

Baseline Characteristics of NSCLC First-Line Immunotherapy Super-Responders in Three European Lung Cancer Centers: An ENDEAVOUR-IMIGO Project

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Disclosure: The authors have declared no conflicts of interest.

Acknowledgements: The authors thank Daiichi Sankyo (Tokyo, Japan) for providing organizational, non-financial support to the project within the ENDEAVOUR lung cancer programme.

Keywords: Adenocarcinoma, checkpoint inhibitor, KRAS, long-term response, neutrophil-to-lymphocyte ratio, programmed death-ligand 1 (PD-L1), squamous-cell carcinoma, systemic steroid.

Citation: Oncol AMJ. 2026;3[1]:89-91.
<https://doi.org/10.33590/oncolamj/US09VJ65>

BACKGROUND AND AIMS

Immune-checkpoint inhibitors (ICI) are an indispensable part of first-line treatment concepts for most patients with metastatic non-small cell lung cancer without targetable driver mutations.¹ Still, long-term response is

rare, and data on predictive biomarkers are limited, with the expression of programmed death-ligand 1 (PD-L1) being the only one used in daily clinical practice.

As part of the Daiichi Sankyo ENDEAVOUR program supporting young lung cancer researchers, the ENDEAVOUR-IMIGO working group was formed to explore novel biomarkers from imaging and genetic testing, including AI methods.

METHODS AND RESULTS

As a first exploratory analysis,² 'super-responders' to first-line ICI treatment with a progression-free survival of ≥ 24 months were identified from three separate registries in Linz (Austria), Groningen (the Netherlands), and Milan (Italy), and compared for their baseline characteristics.

Of interest, the rate of super-responders was very similar in the three cohorts, with 50/402 (12.4%) in the Linz, 46/428 (10.7%) in the Groningen, and 45/283 (15.9%) in the Milan cohort. Baseline characteristics of the respective cohorts are shown in [Table 1](#), showing predominantly adenocarcinomas with a high average PD-L1 expression. Of interest, nearly half of the patients across all three cohorts had KRAS mutations.

To further elucidate possible factors associated with a 'super-responder' status, the Linz cohort was matched for age, sex, histology, PD-L1 positivity, stage, and Eastern Cooperative Oncology Group (ECOG) performance status with non-responders (progression-free survival <6 months). Marked differences were seen concerning a higher rate of chemo-immunotherapy combination treatment, lower use of systemic

Table 1: Baseline characteristics for ICI super-responders as compared to non-responders in the Linz cohort, as well as for super-responders in the Milan and Groningen cohorts.

	Linz (n=100)			Milan (n=45)	Groningen (n=46)
	<6M n=50 (matched)	≥2Y n=50	p value <6M vs ≥2Y	≥2Y n=45	≥2Y n=46
Male sex, n (%)	24 (48)	25 (50)	0.841	34 (75.5)	22 (48)
Age <70, n (%)	14 (28)	15 (30)	0.826	15 (33.3)	34 (74)
ECOG performance status, n (%)					
0	25 (50)	24 (48)	0.768	21 (47)	18 (39)
1	16 (32)	19 (38)		23 (51)	23 (50)
2+	9 (18)	7 (14)		1 (2)	5 (11)
Histological subtype, n (%)					
Adenocarcinoma	36 (72)	36 (72)	0.341	30 (67)	33 (72)
Squamous cell carcinoma	12 (24)	14 (28)		6 (13)	7 (15)
Other	2 (4)	0 (0)		9 (20)	6 (13)
PD-L1 expression %, mean (SD)	41.9 (36.8)	48.9 (38.8)	0.403	52.3 (35.4)	54.0 (39.0)
Brain metastases, n (%)	16 (32)	13 (26)	0.509	14 (31)	7 (15)
KRAS mutation, n (%)	12 (35)	18 (50)	0.214	19 (42)	23 (50)
Treatment, n (%)					
Chemo-ICI combination	29 (58)	38 (76)	0.056	18 (40)	19 (41)
ICI-monotherapy	21 (42)	12 (24)		27 (60)	27 (59)
Systemic steroid treatment, n (%)	17 (34)	6 (12)	0.009	12 (27)	N/A
Absolute neutrophil count (G/L), mean (SD)	11.5 (8.7)	7.7 (2.9)	0.015	6.8 (3.2)	7.3 (2.6)
Absolute lymphocyte count (G/L), mean (SD)	1.7 (3.7)	1.4 (0.7)	0.071	1.9 (0.7)	1.6 (0.7)
Neutrophil-to-lymphocyte ratio, mean (SD)	13.4 (11.0)	7.2 (5.2)	0.006	4.4 (3.6)	5.9 (4.0)

ECOG: Eastern Cooperative Oncology Group; M: months; ICI: immune checkpoint inhibitor; PD-L1: programmed death-ligand 1; vs: versus; Y: years.

steroids at treatment initiation, and lower neutrophil-to-lymphocyte ratio in super-responders (Table 1).

CONCLUSION

The authors concluded that 'super-responders' to first-line ICI therapy may represent a distinct patient phenotype that

showed consistent characteristics across three independent registries. Matched exploratory analyses from only the Linz cohort also showed possible implications of tumor characteristics, co-medication, and the patient's baseline inflammatory state, which warrant further, more detailed analyses.

FUTURE DIRECTIONS

Planned next steps in the ENDEAVOUR-IMIGO project include harmonization of the national registry data and establishment of a multi-national control group, and the inclusion of broad-panel next-generation sequencing data and variables derived from CT and 18F-FDG-PET/CT into more complex models.

References

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