

## Cytoreduction should not uniformly precede allogeneic transplant for MDS

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MDS patients who are candidates for allogeneic transplantation are frequently offered cytoreductive therapies prior to transplant. In this talk, I will argue that *routine* cytoreduction prior to transplant is not supported by available evidence and can in some cases be counterproductive.

**Definitions:** “Cytoreduction” in the context of MDS can either refer to the administration of a hypomethylating agent, with or without venetoclax, or to conventional induction chemotherapy. The term is most commonly used to refer to patients with excess blasts, in whom the goal of cytoreduction is to reduce the blast count to less than 5% of bone marrow cellularity. In some cases, however, the term is used less precisely to refer to any administration of cytotoxic drugs, irrespective of blast count.

The use of pre-transplant cytoreduction can be considered in two distinct scenarios:

- 1. Cytoreduction should not generally be employed in MDS patients without excess blasts.** The primary benefit of cytoreduction in MDS is the prevention of progression to acute myeloid leukemia.
  - Patients without excess blasts are generally at low risk of imminent transformation, especially when transplant is planned in the near future, and thus do not derive this benefit.
  - In such patients, cytoreduction can lead to cytopenias and associated complications (infections, bleeding) that delay transplant (Kröger et al, JCO 2021).
- 2. In patients with excess blasts, the use of cytoreduction depends on the trajectory of disease**
  - Blast percentage should be interpreted in the context of MDS dynamics, and not as a static number.
  - In some patients, > 5% blasts does not connote imminent transformation to acute leukemia.
    - o This is frequently the case in MDS/MPN overlap cases in whom blasts are part of a spectrum of increased immature myeloid cells.
    - o It may also be the case in slowly progressive MDS in which the blast count is gradually increasing.
    - o In some older or frail patients with MDS, there is a limited window for administration of cytotoxic therapy, and it may be more productive to respond to an increasing blast count in these patients by moving quickly to transplant rather than spending time on cytoreduction.
  - On the other hand, patients with rapidly increasing blasts counts, or patients found to have blast counts > 10% at the time of MDS diagnosis, are likely in the process of AML transformation. In these cases, cytoreduction may help control disease and improve the likelihood of successful transplant, particularly in patients receiving reduced intensity conditioning regimens.
  - Of note, the American Society for Transplantation and Cellular Therapy’s guidelines for transplant in MDS patients do not recommend routine administration of cytotoxic therapy prior to transplant and rate the evidence supporting this practice a “C” (DeFilipp et al, TCT 2023).

### References:

DeFilipp Z, Ciurea SO, Cutler C, et al. Hematopoietic Cell Transplantation in the Management of Myelodysplastic Syndrome: An Evidence-Based Review from the American Society for Transplantation and Cellular Therapy Committee on Practice Guidelines. *Transplant Cell Ther.* 2023;29(2):71-81.

Kröger N, Sockel K, Wolschke C, et al. Comparison between 5-azacytidine treatment and allogeneic stem cell transplantation in elderly patients with advanced MDS according to donor availability (VidazaAllo Study). *J Clin Oncol* 2021;39(30):3318-3328.