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.

“Of the important take-home findings from our study so far is that patience 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 30% fewer colonoscopies nationwide than usual. “It was just astounding,” May says. “It was as
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 thrombocytopenia, 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, JAK2V617F, are illustrative. In a patient diagnosed with essential thrombocytopenia at age 20, the JAK2V617F 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 JAK2V617F 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...