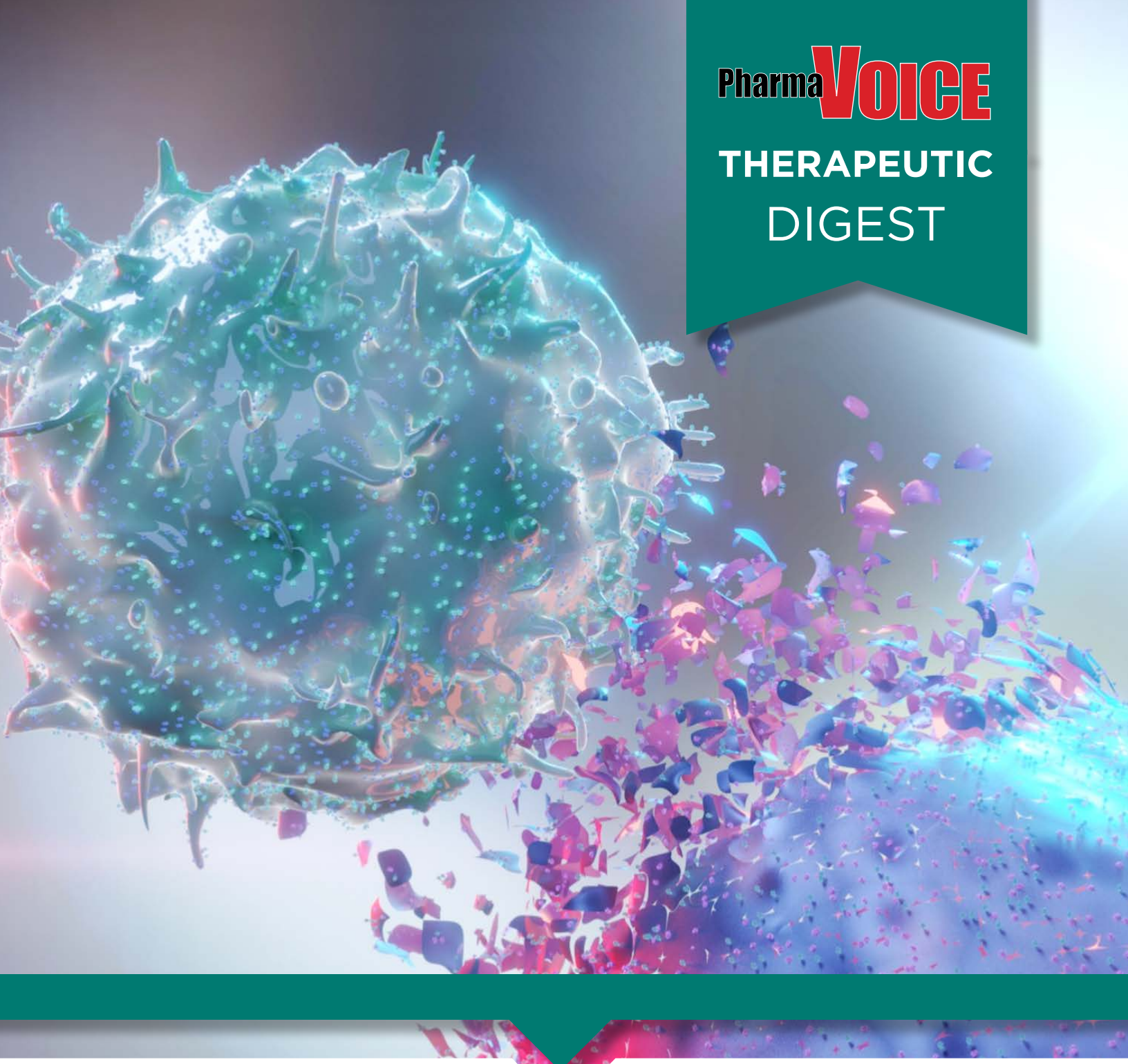

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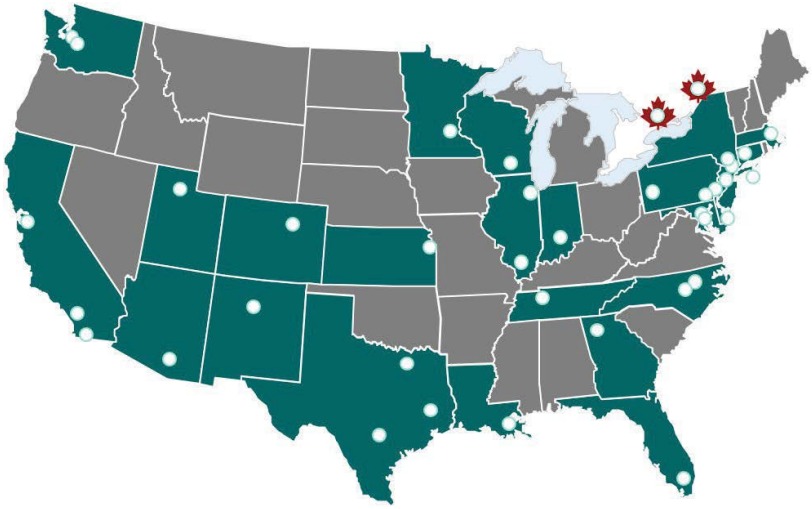

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Written by Kristina Erfe Pines

ONCOLOGY

Progress Against Cancer

2020 was filled with unexpected challenges for cancer research and patient care. As many of us shifted our lives online in the wake of the COVID-19 pandemic, cancer research was paused, clinical trials were put on hold, appointments were rescheduled, and conferences were cancelled or reformatted.

All this occurred amidst a global pandemic that has killed more than 1.9 million people worldwide, a plummeting economy with record unemployment levels, and a national reckoning with racism and racial disparities in all facets of society—including healthcare.

There were twenty-one novel oncology drugs approved by the FDA in 2020.

But there is also progress. An unprecedented level of scientific collaboration and dissemination led to rapid research advances, culminating in the authorization of three vaccines against COVID-19 within a year of the first reported COVID-19 cases. There were twenty-one novel oncology drugs approved by the FDA in 2020, including for difficult-to-treat cancers such as triple-negative breast cancer, and certain gastrointestinal stromal tumors. The first liquid biopsy next-generation sequencing tests were approved, the first in-human trial of off-the-shelf CAR-T cell therapy was launched, and the first comprehensive report on cancer disparities was released by the AACR.

Yes, 2020 was a year rife with struggles, but it wasn't without progress.

ADVANCES IN GI CANCERS

Molecular Profiling

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.

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[1].

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, epi- genetic 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-Drugs

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[2]. Standard secondary therapy consists of chemo- therapy with paclitaxel plus the monoclonal antibody ramucirumab, which acts on vascular endothelial growth factor 2, reducing blood supply to tumors[3]. 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 [4,5,6].

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[7].

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[8],

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.

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

Pembrolizumab

Approximately 5% of patients with metastatic colorectal cancer have high microsatellite instability with deficient mismatch repair (MSI-H/dMMR)[9], 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[10], first-line treatment with 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[11].

