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General AML

Phase II study of cladribine plus low-dose cytarabine alternating with decitabine in elderly patients with acute myeloid leukemia

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In the August 2018 issue of Lancet Haematology, a group of researchers from the MD Anderson Cancer Center, Houston, TX, published data from an open-label phase II study (NCT01515527), which is assessing a new low-intensity regimen of cladribine plus low-dose cytarabine (LDAC) alternating with decitabine in elderly or unfit patients with newly diagnosed acute myeloid leukemia (AML).

One hundred and eighteen elderly or unfit patients (median age = 69 years, range 65–73) with newly diagnosed AML were enrolled sequentially into this phase II study. Patients received cladribine plus LDAC for two 28-day cycles alternating with decitabine for two 28-day cycles for up to 18 cycles. For induction, patients received cladribine (5 mg/m^2 on days 1–5) plus LDAC (20 mg subcutaneously on days 1–10 [cycle A]). Patients who achieved remission then received a consolidation therapy consisting of cladribine (5 mg/m^2 on days 1–3) and LDAC (20 mg subcutaneously on days 1–10) alternating with decitabine (20 mg/m^2 intravenously on days 1–5 [cycle B]). The primary objective of the study was disease-free survival (DFS).

Key findings:

Efficacy

- Median follow-up: 37.2 months
- Objective response: 68% (80/118)
  - Complete response (CR): 58% (69/118)
  - CR with incomplete count recovery: 9% (11/118)
- Median duration of remission in responders: 14.7 months (7.0–not reached)
- Median overall survival in all patients: 13.8 months (6.9–28.6 months)
- Median OS in responders and non-responders: 16.2 *vs* 4.7 months
- Median DFS in all patients: 10.8 months (5.4–25.9 months)

Minimal residual disease (MRD)

- MRD was performed at the time of response assessment (at day 30 and 60) in 71 patients
- At day 30, 27 (52%) of the 52 patients who achieved objective response with MRD data were MRD negative
- At day 60, 13 (50%) of the 26 patients who achieved objective response with MRD data were MRD negative
- MRD positivity at day 60 associated with inferior OS

Safety

- The most common study-related adverse events were elevated total bilirubin, rash, and nausea
- Four-week mortality rate: 1% (1/118)
- 8-week mortality rate: 7% (8/118)

In summary, this new low-intensity regimen of cladribine plus LDAC alternating with decitabine was well tolerated and effective in elderly or unfit patients with AML. Additionally, “response to therapy was associated with longer survival”.

Key limitations of this study include the risk of selection bias, the inclusion criteria were not flexible enough to allow a broad enrollment of patients and lack of information about subsequent treatment for patients whose AML relapsed during the study.

References

1. Kadia T. M. *et al*. Cladribine and low-dose cytarabine alternating with decitabine as front-line therapy for elderly patients with acute myeloid leukaemia: a phase 2 single-arm trial. Lancet Haematol. 2018 Aug 13. DOI: 10.1016/S2352-3026(18)30132-7. [Epub ahead of print].