

Thank you very much for taking the time to review this manuscript, for recognizing the content of our article, and for allowing us to make changes according to your suggestions. Please find the detailed responses below and the corrections that were made, highlighted in **green** in the re-submitted files.

1. In line 53 the authors mention the importance of CD4+ CD25+ T cells in desensitization, but below on line 239, it is mentioned that CD4+CD25+CD134+ T cell counts tend to decrease thanks to desensitization. Please clarify, taking into account the true function of CD4+CD25+ T cells, specifically CD134+ cells.

Response: Thank you for the comment. In a study by Teraki et al, it was demonstrated that the number of lesional CD4+ CD25+ T in fix drug eruptions (FDE) is increased significantly after desensitization, whereas the number of lesional CD8+ T cells decreased. It is suggested that the CD25+ CD4+ T cells found in the epidermis of FDE lesions after desensitization, might have a regulatory function, thereby suppressing the effector function of CD8+ T cells in FDE lesions. The CD25+CD4+ T cells in the epidermis of FDE lesions after desensitization are likely the result of continual migration of CD25+CD4+ T cells into the epidermis due to repeated administrations of the drug (reference 25).

On the other hand, in the study by Klaewsongkram et al, the authors investigated the proportion of drug –induced CD4+CD25+CD134+ T-cell changes in peripheral blood in patients with a history of imatinib-induced non-immediate reactions undergoing drug desensitization. The CD134, or OX40, a member of the tumor necrosis factor receptor family, is characterized as a costimulatory molecule regulating both TH1- and TH2-mediated reactions and has a critical role in the maintenance of an immune response. The coexpression of CD134 and CD25 after 48 hours of antigen stimulation can be used as a marker for antigen-specific CD4+ T-cells. The authors reported a successful desensitization protocols, and observed a reduction in imatinib-induced CD4+CD25+CD134+ T-cell percentages in peripheral blood after tolerance induction in these patients. It remained low even after discontinued use of steroids.

(reference 10).

We have added this in lines 238-255.