# Weekly Carfilzomib, Lenalidomide and Dexamethasone until progression in Relapsed Refractory Multiple Myeloma

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## Introduction

- Carfilzomib, Lenalidomide and Dexamethasone association (KRd) has led to approval in early Relapsed Refractory Multiple Myeloma
- Carfilzomib is an epoxyketone proteasome inhibitor that binds selectively and irreversibly to the constitutive proteasome and immunoproteasome.
- On ASPIRE International phase 3 study Carfilzomib was used on a twice a week basis at 27mg/m² and limited to 18 months exposure.

KRd on a weekly basis at 56 mg/m² had similar and safe properties

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

## Methods

**28 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 $10^{-6}$)

## Results

### 1/ Characteristics of the patients at baseline (n=28)

| | n (%), unless specified |
|---|---|
| Cardiac comorbidities | |
| Yes | 10 (36) |
| ECOG performans status | |
| 2 | 2 (7) |
| High risk | |
| Cytogenetic high risk | 7 (25) |
| ISS 3 | 5 (18) |
| R ISS 3 | 1 (4) |
| EMD | 8 (28) |
| Median previous regimens (range) | 1 (1–3) |
| Previous therapies | |
| Bortezomib | 28 (100) |
| Lenalidomide | 12 (43) |
| Disease refractory | |
| Bortezomib | 2 (7) |
| Lenalidomide | 0 (0) |

### 2/ Treatment responses of the patients (n=28)

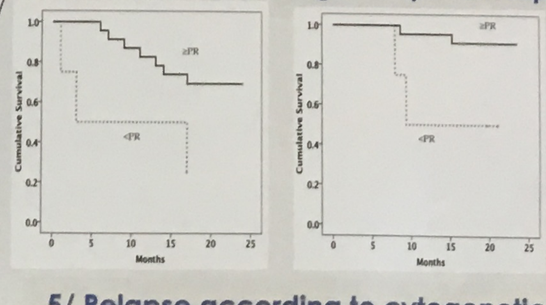
- With a median follow up of 30 months, 50% of patients relapsed and 39% died
- Median duration of response was 13 months
- **8/28 patients are still on treatment with duration > 24 month including 6 patients with duration > 30 months**

| | n (%), unless specified |
|---|---|
| ORR (≥PR) | 24 (85,7) |
| ≥ CR | 13 (46,4) |
| MRD negative $10^{-6}$ | 6 (21,4) |
| ≥ VGPR | 20 (71,4) |
| ≥ PR | 24 (85,7) |
| CBR (≥PR) | 25 ((89,3) |
| ≥ Minor response | 24 (85,7) |

- The median PFS and EFS was at **29 months.** At 42 months, the expected-relapse rate is 60%
- These results are similar to those of the ASPIRE study.

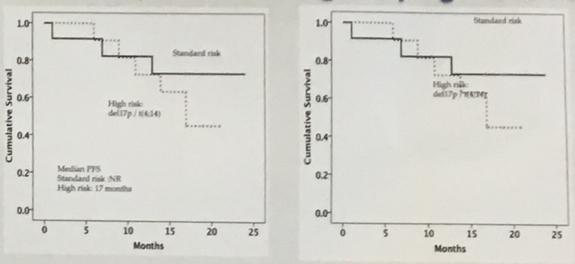
## Results

### 4/ Survival according to depth of response




As demonstrated in ASPIRE, depth of response has an impact on survival, though 86% did have benefit from KRd weekly.

### 5/ Relapse according to cytogenetic markers




Patients with cytogenetic and ISS poor risk features had a lower benefit in terms of survival with KRd weekly median 17 months herein versus approximately 20 months in ASPIRE.

### 6/ Adverse Events of interest

- 3/28 patients stopped Carfilzomib for cardiac events : 1 for thrombosis, 1for thrombotic microangiopathy and 1 for Brugada syndrome
- 2/28 patients stopped Carfilzomib for confort
- 6/7 patients who stopped Carfilzomib received Ixazomib, Lenalidomide and Dexamethasone
- 10% patients had significant adverse event responsible for the interruption of the treatment.
- No patient died related to adverse events.

## Conclusion

- KRd weekly at 20/56mg/m² was effective and safe with manageable toxicities to early RRMM patients. This weekly regimen was far less inconvenient to patients.
- Carfilzomib can be used until progression and a long exposure is effective and safe in RRMM.
- Further studies are warranted to confirm this data on a larger MM population.