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To view this report online and learn more about progress against cancer, visit ASCO.org/CCA. This report was also published in the *Journal of Clinical Oncology* at ascopubs.org/journal/jco on February 1, 2017.
A MESSAGE FROM ASCO’S PRESIDENT

I am pleased to present Clinical Cancer Advances 2017, which highlights the most promising advances in patient-oriented cancer research over the past year. The report gives us an opportunity to reflect on what an exciting time it is for cancer research and how swiftly our understanding of cancer has improved.

One year ago, the White House announced the national Cancer Moonshot program to accelerate progress against cancer. This shared vision of progress has reinvigorated the research community, identified new areas of scientific collaboration, and raised our ambitions regarding what may be possible beyond the progress we have already made.

When I entered the field 35 years ago, I could not have imagined where we would be today. We can now detect cancer earlier, target treatments more effectively, and manage adverse effects more effectively to enable patients to live better, more fulfilling lives. Today, two of three people with cancer live at least 5 years after diagnosis, up from roughly one of two in the 1970s.

This progress has resulted from decades of incremental advances that have collectively expanded our understanding of the molecular underpinnings of cancer. There is no better current example of this than ASCO’s 2017 Advance of the Year: Immunotherapy 2.0.

Over the last year, there has been a wave of new successes with immunotherapy. Research has proven this approach can be effective against a wide range of hard-to-treat advanced cancers previously considered intractable. Researchers are now working to identify biologic markers that can help increase the effectiveness of treatment and determine who is most likely to benefit from immunotherapy. This knowledge will enable oncologists to make evidence-based decisions so as many patients as possible might benefit from this new type of treatment.

Each successive advance builds on the previous hard work of generations of basic, translational, and clinical cancer researchers. Importantly, the advances described in this report would not have been possible without the individuals who volunteered to participate in clinical trials as part of their treatment.

To turn the promising vision of a cancer moonshot into meaningful advances, we need sustained, robust federal funding for continued research and innovation. Approximately 30% of the research highlighted in this report was funded, at least in part, through federal dollars appropriated to the National Institutes of Health or the National Cancer Institute. Without this federal investment—unique internationally in scale, duration, and impact for decades—I fear we may lose the forward momentum needed to further the progress we see highlighted in this report.

Federal lawmakers can further fuel progress by advancing initiatives that facilitate the use of big data to achieve the common good of high-quality care for all patients. Such programs, like ASCO’s CancerLinQ, will rapidly increase the pace of progress and dramatically expand the reach of treatment advances to the millions of patients who are living with cancer today or who will do so in the future. This investment will yield medical, scientific, economic, and societal benefits for years to come.

Much work still lies ahead. Many questions remain about how cancer develops and spreads and how best to treat it. As you read through Clinical Cancer Advances 2017, I hope you are as inspired as I am by the gains the clinical cancer research community has made over the past year and by the promise of a new era of advances just over the horizon.

Daniel F. Hayes, MD, FASCO, FACP
ASCO President, 2016 to 2017
EXECUTIVE SUMMARY

Cancer is one of the world’s most pressing health care challenges. On the whole, research progress from one year to the next is incremental, and true breakthroughs are exceptional. Nevertheless, every year brings new knowledge and insights that help direct further research and ultimately improve the outlook for patients with cancer. This report highlights the most important clinical advances of 2016 and previews where cancer science is headed.

Accelerated by the National Cancer Act of 1971 and then by a responsive research infrastructure and increasingly innovative regulatory environment, cancer research today delivers new treatments to patients faster than ever. In just 1 year’s time (from November 2015 through October 2016), the US Food and Drug Administration (FDA) has approved 20 therapies for more than a dozen different types of cancer (Table 1). An example of this accelerating progress is cancer immunotherapy.
WHAT’S NEXT FOR CANCER IMMUNOTHERAPY?

A hundred years in the making, cancer immunotherapy is now a standard treatment option for people with a growing number of different cancers. In 2016 alone, the FDA approved immunotherapies for advanced forms of lung, kidney, bladder, and head and neck cancers, as well as Hodgkin lymphoma.

For some people with these advanced-stage cancers, the advent of cancer immunotherapy is truly life changing. It often offers the only chance to live longer and better. And many believe that this first wave of success with cancer immunotherapy is just the beginning.

Building on our initial success, a key next step is to understand why fewer than half of patients currently selected for treatment actually benefit from immunotherapy and why the benefit, if it occurs, may be short lived. In 2016, several reports revealed early insights into patient and cancer characteristics (ie, biomarkers) that might predict whether immunotherapy could work well in an individual patient. For example, it seems that for some cancers, the subset of tumors with many genetic mutations can be more responsive to current immunotherapy options.

While we are trying to identify who will benefit, we are also exploring whether combining immunotherapy treatments with one another or with other cancer treatments, such as radiation therapy and chemotherapy, might extend the impact of this new group of therapies. Together, these efforts mark the next phase of immunotherapy: Immunotherapy 2.0: Expanding Use and Refining Patient Selection, the American Society of Clinical Oncology’s (ASCO) Advance of the Year.

PRECISION MEDICINE

The advances highlighted in this report attest to a key trend that is driving progress against cancer today: cancer therapies are becoming increasingly precise, thereby enabling a more personalized approach to treatment selection. The research into cancer biology is propelling rapid development of novel treatments targeting the key molecules that allow cancers to grow and spread. In 2016 alone, this strategy resulted in new targeted therapies for people living with advanced cancers of the lung, breast, and kidney, as well as several hard-to-treat forms of blood cancer.

Today, new molecular technologies can quickly pinpoint molecular changes in the tumor or free-floating cancer DNA in the blood. For a growing number of patients, such changes can be matched to either existing targeted treatments or experimental treatments that are being tested in clinical trials. Although this approach is not yet routine, early research suggests it could open viable new treatment options for patients with a wide range of hard-to-treat cancers (as described in Looking to the Future).

Cancer by the Numbers

The World Health Organization projects that the number of new cancer diagnoses will reach 22 million per year in the next two decades, up from 14 million in 2012. In the same timeframe, cancer-related deaths may increase by as much as 70%. Seven of 10 deaths resulting from cancer occur in Africa, Asia, and Central and South America, regions of the world with limited access to cancer screening and treatment.¹

In the United States, an estimated 1.7 million people were diagnosed with cancer in 2016.² Because of the growing population of older adults and changing demographics, US annual cancer incidence is expected to reach 2.2 million per year by 2030.³

The good news is that, for most people, a diagnosis of cancer is not as grim as it used to be. Today, 68% of adults and 81% of children with cancer will be alive at least 5 years after a diagnosis. This is a big improvement from the 1970s, when only 50% of adults and 62% of children were surviving 5 years.⁴ Although annual US cancer death rates have been declining in the last 20 years, the number of deaths resulting from cancer remains high because of overall population growth.

CARING FOR THE WHOLE PATIENT

In the 21st century, people with cancer are not only living longer than ever, but also enjoying a better quality of life than before. Indeed, an entire field of cancer survivorship has emerged—studying ways to improve life as well as extend it. Although treating the physical illness remains a priority, more and more attention is being paid to caring for the whole patient, which includes his or her emotional and psychosocial needs.

With increased access to health information, patients today can be more active partners in their health care. A patient’s values and preferences are critical when it comes to decisions about cancer screening and prevention measures, as well as cancer therapy selection. Indeed, lifestyle and environmental factors along with genomics represent the keys to precision medicine.

This report features efforts to ensure that every patient with cancer receives the best possible care. Among these efforts are Web-based tools for self-monitoring symptoms, education and navigation programs for underserved populations, and a better way to prevent nausea triggered by chemotherapy. Lastly, this report reviews clinical research addressing a long-standing unresolved question in a common malignancy: prostate cancer.

FEDERAL FUNDING SUPPORTS PIONEERING RESEARCH

Clinical cancer research in the United States is made possible through funding from both public and private sectors. When it comes to high-risk, pioneering research, federal funding is often indispensable and has been a unique asset over the decades since World War II. Often only federal funding can support research that the private sector typically does not pursue, such as cancer prevention and screening and treatment comparisons.

Funding from the US National Institutes of Health (NIH) supported approximately one-third of the top advances highlighted in this report. Among the most notable are:

- Early evidence that immunotherapy is effective against an aggressive, nonmelanoma skin cancer
- A new, life-extending targeted treatment of an aggressive blood cancer
- Improved therapies for children with high-risk neuroblastoma and adults with glioma
- First insight into how genetic changes evolve during the development of melanoma
- Discovery of two genes linked to increased risk of ovarian cancer
- Identification of heritable genetic mutations in children with cancer and people with suspected Lynch syndrome
- Applications of liquid biopsy testing in cancer care

CALL TO ACTION

ASCO is calling on lawmakers to continue to build on investments in NIH and NCI with predictable and sustainable future funding increases to meet the promise of today’s research.
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

- **23% DECLINE IN CANCER DEATH RATE**
  Since a peak in 1991¹

- **90+ CANCER DRUGS APPROVED BY THE FDA SINCE 2006²**

- **INCREASED 5-YEAR SURVIVAL**
  2 out of 3 people with cancer live at least 5 years after diagnosis³

- **14.5M CANCER SURVIVORS**
  Up from 11.4 million in 2006¹

Yet, while the NIH received its first significant budget increase in over a decade in 2016...

NCI’s budget, when adjusted for inflation, remains below prerecession levels³

**FUNDING FOR NCI RESEARCH**³

Source: National Cancer Institute

Increased federal funding is urgently needed to accelerate life-saving research and new cancer breakthroughs

Current research priorities include:⁴,⁵

- **IMMUNOTHERAPY RESEARCH**
  Support mechanisms to identify, test and validate new predictive biomarkers

- **ENHANCED DATA SHARING**
  Create a national ecosystem for sharing and analyzing data

- **EXPANDED PREVENTION AND DETECTION STRATEGIES**
  Boost prevention research and increase testing to identify high-risk patients

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.

Sources:

NIH = National Institutes of Health  NCI = National Cancer Institute

Fig 1. Robust federal funding needed to accelerate cancer research.
Sustained and steady funding of the NIH and National Cancer Institute (NCI) is critical to maintaining the pace of scientific discovery and continued progress against cancer. However, although the NIH received its first budget increase in more than a decade in 2016, the budget of the NCI, when adjusted for inflation, remains below prerecession levels (Fig 1). Failure to sustain the historic US investment in research places health outcomes, scientific leadership, and economic growth at risk.

ABOUT CLINICAL CANCER ADVANCES

ASCO developed this annual report, now in its 12th year, to document the important progress being made in clinical cancer research and highlight emerging trends in the field. Clinical Cancer Advances serves to outline to the public progress achieved in clinical cancer research and care each year. As a whole, this document attests to the exciting current state of the science and envisions future directions of cancer research.

The content of Clinical Cancer Advances was developed under the direction of a 20-person editorial board composed of experts in a wide range of oncology subspecialties. The editors reviewed research reports published in peer-reviewed scientific and medical journals or presented at major scientific meetings over a 1-year period (October 2015 to October 2016). The advances highlighted in this report cover the full range of clinical research disciplines: prevention, treatment, patient care, and tumor biology.

ABOUT THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY

Founded in 1964, ASCO is committed to making a world of difference in cancer care. As the world’s leading organization of its kind, ASCO represents more than 40,000 oncology professionals who care for people living with cancer. Through research, education, and promotion of the highest-quality patient care, ASCO works to conquer cancer and create a world where cancer is prevented or cured, and every survivor is healthy. ASCO is supported by its affiliate organization, the Conquer Cancer Foundation. Learn more at ASCO.org, explore patient education resources at Cancer.Net, and follow us on Facebook, Twitter, LinkedIn, and YouTube.

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.
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, the foundation works to conquer this disease by funding breakthrough cancer research, sharing cutting-edge knowledge with patients and physicians worldwide, and by improving quality of care and access to care, enhancing the lives of all who are touched by cancer.

Over 33 years, more than $105 million in funding has been provided through the Conquer Cancer Foundation Grants and Awards Program to support clinical and translational scientists at all levels of their careers, working around the globe to address the full spectrum of oncology—from prevention through survivorship and end-of-life care. The foundation has given more than 1,700 grants and awards in 68 countries. Foundation grants have helped researchers launch successful careers and make discoveries that benefit patients with cancer.

Several of the studies featured in this year’s Clinical Cancer Advances report were led by past Conquer Cancer Foundation grant recipients who have continued their careers in oncology research.
This year, ASCO has named Immunotherapy 2.0 as the advance of the year. This selection recognizes the growing wave of progress using cancer immunotherapy, which has extended and improved the lives of patients, many of whom had few other effective treatment options.

It has taken scientists more than a century to learn how to harness the immune system to fight cancer. A number of strategies to achieve this have been tried, but one approach—blocking immune checkpoints—has been particularly effective against a range of different cancers. Immune checkpoints are specialized proteins that act as brakes on the immune system, ensuring that immune defenses are engaged only when they are needed and for as long as they are needed. They prevent the immune system from becoming overactive, which can lead to excessive inflammation or autoimmune disease.
When a cancer cell encounters a T cell (a type of immune cell), the interaction between the major histocompatibility complex (MHC) and the T-cell receptor (TCR) molecules activates the T cell. But when the PD-L1 checkpoint protein on the cancer cell attaches to the PD-1 checkpoint receptor on the T cell, the T cell is deactivated.

New immune checkpoint inhibitor therapies prevent the PD-L1 checkpoint protein from attaching to the PD-1 checkpoint receptor. This allows the MHC and TCR interaction to activate the T cell and unleash the immune system to attack cancer.

