Oncology Update

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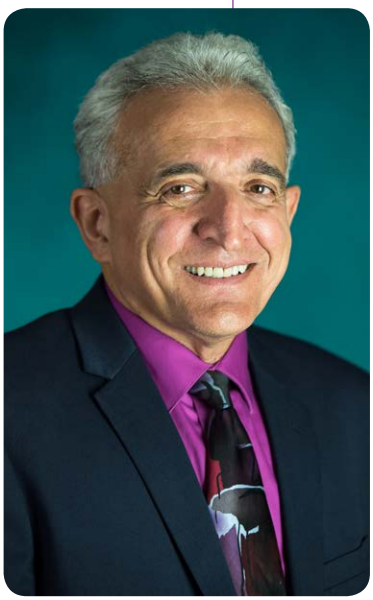
Mary Lanning HEALTHCARE
Morrison Cancer Center

A quarterly newsletter from Mary Lanning Healthcare Morrison Cancer Center
The future of cancer care in central Nebraska
The definition of excellence in comprehensive community cancer care



Dear colleagues,
It is with great pleasure and honor that I share our October Oncology Update newsletter from my new cancer team at Mary Lanning Healthcare Morrison Cancer Center. Over the past several years, you have received this quarterly newsletter produced by me and my cancer team, designed to stay in touch with you, our distinguished referring colleagues and providers in Nebraska. The goal of this newsletter has been to share new preventative, diagnostic, therapeutic, supportive and palliative care-related advances in the hematology/oncology arena, as well as recently published practice-changing data useful and relevant to the care of our shared patients.

Cancer care continuum is a team effort. My cancer team starts with you, our referring physicians, then includes the entire spectrum of disciplines from primary care to surgery to pathology, radiology/interventional radiology, radiation oncology and to all other specialties through which we share patients. Because of this crucial multidisciplinary involvement, I aim to highlight new procedures, practices and accomplishments involving all providers. Featured clinical trials, recent FDA hematology/oncology drug approvals and peer-reviewed publications from my cancer program constitute other aspects of this newsletter.

Oncology Update will continue to be delivered to you quarterly in the same high-quality print format, but from my new cancer team at Mary Lanning Healthcare Morrison Cancer Center, the future of cancer care in central Nebraska. Your precious feedback and great support have been the driving force behind the success of this newsletter for many years.

As always, we welcome any subject or area of interest that you would like to see covered in this newsletter or any medical/surgical services that you provide and wish to share and publicize with our medical community. For more information on any of the topics presented or to provide feedback, please do not hesitate to contact us at **mehmet.copur@marylanning.org**. As always, we love to hear from you. Thank you for your interest and continued support in our newsletter.

Cordially,

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This issue

MCC touts complete multidisciplinary thoracic oncology program

One of the reasons aggregate lung cancer survival in the United States has not improved during the past three decades is the gap between the quality of care patients receive at academic research centers versus community-based cancer centers. Eighty percent of lung cancer patients receive care in their community where there is not always a complete multidisciplinary thoracic oncology team available.

People with lung cancer, esophageal cancer, mesothelioma, thymic cancer or other cancers that involve the chest cavity usually need several different types of treatment by a multidisciplinary team of providers. Specialist physician and non-physician providers with expertise in cardiothoracic surgery, pulmonology, radiology/interventional radiology, pathology, medical oncology, radiation oncology, pharmacy, genetic counseling, dietary and social work are indispensable components of a comprehensive thoracic oncology program. Thoracic oncology teams meet regularly to review and discuss their cases in multidisciplinary tumor boards and offer a comprehensive, coordinated approach for each individual patient. Only through this kind of a program can individualized care for each patient be delivered in a coordinated manner.

