Durvalumab in treatment-naive, stage IV non-small cell lung cancer (NSCLC) patients, with ECOG PS 2-3 and high PD-L1 tumor expression: results of the IFCT-1802 SAVIMMUNE Phase II Trial

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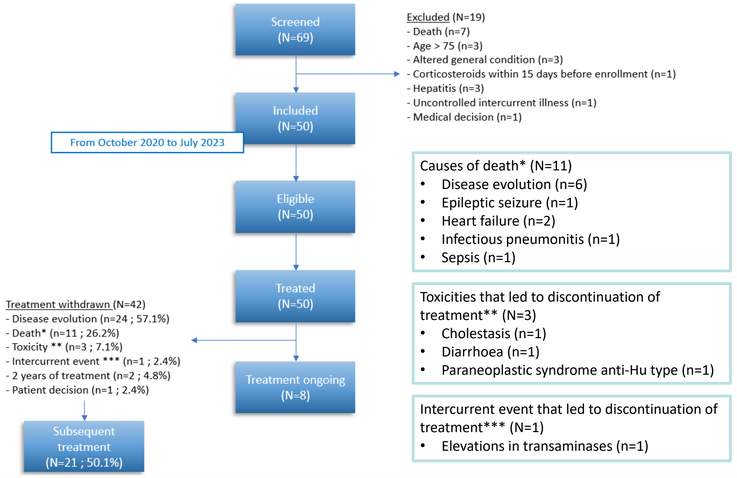
Background

Performance Status (PS) 2-3 is a prognostic factor associated with poor survival (median OS in PS2 pts was 3-5 months with single agent chemotherapy, and 6-9 months with combination chemotherapy; and less than 2 months in PS3 pts) and higher incidence of chemotherapy-related adverse events (AE), while the impact of poor PS on immunotherapy safety and efficacy is less documented. We sought to prospectively assess front-line durvalumab (anti-PD-L1) in PS2-3 pts with advanced NSCLC and high PD-L1 expression.

Methods and Objectives

In this single-arm, multicentre (n=22), phase II trial, PS2-3 pts, **aged 18-75**, with metastatic NSCLC, **PD-L1 positive (TPS ≥25%)**, without brain metastases, received 1500mg durvalumab every 4 weeks until progression, toxicity or completion of 2 years of therapy. Primary endpoint was safety defined as the incidence of grade ≥3 treatment-related AE (TRAE) during the first 8 weeks (NCI CTCAE v.5.0). Using a 2-step binomial proportion test (O'Brien-Fleming's procedure), 67 pts were to be included, to achieve 95% power, with 5% type I error rate, to observe <40% (H0) G3-5 TRAE. Secondary objectives included intent-to-treat (ITT) blinded independent centrally reviewed (BICR) ORR and PFS, DoR, OS and PS improvement at 8 weeks.
At the data cutoff (30NOV2023), median duration of follow-up was 15.7 months [9.72-21.81].

Patient disposition



Baseline characteristics

Patients characteristics			ITT (N=50)
Sex	**Female**	N (%)	15 (30)
	Male	N (%)	35 (70)
Age		Median [Min-Max]	68.3 [47.2-75.3]
Smoking status	**Current**	N (%)	30 (60)
	Former	N (%)	19 (38)
	Never	N (%)	1 (2)
PS	**2**	N (%)	40 (80)
	3	N (%)	10 (20)
Medical history	**Diabetes**	N (%)	12 (24)
	Renal	N (%)	1 (2)
	Respiratory	N (%)	19 (38)
	Cardiac	N (%)	18 (36)
Charlson score		Median [Min-Max]	8 [0.0-15.0]
Skeletal Muscle Index		Median [Min-Max]	38.8 [22.5-80.8]
Sarcopenia		Yes	41 (87.2)
		No	6 (12.8)
		UK	3

