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RADIOPHARMACEUTICALS ON DECK.

A new approval, new evidence, and a full pipeline of new products suggest more patients with cancer will be treated with the ultimate “targeted therapies,” [SP181](#).

ACCELERATED APPROVALS. Two pharmacy experts weigh in on a January 2025 report from the HHS Office of Inspector General that recommended reforms to the FDA accelerated approval process, [SP184-SP185](#).

EXPANDING ACCESS. Clinical trials for renal cell carcinoma take place mostly in wealthy countries, even though poverty is strongly linked to poor outcomes in this disease, according to Regina Barragan-Carrillo, MD, a City of Hope postdoctoral researcher who said expanding trials to more countries has scientific benefits, [SP185](#).



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“TRANSFORMATIVE” RESULTS.

Combining enfortumab vedotin (Padcev) with pembrolizumab offered patients with advanced urothelial carcinoma “transformative” benefits over chemotherapy, data from the phase 3 EV-302 trial showed during the American Society of Clinical Oncology Genitourinary Cancers Symposium, [SP208](#).



VIMSELTINIB APPROVED.

Recent FDA approvals include vimseltinib (Romvimza; Deciphera Pharmaceuticals), used to treat patients with symptomatic tenosynovial giant cell tumor in cases where surgical resection may cause worsening functional limitation or severe morbidity, [SP223](#).



PRECISION MEDICINE

Technology, Partnerships, Data, and Culture Are Keys to Bringing Precision Medicine to Community Oncology

Mary Caffrey

IN JANUARY 2025, former FDA Commissioner Stephen Hahn, MD, and fellow panelists at the JP Morgan investors conference observed that pharma no longer follows a path of establishing a presence in one tumor type before moving to the next—today’s news is all about targets, regardless of where cancer emerges.¹

This approach, Hahn said, relies on patients receiving timely diagnostic testing. However, he described the testing arena as “a bit of a mess right now.”¹ Cutting-edge tools used at academic centers, such as Hahn’s former employer The University of Texas MD Anderson Cancer Center, may not be available in a community clinic.

Advances in diagnostics, used to catch cancer as early as possible, and the use of biomarkers, to guide treatment, have reached patients at highly uneven rates. Alongside Hahn on the panel was Dan Malarek, PhD, who is CEO of Foundation Medicine; he previewed the company’s FoundationOne Monitor assay, a blood test that will measure circulating tumor DNA (ctDNA) for both responses and resistance to therapy.² Meanwhile, panel moderator John Carroll of Endpoints News, a cancer survivor, said he’s had tests that have been in use for 50 years.

More than 5 years ago, the American Society of Clinical Oncology (ASCO) warned that the rise of precision medicine, in which genomic tests drive personalized approaches, matching treatments with

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An Exact Sciences laboratory employee in Madison, Wisconsin. Flatiron Health and Exact Sciences’ new partnership will speed the delivery of testing data into clinical evidence. [See Sidebar, SP233](#).

HEALTH EQUITY

Trump’s Stance Doesn’t End Need for Diversity in Clinical Trials

Mary Caffrey

IN DECEMBER 2024, Rachel E. Rau, MD, brightened when asked about data that showed a new regimen for pediatric leukemia worked exceptionally well in Hispanic children.¹

Rau, an associate professor of pediatrics at Seattle Children’s, shared results that showed adding blinatumomab (Blinicyto; Amgen Inc) to chemotherapy boosted disease-free survival by 61% in children with B-cell acute lymphoblastic leukemia. This disease has worse outcomes in Hispanic children, possibly due to a variant in the *IKF1* gene seen among those of indigenous American ancestry.^{1,2} For these children, the survival benefit was even higher at 71%, compared with chemotherapy alone.^{1,3}

The results were “super exciting,” Rau said, recalling the 11 years she had spent treating young patients in Houston, Texas. “Our population in Texas was 65%

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PRACTICE TRANSFORMATION

Making PIN and Telehealth Work Together—It Can Be Done

Grace Showalter, MHIIM, BSN, RN

WHEN CMS DECLINED to add Principal Illness Navigation (PIN) to the Medicare telehealth list in the 2024 Physician Fee Schedule (PFS) Final Rule,¹ many providers were confused.

Providers had waited for years for CMS to add PIN codes to the 2024 PFS, citing evidence of the value of navigation in care and resulting improvements in patients.²⁻⁴ Medicare had repeatedly touted PIN as a service designed to improve health equity and access to care while simultaneously communicating that the service was not able to be billed as a telehealth service, which limited access to these services for patients experiencing barriers to in-person care.

However, what appears to be contradictory messaging from Medicare is more likely an example of the disconnect between “Medicare-ese” and the language providers use to talk about how we deliver health care.

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Find podcasts, webinars, and expert interviews at www.ajmc.com

Scout: Revolutionizing AI-Powered Oncology Research

MORE THAN A DECADE AGO, Pew Research Center found that most patients looked up health information online before coming in for a medical appointment.¹ Using the internet to get health care answers can be good or bad. Online information may help patients piece together symptoms they would otherwise ignore, but most online searches do not separate high-quality sources from irrelevant or unreliable health information.

How can physicians or patients separate fact from fiction? At MJH Life Sciences®, artificial intelligence (AI) is helping us learn.

In March, we launched Scout, an AI-powered search tool informed by the high-quality articles and expert opinions we collect while speaking with physicians, pharmacists, and others on the health care team. Scout's ability to absorb video content from interviews, Peer Exchanges, and other MJH Insights programs sets it apart. Powered by a customized large language model, Scout delivers highly relevant, precise, and actionable results by understanding the context of complex clinical queries.

Unlike other tools, Scout is a unique, validated resource that can offer insights to patients and physicians alike. Answers to questions such as, "How does trastuzumab deruxtecan compare with other treatments in efficacy for HER2-positive breast cancer?" provide a plain-language response and links to related articles if the reader wants to know more.

We previewed Scout at the 42nd Annual Miami Breast Cancer Conference, held March 6 to 9, 2025. The feedback was largely positive, but we are looking for more. We are testing Scout on our OncLive.com website before it becomes available through other MJH Life Sciences brands. Give Scout a try, and let us know what you think.

PCOC 2025:

Our Meeting Is More Important Than Ever

Preparations are in full swing for the signature event of *The American Journal of Managed Care*—our annual Patient-Centered Oncology Care® (PCOC) meeting, taking place September 25 to 26, 2025, at the JW Marriott Nashville in Tennessee. This year's theme, *Finding Our Rhythm: Embracing Change in Oncology Care*, highlights the importance of reaching out to colleagues for collaboration and support during periods of uncertainty. Whether change is positive—such as new AI solutions—or challenging—such as the shifts in federal research funds, the best response is to learn from each other. PCOC was created with this belief in mind.

We encourage you to visit our PCOC website, <https://pcoc.ajmc.com/>, for more information and to register for the 2025 meeting. ♦

Sincerely,
Mike Hennessy Jr
PRESIDENT & CEO

REFERENCE

Fox S, Duggan M. Health Online 2013. Pew Research Center. January 15, 2013. Accessed March 24, 2025. <https://www.pewresearch.org/inter-net/2013/01/15/health-online-2013/>

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Radiopharmaceuticals are commonly used in diagnostics, but therapeutics are gaining notice. Photo: Bayer

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Unpredictable, but Inevitable

MARY CAFFREY

IN JUNE 1990, Anthony Fauci, MD, then early in his term as director of the National Institute of Allergy and Infectious Disease (NIAID), gave an extraordinary address to the Sixth International Conference on AIDS. Although his talk is remembered for its olive branch to AIDS activists, Fauci opened by seeking a “renewed commitment” to basic research: Progress against AIDS, he said, would be impossible without decades of earlier work in molecular biology, immunology, and other fields.

Basic research is “not only critical” to fighting AIDS, Fauci said, “but it is a solid investment in our future fight against other diseases, many of which are totally unrelated to AIDS. For that is the nature of basic biomedical research. Its dividends are unpredictable but inevitable.”

The prediction foretold how the research agenda Fauci outlined that day would propel work on genetically modified T cells to attack HIV-infected cells, and how the resulting knowledge would be shifted to the fight against cancer. Nearly 35 years later, chimeric antigen receptor (CAR) T-cell therapy is one of the most potent weapons against leukemia and lymphoma—a consequence of decades of investment and an ethos to go where the science leads.

Fast forward to March 26, 2025, when oncologist Monica Bertagnolli, MD, the recently departed director of the National Institutes of Health (NIH), told Democratic senators how the Trump administration’s quest to rein in universities and destroy anything labeled “Diversity, Equity, and Inclusion,” has caused the cancellation of 300 NIH grants and the delay of \$1.5 billion in research funding. With Bertagnolli was Whitney Wharton, PhD, an Emory University Alzheimer disease (AD) investigator, who has lost 2 grants for projects that explored why the disease disproportionately affects those from under resourced groups; per the original requirements, Wharton has enrolled participants who are Black, female, and members of the LGBTQ community with a family history of AD.

Wharton read aloud her February 28, 2025, NIH termination letter, versions of which have

been sent to hundreds of scientists: “Research programs based on gender identity are often unscientific, have little identifiable return on investment and *do nothing to enhance the health of many Americans.*”

Such a claim is both chilling and inaccurate. Even in the 1980s, those who singled out gay men for political sport did not succeed in snuffing out the research at NIH. Fauci, after reading about the first cases in 1981, redirected his entire lab to focus on this mysterious disease.

At the time, President Ronald Reagan failed to utter the word AIDS until the 1985 death of Rock Hudson, and he was famously stingy with research funding. But even Reagan didn’t try to block all work on HIV by claiming it served no purpose. He didn’t fire Surgeon General C. Everett Koop, MD, DSc, whose profile grew after his 1986 report on the threat AIDS posed to the population. Nor did Reagan threaten Admiral James Watkins, who led a commission that harshly judged the administration’s handling of the epidemic.

For the past 30 years, funding for NIH enjoyed bipartisan support; the parties have differed on funding levels at various points, but both acknowledge links between basic research and economic growth, along with incalculable benefits to patients. NIH cuts are being challenged in court, but for many, the damage is done. The real tragedy, however, is that patients with rare cancers or conditions such as AD will wait longer for cures that for some may never come. Both Bertagnolli, a cancer survivor herself, and Wharton told senators this is where funding cuts will be felt most.

While lost grants “are devastating for me and my team, particularly junior faculty and students,” Wharton said, “my primary concern is for the patients, research participants, and the families who are already being impacted by the NIH’s recent radical shift in funding priorities.”

Perhaps someday scholars will calculate how many patient deaths were caused by the cuts being made today, or how many cures went undiscovered. Unpredictable? Yes. But inevitable. ♦

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To present policy makers, payers, and providers with the clinical, pharmacoeconomic, and regulatory information they need to improve efficiency and outcomes in cancer care.

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Meeting the Financial Needs of Patients With Chronic Conditions

TIARA GREEN, MSED | PRODUCED BY MARY CAFFREY



GREEN

Tiara Green, MSED,
president, Accessia Health.

THE TERM FINANCIAL TOXICITY entered the discussion of cancer care more than a decade ago¹ to highlight the effect a patient's ability to pay for care would have on the course of their disease. Since then, cancer regimens have become more complex,² and concerns are growing about increasing numbers of young adults being diagnosed with cancer; this population is known to have issues with the cost of care.³

Despite the rise of financial assistance programs inside and outside pharmaceutical companies, gaps remain, especially for those who will deal with a disease over many years. Accessia Health, founded in 1989, seeks to address the needs not covered by traditional assistance programs.⁴ Tiara Green, MSED, president of Accessia Health, answered questions from *Evidence-Based Oncology (EBO)* about the nonprofit organization and its mission.

EBO: What inspired the creation of Accessia Health? What is your mission?

GREEN: Accessia Health is a national charitable patient assistance organization that provides programs and services to people of all ages with a rare or chronic health condition. Although navigating health care is challenging for most individuals and families, those battling rare or chronic diseases face even greater challenges with delayed diagnoses, limited treatment options due to their conditions, and restricted access to quality specialist care. These challenges are further compounded by financial constraints that leave many struggling to obtain the care they need.

Founded by a patient with a rare condition, Accessia Health's mission is to provide a financial safety net, products, services, and assistance to individuals with rare or chronic health conditions and their families. We're committed to breaking down the financial and systemic barriers that hinder one's ability to access lifesaving treatments and services. Our holistic approach includes financial support that extends beyond traditional co-pay assistance to cover other medical expenses such as travel, medical equipment, diagnostic testing, and even dental treatments. Through this model, patients have the ability to focus on their health and getting better rather than worrying about how to afford essential care.

EBO: Do you provide services for patients and physicians?

GREEN: Accessia Health provides flexible financial assistance and services that help patients and families navigate the evolving world of health care regulations and policy. In addition to financial assistance, we offer educational resources and legal support for disability claims, all aimed at improving a person's ability to make informed health care decisions.

However, our work coincides with [the work of] providers. The resources we provide streamline access to timely care, including early detection and necessary treatment options. Many individuals with costly conditions struggle to afford health care expenses that impact their ability to follow care plans recommended by their providers, leading to poorer health outcomes. By working in tandem with providers, we address the root cause of gaps in care and ensure that financial pressures do not prevent people from receiving the care they need or force them to choose between their health and paying for basic necessities.

EBO: What is your business model? Is there a cost for the patients?

GREEN: Our programs rely on funding and donations from individuals, corporations, and foundations. Patients can access resources and apply for financial assistance at no cost. Accessia Health provides financial assistance to those who meet eligibility criteria. Our program model, Your Assistance, Your Choice, allows patients to allocate those funds based on their needs and circumstances. This is a unique model that differs from traditional assistance programs, which have historically only covered costs associated with medication co-pays or health insurance premiums.

EBO: You help patients with rare and chronic diseases. How do you determine if a patient can receive funding from your organization?

GREEN: Accessia Health offers financial assistance for various rare and chronic conditions. If an individual has a qualifying condition, [a list of] which can be found on our website,⁴ they begin by submitting an application. Eligibility is determined by a variety of factors, including diagnosis, household income, and program availability. We strive to accommodate as many patients as possible and continue to expand our offerings with new assistance programs each year. Financial need is assessed to ensure that support reaches those who need it most, and our team members help support this process by connecting patients with additional resources and helping them understand their insurance options and benefits.

EBO: From your vantage point, are financial toxicity challenges improving or worsening?

GREEN: Financial toxicity continues to be one of the most pressing challenges in health care, with people facing the overwhelming burden of affording essential treatments and services. This concern is even more pressing for those with rare or chronic conditions due to the high price tags associated with specialized, often experimental, therapies.

Recent data show that Americans collectively hold \$220 billion in medical debt, with nearly 3 million people owing more than \$10,000 each.⁵ Legislative efforts such as the Inflation Reduction Act of 2022 aim to address financial toxicity by capping out-of-pocket expenses for Medicare beneficiaries and lowering prescription drug costs. Although these changes are a step in the right direction, gaps in coverage persist, and many still struggle to access affordable health care.

High out-of-pocket costs and health insurance premiums continue to put a strain on individuals and families. Those we serve often must choose between paying for essential care and covering basic living expenses. Our goal is to help lighten their financial burden, ensuring no one has to choose between paying for their health care needs or paying their rent.

EBO: Approximately what percentage of the patients you work with have cancer?

GREEN: Cancer treatment often requires costly therapies that can place significant financial strain on patients and their families.

To date, nearly 25% of our patient population has a cancer diagnosis.

EBO: We still hear about problems with reimbursement for diagnostics. What does the landscape look like from your perspective?

GREEN: Reimbursement and insurance coverage challenges for diagnostic testing continue to be a major issue, particularly for those with rare conditions who require specialized testing to confirm their diagnosis. Insurance coverage for diagnostics is often limited, leading to significant out-of-pocket costs and delays in diagnosis. In many cases, early intervention can lead to better health outcomes.

At Accessia Health, we recognize the importance of diagnostics in a person's health care journey. That's why our model allows patients to use their financial assistance for diagnostic testing if needed. By providing this flexibility, we help reduce financial constraints that could delay critical health care decisions.

EBO: Is there anything you would like to add?

GREEN: In order to offer a truly holistic care model, it is critical for charitable patient assistance organizations to consider social determinants of health when offering programs and services. At Accessia Health, we supplement our flexible financial assistance programs by offering educational content that builds health literacy and partnering with local community organizations to connect patients with essential resources.

In addition, we prioritize equitable access, which means underserved and often marginalized communities are able to utilize our services as readily as any other individual. Our case managers assist with navigating the evolving complexities of the health care system, including regulations and policy changes. By combining financial assistance with education and advocacy, we empower patients with the knowledge and tools to obtain quality, affordable care. ♦

AUTHOR INFORMATION

With more than 20 years of expertise in public health and nonprofit sectors, Tiara Green, MSEd, drives strategic initiatives and health equity programs for Accessia Health to address unmet needs in health care and offer comprehensive support to individuals facing rare or chronic diseases.

REFERENCES

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THERAPEUTIC ADVANCES

Will the Coming Radiopharmaceutical Wave Reach More Patients With Cancer?

MARY CAFFREY

RIISING INTEREST IN solutions that target cancer therapies directly has fueled growth in radiopharmaceuticals, a sector witnessing new studies, banner trial results, and, most recently, an FDA approval that promises to greatly expand who can receive treatment.

Radiopharmaceuticals pinpoint delivery of radionuclides to targeted lesions to diagnose and treat multiple diseases. In cancer care, radioligand therapy (RLT) combines a radioisotope with a ligand, which binds the agent to markers on specific cancer cells. RLTs have gained notice as the need grows for treatments in refractory tumor types that do not respond to existing therapies.¹ The sector has seen billions in merger and acquisition activity in recent years; a September 2024 analysis by Insight Partners estimated the value of the global radiopharmaceuticals sector, including cancer treatments, would grow from \$9.07 billion in 2023 to \$26.51 billion by 2031.²

The FDA's March 28, 2025, approval of an added indication for lutetium Lu 177 vipivotide tetraxetan (Pluvicto; Novartis Pharmaceuticals Corporation) in metastatic castration-resistant prostate cancer (mCRPC) could triple the number of patients eligible for the therapy, company officials said in a statement. The new indication allows treatment for prostate-specific membrane antigen (PSMA)-positive disease following androgen receptor pathway inhibitor (ARPI) therapy in patients for whom it is "considered appropriate to delay chemotherapy," Novartis officials said.³ This follows the March 2022 approval for patients with PSMA-positive mCRPC treated with ARPI therapy and taxane-based chemotherapy.⁴

Use of the RLT earlier on during treatment could be a game-changer, Michael J. Morris, MD, prostate cancer section head, genitourinary oncology, Memorial Sloan Kettering Cancer Center, said

in the statement. "The earlier indication...could really change our treatment paradigms for patients with mCRPC," said Morris, who led the key study driving the approval. "It offers a targeted therapy that better delays disease progression compared [with] a second ARPI."³

Novartis leaders aren't the only ones backing the idea that more patients could benefit from earlier treatment with radiopharmaceuticals. An official from Bayer, whose radium Ra 223 dichloride (Xofigo) was approved in 2013 to treat patients with CRPC and symptomatic bone metastases,⁵ told *Evidence-Based Oncology (EBO)* in a February interview that groundbreaking new data for Ra 223 have generated renewed interest in the therapy, and more patients should benefit.

Jorge Ortiz, MD, global medical affairs head for Xofigo at Bayer Oncology, referenced PEACE-3 (NCT02194842),⁶ an investigator-initiated trial presented at the European Society for Medical Oncology (ESMO) in Barcelona, Spain, in October 2024. PEACE-3 data showed that adding Ra 223 to enzalutamide improved radiographic progression-free survival (rPFS) in untreated mCRPC and could offer a new first-line option.^{6,7}

"It's about making sure the right patient gets treated with radium at the right time," Ortiz said. "That right time is first-line mCRPC, and that's where we saw the benefit."

Enthusiasm for radiopharmaceuticals is spreading among clinicians despite recognized management challenges. RLTs have a limited treatment window due to their short half-life, so orders must be handled with great care, Naga Vara Kishore Pillarsetty, PhD, a radiochemist at Memorial Sloan Kettering Cancer Center, said in a February interview with *EBO's* sister publication, *Pharmacy Times*.⁸ (The half-life for Ra 223 is 11.4 days; it is 6.7 days for Lu 177). Pillarsetty



ORTIZ

Jorge Ortiz, MD, global medical affairs, Xofigo, Bayer Oncology.



MORRIS

Michael J. Morris, MD, prostate cancer section head, GU Oncology, Memorial Sloan Kettering Cancer Center.



PILLARSETTY

Naga Vara Kishore Pillarsetty, PhD, radiochemist, Memorial Sloan Kettering Cancer Center.

noted that the very first “targeted therapy” was radioiodine (iodine 131), following studies by Saul Hertz, MD, in the 1940s whose data showed the effectiveness of iodine 131 in treating hyperthyroidism, leading to its use in thyroid cancer.^{8,9}

Safety has always been a concern. Using a ligand to get the radioactive molecule to its precise target has significantly helped prevent organ damage, according to a January 2025 review article in *Signal Transduction and Targeted Therapy*.¹ 2019 FDA guidance outlined steps for industry to promote safety in developing RLTs in oncology.¹⁰ Posttreatment protocols vary; although patients receiving iodine 131 are advised to avoid small children for several days, Ra 223 is expelled in the urine and feces, so the Oncology Nursing Society advises routine good hygiene as sufficient.¹¹

Ortiz and Pillarsetty agreed that more must be done to educate doctors and patients about radiopharmaceuticals—and dispel myths as well.

It’s “absolutely true” that a patient may balk at hearing the word *radium* associated with their cancer treatment, Ortiz said. “We can all do a better job—pharma, clinicians, and patient advocacy groups—because it’s not only a very safe treatment in terms of the side effect profile,” he said, “but the delivery is easy.”

For patients treated with Ra 223, “it’s a 1-minute injection, and they then can go home,” Ortiz said.

To that end, leaders from the American Oncology Network (AON), which includes many small oncology practices, will discuss the use of radiopharmaceuticals at the community level on April 28, 2025, during the Community Oncology Alliance (COA) annual conference, in Lake Buena Vista, Florida.¹²

PEACE-3 Results Spur Interest

Ra 223 was approved based on findings in the ALSYMPCA trial (NCT00699751), which evaluated 921 patients and demonstrated a 30% overall survival (OS) benefit with Ra 223 compared with placebo among patients who had previously received, were not eligible for, or had declined chemotherapy. Median OS was 14.9 months for the Ra 223 group and 11.3 months for the placebo group (HR, 0.70; 95% CI, 0.58-0.83; $P < .001$).¹³

ERA-223 (NCT02043678), a combination study whose findings were published in 2019, proved to be a setback, Ortiz said. That study paired Ra 223 with abiraterone acetate, a therapy typically given in the first line in patients with mCRPC who are progressing on androgen deprivation therapy. The combination did not improve symptomatic skeletal event-free survival in the population covered by the FDA approval, and study authors reported an increase in fractures.¹⁴

However, a pair of investigator-initiated studies were still in progress: one was PEACE-3 (NCT02194842), which paired Ra 223 with enzalutamide, the other standard first-line treatment. Following the results for ERA-223, investigators changed the protocol to require bone-protecting agents. Results presented by Silke Gillessen, MD, head of the Department of Medical Oncology, Università della Svizzera Italiana, and medical and scientific director, Oncology Institute of Southern Switzerland, showed this new combination was associated with a 31% improvement in rPFS—19.4 months vs 16.4 months in the enzalutamide only arm (HR 0.69; 95% CI, 0.54-0.87; $P = .0009$). At 24 months, 45% of patients in the Ra 223 arm were free of radiographic progression compared with 36% in the monotherapy arm.⁶

“The primary end point, rPFS, was met, but the most surprising and exciting piece was the overall survival data,” Ortiz said. Early results show the combination demonstrated a 31% reduction in risk of death compared with the monotherapy arm, with median OS rising from 35 months to 42.3 months. A final OS analysis will be forthcoming, the study authors reported.^{6,7}

Mechanisms of Action: A-Emitters vs B-Emitters

The radiopharmaceutical sector is evolving from its historic focus on diagnostics, according to the *Signal* review article.¹ Zhang et al write, “Therapeutic isotopes with higher linear energy transfer and

longer half-lives have been introduced...in recent years, as the major demand for radiopharmaceutical discovery has shifted from diagnostic imaging to targeted therapy.”

Among radionuclides, the authors outline differences between the α -emitters, of which Ra 223 is the only FDA-approved therapy, and β -emitters, which include Lu 177, iodine 131, and several agents used in positron emission tomography (PET) and single photon emission computed tomography (SPECT) imaging. (The authors also discuss smaller categories, such as Auger electron emitters.)

“The natural characteristics of α -particles (such as their short range and high energy) can cause irreversible damage to the DNA of cancer cells,” the authors write, making this group of agents an active research area with several therapies in development.¹

β -emitters, note the authors, “are cytotoxic against relatively large cancer deposits due to their emission of high-energy electrons in the medium tissue range.” Although these are more commonly used in practice, the authors cite some limitations: “ β -emitters have relatively low energy and poor tissue penetration, resulting in lower treatment efficacy for larger and malignant tumors.”¹

In the interview, Ortiz emphasized Ra 223’s benefits as an α -emitting therapy. Bone metastases, which the therapy is designed to treat, affect 90% of patients with prostate cancer, he said. The α therapy “goes to places where there’s bone turnover, and those are bone metastases,” offering better survival than earlier β -emitter bone therapies.

The α therapies, he said, “are unique because they have very high linear energy transfer—meaning the load of energy that is transferred is really high, so that it creates a double DNA strand break, and these cells generally are not able to recover from that.” Ortiz emphasized that these therapies “travel a very short distance, so they act where they are supposed to act, without affecting other cells.”

He noted that radium mimics the bone’s calcium in traveling to it. When bone metastases appear, they kill off existing bone, which tries to recover by creating new bone. Because the radium follows where the calcium is being pulled to kill the cancer, Ortiz said, it behaves as a targeted therapy.

Observers note the PEACE-3 trial could represent a change of fortune for Ra 223 following ERA-223. Writing for *UroToday*, Zachary Klaassen, MD, MSc; and Rashid Sayyid, MD, MSc, said the results demonstrate the importance of using bone-protecting agents with the combination. “These results potentially elevate 6 cycles of radium 223 into the first-line mCRPC disease space in combination with enzalutamide, with the caveat that patients being considered for this combination must have no evidence of visceral metastases and have asymptomatic/mildly symptomatic bone metastases,” unlike ALSYMPCA, where patients had symptomatic bone metastases.⁷

Activity in the Marketplace

A look at recent transactions involving radiopharmaceuticals highlights their growing importance:

BAYER. In May 2023, Bayer announced a strategic partnership with Bicycle Therapeutics, which is developing several α -emitter candidates, including therapies in prostate cancer. The potential value of this deal is \$1.7 billion.¹⁵

NOVARTIS. Along with lutetium Lu 177 vipivotide tetraxetan, Novartis already owns lutetium Lu 177 dotatate (Lutathera), approved to treat somatostatin receptor-positive (SSTR) gastroenteropancreatic neuroendocrine tumors (GEP-NETs).¹⁶ Zhang et al cite therapies targeting SSTR as one of the most promising research areas, and multiple transactions involve drugs for this target.¹

In May 2024, Novartis acquired Mariana Oncology, which is developing therapies involving actinium-225, an α -emitter. These include MC-339, which is now being studied in small cell lung cancer (SCLC).¹⁷ If Mariana achieves several milestones, the deal’s total value could rise to \$1.75 billion.

BRISTOL MYERS SQUIBB. Another actinium-225 therapy in development is RYZ101, or ²²⁵Ac-DOTATATE, an SSTR-targeting therapy developed by RayzeBio, which Bristol Myers Squibb acquired in February 2024 for \$4.1 billion.^{18,19} ClinicalTrials.gov includes several studies evaluating RYZ101: a phase 1/2 trial in patients with ER-positive, HER2-negative unresectable or metastatic breast cancer expressing SSTRs (TRACY-1; NCT06590857); a phase 1 trial for extensive-stage SCLC (NCT05595460); and a phase 3 trial for GEP-NETS (ACTION-1; NCT05477576).²⁰⁻²²

ELI LILLY AND COMPANY. Previously an investor in Mariana Oncology, Eli Lilly acquired POINT Biopharma Global Inc for \$1.4 billion in December 2023; its statement highlighted Lu 177 PNT2002, a PSMA-targeted radioligand therapy for mCRPC, and Lu 177 octreotate PNT2003, an SSTR-targeted radioligand therapy to treat GEP-NETS.²³ POINT Biopharma is also developing a candidate to target FAP- α , another area the Zhang article highlights.^{1,23}

ASTRAZENECA. The global pharmaceutical company, which has made its mark in antibody-drug conjugates in recent years, acquired Fusion Pharmaceuticals Inc in March 2024 for \$2 billion. A statement described interest in developing “next-generation radioconjugates,” including those targeting PSMA in prostate cancer.²⁴

LANTHEUS HOLDINGS, INC. In January 2025, Lantheus acquired Evergreen Theragnostics, Inc for \$1 billion, betting on the combination of its diagnostics and a generic version of Lutathera now under development.²⁵

Overcoming Patient Resistance

MSKCC’s Pillarsetty said Novartis’ approvals for Lu 177-dotatate for neuroendocrine tumors and Lu 177 vipivotide tetraxetan for PSMA-positive prostate cancer set in motion the latest wave of interest in radiopharmaceuticals but work remains to eliminate the concerns persisting around these therapies. Over the years, he said, pharmaceutical companies have not done the best job communicating the benefits.

“The biggest stigma is that for patients,...this is usually something that’s harmful, but that’s not the case,” Pillarsetty said in the interview. Millions have been treated with radioiodine, he noted, and the risk of secondary cancers down the road is no worse than that from treatment with chemotherapy. “This is something [that] patients have to be reminded [about] all the time.”⁸

Ortiz, who spoke with *EBO* during the American Society of Clinical Oncology Genitourinary Cancers (ASCO GU) Symposium, agreed that patient and payer education would be critical to moving radiopharmaceuticals to the front of the treatment queue. At ASCO GU, Bayer presented a review of 48 real-world studies involving 15,000 patients treated with Ra 223 after adopting androgen pathway inhibitors. The authors concluded that patients who have at least 5 cycles of the therapy live longer than those who do not, yet Ra 223 is often given after other treatments, “which may limit its full effectiveness.”²⁶

“The findings highlight the survival benefits of early-use Ra 223 with completion of 5 [or more] cycles, a favorable safety profile, and low rates of fracture when guideline-recommended

[bone-protecting agents] are used,” the authors wrote. Also at ASCO GU, findings from the Netherlands showed that retreatment with Ra 223 is safe in mCRPC.²⁷

Ortiz said more results involving Ra 223 are imminent, including a dosing study combining Ra 223 with the PARP inhibitor olaparib (NCT03317392). As Zhang et al explained, because the PARP pathway helps control the DNA repair pathway, PARP inhibitors may help radiopharmaceuticals block attempts to repair DNA damage.^{1,28}

Education is key as radiopharmaceuticals enter this new phase, Ortiz said. “We need to make a significantly better effort at communicating this to clinicians—especially in the community—to patients, and patient advocates because otherwise, lack of knowledge is probably going to be one of our highest challenges,” he said. Based on the results presented at ESMO, “the evidence is there.” ♦

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Evolent's Wonsettler Sees Outcomes-Based Reimbursement as "A Healthy Tool"

TERRA WONSETTLER, PHARMD, MBA | INTERVIEW BY MARY CAFFREY



WONSETTLER

Terra Wonsettler, PharmD, MBA, vice president for clinical evidence, policy, and oncology pharmacy, Evolent.

ARE THERE LESSONS to be gained from FDA's 2021 accelerated approval of aducanumab (Aduhelm), the monoclonal antibody some thought would offer hope for patients with Alzheimer disease? The controversial decision set off a wave of press coverage and an investigation by Congress. Ultimately, Biogen pulled the drug from the market after Medicare offered limited coverage.

