ADVANCES IN ONCOLOGY

- The latest in breast cancer
- Lung cancer biomarkers
- CAR-T cell therapy

PLUS

Pharmacy/Formulary Development
Payers ramp up vaccination efforts

Technology
10 telehealth takeaways

Industry Analysis
The SDOH craze
We are raising the bar in cancer care to deliver the best possible life outcomes

21st Century Oncology is now part of GenesisCare, which means your members and patients benefit from the collective expertise of 5,000 global physicians and healthcare professionals. In the US, we have 300 cancer centers with over 125 radiation oncology locations to help bring the right care close to home.

We are dedicated to delivering cutting edge, high-quality and cost-effective cancer treatments.

All of this means that we are providing access to world-class cancer care to deliver the best possible life outcomes for cancer patients.

genesiscare.com/USA
Chairman’s Letter

Dethroning the emperor

We often find eloquence in dire circumstances, limning dark topics and fearsome subjects. Siddhartha Mukherjee’s Pulitzer Prize-winning *The Emperor of All Maladies* is such a place. Explanations that in other hands turn abstruse and jargon-choked become clear in his. Cancer occurs, Mukherjee writes, when the powerful genetic circuits that regulate cell division break down. “Cancer cells grow faster, adapt better,” he writes. “They are more perfect versions of ourselves.”

Mukherjee’s book and the new therapies that disable these more perfect versions of ourselves came to mind as we were putting together the stories about oncology advances featured in this issue of Managed Healthcare Executive.

Karen Appold’s story on new breast cancer treatments mentions Trodelvy (sacituzumab govitecan-hzly) and Enhertu (fam-trastuzumab deruxtecan-nxki) are search-and-destroy agents that first recognize cancer cells and then a drug is deployed to disable them. Keith Loria’s piece on lung cancer biomarkers reports on the growing number of therapies designed to attack cancer cells in bespoke fashion. The National Comprehensive Cancer Network’s guidelines for non-small-cell lung cancer recommends testing for seven different types of biomarkers, a list that is only going to get longer. Questions remain about the best way to conduct these tests; with next-generation sequencing means they can be done in, basically, one fell swoop. But as Loria’s story mentions, the excitement about biomarker-guided therapy shouldn’t cloud clinical judgment. Standard therapy is still going to be the best choice for many patients.

Mukherjee book came out in 2010, so it predates CAR-T cell therapy and current era of immunotherapy. That’s a reminder about the pace of innovation in oncology in recent years. And Mary Caffrey’s Q&A with Duncan Allen, M.H.A., vice president of clinical services for OneOncology, brings up the prospect of moving CAR-T cell therapy out of rarefied academic centers into community settings. The pathway from cutting edge to commonplace seems to be getting shorter.

We’re long ways from vanquishing cancer. But perhaps we are headed to a time when the emperor of all maladies is less ominous, a disease more managed and outsmarted than dreaded and deadly.

Mike Hennessy Sr.
Chairman and Founder
of MJH Life Sciences
COVER STORY

DRUGS IN THE PIPELINE
8 Positive results for Darzalex, Jakavi to be reported at ASH

PHARMACY/FORMULARY DEVELOPMENT
24 Insurers take up mantle to ensure immunizations

TECHNOLOGY
26 10 takeaways about the telehealth boom

POPULATION HEALTH MANAGEMENT
30 Using “nudges” to change healthcare

INDUSTRY ANALYSIS
32 Addressing SOOH: Can healthcare take them on effectively?

DEPARTMENTS
4 Editorial Advisory Board
5 In Brief

ADVANCES IN ONCOLOGY

11 Five important developments in breast cancer treatment
14 Biomarkers for guiding lung cancer treatment
16 Bringing CAR-T cell therapy to the community
22 Headed in the right direction: Cancer mortality rates are going down

© 2020 MultiMedia Medical LLC. All rights reserved. No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including by photocopy, recording, or information storage and retrieval without permission in writing from the publisher. Authorization to photocopy items for internal/educational or personal use, or for the internal/educational or personal use of specific clients is granted by MJH Life Sciences™ for libraries and other users registered with the Copyright Clearance Center, 222 Rosewood Dr., Danvers, MA 01923, 978-750-8400 fax 978-646-8700 or visit http://www.copyright.com online. For uses beyond those listed above, please direct your written request to the Permissions Dept. email: etemple-morris@mmhgroup.com

Managed Healthcare Executive® (ISSN 1533-9300, Digital ISSN 2150-7120) is published monthly by MJH Life Sciences™, 2 Clarke Drive, Suite 100, Cranbury, NJ 08512. Subscription rates: 1 year $99.00, 2 years $145.00 in the United States & Possessions; 1 year $122.00, 2 years $173.25 in Canada and Mexico; 1 year $192.00, 2 years $295.00 in all other countries. For air-expedited service, include an additional $87.00 per order annually. Single copies (prepaid only): $9.00 in the United States, $22.00 all other countries. Back issues, if available: $15.00 in the U.S.; $17.00 all other countries. Include $6.85 per order plus $2 per additional copy for U.S. postage and handling. If shipping outside the U.S., include an additional $10 per order plus $3 per additional copy. Periodicals postage paid at Trenton, NJ 08650 and additional mailing offices. POSTMASTER: Please send address changes to Managed Healthcare Executive®, PO Box 457, Cranbury NJ 08512-0457.

© 2020 MultiMedia Medical LLC. All rights reserved. No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including by photocopy, recording, or information storage and retrieval without permission in writing from the publisher. Authorization to photocopy items for internal/educational or personal use, or for the internal/educational or personal use of specific clients is granted by MJH Life Sciences™ for libraries and other users registered with the Copyright Clearance Center, 222 Rosewood Dr., Danvers, MA 01923, 978-750-8400 fax 978-646-8700 or visit http://www.copyright.com online. For uses beyond those listed above, please direct your written request to the Permissions Dept. email: etemple-morris@mmhgroup.com

Managed Healthcare Executive® (ISSN 1533-9300, Digital ISSN 2150-7120) is published monthly by MJH Life Sciences™, 2 Clarke Drive, Suite 100, Cranbury, NJ 08512. Subscription rates: 1 year $99.00, 2 years $145.00 in the United States & Possessions; 1 year $122.00, 2 years $173.25 in Canada and Mexico; 1 year $192.00, 2 years $295.00 in all other countries. For air-expedited service, include an additional $87.00 per order annually. Single copies (prepaid only): $9.00 in the United States, $22.00 all other countries. Back issues, if available: $15.00 in the U.S.; $17.00 all other countries. Include $6.85 per order plus $2 per additional copy for U.S. postage and handling. If shipping outside the U.S., include an additional $10 per order plus $3 per additional copy. Periodicals postage paid at Trenton, NJ 08650 and additional mailing offices. POSTMASTER: Please send address changes to Managed Healthcare Executive®, PO Box 457, Cranbury NJ 08512-0457.
Mission
Managed Healthcare Executive® provides healthcare executives at
health plans and provider organizations with analysis, insights, and strategies
to pursue value-driven solutions.
Prime research a thumbs-up for Entresto — with caveats

Entresto (sacubitril-valsartan) didn’t get a lot of love from payers after it was approved in 2015 because of its expense and the crowded armamentarium for heart failure. But Entresto has since made its way into guidelines for reduced ejection fraction heart failure, sometimes called systolic heart failure. And now research done by pharmacy benefit manager (PBM) Prime Therapeutics may give the combination drug a further boost, although there some catches.

Patrick Gleason, Pharm.D., the PBM’s assistant vice president of health outcomes, presented findings at the Academy of Managed Care Pharmacy Nexus meeting in October that showed Entresto reduced annual total cost of care for reduced ejection heart failure patients by $10,177, on average, a 22% decrease. The study, a before-and-after Entresto comparison, included 658 commercially insured patients.

Their annual pharmacy costs went up by $5,547 after they started taking Entresto, but that was offset by a $15,724 decrease in their medical costs, most of it coming from reduced hospitalizations.

Gleason says the results support removing prior authorization requirements for Entresto. Prime has negotiated a value-based contract for Entresto with the drug’s maker, Novartis, that is based on the total cost of care. That contract was the impetus for Prime removing prior authorization for Entresto, according to a company press release about Gleason’s research.

One possible problem with this research is the use of patients as their own historical controls. Such a design can invite confounding. But more importantly, the 658 patients were adherent patients and so a best-case scenario. When the analysis included 378 nonadherent patients, the total cost of care decreased by 2% instead of 22%. The clear implication is that for health plans and PBMs to realize savings from Entresto, they will have to work at making sure people take the drug as prescribed.

U.S. looks bad in international COVID-19 comparisons

The United States usually doesn’t fare very well in international health comparisons. The country’s healthcare ranks among, if not the, most expensive. The outcomes, as measured by metrics such as life expectancy at birth, are not top tier, especially when the U.S. is compared to well-off countries in Europe and Asia. The story with COVID-19 is similar, according to data reported recently by Kaiser Family Foundation. Among the dozen developed countries included in the foundation’s analysis, only Belgium, at 90.4 COVID-19-related deaths per 100,000 population, was worse than the U.S., at 66.5 COVID-19 deaths per 100,000. By contrast, Japan’s rate of 1.3 COVID-19 deaths per 100,000 is stunningly low, as is Australia’s (3.6 per 100,000) and Germany’s (11.7 per 100,000).

Kaiser’s ranking of the leading causes of death is also sobering. COVID-19 is on course to being the third leading cause of death in the U.S. in 2020, behind only the perennial leaders, heart disease and cancer. In Japan, COVID-19 is on track to being the 29th leading cause of death and in Germany, the 17th.

Managed Healthcare Executive.com
In Brief

ACOs edging toward downside risk

The Trump administration’s push to get more Medicare Shared Savings Program (MSSP) ACOs to take on downside risk is having an effect, but there are still many nontakers.

According to tallies in an analysis published on the Health Affairs blog last month, 53% of the 139 MSSP ACOs that migrated out of the regular MSSP program last year into the administration’s Pathways to Success program took on downside risk. That makes sense because the Pathways program is designed to encourage ACOs to take on downside risk. But a greater proportion (309 out of 514, or 60%) of the MSSP ACOs stayed in the legacy program and only 17% of those ACOs took on downside risk.

Trump administration health officials — and a number of experts outside the administration — have argued that the ACOs will realize their value-base care potential only if they take on downside risk, the shorthand way of saying that penalties would be assessed if the ACO exceeds financial benchmarks.

The analysis was conducted by Mark McClellan, M.D., Ph.D., director the Duke-Margolis Center for Health Policy at Duke University, and his colleagues.

McClellan, who was FDA commissioner and CMS administrator during the George W. Bush administration, and his co-authors say cost and quality metrics for ACOs this year will be “muddled” because of the COVID-19 pandemic and uncertainty about the effects of the adjustments CMS has made in the program. They note, though, that the dire scenario of an exodus of ACOs because of the Pathway of Success rules didn’t happen last year.

Telehealth question: Can we talk — just on the phone?

It’s become COVID-19 pandemic cliché that telehealth is here to stay. But there are fault lines ahead. Will all payment and other “flexibilities” that CMS granted be made permanent? For example, vendors who have invested heavily in technology that is HIPAA-compliant want to see the HIPAA requirements come back, partly out of self-interest.

Another open question is whether reimbursable telehealth visits will continue to include audio-only telephone calls. “It was telephonic care that saved us,” said Andie Martinez Patterson during a recent Leonard Davis Institute of Health Economics webinar on the pandemic’s effect on the finances of healthcare providers.

Patterson, M.P.P., is vice president of government affairs for the California Primary Care Association, which represents not-for-profit community health centers and regional clinic associations in the state.

“We tried hard with telehealth (audio and visual), but the technology was difficult for a lot of the patient population,” Patterson said. “Some of our elderly patients were really not into it.”

Meet our board!

