

General AML

## Phase II randomized study of high-dose LEN and AZA in newly-diagnosed AML

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This month, in *Haematologica*, [Bruno C. Medeiros](#) from [Stanford University School of Medicine](#), Stanford, CA, USA, and colleagues [published](#) results of their randomized open-label phase II study ([NCT01358734](#)) which compared the safety and efficacy of continuous high-dose lenalidomide (LEN), sequential azacitidine (AZA) and LEN or AZA alone in patients aged  $\geq 65$  years with newly diagnosed Acute Myeloid Leukemia (AML).

Overall, 88 newly diagnosed AML patients were randomized to receive either high-dose continuous LEN (n = 15, median age = 80 years), sequential AZA and LEN (n = 39, median age = 76 years) or AZA alone (n = 34, median age 75 years).

### Key Findings:

- All patients discontinued treatment in the high-dose LEN cohort due to adverse events (AEs [n = 4]), death (n = 3), progressive disease (n = 5), consent withdrawal (n = 6) and other reasons (n = 2)
- Thirty-seven patients in the sequential AZA plus LEN cohort discontinued treatment due to AEs (n = 7), lack of efficacy (n = 1), consent withdrawal (n = 6), death (n = 7), progressive disease (n = 11) and other reasons (n = 5)
- Twenty-nine patients in the AZA alone cohort discontinued treatment due to AEs (n = 3), lack of efficacy (n = 3), consent withdrawal (n = 3), death (n = 2), progressive disease (n = 13), non-compliance with study drug (n = 1) and other reasons (n = 4)
- One-year survival
  - High-dose LEN = 21% (95% CI, 0, 43%)
  - Sequential AZA and LEN = 44% (95% CI, 28, 60%)
  - AZA alone = 52% (95% CI, 35, 70%)
- Hazard of death in the first four-months post randomization
  - Patients in the high-dose LEN cohort had a higher hazard of death than patients in the AZA cohort; Hazard Ratio (HR) = 5.73,  $P = 0.002$
  - Patients in the high-dose LEN cohort had a higher hazard of death than patients in the sequential AZA plus LEN cohort; HR = 2.19,  $P = 0.071$
  - Patients in the sequential AZA plus LEN cohort had a higher hazard of death than patients in the AZA cohort; HR = 2.51,  $P = 0.081$

In summary, high-dose continuous LEN was not well tolerated and led to a high rate of discontinuation and an increased hazard of death compared to sequential AZA and LEN or AZA alone in patients aged  $\geq 65$  years with newly diagnosed AML.

Medeiros *et al.*, suggested that based on the early HR for death observed in their study, their data does not support the use of continuous high-dose LEN or sequential AZA plus LEN over AZA alone in patients aged  $\geq 65$  years with newly diagnosed AML.

### Abstract

Therapy of acute myeloid leukemia in older persons is associated with poor outcomes because of intolerance to intensive therapy, resistant disease and co-morbidities. This multi-center, randomized, open-label, phase-2 trial compared safety and efficacy of three therapeutic strategies in persons  $\geq 65$  years with newly-diagnosed acute myeloid leukemia: (1) continuous high-dose lenalidomide (N=15); (2) sequential azacitidine and lenalidomide (N=39); and (3) azacitidine (N=34) only. The efficacy endpoint was 1-year survival. Median age was 76 years (range, 66-87 years). Thirteen subjects (15%) had prior myelodysplastic syndrome and 41 (47%), adverse cytogenetics. One-year survival was 21% (95% confidence interval, 0, 43%) with high-dose lenalidomide, 44% (28, 60%) with sequential azacitidine and lenalidomide, and 52% (35, 70%) with azacitidine only. Lenalidomide at a continuous high-dose schedule was poorly-tolerated resulting in a high rate of early-therapy discontinuations. Hazard of death in the 1st 4 months was greatest in subjects receiving continuous high-dose lenalidomide; hazards of death thereafter were similar. These data do not favor use of continuous high-dose lenalidomide or sequential lenalidomide and azacitidine over the conventional dose and schedule of azacitidine only in persons aged  $\geq 65$  years with newly-diagnosed acute myeloid leukemia. The study is registered at ClinicalTrials.gov (NCT01358734).

### References

1. Medeiros, B. C. et al. Randomized Study Of Continuous High-Dose Lenalidomide, Sequential Azacitidine And Lenalidomide Or Azacitidine In Persons  $\geq 65$  Years With Newly-Diagnosed Acute Myeloid Leukemia. Haematologica. 2017 Nov 2. DOI: [10.3324/haematol.2017.172353](https://doi.org/10.3324/haematol.2017.172353). [Epub ahead of print].

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