Addition of Daratumumab to Drug Regimens in the Treatment of Multiple Myeloma: A Systematic Review and Meta-analysis of Randomized Clinical Trials.

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Background

Despite improvement in the treatment of multiple myeloma (MM), a significant number of patients do not respond to the existing drug regimens. Daratumumab is a human monoclonal antibody targets CD38 that is overexpressed on multiple myeloma cells. Preclinical studies have shown that daratumumab induces Multiple Myeloma cell death through several mechanisms, including complement-dependent cytotoxicity (CDC), antibody-dependent cell-mediated cytotoxicity, antibody-dependent cellular phagocytosis, and apoptosis.

Objective

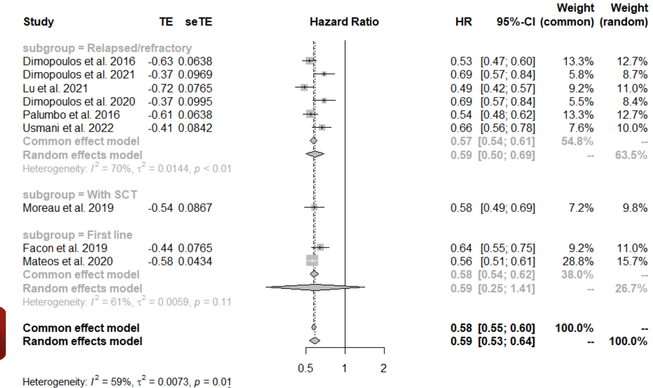
Assess the efficacy of daratumumab addition to drug regimens and stem cell transplant in patients with multiple myeloma tested in randomized clinical trials.

Methods

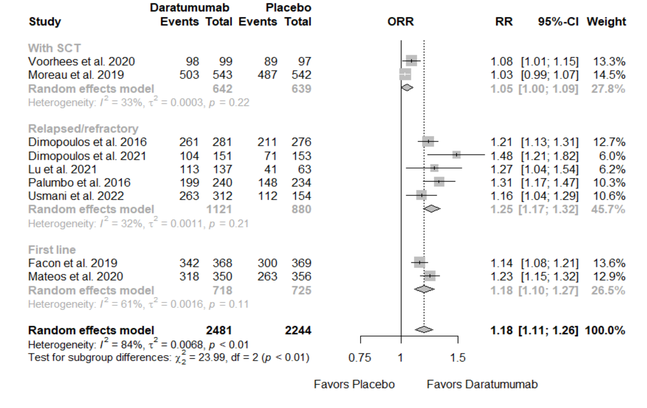
A literature search was performed on PubMed, Embase, Web of Science, Cochrane, and clinicaltrials.gov with Mesh and Emtree terms, “daratumumab” and “multiple myeloma” from the inception of data to 27 March 2022. “R” software was used to conduct the meta-analysis.

Results

4,564 articles were screened and 9 randomized clinical trials (RCTs, N=4,725) were included. All patients were adults (>18 years). Daratumumab was given to 2,481 patients in combination with regimens including lenalidomide+ dexamethasone (N=649), pomalidomide+ dexamethasone (N=151), bortezomib+ dexamethasone (N=377), bortezomib+ melphalan+ prednisone (N=350), bortezomib+ thalidomide+ dexamethasone (N=543), carfilzomib+ dexamethasone (N=312), and lenalidomide+ bortezomib+ dexamethasone (N=99) while no daratumumab was given to 2,244 patients. In relapsed/refractory multiple myeloma (RRMM) patients (N=2,001), RR of OR was 1.25 (95% CI=1.17-1.32, I^2=32%), CR was 2.46 (95% CI=2.02-3, I^2=31%), and HR of PFS was 0.59 (95% CI=0.50-0.69, I^2=70%) all in favor of daratumumab vs. control. In stem cell transplant (SCT) eligible patients (N=1,281), RR of OR was 1.05 (95% CI=1-1.09, I^2=33%), CR was 1.4 (95% CI=1.16-1.69, I^2=32%), and HR of PFS was 0.58 (95% CI=0.49-0.69, I^2=0%) all in favor of daratumumab vs. control as induction and consolidation therapy. In SCT ineligible patients (N=1,443), RR of OR was 1.18 (95% CI=1.10-1.27, I^2=61%), CR was 1.86 (95% CI=1.6-2.15, I^2=0%), and HR of PFS was 0.59 (95% CI=0.52-0.68, I^2=61%), all in favor of daratumumab vs. control as first therapy.



HR of PFS in randomized clinical trials. Subgroup 1= relapsed refractory patients, group 2= maintenance after Stem cell transplant. Group 3= newly diagnosed patients.



Summary

The addition of daratumumab to chemotherapy regimens or stem cell transplant significantly improved PFS and response rates in patients with RRMM, SCT eligible MM, or SCT ineligible MM. More RCTs are needed to confirm these results.

References

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