Les Transversales « by IFODS »

IFODS

on behalf of Cours St-Paul

International and French Oncology Days

Journées Franco-Internationales d'Oncologie

Cancers bronchiques non à petites cellules
Immunothérapie

Pr. Nicolas Girard

Institut Curie,
INSERM U932,
Université Paris-Saclay

Liens d'intérêt

- Recherche clinique:
- Amgen
- Astra-Zeneca
- Abbvie
- Blue
- BMS
- Boehringer-Ingelheim
- Janssen
- Hoffmann-La Roche
- Lilly
- Merck
- MSD
- Novartis
- Sivan

- Symposia:
- Amgen
- Astra-Zeneca
- BMS
- Janssen
- Mirati
- MSD
- Pfizer

- Congrès:
- Astra-Zeneca
- MSD

- ITMIG: Président

- Réunions d'experts:
- Amgen
- Astra-Zeneca
- BMS
- Boehringer-Ingelheim
- Janssen
- Hoffman-La Roche
- Lilly
- Novartis
- Merck
- MSD
- Pfizer
- Sanofi

Déclaration publique d'intérêt
https://dpi.sante.gouv.fr/dpi-public-webapp/app/recherche/declarant

Les cancers thoraciques

Non à petites cellules

- Stades précoces
- Dépistage
- Localement avancés
  - Résécables
  - Non résécables
- Métastatiques
  - Oncogène addictif
  - Sans oncogène addictif

Petites cellules

- Localement avancés
- Métastatiques

Mésothéliome

Tumeurs thymiques

Immunothérapie
Cancers bronchiques non à petites cellules

Immunothérapie *en remplacement* de la chimiothérapie

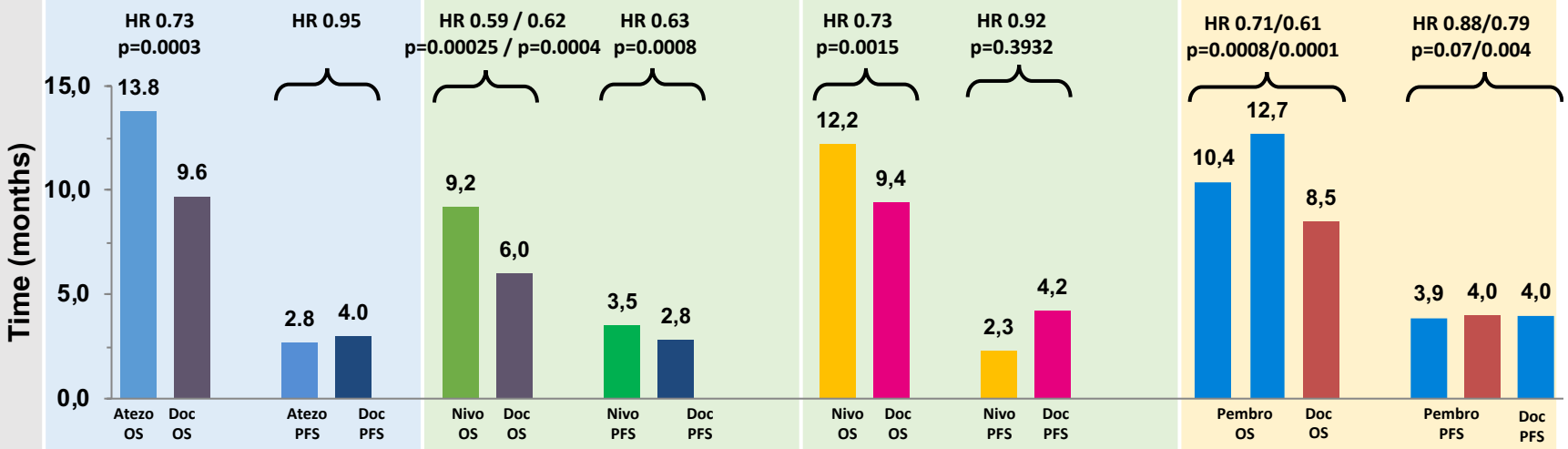
Immunothérapie en combinaison avec la chimiothérapie

#1 Immunotherapy to replace chemotherapy

Second line
vs.
Docetaxel

#1 Immunothérapie en remplacement de la chimiothérapie

Seconde ligne vs. Docetaxel

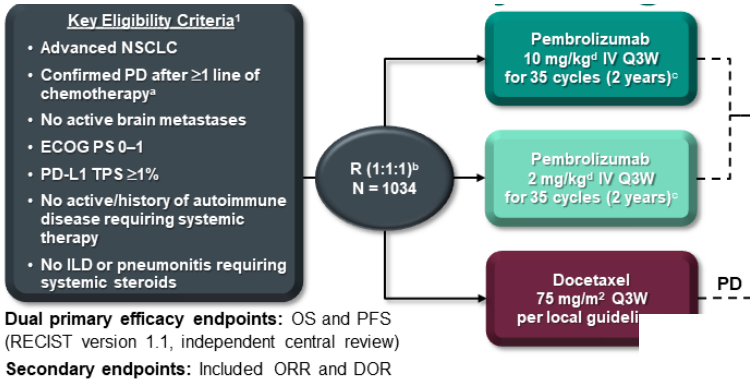
	Atezolizumab	Nivolumab		Pembrolizumab
	OAK PhIII allcomer 2/3L atezo vs. doc (n=850)	CheckMate 017 PhIII 2L Sq nivo vs. doc (n=272)	CheckMate 057 PhIII 2/3L NSq nivo vs. doc (n=582)	KEYNOTE-010 PhIII PDL1+ ≥2L pembro vs. doc (n=1034)
				
OR %	**Atezo 14% vs doc 13%**	**Nivo 20% vs doc 9%**	**Nivo 19% vs doc 12%**	**Pembro 18% vs doc 9%**
Notes	G3–4 treatment-related AEs: 15 vs 43%	G3–4 treatment-related AEs: 8 vs 56% *Reduction from baseline in lung cancer symptoms with nivolumab*	G3–4 treatment-related AEs: 10 vs 54%	G3–5 treatment-related AEs: 13-16 vs 35%
	ALL histologies ALL PD-L1	**2 trials for 2 histologies ALL PD-L1**		**ALL histologies PD-L1≥1%**

Cross-study comparisons are not intended.

Felip E et al. J Clin Oncol 2017;
Herbst RS et al.
Rittmeyer A et al. *Lancet.* 2017;389:255

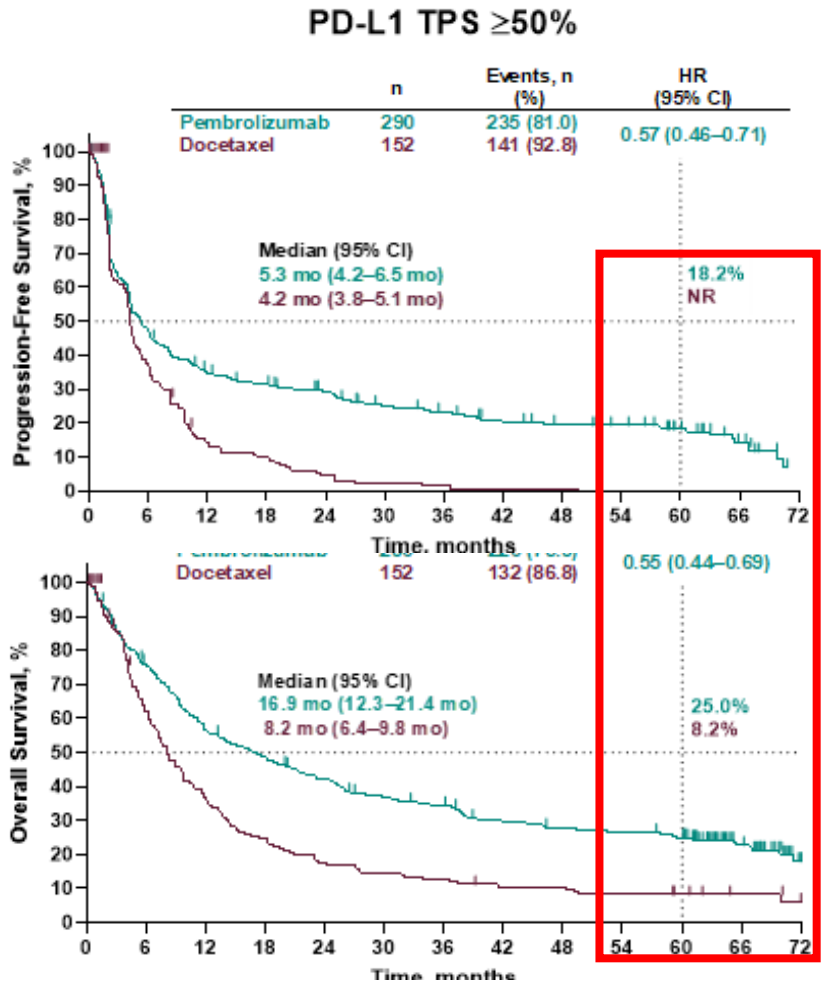
Immune checkpoint inhibitors
Prolonged survival in responders: 5-year OS is reachable

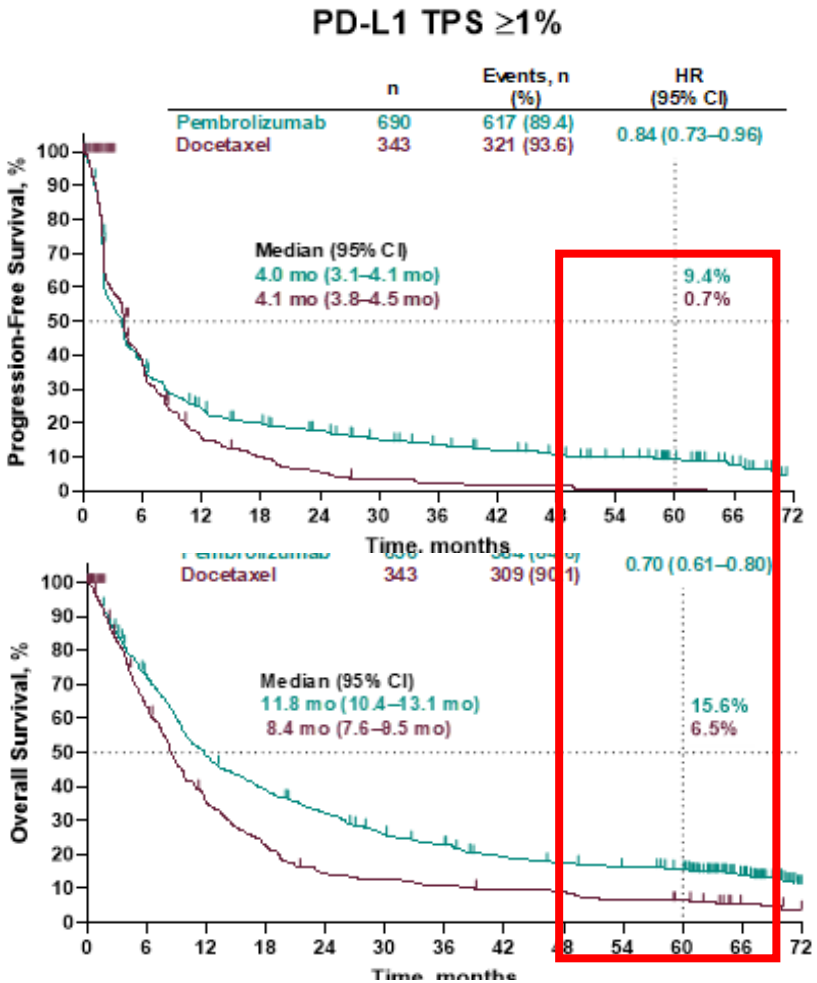
KEYNOTE-010: Pembrolizumab



Dual primary efficacy endpoints: OS and PFS (RECIST version 1.1, independent central review)

Secondary endpoints: Included ORR and DOR





Herbst R et al. Abstr FP13.01 WCLC 2020

#1 Immunothérapie en remplacement de la chimiothérapie

Seconde ligne
vs.
Docetaxel

Première ligne
vs.
chimiothérapie

#1 Immunothérapie en remplacement de la chimiothérapie

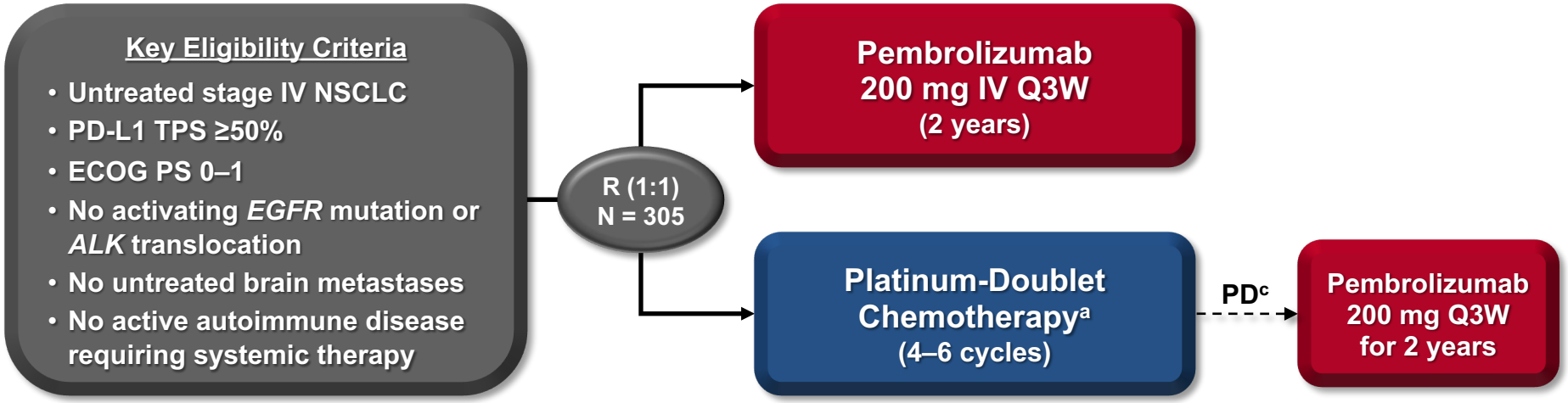
Seconde ligne
vs.
Docetaxel

Sélection
PD-L1≥50%

Première ligne
vs.
chimiothérapie

Immunotherapy to replace chemotherapy
Selection based on PD-L1≥50%

KEYNOTE-024: design



End Points

Primary:	PFS (RECIST v1.1, blinded independent central review)
Key secondary:	OS
Secondary:	ORR, safety
Exploratory:	DOR

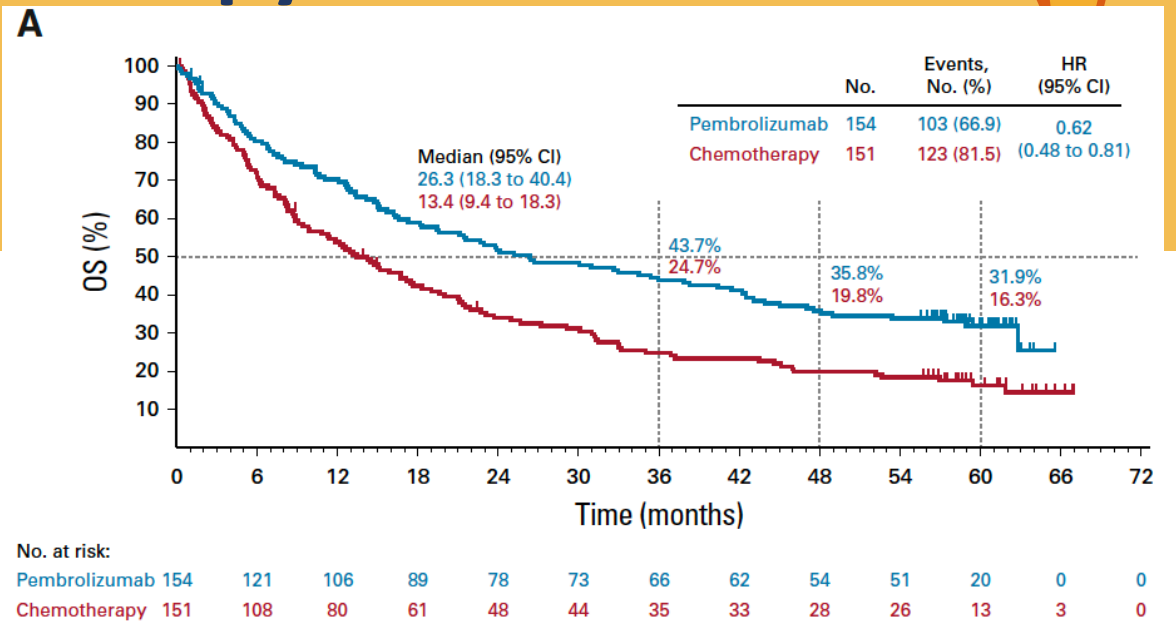
[a]Optional pemetrexed maintenance therapy for nonsquamous disease. [b]Permitted for nonsquamous disease only.
[c]Prior to the DMC recommendation and amendment 6, which permitted those in the chemotherapy arm to be offered pembrolizumab (based on interim analysis 2 data), patients were eligible for crossover when PD was confirmed by blinded, independent central radiology review.

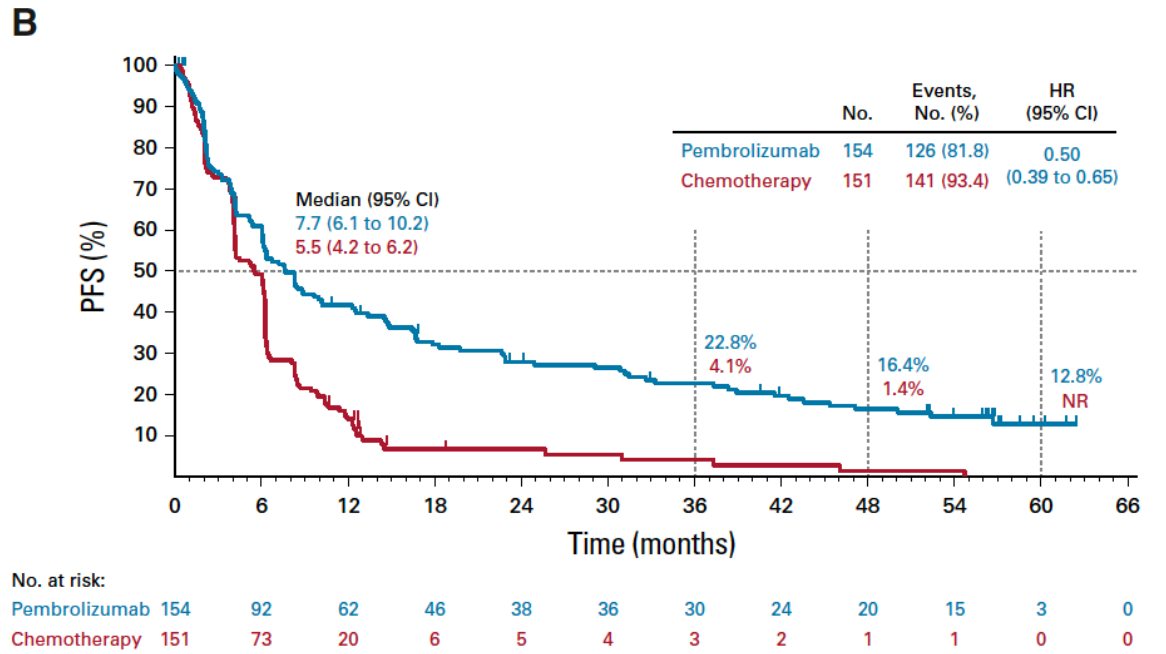
Reck et al. N Engl J Med 2016; 375:1823

Immunotherapy to replace chemotherapy
Selection based on PD-L1≥50%

Five-Year Outcomes With Pembrolizumab Versus Chemotherapy for Metastatic Non–Small-Cell Lung Cancer With PD-L1 Tumor Proportion Score ≥ 50%

Martin Reck, MD, PhD[1]; Delvys Rodríguez-Abreu, MD, PhD[2]; Andrew G. Robinson, MD, MSc[3]; Rina Hui, MBBS, PhD[4]; Tibor Csőszi, MD[5]; Andrea Fülöp, MD[6]; Maya Gottfried, MD[7]; Nir Peled, MD, PhD[8]; Ali Tafreshi, MD[9]; Sinead Cuffe, MD[10]; Mary O'Brien, MD[11]; Suman Rao, MD[12]; Katsuyuki Hotta, MD, PhD, MPH[13]; Ticiana A. Leal, MD[14]; Jonathan W. Riess, MD, MS[15]; Erin Jensen, MS[16]; Bin Zhao, MD, PhD[16]; M. Catherine Pietanza, MD[16]; and Julie R. Brahmer, MD[17]

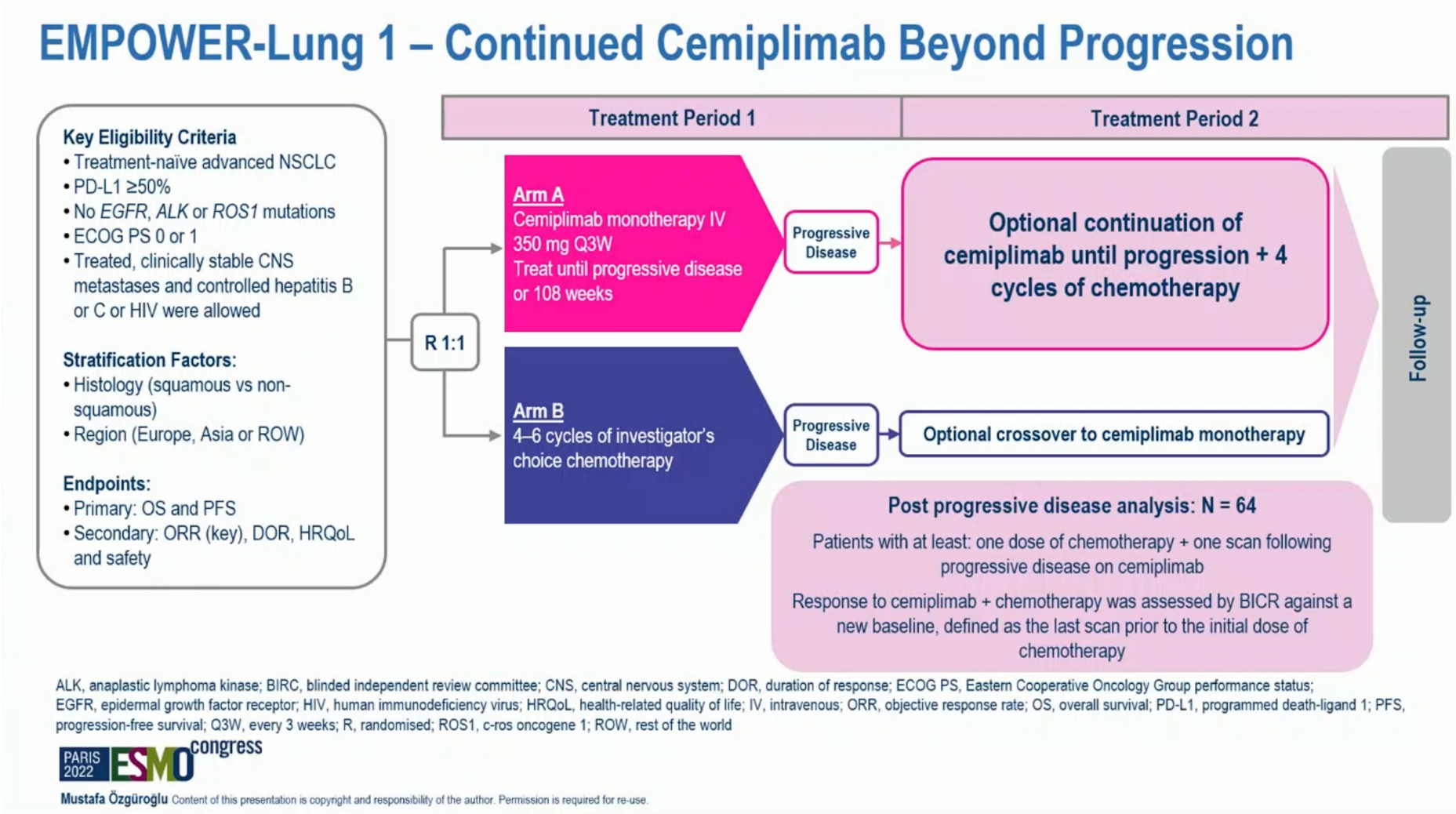




J Clin Oncol 39:2339-2349

Immunotherapy to replace chemotherapy
Selection based on PD-L1≥50%

EMPOWER-Lung-1



Ozroglu et al. ESMO 2022

Immunotherapy to replace chemotherapy
Selection based on PD-L1≥50%

EMPOWER-Lung-1

	Cemiplimab Beyond Progression N=64	
OS	Period 1+2 Randomization to Death	Period 2 Day 1 of Continued Treatment to Death
Median (95% CI, months)	27.4 (23.0, 31.8)*	15.1 (11.3, 18.7)
Estimated Survival Probability, % (95% CI)		
6 months	100 (NE, NE)	91.9 (81.6, 96.5)
12 months	91.8 (81.4, 96.5)	56.8 (43.0, 68.5)
24 months	60.5 (46.6, 71.8)	26.2 (14.3, 39.8)
36 months	32.3 (20.1, 45.1)	NE (NE, NE)

*Includes the 15.1 months of survival beyond progression. CI, confidence interval; OS, overall survival; NE, non-evaluable

Data cutoff date: March 4, 2022

Continued cemiplimab with addition of chemotherapy beyond progression appears superior to historical data for chemotherapy in the 2nd line setting where median OS is 8.4 months (range: 5.6 - 11.2) (Bersanelli et al., Lung Cancer, 2020)

	Cemiplimab Beyond Progression N=64	
PFS	Period 1	Period 2
Median (95% CI, months)	6.2 (4.2, 8.2)	6.6 (6.1, 9.3)
Estimated Event-Free Probability, % (95% CI)		
6 months	50.7 (37.0, 62.9)	66.2 (53.0, 76.5)
12 months	24.1 (13.3, 36.6)	31.2 (19.5, 43.7)
18 months	0 (NE, NE)	15.7 (7.2, 27.2)
24 months	0 (NE, NE)	8.4 (2.0, 20.7)

CI, confidence interval; PFS, progression free survival; NE, non-evaluable

	Cemiplimab Beyond Progression N=64	
	Period 1	Period 2
Objective Response Rate (ORR: CR+PR), n (%)	**19 (29.7)**	**20 (31.3)**
95% CI for ORR (range %)	(18.9, 42.4)	(20.2, 44.1)
Best Overall Tumor Response, n (%)		
Complete Response (CR)	0	3 (4.7)
Partial Response (PR)	19 (29.7)	17 (26.6)
Stable Disease (SD)	28 (43.8)	35 (54.7)
Non-CR/Non-PD	0	0
Progressive Disease (PD)	13 (20.3)	9 (14.1)
Not Evaluable (NE)	4 (6.3)	0

CI, confidence interval

Data cutoff date: March 1, 2020 – Left Column; Oct 1, 2021 – Right column

Ozroglu et al. ESMO 2022

#1 Immunothérapie en remplacement de la chimiothérapie

Seconde ligne
vs.
Docetaxel

Première ligne
vs.
chimiothérapie

Sélection
PD-L1≥50%

Comment
optimiser?

Duration of immunotherapy in the first-line setting
DICIPLE

Trial design and endpoints

IFCT-1701 D.I.C.I.P.L.E
Double Immune Checkpoint Inhibitors in any PD-L1 stage IV non-small Lung CancEr

Multicenter, non-inferiority, randomized phase III trial

Histogically-proven stage IV NSCLC:
- Measurable disease
- PS 0-1
- 18 – 75 years
- Any PDL1
- w/o EGFR/ALK alterations
- chemo & i.o naive

n = 1360

Nivolumab 3mg /kg q2w + **Ipilimumab** 1 mg/kg q6w

At 6 months patients with disease control Randomized 1:1

n = 868

Stratification factors:
- SCC/non-SCC
- PD-L1 (<1%, 1-49%, ≥50%)
- Ever smokers/never-smokers
- response: PR/SD

Arm A → **Nivolumab** 3mg /kg q2w + **Ipilimumab** 1 mg/kg q6w → *Prog* → **Platinum-based doublet recommended**

Arm B → **Observation** → *Prog* → **Nivolumab** 3mg /kg q2w + **Ipilimumab** 1 mg/kg q6w

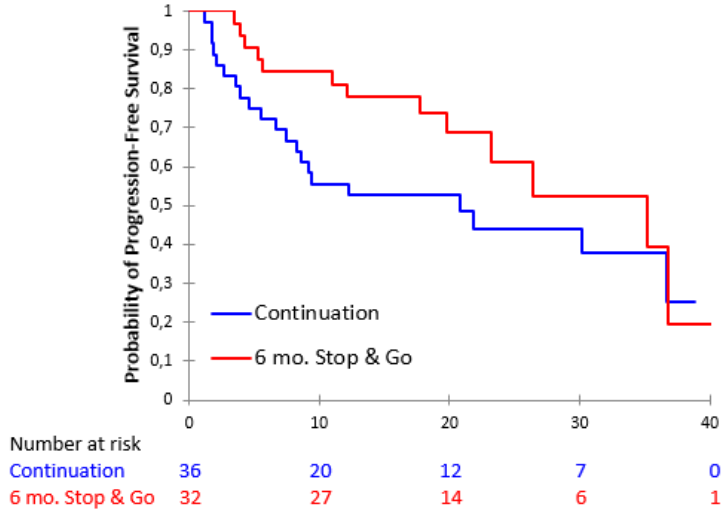
- Primary endpoint : **PFS from randomization**
- Secondary endpoints : safety and tolerance, overal quality of life, PD-L1 tumour expression prognostic and predictive value
- CT-scan f.u q8 weeks for 1 year, then q12 weeks i arms

Exploratory biomarkers studies

ClinicalTrials.gov: NCT03469960

Efficacy: Progression-Free Survival

Per protocol population (primary endpoint)



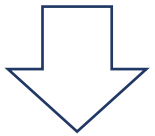
	A – Continuation (N= 36)	B – Stop & Go (N = 32)
Event : N (%)	21 (58.3)	13 (40.6)
Median PFS: months [95% CI]	**20.8** co	**35.2** [19.8-NR]
6-m PFS: % [95% CI]	72.2 [54.5-84.0]	84.4 [66.5-93.2]
12-m PFS: % [95% CI]	**55.6 [38.0-69.9]**	**81.2 [62.9-91.1]**
p=0.12		

Median follow-up [95% CI] : 25 months [20-31] from randomization

Zalcman et al. ESMO 2022

#1 Immunothérapie en remplacement de la chimiothérapie

Seconde ligne
vs.
Docetaxel



**Première ligne
vs.
chimiothérapie**

**Sélection
PD-L1≥50%**

Comment
optimiser?

Sélection
PD-L1
inférieur?

Immunotherapy to replace chemotherapy
Selection based on PD-L1 1-49%

KEYNOTE-042 Study Design

Key Eligibility Criteria
- Untreated locally advanced or metastatic NSCLC of any histology
- PD-L1 TPS ≥1%[a]
- No sensitizing *EGFR* or *ALK* alterations
- ECOG PS 0 or 1
- No untreated or unstable CNS metastases
- No history of pneumonitis that required systemic corticosteroids

Stratification Factors
- Region (east Asia vs rest of the world)
- ECOG PS (0 vs 1)
- Histology (squamous vs nonsquamous)
- PD-L1 TPS (≥50% vs 1%–49%)

Randomize 1:1

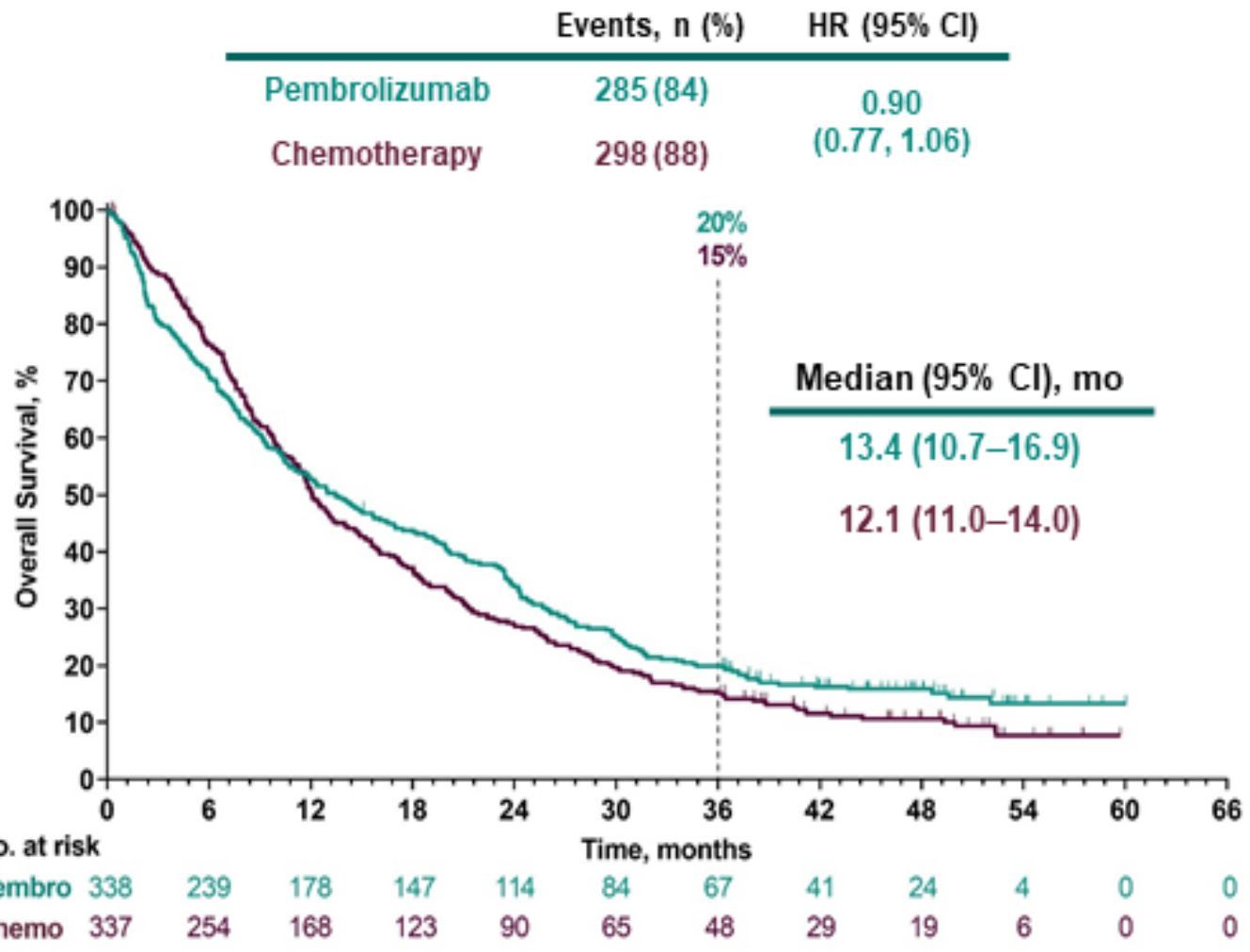
N = 637 → Pembrolizumab 200 mg Q3W for up to 35 cycles

N = 637 → Carboplatin AUC 5 or 6 Q3W + Paclitaxel 200 mg/m² Q3W[b] OR Carboplatin AUC 5 or 6 Q3W + Pemetrexed 500 mg/m² Q3W[b] for up to 6 cycles

End points
- Primary: OS in PD-L1 TPS ≥50%, ≥20%, and ≥1%
- Secondary: PFS and ORR in TPS ≥50%, ≥20%, and ≥1%; safety in TPS ≥1%

Current analysis planned to occur ~45 months after study start

CNS, central nervous system.



Cho BC et al. Abstr FP13.04 WCLC 2020

Immunothérapie
Cancers bronchiques non à petites cellules

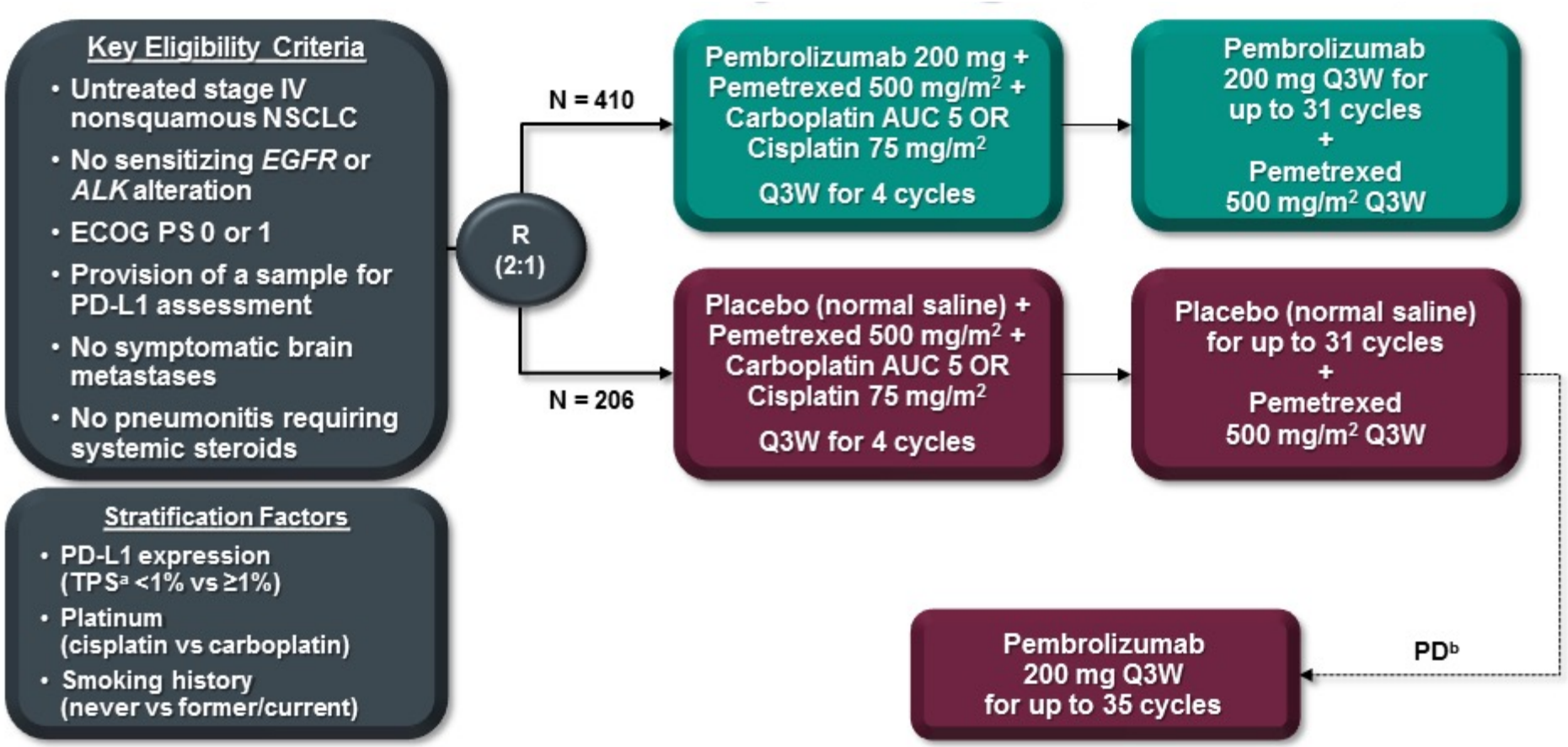
Immunothérapie en remplacement de la chimiothérapie

Immunothérapie *en combinaison* avec la chimiothérapie

Immunothérapie en combinaison avec la chimiothérapie Non-épidermoïdes

Placebo
Stratification on PD-L1
Exclusion of EGFR/ALK

KEYNOTE-189: design



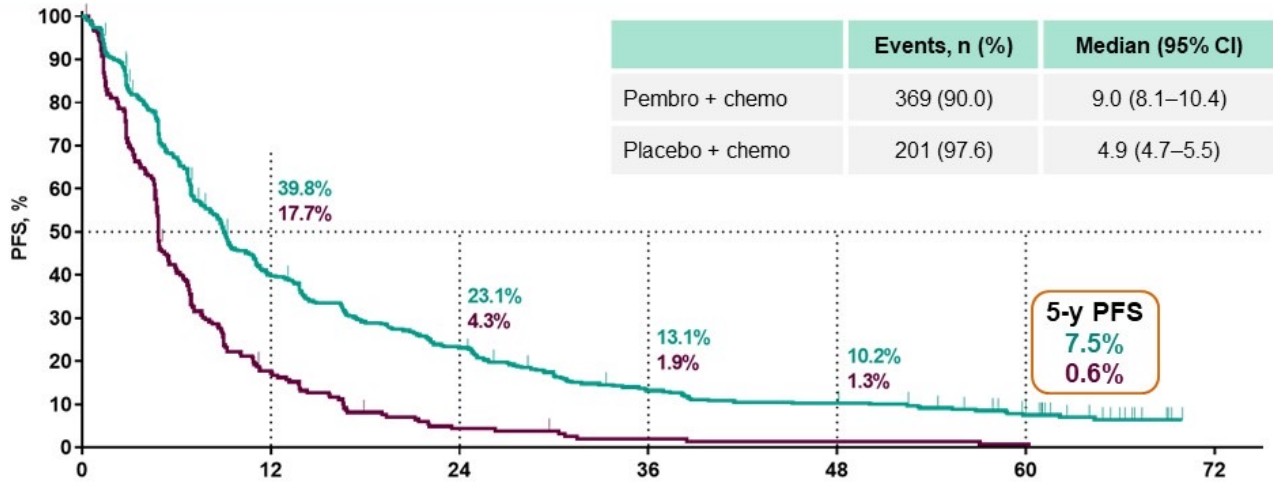
[a]Percentage of tumor cells with membranous PD-L1 staining assessed using the PD-L1 IHC 22C3 pharmDx assay. [b]Patients could crossover during the induction or maintenance phases. To be eligible for crossover, PD must have been verified by blinded, independent central radiologic review and all safety criteria had to be met.

