SAFETY AND EFFICACY OF POMALIDOMIDE + LOW-DOSE DEXAMETHASONE IMMEDIATELY FOLLOWING LENALIDOMIDE-BASED TREATMENT FAILURE IN PATIENTS WITH RELAPSED AND/OR REFRACTORY MULTIPLE MYELOMA

Author(s): David S. Siegel, et al.

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Background

Pomalidomide (POM) + low-dose dexamethasone (LoDEX) is a standard of care for the treatment (Tx) of patients (pts) with relapsed and/or refractory multiple myeloma (RRMM). This regimen is being investigated in the MM-014 (NCT01946477) trial as a third-line Tx in pts with RRMM in whom last prior therapy with lenalidomide (LEN) failed (cohort A). As LEN becomes increasingly established in earlier lines of Tx, it is pertinent to demonstrate efficacy in pts who have exhausted the benefit of LEN as their last Tx.

Aims

To present safety and efficacy results of POM + LoDEX as a third-line Tx immediately after LEN in cohort A of the MM-014 trial, including a subset analysis of pts who were previously treated with proteasome inhibitors (PI) and/or bortezomib (BORT).

Methods

Eligibility criteria included age ≥ 18 y, documented MM, 2 prior Tx lines, and progressive disease (PD) after ≥ 2 cycles of second-line LEN-based therapy. Pts received 28-d cycles of POM 4 mg/d on d 1-21 + LoDEX 40 mg/d (20 mg/d if > 75 y) on d 1, 8, 15, and 22, with mandatory thromboprophylaxis. The primary endpoint was overall response rate (≥ partial response per modified International Myeloma Working Group criteria). The clinical benefit rate was defined as the percentage of pts achieving complete response, very good partial response, partial response, or minimal response. Key secondary endpoints included progression-free survival (PFS), safety, and second primary malignancies (SPMs). All pts provided informed consent.

Results

A total of 56 pts were enrolled in cohort A. Median age was 68 y, with 62.5% of patients aged > 65 y in the intention-to-treat (ITT) population (prior PI, 63.4% [n = 41]; prior BORT, 64.1% [n = 39]) and 57.1% overall (prior PI, 58.5%; prior BORT, 56.4%) were male. Most pts had an ECOG performance status of 0/1: 92.9%, 95.1%, and 94.9%, respectively. All pts were refractory or relapsed to their most recent LEN-containing regimen, and 91.1%, 92.7%, and 92.3% of pts were LEN refractory, respectively. A majority of patients had prior stem cell transplant: 64.3% overall, 63.4% with prior PI, and 61.5% with prior BORT. Cytogenetic data by FISH were available for 50 pts: 4 were positive for del(17p), 4 for t(4;14), and 2 for t(14;16). Median duration of prior LEN-containing Tx was 23.6 mos (range, 3.5-107.0 mos), and in 60.7% of pts, the most recent LEN dose was 25 mg/d. Median follow-up was 19.0 mos at the data cutoff (10/2/2017). Responses and PFS outcomes are reported in the table. Of the 56 pts in the ITT population, 52 discontinued Tx, 31 (59.6%) due to PD, 7 withdrawal, 5 adverse events (AEs), 3 lack of efficacy, 2 death, and 3 other reasons. The most common grade 3/4 treatment-emergent AEs included anemia (25.0%), neutropenia (10.7%), fatigue (14.3%), and infections (25.0%, including pneumonia [14.3%]). Grade 3/4 pulmonary embolism was reported in 2 pts, and 1 pt had an SPM. Similar safety results were noted in pts with prior exposure to PI or BORT.

Outcome	Cohort A (n = 56)	Prior PI Exposure (n = 41)	Prior BORT Exposure (n = 39)
ORR, %	33.9	31.7	28.2
VGPR	12.5	9.8	7.7
CBR, %	44.6	41.5	38.5
PFS, median, months			
ITT (n = 56)	9.6	7.9	7.9
EE (n = 53)	13.8		

BORT, bortezomib; CBR, clinical benefit rate; EE, efficacy evaluable; ORR, overall response rate; PFS, progression-free survival; PI, proteasome inhibitor; VGPR, very good partial response.

Conclusion

POM + LoDEX is a safe and effective third-line Tx for pts with RRMM following second-line failure of LEN-based Tx, including pts with prior exposure to PI or BORT. All pts, including those with prior PI or BORT Tx, experienced lower rates of hematologic AEs and longer median PFS than what has been previously reported for other studies using POM + LoDEX in later lines of Tx.

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