Studies Highlight Progress in Preventing and Treating Blood Cancers and Pre-Cancerous Conditions

Advances show promise for patients with smoldering multiple myeloma, chronic lymphocytic leukemia and acute myeloid leukemia.

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Studies being presented at the 66th American Society of Hematology (ASH) Annual Meeting and Exposition highlight progress in preventing and treating blood cancers.

“It’s very encouraging to see advances being made across the continuum of care for blood cancers,” said Surbhi Sidana, MD, an associate professor of medicine at Stanford University in California, who moderated the briefing Diagnosing and Treating Blood Cancers and “Almost” Cancers.

“In this set of studies, investigators are focused on improving our understanding of environmental exposures that can increase cancer risk, ascertaining whether early intervention can improve outcomes for patients with a high-risk precancerous condition, identifying promising new treatment approaches for patients for whom existing options fall short, and shedding light on the ways in which socioeconomic factors may limit patients’ access to a potentially life-saving treatment,” Dr. Sidana said.

In the first study, the drug daratumumab [Darzalex Faspro] cut the risk of disease progression by half in patients who faced a high risk of developing multiple myeloma (a cancer of plasma cells, which are found in the bone marrow and are part of the immune system) within two years.

The second and third studies involved patients with chronic lymphocytic leukemia (CLL), the most common form of leukemia in adults in the United States. In previously untreated patients, a combination regimen of two oral drugs significantly lengthened the time until the disease worsened and caused fewer adverse effects compared with a standard treatment regimen. And in early results of an ongoing trial, patients with returning CLL after at least two prior treatments responded well to epcoritamab [Epkinly], a biologic agent that is a bispecific CD20/CD3 T cell engager.

In the fourth study, researchers found that first responders who worked at the World Trade Center site following the September 11, 2001, attacks were three times more likely to have genetic changes associated with an increased risk of blood cancer compared with non-exposed first responders or members of the public. Those with the genetic changes also have as much as a five-fold increased risk for leukemia.

And in the last study, researchers showed that, for patients with acute myeloid leukemia, socioeconomic factors can limit access to a potentially curative transplant of blood-forming stem cells from a healthy donor. Patients were less likely to receive such a transplant and more likely to die without receiving one if they lived in neighborhoods where more residents had less than a high school education, had incomes below the federal poverty level, or received benefits from federal assistance programs.

Daratumumab Cuts Risk of Progression by Half in Smoldering Multiple Myeloma

Abstract 773: Phase 3 Randomized Study of Daratumumab Monotherapy Versus Active Monitoring in Patients with High-Risk Smoldering Multiple Myeloma: Primary Results of the Aquila Study

Patients at high risk for developing multiple myeloma who received the drug daratumumab for up to three years saw a 51% reduction in their risk of disease progression compared with similar patients who were actively monitored but not treated.

“Compared with active monitoring, single-agent treatment with daratumumab had an acceptable safety profile and showed a clinically meaningful benefit in preventing or delaying progression to active multiple myeloma in high-risk patients,” said principal investigator Meletios A. Dimopoulos, MD, professor and chairman of the department of clinical therapeutics at the National and Kapodistrian University of Athens School of Medicine. “These results represent a new option for high-risk patients and their physicians to consider when weighing the pros and cons of treatment versus active monitoring.”

Patients enrolled in the AQUILA study, a randomized phase III clinical trial conducted in 24 countries, had been diagnosed with high-risk smoldering multiple myeloma, a precancerous condition with features that put them at more than 50% risk of developing active cancer within two years. The decision to treat these patients or not is controversial among hematologists. Active monitoring, in which patients are closely evaluated by their doctors for any signs that their condition is getting worse, is currently the standard of care.

A total of 390 patients were enrolled. Patients’ median age was 64 and 48% were men. Patients were randomly assigned to receive either subcutaneous daratumumab every 28 days or active monitoring for up to 36 months or until their condition progressed to multiple myeloma, whichever came first.