Gandhi et al. NEJM 2018;378:2078

Immunothérapie en combinaison avec la chimiothérapie Non-épidermoïdes

KEYNOTE-189: résultats

PFS[a]: ITT Population



	Events, n (%)	Median (95% CI)	HR (95% CI)
Pembro + chemo	369 (90.0)	9.0 (8.1–10.4)	0.50 (0.42–0.60)
Placebo + chemo	201 (97.6)	4.9 (4.7–5.5)	

No. at risk							
Pembro + chemo	410	158	91	49	37	21	0
Placebo + chemo	206	35	8	3	2	1	0

	PD-L1 TPS ≥50%		PD-L1 TPS 1%–49%		PD-L1 TPS <1%	
	Pembro + chemo (n = 132)	Placebo + chemo (n = 70)	Pembro + chemo (n = 128)	Placebo + chemo (n = 58)	Pembro + chemo (n = 127)	Placebo + chemo (n = 63)
PFS HR (95% CI)	0.35 (0.25–0.49)		0.57 (0.41–0.80)		0.67 (0.49–0.92)	
5-y PFS rate,[b] %	12.8	0	6.5	1.9	2.4	0

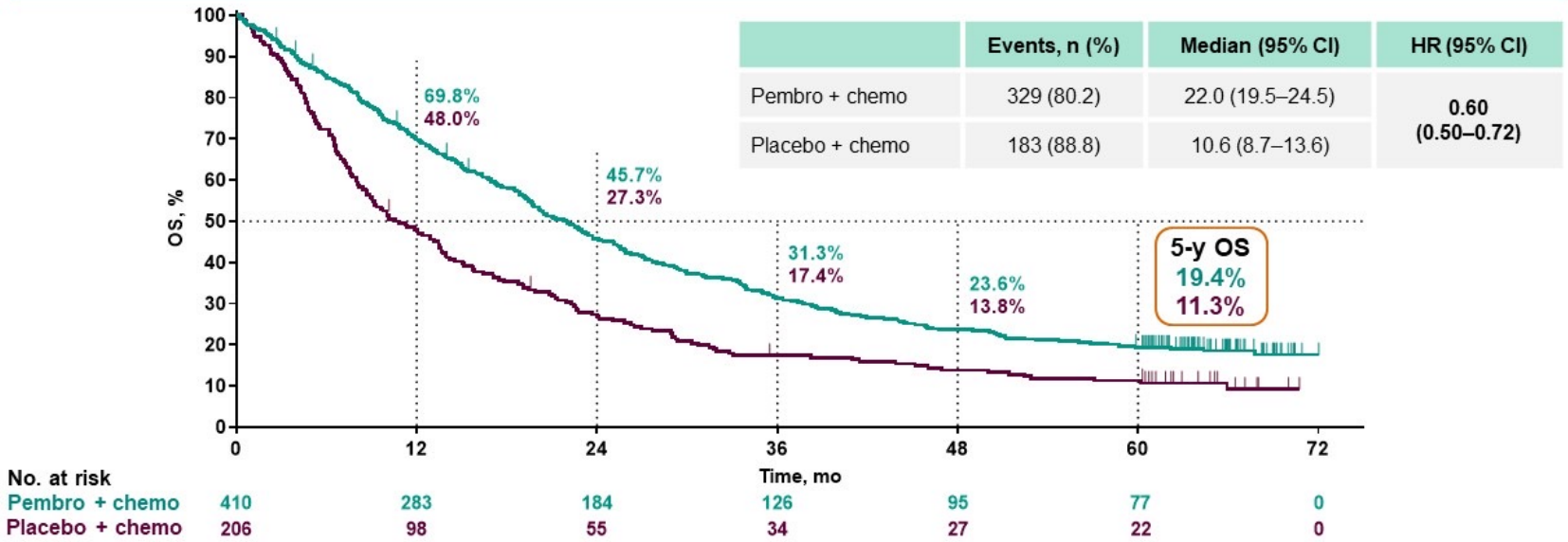
[a]Per RECIST version 1.1 by BICR. [b]Kaplan-Meier estimate. Data cutoff date: March 8, 2022.

Garassino et al. ESMO 2022

Immunothérapie en combinaison avec la chimiothérapie Non-épidermoïdes

KEYNOTE-189: résultats

OS: ITT Population



	Events, n (%)	Median (95% CI)	HR (95% CI)
Pembro + chemo	329 (80.2)	22.0 (19.5–24.5)	0.60 (0.50–0.72)
Placebo + chemo	183 (88.8)	10.6 (8.7–13.6)	

	PD-L1 TPS ≥50%		PD-L1 TPS 1%–49%		PD-L1 TPS <1%	
	Pembro + chemo (n = 132)	Placebo + chemo (n = 70)	Pembro + chemo (n = 128)	Placebo + chemo (n = 58)	Pembro + chemo (n = 127)	Placebo + chemo (n = 63)
OS HR (95% CI)	0.68 (0.49–0.96)		0.65 (0.46–0.90)		0.55 (0.39–0.76)	
5-y OS rate,[a] %	29.6	21.4	19.8	7.7	9.6	5.3

[a]Kaplan-Meier estimate. Data cutoff date: March 8, 2022.

Garassino et al. ESMO 2022

Immunothérapie en combinaison avec la chimiothérapie Epidermoïdes

KEYNOTE-407: design

Placebo
Stratification on PD-L1

Key Eligibility Criteria

- Untreated stage IV NSCLC with squamous histology
- ECOG PS 0 or 1
- Provision of a sample for PDL-1 assessment
- No symptomatic brain metastases
- No pneumonitis requiring systemic steroids

R (1:1)

Pembrolizumab 200 mg Q3W[b] + Carboplatin AUC 6 Q3W + Paclitaxel 200 mg/m² Q3W OR nab-paclitaxel 100 mg/m² Q1W[c] for 4 cycles (each 3 wks)

→ **Pembrolizumab 200 mg Q3W for up to 31 cycles[d]**

Placebo (normal saline) Q3W + Carboplatin AUC 6 Q3W + Paclitaxel 200 mg/m² Q3W OR nab-paclitaxel 100 mg/m² Q1W[c] for 4 cycles (each 3 wks)

→ **Placebo (normal saline) Q3W for up to 31 cycles[d]**

PD[e] → **Optional Crossover[b] Pembrolizumab 200 mg Q3W for up to 35 cycles**

Stratification Factors

- PD-L1 expression: TPS[a] <1% vs TPS ≥1%
- Choice of taxane: paclitaxel vs nab-paclitaxel
- Geographic region: East Asia vs rest of world

Endpoints

- Primary: PFS (RECIST v1.1, BICR) and OS
- Secondary: ORR and DOR (RECIST v1.1, BICR), safety

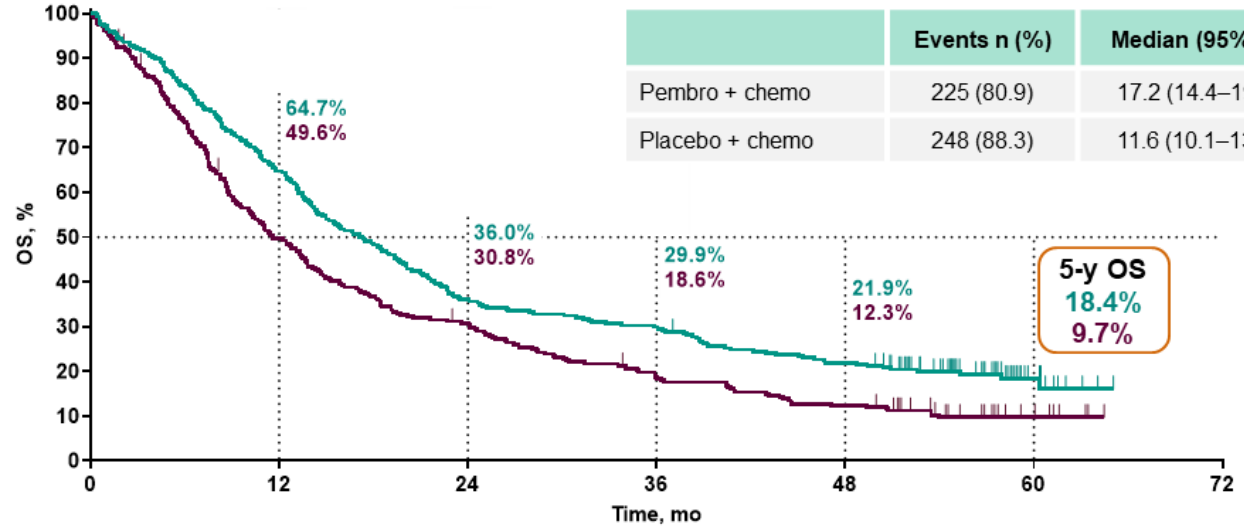
AUC, area under the curve; BICR, blinded independent central review; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; PD, progressive disease; Q1W, every week; Q3W, every 3 weeks; R, randomization; TPS, tumor proportion score.
[a]Percentage of tumor cells with membranous PD-L1 staining assessed using the PD-L1 IHC 22C3 pharmDx assay (Agilent Technologies, Carpinteria, CA, USA).
[b]Patients with documented disease progression who were benefiting clinically could continue open-label pembrolizumab monotherapy to complete a total of 35 cycles.

Paz-Ares et al. ESMO 2019

Immunotherapy in addition to chemotherapy Squamous cell carcinomas

KEYNOTE-407: results

OS: ITT Population



	Events n (%)	Median (95% CI)	HR (95% CI)
Pembro + chemo	225 (80.9)	17.2 (14.4–19.7)	0.71 (0.59–0.85)
Placebo + chemo	248 (88.3)	11.6 (10.1–13.7)	

No. at risk							
Pembro + chemo	278	180	100	83	60	10	0
Placebo + chemo	281	137	84	50	33	7	0

	PD-L1 TPS ≥50%		PD-L1 TPS 1%–49%		PD-L1 TPS <1%	
	Pembro + chemo (n = 73)	Placebo + chemo (n = 73)	Pembro + chemo (n = 103)	Placebo + chemo (n = 104)	Pembro + chemo (n = 95)	Placebo + chemo (n = 99)
OS HR (95% CI)	0.68 (0.47–0.97)		0.61 (0.45–0.83)		0.83 (0.61–1.13)	
5-y OS rate,[a] %	23.3	8.3	20.6	7.6	10.7	13.1

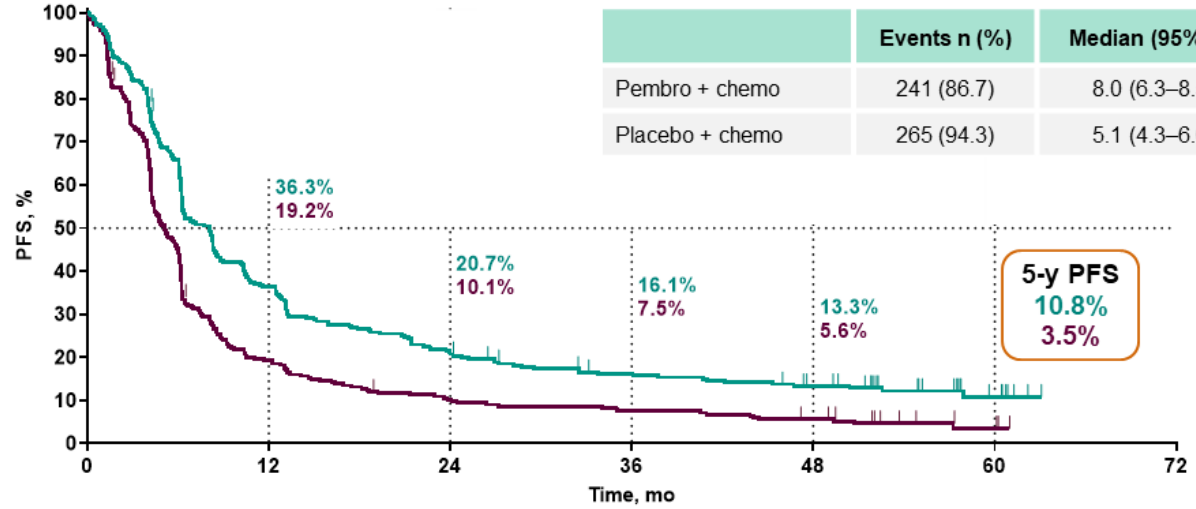
[a]Kaplan-Meier estimate. Data cutoff date: February 23, 2022.

Novello et al. ESMO 2022

Immunotherapy in addition to chemotherapy Squamous cell carcinomas

KEYNOTE-407: results

PFS[a]: ITT Population



	Events n (%)	Median (95% CI)	HR (95% CI)
Pembro + chemo	241 (86.7)	8.0 (6.3–8.5)	0.62 (0.52–0.74)
Placebo + chemo	265 (94.3)	5.1 (4.3–6.0)	

No. at risk							
Pembro + chemo	278	100	56	40	30	7	0
Placebo + chemo	281	53	27	20	14	1	0

	PD-L1 TPS ≥50%		PD-L1 TPS 1%–49%		PD-L1 TPS <1%	
	Pembro + chemo (n = 73)	Placebo + chemo (n = 73)	Pembro + chemo (n = 103)	Placebo + chemo (n = 104)	Pembro + chemo (n = 95)	Placebo + chemo (n = 99)
PFS HR (95% CI)	0.48 (0.33–0.69)		0.60 (0.45–0.81)		0.70 (0.52–0.95)	
5-y PFS rate[b], %	15.0	NR	11.8	NR	7.1	6.7

[a]Per RECIST v1.1 by BICR. [b]Kaplan-Meier estimate. Data cutoff date: February 23, 2022.

Novello et al. ESMO 2022

Immunothérapie
Cancers bronchiques non à petites cellules

Immunothérapie en remplacement de la chimiothérapie

Immunothérapie *en combinaison* avec la chimiothérapie

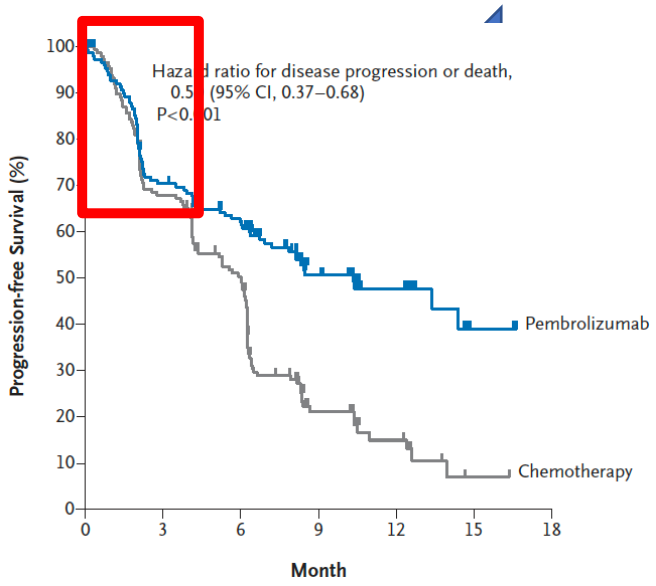
#2 Immunotherapy in addition to chemotherapy

Immunotherapy to replace chemotherapy

Immunotherapy *in addition* to chemotherapy

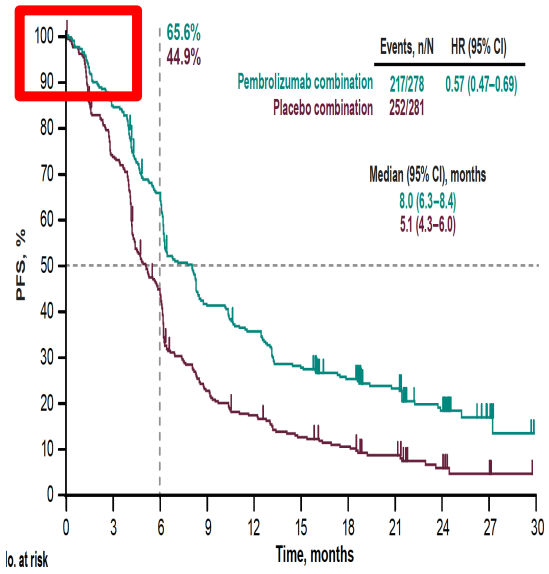
PD-L1≥50%
Question: pembrolizumab alone or with chemotherapy?

Pembrolizumab alone
All histologies



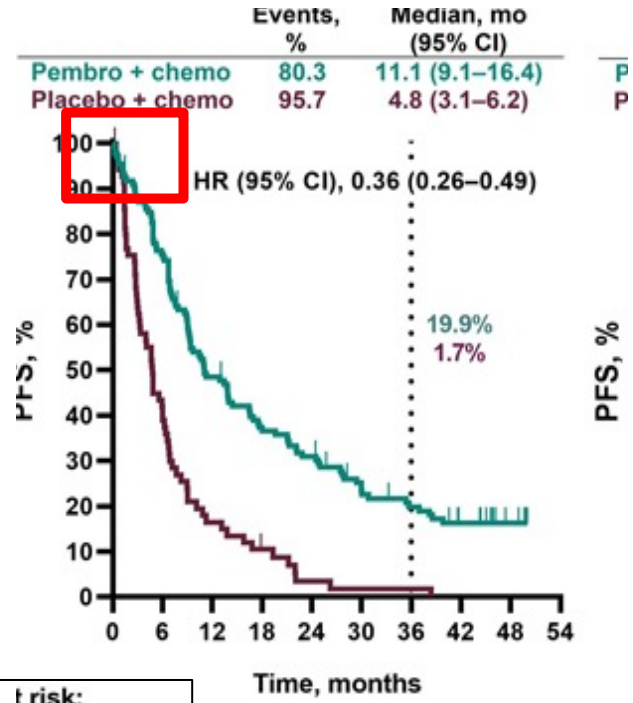
30% early PD

Pembrolizumab plus chemo



Squamous

Non-Squamous

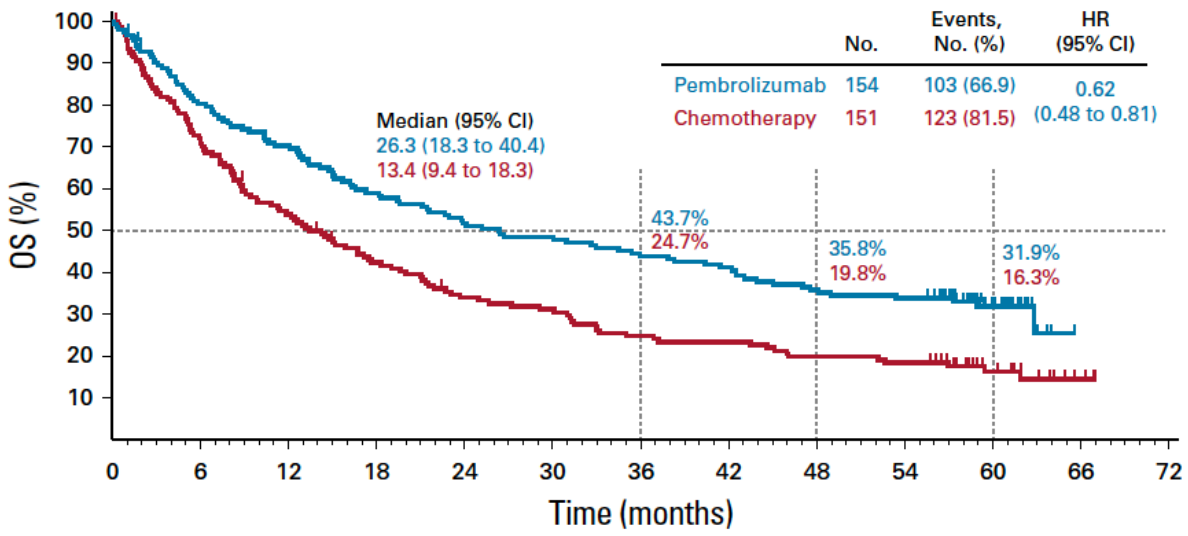


10% early PD

Reck et al. WCLC 2019; Gfadgeel et al. ASCO 2019; Reck et al. NEJM 2016;375:1823; Paz-Ares et al. ESMO 2019; Peters et al. ESMO 2019

PD-L1≥50%
Question: pembrolizumab alone or with chemotherapy?

Pembrolizumab alone
All histologies



Pembrolizumab plus chemo
Squamous

	PD-L1 TPS ≥50%	
	Pembro + chemo (n = 73)	Placebo + chemo (n = 73)
OS HR (95% CI)	0.68 (0.47–0.97)	
5-y OS rate,[a] %	23.3	8.3

plan-Meier estimate. Data cutoff date: February 23, 2022.

Non-Squamous

	PD-L1 TPS ≥50%	
	Pembro + chemo (n = 132)	Placebo + chemo (n = 70)
OS HR (95% CI)	0.68 (0.49–0.96)	
5-y OS rate,[a] %	29.6	21.4

[a]Kaplan-Meier estimate. Data cutoff date: March 8, 2022.

Garassino et al. ESMO 2022; Novello et al. ESMO 2022

Post-IO stratégies?

Targeted agents for oncogene addictions
KRAS, BRAF, ROS1
MET, HER2, RET, EGFR exon 20, NTRK…

Rechallenge

Docetaxel
Single agent chemos

New targets for non oncogene addicted tumors
CEACAM, TROP-2, HLA-A2, MET, HER3

TROP2: Datopotamab deruxtecan

Background

- Dato-DXd is an ADC composed of a humanized TROP2 IgG1 mAb covalently linked to a topoisomerase I inhibitor payload via a stable tetrapeptide-based cleavable linker
- TROPION-Lung02 is a phase 1b study evaluating Dato-DXd + pembrolizumab (pembro) ± platinum CT[a] in advanced NSCLC without actionable genomic alterations (NCT04526691)
- Study approach: safety of Dato-DXd + pembro "doublets" was established prior to evaluation of platinum-containing "triplets"
  - Safety of Dato-DXd 4-mg/kg combinations was established prior to evaluation of 6-mg/kg combinations

Key eligibility
- Advanced/metastatic NSCLC
- Dose confirmation[b]: ≤2 lines of prior therapy[c]
- Dose expansion
  - ≤1 line of platinum-based CT (cohorts 1 and 2)[c]
  - No prior therapy (cohorts 3-6)[c]

	Dato-DXd IV Q3W	+	pembro IV Q3W	+	platinum CT IV Q3W	
Cohort 1 (n=20)[d]:	4 mg/kg	+	200 mg			"Doublet"
Cohort 2 (n=20)[d]:	6 mg/kg	+	200 mg			
Cohort 3 (n=17)[d]:	4 mg/kg	+	200 mg	+	carboplatin AUC 5	"Triplet"
Cohort 4 (n=20)[d]:	6 mg/kg	+	200 mg	+	carboplatin AUC 5	
Cohort 5 (n=7)[d]:	4 mg/kg	+	200 mg	+	cisplatin 75 mg/m²	
Cohort 6 (n=4)[d]:	6 mg/kg	+	200 mg	+	cisplatin 75 mg/m²	

- **Primary objectives:** safety and tolerability
- **Secondary objectives:** efficacy, pharmacokinetics, and anti-drug antibodies

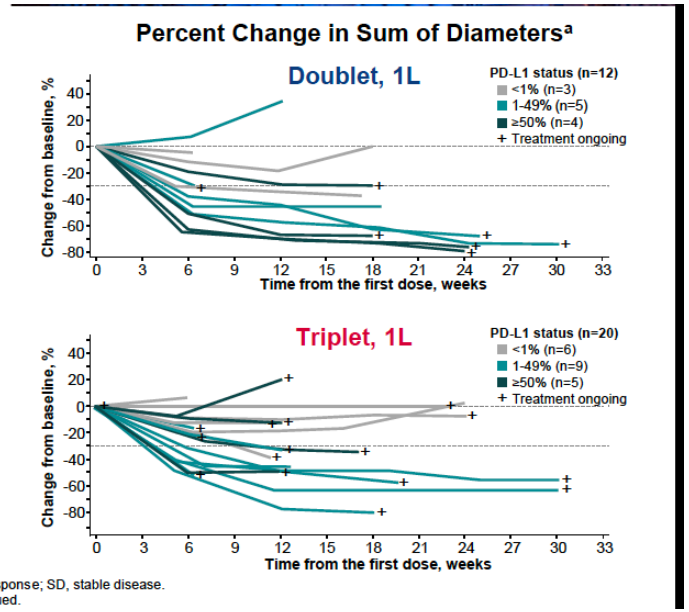
Antitumor Activity

In the overall population:
ORRs (confirmed + pending) of 37% and 41% were seen with doublet (n=38) and triplet (n=37) therapy, respectively; both groups had 84% DCR

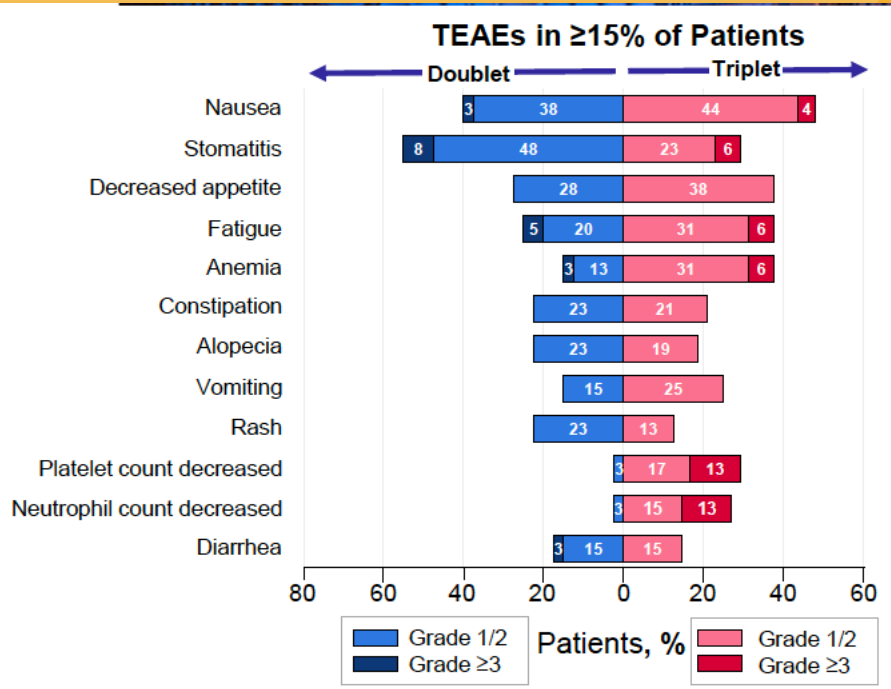
BOR With 1L Therapy For Advanced NSCLC[a,b]

Response, n (%)	Doublet (n=13)	Triplet (n=20)
ORR confirmed + pending	**8 (62%)**	**10 (50%)**
CR	0	0
PR confirmed	8 (62%)	7 (35%)
PR pending	0	3 (15%)
SD	5 (39%)	8 (40%)
DCR	13 (100%)	18 (90%)

- As 1L therapy, the doublet and triplet yielded ORRs (confirmed + pending) of 62% and 50%, respectively
- As 2L+ therapy, respective ORRs (confirmed + pending) were 24% and 29%



Data cutoff: May 2, 2022.
BOR, best overall response; CR, complete response; DCR, disease control rate; ORR, overall response rate; PR, partial response; SD, stable disease.
[a] By investigator. [b] BOR is based on response evaluable patients who have ≥1 postbaseline tumor assessment or discontinued.



Levy et al. WCLC 2022

CAECAM-5

Tusamitamab ravtansine

ABSTRACT 9039

Safety and efficacy of tusamitamab ravtansine (SAR408701) in long-term treated patients with nonsquamous non-small cell lung cancer expressing carcinoembryonic antigen-related cell adhesion molecule 5

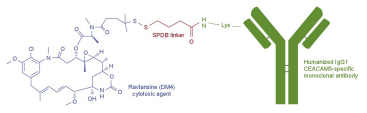
Charles Ricordel[1], Fabrice Barlesi[2], Sophie Cousin[3], Byoung Chul Cho[4], Emiliano Calvo[5], Tae Min Kim[6], Carole Hélissey[7], Jin-Soo Kim[8], Maria Vieito[9], Valentina Boni[10], Francois Ghiringhelli[11], Mustapha Chadjaa[12], Nina Masson[13], Christine Soufflet[12], and Anas Gazzah[14]

[1]Service de Pneumologie, CHU Rennes, Rennes, France; [2]Aix-Marseille University, INSERM, CNRS, CRCM, APHM, CEPCM CLIP2, Marseille, France; [3]Department of Medicine, Institut Bergonié, Bordeaux, France; [4]Severance Hospital, Yonsei University Health System, Seoul, Republic of Korea; [5]START Madrid-CIOCC, Centro Integral Oncológico Clara Campal, Madrid, Spain; [6]Department of Internal Medicine, Seoul National University Hospital, Seoul, Republic of Korea; [7]Clinical Research Unit, Department of Medical Oncology, HIA Bégin, Saint-Mandé, France; [8]Department of Internal Medicine, Seoul National University Hospital and Boramae Medical Center, Seoul, Republic of Korea; [9]Vall d'Hebron Institute of Oncology, Barcelona, Spain; [10]NEXT Madrid, Universitario Hospital Quirónsalud Madrid, Madrid, Spain. At the time of the study: START Madrid-CIOCC, Centro Integral Oncológico Clara Campal, Madrid, Spain; [11]Centre Georges-Francois Leclerc, Dijon, France; [12]Sanofi, Paris, France; [13]IT&M Stats on behalf of Sanofi, Paris, France; [14]Department of Drug Development (DITEP), Gustave Roussy, Villejuif, France

BACKGROUND

- Carcinoembryonic antigen-related cell adhesion molecule 5 (CEACAM5), a cell surface glycoprotein, is overexpressed in several tumor types, including nonsquamous non-small cell lung cancer (NSQ NSCLC)[1]
- Tusamitamab ravtansine (SAR408701) is a novel antibody-drug conjugate that selectively targets CEACAM5 (**Figure 1**)[2]

Figure 1. Structure of tusamitamab ravtansine



Drug-to-antibody ratio is 3.8.[2]
CEACAM5, carcinoembryonic antigen-related cell adhesion molecule 5; DM4, ravtansine; IgG1, immunoglobulin G1; SPDB, N-succinimidyl 4-(2-pyridyldithio)butyrate.

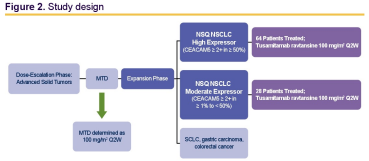
- In previously reported results from an open-label Phase 1/2 study (NCT02187848), tusamitamab ravtansine showed promising antitumor activity in patients with heavily pretreated NSQ NSCLC[4]
  - Among 64 patients with high CEACAM5 expression, 13 (20.3%) had a confirmed partial response (PR) and 28 (43.8%) had stable disease (SD)
  - Of 28 moderate expressors of CEACAM5, 2 (7.1%) had confirmed PR and 15 (53.6%) had SD
- Herein we report results for patients with NSQ NSCLC and high or moderate CEACAM5 expression who were treated with tusamitamab ravtansine for ≥ 12 months as of April 14, 2022

METHODS

Study Design

- This Phase 1/2 study (NCT02187848) was a first-in-human study for the evaluation of the safety, pharmacokinetics, and antitumor activity of tusamitamab ravtansine in patients with advanced solid tumors (**Figure 2**)[3]

Figure 2. Study design



CEACAM5, carcinoembryonic antigen-related cell adhesion molecule 5; MTD, maximum tolerated dose; NSCLC, non-small cell lung cancer; NSQ, nonsquamous; Q2W, every 2 weeks; SCLC, small cell lung cancer.

- In the dose-escalation phase of the study, the maximum tolerated dose was determined to be 100 mg/m² every 2 weeks (Q2W)[3]
  - Patients in the expansion phase were treated with tusamitamab ravtansine 100 mg/m² Q2W[3]
- The expansion phase NSQ NSCLC cohorts included patients, in two separate cohorts, with high or moderate CEACAM5 expression via immunohistochemistry on the most recent archival tissue sample[4]
  - High expression was defined as CEACAM5 ≥ 2+ intensity in ≥ 50% of tumor cells
  - Moderate expression was defined as CEACAM5 ≥ 2+ intensity in ≥ 1% to < 50% of tumor cells

Analyses

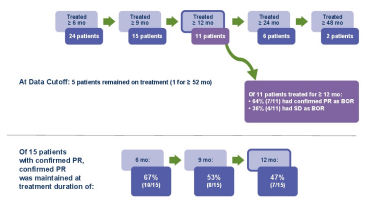
- Antitumor activity was evaluated every 4 cycles (8 weeks) using Response Evaluation Criteria in Solid Tumors guideline v1.1
  - To be documented as a confirmed response, confirmation of response was required with a second examination done at least 4 weeks apart from the first
  - Endpoints included best overall response (BOR) and best tumor shrinkage from baseline
- Incidence of treatment-emergent adverse events (TEAEs) was assessed with severity graded according to National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03 criteria
- These descriptive analyses focused on the group of patients treated with tusamitamab ravtansine for ≥ 12 months

RESULTS

Treatment History of Patients with NSQ NSCLC

- 92 patients (64 with high and 28 with moderate expression of CEACAM5) with NSQ NSCLC were included in the expansion phase
  - The last patient to enroll received first treatment on October 8, 2019
- Of these, 11 patients remained on treatment after 12 months (**Figure 3**)
  - At data cutoff (April 14, 2022), 5 patients remained on treatment, including 1 patient who had been treated for > 4.3 years

Figure 3. Treatment history and duration of partial response



BOR, best overall response; mo, months; PR, partial response, SD, stable disease.

- Among patients treated for ≥ 12 months, median (range) treatment duration was 29.6 (12.1–52.0) months
- Of 15 patients with PR in both NSQ NSCLC cohorts, 7 (47%) maintained PR at 12 months (**Figure 3**)
- Four of 11 patients (36%) treated for ≥ 12 months had SD as BOR

Characteristics of Patients Treated For ≥ 12 Months (n = 11)

- Of 11 patients treated for ≥ 12 mo, 9 had high CEACAM5 expression and 2 had moderate CEACAM5 expression; most had prior treatment with an anti-programmed cell death protein 1 (PD-1)/programmed death ligand 1 (PD-L1) agent (**Table 1**)
  - Patients treated for ≥ 12 months had better ECOG PS scores and fewer prior treatments compared with the overall group of patients with NSQ NSCLC (**Table 1**)

Table 1. Baseline characteristics of overall group and patients completing ≥ 12 months of treatment

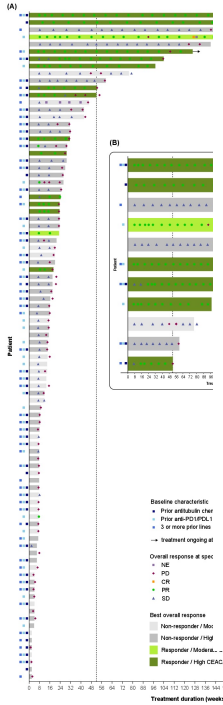
Characteristic	Total (n = 92)	Treated ≥ 12 mo (n = 11)
Age, years, median (range)	62.5 (31–91)	61.0 (41–81)
Race, n (%)		
White	77 (83.7)	8 (72.7)
Asian	15 (16.3)	3 (27.3)
Sex, n (%)		
Male	47 (51.1)	4 (36.4)
Female	45 (48.9)	7 (63.6)
CEACAM5 expression, n (%)		
High	64 (69.6)	9 (81.8)
Moderate	28 (30.4)	2 (18.2)
ECOG PS, n (%)		
0	26 (28.3)	7 (63.6)
1	65 (70.7)	4 (36.4)
≥ 3 organs involved, n (%)	52 (56.5)	5 (45.5)
Number of prior regimens for advanced disease, median (range)	3.0 (1–10)	2.0 (1–6)
Prior treatment, n (%)		
Anti-tubulin	56 (60.9)	5 (45.5)
Anti-PD-1/PD-L1	69 (75.0)	6 (54.5)

CEACAM5, carcinoembryonic antigen-related cell adhesion molecule 5; ECOG PS, Eastern Cooperative Oncology Group Performance Status; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1.

Efficacy Outcomes of Patients Treated for ≥ 12 Months (n = 11)

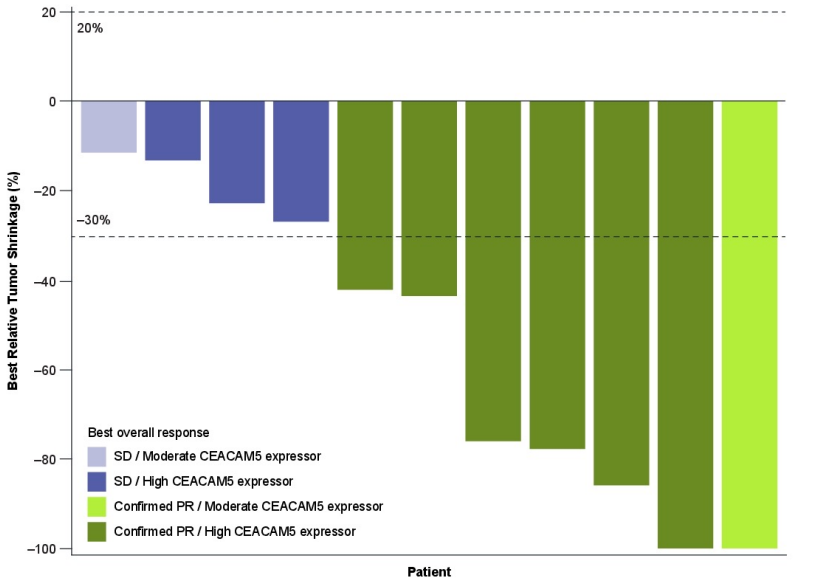
- Among 11 patients who were treated for ≥ 12 months, 7 (64%) had confirmed PR and 4 (36%) had SD as the best overall response (**Figure 3**)
  - For the 7 patients with confirmed PR, median (range) duration of response was 23.9 (8.5–44.9) months
- Findings for individual patients are shown in **Figure 4** and **Figure 5**

Figure 4. Duration of treatment, overall response … overall response for the total group (A) and for p…



For best overall response, responders were patients with either confirmed CR or confirmed PR.
CR, complete response; NE, not evaluable; PD, progressive disease; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1; PR, partial response; SD, stable disease.

Figure 5. Best overall response in patients treated ≥ 12 months (n = 11)



Dotted lines indicate cutoffs for progressive disease (≥ 20% increase in the sum of diameters of target lesions), SD (+20% to −30%), and PR

Safety Outcomes of Patients Treated for ≥ 12 Months (n = 11)

- Keratitis/keratopathy were the most frequent TEAEs, occurring in 8 patients (72.7%); 4 (36.4%) with Grade ≥ 3 (**Table 3**)
  - 7 patients had subsequent treatment modification (cycle delay with or without dose reduction or interruption) due to these events
  - No corneal TEAE was serious or led to treatment discontinuation

No	6	3 (50.0)
Any prior anti-PD-1/PD-L1 therapy		
Yes	6	5 (83.3)
No	5	2 (40.0)

*Responders are patients with confirmed PR as best overall response.
†Percentage of responders is calculated out of the number of patients in each category (shown in the center column).
CEACAM5, carcinoembryonic antigen-related cell adhesion molecule 5; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1; PR, partial response.

