Clinical Cancer Advances 2021: ASCO's Report on Progress Against Cancer

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EXECUTIVE SUMMARY

Clinical Cancer Advances 2021: ASCO's 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. This year's report also discusses the critical issue of health equity in cancer research and solutions to ensure that every patient with cancer, everywhere, can access the latest advances.

Achieving Equity in Cancer Research

Overall cancer mortality has decreased in the United States[1] thanks to tremendous progress in cancer prevention, early detection, and treatment—underpinned by decades of research progress.[2]

Unfortunately, not all individuals with cancer have benefited equitably from this success, as Blacks,[3] patients living in rural areas,[4] populations with lower income and education levels,[5] and others continue to experience lower survival and higher mortality rates for many cancers.

> *As clinicians, we are committed to providing evidenced-based, high-quality cancer care to every patient, every day, everywhere. But, if clinical trials don't represent the individuals we treat, including those from racial, ethnic, and other minority populations, the state of science suffers, and patients with life-threatening conditions may not receive the best—perhaps only—treatment option for their condition.*
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> *—Lori J. Pierce, MD, FASTRO, FASCO, ASCO President, 2020-2021*

Disparities in cancer research is a complex, multifaceted issue requiring a multifactorial response that addresses (1) specific interrelated barriers precluding certain populations from trial participation, and (2) structural and systemic challenges that limit the cancer community's pursuit of research that would benefit underserved populations.

Disparities in cancer outcomes are rooted, in some respects, in the development of novel diagnostics and therapeutics—the clinical research that demonstrates the efficacy and safety of new cancer treatments.

Patients with cancer who might, otherwise, be candidates for clinical trials continue to face multiple barriers, which must be thoroughly understood and appropriately addressed before the cancer community can learn from every individual with cancer.

All populations should have an equal opportunity to participate in, be recognized for, and benefit from research across the spectrum, including clinical trials, health services research, and other types of research studies and methodologies. A collective effort by all stakeholders—including patients, caregivers, providers, policy leaders, pharmaceutical organizations, and advocacy groups—is needed to develop appropriately targeted approaches to achieve this goal.

Advance of the Year: Molecular Profiling Drives Progress in GI Cancers

Surgery, radiotherapy, and chemotherapy have been the mainstay of treatment for GI cancer but have limited effect and can take a heavy toll on quality of life. The development of more effective therapies for GI

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ASSOCIATED CONTENT

Appendix

Author affiliations and support information (if applicable) appear at the end of this article.

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cancer has lagged. Molecular profiling has helped change the outlook for patients with GI cancer by identifying the molecular and genetic signatures that allow oncologists to deliver treatments that are highly specific to a tumor. For these reasons, ASCO has identified molecular profiling driving progress in GI cancer as the 2021 Advance of the Year. This selection recognizes the treatment advances made possible by molecular testing for patients with GI cancers.

GI cancer includes cancers of the esophagus, stomach, small bowel, gallbladder and biliary tract, pancreas, colon, rectum, and anus and accounts for 26% of the global cancer incidence and 35% of all cancer-related deaths.[6] The ability to molecularly profile a GI tumor has expanded the treatment options for individual patients with GI cancers—extending survival, while minimizing adverse effects. Specific genetic mutations, amplifications or fusions, epigenetic profile, protein expression, or other molecular features allow oncologists to choose targeted therapies matched to the molecular profile of their patients' tumor. In the past year, research has shown that targeting human epidermal growth factor receptor 2 (HER2) improves survival in gastric cancer and shows promise for patients with HER2-positive colorectal cancer. Therapy is now approved that targets specific DNA mutations in metastatic colorectal cancer. These advances are moving the treatment of GI cancers closer to personalized medicine.

Additional Major Advances

Advances featured in this year's report reflect progress in a range of cancers and across prevention and treatment, including:

- Progress in bringing targeted therapies to patients with earlier-stage disease.
- Biomarker-driven treatment approaches that offer more personalized care for lung, colorectal, and gastric cancers.
- Combinations of different therapies that extend survival without increasing toxicity.
- A growing number of targeted therapies are offering extended survival for more patients with difficult-to-treat cancers.

ASCO Research Priorities to Accelerate Progress

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, each year ASCO issues its list of top Research Priorities to Accelerate Progress Against Cancer. As cancer care becomes more complex and personalized, the research behind new advances must include all populations who stand to benefit and consider the impact of social determinants of health, such as the social, economic, and cultural factors that influence cancer risk and outcomes.

Research priorities for 2021, listed below in no particular order, represent promising areas of research that have the potential to significantly improve the knowledge base for clinical decision making and address vital unmet needs in cancer care. This year's list includes a newly added priority on artificial intelligence, recognizing its growing potential to solve complex problems and drive diagnostic, therapeutic, and translational research across the spectrum of cancer prevention and care.

- Develop and Integrate Artificial Intelligence and Deep Learning in Cancer Research
- Identify Strategies That Predict Response and Resistance to Immunotherapies
- Optimize Multimodality Treatment for Solid Tumors
- Increase Precision Medicine Research and Treatment Approaches in Pediatric and Other Rare Cancers
- Optimize Care for Older Adults With Cancer
- Increase Equitable Access to Cancer Clinical Trials
- Reduce Adverse Consequences of Cancer Treatment
- Reduce Obesity's Impact on Cancer Incidence and Outcomes
- Better Identify Potentially Malignant Lesions and Predict When Treatment is Needed

Progress Against Cancer: Why Federal Support Matters

We are in an exciting and promising era of medical research, and new discoveries are leading to major improvements in the way we prevent, diagnose, treat, and even cure cancer.

Every major medical breakthrough in cancer started with research funded by the National Institutes of Health (NIH) and the National Cancer Institute (NCI). This year marks the 50th anniversary of the December 1971 signing of the National Cancer Act,

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which led to the establishment of the National Cancer Program and significantly expanded the authorities and responsibilities of NCI. Through the research, training, and infrastructure programs of NCI, cancer care and research expanded from a few pioneering research institutions to cancer centers, community hospitals, and oncology practices across the United States.

Research funded by NIH and NCI generates biomedical innovations that fuel the entry of new therapies into the market—helping to make the United States the global leader in developing new cancer treatments. They also fund vital cancer research that private industry has little incentive to conduct, such as studies focused on prevention and screening, identifying treatments for rare cancers, and comparing the effectiveness and safety of similar treatments.

Over the past few decades, federal investment in cancer research has helped lead to:

- 29% decline in overall cancer death rates (since peak in 1991)[7]
- 2.9 million+ cancer deaths averted in the United States[7]
- 150+ new cancer drugs or indications approved by the US Food and Drug Administration (FDA) since 2006

Sustaining the national commitment to cancer research is essential to transform research discoveries into new treatments and improve care for millions of people with cancer.

Progress in a Pandemic: Cancer Research Funding at Risk

Recently, there has been broad, bipartisan support in Congress for increased investment in NIH. In fiscal year (FY) 2020, Congress provided a $2.6 billion (in US dollars) funding increase for NIH, including a $300 million increase for NCI.[8]

However, the COVID-19 public health emergency threatens to reverse years of momentum. Laboratories conducting cancer research have closed or space has been redirected to COVID-19 research. Clinical trials have halted or slowed, creating a costly loss in research progress and delays in patient access to potentially life-saving treatments. NIH and NCI need emergency funding on top of a robust annual increase to their baseline budgets to mitigate disruptions caused by the pandemic and get the nation's biomedical research enterprise up and running again. However, tight budget caps and shifting funding priorities as a result of the public health emergency have complicated the annual funding process, causing uncertainty for future funding for NIH and NCI.

We know that even minor funding cuts can have a major impact on cancer research. After the last financial crisis, federal funding for cancer research declined by nearly 25%, and even with recent continued increases, NIH's purchasing power is only now beginning to reach pre-2006 levels (adjusted for inflation).[9] NCI's budget is still $1.1 billion less than it would be if funding had kept pace with biomedical inflation since FY 2003.[10] We cannot repeat history.

> *Stable, predictable funding increases will allow our nation to continue to build on the promise of today's research and improve outcomes for all patients with cancer.*
> *—Richard L. Schilsky, MD, FACP, FSCT, FASCO, Chief Medical Officer (CMO) and Executive Vice President of ASCO*

COVID-19 has caused immense personal suffering and disruptions across nearly every aspect of society. We cannot let this pandemic stop our progress against cancer and disrupt essential innovation any further.

Progress Needs You: Take Action to Support Federal Investment in Cancer Research

Increased federal funding for cancer research is more important than ever to help the research community tackle new setbacks while pursuing the life-changing research that patients with cancer and their families rely on.

Lend your voice. Together, nothing will stop us from conquering cancer. Use the Association for Clinical Oncology's ACT Network to contact your Members of Congress and urge them to support an increase in funding for NIH and NCI. Visit ASCO.org/actnetwork to take action.

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 16th edition, is developed by a 26-member editorial board of experts in a range of cancer types, subspecialties, and care issues. The editors reviewed scientific literature published in peer-reviewed journals or presented at major medical conferences, primarily from October 2019 to September 2020, 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.

