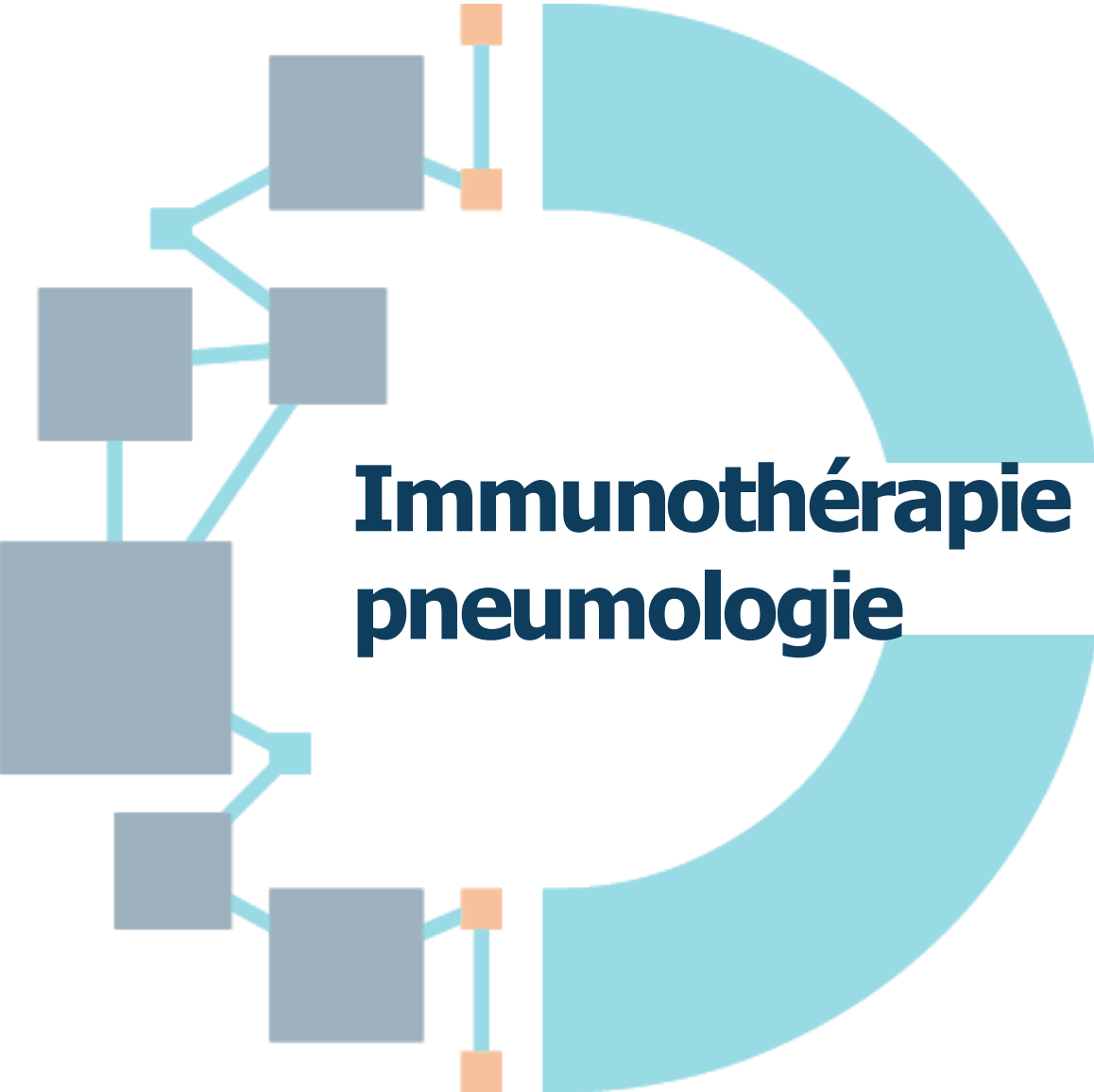




Immunothérapie en pneumologie

11 avril 2025

Bordeaux

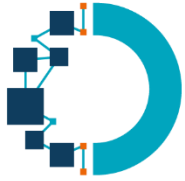
Thomas Egenod
Unité d'oncologie thoracique
CHU Limoges

4EME RENCONTRE D'ONCOGERIATRIE EN NOUVELLE-AQUITAINE



Liens d'intérêts

- **Invitation congrès** : Roche, BMS, MSD, Astra Zeneca, Novartis, Pfizer, Olympus, Novatech
- **Rénumération pour présentations** : Roche, BMS, MSD, Astra Zeneca, Novartis
- **Activité d'expertise** : Consultant pour PulmonX



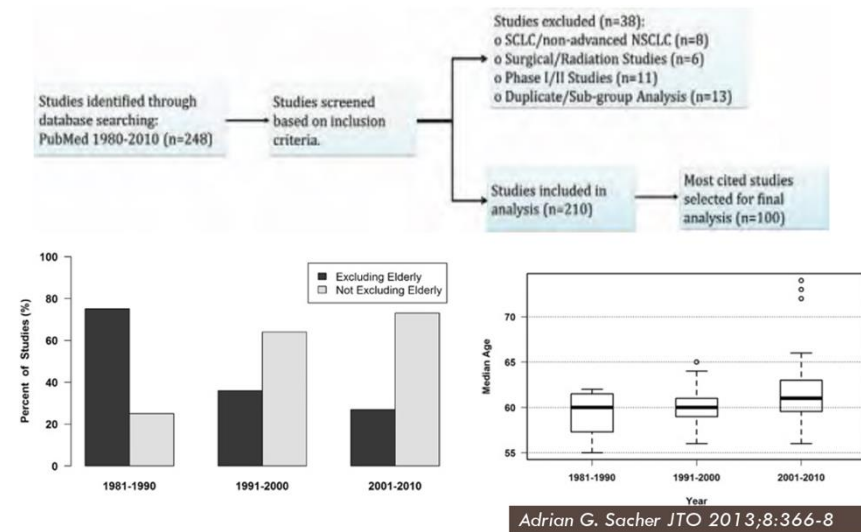
Introduction

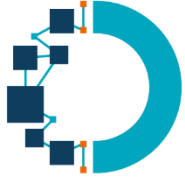
Qui est concerné ?
65 ans (OMS) ? **70 ans ? 75 ans ?**



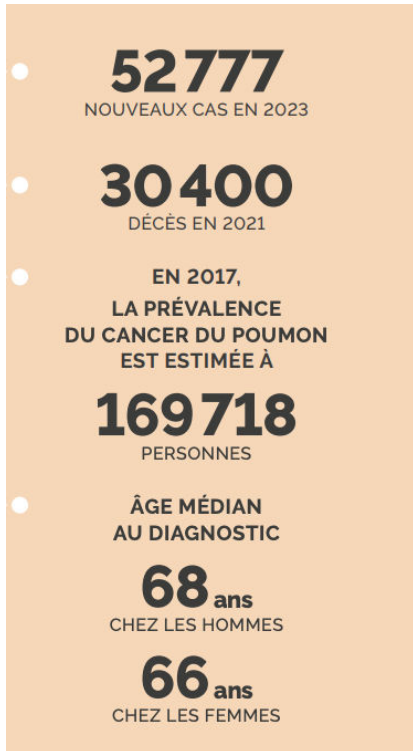
Manque de visibilité dans les
essais cliniques

Elderly Patients with Advanced NSCLC in Phase III Clinical Trials: Are the Elderly Excluded from Practice-Changing Trials in Advanced NSCLC?

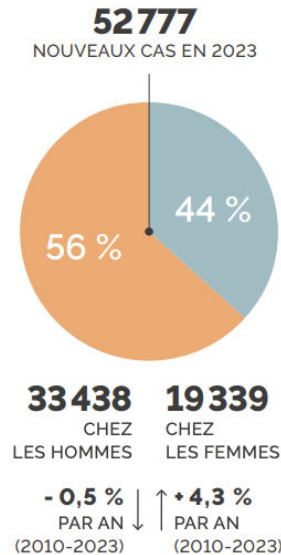




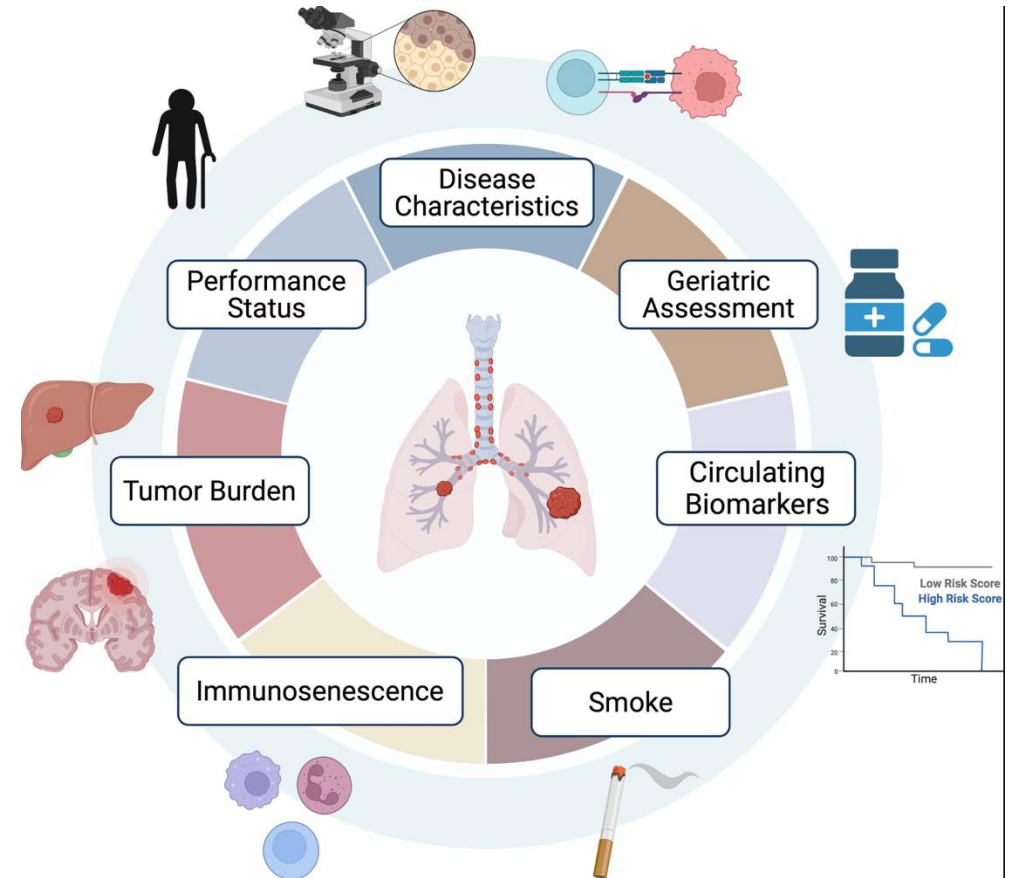
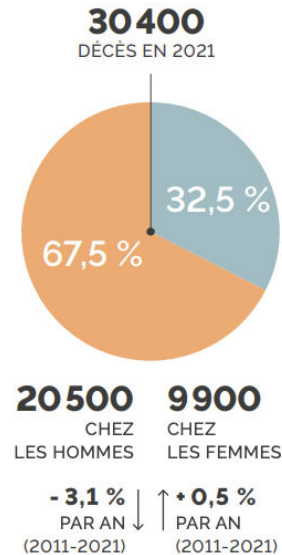
CBNPC et sujet âgé

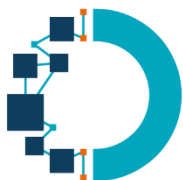


**2° CANCER LE PLUS
FRÉQUENT CHEZ LES
HOMMES ET 3° CHEZ
LES FEMMES EN FRANCE**



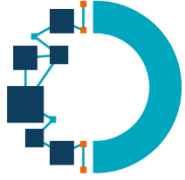
**1° CAUSE DE DÉCÈS
PAR CANCER
EN FRANCE**



