Oncology Update

Winter 2021

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Mary Lanning HEALTHCARE
Morrison Cancer Center

A quarterly newsletter from Mary Lanning Healthcare's Morrison Cancer Center
Local and national cancer authority
The definition of excellence in a comprehensive, academic, community cancer program.

Happy New Year and ninth year of the Oncology Update

This issue

Dear colleagues,
January 2021 marks the nine-year anniversary of the launch of our Oncology Update newsletter! It is hard to believe that we are approaching a decade of publication. I would like to thank all our loyal readers and referring healthcare providers. Your support and feedback have been instrumental in keeping the newsletter going. This year has certainly been challenging due to the COVID-19 pandemic.

Morrison Cancer Center has been on the frontline, fighting non-stop against cancer despite the pandemic. 2020 was another giant year for our cancer program with several landmark accomplishments, ranging from expanding our patient referral base and acquiring new staff members, to publication in numerous national journals, public education through local and national media, partaking in ASCO initiatives and participating in the NCI-designated Buffet Cancer Center Community Outreach program. The year 2020 shows the indisputable performance of the Morrison Cancer Center, a local and national cancer authority.

Cancer care continuum is a team effort that starts with you, our distinguished referring providers. The goal of the newsletter is to keep in touch and communicate quarterly happenings in the hematology/oncology world, highlight advancements, share MCC accomplishments and advances in your individual practices. Let us know of any stories you would like included by emailing mehmet.copur@marylanning.org. We would love to hear from you.

Cheers to a healthy, happy, prosperous new year full of meaningful accomplishments.

Cordially,

Mehmet Sitki Copur, MD FACP
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New employees, changes at MCC

New Director named in November

David Jones accepted the position of the Morrison Cancer Center Director in November.

Jones has 24 years of radiation therapy/ oncology experience.

He most recently was the Service Leader for the Radiation Oncology & Gamma Knife Center at Nebraska Methodist Hospital in Omaha.

Jones holds a Bachelor of Science Degree in Radiation Therapy from Methodist College in Omaha, as well as an Associate's Degree in Radiologic Technology.

PA-C joins MCC oncology provider staff

Anne Roberts, PA-C, will begin seeing patients in January as part of the Morrison Cancer Center medical oncology team.

Roberts is a Grand Island native who has worked in healthcare since 1997. She received her Bachelor of Science Degree in Business Development from Bellevue University in 2003. After several years working in lab and radiology departments, she pursued a path as a physician assistant. She graduated with a Master's Degree in Physician Assistant studies from Union College in Lincoln in 2008. She has worked in the areas of pain management, women's health, urgent care, family practice, emergency and dermatology.

"As an experienced physician assistant, I want a position where I can care for patients with skill and compassion. The Morrison Cancer Center is the place where I hope to accomplish this goal," Roberts said.

Social worker and nurse join staff

Stephanie Earl, CSW, (left) and Wendy League, RN (right) recently joined the MCC family.

Earl received her Social Work Degree from the University of Nebraska at Kearney. She worked at AseraCare hospice for seven years.

"When a person is diagnosed with cancer, it seems everyone is focused, and rightly so, on that person's physical wellbeing, treatments, side effects, doctor's visits, tests. But we know there are other parts of life affected by cancer: self-image, work, family, friendships and the approach to living. As an oncology social worker, I understand these complex issues and look for ways to help patients cope. My goal is to help patients and bring a sense of relief to the patient and their loved ones."

League graduated from Central Community College with a Nursing Degree. She worked as a nurse manager at Convenience Care.

"Oncology nursing is a great career for those who enjoy ongoing relationships with patients and their families. There is a special bond when you get to care for someone during their first treatment, then work with them during their entire cancer journey. Knowing the patient helps me give better care. I am excited to be part of the MCC family.

Dr. M. Sitki Copur named Medical Director at MCC

Dr. M. Sitki Copur became MCC's Medical Director of Oncology on November 1. He serves as the professional head of the oncology program, working with physicians, providers, administrators and management in directing goals for the program.