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About ASCO and the Association for Clinical Oncology

ASCO (the Society) and the Association for Clinical Oncology (the Association) are committed to the principle that knowledge conquers cancer. ASCO represents nearly 45,000 oncology professionals who care for people living with cancer. Through research, education, and promotion of high-quality and equitable patient care, the Society works to conquer cancer and create a world where cancer is prevented or cured, and every survivor is healthy. The Association works to ensure that all individuals with cancer have access to high-quality and equitable care; that the cancer care delivery system supports optimal cancer care; and that our nation supports robust federal funding for research on the prevention, screening, diagnosis, and treatment of cancer. Learn more about the Society at www.ASCO.org, explore patient education resources at www.Cancer.Net, and follow us on Facebook, Twitter, LinkedIn, Instagram, and YouTube. Learn more about the Association at www.ascoassociation.org and follow us on Twitter.

About Conquer Cancer, the ASCO Foundation

Conquer Cancer, the ASCO Foundation 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. Nearly a third of the clinical trials included in this report were conducted by researchers previously funded by Conquer Cancer.

ACHIEVING EQUITY IN CANCER RESEARCH

Disparities in Cancer Research: A Precursor to Disparate Cancer Outcomes

Overall cancer mortality has decreased in the United States[1] thanks to tremendous progress in cancer prevention, early detection, and treatment—underpinned by decades of research progress.[2,3]

Unfortunately, not all individuals with cancer have benefited equitably from this success, as Blacks, patients living in rural areas,[4] populations with lower income and education levels,[5] and others continue to experience lower survival and higher mortality rates for many cancers.

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Disparities in cancer outcomes are rooted, in some respects, in the development of novel diagnostics and therapeutics—the clinical research that demonstrates the efficacy and safety of new cancer treatments.

Although most patients express a willingness to participate in clinical research, only approximately 8% of adult cancer patients enroll in cancer clinical trials,[11] and the percentage of minorities participating in clinical trials, overall, is much lower when compared to the general population of the United States. Blacks, Hispanics, and other minority groups, for example, continue to be underrepresented in clinical trials. Recent analyses of cancer treatment trials found that only 4%-6% of clinical trial participants are Black, and 3%-6% are Latino, despite representing 15% and 13% of all patients with cancer, respectively.[12,13] The under-representation of minority groups in cancer research contributes to disparities in cancer care and outcomes by failing to provide the evidence that clinicians need to safely treat minority patients with cancer.

In contrast, progress in pediatric oncology tells a different story. With a greater than 50% enrollment rate of affected children, pediatric cancer clinical trials have always been more inclusive and diverse, contributing to a decline in

pediatric cancer mortality rates over more than four decades, while the rate for adults has been declining for just the past two-plus decades.[14]

The COVID-19 pandemic may exacerbate disparities in cancer research, as the coronavirus has been yet another reminder of disparities in access to care and outcomes in the United States. COVID-19 took a greater toll with higher hospitalizations and death rates in American Indian and Native Alaskan, Black, and Hispanic communities,[15] and among Black and Hispanic patients with cancer, in particular.[16] Loss of employment and employment-based insurance coverage have also hit these communities the hardest, presenting additional barriers to participating in clinical research.

Disparities in cancer research is a complex multifaceted issue requiring a multifactorial response that addresses specific inter-related barriers that preclude certain populations from trial participation, as well as structural and systemic challenges that limit the cancer community's ability to conduct research that would benefit underserved populations.

In August 2020, ASCO published its Cancer Disparities and Health Equity Policy Statement, which included a focus on ensuring equitable access to cancer research and stressed that all populations should have an equal opportunity to participate in, be recognized for, and benefit from research across the spectrum, including clinical trials, health services research, and other types of research studies and methodologies. The statement underscores that a collective effort by all stakeholders—including patients, caregivers, providers, policy leaders, pharmaceutical organizations, and advocacy groups—is needed to develop appropriately targeted approaches to achieve this goal.

Evidence Gaps in Health Disparities Cancer Research

Health disparities research is a foundational discipline that addresses population-based inequities in cancer research and crosses large areas of inquiry, including biologic and environmental determinants of cancer incidence; biologic, environmental, and system-level determinants of postdiagnosis survival; and social determinants of health. Spanning transdisciplinary fields, health equity cancer research integrates basic science, clinical science, policy, epidemiology, and the social sciences.

In 2017, four leading cancer organizations, the American Association for Cancer Research, the American Cancer Society, ASCO, and NCI, released a joint position statement entitled Charting the Future of Cancer Health Disparities Research.[17] This statement presented a unified strategy to promote cooperation among investigators in all areas of cancer research to ensure that cancer research benefits all populations and patients regardless of race, ethnicity, age, gender identity, sexual orientation, socioeconomic status, or the communities in which they live.

The statement identified gaps in data available about patients and their communities. Routine collection and reporting of data regarding demographic and clinical characteristics of research participants can increase the likelihood that research will acknowledge and potentially address health disparities,[18] including differences in treatment effectiveness, tolerance, and outcomes. Studies should routinely collect and publicly report aggregated data on demographic and clinical factors (including race/ethnicity, sexual orientation and gender identity, nativity, ability status, socioeconomic status, age, comorbidities, and treatment, among others).

Another avenue for making research more inclusive is through postmarket data collection. Using a larger, more representative sample gives physicians and researchers the ability to generate new hypotheses and apply those insights to improve care in real-world settings. CancerLinQ, a real-world oncology data platform developed by ASCO, supports this goal by securely compiling, analyzing, and de-identifying vast amounts of information on patient characteristics using data from 1.5 million patients from across the nation in oncology practices of all sizes and settings.

Barriers to Equitable Cancer Research

Patients with cancer who might, otherwise, be candidates for clinical trials continue to face multiple barriers, which must be thoroughly understood and appropriately addressed before the cancer community can learn from every individual with cancer.

The barriers that patients face have been broken down into five categories:[14]

- Structural barriers—having access to a clinic or site offering a clinical trial, including factors such as transportation and its associated costs, health insurance status, and dependent care.
- Clinical barriers—a patient must be eligible to participate in a particular trial.
- Patient attitudes toward clinical trials—historically, patients often have reported being nervous about the idea of participating in a clinical trial, although educational efforts and easily understandable informed consent documents may mitigate this.
- Physician attitudes—while most oncologists agree that clinical trials are a high-quality option for many patients, many still fail to offer patients the opportunity to enroll in a clinical trial or treat their patients off-protocol rather than officially enroll a patient in the trial in an effort to not accrue additional administrative burden and regulatory liability.

- Demographic and socioeconomic disparities—the most common demographic disparity is age of the patient; race as a factor is more mixed, depending on the type of trial and disease being studied.

Other reasons for low participation rates for all populations range from trial eligibility that excludes patients with comorbidities, financial hardships, and patient misconceptions about clinical trials. When combined, these structural and clinical barriers make trial participation unachievable for more than three of four patients with cancer.[19]

Strategies to Improve Equity in Cancer Research

There are some strategies and actions that can be used to lower the barriers to clinical trial participation and thereby increase the pool of participants:

Eligibility criteria. One way to make clinical trials available to more patients while simultaneously gathering evidence from a wider swath of the population is to broaden trial eligibility criteria. ASCO and Friends of Cancer Research have worked to support the FDA in doing this, and in July 2020, the FDA finalized four new Guidance for Industry documents that recommended broadening eligibility criteria for clinical trials by lowering the minimum age to possibly incorporate adolescent patients and by including patients with brain metastases who have been treated and are stable, and not automatically excluding patients with active brain metastases or patients with leptomeningeal disease. The guidance documents also address inclusion of patients with HIV, hepatitis B, and hepatitis C, and patients with prior or concurrent malignancies and recommend less restrictive renal, cardiac, and hepatic function criteria. The FDA also released draft guidance to encourage greater trial participation by older adults, the population that experiences the majority of cancer diagnoses and deaths.[20]

More recently, the FDA issued final guidance that recommends approaches that sponsors of clinical trials can take to increase diversity in their trials—with an emphasis on real-world data.[21]

Umbrella and basket trial design. Another method by which to expand clinical trial participation is by using umbrella and basket trials, both of which can test several treatments at once across more than one cancer population simultaneously, which potentially could examine and compare the experience of underserved populations.[22] An umbrella trial tests how well new therapies work in patients with the same type of cancer but different gene mutations or biomarkers. A basket trial tests how well a therapy works in patients with different types of cancers that have the same gene mutations or biomarkers. For example, ASCO's TAPUR Study is a basket trial designed to learn from the greatest number of patients possible by having minimal eligibility criteria, which is possible because the study involves only FDA-approved, targeted drugs. This is different than most clinical trials, which have traditionally left out large swaths of the population and skew younger and healthier than the typical patient with cancer.

Trial availability. Geography presents yet another significant barrier in clinical trial enrollment, even after a match has been made between an ongoing trial and a patient's cancer type and stage. A 2020 study published in the *Journal of the American Medical Association* examined the location of clinical trials relative to population and found that a lack of a convenient trial location explained 87% of disparities in clinical trial participants. This is especially true for patients in rural areas but even for those in more populous regions who lack ease of transportation to a particular site.[23] The FDA's 2020 final guidance noted previously also recommends sending medical professionals to visit trial participants instead of requiring extensive participant travel—a step that could appreciably address this barrier.

