(PF763) UPDATED RESULTS OF A PHASE 1 FIRST-IN-HUMAN STUDY OF CEMSIDOMIDE, A NOVEL MONODAC® DEGRADER, WITH DEXAMETHASONE (DEX) IN PATIENTS WITH (RRMM)

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

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Background

Cemsidomide (CFT7455) is a novel and highly potent Ikaros Family Zinc Finger Protein 1/3 (IKZF1/3) MonoDAC® cereblon-based degrader. Cemsidomide has demonstrated best-in-class activity in MM preclinical models and induces immune activation.

Aims

To report updated results with additional pts and longer follow-up from the cemsidomide plus dexamethasone (DEX) phase 1 dose escalation and expansion cohorts.

Methods

CFT7455-1101(NCT04756726) is an open-label, phase 1/2, multi-center, first-in-human study evaluating safety, efficacy, pharmacokinetics (PK), and pharmacodynamics (PD) of cemsidomide in pts with RRMM and R/R NHL. Eligible MM pts must have received lenalidomide, pomalidomide, a proteasome inhibitor, and an anti-CD38 antibody. The primary objective is to characterize the safety and tolerability of cemsidomide in combination with DEX and to determine the MTD and/or RP2D. Secondary objectives include antimyeloma activity per IMWG response criteria, PK, and PD. Dose escalation was guided by a Bayesian logistic regression model with cohorts of 3-6 pts and a provision for additional pts at doses declared safe.

Results

As of November 26, 2025, 73 MM pts have been treated with cemsidomide plus DEX. Enrollment is completed and 8 pts remain on treatment. The median age is 67 (range 39-90) and pts received a median of 7 prior lines (range 3-22). 81% of pts were penta-drug exposed and 75% had previous CAR-T therapy or a bispecific antibody. 32% of pts have extramedullary disease. Cemsidomide doses explored included 50 µg MWF (n=6), 37.5 µg QD (n=12), 62.5 µg QD (n=16), 75 µg QD (n=20), and 100 µg QD (n=19), all on a 14 day on/14 day off dosing schedule. All doses were declared safe and 100 µg was the maximum administered dose. Systemic exposure of cemsidomide increased dose proportionally. Across doses, cemsidomide produced greater than 50% and 80% of IKZF1 and IKZF3 degradation respectively, and T-cell activation by flow cytometry and cytokine expression. 4 pts had a dose-limiting toxicity: 1 pt at 62.5 µg had grade 4 neutropenia >7 days; 3 pts at 100 µg had 5 DLT events (grade 4 neutropenia >7 days, grade 3 ALT increase, grade 3 febrile neutropenia, grade 3 pneumonia in 2 subjects). Grade 3-4 treatment emergent adverse events (AEs) occurring in ≥10% of pts included neutropenia (58%), infections (30%), anemia (25%), leukopenia (25%), thrombocytopenia (11%), lymphopenia (11%). The majority of grade ≥3 neutropenia occurred in cycles 1-2. 45% of pts received G-CSF and 6% of pts experienced grade 3-4 febrile neutropenia. No pts experienced grade 3-4 rash, fatigue, nausea, or vomiting. 4 pts had AEs resulting in dose reduction and 4 pts had an AE resulting in discontinuation (none considered related). The median relative dose intensity of cemsidomide is 0.942. The ORR among all pts is 36% (26/72) with a clinical benefit rate (MR or better) of 50% (36/72). The ORR at the 75 µg and 100 µg doses is 40% (8/20) and 53% (10/19).

Summary/Conclusion

Oral cemsidomide with DEX demonstrates compelling efficacy, tolerability and PK/PD in a heavily pre-treated RRMM population, the majority of whom had received a CAR-T or bispecific antibody. Grade 3-4 toxicities were primarily cycle 1-2 myelosuppression, which were manageable with limited dose reductions and discontinuations. Further development includes a phase 2 MOMENTUM study (NCT07284758) and a phase 1 b study of cemsidomide and elranatamab (NCT07280013). Updated safety and antimyeloma endpoints will be presented at the conference.