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Introduction

- Carfilzomib, Revlimid and Dexamethasone (KRd) combination has emerged in recent years as a promising treatment for relapsed and refractory multiple myeloma (RRMM)
- Carfilzomib administered weekly (20/56 mg/m²) showed results equivalent to the twice-weekly regimen in terms of safety and efficacy.
- Several studies, like POLLUX study, conducted in the early RRMM have showed the importance of prolonged triplet-based treatment.

We report the long-term exposure data on KRd weekly given at 56 mg/m² until progression in RRMM

Methods

- 42 patients** received KRd weekly regimen in 28-day cycles until disease progression or until occurrence of unacceptable toxic effects.
- Carfilzomib was administered as a 30-minute infusion on days 1,8,15 (starting dose, 20mg/m² on day 1 of cycle 1 ; target dose, 56mg/m² thereafter).
- Lenalidomide (25mg) was given on days 1 through 21.
- Dexamethasone (40mg) was administered weekly.
- All assessments were made according to IMWG. MRD measurement was studied by NGS (sensitivity level 10⁻⁶)

Characteristics of the patients at baseline (n=42)

| | n (%), unless specified |
|----------------------------------|-------------------------|
| Age > 65 | |
| Yes | 8 (19) |
| High risk | |
| Cytogenetic high risk | 7 (25) |
| ISS 3 | 8 (19) |
| R ISS 3 | 5 (12) |
| EMD | 11 (26) |
| Median previous regimens (range) | 1 (1-3) |
| Previous therapies | |
| Bortezomib | 42 (100) |
| Lenalidomide | 15 (36) |
| Disease refractory | |
| Bortezomib | 2 (5) |
| Lenalidomide | 0 (0) |

Treatment responses of the patients (n=42)

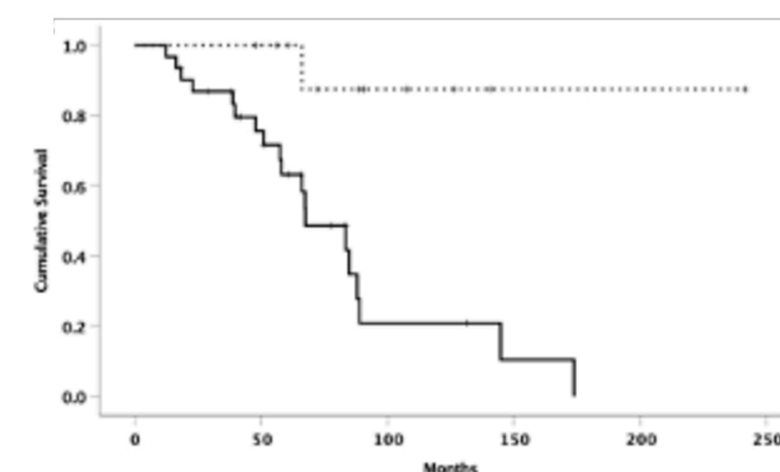
| | n (%), unless specified |
|-------------------------------|-------------------------|
| ORR | 35 (83) |
| MRD negative 10 ⁻⁶ | 5 (12) |
| ≥ CR | 19 (45) |
| ≥ VGPR | 31 (74) |
| ≥ PR | 35 (84) |

- With a median follow-up from start of KRd at 43.5 months, 47,6% died and 50% relapsed
- The median number of KRd cycles was 24 (range 1-51), with 11 (27%) patients who received more than 30 cycles

Results

PFS and OS

The median PFS from start of KRd regimen is 22,6 months (11,2 – 33,9)
The median OS from diagnosis was 88,0 (66,5 - 109,4)



Adverse Events of interest

- 3/28 patients stopped Carfilzomib for cardiac events : 1 for thrombosis, 1 for thrombotic microangiopathy and 1 for Brugada syndrome
- 2/28 patients stopped Carfilzomib for confort
- 7/8 patients who stopped Carfilzomib received Ixazomib, Lenalidomide and Dexamethasone and will not relapsed.
- 10% patients had significant adverse event responsible for the interruption of the treatment.
- No patient died related to adverse events.

Conclusion

- Prolonged exposure to weekly KRd shows promising results in terms of overall survival and progression-free survival even in poorly prognostic disease.
- Prolonged KRd treatment can improve the depth of response with an acceptable tolerance profile even on frailty patients.
- Further studies are warranted to confirm this data on a larger population