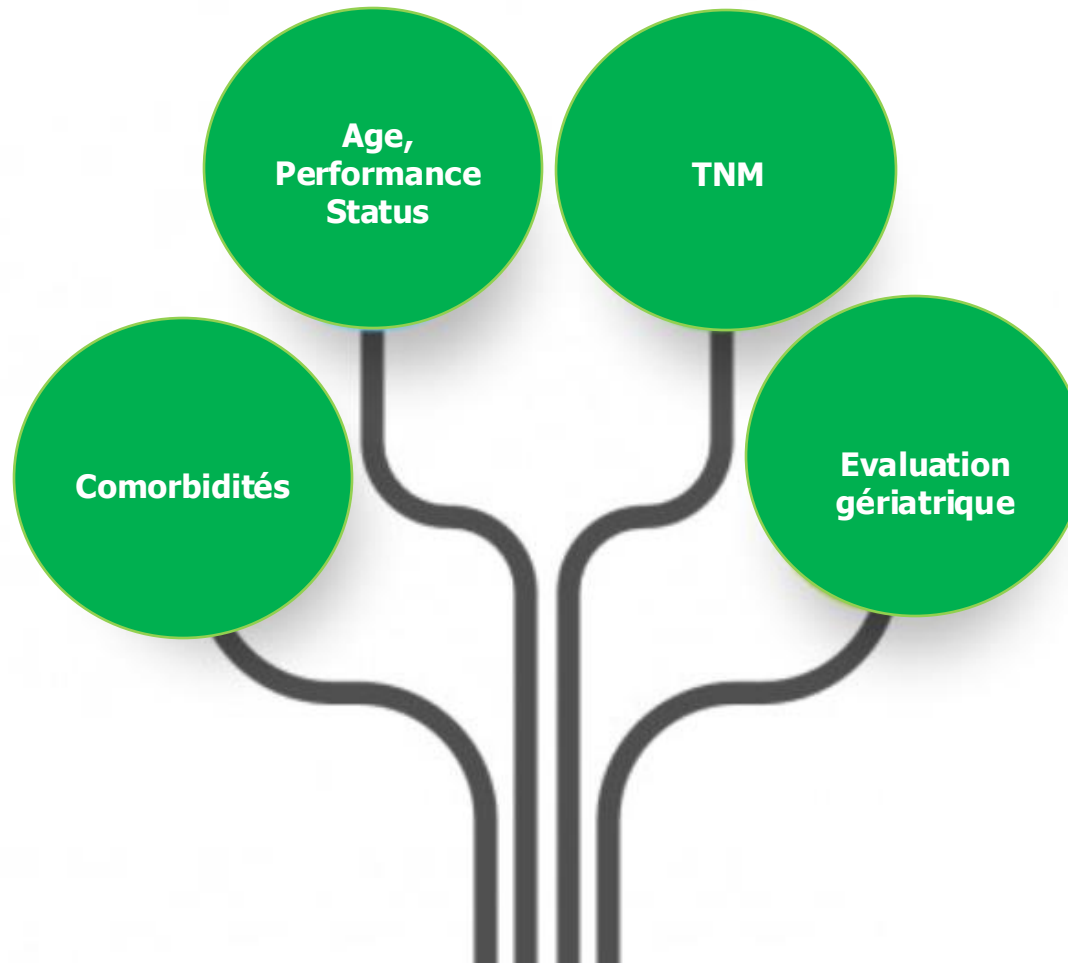


Présentation clinique

	All Patients (n = 193)	Patients ≥ 70 Years (n = 92)	Patients < 70 Years (n = 101)	P Value
Age: Median (Range)	68.5 (35.5-93.4)	78.2 (70.2-93.4)	60.4 (35.5-69.7)	$P < .0001^a$
Sex: Men/Women	135/58 (69.9/30.1)	61/31 (66.3/33.7)	74/27 (73.3/26.7)	$P = .109^b$
PS				$P = .001^b$
0-1	150 (78)	61 (66.3)	89 (88.1)	
2	30 (15)	22 (23.9)	8 (7.9)	
3-4	13 (7)	9 (9.8)	4 (4)	
Tobacco Status: Never/Former/Current Smoker	16/97/78 (8/50/40)	9/60/22 (9.8/65.3/23.9)	7/37/56 (6.9/36.6/55.4)	$P < .0001^b$
Married or Couple: Yes/No	98/64 (52/33)	45/33 (57.7/42.3)	53/31 (63.1/36.9)	$P = .482^b$
Charlson Score: Median (IQR)	1 (0-2)	2 (1-3)	1 (0-2)	$P < .0001^a$
Histologic Type				$P = .024^b$
Adenocarcinoma	94 (49)	36 (39.1)	58 (57.4)	
Squamous cell	36 (19)	25 (27.2)	11 (10.9)	
Large-cell	23 (12)	10 (10.9)	13 (12.9)	
Large-cell with neuro- endocrine component	2 (1)	2 (2.2)	0 (0)	
Adenosquamous	1 (0.5)	0 (0)	1 (1)	
Small-cell	26 (13)	12 (13)	14 (13.8)	
NOS	11 (5.5)	7 (7.6)	4 (4)	
Stage: I/II/III/IV	27/16/35/115 (14.0/8.3/18.1/59.6)	12/4/17/59 (13.0/4.3/18.5/64.1)	15/12/18/56 (14.9/11.9/17.8/55.4)	$P = .258^b$



Processus décisionnel

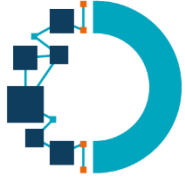


Oncodage ou G8	
8 items	Patients âgés ≥ 75 ans
• Appétit	
• Perte de poids (< 3 mois)	
• Motricité	
• Troubles neuro-psychologiques	
• Indice de Masse Corporelle	
• Plus de 3 médicaments	
• Etat de santé perçu par le patient	
• Age	
Score > 14	Décision de traitement adapté
Score ≤ 14	Révéle une vulnérabilité / fragilité Evaluation gériatrique recommandée

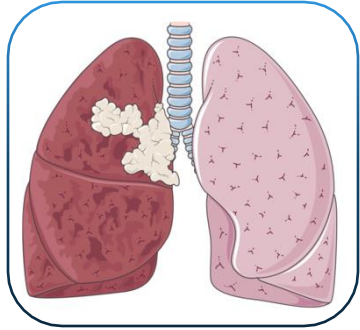
Balducci 1	• Patients en forme, vieillissement réussi, autonome, pas de facteur de fragilité • Traitement oncologique identique à celui du patient jeune.
Balducci 2	• Patients ayant 1 ou 2 comorbidités, 1 syndrome gériatrique (chutes, troubles cognitifs, syndrome dépressif sévère, incontinence, troubles visuels) • Traitement oncologique à adapter prise en charge oncogériatrique
Balducci 3	• Patients fragiles, ayant ≥ 1 dépendance (IADL), ≥ 3 comorbidités, ≥ 1 syndrome gériatrique • Traitement palliatif

Référentiels AURA 2025 :

“L'utilisation de scores gériatriques chez les patients de plus de 70 ans est recommandé, même si **aucun score gériatrique n'est actuellement validé en cancérologie thoracique**



IO en oncologie thoracique

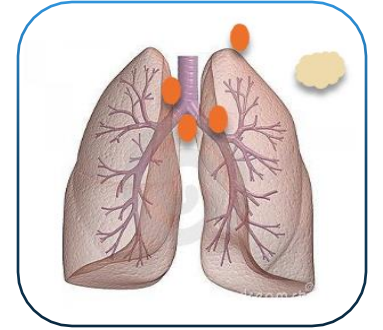


STADES PRECOCES

CT-IO néoadjuvante 3 à 4 cures
+/-
IO adjuvante 1 an

STADES III

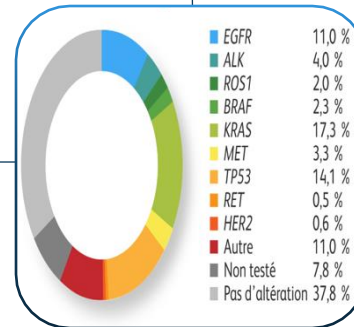
CT-RT
+/-
IO adjuvante 1 an si pas de PD



STADES IV

Première ligne
- PDL1 < 50% : CT-IO*
- PDL1 ≥ 50% : IO 2 ans ou CT-IO
4 cures puis maintenance 2 ans

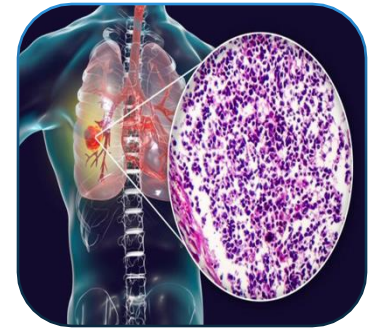
Deuxième ligne : IO monothérapie si
PD après CT exclusive (exceptionnel)

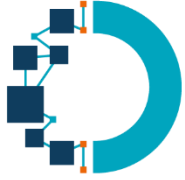


CPC

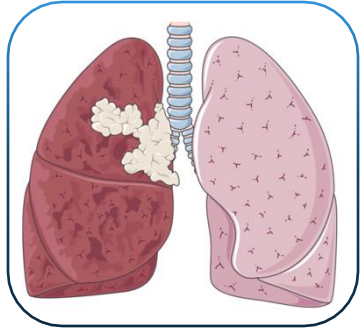
Formes localisée au thorax :
CT-RT +/- IO adjuvante 1 an si pas de PD

Stades métastatiques : CT-IO 4 cures puis
maintenance IO seule si pas de PD





IO en oncologie thoracique

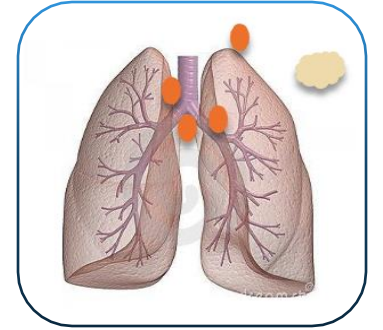


STADES PRECOCES

CT-IO néoadjuvante 3 à 4 cures
+/-
IO adjuvante 1 an

STADES III

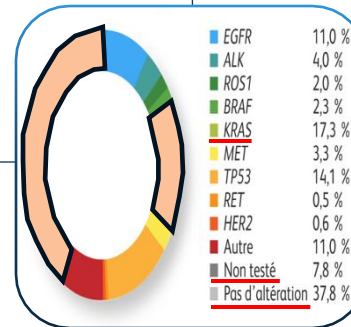
CT-RT
+/-
IO adjuvante 1 an si pas de PD



STADES IV

Première ligne
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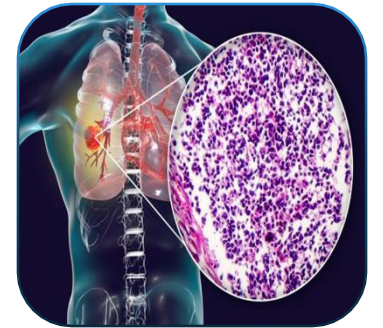
Deuxième ligne : IO monothérapie si
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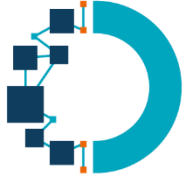


CPC

Formes localisée au thorax :
CT-RT +/- IO adjuvante 1 an si pas de PD

Stades métastatiques : CT-IO 4 cures puis
maintenance IO seule si pas de PD



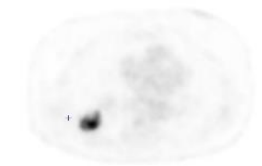
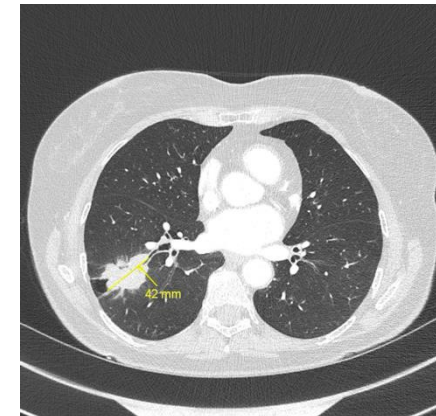
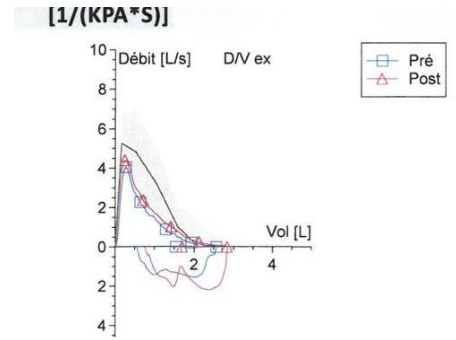


