

PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 73320

Title: Intrathecal methotrexate in combination with systemic chemotherapy in glioblastoma patients with leptomeningeal dissemination: a retrospective analysis

Provenance and peer review: Unsolicited manuscript; externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05631502

Position: Peer Reviewer

Academic degree: BSc, MBBS, MD

Professional title: Academic Research, Doctor

Reviewer's Country/Territory: Qatar

Author's Country/Territory: China

Manuscript submission date: 2021-11-23

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-12-22 03:09

Reviewer performed review: 2021-12-29 08:57

Review time: 7 Days and 5 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous
	Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No

SPECIFIC COMMENTS TO AUTHORS

I would like to thank the authors to take out time to conduct this important study. I have a few comments (major and minor) as below and I believe they need to be addressed before this article can be considered for a potential publication

- One of the major limitations of the study is the design, as the authors are building a case for efficacy of a medication, which can be best done in a prospective clinical trial or at-least prospective observational designs. This has to be addressed in more details in the limitations. Additionally, the title needs to have the word retrospective analysis or any alternate work clearly indicating the study design.
- Another concern that I have is that there is no comparative group, even if this is a retrospective design there could have been a comparative group of patients who for one reason or the other did not receive ITC MTX. I do not think in this current scenario it is appropriate to comment on effectivity and safety profile as these measures need a comparator. Authors can address this by changing the theme of the manuscript from effectivity and safety to something like “clinical outcomes of GBM patients who received ITC MTX”
- Sample size is small and has not been justified as to what level of power will this sample size give to inference these results.
- I do understand that the authors have touched on all the above limitations and rightfully so, I would advise them to change the theme of this manuscript away from finding effectiveness and safety profile.
- Some important and highly relevant studies have not been discussed (such as 10.1007/s11060-014-1486-2)
- Minor grammar polishing is required throughout the manuscript.

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Provenance and peer review: Unsolicited manuscript; externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05689039

Position: Peer Reviewer

Academic degree: PhD

Professional title: Postdoctoral Fellow

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2021-11-23

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-12-30 21:23

Reviewer performed review: 2022-01-12 04:14

Review time: 12 Days and 6 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

**Peer-reviewer
statements**

Peer-Review: [☒] Anonymous [☐] Onymous

Conflicts-of-Interest: [☐] Yes [☒] No

SPECIFIC COMMENTS TO AUTHORS

Glioblastoma is a fast-growing and aggressive brain tumor with a median survival of only 12-15 months. Leptomeningeal dissemination (LMD) is a severe complication of GBM raising diagnostic and therapeutic challenges in clinical routine. In this study, the authors combined methotrexate with systemic chemotherapy to treat LMD patients. They revealed the median overall survival of glioblastoma patients with leptomeningeal dissemination after receiving systemic chemotherapy in combination with intrathecal methotrexate is a bit longer than the regular chemotherapy regimen. The major issue for the combination regimen is the mild improvement in median overall survival time and the small patient number. There are several minor issues listed as follows. Line number is recommended to put forward opinions about revision. Are there patients who were only treated with a regular chemotherapy regimen in the trial? Or all of the 26 patients were treated in a combination of methotrexate? Fig 2, please indicate what is the chemotherapy in this combination therapy. Is it TMZ or other chemotherapy drugs?

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Reviewer's code: 05631502

Position: Peer Reviewer

Academic degree: BSc, MBBS, MD

Professional title: Academic Research, Doctor

Reviewer's Country/Territory: Qatar

Author's Country/Territory: China

Manuscript submission date: 2021-11-23

Reviewer chosen by: Ji-Hong Liu

Reviewer accepted review: 2022-02-18 09:38

Reviewer performed review: 2022-02-18 09:46

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
<https://www.wjgnet.com>

statements

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

SPECIFIC COMMENTS TO AUTHORS

I appreciate the efforts of the authors to revise the study. Most of the concerns have been adequately addressed. I still have one concern with regards to a still-present strong message of the efficacy of intrathecal MTX. This is still visible in the core tip and elsewhere too. If the authors agree, they can change it to keep the results in accordance with the study design.