ImmunoScience Academy

Partnering for Education & Optimizing Treatment in ImmunoScience

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Workshop B2

Use of CPI in patients with specific medical conditions and challenges raised by therapies

Convention room 2, Floor 1

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Cliniques Universitaires Saint-Luc, Brussels

Mercury number : ONCBE1908737-06
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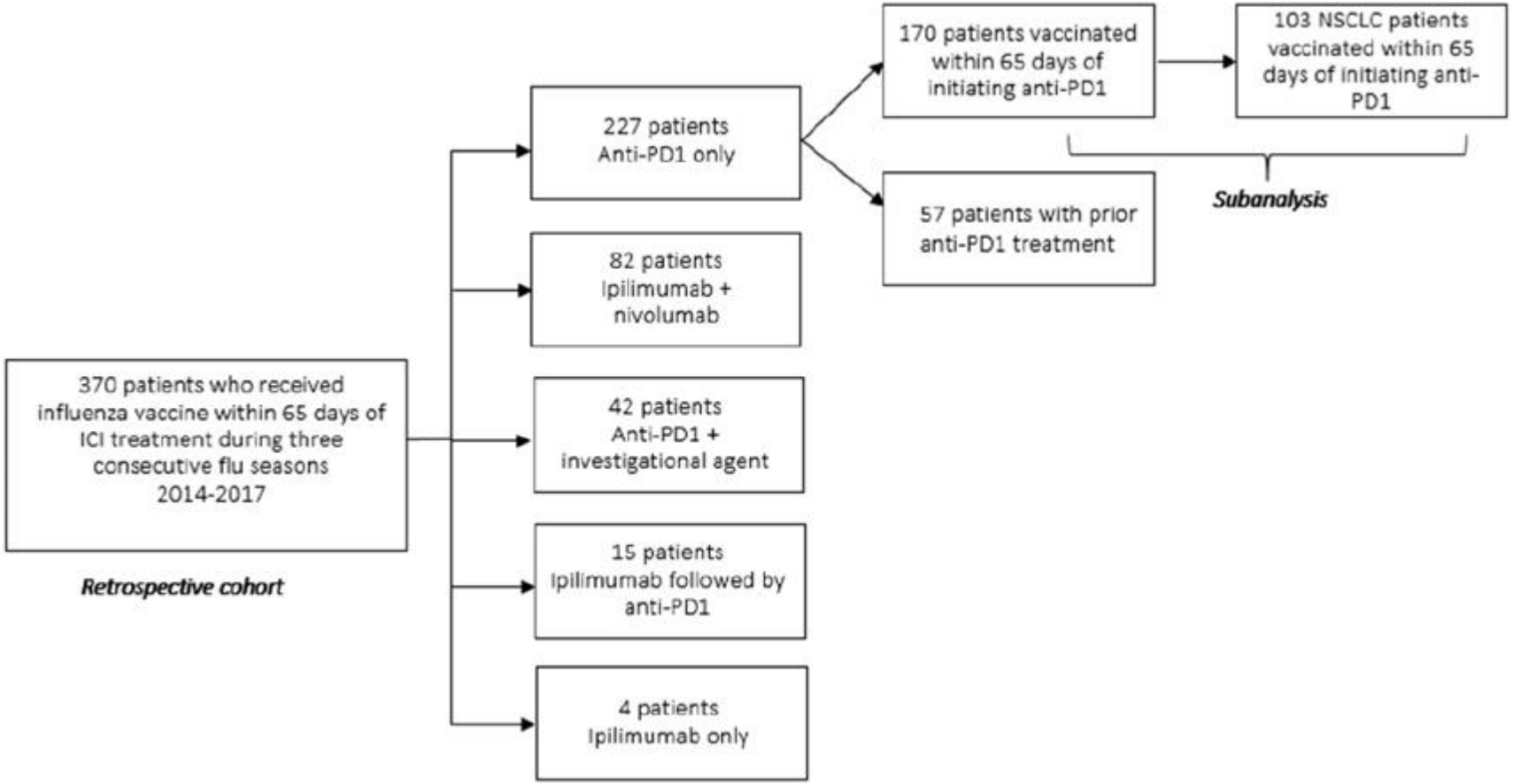
Agenda

- CPIs and flu vaccine
- HIV/hepatitis B/C positive patients
- Patients with brain metastases
- Elderly pts with solid tumours
- Hyperprogression / pseudoprogression
- Patients with organ transplants

Safety of Inactivated Influenza Vaccine in Cancer Patients Receiving Immune Checkpoint Inhibitors

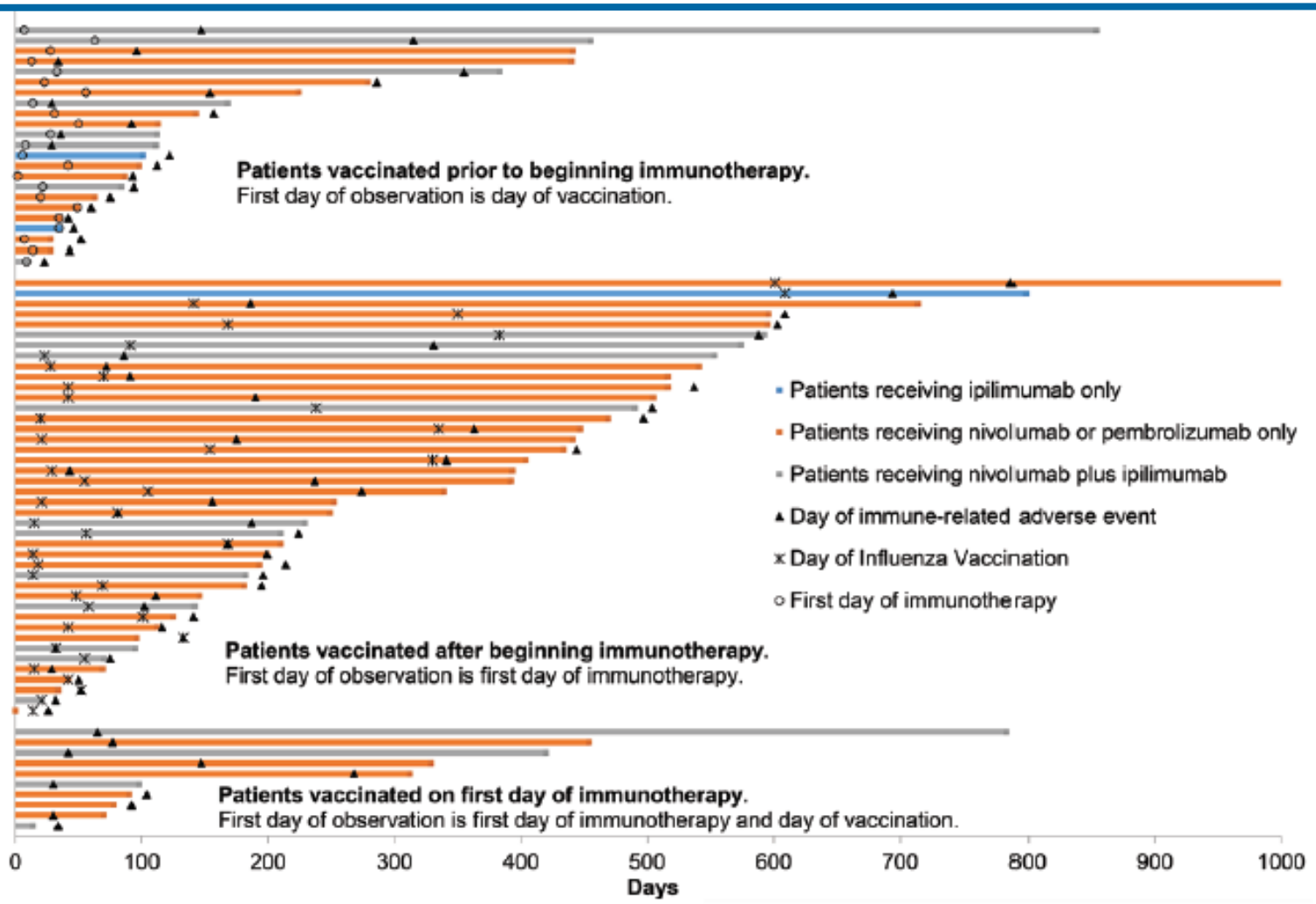
Curtis R. Chong,[1] Vivian J. Park,[2] Bevin Cohen,[2,4] Michael A. Postow,[5] Jedd D. Wolchok,[5] and Mini Kamboj[6,7]

Flow diagram shows type of ICI for entire study cohort and population included in subset analysis (vaccinated patients who were newly treated with anti-PD-1 agents)



