

Supplementary Online Content

Simonaggio A, Michot JM, Voisin AL, et al. Evaluation of readministration of immune checkpoint inhibitors after immune-related adverse events in patients with cancer. *JAMA Oncol*. Published online June 6, 2019.
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eFigure 1. Study Design

eFigure 2. Outcome After Anti-PD-1 or Anti-PD-L1 Rechallenge

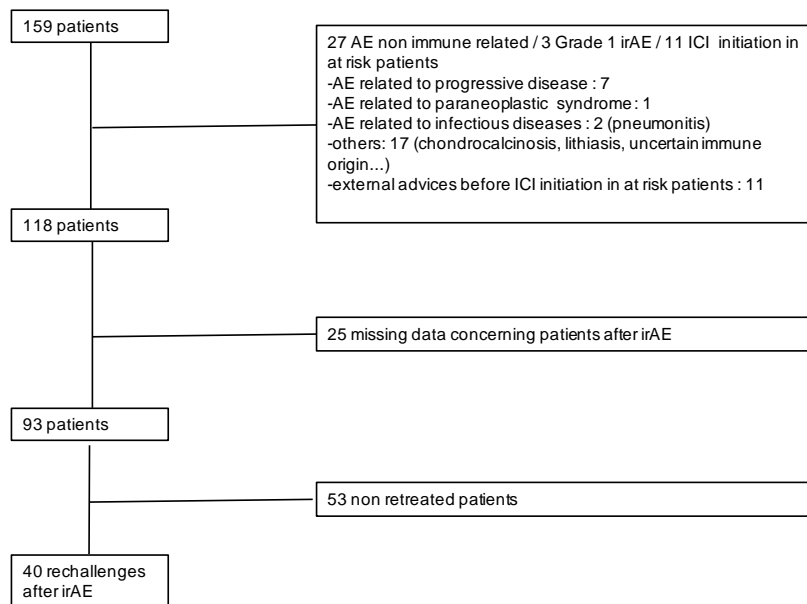
eFigure 3. Severity Grade: Comparison of the Initial and Second irAEs

eFigure 4. Kaplan-Meier Curves for PFS (A) and OS (B) in Patients in the Retreated Group (n = 40) and the Non-retreated Group (n=37)

eTable. Summary of the Main Studies of ICI Rechallenge After an irAE

This supplementary material has been provided by the authors to give readers additional information about their work.

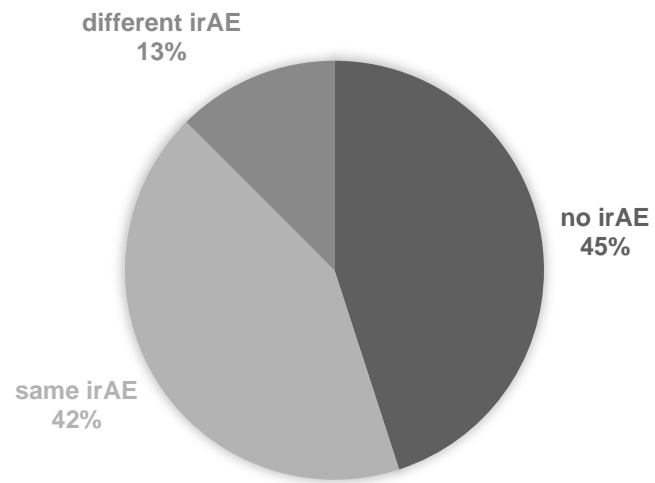
eFigure 1. Study Design



One hundred fifty-nine patients were referred to the ImmunoTOX board. Twenty-seven had no irAEs, 3 had Grade 1 irAE, 11 were addressed for guidance before anti-PD(L)-1 initiation and 25 had missing data concerning rechallenge (external advices). Ninety-three patients were analyzed for irAE description. Forty patients (40/93) were retreated with anti-PD(L)-1 after first irAE.

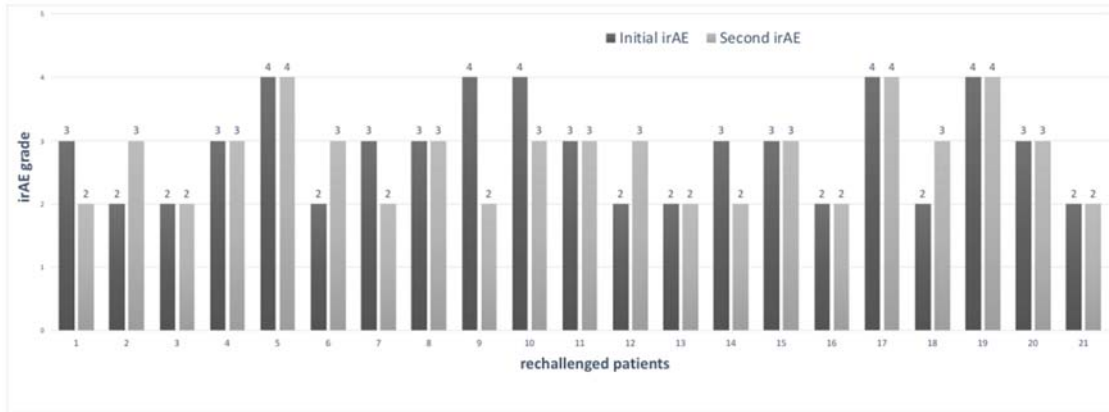
Abbreviations: AE: adverse event, irAE: immune related adverse event, ICI: immune checkpoint inhibitor.

