

General AML

## Transplant conditioning with treosulfan/fludarabine with or without TBI in patients with AML and MDS

 Anna Bartus  Cynthia Umukoro | Feb 06, 2018

In an article published in [Biology of Blood and Marrow Transplantation](#), [H. Joachim Deeg](#) from [Fred Hutchinson Cancer Research Center](#), Seattle, WA, and colleagues discussed results from their prospective randomized phase II study ([NCT01894477](#)), which assessed whether the addition of 2 Gy Total Body Irradiation (TBI) to treosulfan/fludarabine can reduce post-transplant relapse incidence and improve Progression-Free Survival (PFS) in patients with Acute Myeloid Leukemia (AML) or Myelodysplastic Syndrome (MDS).

This phase II study was initially designed for 80 patients. Patients were randomly assigned to receive either treosulfan (14 g/m<sup>2</sup>/day, Days -6 to -4) and fludarabine (30 mg/m<sup>2</sup>/day, Days -6 to -2) alone (Non-TBI arm) or with a single dose of 2 Gy TBI (Day 0 [TBI arm]). A planned preliminary analysis of ≥ 20 patients in each arm who were followed for ≥ 6 months, demonstrated that patients in the TBI arm had a significantly superior PFS ( $P = 0.04$ ) than patients in the non-TBI arm. As a result, enrolment into the Non-TBI arm was terminated. The protocol of the study was amended to enrol more patients and the remaining were enrolled in the TBI arm.

Thus, a total of 100 patients (median age = 57 years) with AML (n = 49), MDS (n = 49), and chronic myelomonocytic leukemia (n = 2) were enrolled in this study between December 2013 and July 2016. Patients were randomly assigned to the TBI (n = 65) and Non-TBI arm (n = 35).

### Key findings:

1-year Relapse rate in the TBI and Non-TBI arms respectively

- In all patients: 22% vs 34%, HR = 0.49,  $P = 0.06$
- In patients with AML: 16% vs 35%; HR = 0.31,  $P = 0.05$
- In patients with MDS: 27% vs 33%, HR = 0.11,  $P = 0.49$

1-year Overall Survival (OS) in the TBI and Non-TBI arms, respectively

- In all patients: 80% vs 69%, HR = 0.71,  $P = 0.34$
- In patients with AML: 84% vs 65%, HR = 0.40,  $P = 0.09$
- In patients with MDS: 76% vs 72%, HR = 1.28,  $P = 0.64$

1-year PFS in the TBI and Non-TBI arms, respectively

- In all patients: 68% vs 54%, HR = 0.64,  $P = 0.15$
- In patients with AML: 75% vs 53%, HR = 0.42,  $P = 0.06$
- In patients with MDS: 61% vs 56%, HR = 0.94,  $P = 0.88$

1-year non-relapse mortality (NRM) in all patient was 9% and did not differ between arms.

Overall, 27 patients died in the TBI and Non-TBI arms due to relapse (7 vs 10), GVHD (8 vs 2), organ failure (2 vs 1), and infection (1 vs 0).

The authors concluded by highlighting that their data confirmed the “excellent tolerability of fludarabine/treosulfan conditioning in patients with AML and MDS”. Furthermore, the addition of 2 Gy TBI to treosulfan/fludarabine appeared to benefit outcomes by reducing relapse risk without increasing toxicity or NRM.

Addition of TBI to fludarabine/treosulfan appeared to benefit patients with AML but had no significant effect in patients with MDS, which the authors noted was “consistent with biological and pathophysiological differences between AML and MDS”.

## References

1. Deeg H.J. et al. Transplant conditioning with Treosulfan/Fludarabine with or without TBI. A randomized phase II trial in patients with MDS and AML. Biology of Blood and Marrow Transplantation. 2017 Dec 20. DOI: [10.1016/j.bbmt.2017.12.785](https://doi.org/10.1016/j.bbmt.2017.12.785) [Epub ahead of print]

---

© 2018 Scientific Education Support Ltd. This PDF is provided for personal use only. For wider or commercial use, please seek permission from [secretariat@scientificeducationsupport.com](mailto:secretariat@scientificeducationsupport.com) and attribute the source as: <<http://www.amlglobalportal.com/medical-information/transplant-conditioning-with-treosulfan-fludarabine-with-or-without-tbi-in-patients-with-aml-and-mds>>