Discontinuation of immune checkpoint inhibitor (ICI) above 18 months of treatment in real-life patients with advanced non small-cell lung carcinoma (NSCLC) : INTEPI, a multicentric retrospective study

Abstract 202
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INTRODUCTION

- The potential for durable responses with immune checkpoint inhibitors (ICIs) treatment for Non Small Cell Lung Cancer (NSCLC), along with their costs and potential risks for toxicity, has fueled interest in understanding long-term outcomes after treatment discontinuation, as well as determining the optimal treatment duration.
- In phase III clinical trials, the duration of treatment was set at 2 years or until disease progression.
- In the Keynote-010 study, 79 patients completed maximum 35 cycles/2 years of pembrolizumab; Overall Survival (OS) and Progression Free Survival (PFS) rates at 12 months after discontinuation were 99% and 72.5% respectively, OS and PFS rates at 24 months were 86% and 57.7% respectively.
- The CheckMate-153 study was in favor of continuing treatment beyond 1 year.
- Available data on melanoma suggest that best overall response at the discontinuation of treatment could be a good predictive factor of relapse risk, and metabolic response according to FDG-PET/CT could be helpful.

OBJECTIVES

- Exploratory study that aimed to describe the outcome of patients with advanced NSCLC treated with ICI monotherapy for at least 18 months and who stopped treatment in the absence of progressive disease (PD). A focus has been made to identify potential predictive biomarkers for relapse after treatment discontinuation.

METHODS

- Among patients who started ICI monotherapy between 1st July 2015 and 1st June 2018 in 7 hospitals with a controlled tumour after at least 18 months of treatment (n=107), those who interrupted ICI were selected (n=54). Their characteristics, the causes of discontinuation of ICI, and their outcome are described.
- Patients received ICI in an expanded access program or according to the label after approval.
- Baseline characteristics, treatment disposition, tumour responses, PFS and OS were collected using electronic databases medical records.
- PFS and OS after treatment discontinuation were calculated from the date of the last cycle to the date of PD or to date of death or last follow-up, and estimated using the Kaplan Meier method and compared using log rank tests.

RESULTS

Table 1. Characteristics n (%) of the 54 patients included in the analysis.

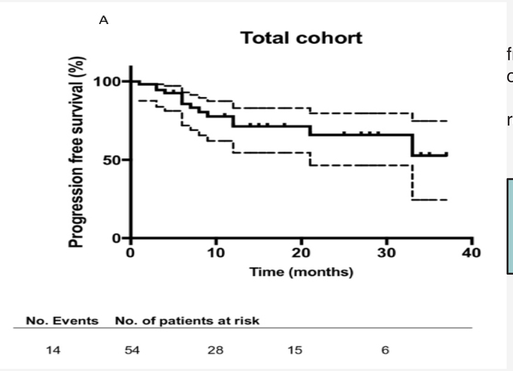
Anti-PD-1 mAb	Nivolumab	51 (94)
	Pembrolizumab	3 (6)
Median age, years (range)		63 (40-82)
Age group	<75 y	48 (89)
	≥75 y	6 (11)
Gender	Male	41 (76)
Smoking status		
	Current or former smoker	50 (93)
	Never	4 (7)
Line of therapy for ICI		
	First-line	4 (7)
	Second-line or higher	50 (93)
ECOG PS	0	18 (33)
	1	31 (58)
	≥2 or Unknown	5 (9)
PDL1 status	<1%	2 (4)
	1-50%	8 (15)
	>50%	8 (15)
	Unknown	36 (66)
Histology		
	Adenocarcinoma	29 (54)
	Squamous Cell	12 (22)
	Other	13 (24)
Positive mutation status		
	KRAS	16 (30)
	BRAF	1 (2)
	HER2	1 (2)
	MET exon 14	2 (4)
Wild type status or unknow		34 (62)
Number of metastatic sites at ICI initiation		
	≤3	44 (81)
	>3	10 (19)
Brain metastases at ICI initiation		11 (20)
Duration of treatment		
	18-24 months	20 (37)
	24-36 months	27 (50)
	>36 months	7 (13)
Median duration of treatment, months (range)		26 (18-48)
Immune-related AEs during treatment		
	yes	44 (81)
	no	10 (19)

- A total of 81% of patients experienced at least one immune-related adverse event (20% grade 3-4), most frequent being cutaneous side effects (55% of the total patients).
- Treatment was stopped by choice of the prescriber and toxicity in 46% and 22% respectively.

