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Poster Session

Lymphoma: Chemotherapy and Clinical Trials Poster I

Results of a Phase II Study of Bortezomib in Patients with Relapsed or Refractory Indolent Lymphoma.

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Abstract

This study was designed to evaluate the efficacy and safety of bortezomib as monotherapy in patients (pts) with indolent B-

cell lymphoma who have relapsed following, or who are refractory to, rituximab therapy. A total of 60 patients enrolled and 59 were treated with 1.3 mg/m^2 of bortezomib (IV bolus over 3–5 secs) Days 1, 4, 8, and 11 for up to eight 21-day cycles; pts with a CR could receive 4 additional cycles. Pts with <CR entered the maintenance phase with bortezomib administered on Days 1, 4, 8, and 11 of each 42- day cycle until progression; 55 patients completed 2 or more cycles and were therefore considered evaluable. Median age was 70 years, 53% female, 88% White, baseline ECOG 0/1/2 was 55%/43%/2%, Ann Arbor stage at baseline was III-IIIE (28%) and IV (65%); 34 pts (58%) had received ^{3}2 prior regimens. At baseline 58% of pts had normal Hgb and 73% had normal LDH. Pts received a median of 4 cycles of bortezomib (range, 1–18); 59% of pts had a dose delay, 25% had a dose reduction, 10% had a delay and reduction. 6 patients (10%) were <CR (including CRu) after 8 cycles went on to receive maintenance therapy. Main reasons for delay were thrombocytopenia or fatigue; doses were reduced mainly due to thrombocytopenia and discontinued mainly due to fatigue. Overall responses were: 1 CR (1.8%), 2 CRu (3.6%), 3 PR (5.5%), 34 SD (61.8%), and 11 PD (20.0%); 4 pts (7.3%) were NE. The clinical benefit rate (CBR: CR+Cru+PR+[SD^{3}6 mo]) was 30.9% (17 pts). For pts who relapsed within 6 months (mos) of prior rituximab, CBR was 16.4% (3.6% PR) vs 14.5% (1.8% CR, 3.6%CRu, 1.8% PR) in pts with relapses >6 mos following rituximab. By histology: follicular pts had CR or CRu (2/38, 5.3%) and PR (3/38, 7.9%); marginal zone pts had CRu (1/6, 16.7%) and no PR, and small lymphocytic pts (n=11) had no CRu or PR. We did not see any correlation between the FLIPI score and response in pts with follicular NHL. Median time to response was 2.2 mos (range 1.2–4.0) and duration of response was 7.5 mos (2.7–23.6). 1-yr survival was 71% and 2-yr survival was 46%. Median survival was 21.3 mos (range, 1.3–30.8), median PFS was 5.2 mos (range, 1.0– 27.7), and median TTP was 5.2 mos (range, 0.2–27.7). Median event-free survival was 2.0 mos (range, 0.1–27.7). For the 6 pts receiving maintenance cycles (median of 4; range, 2–10) the median PFS was 11.1 mos (range, 9.0–19.1). The most frequent treatment-related Grade 3–4 AEs included: thrombocytopenia (22%), fatigue (10%), neutropenia (8.5%), and neuropathy and diarrhea (6.8%, each). Reasons off treatment include: 24 (40%) disease progression; 19 (32%) AEs, primarily fatigue, neuropathy, nausea, diarrhea, or thrombocytopenia; 8 (13%) investigator request; 4 (7%) patient request; 2 (3%) other, 1 (2%) normal completion. 2 pts (3%) remain on treatment. Causes of death (n=23) were disease progression (n=19) and 1 each MDS, pneumonia, pneumonitis, and unknown (no autopsy performed). In conclusion, this study (the largest to date) reports the activity of single-agent bortezomib in low grade lymphoma. It demonstrates activity primarily in marginal zone (CBR = 50%) and in follicular lymphoma (CBR = 38%). We saw no activity in small lymphocytic disease; however, the sample size was small in this subset (n=11). As previously reported, the main toxicities were thrombocytopenia, fatigue, and neuropathy. Thus bortezomib should be considered a new, active agent for low-grade lymphoma. Maintenance resulted in increased PFS and should be explored further. Results of an ongoing phase 3 study in 670 pts comparing bortezomib combined with rituximab vs rituximab alone will be of interest in planning future studies for this disease. This research was supported, in part, from a research grant from Millennium Pharmaceuticals, Inc.

Footnotes

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Disclosures: Taetle: *Millennium:* Membership on an entity's Board of Directors or advisory committees. **Lyons:** *Amgen:* Consultancy; *GlaxoSmithKline:* Consultancy; *Novartis:* Consultancy. **Off Label Use:** VELCADE® (bortezomib) for Injection is a small molecule proteasome inhibitor developed by Millennium Pharmaceuticals, Inc., (MPI) as a novel agent to treat human malignancies. VELCADE® (bortezomib) for Injection is indicated for the treatment of patients with multiple myeloma. It is also indicated for the treatment of patients with mantle cell lymphoma who have received at least 1 prior

therapy..

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