Concerns about trial availability also showed up in a 2020 study for the Oncology Nursing Society that found patients were willing and able to travel approximately 11 miles to a clinical trial site, with differences among ethnic groups. The study advocated that nurses could be a crucial element in understanding these geographic disparities and helping guide patients to relevant trials that would be feasible for them.[24]

Patient education, recruitment, and support. A recent ASCO survey[25] found significant misperceptions among Americans about clinical trials. Nearly half of all respondents (48%) believe patients with cancer who participate in clinical trials are not receiving the best possible care, although clinical trials may offer the best options for initial treatment and, when the current standard of care is not working for a patient, they may provide a treatment option when no other treatments are available. Additionally, 75% of Americans, including 87% of patients with cancer, believe that some people who participate in cancer clinical trials receive a placebo rather than actual treatment—although placebos are rarely used in cancer clinical trials and are only used when there is no standard treatment available.

Increased physician-to-patient education and expanded community outreach could address this lack of understanding about the true nature of clinical trials. Researchers should be encouraged to use recruitment strategies that ensure adequate representation of populations afflicted with the disease being studied and those at risk of disparate outcomes, including, but not limited to, populations with diverse socioeconomic status, race/ethnicity, and geographic location (urban or rural). Social media and use of patient-centered recruitment messaging is also gaining traction in assisting with recruiting patients for clinical research who may traditionally have been under-represented.[18]

Patient navigation. Other programs that have improved inclusion in research include patient navigation, educational efforts led by community health workers, and partnerships with community and advocacy organizations. Such efforts can assist with overcoming other known barriers to participation in research, such as transportation and childcare.

Novel consent strategies. Novel strategies include informed consent practices that are more accessible and understandable to participants from a wide range of cultural and linguistic backgrounds. Methods include multimedia consent content with concise text blocks, visual icons, and videos on smartphone-optimized web interfaces.[18]

Financial assistance. Although health insurance coverage of costs associated with clinical trial participation are, generally, covered by Medicare and private payers, Medicaid is not federally required to cover routine care costs (including physician visits and laboratory studies). With nearly 20% of Americans covered under Medicaid, a large swath of individuals with cancer—including those from under-represented minority and ethnic groups not well-represented in clinical trials—are financially unable to participate in potentially life-saving research.

ASCO has joined with numerous other organizations in urging Congress to pass the bipartisan CLINICAL TREATMENT Act, which would guarantee coverage of the routine care costs of clinical trial participation for Medicaid enrollees with life-threatening conditions. This legislation would improve the validity of clinical research data, thereby delivering better treatments to all patients while helping to reduce health disparities and ensure all patients have access to high-quality, high-value cancer care.

Discussion: Lessons From the Pandemic

The COVID-19 pandemic has provided a unique opportunity to re-envision cancer research and examine, in particular, disparities in clinical trials participation. Cancer clinical trials were upended in the early months of the outbreak, with widespread interruptions in trial enrollment preventing some patients from receiving experimental cancer therapies. Within the first weeks of the pandemic, some 60% of research institutions halted patient screening and enrollment for at least some trials.[26] Similar numbers halted patient visits focused only on research, blood draws, or tissue collections, prioritizing only those visits that were essential to sustain patients' health.

Yet, research sponsors and regulators acted quickly to create more flexible research practices averting a total shutdown of trials. The FDA and NCI quickly issued guidance and workarounds to give researchers and trial sponsors new flexibility while preserving the integrity of research. Along with remote patient monitoring and drug administration, the guidance allowed virtual consent using e-signatures, limited collection of research-only biospecimens, and blood draws or imaging scans done by local healthcare providers close to home. As a result, most patients were able to continue their treatments, and most trials were able to resume after just a few weeks or months of interruption.

The COVID-19 pandemic brought racial and other health disparities into sharp relief. At the same time, it was also clear that the healthcare system—and the oncology community in particular—has the agility to respond quickly to substantial and unexpected disruptions to both clinical trials and clinical care. This same ingenuity and flexibility can and should be applied to improving health equity for all individuals, so that right treatment truly is delivered to the right patient at the right time, everywhere.

ADVANCE OF THE YEAR: MOLECULAR PROFILING DRIVES PROGRESS IN GI CANCERS

Surgery, radiotherapy, and chemotherapy have been the mainstay of treatment for GI cancers but have limited effect and can take a heavy toll on quality of life. The development of more effective therapies for GI cancers has lagged. Molecular profiling has helped change the outlook for patients with GI cancer by identifying the molecular and genetic signatures that allow oncologists to deliver treatments that are highly specific to a tumor. For these reasons, ASCO selected molecular profiling driving progress in GI cancers as the 2021 Advance of the Year. This selection recognizes the treatment advances made possible by molecular testing for patients with GI cancers.

GI cancers include cancers of the esophagus, stomach, small bowel, gallbladder and biliary tract, pancreas, colon, rectum, and anus and account for 26% of the global cancer incidence burden and 35% of all cancer-related deaths.[6] The ability to molecularly profile a tumor has expanded the treatment options for individual patients with GI cancers—extending survival, while minimizing adverse effects. Specific genetic mutations, amplifications or fusions, epigenetic profile, protein expression, or other molecular features allow oncologists to choose targeted therapies matched to the molecular profile of their patient's disease. In the past year, research has shown that targeting HER2 improves survival in gastric cancer and shows promise for patients with HER2-positive colorectal cancer. Therapy is now approved that targets specific DNA mutations in metastatic colorectal cancer. These advances are moving the treatment of GI cancers closer to personalized medicine.

Antibody-Drug Shows Promise in GI Cancers

HER2 is a protein that promotes the growth of cancer cells. Overexpression of HER2 occurs among patients with

breast, lung, gastric, and gastroesophageal junction cancers, among others. Trastuzumab is a monoclonal antibody that targets HER2, tamping down accelerated cancer cell growth and promoting cell death.

Trastuzumab plus chemotherapy is the standard initial treatment for HER2-positive gastric and gastroesophageal cancers, which account for around 20% these types of cancers.[27] Standard secondary therapy consists of chemotherapy with paclitaxel plus the monoclonal antibody ramucirumab, which acts on vascular endothelial growth factor 2, reducing blood supply to tumors.[28] A number of treatments have been investigated for the treatment of gastric and gastroesophageal junction cancers following progression after standard first- and second-line therapies.[29-31]

Trastuzumab deruxtecan is a novel antibody-drug conjugate that links anti-HER2 trastuzumab with deruxtecan—an anticancer drug that interrupts DNA replication in cancer cells. Essentially, trastuzumab deruxtecan delivers a highly targeted payload of the replication-interrupting drug into tumor cells, further triggering cell death.[32]

Following the promising results in a phase I trial of trastuzumab deruxtecan, researchers evaluated efficacy and safety in a phase II trial of patients with HER2-positive gastric or gastroesophageal cancers that progressed despite treatment with trastuzumab. In the DESTINY Gastric-01 study (ClinicalTrials.gov identifier: NCT03329690),[33] patients were randomly assigned to receive trastuzumab deruxtecan (125 patients) or the treating clinician's choice of chemotherapy (62 patients). Among patients who received the antibody-drug conjugate, 51.3% experienced an objective response compared with 14.3% of patients who received chemotherapy. Overall survival was also improved with trastuzumab deruxtecan (12.5 months) compared with chemotherapy (8.4 months). The most common grade 3 or greater adverse events were decreased neutrophil count, anemia, and decreased WBC count, all of which were more frequent among patients receiving trastuzumab deruxtecan. Twelve patients (10%) who received the antibody-drug conjugate developed drug-related interstitial lung disease or pneumonitis, mostly grade 1 or 2; no cases occurred in the chemotherapy group.

Additional data were presented at the virtual scientific program of the 2020 ASCO Annual Meeting. A study of trastuzumab deruxtecan in HER2-positive colorectal cancer showed similarly promising results. The phase II DESTINY-CRC01 trial (ClinicalTrials.gov identifier: NCT03384940)[34] included patients with HER2-expressing metastatic colorectal cancer that had progressed after two or more treatment regimens. In this trial, nearly half of patients (45.3%) experienced an objective response—one patient had complete response and 23 had partial response. The most common grade 3 or greater adverse events were decreased neutrophil count and anemia. Five patients developed interstitial lung disease.

If approved, trastuzumab deruxtecan could fill a significant unmet need for patients with previously treated HER2-positive metastatic gastric and/or colorectal cancer.

Pembrolizumab Doubles Time to Disease Progression in Patients With Advanced Colorectal Cancer With DNA Mismatch Repair Deficiency

Approximately 5% of patients with metastatic colorectal cancer have high microsatellite instability with deficient mismatch repair (MSI-H/dMMR),[35] which can be detected when a cell is unable to repair mistakes that are made during the process of copying DNA. When this happens, mutations in the DNA start accumulating and may cause cancer. Pembrolizumab is an immune checkpoint inhibitor that blocks the activity of a receptor called PD-1, a protein that helps keep the immune system in check, thereby allowing the immune system to attack cancer cells.

In the phase III KEYNOTE-177 trial (ClinicalTrials.gov identifier: NCT02563002),[36] first-line treatment with

TAPUR

ASCO's Targeted Agent and Profiling Utilization Registry Study (TAPUR; ClinicalTrials.gov identifier: NCT02693535), now in its fifth year, continues to enroll patients with advanced cancer with tumors that harbor a potentially actionable genomic alteration and report findings on patient outcomes. TAPUR evaluates antitumor activity of commercially available, targeted anticancer drugs when used outside of their FDA-approved indications. The study identifies potential new uses for existing, effective treatments that target a tumor genomic alteration.

