Reviewer’s report

Title: Case series discussion of cardiac and vascular events following carfilzomib treatment: possible mechanism, screening, and monitoring

Version: 2
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Reviewer: Prem Sinha

Reviewer’s report:

In the present manuscript authors have reviewed the medical records of 67 patients with relapsed and/or refractory multiple myeloma that were treated with carfilzomib, a proteasome inhibitor. From a comprehensive analysis they report that a significant percentage of patients (12 out of 67) underwent cardiac and vascular related adverse events that were already at the border of cardiac related risk. Further, they describe how patients with cardiac risk factors can be monitored closely during the drug treatment. Finally, the authors put forward the hypothesis that adverse events may be the result of a dose response-dependent perturbation in endothelial nitric oxide synthase (eNOS) activity and NO synthesis that adversely affect cardiac and endothelial cells.

This report is highly significant for treating patients with cardiac complications, especially due to lack of existing published material/reports of such nature.

Minor Essential Revisions/Discretionary Revisions:

1. The authors report that 9 out of 12 patients had prior autologous stem cell transplant. Did the authors come across any patients who had autologous stem cell transplant but did not experience cardiac or vascular related adverse events. If so, it will be beneficial to include this case study as well.

2. One of the future management plans includes decreasing or eliminating hydration in certain patients. It would be important to explain how decrease in hydration will have beneficial effect.

3. It will be useful for a general reader to understand the logic of grading system for the adverse events in patients (for example, what is grade 3 Vs grade 4 etc.)

4. in vivo (line 86 and line 318) and in vitro (line 311) should be in italics.

5. In the list of abbreviations, Durie-Salmon and DS are written in two separate lines.

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests