



**ASCO**<sup>®</sup>  
AMERICAN SOCIETY OF  
CLINICAL ONCOLOGY

# Clinical Cancer Advances 2018



ASCO'S ANNUAL REPORT ON PROGRESS AGAINST CANCER

# About Clinical Cancer Advances

ASCO develops this annual report, now in its 13th edition, to outline the progress that has been achieved in clinical cancer research and care each year. As a whole, *Clinical Cancer Advances* highlights current trends in the field and previews future directions of cancer research.

The content of this report was developed under the direction of a 20-person editorial board composed of experts in a wide range of cancer types, as well as surgical oncology, radiation oncology, cancer prevention and screening, quality of care, health disparities, and tumor biology and developmental therapeutics.

The editors reviewed scientific literature that was published in peer-reviewed journals or presented at major medical conferences from October 2016 through September 2017 and selected advances according to formal criteria.

Primarily, advances must improve meaningful patient outcomes, such as survival or quality of life, and have a strong scientific impact.

To view this report online and learn more about progress against cancer, visit [ASCO.org/CCA](https://www.asco.org/CCA). This report was also published in the *Journal of Clinical Oncology* at [ascopubs.org/journal/jco](https://ascopubs.org/journal/jco) on January 30, 2018.

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# A Message from ASCO's President

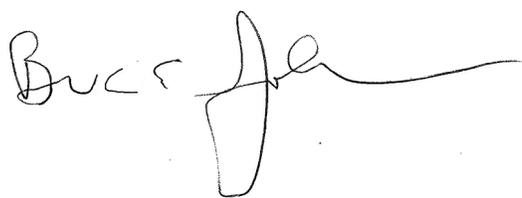
I remember when ASCO first conceived of publishing an annual report on the most transformative research occurring in cancer care. Thirteen reports later, the progress we have chronicled is remarkable, and this year is no different. The research featured in the ASCO's *2018 Clinical Cancer Advances* report underscores the impressive gains in our understanding of cancer and in our ability to tailor treatments to tumors' genetic makeup.

The ASCO 2018 Advance of the Year, **adoptive cell immunotherapy**, allows clinicians to genetically reprogram patients' own immune cells to find and attack cancer cells throughout the body. Chimeric antigen receptor (CAR) T-cell therapy—a type of adoptive cell immunotherapy—has led to remarkable results in young patients with acute lymphoblastic leukemia (ALL) and in adults with lymphoma and multiple myeloma. Researchers are also exploring this approach in other types of cancer.

This advance would not be possible without robust federal investment in cancer research. The first clinical trial of CAR T-cell therapy in children with ALL was funded, in part, by grants from the National Cancer Institute (NCI), and researchers at the NCI Center for Cancer Research were the first to report on possible CAR T-cell therapy for multiple myeloma. These discoveries follow decades of prior research on immunology and cancer biology, much of which was supported by federal dollars. In fact, many advances that are highlighted in the *2018 Clinical Cancer Advances* report were made possible thanks to our nation's support for biomedical research. Funding from the US National Institutes of Health and the NCI helps researchers pursue critical patient care questions and addresses vital, unmet needs that private industry has little incentive to take on. Federally supported cancer research generates the biomedical innovations that fuel the development and availability of new and improved treatments for patients. We need sustained federal research investment to accelerate the discovery of the next generation of cancer treatments.

Another major trend in this year's report is progress in precision medicine approaches to treat cancer. Although precision medicine offers promise to people with cancer and their families, that promise is only as good as our ability to make these treatments available to all patients. My presidential theme, "Delivering Discoveries: Expanding the Reach of Precision Medicine," focuses on tackling this formidable challenge so that new targeted therapies are accessible to anyone who faces a cancer diagnosis. By improving access to high-quality care, harnessing big data on patient outcomes from across the globe, and pursuing innovative clinical trials, I am optimistic that we will speed the delivery of these most promising treatments to more patients.

Sincerely,



**Bruce E. Johnson, MD, FASCO**

ASCO President, 2017 to 2018



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# Executive Summary

Approximately 1.7 million people received a cancer diagnosis in the United States in 2017.<sup>1</sup> Today, more than 15 million Americans, nearly one in 20, is a survivor, which means that they have had or are living with cancer.<sup>2</sup> The number of survivors is growing steadily; experts estimate that there will be 26 million by 2040, with 73% 65 years of age or more.<sup>3</sup>



At the same time, the rate of cancer death has been decreasing, and people are living longer with cancer than ever before. Approximately 64% of US patients diagnosed with cancer in 2005 have lived 10 years or more beyond diagnosis, up from 35% for those diagnosed in 1975.<sup>4</sup> These trends reflect our and other nations' investments in cancer research and the relentless efforts to advance discovery and care. The volume and pace of cancer research is growing rapidly. For example, the number of medical journal articles with the word "cancer" in the title quadrupled in the last decade, from approximately 28,000 in 2007 to 120,000 in 2017. Yet more work lies ahead. Because of the aging and growing population, there will be more new patients with cancer every year, both in the United States and worldwide. For every life saved, there are still many people waiting for the next breakthrough for themselves or their loved ones.

This report highlights the most important clinical advances of 2017 and previews where cancer science is headed. New treatments help patients with melanoma and ovarian, lung, bladder, brain, and prostate cancer live longer, and many other new therapies delay cancer worsening or lower the chance of recurrence. In the span of just 1 year—from November 2016 through October 2017—the US Food and Drug Administration (FDA) approved 31 new therapies for more than 16 types of cancer. Among the new approvals are two firsts: an adoptive cell immunotherapy—the ASCO Advance of the Year—and a tumor agnostic therapy, that is, treatment that works against different types of cancers that share a common genetic abnormality.

# First Adoptive Cell Immunotherapy and Gene Therapy for Cancer

In August 2017, the FDA approved the first adoptive cell immunotherapy, also known as CAR T-cell therapy, and the first gene therapy for cancer, tisagenlecleucel. This double first approval stems from decades of research on how to train the patient's own immune cells to fight cancer.

Even more important than the historic significance of this achievement is the medical need this unique new therapy is poised to fill. Tisagenlecleucel may be the

first treatment to truly turn the tables on recurrent pediatric acute lymphoblastic leukemia (ALL), one of the most common cancers in children. In a clinical trial, in four of five patients, cancer went into remission after the treatment, which was custom prepared in the laboratory from the patients' own blood cells.

In October 2017, the FDA approved the second CAR T-cell therapy, axicabtagene ciloleucel, to treat adults with certain types

of lymphoma. Other CAR T-cell therapies seem promising in clinical trials of people with multiple myeloma. CAR T-cell therapy represents an exciting innovation that has the potential to transform cancer care. It also raises the ongoing issue of cost and reminds us that, as a community, we need to find solutions that will assure that every patient with cancer has access to the care they need (see Advance of the Year: Adoptive Cell Immunotherapy).

## Precision Oncology

The other historic first among FDA approvals in 2017 marks a milestone in precision oncology. The immune checkpoint inhibitor pembrolizumab became the first cancer treatment to receive a tumor-agnostic indication.

It received accelerated approval to treat any type of solid tumor that has mismatch repair deficiency, a defect that undermines the cell's ability to repair DNA damage. This approval provides patients with a wide range of different cancers an effective way to control the disease.

Another promising treatment, larotrectinib, which homes in on a different, rare genomic abnormality in the tumor known as *tropomyosin receptor kinase (TRK)* gene fusion, also seems to work across tumor types and in both adults and children. Larotrectinib has the potential to become the first tumor-agnostic targeted therapy for cancer.

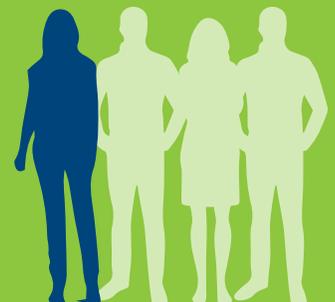
Meanwhile, fundamental cancer biology research is uncovering new molecular pathways that are being explored as potential therapeutic targets. In 2017 alone, the FDA approved more than 13 new targeted medicines for people with leukemia, and multiple myeloma, as well as ovarian, breast, and lung cancer.

## Immunotherapy for Lung Cancer Could Save 250,000 Years of Life



ASCO estimates that immune **checkpoint inhibitors would save 250,000 years of life** if all US patients with advanced lung cancer for whom checkpoint inhibitors are currently indicated receive the treatment.

In addition, **one in four** patients with newly diagnosed cancer and one in 10 with previously treated disease **may live well beyond 5 years after treatment initiation**. The estimates were based on an analysis of clinical trial results and cancer incidence and population data conducted by the ASCO Center for Research and Analytics (CENTRA).



# Targeted Agent and Profiling Utilization Registry Study

In 2017, ASCO's Targeted Agent and Profiling Utilization Registry (TAPUR) Study continued expanding. As of November 2, 2017, there were more than 495 participants enrolled on a study drug at more than 83 sites in 18 states, each offering 17 different targeted therapy options provided by the seven participating pharmaceutical companies.

In addition, the study protocol was

revised to lower the age of eligibility for the trial from 18 years to 12 years to extend the opportunity for participation to adolescent patients with advanced cancer in cases in which there is a defined adolescent dose for the study drugs.

The objective for the TAPUR Study is to evaluate molecularly targeted cancer drugs and collect data on clinical outcomes to learn about additional uses of these drugs

outside of the indications already approved by the FDA.

The TAPUR Study (ClinicalTrials.gov identifier: NCT02693535) is registered with a full list of inclusion and exclusion criteria and other information. Prospective patients, researchers, and practices interested in participating can visit the TAPUR website, TAPUR.org, or e-mail the TAPUR Study team at TAPUR@asco.org.

“ The only failure in cancer research is when you quit or are forced to quit because of a lack of funding. It takes decades of sustained research investment to test the safety and efficacy of cancer drugs. Congress needs to give researchers resources to discover the treatments that lead to better outcomes for those individuals with cancer. ”

Representative Brian Higgins (D-NY-26), Co-Chair, House Cancer Caucus



## Patient-Centered Care

As life expectancy after a cancer diagnosis continues to improve, there is growing recognition of the need to address patients' emotional and psychosocial needs from the time of diagnosis through treatment and survivorship.

*Clinical Cancer Advances 2018* highlights efforts to preserve patient quality of life by avoiding unnecessary treatment or by lowering therapy dose or duration.

Furthermore, new tools that engage patients in their own care, such as Web programs for symptom monitoring, psychological support, and end-of-life planning, are showing benefits for both patients and health care systems.

Finally, we are entering a new era in care in which biomedical research is no longer solely driven by researchers and physicians, but also by patients who are

more and more directly engaged in driving progress forward.

By donating tissue samples and clinical information, or by helping to design research studies and formulate practice guidelines, patients are providing valuable perspectives and contributing to better care for other patients now and in the future.



## A Call to Action to Congress

Americans are counting on our leaders to invest in biomedical innovation that will deliver the next generation of cancer cures to patients. ASCO urges Congress to give hope to millions of Americans with cancer by continuing to build on its investment in cancer research and providing predictable funding increases to NIH and NCI.

# Federal Support for Cancer Research Is Critical

Federally funded cancer research has driven many of the major prevention and treatment advances of the past 50 years, and has led to substantial improvements in patient survival and dramatic improvements in quality of life for people with cancer.

The National Cancer Institute (NCI) funds studies in areas that private industry has little incentive to address, such as research on cancer prevention, screening, and rare cancers, as well as groundbreaking foundational research.

The US National Institutes for Health (NIH) is the single largest public funder of biomedical research in the world. Federally funded biomedical research helps keep the United States globally competitive by contributing \$65 billion in economic growth, supporting 380,000 jobs, and generating \$2.21 dollars in local economic growth for every dollar in NIH funding.<sup>5,6</sup> It is estimated that NIH-funded basic research provides a positive return to public investment of 43%.<sup>7</sup>

Research funded by the NIH also fuels the innovation on which companies depend

to bring new treatments to the marketplace, helping make the United States the global leader in developing treatments. Studies show that NIH investments in biomedical research stimulate increased private investment: Every dollar of increase in public clinical research stimulates \$2.35 dollars of industry investment at 3 years.<sup>7</sup>

Funding from the NIH and other federal agencies supported more than 25% of the top advances featured in this report. Among the most notable are studies that have found:

- Prolonged survival with new approaches:
  - A new treatment regimen helps women with recurrent ovarian cancer live longer.
  - A Web-based tool for self-reporting symptoms during chemotherapy helps patients with advanced cancer live longer.
- Longer hormone therapy reduces the risk of breast cancer recurrence.
- Reduced adverse effects with less treatment:

- Shortening the duration of adjuvant chemotherapy for stage III colorectal cancer is safe and reduces adverse effects.
- In patients with melanoma, less extensive surgery lowers the risk of lymphedema without compromising survival.
- Lowering the radiation dose for oropharyngeal cancer reduces health complications without compromising survival.
- Effective strategies to help patients with advanced cancer understand and cope with their prognosis.
- For cancer-related fatigue, exercise and psychological support are more effective than medication.
- New insights on the adverse effects of certain prostate cancer and lung cancer treatments will help inform treatment and survivorship discussions.

In the last year, Congress has made critical investments to improve and accelerate cancer research through

## Join Us: Tell Your Representatives to Support Cancer Policy Priorities



More than 100 ASCO members from across the country came to the US Capitol in September 2017 for ASCO's annual Advocacy Summit, where members urged Congress to support issues critical to improving cancer research and care.

During meetings with members of Congress and staff, ASCO members asked Congress to support policies to increase federal research funding, ensure access to chemotherapy services for patients enrolled in Medicare, and improve the affordability of cancer drugs.

ASCO members have an opportunity to make their voices heard throughout the year by engaging with their members of Congress on key issues related to cancer policy. To learn more about participating in ongoing advocacy efforts, visit [asco.org/ACTNetwork](http://asco.org/ACTNetwork).

supplemental funding for the Cancer Moonshot Initiative and the 21st Century Cures Act. In addition, Congress included a boost in funding for NIH and NCI in fiscal year 2017; however, despite these funding increases, NCI's budget, when adjusted for inflation, remains below prerecession levels<sup>8</sup> (Fig 1).

One manifestation of this reduced

budget is that it is more difficult for researchers to secure funding. For example, in 2015, only 16% of new research proposals received funding compared with 27% in 2001.<sup>9</sup>

This decline in funding means that it is more difficult for the field to recruit and retain young researchers, which threatens future progress against cancer. Flat funding and

budget cuts translate into less innovation, fewer studies launched, fewer patients enrolled in clinical trials, fewer researchers entering the field, and fewer discoveries. Predictable funding increases are critical to sustain progress against cancer. Dependable and robust funding is essential for planning and conducting multiyear trials that advance new treatments.



## Federal Funding Badge

ASCO has created a badge to highlight research that has received federal funding. Studies in this report that have received federal funding are denoted with this badge. For more information, please visit [asco.org/nihfunding](http://asco.org/nihfunding).

## CANCER RESEARCH FUNDING

**91%**

More than nine (91%) in 10 Americans believe that the US government should dedicate substantial funding to diagnose, prevent, and treat cancer.

### Support for government action, especially on research

AMERICANS SAY THE GOVERNMENT SHOULD SPEND MORE ON THE FOLLOWING CANCER PRIORITIES, EVEN IF IT MEANS HIGHER TAXES OR ADDING TO THE DEFICIT:

**73%**

Find treatments and cures for cancer

**54%**

Help Americans afford cancer screenings and care

**49%**

Cancer prevention

# FEDERAL FUNDING IS CRITICAL TO ADVANCING OUR NATION'S CANCER PROGRESS

People with cancer are living better and longer, thanks to our nation's investment in cancer research

▼ **25%**

**DECLINE IN CANCER DEATH RATE**

Since a peak in 1991<sup>1</sup>

**110+**

**NEW CANCER DRUGS OR INDICATIONS**

Approved by the FDA since 2006<sup>2</sup>



**INCREASED 5-YEAR SURVIVAL**

2 out of 3 people with cancer live at least 5 years after diagnosis<sup>1</sup>

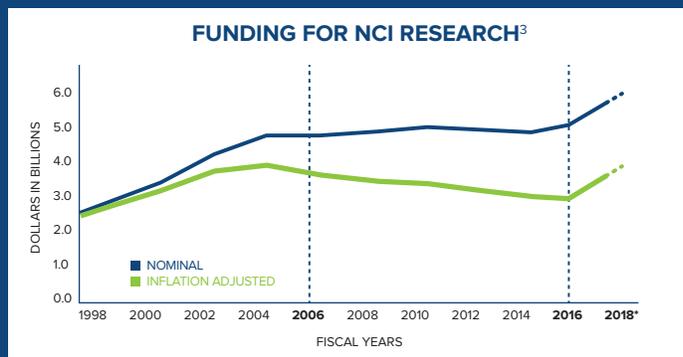
▲ **15.5M**

**CANCER SURVIVORS**

Up from 11.4 million in 2006<sup>1</sup>

NCI's budget, when adjusted for inflation, remains below prerecession levels<sup>3</sup>

**Congress needs to build on its investment**



NIH = National Institutes of Health NCI = National Cancer Institute

\*Figures do not include additional funding from the 21st Century Cures Act.