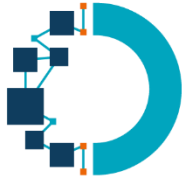
Cas Clinique stade précoce

- Mme K 75 ans
- Tabac 30PA
- Bilan de toux chronique
- PS 0

➔ Minisonde + EBUS : ADK
T2aN1M0 (stade IIB) PDL1
80% - NGS neg. **CAT ?**

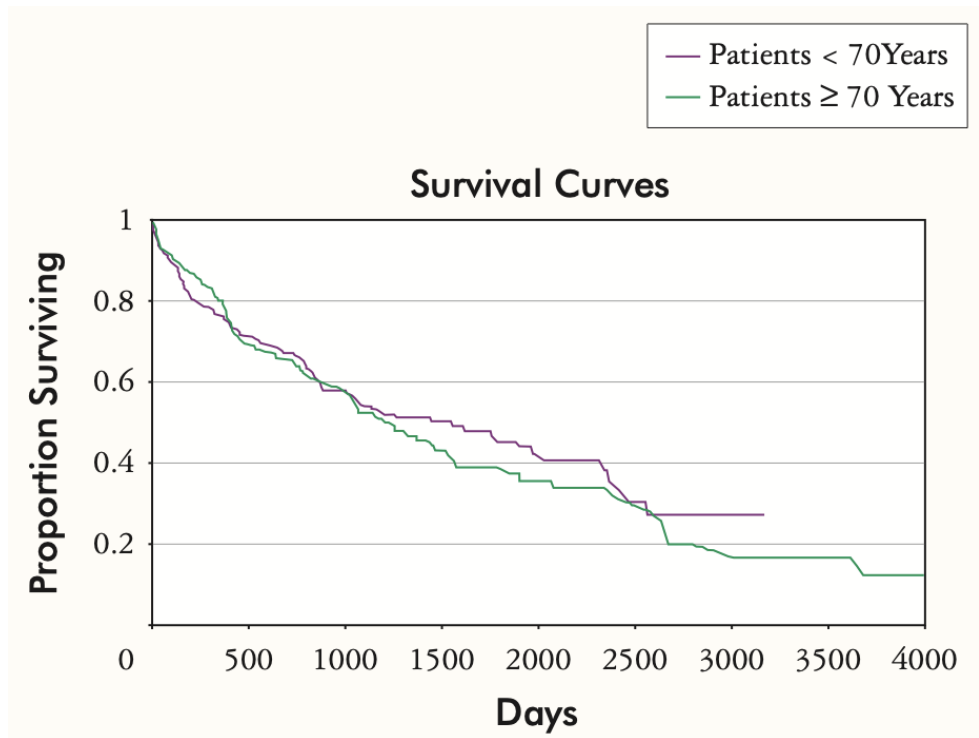
CVF	[L]	1.40	2.11	2.82	2.56	121	2.83	134	10
VEMS	[L]	1.11	1.73	2.36	1.53	89	1.69	97	10
VEMS % CVF	[%]	41.66	82.05	122.43	59.97		59.74	73	-0
VEMS % CV MAX	[%]	65.09	75.80	86.51	59.97		59.74	79	-0
DEP	[L/s]	3.78	5.26	6.74	4.05	77	4.40	84	8
DEM 75	[L/s]	2.59	4.81	7.03	2.27	47	2.37	49	4
DEM 50	[L/s]	1.37	3.18	4.99	0.89	28	1.03	32	15
DEM 25	[L/s]		0.98	2.11	0.22	22	0.26	27	21
DEMM 25/75	[L/s]	1.07	2.46	3.86	0.65	26	0.71	29	10
VIMS	[L]				1.42		1.75		24
DEM 50 % DIM 50	[%]				66.67		73.46		10
Capacité Vitale...	[L]	1.53	2.22	2.91	2.44	110	2.83	127	16
CPT	[L]	3.39	4.37	5.36	5.01	114			
VR	[L]	1.33	1.91	2.48	2.56	134			





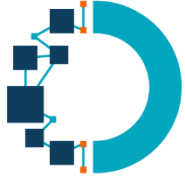
Chirurgie carcinologique et sujet âgé

A discuter au cas par cas, si contre indication → stéréotaxie



Complication	No. of Evaluable Patients	No. of Patients		
		Age < 70 Years	Age ≥ 70 Years	P Value
All Types	269	84 (51.2%)	64 (61.0%)	NS
Arrhythmia	268	61 (37.2%)	46 (44.2%)	NS
Pulmonary	264	46 (28.0%)	33 (33.0%)	NS
Deaths Within 30 Days	279	11 (6.7%)	7 (6.1%)	NS
Median Length of Hospital Stay, Days (Range)	280	9 (1-144)	11 (5-107)	0.0006

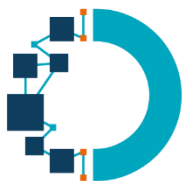
Hanna et al. Clinical Lung Cancer 2002



Cas Clinique stade précoce

	Adjuvant IO 	Neoadjuvant CT-IO 	Neoadjuvant CT-IO, adjuvant IO
Efficacy	N'augmente pas la SG vs CT dans méta analyse	Augmente SG vs CT dans méta analyse	N'augmente pas la SG vs CT-IO dans méta analyse
Authorization	. IMPr01, PD-L1 ≥1%; PD-L1 ≥50% . KN091,	. CM816, ; PD-L1 ≥1%	. KN671, . AEGAN,
Compliance	. Surgery . CT . IO 100%, pCR:0% 60% 70%/60% 12 cycles	81-91%, pCR:20% 95% 95%/3 cycles	81-91%, pCR:20% 95% ?%/60% 12 cycles
Toxicity	S (+); CT (+); IO 1 yr (++)	CT-IO (+); S (+)	S (+); CT-IO (+); IO 1 yr (++)
Cost	+++	+	+++

Wu et al. Cancer 2023



Cas Clinique stade précoce

Subgroup	No. of Patients	Pathological Complete Response (95% CI)		Unweighted Difference, Nivolumab plus Chemotherapy minus Chemotherapy Alone (95% CI)	percentage points
		Chemotherapy alone (N=179)	Nivolumab plus chemotherapy (N=179)		
		%	%		
Overall	358	2.2 (0.6–5.6)	24.0 (18.0–31.0)		21.8 (15.2 to 28.7)
Age					
<65 yr	176	0 (0–4.3)	26.9 (18.2–37.1)		26.9 (17.8 to 36.7)
≥65 yr	182	4.2 (1.1–10.3)	20.9 (12.9–31.0)		17.8 (7.3 to 26.8)

CM 816

B Subgroup Analysis of Event-free Survival

Subgroup	Pembrolizumab Group	Placebo Group	Hazard Ratio for Event or Death (95% CI)
	no. of events/no. of participants	no. of events/no. of participants	
All patients	139/397	205/400	0.58 (0.46–0.72)
Age			
<65 yr	74/221	113/214	0.53 (0.39–0.71)
≥65 yr	65/176	92/186	0.64 (0.46–0.88)

KN 671

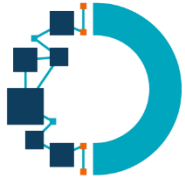
B Subgroup Analysis

Subgroup	No. of Patients	Median Event-free Survival (95% CI)		Hazard Ratio for Disease Progression, Recurrence, or Death (95% CI)
		Durvalumab	Placebo	
All patients	740	NR (31.9–NR)	25.9 (18.9–NR)	0.68 (0.53–0.88)
Age at randomization				
<65 yr	358	NR (NR–NR)	NR (18.9–NR)	0.71 (0.47–1.04)
≥65 yr	382	NR (17.9–NR)	24.5 (13.6–31.1)	0.69 (0.48–0.97)

AEGAN

Neoadjuvant CT-IO	Neoadjuvant CT-IO, adjuvant IO
Augmente SG vs CT dans méta analyse	N'augmente pas la SG vs CT-IO dans méta analyse
. CM816, ; PD-L1 ≥1% >65ans : 50.8%	. KN671, >65ans : 45.2% . AEGAN, >65ans : 47.8%
81-91%, pCR:20% 95% 95%/3 cycles	81-91%, pCR:20% 95% ?%/60% 12 cycles
CT-IO (+); S (+)	S (+); CT-IO (+); IO 1 yr (++)
+	+++

Wu et al. Cancer 2023



Suivi

Inclusion dans l'étude **NeoCOAST** :
4 cures de CT + Durvalumab / Monalizumab.

Tolérance parfaite



Evaluation à 4 cures

Réponse métabolique partielle importante



Lobectomie inf droite

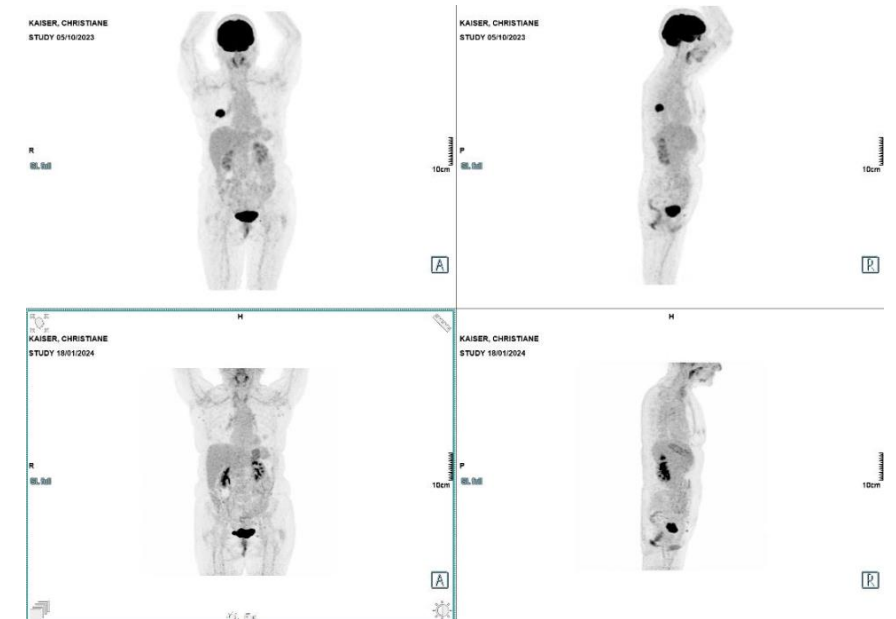
REPONSE PATHOLOGIQUE COMPLETE

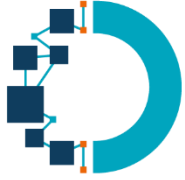


Durvalumab / Monalizumab 12 mois
Pas de complication (fin en nov 24)



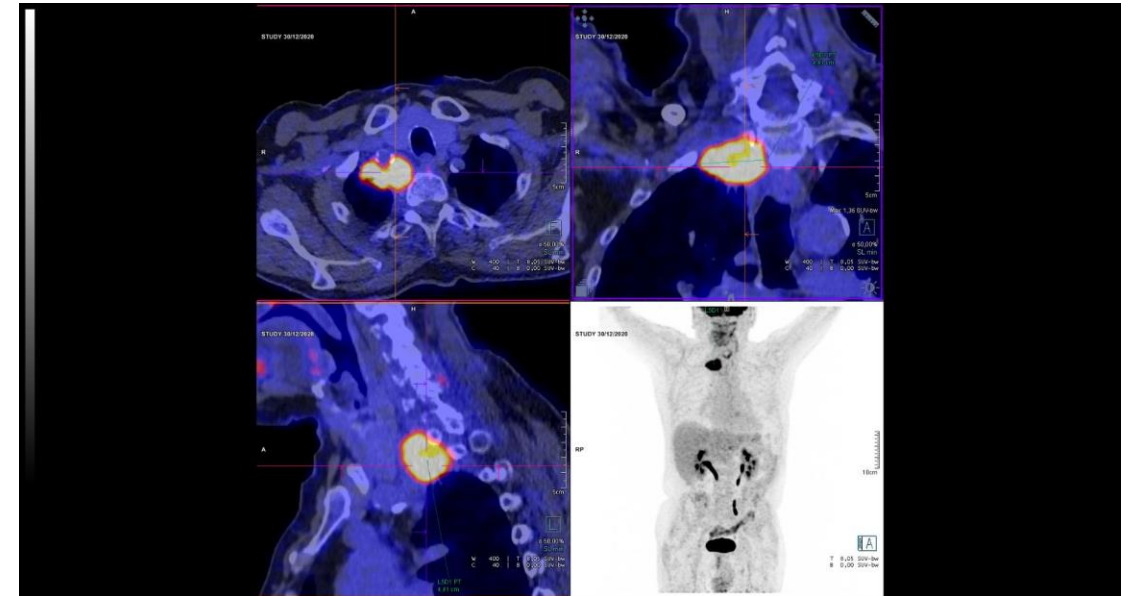
Poursuite de la rémission au 07 avril 2025



