Blood Abstracts: 54th ASH Annual Meeting Abstracts; Vol. 120, Issue 21, 16 Nov 2012

Abstract 1855 Combined Bendamustine, Prednisone and Bortezomib (BPV) in Patients with Relapsed or Refractory Multiple Myeloma

Wolfram Poenisch[1*], Malvina Bourgeois[1*], Barbara Moll[1*], Simone Heyn[2*], Nadja Jäkel[3*], Robert Rohrberg[4*], Hans Juergen Hurtz[5*], Marion Schmalfeld[6*], Michael Assmann[7*], Thomas Edelmann[8*], Martin Mohren, MD[9], Franz-Albert Hoffmann[10*], Andreas Schwarzer, MD[11], Gerald Hensel[12*], Kerstin Loeschcke[1*], Cornelia Becker, MD[13*], Rainer Krahl, MD[14*], Ina Wagner[2*], Haifa K. Al-Ali, MD[15*] and Dietger Niederwieser[1]

[1]University of Leipzig, Leipzig, Germany
[2]Hematology, Oncology and Hemostaseology, University Clinical Center, Leipzig, Germany
[3]Hematology, Oncology and Hemostaseology, University of Leipzig, Leipzig, Germany
[4]Gemeinschaftspraxis, Halle, Germany
[5]Internistische Gemeinschaftspraxis, Halle, Germany
[6]Gemeinschaftspraxis Hämatologie/Onkologie, Halle
[7]MVZ Elblandpolikliniken, Riesa, Germany
[8]Medcenter Nordsachsen, Schkeuditz, Germany
[9]Johanniter Krankenhaus Genthin-Stendal gGmbH, Stendal, Germany
[10]Praxis für Haematologie und Onkologie, Leipzig, Germany
[11]Private Practice, Leipzig, Germany
[12]Univerity of Leipzig, Leipzig, Germany
[13]Hematology and Oncology, University of Leipzig, Leipzig, Germany
[14]Hematology / Oncology, University of Leipzig, Leipzig, Germany
[15]Department of Hematology, Oncology and Hemostaseology, University of Leipzig, Leipzig, Germany

Introduction: Bortezomib and bendamustine have turned out to be effective, rapid action drugs in the treatment of multiple myeloma (MM). Bortezomib is a proteasome inhibitor that has shown important clinical efficacy either as a single agent or in combination with other cytostatic agents in MM. Bendamustine is a bifunctional alkylating agent with low toxicity that produces both single- and double-strand breaks in DNA, and shows only partial cross resistance with other alkylating drugs. The combination of bendamustine and prednisone with bortezomib (BPV) was assessed to determine the efficacy and toxicity of this regimen in patients with relapsed or refractory MM.

Methods: Between January 2005 and December 2011, 78 patients (median age 62; range 31-81 years) with relapsed or refractory MM were treated with bendamustine 60 (-120)

mg/qm on day 1 and 2, bortezomib 1.3 mg/qm on days 1, 4, 8 and 11, and prednisone 100 mg on days 1, 2, 4, 8 and 11. Cycles were repeated every 21 days until maximum response or progressive disease. Maximum response was achieved if three weeks of therapy did not further reduce myeloma protein by more than 10 %.

The median number of prior therapies was 2 (range 1-9). Previous therapies included 31 x thalidomide, 10 x lenalidomide, 14 x bortezomib, 24 x autologous PBSCT, and 19 x autologous-allogeneic PBSCT.

In contrast to other clinical studies, patients with pronounced pancytopenia due to stem-cell toxic pre-treatment or advanced disease were also included. Patients were divided into two groups: group A (n = 45) comprised patients with normal bone marrow function and group B (n = 33) patients with pre-existing restricted bone marrow function and pronounced pancytopenia (CTC-Criteria grade III and IV). Patients were excluded from this retrospective analysis if they had other secondary malignancies. To exclude myelodysplastic syndroma or secondary acute myeloid leukemia cytological and cytogenetic examination of bone marrow was performed in patients with pre-existent severe pancytopenia. Response was assessed using EBMT criteria modified to include near complete remission (nCR) and very good partial remission (VGPR).

Results: The median number of BPV-treatment cycles was 2 (1-7). 54 patients (69 %) responded after at least one cycle of chemotherapy with 3 CR, 10 nCR, 10 VGPR, and 31 PR. Nine patients had MR, 9 patient's stable disease and 6 patients underwent progression. A follow up of surviving patients at a median of 34 months revealed median PFS and OS for patients without preexisting severe haematological toxicities (group A) of 11 months and 50 months respectively. Outcome was significantly better than that of patients with pre-existing severe haematological toxicities (group B) who had a median PFS, and OS of 3 months and 5 months, respectively ($p < 0.001$).

The regimen was well-tolerated with few significant side effects in patients without preexisting severe haematological toxicities. New cytopenias occured infrequently with thrombocytopenia grade 3 in 11 patients, grade 4 in 8 patients and neutropenia grade 3 in 7 patients. Six patients experienced a moderate new polyneuropathy (grade 2).

Summary: BPV therapy was well tolerated in patients with relapsed/refractory MM, with a response rate of approximately 70 %. The high efficacy and the favourable toxicity profile of BPV warrant further evaluation in clinical trials.

Disclosures: Poenisch: *Mundipharma:* Honoraria, Research Funding; *Janssen:* Honoraria, Research Funding.

[*] *signifies non-member of ASH*