Cancer treatments known as immune checkpoint inhibitors unleash the immune system to attack cancer (Fig 2). Since the first remarkable reports of immune checkpoint inhibitors shrinking advanced melanoma in 2011, research in this area has taken off at an incredible pace. Over the past year, the FDA approved five new uses for immune checkpoint inhibitors: lung cancer, head and neck cancer, bladder cancer, kidney cancer, and Hodgkin lymphoma. However, many other patients with the same types of cancer either do not benefit from immunotherapy at all or experience a benefit that is short lived. New research reported in 2016 is advancing the ability to identify patients who are most likely to benefit from immunotherapy, while sparing others from its high cost and adverse effects.

**PROGRESS WITH IMMUNE CHECKPOINT INHIBITORS**

**Immunotherapy extends long-term survival in advanced melanoma.**

The number of people diagnosed with melanoma has risen sharply over the last three decades and is continuing to increase worldwide. In 2016, an estimated 76,380 adults in the United States were diagnosed with melanoma of the skin. Melanoma is the fifth most common cancer among men and the seventh most common cancer among women.

Although it accounts for only 1% of all skin cancers, melanoma causes the vast majority of deaths resulting from skin cancer. It is estimated that 10,130 deaths resulting from melanoma occurred last year.

Most people with melanoma are cured with surgery alone. However, among patients with metastatic melanoma, only 17% will live 5 years after their diagnosis.

In just a few short years, immunotherapy has transformed the outlook for this disease. Given the lasting responses seen in a large proportion of patients who have received immunotherapy, experts are beginning to speculate that a cure may be within reach, at least for a fortunate few patients.

Approval of the checkpoint inhibitor ipilimumab marked the first treatment that could prolong life for patients with advanced melanoma (ipilimumab blocks the immune checkpoint cytotoxic T-cell lymphocyte-4 [CTLA-4]). By the end of 2014, the FDA had approved two additional checkpoint inhibitors for use in patients with advanced melanoma: pembrolizumab and nivolumab. In research studies, both proved to be even more effective than ipilimumab, while causing fewer adverse effects.
In 2014, Rebecca found out that the lung cancer that she had been previously diagnosed with had returned and spread to other areas. Her doctors quickly ran out of treatment options and suggested hospice. It was then that Rebecca learned about a clinical trial investigating a type of immunotherapy called nivolumab for advanced lung cancer. After one month on the trial, her tumor began to shrink, and the severe pain Rebecca had felt for the last year finally began to subside. Today, the cancer is in remission.

Rebecca is an active participant in the #LCSM Twitter community and is pictured left with her oncologist Katherine Wang, MD, PhD.

\[\text{VOICES OF CANCER RESEARCH}\]

**REBECCA HILL**

“I’m in remission— I can’t believe it myself.”

In 2014, Rebecca found out that the lung cancer that she had been previously diagnosed with had returned and spread to other areas. Her doctors quickly ran out of treatment options and suggested hospice.

It was then that Rebecca learned about a clinical trial investigating a type of immunotherapy called nivolumab for advanced lung cancer. After one month on the trial, her tumor began to shrink, and the severe pain Rebecca had felt for the last year finally began to subside. Today, the cancer is in remission.

Rebecca is an active participant in the #LCSM Twitter community and is pictured left with her oncologist Katherine Wang, MD, PhD.
(PD-L1)–positive NSCLC. Among all patients treated in the study, the median survival was 10.4 months with pembrolizumab versus 8.5 months with docetaxel. In the group of patients with higher levels of PD-L1 (at least 50% of cells positive for PD-L1), the median survival with pembrolizumab was even longer (14.9 vs 8.2 months). In addition, the rate of severe adverse effects was much lower with pembrolizumab than with docetaxel (16% vs 35%). Not only does immunotherapy offer patients with NSCLC the chance to live longer, it is also far easier to tolerate than chemotherapy for many patients.

These findings established pembrolizumab as a new standard option for patients with previously treated, advanced NSCLC. The study also sparked a national conversation about the importance of PD-L1 biomarker testing to select patients who are most likely to benefit from immune checkpoint inhibitors.

Meanwhile, findings from a large clinical trial suggest that pembrolizumab may be more effective than chemotherapy as an initial treatment for patients who have metastatic NSCLC with high levels of PD-L1 (> 50% of cancer cells are PD-1 positive), whereas a similar study failed to demonstrate superiority of nivolumab to chemotherapy in this setting.

These findings will change initial treatment of metastatic NSCLC in that every newly diagnosed patient will need to be tested for PD-L1. Patients with high PD-L1 levels will likely receive immunotherapy rather than chemotherapy.

Another immune checkpoint inhibitor, atezolizumab, was approved by the FDA in 2016 for patients with previously treated, metastatic NSCLC. The approval was based on two large clinical trials, which showed that patients who received atezolizumab lived longer (13.8 and 12.6 months, respectively) than those who received standard docetaxel chemotherapy (9.6 and 9.7 months, respectively). The most common adverse effects related to treatment with atezolizumab included fatigue, decreased appetite, shortness of breath, cough, and nausea. Atezolizumab is a PD-L1 inhibitor previously approved for treatment of bladder cancer.

In October 2016, the FDA approved pembrolizumab for use as first-line treatment for patients with advanced, PD-L1–positive NSCLC. A breakthrough therapy designation had previously been granted for the same use. These studies collectively mean that the historical standard treatment of advanced lung cancer (ie, chemotherapy) has finally been displaced by immunotherapy as either first- or second-line treatment.

First new treatment for bladder cancer in three decades. An estimated 76,960 people were diagnosed with bladder cancer in the United States in 2016, and 430,000 were diagnosed worldwide in 2012. Bladder cancer is more common among men than women. In fact, bladder cancer is the fourth most common cancer among men.

It is estimated that 16,390 deaths resulting from bladder cancer occurred in the United States in 2016. The most commonly diagnosed type of bladder cancer is superficial bladder cancer (ie, cancer that has not yet spread outside of the bladder), which can typically be treated successfully. However, people who have advanced bladder cancer are in desperate need of better therapies. Only 15% of patients with bladder cancer that has spread to distant parts of the body live 5 years after diagnosis. Cancer.Net provides details about bladder cancer for patients, caregivers, and others seeking reliable information.

There had been little progress in the treatment of advanced bladder cancer for several decades until the FDA approval of the immunotherapy atezolizumab in May 2016. Atezolizumab was also the first PD-L1 checkpoint inhibitor to gain FDA approval for any use.

The approval of atezolizumab was based on an early clinical trial of patients with previously treated metastatic urothelial cancer, the most common type of bladder cancer. Among patients with
This clinical trial saved my life."

SUSAN CORCORAN

When Susan’s bladder cancer returned in 2013, doctors told her the cancer had spread, and treatment would only slow its growth temporarily. Now, nearly four years later, Susan is cancer-free, thanks to a clinical trial of an immunotherapy called atezolizumab.

Susan has been on the trial for more than two years now, receiving an infusion of atezolizumab once every three weeks. She has spent this time traveling with her husband, dragon boating with fellow cancer survivors, and visiting her grandchildren.

Susan is a member of the Bladder Cancer Advocacy Network (BCAN).

Immunotherapy extends life after head and neck cancer recurrence. More than 600,000 people around the world are diagnosed with head and neck cancer every year, with nearly 50,000 in the United States alone. This type of cancer is difficult to treat, particularly if it recurs or spreads (ie, metastasizes). Patients with squamous cell head and neck cancer that worsens within 6 months of treatment with chemotherapy have no life-extending therapy options.

However, a recent clinical trial suggests that nivolumab may offer such patients a chance to live longer. The estimated 1-year survival rate was more than two-fold higher among patients treated with nivolumab than that among those treated with standard chemotherapy (36% vs 17%). The median survival was 7.5 months in the nivolumab group and 5.1 months in the chemotherapy group.

Fewer patients in the nivolumab group (13% vs 35%) had severe treatment-related adverse effects. In addition, quality of life remained stable among patients who received nivolumab but deteriorated among those who received chemotherapy. Based on the results of this trial, the FDA approved nivolumab for the treatment of patients with recurrent or metastatic squamous cell carcinoma of the head and neck in November 2016.
Ongoing clinical trials are exploring whether combining nivolumab with ipilimumab may further improve patient outcomes (ClinicalTrials.gov identifiers: NCT02741570 and NCT02823574). Meanwhile, pembrolizumab is already approved as treatment for patients with recurrent or metastatic head and neck cancer.

**Chance to slow ovarian cancer progression.** Compared with other cancers, ovarian cancer is relatively uncommon, with an estimated 22,280 new diagnoses in the United States in 2016.²³ Worldwide, 239,000 women were diagnosed with ovarian cancer in 2012.⁷ Nonetheless, ovarian cancer is the fifth most common cause of cancer-related death among US women, causing an estimated 14,240 deaths in 2016.²³ Because of the lack of specific symptoms, ovarian cancer has often reached an advanced stage by the time of diagnosis. Despite surgery and chemotherapy, more than 70% of women with ovarian cancer that goes into remission eventually experience a relapse. Fewer than half of such women live 5 years after diagnosis.

Early research published in 2015 suggests that nivolumab may help some women with ovarian cancer that has relapsed after platinum-based chemotherapy. In an early clinical trial of 20 women, three (15%) experienced tumor shrinkage after treatment with nivolumab, and an additional six (30%) had stable disease (ie, tumors neither shrinking nor growing).²⁴ Two women experienced complete remission, one of whom had a type of ovarian cancer particularly resistant to chemotherapy (clear cell carcinoma).

These early findings have spurred further research on how best to incorporate immunotherapy into the treatment of ovarian cancer. Several ongoing clinical trials are exploring nivolumab in combination with other immunotherapies for women with recurrent ovarian cancer (ClinicalTrials.gov identifiers: NCT02737787, NCT02335918, and NCT01928394).

**Hodgkin lymphoma seems particularly susceptible to PD-1 inhibitors.** Hodgkin lymphoma is a cancer of the lymphatic system. It is a fairly uncommon cancer, with an estimated 8,500 people diagnosed in the United States in 2016.²⁵ Hodgkin lymphoma is more common among young adults and men than it is among women.

Classic Hodgkin lymphoma is the most common type of Hodgkin lymphoma, accounting for 95% of all cases. The survival rate for classic Hodgkin lymphoma has been increasing for the past 40 years as a result of treatment improvements. Most patients with classic Hodgkin lymphoma achieve good outcomes with initial chemotherapy, and 86% will live 5 years after diagnosis.

However, in approximately 20% to 30% of patients, classic Hodgkin lymphoma will relapse after initial treatment or will not respond to therapy at all. Such patients require further, more intensive treatment, such as high-dose chemotherapy followed by autologous stem-cell transplantation (ASCT). If the cancer relapses after ASCT, a newer regimen combining a targeted drug with chemotherapy, brentuximab vedotin, can extend survival, but in many patients, the lymphoma eventually worsens despite treatment.

Research reported in 2016 led to a new treatment option for such patients: nivolumab.²⁶ This advance stems from an earlier discovery of genetic changes in malignant classic Hodgkin lymphoma cells called Reed-Sternberg cells. The genetic changes result in an abundance of immune checkpoint molecules PD-L1 and PD-L2, which help the cancer cells dampen immune responses through the PD-1/PD-L1 checkpoint. This insight suggests that classic Hodgkin lymphoma may be particularly susceptible to PD-1 and PD-L1 immune checkpoint inhibitors.

A recent analysis of biopsy samples from newly diagnosed patients with classic Hodgkin lymphoma showed that the genetic changes that lead to an abundance of PD-L1 and PD-L2 markers (polysomy, copy gain, and amplification) are extremely common.²⁷ Such genetic changes were found in 97% of the 108 specimens tested. This genetic underpinning maybe the reason the response rates to PD-1 inhibitors are higher in classic Hodgkin lymphoma than in any other type of cancer studied to date.

The FDA approval of nivolumab for classic Hodgkin lymphoma was based on an early clinical trial in which lymphoma went into remission in 53 (66%) of 80 patients and disappeared entirely in seven.²⁸ Nearly all patients with classic Hodgkin lymphoma who responded to the treatment had at least a 50% reduction in the amount of cancer in the body, and responses lasted 8 months, on average. Nivolumab was generally well tolerated. The most common adverse effects of any grade were fatigue, infusion-related reaction, and skin rash. Severe adverse effects, such as low blood counts (neutropenia) and liver enzyme abnormalities (increased lipase), occurred in only 5% of patients.

In another early trial, pembrolizumab was also effective among young patients with relapsed or
The next chapter of immunotherapy research will focus on answering these questions. Given the high cost and considerable adverse effects of immunotherapy approaches, it is all the more important to be able to determine who is likely to benefit the most. Although there can never be complete certainty about whether a cancer will respond to treatment, in most cases physicians can at least estimate the likelihood of benefit, based on the biologic characteristics or biomarkers of the patient and the tumor.

Scientists are only beginning to unravel the biomarkers that may predict a favorable response to immunotherapy. For example, researchers expected that cancers with high levels of PD-L1 would respond well to PD-1 checkpoint inhibitors and that those without PD-L1 would not benefit at all. However, in a number of different cancers, such as ovarian cancer and melanoma, the relationship between PD-L1 and response to PD-1 checkpoint inhibitors has been less clear. In several clinical trials, cancers with even low levels of PD-L1, including some lung cancers, responded to PD-1 inhibitors.

