The lives of countless cancer patients worldwide rest on us speaking out. We must be bold in our commitment and actions for equitable care. It’s our time. It’s our responsibility. And I firmly believe it’s ASCO’s destiny.

Lori Pierce, MD, FASTRO, FASCO
University of Michigan, ASCO President, 2020-2021

The first randomized controlled trial to my knowledge of adjuvant immunotherapy in renal cell cancer was interferon, and this was presented at the 1992 ASCO meeting...Now, 29 years later finally—finally—we have a positive adjuvant event study in renal cell cancer.

Toni K. Choueiri, MD
Dana-Farber Cancer Institute, Harvard Medical School

Differences in economic stability, housing, education, food, community, and access to the health care system all play a role in our access to cancer care and our risk of getting cancer.

Jennifer Young Pierce, MD, MPH
Mitchell Cancer Institute, University of South Alabama

HIGHLIGHTS FROM THE MEETING

• STUDY FINDS GENOMICS, PRECISION MEDICINE, MAY EXACERBATE DISPARITIES IN PROSTATE CANCER, SP173.

• DATA IN PACIFIC STUDY SHOW OVERALL SURVIVAL OF MORE THAN 30% AT 5-YEAR MARK, SP178.

• ADDING OLAPARIB TO TREATMENT FOR EARLY-STAGE BRCA-MUTATED BREAST CANCER OFFERS BENEFITS, SP180.

• COSTS IN THE OCM WERE LESS THAN IN ROUTINE CARE, SP189.

• CANCER AND THE RISK OF HOSPITAL READMISSION, SP190.
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Questions Linger About COVID-19’s Origins

The incredible strength and collaboration of the scientific community have allowed us to regain some sense of normalcy. The development and rollout of multiple effective vaccine options have been the medical miracle of our lifetime.

We may never know where this virus came from and what triggered the global pandemic that has claimed more than 3.8 million lives. And we won’t know the long-term effects until enough time has elapsed. What we do know for certain is that the incredible strength and collaboration of the scientific community have allowed us to regain some semblance of normalcy. The development and rollout of multiple effective vaccine options have been the medical miracle of our lifetime.

Sincerely,

Mike Hennessy Sr
CHAIRMAN AND FOUNDER
MJH LIFE SCIENCES™

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

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FROM THE CHAIRMAN

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Questions Linger About COVID-19’s Origins

WAS IT NATURAL ZOONOTIC SPILLOVER that catastrophically catapulted SARS-CoV-2 from an emerging virus into a pandemic pathogen, or was it something much more sinister? Could a lab leak in Wuhan, China, have lit the fuse?

Early on, whispers of a potentially engineered virus out of China were so pervasive that, in February 2020, a group of 27 public health scientists published a letter in The Lancet disputing the lab leak theory.

Analyses of the genomic sequence of the virus subsequently pointed to natural origins, but questions regarding China’s role persisted.

Fast-forward to June 2021, and The Lancet has updated the February 2020 letter with an addendum with revised disclosure statements from virologist and investigator Peter Daszak, one of the 27 authors. Daszak noted that his remuneration is paid solely in the form of a salary at EcoHealth Alliance, a New York-based nonprofit research foundation of which he is president. The foundation has reportedly worked directly with Wuhan laboratories and funded research at the Wuhan Institute of Virology.

In addition, recent reports have uncovered financial ties between Google and EcoHealth Alliance. The tech giant was accused of censoring lab leak “conspiracy theory” stories in its search results, but Google’s health lead, David Feinberg, MD, insisted that the company simply took steps to protect users from unverified information.

Are these coincidences or “where there’s smoke, there’s fire” situations? It’s unclear.

The questions extend beyond origin theory, though. With the FDA’s green lighting of vaccines for adolescents and young adults comes hesitation over long-term effects on fertility and cases of heart inflammation. Robert Malone, MD, the inventor of the messenger RNA (mRNA) vaccine technology, recently expressed concern over the risk-benefit analysis of vaccination for young adults. A CDC advisory committee met recently to discuss cases of myocarditis or pericarditis in people aged 30 and younger who have received an mRNA COVID-19 vaccine.

The incredible strength and collaboration of the scientific community have allowed us to regain some sense of normalcy. The development and rollout of multiple effective vaccine options have been the medical miracle of our lifetime.

We may never know where this virus came from and what triggered the global pandemic that has claimed more than 3.8 million lives. And we won’t know the long-term effects until enough time has elapsed. What we do know for certain is that the incredible strength and collaboration of the scientific community have allowed us to regain some semblance of normalcy. The development and rollout of multiple effective vaccine options have been the medical miracle of our lifetime.

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TABLE. Impact of Clinical Trial Enrollment on Episode Costs in the Oncology Care Model (OCM)

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<tr>
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<td>17.5</td>
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<tr>
<td>Multiple Myeloma</td>
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<td>Small Intensive / Colorectal</td>
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<tr>
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<tr>
<td>All other</td>
<td>9.4</td>
</tr>
<tr>
<td>Total</td>
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SP169 PRESIDENT’S ADDRESS
ASC0’s Pledge on Equity in Cancer Care: “History Has Its Eyes on Us”

SP172 DISPARITIES
Addressing Disparities in Women’s Cancer Care, at Home and Abroad
Study Finds Genomics, Precision Medicine May Exacerbate Racial Disparities in Prostate Cancer
Community-Based Initiative Doubles Accrual Rate of Black Participants in Cancer Trials

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Telehealth Will Stay, but Not For Every Visit, Oncologists Report
Impact of COVID-19 on Disparities in Cancer Outcomes Spans Various Groups of Patients

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Higher Medicaid Income Limits Linked to Longer Cancer Survival

SP177 IMMUNO-ONCOCY
“Practice-Changing” Results Seen for Pembrolizumab in Adjunct Setting for Renal Cell Carcinoma
At 5 Years, More Than 30% of Patients in PACIFIC Had Stable NSCLC, Data Show

CLINICAL SPOTLIGHT: Camille Hertzka Addresses 5-Year PACIFIC Trial Findings, Future Ambitions for Durvalumab

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Adding Olaparib to Treatment for Early-Stage BRCA-Mutated Breast Cancer Yields Benefits, Study Shows
Sotorasib, First Approved KRAS-targeting Cancer Drug, Looks Promising

SP184 CAR T-CELL THERAPY
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Studies Offer Promising Data on CAR T-Cell Therapy in B-ALL, Multiple Myeloma

SP186 LEUKEMIA & LYMPHOMA
Phase 2 Data for Tisagenleucel, Tafasitamab Show Objective Responses in More Than Half of Patients

CLINICAL SPOTLIGHT: Christopher Arendt, PhD, on OPTIC Findings for Dose Optimization of Ponatinib in Patients With CP-CML

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SP189 ADVERSE EVENTS
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SP190 HEALTH-RELATED QUALITY OF LIFE
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CLINICAL SPOTLIGHT: Kirk Shepard, MD, Highlights HRQOL Findings of Lenvatinib/Pembrolizumab Combination Therapy in Advanced Endometrial Carcinoma

SP168 JULY 2021 | AJMC.COM
AFTER A YEAR LIKE NO OTHER, when COVID-19 laid bare the disparities that have long persisted in health care and beyond, the president of the American Society of Clinical Oncology (ASCO) opened the group’s annual meeting on June 5, 2021, by calling it like she sees it.

Equity in care is not sufficient, said Lori Pierce, MD, FASTRO, FASCO, a radiation oncologist from the University of Michigan. Achieving equity—which means that patients have similar outcomes in cancer care, regardless of circumstance—is harder to achieve, in part because it requires overcoming the structural racism that exists not just in society but in health care specifically.

Equity was a theme across this year’s ASCO meeting, held in a virtual format for the second year due to the pandemic. As Clifford Hudis, MD, FACP, FASCO, the group’s CEO, introduced Pierce, he said that in 2018, when she was selected as the 2020-2021 ASCO president, no one could have foreseen the role she would play in leading the organization during the pandemic.

“History has its eyes on us. We are a pivotal time in the history of our society and the social history of the world. We must capitalize on the momentum and hold ourselves accountable.”

—Lori Pierce, MD, FASTRO, FASCO, president, American Society of Clinical Oncology, 2020-2021

At this year’s meeting, Hudis said that Pierce proved to be the right person at the right time. “Sometimes it is said that leaders have to grow and rise to meet the moment, but that was not the case this year,” he said.

Throughout her career, Pierce has worked to address equity issues in health care generally and cancer care specifically. The pandemic has highlighted gaps in access to care and outcomes, and from the start oncologists have braced for treatment regimen alterations due to pandemic protocols, and a potential wave of late-stage diagnoses as patients miss screenings and follow-up care.

In her remarks, Pierce drew on her own experience, growing up in the 1960s, of how laws may change but inequities persist. As a child, she was aware of the civil rights movement. “Although I didn’t realize it at that time, I was observing segregation’s impact on health care,” she said. When she visited her father’s family in Ahoskie, North Carolina, “White residents had access to many high-quality health care options” but “Black people were largely treated by a single African American doctor.

“Looking back, no matter how skilled he was, he was still one doctor treating an entire community—every person, every age, every condition. And that, by definition, is limited,” Pierce said.

“As I got older, attending college and then medical school, I became more aware that while the legal segregation I saw in North Carolina in the 1960s was over, health care inequality remained firmly entrenched in the United States and worldwide. As a resident in radiation oncology, and then as a breast cancer physician and researcher, I became increasingly committed to improving outcomes for all people with cancer.”

In August 2020, ASCO issued an updated statement on cancer disparities and health equity, and in May 2021, Pierce followed up with a specific statement on closing gaps for Black patients with cancer. She cited passage of the Clinical Treatment Act, which takes effect in January 2022. ASCO advocated for the law, which will require Medicaid to cover the costs of any insured members who participate in research; Pierce said the law should help boost the number of Black patients who participate in trials. Right now, Black patients account for about 15% of those with cancer in the United States but only about 5% of patients enrolled in clinical trials.

Before Pierce began her talk, she welcomed a trio of speakers to address the theme of equity: the director of the National Cancer Institute (NCI), Norman E. “Ned” Sharpless, MD; Julio Frenk, MD, PhD, MPH, president of the University of Miami and former minister of health for Mexico; and Rhea Boyd, MD, MPH, a pediatrician, community health advocate, and expert on the intersection of structural racism, inequity, and health.

NCI Seeks Diverse Workforce

Sharpless said the year 2021 marks the 50th anniversary of the National Cancer Act, and while survival rates have improved and tobacco use has declined, the NCI is aware that success has not been felt evenly. Diversifying trials and improving outcomes starts with a modified workforce, and he said the agency is seeking input on how to recruit more Black and Hispanic scientists and how to fund investigators from more diverse backgrounds.

