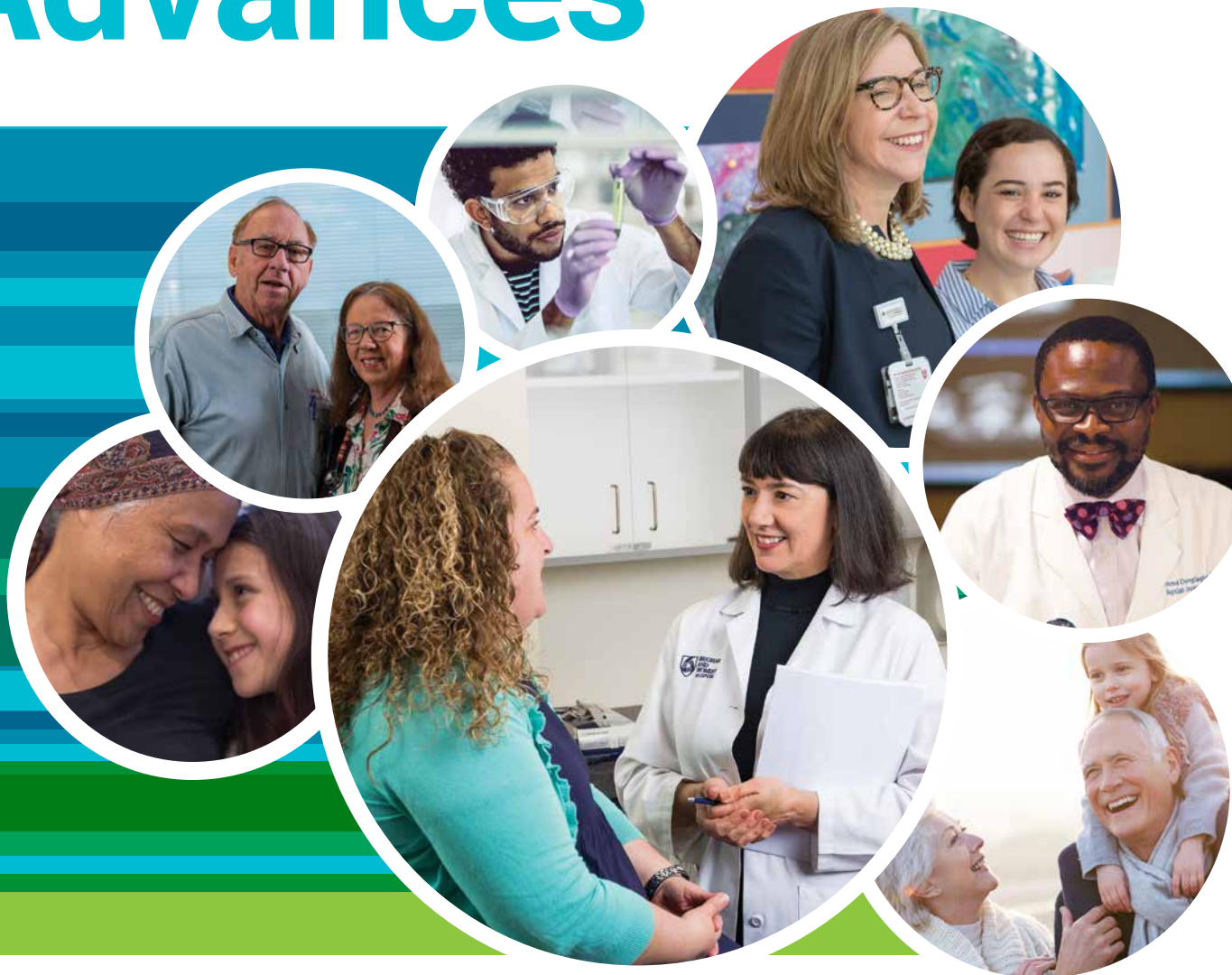


# Clinical Cancer Advances



# 2019

ASCO's Annual Report on Progress Against Cancer



## EXECUTIVE EDITORS

Bruce E. Johnson, MD, FASCO, ASCO Immediate Past President, Dana-Farber Cancer Institute, Boston, MA

Sumanta K. Pal, MD, City of Hope Comprehensive Cancer Center, Duarte, CA

Richard L. Schilsky, MD, FACP, FSCT, FASCO, ASCO Senior Vice President and Chief Medical Officer, Alexandria, VA

## RESEARCH PRIORITY EDITORS

Mariana Chavez-MacGregor, MD, University of Texas MD Anderson Cancer Center, Houston, TX

Heidi D. Klepin, MD, MS, Wake Forest Baptist Medical Center, Winston Salem, NC

Elizabeth A. Mittendorf, MD, PhD, Dana-Farber Cancer Institute, Boston, MA

## SPECIALTY EDITORS

Neeraj Agarwal, MD, Huntsman Cancer Institute, Salt Lake City, UT

Susan Marina Chang, MD, University of California, San Francisco, CA

Ezra Cohen, MD, FRCPC, University of California, San Diego, CA

Suzanne Cole, MD, FACP, Mercy Clinic Oncology and Hematology, Oklahoma City, OK

William Dale, MD, PhD, City of Hope National Medical Center, Duarte, CA

Catherine S. Magid Diefenbach, MD, New York University Cancer Center, New York, NY

Mary L. Disis, MD, FASCO, University of Washington, Seattle, WA

Robert Dreicer, MD, MS, MACP, FASCO, University of Virginia Cancer Center, Charlottesville, VA

David L. Graham, MD, FASCO, Levine Cancer Institute, Charlotte, NC

N. Lynn Henry, MD, PhD, FACP, Huntsman Cancer Institute, Salt Lake City, UT

Joshua Jones, MD, MA, University of Pennsylvania Health System, Philadelphia, PA

Vicki Keedy, MD, Vanderbilt University Medical Center, Nashville, TN

Merry Jennifer Markham, MD, FACP, University of Florida, Gainesville, FL

Carlos Rodriguez-Galindo, MD, St. Jude Children's Research Hospital, Memphis, TN

Michael S. Sabel, MD, FACS, University of Michigan, Ann Arbor, MI

Mario Sznol, MD, Yale School of Medicine, New Haven, CT

William D. Tap, MD, Memorial Sloan Kettering Cancer Center, New York, NY

Shannon Neville Westin, MD, University of Texas MD Anderson Cancer Center, Houston, TX

## ACKNOWLEDGEMENT

The editors would like to thank Michael J. Miller, MS, MPH, for his work drafting this report.

The editors would also like to thank Edward S. Kim, MD, and Jennifer Ligibel, MD, for their input, and posthumously thank Arti Hurria, MD, FASCO, an oncologist whose life-long commitment to improving the care of geriatric patients with cancer has forever made a difference.

*Disclosures for editorial board members can be viewed on page 46.*

# A Message from ASCO's President

Extraordinary progress has been made over the last 70 years to understand, prevent, diagnose, and treat cancer—progress that gives hope to many people facing a cancer diagnosis. The lynchpin of this progress has always been, and continues to be, clinical research—a process through which we learn from and build on the efforts of untold numbers of researchers, clinicians, and patients. ASCO's *Clinical Cancer Advances* report, our 14th edition, examines the most transformative research of the past year and, for the first time, offers our vision for future research priorities.

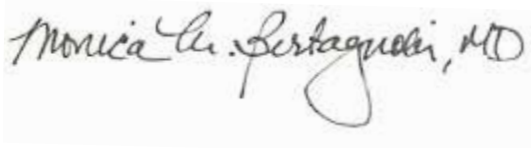
ASCO's 2019 Advance of the Year, **Progress in Treating Rare Cancers**, reflects the impressive gains we've made in understanding these so-called 'orphan diseases' and in tailoring treatments to target their unique characteristics. This year, we are highlighting five remarkable achievements in rare cancers that hold real promise for patients.

Much of the progress we've made against cancer has been driven by federally funded research, and this past year is no different. For example, funding from the US government, including the National Institutes of Health (NIH) and National Cancer Institute (NCI), supported three of the five advances in rare cancers and nearly a third of the studies highlighted in the report. With the number of new US cancer cases set to rise by roughly a third over the next decade, it is crucial that our nation continues to invest in the next generation of cures for patients.

Although survival rates are increasing for many cancers, our work is far from over. **ASCO's Research Priorities to Accelerate Progress Against Cancer** are intended to serve as a guidepost for steering future research in directions we believe have the greatest potential to accelerate the pace of progress. We identified a list of research priorities that help fill critical gaps in cancer prevention and care—from increasing diversity in clinical trials, to better predicting responses to immunotherapy, to reducing the impact of obesity on cancer incidence and outcomes.

Cancer treatment advances are only as good as patients' ability to access them. But, for far too many patients, high-quality cancer care and clinical trials are out of reach. We have much work to do before everyone with cancer has equal access to the best treatments and the opportunity to participate in research. By working together as a community, I know we can find solutions that will help ensure that the advances that are discussed on the following pages reach every patient who could benefit from them.

Sincerely,



**Monica M. Bertagnolli, MD, FACS, FASCO**

ASCO President, 2018 to 2019



# TABLE OF CONTENTS

<i>CLINICAL CANCER ADVANCES 2019: AT A GLANCE</i>	6
<b>ADVANCE OF THE YEAR: PROGRESS IN TREATING RARE CANCERS</b>	11
<b>ADVANCES IN CANCER TREATMENT</b>	15
<b>ADVANCES IN DIAGNOSTICS</b>	21
<b>ADVANCES IN PATIENT CARE</b>	24
<b>THE MICROBIOME AND CANCER</b>	28
<b>NINE RESEARCH PRIORITIES TO ACCELERATE PROGRESS AGAINST CANCER</b>	31
<b>REFERENCES</b>	38
<b>APPENDIX</b>	40



# Clinical Cancer Advances 2019

## AT A GLANCE

*Clinical Cancer Advances 2019: ASCO's Annual Report on Progress Against Cancer* highlights the most important clinical research advances of the past year and identifies priority areas where ASCO believes research efforts should be focused moving forward.

Since 1992,<sup>1</sup> there have been nearly 25 consecutive years of decline in overall incidence and mortality rates for all types of cancer.<sup>2</sup> In addition, the number of people living 5 years or more after a cancer diagnosis is projected to rise 31% by 2026,<sup>3</sup> representing an increase of more than four million survivors in less than a decade. Cancer research, including the advances in this report, helps make progress possible.

## Advance of the Year: Progress in Rare Cancers

This year, ASCO names Progress in Treating Rare Cancers as the Advance of the Year. In the United States, rare cancers account for about 20% of all cancers diagnosed each year, and incidence rates vary worldwide.<sup>4</sup> Progress has historically lagged behind the achievements made in more common cancers; however, five major studies this past year offer significant steps forward, making this a notable year for advances in rare cancers:

1

**A new combination of targeted therapies for a rare, hard-to-treat form of thyroid cancer** produced responses in over two thirds of patients

2

Sorafenib became the **first treatment to improve progression-free survival for desmoid tumors**, a rare type of sarcoma

3

Lutetium Lu 177 dotatate (<sup>177</sup>Lu-Dotatate), a new therapy that delivers targeted radiation to tumor cells, **lowered the risk of disease progression or death by 79% for patients with advanced midgut neuroendocrine tumors**, compared to standard treatment

4

Trastuzumab, a standard treatment for HER2-positive breast cancer, **significantly slowed progression of HER2-positive uterine serous carcinoma**

5

**The first promising therapy**—the colony-stimulating factor-1 inhibitor pexidartinib—**for a rare cancer of the joints known as tenosynovial giant cell tumor, showed an overall response rate of 39.3%**, v 0% for those taking a placebo

“

*Progress is moving at a quicker pace than ever before. From new success with immunotherapies and targeted therapies, to new insights for molecular diagnostics and the microbiome, we've seen truly impactful advances in many types of cancer, especially in rare cancers.”*

—Monica Bertagnolli, MD, FACS, FASCO,  
ASCO President (2018-2019)

”

This progress in rare cancers can be attributed, in part, to ongoing efforts of several major initiatives sponsored and led by the National Institutes of Health, including The Cancer Genome Atlas (TCGA). The systematic characterization of a broad range of tumors by TCGA has led to effective targeting of activated pathways. Future funding of these and other similar efforts is vital to accelerating progress in rare cancers.



## Additional Major Advances



**Landmark advances in molecular diagnostics continue**, with the most significant achievement made with the TAILORx breast cancer study. This study demonstrated that as many as 70% of women with hormone receptor-positive, node-negative breast cancer could safely forgo adjuvant chemotherapy, based on results from a 21 gene assay.



**New successes are being achieved with targeted therapies**, including the introduction of medicines that delay the progression of breast and lung cancers.



**Growing microbiome research field** identifies specific bacteria possibly associated with risk for certain head and neck cancers.



**Immunotherapy advances continue to grow**, expanding to cancers where there have been few immunotherapy treatment successes to date:

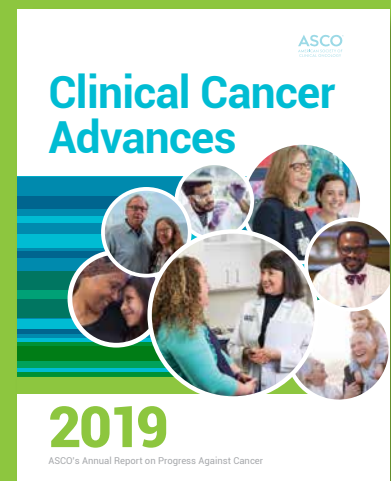
- A new combination immunotherapy regimen was proven to boost overall survival in patients with renal cell cancer, gaining Food and Drug Administration (FDA) approval and becoming the new standard of care.
- An investigational PD-1 inhibitor showed promise for advanced squamous cell cancer of the skin, which has few other treatment options.

## ASCO Research Priorities to Accelerate Progress

For the first time, ASCO is identifying areas on which future research efforts should be focused to help accelerate progress against cancer. These priority areas, listed in no particular order, address an unmet need or help fill a knowledge gap in areas critical to improving patient care and outcomes:

- 1 **Identify strategies** that better predict response to immunotherapies
- 2 **Better define** the patient populations that benefit from postoperative (adjuvant) therapy
- 3 **Translate innovations** in cellular therapies to solid tumors
- 4 **Increase precision medicine research** and treatment approaches in pediatric cancers
- 5 **Optimize care** for older adults with cancer
- 6 **Increase equitable access** to cancer clinical trials
- 7 **Reduce the long-term consequences** of cancer treatment
- 8 **Reduce obesity** and its impact on cancer incidence and outcomes
- 9 **Identify strategies** to detect and treat premalignant lesions

These priorities build on an understanding gleaned from years of research efforts and over time will evolve with the cancer research landscape.



Read the full report on [asco.org/cca](https://asco.org/cca) or as published in the Journal of Clinical Oncology at [ascopubs.org/jco](https://ascopubs.org/jco).



## Voices for Cancer Research



*Clinical Cancer Advances 2019* includes the personal stories of oncologists who have dedicated their lives to clinical cancer research and the patients who inspire them to continue their work. These researchers and patients are featured in ASCO's "I Live to Conquer Cancer" campaign, which aims to put a human face on cancer research and underscore the importance of federally funded research in making progress against cancer. To read these inspiring stories, visit [asco.org/cca](http://asco.org/cca).