A major issue is the lack of standardization of PD-1 and PD-L1 analyses. It is unclear which assay or reagent is optimal or whether expression in only the cancer cells or in cancer cells plus surrounding stromal and/or immune cells should be counted. Furthermore, even using one assay and one method of analysis, cutoffs have varied. These issues need to be resolved before this marker can be considered sufficiently robust for clinical decisions.

In 20 (64%) of 31 patients, the cancer went into remission, and of those patients, five experienced complete remission. Nearly all patients had some reduction in tumor size, and most responses lasted more than 24 weeks. In April 2016, the FDA granted pembrolizumab breakthrough therapy designation for treatment of relapsed classic Hodgkin lymphoma.

Further research into PD-1 checkpoint inhibitors as therapy for relapsed as well as newly diagnosed classic Hodgkin lymphoma is underway. Ongoing clinical trials are exploring combinations of nivolumab with brentuximab vedotin and ipilimumab (ClinicalTrials.gov identifiers: NCT02758717, NCT01896999, and NCT02304458). Pembrolizumab is also being tested in a range of other hematologic malignancies, as well as in multiple myeloma (ClinicalTrials.gov identifier: NCT01953692).

EMERGING CLUES ON PATIENT SELECTION

Despite the broadening landscape of immunotherapy use, a difficult biology puzzle remains to be solved. Why do immune checkpoint inhibitors work so well in some cancers and not at all in others? Among patients with the same type of cancer, why do some respond to immunotherapy while others do not?
CHECKPOINT INHIBITORS WORK WELL AGAINST HYPERMUTATED CANCERS

Although research on biomarkers for immune checkpoint inhibitors and other types of immunotherapy is still evolving, a few key clues have emerged. For one, it seems that tumors with a large number of mutations are more susceptible to checkpoint inhibitors. The likely explanation for this is that tumors with more mutations make more abnormal proteins (antigens) that the immune system recognizes as foreign.

Several tests have been proposed to evaluate mutational burden. One involves sequencing the entire genome of the cancer and simply counting the number of mutations. Yet another approach is to sequence only a selected panel of representative genes and again determine the rate of mutations within the panel. A third is to evaluate surrogate markers of mutational frequency. Another assay determines the presence of a hypermutable phenotype, such as apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like (APOBEC) enzymes.

Cancers with a large number of mutations, so-called hypermutated cancers, are primarily those caused by tobacco (e.g., lung, head and neck, and bladder cancers) or UV light exposure (e.g., melanoma and head and neck cancer). In fact, tobacco and UV light exposure have been linked to unique patterns of genetic changes or genetic signatures. It is therefore not surprising that in clinical trials to date, those are the cancers in which immune checkpoint inhibition has been the most effective.

Scientists have also reported that cancers of patients who have a genetic abnormality called mismatch repair (MMR) deficiency, which undermines the ability of a cell to repair DNA damage, also have many mutations. Early research suggests that patients with MMR-deficient colorectal or brain cancer benefit from checkpoint inhibitors. These treatments, however, have low efficacy in patients with the same cancers that are not MMR deficient.

Taken in total, these exciting data are promising but preliminary. It is hoped that ongoing studies will help to determine if one or more tests can be used to focus immune checkpoint inhibitor therapy on those patients most likely to benefit.
deficiency and response to immune checkpoint inhibitors (this study was funded in part by a grant from the NIH). Among patients with MMR-deficient colorectal cancers, four of 10 responded to the PD-1 checkpoint inhibitor pembrolizumab. In contrast, none of the 18 patients without MMR deficiency responded to pembrolizumab. Patients with MMR deficiency had a mean of 1,782 mutations per tumor, whereas those with normal MMR function had only 73 mutations per tumor.

Although more research is needed, these early findings suggest that testing for MMR deficiency or the number of mutations in the tumor, so-called mutational load, may help identify patients who are likely to benefit from PD-1/PD-L1-directed immunotherapy. Such tests are already available in the clinic.

Childhood brain cancer. In 2016, researchers reported that another MMR-deficient cancer may be susceptible to checkpoint inhibitors: pediatric glioblastoma multiforme (GBM). This is a hard-to-treat cancer. Most children with GBM will experience a recurrence of cancer despite surgery, radiation therapy, and chemotherapy. With a median survival of 6 months, children with recurrent GBM are in urgent need of effective therapies.

The study focused on children with a rare childhood cancer predisposition syndrome known as biallelic MMR deficiency. All children with this syndrome develop cancer in the first two decades of life, most commonly brain, blood, or GI cancer.

The researchers analyzed the rates of genetic mutations in 37 biallelic MMR-deficient tumors from different tissues. Although all high-grade tumors had large numbers of mutations (1,589 on average), biallelic MMR-deficient GBMs had the highest by far (17,740 mutations on average), and biallelic MMR-deficient GBMs had significantly more mutations than all other pediatric or adult brain cancers.

Given previous research suggesting that tumors with a large number of mutations respond well to immune checkpoint inhibitors, researchers expected to see good results in pediatric biallelic MMR-deficient GBM. In this pilot study, two siblings with recurrent biallelic MMR-deficiency were treated with nivolumab. After 12 weeks of therapy with nivolumab, tumors shrank in both children, and their health condition improved. After 9 and 5 months of therapy, respectively, the sister and brother had resumed schooling and daily activities.

According to the authors, this is the first report of durable responses to immune checkpoint inhibitors for recurrent GBM. These findings are encouraging, because most children with recurrent GBM experience disease worsening within only 1 or 2 months from time of recurrence and die within 3 to 6 months.

The findings may also have implications for adult patients with GBM, as well as in other cancers with MMR deficiency. More broadly, this research underscores the possible utility of genetic testing to select patients for immune checkpoint inhibitor therapy.
Merkel cell carcinoma.

Another rare cancer that seems to be susceptible to PD-1 checkpoint inhibitors is an aggressive skin cancer called Merkel cell carcinoma. Advanced Merkel cell carcinoma typically worsens within 3 months of initial treatment with chemotherapy.

As with other skin cancers, Merkel cell carcinoma is caused by exposure to UV light. In addition, approximately four of five occurrences of Merkel cell carcinoma are linked to infection with the Merkel cell polyomavirus (MCPyV).

PD-L1 is found in half of Merkel cell carcinomas, and PD-1 is present on both the cancer-specific and the MCPyV-specific immune cells. Furthermore, the median number of mutations in MCPyV-negative Merkel cell carcinoma (ie, 1,121) is greater than that reported for other cancers that respond to PD-1/PD-L1 checkpoint inhibitor therapy. This high number of mutations, coupled with PD-1 and PD-L1 markers, suggests that Merkel cell carcinoma may be well suited for treatment with a PD-1 checkpoint inhibitor.

In a pilot study, tumors shrunk in 14 (56%) of 26 patients with advanced Merkel cell carcinoma on treatment with pembrolizumab (this study was funded in part by a grant from the NCI). The treatment responses lasted from 2.2 to 9.7 months. In another clinical trial, 28 (32%) of 88 patients with chemotherapy-resistant Merkel cell carcinoma experienced tumor shrinkage after treatment with the PD-L1 inhibitor avelumab. Although longer follow-up and larger studies are needed, these early findings suggest that checkpoint inhibitors may slow the growth of Merkel cell carcinoma.

Merkel cell carcinomas associated with MCPyV have 100 times fewer mutations (median, 12 mutations) than MCPyV-negative cancers. In fact, MCPyV-positive tumors have fewer mutations than reported for cancers that respond poorly to PD-1 inhibitors, such as prostate and pancreatic cancers. Despite this small number of mutations, MCPyV-positive tumors have higher response rates to pembrolizumab (62%) than MCPyV-negative tumors (44%).

Researchers postulate that MCPyV-positive tumors may respond well to immunotherapy because viral proteins (antigens) trigger an immune response. This means that when PD-1 checkpoint inhibitors unleash the immune system, it is already primed to react against the cancer. This finding may have implications for treatment of other cancers linked to viruses.

For additional notable advances in cancer immunotherapy, please see Appendix Table A1.
In 2016, a growing understanding of cancer biology has spurred new insights into genetic mutations that predispose people to different cancers. Knowing that a person carries a mutation in a cancer susceptibility gene is important, because outcomes can be improved through frequent cancer screening and preventive surgery. In addition, identifying cancer susceptibility factors can help direct cancer treatment decisions and inform family planning.

Every opportunity to prevent cancer is welcome news. Last year, researchers reported on a new way to reduce the risk of nonmelanoma skin cancer: a simple vitamin B pill. In addition, ASCO issued a policy statement outlining recommendations to increase the uptake of human papilloma virus (HPV) vaccination. These vaccines prevent cervical and other HPV-related cancers and have the potential to save millions of lives. Meanwhile, researchers identified a range of barriers that contribute to lower cervical and breast cancer screening rates among Latina women.
GENETIC TESTING

Genetic counseling and testing has become a growing part of cancer risk assessment, diagnosis, and treatment planning. Through policy statements, expert guidelines, and quality programs, ASCO is helping oncology professionals integrate genetic counseling and testing into clinical practice.

In the context of cancer, genetic testing can be used to confirm or rule out a hereditary predisposition to cancer (approximately 5% to 10% of cancers are hereditary) and to identify genetic changes in cancer cells that may respond to specific molecularly targeted cancer treatments, helping a physician and patient identify the best treatment option.

During the past year, some insurance companies have adopted policies that hinder oncologists’ ability to order genetic tests for their patients. ASCO opposes any policy that introduces an unnecessary barrier to the appropriate use of genetic testing services or has the potential to negatively affect patient care.
because steps can be taken to lower ovarian cancer risk. The findings from this study have led to a change in the national guidelines on genetic testing. The updated guidelines recommend consideration of surgery (salpingo-oophorectomy) to reduce the risk of ovarian cancer in women who have mutations in RAD51C or RAD51D genes. For women with high-risk gene mutations, such as BRCA1 and BRCA2, the genes related to Lynch syndrome, and others, having the ovaries and fallopian tubes surgically removed can reduce ovarian cancer risk by 70% to 96%.

For women who are already diagnosed with ovarian cancer, testing for RAD51 gene mutations can also inform treatment decisions. Past research has suggested that women who have such mutations may respond well to a novel class of drugs known as poly (ADP-ribose) polymerase (PARP) inhibitors.

**PANCREATIC CANCER SUSCEPTIBILITY GENES IDENTIFIED, AND NEW OPPORTUNITIES FOR SCREENING AND PREVENTION**

Approximately one in 10 pancreatic cancers is associated with a gene mutation that is passed on in a family from one generation to the next. When pancreatic cancer occurs in two or more first-degree relatives, it is referred to as familial pancreatic cancer. Predisposition to pancreatic cancer has been linked to mutations in a number of different genes, including BRCA1 and BRCA2. In 2015, a prospective study found BRCA mutations in 5% of patients with the most common type of pancreatic cancer: pancreatic ductal adenocarcinoma.58

However, the frequency of BRCA mutations was higher (12%) among 33 patients of Ashkenazi Jewish descent. (According to prior studies, BRCA mutations are also more common among Ashkenazi women with breast or ovarian cancer, compared with the general population). Although the numbers were small, this finding led to a change in national genetic testing guidelines so that every Jewish individual with pancreatic cancer is recommended to undergo BRCA1/2 testing. Relatives of BRCA1/2 mutation carriers who are found to have the familial mutation can be offered appropriate preventive strategies, including screening to detect pancreatic cancer at an early stage.

Given that the average person has only a 1% chance of developing pancreatic cancer over a lifetime, general screening for pancreatic cancer is not recommended. However, selective screening of people who are at high risk for pancreatic cancer may detect premalignant tumors or early-stage cancers, both of which are potentially curable with surgery.

The benefit of such screening was evaluated in a recent prospective screening study of 411 asymptomatic people with familial pancreatic cancer or mutations in known pancreatic cancer susceptibility genes (eg, CDKN2A, BRCA1/2, and PALB2).59 Screening tools included annual magnetic resonance imaging, magnetic resonance cholangiopancreatography, and endoscopic ultrasound. The median follow-up time was 32 months.

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**VOICES OF CANCER RESEARCH**

**DAVID DESSERT**

In 2010, a pancreatic cancer diagnosis confirmed it: David carried a BRCA2 gene mutation that increased his risk of certain cancers. The treatment David received at the time was successful, but the risk of his cancer returning was high. A clinical trial, however, gave him new hope. For the past three and a half years, David has been receiving the GVAX vaccine, an immunotherapy designed to reduce the risk of pancreatic cancer recurrence.

“Every treatment we have right now, we have because someone else tried it in a clinical trial,” David said. “Hopefully this will help somebody else down the line.”

David is a pancreatic cancer forum moderator at cancerforums.net, a member of the peer navigator program at Facing Our Risk of Cancer Empowered (FORCE), and a blogger for pancreatica.org.

“I knew that I had a BRCA2 mutation in the family, but I had not yet been tested.”
Pancreatic ductal adenocarcinoma was detected in 13 (7%) of 178 CDKN2A mutation carriers, nine of whom underwent surgery. The 5-year survival rate was 24%, which is five-fold higher than the 5-year survival rate for all patients diagnosed with this cancer. In addition, screening detected pancreatic cancer in only two (0.9%) of 214 individuals with familial pancreatic cancer and one (5%) of 19 patients with BRCA mutations.

This study is the first to our knowledge to demonstrate success in detecting early cancers and favorable outcomes with surgery using pancreatic cancer screening in a high-risk population. Although screening was clearly useful in detecting pancreatic cancer among patients with CDKN2A mutations, more research is needed to assess the benefit of screening in other high-risk groups, such as people with familial pancreatic cancer or BRCA mutations.

