

Patients eligible for transplant

Meta-analysis of lenalidomide maintenance after autologous stem-cell transplantation

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Currently, the standard of care for healthy patients with Newly Diagnosed Multiple Myeloma (NDMM) is treatment with high-dose melphalan (HDM) followed by Autologous Stem-Cell Transplantation (ASCT). However, this is not curative and a prolonged course of maintenance therapy is required for long-term control. Lenalidomide treatment has been found to be a suitable agent as it has a tolerable safety profile and significantly prolongs Progression Free Survival (PFS). However, few of the Randomized Controlled Trials (RCTs) were powered to assess Overall Survival (OS). Therefore, in order to further evaluate the available data, a meta-analysis of three RCTs to assess the efficacy of lenalidomide maintenance therapy after ASCT (in NDMM), was conducted by [Philip McCarthy](#) from the [Roswell Park Cancer Institute](#), Buffalo, New York, and colleagues. Their findings were published in [Journal of Clinical Oncology](#) in July 2017.

The three RCTs chosen for analysis were the Cancer and Leukemia Group B 100104, the Gruppo Italiano Malattie Ematologiche dell'Adulto RV-MM-PI-209, and the IFM (Intergroupe Francophone du Myélome) 2005-02. The number of patients (pts) included in the study was 1,208; lenalidomide group (n=605) and placebo or observational group (n=603). The primary endpoint for the meta-analysis was Overall Survival (OS).

Key findings

- Median follow-up time = 79.5 months for OS
- Median OS: lenalidomide = not reached and placebo or observation group = 86.0 months; HR = 0.75 (95% CI, 0.63–0.90), P = 0.001
- Therefore, a 25% reduction in the risk of death with lenalidomide maintenance therapy was achieved
- Median PFS: lenalidomide = 52.8 months and placebo or observation = 23.5 months; HR = 0.48 (95% CI, 0.41–0.55)
- 7-year survival rate: lenalidomide = 62% and placebo or observation = 50%
- Pts alive at median follow-up of 79.5 months: lenalidomide = 64% and placebo or observation = 54%
- OS benefit was greater for lenalidomide maintenance patients when they had received lenalidomide-based induction treatment
- Median OS with extended follow-up: lenalidomide = 111 months vs. placebo or observation = 86.9 month; HR = 0.77, (95% CI, 0.65-0.91); P = 0.002
- PFS2: lenalidomide = 73.3 months vs. placebo or observation = 56.7 months; HR = 0.72 (95% CI, 0.62–0.84)
- Pts starting second myeloma treatment: lenalidomide group = 52.6% vs. placebo or observation = 70.8%
- Time to second treatment was delayed in the lenalidomide group vs. placebo or observation: HR = 0.72 (95% CI, 0.62-0.84)

- Treatment-emergent adverse events (TEAEs) resulting in discontinuation of treatment: lenalidomide= 29.1% and placebo or observation = 12.2%
- Time to death as a result of MM was longer for lenalidomide group vs. placebo or observation: HR = 0.66; 95% CI, 0.53-0.81 ($P<0.001$)

Conclusion

This meta-analysis confirmed significant PFS and OS benefit with lenalidomide maintenance after ASCT therapy in patients with NDMM, compared with patients receiving the placebo or in the observation group. Interestingly, the PFS benefit was lower in patients over the age of 60 and for females. Limitations of this analysis include the small number of trials included in the study and the differences between studies, such as length of maintenance therapy.

Abstract

Purpose: Lenalidomide maintenance therapy after autologous stem-cell transplantation (ASCT) demonstrated prolonged progression-free survival (PFS) versus placebo or observation in several randomized controlled trials (RCTs) of patients with newly diagnosed multiple myeloma (NDMM). All studies had PFS as the primary end point, and none were powered for overall survival (OS) as a primary end point. Thus, a meta-analysis was conducted to better understand the impact of lenalidomide maintenance in this setting. **Patients and Methods:** The meta-analysis was conducted using primary-source patient-level data and documentation from three RCTs (Cancer and Leukemia Group B 100104, Gruppo Italiano Malattie Ematologiche dell'Adulto RV-MM-PI-209, and Intergroupe Francophone du Myélome 2005-02) that met the following prespecified inclusion criteria: an RCT in patients with NDMM receiving ASCT followed by lenalidomide maintenance versus placebo or observation with patient-level data available and achieved database lock for primary efficacy analysis. **Results:** Overall, 1,208 patients were included in the meta-analysis (605 patients in the lenalidomide maintenance group and 603 in the placebo or observation group). The median PFS was 52.8 months for the lenalidomide group and 23.5 months for the placebo or observation group (hazard ratio, 0.48; 95% CI, 0.41 to 0.55). At a median follow-up time of 79.5 months for all surviving patients, the median OS had not been reached for the lenalidomide maintenance group, whereas it was 86.0 months for the placebo or observation group (hazard ratio, 0.75; 95% CI, 0.63 to 0.90; $P = .001$). The cumulative incidence rate of a second primary malignancy before disease progression was higher with lenalidomide maintenance versus placebo or observation, whereas the cumulative incidence rates of progression, death, or death as a result of myeloma were all higher with placebo or observation versus lenalidomide maintenance. **Conclusion:** This meta-analysis demonstrates a significant OS benefit and confirms the PFS benefit with lenalidomide maintenance after ASCT in patients with NDMM when compared with placebo or observation.

References

1. [McCarthy PL](#), et al. Lenalidomide maintenance after autologous stem-cell transplantation in newly diagnosed multiple myeloma: a meta-analysis. *Journal of Clinical Oncology*. 2017 Jul 25. DOI: [10.1200/JCO.2017.72.6679](#). [Epub ahead of print]