Oncology Update

Fall 2021

Mary Lanning HEALTHCARE
Morrison Cancer Center

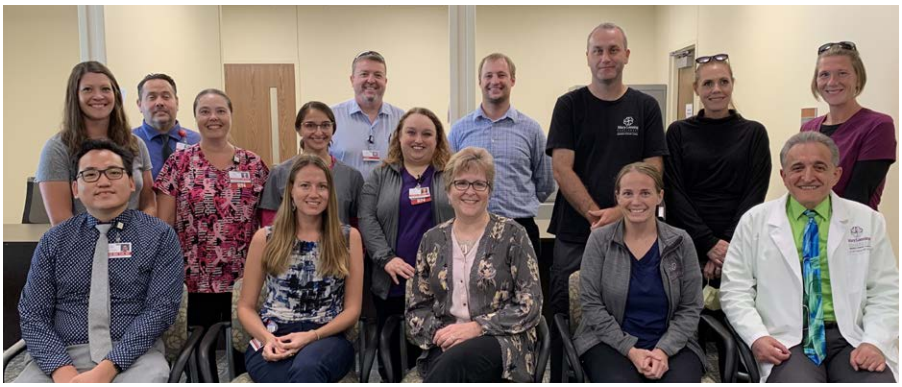
A quarterly newsletter from Mary Lanning Healthcare's Morrison Cancer Center
Local and national cancer authority
The definition of excellence in a comprehensive, academic, community cancer program.

MCC opening in Grand Island

The Morrison Cancer Center in Grand Island opened its doors to patients in late September.

An open house celebration is planned for sometime in October. Details will come soon.

M. Sitki Copur, MD FACP, Medical Director, said the new 15,000-square-foot, state-of-the-art cancer and infusion center is located on the campus of Grand Island Regional Medical Center. MCC is now providing a full spectrum of medical oncology and hematology, including outpatient/inpatient consults and follow-ups, chemotherapy, biologic therapy, immunotherapy, lab services and administration of fluids and blood products.
Radiation therapy services will open in the near future in Grand Island but are currently available at the Hastings location.



The Morrison Cancer Center team meets to officially open the new Grand Island location recently.

"With our academic, community-based approach, 24/7 seamless inpatient/outpatient, comprehensive, passionate, high-level care, we are now fulfilling a long unmet need in cancer care for the central Nebraska population," Copur said. "Our academic affiliation with NCI-designated Fred and Pamela Buffet Cancer Center and the University of Nebraska Medical Center, empowers us with the unique ability to bring academic, community-based cancer care to rural central Nebraska, where it is most needed."

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Morrison Cancer Center

M. Sitki Copur, MD FACP,
Medical Director

New hematologist/oncologist at MCC

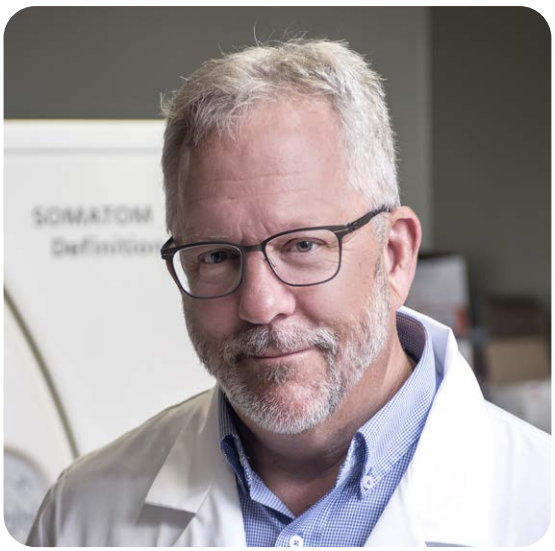
Soe Min Tun, MBBS MBA MSc, joined the Morrison Cancer Center team in July.

Dr. Tun received his Bachelor of Medicine and Bachelor of Surgery Degree at the University of Medicine 2 in Yangon, Myanmar in 2009. He completed an Internal Medicine residency at Woodhull Medical and Mental Health Center program in Brooklyn, NY. In 2021, he completed a fellowship at the University of Massachusetts Medical School - Baystate program in Springfield, Massachusetts. He is board certified in Internal Medicine.

In addition to his medical training, Dr. Tun has a Master of Business Administration Degree from the S.P. Jain School of Global Management in Singapore and a Master of Science Degree in Biomedical Engineering.

"The Morrison Cancer Center is a dream place to work as an oncologist/hematologist," Tun said. "It not only offers the best of the two worlds — i.e. academic and community-based cancer care — but also an amazing team of people with unmatched skills, experience, dedication and passion. I could not be more excited to be part of this dream team."

New radiation oncologist at MCC



Randall Duckert, MD, joins the Morrison Cancer Center team in October.

Dr. Duckert is a board-certified radiation oncologist who has been practicing for nearly 30 years. Originally from Wisconsin, he graduated from the Medical College of Wisconsin in 1988. He completed his internship at LDS Hospital and residency training at the University of Utah in 1992. Before joining the MCC team, he was affiliated with Methodist Eastbrook Cancer Center and Methodist Jennie Edmundson Hospital, where he gained extensive experience delivering brachytherapy treatments, in addition to external beam radiotherapy.

"I've had the good fortune to pursue a career in medicine which has been a calling in the truest sense," Duckert said. "It has been a privilege and responsibility. My particular technical interests are in radiosurgery and brachytherapy but I find my greatest pleasure in educating families on the science of medicine, presenting treatment options and being present with them along their way. Over the years I have seen a vast array of complicated oncologic issues, educating me along my way. I look forward to new learning at Mary Lanning Healthcare, and hope to share my experience in central Nebraska. My friends, family and colleagues, along with the great outdoors, are my greatest pleasures. I see no better guidepost than the golden rule."

New 'Ask the Expert' topics posted

The KHAS radio "Ask the Expert" segments for July, August and September can be found on the Mary Lanning website.

Topics for this quarter included radiation oncolog for July, anal cancer for August and the Covid-19 booster vaccine for September. 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/

Buffet Cancer Center CAB meeting

During its August meeting, the Fred and Pamela Buffet Cancer Center Community Advisory Board announced one-year pilot grants.

