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941TiP **Pembrolizumab in combination with pomalidomide and low-dose dexamethasone in refractory or relapsed and refractory multiple myeloma (rrMM): Randomized, phase 3 KEYNOTE-183 study**

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Background: Even with use of proteasome inhibitors and immunomodulatory drugs for rrMM, response rates remain low. In the phase 1 KEYNOTE-023 study, pembrolizumab + lenalidomide and low-dose dexamethasone showed an acceptable safety profile and promising preliminary efficacy in patients with rrMM, supporting further evaluation of pembrolizumab with immunomodulatory agents. The randomized, open-label, phase 3 KEYNOTE-183 study (ClinicalTrials.gov, NCT02576977) was designed to compare the efficacy of pomalidomide and low-dose dexamethasone with or without pembrolizumab in patients with rrMM.

Trial design: Key eligibility criteria include age ≥18 years, confirmed diagnosis of MM with measurable disease, receipt of ≥2 lines of prior treatment, and documented progression on the last line of therapy. Patients must have been previously exposed to an immunomodulatory drug such as lenalidomide or thalidomide and a proteasome inhibitor such as bortezomib, ixazomib, or carfilzomib, and be refractory or relapsed/refractory to at least one. Patients are being randomly assigned 1:1 to receive pomalidomide 4 mg daily on days 1-21 and low-dose dexamethasone 40 mg daily on days 1, 8, 15, and 22 of repeated 28-day cycles, with or without pembrolizumab 200 mg every 3 weeks. Stratification is based on prior lines of treatment (2 vs ≥3) and disease status (refractory vs sensitive to lenalidomide). Treatment will continue until disease progression or unacceptable toxicity. Response will be assessed every 28 days by Clinical Adjudication Committee blinded central review and investigator review based on International Myeloma Working Group (IMWG) 2011 response criteria. Adverse events (AEs) will be assessed throughout treatment and for 30 days thereafter (90 days for serious AEs) and graded per NCI CTCAE v4.0. The primary end point is progression-free survival (PFS) based on IMWG criteria and overall survival; secondary end points are overall response rate, safety and tolerability, disease control rate, duration of response, and second PFS. KEYNOTE-183 will enroll ~300 patients from multiple sites.

Clinical trial identification: NCT02576977

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