Addition of Carfilzomib as a Third Agent in Lenalidomide-Refractory Multiple Myeloma Switching From Doublet to Triplet

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Context

Carfilzomib is a second generation epoxyketone proteasome inhibitor, proven to be effective and safe in relapsed and refractory multiple myeloma (rrMM), in combination with dexamethasone or lenalidomide and dexamethasone.

Objective

In this retrospective observational trial, we 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.

Patients

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 KRD regimen (ASPIRE trial schedule) for a median of 8 treatment cycles (r 2-18). 61% (19/31) of them had undergone at least one ASCT.

Keywords: carfilzomib, multiple myeloma, relapsed, refractory, lenalidomide

Results

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 is 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 needing blood transfusions; 29% (12/41) grade 3-4 neutropenia (pegfilgrastim in primary prophylaxis was given, no hospitalization was required, no septic shock was 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, pneumonia was observed 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).

Conclusions

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

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