Dear Editor,

Thank you very much for your decision letter and advice on our manuscript (Manuscript #67467) entitled "Low-dose Intralesional Injection of 5-Fluorouracil and Triamcinolone Reduces Tissue Resident Memory T cells in Chronic Eczema". We also thank the reviewers for their constructive comments and suggestions. We have revised the manuscript accordingly, and all amendments are indicated by red font in the revised manuscript. In addition, our point-by-point responses to the comments are listed below this letter.

This revised manuscript has been edited and proofread by *Medjaden,* Inc.

We hope that our revised manuscript is now acceptable for publication in your journal and look forward to hearing from you soon.

With best wishes,
Yours sincerely,

Jianbiao Fei

Department of Dermatology
Shanghai University of Medicine & Health Sciences Affiliated Zhoupu Hospital
Shanghai, China

First of all, we would like to express our sincere gratitude to the reviewers for their constructive and positive comments.

Replies to Reviewer 1

Specific Comments

This is an interesting clinical trial study concerning new method of eczema pharmacotherapy. The theoretical part brings useful information concerning eczema treament and its immunological aspects and experiments including statistical analysis are well designed and described in detail. This article may be useful source of knowledge for all medical practicioners who in their practice meets questions of eczema treatment. It should be emphasised that immunological aspects of this issue were presented which are rather rarely explored in clinical studies of eczema treatment. For these reasons, I recommend this paper for publication in World Journal of Clinical Cases.

Response: We thank the reviewer for the positive comments.

Replies to Reviewer 2

Specific Comments to Authors:

1. I have included all my comments in the word document in red. A really good article to read through and see its potential effect in the field of dermatology. I corrected most of the grammatical mistakes and pointed to a few queries that need to be addressed.

Response: We thank the reviewer for the thoughtful suggestion. We have added the side effects of long-term use of oral corticosteroids and immunosuppressants as highlighted in the revised manuscript (page 6, lines 16-18).

2. Were COPD patients also excluded

Response: According to our exclusion criteria, we excluded COPD patients because these patients often have respiratory tract infections. We have specifically clarified this in the revised manuscript (page8, lines9-10).

3. Were environmental factors or occupations taken as any possible outliers

Response: We thank the reviewer for the insightful comment. As indicated in the guideline, risk factors

for adult eczema include environmental factors, sweating, physical irritation (including scratching), microbes, stress, and food. In this study, all participants attended our hospital, were local residents of Shanghai, and had similar dietary habits. To reduce the interference from weather, our follow-up time was more than 1 year. However, we could have considered the differences in patients' occupations. We have included this as a limitation of our study, as highlighted in the revised manuscript (page 16, lines10-11).

4. isn't the whole treatment and follow-ups for 18months

Response: The whole period for one time treatment and follow-up was 13 months.

5. what was the p-value for the 5-FU+TA group

Response: The p-value for the comparison of the average ADSI scores between the 5-FU+TA and TA groups was 0.154. This was added in the revised manuscript.

Replies to Reviewer 3

1. The types of chronic eczema should be classified as each type has different response rate

Response: There is no defined classification for chronic eczema according to the eczema treatment guideline. Physical irritation (including scratching) is a risk factor for inducing eczema. Anatomical sites such as neck or limbs are exposed and easy to scratch. However, in this study, when we stratified cases according to the anatomical sites of neck, trunk and limbs, no significant difference in the number of patients was observed. Additionally, we also did not find significant differences in the treatment period or average ADSI score between groups.

2. Why author select ADSI for scoring the chronic eczema? Were all chronic eczema of atopic type?

Response: Eczema is also commonly known as atopic dermatitis. There are various scoring systems for assessing the symptoms of eczema, for example, the Eczema Area and Severity Index (EASI), Scoring Atopic Dermatitis (SCORAD) and the Atopic Dermatitis Severity Index (ADSI). Both the EASI and SCORAD evaluate the eczema areas. In this study, the eczema areas of both the 5-FU+TA and TA treatment groups were small and similar. We did not evaluate eczema areas as main criteria. Thus, we think ADSI is the more suitable index for scoring the chronic eczema in this study.

3. As author selected a broad age group from 28-80 years and there are some age specific chronic eczema that has different response rate should be discussed.

Response: As the reviewer suggested, we have performed a stratified analysis for different age groups: 28-45 years, 45-60 years, and older than 60 years. We did not find significant differences between these groups, and the data have been included in Table 1.

4. Author should also mentioned total cumulative dose of TA in each patient as the higher dose of intralesional TA can give systemic effects

Response: As mentioned in the third paragraph of Discussion section, the single dosage of TA is 10 mg for local injection, which is much lower than the dosage used for keloids (10–40 mg at least three times).

5. Author should also mention the confounding variables in the study.

Response: We thank the reviewer for the constructive comment. We have included a discussion of possible confounding variables in the third paragraph of the Discussion section (page14, lines21-24 and page 15, lines1-2).

In addition, the text format of all figures has been modified according to the requirements of the journal.

Due to the low resolution, we replaced the previous figures with high-quality versions, which are images of immunohistochemical staining of CD103 from before and 2 weeks after treatment in the 5-FU+TA group and images of immunohistochemical staining CD8 and CD103 from before the treatment in the TA group in Figure 4.