Older adults with aggressive blood cancer are responsive to treatment and show prolonged survival: Study

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Standard of care treatment for acute myeloid leukemia (AML) is safe and effective for adults over 80, according to a study published in *Blood Neoplasia*. For roughly a quarter of patients, this treatment can durably

prolong survival.

AML is an aggressive and often deadly form of blood cancer that can be difficult to treat. For older adults with AML, the conventional treatment consists of a medication called venetoclax combined with a hypomethylating agent (HMA), also known as VEN-HMA. AML treatment is often intensive and can significantly suppress the immune system and put one at risk of other health complications. As a result, some adults with AML, especially those of advanced older age, may be considered ineligible to receive treatment at all and be recommended to pursue palliative care.

"Our study reveals that a significant portion of these patients at the extremes of older age still derive benefit from the VEN-HMA regimen—which is the standard of care for older AML patients and those who are ineligible to receive intensive chemotherapy," said Justin Watts, MD, a hematologist at the University of Miami Sylvester Comprehensive Cancer Center, in Miami, Florida, and the study's corresponding author.

"While acknowledging it certainly isn't for everyone, we hope our findings encourage health care providers to thoughtfully explore all treatment avenues for elderly patients with AML, rather than prematurely resorting to HMA alone, best supportive care, or hospice care."

Researchers sought to understand overall survival and remission rates among octo- and nonagenarians (those 80–90 and older) who received VEN-HMA treatment to determine its effectiveness. They analyzed electronic medical records from 154 patients with AML treated with VEN-HMA for the first time between March of 2015 and April of 2022 across six medical institutions in the United States and Italy. Participants had a median age of 82 (range 80-92) and 69% were male. Seventy-

seven percent of patients included in the study were newly diagnosed, 10% had relapsed or refractory AML, and for 14%, disease status was unknown.

Sixty-seven percent of patients started treatment with the standard dose and treatment schedule of VEN-HMA, and 72% of the cohort had subsequent modifications of their venetoclax dose or schedule after cycle 1 (e.g., reduction in venetoclax duration). Across the cohort, patients were administered a final median venetoclax dose of 400 mg for 21 days, repeated every 35 days. Patients who demonstrated a response to treatment received a final median venetoclax dose of 200mg of venetoclax for 21 days, in 35-day cycles.

Approximately 20 to 25% of all treated patients experienced prolonged survival, which encompassed roughly 40% of those who responded to treatment. Median overall survival was 8.1 months, and for those who responded to treatment, it was 13.2 months. At just under eight months follow-up, 23% of patients remained in remission, while 20% were still receiving treatment. Death rates within 30 and 60 days of treatment were 8.5% and 17%, respectively, comparable to VIALE-A.

For patients with newly diagnosed AML without a prior myelodysplastic syndrome (MDS), 73% achieved complete remission or complete remission with incomplete count recovery (CRc), a classification given when a patient's leukemia cell counts are undetectable, but blood cell counts have not fully returned to normal levels. For patients who achieved CRc, those who received a final venetoclax duration of 14 days or less per cycle had a better average survival time (median of 24.0 months).

Patients whose cancer cells had a mutation in TP53—a protein vital to preventing abnormal cell growth—exhibited poorer overall survival. Patients with a mutation in the NPM1 protein had very favorable

survival, and interestingly, patients with K/NRAS or FLT3-ITD mutations did not have inferior survival compared to those without.

Notably, this treatment regimen can lead to myelosuppression, reducing the bone marrow's ability to produce healthy blood cells and weakening the immune system. Older patients, especially those over 80, may be more vulnerable to experiencing myelosuppression, and because of this, researchers suggest reducing the dose and duration of treatment for those at increased risk.

"A second major theme here is that treating this patient population requires adjusting the dosage and duration of VEN-HMA," explained Dr. Watts. "Unlike typical adult AML cases, these patients exhibit lower tolerance to venetoclax, suggesting that they may benefit from a reduced dosage."

This study is limited by its retrospective format. Further, the median follow-up duration was approximately 7.7 months, and researchers acknowledge that their data might have been stronger if this was extended.

Researchers said they plan to study the optimal dose and treatment schedule for this population to further enhance health outcomes. They want to explore the relationship between minimal residual disease (MRD) and molecular subtype on venetoclax exposure and ultimately stopping venetoclax in a subset of durably responding patients. Researchers said they are also interested in developing a better understanding of how treatment affects quality of life.

More information: Venetoclax and Hypomethylating Agents in Octo- and Nonagenarians with Acute Myeloid Leukemia, *Blood Neoplasia* (2024). www.sciencedirect.com/science/ … ii/S2950328024000165

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