

Le cancer bronchique en 2025 : dépistage, santé publique et nouveaux traitements

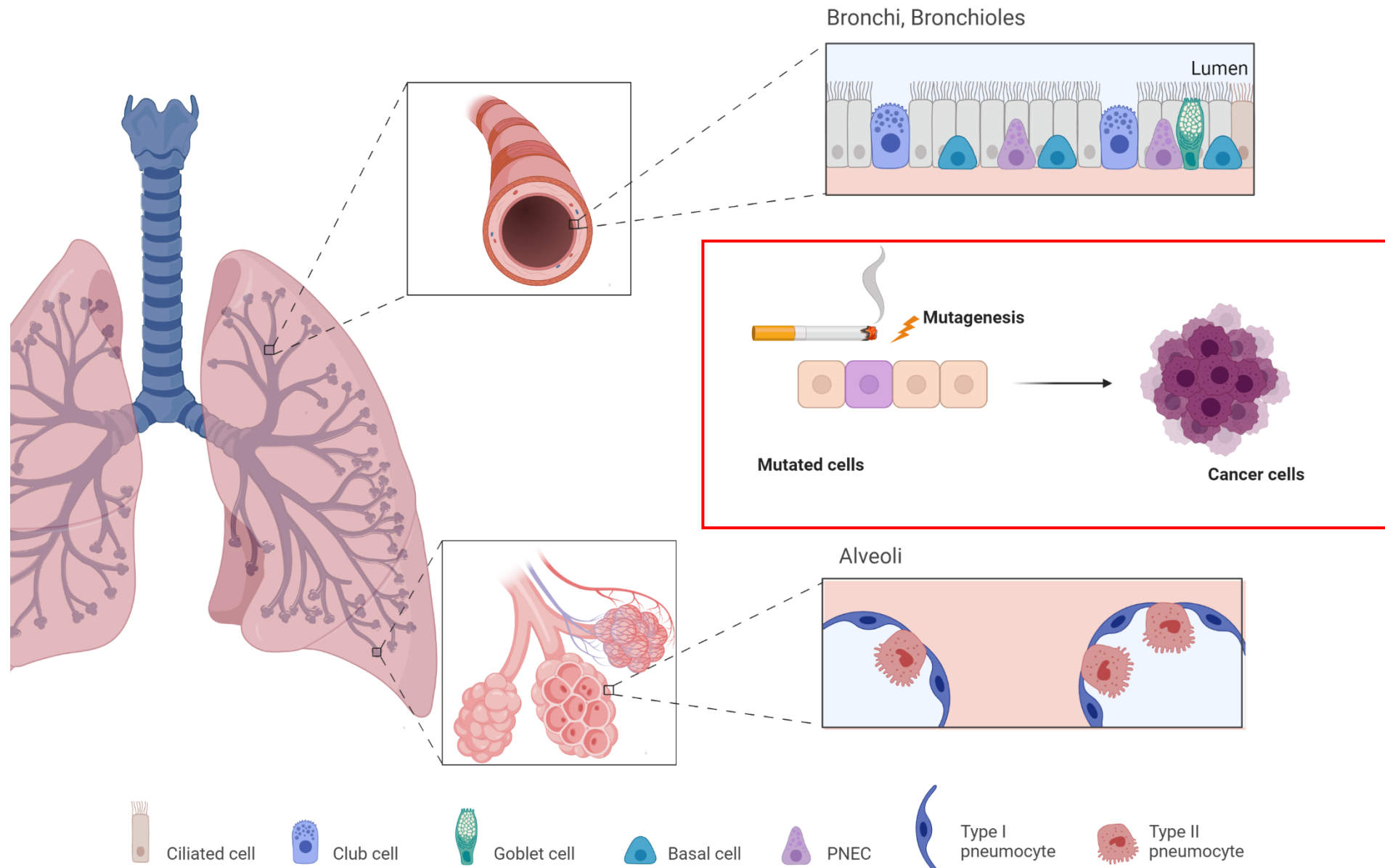
Frank Aboubakar, MD-phD

Pneumologie/Oncologie thoracique

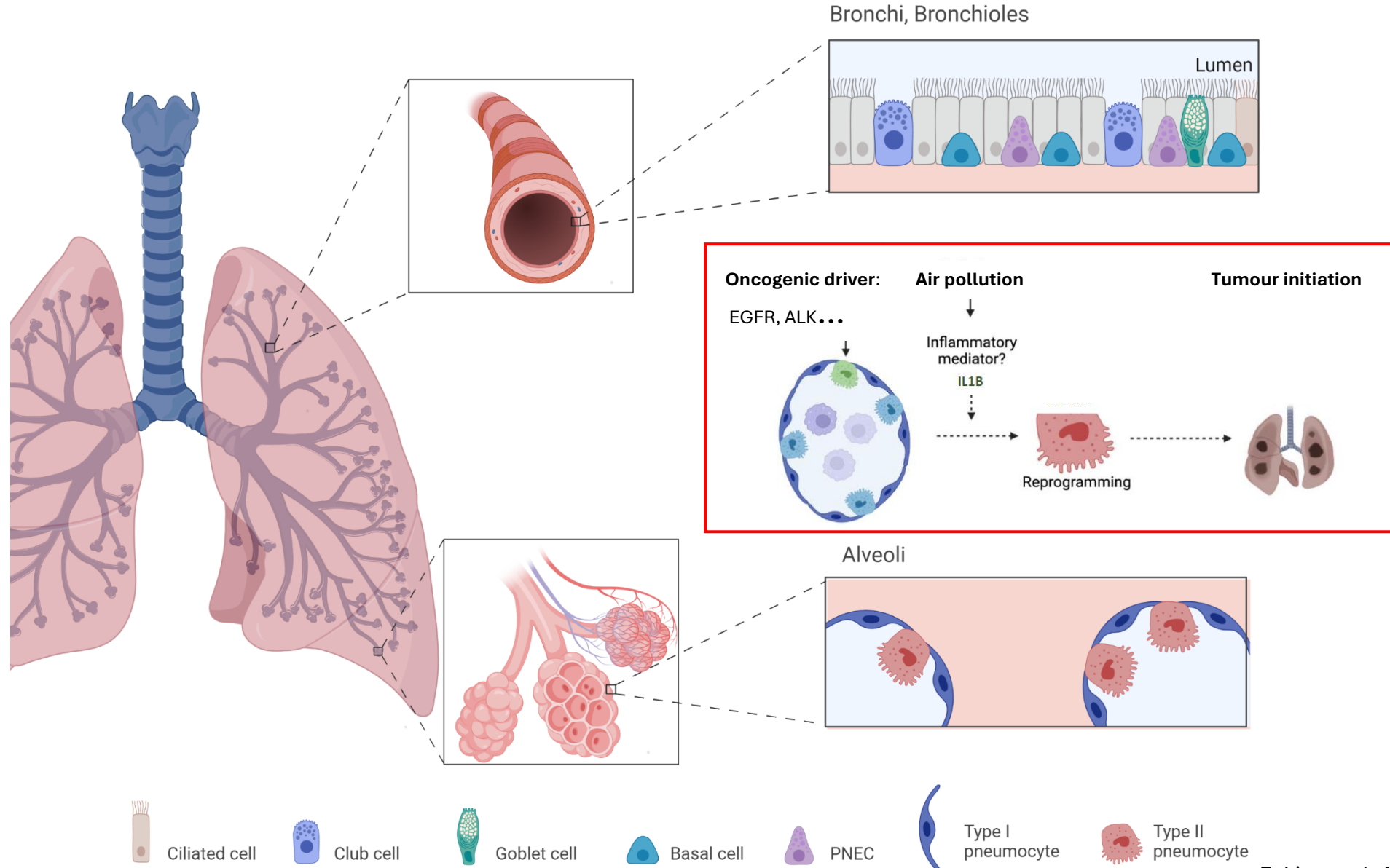
Institut de duve/TILS



Etiology of Lung Cancer: Tobacco

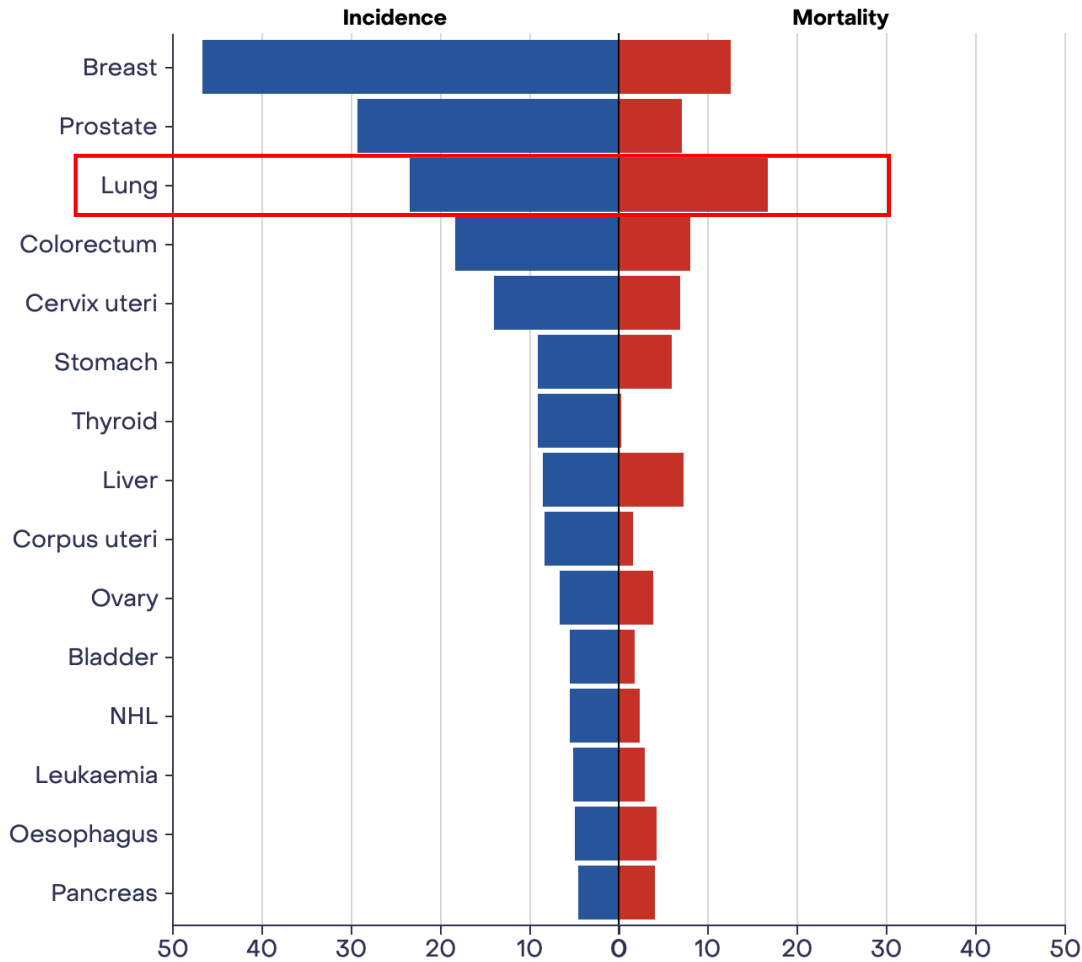


Etiology of Lung Cancer: Air Pollution



Lung cancer incidence and mortality

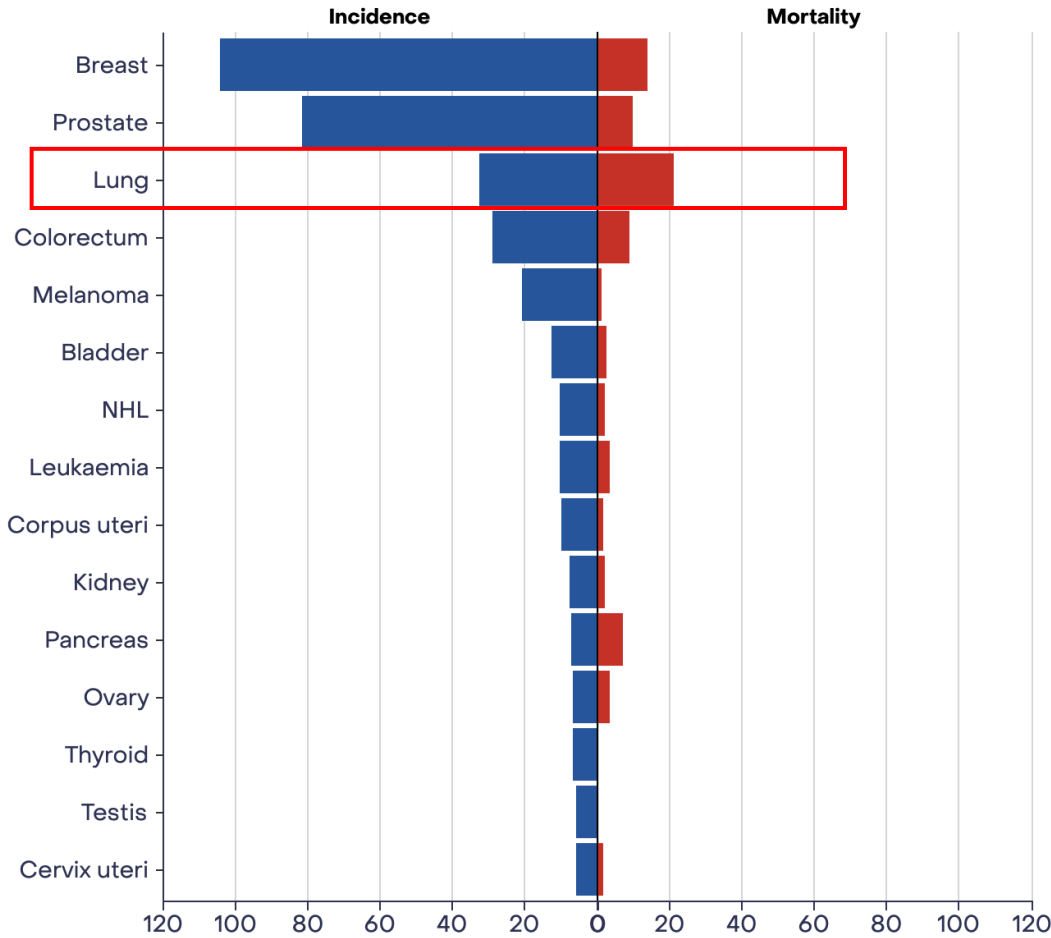
Worldwide



ASR (World) per 100 000

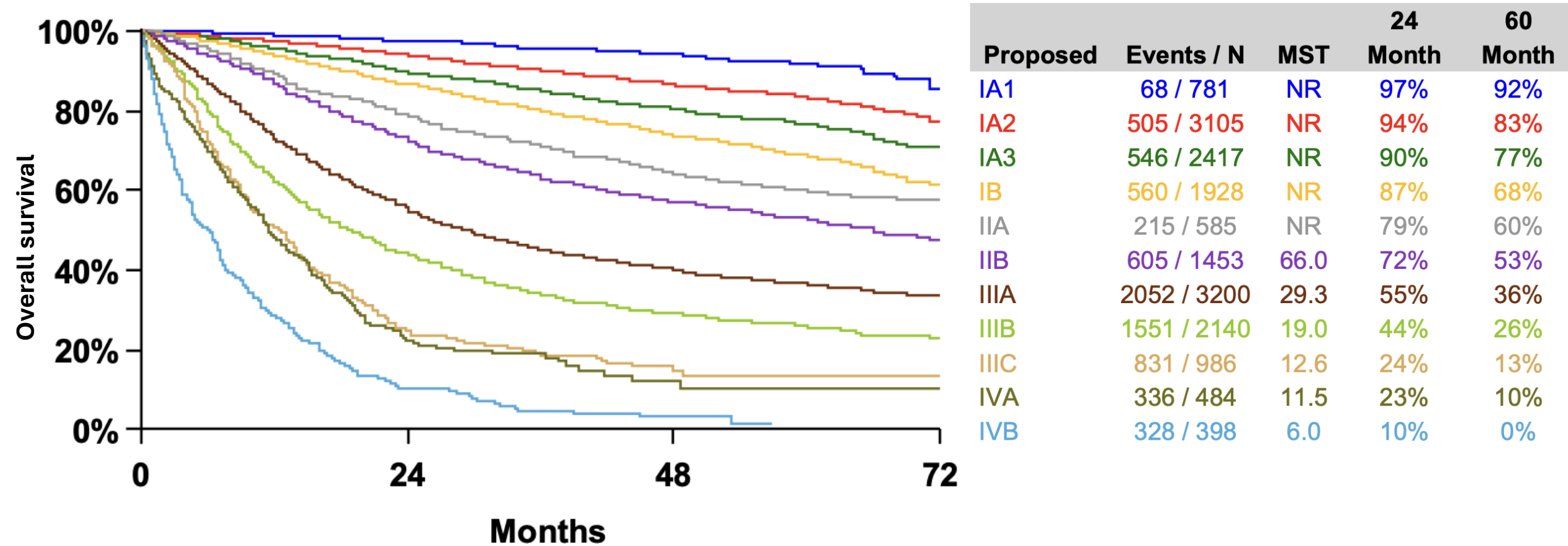
ASR= Age-Standardized Rate

Belgium

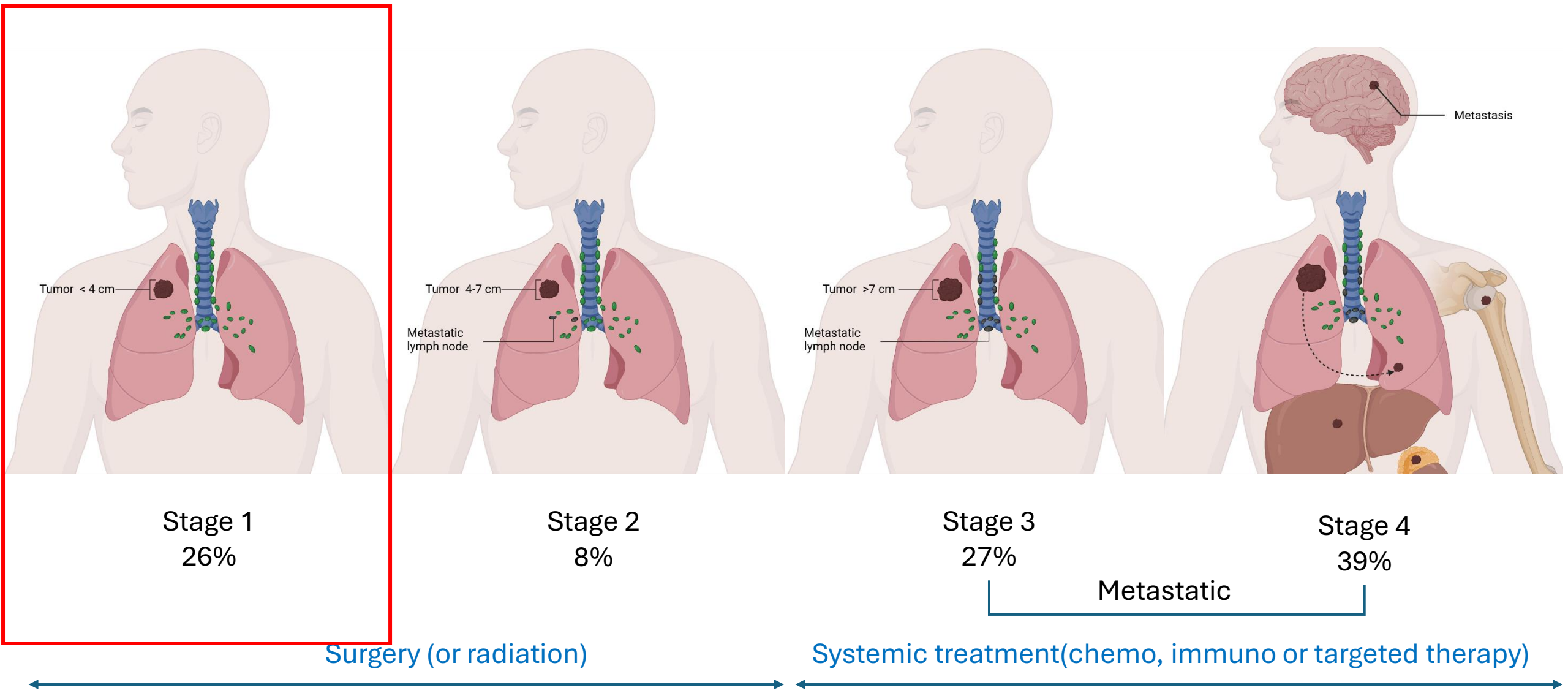


ASR (World) per 100 000

Lung cancer prognosis: overall survival according stage disease



Treatment of lung cancer depends on the disease stage at diagnosis



Dépistage: médecine préventive, régionale

Patient de 55 ans , fumeur actif, depuis l'âge de 20 ans , 35 AUP

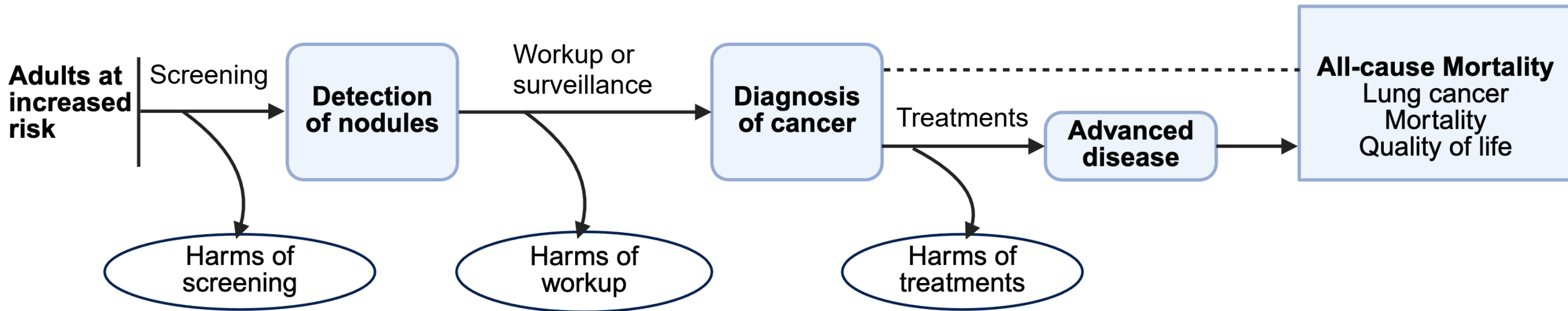
Docteur est ce que vous pouvez me réaliser
des examens de dépistage du cancer
cancer poumon ?

1- OUI

2-NON

3-Eventuellement

Screening workflow, outcome and pitfalls

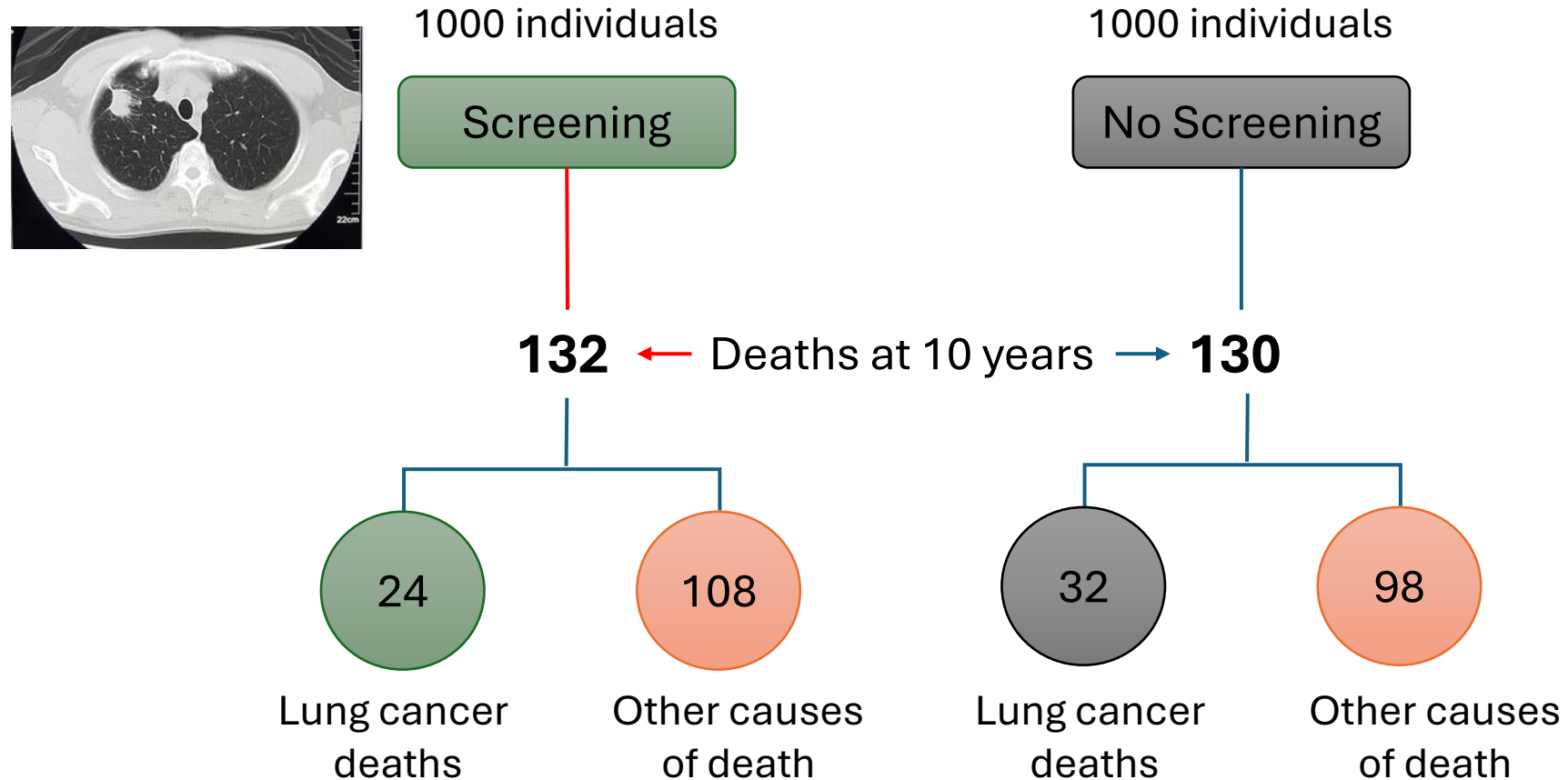


Low-Dose Computed Tomographic Screening for Lung clinical trials

Clinical trial (year), country	Comparison/control group	Eligible subjects	Rate of adherence	Rate of positive screening LDCT	Lung cancer incidence	Lung cancer mortality	All-cause mortality
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Study	Intervention	Comparison	Age	Sex	Smoking	Duration	Quit	Outcome	HR	95% CI	p
NLST (2011), ¹ United States	3 annual screenings with LDCT vs single-view posteroanterior chest radiography	I. 55–74 years II. Male or female III. 30 pack-years IV. Quit within 15 years	>90%	24.2%	645 vs 572 (per 100,000 person-years) (RR: 1.13, [1.03–1.23])	247 vs 309 (RRR:20%, [6.8 to 26.7]; p= 0.004)	6.7% (95% CI, 1.2 to 13.6; p = 0.02)	n= 53 454 participants			
DANTE (2015), ³ Italy	4 annual screenings with LDCT vs no screening	I. 60–74 years old II. Male smokers or former smokers III. 20 pack-years IV. Quit less than 10 years	N/A	37%	8.23% vs 6.07% (p=–.0418)	543 vs 544 (HR: 0.993; 95% CI, 0.688–1.433) [Not significant]	1655 vs 1742 per 100,000 person-years (HR: 0.947; 95% CI, 0.769–1.165) [Not Significant]				
ITALUNG (2017), ⁴ Italy	4 annual screenings with LDCT vs no screening	I. 55–69 years old II. Male or female III. 20 pack-years IV. Quit less than 10 years	81%	N/A	67 vs 71 ((RR)=0.93; 95% CI 0.67 to 1.30)	30% reduction (RR=0.70; 95% CI 0.47 to 1.03) [Not significant]	17% reduction (RR=0.83; 95% CI 0.67 to 1.03) [Not significant]				
LUSI (2019), ⁵ Germany	5 annual screenings with LDCT vs no screening	I. 50–69 years old II. Male or female III. >15 cigarettes a day for >25 years or >10 cigarettes a day for >30 years IV. Quit less than 10 years	>90%	4–22%	85 vs 67 (p=0.16)	HR: 0.74 (95% CI: 0.46–1.19; p = 0.21) [Not significant]	HR = 0.99 [95% CI: 0.79–1.25], p =0.95 [Not significant]	n= 15 792 participants			
NELSON (2020), ⁶ Netherlands	4 annual screenings with LDCT vs no screening	I. 50–74 years old II. Male III. >15 cigarettes a day for >25 years or >10 cigarettes a day for >30 years IV. Quit less than 10 years	90%	2.1%	5.58 vs 4.91 cases per 1000 person-years	2.50 deaths vs 3.30 deaths per 1000 person-years (CR: 0.76 (M) (0.61 to 0.94; P = 0.01)	13.93 vs 13.76 deaths per 1000 person-years, RR: 1.01 (0.92–1.11)				

Is lung cancer screening the way forward?

