

Triple-drug therapy for post-transplant management of multiple myeloma

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Researchers from the University of Chicago Medicine Comprehensive Cancer Center and colleagues in Poland report promising results from their ongoing ATLAS trial, published on January 12, 2023 in the journal

[*Lancet Oncology*](#).

The results of this study indicate that [maintenance therapy](#) (a term researchers use to describe therapy with aim to preventing disease progression or death) with a combination of three drugs, carfilzomib, lenalidomide, and dexamethasone (known as KRd) may improve progression-free survival (a term clinicians use to describe the time to disease progression or death) when compared to the current standard of single agent lenalidomide treatment in patients with newly diagnosed multiple myeloma who have undergone initial induction treatment followed by autologous stem cell transplantation.

ATLAS Phase 3 Trial

The ATLAS trial, is an investigator-initiated, open-label, randomized, phase 3 clinical study conducted at 12 academic and clinical centers in the United States and in Poland. Between June 10, 2016 and October 21, 2020, the study enrolled 180 patients who were randomly assigned to receive either KRd or lenalidomide alone. The key eligibility criteria included the completion of transplantation after any initial pre-transplantation therapy with no progression within twelve months from initiation of pre-transplantation therapy.

The KRd arm received either 8 or 36 cycles of KRd treatment based on the minimal residual disease (MRD) status—the amount of cancer cells that remain in the body during or after treatment—and presence or absence of disease risks for progression. Patients who had standard risk disease and achieved MRD-negativity at the end of 6 cycles of KRd maintenance, received a total 8 cycles of KRd followed by lenalidomide maintenance, the remaining patients continued KRd for 36 cycles followed by lenalidomide maintenance.

The primary endpoint of the study was progression-free survival, and the

secondary endpoints included MRD-negativity rates, safety, and tolerability. The study was coordinated by the University of Chicago in collaboration with investigators from the Polish Myeloma Consortium led by the first author of the report Dominik Dytfeld, MD, Ph.D.

After median follow-up of 33.8 months, median progression-free survival for the KRd arm was 59.1 months compared to 41.6 months for the lenalidomide arm, which represents a 49% reduction in the risk of progression or death. This risk reduction was observed despite a shorter duration (8 cycles) of KRd treatment in 44% patients on the KRd arm with standard risk and MRD-negativity after cycle 6. The improvement of progression-free survival was associated with higher rate of MRD-negativity in the KRd arm compared to the lenalidomide arm at the completion of 6 cycles (53% vs 31%). As expected, patients in the KRd-treated arm experienced higher rates of toxicity but the differences did not translate into higher rates of treatment discontinuation or dose reductions, the authors noted. Based on these results, investigators concluded that MRD- and risk-adapted KRd can be considered as a new option for post-transplant maintenance in newly diagnosed myeloma.

Overall, the efficacy and toxicity results of this study indicate a favorable therapeutic index, making KRd a compelling consideration for post-transplant treatment after autologous stem-cell transplantation, said [Andrzej Jakubowiak, MD, Ph.D.](#), the Director of the Myeloma Program at the University of Chicago and the overall Principal Investigator of the ATLAS study.

ATLAS Trial Limitations

Some of the limitations of the study included the low number of patients in both arms (which was sufficient to evaluate progression-free survival, the primary end-point of the study, but not the secondary outcomes), and interim nature of the published analysis.

Longer follow-up of the ATLAS study is required for confirmation of these results and to provide more information on the duration of MRD—negativity in both arms, outcome in the study subsets, including in high-risk patients, as well as on overall tolerability and overall survival, said Jakubowiak.

ATLAS Trial Results in Context

Investigators note that these interim results of phase 3 ATLAS trial are in line with the results of the phase 2 FORTE trial published in 2021, where an improvement in [progression-free survival](#) in the maintenance phase of the trial was reported with an addition of carfilzomib to lenalidomide in comparison with [lenalidomide](#) alone in patients who completed initial therapy with carfilzomib-based induction followed by transplant and consolidation or extended KRd induction with deferred transplant. Post-transplant treatment strategies are currently intensively evaluated in a number of ongoing randomized trials.

More information: Dominik Dytfeld et al, Carfilzomib, lenalidomide, and dexamethasone or lenalidomide alone as maintenance therapy after autologous stem-cell transplantation in patients with multiple myeloma (ATLAS): interim analysis of a randomised, open-label, phase 3 trial, *The Lancet Oncology* (2023). [DOI: 10.1016/S1470-2045\(22\)00738-0](https://doi.org/10.1016/S1470-2045(22)00738-0)

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