We hope you’ve been listening to our new weekly podcast, “Tuning Into The C-Suite,” hosted by Associate Editor Briana Contreras.

One of our recent episodes features Art Papier and Nada Elbuluk of VisualDx. Contreras spoke with them about how providers can leverage health IT to reduce cognitive bias and racial disparities in healthcare.

And be sure to listen to our new “Meet the Board” series. Over the next several months, Contreras and Senior Editor Peter Wehrwein are having conversations with all of the members of MHE’s editorial advisory board. The latest guest was Don Hall, M.P.H., principal of consulting practice DeltaSigma LLC and a longtime member of our board. Listen in, learn a lot.

To tune in, visit www.managedhealthcareexecutive.com/podcasts or find us on Spotify, iHeart Radio and Apple podcasts.

With easy viewing access on all our sites, you will be among the first to hear about the following:

• Breaking health care news
• Live updates and opinions on what’s happening, with leading experts answering the tough questions
• Cross-specialty feedback for multidisciplinary approaches to treatment and guidelines

MJHLifeSciences.com/news-network
A Comprehensive Approach to Long-Term Narcolepsy Management Is Important for Patients During Their Journey

Studies show that patients with narcolepsy are more likely to have certain comorbid medical conditions than those without narcolepsy.

Narcolepsy is associated with substantial medical and economic burden, which may include emergency room visits, hospital visits, and/or absenteeism.


For more information, contact your Jazz Account Manager or visit NarcolepsyLink.com.
The American Society of Hematology (ASH) will present its annual meeting and exposition virtually Dec. 5-8. Even though the meeting is not happening in person, attendees will still have the opportunity to review thousands of scientific abstracts dealing with the buzziest news and most talked-about topics in hematology today.

Robert A. Brodsky, M.D., ASH secretary and director of hematology at Johns Hopkins University School of Medicine in Baltimore, says the topics will include advances in areas including gene therapy, genome editing, bone marrow transplantation and hematologic malignancies, and a lot of basic research involving stem cells, leukemia progression and immunology.

As for the latest in drug treatments in the pipeline, Brodsky believes two large phase 3 trials will likely garner the most interest.

"The first is the APOLLO trial, a phase 3 randomized study of subcutaneous daratumumab plus pomalidomide and dexamethasone versus pomalidomide and dexamethasone alone," he says, referring to a closely watched trial of treatments for multiple myeloma. "There is also the REACH3, a phase 3 randomized study of ruxolitinib versus best-available-therapy," says Brodsky, referring to a chronic graft-versus-host-disease (GvHD) trial.

Breakthroughs of REACH3

David Feltquate, M.D., Ph.D., global head of Novartis' hematology disease unit, notes that chronic graft-versus-host disease is a common and very serious complication of allogeneic (from one person to another) stem cell transplantation, and patients frequently become resistant or dependent on steroids. GvHD occurs when the new T cells generated by the stem cell transplant recognize the recipient's cells as "foreign" and mount an immunological attack. The skin, gut and liver are most commonly affected. Estimates of how common GvHD occurs vary greatly, and the risk of occurrence depends, in part, on the degree of tissue compatibility between the donor and the recipient. GvHD is conventionally divided into the acute form, which occurs within 100 days of the stem cell transplant, and the chronic one that occurs afterward. The condition can have major effect on people's quality of life and serious cases can be deadly.

"This is why we are so excited about the results of REACH3, a phase 3 study that looked at Jakavi (ruxolitinib) in patients with steroid-refractory or steroid-dependent chronic GvHD," he says. "What we know now is that
Jakavi met the primary endpoint of the study, defined as superior overall response rate after 24 weeks, compared to best available therapy. We also know that Jakavi met two very important secondary endpoints, which were improvements in failure-free survival and also patient-reported symptoms.

Jakavi is an oral inhibitor of the JAK 1 and JAK 2 tyrosine kinases approved in Europe as a treatment for adult patients with polycythemia vera (PV) who are resistant to, or intolerant of, hydroxyurea, and for the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis (MF), post-polycythemia vera MF or post-essential thrombocythemia MF. Novartis licensed ruxolitinib from Incyte Corp. for development and commercialization outside the United States. The drug is marketed in the United States by Incyte as Jakafi.

The REACH3 trial has forerunner, REACH2, which was designed to study Jakavi in people with the acute form of GvHD. The REACH2 results were published in the May 7, 2020, issue of The New England Journal of Medicine. The investigators randomized 309 acute GvHD patients for whom glucocorticoids were not effective (“glucocorticoid-refractory”), 154 to Jakavi and 155 to a control group that was treated with a therapy chosen by the investigator from list of nine options (the large number of choices is indicative of just how unsettled treatment of GvHD is). The primary endpoint was overall response 28 days after the treatment started. The results showed that 62% of the patients in the Jakavi group met that end point compared with 39% of those in control group. The patients on Jakavi also fared better on various other endpoints.

“This is a major improvement in outcomes for acute GvHD patients and taken together with the results seen in chronic GvHD, could mean a change to standard of care for a very difficult-to-treat disease,” Feltquate says. “Based on these data, we plan to file for marketing authorization in GvHD in Europe and other countries.”

The full data from the REACH3 study is expected to be presented at a medical meeting in early 2021. “Jakavi is now the first treatment to demonstrate efficacy in a large-scale randomized clinical trial in steroid-refractory or steroid-dependent chronic GvHD,” Feltquate says. “This is potentially practice-changing news in a disease area where unmet need and patient impact are very high.”

**APOLLO taking off**

In the phase 3 APOLLO randomized study comparing subcutaneous Darzalex (daratumumab) in combination with (Pomalyst) pomalidomide and dexamethasone compared with Pomylastr and dexamethasone alone in relapsed or refractory multiple myeloma, the daratumumab combination met the primary endpoint of improving progression-free survival.

“We are pleased with these positive results for daratumumab, administered as a subcutaneous formulation, in combination with pomalidomide and dexamethasone,” Jan van de Winkel, Ph.D., CEO of Genmab, said in a company press release issued in late July. Janssen bought the development and marketing rights to Darzalex in 2012.

As a phase 3 trial of treatment of a blood cancer with an increasing incidence in some populations, the APOLLO trial is noteworthy, but the results won’t break new ground. The FDA approved the Darzalex-Pomalyst-dexamethasone combination three years ago based on favorable results from a single-arm, phase 1 study. And in August of this year, the FDA approved another “triplet therapy” for relapsed or refractory multiple myeloma that includes Darzalex, Kyprolis (carfilzomib) and dexamethasone.

**Other ASH news**

In addition to the APOLLO and REACH3 trial results, Brodsky says the ASH schedule includes presentation of results from a multicenter trial comparing reduced-intensity allogeneic hematopoietic cell transplantation to hypomethylating therapy or best supportive care.

“It shows an important survival advantage in older patients with advanced myelodysplastic syndrome,” he says. “This will be the new standard of care.”

Another notable area of research is bone marrow transplant, including markedly expanded access to this potentially curative therapy with haploidentical donors, says Brodsky, who also foresees discussion about new research into sickle cell disease during the ASH meeting.

“There are exciting data in curative intent therapies,” he says. “Haploidentical bone marrow transplant results continue to be outstanding. Cure rates are approaching 90%. There are gene therapy and editing approaches showing encouraging early data in small numbers of patients. And there is exciting data for fixed-dose hydroxyurea in Africa.”

Keith Loria, a regular contributor to Managed Healthcare Executive, is freelance writer in the Washington, D.C., area.
Five important advances in breast cancer treatments
Lung cancer treatment: Bespoke and guided by biomarkers
Bringing CAR-T cell therapy to the community
Headed in the right direction: Cancer mortality is going down
Although there isn’t a cure for breast cancer, more effective treatments continue to emerge. Here’s a look at five developments for breast cancer treatment in the last two years.

**FDA approval of Trodelvy**
Trodelvy (sacituzumab govitecan-hzly) was approved by the FDA in April to treat metastatic triple-negative breast cancer. It is called triple-negative because the cancer cells lack estrogen and progesterone receptors and the human epidermal growth factor receptor 2 (HER2) protein. Roughly 15% of breast cancers are triple-negative breast cancers, and they are more commonly diagnosed in women younger than 40. Triple-negative breast cancer is aggressive and is more likely to be diagnosed at a later stage than breast cancers with the receptors it lacks.

Trodelvy, which is administered intravenously, was approved to treat metastatic triple-negative breast cancer that has not responded to standard chemotherapy. The drug is an antibody-drug conjugate, which works like a smart bomb, says David Riseberg, M.D., chief of medical oncology and hematology at Mercy Medical Center in Baltimore. Antibody-drug conjugates are agents that combine antibodies and chemotherapy agents. With Trodelvy, it is the antibody’s job to recognize the trophoblast cell-surface antigen 2 — Trop-2, for short — receptor on the surface of triple-negative breast cancer cells. When that happens, it delivers a topoisomerase inhibitor that is toxic to the cancer cell. This approach of pairing recognition with a chemotherapy agent means the treatment is more precisely directed than chemotherapy alone.

In the ASCENT study that led to Trodelvy’s approval, a third of patients responded to the treatment as measured by overall response rate. “This is generally better than what would be expected in patients with triple-negative breast cancer who were previously treated with prior chemotherapy agents,” says Shannon Puhalla, M.D., a medical oncologist at the UPMC Hillman Cancer Center in Pittsburgh. However, Trodelvy was approved with a boxed warning about severe neutropenia and diarrhea.

The commercial prospects for Trodelvy—and the antibody-drug conjugates in general—are bright judging by Gilead’s recent $21 billion acquisition of Immunomedics, the company that developed Trodelvy.

**FDA approval of Enhertu**
Enhertu (fam-trastuzumab deruxtecan-nxki) is another antibody-drug conjugate. Trodelvy and Enhertu show that drug developers believe there is a lot of promise in the find-and-treat approach of the antibody-drug conjugates. The FDA approved Enhertu in late 2019 as therapy as for metastatic HER2-positive breast cancer among patients who have been previously treated with two or more other types of treatments. With Enhertu, trastuzumab recognizes the cancer cell and the deruxtecan portion causes DNA damage in cancer cells that kills them off. Trastuzumab, a monoclonal antibody, ushered in the current era of cancer treatment that depends on agents that disable molecular-level pathways that feed cancer growth and spread. It was approved more than two decades ago, in 1998, and is sold under the brand name Herceptin, although there are now a number of biosimilars on the market: Herzuma, Trazimera, Kanjinti, and Ogivri.

Enhertu is administered intravenously and is usually given through a subcutaneous port, which allows for direct access to a large chest vein, says Hadeel Assad, M.D., a medical oncologist at the Karmanos Cancer Institute in Detroit. “The treatment (Enhertu) offers a much-needed advancement in treating HER-2 positive breast cancers,” says Jonathan S. Goldberg, M.D., medical oncologist at CareMount Medical in Mount Kisco, New York, and medical director of cancer clinical trials at Northern Westchester.

Five important advances in breast cancer treatments

Two newly approved antibody-drug conjugates and changes in radiation therapy lead the way

*by KAREN APPOLD*
Five important advances in breast cancer treatment

Oncology

“...enough to seek regulatory approval...”

KAUFMAN

Balixafortide is a biologic therapy that blocks CXCR4, a protein found on the surface of many types of cancer cells. CXCR4 allows tumor cells to spread to other body parts, explains Peter Kaufman, M.D., an oncologist at the University of Vermont Medical Center in Burlington, Vermont. The FDA granted balixafortide fast-track status in 2018, and this summer Kaufman and a team of investigators presented positive findings for the drug at the annual meeting of the American Society of Clinical Oncology. Results from the phase I trial that enrolled 56 women with metastatic breast cancer that had been treated previously showed a greater response from a combination of balixafortide and eribulin, a chemotherapeutic agent sold under the brand name Halaven, than eribulin alone.