BROADER TESTING UNCOVERS UNEXPECTED CANCER PREDISPOSITION GENE MUTATIONS

People with Lynch syndrome have a markedly increased risk of developing colorectal, endometrial, ovarian, gastric, pancreatic, urinary tract, and other cancers, often at a young age. The syndrome is caused by mutations in the following genes: MLH1, MSH2, MSH6, PMS2, or EPCAM. Conventional Lynch syndrome testing only screens for mutations in these five genes. However, up to half of families with suspected Lynch syndrome test negative for such mutations, which suggests that other genetic changes may be causing increased risk of cancer.

To address this question, researchers used a new technology known as multigene panel testing, which can rapidly analyze numerous cancer susceptibility genes (this study was funded by a grant from the NCI). They evaluated 25 cancer predisposition genes among 1,260 people who were referred for Lynch syndrome testing.

Although 114 (9%) participants had a mutation in one of the Lynch syndrome genes, 71 (6%) had mutations in other cancer predisposition genes. For example, 15 people had mutations in BRCA1 or BRCA2 genes (linked to increased chance of developing breast, ovarian, and other cancers), and nine other individuals had a mutation in a colorectal cancer susceptibility gene.

This study shows that multigene panel testing may yield clinically useful information that could be missed by the more limited, traditional Lynch syndrome testing. It could reveal genetic changes that would not be suspected based on family history alone, allowing for preventive measures such as screening and surgery.

One downside of broad-based genetic testing, however, is the possibility of discovering genetic mutations that have an uncertain clinical significance. Such findings can cause considerable anxiety in patients. In this study, 38% of the people tested had one or more such uninformative findings.

MANY CHILDREN WITH CANCER MAY CARRY HEREDITARY GENE MUTATIONS

The reasons a child develops cancer are often poorly understood. It is largely unknown how common hereditary mutations in cancer predisposition genes arise in children with cancer. A better understanding of the genetic basis for childhood cancer susceptibility would inform treatment choices as well as genetic counseling for patients’ families.

To address this gap in knowledge, researchers conducted a large-scale genomic study of children diagnosed with cancer before the age of 20 years (this study was funded in part by a grant from the NCI). The analysis focused on 565 genes, including 60 that have previously been associated with cancer predisposition syndromes.

They detected mutations in genes thought to be linked to increased cancer risk in 8.5% of 1,120 children with cancer, a rate that was much higher
A POLICY FOCUS: ASCO CALLS FOR INCREASED USE OF HPV VACCINATION TO PREVENT CERVICAL CANCER

In April 2016, ASCO released a policy statement calling on its member oncologists to help lead the push for all adolescents and young adults to be vaccinated against cervical and other cancers. Published in the Journal of Clinical Oncology, the statement outlines current barriers to the use of human papillomavirus (HPV) vaccination, and recommendations to promote the uptake of these vaccines, which have the potential to save millions of lives.

ASCO supports the recommendation to markedly increase the proportion of young boys and girls receiving the HPV vaccine in the United States and worldwide because research has shown that it is effective in preventing cancer. Ongoing research confirms the public health benefit of HPV vaccines for preventing cervical cancer.

To this end, ASCO believes oncologists can play a vital role in increasing the uptake of HPV vaccines. Although most oncologists are not the direct health care providers for these preventive measures, they play an important role through research and advocacy. ASCO encourages oncologists to advocate for and actively promote policy changes to increase the use of HPV vaccination.


DAILY VITAMIN B REDUCES SKIN CANCER RISK

Excessive sun exposure is a widely recognized risk factor for skin cancer. Despite sun protection campaigns, the rates of skin cancer continue to rise worldwide. Nonmelanoma skin cancer is the most common type of cancer in fair-skinned populations worldwide. More than one in two Australians will develop a nonmelanoma skin cancer in their lifetime. In the United States, 5 million people are treated for skin cancer every year. Although nonmelanoma skin cancer is rarely fatal, its treatment poses a significant burden on health care systems.

than that observed in a control group of 1,000 people without cancer (1.1%). Interestingly, the majority (60%) of children with a hereditary cancer predisposition mutation did not have a family history of cancer.

These findings argue for greater screening for hereditary genetic predisposition in children with cancer, even in the absence of a family history of cancer. For the patient, identification of hereditary mutations may influence treatment selection and guide family planning. For the patient’s relatives, having this information can prompt them to request their own genetic testing and/or consider cancer prevention measures.
Although prior research has explored extrinsic sources of disparity in screening adherence, such as limited access to care and lack of health insurance, relatively little is known about intrinsic factors, such as perceptions and attitudes. A survey of 87 Latina women from New York and Arkansas who were enrolled in a culturally tailored education program to increase breast and cervical cancer screening adherence has provided a wealth of information on a variety of factors.45

Despite completing the education program, the women were noncompliant with at least one of the recommended screening examinations (clinical breast examination or mammogram for breast cancer; Pap test for cervical cancer). The most commonly reported reasons for noncompliance were logistic and organizational barriers (eg, being out of the country for long periods of time, forgetting to schedule an appointment), lack of time (eg, inability to take time off from work), and lack of interest in having a screening test. In addition, several women were confused about when they were due for an examination, and others believed they did not need an examination as often as guidelines recommend.

These new insights into factors that contribute to perceptions of cancer screening may enable development of tailored programs to improve screening rates. Similar methodology can be used to direct interventional programs related to other aspects of cancer care.

For additional notable advances in cancer prevention and screening, please see Appendix Table A1.
The past year has brought advances in the treatment of a broad range of cancers. From November 2015 through October 2016, the FDA approved eight new cancer treatments and 12 new uses of previously approved cancer therapies (Table 1). The new approvals include immunotherapies for bladder cancer and multiple myeloma and targeted treatments for hard-to-treat forms of lung and kidney cancers, chronic lymphocytic leukemia (CLL), and multiple myeloma. New-use approvals have broadened treatment options for patients with melanoma, sarcoma, CLL, lymphoma, neuroendocrine tumors, and breast, lung, kidney, and head and neck cancers. In addition, the FDA approved the first liquid biopsy test in 2016.

Each year, 14 million people around the world learn that they have cancer. Because cancer is mostly a disease of aging, cancer occurrences are expected to increase as human lifespans are extended. Although prevention is the ultimate goal, many factors that contribute to cancer cannot be controlled. Advances in cancer treatment will therefore remain a key part of reducing the global burden of cancer.
<table>
<thead>
<tr>
<th>Name of Drug</th>
<th>Indications</th>
<th>Date</th>
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<tbody>
<tr>
<td><strong>NEW APPROVALS</strong></td>
<td></td>
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<tr>
<td>Osimertinib (Tagrisso)</td>
<td>Metastatic EGFR T790M mutation-positive NSCLC, as detected by FDA-approved test, progressing during or after EGFR TKI therapy</td>
<td>November 2015</td>
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<tr>
<td>Daratumumab (Darzalex)</td>
<td>Multiple myeloma after three or more prior lines of therapy, including PI and immunomodulatory agent, or disease double refractory to PI and immunomodulatory agent</td>
<td>November 2015</td>
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<tr>
<td>Ixazomib (Ninlaro)</td>
<td>In combination with lenalidomide and dexamethasone for multiple myeloma after one or more prior therapy</td>
<td>November 2015</td>
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<tr>
<td>Necitumumab (Portrazza)</td>
<td>In combination with gemcitabine and cisplatin for first-line treatment of metastatic squamous NSCLC</td>
<td>November 2015</td>
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<tr>
<td>Alectinib (Alecensa capsules)</td>
<td>ALK-positive metastatic NSCLC progressing with or intolerant to crizotinib</td>
<td>December 2015</td>
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<tr>
<td>Venetooclax (Venclexa tablets)</td>
<td>CLL with 17p deletion, as detected by FDA-approved test, after one or more prior therapy</td>
<td>April 2016</td>
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<tr>
<td>Cabozantinib (Cabometyx)</td>
<td>Advanced RCC after prior antiangiogenic therapy</td>
<td>April 2016</td>
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<tr>
<td>Atezolizumab (Tecentriq)</td>
<td>Locally advanced or metastatic urothelial carcinoma progressing during or after platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy</td>
<td>May 2016</td>
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<tr>
<td><strong>NEW USES</strong></td>
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<tr>
<td>Trametinib (Mekinist) and dabrafenib (Tafinlar)</td>
<td>In combination for unresectable or metastatic melanoma with BRAF V600E or V600K mutation as detected by FDA-approved test</td>
<td>November 2015</td>
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<tr>
<td>Nivolumab (Opdivo)</td>
<td>Advanced RCC after prior antiangiogenic therapy</td>
<td>November 2015</td>
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<tr>
<td>Ofatumumab (Arzerra injection)</td>
<td>Extended treatment for patients in complete or partial response after two or more lines of therapy for recurrent or progressive CLL</td>
<td>January 2016</td>
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<tr>
<td>Erubulin (Halaven injection)</td>
<td>Unresectable or metastatic liposarcoma after prior anthracycline-containing regimen</td>
<td>January 2016</td>
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<tr>
<td>Palbociclib (Ibrance capsules)</td>
<td>In combination with fulvestrant for hormone receptor-positive, HER2-negative advanced or metastatic breast cancer progressing after endocrine therapy</td>
<td>February 2016</td>
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<tr>
<td>Obinutuzumab (Gazyva injection)</td>
<td>In combination with bendamustine followed by obinutuzumab monotherapy for treatment of FL relapsing after or refractory to rituximab-containing regimen</td>
<td>February 2016</td>
</tr>
<tr>
<td>Everolimus (Afinitor)</td>
<td>Progressive, well-differentiated, nonfunctional NET of gastrointestinal or lung origin (unresectable, locally advanced, or metastatic disease)</td>
<td>February 2016</td>
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<tr>
<td>Crizotinib (Xalkori)</td>
<td>Metastatic NSCLC with ROS1-positive tumors</td>
<td>March 2016</td>
</tr>
<tr>
<td>Lenvatinib (Lenvima)</td>
<td>In combination with everolimus for advanced RCC after one prior antiangiogenic therapy</td>
<td>May 2016</td>
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<tr>
<td>Nivolumab (Opdivo)</td>
<td>Classic HL relapsing or progressing after autologous HSCT and post-transplantation brentuximab vedotin (Adcetris)</td>
<td>May 2016</td>
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<tr>
<td>Liquid biopsy test (cobas)</td>
<td>Detection of exon 19 deletions or exon 21 (L858R) substitution mutations in EGFR gene to identify patients with metastatic NSCLC eligible for treatment with erlotinib (Tarceva)</td>
<td>June 2016</td>
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<tr>
<td>Pembrolizumab (Keytruda)</td>
<td>Recurrent or metastatic HNSCC progressing during or after platinum-containing chemotherapy</td>
<td>August 2016</td>
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<tr>
<td>Atezolizumab (Tecentriq)</td>
<td>Metastatic NSCLC progressing during or after platinum-containing chemotherapy</td>
<td>October 2016</td>
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Abbreviations: ALK, anaplastic lymphoma kinase; CLL, chronic lymphocytic lymphoma; EGFR, epidermal growth factor receptor; FDA, US Food and Drug Administration; FL, follicular lymphoma; HER2, human epidermal growth factor receptor 2; HL, Hodgkin lymphoma; HNSCC, head and neck squamous cell carcinoma; HSCT, hematopoietic stem-cell transplantation; NET, neuroendocrine tumor; NSCLC, non-small-cell lung cancer; PI, proteasome inhibitor; RCC, renal cell carcinoma; TKI, tyrosine kinase inhibitor.
TARGETED THERAPY

In addition to the growing success seen with immunotherapy, 2016 was marked by a wave of advances in precision medicine–based approaches. They include treatments directed at novel molecular targets, new types of treatment, and new ways to combine traditional cancer treatments.

After 20 years, a promising new treatment of acute myeloid leukemia. Acute myeloid leukemia (AML) is the second most common type of leukemia diagnosed in both adults and children. In 2016, an estimated 19,950 people of all ages in the United States were diagnosed with AML. This type of cancer is difficult to treat, and only 27% of patients survive 5 years after diagnosis. More information on AML can be found on Cancer.Net. There have been no effective new treatments for AML since the 1990s. In 2015, researchers reported preliminary findings, which may lead to a new standard of care for approximately one-third of patients with AML, those with mutations in a gene called FLT3 (this study was funded in part by a grant from the NCI). Patients with FMS-related tyrosine kinase 3 (FLT3)-positive AML have a poor prognosis and a high chance of relapse.

In a large clinical trial, previously untreated patients who received a therapy targeting FLT3 called midostaurin, combined with standard chemotherapy, lived years longer than those who received chemotherapy alone. The median survival was 75 months among patients who received midostaurin with chemotherapy and only 26 months among those who received placebo with chemotherapy. Midostaurin also more than doubled the median event-free survival (defined as death, relapse, or no complete remission within 61 days) achieved with chemotherapy alone (8 v 3.6 months).

The overall rates of severe adverse effects and treatment-related deaths were similar between the midostaurin and placebo groups. With 717 patients, this is the largest clinical trial of patients with FLT3-positive AML to date to our knowledge.

New treatment targeting common marker improves outcomes after acute lymphoblastic leukemia relapse.

In 2016, an estimated 2,636 adults in the United States were diagnosed with acute lymphoblastic leukemia (ALL). Although a majority of adults with ALL achieve complete remission after initial therapy, many eventually relapse. The prognosis for such patients is poor, and more effective treatments are urgently needed.