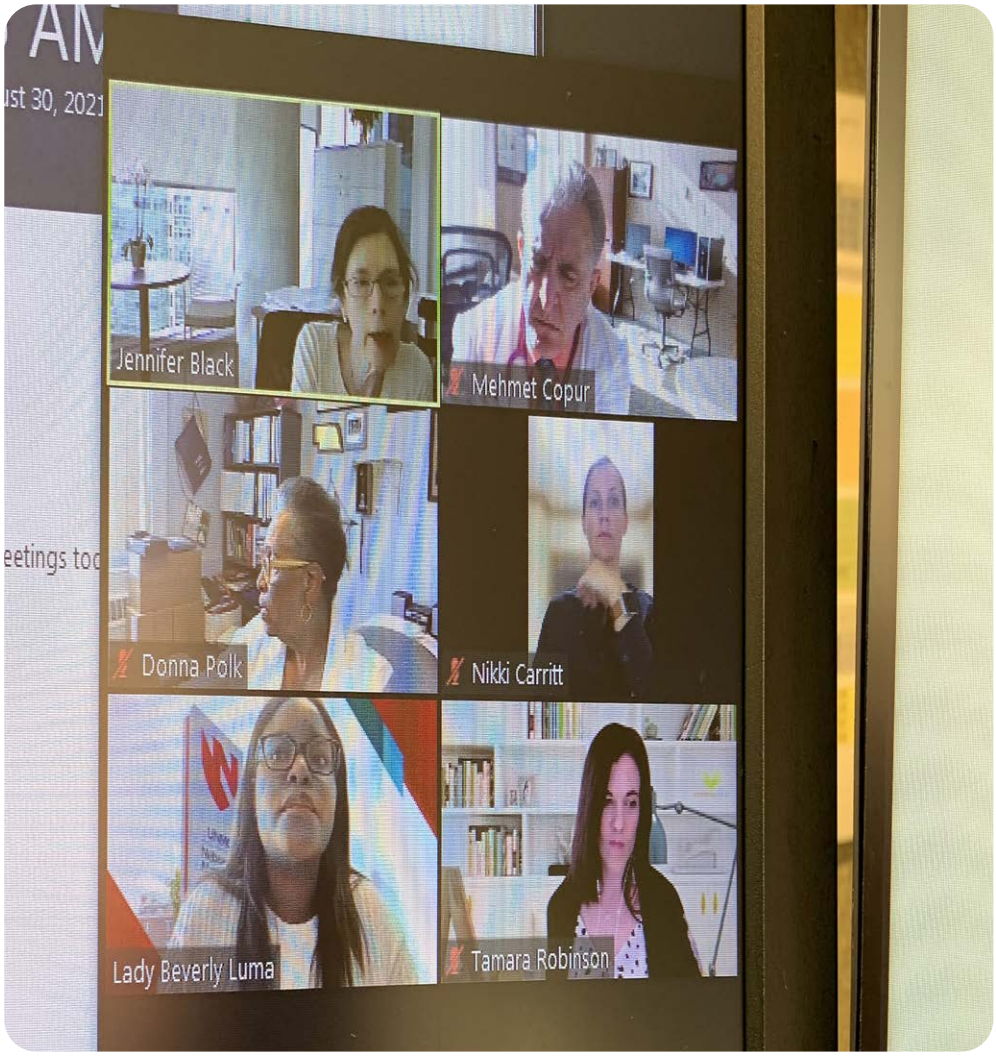
Dr. M. Sitki Copur attended the virtual, quarterly meeting.

The grants support new and existing cancer prevention and control activities conducted by a community organization.

The goal is to provide the resources needed to support vital community activities to reduce the cancer burden and eliminate cancer health disparities in Nebraska.

The Morrison Cancer Center plans to apply with two cancer prevention and control activity projects: Radon Risk Awareness for Lung Cancer Prevention and Low Dose CT Lung Cancer Screening.

The Fred and Pamela Buffet Cancer Center Community Advisory Board is made up of patient advocates, clinicians, community members and government agency representatives. The board's mission is to reduce the burden of cancer, promote health equity and eliminate cancer health disparities in Nebraska. The board works in collaboration with community, clinical and public health partners. The program aims to facilitate development and implementation of cancer research of particular relevance to Nebraska and engage diverse populations across the state.



Prominent agenda items for August included the Community Grant RFA release, presentation of the Gastrointestinal Cancer Program and Cancer Needs Assessment focus group results.

Several new employees join MCC

The following are some news employees at the Morrison Cancer Center:

Kati Brunt
Originally from Cairo, Kati received her LPN in 2015 and her RN in 2020. She worked in long-term care and hospice prior to joining MCC.

"Since coming to MCC, I feel I have found a true passion for oncology, challenging and exciting. I enjoy working with the people at MCC. Everyone is pleasant and willing to teach. The patients are wonderful, and it is a great experience to celebrate their milestones and accomplishments."

Heather Behmerwohld
Born and raised in Mason City, Heather has been a nurse for more than 20 years with experience including med/surg/ortho, labor and delivery, NICU, pediatrics, clinical, hospice and management.

"I am excited to be part of the MCC team. I love the teamwork and independence while building relationships with our patients as we support them through their journey."

Jessica Forbes
A Palmer native, Jessica previously worked in an emergency department.

"I was on the search for a workplace environment that was less stressful and more pleasant, and I found that at Morrison Cancer Center. **Cont. on page 4**

MCC member of ACS organization

The Morrison Cancer Center recently became a member of the American Cancer Society Cancer Action Network Nebraska Health Equity Council.

MCC team members Carlene Springer, APRN; Leslie Robbins, APRN; and Dr. M. Sitki Copur joined the ACS-CAN meeting on August 30

ACS-CAN is sponsoring an event, Nebraska Cancer Research Forum, which will bring together leaders in business, education, medicine, government and research. Discussion will center on potential clinical trials to impact the fight against cancer for those living with the disease. Dr. Copur and his team will take patient testimonials to the forum, which takes place October 27.

ACS-CAN makes cancer a priority for public officials and candidates at the federal, state and local levels. The organization is an evidence-based group and a public health community leader, which engages scientists, researchers, medical providers, advocate and patients. They work to influence critical public health policies important to cancer mission.

As the ACS's non-profit, non-partisan advocacy affiliate, ACS-CAN is critical to the fight for a world without cancer. Staff members work closely with ACS research and cancer control leadership to identify and develop key public policies firmly rooted in scientific evidence. These policies promote access to prevention and early detection, treatment and follow-up care.