“We know that the research workforce still does not reflect the population of the people we serve,” Sharpless said, noting that it’s important “to build a pipeline of talent.”

A Call for Innovation

For all the weakness of the public health infrastructure that COVID-19 exposed, Frenk commented, it also inspired tremendous scientific collaboration and energy. With the right support, the experience could inspire a generation of public health leaders. He called for the enactment of 3 “constructive proposals” that he said “may make the world safer and better prepared for the next pandemic.”

First, he envisions a global network of “sentinel” health care facilities to rapidly collect and share data on emerging diseases—and avoid coverups of outbreaks. Second is a technology platform that would allow diagnostic tests, vaccines, therapies, and other disease-fighting tools to be developed as quickly and collaboratively as possible. Finally, Frenk advocates for a “rapid deployment force” that he described as composed of teams of international public health foot soldiers, ready to make use of the tools in the aforementioned technology platform if an outbreak occurs.

Calling Out Racism

Boyd’s message was direct: We can’t end racism in health care if we don’t call it what it is. Too often, he said, journal articles...
find more "delicate" terms to use to avoid the ugly truth. Quoting the author Ta-Nehisi Coates, Boyd said that racism in health care is often a visceral experience: "Racism inflicts violence upon the body." Health inequities among certain populations are far from inevitable—they exist because some groups are denied protections and supports—yet the words "institutionalized racism" are rarely used in the literature, Boyd pointed out. She cited a 2018 review of 50 high-impact journals over a 13-year period and found only 25 citations of the term in a title or abstract.

The Tools of Change

Pierce said health equity has "always been at the heart of ASCO," and it can be achieved through the pillars of research, education, and quality care. ASCO has formed a partnership with the Association of Community Cancer Centers to increase community-level participation in trials. In May 2021, she said, "we began recruiting at more than 40 clinical trial sites to test practical strategies designed to increase screening and participation of Black and Latinx patients. The strategies include a clinical trial site assessment tool as well as education to mitigate biases."

While the news out of ASCO highlighted that progress is being made, it was clear that plenty of work remains (see SP172-SP174). The University of Pennsylvania's Abramson Cancer Center announced its presentation of an abstract showing that a 5-year effort to diversify participation in its clinical trials had doubled the share of participation by Black patients, from 12% to 24%. On the flip side, though, Foundation Medicine presented results at the 2021 ASCO Annual Meeting of a survey conducted by ASCO showed that patients' attention to weight management improved during cancer treatment. Pierce also wants to learn from a successful colorectal cancer screening program in Delaware that has "virtually eliminated disparities" and saved millions of dollars.

"History has its eyes on us," Pierce said. "We are at a pivotal time in the history of our society and the social history of the world. We must capitalize on the momentum and hold ourselves accountable."

"In the 1965, the Reverend Dr Martin Luther King Jr said that a man dies when he refuses to stand up for that which is right. The lives of countless cancer patients worldwide rest on us speaking out. We must be bold in our commitment and actions for equitable care," Pierce said. "It's our time. It's our responsibility. And I firmly believe it's ASCO's destiny." 

REFERENCES

CONSIDERATIONS FOR PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER

PSMA: A POTENTIAL PHENOTYPIC BIOMARKER IN PROSTATE CANCER

PSMA may bring the potential of phenotypic precision medicine to the mCRPC population

- Highly expressed in >80% of men with advanced prostate cancer¹
- Can be detected noninvasively by PSMA-targeted PET/CT imaging, which has shown high sensitivity and specificity in detecting tumor lesions²-⁴
- Is a potential therapeutic target associated with oncogenic signaling pathways that promote cell proliferation, cell survival, and angiogenesis⁵-⁸,*


References


¹*Clinical significance has not been established and research is ongoing.*

mCRPC, metastatic castration-resistant prostate cancer; PET/CT, positron emission tomography/computed tomography; PSMA, prostate-specific membrane antigen.
**Addressing Disparities in Women’s Cancer Care, at Home and Abroad**

MARY CAFFREY

**FROM BOTSWANA TO BANGLADESH** to Alabama, disparities in cancer care are a worldwide problem for women with gynecological cancers, whether it’s a delay in starting treatment that allows disease to progress, poverty that puts medication out of reach, or what one speaker called the “systemic racism” that keeps Black patients from joining clinical trials.

“Equality in Care for All Women: Addressing Disparities in Gynecologic Malignancies” came on the first day of the 2021 annual meeting of the American Society of Clinical Oncology. Health equity was a theme throughout the 5-day virtual meeting. This session, moderated by Surbhi Grover, MD, MBA, of the University of Pennsylvania, also featured Arunangshu Das, MBBS, of Square Hospital in Dhaka, Bangladesh, and Jennifer Young Pierce, MD, MPH, of Mitchell Cancer Institute at the University of South Alabama.

**Grover**

Surbhi Grover, MD, MBA, University of Pennsylvania

**Das**

Arunangshu Das, MBBS, Square Hospital, Dhaka, Bangladesh

**Pierce**

Jennifer Young Pierce, MD, MPH, Mitchell Cancer Institute, University of South Alabama

“**It’s important to note that differences in screening do account for differences in mortality: Up to 50% of women dying of cervical cancer [did not have] recent screening.**”

—Jennifer Young Pierce, MD, MPH, Mitchell Cancer Institute, University of South Alabama

**Botswana**

Grover has developed a practice of global radiation oncology at the Princess Marina Hospital in Gaborone, Botswana. She presented data showing that disparities in care in Africa start with the limited number of radiotherapy machines in the central part of the continent, which leads to delays treatment for women with locally advanced cervical cancer.

Botswana has high HIV rates: About 20% of adults are HIV positive, with rates among women of reproductive age even higher. Most people know their HIV status and those who are positive are receiving treatment, noted Grover. “More than 95% of the ones who are on treatment are actually virally suppressed,” she said.

But that immunosuppression increases the risk of cervical cancer. If cancer occurs, “These are the patients who will need radiotherapy,” she said. “Overall survival for all patients at 2 years is close to 67%; at 5 years, it’s close to 56%.”

The challenge is getting patients treated in a reasonable time frame. It could take 25 days from a clinic visit to get the pathology report, and by the time the patient gets to the first radiation conference, 40 days have passed. Government-funded care doesn’t mean it’s fast, Grover explained. “During this period, a lot of the patients potentially get lost or get sicker. And that has a huge impact on their outcomes,” she said.

In 2015, work began on a clinic within Grover’s hospital to set up care navigation to speed the process, connect the various physicians and laboratory staff, and cut down the number of days from diagnosis to treatment. “Just with this simple intervention, we were able to reduce the [time] from biopsy to treatment from 120 days to 60 days, and we’re reanalyzing these data again, since this [outcome] was last looked at in 2017,” she said.

Other interventions involve addressing problems with electronic medical records and using phone apps to track patients, which has allowed the hospital to record “every single patient” in an application, which eliminates paper and makes it easier to keep tabs on patients. Ninety percent of patients as well as providers found this “really useful,” said Grover, and patients are permitted to send free messages if they need to reschedule.

Other projects include using technology to figure out why some women do not follow up for radiation for their cervical cancer, to improve screening rates, and to adjust screening guidelines given the needs of patients who come to their clinic.

**International Disparities**

Das said the “striking disparities” in cancer management between rich and poor countries reach every aspect of care, whether it’s surgery, chemotherapy, radiotherapy, or pathological service. “Almost 100% of these components are available in the public sector of high-income countries. But if we look at the low-income countries, we can see that only 40% of these essential components are available [on average] in the public sector,” he said.

Large numbers of patients with gynecological cancers—cervical, endometrial, and ovarian—live in Africa and Asia, Das explained. But the global burden of where deaths occur does not align with where the resources are.

Each year, Das said, about 207,000 women die of ovarian cancer; 300,000 women die of cervical cancer, and 80% of new cervical cancer diagnoses and deaths happen in Asia and Africa. “There are 3 important components of cervical cancer management: vaccination, screening, and treatment. Human papillomavirus (HPV) vaccination lowers the risk of cervical cancer in a person. However, huge disparities persist in the distribution of the HPV vaccine throughout the world,” Das said, pointing to maps and data from the New England Journal of Medicine to show that low- and middle-income countries are not keeping pace. Other data show that 19% of eligible women are screened for cervical cancer in low-income countries, compared with 63% of women in high-income countries.

As for treatment, access to the most modern therapies is often limited by price—for example, the cost of bevacizumab, he said, is typically beyond the reach of a wage-earner in a country like Bangladesh. And technologies like next-generation sequencing, which are essential for today’s precision medicine strategies, may not even be available in some parts of the world, or even to some poor patients in developed countries.

Das noted how the revelation of disparities in care that were made clear during the COVID-19 pandemic had become a political issue. “Collaboration to reduce the gap is needed,” he said. Access to resources and “the commitment of international societies and organizations is needed to ensure equality.”

**Disparities at Home**

Pierce was direct in taking on the “paradox of ongoing disparities and emerging technology,” showing a map of the United States to
highlights how cervical cancer rates vary by state and by population. “Specifically, by race, we see higher rates of mortality in Black, Hispanic, and Native American women,” she said, noting, however, that disparities have decreased and access to guideline-based care has improved.

Still, “race is not the only category in which we see ongoing disparities. In each state, there are a multitude of differences that each county within a state can have,” she said. Using maps from Alabama, she showed the overlap of HPV-associated cancer incidence and poverty.

“We know that in the United States, race is just a marker for other social determinants of health due to systemic racism. And yet this can be true in other parts of the world as well,” Pierce said. “Differences in economic stability, housing, education, food, community, and access to the health care system all play a role in our access to cancer care and our risk of getting cancer.”

Pierce addressed several realities of vaccination:

• Rates of HPV vaccination range from 39% to 60%, and Pierce said uptake can be affected by cultural concerns that vaccination of young adolescents is akin to an invitation to engage in premature sex.
• In Alabama, those with public insurance are more likely to get the HPV vaccine than those with private coverage.

Guidelines that call for HPV screening and testing, along with Pap screening, and take into account a patient’s history and near- and long-term risk, may help. Such factors “ultimately result in a recommendation that is specific to that patient on that day,” Pierce said, but they may not be helpful in other countries.

Social determinants play a role in many aspects of health care, ranging from lack of transportation to reach facilities and not having child care (leading to missed appointments) to not being enrolled in clinical trials. “It’s important to note that differences in screening do account for differences in mortality: Up to 50% of women dying of cervical cancer [did not have] recent screening. However, these differences do not account for the disparities,” Pierce said.

