

EP07.53: Histological subtype, PD-L1 status and KRAS mutation as predictors of pathological response to neoadjuvant chemoimmunotherapy in resectable NSCLC: retrospective multicenter study.

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INTRODUCTION

Surgery remains the primary curative-intent treatment for patients with resectable non-small-cell lung cancer (NSCLC). Perioperative immunotherapy with neoadjuvant chemotherapy has recently emerged as a promising strategy to improve outcomes. Good patient selection remains important factor for successful treatment. Treating PD-L1 positive only or introducing KRAS inhibitors to perioperative regimens are ways to boost results.

The aim of this study was to compare pathological outcomes with histological and molecular features.

METHODS

Who:

Patients with newly diagnosed, previously untreated, resectable stage IIA–IIIB NSCLC without *EGFR* mutations or *ALK* rearrangements and known NGS status were selected from hospital database.

Staging was always based on PET-CT and head MRI or CT with i.v. contrast.

Where:

Three major Polish lung cancer centers (pulmonology, oncology and thoracic surgery in one location).

What:

Treatment was carried out in routine practice - regimen consisted of 3–4 cycles of histology-based chemotherapy with nivolumab, durvalumab or pembrolizumab. Pathological response was evaluated by pathologist in post-surgical specimen examination.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- The use of neoadjuvant chemoimmunotherapy results in high proportions of MPR in our patient's population.
- Non-squamous histology is a negative predictive factor for response.
- PD-L1 high tumors were associated with high probability of MPR.
- No negative value of KRAS mutation or PD-L1 negative expression was demonstrated.

Future Direction for Research

- As we demonstrated neoadjuvant treatment should not be limited based on any known histological or molecular feature.
- Further search for positive and negative predictors of response to neoadjuvant chemoimmunotherapy is important, patient selection may result in better outcomes and wit less unnecessary toxicities.

REFERENCES & ACKNOWLEDGEMENTS

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RESULTS

A total of 120 patients were included. Baseline characteristics of patients and treatment is summarized in Table 1 below.

Characteristics	Overall N=120
Age, years, median	68
Sex, n (%)	
Male	70 (58.8%)
Female	50 (41.2%)
Histology, n (%)	
Squamous cell carcinoma	71 (59.2%)
Adenocarcinoma	42 (35%)
NOS	7 (5.8%)
Clinical stage by 8th TNM, n (%)	
II	33 (27.5%)
III	87 (72.5%)
PD-L1 expression, TPS, n (%)	
TPS <1%	24 (20%)
TPS 1-49%	50 (41.6%)
TPS ≥50%	46 (38.3%)
Immunotherapy used, n (%)	
Pembrolizumab	53 (44.2%)
Nivolumab	44 (36.7%)
Durvalumab	23 (19.2%)
Time to surgery from last cycle, weeks, median	7

Most patients were male, squamous histology was predominant. High tumor PD-L1 expression was assessed in 46 cases, whereas PD-L1 negative tumor cells were present in 24 cases.

Among 49 patients with non-squamous histology, KRAS mutation was present in 24 cases.

Pembrolizumab was the most used antibody.

Surgery was performed in 109 patients, pneumonectomy was performed in 12.8% of cases, R0 was achieved in 93.6%.

Pathological complete response (pCR) was present in 32% of cases (35/109), as major pathological response (MPR) (including pCR) was present in 65 cases (59.6% of total cases). MPR rate for non-squamous histology was 40.4, and this histological subtype was associated with significantly lower chances of achieving MPR (chi2, p<0.0001).

Among patient with KRAS positive tumors MPR was present in 43.5% of cases, thus KRAS mutation was not associated with lower chances of MPR (chi2, p=0.075).

In PD-L1 high subgroup chance of MPR was significantly higher (chi2, p=0.01). In contrast, in the PD-L1 negative subgroup, no increased risk of not achieving MPR (more than 10% of viable tumor cells) was observed (chi2, p=0.13).