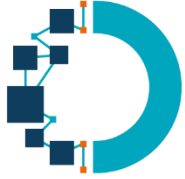


Cas Clinique stade localement avancé

- M. S 77ans
- HTA, CMI (stent)
- BPCO post tabagique (VEMS 2L)
- Bilan de douleurs d'allure pleurales
- Balducci 1



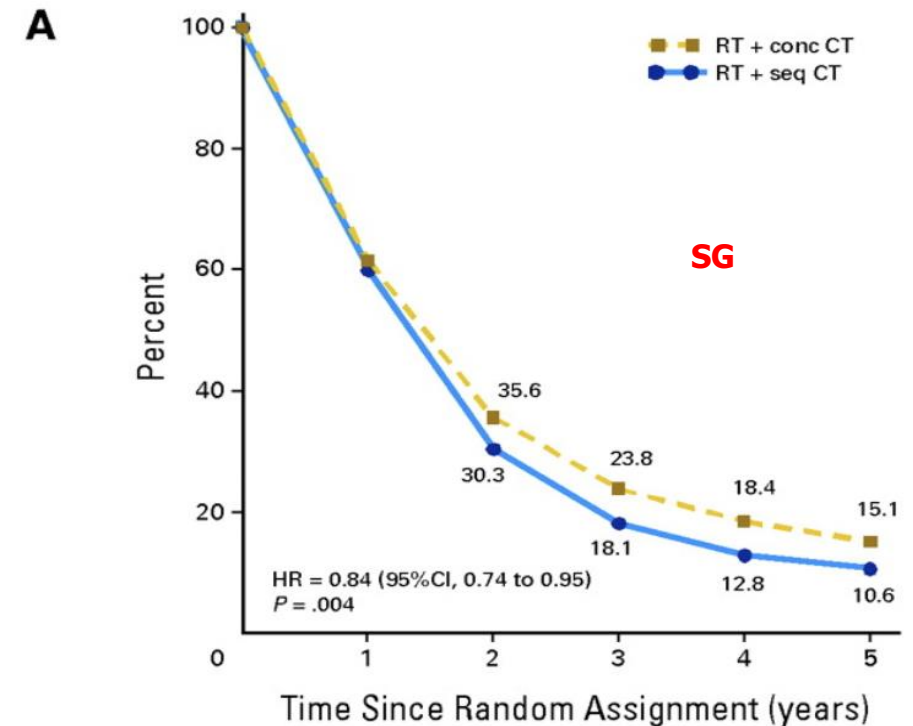
➡ EUS epidermoïde PDL1 40%



CTRT conco vs séquentiel

Stades III non résécables
doivent être traités par CTRT :

- Recommandations : 66Gy de RT avec chimio "à base de sels de platine"
- conco > CTRT séquentiel mais possible uniquement si PS 0-1 et < 70ans (sauf cas hypersélectionnés)

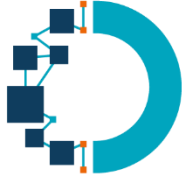


C

Category	No. Deaths/ No. Entered		Hazard Ratio	P of Interaction trend* test
	RT + Conc CT	RT + Seq CT		
Age				.38
Less than 60	239/273	217/246		*.24
60-64	95/114	100/111		
65-69	123/140	122/130		
70 or over	64/76	106/113		

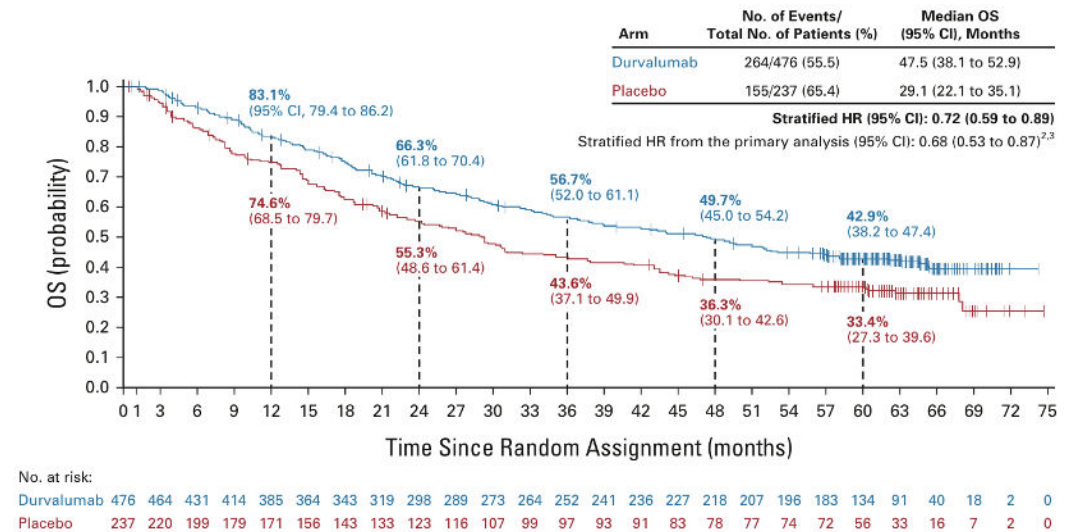
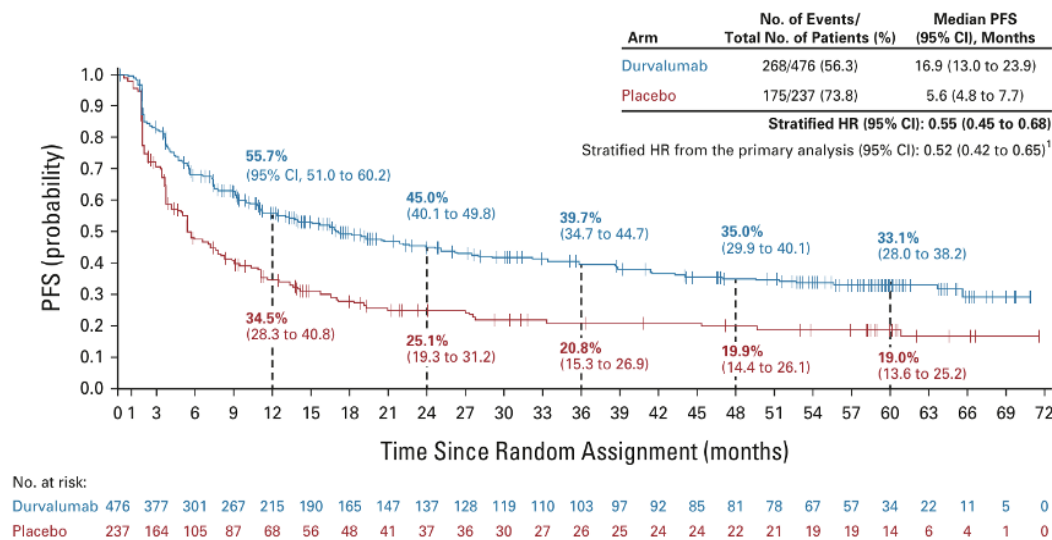
	Deaths/Person-Years by Period				
	0y-1y	1y-2y	2y-3y	3y-4y	> 4y
RT+ conc CT (n = 603)	240/498	147/276	67/171	30/116	37/186
RT+ seq CT (n = 602)	253/491	171/242	70/129	30/ 83	23/126

Auperin et al. *JCO* 2010

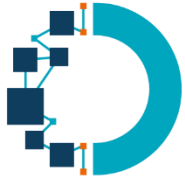


L'IO après CTRT : l'étude PACIFIC

CTRT conco suivie par 1 an de DURVALUMAB en l'absence de PD en fin de CTRT
(début < 42j après la fin de la RT)



65% des patients avaient >65ans (>70 ??)



Etude PACIFIC 6 : Durva après CTRT séquentielle

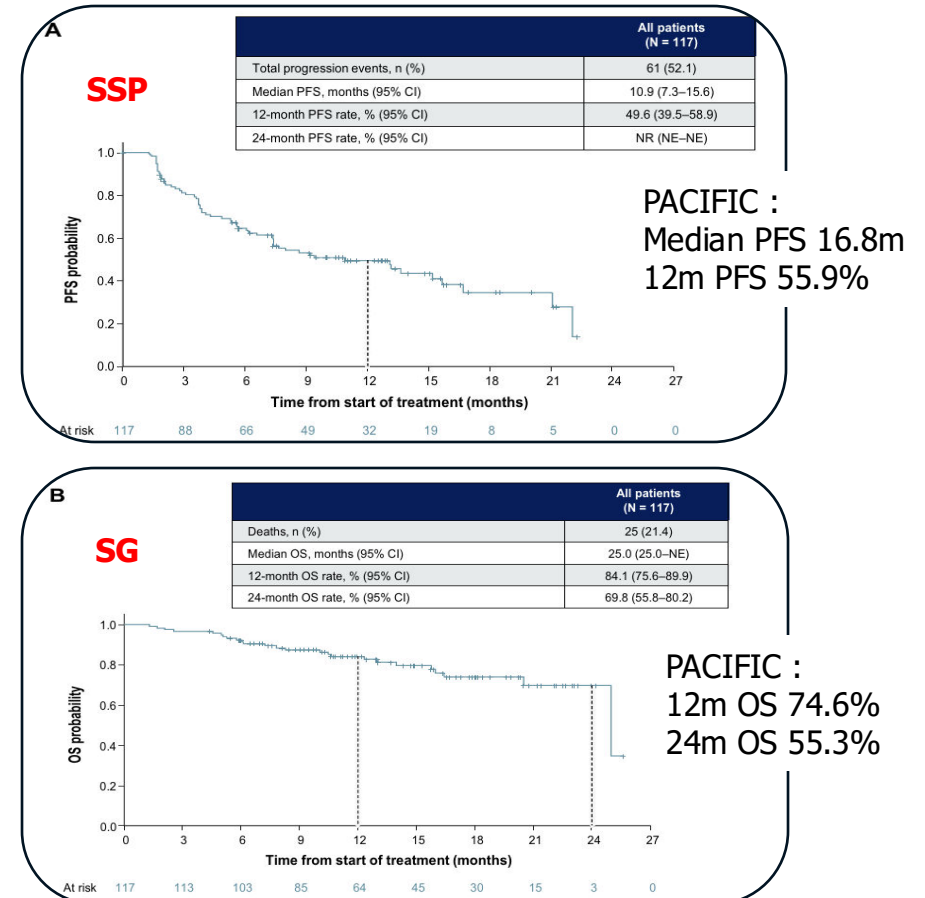
Table 1. Baseline Patient and Disease Characteristics

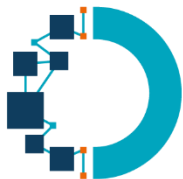
Characteristic	ECOG PS 0 or 1 (n = 114)	ECOG PS 2 (n = 3)	All Patients (N = 117)
Median age (range), y	68.0 (39-85)	65.0 (53-77)	68.0 (39-85)
Age group, n (%)			
<65 y	39 (34.2)	1 (33.3)	40 (34.2)
≥65 y	75 (65.8)	2 (66.7)	77 (65.8)
≥75 y	20 (17.5)	1 (33.3)	21 (17.9)
Sex, n (%)			
Men	71 (62.3)	2 (66.7)	73 (62.4)
Women	43 (37.7)	1 (33.3)	44 (37.6)
Race, n (%)			
White	101 (88.6)	3 (100.0)	104 (88.9)
Unknown	13 (11.4)	0	13 (11.1)
Smoking history, n (%)			
Never smoker	9 (7.9)	0	9 (7.7)
Former smoker	73 (64.0)	2 (66.7)	75 (64.1)
Current smoker	32 (28.1)	1 (33.3)	33 (28.2)
ECOG PS, n (%)			
0	47 (41.2)	0	47 (40.2)
1	67 (58.8)	0	67 (57.3)
2	0	3 (100.0)	3 (2.6)
Histologic type, n (%)			
Adenocarcinoma	63 (55.3)	0	63 (53.8)
Squamous cell	42 (36.8)	3 (100.0)	45 (38.5)
Other	9 (7.9)	0	9 (7.7)
Disease stage at baseline, n (%)			
IA	1 (0.9)	0	1 (0.9)
IIIA	44 (38.6)	0	44 (37.6)
IIIB	58 (50.9)	1 (33.3)	59 (50.4)
IIIC	11 (9.6)	2 (66.7)	13 (11.1)
PD-L1 expression on TCs, n (%)			
<1%	34 (29.8)	0	34 (29.1)
≥1%	33 (28.9)	3 (100.0)	36 (30.8)
Missing	47 (41.2)	0	47 (40.2)

ECOG, Eastern Cooperative Oncology Group; PD-L1, programmed cell death-ligand 1; PS, performance status; TC, tumor cell.