"It is a great privilege and honor to serve with so many talented and distinguished people at MCC," Dr. Copur said. "MCC has become a local and national cancer authority. My goal is to continue building and providing exemplary academic/community-based cancer care — an unmet need for central Nebraska."

Patient gives back with painting gift

MCC patient Joyce Nelson recently presented the MCC staff with a special gift.

Since her diagnosis with metastatic breast cancer, Nelson had been unable to pursue her hobby of painting. After a year battling the disease and beating it down to complete clinical remission, Nelson's first painting was these amaryllis flowers. The real flowers, located at MCC, were an inspiration to her during her treatments.

Nelson's painting is now on display at MCC in honor of her fight, and victory, against breast cancer.

Right: Cancer patient Joyce Nelson and Dr. M. Sitki Copur are pictured with Nelson's painting.

October fun

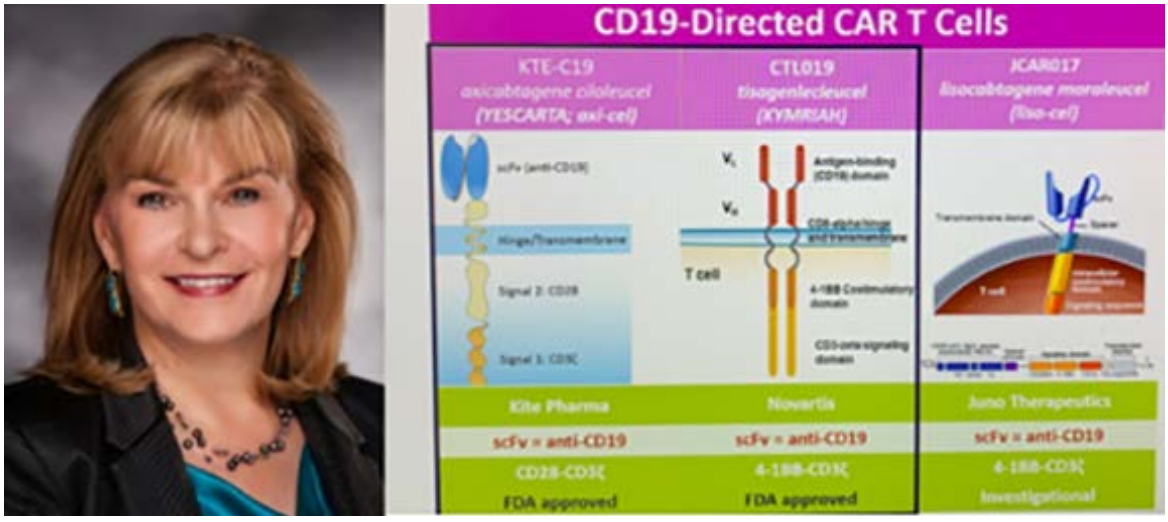
The Morrison Cancer Center staff decked out as grandmas in curlers for Halloween this year.

Special 'Ask the Expert' deals with COVID-19

As our world has come to grips with the coronavirus, other important medical care has sometimes been deprioritized, delayed or discontinued. Cancer communities all across the country have been forced to deal with shifting and conflicting directions from the government, public health officials and professional societies who were blindsided by the pandemic. Knowing what we have learned, it is clear that a diagnosis of active cancer or recent anticancer therapy do not predict worse outcomes for those with COVID-19 infections.

Patients with cancer, but limited comorbidities, can continue their treatments safely. This is important practice-changing information. Dr. Copur shared a special `Ask the Expert' radio talk on November 20 to talk about COVID-19 and cancer. To listen to the talk, please access it via the Mary Lanning web page:

www.marylanning.org/our-services/cancer-care/in-the-news/



Dr. Vose gives grand rounds at MCC

Julie Vose, MD MBA, was the speaker for a CME Grand Rounds about CAR-T cell therapy on December 1.

