Peer Review File

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Review comments-Reviewer A

Comment 1: Were poor performance status (PS) cases included in the present study? Was there a difference in PS between high CRP and low LDH groups and the other group?
Reply 1: Patients with poor basic status (PS >2) have been excluded at the time of inclusion. We have modified our text as advised.
Changes in the text: Page 4, line 125-126.

Comment 2: Were any of the cases positive for driver gene mutations?
Reply 2:33 of patients have positive driver gene mutations. PD-1/PD-L1 inhibitors are treated as second-line and subsequent treatment after drug resistance.
Changes in the text: None.

Comment 3: Were the PD-L1 expression of 83 cases unmeasured?
Reply 3: Yes, this part of the patient are unmeasured before treatment.
Changes in the text: None.

Comment 4: Regarding immunotherapy, what regimens were used for single-agent and combination immunotherapy? Was there a difference in treatment regimen between high CRP and low LDH groups and the other group?
Reply 4: Patients treated with single or combined therapy were both included in this study. All patients use at least one of the following drugs: Pembrolizumab, Tislelizumab, Sintilimab, Camrelizumab, Nivolumab, Toripalimab, Atezolizumab. The combined therapy regimen is platinum-containing dual-drug chemotherapy, determined according to tumor histology. Both high CRP and low LDH groups and the other group have same composition of patients. We have revised the expression of the relevant paragraph.
Changes in the text: Page4, lines121-124.

Comment 5: Kaplan-Meier curves should include number at risk.
Reply 5: We have modified our figures and related data as advised.
Changes in the text: Page13, Figure 2 and Figure 3, Page15 Table2, Page6, lines 177-178, Page13, lines 396-397, Page14, lines 404-407.

Comment 6: There have been many reports that high CRP levels are a poor prognostic factor for malignant tumors, but why was PFS better for non-small cell patients with high CRP levels

in this study? An explanation arguing the necessity is required in the discussion.

Reply 6: We think that we had preliminary explained the reasons why was PFS better for NSCLC patients with high CRP levels (see page 7, lines 215-235), Further explanation data has been added to make it clearer (see page 7-8, lines 235-241).

Changes in the text: page 7-8, lines 235-241.Page 12, line 372-375.

Review comments-Reviewer B

Comment: Is there any difference with ICI monotherapy compared to chemo-ICI treated patients in the CRP and LDH outcomes?

Reply: Less than 10% of patients use ICI monotherapy, so we did not perform further analysis.

Changes in the text: None.

Review comments-Reviewer C

1. Please check if any more references need to be added in the below 2 sentences since you mentioned "Studies", but only one reference was cited. If not, "studies" should be changed to "a study/a previous study".

70 non-small cell lung cancer (NSCLC) range from 20% to 50% (2). Studies have pointed
71 out that compared with chemotherapy and immunotherapy, immunocombination
72 chemotherapy can further improve the quality of life and survival of patients with
73 advanced NSCLC (3).

97 therapeutic effect for tumor patients. Various studies have shown that inflammatory
98 markers have far-reaching effects on cancer development and the innate immune
99 system (13), but the presumptive prognostic value of combined serum inflammatory

Reply: We have modified our text as advised.

2. Please add citation of reference for below "one study".

91 in the occurrence and development of many kinds of malignant tumors. For example,
92 one study suggested that increased preoperative CRP levels are associated with the
93 inability to achieve complete resection in patients with NSCLC, and another study
94 showed that changes in CRP in the early stage can predict response to checkpoint
95 inhibitor treatment (12). It is suggested that systemic inflammatory response plays an

Reply: We have added citation and modified our text as advised.

3. It's suggested to add citation of reference for RECIST used.

114 survival (PFS) was the primary endpoint and was assessed by investigators according
115 to the Response Evaluation Criteria in Solid Tumors (RECIST). All baseline

Reply: We have added citation of iRECIST.

4. Please check all abbreviations in the abstract and main text, such as below. All abbreviated terms should be full when they first appear.