(delay with or without reduction)

- The observed long-term clinical benefit and safety profile of tusamitamab ravtansine support its further clinical development
  - A Phase 3 study (CARMEN-LC03; NCT04154956) is ongoing to evaluate tusamitamab ravtansine monotherapy in previously treated patients with high CEACAM5 expressing NSQ NSCLC

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CR has served in a consulting or advisory role for AstraZeneca/MedImmune, Bristol-Myers Squibb, and Takeda. **FB** has served in a consulting or advisory role for AstraZeneca/MedImmune, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Lilly, Merck Sérono, Mirati Therapeutics, MSD Oncology, Novartis, Pfizer, Pierre Fabre, Roche/Genentech, and Takeda; reports travel/accommodations/other expenses from AstraZeneca/MedImmune, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, MSD Oncology, and Roche/Genentech; reports honoraria from AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Genentech/Roche, Lilly, Merck Sérono, Mirati Therapeutics, MSD Oncology, Novartis, Pfizer, Pierre Fabre, Roche/Genentech, ServierMavenis, and Takeda. **SCC** has served in a consulting or advisory role for AstraZeneca, Blueprint Medicines, Boehringer Ingelheim, Bridgebio, Bristol-Myers Squibb, Cyrus Therapeutics, Guardant Health, r-Pharm, Daiichi Sankyo, Dong-A ST, GI Innovation, Hanpharm Bio, Janssen, Lilly, MedPacto, Mogam-Institute, Regeneron, Roche/Genentech, Samsung Bioepis, Sanofi, Servier, Sysmex, Takeda, Yuhan, and Zymeworks; has received research funding from Abbvie, AstraZeneca, Bayer, Blueprint Medicines, Chemocentryx, Daiichi Sankyo, Dong-A ST, Eli Innovation, Hanpharm Bio, Janssen, Lilly, MedPacto, Mogam-Institute, Regeneron, Roche/Genentech, Samsung Bioepis, Sanofi, Servier, Sysmex, Takeda, Yuhan, and Zymeworks; and has stock and other ownership interests in Cyrus Therapeutics. **TMK** has served in a consulting or advisory role for AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Eisai, Genexine, Genosco, Hanmi Pharm, Ildong, Janssen, Lilly, Merck Sharp & Dohme, Merck Serono, Novartis, Ono Pharmaceutical, Pfizer, Roche, Samsung Bioepis, Sanofi, Takeda, Taiho, and Yuhan; reports travel/accommodations/other expenses from AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Eisai, Genexine, Hanmi Pharm, Ildong, Janssen, Lilly, Merck Sharp & Dohme, Merck Serono, Novartis, Ono Pharmaceutical, Pfizer, Roche, Samsung Bioepis, Sanofi, Takeda, Taiho, and Yuhan; and has received research funding from AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Eisai, Genexine, Hanmi Pharm, Ildong, Janssen, Lilly, Merck Sharp & Dohme, Merck Serono, Novartis, Ono Pharmaceutical, Pfizer, Roche, Samsung Bioepis, Sanofi, Takeda, Taiho, and Yuhan. **JSK** has served in a consulting or advisory role for Celltrion, Daiichi Sankyo, Eisai, Genexine, Hanmi Pharm, Ildong, Janssen, Lilly, Merck Sharp & Dohme, Merck Serono, Novartis, Ono Pharmaceutical, Pfizer, Roche, Samsung Bioepis, Sanofi, Takeda, Taiho, and Yuhan; reports travel/accommodations/other expenses from Celltrion, Daiichi Sankyo, Eisai, Genexine, Hanmi Pharm, Ildong, Janssen, Lilly, Merck Sharp & Dohme, Merck Serono, Novartis, Ono Pharmaceutical, Pfizer, Roche, Samsung Bioepis, Sanofi, Takeda, Taiho, and Yuhan; and has received research funding from Celltrion, Daiichi Sankyo, Eisai, Genexine, Hanmi Pharm, Ildong, Janssen, Lilly, Merck Sharp & Dohme, Merck Serono, Novartis, Ono Pharmaceutical, Pfizer, Roche, Samsung Bioepis, Sanofi, Takeda, Taiho, and Yuhan. **VB** has served in a consulting or advisory role for Roche and reports travel/accommodations/other expenses from Roche. **YB** is an employee of NEXT Oncology and Quirónsalud; holds leadership roles in NEXT Oncology; reports honoraria from Amunix, Duckpoint Global, OEA Bioscience, Lava, and Puma Biotechnology; has served in a consulting or advisory role for Duckpoint Global and CrossAt; has served in a speakers bureau for Lilly, Sotio, and Tactics; reports their institution has received research funding from Abbvie, Adaptimmune, Alkermes, Amgen, Array BioPharma, AstraZeneca, Bayer, BioNTech, Boehringer Ingelheim, Bristol-Myers Squibb, Cytomx Therapeutics, Genmab, Incyte, Janssen, Kura Oncology, Lilly, Loxo, Menarini, Merck, Merus, Novartis, Pfizer, Puma Biotechnology, Roche/Genentech, Sanofi, Seattle Genetics, Synthon, Tesaro, and Zentrin Epigenetics; and reports travel/accommodations/other expenses from Bayer and START. **FG** reports travel/accommodations/other expenses from Amgen and Roche/Genentech; reports honoraria from Roche, and reports their institution has received research funding from AstraZeneca/MedImmune. **SC** is an employee of Evaxia, a contractor for Sanofi. **NC** is an employee of Sanofi. **SC, HM,** and **AG** have no disclosures to report.

REFERENCES:
1. Hammarström S, et al. Semin Cancer Biol. 1999;9(2):67–81.
2. Deckert S, et al. Clin Cancer Res. 2021;26(24):6588–6598.
3. Decker S, et al. Cancer Res. 2015;75(15 suppl):Abs. 1988.
4. Gazzah A, et al. J Clin Oncol. 2020;38(15 suppl):Abs. 9505.
5. Gazzah A, et al. Ann Oncol. 2022;33:416–425.

For additional information, please contact Charles.RICORDEL@chu-rennes.fr

ASCO 2022

HLA-A2: TEDOPI

- Advanced/metastatic NSCLC
- EGFRwt, ALK-negative, all PD-L1 status
- HLA-A2+ (blood)
- Failure to platinum-based CT and IO, combined or sequenced
- IO last line with primary or secondary resistance*
- Brain metastases allowed if asymptomatic & treated
- ECOG PS 0 to 1

R 2:1

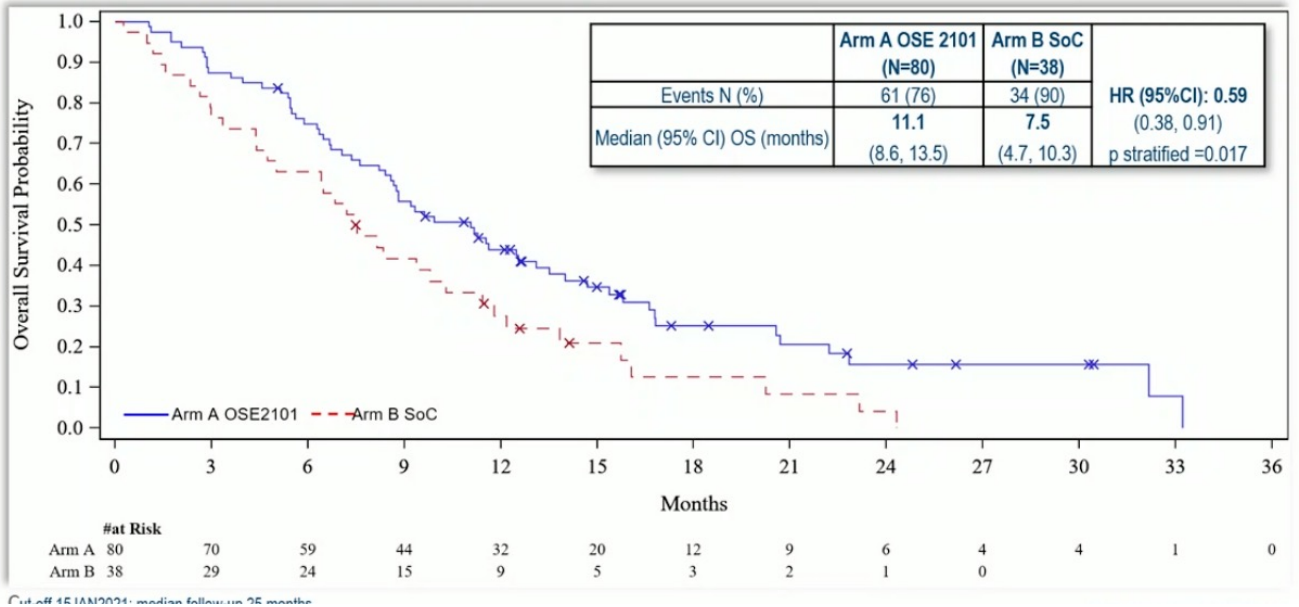
Arm A: OSE2101 Q3W for 6 subcutaneous injections, then Q8W up to Year 1, then Q12W until progression or toxicity

Arm B: SoC (docetaxel or pemetrexed) Q3W until progression or toxicity

Stratification:
- Histology
- Best response to 1st line
- Line rank of prior IO

Primary endpoint: OS

Overall Survival in PoI



	Arm A OSE 2101 (N=80)	Arm B SoC (N=38)	
Events N (%)	61 (76)	34 (90)	HR (95%CI): 0.59 (0.38, 0.91) p stratified =0.017
Median (95% CI) OS (months)	11.1 (8.6, 13.5)	7.5 (4.7, 10.3)	

- Step-1 primary endpoint was achieved (cut off February 2020; 103 patients)[1]:
  1-year OS rate 46% versus 36% in SoC (Fleming design); HR for OS=0.71
- Due to the risk of COVID-19 on data integrity, the study was prematurely stopped in April 2020 upon the Independent Data Monitoring Committee recommendation:
  219 pts instead of initial ≈400 pts were enrolled
- Population of Interest (PoI) was identified from Step-1:
  patients with IO secondary resistance after sequential IO; HR for OS=0.65
- PoI and revision of statistical plan were discussed with FDA in July 2021 before database lock
- The final primary analysis was done in the PoI:
  the initial hypothesis of 278 events for HR 0.7 was not reachable
  revised statistical hypothesis in PoI: 90 events for HR=0.55; power 80%, 2-sided level of 5%

Besse et al. ESMO 2021

Les cancers thoraciques

Non à petites cellules

- Stades précoces
  - Dépistage
- Localement avancés
  - Résécables
  - Non résécables
- Métastatiques
  - Oncogène addictif
  - Sans oncogène addictif

Petites cellules

- Localement avancés
- Métastatiques

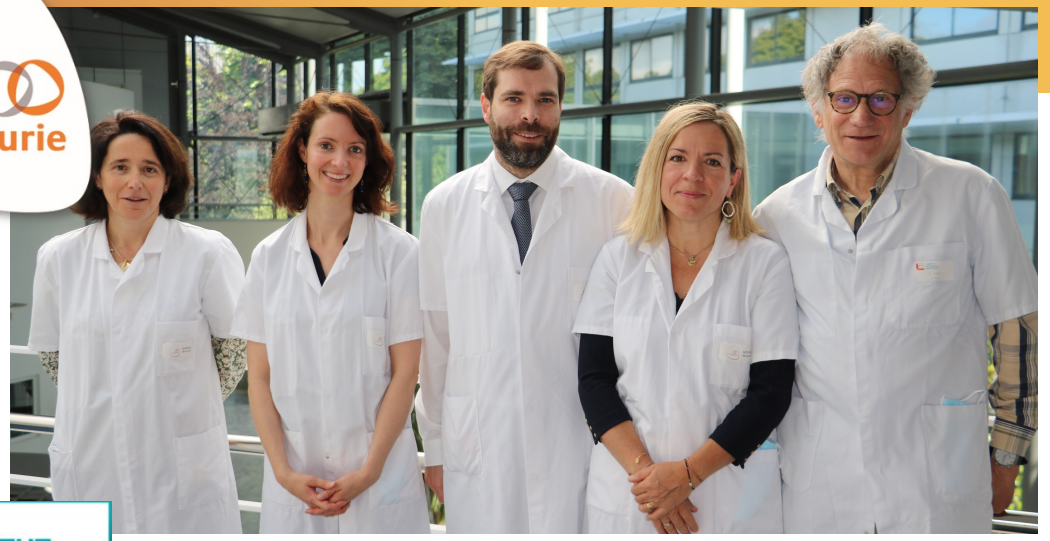
Mésothéliome

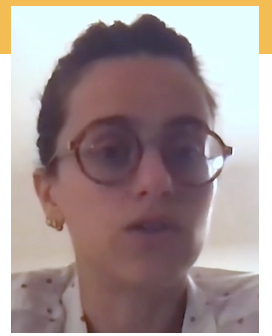
Tumeurs thymiques

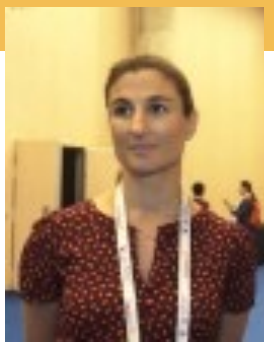
Merci!

Institut du thorax
Curie - Montsouris

institutCurie







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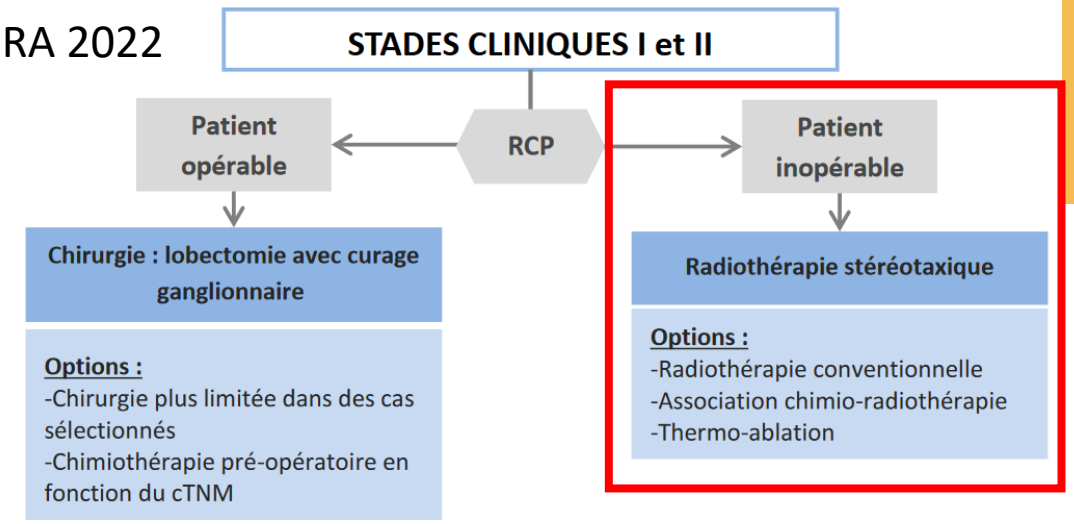
Actualités et enjeux de la radiothérapie

Pr Delphine Antoni
ICANS | Institut de cancérologie Strasbourg Europe

La RCS* dans les CBNPC de stade I et II: une révolution

AURA 2022



TROG 09.02 CHISEL: RCS vs RTC3D stade 1 Tumeurs périphériques

RCS : 54Gy - 3fr x 18Gy ou 48Gy - 4fr x 12Gy
RTC3D : 66Gy - 33fr x 2Gy ou 50Gy - 20fr x 2,5Gy

	CL 2 ans (%) (p=0,008)	Med SG (p=0,027)
RTC3D (#35)	69	3 ans
RCS (#66)	86	5 ans

Ball et al. Lancet Oncol 2019

LUSTRE: RCS vs RT hypofractionnée stade 1 Tumeurs périphériques ou centrales

RCS : 48Gy - 4fr x 12Gy ou 60Gy - 8fr x 7,5Gy
RT hypofr. : 60Gy - 15fr x 4Gy

	CL 3 ans (%) p=0,15
RT hypofr. (#79)	81,2
RCS (#154)	87,6

Swaminath et al. ASTRO 2022

BED > 100 Gy : facteur pronostique de contrôle local

* radiothérapie en conditions stéréotaxiques

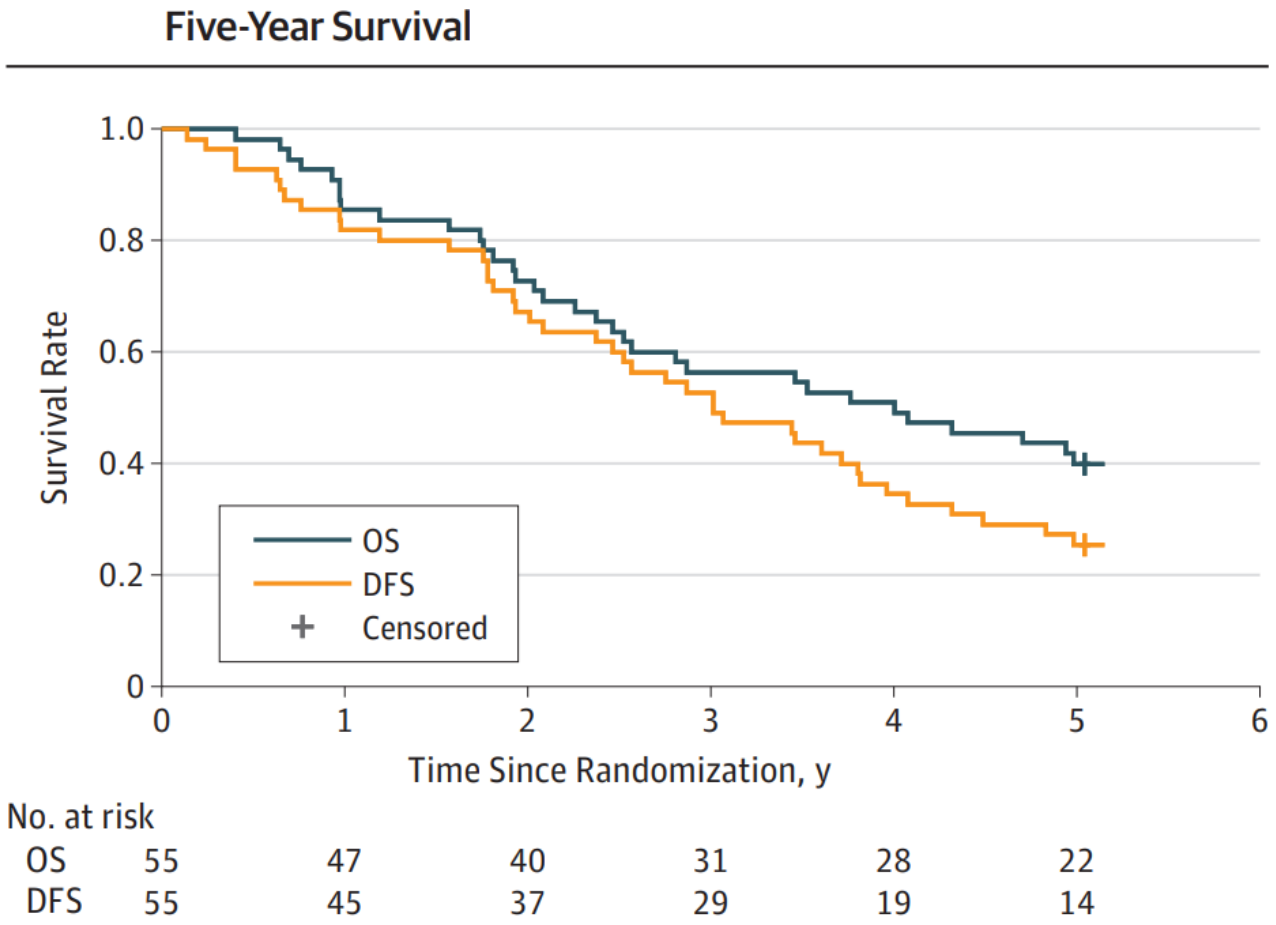
La RCS* dans les CBNPC de stade I et II: une révolution

Traitement efficace et sûre

- Contrôle local à 2 et 5 ans: 95% et 90%

- Toxicité gr 3 : 11%; gr 4 : 2% (CHISEL)
- Toxicité gr 3 : 15% (RTOG 0618)

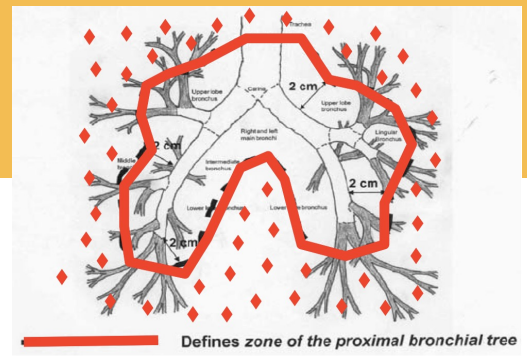
RTOG 0236



Ball et al. Lancet Oncol 2019, Timmerman et al. Jama Oncol 2018

La RCS pour les tumeurs centrales ou hypercentrales

Safety and Efficacy of a Five-Fraction Stereotactic Body Radiotherapy Schedule for Centrally Located NSCLC: NRG Oncology/RTOG 0813 Trial

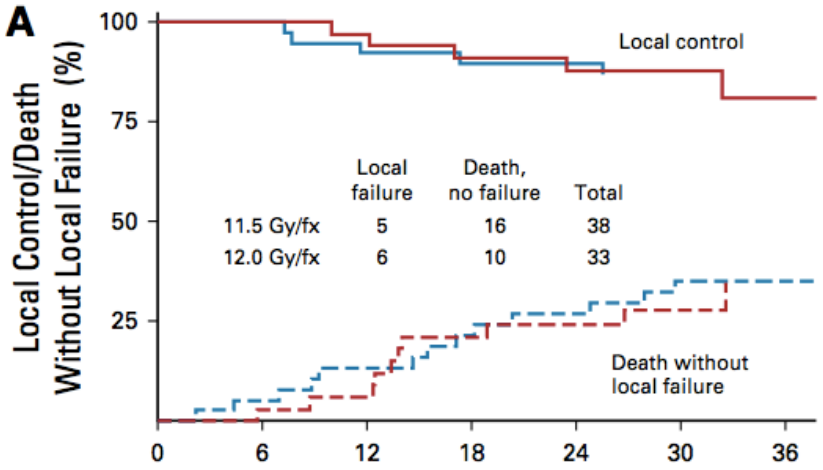


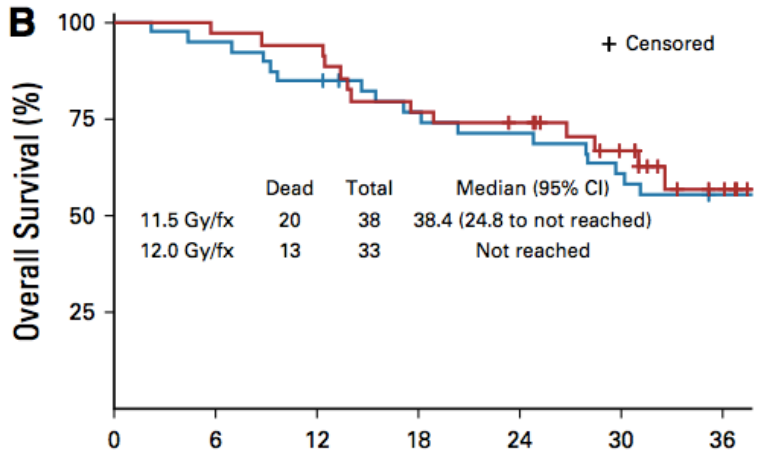
Médiane de suivi : 37,9 mois

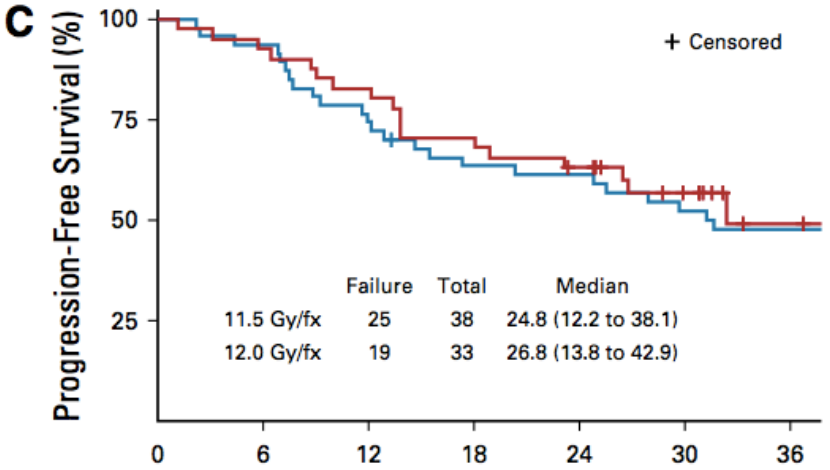
CL à 2 ans: 87,9%

SG à 2 ans: 72,7%

SSP à 2 ans: 54,5%







11.5 Gy
12.0 Gy

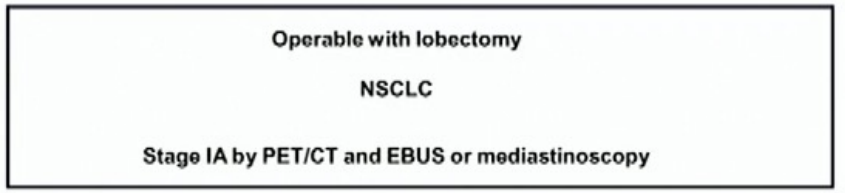
Dose maximale tolérée 12Gy / fraction (7,2% de probabilité de toxicité)

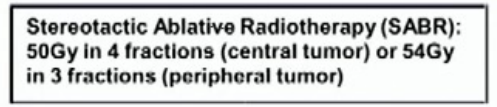
Bezjak et al. JCO 2019

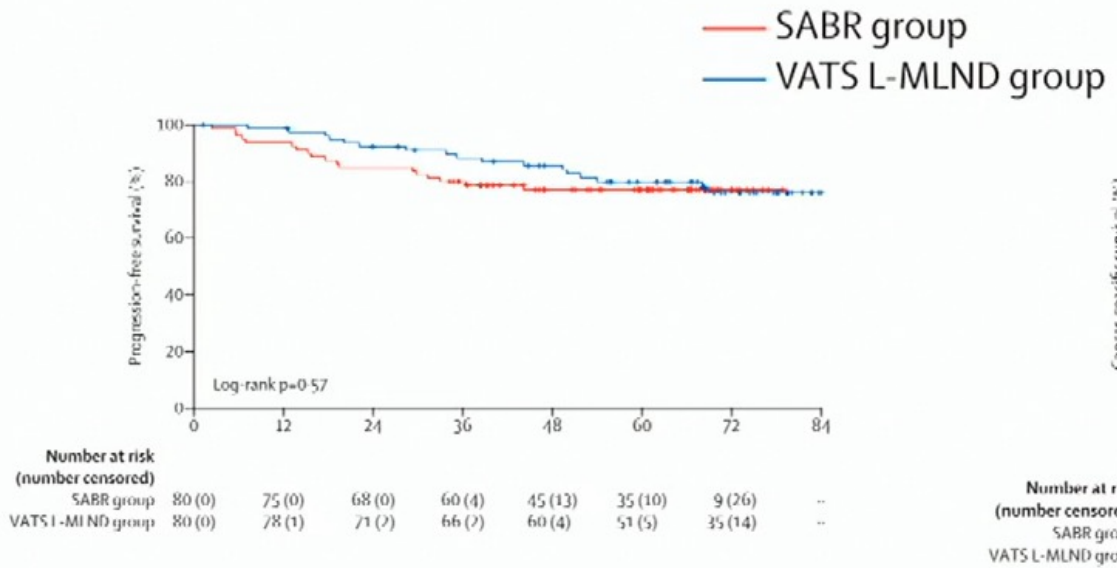
La RCS pour les tumeurs stade IA opérable

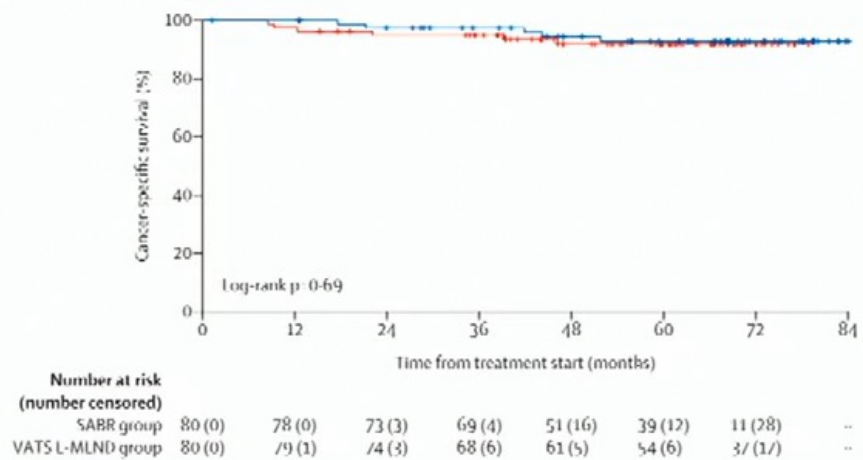
Plusieurs tentatives d'essais randomisés
ROSEL (960 pts), STARS (1030 pts), RTOG (420 pts), SABRTooth (670 pts)

Revised stars:
Cohorte prospective de RCS chez patients opérables
Cohorte prospective chirurgicale
Tumeur de moins de 3 cm





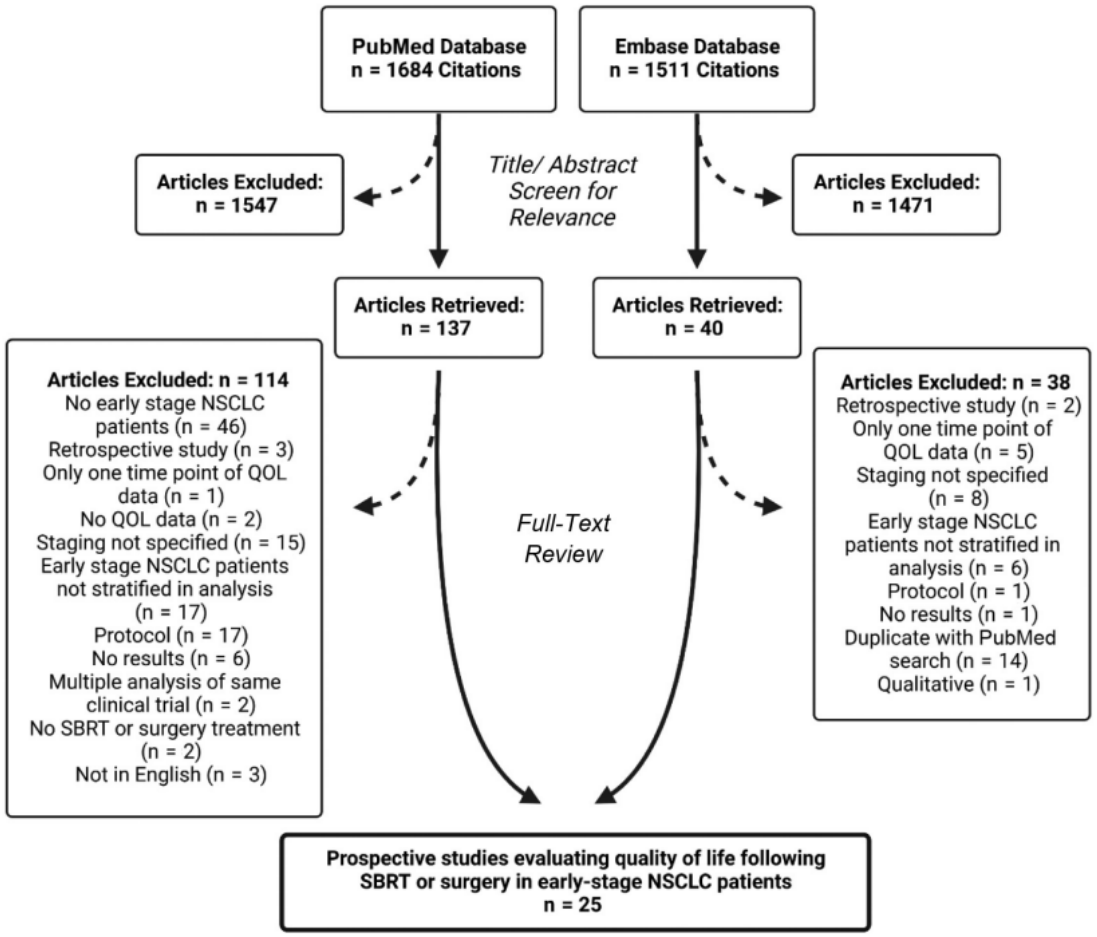


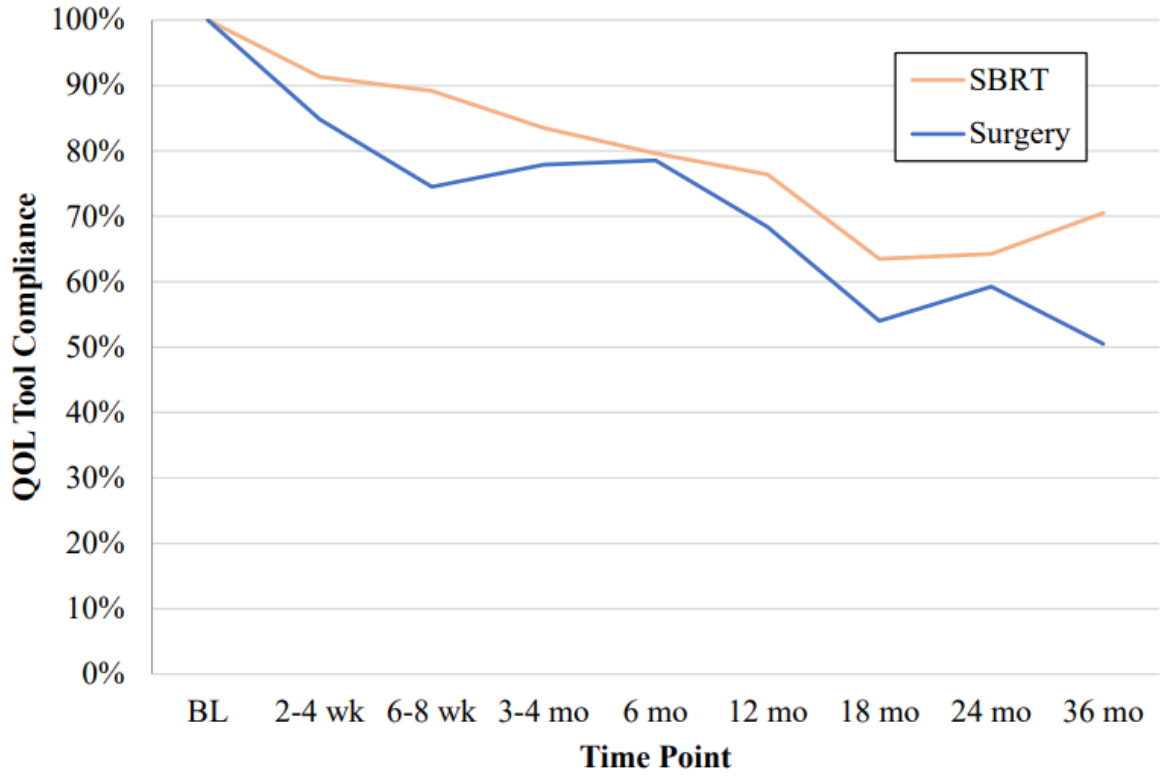


→ RCS non inférieure à la chirurgie

Chang et al. Lancet Oncol 2021

La RCS : impact sur la qualité de vie



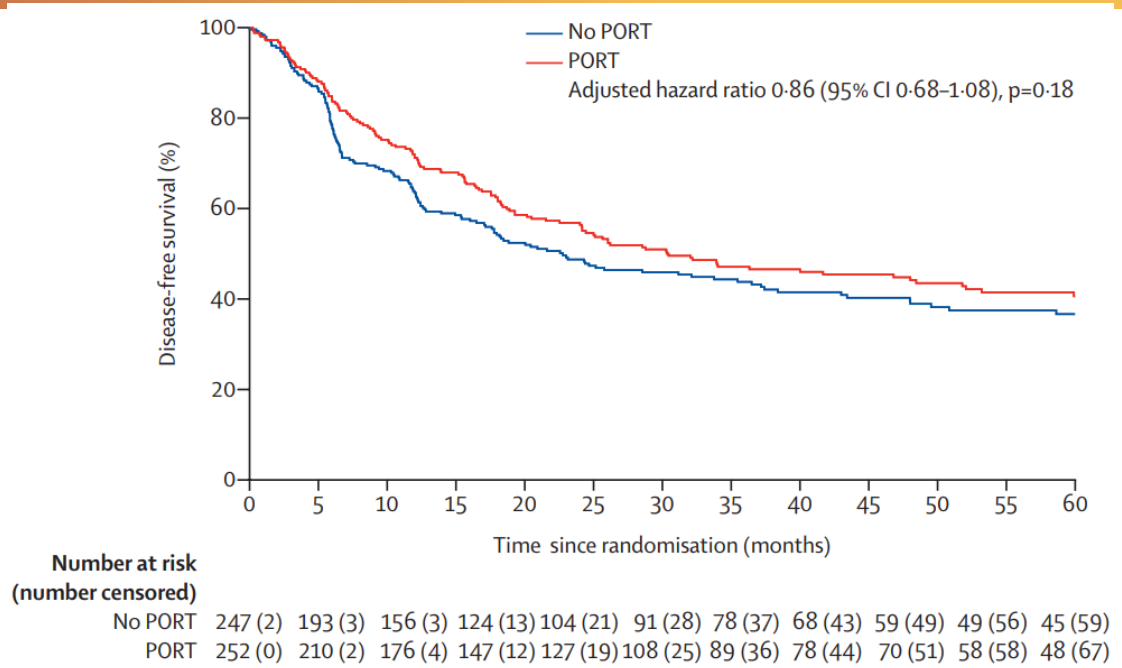


Number at risk

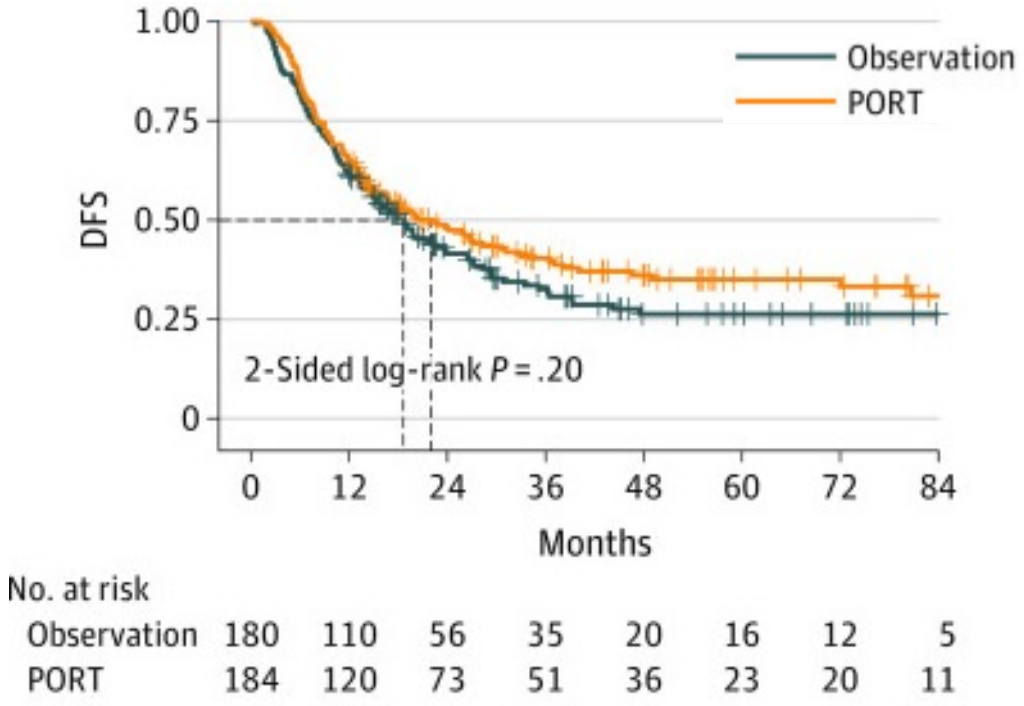
SBRT	1597	194	294	1085	1057	926	148	285	39
Surgery	1652	583	354	991	737	909	114	213	14

Iovoli et al. JTO 2022

Stade III pN2: radiothérapie adjuvante ?