PREVENTION

Aspirin

Aspirin has been 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[12,13]. Accumulated data from observational studies and registries suggest a protective benefit associated with aspirin in patients with Lynch syndrome[14].

Twenty-year follow-up was planned as part of the CAPP2 study, 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[15]. 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.

COMBINATION THERAPIES

Tucatinib + Standard Therapy

Brain metastases have long been a challenge for patients with HER2-positive breast cancer, developing in up to half of patients[16]. These metastases progress quickly, typically within 6-12 months, due to a lack of effective treatments beyond localized therapy[17,18].

Results from the randomized, placebo-controlled HER2- CLIMB study[19], 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 com- bination with trastuzumab and capecitabine for this patient population[20].

Immunotherapy + Surgery

Triple-negative breast cancer is the most aggressive subtype of breast cancer[21]. 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[22], 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[23,24,25].

The immunotherapy drug pembrolizumab has shown promise in patients with early triple-negative disease[26]. With the phase III KEYNOTE 522 trial[27], 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.

CDK4/6 Inhibitor

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[28]. 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[29].

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[30]. 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[31].

In the phase III randomized monarchE trial[32], researchers valuated 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 endo- crine 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. These early findings are encouraging and represent the first treatment advance in 20 years in the adjuvant setting for this form of breast cancer.

Nivolumab + Ipilimumab

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[33]. 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[34], 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 + Chemotherapy

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[35]. 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[36]. Rituximab destroys both normal and malignant B cells, and although effective in treating B-cell cancers, it carries the risk of serious adverse effects[37].

Investigators conducted an open-label, randomized phase III study[38], 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.