Balixafortide, which is being tested and developed by Polyphor, a Swiss biotech company, is being evaluated in a phase 3 study of close to 400 patients with HER2 negative metastatic breast cancer. “If similar results are reproduced in this study, it may be enough to seek regulatory approval without conducting more studies,” says Kaufman.

Promising results for balixafortide

Balixafortide is being evaluated in a phase 3 study of close to 400 patients with HER2 negative metastatic breast cancer. “If similar results are reproduced in this study, it may be enough to seek regulatory approval without conducting more studies,” says Kaufman.

Fewer adjuvant radiation treatments

Women with breast cancer are frequently treated with between 15 and 20 radiation treatments over a three- or four-week period after breast-conserving surgery. New research suggests that fewer treatments over just a week’s time may be needed. Results from the FAST-Forward trial published in The Lancet this year showed that five treatments were noninferior to 15, notes Sushil Beriwal, MD, deputy director of radiation services at the University of Pittsburgh Hillman Cancer Center. Fewer treatments are less expensive and time-consuming for patients and sometimes there’s a lower chance of adverse effects.

A CT scan is used to map the target for radiation. Then, radiation oncologists mark the tumor’s boundaries and determine the necessary dosage using sophisticated computer programs, Beriwal says. This enables them to administer the radiation with a high level of accuracy. The patient is positioned on a treatment table and images or scans are taken before each treatment to make sure the radiation beams are targeted to the desired area.

Targeted intraoperative radiation therapy

Targeted intraoperative radiation therapy (TARGIT-IORT) is given in the operating room at the time of a patient’s initial lumpectomy to remove local breast cancer, says Valery Uhl, MD, a radiation oncologist in Northern California and president of the board of TARGIT Collaborative Group (TCG) in Sacramento, California. TARGIT-IORT consists of a single, highly precise dose of radiation given directly to the area where breast cancer was surgically removed. “This is ideal for patients with small breast cancers who choose lumpectomy as a treatment,” says Roshni Rao, M.D., chief of the breast surgery program at NewYork-Presbyterian Hospital in New York. “The treatment involves having a breast surgeon remove the cancer from the breast, along with a small area of normal tissue around the edges. It decreases the side effects to the skin and allows patients to recover promptly.”

Intraoperative treatment radiation therapy has been used for many years, and results of a study with more than eight years of follow-up were published in The BMJ in August. They showed that intraoperative treatment was just as effective as the more traditional adjuvant therapy.

The risk of cancer returning within the breast is less than 3% with intraoperative radiation, says Rao, and it’s less costly and more convenient for patients because it eliminates the need for follow-up visits for radiation.

“If the United States embraced TARGIT-IORT, the healthcare system would save millions,” says Uhl. “There are also advantages for the patient, such as convenience, reduced travel and personal costs, improved quality of life, and fewer side effects.”

Karen Appold is a medical writer in the Lehigh Valley region of Pennsylvania.

Karen Appold is a medical writer in the Lehigh Valley region of Pennsylvania.
Partners in Primary Care Finds Success in Addressing Seniors’ Social Determinants of Health

By Renee’ Buckingham, President, Partners in Primary Care

There is growing recognition among health care providers and payers that disease prevalence is inextricably tied to social and environmental factors that impact health. In fact, clinical care accounts for an estimated 20 percent of health outcomes, while 80 percent are the result of social determinants of health (SDOH).

Millions of older Americans live in a precarious financial situation. Nearly one in four seniors has difficulty paying monthly living expenses, 24 percent are food insecure, many struggle with the cost of housing and homelessness is on the rise among this population. Many seniors lack access to transportation, preventing them from securing essential goods and necessary medical care and increasing their isolation.

These SDOH factors compound already high rates of mental health conditions among seniors, which, in turn, negatively impact their health.

Barriers to Addressing SDOH

Multiple obstacles, structural and attitudinal, make it difficult to address SDOH within the traditional care model. Physicians recognize the negative effects these factors have on health, but time and resources limit their ability to treat them. A study published in JAMA Network Open revealed that only 16 percent of physician practices screen for key social needs: food insecurity, housing instability, utility needs, transportation needs and interpersonal violence.

Lack of awareness of available social supports is one problem. Another is older patients’ hesitancy to share their nonmedical struggles with clinicians. There is also little incentive or bandwidth for physicians to address these issues within the fee-for-service model.

Traditional Medicare provides limited reimbursements for treating SDOH, making it infeasible for most practices to expand staff roles to address unmet social service needs.

Transforming Senior Care to Meet Medical and Socioeconomic Needs

Recent changes to Medicare Advantage Plans have enabled more holistic approaches to patient care by expanding the definition of supplemental benefits. The push toward value-based care has also significantly elevated the role of SDOH in treating patients, given their outsized impact on health outcomes.

These changes have created new models of senior care. One example is Partners in Primary Care, a network currently operating 56 senior-focused primary care centers – with 7 more that will open by the end of Q1 – throughout seven states. Partners accepts patients with any Medicare Advantage Plan and people eligible for both Medicare and Medicaid (dual eligible). These practices are made up of care teams that include a behavioral health specialist and a social worker who helps connect patients with needed services so mental health and SDOH issues can be addressed during visits.

Efficiencies gained across our centers allow our physicians to spend, on average, 45 minutes with each patient – triple the time most physicians can manage. Our value-based care model, focused on a whole-person health approach, encourages patients to be seen more frequently, not just when they’re sick. In the past three years, patients have had an average of five visits per year. That number of visits – plus the increased time per visit – enables stronger relationships to develop between the patient and our care team, creating a level of trust that allows patients to discuss their nonmedical challenges and to accept assistance.

This holistic approach benefits both patients and payers. Data from our South Carolina centers showed that in 2019, 30-day hospital readmission rates for our patients were almost 60 percent lower than those of the general Medicare population. And, our rate of hospital admissions was 186 per 1,000, significantly lower than the national rate for this age group, which ranges from 233 per 1,000 (65 to 84 years old) to 456 per 1,000 (age 85+).

These value-based care-team models are reshaping patient care not just in treating their medical symptoms, but also in addressing the circumstances that often underlie those problems. Doing so can improve patients’ health and quality of life as well as reduce overall costs.

Renee’ Buckingham

Renee’ Buckingham is President, Care Delivery for Humana. Humana’s Care Delivery Organization includes Partners in Primary Care – wholly owned, de Novo senior focused, payer agnostic primary care clinics; Family Physicians Group, a large senior focused primary care group located in Orlando, FL; and various provider joint ventures and partnerships. As President, Renee’ is responsible for business operations, performance and national expansion of these Primary Care businesses.

Until January 2018, Renee’ was Vice President and North Division Leader, in Humana’s Medicare business, where she led Market Operations for one of Humana’s largest Divisions. The North Division includes 20 states spanning from Maine to Montana serving nearly 800,000 of Humana’s Medicare Advantage members.

Prior to joining the Medicare Segment in October 2014, Renee’ led Humana’s Provider Development Center of Excellence as an Enterprise Vice President and was responsible for both building and deploying programs and capabilities designed to support providers as they moved from transactional care to value-based care. Under her leadership, Humana grew Value Based Agreements to more than 900 accountable relationships.

Renee’ has been with Humana for 21 years and has held several other leadership positions including Vice President, Provider Contracting, Regional Vice President Provider Contracting and National Vice President, Provider Engagement and Value Based Programs.

Support provided by Humana. Copyright 2020 and published by MJH Life Sciences™. No portion of this program may be reproduced or transmitted in any form, by any means, without the prior written permission of MJH Life Sciences™. The views and opinions expressed in this material do not necessarily reflect the views and opinions of MJH Life Sciences™, or Managed Healthcare Executive.
Precision is a virtue in most things and cancer treatment is no exception. Rather than attacking all dividing cells in hopes of cutting down the cancerous ones, many treatments today home in on and disable genetic and other anomalies that allow cancer cells to run rampant, metastasize and kill.

Lung cancer treatment has become especially targeted partly because there is such a need. The American Cancer Society estimates that about 228,000 people in the U.S. will be diagnosed with lung cancer this year, an incidence total second only to breast cancer. Moreover, lung cancer is far and away the deadliest cancer in the U.S. as measured by the total number of deaths. The American Cancer Society estimates that there will be 135,000 lung cancer deaths this year in this country, more than deaths caused by colon, breast and prostate cancer combined.

Targeted therapy for lung cancer became possible because researchers have characterized in greater and greater detail an increasing number of the genetic and other molecular-level events that trigger the initiation and growth of lung cancer tumors. Along with the lengthening roster of targeted therapies are a growing number of biomarkers that clinicians need to test for to help them decide which, if any, of those targeted therapies to prescribe. The National Comprehensive Cancer Network's 2020 clinical practice guidelines for non-small-cell lung cancer (NSCLC), which comprises 90% of all lung cancers, now includes seven biomarkers.

Shyama Kazmi, M.D., RPh, a medical oncologist and hematologist at the Cancer Treatment Centers of America in Philadelphia, notes that lung cancer has more identified biomarkers than any other solid tumor cancer. These activating mutations and genetic aberrations have multiple treatment modalities that are effective and can spare patients harsh chemotherapy, she adds.

"It is imperative to test all lung cancers for biomarkers and genomic aberrations as targeted therapies and immunotherapies have shown to be highly effective initial therapies in this group," Kazmi says. She mentions a patient who was diagnosed with metastatic lung cancer in 2014. "Due to the patient’s EGFR mutations and targeted therapies, chemotherapy has not yet been necessary and the patient continues to function in full capacity with oral medications that are not toxic."

Kim Norris, co-founder and president of the Lung Cancer Foundation of America, an industry-sponsored group that advocates for lung cancer patients and research, says the rapid pace of discovery in lung cancer research is giving patients more treatment options than ever.

“I am confident we will continue to see a dramatic increase in the five-year survival rate for lung cancer.”

However, advances in lung cancer treatment and the growing number of biomarkers guiding treatment choices are presenting clinicians and patients with a number of difficult issues. Many biomarker tests are performed as a series of tests, which can be a costly and time-consuming process. Some experts argue that next-generation sequencing, which can test for many genetic markers at once, would be more efficient and less costly. "As more and more gene targets have emerged it would be beneficial to switch to broader NGS (next-generation sequencing)-based assays that can evaluate all proven and emerging biomarkers in a single test," wrote Nathan Pennell, M.D., Ph.D., and his co-authors in an article on biomarkers in last year’s American Society of Clinical Oncology’s (ASCO) Education Book. Pennell is a medical oncologist at Cleveland Clinic. He and his co-authors say NGS tests can be grouped into two basic categories: amplicon-based tests that cover smaller “hot spots” of the genome and don’t detect certain types of mutations, and targeted hybridization capture tests that are more encompassing but also more complex. The turnaround time on an NGS targeted hybridization test is 15 to 20 days, according to Pennell and his colleagues.

So-called liquid biopsies that detect tumor DNA in blood plasma...
There are another testing option for clinicians and patients to consider. In August, the FDA approved Guardant360 CDx, which the agency said was the first liquid biopsy that also uses next-generation sequencing. The test is approved to find mutations in the epidermal growth factor receptor (EGFR) gene.

One pitfall in the current enthusiasm for biomarker-guided, targeted lung cancer treatment is overusing the expensive treatments. Pennell and his colleagues touch on the subject in their ASCO article. "For the majority of patients, standard treatments will offer more compelling evidence of clinical benefit than those based on molecular alterations, particularly if suggested targeted options are predicated only on preclinical or very limited evidence thus far," they wrote.

They also warned that targeted treatment might be detrimental if it's used instead of standard treatments that are more effective.