Chong et al., CID 2019

Time (days) from receipt of vaccine and immune checkpoint inhibitor (ICI; immunotherapy) to immune-related adverse event for the 75 patients who experienced these events



Chong et al., CID 2019

Safety of inactivated Influenza Vaccine in cancer patients receiving Immune Checkpoints inhibitors: Results (N = 370 pts) (1)

- 20% experienced a new onset IRAE (any grade) / Gr 3/4: 8%
- IRAEs: G1 (7%); G2 (53%); G3 (36%); G4 (4%); G5 (0%)
- Types of IRAEs: Endocrine (28%); pneumonitis (25%); colitis (13%), transaminitis (12%)
- IRAEs:

	Ipi + Nivo	Anti PD1
Any grade	30%	17%
Gr 3/4	13%	6.6%

Chong et al., CID 2019

Differences Between Patients Who Developed an Immune-related Adverse Event and Those Who Did Not Among All Patients Who Received Checkpoint Inhibitors and Influenza Vaccine

Variable	IRAE (n = 75)	No IRAE (n = 295)	*P* Value
Age at vaccination, y	65.9 (11.9)	62.2 (14.1)	.04
Sex			.52
Male (N = 200)	43 (21%)	157 (79%)	…
Female (N = 179)	32 (19%)	138 (81%)	…
Tumor type			.86
Lung (N = 165)	32 (19%)	133 (81%)	…
Melanoma (N = 71)	16 (23%)	55 (77%)	…
Other (N = 134)	27 (20%)	107 (80%)	…
Therapy type			.13
Ipilimumab only (N = 4)	1 (25%)	3 (75%)	…
Ipilimumab followed by anti–PD-1 (N = 15)	3 (20%)	12 (80%)	…
Ipilimumab and anti–PD-1 concurrently (N = 82)	25 (30%)	57 (70%)	…
Anti–PD-1 only (N = 227)	38 (17%)	189 (83%)	…
Other[a] (N = 42)	8 (19%)	34 (81%)	…
Season			.76
2014–2015 (N = 36)	9 (25%)	27 (75%)	…
2015–2016 (N = 137)	27 (20%)	110 (80%)	…
2016–2017 (N = 197)	39 (20%)	158 (80%)	…
Vaccine dose			
High (N = 171)	41 (24%)	130 (76%)	.10
Standard (N = 199)	34 (17%)	165 (83%)	…
Vaccine coverage			.03
Quadrivalent (N = 163)	25 (15%)	138 (85%)	…
Trivalent (N = 207)	50 (24%)	157 (76%)	…
Order of administration			.20
Immunotherapy first (N = 232)	43 (19%)	189 (81%)	…
Vaccine first (N = 107)	22 (21%)	85 (79%)	…
Same day (N = 31)	10 (32%)	21 (68%)	…

Chong et al., CID 2019

Safety of inactivated Influenza Vaccine in cancer patients receiving Immune Checkpoints inhibitors: Results (N = 370 pts) (2)

- Anti PD-1 agents: IRAE rates did not vary with order of vaccine administration
- Conclusion: Routine seasonal flu vaccination seems to be safe in pts on ICIs

Chong et al., CID 2019

Hepatitis B and ICI

Hepatitis B outcomes	
Demographics	**Results**
Sample size	12
Malignancy	8 melanoma 1 urothelial carcinoma 1 hepatocellular carcinoma 1 gastric cancer 1 glioblastoma
Immunotherapy	7 pembrolizumab 4 nivolumab 1 pembrolizumab + ipilimumab (sequential)
Virologic response	2 virologic response 1 virologic failure (patient not on antiviral therapy)
Response	1 CR 1 PR 8 SD 2 PD
Immune related adverse events	**4 events** grade 2 pneumonitis on nivolumab grade 2 rash on pembrolizumab grade 1 rash on pembrolizumab grade 1 vitiligo on nivolumab

Hepatitis C and ICI

Hepatitis C outcomes	
Demographics	**Results**
Sample size	14
Malignancy	9 melanoma 2 urothelial carcinoma 1 renal cell carcinoma 1 non-small cell lung cancer 1 mesothelioma
Immunotherapy	1 atezolizumab 4 pembrolizumab 5 nivolumab 4 PD-1 inhibitor + ipilimumab
Virologic response	0 virologic response 0 virologic failure
Response	2 CR 1 PR 8 SD 3 PD
Immune related adverse events	**5 events** grade 4 colitis/duodenitis on nivolumab + ipilimumab grade 3 autoimmune hepatitis on nivolumab + ipilimumab grade 3 adrenal insufficiency on pembrolizumab grade 1 rash on nivolumab grade 1 arthralgia on nivolumab

HIV and ICI : Case Series / Systematic Review

Safety and Efficacy of Immune Checkpoint Inhibitor Therapy in Patients With HIV Infection and Advanced-Stage Cancer
A Systematic Review

Table 2. Select Studies of Immune Checkpoint Inhibitor Therapy in Patients With Advanced-Stage Cancer

Source	Sample Size	Study Type	Tumor Type (No.)	ICI Therapy (No.)	Adverse Events (No.)	HIV Load	CD4 Cell Count	Best Response
Ostios-Garcia et al,[20] 2018	7	Retrospective case series	NSCLC (7)	Pembrolizumab (5), nivolumab (2)	Grade 1 arthralgia (1), grade 1 fatigue (1), grade 1 headache (1), grade 1 chest pain (1), grade 2 arthralgia (2)	Remained suppressed[a]	Stable[b]	Stable disease (2), PR (3), PD (2)
Samri et al[28] 2017	12	Retrospective case series	NSCLC (12)	Nivolumab (12)	Grade 1 hepatitis (1), hypereosinophilia (1)	Remained suppressed[c]	Stable	Stable disease (4), PR (3), PD (5)
Heppt et al,[17] 2017	10	Retrospective case series	Melanoma (9), Merkle cell carcinoma (1)	Nivolumab (1), pembrolizumab (3), ipilimumab (3), ipilimumab plus nivolumab (3)	Grade 1 pneumonitis (1), grade 1 fatigue (1)	Remained suppressed	Stable[d]	PR (1), CR (2), PD (6), NR (1)
Park et al,[27] 2018	8	Retrospective case series	HNSCC (3), melanoma (2), cutaneous SCC (2), SCC (1)	Anti-PD-1 (7), ipilimumab plus nivolumab (1)	Anti-PD-1, grade 1 fatigue (4), grade 1 rash (2); ipilimumab plus nivolumab, grade 3 hepatitis (1)	Remained suppressed	Upward trend[e]	PR (4), CR (1), PD (2), NR (1)
Galanina et al,[26] 2018	8	Retrospective case series	Kaposi sarcoma (8)	Nivolumab (8)	No grade ≥2 toxic effects reported[f]	Pretreatment median (range): 20.5 /mL (0-116 706 mL); posttreatment median (range): 64 /mL (0-1 390 000 mL)	Upward trend (mean increase by 80.5 /μL)	PR (4), CR (1), stable disease (3)
Uldrick,[29] 2017	21	Prospective clinical trial	Primary effusion lymphoma (2), Kaposi sarcoma (1), diffuse large B-cell lymphoma (1), anal cancer (5), head and neck (5), SCC (1), NSCLC (2), HCC (1), transitional cell carcinoma (1), pancreatic cancer (1), cholangiocarcinoma (1)	Pembrolizumab (21)	Most treatment-emergent AEs were grades 1-2 (93%),[9] immune-related AEs, grade 1 hypothyroidism (2), grade 1 ALT increase (1), grade 1 joint stiffness (1), grade 1 pneumonitis (1), grade 2 pneumonitis (2), grade 2 hypothyroidism (4), grade 3 ALT increase (1)	Remained suppressed	Upward trend	NR

HIV Load stable to upward trend
CD4 cell count stable
irAEs : 9%
No unexpected safety signal
Efficacy present

Cook M.R. Jama Oncol, 2019

PD-1/PD-L1 immunotherapy in pts with hepatitis B/C

Hepatitis B: **12 pts**

Hepatitis C: **14 pts**

<u>Conclusion</u>: PD-1/PD-L1 immunotherapy did not appear to worsen viral control in hepatitis B or C patients and that these pts may benefit from this therapy

HIV and ICI: Clinical Trial

Study Objectives and Design: DURVAST (NCT 03094286)

1. **Primary endpoint:** Feasibility /Safety

2. **Secondary endpoint:** ORR (RECIST v1.1), PFS, OS

Inclusion Criteria
- -HIV-1 infection
- -Advanced cancer
- -Naive or pretreated patients
- - Effective ART

