Comparison of PD-L1 expression before and after neoadjuvant chemoradiation or chemotherapy in stage III non-small cell lung cancer (NSCLC)

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Poster # 5P

Background

- The incorporation of immune-checkpoint inhibitors (ICIs) into the multimodal treatment of operable stage III NSCLC is likely to change future treatment standards.
- Programmed cell death ligand-1 (PD-L1) expression on tumor cells is a predictive biomarker for sensitivity to ICIs targeting the PD-1/PD-L1 axis.
- Little is known on the impact of treatment modalities such as chemo-, radiotherapy and/or combinations on PD-L1 expression level.

Methods

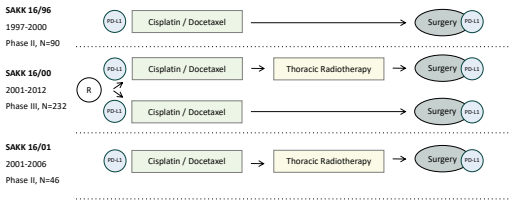
Study design

- We collected formalin-fixed, paraffin-embedded tumor tissue samples from patients enrolled in the Swiss Group for Clinical Cancer Research (SAKK) trials 16/96 [1], 16/00 [2], 16/01 [3], and analyzed PD-L1 expression (Tumor Proportion Score) by immuno-histochemistry using the Ventana PD-L1 (SP263) assay.
- The SAKK 16/96, 16/00 and 16/01 trials included patients with operable stage III NSCLC. All patients were treated with 3 cycles of induction chemotherapy (cisplatin/docetaxel), followed in some patients by radiotherapy (44 Gy, 22 fractions) (bimodal and trimodal cohort) (**Figure 1**).
- We analyzed diagnostic tumor tissue samples (pre-neoadjuvant samples) and tumor resection specimens (post-neoadjuvant samples).

Objective

- To investigate the impact of chemotherapy and chemoradiation on the PD-L1 expression in patients with stage III NSCLC.

Figure 1. SAKK 16 trials and PD-L1 analysis.



SAKK 16/96 and 16/00 included T1-3 N2 patients only. SAKK 16/01 enrolled patients with T4 N0-3 or T1-4 N3.
Chemotherapy: Cisplatin 100 mg/m² and docetaxel 85 mg/m², given once every 3 weeks.
Thoracic Radiotherapy: 44 Gy in 22 fractions in 3 weeks with accelerated concomitant boost radiotherapy.

Results

- We obtained matched pre- and post-neoadjuvant tumor tissue samples from 100 patients. Due to low PD-L1 expression and significant inter-trial heterogeneity (SAKK 16/00 vs. 16/96, p = 0.0038), the samples from SAKK 16/96 trial were excluded.
- Overall, pre- and post-neoadjuvant samples from 83 patients were included in the final analysis (**Table 1**).

Table 1. Patient demographics and disease characteristics.

	Overall (N=83)
Trial	
• SAKK 16/00	72 (86.7%)
• SAKK 16/01	11 (13.3%)
Therapy group	
• Bimodal	41 (49.4%)
• Trimodal	42 (50.6%)
Age (years)	
• median (min, max)	59.0 (39.0-74.0)
Sex	
• Female	29 (34.9%)
• Male	54 (65.1%)
ECOG performance status	
• 0	62 (74.7%)
• 1	21 (25.3%)

Tobacco use history	
• Continued	32 (38.6%)
• Stopped	46 (55.4%)
• Never	5 (6.0%)
Smoking burden (pack-years) [1]	
• median (min, max)	45 (5-100)
Histology	
• Adenocarcinoma	31 (37.3%)
• Squamous cell carcinoma	30 (36.1%)
• Large cell carcinoma	4 (4.8%)
• Poorly differentiated NSCLC	17 (20.5%)
• Not otherwise specified	1 (1.2%)
Stage (TNM 7th edition)	
• IIIA	76 (91.6%)
• IIIB	7 (8.4%)

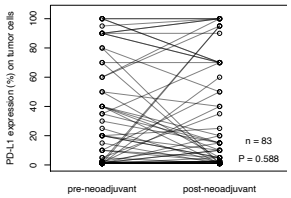
[1] Data collected for 74 patients.

- PD-L1 expression levels are presented in **Table 2**.
- Median pre- and post-neoadjuvant PD-L1 expression did not differ significantly (Wilcoxon test, p = 0.588) (**Figure 2**).

Table 2 and **Figure 2.** PD-L1 expression (all patients).

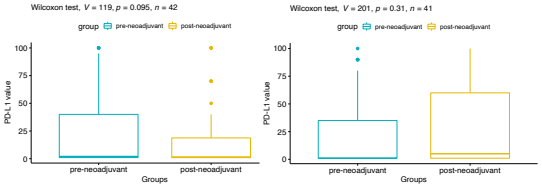
PD-L1 status [1]	
All patients (N=83)	Patients (%)
• PD-L1 <1%	34 (41%)
• PD-L1 1-49%	31 (37%)
• PD-L1 ≥50%	18 (22%)
Median PD-L1 expression	
All patients (N=83)	Median (min; max)
• pre-neoadjuvant	1% (<1; 100)
• post-neoadjuvant	1-4% (<1; 100)
Trimodal cohort (N=42)	
• pre-neoadjuvant	1-4% (<1; 100)
• post-neoadjuvant	1-4% (<1; 100)
Bimodal cohort (N=41)	
• pre-neoadjuvant	<1% (<1; 100)
• post-neoadjuvant	5% (<1; 100)

[1] pre-neoadjuvant values.



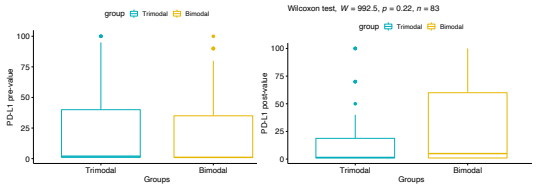
- There was no significant difference in either of the cohorts (trimodal and bimodal) for the median PD-L1 expression between the pre- and the post-neoadjuvant samples (**Figure 3**).

Figure 3. PD-L1 expression in the trimodal (left) and the bimodal cohort (right).



- In the comparison of the treatment arms (trimodal vs. bimodal cohort) there was no statistically significant difference for the median PD-L1 expression after neoadjuvant treatment (p = 0.22) (**Figure 4**).

Figure 4. PD-L1 expression in the pre-neoadjuvant (left) and the post-neoadjuvant samples (right).



Conclusions

- Neoadjuvant treatment did not impact on PD-L1 expression. This was the case for both neoadjuvant chemotherapy as well as neoadjuvant chemoradiation.
- If the observation that radiotherapy can sensitize to treatment with ICIs holds true, it is unlikely to be mediated through an upregulation of PD-L1 expression.

References:
[1] Betticher DC, et al. J Clin Oncol. 2003;21(9):1752-9.
[2] Stupp R, et al. Lancet Oncol. 2009;10(8):785-93.
[3] Pless M, et al. Lancet. 2015;386(9998):1049-56.

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