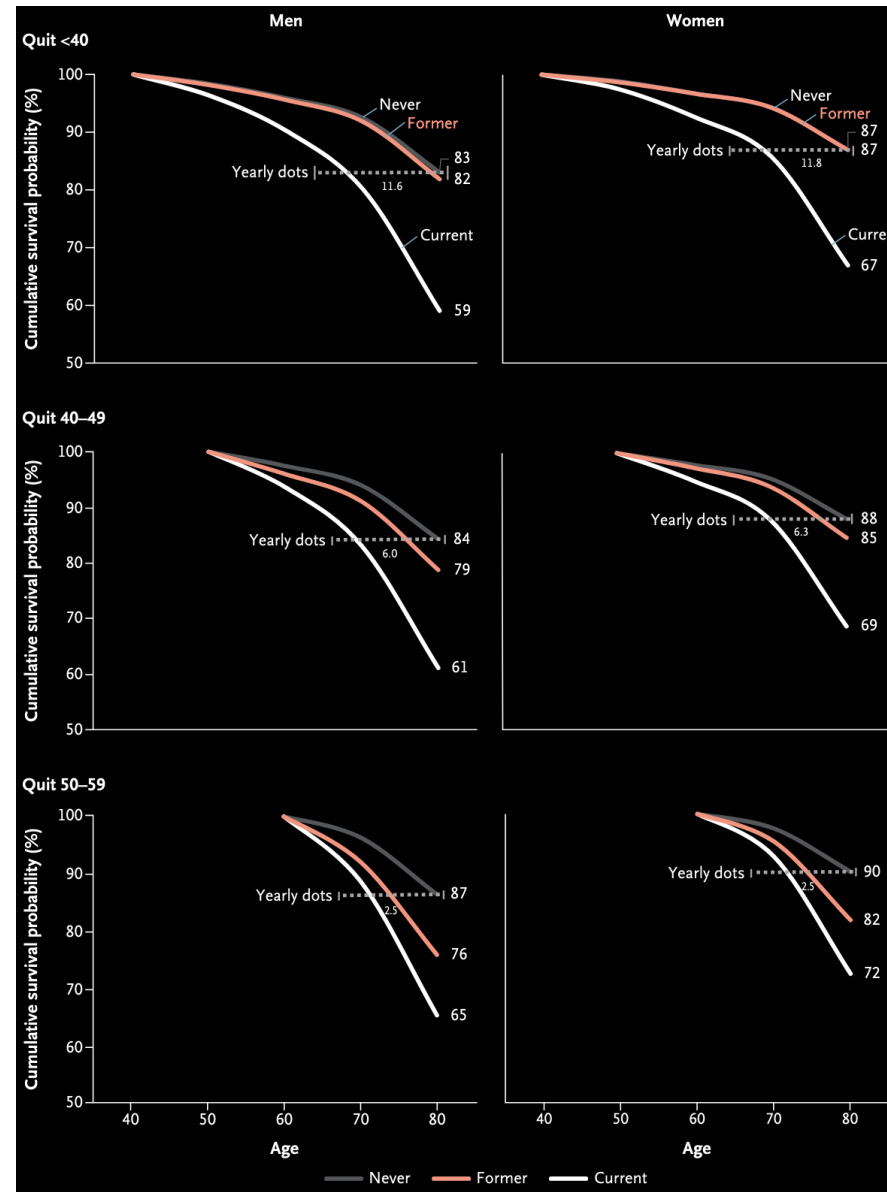


Impact of Smoking Cessation Age on Long-Term Survival: It's Never Too Late to Quit — But the Sooner, the Better

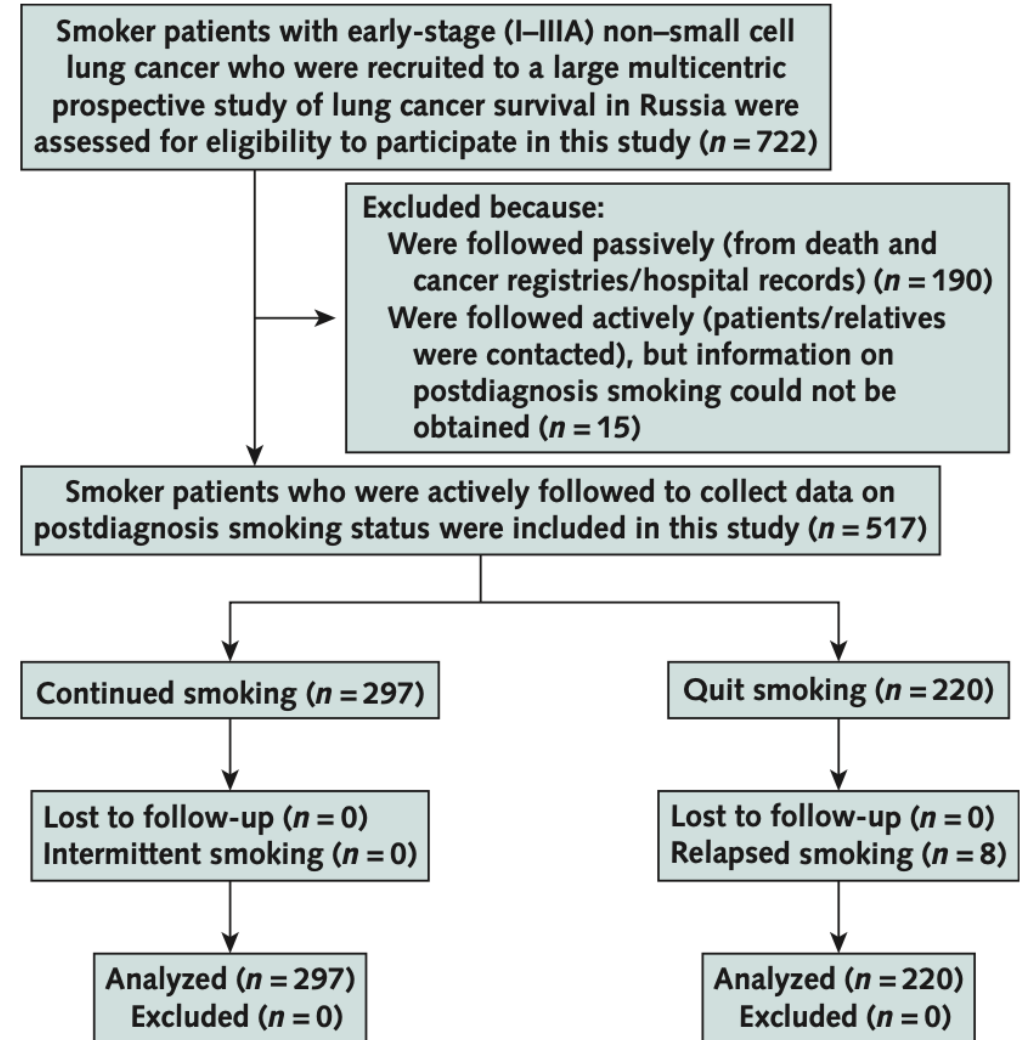
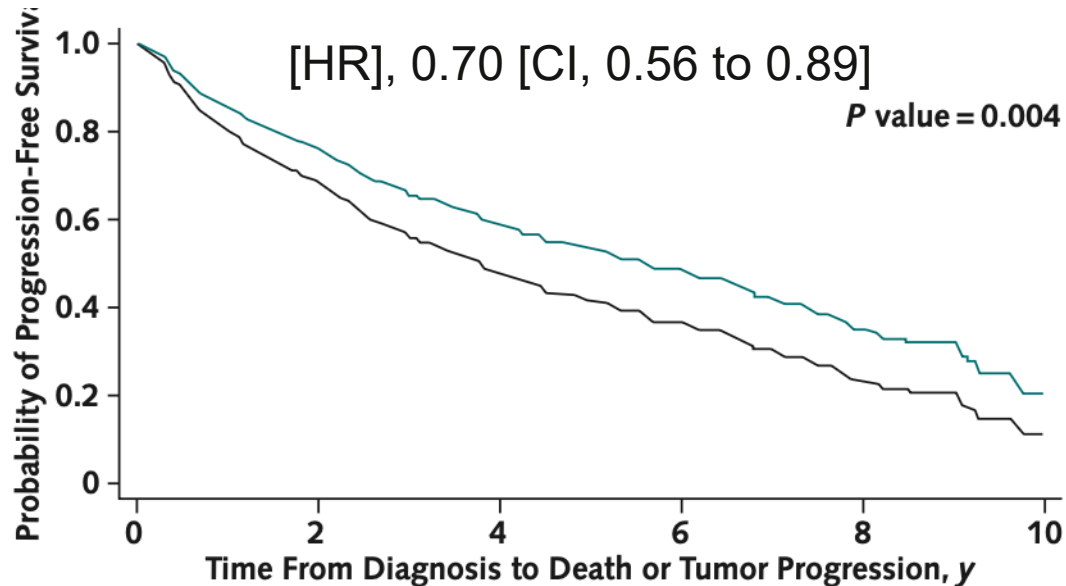
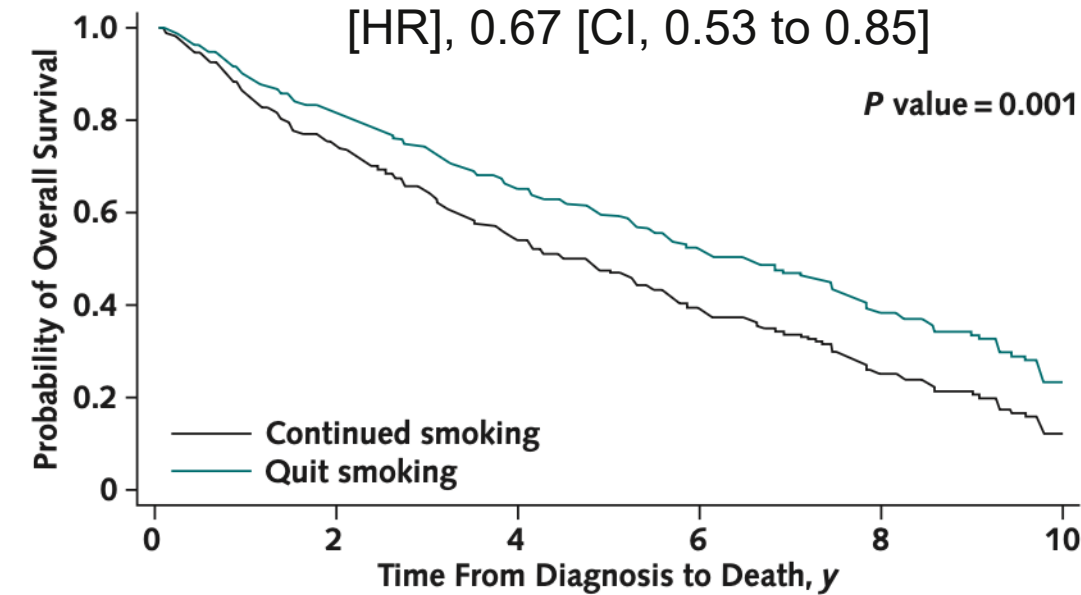
Arrêter de fumer avant 40 ans
+11,5 ans de survie globale

Arrêter de fumer entre 40-49 ans
+6 ans de survie globale

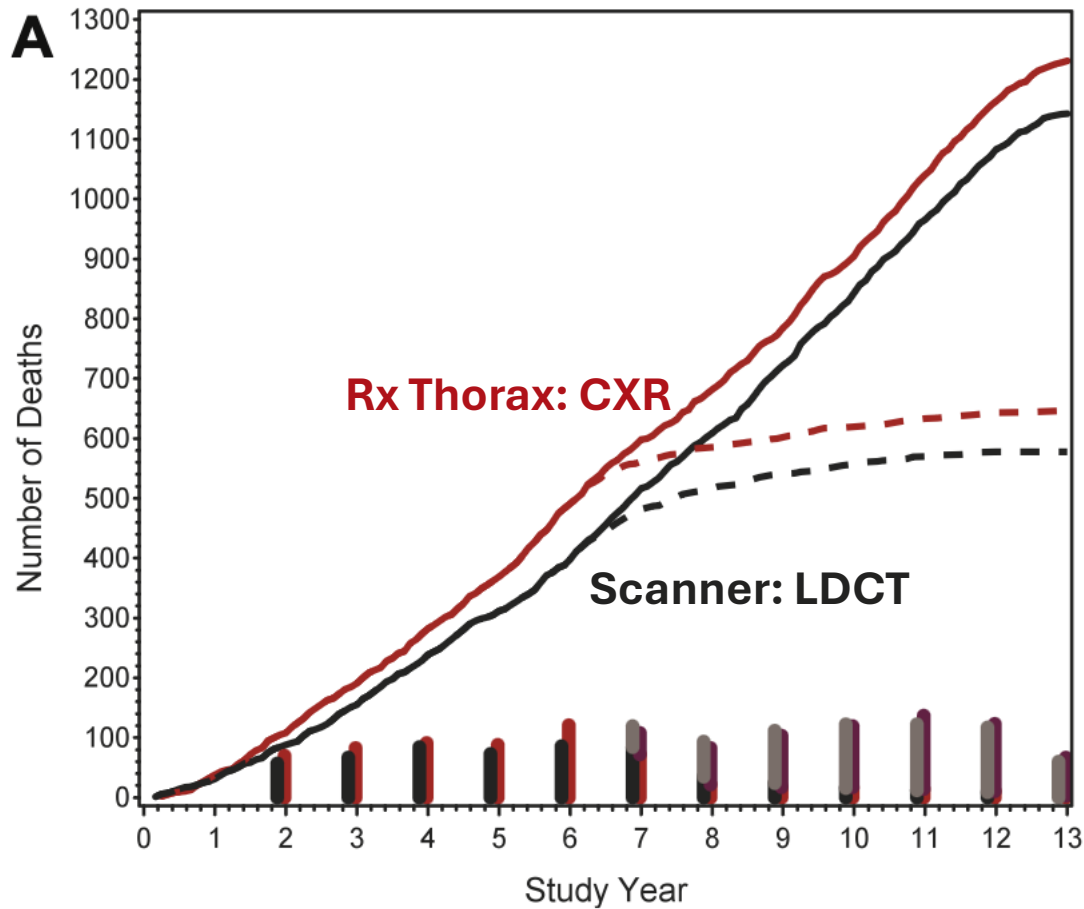
Arrêter de fumer entre 50-59 ans
+2,5 ans de survie globale



Stopping Smoking After Lung Cancer Diagnosis Saves More Lives Than Chemotherapy

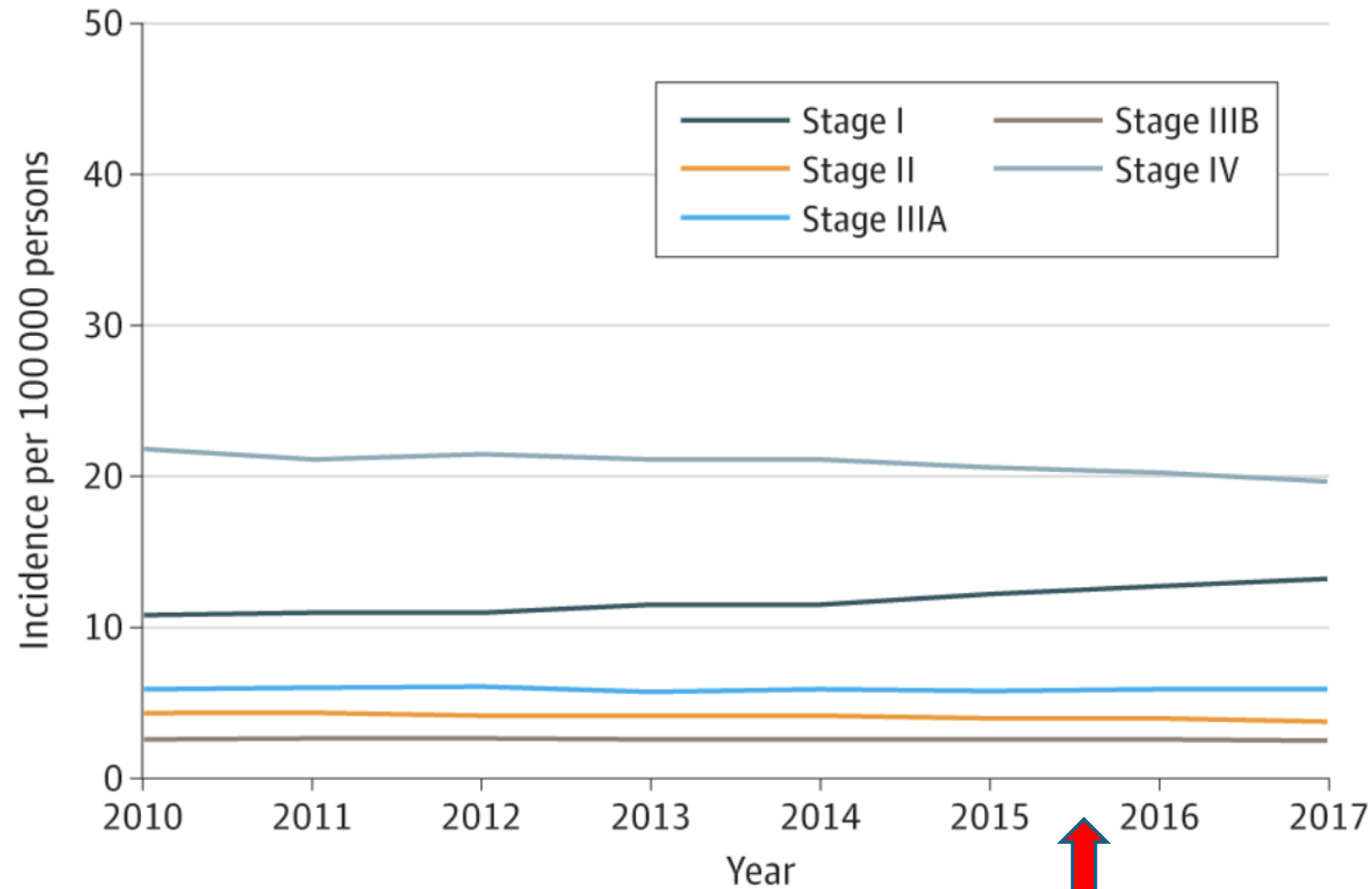


Is lung cancer screening the way forward?



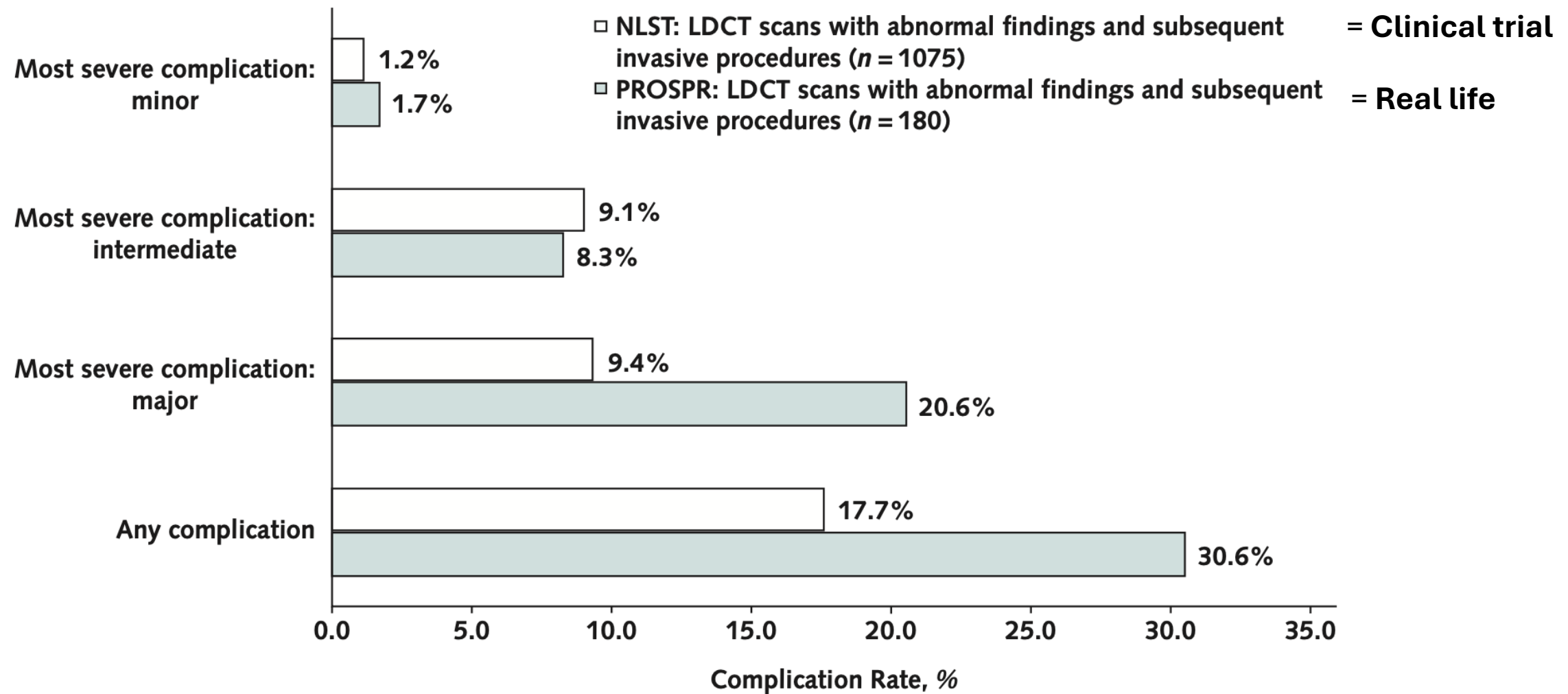
Outcome	LDCT, n (per 1000 subjects)	CXR, n (per 1000 subjects)	Difference across Arms per 1000 Subjects (95% CI) (CXR Minus LDCT)	RR (95% CI)	p Value Interaction ^a
All lung cancer deaths					
All subjects	1147 (42.9)	1236 (46.2)	3.3 (-0.2 to 6.8)	0.92 (0.85-1.00)	
Men	733 (46.5)	755 (47.9)	1.4 (-3.3 to 6.1)	0.97 (0.87-1.07)	0.17
Women	414 (37.8)	481 (43.9)	6.1 (0.8-11.3)	0.86 (0.75-0.98)	
Current smoker	724 (56.3)	818 (63.4)	7.1 (1.3-12.9)	0.88 (0.80-0.97)	0.12
Former smoker	423 (30.5)	418 (30.2)	-0.3 (-4.3 to 3.8)	1.01 (0.88-1.15)	
Age 55-64 y at randomization	641 (32.7)	739 (37.7)	5.0 (1.3-8.6)	0.86 (0.78-0.96)	0.051
Age 65-74 y at randomization	506 (71.2)	497 (69.9)	-1.3 (-9.7 to 7.2)	1.01 (0.90-1.15)	
Overall mortality (all subjects)	5253 (196.6)	5366 (200.7)	4.2 (-2.6 to 10.9)	0.97 (0.94-1.01)	
Overall mortality excluding lung cancer deaths (all subjects)	4106 (153.7)	4130 (154.5)	0.9 (-5.3 to 7.0)	0.99 (0.95-1.03)	

Is lung cancer screening the way forward?