More than 3,000 participants have been registered and more than 2,000 treated with a TAPUR study therapy. Based on treatment responses in the first stage of the enrollment, patient cohorts are either expanded to stage II for further study or permanently closed. This past year alone, TAPUR researchers have presented or published findings for 10 cohorts. Of these 10 cohorts, six reported positive findings, including positive cohorts for patients with HER2-amplified metastatic colorectal cancer (mCRC) treated with trastuzumab plus pertuzumab and patients with *BRAF*-mutant mCRC treated with cobimetinib plus vemurafenib. For the latest updates of all available results, closures, expansions, and listing of publications and presentations, visit the TAPUR website at tapur.org.

pembrolizumab doubled the time to disease progression (16.5 months) compared with patients who received conventional chemotherapy (8.2 months). The findings come from an interim analysis presented during the virtual scientific program of the 2020 ASCO Annual Meeting. Severe treatment-related adverse events (grade 3 or greater) were less common with pembrolizumab (22%) than chemotherapy (66%).

The FDA approved pembrolizumab for the first-line treatment of patients with unresectable or metastatic MSI-H/dMMR colorectal cancer in June 2020.[35]

PREVENTION

Aspirin Linked to Long-Term Reduction in Cancer Risk in Patients With Hereditary Cancer Predisposition

Lynch syndrome is an inherited condition associated with an increased risk of multiple types of cancers, including colorectal cancer. The lifetime risk of colorectal cancer is estimated to range from 20% to 80% among patients with this condition versus 4%-5% for the general population.[37,38] Accumulated data from observational studies and registries suggest a protective benefit associated with aspirin in patients with Lynch syndrome.[39]

Twenty-year follow-up was planned as part of the CAPP2 study (ISRCTN registry, number ISRCTN59521990), which included 427 individuals randomly assigned to receive daily aspirin or placebo for 2 years. The analysis showed a significant, meaningful decrease of 44% in colorectal cancers among Lynch syndrome carriers who took aspirin compared with those who took a placebo.[40] This benefit took more than 5 years to become detectable but persisted beyond 20 years. Serious adverse events were comparable for the two groups. The optimal dosage and treatment duration remain to be determined.

ADDITIONAL ADVANCES

Combination Therapies

Tucatinib plus standard therapy delays progression of brain metastases in patients with HER2-positive breast cancer. Brain metastases have long been a challenge for patients with HER2-positive breast cancer, developing in up to half of patients.[41] These metastases progress quickly, typically within 6-12 months, due to a lack of effective treatments beyond localized therapy.[42,43]

Results from the randomized, placebo-controlled HER2-CLIMB study (ClinicalTrials.gov identifier: NCT03975647),[44] changed this by showing that adding a new HER2 targeted therapy, called tucatinib, to standard trastuzumab and capecitabine significantly reduced the risk of brain metastases progression or death. Over the course of the study, this risk fell by just over two thirds (68%) compared with patients who received placebo with trastuzumab and capecitabine. Patients taking tucatinib also had longer overall survival—18.1 versus 12.0 months.

These strong efficacy results established tucatinib as a new standard of care for patients with advanced unresectable or metastatic HER2-positive breast cancer, including patients with brain metastases, who have received one or more prior anti-HER2-based regimens in the metastatic setting. The FDA approved tucatinib in combination with trastuzumab and capecitabine for this patient population.[45]

Immunotherapy before surgery may improve prognosis of early-stage, triple-negative breast cancer. Triple-negative breast cancer is the most aggressive subtype of breast cancer.[46] In this cancer, the three most common growth factor receptors that drive breast cancer growth are not expressed—estrogen receptor, progesterone receptor, and HER2. Advanced triple-negative breast cancer has an extremely poor prognosis,[46] so preventing progression in patients with early-stage disease is a high unmet medical need and a critical area for research. A number of studies have demonstrated that achieving pathologic complete response—when no cancer cells remain in the breast or lymph nodes—from chemotherapy given prior to surgery (neoadjuvant chemotherapy) is strongly associated with better prognosis.[47–49]

The immunotherapy drug pembrolizumab has shown promise in patients with early triple-negative disease.[50] With the phase III KEYNOTE 522 trial (ClinicalTrials.gov identifier: NCT03036488),[51] patients with stage II or III triple-negative breast cancer were randomly assigned to receive neoadjuvant standard platinum-based chemotherapy with either pembrolizumab or placebo, followed by anthracycline and cyclophosphamide with either pembrolizumab or placebo. Patients then went on to surgery, followed by treatment with pembrolizumab or placebo. The addition of pembrolizumab to chemotherapy improved pathologic complete response (64.8%) compared with chemotherapy alone (51.2%) as well as event-free and overall survival. Pathologic complete response occurs when no signs of cancer can be found in tissue samples. These promising results suggest that the combination of chemotherapy with immunotherapy may improve long-term outcomes for patients with this disease.

This study supports progress in an area noted in ASCO's Research Priorities to Accelerate Progress Against Cancer, most notably the increased use of immunotherapy in a difficult-to-treat disease. Patients who have a complete response to neoadjuvant (given prior to surgery) chemotherapy are more likely to have the option of breast conservation than those who have significant residual disease.

CDK4/6 inhibitor reduces risk of early recurrence for high-risk early-stage HR-positive, HER2-negative breast cancer. It is estimated that up to 20% of patients with hormone receptor (HR)–positive, HER2-negative breast cancer will experience disease recurrence in the first 10 years after diagnosis.[52] These recurrences are typically distant metastases and are often incurable. Given that over 150,000 patients are diagnosed with HR-positive HER2-negative breast cancer each year in the United States alone, advances in the treatment of this disease may have substantial impact on the population.[53]

Abemaciclib is a cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitor that works by blocking certain proteins to slow down the growth of cancer cells.[54] It is approved by the FDA as initial therapy for advanced HR-positive, HER2-negative breast cancer based on clinical trials that showed substantially improved outcomes for women treated with abemaciclib and traditional endocrine therapy compared with endocrine therapy alone.[55]

In the phase III randomized monarchE trial (ClinicalTrials.gov identifier: NCT03155997),[56] researchers evaluated the addition of abemaciclib to standard adjuvant endocrine therapy in patients with HR-positive, HER2-negative early breast cancer with positive lymph nodes and a high risk of recurrence within 5 years of cancer diagnosis. Abemaciclib combined with endocrine therapy showed a significant improvement in invasive disease-free survival at 2 years (92.2%), compared with standard therapy alone (88.7%). Most patients in the trial experienced at least one treatment-related adverse effect (97.9% in the abemaciclib group and 86.1% in the standard care group). The most frequent adverse effects were diarrhea, neutropenia, and fatigue in the abemaciclib group and arthralgia, hot flushes, and fatigue in the standard care group. There was a 16.6% treatment discontinuation rate in the abemaciclib arm.

Additional translational studies will help identify who is most likely to benefit from the addition of this therapy; longer follow-up will help determine whether the use of adjuvant abemaciclib will improve overall survival. However, these early findings are encouraging and represent the first treatment advance in 20 years in the adjuvant setting for this form of breast cancer.

Combination offers chemotherapy-free alternative first-line treatment for patients with advanced non–small-cell lung cancer. Over the past two decades, treatment has improved for non–small-cell lung cancers (NSCLC) with certain identifiable driver mutations, and in the last 5 years, immune checkpoint inhibitors have further transformed the treatment outlook—especially for patients with cancers that do not harbor driver mutations. Checkpoint inhibitors help the immune system identify and target cancer cells. Nivolumab and ipilimumab target different but complementary immune checkpoints.[57] Nivolumab targets programmed death-ligand 1 (PD-L1), a protein that can slow down the immune system's ability to target some cancer cells, whereas ipilimumab acts on a different protein.

In the open-label phase III randomized CheckMate 227 study (ClinicalTrials.gov identifier: NCT02477826),[58] investigators demonstrated the nivolumab-ipilimumab combination significantly improved overall survival compared with chemotherapy alone (17.1 *v* 14.9 months) in patients newly diagnosed with advanced NSCLC and with PD-L1 levels of at least 1% (PD-L1 positive). Median overall survival was also improved with the combination therapy in patients with a PD-L1 expression level of less than 1%—17.2 months with nivolumab-ipilimumab compared with 12.2 months with chemotherapy alone. Treatment-related serious adverse events of any grade were more common with the combination immunotherapy regimen (24.5%) than with chemotherapy alone (13.9%). Treatment-related adverse events leading to discontinuation were also greater with the combination immunotherapy therapy (18.1%) than with chemotherapy (9.1%).

The combination therapy allows certain patients to avoid chemotherapy, which can significantly limit quality of life. In May 2020, the FDA approved this combination for the treatment of patients with advanced NSCLC with a PD-L1 expression of 1% or greater.