**Important lung cancer biomarkers**
The number of possible lung cancer biomarkers seems to grow almost daily. The Wolters Kluwer UpToDate article on personalized therapy for advanced NSCLC by Lecia Sequist, M.D., M.P.H., and Joel Neal, M.D., M.P.H., provides a rundown on many of the most clinically relevant mutations. Here are three of them:

**EGFR mutation.** Mutations in the EGFR gene occur in about 15% of NSCLC adenocarcinomas diagnosed in the U.S. and the mutations occur most commonly in nonsmokers. (Adenocarcinoma of the lung arises from the mucosal glands and accounts for about 40% of all lung cancers.) The incidence of EGFR mutations is higher in Asian populations. The College of American Pathologists and two other groups issued guidance for testing for EGFR mutations in 2013 and ASCO endorsed the guidance a year later. In advanced NSCLC, EGFR mutations are associated with a more favorable prognosis. Lung cancers with EGFR mutations can be treated with a number of EGFR tyrosine kinase inhibitors, such as Tarceva (erlotinib), Iressa (gefitinib), Gilotrif (afatinib), Vizimpro (dacomitinib) and Tagrisso (osimertinib).

**ALK rearrangements.** Rearrangements of the anaplastic lymphoma kinase (ALK) gene occur in about 4% of NSCLC adenocarcinomas. The rearrangements are more common in the lung cancers of young patients and among those who haven't smoked. Most NGS tests can identify the ALK rearrangements. ALK-positive lung cancers are sensitive to the cancer-fighting effects of ALK tyrosine kinase inhibitors, such as Xalkori (crizotinib), Zykadia (ceritinib), Alecensa (alectinib) and Alunbrig (brigatinib).

**ROS1 rearrangements.** c-ROS oncogene 1 (ROS1) is the causative factor in 1% to 2% of cases of NSCLC. In ROS1 rearrangements, part of the gene is out of place, or "translocated," and inserted in another gene in the genome. ROS1-positive lung cancers are more commonly seen in adenocarcinomas than not, in younger people, and in those who haven't smoked. Xalkori (crizotinib) and Rozlytrek (entrectinib) are FDA-approved for patients with ROS1 translocation.

**In the future**
The search for additional targeted therapies and the biomarkers that can guide their use is continuing. Researchers have discovered, for example, that some NSCLC tumors have mutations in the human epidermal growth factor receptor 2 (HER2) gene that has been a breast cancer biomarker for more than 20 years.

Keith Orford, M.D., Ph.D., chief medical officer of Calithera Biosciences, speaks of the recently emerging science that suggests that the KEAP1/NRF2 molecular pathway may identify a unique vulnerability in the subset of NSCLC patients. “Mutations in the KEAP1/NRF2 pathway, which occur in an estimated 20% of NSCLC patients, are associated with aggressive tumor growth,” Orford says. “Recently presented clinical data demonstrate that activation of this pathway, either through the loss of KEAP1 function or activation of NRF2, is associated with poor clinical outcomes among patients with NSCLC receiving front-line standard-of-care chemoimmunotherapy.”

“Interestingly,” Orford continues, “we are also observing in preclinical research that the activation of the KEAP1/NRF2 pathway makes tumors dependent on glutaminase activity for growth and survival, making these tumors exquisitely sensitive to inhibition of glutaminase activity.”

His company is currently developing the first-in-clinic glutaminase inhibitor telaglenastat, which is being evaluated in the phase 2 KEAPSAKE trial for the treatment of NSCLC in combination with standard-of-care chemoimmunotherapy.

Keith Loria, a regular contributor to Managed Healthcare Executive®, is a freelance writer in the Washington, D.C., area.

---

**The American Cancer Society estimates that there will be 135,000 LUNG CANCER DEATHS this year in this country, more than deaths than caused by colon, breast and prostate cancer combined.**
When FDA approved Kymriah (tisagenlecleucel), the first CAR-T cell therapy, in August 2017, then-Commissioner Scott Gottlieb, M.D., heralded the arrival of “a new frontier in medical innovation,” which offered hope of treating the deadliest cancers. But with that early promise came problems, some because the therapy was on the steepest pitch of the learning curve. Kymriah was complex to administer. Patients and caregivers were required to stay in a nearby hotel and hospital stays of a week or more were common. Some patients suffered cytokine release syndrome, a torrent of the immune system’s signaling proteins that results in a raft of symptoms—fever, nausea, rashes—that in extreme cases can be fatal. And there was the then-shocking price of $475,000.

But now CAR-T cell therapy might have reached a new phase when it is no longer solely in the province of academic medical centers. More therapies in the class have been approved and are on the market. Shortly after giving Novartis’ Kymriah its blessing, the FDA approved Gilead’s Yescarta (axi-cabtagene ciloleucel) for relapsed or refractory large B-cell lymphoma. In July 2020, the agency approved a third CAR T-cell therapy, Gilead’s Tecartus (brexicabtagene autoleucel) for relapsed or refractory mantle cell lymphoma, and it may soon approve a fourth, Bristol Myers Squibb’s liso-cel (lisocabtagene maraleucel), which would also be for treatment of large B-cell lymphoma that hasn’t responded to previous treatment. Liso-cel seems poised to enter into community oncology practice, partly because its manufacturing process separates CD8+ and CD4+ T-cells and creates a therapy with a set ratio of CARs.

Duncan Allen, M.H.A., vice president of clinical services for OneOncology, a network of 170 community oncology practices headquartered in Nashville, Tennessee. Allen previously managed one of the nation’s first CAR-T cell therapy programs at Vanderbilt University Medical Center in Nashville.

Managed Healthcare Executive® spoke with Allen recently about bringing CAR-T cell therapy to community oncology practices.*

What are the challenges of bringing CAR-T cell therapy into the community practice?

The emergence of the immune effector cell therapeutic class in general—and specifically CAR-T, the most successful therapy in that class today—has been groundbreaking for patients suffering from specific hematologic malignancies.

Where the challenge lies with CAR-T therapy is that the scientific data is relatively new, and this presents some challenges when trying to determine how these half-million-dollar, cutting-edge therapies should be thought of in relation to their therapeutic peers.

In addition, the therapy brings certain manufacturing complexities. It requires two weeks or more to make. There are specific toxicity considerations that require the use of a specialized steroid, which

**CAR-T CELL THERAPY** Chimeric antigen receptor (CAR) T-cell therapy outfits a patient’s own T-cells with receptors, which lets the resulting “CARs” hunt down and do battle with cancer cells. The multistep process involves harvesting the patient’s T cells, modifying them, and then infusing them.
costs upwards of $2,000 per administration. And, quite frankly, this is a very resource-intensive treatment process that requires intense monitoring of the patient for over 30 days.

There are a significant number of challenges in the current generation of CAR products, but I do see that changing over time.

Are there advantages of administering CAR-T cell therapy at the community practice level?
Absolutely. CAR-T administration is largely in its infancy in the community setting. As this therapeutic class evolves from our current generation of CARs into future generations where you may have (allogenic) off-the-shelf products, the advantages of administering and monitoring in a community setting are relatively straightforward. There’s access to timely administration and convenience in close-to-home treatments, which I think is very important given the level of monitoring required and the ability to administer in a REMS (risk evaluation and mitigation strategy)-certified outpatient facility. I think that really is a game changer, and really makes the community setting ideal for future CAR generations.

What is holding back the growth of CAR-T cell therapy as a primary treatment?
Many of the initial barriers to reimbursement and administration have begun to be addressed after intensive efforts to push for payment out of CMS. I think there are still many questions about how to sustain coverage for CAR-T cell therapy given the price tags.

With the advent of value-based care, a core tenet of OneOncology, we’ve seen that we must address matching price to outcome — and CAR-T cell therapy is at the top of that list.

I think last time I looked there were over 1,000 trials for cellular therapies, and many are beginning to be tested on solid tumors. We’ll have to think ahead about the scalability of cellular therapy, should solid tumor come into play in the future, so we can ensure that patients have access to these cutting-edge therapies. I think the community setting is uniquely positioned to help with that scale.

How does reimbursement today compare with reimbursement three years ago?
As someone who personally has sat with families and walked them through the reimbursement journey for CAR-T, I can tell you that it has gotten much better.

There were periods where patients simply would be waiting on their payer to cover their therapy. Luckily, I think we’ve seen the maturation of the coding and reimbursement environment over the past two years, largely thanks to that advocacy from the American Society for Transplantation and Cellular Therapy and the American Society of Hematology. Today, around 90% of plans have coverage for CAR-T.

But they’re still nuances. For starters, it’s not just about the cost of the therapy, but the associated costs for delivering a therapy, including leukapheresis, the administration of steroids and other related costs. The coding considerations have not been inclusive of the full cost surrounding CAR therapy and this has been presented in a number of forums. But it impacts patients and providers and practices, and I would like to see this improve over time as cellular therapy becomes mainstream. I think with increased policy advocacy, we can definitely get to a healthier state.

Are some CAR-T therapies and indications more appropriate for the community setting than others?
As different products are tested, there will be clear winners that are more suitable for the community setting. And those will likely (be) therapies that have lower toxicity profiles, so that you can ensure you’re not going to have to admit your patient to the hospital.

With the current generation of CAR-T therapies, most folks would say that there have been different experiences with the two primary players. But over time, I think we will definitively determine which immune effector cells are more appropriate from an outpatient perspective and which are more suitable for inpatient administration.

So I think the verdict is still largely out.

*This transcript has been edited for clarity and length.

Oncology section continues on page 22
**INDICATION**

TRODELVY® (sacituzumab govitecan-hziy) is indicated for the treatment of adult patients with metastatic triple-negative breast cancer (mTNBC) who have received at least 2 prior therapies for metastatic disease. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

**IMPORTANT SAFETY INFORMATION**

**WARNING: NEUTROPENIA AND DIARRHEA**

TRODELVY can cause severe or life-threatening neutropenia. Withhold TRODELVY for absolute neutrophil count (ANC) below 1500/mm³ on Day 1 of any cycle or ANC below 1000/mm³ on Day 8 of any cycle. Withhold TRODELVY for neutropenic fever.


- Dose modifications may be required due to neutropenia. Febrile neutropenia occurred in 6% (24/408) of patients treated with TRODELVY, including 8% (9/108) of patients with mTNBC after at least 2 prior therapies. Less than 1% (1/408) of patients had febrile neutropenia leading to permanent discontinuation. The incidence of Grade 1-4 neutropenia was 64% in patients with mTNBC (n=108). In all patients treated with TRODELVY (n=408), the incidence of Grade 1-4 neutropenia was 54%; Grade 4 neutropenia occurred in 13%. Less than 1% (2/408) of patients permanently discontinued treatment due to neutropenia.

Severe diarrhea may occur. Monitor patients with diarrhea and give fluid and electrolytes as needed. Administer atropine, if not contraindicated, for early diarrhea of any severity. At the onset of late diarrhea, evaluate for infectious causes and, if negative, promptly initiate loperamide. If severe diarrhea occurs, withhold TRODELVY until resolved to ≤ Grade 1 and reduce subsequent doses.

- Diarrhea occurred in 63% (68/108) of patients with mTNBC and 62% (254/408) of all patients treated with TRODELVY. In each population, events of Grade 3 occurred in 9% (10/108) of mTNBC patients and 9% (36/408) of all patients treated with TRODELVY. Four out of 408 patients (<1%) discontinued treatment because of diarrhea. Neutropenic colitis was observed in 2% (2/108) of patients in the mTNBC cohort and 1% of all patients treated with TRODELVY.

Contraindications: Severe hypersensitivity reaction to TRODELVY.

**Hypersensitivity**

- TRODELVY can cause severe and life-threatening hypersensitivity, including anaphylactic reactions. Hypersensitivity reactions occurred within 24 hours of dosing in 37% (151/408) and Grade 3-4 hypersensitivity occurred in 1% (6/408) of all patients treated with TRODELVY. The incidence of hypersensitivity reactions leading to permanent discontinuation of TRODELVY was 1% (3/408).