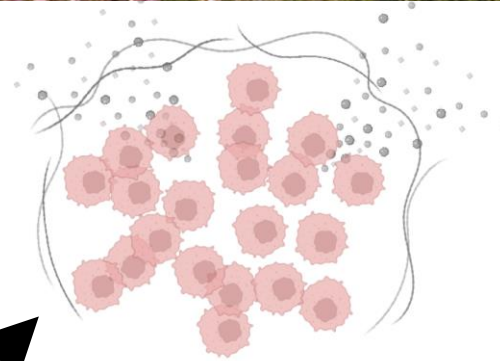
Screening in USA

Rates of complications after subsequent invasive procedures in PROSPR (real life) vs. NLST (clinical trial) patients



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1988



Human tumor cells
melanoma



CD8 T lymphocyte



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HOME > SCIENCE > VOL. 254, NO. 5038 > A GENE ENCODING AN ANTIGEN RECOGNIZED BY CYTOLYTIC T LYMPHOCYTES ON A HUMAN MELANOMA

[REPORT](#)



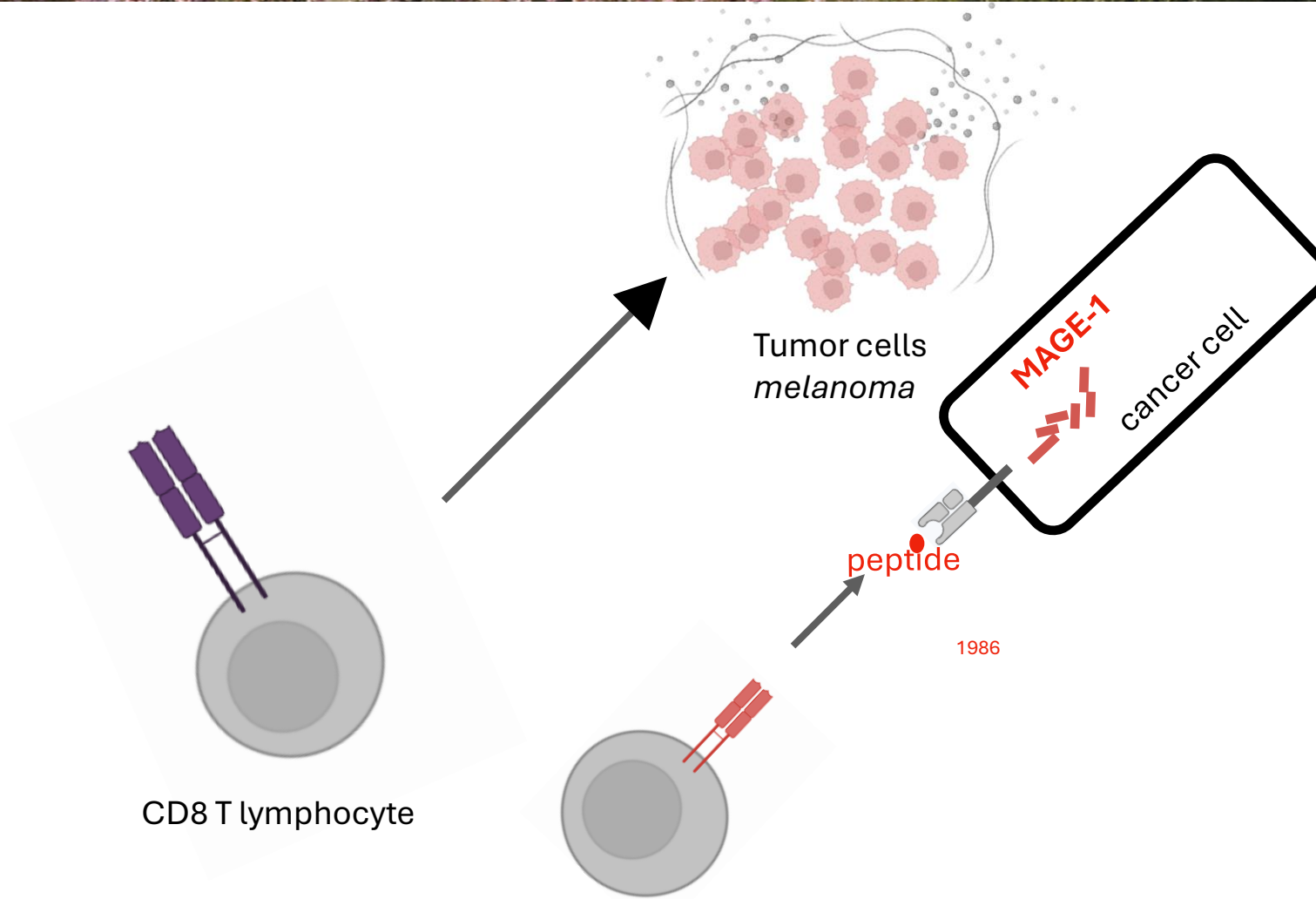
A Gene Encoding an Antigen Recognized by Cytolytic T Lymphocytes on a Human Melanoma

P. VAN DER BRUGGEN, C. TRAVERSARI, P. CHOMÉZ, C. LURQUIN, E. DE PLAEN, B. VAN DEN EYNDE, A. KNUTH, AND T. BOON [Authors Info & Affiliations](#)

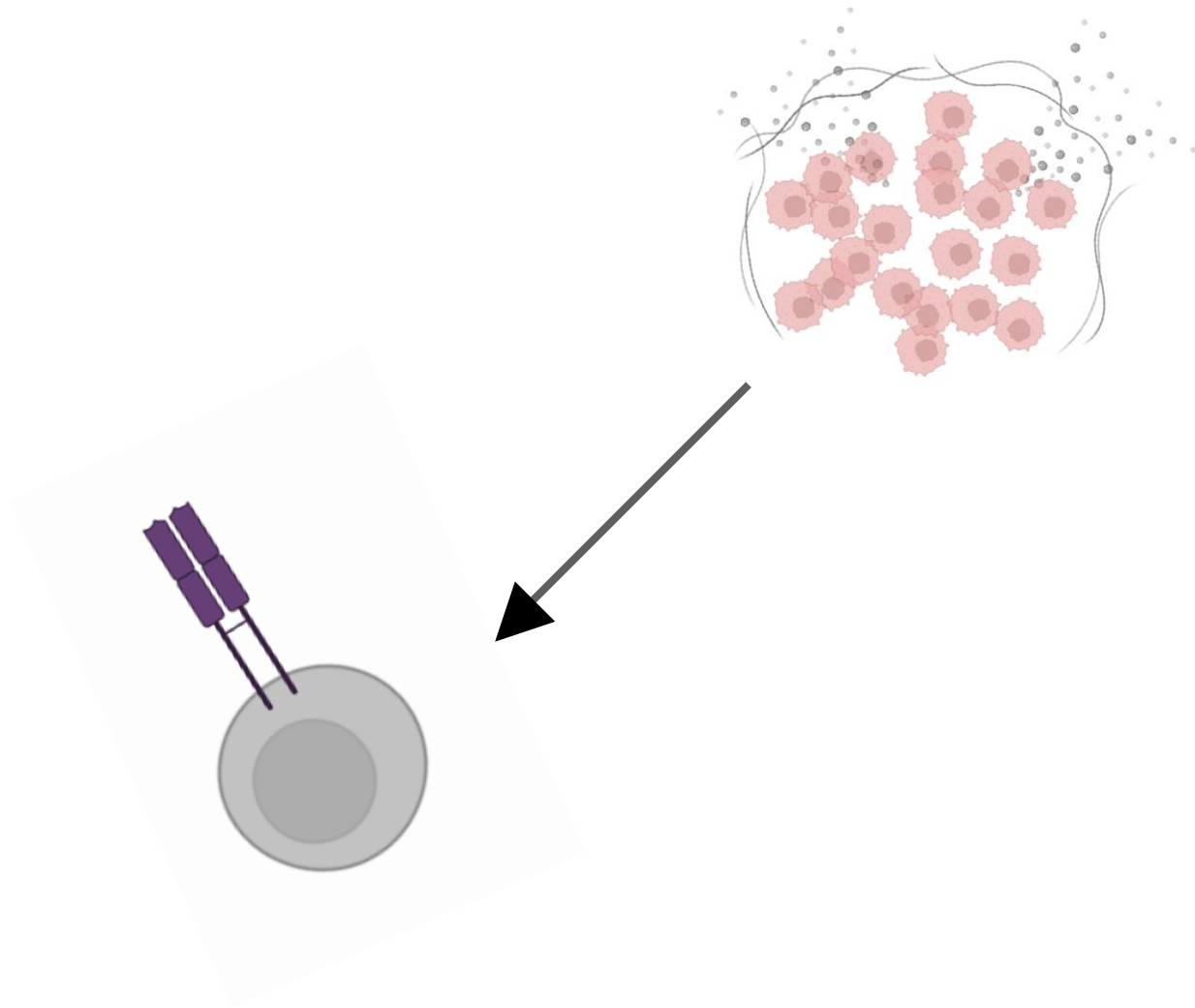
SCIENCE • 13 Dec 1991 • Vol 254, Issue 5038 • pp. 1643-1647 • DOI:10.1126/science.1840703

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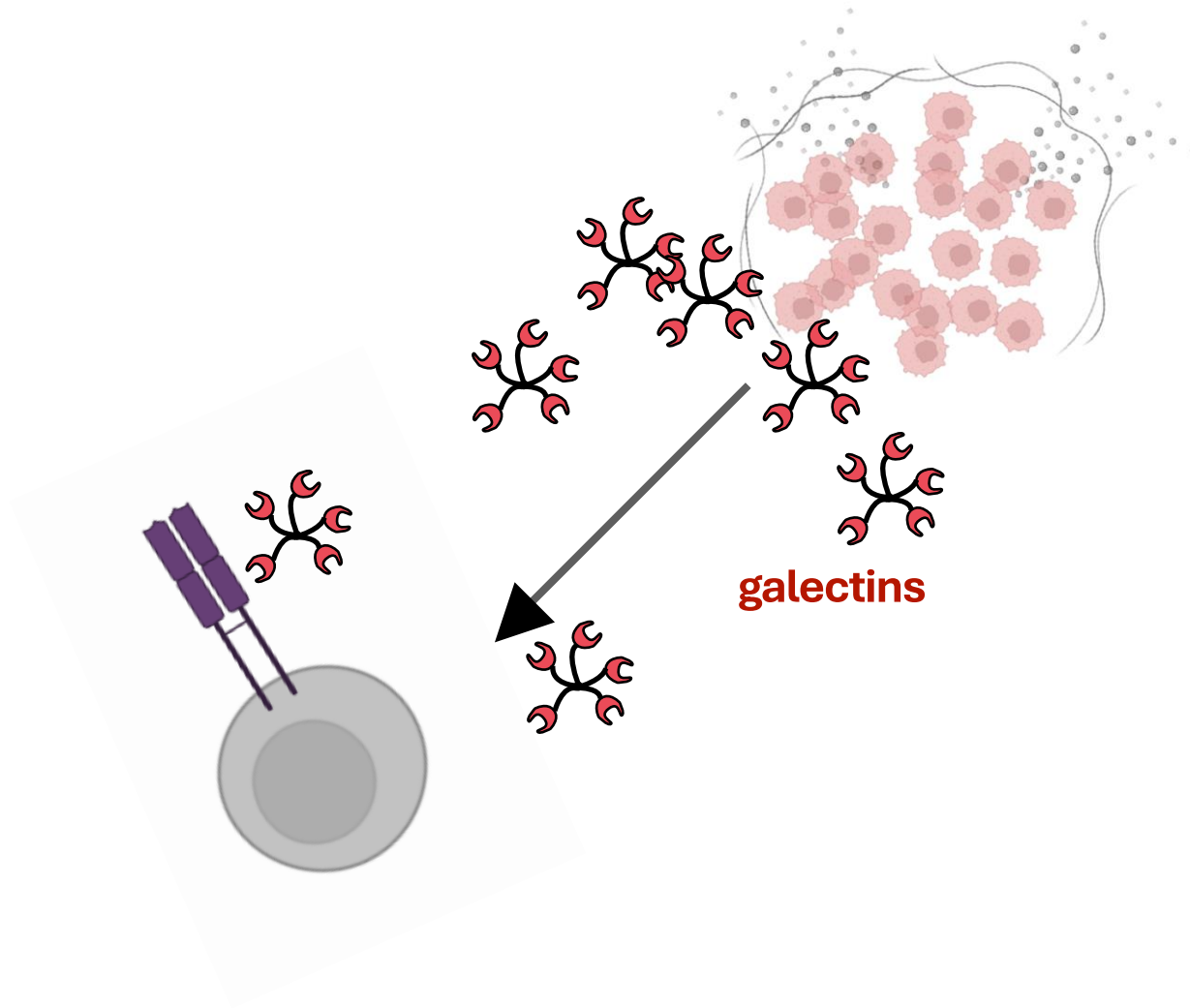
1988



How do tumor cells resist T-cells?



How do tumor cells resist T-cells?possibly by secreting galectins



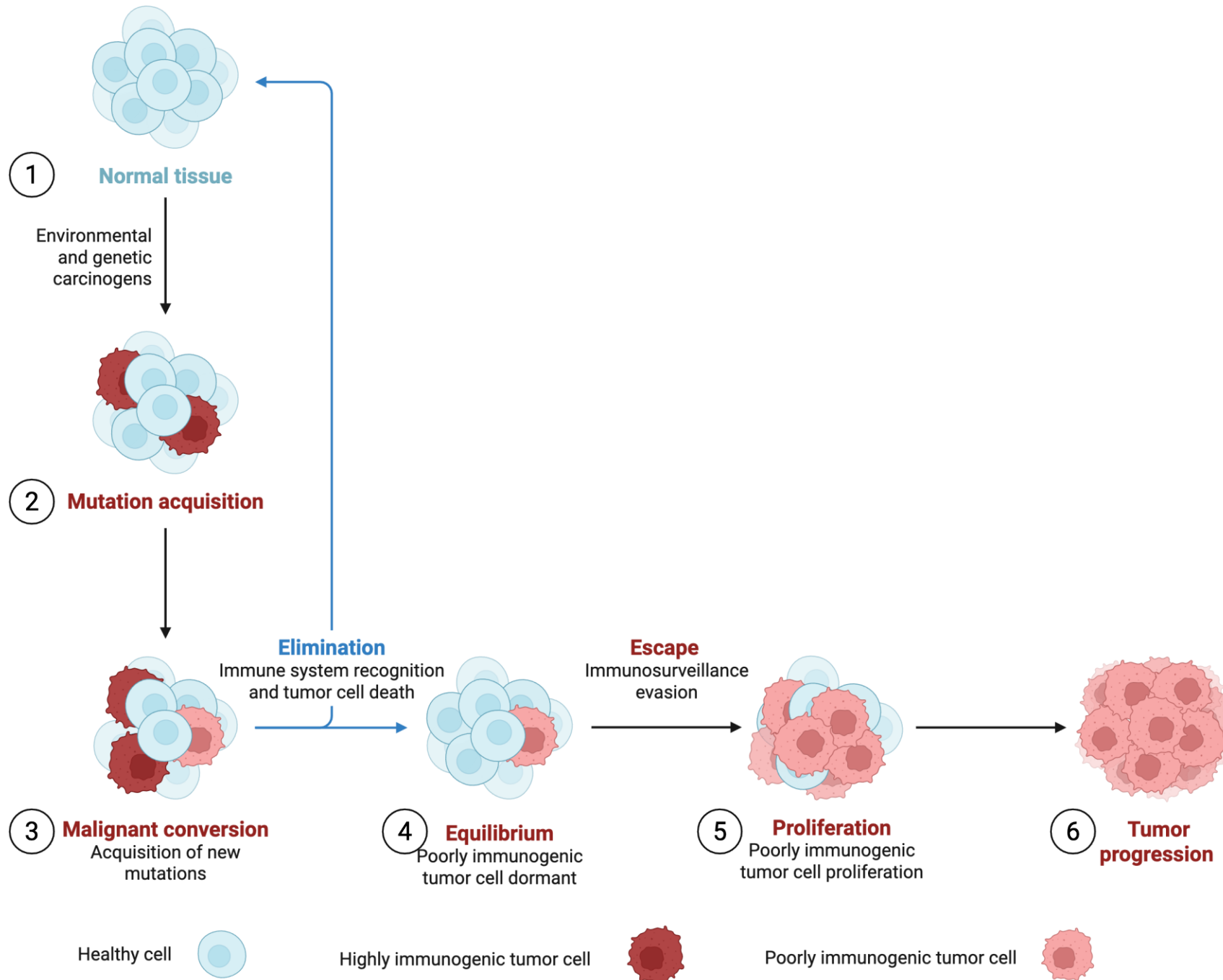
ARTICLE

DOI: [10.1038/s41467-017-00925-6](https://doi.org/10.1038/s41467-017-00925-6)

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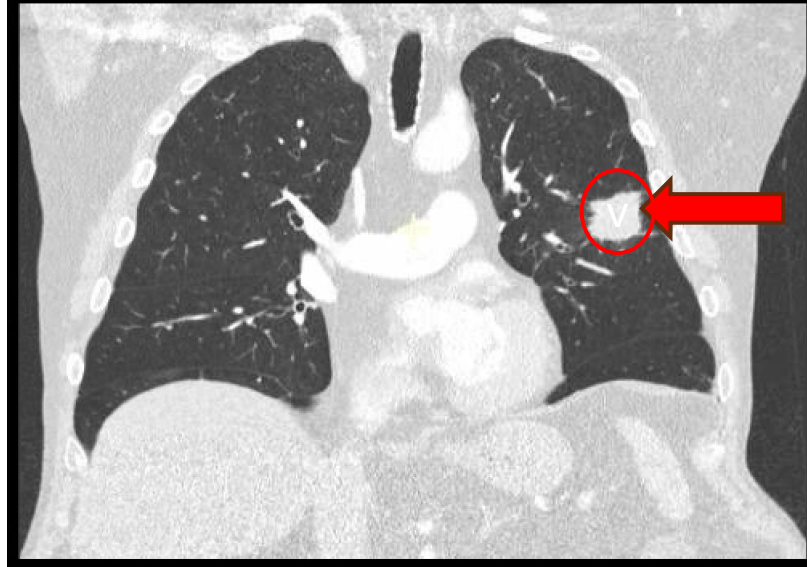
Galectin-3 captures interferon-gamma in the tumor matrix reducing chemokine gradient production and T-cell tumor infiltration

Monica Gordon-Alonso^{1,2}, Thibault Hirsch¹, Claude Wildmann^{1,2} & Pierre van der Bruggen^{1,2}

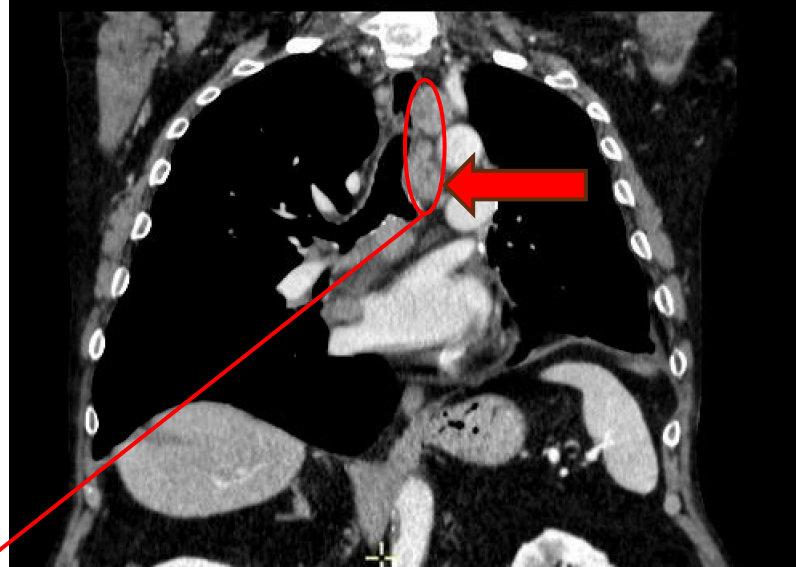


Unusual clinical history

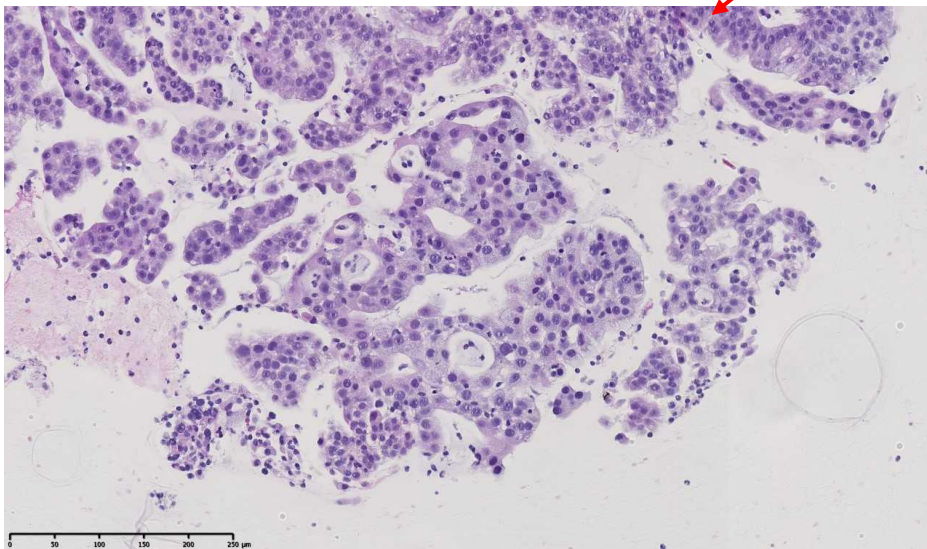
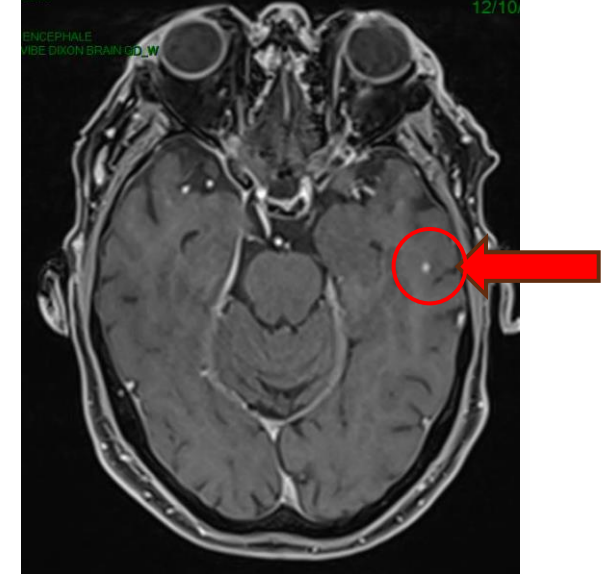
Oct 2022