In January 2025, the HHS Office of Inspector General (OIG) issued its report on the matter.¹ It found deviations from recommended practices in 3 approvals of 24 drugs it reviewed and offered 2 recommendations:

1. FDA agreed it should "take steps to ensure that appropriate documentation of meetings with sponsors is included in drug approval administrative files."
2. FDA should "define specific factors that would require FDA's accelerated approval council to advise on certain drug applications." The agency did not agree with this recommendation.¹

The aducanumab approval is an outlier case; the more typical issues surrounding accelerated approvals involve drugs where confirmatory trials fail to produce evidence that matches a drug's early promise. In recent years, some sponsors have withdrawn drugs from the market following disappointing results in confirmatory trials, which experts say should be expected as use of the pathway matures.

For additional insight on the recent HHS OIG report, *The American Journal of Managed Care (AJMC)* spoke with Terra Wonsettler, PharmD, MBA, vice president for clinical evidence, policy, and oncology pharmacy, Evolent. Last year, Wonsettler wrote a commentary for *AJMC's* publication, *Evidence-Based Oncology*, "Cancer drugs speed to accelerated approvals, then hit the brakes in timely, clinically beneficial confirmatory trials."²

AJMC: The HHS OIG overview was sought in response to the aducanumab episode. Although the report spends considerable time on that case, it also addresses more routine issues that come up with use of the accelerated approval pathway. What observations in the report did you think were fair? Were any observations unfair?

WONSETTLER: That's a great question. Thinking back to those 3 observations and just bringing those back to the top, OIG really highlighted the deviation from recommended practices. In those instances, the FDA evaluated those analyses [were] not included in the sponsor's original plans, which deviated from best practices.

There were concerns from reviewers as well as the advisory committees in 3 of those 24 drugs in the sample size. Despite those concerns, those drugs [were] pushed through to approval.

The third observation was incomplete documentation, [as] some of those meetings with the sponsors were either missing or incomplete from the administrative file. The FDA is required to document a basis for decisions, including those relevant meeting minutes. So certainly, they are fair observations, as

they're ultimately underscoring the need for more stringent documentation and adherence to the accelerated approval pathway, which already grants—as quoted in the report—tremendous latitude in decision-making.

AJMC: As you explained in your commentary, the accelerated approval pathway seeks to strike a balance between bringing life-saving therapies to patients as quickly as possible and generating evidence to support ongoing approval. Do the HHS OIG recommendations support this balance?

WONSETTLER: ...Those 2 recommendations were ultimately made to strengthen those guardrails, ensuring appropriate and consistent use of the accelerated approval pathway. For a process-oriented retrospective review of that smaller sample size of 24 medications, these steps do support a path to a more documented, escalated review process to ultimately support the defense of a decision. They're looking for complete, comprehensive documentation to help maintain that transparency, which is especially critical, as well as the accountability and the evidence, [and for] the council to advise in those drug applications [when there is] a lack of uniform consensus, concern, or review of analysis outside that prespecified plan.

"Proper documentation with clear records and decisions provides transparency and also gives a trail of supporting decisions. They improve accountability, facilitate that oversight, and identify those deviations from those standard processes. So while the FDA did concur that it is important to ensure appropriate documentation, and they're updating internal procedures, there remains that greater opportunity for transparency proactively, especially for patients taking these therapies."

—Terra Wonsettler, PharmD, MBA, vice president for clinical evidence, policy, and oncology pharmacy, Evolent

AJMC: One recommendation called for doing more to ensure that all meetings between sponsors and FDA are properly documented. What are your thoughts on this recommendation in light of the report's findings about the [aducanumab] approval?

WONSETTLER: Proper documentation with clear records and decisions provides transparency and also gives a trail of supporting decisions. They improve that accountability, facilitate that oversight, and identify those deviations from those standard processes. So while the FDA did concur that it is

SPOTLIGHT

Price Caps During Accelerated Approval Would Help Address Financial Toxicity for Patients, Jensen Says

Chelsee Jensen, PharmD, BCPS | Interview by Mary Caffrey



JENSEN

CHELSEE JENSEN, PHARM.D, BCPS, director of formulary management, Mayo Clinic.

A RECENT REPORT from the HHS Office of the Inspector General (OIG) addressed challenges with the current accelerated approval pathway, which was created in 1992 to offer patients a way to gain access to novel therapies ahead of the final results of a phase 3 trial.¹

Although the report released January 14, 2025, was triggered by events surrounding approval of aducanumab (Aduhelm; Biogen) for Alzheimer disease, its scope and recommendations addressed the widespread use of the accelerated pathway in oncology. A 2024 presentation at the American Association for Cancer Research annual meeting found that 59 cancer drugs received approval under the accelerated pathway from 2013 to 2023.² The HHS OIG report highlighted instances where drugs stayed on the market for years at full price while confirmatory trials were delayed; some of these drugs were pulled from the market when data from follow-up trials failed to confirm the early benefit.¹

In its report, HHS OIG recommended that FDA “strengthen guardrails in certain circumstances to ensure appropriate and consistent use of the accelerated approval pathway.” It called for 2 specific steps:

- FDA should “define specific factors that would require FDA’s accelerated approval council to advise on certain drug applications.” The agency did not agree with this recommendation, although the internal council has met several times.
- FDA agreed it should “take steps to ensure that appropriate documentation of meetings with sponsors is included in drug approval administrative files.”¹

For insight on the implications of the report and its recommendations in clinical practice, *The American Journal of Managed Care (AJMC)* spoke with Chelsee Jensen, PharmD, BCPS, director of formulary management at Mayo Clinic. Jensen cited the example of the July 2021 safety alert of melphalan flufenamide (Pepaxto; Oncoceptides AB) to treat multiple myeloma, coming just after the accelerated approval; this was followed by FDA’s final decision under the process spelled out in the Food and Drug Omnibus Reform Act of 2022.³

AJMC: The HHS OIG report on the accelerated approval pathway discussed the use of an Accelerated Approval Coordinating Council, which met 3 times during 2024. Is it useful to have this council as an internal mechanism?

JENSEN: I do think it is useful to have some sort of council as an internal mechanism. The bottom line is really we need accountability to track outcomes on accelerated approval agents to ensure confirmatory trials are being completed in a timely manner. I’m not exactly sure if it was that Accelerated Approval Coordinating Council or the OCEAN

investigators, but I do think it was really good that the safety signals for melphalan flufenamide were caught in a timely manner in order to facilitate its removal from the market.

Melphalan flufenamide was approved in February of 2021,⁴ the OCEAN trial [NCT03151811] FDA safety alert came out in July of 2021,⁵ and [the drug] was withdrawn from the market in October of 2021, so I think that was a very timely time frame in order to address those safety signals and get that off the market.

AJMC: What challenges do clinicians face when they have started a patient on a cancer drug that was approved through the accelerated process and then the therapy is pulled off the market?

JENSEN: I have not had direct patient conversations about this, but I have heard that these conversations are very difficult, especially when an accelerated approval agent is withdrawn and a patient’s on it and responding. With those patients, you have to have a difficult conversation of [whether we] can continue the therapy. Sometimes there’s a venue through a compassionate use program, but other times there is not. Getting that patient onto a different drug altogether, whether there’s a drug available in that line of treatment, has to be a difficult conversation. In addition, I have seen recent trends that sometimes commercial insurance will not even cover accelerated approval drugs because these therapies are considered investigational. So it’s still unclear for those patient populations whether they would have a venue to access the drug through a clinical trial, or whether they would have access at all. I think that’s an interesting trend that needs to be followed, especially if we continue to see an increase in certain commercial insurers not covering drugs under accelerated approval.

AJMC: One challenge has been the length of time that has occurred in some cases between the accelerated approval, when the drug enters the marketplace, and when the confirmatory trial happens. This is an issue that the OIG report did highlight; the report noted how much money Medicare and Medicaid have spent on some of these drugs under accelerated approval. Should Congress authorize Medicare and Medicaid to perhaps pay less for these drugs, or authorize an assessment on the pharmaceutical companies that take too long to complete confirmatory trials?

JENSEN: While I do think the penalty obviously would offset costs [to] CMS directly, it really does not address that financial toxicity that patients might incur, that health care institutions might incur, and other insurance companies may incur for offering an accelerated approval drug. I personally do feel it would be a better path for Congress to set price limits for accelerated approval drugs, limiting them to a \$150,000 to \$200,000 annualized wholesale acquisition cost. In my opinion, the price cap should be in place for the duration of its accelerated approval. And once it does get granted full approval, then [pharmaceutical companies] would be authorized to adjust the price as they see fit. But I really do think that we need to have more price controls on the front end in order to reduce financial toxicity to patients and to that health care institution as a whole.

AJMC: Is there anything else you would like to add?

JENSEN: Often, when we do have a drug that’s coming to market, the

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manufacturer is not going to offer a health care institution a discount on that drug. Yet they might be aggressively discounting it to certain insurance companies to maintain formulary status. Again, if the population served by the institution is heavily [enrolled in] Medicare and Medicaid, it may not be financially feasible for that institution to offer the medication without taking a significant loss. That's why I do think a pricing limit on the front end for accelerated approval drugs would be more impactful and equitable to the system vs reimbursement limits or a penalty. ♦

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important to ensure appropriate documentation, and they're updating their internal procedures, there remains that greater opportunity for transparency proactively, especially for the patients taking these therapies.

In the report, the OIG did note a risk-to-benefit profile allowing drug sponsors to use the surrogate end points in the accelerated approval process where the risk of the drug may not ultimately provide a benefit that's predicted. These are the resources called for in [the article] "Cancer Drugs Speed to Accelerated Approvals Then Hit the Brakes in Timely, Clinically Beneficial Confirmatory Trials."² Resources such as educational materials and guidance on the accelerated pathway highlight the risks and benefits, which enhance these patient conversations. It's critical to get this information to our patients as well.

AJMC: FDA did not support the other recommendation regarding guardrails to trigger meetings of the accelerated approval council. What are your thoughts on this recommendation?

WONSETTLER: Yes, of course; while the need for these resources does require consideration, this is a call-to-action opportunity for a cost-to-benefit analysis, weighing the clinical resources required vs the tragic time lost, the outcomes, and the financial toxicity incurred in nonefficacious treatment to patients.

AJMC: Do payers have a fair argument that some compensation is warranted if a therapy fails to live up to expectations?

WONSETTLER: Absolutely. As we pan out and [compare] the United States [with] other countries

[around] the globe, we in the US far outpace other nations and expect to exceed 20% of our GDP on health care spending over just the next 10 years. Meanwhile, the US also lags on health outcomes. So, with that setting and that foundation, patients also deserve high-value care. Outcomes-based reimbursement can be a healthy tool, aligning the entire health continuum from the start of the drug manufacturer to, ultimately, the patient. ♦

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SPOTLIGHT

“Expanding Access Isn’t Just About Being Fair,” It’s About Building Better Treatments for Everyone

Mary Caffrey



BARRAGAN-CARRILLO

REGINA BARRAGAN-CARRILLO, MD, is a postdoctoral fellow in the Genitourinary Clinic, Medical Oncology and Medical Therapeutics, City of Hope, Duarte, California.

GLOBAL HEALTH SAW PLENTY of upheaval in early 2025. First came news that the United States would sever ties with the World Health Organization (WHO).¹ Then came the decision by the Trump administration to all but shutter the US Agency for International Development (USAID), which brought at least 30 international clinical trials to a sudden halt.²

All this provided an ironic backdrop for Regina Barragan-Carrillo, MD, a postdoctoral fellow at City of Hope in Duarte, California, who traveled to San Francisco to present study results that show clinical trials in renal cell carcinoma (RCC) mostly take place in wealthy countries, even though poverty is strongly linked to poor outcomes in this disease.³ Barragan-Carrillo presented her findings at the American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO GU), held February 13-15, 2025.⁴

ASCO, as well as the National Cancer Institute and the FDA, have called for academic investigators and pharmaceutical companies to take steps to ensure that clinical trial enrollment for new therapies more closely matches the population of patients who will take the drugs. But data show it has been an uphill battle. The Lazarex Cancer Foundation reported in 2024 that Black patients make up 5% of clinical trial participants, although they are 13% of the US population, and Hispanic patients are only 1% of trial participants, even though they are 16% of the population.⁵

Barragan-Carrillo’s study focused on a key problem: Too few studies go where the patients are.⁶ *The American Journal of Managed Care*® (AJMC®) spoke with Barragan-Carrillo during ASCO GU about her findings and their importance, given the shifting landscape over support for diversity and equity initiatives in health care.

This interview has been lightly edited for clarity.

AJMC: What do we know about the connections between RCC and poverty?

BARRAGAN-CARRILLO: We know that lower socioeconomic status is linked to both a higher risk for developing RCC and worse survival outcomes. These survival outcomes [affected by] later diagnosis and worse access to care, as well as less access to novel systemic therapy.

For example, here in the US, Black patients [with RCC] have a 16% higher mortality rate compared with their non-Hispanic White counterparts.³ In Arizona, when we’re talking about patients of Latino origins, it’s been documented that these patients are twice as likely to be diagnosed in advanced stages and have nearly double the risk of dying from early-stage disease compared with non-Hispanic White patients.⁷

This does not stop at the individual patient level. On a global scale, people [with] lower incomes face even greater barriers to care, with 5-year survival rates up to 50% lower than in wealthier countries.⁸ There definitely is an important risk, not only from a biological standpoint, but more from

contamination and exposure to environmental factors that could increase the risk for developing RCC. Access to care also plays a very important role.

AJMC: Your findings show that 76% of the trials in RCC were conducted exclusively in high-income countries and that none were available in low-income countries.⁴ Beyond the fact that the trials fail to reflect racial and ethnic diversity, what knowledge do we lack about drug delivery in low-income countries when we fail to include them in trials?

“Beyond equity, there are scientific benefits to expanding clinical trials globally. Genetic diversity matters, and it matters a lot in oncology. It matters a lot when you talk about pharmacodynamics and pharmacokinetics; the way patients respond to different cancer treatments can vary [dramatically based] on genetic background, environmental exposures, and underlying health conditions. Including low-income countries in trials gives us more representation on data, and it leads to better and more universally effective treatments.”

—Regina Barragan-Carrillo, MD,
postdoctoral fellow,
City of Hope

BARRAGAN-CARRILLO: What do we not learn about that process when we don’t do the trials in low-income countries? We do not learn a lot, to be quite frank, when these trials are not conducted in all sorts of [communities]. In low-income countries, we are missing critical information about how the treatments work in the real-world setting, as well as how drug distribution works.

For example, how do we ensure that hospitals have the capability to handle the drug and the correct refrigeration system to ensure the quality of the drug is going to be maintained, that it [matches] the quality when they were doing the research in high-income countries? The fact that we’re not annotating for that, and we don’t have the evidence to support it, also leads to fewer opportunities to improve it.

It’s going to be very difficult to have specific steps to improve the quality of care, even for patients who are living in remote areas of the US. We’re missing out on a lot of critical information.

AJMC: What are other challenges with drug delivery that we could learn about during a clinical trial?

BARRAGAN-CARRILLO: Many patients in [low-to-middle-income countries] have coexisting conditions, such as malnutrition, parasitic infection, or environmental exposures, that do not happen in high-income countries and could alter the drug’s effectiveness. It’s difficult to pinpoint a single thing,

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but the one sure thing is that populations do look very different across the US and across the globe—so all these external factors that are seen more often in other countries are not being shown in the clinical trials. And we're not sure whether the interventions that have proven to be effective for patients in high-income countries are going to be as effective for patients in other regions of the world.

AJMC: Your results highlight the disproportionate role that pharma plays in funding trials. Almost all of the time, pharma sponsors trials for their own investigational drugs—not for generic drugs that low-income countries would be more likely to afford. Whose job should it be to maintain the infrastructure to pay for those kinds of studies?

BARRAGAN-CARRILLO: That's the million-dollar question, to be completely honest. Right now, no one is really taking ownership. If I can be very transparent, pharma companies clearly focus on profit and patents in drug trials, meaning they rarely invest in trials for generics. And even though generics could be game changers for low-income countries, it's something that does not have an economic interest where we ask ourselves, "Who should be the one stepping up?" It has to be a collaborative effort.

First, governments must take a more active role, particularly through public health care agencies and funding bodies and international agencies. For example, the WHO should step up to help coordinate the effort and establish funding mechanisms. [Nongovernmental organizations] have a role to play, especially in implementation; patient advocacy and public and private partnerships can offer a way forward, pairing the infrastructure and expertise from the industry with the public sector funding and global priorities.

An important example that I love to highlight is the Drugs for Neglected Diseases initiative.⁹ It's a very good model in the sense that it brings together different stakeholders to fund research on diseases that disproportionately affect low-income regions. We need to do something similar in the space of not only RCC but oncology in general to help patients worldwide.

AJMC: Why should it matter to wealthy countries whether poor countries have access to clinical trials? How does everyone benefit when everyone has access?

BARRAGAN-CARRILLO: First, I think of fairness. Cancer is not a problem of only wealthy countries, so why should clinical research be concentrated there? If we test new therapies only in high-income settings, we end up with treatments that may not be applicable, accessible, or even effective for a large portion of the world's population.

Right now, we're overwhelmingly concentrated on high-income countries, which is leaving out the majority of the world's patients who have cancer; 70% to 75% of all new cancer cases are happening in lower- and middle-income countries,¹⁰ so we're talking about almost three-fourths of our worldwide patient population. And expanding access isn't just about being fair; it's also about making treatments better, stronger, and more effective for everyone.

Beyond equity, there are scientific benefits to expanding clinical trials globally. Genetic diversity matters, and it matters a lot in oncology. It matters a lot when you talk about pharmacodynamics and pharmacokinetics; the way patients respond to different cancer treatments can vary [dramatically based] on genetic background, environmental exposures, and underlying health conditions. Including low-income countries in trials gives us more representation on data, and it leads to better and more universally effective treatments.

Another thing I'd like to mention is that we learn how to make treatments in health care environments. Not every country is going to have the same access to high-tech imaging, robotic surgery, or expensive immunotherapies. Understanding how to adapt the treatments for different levels of health care infrastructure can make them more scalable and accessible worldwide.

AJMC: So we might actually learn how to do things in a less expensive way?

BARRAGAN-CARRILLO: Yes, 100%. There's what we call reverse engineering, where we learn how to adapt certain information in a lower-income setting and then bring it back to a higher-income setting to be much more cost-effective. That can allow patients to have access to care without so much financial toxicity.

AJMC: Obviously, you worked on this study for a long time. But you happen to be presenting these results just as the new presidential administration is pulling back on personnel, on funding that supported a lot of this kind of research, and on the infrastructure that supported this work. Many of these decisions, of course, are being contested. What are the implications of presenting your research in this changing environment?

BARRAGAN-CARRILLO: I think scaling back this type of funding is a major step in the wrong direction. From a scientific point of view, cutting funding from global health research doesn't just slow down the progress, it actively worsens these priorities. The broader implications are quite concerning. It could mean less innovation....

This could lead to worse patient outcomes. If trials only happen in wealthy regions, we'll continue to see major inequities in who benefits from scientific answers. It also leads to weaker international collaboration, which has an impact not only on health care but also on economic and social development.

Global health efforts rely not only on partnerships but also on collaboration among groups and countries. When funding disappears, these partnerships end up breaking down. Rebuilding them will take years. At a time when we should be looking at expanding clinical trial access, these cuts do the exact opposite by shrinking opportunities, limiting research, and ultimately costing lives. ♦

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Cancer Mortality Rates Still High Among Black Patients, Despite Overall Decline

JULIA BONAVIDACOLA



SIEGEL

Rebecca Siegel, MPH, senior scientific director, Cancer Surveillance Research, American Cancer Society.

DESPITE A SIGNIFICANT decrease in mortality related to cancer in Black men and women, the incidence of mortality was still higher in Black individuals compared with other populations, according to a new report, *Cancer Statistics for African American and Black People, 2025*, published by the American Cancer Society.¹

This report, published in *CA: A Cancer Journal for Clinicians*, used population-based science from the National Cancer Institute and the CDC to collect data on the incidence, mortality, screening, survival, and risk factors of cancer in Black individuals. The data used for the report were the most recent available in the databases.

The authors found that there will be an estimated 248,470 diagnoses and 73,240 deaths related to cancer in Black individuals, accounting for the second-leading cause of death in Black individuals in 2025. Overall, the mortality rate associated with cancer declined from 49% in 1991 to 33% in 2022. Black men experienced the highest decline in mortality related to cancer compared with Black women, White men, and White women, with a 65% to 67% drop among Black men aged 40 to 59 years.

However, the risk of cancer death was still high among Black individuals. Myeloma and prostate, endometrial, and stomach cancers had a risk of cancer death in Black individuals that was 2-fold higher compared with White individuals. Colorectal, breast, cervical, and liver cancers all had a 40% to 50% higher risk of death in Black individuals.

The most reported cancers diagnosed in Black individuals were prostate (44% in men), breast (34% in women), lung (10%), and colorectal (8%) cancers. These cancers also made up 58% of all new diagnoses. The likelihood of dying from breast cancer was 38% higher in Black women compared with White women, whereas the likelihood of being diagnosed with breast cancer was 5% lower in Black women. The incidence rate of prostate cancer was also 67% higher in Black men compared with White men, with Black men twice as likely to die. The incidence of endometrial cancer also increased in Black women by 2% each year.

“Overall declines in cancer mortality rates in Black people largely reflect behavioral changes, such as historical declines in cigarette smoking among Black teens, as well as advances in treatment and earlier detection for some cancers. Yet, this population persistently

experiences a much higher mortality burden than other racial and ethnic groups for many cancers. We must reverse course,” said Rebecca Siegel, MPH, senior scientific director for cancer surveillance research at the American Cancer Society and senior author of the report, in a statement.¹

These results are in line with past research that has found a continuing disparity in both diagnoses and health care related to health care in Black individuals. Researchers have found that Black women are less likely to receive care according to guidelines when compared with White women, and an increased mortality in Black women due to these care disparities.² Racial discrimination has also been a source of disparities in outcomes among Black individuals, with most participants of a study published by the *Journal of the National Cancer Institute* reporting that they had experienced racial discrimination when accessing health care related to cancer.³

“This report highlights the disparities the Black community has faced for decades. While the decline in cancer mortality rates is encouraging, the stark inequities in incidence and survival for many cancers underscore the urgent need for targeted research and interventions,” said Wayne A. I. Frederick, MD, MBA, interim chief executive officer of the American Cancer Society and the American Cancer Society Cancer Action Network.¹ ♦

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Supreme Court Case Could Threaten Free Colorectal Cancer Screenings

PEARL STEINZOR

THE AMERICAN COLLEGE of Gastroenterology (ACG) is urging the US Supreme Court to uphold the authority of the US Preventive Services Task Force (USPSTF), warning that millions of Americans could lose access to essential colorectal cancer (CRC) screenings.¹ In an amicus brief filed Monday in *Kennedy v Braidwood*, the ACG

highlighted the potential consequences of limiting the USPSTF’s role in guiding preventive care coverage under the

“Simply put, the implications of the court’s upcoming decision on patient care and public health should not be understated,” said Amy S. Oxentenko, MD, FACP, president of the ACG, in

a statement. “We informed the Supreme Court of how much progress we’ve made in recent decades in preventing colorectal cancer deaths through colonoscopy with polypectomy, but also warned the justices how much is at stake in this moment—especially as incidence rates continue to rise among younger Americans.”

The court will rule this spring on the validity of the USPTSF and its recommendations under the Affordable Care Act (ACA). The ACG represents the interests of gastrointestinal clinicians and their patients. In the brief, the group outlined the success and importance of CRC screening for public health, while also emphasizing the need to reduce barriers to access.

Since the USPSTF updated its recommendations that patients aged 45 to 49 years be screened for CRC, research found disparities based on socioeconomic status and area of residence, emphasizing a need for interventions in these areas to increase screening in all patients.² Furthermore, CRC is the second leading cause of cancer-related deaths in the US. CRC has also been found to increasingly affecting younger adults, with diagnoses among those under age 55 years nearly doubling over the past decade.

The Supreme Court case comes at a critical moment in the fight against CRC. Although

overall incidence rates have dropped nearly 50%—largely due to increased screening—early-onset CRC is on track to become the leading cause of cancer death in people aged 20 to 49 by 2030, according to the ACG.

The ACA's preventive services mandate has eliminated cost-sharing for screenings, removing a key barrier to care. Research shows that out-of-pocket costs deter patients from getting screened, particularly those from lower-income backgrounds. If the court upholds the lower court's ruling in *Braidwood*, the ACG warns that screening rates could decline—leading to more late-stage diagnoses and higher mortality rates.

Although the ACG steered clear of constitutional arguments, it underscored the public health stakes. Beyond ACA-regulated insurance plans, the USPSTF's recommendations influence screening mandates in 16 states. A ruling against the task force's authority could trigger further legal

battles over state mandates, leaving millions of Americans in limbo.

“Colorectal cancer screening includes colonoscopies and other, noninvasive tests that can detect warning signs before colorectal cancer develops,” the brief outlined. “The data are clear: colorectal cancer screening saves lives by stopping colorectal cancer—the second most common cause of cancer mortality in the US—in many cases even before it happens.” ♦

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SPOTLIGHT

How Pharmacists Can Help Patients Navigate Costs, Access to Breast Cancer Therapies

Pearl Steinzor



MENG

TIFFANY MENG, PHARM.D,
oncology pharmacist, UCSF Health.

INSURANCE FORMULARIES, patient assistance programs, and financial counselors play a significant role in reducing financial toxicity and removing barriers to care for patients struggling to afford breast cancer therapy, Tiffany Meng, PharmD, an oncology pharmacist with UCSF Health, said in a recent interview with *Evidence-Based Oncology (EBO)*.

EBO: How do formulary decisions and utilization management strategies impact patient access to targeted therapies for breast cancer?

MENG: I think when it comes to formulary decisions, it's kind of 2-fold. When we're talking about formulary, the first thing we usually need to think about is what's on the insurance formulary. I work in an outpatient infusion center, so we often deal with many different kinds of insurance, depending on the patients that we're seeing. Insurance formulary will often dictate what medication could be covered for the patient and what wouldn't be, and that essentially will impact patients' access to therapies.

Generally speaking, at our institution, the billing and central authorization team work together with the insurance, dealing with appeals [and] prior authorization, and help facilitate peer-to-peer discussions, where the providers of each individual clinic will get involved at that point. We also have patient assistance programs that are offered by various drug manufacturers, and we have a team of financial counselors that can try to

help make sure that patients can get access to these higher-cost targeted therapies for breast cancer.

From a pharmacy standpoint, because I work in an outpatient infusion center, generally speaking, if a medication is covered by insurance, we do our best to obtain the drug because we want to be able to provide that for our patients. As long as the insurance allows it, our health system is able to obtain it. We're fortunate in the sense that we're a lot less restrictive when handling these high-cost targeted therapies compared to inpatient setting or ambulatory care setting. Also, we help deal with patient assistance program medications. We help run the inventory and whatnot. So that's what we do to, hopefully, do our best to help make sure that patients get access to these medications.

EBO: When evaluating biosimilars for HER2-positive breast cancer treatment, what are the key considerations?

MENG: I think when talking about biosimilars, it's really important that we...make sure they have comparable clinical outcomes and safety profiles to their reference biologics. So that way, we can make sure it is clinically safe and an effective alternative when we're swapping them out for treatment. Once we establish that it is effective and safe, and switching them out is going to be safe and continue the efficacy, then we can start considering, "OK, what's more cost-effective?"

The market now has so many different biosimilars for the same drug, and every biosimilar could have a different contracting price, whether you're talking about insurance, whether you're talking about a health system, and that will determine what the cost is. Also, certain insurance will prefer one biosimilar over the other biosimilar, and that's something that, working in a health system, we have to figure out what makes the most sense for our system. Also, being able to cover most of what our patient population insurance would be willing to cover and what our patients can actually get access to. That's kind of how we approach it. ♦

Experts Issue a Call to Action for Oncology Care Equity

MAGGIE L. SHAW

NASHVILLE REGIONAL

ACHIEVING HEALTH EQUITY is a persistent challenge in cancer care, shaped by socioeconomic disparities, health policy, insurance benefit design, and site-of-care restrictions that disproportionately affect some communities. Further, although therapies can offer transformative potential, significant challenges and payer-related barriers often limit equitable care access and delivery. Therefore, expanding access to advanced cancer therapies and elevating the value of current and future care require trusted strategic academic-community partnerships among community oncology practices, hospitals, and key industry stakeholders.

Mitigating barriers is crucial to ensuring all patients receive high-quality, timely treatment. Standardizing care across networks, implementing structured education for health care professionals and patients, fostering multidisciplinary expertise, and empowering physician champions to drive treatment are essential to more equitable oncology care.

Part of the Elevating Value in Cancer Care regional series, the January 30, 2025, Institute for Value-Based Medicine® event in Nashville, Tennessee, brought together experts from the top cancer centers, hospitals, and care networks in the region to address how collaboration can bridge critical gaps in care delivery. Panelists and presenters alike emphasized the need to address social determinants of health and health-related social needs to ensure timely and equitable access to treatment.

They examined the broader societal and systemic conditions that influence health and the immediate, tangible needs that affect an individual's ability to receive care. Additionally, they explored the intersection of health equity and value-based cancer care, emphasizing the importance of innovative collaborations and systemic changes to ensure all patients, regardless of background, have access to high-quality treatment.

Health Equity in Cancer Care Delivery

"I think it's important if we are in the system, if we want to make an impact, if we want to think about equity, particularly in today's climate when there are pushbacks against accessibility and equity—because, unfortunately, the terms *DEI* [diversity, equity, and inclusion] and *equity* have been conflated, [and] they're not the same—[that] we... understand the difference so...we can advocate to make sure we're reducing barriers in terms of cancer care and cancer care delivery," said Karen Winkfield, MD, PhD, Ingram Professor of Cancer Research at Vanderbilt Ingram Cancer Center, professor of radiation oncology, Vanderbilt University Medical Center; professor of medicine at ; and executive director of the Meharry-Vanderbilt Alliance, who moderated this panel discussion.

Winkfield was joined by Kate Baker, MD, MMHC, medical oncologist and medical director of value-based care at Tennessee Oncology; Cathy Eng, MD, FACP, FASCO, gastrointestinal program leader for research, executive director of the young adult cancers program, and associate director for research partnerships, School of Global Health, Vanderbilt Ingram Cancer Center; and Ricky Martin, MD, MPH, medical oncologist and medical director for health equity and community engagement at Tennessee Oncology.

Their overall message was that for meaningful and lasting change to advance health equity, there must be sustainable and genuine engagement through community-driven solutions from everyone

involved. These solutions need to look at the short- and long-term future of health equity through the lens of social determinants of health, the wide-sweeping but often nuanced societal shortcomings that shape patient health, and health-related social needs, which are more immediate and tangible and directly impact the ability to even receive care.

"There are microenvironments that exist, and it's [a matter of] recognizing that those landscapes are fairly intentional...there are societal reasons for the conditions that exist and the people who have to live their lives in those settings, and...there is the capacity to change them," Martin said. Social determinants are modifiable, he emphasized, and they can be changed through targeted interventions.

These structural barriers point to policy as a principal determinant of health disparities in cancer care, evidenced through insurance benefit design and how that influences financial toxicity. For an accurate representation of how this is playing out in Tennessee, one need look no further than the nonexpansion of Medicaid and the apparent hoops of qualification individuals must jump through to qualify for coverage.

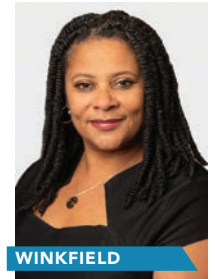
Tennessee is 1 of 10 states that have not expanded Medicaid coverage under the Affordable Care Act as of 2025.¹ However, in 2024, the state expanded eligibility for low-income parents from 89% to 105% of the federal poverty level.² Frequently, the result is a coverage gap, where individuals seeking assistance through Medicaid have too high an income to qualify for coverage but are still unable to afford coverage through private insurance. Winkfield noted that these challenges are sometimes mistakenly assumed to affect only individuals in lower socioeconomic brackets, but those with midrange salaries also may encounter this form of financial toxicity due to a lack of affordable insurance options. This underscores the pervasive nature of the problem, which extends beyond traditional notions of poverty.

Health equity in cancer care does not merely concern race, according to the panel. The impact of insurance benefit design on health disparities was one of the most pressing issues they highlighted. Baker pointed out how "formulary coverage and high deductibles" can create significant barriers to care. She shared the story of a patient who "had to be admitted twice to get inpatient chemotherapy because she wasn't able to get the intravenous access...she needed...to get outpatient chemo, and that was really just because of the insurance that she had."

