Taxanes plus immunotherapy might be a potential option for *HER2*-altered NSCLC beyond first-line progression: a retrospective real-world study

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Background

- Currently, there is limited research focusing on the treatment for *HER2*-altered advanced non-small cell lung cancer (NSCLC) progressed beyond first-line treatment, especially on evaluating the benefit of taxanes in the second or third-line setting.
- The retrospective real-world study aimed to assess the efficacy of various kinds of taxanes, including nab-paclitaxel, paclitaxel, and docetaxel. The research further compared the efficacy of taxanes-based chemotherapy alone (C), and combined with angiogenesis inhibitors (C+A) or immune checkpoint inhibitors (C+I) for *HER2*-altered NSCLC.

Methods

- *HER2*-altered NSCLC patients who received taxanes-based treatment as the second or third-line setting between November 2015 and September 2021 were screened.
- Patients treated with different kinds of taxanes and various strategies including C, C+I, or C+A were included for final efficacy analysis. Progression-free survival (PFS) was compared between subgroups.

Results

- A total of 52 patients were finally included.
- C+I achieved longer PFS than C (median, 5.70 vs.4.27 months, hazard ratio 0.39, 95% CI: 0.16-0.92, p=0.003). There was no difference between C+I and C+A (median, 5.70 vs.4.03 months, hazard ratio 0.92, 95% CI: 0.46-1.85, p=0.87), despite of PD-L1 expression or tumor mutational burden.
- A clinically meaningful improvement in PFS was observed among patients in the nab-paclitaxel group compared with those in the docetaxel group (median, 6.40 vs. 4.03 months, hazard ratio 0.34, 95%CI: 0.16-0.71, p=0.003).

Results

Table 1. Clinicopathological characteristics

Characteristics	Total (n=52)	C (n=12)	C+A (n=20)	C+I (n=20)	*p*-value
Age (years)	53.9±9.2	52.8±8.0	53.1±9.0	55.4±10.2	0.67
Gender					0.82
Male	27 (51.9%)	7 (58.3%)	11 (55.0%)	9 (45.0%)	
Female	25 (48.1%)	5 (41.7%)	9 (45.0%)	11 (55.0%)	
Smoking History					0.19
Never	31 (59.6%)	5 (41.7%)	11 (55.0%)	15 (75.0%)	
Current/former	21 (40.4%)	7 (58.3%)	9 (45.0%)	5 (25.0%)	
CNS metastases					0.63
Absence	46 (88.5%)	10 (83.3%)	19 (95.0%)	17 (85.0%)	
Presence	6 (11.5%)	2 (16.7%)	1 (5.0%)	3 (15.0%)	
NGS specimen					0.62
Tumor tissue	47 (90.4%)	10 (83.3%)	18 (90.0%)	19 (95.0%)	
Plasma	5 (9.6%)	2 (16.7%)	2 (10.0%)	1 (5.0%)	
***HER2* variants**					0.86
Ex20ins	42 (80.8%)	11 (91.7%)	16 (80.0%)	15 (85.0%)	
Missense	6 (11.5%)	1 (8.3%)	2 (10.0%)	3 (15.0%)	
Amplification	4 (7.7%)	0 (0.0%)	2 (10.0%)	2 (10.0%)	
PD-L1 expression					0.05
Negative	10 (19.2%)	4 (33.3%)	1 (5.0%)	7 (35.0%)	
1≤TPS<50%	7 (13.5%)	0 (0.0%)	3 (15.0%)	2 (10.0%)	
TPS≥50%	6 (11.5%)	0 (0.0%)	2 (10.0%)	4 (20.0%)	
NA	29 (55.8%)	8 (66.7%)	14 (70.0%)	7 (35.0%)	
TMB value (Mb/Muts)					0.34
<10	8 (15.4%)	1 (8.3%)	2 (10.0%)	5 (25.0%)	
≥10	2 (3.8%)	0 (0.0%)	2 (10.0%)	0 (0.0%)	
NA	42 (80.8%)	11 (91.7%)	16 (80.0%)	15 (75.0%)	
Treatment line					0.66
2nd-line	48 (92.3%)	12 (100.0%)	18 (90.0%)	18 (90.0%)	
3rd-line	4 (7.7%)	0 (8.3%)	2 (10.0%)	2 (10.0%)	

C, chemotherapy alone. C+A, chemotherapy plus angiogenesis inhibitors. C+I, chemotherapy plus immune checkpoint inhibitors. CNS, central nervous system. NGS, next-generation sequencing. Ex20ins, exon 20 insertion. NA, not available. TMB, tumor mutational burden. TPS, tumor proportion score.

Figure 1. The detailed molecular landscape

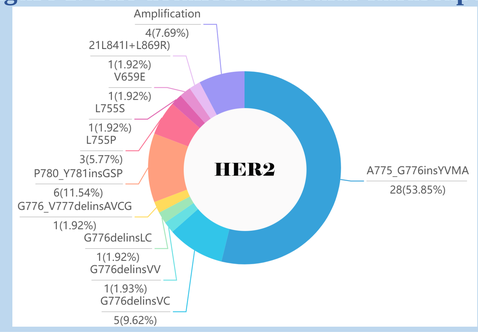


Figure 2. The K-M curve of PFS in taxanes

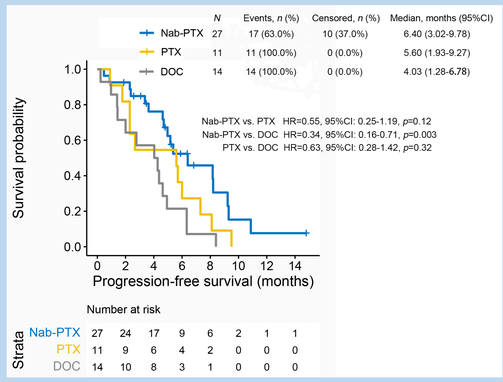


Figure 3. The K-M curve of PFS in treatments

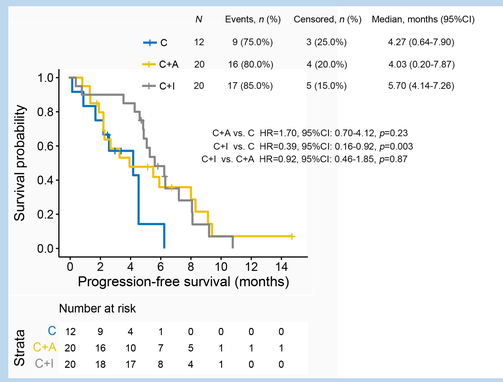
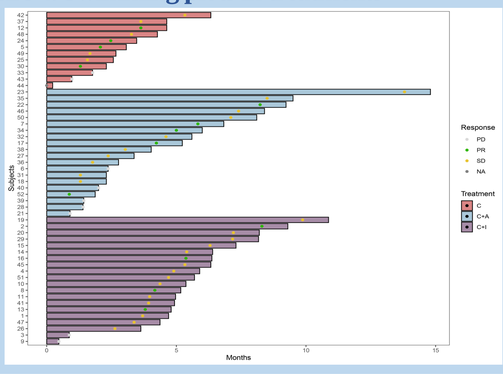
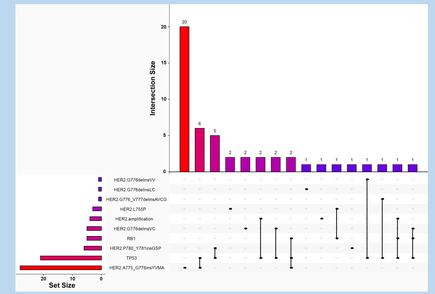


Figure 4. Swimming plots in treatments



Results

Figure 5. Top 10 altered genes



Limitations

- It inevitably exists selective bias due to the retrospective nature.
- Less than half of the patients received large panels of NGS testing, with no adequate data for molecular analysis.
- Results should be interpreted with caution due to the limited sample size receiving immunotherapy in this study

Conclusions

- In the taxanes, nab-paclitaxel appears to be a reasonable alternative to docetaxel for *HER2*-altered patients.
- Chemotherapy plus immune checkpoint inhibitors might yield more survival benefits than chemotherapy alone in the second or third-line setting in *HER2*-altered NSCLC.

Acknowledgements

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