Peer Review File

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Reviewer A

This is a good article which tries to show relation between CEA levels and prognosis of CTD-ILD.
It has a correct design and the results are clearly exposed.
I think it should be useful to explain with a graphic or more clearly which is the role of tumor biomarkers in ILD (both in introduction and in the discussion of the results), for a better understanding of the study purposes.
Reply : We thank the reviewer's suggestive comments. An abstract graphic was added in the supplementary appendix to illustrate the role of tumor biomarkers in CTD-ILD.
Changes in the text: The significant correlations emerged between serum CEA levels, progressive pulmonary fibrosis, acute exacerbation, and all-cause mortality in the patients with CTD-ILD, suggesting CEA as a potential biomarker (Figure S6) (see, page 15, lines 325-327).

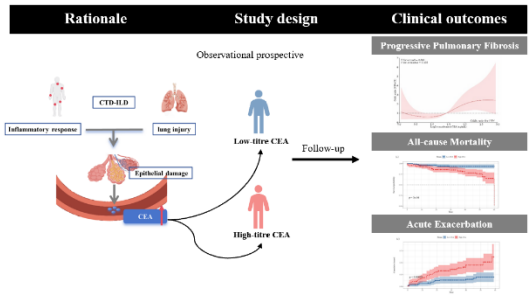

Figure S6 Graphical abstract

Reviewer B

Interesting manuscript.
My rationale for my recommendations are as follows:
1. Bio markers to identify progression in CTD-ILD is a narrow topic and I commend the authors for undertaking this topic but it seems more exploratory in nature.
Reply: We thank the reviewer's valuable comments. We truly appreciate the recognition of our efforts in exploring biomarkers for identifying progression in CTD-ILD, even though the topic is indeed narrow and exploratory. To address this, we have added a graphical abstract that outlines the potential mechanisms based on current knowledge, while acknowledging that this representation may still be somewhat superficial. We fully agree that further investigation is essential to deepen our understanding and validate the clinical potential of these biomarkers.
Changes in the text: Although we observed a potential link between CEA levels and fibrosis, the underlying mechanisms remain unclear and warrant further investigation (see page 15, lines 314-316). The significant correlations emerged between serum CEA levels, progressive pulmonary fibrosis, acute exacerbation, and all-cause mortality in the patients with CTD-ILD, suggesting CEA as a potential biomarker (Figure S6) (see page 15, lines 325-327).

2. The sample size is small and there are rather few RAILD patients which may not represent true CTD-ILD.
Reply: We thank the reviewer's comments. We acknowledged that the single-center study and limited number of RA-ILD patients may raise concerns about generalizability to the broader

CTD-ILD population. This study was conducted based on available resources and patients during the study period. The number of enrolled patients fulfilled the sample size evaluation statistically. The limitation and its potential impact on the results was discussed, and recommend future studies with larger, more diverse populations to validate our findings.
Changes in the text: The study was based in a single medical center with a limited sample size, including relatively few RA-ILD patients. As a result, our data may not fully represent the broader CTD-ILD population, potentially limiting the generalizability of our findings (see page 14, lines 305-308).

3. There is a LOT of analysis in this manuscript which makes it less readable. There are many subgroup analyses and figures, especially in the supplement. Making it more concise would be helpful.
Reply: We thank the reviewer's suggestive comments. To address this, we have carefully reviewed and reduced the number of figures and tables in the supplementary appendix.
Changes in the text:
3.1 Notably, patients with PPF only presented significantly higher serum CEA (median level 2.09 versus 1.48 ng/mL, P=0.002) and CA125 (median level 17.4 versus 13.5 ng/mL, P=0.031) than those without PPF (Table S4) (see page 9, lines 185-188).
3.2 Serum CA125 level was negatively correlated with DLCO% pred. ($r = -0.282$, $P < 0.001$) (Table S5) (see page 10, lines 202-203).
3.3 Subgroup analysis of diagnoses indicated a potential association between elevated CEA levels and PPF within the IIM (P=0.045) and UCTD (P=0.01) subgroups (Table S7) (see page 11, lines 233-234).
3.4 After excluding acute worsening (Table S10), a higher CEA concentration was associated with PPF (OR 1.67, 95% CI: 1.05-2.66, P = 0.032). After excluding patients with emphysema (Table S11), a higher CEA concentration was still associated with PPF (OR 1.76, 95% CI: 1.12-2.76, P = 0.015) (see page 11, lines 236-238).