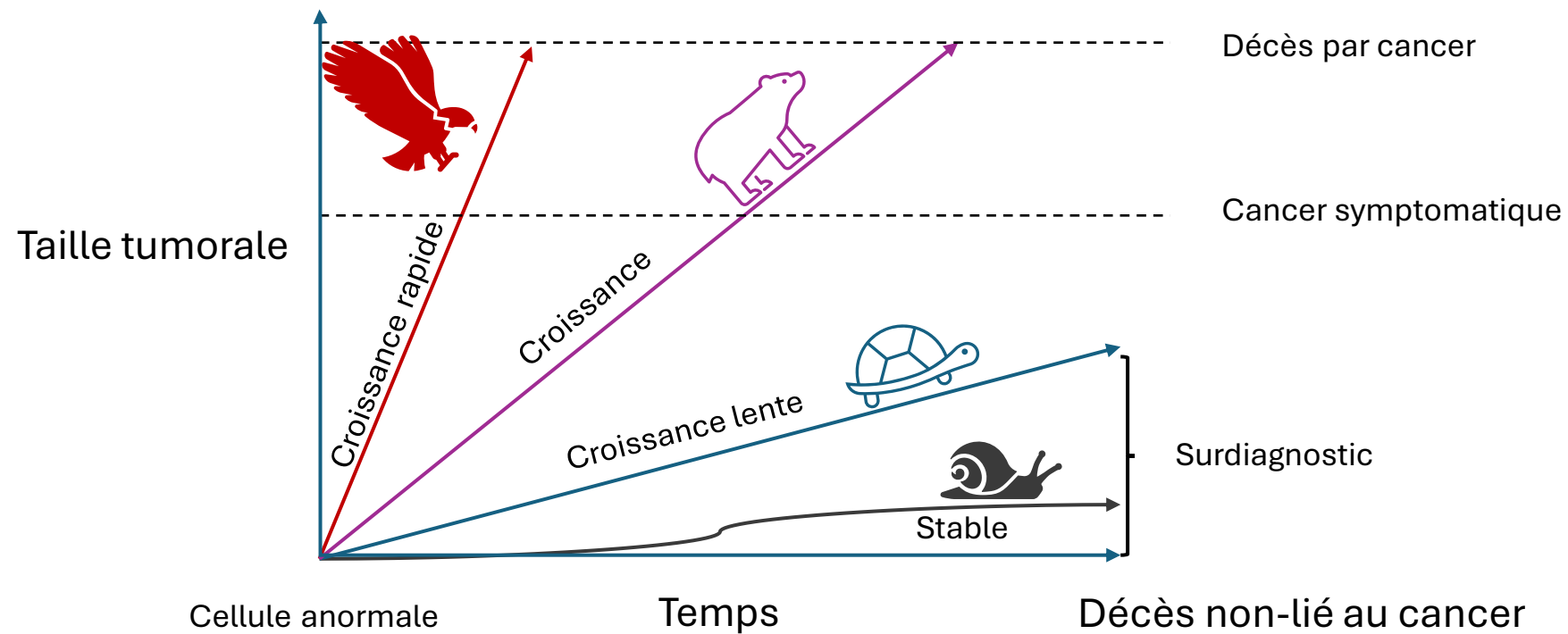
Aug 2024



Aug 2024



Techniques de Détection et de Diagnostic: Le surdiagnostic



Patient de 55 ans , fumeur actif, depuis l'âge de 20 ans , 35 AUP

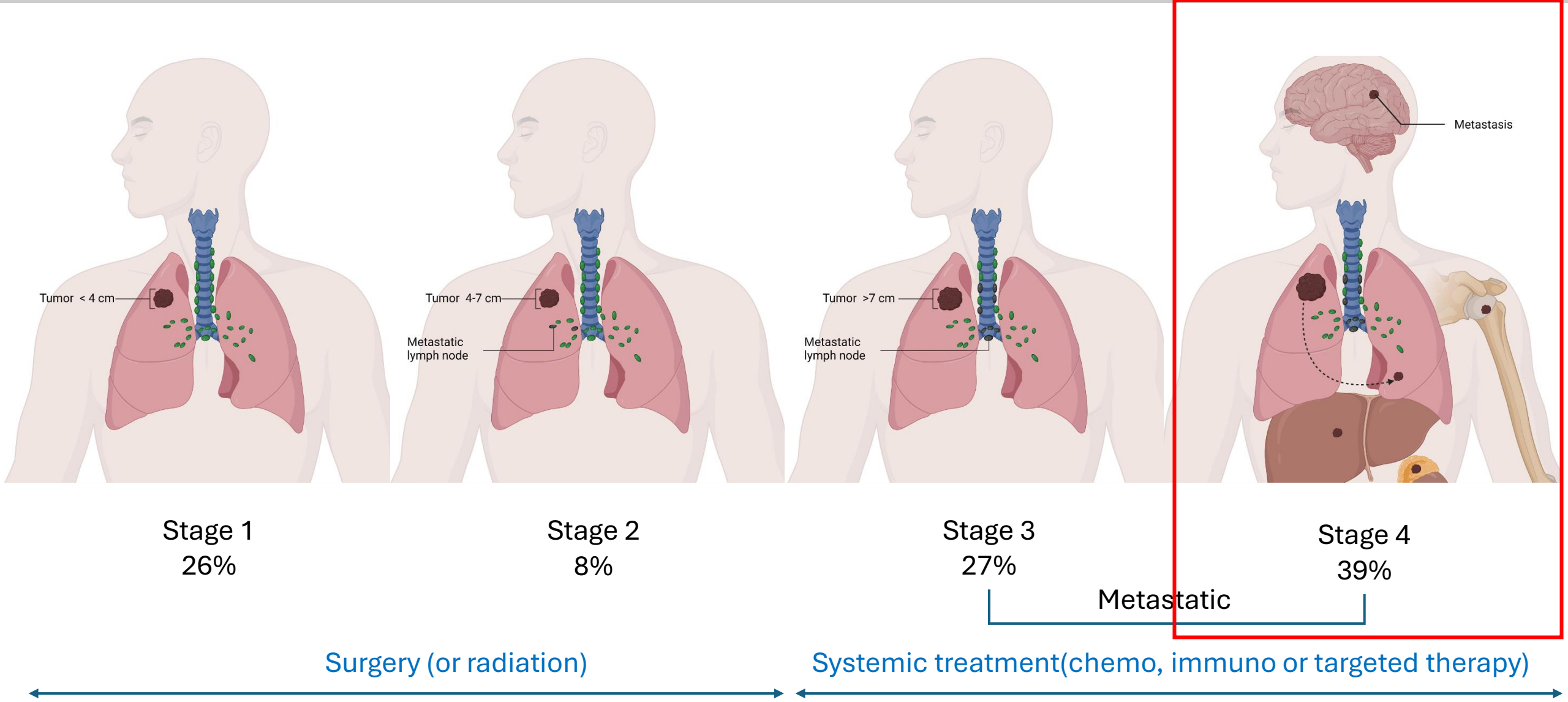
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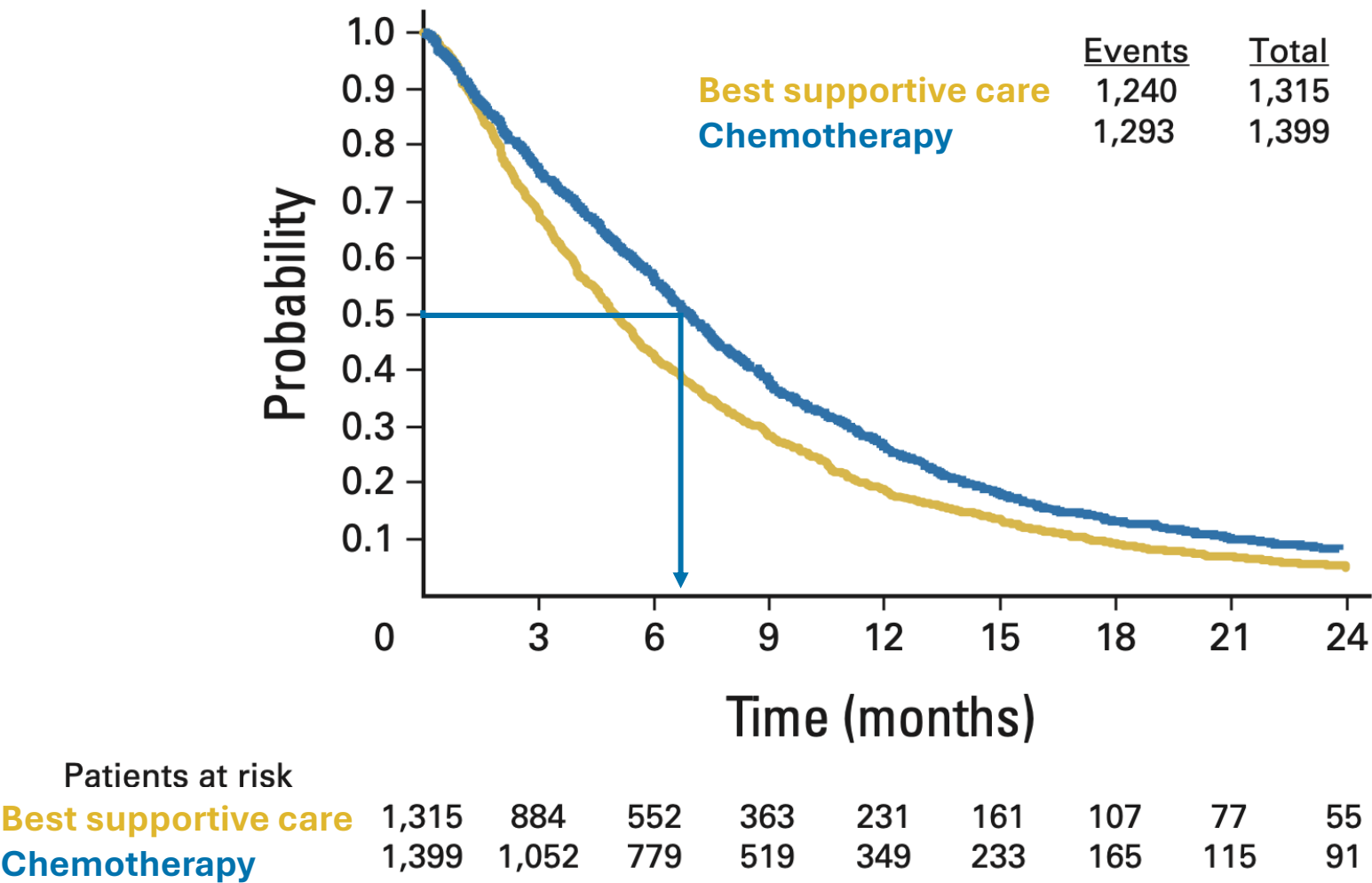
3-Eventuellement

Treatment of lung cancer depends on the disease stage at diagnosis

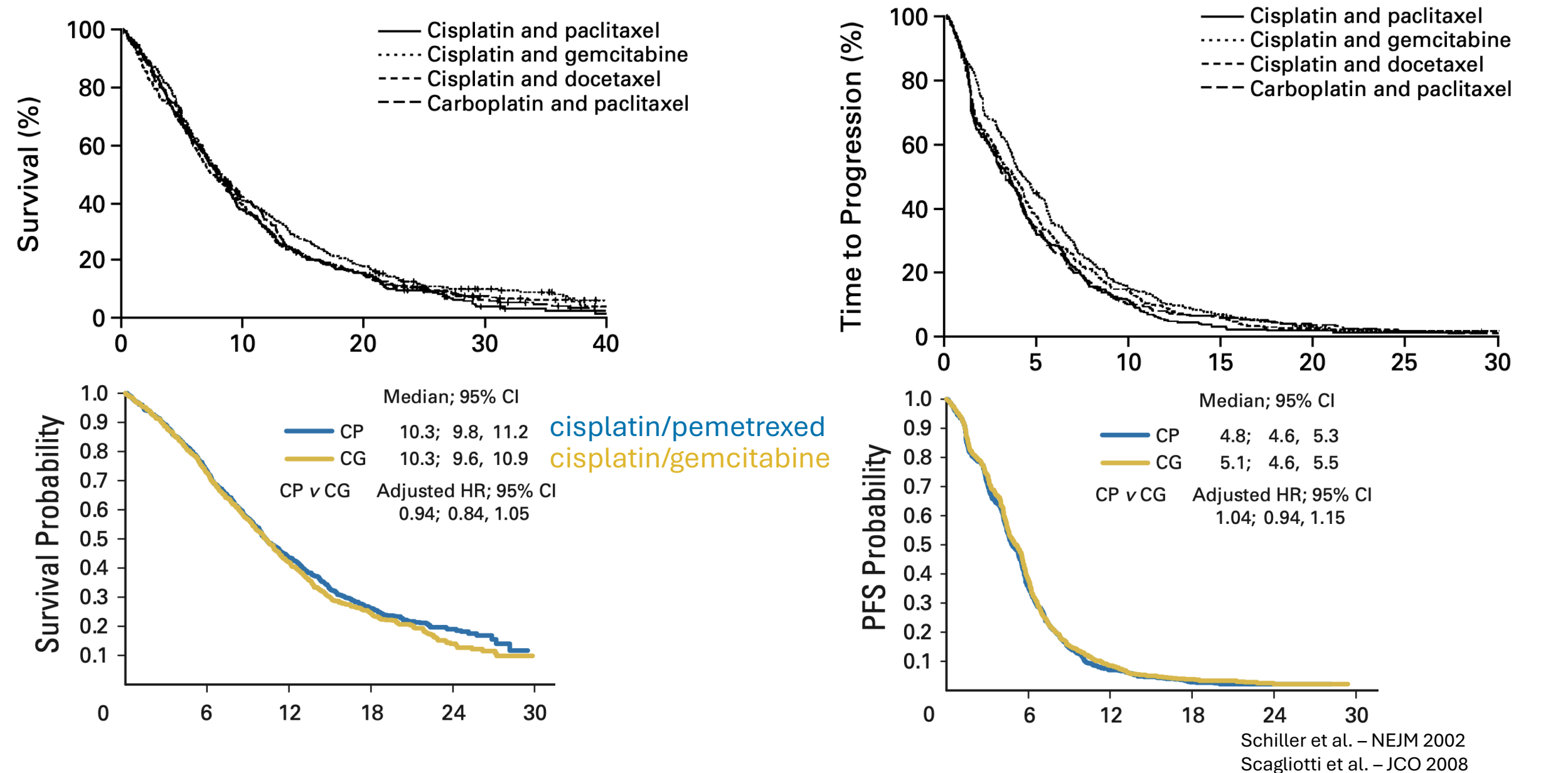


Chemotherapy improves survival in metastatic NSCLC — But does not offer a cure

Median overall survival of 6 months (+ 1,5 months)



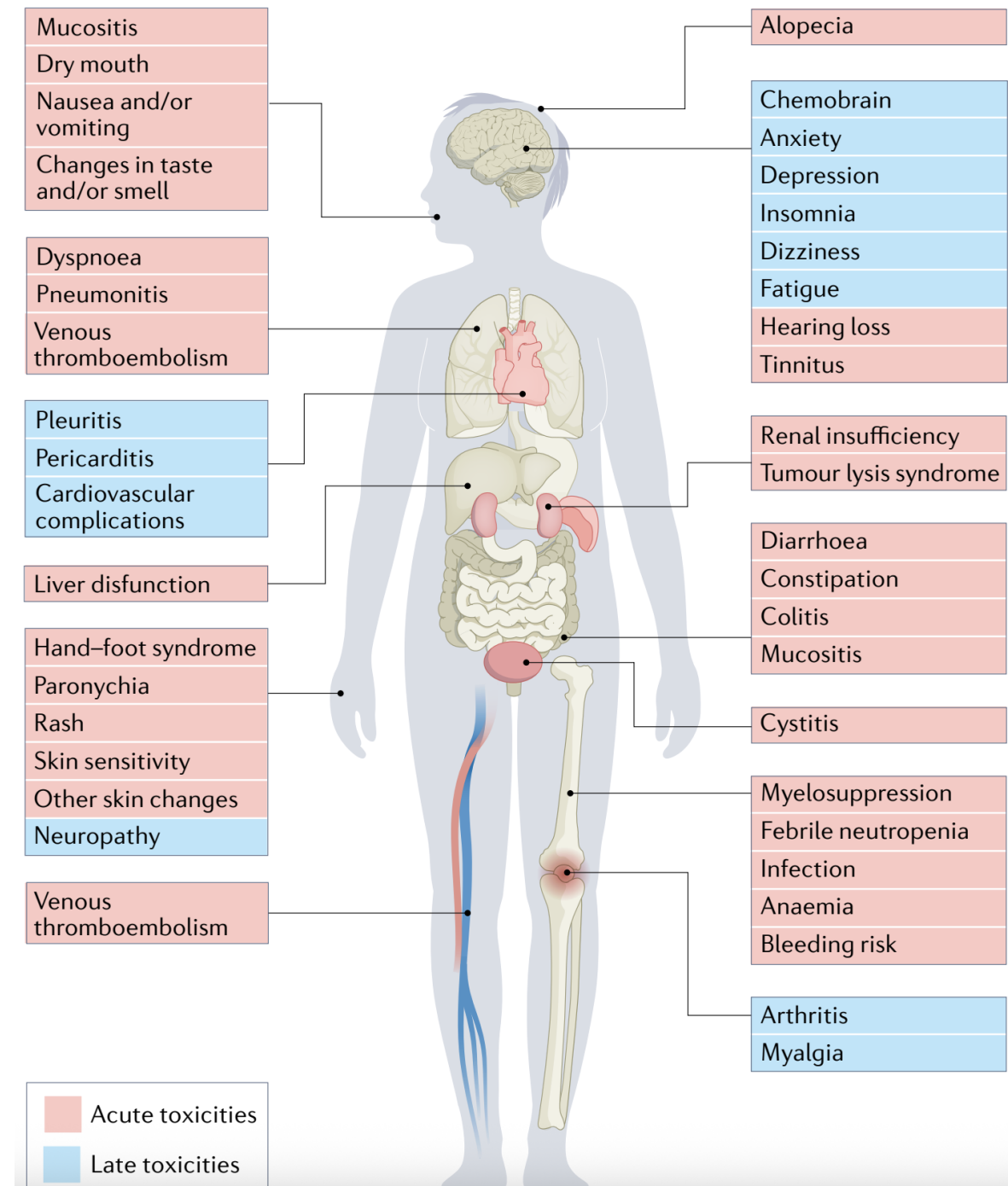
All roads lead to Platinum doublets in NSCLC : similar survival, choice driven by tolerance



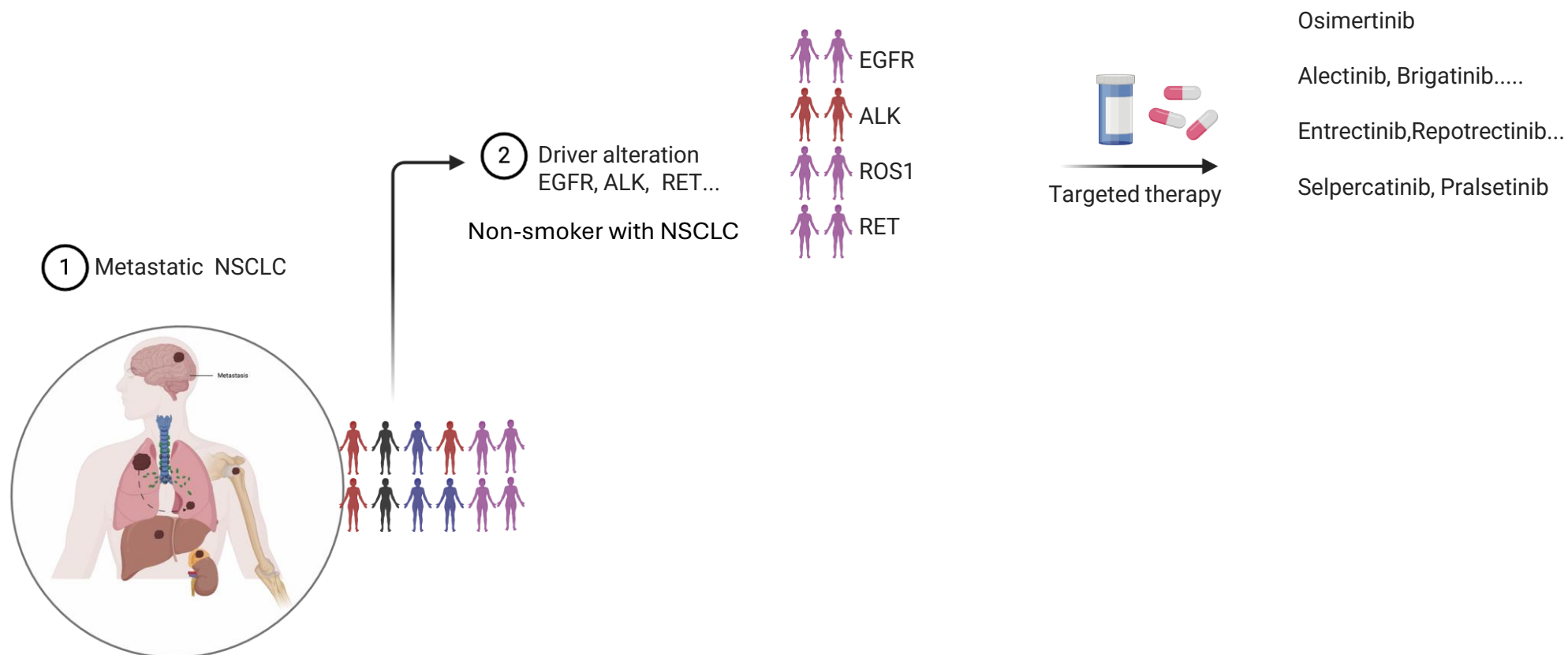
Acute and long-term chemotherapy associated adverse events in patients with cancer

M.B. Lustberg et al. nature reviews clinical oncology 2023

M. Kuderer et al. nature reviews clinical oncology 2023



Immunotherapy is not effective in NSCLC with actionable driver alterations



7/2/2019: Patiente 49 ans, institutrice, 1 fille de 6,5 ans

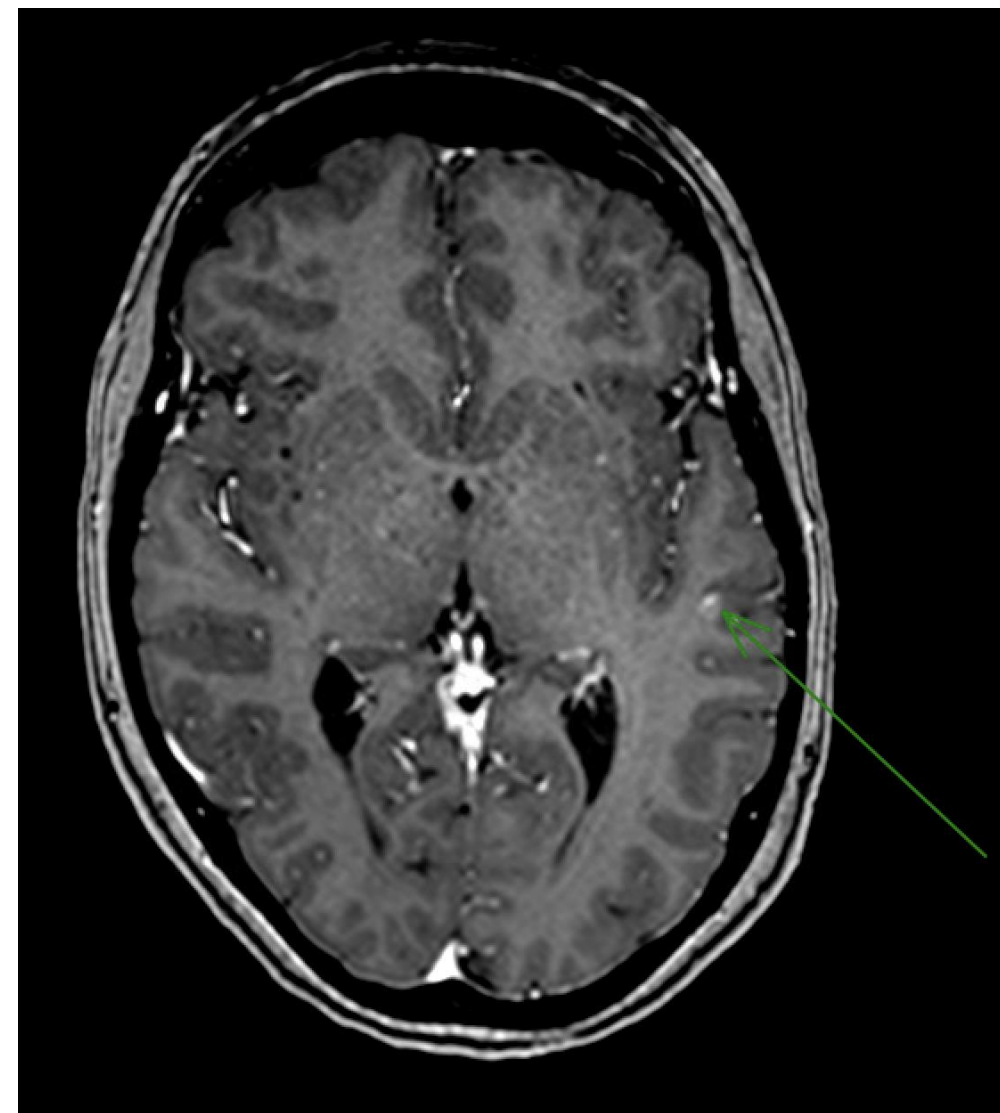
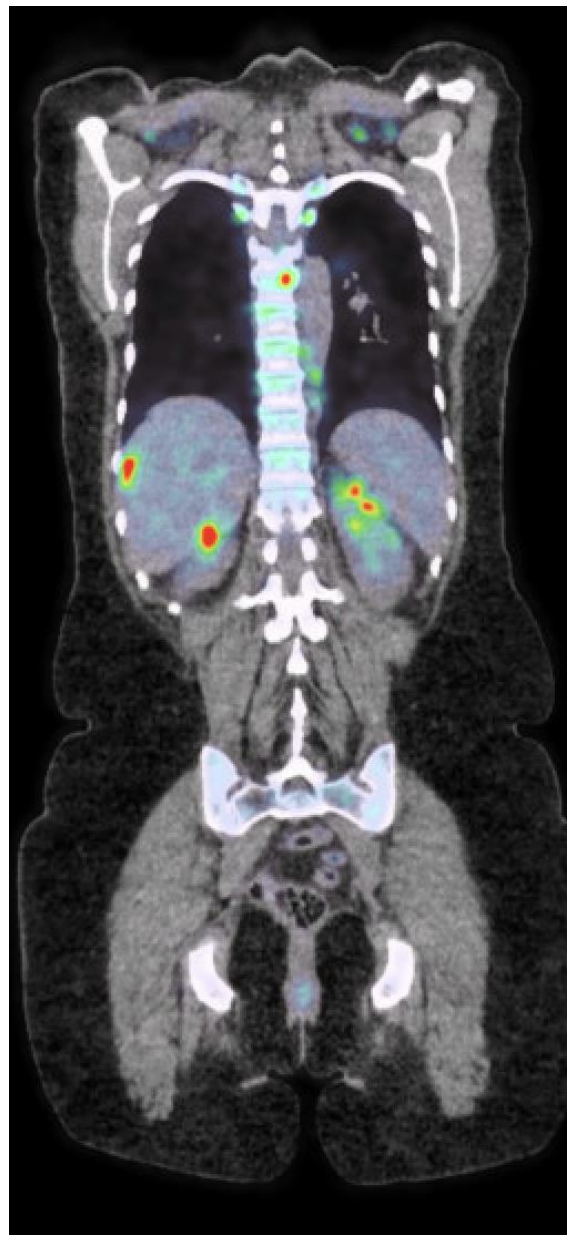
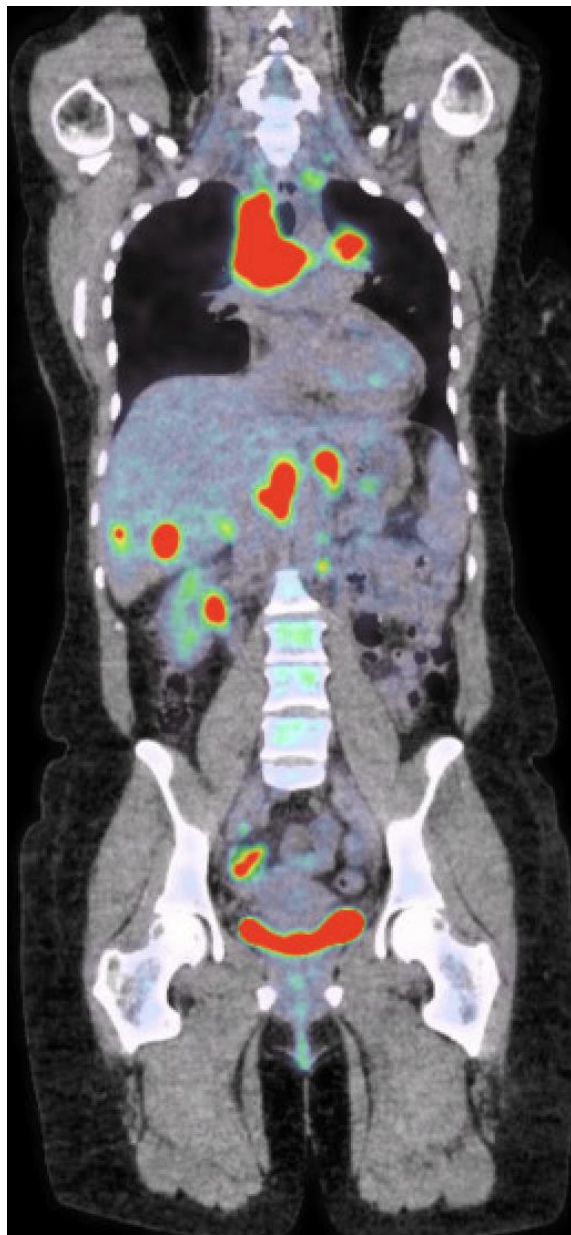
Dyspnée présente depuis 3 semaines, d'apparition brutale. Dyspnée d'effort ainsi que d'une fatigue. Pas de douleur thoracique.