The lifetime probability of developing prostate cancer is 18.2% among Black men compared with 13.3% among White men. Black men are also significantly more likely to die of prostate cancer than White men (4.4% vs 2.4%).1

Although the advances in genomics and precision medicine promise to improve risk prediction and outcomes for many cancers, they may also actually exacerbate these disparities. In a study presented as an abstract by Foundation Medicine and collaborators, Brandon Mahal, MD, assistant professor of radiation oncology and assistant director of community outreach and engagement at the Sylvester Comprehensive Cancer Center, and colleagues looked at how patterns of comprehensive genomic profiling and treatment varied by race.1

The data, coming from the largest known cohort of its kind, revealed that despite having similar frequency of actionable gene alterations, men of African descent were less likely than men of European ancestry to receive early comprehensive genomic profiling and to be enrolled in clinical trials.

The researchers collected data on more than 11,000 patients with advanced prostate cancer with comprehensive genomic profiling, including 1400 men of African descent and 9200 patients of European descent. They also analyzed real-world data from nearly 900 patients from Foundation Medicine and Flatiron Health’s clinic-genomic database.

The rates of alterations in BCRA1/2, AR, DNA damage response pathway genes, and actionable genes were similar across the 2 ancestry types. And while both groups were just as likely to receive immunotherapy and PARP inhibitor treatment, men of African descent were nearly 3 times less likely to receive an investigational treatment in a clinical trial compared with men of European descent (11% vs 30%). This remained true even among men with actionable alterations (1% vs 6%).

“Men of African ancestry experience the greatest burden of disease in prostate cancer, and this research indicates that differences in cancer care are not solely based on biological factors, but rather points to socioeconomic factors such as access to comprehensive genomic profiling and clinical trial enrollment,” Mahal said in a statement.1 “To ensure equitable opportunities for precision medicine, we need to expand access to and awareness of advances that impact patient care and outcomes, including timely use of genomic testing to help make informed treatment decisions.”

Reference

Study Finds Genomics, Precision Medicine May Exacerbate Racial Disparities in Prostate Cancer

JAIME ROSENBERG

RACIAL DISPARITIES IN HEALTH OUTCOMES, including in cancer, are well documented. However, it’s not always clear how biological or socioeconomic factors affect these disparities, or whether advances in genomics and precision medicine have an impact.

Now, new research presented at the 2021 American Society of Clinical Oncology Annual Meeting is painting a clearer picture of what drives differences in mortality and outcomes for patients with prostate cancer, which has higher incidence and mortality among Black men.

The lifetime probability of developing prostate cancer is 18.2% among Black men compared with 13.3% among White men. Black men are also significantly more likely to die of prostate cancer than White men (4.4% vs 2.4%).1

Although the advances in genomics and precision medicine promise to improve risk prediction and outcomes for many cancers, they may also actually exacerbate these disparities. In a study presented as an abstract by Foundation Medicine and collaborators, Brandon Mahal, MD, assistant professor of radiation oncology and assistant director of community outreach and engagement at the Sylvester Comprehensive Cancer Center, and colleagues looked at how patterns of comprehensive genomic profiling and treatment varied by race.1

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“Men of African ancestry experience the greatest burden of disease in prostate cancer, and this research indicates that differences in cancer care are not solely based on biological factors, but rather points to socioeconomic factors such as access to comprehensive genomic profiling and clinical trial enrollment,” Mahal said in a statement.1 “To ensure equitable opportunities for precision medicine, we need to expand access to and awareness of advances that impact patient care and outcomes, including timely use of genomic testing to help make informed treatment decisions.”

Why, Pierce asked, are women of different races with cervical cancer at the same stage often given different surgical recommendations? It’s a big problem if patients are receiving guideline-based care and yet even in a high-volume hospital the disparities are not completely eliminated, she said.

“Genetic alterations may contribute to these disparities, and increasingly, data support molecular differences at the tumor level by race and other cancers,” Pierce said. “These genetic differences may play a role in the treatments that we are offering patients and their response to treatment,” Pierce said.

The problem: White women account for most of the patients in the studies used to develop the guidelines.

For women of other races, “if we want to find different treatments that may work differently, we’ve got to look harder,” she said.

REFERENCE
During a separate presentation, Mahal explained that most genomic studies are based on Eurocentric cohorts, with approximately 80% of patients included in the genome-wide association study being of European descent despite accounting for 16% of the population, leaving the door open to worsening disparities due to a lack of representative studies. Mahal outlined several approaches that could be taken to both study and address disparities in prostate cancer, including:

- transdisciplinary research that bridges basic, clinical, and epidemiological research;
- trials that include diverse populations;
- precision medicine used as a means to identify mechanisms of disparity; and
- outreach programs to bring care delivery and cutting-edge science to diverse communities.

**REFERENCES**


**Community-Based Initiative Doubles Accrual Rate of Black Participants in Cancer Trials**

**LAUREN MASSARO**

**A 5-YEAR INITIATIVE** to encourage the enrollment of Black participants in cancer clinical trials was associated with improved accrual rates at the Abramson Cancer Center (ACC) at the University of Pennsylvania, according to research results published during the 2021 annual meeting of the American Society of Clinical Oncology.

Using targeted community outreach and engagement strategies, the effort aimed to address the broader issue of underrepresentation of Black participants in cancer research—nationwide, only 5% of Black patients are enrolled in clinical trials, although Black individuals comprise about 14% of the overall US population.

In 2014, baseline findings of the 12-county catchment area near Philadelphia showed that while Black residents comprised 19.0% of the population and 16.5% of patients with cancer, only 11% of ACC patients were Black. The rates of enrollment of Black participants in 3 kinds of trials—treatment, nontherapeutic interventional, and noninterventional—were 12.2%, 8.3%, and 13.0%, respectively.

The ACC launched the community-based engagement initiative to address these gaps. The program implemented culturally tailored marketing strategies for cancer clinical trials; protocol-specific plans to facilitate Black participant enrollment; new partnerships with faith-based organizations serving Black communities to conduct educational events about clinical trials; and pilot programs with Lyft and Bide Health to address transportation barriers. It also promoted patient education by nurse navigators regarding cancer and clinical trials and established an improved informed consent process.

Using formats ranging from educational forums to wellness fairs, the program reached more than 10,000 individuals in venues such as churches, neighborhood community centers and parks, and health centers.

By 2018, the outreach was bearing fruit, with the percentage of Black patients treated at the ACC increasing to 16.2%, an approximate 5% increase over 2014. It matched the percentage of Black cancer patients in the areas around the hospital.
PATIENTS WITH CANCER had different outcomes during the COVID-19 pandemic depending on their ethnic background or economic status, according to a pair of studies presented during the 2021 American Society of Clinical Oncology (ASCO) annual meeting.

Abstracts revealed that end-of-life experiences are worse for patients with Medicaid than they are for patients with commercial insurance, and that Black patients with breast cancer fare poorly compared with other ethnic groups when it comes COVID-19 outcomes.

Disparities in health outcomes by race and ethnicity or have been studied for years, but the arrival of COVID-19 has added a new dimension and elevated awareness about health and coverage gaps as the pandemic made its way through the country.

BREAST CANCER AND COVID-19. With Black and Hispanic patients having a higher risk of acquiring the virus that causes COVID-19, investigators of the first study abstract aimed to see how 1000 patients of different ethnicities with breast cancer fare after contracting the disease. Across all ethnic groups, Black patients were significantly more likely to have more severe illness and die of the virus. Black patients were more likely than White and Hispanic patients to be hospitalized for COVID-19 (49% vs 34% vs 34%, respectively) and require mechanical ventilation (9% vs 3% vs 3%).
COVID-19

Higher Medicaid Income Limits Linked to Longer Cancer Survival

Mary Caffrey

States with higher Medicaid income limits—allowing more people to have health coverage—had better cancer survival rates among those newly diagnosed with cancer, according to study released this week ahead of the annual meeting of the American Society of Clinical Oncology (ASCO).

The study tracks 1.5 million adults who were diagnosed with cancer between 2010 and 2013, just before the effects of Medicaid expansion, allowed states to include households earning up to 138% of the federal poverty line (FPL). But some states opted not to participate, and because Medicaid has always been a shared program between the federal and state governments, there has been wide variation in income limits for Medicaid over the past decade for adults aged 19 to 64 years.

Using the National Cancer Database, researchers tracked the patients through December 31, 2017, for up to 8 years of follow-up. They put states into 3 categories based on their Medicaid income limit: (1) 50% of the FPL or less, (2) 51% to 137%, or (3) 138% of the FPL or greater.

The study team compared results for 17 common cancers. Among those diagnosed with early-stage breast cancer, the death rate due to any cause was 31% higher in states with Medicaid income eligibility limits capped at 50% of FPL, and 17% higher in states with limits between 51% and 137% FPL, compared with similar patients in the 11 states with Medicaid income eligibility limits of 138% FPL or greater prior to 2014.

This is not the first study presented at ASCO linking Medicaid expansion to improvements in cancer care. A late-breaking abstract presented in 2019 found that expansion led to better cancer care for Black patients newly diagnosed with cancer, including the ability to get timely care. Lead author Jingxuan Zhao, MPH, an associate scientist at the American Cancer Society, said the variation that exists today was present at the start of the study as well. In Texas, home to the largest number of uninsured, the Medicaid eligibility cap was only 27% of the FPL.

The number of states opting for Medicaid expansion has increased since 2014, and now stands at 38 plus the District of Columbia. The remaining 12 include some of the poorest states in the country, which have high rates of comorbidities. Congress recently offered more incentives to woo these states to expand Medicaid under the Affordable Care Act.

“This study shows that states with expanded Medicaid income eligibility limits have improved cancer survival rates, consistent across cancer type and stage. Health insurance coverage is associated with improved access to cancer prevention, diagnosis, and treatment, allowing us better opportunities to provide the right care to the right patient at the right time,” said ASCO President Lori J. Pierce, MD, FASTRO, FASCO.

“I think these data can be used to encourage those states who have chosen not to expand Medicaid coverage to strongly reconsider, since people who are uninsured are very likely to forego screening, and miss detection of early lesions, when a cure would be far more likely,” Pierce said.

“Those who are uninsured are unlikely to receive cancer care. And for those who are able to start cancer treatment, they’re unlikely to complete their cancer here. So, equity of care is very, very critical.”

References
"Practice-Changing” Results Seen for Pembrolizumab in Adjuvant Setting in Renal Cell Carcinoma

MARY CAFFREY

TREATING PATIENTS WITH a common type of kidney cancer with the checkpoint inhibitor pembrolizumab (Keytruda; Merck) after surgery cut the risk of disease recurrence or death by 32% over a 2-year period, according to results presented in June during the annual meeting of the American Society of Clinical Oncology (ASCO).

The KEYNOTE-564 interim results, which capped the meeting’s plenary session, were described as “practice-changing” by a scientist asked to comment, although more time is needed to learn whether a clear benefit in disease-free survival (DFS) fully extends to overall survival (OS).1

Merck funded the study.