17% cisplatine

Tox similaire à
PACIFIC





Suivi

Chimio radiothérapie séquentielle.

1 épisode de neutropénie IV non compliqué sans
récidive après concession de dose



Evaluation le jour de la dernière séance de RT

Réponse métabolique complète



DURVALUMAB 1 an (fin 05/22)

Poursuite de la Réponse complète

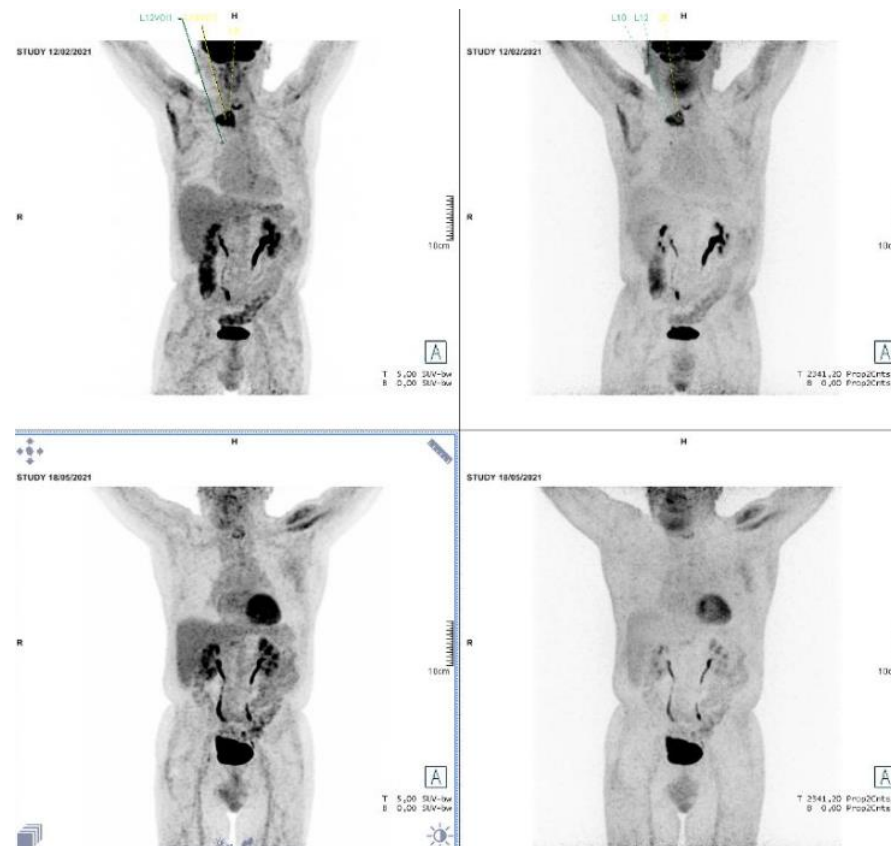
Polyarthralgies G1 sous IO



Oligoprogression cérébrale en 2024 stereo exclusive



Pas de récurrence au 07 avril 2025

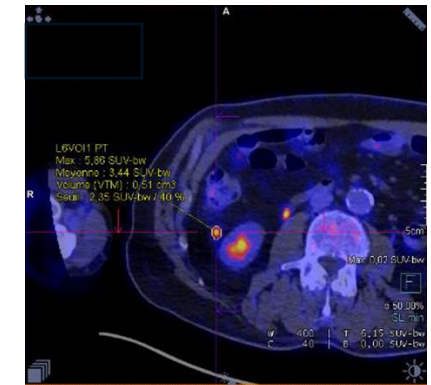
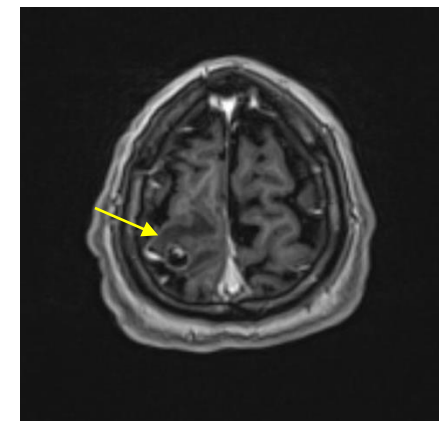


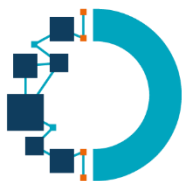


Cas Clinique CBNPC IV L1

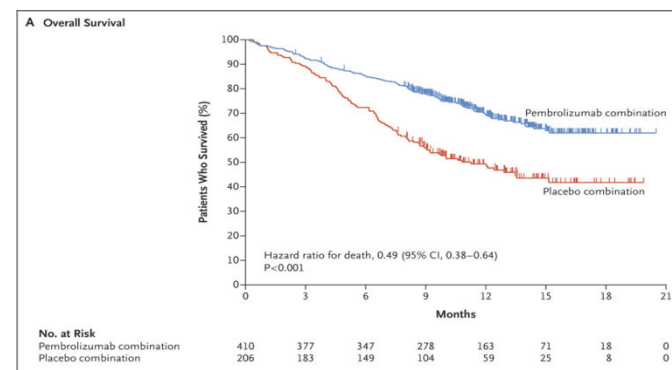
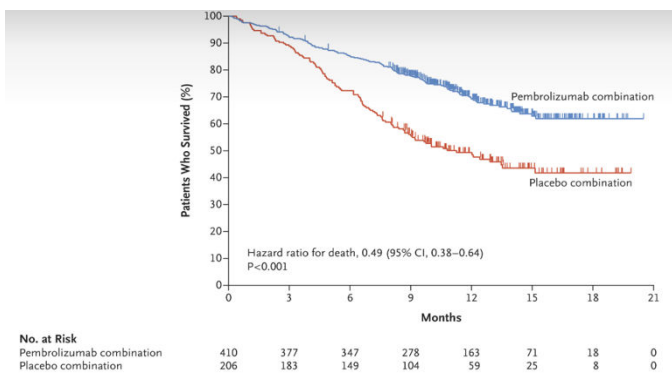
- M. F 77ans
- Diabète, Tabac 40 PA
- Deficit l'hémicorps gauche
- PS **1** – Balducci 1

➔ PTT : ADK IV PDL1 **20%**, NGS neg



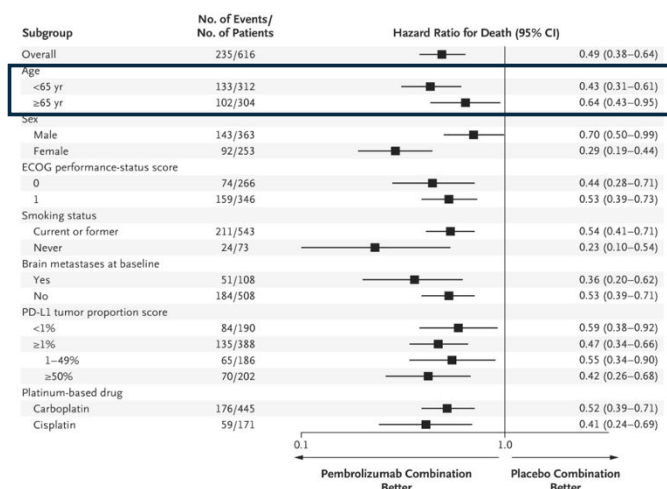


L1 tout PDL1, PS 0 ou 1 : Combo CT-IO vs CT



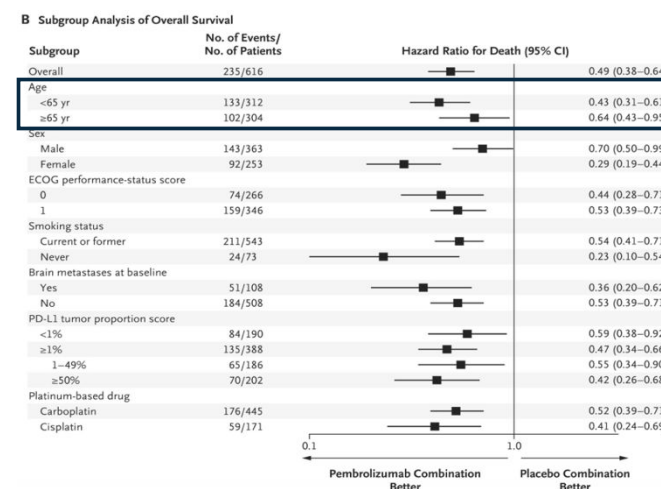
ADK

> 70ans : $n = 18$

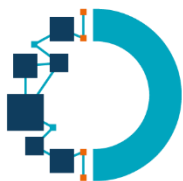


CANCERS
EPIDERMOIDES

> 70ans : $n = 14$

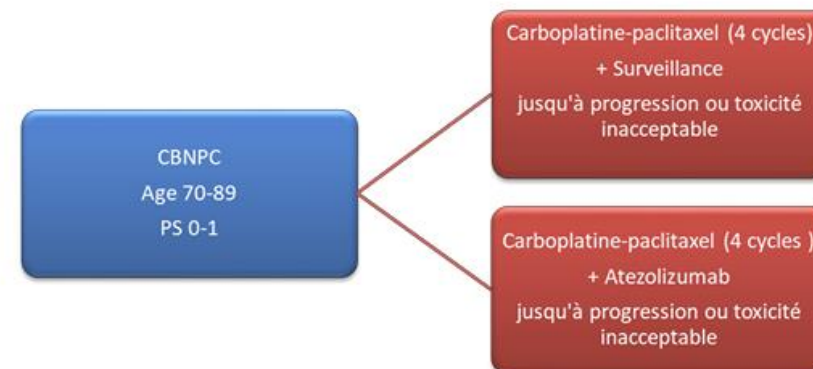


Ghandi et al. *NEJM* (2019)



