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q 21 D. Pts were dose escalated to 70 mg/m² in Arm 1 and 14 mg/m² in Arm 2 if no Grade(G) 3 or 4 toxicities were observed in cycle 1. Assuming 310 eligible pts in each arm, the study had 0.80 power to detect a 33% difference in survival. All p-values reported are two-sided.

Results

Pt Characteristics: Eligible pts Arm 1:334; Arm 2 :332. Pretreatment characteristics were equally balanced for age, race, performance status, PSA and symptoms.

Response and Survival

The median survival of men treated on Arm 1 was 18 months and Arm 2 was 15 months (logrank p=.008) The hazard ratio was 0.77 (95% confidence interval 0.64, 0.94). Arm 1 also demonstrated a superior median time to progression (6 months) compared to Arm

2 (3 months) logrank p<0.0001. The measurable disease response rates in arm 1 and 2 were 17% and 10% (p=.30), respectively.

Toxicity

G 3 or 4 toxicity was reported in 175 pts (54%) on Arm 1 and 109 pts (34%) on arm 2, due to higher rates of gastrointestinal (63pts vs. 21pts) and cardiovascular (44pts vs 20pts) events on arm 1. There was no significant difference in toxic deaths observed Arm 1 (n=7, 2%) vs. Arm 2 (n=4, 1%).

Conclusions

The 23% improvement in survival in men treated with D+E supports its use as first line therapy for AIPCA. This is the first large randomized trial demonstrating a survival advantage in AIPCA. ■

Abstract #6511

Bortezomib vs. Dexamethasone in Relapsed Multiple Myeloma

A Phase 3 Randomized Study

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Background

Bortezomib (Velcade, Millennium Pharmaceuticals), a novel proteasome inhibitor, is effective in refractory multiple myeloma (MM). For the APEX Study Group we present the interim results of an international, randomized phase 3 study conducted at 95 sites.

Methods

Between June 2002 and Oct 2003 669 patients (pt) with relapsed MM previously treated with 1-3 prior therapies were randomized to bortezomib (Vc) (327 pts) 1.3 mg/m² IV days 1,4,8,11 q 3 weeks for 8 cycles followed by 1.3 mg/m² IV days 1,8,15,22 q 5weeks for 3 cycles versus dexamethasone (D) (330 pts) 40 mg po days 1-4, 9-12, 17-20 q 5 weeks for 4 cycles followed by 40mg po days 1-4 every

28 days for 3 cycles. The primary endpoint was time to progression (TTP) using EBMT criteria for progressive disease (PD). Secondary endpoints were overall survival (OS), incidence of ≥grade 3 infection and time to skeletal event (TSE). Pt progressing on D were offered Vc on a companion study.

Results

Median age was 62 with no apparent differences in baseline characteristics. At the interim analysis (IA) 254 PD events had occurred. Pt receiving Vc demonstrated a highly significant benefit in TTP. Median TTP was 5.7 months (95% CI: 5.0, 7.9) on Vc and 3.6 months (95% CI: 3.2, 4.8) on D (p<0.0001, log-rank test). Overall survival was longer on Vc (p=0.038, log-rank test), with 13 deaths on Vc and 24 on D, but

median survival was not reached on either arm. A trend towards a lower incidence of ≥grade 3 infections was also noted with 22 (6.7%) on Vc vs 35 (10.6%) on D (p=0.096, Fisher's exact test). No difference was noted in TSE (p=0.954, log-rank test). No other major safety differences were noted. Following the interim analysis, the Data Monitoring Committee recommended that treatment on the D arm be halted, and patients randomized to D were allowed to receive Vc.

Conclusions

At the IA bortezomib was significantly more effective than dexamethasone for patients with relapsed MM. Further evaluation of survival, response duration, response rate, and safety are ongoing. ■