Reviewer’s report

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

Version: 2
Date: 22 August 2014

Reviewer: Pratik Nagaria

Reviewer’s report:

In this case report, the authors retrospectively examine the records of 67 patients with relapsed and/or refractory multiple myeloma (MM) treated at Mt. Sinai Medical Center, NY. The authors describe 12 patients amongst the 67 who experienced cardiac or vascular-related adverse events subsequent to Carfilzomib-based treatment. While several of the described adverse effects have also been described by other independent observations, the records examined by the authors indicate that most of these patients had a prior history of the specific cardiac or vascular adverse event they exhibited.

Thus, this case report falls under ‘Findings that shed new light on the possible pathogenesis of a disease or an adverse effect.’

No ‘Major Compulsory Revisions’ are recommended

Minor Essential Revisions

• From the described case-studies the criteria for the selection of 67 patients is not clear. Were these the total number of patients diagnosed with refractory or relapsed MM and treated with Carfilzomib or these were randomly selected Carfilzomib-treated patients? This needs clarification.

• Table 2: It is not clear whether the patients who demonstrated grade > adverse event (column 1) were the ones who also had a prior history of adverse effects (column 2). This needs to be clarified.

• Some of the recommendations provided in Table 3 here have also been provided by Carfilzomib drug-manufacturers (http://www.kyprolis.com/starting-kyprolis/side-effects). The authors should comment on how the recommendations that they provide in this study differ/or add to those from the manufacturers.

Discretionary Revisions

• A brief description of Carfilzomib pharmacokinetics (Drug clearance, metabolism) needs to be provided in the section starting on Line 71.

• It is recommended that the discussion on ‘Potential mechanisms of proteasome inhibition-mediated endothelial dysfunction and heart failure’ (line 295) can be shortened. A review (e.g. Kortuem and Stewart, Blood 2013), could be cited.

• To be consistent between the different case studies, it would be beneficial to
readers if the total cumulative dose of carfilzomib before the occurrence of the described adverse events is listed.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests