PEOPLE


Roswell Park Comprehensive Cancer Center

In January, **Kelvin Lee, MD,** became director of the Indiana University (IU) Melvin and Bren Simon Comprehensive Cancer Center in Indianapolis, succeeding Patrick Loehrer, MD. In addition, Lee became the senior associate dean of cancer research at IU School of Medicine. Previously, he served as the chair of immunology at Roswell Park Comprehensive Cancer Center in Buffalo, NY, where he also co-led the center's Tumor Immunology and Immunotherapy Program. He is an investigator on clinical trials of immunotherapy for multiple myeloma and maintains a clinical practice.


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Jan Kitajewski, PhD, became director of the University of Illinois Cancer Center in Chicago in November; he served as interim director since December 2019. He will continue as head of the Department of Physiology and Biophysics and as a professor of basic sciences at the center. Kitajewski previously held various positions at Columbia University in New York, NY, including head of the Division of Reproductive Sciences in the Department of Obstetrics and Gynecology. His research has uncovered mechanisms of embryonic, ovarian, retinal, and tumor angiogenesis.

Survival Factors ID'd for Patients with Blood Cancer + COVID-19

Researchers launched the American Society of Hematology (ASH) Research Collaborative COVID-19 Registry for Hematology in April 2020 to gather real-time data on patients with hematologic malignancies who develop COVID-19 (see www.ashresearchcollaborative.org/s/covid-19-registry). Now, an analysis of the data reveals that around a third of patients with blood cancers who required hospitalization for COVID-19 died. Risk factors included older age, forgoing intensive treatment, and poor prognosis before infection. Findings were presented at the 2020 ASH Annual Meeting, held virtually December 5–8.

As COVID-19 emerged in early 2020, "many ... were concerned initially that individuals with underlying cancer—and especially those with hematologic malignancies—could be at increased risk of adverse outcomes following COVID-19 infection," said William Wood, MD, MPH, of the University of North Carolina (UNC) at Chapel Hill, who presented the results. Preliminary reports from China and the UK suggested that this may be the case, prompting researchers to launch the ASH COVID-19 registry to investigate further.

Wood reported on 656 patients with hematologic malignancies: a little more than half had leukemia and a quarter had lymphoma. The mortality rate was 20% overall and 33% for those who required hospitalization. COVID-19 severity and death were linked to cancer status: 50% of patients in remission developed moderate or severe infection and 13% died, compared with 69% and 21%, respectively, of those receiving initial treatment. Those with relapsed or refractory cancer fared the worst, with 79% developing moderate or severe COVID-19 and 36% dying. Age was also a risk factor: 47% of patients ages 19 to 39 had moderate or severe COVID-19 and 6% died, compared with 62% and 18%, respectively, of those ages 40 to 69. Of patients 70 and older, 70% developed moderate or severe COVID-19 and 33% died.

Further, patients expected to live longer than 12 months prior to COVID-19 infection had a 58% rate of moderate or severe COVID-19 and a 13% rate of death, compared with 79% and 51% in those expected to live for less than 12 months. In addition, those who declined treatment in the intensive care unit had a mortality rate of 73%, compared with 13% for those who did not forgo such care.

"One of the important take-home findings from our study so far is that patients with underlying hematologic malignancies are in fact a medically vulnerable population when it comes to complications from COVID-19 infection, including severity and mortality," Wood said. As the registry continues to accrue patients, he hopes to explore questions related to specific blood cancers, treatments, and risk factors.

The data "are important and informative," said Ross Levine, MD, of Memorial Sloan Kettering Cancer Center in New York, NY, who is not involved in the work. "An effort like this highlights the important link between blood cancers and COVID-19 severity," he added, although more data are needed to understand disease- and treatment-related interactions and implications.

For Alisa Wolberg, PhD, of UNC Chapel Hill, who is also not connected to the registry, it fills a significant knowledge gap. "We can't begin studies to understand molecular mechanisms and potential treatments and approaches until we understand severity and mortality—and risks for adverse clinical outcomes."

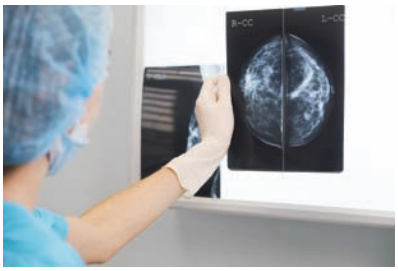
The registry, which is open to patients with other hematologic disorders, also illustrates the value of large, coordinated research efforts. "It shows what the hematology/heme malignancies community can do when it works together," Levine said. "Such efforts—and the cooperation they require—are what our patients expect and what the field needs." –*Catherine Caruso* ■

As Pandemic Continues, Screening Concerns Grow

When the COVID-19 pandemic began, oncologists were mildly concerned about how it might affect cancer screening (Cancer Discov 2020;10:OF4). Many months later, amid the continuing pandemic, their concerns about how extensively COVID-19 has disrupted screening have grown—along with their fears about the consequences.

"There's so much attention on COVID-19—and rightfully so—but I think people are forgetting that preventive services need to continue," says Folasade May, MD, PhD, of the University of California, Los Angeles (UCLA).

UCLA and most other medical centers paused colorectal cancer screening for several weeks in March and April, leading to 90% fewer colonoscopies nationwide than usual. "It was just astounding," May says. "It was as



though someone took all the endoscopes overnight." Moreover, colorectal cancer diagnoses dropped by 32%, even though "we know cancer didn't stop."

Similarly, breast cancer screening largely halted. Constance Lehman, MD, PhD, of Massachusetts General Hospital (MGH) in Boston, estimates that more than 90% of mammograms were canceled in the United States due to the shutdown, including about 15,000 at MGH alone. The result: About half as many breast cancers as usual were diagnosed in April.

Skipped screenings or lengthy delays are concerning, May says, because the survival rate for stage I colorectal cancer is 90%, compared with 11% to 15% for stage IV disease. "I think, unfortunately, we'll have later stage at time of diagnosis for a while."

Lehman has already seen this play out at MGH, where more than 90% of patients diagnosed with breast cancer through screening typically have early-stage disease, a percentage that has dropped to around 65%. Also concerning, Tari King, MD, of Brigham and Women's Hospital (BWH) in Boston has patients who felt a breast lump early in the pandemic but waited 6 or 7 months to seek care, resulting in more advanced disease.

Although screening centers now have COVID-19 safety measures in place, some patients are hesitant to reschedule. To combat this, providers are educating patients about precautions they're taking, and May emphasizes that no patients screened at the UCLA endoscopy unit have contracted coronavirus. "We're trying to use a data-driven approach to help patients feel [comfortable] coming in," she says.

Eric Flenaugh, MD, of Morehouse School of Medicine and Grady Hospital in Atlanta, GA, who saw lung cancer screening drop by about 50%, has turned to public service announcements and a Facebook Live event to draw patients back.

Concerns remain, however, that that won't happen as patients juggle work and childcare—and deal with challenges such as losing health insurance. In particular, the pandemic may increase existing screening disparities for Black and Latino patients, who are disproportionately essential workers. "I'm a little bit worried that we're going to lose some of the success we've had in minimizing disparities," May says.

King agrees. "The underrepresented minority population is the group that is not rescheduling" breast cancer screening, she says.

Flenaugh largely cares for medically underserved African American patients, who are at higher risk of disease yet often resistant to lung cancer screening. His center uses automatic reminders and presses primary care physicians to recommend screening. "Every institution is going to have to assess its patient population and come up with strategies to get these patients back in," he says.

Yet there are some positive signs: May and Flenaugh are seeing screening rates for colorectal and lung cancer, respectively, rebound at their institutions. Breast cancer screening at MGH and BWH now tops 100% of the usual volume, in part due to centers opening on nights and weekends.

However, Flenaugh worries that screening may flag as coronavirus cases balloon again. "We will prioritize, we will take care of the acutely ill, we will get through this crisis," he says, "but we also need to stay preventative." *–Catherine Caruso* ■

MPN Driver Mutations May Occur *In Utero*

A lingering question regarding myeloproliferative neoplasms (MPN)—including polycythemia vera, essential thrombocythemia, and myelofibrosis—is how rapidly they develop. Many patients with MPNs present with normal blood counts just months before diagnosis, supporting a rapid-development model. However, driver mutations are present in the blood of healthy individuals with age-related clonal hematopoiesis, and these may slowly or never evolve into cancer.

"As physicians, some of the commonest questions we get asked by our patients with blood cancers are, 'How long have I had it for?' and 'How fast did it grow?'" said Jyoti Nangalia, MD, PhD, of the Wellcome Sanger Institute in Hinxton, UK, in a presentation at the 2020 American Society of Hematology Annual Meeting, held virtually December 5–8. Nangalia and her team set out to answer this question using genomic studies—generating highly provocative findings.

The group performed genomic analyses on bone marrow or peripheral blood samples collected from 10 patients diagnosed with MPNs between the ages of 20 and 76. These samples were used to grow single cell–derived hematopoietic colonies, which were subjected to whole-genome sequencing, enabling construction of phylogenetic trees for each patient's clones.

Results from three of the patients, all of whom harbored the most common driver mutation in MPNs, *JAK2*^{V617F}, are illustrative. In a patient diagnosed with essential thrombocythemia at age 20, the *JAK2*^{V617F} mutation occurred between 6.2 weeks after conception and 1.3 years of age. In a patient with polycythemia vera diagnosed at age 31, the *JAK2*^{V617F} mutation became established between 4.2 weeks postconception and 8.6 years of age. Even in the third patient, diagnosed with polycythemia vera at age 65, the mutation was entrenched between 1.8 weeks after conception to 11.4 years of age. The upshot: MPN driver mutations can occur very early in life, perhaps even *in utero*, and may take decades to progress to full-blown MPNs.

"At any one snapshot in time in our life, the mutations within individual cells represent natural barcodes that can be used to trace back the ancestry of the cells right to the start of life," Nangalia explained. Using the phylogenetic trees to depict the relative timing of driver-mutation acquisition, the absolute timing of mutation acquisition was determined using patient- and clone-specific mutation rates, revealing the age range during which the mutations likely occurred.

The rate of a clone's growth determined the time between driver mutation and diagnosis. Slower-growing clones could take 50 years to evolve into MPNs, whereas faster-growing clones could become MPNs within 10 years. "For slow-growing *JAK2*[-mutant] clones, with sensitive assays, we would