POMALIDOMIDE + LOW-DOSE DEXAMETHASONE + DARATUMUMAB IN PATIENTS WITH RELAPSED AND/OR REFRACTORY MULTIPLE MYELOMA AFTER LENALIDOMIDE-BASED TREATMENT FAILURE

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Background

MM-014 (NCT01946477) was designed to assess outcomes with pomalidomide (POM)-based treatment in patients with lenalidomide (LEN) treatment failure immediately before study entry. POM + low-dose dexamethasone (LoDEX) + daratumumab (DARA) was approved in the United States for use in patients with multiple myeloma (MM) who have received ≥ 2 prior therapies, including LEN and a proteasome inhibitor. However, data on the use of this triplet regimen in earlier lines of therapy and immediately after LEN-based treatment are limited. Cohort B of the MM-014 trial is investigating POM + LoDEX + DARA in this setting.

Aims

To present efficacy and safety analyses of cohort B of the MM-014 trial in which POM + LoDEX + DARA was given as second-line or greater treatment in patients with relapsed and/or refractory MM (RRMM).

Methods

Patients with RRMM who had received 1 or 2 prior lines of treatment, had a LEN-based treatment immediately before the study, and had progressive disease (PD) were eligible. In 28-day cycles, patients received POM 4 mg/day orally on days 1 to 21 + LoDEX 40 mg/day (20 mg/day if aged > 75 years) on days 1, 8, 15, and 22 + DARA 16 mg/kg intravenously on the LoDEX dosing days of cycles 1 and 2, then days 1 and 15 of cycles 3 to 6, then day 1 of cycles 7 onward. Thromboprophylaxis was mandatory. The primary objective was overall response rate (ORR) by modified International Myeloma Working Group criteria. All patients provided informed consent.

Results

The intention-to-treat population (ITT) included 46 patients. The median follow-up was 7.8 months; 13 patients discontinued treatment because of PD (n = 7), adverse events (n = 2), or other reasons (n = 4). Patients were refractory to (n = 36 [78%]) or had relapsed after (n = 10 [22%]) LEN-based treatment. The median duration of prior LEN-based treatment was 23.6 months, and 20 patients (43%) received LEN 25 mg/day as their last LEN-based treatment. Efficacy outcomes in the ITT population and grade 3/4 treatment-emergent adverse events in the safety population (n = 46; defined as all patients who received ≥ 1 dose of study drug) are shown in the table. The ORR was 76.7% in the efficacy-evaluable population (n = 43; defined as all patients who received ≥ 1 dose of study drug and had ≥ 1 post-baseline assessment for response), 72.2% in LEN-refractory patients, and 75.0% in patients who received LEN 25 mg/day as their last LEN-based treatment. Clinical benefit (defined as complete response, very good partial response, partial response, or minimal response) was achieved in 78.3% of patients, and the 1-year progression-free survival rate was 76.9%. At baseline, 10 patients (21.7%) had grade ≥ 2 neutropenia. Grade 3/4 pulmonary embolism and peripheral neuropathy occurred in 1 patient each. Any-grade infusion-related reactions occurred in 13 patients. The primary reasons for dose interruptions were neutropenia (POM and DARA) and infusion-related reactions (DARA only).

Table. Efficacy and Safety

Outcomes, %	N = 46
Efficacy	
ORR	71.7
CR	4.3
VGPR	21.7
PR	45.7
Minimal response	6.5
Clinical benefit (CR + VGPR + PR + MR)	78.3
SD	8.7
PD	6.5
1-year PFS	76.9
Safety	
Grade 3/4 TEAEs (occurring in ≥ 10% of patients)	
Neutropenia	71.7
Thrombocytopenia	23.9
Anemia	17.4
Infection	28.3

CR, complete response; MR, minimal response; PFS, progression-free survival; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease; TEAE, treatment-emergent adverse event; VGPR, very good partial response.

Conclusion

These results indicate that POM + LoDEX + DARA is an effective and tolerable regimen when sequenced in earlier lines of therapy in patients with RRMM and in whom first- or second-line therapy with a LEN-based treatment failed.

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