Eng brought attention to the unique challenges young adults face and illustrated the profound impact of systemic failures on individuals and families. For young adults, the top issues are "job security and insurance issues" and advocating for their care. Often, they are forced to take months off work for treatment or laid off from their jobs, and their care team must jump in and appeal, according to Eng. She also shared her parents' experiences with language barriers and insurance issues, describing them as "horrible health care."

The panel also explored potential solutions and initiatives aimed at fostering health equity. Baker discussed Tennessee Oncology's efforts to "decrease the cost of care and participate in the Enhancing Oncology Model" of payment for value and quality vs fee-for-service-based payment. Eng emphasized the importance of "multidisciplinary efforts and working with social workers and pharmacists to support patients," mentioning various programs and foundations providing essential patient resources, such as counseling.

Martin stressed the significance of "showing up and building trust with patients" and the necessity for "sustainability in health



WINKFIELD

Karen Winkfield, MD, PhD



BAKER

Kate Baker, MD, MMHC



ENG

Cathy Eng, MD, FACP, FASCO



MULLANGI

Samyukta Mullangi, MD, MBA



RICHEY

Sylvia Richey, MD



MAYNARD

Angie Maynard, PharmD, MS, CPGx



KURBEGOV

Dax Kurbegov, MD



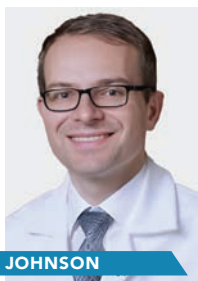
ARROWSMITH

Edward "Ted" Arrowsmith, MD, MPH



IAM

Wade Iams, MD, MSCI



JOHNSON

Douglas Johnson, MD, MSCI

equity programs." He highlighted the crucial role of "community advisory boards and the importance of co-ownership in health equity initiatives," advocating for a collaborative approach to addressing these issues.

Winkfield concluded the discussion by emphasizing the importance of "inclusive participation in clinical trials"—a call to action that underscored health care professionals' collective responsibility to bridge the gap between research and real-world application, ensuring that advancements in medicine benefit all members of society. She expressed this sentiment in a previous interview with *The American Journal of Managed Care*, sister publication to *Evidence-Based Oncology*, where she said, "It's important for our researchers to be able to articulate their research in a way that is meaningful to the community. [They] must learn how to talk about their research in a way that the communities...we serve can really understand."³

Academic, Hospital, and Community Partnerships

This panel discussion focused on improving patient access to safe and effective advanced cancer therapies across an evolving oncology landscape. The panelists addressed why partnerships between academic hospitals, community oncology practices, and private institutions are essential to achieving this outcome.

"How can we scale delivery and access to novel drug therapies?" Samyukta Mullangi, MD, MBA, senior medical director at Thyme Care and medical oncologist at Tennessee Oncology, asked the gathered experts. "This includes relatively increasingly off-the-shelf interventions, like CAR T [chimeric antigen receptor T-cell therapy] and bispecific antibodies, but also access to clinical trials."

Sylvia Richey, MD, medical oncologist and chief medical officer at West Cancer Center and Research Institute, explained that selecting hospital partners that accept all payers is critical to expanding access. However, it is also crucial to have plans in place to help manage patients as they go through treatment, especially when these treatments cause serious complications, such as the systemic inflammation seen with cytokine release syndrome. To this end, having trained staff and well-defined admission protocols are essential.

Standardizing care through multidisciplinary collaboration is also vital, with embedded specialized care hubs and training programs being essential to facilitating community-based practices offering complex therapies, explained Dax Kurbegov, MD, senior vice president at Sarah Cannon Cancer Network. At the center of this is balancing accessibility with volume-driven proficiency to ensure that specialized centers can maintain their expertise by not becoming overburdened with excessive patient loads.

"Ensuring that centers see enough cases to maintain proficiency is critical to balancing access with expertise," he explained.

Sandhya Mudumbi, MD, palliative care physician and medical director of supportive care teams (psychosocial oncology, palliative care, and integrative health) at Tennessee Oncology, explained that with the increasing complexity of some cancer treatments, community practices need to invest time and resources in fostering bidirectional partnerships so that everyone benefits and can overcome organizational hurdles. Each party that comes to the table through these interactions must align on their core values and mission, have strong data capabilities for tracking outcomes, and be committed physician champions.

Precision Medicine in Value-Based Care

The third panel discussion of the evening explored the intersection of precision medicine and value-based care in oncology, focusing on the challenges and opportunities in implementing genomic testing and precision treatment strategies. Edward "Ted" Arrowsmith, MD, MPH, executive vice president of therapeutics at Tennessee Oncology and medical director for pathways at OneOncology, was joined by Wade Iams, MD, MSCI, director of lung cancer research at Tennessee Oncology, and Douglas Johnson, MD, MSCI, coleader of

the Translational Research and Interventional Oncology Research Program at Vanderbilt-Ingram Cancer Center.

"One of the biggest breakthroughs we've had over the last 20 years has been the development of targeted, precise therapies for our patients," Arrowsmith said. "But there are barriers to delivering that across the full spectrum of patient populations."

The trio addressed several hot topics, such as reflex next-generation sequencing for non-small cell lung cancer (NSCLC)—the standardization of which remains a top challenge. This key component of precision medicine is when a pathologist automatically initiates additional genetic testing on a tumor sample after initial results reveal a predefined mutation, eliminating the need for orders from an oncologist.⁴ Universal testing is a top priority of many advocates, the panel noted, but debate is ongoing over its necessity in specific populations, such as patients with squamous NSCLC or a history of smoking. The development of guidelines to define its appropriate applications is crucial.

Another highlight of this discussion was the need for standardized molecular testing processes and the importance of timely, early-stage testing for high-risk patients—supported by payer-aligned guidelines—and longitudinal testing to help monitor resistance mutations. The panelists also discussed the complexities of minimal residual disease testing, which is quickly gaining traction as a surrogate treatment end point⁵ but still lacks robust prospective data to endorse its widespread adoption.

"I think systems and physicians are going to continue to get more and more pressure to use these tests before we have the ideal prospective data sets that we need," Iams cautioned.

Beyond testing, the 3 experts highlighted the importance of communication and streamlining provider coordination, particularly in integrating genomic data into electronic medical records.

Like Mudumbi, Johnson emphasized the importance of bidirectional communication, "especially when patients go back and forth between academic and community sites or from one site to another. That communication piece is really important and can be lifesaving."

Addressing access disparities is also crucial due to the impact of socioeconomic factors on testing availability and access. The discussants called for continued investment in clinical trials, health literacy efforts, and systematic solutions to ensure equitable access to precision oncology.

Pharmacy Decision-Making in Oncology

Jerrick White, PharmD, director of pharmacy services at Tennessee Oncology, moderated the final panel discussion of the evening, which focused on advancing oncology care with innovative delivery methods, multidisciplinary collaboration, and pharmacy-led initiatives. Angie Maynard, PharmD, MS, CPGx, assistant professor of pharmacy practice at Lipscomb University College of Pharmacy, and Amanda Cass, PharmD, BCSCP, clinical pharmacist specialist in thoracic oncology at Vanderbilt University Medical Center, were his copanelists.

The first key topic they addressed was outpatient delivery models for bispecific antibodies and CAR T. Vanderbilt is exploring outpatient administration with remote patient monitoring, and Tennessee Oncology is employing hub sites for step-up dosing and a thorough screening process for CAR T referrals.

"A lot of steps go into this, but so far, we've treated 8 patients," White noted, "and we have another 4 in the pipeline."

The panelists also discussed challenges with optimizing care from fragmented care models, especially for underinsured patients, and they emphasized the importance of strong nurse navigation and multidisciplinary collaboration for seamless patient transitions. "This has been a theme throughout the night from every panel that's been up here. There needs to be some continuity and good communication between each place that's involved in a patient's care," Maynard emphasized. "We do the best we can but having a

good multidisciplinary care team and a good nurse navigator, [and] pharmacist, if they are involved in that [aspect] of care, is imperative.”

Specialty pharmacies also place a vital role in improving treatment access and affordability by finding novel solutions to facilitate medication dispensing while reducing waste. For example, Vanderbilt licensed automatic dispensing machines in clinics to facilitate the dispensing of chemotherapy medications and enable the restocking of unused medications in the case of dose changes.

Lastly, the experts highlighted the role of pharmacists in oncology clinics, noting they provide telehealth services, manage supportive care, and reduce physicians’ workloads. The panel praised telehealth for improving patient engagement, reducing travel time, and enhancing adherence.

“I think it’s helped expedite care for these patients and streamline care,” Cass noted,” as well as hopefully prevent some toxicities from some of these more high-risk therapies.”

Where to Go From Here

Health care is a deeply personal experience and one that extends beyond mere policy and procedure. Addressing systemic disparities and prioritizing patient-centered care can drive a more equitable system in which the future of community oncology will hinge on collaboration between community and academic centers, strong leadership, and coordinated care transitions as keys

to safely delivering advanced therapies in nonacademic, diverse settings. Challenges include site-of-care mandates, use of telehealth in patient management, and the need for real-world data to inform cost-effectiveness. Expanding patient assistance programs, and addressing socioeconomic barriers are critical to ensuring equitable access to care. ♦

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SPOTLIGHT

Elevating Cancer Care Through Personalized Treatment

Cathy Eng, MD, FACP, FASCO | Interview by Maggie L. Shaw



ENG

CATHY ENG, MD, FACP, FASCO, codirector, Gastrointestinal (GI) Oncology; coleader, GI Cancer Research Program; director, Young Adult Cancers Program, Vanderbilt-Ingram Cancer Center.

EARLIER THIS YEAR, for a oncology-focused Institute for Value-Based Medicine event, *The American Journal of Managed Care* partnered with several prominent health care institutions from across the Nashville region to elevate value in cancer care by discussing the roles that academic, hospital, and community partnerships; precision medicine; pharmacy; and health equity fulfill when delivering care in the oncology space.

Lipscomb University and Metropolitan General Hospital, Meharry Medical College, Sarah Cannon, Tennessee Oncology, Thyme Care, Vanderbilt-Ingram Cancer Center, Vanderbilt University Medical Center, and West Cancer Center were represented.

In this discussion with Cathy Eng, MD, FACP, FASCO, codirector, Gastrointestinal (GI) Oncology; coleader, GI Cancer Research Program; and director, Young Adult Cancers Program, Vanderbilt-Ingram Cancer Center, she illustrates how Vanderbilt works to specify each individual patient’s cancer care regimen and treatment path. Eng participated on the panel discussion, “Health Equity in Cancer Care Delivery.”

This transcript has been lightly edited for clarity.

AJMC: How does Vanderbilt integrate its mission to elevate cancer care across its care offerings?

ENG: I would say that Vanderbilt-Ingram Cancer Center and the Vanderbilt University Medical Center—because many of our consultants are part of the university medical center—what we truly try to do for our cancer patients is really try to focus on their unmet needs. Especially in regards to cancer treatment nowadays, the focus of a lot of therapy is more personalized, biomarker-driven therapy.

I think because we are fortunate enough to be a large academic institution, we have good rapport with pharma, and as a result, have historically been involved in many pivotal clinical trials. Just for the audience, I’m largely a GI medical oncology specialist, but I do assist with strategic initiatives regarding pharma interests in the cancer center itself.

I think that when we’re talking about elevating value in cancer care, I think it’s really important to try to be able to offer patients care more specific to their malignancy. We recognize the importance that in the majority, at least solid tumors, next-generation sequencing or mutation analysis, or any type of amplification or any type of fusion protein, is noted based upon the patient’s existing tumor, and we will work with other companies to identify those various molecular alterations. That way we can provide patients the most optimal care in regards to treatment.

But also, I think the value arises when we work very much so in a multidisciplinary team effort with our surgical colleagues, radiation colleagues, pathology, etc, and a lot of our treatment planning is discussed in our tumor board, so you’re getting multiple opinions of people, even though you may have only had 1 consultation with 1 doctor—you’re getting multiple opinions within 1 meeting about the best approach to your cancer. I think that that really helps optimize the value for a cancer care patient, plus all the supportive services that are available at Vanderbilt, such as social work, supportive care, oncology clinic, to optimize the overall well-being of the patient, nutrition, wound care, etc. ♦

Making Novel Cancer Therapies Available Requires Choices Because Resources Are Limited

KYLE MUNZ



GILLESPIE

Theresa W. Gillespie, PhD, MA, FAAN



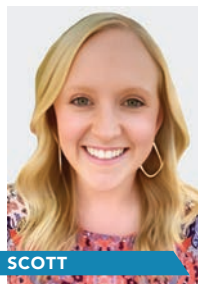
SACKS

Ruth Sacks, MD



JONES

Jade E. Jones, MD



SCOTT

Sara Scott, PharmD, BCOP



AYYAPPAN

Sabarish Ayyappan, MD

IVBM ATLANTA

MOVING FORWARD IN clinical research involves answering simple questions: Can you explain why it matters? Can you get someone to pay for it?

These are questions of health policy, said Theresa W. Gillespie, PhD, MA, FAAN, associate director for cancer health equity and community engagement at Winship Cancer Institute of Emory University. “If you can’t get it to a policy level where it’s going to be approved, where it’s going to be paid for, where it’s going to be accessible, then we’re not going to make the progress that we want to make.”

Gillespie is not alone in this view, as other experts have drawn attention to the influence of the Inflation Reduction Act (IRA) and CMS on patient care and access to novel medications. These topics, as well as crucial advancements in the treatment of non-small cell lung cancer (NSCLC), chronic lymphocytic leukemia (CLL), and other hematologic malignancies, were highlights of the Institute for Value-Based Medicine event held February 13, 2025, in Atlanta, Georgia.

These sentiments resonated throughout the discussion of various immunotherapies, and the panels highlighted the central role of health care policy in elevating value in cancer care.

Addressing social determinants of health (SDOH), or the “hidden factors,” as Ruth Sacks, MD, assistant professor, Department of Hematology and Medical Oncology at Emory University School of Medicine, put it, requires an ongoing commitment from institutions, sponsors, and health systems to fill in gaps that policy alone cannot remedy. “You can be an advocate, but the institution has to care to put those resources in place,” and “it has to come from top to bottom,” said Jade E. Jones, MD, medical oncologist at Emory Winship Cancer Institute. Social workers, patient navigators, and community partnerships are vital in these initiatives.

In the realm of chimeric antigen receptor (CAR) T-cell and bispecific therapies, community partnerships can help facilitate Risk Evaluation and Mitigation Strategy (REMS) and educational initiatives. “One piece of it is early referral to a center who [has such therapies] to establish that relationship early [on] before these therapies are needed in an emergency,” argued Sara Scott, PharmD, BCOP, clinical pharmacy specialist at Emory Healthcare, as she highlighted the value of collaborating at the community level to operationalize CAR T-cell and bispecific interventions.

Making bispecific and CAR T-cell therapies accessible in community settings also requires partnering with larger academic institutions, noted Sabarish Ayyappan, MD, medical director for hematologic malignancies at City of Hope Cancer Center, Atlanta. These relationships can better equip physicians to manage step-up dosing and risks for cytokine release syndrome in patients with multiple myeloma or lymphoma, he added.

“No patient with myeloma should die without seeing a bispecific,” declared Nisha Joseph, MD, associate professor, Department of Hematology and Medical Oncology, Emory School of Medicine. “So, it’s...important that we’re having these kinds of conversations and talk[ing] about how to pragmatically get into the community more.”

“There really needs to be more accountability in terms of helping these patients navigate the system,” Sacks continued. “On a policy level, we need to move forward with advocating for patients across the board, especially patients [with cancer who] are in a very vulnerable position.” The panel emphasized the need to help connect patients with transportation while assisting them in addressing challenges related to insurance coverage, clinical trial access, financial toxicities, and preventive services in oncology care.

Gillespie criticized the use of household income as a benchmark for assessing patients’ financial status when deciding if they qualify for specific assistance. She referenced the hidden factors Sacks alluded to, citing how some treatments can cause income loss when patients must take time off work. Additionally, many travel and lodging expenses are not factored into these financial assessments.

“No patient with myeloma should die without seeing a bispecific. So it’s...important that we’re having these kinds of conversations and talk[ing] about how to pragmatically get into the community more.”

—Nisha Joseph, MD, associate professor, Department of Hematology and Medical Oncology, Emory University School of Medicine

The experts also discussed the need for Medicaid expansion, as Gillespie and Jones mentioned how many patients—who fear financial toxicity or have travel or insurance barriers—delay care and, as a result, show up later in the course of their disease. Given that care delays can critically affect patient outcomes, it is critical to do more to offer accessible screening and prevention services to catch cancer early on. “An ounce of prevention is worth a pound of cure, but we need to be thinking about access for all kinds [of individuals] and value in cancer care across all levels,” Gillespie said.

The IRA and CMS price negotiations, in particular, could significantly improve access to newer, more effective Bruton tyrosine kinase (BTK) inhibitors in CLL, such as zanubrutinib (Brukinsa; BeiGene USA, Inc) and acalabrutinib (Calquence; AstraZeneca Pharmaceuticals LP).

“We just don’t have unlimited resources anymore, and a huge proportion of health care costs comes from cancer therapy,” said Eiran A. Warner, MD, oncologist/hematologist at Piedmont Cancer Institute. “Choices are going to have to be made, and one way of trying to help the health system is to lower cost through [the IRA]. That’s probably where the future is,” he continued, expressing optimism for legislation to dictate more cost-conscious care. However, a provider’s autonomy needs to remain a

priority because “the ultimate decision, which is the best agent, rests in the expertise of the treating physician,” said Andres Chang, MD, PhD, instructor, Department of Hematology and Medical Oncology at Emory University School of Medicine.

“These drugs are not cheap by any means, and if you’ve got to take [them] lifelong, [they] can make anybody bankrupt.”

—Vipin R. Lohiya, MD, oncologist/hematologist, Piedmont Cancer Institute

Evaluating outcomes and gathering data associated with minimal residual disease (MRD) or fixed-duration interventions are essential for cost-benefit analyses because “these drugs are not cheap by any means, and if you’ve got to take [them] lifelong, [they] can make anybody bankrupt,” Vipin R. Lohiya, MD, oncologist/hematologist at Piedmont Cancer Institute, added. Jean Koff, MD, MS, a hematologist at Emory Winship Cancer Institute, echoed this sentiment and alluded to the variety of patient characteristics that influence clinical decisions for BTK inhibitors. She stated, “It’s not going to be one size fits

all” when it comes to a patient’s intervention, the influence of doublet or triplet therapy, or the role of MRD. Furthermore, with compelling data to guide treatment decisions, providers may be able to “reach back into [their] pocket and not even have to use a new therapy.”

Role of Specialty Pharmacy in NSCLC

Building on these topics, a panel of NSCLC experts discussed the importance of strong specialty pharmacy programs to aid with high-cost therapies. “There needs to be a team of people that can really coordinate the care and communicate so that we can get these treatments approved in time,” Pauline Kim, PharmD, BCOP, who at the time was a clinical pharmacy specialist with Emory Healthcare, explained. “It needs different coordination from the insurance company, from the clinic, right from the specialty pharmacy,” she added.

NSCLC panelists also emphasized the need for policy-level changes to improve access to molecular testing and quicken turnaround times. “I would argue that an NGS [next-generation sequencing] panel for lung cancer is just as important as ER [estrogen receptor], PR [progesterone receptor], [and] HER2 [are] for breast cancer, and we need to push [so] that this is done reflexively on a national level and not piecemeal,” stated Jennifer Carlisle, MD assistant professor, Department of Hematology and Medical Oncology, Emory School of Medicine. Additionally, Ioana Bonta, MD, medical oncologist at Georgia Cancer Specialists, mentioned how including genomic testing as part of a cancer institute’s quality measures can be a valuable strategy.

Ultimately, the panelists in the evening discussions expressed an urgent need for action. Looking ahead, deep institutional commitments, strategic partnerships, policy reform, and continued advocacy will be essential to elevate value in cancer care. ♦



JOSEPH

Nisha Joseph, MD



CHANG

Andres Chang, MD, PhD



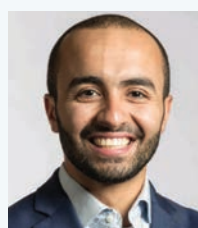
KIM

Pauline Kim, PharmD, BCOP

SPOTLIGHT

Embracing EOM, Enhancing Collaboration and Cost Management

Kirollos Hanna, PharmD, BCPS, BCOP, FACCC, FAPO | Produced by Kyle Munz



HANNA

KIROLLOS HANNA, PHARM.D, BCPS, BCOP, FACCC, FAPO, director of pharmacy, Minnesota Oncology.

This interview is edited for clarity. It took place during an Institute for Value-Based Medicine event with Minnesota Oncology.

AJMC: Compared with the Oncology Care Model (OCM), fewer practices joined the Enhancing Oncology Model (EOM). Can you explain why your practice decided to join EOM after not doing OCM?

HANNA: My practice within Minnesota Oncology was really driven to be part of the EOM when CMS...came out with this particular model. ... We have always been in conversations with local payers, national payers, and

various entities around value-based care delivery. We have partnerships with local organizations under a value-based enterprise type of model; we have very strong relationships with Blue Cross [and] Blue Shield of Minnesota in terms of being able to demonstrate, [that] our cost of care can be lower without taking away from the outcomes—the clinical benefit—of our patients. So, EOM...to us, was almost a no-brainer.

We knew that drug costs [were] driving up health care spend[ing]. So Medicare came and said, “Hey, you know what? That’s going to be 70% of... this EOM analysis in these top 7 disease states. And what could you do to help show that you can reduce the total cost of care around certain drugs?” So that’s where we navigate things like biosimilars, be heavy adopters of biosimilars as soon as they’re coming to market. Looking at our pathways, [they] take into consideration the total cost of care and where there could be opportunities to contain cost if the clinical profile of particular regimens [doesn’t] really differ significantly, or [at all], by any means. Then [there are] other things...like social determinants of health.

It was really nice to see this EOM model come out, and it tied a lot of factors that we have maybe worked on in the past or currently are working on. ... EOM, for us, was just an opportunity to...continue to demonstrate that value and show that value. ♦

More Is Not Always Better: Innovations in Oncology Treatment and Diagnostics

ROSE MCNULTY



HUMPHREYS

Sophia Humphreys,
PharmD, MHA, BCBS.



CHIN

Alan Chin, PharmD.



OYEKAN

Elizabeth Oyekan,
PharmD, FCSHP, CPHQ.



BUCKLE

Geoffrey Buckle, MD, MPH.

IVBM SAN FRANCISCO

ONCOLOGY HAS SEEN WAVES of innovation in diagnostics, treatment, and patient management in recent years. However, with novel options comes a need for more nuanced decision-making for providers and patients. Speakers at an Institute for Value-Based Medicine event held in San Francisco, California, on February 27, 2025, discussed the complexities of treatment decision-making across cancer types and strategies to drive value in cancer care. The event, *Elevating Value in Cancer Care: San Francisco*, brought together stakeholders in the oncology treatment space to share their insight into value-based medicine in oncology.

The first session centered on pharmacy decision-making in oncology. Moderated by Sophia Humphreys, PharmD, MHA, BCBS, executive director of pharmacy, Providence Health System, the panel included Elizabeth Oyekan, PharmD, FCSHP, CPHQ, chief pharmacy officer at Stanford Health; Alan Chin, PharmD, clinical oncology pharmacist at UCSF Health; and Tiffany Phung, PharmD, specialty pharmacy director at UC Davis Health.

The discussion began with the logistics and value of delivering bispecific antibodies or even chimeric antigen receptor (CAR) T-cell therapies, traditionally administered in the inpatient setting, as outpatient treatments. Delivering these high-cost, high-risk therapies in the outpatient setting can reduce hospital stays and health care costs overall, Chin noted.

“For patients themselves, it definitely offers a greater convenience for them and greater patient satisfaction, which is most important of all,” Chin said. “These patients don’t need to be admitted for the entire week anymore, so it increases the flexibility of scheduling for these patients. It offers them care closer to home, and overall, these patients have [a] greater quality of life and adherence as well.”

Reimbursement models have also adapted to this trend, Chin explained. He said that as more data emerge confirming safety, this strategy may become increasingly popular for CAR T-cell therapies and bispecific antibodies. To manage treatment-induced toxicities, uniform inpatient and outpatient workflows are crucial. These will vary between therapies, but there may also be opportunities to consolidate strategies when multiple therapies have similar toxicity management protocols, Chin said.

In response to a question about the fragmentation that can occur with payer mandates regarding sites of care, Oyekan said although it poses challenges, this issue is part of a larger push for delivering care at lower price points and will likely need to be navigated. With patients increasingly being steered from expensive sites of care, such as large academic centers, clinically integrated networks (CINs) and teleoncology are 2 elements that could facilitate better communication, lower costs, and optimal patient outcomes, she added.

“We know site of care is coming, and the question for us is, ‘What are we going to do to keep the communication lines going?’ The other thing we’re thinking about is CINs,” Oyekan said. “What we’re doing there is looking to see, how do we bring [in] the hospitals that we work with? How do we bring the providers in the community, the specialty pharmacies

and other entities we’re working with, and how do we form an alliance?”

Phung spoke to the pharmacists’ role in driving value alongside oncology teams, emphasizing the importance of collaboration to optimize outcomes. She pointed to a study that characterized a multidisciplinary team’s role in hospital discharge for patients with acute myeloid leukemia receiving the BCL2 inhibitor venetoclax with hypomethylating agents.¹

“What they saw was [that] when pharmacists were involved in managing the care from inpatient to out—getting those prior authorizations, making sure that the medication is in hand—for the patient, the length of stay in the hospital was reduced significantly,” Phung said. This demonstrated that working with inpatient and outpatient pharmacists can allow patients to be safely discharged with good outcomes. At UC Davis Health, she continued, pharmacists also conduct post-discharge calls to ensure patients are adhering to treatment appropriately. “Under this collaborative practice agreement, we’re able to prescribe the supportive care that’s needed,” she said.

Oyekan and Chin echoed the importance of this strategy, adding that Stanford Health and UCSF employ similar best practices.

“... [W]hen pharmacists were involved in managing the care from inpatient to out—getting those prior authorizations, making sure that the medication is in hand—for the patient, the length of stay in the hospital was reduced significantly.”

—Tiffany Phung, PharmD,
specialty pharmacy director,
UC Davis Health

Innovations and Best Practices in Breast and Gastrointestinal Cancers

Laura Huppert, MD, breast oncologist at UCSF Health, moderated a session on innovations in breast cancer treatment. Panelists Aditi Choudhry, MD, a hematologist/medical oncologist at John Muir Health; Lidia Schapira, MD, FASCO, professor of medicine at Stanford University School of Medicine; and Tiffany Meng, PharmD, oncology pharmacist at UCSF, discussed the latest developments in the breast cancer treatment space and how best to serve patients with breast cancer.

Huppert opened the discussion with a question about CDK4/6 inhibitors for patients with early-stage hormone receptor-positive, HER2-negative breast cancer—specifically, the efficacy of these therapies and barriers to receiving them. Schapira said because early-stage breast cancer is treated with curative intent, patient preference is an integral part of the conversation.

“Ultimately, the person who decides on the value, I think, is the patient—if they can afford it and if they can physically have it,” Schapira said. However, she noted the significant toxicity associated with CDK4/6 inhibition, and a lack of evidence that survival improves with these treatments.

“Patients are often not at their best, and you hopefully don’t want them to make a decision from a place of fear, saying, ‘Just give me everything,’ which is often the way some of the adjuvant conversations are framed,” Schapira said. “And I don’t think that is really fair. I don’t think it’s really helping the patient either.”

Choudhry added that she offers CDK4/6 inhibitors to eligible, younger high-risk patients; however, she explains to patients that although approved options exist, there isn’t a proven overall survival (OS) benefit.

“Once you tell a patient that this is approved, they automatically just want to grasp for it without realizing that there isn’t [an] OS benefit,” Choudhry said. “That’s a conversation I’m having with my patients. I’m still offering it to the high-risk, younger, node-positive patients, and then having a more detailed, in-depth discussion with node-negative, especially postmenopausal, older patients.”

Schapira cautioned against overtreatment, explaining that more treatment and higher doses are not always better. Treatment should be planned methodically, carefully, and calmly; every patient is unique in their needs and treatment responses.

From the pharmacy perspective, Meng discussed the challenges of getting coverage for newer therapies and defining value from the patient’s perspective. Patients may come to the pharmacy intending to proceed with a treatment, only to learn that the copay is unmanageable, or that insurance did not grant approval. Pharmacists can help patients by navigating prior authorization, peer-to-peer appeals, and options such as co-pay cards, grants, patient assistance programs, or other routes of assistance, Meng said.

“It’s exploring all these options with the patients to see what would be reasonable for them and make it accessible for them,” Meng said. “And then it’s adherence. You might feel like, ‘Oh, I’m ready to take this medication,’ and then you start taking it, and it’s really intolerable. And then the conversation needs to be had about how you help them stay on the regimen.”

Schapira explained that supporting patients through services like financial navigation is also important, although these services are often underused. Expanding supportive services, especially at academic centers providing cancer care, is essential.

“I think our cancer centers need to understand that supporting patients is part of the business of giving cancer care,” Schapira said.

Curtis Chong, MD, PhD, MPhil, FACP, medical oncologist at Stanford Medicine, moderated the session, Best Practices in Screening and Testing in GI Oncology. Discussants included Geoffrey Buckle, MD, MPH, gastrointestinal (GI) oncologist at UCSF; Andrew Ko, MD, also a GI oncologist at UCSF; and Margaret Tempero, MD, medical oncologist and director, UCSF Pancreas Center.

Circulating tumor DNA (ctDNA), a relatively novel tool, holds value in various scenarios, Chong began, including therapy selection in the metastatic setting and chance of recurrence in the adjuvant and neoadjuvant settings. Tempero spoke about ctDNA use in the realm of multicancer early detection (MCED) testing, where evidence is still accumulating.

“There’s still much to be done to prove this is of any value, and it probably is going to require some other analytes besides ctDNA, if we’re really serious about early detection of cancer,” Tempero said. A major challenge with MCED, Chong said, is decision-making after ctDNA testing shows a positive result, but nothing is found in subsequent screening. Tempero said having the appropriate imaging instrumentation and multidisciplinary clinical staff to perform comprehensive diagnostic testing is helpful in fast-tracking patients to diagnosis, but this is uncommon in the community setting.

Chong asked the panel about their approaches to colorectal cancer screening tests, such as the FDA-approved Shield and Cologuard tests. Buckle noted these don’t hold value for surveillance in patients already diagnosed with colorectal cancer.

“Taking a step back from the problems that primary care providers and population health face, which are quite different, there’s definitely an implementation challenge of getting access to colonoscopies, getting people to do preps, and long wait times. I think that these tools can help serve an implementation gap, in essence, getting more people tested.” Although increasing testing rates via ctDNA screening tests could save lives, colonoscopy should be prioritized because it is both diagnostic and therapeutic, as polyps that pose a risk can be removed, Buckle said.

A crucial setting for ctDNA is in the detection of minimal residual disease (MRD), Ko explained, adding that data are more robust in colorectal cancer than some other cancer types in this setting. He noted that BESPOKE trial (NCT04264702) results presented at the 2025 American Society of Clinical Oncology Gastrointestinal Cancers Symposium suggested there was no benefit to adjuvant therapy among patients who tested negative for ctDNA,² but that the evidence is not compelling enough to not give adjuvant chemotherapy to patients with stage III disease. Buckle agreed, adding that data from the VEGA trial (NCT03662542), which is looking at both intensification and de-escalation of therapy,³ may help answer this question.

“I think it’s fair to say we’re not ready to deescalate therapy based upon very large randomized controlled trials of 12,000 patients that help inform current practice,” Buckle said, “but I think that we have observational data is sufficient to then allow for intensification.... If you have a stage II patient, we know that those patients fare worse if they’re positive vs stage III with negative ctDNA.” ♦

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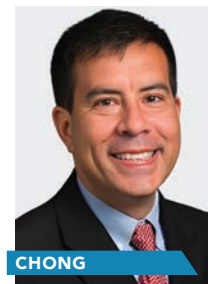
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Standardized Testing, Moves to Oral Therapy, and Cost Challenges Get Attention

PEARL STEINZOR



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IVBM TAMPA

PRECISION MEDICINE IS transforming the treatment landscape for hematologic and solid tumors. On March 6, 2025, experts highlighted breakthroughs in multiple myeloma, lung cancer, and chronic lymphocytic leukemia (CLL) at an Institute for Value-Based Medicine (IVBM) event in Tampa, Florida.

