Peer Review File

Reviewer A

Comment 1: Please try to include recent meta-analyes in your work e.g., PMID: 36168110

Reply 1: Thanks to the reviewer's suggest, we added the content of this article and quoted it.

Changes in the text: PD-L1 is a relatively popular biomarker at present. A meta-analysis of seven trials involving 1132 patients with PD-L1 negative and driver gene negative advanced non squamous NSCLC showed that compared to chemotherapy alone, immunotherapy combined with chemotherapy as a first-line treatment for patients with PD-L1 negative advanced non squamous NSCLC achieved better ORR (odds ratio 2.81, 95% CI 1.69-4.65), PFS(HR 0.63, 95% CI 0.55-0.74, $p < 0.001$) and OS (HR 0.68, 95% CI 0.56-0.82, $p<0.001$)(78).

Comment 2: if possible, please comment on the complications and cost associated with the use of such Immunotherapy e.g., PMID: 31088241, PMID: 30470252, and PMID: 30962996.

Reply 2: Thanks to the reviewer's suggest, we added the content of the complications and cost associated with the use of such Immunotherapy and quoted those articles.

Changes in the text: A previous study (7) has shown that for a general cohort with non-small cell lung cancer (NSCLC), nivolumab was not cost-effective, but increasing PD-L1 cutoffs resulted in acceptable cost-effectiveness (CE). On the other hand, pembrolizumab was found to be cost-effective for both previously treated and newly-diagnosed metastatic NSCLC. Overall, there are limitations to the cost-effectiveness of ICIs. More CE investigations and clinical trials are needed in the future.

Despite the significant and durable clinical efficacy of anti-PD/PD-L1 immune therapy in many cancer types, its use is also associated with high rates of skin, gastrointestinal, and endocrine adverse effects. Studies (8,9) have found that anti-PD-1 immune therapy increases the incidence of both high-grade and any-grade pneumonitis compared to chemotherapy, while there is no significant difference for anti-PD-L1 immune therapy.

Comment 3: Table 1 and 2: Please add the reference in the "Trial" column.

Reply 3: we added the references in the table 1 and 2.

Changes in the text: Table 1 and 2

Comment 4: Table 2: Please specify the groups that you reported in OS, PFS, and ORR e.g., 34.5m vs. 16.7m and 17.2m vs. 15.2m vs.12.2m. This could be specified in the table footnote. Also: please specify the unit for this e.g., 0.62 (0.41–0.94) for example HR 0.62 (95%CI 0.41–0.94). etc.

Reply 4: We have modified Table 2 according to your suggestion.

Changes in the text: Table 2

Comment 5: If possible, please try to report PRISMA flowchart of your included studies.

Reply 5: Since there is already a table corresponding to the detection strategy, we did not make repeated flowchart. Thank you very much.

<mark>**Reviewer B**</mark>

1. Please check all "narrative literature review" in your whole manuscript, including your Title. "narrative review" or "literature review", please just use one.

Reply 1: We've changed all of "narrative literature review" to "literature review".

Changes in the text: "Immunotherapy for advanced non-small cell lung cancer with negative PD-L1 expression: a literature review."

"We performed a literature review to identify relevant data published until September 2022."

2. Please add citation of reference for below mentioned studies.

study, Hwang et al. found that the expression rate of PD-L1 was higher in those with epidermal growth factor receptor (*EGFR*) wild type (WT), squamous cell carcinoma, and metastatic tumors (P<0.001).

considered to be treated with nivolumab in second-line therapy. The CheckMate-078 and CheckMate-870 studies both suggest that nivolumab should also be attempted in second- and third-line therapy for patients with advanced NSCLC with negative PD-L1 expression in the Chinese population. The value of camrelizumab in second-line

Reply 1:   I have added citation of reference for above mentioned studies.

Changes in the text: "In their study, Hwang et al. found that the expression rate of PD-L1 was higher in those with epidermal growth factor receptor (EGFR) wild type (WT), squamous cell carcinoma, and metastatic tumors (P<0.001) (47)."

"The CheckMate-078 (23) and CheckMate-870 (24) studies both suggest that nivolumab should also be attempted in second- and third-line therapy for patients with

advanced NSCLC with negative PD-L1 expression in the Chinese population. "

3. Please check whether references cited in your Table 1-2 are correct and match with Trials names. For example, should the below Camel-sq be reference (59), not (54)?

Camel (58)	1	NCT03134872	III	Non-squamous NSCLC
Camel-sq [54]	1	NCT03668496	III	Squamous NSCl
SHR-1210-II-201_ (61)	2	NCT03085069	II	NSCLC

59. Ren S, Chen J, Xu X, et al. Camrelizumab Plus Carboplatin and Paclitaxel as First-Line Treatment for Advanced Squamous NSCLC (CameL-Sq): A Phase 3 Trial. J Thorac Oncol 2022;17:544-57.

Reply 1: we checked Table 1-2 to match with Trials names. Camel-sq should be reference (59), not (54).

Changes in the text: Table 1-2