3. RELAPSED/REFRACTORY MULTIPLE MYELOMA

CEVOSTAMAB PLUS POMALIDOMIDE AND DEXAMETHASONE IN PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA: BIOMARKER ANALYSES FROM CAMMA 1 ARM B

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Background. Cevostamab is a FcRH5xCD3 T-cell-engaging bispecific antibody that has shown promising activity and manageable safety as monotherapy in pts with late-line RRMM (Richter et al. ASH 2024). Anti-myeloma agents that augment T-cell activity could enhance the activity of cevostamab. Cevostamab plus pom-dex induced durable responses and had manageable safety in B-cell maturation antigen (BCMA) therapy-naïve pts with RRMM who were enrolled into the Arm B randomised dose-expansion stage of the Phase Ib CAMMA 1 study (NCT04910568) (Mian et al. IMS 2025). We report exploratory biomarker analyses in BCMA-naïve pts from Arm B.

Methods. Eligible pts were those with RRMM who had received ≥1 prior immunomodulatory drug and ≥1 prior proteasome inhibitor as part of ≥1 prior line. Pts were randomised (1:1) to receive 70 mg or 105 mg cevostamab given Q2W in Cycles (C) 1–6 (28-day cycle) and Q4W in C7+, after a pre-phase with double or triple step-up dosing. From C1+, pom (2 mg Day [D] 1–21) and dex (20 mg D1, 8, 15 and 22) were given. Treatment was continued until unacceptable toxicity or disease progression. Soluble BCMA (sBCMA) was measured in plasma using LC/MS and multiplex ELISA assays on ELLA platform. Minimal residual disease (MRD) was assessed in bone marrow aspirate using next-generation sequencing.

Results. As of 6 September 2025, 64 pts had been randomised and treated in the Arm B dose-expansion cohorts (n=32 in each). Of these, 29 pts in the 70 mg group and 25 pts in the 105 mg group were BCMA naïve. Among these pts, median age was 65 years in both groups, median number of prior lines of therapy was 2 [range: 1–6] in both groups and the majority were refractory to their last line of therapy (70 mg, 72.4%; 105 mg, 68.0%). Baseline sBCMA levels were comparable in the 70 mg and 105 mg groups. Median time on study was 13.2 months (range: 9.1–18.3) in the 70 mg group and 11.2 months (range: 3.3–18.6) in the 105 mg group. Objective response rates were 86.2% and 88.0%, respectively, while very good partial response or better rates were 72.4% and 76.0%. At cut-off, 80.0% of responders in the 70 mg group and 81.8% in the 105 mg group had ongoing responses. Overall, 96.0% of pts in the 70 mg group and 90.9% in the 105 mg group had a duration of response of ≥6 months. Combination treatment induced rapid, deep and durable declines in sBCMA levels. Median sBCMA decreases were 54.9% by C1D1 pre-infusion (after the first target dose in the cevostamab pre-phase), 83.0% by C1D15 and 90.9% by C2D1 pre-infusion. No significant difference in sBCMA kinetics were observed between the dose groups. Twenty-eight pts achieved a complete response or better (CR+), 23 of whom were evaluable for MRD. Of these, 18 pts achieved best MRD negativity at the 10^{-6} threshold level and 3 pts at the 10^{-5} threshold. One CR+ patient had ID clone failure and 4 CR+ pts were not available at cut-off. Among MRD-evaluable CR+ pts, the CR+MRD-negativity rate at the 10^{-5} threshold was not significantly different between the 70 mg (10/11, 90.9%) and 105 mg (11/12, 91.7%) groups.

Conclusions. Cevostamab plus pom-dex induced deep and durable remissions in BCMA-naïve pts with RRMM. Rapid, deep and durable declines in sBCMA levels and high rates of CR+MRD-negativity were also observed. *Acknowledgments: This study was sponsored by F. Hoffmann-La Roche Ltd.*