Rituximab plus chemotherapy improves survival for children with mature B-cell non-Hodgkin lymphoma. Over the last 30 years, therapies have been refined for children and adolescents diagnosed with mature B-cell non-Hodgkin lymphoma (primarily Burkitt lymphoma or diffuse large B-cell lymphoma) and resulted in improved outcomes.[59] However, treatment options are still limited for those patients with high-risk features (higher stage, elevated levels of the protein lactate dehydrogenase, and CNS involvement) or those with cancer that does not respond to initial therapy. Although the addition of rituximab to standard chemotherapy has been shown to be effective in adults, it has not been tested in children and adolescents.[60] Rituximab destroys both normal and malignant B cells, and although effective in treating B-cell cancers, it carries the risk of serious adverse effects.[61]

Investigators conducted an open-label, randomized phase III study (ClinicalTrials.gov identifier: NCT01516580)[62] including 328 children and adolescents 2-17 years with high-grade, high-risk, mature B-cell non-Hodgkin lymphoma. Initially, patients were randomly assigned to receive standard-of-care chemotherapy alone or with rituximab. Random assignment was stopped, however, after the first interim analysis because of high efficacy of the rituximab-chemotherapy combination, and all enrolled patients were allowed to receive the combination therapy. At 3 years, 93.9% of those who had received rituximab-chemotherapy and 82.3% in the chemotherapy-only group had no primary refractory disease, progression, relapse, a second cancer,

or death from any cause. Overall survival at 3 years was also greater for those who received rituximab (95.1%) than those who received chemotherapy only (87.3%). However, patients who received rituximab experienced greater adverse effects, suggesting that longer-term monitoring, particularly for infectious complications, may be required. One-third of patients had infusion reactions during the first rituximab treatment, although this decreased with subsequent infusions. After the initial chemotherapy, grade 4 or greater adverse events were seen in the rituximab-chemotherapy group (33.3%), compared with the chemotherapy-only group (24.2%). Grade 4 or greater neutropenia with fever and infection were both more common among patients who received rituximab.

Adding rituximab to chemotherapy has been adopted as standard of care for patients with high-risk disease. This study was funded in part by NCI.

First new treatment for hepatocellular carcinoma approved in more than ten years. Hepatocellular carcinoma (HCC) is the fifth most common cancer worldwide and the second leading cause of cancer-related death.[63,64] When most patients with HCC initially seek care, they have tumors that cannot be removed surgically and have a poor prognosis.[65] The targeted therapy sorafenib has been the mainstay of treatment for HCC that is inoperable, although adverse effects are common and often impair quality of life.[66]

In early trials, the combination of atezolizumab and bevacizumab showed antitumor activity against inoperable HCC and adverse effects were generally tolerable.[67] Atezolizumab is a type of immunotherapy known as a PD-L1 inhibitor that helps the body's immune system attack cancer cells.[68] Bevacizumab is a vascular endothelial growth factor inhibitor that helps limit the blood supply to tumors.[69]

Researchers confirmed the earlier findings of antitumor activity in the large, randomized phase III IMbrave150 trial (ClinicalTrials.gov identifier: NCT03434379),[70] which included 501 patients not previously treated with systemic therapy. Patients were randomly assigned to receive either the atezolizumab-bevacizumab combination or sorafenib. Overall survival at 12 months was 67.2% for patients who received the combination compared with 54.6% for those in the sorafenib group. In addition, the estimated median time until the cancer progressed was 6.8 months for the combination treatment and 4.3 months for sorafenib alone. Serious adverse events were more common among patients who received atezolizumab plus bevacizumab—38% as compared with 30% with sorafenib. Grade 5 adverse events occurred in 4.6% of patients who received the combination compared with 5.8% with sorafenib.

The combination of atezolizumab and bevacizumab was approved by the FDA in May 2020 for the treatment of patients with unresectable or metastatic HCC who have not received prior systemic therapy.[71] Inoperable HCC has been an area of great clinical need, and the approval marks the first immunotherapy combination to be approved for this cancer.

Drug combination extends survival in older patients with acute myeloid leukemia. Acute myeloid leukemia (AML) can occur in people of any age, but the disease more commonly affects older individuals, with an average age of diagnosis of 68 years.[72,73] Yet, older patients with cancer typically receive less aggressive treatment, often as a result of competing health issues or, in some cases, a lack of proven therapies.[74] Azacitidine is a drug that blocks a protein that slows down cancer cell death.[75] Early studies had suggested that adding venetoclax (a drug that works in a similar way) to azacitidine may improve survival over other available treatments.[76]

In the phase III VIALE-A trial (ClinicalTrials.gov identifier: NCT02993523),[77] researchers compared the azacitidine-venetoclax combination with azacitidine and placebo among patients age 75 or older who had not received prior treatment and could not safely undergo intensive standard care. They found that overall survival was longer for patients who received the azacitidine-venetoclax combination (14.7 months) compared with those who received azacitidine and placebo (9.6 months). Serious side effects were common in both groups, occurring in 83% of patients who received the combination therapy and 73% who received azacitidine and placebo. Grade 3 or higher hematologic side effects included thrombocytopenia, neutropenia, and febrile neutropenia.

Based on these results, in October 2020 the FDA approved venetoclax in combination with azacitidine, or decitabine, or low-dose cytarabine in adults age 75 or older newly diagnosed with AML who are ineligible for intensive chemotherapy or who have comorbidities that preclude the use of intensive induction chemotherapy. This approval provides an important new effective treatment option for older patients with AML.

Targeted Therapies

Response to HER2-targeting antibody-drug conjugate seen in patients with lung cancer. Trastuzumab deruxtecan has shown efficacy in the treatment of patients with breast cancer and gastric cancer that makes too much of a protein called HER2-positive (see Antibody-Drug Shows Promise in GI Cancers). The treatment has also shown promise for NSCLC. HER2 positivity has been recognized in lung adenocarcinoma for some time, occurring in about 2% of cases.[78] However, trials of HER2 inhibitors to date have disappointed.

Data from the phase II DESTINY-Lung01 trial (ClinicalTrials.gov identifier: NCT03505710),[79] which was presented in the virtual scientific program of the 2020 ASCO Annual Meeting, were more encouraging. In the data presented, 61.9% of pretreated patients with advanced HER2-positive

NSCLC who received trastuzumab deruxtecan had a confirmed response. The time to disease progression was estimated to be 14 months. More than half (52.4%) of patients had treatment-related adverse events of grade 3 or greater, including decreased neutrophil count and anemia. Five patients developed drug-related interstitial lung disease. Although longer-term data are needed, trastuzumab deruxtecan represents the most promising treatment to date for this population of patients with lung cancer.

Postsurgery targeted therapy doubles disease-free survival in early, EGFR-positive non–small-cell lung cancer. Platinum-based chemotherapy following surgery has been the recommended treatment for patients with stage II-IIIA NSCLC, although this treatment only reduces the risk of recurrence or death by around 16% compared with surgery alone.[80,81] Data from the phase III ADAURA trial (ClinicalTrials.gov identifier: NCT02511106)[82] offer a promising new option for patients with tumors that have a mutated epidermal growth factor receptor gene (*EGFR*). The trial found that giving the *EGFR*-targeted drug osimertinib after surgery with or without platinum-based chemotherapy at the clinician's discretion improved 24-month disease-free survival (the time from treatment to either disease return or death) to about 90%, compared to 44% among patients who received the same surgery and chemotherapy regimen plus placebo. In fact, the trial was unblinded early after this dramatic improvement. Of patients with stage II-IIIA NSCLC receiving osimertinib after surgery, the risk of disease recurrence or death was reduced by 83%.

The improvement in disease-free survival seen in this study strongly supports the use of this targeted therapy in earlier-stage disease and is practice-changing for resected, early-stage *EGFR*-mutation-positive NSCLC.

Targeted therapy prompts response in patients with NSCLC carrying specific mutation. It is estimated that 1%-2% of patients with NSCLC carry a type of genetic mutation called *RET* fusion, which is involved in the production of abnormal proteins that promote the growth of cancer cells.[83] Selpercatinib is a targeted therapy that works to block these proteins. In the phase I-II LIBRETTO-001 trial (ClinicalTrials.gov identifier: NCT03157128),[84] researchers evaluated the efficacy and safety of the drug in patients with *RET* fusion–positive NSCLC who had previously received platinum-based chemotherapy (49 patients) and also those who were previously untreated (39 patients). Across both patient groups, researchers observed high, long-lasting responses. Of patients who had received previous treatment, 64% had an objective response, defined as complete or partial response, or disease that did not progress; responses lasted for a median of 17.5 months. Among patients who had not previously been treated, 85% had a response; 90% of these patients continued to respond at 6 months of follow-up. Grade 3 or 4 hypertension was the most common adverse event. Six grade 5 adverse events were observed, although these were not determined to be related to selpercatinib. Overall, treatment-related adverse events did not require dose interruption or modification. Although larger trials are needed to confirm these findings, the efficacy of selpercatinib combined with its safety holds promise for patients with NSCLC that harbors *RET* fusion alterations. The FDA approved selpercatinib for the treatment of adult patients with metastatic *RET* fusion–positive NSCLC in May 2020.[85]

PARP inhibitor doubles progression-free survival for men with hormone therapy-resistant prostate cancer. Metastatic prostate cancer that grows and continues to spread despite hormone therapy is often referred to as metastatic castration-resistant prostate cancer (mCRPC). Although there have been significant therapeutic developments in this setting, it remains an incurable disease.[86] Recent evidence demonstrates that about a third of patients with mCRPC harbor specific gene mutations that inhibit the repair of DNA damage, with the most prominent of these being mutations in *BRCA 1/2* and *ATM*. Data suggest that men with these gene mutations may benefit from treatment with poly(adenosine diphosphate-ribose) polymerase (PARP) inhibitors, such as olaparib and rucaparib.[87-89]

The phase III PROfound trial (ClinicalTrials.gov identifier: NCT02987543)[90] examined the efficacy and safety of olaparib. Patients with mCRPC with at least one alteration in *BRCA 1*, *BRCA 2*, or *ATM* were randomly assigned 2:1 to receive olaparib (162 patients) or the treating clinician's choice of enzalutamide or abiraterone (83 patients). At the time of data cutoff, the median time to disease progression was twice as long for patients receiving olaparib (7.4 months) compared with those receiving enzalutamide/abiraterone (3.6 months). The median overall survival was significantly longer in the olaparib group (19.1 months) than in those receiving enzalutamide or abiraterone (14.7 months). There were more grade 3 and 4 events in the olaparib arm with the most common toxicities being anemia, nausea, fatigue, and loss of strength.