One new treatment, inotuzumab ozogamicin, may improve outcomes for older people with recurrent ALL, according to an ongoing clinical trial. Inotuzumab ozogamicin belongs to a new class of cancer treatments known as antibody–drug conjugates (ADCs). These comprise an antibody chemically linked to a powerful cancer drug called calicheamicin. The antibody targets the CD22 molecule, found on tumor cells in 90% of patients with B-cell ALL, and helps deliver calicheamicin to leukemia cells.

In this late-stage trial, patients were randomly assigned to receive inotuzumab ozogamicin or standard intensive chemotherapy. The rate of complete remission was more than two-fold higher in the inotuzumab ozogamicin group compared with the standard therapy group (81% v 29%). The median time until cancer worsened was longer in the inotuzumab ozogamicin group than in the standard therapy group (5 v 1.8 months), and the median survival was longer as well (7.7 v 6.7 months).

A major adverse effect of inotuzumab ozogamicin was veno-occlusive liver disease, which occurred in 11% of patients. Inotuzumab ozogamicin is likely to become a new standard of care for older adult patients with relapsed or refractory B-cell ALL.

Progress in treating advanced, ALK-positive NSCLC.

Approximately 3% to 7% of NSCLCs are anaplastic lymphoma kinase (ALK) positive, meaning that the cancers carry a genetic change known as ALK gene rearrangement. The first treatment to specifically target ALK-positive tumors, crizotinib, was approved by the FDA in 2011. Although crizotinib shrinks tumors in a large proportion of patients, most experience a relapse within the first year of treatment.

To address the challenge of crizotinib resistance, researchers have been developing more potent, next-generation ALK inhibitors. One such treatment, alectinib, has shown encouraging results in patients with crizotinib-resistant, advanced NSCLC, including those with brain metastases. In an early-stage clinical trial, 48% of patients responded to alectinib, with a median duration of response of 13.5 months.

Notably, in 75% of patients with NSCLC and brain metastases, brain lesions shrank with alectinib. This is a promising finding, because chemotherapy...
has had limited efficacy in the central nervous system (CNS), with response rates of only 45%. In late 2015, the FDA approved alectinib for people with ALK-positive NSCLC who cannot tolerate crizotinib or whose cancer worsens after crizotinib.\(^5\) Overall, alectinib was well tolerated, with the most frequently reported adverse effects being nausea and diarrhea. Severe liver enzyme abnormalities occurred in 6% of patients.

Preliminary findings from an ongoing late-stage clinical trial suggest that alectinib may also help previously untreated patients with advanced, ALK-positive NSCLC.\(^5\) In this study, tumors shrank in 92% of patients treated with alectinib compared with 79% of those treated with crizotinib. Patients who received alectinib had a 66% lower risk of disease worsening than those treated with crizotinib.

Moreover, alectinib was better tolerated than crizotinib, causing fewer adverse effects. Only one adverse effect, constipation, occurred in more than 30% of patients in the alectinib group. In contrast, several adverse effects, including nausea, diarrhea, vomiting, and visual disturbance, occurred in more than half of patients treated with crizotinib. Another worldwide phase III trial of this same treatment comparison (ClinicalTrials.gov identifier: NCT02075840) is underway.

**New regimen halts multiple myeloma progression.**

Multiple myeloma is a cancer of plasma cells, which are found in the bone marrow and make antibodies to fight infections. Abnormal plasma cells can crowd out or suppress the growth of other cells in the bone marrow, resulting in anemia, excessive bleeding, and decreased ability to fight infections.

In 2016, an estimated 30,300 people in the United States were diagnosed with multiple myeloma.\(^5\) Multiple myeloma often recurs despite treatment. Fewer than half of people with multiple myeloma will live 5 or more years after diagnosis.

Early findings from a late-stage trial suggest that a three-drug combination may improve outcomes for patients with recurrent or treatment-resistant multiple myeloma.\(^5\) The new regimen adds the novel therapy daratumumab to a standard combination of bortezomib and dexamethasone.

Treatment that incorporated daratumumab resulted in a 70% lower risk of cancer progression than the standard two-drug regimen. In addition, partial response rates were increased from 29% to 59% with daratumumab, and complete response rates from 9% to 19%. Treatment-related adverse effects were generally similar between the two groups. However, low platelet counts, peripheral neuropathy, diarrhea, and anemia occurred more frequently with the daratumumab regimen.

Daratumumab targets a molecule on plasma cells called CD38. It is one of the first cancer treatments with a two-pronged mode of action: it has the ability to destroy cancer cells directly and coax the immune system to attack the cancer. On the basis of results of an earlier clinical trial, the FDA granted daratumumab accelerated approval for the treatment of multiple myeloma in 2015.

Longer patient follow-up is required to determine if the addition of daratumumab helps patients live longer. Meanwhile, a clinical trial of daratumumab combined with a different standard regimen for patients with recurrent multiple myeloma is underway (ClinicalTrials.gov identifier: NCT01615029). Additional clinical trials testing various daratumumab-based regimens in patients with previously untreated multiple myeloma are also in progress (ClinicalTrials.gov identifiers: NCT02252172 and NCT02195479).

**New class of targeted treatments for advanced breast cancer.**

Hormone receptor–positive breast cancer is the most common type of breast cancer. Although hormone (antiestrogen) therapy is the standard of care for patients with hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer, its clinical benefit is modest, and treatment resistance remains a significant challenge.

In 2016, researchers reported updated results from a large clinical trial of a new targeted treatment of metastatic breast cancer: palbociclib.\(^5\) Palbociclib is a pill that works by blocking two molecules involved in breast cancer resistance to hormone therapy: cyclin-dependent kinase 4 (CDK4) and cyclin-dependent kinase 6 (CDK6). CDK4/6 inhibitors are a new class of targeted treatments that may have a role in many different types of cancer in the future.

The study enrolled women with hormone receptor–positive, HER2-negative metastatic breast cancer that had worsened with prior hormone therapy. Women were randomly assigned to treatment with palbociclib plus a standard hormone therapy (ie, fulvestrant) or placebo plus fulvestrant. In the trial, the addition of palbociclib to hormone therapy nearly doubled the median time until the cancer worsened to 9.5 months, compared with 4.6 months with fulvestrant plus placebo. Approximately two-thirds of women experienced clinical benefit from the palbociclib regimen, and one-quarter experienced tumor shrinkage. The benefit of palbociclib was seen regardless of degree of hormone therapy resistance, hormone receptor level, and PIK3CA mutational status. However, the rates of severe adverse effects were substantially higher in the palbociclib group (73% v 22%). The most common adverse effects were low blood counts (neutropenia, anemia, and leucopenia).

Palbociclib has also been studied as initial treatment for advanced breast cancer in combination with hormone therapy. In a large
clinical trial, postmenopausal women with estrogen receptor (ER)-positive, HER2-negative breast cancer were treated with either letrozole plus placebo or letrozole plus palbociclib. Palbociclib extended the median time until the cancer worsened from 14 to 25 months in this study.\(^{56}\) The adverse effects among patients treated with palbociclib plus letrozole were similar to those seen previously with palbociclib in combination with fulvestrant (ie, low blood counts, fatigue, and nausea).

In another clinical trial of first-line therapy for ER-positive, advanced breast cancer, patients were randomly assigned to receive letrozole plus placebo or letrozole plus ribociclib, a CDK4/6 inhibitor.\(^{57}\) In this trial, ribociclib markedly slowed cancer progression. After 18 months, cancer had not worsened in 63% of patients in the ribociclib group, compared with 42% of patients in the placebo group. The clinical outcomes and adverse effects for ribociclib and palbociclib seemed nearly identical.

It is not yet clear if palbociclib or ribociclib will extend overall survival because follow-up has not been sufficiently long nor have any biomarker tests been shown to predict who will or will not benefit from addition of these drugs. However, these findings have already changed the standard of care for patients with hormone receptor-positive metastatic breast cancer. The FDA approved palbociclib plus fulvestrant for women with disease progression after hormone therapy in February 2016.\(^{58}\) Palbociclib was previously approved for use with letrozole as initial hormone therapy for patients with ER-positive, HER2-negative advanced breast cancer.

**More effective treatments for advanced kidney cancer.**

An estimated 62,700 adults were diagnosed with kidney cancer in the United States in 2016.\(^{59}\) Renal cell carcinoma (RCC) is the most common type of kidney cancer in adults. At the time of diagnosis, nearly one-third of patients with RCC have metastatic cancer. The 5-year survival for people with metastatic RCC is only 12%. More information on kidney cancer can be found on Cancer.Net.

Advances in understanding kidney cancer biology led to the development of treatments targeting two molecular pathways: vascular endothelial growth factor receptor (VEGFR) and mammalian target of rapamycin (mTOR). Introduced approximately a decade ago, the treatments extend median survival for patients with advanced kidney cancer from 1 to 3 years. The current standard-of-care treatment for patients with recurrent, advanced kidney cancer includes VEGFR inhibitors axitinib and sorafenib and mTOR inhibitor everolimus.

In 2016, researchers reported findings from a large clinical trial suggesting an even more effective targeted treatment for relapsed RCC.\(^{60}\) Cabozantinib is an oral treatment that blocks several different targets in cancer cells, including tyrosine kinases MET, VEGFR2, and AXL. The median overall survival was 16.5 months in the group of patients treated with standard-of-care everolimus and 21.4 months in the group treated with cabozantinib. Patients who received cabozantinib had a 49% lower risk of cancer progression and substantially higher tumor shrinkage rates (17% v 3%).

Severe-grade adverse effects that occurred more frequently with cabozantinib than with everolimus included high blood pressure, diarrhea, and fatigue. Anemia was more common in the everolimus group. On the basis of the findings from this study, the FDA approved cabozantinib in 2016 for the treatment of advanced RCC in patients who had received prior VEGFR inhibitor therapy.\(^{61}\)

Two other large clinical trials explored VEGFR inhibitors in patients with advanced, nonmetastatic RCC who are at high risk of recurrence after surgery. Up to 40% of patients with stage III RCC experience a relapse with metastasis after kidney cancer surgery.\(^{62}\) There is currently no standard treatment for such patients, and the standard of care after surgery is surveillance.
In the S-TRAC (Sunitinib Treatment of Renal Adjuvant Cancer) trial, patients with stage III clear cell RCC were randomly assigned to treatment with sunitinib or placebo after surgery to remove the tumor. Sunitinib blocks VEGFR and several other molecular targets. The period until the cancer worsened was significantly longer in the sunitinib group (median, 6.8 years) than in the placebo group (median, 5.6 years). The rate of severe adverse effects, such as skin rash, high blood pressure, and fatigue, was higher in the sunitinib group than in the placebo group (63% v 22%). Although these findings are encouraging, longer follow-up is needed to determine whether treatment with sunitinib in this setting prolongs survival.

In contrast, a much larger clinical trial, ASSURE (Adjuvant Sorafenib or Sunitinib for Unfavorable Renal Carcinoma; ECOG-ACRIN E2805), found no significant difference in the duration of disease-free survival between patients who received placebo (median, 6.6 years), sunitinib (median, 5.8 years), or sorafenib (median, 6.1 years) after surgery (this study was funded in part by a grant from the NCI). The most common severe adverse effects in the sunitinib and sorafenib groups were high blood pressure, hand-foot reaction, rash, and fatigue. Five deaths related to treatment occurred: one in the sorafenib group and four in the sunitinib group. The study authors concluded that neither sunitinib nor sorafenib should be used as adjuvant treatment for high-risk, advanced RCC.

Adjuvant VEGFR inhibitors should not be administered in the clinic until additional data are available to reconcile the differing results from the S-TRAC and ASSURE trials. A more compelling signal would be a trend toward survival benefit in either study, which currently does not exist. With multiple other adjuvant VEGFR studies underway, more data should be available to adjudicate the role of this treatment strategy. Physicians should continue to encourage enrollment of patients in ongoing trials that further explore the question.

Promising treatment for ovarian cancer. With survival in the range of 12 to 18 months, women with recurrent ovarian cancer are in desperate need of better therapies. Research findings reported in 2016 may lead to a new approach to treat this difficult cancer. In an early-stage clinical trial, four of 10 women with folate receptor alpha–positive ovarian
cancer resistant to standard platinum chemotherapy experienced tumor shrinkage after receiving IMGN853 (mirvetuximab soravtansine). The most common adverse effects were diarrhea, eye problems, cough, fatigue, and decreased appetite. IMGN853 belongs to the new class of cancer therapies known as ADCs. It comprises an antibody targeting folate receptor alpha (a marker found in most ovarian cancers) and a potent anticancer drug called DM4, which blocks cell division and growth. Additional clinical trials of IMGN853 in women with folate receptor alpha-positive ovarian cancer are already underway (ClinicalTrials.gov identifiers: NCT02631876 and NCT02606305).

**COMBINED MODALITY THERAPY**

It is common that patients with cancer receive two or more treatments at a time, at least at some point during the course of their illness. Such common modality therapies can work better than standalone treatments, but this improved efficacy often comes with more adverse effects. As with all new approaches, before any new combination of treatments becomes part of routine care, its benefits and safety need to be evaluated in a clinical trial against a standard treatment regimen. Last year, clinical trials delivered important advances in combined modality therapies for brain cancer, neuroblastoma, and colorectal cancer.

**Adding chemotherapy to radiation therapy extends glioma survival.** In 2016, scientists reported long-awaited results from a federally funded clinical trial of patients with grade 2 glioma (this study was funded by a grant from the NCI). Grade 2 gliomas are rare, accounting for only 5% to 10% of all brain tumors, and often occur in younger people. Although low-grade gliomas grow slower than other types of brain cancer, they lead to worsening neurologic symptoms and often premature death.

