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**Reviewer A**

In Figure 3F, the study showed significant difference between 1st line and other lines.
These figures might be univariate analysis, I think. It may be enough to use HR, but multivariate analysis should be added if possible. Possibly some factors, such as PS or PD-L1 expressions might be confounding factor.
***Response:*** *Thanks for your constructive comments and suggestions. We have added the univariate and multivariate analysis results, as shown in the Table below (Main text and Supplementary Table 1 and 2). As for some factors, such as PD-L1 expression, only the univariate analysis was performed due to the small subset of patients tested. We have added the limitation in the discussion section and sincerely hope it will meet with your approval;*

**Table S1** Univariate and multivariate COX regression analysis of PFS

| Variables | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | HR (95%CI) | *p* | HR (95%CI) | *p* |
| **Age** | | | | |
| <70 years | REF. | | REF. | |
| ≥70 years | 0.887(0.641, 1.226) | 0.466 | 1.218(0.862, 1.722) | 0.264 |
| **Sex** | | | | |
| Female | REF. | | REF. | |
| Male | 1.235(0.876, 1.743) | 0.229 | 0.924(0.632, 1.352) | 0.685 |
| **Smoking history** | | | | |
| No | REF. | | REF. | |
| Yes | 0.722(0.454, 1.148) | 0.169 | 0.735(0.452, 1.195) | 0.215 |
| **ECOG performance status** | | | | |
| 0–1 | REF. | | REF. | |
| ≥2 | 1.004(0.659, 1.531) | 0.984 | 0.898(0.582, 1.384) | 0.625 |
| **Histology** | | | | |
| Squamous cell carcinoma | REF. | | REF. | |
| Non-squamous cell carcinoma | 0.959(0.693, 1.328) | 0.803 | 1.005(0.344, 2.936) | 0.993 |
| Unspecified | 1.321(0.478, 3.649) | 0.592 | 1.152(0.405, 3.267) | 0.790 |
| **Clinical stage** | | | | |
| III | REF. | | REF. | |
| IV | 0.661(0.425, 1.029) | 0.067 | 1.489(0.927, 2.391) | 0.100 |
| **Brain metastatic** | | | | |
| No | REF. | | REF. | |
| Yes | 1.108(0.681, 1.522) | 0.930 | 0.926(0.600, 1.429) | 0.728 |
| **Liver metastatic** | | | | |

| | | | | |
|---|---|---|---|---|
| No | REF. | | REF. | |
| Yes | 0.806(0.514, 1.264) | 0.348 | 1.169(0.733, 1.862) | 0.512 |
| **Adrenal gland metastatic** | | | | |
| No | REF. | | REF. | |
| Yes | 0.935(0.475, 1.838) | 0.845 | 0.985(0.487, 1.993) | 0.966 |
| **Treatment line** | | | | |
| First line | Ref | | REF. | |
| Second line | 1.168(0.797, 1.711) | 0.426 | 1.189(0.792, 1.786) | 0.403 |
| Third or later line | 1.375(0.923, 2.048) | 0.118 | 1.328(0.857, 2.058) | 0.204 |
| **Treatment patterns** | | | | |
| Camrelizumab monotherapy | REF. | | REF. | |
| Camrelizumab plus chemotherapy | 1.664(0.915, 3.024) | 0.095 | 1.669(0.899, 3.098) | 0.105 |
| Camrelizumab plus others* | 1.821(0.961, 3.452) | 0.066 | 1.762(0.903, 3.439) | 0.097 |

*, others including anti-angiogenesis therapy or plus chemotherapy, or targeted therapy. PFS, progression-free survival; HR: hazard ratio; CI: confidential interval; REF.: reference; ECOG, Eastern Cooperative Oncology Group.