Based on data from the PROfound trial, in May 2020 the FDA approved olaparib for mCRPC with mutations in certain genes involved in DNA repair, in disease that has progressed following prior treatment with enzalutamide or abiraterone.[91]

Targeted therapy improves survival and symptoms in lung cancers that spread to CNS. Leptomeninges are part of the inner layers of the tissue surrounding the brain and spinal cord, which protect the CNS. Although metastasis to the leptomeninges is not common in patients with advanced lung cancer (3%-4%), the incidence of leptomeningeal metastasis is greatest (9%) among patients with *EGFR*m NSCLC.[92,93]

A phase I trial, the BLOOM study (ClinicalTrials.gov identifier: NCT02228369)[94] showed dramatic reductions in leptomeningeal metastases and related symptoms among patients with *EGFR*m NSCLCs with the use of osimertinib, a drug that targets a specific mutation in *EGFR*. In a disease state where median overall survival has traditionally been measured in weeks, median overall survival for the 41 patients in the trial was 11 months. Median progression-free survival was 8.6 months. In addition, over half of the patients who had neurologic symptoms at baseline (57%) improved with treatment. Adverse events and tolerability of osimertinib were similar to those that typically accompany treatment with the drug. The most common adverse events of any grade were rash or acne, diarrhea, and nausea.

Other Therapies

Maintenance immunotherapy following chemotherapy extends survival for patients with advanced urothelial cancer. The introduction of immunotherapies—including checkpoint inhibitors—over the last several years has improved the care of patients with metastatic urothelial cancer. Checkpoint inhibitors target the proteins PD-1 or PD-L1, blocking cancer cells from turning off the immune system.

In the JAVELIN Bladder 100 trial (ClinicalTrials.gov identifier: NCT02603432),[95] researchers explored the addition of the PD-L1 inhibitor avelumab to best supportive care in patients with metastatic urothelial cancer that was stable or had responded to platinum-based chemotherapy. The researchers found that maintenance therapy with avelumab extended overall survival (21.4 months) compared with best supportive care alone (14.3 months). Best supportive care is aimed at improving quality of life for patients. Adverse events of grade 3 or higher occurred more frequently (47.4%) in patients who received avelumab compared with those who did not (25.2%).

The study results represent the largest survival benefit seen in advanced urothelial cancer following chemotherapy.

Improved survival with androgen receptor inhibitors in castration-resistant prostate cancer. Initial evidence from phase III trials demonstrated that three novel androgen receptor inhibitors—enzalutamide, apalutamide, and darolutamide—could improve metastases-free survival in patients who have castration-resistant prostate cancer and certain biomarkers.[96,97] However, an overall survival benefit has not yet been seen.[98,99]

The phase III PROSPER trial (ClinicalTrials.gov identifier: NCT02003924)[100] of nearly 1,400 patients showed that adding enzalutamide to hormone therapy more than doubled metastases-free survival (36.6 months) in this population of patients compared with hormone therapy alone (14.7 months). Long-term data from this study showed an overall survival benefit with enzalutamide (67 months) compared with hormone therapy alone (56.3 months). Results from two other large phase III studies produced similar findings with the use of apalutamide and darolutamide compared with hormone therapy alone. Overall survival with apalutamide was longer (73.9 months) compared with hormone therapy alone (59.9 months). Three-year overall survival was longer with darolutamide (83%) compared to hormone therapy only (77%).[101,102]

These findings can help guide treatment discussions between doctors and patients with nonmetastatic castration-resistant prostate cancer.

Adding local radiotherapy to standard chemotherapy boosts survival for nasopharyngeal carcinoma. Although nasopharyngeal carcinoma (cancer located behind the nose and above the back of the throat) is not common in the United States, it occurs frequently in Southeast Asian and native Alaskan populations.[103] For patients with metastatic disease, chemotherapy using gemcitabine and cisplatin is the standard of care as first-line treatment.[104] The use of local therapy, however, has proven beneficial in two previous randomized clinical trials involving this type of cancer.[105,106]

Researchers administered local radiotherapy to patients with newly diagnosed metastatic nasopharyngeal carcinoma to determine if survival could be improved. In the study (ClinicalTrials.gov identifier: NCT02111460),[107] 63 patients were randomly assigned to undergo local or regional radiation treatment in addition to chemotherapy with cisplatin and fluorouracil while 63 received chemotherapy alone. Overall survival at 24 months was significantly longer for the group that received localized radiation (76.4%) compared with those on chemotherapy alone (54.5%). Radiotherapy was associated with grade 3 or higher dermatitis, mucositis, and xerostomia. Harmful adverse effects in the blood, liver, kidneys, and GI tract were comparable between the groups. These results improve standard treatment for metastatic nasopharyngeal carcinoma and add to a growing body of data demonstrating local therapies can play an important role in the treatment of metastatic cancer.

First-in-class drug reduces transfusion dependence in patients with lower-risk myelodysplastic syndromes. Myelodysplastic syndromes (MDS) are a group of cancers in which patients' bone marrow produces too few healthy blood cells. One of the most common signs of MDS is anemia.[108] Patients with lower-risk MDS who are anemic are typically treated with red blood cell (RBC) transfusions and erythropoietin-stimulating agents; however, not all patients are able to tolerate these therapies. Some patients may develop side effects that are difficult to tolerate, limiting the use of these medicines. Some patients who are unable to tolerate these side effects can require repeated transfusions to replace red blood cells, which can affect quality of life and carry risk as well. Patients with low-risk disease (disease unlikely to progress to acute leukemia) can require transfusions for long periods of time. Therefore, there is a significant need for new treatments that can improve anemia.[109-112]

Luspatercept is a new type of drug that helps RBC precursors become red blood cells, thereby increasing the RBC count.[113] The phase III MEDALIST trial (ClinicalTrials.gov identifier: NCT02631070)[114] evaluated the efficacy and safety of luspatercept in patients with lower-risk MDS with ring sideroblasts (faulty RBC precursors), who had been receiving regular RBC transfusions and had disease that was refractory or unlikely to respond to erythropoiesis-stimulating drugs, or who experienced side effects causing them to discontinue treatment. Patients were randomly assigned to receive luspatercept (153 patients) or placebo (76 patients). More patients in the luspatercept arm (38%) no longer required transfusions (the study's primary end point) for 8 weeks compared with those in the placebo arm (13%). Grade 3 or 4 serious adverse events were comparable in the two groups, seen in 42% of those receiving luspatercept and in 45% receiving placebo. The findings of this trial led to the approval of luspatercept by the FDA for lower-risk myelodysplastic syndromes with ringed sideroblasts.[115]

CAR T cell treatment improves survival for majority of patients with relapsed or refractory mantle cell lymphomas, established as new treatment option. Mantle cell lymphoma is an aggressive type of B-cell non-Hodgkin lymphoma and is generally considered incurable without an allogeneic stem-cell transplant. Standard therapy with chemoimmunotherapeutic regimens, particularly using certain targeted drugs (BTK inhibitors), has led to a significant survival improvement for patients with relapsed or refractory disease.[116,117] However, patients with cancer that has progressed further typically have poor survival (less than 12 months).[118]

KTE-X19 is a chimeric antigen receptor (CAR) T cell treatment. CAR T cells are immune cells collected from a patient's blood that are genetically altered to better target cancer cells and then infused back into the patient as a one-time treatment.[119] KTE-X19 targets the CD19 antigen found on the surface of B cells, which are commonly associated with mantle cell lymphoma.

In the phase II ZUMA-2 trial (ClinicalTrials.gov identifier: NCT02601313),[120] patients with relapsed and/or refractory disease who had undergone up to five previous treatments, including BTK inhibitors, were treated with KTE-X19. Responses were observed in 85% of the 60 patients included in the analysis, and 59% had a complete response. At a median of 12.3 months of follow-up, 57% of patients were in remission. At 12 months, progression-free survival was 61%, and overall survival 83%. The toxicity profile was similar to that of other CAR T therapies, including grade 3 or higher cytokine release syndrome and neurologic events in 15% and 31% of patients, respectively. None of these was fatal.

Based on these results, the FDA granted accelerated approval to KTE-X19 (brexucabtagene autoleucel) for the treatment of adult patients with relapsed or refractory mantle cell lymphoma.[121] This marks the third FDA-approved CAR T therapy and the first for patients with advanced mantle cell lymphoma.