Several new employees join MCC

Continued from page 3

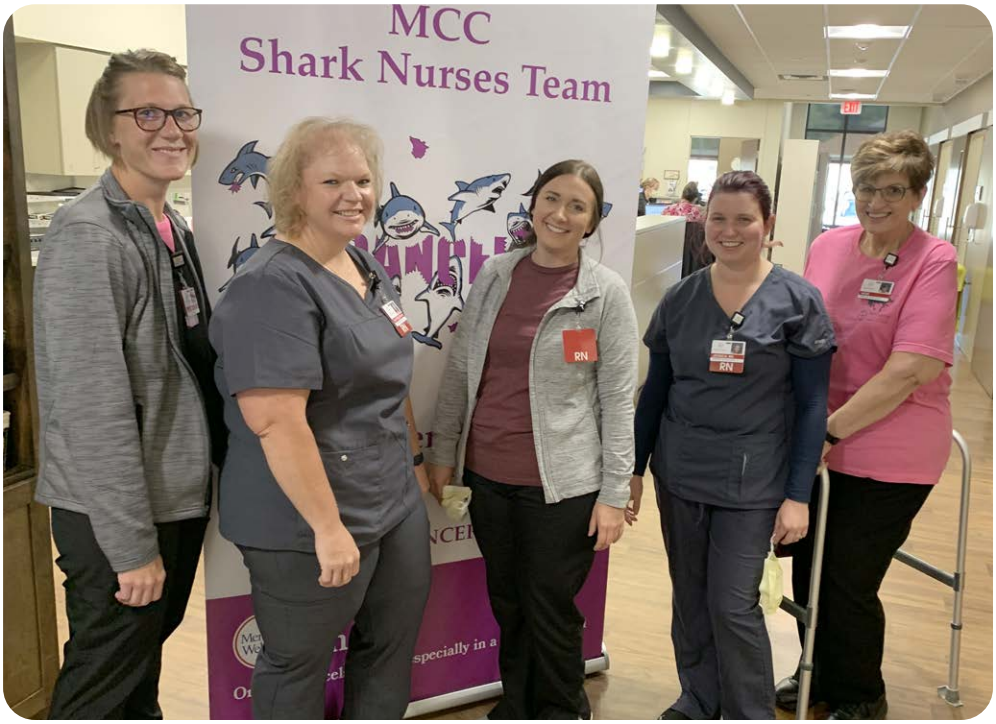
"I am currently enrolled at Nebraska Methodist to further my education. I am always looking for opportunities to learn and more often than not, I have my face buried in a book of some sort. I enjoy the teamwork and the welcoming environment at MCC I also enjoy being able to get to know my patients! I look forward to learning more and becoming a part of the team."

Jordan Sukup

"I am proud to be part of the MCC team. To be able to possibly put a smile on a patient's face or be a listening ear in a time of need brings me a sense of fulfillment. I am extremely grateful to serve our patients along their treatment journey and am excited for my future with MCC."

Vickie Hurley

"After working in oncology for the past 25 years, I am excited to join MCC. I look forward to being part of the most competent and caring oncology team there is. I know first-hand the bond we make with our patients as we help them with this journey, and I am thankful to be part of MCC."



Pictured are Kati Brunt, Heather Behmerwohld, Jordan Sukup, Jessica Forbes and Vickie Hurley, all new MCC employees.

Kool-Aid Days & Melon Roasters Car Show

Members of the Morrison Cancer Center staff provided public education during two Hastings summer events, Kool-Aid Days and the Melon Roasters Car Show.

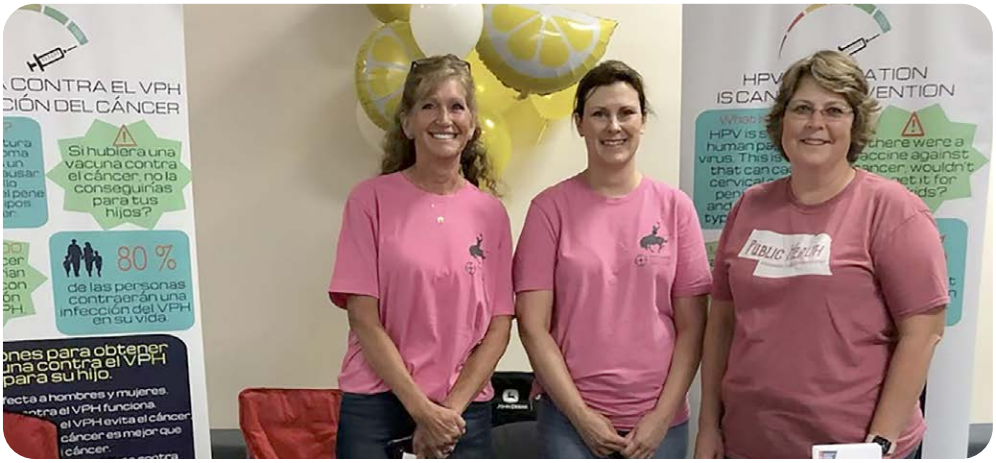
Both were great opportunities for our cancer program to provide valuable educational materials and facilitate discussions about the importance of cancer prevention.

During Kool-Aid Days on August 21, MCC partnered with the South Heartland District Health Department to educate about the importance of the HPV vaccine. The vaccine can help prevent cancers including cervical, tonsil, tongue, vulvar, vaginal, penile and anal. American Cancer Society materials were shared.

More than 2,500 people attended Kool-Aid Days. The MCC booth was near those of other non-profit organizations and children's games. the MCC team talked to parents and grandparents plus young adults and young adults and adolescents for whom the vaccine is recommended.

During the Melon Roasters Car Show on August 222, MCC provided information about cancer risk and screenings.

The outdoor car show drew more than 1,500 people and provided a chance for the radiation oncology team to be visible within the community.



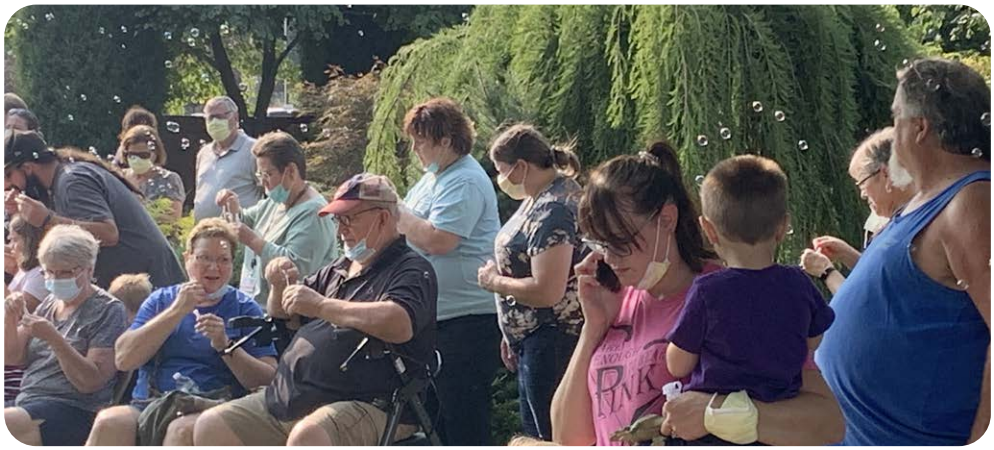
Above: MCC team members are pictured during summer events, including Kool-Aid days) top) and the Melon Roasters Car Show (bottom).

