Article Tools

LYMPHOMA AND PLASMA CELL DISORDERS

Phase II, randomized, double blind, placebo-controlled study comparing siltuximab plus bortezomib versus bortezomib alone in pts with relapsed/refractory multiple myeloma.

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Abstract Disclosures

Abstract

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Background: Preclinical studies of siltuximab (S), a chimeric anti-IL-6 mAb, in combination with bortezomib (B) indicate an additive to synergistic effect in multiple myeloma (MM) cell lines. This randomized study evaluated the safety and efficacy of S+B compared with placebo (plc)+B in pts with relapsed/refractory MM after 1−3 prior tx lines, measurable disease but no prior B exposure. **Methods:** 286 pts were randomized 1:1 to S+B: B+plc. S 6 mg/kg or plc was given IV q2w. B 1.3 mg/m^2 was given IV on d 1, 4, 8, 11, 22, 25, 29, 32 for a max of 4 of 42-d cycles and then reduced to q1w for 35-d cycles. B was stopped for pts with PD/intolerability, and high dose oral dexamethasone (dex) 40 mg could then be started qd on d 1−4, 9−12, 17−20 for a max of 4 of 28-d cycles and on d 1−4 of subsequent cycles until PD, while S/plc continued. Primary endpoint was PFS by EBMT criteria censored at the start of dex/subsequent tx. Secondary endpoints included overall response rate (ORR), OS, and safety before dex. **Results:** 142 and 144 pts received S+B and B+plc, respectively. Baseline demographics and disease characteristics were well balanced across S+B and B+plc, except for age (median 64 vs. 61 yrs) and myeloma type (IgG 65 vs. 71%, IgA 27 vs. 20%). Median tx duration was 5.1 mo in both grps.

Median PFS was 8.1 mo in S+B and 7.6 mo in B+plc (HR 0.869, p = 0.345). ORR (CR+PR) was 55% in pts on S+B and 47% on B+plc (p = 0.213); CR rates were 11 and 7% (p = 0.342), respectively. With 24.5 mo median follow up, median OS was 30.8 mo for S+B and 36.9 mo for B+plc (HR 1.353 for S+B, p = 0.103). Fewer pts on S+B than B+plc moved to dex (23 vs. 31%) and had subsequent SCT (5 vs. 11%). Gr ≥3 AEs occurred in 91% on S+B and 74% on B+plc. Common gr ≥3 AEs in S+B were neutropenia (49%), thrombocytopenia (48%), leukopenia (14%). SAEs occurred in 29% on S+B and 24% on B+plc. Death occurred within 30 d of last study agent administration pre-dex in 8% on S+B and 5% on B+plc.

Conclusions: The combination of S+B had higher response rates but did not prolong survival compared with B+plc. A negative survival trend heavily influenced by differences in dex and SCT rescue was noted. S+B appears to be generally well tolerated but had a higher incidence of hematologic AEs.