**Table S2** Univariate and multivariate COX regression analysis of OS

| **Variables** | **Univariate analysis** | | **Multivariate analysis** | |
|---|---|---|---|---|
| | **HR (95%CI)** | ***p*** | **HR (95%CI)** | ***p*** |
| **Age** | | | | |
| <70 years | REF. | | REF. | |
| ≥70 years | 1.072(0.669, 1.719) | 0.772 | 0.908(0.549, 1.502) | 0.708 |
| **Sex** | | | | |
| Female | REF. | | REF. | |
| Male | 0.953(0.570, 1.592) | 0.854 | 1.337(0.767, 2.331) | 0.306 |
| **Smoking history** | | | | |
| No | REF. | | REF. | |
| Yes | 0.929(0.504, 1.713) | 0.814 | 0.849(0.448, 1.609) | 0.615 |
| **ECOG performance status** | | | | |
| 0–1 | REF. | | REF. | |
| ≥2 | 0.957(0.534, 1.715) | 0.882 | 0.919(0.504, 1.674) | 0.783 |
| **Histology** | | | | |
| Squamous cell carcinoma | REF. | | REF. | |
| Non-squamous cell carcinoma | 0.752(0.482, 1.172) | 0.208 | 0.559(0.338, 0.924) | **0.023** |
| Unspecified | 0.541(0.074, 3.964) | 0.545 | 0.392(0.050, 3.057) | 0.371 |
| **Clinical stage** | | | | |
| III | REF. | | REF. | |
| IV | 0.550(0.283, 1.067) | 0.077 | 1.753(0.866, 3.548) | 0.119 |
| **Brain metastases** | | | | |

| | | | | |
|---|---|---|---|---|
| No | REF. | | REF. | |
| Yes | 0.871(0.504, 1.506) | 0.622 | 1.152(0.636, 2.089) | 0.641 |
| **Liver metastases** | | | | |
| No | REF. | | REF. | |
| Yes | 0.679(0.368, 1.254) | 0.217 | 1.374(0.730, 2.587) | 0.325 |
| **Adrenal gland metastases** | | | | |
| No | REF. | | REF. | |
| Yes | 0.530(0.243, 1.155) | 0.110 | 0.798(0.278, 2.294) | 0.676 |
| **Treatment line** | | | | |
| First line | REF. | | REF. | |
| Second line | 1.575(0.879, 2.823) | 0.127 | 1.981(1.072, 3.662) | **0.029** |
| Third or later line | 1.995(1.102, 3.613) | 0.023 | 2.481(1.285, 4.790) | **0.007** |
| **Treatment pattern** | | | | |
| Camrelizumab monotherapy | REF. | | REF. | |
| Camrelizumab plus chemotherapy | 1.326(0.602, 2.923) | 0.484 | 1.326(0.585, 3.003) | 0.499 |
| Camrelizumab plus others* | 1.566(0.671, 3.655) | 0.300 | 1.564(0.642, 3.807) | 0.325 |

*, others including anti-angiogenesis therapy or plus chemotherapy, or targeted therapy. OS, overall survival; HR: hazard ratio; CI: confidential interval; REF.: reference; ECOG, Eastern Cooperative Oncology Group.

**Reviewer B**

The real-world experience presented by Wang et al. highlights further evidences about the efficacy of immunotherapy in the management of NSCLC. Camrelizumab has not been widely advertised outside the Eastern market, nevertheless phase III trials reported results absolutely comparable to other Immune-checkpoint inhibitors, such as Pembrolizumab. In my opinion, this multicenter analysis has extremely interesting hot topics:

- first of all, 30% of patients are elderly, therefore clinicians treated a population with potentially greater comorbidities;
- 35.7% of enrolled patients are non-smokers, historically a potentially "biomarker-driven" subgroup, with all the implications of potentially poor response to immunotherapy;
- 16% of patients have brain metastases, prognostically more unfavorable.

So it appears clear how enrollment is very different from phase III trial, reflecting the day-to-day outpatient activity.

Moreover, it is very interesting to highlight an absolutely infrequent toxicity rather than other ICIs, the Reactive Cutaneous Capillary Endothelial Proliferation (RCCEP). It was described in 75 (18.6%) participants as a grade 1-2 adverse event. However only 10% of patients interrupt immunotherapy, showing an excellent easy management in clinical practice.

The authors underline that it is essential to propose Camrelizumab in first line setting, considering an ORR of 50% and a DCR of 88.9% with a halving of ORR from second line.