- Pre-infusion medication for patients receiving TRODELVY is recommended. Observe patients closely for infusion-related reactions during each TRODELVY infusion and for at least 30 minutes after completion of each infusion. Medication to treat such reactions, as well as emergency equipment, should be available for immediate use.

**Nausea and Vomiting**

- TRODELVY is emetogenic. Nausea occurred in 69% (74/108) of patients with mTNBC and 69% (281/408) of all patients treated with TRODELVY. Grade 3 nausea occurred in 6% (7/108) and 5% (22/408) of these populations, respectively. Vomiting occurred in 49% (53/108) of patients with mTNBC and 45% (183/408) of all patients treated with TRODELVY. Grade 3 vomiting occurred in 6% (7/108) and 4% (16/408) of these patients, respectively.
TRODELVY for absolute neutrophil count (ANC) below 1500/mm³

TRODELVY can cause severe or life-threatening neutropenia. Withhold treatment in confirmatory trials.

response rate and duration of response. Continued approval for this indication is approved under accelerated approval based on tumor shrinkage in 13%. Less than 1% (2/408) of patients permanently discontinued treatment because of diarrhea. Neutropenic colitis was observed in 2% (2/108) of patients due to neutropenia.

Severe diarrhea may occur. Monitor patients with diarrhea and give fluid and electrolyte replacement and supportive measures when resolved to ≤ Grade 1. Additional antiemetics and other supportive measures may also be employed as clinically indicated. All patients should be given take-home medications with clear instructions for prevention and treatment of nausea and vomiting.

Use in Patients with Reduced UGT1A1 Activity

• Individuals who are homozygous for the uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1)*28 allele are at increased risk for neutropenia and may be at increased risk for other adverse events following initiation of TRODELVY treatment. Closely monitor patients with reduced UGT1A1 activity for severe neutropenia. The appropriate dose for patients who are homozygous for UGT1A1*28 is not known and should be considered based on individual patient tolerance to treatment.

• In 84% (343/408) of patients who received TRODELVY (up to 10 mg/kg on Days 1 and 8 of a 21-day cycle) and had retrospective UGT1A1 genotype results available, the incidence of Grade 4 neutropenia was 26% (10/39) in patients homozygous for the UGT1A1*28 allele, 13% (20/155) in patients heterozygous for the UGT1A1*28 allele, and 11% (16/149) in patients homozygous for the wild-type allele.

Embryo-Fetal Toxicity

• TRODELVY contains a genotoxic component and can cause teratogenicity and/or embryo-fetal lethality when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus.

For patients with mTNBC who have received at least 2 prior therapies for metastatic disease

A WAY IN WITH TRODELVY

TRODELVY attacks metastatic triple-negative breast cancer (mTNBC) with an antibody-drug conjugate (ADC) that binds to Trop-2

Based on pre-clinical data. May not correlate with clinical outcomes.

VISIT TRODELVY.COM TO LEARN MORE.
TRODELVY can cause severe diarrhea. Withhold TRODELVY for Grade 3-4 diarrhea at the time of scheduled treatment. Diarrhea is a common adverse reaction occurring in ≥10% of patients with mTNBC in the IMMU-132-01 study. Withholding TRODELVY may be required if diarrhea continues for ≥3 days at any severity. In a clinical trial, planned doses of up to 18 mg/kg (approximately 1.8 times the maximum recommended dose of TRODELVY) were received by 4 patients (0.4%) with Grade 5 (severe) diarrhea. Based on findings in animals, TRODELVY may impair fertility in females of reproductive potential. Verify the pregnancy status of females of reproductive potential prior to the initiation of TRODELVY.

Hypersensitivity

TRODELVY can cause severe and life-threatening hypersensitivity. Anaphylactic reactions have been observed in clinical trials with TRODELVY.

Hypersensitivity reactions within 24 hours of dosing occurred in 37% (131/440) of patients treated with TRODELVY. Grade 3-4 hypersensitivity occurred in 1% (6/440) of patients treated with TRODELVY. The incidence of hypersensitivity reactions leading to permanent discontinuation of TRODELVY was 1% (1/440).

Pre-infusion medication for patients receiving TRODELVY is recommended. Observe patients closely for infusion-related reactions during each TRODELVY infusion and for at least 30 minutes after completion of each infusion. Medication to treat such reactions, as well as emergency equipment, should be available for immediate use.

Nausea and Vomiting

TRODELVY is emetogenic. Nausea occurred in 69% (74/108) of patients with mTNBC and 69% (281/408) of all patients treated with TRODELVY. Grade 3 nausea occurred in 6% (7/108) and 5% (22/408) of these populations, respectively. Vomiting occurred in 49% (53/108) of patients with mTNBC and 48% (192/408) of all patients treated with TRODELVY. Grade 3 vomiting occurred in 6% (7/108) and 4% (16/408) of these patients, respectively. Premedicate with a two or three drug combination regimen (e.g., dexamethasone with either a 5-HT3 receptor antagonist or an NK-1 receptor antagonist as well as other drugs as indicated) for prevention of chemotherapy-induced nausea and vomiting DNX.

With TRODELVY treatment, Grade 3-4 vomiting at the time of scheduled treatment administration and resume with additional supportive measures when resolved to ≤ Grade 1.

Use in Patients with Reduced UGT1A1 Activity

Individuals who are homozygous for the uridine diphosphate glucuronosyl transferase 1A1 (UGT1A1)*28 allele are at increased risk for neutropenia and may be at increased risk for other adverse reactions following initiation of TRODELVY treatment.

In 84% (34/41) of patients who received TRODELVY (up to 10 mg/kg on Days 1 and 8 of a 21-day cycle) and had retrospective UGT1A1 genotype results available, the incidence of Grade 4 neutropenia was 26% (10/39) in patients homozygous for the UGT1A1*28 allele, 13% (20/155) in patients heterozygous for the UGT1A1*28 allele and 11% (16/149) in patients homozygous for the wild-type allele.

Closely monitor patients with reduced UGT1A1 activity for severe neutropenia. The appropriate dose for patients who are homozygous for UGT1A1*28 is not known and should be considered based on individual patient tolerance to treatment.

Embryo-Fetal Toxicity

Based on its mechanism of action, TRODELVY can cause teratogenicity and/or embryofetal lethality when administered to a pregnancy woman. TRODELVY contains a genotoxic component, SN-38, and targets rapidly dividing cells. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TRODELVY and for 6 months after the last dose. Advise men with female partners of reproductive potential to use effective contraception during treatment with TRODELVY and for 3 months after the last dose (see Use in Specific Populations).

ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the label:

- Neutropenia (see Warnings and Precautions)
- Diarrhea (see Warnings and Precautions)
- Hypersensitivity (see Warnings and Precautions)
- Nausea and Vomiting (see Warnings and Precautions)

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The data described in the Warnings and Precautions section reflect exposure to TRODELVY as a single-agent in a single-arm, open-label study (IMMU-132-01) in 408 patients with mTNBC and other malignancies who had received prior systemic therapeutic regimens for advanced disease. TRODELVY was administered as an intravenous infusion once weekly on Days 1 and 8 of 21-day treatment cycles at doses up to 10 mg/kg until disease progression or unacceptable toxicity.

The data in Table 2 reflect exposure to TRODELVY in a subset of 108 patients with mTNBC who had received at least two prior treatments for metastatic disease in study (IMMU-132-01). Patients received TRODELVY 10 mg/kg via intravenous infusion on Days 1 and 8 of 21-day treatment cycles until disease progression or unacceptable toxicity. The median treatment duration in these 108 patients was 5.1 months (range 0.5-81 months).

Serious adverse reactions were reported in 31% of the patients. The most frequent serious adverse reactions (reported in >1%) of the patients receiving TRODELVY were febrile neutropenia (6%), vomiting (5%), nausea (3%), dyspnea (3%), diarrhea (4%), anemia (2%), pleural effusion, neutropenia, pneumonia, dehydration (each 2%).

TRODELVY was permanently discontinued for adverse reactions in 2% of patients. Adverse reactions leading to discontinuation were anaphylaxis, anemia, fatigue, and headache (each <1%, 1 patient each for each). Forty-five percent (45%) of patients experienced an adverse reaction leading to treatment discontinuation. The most common adverse reaction leading to treatment interruption was neutropenia (31%). Adverse reactions leading to dose reduction occurred in 33% of patients treated with TRODELVY, with 24% having one dose reduction and 9% with two dose reductions. The most common adverse reaction leading to dose reductions was neutropenia/fetal/neutropenia. Adverse reactions occurring in ≥ 10% of patients with mTNBC in the IMMU-132-01 study are summarized in Table 2.

Table 2: Adverse Reactions in ≥ 10% of Patients with mTNBC in IMMU-132-01

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>TRODELVY (n=108)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any adverse reaction</td>
<td>100 (71)</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>95 (21)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>69 (6)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>63 (9)</td>
</tr>
<tr>
<td>Constipation</td>
<td>49 (6)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>34 (5)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>26 (26)</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td></td>
</tr>
<tr>
<td>Pyrexia</td>
<td>77 (9)</td>
</tr>
<tr>
<td>Edema</td>
<td>57 (8)</td>
</tr>
<tr>
<td>Pericarditis</td>
<td>57 (8)</td>
</tr>
<tr>
<td>Hematologic and lymphoid system disorders</td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>44 (43)</td>
</tr>
<tr>
<td>Anemia</td>
<td>52 (12)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>14 (3)</td>
</tr>
<tr>
<td>Metabolic and nutrition disorders</td>
<td></td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>68 (22)</td>
</tr>
<tr>
<td>Decreased phosphorus</td>
<td>30 (1)</td>
</tr>
<tr>
<td>Decreased potassium</td>
<td>24 (4)</td>
</tr>
<tr>
<td>Decreased serum creatinine</td>
<td>21 (5)</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>19 (1)</td>
</tr>
<tr>
<td>Hypophosphatemia</td>
<td>16 (2)</td>
</tr>
<tr>
<td>Dehydration</td>
<td>13 (5)</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
</tr>
<tr>
<td>Alopecia</td>
<td>63 (4)</td>
</tr>
<tr>
<td>Rash</td>
<td>48 (0)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>31 (3)</td>
</tr>
<tr>
<td>Dry skin</td>
<td>17 (0)</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>37 (5)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>32 (2)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>24 (0)</td>
</tr>
<tr>
<td>Somnolence</td>
<td>11 (0)</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>54 (5)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>31 (3)</td>
</tr>
<tr>
<td>Infertility</td>
<td>17 (0)</td>
</tr>
</tbody>
</table>
CONTRAINDICATIONS

TRODELVY is contraindicated in patients who have experienced a severe hypersensitivity reaction to TRODELVY received at least two prior therapies for metastatic disease. TRODELVY is indicated for the treatment of adult patients with metastatic triple-negative breast cancer (mTNBC) who have received at least two prior therapies.

PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

PATIENT INFORMATION

Advise patients of the risk of neutropenia. Instruct patients to immediately contact their healthcare provider if they experience fever, chills, or other signs of infection (see Warnings and Precautions).

Nausea/Vomiting

Advise patients of the risk of nausea and vomiting. Premedication according to established guidelines with a two or three drug regimen for prevention of chemotherapy-induced nausea and vomiting [CINV] is also recommended. Additional antinemetics, sedatives, and other supportive measures may also be employed as clinically indicated. All patients should receive take-home medications for preventing and treating delayed nausea and vomiting, with clear instructions. Instruct patients to immediately contact their healthcare provider if they experience uncontrollable nausea or vomiting (see Warnings and Precautions).

Embryo-Fetal Toxicity

Advisive females to patients to contact their healthcare provider if they are pregnant or become pregnant. Instruct female patients of the risk of a fetus and potential loss of the pregnancy (see Use in Specific Populations).

Contraindications

Advise patients of patients of reproductive potential to use effective contraception during treatment and for at least 6 months after the last dose of TRODELVY (see Use in Specific Populations).