Source: National Cancer Institute

**Increased federal funding is urgently needed to accelerate life-saving research and new cancer breakthroughs<sup>4,5</sup>**

**EXPANDED PREVENTION AND DETECTION STRATEGIES**

Boost prevention research and increase testing to identify high-risk patients



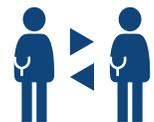
**PRECISION MEDICINE AND IMMUNOTHERAPY RESEARCH**

Support mechanisms to identify, test and validate new predictive biomarkers



**ENHANCED DATA SHARING**

Create a national ecosystem for sharing and analyzing data



**Millions of Americans living with cancer and their loved ones are waiting for new breakthroughs**

**ASCO calls on Congress to build on critical investments by increasing funding to the NIH and NCI.**

For more information visit [asco.org/nihfunding](http://asco.org/nihfunding).

**ASCO**



Sources: 1. American Cancer Society. Cancer Facts & Figures 2017. Atlanta: American Cancer Society; 2017. 2. U.S. Food and Drug Administration. Approved Drugs – Oncology Drugs. Available at: <http://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm>. Accessed on November 9, 2017. 3. National Cancer Institute. NCI Budget and Appropriations. Available at: <https://www.cancer.gov/about-nci/budget>. Accessed on November 9, 2017. 4. The White House. Fact Sheet: Investing in the National Cancer Moonshot. Available at: <https://www.whitehouse.gov/the-press-office/2016/02/01/fact-sheet-investing-national-cancer-moonshot>. Accessed on November 9, 2017. 5. Hayes, Daniel F., MD. "Request for Recommendation of Immediate Actions for the National Cancer Moonshot." Letter to The Vice President. 6 Sept. 2016. MS, Alexandria, VA

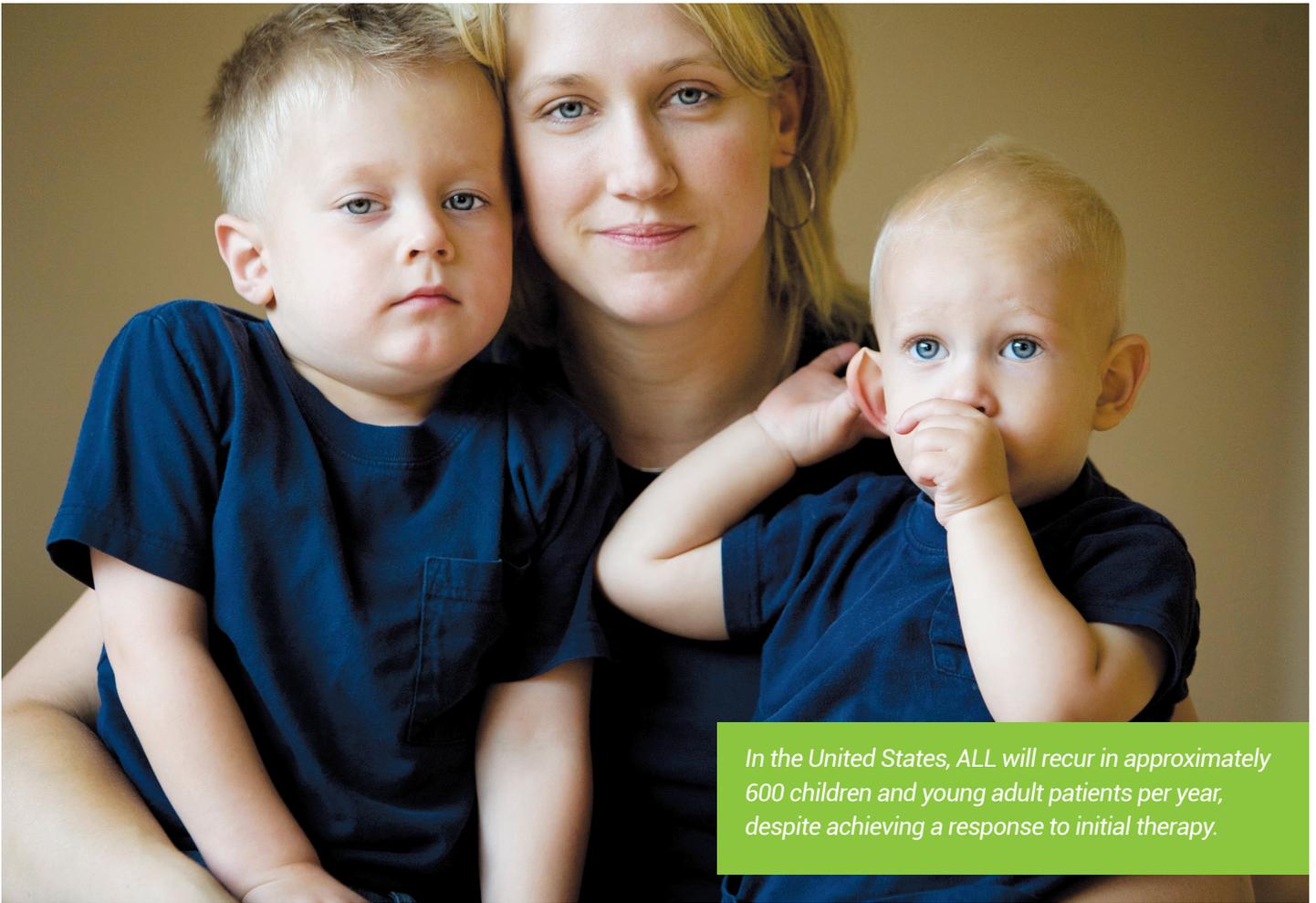
**Fig 1.** Sustained federal funding needed to accelerate cancer research. FDA, US Food and Drug Administration; NCI, National Cancer Institute; NIH, National Institutes of Health.

# 1 Advance of the Year

## ADOPTIVE CELL IMMUNOTHERAPY

This year, ASCO named adoptive cell immunotherapy as the clinical cancer **Advance of the Year**. After decades of research, this powerful and decidedly unique way of treating cancer has become available to certain patients with an otherwise incurable blood cancer.





*In the United States, ALL will recur in approximately 600 children and young adult patients per year, despite achieving a response to initial therapy.*

## CAR T-Cell Therapy Is Poised to Transform Childhood ALL Treatment

In 2017, researchers demonstrated that a CAR T-cell therapy known as tisagenlecleucel, can eradicate relapsed ALL in children. This represents one of the most remarkable advances in the treatment of childhood cancer in the last decade and could dramatically change treatment paradigms for this disease. Tisagenlecleucel targets a protein, known as CD19, on malignant and normal B cells.

In the United States, ALL will recur in approximately 600 children and young adults per year, despite achieving a response to initial therapy.

After a relapse, ALL is difficult to treat, and survival is usually measured in weeks to months. Remission rates with current standard therapies in prior clinical trials have been only 20% with chemotherapy and 33% with targeted therapy.<sup>10,11</sup>

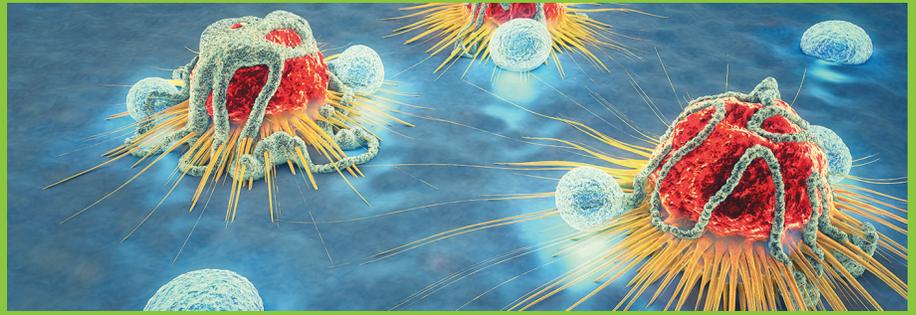
In a clinical trial of children and young adults with relapsed or refractory ALL, cancer went into remission within 3 months of receiving tisagenlecleucel in 52 (82%) of 63 patients, and 75% of patients remained relapse free at 6 months.<sup>12,13</sup> On the basis of these findings, the FDA approved tisagenlecleucel for the treatment of children and



# What Is Adoptive Cell Immunotherapy?

Immune cells navigate the body looking for anything that does not belong—bacteria, viruses, and even cancer cells. They do so by using their molecular feelers, or receptors, to scan for foreign molecules that intruder cells display on their surface. Once an intruder is detected, a class of immune cells, known as cytotoxic T cells, move in to eliminate it.

Unfortunately, cancers have a number of ways to hide from immune cells and avoid their attack. The recently successful immunotherapy approaches aim to remedy this by taking the brakes off the immune system with the use of targeted drugs, known as immune checkpoint inhibitors. Whereas adoptive cell immunotherapy also boosts the body's immune defenses against cancer, it does so in a completely different way—by genetically re-engineering a patient's own immune T cells. In the late 1980s, an immunologist was the first to experiment



with genetically reprogramming T cells, now known as CAR T cells.

CAR T cells are custom made to work against the cancer in each individual patient. To create these cells, researchers collect immune T cells from the patient and insert an artificial gene into the cells.

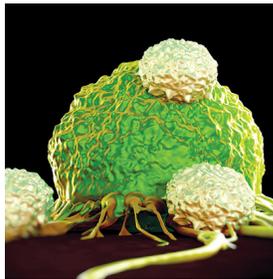
The gene is designed to endow T cells with chimeric antigen receptors that can detect unique molecules on cancer cells after CAR T cells are multiplied in the laboratory and injected back into the patient. In essence, CAR T-cell

therapy is both a gene therapy and an immunotherapy.

When the CAR T-cell receptor attaches to a molecule on a cancer cell, it sends a signal to turn on the destruction machinery of the T cell. Unlike traditional cancer treatments, this living therapy needs to be given to the patient only once, because CAR T cells continue to multiply in the patient's body. As a result, the anticancer effects of CAR T cells can persist and even increase over time.

young adults with B-cell ALL in August 2017.<sup>14</sup>

This global clinical trial confirmed the high efficacy that was demonstrated in prior, single-institution trials; however, the rate of immune-related adverse effects was high with tisagenlecleucel.



Nearly 50% of patients experienced severe cytokine release syndrome (CRS), a complication during which CAR T cells produce a storm of inflammatory molecules. CRS can cause prolonged fever, low blood pressure, difficulty breathing, and problems with multiple organs.

If severe, CRS may require intensive medical care, such as the use of a ventilator or medications known as pressors to increase blood pressure, and seizure medication. Although CRS can be serious and even life threatening, doctors now

have an effective medicine (tocilizumab) with which to curb and, in most cases, fully reverse the symptoms.

In addition, neurologic complications occurred in 15% of patients in the study. A broad range of neurologic problems, including word

recall issues, difficulty speaking, reduction of alertness, delirium, hallucinations, seizures, and coma, have been reported in prior clinical trials with CAR T-cell therapies.

In most patients, such symptoms resolved on their own within a few days without long-term consequences, but several deaths have occurred, with severe neurologic complications in other CAR T-cell trials. In this ALL trial, there were no deaths related to either CRS or neurologic complications.

The global ALL trial also helped to prove

that patient access to this novel treatment could be broadened. It was the first time CAR T cells were produced from patient blood cells in an industrial manufacturing facility and distributed to patients via a global supply chain that included 25 centers in the United States, Canada, Europe, Australia, and Japan.

Until then, the production of CAR T cells was limited to few academic laboratories, without the ability to ship the cell product to patients around the world.

In a clinical trial of young patients with recurrent ALL, for the majority of patients cancer went into remission within 3 months of receiving CAR T-cell therapy.

82%

# CAR T-Cell Therapy Is Effective Against Hard-to-Treat Lymphoma in Adults

CAR T cells that target CD19 have also been proven to be promising against another hard-to-treat cancer, diffuse large B-cell lymphoma (DLBCL), which is the most common type of non-Hodgkin lymphoma. In a multicenter clinical trial of patients with DLBCL that worsened after at least two prior therapies, the cancer responded to tisagenlecleucel in 59% of patients and went into remission in 43% of patients.<sup>15</sup> At 6 months, 79% of patients had

not had a recurrence of lymphoma. Severe CRS occurred in 25% of patients, and neurologic complications in 13%.

In a different clinical trial, patients with relapsed or refractory DLBCL, refractory primary mediastinal B-cell lymphoma, or transformed follicular lymphoma, received another CAR T-cell product called axicabtagene ciloleucel that also targets CD19.<sup>16</sup> Among the first 92 patients who

were treated, the response rate was 82%, with complete remissions occurring in 54% of patients. At a median follow-up of 8.7 months, 39% of patients were still in complete remission. Severe CRS occurred in 13% of patients; neurologic adverse effects occurred in 28% of patients. In late 2017, the FDA approved axicabtagene ciloleucel to treat adults with DLBCL that has not responded to, or has recurred, after at least two prior therapies.<sup>17</sup>

# CAR T-Cell Therapy Sends Multiple Myeloma Into Remission

A different type of CAR T-cell therapy that targets a biomarker known as B-cell maturation antigen (BCMA) seems to be effective against multiple myeloma.

Despite recent advances in treatment, multiple myeloma—a cancer of plasma cells

that make antibodies to fight infections—remains an incurable disease, with only approximately one half of patients living 5 years after diagnosis.

In an early clinical trial, the cancer responded to BCMA CAR T cells in 33 (94%)

of 35 patients, and went into complete remission in 14 patients<sup>18</sup> (Updated data presented at the 2017 ASCO Annual Meeting in Chicago, IL). Only two patients experienced severe CRS, and none experienced neurologic complications from CAR T-cell therapy.



## VOICES OF CANCER RESEARCH

### Melinda Bachini

At 41 years old, Melinda received a diagnosis of a rare cancer: cholangiocarcinoma, also known as bile duct cancer. Currently, there are very few treatments available for this disease. Melinda had five surgeries and several rounds of chemotherapy before eventually running out of options.

Then, Melinda joined a clinical trial at the National Institutes of Health. The study investigated a type of adoptive cell immunotherapy using immune cells from around the tumor (tumor infiltrating lymphocytes). This and another type of immunotherapy she received later on helped shrink the tumors for several years. Melinda has not needed cancer treatment for almost a year, and she calls her quality of life “amazing.”

“Cancer research has saved my life and I couldn’t be happier,” Melinda says, five years after beginning the trial. “It has allowed me to continue to be a wife, mother, and patient advocate.” She hopes that clinical trials will continue to lead to new and better treatment options for patients like her.

*Melinda is a volunteer with The Cholangiocarcinoma Foundation, NCI Hepatobiliary Task Force, and NCI Patient Advocacy Steering Committee (PASC).*

“ I am still alive today because of a clinical trial. ”

# 2 Advances in Cancer Prevention



Cancer prevention efforts, including cancer screening, vaccination, tobacco control, healthy eating, and physical activity, remain key to reducing the effect of cancer and improving outcomes across communities worldwide.

In fact, researchers estimate that 50% of cancer cases and deaths in the United States could be prevented if people adopted simple healthy lifestyle choices that include avoiding smoking and alcohol, maintaining a healthy weight, and exercising regularly.<sup>19</sup>

The top three causes of cancer-related death in low-resource countries—liver cancer, stomach cancer, and cervical cancer—are largely preventable through screening or vaccination. In higher-resource countries, two leading causes of cancer-related deaths—lung and colorectal cancer—can be lowered through lifestyle changes, such as increased physical activity and avoidance of alcohol, tobacco, and processed meat.

The same healthy habits can help prevent dozens of other cancers. Emerging research suggests that human papillomavirus (HPV) vaccination, mainly used for the prevention of cervical cancer, may also help reduce head and neck cancers by lowering oral HPV infections.<sup>20</sup> Finally, safe sun exposure practices and avoidance of indoor tanning can substantially lower the risk for melanoma.

**50%**  
of cancer cases and deaths in the US could be prevented if people adopted simple healthy lifestyle choices.



## Preventive Actions to Lower Cancer Risk

Although most Americans (66%) do not smoke, less than half take other important preventive actions to lower their risk of cancer:

Use sunblock or limit sun exposure without sunblock



48%

Exercise regularly



48%

Maintain a healthy body weight



41%

Limit alcohol consumption



38%

ASCO's National Cancer Opinion Survey, 2017

### AVOIDABLE CANCER RISK FACTORS:

## Indoor Tanning

UV radiation exposure from indoor tanning is a cause of malignant melanoma. Characterizing the risk of melanoma associated with use of UV radiation-emitting devices is critical for developing policies that reduce the use of such devices, but much of the evidence on this topic has come from case-control studies. In the past year, a large, prospective study was reported that adds new weight to such policy efforts, finding that the risk for melanoma rose with an increasing number of indoor tanning sessions.<sup>23</sup>

Compared with those who never used indoor tanning, women who started indoor tanning before 30 years of age had a 30% higher risk for melanoma, which suggests that the harmful effects of indoor tanning are greater at a younger age. For more information on risk factors for melanoma, visit [Cancer.Net](http://Cancer.Net).