Pictured from left are Abby Gallagher, APRN, Matthew Stritt, MD, Jessica Gregg, APRN, and Kalpesh Ganatra, MD, all with Hastings Pulmonary & Sleep Clinic; Thomas Zusag, MD, with Morrison Cancer Center; Rudy Lackner, MD, cardiothoracic surgeon with UNMC; Pornchai Jonglertham, MD, and M.Sitki Copur, MD, both with Morrison Cancer Center; and Rose Meisinger, RN, with UNMC.

The Thoracic Oncology Program at Mary Lanning Healthcare Morrison Cancer Center provides exactly this full spectrum of services by a complete multidisciplinary team of cardiothoracic surgeon Dr. Rudy Lackner, pulmonologists Dr. Kalpesh Ganatra and Dr. Matthew Stritt, radiologists Drs. Paul Rodriquez, Jon Hart, Dan Herold, Shannon Smith, and John Allen, pathologists Drs. Adam Horn and Whitney Wedel, medical oncologists Drs. Pornchai Jonglertham and M. Sitki Copur and radiation oncologist Dr. Thomas Zusag. This team meets every two weeks and discusses the cases in a multidisciplinary tumor board attended by all specialties.

This is just one of the many strengths of Mary Lanning Healthcare Morrison Cancer Center, a comprehensive community cancer program and the future of cancer care in the region.

Above and right: The multidisciplinary thoraric oncology team at Mary Lanning Healthcare meets recently to discuss individualized treatment plans for patients.

Potentially Practice Changing DATA

Atezolizumab for first-line treatment of metastatic nonsquamous NSCLC

The cancer-cell–killing property of atezolizumab may be enhanced by the blockade of vascular endothelial growth factor–mediated immunosuppression with bevacizumab. This open-label, phase 3 study evaluated atezolizumab plus bevacizumab plus chemotherapy in patients with metastatic nonsquamous non–small-cell lung cancer (NSCLC) who had not previously received chemotherapy. Authors randomly assigned patients to receive atezolizumab plus carboplatin plus paclitaxel (ACP), bevacizumab plus carboplatin plus paclitaxel (BCP), or atezolizumab plus BCP (ABCP) every 3 weeks for four or six cycles, followed by maintenance therapy with atezolizumab, bevacizumab, or both. The two primary end points were investigator-assessed progression-free survival both among patients in the intention-to-treat population who had a wild-type genotype (WT population; patients with EGFR or ALK genetic alterations were excluded) and among patients in the WT population who had high expression of an effector T-cell (Teff) gene signature in the tumor (Teff-high WT population) and overall survival in the WT population.

The ABCP group was compared with the BCP group before the ACP group was compared with the BCP group. In the WT population, 356 patients were assigned to the ABCP group, and 336 to the BCP group. The median progression-free survival was longer in the ABCP group than in the BCP group (8.3 months vs. 6.8 months; hazard ratio for disease progression or death, 0.62, P<0.001), the corresponding values in the Teff-high WT population were 11.3 months and 6.8 months (hazard ratio, 0.51, P<0.001). Progression-free survival was also longer in the ABCP group than in the BCP group in the entire intention-to-treat population (including those with EGFR or ALK genetic alterations) and among patients with low or negative programmed death ligand 1 (PD-L1) expression, those with low Teff gene-signature expression, and those with liver metastases. Median overall survival among the patients in the WT population was longer in the ABCP group than in the BCP group (19.2 months vs. 14.7 months; hazard ratio for death, 0.78, P=0.02). The safety profile of ABCP was consistent with previously reported safety risks of the individual medicines. Authors concluded that the addition of atezolizumab to bevacizumab plus chemotherapy significantly improved progression-free survival and overall survival among patients with metastatic nonsquamous NSCLC, regardless of PD-L1 expression and EGFR or ALK genetic alteration status.

Reference: Socinski MA, Jotte RM, Cappuzzo F et al. Atezolizumab for First-Line Treatment of Metastatic Nonsquamous NSCLC. N Engl J Med 2018; 378:2288-2301.

