

Dear Editor, Please find here our point-to-point answers to the reviewers

Reviewer 00012309:

Thank you very much for your detailed review. Here, we provide a point-to-point answer to your suggested corrections.

1. As suggested by the reviewer, we added information about TPMT deficiency in 0.3% to this section. However, as we already addressed in this subheading, we do not systematically determine TPMT activity in our patients, as patients with normal TPMT activity might also develop myelosuppression, and we choose to closely monitor all patients on thiopurine therapy, especially in the first 3 months of therapy.
2. Deep prolonged remission is defined as “no signs of active disease on clinical, biochemical, endoscopic, histological and radiologic evaluation for at least 2-3 years”, as specified later in the subheading.

Reviewer 00055041:

The authors would like to express their gratitude to this reviewer for the review of our manuscript.

Reviewer 03478404

Thank you very much for your detailed review and praised comments. Here, we provide a point-to-point answer to your suggested corrections.

1. In our center, we do not routinely use 5-ASA to optimize thiopurine therapy. For this reason, we chose not to mention mesalazine in the abstract, but this strategy is mentioned in the subheading “Measuring metabolites”.
2. We agree with the reviewer and added a phrase to this section.
3. As suggested by the reviewer, we added information about TPMT deficiency in 0.3% to this section. However, as we already addressed in this subheading, we do not systematically determine TPMT activity in our patients, as patients with normal TPMT activity might also develop myelosuppression, and we choose to closely monitor all patients on thiopurine therapy, especially in the first 3 months of therapy.
4. We agree with the reviewer and added a sentence about EBV-associated HSTCL to this section. Furthermore, as we described in the “cancer risk” paragraph, we do not systematically refer patients to dermatologists. However, patients are informed of a higher risk of skin cancer and are advised to mention new skin abnormalities directly.
5. Since this paper is about thiopurine therapy in adult IBD patients, we added one sentence in the introduction to refer readers to a paper in the pediatric population.
6. We added histological remission to the sentence.
7. Whereas elevated 6-MMP can cause hepatotoxicity, it can also inhibit the *de novo* purine synthesis, thus causing myelotoxicity. We added hepatotoxicity to the table, as suggested by the reviewer.

With kind regards, On behalf of all authors,

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