*"In an age of rapid discovery, these advances are not being applied fast enough to the places where people really need them—we have to bridge that gap. This is what drives me every day."*

—Raymond U. Osarogiagbon, MD, FACP



*"In medical school the doctors I worked with were so hopeful that we would find something better to offer our patients, and indeed, every year, thanks to cancer research, there has been something new."*

—Judith Kaur, MD



*"Pediatric oncology is one of the great success stories of medicine because of our nation's commitment to curing this disease."*

—Tara Henderson, MD, MPH



*"Because of cancer research and the people who have participated in clinical trials, I have a good quality of life. I can do the things I want to do."*

—Gina Hollenbeck



*"There are real lives at stake, and they're at stake every day. As long as we have people who are dying of cancer, as long as we have people who suffer long-term effects related to cancer or its treatment, we can do better, and we must do better."*

—Alan P. Lyss, MD




*"We wouldn't be here today if it weren't for what research did for us in 2009. I never even had to think about my son participating in a clinical trial—some other mother gave permission for her child so that my child could be in the position he is in today. It's a domino effect."*


—Renee Bakos-Pournaras, pictured with son Yano




# Cancer Research: Why Federal Support Matters

Research funded by the National Institutes of Health (NIH) and National Cancer Institute (NCI) has played a pivotal role in advances in cancer prevention, diagnosis, and treatment. In fact, federal funding supported three of the five advances in rare cancers and nearly one third of the studies highlighted in this year's *Clinical Cancer Advances* report. **What the nation's investment in research means for people with cancer.**

**27%**   
decline in cancer death rates (since peak in 1991)<sup>5</sup>

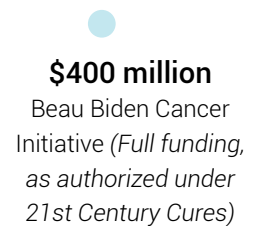
**130+**   
new cancer drugs or indications approved by FDA since 2006<sup>6</sup>

**5-year**   
cancer survival rate increases (2 out of 3 people with cancer live at least 5 years after diagnosis)<sup>7</sup>

**15.5 million**   
cancer survivors (up from 11.4 million in 2006)<sup>5</sup>

## Fiscal Year 2019 Funding<sup>8</sup>

After more than 10 years of stagnant funding, Congress has demonstrated tremendous bipartisan leadership by passing four annual consecutive NIH and NCI funding increases. Most recently, lawmakers passed a \$2 billion (5.4%) NIH funding increase for Fiscal Year 2019.



## But our work is far from over.



**1/3 increase** in new US cancer cases expected over next decade<sup>9</sup>



We're only now nearing **pre-recession NCI funding levels**<sup>8,10</sup>



Despite increases, NCI is still only able to **fund a small fraction** of new research proposals (12% in 2017 v 28% in 1997)<sup>11</sup>



**75% drop** in the number of studies presented at ASCO's Annual Meeting (from 2008-2017) that were primarily funded by NIH<sup>12</sup>

## When we invest in cancer research, everyone benefits.

**\$69 billion** NIH generates new economic activity across the country and **supports 402,816 jobs nationwide** (directly and indirectly)<sup>13</sup>

**67%** of Americans say the US government should **spend more money on finding treatments and cures** for cancer, even if it means higher taxes or adding to the deficit<sup>14</sup>

As long as cancer continues to be the life-threatening burden it is today, our nation must continue to prioritize investment in cancer research. ASCO is hopeful that recent budget increases represent a promising future of renewed focus on federally funded cancer research.



**Contact your Members of Congress** to urge their continued support for NIH and NCI funding. ASCO makes it easy for you to reach them directly. Just visit ASCO's ACT Network at [asco.org/actnetwork](http://asco.org/actnetwork).



AMERICAN SOCIETY OF CLINICAL ONCOLOGY

Founded in 1964, the American Society of Clinical Oncology, Inc. (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 45,000 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.

## CONQUER CANCER® THE ASCO FOUNDATION

Conquer Cancer funds research into every facet of cancer to benefit every patient, everywhere. As ASCO's foundation, Conquer Cancer helps turn science into a sigh of relief for patients around the world by supporting groundbreaking research and education across cancer's full continuum. Several of the top advances featured in this report (about 20%) were made possible by funding from Conquer Cancer or were led by past grantees who have continued their careers in oncology research.

### About Clinical Cancer Advances

ASCO's *Clinical Cancer Advances* report highlights current trends in the field and identifies cancer research priorities that have great potential to advance progress against cancer. The report, now in its 14th edition, is developed by a 20+ member editorial board of experts in a range of cancer types, subspecialties, and care issues. The list of editorial board members and their disclosures can be viewed with the report at [ascopubs.org/doi/abs/10.1200/JCO.18.02037](https://ascopubs.org/doi/abs/10.1200/JCO.18.02037). The editors reviewed scientific literature published in peer-reviewed journals or presented at major medical conferences, primarily from October 2017 to September 2018, and selected advances that improve meaningful patient outcomes and have a strong scientific impact. The editors also proposed priority areas of research that address vital unmet needs in cancer care and have the potential to improve the knowledge base for clinical decision-making.



ADVANCE OF THE YEAR

# Progress in Treating Rare Cancers

*This year, ASCO names Progress in Treating Rare Cancers as the Advance of the Year. Rare cancers have been defined as those that account for less than six of 100,000 diagnosed cancers and for 20% of all cancer cases each year in the United States, though definitions and incidence rates differ around the world.<sup>4</sup>*

*There is wide variation in the availability and effectiveness of treatment options for rare cancers due to the enormous diversity in clinical presentation and underlying biology. It often takes longer to recruit significant numbers of people to participate in clinical trials that are testing new treatments for rare cancers, and there are unique hurdles to developing and designing specialized therapies.*



Photo by Glenn Davenport

Recently, however, the decades of research progress in understanding cancer are translating into better treatments for multiple rare cancers. In fact, clinical research this past year identified effective therapies for rare forms of uterine, neuroendocrine, joint, and thyroid cancers, as well as sarcomas, which for decades have been challenging to treat effectively. What follows are some of the more prominent achievements in rare cancers this past year.

### **New Combination of Targeted Therapies Identified for Rare Form of Thyroid Cancer**

Anaplastic thyroid carcinomas (ATCs) comprise less than 2% of all thyroid cancers diagnosed in the United States and have a worse prognosis than other more common forms of thyroid cancer.<sup>15</sup> Not only do they tend to be aggressive, but also ATCs are usually diagnosed at an advanced stage and have low 1-year survival rates.<sup>16</sup>

This year, the FDA approved the first treatment of ATCs in almost 50 years,<sup>17</sup> a targeted therapy combination of dabrafenib (Tafinlar), a BRAF inhibitor, plus trametinib (Mekinist), a MEK inhibitor, for people with *BRAF*-mutated ATC.

The approval was based on a 2018 finding from a single-arm phase II trial.<sup>18</sup> The federally funded trial assessed 100 patients for eligibility

and enrolled 16 patients with *BRAF*-mutated tumors, all of whom had received prior radiation, surgery, and/or chemotherapy. Of these patients, 69% responded to the drug combination (this study was funded, in part, by NIH). At the time the study was published, seven patients, or nearly half of those enrolled, were experiencing ongoing responses to the therapy. Although overall survival and progression-free survival could not be assessed at the time, clinicians estimated that at least 80% of the patients with tumors that responded would achieve improvements in both outcomes.



Before this study, no chemotherapy treatment for ATC prolonged survival or improved quality of life. This new combination therapy has now become the standard of care for these patients.

### **Sorafenib Becomes First Treatment to Improve Progression-Free Survival for Rare Sarcoma**

This past year brought the first randomized, global phase III trial, Alliance A091105 (ClinicalTrials.gov identifier: NCT02066181)<sup>19</sup> for patients with a rare type of sarcoma called a desmoid tumor. Before this federally funded trial, patients with desmoid tumors were often treated with off-label treatments. Designing a trial for desmoid tumors has historically been challenging because there



are few patients to study and the tumors are known to periodically regress without systemic treatment. Indeed, approximately 20% of the cancers regressed or did not progress in patients who received a placebo in this trial.

Eighty-seven patients with unresectable progressive desmoid tumors were randomly assigned to receive either the tyrosine kinase inhibitor sorafenib (Nexavar) or a placebo. The trial achieved its primary endpoint, with 87% of those taking sorafenib experiencing improved 1-year progression-free survival compared with 43% of patients on placebo (this study was funded, in part, by NCI).



The study authors attribute part of the success of the trial to the relatively robust patient enrollment for a rare cancer. Enrollment was facilitated by NCI's National Clinical Trials Network, a collection of organizations, hospitals, and clinicians that coordinates and supports cancer clinical trials.

### **New Radiolabeled Drug Substantially Lowers the Risk of Progression or Death in Patients With Midgut Neuroendocrine Tumors**

Midgut neuroendocrine tumors are rare, estimated to affect fewer than three per 100,000 people annually.<sup>20</sup> Patients with advanced midgut neuroendocrine tumors are usually treated with somatostatin, a growth hormone inhibitor, or octreotide, a synthetic form of somatostatin that has a long-acting release.

GENEBIOLuNet (ClinicalTrials.gov identifier: NCT03667092), an international phase III trial,<sup>21</sup> was the first study to evaluate the safety and efficacy of <sup>177</sup>Lu-Dotatate in patients with an advanced form of this disease. The medicine is composed of the radioisotope <sup>177</sup>Lu attached to octreotide. The radionuclide-octreotide analog binds to the neuroendocrine tumor cell, enabling radiation to be directly delivered to the cancer cell, inhibiting tumor growth.

In the trial, 229 people were randomly assigned to receive either <sup>177</sup>Lu-Dotatate or octreotide. The estimated progression-free survival after 20 months was 65.2% in the <sup>177</sup>Lu-Dotatate group and 10.8% in the octreotide group. The risk of disease progression or death was 79% lower in people who received <sup>177</sup>Lu-Dotatate compared with those who received octreotide. Results of an interim analysis

suggest longer overall survival with the new treatment; 14 deaths occurred in the group that received <sup>177</sup>Lu-Dotatate compared with 26 deaths in the group that received octreotide.

The FDA approved <sup>177</sup>Lu-Dotatate for treatment of adults with midgut neuroendocrine tumors in January 2018.<sup>22</sup> A follow-up study,<sup>23</sup> published in September 2018, showed that the new treatment also provided important quality-of-life benefits. Investigators found that in addition to improving survival, <sup>177</sup>Lu-Dotatate, compared with octreotide, provided 28.8 v 6.1 months of overall better health and 25.2 v 11.5 months of better physical functioning, respectively.

### **Trastuzumab Effective for a Rare Form of Endometrial Cancer**

Uterine serous carcinoma is a rare and aggressive type of cancer that accounts for 10% of endometrial cancer cases and up to 40% of recurrences and deaths from endometrial cancer.<sup>24</sup> The *HER2* gene is overexpressed in approximately 30% of uterine serous tumors. This year, researchers demonstrated that trastuzumab (Herceptin), a *HER2*-targeted treatment used primarily in women with *HER2*-positive breast cancer, is effective in these tumors.

The phase II trial<sup>25</sup> compared a chemotherapy combination of a platinum-based drug, carboplatin, added to paclitaxel with and without trastuzumab among 61 women with stage III or IV *HER2*-positive uterine serous carcinoma. The median time before disease progression was 12.6 months for women who received trastuzumab compared with 8 months for those who did not. This study is one of the first to demonstrate improved progression-free survival with the addition of a targeted therapy to standard platinum-based chemotherapy in women with this form of uterine cancer.

### **First Promising Therapy Identified for Rare Cancer of the Joints That Typically Occurs in Younger Adults**

With global collaboration, ENLIVEN (ClinicalTrials.gov identifier: NCT02371369)<sup>26</sup>, a trial studying a novel treatment for tenosynovial giant cell tumors—a rare, debilitating tumor that is generally found in younger, working-age adults—was able to enroll and treat 120 patients. The disease is associated with severe loss of function and

## **TAPUR**

ASCO's Targeted Agent and Profiling Utilization Registry (TAPUR; ClinicalTrials.gov identifier: NCT02693535) Study continues to enroll patients and achieve milestones as patient outcomes are reached. The TAPUR Study evaluates antitumor activity of commercially available, targeted anticancer drugs when used outside of their FDA-approved indications. It aims to identify new uses for existing, effective treatments that target tumor genomic profiles.

More than 1,600 participants have been registered and more than 1,200 treated with a TAPUR Study drug. Based on treatment responses in Stage I, patient cohorts are either expanded to Stage II for further study or permanently closed. To see the full list of patient cohort updates, visit [tapur.org/news](http://tapur.org/news).

morbidity and frequently affects physical ability and job function. There is no current standard of care; two systemic therapies that have been tested in clinical trials to treat these tumors have shown poor overall responses.

Surgery remains the standard initial treatment of tenosynovial giant cell tumors. Some patients undergo multiple synovectomies (surgery to remove the membrane, or synovium, that lines a joint, most typically the knee), and some even need full-joint replacements.

The phase III federally funded trial<sup>26</sup> randomly assigned patients with advanced, symptomatic disease to first receive either the CSF-1 inhibitor pexidartinib or a placebo. CSF-1 is a molecule that increases the recruitment of certain tumor-promoting immune cells to the tumor; therefore, an inhibitor of CSF-1 removes these from the milieu. The overall response rate was 39.3% for patients taking pexidartinib compared with 0% for those on placebo. All patients were able to cross over to receive open-label pexidartinib in the second part of the trial.



There was a statistically significant improvement in pain scores, range of motion, and physical function in patients who received the study drug (this study was funded, in part, by NIH).

The use of CSF-1 inhibitors holds promise in this disease and continues to be investigated in new clinical trials. CSF-1 inhibitors, including pexidartinib, are not yet recommended for general use as a result of serious liver toxicities that occurred in some trial

participants. The toxicity is part of the focus of an ongoing study to clarify safety concerns.

### Federal Funding Is Vital to Advancing Progress in Rare Cancers

Progress in rare cancers is being advanced, in part, by ongoing efforts of several major federally funded initiatives:



- The Cancer Genome Atlas (TCGA) cataloged key genomic changes in 33 types of cancer, of which 10 were rare cancers.
- In the Molecular Analysis for Therapy Choice (MATCH; ClinicalTrials.gov identifier: NCT02465060) precision medicine trial, patients receive treatment based on genomic changes in the tumor. More than 60% of enrollees have cancers other than the four most common types.
- The Dual Anti-Cytotoxic T-Cell Lymphocyte-4 and Anti-PD-1 Blockade in Rare Tumors (DART) immunotherapy trial is studying nivolumab (Opdivo) and ipilimumab (Yervoy) in people with rare types of cancers that are usually ineligible for current immunotherapy trials.

Future funding of these and other similar efforts is vital to accelerating progress in rare cancers.







# Advances in Cancer Treatment

*Treatment advances across the spectrum of cancers have continued at a rapid pace. Lung cancer experienced significant treatment breakthroughs this year, primarily in immunotherapy, as it has in the past several years. Other immunotherapy trials brought new treatment options to patients with a range of solid tumor and blood cancers. In addition, in 2018, a Nobel Prize was awarded to the researchers who found that the immune system could be harnessed to attack cancer, highlighting the significance of research advances seen in this area.*

*Progress in treatment was also seen in systemic chemotherapy, targeted chemotherapy, surgery, and radiotherapy.*

## Immunotherapy Advances

This year, research expanded the reach and impact of multiple forms of immunotherapy. Key studies of checkpoint inhibitors showed survival gains when the medicines were offered earlier in the course of treatment and in combination with other treatments, including other immunotherapies and chemotherapy. In adoptive cell therapy, longer-term data provided deeper insight on the benefits and risks of this approach in various blood cancers. The year also brought the FDA approval of several new immunotherapies (Appendix Table A2).

### Checkpoint inhibitors proven valuable as initial therapy for advanced lung cancer.

In advanced non–small-cell lung cancer (NSCLC), two trials demonstrated that checkpoint inhibitor therapies have a role in first-line treatment. The phase III IMpower150 (ClinicalTrials.gov identifier: NCT02366143) trial<sup>27</sup> tested combinations of carboplatin, paclitaxel, and bevacizumab (Avastin) with or without the immunotherapy agent atezolizumab (Tecentriq), which targets the programmed death ligand-1 (PD-L1) protein. Median progression-free survival was 8.3 months for all patients who received the standard treatment plus immunotherapy compared with 6.8 months for those who received conventional chemotherapy with bevacizumab.