The evening opened with a panel discussion on best practices for testing in multiple myeloma. Featured experts included Melissa Alsina, MD, specialist in multiple myeloma and bone marrow transplantation at Moffitt Cancer Center; Gustavo A. Fonseca, MD, FACP, hematologist and oncologist at Florida Cancer Specialists and Research Institute; and Ariel F. Grajales-Cruz, MD, hematologist-oncologist at Moffitt Cancer Center.

The speakers discussed how multiple myeloma has progressed over the past decade, including the impact of CD38 monoclonal antibodies such as daratumumab (Darzalex; Janssen Biotech, Inc) and isatuximab (Sarclisa; Sanofi-Aventis US LLC) on treatment outcomes.

Additionally, the panelists touched on the use of CD38 antibodies in frail patients and the pros and cons of bispecific antibodies and chimeric antigen receptor (CAR) T-cell therapies, highlighting their potential to provide deep responses while also managing toxicities using minimal residual disease (MRD) testing.

“The toxicit[ies] [these therapies] present are toxicities that we as oncologists are all used to dealing with, like infections or immunosuppression, these types of things,” said Alsina. “These [bispecifics] are things that definitely can be given in the community, in contrast to CAR T. Still, you need a more specialized center, like a center that would do transplants, cellular therapies, and [so on].”

The second panel was on advancements in precision medicine in lung cancer and featured speakers Christopher Elder, PharmD, BCOP, associate director of pharmacy clinical services at Florida Cancer Specialists and Research Institute; J. Kevin Hicks, PharmD, PhD, FCCP, personalized medicine specialist at Moffitt Cancer Center; Maen Hussein, MD, medical oncologist and hematologist and at Florida Cancer Specialists and Research Institute; and Sonam Puri, MD, medical oncologist at Moffitt Cancer Center.

Topics of discussion involved advancements in personalized therapy for non-small cell lung cancer, including targeted therapies and immunotherapies. The panelists noted the importance of comprehensive molecular testing for all stages of lung cancer, including the impact of biomarkers such as *EGFR*, *ALK*, and *KRAS* on treatment decisions.

As for best practices for molecular testing in lung cancer, the speakers discussed the importance of integration, the need for heterogeneity, and standardized panels. Data management and the potential for artificial intelligence and machine learning are also factors that facilitate accurate and timely molecular testing.

“At Moffitt, we do have a cloud-based security platform to where all our NGS [next-generation sequencing] results are available,” explained Hicks. “They’re discrete, and then, sort of like a spoke and wheel model, you can have these different

data marks. We do have a precision medicine data mark that basically drives our clinical services, both from day to day with the consult notes plus with the molecular tumor boards. We use that to drive [decisions] as well,...so we can go in and build cohorts of patients.”

The third panel of the evening discussed the patient’s journey in CLL treatment, including personalizing therapy based on patient lifestyle choices, unmet needs, and financial toxicity associated with different CLL therapies.

Speakers included D. Alan Kerr II, MD, PhD, hematologist-oncologist and physician-scientist at Tampa General Hospital Cancer Institute; Jose Sandoval Sus, MD, FACP, hematologist and oncologist at Moffitt Cancer Center; Nikesh Shah, MD, hematologist and oncologist at Tampa General Hospital Cancer Institute; and Sarah Rockwell, PharmD, BCOP, clinical oncology pharmacist at Florida Cancer Specialists and Research Institute.

The panelists highlighted the shift from traditional chemotherapy to personalized oral therapies, with options increasingly based on patient factors such as age, fitness, and lifestyle. As for unmet needs in CLL, Richter transformation remains a significant challenge, with emerging treatments including new BCL-2 inhibitors, bispecific antibodies, and Bruton tyrosine kinase (BTK) degraders under investigation.

“I think the other thing to mention is this kind of new class of BTK degraders that are being studied on trial, and I think we’re seeing some promising early results there,” said Shah. “I’m curious to see, and I’m kind of excited to see, how those are going to play out because those may be BTK-mutation agnostic. They may still work for patients who have had prior BTK mutations.”

Regarding cost and value-based care, the panelists addressed financial toxicity and the impact of treatment-related visit burdens. They explained that fixed-duration therapies can reduce long-term costs, although upfront expenses may be higher.

The speakers also emphasized the importance of ongoing research to advance therapies, particularly for high-risk patients, to further improve outcomes in CLL.

“In terms of ongoing BTK inhibitors, I try to limit it to patients with very high risk,” said Sandoval Sus. “For example, with *TP53* mutations or deletion 17p, we should be doing a FISH [fluorescence in situ hybridization] every time... we diagnose the patient and the type of relapse, as well as an NGS panel.”

The final panel covered the role of pharmacy in decision-making in oncology, featuring Kristen Boykin, PharmD, RPh/CPh, BCOP, BCPS, director of pharmacy operations at Florida Cancer Specialists and Research Institute; Paul Chadwick, chief value and procurement officer at Florida Cancer Specialists and Research Institute; Ken Komorny, PharmD, BCPS, vice president and chief pharmacy officer at Moffitt Cancer Center; and Frank Scimeca, PharmD, MBA, BCOP, vice president of pharmacy services at Florida Cancer Specialists and Research Institute.

Panelists discussed the challenges and opportunities of CAR T-cell therapy and bispecific antibodies. Komorny highlighted Moffitt’s experience treating 1860 patients and reducing



Ken Komorny,
PharmD, BCPS

hospital stays from more than 30 days to 7. Boykin addressed the financial strain of therapies reimbursed only at cost, stressing the need for sustainable models.

“You have to have your financial teams involved [and] your operations teams involved, [and] everyone who touches that patient through their journey needs to be involved and...know what’s going on in order to make it successful,” said Boykin. “It’s just [become] so complicated, and everyone has...different pieces of expertise that they can bring to the table. I think that’s why a number of our more recent collaborations have been successful,...understanding that really, we need to have all the experts at the table, and not one person is expected to know everything.”

In discussing real-world evidence and patient care, the panelists emphasized the critical differences between controlled clinical trial environments and actual patient experiences. They discussed how medically integrated pharmacies can provide more comprehensive patient monitoring, connecting electronic medical records (EMRs) with direct patient interactions to track real-world treatment outcomes. Additionally, Komorny explained that medically integrated pharmacies significantly improved prescription filling speed and refill accuracy compared with out-of-state specialty pharmacies.



Kristen Boykin, PharmD,
RPh/CPh, BCOB, BCPS

“We’ve done some work a little bit in this space to look at some surrogate markers [in] time-to-fill percent of late refills,” explained Komorny. “We’ve demonstrated that if we’re filling the prescription, it’s 3 times as quick as if it’s going to an out-of-state big box specialty pharmacy. Late refills are twice as high if [the refill] goes to a big box specialty pharmacy vs if it’s filled by ours.”

Moreover, the panelists emphasized that real-world evidence goes beyond clinical trial data. It involves continuous patient monitoring, proactive adverse effect management, and adapting protocols based on patient experiences to improve treatment success and reduce health care costs.

“One of the amazing things about a medically integrated pharmacy is the ability to look at that information, connect with your EMR, and see the physician’s notes—not just what you’re seeing on your end as you fill the script, but also interacting with the patients, to have those phone calls with them, those touch points,” Boykin said. “[Adjusting] your protocols and changing your follow-ups with patients to make sure that if you keep patients on therapy, they’re going to be more successful [will] drive down the cost of care.”

It’s crucial, she said, to address these issues up front, “and not wait to have someone else tell you what the real-world evidence is [by] examining your own.” ♦

SPOTLIGHT

Cost-Effectiveness Strategies Are Vital for Streamlining Care in Hematologic Malignancies

Sabarish Ayyappan, MD | Interview by Kyle Munz



AYYAPPAN

SABARISH AYYAPPAN, MD, medical director of hematologic malignancies, City of Hope, Atlanta.

ONE OF THE PROMINENT GAPS in hematologic research, argues Sabarish Ayyappan, MD, City of Hope Cancer Center, Atlanta, is the lack of cost-effectiveness studies. Ayyappan recently took part in the Institute for Value-Based Medicine event in Atlanta, presented by *The American Journal of Managed Care (AJMC)*. Efforts to unveil cost-related outcomes and compile more data in this area can ultimately alleviate health system burden and elevate care for patients with hematologic malignancies, such as multiple myeloma and lymphoma, who receive chimeric antigen receptor (CAR) T-cell or bispecific antibody therapies.

This transcript has been lightly edited for clarity.

AJMC: What future innovations or policy changes do you believe could further streamline the implementation of bispecifics and CAR T-cell therapies?

AYYAPPAN: I think at this point it’ll be good to do more cost-effectiveness studies to see if a patient is being treated in the outpatient rather than being admitted for the step-up dosing or inpatient hospital stays—although sometimes the drugs are now offered for free by some of the companies. Hospital stays, the patients occupying beds to be monitored for cytokine release syndrome, and the fact that the patient is in the hospital also is not something that’s appealing to the patients. Those kinds of things could be looked at.

As we are learning more [about] how we could safely administer both CAR T-cell therapy and bispecific antibody therapies with adequate infrastructure support, you need a hospital with an emergency room [and] trained people at night who could [tend] to these patients if they have any sort of toxicity, like cytokine release syndrome or ICANS [immune effector cell-associated neurotoxicity syndrome]. Also, using some of these novel technologies, like remote monitoring devices where they could monitor their vitals, blood pressure, and other things, which can actually pass on the information very quickly to the treating physician or the team, so that they can act on these patients very well.

I could envision these patients mostly getting these therapies as outpatient, and that way you reduce the burden of them being admitted for either monitoring, for that cytokine release syndrome or for ICANS, and other things as inpatient, reducing the burden on the inpatient service that way. It kind of saves the hospital bed that could be used for other patients. And I think cost effectiveness and looking at all that would help the negotiation between the hospitals and payers to do this more frequently. ♦

COVERAGE BY MARY CAFFREY

ASCO GU

Powles Highlights “Transformative” Benefit of EV Plus Pembro While Sharing Long-Term Data for EV-302

COMBINING THE ANTIBODY-DRUG conjugate enfortumab vedotin (EV) with the immunotherapy pembrolizumab offers patients with advanced urothelial carcinoma (aUC) “transformative” benefits over chemotherapy, including a 74% likelihood of maintaining a confirmed complete response at 2 years,¹ the lead investigator of the phase 3 EV-302 trial (NCT04223856) told those gathered February 14, 2025, for the American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO GU) in San Francisco, California.

In a rapid oral abstract session, Thomas Powles, MD, PhD, professor of genitourinary oncology at Barts Cancer Centre in London, England, added new details to results announced ahead of ASCO GU. Long-term data on EV-302 released just before the symposium showed patients newly diagnosed with aUC cut their risk of death by 49% taking the combination compared with those taking chemotherapy, which had been the standard of care for these patients.²



POWLES

Powles shared an additional year’s worth of data for a median follow-up of 2.5 years, on top of results that had already brought a pair of accelerated approvals for the EV plus pembrolizumab combination in the first-line setting: the first came in April 2023 for patients not eligible for cisplatin³; the second came in December 2023, about 5 months ahead of the FDA’s deadline, for all newly diagnosed patients regardless of cisplatin eligibility.⁴ Enfortumab vedotin is marketed as Padcev (Astellas/Pfizer), and pembrolizumab is marketed as Keytruda (Merck).

The combination, Powles said, “has doubled median progression-free survival [PFS] and overall survival in frontline metastatic disease at high response rates, resulting in transformative care across the world.” Updated data at 29.1 months show the following¹:

- Fifty-four patients (12%) remain on treatment in the combination arm, and no patients remain on treatment in the chemotherapy arm.
- Overall, 218 patients (49%) in the combination arm and 131 patients in the chemotherapy arm (30%) remained in the study.
- Median PFS is 12.5 months in the combination arm (95% CI, 10.5-16.6) vs 6.3 (95% CI, 6.2-6.5), $P < .00001$.
- Median overall survival (OS) is 33.8 months in the combination arm (95% CI, 26.1-39.3) vs 15.9 months (13.6-18.3) in the chemotherapy arm.

He highlighted the OS curves, noting that “they go apart and stay apart,” remaining stable at the 2-year mark. Powles said he recalls that when he began working with patients with aUC, survival of 12 to 14 months was an achievement; with the EV and pembrolizumab regimen, OS is now nearly 34 months. “A big difference has been made,” he said.

Powles highlighted that 74.3% maintained a response at the 2-year mark. “But we also showed that 30% of patients had a complete response, which, again, was unprecedented in this setting,” he said.

The OS showed good overall results among subgroups; of note, 22.6% of the patients in the combination arm evaluated for OS were non-White, and these patients had better median OS (36.3 months) than the White patients (26.1 months). Patients from Europe and North America accounted for 62.2% of the population in the combination arm.

Powles reviewed adverse events (AEs) and described attention to AEs as “a core component of this work.” He said there were no new safety signals; 57% of patients in the combination arm experienced a grade 3 or higher event in the final year of follow-up, most of which were diarrhea or rash.

Given the durable responses and how long some patients are on therapy, Powles was asked: Is it time to examine the optimal time to remove patients

from treatment? He agreed this was the right question to ask but a tough one to answer. For many patients with aUC, the prognosis had been quite grim before the EV and pembrolizumab combination was available.

“The patients I see don’t want to come off therapy,” he said. “My gut feeling on this is 5 years is too long; I think we will agree on that. A year or 6 months is too short for me,” Powles said. “I think we do need to get together with people to start addressing the issue.” ♦

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SPOTLIGHT



Analysis Looks at Benefits, Toxicity of ADC Combinations in Advanced Bladder Cancer

Mary Caffrey



JAIME-CASAS

SALVADOR JAIME-CASAS, MD, is a postdoctoral research fellow, Department of Genitourinary Oncology, City of Hope, Los Angeles, California.

ANTIBODY-DRUG CONJUGATES (ADCs), used with and without immunotherapy, have been game-changers in treating advanced urothelial carcinoma (aUC), a bladder cancer that spreads to other parts of the body. Yet there have been tradeoffs: In some cases, patients see results but experience adverse events (AEs), including skin rashes.

To gain a better understanding of the data on ADC combinations in aUC, investigators led by Salvador Jaime-Casas, MD, a postdoctoral research fellow in the Department of Genitourinary Oncology at City of Hope, in Los Angeles, California, led a systematic review of 5 recent trials involving the use of sacituzumab govitecan (Trodelvy; Gilead Sciences, Inc) and enfortumab vedotin (Padcev; Astellas Pharma US, Inc/Seagen Inc) in combination regimens. Jaime-Casas presented the data in a poster¹ at

continued ▶

SPOTLIGHT

the American Society of Clinical Oncology Genitourinary (ASCO GU) Cancers Symposium, which took place February 13 to 15, 2025, in San Francisco, California.

The 2 ADC therapies have had different paths in the bladder cancer field. Sacituzumab govitecan (SG) received accelerated approval as a monotherapy in April 2021 for patients with previously treated aUC. However, Gilead voluntarily withdrew it from the market last fall after follow-up data failed to meet end points for overall survival (OS).² A recent report from the Department of Health and Human Services Office of the Inspector General highlighted the frequency of cancer therapies being pulled from the market, sometimes years after receiving an accelerated approval, when long-term data fail to meet end OS targets.³

Enfortumab vedotin (EV), meanwhile, received a regular approval for previously treated patients with locally advanced or metastatic UC in July 2021.⁴ Then, in December 2023, a combination with pembrolizumab (Keytruda; Merck) received accelerated approval to treat all newly diagnosed patients with aUC, based on results from the phase 3 EV-302 trial.⁵

Final OS data from the EV-302 trial, announced ahead of ASCO GU and presented on February 14, 2025,⁶ showed that the combination of EV and pembrolizumab reduced the risk of death by 49% compared with chemotherapy (see **Related Article**).

The trials in the review presented at ASCO GU included the phase 1 DAD trial (NCT04724018) that studied the dual ADC combination of sacituzumab govitecan (SG) and EV; the EV-302 trial (NCT04223856) combining EV and pembrolizumab; EV-301 (NCT03474107), cohort K, a phase 1b/2 study that also evaluated EV plus pembrolizumab; EV-103 (NCT03288545), cohort A, also phase 1b/2; and TROPHY U-01 (NCT03547973), the phase 2 study evaluating SG plus pembrolizumab.

Investigators identified 627 evaluable patients from these 5 trials; they recorded an objective response rate (ORR) of 66.2%, and 366 patients across all studies had AEs of grade 3 or higher, for a risk rate (RR) of 58.4%. The most common AE of at least grade 3 was neutropenia (RR, 0.14), followed by anemia (RR, 0.10) and maculopapular rash (RR, 0.10). Data presented in the poster showed a higher incidence of AEs of at least grade 3 in the SG-based regimens than in EV-based ones.

During ASCO GU, Jaime-Casas joined *The American Journal of Managed Care* (AJMC) for an interview about the findings and their meaning in the context of recent news surrounding ADCs.

This interview has been lightly edited for length and clarity.

AJMC: Your findings note that the AE incidence varied by regimen, with events being more common in SG-based regimens. Last fall, Gilead announced it was withdrawing an indication for SG in aUC based on overall survival data. Do the data in your study offer support for that decision?

JAIME-CASAS: The systematic review evaluated 5 prospective clinical trials using either...EV or SG as combination-based regimens. So for most of these trials, it was SG or EV in combination with immunotherapy. And although we did not analyze overall survival, recurrence-free survival, which was part of the reason why SG was pulled off the market, because the TROPiCS-04 trial [NCT04527991] failed to show this improved survival compared to chemotherapy, we also mirror these results by showing that there is a modest improvement in the objective response rate that comes at the cost of a high rate of adverse events, particularly grade 3 or above adverse events. And these were actually very similar if you look at the TROPiCS-04 [results]⁷ and our results; we also recorded that one of the highest adverse events for patients receiving sacituzumab govitecan was neutropenia. We record hematological adverse events such as neutropenia, anemia, and diarrhea.

So I would say, although our analyses are not the same because we do not assess in our paper the recurrence-free survival overall survival, they do reflect the same trend, and that is [that] even if there is some benefit to receiving this therapy, it is modest at best, and it comes at the cost of a high rate of adverse events.

AJMC: How should payers view these results? Are there steps that payers should support or encourage to mitigate AEs?

“Essentially, we know that patients who have a high chance of encountering things like hematological toxicity, neutropenia, or anemia may require more frequent blood evaluation. Some patients may even require transfusions of blood units or even...colony-stimulating factors. At least from the perspective of a [genitourinary] clinic, this is very multidisciplinary in nature. I think one of the associated costs that payers should focus on would be multidisciplinary teams that include medical oncologists, but [they should] also consider dermatologists and even pharmacists who are able to make modifications to the dosages if we encounter these toxicities.”

—Salvador Jaime-Casas, MD,
postdoctoral fellow, Department of Genitourinary Oncology,
City of Hope

JAIME-CASAS: Definitely. In the context of EV, it's a little bit [safer] to say that payers should invest more money, as we know that EV-[pembrolizumab] has been recently approved in the metastatic setting in patients who have previously been untreated. But I think, in particular for sacituzumab govitecan-based regimens and combination regimens, payers should be a little bit more cautious, not only because of the cost of medication but also because of the cost associated with care for these adverse events.

Essentially, we know that patients who have a high chance of encountering things like hematological toxicity, neutropenia, or anemia may require more frequent blood evaluation. Some patients may even require transfusions of blood units or even...colony-stimulating factors. At least from the perspective of a [genitourinary] clinic, this is very multidisciplinary in nature. I think one of the associated costs that payers should focus on would be multidisciplinary teams that include medical oncologists, but [they should] also consider dermatologists and even pharmacists who are able to make modifications to the dosages if we encounter these toxicities.

AJMC: Do we know how AE differences compare when ADCs were given in second- vs first-line treatment?

JAIME-CASAS: I would say right now we do not have very mature data to strictly say what...things we could expect for patients who receive an ADC first line. We can definitely expect a much better functional baseline status,

continued ▶

SPOTLIGHT

CONTINUED FROM PREVIOUS PAGE

and patients may be able to tolerate a little bit more toxicity before withholding or discontinuing the drug completely, in contrast with patients who may be receiving it as their second- or third-line treatment. So for instance, if we talk about EV-302 we know that in this case, the EV and [pembrolizumab combination], which is part of our poster in our systematic review, ... was given [to] patients who were treatment naive. So it was given [in the] first line, and patients were able to tolerate it more. But when we talk about, for instance, the TROPICS-04 patients, this was a heavily pretreated patient population. This frailty may also impact the results, as these patients already have some hematological malignancies, myelosuppression, or even peripheral neuropathy from previous platinum-based chemotherapy.

AJMC: During part of the period your data covers, we were experiencing a severe cisplatin shortage. AJMC was talking in real time with doctors who used ADCs instead of cisplatin to treat patients because sometimes nothing else was available, although the National Comprehensive Cancer Network (NCCN) guidelines indicate cisplatin for first-line treatment. Can physicians look at your data and gain comfort from those decisions, especially if someone confronts them someday about not having cisplatin available?

JAIME-CASAS: In our data, what we did find is there is a promising objective response rate seen overall for these 5 included studies. Three of the studies that we included, EV-302, and EV-103 cohort A and cohort K were given [an ADC] in the context of EV plus immunotherapy. And you know, for EV-103, for that study, ... one of the inclusion criteria was patients who were cisplatin ineligible already. So I think the comfort here is that at least in the context of EV therapy, we could say that it was good at that moment before it was approved; it was a good alternative when you were encountering a patient with advanced urothelial carcinoma, and you had this context of a cisplatin shortage. Giving EV in this disease setting was not a bad option because we do see that there is a tolerable adverse event profile and optimal response. And in the end, we now know that EV and pembrolizumab [were] approved in the metastatic setting first line, while the same could not be said for sacituzumab govitecan.

To sum up, we do believe that data for [sacituzumab govitecan are] still necessary, as we see that it may not be superior in terms of survival according to TROPICS-04 trial [data] when compared [with] chemotherapy.

AJMC: If there's a key data point from your presentation that you'd like to highlight for our readers, what would that be?

JAIME-CASAS: We found only 1 clinical trial that was evaluating 2 antibody-drug conjugates in combination. There was a single phase 1 clinical trial evaluating EV and sacituzumab govitecan. This is a very small phase 1 clinical trial, but I think it shows promise in the sense that antibody-drug conjugates, by having different structures, by having different payloads, and even by having different linkers and then a nonoverlapping adverse event profile, ... show promise for the future where new antibody-drug conjugates will come into the market. And clinical trials could potentially be designed around combining these either with immunotherapy or another antibody-drug conjugate. ♦

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TALAPRO-2 Overall Survival Data Suggest New Standard of Care in mCRPC, Regardless of Genomic Status

A THERAPEUTIC COMBINATION previously approved for men with genetic-mutated advanced prostate cancer could become standard of care for all patients with this disease, regardless of their genomic status, based on data presented February 13, 2025, at the American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO GU) in San Francisco, California.¹

Final data from TALAPRO-2 (NCT03395197), a phase 3 trial of talazoparib (Talzenna; Pfizer) and enzalutamide (Xtandi; Astellas/Pfizer) in men with metastatic castration-resistant prostate cancer (mCRPC), showed that the combination reduced the risk of death by 20.4% in patients whether or not they had homologous recombination repair (HRR) gene alterations.

Data from this larger group of patients in the study, called the unselected cohort because they were enrolled regardless of their genomic status, were

presented at the opening session by global lead investigator Neeraj Agarwal, MD, FASCO, of Huntsman Cancer Institute, University of Utah, Salt Lake City. Agarwal said the trial offered the first meaningful survival benefit from 2 key drug classes in prostate cancer—a PARP inhibitor and an androgen receptor pathway inhibitor (ARPI).

HRR deficiency affects 20% to 30% of men with mCRPC.² During the past decade, its presence has indicated the potential use of PARP inhibitors, of which talazoparib is a newer-generation example. Enzalutamide, meanwhile, is an ARPI that interrupts the AR signaling process at several points.

“In the real world, overall survival [OS] for patients with metastatic castration-resistant prostate cancer, or mCRPC, is less than 3 years, and nearly half of these patients receive only 1 systemic therapy,” Agarwal said. He showed a diagram that demonstrated how simultaneously inhibiting PARP and ARPI may work together to have an effect greater than the sum of these mechanisms working separately, “and may extend to those patients with mCRPC who do not have HRR alterations.”

Discussant Tanya B. Dorff, MD, of City of Hope Comprehensive Cancer Center, Duarte, California, noted that some colleagues in the field had questioned this synergy, but she points to an mCRPC study



AGARWAL



DORFF

by Maha Hussain, MD, the phase 2 BRCAway trial (NCT03012321), which found that the combination of abiraterone and olaparib worked better in combination and was better tolerated than the therapies in sequence.³

“Obviously, more data are needed, but this really does suggest there is synergy. Importantly, we don’t see synergy in terms of toxicity. We did not see any safety signals when combining these classes of drugs, compared with using them alone,” Dorff said.

In an interview with *The American Journal of Managed Care*, Dorff elaborated on how talazoparib and enzalutamide effectively interact against cancer without increased toxicity. Often, she said, “When we put 2 drugs together, we get more than the typical toxicity that you see with one drug or the other. But in this case, the [adverse] effect [AE] profile was essentially exactly the same, at least in TALAPRO-2,” compared with using talazoparib alone or enzalutamide alone. This is good news, given the length of time patients must take the combination, Dorff said. Dose reductions may occur due to anemia, but these occur with or without a combination regimen, she said.

Two Cohorts in Study

Agarwal presented data from cohort 1, the unselected group, which randomly assigned 805 patients who enrolled in the trial regardless of genomic status. After 52.5 months of follow-up, the median OS was 45.8 months for the patients receiving the combination and 37.0 months for those receiving enzalutamide plus placebo. The HR for patients receiving the combination compared with those receiving enzalutamide only was 0.796 (95% CI, 0.661-0.958; 2-sided $P = .0155$).¹

Agarwal noted that the benefits of the combination were seen across subgroups and in an exploratory analysis. There were no new safety signals, and treatment-emergent AEs were generally manageable. A total of 86 patients stopped taking talazoparib due to AEs.

Cohort 2 involved 399 patients whose tumors had known HRR alterations. These results were presented in a separate late-breaking poster by Karim Fizazi, MD, PhD, a professor at Institut Gustave Roussy, University of Paris-Saclay, in Villejuif, France.⁴ After 44.2 months, the median OS for this cohort was 45.1 months in the combination group vs 31.1 months in the enzalutamide-only group (HR, 0.62; 95% CI, 0.48-0.81; $P = .0005$), for a 38% reduction in the risk of death. An exploratory analysis showed that OS benefits were seen in patients with *BRCA* alterations and other alterations.

“Wisely, the investigators chose not to ignore genomics, and the patients with homologous recombination repair alteration are clearly going to derive benefit in a different way than patients without an alteration,” Dorff explained during the session.

For the TALAPRO-2 combination, it has been a matter of waiting for the data. In June 2023, the combination of talazoparib and enzalutamide received FDA approval based on radiographic progression-free survival data for patients with HRR deficiencies.⁵ OS data were not mature. In October 2024, Pfizer announced the OS data for TALAPRO-2 were positive.⁶ In a statement, Roger Dansey, MD, Pfizer’s chief oncology officer, said the company looked forward to working with regulatory officials on label updates to reflect these new data.⁷

“Survival rates in metastatic castration-resistant prostate cancer are poor due to the advanced and aggressive stage of the disease. Today’s results demonstrate the potential for [this combination] to be a practice-changing treatment to help improve patient survival in mCRPC,” Agarwal said in a statement from Pfizer.⁷ ♦

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Pursuit of ADCs in Bladder Cancer Brings Questions About Toxicity, Cost

THERE IS NO QUESTION that antibody-drug conjugates (ADCs) have revolutionized the treatment of patients with bladder cancer, and hope abounds with increased survival times and more drugs and combinations in the pipeline.

The promise of ADCs—delivering the cytotoxic payload directly to the tumor—remains a work in progress, as scientists work to limit off-target effects. As with many therapies, ADCs were first given when other treatments had failed, but now it seems they offer the best hope early on by sparing healthy tissue for the long battle ahead.

Yet the enthusiasm for these cancer “smart bombs” is tempered with many challenges: how to manage toxicity, how to understand sequencing, and how to ensure access when the cost of some combinations is projected to exceed \$400,000 a year.

Speakers addressed these issues at the February 14, 2025, session, The ABCs of ADCs: Unleashing the Power of Antibody-Drug Conjugates in Advanced Bladder Cancer, during the American Society of Clinical Oncology Genitourinary Cancers Symposium, held in San Francisco, California.

NOT ALL ALIKE. Although they have common elements, such as the antibody that binds to the tumor antigen, the linker, and cancer-killing payload, ADCs can vary greatly, said Di “Maria” Jiang, MD, MSc, FRCPC, of Princess Margaret Cancer Center at the University of Toronto. She offered examples of how well-known ADCs use different biomarkers—or none—different antibodies, and different linkers and how varying mechanisms of action affect outcomes.

“Many ADCs exhibit bystander effects,” said Jiang, in which the payload kills tumor cells regardless of their target expression. “ADCs also engage with the immune system and promote immunogenic cell death via the antibody and also the payload activity.”

TARGETING HER2. Funda Meric-Bernstam, MD, FASCO, of The University of Texas MD Anderson Cancer Center, explained how ADCs that target HER2 have opened a new frontier in treating bladder cancer. She explained that next-generation sequencing (NGS) is not a substitute for immunohistochemistry (IHC) testing to find patients who may have HER2 amplification that does not appear on NGS.

She shared data for trastuzumab deruxtecan (Enhertu; Daiichi Sankyo, Inc), well known for its efficacy in certain patients with breast cancer, and highlighted subsets of patients with colorectal cancer within the application for the tumor-agnostic approval granted to this ADC for patients with HER2 IHC 3+ tumors.¹ Like Jiang, Meric-Bernstam suggested that first-line treatment may be the opportunity to use ADCs.

Meric-Bernstam expects new drugs with different payloads and more activity with bispecifics, as there are other mutations in bladder cancer and opportunities with small molecules. Combinations will continue to be important, she said.

“There’s a lot of acceptance from [immuno-oncology] combinations, potentially for ADC combinations, potentially combining targeted therapies with other ADCs, as well as other novel combinations to enhance the activity,” Meric-Bernstam said. “Sequence of therapy is going to be a very interesting area to watch.”



JIANG



MERIC-BERNSTAM

MANAGING TOXICITY. Daniel Castellano, MD, of Hospital Universitario 12 de Octubre in Madrid, explained how the complex, 3-part mechanism of ADCs contributes to the toxicity challenges, which are generally divided into off-target and on-target effects. Despite their design to reduce the footprint of the cytotoxic payload, most end up with toxicity levels that are nearly the same, he said; notably, 55% of patients can develop skin reactions.



CASTELLANO

Biomarker development will help, allowing clinicians to identify patients who will gain the most from treatment with an ADC. Dose de-escalation strategies and pinpointing who will benefit will also be important.

COMBINATIONS ABOUND. Terry Friedlander, MD, of UCSF Helen Diller Family Comprehensive Cancer Center, reviewed what's ahead in combinations with ADCs, starting with why they are needed. Data show that only 48% of newly diagnosed patients get to first-line systemic therapy, only 17% reach second-line therapy, and only 6% get to third-line therapy.



FRIEDLANDER

"We should be giving our best therapies first," Friedlander said. As others have argued, ADCs offer the chance to give patients with bladder cancer a powerful, targeted attack against the tumor. Striving for synergistic combinations can promote the ADC bystander effect, limit overlapping toxicity, and help overcome ADC resistance.

The approach requires balance, however. There is the risk of increased adverse effects (AEs) and financial toxicity. Friedlander shared a sobering chart about the cost of ADC combinations: Those he highlighted ranged from \$120,494 to \$438,660 annually.

Still, he highlighted some trials worth watching. One is examining erdafitinib (Balversa; Janssen Products, LP) plus enfortumab vedotin (Padcev; Astellas Pharma US, Inc) in metastatic urothelial cancer with *FGFR 2/3* alterations, which has presented promising phase 1b data. Another study is investigating enfortumab vedotin plus cabozantinib (Cabometyx; Exelixis, Inc) in phase 1/2 studies in several cancers, including bladder cancer.