#### AVOIDABLE CANCER RISK FACTORS:

## E-Cigarettes May Spur Increases in Smoking

In 2017, two federally funded studies provided the clearest estimates of how e-cigarette use may lead to a future habit of smoking cancer-causing traditional tobacco cigarettes. The first study found that people 14 to 30 years of age who used e-cigarettes were 3.6 times more likely to begin smoking traditional cigarettes than those who never used e-cigarettes (this study was funded, in part, by grants from the NCI, the FDA, and the National Institute on Drug Abuse).<sup>21</sup>



These findings indicate that e-cigarettes are not merely a substitute for traditional cigarettes, but are also a strong risk factor for future smoking. In fact, experts caution that e-cigarette use may lead to an upsurge in smoking prevalence in the long term.

Another study found that, among US teenagers 12 to 17 years of age, the rate of e-cigarette use is already approaching the rate of tobacco cigarette use; 3.1% smoked

e-cigarettes compared with 4.6% who smoked tobacco cigarettes in the last 30 days (this study was funded, in part, by grants from the National Institute on Drug Abuse, NIH, and the FDA).<sup>22</sup> However, among adults, e-cigarette use still lags far behind tobacco cigarette use (6.7% v 22.5%). In addition, among those who used more than one tobacco product, 15% of teenagers and 23% of adults used both e-cigarettes and traditional cigarettes.

There is clear evidence that e-cigarettes, smokeless tobacco, and water pipes may cause serious health problems, including cancer. Because of these potential health risks, the FDA began regulating these products, along with other tobacco products, on August 8, 2016.

The US Centers for Disease Control and Prevention calls on the public, including parents, health care providers, and teachers, to discourage e-cigarette use among youth. ASCO's Cancer.Net provides information on the risks of e-cigarettes and smokeless tobacco.

### Cancer Spending

49%

Almost one half (49%) of Americans believe the government should spend more money on cancer prevention.

54%

54% think the government should spend more to help Americans afford cancer screenings and care.

ASCO's National Cancer Opinion Survey, 2017



## ASCO Issues Statement on Alcohol as It Relates to Cancer Prevention

In 2017, ASCO issued a statement on alcohol and cancer aimed at drawing attention to alcohol consumption as a contributing factor to the overall cancer burden.<sup>24</sup> ASCO cites between 5% and 6% of new cancer cases and deaths globally as being directly attributable to alcohol. This is particularly concerning as 70% of Americans do not recognize drinking alcohol as a risk factor for cancer, according to the National Cancer Opinion Survey, conducted by ASCO in 2017.

Because drinking alcoholic beverages is a potentially modifiable risk factor for cancer, it can be targeted with preventive interventions at both the policy and individual levels to reduce the incidence of cancer. The evidence-based policy recommendations to reduce excessive alcohol consumption listed in the statement, which was published in the *Journal of Clinical Oncology*, are:

- Provide alcohol screening and brief interventions in clinical settings;
- Lower the number of alcohol retailers per capita;
- Increase alcohol taxes and prices;

- Maintain limits on days and hours of sale;
- Enhance enforcement of laws that prohibit sales to minors;
- Restrict youth exposure to advertising of alcoholic beverages;
- Resist additional privatization of retail alcohol sales in communities with current government control;
- Include alcohol control strategies in comprehensive cancer control plans;
- Support efforts to eliminate the use of “pinkwashing” to market alcoholic beverages (ie, discourage alcoholic beverage companies from exploiting the color pink or pink ribbons to show a commitment to finding a cure for breast cancer) given the evidence that alcohol consumption is linked to an increased risk of breast cancer.

In addition, not only does excessive alcohol consumption cause cancer, it also can delay or negatively affect cancer treatment. Oncologists are uniquely

positioned to identify strategies to help their patients reduce alcohol use; address racial, ethnic, gender, and sexual orientation disparities that may place these populations at increased risk of cancer; and serve as community advisors and leaders to raise awareness of alcohol as a cancer risk behavior.

The link between alcohol use and cancer treatment is one of the most-needed areas for future research in the oncology community, particularly in studying the effect of alcohol consumption while undergoing cancer treatment, including chemotherapy, radiation, and surgery.

Other underexplored research areas include the effect of alcohol consumption on postoperative morbidity and targeted therapies, such as immunotherapy and radiation.

By increasing the community's knowledge of the ways in which alcohol affects cancer and cancer treatments, oncologists and researchers may have a better understanding of its role in disease progression and therapeutic responsiveness and toxicity.

# 3 Advances in Cancer Treatment



**This year, more than 14 million people worldwide will learn they have cancer. According to the latest global statistics, nearly 9 million people a year lose their lives to cancer. That equates to approximately 22,000 cancer deaths per day.<sup>25</sup>** The global cancer burden is expected to grow in the future, reaching 21 million patients with cancer and 13 million deaths per year by 2030, as the world's population expands and ages. These sobering statistics underscore the urgency of finding better treatments for patients today and in the future.

The number of new FDA approvals in oncology in recent months is reflective of the scientific fervor and innovation underway to fill this need. From November 2016 through October 2017, the FDA approved a record 18 new cancer therapies and 13 new uses of cancer therapies (Appendix, Table A1). By comparison, in the same timeframe in the previous year, there were eight new cancer therapies and 13 new uses approved, and a similar number in 2015. Most, if not all, of these new and expanded uses are associated with an improvement in patient survival and/or quality of life.

Also historic, 2017 marked the first approval of a tumor-agnostic therapy and the first adoptive T-cell and gene therapy for cancer, demonstrating that the breakthrough therapy designation and other new approaches in oncology drug development have allowed for a more efficient review and approval process. Research results on other immunotherapies and targeted therapies released in 2017 have changed the treatment paradigms for lung, prostate, and bladder cancer.

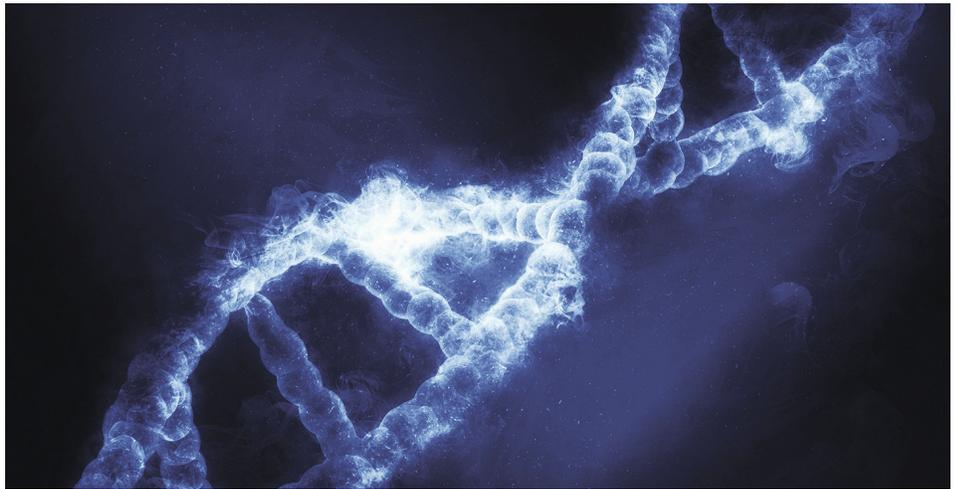
## EMERGENCE OF TISSUE-AGNOSTIC THERAPIES:

# Treating Patients on the Basis of the Tumor's Genetics, Rather Than Its Location

Historically, cancer therapies have been approved for use on the basis of the tumor's location in the body and stage of cancer.

Last year marked a milestone in the history of precision cancer medicine and cancer drug approvals: In May, the FDA approved the first tissue-agnostic treatment, which means that it was approved for use solely on the basis of the genetic make-up of a person's cancer, rather than the type of cancer or its location in the body.<sup>26</sup> Pembrolizumab was approved for the treatment of adults or children with advanced solid tumors that harbor specific genomic changes—mismatch repair (MMR) deficiency or high microsatellite instability (MSI-H).

FDA approval was based on findings from 149 patients with MMR-deficient or MSI-H solid tumors—90 had colorectal cancer and 59 had one of 14 other types of cancer—who were enrolled in five clinical trials.



Tumors shrank in 40% of patients, and in 78% of those patients, tumor response lasted 6 months or more. In one of the studies that included patients with 12 different types of cancer, and in 21% of patients, cancer went into complete remission (this study was funded, in part, by grants from the NIH).<sup>27</sup>



Cells with MMR deficiency have a lower ability to repair damage to their genetic material or DNA and, as a result, accumulate a high number of mutations and make many abnormal proteins. Recent research has shown that programmed death-1/programmed death ligand-1 immune checkpoint inhibitors, which work by unleashing the immune response to



**“ People with cancer can get tomorrow's medicines today by participating in a clinical trial. ”**

## VOICES OF CANCER RESEARCH

### Erin Miller

Erin was the primary caregiver for her husband Mike, who was diagnosed with pancreatic cancer. He received several rounds of chemotherapy but eventually became too sick to continue treatment. They were told that he only had a few months to live.

Erin says it was then that Mike began a gene therapy clinical trial for pancreatic cancer. Soon after, he was feeling better and was well enough to coach his daughter's tee-ball team, go camping with his two sons, and take a ski trip with the family.

Erin is thankful that their family received additional time with Mike, who passed away 19 months after starting the trial.

“My daughter, who was 4 when Mike was diagnosed, would probably not have remembered him had he not lived those extra months,” Erin says. “Every day was a treasured gift to us.”

*Erin, pictured here with her husband Mike, is a Program Services Coordinator at the Lazarex Cancer Foundation.*

cancer, are particularly effective against tumors with MMR deficiency. The reason for this is thought to be a stronger immune response to tumors with more abnormal proteins that the immune system recognizes as foreign.

With this approval, subsets of patients with various types of cancer that are otherwise resistant to treatment gained a highly effective treatment option for controlling the disease, potentially long term. Testing for MMR deficiency or MSI-H will become part of routine diagnostic workup for many patients with solid tumors.

In 2017, researchers presented the early findings from a study of another treatment that seems to work well across many different types of adult and pediatric cancers. The treatment, called larotrectinib, selectively targets a rare genomic

abnormality, the *tropomyosin receptor kinase (TRK)* gene fusion.

It is estimated that this abnormality occurs in approximately 0.5% to 1% of many common cancers. In addition, more than 90% of certain rare cancers, such as salivary gland cancer, pediatric breast cancer, and infantile fibrosarcoma, have *TRK* fusions.

Of the first 50 adults and children with 17 different cancer types who received larotrectinib in clinical trials, treatment response rate was nearly 80%.<sup>28</sup> Responses to larotrectinib have been long lasting, with 79% ongoing at 12 months after starting treatment. The most common adverse effects were fatigue and mild dizziness, which were expected, as the normal *TRK* protein has a role in controlling balance. No patients needed to stop treatment as a

result of adverse effects.

In another clinical trial that enrolled 12 young children with different cancers that harbored *TRK* fusions (infantile fibrosarcoma, other sarcomas, and papillary thyroid cancer) the response rate to larotrectinib was 92%, and responses were also durable. At 6 months, the cancer had worsened in only one patient.<sup>29</sup>

These trials that show strong tumor responses in tumors with *TRK* fusions, regardless of histology, represent a major development in the field. These findings pave the way for a new class of drugs for rare tumors and define a new era in oncology. Equally important, they set a new milestone in precision medicine for pediatric oncology, for which it is just starting to be applied.



“ Funding cancer research is a moral, fiscal, and national security imperative, and is the priority of every family in every neighborhood of America, regardless of their political party. I will fight to provide researchers with the necessary resources so that they can find cures and save lives. ”

— Representative Kevin Yoder (R-KS-03), Co-Chair, Cancer Caucus



A POLICY FOCUS:

## FDA's New Plan to Increase Medical Innovation

The FDA has launched a new Medical Innovation Development Plan designed to facilitate the development of innovative drugs by updating FDA's regulatory tools and policies. FDA intends to use the new plan to streamline the path to market for targeted therapies and other novel drugs to encourage innovation in therapies.

In particular, the plan will focus on facilitating the approval of tumor-agnostic therapies—medicines that work comparatively well in many different types of cancer. As part of the plan, FDA will develop guidance on strategies to improve the efficiency of clinical trials, including adaptive trial designs.

# New Treatments Slow Advanced Lung Cancer Growth

Lung cancer is among the most common types of cancer and the leading cause of cancer death in men and women worldwide. Last year, an estimated 156,000 people died of this disease in the United States.<sup>30</sup>

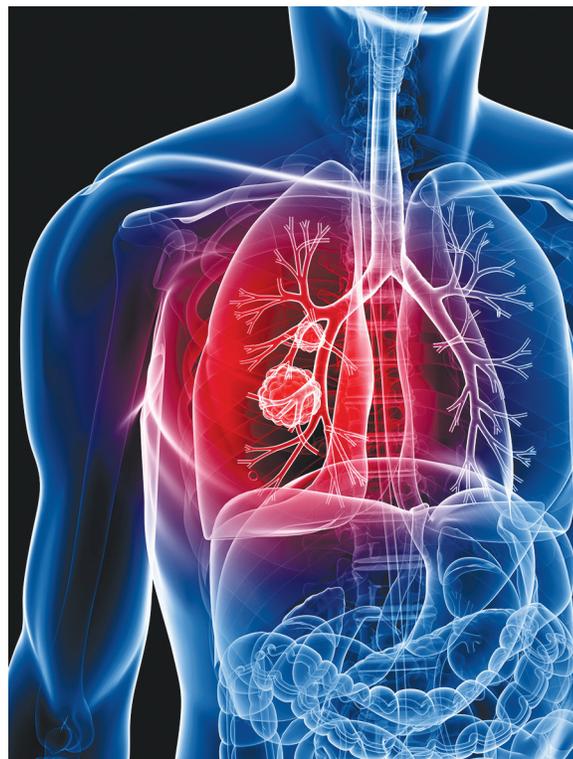
The good news is that these grim statistics have been steadily improving. After decades of increases, rates of lung cancer deaths began to decline in the early 1990s and have been falling, on average, 2.5% each year between 2005 and 2014. The 5-year survival rate increased from only 11% in 1975 to 18% in the most recent time period measured (2007 to 2013).<sup>30</sup> For more information about lung cancer, visit Cancer.Net.

This progress is directly tied to changes in therapy that have occurred

during the past two decades, with the development of new therapies that not only work better, but that often also have fewer adverse effects than standard chemotherapy, radiation, and surgery.

In 2017, two new regimens were introduced for the initial treatment of the most advanced form of non-small-cell lung cancer (NSCLC)—a targeted medicine, alectinib, and an immune checkpoint inhibitor, pembrolizumab, combined with chemotherapy.

For patients with earlier-stage disease, a clinical trial demonstrated that administering a new immune checkpoint inhibitor, durvalumab, after standard chemotherapy and radiation dramatically slowed cancer growth.



## Changing Paradigms in Lung Cancer Treatment

The first paradigm shift occurred in the mid-1990s with research that demonstrated that giving chemotherapy after surgery, known as adjuvant therapy, helps patients live longer, and that combining chemotherapy with radiation therapy can additionally improve the outlook for some patients with lung cancer. Several new chemotherapies were introduced, such as paclitaxel, docetaxel, gemcitabine, and pemetrexed.

The second paradigm shift in the treatment of advanced lung cancer occurred in 2004, when scientists discovered the association between certain mutations in the *epidermal growth factor receptor (EGFR)* and response to EGFR-targeted drugs, such as gefitinib. EGFR is a protein that helps cancer cells grow and is mutated in

25% of lung cancers. In the ensuing years, several EGFR-targeted drugs were developed (erlotinib, afatinib, and osimertinib) as well as treatments that target less common genetic alterations (*BRAF* gene mutations [dabrafenib plus trametinib] and *ALK* gene rearrangements [crizotinib, ceritinib, and alectinib]).

Finally, the introduction of immunotherapy in 2015 marks the third paradigm shift in the treatment of lung cancer. Immune checkpoint inhibitors, pembrolizumab and nivolumab, were first approved for the treatment of advanced NSCLC that worsens during or after standard chemotherapy, and atezolizumab was approved in 2016. That same year, the FDA approved the first use of immunotherapy

for previously untreated advanced NSCLC, pembrolizumab. Currently, immunotherapy is also being studied in earlier stages of disease. In a clinical trial of patients with locally advanced, stage III NSCLC, the checkpoint inhibitor durvalumab delayed disease worsening by nearly 1 year. The ongoing ALCHEMIST immunotherapy trial (ClinicalTrials.gov identifier: NCT02595944) explores whether giving nivolumab after standard treatment of early-stage lung cancer can reduce recurrences and help patients live longer.