The study’s primary endpoint was the elapsed time between randomization to treatment and a

multiple myeloma diagnosis. Disease progression was assessed by an independent review committee using internationally accepted diagnostic criteria. Secondary endpoints included patients' overall response rate, progression free survival on first-line treatment, and overall survival.

After a median follow-up of 65.2 months (about five and a half years), Dimopoulos and his colleagues estimated that 63.1% of the patients assigned to daratumumab had not progressed to active multiple myeloma at five years, compared with 40.8% of those assigned to active monitoring. For patients who received active monitoring, the median time to a multiple myeloma diagnosis was 41.5 months (about three and a half years).

The overall response rate was 63.4% among patients receiving daratumumab, compared with 2.0% for those being actively monitored. In the daratumumab group, 33% of patients began treatment for active multiple myeloma, compared with 52% of those in the active monitoring group.

Adverse events requiring treatment occurred in 40.4% of patients who received daratumumab, compared with 30.1% of those who were actively monitored. In both groups, the most common moderate-to-severe adverse effect was high blood pressure. A total of 41 patients died, 15 (7.7%) of those treated with daratumumab, compared with 26 (13%) who received active monitoring. This difference was statistically significant.

"This is the first study to show improved outcomes with an agent that is not chemotherapy in patients with a myeloma-related condition. Furthermore, the observed benefit in the overall survival of the daratumumab-treated patients is very encouraging," Dr. Dimopoulos said.

Daratumumab is a biologic therapy made from living cells that works by attaching to proteins found on the surface of cancer cells. It both kills cancer cells directly and stimulates cells from the patient's immune system to multiply and kill cancer cells. Daratumumab is approved by the U.S. Food and Drug Administration for use either alone or in combination with standard-of-care drug regimens for patients with newly diagnosed multiple myeloma or myeloma that has come back or not responded to other treatments.

Dr. Dimopoulos cautioned that the findings apply only to patients whose smoldering multiple myeloma has specific features that place them at the highest risk for developing active cancer. Future studies should test whether using daratumumab in combination with other agents can further improve outcomes for these patients, he said.

This study was funded by Janssen Research & Development, LLC, a sister company of Janssen Biotech, Inc., which manufactures daratumumab. Both companies are subsidiaries of Johnson & Johnson.

The study was simultaneously published in the New England Journal of Medicine.

Combination of Two Oral Agents Improves Progression-Free Survival in Previously Untreated Chronic Lymphocytic Leukemia

Abstract 1009: Fixed-Duration Acalabrutinib Plus Venetoclax with or without Obinutuzumab Versus Chemoimmunotherapy for First-Line Treatment of Chronic Lymphocytic Leukemia: Interim Analysis of the Multicenter, Open-Label, Randomized, Phase 3 AMPLIFY Trial

Among patients with previously untreated chronic lymphocytic leukemia, those who received a combination regimen of the oral medications acalabrutinib [Brukinsa] and venetoclax [Venclexta] had significantly better survival without their cancer getting worse and experienced fewer serious adverse events than patients who received one of two standard multidrug treatment regimens for CLL. Patients who also received a third agent, obinutuzumab [Gazvya], had even better survival free of disease progression, but also experienced a higher rate of serious adverse events.

“The study met its primary endpoint, demonstrating superior progression-free survival (PFS) for the acalabrutinib-venetoclax combination regimen compared with standard therapy, said principal investigator Jennifer R. Brown, MD, PhD, director of the CLL Center at Dana-Farber Cancer Institute and the Worthington and Margaret Collette Professor of Medicine in the field of Hematologic Oncology at Harvard Medical School in Boston. “Findings were similar when obinutuzumab was added to the two oral agents, and both regimens had manageable safety profiles.”

The acalabrutinib-venetoclax combination offers the first fixed-duration regimen consisting of all oral agents for patients with previously untreated CLL that is expected to be approved in the U.S., Dr. Brown explained. “It’s a simple regimen that will be easier for patients to take,” she said.