In another phase III trial, KEYNOTE-189 (ClinicalTrials.gov identifier: NCT02578680),<sup>28</sup> researchers randomly assigned participants to receive chemotherapy drugs pemetrexed and cisplatin or carboplatin, followed by the PD-1 inhibitor pembrolizumab or a placebo. Both 1-year overall survival rate (69.2% in the pembrolizumab group v 49.4% in the chemotherapy-alone group) and median progression-free survival time (8.8 months in the pembrolizumab group v 4.9 months in the chemotherapy-alone group) were greater among patients in the pembrolizumab group compared with patients who received chemotherapy alone.

### Combination immunotherapy boosts renal cell cancer survival, established as new standard.

The combination of two immunotherapy agents, nivolumab and ipilimumab, is used routinely in melanoma and is now being explored in other types of cancer. A phase III trial (CheckMate214; ClinicalTrials.gov identifier: NCT02231749)<sup>29</sup> evaluated this new combination immunotherapy regimen in patients with intermediate- or high-risk renal cell carcinoma, finding it improved the 18-month overall survival rate compared with the tyrosine kinase inhibitor sunitinib (Sutent), 75% for the combination v 60% for sunitinib. Remarkably, 9% of patients receiving nivolumab with ipilimumab had complete regression of the cancer.

Although not without the potential for serious toxicities, this combination of immunotherapies is now the standard of care for patients with higher risk metastatic disease. The combination recently received FDA approval in high- and intermediate-risk advanced renal cell cancer,<sup>30</sup> but it has not yet been established as

an effective treatment for patients with low-risk disease.

### Combination immunotherapy can reduce brain metastases in people with melanoma.

Advanced melanoma is one of the few cancers that often metastasizes to the brain. These metastases can cause severe neurologic symptoms and lead to death within a year.

A phase II federally funded study, CheckMate204 (ClinicalTrials.gov identifier: NCT02320058),<sup>31</sup> looked at the combination of nivolumab and ipilimumab (the same combination tested for renal cell cancer) in people with melanoma who had untreated metastases in the brain. Clinicians observed 94 people for 14 months after completion of treatment and found that 26% of patients had no detectable brain metastases and 30% had some reduction in metastases. An impressive 82% of patients were alive after a year, whereas survival had previously been measured at weeks and months for patients receiving standard treatment (this study was funded, in part, by NCI).



Significant side effects were seen in 55% of people on the trial, some of which affected the central nervous system. However, the study authors noted that, as a result of the impressive benefits seen in this study, this checkpoint combination could be explored in other cancers that have spread to the brain.

### Investigational PD-1 inhibitor shows promise for a skin cancer with few treatment options.

In September 2018,<sup>32</sup> the FDA approved a new anti-PD-1 checkpoint inhibitor, cemiplimab (Libtayo), for cutaneous squamous cell carcinoma. The approval was based on a nonrandomized phase II trial<sup>33</sup> of 59 patients with metastatic disease in whom cemiplimab showed remarkable activity; tumors shrank in nearly half (28) of the patients enrolled onto the trial.

Cutaneous squamous cell carcinoma is the second most common skin cancer, with more than one million patients diagnosed annually. Although most of these cancers can be cured with surgical excision, this newer treatment could have an important impact for the small but significant proportion of patients with cancer that persists or metastasizes. Prior research has shown this cancer to be relatively unresponsive to other forms of treatment, including chemotherapy.

### Pembrolizumab provides greatest benefit in head and neck cancers with high PD-L1 expression.

The KEYNOTE-040 (ClinicalTrials.gov identifier: NCT02252042) phase III trial compared pembrolizumab (Keytruda) to standard chemotherapy in 495 people with recurrent or metastatic head and neck squamous cell carcinoma that was not responsive to platinum-based chemotherapy drugs.<sup>34</sup> This trial further evaluated whether a marker—PD-L1 protein expression in more than 50% of tumor cells—affected outcomes.

The trial showed that pembrolizumab, compared with standard





chemotherapy, modestly improved median overall survival time (8.7 v 7.1 months, respectively) if PD-L1 expression levels were greater than 1%. Median overall survival was approximately 4 months greater among people with tumors that expressed PD-L1 at a level greater than 50%. This is the first phase III trial to demonstrate the impact of PD-L1 expression on the efficacy of pembrolizumab in this form of cancer.

### **Chimeric antigen receptor T-cell (CAR-T) therapy trials show longer term benefits.**

In 2018, CAR-T therapy, also known as adoptive cell immunotherapy, was named the Advance of the Year by ASCO. Unlike checkpoint inhibitors, this form of immunotherapy boosts the ability of the body's immune system to fight cancer using a patient's own genetically re-engineered T cells.

An early-phase clinical trial formed the basis of the 2017 FDA approval<sup>35</sup> of the anti-CD19 CAR-T therapy tisagenlecleucel (Kymriah) for acute lymphoblastic leukemia, the most common cancer in children. CD19 is an important biomarker for this cancer because it is present on the surface of malignant B cells, thus making it an effective target for CAR-T cells.

More recently, a global phase II trial (ClinicalTrials.gov identifier: NCT03123939)<sup>36</sup> confirmed preliminary data and established the feasibility of delivering this treatment to children. Of the 75

children in the trial, 81% showed decreased signs and symptoms of disease 3 months after completion of treatment. Persistence of tisagenlecleucel in the blood was observed for as long as 20 months. Overall survival decreased over time but was still significant, with 90% of children living 6 months or longer and 50% of children living 12 months or longer.

Severe but transient adverse events were observed in 73% of the children treated with tisagenlecleucel. The next step will be to test this approach in larger numbers of children and in broader age ranges so that long-term persistence of the engineered cells can be studied along with long-term patient outcomes.

ZUMA-6 (ClinicalTrials.gov identifier: NCT02926833), a phase II trial of a second type of anti-CD19 CAR-T therapy, called axicabtagene ciloleucel (Yescarta), enrolled 111 adults with refractory large B-cell lymphoma.<sup>37</sup> After a median time of 15.4 months, 82% of patients had decreased signs and symptoms of disease and 54% experienced a complete regression of disease. Furthermore, 52% of patients were alive 18 months after treatment. There were some significant adverse effects, including myelosuppression, cytokine release syndrome, and neurologic events. The FDA approved the drug for use in this population in October 2017.<sup>38</sup>

In a third anti-CD19 CAR-T therapy trial (ClinicalTrials.gov identifier: NCT03483688), this time with a newer investigational approach, researchers isolated specific T cells that express a CD19-directed

chimeric antigen receptor, called CTL019, from patients and re-engineered them in the laboratory. They reinfused the new cells into the patients as part of a phase II federally funded study.<sup>39</sup> Clinicians tested the CTL019 therapy in 14 adults with relapsed or refractory diffuse large B-cell lymphoma and 14 adults with follicular lymphoma. Results showed that the re-engineered CTL019 cells rapidly induced complete remission in six patients (43%) with B-cell lymphoma and 10 patients (71%) with follicular lymphoma (this study was funded, in part, by NIH). These results suggest that anti-CD19 CAR-T therapy is a promising option for people with multiple, relapsed, and refractory diffuse large B-cell lymphomas whose survival expectancies have previously been limited.



## Targeted Therapy Advances

Targeting medicines to specific gene mutations in a cancer cell, as opposed to administering systemic chemotherapy that can affect every cell in the body, is still an exciting and productive frontier in oncology. With more than a decade of trials and evidence at hand, targeted therapies are expanding to new types of cancer that have been resistant to more conventional approaches.

### New EGFR inhibitor delays lung cancer progression.

One of the more frequently mutated genes in lung cancer is *EGFR*, and it can mutate in different ways and at different locations along its stretch of DNA. Some of the mutations that occur are responsive to first-generation targeted therapies, such as gefitinib (Iressa) and erlotinib (Tarceva). However, resistance mutations commonly emerge during treatment with these agents.

Two recent trials tested a new, second-generation drug, osimertinib (Tagrisso), that was developed to treat NSCLC with resistant or less common *EGFR* mutations. The oral medicine was approved by the FDA in 2018 based on a phase III international trial, FLAURA (ClinicalTrials.gov identifier: NCT02296125),<sup>40</sup> in which 556 patients with *EGFR*-positive, unresectable or metastatic NSCLC were randomly assigned to initial treatment with osimertinib or the standard *EGFR*-targeted treatments gefitinib or erlotinib. Progression-free survival in patients who received osimertinib was 18.9 months compared with 10.2 months in patients who received a first-generation EGFR inhibitor. A second trial of osimertinib, AURA

(ClinicalTrials.gov identifier: NCT01802632),<sup>41</sup> primarily explored safety and effectiveness (phase I/II) with two different dosages of the medicine (80 and 160 mg) and reported that patients who received the medicine did not experience disease progression for between 16 and 19 months, regardless of the dosage.

Together, the trials showed that osimertinib almost doubled the time to disease progression achieved with older medicines. On the basis of these data, osimertinib has become the new initial treatment of choice in patients with NSCLC with certain *EGFR* mutations, including those not responsive to older *EGFR*-directed therapies.

### New protein-targeted therapy delays cancer progression and gains approval for certain advanced breast cancers.

*HER2/neu* was the first gene mutation in breast cancer for which a targeted therapy, trastuzumab, was developed. Since trastuzumab's approval by the FDA in 1998,<sup>42</sup> a handful of other targeted drugs for breast cancer have been developed. Abemaciclib (Verzenio), a newer drug, inhibits activity of the CDK4/6 proteins that regulate the rate of cell division as opposed to targeting a specific gene mutation.

In two phase III trials, abemaciclib showed activity against previously treated metastatic hormone receptor–positive, *HER2*-negative breast cancer. The MONARCH 2 (ClinicalTrials.gov identifier: NCT02107703) clinical trial<sup>43</sup> randomly assigned 669 women with breast cancer who had disease progression, despite prior endocrine therapy, to fulvestrant (Faslodex) plus abemaciclib or fulvestrant plus a placebo. Fulvestrant is a medicine that degrades the estrogen receptor. Women taking abemaciclib plus fulvestrant had a median progression-free survival time of 16.4 months compared with 9.3 months for women who received fulvestrant plus a placebo.

The MONARCH 3 (ClinicalTrials.gov identifier: NCT02246621) trial<sup>44</sup> tested nonsteroidal aromatase inhibitors—either anastrozole or letrozole—plus either abemaciclib or a placebo in 493 women. In both trials, treatment with an aromatase inhibitor plus abemaciclib resulted in longer life without disease progression. The findings of these trials (and the previously conducted MONARCH 1 [ClinicalTrials.gov identifier: NCT02102490] trial) led to FDA approval in February 2018 of abemaciclib in combination with an

## Medicaid Coverage of Clinical Trials Services

This past year saw the introduction of the CLINICAL TREATMENT Act (HR 6836 in the 115th Congress) by Representatives Gus Bilirakis (R-FL) and Ben Ray Lujan (D-NM). This important measure, which ASCO supported, would require states to cover the routine clinical care costs of participation in an approved clinical trial for Medicaid enrollees. Routine care costs include the nonexperimental costs of treating a patient who is participating in a clinical trial, such as routine physician visits and laboratory studies.

While Medicare and private and commercial payers already guarantee this coverage, Medicaid is the only major payer that is not required by federal law to do so. With Medicaid insuring nearly one fifth of the US population, it is critical to close this gap and ensure that Medicaid beneficiaries have access to trials that may be the best clinical option for many patients.

aromatase inhibitor.<sup>45</sup>

### **Novel combination treatment shows promise for elderly patients with acute myeloid leukemia (AML).**

Combining medicines with innovative mechanisms of action can lead to effective therapies in certain unique or hard-to-treat groups of patients. In AML, this approach is being pursued to improve care for older patients who are generally not healthy enough to tolerate conventional therapies.

Medicines such as azacytidine (Vidaza) and decitabine (Dacogen), which affect the DNA methylation process, have shown some short-lived benefit in these patients. To further boost their therapeutic impact, researchers turned to an oral medicine called venetoclax (Venclexta), which provokes cancer cell death by targeting the BCL2 protein.

A phase I trial (ClinicalTrials.gov identifier: NCT02203773)<sup>46</sup> combining azacytidine and venetoclax was designed to see whether this combination could boost remission of AML in older people. Of the 57 patients initially enrolled, 35 patients achieved either complete remission or complete remission with incomplete restoration of bone marrow function. These results were promising enough to convince the investigators to continue studying this combination in larger groups of people.

### **Other Therapeutic Approaches**

Beyond immunotherapy and targeted treatments, clinical trials brought new advances in several hard-to-treat cancers using a broader range of treatment strategies.

### **New modified chemotherapy regimen proves more potent in pancreatic cancer.**

For patients with pancreatic cancer who have had surgery, the standard postsurgery treatment until now has been gemcitabine, a chemotherapy drug that blocks tumor cells from multiplying. Despite this treatment, more than 70% of patients typically experience cancer recurrence within 2 years of surgery. This year, a trial identified a new, more effective approach using a combination of chemotherapy drugs.

In a phase III clinical trial (ClinicalTrials.gov identifier: NCT01526135)<sup>47</sup> 493 postsurgery patients were randomly assigned to either gemcitabine or a modified fluorouracil, leucovorin, irinotecan, and oxaliplatin (FOLFIRINOX) chemotherapy regimen. The modified version tested in this trial was more tolerable, with reduced dosages of some medicines to minimize toxicity.

At a follow-up of 33.6 months, the median length of time without recurrence of pancreatic cancer (disease-free survival) was much longer in the FOLFIRINOX group than in the gemcitabine group (21.6 v 12.8 months, respectively), as was the median overall survival

(54.4 v 35.0 months, respectively). Both regimens were found to be safe; however, modified FOLFIRINOX was more effective, albeit with higher toxicities. On the basis of this trial, modified FOLFIRINOX is now considered the standard of care after pancreatic cancer resection.

### **Less is more for certain ovarian cancers.**

In ovarian cancer, a recent trial (ClinicalTrials.gov identifier: NCT00565851)<sup>48</sup> helped resolve an ongoing debate about whether aggressive surgery is beneficial. This phase III clinical trial evaluated the benefit of secondary surgery for women with ovarian cancer that was successfully treated with platinum-based chemotherapy, with or without bevacizumab, in patients who were physically able to undergo additional surgical resection.

Researchers randomly assigned 485 women to secondary surgery followed by paclitaxel and carboplatin chemotherapy or chemotherapy with no additional surgery. There was no increase in survival with additional surgery; the median overall survival time was 53.6 months for patients who received the secondary surgery compared with 65.7 months for patients who only received chemotherapy.

These findings may be practice changing, as earlier studies and conventional wisdom previously supported secondary cytoreductive surgery. Although survival was over a year longer with just chemotherapy, the results need to be confirmed by studies that are now ongoing.

### **Two drugs show promise in men with prostate cancer resistant to hormone therapy.**

For men with early-stage prostate cancer, there is evidence demonstrating the benefits and risks of watching and waiting before commencing treatment. If prostate-specific antigen (PSA)



*Our nation must continue to invest in research so that we can make certain that cutting-edge cancer treatments are available to all patients. Federal research is the roadmap to renewed hope that you can bring to people's bedsides each and every day.*

– Representative Paul Tonko (D-NY)





levels rise, indicating that the cancer has progressed, the disease is typically treated with radiation, surgery, or drugs that block the androgen hormones that fuel the cancer's growth. In patients who have received hormone therapy, however, if such cancers do not respond, researchers have determined that approximately 40%, or more than 250,000 men in the United States, will develop metastases and potentially die within a 16-month time interval.