The event at MCC, in collaboration with the University of Nebraska Medical Center, featured Vose, a Neumann M. and Mildred E. Harris Professor and Cheif in the UNMC Oncology/Hematology Division. She talked about CAR-T cell treatment options available in Nebraska.

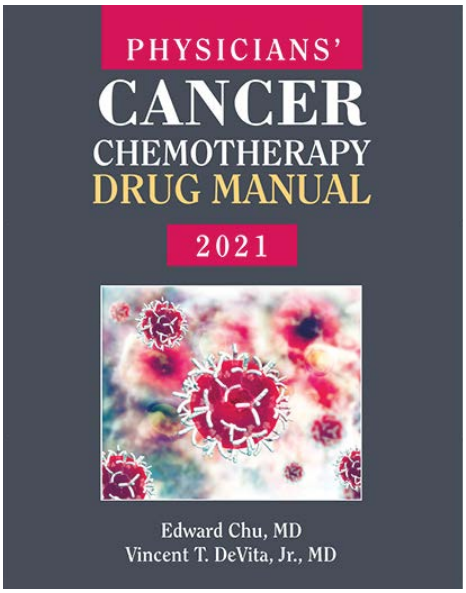
MCC and UNMC continue to be proud to work together,

MCC contributes to popular oncology textbook

The Morrison Cancer Center is listed as a contributing institution in the national/international oncology text, "The Physicians' Chemotherapy Drug Manual."

Written by world-clas experts in clinical cancer therapeutics, this reference textbook provides powerful, complete, user-friendly and up-to-date information on cancer treatment.

Dr. M. Sitki Copur has been among the contributing authors since the book's inception in 2000.



New 'Ask the Expert' topics posted

The KHAS radio "Ask the Expert" segments for October, November and December can be found on the Mary Lanning website.

Topics for the quarter include a Breast Cancer Update for October Breast Cancer Awareness Month, Myelodysplastic Syndromes for November and Hepatocellular Cancer for December. The interviews are broadcast on the first Wednesday and third Friday of each month on KHAS (1230 AM) radio.

www.marylanning.org/our-services/cancer-care/in-the-news/

Publications since our last issue

• **Copur, M.S., Lackner R., Rodriguez P., Horn A., Faris S., Zusag T.** Recurrent EGFR-Mutated Non–Small Cell Lung Cancer Discovered by Abnormal Mammogram:Adjuvant/Frontline Metastatic Management Options. Oncology (Williston Park). 2020; 34:9 **(Published)**

• **Adam Horn, MD; Lisa McCormick, MT(ASCP); Whitney Wedel, MD; Nick Lintel, MD; Mehmet S. Copur, MD; Shari Fiala, CTR; Sally Molnar, MBA, BS, RT(R)(M).** Consolidating Molecular Pathology Data: A Low-Cost Composite Report Prototype. **(Published)**

• **Dianna Uhrich, HT(ASCP); Terri Brown, MHA, MT(ASCP), LSSGB; Whitney Wedel, MD; Nick Lintel, MD; Adam Horn**, MD Progressive Reduc-tion of Surgical Pathology Turnaround Time in a Community Setting: A Multi-Modal Approach. **(Published)**

• Chu E, Harrold LJ, **Copur, M.S.** Chemotherapeutic and Biologic Drugs. In: Physicians Cancer Chemotherapy Drug Manual. Chu E, De Vita ed. 2021. **(Published)**

• Harrold LJ, **Copur, M.S.**, Chu E. Guidelines for Chemotherapy and Dosing Modifications. In: Physicians Cancer Chemotherapy Drug Manual. Chu E, DeVita ed.2012. **(Published)**

• **Copur, M.S.**, Harrold LJ, Chu E. Common Chemotherapy Regimens in Clinical Practice. In: Physicians Cancer Chemotherapy Drug Manual. Chu E, De Vita ed.2021. **(Published)**

