IFCT-1502 CLINIVO: Real-life experience with nivolumab in patients (pts) with advanced Non-Small Cell Lung Cancer (NSCLC): efficacy and safety of nivolumab and post-nivolumab treatment in the French Expanded Access Program (EAP)

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Background

Nivolumab is a standard option for second-line treatment in pts with advanced NSCLC. However data regarding the efficacy of nivolumab as well as post-nivolumab treatment in large cohorts of patients treated in a real-life setting, are lacking.

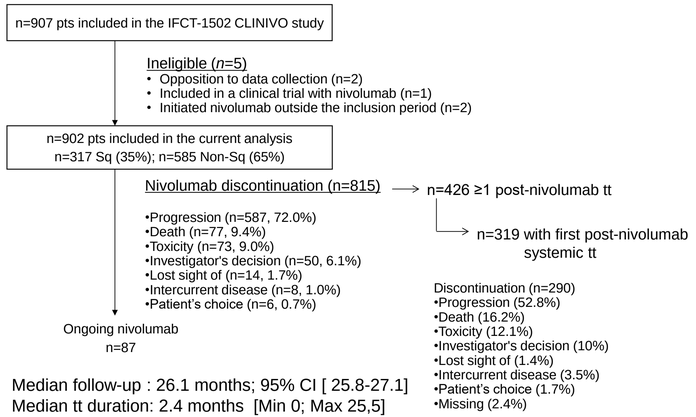
Objectives

- Overall survival (OS)
- Best response, progression-free survival (PFS) to nivolumab
- Best response, progression-free survival (PFS) to post-nivolumab treatment (tt)
- Predictors of response and survival to nivolumab and first post-nivolumab tt
- Maximal toxicity of nivolumab

Methods

This analysis included 902 pts with stage IIIB/IV NSCLC who initated ≥1 dose of nivolumab 3mg/kg q2w through the French EAP from 01/2015 for Squamous (Sq) and 06/2015 for Non-Sq NSCLC, until 08/2015.
Data were collected from pts medical records at each site of the study.

Study flowchart



Median follow-up : 26.1 months; 95% CI [25.8-27.1]
Median tt duration: 2.4 months [Min 0; Max 25,5]

Baseline characteristics

			Sq (N= 317)	Non-Sq (N=585)	Total (N= 902)
Sex	F	N (%)	58 (18.3)	215 (36.8)	273 (30.1)
Age (years)		Median	66.41	62.64	64.18
		Range	[36.4-86.6]	[19.9-88.2]	[19.9-88.2]
Smoking	Non-smoker	N (%)	22 (6.9)	94 (16.2)	116 (12.8)
	Smoker	N (%)	295 (93.1)	487 (83.8)	782 (86.2)
Number of pack-years		Median	40.00	35.00	40.00
		Range	[2.0-130.0]	[0.3-132.0]	[0.3-132.0]
Number of prior lines	1	N (%)	82 (25.9)	164 (28.1)	246 (27.3)
	2	N (%)	115 (36.4)	169 (28.9)	284 (31.5)
	3	N (%)	63 (19.9)	112 (19.2)	175 (19.4)
	4	N (%)	44 (13.9)	71 (12.2)	115 (12.7)
	>4	N (%)	12 (3.8)	68 (11.6)	80 (8.9)
Brain metastasis (at initiation of nivolumab)	No	N (%)	277 (87.4)	428 (73.2)	705 (78.2)
	Yes	N (%)	40 (12.6)	157 (26.8)	197 (21.8)
PDL1 (IHC)	Negative	N (%)	18 (85.7)	37 (63.8)	55 (6.1)
	Positive	N (%)	3 (14.3)	21 (36.2)	24 (2.7)

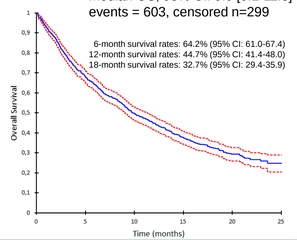
Maximal toxicity of nivolumab

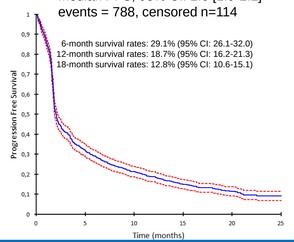
	All N (%)	Grade 2 N (%)	Grade 3 N (%)	Grade 4 N (%)	Grade 5 N (%)
All	313 (34.7%)	215 (23.8%)	82 (9.1%)	9 (1.0%)	7 (0.8%)
General	81 (9%)	65 (7.2%)	15 (1.7%)	1 (0.1%)	0 (0%)
Skin	76 (8.4%)	67 (7.4%)	8 (0.9%)	1 (0.1%)	0 (0%)
Endocrine	79 (8.8%)	70 (7.8%)	8 (0.9%)	1 (0.1%)	0 (0%)
Digestive	63 (7.0%)	48 (5.3%)	13 (1.4%)	1 (0.1%)	1 (0.1%)
Pulmonary	48 (5.3%)	20 (2.2%)	20 (2.2%)	2 (0.2%)	6 (0.7%)
Muscular	38 (4.2%)	28 (3.1%)	10 (1.1%)	0 (0%)	0 (0%)
Hepatic	28 (3.1%)	14 (1.6%)	10 (1.1%)	4 (0.4%)	0 (0%)
Blood and lymphatic	11 (1.2%)	10 (1.1%)	1 (0.1%)	0 (0%)	0 (0%)
Renal and urinary	15 (1.7%)	11 (1.2%)	4 (0.4%)	0 (0%)	0 (0%)
Nervous system	7 (0.8%)	6 (0.7%)	1 (0.1%)	0 (0%)	0 (0%)

