

## Optimizing Bortezomib-based Therapies

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**Introduction:** Bortezomib is active in non-Hodgkin lymphomas. A study was conducted to determine:

- the response rate to Bortezomib when combined with the monoclonal antibody, Rituximab
- the side effects associated with this regimen
- the best way of giving Bortezomib, either once or twice weekly

**Patients and Methods:** A total of 45 patients with recurrent follicular lymphoma, mantle cell lymphoma or Waldenström Macroglobulinaemia received Bortezomib alone, or the drug given in conjunction with Rituximab. Patients in the latter group were randomised to receive either: 1.3mg/m<sup>2</sup> given twice weekly or 1.6mg/m<sup>2</sup>, weekly. The median age of the 17 patients with WM was 67 years (range 45-71 years) and the median number of previous treatments was 1.5 (range 1-4). All needed treatment because of bone marrow involvement i.e. they were anaemic and/or had a low number of white cells and/or platelets.

**Results:** Overall, a partial response was observed in 12/17 (71%) with WM, (4/7 treated with Bortezomib alone and 8/10 receiving the combination). In all responding patients, the blood count improved significantly and a further 2 no longer required blood transfusions. In terms of toxicity, looking at all 45 patients treated, the neutrophil and platelet counts fell significantly in 25% and 22% of patients respectively. The other most common side effects were fatigue (76%), nausea and diarrhoea (each 56%) and lethargy (46%). Neurological toxicity (almost always, pain in the legs or 'pins and needles') occurred in 19 patients (46%) but was always reversible. The dose of Bortezomib needed to be reduced in 7 patients. The weekly schedule was as effective and obviously more convenient than the twice weekly one and was not more toxic.

**Conclusion:** Bortezomib given in combination with Rituximab is clearly active in patients with recurrent WM, even in those who have received multiple previous therapies. The combination will therefore be evaluated in the next national trial for patients with recurrent WM in the UK.