Oedème du visage apparaissant le matin depuis 3 semaines ayant débuté avec les paupières et s'étendant par la suite à l'ensemble du visage.

Présence d'une toux sèche, sans expectorations pouvant être associé à son RGO d'après la patiente

Perte de poids de 4 kg en 2-3 mois, dans le cadre d'un diagnostic d'ulcère gastrique.

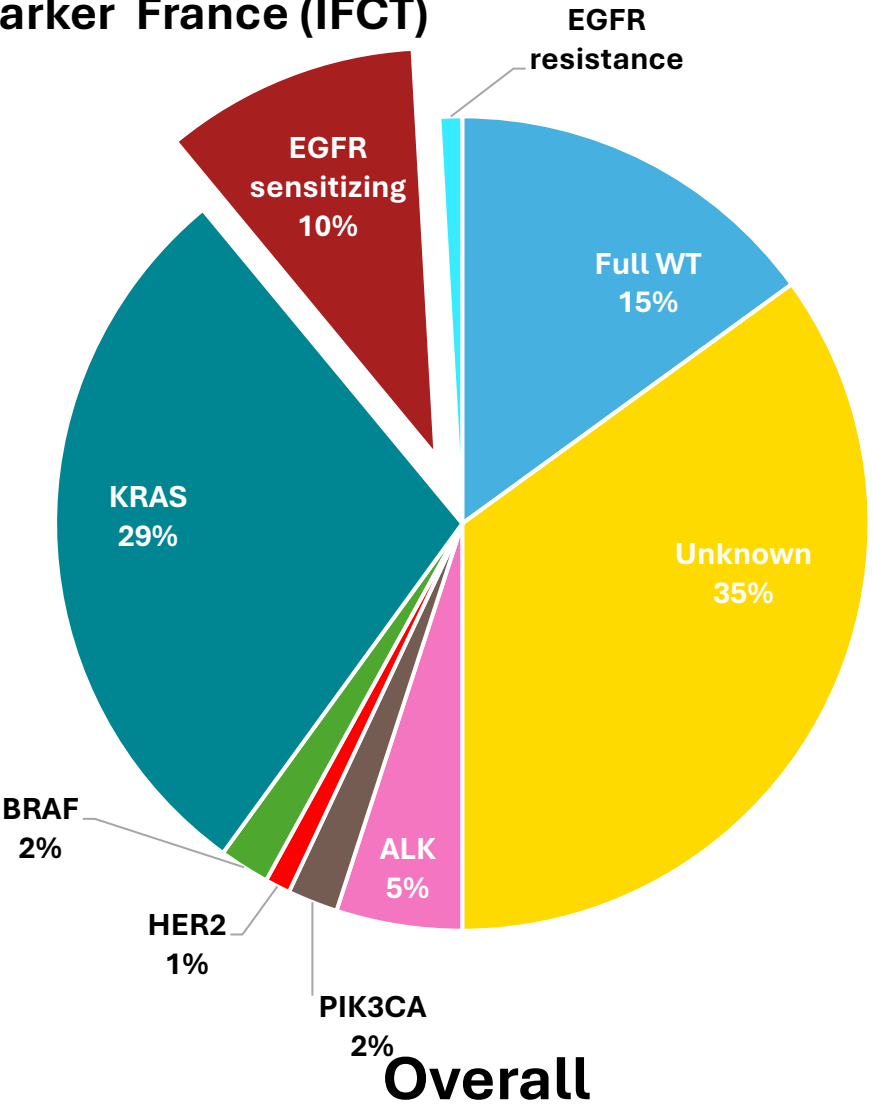
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Quel élément simple dans l'anamnèse peut déjà orienter le type de cancer du poumon dont souffre le patient ?

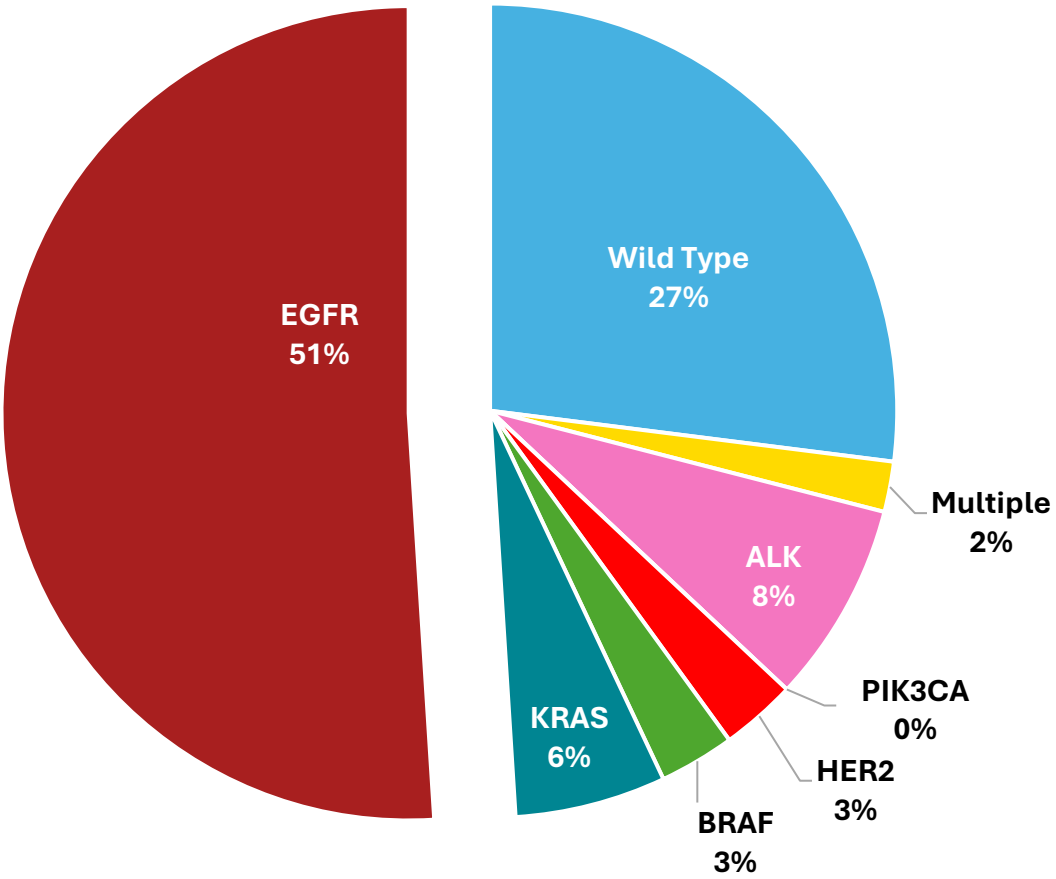
Genetic alterations in NSCLC

Biomarker France (IFCT)



Overall

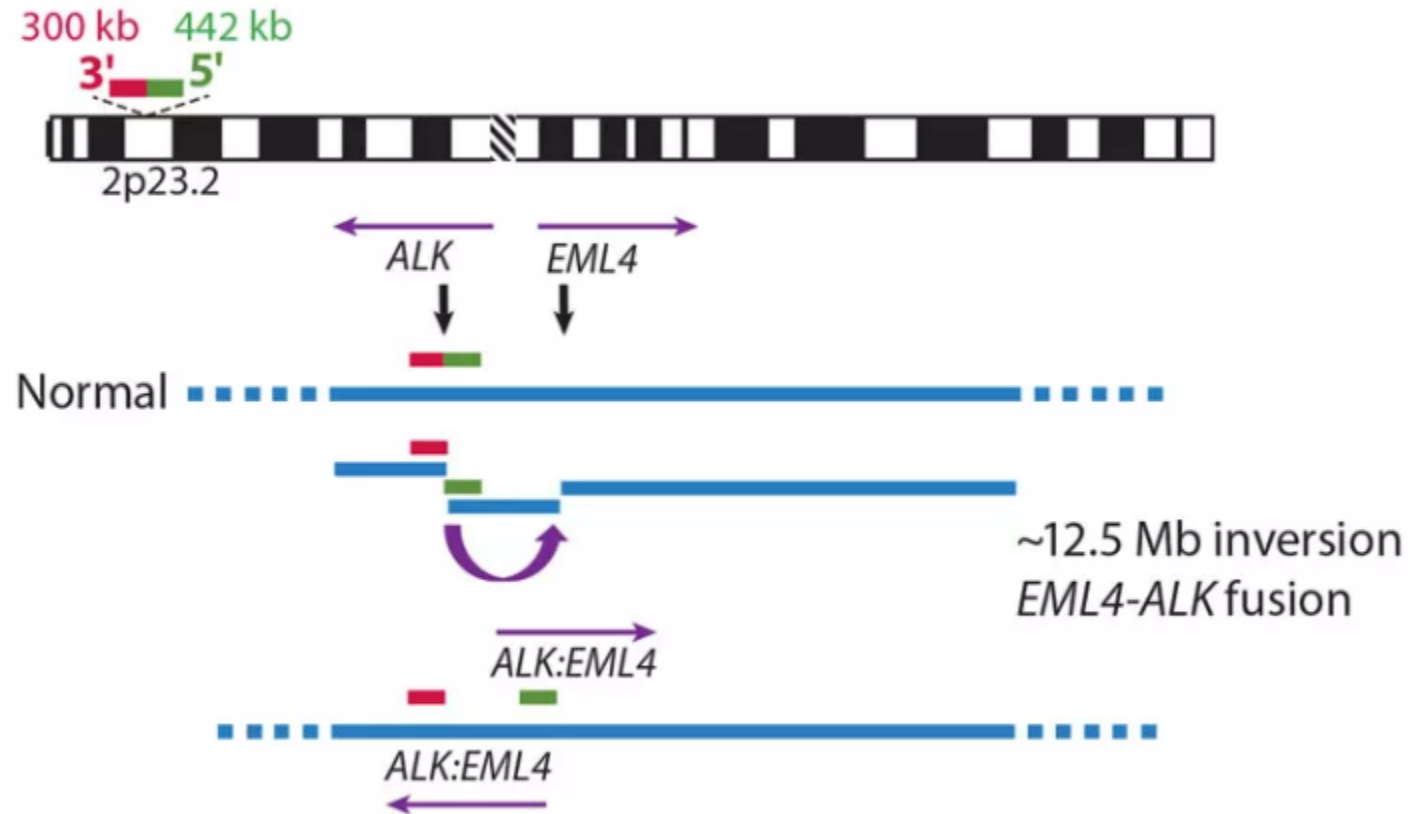
BioCAST (IFCT)



Never-smokers

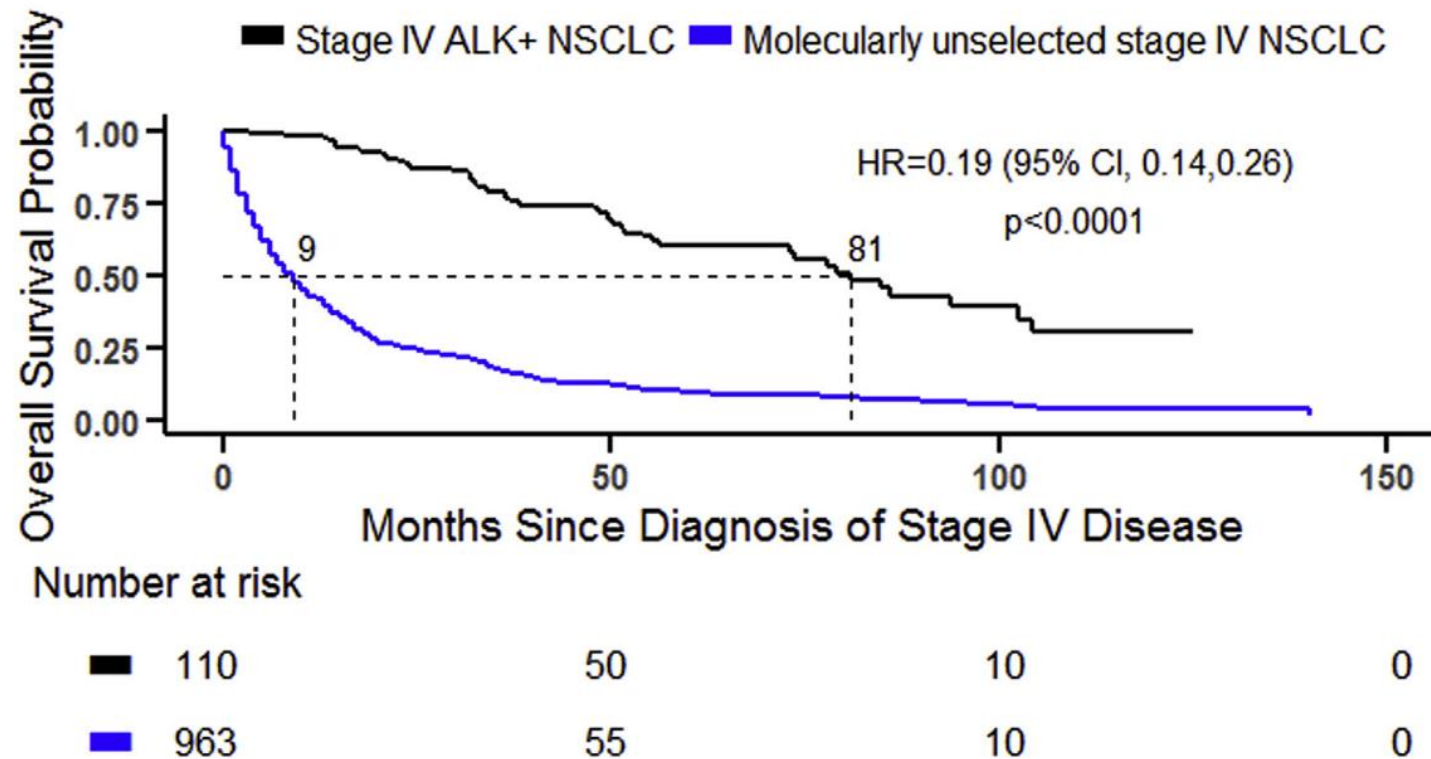
Sun S. Nature rev. Ca. 2007
Barlesi F, Lancet 2016
Couraud S, ERJ 2015

ALK Fusion



Targeted therapy with ALK TKIs is improving outcomes of patients with ALK+ NSCLC

The historical 5 years OS rate for molecularly unselected stage IV NSCLC is 6%

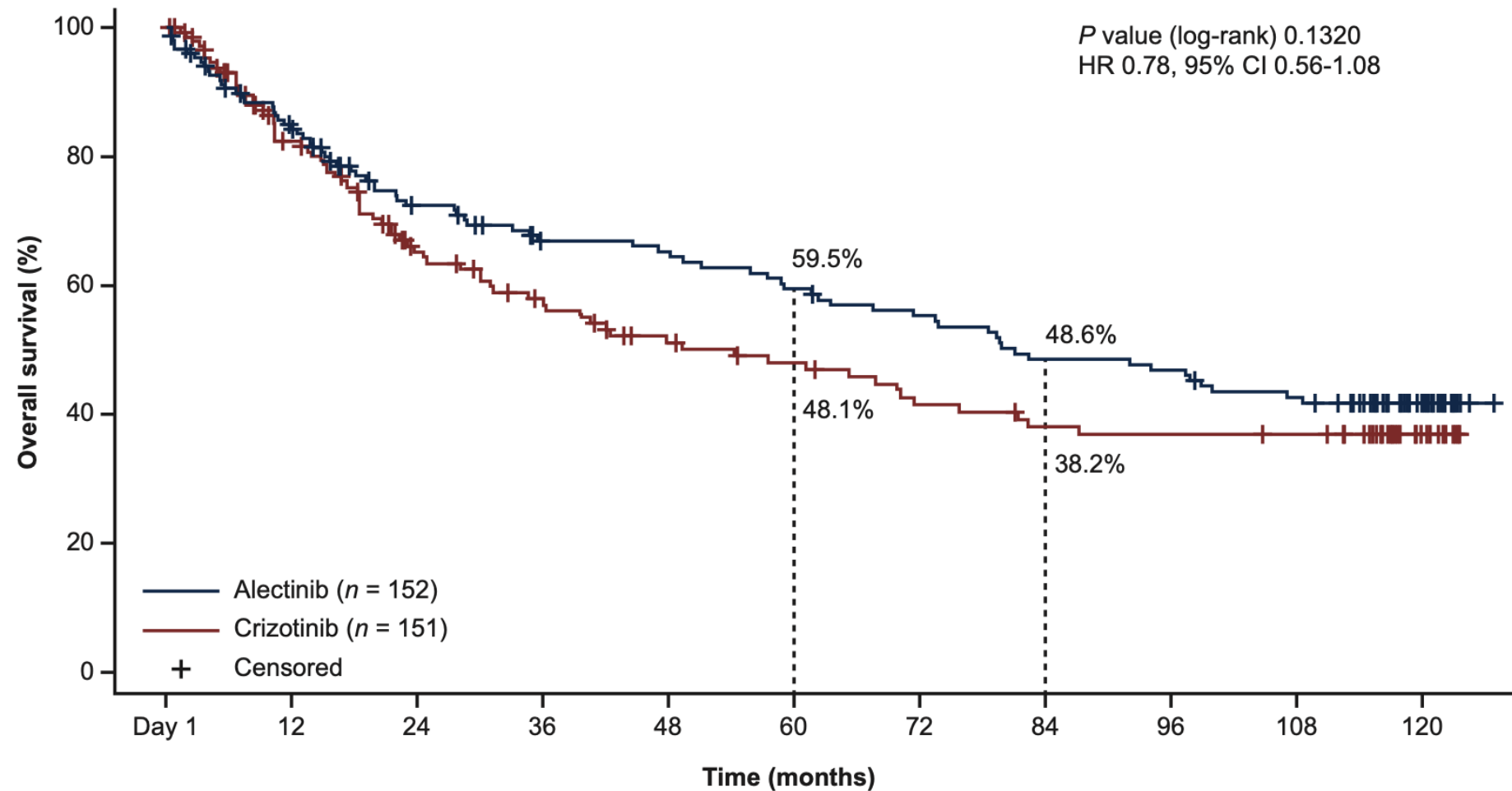


Patients treated with ALK TKIs:

- 5 years OS of 60%
- Median OS of 6,8 years (81 months) from diagnosis of stage IV disease

Targeted therapy with ALK TKIs is improving outcomes of patients with ALK+ NSCLC

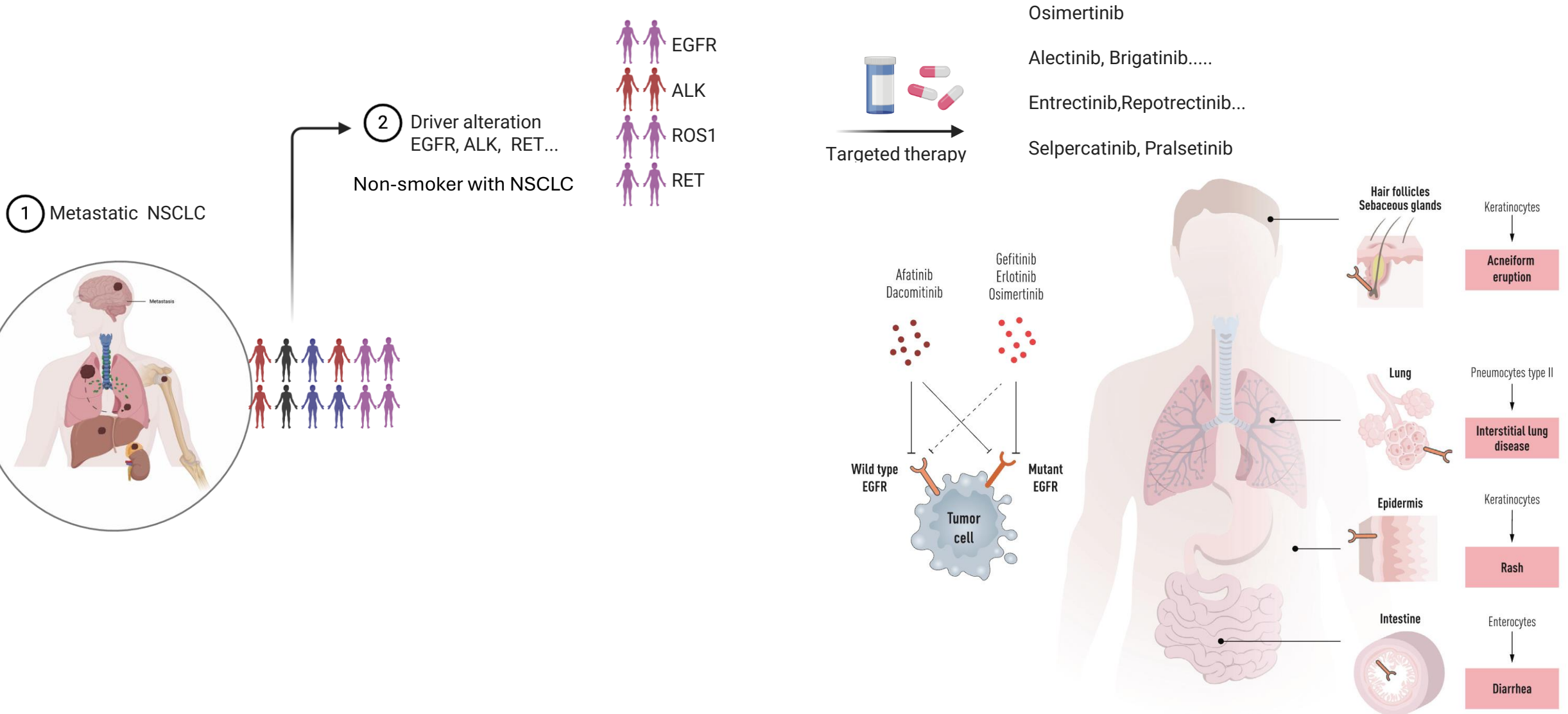
7-years OS rate : 48,6% with alectinib



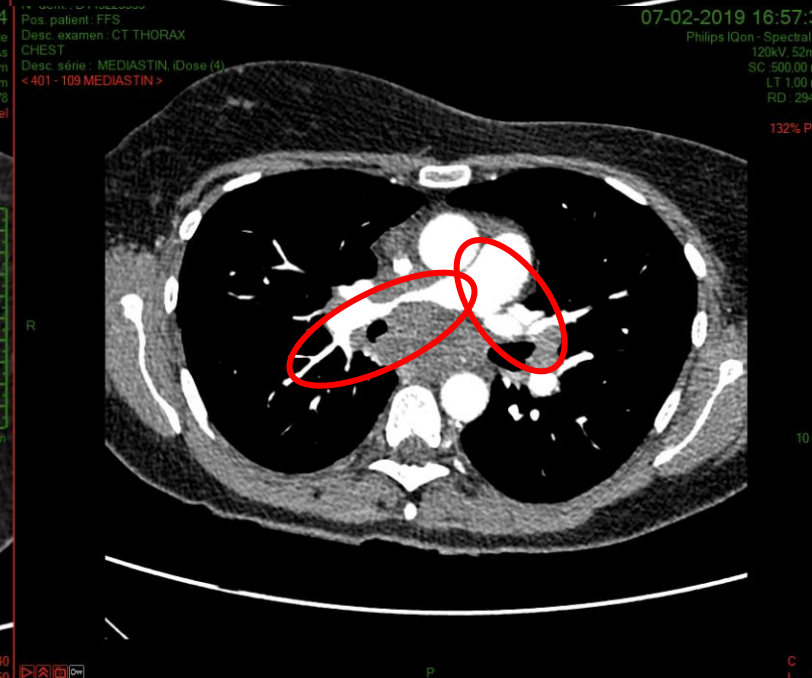
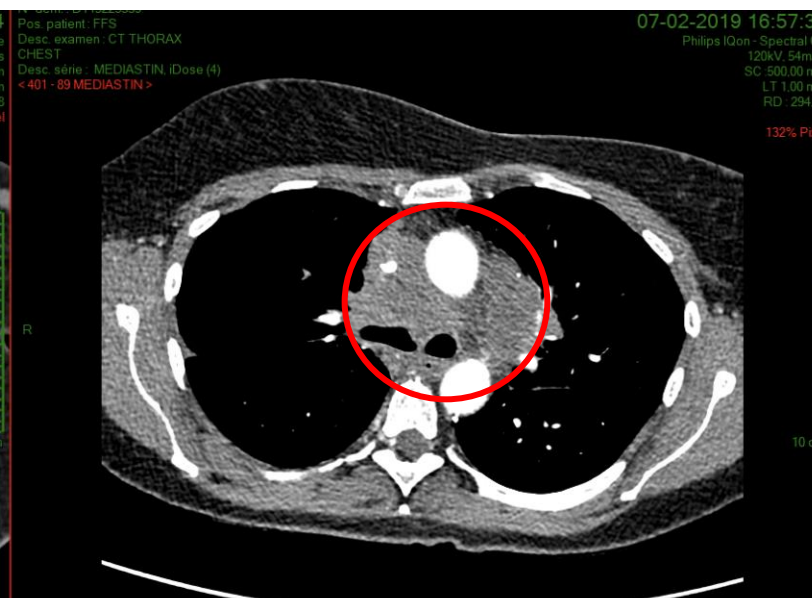
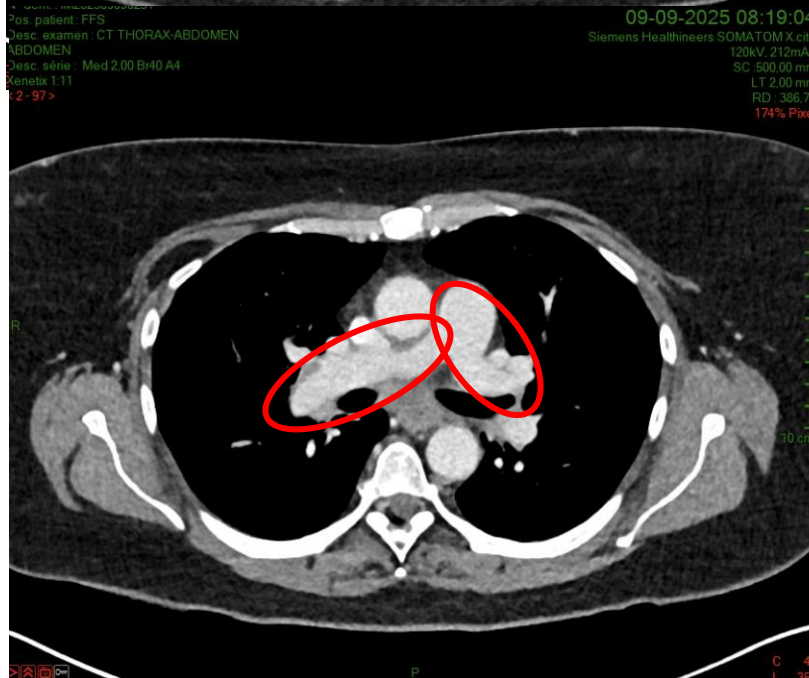
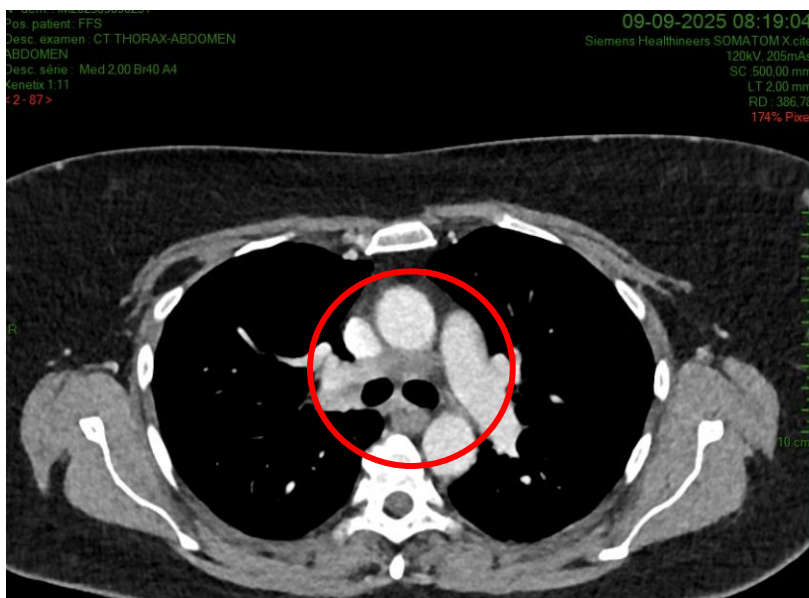
No. of patients at risk