• Maguire W, **Copur, M.S.**, Harrold LJ, Chu E. Antiemetic Agents for the treatment of Chemotherapy-Induced Nausea and Vomiting. In: Physicians Cancer Chemotherapy Drug Manual. Chu E, DeV ita ed. 2012. **(Published)**

• **Copur M.S.,** Vargas L, Merani S, wedel W, Cushman AV, Drincic A. Pancreatic Neuroendocrine Tumor with Humoral Hypercalcemia, and High Tumor PD-L1 Score. Oncology (Williston Park). 2020; 34:10 **(Published)**

• **Copur M.S., Bell S., Rodriguez P., Zusag T., Wedel W., Allen J.** A 65-Year-Old Man with Back Pain and Imaging Findings of Spinal Cord Compression Oncology (Williston Park). 2020; 34:10 **(Submitted for publication)**

MCC shines with CoC survey

Mary Lanning Healthcare and Morrison Cancer Center staff hear about the three-year accreditation given to MCC by the Commisson on Cancer of the American College of Surgeons.

The Morrison Cancer Center has been granted three-year accreditation with Gold Level Commendation from the Commission on Cancer of the American College of Surgeons.

To earn CoC accreditation, a cancer program must meet or exceed 34 CoC quality care standards, be evaluated every three years through a survey and maintain levels of excellence in the delivery of comprehensive patient-centered care. The Morrison Cancer Center is one of the top 5% cancer programs in the nation to receive this recognition in 2020.

MCC was first accredited by the CoC in 1990, and has received commendations every three years since.

This year's surveyor commented: "This is really a great rurual hospital program that has maximized its reach in oncology with great collaboration with the University of Nebraska. I think they have a winning team and are well suited for meeting the challenges of the evolving 2020 standards in their program."

As a CoC-accredited cancer center, the Morrison Cancer Center takes a multidisciplinary approach to treating cancer as a complex group of diseases that requires consultation among surgeons, medical and radiation oncologists, diagnostic radiologists, pathologists and other cancer specialists. This multidisciplinary partnership results in comprehensive patient care.

The Morrison Cancer Center maintains a cancer registry and contributes data to the National Cancer Data Base (NCDB), the largest clinical disease registry in the world. Data on all types of cancer are tracked and analyzed through the NCDB and used to explore trends in cancer care.

Effects of Tranexamic Acid Prophylaxis on bleeding outcomes in hematologic malignancy: The a-TREAT Trial

Despite optimal prophylactic platelet transfusion therapy for severe thrombocytopenia in patients undergoing treatment for hematologic malignancy, WHO Grade 2 or greater bleeding continues to occur at rates of 43% to 70%.

Evidence in therapy-induced thrombocytopenia in hematologic malignancy is lacking. In a double blind placebo controlled randomized clinical trial, patients undergoing treatment for hematologic malignancy at 3 US academic medical centers with hematologic malignancy were enrolled.

Patients received study drug intravenously (1,000mg Tranexamic Acid or saline) or orally (1300mg TXA or placebo) every 8 hours beginning when the platelet count was ≤30,000/μL and continued until platelet count recovery >30,000/ul or if a diagnosis of thrombosis was made. Patients were transfused prophylactically for counts of ≤10,000/μL or if indicated in the judgement of the treating physician.

The primary endpoint was the proportion of patients with bleeding of WHO grade 2 or above over 30 days after activation of study drug. 330 patients were evaluable; 327 received at least one dose of study drug.

The average number of days with thrombocytopenia or bleeding was similar across treatment arms (9.2 [SD=6.7] Tranexamic Acid vs. 9.1 [6.2] placebo). The hazard ratio of time to grade 2+ bleeding or death was 0.96 (95% CI: 0.43, 2.16; p-value=0.92). An increased incidence of line occlusion in the TXA arm was observed but no increase in other types of thrombotic events was detected.