Atezolizumab + Bevacizumab

Hepatocellular carcinoma (HCC) is the fifth most common cancer worldwide and the second leading cause of cancer-related death[39,40]. When most patients with HCC initially seek care, they have tumors that cannot be removed surgically and have a poor prognosis[41]. 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[42].

In early trials, the combination of atezolizumab and bevacizumab showed antitumor activity against inoperable HCC and adverse effects were generally tolerable[43]. Atezolizumab is a type of immunotherapy known as a PD-L1 inhibitor that helps the body's immune system attack cancer cells[44]. Bevacizumab is a vascular endothelial growth factor inhibitor that helps limit the blood supply to tumors[45].

Researchers confirmed the earlier findings of antitumor activity in the large, randomized phase III IMbrave150 trial[46], 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[47]. Inoperable HCC has been an area of great clinical need, and the approval marks the first immunotherapy combination to be approved for this cancer.

Azacitidine + Venetoclax

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[48,49]. 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[50]. Azacitidine is a drug that blocks a protein that slows down

cancer cell death[51]. Early studies had suggested that adding venetoclax (a drug that works in a similar way) to azacitidine may improve survival over other available treatments[52].

In the phase III VIALE-A trial[53], 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.

CONCLUSION

The development of additional molecularly targeted therapies and search for enhanced immunotherapy regimens are expected to permeate the oncology landscape across a broad range of malignancies as 2021 unfolds. Many of the expectations for this year grew out of the advances of 2020, in which new targeted therapies emerged for patient subsets across multiple tumor types and novel immunotherapies continued to expand.

These developments include FDA approvals for the first RET inhibitors, selpercatinib (Retevmo) and pralsetinib (Gavreto), in NSCLC and thyroid cancer settings, and a third chimeric antigen receptor (CAR) T-cell therapy for an oncology indication, brexucabtagene autoleucel (Tecartus) for mantle cell lymphoma. Continued progress in the optimal use of antibodies at immune checkpoints is anticipated. This year will mark a decade since the first checkpoint inhibitor, the anti-CTLA-4 antibody ipilimumab (Yervoy), gained FDA approval for patients with unresectable or metastatic melanoma. Since then, antibodies directed at the PD-1/PD-L1 pathway have dominated the field. The research findings of 2021 are expected to shed light on how best to use these agents in combinations, as well as new checkpoint therapies. All in all, an optimistic year for cancer research.

NOTES

[1] Arnold M, et al. "Global burden of 5 major types of gastrointestinal cancer." Gastroenterology. 2020.

[2] Torre LA, et al. "Global cancer incidence and mortality rates and trends: an update." Cancer Epidemiology, Biomarkers & Prevention. 2016.

[3] National Comprehensive Cancer Network: Gastric cancer: clinical practice guidelines in oncology. 2019.

[4] Kang YK, et al. "Nivolumab in patients with advanced gastric or gastro-oesophageal junction cancer refractory to, or intolerant of, at least two previous chemotherapy regimens (ONO-4538-12, ATTRACTION-2): A randomized, double-blind, placebo-controlled, phase 3 trial." Lancet. 2017.

[5] Shitara K, et al. "Trifluridine/tipiracil versus placebo in patients with heavily pretreated metastatic gastric cancer (TAGS): a randomized, double-blind, placebo-controlled, phase 3 trial." Lancet Oncology. 2018.

[6] Tabernero J, et al. "Pertuzumab plus trastuzumab and chemotherapy for HER2-positive metastatic gastric or gastro-oesophageal junction cancer (JACOB): final analysis of a double-blind, randomized, placebo-controlled phase 3 study." Lancet Oncology. 2018.

[7] National Cancer Institute: NCI Drug Dictionary: fam-trastuzumab deruxtecan-nxki. Cancer.gov

[8] Shitara K, et al. "Trastuzumab deruxtecan in previously treated HER2-positive gastric cancer. New England Journal of Medicine. 2020.

[9] US Food and Drug Administration: FDA approves first-line immunotherapy for patients with MSI-H/dMMR metastatic colorectal cancer." FDA.gov

[10] Andre T, et al. "Pembrolizumab in microsatellite instability high advanced colorectal cancer." New England Journal of Medicine. 2020.

[11] US Food and Drug Administration: FDA approves first-line immunotherapy for patients with MSI-H/dMMR metastatic colorectal cancer." FDA.gov

[12] Lynch Syndrome. Cancer.net

[13] American Cancer Society: key statistics for colorectal cancer.

[14] Flossman E, Rothwell PM, "Effect of aspirin on long term risk of colorectal cancer: consistent evidence from randomized and observational studies." Lancet. 2007.

