Management of biochemical relapse during lenalidomide maintenance therapy post ASCT in multiple myeloma: a descriptive observational study of a single institution

Rola El Sayed1, Yolla Haibe1, Nour Moukalled1, Radwan Massoud1, Basel Haffar1, Charbel Matar1, Ammar Zahreddine1, Ali Bazarbachi1 and Jean El-Cheikh1

1Bone Marrow Transplantation Program and Division of Hematology and oncology, Department of Internal Medicine, Beirut, Lebanon

Patients with multiple myeloma (MM) who underwent autologous stem cell transplantation (ASCT), are known to benefit from maintenance therapy post-transplant. With signs of early relapse, physicians can either optimize maintenance therapy or use a new therapeutic regimen.

**BACKGROUND**

Between January 2011 and May 2017, we included 51 patients with MM who underwent ASCT and received lenalidomide (R) or Bortezomib (V) or shift to different lines of treatment are possible.

**OBJECTIVE**

The purpose of this study is to analyze the clinical outcomes beyond biochemical relapse of patients with MM on maintenance therapy. Time to next treatment (TNT), progression free survival (PFS) and overall survival (OS) are assessed. Different approaches for treatment of relapse such as increase in lenalidomide (R) dose, addition of dexamethasone (D) or Bortezomib (V) or shift to different lines of treatment are possible.

**METHODS**

Between January 2011 and May 2017, we included 51 patients with MM who underwent ASCT and received Bortezomib/Lenalidomide/Dexamethasone (VRD) consolidation and maintenance therapy, mainly lenalidomide (R) 10mg/day for 21 days every 28 days.

**RESULTS**

### Patient Characteristics

**Variable**

- Number of patients included in the study: 51
- Median age at diagnosis (years): 54 (25-74)
- Median age at transplant (years): 52 (46-75)
- Staging (Salmon and Durie)
  - Stage I: 28 (51)
  - Stage II: 15 (29)
  - Stage III: 11 (21)
- Sex: Female: 30 (59)
  - Male: 21 (41)
- High-risk features
  - IgG: 46 (90)
  - IgA: 8 (15)
  - IgD: 1 (2)
  - IgE: None
  - Type of MM
    - II: 16 (31)
    - III: 15 (29)
    - IV: 1 (2)
    - Mixed component: 1 (2)
  - Disease status post transplant
    - SD: 2 (4)
    - PR: 4 (8)
    - VGPR: 34 (67)
    - CR: 27 (53)
  - Observation
    - Lenalidomide increased/Dexamethasone added: 6 (11)
    - Treatment changed: 13 (25)
  - Patient status with biochemical relapse requiring only observation or alteration of maintenance
    - Progessed: 10 (20)
    - Untreated: 23 (45)
    - Patients with signs of biochemical relapse requiring change of treatment
      - Dose reduction/Dose interruption: 13 (25)
      - Death: 3 (6)

**Treatment beyond progression post transplant**

- VRD: 4 (8)
- VTD: 32 (63)
- VRD: 29 (57)
- VCD: 8 (15)
- VTD: 11 (22)
- VD: 5 (10)
- VCD: 4 (8)
- VRD: 26 (51)
- VTD: 23 (45)
- VD: 9 (17)
- VCD: 4 (8)

**Progressive Disease**

- Stage I: 2 (4)
- Stage II: 4 (8)
- Stage III: 2 (4)

**Conditioning regimen**

- Melphalan 200 mg/m2: 6 (12)
- Melphalan 140 mg/m2: 32 (63)
- Melphalan -velcade: 46 (90)

**Type of MM**

- II: 15 (29)
- III: 17 (33)
- IV: 1 (2)

**Outcome**

- Median age at transplant was 55 years (46-75). Forty-six (90%) of patients received R maintenance, 3 patients received VRD maintenance for higher risk features. Median duration of R maintenance was 22 months (3-62). R dose was changed for toxicity (grade I-II) in 17 (33%) patients. Twenty-nine (57%) patients relapsed: 13 (25%) patients were shifted to different treatment protocols (treatment change), 6 patients (11%) were kept on the same R maintenance (observation group) and 10 (20%) patients had increased lenalidomide dose with dexamethasone (R/D group). 6 patients (37%) of the last 2 groups required change of treatment later. The median follow up was 38 months (1-85). Median TNT was 32 months (7-62). At 2 years, the estimated PFS and OS were 39% and 97.5% respectively. The median OS and PFS2 (from change of therapy) were 54 and 29 months for patients in the observation group, versus 52 and 27 months in the R/D group, and 45 and 33 months with treatment change, respectively. No statistically significant difference was noted.

**CONCLUSION:**

Our small monocentric study is limited by its retrospective design and small sample size. However, it suggests that increasing lenalidomide dose as well as adding dexamethasone in selected patients can postpone change to different lines of treatment without affecting survival.