PHASE 1 RESULTS. The session concluded with the presentation of data from a phase 1 study of SHR-A2102, a novel ADC that targets nectin-4, a cleavable linker, and a payload with high membrane permeability. Preliminary findings in urothelial cancer to assess safety and tolerability confirmed an objective response rate of 38.4% in all patients, with 32.3% in the 6 mg/kg group and 50.0% in the 8 mg/kg group. The 6-month duration of response was 59.3% in all patients, with 66.7% and 54.0% in the 6 and 8 mg/kg doses, respectively. Grade 3 or higher treatment-related AEs were seen in 43.8% of patients, the most common being anemia, decreased white blood cell count, and decreased neutrophil count. Investigators concluded that the study drug showed promising antitumor activity in advanced urothelial cancer, even after prior ADC therapy.² ♦

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Getting More Doctors to Record a Life-Saving Prostate Cancer Calculation

WHAT IF YOUR ABILITY to receive the proper treatment for prostate cancer came down to whether a doctor wrote down a math problem?

It sounds far-fetched, but it's not: The math calculation in question is called prostate-specific antigen doubling time (PSADT), the number of months it takes for the patient's PSA level to double.

This measure of how quickly PSA is increasing is used to monitor cancer recurrence, and it is considered one of the best predictors of outcomes

for patients who have been treated for prostate cancer. Physicians use the PSADT metric to gauge a patient's risk level and to decide if they need to start salvage androgen deprivation therapy (ADT).

So what is the issue? According to Alicia Morgans, MD, MPH, genitourinary medical oncologist and director of the Survivorship Program at Dana-Farber Cancer Institute, the PSADT metric is well-known to physicians, but many may be estimating it instead of fully calculating it—or they may be calculating the PSADT but not recording it in their notes.



MORGANS

"It takes time," Morgans said in an interview with *The American Journal of Managed Care*. "You have to pull up the calculator, then you type in the numbers, then you type in the PSA and the date. And you have to do this several times so you can look at a period of time to calculate that doubling time. So it does take effort."

According to data that Morgans presented recently at the American Society of Clinical Oncology Genitourinary Cancers Symposium in San Francisco, all this leads to incomplete or inconsistent recording of PSADT data, which can mean some patients are not receiving the proper care.

Methods

Morgans' study involved a chart review of patients who recorded a high risk (HR) of biochemical recurrence (BCR) from the Cardinal Health Oncology Provider Extended Network from 2018 to 2020 in the United States.¹ The HR BCR definition was at least 9 months with a PSA at or above the threshold of the EMBARK trial, which had evaluated enzalutamide (NCT02319837).² Follow-up was from the date the HR BCR was met until disease progression, the last follow-up, or death through 2022.

Physicians were asked to report PSADT in case reports, using doubling time from labs, clinical judgment, or an online calculator. If none of these were available, PSADT was calculated retrospectively based on values entered into the case reports; these were listed in the study as unknown PSADT. The study also looked at time to treatment.

Results

Among 284 patients with HR BCR, the median time from prostate cancer diagnosis to the end of follow-up was 39.1 months. Most patients had known PSADT. Other data were as follows:

- A higher share of patients with unknown PSADT had PSADT that rapidly doubled (61% vs 20%; $P < .001$)
- A higher share of patients with known PSADT (64%) compared with unknown PSADT (17%) received treatment within 60 days after the index date, with a shorter median time to treatment (1.0 vs 6.7 months; HR, 3.4; 95% CI, 2.6-4.4; $P < .0001$).
- Patients with known PSADT were more likely to be older, have slower doubling time, and receive treatment than patients with unknown PSADT. The authors of the abstract wrote that this could mean treatment opportunities are being missed in clinical practice, and some patients are not getting treatment that could delay disease progression.

Explaining the Results

Morgans suspects that many doctors are looking at the numbers and dates and estimating the approximate doubling time, "which is probably overestimating the doubling time as we suggest in the paper.... They're doing some form of [PSADT], but they're not doing it in a structured, standardized way."

Could software in the electronic health record be modified to perform the PSADT calculation for the doctors? "That would be fantastic," Morgans said. "That would be very, very helpful because if there is a standardized approach to [the] calculation that gets you the true number, then that would be used in the regulatory approval of the drugs that we use for those high-risk patients with the shorter doubling time."

Another possibility is to add a quality measure based on whether doctors record PSADT, but that also raises issues of administrative burden.

Morgans noted that the study data also revealed that if doctors overestimate the doubling time, they, in turn, also underestimate how aggressive the cancer is; thus, they underestimate the risk of metastasis in that individual patient.

If a patient's calculation is off and not listed as—when in fact the cancer is aggressive—that could mean the patient may not be approved for the treatment needed.

“True,” Morgans said. “It may also lead to [the physician] not treating the patient when it's absolutely appropriate, and they're not taking that opportunity to prevent metastasis, which is associated with all kinds of other complications—pain, bleeds, other therapies.”

She added, “It can also be quite expensive for other interventions.”

Performing the calculation correctly doesn't cost or inconvenience the patient—it is strictly a matter of getting doctors to perform PSADT correctly and record it consistently. Morgans said that because the study was relatively small, the group doesn't have information on which doctors are most likely to carry out PSADT correctly and consistently.

“I can't say, except...that I think every doctor is actually at risk for not calculating it because of the time issues, because of the pressures that they have,” Morgans said. ♦

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Can a New Therapeutic Combo Address a Rare Form of RCC?

INVESTIGATORS FROM Shanghai, China, may have found a new treatment combination for a rare form of renal cell carcinoma, one that is largely inherited, progresses quickly, and primarily affects young adult patients.

In the closing hours of the 2025 American Society of Clinical Oncology Genitourinary Cancers Symposium, Wen Kong, MD, assistant professor in the Department of Urology at Renji Hospital, Shanghai Jiao Ton University School of Medicine in China, offered preliminary data from a phase 2 study of 17 patients with advanced or metastatic fumarate hydratase-deficient renal cell carcinoma (FH-RCC), an aggressive subtype of the disease with a poor prognosis.



KONG

Results for 15 patients who could be assessed at data cutoff showed that combining lenvatinib (Lenvima; Eisai Inc) plus tislelizumab (Tevimbra; BeiGene USA, Inc) produced an objective response rate (ORR) of 93.3%, with a complete response (CR) rate of 20.0% (3/15).¹

PRELIMINARY RESULTS. The median time to response was 6 weeks, with 1 progression-free survival (PFS) and 1 overall survival (OS) event; neither PFS nor OS were reached. All-grade adverse events (AEs) were seen in 16 patients

SPOTLIGHT



PROs Similar With Tivozanib Monotherapy and Combination in RCC

Produced by Rose McNulty



BECKERMANN

KATY BECKERMANN, MD, PHD, assistant professor, Vanderbilt University Medical Center; medical director of genitourinary clinical research, Tennessee Oncology.

PATIENT-REPORTED OUTCOMES (PROS) were similar among patients treated with tivozanib monotherapy and those who received combination tivozanib and nivolumab for renal cell carcinoma (RCC) in the TiNivo-2 study (NCT04987203). The data were presented at the American Society of Clinical Oncology Genitourinary Cancers Symposium, held February 13 to 15, 2025, in San Francisco, California.¹

Study author Katy Beckermann, MD, PhD, assistant professor of medicine at Vanderbilt University Medical Center and medical director of genitourinary clinical research at Tennessee Oncology, explained how PROs were measured in the study and the findings to *The American Journal of Managed Care* (AJMC).

This transcript has been lightly edited.

AJMC: How was the patient-reported quality-of-life evaluation here, and what were the completion and adherence rates?

BECKERMANN: I think it's a really important question that we should

obviously take into account. How [is] patients' quality of life in the refractory space if we're essentially dose intensifying or if we're adding treatment regimens? Is that going to add any toxicity, and does that affect quality of life?... This was an exploratory end point in the clinical trial using 2 different metrics: the EORTC [European Organisation for Research and Treatment of Cancer] questionnaire and the FKSI [Functional Assessment of Cancer Therapy–Kidney Symptom Index] questionnaire. You'll see across the treatment arms it was taken at baseline and at day 1 of every single cycle, and the completion rate was equivalent among the arms.... So we then tried to assess what the quality-of-life metrics were. And tivozanib kept these QOL [quality of life] measures even from the beginning to the end of [the] study,... based on FKSI and [data from] the EORTC studies.

AJMC: Adding nivolumab to tivozanib provided no additional benefit vs tivozanib alone. However, what benefits might justify using a monotherapy vs a combination therapy for patient satisfaction and quality of life?

BECKERMANN: Well I think from this clinical trial, because it was a negative clinical trial, we would [never] recommend the combination treatment based on efficacy. And then...based on [data from] TiNivo-2 [and] TIVO-3 [NCT02627963], tivozanib is certainly an FDA-approved, NCCN [National Comprehensive Cancer Network]–recommended option in the treatment [of] patients with refractory kidney cancer. ♦

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(94.1%), and grade 3 or higher events were seen in 4 patients (23.5%). Eight patients had to have dose reductions or stop treatment (47.1%). One patient died due to unrelated lung metastases.

What Is FH-RCC?

Driven mostly by germline mutations, FH-RCC tends to affect adults in their mid-30s or early 40s. It is hard to diagnose, as its symptoms may be mistaken for normal abdominal pain. It metastasizes early, even when tumors are small. Genetic testing is encouraged when families are known to carry the FH mutation, which brings an estimated 15% lifetime risk of developing RCC.

According to Linder et al, FH-RCC occurs when the loss-of-function mutation in the FH gene leads to the accumulation of fumarate, which in turn activates hypoxia-inducible factor (HIF). Then HIF triggers tumor growth through several mechanisms involving both VEGF and EGFR; thus, therapeutic targets can include an anti-EGFR blockade.

Why Look for Something New?

As Kong explained, a combination appearing in the National Comprehensive Cancer Network guidelines featured bevacizumab (Avastin; Genentech), an anti-VEGF monoclonal antibody, and erlotinib (Tarceva; Genentech), an anti-EGFR tyrosine kinase inhibitor (TKI).

But the study whose data led to that recommendation is more than 10 years old, Kong said, “and the landscape for RCC treatment has dramatically changed.”

The addition of checkpoint inhibitors and newer-generation TKIs warranted a second look, and Kong’s center did just that in a 2023 retrospective study of how patients with FH-RCC fared when treated with different combinations in centers across China.

In that paper, of which Kong was the second coauthor, the authors revealed better survival rates when combining a TKI with an immune checkpoint inhibitor.²

The PD-1 inhibitor tislelizumab is known to be effective with chemotherapy for patients with *EGFR*-mutated nonsquamous non-small cell lung cancer who have progressed on EGFR TKI therapy.³

Lenvatinib, meanwhile, is a TKI that works on multiple targets to block new blood vessel formation, thereby limiting blood supply to the tumor; among its targets are VEGF receptors (VEGFR1-3).

Background and Methods

Eligible patients were 18 to 80 years old and diagnosed with pathologically confirmed, unresectable advanced or metastatic FH-RCC and had not received systemic therapy. The diagnosis was confirmed with DNA sequencing. Patients received concurrent therapy, with lenvatinib 20 mg administered by mouth daily and tislelizumab 200 mg intravenously every 3 weeks until disease progression, intolerable toxicity, or withdrawal of consent.

The primary end point is ORR; secondary end points are disease control rate, PFS, duration of response, 1-year and 2-year OS rate, and safety.

Patients enrolled in the trial from September 2023 to October 2024; 14 were male, and 3 were female. The median age was 37 years (range, 24-61). FH germline alterations were found in 12 patients, with 5 carrying somatic mutations. The median follow-up was 7.0 months (range, 1.0-12.0).

Kong shared before-and-after photos showing tumor shrinkage. He acknowledged that the data are immature, and many questions remain, but concluded, “This combination might become a promising alternative option” for patients with FH-RCC. ♦

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ACCC 2025

The Weapons for Getting Paid: Bringing Data, Technology, and Advocacy to the Battle

IN RECENT YEARS, advances in clinical oncology have been offset by administrative burdens: more requirements from Medicare, more quality improvement tasks from payers, and especially more proof that a patient needs a drug or test before reimbursement happens.

Speakers at the March 6, 2025, Association of Cancer Care Centers (ACCC) 51st Annual Meeting and Cancer Center Business Summit session “Payer-Driven Challenges and Solutions” reviewed strategies to deal with common complaints such as prior authorization and contract shortchange. Increasingly, oncologists and cancer center leaders are heading to their state legislatures for relief. Susanne Tameris, MHA, senior director of cancer services at Luminis Health, Anne Arundel Medical Center, DeCesaris Cancer Institute, served as event moderator.

Bringing Data to the Payer Contract Battle

Providers must know every detail of payer contracts and come to contract talks armed with data to back up their arguments, said Matt Mulherin, chief growth officer for AC3 Health.

“You have lots of data,” Mulherin said. “It’s how you pull it together. How do you harness that power and leverage it?”

Gaining insights into Medicare data is relatively easy; for other payers’ data, it is challenging. Drug costs change for every payer every quarter, and timelines for when they change are variable. “If I want to be cynical, it’s complicated by design,” Mulherin said. Constant change makes it harder for providers to keep track of what they should be paid, he explained, making it hard for them to hold payers accountable.



MULHERIN

“Maybe nobody’s paying you as fast as you want, but it’s important to understand how one payer is doing compared [with] the rest of your payers and being able to see them side by side. It helps you to understand who’s good, who’s bad. Also, it does matter. We might not think that it does, but it...matters to a payer.”

—Matt Mulherin,
chief growth officer,
AC3 Health

However, providers must do the legwork necessary to hold payers to the terms of a contract. “You have to understand it, and it takes some time and some energy and some resources to do that, but you can’t hold someone accountable [for] paying you correctly—which is an important piece of the accountability puzzle—if you don’t know what you’re supposed to be getting paid.”

Mulherin offered several key pieces of advice for revenue cycle managers:

- Use payer scorecards and key performance indicators (KPIs) to identify “problem payers,” and use these tools to negotiate better reimbursement rates based on underpayment or slow payment.
- Understand which payers put more clinical burden on the staff.
- Use artificial intelligence (AI), or “payer contract intelligence” to accelerate the identification of errors and the development of performance metrics.
- Use benchmarking when setting fee schedules to improve financial performance.

- Make sure you are paid and that you are paid correctly.
- Ensure that data are accessible to the leadership, payer contracting, and revenue cycle teams and that everyone knows how to use it.

Aligning the billing and practice management systems is essential, Mulherin said. Otherwise, it is hard to know if what you are paid reflects the performance specifications in the contract. “There might be certain metrics that they have to adhere to or that you have to adhere to,” he said, and revenue cycle managers must know and track KPIs that center on denials and time to pay.

What about value-based care? “I think there [are] lots of opportunities for us to innovate with payers,” Mulherin said. “But one thing that often gets overlooked is we’re not really following well on a fee-for-service model.” A value-based contract for some things may be acceptable, but that doesn’t mean the provider shouldn’t be paid on the portions of the contract that are still fee-for-service.

He encouraged those in attendance to keep track of who the good actors are. “Maybe nobody’s paying you as fast as you want, but it’s important to understand how one payer is doing compared [with] the rest of your payers and [be] able to see them side by side. It helps you to understand who’s good, who’s bad. Also, it does matter. We might not think that it does, but it... matters to a payer.”

It is one thing to tell a payer they are one of the worst in terms of time to pay, but it is another to have data showing their denial rate is 1.5 times higher than most payers, Mulherin said. “They don’t have that data, and it’s going to put them on the defensive, or at least it’s going to establish that you have some credibility and some power in the relationship.”

Advocacy Makes a Difference in PBM Reform

When patients arrive at the Texas Oncology clinic in Paris, Texas, Sucharu “Chris” Prakash, MD, who has been medical director for almost 25 years, is determined they receive treatment that day.

Many have traveled long distances. “They are undergoing hardships; there are socioeconomic disparities,” said Prakash, who has served as Texas Oncology’s director of quality services since 2022.

Having to jump through hoops with a pharmacy benefit manager (PBM), or what Prakash calls a middleman, doesn’t help. The Big 3—Express Scripts, Caremark, and Optum—control 80% of the market and not only negotiate prices but also dictate who gets to fill the prescription. So much so that pharmacies that served places like Paris, Texas, have closed all over rural America.

Bipartisan frustration with these practices and others has kept alive a Federal Trade Commission (FTC) lawsuit against the 3 largest PBMs, despite the change in administration and the departure of former FTC Chair Lina Khan, JD. Republicans on the House Oversight Committee have been equally aggressive in calling for reforms. PBM reform is a top agenda item for ACCC and the Community Oncology Alliance (COA), which included the item in the recent COA Prescription for Health Care Reform document.

“The power of the top 3 PBMs—they hold all the cards,” Prakash said.

He described the cascade of issues that harm patients: PBMs restrict formularies, making it harder for patients to get certain cancer drugs. They charge patients too much for drugs, causing high out-of-pocket costs. They steer patients to affiliated pharmacies, even if these are mail-order outfits that cannot offer same-day service. Independent pharmacies are vanishing, crushed by high direct and indirect remuneration fees or “clawbacks” the PBMs charge after a drug is dispensed. And until some states passed transparency laws, no one was sure where drug manufacturer rebates were ending up.

“What [would] utopia look like if you were to solve all the problems [and] lower prescription drug costs for the patient so the prescriptions cost less?” Prakash asked.

He outlined his prescription for reform:

- Increase transparency, including disclosing the use of manufacturer rebates;
- Limit out-of-pocket costs; this would mean banning co-pay accumulators, which prevent co-pay assistance from counting toward out-of-pocket costs; and
- End spread pricing, in which the PBM charges payers, including Medicaid, more than they pay the pharmacy for a medication, with the PBM keeping the “spread.”



PRAKASH

Then Prakash offered a rundown of how advocacy efforts in Texas had curtailed many PBM practices.

- In 2017, Senate Bill (SB) 680 limited insurers’ use of step therapy, requiring protocols based on clinical evidence, not cost, and giving patients a faster appeals process. SB 1076 also passed that year, barring health plans from overcharging for drugs at the point of sale.
- In 2021, which Prakash called a landmark year, oncologists focused on business practices. Governor Greg Abbott signed 2 more measures: House Bill (HB) 1919, which bars PBMs from steering patients to affiliated pharmacies, and HB 1763, which ensures patient access to prescription drugs.
- Most recently, HB 1647, which took effect on September 1, 2023, bars certain health plans from white bagging, in which patients with cancer or other complex conditions are forced to have drugs shipped to their physician from a central pharmacy for administration. Physicians said the practice leads to treatment delays and waste because if bloodwork in the clinic shows the need for a change in dose, the shipped medication cannot be used.

Prakash elaborated on the importance of HB 1763, which he said bars PBMs from limiting pharmacies’ ability to deliver drugs to patients who live far away. If patients have the prescription, “they don’t have them drive over and have the prescription in their hand, but you can...deliver it through the mail.”

He also highlighted the importance of eliminating step therapy. “Don’t tell me to treat the patient with ibrutinib first if I want to do acalabrutinib” for certain blood cancers, he said. “The provider should be able to make that decision.”

The problem, Prakash said, is that Texas reforms do not apply to Employee Retirement Income Security Act (ERISA) plans. In the future, this could change. He highlighted a key case in Arkansas “that was a precedent-setting case where...the Supreme Court said that the policy should lie in the hands of the state, that if there’s any PBM regulation passed that’s in Texas, it should override ERISA plans or include ERISA plans.”

How a Centralized Prior Authorization Team Made a Difference

Orlando Health Cancer Institute (OHCI) created a centralized prior authorization team to boost the use of prospective prior authorizations (PAs), in which the use of AI tools and pharmacist involvement on the front end of the process decreased patient wait times for medications to an average of less than 48 hours, according to Andrea Ledford, PharmD, MBA, BCOP, BCSCP, FASHP, FHOPA, senior pharmacy director of oncology services at OHCI.

Ledford started her talk by outlining PAs’ purported goals: optimizing patient outcomes and reducing errors, waste, and unnecessary drug costs. She cited several articles from *JAMA* and the ACCC’s journal that indicate oncologists say the opposite is true.

“What we’ve really found is it’s actually a barrier to timely, quality health care. I think we would all agree...that the average length of time for a PA is about 2 to 5 days,” she said. At her own clinic, it was easy to walk through the clinic and see nurses on headsets doing PAs nonstop. Patients, physicians, and administrative staff are all frustrated.

What PA does, she said, is create an “increased administrative burden in our clinics and an increase in patient anxiety as they’re waiting for their life-saving medications.”

Through a pilot project, OHCI decided to put the oncology pharmacy team in the mix on the front end. The pilot occurred just as Florida made a policy change requiring additional PAs, and Ledford distinguished between retrospective and prospective PAs. The process is handled through an automated form built into the electronic medical record (EMR) platform, and the oncology pharmacist fills out answers to a host of required questions on the PA within 24 hours. Then the prescription is released to the pharmacy with the oncology pharmacist’s answers attached.

The shift required EMR training. “We used pharmacy technicians; we taught them where to look for the information in the EMR. We had to grant them more access so they could see the ICD 10 codes and the CPT codes and just where the physicians were documenting the ...relevant information that we needed to support the claim.”



LEDFORD

The change also required a structured process to create an online chat to eliminate calls and resolve questions and keep all communication within the EMR. “What [we] found is we were able to leverage that EMR,” Ledford said. “We really spent time working on the workflow.”

At first, some nurses did not want to let go of the PA process. But later on, some PBMs required the pharmacy team to use their platforms, which Ledford said would have created issues for the nurses alongside their other work. After a year, the process is being handled by 2 pharmacy full-time equivalent staff. The redeployment has vastly improved efficiency and patient experience, Ledford said.

“We looked at only the retrospective [PAs] because we weren’t using any of the prospective before we started. We had lots of faxes and papers all over the clinics. Nursing was on the phone. We had delays both for patients in the clinics and patients waiting for authorization,” she said. “You couldn’t room patients because people were stuck on the phone, and then patients were waiting in the rooms longer because people were on the phone.”

Initially, the pharmacy team handled 28 clinics, but now they handle 36. “We’ve done [a lot] to make it more attractive to the pharmacy techs. I have not had anybody turn over on the pharmacy tech team now in about 18 months, and what we do is we let them work remotely from home, so it’s a good job for them.”

“The physicians, the clinic staff, they just loved it. You do have enhanced communication between the teams. And we’ve already started on our next step, which we’re all tired of, the peer to peer in the appeals for all the targeted agents.

Ledford has met with payers and is developing a structured note based on successful peer-to-peer encounters, and clinical pharmacists will fulfill this role.

Most of all, patients are happier. “We did do the statistics on it, and it was statistically significant for our team.” The control group received a 93.5% approval rate, and the group using the new system received 97.4%. ♦

AI Use Enables Health System to Find Early-Stage Lung Cancer

FOR AMIE J. MILLER, MSN, APRN, AOCNP, ACHPN, CTTS, November always brings opportunity and a little frustration.

Miller was excited at how many attendees at the Association of Cancer Care Centers (ACCC) 51st Annual Meeting and Cancer Center Business Summit knew that November was Lung Cancer Awareness Month. But she admitted it is tough following the annual show of pink to promote Breast Cancer Awareness Month, which comes every October.

Lung cancer, she notes, kills more Americans than breast, colon, and prostate cancer combined.

Miller shared this observation at the March 6, 2025, ACCC session on how artificial intelligence (AI) and business intelligence solutions can help health systems make practice improvements. She runs an AI-fueled effort that saves lives and brings more than \$1 million yearly to Sarasota Memorial Health Care System in southwest Florida.

At Sarasota’s Brian D. Jellison Cancer Institute, Miller is coordinator of the Lung Cancer Early Detection and Prevention Program, which features an initiative to follow up on incidental pulmonary nodules (IPNs) detected through AI. IPNs are asymptomatic lesions that can be detected on a CT scan during an emergency department visit or other intervention; they could signal early lung cancer but often go unaddressed.

Recent therapeutic advances in lung cancer treatment mean survival rates are vastly improved—if cancer is caught early on. However, as data from a 2024 report from the American Lung Association showed,¹ disparities are widening in biomarker testing and lung cancer screening, meaning that whether one dies of lung cancer may depend on access. Miller said national lung cancer screening rates remain stubbornly low at 18.1%, although pockets of the country exceed this rate, such as the catchment area for St. Elizabeth’s Healthcare in Kentucky, where about 45% of the eligible population is screened.

As Miller explained, understanding who is eligible for screening is key. Recommendations from the US Preventive Services Task Force call for screening individuals aged 50 to 80 years who are current smokers or who have quit within



MILLER

the past 15 years after smoking for 20 years or more.² “When we look at the data, only about 42% of [patients with] lung cancer qualified for lung cancer screening,” she said. “So that’s a real issue.”

Thus, 44% of lung cancers are diagnosed at a late stage, when survival rates are significantly lower than if the cancer is caught at stage I or II. That’s where an IPN program can make a difference, Miller said. According to findings from a 2022 study by Penn Medicine, about 10% of patients with an IPN greater than 8 mm will receive a lung cancer diagnosis.³

“With cancer screening, you have people who are well insured; they’re well connected to their primary care doctor, they’re educated.... Whereas with [incidental pulmonary nodules], these patients are oftentimes within the emergency [department] for their health care...oftentimes they are uninsured.”

—Amie J. Miller, MSN, APRN, AOCNP, ACHPN, CTTS,
Brian D. Jellison Cancer Institute,
Sarasota Memorial Health Care System

So who are these patients?

“Incidental pulmonary nodules are a different animal than lung cancer screening,” Miller said. “With cancer screening, you have people who are well insured; they’re well connected to their primary care doctor, they’re educated, and they’re advocating for themselves. Whereas with IPNs, these patients are oftentimes within the emergency [department] for their health care, oftentimes they don’t have a primary care physician, [and] oftentimes they are uninsured.”

Miller took the audience step by step through Sarasota’s journey with its AI-driven lung cancer screening and IPN initiative:

- Sarasota Memorial Health Care System invested in AI-driven software in 2019, which boosted its lung cancer screening program and allowed the launch of an IPN program designed to catch cancers at earlier stages.
- The AI technology reads close to 150,000 CT scans that come in across the 1100-bed system each year. A radiologist will accurately report what is on the scan; almost always, patients do not receive a scan for a lung nodule.
- Previously, the patients would be discharged to a primary care physician who would be unaware of the IPN; a patient with very early-stage lung cancer might return several years later with late-stage lung disease. Miller said, “This is something that is happening in all...your emergency rooms today. I guarantee it.”
- Under the IPN program, the AI flags IPNs that merit follow-up, and information on these patients is forwarded for follow-up. A communication tool kit was developed to help reach out to patients and educate them on the CT scan and next steps.
- After integrating AI, Sarasota’s annual screening volume rose by 99%, from 676 patients in 2019 to 1342 patients in 2023. Screening rates surpass national benchmarks for early detection, with 70% of lung cancer screening cases and 44% of IPN cancer cases diagnosed at stages I and II.

Miller emphasized that the AI program has more than paid for itself: She wrote that the health care system produced a return rate of more than 85% for patients with high-risk lung cancer, with an average of 91% from 2019 through the second quarter of 2024, compared with the national average of 22.3%.

According to the session abstract, “The AI solution helped generate \$8321,128 in downstream charges and \$803,106 in contribution margin from 1702 cases and \$5559,125 in charges and \$349,121 in contribution margin from 275 cases from the lung cancer screening and incidental pulmonary nodule programs, respectively.”⁴

A key to the AI program’s success is that it doesn’t interrupt the workflow but tracks the patients and allows IPNs to be caught promptly. Each day, the

program scans CT scans and pulls what Miller calls a “work list” of patients who need follow-up. “And I guarantee you, every single day I call a patient and say, ‘By the way, you were in the in the emergency [department] last week having your CT scan done because you had a kidney stone—you actually have a spot on your lung, and it measures 10 mm.’ And I can’t tell you how many times patients [say], ‘I had no idea.’”

There’s now a weekly meeting among a team of pulmonologists and a thoracic surgeon to discuss high-risk cases that emerge from the AI-driven caseload. Miller said they cover 10 cases in 30 minutes, and over time, they are building awareness about IPNs.

“There is ongoing community physician outreach,” she said. “This is something that will generate increases in our screening numbers.... That’s something I talk about every day—how can we increase our screening volumes by engaging physicians and empowering and educating the communities.” ♦

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With Subcutaneous Immunotherapy Coming, “Patient Preference Has to Be the Key”

THE RECENT APPROVAL of a nivolumab plus hyaluronidase-nvhy subcutaneous injection (Opdivo Qvantig; Bristol Myers Squibb) marks the next step in the evolution of cancer therapy—and one that promises new solutions for patients and cancer centers alike, according to an oncologist who spoke at the Association of Cancer Care Centers’ 51st Annual Meeting & Cancer Center Business Summit.

Raghava Reddy Induru, MD, an oncologist for Atrium Health Levine Cancer Institute based in Albemarle, North Carolina, walked attendees through the trajectory of the “pillars” of cancer treatment, from the surgery practiced by the ancient Greeks to the discovery of radiation in the 1800s, to the rise of chemotherapy and targeted therapies. More recently, the field has seen the approval of the first immunotherapies, coupled with a shift to genomic-based treatment.

But new treatments are only part of the story, Induru noted. “Evolution comes from many, many different angles, and part of the evolution is how we administer these medications,” he said.

In the 1940s, the launch of chemotherapy came with intravenous (IV) administration. “It’s considered the gold standard...because it’s predictable. We understand the bioavailability very easily,” Induru said.

Oral medications arrived in the mid-1990s. Induru said that, at first, there were challenges because the bioavailability compared with IV administration was not well understood, “but we have made the transition.”

More recently, hematology and oncology have embraced subcutaneous delivery, where therapy is delivered directly under the skin. This method allows rapid delivery of the medication relative to the time needed for IV administration. Induru cited data that showed an average savings of 54 minutes per patient, although the time saved has varied by country.

Subcutaneous delivery has been used for some time, including for well-known therapies such as trastuzumab (Herceptin), which is used in HER2-positive breast cancer, and bortezomib (Velcade), and daratumumab (Darzalex), both used in multiple myeloma. However, the FDA’s December 27, 2024, approval of a subcutaneous formulation of nivolumab across multiple solid tumors marks the



INDURU

first time a checkpoint inhibitor will be delivered this way, which Induru said is a significant step.¹

Although J-codes are not yet available, he said, they are coming soon, and subcutaneous versions of other immune checkpoint inhibitors will follow. He predicts that health systems will see clinical and operational benefits, and patients will also benefit.

“This is unstoppable,” he said. “But how we embrace this is really [what] we need to think of.”

Induru shared a few case studies of patients for whom a subcutaneous option offered benefits. A 54-year-old woman with HER2-positive progressive breast cancer would need a multidisciplinary regimen. She had adjuvant therapy with trastuzumab and pertuzumab (Perjeta) for 4 cycles, and she experienced neutropenic fever and had COVID-19 prior to surgery, which complicated her care. However, she had a complete pathological response. What would come next? The standard of care would be trastuzumab and pertuzumab for 4 months, but this patient no longer had a port.

“A good clinical trial is always the best option for my patients, right?” Induru said. The clinical trial options were IV trastuzumab vs subcutaneous trastuzumab; the trial called for a longer duration of treatment, and IV would be a challenge for a year. “Subcutaneous would be a great option,” he said, but it is “confounded with the whole challenge of getting approval.”

Another case involved a 48-year-old man with symptomatic multiple myeloma who ran his own trucking company. The patient had 5 children; he declined the port and wanted early morning or late day appointments because of his work schedule.

This story reflects what Induru sees in the rural area he serves. His patient “can’t just stop working because he is self-insured. These are very critical components of his life. He is a young male supporting his family.... What are his choices?”

Induru ran through various well-known triplets and quadruplets that were approved in recent years for multiple myeloma. After noting that the regimen of daratumumab, bortezomib, lenalidomide (Revlimid), and dexamethasone can be given with a mix of subcutaneous and oral options, he added, “I don’t have an answer, but [I’m] just helping people to think about who my patient is, and what is the right choice for them.”