Lactation

Advisive females to patients of reproductive potential that TRODELVY may impair fertility (see Use in Specific Populations).

Manufactured by: Immunomedics, 300 The American Road Morris Plains, NJ 07950, USA U.S. License No. 1737.
In 1971, President Richard Nixon declared a war on cancer. Many oncologists and patients now reject the bellicose analogy but coming up to the 50th anniversary of Nixon’s statement, the progress that has been made against the second leading killer of Americans is notable. Because of a combination of public health policies, medical advances, and social reforms, the overall, age-adjusted cancer death rate has been falling since 1991 when it peaked at 215 cancer deaths per 100,000 people. The death rate from cancer declined by 2.2% from 2016 to 2017, the largest single-year drop ever, according to the American Cancer Society’s Cancer Facts & Figures 2020 report.

Earlier diagnosis, more precise treatment, and reduced exposure to known carcinogens — principally cigarettes — have had a favorable effect on five-year survival rates, which now stand at 70% for Whites and 64% among Blacks, as well as on mortality rates.

Lung, colorectal, breast, and prostate cancer are among the most common types of cancer, so declines in their death rates account for much of the drop in the overall death rates. Here are mortality rate trends for those cancers as reported in cancer society’s 2020 report:

- Breast cancer death rates declined 40% from 1989 to 2017 among women.
- Prostate cancer death rates declined 52% from 1993 to 2017 among men.
- Colorectal cancer death rates declined 53% from 1980 to 2017 among men and by 57% from 1969 to 2017 among women.

The cancer society also noted a steep decline in melanoma deaths that it attributes to treatment advances. “The accelerated drops in lung cancer mortality as well as in melanoma that we’re seeing are likely due at least in part to advances in cancer treatment over the past decade, such as immunotherapy,” said William Cance, M.D., the chief medical and scientific officer for the American Cancer Society, in a statement. “They are a profound reminder of how rapidly this area of research is expanding, and now leading to real hope for cancer patients.”

It is important to understand the journey of cancer research and treatment that led to the 25-year decline in deaths, but also to set new goals to ensure treatment is more personalized and equitable in years to come.

“There are certain cancers that have very poor prognoses and high fatality rates. Some of these cancers could benefit from making preventive healthcare and better lifestyles become accessible to all,” notes Smita Bhatia, M.D., M.P.H., director of the Institute for Cancer Outcomes and Survivorship at the University of Alabama, Birmingham. Others, such as pancreatic cancer, she says, require ongoing scientific discovery, and equal access of the scientific discovery to all, in order for death rates to continue to decline.

More survivors

Maybe one of the more underappreciated facts about cancer in the United States is huge growth in the number of Americans who have had cancer who are still living: cancer survivors. In an opinion article published in the New England Journal of Medicine in September, Richard Schilsky, M.D., chief medical officer and executive vice president of the American Society of Clinical Oncology (ASCO), and his coauthors noted that there were 3 million cancer survivors in the United States in 1970. Now there are almost 17 million. The country has a larger population, and the cancer incidence—the number of new cases diagnosed each year—has tripled from just over 600,000 in 1970 to a projected 1.8 million cases this year, Schilsky and his colleagues noted. Earlier detection because of screening and treatment advances factor into survivorship. In 1970, the five-year survival rate was 49%. Now it is about 70%.

Managed Healthcare Executive.com
“It was a very different landscape both in understanding risk factors for cancer, understanding cancer biology, and having a wide array of cancer-specific treatments,” Schilsky said in a podcast that accompanied the article.

In the NEJM article, Schilsky and his colleagues credit the 1971 National Cancer Act, championed by Nixon as launching a war on cancer, as catalyzing the progress in cancer treatment over the past 50 years. They credit the law with increasing funding for research and creating the network of comprehensive cancer centers, which, in turn, led to new treatment strategies (including palliative care), a better understanding of risk factors, and a national network of clinical trials.

In the podcast, Schilsky talked about risk factors “coming into much clearer focus” and efforts to mitigate those risks, including prophylactic breast surgery for women with the highly penetrant BRCA gene mutations, sunscreen to prevent skin cancer, programs to encourage Americans to quit smoking, and vaccination against the human papillomavirus to protect against cervical and anal cancer.

The role of screening
All of this occurred against the backdrop of recognizing that early detection of cancer is associated with better outcomes and that has led to the widespread implementation of cancer screening strategies, said Schilsky, who mentioned screening for cervical, colorectal, breast, and lung cancer specifically.

But cancer screening is controversial. Otis Brawley, M.D., a professor at Johns Hopkins University in Baltimore and a member of the Managed Healthcare Executive editorial advisory board, has been outspoken about what he sees as overscreening that leads to false positives, overtesting, and overtreatment. “Yes, we are still overscreening, but it is not as bad as it once was, especially in prostate cancer,” Brawley said in a recent interview with the MHE editors.

A 2018 article posted on the National Cancer Institute’s website titled “Crunching Numbers: What Cancer Screening Statistics Really Tell Us” goes through some of the explanations and arguments for how screening may skew cancer mortality statistics, including lead-time and length bias. Moreover, any relative risk reduction seen in a cancer screening program that covers the general population is likely to translate into reductions in absolute risk that are quite small for the simple reason that for a general population the risk of developing cancer is small.

Addressing disparities
Although overall cancer mortality figures are encouraging, the disaggregated numbers paint a different picture. Survival rates are lower for Black patients (62%) than for White patients (68%) for every type of major cancer except for kidney and pancreatic cancer, for which they are roughly the same, according to Cancer Facts & Figures 2020.

The American Association for Cancer Research (AACR) published a 156-page report about disparities in September. “In recent years, some strides have been made in combating cancer health disparities, as illustrated by narrowing of racial and ethnic disparities in the overall cancer incidence and death rates,” the report notes. “However, progress has come too slowly, and the cost of all health disparities, including cancer and COVID-19 health disparities—in terms of premature deaths, lost productivity, and the impact on communities—remains monumental and must be addressed.” AACR recommendations for closing the disparity gap include increasing funding for efforts to close the gap and enrolling diverse populations in clinical trials.

Donna Marbury is a freelance writer in Columbus, Ohio.

“There are certain cancers that have very poor prognoses and high fatality rates. Some of these cancers could benefit from making preventive healthcare and better lifestyles become accessible to all.”

— SMITA BHATIA, M.D., M.P.H., DIRECTOR OF THE INSTITUTE FOR CANCER OUTCOMES AND SURVIVORSHIP AT THE UNIVERSITY OF ALABAMA, BIRMINGHAM
Although resistance to vaccination hasn’t a major challenge for health plans, they are not sitting back and letting preventive care fall through the cracks. Instead, many insurers have strategies for promoting vaccination — against a variety of childhood diseases, the flu and COVID-19, once a vaccine becomes available — and are encouraging providers to dispense them and ensure patients are receiving them.

That’s not to say that anti-vaccination sentiment doesn’t exist. California State Sen. Richard Pan, a pediatrician, says he has been a victim of such opinions by some who use ratings sites to downgrade providers and file complaints with their employers. He introduced legislation, which was signed into law last year, that requires health officials to approve requests for medical exemptions to school-required vaccinations and grants officials the authority to revoke medical exemptions if they are found to be fraudulent or inconsistent with state guidelines. The law red-flags any provider who issues more than five vaccine exemptions a year and schools that fall below a 95% immunization rate.

“We are on top of the flu vaccination because a healthcare system can ill afford to let additional patients get sick and have to visit the ER,” says Steve Miller, M.D., chief clinical officer for Cigna. “In addition, paying attention allows us to develop a vaccination infrastructure for COVID-19, which will be different because patients can’t stand in line and wait for a vaccination. A plan also helps establish trust in the healthcare system.

“A flu shot is usually pretty straightforward but atypical today; there is no employer-sponsored campaign when employees are working at home so we need a broader provider network to ensure vaccinations are more readily available,” Miller says. Childhood vaccinations and preventive care, in general, are down as fewer people are getting routine check-ups and screenings because of COVID-19, he says.

Jaja Okigwe, MBA, president and CEO of First Choice Health, a healthcare benefits administrator based in Seattle, says the root of barriers to vaccines is reluctance of beneficiaries to visit a doctor because off the pandemic. Fifty-one percent of U.S. adults now say they would definitely or probably get a vaccine to prevent COVID-19 if it were available, according to the Pew Research Center. That is a significant drop from May, when 72% indicated they would be willing to get vaccinated.

Partly because immunization rates are part of the Healthcare Effectiveness Data and Information Set (HEDIS) measures, health plans and providers have an incentive to keep immunization rates high.

Cigna has created three pilot programs to manage the flu vaccination for underserved populations in Houston, Memphis, Tennessee, and South Florida. The program provides participants with personal protective equipment kits that include masks and sanitizers, connects them with primary care physicians, and provides bus transportation. The response has been positive.

“The pilots also use spokespeople whom members trust, such as local sports stars, clergy, and political leaders, to get the message across to get a flu shot. “There are many social influencers besides doctors that will resonate with members and build confidence,” Miller says. “This has been a true campaign, not just a one-time thing. It’s time to break the code of serving these populations and positively impact these communities.”

Cigna also encourages its providers to build trusted rela-
Insurers take up mantle to ensure immunizations

Creating vaccine strategies
Kristine Grow, senior vice president of communications for America’s Health Insurance Plans, says insurers have an essential role to play as vaccines are approved, in pricing and distribution models, vaccine administration, coverage (they will be covered like other vaccines), and payment and post-market monitoring. They are preparing to:

- Follow prioritization recommendations and weigh in if needed to make recommendations.
- Leverage claims data in advance to identify members who meet the criteria to receive the vaccine and remind them to get the appropriate doses in the right time frames.
- Collaborate with national, state, and local stakeholders to get the vaccines to the public.
- Help educate Americans on safety and effectiveness of a COVID-19 vaccine.

“Our role is to pay for vaccinations and for our providers to dispense them,” says Bob Freeman, CEO of CenCal Health, a Medicaid plan that covers 186,000 people in Santa Barbara and San Luis Obispo counties in California.

“Our emphasis is on how to make easier to get vaccinations and what vehicle to use to communicate most effectively,” Freeman says. “Resistance is not a big problem in the Medicaid population; most are hungry to get vaccinations.”

CenCal has developed a comprehensive program educating and notifying members about obtaining preventive and primary care.

It includes:
- Mailers sent to parents and caregivers of infants and children up to 6 years old who have not received a checkup or well check within the past six months.
- CenCal Health’s member newsletter sent to all member households with age-specific preventive health guidelines for adults and children; education for parents about the importance of pediatric well visits; and assurances of safe visits.
- Website with content focused on what provider offices are doing to prevent spreading COVID-19 to well patients and encouraging parents to call their primary care provider about specifics.
- Media campaigns — television, radio, newspaper, and social media — in English and Spanish featuring recognized local physicians and clinics explaining their safety measures, such as drive-through vaccine clinics for children.

Despite resistance being at a low level, Freeman says the importance of vaccinations should be reinforced. CenCal does not yet have messaging for COVID-19 because “we don’t want to get ahead of the public health department whose direction we follow,” Freeman says.

Texas Children’s Health Plan, a Medicaid health plan in the Houston area, ensures children and women have broad access to vaccines as an integral part of its mission. “We know vaccines are critical in preventing the spread of diseases, which is why we encourage our members to stay up to date on their vaccine schedule and to get a flu vaccine each year,” says Anna Mateja, the health plan’s vice president.

“As a Medicaid managed care organization, we will adhere to the guidelines set forth by state and federal health authorities regarding a COVID-19 vaccine when that becomes available, as we do with the flu vaccine and others,” Mateja says.

PBM s play role
Prime Therapeutics, a PBM based in Minnesota’s Twin Cities metro area, is using efficacy and safety data to study each COVID-19 vaccine option and will rely on the FDA’s labeling to ensure the vaccines are being provided to members in an appropriate manner.