Potentially Practice Changing DATA

Phase 3 trial of Ibrutinib plus Rituximab in Waldenström's Macroglobulinemia

Single-agent ibrutinib has shown substantial activity in patients with relapsed Waldenström's macroglobulinemia, a rare form of B-cell lymphoma. In this trial, the effect of adding ibrutinib to rituximab, both in those who had not received previous treatment and in those with disease recurrence was evaluated. 150 symptomatic patients were randomly assigned to receive ibrutinib plus rituximab or placebo plus rituximab. The primary end point was progression-free survival, as assessed by an independent review committee. Key secondary end points were response rates, sustained hematologic improvement from baseline, and safety. The mutational status of MYD88 and CXCR4 was assessed in bone marrow samples. At 30 months, the progression-free survival rate was 82% with ibrutinib–rituximab versus 28% with placebo–rituximab (hazard ratio for progression or death, 0.20; P<0.001). The benefit in the ibrutinib–rituximab group over that in the placebo–rituximab group was independent of the MYD88 or CXCR4 genotype. The rate of major response was higher with ibrutinib–rituximab than with placebo–rituximab (72% vs. 32%, P<0.001). More patients had sustained increases in hemoglobin level with ibrutinib–rituximab than with placebo–rituximab (73% vs. 41%, P<0.001). The most common adverse events of any grade with ibrutinib–rituximab included infusion-related reactions, diarrhea, arthralgia, and nausea. Among patients with Waldenström's macroglobulinemia, the use of ibrutinib–rituximab resulted in significantly higher rates of progression-free survival than the use of placebo–rituximab, both among those who had received no previous treatment and among those with disease recurrence.

Reference: Dimopoulos, MA, Tedeschi A, Trotman J, et al. Phase 3 Trial of Ibrutinib plus Rituximab in Waldenström's Macroglobulinemia. N Engl J Med 2018;378:2399-2410.

Mary Lanning Healthcare and Morrison Cancer Center officials meet Sept. 18 at the Morrison Cancer Center in Hastings with the UNMC Hematology/Oncology team led by Julie Vose, MD FASCO MBA (pictured center front).

UNMC and MCC collaborate

As the only National Cancer Institute (NCI)-designated cancer center in Nebraska, the Fred & Pamela Buffett Cancer Center, which is a collaboration of UNMC and Nebraska Medicine, brings together a powerhouse team of more than 200 oncologists and researchers to find better ways to diagnose, treat and prevent cancer. At the Fred & Pamela Buffett Cancer Center, Nebraska Medicine offers treatment options and clinical trials not found elsewhere.

Mary Lanning Healthcare, Morrison Cancer Center has already taken part in several projects with UNMC, Nebraska Medicine and the Fred & Pamela Buffett Cancer Center. The Comprehensive Data and Biospecimen Bank known as the Integrated Cancer Repository for Cancer Research (iCaRe2) is one of the projects with a data registry and biospecimen bank. It provides core support services for future multidisciplinary research on cancer and other chronic diseases carried out by members of the Fred & Pamela Buffett Cancer Center.

The Morrison Cancer Center team now is gearing up to increase its collaboration with the Nebraska Medicine cancer team. On September 18, the Morrison Cancer Center team and the Nebraska Medicine Cancer team, led by Julie Vose, MD, FASCO, MBA, hematologist oncologist and UNMC Chief of Hematology Oncology, came together at the Morrison Cancer Center to discuss and implement the next steps in increasing Morrison Cancer Program's existing collaboration with Nebraska Medicine. The focus of the meeting was to expedite the startup of clinical trials at the Morrison Cancer Center. A clinical trial infrastructure for Nebraska Medicine/UNMC Institutional Clinical Trials, NCI Cancer Trials Network trials, and Investigator Initiated Trials is being put in place to facilitate our cancer patients' enrollments on high quality cutting-edge local and national clinical trials.