Two phase III trials (ClinicalTrials.gov identifier: NCT01946204 and NCT02003924, respectively) evaluated apalutamide (Erleada)<sup>49</sup> and enzalutamide (Xtandi)<sup>50</sup> versus placebo in men with nonmetastatic prostate cancer who have increasing PSA levels and in whom the cancer is resistant to hormone therapy. These medicines work by blocking a key driver of prostate cancer, the androgen receptor, in a much more potent fashion than previous drugs.

Each study found a significant improvement in metastasis-free survival. Median metastasis-free survival was 40.5 months in the apalutamide group compared with 16.2 months in the placebo group in one study. In the other study, median metastasis-free

survival was 36.6 months in the enzalutamide group compared with 14.7 months in the placebo group.

These results led to the FDA approval of apalutamide in February 2018,<sup>51</sup> as well as a broadening of the FDA label for enzalutamide in July 2018,<sup>52</sup> meaning that it could be used for indications beyond the initial approval for late-stage castration-resistant prostate cancers. The researchers' next aim is to analyze molecular and circulating markers from blood samples to identify patients who benefited the most from the therapies.

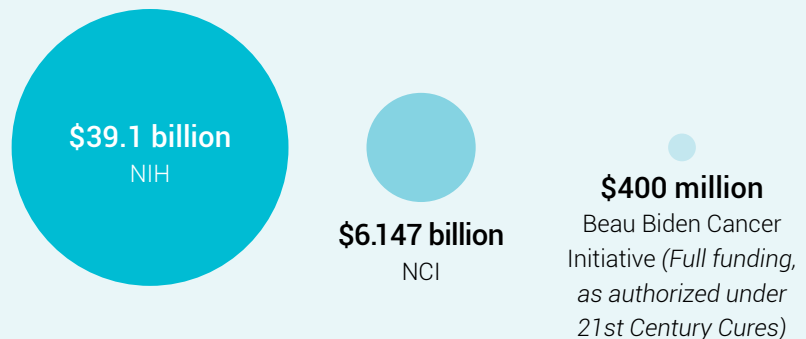
### FDA Approvals

The number of new FDA approvals in oncology continues at a rapid pace. From November 2017 through October 2018, the FDA approved 11 new cancer therapies and 39 new uses of cancer therapies (Appendix Table A2). In the same time frame in the previous year, there were 18 new cancer therapies and 13 new uses approved.

## Cancer Research: Why Federal Support Matters

### Fiscal Year 2019 Funding<sup>8</sup>

After more than 10 years of stagnant funding, Congress has demonstrated tremendous bipartisan leadership by passing four annual consecutive NIH and NCI funding increases. Most recently, lawmakers passed a \$2 billion (5.4%) NIH funding increase for Fiscal Year 2019.



### But our work is far from over.



**1/3 increase** in new US cancer cases expected over next decade<sup>9</sup>



We're only now nearing **pre-recession NCI funding levels**<sup>8,10</sup>



Despite increases, NCI is still only able to **fund a small fraction** of new research proposals (12% in 2017 v 28% in 1997)<sup>11</sup>



**75% drop** in the number of studies presented at ASCO's Annual Meeting (from 2008-2017) that were primarily funded by NIH<sup>12</sup>





# Advances in Diagnostics

*This year marked a major advance with a molecular test that can help many women with early-stage breast cancer safely forgo chemotherapy. There were also advances in the use of liquid biopsies for refining treatment in several major cancers.*

## Investigational Blood Test Detects Common Cancers

Early detection of cancers by a simple blood test, often called a liquid biopsy, is another facet of diagnostics that has been gaining traction. Some recent studies have shown that a blood test that assesses multiple potential markers, including both genes and proteins, may be sensitive enough to potentially diagnose cancer. One such test, CancerSEEK, was able to detect eight common types of cancer by assessing eight protein biomarkers and tumor-specific mutations in circulating DNA found in blood samples.

The federally funded study<sup>53</sup> analyzed the blood of approximately 1,000 patients previously diagnosed with cancers of the ovary, liver, stomach, pancreas, esophagus, colorectum, lung, or breast and compared those results to blood sample analyses from 850 healthy people. CancerSEEK was able to detect evidence of cancer with a sensitivity (the positive results were accurate) of 69% to 98% and a specificity (the negative results were accurate) of greater than 99% (this study was funded, in part, by NCI and the National Institute of General Medical Sciences). The authors suggest that CancerSEEK may be able to be developed as a universal blood test for the early diagnosis of cancer.



## Major Trial Identifies Women Who Can Safely Skip Adjuvant Chemotherapy for Breast Cancer

An international, federally funded clinical trial<sup>54</sup> of more than 10,000 women with hormone receptor-positive, HER2-negative, lymph node-negative breast cancer delivered practice-changing findings. The results of the trial showed that women older than age 50 years with low and intermediate recurrence risk scores (0 to 10 and 11 to 25, respectively), as determined by a 21-gene expression assay, did not benefit from adding adjuvant chemotherapy to standard adjuvant endocrine therapy (this study was funded, in part, by NCI).



The results from TAILORx also showed that women age 50 years and younger, especially those with recurrence scores of 21 to 25, could accrue some benefit from adjuvant chemotherapy. This clinical trial is a significant advance in precision medicine. Up until now, women older than age 50 years with scores between 11 and 25 on the *Oncotype DX* gene expression assay were usually recommended to receive adjuvant chemotherapy. These women can now safely receive just endocrine therapy, which both reduces the cost of care and spares them the short- and long-term adverse effects of chemotherapy.



## Voices for Cancer Research

### Gina Hollenbeck

Gina is a mother of two, an active runner and tennis player, and a non-smoker. Despite living a healthy lifestyle, a persistent cough brought her to the doctor where they revealed that she had a collapsed left lung with multiple tumors. At 38 years old, Gina was diagnosed with adenocarcinoma—the most common type of lung cancer seen in non-smokers.

Gina was then introduced to her oncologist, Dr. Osarogiagbon, and additional scans showed that the cancer had spread to her brain and lymph nodes. She underwent several surgeries and is being treated with therapies that specifically target a genetic mutation in the cancer.

A nurse and an avid researcher, Gina was determined to maintain an integral role in her own care with Dr. Osarogiagbon. "Dr. O has been an answer to prayer. He has let me be an active participant in my care, and we make informed decisions together. I think that has helped a lot in my care—to feel like I have a voice."

Gina credits her quality of life to clinical trials and federally funded research. "I'm grateful for clinical trials—I think they are the way we make progress in medicine. Even 5 years ago, stage IV lung cancer would have been a death sentence. Now, thanks to cancer research, people have a range of personalized therapies available to them with minimal side effects."

*Gina is the President of ALK Positive Outreach, a Facebook support group for patients with ALK-positive non-small-cell lung cancer and their caregivers.*

*"Because of cancer research and the people who have participated in clinical trials, I have a good quality of life. I can do the things I want to do."*

## Voices for Cancer Research

# Raymond U. Osarogiagbon, MD, FACP

Dr. Osarogiagbon always knew that he wanted to work on a disease where the outlook was poor and the opportunity to make a difference was great. After attending medical school in Nigeria, he came to the United States to focus on sickle-cell disease research. Later, however, he developed an interest in lung cancer.

"The development of a lung cancer is not just a personal tragedy, it affects families, communities, and populations. There is a tremendous loss of life, productivity, and happiness," said Dr. Osarogiagbon.

Findings from Dr. Osarogiagbon's early research using Veteran's Affairs (VA) electronic health records, led to the development of multidisciplinary care clinics within the VA health system. Dr. Osarogiagbon wanted to expand this multidisciplinary approach to community settings where the majority of lung cancer care is delivered. In 2005, he relocated to Memphis, Tennessee, to address what he calls the "triple whammy"—that the poorest states with the least well-developed health care infrastructure have the highest burden of disease.

"In an age of rapid discovery, these advances are not being applied fast enough to the places where people really need them—we have to bridge that gap. This is what drives me every day," said Dr. Osarogiagbon.

With the help of NIH funding, Dr. Osarogiagbon and his colleagues have developed a simple, color-coded kit to help surgical teams efficiently collect the full scope of information needed to recommend the best care for each patient with lung cancer. Dr. Osarogiagbon notes that within 5 years, the kit has helped improve the quality of lung cancer surgery by increasing the proportion of cases that meet the National Comprehensive Cancer Network's quality standard from 4% to over 80%, and significant improvements are already being seen in patient survival. He stresses the importance of federally funded studies and that now is the time to invest even more.

*Dr. Osarogiagbon is the director of the Multidisciplinary Thoracic Oncology Program at the Baptist Cancer Center, in Memphis, Tennessee. Disclosures include stock and other ownership interests with Lilly and Pfizer; honoraria from Genentech/Roche; consulting or advisory roles with Genentech/Roche, Lilly; paid research consultant for the Association of Community Cancer Centers; speakers' bureau with Genentech/Roche; a patent for a Lung Cancer Specimen Kit.*

To learn more about why Dr. Osarogiagbon lives to conquer cancer, visit [asco.org/live-to-conquer-cancer](https://asco.org/live-to-conquer-cancer).



*"We are at a point in the evolution of medical science where a lot of investments in cancer biology and care delivery are now coming together to bear fruit. Applying this knowledge to the people who will benefit most is part of the reason why we need ongoing—greater even—funding for cancer research."*





# Advances in Patient Care

*Recent findings point to new approaches that improve patient outcomes and quality of life during and after treatment. These include ways to ease treatment for people with blood cancers, to mitigate hearing loss in children undergoing intensive chemotherapy, to lessen repeated testing of people who have had surgery for colorectal cancer, and to better inform people about the risks of alternative medicine.*

## Palliative Interventions Beneficial Among Patients Undergoing Potentially Curative Treatment of Blood Cancer

Building on prior research showing the benefits of early initiation of supportive care, including palliative care, in patients with advanced cancer, a new study, SHEILD (ClinicalTrials.gov identifier: NCT02207322),<sup>55</sup> looked at the approach in 160 people with hematologic malignancies undergoing potentially curative hematopoietic stem-cell transplantation.

The study randomly assigned people to routine transplantation care or transplantation care with integrative supportive and palliative care. At the start of the study and at 6 months after transplantation, the investigators assessed quality of life, anxiety, and symptom burden, among other factors. The researchers found that patients in the intervention arm (integrated palliative care) had lower depression symptoms and lower post-traumatic stress disorder symptoms, but there was no benefit for quality of life or anxiety. On the basis of this study, incorporating inpatient

### Voices for Cancer Research

## Alan P. Lyss, MD

As a clinician researcher, one of Dr. Lyss' missions is to provide advanced care and treatment options to patients through cutting-edge research. For many of his patients who live in a rural setting, access to proper care can be a real challenge and often leads to delays in diagnosis and treatment. Support from the NCI Community Oncology Research Program (NCORP) has helped Dr. Lyss bridge the gap for his patients, allowing them to gain access to clinical trials in their communities rather than having to travel long distances to receive care.

Dr. Lyss specializes in breast cancer prevention and treatment, aiming to improve the quality of life for his patients. Among the studies available through NCORP, he offers a simple but important study evaluating whether aspirin can help prevent recurrence in women with node-positive, HER2-negative breast cancer. He and his colleagues are also helping test strategies to decrease the number of lymph nodes removed during surgery for women with locally advanced breast cancer, lessening the chance of arm swelling after surgery.

Dr. Lyss pins a bright red "Research Cures Cancer" button on his white coat every day to remind himself of the importance of cancer research. "There are real lives at stake, and they're at stake every day. As long as we have people who are dying of cancer, as long as we have people who suffer long-term effects related to cancer or its treatment, we can do better, and we must do better," said Dr. Lyss.

*Dr. Lyss is an oncologist at Missouri Baptist Medical Center, Heartland Cancer Research NCORP, in St. Louis, Missouri. Disclosures: none.*

*To learn more about why Dr. Lyss lives to conquer cancer, visit [asco.org/live-to-conquer-cancer](https://www.asco.org/live-to-conquer-cancer).*



*"NCI-funded research helps to level the playing field and assure that the latest innovations are available to people who need them—wherever they live, whatever their social circumstances, whatever their race, ethnicity, age, or gender."*

palliative care into routine transplantation could lead to decreased psychological distress that typically persists 6 months after the transplantation.

### Alternative Medicine Is Not a Substitute for Conventional Therapy

Studies quantifying benefits and risks of alternative and unproven therapies in many cancers have not been extensive. An observational study<sup>56</sup> of data from the National Cancer Database confirmed that there is a much higher likelihood of death among patients diagnosed with early-stage or curable breast, lung, or colon cancers who only received alternative medicine, compared with those treated with standard therapy. In this study, which included data from 840 patients treated between 2004 and 2013, authors defined alternative therapies as unproven cancer treatments given by nonmedical personnel.

The 5-year survival rate for patients treated with alternative medicine was 54.7% compared with 78.3% for those who received standard therapy. Cancer-specific 5-year survival rates were also higher for patients with breast, lung, and colorectal cancer who were treated with conventional therapy. The rates were lower, however, for patients treated with conventional therapy for prostate cancer. Researchers suspect this can be attributed to the typically slower progression of prostate cancer.

### Alternative Medicine: Widespread Misconceptions



A surprising number of Americans believe that cancer can be cured solely through alternative therapies

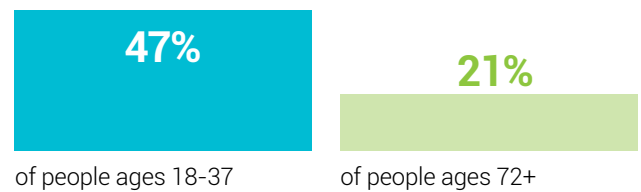
Nearly **4 in 10** Americans



**38%** of caregivers to cancer patients

**22%** of people who have/had cancer

**Younger people** are most likely to hold this view



### Voices for Cancer Research

## Sarah Bryan Miller

Sarah Bryan was 58 when she was diagnosed with a rare form of breast cancer, stage III inflammatory disease, which was followed by a second diagnosis 2 years later of ductal carcinoma in situ. The treatments she received—including chemotherapy, radiation therapy, and multiple surgeries—have helped to prolong her life but have also resulted in mobility issues.

However, as a former professional opera singer, a current member of her church choir, and the classical music critic at the *St. Louis Post-Dispatch*, Sarah Bryan was determined to continue supporting herself financially and to participate in the activities she loves. She credits cancer research and her “honest, straightforward, caring” oncologist, Dr. Lyss for enabling her to keep working and living independently.

Since her initial diagnosis, Sarah Bryan has participated in multiple clinical trials. She believes the federal government has the power to make a positive effect by funding cancer research.

“I’m grateful to live in a time when discoveries are being made and new treatments are being developed,” said Sarah Bryan. “I benefited from research that others have participated in, and it makes going through all of this a little more meaningful, if my participation in a trial helps other people, too.”

*Sarah Bryan is an active volunteer with her local cancer support community in St. Louis, Missouri.*



*“On one side, you may benefit personally from participating in a clinical trial, and on the other, you may be helping someone else. That’s a pretty compelling argument to me.”*



According to the National Cancer Opinion Survey conducted by ASCO in 2018, nearly four in 10 Americans, or 39%, believe cancer can be cured solely through alternative therapies, such as enzyme and oxygen therapy, diet, vitamins, and minerals. The survey also found that younger people (47% of survey respondents age 18 to 37 years and 44% of participants age 38 to 53 years) are the most likely to hold these views.<sup>14</sup>

The National Cancer Database study provides important information to help guide patient decisions about care and might help mitigate concerns about the use of conventional therapies compared with alternative approaches. The researchers also emphasized that alternative medicine should not be confused with integrative or complementary medicine.

### New Combination Treatment Halves Hearing Loss Risk in Children With Hepatoblastoma

Hepatoblastoma, a form of liver cancer that develops in infants and children, can often be treated effectively with a combination of cisplatin chemotherapy and surgery. Cure rates for standard-risk hepatoblastoma are now consistently greater than 80%, and close to 50% of children with high-risk disease can also be cured. The intensive use of cisplatin in young children, however, is associated with irreversible hearing loss.