Alectinib	152	120	94	81	79	72	66	58	56	50	20
Crizotinib	151	104	73	60	50	45	38	34	33	32	9

Complications following novel therapies for non-small cell lung cancer



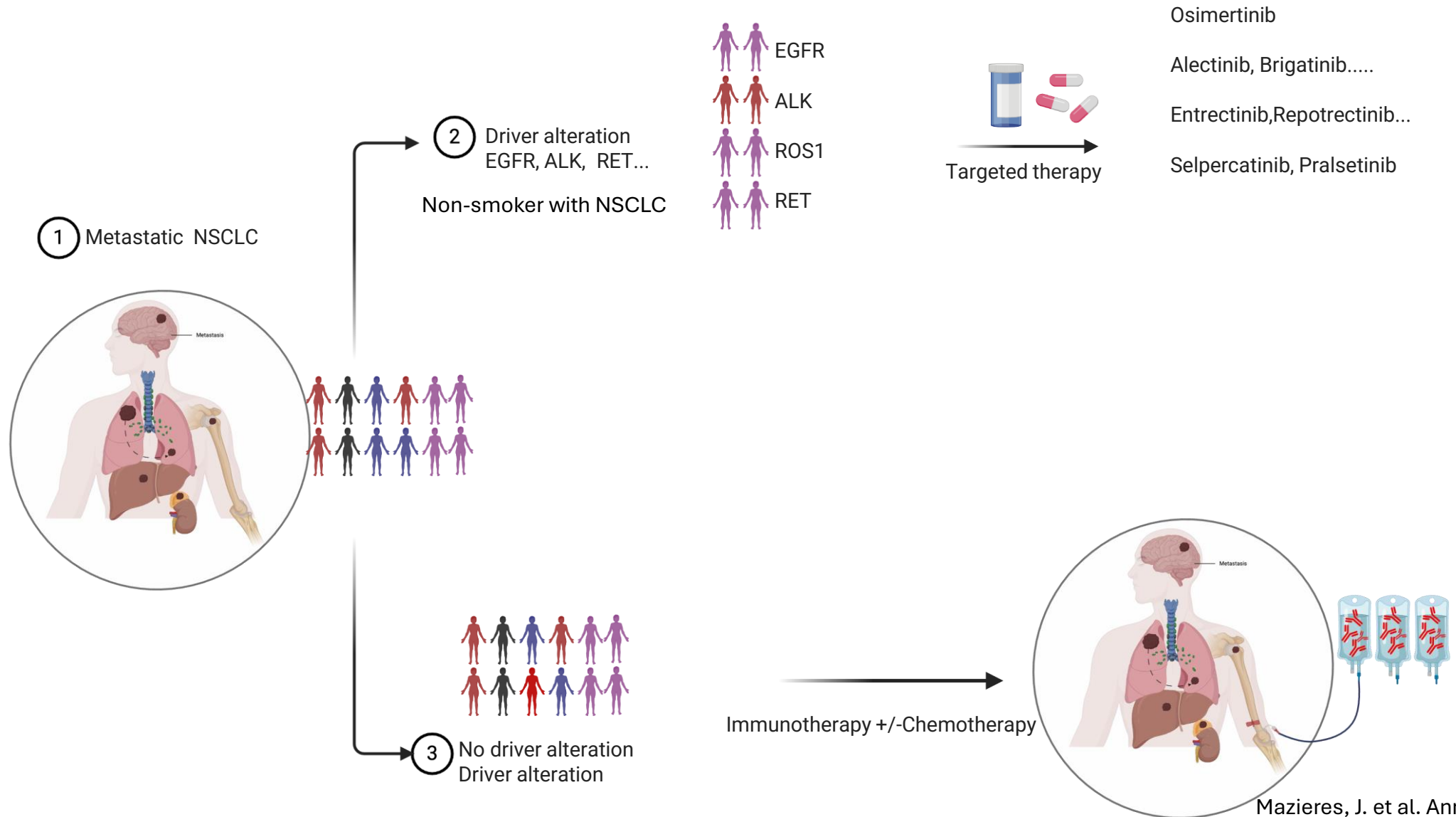
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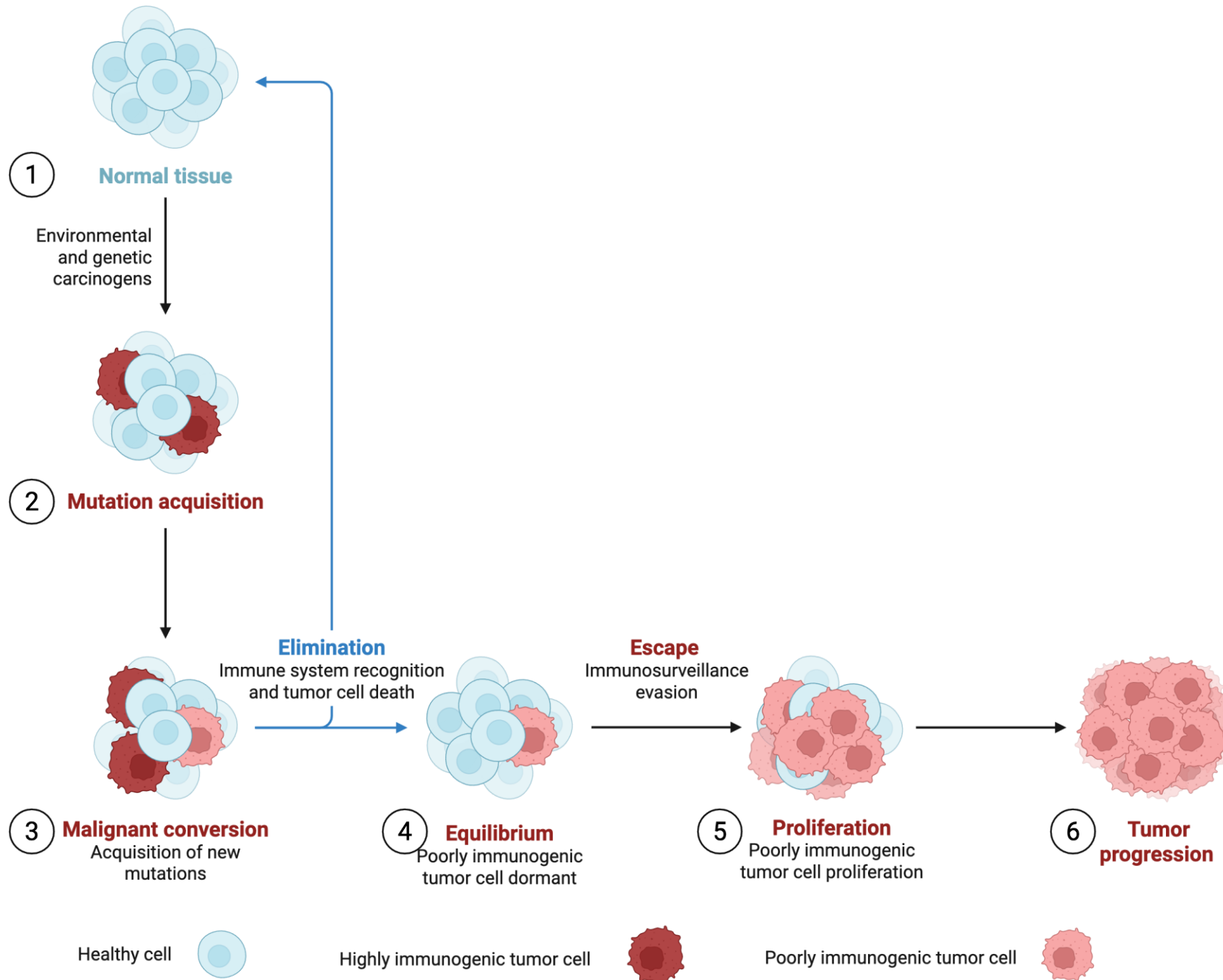


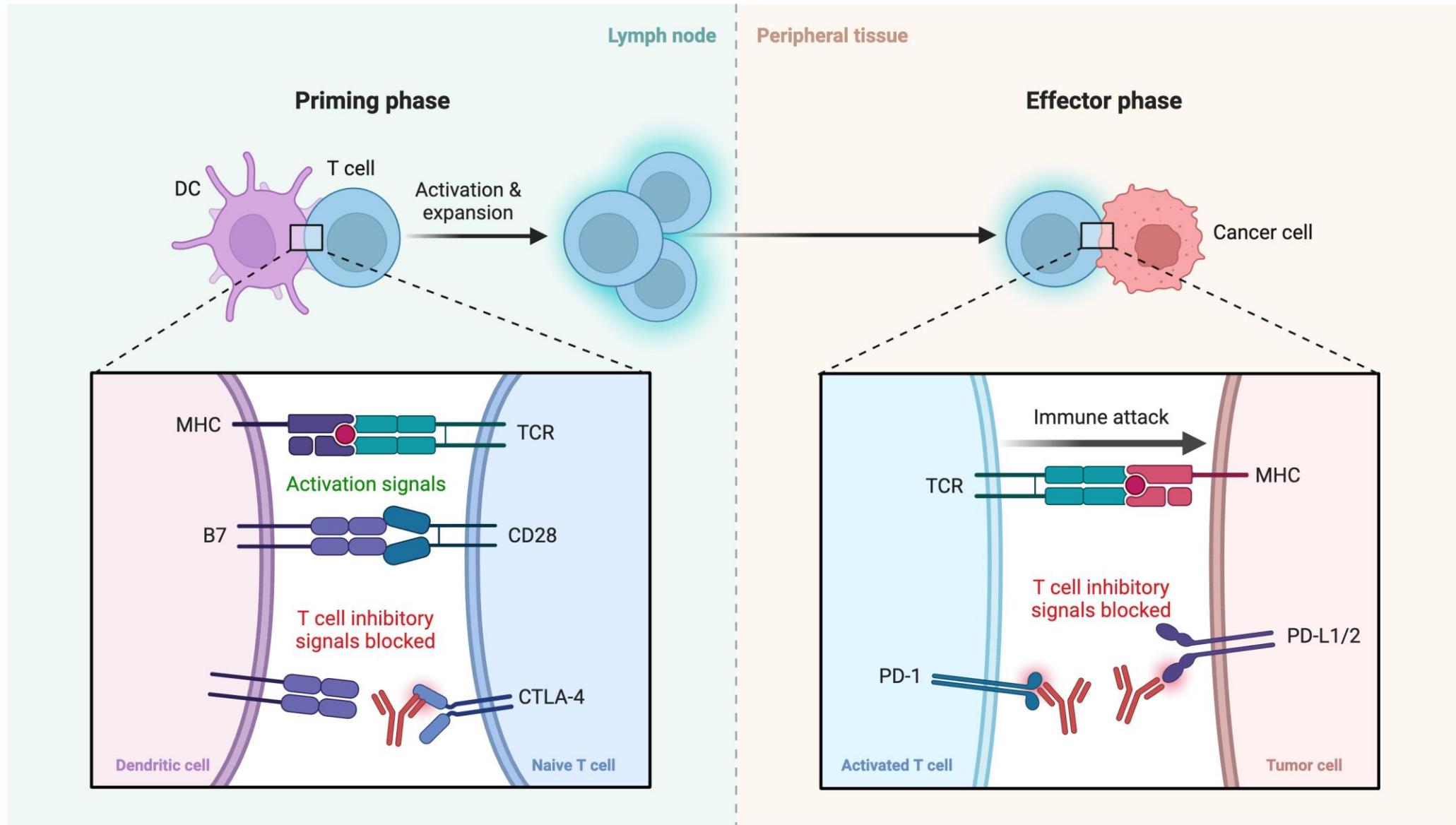
Syndrome cave

Dyspnée

Immunotherapy is not effective in NSCLC with actionable driver alterations

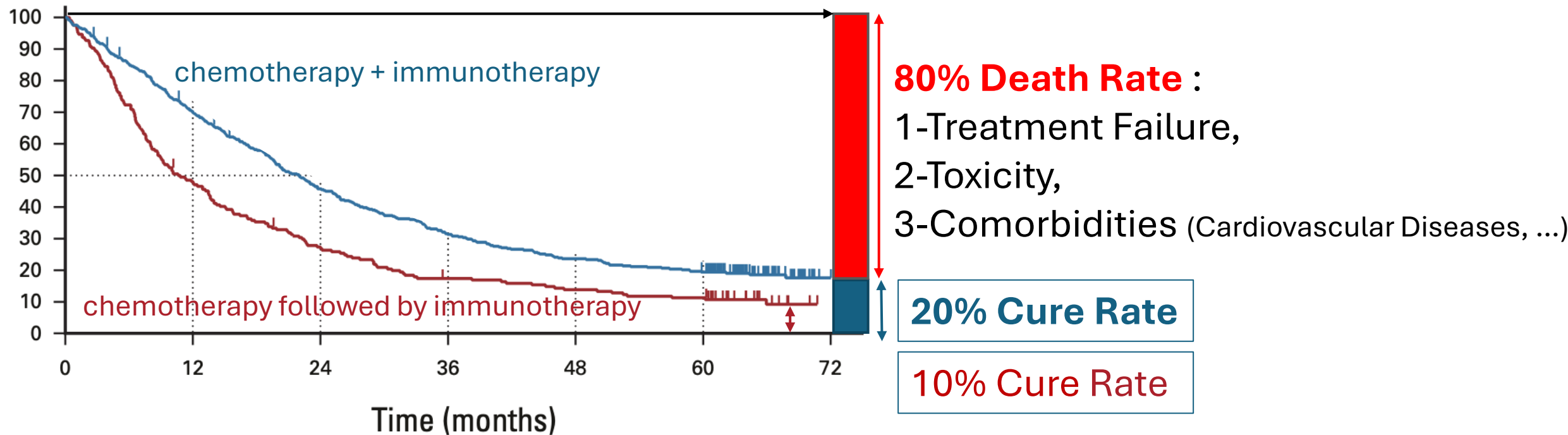




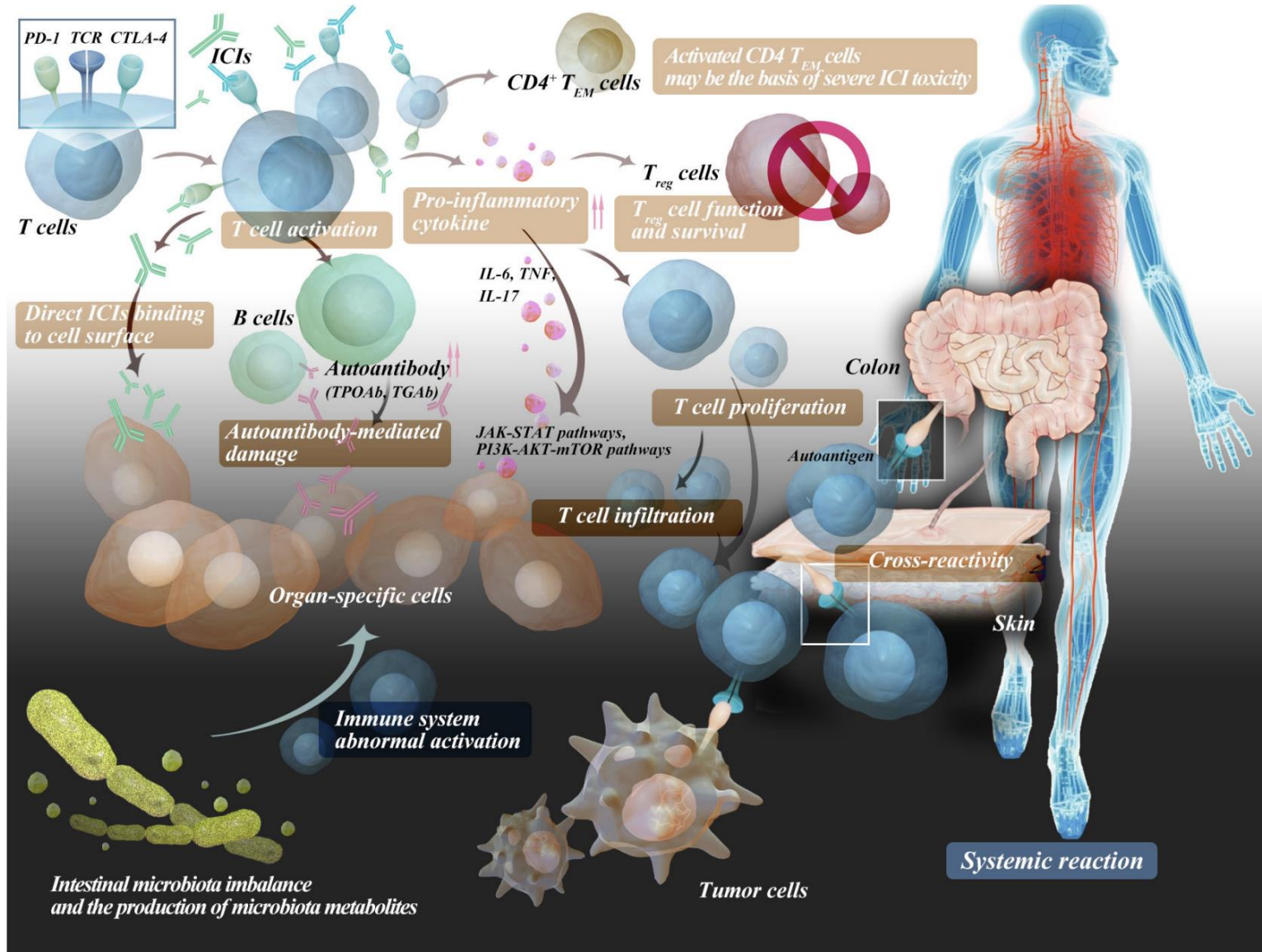


Metastatic NSCLC : Efficacy of Immunotherapy based backbone

Overall survival



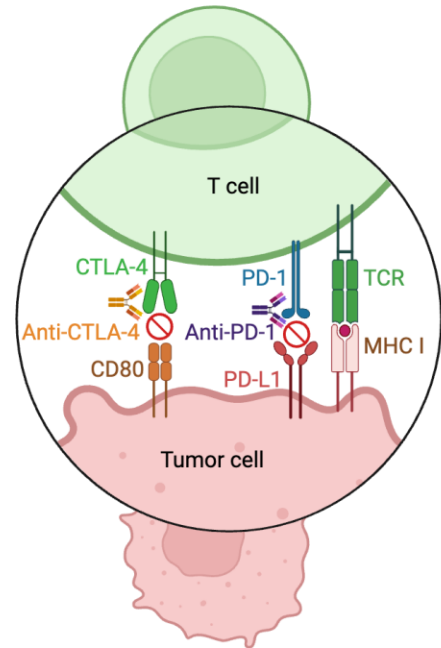
immune checkpoint inhibitors related adverses events



Adverse Events Associated With Immune Checkpoint Inhibitors

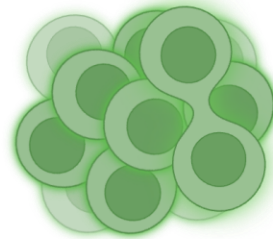
Tumor cells upregulate PD-L1 and CD80 to evade immune surveillance

PD-1 and **CTLA-4** are immune checkpoints expressed by T cells that inhibit immune responses; their interaction with tumor cells by its ligands causes immune evasion

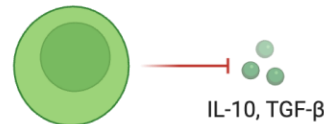


Immune checkpoint inhibitors like **anti-CTLA-4** and **anti-PD1** reverse this, activating immune response against tumor cells

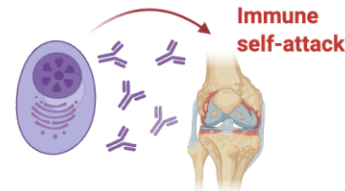
Immune checkpoint inhibitors can also excessively enhance the immune system



T cell
upregulation of proliferation and activation



T reg cell
downregulation and abrogates its functions



Plasma cell
humoral autoimmunity reaction

Due to this upregulation, immune cells widely infiltrate different organs, leading to diverse immune-related adverse events

Brain

- Encephalitis
- Meningitis
- Polyneuropathy

Eyes

- Uveitis
- Sjögren syndrome
- Conjunctivitis/blepharitis

Thyroid

- Hypo/hyperthyroidism
- Thyroiditis

Lungs

- Pneumonitis
- Pleuritis
- Sarcoid-like granulomatosis

Heart

- Myocarditis
- Pericarditis

Liver

- Hepatitis

Stomach

- Gastritis

Skin

- Skin rash
- Pruritus
- Vitiligo
- Psoriasis
- Stevens–Johnson syndrome

Intestine

- Colitis
- Enteritis

Vessels

- Anaemia
- Neutropenia
- Thrombocytopenia
- Acquired haemophilia
- Vasculitis

Joints

- Arthralgia
- Arthritis
- Myositis
- Dermatomyositis









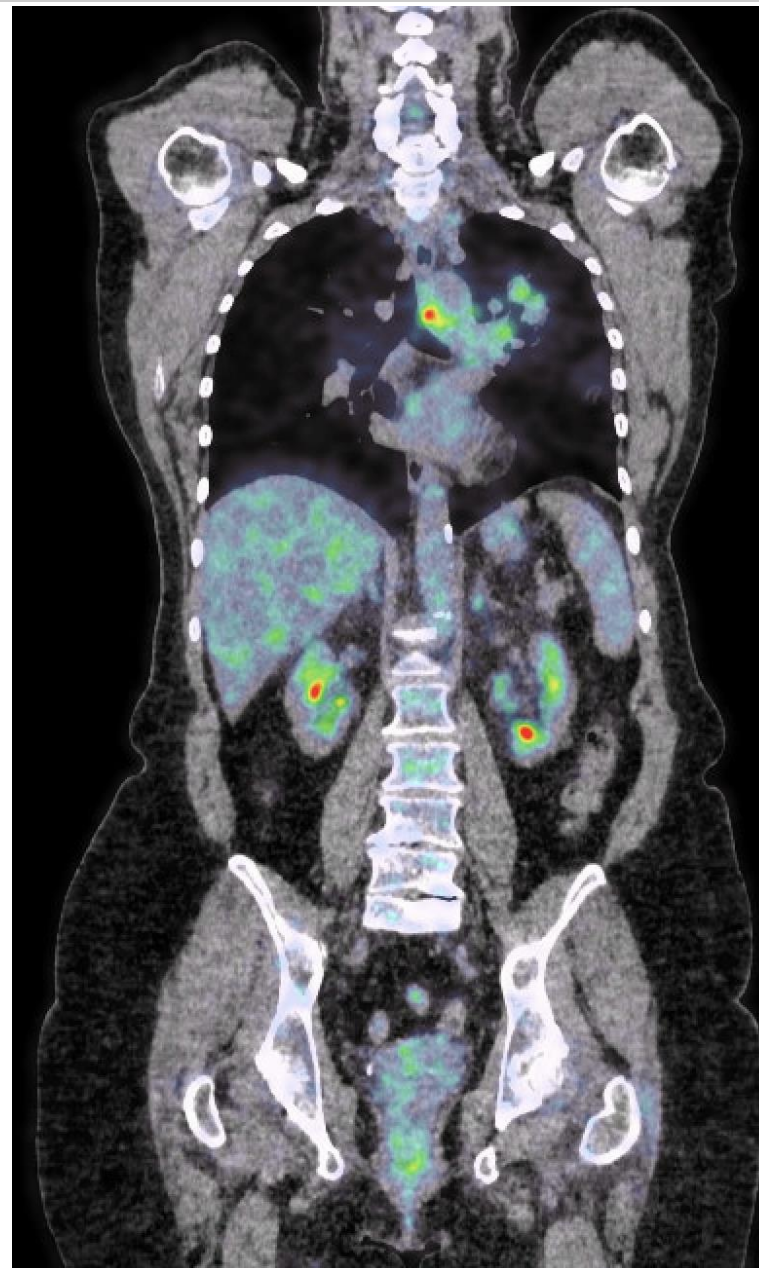
6/2025: Patiente 65 ans

avec atcd d'asthme allergique.