45 **Methods:** This study retrospectively analyzed 116 NSCLC patients treated with anti-
46 PD-1 monoclonal antibodies. Clinical data of the patients were collected before

119 **##Patients**
120 Patients were included in the study if they had inoperable stage III–IV NSCLC
121 confirmed by histopathology and were eligible to receive anti-PD-1/PD-L1
122 immunotherapy (single or combination regimen). All patients use at least one of the
123 following ICIs: Pembrolizumab, Tislelizumab, Sintilimab, Camrelizumab, Nivolumab,

Reply: We have checked and modified our text as advised.

5. Table 1:

1) The data below in your main text don't match with your Table 1.

190 inhibitors between January 2019 and June 2022 are shown in Table 1. They included
191 88 (75%) men and 28 (25%) women. The median age of patients was 59.5 years (range,

Gender, n [%]	
Male	88 [75.9]
Female	28 [24.1]

2) Please indicate the full name of "PD-L1" in Table 1 footnote.

Reply:

1) We have modified our text as advised.

2) We have indicated the full name of "PD-L1" in Table 1 footnote.

6. Table 3:

1) The data below in your main text don't match with your Table 3.

227 P=0.011) and PD-L1 status (HR, 0.568; 95% CI, 0.345–0.937, P=0.027) showed a
228 statistical significance (Table 3). Because some of the variables in the univariate

2) Please indicate the full name of "PFS", "CRP", "LDH" "PD-L1" in Table 3 footnote.

Reply:

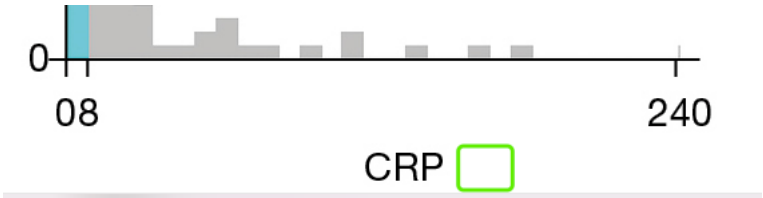
1) We have checked and modified as advised

2) We have indicated the full name of "PFS", "CRP", "LDH" "PD-L1"and "PD-1""HR""CI" in Table 3 footnote

7. Figure 1:

1) Is there any meaning for below bar in your Figure 1?

2) Please add unit for CRP in the x-axis.



Reply:

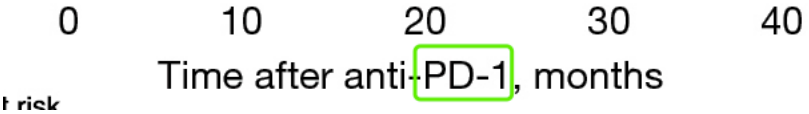
1) It is the $\chi 2$ log-rank values, produced when we dividing the cohort into 2 parts, We have modified figure and text to make it more clear.

426 inhibitors. The χ^2 log-rank values created when the cohort was divided into two groups

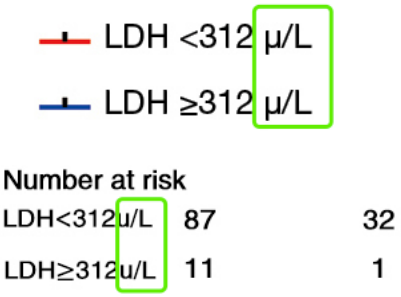
2) We have added unit of CRP as advised.

8. Figure 2:

1) Please check whether "PD-1" is correct in Figure 2. It's "PD-L1" in the legend.



2) The unit is inconsistent with "U/L". Please unify.



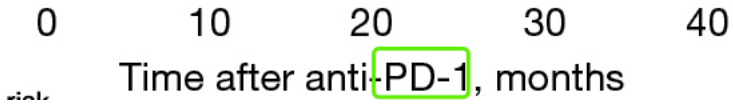
Reply:

1) We have changed the figure with PD-1/PD-L1 instead.

2) We have checked and modified as advised.

9. Figure 3:

1) Please check whether "PD-1" is correct in Figure 3.



2) The data below in your Figure 2B is inconsistent with Figure 2 legend.

414 CRP_{Low} with LDH_{High} (n=2) (P=0.002). (B) Red line, CRP_{High} with LDH_{Low} (n=38); blue
415 line, other combinations (n=44). CRP, C-reactive protein; LDH, lactic dehydrogenase.

Reply:

1) We have checked Figure 3 and modified as advised.

2) We have checked Figure 3B and modified as advised.