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General AML

ASCO 2018 | Venetoclax in combination with decitabine or azacitidine in elderly patients with AML induces durable response

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In February 2018, the AGP reported data as of cut-off date of June 2016 from a dual-stage, non-randomized phase Ib study (NCT02203773), which is assessing the safety and efficacy of venetoclax (VEN), a BCL2 inhibitor, in combination with decitabine (DEC) or azacitidine (AZA) in previously untreated older acute myeloid leukemia (AML) patients who are ineligible for standard induction therapy. Preliminary findings of this study demonstrated that VEN plus AZA or DEC was "well tolerated" in newly diagnosed patients with AML who are unfit for standard chemotherapy with promising preliminary efficacy and low early mortality rate.[1]

The updated data from this phase Ib study was presented by Courtney DiNardo at the 2018 American Society of Oncology (ASCO) Annual Meeting. Overall, 145 patients (median age = 74 years, range: 65–86) were enrolled and administered either VEN at a dose of 400 mg (n = 60), 800 mg (n = 74) or 1200 mg (n = 11) co-administered daily with 20 mg/m^2 of DEC on days 1–5 or 75 mg/m^2 of AZA on days 1–7, each 28-day cycle.[2]

Key findings:

- Safety
  - Most common grade 3–4 adverse events (AEs) occurring in ≥ 25% of patients include febrile neutropenia (43%), thrombocytopenia (24%), decreased WBC count (31%) and anemia 25%)
  - 30-day mortality rate: 3% (5/145)
- Efficacy
  - CR/CRi rate in all patients: 67% (97/145)
    - Median duration of CR/CRi: 11.3 months
  - CR/CRi rate in patients receiving VEN (400 mg) plus AZA: 76%
    - Median duration of response CR/CRi: NR (5.6–NR)
  - CR/CRi rate in patients receiving VEN (800 mg) plus AZA: 71%
  - Median OS: 17.5 months (12.3–NR)
  - Median OS in patients receiving 400 mg VEN: NR (11.0–NR)
- Minimal residual disease (MRD) assessment demonstrated that 29% (28/97) of patients with CR/CRi achieved MRD negative status (MRD negativity was defined as less than 10^{-3} leukemic cells at any measurement in bone marrow aspirates)

The speaker concluded by stating that the “preliminary data suggest that 400 mg of VEN has the optimal benefit-risk profile in combination with DEC or AZA, which demonstrated a tolerable safety profile with deep responses and durable outcomes in elderly patients with AML”. Courtney DiNardo discusses this study in an interview with the AML Global Portal.

References

1. DiNardo C. D. *et al.* Safety and preliminary efficacy of venetoclax with decitabine or azacitidine in elderly patients with previously untreated acute myeloid leukaemia: a non-randomised, open-label, phase 1b study. Lancet Oncol. 2018 Feb; 19(2): 216–228. DOI: 10.1016/S1470-2045(18)30010-X. Epub 2018 Jan 12.
2. DiNardo C. D. *et al*. Durable response with venetoclax in combination with decitabine or azacitadine in elderly patients with acute myeloid leukemia (AML). J Clin Oncol. 36, 2018 (suppl; abstr 7010).

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