

[366] Frequency, Characteristics, and Reversibility of Peripheral Neuropathy (PN) in the APEX Trial.

Session Type: Oral Session

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Introduction: Bortezomib (Bz, VELCADE) is a proteasome inhibitor proven safe and effective for patients (pts) with relapsed and/or refractory multiple myeloma (MM). Pts in SUMMIT (NEJM 2003;348:2609) and CREST (BJH 2004;127:165) underwent rigorous testing (neurologic evaluations, FACT/GOG-Ntx questionnaires, nerve

conduction studies) to determine the incidence, characteristics and reversibility of PN. In these phase 2 trials, the PN rate was 31–41% (grade [G] ≥ 3 in 11–12%). Specific dose modification (DM) guidelines for PN were not incorporated into the phase 2 trials but were developed for subsequent studies. The objective of this report was to evaluate the frequency, characteristics and reversibility of PN in an updated analysis of the randomized phase 3 APEX trial (NEJM 2005;352:2487), in which specific DM guidelines for PN were implemented.

Methods: Pts with relapsed MM were randomized to Bz 1.3 mg/m² IV on d 1, 4, 8, 11 q3wk for 8 cycles then 3 cycles on d 1, 8, 15, 22 q5wk, or dexamethasone (Dex) 40 mg PO on d 1–4, 9–12, 17–20 q5wk for 4 cycles, then 5 cycles on d 1–4 q4wk. Pts with G ≥ 2 PN were excluded. Data were collected on incidence, severity and reversibility of PN.

Results: Of 331 pts safety evaluable enrolled on Bz, 120 (36%) developed PN,

including 30 (9%) with G ≥ 3 . PN was classified as sensory or not specified in the vast majority of cases; motor neuropathies were rare. Of 91 pts with G ≥ 2 PN, 68 had DM, including 37 with doses reduced, held or schedule modification and 31 with Bz discontinuation (DC); 23 pts not following DM protocol. The majority (58 pts; 64%) of the 91 pts improved (9%) or had complete resolution (55%) of symptoms. Of 37 pts with DM without Bz DC, the majority (26 pts; 70%) had improvement, all with complete resolution of PN to baseline, with a median time to resolution of 78 d. Of 31 pts requiring Bz DC, 2 (6%) improved and 17 (55%) had complete resolution of PN with a median time to improvement/resolution of 121 d. Of 23 pts who did not follow the DM protocol, 12 (52%) had complete resolution with a median time to resolution of 106 d. The rates of PN (any G, G ≥ 3) were similar regardless of pt age or number/type of prior therapies. The median TTP of 91 pts

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[2547] Bortezomib Continues Demonstrates Superior Efficacy Compared with High-Dose Dexamethasone in Relapsed Multiple Myeloma: Updated Results of the APEX Trial.

Session Type: Poster Session 751-II

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Introduction: In the international, multicenter phase 3 APEX trial, 669 patients (pts) with multiple myeloma (MM) who had relapsed after 1–3 prior therapies were randomized to receive bortezomib (VELCADE®) 1.3 mg/m² IV d 1, 4, 8, 11 q3wk for 8 cycles followed by 3 cycles on d 1, 8,

15, 22 q5wk, or dexamethasone (Dex) 40 mg PO d 1–4, 9–12, 17–20 q5wk for 4 cycles followed by 5 cycles on d 1–4 q4wk. Pts refractory to Dex were excluded, and those with progressive disease on Dex were eligible to cross over to bortezomib. Pts receiving bortezomib achieved significant improvement in time to progression (TTP, primary end point), response rate (CR + PR using EBMT criteria), and survival (Richardson. NEJM. 2005;352:2487), which resulted in early closure of the trial. The duration of response (DOR) was longer with bortezomib, and infections ? grade 3, time to skeletal events, grade 4 adverse events (AE), serious AE, and discontinuations due to AE were similar in the 2 treatment arms.

Methods: In this analysis, updated response rates, time to response (TTR), DOR, survival, and TTP are presented after extended follow-up. A matched-pairs analysis comparing survival and TTP of pts

on bortezomib in APEX with those in another trial of MM pts who received bortezomib after Dex will also be presented.

Results: 669 pts received a median of 7 cycles of therapy. Based on a median follow-up of 15.8 months, the median TTP, 1-year and overall survival (OS), response rates, median TTR, and median DOR for pts receiving bortezomib are shown in the table. Median duration of therapy for responders (CR + PR) was 7.2 months. Improved response with longer therapy (after cycle 6) was observed in 76 pts (56% of responders) in the bortezomib arm (20 pts improved from MR or PR to CR, and 56 pts improved from MR to PR). Furthermore, 28 of 135 responders (21%) achieved first response (CR/PR) after cycle 4, including 18 pts (13%) on or after cycle 6, and 10 pts (7%) on or after cycle 8. OS increased

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