[15] Burn J, et al. "Cancer prevention with aspirin in hereditary colorectal cancer (Lynch syndrome), 10-year follow-up and registry based 20-year data in the CAPP2 study: a double-blind, randomized, placebo-controlled trial." Lancet. 2020.

[16] Leyland Jones B. "Human epidermal growth factor receptor 2-positive breast cancer and central nervous system metastases." Journal of Clinical Oncology. 2009.

[17] Mahajan A, et al. "Post-operative stereostatic radiosurgery versus observation for completely resected brain metastases: a single-centre, randomized, controlled, phase 3 trial." Lancet Oncology. 2017.

[18] Mahajan A, et al. "Post-operative stereostatic radiosurgery versus observation for completely resected brain metastases: a single-centre, randomized, controlled, phase 3 trial." Lancet Oncology. 2017.

[19] Lin NU, et al. "Intracranial efficacy and survival with tucatinib plus trastuzumab and capecitabine for previously treated HER2-positive breast cancer with brain metastases in the HER2CLIMB trial." Journal of Clinical Oncology. 2020.

[20] US Food and Drug Administration: FDA approves tucatinib for patients with HER2-positive metastatic breast cancer. 2020.

[21] US Food and Drug Administration: FDA approves tucatinib for patients with HER2-positive metastatic breast cancer. 2020.

[22] American Cancer Society: survival rates for triple-negative breast.

[23] Cortazar P, et al. "Pathological complete response and long-term clinical benefit in breast cancer: The CTNeoBC pooled analysis." Lancet. 2014.

[24] Huang M, et al. "Evaluation of pathological complete response as a trial-level surrogate for long-term survival outcomes among triple-negative breast cancer patients receiving neoadjuvant therapy." ESMO Breast Cancer. 2019.

[25] US Food and Drug Administration: guidance for industry: pathological complete response in neoadjuvant treatment of high-risk early-stage breast cancer. 2014.

[26] Schmid P, et al. "Pembrolizumab (pembro) + chemotherapy (chemo) as neoadjuvant treatment for triple negative breast cancer (TNBC): preliminary results from KEYNOTE-173." Journal of Clinical Oncology. 2017.

[27] Schmid P, et al. "Pembrolizumab for early triple-negative breast cancer." New England Journal of Medicine. 2020.
[28] Howlader N, et al. "US incidence of breast cancer subtypes defined by joint hormone receptor and HER2 status." Journal of the National Cancer Institute. 2014.
[29] American Cancer Society: breast cancer facts and figures. 2019-2020.
[30] Sledge GW, et al. "MONARCH 2: Abemaciclib in combination with fulvestrant in women with HR1-HER2-advanced breast cancer who had progressed while receiving endocrine therapy." Journal of Clinical Oncology. 2017.
[31] US Food and Drug Administration: FDA approves abemaciclib as initial therapy for HR-positive, HER2-negative metastatic breast cancer. 2018.
[32] Johnston SRD, et al. "Abemarciclib combined with endocrine therapy for the adjuvant treatment of HR1, HER22, node-positive, high-risk, early breast cancer (MONARCHe). Journal of Clinical Oncology. 2020.
[33] Hellman MD, et al. "Nivolumab plus ipilimumab as first-line treatment for advanced nonsmall cell lung cancer." Lancet Oncology. 2017.
[34] Hellman MD, et al. "Nivolumab plus ipilimumab in advanced non-small-cell lung cancer." New England Journal of Medicine. 2019.
[35] Minard-Colin V, et al. "Progress through effective collaboration, current knowledge, and challenges ahead." Journal of Clinical Oncology. 2016.
[36] Minard-Colin V, et al. "Results of the randomized intergroup trial inter-b-NHL ritux 2010 for children and adolescents with high-risk B-cell non-Hodgkins lymphoma (B-NHL) and mature acute leukemia (B-AL): evaluation of rituximab efficacy in addition to standard LMB chemotherapy (CT) regimen." Journal of Clinical Oncology. 2016.
[37] Havelange V, et al. "Genetic differences between pediatric and adult Burkitt lymphomas." British Journal of Haemotology. 2016.
[38] Minard-Colin V, et al. "Rituximab for high-risk, mature B-cell non-Hodgkin's lymphoma in children." New England Journal of Medicine. 2020.
[39] Bray F, et al. "Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries." A Cancer Journal for Clinicians. 2018.
[40] Petrick JL, et al. "Future of hepatocellular carcinoma incidence in the United States forecast through 2030." Journal of Clinical Oncology. 2016.
[41] Lau WY, et al. "Preoperative systemic chemoimmunotherapy and sequential resection for unsresectable hepatocellular carcinoma." Annals of Surgery. 2001.
[42] Zhou K, Fountzilas C. "Outcomes and quality of life of systemic therapy in advanced hepatocellular carcinoma." Cancers. 2019.
[43] Lee MS, et al. "Randomized efficacy and safety results for atezolizumab (ATEZO) + bevacizumab (BEV) in patients with previously untreated, unresectable hepatocellular carcinoma (HCC). Annals of Oncology. 2019.
[44] National Cancer Institute: dictionary of cancer terms.
[45] National Cancer Institute: angiogenesis inhibitors.
[46] Finn RS, et al. "Atezolizumab plus bevacizumab in unresectable hepatocellular carcinoma." New England Journal of medicine. 2020.
[47] US Food and Drug Administration. "FDA approves atezolizumab plus bevacizumab for unresectable hepatocellular carcinoma.
[48] Howlader N, et al. "SEER cancer statistics review, 1975-2016." National Cancer Institute. 2019.
[49] Song X, et al. "Incidence, survival, and risk factors for adults with acute myeloid leukemia not otherwise specified and acute myeloid leukemia with recurrent genetic abnormalities." Acta Haemotolgica. 2018.
[50] Dohner H, et al. "Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. Blood. 2017.
[51] Mehta SV, et al. "Overexpression of BcI2 protein predicts chemoresistance in acute myeloid leukemia: its correlation with FLT3." Neoplasma 60. 2013.
[52] DiNardo CD, et al. "Safety and preliminary efficacy of venetoclax with decitabine or azacytidine in elderly patients with previously untreated acute myeloid leukemia: a non-randomized, open-label, phase 1b study." Lancet Oncology. 2018.
[53] DiNardo CD, et al. "Azacitidine and venetoclax in previously untreated acute myeloid leukemia." New England Journal of Medicine. 2020.