FDA hematology/oncology drug approvals since last issue

• **Moxetumomab pasudotox-tdfk (LUMOXITI, AstraZeneca Pharmaceuticals LP)**, a CD22-directed cytotoxin for adult patients with relapsed or refractory hairy cell leukemia who received at least two prior systemic therapies, including treatment with a purine nucleoside analog (PNA). **September 13, 2018**.

• **Pembrolizumab (KEYTRUDA, Merck & Co., Inc.)** in combination with pemetrexed and platinum for first-line treatment of patients with metastatic, non-squamous non-small cell lung cancer, with no EGFR or ALK genomic tumor aberrations. **August 20, 2018**.

• **Nivolumab (Opdivo, Bristol-Myers Squibb Company Inc.)** for patients with metastatic small cell lung cancer with progression after platinum-based chemotherapy and at least one other line of therapy. **August 16, 2018**.

• **Lenvatinib capsules (Lenvima, Eisai Inc.)** for first-line treatment of patients with unresectable hepatocellular carcinoma. **August 16, 2018**.

• **Mogamulizumab-kpkc (Poteligeo, Kyowa Kirin, Inc.)** for adult patients with relapsed or refractory mycosis fungoides or Sézary syndrome after at least one prior systemic therapy. **August 8, 2018**.

• **Lusutrombopag (Mulpleta, Shionogi Inc.)** for thrombocytopenia in adults with chronic liver disease who are scheduled to undergo a medical or dental procedure. **July 31, 2018**.

• **Iobenguane I 131 (AZEDRA, Progenics Pharmaceuticals, Inc.)** for adult and pediatric patients (12 years and older) with iobenguane scan-positive, unresectable, locally advanced or metastatic pheochromocytoma or paraganglioma (PPGL) who require systemic anticancer therapy. **July 30, 2018**.

• **Ivosidenib (Tibsovo, Agios Pharmaceuticals, Inc.)** for adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible IDH1 mutation as detected by an FDA-approved test. **July 20, 2018**.

• **Ribociclib (Kisqali, Novartis Pharmaceuticals Corporation)** in combination with an aromatase inhibitor for pre/perimenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer, as initial endocrine-based therapy. **July 18, 2018**.

• **Enzalutamide (XTANDI, Astellas Pharma US, Inc.)**, for patients with castration-resistant prostate cancer (CRPC). **July 13, 2018**.

Oregon Trail Rodeo partners with Morrison Cancer Center

The Oregon Trail Rodeo has partnered with the Morrison Cancer Center at Mary Lanning Healthcare to raise funds for the center's From the Heart program.

The rodeo donates $1 for every rodeo fan who wears pink during the Saturday rodeo session. The 2018 Pink Rodeo Night took place August 25. Rodeo organizers also pass a pink bucket, asking for voluntary donations, during the performance.

The Morrison Cancer Center From the Heart program provides money to patients undergoing cancer treatment. The money is used for fuel or for other necessities like medicine. This year's event was attended by Morrison Cancer Team members Drs. Jonglertham, Zusag and Copur and Carlene Springer, APRN (pictured below right) as well as other cancer team members (pictured above right). It was a fun-filled night that benefits MCC cancer patients

Above: Morrison Cancer Center staff members gather at Pink Night at the Oregon Trail Rodeo. Left: Morrison Cancer Center staff members receive a check for the From the Heart program from the Oregon Trail Rodeo. The rodeo raised $2,305 in 2018 to benefit MCC patients.