David Lassen, chief clinical officer, says Prime will place COVID-19 vaccines on its national formulary as it does for all vaccinations recommended by CDC, whose guidance the PBM follows. He doesn’t anticipate prior authorization or other utilization management programs for COVID-19 vaccines.

“Our goal will be to ensure the shortest turnaround time from product launch to claim adjudication and administration to our members,” Lassen says. “We will be working with our health plans to encourage members to get the vaccine just as they would any flu vaccine, as both are important protections for the health of the member as well as the community.”

He sees the entire pharmacy supply chain working together to ensure beneficiaries receive a COVID-19 vaccine. Insurers would ensure access to the pharmacy benefit and coverage and pharmacy networks would distribute the vaccines. “Everyone is stepping up so we can be ready to serve the public when the vaccines are available,” Lassen says.

Mari Edlin is a healthcare writer in Sonoma, California.

Managed Healthcare Executive.com   MANAGED HEALTHCARE EXECUTIVE   NOVEMBER 2020
The COVID-19 pandemic has been a bumpy ride in the United States, featuring one controversy after another. One of the few areas of agreement is that the widespread adoption of telehealth amid the pandemic has been, by and large, a positive development.

Here are 10 takeaways about the telehealth boom.

1. It wouldn’t have happened without CMS loosening its rules and paying for it

Earlier this year, CMS enacted new rules to provide practices with the flexibility to use telehealth solutions in response to COVID-19. They included providing payment parity for telehealth visits, allowing payment for many codes that were previously considered nonpayable, and the willingness of the federal Office for Civil Rights to waive enforcement of the HIPAA privacy rules allowing the use of non-HIPAA compliant technologies like FaceTime and Zoom to conduct visits.

"The COVID-19 pandemic led to a quantum leap in moving telehealth forward, almost overnight," says Ronald Hirsch, M.D., FACP, vice president of regulations and education for physician advisory solutions at R1 RCM, a revenue cycle management company in Chicago. "However, this would not have happened without the regulatory flexibilities provided by CMS and other payers."

In October, CMS announced it will reimburse providers for 11 more telehealth services, bringing the total to more than 140. Its proposed 2021 Physician Fee Schedule also paves the way for greater use of telehealth and would make some changes permanent instead of being tied to the federal government’s January 31 declaration of a public health emergency.

Of course, there was telehealth before the pandemic. It was gaining a foothold in many areas of the healthcare system but it seemed stuck on the margins, particularly among large health systems on the East Coast.

“The slow adoption was largely due to the lack of reimbursement and payment parity when there was reimbursement at all,” says Iris Berman, M.S.N., RN, vice president of telehealth services at Northwell Health, the 23-hospital health system in the New York metropolitan area. "Much of the reimbursement directed by CMS was to rural communities, which excluded many of our most vulnerable in urban population centers."

2. There’s no going back partly because telehealth has become so popular

Peter Antall, M.D., chief medical officer of Amwell, a Google-backed telemedicine provider that went public in September, says the average monthly visit volume on his company’s platform increased by about 300% between April and June compared with the first three months of the year.

"Today telehealth is no longer a nice-to-have but rather seen as necessary part of the care journey, and we expect this momentum to largely continue post-pandemic," Antall says. "Ultimately, you can’t put the toothpaste back in the tube. Now that both patients and providers have experienced the convenience of telehealth, we don’t anticipate healthcare to ever go back to how it was."

Adoption and acceptance grew as both the public and the providers realized gains such as improved scheduling, reduced travel time, and easier access to specialists, which sometimes occurred in a matter of minutes or hours instead of days and weeks. "Time will tell what
the future holds for telehealth but we won’t return to the baseline we were at before the pandemic,” says Natalie Pageler, M.D., M.Ed., chief medical information officer at Stanford Children’s Health and clinical professor of pediatric critical care at Stanford University. “Now that both patients and physicians have tried it and learned how to use it, they see the value and incentive to continue using virtual visits.”

Before the pandemic, Stanford Children’s Health was conducting about 20 telehealth visits per day in the ambulatory setting. Within a matter of weeks, that number grew to 700 to 800 per day. “In May, we began resuming care that had been delayed by COVID-19. But even now as our in-person visits are continuing to increase further, we’re still seeing almost the same number of telehealth visits,” Pageler says. “With the increase in awareness of the capabilities of telehealth and digital health, we are seeing many lessons learned from both the provider perspective as well as the patient/family perspective about the value of telehealth visits and the type of care that can be delivered via telehealth.”

George Valentine, a telehealth executive at Cox Communications, a regional telecommunications company headquartered in Atlanta, Georgia, shares the opinion that telehealth is winning the popularity contest. Valentine pointed to survey data collected by consulting company McKinsey & Co. that found that 74% of telehealth users reported high satisfaction, that 57% of providers are more comfortable using it now than ever.

3. Necessity is the mother of adoption

Once COVID-19 arrived, the slow-and-steady-wins-the-race pace turned into a sprint. Healthcare providers started working around the clock to start telehealth programs and improve connectivity. Part of the motivation was making up for revenue lost by the lack of office visits.

Forrester Research issued a report in October that made bullish predictions for telehealth next year. The report noted the sharp drop-off in primary care visits because of the COVID-19 pandemic and the rise of telehealth (and the health clinics inside retailers) to take their place.

“Primary care as we know it today stands in the crosshairs, with new entrants vying for the hearts of consumers who legacy healthcare ignored for too long,” said a Forrester blog post about the report.

4. This is your father’s telehealth

Millennials and their demographic successors in Generation Z have grown up in immersed in an online, digital environment. It has been a truism of telehealth that it would appeal most to younger people who are used to conducting so much of life remotely via their phones and other devices. But recent surveys have shown that age may be less of a factor in telehealth acceptance than many thought, and that those older than 65 have seen the value and convenience of using telehealth services.

“Used correctly, it is an adjunct to in-office visits that saves time in travel and can actually improve coordination of care,” Berman says. “That could be especially important for older people because they are more likely to have multiple and complex health problems. In the past, people with complex medical problems would have to make separate trips to see, say, their pulmonologist, cardiologist and oncologist. Each of these visits required arranging transportation and carving out several hours out of the day. Telehealth will not replace the in-person visits if only because of the tests that must be done in person; the tele-MRI scan is not available yet. Still, with telehealth, it is conceivable that separate specialists could be convened for the same patient visit and the care coordination that is much talked about but realized much less often might actually occur.

About 80% of visits are about seeing and talking with patients,
sometimes with significant others present, with no physical presence required, Berman notes. “Using telehealth for these types of visits affords more efficiency and less wait time in offices for the patient,” Berman says. “Provider quality of life can improve as well. All of this, of course, is with appropriate and well-planned use in conjunction with good workflows. We must think about telehealth as being a tool in the tool chest.”

5. But telehealth could be boon for pediatric care, too
Pediatrics requires some in-person care; a vaccine can’t be administered digitally. And typically children are not dealing with chronic conditions that require medication, tests and so on. Still, childhood is a period of relatively high use of healthcare services, some of which might improve with telehealth. Pageler says telehealth could be important for child health because it allows some services to be provided without disrupting school, sports, and other extracurricular schedules. Unless the condition warrants intensive hospital care or specific in-person procedures or exams, telehealth would allow physicians to see patients who require ongoing care for follow-up appointments, she says.

6. Telehealth has a role in inpatient care
Doctors attending to patients who are at home has fueled the COVID-19 telehealth boom, but telehealth is also playing a role in inpatient care. “During [the pandemic], we also found ways to implement telehealth among our inpatients in the hospital,” Pageler says. “This allowed physicians to care for patients in isolation while minimizing the spread of infection and conserving personal protective equipment, such as masks and gowns.”

Antall says many overwhelmed hospitals have had to “beam in” specialists from parts of the country with fewer COVID-19 cases. “We also saw telehealth as an important way for the ‘worried well’ to see a doctor from the comfort of their home so they didn’t have to take up critical space in emergency rooms if not necessary,” he says.

Northwell Health uses two telehealth platforms that involve some inpatient care, according to Berman: eICU, which utilizes Philips eCareManager software and consists of hardwired beds in ICUs that contain high-definition cameras, speakers, a monitor and a button that if pressed calls directly into a remote critical care team located in a command center that can supplement the bedside direct care team 24/7; and DTC (direct to consumer), which is being used for home televisits, clinic-to-clinic and consultations to the ER, and floor care of the hospitals.

7. Telehealth could widen, deepen the digital divide
Could the current go-go attitude about telehealth be going too far? There are some skeptics who argue that some nuanced information and connection is lost for lack of in-person care.

Emphasizing telehealth may deepen a digital divide that those with access to Wi-Fi, broadband, and fast, smart devices don’t experience and therefore may underestimate. According to the Federal Trade Commission, 19 million Americans lack access to fixed broadband service at threshold speeds, a problem

“Ultimately, you can’t put the toothpaste back in the tube. Now that both patients and providers have experienced the convenience of telehealth, we don’t anticipate healthcare to ever go back to how it was.”

— PETER ANTALL, M.D., CHIEF MEDICAL OFFICER OF AMWELL
much more acute in rural areas. Pew Research found that 19% of Americans do not own a smartphone. And there’s the irony that many of those without access to broadband or a smartphone are the very people who might benefit the most from telehealth because of access, mobility, and transportation issues.

“One trend we must be cautious of as this evolves is that we do not leave other at-risk populations behind—those who do not have adequate broadband coverage or access to devices either because of cost or location,” Berman says. “If we solve for that, we are on our way to a very new world of health care.”

8. Fraudsters see a telehealth opening — and take it

Almost every boom presents an opportunity for fraud, and the telehealth boom is no exception. In late September, the Justice Department announced it had charged 86 people with submitting $4.5 billion in fraudulent claims related to telemedicine. According to a press release about the charges, the defendants are accused of paying doctors and nurses to order unnecessary durable medical equipment, genetic and other kinds of diagnostic testing, and pain medication. The Justice Department press release also said that apart from the criminal cases, the CMS Center for Program Integrity had revoked the Medicare billing privileges of 256 medical professionals because of their involvement in telemedicine schemes.

9. State licensing requirements could become an obstacle

As the COVID-19 pandemic escalated in the spring and the demand for telehealth became apparent, many states moved to relax licensing rules that allowed healthcare professionals from other states to provide telehealth services. Those changes were another key ingredient in the telehealth boom recipe. But in some cases, the licensing rules were relaxed on a temporary basis and they might be tightened up if and when the COVID-19 pandemic eases up.

“For pediatric care especially, where specialists are often few and far between, we need to advocate for those state licensing changes to remain,” Pageler says.

10. Telehealth, in-person: Tis not an either/or

The course of the COVID-19 pandemic over the next several months is difficult to predict with any certainty. There are too many variables, including but not limited to the availability of a vaccine, adherence to social distancing and mask wearing, treatment advances, and the consequences of the election. But there has been resumption of some in-person care and indications that the demand for telehealth has slackened relative to the zenith in April and May when remote care was essentially the only option short of an outright emergency or absolute necessity.

“There are always going to be people who prefer to get their care in person, and there are always going to be some scenarios for which in-person care is better,” Antall says. His company believes in a hybrid-care model that offers support whether patients receive virtual or in-person care. “We want this to be a seamless experience,” Antall says.

— NATALIE PAGELER, M.D., M.ED., CHIEF MEDICAL INFORMATION OFFICER AT STANFORD CHILDREN’S HEALTH AND CLINICAL PROFESSOR OF PEDIATRIC CRITICAL CARE AT STANFORD UNIVERSITY.

Keith Loria, a regular contributor to Managed Healthcare Executive®, is a healthcare writer in the Washington, D.C., area.
A physical nudge is not a push or shove, but a gentle prod (often with the well-placed elbow) to pay attention, to wake up, to look over there.

