Peer Review File

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Reviewer A

Comment 1: While the review is well written, it is light on details as evidenced by only 37 references

Reply 1: More in-depth review of new literature has been done and the number of references has been increased to 75

Comment 2: The role of Tregs, TAMs and MDSCs and the agents exploited

Reply 2: This has now been elucidated with references (lines 138 – 203)

Comment 3: Rationale for CTLA4 and PD-1 is not clearly stated. Overall manuscript is light on details

Reply 3: Several more details related to CTLA-4 and PD-1 has been added. More references and data has been added (lines 70 -72)

Comment 4: Synthesizing the information in figures and a table (to summarize approaches) would also greatly benefit this manuscript in its current form.

Reply 4: A figure highlighting the current approaches has now been added

Reviewer B

Comment 1: In the "phenotypes of immunosuppression are malleable" section, the authors discussed the role of TAM in sarcoma. A recent article that was published that analyzed the role of TAM in than 10000 sarcoma patients was not included (Dancok 2020 Oncoimmunology). In this manuscript, many sarcoma subtypes are analyzed and should provide more insight regarding TAM other than GIST. The other is TAM in LMS, where the Stanford Group (van deRijn) has provided a much detailed analysis of TAM's role in LMS, which may also be one of the explanations why LMS are typically non-responsive to immune checkpoint inhibitors.

Reply 1: These 2 important studies have been added and discussed (lines 175 - 195)

Comment 2: In referencing the Phase 2 study of Wilky et al. (axitinib + pembrolizumab), the authors did not mention of why this combination could convert the TAM immunosuppressive function. The other agent mentioned in the same paragraph is imatinib, which is not an anti-angiogenic agent. A more

detailed explanation of the correlation between anti-angiogenic treatment and polarization of the TAM is recommended.
Reply 2: The importance VEGF inhibition and its effect on MDSCs and TAMs has now been discussed in lines 137 -162 and lines 207 -213

Comment 3: In the T-cell approach section, a more detailed description of methods of adoptive T cells for synovial sarcoma is recommended, especially that these TCR-adopted T cells are different from the more popular CAR-T that is generally provided in hematological malignancies
Reply 3: This has now been added lines 315-326

Reviewer C
Comment 1: I agree with the authors in their review of the literature; however, their command of the English language was poorly demonstrated in the first part of the manuscript.
Lines 28-30
Lines 96-97
Lines 102-103
Lines 106-108
Line 112: What is objective response? Too vague.
Lines 116-117
Line 120
Lines 131-132
Line 136
Line 337: correct NYESO
Reply 1: The lines mentioned as well as the whole manuscript has been corrected for language and grammatical errors has been corrected.

Comment 2: In addition, the section about adjuvant therapy combining RA to stimulate tumors was a significant finding in the field and requires more attention than a passing reference in the conclusion section. I would like to see it expanded in a section that discusses molecules like RA and interleukins that are used to stimulate immune responses in cancer immunotherapy.
Reply 2: A paragraph attributed to the discussion with RA has been added lines 162-173