# ONCE-WEEKLY VS TWICE-WEEKLY CARFILZOMIB DOSING PLUS DEXAMETHASONE IN PATIENTS WITH RELAPSED AND REFRACTORY MULTIPLE MYELOMA (RRMM): RESULTS OF THE RANDOMIZED PHASE 3 STUDY A.R.R.O.W.

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**Abstract:** S849

**Type:** Oral Presentation

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**Location:** Room A1

**Background**

Twice-weekly carfilzomib (K) at 20/27 mg/m$^2$ is approved for the treatment of RRMM. To develop a more convenient K regimen, once-weekly K plus dexamethasone (d) was assessed in the phase 1/2 CHAMPION-1 study, establishing a maximum tolerated dose of K 20/70 mg/m$^2$ for RRMM pts.

**Aims**

To present results from the pre-planned interim analysis of the phase 3 study A.R.R.O.W. comparing Kd once-weekly at 20/70 mg/m$^2$ (once-weekly group) vs twice-weekly at 20/27 mg/m$^2$ (twice-weekly group).

**Methods**

Pts with 2–3 prior therapies and prior exposure to proteasome inhibitor and immunomodulatory agent were eligible. Pts were randomized 1:1 to receive either once- or twice-weekly K plus d. The once-weekly group received K (30-min IV) on days (D) 1, 8, and 15 of all cycles (20 mg/m$^2$ on D1 [cycle 1]; 70 mg/m$^2$ thereafter). The twice-weekly group received K (10-min IV) on D1, 2, 8, 9, 15, and 16 (20 mg/m$^2$ on D1 and 2 during cycle 1 and 27 mg/m$^2$ thereafter). All pts received d at 40 mg on D1, 8, 15 (all cycles), and 22 (cycle 1–9 only). Treatment was given in 28-day cycles until disease progression or unacceptable toxicity. The primary endpoint was progression-free survival (PFS). Secondary endpoints were overall response rate (ORR), overall survival, safety, and pharmacokinetics.

**Results**

Baseline characteristics were generally balanced. Median PFS (once- vs twice-weekly) was 11.2 mo vs 7.6 mo (hazard ratio = 0.69; 1-sided *P*=0.0014). ORR (once- vs twice-weekly) was 62.9% vs 40.8% (*P*<0.0001); 7.1% vs 1.7% had a complete response or better. Grade ≥3 adverse events (AEs) occurred in 67.6% (once-weekly) and 61.7% (twice-weekly). Treatment-related grade 5 AEs occurred in 5 pts (2.1%) (once-weekly) and 2 pts (0.9%) (twice-weekly). The incidence of grade ≥3 hypertension and cardiac failure (once- vs twice-weekly) was 5.9% vs 5.5% and 2.9% vs 4.3%, respectively.

**Conclusion**

Once-weekly Kd at 20/70 mg/m$^2$ significantly improved PFS and ORR vs twice-weekly Kd at 20/27 mg/m$^2$. The incidence of AEs was comparable between groups. No new safety risks were found in the once-weekly group. Overall, once-weekly Kd showed favorable benefit-risk profile with a convenient dosing regimen vs twice-weekly Kd.

**Session topic:** 14. Myeloma and other monoclonal gammopathies - Clinical

**Keyword(s):** Clinical Trial, Multiple Myeloma, Phase III, Proteasome inhibitor