CLL is a cancer that starts in the blood-forming cells of the bone marrow. It is the most common form of leukemia in adults in the United States, with around 19,000 new cases diagnosed annually, mostly in people aged 65 or older. It is more common in men than in women. Roughly half of patients with CLL carry mutations in a gene from a family of genes known as IgHV; in these patients, the cancer tends to grow more slowly and, with treatment, can go into remission for many years. In patients with unmutated IgHV, the cancer is more aggressive and tends to relapse more quickly after treatment.

Treatment regimens for CLL have included acalabrutinib and a slightly older drug, ibrutinib, which are in a class known as BTK inhibitors, and venetoclax, which is in a class known as BCL2 inhibitors, said Dr. Brown. However, the BTK inhibitors usually need to be taken indefinitely, which can lead to an accumulation of adverse effects, she said. Venetoclax is often combined with obinutuzumab, which is given as an infusion, a regimen that can be burdensome for patients, as it involves more clinic visits, Dr. Brown said.

This study, known as AMPLIFY, tested the effectiveness of combining the BTK inhibitor acalabrutinib with the BCL2 inhibitor venetoclax, and adding obinutuzumab to the two oral medications, in patients with previously untreated CLL. The randomized phase III clinical trial was

conducted in 27 countries.

A total of 867 patients (median age 61, 64.5% male) were randomly assigned to one of three study arms. Patients in Arm A received acalabrutinib and venetoclax (AV); in Arm B, acalabrutinib, venetoclax, and obinutuzumab (AVO); and in Arm C, the control arm, one of two combination regimens chosen by their doctor: fludarabine, cyclophosphamide, and rituximab (FCR) or bendamustine and rituximab (BR).

Around 60% of patients enrolled in the trial had unmutated IgHV. Patients with the highest risk CLL, in which a gene called TP53 is mutated or deleted, were not enrolled in the AMPLIFY trial because this form of the disease usually does not respond to the chemotherapy used in the control arm of the trial, Dr. Brown said.

PFS, the primary endpoint, was defined as the elapsed time from random assignment to worsening of the cancer among patients in Arm A (AV) compared with those in Arm C. Disease progression was assessed by an independent review committee using internationally accepted criteria. Secondary endpoints included PFS in Arm B (AVO) versus Arm C. All patients were treated for 14 months or until their cancer showed signs of worsening.

After a median follow-up period of 41 months, both the AV and AVO regimens showed a statistically significant improvement in PFS compared with the control regimen of FCR or BR. Dr. Brown and her colleagues estimated that 76.8% of patients who received AV and 83.1% of those who received AVO were free of disease progression at three years, compared with 66.5% of patients who received FCR or BR.

Serious adverse events occurred in 24.7% of patients who received AV, 38.4% of those who received AVO, and 27.4% of those who received FCR or BR. A low white blood cell count was the most common serious adverse event across all three treatment arms. The trial was carried out during the COVID-19 pandemic and a total of 56 patients (10 in the AV group, 25 in the AVO group, and 21 in the control group) died of COVID complications.

“The addition of obinutuzumab to acalabrutinib and venetoclax improved efficacy but also led to more adverse effects and more COVID deaths,” Dr. Brown said. “Our next steps will include trying to better understand which patients get the most benefit from adding obinutuzumab and what factors lead to some patients relapsing sooner.”

A limitation of the study is that FCR and BR, the combination regimens used to treat patients assigned to the control group, which were considered to be the standard of care for initial treatment of CLL when the AMPLIFY trial began in 2019, are no longer considered standard of care in the U.S. This is a common challenge for clinical trials, Dr. Brown said, as standards of care can evolve quickly whereas it usually takes several years to obtain results from a large clinical trial. She noted that although FCR has higher rates of adverse effects than some other therapies, it remains a highly effective treatment option that is widely used around the world and can be curative in a subset of patients.

This study was funded by AstraZeneca, the manufacturer of acalabrutinib.