Suivi

Inclusion étude ELDERLY après stéréotaxie
Bras expérimental



Recrutement terminé



Suivi

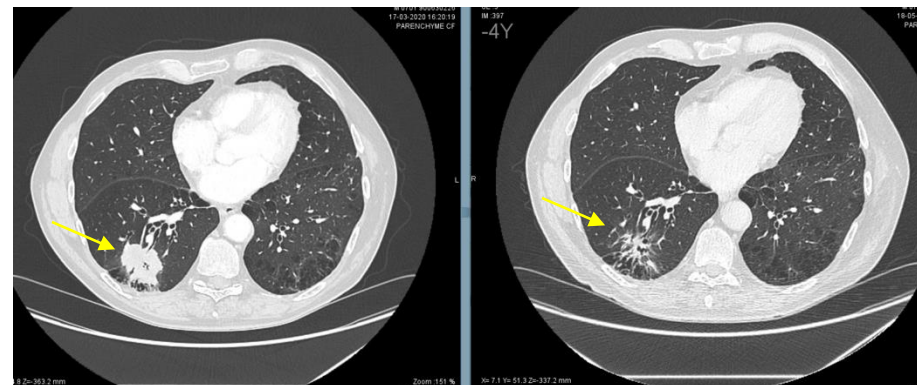
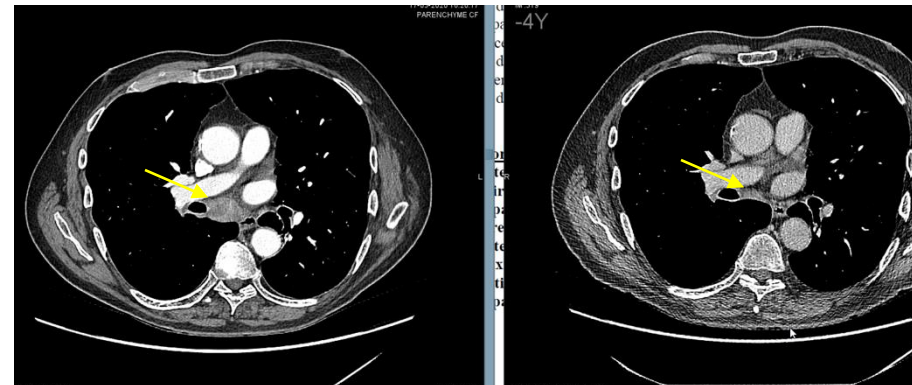
Inclusion étude ELDERLY après stéréotaxie

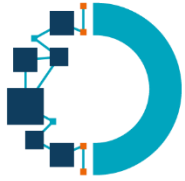
Bras experimental



Bilan après 4 cures d'induction CT-IO

Réponse partielle





Suivi

Inclusion étude ELDERLY après stéréotaxie
Bras experimental



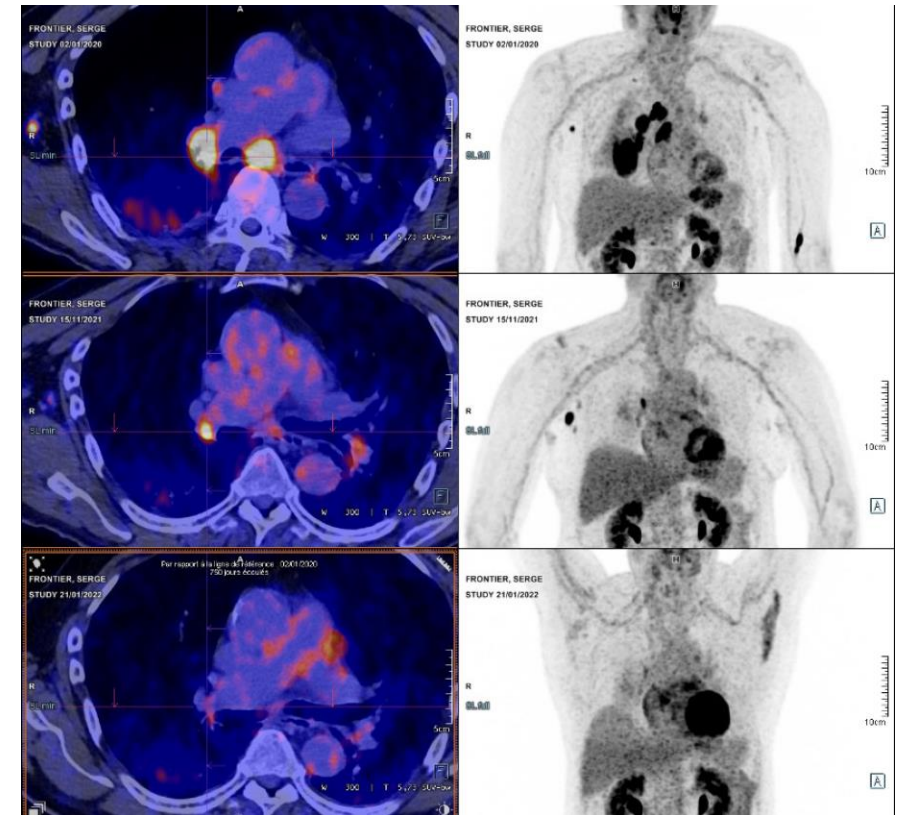
Bilan après 4 cures d'induction CT-IO
Réponse partielle



A 2 ans de la fin de la sequence, RC IRM crane et TAP
Décision de stopper les ttt et de réaliser un TEP
RC métabolique donc pas de RT de "cloture"



Pas de récidence au 07 avril

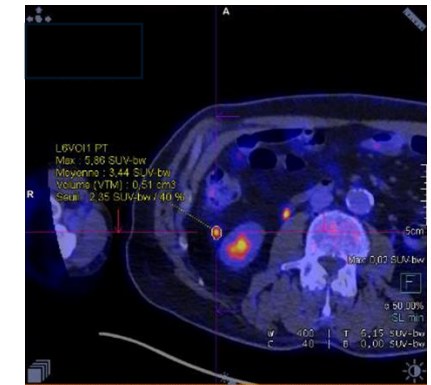
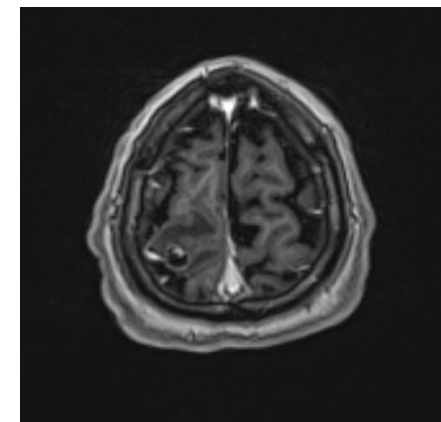


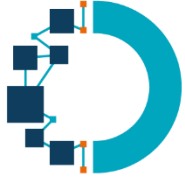


Cas Clinique CBNPC IV L1

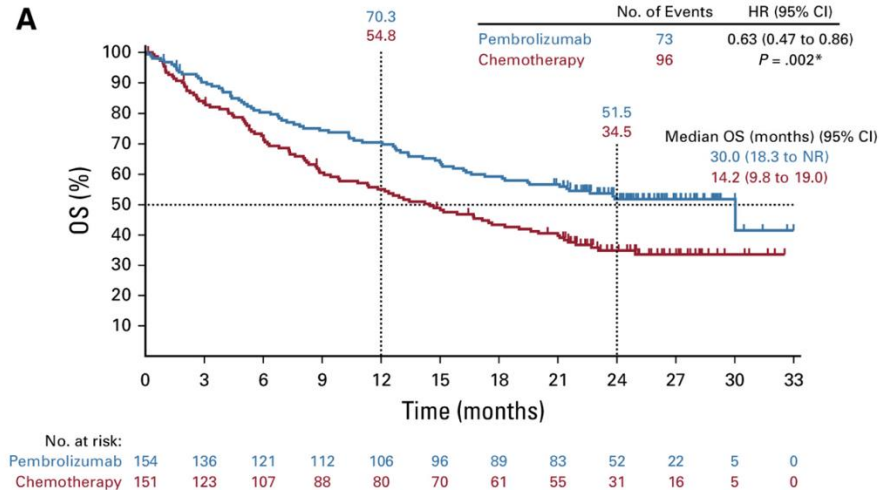
- M. F 77ans
- Diabète, Tabac 40 PA
- Deficit l'hémicorps gauche
- PS 1

➔ PTT : ADK IV PDL1 **80%**, NGS neg

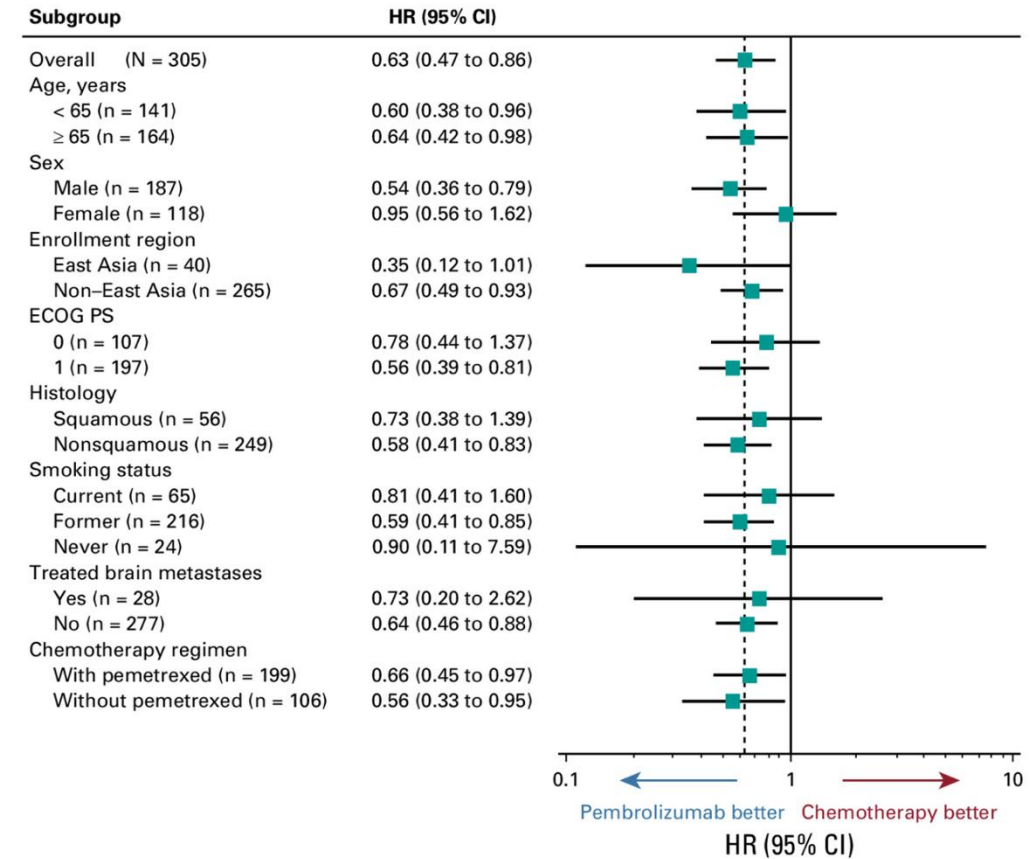




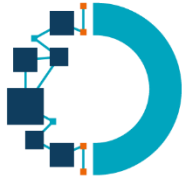
L1 PDL1 > 50% PS 0 ou 1 : IO seule vs Chimio