Reflecting on these developments, ASCO's clinical practice guideline for advanced NSCLC was revised in 2017 to add immunotherapy as a standard treatment approach for either first-line or second-line settings.<sup>31</sup>

## NEW TARGETED MEDICINE WORKS BETTER THAN CHEMOTHERAPY, WITH FEWER ADVERSE EFFECTS

Up to 7% of NSCLCs have a genetic change known as *anaplastic lymphoma kinase (ALK)* rearrangement that results in an abnormal ALK protein that causes cells to grow and spread. The first medicine that targets ALK, crizotinib, was approved by the FDA in 2011, and more potent medicines have been introduced since that time. In 2017, two clinical trials showed that one new ALK medicine, alectinib, is more effective than crizotinib for patients with previously untreated NSCLC, and also causes fewer adverse effects.<sup>32,33</sup>

In the larger of the two trials, during a median follow-up of 18 months, 41% of patients who received alectinib had their cancer worsen, or died, compared with 68% of those who received crizotinib.<sup>33</sup> Alectinib was also better at curbing the growth of cancer that had spread to the brain; only 12% of patients had worsening brain

metastases compared with 45% of those who received crizotinib.

## ROLE OF IMMUNOTHERAPY CONTINUES TO EXPAND, SLOWING ADVANCED CANCER GROWTH

In 2017, the FDA granted accelerated approval to pembrolizumab combined with standard chemotherapy (carboplatin and pemetrexed) as an initial treatment of metastatic NSCLC.<sup>34</sup> The approval was based on an early clinical trial that found that the chance of cancer worsening was cut nearly in half by adding pembrolizumab to chemotherapy.

The median time until cancer worsening was 13 months with pembrolizumab and chemotherapy, versus 9 months with chemotherapy alone; however, the incidence of serious treatment-related adverse effects was higher with combined modality treatment (41%) than chemotherapy alone (28%). An international phase III clinical trial is underway to confirm these findings (ClinicalTrials.gov

identifier: NCT02578680).

A newer immune checkpoint inhibitor, durvalumab, also seems to have a role in lung cancer treatment. These findings mark the first advance in years for the treatment of stage III, locally advanced NSCLC. This type of cancer accounts for approximately one third of all NSCLCs.

The standard treatment of patients with tumors that cannot be surgically removed is chemotherapy with radiation, or chemoradiotherapy. Despite this treatment, cancer quickly worsens, and only 15% of patients are alive 5 years after diagnosis.

In this trial, patients whose cancer did not worsen after chemoradiotherapy were randomly assigned to receive durvalumab or placebo.<sup>35</sup> The median time until cancer worsening was 16.8 months with durvalumab and 5.6 months with placebo, and the median time until patients died or the cancer spread to distant parts of the body was 23.2 months versus 14.6 months, respectively.

# Immunotherapy for Lung Cancer Could Save 250,000 Years of Life

Immune checkpoint inhibitors have transformed treatment for advanced NSCLC. There are currently 3 FDA-approved checkpoint inhibitors for previously treated NSCLC (nivolumab, pembrolizumab, and atezolizumab) and pembrolizumab is approved as an initial therapy for certain patients. In clinical trials, patients who received these immunotherapies have lived longer, on average, than those who received standard chemotherapy. However, given that checkpoint inhibitors have been in use for only a few years, their impact on long-term survival is not yet known.

ASCO estimates that 250,000 years of life would be saved in

the United States if all patients with NSCLC for whom checkpoint inhibitors are currently indicated received the treatment. While the average number of years of life saved is 2.5, up to 25% of people who receive checkpoint inhibitors as an initial treatment and 10% of those who receive them as a second-line treatment may live well beyond 5 years after treatment initiation.

The estimates were based on an analysis of clinical trial results and cancer incidence and population data conducted by the ASCO Center for Research and Analytics (CENTRA). The researchers accounted for differences by race and gender in NSCLC incidence and life expectancy.



# Continued Research on Immune Checkpoint Inhibitors

Uses for immune checkpoint inhibitors—treatments that help unleash the body's immune response to cancer—continue to expand to more cancer types, which has affirmed the role of this strategy, and particularly agents that target the programmed death-1/programmed death ligand-1 checkpoint in cancer treatment. Key recent studies in this area are listed in Table 1.

**Table 1.** Notable Recent Advances With Immune Checkpoint Inhibitors

CANCER TYPE	KEY FINDING	FIRST AUTHOR
Breast cancer	Addition of pembrolizumab to standard neoadjuvant therapy for high-risk, HER2-negative breast cancer increased rates of pathologic complete response, especially in women with triple-negative breast cancer—a 50% higher rate.	Nanda <sup>36</sup>
Head and neck cancer	Patients with recurrent or metastatic squamous cell head and neck cancer who received nivolumab lived a median of 2-3 months longer than did those who received standard therapy of investigator's choice.	Gillison <sup>37</sup>
Head and neck cancer	Compared with patients with recurrent or metastatic squamous cell head and neck cancer who received standard therapy of investigator's choice, those who received nivolumab had fewer symptoms and better quality of life for 15 weeks.	Harrington <sup>38</sup>
Kidney cancer	Response rate was higher in patients with advanced kidney cancer who received nivolumab as initial treatment than in those who received standard sunitinib (42% v 26%, respectively), and time until cancer worsening was longer (median, 11.6 months v 8.4 months, respectively).	Escudier <sup>39</sup>
Liver cancer	In an early clinical trial of patients with advanced liver cancer, response rate to nivolumab was 20% and adverse effects were manageable.	El-Khoueiry <sup>40</sup>
Lung cancer	In a clinical trial of patients with advanced small-cell lung cancer, 1-year survival rate was 30% for those who received nivolumab and 42% for those who received nivolumab with ipililumab.	Hellmann <sup>41</sup>
Lung cancer	Treatment with checkpoint inhibitor durvalumab after standard chemotherapy and radiation delayed worsening of stage III NSCLC by 11 months.	Antonia <sup>42</sup>
Skin cancer	Compared with patients with advanced melanoma who received adjuvant ipililumab, those who received nivolumab had a higher rate of recurrence-free survival at 12 months (70% v 61%, respectively) and a lower rate of severe adverse effects (14% v 46%, respectively).	Weber <sup>43</sup>
Skin cancer	In patients with advanced melanoma, 3-year survival rate was higher with nivolumab and ipililumab combined (55%) than with either nivolumab alone (52%) or ipililumab alone (32%).	Wolchok <sup>44</sup>
Skin cancer	In a clinical trial of patients with advanced Merkel cell carcinoma, response rate to PD-L1 inhibitor avelumab was 32% during a median follow-up of 10 months.	Kaufman <sup>45</sup>
Skin cancer	An early clinical trial suggests that a new PD-1 inhibitor, REGN2810, may be effective against a common skin cancer, cutaneous squamous cell carcinoma. Response rate in patients with advanced disease was 52%.	Papadopoulos <sup>46</sup>
Stomach cancer	A large clinical trial shows that nivolumab is effective as a salvage therapy for people with advanced gastric or gastroesophageal junction cancer that worsens despite chemotherapy. At 12 months, 27% of patients were alive compared with 11% of those who received placebo.	Kang <sup>47</sup>
Stomach cancer	Pembrolizumab showed promising efficacy in a clinical trial of patients with previously treated, advanced stomach or gastroesophageal junction cancer. Response rate was 11% and 12-month survival rate was 23%.	Fuchs <sup>48</sup>

# Immunotherapy Changes the Treatment Paradigm for Bladder Cancer

Bladder cancer is another type of cancer for which immunotherapy has transformed the outlook for patients. The most common type of bladder cancer, urothelial cancer, is difficult to treat at advanced stages. With standard chemotherapy, only 5% of patients are alive 5 years after diagnosis. For more information about bladder cancer, visit Cancer.Net.

After 30 years of limited progress, the outlook for these patients is now improving with the arrival of a series of immunotherapies (Table 2). For some patients, immunotherapy has opened a treatment option where none previously existed. For others, it offers a chance to live longer with fewer treatment-related adverse effects.

In May 2016, atezolizumab became the first immune checkpoint inhibitor to receive FDA approval for the treatment of advanced bladder cancer.<sup>49</sup> In 2017, the FDA approved four other immune checkpoint inhibitors for patients with previously

treated urothelial cancer that worsened, despite platinum-based chemotherapy—nivolumab, avelumab, pembrolizumab, and durvalumab.<sup>50-53</sup> In a large clinical trial that led to the approval of pembrolizumab, patients who received the immunotherapy lived approximately 3 months longer than those who received chemotherapy. Meanwhile, the rate of serious treatment-related adverse effects was more than three times lower in the pembrolizumab group than in the chemotherapy group (15% v 49%).<sup>54</sup>

Recent clinical trials also point to the potential use of immunotherapy as an initial treatment for advanced bladder cancer. As a result of physical frailty and certain health conditions, up to two thirds of patients are not eligible for cisplatin-based chemotherapy, which is the standard initial treatment of this disease. Alternative chemotherapies exist, but are less effective; therefore, many such patients receive only supportive care.

In 2017, the FDA granted accelerated approval to pembrolizumab for this indication.<sup>53</sup> The approval was based on a clinical trial of patients with locally advanced or metastatic urothelial cancer who were not eligible for cisplatin-containing chemotherapy.<sup>55</sup> At a median follow-up of 8 months, treatment response rate was 28%, and responses lasted up to 18 months (median duration not reached). Pembrolizumab was well tolerated, with serious adverse effects occurring in 18% of those treated.

In another clinical trial, atezolizumab also was proven to be effective as an initial therapy for patients with advanced urothelial cancer who cannot receive cisplatin-containing chemotherapy.<sup>56</sup> At a median follow-up of 18 months, the treatment response rate was 23% and median survival was nearly 16 months. These advances have defined new standards of care for patients with advanced bladder cancer.

**Table 2.** Recent US Food and Drug Administration Approvals of Immunotherapies for Bladder Cancer

DRUG NAME (TRADE NAME)	INDICATION	DATE APPROVED
Atezolizumab (Tecentriq)	For treatment of patients with locally advanced or metastatic urothelial carcinoma who experience progression during or after platinum-containing chemotherapy or within 12 months of treatment with platinum-containing chemotherapy.	May 2016
Nivolumab (Opdivo)	For treatment of patients with locally advanced or metastatic urothelial carcinoma who experience disease progression during or after platinum-containing chemotherapy or who experience disease progression within 12 months of neoadjuvant or adjuvant treatment with a platinum-containing chemotherapy.	February 2017
Avelumab (Bavencio)	For patients with locally advanced or metastatic urothelial carcinoma who experience disease progression during or after platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.	May 2017
Durvalumab (Imfinzi)	For treatment of patients with locally advanced or metastatic urothelial carcinoma who experience disease progression during or after platinum-containing chemotherapy or who experience disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.	May 2017
Pembrolizumab (Keytruda)	For patients with locally advanced or metastatic urothelial carcinoma who experience disease progression during or after platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.	May 2017

# New Approaches Help People With Brain Cancer Live Longer

## TWO NEW REGIMENS EXTEND SURVIVAL IN PATIENTS WITH GLIOBLASTOMA

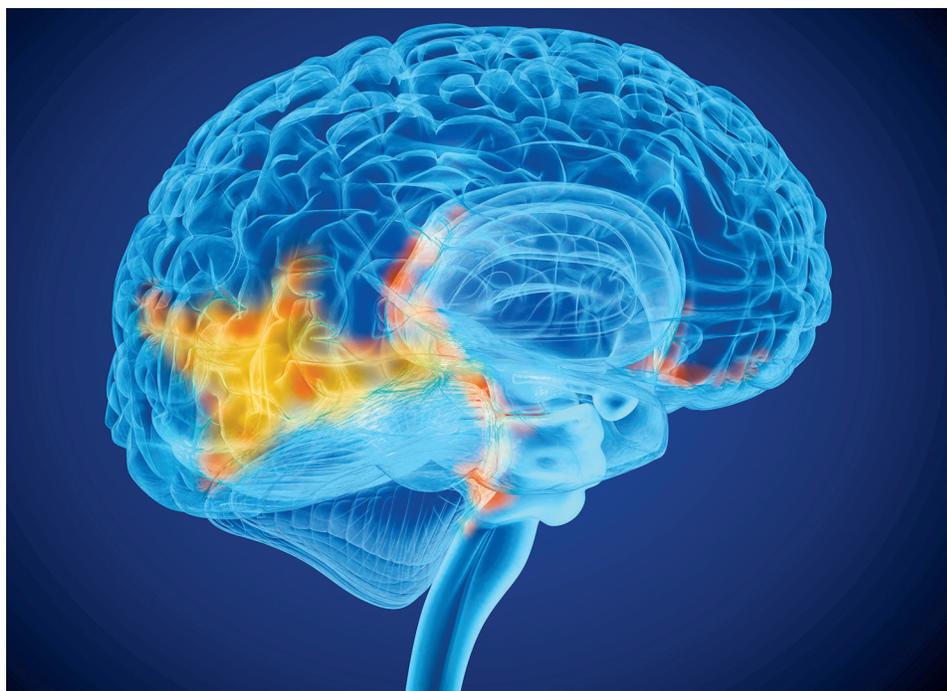
Grade IV glioma, or glioblastoma (GBM), is one of the most common and deadliest types of brain cancer in adults. With current therapies, fewer than one in 10 patients live 5 years after a diagnosis of GBM. There are now two new strategies that can possibly lengthen life for people with GBM. For more information about GBM and other brain tumors, visit Cancer.Net.

The first involves a novel technology known as tumor-treating fields (TTFs). These are low-intensity electrical fields that are thought to slow cancer growth by blocking cell division. TTFs are delivered to the brain tumor through the skin from a device that patients wear on their head continuously at least 18 hours a day.

Preliminary findings from a clinical trial of TTFs led to FDA approval of the device in 2015 for use in combination with temozolomide chemotherapy, after surgery, chemotherapy, and radiation, for patients with newly diagnosed GBM.<sup>58</sup> In 2017, researchers reported longer follow-up findings from the same clinical trial.<sup>59</sup>

The risk of death was reduced by 37% for patients who used the device compared with those who received chemotherapy alone, with a median survival of 21 months with TTFs and chemotherapy, versus 16 months with chemotherapy alone. The addition of TTFs also doubled the 5-year survival rate, from 5% to 13%.

The second advance is the discovery that adding temozolomide chemotherapy to short-course radiotherapy results in longer survival than radiotherapy alone in elderly patients with GBM.<sup>60</sup> The prognosis for elderly patients with GBM is poor and questions remain about the optimal treatment of older patients.



In the study, patients who received temozolomide with radiotherapy had a 33% lower risk of death and lived longer than those who received radiotherapy alone (median, 9.3 months v 7.6 months, respectively), whereas quality of life was similar between the two groups.

Researchers also confirmed prior findings that suggested that a genomic biomarker, methylation of the *O6-methylguanine-DNA methyltransferase (MGMT)* gene, predicts better outcomes in patients with GBM. Among patients with methylated MGMT, median survival with radiotherapy plus temozolomide was 13.5 months compared with 7.7 months with radiotherapy alone.

## ADDING CHEMOTHERAPY TO RADIATION SLOWS GLIOMA GROWTH

Grade III glioma, or anaplastic glioma, commonly occurs in young adults. This type of brain tumor can grow quickly and can recur as GBM despite treatment.

For patients with anaplastic glioma with

a genomic abnormality known as 1p19q codeletion (loss of chromosome arms 1p and 19q) there is clear evidence that adding chemotherapy to radiation therapy improves survival; however, there are conflicting reports of the value of adjuvant (postsurgery) chemotherapy for anaplastic glioma without 1p19q codeletion. Preliminary findings from a large clinical trial have clarified the role of adjuvant temozolomide in this patient population.<sup>61</sup>

The 5-year survival rate was markedly longer when temozolomide was added to radiation therapy (56%) than when patients received radiation therapy alone (44%). Addition of temozolomide after radiation therapy delayed disease worsening by more than 2 years (median, 43 months v 19 months, respectively).

Temozolomide was well tolerated, with serious adverse effects occurring in only 12% of patients. These findings have established this regimen as a new standard of care for patients with anaplastic glioblastoma without 1p19q codeletion.

# New Targeted Therapy Regimens for Breast Cancer

## FOR BRCA-RELATED BREAST CANCER, OLAPARIB IS MORE EFFECTIVE THAN CHEMOTHERAPY

Findings from a large clinical trial of women with advanced, BRCA-related breast cancer point to a new type of treatment for the disease—poly (ADP-ribose) polymerase (PARP) inhibitors. Compared with standard chemotherapy, the PARP inhibitor olaparib lowered the risk of cancer worsening by 42% and extended the time until the cancer worsened by approximately 3 months.<sup>62</sup> Severe adverse effects were less common with olaparib, occurring in 37% of patients compared with 50% of those who were treated with chemotherapy. For more information about advanced breast cancer, visit [Cancer.Net](http://Cancer.Net).