Exclusion Criteria
- -Previous treatment with anti PD-1/PD-L1 antibodies
- -Co-infections (TB, HBV, HCV)

N 20 → **Durvalumab iv 1500 mg Q 4w**

Follow-up
Treatment until PD*
or toxicity
*Treatment continuation was allowed in case of PD with clinical benefit

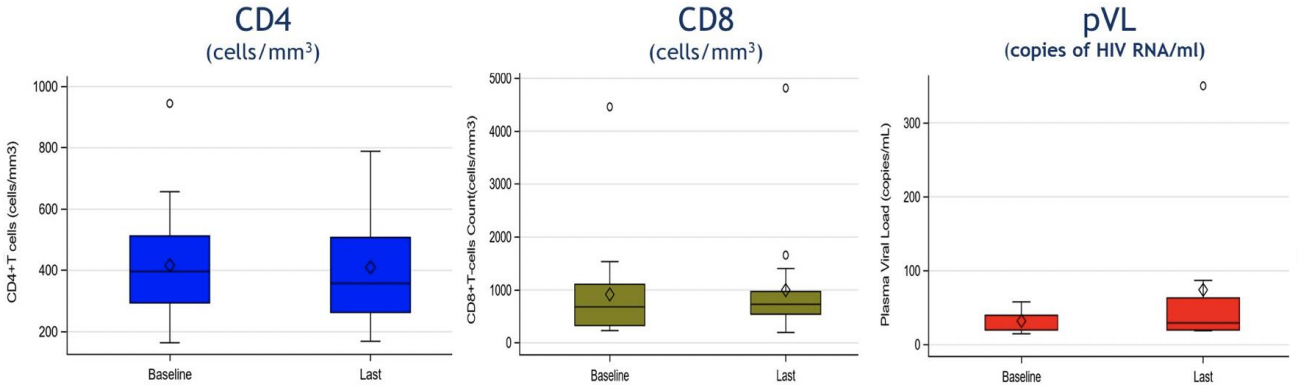
3. **Exploratory endpoints:**
3.1. HIV reservoir, virus replication, composition of circulating T cells
3.2. Molecular predictive factors of antitumoral activity/safety

HIV and ICI: DURVAST trial

Adverse Events (AEs)

Non-Drug related AEs, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Any	23 (75%)	10 (50%)	1 (5%)	1 (5%)	2 (10%)
Respiratory infection	1 (5%)	1 (5%)	1 (5%)	0	1 (5%)
Neurological	0	0	0	0	1 (5%)
Arterial ischemia	0	0	0	1 (5%)	0
Hypotension	0	3 (15%)	0	0	0
Fever	2 (10%)	2 (10%)	0	0	0
Arthromyalgia	11 (55%)	2 (10%)	0	0	0
Asthenia	9 (45%)	2 (10%)	0	0	0
Nausea-vomiting	5 (25%)	0	0	0	0
Constipation	2 (10%)	1 (5%)	0	0	0
Disphagia	2 (10%)	1 (5%)	0	0	0
Diarrhoea	2 (10%)	2 (10%)	0	0	0
Skin AEs	3 (15%)	0	0	0	0
Neutropenia	0	1 (5%)	0	0	0

T cell count and plasma viral load

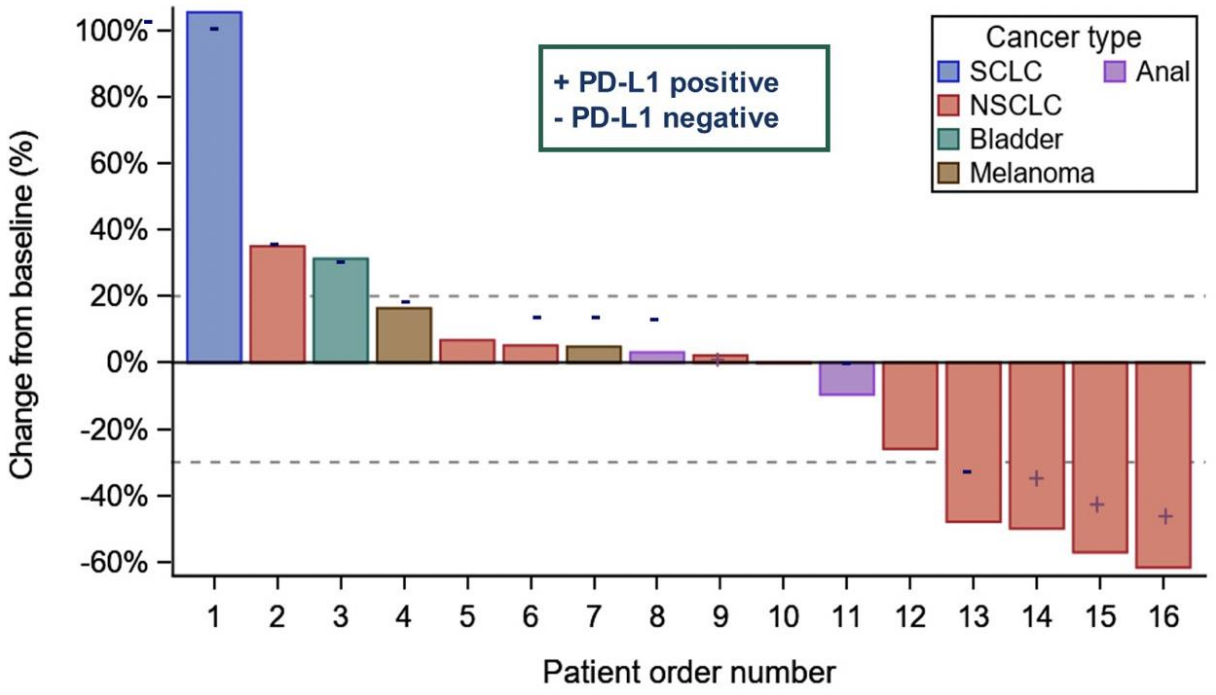


	CD4 Baseline	CD4 Last	CD8 Baseline	CD8 Last	pVL Baseline	pVL Last
Mean (SD)	417 (181)	410 (202)	915 (945)	998 (1088)	32 (13)	74 (113)
Median	397	358	680	729	40	29
[Q1,Q3]	[294, 513]	[263,508]	[327, 1108]	[542, 972]	[20, 40]	[20, 63]
Min, Max	164, 945	169, 789	232, 4460	197, 4815	15, 58	19, 350

Gonzalez-Coa M. ASCO, 2019

HIV and ICI: DURVAST trial

Response	All (n=20)
PR, n (%)	4 (20%)
SD, n (%)	5 (25%)
DCR, n (%)	8 (40%)
PD, n (%)	11 (55%)
RECIST	7 (35%)
NE	4 (20%)
DOR, months median (range)	6.5 (3.5-17 +)



Brain M+ and ICI: Considerations

- High frequency: M+ NSCLC up to 40 %, Melanoma, TNBC, HER2+ BC up to 50%
- Specific Tumour microenvironment
- Underrepresented in pivotal trials
  - Discrepancy between trials
- Brain metastasis categories
  - Treated
  - Untreated (Active)
    - Stable without corticosteroids
    - Stable with corticosteroids
    - Symptomatic
- Concurrent RT and ICI ? (seems feasible but still investigational)

Courtesy S. Holbrechts

Brain M+ and ICI: Clinical Trials

Ref.	Phase	Histology	ICI / Brain M+ categories	N	Brain DCR % / Extracranial DCR %	Brain ORR % / Extracranial ORR %	AE grade ≥ 3 % / AE neuro * grade ≥ 3 %	OS
Margolin, Lancet oncol, 2012	II (subpop)	Melanoma	Nivo / Asympto Nivo /Sympto controlled CS	51 21	24 vs 28 10 vs 5	16 vs 14 5 vs 5	NR/ 4 NR/ 0	OS 12 m : 31% OS 12 m : 12%
Tawbi,NEJM, 2018	II	Melanoma	Nivo + Ipi untreat.	94	58 vs 56	50 vs 50	55 / 7	OS 12 m : 81%
Long, Lancet Oncol,2018	II r	Melanoma	Nivo+ Ipi asympto untreat. Nivo Asympto untreat. Nivo sympto	36 27 16	57 vs 60 21 vs 31 19 vs 33	46 vs 57 21 vs 29 6 vs 25	63 /6 16 / 0 13 / 19	OS 12 m: 60% OS 12m : 60% OS 12m: 30 %
Golberg, Lancet Oncol, 2016 JCO , 2018 (OS)	II	Melanoma NSCLC	Pembro Asympto untreat Pembro Asympto untreat	18 18	NR	22 vs 22 33 vs 33	6 / 6 10 / 10	OS 2 Y : 31%
Flippot, JCO, 2019 (subgroup)	II	RCC	Nivo untreated Nivo treated asympto	39 34	50 vs 51	12 (< 10mm) vs 21	10 / 12 15 / NR	OS 12m : 66.7% OS 12m: 58.8%