High Response Rate, Manageable Adverse Effects Seen with Epcoritamab in Pretreated R/R CLL

Abstract 883: Epcoritamab Monotherapy in Patients (Pts) with Relapsed or Refractory (R/R) Chronic Lymphocytic Leukemia (CLL): Results from CLL Expansion and Optimization Cohorts of Epcore CLL-1

In early results from a nonrandomized study, the biologic agent epcoritamab, which leverages patients' own immune systems to find and kill cancer cells, showed promise in patients with chronic lymphocytic leukemia that had come back or not responded to at least two prior treatments.

"In heavily pretreated CLL, single-agent epcoritamab had a high overall response rate and a manageable safety profile," said principal investigator Alexey Danilov, MD, PhD, a professor in the department of hematology & hematopoietic cell transplantation at City of Hope National Medical Center in Duarte, California.

Two classes of targeted drugs known as BTK and BCL2 inhibitors are the standard of care for both previously untreated CLL and CLL that has come back after treatment, Dr. Danilov said. However, some patients do not respond well to these agents. Moreover, in almost all patients with CLL, these classes of drugs eventually stop working.

"To date, no treatments have been shown in randomized trials to be effective for patients whose CLL has worsened after treatment with both BTK and BCL2 inhibitors," he said. "There is an unmet need for new treatment options for this group of patients."

Epcoritamab, which is given as an injection under the skin, belongs to a class of drugs known as bispecific T-cell engagers. It works by attaching to proteins on the surfaces of both cancer cells and healthy T cells (cells in the immune system that help kill cancer cells). This brings the cancer cells and the T cells closer to each other, which enables the T cells to more effectively kill the cancer cells. Epcoritamab is approved by the U.S Food and Drug Administration to treat two types of lymphoma that have come back or not responded to at least two prior therapies.

"CLL cells have learned how to persist in the body by making themselves invisible to the patient's immune system," Dr. Danilov said. "Epcoritamab essentially works as a bridge between the body's immune cells and the CLL cells, boosting the ability of the immune cells to find, attack, and kill the cancer cells."

The ongoing EPCORE CLL-1 trial is testing the effectiveness of epcoritamab in patients with CLL and other blood cancers that have come back after treatment with at least two different agents, including a BTK inhibitor. The trial, which is being conducted in 12 countries, will enroll a total of 184 patients.

The current study reports early results for the first 40 patients (median age 71.5, mostly male) enrolled in the trial. Most had CLL with features that make it more challenging to treat, such as a mutation in the TP53 gene or a chromosomal abnormality known as 17p deletion. Everyone was treated with the same dose of epcoritamab, with the first group (the EXP cohort, 23 patients) receiving the drug in three gradually increasing doses, while the second group (the OPT cohort; 17 patients), who were enrolled later, received it in four increasing doses.

The primary endpoint for the EXP cohort was the overall response rate (ORR), defined as the proportion of patients in whom signs of cancer either completely cleared or reduced by at least half. Secondary endpoints included the time until patients' cancer showed signs of worsening, overall survival, and minimal residual disease (MRD), which refers to cancer cells that remain in the blood or bone marrow at a level that can be detected only with highly sensitive tests. For the OPT cohort, the primary endpoints included the number and severity of new cases of common side effects.

In the EXP cohort, after a median follow-up period of 22.8 months, the ORR was 61%. Among responding patients, 39% had a complete response, meaning that signs of cancer completely cleared. For all patients in this cohort, the median time until their cancer showed signs of worsening was 12.8 months. After about 15 months of follow-up, an estimated 65% of patients (15 people) were still alive. Among 12 responding patients (52%) who underwent MRD testing, nine (75%) had undetectable MRD in tests based on the standard sensitivity level.

"The response rate was very impressive for a single agent, especially considering that most patients had already been treated with both BTK and BCL2 inhibitors without success and had disease features that are difficult to treat," Dr. Danilov said.