Whereas several PARP inhibitors are already approved by the FDA for the treatment of ovarian cancer, this is the first study to demonstrate clinical benefit from this approach in patients with breast cancer. Several other large clinical trials of olaparib in breast cancer are underway (ClinicalTrials.gov identifiers: NCT02032823 and NCT03167619).

Up to 3% of all breast cancers occur in women who carry inherited changes in genes *BRCA1* and *BRCA2*. These changes undermine the ability of the cell to repair damaged DNA. Because of their underlying defect in DNA repair, cancer cells with *BRCA* mutations are particularly vulnerable to treatments that target PARP, another key component of the cell's DNA repair machinery.

## DUAL TARGETED THERAPY LOWERS THE RISK OF INVASIVE BREAST CANCER IN SOME WOMEN

A clinical trial of nearly 5,000 women with early, human epidermal growth factor



receptor 2 (HER2)—positive breast cancer has suggested that adding a second HER2-targeted medicine, pertuzumab, to the standard regimen of the HER2-blocking therapy trastuzumab and chemotherapy may help some women.<sup>63</sup>

Recurrences were reduced by approximately one fifth in patients who received pertuzumab with trastuzumab after surgery compared with those who received trastuzumab and placebo. At 3 years, an estimated 94.1% of patients in the pertuzumab group were free of invasive breast cancer compared with 93.2% of patients in the placebo group. Addition of pertuzumab did not increase the rate of heart problems, which is the greatest concern with HER2-targeted therapy.

Treatment benefit was particularly evident in patients with breast cancer that

had spread to lymph nodes—an estimated 92% were free of invasive cancer compared with 90.2% of those who received placebo at 3 years. In contrast, in patients with node-negative cancer, pertuzumab did not improve invasive disease-free survival.

These findings may set a new standard of care for some patients with node-positive, HER2-positive, hormone receptor-negative breast cancer who have a higher risk of developing invasive breast cancer. Meanwhile, researchers are trying to identify biomarkers that may help predict which groups of patients will benefit most from pertuzumab.

The good news from this trial is that patients with HER2-positive breast cancer—the group of patients that used to have the worst prognosis—are doing so well on trastuzumab alone.

## Teri Pollastro

At 43 years old, Teri received her second breast cancer diagnosis, though this time the cancer had spread to other parts of her body. "I had very little hope," she says.

Teri had two young daughters to raise, so she focused intently on finding new therapies that could treat metastatic cancer, trying different therapeutic approaches over the years. She is thankful that she had access to state-of-the-art treatments not available in many parts of the world, as well as innovative clinical trials evaluating vaccine therapy and stereotactic radiation.

Teri is grateful to cancer research for giving her more than 14 years with her family since her diagnosis.

"Without advances in cancer research, I would not have been able to raise my two daughters," says Teri, who celebrated her 25th wedding anniversary with her husband in November. "With the novel treatments I continue to receive, I am able to enjoy 'the good stuff' in life. Additionally, I am able to advocate for myself and those who cannot for more metastatic cancer research with the hope of finding cures."

**“ My wish is for every person with metastatic cancer to have treatments available that allow them to live a 'normal' life like me. ”**

Teri is a volunteer with the Seattle Cancer Care Alliance, MBC Alliance, Susan Komen Puget Sound, and Translational Breast Cancer Research Consortium. Teri (center) is pictured with her cancer care team, ASCO members (from left to right) Sasha Stanton, MD, PhD, Julie Gralow, MD, FASCO, and Ray Yeung, MD, as well as Denise Bundow (second from right).

## Research Supports Extended Hormone Therapy for Patients With Higher-Risk Breast Cancer

To lower the chance of cancer recurrence, many women with early-stage breast cancer receive hormone therapy after surgery. Until recently, the recommended standard duration of such therapy had been 5 years, but new research findings suggest that extending hormone therapy may benefit some patients.

In 2016, a large clinical trial found that, in women with hormone receptor–positive, early breast cancer who received the aromatase inhibitor letrozole for 10 years, breast cancer recurrences or new cancers in the opposite breast were reduced by approximately one third compared with women who received 5 years of aromatase inhibitor therapy.<sup>64</sup>

Later that year, an even larger trial

reported a similar (29%) reduction in the risk of breast cancer recurrence or cancer in the opposite breast for women who received 5 additional years of letrozole after 5 years of aromatase inhibitor therapy (this study was funded, in part, by a grant from the NCI).<sup>65</sup>

However, longer hormone therapy did not improve overall or disease-free survival—the primary end point of the study—and was accompanied by a small increase in the risk of blood clots. In late 2017, researchers reported on an improvement in disease-free survival for women who received extended aromatase inhibitor therapy after tamoxifen.<sup>66</sup> In that clinical trial, 5-year disease-free survival was 83% among women who received anastrozole for 6



years, and 79% among those who received it for 3 years; however, patients in the 6-year therapy group had more adverse effects, including joint and muscle pain.

Taken together, these findings support longer hormone therapy for women with early breast cancer who have a higher risk for recurrence on the basis of tumor features and patient-specific factors. Discussion of therapy duration should take into consideration the adverse effects the patient experienced during initial hormone therapy as well as ongoing health conditions.

If patients are carefully selected for extended hormone therapy, breast cancer mortality can be additionally reduced without overtreatment.

# Bevacizumab May Help Some Women With Ovarian Cancer Live Longer

Women with recurrent ovarian cancer have a short life expectancy and limited treatment options. In late 2016, the FDA approved a new regimen that improves their outlook—adding bevacizumab to standard platinum-based chemotherapy.

This was the first approval of a new treatment of platinum-sensitive ovarian cancer in more than a decade. Bevacizumab had been previously approved for the treatment of women with platinum-resistant ovarian cancer. For more information about

ovarian cancer, visit [Cancer.Net](http://Cancer.Net).

This new approval was based on a clinical trial in which women received standard chemotherapy alone or bevacizumab with standard paclitaxel plus carboplatin chemotherapy, followed by maintenance therapy with bevacizumab (this study was funded, in part, by a grant from the NCI).<sup>67</sup> Addition of bevacizumab significantly extended median time until cancer



worsening to 13.8 months compared with 10.4 months with chemotherapy alone.

Overall survival was also longer with bevacizumab than with chemotherapy alone (median, 42 months v 37 months), but this difference was not statistically significant; however, the rate of severe adverse effects was higher in the bevacizumab group (96%) than in the standard therapy group (86%), with high blood pressure and fatigue being the most common adverse effects with bevacizumab.

## A POLICY FOCUS:

# Learning More About Older Adults With Cancer

More than 60% of cancer diagnoses in the United States occur in people age  $\geq 65$  years—a population that will grow rapidly over the coming years. Whereas 70% of cancer deaths occur in older adults, and older adults make up the majority of survivors of cancer, the evidence base for treating this population is sparse. Older adults are under-represented in clinical trials, and trials designed specifically for older adults are rare.

ASCO and the FDA held a workshop in November 2017 to discuss ASCO's recommendations to improve the evidence base for treating older adults. ASCO is continuing to urge federal agencies and the cancer research community to increase the enrollment of older adults in clinical trials and use other strategies to collect evidence on this population of patients.



# New Maintenance Therapies Keep Recurrent Ovarian Cancer From Worsening

Maintenance therapy for ovarian cancer is critical because of the high rate of recurrence, despite initial response to standard platinum-based chemotherapy. In 2017, the FDA approved a new maintenance treatment, the PARP inhibitor olaparib, for women with recurrent ovarian cancer who responded to platinum-based chemotherapy.<sup>68</sup>

Approval was based on a clinical trial in which olaparib was demonstrated to markedly slow cancer growth.<sup>69</sup> Median time until cancer worsening was 19.1 months

with olaparib versus 5.1 months with placebo. The most common severe adverse effects of olaparib were anemia and fatigue.

Meanwhile, in a clinical trial of maintenance therapy with the PARP inhibitor rucaparib, the growth of platinum-sensitive, recurrent ovarian cancer was also slowed.<sup>70</sup> Overall, rucaparib delayed cancer worsening by approximately 5 months longer than placebo (10.8 months v 5.4 months, respectively).

Benefit was greatest among women with

*BRCA* mutations (median time until cancer worsening was 16.6 months with rucaparib v 5.4 months with placebo), as well as women with tumors that harbored defects in DNA repair machinery (median time until cancer worsening was 13.6 months with rucaparib v 5.4 months with placebo). The most common severe adverse effects of rucaparib were anemia and liver enzyme abnormalities. These findings have been submitted to the FDA for the approval of rucaparib in this setting.

## Kenneth Monarrez

“It has made the word ‘legacy’ mean something completely different to me now, because my family’s genetics can play a small role in finding a therapy.”



Kenneth is a father, coach, marathon runner, and manager of a small company. He was diagnosed with kidney cancer on New Year’s Day, 2013, and had a recurrence several years later.

Genetic testing revealed that Kenneth had a mutation in the *BAP1* gene, which left him with no proven treatment options. He now participates in clinical studies where researchers monitor his progress closely with scans every three months while working to develop new medicines that target this particular gene.

“By participating in research, you are taking a risk,” Kenneth says, “but serving a greater good.”

*Kenneth, pictured with his family, is a board member at the Gateway for Cancer Research.*

# Precision Medicine Helps People With Melanoma Live Longer

Whereas early-stage melanoma is curable with surgery, patients with stage III melanoma face a much higher chance of recurrence after surgery, and many ultimately die of metastatic disease. New findings suggest that a precision medicine approach that combines two targeted medicines can improve outcomes for a subset of patients.

The study was conducted in patients with tumors that harbored *BRAF* gene mutations, which occur in approximately 40% of all melanomas. *BRAF* mutations turn on a molecular pathway known as mitogen-activated protein kinase. Prior research has demonstrated that blocking this pathway with two medicines in combination—dabrafenib and trametinib—helps patients with metastatic, *BRAF*-mutated melanoma live longer (the FDA approved this regimen in 2014).

In 2017, researchers reported that the combination of dabrafenib and trametinib can also help patients with stage III melanoma by lowering the risk for recurrence after surgery.<sup>71</sup> Estimated 3-year



relapse-free survival rates were 58% with targeted therapy and 39% with placebo. Overall survival rates were 86% with targeted therapy versus 77% with placebo.

Combined targeted treatment was associated with a considerable rate of serious adverse effects (36%), including potentially fatal pneumonia. Overall, 26% of

patients had to stop treatment earlier than the planned 12-month duration as a result of adverse effects.

Currently, there is insufficient evidence to inform the most beneficial duration of adjuvant therapy for stage III melanoma. For more information about melanoma, visit [Cancer.Net](http://Cancer.Net).

# New Treatment Paradigms Help Men With Prostate Cancer Live Longer

## ADDING HORMONE THERAPY TO RADIATION BOOSTS THE LONG-TERM SURVIVAL RATE

More than 30% of men who receive surgery for localized prostate cancer experience a recurrence of cancer. Patients who experience a local recurrence after surgery receive radiation therapy, but despite the therapy, the cancer eventually worsens in up to 50% of men. For more information about prostate cancer, visit Cancer.Net.

A recent large clinical trial found that adding androgen-deprivation therapy to radiation therapy helps men, who experience a local recurrence after surgery, live longer (this study was funded, in part, by a grant from the NCI).<sup>72</sup>



The study enrolled men with prostate-specific antigen (PSA) levels between 0.2 ng/mL to 4 ng/mL at least 8 weeks after surgery. Men were randomly assigned to receive androgen-deprivation therapy bicalutamide during and 24 months after radiation therapy or radiation therapy and placebo.

Survival rate at 12 years was 76% in the bicalutamide group versus 71% in the placebo group. More men in the placebo

group developed metastatic prostate cancer (23% v 14%, respectively) and more died of the disease (13% v 6%, respectively). Late effects of radiotherapy were similar between groups, but gynecomastia (swelling of breast tissue) was much more common with bicalutamide, occurring in 70% of men compared with 11% of those who received placebo.

Whereas other clinical trials are investigating the use of newer hormonal therapies with radiation therapy after prostate cancer surgery (ClinicalTrials.gov identifiers: NCT00541047 and NCT00423475), these findings provide strong evidence to support the combination of androgen-deprivation therapy with radiation therapy for men who experience a local recurrence after surgery.

## A NEW STANDARD OF CARE FOR ADVANCED PROSTATE CANCER

Two large studies presented in 2017 demonstrated that adding abiraterone to standard androgen-deprivation therapy helps men with metastatic prostate cancer live longer. Whereas androgen-deprivation therapy slows prostate cancer growth by preventing the testicles from making testosterone, certain other organs in the body continue making small amounts of

testosterone and other androgens.

Abiraterone stops the production of both testosterone and other androgens throughout the body by blocking an enzyme that converts other hormones to androgens.

In the first study, patients with high-risk metastatic prostate cancer were randomly assigned to receive androgen-deprivation therapy with either abiraterone or placebo.<sup>73</sup> At a median follow-up of 30 months, men who received abiraterone had a 38% lower risk of death than did those who received placebo. Abiraterone also more than doubled the median time until cancer worsening from 15 months to 33 months.

The second study, which included men with high-risk, locally advanced or metastatic prostate cancer, found that patients who received abiraterone with standard androgen-deprivation therapy had a 37% lower risk of death than those who received androgen-deprivation therapy alone.<sup>74</sup> The 3-year survival rate was 76% with standard therapy alone and 83% with standard therapy plus abiraterone.

Taken together, these findings define a new standard of care for men with metastatic prostate cancer.

## A POLICY FOCUS:

# Promoting Patient Participation in Clinical Trials

Clinical trials are critical for the advancement of new cancer treatments, but only a small percentage of patients (< 3%) in the United States participate in clinical trials.<sup>57</sup>

In clinical trials, eligibility criteria define the trial population and protect the safety of trial participants, particularly those who may be more vulnerable to the adverse effects of treatment in a clinical trial; however, overly restrictive eligibility

criteria can make trial findings more difficult to apply to the treatment of real-world patients with cancer.

ASCO, in collaboration with the nonprofit advocacy organization, Friends of Cancer Research, issued a joint research statement calling for the use of more inclusive eligibility criteria for cancer clinical trials. The statement, published in the *Journal of Clinical Oncology*, provides recommendations

to address eligibility criteria in five areas: minimum age requirements for trial enrollment, patients with HIV/AIDS, patients with brain metastases, patients experiencing organ dysfunction, and patients with prior and concurrent malignancies.

ASCO is working with the FDA and clinical trial sponsors to identify additional opportunities to safely expand eligibility criteria for oncology trials.

# Research Informs Decision Making for Early Prostate Cancer Treatment

Men with early (localized) prostate cancer can choose one of three standard treatments, which include surgery, radiation therapy, or active surveillance. A recent clinical trial found no significant differences in 10-year survival with any approach, although active surveillance was associated with a higher risk of cancer worsening and metastasis.<sup>75</sup>

A subsequent analysis of patient-reported outcome data from the same clinical trial showed that adverse effects differed among the three approaches.<sup>76</sup>

Surgery had a greater negative impact on sexual function and urinary continence than either radiation therapy or active surveillance. In the active surveillance

group, sexual and urinary function declined gradually. Bowel function problems were worse in the radiotherapy group than in the other two groups at 6 months, but subsequently recovered somewhat.

There were no significant differences among the treatment groups in anxiety, depression, or general health-related or cancer-related quality of life.

Another clinical trial that compared surgery with active surveillance found that men who received surgery had more sexual dysfunction and urinary incontinence through 10 years than did those who received active surveillance (this study was funded, in part, by grants from the US Department of Veterans Affairs, the Agency

for Healthcare Quality and Research, and the NCI).<sup>77</sup>

Limitations in activities of daily living through 2 years were also greater in the surgery group. In addition, two large, population-based studies that observed men with localized prostate cancer for 3 years also found that patterns of adverse effects differed depending on the type of treatment men received.<sup>78,79</sup>

Taken together, these findings from clinical trial participants as well as real-world patients will help clinicians better counsel patients about the risks and benefits of various treatments for localized prostate cancer.