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, each year, ASCO issues its list of top Research Priorities to Accelerate Progress Against Cancer. As cancer care becomes more complex and personalized, the research behind new advances must include the representation of all populations who stand to benefit and consider social determinants of health, such as the social, economic, and cultural factors that influence cancer risk and outcomes.

Research priorities for 2021, listed below in no particular order, represent promising areas of research that have the potential to significantly improve the knowledge base for clinical decision making and address vital unmet needs in cancer care. This year's list includes a newly added priority on artificial intelligence, recognizing its growing potential to solve complex problems and drive diagnostic, therapeutic, and translational research across the spectrum of cancer prevention and care.

Develop and Integrate Artificial Intelligence and Deep Learning in Cancer Research

Artificial intelligence (AI) is a rapidly growing and complex field of medical research, with potential to integrate innumerable data points into a clinically useful context. There are several types of AI, including deep learning methods, which use algorithms in an iterative process to identify relationships within data to solve complex problems. AI has the potential to drive diagnostic, therapeutic, and translational research across the spectrum of cancer prevention and care. It will be critical to educate oncologists about the fundamentals, advantages, and potential pitfalls of AI and deep learning techniques to support effective application in real-world cancer care.

Primary focus areas:

- Develop deep learning methodologies that aid in cancer diagnosis based on biospecimen analysis, including the detection of molecular variants that may affect prognosis or treatment decisions.
- Investigate the utility of AI to enhance and improve radiographic imaging, analysis, and reporting.
- Implement and assess AI systems that integrate large amounts of clinical data to aid clinical decision making and measurement of clinical outcomes.

Identify Strategies That Predict Response and Resistance 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 by producing long-lasting remissions. For others, however, despite initial response to immunotherapy, resistance to treatment can develop and the cancer can recur. Immunotherapies can also cause substantial adverse effects that can be life-threatening and, in some cases, permanent. The ability to adequately assess, and potentially predict, response and resistance to immunotherapy will lead to better outcomes for patients.

Priority focus areas:

- Identify blood- and tissue-based biomarkers relevant to immunotherapies that can predict initial response, long-term disease control, adverse events, and resistance.
- Develop predictive models and algorithms that assign risk of severe immune-related toxicities based on readily available patient data.

Optimize Multimodality Treatment for Solid Tumors

A wide range of therapies are recommended to patients around the time of surgery (perioperative) as well as before and after it (neoadjuvant and adjuvant treatment). These therapies aim to achieve local control of the tumor as well as reduce the risk of recurrence and cancer-related death associated with microscopic tumor spread. 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 these therapies are the ones most likely to benefit. Limiting their use in those who are unlikely to benefit will be an important step in optimizing care and eliminating unnecessary adverse effects and costs for patients in whom the benefits are unlikely to outweigh the risks.

Priority focus areas:

- 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.
- Define the patient populations that benefit from perioperative, neoadjuvant, and adjuvant therapies, including clinical, pathologic, genomic, biochemical, immunologic, and environmental or social factors that affect the likelihood of benefit
- Study treatment de-escalation strategies that maximize benefit while reducing risk.

Increase Precision Medicine Research and Treatment Approaches in Pediatric and Other Rare Cancers

Genomic tools have been widely deployed in adult patients with cancer to characterize the tumor mutation profile and guide therapy selection. In certain cancers, the use of these tools has accelerated the 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 as well as other rare cancers.

Priority focus areas:

- Identify genomic and other molecular alterations in pediatric and rare cancers that can serve as potentially actionable treatment targets.
- Develop effective therapeutic agents that can target genomic or other molecular alterations in childhood and rare cancers.
- Explore the efficacy of existing targeted therapies in pediatric patients and patients with rare cancers that have mutations shown to be responsive to medicines that work in adult populations.

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 that 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 younger clinical trial participants. Researchers must make use of available practice-based, real-world data to study and drive improvements in caring for older adults with cancer. The lack of evidence 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, biomarkers of aging, and clinical pharmacology in older adults, to more reliably predict risk of treatment-related adverse effects in older patients with cancer.
- Use practice-based data to better understand the efficacy and toxicities of cancer treatments, including the impact on physical function, cognition, and quality of life, particularly among older adults most underrepresented in clinical trials, such as those with impaired functional status, comorbidities, or frailty.

- Test the role of geriatric assessment-guided management in improving outcomes using personalized care; important focus areas include strategies that minimize undertreatment of fit patients and overtreatment of vulnerable or frail patients, supportive care interventions, and care delivery interventions.

Increase Equitable Access to Cancer Clinical Trials

Certain patient populations are consistently underrepresented in cancer clinical trials. These include patients from racial and ethnic minorities, rural areas, and lower socioeconomic groups and patients older than 65 years as well as adolescents and young adults age 15-39 years. Decreased representation of 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 biologic, 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 population (examples may include use of educational tools, telehealth, 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 underrepresented groups and the physicians treating them.
- Make use of clinical practice data to study differences in cancer incidence, prevalence, natural history of disease, and treatment experience, including efficacy and toxicity, among underrepresented populations.

Reduce Adverse Consequences of Cancer Treatment

Advances in cancer treatment have resulted in a record number of cancer survivors—more than 15.5 million in the United States at present. Many survivors face acute and chronic consequences of cancer, including pain and adverse effects of cancer therapies—such as peripheral neuropathy, cognitive impairment, and cardiotoxicity—that affect quality of life and pose a substantial burden not only to patients but also to the healthcare system. Identifying strategies to minimize cancer-associated pain and treatment effects is an urgent area of research.

Priority focus areas:

- Develop and test strategies to mitigate and manage chronic toxicities associated with cancer treatment, including optimization of drug and radiation dosing.
- 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.
- Expand understanding and use of the range of pain management options for patients with cancer.
- Develop new tools to facilitate long-term tracking of patient outcomes that include patient-reported measures.

Reduce Obesity's Impact on Cancer Incidence and Outcomes

The incidence of obesity has dramatically increased over the past several decades.[122] Despite being the second leading preventable cause of cancer, an ASCO survey found that only 35% of Americans recognize excess body weight as a cancer risk factor.[123] Obesity is associated with poorer cancer survival and can contribute to increased risk of treatment-related adverse 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 and will surpass smoking as the leading preventable cause of cancer.[124]

Priority focus areas:

- Improve the understanding of the mechanisms by 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.

Better Identify Potentially Malignant Lesions and Predict When Treatment Is Needed

Many cancers begin as high-risk lesions that invariably progress to invasive cancer, whereas other premalignant lesions may never require treatment. Currently, little is known about the genetic makeup, heterogeneity, and microenvironment of premalignant lesions, and what causes some to progress to invasive cancer. Increased knowledge will help guide new approaches to intercept and eradicate high-risk lesions before their transformation to

malignancy and to spare patients from unnecessary treatments for lesions with a low risk of progression.

Priority focus areas:

- Address barriers to screening and early treatment of potentially malignant disease.
- Identify potentially malignant lesions with a high risk for progression based on specific features and develop appropriate treatment strategies, while also identifying potentially malignant lesions that do not require intervention.
- 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 potentially malignant lesions that are associated with progression to invasive disease.
- Investigate novel methods for evaluation of potentially malignant lesions to better inform the risk or likelihood of progression to invasive disease.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Clinical Cancer Advances 2021: ASCO's Report on Progress Against Cancer

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APPENDIX

TABLE A1. FDA Approvals of Anticancer Therapies (October 2019-November 2020)

New Approvals	Comments
New therapies or tests	
October 2020	
NGS-based FoundationOne CDx test	A companion diagnostic to identify fusions in neurotrophic receptor tyrosine kinase (*NTRK*) genes, *NTRK1*, *NTRK2*, and *NTRK3*, in DNA isolated from tumor tissue specimens from patients with solid tumors eligible for treatment with larotrectinib
September 2020	
Pralsetinib (GAVRETO)	For adult patients with metastatic RET fusion–positive non–small-cell lung cancer (NSCLC) as detected by an FDA-approved test
Azacitidine tablets (ONUREG)	For continued treatment of patients with acute myeloid leukemia who achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy and are not able to complete intensive curative therapy
August 2020	
FoundationOne Liquid CDx test	A companion diagnostic to identify mutations in *BRCA*1 and *BRCA*2 genes in cell-free DNA isolated from plasma specimens from patients with metastatic castration-resistant prostate cancer (mCRPC) eligible for treatment with rucaparib (RUBRACA)
Belantamab mafodotin-blmf (BLENREP)	For adult patients with relapsed or refractory multiple myeloma who have received at least 4 prior therapies, including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent
July 2020	
Brexucabtagene autoleucel (TECARTUS)	A CD19-directed genetically modified autologous T cell immunotherapy, for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL)
June 2020	
Tazemetostat (TAZVERIK)	An EZH2 inhibitor, for adult patients with relapsed or refractory (R/R) follicular lymphoma (FL) whose tumors are positive for an EZH2 mutation as detected by an FDA-approved test and who have received at least 2 prior systemic therapies, and for adult patients with R/R FL who have no satisfactory alternative treatment options
Lurbinectedin (ZEPZELCA)	For adult patients with metastatic small-cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy
May 2020	
Brigatinib (ALUNBRIG)	For adult patients with anaplastic lymphoma kinase (ALK)–positive metastatic non–small-cell lung cancer (NSCLC) as detected by an FDA-approved test
Ripretinib (QINLOCK)	For adult patients with advanced GI stromal tumor (GIST) who have received prior treatment with 3 or more kinase inhibitors, including imatinib
Capmatinib (TABRECTA)	For adult patients with metastatic non–small-cell lung cancer (NSCLC) whose tumors have a mutation that leads to mesenchymal-epithelial transition (MET) exon 14 skipping as detected by an FDA-approved test
Daratumumab and hyaluronidase-fihj (DARZALEX FASPRO)	For adult patients with newly diagnosed or relapsed or refractory multiple myeloma. This new product allows for subcutaneous dosing of daratumumab
April 2020	
Sacituzumab govitecan-hziy (TRODELVY)	For adult patients with metastatic triple-negative breast cancer who received at least two prior therapies for metastatic disease