- **Observations from phase II**

  - **Brain M+ versus extracranial M+ : same range of efficacy**
  - **No specific / new safety signal**
  - **Immuno combination better than Immuno monotherapy**
  - **Lower control rate (IC and EC) and lower OS of symptomatic metastasis (CS?)**

* AE nervous system : headache , dizziness

Courtesy S. Holbrechts

Elderly and ICI: meta analysis

Table 1 Characteristics of included studies. Abbreviations: NSCLC (non-small lung cancer); S-NSCLC (squamous non-small lung cancer); NS-NSCLC (non-squamous non-small lung cancer); RCC (renal cell cancer); H&N (head & neck); NR (not reported); Q (every); W (weeks)

	Study Name	Drug	Phase	Malignancy	First line	Arm 1	Arm 2	Arm 3	Patient' number	Age median	Age range	Age mean	n (%) < 65 y	n (%) ≥ 65 y
Rittmeyer 2016 [33]	OAK	Atezolizumab	3	NSCLC	N	Atezolizumab 1200 mg Q 3 W	Docetaxel 75 mg/m^2 Q 3 W		850	64	33–85	63	453 (53)	397 (47)
Fehrenbacher 2016 [26, 34]	POPLAR	Atezolizumab	2	NSCLC	N	Atezolizumab 1200 mg Q 3 W	Docetaxel 75 mg/m^2 Q 3 W		287	62	36–84	61.5	174 (61)	113 (39)
Brahmer 2015 [5]	Checkmate-017	Nivolumab	3	S-NSCLC	N	Nivolumab 3 mg/kg Q 2 W	Docetaxel 75 mg/m^2 Q 3 W		272	63	39–85	63	152 (56)	120 (44)
Borghaei 2015 [6]	Checkmate-057	Nivolumab	3	NS-NSCLC	N	Nivolumab 3 mg/kg Q 2 W	Docetaxel 75 mg/m^2 Q 3 W		582	62	21–85	NR	339 (58)	243 (42)
Motzer 2015 [4]	Checkmate-025	Nivolumab	3	RCC	N	Nivolumab 3 mg/kg Q 2 W	Everolimus 10 mg daily		821	62	18–88	61.3	497 (61)	324 (39)
Robert 01–2015 [29]	Checkmate-066	Nivolumab	3	Melanoma	Y	Nivolumab 3 mg/kg Q 2 W	Dacarbazine 1000 mg/m^2 Q 3 W		418	65	18–87	62.7	200 (48)	218 (52)
Ferris 2016 [2]	Checkmate-141	Nivolumab	3	H&N	N	Nivolumab 3 mg/kg Q 2 W	Chemotherapy		361	60	28–83	59.1	248 (69)	113 (31)
Herbst 2016 [8]	Keynote-010	Pembrolizumab	2/3	NSCLC	N	Pembrolizmab 2 mg/kg Q 3 W	Pembrolizumab 10 mg/kg Q 3 W	Docetaxel 75 mg/m^2 Q 3 W	1033	NR	NR	62	604 (58)	429 (42)
Robert 06–2015 [9]	Keynote-006	Pembrolizumab	3	Melanoma	N	Pembrolizumab 10 mg/kg Q 2 W	Pembrolizumab 10 mg/kg Q 3 W	Ipilimumab 3 mg/kg Q 3 W	834	NR	NR	60.3	467 (56)	367 (44)

Table 2 Summary of HR for OS by Age

Age	HR (95% CI)
Age < 65 years	0.68 (0.61 to 0.75)
Age ≥ 65 years	0.64 (0.54 to 0.76)

Table 3 Summary of HR for PFS by Age

Age	HR (95% CI)
Age < 65 years	0.73 (0.61 to 0.88)
Age ≥ 65 years	0.74 (0.60 to 0.92)

Elias R. J for Immunoth, 2018

Elderly and ICI : age ≥ 70 and PS 2

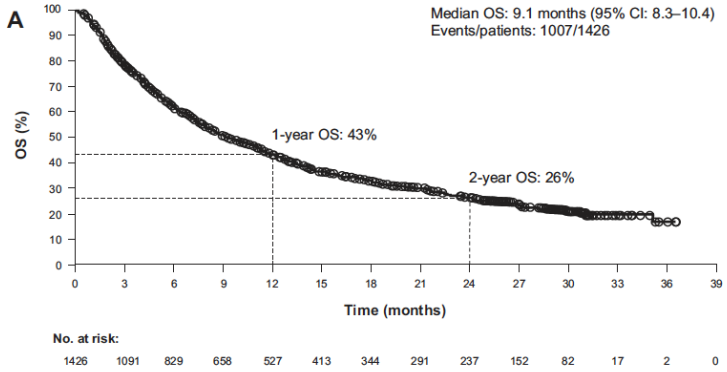
Safety, Efficacy, and Patient-Reported Health-Related Quality of Life and Symptom Burden with Nivolumab in Patients with Advanced Non-Small Cell Lung Cancer, Including Patients Aged 70 Years or Older with Poor Performance Status (CheckMate 153)

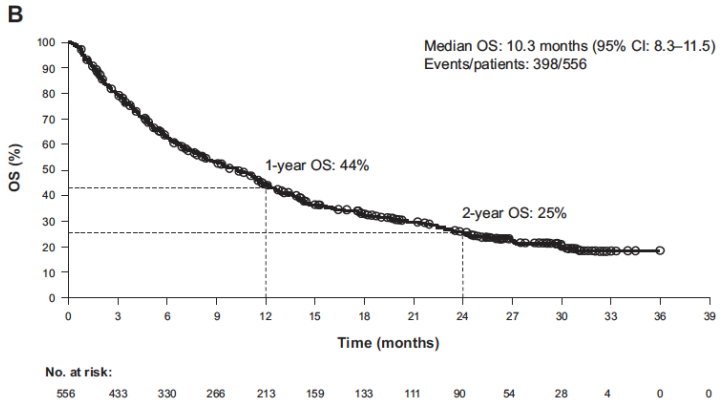
Phase III /IV previously treated

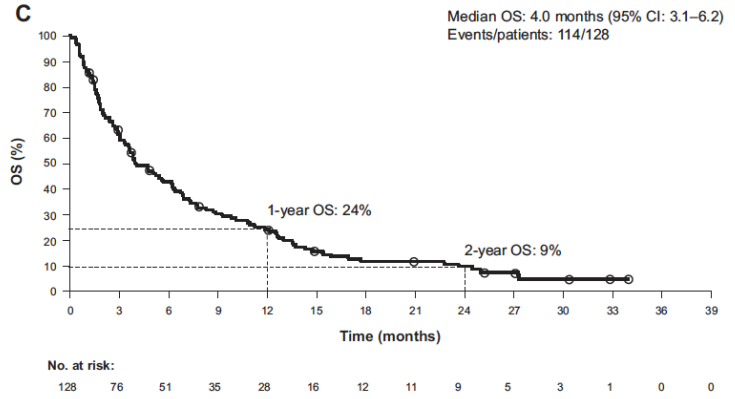
N all : 1426 (PS 2 : 128)

N ≥ 70 : 556 patients (PS 2 : 63)

	All	≥ 70	PS 2
OS m	9.1	10.3	4
2Y OS	26 %	25 %	9
AE grade ≥ 3	6 %	6 %	9 %







Spigel D, JTO, 2019

Elderly and ICI: Belgian Real World Data

Real life safety and effectiveness of nivolumab in older patients with non-small cell lung cancer: results from the Belgian compassionate use program

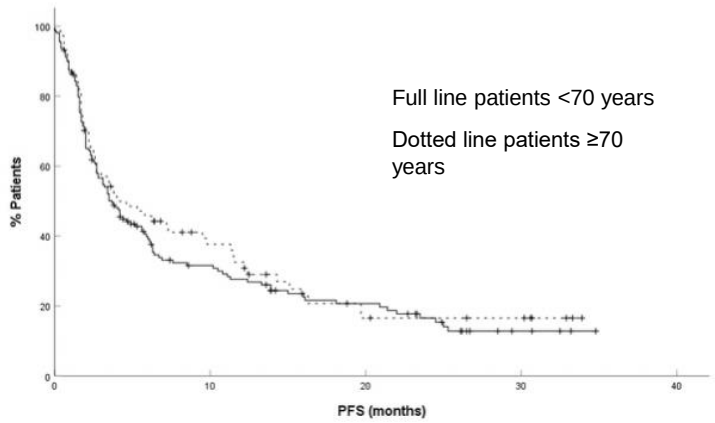
All patients (N=324)	Patients <70 (N=216)	Patients ≥70 (N=108)	Patients ECOG-PS 0-1 (N=224)	Patients ECOG ≥ 2 (N=87)