In my opinion, it would have been very interesting to stratify PD-L1 with CPS in such a way as to highlight any (probable) correlations with PFS, OS and ORR as well as a more in-depth study of molecular biomarkers especially in non-smoking population, also considering the well-

known different biological and molecular characteristics of the Eastern population compared to the Western.

***Response:*** *Thanks for your constructive comments and suggestions. We have explored the prognostic correlation of molecular biomarkers, PD-L1 expressions and EGFR/ALK mutation, in patients underwent tests and with known expression/mutation status. Neither PD-L1 expression nor EGFR/ALK mutation status was found to be associated with PFS/OS (Figure 1-4 below). Unfortunately, due to the limited number of patients and potential selection bias, further exploration analysis in a specific subgroup of patients was not performed. We have added some information in the limitation section and sincerely hope it will still meet with your approval;*

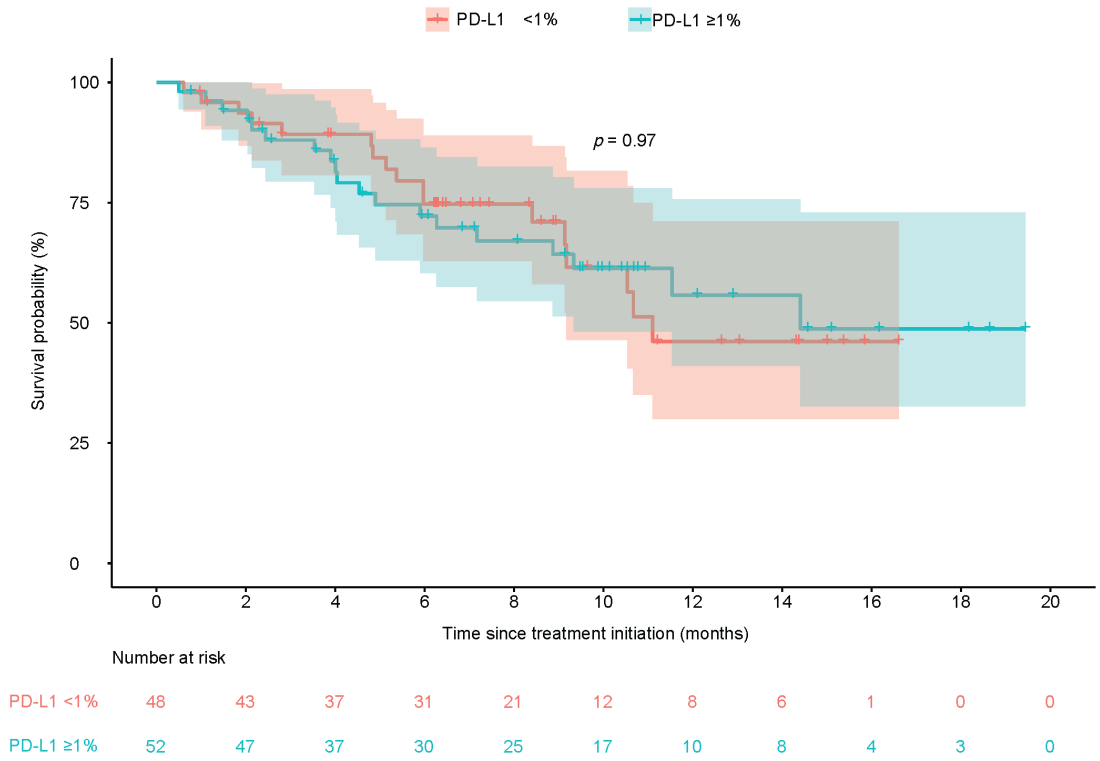


**Figure 1** Progression-free survival analysis stratified by PD-L1 expression status

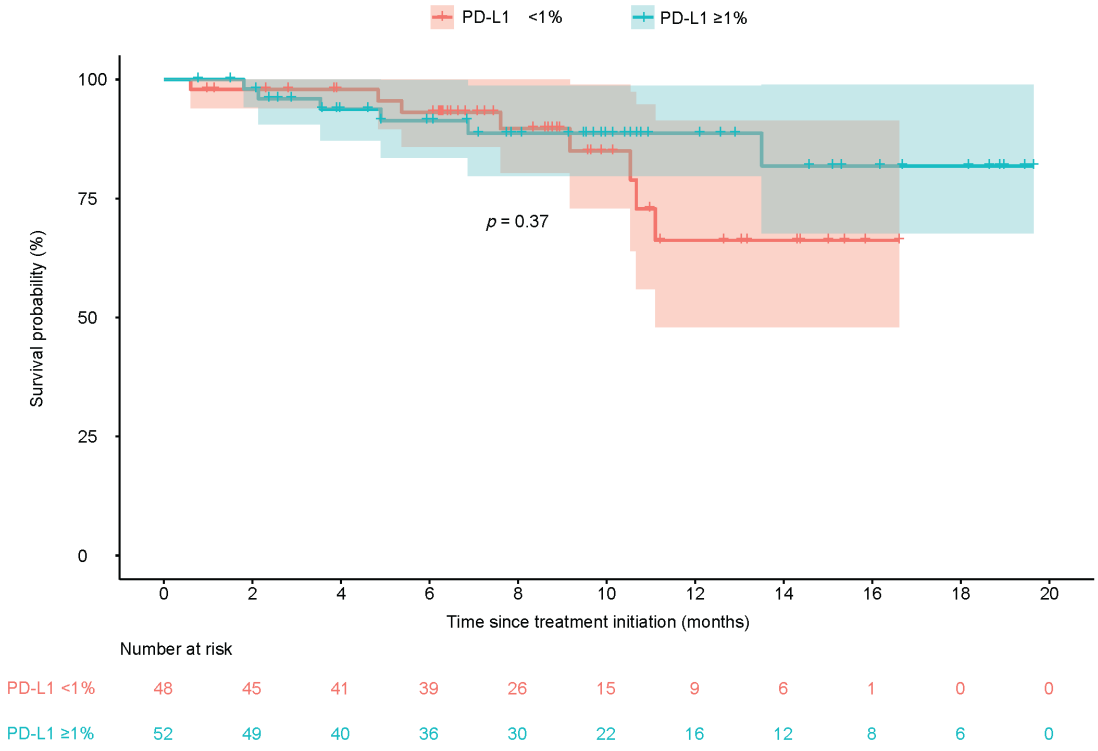


