

## Author's response to decision letter

### Response to Reviewer 1:

**Comment 1:** The significance of  $^{18}\text{F}$ -FDG avidity before and after treatment should be discussed as the topic focusing the PET finding.

**Response:** We appreciate it lot for your good suggestion. Since the significance of  $^{18}\text{F}$ -FDG avidity before and after treatment is very important, we have carefully discussed the two parts in the revised manuscript respectively, as “Although two early retrospective studies of Hoffman *et al.* reported absence of  $^{18}\text{F}$ -FDG avidity in total 24 patients with MALT lymphoma, increasing data indicated that imaging with  $^{18}\text{F}$ -FDG-PET is useful for lesion detection. In the consensus of the International Conference on Malignant Lymphomas Imaging Working Group, the  $^{18}\text{F}$ -FDG avidity of MALT lymphoma varied from 54% to 81% before treatment. Beal *et al.* retrospectively reviewed 42 patients with MALT lymphoma and reported that 81% of the lesions demonstrated  $^{18}\text{F}$ -FDG avidity with a median  $\text{SUV}_{\text{max}}$  of 5.5. Karam *et al.* compared the sensitivity of PET and CT. PET outperformed CT in the depiction of MALT lymphoma with sensitivity of 85% *versus* 57%. Based on the theory that integrating the PET scanner and helical CT provides more sensitive and specific images, Carrillo-Cruz *et al.* analyzed PET/CT images of 40 patients with marginal zone B-cell lymphoma and found that PET/CT had a significant advantage in detecting more involved lesions through abnormal FDG avidity. The sensitivity of PET/CT was as high as 95.5% for extranodal lesions, while the sensitivity of CT was only 67%. Apart from the important roles in discovering lesions and staging, the exceptionally high FDG avidity before treatment can also present suspicion of DLBCL transformation and help to determine the repeat biopsy site. In the retrospective study of Carrillo-Cruz *et al.*, there was a case of MALT lymphoma showing DLBCL transformation with  $\text{SUV}_{\text{max}}$  as 37. Karam *et al.* reported that the mean  $\text{SUV}_{\text{max}}$  was 11.2 in large B-cell transformed MATL lymphoma, while for non-transformed MALT lymphoma, the mean  $\text{SUV}_{\text{max}}$  was 3.7.

<sup>18</sup>F-FDG / PET is essential for initial staging of MALT lymphoma, while studies have presented that the even more clinically important role is its ability to evaluate response to treatment through FDG avidity changes and direct subsequent clinical decision-making. In the research of Mayerhoefer et al., it showed that interim <sup>18</sup>F-FDG-PET can predict the end-of-treatment outcome after three cycles of rituximab-based therapy in patients with MALT lymphoma. Lesion-based cut-off value for separation of complete remission from other outcomes (i.e., CR vs. PR + SD) was -11.74% for  $\Delta\text{SUV}_{\text{max}}$ , which meant that patients with a  $\text{SUV}_{\text{max}}$  reduction more than 11.74% would have a better prognosis. In the series of Beat et al., eight patients with MALT lymphoma accepted a PET/CT examination after first-line treatment. Among them, 3 patients attained a complete remission with no focal or diffuse FDG avidity above background in a location incompatible with normal anatomy/physiology, and 2 patients reached a partial response without relapse after 6 and 18 months. Carrillo-Cruz et al. evaluated patients' post-treatment response with PET/CT, which revealed 10 of 15 patients had a negative PET/CT. Remarkably, none of them relapsed, and the 3-year OS reached 100%, reflecting a negative predictive value of 100%. Perry et al. followed up 12 patients with MALT lymphoma using PET/CT [median follow up 21 months (6–48 months)]. PET/CT showed subsequent biopsy proven relapse in three patients and disease progression in another patient”.

**Comment 2:** Did this patient receive any radiochemotherapy after sigmoid colon resection?

**Response:** Thanks a lot for your valuable comments. After surgery, the pathological diagnosis of the patient presented moderately differentiated ulcerative sigmoid adenocarcinoma of T3N0M0 and there was no high risk factor. According to the NCCN guidelines, the patient didn't receive any radiochemotherapy after sigmoid colon resection. We have revised the manuscript as “Pathological diagnosis presented moderately differentiated ulcerative sigmoid adenocarcinoma of T3N0M0 without any

high risk factors. As a consequence, the patient was released from our hospital, eschewing adjuvant radiochemotherapy”.

**Comment 3:** The colonoscopic illustrations before and after chemotherapy should be offered for comparison.

**Response:** We are deeply sorry for the neglect of patient’s post-treatment colonoscopic illustrations. In the revised manuscript, we have presented the colonoscopic picture with legend as “Follow-up colonoscopy showed a smooth anastomosis without any mass.”



**Figure 6.** Colonoscopy findings after treatment. Follow-up colonoscopy showed a smooth anastomosis without any mass.

**Comment 4:** Figure 1 is unnecessary. Were Figures 8&9 originally made by the authors? If not the copyright should be considered.

**Response:** Thank you very much for your good suggestion. We are sorry for inserting the unnecessary Figure 1. We have deleted it in the revised manuscript to make the manuscript more concise. Figures 8 and figure 9 were originally made by the authors with the software Pathway Builder tool.

**Comment 5:** “Discussion” is too long and not to the point and must be shortened extensively.

**Response:** Thanks a lot for your valuable comments. MALT lymphoma arising at the colorectal anastomosis has not been thoroughly

investigated, including the etiopathogenesis, PET/CT characteristics, and treatment strategy. So, in the revised discussion, we emphasized these three parts and delete the section as “postoperative follow-up for patients with colonic adenocarcinoma” which was not closely associated with the case. Furthermore, the whole discussion section was shortened accordingly. In addition, we carefully discussed the significance of FDG avidity before and after treatment.

**Comment 6:** “References” too long.

**Response:** Thank you very much for your useful suggestion. Due to a long discussion section, we inserted too many references, among which there were less important ones. We have checked the references one by one according to the manuscript and deleted unnecessary references.

We also edited the manuscript for language and presentation.

Thank you for your great review. We sincerely hope that our revised manuscript would win your satisfaction.