Considerations for Bringing Subcutaneous Drugs Into Practice

Practical considerations for health systems include looking at clinical trials comparing IV and subcutaneous formulations and how costs compare, Induru said. At this point, most studies are designed to show noninferiority with IV formulations, he said. The phase 3 Checkmate-67T study (NCT04810078) involving 495 patients met the pharmacokinetic, overall response rate, and safety end points.²

Savings, he explained, cannot be evaluated simply within the comparison of therapies themselves. The large reduction in administration time will make scheduling more manageable and allow a complete rethinking of workforce optimization.

“It reduces the hospital and clinic burden—no question about it,” he said. In the institution’s area where subcutaneous therapy is given, he said, “The way we staff that is different, and how we look at the utilization of the time is different than what we’re doing with the infusion [area].”

If more patients can be treated with subcutaneous therapy, “I may have more people now who could make sure that the patients are coming for their appointments, or [staff] who could use the time to coordinate these appointments,” Induru said. With help from artificial intelligence, he added, “That’s how I [will] better use my resources.”

Induru said the most important consideration is what the patient wants. With the arrival of the subcutaneous option, home therapy administration is not out of the question. Although IV administration has some advantages, “patient preference has to be the key,” Induru said. ♦

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Texas Oncology to Roll Out Canopy for ePROs After Head-to-Head Pilot Trial

MARY CAFFREY AND ROSE MCNULTY



PATT

Debra Patt, MD, PhD, MBA, executive vice president for public policy and strategy, Texas Oncology.



KWIATKOWSKY

Lavi Kwiatkowsky, CEO and founder, Canopy.

TEXAS ONCOLOGY, a community oncology giant with nearly 1000 providers across 280 locations, announced today it would form a multiyear partnership with Canopy, a continuous care platform that helps practices collect and manage patient feedback. The goal is to prevent hospital stays and improve outcomes.

Canopy, which has grown to serve 2000 providers in a dozen practices, is poised to make its biggest leap yet by scaling to serve one of the largest and best-known practices in the country. Part of The US Oncology Network, Texas Oncology sees 71,000 new patients each year and is a leader in value-based care and clinical research; it is enrolled in the Enhancing Oncology Model (EOM), a Medicare program that requires practices to meet certain performance benchmarks to qualify every 6 months for additional payments.

“Oncologists are seeing the fastest rate of therapeutic innovation in history. With this growing complexity, our practice must also evolve,” R. Steven Paulson, MD, president and CEO of Texas Oncology, said in a statement.¹ “This partnership with Canopy ensures that we remain at the forefront of cancer care, allowing us to set new standards in our approach to each patient’s unique journey.”

In an interview with *The American Journal of Managed Care* (AJMC), Debra Patt, MD, PhD, MBA, executive vice president of public policy and strategy for Texas Oncology, said, “Canopy has been our partner in innovation. It’s one of the things that we really like about working with them. They’re quick to adapt the technology when we need it to adapt with additional functionality, thinking about the need to support patients on oral oncolytics [and] thinking about specific disease states that need different kinds of support or therapy interventions that require different types of support. They’ve been great collaborators as we innovate and change.”

“Partnering with Texas Oncology is a pivotal step in our mission to make continuous care the standard for all cancer patients,” Lavi Kwiatkowsky, CEO and founder of Canopy, said in the statement. “Texas Oncology’s forward-thinking approach and dedication to embracing innovation make them an ideal partner. Together, we aim to set a new benchmark for AI [artificial intelligence]–powered, continuous oncology care.”¹

Today’s announcement follows a recent pilot trial in Texas Oncology’s Amarillo clinic, in which Patt said Canopy had “had substantially higher adoption rates” than another platform in use at the clinic.

“This means the symptom management tools have a better opportunity to serve patients,” Patt said.

During the pilot, which began in October 2024 and ran through February 2025, Patt said Texas Oncology received positive feedback from both the nursing staff and patients.

“The feedback from our nursing staff has been that they’re able to spend less time on the documentation burden because there are digital tools—AI among them—that allow Canopy’s use of symptom management pathways and documentation [for] patients and in the medical record to be more seamless,” she said.

“If we thought that our nurses were spending 50% of their time being nurses and 50% of their time on the administrative burden of the tasks at hand of patient symptom management, we see that migrating to closer to an 80:20 shift. I think that evolution is important in the wake of a staffing crisis that we all see. And



anchoring on to where we started, Texas Oncology has continued to make investments in value-based care, and we want our people to act top of license so we can do that efficiently and effectively.”

Texas Oncology, as a practice, and Patt individually were early leaders in the use of technology for symptom management to improve patient outcomes. Patt previously led studies involving a different platform, Navigating Cancer, which Texas Oncology selected as a triage management tool in 2020.²

“Canopy has been our partner in innovation. It’s one of the things that we really like about working with them. They’re quick to adapt the technology when we need it to adapt with additional functionality, thinking about the need to support patients on oral oncolytics [and] thinking about specific disease states that need different kinds of support or therapy interventions that require different types of support. They’ve been great collaborators as we innovate and change.”

—Debra Patt, MD, PhD, MBA, executive vice president, public policy and strategy, Texas Oncology

In September 2024, a different community oncology network, OneOncology, purchased Navigating Cancer.³ Patt said Texas Oncology would continue to have a relationship with Navigating Cancer.

To prepare for the partnership’s launch, Canopy has integrated with iKnowMed, the electronic health record (EHR) developed by Ontada, the McKesson oncology technology and insights company. Canopy has become a member of the Ontada Developer Marketplace. McKesson supports The US Oncology Network, whose member practices remain independent.

In an interview with AJMC, Kwiatkowsky shared how he created Canopy in 2018 after seeing family members suffer needlessly with cancer. He was inspired by research findings presented in 2017 by Ethan Basch, MD, MSc, at the American Society of Clinical Oncology (ASCO) plenary session, which showed that electronic

remote symptom monitoring could improve overall survival by 5 months—as good as some novel therapies at a far lower cost.⁴

Kwiatkowsky described how Canopy took on one challenge at a time in its early work with Highlands Oncology, a small but highly regarded practice in Northwest Arkansas.

“It was very clear to us that to make this successful, we need to make the practice successful,” he said. “So it doesn’t matter how many life-threatening symptoms or issues or adverse events we find, if the practice doesn’t tackle them quickly and efficiently in a standardized fashion, it’s not going to help anyone. It’s going to sit on some queue somewhere.”

The system launched with Highlands in 2020 has been slowly refined ever since. “We started with remote monitoring,” Kwiatkowsky said. Next came algorithms to triage the most urgent matters, then came support for nurses, followed by workflows and decision support.

Results for Canopy’s early work with Highlands drew attention. Results published in 2022 by ASCO included a 45% improvement in treatment persistence,⁵ a 22% reduction in hospitalizations and emergency department visits per 100 patient months,⁶ and 88% patient engagement sustained at 6 months.⁷

More recent data published at the 2024 American Society of Hematology meeting showed improved early detection of toxicity among patients being treated with bispecifics and a 37% reduction in treatment discontinuation.^{8,9}

Reimbursement. Because Canopy allows practices to identify and address symptoms that patients experience between visits, practices can capture reimbursement through programs available through CMS, such as principal care management and chronic care management and remote therapeutic monitoring.

Today, the move is on to bring complex therapies into community practice settings. Kwiatkowsky said Canopy is working on tools to help practices administer bispecific antibodies and antibody-drug conjugates.

In addition to supporting Texas Oncology and Highlands, Canopy supports New York Cancer & Blood Specialists in New York and Oncology Consultants in Houston, Texas. ♦

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SPOTLIGHT



How Do Infusion Pharmacies Support Financial Sustainability in Oncology?

Jorge García, PharmD, MS, MBA, MHA, FACHE, FACCC | Interview by Hayden E. Klein



GARCIA

JORGE GARCIA, PHARM.D, MS, MBA, MHA, FACHE, FACCC, assistant vice president, system oncology pharmacy services and nononcology infusion, Baptist Health South Florida.

WITH RISING ONCOLOGY treatment costs and potentially billions of dollars anticipated in health care cuts, providers must optimize infusion pharmacy services to navigate reimbursement challenges, says Jorge García, PharmD, MS, MBA, MHA, FACHE, FACCC, assistant vice president of system oncology pharmacy services and nononcology infusion pharmacy services at Baptist Health South Florida.

In an interview with *The American Journal of Managed Care (AJMC)*, García notes that value-based care in oncology has faced challenges, but he sees emerging models as promising strategies to align cost containment with quality care.

This transcript has been lightly edited for clarity.

AJMC: With rising treatment costs and reimbursement challenges, how can infusion pharmacy optimization help cancer centers improve financial sustainability while maintaining high-quality patient care?

GARCIA: When I think about high cost in oncology, the large majority of the pharmacotherapy services that we provide our patients [with] does take place in the outpatient setting. That is a buy-and-bill setting. I think the dynamics there is a little bit different than when we consider services in the inpatient setting with a DRG [diagnosis related group] kind of payment.

For me, it’s really important to identify best practices establishing access in both of those settings, and that requires a slightly different approach and a strategy to make sure that it is sustainable and that it could be done in a viable way. But in the cancer space, we continue to see viable avenues to support the services.

I think as we move into the near future, we know that there are expectations to cut health care costs. I think we’re [talking about]...\$800 billion in cuts, so that is little bit concerning. Understanding how much of that may come out of Medicare reimbursement, other CMS services, [or] potential Medicaid eligibility is something that we need to continue

to track very closely to understand how it's going to impact our patients and our practices going forward.

AJMC: How can infusion pharmacies align with cost-containment efforts set by value-based care models without compromising treatment access?

GARCIA: I think we've talked about value-based care in oncology [for] a long time, with somewhat limited success. I think value-based care has found its way into chronic conditions, hypertension, diabetes, and others.

I think in oncology, just given the nature of oncology [and] the outpatient nature of it, it's been a little bit more challenging. But I begin to see some value-based [and] some at-risk sort of arrange-

ments that make a lot of sense in oncology, especially around high-cost pharmaceuticals, where you would see...the life science organization provide a credit for the drug if the clinical outcomes are not met for that patient, and I think that that's tremendously helpful for some of the therapies. But also [it's important to understand] how the health plans may be able to partake in the risk of a therapy that may be provided to a patient where the patient may not be achieving outcomes.

I think we're just beginning to understand how this fits in in oncology with some few examples, but I think we're going to continue to make progress in this space to ensure that as stakeholders that participate in cancer care—the provider, the health plan, the life science organizations—we're all invested in the success of therapies. I'm excited to see what's in store there as we...go into the future. ♦

Moffitt's Locke Discusses Gene Editing Process to Create Cema-Cel

INTERVIEW BY MAGGIE L. SHAW



LOCKE

Frederick L. Locke, MD, chair, Department of Blood and Marrow Transplant and Cellular Immunotherapy, Moffitt Cancer Center.

THE INVESTIGATIONAL ALLOGENEIC chimeric antigen receptor (CAR) T-cell therapy cema-cel (cema-cel; Allogene Therapeutics) is being evaluated in the ALPHA (NCT03939026) and ALPHA2 (NCT04416984) trials for relapsed/refractory large B-cell lymphoma, a type of non-Hodgkin lymphoma, and in the ALPHA3 trial (NCT06500273) in patients with a low disease burden who have received cema-cel as consolidation treatment in the first line.

Frederick L. Locke, MD, lead investigator on ALPHA and ALPHA2 and chair of the Department of Blood and Marrow Transplant and Cellular Immunotherapy at Moffitt Cancer Center and Research Institute, spoke with *Evidence-Based Oncology (EBO)* about how the therapy is genetically engineered to lessen the risk of patient rejection.

This transcript was lightly edited for clarity.

EBO: Can you describe the gene editing process involved in creating cema-cel to mitigate the risk of graft-vs-host disease?

LOCKE: Cema-cel is an allogeneic CAR T-cell therapy, which targets CD19, and cema-cel is what we tested out in the ALPHA and ALPHA2 clinical trials. Cema-cel takes healthy donor T cells, and using a gene-editing technique called TALEN [transcription activator-like effector nucleases], it removes 2 genes, and thereby 2 proteins, from the donor's T cells.

One of those is CD52—that's just the name of a cell surface protein. CD52 exists on all the immune cells in the body, or all the lymphocytes in the body, and other immune cells. By removing that protein from the donor's CAR T cells, it allows us to use a monoclonal antibody against CD52 during the lymphodepletion regimen, so that we can lower patients' immune cells and allow the cema-cel to be infused and expand in the patient's body.



It gives us an extra advantage so that those donor cells aren't rejected by the patient's immune cells.

The other gene that's deleted in cema-cel is the *TRAC* gene.... *TRAC*...is a gene and a protein that's necessary for the expression of the T-cell receptor. Each T cell recognizes a different target, and those T-cell receptors—if we get T cells infused into our blood from a healthy donor—...could recognize the proteins of our body as abnormal because they're not used to our body. We need to remove the T-cell receptor from the donor cells so that when they are infused into the patient, they don't cause graft-vs-host disease, [and] they don't attack the patient's body, recognizing it as foreign. Then, of course, the CAR, the chimeric antigen receptor, is a gene that's expressed in cema-cel against CD19.

We're not replacing all the patient's blood cells with donor cells. We're simply giving a single infusion of cema-cel: healthy donor T cells that are engineered to react against the patient's lymphoma cells and not be rejected or cause graft-vs-host disease. We do have to lymphodeplete; all CAR T-cell patients get lymphodepletion. We transiently lower the normal lymphocytes and immune cells in the body, so that when the CAR T cells are infused into the blood, they have less competition. We do that with cema-cel as well with 2 drugs, fludarabine and cyclophosphamide, just like autologous CAR Ts, and we also use ALLO-647, which is a monoclonal antibody, against CD52. ♦

ASHLEY CHAN, HAYDEN E. KLEIN, ROSE MCNULTY, CAMERON SANTORO, MAGGIE L. SHAW, PEARL STEINZOR, AND ASHLING WAHNER.

FDA ACTIONS

FDA Approves Vimseltinib for Symptomatic Tenosynovial Giant Cell Tumor

THE FDA APPROVED vimseltinib (Romvimza; Deciphera Pharmaceuticals) on February 15, 2025, for the treatment of patients with symptomatic tenosynovial giant cell tumor (TGCT) for whom surgical resection may cause worsening functional limitation or severe morbidity.¹

This regulatory decision was supported by findings from the phase 3 MOTION trial (NCT05059262), in which vimseltinib elicited a 40% (95% CI, 29%-51%) overall response rate (ORR) at week 25 vs 0% (95% CI, 0%-9%) with placebo in the intent-to-treat (ITT) population (difference, 40%; 95% CI, 29%-51%; $P < .0001$).^{1,2} The median duration of response (DOR) was not reached with vimseltinib. At an additional 6 months of follow-up, 85% of responders had achieved a DOR of at least 6 months, and 58% had a DOR of at least 9 months.

“We’re very excited to have vimseltinib recently approved,” William D. Tap, MD, of Memorial Sloan Kettering Cancer Center in New York, New York, said in an interview with *OncLive*.[®] “TGCT, especially the diffuse type, can be a very devastating disease for people. It’s not something that generally threatens their life, but it can really alter the trajectory of their life. People live with the disease for long periods...and can have tremendous symptoms and a lot of disability from it, so to have medical options for TGCT is critical for us.”

The multicenter, double-blind MOTION trial enrolled patients at least 18 years of age with histologically confirmed TGCT for whom surgical resection might worsen functional limitations or cause severe morbidity.

Between January 21, 2022, and February 21, 2023, 123 patients were randomly assigned 2:1 to receive vimseltinib at 30 mg orally twice weekly ($n = 83$) or placebo ($n = 40$), each given in 28-day cycles for 24 weeks.

The ORR at week 25 assessed by independent radiological review (IRR) per RECIST 1.1 criteria in the ITT population served as the primary end point. Secondary end points included ORR by IRR per tumor volume score (TVS), change from baseline in active range of motion (ROM) of the affected joint, change from baseline in TGCT-specific Patient-Reported Outcomes Measurement Information System physical function (PROMIS-PF), worst stiffness numeric rating scale (NRS), EuroQoL visual analogue scale (EQ-VAS) health status, and Brief Pain Inventory (BPI) worst pain response rate.

Additional findings from the study, presented at the 2024 American Society of Clinical Oncology Annual Meeting and concurrently published in *The Lancet*, showed that treatment with vimseltinib led to a statistically significant ORR advantage over placebo in almost every prespecified patient subgroup. Furthermore, 95% of patients in the vimseltinib arm experienced a decrease in tumor size per RECIST criteria. At a data cutoff date of August 22, 2023, the median DOR for patients who achieved an objective tumor response at week 25 was not reached (NR; range, 0.03-11.7 months).

The ORR by IRR per TVS at week 25 was also significantly higher in the vimseltinib arm vs the placebo arm, at 67% vs 0% (difference, 67%; 95% CI, 56%-77%; $P < .0001$). In total, 5% and 63% of patients in the vimseltinib arm had a complete response and partial response, respectively, per TVS. The median DOR by IRR per TVS was NR (range, 0.03-13.9 months).

The least squares (LS) mean change in active ROM from baseline in the affected joint at week 25 was significantly higher in the vimseltinib arm vs the placebo arm, at 18.4% (SE, 6.5) vs 3.8% (SE, 7.2), respectively (difference, 14.6%; 95% CI, 4.0%-25.3%; $P = .0077$). Significant improvements in physical function, as measured by PROMIS-PF, were also noted with vimseltinib vs placebo (LS mean change from baseline difference, 3.3; 95% CI, 1.4-5.2; $P = .0007$). The PROMIS-PF response rates were 43% and 25% in these respective arms (difference, 18%; 95% CI, 1%-36%; $P = .046$).

Treatment with vimseltinib also significantly improved stiffness, inducing an LS mean change from baseline of -2.1 (SE, 0.2) vs -0.3 (SE, 0.3) with placebo

(difference, -1.8 ; 95% CI, -2.5 to -1.1 ; $P < .0001$). The worst stiffness NRS response rates were 39% and 15%, respectively (difference, 24%; 95% CI, 8%-39%; $P = .008$).

The EQ-VAS response rate was numerically higher in the vimseltinib arm, at 37% vs 25% in the placebo arm, although this difference was not statistically significant (difference, 12%; 95% CI, -5% to 29%; $P = .16$). The LS mean change in EQ-VAS from baseline was 13.5 (SE, 2.4) in the vimseltinib arm vs 6.1 (SE, 2.9) in the placebo arm (difference, 7.4; 95% CI, 1.4-13.4; $P = .016$). The BPI worst pain response rates were 48% and 23% in these respective arms (difference, 26%; 95% CI, 4%-42%; $P = .0056$).

Grade 3 or 4 treatment-emergent adverse effects (TEAEs) occurred in 37% of patients in the vimseltinib safety population ($n = 83$) and 10% of those in the placebo safety population ($n = 40$). The most common TEAEs reported in the vimseltinib arm were periorbital edema (any-grade, 45%; grade 3/4, 4%), fatigue (33%; 0%), facial edema (31%; 1%), pruritus (29%; 2%), headache (28%; 1%), asthenia (27%; 1%), nausea (25%; 0%), increased blood creatine phosphokinase levels (24%; 10%), and increased aspartate aminotransferase levels (23%; 0%).

Grade 3 or 4 treatment-related AEs occurred in 30% of patients in the vimseltinib arm and 3% of those in the placebo arm.

Notably, investigators did not observe evidence of cholestatic hepatotoxicity or drug-induced liver injury. ♦

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FDA Accepts Resubmission of BLA for Odronextamab in R/R Follicular Lymphoma

THE FDA HAS ACCEPTED a resubmission of the biologics license application (BLA) seeking approval of odronextamab (Ordspono) for the treatment of patients with relapsed/refractory follicular lymphoma after 2 or more lines of systemic therapy.¹

The BLA resubmission was accepted following a complete response letter (CRL) issued by the FDA in March 2024.² According to Regeneron Pharmaceuticals, the agent’s developer, the CRL was related to the enrollment status in confirmatory trials and did not establish any issues regarding efficacy, safety, trial design, or manufacturing of odronextamab.

The FDA set a new Prescription Drug User Fee Act date of July 30, 2025, for odronextamab.¹

The BLA resubmission and acceptance from the FDA followed the achievement of the phase 3 confirmatory OLYMPIA-1 trial (NCT06091254) for patients with relapsed/refractory follicular lymphoma. However, data from the phase 1 ELM-1 (NCT02290951) and phase 2 ELM-2 (NCT03888105) trials supported the BLA resubmission, which demonstrated an overall response rate (ORR) of 80% ($n = 103$), with 74% of patients ($n = 95$) achieving complete responses (CRs). Serious adverse effects (AEs) occurred in 67% of patients and included cytokine release syndrome (CRS), COVID-19, and pneumonia in at least 10%.

In August 2024, the European Commission approved odronextamab for the treatment of adult patients with relapsed/refractory follicular lymphoma and relapsed/refractory diffuse large B-cell lymphoma who previously received at least 2 lines of systemic therapy.³ The regulatory decision was based on data from the ELM-1 and ELM-2 trials.

In ELM-2, at a data cutoff of October 20, 2023, the median duration of efficacy follow-up was 20.1 months among patients with relapsed/refractory follicular lymphoma.⁴ The ORR by independent central review was 80% (95% CI, 72.5%-86.9%; n = 103/128), with a CR rate of 73% in more than 90% of responders. ORR and CR rates per local investigators were 82% and 73%, respectively. A reduction in tumor size was recorded in 95% of all evaluable patients.

Findings from the ELM-1 study demonstrated that treatment of odronextamab led to an ORR of 51% (95% CI, 42%-59%) and a CR rate of 37% (95% CI, 29%-45%) in efficacy-evaluable patients with non-Hodgkin lymphoma (n = 142).⁵ Notably, patients with relapsed/refractory follicular lymphoma who received odronextamab at 5 mg or greater (n = 32) had an ORR of 91% (95% CI, 75%-98%) and a CR rate of 72% (95% CI, 53%-86%). The estimated median duration of response was 15.8 months (95% CI, 6.4-not estimable), with the longest ongoing CR being 53.0 months; responses occurred early on, with a median time to first CR of 2.6 months (IQR, 2.5-2.9).

ELM-2 Trial

In the follicular lymphoma cohort (n = 128), patients were at least 18 years of age. They had grade 1 to 3a follicular lymphoma with central histopathologic confirmation; had relapsed on or had disease refractory to 2 or more prior lines of systemic therapy, which included an anti-CD20 antibody and alkylator; were not considered for treatment with rituximab (Rituxan)/lenvatinib (Lenvima); and had an ECOG performance status of 0 or 1.⁴

Patients were treated with intravenous (IV) odronextamab in 21-day cycles, during which step-up dosing was implemented in cycle 1 to mitigate risks of CRS; this was followed by odronextamab at 80 mg on days 1, 8, and 15 in cycles 2 to 4. Maintenance dosing continued with odronextamab at 160 mg every 2 weeks until disease progression or treatment discontinuation based on another protocol-defined reason.

Regarding safety, any-grade treatment-emergent AEs (TEAEs) occurred in all patients, with 92% experiencing at least 1 treatment-related AE (TRAE). The most common TEAEs of any grade included CRS (56%), neutropenia (39%), and pyrexia (38%); the most common grade 3/4 TEAEs included neutropenia (32%), anemia (12%), and decreased neutrophil levels (12%).

ELM-1 Trial

Patients included in the study (n = 145) had documented B-cell non-Hodgkin lymphoma defined by 2007 National Cancer Institute Working Group criteria and at least 1 measurable lesion of at least 1.5 cm on the longest diameter. Additionally, they had to have received at least 1 previous treatment with an anti-CD20 antibody, have an ECOG performance status of 0 or 1, and have adequate hematological and organ function.⁵

Patients received IV odronextamab in 21-day cycles based on a step-up dose in cycle 1, then treatment once per week at doses ranging from 0.1 mg to 320 mg on days 1, 8, and 15 during cycles 2 to 4. Following cycle 4, they received maintenance therapy every 2 weeks until disease progression or unacceptable toxicity.

All patients experienced at least 1 TEAE of any grade, and 93% had at least 1 TRAE. Grade 3 or greater TEAEs occurred in 82% of patients, which included anemia (25%), lymphopenia (19%), hypophosphatemia (19%), neutropenia (19%), and thrombocytopenia (14%). Notably, most CRS events were grades 1 or 2 (36% and 19%, respectively) and mainly occurred in cycle 1 of treatment during step-up dosing. ♦

This article first appeared on OncLive.

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FDA Approves Generic Lenalidomide Capsules in Multiple Strengths

THE FDA HAS APPROVED Amneal Pharmaceuticals' generic lenalidomide capsules in multiple strengths, the company announced on February 19, 2025.¹ Amneal will be granted a license to manufacture and sell the product, which references Celgene's Revlimid.

Lenalidomide, a thalidomide analogue, is indicated for the treatment of several blood cancers and myelodysplastic syndrome (MDS). Amneal's generic lenalidomide was approved in 2.5-mg, 5-mg, 10-mg, 15-mg, 20-mg, and 25-mg strengths.

Lenalidomide (Revlimid; Celgene) was initially approved in the US in 2005 and has since been approved for the treatment of patients with multiple myeloma, anemia due to MDS, relapsed or progressing mantle cell lymphoma following 2 prior therapies, follicular lymphoma, and marginal zone lymphoma.² Celgene will provide Amneal a license to the patents needed to manufacture and sell generic lenalidomide capsules in the US starting January 31, 2026, according to the news release.¹

Amneal also announced the launch of mesalamine 800-mg delayed-release tablets referencing Asacol HD (Allergan Pharmaceuticals).¹ Mesalamine is an aminosalicilate first approved in 1987 for the treatment of moderately active ulcerative colitis.³ The first once-daily mesalamine, Lialda (Takeda Pharmaceuticals), was approved in 2007.⁴

"Our ability to execute and continuously launch complex products is expanding our portfolio of affordable medicines and driving the sustainable growth of our business," Andy Boyer, executive vice president and chief commercial officer of affordable medicines at Amneal, said in the news release.¹ "Mesalamine is a difficult-to-make product with a limited number of suppliers, and this approval highlights the strength of our [research and development] capabilities. Additionally, the approval of lenalidomide represents another key product approval in a large market that will be a future growth driver for us." ♦

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Denosumab Biosimilars Are Approved With Interchangeability to Address Osteoporosis, Fracture Risk

DENOSUMAB-DSSB BIOSIMILARS OSPOMYV and Xbryk, which reference Prolia and Xgeva, respectively, have received FDA approval for treating osteoporosis and bone loss, Samsung Bioepis announced on February 15, 2025.¹ The FDA has granted interchangeability designation for both

Ospomyv (60-mg prefilled syringe) and Xbryk (120-mg vial), marking the company's first approval for an endocrinology biosimilar, according to a company news release.

Ospomyv is used to treat osteoporosis in postmenopausal women at high risk for fracture, increase bone mass in men at high risk for fracture (including those receiving androgen deprivation therapy for nonmetastatic prostate cancer), and boost bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.²

Xbryk prevents skeletal-related events in patients with multiple myeloma and patients with bone metastases from solid tumors. It also treats adults and skeletally mature adolescents with giant cell tumors in the bone that are unresectable or where surgical resection is likely to result in severe morbidity. Additionally, it treats hypercalcemia of malignancy refractory to bisphosphonate therapy.

"The FDA approval of Ospomyv and Xbryk marks a key step in improving patient access and alleviating treatment costs for patients with osteoporosis and cancer-related bone loss in the US," Byoungin Jung, vice president and regulatory affairs team leader at Samsung Bioepis, said.¹



JUNG

A phase 1 study (NCT04621318) showed equivalence among the biosimilar denosumab, the European Union (EU)-sourced denosumab, and the US-sourced version in healthy male participants.³ Participants were randomly assigned to receive a single 60-mg dose of denosumab-dssb, the EU denosumab, or the US denosumab. The study met the primary end point regarding area under the concentration-time curve (AUC) from time zero to infinity, AUC from time zero to the last quantifiable concentration, and maximum serum concentration.

A phase 3 study (NCT04664959) demonstrated equivalent efficacy and comparable safety, immunogenicity, pharmacokinetics, and pharmacodynamic profiles between denosumab-dssb and reference denosumab in patients with postmenopausal osteoporosis.⁴ Researchers randomly assigned patients 1:1 to receive either 60-mg denosumab-dssb or reference denosumab subcutaneously at months 0 and 6.

At month 12, researchers again randomly assigned patients to continue with the assigned treatment or switch from the reference product to the biosimilar up to month 18. The study met the primary end point of percent change at baseline in lumbar spine bone mineral density at month 12. Follow-up data up to month 18 showed comparable efficacy, pharmacokinetics, pharmacodynamics, safety, and immunogenicity after switching to denosumab-dssb from the reference product.

Patients with postmenopausal osteoporosis who received Ospomyv experienced several common adverse events (AEs), including back pain, extremity pain, hypercholesterolemia, musculoskeletal pain, and cystitis.² Men with osteoporosis experienced back pain, arthralgia, and nasopharyngitis (> 5%). Back pain, hypertension, bronchitis, and headache were the most common AEs in patients with glucocorticoid-induced osteoporosis.

Patients with bone metastasis from solid tumors who received Xbryk experienced AEs such as fatigue, hypophosphatemia, and nausea. Patients with multiple myeloma experienced diarrhea, nausea, anemia, back pain, thrombocytopenia, peripheral edema, hypocalcemia, upper respiratory tract infection, rash, and headache. Patients with giant cell tumors of bone and hypercalcemia of malignancy experienced similar AEs.

Samsung Bioepis' FDA approval for both denosumab biosimilars marks the company's ninth and tenth approved medications.¹ This achievement has the potential to expand patient access to biosimilar treatments in this therapeutic space. ♦

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MANAGED CARE UPDATES

Data Show a Rural-Urban Gap in Cervical Cancer Mortality, but HPV Vaccine Appears to Be Working

CERVICAL CANCER IS on the rise in the US, and some women may be at greater risk than others, as data show that women living in rural areas and those in minority groups face a higher mortality risk.^{1,2}

Data in a new report published March 3, 2025, in *JAMA Network Open* show how suboptimal screening and diagnostic and therapeutic care may be driving disparities in the likelihood of death from cervical cancer among rural- and urban-dwelling women in the US.³ If cervical cancer is caught early on, the 5-year survival rate can be 91% vs 19% for later-stage diagnosis with distant metastasis.⁴

Amid this bad news, however, some hope exists: an analysis published by the CDC prior to the article above showed that rates of cervical precancer fell by 79% between 2008 and 2022 among women in their early 20s, the first generation to receive the human papillomavirus (HPV) vaccine.⁵

Disparities Between Rural and Urban Women

Using data on cervical cancer cases and mortality from 2001 through 2019, gathered from the National Program of Cancer Registries and Surveillance, Epidemiology, and End Results database and the National Center for Health Statistics, respectively, the *JAMA* authors estimated 5-year mortality and annual rates for cervical cancer.³ They also used data from the Behavioral Risk Factor Surveillance System to adjust for survey-weighted smoothed hysterectomy prevalence. Rates were estimated per 100,000 women.

The study authors found 222,425 cases of cervical cancer in the US between 2001 and 2019, with a majority seen among non-Hispanic White women (59.9%) who lived in an urban county (84.3%). However, when corrected for hysterectomy, the incidence per 100,000 was 17.35% higher in a rural vs an urban county, at 11.9 vs 10.0.

"The data are consistent with a considerable impact from the US HPV vaccination program on cervical precancers, with the largest decreases in the youngest age group for which benefit of vaccination would first be observed."

—CDC authors

Additional differences became apparent after comparing 2 time periods:

- For rural counties, there was a 0.85% annual increase (95% CI, 0.08%-2.05%) in the incidence of cervical cancer between 2012 and 2019 after a decrease between 2001 and 2012
- For urban counties, the annual percentage change (APC) was -0.03 (95% CI, -0.89% to 2.00%) between 2013 and 2019, which the authors noted was a plateaued rate after decreasing from 2001 to 2013

The authors explain that these data illustrate an overall widening gap in rural and urban incidence from 2013 to 2019, with rate ratios (RRs) of 1.16 (95% CI, 1.10-1.22) and 1.25 (95% CI, 1.19-1.31), respectively.

Mortality was 1.42 (95% CI, 1.33-1.51) times higher in the rural vs the urban counties.