Low blood counts were common in patients in the EXP cohort. However, most patients had low blood counts when they enrolled in the study, Dr. Danilov said, suggesting that the low counts were often caused by the cancer rather than by the study treatment. Cytokine release syndrome, or CRS (which includes symptoms like fever, nausea, headache, rash, rapid heartbeat, low blood pressure, and trouble breathing), was the most frequent non-blood-related adverse effect, occurring in 96% of patients. In most cases, CRS was mild, Dr. Danilov said, and mostly occurred after the first full dose of epcoritamab. Other common side effects were diarrhea, fatigue, and swelling in the hands or lower legs. Four patients in the EXP cohort (17%) died, all of causes other than CLL.

Follow-up for patients in the OPT cohort, who were enrolled in the study later than those in the EXP cohort, was just 2.9 months. Because of the brevity of follow-up to date, data on the effectiveness of epcoritamab treatment in this cohort are not yet available, Dr. Danilov said. Eighty-four percent of patients had mild CRS; none had severe CRS. To date, no patients in the OPT cohort have died. No patients in either cohort have discontinued treatment because of adverse effects, Dr. Danilov said.

He cautioned that these are early results from just 40 patients. "We will need to treat more

patients, follow them for a longer period of time, and conduct randomized studies to validate these findings," he said.

"We also want to test epcoritamab in patients with CLL who have had fewer prior therapies," he said. "There is reason to believe it could be even more effective if used earlier in the disease course, when a patient's immune system is less compromised."

This study was funded by GenMab, co-developer of epcoritamab with AbbVie.

Study Finds Genetic Changes, Elevated Leukemia Risk in Ground Zero First Responders

Abstract 943: Elevated Clonal Hematopoiesis in Environmentally Exposed Responders Has Distinct Age-Related Patterns and Relies on IL1RAP for Clonal Expansion

First responders who worked at Ground Zero in the aftermath of the 2001 attacks on the World Trade Center in New York City were three times more likely to have genetic changes associated with an increased risk of blood cancer compared with other first responders or members of the public who were not exposed to Ground Zero.

Moreover, younger first responders (under age 60) who had worked at the site not only showed these genetic changes, which are rarely seen in people under 70, but the changes were unlike any previously seen in this condition, which commonly occur during normal aging. Ground Zero first responders with these genetic changes have as much as a five-fold increased risk for leukemia.

Interestingly, when researchers exposed laboratory mice to dust from Ground Zero at a level equivalent to what first responders were exposed to in an eight-hour shift, the mice developed the same genetic changes seen in the responders. In particular, exposing the mice to the toxic dust led to overproduction of a protein called IL1RAP, which stimulates inflammation and increases the risk of cancer development. Deleting the gene for this protein halted the precancerous genetic changes and expansion of mutant blood cells.

"Our study has shown not only an increased risk of developing leukemia in Ground Zero-exposed first responders, but also a distinct spectrum of precancerous genetic changes in younger exposed responders," said principal investigator Divij Verma, PhD, of Albert Einstein College of Medicine in the Bronx, New York. "We have also demonstrated that inflammation induced by exposure to toxic dust is the likely mechanism for these genetic changes, and that turning off the IL1RAP gene, in particular, may be a promising strategy to delay or inhibit the development of these genetic changes or prevent progression to leukemia."

The genetic changes, known as clonal hematopoiesis (CH), have no signs or symptoms and are generally detected only when a person undergoes genetic testing for another condition such as a solid tumor or an unexplained low blood count. CH occurs in about 10% of people aged 70 and older, but is rare in people under 70. Studies have shown that people with CH have about a 1% per year chance of developing leukemia or another blood cancer; they are also at elevated risk for

heart and liver diseases.

Dr. Verma and his colleagues collected blood samples from 988 firefighters and emergency medical personnel who were exposed to high levels of airborne dust, gases, and potential cancer-causing substances at Ground Zero and examined their genomes to determine how many had CH and how many of those with CH developed leukemia. On average, the blood samples were collected 10 years after exposure; at the time of the blood draw, the responders' median age was 56. The investigators then compared the Ground Zero-exposed responders with 255 firefighters who had not been at the site but had occupational exposures to pollutants and potentially toxic substances, and to 195 people from the general population who were not first responders and had not been at Ground Zero.