Commentator Rana McKay, MD, associate professor of medicine and urology at the University of California San Diego, and Genitourinary Oncology co-lead at Moores Cancer Center, said that while it will be important to wait for OS data to mature, she did not hesitate to describe the results as “practice-changing.”

“The data represent a paradigm shift as the first positive phase 3 study of adjuvant immunotherapy in RCC,” McKay said. “DFS prolongation represents clinical benefit, given the magnitude of benefit and limited toxicity.”

If pembrolizumab after surgery is adopted as the new standard of care for these patients, McKay said, “new questions will arise, including, ‘Will there be broad implementation for all patients? What about the application for non–clear cell patients? And if recurrence does develop, how does this alter first-line treatment?’

"Ultimately,” McKay said, "this is a quantum leap forward for our patients and provides additional options for individuals with renal cell carcinoma.”

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—Rana McKay, MD, associate professor of medicine and urology, University of California, San Diego

Renal cell carcinoma (RCC) kills 175,000 people worldwide each year, and its incidence has been slowly rising, due to an aging population and better detection.2 Half of patients who have surgery to remove an initial tumor see their cancer return, so the search has been on for treatment that could prevent cancer from reaching an advanced stage. Until now, adjuvant studies have inconsistent or negative. However, pembrolizumab’s effectiveness in metastatic RCC raised the possibility that the PD-1 inhibitor could work in the adjuvant setting.3

The phase 3 study is the first with a checkpoint inhibitor in the adjuvant setting to improve DFS in patients with high-risk clear cell RCC who have had surgery to remove a tumor or the entire kidney. Toni K. Choueiri, MD, director of the Lank Center for Genitourinary Oncology at the Dana-Farber Cancer Institute and lead author of the study, characterized how long researchers in the field have searched for an adjuvant treatment for high-risk RCC patients after surgery.

"To my knowledge, the first randomized control trial of adjuvant immunotherapy in RCC [utilized] interferon, and this was presented at the 1992 ASCO meeting. At that time, I wasn’t done with high school,” Choueiri said during the presentation. "Now, 29 years later, we finally—finally—have a positive adjuvant event study in RCC.”

Details of KEYNOTE-564

The study randomized 994 patients 1:1 to receive either pembrolizumab or placebo at least 12 weeks after surgery. The primary end point was DFS, with OS as a secondary end point. Patients at various risk levels were enrolled: intermediate-high risk, high risk, or no evidence of disease after a primary tumor and soft tissue metastases completely resected at least 1 year from nephrectomy. Results showed:

• The 24-month DFS rate was 77.3% with pembrolizumab, compared with 68.1% with placebo (HR, 0.68; 95% CI, 0.53-0.87; P = .001). The benefit was consistent across subgroups.

• The estimated preliminary OS rate at 24 months was 96.6% with pembrolizumab, compared with 93.5% with placebo; however, the number of events was small, and Choueiri said the results (HR, 0.54; 95% CI, 0.30-0.96; P = .0164) “should be interpreted with caution.”

• Adverse events (AEs) of grade 3 or higher were more common with pembrolizumab than placebo: 32.4% vs 17.7%. No treatment-related deaths were seen in the pembrolizumab group.

"Ultimately,” McKay said, “this is a quantum leap forward for our patients and provides additional options for individuals with renal cell carcinoma.”

REFERENCES


LUNG CANCER REMAINS the leading cause of cancer death in the United States, projected to take 131,000 lives this year.1 But recent news in lung cancer has been positive—fewer new cases and fewer deaths—due to lower smoking rates, improved screening, and much better therapies.

Results presented at the 2021 American Society of Clinical Oncology (ASCO) annual meeting showed the durability of a practice-changing immunotherapy, as 5-year results for durvalumab (Imfinzi; AstraZeneca) showed that 43% of certain patients with non–small cell lung cancer (NSCLC) were alive after 5 years and 33% of those who received the agent had no advancing disease.2

Those rates are double or triple what would have been expected in the past, according to an investigator for the phase 3 trial, called PACIFIC. The trial evaluated the effectiveness of giving durvalumab for 1 year to patients with stage III NSCLC whose disease had not progressed after receiving platinum-based chemoradiotherapy.

David Spigel, MD, chief scientific officer at the Sarah Cannon Research Institute and an investigator in the PACIFIC trial, said patients were included regardless of their PD-L1 status, even though durvalumab binds to PD-L1. The monoclonal antibody blocks the interaction with PD-1 and CD80 to deter a tumor’s ability to work around the immune system.

Results from the abstract presented at ASCO showed:

- Overall, 473 patients in PACIFIC were randomized to receive durvalumab and 236 received placebo. The last patient completed treatment in May 2017. As of January 2021, median follow-up was 34.2 months.
- The 60-month overall survival (OS) rates were 42.9% for durvalumab and 33.4% for placebo (stratified HR, 0.72; 95% CI, 0.59-0.89).
- The 60-month progression-free survival (PFS) rates were 33.1% for durvalumab and 19.0% for placebo (stratified HR, 0.55; 95% CI, 0.45-0.68).

Several initiatives are underway to boost lung cancer screening rates to catch cancer earlier. The US Preventive Services Task Force recently recommended that screening should begin for smokers or former smokers at age 50 years instead of 55 years.3

Although most patients present with NSCLC at stage III, multiple ongoing trials are examining the use of durvalumab in earlier stages of NSCLC, and the immunotherapy is also being tested in combination with other therapies in the stage III unresectable setting and in the neoadjuvant early-stage setting. If screening rates improve and patients are tested at younger ages, more patients can be treated when NSCLC is at a curable stage.

In presenting the results, Spigel said the 5-year data establish “a new benchmark for the standard of care in the unresectable stage III NSCLC setting.”

“Historically,” he said, “only 15% to 30% of these patients survived 5 years.”

When Another Option Is Needed

The practice-changing results from PACIFIC don’t apply to every patient with stage III unresectable NSCLC, according to Helen Ross, MD, a medical oncologist at Banner MD Anderson Cancer Center in Gilbert, Arizona, who presented results from the phase 2 AFT-16 study.4

“Unfortunately, many, if not most, of our unresectable stage III NSCLC patients won’t be eligible for adjuvant checkpoint inhibitor treatment,” she said. “We hypothesize that neoadjuvant atezolizumab given before chemoradiotherapy might allow more of our eligible patients to receive the potential benefit of a checkpoint inhibitor. And they would be able to continue adjuvant immune checkpoint inhibitor therapy after chemoradiotherapy, if they still had good performance status and no progression of disease.”

Ross explained the study schema:

- Patients with unresectable stage IIIA and IIIB NSCLC received 4 cycles of atezolizumab, with restaging after cycles 2 and 4.
- Those who had not progressed went on chemoradiotherapy chest radiation with weekly carboplatin/paclitaxel, and they were also eligible for standard consolidation therapy.
- Those who still had not progressed after restaging were eligible to complete 1 year of atezolizumab.
- Of the population of 64 patients with unresectable stage III disease, data from 62 who received at least 1 dose of atezolizumab were presented.

The average age of patients in the study was 63.9 years; 51.6% of the patients were female, 77.4% were white, 61.3% were former smokers, 11.3% were never smokers, and 56.5% had an ECOG performance stage of 1.

RESULTS. The median PFS was 23.7 months; the 12- and 18-month PFS rates were 66% and 57%, respectively. The 18-month OS rate was 84%, with the median OS not estimable. Adverse events included one each of grade 3 pneumonitis, pneumonia, and colitis, and one event of grade 4 Guillain-Barre syndrome.

Ross explained that the study team then undertook an exploratory analysis “to look at outcomes, including PFS from the end of chemoradiotherapy, to try to mirror the findings of the PACIFIC trial.”

“Our PFS [rates] at 12 and 18 months from the end of chemoradiotherapy were 78% and 72%, respectively,” she said. “The PACIFIC trial reported PFS at 12 months of 55.9%, and at 18 months of 44.2%.”

Based on these phase 2 findings, Ross said, “We think the neoadjuvant approach merits further study in unresectable stage III NSCLC.”

REFERENCES

Camille Hertzka Addresses 5-Year PACIFIC Trial Findings, Future Ambitions for Durvalumab

Produced by Matthew Gavidia

Camille Hertzka, vice president and head of oncology, US Medical, AstraZeneca, discussed updated findings of the PACIFIC trial indicating that a third of patients with unresectable non–small cell lung cancer are stable at 5 years.

Updated findings of the PACIFIC trial showed an overall survival (OS) rate of 43% in patients with unresectable non–small cell lung cancer (NSCLC) after 5 years of treatment with durvalumab,1 which is a promising trend that will continue to be investigated in future clinical trials, said Camille Hertzka, vice president and head of oncology, US Medical, AstraZeneca. FDA approved durvalumab, sold as Imfinzi, in this setting in February 2018.2 This interview has been edited lightly for clarity.

EVIDENCE-BASED ONCOLOGY™ (EBO): As you report 5-year data on PACIFIC, what percentage of stage III NSCLC patients are receiving the regimen of concurrent chemotherapy followed by durvalumab?

HERTZKA: We’ve seen from the very beginning—from the first presentation [of results], and after the FDA approval—a lot of enthusiasm around these data. And now, we see that approximately 70% of patients are currently being treated with the PACIFIC regimen.3

EBO: Updated results on subgroups will be reported later, but OS data suggest favorable outcomes for several patient groups. Do the subgroup analyses generally hold up?

HERTZKA: Let me start first with the overall benefit that we see in the study. In the primary analysis we reported a couple of years ago, [there was] an improvement in [progression-free survival] as well as OS. During these analyses at [the American Society of Clinical Oncology annual meeting], we presented a 5-year follow up, which is a critically important milestone when you think about lung cancer, and unresectable stage III lung cancer.

We reported that 43% of the patients included in this study who were treated with durvalumab [were] alive 5 years later, which is really significant for this disease. To me, what is [also] extremely important to consider is the number of patients who have not progressed during these years: One-third of patients who were treated with durvalumab were still progression-free at 5 years.

[More specifically], they were treated for a year with durvalumab after chemoradiation, which means that for this one sort of patient, they have been free of treatments and free of progression for 4 years. It’s really significant for patients.

That is a preliminary analysis, where we had power to demonstrate results into the primary end point. If we look at the subgroup analysis, it has been really consistent over time that the benefits were reported and observed across the different subgroups. What we’ve seen from the very beginning was a tendency of having women, patients who are younger, or patients with earlier stage [of having] a slightly better benefit, but it’s very difficult to say if it’s a better benefit or if it’s just prognostic of these patients.

