(PS1883) UPDATED RESULTS FROM RANDOMIZED PHASE II DOSE OPTIMIZATION STUDY OF INOBRODIB (CCS1477), IN COMBINATION WITH POMALIDOMIDE AND DEXAMETHASONE IN RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM)

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

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Background

Inobrodib (CCS1477) is a first-in-class, oral inhibitor of the p300/CBP bromodomains with demonstrated anti-myeloma activity and synergy with pomalidomide (Pom). In combination with Pom and dexamethasone (dex) (InoPd), it has previously shown manageable safety profile and clinical activity in heavily pretreated relapsed/refractory multiple myeloma (RRMM).

Aims

To determine the optimal dose (RP2D) of InoPd in patients with RRMM (NCT04068597).

Methods

Eligible RRMM patients had exhausted standard therapies or received ≥2 prior lines including lenalidomide and a proteasome inhibitor (if Pom-naïve). Patients were randomized to inobrodib 20, 30, or 40 mg taken twice daily, irrespective of food intake (4 days on/3 days off) plus Pom 4 mg (days 1–21) and age-adjusted dex (20–40 mg) in 28-day cycles. Randomization was stratified by prior Pom esposure. Adverse events (AEs) were graded per CTCAE v5.0; responses were assessed by IMWG criteria.

Results

Enrolment has completed (63 pts total) and as of 16Feb2026 median follow-up was 217 day (range 11-427). Median age was 70 years (44–83); 78% patients had ECOG 1. Poor prognostic features, such as high risk by the IMWG Consensus Genomic Staging (37%), were noted in significant proportion of patients. Median number of prior therapies was 5 (2–17); 60% had 1-2 prior transplants, 54% were Pom-refractory, 73% triple-class refractory, 25% penta-drug refractory, and 65% had prior BCMA- and/or T-cell engager–directed therapy.
Grade 3/4 treatment-emergent AEs occurred in 71% of patients, mainly hematologic (thrombocytopenia 36%, neutropenia 34%, anemia 20%). Thrombocytopenia was the primary overlapping toxicity for inobrodib and pomalidomide. At the 20-mg dose, the frequency of G3/4 thrombocytopenia 29%, neutropenia 24% and anaemia 24% was comparable with published Pom/dex data. Non-haematological events were mostly mild or moderate, with fatigue being most frequent at 51%. Two patients (3%) discontinued treatment due to adverse event and 52% due to progressive disease.
Overall response rates (ORR) were 67%, 60%, and 41% in the 20-, 30-, and 40-mg cohorts, respectively. The lower ORR in the 40mg cohort was likely due to a higher interruption rate in the initial cycles which resulted in early discontinuations due to progression. In high unmet-need subgroup (Pom-refractory and prior BCMA/TCE), ORR was 67% at 20 and 30 mg. Median time to response was ~1 month, with deepening over time; deep responses (CR with MRD negativity) were noted in each dose level; and VGPR+ rates were 33% and 35% at 20 and 30 mg. In non–Pom-refractory patients (n=11, of which 55% were also post BCMA/TCE) at 20 mg, ORR was 91%. DOR and PFS are maturing.

Summary/Conclusion

InoPd shows manageable safety and encouraging activity in heavily pretreated RRMM, including patients previously treated with anti-BCMA therapy and/or T-cell engagers. The 20-mg dose provided the most favorable balance of safety and efficacy and was selected for the pivotal trials DOMMINO-1 and DOMMINO-2.