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Phase 3 QUAZAR AML-001 Trial Finds Oral Azacitidine Extends Survival in Older Adults with AML

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Results from the randomized, double-blind, placebo-controlled phase 3 QUAZAR AML-001 trial (NCT01757535) revealed that oral azacitidine (Onureg; CC-486) as maintenance was associated with significantly longer overall and relapse-free survival (RFS) as compared with placebo in older patients with acute myeloid leukemia (AML) who were in remission following intensive chemotherapy.[1]

Importantly, quality-of-life (QOL) measures were sustained throughout treatment.

"After intensive chemotherapy, the risk of AML relapse is high. Many older patients are not eligible to receive a stem cell transplant and so a less toxic option to reduce disease recurrence is desirable, rather than just being monitored and waiting for the disease to come back," Andrew H. Wei, MB, BS, PhD, of the Monash University Australian Centre for Blood Diseases and a Hematologist at Alfred Health, said in a press release.[2] "Based on the results of the QUAZAR study, it is very exciting to think that, by taking a tablet that is relatively well-tolerated, we can help reduce relapse risk and improve survival."

In the trial, 472 patients who were 55 years of age or older with AML in first remission after induction chemotherapy, with or without consolidation chemotherapy, who were not candidates for hematopoietic stem-cell transplantation (HSCT) at trial entry were randomized to receive either 300 mg oral azacitidine (n = 238) or placebo (n = 234) once daily for 14 days of each 28-day cycle.

The primary end point of the study was overall survival (OS) and key secondary end points included RFS and health-related QOL.

As of the data cutoff of July 15, 2019, 193 patients (81%) had discontinued treatment with oral azacitidine, and 208 (89%) had discontinued placebo. The median time to discontinuation was 11.4 months (95% CI, 9.8-13.6) and 6.1 months (95% CI, 5.1 to 7.4) in the oral azacitidine and placebo groups, respectively.

The median duration of treatment with oral azacitidine was 12 cycles (range, 1-80) compared with 6 cycles (range, 1-73) for placebo.

At a median follow-up of 41.2 months, median OS from randomization was significantly longer with oral azacitidine at 24.7 versus placebo at 14.8 months ($P < .001$). Additionally, median relapse-free survival was also significantly longer with oral azacitidine (10.2 months vs 4.8 months with placebo; $P < .001$).

Regarding safety, the most commonly reported grade 3/4 adverse events (AEs) were neutropenia (41% with oral azacitidine vs 24% with placebo) and thrombocytopenia (22% vs 21%, respectively). The most common serious AEs were infections, which were reported at rates of 17% and 8% for the oral azacitidine and placebo groups, respectively. Gastrointestinal AEs accounted for the most common grade 1/2 events

According to Wei, these data are likely to establish a new standard of care among older adults with AML.

"This is a very significant advance because the drug is easy to administer and means that adults with AML don't have to spend extra time in hospital," said Wei.

It is still unknown whether oral azacitidine may benefit patients with AML when used in other clinical contexts, thus its use for other indications requires further investigation. Results from an open-label, phase 2 study indicated that oral azacitidine may provide effective maintenance therapy following HSCT (NCT01835587), however larger, controlled trials are still needed.

References:

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2. Drug clinical trial improves survival for AML patients. News release. Monash University. Published December 29, 2020. Accessed January 6, 2021. https://www.monash.edu/medicine/news/latest/2020-articles/drug-clinical-trial-improves-survival-for-aml-patients