When you look across studies in lung cancer, you will always see that women have a slightly better prognosis than men; you would [also] always see that younger patients would have a better prognosis. So, I think when we look at these subgroups, it’s important to consider what is predictive and what is prognostic. From what we’ve learned, there was nothing that really stood out that was a surprise. And it’s consistent over time; nothing really changed at the 4-year or 5-year mark.

EBO: Do the 5-year data support new screening guidelines that will call for screening patients for lung cancer at earlier ages? What can be done to boost screening rates?

HERTZKA: That’s a really good question. To me, the priority at this stage is that we need to get all patients who should be screened to be screened. That is a first step.

We see so many patients, and especially medically underserved patient populations, who are not doing the screening as they should. We see so many smokers who feel that they don’t want to hear about bad news so they will wait a little bit longer. [This] is associated sometimes with this fear of feeling guilty that they did something.

It’s also important that we raise greater awareness about the importance of screening in general. So, what can we do? Raise awareness, make noise, tell everybody how important it is to do screening because of the impact it can have. And PACIFIC is a way to tell the story of what an impact it can make, because if you’re not treated early, you will have a late-stage disease and the outcome will be totally different.

I don’t think the 5-year milestone is the main point. I think PACIFIC in general [is the point], plus all the other studies—specifically, [I’d like to] mention ADAURA, which was presented last year with osimertinib in [an] earlier stage. That is another very important milestone.4

The advances we are making in the early stage are going to be even more impactful if more patients are diagnosed earlier. So, we need to do everything [possible] to get to patients who should be screened earlier for lung cancer and beyond lung cancer, I have to say. And [I’d like to] add that a lot of technologies are being assessed to improve screening rates.

REFERENCES
Targeted Therapy

Adding Olaparib to Treatment for Early-Stage BRCA-Mutated Breast Cancer Yields Benefits, Study Shows

MARY CAFFREY

Adding Olaparib to Treatment for Early-Stage BRCA-Mutated Breast Cancer Yields Benefits, Study Shows

The 3-year distant disease–free survival was 87.5% in the olaparib group and 80.4% in the placebo group, for a difference of 7.1 percentage points (95% CI, 3.0-11.1). The HR for distant disease or death was 0.57 (99.5% CI, 0.39-0.83; P < .001).

The 3-year estimated overall survival was greater with olaparib but not statistically significant at the time of the interim analysis.

Adverse events (AEs) were consistent with those in earlier studies with olaparib. Serious AEs did not occur more frequently with olaparib than with placebo.

"Olaparib had limited effects on global patient-reported quality of life," the authors wrote in NEJM.

The results are the first to report the effects of a PARP inhibitor as an adjuvant therapy on survival end points. As such, lead author Andrew Tutt, MB ChB, PhD, of the Institute of Cancer Research, King’s College, said that they suggest a possible addition to the standard of care for patients with germline BRCA1/2 mutation–associated early breast cancer whose risk of cancer recurrence is higher. More follow-up is planned.

Olaparib is sold as Lynparza by AstraZeneca/Merck; AstraZeneca funded the study with the National Cancer Institute.

REFERENCES

Sotorasib, First Approved KRAS-Targeting Cancer Drug, Looks Promising

PETER WEHRWEIN

Sotorasib, First Approved KRAS-Targeting Cancer Drug, Looks Promising

Sotorasib, taken as a daily pill, targets mutated versions of the KRAS gene. Researchers have long identified these mutations as instrumental in the development of cancer, but the gene has...
been an elusive target for treatment for decades. Skoulidis explained that the gene has a “smooth and featureless surface” that makes it difficult for treatment agents to latch onto, making it possibly “undruggable.”

Cost issues could be a hurdle. Media reports suggest that Amgen plans to price the drug at $17,900 a month, a price that payers may balk at depending on how the drug stacks up against its alternatives.

About 1 in 8, or 13%, of patients with nonsquamous NSCLC have tumors with the KRAS G12C–mutated genes that sotorasib targets, according to Skoulidis. He said that each year, about 13,000 US patients will be eligible to take the drug based on its current indications.

Sotorasib has the history-making distinction of being the first FDA-approved drug to target the KRAS gene, but the drug’s clinical and commercial fate is not certain. A current phase 3 trial, CodeBreak200, is comparing sotorasib with the established cancer drug docetaxel. Skoulidis said that results from previous studies suggest that sotorasib is more effective but that such comparisons must be interpreted with caution; they aren’t as valid as head-to-head comparisons.

Sotorasib may also face competition: Mirati Therapeutics reported positive results for adagrasib, its KRAS G12C inhibitor, at an American lung cancer meeting earlier this year.2 Also, second-generation KRAS-targeted drugs that are at various stages of development could overshadow sotorasib, despite its first-out-of-the-gate status.

Cost issues could be another hurdle. Media reports suggest that Amgen plans to price the drug at $17,900 a month, a price that payers may balk at depending on how the drug stacks up against its alternatives.3 Amgen included many of the results of the phase 2 trial, called CodeBreak100, in its previous announcement of the FDA approval, so results presented at the ASCO meeting and published simultaneously in the New England Journal of Medicine were somewhat anticlimactic. The results showed that 46 of 124 patients (37%) included in the analysis had an objective response to sotorasib; the median duration of response was 11.1 months, median progression-free survival was 6.8 months, and median overall survival was 12.5 months. Most patients (69.8%) experienced treatment-related adverse events; for 20.6%, they were serious.

According to Skoulidis, among the most important findings of the phase 2 trial may be response seen in patients with a co-occurring mutation in the STK11 gene and an unmutated KEAP1 gene. “Sotorasib works only in patients with KRAS G12C–mutated NSCLC, but it appears, based on these data, that there is a signal that it might work better in KRAS G12C–mutated NSCLC that harbors a co-mutation in STK11, particularly when KEAP1...is wild type,” Skoulidis said.

If the finding is confirmed in larger trials, it might point to a subgroup of patients who particularly benefit from Amgen’s KRAS-targeted drug and perhaps to its use as a first-line drug, noted Skoulidis. Only 2 of 126 patients in the phase 2 trial were Black, Skoulidis said both Amgen and the participating academic institutions are aiming to improve inclusion of underserved and underrepresented patient populations in the follow-up phase 3 trial. He also hopes that the approval of sotorasib will “galvanize and activate efforts to routinely obtain comprehensive genetic profiling of basically any patient with locally advanced or metastatic NSCLC.”

REFERENCES
Findings of an extended follow-up of larotrectinib in patients with tyrosine receptor kinase (TRK) fusion cancer indicate that this neurotrophic TRK (NTRK) inhibitor is more effective than any other treatment for this patient population, said Antoine Italiano, MD, PhD.

**EVIDENCE-BASED ONCOLOGY™ (EBO):** Can you speak on the goals of this study in assessing longer follow-up of larotrectinib use in patients with TRK fusion cancer?

**ITALIANO:** The main point we have investigated in this study is a specific end point called the growth modulation index [GMI]. This represents the ratio of progression-free survival [PFS] on an investigational treatment, larotrectinib, vs the PFS on a previous line of treatment the patient received.

This end point, GMI, is particularly useful in settings where it’s very challenging to perform a randomized study and therefore to have a control arm. This is the case, for instance, with NTRK fusion, which is very rare. GMI allows [us to] use the patient as [their] own control, and we consider a GMI ratio of more than 1.33 to indicate very promising activity.

In this study, we analyzed the GMI for all the patients who received a previous line of therapy, and then larotrectinib, based on the presence of NTRK fusion. [A total of] 122 patients were included in the analysis, and we observed the GMI to be more than 1.33 in about 74% of patients. [This] means, clearly, that the most efficient systemic treatment in this specific population is the NTRK inhibitor.

**EBO:** Can you speak on the significance of the observed rise in GMI for those undergoing larotrectinib use in patients with TRK fusion cancer?

**ITALIANO:** Since we don’t have [a] randomized study, this intrapatient comparison, in which the patient is used as their own control, clearly indicates that larotrectinib is more effective than conventional treatment the patient has [previously] received. For me, this clearly suggests that at least for patients with NTRK fusion, the best systemic treatment is the NTRK inhibitor, larotrectinib.

"Since we don’t have [a] randomized study, this intrapatient comparison, in which the patient is used as their own control, clearly indicates that larotrectinib is actually more effective than conventional treatment the patient has [previously] received. For me, this clearly suggests that at least for patients with NTRK fusion, the best systemic treatment is the NTRK inhibitor, larotrectinib."

—Antoine Italiano, MD, PhD

**REFERENCE**


**SPOTLIGHT**

**CONFERENCE**

ASCO 2021 Annual Meeting: Late-Breaking Late-Stage and Leading Edge Late-Stage Presentations - Friday, June 4, 2021

**THERAPEUTIC AREA**

Targeted Therapy

**AUTHOR**

Matthew Gavidia, PhD

**PRODUCER**

Matthew Gavidia

**IMAGE**

Antoine Italiano, MD, PhD, on Extended Follow-up Findings of Larotrectinib in Patients With TRK Fusion Cancer

**PRODUCED BY**

Matthew Gavidia
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Larry Anderson, MD, PhD, Discusses High Response Rates of Ide-Cel in Multiple Myeloma, Protocols During COVID-19

Produced by Matthew Gavidia

Larry D. Anderson, MD, PhD, is the director of the Myeloma, Waldenström’s, and Amyloidosis Program and associate professor, Internal Medicine, Division of Hematology/Oncology, UT Southwestern Medical Center in Dallas, Texas.

ANDERSON: This is an updated analysis from the KarMMa study presented at ASCO 2021 that shows longer-term efficacy and safety results in patients treated with ide-cel in the KarMMa trial overall, and broken down by number of prior lines of therapy, vs 3 vs 4 or more, [because] the FDA label is requiring at least 4 prior lines of therapy and the study only required 3.

Our results showed a 24.8-month median overall survival in triple class-exposed, relapsed refractory multiple myeloma now at a median follow-up of 24.8 months, the longest follow-up to date for a global clinical trial of CAR T-cell therapy for myeloma.

Overall survival was similar after 3 vs 4 or more prior lines of therapy. And of note, it was over 20 months for those with extramedullary disease and with triple class refractory. Overall, 128 patients were infused with ide-cel in this study, with a range of 150 [million] to 450 million CAR T-cells infused. These were patients that had received a median of 6 prior lines of therapy, ranging from 3 to 16.

The overall response rate was 73%. Median progression-free survival [PFS] was 8.6 months. This study showed an average response rate that wasn’t affected by the number of prior lines of therapy. However, the patients that received the highest target dose of 450 million CAR T-cells did have higher response rates of 81% and the complete response rate was higher at 39% and the median PFS was 12.2 months.

