MultipleMyelomaHub

Patients non-eligible for transplant

ASH 2017 | Bortezomib and lenalidomide induction regimens for high-risk transplant-ineligible NDMM patients

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On Monday 11 December 2017, an oral abstract session was held entitled: *Session: 653. Myeloma: Therapy, excluding Transplantation I.* The talk was presented by Alessandra Larocca from the Myeloma Unit, Division of Hematology, University of Torino, Torino, Italy and entitled: *Abstract 744: Impact of Bortezomib- or Lenalidomide-Based Induction Treatment on High Risk Cytogenetic Transplant-Ineligible Patients with Newly Diagnosed Multiple Myeloma Enrolled in the Gimema-MM-03-05 and EMN01 Trials.* This study assessed the impact of cytogenetics on outcomes in transplant-ineligible patients with newly diagnosed MM (NDMM) treated with bortezomib-based induction (BORT) or lenalidomide-based (LEN) treatment.

In the GIMEMA-MM-03-05-trial, patients (pts) were randomized to bortezomib-melphalan-prednisone-thalidomide for 9 cycles followed by maintenance with bortezomib-thalidomide (VMPT-VT) and compared to bortezomib-melphalan-prednisone (VMP) for 9 cycles, without maintenance. In the EMN01-trial, patients were randomized to melphalan-prednisone-lenalidomide (MPR) or cyclophosphamide-prednisone-lenalidomide (CPR) or lenalidomide plus low-dose dexamethasone (Rd) for 9 cycles, followed by maintenance with either lenalidomide alone or lenalidomide plus prednisone continuously.

Key Findings:

- VMP *vs* Rd (≤ 75 yrs):
  - Median PFS: 24.8 *vs* 18.8 months, HR = 0.77 (95% CI, 0.60–0.99, *P* =0.04)
  - Median OS (4 yrs): 65% *vs* 59%, HR = 0.69 (95% CI, 0.49–0.96, *P* =0.03)
- VMP *vs* Rd (> 75 yrs):
  - Median PFS: 27.5 *vs* 17.8 months, HR = 0.93 (95% CI, 0.61–1.41, *P* =0.72)
  - Median OS (4 yrs): 49% *vs* 54%, HR = 1.44 (95% CI, 0.87–2.38, *P* =0.15)
- Median follow-up for both arms: Gimema-MM-03-05 (BORT-based) - 72.3 months; EMN01 (LEN-based) = 65.8 months
- Median age of pts: BORT = 71 yrs; LEN = 73 yrs
- Pts were characterized via cytogenetic risk group according to IMWG consensus:
  - High-risk: del(17p) ≥10% or t(4;14) ≥15% or t(14;16) ≥15%
  - Standard-risk group: all other pts
- Median follow-up is 69.9 months for VMP *vs* VMPT *vs* Rd *vs* CPR *vs* MPR

Treatments	Median PFS (months)	Median OS (months)
VMPT	33.8	NR
VMP	25.1	71
Rd	18.6	62
CPR	18.9	67.5
MPR	22.2	66.2

- There is a higher PFS in VMPT-treated pts and a higher OS in LEN-based pts
- Data for standard-risk subset of MM patients (BORT *vs* LEN):
- Median PFS (29.1 *vs* 21.7 months), HR = 0.84 (95% CI, 0.70–1.01, *P* =0.07)
- Median OS (78.1 *vs* 79.9 months), HR = 1.03 (95% CI, 0.80–1.32, *P* =0.81)
- Data for high-risk subset of MM patients (BORT *vs* LEN):
  - Median PFS (30.8 *vs* 14.8 months), HR = 0.54 (95% CI, 0.41–0.72, *P* <0.001)
  - Median OS (62.4 *vs* 43.2 months), HR = 0.65 (95% CI, 0.45–0.92, *P* =0.02)
- Pts with combined lesions were identified having one or more of the following cytogenetic abnormalities: t(4;14) or t(14;16) or del(17p)
- Data for Combined lesions (BORT *vs* LEN):
- 1 abnormality
  - Median PFS (31.5 *vs* 15.1 months), HR = 0.54 (95% CI, 0.39-0.74, *P* <0.001)
  - Median OS (61 *vs* 44%), HR = 0.71 (95% CI, 0.48-1.05, *P* =0.09)
- ≥ 2 abnormalities:
  - Median PFS (19.8 *vs* 11.8 months), HR = 0.51 (95% CI, 0.25-1.03, *P* =0.03)
  - Median OS (63 *vs* 33%), HR = 0.37 (95% CI, 0.15-0.90, *P* =0.03)
- Data for chromosomal abnormalities (BORT *vs* LEN):
- Del17p
  - Median PFS: 18 *vs* 13 months, HR = 0.72 (95% CI, 0.49-1.05, *P* =0.09)
  - Median OS: 56 *vs* 43%, HR = 0.75 (95% CI, 0.47-1.20, *P* =0.23)
- t(4;14)
  - Median PFS: 32 *vs* 15 months, HR = 0.41 (95% CI, 0.27-0.61, *P* <0.001)
  - Median OS: 63 *vs* 43%, HR = 0.56 (95% CI, 0.33-0.94, *P* =0.03)
- t(14;16)
  - Median PFS: 36 *vs* 10 months, HR = 0.34 (95% CI, 0.16-0.75, *P* =0.008)
  - Median OS: 86 *vs* 31%, HR = 0.14 (95% CI, 0.05-0.45, *P* <0.001)

Dr. Larocca concluded that BORT-based treatments (i.e VMP) displayed an advantage for high-risk NDMM patients that are ineligible for transplant. In standard-risk patients, the choice of treatment should be based upon comorbidities (such as renal impairment), fitness/age, compliance and patient preference. Additionally, the study detected a higher overall survival in patients over the age of 75 years of age, when administered LEN-based treatments. It was suggested that FISH analysis should be performed in all NDMM for risk stratification and that better treatment options and newer combinations in the high-risk subtype, as classified in this study, are needed.

References

1. Larocca *et al*. Impact of Bortezomib- or Lenalidomide-Based Induction Treatment on High Risk Cytogenetic Transplant-Ineligible Patients with Newly Diagnosed Multiple Myeloma Enrolled in the Gimema-MM-03-05 and EMN01 Trials. #Abstract 744. 59th ASH Annual Meeting and Exposition 2017, December 2017, Atlanta, GA.