Potentially Practice Changing DATA

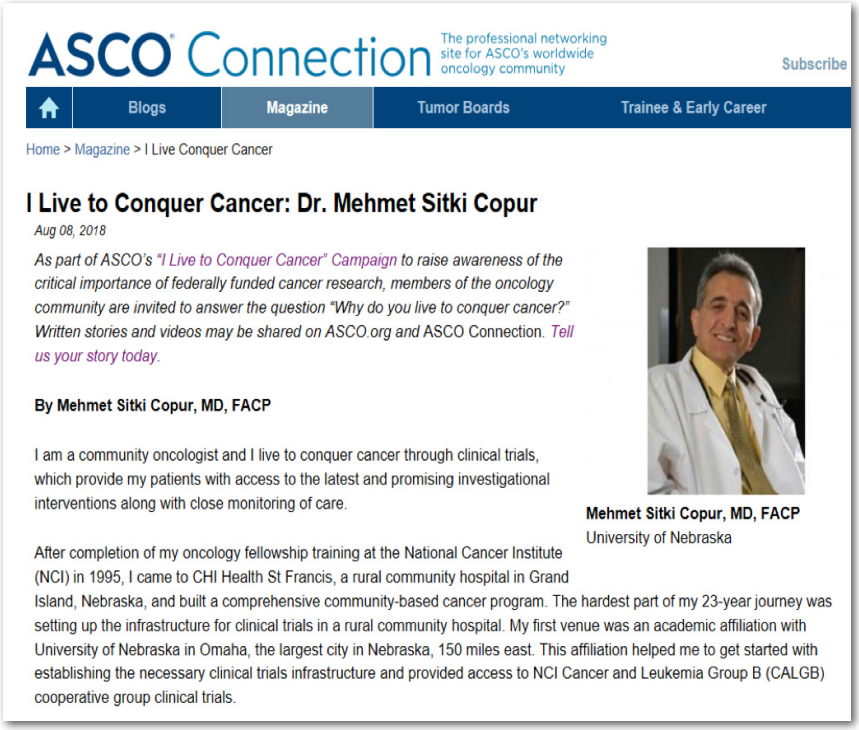
Enzalutamide in men with no metastatic, castration-resistant prostate cancer

Men with nonmetastatic, castration-resistant prostate cancer and a rapidly rising prostate-specific antigen (PSA) level are at high risk for metastasis. Enzalutamide, which prolongs overall survival among patients with metastatic, castration-resistant prostate cancer was evaluated to see if it would delay metastasis in men with nonmetastatic, castration-resistant prostate cancer and a rapidly rising PSA level. Men with nonmetastatic, castration-resistant prostate cancer and a PSA doubling time of 10 months or less who were continuing androgen-deprivation therapy were randomly assigned to receive enzalutamide (at a dose of 160 mg) or placebo once daily. The primary end point was metastasis-free survival (defined as the time from randomization to radiographic progression or as the time to death without radiographic progression).

A total of 1401 patients (median PSA doubling time, 3.7 months) underwent randomization. The median metastasis-free survival was 36.6 months in the enzalutamide group versus 14.7 months in the placebo group (hazard ratio 0.29, P<0.001). The time to the first use of a subsequent antineoplastic therapy was longer with enzalutamide treatment than with placebo (39.6 vs. 17.7 months). At the first interim analysis of overall survival, 103 patients (11%) receiving enzalutamide and 62 (13%) receiving placebo had died. Adverse events of grade 3 or higher occurred in 31% of the patients receiving enzalutamide, as compared with 23% of those receiving placebo. Among men with nonmetastatic, castration-resistant prostate cancer with a rapidly rising PSA level, enzalutamide treatment led to a clinically meaningful and significant 71% lower risk of metastasis or death than placebo.

Reference: Hussain M, Fizazi K, Saad F et al. Enzalutamide in Men with Nonmetastatic, Castration-Resistant Prostate Cancer. N Engl J Med 2018;378:2465-2474.

ASCO 'I Live to Conquer Cancer' initiative



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I Live to Conquer Cancer: Dr. Mehmet Sitki Copur

Aug 08, 2018

As part of ASCO's "I Live to Conquer Cancer" Campaign to raise awareness of the critical importance of federally funded cancer research, members of the oncology community are invited to answer the question "Why do you live to conquer cancer?" Written stories and videos may be shared on ASCO.org and ASCO Connection. *Tell us your story today.*

By Mehmet Sitki Copur, MD, FACP

I am a community oncologist and I live to conquer cancer through clinical trials, which provide my patients with access to the latest and promising investigational interventions along with close monitoring of care.

