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PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Oncology*

Manuscript NO: 82399

Title: Interaction between age and gender on survival outcomes in extramedullary multiple myeloma over the past two decades.

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05601558
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: United States

Manuscript submission date: 2022-12-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-01-16 05:19

Reviewer performed review: 2023-01-26 06:32

Review time: 10 Days and 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors uncovered interesting aspects regarding an unmet need of a subtype of high-risk multiple myeloma. However, several points should be addressed: 1.There is many potential biais in this study that have to be discussed in the manuscript as the authors performed many statistical analysis that could conduct to a false correlation between those factors. It should have been interesting to confirm this hypothesis on a external validation cohort. 2.Another question is the accuracy of clinical data about the exact nature of these EMM manisfestation (primary vs. secondary spread) and the anatomical characteristics (bone-related vs. ematogenous spreading) in the data base and the possible interaction between the higher rate of EMM in relapsed and refractory vs. newly diagnosed. 3. Did the authors also check for plasma cell leukemia (PCL)? Are these data really reliable? Is this data set already audited on this topic (as far as I understand is a retrospective registry) 4. The manuscript have to be improved as there is no references in the introduction to focus on the byological background (i.e. several reports have been published regarding the genomic landscape of particular EMM (i.e. central nervous system CNS), as a main principal results about genomic and cytogenetic

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makeup are not described clearly in the tables 5. This study opens the way to trials for targeted therapies in EMM. In the discussion section you talk about novel approaches (such as RNA based and altrenatives) indeed, utilizing new tools miRNAs as potential targets in the diagnosis, prognosis and treatment of MM, which can be useful for future clinical management. 6. In the frame of point 5 thinking, bind to target miRs modulating gene expression at post-transcriptional levels. Here, we present an overview of miRs deregulation in the pathogenesis of multiple myeloma (MM), and discuss the potential use of miRs/nanocarriers association in clinic. Since miRs can act as oncogenes or tumor suppressors, strategies based on their inhibition and/or replacement represent the new opportunities in cancer therapy. The miRs delivery systems include liposomes, polymers, and exosomes that increase their physical stability and prevent nuclease degradation. Phase I/II clinical trials support the importance of miRs as an innovative therapeutic approach in nanomedicine to prevent cancer progression and drug resistance. Results in clinical practice are promising. Can you explain more precisely the action and the possible combinations with current therapeutics (please refer to PMID: 32349317 and expand the biological discussion or the potential explanation for the authors findings in the introduction/discussion section briefly mentioning the biological landscape).

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Peer-review model: Single blind

Reviewer's code: 06497461
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: United Kingdom

Author's Country/Territory: United States

Manuscript submission date: 2022-12-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-01-27 13:56

Reviewer performed review: 2023-02-07 11:30

Review time: 10 Days and 21 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Manuscript is well-written and findings are communicated clearly. Discussion of the results and the implications of these results could be improved - the explanation of results (hypotheses behind them) could be expanded upon and the "so what" is missing.

Sample size might be considered small when looking at certain groups of patients and should be considered.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Clinical Oncology*

Manuscript NO: 82399

Title: Interaction between age and gender on survival outcomes in extramedullary multiple myeloma over the past two decades.

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05601558

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: United States

Manuscript submission date: 2022-12-17

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2023-02-23 03:18

Reviewer performed review: 2023-02-23 03:26

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[Y] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

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statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors have clarified several of the questions I raised in my previous review. Most of the major problems have been addressed by this revision.