	No PORT	PORT
SSM Médiane	22,8 mois	30,5 mois
SSM 3 ans	43,8%	47,1%
Rechute médiastinale	46%	25%
Décès	5%	15%
Tox. Cardio-pulm gr 3-4	5%	11%

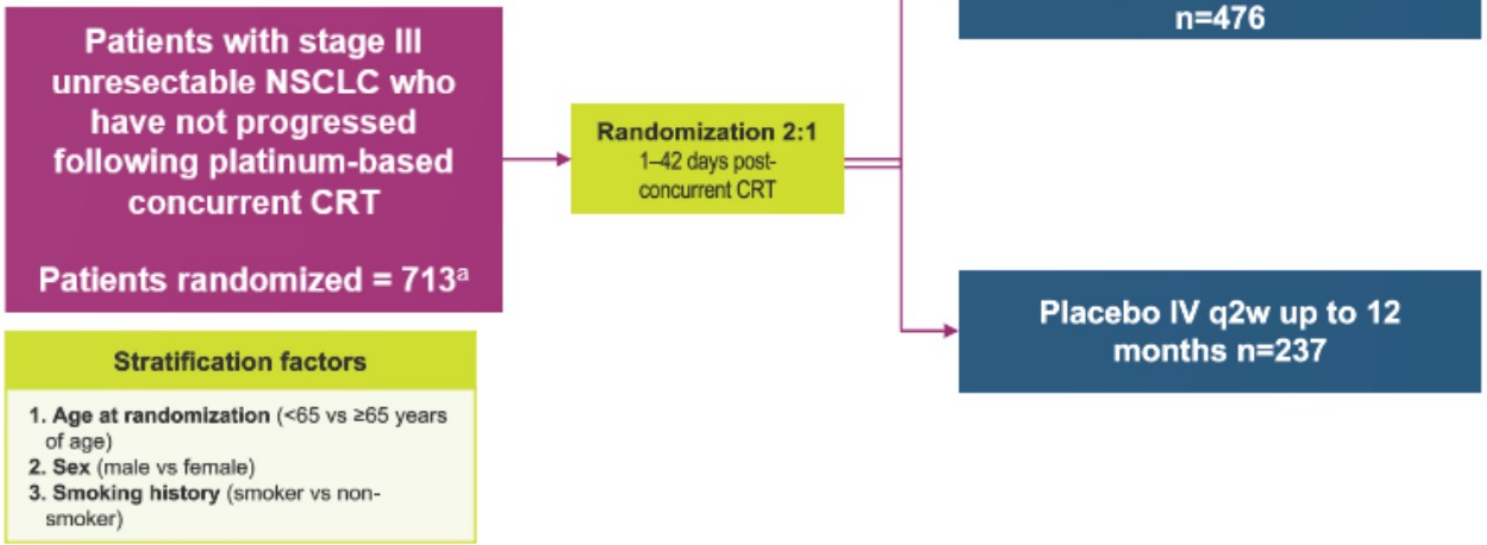


Le Pechoux et al. Lancet Oncol 2022

Hui et al. JAMA Oncol 2021

Stade III : chimioradiothérapie combinée à l'immunothérapie

PACIFIC : essai de phase 3, randomisé, en double-aveugle contre placebo, multicentrique, international



Co-primary endpoints

- PFS[b] by BICR
- OS

Secondary endpoints

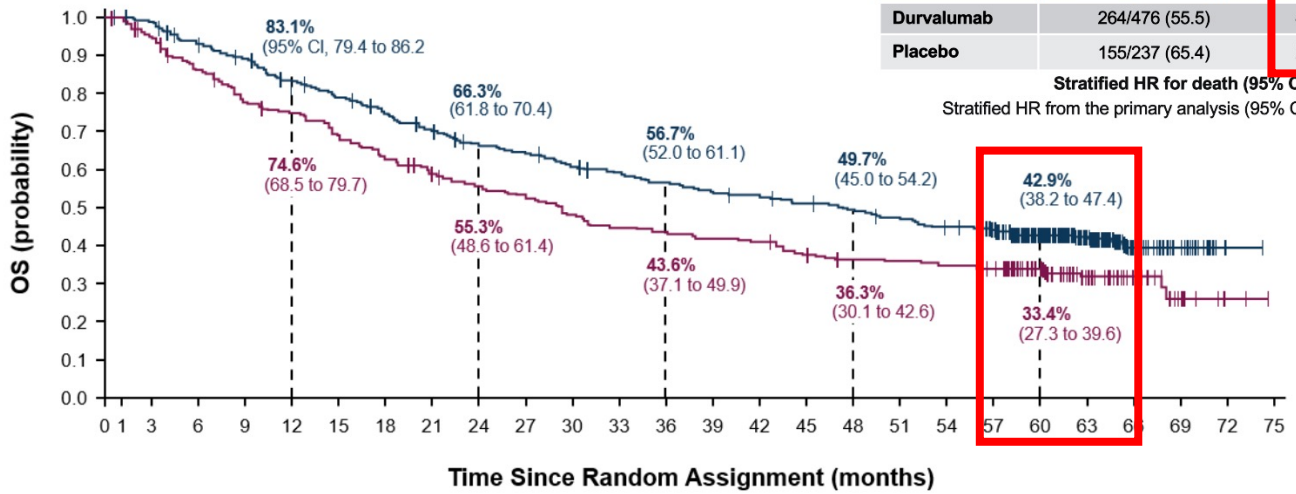
- OS24
- DoR (per BICR)
- ORR (per BICR)
- APF12 and APF18
- TTDM
- Safety and tolerability
- PROs
- PK and immunogenicity

Antonia et al. N Engl J Med. 2018

PACIFIC

Arm	No. of events / No. of patients (%)	Median OS (95% CI) months
Durvalumab	264/476 (55.5)	47.5 (38.1–52.9)
Placebo	155/237 (65.4)	29.1 (22.1–35.1)

Stratified HR for death (95% CI): 0.72 (0.59–0.89)
Stratified HR from the primary analysis (95% CI): 0.68 (0.53–0.87)

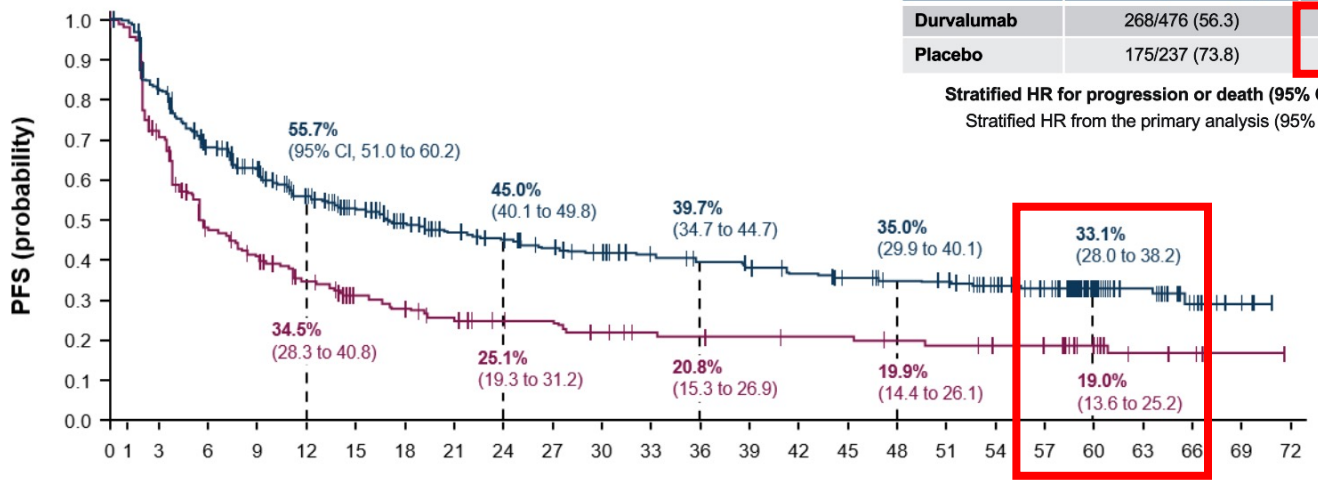


No. at risk

Durva.	476	464	431	414	385	364	343	319	298	289	273	264	252	241	236	227	218	207	196	183	134	91	40	18	2	0
Placebo	237	220	199	179	171	156	143	133	123	116	107	99	97	93	91	83	78	77	74	72	56	33	16	7	2	0

Arm	No. of events / No. of patients (%)	Median PFS (95% CI) months
Durvalumab	268/476 (56.3)	16.9 (13.0–23.9)
Placebo	175/237 (73.8)	5.6 (4.8–7.7)

Stratified HR for progression or death (95% CI): 0.55 (0.45–0.68)
Stratified HR from the primary analysis (95% CI): 0.52 (0.42–0.65)



No. at risk

Durva	476	377	301	267	215	190	165	147	137	128	119	110	103	97	92	85	81	78	67	57	34	22	11	5	0
Placebo	237	164	105	87	68	56	48	41	37	36	30	27	26	25	24	24	22	21	19	19	14	6	4	1	0

Spigel et al. JCO. 2022

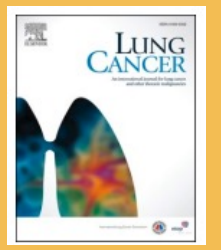
PACIFIC

Adverse events, n (%)	Durvalumab (n=475)		Placebo (n=234)	
	Any grade[b]	Grade 3 or 4	Any grade[b]	Grade 3 or 4
Any event	460 (96.8)	145 (30.5)	222 (94.9)	61 (26.1)
Cough	167 (35.2)	2 (0.4)	59 (25.2)	1 (0.4)
Fatigue	114 (24.0)	1 (0.2)	48 (20.5)	3 (1.3)
Dyspnea	106 (22.3)	7 (1.5)	56 (23.9)	6 (2.6)
Radiation Pneumonitis[c]	96 (20.2)	7 (1.5)	37 (15.8)	1 (0.4)
Diarrhea	88 (18.5)	3 (0.6)	46 (19.7)	3 (1.3)
Pyrexia	72 (15.2)	1 (0.2)	22 (9.4)	0
Nausea	68 (14.3)	0	31 (13.2)	0
Decreased appetite	68 (14.3)	1 (0.2)	30 (12.8)	2 (0.9)
Pneumonia	63 (13.3)	21 (4.4)	18 (7.7)	9 (3.8)
Pneumonitis[c]	60 (12.6)	9 (1.9)	18 (7.7)	4 (1.7)
Arthralgia	59 (12.4)	0	26 (11.1)	0
Upper respiratory tract infection	59 (12.4)	1 (0.2)	24 (10.3)	0
Pruritus	59 (12.4)	0	12 (5.1)	0
Rash	58 (12.2)	1 (0.2)	18 (7.7)	0
Constipation	56 (11.8)	1 (0.2)	20 (8.5)	0
Hypothyroidism	55 (11.6)	1 (0.2)	4 (1.7)	0
Headache	52 (10.9)	1 (0.2)	21 (9.0)	2 (0.9)
Asthenia	51 (10.7)	3 (0.6)	31 (13.2)	1 (0.4)
Back pain	50 (10.5)	1 (0.2)	27 (11.5)	1 (0.4)
Musculoskeletal pain	39 (8.2)	3 (0.6)	24 (10.3)	1 (0.4)
Anemia	36 (7.6)	14 (2.9)	26 (11.1)	8 (3.4)

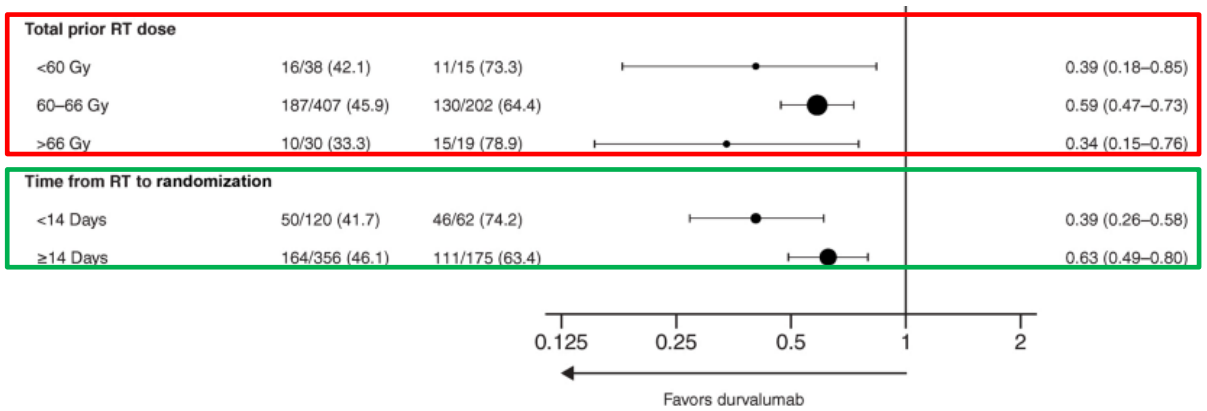
Antonia et al. N Engl J Med. 2018

Impact of prior chemoradiotherapy-related variables on outcomes with durvalumab in unresectable Stage III NSCLC (PACIFIC)

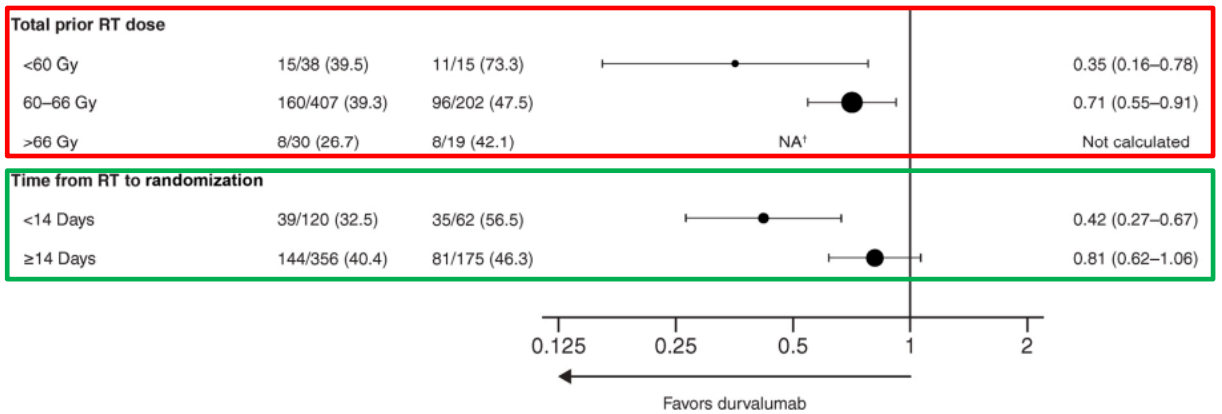
Corinne Faivre-Finn [a,b,*], David R. Spigel [c,d], Suresh Senan [e], Corey Langer [f], Bradford A. Perez [g], Mustafa Özgüroğlu [h], Davey Daniel [c,d], Augusto Villegas [i], David Vicente [j], Rina Hui [k], Shuji Murakami [l], Luis Paz-Ares [m], Helen Broadhurst [n], Catherine Wadsworth [o,1], Phillip A. Dennis [p], Scott J. Antonia [g]



PFS



OS



Faivre-Finn et al. Lung Cancer 2021

Characterizing immune-mediated adverse events with durvalumab in patients with unresectable stage III NSCLC: A post-hoc analysis of the PACIFIC trial

Immune-mediated adverse events in patients receiving durvalumab or placebo by time elapsed from completion of RT to randomization (<14 days vs. ≥ 14 days) (as-treated population).

	Randomization < 14 days after RT				Randomization ≥ 14 days after RT			
	Immune-mediated pneumonitis		Non-pneumonitis imAEs		Immune-mediated pneumonitis		Non-pneumonitis imAEs	
	Durvalumab (n = 120)	Placebo (n = 60)	Durvalumab (n = 120)	Placebo (n = 60)	Durvalumab (n = 355)	Placebo (n = 174)	Durvalumab (n = 355)	Placebo (n = 174)
Any-grade, n (%)	13 (10.8)	2 (3.3)	18 (15.0)	1 (1.7)	38 (10.7)	14 (8.0)	53 (14.9)	4 (2.3)
Treatment-related, n (%)[a]	8 (6.7)	1 (1.7)	18 (15.0)	0	30 (8.5)	8 (4.6)	49 (13.8)	2 (1.1)
Grade 3/4, n (%)	2 (1.7)	1 (1.7)	1 (0.8)	0	7 (2.0)	5 (2.9)	7 (2.0)	0
Treatment-related, n (%)[a]	1 (0.8)	1 (1.7)	1 (0.8)	0	6 (1.7)	3 (1.7)	7 (2.0)	0
Fatal, n (%)	0	1 (1.7)	0	0	4 (1.1)	3 (1.7)	0	0
Treatment-related, n (%)[a]	0	0	0	0	4 (1.1)	3 (1.7)	0	0
Serious, n (%)[b]	3 (2.5)	2 (3.3)	1 (0.8)	0	12 (3.4)	7 (4.0)	5 (1.4)	0
Treatment-related, n (%)[a]	3 (2.5)	1 (1.7)	1 (0.8)	0	12 (3.4)	5 (2.9)	5 (1.4)	0

Fin de la RT (< 14 j ou ≥ 14 j) : pas d'impact sur l'incidence ou la sévérité des EI

Naidoo et al. Lung Cancer 2022

Quel impact de la RCMI ?

Impact of Intensity-Modulated Radiation Therapy Technique for Locally Advanced Non–Small-Cell Lung Cancer: A Secondary Analysis of the NRG Oncology RTOG 0617 Randomized Clinical Trial

JOURNAL OF CLINICAL ONCOLOGY

	3D-CRT	IMRT	p
Nombre de patients	254	228	
Dose *(74 Gy versus 60 Gy)*	42.9	40.8	0.64
Cetuximab *(yes versus no)*	47.6	47.4	0.95
Age *(median)*	64	64	0.9
OMS *(0 versus 1)*	59.8	54.8	0.27
PET-CT *(yes versus no)*	88.2	94.3	0.02
Histology (Squamous versus others)	46.5	39.9	0.24
Stage *(IIIA versus IIIB)*	69.7	61.4	0.06

Chun et al. JCO 2017

Quel impact de la RCMI ?

Dosimetric Factor	3D-CRT Median	3D-CRT Q1-Q3	IMRT Median	IMRT Q1-Q3	P
PTV volume, mL	426.7	298.1-586.5	486.2	347.6-677.3	.005*
Volume of lung excluding CTV, mL	3,331.4	2,676.7-4,045.0	3,215.7	2,754.6-4,020.0	.779*
PTV volume:lung volume ratio	0.13	0.09-0.19	0.15	0.10-0.21	.013*
Minimum dose to PTV, Gy	55.2	49.8-60.2	53.4	48.0-57.3	< .001†
Maximum dose to PTV, Gy	68.8	66.1-80.8	70.2	66.1-80.9	.256†
Dose to cover 95% of PTV, Gy	60.8	60.0-72.3	60.7	60.0-73.0	.088†
PTV covered by 100% Rx dose, %	94.8	87.0-96.4	95.1	92.1-97.0	.058*
Mean lung dose, Gy	18.1	15.4-20.6	17.7	14.4-20.1	.088†
Volume of lung, %					
V5	54.8	43.3-65.9	61.6	52.1-70.4	< .001†
V20	30.5	25.3-35.1	29.9	24.0-34.7	.297†
Mean esophagus dose, Gy	27.6	22.1-32.8	25.6	20.2-32.6	.078†
Volume of esophagus, %					
V20	47.6	39.4-56.9	46.8	36.7-56.7	.466†
V60	19.7	5.2-30.4	18.4	3.6-29.3	.927†
Volume of heart, %					
V20	23.5	7.8-46.0	19.3	5.2-36.5	.049†
V40	11.4	1.7-25.9	6.8	0.6-15.5	.003†
V60	2.4	0.0-8.3	1.4	0.0-5.0	.045†
Volume of heart inside PTV, mL	2.05	0.00-16.46	3.56	0.00-16.73	.183*
Maximum dose outside PTV, Gy	69.9	66.3-80.8	69.55	65.6-79.9	.026†

≥ Grade 3 Toxicity	3D-CRT, % (No.)	IMRT, % (No.)	P
No. of patients	254	228	
Pneumonitis	7.9 (20)	3.5 (8)	.039
Esophagitis/dysphagia	15.4 (39)	13.2 (30)	.534
Weight loss	2.8 (7)	3.9 (9)	.419
Cardiovascular	8.3 (21)	4.8 (11)	.131

Table 5. Multivariable Logistic Regression Analysis of CTCAE ≥ Grade 3 Pneumonitis

Covariate	Comparison	OR (95% CI)	P
RT technique	3D-CRT (RL) *v* IMRT	0.410 (0.171 to 0.986)	.046
AJCC stage group	IIIA (RL) *v* IIIB	2.276 (1.009 to 5.137)	.048
Lung V20, %	Continuous	1.071 (1.008 to 1.137)	.026
PTV, mL	Continuous (log-transformed)	1.701 (0.708 to 4.085)	.235

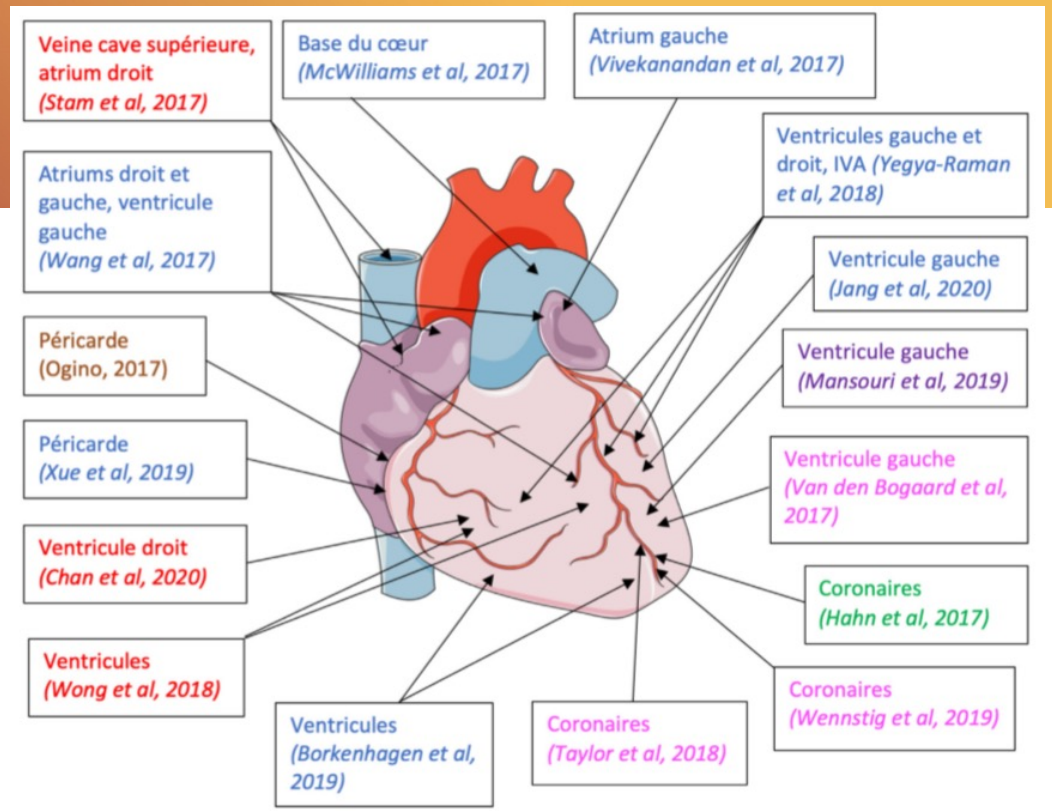
Chun et al. JCO 2017

Immunothérapie et CRT dans les CBNPC de stade III

Essai	Phase	Stade IIIB/C	Dose RT	RCMI	Immunothérapie	PNP ≥ G3	PNP G5
RTOG 0617[1]	2	34%	60 Gy	59,2%	non	7%	1%
PACIFIC[2]	3	44,7%	60 à 66 Gy	ND	Durvalumab sequentiel	3,4%	0,8%
KEYNOTE-799[3]	2	63,4%	60 Gy	89,3%	Pembrolizumab concomitant	8%	3,6%
NICOLAS[4]	2	63,3%	66 Gy	ND	Nivolumab concomitant	11,7%	0%

1 Bradley et al. JCO 2020, 2 Antonia et al. N Engl J Med. 2018, 3 Jabbour et al. Jama Oncol 2021, 4 Peters et al. JTO 2021

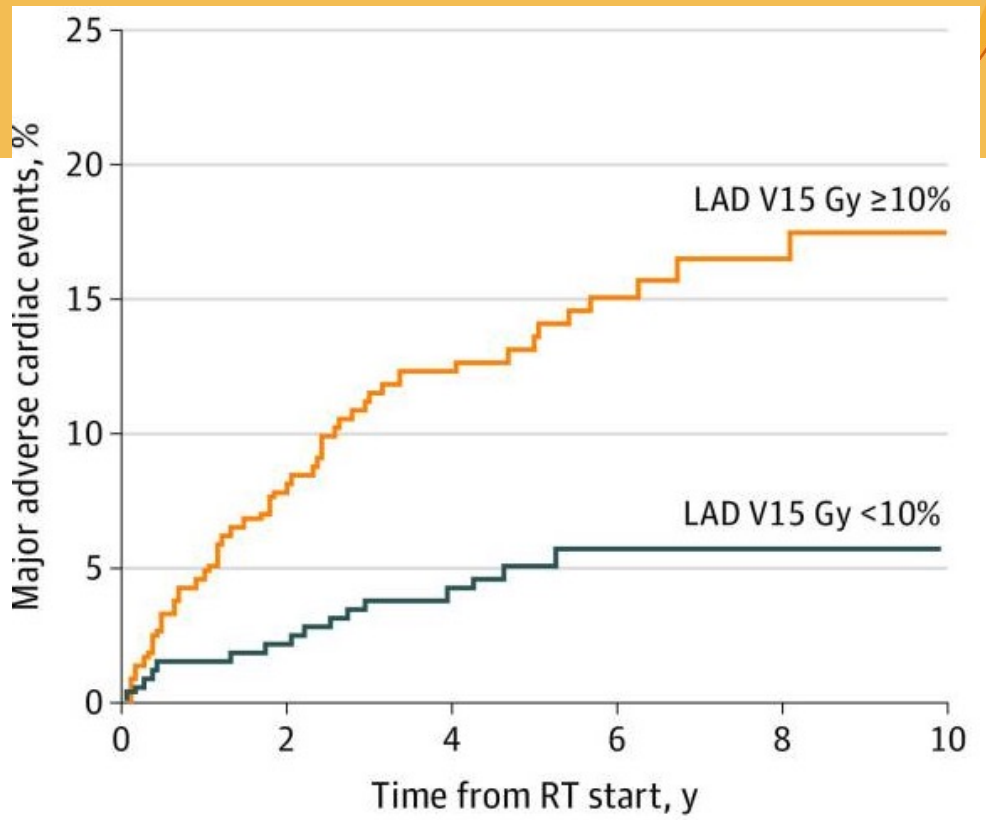
Cardiotoxicité de la radiothérapie



Sous-structures cardiaques significativement associées à des ev. cardiaques et à la SG:

Bleu: CBNPC fractionnement classique
Rouge: CBNPC RCS
Rose: cancers du sein
Violet: cancers pédiatriques
Vert: lymphomes
Marron: cancers de l'œsophage

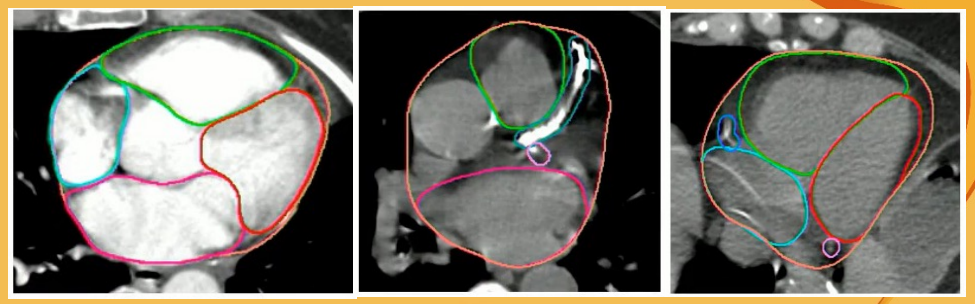
Eber J. et al. Cancer Radiother 2021



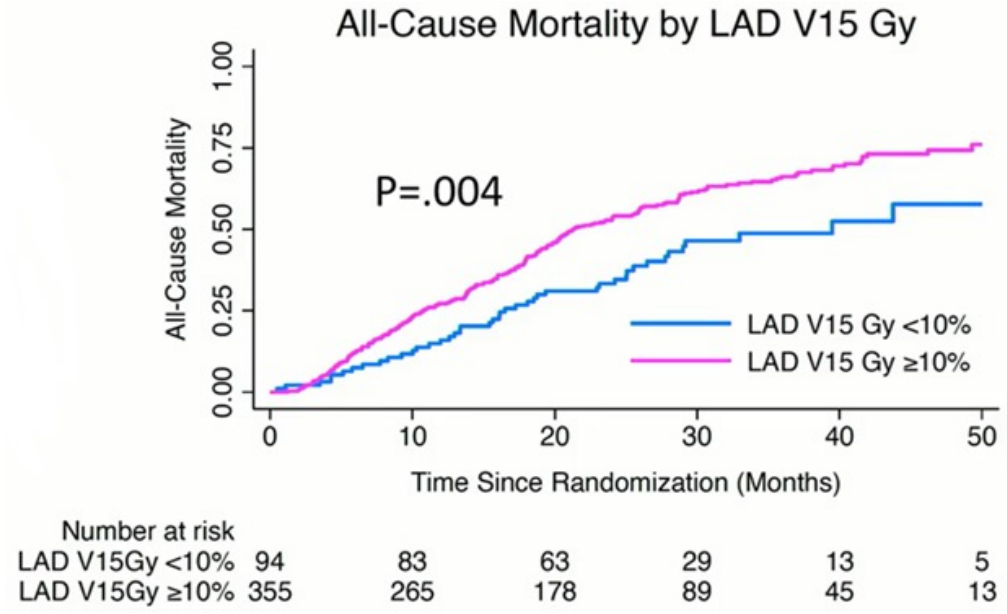
V15Gy ≥ 10%
Facteur de risque indépendant de survenue de toxicité cardiaque

Atkins et al. Jama Oncol 2021

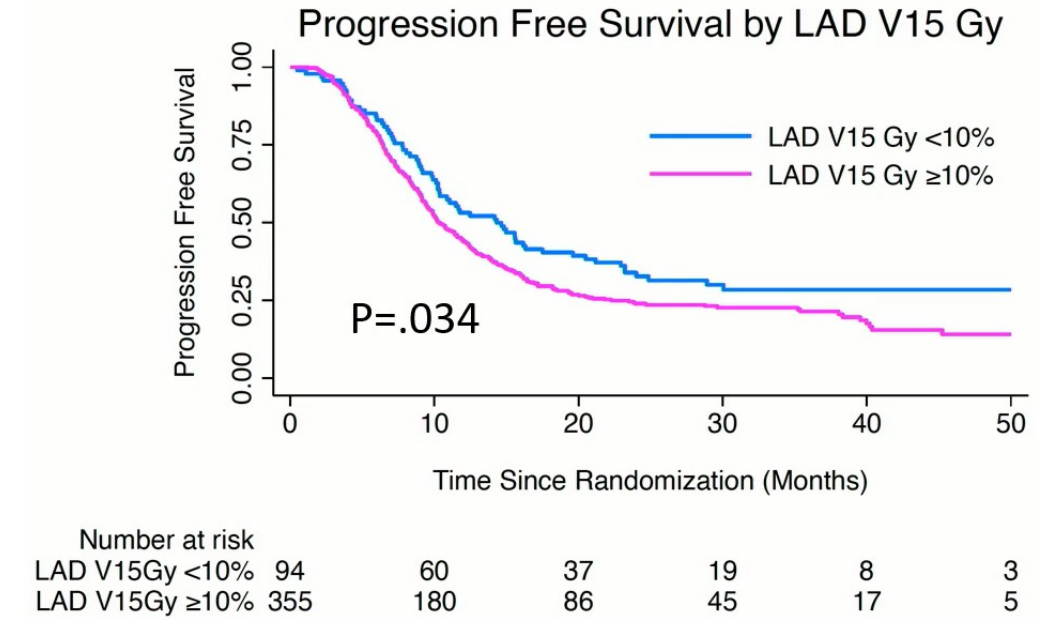
Cardiotoxicité de la radiothérapie



Left Anterior Descending Coronary Artery Radiation Dose Association withe All-Cause Mortality in NRG Oncology Trial RTOG 0617



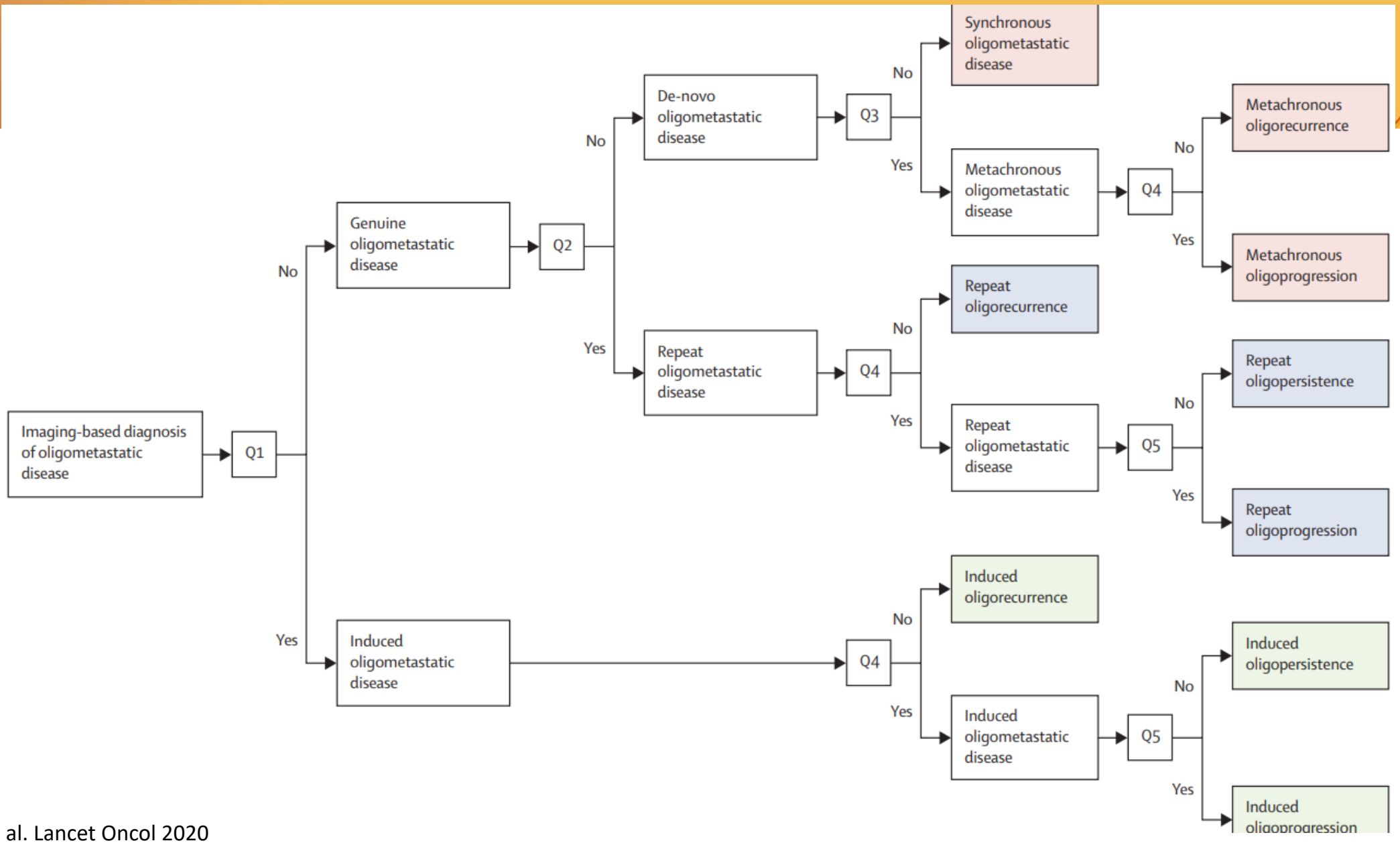
IVA V15 Gy	≥ 10%	< 10%	p
SG médiane	20 mois	25 mois	0,004
SG 2 ans	47%	67%	0,004



IVA V15 Gy	≥ 10%	< 10%	p
SSP médiane	6 mois	8 mois	0,016
SSP 1 an	44%	52%	0,034

McKenzie et al. ASTRO 2022

L'oligo-paradigme : une approche multidisciplinaire



Guckenberger et al. Lancet Oncol 2020

ORIGINAL ARTICLE

Definition of Synchronous Oligometastatic Non-Small Cell Lung Cancer—A Consensus Report

Results: It was determined that definition of sOM NSCLC is relevant when a radical treatment that may modify the disease course (leading to long-term disease control) is technically feasible for all tumor sites with acceptable toxicity. On the basis of the review, a maximum of five metastases and three organs was proposed. Mediastinal lymph node involvement was not counted as a metastatic site. Fludeoxyglucose F 18 positron emission tomography–

Dingemans et al. JTO 2019

Approche multidisciplinaire dans la maladie oligométastatique: essais phase II randomisés

Essai	tumeur primitive	Nb. de patients	Nb. de métastases	Suivi (mois)	Séquence de traitement	SSP (mois) TL vs ctrl	SG (mois) TL vs ctrl	Toxicité (grade)
Palma et al. [1]	poumon, sein, prostate, CR, autres	99	≤ 5	51	Pas de TS requis avant TL (RT)	11,6 vs 5,4	50 vs 28	29% (≥2)
Gomez et al. [2]	CBNPC	49	≤ 3	38,8	TS - > TL (RT ou chirurgie)	14,2 vs 4,4	41,2 vs 17,0	20% (≥3)
Iyengar et al. [3]	CBNPC	29	≤ 5	9,6	TS - > TL (RT)	9,7 vs 3,5	NR	8,3% (≥3)
Wang et al. [4]	CBNPC EGFR+	133	≤ 5	23,6	TKI seul vs TKI et RT	20,2 vs 12,5	25,5 vs 17,4	6% (≥3)
Tsai et al. [5]	CBNPC sein	106	≤ 5 (OP)		TS vs TS + RT sur tous les sites OP	CBNPC 10 vs 2,2 **Tps médian chgt de TS : 8,1 vs 5,3 mois**		61% (≥2)

1 Palma et al. JCO 2020, 2 Gomez et al. Lancet oncology 2016, 3 Iyengar et al. JAMA oncology 2017, 4 Wang et al. J Natl Cancer Inst 2021, 5 Tsai et al. ASTRO 2022

Les enjeux et perspectives

- RCS dans les stades localisés et dans la maladie oligométastatique
- Pas de RT complémentaire dans les stades III pN2
- RCMI dans les stades 3
- Combinaison RT-immunothérapie à tous les stades

  - Volumes cibles et organes à risque
  - Dose / fractionnement
  - Objectifs de traitement / Effet recherché
  - Séquences thérapeutiques
  - Radiothérapie adaptative

Nouveaux Parcours Peri-opératoires

Pr Marie Wislez

Unité d'oncologie thoracique, Service de Pneumologie, Hôpital Cochin, AP-HP

Equipe "cancer, immune control and escape » Inserm U1138

Université de Paris

Université de Paris

Institut du cancer PARIS CARPEM

CANCER RESEARCH FOR PERSONALIZED MEDECINE

AP-HP.Centre-Université de Paris

Liens d’intérêts

Investigateurs essais thérapeutiques : AZ, Roche, BMS, MSD, Novartis, Amgen, Lilly

Symposium : AZ, Roche, MSD, Pfizer, Lilly, Amgen, Takeda

Expertise : AZ, Roche, BMS, MSD, Novartis, Amgen, Lilly, Neogene

Les stades non métastatiques

TNM	Survie à 5 ans
IB	68%
IIA	60%
IIB	53%
IIIA	36%

Améliorer la survie

- Diminuer le risque de récidive
- Diminuer les métastases occultes non détectables avant la chirurgie

J Thorac Dis 2019;11(7):2955-2964

Les stades localisés

Adjuvant Chemotherapy OS benefit

2004

Adjuvant Osimertinib DFS benefit

2020

Neo adjuvant Nivolumab CT CM816 MPR cPR DFS

Adjuvant atezolizumab IMpower 010 DFS

Adjuvant pembrolizumab Keynote 091 DFS

2014

MAGRIT adjuvant vaccine trial

2016

ECOG 1505 adjuvant angiogenesis inhibition

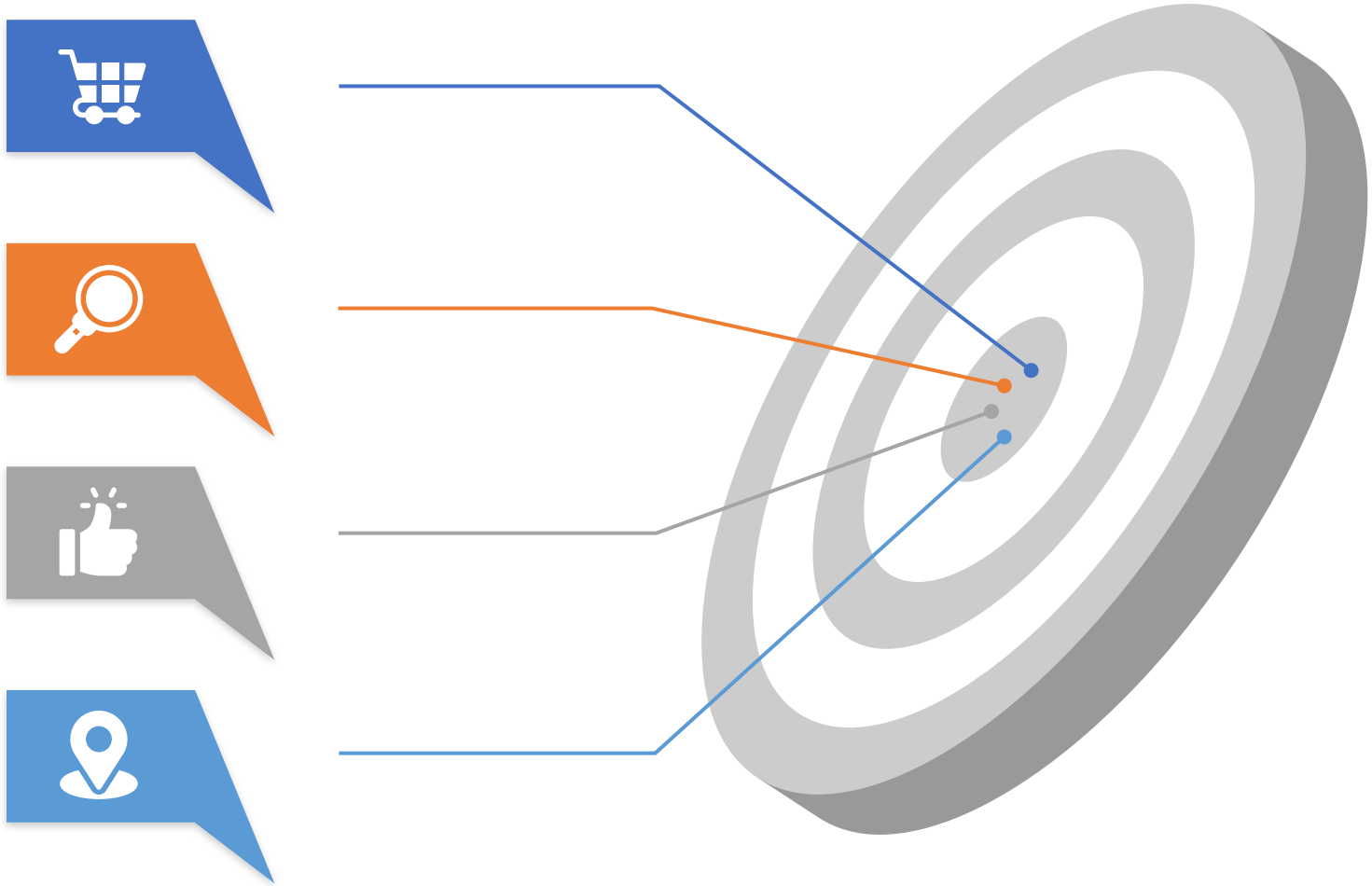
Quels sont les points à connaitre ?

