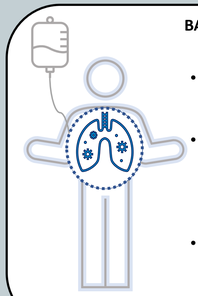
Safety and efficacy of immunotherapy rechallenge following a previous immune-induced interstitial lung disease.

C. Joseph[1] (no conflict of intrest), J. Mazieres[1], M. Delaunay[1], A. Lusque[2], J.-M. Michot[3], J. Le Pavec[4], R. Veillon[5], M. Wislez[6], P. Tomasini[7] , E. Giroux-Leprieur[8] , M. Duruisseaux[9], M. Pérol[10], C. Decroisette[11], B. Duchemann[12], S. Couraud[13], J. Milia[1], S. Collot[14], G. Prevot[1]
[1]Hôpital Larrey, Toulouse, France; [2]Institut Claudius Rigaud, Toulouse, France; [3]Institut Gustave Roussy, Villejuif, France; [4]Hopital Saint Joseph, Paris, France; [5]Hôpital Haut Lévêque, Pessac, France; [6]Hôpital Cochin, Nogent Sur Marne, France; [7]Hôpital Nord, Marseille, France; [8]Hopital Ambroise Pare AP-HP, Boulogne-Billancourt, France; [9]Hopital Louis Pradel, Lyon, France; [10]Centre Léon Bérard, Lyon, France; [11]Centre Hospitalier Annecy Genevois, Annecy, France; [12]Hôpital Avicenne, Bobigny, France; [13]Lyon Sud Hospital Center, Pierre-Bénite, France; [14]Hôpital Larrey, Toulouse, France

BACKGROUND



- ILD incidence : 2,7%
  ⚠10% in combination
- Guidelines :
  - grade I – II : hold +/- oral CSI
  - grade ≥ 3 : stop + oral CSI +/- immunosupressor treatment
- Beneficial impact of IRAes on survival outcomes

STUDY DESIGN

- Retrospective
- Multicentric
- ICI-ILD anteriority
- Nov. 2013 – May 2019
- More than 18 yrs
- ICI rechallenge

PATIENTS CARACTERISTICS

		Patients n	Frequency %
Sex	*Male*	*25*	78,1
(n = 32)	*Female*	*7*	21,9
Age at diagnosis (median yrs)	*58,5*		
Smoking history	*Never smoker*	*5*	*17,9*
(n=28)	*Current smoker*	*14*	*50*
	Ex smoker	*9*	*32,1*
Diagnosis of tumour	*Lung cancer*	*21*	*65,6*
(n=32)	*Melanoma*	*7*	*21,9*
	Others	*4*	12,5
Treatment before ICI	*≥ 1 line*	*22*	*68.7*
(n=32)	*Chemotherapy*	*21*	*65,6*
	Targeted therapy	*1*	*3,1*
	Thoracic radiotherapy	*9*	*28,1*

FIRST EPISOD OF ICI-ILD

ICI perfusion :
. 15,6% anti-CTLA-4 + anti-PD-1
. 56,3% nivolumab
. 28,1% pembrolizumab

n = 32

Median time to ICI – ICI-ILD : 3 MONTHS

ICI-ILD grade (nci-ctc) **:**

III	18,8%
II	56,2%
I	25%

Treatments :
- Antibiotherapy : 31,3%
- Corticotherapy : 78,1%
- Oxygenotherapy : 18,8%

Best Objective Response :

CR/PR	SD	PD	UK
56,2%	25%	3,1%	15,7%

SECOND EPISOD OF ICI-ILD

ICI perfusion (n = 32) **:**
. 3,2% anti-CTLA-4 + anti-PD-1
. 6,2% anti-CTLA-4
. 65,6% nivolumab
. 25% pembrolizumab

40,6% (n = 13)

38,3% had grade III

Median time from rechallenge to ICI – ICI-ILD recurrence : 0,9 MONTHS

ICI-ILD grade (nci-ctc) **:**

V	7,7%
III	30,8%
II	46,2%
I	15,4%

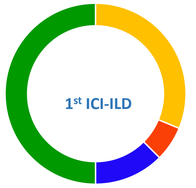
Treatments :
- Antibiotherapy : 46,2%
- Corticotherapy : 84,6%
- Oxygenotherapy : 38,5%

Best Objective Response :

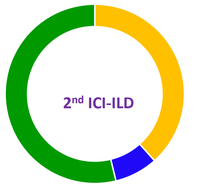
	CR/PR	SD	PD
n = 13	23%	38,5%	38,5%
n = 32	18,8%	34,4%	46,9%

RADIOLOGICAL DESCRIPTION

Radiological Pattern :

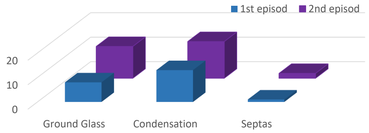


Same pattern between 1st and 2nd episod = 53,8%



ICI-ILD Recurrence :

- **Lesion Intensity**
  (+ = 1/ ++ = 2/ +++ = 3)
  NA = 5

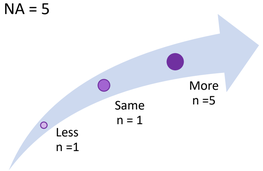


- **Number of lobes involves** (1 to 5)
  NA = 1

1	n = 3
2	n = 2
3	n = 2
4	n = 1
5	n = 4

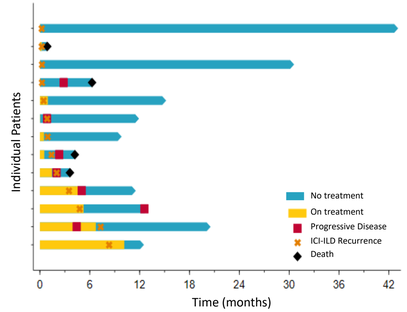
n = 3	1
n = 1	2
n = 3	3
n = 1	4
n = 4	5

- **Radiologist's assessment of the severity** :
  NA = 5



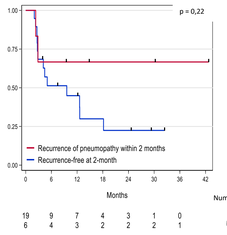
71.4% of the CT-TDM in the 2nd episode are considered more severe than in the first one.

ICI ILD 2nd EPISOD EVENTS

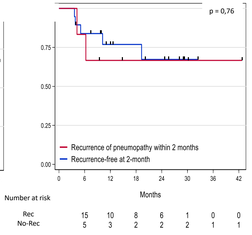


OVERALL SURVIVAL AND PROGRESSION FREE SURVIVAL

PFS : median = 4,1 months



OS : median = 38,1 months



Three months after the rechallenge, 15 patients (46.9%) had progressive disease : 55.6% in the recurrence group and 43.6% in the no recurrence group.

CONCLUSION

- 40.6% of patients had a recurrence of ICI-ILD after rechallenge with ICI.
- The second episode of ICI-ILD appears to have similar radiological patterns but to be more severe and to occur earlier than the first one.
- PFS and OS were not statistically different in patients who experienced ICI-ILD recurrence vs not.