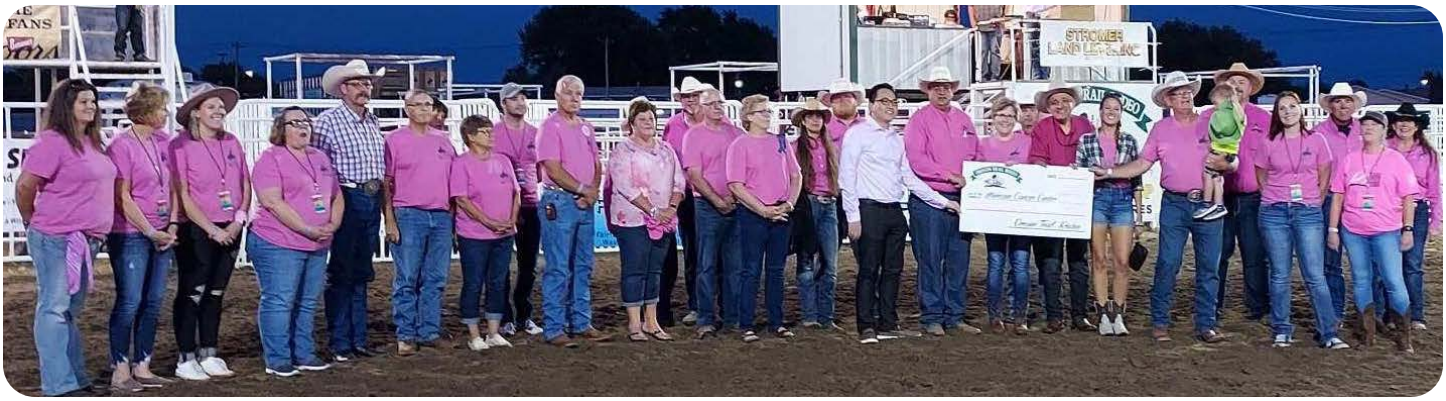
MCC teams with GRACE foundation

The Morrison Cancer Center and the GRACE Cancer Foundation teamed up on a butterfly release event in August.

The butterflies were released as a symbol of hope, transformation and renewal of life in honor of cancer patients. A shipping glitch caused the butterflies to arrive a day late. However, the event went on as scheduled with bubbles, words of encouragement and music.

The following day. MCC staff and patients were honored to let the butterflies go in the Perkins-Spady Memorial Garden.





Above: The Oregon Trail Rodeo Association presents a check to the Morrison Cancer Center for $3,150, proceeds from Tough Enough to Wear Pink night. Below: MCC team members man the t-shirt sales booth at the Oregon Trail Rodeo.

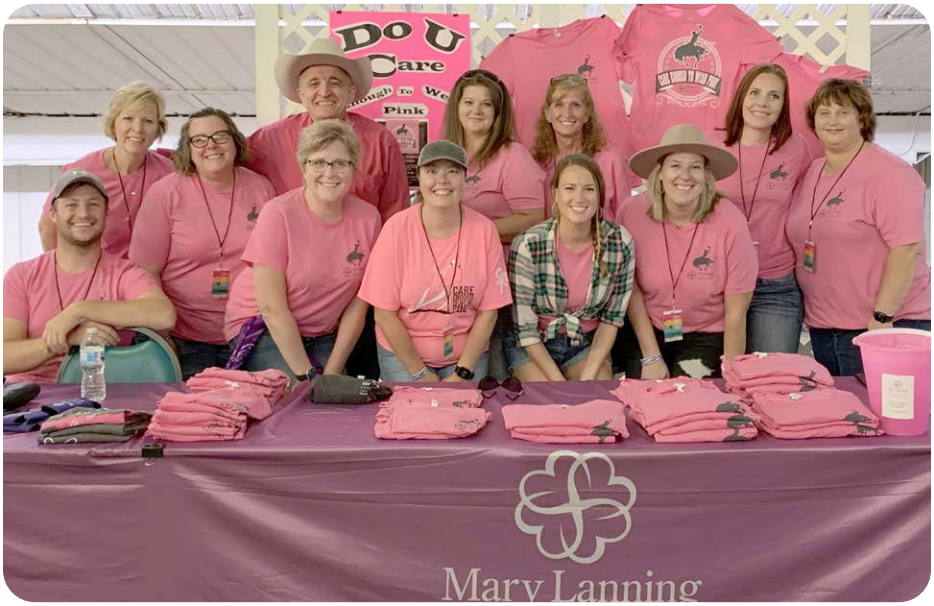
Pink Night at the Oregon Trail Rodeo

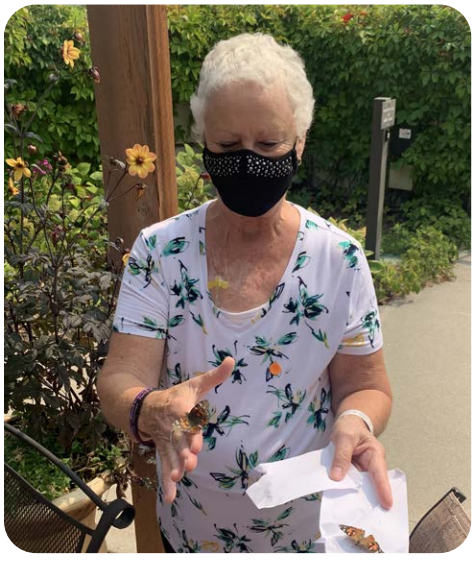
Many members of the Morrison Cancer Center team attended the Tough Enough to Wear Pink night at the Oregon Trail Rodeo.

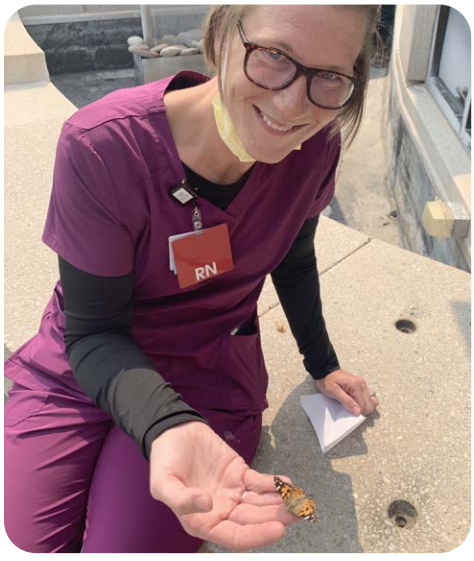
The Oregon Trail Rodeo Association donates money for every audience member who wears pink to the From the Heart Fund at MCC as part of the event. The MCC staff also sold pink rodeo shirts to raise money during the Oregon Trail Rodeo and the Webster County Rodeo in July.

