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RESPONSES TO IMMUNOTHERAPY BASED ON PROGRAMMED DEATH-LIGAND 1 (PD-L1) COPY NUMBER VARIATION (CNV) STATUS IN PATIENTS WITH ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC)

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Background Immunotherapy has shown promise in treating patients with metastatic NSCLC, but response rates vary. This study aims to investigate the relationship between PD-L1 CNV and response to immunotherapy in patients with NSCLC.

Methods We conducted a retrospective analysis of patients who received immunotherapy, and were identified to have information on CNV status for PD-L1 through the MayoComplete Solid Tumor Panel (MCSTP) Next Generation Sequencing (NGS) assay. Response to therapy was evaluated using evidence of radiographic progression, date of death or date of last follow-up. Progression-free survival (PFS) and Overall survival (OS) were defined as time interval between data of initiation of immunotherapy to date of radiographic progression and date of death respectively.

Results 98 patients were included in the study, most of whom had received immunotherapy as a first-line treatment (77%). The median age was 70.5 years (range: 39–88), and 64% were male. The most common histology was adenocarcinoma (68%), followed by squamous cell carcinoma (16%) and

others (16%). We found that PD-L1 CNV was altered in 54% of patients with either heterozygous deletion (34%) or copy number gain (20%). We observed higher median PD-L1% in patients with PD-L1 CNV copy number gain compared to normal/deletions (80% vs 5%, $p=0.0172$) (table 1).

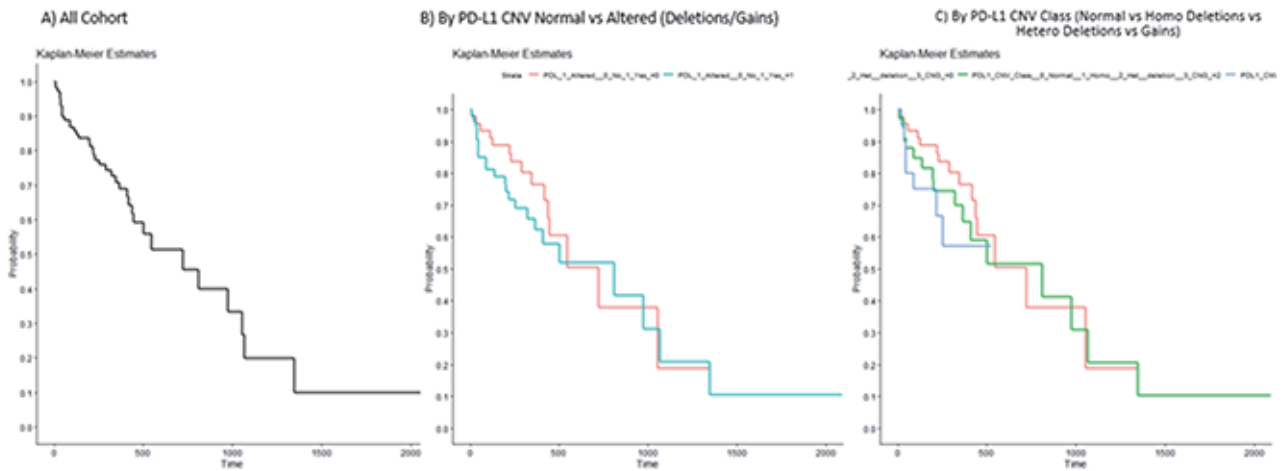
In terms of smoking status, 94% of patients had a history of smoking (84% former smokers, 10% current smokers and 6% never smokers). Most patients had stage IV disease at treatment initiation (68%), and the ECOG performance status was mostly 0 or 1 (78%). The median PFS and OS for the cohort was 5.4 and 23.8 months respectively (table 1). We observed improved response to immunotherapy with higher PDL1 IHC% as has been reported previously. However, we did not find any significant differences in median PFS by presence (7.5 [normal] vs 5.0 months [altered], $p=0.28$) and type (7.5 [normal] vs 5.5 [deletion] vs 4.4 months [gain], $p=0.56$) of PD-L1 CNV alteration. Similarly, there were no significant differences in OS by presence (23.8 [normal] vs 26.6 [altered] months, $p=0.38$) and type (23.7 [normal] vs 26.6 [deletion] vs not reached [gain] months, $p=0.51$) of PD-L1 CNV alteration (figure 1).

Conclusions Our study did not find any significant difference in median PFS and OS between patients with normal PD-L1 CNV and those with altered PD-L1 CNV, including different types of PD-L1 CNV alterations. Our study suggests that PD-L1 CNV status may not be a reliable predictive biomarker for response to immunotherapy in patients with advanced NSCLC.

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| Variable | Category | Count (n) | Proportion (%) | Mean | Median |
|-----------------------|-----------------------|-----------|----------------|------|-----------------|
| Age | | 98 | | 69.6 | 70.5 |
| Sex | Male | 63 | 64 | | |
| | Female | 35 | 36 | | |
| Histology | Adenocarcinoma | 67 | 68 | | |
| | Squamous | 16 | 16 | | |
| | Other | 15 | 16 | | |
| PD-L1 Status | <1% | 24 | 24 | | |
| | 1-49% | 38 | 39 | | |
| | >=50% | 33 | 34 | | |
| | Missing | 3 | 3 | | |
| CNV Classification | Normal | 45 | 46 | | |
| | Heterozygous Deletion | 33 | 34 | | |
| | Copy Number Gain | 20 | 20 | | |
| Smoking Status | Never | 7 | 6 | | |
| | Former | 82 | 84 | | |
| | Current | 9 | 10 | | |
| Stage | I | 3 | | | |
| | II | 2 | | | |
| | III | 25 | | | |
| | IV | 68 | | | |
| ECOG | 0 | 31 | 32 | | |
| | 1 | 45 | 46 | | |
| | 2 | 16 | 16 | | |
| | 3 | 6 | 6 | | |
| CNS Disease | No | 71 | 72 | | |
| | Yes | 27 | 28 | | |
| Line of Immunotherapy | First | 75 | 77 | | |
| | Second | 22 | 22 | | |
| | Third or more | 1 | 1 | | |
| PFS (months) | | 66 | | | 5.4 (167 days) |
| OS (months) | | 38 | | | 23.8 (723 days) |

Figure 1: Overall Survival (days)



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