In a recent federally funded study, SIOPEL6 (ClinicalTrials.gov identifier: NCT00652132),<sup>57</sup> 109 children with standard-risk hepatoblastoma were randomly assigned to receive cisplatin or cisplatin plus sodium thiosulfate treatment (this study was funded, in part, by NIH and the US Department of Veterans Affairs). Sodium



thiosulfate is a basic chemical compound that is on the World Health Organization list of essential, safe medicines.<sup>58</sup>

In the study, the two medicines were given over four courses before surgery and two courses after surgery. Hearing loss of any grade was nearly halved with the combination treatment. Grade 1 or greater hearing loss (on a scale with grade 1 being the least loss of hearing and grade 4 the most) occurred in 33% of children in the cisplatin plus sodium thiosulfate group compared with 63% of children in the cisplatin-alone group. Survival was not affected by adding sodium thiosulfate to cisplatin, suggesting that the addition did not have a tumor-protective effect.

### Surveillance of Postsurgical Patients With Colorectal Cancer Could Effectively Be Lessened

The optimal frequency of follow-up testing for people who have been treated for colorectal cancer has not been quantified. In an unblinded trial, COLOFOL (ClinicalTrials.gov identifier: NCT00225641),<sup>59</sup> conducted in Sweden, Denmark, and Uruguay, more than 2,500 people with stage II or III colorectal cancer were randomly assigned to either low-frequency follow-up (computed tomography of the chest, abdomen, and pelvis and measurement of carcinoembryonic antigen, a blood antigen, at 12 and 36 months after surgery) or high-frequency follow-up (the same tests at 6, 12, 28, 24, and 36 months after surgery). Primary outcomes showed no difference in the number of deaths overall after 5 years as a result of colorectal cancer or any other cause.

The finding—that less frequent surveillance does not result in worse survival outcomes—indicates that it is safe for patients to have less testing over time, a finding that should reduce health care costs as well as reduce patients' exposure to unnecessary radiation from computed tomography scans.

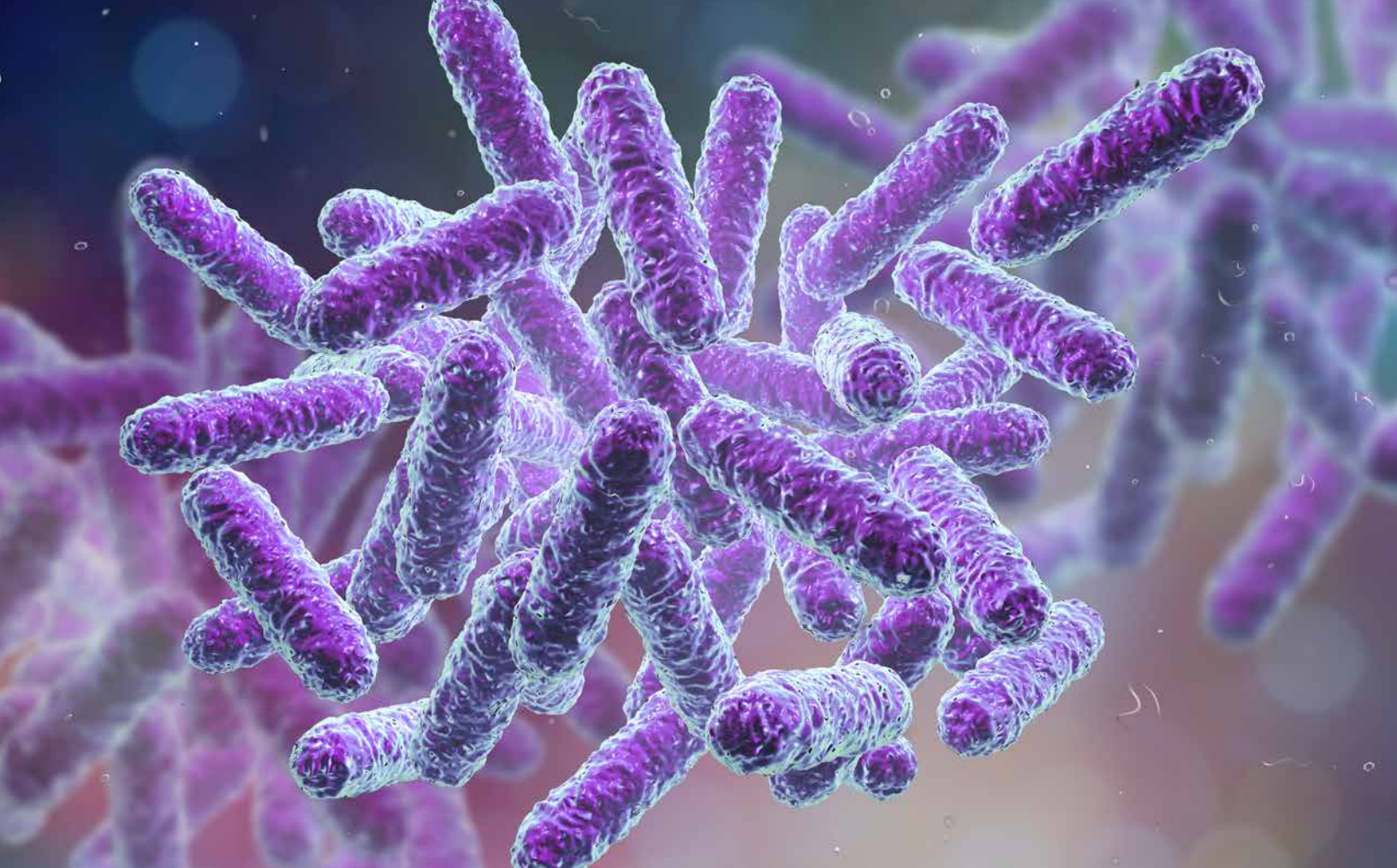
“

*I am proud that the 21st Century Cures Act included funding increases for NIH signed into law on a bipartisan basis. Oncologists and lawmakers both care about people with cancer, and, together, we can work toward even greater increases for NIH to find answers that will improve treatments patients receive.*

— Representative Fred Upton (R-MI)

”





# The Microbiome and Cancer

*The human body's microbial community is thought to have such intricate and profound effects on human health that it is often referred to as the hidden organ. By evolving together over thousands of years, indwelling microbes and their human hosts have developed a mutually beneficial relationship. The relationship is so intertwined that one can think of the human body as one superorganism made of both human and microbial cells.<sup>60</sup>*

*From birth through the early years of life, countless different bacteria colonize the body. These trillions of microbes form the human microbiome, which is influenced by genetic, environmental, and lifestyle factors (such as diet, medication use, and physical activity). Because of this, the composition of the microbiome varies from one person to the next.<sup>60</sup>*



Recent research has shown that the microbiome plays an important role in maintaining and influencing key physiologic activities, including normal metabolism and immune function. Laboratory and clinical evidence suggest that changes in specific organisms in the microbiome may lead to the development of disease, including cancer.

When it comes to cancer, the body's microbes can be both harmful and beneficial. Although certain microbes may promote cancer growth, others seem to bolster the body's immune defenses against cancer or help cancer treatments work better.<sup>60</sup>

Microbiome research is a young and fast-growing field; however, it is not yet clear that specific microbes have beneficial or detrimental roles in cancer development. As such, research efforts are expanding.

### The Microbiome Shapes Cancer Risk

While much work has focused on the gut microbiome, researchers have found that changes in oral and vaginal microbiomes could be associated with modified disease risk as well. Many investigations have found links between the abundance of specific organisms that comprise the microbiome and the risk of colon, squamous cell, and esophageal cancers. These observations suggest that modulating the microbiome in individuals at high risk of developing certain malignancies may be a cancer prevention strategy worth exploring.

Over the past several years, two federally funded studies looked at oral mouthwash samples from people to determine the presence of specific bacterial microbes. One study enrolled 383 patients and controls to examine how the microbiome might influence head and neck squamous cell cancer.<sup>61</sup> Researchers noted that people who



developed this disease were more often current tobacco smokers, consumed moderate to high levels of alcohol, and were human papillomavirus type 16 positive (this study was funded, in part, by NCI).

For patients with head and neck squamous cell cancer, researchers found that while the overall composition of the microbiome was not associated with increased cancer risk, an abundant amount of *Corynebacterium* and *Kingella* bacteria was associated with a decreased risk.

Another study looked at the prevalence of oral bacteria in 106 patients with esophageal adenocarcinoma (EAC) and esophageal squamous cell carcinoma (ESCC)<sup>62</sup> (this study was funded, in part, by NCI). The periodontal pathogen *Tannerella forsythia* was associated with higher risk of EAC, whereas depletion of *Neisseria* and *Streptococcus pneumoniae* bacteria was associated with lower EAC risk. For ESCC, the abundance of the periodontal bacterium *Porphyromonas gingivalis* conveyed higher risk of the cancer.



It is too soon to offer a strategy for using the microbiome to modify cancer risk or progression; however, the findings of these two studies could inform the basis for future research on effective approaches for prevention or treatment of some head and neck cancers.

Though there are still many questions to answer about the microbiome, it is known that a lifestyle involving a well-balanced diet and exercise can promote a diverse microbiome associated with good health. In the future, cancer care may even include an analysis of the patient's microbiome at diagnosis to inform personalized treatment planning. ASCO will continue to monitor progress in this complex but fascinating field of research and will report on progress in understanding the microbiome and cancer in future editions of *Clinical Cancer Advances*.





## Voices for Cancer Research

# Judith Kaur, MD

Dr. Kaur grew up in the inner city of Chicago and was the first in her family to graduate from high school and college. As a young female student with a passion for science and an admiration for teachers, in the 1960s Dr. Kaur was encouraged to pursue one of the few professions thought to be suitable for women at that time—science teacher. It wasn't until her husband challenged her to go to medical school that she seriously considered it. Dr. Kaur was later accepted to the Indians into Medicine Program at the University of North Dakota, a federal program that recruits Native Americans, like Dr. Kaur, into medical school.

Later, Dr. Kaur received the very first Young Investigator Award from the Conquer Cancer Foundation of ASCO, which provides grant funding to early-career researchers to begin and establish the direction of their cancer research. She received the award for her innovative work in creating monoclonal antibodies for use in melanoma, a treatment unheard of at the time but now a standard of care.

Dr. Kaur has become a pioneer in women's cancer research and education, particularly in breast and cervical cancers. She incorporates her love for teaching into her clinical practice every day and stresses the importance of personalized education to overcome cancer health disparities across the country. "It comes down to having the best treatment for the right patient for the right reason, every time you see them," said Dr. Kaur.

*"In medical school the doctors I worked with were so hopeful that we would find something better to offer our patients, and indeed, every year, thanks to cancer research, there has been something new."*

Today, Dr. Kaur leads the Spirit of Eagles, a program that focuses on including Native Americans in research training and education and provides culturally tailored materials for tribes across the country. Through her leadership and research, Dr. Kaur's efforts are increasing clinical trial participation, improving cancer prevention, and supporting students interested in pursuing careers in medicine.

*Dr. Kaur, pictured center above, is an oncologist and medical director for the Native American Programs in the Mayo Clinic Cancer Center in Jacksonville, Florida. Disclosures include honoraria and travel, accommodations, and expenses from Lilly.*

*To learn more about why Dr. Kaur lives to conquer cancer, visit [asco.org/live-to-conquer-cancer](https://asco.org/live-to-conquer-cancer).*





# Nine Research Priorities to Accelerate Progress Against Cancer

*As the organization that represents and connects the global community of clinicians who discover new treatments for cancer and deliver the latest advances to patients, ASCO has developed, for the first time, a set of Research Priorities to Accelerate Progress Against Cancer. These priorities represent promising areas of research that urgently need greater attention and have the potential to significantly improve the knowledge base for clinical decision-making and address vital unmet needs in cancer care.*

The current list reflects ASCO's mission—conquering cancer through research, education, and promotion of the highest quality patient care—as well as the diversity of needs and opportunities in oncology. It focuses on cancer prevention strategies, increasing equity in access to and participation in research, optimizing treatment, and improving long-term health for the growing number of cancer survivors around the world.

Over time, ASCO's Research Priorities will evolve with the cancer research landscape and will be periodically updated to reflect advancing science and unmet clinical needs. Current priorities are listed in no particular order.

## 1 Identify Strategies That Better Predict Response to Immunotherapies

Cancer immunotherapy encompasses a broad range of medicines and treatment approaches, including vaccines, immune checkpoint inhibitors, and most recently, cellular therapies. These interventions have improved the outlook for multiple cancers, producing long-lasting remissions that can last for years in some patients. At present, however, long-term disease control occurs in just a minority of patients. In addition, immunotherapies can cause substantial side effects that can be life-threatening, and in some cases, permanent. Methods to identify patients most likely to benefit from immunotherapy and those at high risk for severe adverse events are urgently needed. The ability to adequately assess benefits and risks of immunotherapy for each individual will lead to better outcomes for patients.

### Priority Focus Areas

- Identify factors that predict response, long-term disease control, prolonged survival, treatment resistance, and adverse events for all types of immunotherapies
- Develop blood and tissue-based biomarkers and novel immune-response signatures that predict treatment benefit

- Develop predictive models and algorithms that assign risk of severe immune-related toxicities based on readily available patient data

## 2 Better Define the Patient Populations That Benefit From Postoperative (Adjuvant) Therapy

A wide range of therapies are recommended to patients after surgery. These therapies, referred to as adjuvant treatments, aim to reduce the risk of recurrence and cancer-related death. Although such therapy has been associated with dramatic improvements in survival for some patients, studies have shown that the risks can outweigh the benefits for others. It is important to ensure that patients who receive adjuvant therapy are the ones most likely to benefit. Eliminating its use in those who do not benefit will be an important step in optimizing care and eliminating unnecessary side effects and costs for patients in whom the benefits are unlikely to outweigh the risks.

### Priority Focus Areas

- Determine factors that identify patients most likely to benefit, or those unlikely to benefit, from adjuvant therapy, including, but not limited to, clinical, pathological, genomic, biochemical, immunological, and environmental/social factors
- Develop analytically and clinically valid biomarker tests with proven clinical utility to identify recurrence risk after treatment of the primary tumor and determine the best options for patients with different degrees of risk

## 3 Translate Innovations in Cellular Therapies to Solid Tumors

Recent FDA approvals of chimeric antigen receptor (CAR) T-cell therapies in leukemia and lymphoma are true milestones in cancer

## A Path Forward to Increase Access to Clinical Trials

ASCO is working with key stakeholders to address under-representation of certain populations in clinical trials. Recently, the society issued a policy statement on the financial barriers that prevent patients from participating in clinical trials. ASCO's recommendations include: improve insurance coverage of routine care costs for clinical trial participants, increase transparency about out-of-pocket costs, remove impediments to ethically appropriate direct payments to patients, and incentivize research on the financial costs of trial participation.

This statement builds on ASCO's work with Friends of Cancer Research to address under-representation in cancer clinical trials through more inclusive eligibility criteria. The two organizations developed comprehensive recommendations to address eligibility criteria in five areas: minimum age requirements for trial enrollment, HIV/AIDS status, brain metastases, organ dysfunction, and prior and concurrent malignancies.

therapy, as signified by ASCO's 2018 Advance of the Year designation. Although cellular therapies that use a patient's modified cells to harness the immune system are transforming care for some patients with blood-based cancers, there are limited data to show whether this strategy can be expanded to patients with solid tumors.

