(PB3387) MOMENTUM: A PHASE 2, OPEN-LABEL, SINGLE-ARM, MULTICENTER STUDY TO EVALUATE THE EFFICACY OF CEMSIDOMIDE + DEXAMETHASONE IN SUBJECTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

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Background

Cemsidomide is a novel, highly potent, cereblon-based, IKZF1/3 MonoDAC® degrader, having a similar mechanism of action as BMS's IMiD® or CELMoD® degraders for MM. Cemsidomide displays catalytic activity enabling rapid and deep target degradation with high binding affinity to overcome resistance due to low cereblon levels. Cemsidomide binds to cereblon to facilitate the recruitment and ubiquitination of IKZF1/3 leading to the proteasomal degradation of both proteins. IKZF1/3 degradation induces multiple myeloma cell death, activation of fully differentiated T-cells which prevents T-cell exhaustion and promotes secretion of key immune stimulating cytokines. In a Phase 1 study, cemsidomide, given orally QD over 14 days with a 14 day "off" period (14/14) in combination with weekly dexamethasone in a heavily pre-treated patient population (7 median prior lines), was well tolerated and demonstrated durable anti-myeloma activity at increasing dose levels. A 53% ORR was observed as the highest dose of 100 µg QD 14/14, with a 36% ORR observed across all dose levels (Dhakal IMS 2025).

Aims

MOMENTUM (NCT07284758) is a Phase 2 multi-center, open-label, single-arm, global study to further evaluate the anti-myeloma activity as well as safety, tolerability, and PK/PD of cemsidomide.

Methods

The study will enroll approximately 100 patients. The patient population eligible for this study include those who have received at least 3 prior antimyeloma regimens, which must have included an IKZF1/3 degrader other than cemsidomide, a proteasome inhibitor, an anti-CD38 antibody, and a TCE or CAR-T therapy (unless not indicated). Prior TCE or CAR-T therapy may be one or more targets including but not limited to: BCMA, GPRC5D, FcRH5, and CD38. Patients must have an ECOG score of ≤2, and adequate organ function prior to dosing. Patients will receive cemsidomide 100 µg QD 14/14 and dexamethasone in a 28-day cycle until progressive disease, AE requiring treatment discontinuation, or withdrawal of consent. The primary endpoint of this study is ORR per IMWG response Criteria (IMS 2025) assessed by an Independent Review Committee (IRC). Secondary endpoints include assessment of DOR, PFS, and OS. Exploratory objectives include antimyeloma activity assessed by investigator, degradation of IKF1/3, quantification of protein expression, and patient QoL assessments. Exposure-response relationships between cemsidomide and relevant markers of safety and efficacy will also be analyzed. A safety review committee and an IRC will be established to oversee safety and efficacy throughout the trial.

Results

The study is open to enrollment as of December 2025 and is currently recruiting.