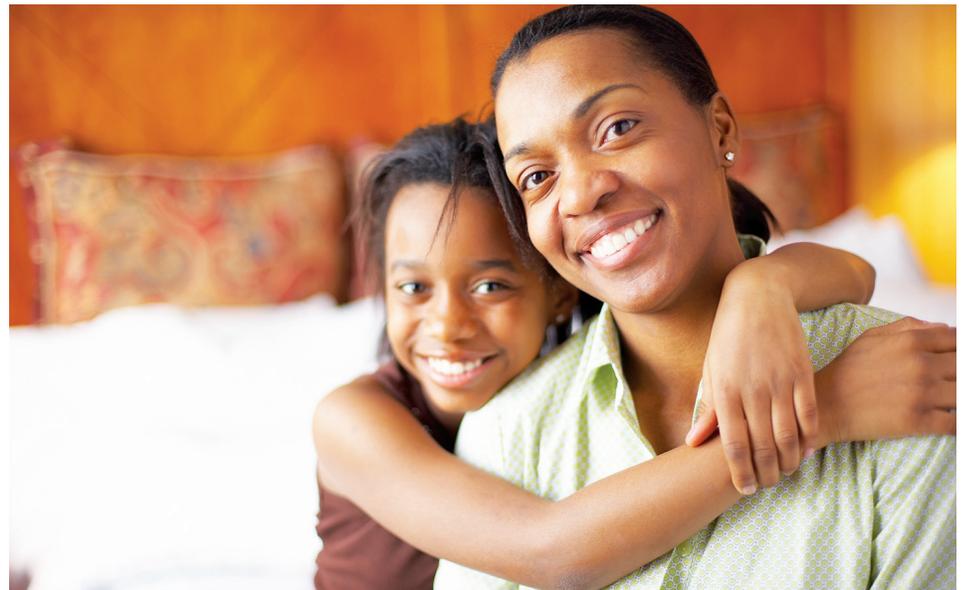
## Less Is More: Preserving Quality of Life With Less Treatment

### SHORTER CHEMOTHERAPY FOR COLON CANCER IS SAFE AND LOWERS THE CHANCE OF NERVE DAMAGE

For patients with stage III colon cancer, administering chemotherapy after surgery (adjuvant chemotherapy) lowers the chance that the cancer will come back. The standard 6-month course of adjuvant oxaliplatin-based chemotherapy can cause peripheral neuropathy.

Symptoms of this condition, which include pain, tingling, numbness, and muscle weakness, sometimes persist indefinitely. Longer chemotherapy also typically means more diarrhea and fatigue, more doctor appointments, blood draws, and time away from work and social gatherings.

Six clinical trials with 12,800 patients in North America, Europe, and Japan explored whether adjuvant chemotherapy regimens that consisted of either FOLFOX (infusional fluorouracil, leucovorin, and oxaliplatin)



or CAPOX (capecitabine and oxaliplatin) could be shortened to 3 months without compromising survival. In 2017, researchers reported on the analysis of pooled data



from the trials (this study was funded, in part, by a grant from the NCI).<sup>80</sup>

The chance of being free from colon cancer at 3 years was only slightly lower with 3 months of chemotherapy than with

6 months (74.6% v 75.5%, respectively). For patients with a lower risk of cancer recurrence (T1 to T3 N1 colon cancer), the chance of being cancer free at 3 years was nearly identical between the two groups—83.1% in those who received a 3-month course and 83.3% in patients who received a 6-month course.

The rate of clinically meaningful nerve damage differed depending on the type of chemotherapy regimen received, but was consistently lower for people who received 3 months versus 6 months of chemotherapy (15% v 45% with FOLFOX and 17% v 48% with CAPOX, respectively).

These findings, relevant to approximately 400,000 patients with stage III colon cancer worldwide, should inform conversations between oncologists and their patients. For patients with lower-risk stage III colon cancer, the shorter 3-month course will likely become the new standard of care.

For patients with higher-risk cancer, decisions on shorter-duration therapy will have to be carefully weighed against the risks of recurrence, patient ability to tolerate chemotherapy, and patient preferences. For more information about colon cancer, visit Cancer.Net.

#### LESS EXTENSIVE SURGERY FOR MELANOMA SPARES PATIENTS COMPLICATIONS

Many patients with intermediate-thickness melanomas (1.2 mm to 3.5 mm) routinely receive sentinel lymph node biopsy, a procedure that removes the first



lymph node to which cancer cells are likely to spread. The lymph node is then checked for cancer. If cancer cells are found in this sentinel node, the patient is more likely to experience a recurrence of melanoma after surgery.

To lower the chances of recurrence in patients with cancer in sentinel nodes, removal of the remaining lymph nodes near the tumor is usually recommended; however, this more extensive surgery increases the risk for complications, particularly long-term swelling of an arm or leg from the build-up of lymph fluid in tissues, known as lymphedema. Experts have therefore questioned the value of this surgical procedure in patients with positive sentinel lymph nodes.

A large clinical trial reported in 2017 suggests that the removal of additional lymph nodes may not be necessary (this study was funded, in part, by a grant from the NCI).<sup>81</sup>



At 3 years, the rate of melanoma-specific survival (the percentage of people who had not died of melanoma) was the same (86%) whether patients received additional surgery to remove lymph nodes or were only observed. Patients who received additional surgery had a lower risk of regional recurrence, but also had more health complications. The rate of lymphedema was four times higher in the surgery group than in the observation group (24% v 6%, respectively). Given that lymph node surgery does not improve survival, it may be possible to avoid this treatment in many patients and spare them an additional surgery with its associated complications.

#### FEWER WOMEN HAVING ADDITIONAL BREAST SURGERY AFTER LUMPECTOMY

Performing a second surgery after initial lumpectomy for early breast cancer was previously common. Second surgery was often recommended as a result of positive or close margins, which means that some cancer cells were found along the edge of the cancer tissue removed by lumpectomy;

### A POLICY FOCUS:

## Streamlining Adverse Events Reporting for Cancer Clinical Trials

Regulations require research sponsors to report certain serious adverse events experienced by patients in a clinical trial to the FDA via an expedited process.

The current challenge with reporting is the high volume of uninformative reports, which hinders patient safety,

imposes a substantial toll on the FDA, research site time, and resources.

In March 2017, ASCO held a workshop on streamlining adverse events reporting. Attended by stakeholders from across the cancer research community, including researchers, industry representatives,

patient advocates, and officials from the FDA and the NCI, the workshop participants discussed ways to decrease over-reporting as well as best practices for adverse events reporting for both sponsors and research sites. Recommendations developed through this effort were published in late 2017 in the *Journal of Clinical Oncology*.

however, there has been controversy over what constitutes a negative margin.

In 2014, the Society of Surgical Oncology and the American Society of Radiation Oncology published an evidence-based consensus statement, endorsed by ASCO, that recommended that if there are no cancer cells adjacent to any inked edge/surface of the surgical specimen, the margins should be considered negative and a second surgery is not required.<sup>82</sup>

A recent large, population-based study assessed the effect of this recommendation on the rates of breast cancer surgery (this study was funded, in part, by a grant from the NCI).<sup>83</sup> From 2013 to 2015, the rate of initial lumpectomy remained stable at 67%, but the rate of second breast surgery declined by 16%, and fewer women underwent a subsequent mastectomy. This study demonstrates the important role of clinical practice guidelines in reducing overtreatment.



#### DELAYING RECTAL CANCER SURGERY LOWERS THE RISK OF COMPLICATION

Radiation therapy before surgery lowers the risk of local recurrence in patients with rectal cancer. In the past, it was considered important to perform surgery soon after the completion of radiation therapy, but a new study in Sweden found that delaying

surgery by a few weeks is safe and results in fewer complications.<sup>84</sup>

There was no difference in local recurrence between patients who received the standard short-course radiation therapy with surgery within 1 week and those who received surgery 4 weeks to 8 weeks after either short-course radiation or long-course radiation therapy. Patients who received short-course radiation therapy with delayed surgery had a nearly 40% lower risk of complications after surgery than those who received standard short-course radiation without a delay in surgery.

Although common in Europe, short-course radiation therapy before surgery is not used in the United States, where the standard approach is chemotherapy and radiation. An ongoing clinical trial is exploring whether radiation therapy can be eliminated from the treatment of high-risk, locally advanced rectal cancer (ClinicalTrials.gov identifier: NCT01515787).

#### LOWERING RADIATION THERAPY DOSE FOR THROAT CANCER REDUCES LONG-TERM COMPLICATIONS

HPV-associated oropharyngeal cancer responds well to treatment, but the standard radiation therapy administered with chemotherapy can lead to debilitating long-term complications. As patients with HPV-associated oropharyngeal cancer tend to be younger, they may carry the burden of

these complications for decades.

Two separate clinical trials found that lowering the standard radiation dose by 15% to 20% in patients with a favorable prognosis (ie, a complete clinical response is achieved with initial chemotherapy) does not compromise survival. In the first study, the 2-year survival rate was 94% for patients who were treated with 54 Gy and 96% for those who received 54 Gy or less, and adverse effects were milder with the lower dose (this study was supported, in part, by grants from the NCI and the US Department of Health and Human Services).<sup>85</sup>



At 12 months, markedly fewer patients in the lower-dose group had difficulty swallowing solids (40% v 89%, respectively) or impaired nutrition (10% v 44%, respectively) compared with patients who received higher doses of treatment. In the second study, where patients with a more favorable prognosis received a dose of 54 Gy and others received 60 Gy, cancer had not worsened for 92% of patients overall at 2 years.<sup>86</sup>

If confirmed in a larger clinical trial, these findings will lead to a change in the standard of care for patients with lower-risk, HPV-related oropharyngeal cancer (eg, those with a minimal smoking history and small tumor size). For more information about oropharyngeal cancer, visit Cancer.Net.



“Cancer research saved my life and is allowing me to watch my family grow up.”

#### VOICES OF CANCER RESEARCH

### T.J. Sharpe

T.J. was 37 years old, and his newborn son only four weeks old, when he was diagnosed with advanced melanoma.

Since then, T.J. has participated in more than one clinical trial. In one study, he was the first patient ever to receive a new combination of immunotherapies for melanoma. When that treatment stopped working, he enrolled in a second trial of a different immunotherapy. Thanks to this trial, five years since his diagnosis, T.J. has no detectable signs of cancer.

“Without patients willing to participate in clinical trials, the pace of drug development, and its life-improving, life-extending, and live-saving results, slows to a trickle,” T.J. says. T.J. is pictured with his oncologist, ASCO member Ena Segota, MD.

# Recent ASCO Clinical Practice Guidelines

Clinical practice guidelines help to distill knowledge about a particular clinical issue and provide recommendations to help clinicians deliver the best treatment and care to every patient. ASCO develops its clinical practice guidelines through a

rigorous, systematic review of relevant medical literature and clinical interpretation from a multidisciplinary panel of experts and patient representatives. In 2017, the ASCO issued more than 14 clinical practice guidelines, guideline updates, and

provisional clinical opinions (Table 3). To view ASCO guidance by clinical area, visit <https://www.asco.org/practice-guidelines/quality-guidelines/guidelines>.

**Table 3.** ASCO Clinical Practice Guidelines, Updates, Endorsements, and Provisional Clinical Opinions from January to October 2017

PUBLICATION DATE	GUIDELINE
<b>Guideline</b>	
January 17	Management of Small Renal Masses: American Society of Clinical Oncology Clinical Practice Guideline Summary
January 30	Screening to Prevent Invasive Cervical Cancer: ASCO Resource-Stratified Clinical Practice Guideline
February 6	Molecular Biomarkers for the Evaluation of Colorectal Cancer: Guideline From the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and the American Society of Clinical Oncology
March 6	Use of Adjuvant Bisphosphonates and Other Bone-Modifying Agents in Breast Cancer: A Cancer Care Ontario and American Society of Clinical Oncology Clinical Practice Guideline
March 17	Primary Prevention of Cervical Cancer: American Society of Clinical Oncology Resource-Stratified Guideline
August 10	Treatment of Nonmetastatic Muscle-Invasive Bladder Cancer: American Urological Association/American Society of Clinical Oncology/American Society for Radiation Oncology/Society of Urologic Oncology Clinical Practice Guideline
September 11	Patient-Clinician Communication: American Society of Clinical Oncology Consensus Guideline
<b>Guideline update</b>	
March 27	Brachytherapy for Patients With Prostate Cancer: American Society of Clinical Oncology/Cancer Care Ontario Joint Guideline Update
April 11	Potentially Curable Pancreatic Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update
April 24	Adjuvant Systemic Therapy and Adjuvant Radiation Therapy for Stages I to IIIA Resectable Non–Small-Cell Lung Cancers: American Society of Clinical Oncology/Cancer Care Ontario Clinical Practice Guideline Update
July 10	Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy for Women With Early-Stage Invasive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline Focused Update
July 31	Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update
August 14	Systemic Therapy for Stage IV Non–Small-Cell Lung Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update
<b>Guideline endorsement</b>	
February 27	Head and Neck Cancer Survivorship Care Guideline: American Society of Clinical Oncology Clinical Practice Guideline Endorsement of the American Cancer Society Guideline
April 25	Second-Line Hormonal Therapy for Men With Chemotherapy-Naïve, Castration-Resistant Prostate Cancer: American Society of Clinical Oncology Provisional Clinical Opinion

For additional advances in cancer treatment, please see Appendix Table A2.

# Explore ASCO's Timeline of Major Advances in Cancer

ASCO's Cancer Progress Timeline provides a historical overview of major advances in cancer that have led to dramatic improvements in patients' survival and quality of life.

This interactive, data-rich resource chronicles more than **400 treatment and prevention advances spanning 170 years** – many of which were made possible by federal investments in cancer research. Recently relaunched with new milestones, the timeline details the history of advances in numerous cancers and types of care.

**1903**  
First use of radiation to treat cancer

**1965**  
Pioneering "combination chemotherapy" cures leukemia

**1970s**  
Less invasive surgery proven safe for early breast cancers

**2003**  
Scientists decode the human genome

**2017**  
First gene therapy for cancer

This badge indicates that a cancer advance has been supported at least in part by federal funding.

Examine key advances in cancer at [asco.org/cancer-progress](https://asco.org/cancer-progress).

# 4 Advances in Patient Care



## Communication and Coping Tools Improve End-of-Life Planning

Having accurate information about prognosis is crucial for patients with late-stage cancer. Having conversations about the end of life helps patients set appropriate goals and potentially avoid intensive medical treatments and hospital death.

However, many patients are misinformed about or misunderstand their prognosis, and others have difficulty coping with the realization that their illness is terminal. Recent research has focused on interventions and tools that may help overcome this gap in patient–doctor communication.

In one study, a communication coaching intervention helped patients with late-stage cancer actively seek information and express preferences about their care (this study was funded, in part, by a grant from the NCI).<sup>87</sup> Oncologists in the intervention group received brief, individualized, skill-based communication training that focused on being receptive to patient questions and concerns. Patients received individualized communication coaching that incorporated a list of questions related to cancer care and end-of-life issues. Oncologists and patients in the control group did not receive any communication training or prompting.



During a subsequent office visit, nearly three times as many patients in the intervention group than in the control group (17% v 6%, respectively) asked about prognosis, and more than twice as many (70% v 33%, respectively) brought up topics that were covered by the communication coaching, such as cancer treatment, current cancer state, and preferences about care at the end of life. Whereas validation of these results in other settings is necessary, they underscore the value of combined patient–doctor interventions to enhance communication.

New online tools are another way of helping patients plan for the end of life. In a recent study of elderly patients with chronic and/or serious conditions, 35% of those who used the interactive, patient-centered advance care planning Web site, PREPARE, along with an easy-to-read advance directive, succeeded in assembling advance planning documentation compared with 25% of those who used the advance directive alone (this study was funded by a grant from the US Department of Veterans Affairs Office of Research and Development).<sup>88</sup>



Given that the Web site used in this study is free to the public and requires no physician involvement, it represents a method of improving end-of-life care with minimal health care system resource expenditure.

Research shows that certain coping strategies can help patients with incurable cancer who accurately understand their diagnosis to be terminal (this study was funded, in part, by grants from the NIH, NCI, and the National Institute of Nursing Research).<sup>89</sup>



For example, patients who used positive reframing (ie, looking for something good in

their situation) and active coping (ie, taking action to try to make their situation better) had improved quality of life and less depression.

It is important that doctors communicate the availability of these tools and help patients both understand and cope with advanced cancer and a terminal prognosis. A new ASCO guideline provides oncologists with recommendations regarding core communication skills that apply across the continuum of cancer care, including discussion of goals of care and prognosis, treatment selection, and end-of-life care.<sup>90</sup> For more information on coping with cancer, visit Cancer.Net.

## CancerLinQ Partners With Federal Agencies and Medical Specialty Societies

In 2017, one of the main focus areas for CancerLinQ was partnering with federal agencies, professional societies, and life sciences companies. The goal of these collaborations was to convene the cancer community around solutions for improving the quality of care for patients with cancer.

By leveraging the expertise of the many stakeholders that span the care continuum, all of whom affect key decision points in a patient's care, we can help make CancerLinQ a system that encompasses all of cancer care. The effort was successful, with 10 collaborations formally signed and announced between June 2016 and June 2017 with

the following organizations:

- *American Academy of Physician Assistants*
- *American Society of Radiation Oncology*
- *Cancer Informatics for Cancer Centers*
- *College of American Pathologists*
- *US Food and Drug Administration*
- *Hematology/Oncology Pharmacy Association*
- *National Comprehensive Cancer Network*
- *National Cancer Institute*
- *Oncology Nursing Society*
- *Society of Gynecologic Oncology*

The organizations with which CancerLinQ has partnered are invited to participate in the CancerLinQ Oncology Leadership Council, the official body of strategic advisors that comprise member representatives from CancerLinQ's official partner organizations and advisory groups.