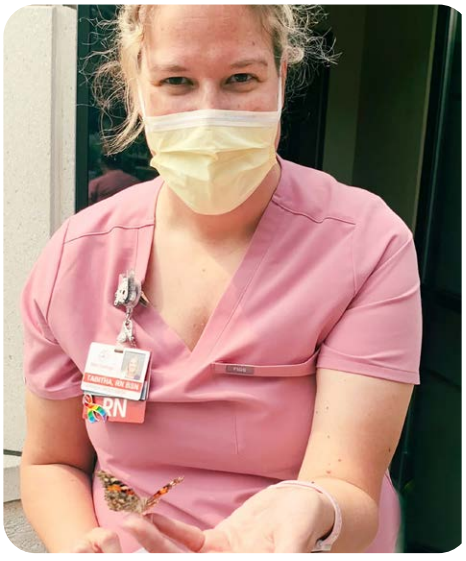
The From the Heart Fund helps patients meet household bills, gas and medication costs and more.

The Rodeo Association presented MCC with a check for $3,150. All funds go to help local patients.









MCC part of ASCO quality measure development

The Morrison Cancer Center recently participated in a feasibility testing for an American Society of Clinical Oncology (ASCO) quality measure.

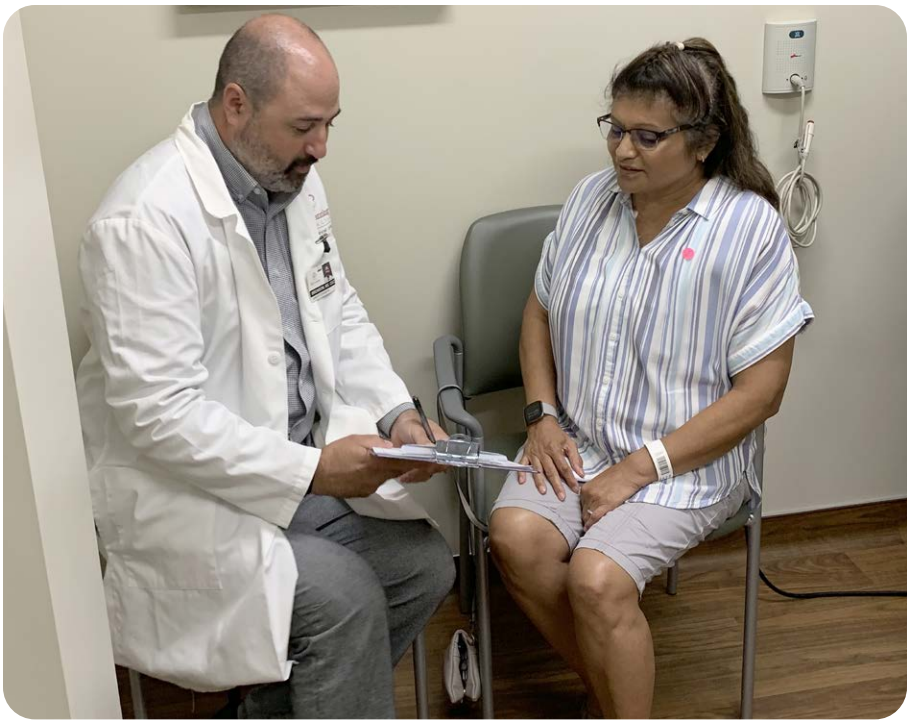
The quality measure was Appropriate Germline Testing for Ovarian Cancer Patients.

Many medical societies recommend genetic testing for all women diagnosed with ovarian cancer. Yet, about 30 percent of women undergo such testing.

ASCO is developing this quality measure to recommend all women diagnosed with epithelial ovarian cancer be offered germline genetic testing for ovarian cancer susceptibility genes at the time of diagnosis. As part of that, ASCO is working with oncology centers across the nation to develop the best way this measure can be implemented by leveraging information in a patient's electronic health record (EHR).

MCC completed a feasibility tool assessing specific data elements within the company EHR, EPIC. ASCO will use the information to gain insight into how and what data is captured in EHRs and, if the information needed is not captured, how hard would it be to implement such capture.

ASCO believes quality measures are essential to improving care quality, resource use and patient outcomes.



Bronson Riley, MS CGC CCRP, meets with a patient recently at the Morrison Cancer Center.

MCC staff highlight: Genetic counselor

When Morrison Cancer Center patients want to know more whether their family members are at risk, our genetic counselor is on hand to meet them.

Bronson Riley, MS CGC CCRP, is a board-certified and licensed genetic counselor who provides cancer risk assessment and counseling to patients and their families.

Bronson received graduate training at Case Western Reserve University. He has been providing genetic counseling since 2006.

In addition to his clinical activities, Bronson is an adjunct assistant professor in the Genetic Counseling Training Program at the University of Nebraska Medical Center and a the Physician Assistant Studies Program at Union College.

He is a director on the American Board of Genetic Counselors.

In 2010, Bronson received The New Leader Award from the National Association of Genetic Counselors.

"The Morrison Cancer Center and our patients are fortunate to have Bronson on our team," said M. Sitki Copur, MD. "With his academic and clinical skills, Bronson is a perfect fit for our academic, community-based cancer center. He is an indispensable team player for so many academic and clinical projects that we will be taking on in the near future."