Mehmet Sitki Copur, MD, FACP
University of Nebraska

After completion of my oncology fellowship training at the National Cancer Institute (NCI) in 1995, I came to CHI Health St Francis, a rural community hospital in Grand Island, Nebraska, and built a comprehensive community-based cancer program. The hardest part of my 23-year journey was setting up the infrastructure for clinical trials in a rural community hospital. My first venue was an academic affiliation with University of Nebraska in Omaha, the largest city in Nebraska, 150 miles east. This affiliation helped me to get started with establishing the necessary clinical trials infrastructure and provided access to NCI Cancer and Leukemia Group B (CALGB) cooperative group clinical trials.

Cancer treatment advances are transforming cancer care and giving hope to the millions of Americans who face a cancer diagnosis each year.

This progress could not be possible without the strong support provided by the National Cancer Institute (NCI) and the passionate work of cancer researchers who are finding new ways to diagnose, prevent and treat cancer.

In June 2018, American Society of Clinical Oncology (ASCO) came up with "I Live to Conquer Cancer" campaign, putting a human face on those who have dedicated their lives to clinical cancer research and to the patients who inspire them to continue their work against cancer. The campaign seeks to highlight the importance of federally funded cancer research and asks members to share why they live to conquer cancer.

As part of Conquer Cancer's "I Live to Conquer Cancer" campaign, Dr. Copur of Morrison Cancer Center contributed to this ASCO initiative with an article which was published online at ASCO website.
Dr. Copur's full article is available at
https://connection.asco.org/magazine/i-live-conquer-cancer/i-live-conquer-cancer-dr-mehmet-sitki-copur

Publications since our last issue

• Copur MS. I Live to Conquer Cancer. ASCO Connection Aug 2018 https://connection.asco.org/magazine/i-live-conquer-cancer/i-live-conquer-cancer-dr-mehmet-sitki-copur (published)

• Copur MS, et al. Miscellaneous Chemotherapeutic Agents. In: Cancer Principles & Practice of Oncology De Vita VT, Hellman S, Rosenberg SA 11th edition: November 2018. (in press)

• Chu E, Harrold LJ, Copur MS. Chemotherapeutic and Biologic Drugs. In: Physicians Cancer Chemotherapy Drug Manual. Chu E, DeVita ed. 5-447:2019. (in press)

• Copur MS, Tiedemann D, Harrold LJ, Chu E. Guidelines for Chemotherapy and Dosing Modifications. In: Physicians Cancer Chemotherapy Drug Manual. Chu E, DeVita ed. 449-472:2019. (in press)

• Copur MS, Harrold LJ, Chu E. Common Chemotherapy Regimens in Clinical Practice. 473-622:2019. (in press)

• Copur MS, Harrold LJ, Chu E. Antiemetic Agents for the treatment of Chemotherapy-Induced Nausea and Vomiting.623-632:2019. (in press)

• Copur MS. Lack of awareness lack of clinical trials in the community where most needed. Oncologist 2018. (submitted for publication)

• Copur et al. Randomized Double-Blind Placebo Controlled Study of Subcutaneous Testosterone in the adjuvant Treatment of Postmenopausal Women with Aromatase Inhibitor Induced Arthralgias. Alliance A221102 Submitted for San Antonio Breast Cancer Symposium (SABCS). (submitted for publication)

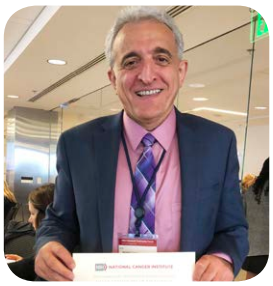
ASCO Research Community Forum 2018

Dr. M. Sitki Copur of the Morrison Cancer Center joined two University of Nebraska Medical Center research team members at the ASCO Research Community Forum recently.