Reference: Gernsheimer TB, Brown SP, Triulzi DJ et al. Effects of Tranexamic Acid Prophylaxis on Bleeding Outcomes in Hematologic Malignancy: The a-TREAT Trial. ASH meeting. Blood 2020 Abstract 2.

Pembrolizumab in microsatellite-instability–high advanced colorectal cancer

Programmed death 1 (PD-1) blockade has clinical benefit in microsatellite-instability–high (MSI-H) or mismatch-repair–deficient (dMMR) tumors after previous therapy.

The efficacy of PD-1 blockade as compared with chemotherapy as first-line therapy for MSI-H–dMMR advanced or metastatic colorectal cancer is unknown. In this phase 3, open-label trial, 307 patients with metastatic MSI-H–dMMR colorectal cancer who had not previously received treatment were randomly assigned, in a 1:1 ratio, to receive pembrolizumab at a dose of 200 mg every 3 weeks or chemotherapy (5-fluorouracil–based therapy with or without bevacizumab or cetuximab) every 2 weeks. Patients receiving chemotherapy could cross over to pembrolizumab therapy after disease progression.

The two primary end points were progression-free survival and overall survival. At the second interim analysis, after a median follow-up (from randomization to data cutoff) of 32.4 months (range, 24.0 to 48.3), pembrolizumab was superior to chemotherapy with respect to progression-free survival (median, 16.5 vs. 8.2 months; hazard ratio, 0.60; 95% confidence interval [CI], 0.45 to 0.80; P=0.0002). The estimated mean survival after 24 months of follow-up was 13.7 months (range, 12.0 to 15.4) as compared with 10.8 months (range, 9.4 to 12.2). An overall response (complete or partial response), as evaluated with Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1, was observed in 43.8% of the patients in the pembrolizumab group and 33.1% in the chemotherapy group. Among patients with an overall response, 83% in the pembrolizumab group, as compared with 35% of patients in the chemotherapy group, had ongoing responses at 24 months.

Pembrolizumab led to significantly longer progression-free survival than chemotherapy when received as first-line therapy for MSI-H–dMMR metastatic colorectal cancer, with fewer treatment-related adverse events.

Reference: Andre T, Shiu KK, Kim TW et al. Pembrolizumab in Microsatellite-Instability–High Advanced Colorectal Cancer. N Engl J Med 2020; 383:2207-2218

Potentially Practice Changing DATA

A multi-center biologic assignment trial comparing reduced intensity allogeneic hematopoietic cell transplantation to hypomethylating therapy or best supportive care in patients age 50-75 with Advanced Myelodysplastic Syndrome: blood and marrow transplant clinical trials network study 1102

Allogeneic hematopoietic cell transplantation, widely used in younger MDS patients and is the only curative therapy for MDS.

While transplantation outcomes among selected older patients with MDS are similar to younger patients with MDS, early transplantation for older patients is infrequently offered. In a multicenter, biologic assignment trial, outcomes of the subjects aged 50-75 with higher risk de novo MDS (IPSS Intermediate-2 (Int-2) or High) who were candidates for reduced-intensity conditioning (RIC) allogeneic HCT, were compared with the outcomes of those with a suitable 8/8 HLA-matched donor to those without a donor.

The primary analysis compared three-year overall survival (OS) between arms using adjusted survival estimates to account for the potential bias resulting from biological assignment. 384 subjects (Donor n=260, No Donor n=124) were enrolled at 34 centers. The study arms were well balanced for age, gender, KPS, IPSS risk, MDS disease duration and responsiveness to hypomethylating therapy (Table).

The median follow-up time for surviving patients was 34.2 months (range: 2.3-38 months) in the Donor arm and 26.9 months (range: 2.4-37.2 months) in the No Donor arm. In an intent-to-treat analysis, adjusted OS at 3 years from study enrollment in the Donor arm was 47.9% (95% CI: 41.3%-54.1%) compared with 26.6% (95% CI: 18.4%-35.6%) in the No Donor arm (p=0.0001, absolute difference 21.3%, 95% CI: 10.2%-31.8%). Leukemia-free survival (LFS) at 3 years was greater in the Donor arm (35.8%, 95% CI: 29.8%-41.8%) compared with the No Donor arm (20.6%, 95% CI: 13.3%-29.1%, p=0.003), with no changes in the sensitivity analysis.