In the study, patients were randomly assigned to receive radiation therapy alone or radiation therapy followed by PCV (procarbazine, CCNU, and vincristine) chemotherapy. The median survival was substantially longer among patients treated with chemotherapy and radiation therapy (13.3 years) than among those who received radiation therapy alone (7.8 years). Addition of chemotherapy also slowed the course of the disease; at 10 years, the cancer worsened in only 21% of patients in this group. In contrast, cancer worsened in 51% of patients treated with radiation therapy alone. This study led to a change in the standard of care for high-risk, low-grade gliomas; PCV chemotherapy is now added to radiation therapy.

**More effective regimen for children with high-risk neuroblastoma.** Neuroblastoma is the second most common solid tumor in children and the most common cancer in infancy. It begins in nerve cells outside of the brain. Approximately 700 children are diagnosed with neuroblastoma each year in the United States, most younger than age 6 years. High-risk neuroblastoma requires intensive treatment, which may include surgery, chemotherapy, radiation therapy, and/or autologous stem cell transplant (ASCT). Despite all these treatments, fewer than half of children will survive 5 years after diagnosis of a high-risk neuroblastoma.

A federally funded trial performed by the Children's Oncology Group found that adding a second autologous stem cell transplant or ASCT to standard therapy can improve patient outcomes (this study was funded in part by a grant from the NCI). At 3 years, cancer had not recurred in 61% of patients who had undergone two transplantations, compared with 48% of patients who had undergone one.

The 3-year survival rate was slightly higher in the double transplantation group than in the single transplantation group (74% vs 69%), but this difference was not statistically significant. This study was not designed to observe a difference in overall survival between the two treatment groups. However, given that most neuroblastoma recurrences occur within 2 to 3 years of diagnosis, patients who had not experienced a recurrence at 3 years had a better chance of long-term survival.

The rates of severe adverse effects, such as infections and liver problems, were similar between the two treatment groups, although fewer treatment-related deaths occurred with double transplantation. Nonetheless, it is important to keep in mind that the combination therapy for high-risk neuroblastoma is one of the most aggressive cancer regimens administered to children. Longer patient follow-up is needed to determine if there are any long-term or late-onset adverse effects of this therapy.

**Colon tumor location: a factor to consider in treatment decisions.** An unexpected factor may help explain why some patients with colorectal cancer do better than others. According to an analysis of data from a large clinical trial, patients with advanced colorectal cancer live longer if the cancer begins on the left side of the colon rather than on the right side.
(this study was funded in part by a grant from the NCI). In the trial, patients received a combination of FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or FOLFIRI (fluorouracil, leucovorin, and irinotecan) chemotherapy with either of the two standard targeted therapies for advanced colorectal cancer: cetuximab or bevacizumab. In prior research, the two treatments yielded similar survival. In this analysis, the median survival for patients with left-sided tumors was 33 months, but it was only 19 months for those with right-sided tumors.

A separate analysis of data from two other clinical trials also found that patients with advanced colorectal cancer that began on the left side of the colon lived longer than those with cancers that began on the right side. Among patients with left-sided tumors, the combination of cetuximab and FOLFIRI was more effective than bevacizumab and FOLFIRI, whereas patients with right-sided tumors experienced limited benefit from either regimen.

For now, the compelling findings from these studies suggest that clinicians should take into account the location of the primary tumor when making treatment decisions for patients with advanced colorectal cancer. For patients with a right-sided colorectal cancer, cetuximab may not provide a benefit. However, for those patients whose tumors originate in the left colon, either a bevacizumab- or cetuximab-based regimen is effective, with cetuximab seeming to produce the best outcomes when combined with chemotherapy.

Finally, an analysis of pooled data from 66 clinical trials and more than 1.4 million patients revealed that left-sided primary colon tumors were associated with a better prognosis than right-sided tumors, irrespective of cancer stage. Overall, patients with left-sided tumors had a 20% lower risk of death. This analysis suggests that the location of primary tumor should be considered when establishing prognosis and designing future clinical trials in both early and advanced colorectal cancers.

**COLORECTAL TUMORS: RIGHT OR LEFT?**
The answer might influence a patient’s survival and treatment choices, according to a new study of patients with advanced colorectal cancers.

**RIGHT**
- Ascending colon
- Cecum
- Descending colon
- Rectum
- Sigmoid colon

**LEFT**
- Colon
- Rectum
- Sigmoid colon

**CHEMOTHERAPY**
Even in the era of precision medicine, chemotherapy remains a key treatment modality for many patients with cancer. Along with development of new chemotherapies, researchers are exploring new ways to use conventional chemotherapies. The past year brought important advances in chemotherapy for treatment of patients with pancreatic cancer and leukemia.

**Pancreatic cancer: two-drug regimen increases chance of living longer.** Pancreatic cancer is often difficult to diagnose. As a result, it is often not found until it has spread from the pancreas to other parts of the body and can no longer be removed with surgery. Overall, only 29% of patients with pancreatic cancer will be alive 1 year after diagnosis. As the fourth leading cause of death resulting from cancer in the United States, pancreatic cancer took an estimated 42,000 lives in 2016.

Patients who are diagnosed early enough for surgical removal of the tumor have a chance of longer survival. For the past two decades, the standard of care after pancreatic cancer surgery has been gemcitabine chemotherapy, which is administered to eliminate remaining cancer cells and reduce the chance of relapse. However, the benefit of gemcitabine is relatively modest, with only 20% of patients surviving 5 years.

A recent clinical trial found that adding a second chemotherapy drug, capecitabine, to gemcitabine can help such patients live even longer. The median survival was 28 months in the group of patients treated with the two-drug regimen and 25.5 months in the group that received gemcitabine alone. Despite a small difference in median survival, addition of capecitabine increased the chance of surviving 5 years from 16% to 29%.

These results have set a new standard of care for use of gemcitabine plus capecitabine as adjuvant (postsurgery) therapy after pancreatic cancer surgery. Gemcitabine and capecitabine are both FDA approved for use in several different cancers and are available as generic medicines.

The combination regimen was well tolerated overall, with no significant increase in adverse effects compared with gemcitabine alone. The safety of the gemcitabine–capecitabine combination allows for the possibility of adding other treatments to this regimen with the goal of further improving patient benefit.

**High-risk AML: new packaging of conventional drugs extends survival.** With current therapy, people with AML live only approximately 6 months after diagnosis. There has been little improvement in AML survival in the last few decades, but last year brought not only a promising new targeted therapy (described under Targeted Therapy), but also an
improved chemotherapy regimen. The new medicine, called CPX-351, packs cytarabine and daunorubicin into a liposome, which helps the chemotherapy slip into leukemia cells. CPX-351 was investigated in a late-stage clinical trial of older patients newly diagnosed with secondary AML. Secondary AML can develop as a result of treatment of another cancer or environmental exposure to radiation or certain chemicals.

In the study, patients who received CPX-351 lived approximately 4 months longer (median survival, 10 months) than those who received standard combination chemotherapy (median survival, 6 months) with the same drugs. At 2 years, 31% of patients were alive in the CPX-351 group versus 12% of patients in the standard chemotherapy group. There were no differences in adverse effects between the two groups of patients.

These findings represent a long-awaited advance in treatment of older adults with high-risk or secondary AML. The FDA has granted CPX-351 a breakthrough therapy designation for treatment of patients with AML.

NEW CONCERNS ABOUT LAPAROSCOPIC RECTAL CANCER SURGERY

In recent years, laparoscopic surgery has emerged as an attractive alternative to the traditional open surgery because of its shorter recovery time and lower rate of complications. The procedure is performed with the aid of a video camera and instruments inserted through small incisions in the abdomen.

Patients with early and locally advanced rectal cancer can be cured with surgery, provided the tumor tissue is completely removed. However, the choice between open and laparoscopic surgery is not easy to make for such patients. Experts have raised concerns that laparoscopic surgery may not remove tumor tissue as completely as open surgery does. As a result, patients who undergo laparoscopic surgery may have a greater chance of cancer recurrence and consequently shorter survival.

In one recent clinical trial, rates of surgical success (ie, complete tumor removal) were found to be substantially lower among patients with rectal cancer who underwent laparoscopic surgery than among those who underwent open surgery (82% v 87%). Similar trends were seen in another large trial, where successful surgery was achieved in 82% of patients undergoing a laparoscopic procedure and 89% of patients undergoing open surgery.

These findings confirm concerns that laparoscopic surgery may lead to more cancer recurrences and shorter survival. Patients enrolled in these two trials will continue to be observed to answer this question. Meanwhile, routine use of laparoscopic surgery is not recommended for patients with stage II or III rectal cancer. In contrast, laparoscopic surgery is a well-accepted procedure for patients with colon cancer.

LONGER HORMONE THERAPY FURTHER REDUCES BREAST CANCER RECURRENT

Breast cancer can recur many years after a woman completes treatment for early-stage, hormone receptor–positive breast cancer. To lower the chance of recurrence, many women receive hormone therapy after surgery. In 2016, researchers reported that extending a form of hormone therapy called aromatase inhibitors from the standard 5 years to 10 years may further reduce the risk of recurrence.

The study enrolled postmenopausal women with early breast cancer who had completed 5 years of aromatase inhibitor hormone therapy either as first-line treatment or after tamoxifen. The women were randomly assigned to receive the aromatase inhibitor letrozole for 5 additional years or placebo.

The chance of breast cancer recurrence or development of a second cancer in the opposite breast was 34% lower in the letrozole group than in the placebo group. At 5 years of follow-up, 95% of women in the letrozole group and 91% of women in

A POLICY FOCUS: ROBUST FEDERAL FUNDING NEEDED FOR CANCER RESEARCH PROGRESS

ASCO continues to urge legislators to make a robust national investment in medical research through the National Institutes of Health (NIH) and the National Cancer Institute.

For much of the past decade, federal funding for biomedical research has been flat, and in inflation-adjusted dollars, the NIH budget was 20% lower in 2016 than it was a decade before. This dramatic drop in funding limits the ability of scientists to conduct important research that advances the prevention, diagnosis, and treatment of cancer for millions of people.

Even under tight budgetary constraints, Congress must provide consistent and predictable funding increases to continue our momentum to prevent cancer and improve cancer treatment for patients.

the placebo group remained breast cancer free. The rates of second breast cancers were lower in the letrozole group (0.2% v 0.5%). Nonetheless, 5-year survival rates were not significantly different between the two groups (letrozole, 94% v placebo, 93%).

Adverse effects of hormone therapy can be difficult to bear, particularly over a long period of time. Although bone pain, fractures, and osteoporosis occurred more frequently with letrozole than with placebo, researchers found no significant differences in either overall quality of life or menopause-specific symptoms.

Furthermore, a separate analysis of more than 45,000 patients who were observed for 15 years after receiving 5 years of hormone therapy provides a more accurate estimate of the risk of breast cancer recurrence according to initial tumor stage, grade, and lymph node status. The findings will help inform decisions about continuing hormone therapy beyond 5 years.

These findings are important to millions of women around the world who receive a diagnosis of hormone receptor–positive breast cancer each year. They provide much-needed direction to physicians and patients discussing whether to extend hormone therapy beyond the previous standard of 5 years, particularly in women who found the first 5 years of treatment acceptable.

For additional notable advances in cancer treatment, please see Appendix Table A1.
Along with other areas of medicine, the cancer community has embraced the concept of patient-centered care. Patients today are encouraged to take an active role in their care from the moment of diagnosis, and the latest research highlights both challenges and solutions for ensuring every patient receives quality cancer care.

First, 2016 marked important milestones in two key initiatives that hold great promise for people with cancer: CancerLinQ, ASCO’s big-data initiative to rapidly improve the quality of cancer care, and the TAPUR (Targeted Agent and Profiling Utilization Registry) study, which is the first clinical trial conducted by ASCO.

In addition, an advance has been made in preventing nausea and vomiting in patients receiving chemotherapy. Researchers have identified a more powerful medication combination that will help ease these challenging adverse effects of treatment. Not only does this advance improve patients’ quality of life, it also helps more people complete the full dose and course of chemotherapy.
A POLICY FOCUS: IMPORTANCE OF DATA SHARING IN CANCER CARE AND RESEARCH

ASCO continues to advance policies that improve the widespread interoperability of electronic health records, which refers to the ability to identify, extract, and use health care data within and among systems. Interoperability is essential for the complex treatment of cancer because multiple health care providers using different information systems need a way to exchange detailed clinical information to coordinate care effectively. Furthermore, interoperability will provide a critical foundation for big-data efforts, including ASCO’s CancerLinQ initiative, which holds great promise in unlocking advances by distilling massive volumes of clinical data from large groups of patients with cancer.

ASCO was a major supporter of the 21st Century Cures Act, and congratulated President Obama, Vice President Biden, and Congress when the legislation was signed into law and funded in December 2016. The law includes provisions to advance interoperability, such as requiring the secure access, transfer, exchange, and use of all electronically accessible health information for authorized purposes, and banning information blocking, which is the practice of knowingly and unreasonably interfering with the exchange or use of electronic health information.

Now that 21st Century Cures Act has been signed into law, ASCO will continue to serve as a resource to policymakers to support implementation.

New tools and programs, such as a Web-based tool for self-monitoring symptoms and patient navigation and education programs for underserved populations with lower health literacy, are being developed to improve care and quality of life. Such programs will become increasingly important in the era of precision medicine.

