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P23: Impact of PDL1 expression on Outcomes of patients with EGFR mutant NSCLC treated with EGFR TKIs: first results of the POET study

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Background

- In EGFR mutant advanced NSCLC (aNSCLC), acquired resistance to EGFR tyrosine kinase inhibitors (TKIs) inevitably occurs.
- Despite some data demonstrated that high PD-L1 expression predicts poor response and de novo resistance to EGFR TKIs, including Osimertinib[1-2], to date, inconclusive results have been published or presented regarding the predictive/prognostic role of PDL1 expression in EGFR mutant NSCLC[3].
- **In the POET study, we aimed to, retrospectively, evaluate the potential prognostic impact of PDL1 expression in EGFR-positive aNSCLC during first, second, and third-generation TKIs treatment.**

Methods

- A retrospective analysis of patients treated with first (Erlotinib/Gefitinib), second (Afatinib) and third generation (Osimertinib) EGFR-TKIs was conducted.
- The main objective was to evaluate the potential correlation between levels of PDL1 expression and anti-EGFR treatment efficacy in terms of overall survival (OS) and progression-free-survival (PFS).

Results - 1

Patients' characteristics

Data from 171 patients (median age 69.0 years) who received EGFR TKIs were gathered. The most common EGFR alteration was ex19del (52.6%). 26 patients (15.2%) showed high PDL1 expression (≥50%). 105 patients (61.4%) were treated with Osimertinib, while 22.2%, 12.3% and 4.1% were treated with Gefitinib, Afatinib and Erlotinib, respectively [Table 1].

Results - 2

Table 1. Clinical and molecular characteristics of the population.

Characteristics	Patients N= 171 (%)
Gender	
Male	60 (35.1)
Female	111 (64.9)
Age in years (median, IQR, range)	69 (59-74) (25-84)
Smoking habits	
Current	16 (9.4)
Former	57 (33.3)
Never	69 (40.4)
Unknown	29 (17.1)
ECOG PS	
0	75 (43.9)
1	75 (43.9)
2-3	21 (12.2)
Stage	
IIIB	7 (4.1)
IV	164 (95.9)
PDL1	
<=49%	145 (84.8)
>=50%	26 (15.2)
Mutations	
Exon 19 (ex19del)	90 (52.6)
Exon 21 (L858R)	68 (39.8)
Others	9 (7.7)
TKIs	
Gefitinib	38 (22.2)
Afatinib	21 (12.3)
Erlotinib	7 (4.1)
Osimertinib	105 (61.4)
Treatment line	
1	162 (94.7)
2	8 (4.7)
3	1 (0.6)

Response and outcome results

In the overall population, the objective response rate was 61%, mPFS 19.1 months (15.1-23.1) and 2-year OS 61.5%.

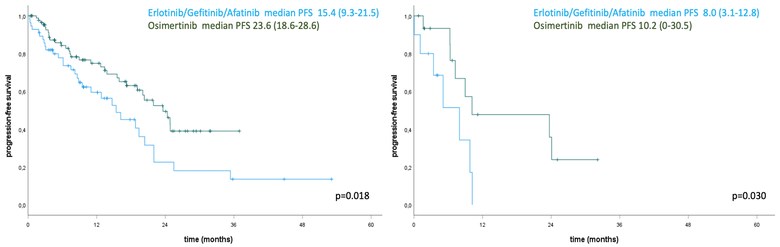
Table 2. Results of multivariate analysis.

	UNIVARIATE HR (95% CI)	MULTIVARIATE HR (95% CI)
ECOG PS	P<0.0001	*P=0.002*
0	1.00	*1.00*
1	1.33 (0.80-2.21)	*1.60 (0.95-2.72)*
2-3	5.09 (2.70-9.60)	*3.73 (1.78-7.82)*
PDL1	P=0.03	P=0.073
<=49%	1.00	1.00
>=50%	1.87 (1.06-3.29)	1.71 (0.95-3.08)
METASTATIC SITES		
Lung	0.80 (0.51-1.26) p=0.34	
Node	0.93 (0.51-1.68) p=0.80	
Pleural	1.06 (0.67-1.66) p=0.80	
Bone	1.25 (0.79-1.97) p=0.35	
Adrenal Gland	2.17 (1.18-3.97) p=0.01	1.36 (0.65-2.84) p=0.41
Liver	3.11 (1.79-5.41) p<0.0001	*1.98 (1.06-3.68) p=0.03*
Brain	1.07 (0.65-1.76) p=0.78	
TKIs	P=0.006	*P=0.001*
Gefitinib/Erlotinib	1.00	*1.00*
Afatinib	0.62 (0.31-1.26)	*0.48 (0.22-1.06)*
Osimertinib	0.45 (0.27-0.73)	*0.36 (0.21-0.61)*
FIRST LINE	P<0.0001	P=0.08
No	1.00	1.00
Yes	0.14 (0.06-0.35)	0.39 (0.13-1.12)

Association between PDL1 expression and outcome

Patients with PDL1 <50% showed mPFS of 15.4 (9.3-21.5) versus 23.6 months (18.6-28.6) with first/second and third generation TKIs, respectively (p=0.018). Patients with PDL1 ≥50% showed mPFS of 8.0 months (3.1-12.8) versus 10.2 months (0-30.5) with first/second and third generation TKIs, respectively (p=0.03) [Figure 1]. In the high PDL1 subgroup, a significant difference in OS was observed (mOS 24.9 versus 31.3 months with first/second versus third-generation TKIs; p=0.030). No statistically significant differences were reported when the analysis was limited to the first-line setting.

Figure 1. PFS in PDL1<50% and in PDL1>=50%, according to the generation of TKIs



PDL1<50% PDL1 >= 50%

Conclusion

- This retrospective and multicentric analysis demonstrates the negative prognostic impact of high PDL1 expression in EGFR mutant NSCLC treated with TKIs.
- To note, our study supports the survival benefit of Osimertinib compared to first/second generation TKIs, regardless of PDL1 expression.
- A larger data collection is ongoing and updated results will be presented/published soon.

References

1. Su S et al. Strong programmed death ligand 1 expression predicts poor response and de novo resistance to EGFR tyrosine kinase inhibitors among NSCLC patients with EGFR mutation. J Thorac Oncol 2018; 13:1668-1675
2. Hsu KH et al. PD-L1 strong expressions affect the clinical outcomes of osimertinib in treatment naïve advanced EGFR-M+ non-small cell lung cancer patients. Sci Rep 2022; 13(12):9753
3. Peng Z et al. Predictive value of pretreatment PD-L1 expression in EGFR-M+ non-small cell lung cancer: a meta-analysis. World J Surg Oncol 2021; 19:145

All authors declare no conflict of interests related to this study.

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