They found that 14% of the exposed first responders had CH, compared with 7% of firefighters and other people who had not been at Ground Zero. Even though DNMT3A and TET2 were the two most common mutated genes in Ground Zero-exposed responders, the subsequent spectrum of mutations was distinct in younger Ground Zero-exposed responders (i.e., those now aged under 60) and included APC (6.6%), KMT2D (4.8%), ATM (4.8%), PIK3CA (4.2%) CREBBP (3.0%), BRCA2 (2.4%), ERBB4 (2.4%), and ARID1A (2.4%), which have not been reported in any previous CH studies.

Notably, in the firefighters and other first responders who had no Ground Zero exposure, the risk of having CH was the same as for people who were not first responders and had not been to the site. Among Ground Zero-exposed first responders with CH, 3.7% developed leukemia, compared with 0.6% of those in the non-exposed comparison groups. Compared with exposed first responders without CH, those with CH had more genetic changes indicating an elevated risk for leukemia or another blood cancer, as well as increased levels of neutrophils and monocytes (types of white blood cells) and red cell width suggestive of greater inflammation.

All Ground Zero-exposed first responders with CH are being contacted and invited to visit the hospital to identify any health problems as early as possible and initiate treatment, if necessary, Dr. Verma said.

He and his team are conducting further research to identify any differences in exposures and their effects among first responders who worked at Ground Zero during the first three days of the disaster versus those who were there later. They are also working to identify the specific toxic components of the dust collected from Ground Zero, the mechanisms by which it causes genetic changes in exposed people, and whether these mechanisms and their effects are unique to Ground Zero exposure or have similarities with those seen in people exposed to wildfires, burn pits, and other environmental exposures.

A limitation of the study is that while deleting the gene for IL1RAP halted precancerous genetic changes in mice, no studies have yet been done to show whether this strategy will work in people. However, Dr. Verma said, IL1RAP is a potentially important target, as it inhibits signaling from several mediators of inflammation. Targeting IL1RAP holds significant potential for reducing

inflammation and combating inflammation-driven malignancies, he said.

This study was funded by grants from the U.S. Centers for Disease Control and Prevention and the National Institutes of Health.

Prospective Study Finds Social and Economic Factors Limit Access to Stem Cell Transplants for Patients with AML

Abstract 6: Impact of Socioeconomic Factors on Access to and Outcomes of Allogeneic Hematopoietic Cell Transplantation (allo-HCT) for Acute Myeloid Leukemia (AML): A Multi-Center Observational Study

Many patients with acute myeloid leukemia (AML) can be cured by a transplant of blood-forming stem cells from a healthy donor, known as an allogeneic hematopoietic cell transplant (HCT). Studies have shown, however, that for a variety of reasons HCT may not be equally available to patients with AML from all backgrounds.

A prospective study examining the impact of social determinants of health on access to and survival after allogeneic HCT for patients with AML has shown that patients living in neighborhoods where more residents had less than a high school education, had incomes below the federal poverty level, or received benefits from federal assistance programs were less likely to receive HCT and more likely to die without receiving it. Among patients who did receive HCT, social and economic barriers, particularly lower education and use of federal assistance programs, were linked with a modest increase in mortality.

“To the best of our knowledge, this is the first prospective, multi-center study to evaluate the impact of specific social determinants of health on access to HCT and survival outcomes,” said first author Natalie Wuliji, DO, an assistant professor at Fred Hutchinson Cancer Center in Seattle. “Our results could set the stage to help identify targeted interventions to improve access to HCT for patients with AML who face socioeconomic barriers.”

AML is a fast-growing cancer of the blood-forming cells in the bone marrow. Previous studies that looked back at the records of patients treated in the past have suggested that patients with AML who have lower incomes or fewer years of education, belong to minority racial or ethnic groups, or lack private health insurance face more barriers to obtaining HCT than other patients. Other research has shown that social determinants of health – defined as the conditions in which people live and work, such as low income, low education level, food insecurity, and housing instability – can significantly affect health outcomes.