#### Priority Focus Areas

- Identify and validate novel antigenic targets uniquely present in solid tumors
- Explore the safety and activity of promising cellular therapies in solid tumors
- Develop strategies that mitigate current challenges in delivering cellular therapies to patients, including exploring the use of cellular products that do not have to be individually manufactured for each patient
- Examine and optimize the cancer care delivery systems needed to safely administer cellular therapies to all who might benefit

## 4 Increase Precision Medicine Research and Treatment Approaches in Pediatric Cancers

Genomic tools have been widely deployed for adult patients to characterize common mutations across different types of cancer. In certain cancers, the use of these tools has accelerated development of new targeted therapies that have improved and extended patients' lives. Despite this success in adult patients, precision medicine treatment approaches have yet to be widely integrated into the treatment of pediatric cancers.

#### Priority Focus Areas

- Identify genomic or other molecular alterations in pediatric cancers that can serve as potentially actionable treatment targets

## Voices for Cancer Research

# Renee Bakos-Pournaras and Yano Pournaras

In 2008, 2-year-old Yano's health began to deteriorate. He developed fevers that would not subside, lost his appetite, and had trouble walking. His mother, Renee, knew something was wrong. "Things were just off, things were not right," she said.

Yano's condition did not improve after multiple visits to the doctor, many rounds of bloodwork, and treatment with intravenous antibiotics. Then one morning he woke up with what appeared to be bruises around his eye sockets. Renee rushed him to the hospital where he underwent scans that revealed a large tumor on his spine. On his third birthday, Yano was diagnosed with stage IV terminal cancer.

Less than 24 hours after his diagnosis, Renee returned to her hometown of Chicago with Yano to begin his treatment. Yano received surgery, chemotherapy, radiation, and stem cell transplants as part of his care. His mother was determined to save his life and served as his biggest advocate, ensuring he received the latest treatment options available.

"He went on almost every clinical trial the doctors presented us with. We tried everything, literally everything," she said. One of the treatments he received as part of a clinical trial is now a standard of care for patients with high-risk neuroblastoma.

Today Yano is a thriving 12-year-old, thanks to the incredible care of his doctors and the clinical trials he was offered. Based on his experience with cancer, Yano is now working on an anti-bullying campaign aimed at helping children with cancer. He knows first-hand that side effects from treatment, such as hair loss, can make children with cancer feel different from their peers and wants to help all children understand and overcome these perceived differences.

Renee has great admiration for her son, "He's truly my miracle." Once Yano finished treatment and went into remission, he officially graduated into long-term care and was introduced to his current oncologist, Dr. Henderson.

"Yano's doctors are the most compassionate people I have ever met. They know all the side effects of his treatments and they are constantly searching for ways to make things better because they truly care," said Renee.



*"We wouldn't be here today if it weren't for what research did for us in 2009. I never even had to think about my son participating in a clinical trial—some other mother gave permission for her child so that my child could be in the position he is in today. It's a domino effect."*





## Voices for Cancer Research

# Tara Henderson, MD, MPH

Fascinated by science at a young age, Dr. Henderson participated in a cancer research laboratory program during her junior year of high school. The experience led her to combine her knack for science and desire to positively impact the world with a career in cancer research.

Today, Dr. Henderson directs a cancer survivor clinic in one of the biggest cities in the United States. The clinic's program is aimed at preventing and treating the long-term health issues that pediatric and adult survivors of cancer may face after treatment. Her ongoing research efforts, many of which are federally funded, are dedicated to keeping patients healthy for the rest of their lives.

"I wake up every day excited to be part of the amazing success story of pediatric oncology," said Dr. Henderson. "I'm working hard to make sure that all kids can live healthy lives like my own children."

Dr. Henderson's current research focuses on better understanding the lingering effects of treatments for children with high-risk neuroblastoma. She wants to ensure that the recent advances in the treatment of pediatric cancers don't lose their momentum. She notes that the overall survival rate for children with cancer is now more than 80%,<sup>63\*</sup> compared with 58% in the mid-1970s.<sup>63\*\*</sup>

Many of these pioneering research advances can be attributed to clinical trials and studies funded by the federal government.

*"Pediatric oncology is one of the great success stories of medicine because of our nation's commitment to curing this disease."*

While Dr. Henderson is proud of the successes in her field, she acknowledges that we still have a long way to go. She believes that federal investment in cancer research must continue now to "make sure that the progress continues in 10, 20, or 30 years for children all over the world." She envisions a future where no child dies of cancer and aspires to ensure a future where no child dies of the consequences of cancer treatment, either.

*Dr. Henderson is a pediatric oncologist and director of the Childhood Cancer Survivors Center at University of Chicago Medicine. Disclosures for Dr. Henderson include research funding from Seattle Genetics and other relationships with the company.*

To learn more about why Dr. Henderson lives to conquer cancer, visit [asco.org/live-to-conquer-cancer](https://www.asco.org/live-to-conquer-cancer).



- Develop effective therapeutic agents that can target genomic or other molecular alterations in childhood cancers
- Explore the efficacy of existing targeted therapies in pediatric patients with tumors that have mutations shown to be responsive to medicines that work in adult populations

## 5 Optimize Care for Older Adults With Cancer

Although adults age 65 years and older represent the majority of people with cancer, few cancer clinical trials focus specifically on this population. Older patients who do participate in clinical trials are generally not representative of the older patients who oncologists typically see in daily practice. As a result, clinicians face challenges applying clinical trial data to older patients who may have additional health conditions, varying levels of functional ability, and different goals from clinical trial participants. The lack of evidence in this area combined with the inherent diversity of aging populations impedes the delivery of high-quality care for the largest and most rapidly growing segment of patients with cancer.

### Priority Focus Areas

- Develop standardized methods to characterize physiologic aging, such as geriatric assessment and biomarkers of aging, to more reliably predict risk of treatment-related side effects in older people with cancer
- Investigate the impact of cancer treatment on physical function, cognition, and quality-of-life to inform tolerability of cancer therapies in older people
- Investigate the efficacy and toxicity of therapies among older adults most under-represented in clinical trials, such as those with impaired functional status, comorbidities, or frailty
- Conduct clinical trials testing the role of geriatric assessment-guided management to improve outcomes using personalized care; important focus areas include strategies that minimize undertreatment for fit patients and overtreatment for vulnerable or frail patients, supportive care interventions, and care delivery interventions

## 6 Increase Equitable Access to Cancer Clinical Trials

Certain patient populations are consistently under-represented in cancer clinical trials. These include patients from racial and ethnic minorities, rural areas, lower socioeconomic groups, and people older than 65 years as well as adolescents and young adults age 15–39 years. Decreased representation among these groups can limit access to the promising treatments offered through these

trials and means that research findings may not fully account for the diversity of biological, social, and cultural factors that influence outcomes. Additional research is needed to ensure that every patient with cancer, regardless of race, ethnicity, age, geographic location, or socioeconomic status, benefits from research advances.

### Priority Focus Areas

- Improve understanding of the barriers to trial enrollment among various under-represented groups, taking into consideration patient, practice, community, and trial-specific factors
- Develop and test interventions that enhance clinical trial enrollment among under-represented populations (examples may include use of educational tools, tele-health, and community-based involvement, and participatory research)
- Evaluate novel strategies to improve access to clinical research resources in areas with large proportions of under-represented minorities
- Develop mechanisms that improve awareness and education about clinical trials among under-represented groups and the physicians treating them
- Investigate differences in cancer incidence, prevalence, natural history of disease, and treatment experience, including efficacy and toxicity, among under-represented populations

## 7 Reduce the Long-Term Consequences of Cancer Treatment

Advances in cancer treatment have resulted in a record number of cancer survivors—over 15.5 million.<sup>63</sup> Although this is a tremendous accomplishment, survivors still face long-term consequences of cancer, including side effects of cancer therapies that affect quality of life. These side effects, which commonly include peripheral neuropathy, cognitive impairment, and cardiotoxicity, pose a substantial burden not only to patients but also to the health care system.

### Priority Focus Areas

- Identify genetic variants associated with increased risk of treatment-related toxicities
- Deepen understanding of the underlying mechanisms of toxicities from targeted treatments, determine their contribution to long-term effects, and develop novel strategies to mitigate or eliminate such toxicities
- Develop new tools to facilitate long-term tracking of patient outcomes that include patient-reported outcome measures



## 8 Reduce Obesity's Impact on Cancer Incidence and Outcomes

The incidence of obesity has dramatically increased over the past several decades.<sup>64</sup> Despite being the second leading preventable cause of cancer, a recent ASCO survey<sup>14</sup> found that only 35% of Americans recognize excess body weight as a cancer risk factor. Obesity is associated with poorer cancer survival and can contribute to increased risk of treatment-related side effects. If current trends continue over the next 20 years, it is estimated that obesity will lead to more than 500,000 additional cases of cancer each year in the United States<sup>65</sup> and will surpass smoking as the leading preventable cause of cancer.

### Priority Focus Areas

- Improve the understanding of the mechanisms through which weight and energy balance, including physical activity and dietary factors, contribute to cancer development and progression
- Investigate how obesity affects response to therapy, risk of cancer recurrence, and long-term cancer outcomes
- Assess the impact of energy balance interventions, such as weight loss, increased physical activity, and improved dietary quality, on cancer risk, recurrence, and mortality

- Identify effective interventions that optimize energy balance in people at risk and who are living with cancer

## 9 Identify Strategies to Detect and Treat Premalignant Lesions

Many cancers begin as high-risk lesions that invariably progress to invasive cancer. Currently, little is known about the genetic makeup, heterogeneity, microenvironment, and what causes some of these lesions to progress to invasive cancer. Increased knowledge will help guide new approaches to intercept and eradicate high-risk lesions prior to their transformation to malignancy.

### Priority Focus Areas

- Identify specific molecular pathways that drive progression of preinvasive lesions to invasive cancer and develop interventions that can delay or prevent progression to malignancy
- Identify features of the microenvironment of premalignant lesions that are associated with progression to invasive disease
- Investigate novel methods for evaluation of premalignant lesions to better inform the risk or likelihood of progression to invasive disease

# BREAKTHROUGHS SAVE LIVES

*Six-time sarcoma survivor Brittany Sullivan (left) and Breelyn Wilky, MD (right)*



Learn how Dr. Wilky's clinical trial led to a breakthrough in research and saved Brittany's life.

**CONQUER CANCER**<sup>®</sup>  
THE ASCO FOUNDATION

Watch their story on  
**CONQUER.ORG**

1. Wingo PA, Ries LA, Rosenberg HM, et al: Cancer incidence and mortality, 1973-1995: A report card for the U.S. *Cancer* 82:1197-1207, 1998
2. Cronin KA, Lake AJ, Scott S, et al: Annual report to the nation on the status of cancer, part I: National cancer statistics. *Cancer* 124:2785-2800, 2018
3. Bluethmann SM, Mariotto AB, Rowland JH: Anticipating the "silver tsunami": Prevalence trajectories and comorbidity burden among older cancer survivors in the United States. *Cancer Epidemiol Biomarkers Prev* 25:1029-1036, 2016
4. National Cancer Institute: The International Rare Cancer Initiative. <https://www.cancer.gov/about-nci/organization/cgh/research/irci>
5. American Cancer Society: Cancer facts and figures 2018. <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2018/cancer-facts-and-figures-2018.pdf>
6. Center Watch: FDA approved drugs for oncology. <https://www.centerwatch.com/drug-information/fda-approved-drugs/therapeutic-area/12/oncology>
7. National Institutes of Health: Yesterday, today, and tomorrow: NIH research timelines. <https://report.nih.gov/nihfactsheets/viewfactsheet.aspx?csid=75>
8. National Institutes of Health: Appropriations. <https://www.nih.gov/about-nih/what-we-do/nih-almanac/appropriations-section-1>
9. Thielking M: Cancer deaths are down—But new cases are on the rise, report says. <https://www.statnews.com/2017/09/13/cancer-deaths-cases-rise/>
10. Bureau of Labor Statistics: CPI inflation calculator. [https://www.bls.gov/data/inflation\\_calculator.htm](https://www.bls.gov/data/inflation_calculator.htm)
11. National Institutes of Health: Research project success rates by NIH institute. [https://report.nih.gov/success\\_rates/Success\\_ByIC.cfm](https://report.nih.gov/success_rates/Success_ByIC.cfm)
12. ASCO: ASCO annual meeting statistics.
13. United for Medical Research: NIH's role in sustaining the U.S. economy: 2018 update. <http://www.unitedformedicalresearch.com/wp-content/uploads/2018/02/NIHs-Role-in-Sustaining-the-U.S.-Economy-2018-Update-FINAL.pdf>
14. ASCO: ASCO 2018 Cancer Opinions Survey. <https://www.asco.org/sites/new-www.asco.org/files/content-files/research-and-progress/documents/2018-NCOS-Results.pdf>
15. National Cancer Institute: SEER cancer stat facts: Thyroid cancer. <https://seer.cancer.gov/statfacts/html/thyro.html>
16. Rao SN, Zafereo M, Dadu R, et al: Patterns of treatment failure in anaplastic thyroid carcinoma. *Thyroid* 27:672-681, 2017
17. US Food and Drug Administration: FDA approves dabrafenib plus trametinib for adjuvant treatment of melanoma with BRAF V600E or V600K mutations. <https://www.fda.gov/drugs/informationondrugs/approveddrugs/ucm606165.htm>
18. Subbiah V, Kreitman RJ, Wainberg ZA, et al: Dabrafenib and trametinib treatment in patients with locally advanced or metastatic BRAF V600-mutant anaplastic thyroid cancer. *J Clin Oncol* 36:7-13, 2018
19. Gounder MM, Mahoney MR, Van Tine BA, et al: Phase III, randomized, double blind, placebo-controlled trial of sorafenib in desmoid tumors (Alliance A091105). *J Clin Oncol* 36, 2018 (suppl; abstr 11500)
20. Dasari A, Shen C, Halperin D, et al: Trends in the incidence, prevalence, and survival outcomes in patients with neuroendocrine tumors in the United States. *JAMA Oncol* 3:1335-1342, 2017
21. Strosberg J, El-Haddad G, Wolin E, et al: Phase 3 trial of 177Lu-Dotatate for midgut neuroendocrine tumors. *N Engl J Med* 376:125-135, 2017
22. US Food and Drug Administration: FDA approves lutetium Lu 177 dotatate for treatment of GEP-NETS. <https://www.fda.gov/drugs/informationondrugs/approveddrugs/ucm594105.htm>
23. Strosberg J, Wolin E, Chasen B, et al: Health-related quality of life in patients with progressive midgut neuroendocrine tumors treated with 177Lu-Dotatate in the phase III NETTER-1 trial. *J Clin Oncol* 36:2578-2584, 2018
24. Fader AN, Boruta D, Olawaye AB, et al: Uterine papillary serous carcinoma: Epidemiology, pathogenesis and management. *Curr Opin Obstet Gynecol* 22: 21-29, 2010
25. Fader AN, Roque DM, Siegel E, et al: Randomized phase II trial of carboplatin-paclitaxel versus carboplatin-paclitaxel-trastuzumab in uterine serous carcinomas that overexpress human epidermal growth factor receptor 2/neu. *J Clin Oncol* 36:2044-2051, 2018
26. Tap WD, Gelderblom H, Stacchiotti S, et al: Final results of ENLIVEN: A global, double-blind, randomized, placebo-controlled, phase 3 study of pexidartinib in advanced tenosynovial giant cell tumor (TGCT). *J Clin Oncol* 36, 2018 (suppl 15; abstr 11502)
27. Socinski MA, Jotte RM, Cappuzzo F, et al: Atezolizumab for first-line treatment of metastatic nonsquamous NSCLC. *N Engl J Med* 378:2288-2301, 2018
28. Gandhi L, Rodríguez-Abreu D, Gadgeel S, et al: Pembrolizumab plus chemotherapy in metastatic non-small-cell lung cancer. *N Engl J Med* 378:2078-2092, 2018
29. Motzer RJ, Tannir NM, McDermott DF, et al: Nivolumab plus ipilimumab versus sunitinib in advanced renal-cell carcinoma. *N Engl J Med* 378:1277-1290, 2018
30. US Food and Drug Administration: FDA approves nivolumab plus ipilimumab combination for intermediate or poor-risk advanced renal cell carcinoma. [www.fda.gov/drugs/informationondrugs/approveddrugs/ucm604685.htm](http://www.fda.gov/drugs/informationondrugs/approveddrugs/ucm604685.htm)
31. Tawbi HA, Forsyth PA, Algazi A, et al: Combined nivolumab and ipilimumab in melanoma metastatic to the brain. *N Engl J Med* 379:722-730, 2018
32. US Food and Drug Administration: FDA approves first treatment for advanced form of the second most common skin cancer. <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm622044.htm>
33. Migden MR, Rischin D, Schmultz CD, et al: PD-1 blockade with cemiplimab in advanced cutaneous squamous-cell carcinoma. *N Engl J Med* 379:341-351, 2018
34. Soulieres D, Cohen E, Le Tourneau C, et al: Updated survival results of the KEYNOTE-040 study of pembrolizumab vs standard-of-care chemotherapy for recurrent or metastatic head and neck squamous cell carcinoma. *Cancer Res* 78:13, 2018 (abstr CT115)