Results by Race and Ethnicity

Regarding differences by race and ethnicity, the data show rural-dwelling women to be at a distinct disadvantage in cervical cancer incidence:

- Among urban Hispanic women for 2001-2012 and 2012-2019, the APCs were -4.20% (95% CI, -4.76% to -3.75%) and -0.34% (95% CI, -1.17% to 0.83%), respectively, whereas for rural Hispanic women, the APC was -2.72% (95% CI, -4.00% to -1.32%) between 2001 and 2019
- Among urban non-Hispanic Black women for 2001-2004 and 2004-2019, the APCs were -5.43% (95% CI, -8.99% to -2.72%) and -2.41% (95% CI, -2.83% to -0.62%), respectively. For rural non-Hispanic Black women, the APCs were -3.23% (95% CI, -7.30% to -2.24%) and 9.07% (95% CI, -2.84% to 17.84%) for 2001-2017 and 2017-2019, respectively
- Among urban non-Hispanic White women for 2001-2003 and 2003-2019, the APCs were -4.95% (95% CI, -6.53% to -1.62%) and -0.40% (95% CI, -0.59% to -0.10%), respectively. For rural non-Hispanic White women, the APCs were -1.60% (95% CI, -2.12% to -1.23%) and 1.05% (95% CI, 0.24% - 2.33%) for 2001-2012 and 2012-2019, respectively

For 2005-2009, 2010-2014, and 2015-2019, the RRs also were elevated in rural compared with urban locations, in most instances:

- **2005-2009:** Among Hispanic women, 1.25 (95% CI, 1.03-1.52); non-Hispanic Black, 1.38 (95% CI, 1.15-1.66); non-Hispanic White, 1.41 (95% CI, 1.30-1.53)
- **2010-2014:** Among Hispanic women, 0.97 (95% CI, 0.78-1.20); non-Hispanic Black, 1.43 (95% CI, 1.18-1.74); non-Hispanic White, 1.40 (95% CI, 1.29-1.51)
- **2015-2019:** Among Hispanic women, 1.33 (95% CI, 1.12-1.58); non-Hispanic Black, 1.58 (95% CI, 1.32-1.90); non-Hispanic White, 1.54 (95% CI, 1.43-1.67)

Making Inroads With the HPV Vaccine

The investigators explain that if not addressed, the care barriers contributing to these outcomes disparities may only worsen, with potential exacerbations from lower HPV vaccine uptake in rural areas.⁶ This is despite clear evidence that the HPV vaccine is presently preventing cancer in the US among women and men.^{5,7}

The HPV vaccine was first recommended for girls in 2006 and for boys in 2011; vaccination is recommended starting at age 9, with catch-up doses being recommended from ages 13 to 26.⁵ The new CDC analysis was based on a comparison of data from 3.4 million people who did or did not get the HPV vaccine. Authors found that rates of HPV precancers, which CDC has been monitoring since 2008, fell for women aged 20 to 24 by 79%, and high-risk precancers decreased for women aged 25 to 29 by 37%.⁵

The CDC authors concluded, “The data are consistent with a considerable impact from the US HPV vaccination program on cervical precancers, with the largest decreases in the youngest age group for which benefit of vaccination would first be observed.”⁵

DISPARITIES WILL “MAGNIFY.” There is already policy-level evidence of cervical cancer disparities in the rural South among Black women living in the Mississippi Delta region. A January 2025 report from the Southern Rural Black Women’s Initiative for Economic and Social Justice and Human Rights Watch details the systemic shortcomings and lack of reproductive care that are likely to blame for a disproportionately higher rate of cervical cancer-related deaths among Black women than White women.⁸ A principal factor involved in these disparate health outcomes is limited access to the HPV vaccine.

The overall message from the authors of the present report is that if preventive care, by way of HPV vaccination and screening, does not improve in and for rural US counties, “disparities are likely to magnify in future years.”³ ♦

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Real-World Findings Show Longer Survival in Academic Centers Than Community Settings in CLL, MCL

PATIENTS WITH chronic lymphocytic leukemia (CLL) and mantle cell lymphoma (MCL) who received care in academic cancer centers had significantly better survival outcomes than those treated in community settings, according to results from a new real-world study.¹

Published in *Leukemia & Lymphoma*, these findings highlight the influence of practice setting on patient outcomes and add to the conversation around treatment gaps in the US.

“This study specifically addressed site of care, a factor that had been suggested in prior research as related to improved outcomes among patients with CLL or MCL,” the study authors wrote.¹ “The results demonstrate a strong statistically significant relationship between care in an academic practice setting and improved clinical outcomes in both diseases.”

“This study specifically addressed site of care, a factor that had been suggested in prior research as related to improved outcomes among patients with chronic lymphocytic leukemia or mantle cell lymphoma. The results demonstrate a strong statistically significant relationship between care in an academic practice setting and improved clinical outcomes in both diseases.”

—study authors

Researchers evaluated nationwide data from 9783 patients with either CLL (n = 6372) or MCL (n = 3411) who received systemic therapy between 2013 and 2022. Of these patients, 13.9% with CLL and 22.2% with MCL were treated in academic settings. The analysis revealed a substantial gap in survival. From the start of first-line therapy for CLL, the median overall survival (OS) was not reached in academic centers; it was 80.5 months in community settings. Meanwhile, the median OS for MCL was 95.6 months in academic settings and 68.7 months in community settings.

Academic centers were more likely to treat younger patients and those with high-risk disease features, such as del(17p) mutations in CLL, and had significantly higher rates of clinical trial enrollment for both cancer types. After researchers adjusted for baseline differences, academic centers still had significantly longer survival outcomes for their patients than community-based practices. Patients with CLL or MCL treated in academic settings were also more likely to participate in a clinical trial than their counterparts in community settings. However, this study did not evaluate any causal relationship between trial participation and patient outcomes.

Covalent Bruton tyrosine kinase inhibitors were more frequently used in both first-line and later-line settings for MCL in academic centers than in community sites, although the duration of treatment was similar across settings. Additionally, the overall use of BCL2 inhibitors (BCL2i) and PI3K inhibitors (PI3Ki) remained low in both settings, with less than 20% of patients with CLL and 10% with MCL receiving BCL2i, and PI3Ki use fell below 1%.

The researchers also found a large gap in chimeric antigen receptor (CAR) T-cell therapy utilization between settings and an overall lack thereof. CAR T-cell therapies are associated with improved outcomes in MCL, yet only 6.2% of patients in academic centers and 1.3% in community practices received the treatment. However, the researchers said this low utilization, although still a concern, does not explain the survival gap between sites of care.

“Similarly, [although] BCL2i-based treatment has demonstrated efficacy, exposure to these therapies was only observed in a small subset of patients in either cohort,” they explained. “Therefore, this was also not likely to be sufficient to impact the differences observed in overall survival.”

Despite the advantages of academic settings shown by this study, the authors also acknowledged the challenges of access and equity. Patients in community settings were generally older and more likely to be on Medicare or uninsured, raising questions about disparities in specialized cancer care—a topic of growing importance as these disparities worsen in rural areas where patients have higher rates of risk factors and cancer centers are often left behind in the latest advancements.²

“Race and ethnicity differences by site of care raise concerns about equity and how the site of care differences may contribute to potential differential outcomes by race,” the authors emphasized.¹ “However, prior research has shown the lack of significant differences in outcomes by race in this same database. The relationship between site of care and race is deserving of further examination in future research.”

Although the study established a clear association between academic settings and better survival, the reasons for this advantage remain complex. The authors suggested that factors such as multidisciplinary tumor boards and higher provider experience may play a role, although more research is needed to better understand the underlying mechanisms. ♦

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SPOTLIGHT

Patients With Ovarian Cancer Had Stable Remission Rates Despite Pandemic, Findings Show

Brooke McCormick



CHAO

CHUN CHAO, PHD, MS,
cancer epidemiologist at Kaiser Permanente Southern California.

IN AN INTERVIEW WITH *The American Journal of Managed Care*® (AJMC®), Chun Chao, PhD, MS, cancer epidemiologist at Kaiser Permanente Southern California, explored the impact of the COVID-19 pandemic on oncology care, particularly for patients with ovarian cancer.

Chao explained the objectives of the study she coauthored, “Clinical Remission Rates in Patients With Epithelial Ovarian Cancer Before and After the Onset of the COVID 19 Pandemic in an Integrated Healthcare Delivery System.”¹ She then offered explanations for the findings and their impact for payers.

This interview is lightly edited for clarity.

AJMC: What was the impact of the COVID-19 pandemic on cancer screening, diagnosis, and treatment, especially for patients with ovarian cancer?

CHAO: Oncology care has definitely been affected in a significant way by the pandemic, and there are several reasons for that. As we know, several of the

cancer types—there’s a sense of urgency to them. Also, oncology care can be very complex, involving [multiple] experts or physicians, so the care pathways are very multidisciplinary. There’s also a demand for frequent contact between the patient and the health care providers. Patients with cancer, when undergoing cancer treatment, are somewhat immunosuppressed, so they are a rather vulnerable population. Because of all these reasons, cancer care was greatly affected by the pandemic.

There are several studies from the US, as well as Europe, that show that there has been a reduction in cancer screening rates, the number of cancers diagnosed in the pandemic year vs prior years, and the number of treatments. Compared with the prepandemic era, you see fewer cancer treatments being provided during the pandemic era.

Ovarian cancer is a pretty aggressive cancer; more than two-thirds of patients were diagnosed with advanced-stage disease. There are also studies that show a significant delay in getting treatment and treatment initiation, as well as treatments being canceled, in the early stage of the pandemic.

Also, we have consistently seen studies report the altered management approach for patients with ovarian cancer. Our guideline bodies, nationally and internationally, highlight the use of neoadjuvant chemotherapy in the pandemic era, so that may be the underlying reason why we see these altered management approaches for ovarian cancer.

AJMC: What was the objective of your study? Why did you decide to investigate this?

CHAO: This study was started in the middle of the pandemic, and we thought it would be important to understand how management approaches toward

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ovarian cancer have evolved, and to understand the short-term outcomes that these patients experienced with these altered approaches.

We may face another pandemic if a newly evolved virus arises in the future. So it is important to learn from the experience of the COVID-19 pandemic. That's why we decided to conduct this evaluation. We wanted to compare the management approaches before and after the onset of the pandemic.

One thing we wanted to explore was physician visits, whether telehealth or in-person. Did they remain stable? Also, monitoring for chemotherapy toxicity: Was that done with the same level of vigilance compared with the prepandemic level?

We wanted to look at whether patient outcomes are comparable with all these alterations in management. You have increased use of neoadjuvant chemotherapy, you have increased use of telehealth, but are patients still achieving remission [at rates similar to those in] the prepandemic era?

AJMC: Your study found no significant differences in complete or clinical remission rates before and after the COVID-19 pandemic. What do you think contributed to these stable outcomes despite disruptions in care?

CHAO: I think there are a few possible explanations for our findings. Similar to other studies, our study found a greater use of neoadjuvant chemotherapy in ovarian cancer management in the pandemic era. The observation that remission rates were similar before and after the onset of the pandemic may suggest that neoadjuvant chemotherapy followed by surgery was a similarly effective management approach as surgery first and then adjuvant chemotherapy; that's one possible reason.

Also, as part of the study, we analyzed data on health care utilization among patients with ovarian cancer during the active treatment phase, and we found comparable rates of physician visits. There was increased telehealth use, but in terms of the number of visits, whether it's telehealth or in-person, that frequency is actually comparable before and after the onset of the pandemic in the Kaiser Permanente Southern California setting. We also found comparable rates of the laboratory tests that were done to monitor chemotherapy toxicity.

Another possible reason is that these patients are still receiving comparable care during their active treatment phase, similar contact with their physicians, and approximately the same monitoring for their chemotherapy. That could also contribute to the stable outcome that we observed.

Another possible factor, which we didn't directly evaluate in our study, was that we did not find evidence for delays in treatment. We did not have evidence of a delay between the time to diagnosis and treatment

initiation in our health care system. That could also be part of why we saw comparable remission outcomes for these patients.

AJMC: What were the key limitations of your study? How might they have impacted your findings?

CHAO: There is always a possibility of unmeasured confounders that we did not account for in our study. Also, not all our patients had follow-up visits that would allow us to assess their remission status.

However, we did have very detailed information on the most important prognostic factors. We did not have the molecular characteristics of these ovarian cancers, but that's one thing that we did not expect to vary, the distribution of the molecular characteristics of ovarian cancer. We did not expect that to vary before and after the onset of the pandemic, so that should not be a huge concern.

In summary, I don't think we expect these limitations to have an important impact on our findings.

AJMC: Since your study focused on an insured population, how do you think remission rates might have differed for uninsured patients?

CHAO: We know that cancer outcomes, including those in ovarian cancer, are generally worse in the uninsured patient populations, and there are several reasons for this. There could be a delay in care seeking, a delay or suboptimal treatment because of cost concerns, and more limited access to specialists. They also may have less optimal adherence to recommended treatments for these reasons.

Our findings may not be generalizable to these other populations, including the uninsured or different types of health care settings. We found the remission rate to be stable before and after the onset of the pandemic. But uninsured patients, for example, may have even greater barriers to seeking care in the pandemic era, so there may be more loss of employment and a greater or new child care need for these patients. All these factors can impose greater barriers for them to seek care and receive adequate treatment.

That's why the findings in an insured population may not apply to the uninsured population when you compare the pre- and postpandemic eras, because people experience different challenges or barriers. ♦

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CLINICAL UPDATES

Cetuximab Plus Chemotherapy May Improve Colorectal Cancer Outcomes

CETUXIMAB (ERBITUX; ELI LILLY AND COMPANY) plus chemotherapy resulted in higher progression-free survival (PFS) and overall survival (OS) for patients with metastatic colorectal cancer (mCRC), according to results from a new study.¹ Findings from the systemic and meta-analysis, published in *BMC Cancer*, offer valuable insights into optimizing mCRC treatment strategies.

"Monoclonal antibodies are effective therapeutic options in mCRC treatment," the researchers wrote. "Cetuximab, an anti-EGFR monoclonal antibody,

demonstrated a significant advancement in managing mCRC when combined with various chemotherapy regimens. When used in conjunction with chemotherapy, cetuximab had a better prognosis for patients with CRC who had metastases by improving both overall and progression-free survival."

Cetuximab was approved in 2004 to treat patients with advanced CRC that has spread to other parts of the body, making it the first monoclonal antibody approved to treat this type of cancer.² In December 2024, the FDA approved encorafenib with cetuximab and mFOLFOX6 for mCRC with *BRAFV600E* mutation, based on results from the phase 3 BREAKWATER trial (NCT04607421).³

In this study, the researchers searched PubMed and Google Scholar for studies on mCRC treatment with anti-EGFR therapy.¹ Primary outcomes included PFS and OS, standardized across studies. Data extraction was independently conducted by 2 reviewers, with discrepancies resolved through discussion. Study quality was assessed using the Newcastle-Ottawa Scale. Statistical analysis employed fixed- or

random-effects models based on heterogeneity, with subgroup analysis and funnel plots used to determine bias.

The 25 studies analyzed included 3788 patients with mCRC, aged 18 to 77 years. Patients receiving cetuximab plus chemotherapy showed significantly improved PFS (HR, 0.79; 95% CI, 0.63-0.96; $P < .01$; $I^2 = 38\%$) and OS (HR, 0.78; 95% CI, 0.60-0.91; $P < .01$; $I^2 = 47\%$) compared with controls. Subgroup analysis of randomized controlled trials confirmed these benefits, with consistent HRs for PFS (HR, 0.77; 95% CI, 0.62-0.93) and OS (HR, 0.76; 95% CI, 0.61-0.88), reinforcing cetuximab's efficacy.

“Our meta-analysis justifies the useful addition of cetuximab to standard chemotherapy regimens for [metastatic colorectal cancer]. This approach could improve patient outcomes and provide a valuable addition to current treatment strategies.”

—study authors

However, the researchers noted some limitations. First, small sample sizes in some studies may have influenced outcomes, and including retrospective and prospective studies could impact result accuracy. Second, methodological differences—such as study design, patient characteristics, treatment protocols,

and follow-up periods—contributed to heterogeneity. Third, restricting the analysis to English-language publications introduced potential publication bias. Lastly, the findings relied on HRs, but not all studies reported these with corresponding confidence intervals, particularly for OS, which may have affected result reliability.

Despite these findings, the researchers believe the study demonstrated significant benefits of combining cetuximab with chemotherapy for patients with mCRC.

“The cetuximab-based therapy is associated with a substantial improvement in progression-free survival and overall survival compared [with] chemotherapy alone,” the researchers wrote.¹ “Our meta-analysis justifies the useful addition of cetuximab to standard chemotherapy regimens for mCRC. This approach could improve patient outcomes and provide a valuable addition to current treatment strategies. Future research is needed to confirm its clinical efficacy, identify patient subgroups that are most likely to benefit, and explore its impact on survival and quality of life for optimal integration into clinical practice. The findings underscore the cetuximab-chemotherapy combination as a promising first-line protocol for mCRC.” ♦

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SPOTLIGHT

NSCLC Advancements Offer Hope, but Disparities Persist

Ioana Bonta, MD | Interview by Kyle Munz



BONTA

IOANA BONTA, MD, medical oncologist, Georgia Cancer Specialists, Atlanta.

IMMUNOTHERAPIES, BISPECIFICS, AND antibody-drug conjugates (ADCs) have transformed the treatment landscape for patients with non-small cell lung cancer (NSCLC). Their advancements have helped tailor more targeted interventions and improved patients' quality of life, said Ioana Bonta, MD, in an interview with *The American Journal of Managed Care (AJMC)*.

These topics and more were explored at a recent Institute for Value Based Medicine event held in Atlanta, Georgia. Bonta, a medical oncologist at Georgia Cancer Specialists in Atlanta, was a presenter at the event.

This transcript has been lightly edited for clarity.

AJMC: What are the most influential advancements in NSCLC treatment in recent years, and how have they shaped patient outcomes?

BONTA: It certainly has been a very dense time for development in non-small cell lung cancer, and the advent of immunotherapy and targeted therapy really have made an impact on the outcomes for our patients. I

think immunotherapy is one of the main advancements. I don't know what other words to use, but more recently, combinations of immunotherapy with targeted therapy and ADCs seem to be making a difference in progression-free survival and, hopefully, overall survival soon.

Bispecific therapies are also coming into the field of non-small cell lung cancer. What is the impact? What we look at is the quality of life. Are those therapies better tolerated by our patients? Are the adverse effects more tolerable than our conventional cytotoxic chemotherapy? And yes, we do see an improvement in the quality of life and also, very importantly, in the outcomes, such as progression-free survival and, very importantly, overall survival of our patients.

AJMC: How have recent advancements in NSCLC helped address care gaps or reduce disparities in access and outcomes?

BONTA: First of all, [the advancements have] allowed us to identify those disparities and see their differences. And we know in minority populations, such as Black populations and Latinx populations, there's been an increase in mortality from lung cancer. And although this is true for the [White] population, for instance, it is actually more pronounced in the minority populations. It was very important to identify that those disparities actually exist. We know that the comorbidities in the minority population are more pronounced, and [this] makes the delivery of immunotherapy, targeted therapy, or any cancer therapy, in general, more difficult.

Also, when talking about disparities, we have to mention access to health care, not only system issues but also patient issues such as cultural acceptance, trust issues, socioeconomic status, and education level. ♦

Technology, Partnerships, Data, and Culture Are Keys to Bringing Precision Medicine to Community Oncology

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CONTINUED FROM COVER

tumor characteristics, could create new disparities in care,^{3,4} particularly for low-income patients treated outside an academic center. Since then, access to biomarker testing has improved, especially when looking at next-generation sequencing (NGS), which can uncover multiple genetic variations at once. However, the landscape for biomarker testing, generally, and NGS, specifically, remains a patchwork of state laws and payer policies that offer clinical, financial, and administrative hurdles for community practices.^{5,6} A July 2024 study in *JAMA Network Open* found that most patients with metastatic prostate and urothelial cancers did not receive NGS testing, and rates were worse for patients who were Black or covered by Medicare or Medicaid.⁷

This conflicted with mandates from Congress and the FDA that called for clinical trials to better reflect populations to be treated with new therapies.⁸ In response, pharmaceutical sponsors have worked with community practices to promote diverse enrollment and achieve precision medicine solutions. At the same time, entrepreneurs have developed artificial intelligence (AI)-driven platforms to match patients with trials or therapies, taking burdens off practice-level staff.⁹⁻¹¹

In recent weeks, the Trump administration's reversal of diversity, equity, and inclusion initiatives prompted the FDA to temporarily remove a draft guidance on clinical trial diversity from its website;¹² the page now states it was restored under a court order. As Hahn said in January, with 85% of new cancer therapies requiring a companion diagnostic, precision medicine "is here to stay."¹

Today, community oncology has developed strong models to bring precision medicine to patients, even in the most remote locations. By leveraging technology and partnerships and by promoting a culture of research, community providers have shown that rapid improvement is possible. New transactions are announced almost daily, and Precedence Research projected on February 26, 2025, the global personalized medicine market would double from \$654.46 billion today to \$1.315 trillion by 2034, with oncology making up the largest market segment at 42%.¹³

The Warning From ASCO

In 2019, ASCO published a series of reports warning that for all its promise, precision medicine could create new problems: It threatened to widen disparities between the haves and the have-nots in cancer care in a multitude of ways.^{3,4}

It was frustrating enough that patients taking part in clinical trials had more access to precision medicine approaches, and that these patients were more likely to be wealthy and White than those in a community clinic. As tissue samples from trial patients filled databases, resources such as the Cancer Genome Atlas became overpopulated with data that did not represent the population; a 2009 study had shown that individuals of European descent made up 95% of participants in genome-wide association studies.^{4,14}

What could be done? Around this time, then-ASCO President Monica Bertagnolli, MD, formed a Rural Cancer Care Task Force¹⁵ to address the fact that clinical trials and novel treatments were bypassing patients who lacked the means to travel to academic centers; an analysis of adjusted annual mortality

rates from 1999 to 2019 would show that the survival gap between urban and rural older adults had increased 25-fold during that time.¹⁶

One ASCO task force member is Sucharu "Chris" Prakash, MD, who has been medical director at Texas Oncology's Paris, Texas, location for nearly 25 years.¹⁷ By 2020, the task force had offered its first report on the challenges of rural cancer care, which he discussed with *Evidence-Based Oncology (EBO)*—rural residents were older, with less education and income than those in cities, and their cancer outcomes were generally worse. "They are diagnosed later," so mortality is higher, Prakash said. "Access to care is a major issue—that impacts screening and treatment. There are major barriers to insurance coverage and transportation."¹⁷

"I would say we test almost every single patient [who] walks in the door in Texas Oncology, no matter where they are. It could be in El Paso; it could be in Austin, downtown Dallas or Paris, Texas."

—Sucharu "Chris" Prakash, MD, director, Quality Services; medical director, Texas Oncology

By 2022, Prakash was Texas Oncology's director of quality services, and he embraced one of the biggest challenges in closing the disparities between rural and urban mortality rates: making NGS the norm for every eligible patient who walked in the door with an advanced solid tumor cancer. In doing so, Prakash would help lead an initiative that would expand genomic testing across all of Texas Oncology.

Texas Oncology's Precision Medicine Quality Initiative

As Prakash took on the quality services mantle, biomarker testing rates immediately hit his radar. Texas Oncology faced a challenge that was common in community settings—only about half the eligible patients were being tested, and sometimes rates were lower. "We were in the same boat as everybody else," he said in a February interview. "So, that's the initiative I thought we should do."

Testing rates had to be consistent no matter where patients were treated, Prakash said, whether it was in an urban center or at a clinic like his, located in eastern Texas at the state's border with Oklahoma. Thus, the goal of the Precision Medicine Quality Initiative was straightforward: All patients with advanced solid tumor cancers eligible for NGS testing should receive it.

But making this happen would require changes. "When we talk about biomarker testing, it's all about making it easy and

intuitive for the provider to order it,” Prakash said. “That’s the major reason why testing is not widely adopted—because it’s difficult, it’s time-consuming, [and] it’s expensive.”

Texas Oncology’s precision medicine program, led by Vice President Lori Brisbin, MS, MLS, partnered with Trapelo Health, creator of an online precision medicine decision support tool that could both integrate with iKnowMed, the existing electronic medical record (EMR) used by practices in The US Oncology Network, and streamline prior authorization.¹⁸ As Prakash explained, “The provider logs on, and then it guides you, step by step, based on the patient’s disease type, the stage, the site of disease, the pathology findings, the histology—and shows you what tests may be on guidelines and what tests you may want to order.”

Physicians at Texas Oncology can select tests from multiple labs, Prakash explained. “Once the order is placed, then our precision medicine team does the legwork on making sure that the specimen is shipped to the appropriate lab.” When tests results come back, they are seen right away, he said.

“Guidelines are continually evolving as advancements are made, and it is nearly impossible for physicians, especially those who are caring for many, many patients, to keep up-to-date all the time.”

—Ezra Cohen, MD,
chief medical officer, oncology,
Tempus AI

Data presented by Prakash and Brisbin at conferences show that pairing Trapelo with the iKnowMed EMR, alongside education efforts with physicians on the importance of biomarker testing, led to an explosion in the number of annual NGS orders in 2022 compared with prepandemic levels. Information presented at the Association of Cancer Care Centers’ 2023 National Oncology Conference showed that orders for solid tumor tests jumped from 4495 in 2019 to 14,702 in 2022.¹⁸ An abstract presented at the 2023 ASCO Quality Care Symposium tracked data from January 2022, prior to the launch of the initiative, through March 2023. It showed that test orders increased 150% during the study period, highlighting the ability of even a large, multisite practice to dramatically expand a precision medicine program with the right technology, partnerships, and commitment.¹⁹

Prakash said NGS via tissue testing remains the first choice, but other testing types are used if that is not feasible. Data from the ASCO Quality abstract show that 79% of the patients received somatic broad panel NGS, 16% received NGS on liquid biopsy, and 5% were single gene/small panel tests.¹⁹

Having centralized precision medicine resources makes all the difference for physicians in far-flung corners of the state, Prakash said, but changing the ethos to “test everyone” has also been an important part of the story. “I would say we test almost every single patient [who] walks in the door in Texas Oncology, no matter where they are. It could be in El Paso; it could be in Austin, downtown Dallas or Paris, Texas.”

The next big hurdle: reimbursement.

Prakash served a term as president of the Texas Society of Clinical Oncology, and during his tenure, the group worked to get state legislators to pass a law requiring biomarker testing, which took effect September 1, 2023.²⁰ This removes a huge barrier to testing because physicians are free from spending hours writing letters of medical necessity for an NGS panel. Before the law took effect, Prakash said he wrote these letters almost daily. And the need is growing, as the number of targetable mutations has exploded in just a few years, across multiple cancers.

“This policy change, to make sure insurance companies pay for testing and patients are not tasked with paying exorbitant fees, has been critical,” he said. “We’ve seen the results.”

Meeting Diverse Needs in Nashville

Through her role as assistant professor of pharmacy practice at Lipscomb University and her practice in Nashville General Hospital at Meharry Medical College, in Tennessee, Angie Maynard, PharmD, MS, CPGx, sees the promise and challenges of precision medicine through several lenses.

“The hospital serves our indigent population, including those [who] are incarcerated, those [who] are underinsured, or not insured at all,” she explained. “We also have some patients who are insured. So, we run the gamut.”

On the plus side, her institution has a strong partnership with Tempus AI, in which the testing company takes the lead in working with insurers, including for patients who are incarcerated. Tempus helps resolve transportation issues and, in some cases, goes to the patient if they cannot come to the hospital for a test, Maynard said. “We’ve been fortunate in that sense,” she said.

Ezra Cohen, MD, Tempus’ chief medical officer of oncology, explained how the partnerships work: Tempus Next, the company’s AI-enabled care pathway intelligence platform, integrates into an EMR to create alerts for individual patients, offering support for physicians to deliver guideline-based care.

“Guidelines are continually evolving as advancements are made and it is nearly impossible for physicians, especially those who are caring for many, many patients, to keep up-to-date all the time,” he said. “This type of technology makes it much easier for physicians to deliver personalized care as it seamlessly identifies care gaps and equips them with actionable insights at the point of care, supporting access to the most up-to-date, guideline-directed treatments.”

Clinical trials, Cohen said, have been shown to offer the best access to novel therapies, and the best outcomes for patients. To reach patients from underserved communities, Tempus’ TIME program works with community hospitals that care for these patients to activate trials on site, which he said makes it easier for patients to take part in studies.

“Through the TIME program, the need to travel and engage with far off academic medical centers in order to participate in clinical trials is eliminated,” Cohen said.

For Maynard, the biggest challenges these days come not with access to testing, but when biomarkers show that a patient with cancer needs a newer therapy, one that will require the patient to apply for financial assistance. Tennessee does not have Medicaid expansion under the Affordable Care Act, and Maynard has seen cases in which patients who are out of work due to cancer still miss qualifying for help. In some scenarios, patients who are too ill to live alone move in with a family caregiver, with unintended consequences.

“That’s our biggest problem. We’ve had several patients who have to live with family members in order to have supplemental care,” triggering a rejection because now the application must capture the entire household income. “You have to report everything for patient assistance, and that family member maybe makes just enough more money [to exceed the standard].”

Both Prakash and Maynard said today’s challenges revolve less around getting access to testing and more around the speed with which oncology care is changing—and the fact that clinical guidelines don’t always keep pace.

“It’s a moving target,” Prakash said, because as technology evolves, ctDNA testing improves, and more care incorporates the use of minimal residual disease testing.

Maynard agreed. “The one thing I’ll say about precision medicine, in the space we work in, is that I wish we had a board just for that—we have a tumor board, but not a board for precision medicine.”

A National Perspective on Payer Coverage

From his vantage point, Tempus’ Cohen has seen both positive changes in precision medicine reimbursement since the ASCO reports, as well as examples where restrictive definitions of “clinical utility” create barriers to access.

“Medicaid coverage for cancer genomic testing varies widely at the state level, because Medicaid is a joint federal-state program, meaning states have flexibility in setting their own coverage policies,” he said in an email to *EBO*. States that with Medicaid expansion have, “in some limited cases, created

broader coverage and reimbursement for precision medicine testing in the form of comprehensive genomic profiling.”

Cohen said that passing laws such as the one in Texas, which seek to cover all genomic testing outside of ERISA plans, offer “a theoretical guarantor of reimbursement in the Medicaid population, although the true impact of these mandates is yet to be realized.”

He explained that reimbursement is subject to interpretation, citing language that says coverage is provided “when the test provides clinical utility as demonstrated by medical and scientific evidence.” Restrictive definitions of clinical utility may be supported by non-current clinical literature citations, which Cohen said create barriers to reimbursement.

“This translates to coverage interpretations of clinical utility specified by a Medicaid payer policy that only reimburses small panel genomic testing mixed with mostly non-NGS technologies,” Cohen said. “These would remain outside of ASCO interpretation of precision medicine cancer care, and in some states, this trend is reducing access to coverage, often when benefits are delegated to a third-party lab benefits management company.”

Using AI to Help Clinicians Make Decisions

Technology gave Texas Oncology the boost it needed to make NGS the norm for solid tumor patients. Now, technology may offer solutions to the challenge Maynard outlined: how to easily interpret test results and make the best treatment choices, given the ever-increasing number of options.

The positive side of NGS is that it captures multiple genomic factors that could be driving cancer. However, the downside is that the FDA regulates the makeup of commercial lab reports, which cannot point physicians in a clear direction if there are multiple potentially actionable targets. That’s where specialized expertise is needed, and in the future, much of this decision-making will be driven by AI.

If 5 years ago community oncology was seen as catching up in precision medicine, today large practices and multipractice networks have the upper hand in a key area: Eighty percent of cancer care happens in the community,²¹ and practices have the data.

Several large practices have created precision medicine subsidiaries as they leverage their data to form partnerships and pursue research. Texas Oncology formed Precision Health Informatics, LLC (PHI); in July 2024, PHI announced a partnership with COTA to develop AI-driven precision medicine models.²² Just before the Florida Cancer Specialists & Research Institute joined The US Oncology Network last year, it formed Vita Nova Insights through its subsidiary CORE Ventures.²³

MiBA, or Meaningful InsightsBiotech Analytics, launched in April 2024, under leadership from the American Oncology Network and Ascend Technologies Group.²⁴ MiBA has lined up several partnerships: Guardant Health, Foundation Medicine, and more recently, Clarified Precision Medicine, which specializes in interpreting test results.