This is the first time that a coalition of this nature has been created and convened. As CancerLinQ creates this community of learning in cancer, these foundational partners offer incredible thought leadership and represent the importance of a team-based approach to delivering high-quality care.

## Rhonda Kokot

“ It’s important for people to know clinical trials are always an option and not just something to consider when all other options have been exhausted. ”



Rhonda was 29 years old when she was diagnosed with acute myeloid leukemia. She eventually needed a stem cell transplant and faced the possibility of major side effects, including life-threatening infections.

A clinical trial using umbilical cord blood for the transplant, however, spared Rhonda many of the expected toxicities. “Today, I live a pretty healthy life with no major side effects,” says Rhonda.

She credits the trial for keeping her alive. Since participating in the study, she has run several half marathons and volunteers her time in support of cancer research.

*Rhonda is a board member at the Gateway for Cancer Research.*

## Managing Common Adverse Effects and Complications

### RADIATION THERAPY FOR LUNG CANCER INCREASES THE RISK FOR HEART PROBLEMS

Radiation has been the backbone of treatment of stage III NSCLC for 3 decades. Despite the known harmful effects that chest radiation can have on the heart, patients with stage III NSCLC still receive high doses of radiation because it is believed that few live long enough to experience heart complications (life expectancy is less than 2 years). A pair of studies published in 2017 challenge this notion by showing that heart problems are relatively common in this patient population and occur earlier than historically understood.

In an analysis of patients who were treated in six clinical trials from 1996 to 2009, 21% of those who received a high dose of radiation ( $\geq 20$  Gy) developed symptomatic heart problems within 2 years (this study was funded by a grant from the NIH).<sup>91</sup> Heart problems were independently linked to high doses of radiation and underlying risk (eg, smoking and cardiovascular disease).



A second analysis of patients who were treated in four clinical trials from 2004 to



2013 demonstrated similar results; 11% developed severe heart problems within 2 years (this study was funded by a grant from the NIH).<sup>92</sup>



As in the other study, patients who received a higher radiation dose and/or had preexisting heart disease were more likely to develop heart problems. Furthermore, both cancer worsening and heart problems were linked to shorter survival.

These findings will inform treatment and survivorship discussions between physicians

and patients with stage III NSCLC. When selecting radiation dose, controlling tumor growth should be balanced with minimizing the risk for heart problems, particularly in patients with an underlying risk of heart disease.

A recent guideline from ASCO recommends that, before the start of therapy, doctors should discuss the potential for heart problems with patients who are at increased risk for such complications and establish a tailored and detailed plan to monitor them during and after cancer treatment.<sup>93</sup>

## SINGLE RADIATION TREATMENT RELIEVES SYMPTOMS OF SPINAL CORD COMPRESSION

As many as one in 10 people with advanced cancer develop spinal cord compression. This condition is a major detriment to quality of life, causing back pain, numbness, tingling, difficulty or inability to walk, and sometimes bowel or bladder incontinence. Radiation therapy can prevent or relieve these symptoms, but it typically requires multiple trips to the clinic for treatment.

Research presented in 2017 demonstrated that a single radiation treatment may be sufficient for patients with a short life expectancy.<sup>94</sup> In a large clinical trial, one-time radiation treatment was as effective as 5 days of treatment in terms of helping patients stay mobile, and median survival was not different between the two groups (approximately 3 months). Shortening radiation therapy allows patients with cancer-related spinal cord compression to spend less time in the hospital and more time doing things they enjoy.

## FOR CANCER-RELATED FATIGUE, EXERCISE AND PSYCHOLOGICAL SUPPORT WORK BEST

Cancer-related fatigue is different from feeling tired after staying up too late. It is a persistent feeling of physical, emotional, or mental exhaustion that interferes with one's daily activities and does not improve with rest. Most people who receive cancer treatment experience fatigue, and approximately one third of survivors of



cancer experience fatigue that lasts for years after finishing treatment.

Numerous approaches for treating cancer-related fatigue have been tested, with variable outcomes; therefore, it has not been clear which treatments work best. An analysis of 113 randomized clinical trials compared the four most commonly recommended treatments, which are exercise, psychological intervention, combined exercise and psychological intervention, and medication (this study was funded in part by grants from the NIH).<sup>95</sup>



Exercise, psychological support, and the combination of the two approaches improved cancer-related fatigue during and after cancer treatment. Benefits of these treatments were greater for patients

with nonmetastatic disease and varied by intervention mode and timing; however, medications were much less effective than behavioral interventions.

These findings confirm a large body of literature in the field and suggest that exercise and psychological interventions should be used before pharmaceutical interventions, which provide minimal benefit. These recommendations are relevant to many patients with cancer.

ASCO recommends that health care providers assess the patient's level of fatigue at diagnosis and repeat this assessment yearly and at any time there are symptoms of fatigue throughout treatment and into recovery.<sup>96</sup> For more information about cancer-related fatigue, visit Cancer.Net.

# ASCO Launches Center for Research and Analytics

In June 2017, ASCO announced the launch of its new Center for Research and Analytics (CENTRA) to make an array of cancer data available to the oncology community and provide consultation and support for research and analysis.

The CENTRA team will help analyze and build an evidence base that can help

to support cancer policy development, advance the practice of oncology, and improve cancer care for patients. This supports ASCO's continuing commitment to helping to advance the field of oncology and improve cancer care through the generation and application of high-quality evidence.

Requests can be made through

CENTRA for data from ASCO sources, such as our quality programs, annual census of oncology practices, and scientific meeting abstracts and presentations. All research requests will be evaluated before being fulfilled. For more information or to submit requests, please contact: [CENTRA@asco.org](mailto:CENTRA@asco.org).

## Andrew Schorr

Without clinical trials, says Andrew, "I think I would have died long ago."

Andrew was diagnosed at age 45 with chronic lymphocytic leukemia and then again at age 61 with myelofibrosis, a rare type of bone marrow cancer. He has participated in multiple clinical trials over the years, including a trial for a regimen that combines chemotherapy with a monoclonal antibody.

Today, Andrew is being treated for a recurrence of leukemia, but he says the treatment allows him to live a normal, active life. He feels grateful for the care he has received and the studies he has participated in.

*Andrew is the founder of Patient Empowerment Network and Patient Empowerment Foundation, as well as the co-founder of Patient Power.*



“ My participation helped me, and I know it has led to the approval of treatments that are now helping others. ”

# Patient Engagement Leads to Improved Care

## WEB-BASED SYMPTOM REPORTING EXTENDS SURVIVAL

The value of patients reporting their own outcomes is increasingly recognized in oncology, and there is interest in integrating patient-reported outcomes into routine practice. A recent study demonstrated that a Web-based, patient-reported outcomes tool can help patients with advanced cancer live longer.<sup>97</sup>

*The findings confirm that patient-reported outcomes should be the standard of care for patients with late-stage cancer.*

With the standard approach of assessing symptoms only during office visits, the health care team can be unaware of patients' symptoms up to half of the time. In a clinical trial, the Web-based tool enabled patients to report common symptoms in real time and triggered alerts to clinicians if symptoms worsened (this study was supported by ASCO's Conquer Cancer Foundation). When appropriate, clinicians took action to relieve symptoms,

such as lowering the chemotherapy dose or providing supportive care.

Patients with metastatic cancer who used the tool while receiving chemotherapy lived a median of 5 months longer than those who did not use the tool (31 months v 26 months, respectively). This improvement in survival was greater than that associated with nearly all cancer drugs that received FDA approval in 2016.

Researchers previously reported that the use of the same tool was associated with better quality of life and fewer visits to the emergency room and hospitalizations. The findings confirm that patient-reported outcomes should be the standard of care for patients with late-stage cancer. A nationwide clinical trial that uses an updated tool that works on both personal computers and mobile devices is under way in community practices across the United States.

## AFTER CANCER DIAGNOSIS, AN ONLINE SUPPORT PROGRAM LOWERS DISTRESS

Patients experience major distress when they first learn of their cancer

diagnosis. Yet amid all the tests, treatment appointments, and family or work decisions, little attention is paid to one's psychological and emotional well-being. In fact, as a result of patients' time constraints and the lack of availability and resources for psychological support, few patients who are newly diagnosed with cancer receive any psychological support.

To address this need, researchers are looking into leveraging Internet-based technologies to provide support to more patients and improve their quality of life. In a recent study, an 8-week Web-based stress management program that was designed by psychologists and oncologists, improved quality of life and lowered distress for patients who were newly diagnosed with cancer.<sup>98</sup>

The program covered different topics, such as bodily reaction to stress, cognitive stress reduction, feelings, and social interactions. For each weekly topic, participants received written and audio information, then completed exercises and questionnaires.

The study demonstrated that delivering



psychological support via an Internet-based program is feasible, but more research is needed to refine and scale up such an approach for broad use. Researchers already have plans to translate the program into other languages (it is currently available only in German).

### **CROWDSOURCING ADVANCES CANCER RESEARCH**

Progress against rare cancers is often slow because of a combination of scarce funding and a limited availability of patients and tumor samples for research. An attractive solution to this problem is crowdsourcing. More and more people with rare and common cancers today have the opportunity to rapidly and directly affect research by sharing their tumor tissue

samples and medical and/or genetic information to help others with the same or similar diseases. In return, researchers share what they learn with participants.

The Metastatic Breast Cancer Project collects health records and tumor and saliva samples to learn why some patients respond differently to cancer treatments than others. The project engages patients to participate via social media, newsletters, blogs, and advocacy organizations.

Two other such projects focused on sarcoma are run by researchers with the support of patient advocacy organizations, the Angiosarcoma Project and the Leiomyosarcoma Direct Research.

Another emerging type of crowdsourced

research engages members of the general public, so-called citizen scientists, to gather ideas, design studies, and perform research-related tasks, such as analysis of scientific images or quantitative data. This approach is particularly helpful in pathology research studies that require manual review of a large quantity of images. The Cell Slider project recruited approximately 100,000 people to classify images of breast tumor tissue according to estrogen receptor status. To assess the volunteers' performance, researchers compared their classification with that of trained pathologists and found that citizen scientists were able to classify tumors with high accuracy.<sup>99</sup>

For additional notable advances in patient care, please see Appendix Table A2.

# 5 Looking to the Future



## New Type of Medicine Tackles Undruggable Molecular Targets

Although targeted therapies have had a profound effect on cancer medicine, only about 20% of proteins in cancer cells can be targeted by currently available medicines.

Many of the undruggable targets include important molecules in pathways that suppress (eg, TP53 and APC) or promote tumor growth (eg, RAS and MYC). One of the reasons these targets are undruggable is that, historically, it has been difficult to block these pathways with small molecules—meaning protein drugs do not easily penetrate the cell.

A new class of drugs, known as stapled peptides, has emerged as a promising way to target protein-protein interactions. These small proteins have an artificial chemical bridge, or staple, that holds them in a specific shape that allows them to penetrate the cell.

In an early clinical trial, researchers demonstrated for the first time that a stapled peptide is effective in patients.<sup>100</sup> The peptide targeted the interaction between MDM2 and MDMX-TP53 in patients with solid tumors and lymphoma without p53 mutations. The treatment, ALRN-6924, stalled cancer growth in 45% of 55 patients. A larger clinical trial is under way (ClinicalTrials.gov identifier: NCT02264613).

# Emerging Role for Precision Medicine in Cancer Prevention

The concept of precision medicine as applied to cancer prevention is in its nascent stages. In this first phase, scientists are focusing on inherited cancer syndromes, such as BRCA-related breast and ovarian cancers and Lynch syndrome.

For patients with inherited genetic susceptibility to cancer, the hope is to one day replace crude, one-size-fits all cancer risk reduction approaches, such as preventive surgery, with personalized approaches that take into account not only a person's genetic makeup and family history, but also the composition of microbes in their body, their diet, lifestyle, and environmental factors.<sup>101</sup>

Scientists are only beginning to

understand how the complex interplay of all these factors raises or lowers the chance of developing cancer in an individual with an inherited cancer gene mutation. It is also not clear why changes in genes with broad functions, such as the DNA repair and MMR genes, predispose people for certain, but not all cancers.

Large-scale genomics studies are providing insights by which to fine-tune cancer risk assessment for each person. For example, it seems that certain changes in mitochondrial DNA lower the risk of breast cancer in patients with BRCA mutations. Genomic information, along with reproductive and family history, lifestyle, and other factors, may help

patients decide whether and when to have preventive surgery.

Scientists are also exploring the possibility of using immune-based approaches, such as vaccines for cancer prevention in healthy people with cancer predisposition syndromes.<sup>102</sup>

The idea is to harness the immune system to recognize and eliminate premalignant cells on the basis of their molecular characteristics. With the new national investment in cancer prevention through the Cancer Moonshot initiative and cutting-edge technologies, such as sequencing the genomes of individual cells, the opportunity to advance this field is closer than ever.

## Impact of Cancer Care Cost

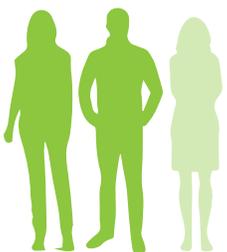
More than one fourth (27%) of Americans who either had cancer themselves or have/had a family member with cancer have taken specific actions to lower treatment costs:

### CONCERNS ABOUT COST OF CARE

**91%** 

of Americans say the cost of cancer drugs is too high.

Among those responsible for paying for a loved one's cancer treatment,

**68%** 

are concerned about cost.

**One in four Americans** who have direct experience with cancer say they or a loved one have taken actions to reduce costs that could **jeopardize the effectiveness of their treatment.**



**9%** skipped **doctor appointments**

**8%** refused **treatment**

**8%** postponed **filling or did not fill prescriptions**

**8%** skipped doses of **prescribed medications**

**7%** cut pills **in half**

(ASCO's National Cancer Opinion Survey, 2017).

# Understanding Health Disparities: The Path to Better Care For All

Cancer is becoming one of the most pressing health care challenges worldwide. Between 2005 and 2015, the number of patients with cancer increased worldwide by 33%.<sup>103</sup> According to the Global Burden of Disease study, issued in late 2017, cancer is the second leading cause of death among noncommunicable diseases, which cause 72% of deaths worldwide.<sup>25</sup>

Whereas many countries have experienced drops in cancer mortality over the last decade, cancer deaths increased in Sub-Saharan Africa and certain other regions lacking in health care infrastructure (this study was funded in part by a grant from the NIH).<sup>103</sup> Seven of 10 cancer deaths occur in regions of Africa, Asia, and Central and South America, where access to cancer screening and treatment is limited in certain areas.<sup>104</sup>



Even within high-resource countries, such as the United States, certain communities experience greater cancer incidence, shorter survival, and more deaths from cancer. During the last 60 years, socioeconomic, education, and racial/ethnic inequities in cancer mortality have persisted and even widened in some cases.<sup>105</sup>

Recently published studies reveal that

the root causes of cancer disparities in the United States are complex. Researchers found that black patients across all socioeconomic groups have higher cancer mortality than white patients. Another study found that people from the poorest communities were more likely to be diagnosed with advanced cancer, regardless of whether they had health insurance.

In addition, patterns of disparity have been changing. For example, during the 1950s, black people had lower all-cancer mortality than did white people, but since the 1960s, all-cancer mortality rates have been significantly higher for black people than for white people across all socioeconomic groups.

Differences are particularly pronounced for some cancers. Within each

## A POLICY FOCUS:

### Giving Medicaid Patients Equal Access to Clinical Trials

Most private insurance plans and Medicare are required to cover the routine costs of care for patients who participate in clinical trials.

Routine care includes items and services that a payer would cover for a patient who is not enrolled in a clinical trial, such as office visits, radiology exams, and laboratory tests; however,

Medicaid is not required to cover these routine costs for patients.

For researchers to understand how different populations respond to cancer treatment and address disparities in cancer outcomes, all types of patients should have the opportunity to participate in cancer trials. Unfortunately, patients from racial and ethnic minority

groups that are over-represented in the Medicaid program make up just a small subset of clinical trial participants.

ASCO strongly encourages policymakers to guarantee that Medicaid covers routine care costs for patients in clinical trials so that more patients with Medicaid can participate in cancer research.

socioeconomic group, black women have a two times higher cervical cancer mortality rate and 50% higher breast cancer mortality rate than white women, and black men have a two times higher prostate cancer mortality rate than white men.<sup>105</sup>

Socioeconomic disparities have also reversed over time. In 1950, people in the most-deprived socioeconomic group had a 27% lower cancer mortality rate than those in the most affluent group, but by 2010 to 2014, the most deprived group had a 22% higher cancer mortality than their most affluent counterparts.<sup>105</sup>

Although patients from disadvantaged communities benefit most from health insurance coverage, insurance alone does not overcome the mortality gap. In one study, patients in the poorest communities were more likely to have advanced cancer at diagnosis and less likely to receive cancer-directed surgery than those from the least disadvantaged communities, regardless of health insurance status (this study was funded in part by a grant from the NIH/NCI).<sup>106</sup>



Another analysis demonstrated

that among people with no health insurance, black patients had rates of cancer mortality that were similar to those of white patients, but had higher mortality rates among either Medicaid or private insurance groups.<sup>107</sup>

Even with access to health care, patients may not seek care for many reasons that include having insurance but health care is not available nearby, not knowing how to access the health care system, or lack of trust in the health care system. Other research suggests that socioeconomic disparities in cancer death rates may, in part, be a result of modifiable behaviors that increase the risk of cancer.