35. US Food and Drug Administration: FDA approves tisagenlecleucel for B-cell ALL. <https://www.fda.gov/drugs/informationondrugs/approveddrugs/ucm574154.htm>
36. Maude SL, Laetsch TW, Buechner J, et al: Tisagenlecleucel in children and young adults with B-cell lymphoblastic leukemia. *N Engl J Med* 378:439-448, 2018
37. Neelapu SS, Locke FL, Bartlett NL, et al: Axicabtagene ciloleucel CAR T-cell therapy in refractory large B-cell lymphoma. *N Engl J Med* 377:2531-2544, 2017
38. US Food and Drug Administration: FDA approves CAR-T cell therapy to treat adults with certain types of large B-cell lymphoma. <https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm581216.htm>
39. Schuster SJ, Svoboda J, Chong EA, et al: Chimeric antigen receptor T cells in refractory B-cell lymphomas. *N Engl J Med* 377:2545-2554, 2017
40. Soria JC, Ohe Y, Vansteenkiste J, et al: Osimertinib in untreated EGFR-mutated advanced non-small-cell lung cancer. *N Engl J Med* 378:113-125, 2018
41. Ramalingam SS, Yang JC, Lee CK, et al: Osimertinib as first-line treatment of EGFR mutation-positive advanced non-small-cell lung cancer. *J Clin Oncol* 36: 841-849, 2018
42. US Food and Drug Administration: FDA approval of Herceptin. [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2010/103792s5250lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/103792s5250lbl.pdf)
43. Sledge GW Jr, Toi M, Neven P, et al: MONARCH 2: Abemaciclib in combination with fulvestrant in women with HR+/HER2- advanced breast cancer who had progressed while receiving endocrine therapy. *J Clin Oncol* 35:2875-2884, 2017
44. Goetz MP, Toi M, Campone M, et al: MONARCH 3: Abemaciclib as initial therapy for advanced breast cancer. *J Clin Oncol* 35:3638-3646, 2017
45. US Food and Drug Administration: FDA approves abemaciclib as initial therapy for HR-positive, HER2-negative metastatic breast cancer. <https://www.fda.gov/drugs/informationondrugs/approveddrugs/ucm598404.htm>
46. DiNardo CD, Pratz KW, Letai A, et al: Safety and preliminary efficacy of venetoclax with decitabine or azacitidine in elderly patients with previously untreated acute myeloid leukaemia: A non-randomised, open-label, phase 1b study. *Lancet Oncol* 19:216-228, 2018
47. Conroy T, Hammel P, Hebbar M, et al: Unicancer GI PRODIGE 24/CCTG PA.6 trial: A multicenter international randomized phase III trial of adjuvant mFOLFIRINOX versus gemcitabine (gem) in patients with resected pancreatic ductal adenocarcinomas. *J Clin Oncol* 36, 2018 (suppl; abstr LBA4001)
48. Coleman RL, Enserro D, Spirtos N, et al: A phase III randomized controlled trial of secondary surgical cytoreduction (SSC) followed by platinum-based combination chemotherapy (PBC), with or without bevacizumab (B) in platinum-sensitive, recurrent ovarian cancer (PSOC): A NRG Oncology/Gynecologic Oncology Group (GOG) study. *J Clin Oncol* 36, 2018 (suppl; abstr 5501)
49. Smith MR, Saad F, Chowdhury S, et al: Apalutamide treatment and metastasis-free survival in prostate cancer. *N Engl J Med* 378:1408-1418, 2018
50. Hussain M, Fizazi K, Saad F, et al: Enzalutamide in men with nonmetastatic, castration-resistant prostate cancer. *N Engl J Med* 378:2465-2474, 2018
51. US Food and Drug Administration: FDA approves apalutamide for non-metastatic castration-resistant prostate cancer. <https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm596796.htm>
52. US Food and Drug Administration: FDA approval for enzalutamide for castration-resistant prostate cancer. <https://www.fda.gov/drugs/informationondrugs/approveddrugs/ucm613543.htm>
53. Cohen JD, Li L, Wang Y, et al: Detection and localization of surgically resectable cancers with a multi-analyte blood test. *Science* 359:926-930, 2018
54. Sparano JA, Gray RJ, Makower DF, et al: Adjuvant chemotherapy guided by a 21-gene expression assay in breast cancer. *N Engl J Med* 379:111-121, 2018
55. El-Jawahri A, Traeger L, Greer JA, et al: Effect of inpatient palliative care during hematopoietic stem-cell transplant on psychological distress 6 months after transplant: Results of a randomized clinical trial. *J Clin Oncol* 35:3714-3721, 2017
56. Johnson SB, Park HS, Gross CP, et al: Use of alternative medicine for cancer and its impact on survival. *J Natl Cancer Inst* 110:121-124, 2018
57. Brock PR, Maibach R, Childs M, et al: Sodium thiosulfate for protection from cisplatin-induced hearing loss. *N Engl J Med* 378:2376-2385, 2018
58. WHO: WHO list of essential medicines. <http://www.who.int/medicines/publications/essentialmedicines/en/>
59. Wille-Jørgensen P, Syk I, Smedh K, et al: Effect of more vs less frequent follow-up testing on overall and colorectal cancer-specific mortality in patients with stage II or III colorectal cancer: The COLOFOL randomized clinical trial. *JAMA* 319:2095-2103, 2018
60. Krilov L: Microbiome: The "hidden organ" that plays a complex role in cancer. <https://www.asco.org/about-asco/press-center/cancer-perspectives/microbiome-hidden-organ-plays-complex-role-cancer>
61. Hayes RB, Ahn J, Fan X, et al: Association of oral microbiome with risk for incident head and neck squamous cell cancer. *JAMA Oncol* 4:358-365, 2018
62. Peters BA, Wu J, Pei Z, et al: Oral microbiome composition reflects prospective risk for esophageal cancers. *Cancer Res* 77:6777-6787, 2017
63. National Cancer Institute: Cancer statistics. <https://www.cancer.gov/about-cancer/understanding/statistics>
- 63\*. Noone AM, Howlander N, Krapcho M, et al. (eds). SEER Cancer Statistics Review, 1975-2015, National Cancer Institute. Bethesda, MD, [https://seer.cancer.gov/csr/1975\\_2015/](https://seer.cancer.gov/csr/1975_2015/), based on November 2017 SEER data submission, posted to the SEER web site, April 2018
- 63\*\*. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. *CA: A Cancer Journal for Clinicians* 68(1):7-30, 2018  
Peters BA, et al. Oral Microbiome Composition Reflects Prospective Risk for Esophageal Cancers. *Cancer Res* 77:23:6777-6787, 2017
64. Whiteman DC, Wilson LF: The fractions of cancer attributable to modifiable factors: A global review. *Cancer Epidemiol* 44:203-221, 2016
65. National Cancer Institute: Take action to decrease your cancer risk: Obesity and its role in cancer health disparities. <https://www.cancer.gov/about-nci/organization/crchd/blog/2015/nmhm15-spotlight>

**Table A1.** Additional Notable Advances (October 2017 to September 2018)

AREA OF RESEARCH	STUDY FINDING	REFERENCE
Trial Design and Outcomes	Evaluation of laboratory parameters in over 400 prostate cancer trials shows that eligibility criteria often disproportionately excludes black patients with the disease.	Vastola ME, et al: JAMA Oncol 4:413, 2018
	Pooled analysis of clinical factors that define which patients with oligometastatic disease have favorable outcomes and are most likely to benefit from metastasis-directed therapy.	Hong JC, et al: PLoS One 13:e0195149, 2018
Treatment	A phase I study using the recombinant nonpathogenic polio-rhinovirus chimera (PVSRIP0) found that it had activity against recurrent glioblastoma.	Desjardins A, et al: N Engl J Med 379:150-161, 2018
	A phase I dose-escalation trial found that the oncolytic adenovirus DNX-2401 was safe to use and had activity against recurrent malignant glioma.	Lang FF, et al: J Clin Oncol 36:1419-1427, 2018
	A phase III trial using pembrolizumab showed significantly longer recurrence-free survival than placebo in patients with resected melanoma.	Eggermont, AMM, et al: N Engl J Med 378:1789-1801, 2018
	The ALCANZA study found the anti-CD30 antibody drug conjugate brentuximab vedotin was superior to standard of care for patients with relapsed cutaneous T-cell lymphoma.	Prince HM, et al: The Lancet 390: 555-566, 2017
	A phase I/II trial of larotrectinib, a highly selective TRK inhibitor, in children with TRK fusion-positive cancers found the children to be responsive to the medication.	Dylon A, et al: N Engl J Med 378:731-739, 2017
	A phase III trial found that patients with metastatic kidney cancer did as well with sunitinib alone compared to surgery plus sunitinib.	Mejean A, et al: N Engl J Med 379:417-427, 2018
	A phase III trial of patients with stage IV gastro-esophageal cancer found better overall survival in those who received nivolumab compared to those who took a placebo.	Yoon-Koo K, et al: The Lancet 390:2461-2471, 2017
Health Disparities	California registry data estimates of cancer-specific survival for patients with prostate, breast, colorectal, and lung cancer for racial/ethnic groups found that stage at diagnosis was the most important factor.	Ellis L, et al: J Clin Oncol 36:25-33, 2017
	Evaluation of registry data for women with early-stage breast cancer identifies insurance as a contributing factor in mortality disparities between non-elderly white and black women.	Jemal A, et al: J Clin Oncol 36:14-24, 2017
Patient Care and Survivorship	Meta-analysis of 88 trials involving over 60,000 women with ER-positive breast cancer who were disease-free after 5 years of endocrine therapy showed that recurrences continued to occur at a relatively steady rate 5 to 20 years after completion of therapy.	Pan H, et al: N Engl J Med 377:1836-1846, 2017
	Combined analyses of the Suppression of Ovarian Function Trial (SOFT) and the Tamoxifen and Exemestane Trial (TEXT) found that both disease-free and overall survival are improved with the addition of ovarian suppression to tamoxifen.	Francis PA, et al: N Engl J Med 379:122-137, 2018
	Trial of 222 cancer survivors with melanoma, breast, and colorectal cancer who had completed treatment found that those who had five face-to-face sessions of ConquerFear, a psychological intervention provided by trained therapists, had lower fears of recurrence than those who received Taking-it-Easy relaxation therapy.	Butow PN, et al: J Clin Oncol 35:4066-4077, 2017

AREA OF RESEARCH	STUDY FINDING	REFERENCE
Tumor Biology	Researchers developed an anatomically based transcriptional atlas of human glioblastoma based on tumors from 41 patients.	Puchalski, RB, et al: Science 360: 660–663, 2018
	IL-23 produced by myeloid-derived suppressor cells can be a driver of castration-resistant prostate cancer in mice and patients with the disease.	Calcinotto A, et al: Nature 559: 363–369, 2018
	Pharmacological modulation of circadian rhythm may be effective against cancer.	Sulli G, et al: Nature 553: 351–355, 2018
	Using the Zika virus as a vector for treatment of glioblastoma shows potential in the lab and in mice in two studies.	Zhu Z, et al: JEM 214:2843-57, 2018
		Kaid C, et al: Cancer Research 78:3363-74, 2017

**Table A2.** FDA Approvals of Anticancer Therapies (November 2017 to October 2018)**New approval**

DRUG	INDICATION
SEPTEMBER 2018	
Cemiplimab-rwlc (Libtayo)	For patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not candidates for curative surgery or curative radiation
Dcomitinib Tablets (Vizimpro)	For the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutations as detected by an FDA-approved test
Duvelisib (Copiktra)	For adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least two prior therapies
Moxetumomab Pasudotox-tdfk (Lumoxiti)	For adult patients with relapsed or refractory hairy cell leukemia (HCL) who received at least two prior systemic therapies, including treatment with a purine nucleoside analog (PNA)
AUGUST 2018	
Mogamulizumab-kpkc (Poteligeo)	For adult patients with relapsed or refractory mycosis fungoides (MF) or Sézary syndrome (SS) after at least one prior systemic therapy
JULY 2018	
Ivosidenib (Tibsovo)	For adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible IDH1 mutation as detected by an FDA-approved test
Iobenguane I 131 (Azedra)	For adult and pediatric patients (12 years and older) with iobenguane scan-positive, unresectable, locally advanced or metastatic pheochromocytoma or paraganglioma (PPGL) that requires systemic anticancer therapy
FEBRUARY 2018	
Apalutamide (Erleada)	For non-metastatic castration-resistant prostate cancer
JANUARY 2018	
Lutetium Lu 177 Dotatate (Lutathera)	A radiolabeled somatostatin analog, for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults
DECEMBER 2017	
Trastuzumab-dkst (Ogivri)	As a biosimilar to Herceptin (trastuzumab, Genentech, Inc.) for the treatment of patients with HER2-overexpressing breast or metastatic stomach cancer (gastric or gastroesophageal junction adenocarcinoma)
FoundationOne CDx (F1CDx)	A next generation sequencing (NGS) based in vitro diagnostic (IVD) to detect genetic mutations in 324 genes and two genomic signatures in any solid tumor type



## New uses

DRUG	INDICATION
OCTOBER 2018	
Talazoparib (Talzenna)	For patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm), HER2 negative locally advanced or metastatic breast cancer
AUGUST 2018	
Pembrolizumab (Keytruda)	In combination with pemetrexed and platinum as first-line treatment of patients with metastatic, non-squamous non-small cell lung cancer (NSqNSCLC), with no EGFR or ALK genomic tumor aberrations
Pembrolizumab (Keytruda) and Atezolizumab (Tecentriq)	To require the use of an FDA-approved companion diagnostic test to determine PD-L1 levels in tumor tissue from patients with locally advanced or metastatic urothelial cancer who are cisplatin-ineligible
Nivolumab (Opdivo)	For patients with metastatic small cell lung cancer (SCLC) with progression after platinum-based chemotherapy and at least one other line of therapy
Lenvatinib Capsules (Lenvima)	For first-line treatment of patients with unresectable hepatocellular carcinoma (HCC)
JULY 2018	
Ribociclib (Kisqali)	In combination with an aromatase inhibitor for pre/perimenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer, as initial endocrine-based therapy
Enzalutamide (Xtandi)	For patients with castration-resistant prostate cancer (CRPC)
Ipilimumab (Yervoy)	In combination with an aromatase inhibitor for pre/perimenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer, as initial endocrine-based therapy
JUNE 2018	
Atezolizumab (Tecentriq) and Pembrolizumab (Keytruda)	Limited the use for patients with locally advanced or metastatic urothelial cancer who are not eligible for cisplatin-containing therapy
Encorafenib (Braftovi) and Binimetinib (Mektovi)	In combination for patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation, as detected by an FDA-approved test
Pembrolizumab (Keytruda)	For the treatment of adult and pediatric patients with refractory primary mediastinal large B-cell lymphoma (PMBCL), or who have relapsed after two or more prior lines of therapy
Bevacizumab (Avastin)	For patients with epithelial ovarian, fallopian tube, or primary peritoneal cancer in combination with carboplatin and paclitaxel, followed by single-agent bevacizumab, for stage III or IV disease after initial surgical resection
Pembrolizumab (Keytruda)	For patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1 (CPS $\geq 1$ ) as determined by an FDA-approved test
Venetoclax (Venclexta)	For patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL), with or without 17p deletion, who have received at least one prior therapy