- Patients characteristics well balanced in both groups
- No difference in Safety
- No difference in OS and PFS by age
- Lower OS and PFS for PS ≥ 2

Joris S. Journal of Geriatric Oncology, accepted

Elderly and ICI: Belgian Real world data

Figure 1a: Progression Free Survival



Full line patients <70 years

Dotted line patients ≥70 years

Figure 1b: Overall Survival

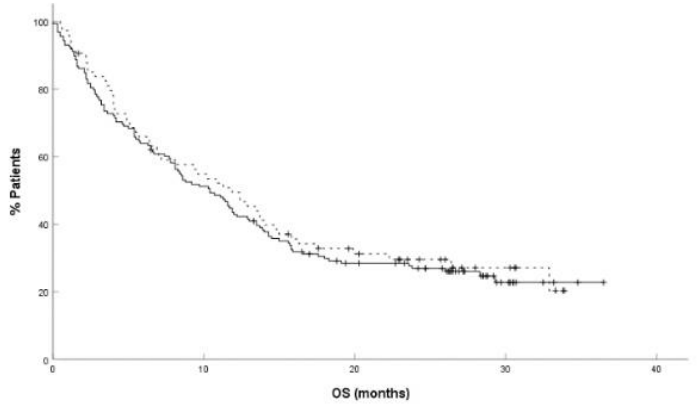
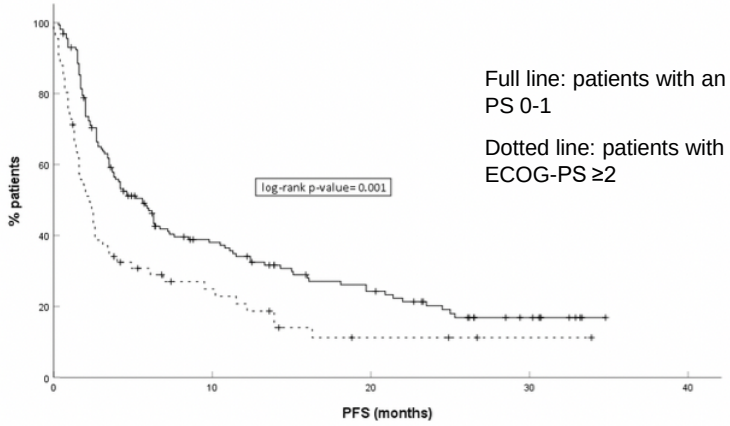


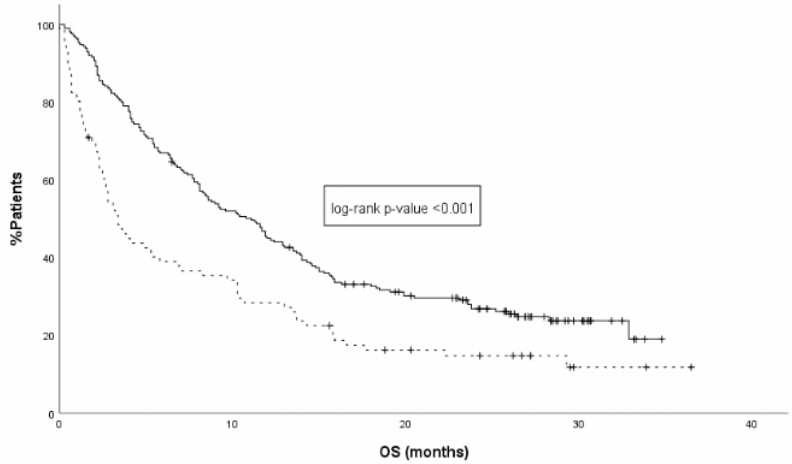
Figure 2a: Progression Free survival



Full line: patients with an ECOG-PS 0-1

Dotted line: patients with an ECOG-PS ≥2

Figure 2b: Overall survival



ImmunoScience Academy

Partnering for Education & Optimizing Treatment in ImmunoScience

Use of immune checkpoint inhibitors in specific medical conditions and challenges raised by therapies

Jean-Pascal Machiels

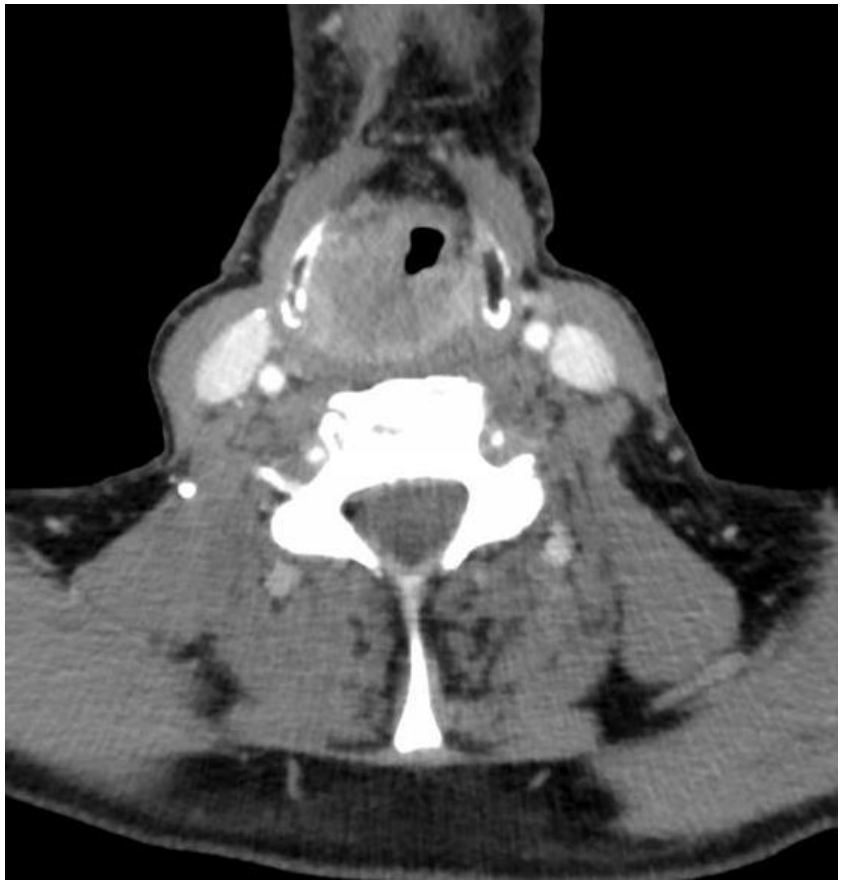
INSTITUT
ROI ALBERT II
CANCÉROLOGIE ET HÉMATOLOGIE
Cliniques universitaires SAINT-LUC I UCL Bruxelles

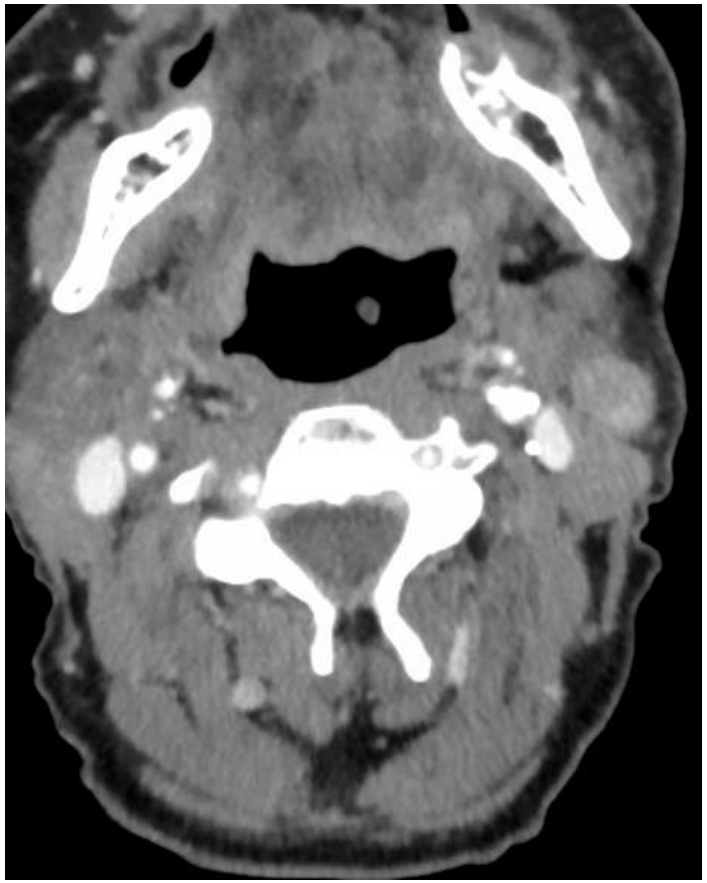
Male °1959

- No relevant past medical history
  - Smoker: 30 UAP
  - Alcohol: 3 units per day