Clarified, highlighted in *EBO* in 2024 for its mission to cover the “last mile” in precision medicine,¹¹ seeks to bridge the interpretation gap by using AI to create ranked treatment recommendations, which are then reviewed by qualified experts. The resulting report highlights which treatment choices are considered first options—and which ones are not recommended, based on evidence that the patient will not respond.^{11,25}

Case studies of how the process works in a real-world setting are presented in a new white paper, “Unraveling the complexity of therapeutic decision-making,” which Clarified published February 26, 2025.²⁵ The white paper states that this technology is especially valuable to managed care and market access teams “to help improve patient outcomes and reduce costs.”

In an interview, Clarified CEO Rajni Natesan, MD, MBA, said community oncology practices were viewed as ideal candidates for the technology early on. But in cancer care today, only a small number of cases will make it to a tumor board, no matter the setting. “Guidelines change,” Natesan said. “Even at an academic center, where there is expertise, there is a scalability problem.”

If keeping pace with innovation is the next challenge, Texas Oncology’s Prakash is ready. Simply put, he said, every patient with advanced cancer eligible for NGS should receive it.

“It’s been a journey,” Prakash said. “It’s been a challenge in a lot of ways. To change habits—to change the culture—is difficult. Back when I started doing this, our testing rates were less than 50% of all advanced cancers...

“This is what we want to do for our patients and for the advancement of oncology.” ♦

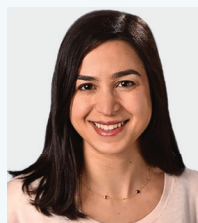
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SPOTLIGHT

Flatiron's Afghahi Addresses Testing Reimbursement Landscape, Opportunities in Exact Sciences Partnership

Produced by Mary Caffrey



AFGHAHI

ANOSHEH AFGHANI, MD, MPH, medical director, Flatiron Health; breast cancer medical oncologist.

ON FEBRUARY 5, 2025, health care technology provider Flatiron Health and testing company Exact Sciences, announced a new partnership to speed the use of clinical evidence generation for Exact Sciences' molecular residual disease (MRD) test, OncoDetect.¹ This is the latest in a series of partnerships Flatiron has announced with collaborators that serve community oncology; Flatiron has also partnered with artificial intelligence (AI) leaders Canopy and DeepScribe.

Flatiron and Exact Sciences have launched a prospective observational study, which will "evaluate the use of a tumor-informed ctDNA test for detecting MRD and predicting cancer recurrence in solid tumors," according to the statement. The study will enroll 1350 patients receiving standard-of-care regimens in community practice settings, collecting data through blood draws during and after therapy for up to 5 years.¹

MRD is becoming more important in treatment decisions in cancer care, and use of following the endorsement of MRD as a clinical trial end point by an FDA advisory panel.² Flatiron is well-positioned to help practices integrate use of MRD into clinical practice, given the footprint of OncoEMR, its oncology-specific, cloud-based electronic medical record (EMR) platform.

To gain insight into the testing and reimbursement landscape, as well as opportunities created through the Exact Sciences partnership, *Evidence-Based Oncology (EBO)* posed questions to Anosheh Afghahi, MD, MPH, medical director at Flatiron Health and a practicing breast medical oncologist.

EBO: What are the main barriers to bringing precision medicine into community practice?

AFGHAHI: Community oncologists adhere to the same national standards as their academic counterparts, however they may be more susceptible to reduced administrative and clinic support, while often caring for a higher volume of patients.

The increased burden faced by community oncologists creates barriers to providing precision medicine for a variety of reasons:

First, there are reimbursement challenges:

- Genomic or precision medicine assays (such as detection of minimal residual disease, or MRD) are inconsistently covered by insurance.
- Additionally, there is often less allotted time and resourcing to assess whether these genomic or precision medicine assays are reimbursed by individual healthcare coverage plans. The complexities of assessing this, and the wish to prevent high out of pocket costs for patients, may serve as a deterrent for many to get the testing done in certain clinical scenarios.

Second, there are challenges with patient and provider adoption:

- Given clinicians' high patient volumes in the community setting, there may be insufficient time to discuss the specific decision support tools in detail with each patient, thereby reducing the likelihood of patients wanting to pursue this option.
- Further, with the large volume of oncology studies conducted, it can be challenging for providers to keep up with evolving treatment guidelines. Decision support tools hold promise to address this challenge and provide a more tailored treatment plan for individual patients, if they can be more widely adopted across different healthcare settings.
- Finally, in addition to barriers specific to precision oncology care, patients in the community setting may also face socioeconomic factors, such as lack of transportation and reduced health literacy, that further contribute to disparities in care access more broadly.

EBO: We hear that payer coverage for testing is better than it was, but still not as good as it should be given the evidence. How would you describe the reimbursement landscape for testing?

"If a precision oncology assay is part of standard-of-care treatment guidelines, it is more readily performed and more consistently reimbursed. However, assays that are ordered based on emerging data or based on extrapolation from other clinical settings may not have guaranteed reimbursement."

—Anosheh Afghahi, MD, MPH, medical director, Flatiron Health

AFGHAHI: The reimbursement landscape for genomic and MRD testing is variable and depends on the disease type and cancer stage as well as individual coverage plans. In addition, even a test covered by insurance can generate out-of-pocket costs for patients.

If a precision oncology assay is part of standard-of-care treatment guidelines, it is more readily performed and more consistently reimbursed. However, assays that are ordered based on emerging data or based on extrapolation from other clinical settings may not have guaranteed reimbursement.

EBO: The partnership between Flatiron and Exact Sciences is focused on patients in the community setting. Why is the study focusing on these patients?

AFGHAHI: The majority of patients with cancer in the United States are treated in community settings. It is important to ensure that these patients have access to oncology trials, and that the results of these trials are representative of the current cancer patient population.

This is particularly relevant in the emerging space of MRD diagnostics, where there are still many questions on how and where these fit into providing high-quality cancer care.

Flatiron Health serves a large network of community oncology centers—including over 4200 clinicians at more than 1000 sites of care treating upwards of 2.5 million patients—where our technology is embedded into daily workstreams. Our established network enables this multi-arm study to be implemented seamlessly into routine practice, thereby reducing the research participation burden for providers and research staff.

EBO: The Exact Sciences announcement noted the need to reach diverse groups of patients. Why is this important? Is it more important in some tumor types than others?

AFGHAHI: It is important to have a diverse group of patients enroll in trials to ensure that learnings are reflective of the entire cancer patient population. Many studies on the effectiveness and safety of cancer treat-

ments and diagnostic tools lack participant diversity, leading to gaps in data that can limit the generalizability of the results in guiding treatment recommendations.

Increasing representativeness is important across many types of studies and tumor types. This is of utmost importance in tumor types that are more often diagnosed in historically underrepresented patient populations.

If we restrict access to a study to a narrower group of patients rather than a large, diverse group, the outcomes of the study may not be reflective of patients treated in real-world settings. ♦

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Trump's Stance Doesn't End Need for Diversity in Clinical Trials

MARY CAFFREY

CONTINUED FROM COVER

Hispanic—so that one tugged at my heartstrings...when I saw that substantial improvement.”³

Rau's presentation at the 66th American Society of Hematology Annual Meeting and Exposition underscored why the FDA and professional societies have spent a decade pushing for clinical trial enrollment to mirror the US population—or, preferably, those most likely to develop the disease being studied. It is the same reason investigators who study multiple myeloma hope to enroll more Black patients⁴ and why specific lung cancer trials enroll more Asian patients⁵: Genetic differences and underlying comorbidities mean some patient populations face greater risk from certain cancers than others. Knowing how drugs will work among the patients most likely to need them is crucial.⁴⁻⁶

In June 2024, the FDA addressed this in a draft guidance, calling for pharmaceutical companies to submit diversity action plans for certain trials and to develop strategies to boost enrollment among underrepresented groups.⁷ But now, the future of the FDA's effort is in doubt. On January 23, 2025, the guidance web page vanished as the Trump administration took early, aggressive steps to eliminate diversity, equity, and inclusion (DEI) programs in the federal government, which included canceling National Institutes of Health (NIH) grants and removing online data sets.^{8,9}

The courts have reversed some actions, and the FDA guidance page was restored with a disclaimer.¹⁰ But elsewhere, the

administration has taken aim at DEI efforts in higher education and the private sector. Although not directed at clinical trials, these steps could affect progress toward building a more diverse workforce, which experts say is necessary to build trust with underrepresented communities.¹¹ Major institutions, such as the Fred Hutchinson Cancer Center, folded their DEI programs to avoid losing federal research funds.¹²

Yet the need for trials that reflect populations taking new drugs has not disappeared. Experts say giving all patients access to trials and making studies reflect the population in need is not a feel-good exercise but a scientific necessity. This is due to gains in precision medicine, demographic shifts, and increased awareness of the role of health-related social needs in clinical outcomes.¹³⁻¹⁵

Martin Makary, MD, MPH, confirmed on March 25, 2025, as the new FDA commissioner, told a Senate committee that he supported diverse clinical trials, but whether that translates into a final guidance remains to be seen. “I believe in common sense, and I believe in clinical trial diversity,...so I believe if you're going to [extrapolate] results to the general population, you should have results in those populations [for which] you're making recommendations,” Makary said.¹⁶

Prior to January, the FDA had made slow but steady progress in its pursuit of broader representation in drug trials. Pharmaceutical companies built stronger ties with community practices, enabling patients to access new drugs without traveling.



RAU

Rachel E. Rau, MD, associate professor, pediatrics, Seattle Children's.



BURRIS

Howard A. “Skip” Burris III, MD, president, Sarah Cannon Research Institute.

“The FDA has been helpful with their guidance to inform biotech about wanting the clinical trial patients to try to mirror the US Census, to have [the population] look like the patients that are going to be prescribed,” said Howard A. “Skip” Burris, MD, president of Sarah Cannon Research Institute, which now extends across 24 states and 250 sites of care.

Concerns about patient access touch on issues beyond race and ethnicity, said Burris, who was president of the American Society of Clinical Oncology (ASCO) from 2019 to 2020. He highlighted efforts by Monica Bertagnolli, MD, formerly ASCO president and recently director of NIH, to give rural patients better trial access.¹⁷ Incidence of cancer types can also vary from country to country, Burris said, and the FDA has worked to ensure that trials enroll enough US patients.

“While clinical trials are very strict in terms of eligibility criteria, the fact is, once that drug has a label, doctors are giving it to everybody,” he said. “So, if it’s not been studied in different ethnic groups and it hasn’t been studied in different populations by age or comorbidities or whatever disparities might exist, you really are flying a little bit blind with those patients.”

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Tanya B. Dorff, MD, a professor in the Department of Medical Oncology and Therapeutics Research and section chief, Genitourinary Disease Program, at City of Hope, agreed that the scientific community would remain committed to improving patient access to trials, regardless of the political environment. Dorff spoke with *Evidence-Based Oncology (EBO)* during the ASCO Genitourinary (GU) Symposium, February 13 to 15, 2025. Some attendees were shaken by reports of NIH funding changes and layoffs.

“We’re always thinking about how to reduce clinical trial burden [and] unnecessary exclusionary criteria that result in bias as to which patients end up enrolling. That’s not going to go away because of whatever is happening now,” Dorff said. “That thought process, and that initiative in how we write our trials, how we talk to patients, how we retain them, [is] not just about enrolling patients but *keeping* them on study. And I am hopeful that we will...continue to make improvements in [the] diversity of our accrual.”

Executive Orders That Could Affect Trials

On the day he returned to office, President Trump issued an executive order (EO) relevant to the FDA draft guidance. As attorneys from Crowell & Moring LLP noted, the order directed all executive departments and agencies to end DEI efforts by

eliminating “discriminatory and illegal preferences, mandates, policies, programs, activities, guidance, regulations, enforcement actions, consent orders, and requirements.”¹⁸ According to the firm’s notice, the order reined in the Office of Federal Contract Compliance Programs’ authority and instead called on agencies to “scrutinize the DEI practices of private sector employers.”¹⁹ As the attorneys pointed out, the EO bars the office from promoting diversity or enforcing affirmative action. However, the attorneys also wrote, “Significantly, the EO is directed at DEI programs and practices that violate federal antidiscrimination laws—not *all* DEI efforts.”¹⁹ Days later, Crowell attorneys noted that the FDA guidance was required under the Food and Drug Omnibus Reform Act (FDORA), which has not been rescinded.²⁰ FDORA requires final guidance to be issued by June 26, 2025.

Following a court order on February 11, 2025, to restore government websites, the FDA draft guidance features a disclaimer referring to a separate EO on the transgender community. The disclaimer states in part, “Any information on this page promoting gender ideology is extremely inaccurate and disconnected from the immutable biological reality that there are two sexes, male and female.”⁷

The Need for Trials to Reflect Populations

Many factors are behind the call for greater diversity in clinical trials, but the most basic one is America’s changing demographics: US Census data released in August 2021 showed that the White population makes up 58% of the United States, the smallest share in the nation’s history. Hispanic Americans now account for 18.7% of the population, with Black Americans at 12.1% and Asian Americans at 7%. Notably, the White population is shrinking; it fell from 223.6 million in 2010 to 204.3 million in 2020.²¹ The FDA reported that White patients are overrepresented in clinical trials, accounting for 75% of participants. In contrast, Black patients (8%) and Hispanic patients (11%) are underrepresented.²²

Lack of representation in clinical trials is one reason Black patients are more likely to die from cancer, according to the American Cancer Society, whose journal featured the article “Cancer Statistics for African American and Black People, 2025” in February.²³ Although outcomes gaps have shrunk due to declining smoking rates among younger patients, over the past 5 years, the authors wrote, “Black men had 16% higher mortality than White men despite just 4% higher incidence, and Black women had 10% higher mortality than White women despite 9% lower incidence.” Mortality rates for Black patients are twice as high in prostate, uterine corpus, and stomach cancers and myeloma and are 40% to 50% higher in colorectal, breast, cervical, and liver cancers.²³

Diversity in enrollment is more important when a given cancer poses a greater risk to minority groups. For example, *EBO* reported in November 2024 that Black patients accounted for about 1% of enrollment in 2 recent trials on cutting-edge quadruplet therapy in frontline multiple myeloma (MM). Meanwhile, Black patients make up 20% of all those with MM and will account for 24% in 2035.⁴ As scientists learn more about the way genetics affect disease progression, the need for more representative trials grows. Findings presented at the most recent meeting of the International Myeloma Society show that race plays a major role in the pace of “immunologic aging,” which tells scientists how quickly precursors to MM will progress to full-blown disease.²⁴

Finally, there is recognition that social factors such as tobacco or alcohol use or access to adequate food, housing, or transportation affect trial outcomes. A patient’s ability to afford cost-sharing may also affect results if patients are less likely to adhere to a medication.²⁵



Martin Makary, MD,
MPH, FDA Commissioner.



Tanya B. Dorff, MD,
professor and GU section
chief, City of Hope.



Karen Winkfield, MD,
PhD, professor, Vanderbilt
-Ingram Cancer Center.



Kasey Boynton, MPH,
senior director, Sanofi.



William L. Dahut, MD,
chief scientific officer,
American Cancer Society.



MAYNARD
Angie Maynard,
PharmD, MS, CPGx,
assistant professor,
Lipscomb University.

Examples like this show why payers are increasingly skeptical about covering expensive cancer drugs when trials fail to show how the drug will work across the population. More payers today rely on real-world evidence (RWE) to gauge the “true performance of therapies,” according to a 2024 report.²⁶

What happens in the clinic when trials don’t produce data on some groups? Burris said a lack of information can create hesitancy in prescribing a newer drug to a patient. For example, if a patient is older than the trial population, “sometimes, without data, you make the decision to cut the dose of a therapy because you want to be cautious” and avoid adverse events. “On the other side of the coin, sometimes you just plow ahead and give the full dose,” which can cause toxicity.

The need for trials to have a mix of patients matching those taking cancer drugs “has been shown time and time again,” he said. “There is a good scientific rationale for the incorporation of all patients.”

“We’re always thinking about how to reduce clinical trial burden [and] unnecessary exclusionary criteria that result in bias as to which patients end up enrolling. That’s not going to go away because of whatever is happening now. That thought process, and that initiative in how we write our trials, how we talk to patients, how we retain them, [is] not just about enrolling patients but keeping them on study. And I am hopeful that we will...continue to make improvements in [the] diversity of our accrual.”

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professor, Department of Medical Oncology
and Therapeutics Research,
section chief, Genitourinary Disease Program,
City of Hope

Strategies for Improving Representation in Trials

Most DEI efforts gained momentum in the years following the COVID-19 pandemic but calls for reducing disparities in cancer care started years ago. In 2009, ASCO published a statement that called for a multipart strategy: boosting awareness of disparities and supporting research into their causes, improving patient access, and increasing the ranks of doctors and trial staff from underrepresented groups.²⁷ In 2017, ASCO offered a specific blueprint for improving workforce diversity,²⁸ and in 2022, partnered with the Association of Cancer Care Centers (ACCC) to educate community oncologists on enrolling patients in clinical trials.²⁹

The lead author of the 2017 ASCO article, Karen M. Winkfield, MD, PhD, is now a professor of radiation oncology and associate director for community outreach and engagement at Vanderbilt University Medical Center and executive director of the Meharry-Vanderbilt Alliance in Nashville. Interviewed at a session of the Institute for Value-Based Medicine, Winkfield said a key to improving clinical trial enrollment rates for everyone is making trials the norm, not the exception.

ASK PATIENTS TO ENROLL. “We know that, first of all, not enough people are participating in clinical trials,” Winkfield said. “Oftentimes, the No. 1 reason people don’t enter into clinical trials is because there’s not one available.... The second most common reason why people don’t enter into clinical trials [is] they’re not asked. Part of what we try to do at Vanderbilt is create a culture where clinical trials are part of the fabric. It’s not something different or extra; it’s part of the offerings.”³⁰

ENROLLMENT CRITERIA MATTER. Burris said work by the FDA and others has shown that broader enrollment criteria can significantly impact who participates. Kasey Boynton, MPH, senior director of global operations and partnerships for Sanofi, highlighted this approach in a poster presented at the recent ACCC Annual Meeting & Cancer Center Business Summit in Washington, DC. Boynton said minor adjustments, such as increasing body mass index criteria by 2 points, could greatly affect enrollment eligibility. Overlaying RWE on trial criteria helped identify these opportunities, she said.³¹

“Applying these tactics to other oncology trials may improve low enrollment of minority groups currently observed in such trials, thereby enabling a better understanding of therapy safety and efficacy in minority populations,” the researchers wrote.

PARTNERSHIPS WORK. A separate poster summarized findings from an October 2024 ACCC multistakeholder summit on removing trial barriers.³² Participants concurred with calls to adjust trial designs to reflect RWE and to better educate the clinical trial workforce. They also cited the necessity of engaging community partners well before trials need patients—long-term relationships and action plans that address social determinants of health are needed. Partnerships also help pharmaceutical companies identify better locations for enrolling patients and conducting studies to keep patients from dropping out of trials.

Angie Maynard, PharmD, MS, CPGx, assistant professor of pharmacy practice at Lipscomb University College of Pharmacy, Nashville, described an extraordinary partnership between Meharry Medical College, where she conducts clinical trials, and state officials who help Meharry give incarcerated patients access to cancer trials. However, it is not an easy process.

“It’s hard to get them enrolled in clinical trials,” Maynard said. If trials are to be open to groups of incarcerated patients, it should be easier to ensure the patients follow all protocols. “We need a more seamless process.”

USING AI TO IDENTIFY PATIENTS. Both ACCC summit participants and Winkfield say using artificial intelligence (AI) can help identify trial participants in less time than a regular appointment would allow.

“It’s really hard when you have a lot of patients walking through the door to screen every single patient for eligibility,” Winkfield said. When a physician’s schedule gets crowded, AI may be able to do screening legwork before a patient arrives, so the physician already knows if a trial is possible.³⁰

What About the Industry?

The pharmaceutical industry has made significant investments in developing trials that reflect patient populations. In 2021, the Pharmaceutical Research and Manufacturers of America, or PhRMA, published a white paper with Deloitte on meeting the challenges of clinical trial diversity. At that time, the authors reported results of an industry survey that found nearly all responding companies (97%) were taking specific measures to address access issues, while 71% of companies “are considering the needs of diverse populations when designing clinical trial protocols,” which included moving clinical trial sites closer to where patients live.³³ By October 2024, when the FDA held a symposium with ACS on reducing clinical trial barriers, at least 80% of the action plans had been proactively submitted.³⁴

As *EBO* went to press, pharmaceutical companies appeared to be leaving policies on clinical trial diversity intact. Four companies—Eli Lilly and Company, Bristol Myers Squibb, Sanofi, and Genentech—confirmed their commitment to trial diversity in statements to Fierce Biotech on February 27, 2025.³⁵ Other pharmaceutical companies with online statements in support of clinical trial diversity as of March 25, 2025, included: Amgen, GSK, Merck, and Pfizer.³⁶⁻³⁹ Johnson & Johnson hosts a page titled Our Race to Health Equity, with

statements on diversity in clinical trials and workforce development, among other topics.⁴⁰

Privately, industry leaders say the biggest threat to clinical trials is the attempted policy change with NIH grants, which would cap indirect cost recovery at 15%. ASCO has been active in a coalition of specialty groups seeking to overturn this change.⁴¹

ACS is moving ahead with diversity initiatives. ACS Chief Scientific Officer William L. Dahut, MD, used his keynote address at the ASCO GU Symposium to spotlight training programs through ACS' Center for Diversity in Cancer Research. He promoted a new study, VOICES of Black Women, that will enroll 100,000 Black women aged 25 to 55 years in the US with no cancer history to collect online surveys and data twice a year, aiming to improve outcomes over time.^{42,43}

To Maynard, collecting good data is the heart of the issue. Like others, she worries about NIH cuts because they will make it harder to run trials that meet today's standards, including enrolling a diverse patient population.

"Historically, we have kept a particular patient population and run the trials based on that patient population, and then we try to extrapolate it...to everyone," she said. "And that's not always the best thing to do. So, the more diverse the population we have, the better data we have." ♦

Maggie L. Shaw contributed to this article.

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Making PIN and Telehealth Work Together—It Can Be Done

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CONTINUED FROM COVER

A Communication Gap

To be clear, health care providers and any community-based organizations they contract with to provide PIN can unequivocally utilize telephone and telehealth technology to render PIN services. When billing for PIN services that utilize telephone and telehealth technology, they are not billed as telehealth services.

CMS has been explicit, stating in a health-related social needs frequently asked questions document on Community Health Integration (CHI), PIN, and PIN-Peer Support (PS) that “CHI, PIN, and PIN-PS can be performed using telecommunications technology... [and] it was not necessary to add these services to the Medicare Telehealth Services List.”⁵

To understand this paradox, we first need to understand what Medicare means when the agency labels a service as a telehealth service.

Federal regulations codify the definition of telehealth that Medicare must follow.⁶ In brief, Medicare telehealth is a technology that enables real-time (synchronous) interactive audio and visual between the patient and provider. When the provider is technologically capable of providing this interactive audio-video technology, but the patient does not consent to, or is not technically capable of, using interactive video, interactive audio-only technology (telephone) can fulfill the telehealth technology requirement for approved services.

However, the services approved for the Medicare Telehealth Services list⁷ aren't simply those that can safely and effectively be delivered via telecommunications technology; they are those that pass a 5-step review and approval process from Medicare. Criteria in each step must be satisfied before proceeding to the next step. Medicare explains the review process in detail in their Review Criteria, published on the CMS website and in the Physician Fee Schedule.⁸ A brief review of the process follows.

STEP 1. Determine whether the service is separately payable under the PFS.

If the service is not approved for payment under the Medicare Physician Fee Schedule, it cannot be approved as a Medicare telehealth service.

STEP 2. Determine whether the service is subject to the provisions of section 1834(m) of the Act.

Not every service paid under the Physician Fee Schedule is subject to the Act that regulates telehealth. To be considered a potential telehealth service, “at least some elements of the service, when delivered via telehealth, are a substitute for an in-person, face-to-face encounter, and, all of [the] face-to-face elements of the service are furnished using an interactive telecommunications system...”⁸ By CMS definition, a service can only be considered a telehealth service if telecommunication technology is used to *replace* an inherently face-to-face patient interaction. Services that are not inherently face-to-face do not meet the threshold to be subject to the Act and are not appropriate to include on the telehealth list.

STEP 3. Review the elements of the service as described by the HCPCS [Healthcare Common Procedure Coding System] code and determine whether each of them is capable of being furnished

using an interactive telecommunications system as defined in 410.78(a)(3).⁹

CMS reviews the long description of the HCPCS code, identifies the required elements of the service, and evaluates whether the nonoptional elements can be rendered via interactive audio-visual technology. Optional elements of the service are not evaluated.

STEP 4. Consider whether the service elements of the requested service map to the service elements of a service on the list that has a permanent status described in final rulemaking.

CMS examines each required element of the service (as identified in step 3) to determine if a permanently approved telehealth service already exists that contains that individual element. In short, has CMS already determined that the individual required elements are safe and effective when provided via telehealth technology?

STEP 5. Consider whether there is evidence of clinical benefit analogous to the clinical benefit of the in-person service when the patient, who is located at a telehealth originating site, receives a service furnished by a physician or practitioner located at a distant site using an interactive telecommunications system.

CMS reviews evidence to determine if patients receive the same benefit when a service is rendered via telehealth as they do when it is provided in person.

In the 2024 Final Rule, CMS explained the reasoning for not adding PIN to the Telehealth List.¹ While CMS makes payment for PIN services, satisfying the first step, these services do not satisfy step 2 criteria. CMS included this logic in the Rule: “The elements of the individual services in the code descriptors may not typically require a face-to-face interaction, and therefore PIN (G0023, G0024, G0140, and G0146) and CHI (G0019, G0022) would not be considered as potential Medicare telehealth services under section 1834(m) of the Act.” Because PIN is not an inherently face-to-face service, it cannot be considered a telehealth service.

This is not unique. CMS has used this same reasoning to explain why other care management services such as Chronic Care Management (99490) and Principal Care Management (99424) are not on the Telehealth List. Digital E/M visits (99421-99423), Virtual Check-Ins (G2012), Ambulatory Blood Pressure Monitoring (93784, 93786, 93788, and 93790), Remote Patient Monitoring (99453, 99454, 99457, and 99458), and e-Consults (99446-99452) are all services that do not—and cannot—appear on the Telehealth List.

However, just because a service is not considered a telehealth service does not mean that telecommunications technology may not be utilized to render the care described in the HCPCS code. For instance, Chronic Care Management (CCM) and Principal Care Management (PCM) are well known to include telephonic care to patients, as well as care that does not include patient interaction, such as communication with other care providers. In the Final Rule, CMS clarifies that “the possible use of asynchronous communications technology to support the provision of [PIN] services suggests that our policies for other communications-based technology services should apply instead.”¹ In subsequent clarifying documentation,⁵ CMS states, “CHI, PIN, and PIN-PS can be performed

using telecommunications technology. Because these services are ordinarily furnished outside of an in-person, face-to-face visit, they are outside the scope of Medicare telehealth services, like other care management services. For this reason, it was not necessary to add these services to the Medicare Telehealth Services List.”

Use Technology—and Submit Claims

Providers can and should utilize telecommunications technology—whether telehealth, telephone, patient portal messages, secure text messages, or otherwise—to furnish navigation services to patients. When submitting claims, it is not necessary to amend the HCPCS code with modifier -93 or -95 because PIN is not billed as a telehealth service.

This is beneficial to providers. Since PIN services are not subject to telehealth rules, they are free of the statutory limitations on telehealth, including rurality requirements for patient eligibility and the necessity for patients to be located at an approved Originating Site when receiving services. If Congress does not act to extend flexibilities or create more permanent expansions to Medicare telehealth access by March 31, 2025, PIN and other care management services will not be impacted. Patients can continue to receive these services regardless of where they live and where they are when they receive communications from the care team.

This does not mean there aren't other challenges to implementing PIN in practice, but we have successfully integrated PIN into the options for care management that we utilize in our dementia clinic. When discussing PIN implementation with other providers, there are several common misconceptions and workflow considerations that have prevented care teams from receiving reimbursement for this important care.

A common misunderstanding is that PIN is for patients with a serious diagnosis; providers may wait to enroll patients in PIN until a diagnosis of a serious condition is made. However, in the 2024 Final Rule, CMS clarifies that “a definitive diagnosis is not required before the practitioner makes a clinical determination that the patient has a serious high-risk condition.”¹¹ While they give examples of suspected or confirmed conditions that are likely to benefit from PIN, including cancer, dementia, heart failure, and HIV/AIDS, they leave the determination that a condition is serious and high risk to the clinical judgment of the provider. The condition, whether suspected or confirmed, must meet the following parameters:

1. The condition is expected to last at least 3 months.
2. The condition places the patient at risk of hospitalization, nursing home placement, acute exacerbation/decompensation, functional decline, or death.
3. The condition requires development, monitoring, or revision of a disease-specific care plan.

Providers are sometimes confused about which care management service a patient needs; when a patient is seen at the initiating visit, it may be difficult to ascertain the patient's exact needs and which care management service will provide the greatest benefit. Some guidelines are clear: If the patient does not have a confirmed qualifying diagnosis or diagnoses, the patient cannot be enrolled in Principal Care Management (PCM) or Chronic Care Management (CCM), leaving PIN as the more appropriate option. When a patient qualifies for multiple services, we have found that the easiest option is to obtain consent for all services that may be applicable to the patient. Then we ensure the need for navigation is clear in the treatment plan and deliver care according to the patient's needs with clear documentation in the medical record. At the end of the month, we review the care delivered to the patient and bill for the appropriate service(s).

Providers are also confused about what types of care are appropriate to document as part of PIN. For this, it's best to look at the long description of the service finalized in the 2024 Rule, which indicates that “tailored support as needed to accomplish the practitioner's treatment plan” is part of the PIN service.¹ This support should address barriers to the treatment plan, which may include:

- Obtaining prior authorization/precertification for services that are part of the treatment plan
- Helping the patient enroll in state, nonprofit, health system, or

pharmaceutical financial assistance programs to address costs associated with their care

- Obtaining and sharing medical records
- Locating and/or assisting the patient/caregiver to access resources to overcome transportation difficulties, food insecurity, or other health-related social needs
- Educating the patient/caregiver about the condition and treatment plan
- Providing emotional support to help the patient cope with the condition and adjust to new routines
- Scheduling appointments or services that are part of the treatment plan
- Addressing questions, concerns, or objections to the treatment plan

Clinically oriented aspects of care, such as medication adjustments and discussion of the patient's adverse effects of treatment, may be a part of navigation but are better represented by other care management services, such as PCM.

A final barrier to PIN is patient cost sharing. Like all forms of care management, cost sharing for PIN is required in traditional Medicare, but patient contributions are set at 20%, subject to the deductible. For 2025, the Part B deductible is \$257.¹⁰ Nationally, the average nonfacility co-pay for PIN services is \$15.59 for the first 60 minutes of care each month, and \$9.70 for each additional 30 minutes of care in the month. While Medicare Advantage plans may have alternative cost-sharing requirements, they are prohibited from charging drastically more than what is charged in traditional Medicare. These plans may even waive cost sharing for select care management services. High patient cost sharing is more typical when patients are insured through a commercial or employer-sponsored plan, which may not cover or may require higher patient cost sharing for Medicare-specific services. Providers may need to contact individual plans to determine the best way to bill for navigation or negotiate a condition-specific management code or payer-specific navigation code for billing these services.

Medicare's approach to PIN services provides significant opportunity for providers to receive reimbursement for navigation while working to improve access to care and ensure a coordinated care experience. The flexibility Medicare has allowed to render these services using a variety of telecommunication technologies reflects their commitment to health equity. ♦

AUTHOR INFORMATION

Grace Showalter MHIIM, BSN, RN, is the founder and CEO of Vitruvian Consulting Group and Mindful Integrative Medicine, both based in Danville, Pennsylvania. Showalter helps health care organizations manage the revenue cycle so they can deliver appropriate patient care while maintaining fiscal stability and care team satisfaction. With expertise in population health, value-based care, and Medicare reimbursement, she advises providers and digital health companies on ways to address patient need, clinical workflows, and reimbursement requirements, with a focus on serving the primary care population.

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