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First clinical (phase 1b/2a) study of iberdomide (CC-220; IBER), a CELMoD, in combination with dexamethasone (DEX) in patients (pts) with relapsed/refractory multiple myeloma (RRMM).

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Abstract Disclosures

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 DEX.

Methods:
A phase 1b/2a multicenter, open-label, dose-escalation study evaluated the maximum tolerated dose (MTD), recommended phase 2 dose (RP2D), safety, and preliminary efficacy of IBER. Eligible pts had RRMM and must have received ≥ 2 prior regimens including lenalidomide (LEN) and/or pomalidomide (POM), and a proteasome inhibitor (PI). All pts 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 pts age > 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 Jan 2019,58 pts 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 transplant

(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%) pts and were not related to dose. Grade 3–4 neutropenia, thrombocytopenia, neuropathy, and fatigue occurred in 26%, 11%, 2%, and 0% pts, respectively. Three pts discontinued treatment due to AEs. Clinical activity occurred early and was observed across all dose levels (Table); 20 of 51 pts remain on treatment (2–27+ cycles).

Conclusions:

IBER + DEX showed favorable efficacy and safety in heavily pretreated pts with RRMM who failed multiple prior therapies. This study is ongoing, including combinations of IBER with DARA or BORT. Clinical trial information: NCT02773030

Efficacy	IBER dose 0.3–1.2 mg + DEX (N = 51 evaluable)
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%)

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