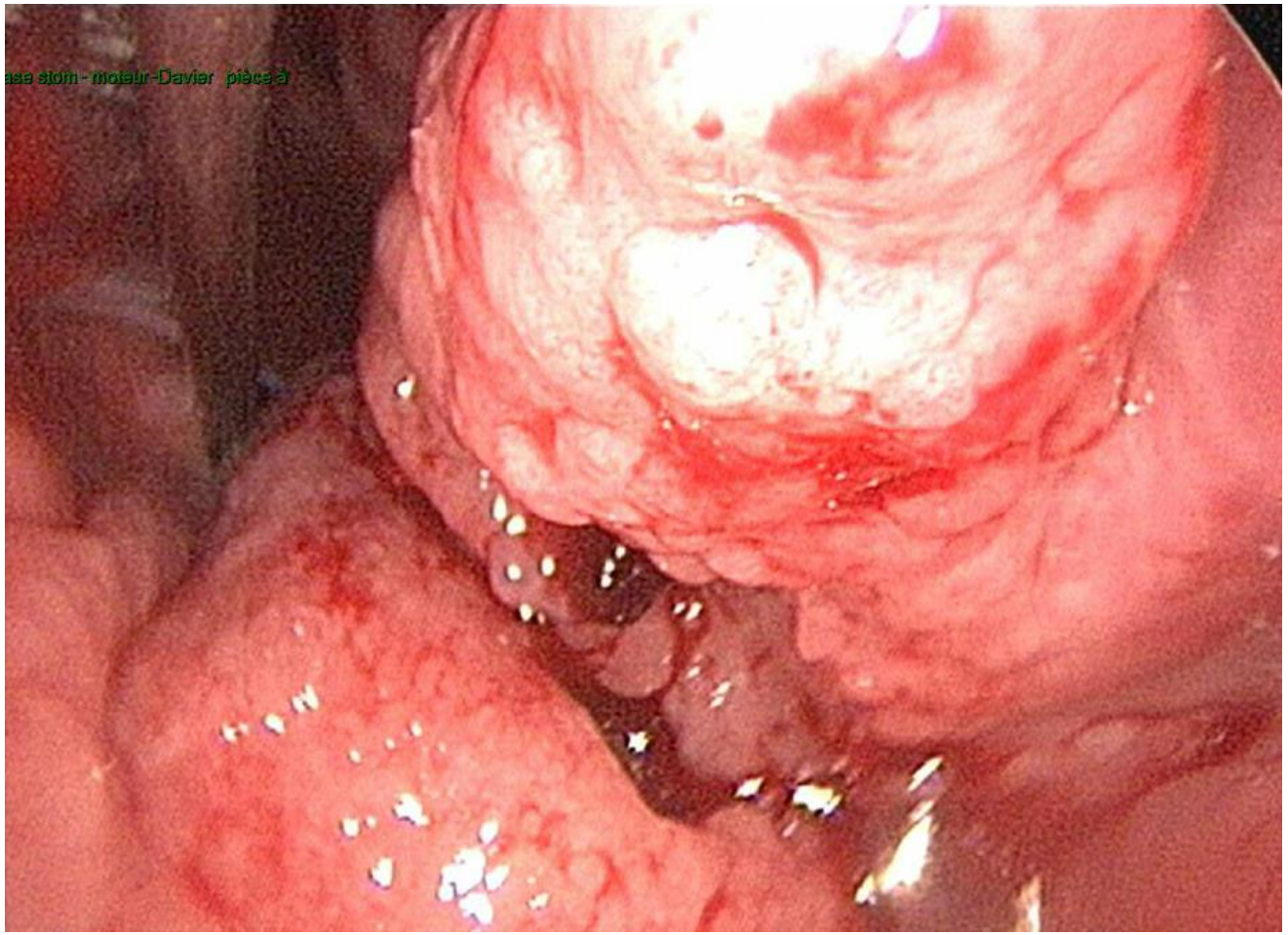
- February 2018: Dysphagia and dysphonia

Male °1959





Male °1959



Male °1959

- Biopsy: Squamous cell carcinoma p16 negative
- FDG-PET: no distant metastases
- cT3N1 right pyriform sinus carcinoma
- Chemoradiation (70 Gy, Cisplatin 100 mg/m2 day 1,22,43) in a clinical trial.
- Phase 3 trial: Chemoradiation with anti-PD1 or placebo

Male °1959

- April 18, 2018: Start anti-PD1 or placebo
- April 25, 2018: Start chemoradiation
  - The patient had dyspnea and stridor
  - Head and neck endoscopy: Laryngeal oedema with airway obstruction
- Tracheostomy. Start chemoradiation.

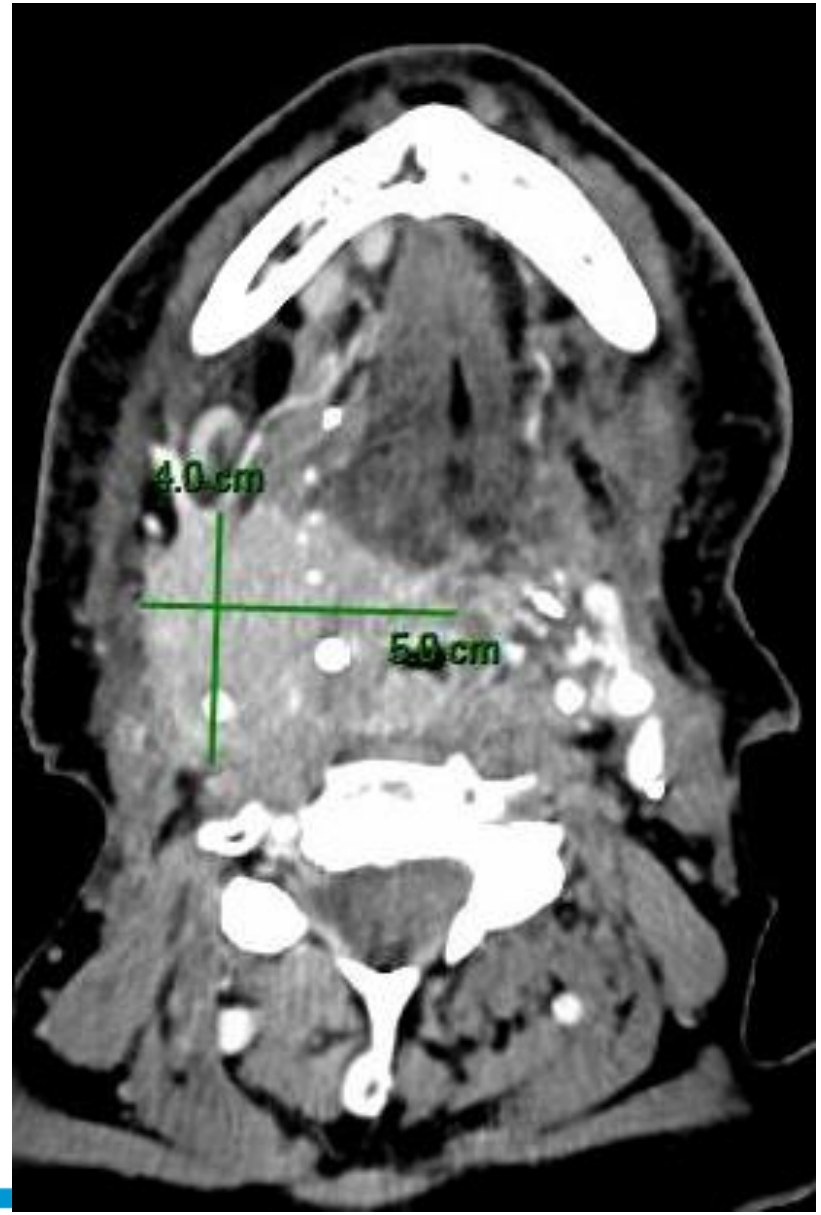
Male °1959

- What is the cause of the oedema ? The surgeon strongly believes that it is due to anti-PD1

- Do you continue treatment (placebo/anti-PD1) ?