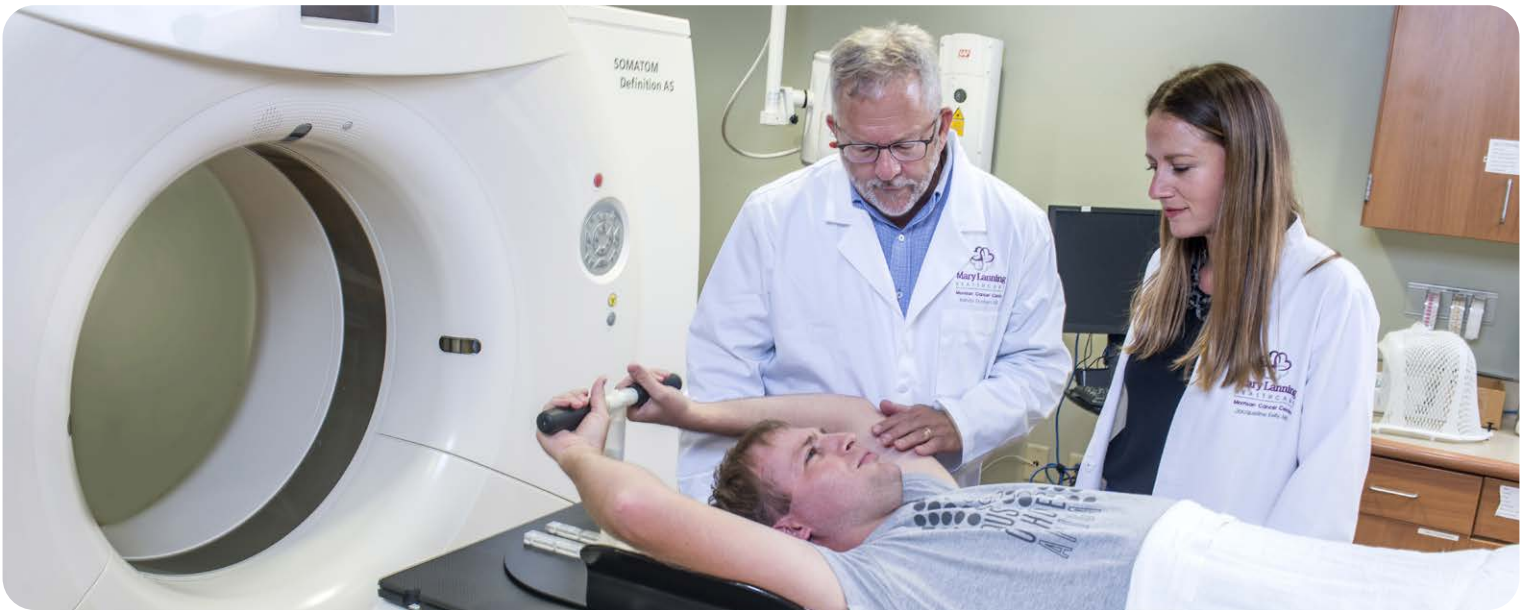
Dr. Kelly receives UNMC appointment

Jacqueline Kelly, MD, recently was appointed to the adjunct faculty of the University of Nebraska Medical Center.

Dr. Kelly will serve with the title of adjunct professor in the College of Allied Health Professions, Division of Radiation Therapy.

She will teach and research, along with other duties as part of the UNMC adjunct faculty. Her expertise will contribute to the education of UNMC students.

Congratulations to Dr. Kelly for this milestone, which aligns with the academic, community-based mission of the Morrison Cancer Center.



Drs. Randall Duckert and Jacqueline Kelly talk with a patient recently at the Morrison Cancer Center.

MCC radiation oncology team highlights

The radiation oncology team at MCC is working to modernize radiotherapy for prostate cancer patients here in central Nebraska.

In August, Dr. Kelly instituted a pathway for ordering Decipher testing, a genomic classifier and risk stratification tool that allows more personalized and tailored treatment recommendations, in appropriate prostate cancer patients.

The radiation team is also working with our colleagues in urology to begin implementing SpaceOAR gel placement prior to initiation of radiation therapy, minimizing rectal dose and thereby ameliorating both acute and late toxicity caused by prostate cancer radiotherapy.

In concordance, the radiotherapy team will be effectuating an intrafraction motion monitoring system that will facilitate more precise targeting of the prostate gland, enabling our facility to offer stereotactic radiation therapy to the prostate in appropriately selected patients.

By being able to offer curative therapy in as few as 5 fractions, we aim to expand our reach and minimize inconvenience for patients with long commutes from more rural areas.

FDA hematology/oncology drug approvals since last issue

• FDA approved **zanubrutinib** (Brukinsa, BeiGene) for adult patients with Waldenström's macroglobulinemia (WM). **September 1, 2021.**

• FDA approved **ivosidenib** (Tibsovo, Servier Pharmaceuticals LLC) for adult patients with previously treated, locally advanced or metastatic cholangiocarcinoma with an isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test. **August 25,2021.**

• FDA approved **nivolumab** (Opdivo, Bristol-Myers Squibb Co.) for the adjuvant treatment of patients with urothelial carcinoma (UC) who are at high risk of recurrence after undergoing radical resection. **August 19, 2021.**

FDA granted accelerated approval to **dostarlimab-gxly** (Jemperli, GlaxoSmithKline LLC) for adult patients with mismatch repair deficient (dMMR) recurrent or advanced solid tumors, as determined by an FDA-approved test, that have progressed on or following prior treatment and who have no satisfactory alternative treatment options. **August 18, 2021.**

• FDA approved **belzutifan** (Welireg, Merck), a hypoxia-inducible factor inhibitor for adult patients with von Hippel-Lindau (VHL) disease who require therapy for associated renal cell carcinoma (RCC), central nervous system (CNS) hemangioblastomas, or pancreatic neuroendocrine tumors (pNET), not requiring immediate surgery. **August 13,2021.**

• FDA approved the combination of **lenvatinib (Lenvima, Eisai) plus pembrolizumab** (Keytruda, Merck) for first-line treatment of adult patients with advanced renal cell carcinoma (RCC).**August 8, 2021.**

• FDA approved **pembrolizumab** (Keytruda, Merck) for high-risk, early-stage, triple-negative breast cancer (TNBC) in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery. **July 26, 2021.**

• FDA approved **pembrolizumab (Keytruda, Merck) in combination with lenvatinib (Lenvima, Eisai)** for patients with advanced endometrial carcinoma that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation. **July 21, 2021.**

• FDA approved **belumosudil** (Rezurock, Kadmon Pharmaceuticals, LLC), a kinase inhibitor, for adult and pediatric patients 12 years and older with chronic graft-versus-host disease (chronic GVHD) after failure of at least two prior lines of systemic therapy. **July 16, 2021.**

• FDA approved **daratumumab and hyaluronidase-fihj (Darzalex Faspro, Janssen Biotech, Inc.) in combination with pomalidomide and dexamethasone** for adult patients with multiple myeloma who have received at least one prior line of therapy including lenalidomide and a proteasome inhibitor. **July 9, 2021.**

• FDA approved **enfortumab vedotin-ejfv** (Padcev, Astellas Pharma US, Inc.), a Nectin-4-directed antibody and microtubule inhibitor conjugate, for adult patients with locally advanced or metastatic urothelial cancer whohave previously received a programmed death receptor-1 (PD-1) or programmed death-ligand (PD-L1) inhibitor and platinum-containing chemotherapy, orare ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy. **July 9, 2021.**

• FDA approved **asparaginase erwinia chrysanthemi** (recombinant)-rywn) (Rylaze, Jazz Pharmaceuticals, Inc.) as a component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LBL) in adult and pediatric patients 1 month or older who have developed hypersensitivity to E. coli-derived asparaginase. **July 1, 2021.**

Adjuvant vs. early salvage radiation therapy for men at high risk for recurrence following radical prostatectomy for prostate cancer and the risk of death

Adjuvant compared with early salvage radiation therapy (sRT) following radical prostatectomy (RP) has not been shown to reduce progression-free survival in randomized controlled trials. However, these trials might have missed a benefit in men with adverse pathology at RP given that these men were under-represented and immortal time bias might have been present.

