



## The 67th ASH Annual Meeting Abstracts

## POSTER

## 654A. MULTIPLE MYELOMA: PHARMACOLOGIC THERAPIES

**Randomized phase II dose optimization study of inobrodib (CCS1477), in combination with pomalidomide and dexamethasone in relapsed/refractory multiple myeloma (RRMM)**

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**Abstract**

**Background** Inobrodib (CCS1477/Ino) is a first-in-class potent, selective, and orally bioavailable inhibitor of the bromodomains of p300 and CBP, two closely related histone acetyl transferases with oncogenic roles in hematological malignancies. Inobrodib exhibits potent anti-tumor cell activity in a range of cell lines including multiple myeloma and demonstrates synergistic activity with pomalidomide (Pom). The combination of Ino with Pom and dexamethasone (dex) (InoPd) was previously shown to have a manageable safety profile and activity in patients (pts) with heavily pretreated RRMM.

**Aims** To determine the optimal dose (RP2D) of InoPd in pts with RRMM (NCT04068597).

**Methods** Eligible pts have confirmed RRMM and must have received at least 2 prior therapies including lenalidomide and a proteasome inhibitor.

Patients are randomised to 3 different dose levels of inobrodib (20mg, 30mg, 40mg) BID on a 4 days on/3 days off intermittent schedule with Pom 4 mg and dex 20-40mg depending on age, all administered on 28-day cycles. Randomization is stratified based on Pom-refractory status.

Adverse events are graded by CTCAE v5.0 and responses are investigator-assessed per IMWG criteria. Pharmacodynamic profiling of paired bone marrow samples and serial peripheral blood mononuclear cell samples, using mass cytometry for IRF4, MYC, and other markers is ongoing.

**Results** Recruitment is ongoing, with 36 of 60 (60%) planned patients enrolled as of the data cut-off (7 July 2025); full enrollment is expected by September 2025. Initial data combining all three dose levels are summarized below. Comprehensive dose-specific data for all patients will be presented at the conference. There are 26 pts in the safety set (received at least one dose), with a median age of 70 yrs (range 44-81). Median number of prior lines of therapy is 5 (range 2-12), 84.6% are triple-class exposed, 15 pts (57.7%) are triple class refractory, and 4 pts (15.4%) received prior BCMA/TCE therapy. In addition, 12 pts (46.2%) were Pom-refractory.

Grade (gr) 3/4 treatment-emergent adverse events (TEAEs) have been reported in 11 of 26 (42%) patients and are predominantly hematologic (neutropenia 15.4%; thrombocytopenia 7.7%; anemia 3.8%). Of note, the main potential overlapping toxicity of this triplet was thrombocytopenia, but there has been no increased frequency or severity to date. Inobrodib monotherapy has not been shown to cause neutropenia. Grade 3/4 infections were uncommon (3.8%), and consistent with the anticipated safety profile of Pom/dex alone.

There are currently 16/26 pts evaluable for response assessment as 10 pts have not yet had a post-baseline efficacy assessment as they were too recently enrolled. To date, responses  $\geq$  PR (including unconfirmed) have been reported in 12/16 (75%) of pts. Responses have been observed in pts refractory to Pom and previously exposed to anti-BCMA and TCE therapies. Median time on treatment was 38.5 days (range 4-106 days). To date, only one pt in the 20mg cohort had discontinued the study to progressive disease and death. Mature data will be presented at the conference. **Summary:** Preliminary results confirm earlier findings that the combination of InoPd has both a manageable safety profile and extremely promising clinical activity in a heavily pretreated population, including those who have received anti-BCMA and/or TCE therapies, and have previously received Pom. Updated results on efficacy and safety for the full cohort will be presented at the meeting. Results from this study will inform the dose for registrational studies, and additional arms on this trial investigating inobrodib in combination with elranatamab and teclistamab are currently ongoing and enrolling.

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