## New uses cont.

DRUG	INDICATION
MAY 2018	
Dabrafenib (Tafinlar) Plus Trametinib (Mekinist)	For anaplastic thyroid cancer with BRAF V600E mutation
Tisagenlecleucel (Kymriah)	A CD19-directed genetically modified autologous T-cell immunotherapy, for adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma
APRIL 2018	
Dabrafenib (Tafinlar) and Trametinib (Mekinist)	In combination for the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection
Osimertinib (Tagrisso)	For the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test
Nivolumab (Opdivo) and Ipilimumab (Yervoy)	In combination for the treatment of intermediate or poor risk, previously untreated advanced renal cell carcinoma
Rucaparib (Rubraca)	For maintenance treatment of recurrent ovarian, fallopian tube, or primary peritoneal cancer
MARCH 2018	
Blinatumomab (Blincyto)	For the treatment of adult and pediatric patients with B-cell precursor acute lymphoblastic leukemia (ALL) in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1%
Nilotinib (Tasigna)	For pediatric patients 1 year of age or older with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia in chronic phase (Ph+ CML-CP) or Ph+ CML-CP resistant or intolerant to prior tyrosine-kinase inhibitor (TKI) therapy
Brentuximab Vedotin (Adcetris)	For adult patients with previously untreated stage III or IV classical Hodgkin lymphoma (cHL) in combination with chemotherapy
FEBRUARY 2018	
Abemaciclib (Verzenio)	In combination with an aromatase inhibitor as initial endocrine-based therapy for postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer
Durvalumab (Imfinzi)	For patients with unresectable stage III non-small cell lung cancer (NSCLC) in who the disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy
Abiraterone Acetate (Zytiga)	Tablets in combination with prednisone for metastatic high-risk castration-sensitive prostate cancer (CSPC)
JANUARY 2018	
Afatinib (Gilotrif)	For a broadened indication in first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have non-resistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test
Olaparib Tablets (Lynparza)	A poly (ADP-ribose) polymerase (PARP) inhibitor, for the treatment of patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm), HER2-negative metastatic breast cancer who have been treated with chemotherapy either in the neoadjuvant, adjuvant, or metastatic setting

DRUG	INDICATION
DECEMBER 2017	
Nilotinib (Tasigna)	To include information on nilotinib discontinuation, post-discontinuation monitoring criteria, and guidance for treatment re-initiation in patients taking nilotinib for Philadelphia chromosome positive (Ph+) chronic myeloid leukemia (CML) who have achieved a sustained molecular response (MR 4.5)
Pertuzumab (Perjeta)	For use in combination with trastuzumab and chemotherapy as adjuvant treatment of patients with HER2-positive early breast cancer at high risk of recurrence
Nivolumab (Opdivo)	For the adjuvant treatment of patients with melanoma with involvement of lymph nodes or in patients with metastatic disease who have undergone complete resection
Bosutinib (Bosulif)	For treatment of patients with newly-diagnosed chronic phase (CP) Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia (CML)
Cabozantinib (Cabometyx)	For treatment of patients with advanced renal cell carcinoma (RCC)

## NOVEMBER 2017

Malate (Sutent)	For the adjuvant treatment of adult patients at high risk of recurrent renal cell carcinoma following nephrectomy
Obinutuzumab (Gazyva)	In combination with chemotherapy, followed by obinutuzumab monotherapy in patients achieving at least a partial remission, for the treatment of adult patients with previously untreated stage II bulky, III, or IV follicular lymphoma (FL)
Dasatinib (Sprycel)	For the treatment of pediatric patients with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in the chronic phase
Brentuximab Vedotin (Adcetris)	For the treatment of adult patients with primary cutaneous anaplastic large cell lymphoma (pcALCL) or CD30-expressing mycosis fungoides (MF) who have received prior systemic therapy
Alectinib (Alecensa)	For treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC), as detected by an FDA-approved test
Vemurafenib (Zelboraf)	For the treatment of patients with Erdheim-Chester Disease (ECD) with BRAF V600 mutation

The following represents disclosure information provided by *Clinical Cancer Advances 2019* editorial board members. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this report. For more information about ASCO's conflict of interest policy, please refer to [asco.org/rwc](http://asco.org/rwc) or [ascopubs.org/jco/site/ifc](http://ascopubs.org/jco/site/ifc).

## Sumanta K. Pal

**Honoraria:** Novartis, Medivation, Astellas Pharma  
**Consulting or Advisory Role:** Pfizer, Novartis, Aveo, Myriad Pharmaceuticals, Genentech, Exelixis, Bristol-Myers Squibb, Astellas Pharma, Ipsen, Eisai  
**Research Funding:** Medivation

## Neeraj Agarwal

**Consulting or Advisory Role:** Pfizer, Exelixis, Medivation/Astellas, Eisai, Merck, Novartis, EMD Serono, Clovis Oncology, Genentech, Bristol-Myers Squibb, AstraZeneca, Nektar, Eli Lilly, Bayer, Foundation One, Argos Therapeutics  
**Research Funding:** Bayer (Inst), Bristol-Myers Squibb (Inst), GlaxoSmithKline (Inst), Medivation (Inst), Takeda (Inst), Novartis (Inst), Pfizer (Inst), BN ImmunoTherapeutics (Inst), Exelixis (Inst), TRACON Pharma (Inst), Rexahn Pharmaceuticals (Inst), Amgen (Inst), AstraZeneca (Inst), Active Biotech (Inst), Bavarian Nordic (Inst), Calithera Biosciences (Inst), Celldex (Inst), Eisai (Inst), Genentech (Inst), Immunomedics (Inst), Janssen (Inst), Merck (Inst), Newlink Genetics (Inst), Prometheus (Inst), Sanofi (Inst)

## Susan Marina Chang

**Consulting or Advisory Role:** Tocagen  
**Research Funding:** Novartis (Inst), Agios (Inst)

## Mariana Chavez-MacGregor

**Employment:** MD Anderson Physician's Network  
**Honoraria:** Pfizer  
**Consulting or Advisory Role:** Genentech  
**Research Funding:** Novartis (Inst)  
**Travel, Accommodations, Expenses:** Pfizer

## Ezra Cohen

**Consulting or Advisory Role:** Merck, Bristol-Myers Squibb, AstraZeneca, Human Longevity, Pfizer, EMD Serono, Mavu Pharmaceutical, Nanobiotix, Incyte

## Suzanne Cole

**Honoraria:** Research to Practice

## Catherine S. Magid Diefenbach

**Stock and Other Ownership Interests:** Gilead Sciences  
**Consulting or Advisory Role:** Seattle Genetics, Bayer, Bristol-Myers Squibb, Genentech, Merck  
**Research Funding:** Seattle Genetics (Inst), Genentech (Inst), Incyte (Inst), LAM Therapeutics (Inst), Merck (Inst), Bristol-Myers Squibb (Inst), Millennium (Inst), MEI Pharma (Inst)

## Mary L. Disis

**Stock and Other Ownership Interests:** Epithany  
**Research Funding:** EMD Serono, Celgene, Janssen, Epithany (Inst), Pfizer  
**Patents, Royalties, Other Intellectual Property:** I am an inventor on patents held by the University of Washington

## Robert Dreicer

**Consulting or Advisory Role:** Astellas Pharma, AstraZeneca, Bristol-Myers Squibb, Genentech, EMD Serono, Incyte, Pfizer  
**Research Funding:** Genentech (Inst), Seattle Genetics (Inst), BioClin Therapeutics (Inst), Janssen Oncology (Inst), Merck (Inst)

## David L. Graham

**Employment:** Medscape  
**Speakers' Bureau:** Biopep Solution

## N. Lynn Henry

**Research Funding:** Innocrin Pharma (Inst), Pfizer (Inst), AbbVie (Inst)

## Vicki Keedy

**Employment:** Zimmer BioMet (I)  
**Consulting or Advisory Role:** Threshold Pharmaceuticals, Janssen Oncology, Karyopharm Therapeutics

**Research Funding:** Pfizer (Inst), CytRx Corporation (Inst), Threshold Pharmaceuticals (Inst), Medpacto (Inst), Plexxikon (Inst), Roche (Inst), Daiichi Sankyo (Inst), Eli Lilly (Inst), BioMed Valley Discoveries (Inst), Immune Design (Inst), GlaxoSmithKline (Inst), TRACON Pharma (Inst), Advenchen Laboratories (Inst)

## Heidi D. Klepin

**Patents, Royalties, Other Intellectual Property:** UpToDate contributor

## Merry Jennifer Markham

**Consulting or Advisory Role:** Astex Pharmaceuticals  
**Research Funding:** Astex Pharmaceuticals (Inst), Aduro Biotech (Inst)

## Elizabeth A. Mittendorf

**Honoraria:** Physician Education Resource  
**Consulting or Advisory Role:** Peregrine Pharmaceuticals, TapImmune, Sellas Life Sciences, Merck  
**Research Funding:** Galena Biopharma (Inst), Genentech, AstraZeneca (Inst), EMD Serono (Inst)

## Carlos Rodriguez-Galindo

**Honoraria:** Novimmune

## Michael S. Sabel

**Patents, Royalties, Other Intellectual Property:** Breast Cancer Ally and Melanoma Ally mobile technologies

## Richard L. Schilsky

**Research Funding:** AstraZeneca (Inst), Bayer (Inst), Bristol-Myers Squibb (Inst), Genentech (Inst), Eli Lilly (Inst), Merck (Inst), Pfizer (Inst)

## Mario Sznol

**Stock and Other Ownership Interests:** Amphivena, Intensity Therapeutics, Adaptive Biotechnologies, Actym Therapeutics, Torque  
**Consulting or Advisory Role:** Bristol-Myers Squibb, Genentech, AstraZeneca/MedImmune, Kyowa Hakko Kirin, Nektar, Novartis, Eli Lilly, Merck Sharp & Dohme, Biodesix, Adaptimmune, Lycera, Theravance, Modulate, Omnio, Seattle Genetics, Inovio Pharmaceuticals, Pierre Fabre, Baxalta/Shire, Newlink Genetics, Molecular Partners, Genmab, Torque, Abbie, Allakos, Hinge, Symphogen, Pieris Pharmaceuticals, Gritstone Oncology, Innate Pharma, Celldex, Incyte, Almac Diagnostics, Immunocore  
**Other Relationship:** Haymarket Media, Research to Practice, TRM Oncology, Physician Education Resource, Imedex, AcademicCME, DAVA Oncology, Clinical Care Options, Vindico, Prime Oncology

## William D. Tap

**Leadership:** Certis Oncology Solutions, Atropos Pharmaceuticals  
**Stock and Other Ownership Interests:** Certis Oncology Solutions, Atropos  
**Consulting or Advisory Role:** EMD Serono, Plexxikon, Janssen, Eli Lilly, Daiichi Sankyo, Novartis, Eisai, Immune Design, Blueprint Medicines, Loxo, Agios, GlaxoSmithKline  
**Research Funding:** Novartis, Eli Lilly, Plexxikon, Daiichi Sankyo, TRACON Pharma, Blueprint Medicines, Immune Design  
**Patents, Royalties, Other Intellectual Property:** Methods of treating metastatic sarcoma using talimogene laherparepvec (T-Vec) and pembrolizumab combination therapy, 62/671,625; companion diagnostic for CDK4 inhibitors, 14/854,329

## Shannon Neville Westin

**Consulting or Advisory Role:** Roche, AstraZeneca, Ovation Sciences, Medivation, Genentech, Vermillion, Casdin Capital, Medscape, Clovis Oncology, Watermark Research Partners, Gerson Lehrman Group, Vaniam Group, Tesaro, Merck, Pfizer, BioAscent  
**Research Funding:** AstraZeneca, Novartis, Biomarin, Karyopharm Therapeutics (I), Celgene (I), Critical Outcome Technologies, Bayer, Tesaro, Kite Pharma (I), Cotinga Pharmaceuticals, Clovis Oncology, Genentech

## Bruce E. Johnson

**Research Funding:** Novartis (Inst), Toshiba (Inst), Novartis (Inst)  
**Patents, Royalties, Other Intellectual Property:** Dana-Farber Cancer Institute

No other potential conflicts of interest were reported.



# Common Or Rare, ASCO Has Trusted Cancer Type Information For Patients, Caregivers, and Families

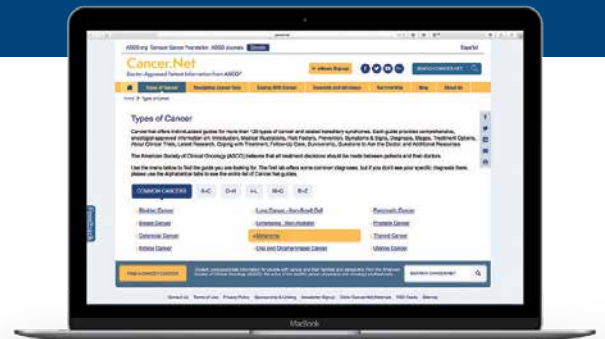
Cancer.Net, the patient information website of the American Society of Clinical Oncology (ASCO), is a respected and award-winning source for comprehensive, peer-reviewed guides for more than 120 types of cancer and related hereditary syndromes.

Visit [www.cancer.net/types](http://www.cancer.net/types)

Each guide includes patient-directed information on:

- Risk Factors
- Symptoms & Signs
- Diagnostic Tests
- Stages & Grades
- Treatment Options
- Clinical Trials & Latest Research
- Coping with Side Effects
- Follow-Up Care & Survivorship
- Questions to Ask the Health Care Team

All content is peer-reviewed by the Cancer.Net Editorial Board, composed of more than 150 medical, surgical, radiation, and pediatric oncologists, physician assistants, oncology nurses, social workers, and patient advocates.



Cancer.Net has information on a wide range of diseases, both common and rare adult and childhood cancers, including individual guides on:

- Sarcomas
- Carcinomas
- Blood Cancers
- Brain Tumors
- Skin Cancers
- Neuroendocrine Tumors

**Do you prefer to learn on the go?**

Cancer type information is also available on Cancer.Net's free mobile app: [www.cancer.net/app](http://www.cancer.net/app)

Information is available in Spanish about the most common cancer types affecting Hispanics/Latinos in the United States.

[www.cancer.net/es](http://www.cancer.net/es)

## Cancer.Net

Doctor-Approved Patient Information from ASCO®

## ASCO®

AMERICAN SOCIETY OF CLINICAL ONCOLOGY

# I Live to Conquer Cancer

“

To find the next frontier in cancer vaccines, we need our nation's support for cancer research.”

—Judith S. Kaur, MD

Mayo Clinic Cancer Center

Pioneer in cancer prevention and education

Congress: Now is the time to invest in the next generation of cancer cures.

Learn more at [asco.org/live-to-conquer-cancer](https://asco.org/live-to-conquer-cancer).

**ASCO**<sup>®</sup>

AMERICAN SOCIETY OF CLINICAL ONCOLOGY



**ASCO<sup>®</sup>**

2318 Mill Road, Suite 800, Alexandria, VA 22314

571.483.1300 • [www.asco.org](http://www.asco.org)