RESOURCES

Andre T, et al. "Pembrolizumab in microsatellite instability high advanced colorectal cancer." New England Journal of Medicine. 2020.

Arnold M, et al. "Global burden of 5 major types of gastrointestinal cancer." Gastroenterology. 2020.

Bray F, et al. "Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries." A Cancer Journal for Clinicians. 2018.

Burn J, et al. "Cancer prevention with aspirin in hereditary colorectal cancer (Lynch syndrome), 10-year follow-up and registry based 20-year data in the CAPP2 study: a double-blind, randomized, placebo-controlled trial." Lancet. 2020.

Cortazar P, et al. "Pathological complete response and long-term clinical benefit in breast cancer: The CTNeoBC pooled analysis." Lancet. 2014.

Finn RS, et al. "Atezolizumab plus bevacizumab in unresectable hepatocellular carcinoma." New England Journal of medicine. 2020.

Flossman E, Rothwell PM, "Effect of aspirin on long term risk of colorectal cancer: consistent evidence from randomized and observational studies." Lancet. 2007.

Havelange V, et al. "Genetic differences between pediatric and adult Burkitt lymphomas." British Journal of Haemotology. 2016.

Hellman MD, et al. "Nivolumab plus ipilimumab as first-line treatment for advanced nonsmall cell lung cancer." Lancet Oncology. 2017.

Hellman MD, et al. "Nivolumab plus ipilimumab in advanced non-small-cell lung cancer." New England Journal of Medicine. 2019.

Howlader N, et al. "US incidence of breast cancer subtypes defined by joint hormone receptor and HER2 status." Journal of the National Cancer Institute. 2014.

Huang M, et al. "Evaluation of pathological complete response as a trial-level surrogate for long-term survival outcomes among triple-negative breast cancer patients receiving neoadjuvant therapy." ESMO Breast Cancer. 2019.

Johnston SRD, et al. "Abemarciclib combined with endocrine therapy for the adjuvant treatment of HR1, HER22, node-positive, high-risk, early breast cancer (MONARCHe). Journal of Clinical Oncology. 2020.

Kang YK, et al. "Nivolumab in patients with advanced gastric or gastro-oesophageal junction cancer refractory to, or intolerant of, at least two previous chemotherapy regimens (ONO-4538-12, ATTRACTION-2): A randomized, double-blind, placebo-controlled, phase 3 trial." Lancet. 2017.