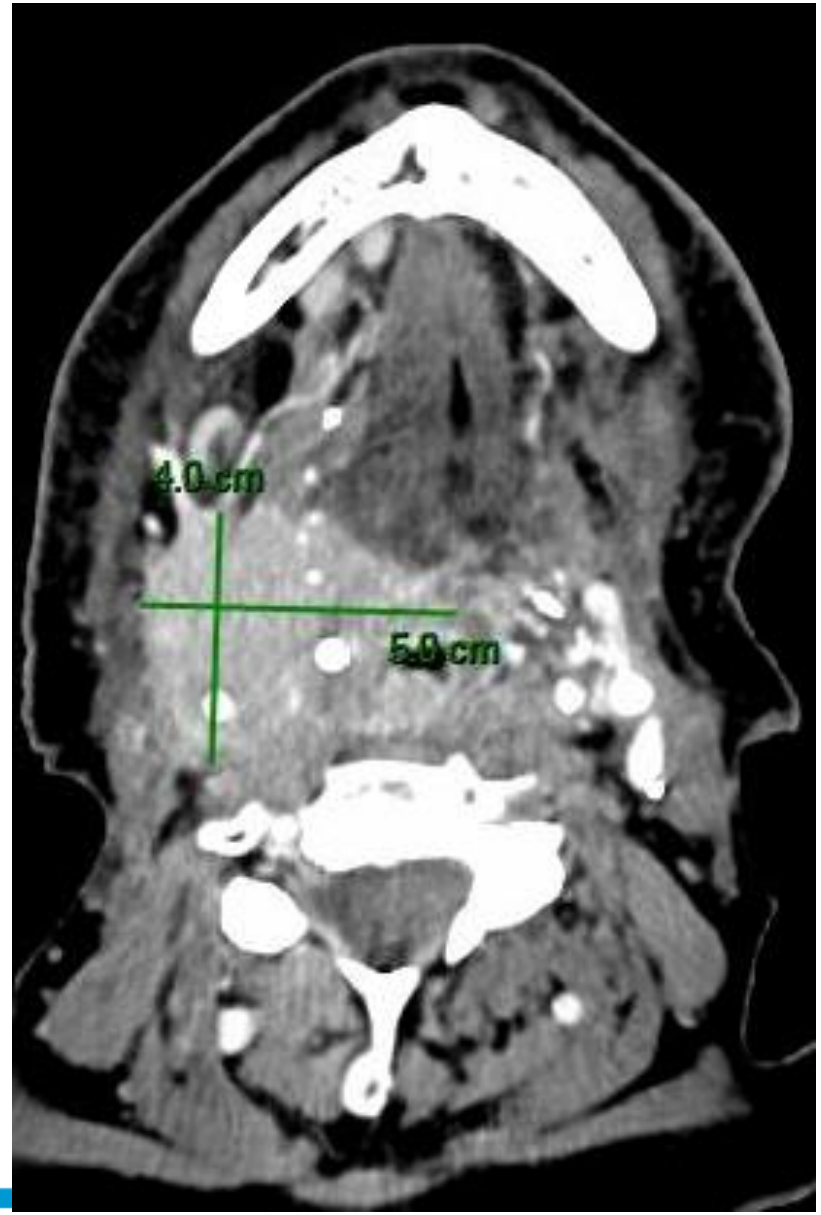
Male °1959

- December 2018 : disease progression
- What do you do ?



Male °1959

- December 2018 : disease progression
- What do you do ?
  - Unblinded: placebo



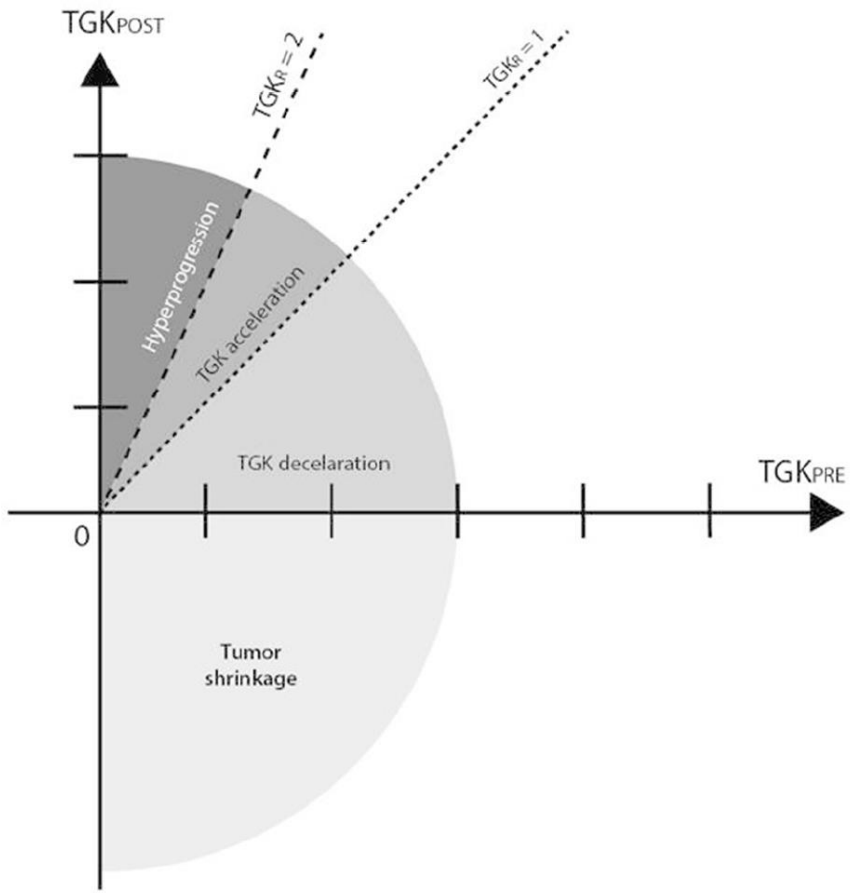
Hyperprogression vs pseudo progression: definitions

- **Pseudoprogression**: Increase in size of the lesion before tumor regression

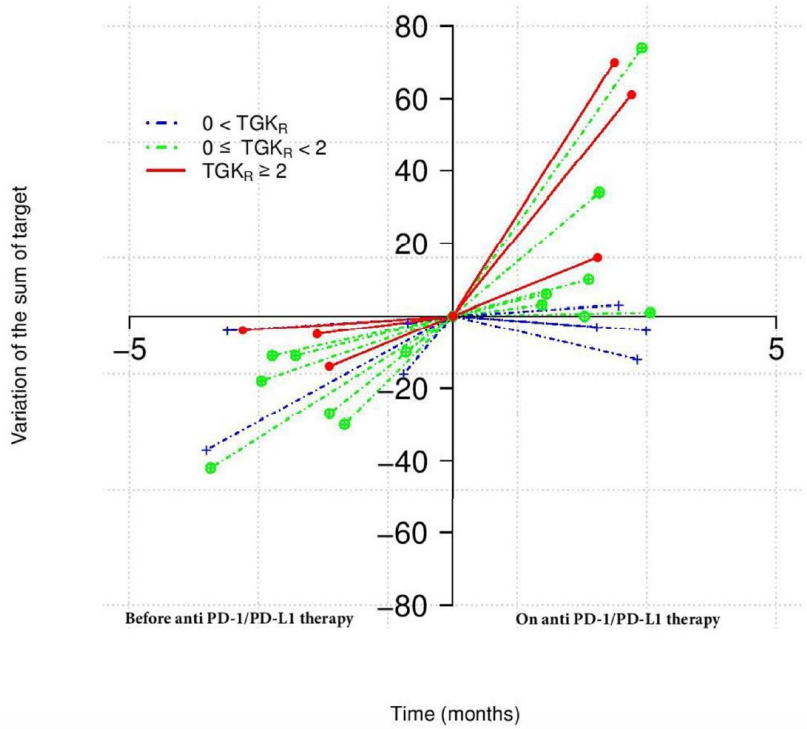
- **Hyperprogression**: ≥ 2 fold increase in tumor growth rate between the pre-treatment and the treatment periods

    - Frequency: 9-30% (using various definitions)[1-5]
    - No placebo arms to control for natural disease evolution

