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Patients with stage IV melanoma treated with immunotherapy for more than 2 years: is an end to treatment possible?

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Background

Immune checkpoint inhibitors anti-PD-1 have significantly improved prognosis of patients with advanced melanoma. Treatment duration in patient who achieved a durable complete response (CR) is still debated. On the basis of some literature findings, it is generally agreed that in CR patients treatment can be interrupted after two years. However, a few data are available for those patients who achieved a long-lasting partial response or stable disease after two years of treatment in a real-life setting.

Materials and Methods

This multicentre study included 328 stage IV melanoma patients from 23 Italian referral centres belonging to IMI (Italian Melanoma Intergroup) who underwent an anti-PD1 treatment for more than 2 years discontinued the treatment after the obtaining of a CR or due to drug-related toxicity or for patient decision.

Results

Out of 328 patients, 237 discontinued treatment because of complete response, toxicity or patient's decision after two years of treatment. 78 patients continued treatment more than two years. Among those patients, we observed a CR in 16 patients, partial response (PR) in 47 patients, stable disease (SD) in 14 patients and disease progression (PD) in 1 patient.

Among the group of patients who interrupted therapy after two years (n 237), 128 patients were in CR.

Out of 158 patients in CR discontinuing treatment, only 17 patients (10.7%) developed relapse and 8 patients (6.3%) died. Moreover, 16 patients of this group (12.5%) underwent surgery and 19 patients (14.8%) received radiotherapy.

Conclusion

In this multicentre study, treatment interruption is a safe decision in patients who achieved CR. Since a great number of patients in CR took advantage of surgery and/or radiotherapy in order to achieve complete response, same benefits can be supposed for the group of patients with PR and SD that are still in therapy since many years. Otherwise, treatment interruption is not advised in this group since, considering our experience, a greater risk of relapse has been proved to be associated with PR and SD at the discontinuation of immunotherapy.

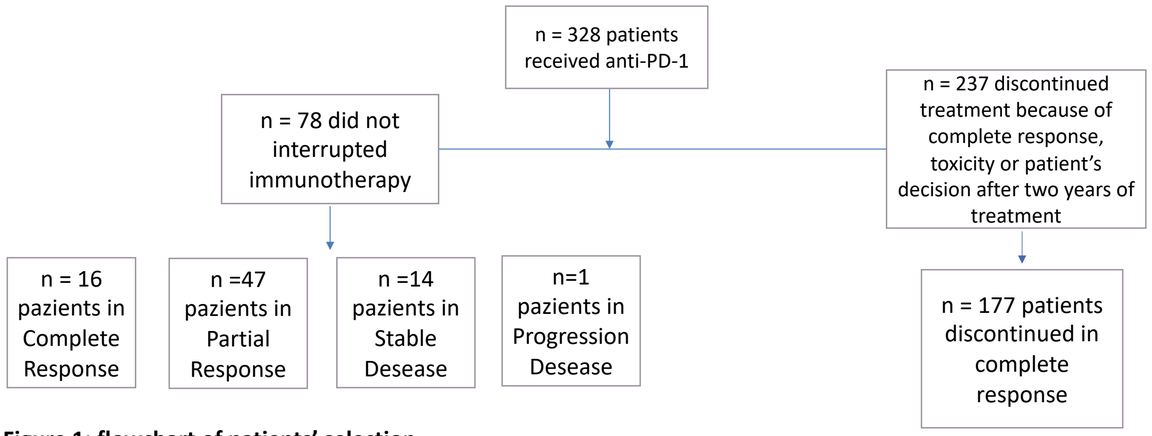
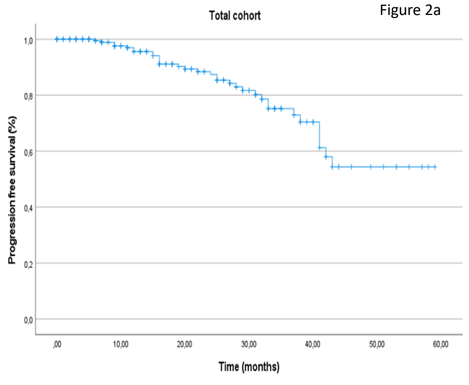


Figure 1: flowchart of patients' selection.

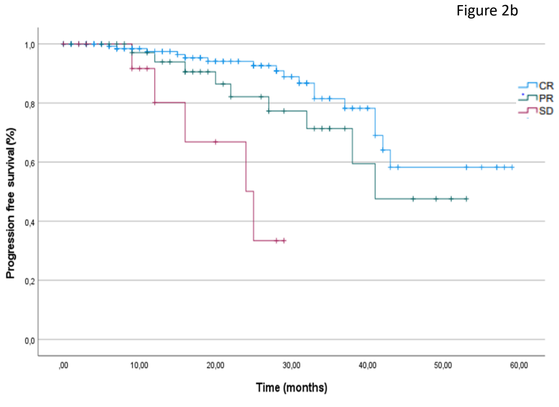
Kaplan–Meier probability curves for progression-free survival from discontinuation of anti-PD-1. (Figure 2a) according to best overall (Figure 2b)

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	72	41	17	7	0
PR	9	44	31	21	13	4	1	0
SD	5	15	9	4	0	0	0	0