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TABLE A1. FDA Approvals of Anticancer Therapies (October 2019-November 2020) (continued)

New Approvals	Comments
Pemigatinib (PEMAZYRE)	For the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as detected by an FDA-approved test
Selumetinib (KOSELUGO)	For pediatric patients, 2 years of age and older, with neurofibromatosis type 1 (NF1) who have symptomatic, inoperable plexiform neurofibromas (PN)
Mitomycin (JELMYTO)	For adult patients with low-grade upper tract urothelial cancer (LG-UTUC)
January 2020	
Tazemetostat (TAZVERIK)	For adults and pediatric patients age 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection
Avapritinib (AYVAKIT)	For adults with unresectable or metastatic GI stromal tumor (GIST) harboring a platelet-derived growth factor receptor alpha (PDGFRA) exon 18 mutation, including D842V mutations
December 2019	
Fam-trastuzumab deruxtecan-nxki (ENHERTU)	For patients with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting
Enfortumab vedotin-ejfv (PADCEV)	For adult patients with locally advanced or metastatic urothelial cancer who have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor, and a platinum-containing chemotherapy in the neoadjuvant or adjuvant, locally advanced, or metastatic setting
November 2019	
Givosiran (GIVLAARI)	For adults with acute hepatic porphyria (AHP)
New uses	
October 2020	
Venetoclax (VENCLEXTA)	In combination with azacitidine, decitabine, or low-dose cytarabine (LDAC) for newly diagnosed acute myeloid leukemia (AML) in adults 75 years or older, or who have comorbidities precluding intensive induction chemotherapy
Nivolumab (OPDIVO) plus ipilimumab (YERVOY)	First-line treatment for adult patients with unresectable malignant pleural mesothelioma
August 2020	
Carfilzomib (KYPROLIS) and daratumumab (DARZALEX)	In combination with dexamethasone for adult patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy
July 2020	
Tafasitamab-cxix (MONJUVI)	A CD19-directed cytolytic antibody, indicated in combination with lenalidomide for adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified, including DLBCL arising from low-grade lymphoma, and who are not eligible for autologous stem-cell transplant
Atezolizumab (TECENTRIQ)	In combination with cobimetinib and vemurafenib for patients with *BRAF* V600 mutation–positive unresectable or metastatic melanoma
June 2020	
Pembrolizumab (KEYTRUDA)	For the first-line treatment of patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer
Pertuzumab, trastuzumab, and hyaluronidase—zzxf (PHESGO)	A new fixed-dose combination for subcutaneous injection for treatment of patients with HER2-positive early breast cancer
Pembrolizumab (KEYTRUDA)	For patients with recurrent or metastatic cutaneous squamous cell carcinoma (cSCC) that is not curable by surgery or radiation

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TABLE A1. FDA Approvals of Anticancer Therapies (October 2019-November 2020) (continued)

New Approvals	Comments
Pembrolizumab (KEYTRUDA)	For the treatment of adult and pediatric patients with unresectable or metastatic tumor mutational burden-high (TMB H) (≥ 10 mutations/megabase [mut/Mb]) solid tumors, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options
Nivolumab (OPDIVO)	For patients with unresectable advanced, recurrent, or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy
Avelumab (BAVENCIO)	For maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) that has not progressed with first-line platinum-containing chemotherapy
May 2020	
Ramucirumab (CYRAMZA)	In combination with erlotinib for first-line treatment of metastatic non–small-cell lung cancer (NSCLC) with epidermal growth factor receptor (*EGFR*) exon 19 deletions or exon 21 (L858R) mutations
Atezolizumab in combination with bevacizumab (TECENTRIQ and AVASTIN)	For patients with unresectable or metastatic hepatocellular carcinoma who have not received prior systemic therapy
Nivolumab (OPDIVO)in combination with ipilimumab (YERVOY) and 2 cycles of platinum-doublet chemotherapy	First-line treatment for patients with metastatic or recurrent non–small-cell lung cancer (NSCLC), with no epidermal growth factor receptor (*EGFR*) or anaplastic lymphoma kinase (*ALK*) genomic tumor aberrations.
Nivolumab (OPDIVO)in combination with ipilimumab (YERVOY)	First-line treatment for patients with metastatic non–small-cell lung cancer whose tumors express PD-L1 (≥ 1%), as determined by an FDA-approved test, with no epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (*ALK*) genomic tumor aberrations
Pomalidomide (POMALYST)	Expanded the indication to include treating adult patients with AIDS-related Kaposi sarcoma after failure of highly active antiretroviral therapy and Kaposi sarcoma in adult patients who are HIV-negative.
Olaparib (LYNPARZA)	Expanded the indication to include its combination with bevacizumab for first-line maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy and whose cancer is associated with homologous recombination deficiency positive status defined by either a deleterious or suspected deleterious *BRCA* mutation, and/or genomic instability
Olaparib (LYNPARZA)	For adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC), who have progressed following prior treatment with enzalutamide or abiraterone
Atezolizumab (TECENTRIQ)	For the first-line treatment of adult patients with metastatic non–small-cell lung cancer (NSCLC) whose tumors have high PD-L1 expression (PD-L1 stained ≥ 50% of tumor cells [TC ≥ 50%] or PD-L1 stained tumor-infiltrating immune cells [IC] covering ≥ 10% of the tumor area [IC ≥ 10%]), with no *EGFR* or *ALK* genomic tumor aberrations
Rucaparib (RUBRACA)	For patients with deleterious *BRCA* mutation (germline and/or somatic)–associated metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor-directed therapy and a taxane-based chemotherapy
Selpercatinib (RETEVMO)	For the following indications: adult patients with metastatic *RET* fusion–positive non–small-cell lung cancer (NSCLC); adult and pediatric patients ≥ 12 years of age with advanced or metastatic *RET*-mutant medullary thyroid cancer (MTC) who require systemic therapy; adult and pediatric patients ≥ 12 years of age with advanced or metastatic RET fusion–positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)

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TABLE A1. FDA Approvals of Anticancer Therapies (October 2019-November 2020) (continued)

New Approvals	Comments
April 2020	
Niraparib (ZEJULA)	For the maintenance treatment of adult patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy
Pembrolizumab (KEYTRUDA)	New dosing regimen of 400 mg every 6 weeks for pembrolizumab (KEYTRUDA) across all currently approved adult indications in addition to the current 200 mg every 3 weeks dosing regimen
Tucatinib (TUKYSAin combination with trastuzumab and capecitabine	For adult patients with advanced unresectable or metastatic HER2-positive breast cancer, including patients with brain metastases, who have received one or more prior anti-HER2-based regimens in the metastatic setting
Encorafenib (BRAFTOVI) in combination with cetuximab	For the treatment of adult patients with metastatic colorectal cancer (CRC) with a *BRAF* V600E mutation, detected by an FDA-approved test, after prior therapy
March 2020	
Durvalumab (IMFINZI) in combination with etoposide and either carboplatin or cisplatin	First-line treatment of patients with extensive-stage small-cell lung cancer
Nivolumab and ipilimumab (OPDIVO and YERVOY))	For patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib
Isatuximab-irfc (SARCLISA) in combination with pomalidomide and dexamethasone	For adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor
February 2020	
Neratinib (NERLYNX) in combination with capecitabine	For adult patients with advanced or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting
January 2020	
Pembrolizumab (KEYTRUDA)	For the treatment of patients with Bacillus Calmette-Guerin (BCG)-unresponsive, high-risk, nonmuscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy
December 2019	
Olaparib (LYNPARZA)	For the maintenance treatment of adult patients with deleterious or suspected deleterious germline *BRCA*-mutated (g*BRCA*m) metastatic pancreatic adenocarcinoma, as detected by an FDA-approved test, whose disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen
Atezolizumab (TECENTRIQ) in combination with paclitaxel protein-bound and carboplatin	For the first-line treatment of adult patients with metastatic nonsquamous non–small-cell lung cancer (NSCLC) with no *EGFR* or *ALK* genomic tumor aberrations
Enzalutamide (XTANDI)	For patients with metastatic castration-sensitive prostate cancer (mCSPC)
October 2019	
Niraparib (ZEJULA)	For patients with advanced ovarian, fallopian tube, or primary peritoneal cancer treated with three or more prior chemotherapy regimens and whose cancer is associated with homologous recombination deficiency (HRD)–positive status. HDR is defined by either a deleterious or suspected deleterious *BRCA* mutation, or genomic instability in patients with disease progression greater than 6 months after response to the last platinum-based chemotherapy