An OS and LFS benefit was seen across all subgroups tested (Figure). No clinically significant differences in QOL between Donor and No Donor arms as measured.

A significant OS advantage was observed in older patients with Int-2 and High IPSS risk de novo MDS who are RIC HCT candidates and have an HLA-matched donor, when compared with those without a donor. Hematopoietic cell transplantation should be offered to all individuals between the ages of 50-75 with Int-2 and High IPSS risk MDS in whom a suitable donor can be identified.

Reference: Nakamura R, Saber W, Martens MJ et al. Multi-Center Biologic Assignment Trial Comparing Reduced Intensity Allogeneic Hematopoietic Cell Transplantation to Hypomethylating Therapy or Best Supportive Care in Patients Aged 50-75 with Advanced Myelodysplastic Syndrome: Blood and Marrow Transplant Clinical Trials Network Study 1102. ASH meeting Blood 2020 Abstract 75

SWOG S1007: Adjuvant trial of randomized ER+ patients who had a Recurrence Score < 25 and 1-3 positive nodes to endocrine therapy (ET) versus ET + chemotherapy

The SWOG S1007-The RxPONDER trial screened 9,383 women with HR-positive, HER2-negative breast cancer and one to three positive lymph nodes to identify those with recurrence scores of 25 or less.

A total of 5,083 such patients were randomly assigned to receive hormone therapy alone or hormone therapy plus intravenous chemotherapy with taxane and/or anthracyclines. Two-thirds of the women in the trial were postmenopausal, and data from 5,015 eligible randomized patients were used in the analysis.

Primary and secondary end points were invasive disease free survival, and overall survival. After a median follow up of 5 years, among postmenopausal women the five-year invasive disease free survival rate was 91.6% for the chemotherapy plus hormone therapy group and 91.9% for the hormone therapy only group. Among premenopausal women the five-year invasive disease free survival rate was 94.2% for the chemotherapy and hormone therapy group compared to 89.0% for the hormone therapy-only group.

This benefit was seen regardless of recurrence score. Premenopausal women also appeared to experience an overall survival benefit at five years, the overall survival rate was 98.6% for those receiving chemotherapy plus hormone therapy and 97.3% for women in the hormone therapy-only group.

Reference: Kalinsky, K. et al. Oral Presentation: [GS3-00]. San Antonio Breast Cancer Symposium; December 2020.

Abemaciclib combined with endocrine therapy for the adjuvant treatment of HR+, HER2–, node-positive, high-risk, early breast cancer (monarchE)

Many patients with HR+, HER2– early breast cancer (EBC) will not experience recurrence or have distant recurrence with currently available standard therapies. However, up to 30% of patients with high-risk clinical and/or pathologic features may experience distant recurrence, many in the first few years. Superior treatment options are needed to prevent early recurrence and development of metastases for this group of patients.

Abemaciclib is an oral, continuously dosed, CDK4/6 inhibitor approved for HR+, HER2– advanced breast cancer (ABC). This open-label, phase III study included patients with HR+, HER2–, high-risk EBC, who had surgery and, as indicated, radiotherapy and/or adjuvant/neoadjuvant chemotherapy. Patients with four or more positive nodes, or one to three nodes and either tumor size ≥ 5 cm, histologic grade 3, or central Ki-67 ≥ 20%, were eligible and randomly assigned (1:1) to standard-of-care adjuvant endocrine therapy (ET) with or without abemaciclib (150 mg twice daily for 2 years).