Lau WY, et al. "Preoperative systemic chemoimmunotherapy and sequential resection for unsresectable hepatocellular carcinoma." Annals of Surgery. 2001.

Lee MS, et al. "Randomized efficacy and safety results for atezolizumab (ATEZO) + bevacizumab (BEV) in patients with previously untreated, unresectable hepatocellular carcinoma (HCC). Annals of Oncology. 2019.

Leyland Jones B. "Human epidermal growth factor receptor 2-positive breast cancer and central nervous system metastases." Journal of Clinical Oncology. 2009.

Lin NU, et al. "Intracranial efficacy and survival with tucatinib plus trastuzumab and capecitabine for previously treated HER2-positive breast cancer with brain metastases in the HER2CLIMB trial." Journal of Clinical Oncology. 2020.

Mahajan A, et al. "Post-operative stereostatic radiosurgery versus observation for completely resected brain metastases:

a single-centre, randomized, controlled, phase 3 trial." Lancet Oncology. 2017.

Markham M, et al. "Clinical cancer advances 2020: annual report on progress against cancer from the American Society of Clinical Oncology." 2020.

Minard-Colin V, et al. "Progress through effective collaboration, current knowledge, and challenges ahead." Journal of Clinical Oncology. 2016.

Minard-Colin V, et al. "Results of the randomized intergroup trial inter-b-NHL ritux 2010 for children and adolescents with high-risk B-cell non-Hodgkins lymphoma (B-NHL) and mature acute leukemia (B-AL): evaluation of rituximab efficacy in addition to standard LMB chemotherapy (CT) regimen." Journal of Clinical Oncology. 2016.

Minard-Colin V, et al. "Rituximab for high-risk, mature B-cell non-Hodgkin's lymphoma in children." New England Journal of Medicine. 2020.

"More innovation is on tap for 2021." OncologyLive. 2021.

National Comprehensive Cancer Network: Gastric cancer: clinical practice guidelines in oncology. 2019.

Pancholi N. "Experts forecast cancer research and treatment advances in 2021." American Association for Cancer Research. 2021.

Petrick JL, et al. "Future of hepatocellular carcinoma incidence in the United States forecast through 2030." Journal of Clinical Oncology. 2016.

Scherer L. "Cancer News Digest: The latest developments in cancer research and treatment for February 2021." Everyday Health. 2021.

Schmid P, et al. "Pembrolizumab (pembro) + chemotherapy (chemo) as neoadjuvant treatment for triple negative breast cancer (TNBC): preliminary results from KEYNOTE-173." Journal of Clinical Oncology. 2017.

Schmid P, et al. "Pembrolizumab for early triple-negative breast cancer." New England Journal of Medicine. 2020.

Shitara K, et al. "Trifluridine/tipiracil versus placebo in patients with heavily pretreated metastatic gastric cancer (TAGS): a randomized, double-blind, placebo-controlled, phase 3 trial." Lancet Oncology. 2018.

Shitara K, et al. "Trastuzumab deruxtecan in previously treated HER2-positive gastric cancer. New England Journal of Medicine. 2020.

Sledge GW, et al. "MONARCH 2: Abemaciclib in combination with fulvestrant in women with HR1-HER2- advanced breast cancer who had progressed while receiving endocrine therapy." Journal of Clinical Oncology. 2017.

Smith S, et al. "Clinical Cancer Advances 2021: ASCO's report on progress against cancer." Journal of Clinical Oncology. 2021.

Tabernero J, et al. "Pertuzumab plus trastuzumab and chemotherapy for HER2-positive metastatic gastric or gastro-oesophageal junction cancer (JACOB): final analysis of a double-blind, randomized, placebo-controlled phase 3 study." Lancet Oncology. 2018.

Torre LA, et al. "Global cancer incidence and mortality rates and trends: an update." Cancer Epidemiology, Biomarkers & Prevention. 2016.

"Year in review: five important clinical advances in cancer in 2020." Memorial Sloan Kettering Cancer Center. 2020.

Zhou K, Fountzilas C. "Outcomes and quality of life of systemic therapy in advanced hepatocellular carcinoma." Cancers. 2019.

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THERAPEUTIC DIGESTS

2021 THERAPEUTIC TOPICS:

Diabetes

Digital Therapeutics

Endocrinology

Vaccines

Cardiology

Oncology

Dermatology

Inflammatory Diseases

Rare Disorders

Neurology

Infectious Disease

Pulmonology