Peer Review File

Article Information: https://dx.doi.org/10.21037/apm-22-691

Reviewer A

1. In the chapter "Infection in patients with HM," I advise the following treatment agents to comment for the authors, because it would be helpful for the readers: (1) primary prophylaxis for fungal infection itraconazole oral solution (ITCZ-OS) harbors better bioavailability than capsule (page 11, line 392), (2) in anti-fungal treatment including prophylactic use, the positioning and role of liposomal amphotericin (or amphotericin) would be reasonably added (page 11, lines 396-413). (3) In empirical therapy (special situations), you mentioned about glycopeptide, probably vancomycin for setting in breakthrough fever. Likewise, I offer to add the description of antifungal coverage as next additive agent for second breakthrough fever (page 10, lines 366-371). (4) for viral infections, you only limited the agent valacyclovir. How about acyclovir (page 11, line 419)?
Answers: All have been supplemented in the revised page 21, line 4 for item (1); page 21, line 15 for item (2) ; page 20, line 5 for item (3) and, page 22, line 10 for item (4).

2. The name of pathogenic microbials should be written in italic style starting with a capital letter. Pneumocyctis "j"iroveci (page 11, line 399).
Answers: It has been amended accordingly (page 21, line 10).

3. You taught me about the efficacy of single- or double-unit red blood cell transfusion (page 6, line 203). How about platelet transfusion? If you know an evidence which is better ten unit or twenty unit (single or double)?
Answers: There is no such evidence for platelet . The usual dose is mentioned in page 12, line 20.

Reviewer B

1. The authors point out that many of the 'evidence-based' recommendations for interventions (including symptom management) for patients with advanced hematologic malignancies are drawn from 'healthier' populations (not those receiving palliative care). I think that this point is worth highlighting repeatedly in the article to ensure that readers do not inappropriately assume that your conclusions and recommendations are the 'gold standard' or 'evidence-based' for patients with advanced disease near the end of life.

Answers: It has been highlighted in the abstract (page 8, line 13) and conclusion (page 34, line 14) of the revised manuscript.

2.Consideration of many interventions (blood products/ESAs, antimicrobial therapy, disease-modifying therapy, etc…) all require careful consideration of the potential risks and benefits and absolutely must consider a patient's goals and wishes. I suggest that the authors ensure that this point comes through in the text and in the summary tables.

Answers: This has been mentioned accordingly (page 34, line19) of the revised manuscript and revised tables 1-4.

3. Finally, I suggest that the authors review some of the recent literature that has discussed hematologic malignancies in palliative care and red blood cell transfusion in palliative care. Since ~2019, there have been several articles published on these topic that would be relevant to discuss and cite.

Answers: The relevant literatures have been updated (page 11, line 9).

4.Abstract and intro lines 149-150: "there are increasing number of patients with advanced HM referred to PC team while they are still on disease treatment". This sentence appears in the abstract and intro, and I recommend you revise it for grammar and terminology. Should it not be "disease-modifying treatment/therapy"?

Answers: This has been revised (pages 8 line 6 & page 9 line 11).

5. Methods: I understand that your review covered a broad scope, but are you able to provide any additional details on your search strategy, as well as data synthesis? How were articles deemed relevant? Who decided this?

Answers This has been mentioned (page 10, line 8-11).

6. Line 176: "While the use of blood product provides effective symptomatic relief" Does the use of blood product always provide effective symptomatic relief? I suggest rephrasing this as "can provide effective symptomatic relief".

Answers: It has been rephrased (page 10, line 21).

7. Lines 187-196: I believe that this summary could be more concise given the scope of your review.

Answers: It has been revised (page 11, line 11-17).

8. Lines 197-207: I would recommend that the authors review and consider discussing/citing some of the recent literature that has discussed transfusion among patients receiving palliative care. There is a body of literature specifically discussing red blood cell transfusion.

Answers: These recent literatures have been updated (page 11, line 9).

9. Lines 679-680: "The roles of PC nurse include both emotional and practical support (e.g Hickman line) to patients and their families." This line is an awkward intro to this section, that diminishes the expertise and value of palliative care nursing. Yes, they provide emotional support but they also have expertise in symptom management (as well as the practical items).

Answers: This has been revised (page 34, line 1).