Chimiothérapie adjuvante et néoadjuvante
Méta-analyse ~ **+ 5% survie à 5 ans**, stade et PS dépendant

Observance à la chimiothérapie en adjuvant > neoadjuvant **(91% vs 61%)**

Réponse histologique majeure et survie pour la chimiothérapie à base de platine

Rationnel préclinique pour l'immunothérapie en néaodjuvant > adjuvant



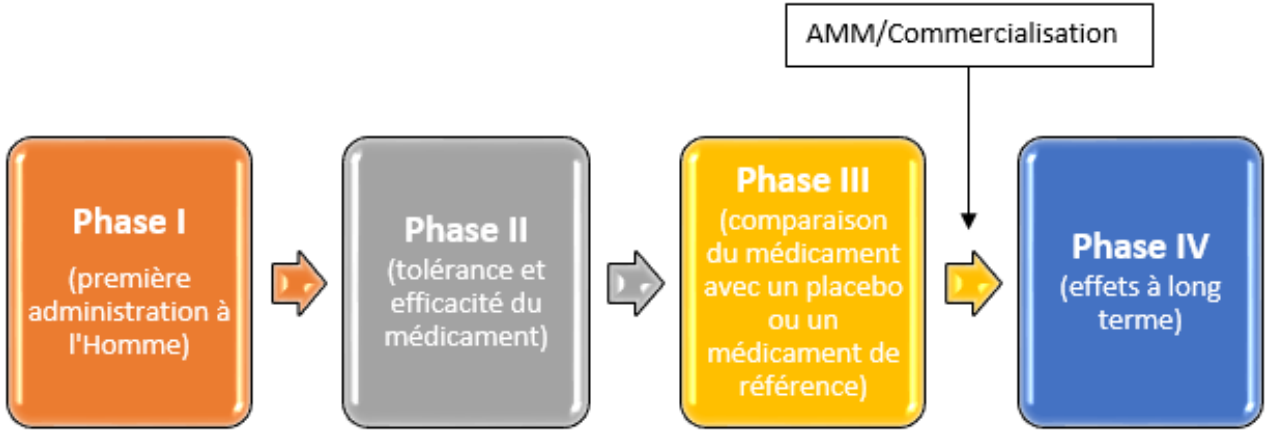
NEJM 00; JNCI 03; EuroJTS 04, NEJM 04; NEJM 05; J Clin Oncol 2008; Lancet Oncology; J Clin Oncol 2010; 28:3138-3145

Immunothérapie en monothérapie néoadjuvante

conclusions des études de phase 2

Difficulté d'analyse des essais

- Multi / monocentrique
- Petits effectifs
- Objectifs principaux
  - réponse histologique vs patients opérés
- Mortalité à 90 jours
- Type histologique C épidermoïde
  - Comorbidités
  - Tabac
  - Tumeurs proximales
  - Pneumonectomie
- Nombre de cycles
- Délais entre le dernier cycle et la chirurgie



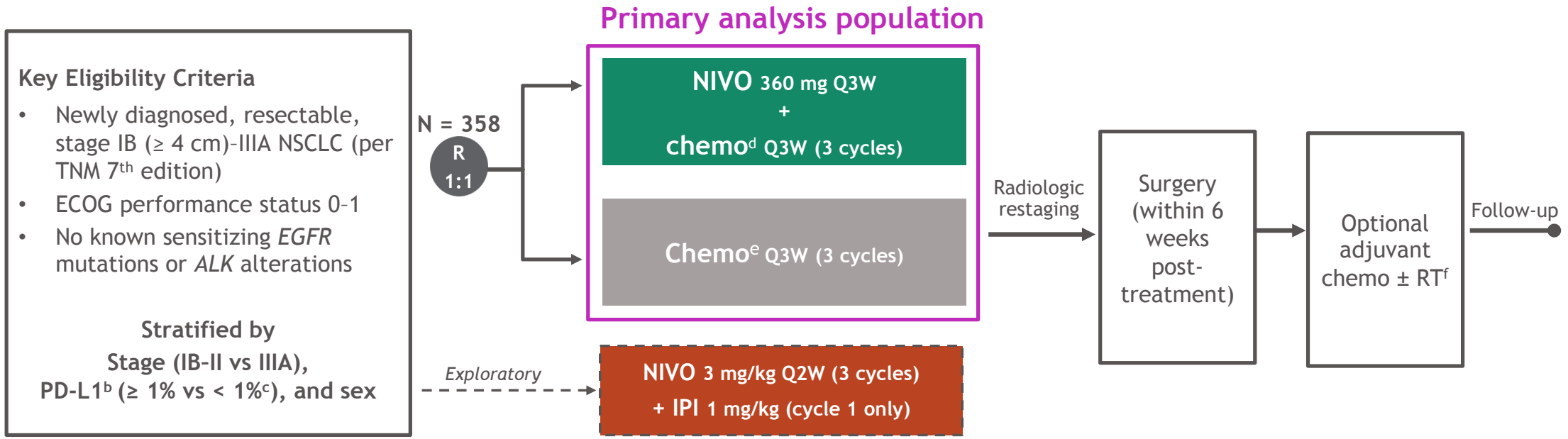
L'immunothérapie néoadjuvante impacte t'elle la chirurgie?

- Complexité de la chirurgie ?
- Flare-up médiastinal
- Effets indésirables immuns

Phase 3 : ICI + chimiothérapie vs chimiothérapie situation néoadjuvante

Sponsor	NCT#	stage	Treatment	Primary end point	N	Estimated completion
CM 816	02998528	IB-IIA	Nivo/Ipi vs. Nivo/Chemo vs. Chemo	EFS pCR	350	May 2023
IMPOWER 030	03456063	II-IIIB	Atezolizumab + chemo vs chemo+Placebo	MPR EFS	450	Nov 2024
KN 671	03425643	IIB-IIIA	Pembro/chemo vs chemo	EFS, OS	786	Jan 2024
Agean	03800134	IIA-IIIB	Durva/Chemo vs. Chemo	MPR EFS	800	Jan 2024

CheckMate-816 : Neoadjuvant immunotherapy



Primary endpoints
- pCR by BIPR
- EFS by BICR

Secondary endpoints
- MPR by BIPR
- OS
- Time to death or distant metastases

Exploratory endpoints
- ORR by BICR
- Predictive biomarkers (PD-L1, TMB, ctDNA[g])

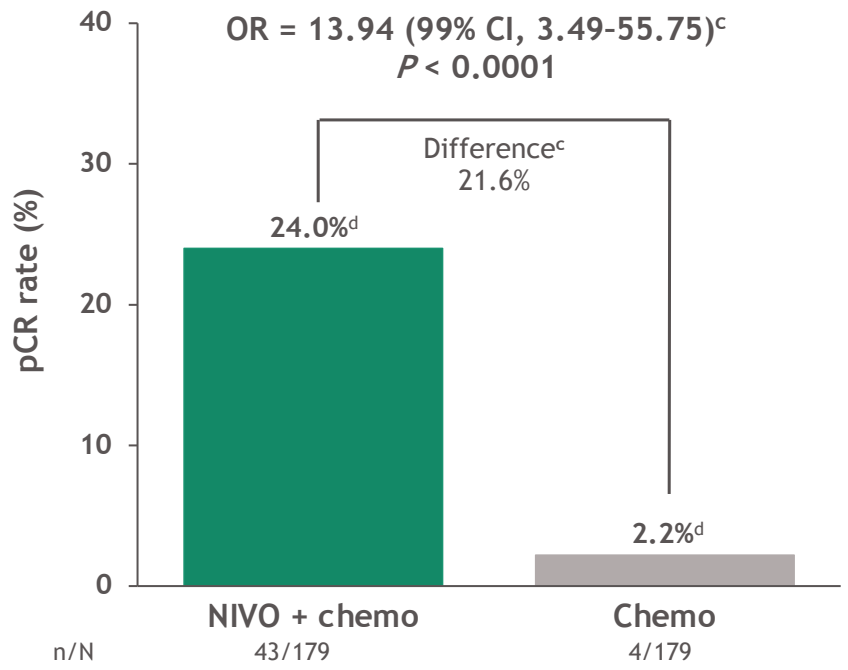
Database lock: September 16, 2020; minimum follow-up: 7.6 mo for NIVO + chemo and chemo arms.

[a]NCT02998528; [b]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako); [c]Included patients with PD-L1 expression status not evaluable and indeterminate; [d]NSQ; pemetrexed + cisplatin; paclitaxel + carboplatin; SQ: gemcitabine + cisplatin; paclitaxel + carboplatin; [e]Vinorelbine + cisplatin, or docetaxel + cisplatin, or gemcitabine + cisplatin (SQ only), or pemetrexed + cisplatin (NSQ only) or paclitaxel + carboplatin; [f]Per HCP choice; [g]Performed using tumor-guided personalized ctDNA panel (ArcherDX PCM).

Forde et al. AACR 2021; Spicer et al. ASCO 2021

CheckMate-816 : Neoadjuvant immunotherapy

Primary endpoint: pCR rate with neoadjuvant NIVO + chemo vs chemo



CM-816: Exploratory Biomarker data

- **pCR rates favored N+CT across PD-L1 levels, although higher rates in the PDL1≥50% subgroup (pCR=45%)**
  - PD-L1 expression as expected (49.7% pts with ≥1%; 22.3% pts with ≥50%)
  - For comparison, in BR31: 57.8% pts with ≥1%; 24.1% pts with ≥50%)

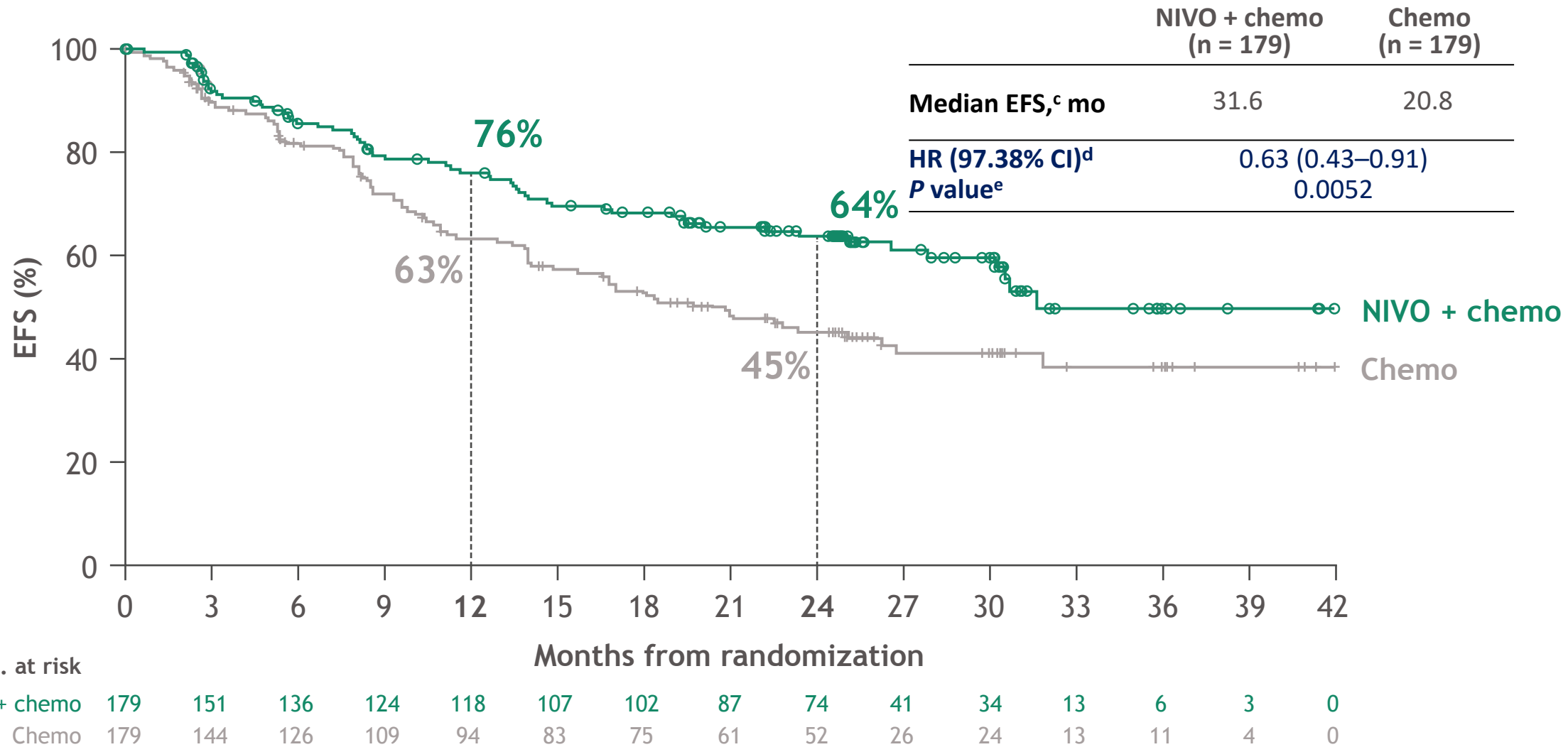
	pCR[a] rate, %		Unweighted pCR difference, % (95% CI)	Unweighted pCR difference, %
	NIVO + chemo (n = 179)	Chemo (n = 179)		
PD-L1 < 1% (n = 155)	17	3		14
PD-L1 ≥ 1% (n = 178)	33	2		30
PD-L1 1-49% (n = 98)	24	0		24
PD-L1 ≥ 50% (n = 80)	45	5		40
TMB < 12.3 mut/Mb (n = 102)	22	2		21
TMB ≥ 12.3 mut/Mb (n = 76)	31	3		28

- pCR rate in the NIVO + IPI arm was 20.4% (95% CI, 13.4-29.0)

[a]per BIPR; pCR: 0% residual viable tumor cells in both primary tumor (lung) and sampled lymph nodes; [b]ITT principle: patients wł
stratified Cochran-Mantel-Haenszel method; [d]pCR rates 95% CI: NIVO + chemo, 18.0-31.0; chemo, 0.6-5.6; [e]Patients who underw

CheckMate-816 : Neoadjuvant immunotherapy

Primary endpoint: EFS with neoadjuvant NIVO + chemo vs chemo

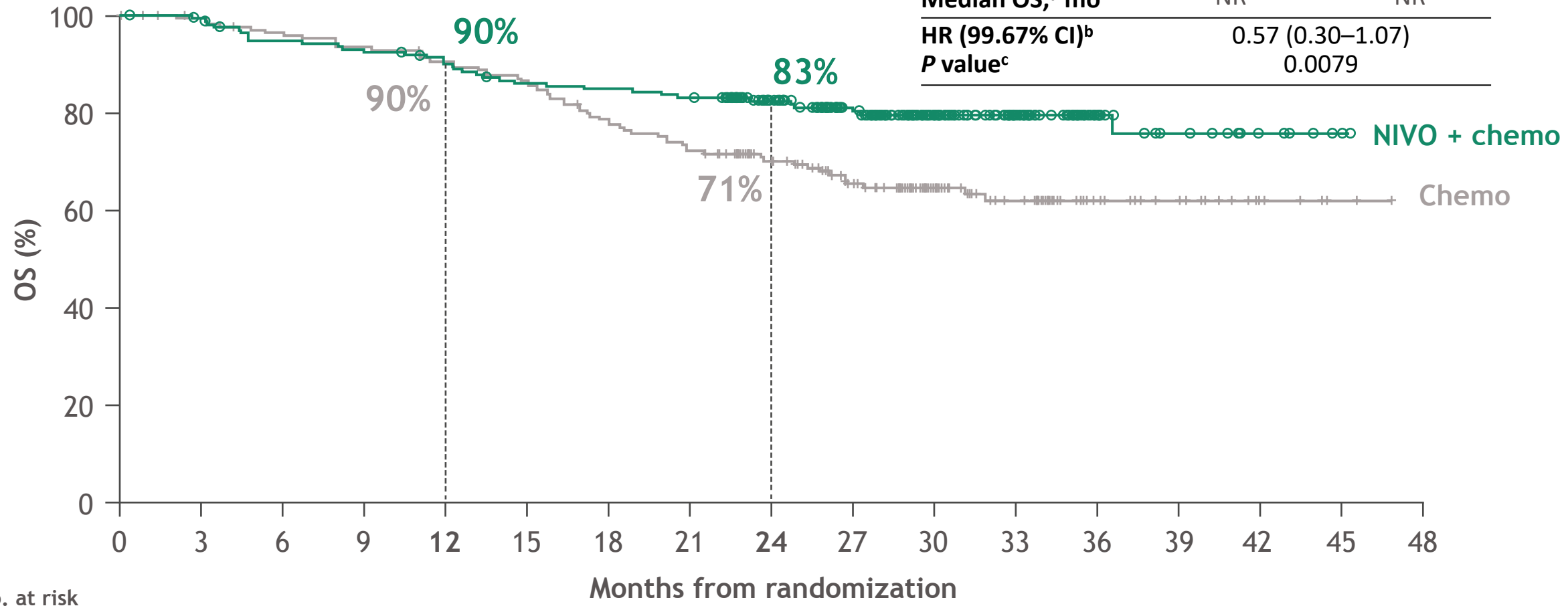


	NIVO + chemo (n = 179)	Chemo (n = 179)
Median EFS,[c] mo	31.6	20.8
HR (97.38% CI)[d]	0.63 (0.43–0.91)	
***P* value[e]**	0.0052	

CheckMate-816 : Neoadjuvant immunotherapy

Overall survival: interim analysis

	NIVO + chemo (n = 179)	Chemo (n = 179)
Median OS,[a] mo	NR	NR
HR (99.67% CI)[b]	0.57 (0.30–1.07)	
***P* value[c]**	0.0079	



No. at risk																
NIVO + chemo	179	176	166	163	156	148	146	143	122	101	72	48	26	16	7	3	0
Chemo	179	172	165	161	154	148	133	123	108	80	59	41	24	16	7	2	0

Minimum follow-up: 21 months; median follow-up, 29.5 months.

[a]95% CI = NR-NR (NIVO + chemo) and NR-NR (chemo); [b]95% CI = 0.38-0.87; [c]Significance boundary for OS (0.0033) was not met at this interim analysis.

Phase 3 : ICI monothérapie en situation adjuvante

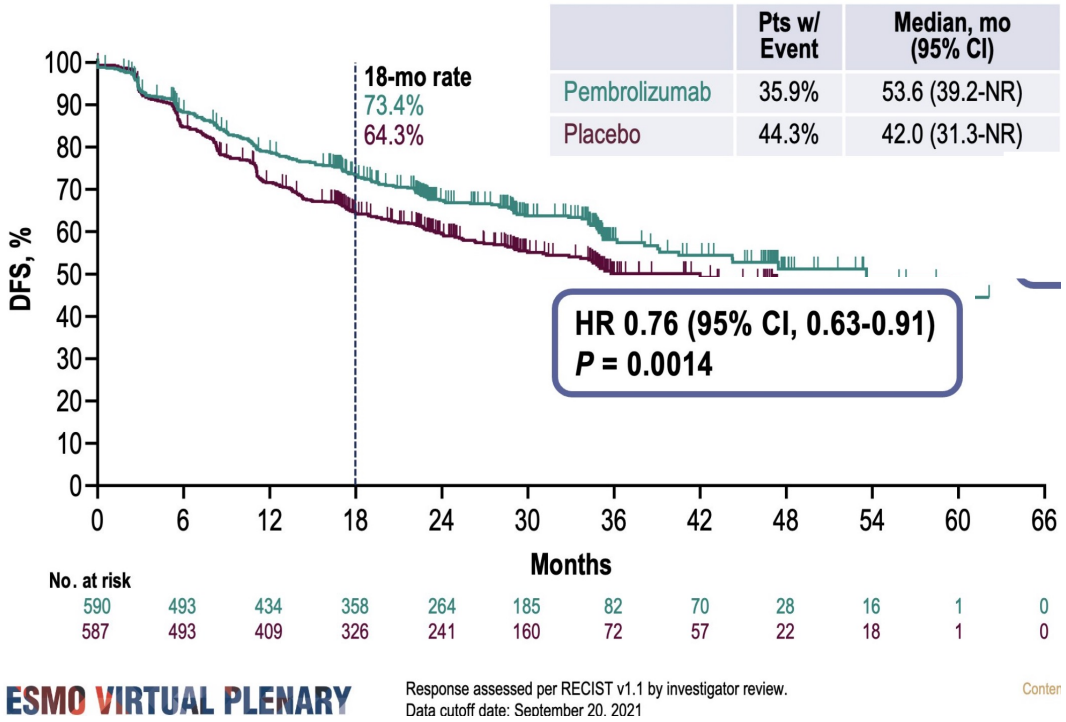
TABLE 2. Phase III Trials of Adjuvant anti–PD-L1 for Resected Non–Small-Cell Lung Cancer

Study	PD-1/PD-L1 Inhibitor	Sample Size	Chemotherapy-Specified	PORT	Placebo	Primary End Points	Status
EA5142/ANVIL (NCT02595944)	Nivolumab	903	No	Yes	No	DFS and OS DFS in PD-L1 ≥ 50% and in ITT	Completed accrual
IMpower010 (NCT02486718)	Atezolizumab	1,280	Yes	No	No	DFS in stage II/III PD-L1+ and all DFS in ITT PD-L1+ and all	Completed accrual
BR.31 (NCT02273375)	Durvalumab	1,360	No	No	Yes	DFS in PD-L1+	Completed accrual
EORTC141/PEARLS (NCT02504372)	Pembrolizumab	1,080	No	Yes	Yes	DFS in all DFS in PD-L1 high	Completed accrual
ACCIO/ALLIANCE (NCT04267848)	Pembrolizumab (concurrent and sequential arms)	1,263	Yes	No	No	DFS and OS in all	Accrual ongoing

Abbreviations: DFS, disease-free survival; ITT, intention to treat; OS, overall survival; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PORT, postoperative radiotherapy.

Adjuvant immunotherapy

PEARLS / KEYNOTE-091
DFS, Overall Population



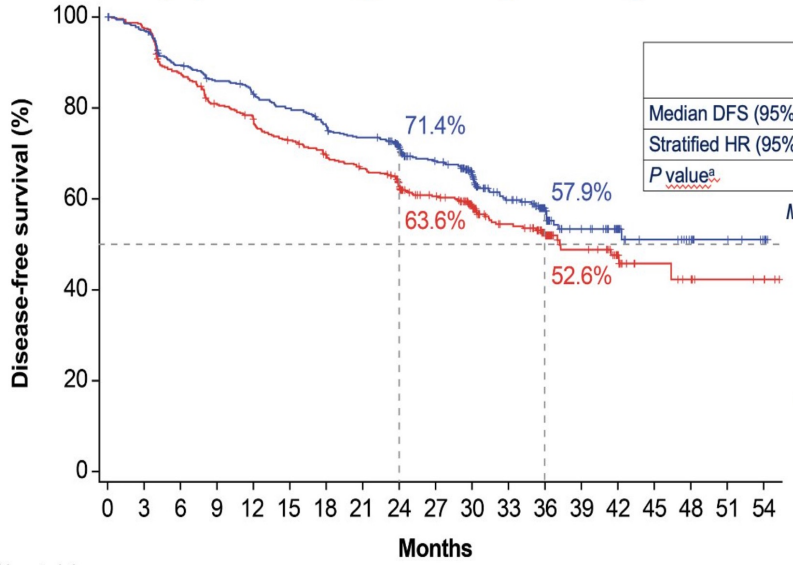
	Pts w/ Event	Median, mo (95% CI)
Pembrolizumab	35.9%	53.6 (39.2-NR)
Placebo	44.3%	42.0 (31.3-NR)

ESMO VIRTUAL PLENARY

Response assessed per RECIST v1.1 by investigator review.
Data cutoff date: September 20, 2021

Paz Ares L, ESMO virtual meeting 2022

IMpower010: DFS in the ITT population (stage IB-IIIA; primary endpoint)



	Atezolizumab (n=507)	BSC (n=498)
Median DFS (95% CI), mo	NE (36.1, NE)	37.2 (31.6, NE)
Stratified HR (95% CI)	0.81 (0.67, 0.99)	
P value[a]	0.04[b]	

Median follow-up: 32.2 mo (range, 0-58.8)

- DFS in the ITT population did not cross the significance boundary at this interim DFS analysis

Clinical cutoff: January 21, 2021. [a] Stratified log-rank. [b] The statistical significance boundary for DFS was not crossed.

Similar HR for DFS in IMpower 010

TKI EGFR en adjuvant

Adjuvant Osimertinib versus Placebo (ADAURA)

Patients with completely resected stage* IB, II, IIIA NSCLC, with or without adjuvant chemotherapy†

Key inclusion criteria:
- ≥18 years (Japan / Taiwan: ≥20)
- WHO PS 0 / 1
- Confirmed primary non-squamous NSCLC Ex19del / L858R‡
- MRI or CT scan of the brain prior to surgery or randomization
- Complete resection with negative margins¶
- Maximum interval between surgery and randomization:
  - 10 weeks without adjuvant chemotherapy
  - 26 weeks with adjuvant chemotherapy

Adjuvant chemotherapy use was per physician and patient choice, and should have consisted of a platinum-based doublet for ≤4 cycles

Stratification by:
stage (IB vs II vs IIIA)
EGFRm (Ex19del vs L858R)
race (Asian vs non-Asian)

Osimertinib 80 mg, once daily

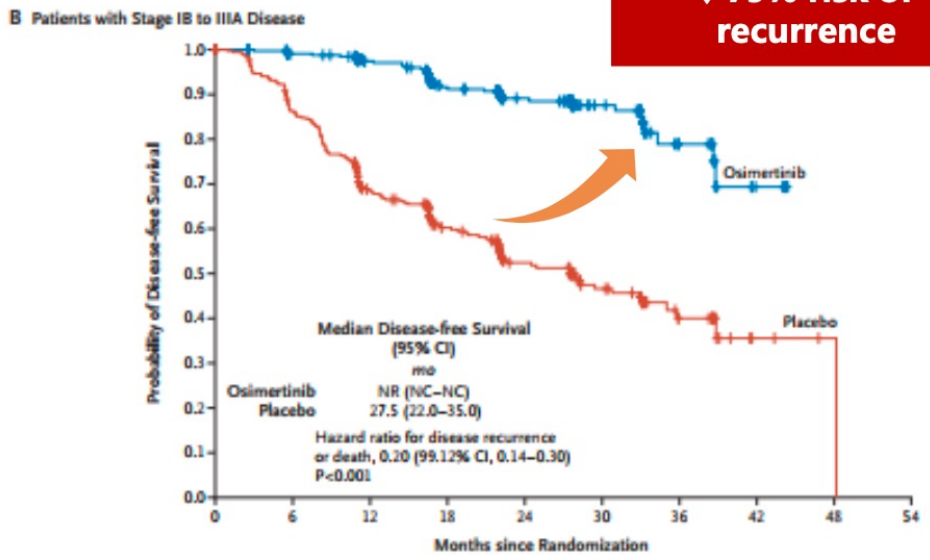
Placebo, once daily

Planned treatment duration: three years

Treatment continues until:
- Disease recurrence
- Treatment completed
- Discontinuation criterion met

Follow up:
- Until recurrence: Week 12 and 24, then every 24 weeks to 5 years, then yearly
- After recurrence: every 24 weeks for 5 years, then yearly

↓ 79% risk of recurrence



2020 ASCO, Presented By Roy Herbst Wu YL et al. 2020 N Engl J Med. 2021 NCCN

EMA Committee for Medicinal Products for Human Use (CHMP) decisions

- Avril 2022

The EMA Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion supporting the approval of adjuvant atezolizumab (Tecentriq), after complete resection and platinum-based chemotherapy, in adult patients with NSCLC with a high risk of recurrence and whose tumors express PD-L1 of 50% or higher and do not harbor *EGFR* mutations or *ALK* alterations.

- Avril 2021

The CHMP adopted a new indication as follows : Tagrisso as monotherapy is indicated for the adjuvant treatment after complete tumour resection in adult patients with stage IB-IIIA NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations.

Discussion …

- Quels patients ?
  - TNM
  - Place du PD-L1 pour l'immunothérapie
  - Place de l'ADN tumoral circulant
- Nouvelles indications de l'adjuvant
  - Quel testing sur la pièce opératoire
  - Durée
- Néoadjuvant
  - Necessité d'un diagnostic histologique pré opératoire
  - Stagging complet documenté
  - Testing sur petites biopsies
  - Délais pour la chirurgie
  - Place de la réponse histologique

Comment opérer le cancer bronchique en 2022

Pr Marco Alifano

Chirurgie Thoracique

HUPC, AP-HP Centre

Université de Paris

Déclaration des liens d'intérêts
J'ai actuellement, ou j'ai eu au cours des trois dernières années, une affiliation ou des intérêts financiers ou intérêts de tout ordre avec les sociétés commerciales suivantes en lien avec la santé.

- Liens d'intérêt :
  Consulting pour BMS, AMGEN, Roche, AstraZeneca

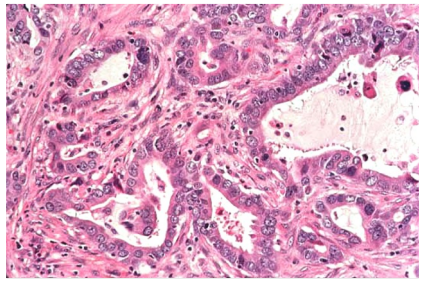
- Liens d'intérêt en relation avec la présentation :
  - Aucun

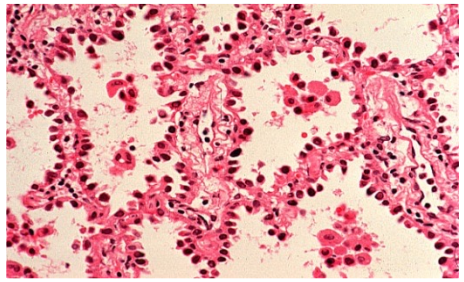
Chirurgie Thoracique: Contexte

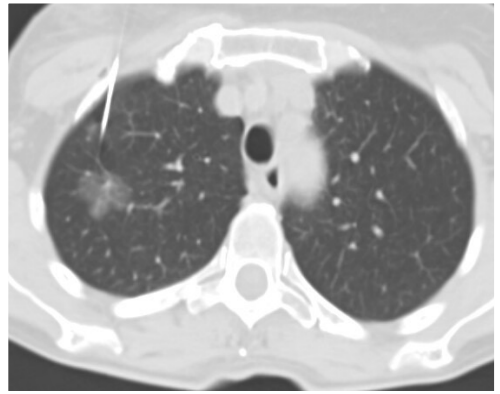
- Demandes « grandissantes » de
  - prises en charge moins agressives en termes de lourdeur des gestes
  - gestion optimale de la douleur
  - réduction des durées d'hospitalisation
  - retour rapide à la vie précédente

- Cependant demande inchangée de prise en charge, médico-chirurgicale, de
  - pathologies lourdes
  - chez des malades âgés ou à fortes comorbidités
  - ambition de traitements mieux tolérés et donc plus acceptables

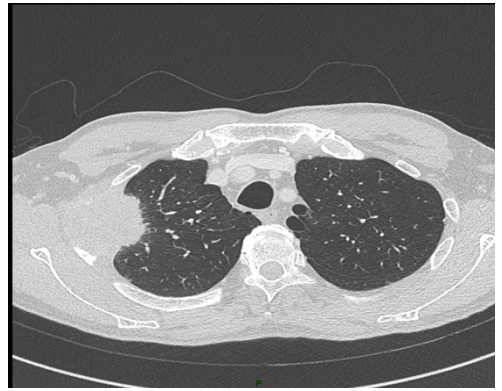
Chirurgie Thoracique: Contexte



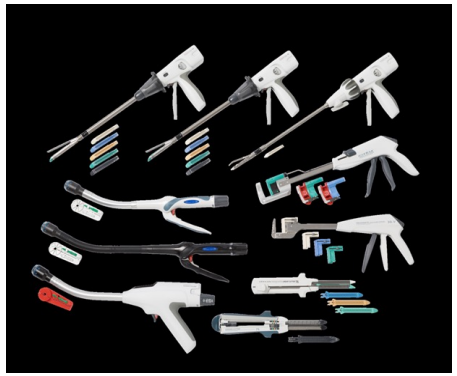




- Les maladies (et leur connaissance) changent aussi :
  - Diagnostics précoces possibles et souvent réalisés
    - Traitements moins agressifs
  - Meilleure connaissance des aspects biologiques
    - De la maladie
    - Du malade
  - Nouvelle cibles thérapeutiques efficaces
  - *+10% d'actes GFFA chaque année en France (jusqu'en 2019)*



Outils

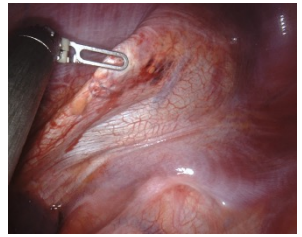


- Bloc opératoires et salles d'endoscopie
  - Equipés
    - Vidéo
    - Robot
    - Connectés
    - Hybrides

- Organisation des services d'hospitalisation et des activités de chirurgie repensé pour prendre en compte/profiter
  - RRAC (« Fast track »)
  - Hôtel patients
  - Hospitalisation conventionnelle aux capacitaires adaptés

- Adaptation de la typologie de secteur critique aux patients qui en relèvent
  - Réanimation (Uni/multi défaillance)
  - Soins intensifs (prise en charge mono-défaillance respiratoire)

- Faciliter la sortie des patients qui ne relèvent plus de l'hospitalisation mais ne sont pas aptes au retour à domicile (y compris problématiques démographiques et sociales)
  - SSR
  - Hôtel patients



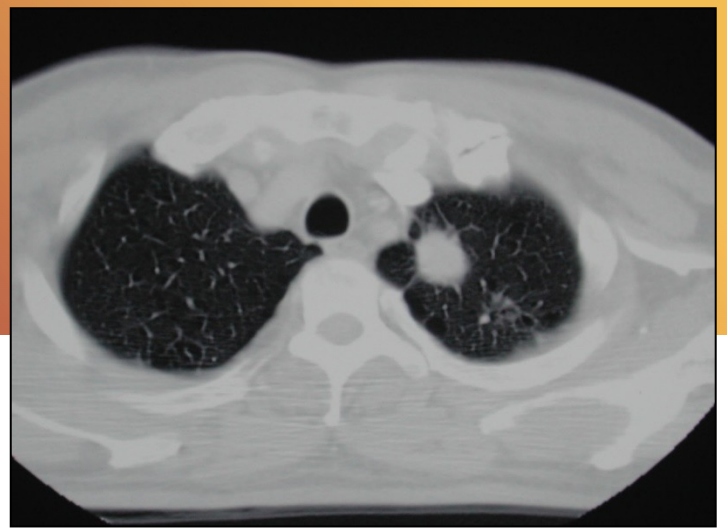
Chirurgie Thoracique Oncologique: Développer la précision dans un contexte vaste

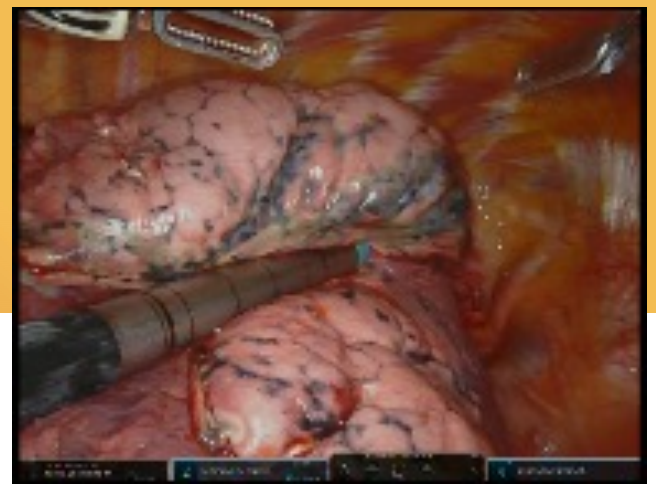
Quelle ambition?

