



Carfilzomib-Lenalidomide-Dexamethasone in the management of Lenalidomide-refractory Multiple Myeloma

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Introduction

Carfilzomib is an epoxyketone proteasome inhibitor of second generation, proved to be effective and safe in relapsed and refractory Multiple Myeloma (rrMM), in combination with dexamethasone or lenalidomide and dexamethasone.

Aims

In this retrospective observational trial, it has been evaluated efficacy and safety of carfilzomib, in combination with lenalidomide-dexamethasone (KRD) as salvage regimen in patients with rrMM, refractory to lenalidomide, where lenalidomide-based regimens have no proven efficacy.

Materials and Methods

41 patients (23 M/18 F), with rrMM, median age at diagnosis 63.7 years (r. 43-82), median age at start of treatment 67 years (r. 48-84) previously treated with several lines of treatments (median 3, r. 2-11), underwent to KRD regimen (ASPIRE trial schedule) for a median treatment cycles of 8 (r 2-18). ISS was equally distributed, and all patients had previously been treated with bortezomib and IMiDs, and were refractory to these agents. 61% (19/31) of them had undergone at least to a single ASCT.

	Numbers of patients	Age at diagnosis	Age Start Treatment	Previous treatments	ORR: (≥PR)	ORR2: (≥SD)	OS from diagnosis	OS from start treatment	TTR
Pom-Dexa	33 (19 M/14 F)	69 (r. 52-84)	76 (r. 56-89)	7 (r. 2-11)	45.4%	78.7%	92 (r. 21-234)	9 (r. 1-25)	2 (r.1-6)
KRD	41 (23 M/18 F)	63.7 (r. 43-82)	67 (r. 48-84)	3 (r. 2-11)	68.2%	87.8%	62 (r. 9-170)	11 (r. 2-18)	1.3 (r.1-4)
BVD	56 (31 M/25 F)	57.3 (r. 36-82)	61.8 (r. 37-83)	6 (r. 2-11)	64%	85.7%	62.7 (r. 6-151)	9.8 (r. 2-36)	1.2 (r.1-3)

Results

According to IMWG criteria, after a median follow-up of 9 months (r. 2-18), ORR was 68,2% (28/41: 9 CR, 12 VGPR, 7 PR) with 5 progressive diseases (PD) and 8 patients in stable disease (SD): this can be considered as an impressive result in this subset of rrMM patients, refractory to lenalidomide. In particular, for 11 patients, KRD was, after having achieved at least a PR, a bridge to second/third autologous SCT. Median time to response was 1.3 months (r.1-4), median OS from diagnosis was 62 months (r. 9-170), median OS from start of Carfilzomib was 11 months (r. 2-18). Carfilzomib was well tolerated, with grade 2 anemia in 39%(16/41) of patients, successfully managed by ESAs, without necessity of blood transfusions; 29% (12/41) grade 3-4 neutropenia (pegfilgrastim in primary prophylaxis was given, no hospitalization was required, no septic shocks were observed); 34% (14/41) grade 2, 21% (9/41) grade 3 and 12% (5/41) grade 4 thrombocytopenia, without hemorrhagic events and transfusion-dependency. Moreover, it was observed pneumonia in 39% (16/41) of patients, treated by common antibiotic drugs and always solved. A cardiac monitoring was performed for all patients: hypertension (grade 2-3) in 34% (14/41) of patients; fatigue in 39% (16/31) of patients.

Conclusions

Carfilzomib-Lenalidomide-Dexamethasone has shown significant efficacy in a particularly severe setting of patients, relapsed and refractory to all available therapeutic resources, also lenalidomide, and it could be considered as a bridge to a second autologous or allogeneic SCT.

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