**Figure 2** Overall survival analysis stratified by PD-L1 expression status

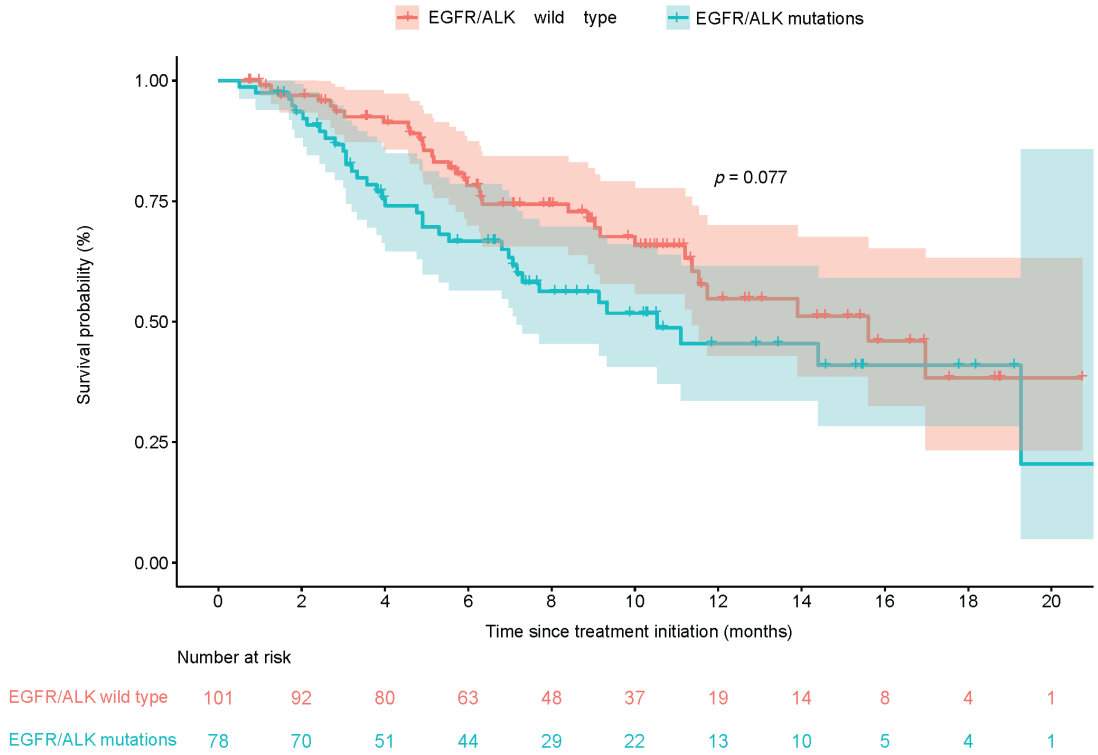


**Figure 3** Progression-free survival analysis stratified by EGFR/ALK mutation status

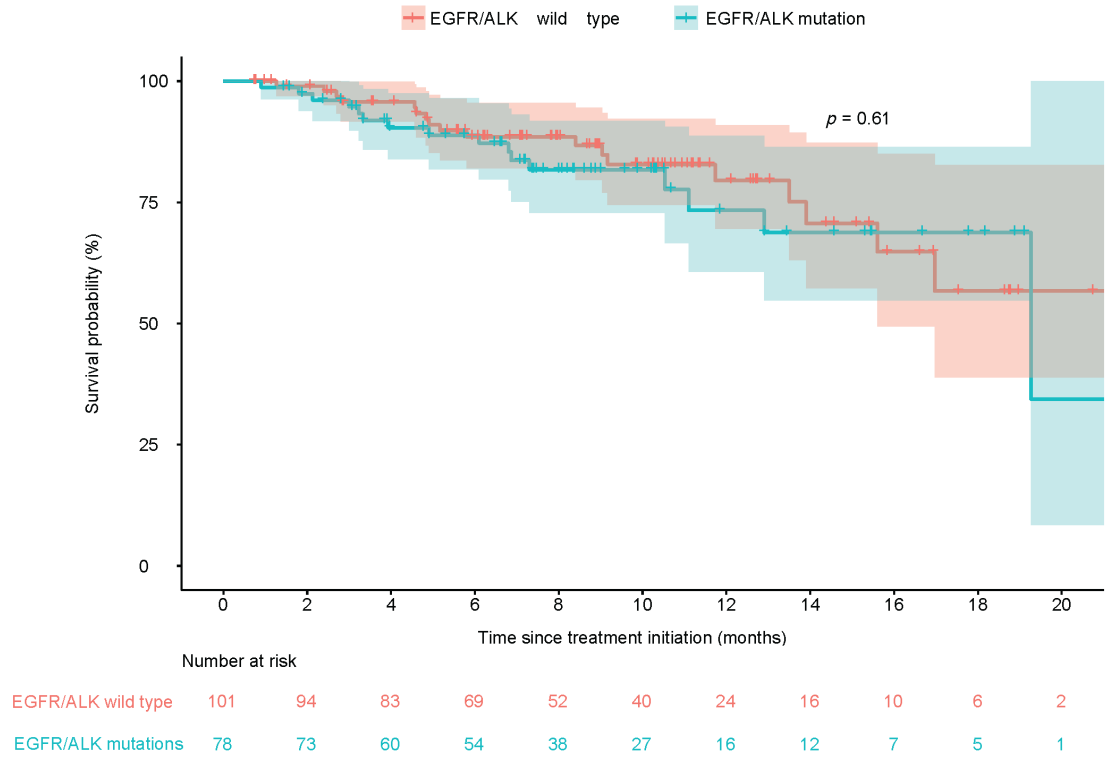


**Figure 4** Overall survival analysis stratified by EGFR/ALK mutation status

**Reviewer C**

1. Based on the results of CameL and CameL-sq clinical studies, camrelizumab has been approved for first-line treatment of driver gene negative advanced non-small cell lung cancer. The results of this observational study are similar to the previous randomized controlled trials whose results are well known. The idea is not novel.

