Title: Reduced Frequency of Intravitreal Methotrexate Lowers the Risk of Keratopathy in Vitreoretinal Lymphoma Patients

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Reviewer: Shahar Frenkel

Reviewer's report:

Dr. Zhou and colleagues tested what most bothers patients treated with IVit MTX for VRL - the keratopathy. Keratopathy is the reason why some clinicians give only partial treatment, see recurrences and erroneously decide that IVit MTX is not good for their patients. As such, this is an important paper. The manuscript is written well and clear. Please see specific comments.

Background:
VRL does NOT involve the uveal tract.
Brackets for the references should be spaced from the text.
Please be consistent - the proper term is vitreo-retinal lymphoma VRL. Intraocular lymphoma also includes to choroidal lymphoma, which is a different entity altogether.
Some articles are missing: "...antibody) are currently THE main treatment...". "Despite THE efforts, intraocular lymphoma..."
This last sentence is also wrong in context in addition to the bad grammar: VRL has a good prognosis. It is the CNS component that entails a bad prognosis. Treatment of the VRL portion does not change the CNS outcome.

M&M:
Diagnosis: The only missing component in this fine description is the lack of PCR analysis of the specimens. I would appreciate a discussion of its absence.
Treatment: Here lies a great flaw: it appears that radiation treatment could have been added. This messes the results, as one would expect to see the results of IVit MTX alone in a study like this.

Results:
Please also add a Snellen equivalent next to each LogMAR result.
Table 2: did WBRT include the eyes in the radiation fields? If so, these patients should be excluded fro this study.
Fig.3 is far from depicting a typical IVit.MTX-type of keratopathy. It is far too gentle.

Discussion:
It appears that the authors follow the recommendation that any CNSL patient undergo routine ophthalmic evaluation repeatedly, and not just at diagnosis of CNSL. This should be stated clearly.
The name of the entity is vitre-RETINAL lymphoma. However, it appears that hardly any of the patients had retinal involvement. This is an important observation to state.
I completely disagree with the authors' cautionary statement on minimizing treatment for patients without CNS disease, as previous publications did not find any effect of the IVit injections on the CNS portion of the disease.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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