FIRST CLINICAL (PHASE 1B/2A) STUDY OF IBERDOMIDE (CC-220; IBER), A CELMOD, IN COMBINATION WITH DEXAMETHASONE IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA

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Background
IBER is a novel cereblon E3 ligase modulator (CELMoD) with enhanced tumoricidal and immunostimulatory activities. Preclinically, IBER overcomes immunomodulatory drug (IMiD) resistance and has synergy with daratumumab (DARA), bortezomib (BORT), and dexamethasone (DEX).

Aims
This phase 1b/2a multicenter, open-label, dose-escalation study (NCT02773030) was conducted to evaluate the maximum tolerated dose (MTD), recommended phase 2 dose (RP2D), safety and preliminary efficacy of IBER in combination with DEX, in patients with relapsed/refractory multiple myeloma (RRMM).

Methods
Eligible patients had RRMM and must have received ≥2 prior regimens including lenalidomide (LEN) and/or pomalidomide (POM), and a proteasome inhibitor (PI). All patients had progressed on or within 60 days of last MM therapy. Escalating doses of IBER were given on days 1–21, in combination with DEX 40 mg (20 mg in patients aged >75 years) on days 1, 8, 15, and 22, of each 28-day cycle. Dose escalation was reviewed by a dose escalation committee.

Results
As of January 2019, 58 patients had received IBER + DEX. Median age was 64.5 years (range 33–79), and median number of prior regimens was 5 (2–12). Prior therapies included autologous stem cell transplantation (79%), LEN (100%), POM (69%), PIs (100%), and DARA (66%). IBER dose ranged from 0.3 to 1.2 mg; MTD/RP2D was not reached. Median duration of therapy was 12+ weeks (range 4–109). Grade 3–4 adverse events (AEs) were reported in 41 (72%) patients and were not related to dose. Grade 3–4 neutropenia, thrombocytopenia, neuropathy, and fatigue occurred in 26%, 11%, 2%, and 0% patients, respectively. Three patients discontinued treatment due to AEs. Clinical activity occurred early and was observed across all dose levels (Table 1); 20 of 51 patients remain on treatment (2–27+ cycles).

Table 1. Responses in evaluable patients

Efficacy	IBER dose 0.3–1.2 mg + DEX (N=51)
Very good partial response	1
Partial response (PR)	15
Minimal response (MR)	10
Stable disease (SD)	19
Progressive disease	6
Overall response (≥PR, %)	16 (31)
Clinical benefit (≥MR, %)	26 (51)
Disease control (≥SD, %)	45 (88)

DEX, dexamethasone; IBER, iberdomide

Conclusion

IBER + DEX showed favorable efficacy and safety in heavily pretreated patients with RRMM who failed multiple prior therapies. This study is ongoing, including combinations of IBER with DARA or BORT.