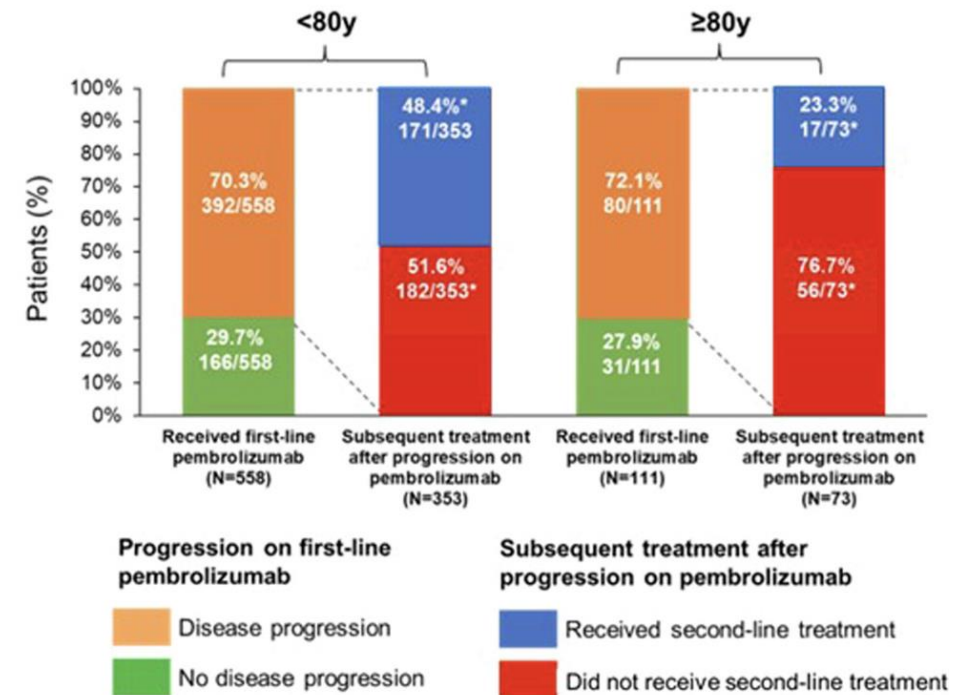
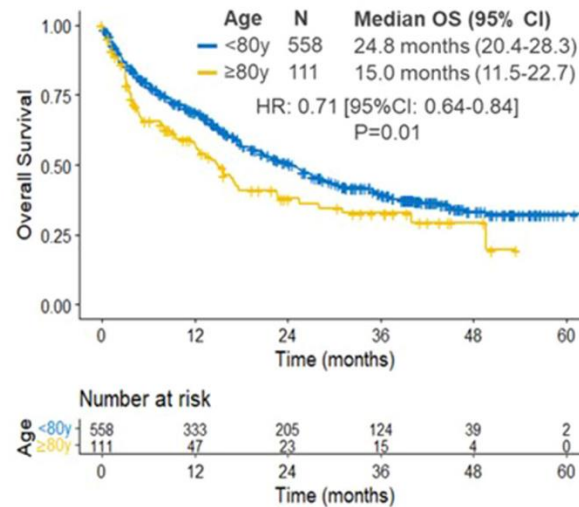
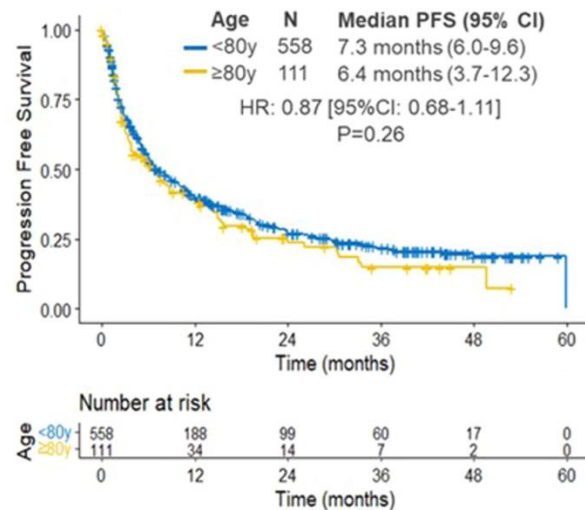
B

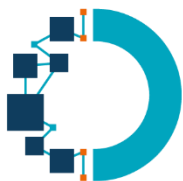


Reck et al. *JCO* 2019

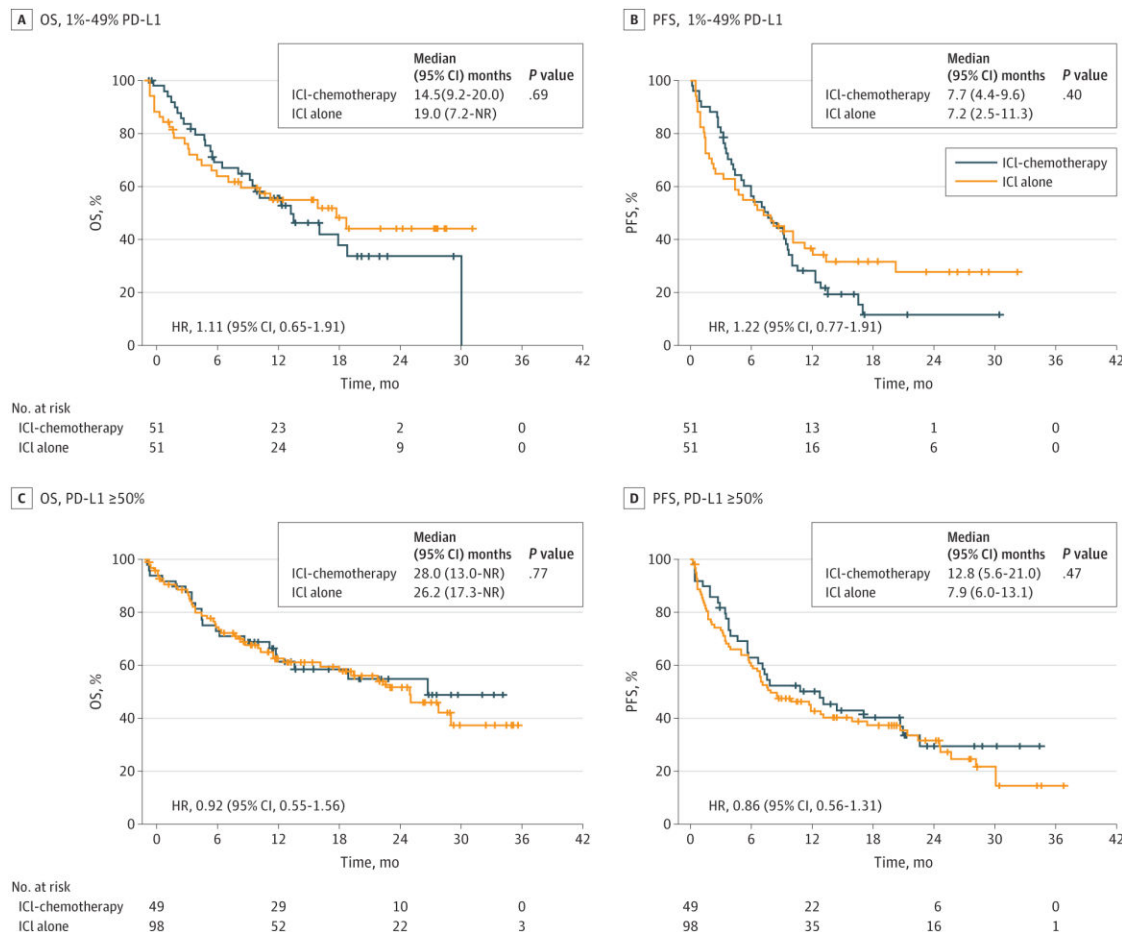


L1 PDL1 > 50% PS 0 ou 1 : l'IO est elle plus efficace chez les "jeunes"





CT-IO vs IO seule > 75ans et PS < 2



irAEs	ICI-chemotherapy		ICI	
	Any grade	Grade ≥3	Any grade	Grade ≥3
All	173 (48.9)	86 (24.3)	171 (40.2)	76 (17.9)
Steroid use due to irAEs	115 (32.5)	NA	105 (24.7)	NA
Pneumonitis	83 (23.4)	41 (11.6)	66 (15.6)	29 (6.8)
Colitis	13 (3.7)	7 (2)	10 (2.4)	1 (0.24)
Thyroid disorder	18 (5.1)	2 (0.6)	16 (3.8)	0 (0)
Skin disorder	27 (7.6)	11 (3.1)	43 (10.1)	13 (3.1)
Liver dysfunction	15 (4.2)	6 (1.7)	14 (3.3)	9 (2.1)
Kidney dysfunction	19 (5.4)	5 (1.4)	4 (0.9)	1 (0.24)
Endocrine disorder	18 (5.1)	13 (3.7)	23 (5.4)	13 (3.1)
Central nervous system disorder	1 (0.3)	1 (0.3)	1 (0.2)	1 (0.24)
Other	16 (4.5)	10 (2.8)	24 (5.6)	11 (2.6)

Faut-il toujours faire de la chimiothérapie chez les sujets > 75ans PDL1 positifs ?

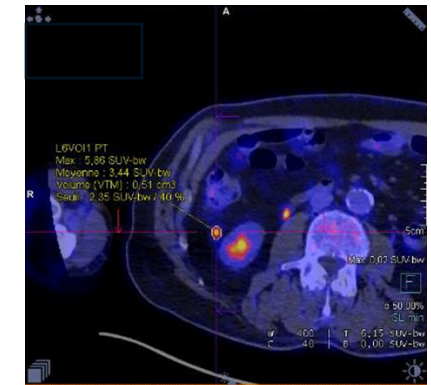
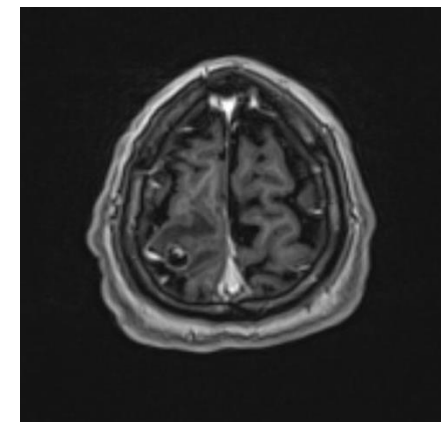
Tsukita et al. *JAMA* 2024

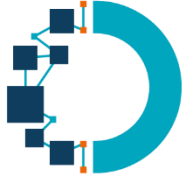


Cas Clinique CBNPC IV L1

- M. F 77ans
- Diabète, Tabac 40 PA
- Deficit l'hémicorps gauche
- PS 2 – Balducci **2**

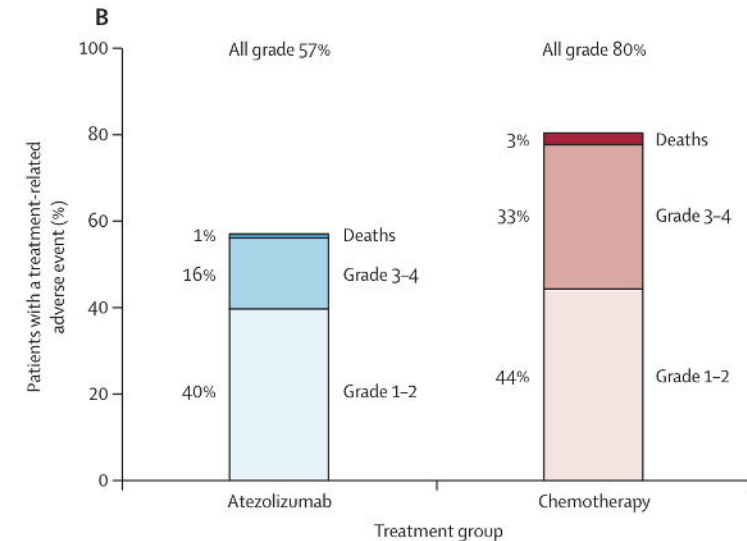
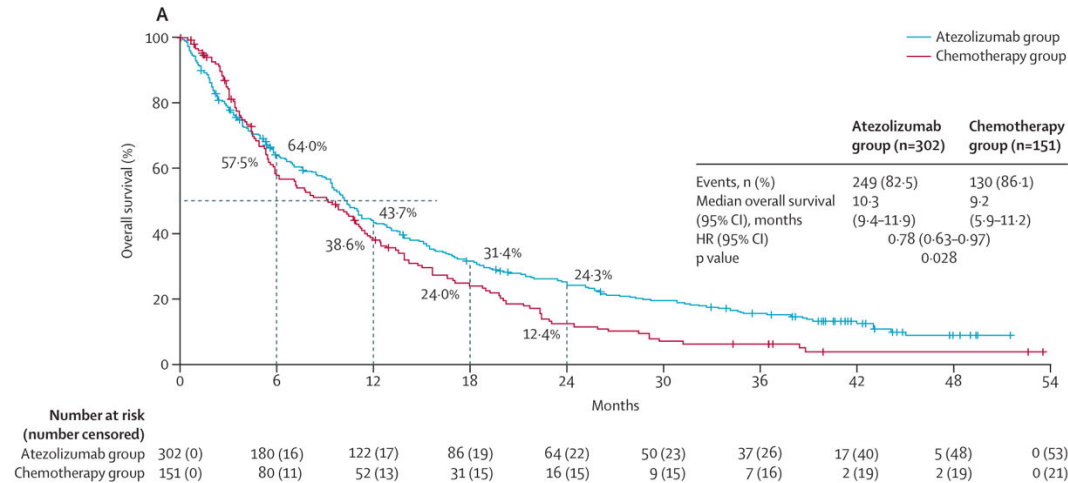
➔ PTT : ADK IV PDL1 **40%**, NGS neg



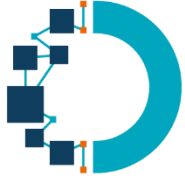


L1 tout PDL1, sujet âgés fragiles monoCT ou IO ?

