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EHA 2018 | Panobinostat, decitabine and donor lymphocyte infusion post-allogeneic transplantation in newly diagnosed poor-risk acute myeloid leukemia

Cynthia Umukoro Gary Nolan | Jul 20, 2018

At the 23rd Congress of the European Hematology Association, there was an oral session on June 16, 2018, in which Jan Cornelissen from Erasmus Medical Center, Rotterdam, NE, on behalf of the HOVON group, presented data from a phase I/II feasibility study (HOVON 116 AML trial) evaluating panobinostat, decitabine, and donor lymphocyte infusion (DLI) post allogeneic hematopoietic stem cell transplantation (allo-HSCT) in newly diagnosed poor-risk acute myeloid leukemia (AML) patients.

The rationale behind this phase I/II study was to exploit the graft versus leukemia (GvL) effect efficiently by early timing of allo-HSCT and application of post-transplant epigenetic therapy and DLI, which can control residual leukemic tumor burden and enhance GvL by increased translation and expression of tumor-associated antigens in AML.

One hundred and forty patients with newly diagnosed poor-risk AML were registered on this study, of these 110 patients (median age = 59 years, range; 18–71) proceeded to allo-HSCT.

The main objective of the phase I portion of this study was to evaluate the feasibility of epigenetic therapy, consisting of either panobinostat (20 mg orally at days 1, 4, 8, 11 of a 4 week-cycle) alone or panobinostat combined with decitabine (10 or 20 mg/m^2 IV at days 1–3 of every 4 week-cycle) post-transplant.

Key findings:

- Dose-limiting toxicity (DLT)
  - Panobinostat alone (dose level 1): 2/13 patients experienced DLT of delayed recovery
  - Panobinostat and decitabine 20 mg/m^2 (dose level 2): 4/12 patients experienced DLT of delayed recovery
  - Panobinostat and decitabine 10 mg/m^2 (dose level 3): 1/11 patients experienced DLT of delayed recovery
  - Dose level 1 and 3 were concluded feasible

Following the feasibility study in the phase I portion of this study, the study proceeded to a phase II phase. The main objective of the phase II portion of the study was to evaluate the feasibility of allo-HSCT shortly followed by panobinostat and decitabine interspersed by DLI in patients with poor-risk AML < 115 days' post-transplant. It was observed that 55% (60/110) of patients received the schedule (panobinostat and decitabine) in time which indicates the feasibility of this study. Additionally, Panobinostat and decitabine post-transplant allowed for DLI administration in 57% (63/110) of transplanted patients which were administered within 115 days from transplant.

The second aim of this phase II portion was to assess efficacy in terms of overall and relapse-free survival, GvHD, non-relapse mortality (NRM), relapse and measurable residual disease (MRD).

Key findings:

- 1- and 2-year overall survival was 71% and 49%, respectively
- 1-and 2-year relapse free survival was 64% and 46%, respectively
    - 1-and 2-year RFS of patients in this phase I/II study compared favorably with historical matched HOVON patients (1- and 2-year RFS = 43% and 39%, respectively)
- 2-year NRM: 11%
- Forty-four patients died due to NRM (n = 17) and relapse (n = 27)
- GvHD after DLI was limited

In summary, allo-HSCT with GVHD-prophylaxis by cyclophosphamide post-transplant allows for early initiation of epigenetic therapy and DLI. Taken together, the findings of this study suggest an "enhanced GVL". The speaker, Jan Cornelissen discussed the findings of this phase I/II feasibility study in an interview with the AGP here.

References

1. Cornelissen J. *et al*. Panobinostat, decitabine, a donor lymphocyte infusion post allogeneic hematopoietic stem cell transplantation: The HOVON 116 study in newly diagnosed poor-risk AML patients. Abstract S858. 23rd Congress of the European Hematology Association; 2018 June 14–17, Stockholm, SE.