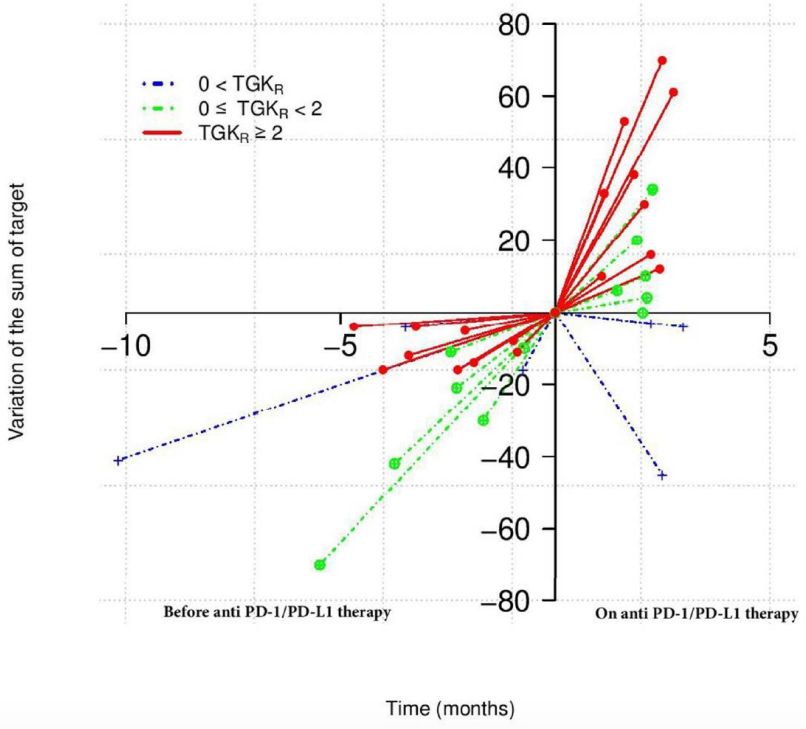
1Champiat et al. Clin Cancer Res 2017; 2Champiat et al. Nat Rev Clin Onco 2018; 3Saada Bouzid et al. Ann of Oncol.2017;
4Kata et al. Clin Cancer Res 2017; 5Ferrara et al. JAMA Oncol 2017



Saada Bouzid et al. Ann Oncol.2017



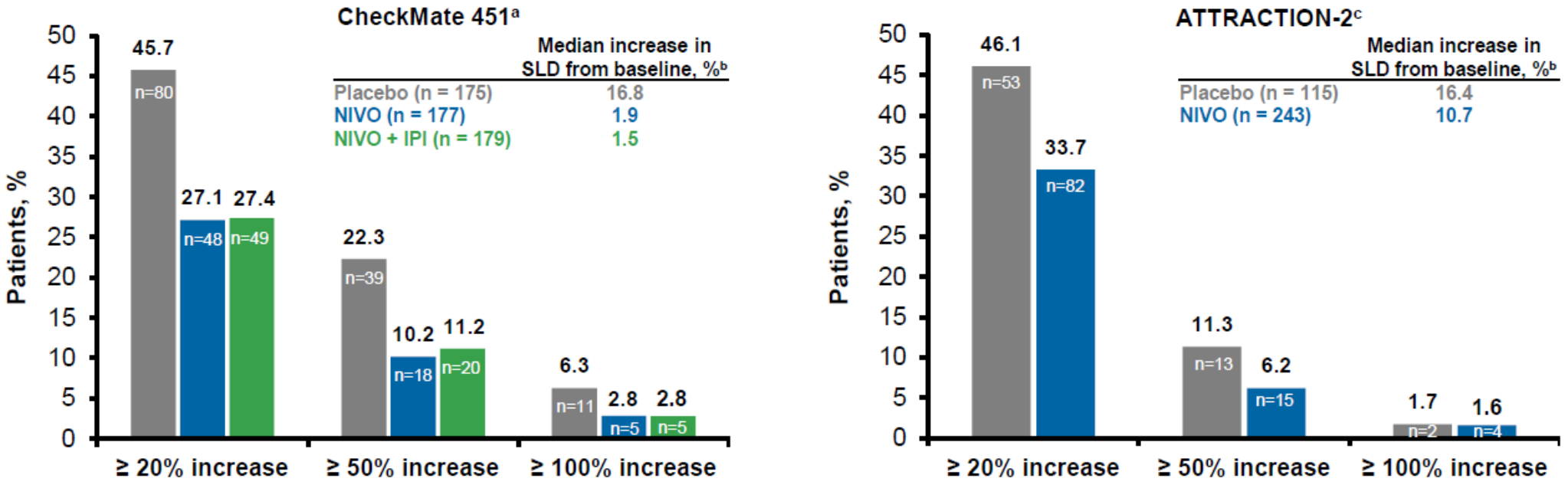
Local recurrence



Regional recurrence

Saada Bouzid et al. Ann Oncol.2017

Does it really exist ?



- In CheckMate 451, descriptive analysis of OS in ≥ 20% vs < 20% populations suggests that greater increases in tumor size are prognostic of poor survival

1Reck et al ESMO 2019; 2 Feng et al. J Immunotherapy Cancer 2018

Male

- Past medical history
  - 1997: non-Hodgkin lymphoma treated with high dose chemotherapy and hematopoietic stem cell familial allograft
  - 1987: malaria
  - 2010: lung tuberculosis
  - 1997: hepatitis B (not active)
  - Tobacco: 20 UAP, no alcohol

- August 2013: Hypopharynx T4aN2bM0

Male

- August 2013: Hypopharynx T4aN2bM0
- January 2016: Liver metastases; Biopsy: squamous cell carcinoma
- 2016-2017: Platinum/5-FU/cetuximab
- 2017: progressive disease. Anti-PD1 ?

Male

- Treated with anti-PD1 during 4 months
- Progressive disease
- No auto-immune related adverse events

Organ transplants and immune checkpoints: discussion

- Transplanted patients receive immusuppressive therapy: antitumor effect may be affected
- Checkpoint blockade may activate anti-graft immune rejection

Organ transplants and immune checkpoints: discussion

- IO **before** allogenic blood or bone marrow transplant: no large studies
- May increase GvHD, immune related AEs, and nonrelapse mortality[1]
- Posttransplant cyclophosphamide might limit this risk[2]
- Further investigations needed

1 Merryman et al. Blood 2017; 2 Schoch et al. Blood Advances 2018

Organ transplants and immune checkpoints: discussion

- IO **after** allogenic blood or bone marrow transplant: no large studies[1,2]
- Cautious: risk of agressive GvHD in immediate posttransplantation
- However, sometimes used with success in case of relapse
- No GvHD and no immunosuppression two years (?) after transplant: probably safe

1 Dada et al. Eur J Haematology 2019; 2 Ijaz et al. Biology of blood and bone marrow transplantation 2019.

Organ transplants and immune checkpoints: discussion

Immune checkpoint blockade regimens with associated risk and timing of allograft rejection based on available reports.

Name of agent	Mechanism of action	Organs involved	% of Total rejected	Time until rejection (weeks)
Ipilimumab monotherapy	CTLA-4 Inhibition	Kidney: 3 [14,31] Liver: 2 [13,32] Heart: 1 [33] N = 6	Kidney: 1/3 = 33% Liver: 0/2 = 0% Heart 0/1 = 0% Total: 1/6 = ~16%	8 [31]
Pembrolizumab monotherapy	PD-1 Inhibition	Kidney: 2 [14,34] Liver: 1 [35] N = 3	Kidney: 2/2 = 100% Liver: 0/1 = 0% Total 2/3 = ~66%	6 [34] 8 [15]
Nivolumab monotherapy	PD-1 Inhibition	Kidney: 3 [36–38] Heart: 2 [16,38] N = 5	Kidney: 2/3 = ~66% Heart: 1/2 = 50% Total: 3/5 = 60%	Kidney: 6 [36,37] Heart: 2 [16]
Ipilimumab followed by Nivolumab (after progression on ipilimumab alone)	CTLA-4 inhibition → PD-1 inhibition (after documented progression)	Kidney: 2 [19,39] N = 2	Kidney: 1/2 = 50% Total: 1/2 = 50%	0.85 [19]
Ipilimumab followed by Pembrolizumab (after progression on ipilimumab alone)	CTLA-4 inhibition → PD-1 inhibition (after documented progression)	Kidney: 1 [2] N = 1	Kidney: 1/1 = 100% Total: 1/1 = 100%	3 [2]

Clinical outcomes of all available cases in which organ transplant recipients received immune checkpoint blockade. These outcomes are organized according to th therapeutic regimen used in each case. Described regimens included monotherapy or combination therapy with CTLA-4 and PD-1 inhibitors.

Chae et al. Cancer Treatment Reviews 2017

Organ transplants and immune checkpoints: discussion

- IO can be active in transplanted patients
- Anti-PD1: high risk of acute rejection
- Anti-CTLA4 appears safer
- Risk/benefice balance:
  - Renal transplant vs the others
  - Expected response to IO
  - ? Concomitant use of steroids or mTOR inhibitor ?

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