The primary end point was invasive disease-free survival (IDFS), and secondary end points included distant relapse–free survival, overall survival, and safety. At a preplanned efficacy interim analysis, among 5,637 randomly assigned patients, 323 IDFS events were observed in the intent-to-treat population.

Abemaciclib plus ET demonstrated superior IDFS versus ET alone (P = .01; hazard ratio, 0.75; 95% CI, 0.60 to 0.93), with 2-year IDFS rates of 92.2% versus 88.7%, respectively. Safety data were consistent with the known safety profile of abemaciclib. Abemaciclib when combined with ET is the first CDK4/6 inhibitor to demonstrate a significant improvement in IDFS in patients with HR+, HER2– node-positive EBC at high risk of early recurrence.

Reference: Johnston SRD, Harbeck N, Hegg R, et al. Abemaciclib Combined With Endocrine Therapy for the Adjuvant Treatment of HR+, HER2–, Node-Positive, High-Risk, Early Breast Cancer (monarchE) J Clin Oncol 38:3987-3998.

FDA hematology/oncology drug approvals since last issue

• FDA approved **osimertinib** (TAGRISSO, AstraZeneca Pharmaceuticals LP) for adjuvant therapy after tumor resection in patients with non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test. **December 18, 2020**

• FDA approved the first oral gonadotropin-releasing hormone (GnRH) receptor antagonist, **relugolix**, (ORGOVYX, Myovant Sciences, Inc.) for adult patients with advanced prostate cancer. **December 18, 2020**

• FDA approved **selinexor** (XPOVIO, Karyopharm Therapeutics Inc.) in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy. **December 18, 2020**

• FDA approved **margetuximab-cmkb** (MARGENZA, MacroGenics) in combination with chemotherapy, for the treatment of adult patients with metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 regimens, at least one of which was for metastatic disease. **December 16, 2020**

• FDA approved **pralsetinib** (GAVRETO, Blueprint Medicines Corporation) for adult and pediatric patients 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy or RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate). **December 1, 2020**

• FDA approved the **Sonalleve MR-HIFU system** (Profound Medical Inc.) for the treatment of osteoid osteoma in the extremities. **November 27, 2020**

• FDA granted accelerated approval to **naxitamab** (DANYELZA, Y-mAbs Therapeutics, Inc.) in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF) for pediatric patients one year of age and older and adult patients with relapsed or refractory high-risk neuroblastoma in the bone or bone marrow demonstrating a partial response, minor response, or stable disease to prior therapy. **November 25, 2020**

• FDA granted accelerated approval to **pembrolizumab** (KEYTRUDA, Merck & Co.) in combination with chemotherapy for the treatment of patients with locally recurrent unresectable or metastatic triple-negative breast cancer (TNBC) whose tumors express PD-L1 (CPS ≥10) as determined by an FDA approved test. **November 13, 2020**

• FDA granted regular approval to **venetoclax** in combination for untreated acute myeloid leukemia. **October 16, 2020**

• FDA extended the approval of **pembrolizumab** (KEYTRUDA®, Merck Sharp & Dohme Corp.) for the following indications: adult patients with relapsed or refractory classical Hodgkin lymphoma (cHL) and pediatric patients with refractory cHL, or cHL that has relapsed after 2 or more lines of therapy. **October 14, 2020**

• FDA approved the combination of **nivolumab** (OPDIVO, Bristol-Myers Squibb Co.) plus ipilimumab (YERVOY, Bristol-Myers Squibb Co.) as first-line treatment for adult patients with unresectable malignant pleural mesothelioma. **October 2, 2020**

• FDA alerted healthcare professionals and oncology clinical investigators about efficacy and potential safety concerns with **atezolizumab** in combination with paclitaxel for treatment of breast cancer. **September 8, 2020.**

• FDA granted accelerated approval to **pralsetinib** (GAVRETO, Blueprint Medicines Corporation) for adult patients with metastatic RET fusion-positive non-small cell lung cancer (NSCLC) as detected by an FDA approved test. **September 4, 2020.**

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