P512 Discontinuation of anti-PD1 in advanced melanoma: an observational retrospective study from the Italian Melanoma Intergroup.

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Background

Immunotherapy has improved the survival of patients with stage IV melanoma. In responding subjects, clinical benefits may be long-lasting and persist even after treatment discontinuation. However, a few data are available on clinical outcomes of patients that discontinued anti-PD1 immunotherapy in a real-life setting.

Objective

The aim of this study was to evaluate the progression of free survival (PFS) in patients with metastatic melanoma who interrupted anti PD-1 treatment in complete response (CR) or due to limiting toxicity.

Materials and Methods

This multicenter study included 328 patients with advanced melanoma, at 23 Italian medical centers belonging to IMI (Italian Melanoma Intergroup). The study investigated the relapse risk in 237 patients who stopped anti-PD1 therapy due to complete response, treatment-related toxicity or by their own choice after a long period of treatment. Patients in disease progression at therapy interruption were excluded during follow-up. Clinical and biological factors associated with recurrence were studied.

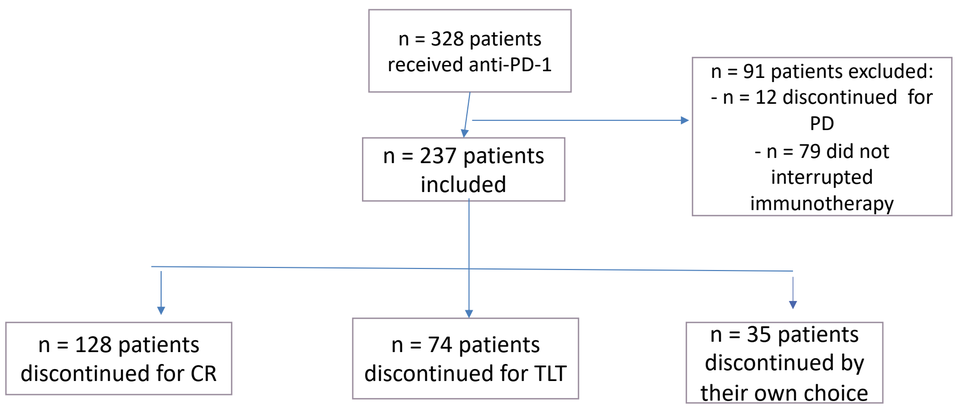


Figure 1: flowchart of patients' selection.

Results

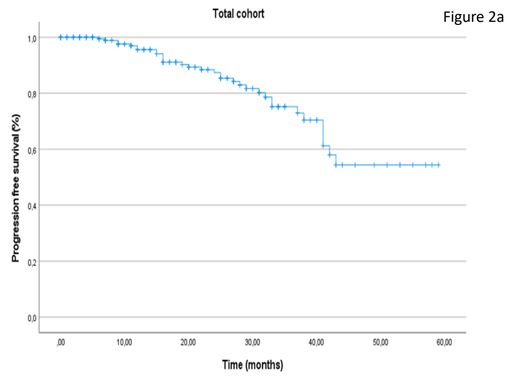
- The median age of patients was 68.9 years (standard deviation: 13; range 33-95). The median time on treatment was 33 months (standard deviation: 18,7; range 1-98). Out of 237 patients, 128 patients (54%) interrupted anti-PD1 for CR, 74 patients (31.2%) for adverse effects (36 patients in CR, 25 patients in partial response (PR), 9 patients in stable disease (SD) and 2 patients in disease progression (PD)) and 35 patients (14.8%) by their own choice (12 patients in CR, 17 patients in PR and 6 patients in SD). After a median follow up of 21 months (range 1-81) after treatment discontinuation, 85.7% of patients remain disease free. 34 patients (14.3%) developed a relapse after a median time of 12 months (range 1-35): 10 patients (29.4%) after discontinuation for CR, 17 patients (50%) after discontinuation for treatment-related toxicity (7 in CR, 5 in PR, 5 in SD) and 7 patients (20.6%) after discontinuation due to the patient's decision (2 in CR, 4 in PR, 1 in SD). Only 7.8% of patients who interrupted for CR (10/128), 23% of patients who interrupted for limiting toxicity (17/74) and 20% of patients who interrupted by their own choice (7/35) developed recurrence.
- Regarding patients who discontinued therapy because of CR, we observed a statistically significant association between recurrence and site of primitive melanoma, particularly visceral/mucosal site (p=<0.05). Moreover, patient with a metastatic disease limited to the lung who obtained a CR were characterized by a lower number of relapses (p=<0.05).
- At last, we observed an association between site of primary melanoma – in particular unknown primary site - and discontinuation for treatment-related toxicity (p=<0.05).
- Sex, ECOG, LDH, mutation of BRAF and NRAS, Breslow's index, Clark's level, site and number of metastases, vitiligo were studied but did not demonstrate any association with relapse rate.

Conclusion

This study confirms in a real life setting that immunotherapy can achieve long-lasting responses that can be maintained after anti-PD1 interruption. In 70.6% of cases, recurrences were observed among patients who had not obtained a CR at treatment discontinuation.

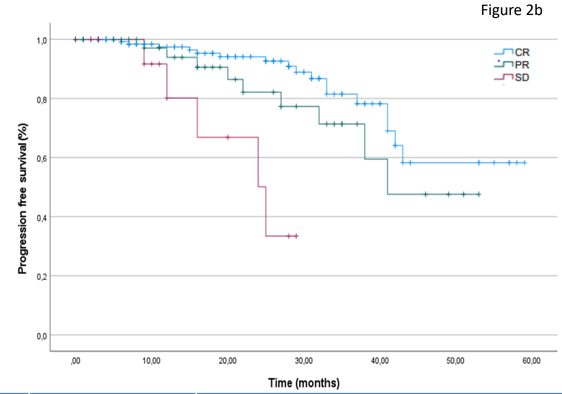
Kaplan–Meier probability curves for progression-free survival from discontinuation of anti-PD-1. (Figure 2a) according to best overall (Figure 2b)

Figure 2a



No Events	No of Patients at Risk						
34	237	149	105	58	21	16	16

Figure 2b



	No of Events	No of Patients at Risk						
CR	19	177	108	74	41	17	7	0
PR	9	44	32	21	13	4	1	0
SD	5	15	9	4	0	0	0	0