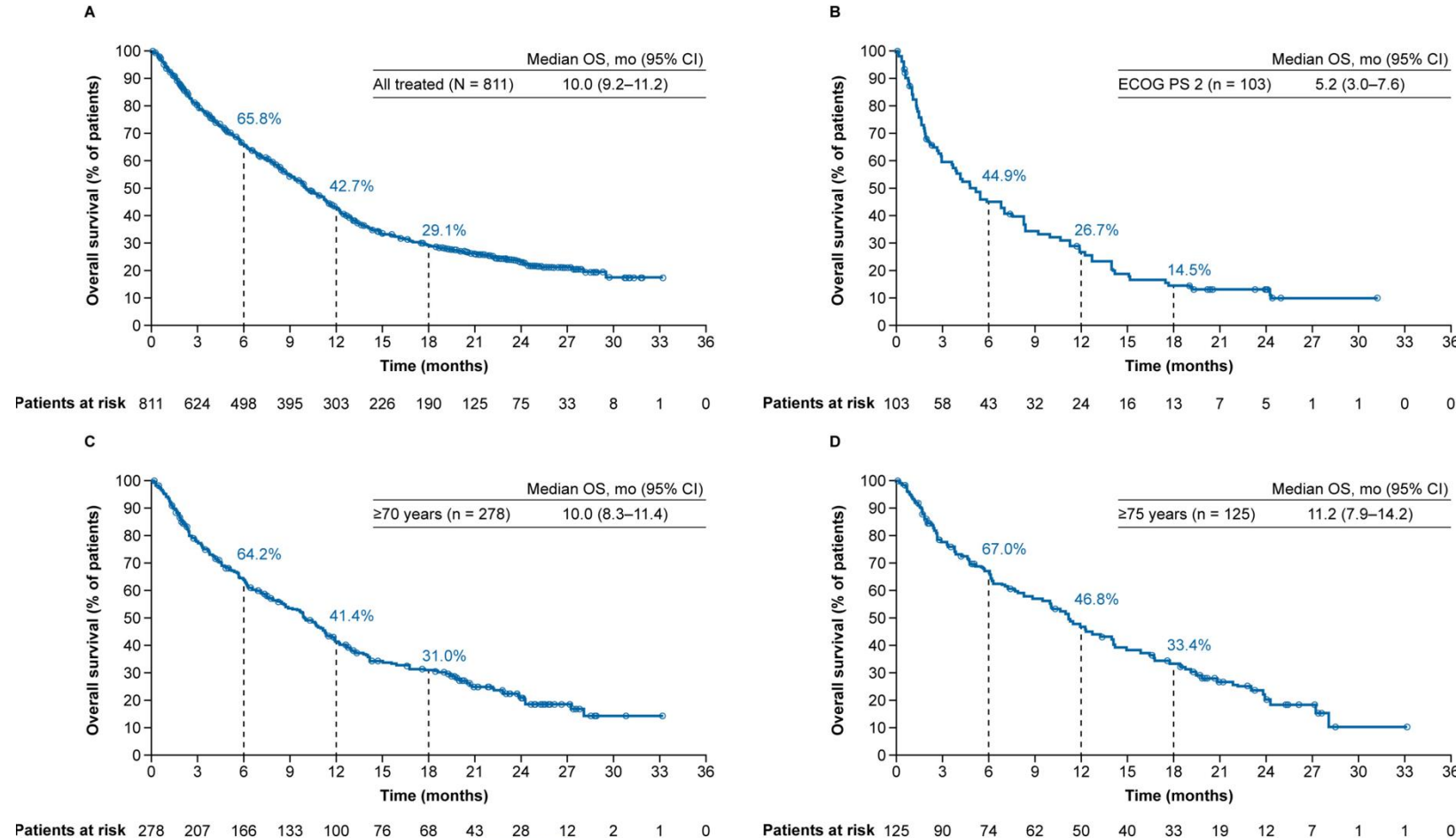
	Events/patients, n/N	Median overall survival, months	Events/patients, n/N	Median overall survival, months	HR (95% CI)
All patients	249/302	10.3	130/151	9.2	0.78 (0.63-0.97)
Age					
≥80 years	87/97	9.9	36/43	9.7	0.97 (0.66-1.44)
70-79 years	105/125	10.3	58/65	6.1	0.68 (0.49-0.94)
<70 years	57/80	11.9	36/43	9.8	0.75 (0.49-1.14)



Ming Lee et al. *Lancet* 2023



IO seule L2 et plus .. Si pas utilisé en L1

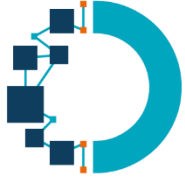


Données issues de la CHECKMATE 171 : phase 2 nivolumab monothérapie chez maladies pré traités :

- 12.7% de PS > 1
- 34.3% > 70 ans
- 15.4% > 75 ans

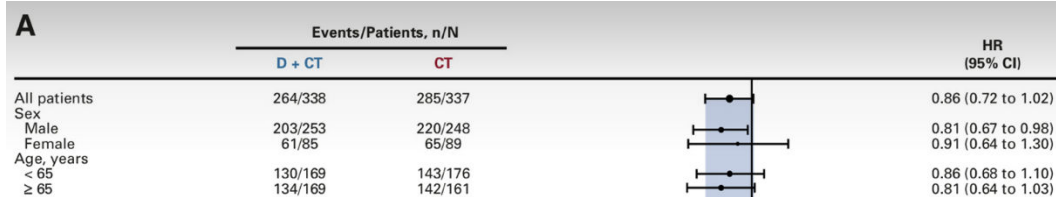
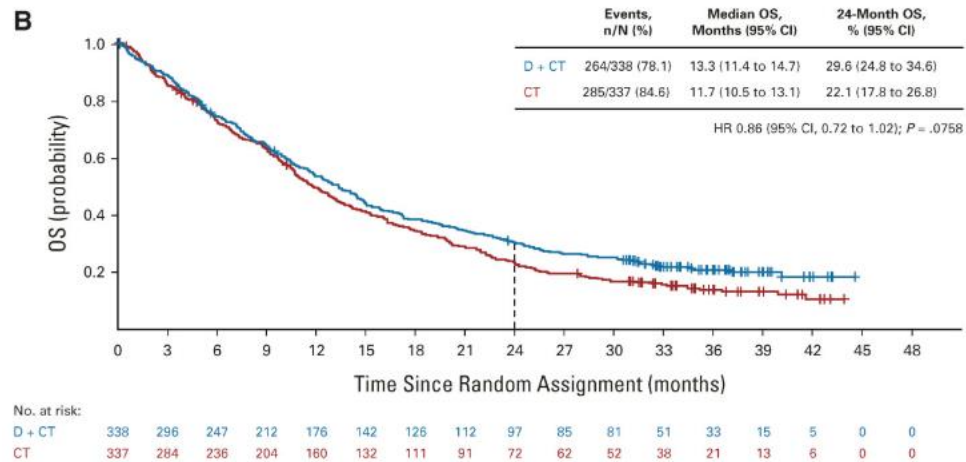
A la différence des PS > 1, chez sujet âgé :

- Efficacité similaire
- Pas de différence sur les AE



Place de l'IO dans les CPC

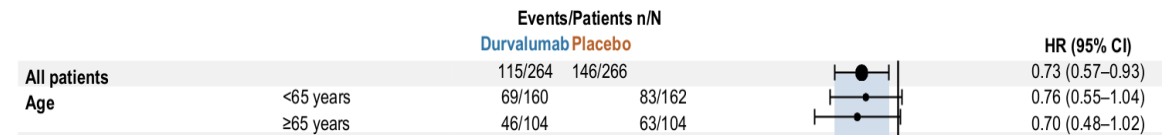
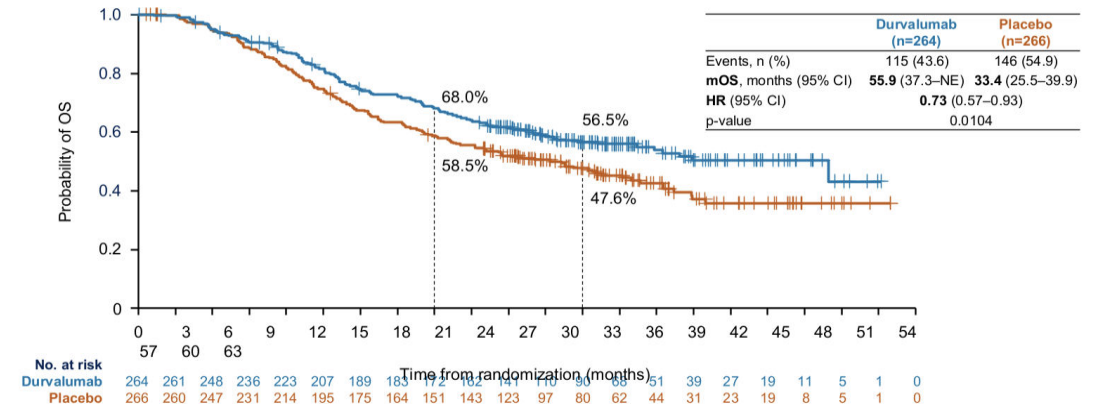
STADE IV



Johnson et al. *JCO* 2022

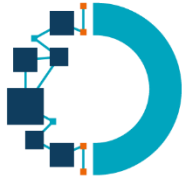
STADE LOCALISE AU THORAX

• Median duration of follow up in censored patients: 37.2 months (range 0.1–60.9)



Bénéfice persistant qqs le sel de platine utilisé
CTRT conço obligatoire ...

Cheng et al. *NEJM* 2024



CONCLUSION – TAKE HOME MESSAGES

- Pas d'arrière pensée (tolérance / efficacité) quant à l'utilisation de l'immunothérapie chez le sujet âgé
- Manque de données chez les patients de plus de 70 ans +++

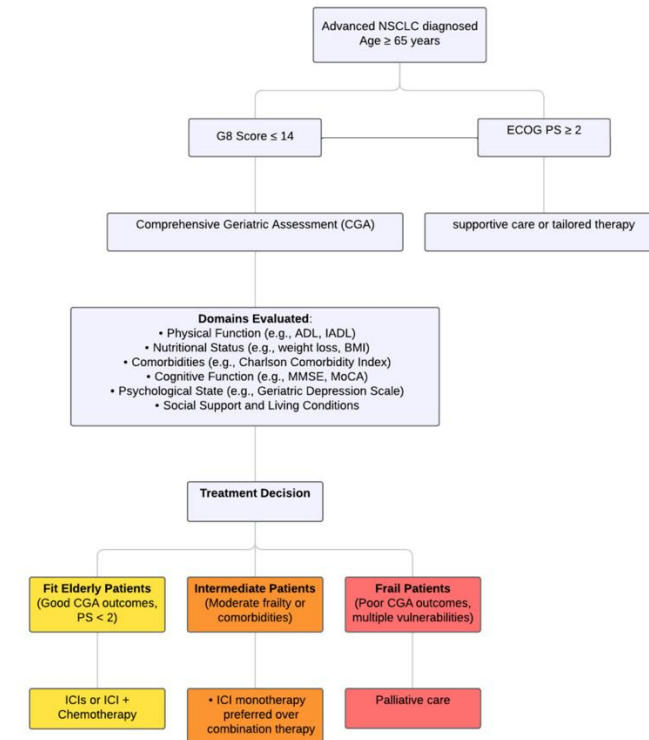


Figure 1. Flowchart of the Comprehensive Geriatric Assessment Process for Elderly Patients with NSCLC, Highlighting Key Decision Points and Treatment Pathways Based on Functional and Physiological Assessments.



CONCLUSION – TAKE HOME MESSAGES

- Pas d'arrière pensée (tolérance / efficacité) quant à l'utilisation de l'immunothérapie chez le sujet âgé
- Manque de données chez les patients de plus de 70 ans +++



RECHERCHE

GFPC 05-2023_PROMETHEE –
R. Corre

PROspective Masterprotocol for
Evaluation of systemic Therapeutics in
Elderly with Thoracic Malignancies