***Response:*** *Thanks for your comments. This study mainly focused on the real-world effectiveness and safety of camrelizumab-containing regimens in advanced NSCLC patients. Unlike the patients recruited in the pivotal clinical trials, all the patients we deal with in daily practice were included for analysis. Also, the treatments were at the discretion of attending physicians in charge without a prespecified protocol. So, the results observed in this study may better reflect our routine clinical practice. We sincerely hope it will meet with your approval;*

2. This study included patients with non-small cell lung cancer who were scheduled to be treated with camrelizumab, but the specific treatment regimens were different. Immunomonotherapy, immunotherapy combined with chemotherapy or immunotherapy combined with anti-angiogenesis therapy may affect the results, but this study has not been analyzed.

***Response:*** *Thanks for your constructive comments and suggestions. In the routine practice, patients are treated by the attending physicians in charge according to their experience and specific situation of the patient. Therefore, the different treatment regimens were used in this study. In subgroup analysis, the ORR was not found to be markedly different among patients*

*receiving different treatment regimes. Also, the PFS and OS were not significantly different (Figure 5 and 6 below). Besides, multivariate COX regression analysis was further performed to determine whether different treatment regimens may affect the results after adjustment for baseline patient characteristics. Treatment regimen was not independently associated with PFS or OS of patients, as mentioned above and shown in the revised main text. We sincerely hope it will meet your requirement;*