“We found that social and economic barriers have a greater impact on the ability to receive a transplant or on the risk of death before transplant than on outcomes after the transplant,” Dr. Wuliji said. “These findings suggest that access to allo-HCT may help level the playing field for AML patients across socioeconomic backgrounds, though further studies are needed to confirm this.”

HCT is costly, available at a limited number of specialized centers, and involves a lengthy hospital stay, Dr. Wuliji said – all of which impose burdens on patients and families who have limited resources, difficulty taking time off work to travel for care, or limited health insurance coverage.

For this study, Dr. Wuliji and her colleagues followed 692 adult patients for a median of 4.5 years after their AML diagnosis. The patients were treated at one of 13 medical centers across the U.S. The researchers collected data on how many patients received HCT and how many died before and after receiving HCT. They classified patients by the zip code in which they lived and examined U.S. Census Bureau data for those zip codes on a range of social and economic factors. These included median household income, the percentage of adults aged 25 or older with less than a high school education, and the percentage of households receiving Supplemental Security Income (SSI, a federal program for people with disabilities and low-income older adults), or Supplemental Nutrition Assistance Program (SNAP) benefits (also known as food stamps).

The research team also documented patient-reported race as a proxy for exposure to discrimination. They then used statistical methods to evaluate the effects of these social and economic factors on the patients' likelihood of receiving HCT, dying without receiving HCT, and dying after HCT.

The patients' median age was 62; 43% were aged 65 or over and 43% were female. Most (77%) had newly diagnosed AML with features associated with a poor outlook. Across all zip codes, 7.3% had less than a high school education; 9.5% had incomes below the federal poverty level; 10.2% received SNAP benefits; and 4.2% received SSI. Most patients (86%) self-identified as white, 6% as Black, 3% as Asian, and 4% as another race. Overall, 46% of patients received HCT; among those aged 65 or over, 31% received HCT.

A total of 291 patients died without receiving HCT. The risk of dying without receiving HCT increased by 24% as the proportion of zip-code residents with less than a high school education increased by 10%, by 40% for each increase in the proportion of residents receiving SSI, by 18% for each 10% increase in the proportion with incomes below poverty, and by 14% for each increase in the proportion receiving SNAP benefits.

The likelihood of a patient receiving HCT decreased by 30% as the percentage of zip-code residents with less than a high school education increased by 10%; by 22% for each 10% increase in households receiving SSI; by 5% for each 10% increase in households with incomes below poverty; and by 9% for each 10% increase in households receiving SNAP benefits.

Compared with white patients, Asian patients had a 34% higher likelihood of receiving HCT, Black patients an 18% reduced likelihood, and those of other races an 11% reduced likelihood. However, given the small percentage of non-white patients in the study, it is difficult to draw definitive conclusions about the impact of race on study outcomes, Dr. Wuliji said. The likelihood of receiving HCT increased by 5% with a $25,000 increase in median income in the zip code.

Among patients who received HCT, the risk of dying after the procedure increased by 17% as the

percentage of zip-code residents with less than a high school education increased by 10%, by 22% as the percentage of households receiving SSI increased by 10%, and by 12% as the percentage receiving SNAP benefits increased by 10%. No increase in the risk of dying after HCT was seen for patients with incomes below poverty.

An ongoing trial aims to increase the participation of patients from groups underrepresented in clinical trials and to develop HCT-focused patient education materials, Dr. Wuliji said. Future plans include exploring novel ways to improve access to HCT for patients who live in neighborhoods with lower education levels or poverty.

The impact of social and economic barriers on mortality among patients receiving HCT needs to be confirmed in future studies, Dr. Wuliji said. Limitations of the study are that its findings on SDOH are based on zip-code level data rather than patient-level data and that patients who could not understand or read English were excluded because patients were required to complete questionnaires and surveys that were available only in English, she said.

This study was funded by grants from the Patient-Centered Outcomes Research Institute, the American Cancer Society, and the American Society of Hematology.

The study was simultaneously published in Blood.

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