Finally, a major study reported in 2016 provides long-awaited answers about outcomes with three standard approaches for early prostate cancer: active surveillance, surgery, and radiation therapy. The findings will inform physician and patient discussions about treatment.

ASCO ADVANCES PATIENT CARE THROUGH PRECISION MEDICINE AND BIG DATA

In early 2016, CancerLinQ—ASCO’s big-data initiative to rapidly improve the quality of care for people with cancer—went live. The number of participating oncology practices grew steadily throughout the year, ranging from small private practices to some of the leading cancer centers in the nation. More than 70 vanguard practices in 40 states and the District of Columbia have signed on to feed patient data into CancerLinQ and use the system in their practices. The rapid-learning system run by CancerLinQ, a wholly owned nonprofit subsidiary of ASCO, is now drawing on more than 1 million patient records from across the United States.

In addition, CancerLinQ has agreements in place with Cancer Informatics for Cancer Centers (CI4CC) and SAP. The collaborative agreement with CI4CC, which represents senior informatics leaders and chief data scientists at NCI-designated cancer centers and other major medical and research institutions across the nation, will bring the nation’s leading clinical, genomic, and biomedical informaticists, academicians, and data scientists together with the oncology community to help improve cancer care through CancerLinQ. The CancerLinQ platform was codeveloped with SAP using the SAP Connected Health platform that runs on SAP HANA, a flexible, in-memory data management and application platform created by SAP.

CancerLinQ is continuing to add new practices and will soon enable the cancer community to begin to gain critical insights from the growing data resources of the system that will improve cancer care and spark new research.

The ASCO TAPUR study (ClinicalTrials.gov identifier: NCT02693535) was also launched in 2016, officially opening patient enrollment on March 14. TAPUR is designed to evaluate molecularly targeted cancer drugs and collect data on clinical outcomes to learn about additional uses of these drugs outside of indications already approved by the FDA. It will offer flexibility, allowing physicians to choose the tumor specimen or blood sample and genomic profiling test; use broad general eligibility criteria; and streamline data collection and reduce the overall amount of data collected.

The precision medicine trial has enjoyed robust expansion in just its first year, continuously adding both patients and participating sites. As of
In the first 24 hours after chemotherapy, the proportion of patients who were nausea free was much higher in the olanzapine group than in the placebo group (74% v 45%), and over a 5-day period after chemotherapy (37% v 22%).

These findings add to evidence from other clinical trials suggesting the benefit of olanzapine in preventing chemotherapy-related nausea and vomiting. Olanzapine is approved by the FDA for treatment of psychosis. The adverse effects typically include mild short-term sedation, weight gain, and increased risk of type 2 diabetes. In this study, patients who received olanzapine had drowsiness on the second day, which subsided in the subsequent days. There were no serious adverse effects related to olanzapine.

PATIENT SELF-REPORTING OF SYMPTOMS IMPROVES CARE

Most patients with advanced cancer will experience symptoms while receiving treatment. Physicians or nurses typically ask patients about their symptoms only during clinic visits, and toxicity data in clinical trials are biased according to selection of patients who enroll in the trials (compared with the average patient in practice who receives the drug) and by the limited nature of gathering the data. As a result, symptoms that are more common in patients who may not be represented in the trials and that appear or change between visits can be missed or simply forgotten and can thus go untreated.

In the past several years, more efficient ways of monitoring symptoms have been proposed. One of these involves collecting symptom information directly from patients through standardized questionnaires, without physician interpretation.

VOICES OF CANCER RESEARCH

LORI WALLACE-PUSHINAITIS

When Lori received her second breast cancer diagnosis in 2014, the cancer had already spread throughout her body. However, despite having advanced disease, Lori spent more than a year on a clinical trial for lurbinectedin, seeing slow and steady improvement for 14 months until the cancer began to grow again.

Still committed to exploring her options, Lori has moved on to other treatments. She is grateful, however, as she feels clinical trials have given her more time with her son.

Lori is a volunteer with the Bay Area Young Survivors (BAYS), Mets in The City (MITC), Facing Our Risk of Cancer Empowered (FORCE), Young Survival Coalition (YSC), and METAvivor.
Patient navigators guide patients through all the complexities of multidisciplinary cancer care. This may include ensuring that patients schedule and attend physician visits, start cancer therapy as soon as possible, and take prescription medicines as directed.

A recent report describes a navigation program designed to reduce the challenges faced by underserved minority patients with cancer. Although minority women in the United States are less likely to develop breast cancer, they are more likely to die as a result of breast cancer than white women. The higher breast cancer death rate among minority women results in part from treatment delays and patients not sticking to treatment.

In the study, patients diagnosed with breast cancer were paired with a patient navigator, while a second group of patients received usual care (ie, without the help of patient navigators). Most of the patients were either African American (45%) or Hispanic (38%), and 72% were enrolled in a program. The navigators met with patients at all radiology and oncology medical appointments, as well as on the day of surgery. They also provided financial consultations and helped negotiate payments, as needed.

Patients who received help from patient navigators began cancer treatment sooner than those who received usual care and had better compliance with treatment after surgery. On average, women in the patient navigation group started chemotherapy approximately 30 days earlier and hormone therapy approximately 95 days earlier than those in the usual care group. Patient compliance with either chemotherapy or hormone therapy was 100% among women in the navigation program. In contrast, among women who received usual care, only 57% were compliant with chemotherapy and 69% with hormone therapy.

This approach is part of a growing recognition of the importance of patient-reported outcomes in medicine and patient-centered health care in general.

A large clinical trial recently showed how one patient-reported outcome tool can have positive effects on the well-being of patients with cancer. In the study, patients receiving chemotherapy for advanced breast, genitourinary, gynecologic, or lung cancer were randomly assigned to the self-reporting group or the usual care group.

Self-reporting was conducted via a Web-based questionnaire that covered 12 common symptoms, such as appetite loss, constipation, cough, diarrhea, and fatigue. The tool triggered e-mail alerts to nurses whenever patients reported symptoms worsening. Usual care consisted of discussing and documenting symptoms during patients’ visits with their oncologists.

Over a 6-month period, more patients in the self-reporting group (34%) had an improvement in health-related quality of life (HRQL) than in the usual care group (18%). Conversely, fewer patients in the self-reporting group (38%) had worsening of HRQL than in the usual care group (53%). HRQL measures mobility, self-care, usual activities, pain or discomfort, anxiety, and depression. More studies are needed to determine if symptom self-reporting would have such a large benefit in other care settings, but this and other studies have proven that this technology holds promise in the supportive care of patients receiving cancer treatment.

PATIENT NAVIGATION PROGRAM IMPROVES COMPLIANCE WITH CANCER THERAPY

The first patient navigation programs were developed nearly three decades ago to improve access to cancer screening. Since then, a variety of such programs have been launched to help people, particularly those in medically underserved communities, overcome barriers to receiving quality care—from diagnosis through treatment and survivorship.

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measure their level of health literacy. The written questionnaire covered knowledge of genetics, participants’ confidence in their ability to use genetic information, and perceived importance of genetic information and family history. Most participants were aware of the importance of family health history and were sure they could talk about it with family members; however, approximately half of participants (47%) were found to have limited health literacy.

People with limited health literacy had lower genetics-related knowledge and lower awareness of the value of knowing family health history. Those with limited health literacy were more likely to think that learning about their genetic information was important, compared with those with adequate health literacy; however, they were less likely to think that family health history information was important. Interestingly, people with limited health literacy were more likely to discuss family health history with their physicians than those with adequate health literacy.

These findings underscore the need for education programs to improve health literacy, particularly with regard to genetics. An informed patient is able to make better decisions regarding genetic testing and screening and how these tools may be used to inform his or her health care.

These findings affirm that use of navigators within cancer centers is vital to improving cancer care, especially in medically underserved and vulnerable populations.

ADDRESSING HEALTH LITERACY IN THE ERA OF PRECISION MEDICINE

Genomics-based targeted cancer therapies have had a major, positive effect on modern cancer therapy. However, the ability to offer truly personalized cancer care to most patients will require lower costs for genomic testing and faster sample processing times. Not all communities and individuals have equal access to genomic testing, and such testing may not even be clinically informative for many patients. Another challenge is that precision medicine and its associated terminology are complex.

Recent research suggests that the public may not fully understand the current possibilities and limitations of genetic or genomic information, including results of genetic testing. One reason may involve the health literacy level of consumers, meaning how much people do or don’t understand health and medical information. For instance, one study shows that understanding health information is an important factor in how people perceive the importance of genetic testing (this study was funded in part by a grant from the NIH). Those with high health literacy scores tended to understand the importance and implications of genetic testing better than those who had low or limited health literacy scores. These findings are relevant whenever genetic testing is used to inform patient care, regardless of disease.

In the study, researchers surveyed more than 600 patients at a primary health clinic of a large hospital, which serves a diverse patient population in the St Louis, Missouri, area. Participants were asked to complete a written questionnaire followed by a set of verbally administered questions to...
CANCER WORSENED IN MORE MEN IN THE ACTIVE SURVEILLANCE GROUP than in men who received either surgery or radiation plus hormone therapy.

Active Surveillance: 20% cancer worsened
Surgery: 8% cancer worsened
Chemotherapy: 8% cancer worsened

EXCELLENT 10-YEAR SURVIVAL FOR PATIENTS WITH EARLY PROSTATE CANCER, REGARDLESS OF TREATMENT

One in eight men will be diagnosed with prostate cancer at some point during his lifetime. In 2016 alone, an estimated 181,000 men received a prostate cancer diagnosis. In recent decades, widespread prostate-specific antigen (PSA) testing has increased prostate cancer diagnoses and treatment. However, because prostate cancer often grows slowly, many men who are diagnosed with early cancer die as a result of other causes before they succumb to prostate cancer. This means that treatment of early prostate cancer is not always necessary. Prostate cancer treatment may also cause complications, such as sexual, urinary, and bowel problems.

In addition, the choice of treatment for men with prostate cancer that is detected on the basis of PSA testing is controversial. A recent clinical trial provided answers to a long-standing question in prostate cancer care: which approach is best in treating localized, early-stage prostate cancer: surgery, radiation therapy, or active surveillance?

The trial randomly assigned 1,643 men diagnosed with localized prostate cancer to either active surveillance, surgery (radical prostatectomy), or radiation therapy with short-course hormone therapy. PSA levels were regularly measured in men assigned to active surveillance, and those with rising PSA levels had the option of continuing surveillance or receiving curative therapy, including surgery and radiation therapy.

After a median follow-up period of 10 years, there were no significant differences among the three groups in rate of prostate cancer-related deaths (approximately 1%). Similarly, there were no differences in the number of deaths resulting from any cause. However, cancer had worsened in more men in the active surveillance group (20%) than in men who received either surgery (8%) or radiation therapy plus hormone therapy (8%). Likewise, the rate of metastasis was higher in the active surveillance group (6%) than in either the surgery (2%) or radiation therapy plus hormone therapy group (3%).

This trial addresses the important question of clinical effectiveness regarding these three approaches to treating early, localized prostate cancer. Although the findings suggest that immediate active treatment is more effective than active surveillance to avoid disease worsening, longer follow-up may be needed to see if there are differences in death rates across the three approaches. Meanwhile, the insights from this study will inform treatment discussions between physicians and patients.

For additional notable advances in patient care, please see Appendix Table A1.
The biology of a cancer is constantly changing. New genetic mutations appear as the tumor grows and spreads, providing new challenges for treatment and also new avenues of research for the development of additional therapies. In 2016, a landmark study provided an in-depth view of the pattern of genetic changes during development of melanoma from precursor lesions (precancer).

Cancers can also develop new genetic mutations that make them resistant to cancer therapy. Two early studies suggested that matching genetic changes in the tumor with specific treatments that target those genetic changes improves outcomes for patients with advanced cancer.
THERAPEUTIC OPTIONS EXPAND WITH PRECISION MEDICINE APPROACHES

Sadly, almost every patient with advanced cancer eventually reaches a point when there are no effective treatments left. In the current era of precision medicine, however, molecular testing of the tumor is opening additional treatment options for some of these patients.

One recent study supports the use of comprehensive genomic testing in patients who have hard-to-treat cancers. Researchers analyzed changes in 236 genes from the tumors of more than 300 patients with different cancers. So-called actionable mutations, or mutations that could be targeted with an existing therapy, were found in nearly all patients (93%), and 38% received a therapy matched to the mutation. Patients with more actionable mutations and matched therapies had more frequent and longer remissions, as well as longer survival.

An ongoing trial is assigning patients with advanced cancer whose prior genetic tests revealed abnormalities in specific molecular pathways to corresponding targeted treatments. The treatment assignments are outside of FDA-approved indications. Tumors shrank in 29 (22%) of the first 129 patients enrolled in the study; these patients had 12 different types of cancer.

For additional notable advances in tumor biology, please see Appendix Table A1.
LIQUID BIOPSIES HELP PERSONALIZE CANCER THERAPY

Nearly every patient with suspected cancer will undergo a tumor biopsy. In fact, tumor biopsy is the main way physicians diagnose most types of cancer and determine their grade or stage. In addition, biopsies can also be used to make treatment decisions. By analyzing the genetic material in the tumor specimen, physicians may uncover genetic changes that can be matched to specific targeted therapies. However, although tumor biopsy has been a critical part of cancer care for decades, depending on the location of the tumor and the patient’s general health, performing a tumor biopsy may not always be feasible or safe.
Physicians have followed circulating tumor biomarkers to monitor patient status for decades, including carcinoembryonic antigen (CEA), cancer antigen 125 (CA-125), CA 15-3/CA 27.29, CA 19-9, and PSA for colorectal, ovarian, breast, pancreatic, and prostate cancers, respectively. Over the last 15 years, strategies to capture and enumerate circulating tumor cells have also been reported. More recently, several investigators have reported the ability to purify and characterize circulating, cell-free tumor DNA. These approaches have been dubbed liquid biopsies. They offer the opportunity to easily and conveniently determine changes in both the amount of tumor burden and the genotype and phenotype of the cancer over time.

