

Bortezomib (VELCADE®) Plus Dexamethasone as Induction Treatment

Prior to Autologous Stem Cell Transplantation in Patients with Newly Diagnosed Multiple Myeloma: Preliminary Results of an IFM Phase II Study

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When patients (pts) with newly diagnosed multiple myeloma (MM) are treated with autologous stem cell transplantation (ASCT), the standard induction therapy is a dexamethasone (Dex) based regimen. Currently, the use of VAD or Dex alone results in a complete remission (CR) rate of <10%. In an ongoing ECOG trial comparing Dex alone to the combination thalidomide plus Dex, preliminary results did not show a clear advantage of the combination (Rajkumar ASCO 2004). Since achievement of CR is a major objective in the treatment of MM, better therapeutic regimens are being investigated.

Bortezomib is currently approved in the US and in the EU for the treatment of relapsed/refractory MM. Both in vitro studies and preliminary clinical experience in relapsed/refractory pts have suggested that the combination of bortezomib and Dex could further improve the results achieved with bortezomib alone.

The IFM group initiated a Phase II open trial assessing the combination of bortezomib and Dex in pts with previously untreated MM and who are candidates for ASCT. The regimen consisted of bortezomib 1.3mg/m² iv on days 1, 4, 8, 11 and Dex 40mg per os days 1-4, 9-12 (for the first 2 cycles, days 1-4 only for the last 2 cycles), administered on 4 consecutive 21 days cycles. Stem cell collection was performed just before cycle 4 after G-CSF priming. The primary objective of the study was CR rate after 4 cycles. As of August 1, 47 pts have been recruited and data is available for the first 18 pts. The median age is 53 years



(38-63) Sixteen/18 pts received 4 cycles: 1 patient progressed after 3 cycles and in one case the last two injections of bortezomib were not performed because of grade 3 neuropathy.

Results

The overall results were as follows: CR (negative electrophoresis) 3; very good partial remission (90% reduction of M component) 2; partial remission (50% reduction of the serum M component or 90% reduction of the urine M component) 10; failure (stable disease or progression) 3. The overall response rate was 83% and the CR rate was 17%. Side effect were usually

mild (grade 1/2); only one grade 3 neuropathy was recorded. In all cases stem cells could be adequately collected. These preliminary results appear to be very encouraging and the bortezomib/Dex combination appears effective and well tolerated in pts with newly diagnosed MM. The results will be updated at time of presentation. If updated analysis confirms currently available data, the IFM will start a large randomized phase III trial comparing VAD and bortezomib/Dex as induction treatment prior to ASCT in pts with newly diagnosed MM up to the age of 65.

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