Outcomes after discontinuation

From discontinuation, OS and PFS were 90% and 71% respectively at 12 months and 82% and 66% respectively at 24 months.

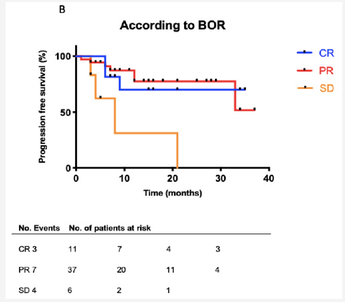
Figure 1. Kaplan-Meier probability curves for PFS from discontinuation of ICI : for the total cohort (A) ; according to best overall response (BOR) RECIST1.1 CT scan (B) ; according to complete response and/or complete metabolic response FDG-PET/CT (C).

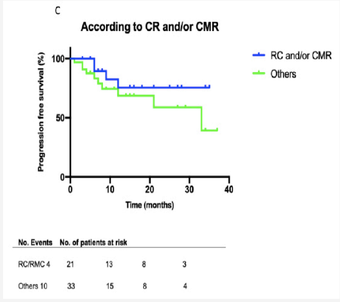


After a median follow up of 16 months (range 2-41) from discontinuation, 74% of patients remained free of progression.

Median time to progression for the 14 patients with relapse was 9 months (range 2-33).

Median PFS not reached, PFS 12 months 71%, PFS 24 months 66%.





PFS rates at 12 months were 70% for complete responders (CR) 77% for partial responders (PR), and 31% for those with stable disease (SD).

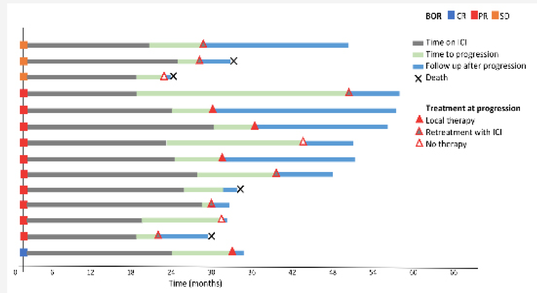
Relapse, n(%)	14 (26)
CR, n(%)	1 (5)
PR, n(%)	10 (27)
SD, n(%)	3 (50)

28 of the 54 patients and 10 of the 14 relapsing patients had a FDG-PET/CT at discontinuation of ICI.

In our analysis of PFS according to FDG-TEP/CT response groups, we could not study PFS according to complete metabolic response but we compared patients with either a RECIST1.1 and/ or a metabolic response with patients without a complete response.

PFS rates at 12 months were 76% for CR and/or CMR and 69% for others.

Figure 2. Swimmer plot indicating time on ICI treatment, PFS, and OS of patients with progression after discontinuation of ICI.



CONCLUSION

- This study provides new insights into the long-term outcomes of patients with advanced NSCLC treated with ICI monotherapy for at least 18 months before discontinuation in the absence of PD.
- Our study in real life shows similar efficacy of durable response after stopping immunotherapy compared to clinical trials.
- Duration of disease control seems to be correlated to tumor response. Unfortunatly we did not have enough patients with FDG-PET/CT at discontinuation to assess a relationship between complete metabolic response and prolonged PFS, yet our results on a limited sample suggest that FDG-PET/CT might be a positive factor for a prolonged tumor control after discontinuation. This needs to be confirmed on a larger sample.
- While these results are encouraging, there remains uncertainty about the disease course of patients who have received at least 18 months of treatment without disease progression. These results can be used as a basis for discussion with the patients in order to make a shared decision on whether or not to continue immunotherapy.

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