The 2015 National Health Index Survey showed that prevalence of smoking, obesity, physical inactivity, and inadequate intake of fruit and vegetables was higher among people with lower education and income levels, and rates of cancer screening were lower.

Taken together, this body of research suggests that addressing cancer disparities and achieving equity calls for multifaceted approaches that are focused on efforts to improve prevention, screening, and access to high-quality cancer care.

## A POLICY FOCUS: Addressing Health Disparities in Cancer Care

Significant cancer health disparities continue to exist in certain populations. Race, ethnicity, socioeconomic status, and geography all affect patient health outcomes, and racial and ethnic minorities and individuals of lower socioeconomic status experience worse cancer outcomes.

To address this issue, ASCO, with the American Association for Cancer Research, the American Cancer Society, and the NCI, released a joint statement to foster cooperation across the cancer research community to ensure that all patients, regardless of demographics, socioeconomic status, or the communities in which they live, benefit from cancer research (the statement was published in the *Journal of Clinical Oncology*<sup>108</sup>).

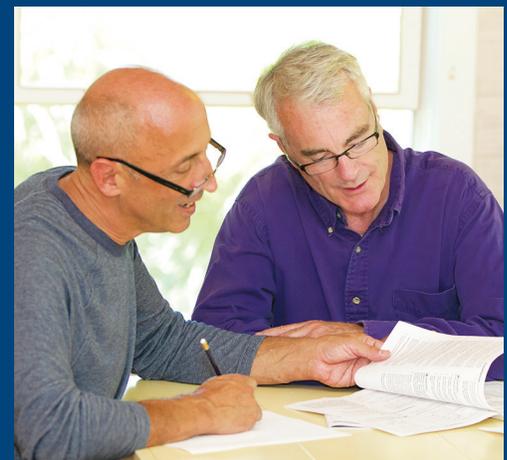
The statement called for defining and improving data measures and tools for cancer disparities research, addressing disparities in cancer incidence, addressing cancer survival disparities, improving community engagement in cancer research, and redesigning clinical trials to acknowledge and address cancer disparities.

## ASCO Issues Recommendations for Reducing Cancer Disparities Among Sexual and Gender Minority Populations

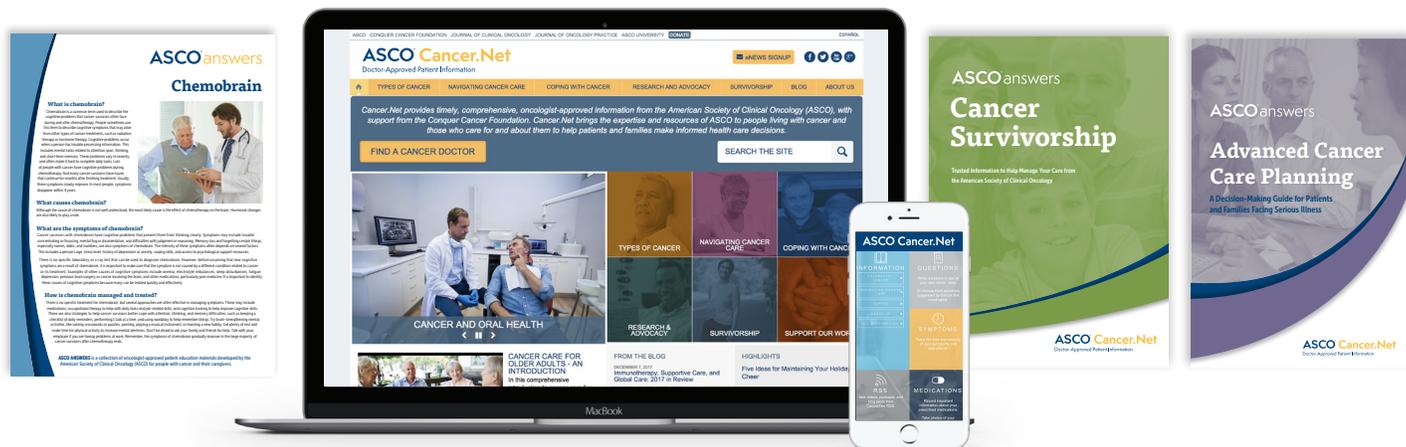
Sexual and gender minority (SGM) populations, including individuals who are lesbian, gay, bisexual, transgender, and intersex, bear a disproportionate cancer burden that stems from several factors, such as lower rates of cancer screening and a hesitancy on the part of SGM patients to disclose their sexual orientation to providers because of a fear of stigmatization.

ASCO issued recommendations to address the needs of SGM

populations as they relate to cancer.<sup>109</sup> The recommendations, published in a policy statement in the *Journal of Clinical Oncology*, are designed to focus attention on the challenges that face the SGM community, including discrimination and greater risk of anxiety and depression, resulting in disparate care. The statement also provides concrete steps that can help minimize health disparities among SGM individuals.



# ASCO Resources for Patients



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**Table A1.** FDA Approvals of Cancer Therapies From November 1, 2016, to October 31, 2017

DRUG	INDICATION	APPROVAL DATE
<b>New approval</b>		
Rucaparib (Rubraca)	For treatment of patients with deleterious <i>BRCA</i> mutation (germline and/or somatic)–associated advanced ovarian cancer who have been treated with two or more chemotherapies.	December 2016
Avelumab (Bavencio)	For the treatment of patients $\geq 12$ years of age with metastatic Merkel cell carcinoma. Avelumab is a PD-L1 blocking human immunoglobulin G1 $\lambda$ monoclonal antibody. This is the first FDA-approved product to treat this type of cancer.	March 2017
Niraparib (Zejula)	Maintenance treatment for adult patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to platinum-based chemotherapy.	March 2017
Ribociclib (Kisqali)	In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer.	March 2017
Brigatinib (Alunbrig)	For treatment of patients with metastatic anaplastic lymphoma kinase–positive NSCLC who experienced disease progression on or who are intolerant to crizotinib.	April 2017
Midostaurin (Rydapt)	For treatment of adult patients with newly diagnosed AML who are FLT3 mutation–positive, as detected by an FDA-approved test, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation.	April 2017
Durvalumab (Imfinzi)	For treatment of patients with locally advanced or metastatic urothelial carcinoma who experience disease progression during or after platinum-containing chemotherapy or who experience disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.	May 2017
Rituximab and hyaluronidase human (Rituxan Hycela)	For adult patients with follicular lymphoma, diffuse large B-cell lymphoma, and chronic lymphocytic leukemia.	June 2017
Neratinib (Nerlynx)	For extended adjuvant treatment of adult patients with early-stage HER2-overexpressed/amplified breast cancer, to follow adjuvant trastuzumab-based therapy.	July 2017
Daunorubicin and cytarabine (Vyxeos)	For treatment of adults with newly diagnosed therapy-related AML or AML with myelodysplasia-related changes, two types of AML that have a poor prognosis.	August 2017
Enasidenib (Idhifa)	For treatment of adult patients with relapsed or refractory AML with an isocitrate dehydrogenase-2 mutation as detected by an FDA-approved test.	August 2017
Inotuzumab ozogamicin (Besponsa)	For treatment of adults with relapsed or refractory B-cell precursor ALL.	August 2017
Tisagenlecleucel (Kymriah)	For treatment of patients $\leq 25$ years of age with B-cell precursor ALL that is refractory or in second or later relapse.	August 2017
Abemaciclib (Verzenio)	In combination with fulvestrant for women with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression after endocrine therapy.	September 2017
Bevacizumab-awwb (Mvasi)	Approved as a biosimilar to bevacizumab (Avastin), bevacizumab-awwb is the first biosimilar approved in the United States for the treatment of cancer.	September 2017

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; EGFR, epidermal growth factor receptor; FDA, US Food and Drug Administration; HCC, hepatocellular carcinoma; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; NSCLC, non–small-cell lung cancer; PD-L1, programmed death-ligand 1.

Table A1 cont.

DRUG	INDICATION	APPROVAL DATE
Copanlisib (Aliqopa)	For treatment of adult patients with relapsed follicular lymphoma who have received at least two prior systemic therapies.	September 2017
Gemtuzumab ozogamicin (Mylotarg)	Newly diagnosed CD33-positive AML in adults and for treatment of relapsed or refractory CD33-positive AML in adults and pediatric patients $\geq 2$ years of age. May be used in combination with daunorubicin and cytarabine for adults with newly diagnosed AML or as a stand-alone treatment of certain adult and pediatric patients.	September 2017
Axicabtagene ciloleucel (Yescarta)	For treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy.	October 2017
<b>New use</b>		
Daratumumab (Darzalex)	In combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy.	November 2016
Nivolumab (Opdivo)	Recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after a platinum-based therapy.	November 2016
Lenalidomide (Revlimid)	Maintenance therapy for patients with multiple myeloma after autologous stem-cell transplantation.	February 2017
Nivolumab (Opdivo)	For treatment of patients with locally advanced or metastatic urothelial carcinoma who experience disease progression during or after platinum-containing chemotherapy or experience disease progression within 12 months of neoadjuvant or adjuvant treatment with a platinum-containing chemotherapy.	February 2017
Osimertinib (Tagrisso)	For treatment of patients with metastatic EGFR T790M mutation-positive NSCLC, as detected by an FDA-approved test, who experienced disease progression on or after EGFR tyrosine kinase inhibitor therapy.	March 2017
Palbociclib (Ibrance)	HR-positive, HER2-negative advanced or metastatic breast cancer in combination with an aromatase inhibitor as initial endocrine-based therapy in postmenopausal women.	March 2017
Pembrolizumab (Keytruda)	For treatment of adult and pediatric patients with refractory classic Hodgkin lymphoma or those who have experienced relapse after three or more prior lines of therapy.	March 2017
Regorafenib (Stivarga)	For treatment of patients with HCC who have been previously treated with sorafenib.	April 2017
Avelumab (Bavencio)	For patients with locally advanced or metastatic urothelial carcinoma who experienced disease progression during or after platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.	March 2017
Pembrolizumab (Keytruda)	In combination with pemetrexed and carboplatin for treatment of patients with previously untreated metastatic nonsquamous NSCLC.	May 2017
Pembrolizumab (Keytruda)	For patients with locally advanced or metastatic urothelial carcinoma who experience disease progression during or after platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.	May 2017
Nivolumab (Opdivo)	For treatment of HCC in patients who have been previously treated with sorafenib.	September 2017
Pembrolizumab (Keytruda)	For patients with recurrent locally advanced or metastatic, gastric, or gastroesophageal junction adenocarcinoma whose tumors express PD-L1 as determined by an FDA-approved test.	September 2017

**Table A2.** Additional Notable Advances (October 2016 to October 2017)

AREA OF RESEARCH	STUDY TITLE	REFERENCE
Screening	Analysis of plasma Epstein-Barr virus DNA to screen for nasopharyngeal cancer	Chan KCA, et al: <i>N Engl J Med</i> 377:513-522, 2017
Treatment	Blinatumomab versus chemotherapy for advanced acute lymphoblastic leukemia	Kantarjian H, et al: <i>N Engl J Med</i> 376:836-847, 2017
	Pomalidomide for symptomatic Kaposi's sarcoma in people with and without HIV infection: A phase I/II study	Polizzotto MN, et al: <i>J Clin Oncol</i> 34:4125-4131, 2016
	Phase Ia and Ib studies of the novel carcinoembryonic antigen (CEA) T-cell bispecific (CEA CD3 TCB) antibody as a single agent and in combination with atezolizumab: Preliminary efficacy and safety in patients with metastatic colorectal cancer (mCRC)	Tabernero J, et al: <i>J Clin Oncol</i> 35, 2017 (suppl; abstr 3002)
	Efficacy and safety of nivolumab (NIVO) plus ipilimumab (IPI) in patients with melanoma (MEL) metastatic to the brain: Results of the phase II study CheckMate 204	Tawbi HAH, et al: <i>J Clin Oncol</i> 35, 2017 (suppl; abstr 9507)
	Adjuvant capecitabine for breast cancer after preoperative chemotherapy	Masuda N, et al: <i>N Engl J Med</i> 376:2147-2159, 2017
	Irinotecan-temozolomide with temsirolimus or dinutuximab in children with refractory or relapsed neuroblastoma (COG ANBL1221): An open-label, randomized, phase 2 trial	Mody R et al: <i>Lancet Oncol</i> 18:946-57, 2017
	Hormonal maintenance therapy for women with low-grade serous cancer of the ovary or peritoneum	Gershenson DM, et al: <i>J Clin Oncol</i> 35:1103-1111, 2017
	A phase I study of convection enhanced delivery (CED) of 124I-8H9 radio-labeled monoclonal antibody in children with diffuse intrinsic pontine glioma (DIPG)	Souweidane MM, et al: <i>J Clin Oncol</i> 35, 2017 (suppl; abstr 2010)
	Midostaurin plus chemotherapy for acute myeloid leukemia with a FLT3 mutation	Stone RM, et al: <i>N Engl J Med</i> 377:454-464, 2017
	Phase III randomized trial of chemotherapy with or without bevacizumab (B) in patients (pts) with recurrent or metastatic squamous cell carcinoma of the head and neck (R/M SCCHN): Survival analysis of E1305, an ECOG-ACRIN Cancer Research Group trial	Argiris A, et al: <i>J Clin Oncol</i> 35, 2017 (suppl; abstr 6000)
	Efficacy of dabrafenib (D) and trametinib (T) in patients (pts) with BRAF V600E-mutated anaplastic thyroid cancer (ATC)	Subbiah V, et al: <i>J Clin Oncol</i> 35, 2017 (suppl; abstr 6023)
	MONARCH 2: Abemaciclib in combination with fulvestrant in women with HR+/HER2- advanced breast cancer who had progressed while receiving endocrine therapy	Sledge GW, et al: <i>J Clin Oncol</i> 35:2875-2884, 2017
Patient care	The impact of exercise on cancer mortality, recurrence, and treatment-related adverse effects	Cormie P, et al: <i>Epidemiol Rev</i> 39:71-92, 2017
	Traveling to a high-volume center is associated with improved survival for patients with esophageal cancer	Speicher PJ, et al: <i>Ann Surg</i> 265:4:743, 2017
	Temporal trends in treatment and subsequent neoplasm risk among 5-year survivors of childhood cancer, 1970-2015	Turcotte LM, et al: <i>JAMA</i> 317:814-824, 2017
	Measuring financial toxicity as a clinically relevant patient-reported outcome: The validation of the Comprehensive Score for financial Toxicity (COST)	De Souza JA, et al: <i>Cancer</i> 123:476-484, 2017
	Long-term results of a phase II randomized controlled trial (RCT) of a psychological intervention (Conquer Fear) to reduce clinical levels of fear of cancer recurrence in breast, colorectal, and melanoma cancer survivors	Beit JM, et al: <i>J Clin Oncol</i> 35, 2017 (suppl; abstr LBA10000)
Tumor biology	Novel molecular subgroups for clinical classification and outcome prediction in childhood medulloblastoma: A cohort study.	Schwalbe EC et al: <i>Lancet Oncol</i> 18:958-971, 2017
	DNA methylation heterogeneity defines a disease spectrum in Ewing sarcoma	Sheffield NC et al: <i>Nat Med</i> 23:386-395, 2017

Abbreviations: ACRIN, American College of Radiology Imaging Network; ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; HR, hormone receptor.

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## Conquer Cancer Foundation

The Conquer Cancer Foundation was created by the world's foremost cancer physicians of ASCO to seek dramatic advances in the prevention, treatment, and cure of all types of cancer. Toward the vision of a world free from the fear of cancer, Conquer Cancer works to conquer this disease by funding breakthrough cancer research and sharing cutting-edge knowledge with patients and physicians worldwide, and by improving the quality of care and access to care, enhancing the lives of all who are touched by cancer.

Over 34 years, more than \$109 million in funding has been provided through the Conquer Cancer's Grants and Awards Program to support clinical and translational scientists, at all levels of their careers and working around the globe, to address the full spectrum of oncology, from prevention through survivorship and end-of-life care. Conquer Cancer has given more than 1,800 Conquer Cancer grants and awards in 71 countries. Foundation grants have helped researchers launch successful careers and make discoveries that benefit patients with cancer.

One of the top patient care advances featured in this report was made possible by funding from Conquer Cancer (see Patient Engagement Leads to Improved Care), and several other studies that are highlighted were led by past Conquer Cancer grant recipients who have continued their careers in oncology research.

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