Responses were durable, with a median duration of response of 10.9 months among all ide-cel-treated patients [and] an increase with depth of response to 21.5 months of duration of response for those achieving complete response.

Although 84% of patients in this study experienced some level of cytokine release syndrome, only 6% had grade 3 or higher, and fortunately, only 18% of patients in the study experienced any grade of neurotoxicity, with only 4% experiencing grade 3 and no grade 4 or 5 neurotoxicity.

So, the safety profile in this study was similar regardless of the number of prior lines of therapy and remained consistent with longer follow up, with similar rates of infections, second primary malignancies, and no unexpected gene therapy-related toxicities. And based on this study, the ide-cel product has now been FDA approved for patients with relapsed refractory multiple myeloma who have received at least 4 prior lines of therapy.

EBO: Can you discuss the long-term data on ide-cel that were presented at the 2021 ASCO Annual Meeting?

ANDERSON: First of all, the long-term data tells us it tells us that we’re not seeing any increasing long-term side effects of CAR T-cell therapy for myeloma, no gene therapy related [adverse effects], no unexpected higher incidence of second malignancies, and no late neurotoxicity. But as far as comparing products, we really don’t have any data to compare between ide-cel versus cilta-cel at this point. …

One other thing of a note, certainly with the ide-cel patients in the KarMMa study where, as I mentioned, we’re only seeing about 18% neuropathy with very low risk of severe neuropathy. Certainly, the studies presented to date with cilta-cel do show some non [central nervous system] neurotoxicity that we’re anxious to follow up on, and see how that pans out with further follow up and see what the true incidence and outcomes are for those patients.

EBO: One of the issues with payers over the cost of CAR T-cell therapy generally has been that even when patients have a good response, they may relapse. Given that the median duration of response for patients with a complete response is still less than 2 years, what have you learned from KarMMa about patient selection to ensure that the best candidates receive ide-cel, and that conditions are optimal for good results?

ANDERSON: Right now, all we can say is that there were similar results if patients had received 3 lines of private therapy versus 4 or more. Certainly, we would like to know more about exactly which patients are going to have a complete response. Obviously, that translates into better outcomes. And in those patients with a complete response, they have a duration of response of 21.5 months; of those with [near complete response], 41% are still in remission at 2 years, and some still in remission, and currently at 3 years. But we don’t have any data yet on trying to pin down which patients specifically are going to be predicted to have the better responses and longer remissions, unfortunately.

So, right now, just compared to all the other options that we have for these patients that provide a very short survival with most other products, certainly, this is still a really good option for these patients. What we’re suspecting though, is that if we can give these CAR T cells even earlier in the course of therapy, when the T cells are more functional or less dysfunctional, we’re hoping that can make even more difference on the outcomes in these patients.
Studies Offer Promising Data on CAR T-Cell Therapy in B-ALL, Multiple Myeloma

JAIME ROSENBERG

TWO ABSTRACTS PRESENTED recently at the American Society of Clinical Oncology annual meeting offered promising data for 2 chimeric antigen receptor (CAR) T-cell therapies, one in relapsed/refractory (R/R) B-cell acute lymphoblastic leukemia (B-ALL), and one in R/R multiple myeloma.

Approved in 2020 for patients with R/R mantle cell lymphoma, brexucabtagene autoleucel (brexu-cel), sold as Tecartus, is now being studied as well in patients with R/R B-ALL, and the recent conference data suggest that the treatment offers clinical benefit in these patients.1

After a median follow-up of 16.4 months, median overall survival was not reached among the patients who responded to brexu-cel. These patients had a mean relapse-free survival of 14.2 months.

Across the 55 patients receiving brexu-cel, 71% achieved a complete response (CR) or CR with incomplete hematologic recovery (CRi), 97% of whom were negative for minimal residual disease.

The patients included in the study were heavily pretreated: 45%, 22%, and 42% had previously undergone an allogeneic stem cell transplant, respectively.

Ninety-five percent of patients experienced grade ≥3 adverse events (AEs), the most common of which included anemia (49%) and neutropenia (49%). Grade 3/4 cytokine release syndrome and neurologic AEs—commonly reported among patients treated with CAR T-cell therapies—were reported in 24% and 25% of patients, respectively, with a median time to onset of 5 days and 9 days, respectively.

According to the researchers, they were generally reversible.

NOVEL THERAPY IN MULTIPLE MYELOMA. During the conference, researchers also offered data from 2 different time points of an ongoing phase 1 study of CART-ddBCMA in R/R multiple myeloma. CART-ddBCMA is an autologous CAR T-cell therapy that uses a novel binding domain to target B-cell maturation antigen (BCMA), and it is designed to reduce the risk of immunogenicity and have high stability.

As of January 29, 2021, there were 9 evaluable patients, all of whom had responded to CART-ddBCMA. Four patients had achieved a stringent CR (sCR), 1 a very good partial response (VGPR), and 4 a PR. One of the patients who achieved a PR had disease relapse and was retreated, while the rest of the patients had ongoing responses.2

Similar findings were seen as of April 2021,3 with all 12 evaluable patients achieving a response, including 5 sCRs, 1 CR, 3 VGPRs, and 3 PRs. Eleven of these responses are ongoing, and study data suggest that responses deepen over time.

According to the researchers, despite previously progressing on BCMA-targeted therapy, 1 patient still achieved a VGPR.

All 12 of these patients have received at least 3 prior lines of therapy, and 10 were pentarefractory.

REFERENCES
Phase 2 Data for Tisagenlecleucel, Tafasitamab Show Objective Responses in More Than Half of Patients

JARED KALTWASSER

DRUGMAKERS UNVEILED POSITIVE new phase 2 data for a pair of therapies targeting 2 types of non-Hodgkin lymphomas during the 2021 American Society of Clinical Oncology Annual Meeting, held June 4 to 8 in a virtual format.

The chimeric antigen receptor (CAR) T-cell therapy tisagenlecleucel (Kymriah) had an overall response rate (ORR) of 86% among patients with relapsed or refractory follicular lymphoma, and the humanized Fc-modified cytolytic CD19-targeting monoclonal antibody tafasitamab (Monjuvi) had an ORR of more than 50% when administered in combination with lenalidomide (Revlimid) to patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL).

TISAGENLECLEUCEL IN FOLLICULAR LYMPHOMA. Novartis AG released the pivotal phase 2 data from its ELARA trial, showing that tisagenlecleucel led to an ORR of 86% (95% CI, 78%-92%) in patients with follicular lymphoma, and a 66% complete response (CR) rate (95% CI, 56%–75%). None of the 97 patients evaluated for safety experienced grade 3 or 4 cytokine release syndrome (CRS), the most common adverse event associated with CAR T-cell therapies, although nearly half (49%) had grade 1 or 2 CRS.

“Our goal as researchers is to continue to explore the potential of CAR-T therapy, and the robust ELARA safety and efficacy findings suggest [that] Kymriah may play an important role in the third-line treatment of relapsed or refractory follicular lymphoma,” said Stephen J. Schuster, MD, of the University of Pennsylvania’s Perelman School of Medicine, in a news release.2

The ELARA trial had a median follow-up of 11 months, by which time the median duration of response (DOR), progression-free survival (PFS), and overall survival (OS) were not reached. Schuster and colleagues estimated DOR for patients with CR at 6 months to be 94% (95% CI, 82%-98%) and 76% for patients with PFS at 6 months (95% CI, 65%-84%). The median number of prior therapies in the cohort was 4 (range, 2-13). Nine percent of patients reported grade 1 or 2 neurological events, and 1 patient had a grade 4 neurological event, although all recovered. The most common grade 3 or higher adverse events in the first 8 weeks following infusion were neutropenia (28%) and anemia (13%). No treatment-related deaths were reported.

Novartis said it is committed to expanding the availability of CAR T-cell therapies, and will push forward with regulatory submissions for the indication as soon as possible.

TAFASITAMAB RESULTS. Meanwhile, Incyte Corp. and MorphoSys US Inc. said its phase 2 L-MIND trial showed tafasitamab had an ORR of 57.5% (46 of 80 patients; 95% CI, 45.9%-68.5%) when given to patients with relapsed or refractory DLBCL in combination with lenalidomide. Forty percent of patients achieved CR, and the median DOR was 43.9 months (95% CI, 26.1 - not reached) and the median PFS was 11.6 months (95% CI, 6.3-45.7).

“The 3-year follow-up data not only show a durable response and consistent safety profile in patients with relapsed or refractory DLBCL treated with tafasitamab plus lenalidomide, it also suggests the combination could potentially lead to durable remission,” said MorphoSys senior vice president Nuwan Kurukulasuriya, in a press release. “We are looking forward to sharing these long-term follow-up findings with the scientific community.”

Tafasitamab in combination with lenalidomide was approved by the Food and Drug Administration via its accelerated approval pathway last July for the treatment in adult patients with relapsed or refractory DLBCL not otherwise specified, including those arising from low-grade lymphoma, who are not eligible for autologous stem cell transplantation.

REFERENCES

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Christopher Arendt, PhD, on OPTIC Findings for Dose Optimization of Ponatinib in Patients With CP-CML

Produced by Matthew Gavidia

Findings of the OPTIC study, which examined dose optimization of ponatinib in patients with chronic phase chronic myeloid leukemia (CP-CML), indicated that the highest dose of 45 mg achieved optimal results. These were maintained after lowering the dosage, said Christopher Arendt, PhD, head, Oncology Therapeutic Area Unit, Takeda.

EVIDENCE-BASED ONCOLOGY™ (EBO): What was the general rationale for the phase 2 OPTIC study? Why are patients taking third-generation tyrosine kinase inhibitors (TKIs) at risk for events such as thrombocytopenia?

ARENDT: This study involved ponatinib (Iclusig), an oral TKI that targets a specific genetic fusion. It’s a fusion of BCR and ABL1 that’s associated with some subtypes of CML, and also [with] Philadelphia chromosome-positive acute lymphoblastic leukemia. [Ponatinib] was developed by computational- and structure-based drug design. That’s interesting is that it’s able to inhibit this lesion, but it’s also uniquely able to inhibit, in addition, a resistance mutation that develops in response to targeted therapies against BCR-ABL1.

That mutation, known as T315I, identifies 1 specific amino acid change and is resistant to second-generation tyrosine kinase inhibitors (TKIs) at risk for events such as thrombocytopenia. So, [ponatinib] is called a third-generation inhibitor. It has this added virtue that it’s able to address so-called gatekeeper mutation, or resistance mutation. There’s a bit of a misconception when it comes to CP-CML that this is a “good” cancer to have, but in reality, there are certainly very resistant forms of disease, as well as intolerant forms that develop, and these are associated with extremely poor outcomes.