Traitements chirurgicaux mieux tolérés et donc plus acceptables

- Intégration de la chirurgie à des prises en charge multimodales
  - Multidisciplinaires
  - Pluri professionnelles
- Amélioration des résultats
  - Morbi-mortalité
  - Survie libre de maladie
  - Survie libre de traitements
  - Survie globale
  - Qualité de vie

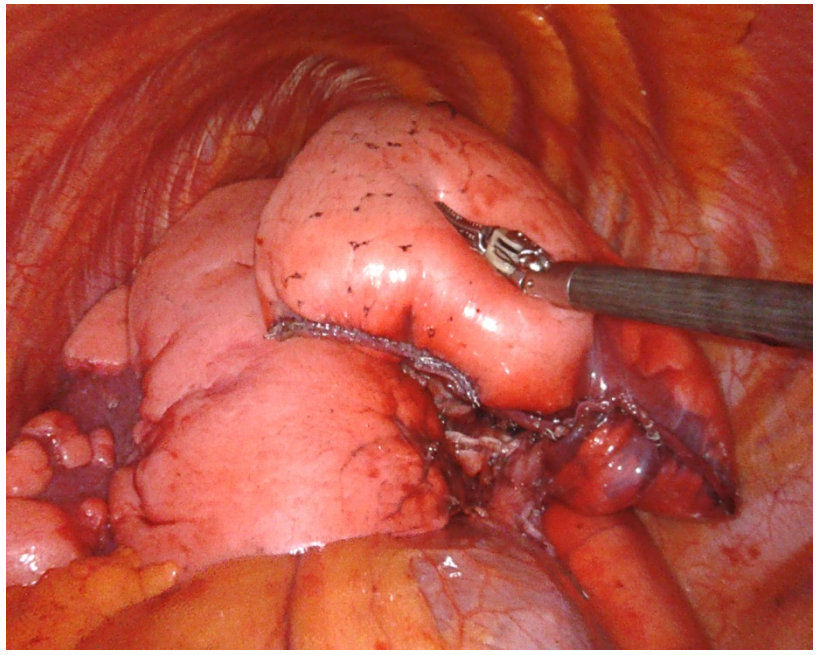
- Soutenabilité économique et sociale des prise en charge et de l'innovation

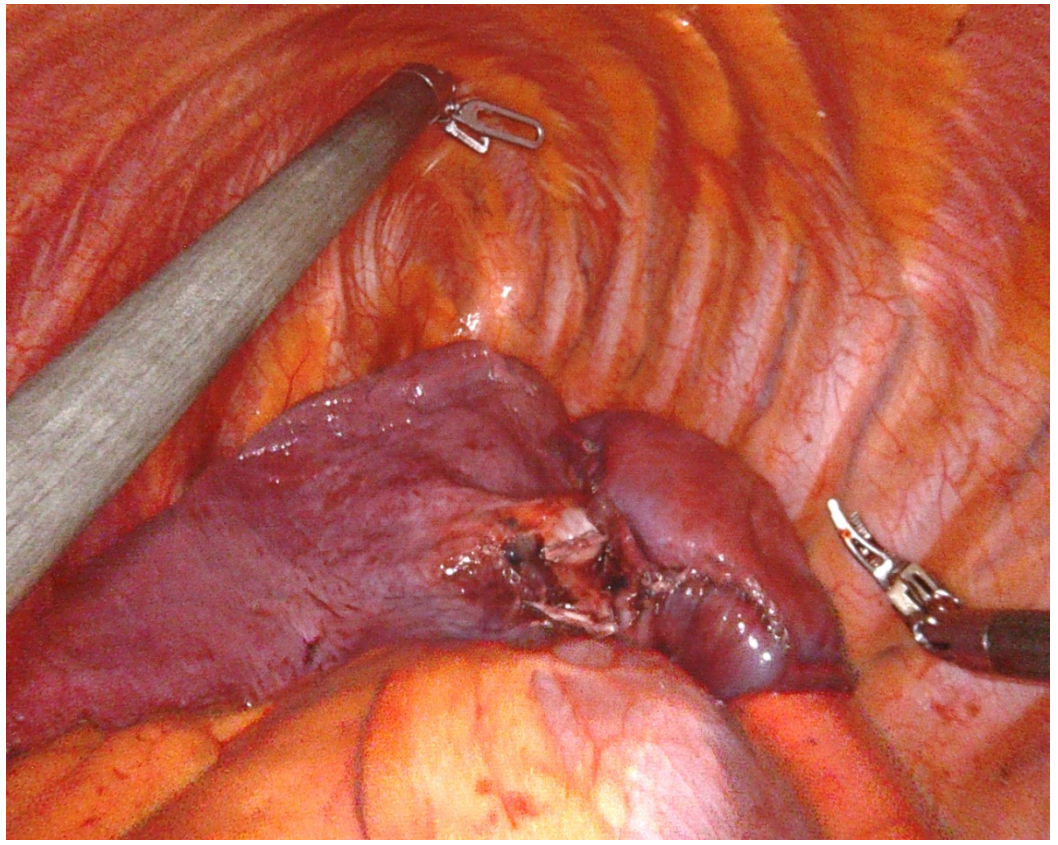


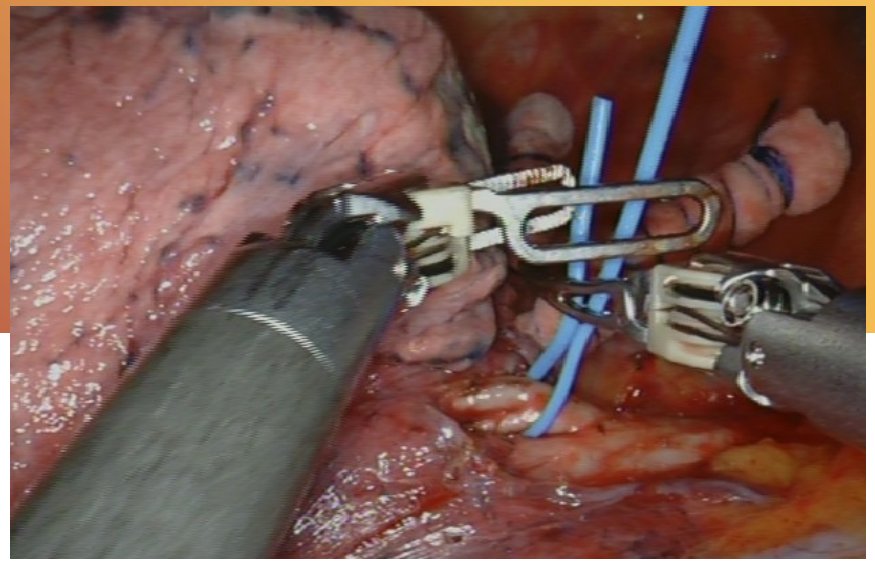


Les outils de l’innovations ou l’innovation et ses outils:

- Chirurgie vidéo ou robot- assistée
- Vision augmentée
- 7 dégrées de liberté dans les mouvements
- Agrafages vidéo et robot





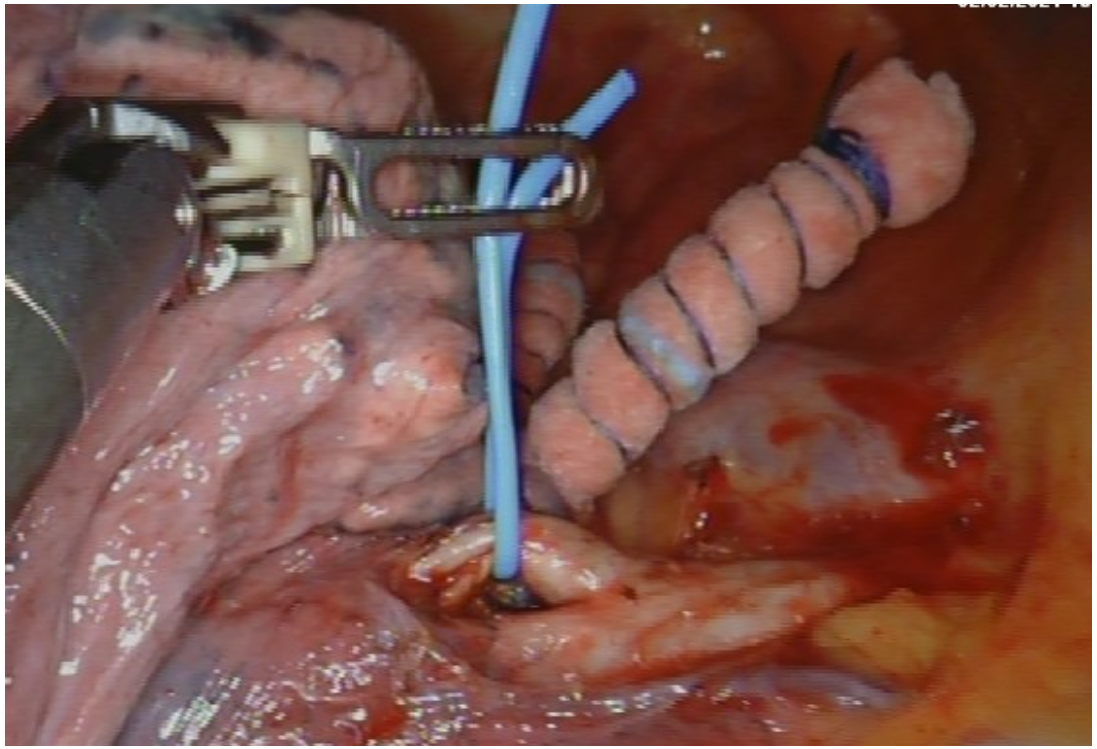


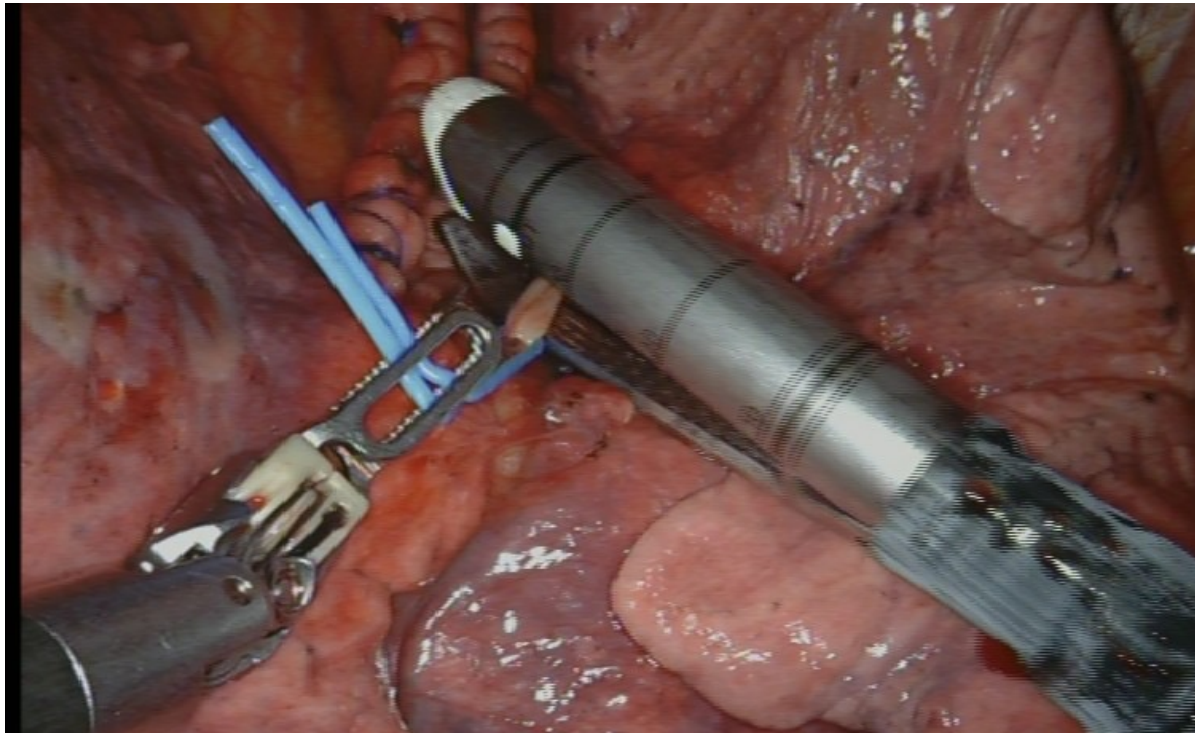
Chirurgie robotique

Vision et mobilité augmentées

Principes similaires à la chirurgie conventionnelle:

- Dissection
- Mise sur lac
- Section-suture
- Tampon disponible pour compression = SECURITE

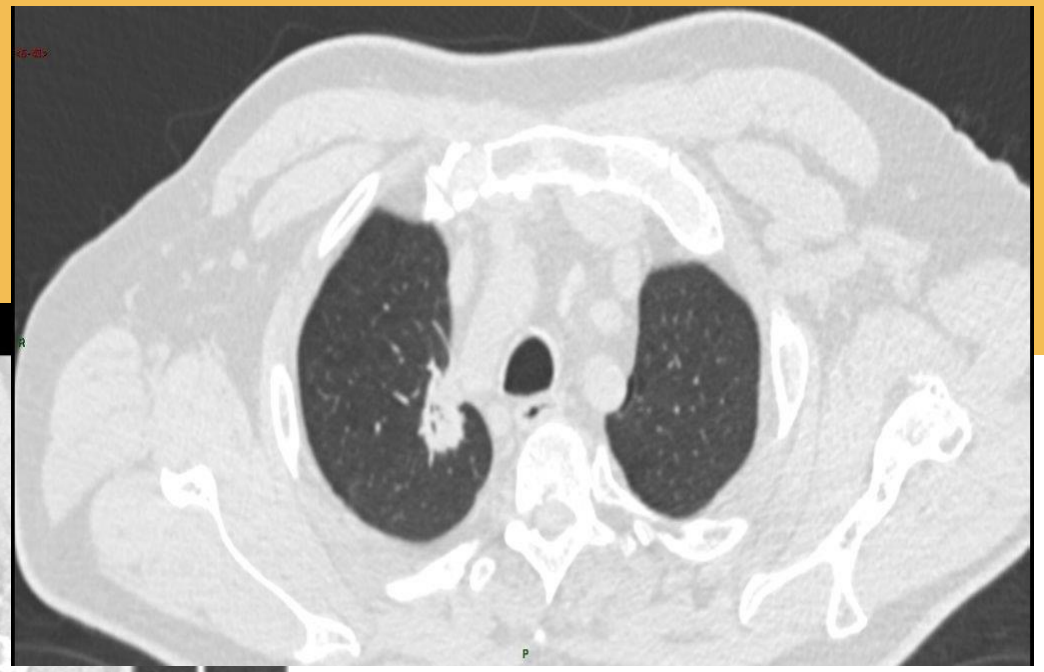


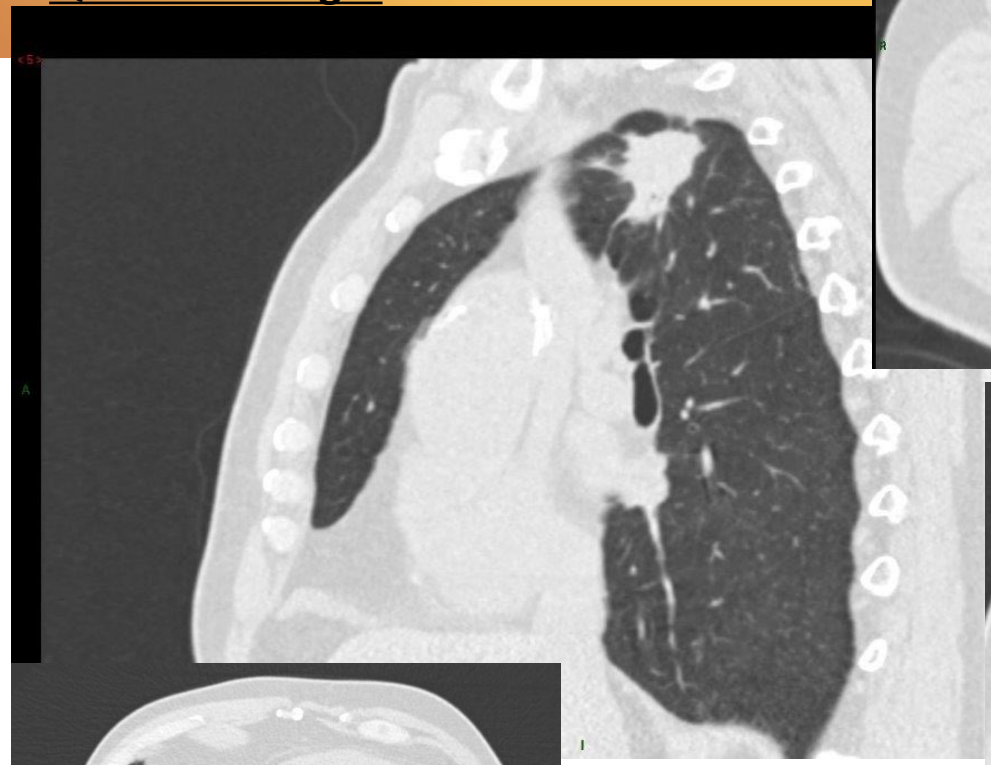


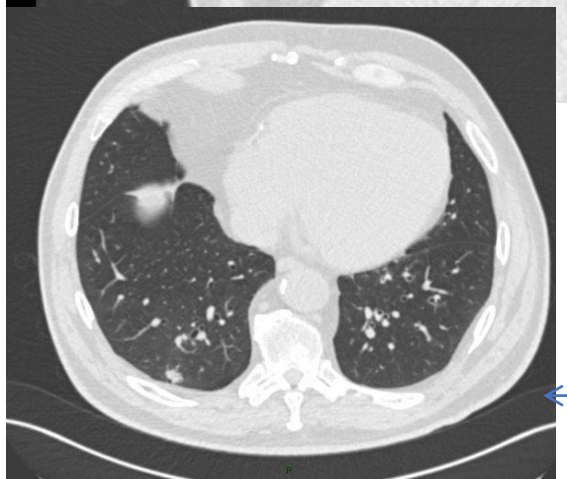
Synchronous homolateral tumors

M, 58 years 22 PA
3 right-side lesixons
FEV1 99%th;
Q Scan 68% right

PET: SUV
Max 7.8

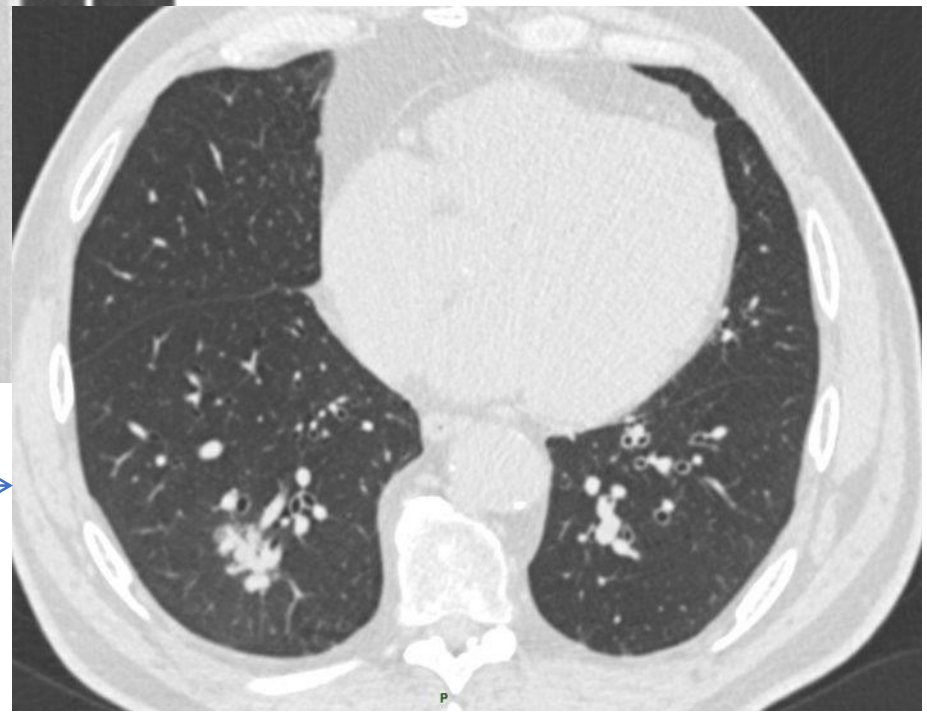




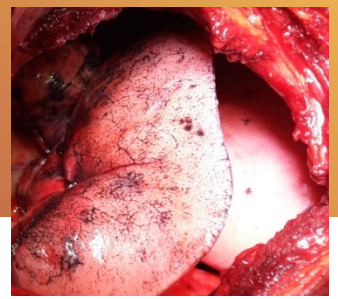


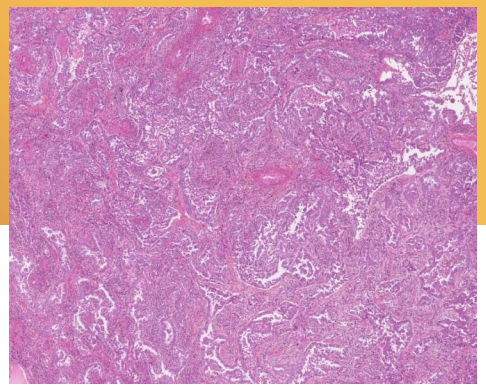
PET: SUV
Max 3.6

PET: SUV
Max 1.2



APICAL ANATOMICAL SEGMENTECTOMY





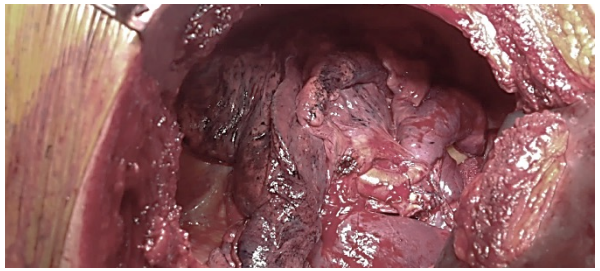
ORIGINAL ARTICLE

IASLC

Proposal for a Combined Histomolecular Algorithm to Distinguish Multiple Primary Adenocarcinomas from Intrapulmonary Metastasis in Patients with Multiple Lung Tumors

Audrey Mansuet-Lupo, MD, PhD,[a,b] Marc Barritault, MD, PhD,[c,d] Marco Alifano, MD, PhD,[e] Aurélie Janet-Vendroux, MD,[b,e] Makmoud Zarmaev, PharmD,[b] Jérôme Biton, PhD,[b] Yoan Velut,[b] Christine Le Hay,[d] Isabelle Cremer, PhD,[b] Jean-François Régnard, MD,[e] Ludovic Fournel, MD,[e] Bastien Rance, PhD,[f] Marie Wislez, MD, PhD,[b,g] Pierre Laurent-Puig, MD, PhD,[c,d] Ronald Herbst, MD, PhD,[h] Diane Damotte, MD, PhD,[a,b,*] Hélène Blons, PharmD, PhD[c,d]

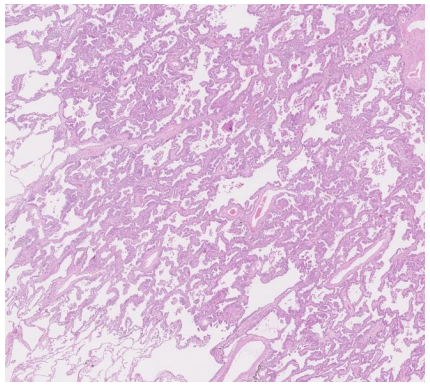
POSTERO-MEDIAL AND POSTERO-LATERAL ANATOMICAL BISEGMENTECTOMY

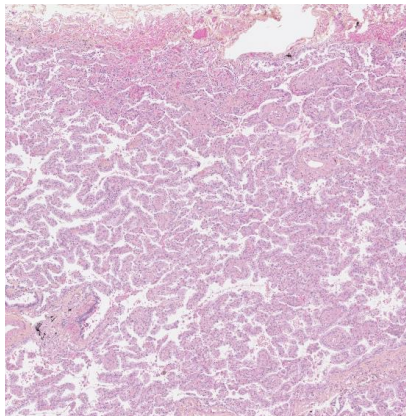


Tumor A

RUL Tubular ADK

MOL BIOL: **Mut c.35G>T, p.Gly12Val** of **KRAS**





Tumor B

RLL Papillary ADK

MOL BIO : Mut **c.34 G>T**, p.GlyCys of **KRAS**

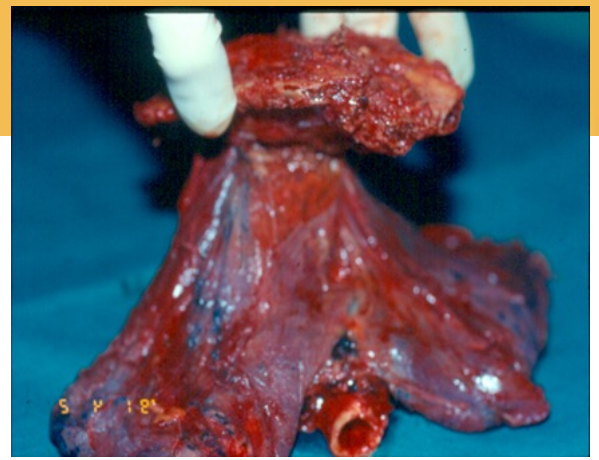
Tumor C

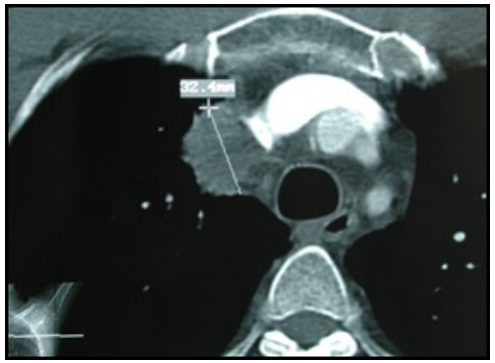
RLL papillary and lepidic ADK

MOL BIOL : Mut **c.34 G>T**, p.GlyCys of **KRAS**

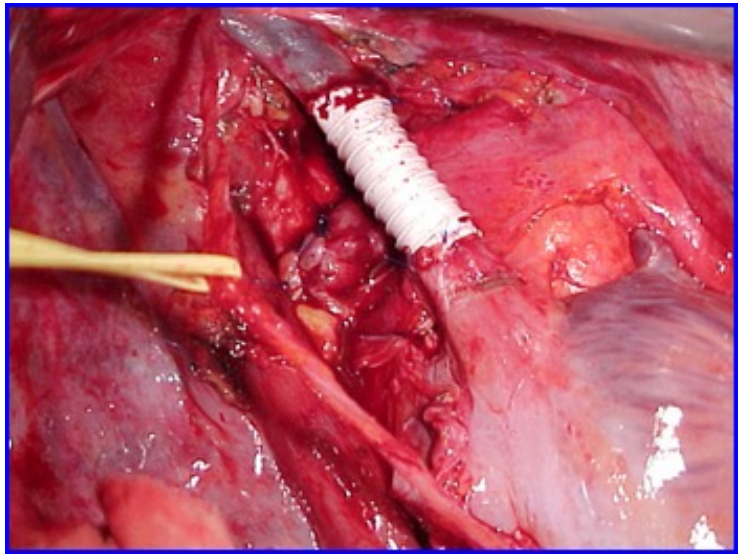
Chirurgie conventionnelle
C’est la culture globale qui évolue
avec les nouveaux outils

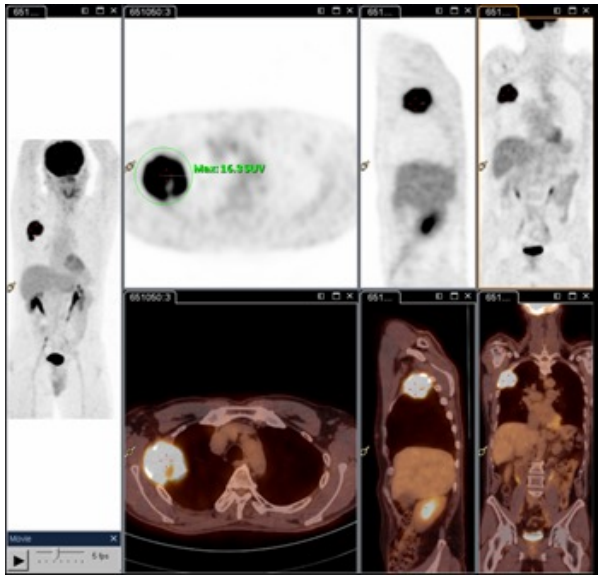
Paroi

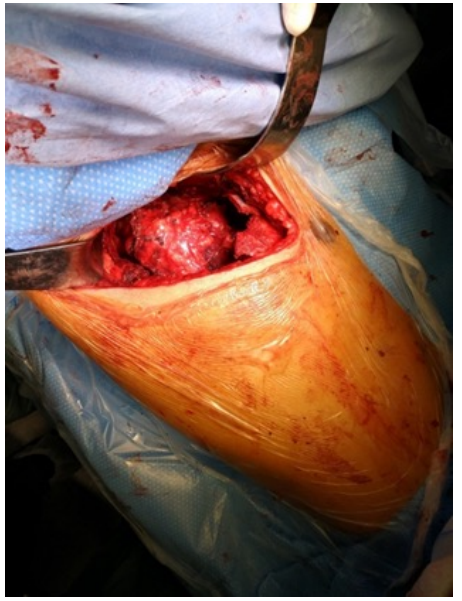


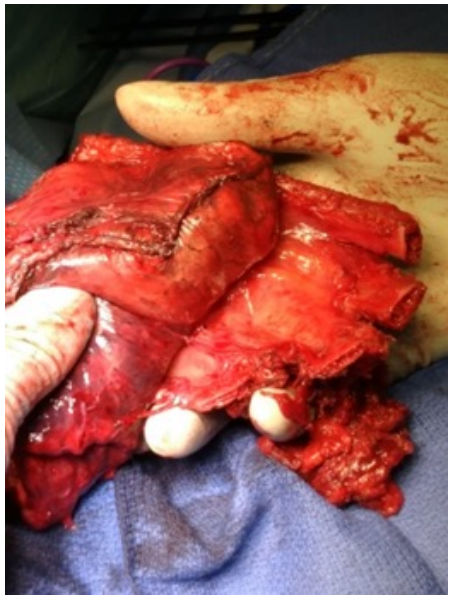


Résection VCS



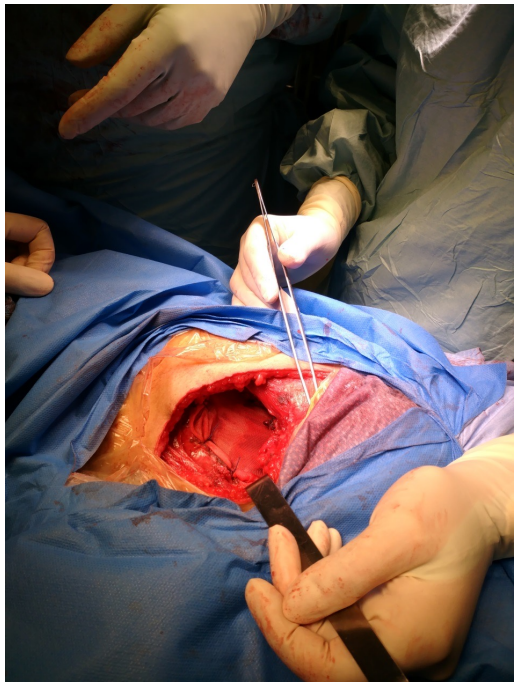


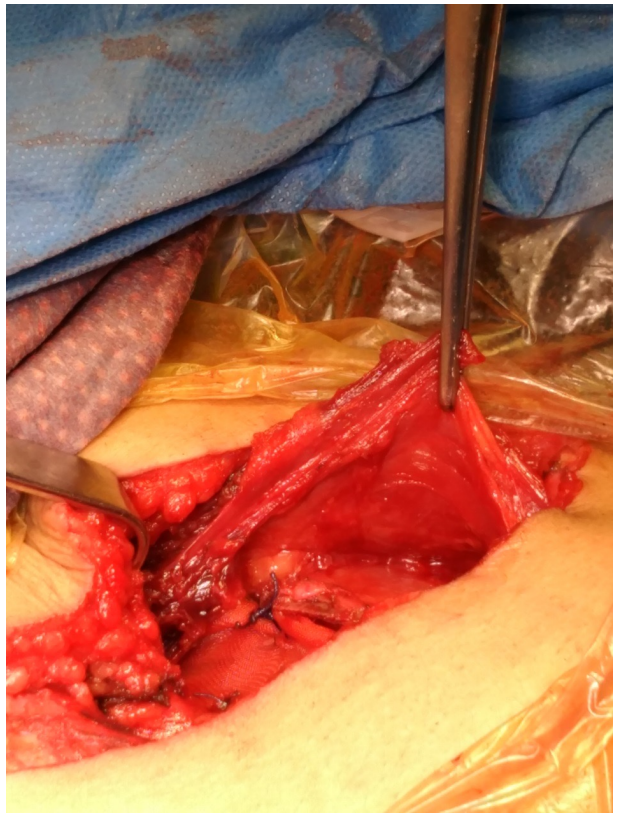


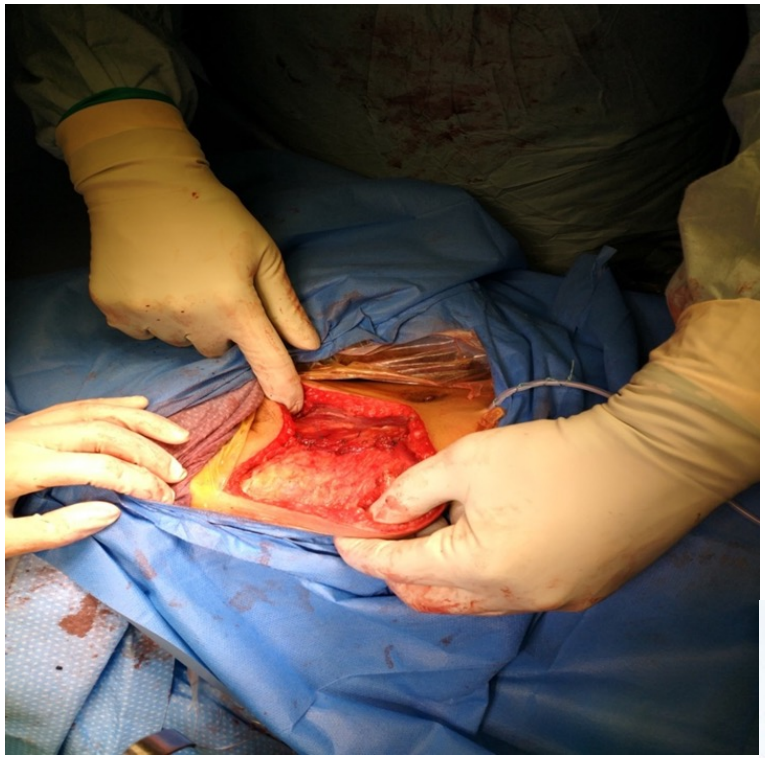


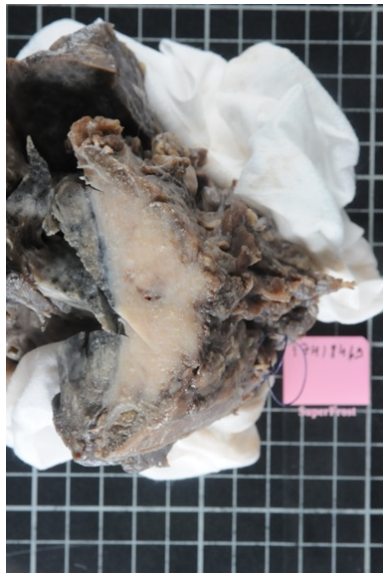
Cancer Pulmonaire T3 Paroi: **LSD + Paroi « en bloc »**

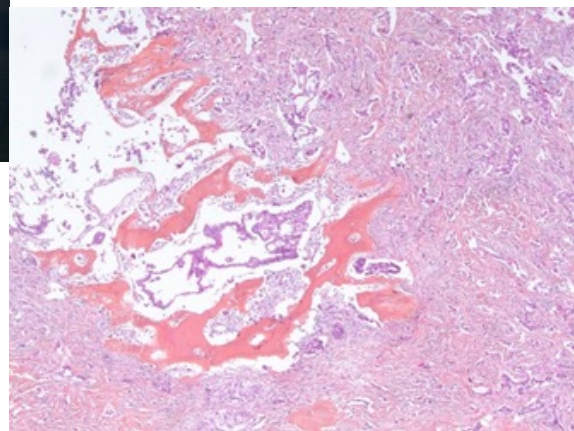
VICRYL MESH, PECTORALIS MAJOR + LATISSIMUS DORSI UNPEDICLED FLAPS





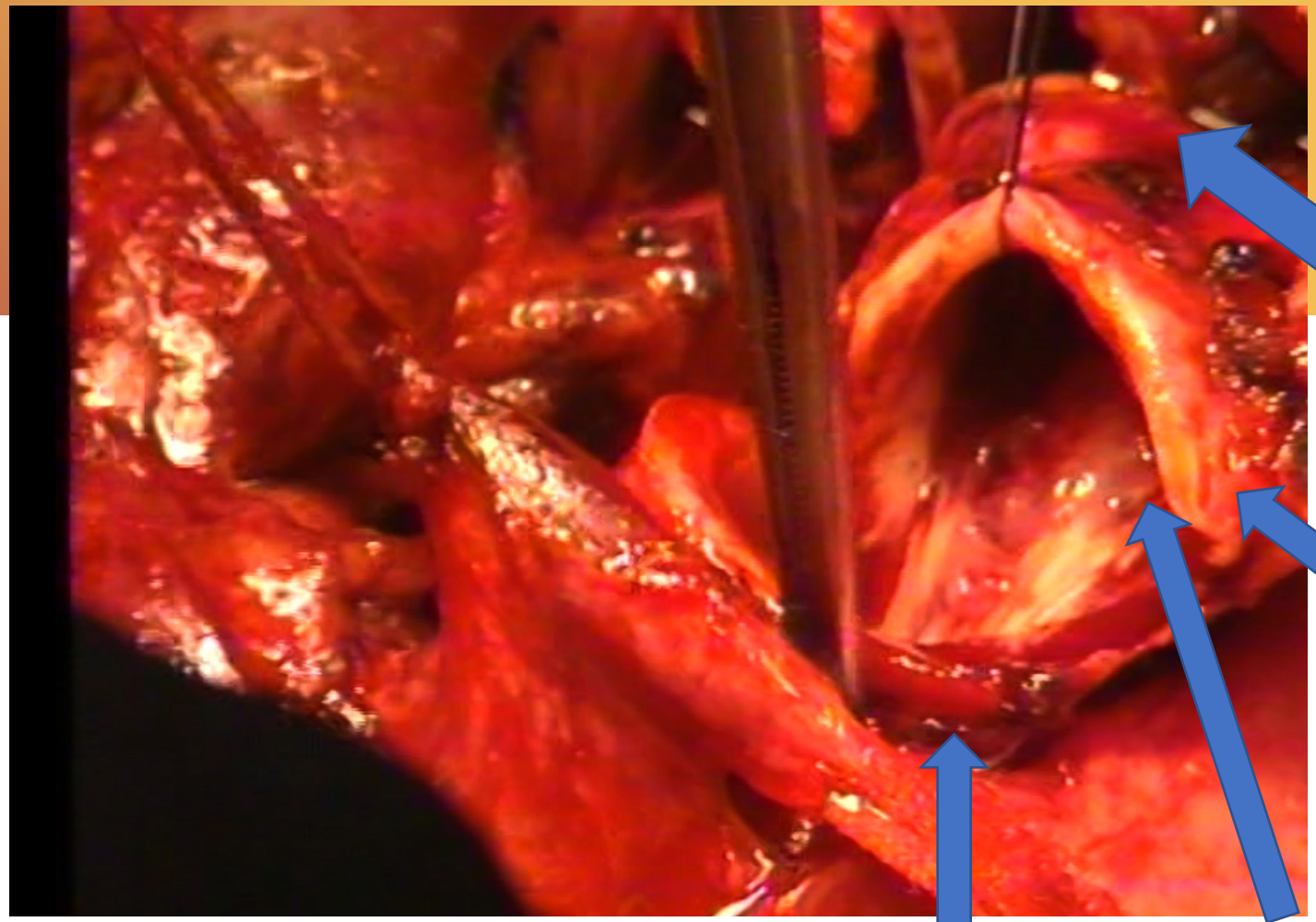






RCP Cancérologie Thoracique: 4 cures Cht adjuvante

Chirurgie conventionnelle
C’est la culture globale qui évolue avec les nouveaux outils