eFigure 2. Outcome After Anti-PD-1 or Anti-PD-L1 Rechallenge



Abbreviations: irAE: immune related adverse events, anti PD-1 : anti-programmed cell death 1, anti-PD-L1 : anti-programmed death ligand 1

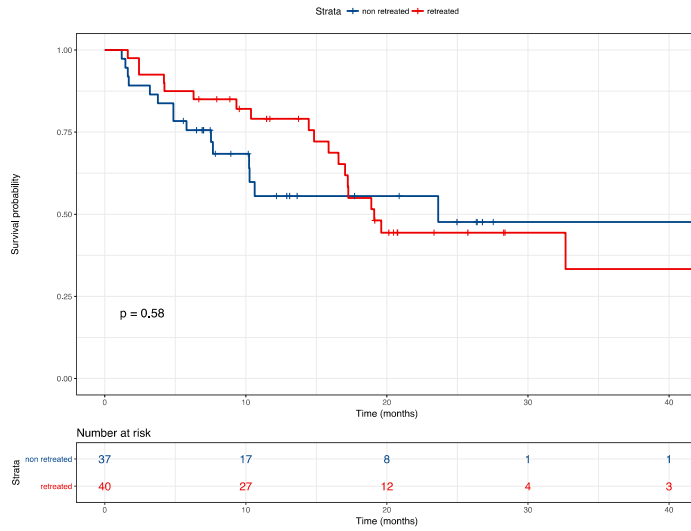
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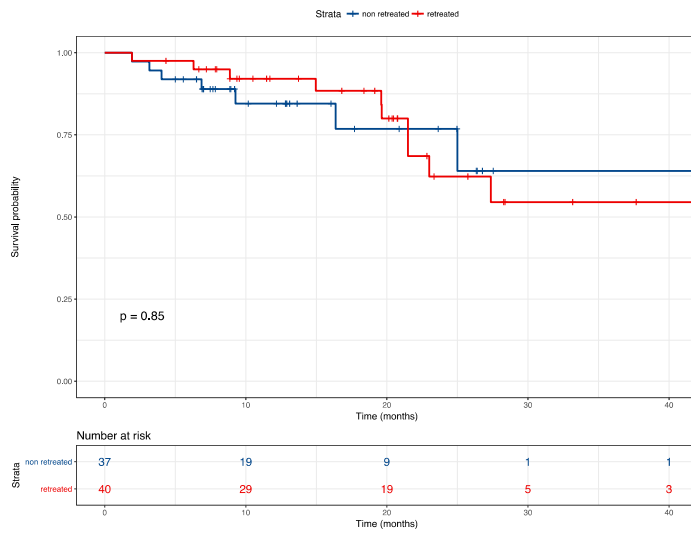
Abbreviations: irAE: immune related adverse events

eFigure 4. Kaplan-Meier Curves for PFS (A) and OS (B) in Patients in the Retreated Group (n = 40) and the Non-retreated Group (n=37)

(A)



(B)



eTable. Summary of the Main Studies of ICI Rechallenge After an irAE

Reference	Study	Tumor type	Initial ICI	ICI rechallenge	N	N rechallenged	toxicities	Outcome / recurrence	comments
Spain et al. 22	Case report	Metastatic melanoma	Nivolumab ipilimumab	Nivolumab ipilimumab	3	3	G3 meningitis G3 hepatitis G3 colitis	2 patients experienced irAE recurrence (G4 cytolytic ans G3 colitis)	No death after rechallenge
Pollack et al. 23	Retrospective multicentric	Metastatic melanoma	Nivolumab ipilimumab	Anti PD1	80	80	Colitis: 41% Hepatitis: 36% Rash: 6% Hypophysitis: 5% Pneumonitis: 4% Grade 2: 31% Grade 3: 61% Grade 4: 8%	18%: recurrence if the same irAE 21%: occurrence of a new irAE	One death after rechallenge (G5 Steven-Johnson Syndrome) Duration of steroid taper, initial irAE severity, use of IS drug did not predict for toxicity on rechallenge
Sanini et al. 24	Retrospective multicentric	NSCLC	Anti PD(L)1	Anti PD(L)1	71	19	Pneumonitis: 21% Colitis: 17% Hepatitis: 13% Grade 2: 54% Grade 3: 42%	26% same irAE 23% new irAE 51% no subsequent irAE	2 deaths after rechallenge Shorter duration of treatment before 1st irAE (<3 months) and hospitalization were associated with irAE recurrence after rechallenge
DeLaunay et al. 27	Retrospective multicentric	Melanoma NSCLC	Anti PD(L)1; 93.1% Anti CTLA4: 6.9%	Anti PD(L)1	64	10	Pneumonitis Grade 1: 15.6% Grade 2/3: 65.6% Grade 4: 9.4% Grade 5: 9.4%	3 Pneumonitis recurrence (33.3%)	No death after rechallenge Duration of treatment before pneumonitis was shorter among NSCLC cohort (2.1 months vs. 5.2 months in melanoma cohort)
Naidoo et al. 17	Retrospective multicentric	Melanoma NSCLC, bladder, lymphoma, others	Anti PD(L)1 +/- anti CTLA4	Anti PD(L)1	49	12	Pneumonitis Grade 1: 40% Grade 2: 33% Grade 3: 23%	3 Pneumonitis recurrence (25%)	No death after rechallenge

Abbreviations: ICI: immune checkpoint inhibitor, irAE: immune related adverse events