Abstract: P1978

Title: PATIENT-REPORTED OUTCOMES FROM THE RANDOMIZED PHASE 3 CANOVA STUDY OF VENETOCLAX-DEXAMETHASONE VS POMALIDOMIDE-DEXAMETHASONE IN PATIENTS WITH T(11;14)-POSITIVE RELAPSED/REFRACTORY MULTIPLE MYELOMA

Abstract Type: e-Poster Presentation

Topic: Myeloma and other monoclonal gammopathies - Clinical

Background:

Venetoclax, a potent BCL-2 inhibitor, has been evaluated as biomarker-directed therapy in t(11;14)-positive relapsed/refractory multiple myeloma (RRMM; Kumar, *Blood*. 2017;130:2401. Kumar, *Lancet Oncol*. 2020;21:1630. Kaufman, *Am J Hematol*. 2021;96:418). In the randomized, global, open-label Phase 3 CANOVA study (NCT03539744) primary analysis, patients (pts) with t(11;14)-positive RRMM had longer median progression-free survival (PFS) with venetoclax and dexamethasone (VenDex) vs pomalidomide and dexamethasone (PomDex; 9.9 vs 5.8 months, respectively; *P*=0.237).

Aims:

To evaluate** patient-reported outcomes (PROs) with VenDex vs PomDex from CANOVA.

Methods:

Pts aged ≥18 years with t(11;14)-positive RRMM per centralized FISH with plasma cell enrichment, an ECOG performance status (ECOG PS) ≤2, and who received ≥2 prior lines of therapy (LOTs) were enrolled. Eligible pts also had progressed on or within 60 days after their last LOT, previously received a proteasome inhibitor (PI), and were refractory to or relapsed on lenalidomide (Len). Pts were randomized 1:1 to Ven (800 mg PO QD, no dose ramp-up) or Pom (4 mg PO Days 1–21) added to Dex (40 mg QW) for each 28-day cycle. Pts were stratified by age at randomization (<65 vs ≥65 years), prior LOTs (2 to 3 vs ≥4), and International Staging System (ISS) stage at screening (I vs II vs III). The primary endpoint was independent review committee–assessed PFS. Time to deterioration in disease symptoms (TTDDS) and** time to deterioration in physical functioning (TTDPF) were key secondary endpoints. TTDDS was measured by the European Organization for Research and Treatment of Cancer (EORTC) QLQ-MY20 disease symptom domain, with worsening defined as a change from baseline (BL; Cycle 1 Day 1) score of ≥10 points. TTDPF was measured by the EORTC QLQ-C30 physical functioning domain,** with worsening defined as a change from BL score of ≤ −10 points. Assessments were completed before dosing and on Day 1 of each odd numbered cycle starting with Cycle 3.

Results:

At the median follow-up of 24.9 months (July 24, 2023 cutoff), 263 pts were randomized (VenDex, n=133; PomDex, n=130). Median (range) age was 67 years (39–85) in the VenDex arm and 66 years (37–89) in the PomDex arm. In the VenDex vs PomDex arms, most pts had an ECOG PS of 0 (47% vs 48%) or 1 (41% vs 47%) and were ISS stage I (50% vs 46%) or stage II (30% vs 35%). At screening, 74% and 75% of pts had received 2–3 prior LOTs in the VenDex and PomDex arms, respectively. Most pts in the VenDex and PomDex arms were refractory to PIs (82% and 73%) and immunomodulatory drugs (96% and 98% [Len, 96% and 96%]). Median (95% CI) TTDDS was 20.3 months (9.2–not estimable) and 9.4 months (5.7–19.7) in the VenDex and PomDex arms, respectively (hazard ratio [HR], 0.769 [95% CI, 0.486–1.216]; *P*=0.260; **Figure**). At the final visit (FV), mean change ± standard deviation (SD) from BL for disease symptoms was −5.9 ± 18.59 in the VenDex arm (BL: 29.4; FV: 23.4; 82% completion) and −1.1 ± 18.95 in the PomDex arm (BL: 25.6; FV: 24.4; 79% completion). Median TTDPF (95% CI) was 13.2 months (9.7–20.1) and 5.6 months (3.8–9.5) in the VenDex and PomDex arms, respectively (HR, 0.494 [95% CI, 0.317–0.770]; *P*=0.002; **Figure**). Mean change ± SD from BL to FV for physical functioning was −0.4 ± 19.98 in the VenDex arm (BL: 63.3; FV: 62.9; 83% completion) and −5.3 ± 19.47 in the PomDex arm (BL: 68.8; FV: 63.5; 81% completion).

Summary/Conclusion:

In CANOVA, pts treated with VenDex had delayed median TTDDS and TTDPF compared with those treated with PomDex. These data support a benefit in these PRO measures with VenDex for t(11;14)-positive RRMM.

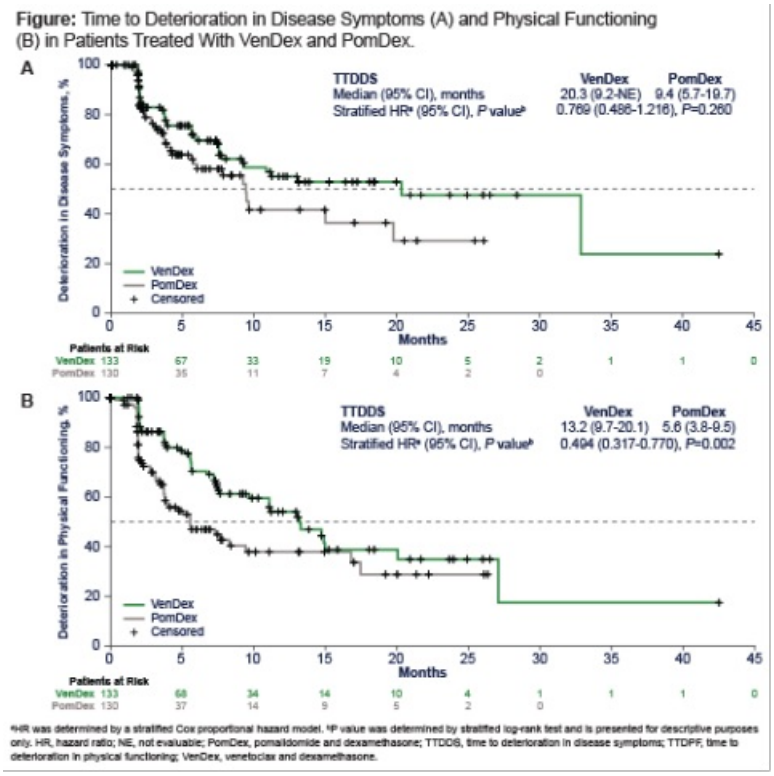

Figure: Time to Deterioration in Disease Symptoms (A) and Physical Functioning (B) in Patients Treated With VenDex and PomDex.

[a]HR was determined by a stratified Cox proportional hazard model. [b]P value was determined by stratified log-rank test and is presented for descriptive purposes only. HR, hazard ratio; NE, not evaluable; PomDex, pomalidomide and dexamethasone; TTDDS, time to deterioration in disease symptoms; TTDPF, time to deterioration in physical functioning; VenDex, venetoclax and dexamethasone.

Keywords: "t(11;14)", Myeloma, Venetoclax, Patient reported outcomes