Tronc intermédiaire

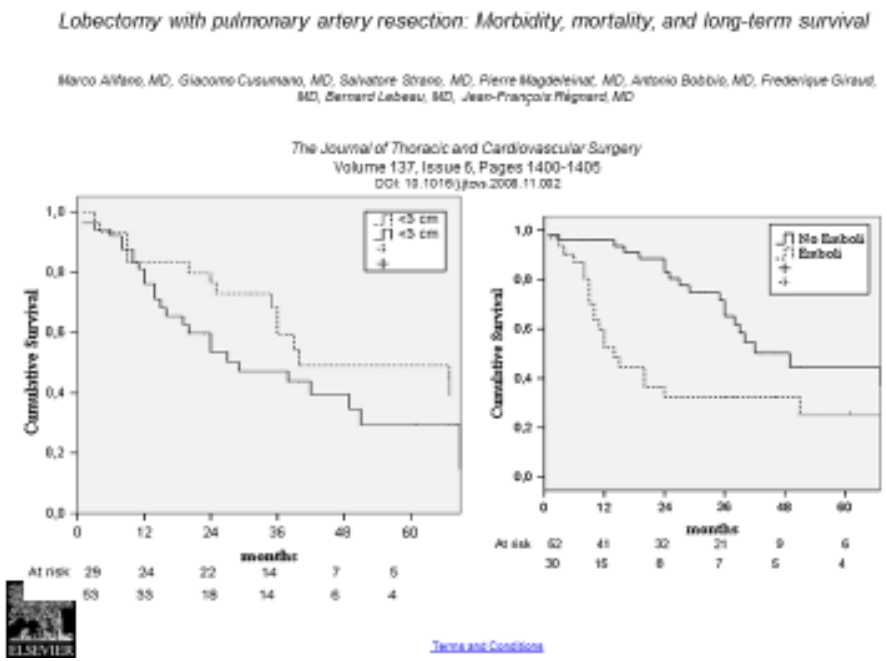
Lobaire sup Droite

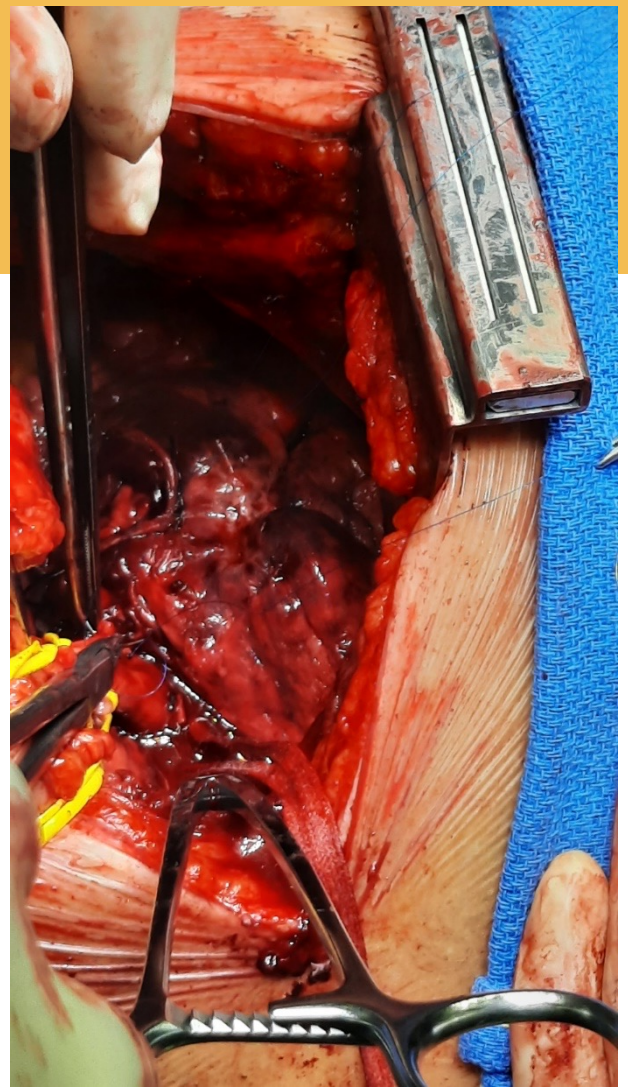
Cancer épidermoïde

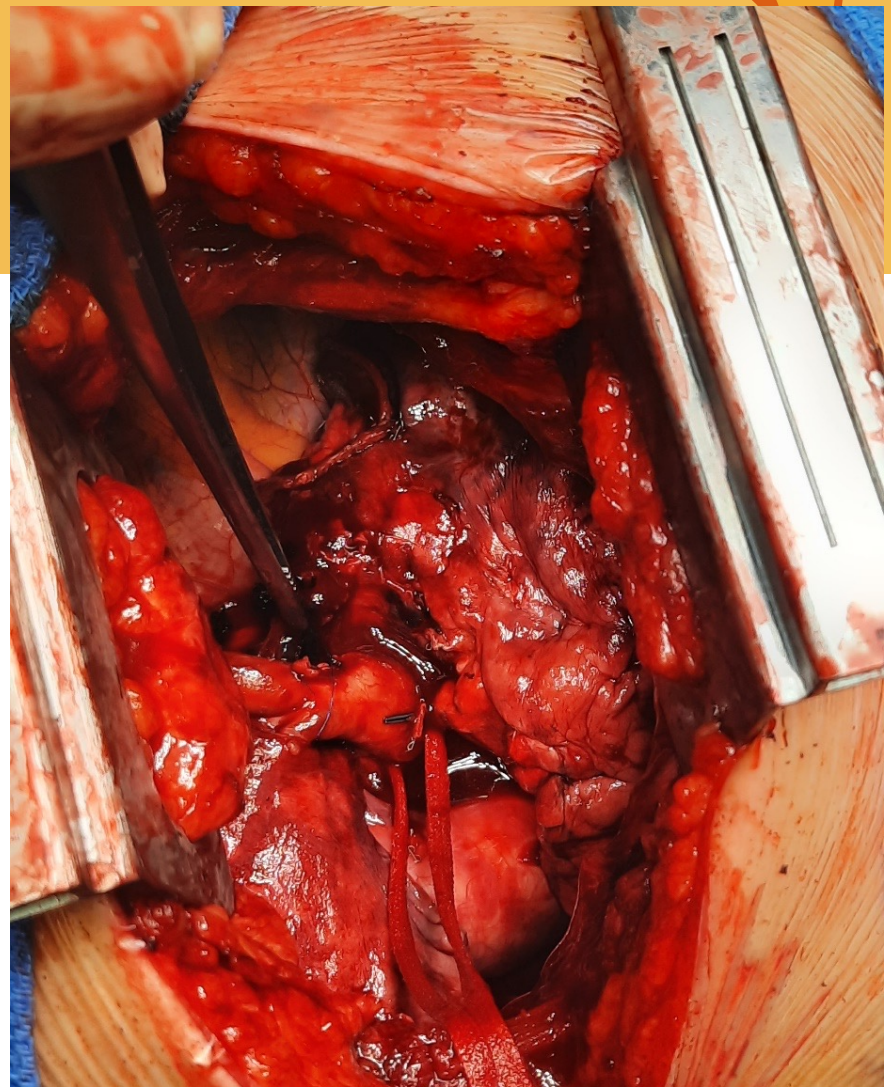
Bronche souche

Résection Anastomose bronchique « Sleeve »

Chirurgie conventionnelle
C’est la culture globale qui évolue avec les nouveaux outils





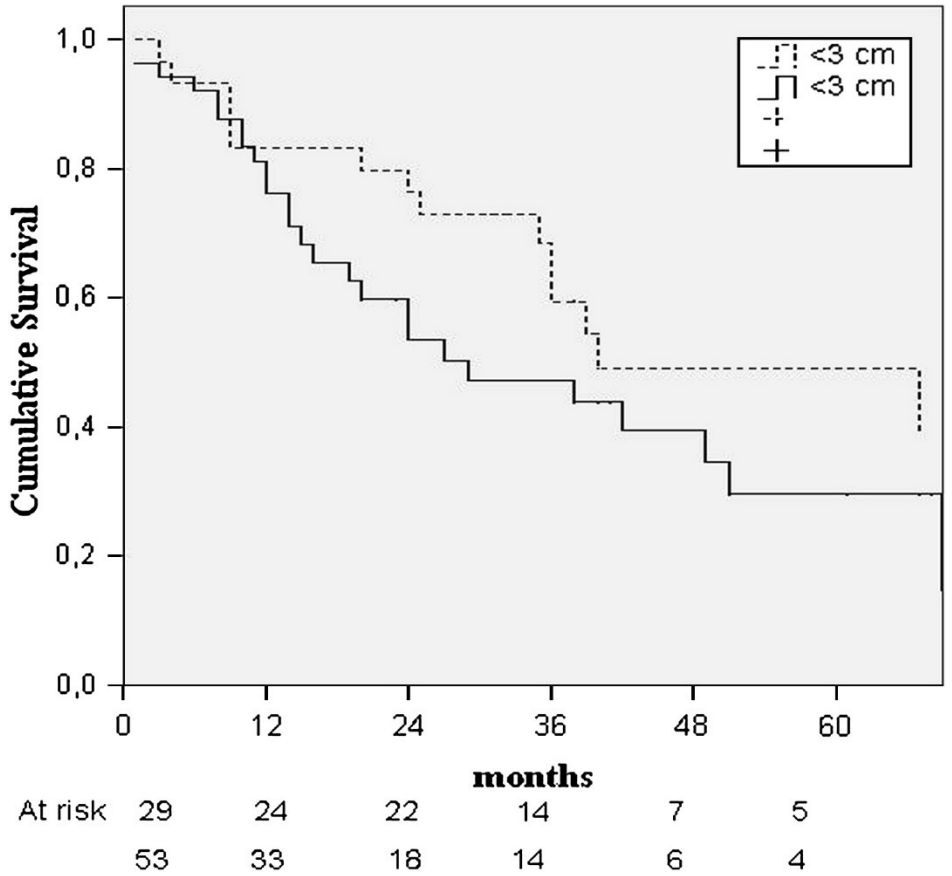


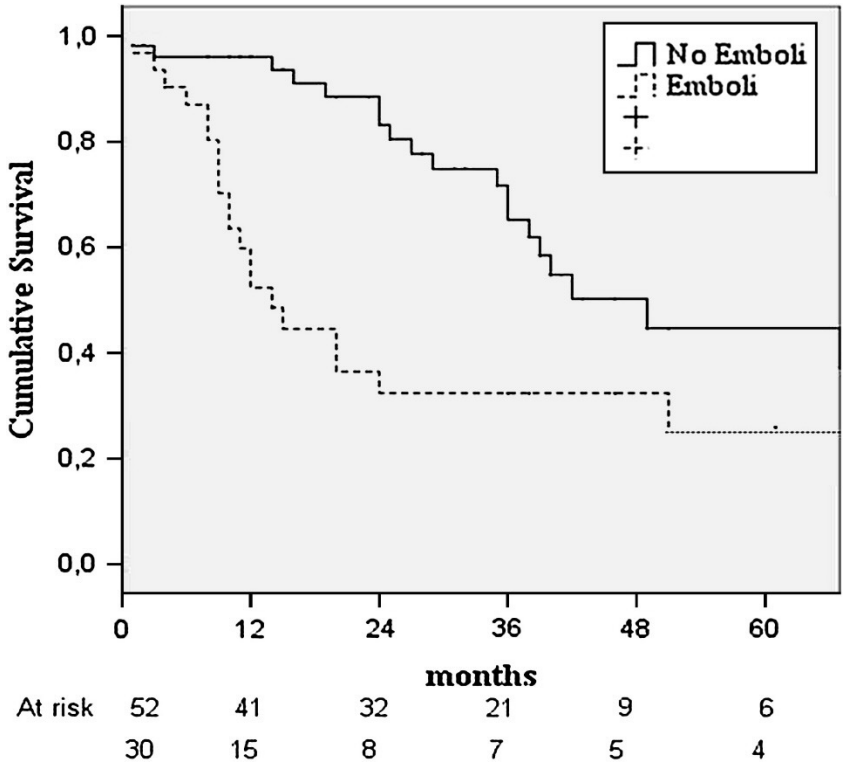
Plastie artérielle

Lobectomy with pulmonary artery resection: Morbidity, mortality, and long-term survival

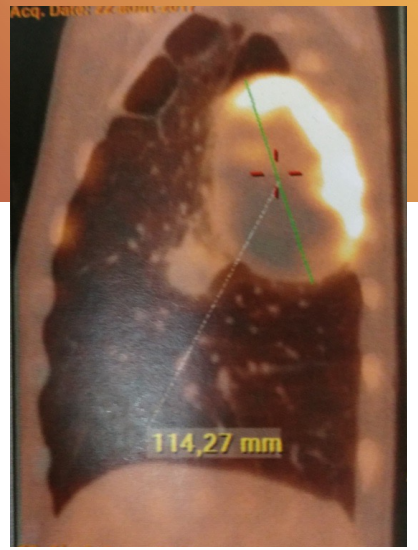
Marco Alifano, MD, Giacomo Cusumano, MD, Salvatore Strano, MD, Pierre Magdeleinat, MD, Antonio Bobbio, MD, Frederique Giraud, MD, Bernard Lebeau, MD, Jean-François Régnard, MD

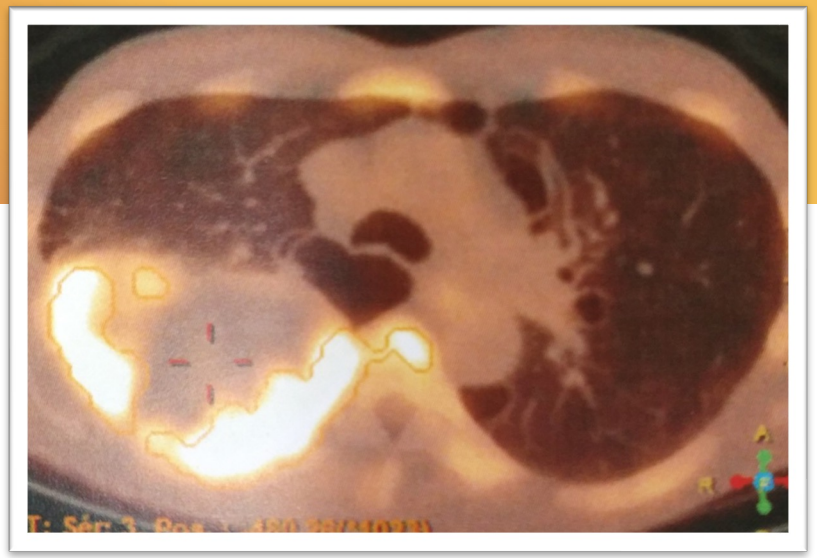
The Journal of Thoracic and Cardiovascular Surgery
Volume 137, Issue 6, Pages 1400-1405
DOI: 10.1016/j.jtcvs.2008.11.002





Cancer Pulmonaire T4 Paroi: **Pneumonectomie+ Paroi**





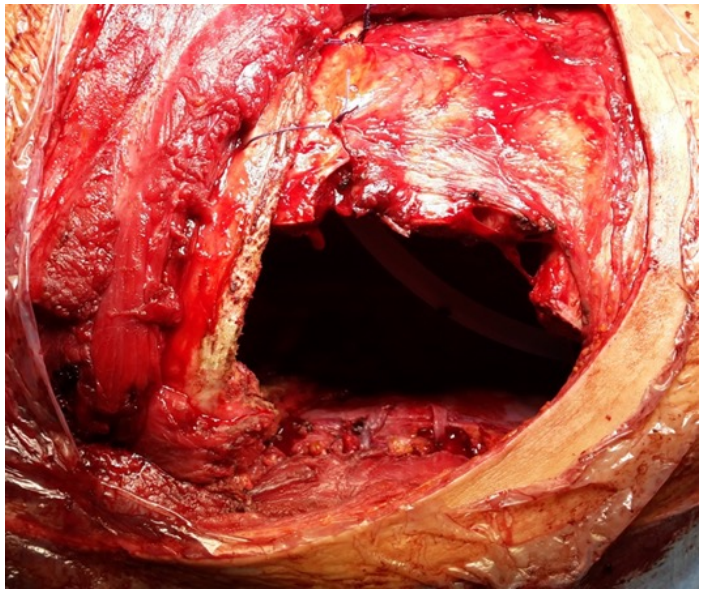
Chirurgie conventionnelle
C'est la culture globale qui évolue
avec les nouveaux outils

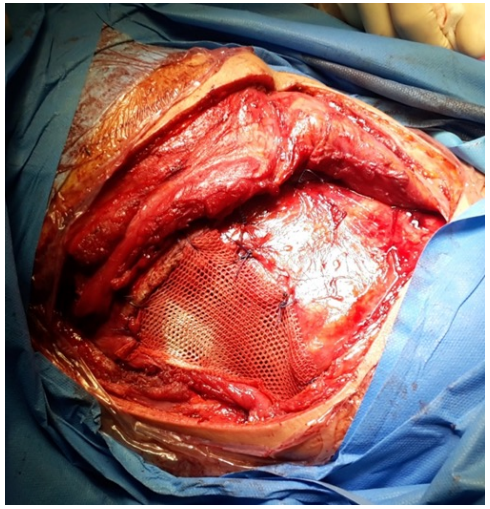
Lung (2015) 193:969–975
DOI 10.1007/s00408-015-9810-y

Which is the Role of Pneumonectomy in the Era of Parenchymal-Sparing Procedures? Early/Long-Term Survival and Functional Results of a Single-Center Experience

Aurélie Janet-Vendroux[2] · Mauro Lo[1] · Antonio Bobbio[1] · Filippo Lococo[1] · Audrey Lupo[2] · Pauline Ledinot[1] · Pierre Magdeleinat[1] · Nicolas Roche[2] · Diane Damotte[3] · Jean-François Regnard[1] · Marco Alifano[2]

293 M ; 105 W; 61,0 ± 10,9 years
Tobacco 84,5%, 40 P/Y (20-50)
History extrathor cancer: 13,7%
Significant comorbidities: 85,0%



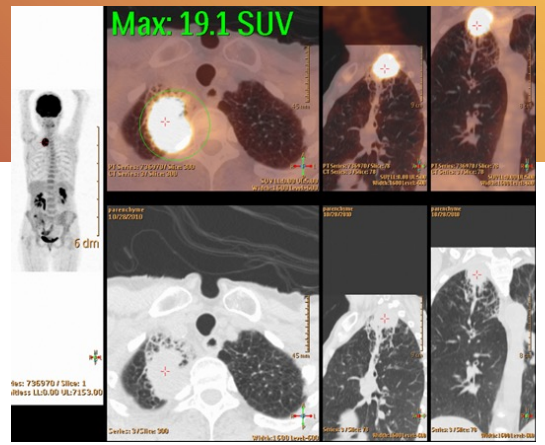


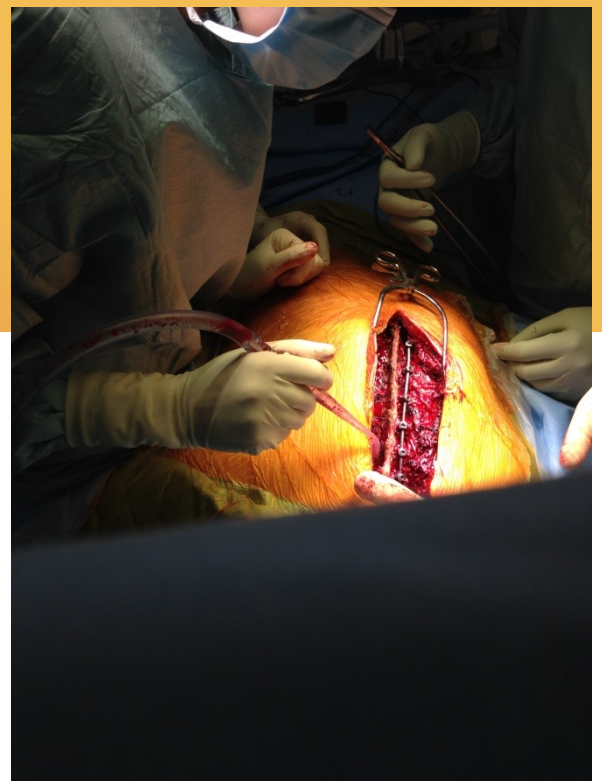
Indications à la pneumonectomie :

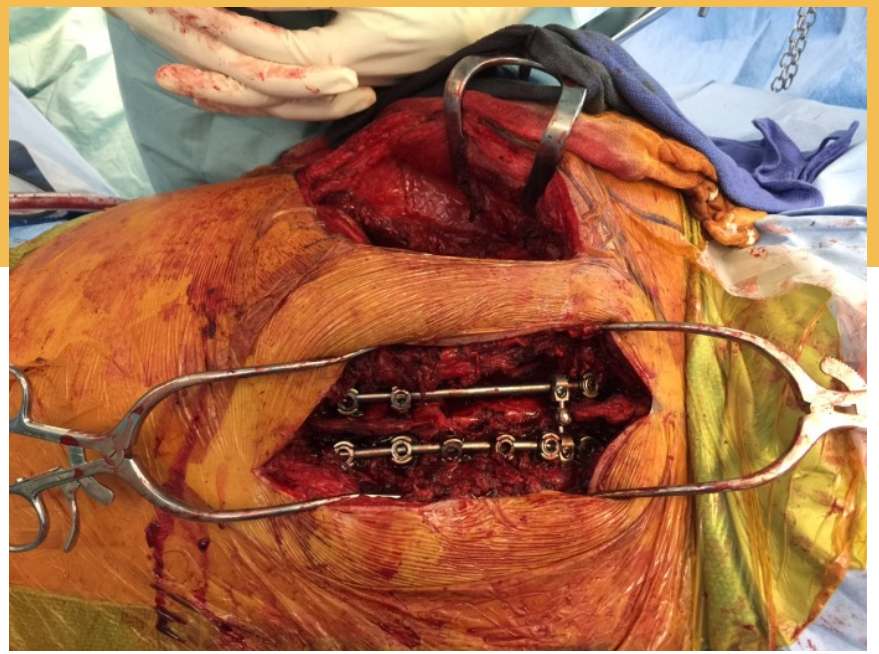
NSCLC	n=350
Other malign	n=30
Benign disease	n=6
« Salvage »	n=12

INDUCTION 37%
Chemiotherapy 33% ; 3 cycles (2-5)
Radiotherapy n=2

NSCLC : c staging	
T1	6%
T2	47%
T3	36%
T4	11%
N0	45%
N1	21%
N2	33%
N3	1%







THE ANNALS OF THORACIC SURGERY

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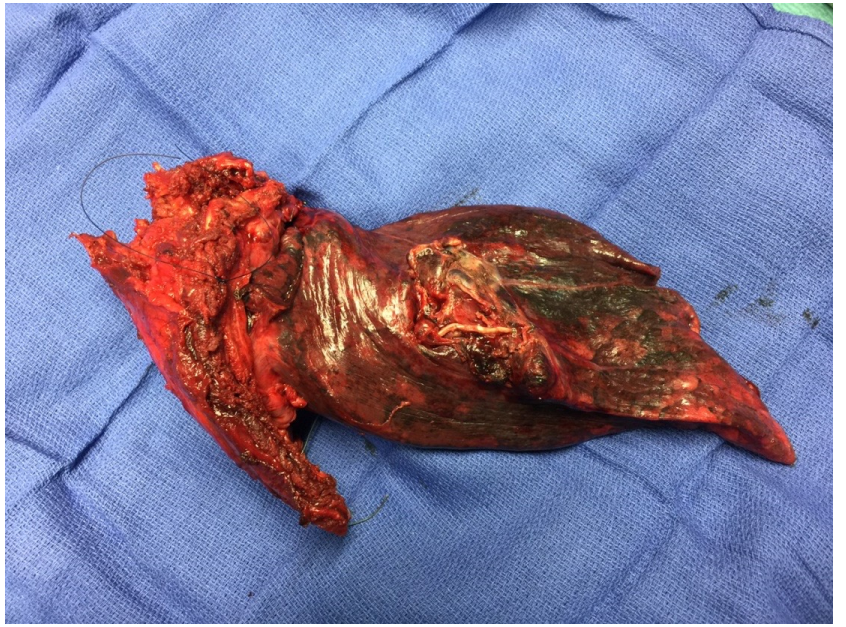
ORIGINAL ARTICLE GENERAL THORACIC | VOLUME 108, ISSUE 1, P227-234, JULY 01, 2019

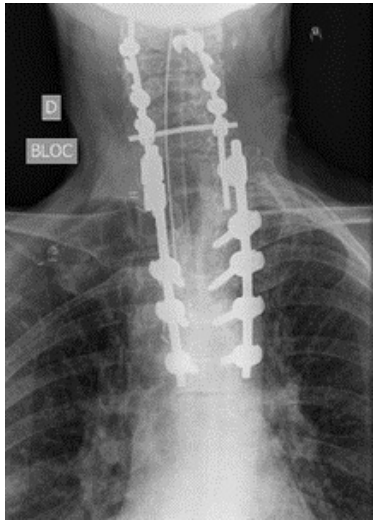
PDF [709 KB] Figures Save Share Reprints Request

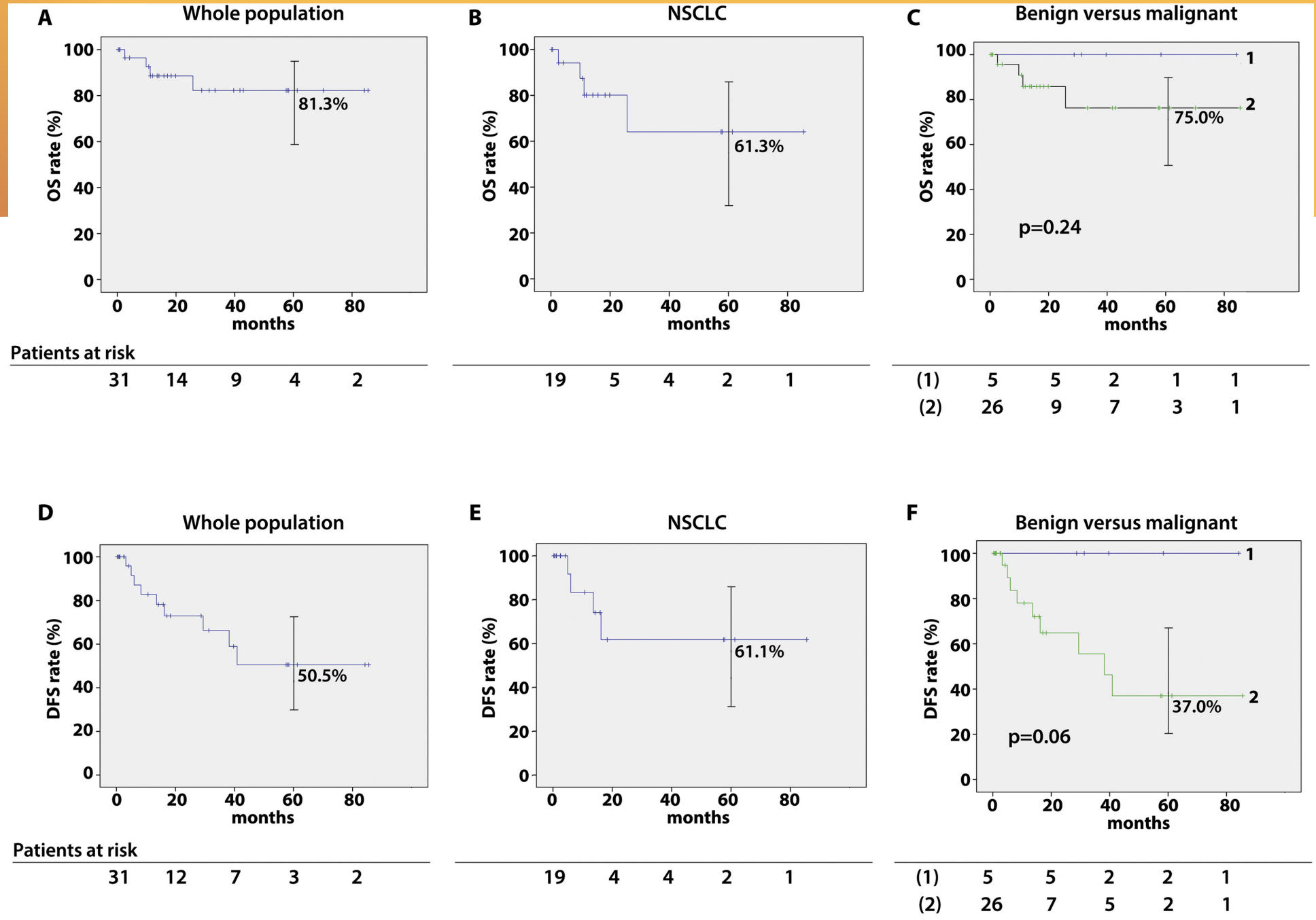
En Bloc Resection of Thoracic Tumors Invading the Spine: A Single-Center Experience

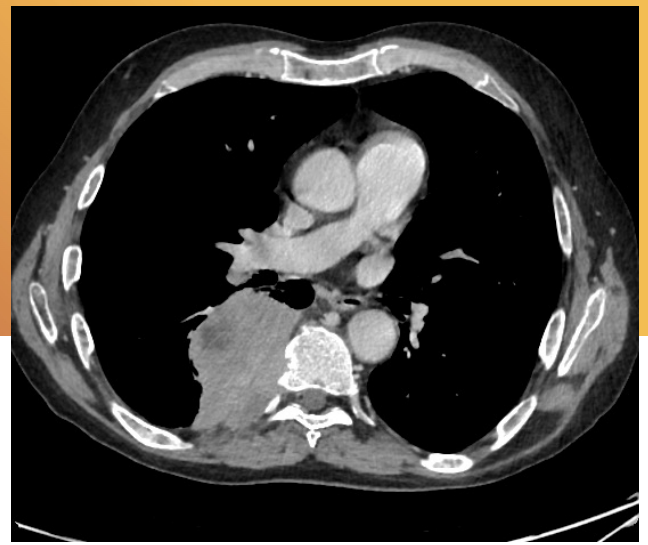
Xiao-Miao Zhang, MD * • Ludovic Fournel, MD * • Audrey Lupo, MD, PhD • ...
Jean-François Regnard, MD, PhD • Frederic Sailhan, MD • Marco Alifano, MD, PhD • Show all authors •
Show footnotes

Published: March 15, 2019 • DOI: https://doi.org/10.1016/j.athoracsur.2019.02.019 • Check for updates PlumX Metrics

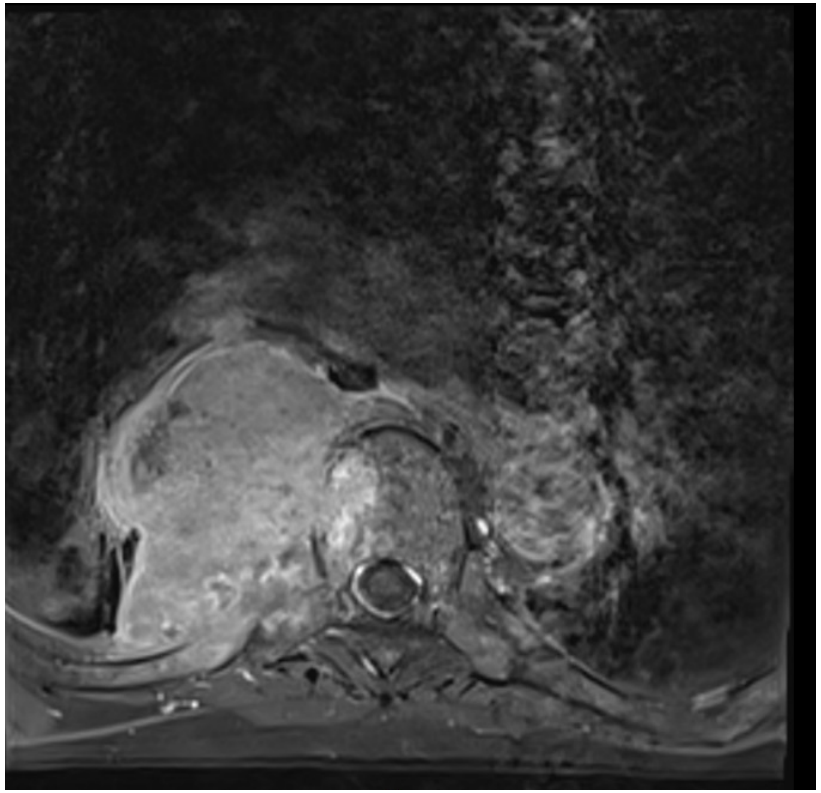


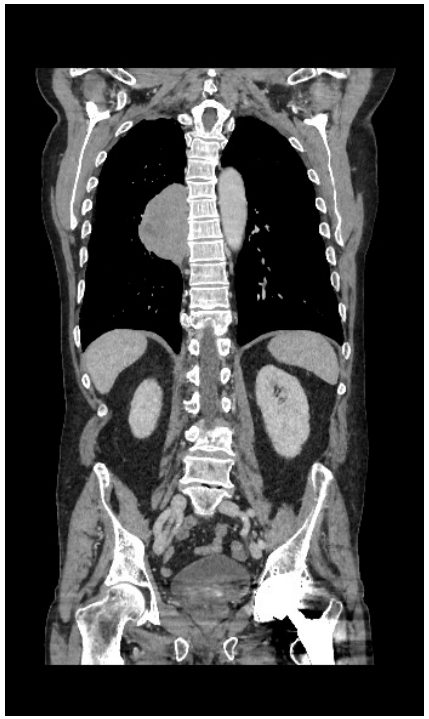



A
Whole population
OS rate (%)
100
80
60
40
20
0
81.3%
0
20
40
60
80
months
Patients at risk
31 14 9 4 2
B
NSCLC
OS rate (%)
61.3%
months
19 5 4 2 1
C
Benign versus malignant
OS rate (%)
1
2
75.0%
p=0.24
months
(1) 5 5 2 1 1
(2) 26 9 7 3 1
D
Whole population
DFS rate (%)
50.5%
months
Patients at risk
31 12 7 3 2
E
NSCLC
DFS rate (%)
61.1%
months
19 4 4 2 1
F
Benign versus malignant
DFS rate (%)
1
2
37.0%
p=0.06
months
(1) 5 5 2 2 1
(2) 26 7 5 2 1

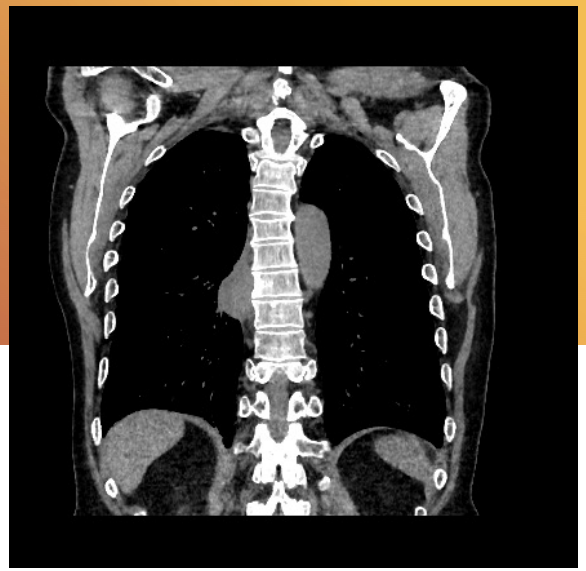


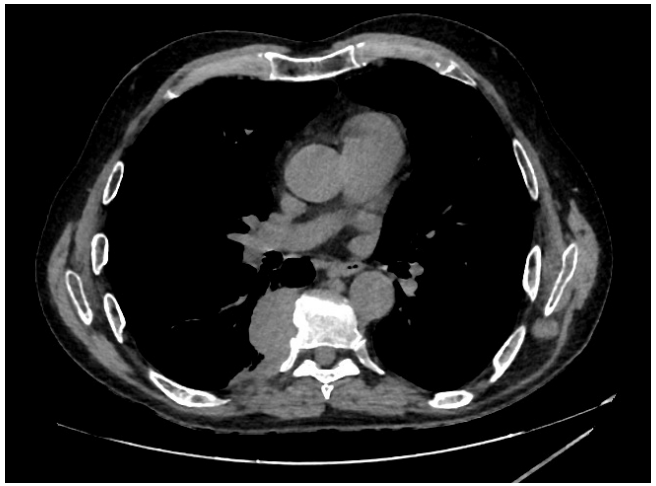
RCP Cancérologie thoracique Essonne (1): Traitement multimodal incluant une chimiothérapie d'induction suivie d'un traitement locorégional
2 cures Cis platine Alimta
Pendant la chimiothérapie:
Augmentation des douleurs





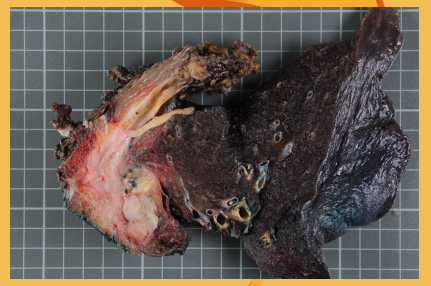
RCP RCP Cancérologie thoracique Essonne (2): PD; Immunothérapie: 3 cures et réévaluation

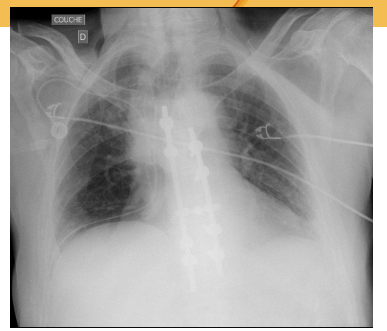




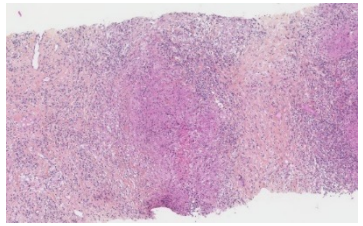
PET SUV max 9
RCP (3): RP (>50%)
Chirurgie

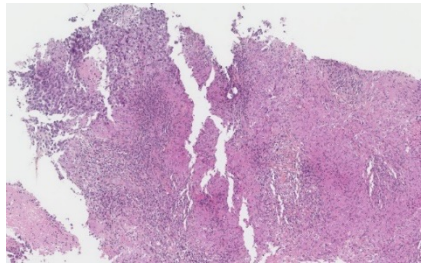
Lobectomie inferieure droite avec curage pariétectomie monobloc de K8 K9 -D8 D9
Instrumentation vertébrale
Temps opératoire: 240 minutes
RRAC
Retrait du drainage à J+2
RAD à J+10



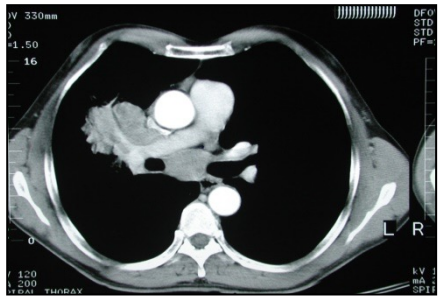


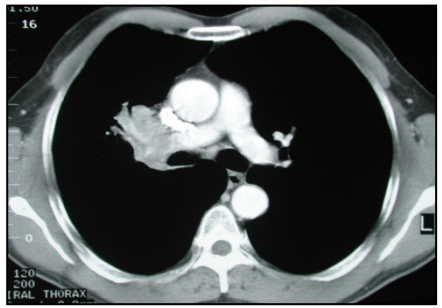
Ana path:
70% tumeur viable
Adénocarcinome peu différencié
35 mm
envahissement corticale des deux vertebres
R0 NO
ypT4N0; RCP: surveillance; pas de récidive à 12 mois

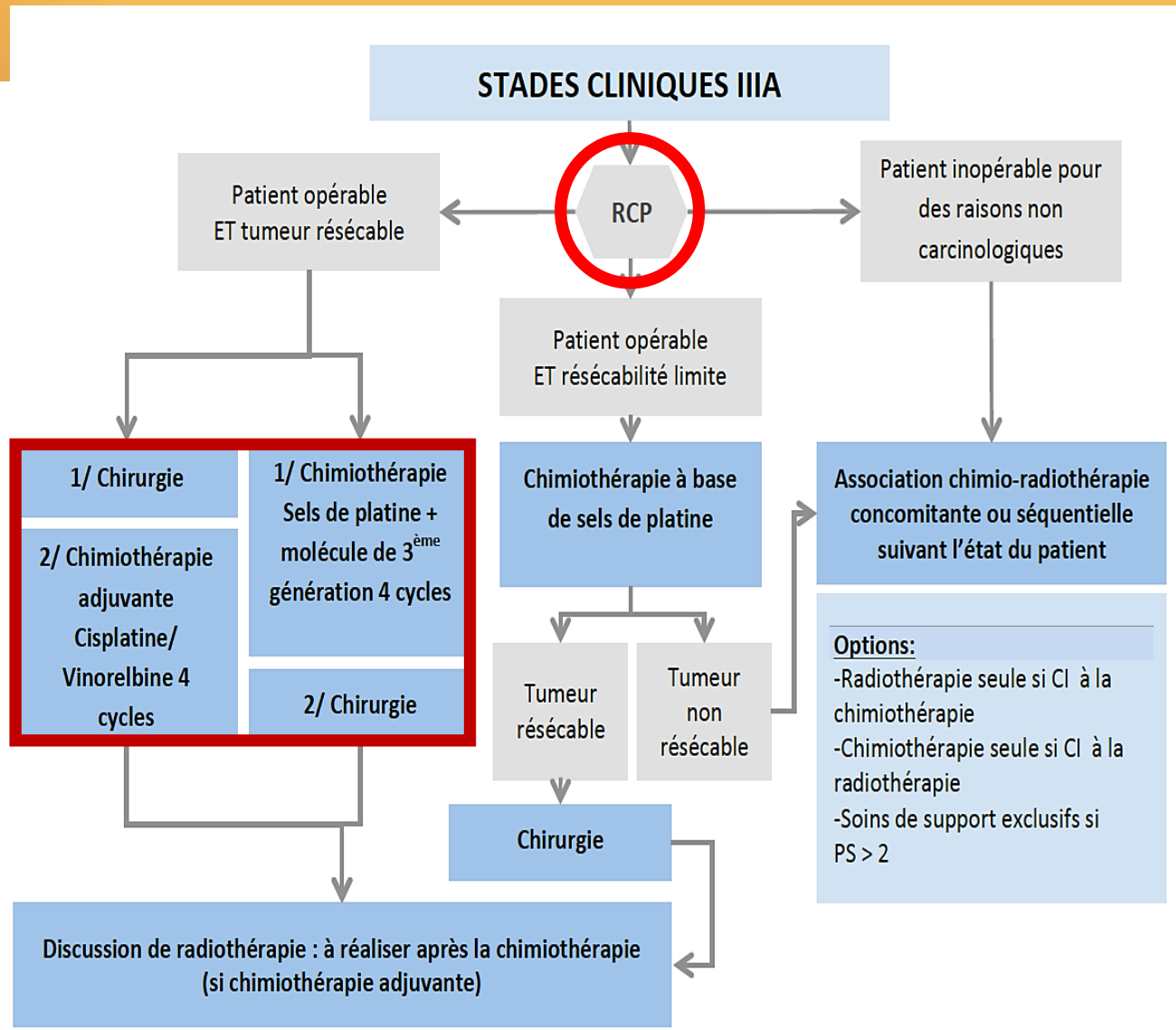




Quelles sont les stratégies possibles?