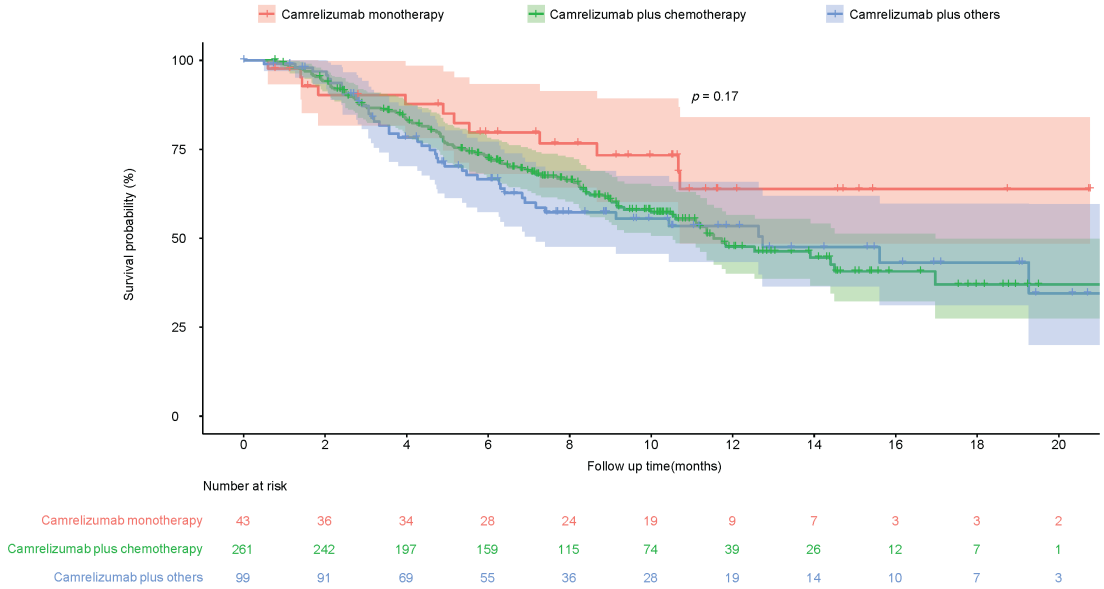


**Figure 5** Progression-free survival analysis stratified by treatment patterns

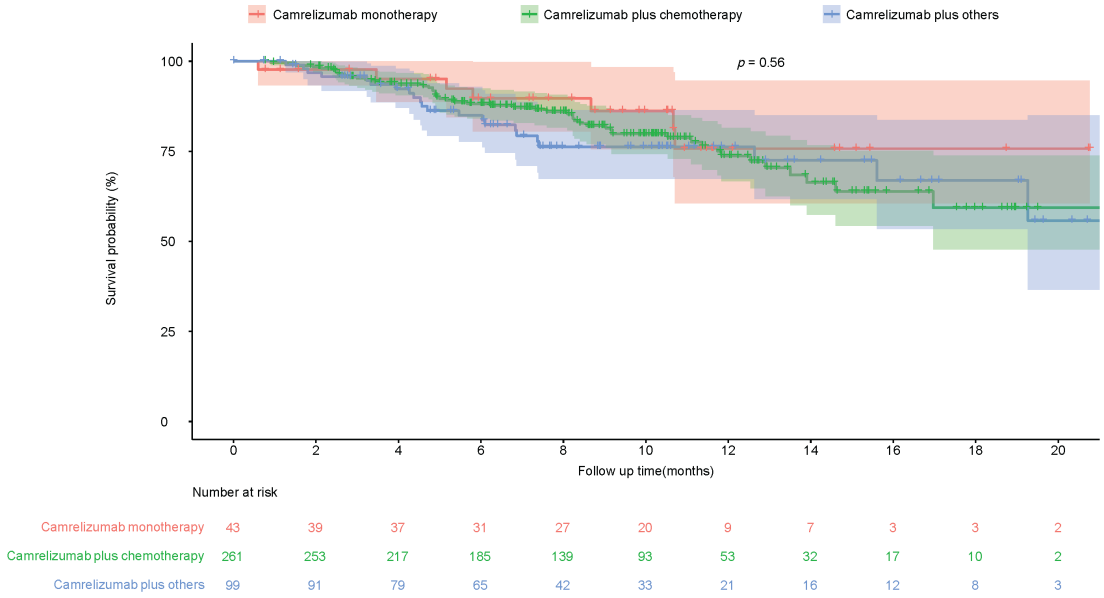


**Figure 6** Overall survival analysis stratified by treatment patterns

3. In the subgroup analysis of OS, the OS of patients treated with first-line, second-line and third or later line of camrelizumab was not comparable, many factors would influence the OS. There may be some methodological problems in this article.

***Response:*** *Thanks for your constructive comments and suggestions. We totally agree with your opinion that many factors, especially treatment line, may influence the survival outcomes. Accordingly, we have established a multivariate COX regression model to identify independent prognostic predictors as mentioned above and sincerely hope it will still meet with your approval;*

**Reviewer D**

This study reported a prospective multicenter cohort study, to investigate the real-world effectiveness and safety of camrelizumab in advanced NSCLC patients, which provides useful study addition to this area. I think this topic is great and fills a research gap. However, there are still some questions that need to be revised as follows:

1. This is a one-arm, non-controlled cohort study. Different study populations have a large influence on patient outcomes. How to control selection bias.

***Response:*** *Thanks for your constructive comments and suggestions. In this study, all consecutive patients who admitted to the study centers and scheduled to receive camrelizumab were asked for potential participation. All those willing to participate were included for analysis to control for potential selection biases. However, only the patients receiving camrelizumab at 43 hospitals in the Jiangsu Province, an economically well-developed area in East China, were included for analysis in this study, which may influence the generalization of the results observed. The corresponding limitation has already been mentioned in the discussion section. We sincerely hope it will still meet with your approval;*

2. For single-arm studies, second-line or more-line therapy may lead to more bias in prognosis and treatment choice. Can you explain the rationality of survival comparison?

***Response:*** *Thanks for your constructive comments and suggestions. We share your concern about potential bias in prognosis and treatment choice regarding increasing line of therapy. We have added the multivariate COX regression results as mentioned above and sincerely hope it will still meet with your approval.*