10. Conclusion: It is good that the authors mentioned similarities and differences of patients with hematologic malignancies in the palliative care setting compared with those with solid organ tumours. I think this article would be improved by introducing this idea early

Answers: This has been revised (page 9, line12).

Reviewer C

1. It would be great to include a sentence or two about the supportive care needs of family caregivers of patients with advanced HMs.
Answers: This has been updated (page 9, line 18).

2. Regarding fatigue (pages 13-14), there is a growing body of literature to support the role of exercise in the management of cancer-related fatigue (see refs below). You may wish to include a sentence or two about exercise as an intervenetion for cancer-related fatigue.
Answers: These have been updated (page 26, line 12).

3.nursing care (page 17, starting at line 678), some clinicians and scholars advocate for all nurses to be able to provide primary palliative care, irrespective of their practice setting/expertise. In this regard, the hematology nurse should possess basic primary palliative care competencies and skills (arguably, all clinicians, including physicians, should be able to provide basic primary palliative care and refer to specialty palliative care as required).
Answers: It has been updated (page 34, line 8).

4. a “good death” (line 671), you may wish to include this article by Kuczmarski & Odejide.
Answers: This has been included in reference 87 (page 33, line10).

Reviewer D

1. One aspect that perhaps is overlooked is the frequent visits to cancer center and time spent in therapy. For certain conditions oral targeted therapy could help to spend less time in cancer center and more time at home. This has not been studied in depth but it is already happening in clinical practice
Answers: This has been updated (page 33, line 15).

2.Another interesting aspect would like to see is that perhaps we may need to redefine the "palliative care goals" of patients with hematologic malignancies

I do not think that same goals apply to all of them. For instance in a patient with Transfusion dependent (red cells and platelets) condition, the goal of spacing out transfusions should be an ideal palliative care objective

Answers : This has been mentioned in revised table 1 and discussion part (page 34, line 18) with yellow highlight.

3.Another aspect is Transfusion at home would be unique in this setting and could contribute to better outcomes

Answers : This has been updated (page 33, line 12).

Reviewer E

1. The authors interchange the terms palliative care and supportive care. This may be simpler in oncology, but in hematological malignancies, supportive care usually refers to care to allow patients to complete treatments with minimal risk.

Answers : This has been further clarified (page 9, line 6).

2. Please frame the target for this review – is it to explain to PC providers how to treat HM patients or to show hematologists how to provide PC for their patients?

Answers: The target has been framed (page 9, line 20).

3. Throughout the discussion on use of blood products – the guidelines provided are based on data applying to mortality – ie – triggers for blood products are based on mortality data rather than patient comfort. Is there any data on the effect on quality of life? Would you recommend transfusions for a patient with <2weeks prognosis and no effect on symptoms?

Answers: This has been discussed as a limitation (page 34, lines 15 &19).

4. The scope of this review is huge – I would suggest a separate review on use of transfusions and growth factors and a separate review of symptom management.
Answers: This has been reviewed separately (page 10, line 13 & 15).

5. I would suggest clarifying the basis for the recommendations for symptom management made – are they based on studies including HM patients and what is the available data?
Answers: based on studies including international guideline on hematology-oncology or oncology. It has been mentioned as a limitation of this study (page 34, line 16).

6. In general there is little discussion of management based on goals of care. It would help if the authors could frame the decision to be made based on patient goals and available data
Answers: This has been supplemented (page 34, line 18) and in revised tables 1-4.

7. Heme-onc emergencies should include hypercalcemia and cord compression among others
Answers: These have been updated in the revised table 2 (page 24, line 1).

8. The source of pain in patients with HM would depend on the disease. Bone pain is common in myeloma but in other cases this is not the case. See for example: Shaulov, A., Rodin, G., Popovic, G. et al. Support Care Cancer (2019) 27: 2789.
Answers. It has been supplemented (page 27, line 6).

9. Little data on pain syndromes more commonly seen in HM is available: Perianal pain, Mucositis treatments, incidental bone pain.
Answers : This has been mentioned as a limitation in the discussion (page 34, line 15).

10. The section on EOL care should discuss site of death – options for death at home for patients with HM are minimal
Answers : This has been updated (page 33, line 11).

11. None of the early palliative care in HM studies are referenced. See JAMA Oncol. 2021;7(2):238-245 and JAMA. 2016;316(20):2094-2103

Answers : These have been supplemented in references 3 & 4 (page 37, line 1).