

## **Reviewer comment reply**

### **Reviewer 1**

An interesting review that discussed the immune microenvironment and check point inhibitors in HCC. Several problems need further revision.

1. "ICI in BCLC stage B" and "ICI and TACE" should be integrated into one section.

**Ans:** We thank the reviewers for their valuable suggestion. "ICI's in surgery" has been included in "ICI in BCLC stage B" section at **Page 11, Paragraph 1, Line 12-15**.

2. It seems that the value of ICIs in surgery was not discussed in the manuscript

**Ans:** The details about "ICIs in surgery" have been included at **Page 12, Paragraph 1 and 2**.

### **Reviewer 2**

1. What happens- suppression of immune system Both MDSCs and macrophages may derive from monocytes, and MDSCs may differentiate into M2 macrophages.

The arrangement of the manuscript is prone to be ambiguity.

**Ans:** We thanks the reviewers for their valuable inputs. The arrangement of the manuscript has been revised and improved to remove any ambiguity.

2. “Cold and Hot tumours concept” It is simple for this definition. Which reference cited ?

**Ans:** The reference has been added **Reference 44 at Page 8, Paragraph 2, Line 4.**

3. M2 TAM is immunosuppression, which should be in Cold or Hot tumors?

**Ans:** Reviewers have asked a good question. The literature research shows increased TAMs in immune active hepatocellular carcinoma meaning Hot tumor. However, we could not find a reference citing specifically about M2 TAM as they are immunosuppressive and are expected to be present in Cold tumors. Hence, the same point has not been added in the manuscript due to lack of available evidence.

4. Why Dendritic cells (DC) are the initiator?

**Ans:** As dendritic cells present antigens to CTLs, their different phenotypes behave differently. The mechanism has been elaborated at **Page 4, Paragraph 2 and Page 5, Paragraph 1 and 2.**

5. The topic of CAF is too brief and you’d better review CAF after Treg.

**Ans:** The CAF details have been elaborated at **Page 7, Paragraph 2, 3 and Page 8, Paragraph 1.**

6. T regulatory cells- suppressors of anti-tumour immunity MDSCs, M2 TAM and N2 TAN are also suppressors of anti-tumour immunity. The title has no characteristic.

**Ans:** The title for all cells has been made “**Immune suppression**” at Page 3, Line 29.

7. The figures should be added M1/M2 TAM, N1/N2 TAN, G/M-MDSC.

**Ans:** The required nomenclature has been added in **Figure 2**.