But today we are enveloped in a swarm of behavioral nudges, partly because we are riveted to our electronic devices. Amazon’s Alexa and Apple’s Siri ping us appointment reminders, tell us when to take the meal out of the oven, and prepare us to take that upcoming left turn at the light.

Nudges—and the technologies to deliver them—are becoming an increasingly important part of American healthcare. They are being used to keep patients safe, steer doctors and consumers to make more cost-effective decisions, and improve the quality of care. The trick to nudges, say experts, is for them to be not too controlling while putting people on a path to the “best” choice. Behavioral nudges, which can include setting defaults and digital reminders to offer chances at small financial rewards, need to anticipate innate flaws in human thinking that tend to overvalue immediate rewards and misjudge probabilistic scenarios.

EHRs are an opportunity
The behavioral nudge is a concept from the field of behavioral economics. In 2017, Richard Thaler won the Nobel Memorial Prize in Economics for his work on behavioral economics, a field that combines economics with the psychology of making decisions. Nudges don’t restrict or force a choice or involve strong monetary incentives but instead help guide a stakeholder to a preferred option, says Mitesh Patel, M.D., MBA, director of the Penn Medicine Nudge Unit, which claims to be the first behavioral “design team” embedded in health system.

In healthcare, nudges originated out of a desire to improve patient safety; among the first nudges were notifications about allergies and adverse reactions to medications. “If a provider tried to order a medication and a patient had a documented allergy or adverse reaction to it, a pop-up would stop the physician and require them to either change the order or give a valid reason why they still wanted to order it,” says Joyce Brown, B.S.N., RN, the clinical informatics coordinator at Deborah Heart and Lung Center, a hospital specializing in cardiovascular and lung disease in southern New Jersey.

Nudging has branched out from there partly because the electronic health record (EHR) makes it relatively easy to use defaults and reminders to guide healthcare decisions. Patient portals and conversations between patients and clinicians also present chances for nudges to take place.

“There are opportunities to work through all of these mediums to align nudges with improved medical decision-making,” Patel says.

Patel and his colleagues at the Penn Medicine Nudge Unit have worked with clinicians from more than a dozen specialties to implement nudges in healthcare. The unit’s success stories include changing default settings in the EHR to increase generic prescribing from 75% to 98%, increasing referrals to cardiac rehabilitation for heart attack patients from 15% to 85%, and decreasing unnecessary imaging among patients with cancer at the end of their life from 68% to 32%. They have also used active choice prompts to remind clinicians to address gaps in care which have increased influenza vaccination, cancer screening and statin prescribing.

Physicians at Deborah Heart and Lung use nudges as reminders of best practices. “They are a way to provide guidance, but ultimately physicians make the decision for the type of care delivered,” Brown says.

Nudges can be used to help providers follow guidelines set by CMS, other government entities, and other organizations. Brown says...
that if certain protocols are required or recommended, nudges can increase the number of clinicians who follow them. If certain protocols are required that involve a number of tests, medications, or treatments, physicians can order all of them at the same time, Brown says.

**Getting the alignment right**

Because nudges can be very powerful, they need to be implemented carefully. “We focus on driving outcomes using national guidelines and evidence-based criteria,” Patel says. “They are most useful when a specific decision point can be targeted to significantly shift decision-making behavior.”

Poorly designed nudges that seem coercive or counterproductive can backfire. Nudges should be designed to create a path of least resistance around a choice so that whoever is being nudged will be receptive to it, experts say. “Nudges can be made difficult to opt out of to increase the likelihood of behavior change, but it is important that a nudge actually aligns with what the people being nudged would see as either in their or society’s best interests,” says Kevin Volpp, M.D., Ph.D., director of the Penn Center for Health Incentives and Behavioral Economics and one of the world’s foremost experts on nudges and behavioral economics in healthcare.

“Well-designed nudges based on clinical evidence make it easier for clinicians to effectively treat patients based on the latest evidence,” Volpp says. “This can save time while also increasing the effectiveness and value of their care.”

But as with any other strategy or tactic designed to influence behavior, nudges can be overdone. In the realm of patient safety, “alarm fatigue” can set in so that safety alerts end up having the opposite of their intended effect because clinicians tune them out. “If a physician receives too many alerts, they may lose their importance,” Brown says.

**Money is an obstacle**

At the University of Pennsylvania, raising generic prescribing rates by using nudges is considered one of the big behavioral economics success stories because it saved the health system about $32 million in the two and a half years after it was implemented.

“Before the prescribing default was changed to generic medications, clinicians weren’t opposed to prescribing generics, but they were unlikely to take the time to sift through a long list of alternatives to find one,” Volpp says. “Making it easy for clinicians to prescribe generics created a pathway whereby nearly 100% of clinicians now prescribe them.”

Volpp says setting generics as a default is a good example of how making the optimum choice easier can guide people to a choice they might have made by themselves had they had more time to consider the decision.

Brown cites Deborah Heart and Lung Center’s sepsis program as one of its greatest successes with nudges. The hospital created a sepsis surveillance board that identified patients with early signs of sepsis. “If they truly show signs of sepsis, we have protocols that include CMS guidelines for sepsis care including timing of labs, fluids, and medications, and electronic documents to prompt the physician with what needs to be charted in order to meet regulations,” Brown said. She believes the program has been successful because physicians have everything they need at their fingertips.

Nudges have their limitations. Volpp says behavior change is unlikely to happen if there are strong financial incentives to stick with the status quo or to make a different change. “Nudges can have a significant influence on what patients and physicians do, but it’s difficult for nudges to overcome strong monetary incentives that induce behaviors,” Volpp says. If, for example, a clinician is compensated primarily for doing procedures, nudges to do fewer procedures are unlikely to have sufficient power to offset the compensation. In contrast, nudges can be highly effective for, say, decreasing antibiotic prescribing rates if there isn’t any countervailing incentive driving that behavior.

Karen Appold is a medical writer in the Lehigh Valley region of Pennsylvania.
We are not finished.

People in treatment for HIV are living longer. That means your members with HIV will face different challenges. At ViiV Healthcare, we’re working to help meet their changing needs.

Learn more about what we are doing at www.us.viivhealthcare.com

Trademark is owned by or licensed to the ViiV Healthcare group of companies.

©2020 ViiV Healthcare or licensor.
HVUADVT200001 February 2020
Produced in USA.
Reading is a struggling small city (population 88,000) in southeastern Pennsylvania with a poverty rate of about 35%. If healthcare providers and providers are to travel “upstream” to address the social determinants of health (SDOH), communities like Reading might be where those efforts would have the biggest effect — or falter because the determinants are deep-seated and intertwined.

Three years ago, Reading Hospital, the 714-bed flagship hospital of Tower Health, a regional nonprofit health system in southeastern Pennsylvania, received a $4.5 million grant from CMS to start a program that teams up community organizations with the hospital. Medicare and Medicaid patients who receive medical treatment at the hospital are asked about their social service needs and care navigators and community health workers help link them with services. Addressing these social needs has helped decrease emergency department visits, saving the hospital $1 million, according to a case study by Reading Hospital released in July. “Working together has a much more powerful impact,” says Desha Dickson, the hospital’s associate vice president for community wellness.

SDOH is a hot ticket in American healthcare these days and the COVID-19 pandemic has made it even more so because of the health and healthcare disparities the pandemic has revealed. The appeal of dealing with the root causes of disease is strong and easy to grasp. But there are also some misgivings. Can the healthcare system realistically take on such big problems? Are the programs longer on public relations than on substance?

Brian Castrucci, president and CEO of the de Beaumont Foundation in Bethesda, Maryland, which focuses on community health, said that while establishing a community food pantry, for example, may be greatly needed, “It only meets the individual patient’s needs for the moment.” Helping an individual address their social service needs by helping them obtain a job or secure housing “extends the treatment of the symptoms, not the treatment of the causes,” he says. “There’s not enough money in healthcare to mitigate these societal-level problems,” Castrucci says “Instead, American healthcare could be more effective using its power to push policymakers to address the social and economic conditions that impact the health of a community.”

Castrucci and the skeptics and critics may have a point. But it also seems reasonable when Dickson and others say SDOH programs take time to bear fruit because the problems they’re addressing — housing, employment, nutrition — are not minor. Besides, even if a program skims the surface or homes in on a fairly narrow problem, it could make a big difference in people’s health status. Granted, the numbers are a little squishy, but by some calculations, up to 80% of a person’s health is influenced by SDOH.

Measuring the effect
Insurers and providers now have enough experience with SDOH programs that they are beginning to amass data measuring the effects of their efforts. Starting in 2018, Humana launched pilot programs in several cities with Papa, a platform that provides “grandchildren on demand” by recruiting college students to spend time with lonely seniors. “There’s a laser focus on social isolation and loneliness,” says Caraline Coats,
MHAS, vice president of Humana’s Bold Goal and Population Health Strategy programs. Using the CDC’s Healthy Days metric, which measures an individual’s physical and mental health, participants in Humana’s program with Papa reported they were physically healthy three more days per month and mentally healthy five more days per month, Coats said.

When the COVID-19 pandemic struck, Papa’s college students shifted to virtual visits with seniors, says Andrew Renda, M.D., associate vice president of population health at Humana.

Humana also used Papa to help address other social determinants of health when COVID-19 flared, Renda says. The students delivered groceries to those who had food insecurity, which allowed for brief social connections with the seniors.

“Social determinants existed before COVID-19, and they’ve been exacerbated by COVID-19,” Renda says. When the insurer surveyed 100,000 Medicare Advantage members after the pandemic began, it found that 40% were feeling a financial strain, about 30% were lonely, more than 25% were food insecure, and almost 10% had insecure housing, Renda says.

In some cases, people who didn’t struggle with social determinants of health before the pandemic are grappling with them now, Renda says. Humana is working with the National Quality Forum, a nonprofit focused on improving healthcare, to develop qualitative measures of food insecurity. “We’re trying to put solid study designs around it,” Renda says. That can help Humana measure outcomes, such as improving patient health and saving money on care.

“No codes for that

Elizabeth Baca, M.D., M.P.A, a specialist leader at the consultancy Deloitte, says value-based care “changes the equation about how we think about health more holistically.” Baca, a physician who practiced medicine and taught at Stanford University, says healthcare traditionally does not have a way for physicians to bill for care that would address SDOH.

She recalls dealing with one immigrant family who lived in a garage. Their son had severe allergies and asthma and had been repeatedly admitted to the intensive care unit. Baca eventually called the California Health and Human Services Agency for help getting the family into a home in order to improve the son’s health. By addressing social determinants, “There’s so much potential to have a real impact for the patient,” Baca says.

More data are getting collected on SDOH, Onlife Health, which is part of GuideWell, the umbrella organization that owns and operates several Florida health insurers, is about to launch the Social Determinants of Health Community-Based Index, a mapping tool that identifies every community’s SDOH vulnerabilities. The tool can be used by certain Blues health plans, such as Florida Blue, Health Care Service Corp., and BlueCross BlueShield of Tennessee, so they can “understand at community levels the vulnerabilities of that community,” says Catherine Bass, Ph.D., M.S., director of informatics at Onlife Health, which is headquartered in Brentwood, Tennessee. After collecting input from its health plan members on topics such as how stress affects their lives or on their eating habits, Onlife can pass the information on to the insurers.

If an individual is dealing with food insecurity, for example, the insurer could help link the person to resources in their community that could help them access healthy food or provide them with information on how to eat healthy on a budget, Bass says.

“Taking such an approach can help improve members’ health and help an insurer attract and retain members because it creates loyalty, as the insurers “know you in a way that feels very personal,” says Bass.

Susan Ladika is an independent journalist in Tampa, Florida, who writes about healthcare and business.

“There’s not enough money in healthcare to mitigate these societal-level problems.”

—BRIAN CASTRUCCI, PRESIDENT AND OF CEO OF THE DE BEAUMONT FOUNDATION IN BETHESDA, MARYLAND