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Daratumumab, Lenalidomide, and Dexamethasone for Multiple Myeloma

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ABSTRACT

BACKGROUND

Daratumumab showed promising efficacy alone and with lenalidomide and dexamethasone in a phase 1–2 study involving patients with relapsed or refractory multiple myeloma.

METHODS

In this phase 3 trial, we randomly assigned 569 patients with multiple myeloma who had received one or more previous lines of therapy to receive lenalidomide and dexamethasone either alone (control group) or in combination with daratumumab (daratumumab group). The primary end point was progression-free survival.

RESULTS

At a median follow-up of 13.5 months in a protocol-specified interim analysis, 169 events of disease progression or death were observed (in 53 of 286 patients [18.5%] in the daratumumab group vs. 116 of 283 [41.0%] in the control group; hazard ratio, 0.37; 95% confidence interval [CI], 0.27 to 0.52; P<0.001 by stratified log-rank test). The Kaplan–Meier rate of progression-free survival at 12 months was 83.2% (95% CI, 78.3 to 87.2) in the daratumumab group, as compared with 60.1% (95% CI, 54.0 to 65.7) in the control group. A significantly higher rate of overall response was observed in the daratumumab group than in the control group (92.9% vs. 76.4%, P<0.001), as was a higher rate of complete response or better (43.1% vs. 19.2%, P<0.001). In the daratumumab group, 22.4% of the patients had results below the threshold for minimal residual disease (1 tumor cell per 10^5 white cells), as compared with 4.6% of those in the control group (P<0.001); results below the threshold for minimal residual disease were associated with improved outcomes. The most common adverse events of grade 3 or 4 during treatment were neutropenia (in 51.9% of the patients in the daratumumab group vs. 37.0% of those in the control group), thrombocytopenia (in 12.7% vs. 13.5%), and anemia (in 12.4% vs. 19.6%). Daratumumab-associated infusion-related reactions occurred in 47.7% of the patients and were mostly of grade 1 or 2.

CONCLUSIONS

The addition of daratumumab to lenalidomide and dexamethasone significantly lengthened progression-free survival among patients with relapsed or refractory multiple myeloma. Daratumumab was associated with infusion-related reactions and a higher rate of neutropenia than the control therapy. (Funded by Janssen Research and Development; POLLUX ClinicalTrials.gov number, NCT02076009.)

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*A complete list of investigators in the POLLUX trial is provided in the Supplementary Appendix, available at NEJM.org.

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