Balancing [a drug’s] clinical efficacy with a safety profile is all about threading that needle, and threading that needle at the level of the dosing schedule. You want that dosing schedule to be just high enough to address the tumor growth, but not so high that there are unwanted [adverse] effects. And so, [ponatinib] was already an approved medicine in CP-CML, but it was relegated to the last line of therapy, which we felt was not optimal for patients who could benefit earlier.

What OPTIC sought to do was to optimize, essentially, the dose and schedule, so it evaluated several different doses. The study found that a starting dose of 45 mg was optimal. The patients were monitored for a clinical response by a blood test, and when that genetic lesion fell to a nearly undetectable level—less than 1% in blood—the dose schedule was reduced to a third of that dose, 15 mg daily.

With this, the safety and efficacy profile was really optimized within the OPTIC study. The trial met its primary end point, and toward the end of last year, the FDA approved the supplemental new drug application for adult patients with CP-CML who had received 2 prior TKIs. This allowed [ponatinib] to move up to an earlier stage of treatment, and we believe that’s going to be very beneficial for patients—again, keeping in mind that resistance ultimately is a hallmark of the first- and second-generation TKIs in this particular treatment setting. Thrombocytopenia is a potential [adverse] effect of this [drug] class, but the mechanistic basis for this is not fully clear. It’s thought to be potentially due to inhibiting some of the signal transduction pathways that [ponatinib] hits that are important in megakaryocytes, which is in the same kind of myeloid lineage that ultimately we’re targeting in this particular disease setting.

EBO: How do the results presented at ASCO contribute to precision medicine in the treatment of CML?

ARENDT: Precision medicine is all about matching the right medicine to a patient who has an identifiable, if you will, kind of biomarker or genetic signature in that disease setting. What’s exciting around the OPTIC study data is that we now have the ability to tailor the treatment with this medicine to patients who can benefit, because they have that driver mutation that can be specifically identified to have become resistant to the other classes in this space. And again, that’s the T315I mutation.

That’s a wonderful example of precision medicine being allowed for that very agile treatment with the appropriate medicine, instead of having to wait and test and allow a cancer to progress when it could benefit from having the right tailored therapy from the start.

Also, clearly, the fact that [ponatinib] moves up in the treatment schedule paradigm allows, we hope, to prevent the development of that particular lesion. To be able to still have that precision, genetic connection between the BCR-ABL1 lesion and offering a patient [ponatinib], and then following that patient with the expectation that the T315I mutation is going to be under a very strong selective pressure from this particular medicine. The hope would be that it doesn’t develop, and the hope would be that patients then can benefit for a longer duration of response.

EBO: What subgroup results are noteworthy?

ARENDT: We looked at different therapeutic doses in the OPTIC study, as I said, and it was all about being able to thread that needle in the best possible way for patient benefit: maximizing responses but ultimately minimizing any [potential] adverse events. So, the most interesting subgroup is the one that received the highest dose that was tested in that study, initially—that was the 45-mg cohort. These patients had the best initial response and then sustained responses. They were dropped down to that 15-mg dose, maintained, and followed over the course of the study.

REFERENCES
ARE CANCER PATIENTS RECEIVING biomarker tests? How is remote patient monitoring working in a real-world setting? Beyond results from major randomized clinical trials, the 2021 annual meeting of the American Society of Clinical Oncology (ASCO) offered an opportunity to present findings from everyday clinical practice, including studies presented by Strategic Alliance Partners of The American Journal of Managed Care®. A sampling of the results are below.

**MYLUNG Consortium Finds Gaps**

The first set of results presented by the MYLUNG Consortium, which includes members of The US Oncology Network, major pharmaceutical partners, and advocacy groups, revealed significant gaps in biomarker testing in non–small cell lung cancer (NSCLC), found that most cancers are detected at stage IV, and showed that the time from diagnosis to the start of first-line therapy takes about 5 weeks.1

**Patients taking oral therapy had better compliance rates. Items about implementation that were addressed included the lack of a second prompt; inconsistent discussion of ePROs during clinic visits; and COVID-19–related changes in the workflow that may affect data collection.**

Makenzi Evangelist, MD, the principal investigator for the MYLUNG Consortium Protocol 2 and an oncologist with New York Oncology Hematology, who presented the results at ASCO, said the retrospective, observational chart study found that testing gaps and delays are keeping patients from getting treatment they need in timely manner.

“There are already several targeted therapies to treat subsets of populations, and many more are in the pipeline that hold incredible potential,” she said. “Unfortunately, barriers exist that prevent the necessary comprehensive biomarker testing that enables the use of these treatments.”

The MYLUNG Consortium is a collaborative study that will conduct 3 protocols over a 5-year period. Protocol 1, presented at ASCO, is a retrospective study of more than 3500 patients with metastatic NSCLC that investigated the following areas: testing rates for ALK, BRAF, EGFR, ROS1, and PD-L1 mutations; use of the full next-generation sequencing panel (NGS); time from NSCLC diagnosis to first-line therapy; turnaround times from biomarker orders to results; and time from NSCLC diagnosis to test results. Protocol 1 found that while 90% of patients were given at least 1 biomarker test, only 46% received testing for 5 or more biomarkers. As a result, many missed out on the chance for a targeted therapy. Also, the median time from diagnosis to first-line therapy was about 5 weeks. Turnaround time from testing orders to results was about 2 weeks, which shows a need to get results to physicians more quickly to develop a treatment regimen. NGS testing improved over time, suggesting that comprehensive testing is increasing. Most of the population was diagnosed with advanced disease, with roughly 80% detected at stage IV.

**Texas Oncology Highlights Tech Improvements to Help Patients**

In a pair of presentations, Texas Oncology’s Lalan Wilfong, MD; and Debra Patt, MD, PhD, MBA, highlighted implementation of patient management technologies to reduce trip to the emergency department (ED)2 and to implement electronic patient-reported outcomes (ePROs)3 across more than 200 sites in the community oncology network.

Through a partnership with Navigating Cancer, Texas Oncology first implemented a new protocol and tracking system to reduce call-back times, which were a consistent source of complaints; failure to respond to patient calls often resulted in patient ED visits during business hours. Wilfong presented data to show that implementation of a new tracking system in February 2020, which tracked 1 million calls for through the end of the year. Average response time for each incident fell from 3.2 hours to 2.2 hours by December 2020. The goal was to resolve most calls in 90 minutes, and by December 2020, 60% of calls were resolved in less than 1 hour. Of note, 8% of symptom-related incidents that would likely have otherwise resulted in an ED visit were averted by nurse intervention.

Patt discussed use of Navigating Cancer technology for collection of ePROs, as many value-based care models encourage the collection of these data to improve patient outcomes, patient satisfaction, and adherence to therapeutic regimens. Texas Oncology began using the platform in July 2020, and data collection reflects the period through December 2020. Patients were given a choice to be prompted via text or email to self-report common symptoms and well-being status on a web site or by smartphone. Severe symptoms could be reported in real time, and such reports triggered an alert to a nurse to address the symptom. Compliance was addressed each week, with an evaluation of barriers to reporting. Over the study period, 4375 patients enrolled in the program and entered baseline data; 61% of the patients were female, and 75% of the patients were older than 55 years. Compliance with weekly reporting began at 72% and fell to 52% over 10 weeks.

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In OCM, Costs in Clinical Trials Were Less Than Those in Routine Care

Does participation in a clinical trial add to a payer’s costs? A study by Tennessee Oncology that examined data from 90 oncologists over a 2-year period suggests that trial participation can, in fact, save money.1 Investigators created matched comparator groups for patients in the Oncology Care Model (OCM) to measure the impact of trial participation on total cost, compared with costs of routine care. Variables considered included cancer type, metastatic status, comorbidities, performance status, and age. Among other factors measured were whether trial participation affected receipt of active treatment in the last 14 days of life. During the study period (2016-2018), 8026 completed OCM episodes met the study criteria; of these, 459 episodes included patients who were participating in a trial. Episodes with trial enrollment cost $5976 less than nontrial episodes on average, with most savings coming from decreased drug costs. There were no differences in end-of-life costs, hospitalization rates, or hospice use in trial vs nontrial episodes.

Remote Monitoring Enables Nurse Intervention in Arkansas Cancer Group

Highlands Oncology Group, which includes 19 medical oncologists in northwest Arkansas, presented results from its implementation of the Explain ePRO system integrated with the electronic medical record.2 Starting in June 2020, the practice offered patients who were being treated with parenteral cancer therapy the opportunity to enroll in the system to monitor symptoms during therapy. According to the abstract, patients could report symptoms based on the National Comprehensive Cancer Network (NCCN) Distress Thermometer and Problem List Instrument. A predefined protocol had threshold points to trigger notifications to a nurse. A review would determine whether nurses would handle the situation remotely or if a patient needed an urgent office visit or trip to the ED. Through January 2021, the practice treated 1261 patients with intravenous chemotherapy; 769 were offered enrollment in Explain and 569 (73.9%) were enrolled, including 419 who were in the OCM. For the most part, those who did not enroll had low symptom burden, did not speak English, or were near the end of treatment. Patients used the mobile app (89.1%) or interactive voice response interface (10.1%) at the following intervals: once a month (12%), twice a month (30%), 3 times a month (35%), and 4 times or more a month (23%). Of those enrolled, 52.7% were still giving reports after 3 months. Of the reports made, 50% met the threshold for a nurse to be notified. The nursing staff followed up with a call for 78.8% of the notifications, and of these calls, 21.2% required an urgent office visit (7% of overall reports). Typical reasons for a visit were high NCCN Distress score (17.1%), fatigue (16.1%), pain (11.5%), nausea (9.4%), and dyspnea (4.5%). The main reasons reports stopped were death, hospice admission, and the end of treatment.

Highlands Oncology Group is a member of the Quality Cancer Care Alliance.

REFERENCES

ADVERSE EVENTS / QUALITY OF LIFE

Analysis From Atezolizumab Trials Shows irAEs Can Predict Longer OS

THE RISE OF IMMUNOTHERAPY in cancer care has brought with it the challenge of managing adverse events (AEs). But immune-related AEs (irAEs) are known to be a sign that the treatment is working, and an analysis of phase 3 trials involving atezolizumab (Tecentriq), presented during the 2021 American Society of Clinical Oncology Annual Meeting, shows that the prevalence of low-grade irAEs can, in fact, predict longer overall survival (OS).

Atezolizumab is currently approved in the first- and second-line settings for advanced non–small cell lung cancer (NSCLC). In an exploratory analysis, investigators pooled data from the IMpower 130, the IMpower 132, and the IMpower 150 studies, which evaluated the anti–PD-L1 agent in various combinations in treatment-naïve patients with nonsquamous stage IV NSCLC. The combinations were as follows:

- IMpower 130: Patients were randomized to carboplatin and nab-paclitaxel alone or with atezolizumab;
- IMpower 132: Patients were randomized to carboplatin or cisplatin alone or with atezolizumab; and
- IMpower 150: Patients were randomized to atezolizumab plus bevacizumab plus carboplatin and paclitaxel, or atezolizumab plus carboplatin and paclitaxel, or bevacizumab plus carboplatin plus paclitaxel.