Authors evaluated the impact of adjuvant versus early sRT on all-cause mortality (ACM) risk in men with adverse pathology defined as positive pelvic lymph nodes (pN1) or pGleason score 8-10 prostate cancer (PC) and disease extending beyond the prostate (pT3/4).

Authors used a treatment propensity score to minimize potential treatment selection bias when estimating the causal effect of adjuvant versus early sRT on ACM risk and a sensitivity analysis to assess the impact that varying definitions of adverse pathology had on ACM risk adjusting for age at RP, PC prognostic factors, site, and the time-dependent use of post-RP androgen deprivation therapy.

After a median follow-up (interquartile range) of 8.16 (6.00-12.10) years, of the 26,118 men in the study cohort, 2,104 (8.06%) died, of which 539 (25.62%) were from PC.

After excluding men with a persistent prostate-specific antigen, adjuvant compared with early sRT was associated with a significantly lower ACM risk among men with adverse pathology at RP when men with pN1 PC were excluded (0.33 [0.13-0.85]; P5.02) or included (0.66 [0.44-0.99]; P5 .04).

Authors concluded that Adjuvant radiation therapy should be considered in men with pN1 or pGleason score 8 to 10 and pT3/4 PC given the possibility that a significant reduction in ACM risk exists.

Ref: J Clin Oncol 39:2284-2293. © 2021 by American Society of Clinical Oncology

Potentially Practice Changing DATA

Clinical response to immunotherapy targeting programmed cell death receptor 1/programmed cell death ligand 1 in patients with treatment-resistant microsatellite stable colorectal cancer with and without liver metastases

Microsatellite stable (MSS) metastatic colorectal cancer has been historically characterized as resistant to immunotherapy. Recent studies have demonstrated limited clinical activity of programmed cell death receptor 1/programmed death ligand 1 (PD-1/PD-L1) targeting in MSS metastatic colorectal cancer.

The association of metastatic disease in the liver with treatment response has not been fully investigated. To investigate the association of liver metastases with response to PD-1/PD-L1–targeting therapy in MSS metastatic colorectal cancer.

The authors of this single-center retrospective cohort study evaluated clinical responses to PD-1– or PD-L1–targeting therapy, with or without other investigational agents, in patients with MSS metastatic colorectal cancer and disease progression after standard of care therapy. Objective response rate (ORR) and progression-free survival (PFS), measured from initiation of PD-1/PD-L1–targeting therapy. Ninety-five patients with MSS metastatic colorectal cancer were identified (54 men [56.8%]; median age, 55 [interquartile range (IQR), 49-64] years).

The overall ORR was 8.4% (8 of 95 patients). Eight of 41 patients without liver metastases achieved an ORR of 19.5%, and no response was observed in 54 patients with liver metastases. The disease control rate was 58.5% (24 of 41) in patients without liver metastasis and 1.9% (1 of 54) in patients with liver metastasis.

Patients without liver metastases at the time of PD-1/PD-L1–targeting treatment had a superior median PFS compared with patients with liver metastases (4.0 [IQR, 2.0-7.5] vs 1.5 [IQR, 1.0-2.0] months; P < .001). In addition, median PFS was 5.5 (IQR, 2.0-11.5) months for patients without any prior or current liver involvement at the time of PD-1/PD-L1–targeting treatment initiation.

Using a multivariate Cox regression model correcting for Eastern Cooperative Oncology Group status, primary tumor location, RAS and BRAF status, tumor mutation burden, and metastatic sites, liver metastases was the variable with the most significant association with faster progression after PD-1/PD-L1 treatment inhibition (hazard ratio, 7.00; 95% CI, 3.18-15.42; P < .001). Findings of this cohort study suggest that patients with MSS metastatic colorectal cancer and without liver metastases may derive clinical benefits from checkpoint inhibitors, whereas the presence of liver metastases was associated with resistance. Further prospective studies are needed to investigate PD-1/PD-L1 inhibitors in patients with MSS metastatic colorectal cancer without liver metastases

Ref: JAMA Network Open. 2021; 4(8):e2118416. Doi: 10.1001/jama networkopen. 2021.18416

Publications since our last issue

• **Copur, M.S.** Cushman, A.V., Padussis, J.C., **Wedel, W., Schroeder, C., Herold, D., Lintel, N., Horn, A.** Mucinous Adenocarcinoma of the Appendix with Histologic Response to Neoadjuvant Chemotherapy- Review of Histologic and Clinical Spectrum of Epithelial Neoplastic Mucinous Lesions of the Appendix," Oncology 2021 June 2021. **(Published)**

• **Copur, M.S., Kelly J., Faris, S., Herold, D., Lintel, N., Horn, A., Wedel, W., Riley, B.** A 64-Year-old Man with BRCA Mutated Breast Cancer-Known and Unknown Aspects of Male Breast Cancer. Oncology 2021 **(Published)**

• Clark, A.S., Hong, F., Finn, R.S., De Michele A.M., Mitchell, E.P., Zwiebel, J., **Copur, M.S.,** et al. Phase II Trial of Palbociclib in CCND 1, 2 or 3 Amplified Non-Breast Tumors: Results from the NCI-MATCH Trial (EAY131) Sub-protocol Z1B. Clin Can Res 2021. **(Accepted for publication)**