Consultation récente pour reprise de dossier et tableau de bronchite asthmatiforme il y a quelques semaines avec sibilances base droite traitée symptomatiquement. Actuellement symptômes résolus, patiente revue sans aucun symptôme respiratoire ni général (pas d'hémoptysie ni dyspnée ni AEG ni symptômes B) mais réalisation d'une Rx de principe avec lésion LSG puis mise au point par CT ce 18/06:

Quel élément simple dans l'anamnèse peut déjà orienter le type de cancer du poumon dont souffre le patient ?

6/2025: Patiente 65 ans



6/2025: Patiente 65 ans

II/ Méthodologie

- Extraction : d'ADN à partir de lames FFPE (Formalin-Fixed, Paraffin-Embedded) après macrodissection des zones tumorale;
- Panel : Capture Custom Panel TE-98036185 hg38 (Twist).

ABL1	BRCA1	CTNNB1	FLI1	KIT	NTRK2	PTEN	SDHD
AKT1	BRCA2	EGFR (HER1-ERBB1)	FLT3	KRAS	NTRK3	RAC1	SMARCA4
AKT2	BRIP1	ERBB2 (HER2-NEU)	FOXL2	MAP2K1 (MEK1)	PALB2	RAD51B	SMARCB1
AKT3	CCND1	ERBB3 (HER3)	GATA3	MAP2K2	PBRM1	RAD51C	SMO
ALK	CCNE1	ERBB4	GNA11	MAP3K3	PDGFB	RAD51D	STK11 (LKB1)
APC	CD274	ERCC2	GNA14	MDM2	PDGFRA	RAD54L	SUFU
AR	CDH1	ESR1	GNAQ	MET	PDGFRB	RAF1	TEK
ARAF	CDK12	EZH2	GNAS	MRE11A	PIK3CA	RB1	TERT promoter
ARID1A	CDK4	FANCA	H3F3A	MTOR	PIK3R1	RET	TP53
ATM	CDK6	FANCL	HIST1H3B	MYC	PIK3R2	RICTOR	TSC1
ATR	CDKN2A	FBXW7	HIST1H3C	NF1	POLD1	RNF43	TSC2
ATRX	CHEK1	FGFR1	HRAS	NOTCH1	POLE	ROS1	VHL
BARD1	CHEK2	FGFR2	IDH1	NRAS	PPP2R2A	SDHA	/
BCOR	CIC	FGFR3	IDH2	NRG1	PRDM6	SDHB	/
BRAF	CSF1R	FGFR4	KDM6A	NTRK1	PTCH1	SDHC	/

IV/ Conclusion

- Présence de cellules porteuses du variant p.(Gly12Asp) (p.(G12D)) dans le gène **KRAS**.
- Ce variant est classé biologiquement comme pathogénique et est de **signification clinique pronostique avérée dans cette pathologie**.
- Pour information : D'autres variants ont été identifiés dans d'autres gènes. Les détails de ces variants sont repris dans le tableau des résultats et le point annexe.

III/ Méthodologie

- Extraction : d'ARN à partir de lames FFPE (Formalin-Fixed, Paraffin-Embedded) après macrodissection des zones tumorales, ou au d
- Panel : FusionPlex® Lung (Archer®).

Gène	Exons testés	Transcript	Gène	Exons testés	Transcript
ALK	2,4,6,10,16,17,18,19,20,21,22,23,26	NM_004304	NRG1	1,8	NM_013957
BRAF	1,3,7,8,10,13	NM_004333	NRG1	1,2,3,4,6	NM_004495
EGFR	1,7,8,9,16,19,20,24,25	NM_005228	NTRK1	2,4,6,8,10,11,12,13	NM_002529
EGFR	Exon 2-7 Skipping (EGFRvIII)	NM_005228	NTRK2	5,7,9,11,12,13,14,15,16,17	NM_006180
FGFR1	2,3,4,5,6,7,8,9,10,11,12,17	NM_015850	NTRK3	4,7,10,12,13,14,15,16	NM_002530
FGFR2	2,5,7,8,9,10,16,17	NM_000141	NTRK3	15	NM_001007156
FGFR3	3,5,8,9,10,16,17,18	NM_000142	RET	2,4,6,8,9,10,11,12,13,14	NM_020630
MET	2,4,5,6,13,14,15,16,17,21	NM_000245	ROS1	2,4,7,31,32,33,34,35,36,37	NM_002944
MET	Exon 14 Skipping	NM_000245			

III/ Résultats

- Evaluation de l'échantillon :
- Quantité de matériel / ARN : Adéquate
- Qualité du séquençage : Optimale

Fusion identifiée :

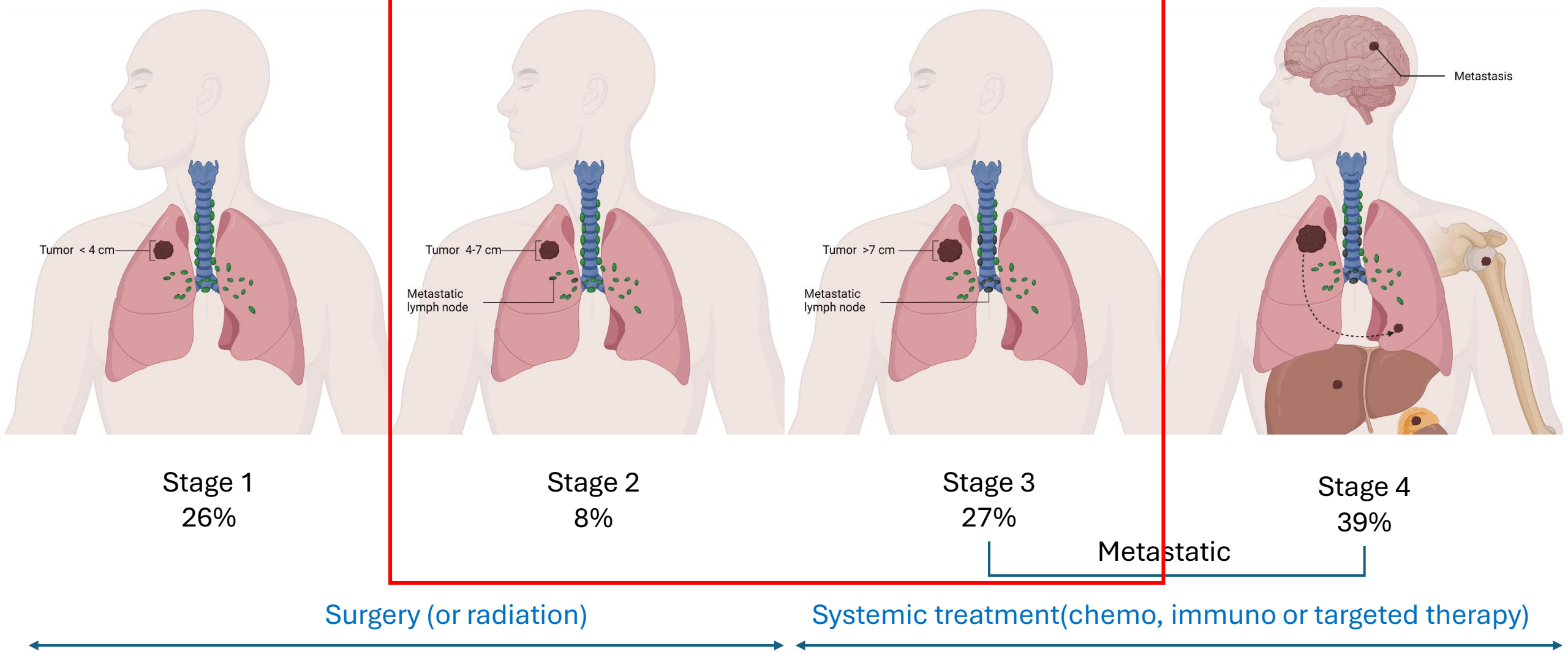
Fusion Gene	Gene A Gene B	Transcript ID A Transcript ID B	Exon A Exon B	Breakpoint A Breakpoint B	Classification Biologique*
/					

* selon le principe de classification recommandé par Sciensano et Belac

IV/ Conclusion

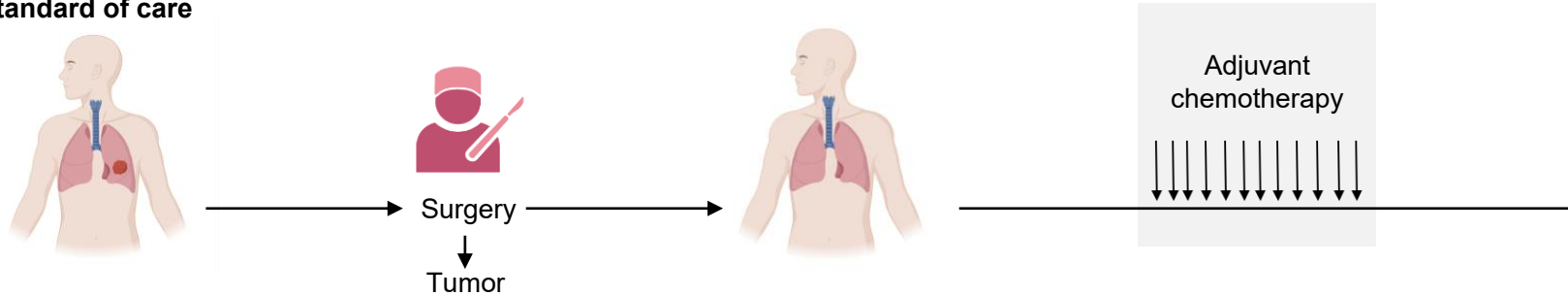
- Absence de transcrit de fusion détecté pour les gènes analysés.
- Pour information : la mutation identifiée précédemment dans le gène KRAS p.(Gly12Asp) a été retrouvée via ce panel FusionPlex Lung (Archer).

Treatment of lung cancer depends on the disease stage at diagnosis

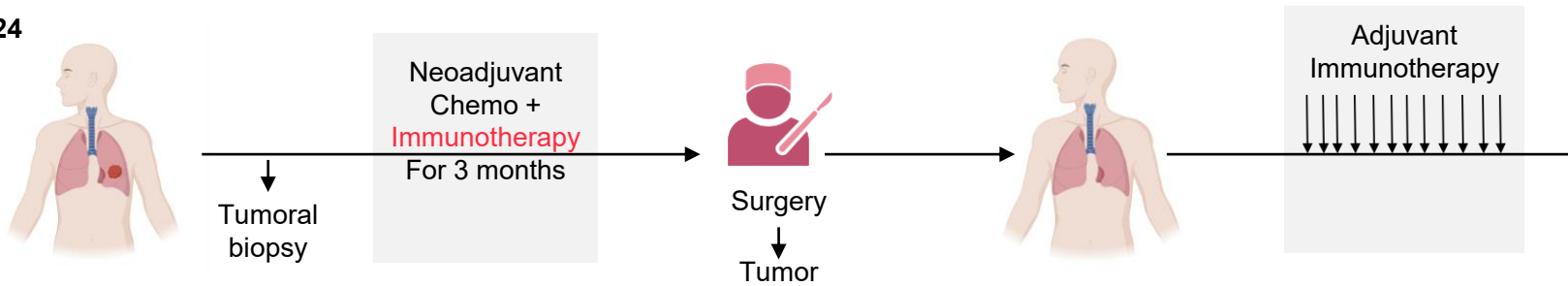


Neoadjuvant chemoimmunotherapy for stage II-III NSCLC patients

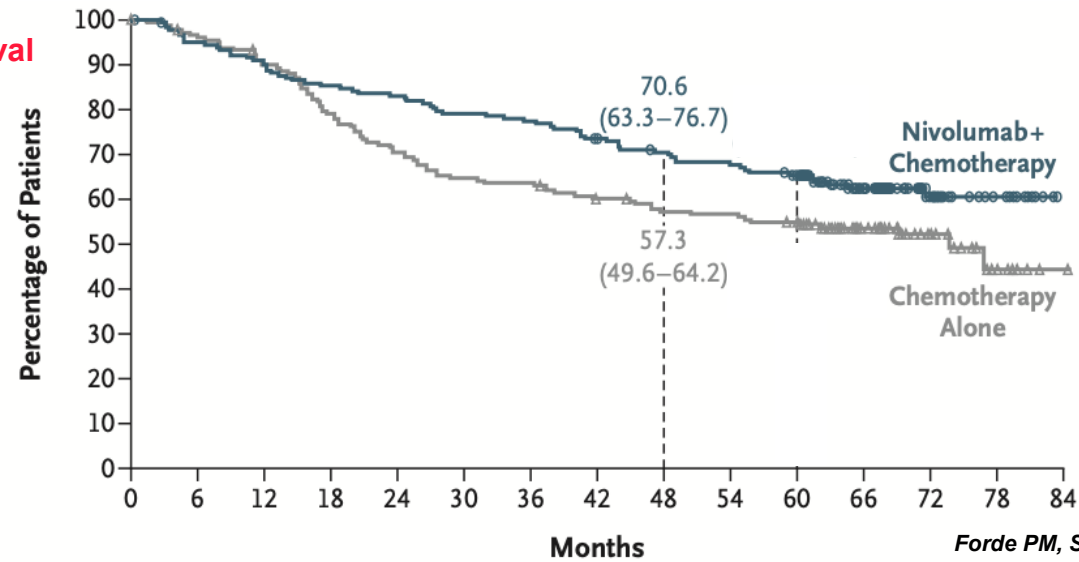
Former standard of care



Since 2024

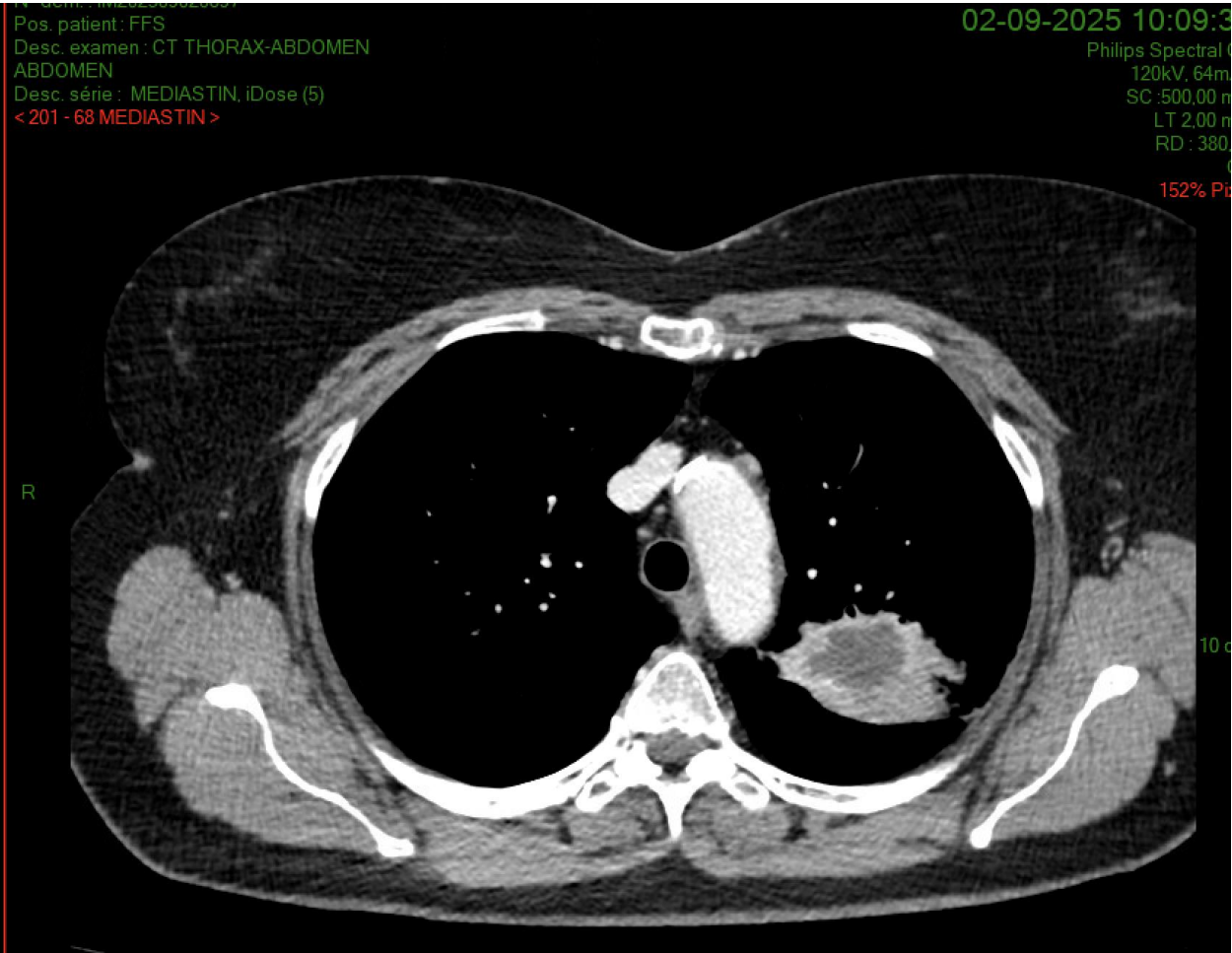
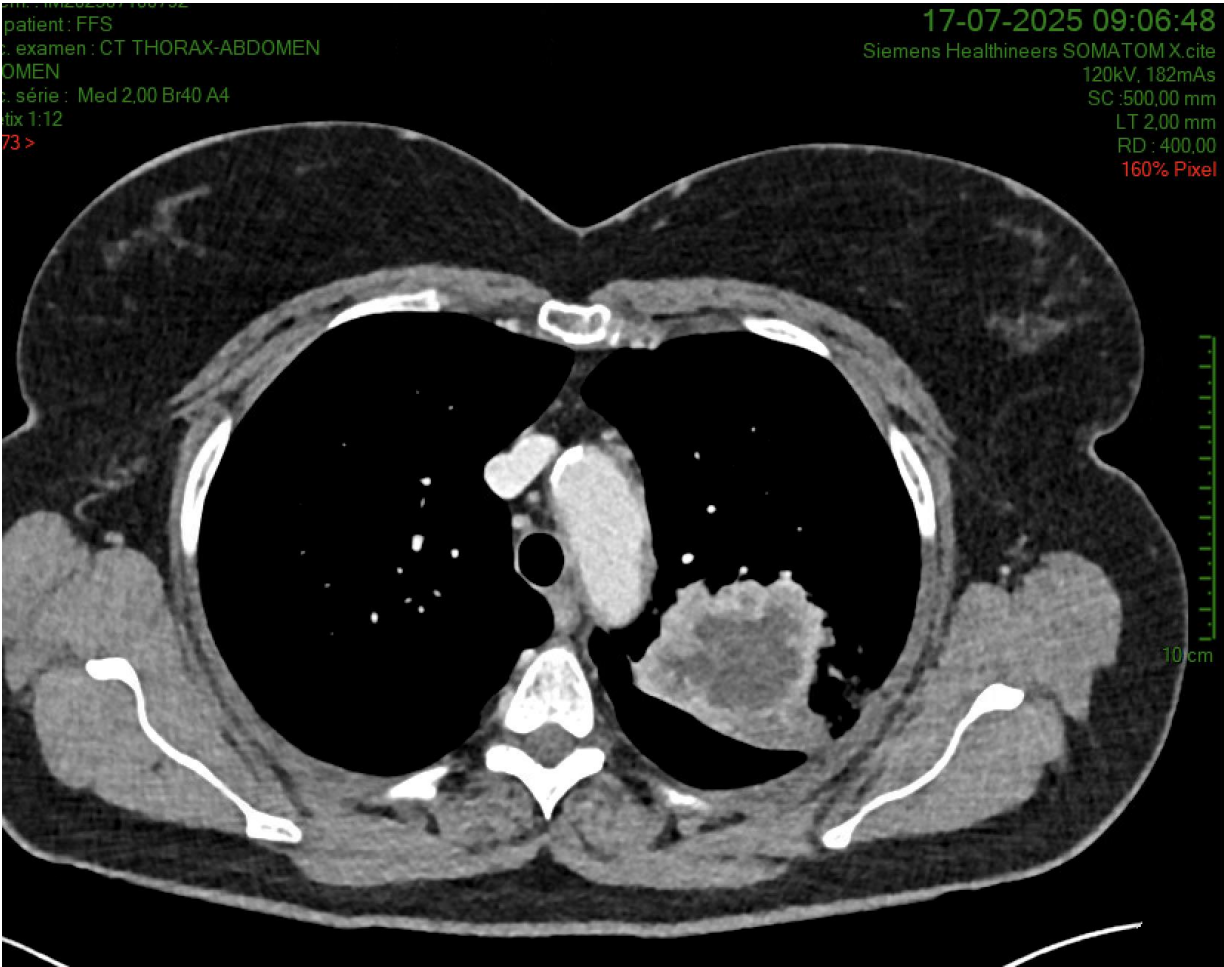