Debbie Vidlack, UNMC Industry Trials Coordinator; Jennifer Messick UNMC Clinical Research Operations Administrator; and Dr. M. Sitki Copur, Morrison Cancer Center.

Established in 2010, the forum was created as a solution-oriented venue for research sites. The forum's annual meeting is geared toward community-based research sites, including those affiliated with academic centers. The meeting offers physician researchers and research staff a unique platform to collaborate and develop solutions to common challenges in conducting oncology clinical trials. This year a record attendance of 165 participants gathered at ASCO's headquarters in Washington DC on September 23-24, 2018. Participants included physicians (38%) and non-physicians (62%) from community-based practices (58%), academic research centers (24%) and several research organizations as well as Federal employees from FDA and NCI.

Dr. Copur and UNMC research team members Jennifer Messick and Debbie Vidlack attended this year's meeting. Dr. Copur serves at ASCO Research Community Forum Resource Development Task Force. He will be sharing his knowledge and experience with the rest of the ASCO Research Community Forum audience in an upcoming article, on the topic of setting up clinical trials infrastructure in the community setting.



Copur receives gold and silver awards

Dr. M. Sitki Copur received two awards during the annual meeting of National Cancer Institute (NCI) Community Oncology Research Program, which was held in Bethesda, Maryland, in September.

Dr. Copur accepted a Gold Certificate of Excellence Award as the Principal Investigator (PI) of NCI Community Oncology Research Program on behalf of CHI NCORP (his prior affiliation). He also received a Silver Certificate of Excellence for his individual exceptional achievement on patient enrollments in NCI Cancer Treatment and Cancer Control Trials during August 2017 through June 2018.

Potentially Practice Changing DATA

Cabozantinib in Patients with Advanced & Progressing Hepatocellular Carcinoma

Cabozantinib inhibits tyrosine kinases, including vascular endothelial growth factor receptors 1, 2, and 3, MET, and AXL, which are implicated in the progression of hepatocellular carcinoma and the development of resistance to sorafenib, the standard initial treatment for advanced disease. This randomized, double-blind, phase 3 trial evaluated cabozantinib as compared with placebo in previously treated patients with advanced hepatocellular carcinoma. A total of 707 patients were randomly assigned in a 2:1 ratio to receive cabozantinib (60 mg once daily) or matching placebo. Eligible patients had received previous treatment with sorafenib, had disease progression after at least one systemic treatment for hepatocellular carcinoma, and may have received up to two previous systemic regimens for advanced hepatocellular carcinoma. The primary end point was overall survival. Secondary end points were progression-free survival and the objective response rate. At the second planned interim analysis, the trial showed significantly longer overall survival with cabozantinib than with placebo. Median overall survival was 10.2 months with cabozantinib and 8.0 months with placebo (hazard ratio for death, 0.76, P=0.005). Median progression-free survival was 5.2 months with cabozantinib and 1.9 months with placebo (hazard ratio for disease progression or death, 0.44, P<0.001), and the objective response rates were 4% and less than 1%, respectively (P=0.009). Grade 3 or 4 adverse events occurred in 68% of patients in the cabozantinib group and in 36% in the placebo group. The most common high-grade events were palmar–plantar erythrodysesthesia (17% with cabozantinib vs. 0% with placebo), hypertension (16% vs. 2%), increased aspartate aminotransferase level (12% vs. 7%), fatigue (10% vs. 4%), and diarrhea (10% vs. 2%). Among patients with previously treated advanced hepatocellular carcinoma, treatment with cabozantinib resulted in longer overall survival and progression-free survival than placebo.

Reference: Abou-Alfa GK, Meyer T, Cheng AL et al. Cabozantinib in Patients with Advanced and Progressing Hepatocellular Carcinoma. N Engl J Med. 2018;379:54-63.

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