In a liquid biopsy, circulating tumor DNA is collected from bodily fluids and analyzed, providing what seems to be representative information about genetic changes in the tumor. Because genetic changes evolve as cancers grow and spread, this information can be used to stop a treatment to which resistance is emerging, as has been done with circulating proteins and tumor cells for years, or, perhaps more exciting, to switch to a different treatment that is tailored to a different mutation as it appears.

Even for patients who are able to undergo a traditional tissue biopsy, a liquid biopsy may be safer, quicker, and more convenient—and perhaps even more informative. For example, a biopsy only represents a single site of disease, and studies of tumor heterogeneity tell us that different tumor sites in the same patient may have different genotypes and phenotypes. Thus, a liquid biopsy may provide a snapshot of the tumor makeup of the entire body, not just that of the biopsied site.

Another advantage of a liquid biopsy is its potential to provide a snapshot of the full landscape of genetic changes present in a tumor. Different parts of the tumor often have genetically distinct groups of cells. Because a tissue biopsy takes only a small piece of the tumor, some key mutations may be missed. Nonetheless, research also shows that liquid biopsies sometimes fail to detect key mutations that are revealed by tissue biopsy tests.

Liquid biopsy informs lung cancer treatment decisions. One liquid biopsy test has already become part of routine care for patients with advanced lung cancer, and others are being developed using a variety of technologies. The test screens circulating tumor DNA from the blood for a specific mutation in the *EGFR* gene: T790M. This mutation occurs in approximately 60% of patients who develop resistance to epidermal growth factor receptor (EGFR)-targeted drugs, afatinib, gefitinib, and erlotinib.

It is important to know whether a patient has the T790M mutation because new treatments that specifically target this genetic change are available (eg, osimertinib and rociletinib). However, patients who do not have the T790M mutation should not receive such treatments, because they are less effective against T790M-negative tumors.

Tumor testing for T790M is now recommended for all patients with EGFR-positive NSCLC that worsens despite EGFR-targeted therapy. However, many patients are not able to have the test done; the tumor may be in an inaccessible location, there may be insufficient tissue available, or a biopsy may not be safe because the patient is in poor health. For such patients, a liquid biopsy test is now available. The blood test, known as cobas *EGFR* Mutation Test v2, was FDA approved in 2015 to identify patients who may benefit from osimertinib. In 2016, the test was also approved for use as a companion diagnostic to help identify patients with a different type of *EGFR* mutation who may benefit from initial treatment with erlotinib. In an early study, the liquid biopsy test identified six in 10 patients who had T790M-positive tumors. This is good news for patients who are unable to undergo a traditional tissue biopsy.

Meanwhile, several other promising liquid biopsy tests for patients with lung cancer are being explored. A blood test using a technique known as BEAMing identified seven of 10 patients with T790M mutations in their tumors (this study was funded in part by a grant from the NIH). A different test that uses so-called droplet digital polymerase chain reaction identified eight of 10 patients with T790M-
positive tumors (this study was funded by a grant from the NCI). The latter test can also screen for other EGFR as well as KRAS mutations.

Finally, another early clinical trial found that response to the EGFR-targeted therapy rociletinib was similar irrespective of whether T790M status was determined through traditional tissue biopsy or liquid biopsy of urine or blood. The researchers used BEAMing technology for blood mutation analysis and a technique known as short footprinting for urine. Blood and urine testing identified several T790M-positive cases that were missed by tissue biopsy.

These studies confirm that the accuracy of molecular testing using either blood or urine samples is high and that such testing predicts outcomes from EGFR therapy similar to those predicted by traditional tumor biopsy. Moreover, early findings show that regardless of how the T790M mutation is detected (liquid or traditional tumor biopsy), patients respond to osimertinib and rociletinib equally well.

However, a negative liquid biopsy test is not as reliable as a negative tumor biopsy test. Therefore, whenever possible, patients with a negative blood or urine test should have tumor tissue tested for confirmation.

Liquid biopsy may open new targeted treatment options. Another liquid biopsy test was reported last year that could rapidly and accurately screen blood samples for a broad panel of genetic changes, including EGFR T790M. An analysis of blood samples from 15,000 patients with 50 different types of cancer showed that the patterns of genetic changes in circulating tumor DNA were similar to those in the tumor.

The blood test detected 94% to 100% of changes in EGFR, BRAF, KRAS, ALK, RET, and ROS1 genes that had been found previously in tumor biopsy analyses from the same patients. It also provided leads for targeted therapy that could be matched to the genetic changes found in the circulating tumor DNA. The researchers identified such additional treatment opportunities for approximately two-thirds of patients who had insufficient tissue available for a biopsy.

Liquid biopsy predicts colon cancer recurrence. In 2016, researchers proposed an entirely different use for liquid biopsies. According to a large study, measuring circulating tumor DNA from the blood can accurately predict which patients with stage II colon cancer are at risk for recurrence (this study was funded in part by a grant from the NIH). Detection of circulating tumor DNA after colon cancer surgery is a sign that some cancer cells have been left behind, and this puts the patient at higher risk of recurrence.

Overall, patients with stage II colon cancer have a low risk of recurrence, and four of five are cured with surgery alone. Patients who are at high risk of recurrence may need additional treatment after surgery to lower the chances of recurrence. This new blood test may help identify more patients who might benefit from receiving chemotherapy after surgery.

In the study, nearly 80% of patients who had circulating tumor DNA detected in the blood after surgery experienced a recurrence of colon cancer. In contrast, only 10% of patients who tested negative for circulating tumor DNA experienced a recurrence. These findings are relevant to more than 300,000 people around the world who are diagnosed with stage II colon cancer each year.

EXPANDING TARGETED THERAPY OPTIONS FOR OVARIAN CANCER

Worldwide, more women die from ovarian cancer than from any other gynecologic cancer. Although initial treatment of ovarian cancer with chemotherapy is usually effective, most patients will eventually experience a recurrence. Patients with recurrent ovarian cancer have limited treatment options, and median survival is generally reported as between 1 and 2 years from diagnosis.

Standard treatments for recurrent ovarian cancer include bevacizumab, which halts cancer growth for approximately 3 months, and the novel targeted treatment olaparib. Olaparib was the first treatment in a new class of targeted therapies that block PARP, a protein that repairs damaged DNA. Although olaparib is more effective than bevacizumab, it is only approved for use in patients with BRCA gene mutations, who account for just 10% to 15% of all women with ovarian cancers.

In 2016, researchers reported that a different PARP inhibitor, niraparib, is effective in a broader range of patients with advanced, recurrent ovarian cancer. The late-stage clinical trial included two groups of patients: women with germline (heritable) BRCA mutations and those without such mutations. Within the group lacking a BRCA mutation, there was a subset of patients with another defect in DNA repair processes called homologous recombination DNA repair deficiency (HRD). All patients had ovarian cancer that responded to platinum-containing chemotherapy.

The patients were randomly assigned to receive niraparib or placebo. Niraparib slowed cancer growth in all patient groups, but it was most effective in patients with BRCA mutations. In this group, the median time until the cancer worsened was 21 months with niraparib and 5.5 months with placebo. Among patients without BRCA mutations, cancer worsened after a median period of 9.3 months with niraparib, compared with 3.9 months with placebo. In the subset of patients with HRD, the
median time to cancer progression was 12.9 months with niraparib and 3.8 months with placebo.

The most common severe adverse effects related to niraparib included low blood counts and anemia. Patients who received niraparib reported a quality of life comparable to that reported by those who received placebo.

These findings suggest that the benefit of niraparib is not restricted to patients with a known germline BRCA1 mutation, expanding access to PARP inhibitors. However, further work is needed to determine the most appropriate strategy for use of PARP inhibitors in this population.

CANCER MOONSHOT: GALVANIZING A RENEWED COMMITMENT TO CONQUERING CANCER

During his final State of the Union address, President Obama launched the Cancer Moonshot to renew the nation’s commitment to conquering cancer. Led by Vice President Joe Biden, the National Cancer Moonshot Initiative aligned the resources of the federal government to accelerate progress in cancer research and encouraged greater collaboration within the entire cancer research community.

Throughout 2016, Biden met with a wide range of stakeholders to better understand the current cancer research and cancer clinical practice environment—both opportunities in and barriers to providing cancer care and conducting cancer research in the United States. Working with the Cancer Moonshot Task Force (which included representatives from all federal agencies involved in cancer clinical care and research), Biden made a series of announcements to take immediate action to improve cancer research.

ASCO worked closely with Biden’s Moonshot team, submitting recommendations to Biden, the Task Force, and NCI Blue Ribbon Panel; speaking at public forums; engaging in strategic discussions; and welcoming Biden to address the world’s cancer leaders who convened at the ASCO Annual Meeting in Chicago in June 2016.

The Cancer Moonshot rightly called for patients with cancer to become our shared and primary focus. President Obama and Biden challenged the cancer community to unite and work together in recognition that the whole will be far greater than the sum of its parts. The Cancer Moonshot also addressed the entire continuum of cancer care to speed advances in cancer prevention, diagnosis, treatment, supportive care, survivorship, and end-of-life care. Biden made an important decision to include all types of cancer.

The Cancer Moonshot Initiative spurred public and private sector organizations into action and jumpstarted collaborations to accelerate the nation’s progress in fighting life-threatening cancers that affect so many. To continue the momentum in our work to conquer cancer, ASCO has urged Congress and the new Administration to take the following steps:

- Advance initiatives to improve interoperability of health care information, which will help improve patient care and support quality measurement and research.
- Identify ways to streamline regulatory and reporting requirements so researchers can spend less time on administrative tasks and more time on developing new ideas and conducting research.
- Provide federal funding for the Cancer Moonshot Initiative and other translational and clinical research efforts.

ASCO is particularly pleased that the Cancer Moonshot Task Force highlighted the continuing work of the FDA with ASCO and Friends of Cancer Research to evaluate clinical trial entrance criteria that may unnecessarily restrict clinical trial access, such as such as brain metastases, HIV status, organ dysfunction, and age restrictions.

With the backing of the new Congress and Administration, we can build on the progress of the Cancer Moonshot and make gains in our fight against cancer.
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### Table A1. Additional Notable Advances (October 2015 – October 2016)

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<td>Soulieres D, et al: J Clin Oncol 34, 2016 (suppl; abstr 6008)</td>
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<td>Results of a phase III randomized, multicenter study of allogeneic stem cell transplantation after high vs. reduced intensity conditioning in patients with myelodysplastic syndrome (MDS) or acute myeloid leukemia</td>
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What is metastatic breast cancer?

Metastatic breast cancer is breast cancer that has spread to other parts of the body. The most frequent sites are bones, lymph nodes, liver, lungs, and brain. It is still called breast cancer, even after it had spread. Metastatic breast cancer is not curable, but it is treatable. Many patients continue to live well for a number of years with metastatic breast cancer.

How can I cope with metastatic breast cancer?

A diagnosis of metastatic breast cancer often comes as a shock. People describe a range of emotions such as fear, anger, or sadness that may change day-to-day or over time. You may have concerns about how this diagnosis will affect many different aspects of your life, such as your relationships, work or career, family and social roles, and finances. You may be worried about suffering or having your life shortened by this disease. It is important to remember you are not alone. Becoming informed about your specific diagnosis and working with your health care team to find professionals who can provide support to you and your family, offer guidance about your treatment options, and identify services to address the needs of your caregivers are key parts of the coping process. Talk openly with your doctors and health care team to express your feelings, preferences, and concerns. They are there to help, and many team members have special skills, experience, and knowledge to support patients and their families.

How is metastatic breast cancer treated?

The primary goal of treatment for metastatic breast cancer is to extend or prolong life and to relieve the symptoms caused by the cancer. This approach, aimed at reducing symptoms and suffering, is often referred to as supportive or palliative care, and it is often given along with treatment to slow or stop the growth of cancer.

Treatment options for women with metastatic breast cancer vary based on characteristics of the tumor—for example, whether the tumor is hormonally sensitive (ER-positive, PR-positive) or HER2-positive, where in the body the cancer has spread, the presence of specific symptoms, and previous cancer treatments. For women with ER- and PR-positive cancers, treatment with hormonal therapy is effective and can be used to control breast cancer for many years. Other common treatments for metastatic breast cancer include chemotherapy and targeted therapy. Because it is not unusual for metastatic breast cancer to become resistant (stop responding) to these drugs, you may need to change therapies fairly often. When making treatment decisions, you may also consider a clinical trial; talk with your doctor often about all treatment options and the goals of each treatment.

Other possible treatments include radiation therapy or non-chemotherapy medications called bisphosphonates to treat bone metastases and surgery to remove a tumor that is causing discomfort. You may receive additional treatment to make sure you are physically comfortable and free from pain.

For information and resources, please visit Cancer.Net.
While nearly 1 in 2 people will get cancer in their lifetime, 2 in 3 will survive it. The research featured in ASCO’s Clinical Cancer Advances report is a testament to the progress forged as new therapies are uncovered, young investigators are funded, and the knowledge of practicing oncologists is pooled. Together, we’re making it harder for cancer to survive.