Analyses of irAEs and survival took place at 1, 3, 6, and 12 months. In total, 2503 patients were included, with 1577 in the atezolizumab arm and 926 in the control arm. Study protocols called for treatment interruption or discontinuation if AEs were grade 3 or higher.

Results showed:

- 48% of patients in the atezolizumab arm had an irAE, vs 32% in the control arm. 11% of those in the atezolizumab arm had irAEs grade 3-5, compared with 5% of those in the control arm.
- The most common irAEs were rash (28% for atezolizumab vs 18% for control), hepatitis (15% vs 10%), and hypothyroidism (12% vs 4%). Median time to onset was 1.7 months for the atezolizumab group vs 1.4 months for control.
- OS hazard ratios (HRs) between patients with irAEs and those without were 0.69 for the atezolizumab arm and 0.82 for the control arm; excluding rash, the OS HRs were 0.75 for the atezolizumab arm and 0.90 for the control.

The authors concluded that patients with grade 1 and 2 irAEs had the longest OS and those with irAEs of grade 3 or higher had the shortest, possibly due to discontinuation of therapy. They wrote that the data offer additional support for atezolizumab with chemotherapy in the first-line setting, with or without bevacizumab.

REFERENCE
HEALTH-RELATED QUALITY OF LIFE

ASCORE STUDIES COVER DATA ON HEALTH CARE UTILIZATION, QUALITY OF LIFE

MARY CAFFREY

DOZENS OF STUDIES presented during the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting involved data measuring health care utilization, the costs of adverse events (AEs) that result from cancer treatment, and patients’ quality of life.

Cost of Treatment-Related Diarrhea
Gastrointestinal AEs occur frequently in cancer treatment, especially when therapies are used in combination. Studies funded by Napo Pharmaceuticals, developers of a treatment to prevent noninfectious diarrhea, examined the cost of cancer-related diarrhea (CRD) to the health system and its effects on patients’ quality of life.1,2 Led by Pablo C. Okhuysen, MD, of The University of Texas MD Anderson Cancer Center; Lee S. Schwartzberg, MD, of West Cancer Center; and Eric Roeland, MD, of Harvard Medical School, the studies examined 104,135 matched pairs of patients with either solid tumor or hematologic cancer, with and without CRD, who received chemotherapy or targeted therapy. Researchers used the IQVIA PharMetrics database to calculate all health care costs over a 12-month period, with the index date being the first cancer claim; patients were reindexed after the first claim based on treatment for diarrhea. Results showed that:

- Patients with CRD incurred significantly higher health care costs than those without: mean, $104,880 vs $39,664, respectively (P < .0001).
- Patients who had inadequate treatment for CRD had the highest mean health care costs, at $129,531; for patients treated adequately for CRD, mean costs were $107,050; and for patients who did not need treatment for CRD, mean costs were $56,350 (P for all comparisons, <.0001).
- Mean pharmacy costs were $35,190 for CRD patients compared with $15,883 for non-CRD patients; emergency department visits cost a mean of $1107 for CRD patients vs $216 for non-CRD patients.
- Patients who reported being terminally ill were less likely to be hospitalized in the last 30 days of life (OR, 0.56; 95% CI, 0.32-0.98; P = .043), and they were more likely to be hospitalized in the last 30 days of life (OR, 2.28; 95% CI, 1.20-4.32; P < .001).

Investigators also used the data set to gain insights about discontinuation rates by type of treatment for patients with and without CRD. Among patients receiving chemotherapy, those with CRD stopped therapy more frequently than those without CRD: 81.5% vs 62.3%. Among patients taking a targeted therapy, those with CRD also stopped more frequently, but the gap was not as large: 69.2% vs 64.3%. Discontinuation rates were highest for patients taking both treatments: 96% for those with CRD and 85.5% for those without (all P < .0001).

More payers, including Medicare, are becoming interested in patient-reported outcomes for cancer therapies, and the FDA recently issued a guidance for industry on the topic.1

Cancer Raises Readmission Risk
Payment models such as the Oncology Care Model have sought to reduce the risk of hospital readmissions within 30 days of discharge. This outcome has been a priority across Medicare under the Affordable Care Act, as such trips back to the hospital boost costs and are typically associated with poor patient outcomes. A study funded by the National Institutes of Health sought to quantify how much having cancer elevated the 30-day readmission risk.4 Using the National Readmission Database, researchers identified nonprocedural hospital readmissions between January and November 2017 including those patients with and without a cancer diagnosis. Results showed that:

- Of 18.9 million weighted readmissions, 1.68 million (8.9%) involved patients who had a cancer diagnosis. A cancer diagnosis, vs no such diagnosis, was associated with a significantly higher risk of readmission: 23.5% vs 13.6% (P < .001).
- However, among readmissions, cancer patients were less likely to have a preventable readmission: 6.5% of readmissions of patients with cancer were seen as preventable, compared with 12.1% among patients without cancer, when both were readmitted for the same non–cancer-related diagnoses (P < .001).
- The site of cancer was the greatest predictor of readmission risk. Patients with liver cancer, pancreatic cancer, and non-Hodgkin lymphoma had the highest readmission rates.

Perceptions Linked to End-of-Life Health Care Use
Patients who have an inaccurate view of their cancer prognosis will be unprepared to make difficult decisions regarding end-of-life care, which can lead to late treatment that will not be effective or to late hospital stays. Investigators funded by the Leukemia and Lymphoma Society conducted a secondary analysis using longitudinal data from a randomized controlled trial of a palliative care intervention for patients with incurable lung or gastrointestinal cancer.1 Using the Prognosis and Treatment Perceptions Questionnaire, they assessed patients at weeks 12 and 24 after diagnosis and conducted a final assessment close to death. There were 350 patients in the parent trial, of whom 80.5% died during the study period and were included in the analysis. Results showed that:

- 59.4% of the patients reported being terminally ill, while 66.1% said their cancer was likely curable at the assessment closest to death.
- The patients who said their cancer was curable were least likely to use hospice (OR, 0.25; 95% CI, 0.10-0.61; P = .002) or to die at home (OR, 0.56; 95% CI, 0.32-0.98; P = .043), and they were more likely to be hospitalized in the last 30 days of life (OR, 2.28; 95% CI, 1.20-4.32; P < .001).
- Patients who reported being terminally ill were less likely to be hospitalized in the last 30 days of life (OR, 0.52; 95% CI, 0.29-0.92; P = .025). However, these patients’ perceptions did not affect hospital length of stay or chemotherapy administration in the last 30 days of life.

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Kirk Shepard, MD, Highlights HRQOL Findings of Lenvatinib/Pembrolizumab Combination Therapy in Advanced Endometrial Carcinoma

Produced by Matthew Gavidia

**RESULTS PRESENTED AT** the American Society of Clinical Oncology (ASCO) 2021 Virtual Annual Meeting showcased similar health-related quality of life (HRQOL) scores among patients with advanced endometrial carcinoma (aEC) undergoing combination therapy vs monochemotherapy. The findings could prove significantly important, particularly for a disease that has not had a specifically approved therapy in 50 years, said Kirk Shepard, MD, chief medical officer, senior vice president, and head of Global Medical Affairs, Eisai.

**EVIDENCE-BASED ONCOLOGY™ (EBO):** Can you discuss what can be derived by measuring HRQOL for a condition such as endometrial cancer (EC), particularly in its advanced stages (aEC)?

**SHEPARD:** It’s extremely important that we measure these parameters in patients, particularly in endometrial carcinoma, and advanced endometrial carcinoma. It’s been 50 years since a drug has been specifically approved for endometrial carcinoma. It’s very important that we don’t just measure the effectiveness [and] efficacy of a drug, but also look at the risk-benefit balance, and of course quality of life is on the other side. So, the health-related quality of life measures, which have come quite far in the last couple of decades—including 2 guidelines, at least, written since 2006—[now inform] FDA about how they appropriately can measure quality of life in patients.

The particular one that we used, the [European Organization for the Research and Treatment of Cancer, Quality of Life Questionnaire], is the one that’s most used. It’s a general measure of parameters of different domains that has been validated in more than 100 validation studies and used in maybe a couple thousand studies through a couple of decades. It’s very important that we use the tools that we have now to measure the quality of life in patients.

**EBO: Results indicate similar mean HRQOL scores for patients with aEC undergoing the combination therapy vs chemotherapy. Can you speak on the significance of this finding?**

**SHEPARD:** We were very happy with the results, as you might imagine, because we were comparing ourselves—Keytruda [pembrolizumab] and Lenvima [lenvatinib]—with one monochemotherapy. And these are traditional chemotherapies. It would be called the physician’s choice of therapy, which is either doxorubicin or paclitaxel.

To come out with numerically the same—in fact, [actually] better,—although [the difference] wasn’t statistically [significant]—quality of life parameters as 2 mono drugs, while we’re giving 2 drugs, was very important.

This is something very valuable because it gives [physicians]—particularly physicians who have treated endometrial carcinoma for 50 years with the same drugs—a window into what’s happening when we offer new advanced drugs, such as an [immuno-oncology] or a [tyrosine kinase inhibitor], such as Lenvima. It shows that, really, the QOL remains quite good. With the great results we got—and I think you’re probably familiar with the 309 Study we presented at the Society of Gynecologic Oncology meeting—it’s really a very acceptable risk-benefit ratio.

**EBO: Were there any notable differences by patient subgroup in HRQOL for those undergoing the combination therapy?**

**SHEPARD:** It’s a great question, [but] we haven’t done subgroup analyses yet. That’s what needs to be done [next]. Of course, we wanted to get the topline results out for SGO as soon as we knew the results; [this way], treating physicians [would know] that this was another group of drugs they could use together to treat patients.

Of course, the quality of life is somewhat topline now also. … But the subgroup analysis, as long as the numbers don’t get too low as we look at the group, is the way that we would want to go next as far as the next step.

It’s been a pleasure to work at a company like Eisai, because they have human health care. Human health care is a platform that was started 30 years ago, where we put the patient first, [and] the caregiver and the family.

This fits in very well with what we’ve done, not only with endometrial carcinoma, but in the same program at ASCO, we are doing a HRQOL study, and it’s being orally presented for renal cell carcinoma. So again, Eisai is very concerned about not just getting good results as far as shrinking tumors, but making sure that we always consider the quality of life of the patient. 

**REFERENCES**


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Hospital Outcomes of Male Breast Cancer in the United States

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