REFERENTIEL oncorif 2021

Department culture of Quality

Participation to the On-going certification of the whole hospital (2017-)

Accreditation of all permanent staff surgeons (HAS)

1 staff surgeon (Dr E Canny) specifically in charge of quality
1 staff surgeon (Dr A. Bobbio)in charge of Morbidity and Mortality Review Meetings

1 weekly department meeting : Staff Surgeons, Fellows, Residents, Chest Radiologist(s), Thoracic Pathologist, Anestesiosogist (s)/Critical Care, Head Nurse of the Ors: GO

Last check by anesthesiologist and staff surgeon in charge of patient
on the morning of operation (No GO)

2 Annual meetings with all the staff members to discuss about morbidity, mortality, rehospitalization, and survival rates, thanks to the department (200 items)
and Epithor (50 items) prospective databases.

• LA RRAC: LE PATIENT AU CENTRE DU RAISONNEMENT

SOMMAIRE

LE LENDEMAIN DE L'OPÉRATION

Je ressens une douleur ■ oui ■ non

Sur une échelle de 0 à 10, mon plus haut niveau de douleur au repos depuis l'opération :

0 1 2 3 4 5 6 7 8 9 10

Et celui lorsque je tousse/je bouge :

0 1 2 3 4 5 6 7 8 9 10

Présente-t-elle une ou plusieurs des caractéristiques suivantes ?

☐ Brûlure ☐ Sensation de froid douloureux ☐ Décharges électriques

Est-elle associée, dans la même région, à un ou plusieurs des symptômes suivants ?

☐ Fourmillements ☐ Picotements

☐ Engourdissements ☐ Démangeaisons

La douleur est-elle provoquée ou augmentée par le frottement ?

☐ oui ☐ non

J'ai ressenti(e) une gêne à cause de :

☐ ma perfusion ☐ ma sonde urinaire ☐ mon drain

Ma respiration et mes déplacements

Je me suis senti(e) encombré(e) : ☐ oui ☐ non

J'ai bénéficié de kinésithérapie respiratoire :

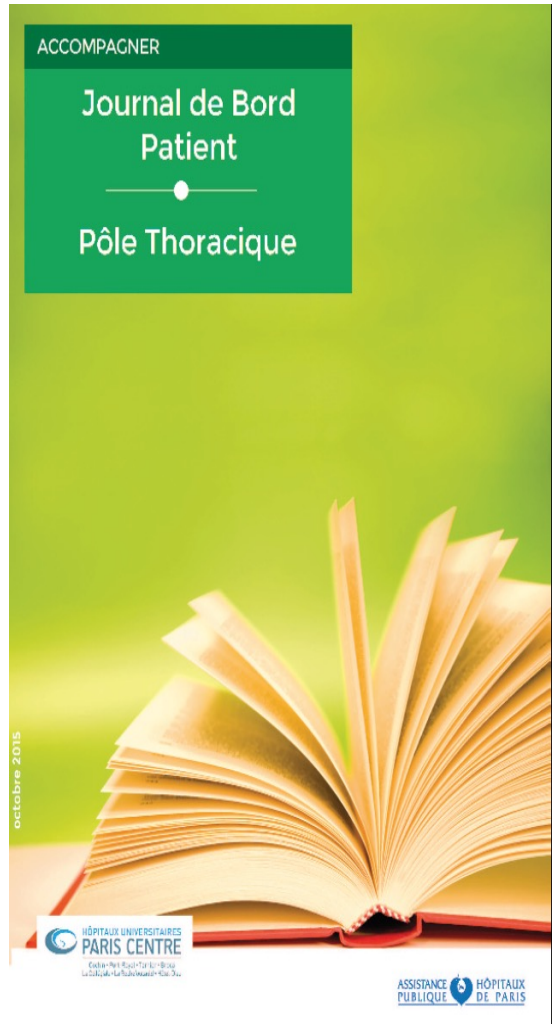
☐ oui (.....fois) ☐ non

J'ai utilisé mon bulleur : ☐ oui (.....fois) ☐ non

Je suis resté(e) au fauteuil :

☐ Plus de 4h ☐ Moins de 4h ☐ Pas du tout

J'ai marché : ☐ oui (.....fois) ☐ non



Cancers (Basel). 2022 Apr; 14(7): 1745.
Published online 2022 Mar 29. doi: 10.3390/cancers14071745
PMCID: PMC8997103
PMID: 35406517

Enhanced Recovery Pathway in Lung Resection Surgery: Program Establishment and Results of a Cohort Study Encompassing 1243 Consecutive Patients

Yen-Lan Nguyen,[1] Elena Maiolino,[2] Vincent De Pauw,[2] Mathilde Prieto,[2] Antonio Mazzella,[2] Jean-Baptiste Peretout,[1] Agnès Dechartres,[3] Christophe Baillard,[1] Antonio Bobbio,[2] Elisa Daffré,[2] and Marco Alifano[2,*]

Yasushi Shintani, Academic Editor

Operative Phase	Elements Already in Place	What We Gave Up	Changes Induced by Our ERP
Pre	Preoperative assessment General patient information including smoking cessation	Stop food and drinks at midnight the day before surgery	Patient empowerment with dedicated information leaflet Carbohydrates intake
Per	Intraoperative warming Prophylactic antibiotics Goal directed fluid therapy Protective ventilation Targeted postoperative nausea prevention Regional anesthesia catheter	No use of non-steroid anti-inflammatory drugs use No strategy of chest tube management	Opiate analgesia avoidance strategy with non-steroid anti-inflammatory drugs use Single chest tube
Post	Venous thromboembolism prophylaxis Targeted postoperative nausea prevention Opioids for breakthrough pain Mobilization within 24 h	Pain evaluation at rest Continuous regional anesthesia Opioids personalized controlled anesthesia Maintenance of intravenous analgesics and fluids Feeding at POD 1 No consensus on chest tube management	Pain evaluation at rest and mobilization Personalized controlled regional anesthesia non-steroid anti-inflammatory drugs use Early infusion withdrawal Early feeding and mobilization at day 0 Consensus on chest tube managemen

Mortalité post-opératoire 1.02%

Contents lists available at ScienceDirect

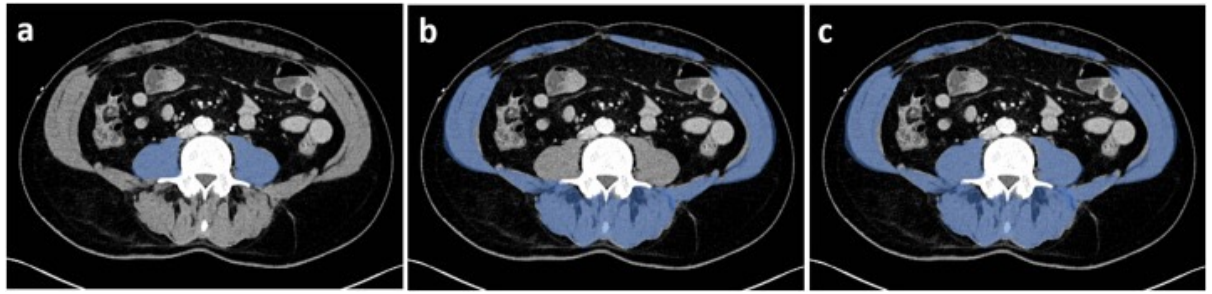
Lung Cancer

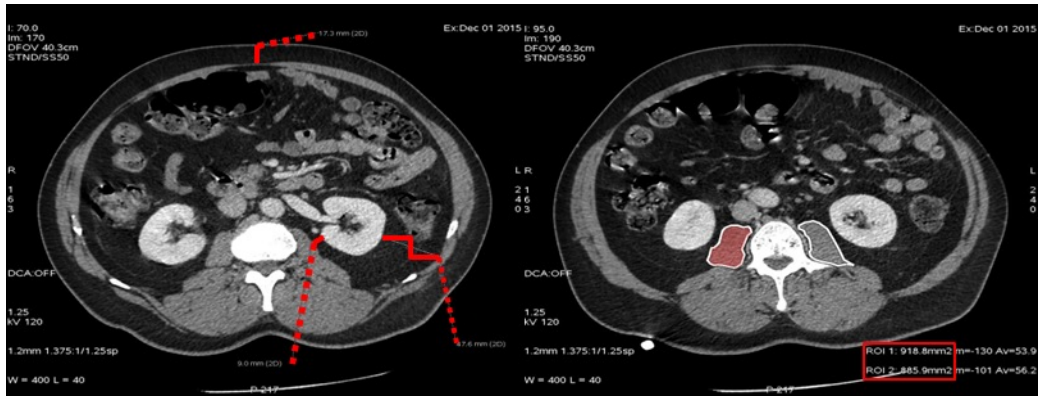
journal homepage: www.elsevier.com/locate/lungcan

Sarcopenia as independent risk factor of postpneumonectomy respiratory failure, ARDS and mortality

Katharina Martini [a,b], Guillaume Chassagnon [a,c], Ludovic Fournel [c,d], Mathilde Prieto [c,d], Trieu-Nghi Hoang-Thi [a,e], Nara Halm [a], Antonio Bobbio [d], Marie-Pierre Revel [a,c], Marco Alifano [c,d,*]

[a] Radiology Department, APHP Centre - Université de Paris, 27 Rue du Faubourg Saint-Jacques, 75014 Paris, France
[b] Diagnostic and Interventional Radiology, University Hospital Sarcopenia as Independent Risk Factor of Postpneumonectomy Respiratory Failure, ARDS and Mortality, Zurich, Rämistrasse 100, 8008 Zurich, Switzerland
[c] University of Paris, Paris, France
[d] Department of Thoracic Surgery, APHP Centre - Université de Paris, 27 Rue du Faubourg Saint-Jacques, 75014 Paris, France
[e] Department Diagnostic Imaging, Vinmec International Hospital – Central Park, Ho Chi Minh City, Viet Nam



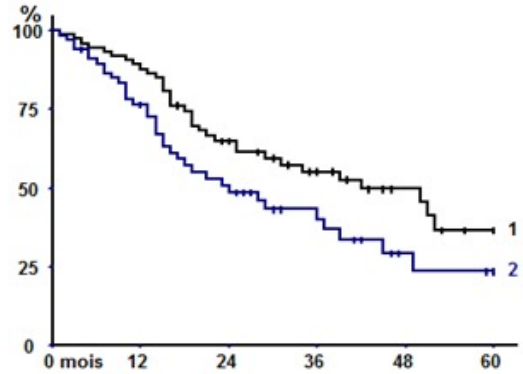


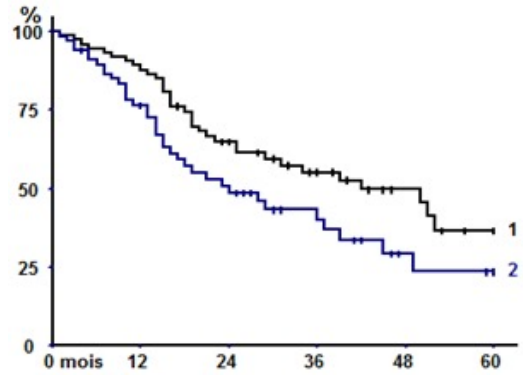
Body Mass Index and Total Psoas Area Affect Outcomes in Patients Undergoing Pneumonectomy for Cancer

Remi Hervochon, MD, Antonio Bobbio, MD, PhD, Claude Guinet, MD, PhD, Audrey Mansuet-Lupo, MD, PhD, Antoine Rabbat, MD, Jean-François Régnard, MD, Nicolas Roche, MD, PhD, Diane Damotte, MD, PhD, Antonio Iannelli, MD, PhD, and Marco Alifano, MD, PhD

Departments of Thoracic Surgery, Radiology, Pathology, and Chest Disease and Intensive Care, Paris Centre University Hospitals, Paris; University Paris Descartes, Paris; and Department of Surgery, Nice University Hospital, Nice, France

GENERAL





cancers

MDPI

Article

Total Psoas Area and Total Muscular Parietal Area Affect Long-Term Survival of Patients Undergoing Pneumonectomy for Non-Small Cell Lung Cancer

Elisa Daffrè [1,†], Mathilde Prieto [1,†], Katharina Martini [2,†], Trieu-Nghi Hoang-Thi [3], Nara Halm [3], Hervè Dermine [4], Antonio Bobbio [1], Guillaume Chassagnon [3,5], Marie Pierre Revel [3,5] and Marco Alifano [1,5,*]

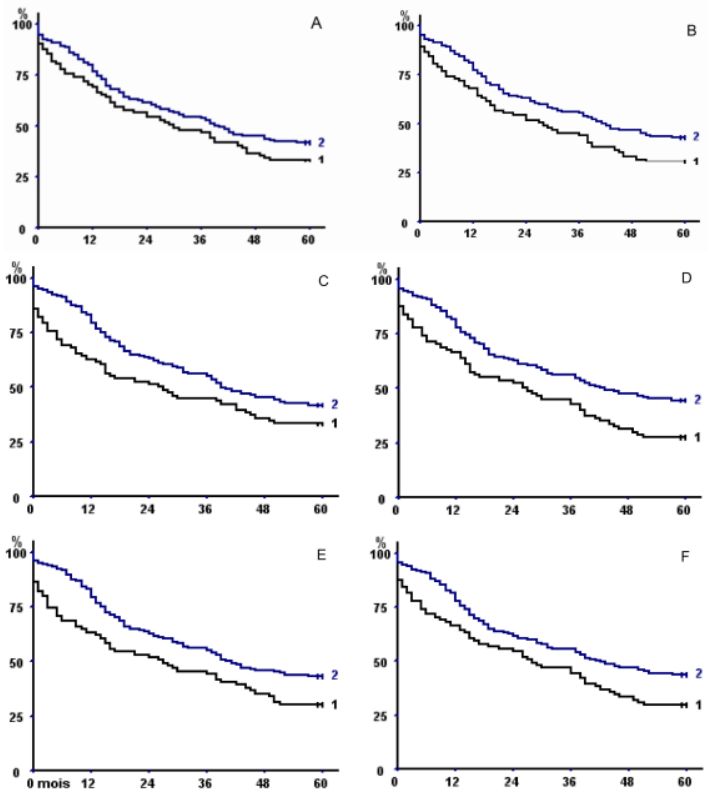


Figure 2. Kaplan–Meier survival curves in the whole population with respect to (**A**) psoas area with fat exclusion, (**B**) total psoas area, (**C**) parietal area with fat exclusion, (**D**) total parietal area, (**E**) total muscle area with fat exclusion, and (**F**) total muscle area. In all of the panels, curve 2 represents patients with sex-specific areas greater than the 33rd percentile versus less than or equal to the 33rd percentile (curve 1).

cancers

MDPI

Article

Pre-Disease and Pre-Surgery BMI, Weight Loss and Sarcopenia Impact Survival of Resected Lung Cancer Independently of Tumor Stage

Philippe Icard [1,2], Olivier Schussler [1], Mauro Loi [3], Antonio Bobbio [1], Audrey Mansuet Lupo [4,5], Marie Wislez [5,6], Antonio Iannelli [7,8], Ludovic Fournel [1,9], Diane Damotte [4,5] and Marco Alifano [1,5,*]

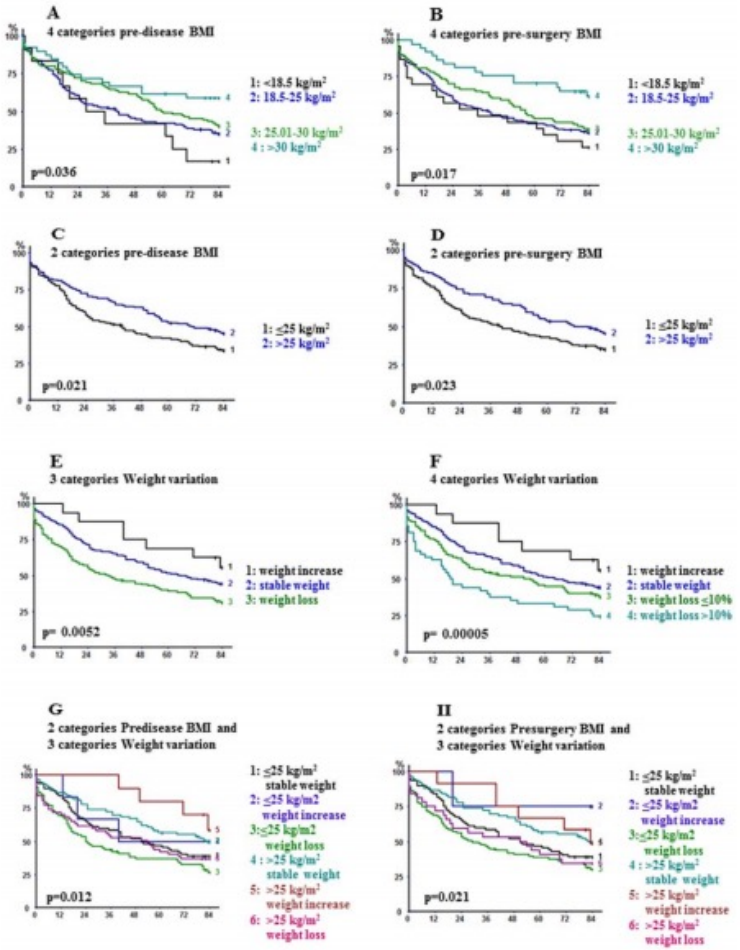


Figure 1. Kaplan–Meier overall survival analyses and log-rank comparisons with respect to: (**A**) pre-disease BMI (four categories: underweight, normal weight, overweight, obesity); (**B**) pre-surgery

European Journal of Cardio-Thoracic Surgery 45 (2014) 652–659
doi:10.1093/ejcts/ezt452 Advance Access publication 23 September 2013

ORIGINAL ARTICLE

National perioperative outcomes of pulmonary lobectomy for cancer: the influence of nutritional status†

Pascal Alexandre Thomas[a,*], Julie Berbis[b], Pierre-Emmanuel Falcoz[c], Françoise Le Pimpec-Barthes[d], Alain Bernard[e], Jacques Jougon[f], Henri Porte[g], Marco Alifano[h] and Marcel Dahan[i] on behalf of the EPITHOR Group

	Operative death				
	Yes (*N* = 490)	No (*N* = 19 145)	*P**	OR a	95% CI
BMI, *N* (%)					
Normal	249 **(2.7)**	9142 (97.3)	**0.002**	1	
Underweight	35 **(4.1)**	822 (95.9)		1.89	[1.30–p2.75]
Overweight	156 **(2.3)**	6565 (97.7)		0.72	[0.59–0.89]
Obesity	50 **(1.9)**	2616 (98.1)		0.54	[0.40–0.74]

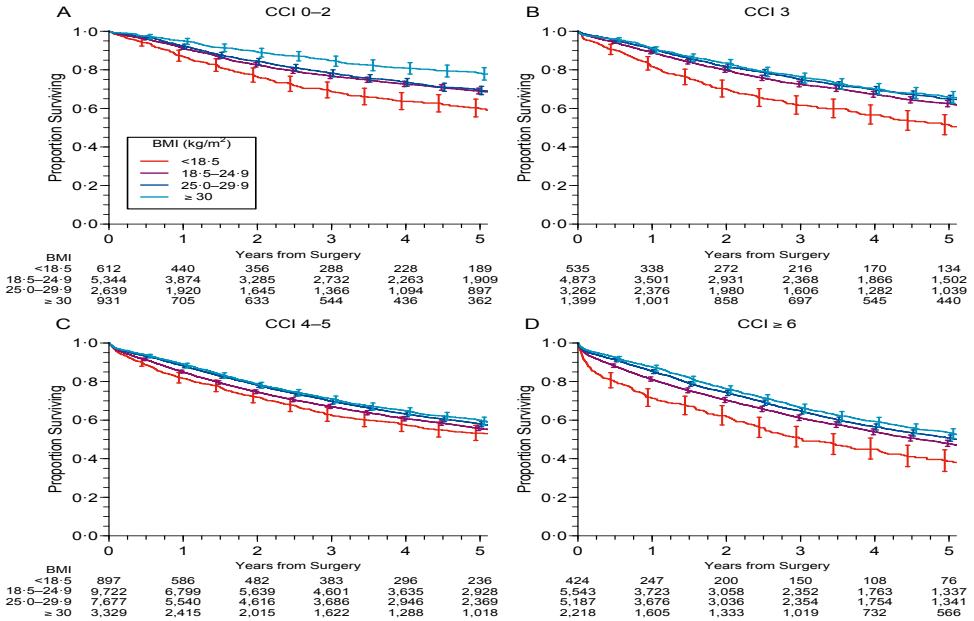
cancers

MDPI

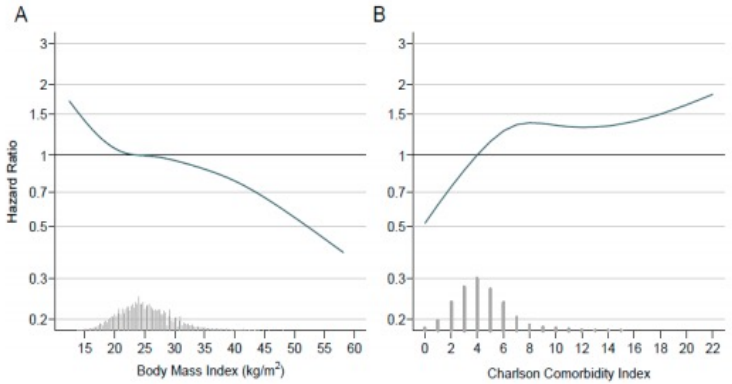
Article

The Reality of Lung Cancer Paradox: The Impact of Body Mass Index on Long-Term Survival of Resected Lung Cancer. A French Nationwide Analysis from the Epithor Database

Marco Alifano [1,*], Elisa Daffré [1], Antonio Iannelli [2], Laurent Brouchet [3], Pierre Emmanuel Falcoz [4], Françoise Le Pimpec Barthes [5], Alain Bernard [6], Pierre Benoit Pages [6], Pascal Alexandre Thomas [7], Marcel Dahan [3] and Raphael Porcher [8]



Survie selon les catégories d'IMC par strat D'index de comorbidité de Charlson (CCI)



Suivi médian: 5.2 ans (IQR 2.3–9.5).
Mortalité à 30 et 90 jours: 2.6% et 4.7%.
Survie à 1, 3, et 5 ans: 87.2%, 69.5%, 58.4%. **Differences de survie selon classe IMC hautement significatives (p<0,0001)**

RR non ajusté:

- **Poids normal: Ref**
- **Insuffisance pondérale**: 1,24 (IC à 95 % 1,16-1,33)
- **Surpoids**: 0,95 (IC à 95 % 0,92-0,98)
- **Obésité**: 0,88 (IC à 95 % 0,84 –0.92)

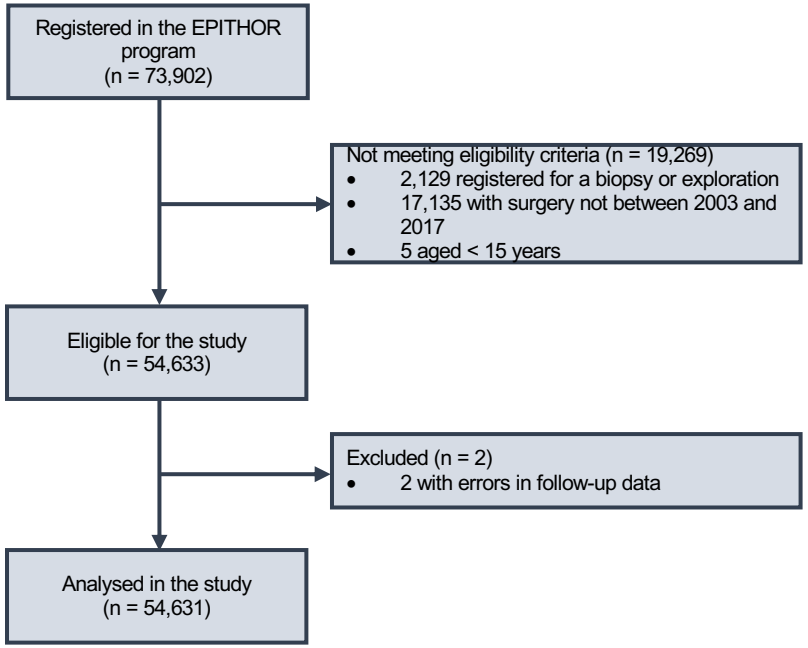
- Participation to the national Thoracic Surgery database (Epithor)

On-site morbidity, mortality, survival
Bench-marking with national data

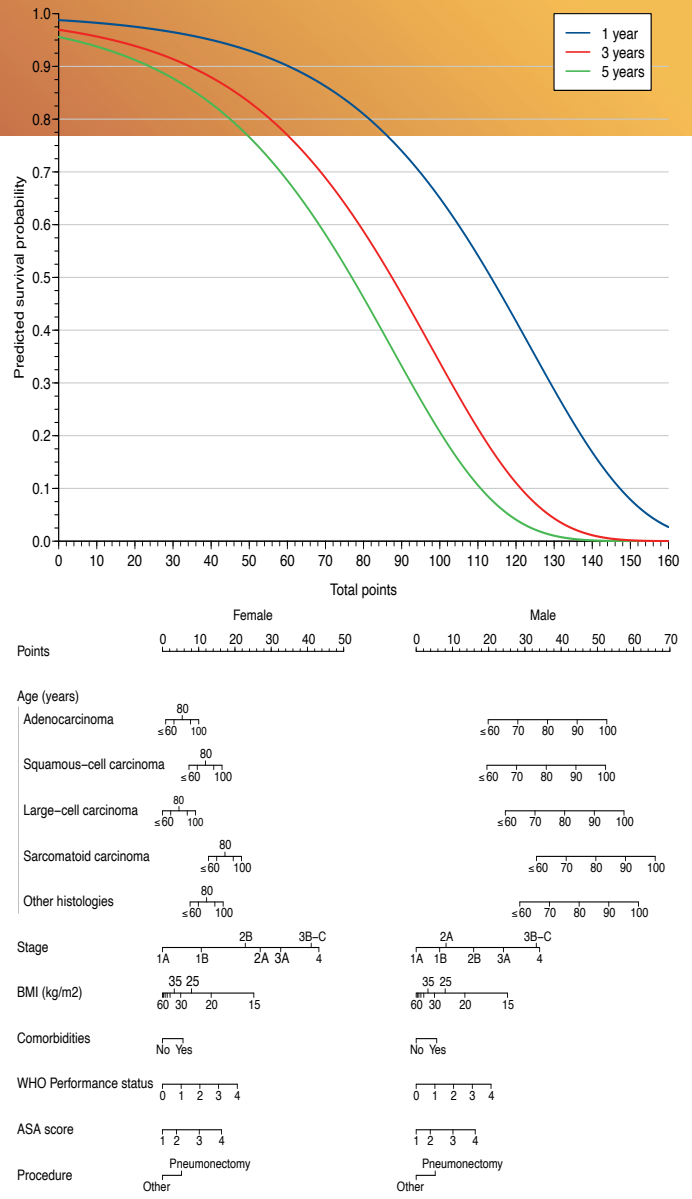
Résultats de l'analyse de la base EPITHOR :
la vraie vie, visualisation de l'impact de nombreux paramètres

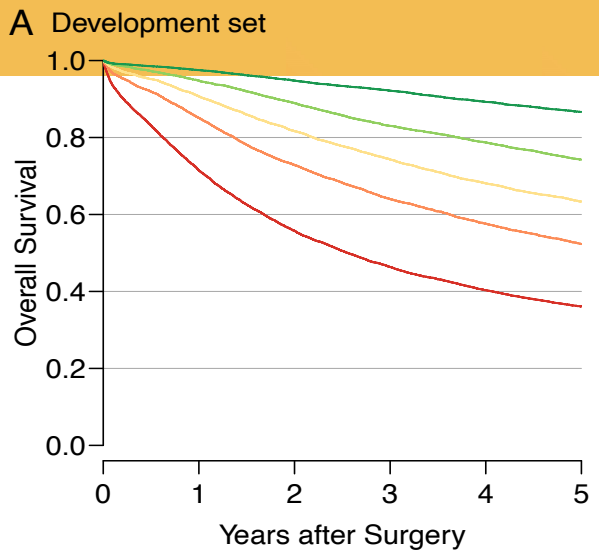
Table S1. Overall survival at specific timepoints. Values are percent survival with 95% confidence interval.

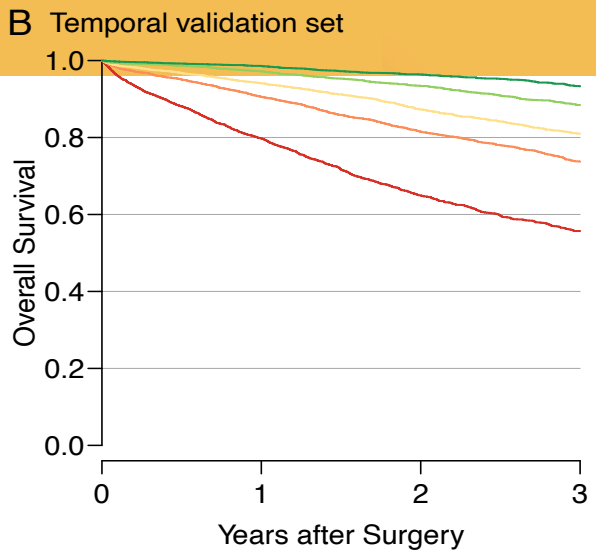
Features	1 month	3 months	1 year	3 years	5 years
Overall cohort	97.4 (97.2–97.5)	95.3 (95.1–95.4)	87.2 (86.9–87.5)	69.5 (69.1–69.9)	58.4 (57.9–58.9)
BMI category					
Underweight	96.0 (95.3–96.8)	92.5 (91.4–93.6)	81.1 (79.4–82.8)	61.8 (59.6–64.0)	52.0 (49.7–54.4)
Normal weight	97.2 (97.0–97.4)	94.8 (94.6–95.1)	86.2 (85.7–86.6)	68.7 (68.1–69.4)	57.9 (57.2–58.6)
Overweight	97.6 (97.4–97.8)	95.8 (95.5–96.1)	88.4 (88.0–88.9)	70.4 (69.7–71.1)	58.7 (57.8–59.5)
Obesity	97.6 (97.3–98.0)	96.3 (95.8–96.7)	89.7 (89.0–90.4)	72.3 (71.2–73.4)	61.3 (60.0–62.6)
Sex					
Female	98.9 (98.7–99.0)	98.0 (97.8–98.3)	94.6 (94.2–95.0)	86.3 (85.7–86.9)	80.7 (80.0–81.5)
Male	96.7 (96.5–96.9)	94.1 (93.9–94.4)	84.3 (84.0–84.7)	63.2 (62.7–63.8)	50.4 (49.8–51.0)
Age, y					
≤ 55	98.6 (98.3–98.8)	97.2 (96.9–97.6)	90.0 (89.4–90.7)	74.0 (73.0–74.9)	65.7 (64.6–66.8)
56–60	98.4 (98.1–98.7)	96.9 (96.5–97.3)	89.5 (88.8–90.2)	72.3 (71.2–73.3)	61.2 (60.0–62.5)
61–65	97.7 (97.4–98.0)	95.9 (95.5–96.3)	88.1 (87.4–88.8)	70.4 (69.4–71.4)	59.5 (58.4–60.7)
66–70	97.5 (97.2–97.8)	95.2 (94.8–95.6)	86.8 (86.1–87.5)	69.5 (68.5–70.5)	58.5 (57.4–59.7)
71–75	96.7 (96.3–97.1)	93.9 (93.4–94.5)	85.7 (84.9–86.5)	67.4 (66.3–68.6)	54.0 (52.8–55.4)
> 75	94.8 (94.3–95.3)	91.8 (91.1–92.4)	82.2 (81.3–83.1)	62.0 (60.8–63.2)	48.9 (47.6–50.2)
Charlson comorbidity index					
0–2	98.9 (98.7–99.2)	97.9 (97.6–98.2)	91.6 (91.0–92.2)	77.4 (76.4–78.3)	69.4 (68.2–70.5)
3	98.3 (98.0–98.5)	96.8 (96.4–97.1)	89.5 (88.8–90.1)	73.2 (72.2–74.2)	63.1 (62.0–64.2)
4–5	97.2 (97.0–97.4)	94.9 (94.6–95.2)	86.6 (86.1–87.1)	68.4 (67.7–69.1)	57.0 (56.3–57.8)
≥ 6	95.8 (95.5–96.2)	92.9 (92.4–93.4)	83.5 (82.9–84.2)	63.1 (62.2–64.0)	49.5 (48.5–50.6)
Performance status					
0	98.5 (98.4–98.7)	97.2 (97.0–97.5)	91.3 (90.9–91.7)	75.3 (74.6–75.9)	64.7 (64.0–65.5)
1	97.0 (96.8–97.3)	94.7 (94.4–95.0)	85.9 (85.4–86.4)	67.3 (66.6–67.9)	55.8 (55.1–56.6)
2–4	93.7 (93.0–94.4)	89.2 (88.3–90.1)	76.6 (75.4–77.9)	56.4 (54.9–57.9)	44.6 (43.0–46.2)
Stage					
0	99.4 (98.3–100.0)	96.9 (94.3–99.6)	93.6 (89.8–97.5)	80.2 (73.7–87.3)	68.4 (60.0–78.0)
I	98.2 (98.0–98.4)	96.9 (96.7–97.2)	93.0 (92.6–93.4)	80.1 (79.5–80.7)	68.9 (68.1–69.6)
II	97.3 (96.9–97.6)	94.9 (94.3–95.4)	85.6 (84.7–86.4)	65.5 (64.3–66.7)	53.6 (52.2–55.0)
III	96.3 (95.9–96.7)	93.1 (92.6–93.7)	79.4 (78.5–80.3)	53.9 (52.7–55.1)	42.3 (41.1–43.6)
IV	96.8 (96.0–97.5)	92.7 (91.6–93.8)	75.1 (73.3–77.0)	46.7 (44.5–49.0)	36.3 (34.1–38.6)
Surgical procedure					
Pneumonectomy	94.1 (93.4–94.7)	90.0 (89.2–90.8)	75.7 (74.5–76.9)	53.7 (52.3–55.2)	44.0 (42.5–45.5)
Other	97.7 (97.6–97.9)	95.9 (95.7–96.1)	88.6 (88.3–88.9)	71.4 (70.9–71.8)	60.1 (59.6–60.6)
Side					
Right	97.1 (96.9–97.2)	94.9 (94.7–95.2)	87.1 (86.7–87.5)	70.0 (69.4–70.6)	59.3 (58.6–59.9)
Left	97.8 (97.6–98.0)	95.7 (95.4–96.0)	87.3 (86.9–87.8)	68.7 (68.1–69.4)	57.1 (56.4–57.9)

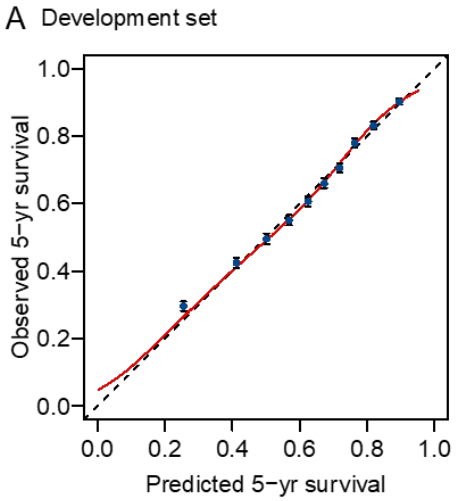


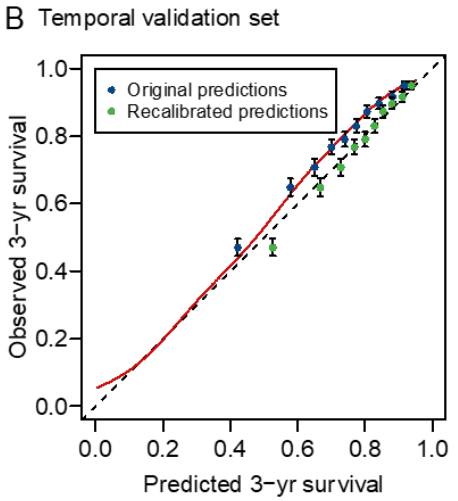
Construction d'un nomogramme de prédiction de la survie du cancer pulmonaire opéré. Base Epithor; analyse de 63.433 pts: 9 paramètres malade/maladie « basic » retenus







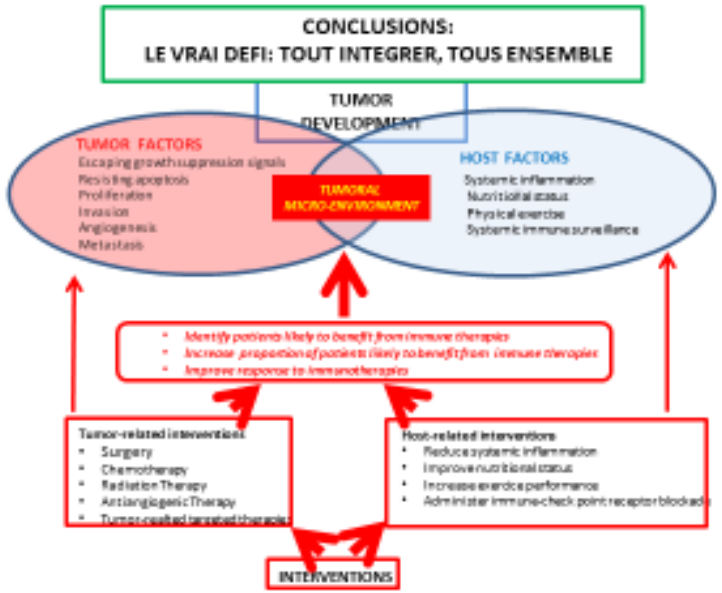




Conclusions :
Les défis des innovations en chirurgie thoracique en 2023

<u>Détermination et optimisation des stratégies de prise en charge en fonction de l'interaction malade/maladie en évaluant les différentes options interventionnelles :</u>

- *Chirurgie*
  - *Conventionnelle*
  - *Mini-invasive* ***(Vidéo –assistée,*** *Robot- assistée****, guidée par l'image)***
- *Management périopératoire:*
  - *RAAC*
  - *Lean management au bloc*
  - ***Pré-habilitation / rehabilitation***
  - *Hospitalisation de courte durée, mais avec nouvelles modalité de* ***maintien de contact avec patients et entourage***
- *Chimiothérapie périopératoire conventionnelle*
- *Thérapies ciblées*
- ***Immunothérapie néoadjuvante- adjuvante***
- *Radiothérapies*
- ***Adaptation des habitudes et du cadre de vie***
  - ***Exercice***
  - ***Nutrition***
  - ***Ergothérapie***
  - ***Education du malade, de l'entourage, des professionnels***



Bobbio A, Alifano M. Immune therapy of non-small cell lung cancer. The future. Pharm Research 2015; 99:217

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