Tumor characteristics			ITT (N=50)
Histology	**Adenocarcinoma**	N (%)	29 (58)
	Squamous cell carcinoma	N (%)	12 (24)
	Others (NOS, Large cell carcinoma)	N (%)	9 (18)
TNM (Stage)	**IVA**	N (%)	18 (36)
	IVB	N (%)	32 (64)
PD-L1 (%)		Median	87.5
PD-L1 expression	**25-49%**	N (%)	6 (12)
	≥ 50%	N (%)	44 (88)
Molecular status	**EGFR mutation**	N (%)	0
	ALK fusion	N (%)	0
	KRAS mutation	N (%)	20 (40)

Treatment-Related Adverse Events (TRAE)

The median number of treatment cycles was 3 [1-26].
During the first 8 weeks, grade ≥3 TRAE occurred in 10% of pts (95% CI 1.7%–18.3%). During the follow-up, any grade TRAE occurred in 50% of pts (95% CI 36.1%–63.9%). No grade 5 TRAE were reported.

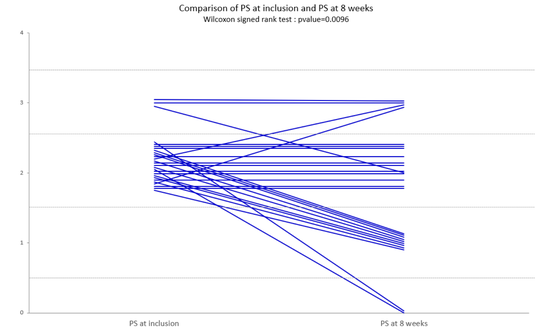
TRAE	Any grade	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
N (%)	25 (50%)	6 (12%)	12 (24%)	6 (12%)	1 (2%)	0 (0%)

ORR at 8 weeks

ORR at 8 weeks (N=50)	According to **Investigators**	According to **BICR**
Partial Response	11 (22%)	13 (26%)
Stable Disease	13 (26%)	9 (18%)
Disease Control	24 (48%)	22 (44%)
Progressive disease	16 (32%)	16 (32%)
Not Evaluable	10 (20%)	12 (24%)

BICR ORR at 8 weeks was 26% (95% CI 13.8%–38.2%) and 24% (95% CI 12.2%–35.8%) were confirmed at 16 weeks.
Median DoR was 11.3 months (95% CI, 6.4 to NR).

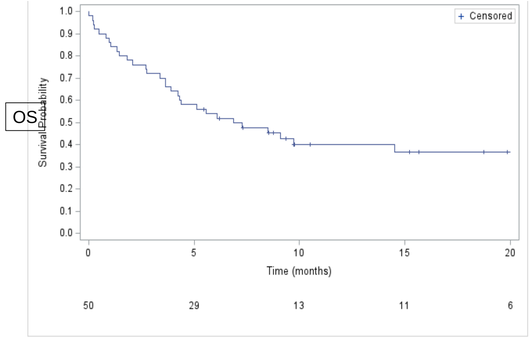
Change of PS at 8 weeks



Each line shows the change of PS of a patient from baseline to 8 weeks. A clinically valuable improvement in 11/50 (22%) of pts was observed (i.e. improvement from PS2-3 at baseline to PS0-1).

PFS and OS

PFS	ITT (N=50)	PS 2 (N=40)	PS 3 (N=10)
Event: N (%)	40 (80%)	30 (75%)	10 (100%)
Median PFS: months [95% CI]	2.3 [1.7-5.6]	3.5 [1.8-9.4]	1.4 [0.2-3.9]
OS			
Event: N (%)	31 (62%)	22 (55%)	9 (90%)
Median OS: months [95% CI]	6.9 [3.9-31.1]	9.7 [4.4-NR]	3.0 [0.2-5.6]
12-m OS: % [95% CI]	40.1 [26.1-53.7]	47.7 [31.0-62.7]	10.0 [0.6-35.8]



Conclusions

In PS2-3 pts with advanced NSCLC and high PD-L1 expression, front-line durvalumab is safe and showed interesting activity. The challenge remains the selection of patients who could actually derive benefits from ICI beyond PDL1 expression.

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