Best response to nivolumab

Best response (%, 95% CI)	
Objective response (OR)	19.0% [16.2 ; 21.7]
Stable disease (SD)	35.5% [32.1 ; 38.9]
Disease Control (OR+SD)	54.5% [50.9 ; 58.0]
Progressive disease (PD)	44.9% [41.4 ; 48.4]
Not evaluable	0.6% [0.1 ; 1.2]

Efficacy of nivolumab





Pronostic factors of OS

	Univariate analysis			Multivariate analysis (n=889)		
Characteristics	HR	95% CI	p	HR	95% CI	p
ECOG PS						
2/3/4 (vs 0/1)	2.24	1.85-2.72	<0.0001	2.21	1.82-2.69	<0.0001
Brain metastasis						
Yes (vs No)	1.39	1.15-1.68	0.001	1.38	1.15-1.67	0.0007

Gender, age at initiation of nivolumab, smoking history, TNM stage, histology were not associated with OS.

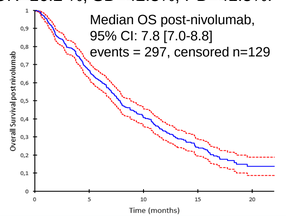
Acces to post-nivolumab tt

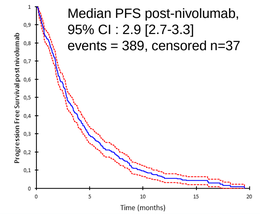
815 (90%) of patients had discontinuated nivolumab. Post-nivolumab tt was administered to 426 (47%) patients. Patients with a PS0/1, with 1 or 2 prior lines and without brain metastasis (at the time of nivolumab initiation) were more common in the population with post-nivolumab tt.

Exclusive systemic tt	**N=319 (74.9%)**		
Single agent chemotherapy	n=210 (49.3%)	Docetaxel	61 (14.3%)
		Gemcitabine	64 (15.0%)
		Paclitacel +/ bevacizumab	38 (8.9%)
		Vinorelbine	24 (5.6%)
		Pemetrexed	20 (4.7%)
		Other	3 (0.7%)
Platin-based doublet	n=35 (8.2%)	Platin-Paclitaxel	21 (4.9%)
		Other	14 (3.3%)
Targeted therapy	n=57 (13.4%)	Erlotinib	43 (10.1%)
		Other	14 (3.3%)
Nivolumab rechallenge	n=15 (3.5%)		
Other/unknown systemic tt	n=2 (0.5%)		
Surgery +/- radiotherapy +/- systemic tt	**N=100 (23.5%)**		
Unknown tt	**N=7 (1.6%)**		

Efficacy of post-nivolumab tt

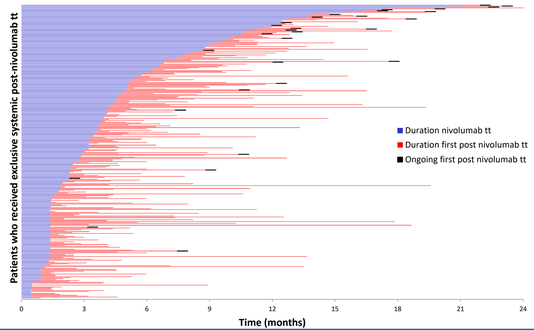
Best response to first post-nivolumab systemic tt (n=319) was: OR=16.2 %; SD=42.3%; PD=41.5%.





Pronostic factors of OS in patients receiving post-nivolumab tt

Cox multivariate analysis confirmed that smoking history (HR=1.42, 95% CI 1.00-2.03), presence of brain metastasis at initiation of nivolumab (HR=1.36, 95% CI 1.02-1.80) had defavourable effect on post-nivolumab prognosis. An OR under nivolumab had favourable effect on post-nivolumab prognosis (HR=0.52, 95% CI 0.29–0.93).
Gender, age, PS at initiation of nivolumab, TNM stage, histology, duration of nivolumab tt were not associated with OS.



Conclusions

Efficacy and safety of nivolumab was in line with data from clinical trials. Post-nivolumab treatment may be delivered in many patients, with highly variable efficacy and impact on OS.

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