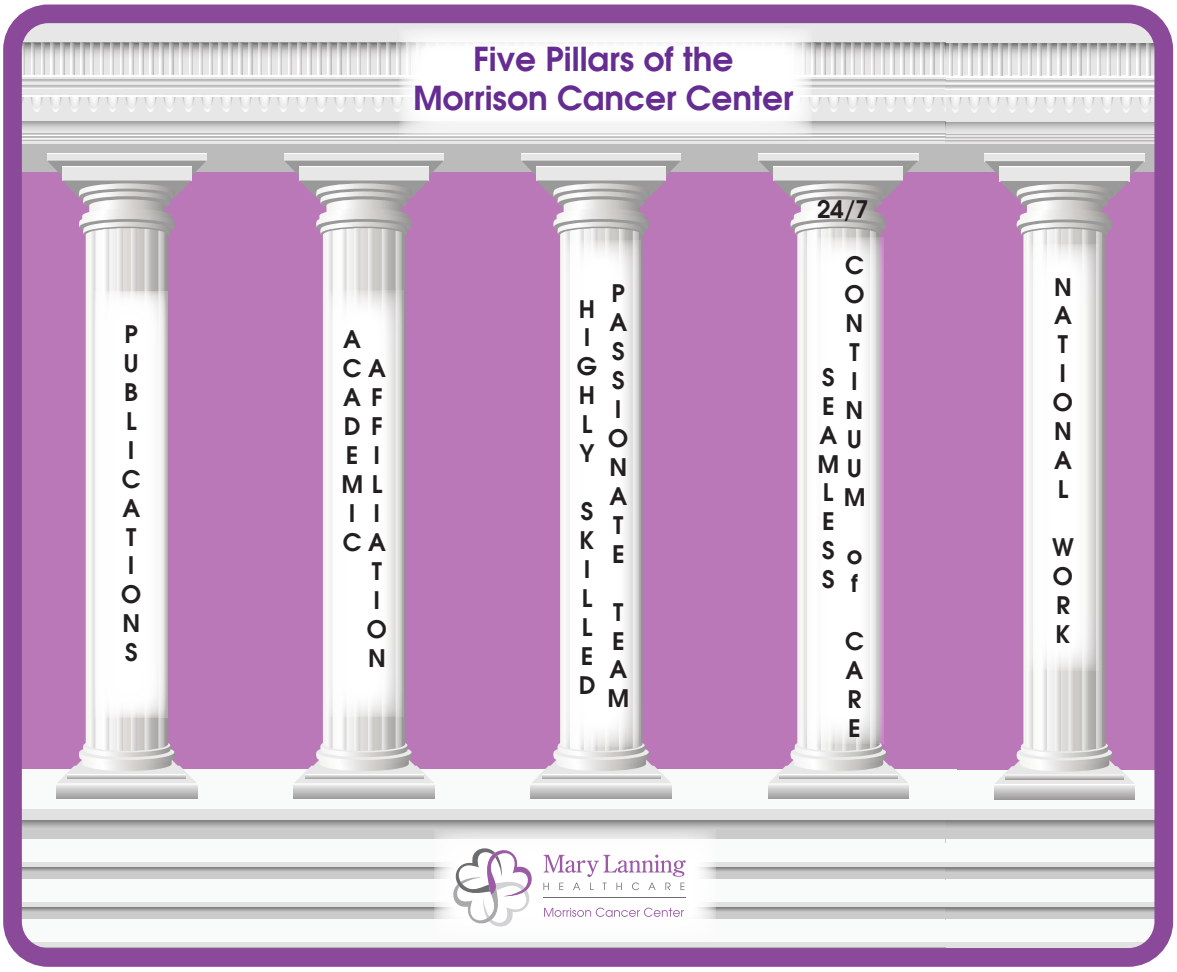
• Chu, E., Harrold., LJ., **Copur, M.S.** Chemotherapeutic and Biologic Drugs. In: Physicians Cancer Chemotherapy Drug Manual. Chu E, De Vita ed. 2022 **(Submitted for publication)**

• Harrold L.J., **Copur, M.S.,** Chu E. Guidelines for Chemotherapy and Dosing Modifications. In: Physicians Cancer Chemotherapy Drug Manual. Chu E, DeVita ed.2022. **(Submitted for publication)**

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

• Maguire, W, **Copur, M.S.**, Harrold, L.J., Chu E. Antiemetic Agents for the treatment of Chemotherapy-Induced Nausea and Vomiting. In: Physicians Cancer Chemotherapy Drug Manual. Chu E, De Vita ed. 2012. **(Submitted for publication)**

• **Copur, M.S., Schroeder, C., Ly, Q., Kelly, J., Wedel, W., Lintel, N., Tun, S.M., Horn A., Rodriguez H., Riley, B.** Pathological Complete Response of Locally Advanced Colon Cancer to Neoadjuvant Chemoimmunotherapy and Oxaliplatin-Induced Fever Associated with IL-6 Release. Oncology 2021. **(Submitted for publication)**



Potentially Practice Changing DATA

Pembrolizumab plus ipilimumab following anti-PD-1/L1 failure in melanoma

Combination of antiprogrammed cell death protein-1 (PD-1) plus anti–cytotoxic T-cell lymphocyte-4(anti-CTLA-4) immunotherapy shows greater response rates (RRs) than anti-PD-1 antibody alone in melanoma, but RR after initial anti-PD-1 and programmed death ligand-1 (PD-L1) antibody progression awaits robust investigation. Anti-CTLA-4 antibody alone after anti-PD-1/L1 antibody progression has a historical RR of 13%.

We report the results of the first prospective clinical trial evaluating ipilimumab 1 mg/kg plus pembrolizumab following progression on anti-PD-1 immunotherapy. Patients with advanced melanoma who had progressed on anti-PD-1/L1 antibody as immediate prior therapy (including non–anti-CTLA-4 antibody combinations) were eligible. Patients received pembrolizumab200 mg plus ipilimumab 1 mg/kg once every 3 weeks for four doses, followed by pembrolizumab monotherapy. The primary end point was RR by irRECIST.

After 35 patients, the trial met the primary end point and was expanded to enroll a total of 70 patients to better estimate the RR.
RESULTS Prior treatments included 60 on anti-PD-1 antibody alone and 10 on anti-PD-1/L1 antibody–based combinations. Thirteen patients had progressed in the adjuvant setting. The median length of prior treatment with anti-PD-1/L1 antibody was 4.8 months. Response assessments included five complete and 15 partial responses, making the irRECIST RR 29% among the entire trial population. The median progression-free survival was 5.0 months, and the median overall survival was 24.7 months. The median duration of response was 16.6 months. There was no difference in median time on prior anti-PD1/L1 or time to PD1 1CTLA4 initiation between responders and non-responders. Grade 3-4 drug-related adverse events occurred in 27% of patients. Responses occurred in PD-L1–negative, non-T-cell–inflamed, and intermediate tumor phenotypes. To our knowledge, this is the first prospective study in melanoma of pembrolizumab plus low-dose ipilimumab after anti-PD-1/L1 immunotherapy failure, demonstrating significant antitumor activity and tolerability.

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