Overall survival

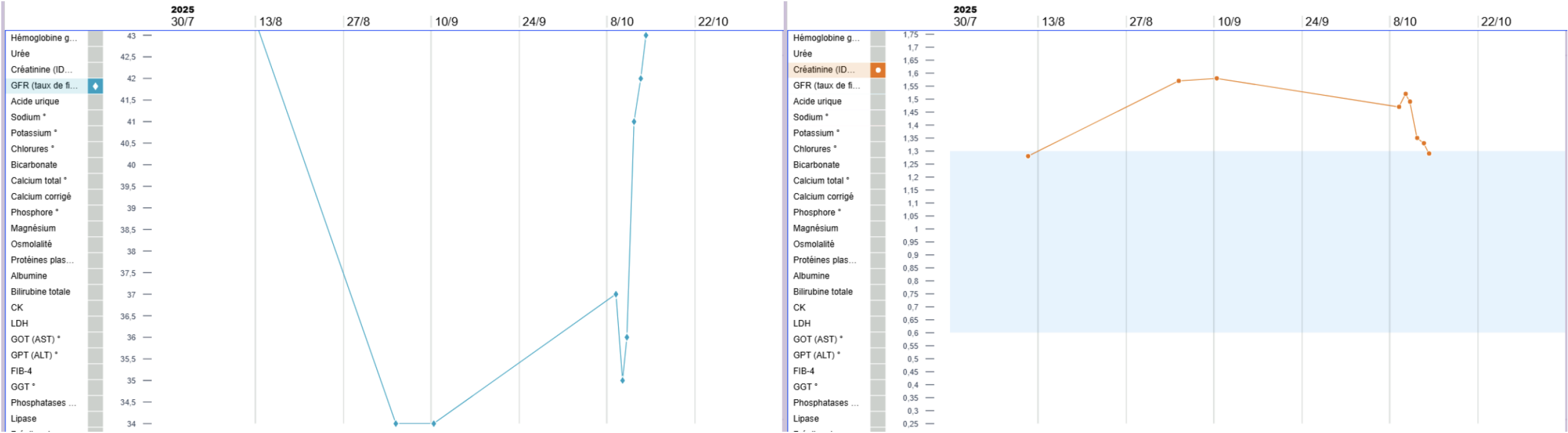


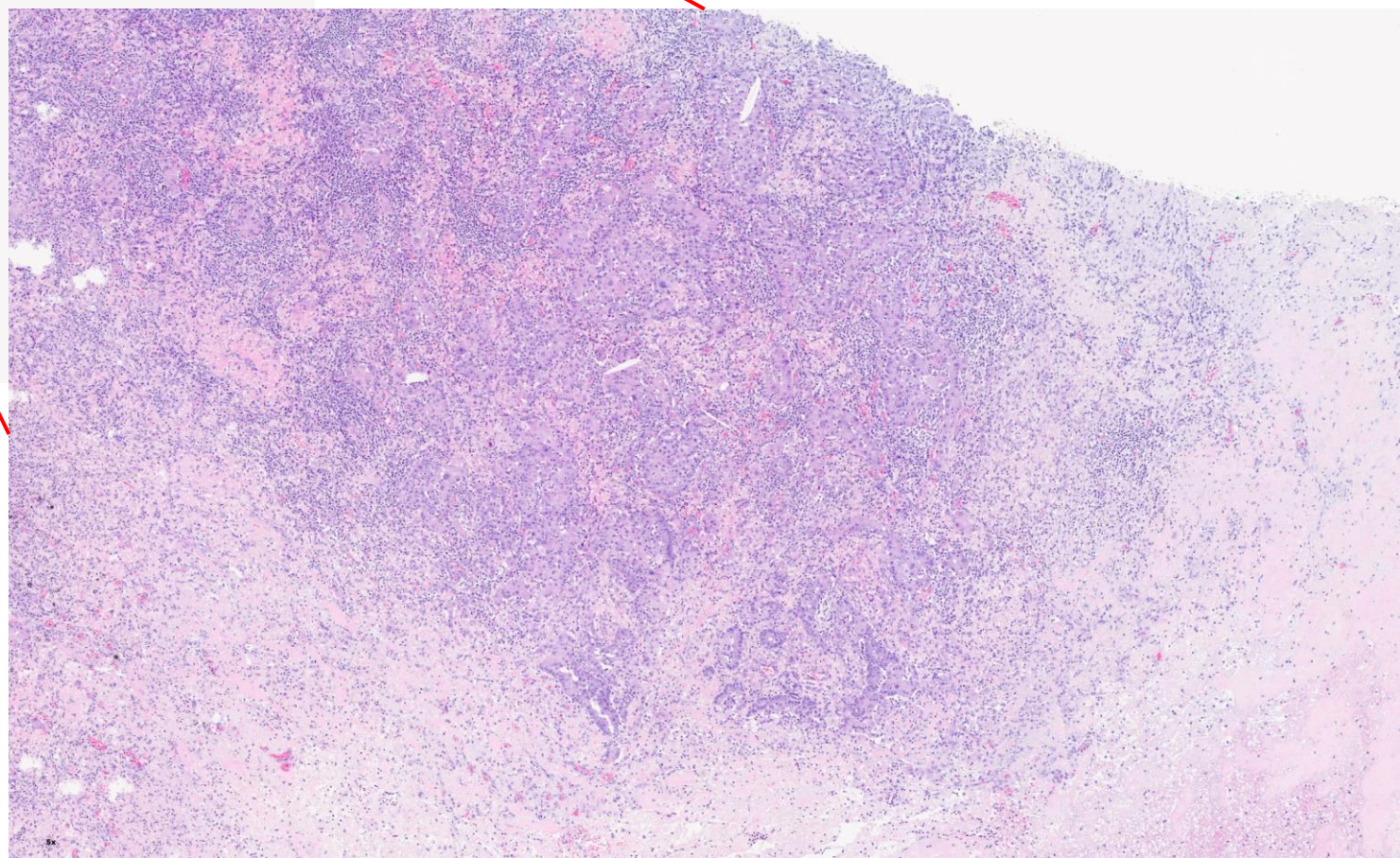
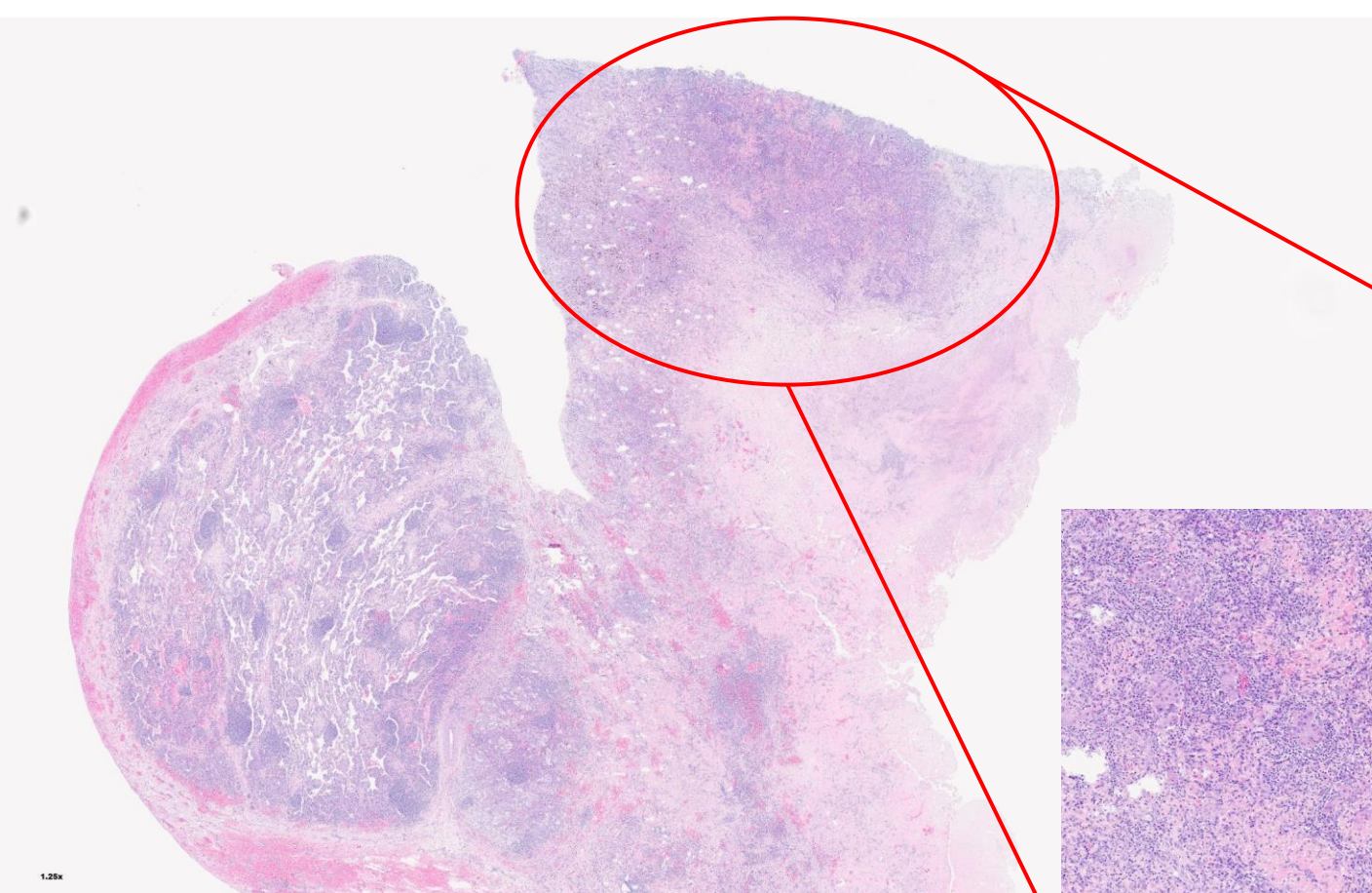
Forde PM, Spicer J, et al., NEJM, 2025

6/2025: Patiente 65 ans



6/2025: Patiente 65 ans





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The patients!



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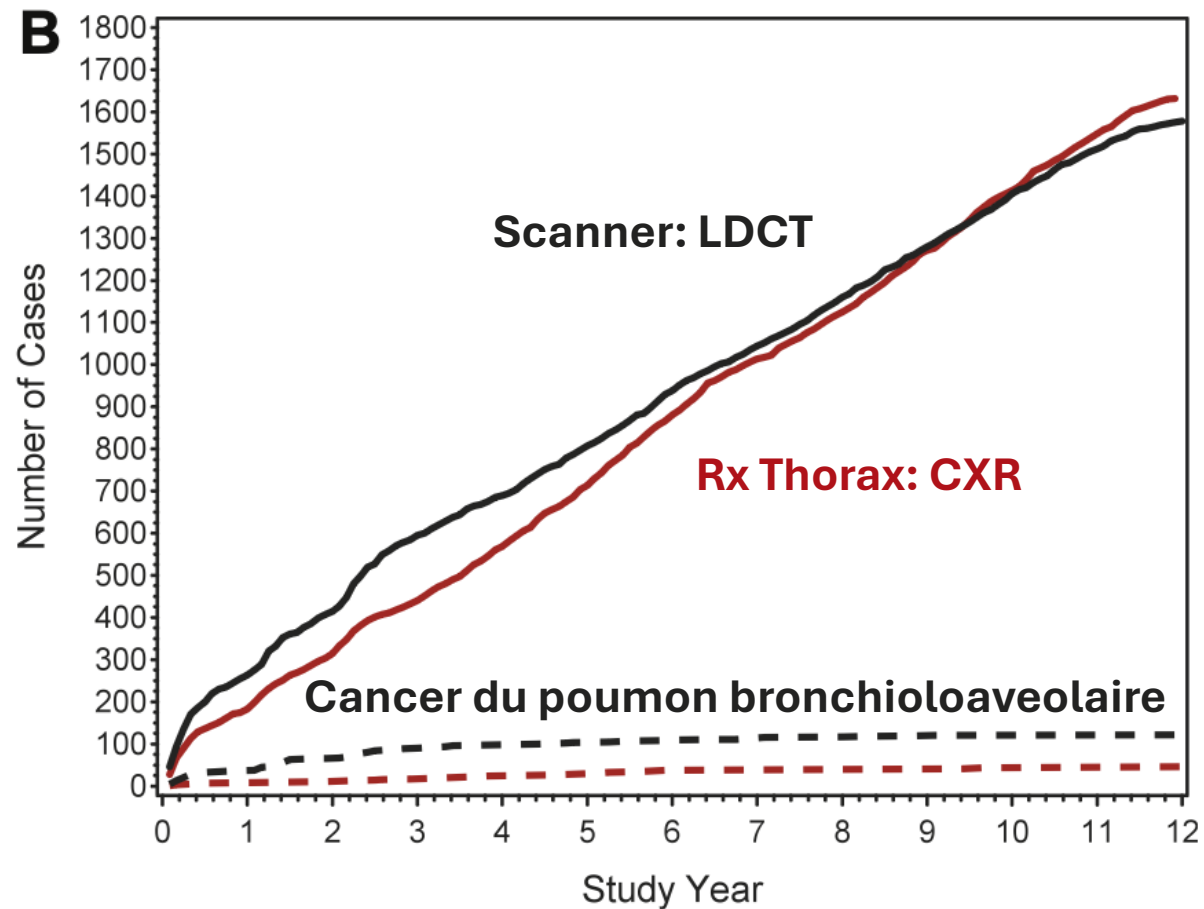
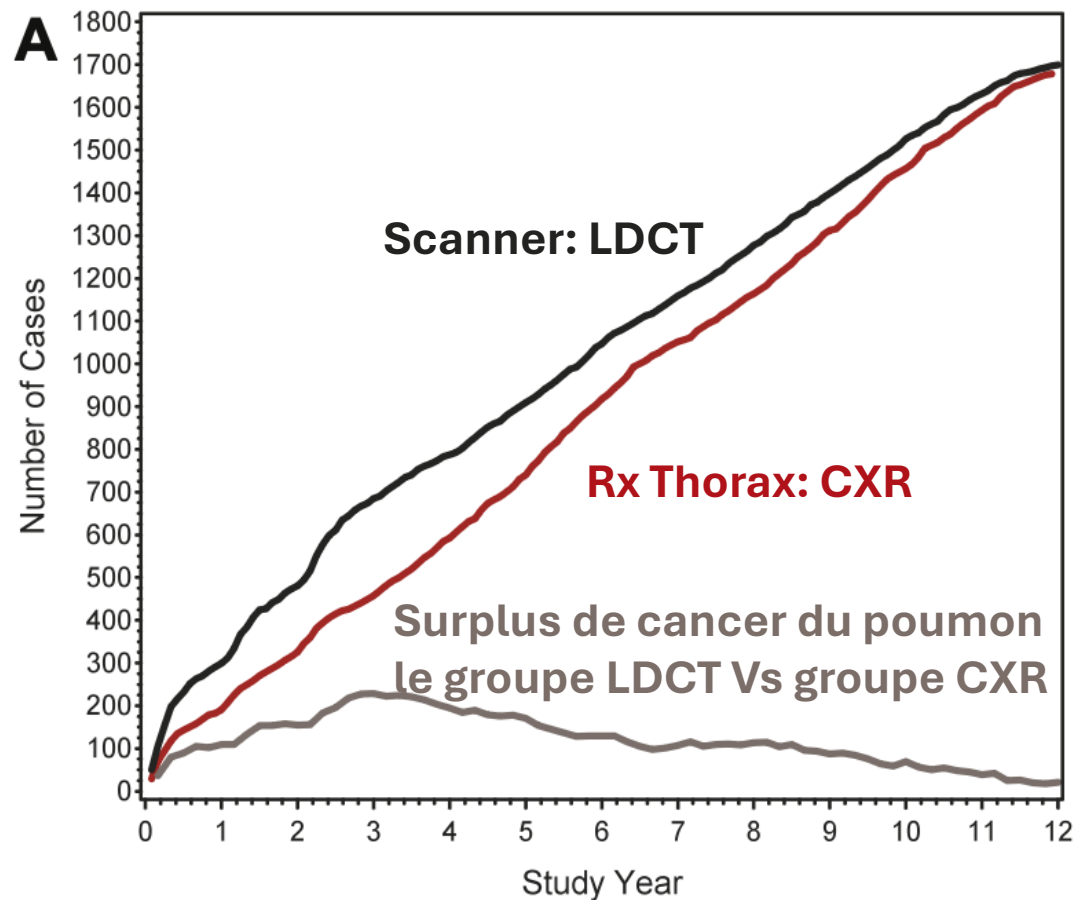
B. Plichon

I. Beaufay

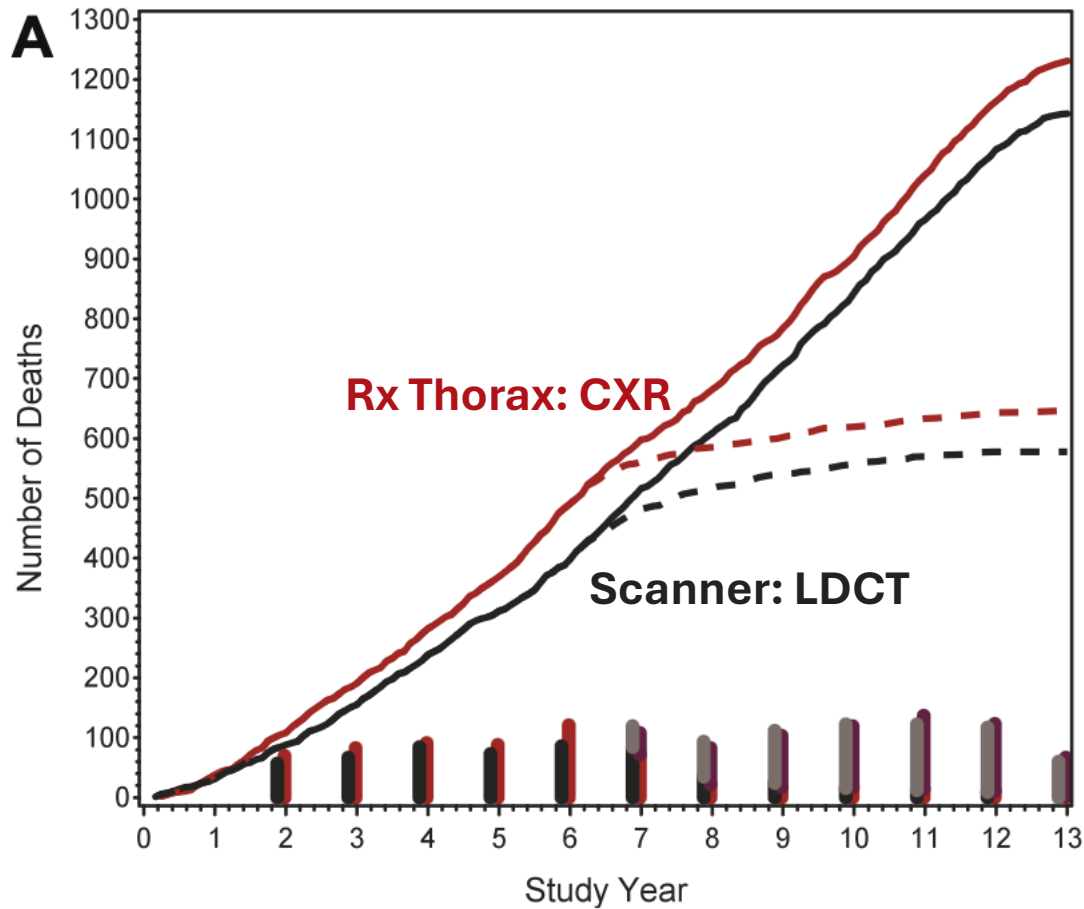
F. Adriaens

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Is lung cancer screening the way forward?

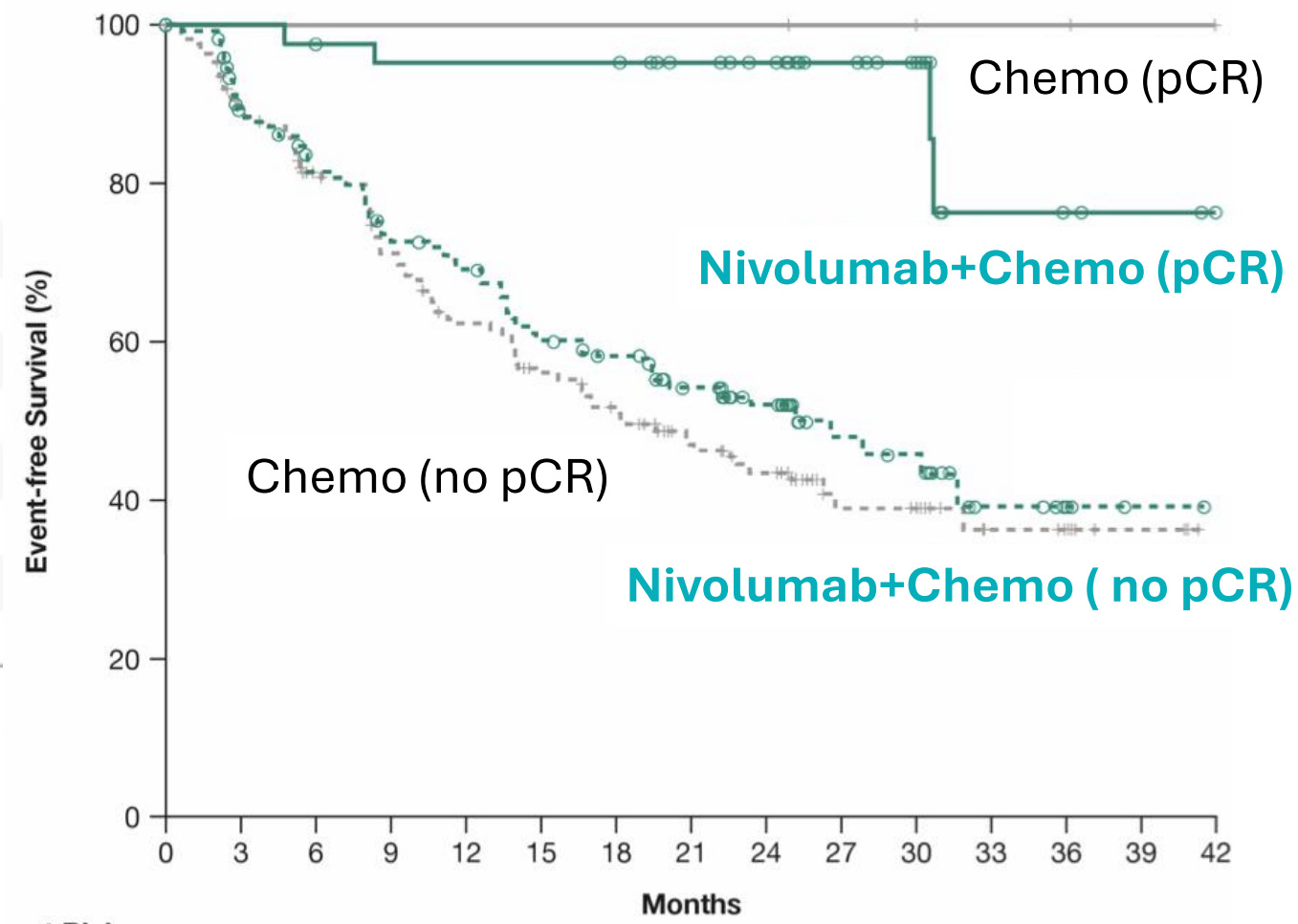
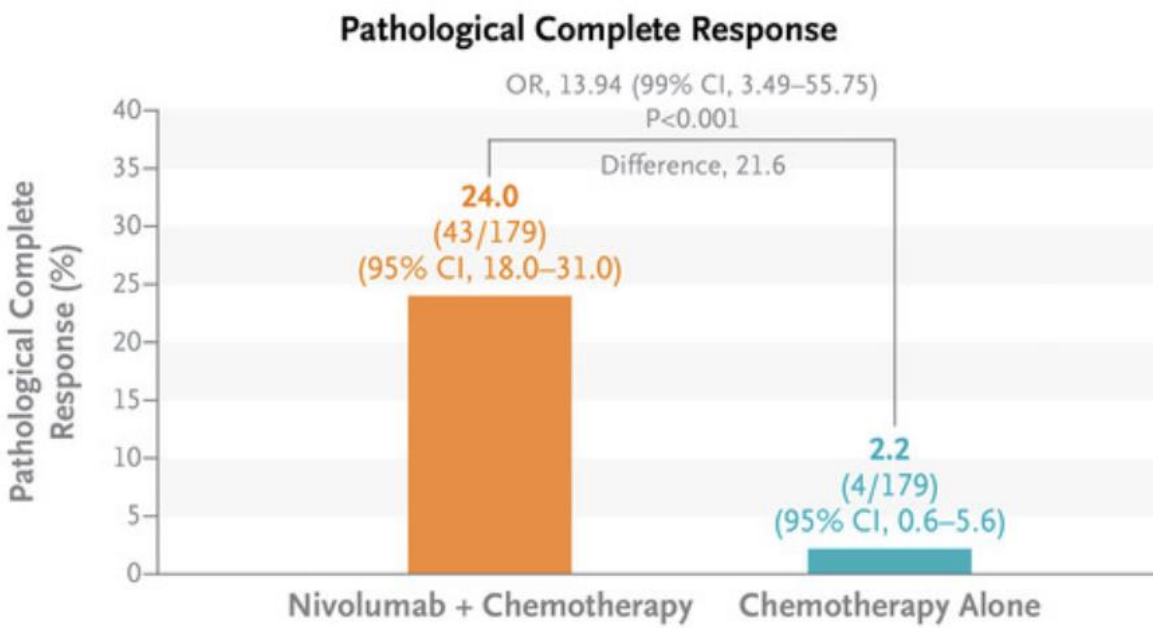


Is lung cancer screening the way forward?



Outcome	LDCT, n (per 1000 subjects)	CXR, n (per 1000 subjects)	Difference across Arms per 1000 Subjects (95% CI) (CXR Minus LDCT)	RR (95% CI)	p Value Interaction ^a
All lung cancer deaths					
All subjects	1147 (42.9)	1236 (46.2)	3.3 (-0.2 to 6.8)	0.92 (0.85-1.00)	
Men	733 (46.5)	755 (47.9)	1.4 (-3.3 to 6.1)	0.97 (0.87-1.07)	0.17
Women	414 (37.8)	481 (43.9)	6.1 (0.8-11.3)	0.86 (0.75-0.98)	
Current smoker	724 (56.3)	818 (63.4)	7.1 (1.3-12.9)	0.88 (0.80-0.97)	0.12
Former smoker	423 (30.5)	418 (30.2)	-0.3 (-4.3 to 3.8)	1.01 (0.88-1.15)	
Age 55-64 y at randomization	641 (32.7)	739 (37.7)	5.0 (1.3-8.6)	0.86 (0.78-0.96)	0.051
Age 65-74 y at randomization	506 (71.2)	497 (69.9)	-1.3 (-9.7 to 7.2)	1.01 (0.90-1.15)	
Overall mortality (all subjects)	5253 (196.6)	5366 (200.7)	4.2 (-2.6 to 10.9)	0.97 (0.94-1.01)	
Overall mortality excluding lung cancer deaths (all subjects)	4106 (153.7)	4130 (154.5)	0.9 (-5.3 to 7.0)	0.99 (0.95-1.03)	

Immunotherapy in resectable advanced (stage 2-3) NSCLC



Niveaux de preuve /recommandations

Levels of evidence in research

There are 5 levels of evidence in the hierarchy of evidence – being 1 (or in some cases A) for strong and high-quality evidence and 5 (or E) for evidence with effectiveness not established.

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LEVEL 1 (higher quality of evidence)

High quality randomized trial or prospective study; testing of previously developed diagnostic criteria on consecutive patients; sensible costs and alternatives; values obtained from many studies with multiway sensitivity analyses; systematic review of Level I RCTs and Level I studies.

LEVEL 2

Lesser quality RCT; prospective comparative study; retrospective study; untreated controls from an RCT; lesser quality prospective study; development of diagnostic criteria on consecutive patients; sensible costs and alternatives; values obtained from limited studies; with multiway sensitivity analyses; systematic review of Level II studies or Level I studies with inconsistent results.

LEVEL 3

Case control study (therapeutic and prognostic studies); retrospective comparative study; study of nonconsecutive patients without consistently applied reference “gold” standard; analyses based on limited alternatives and costs and poor estimates; systematic review of Level III studies.

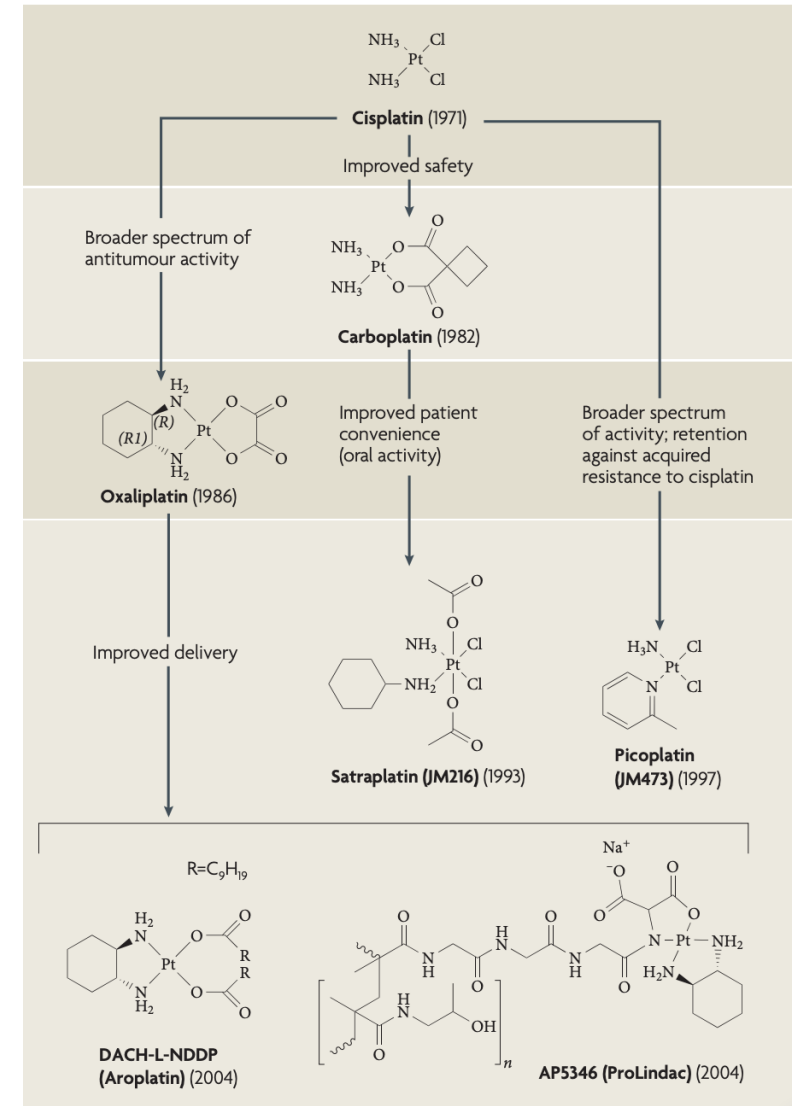
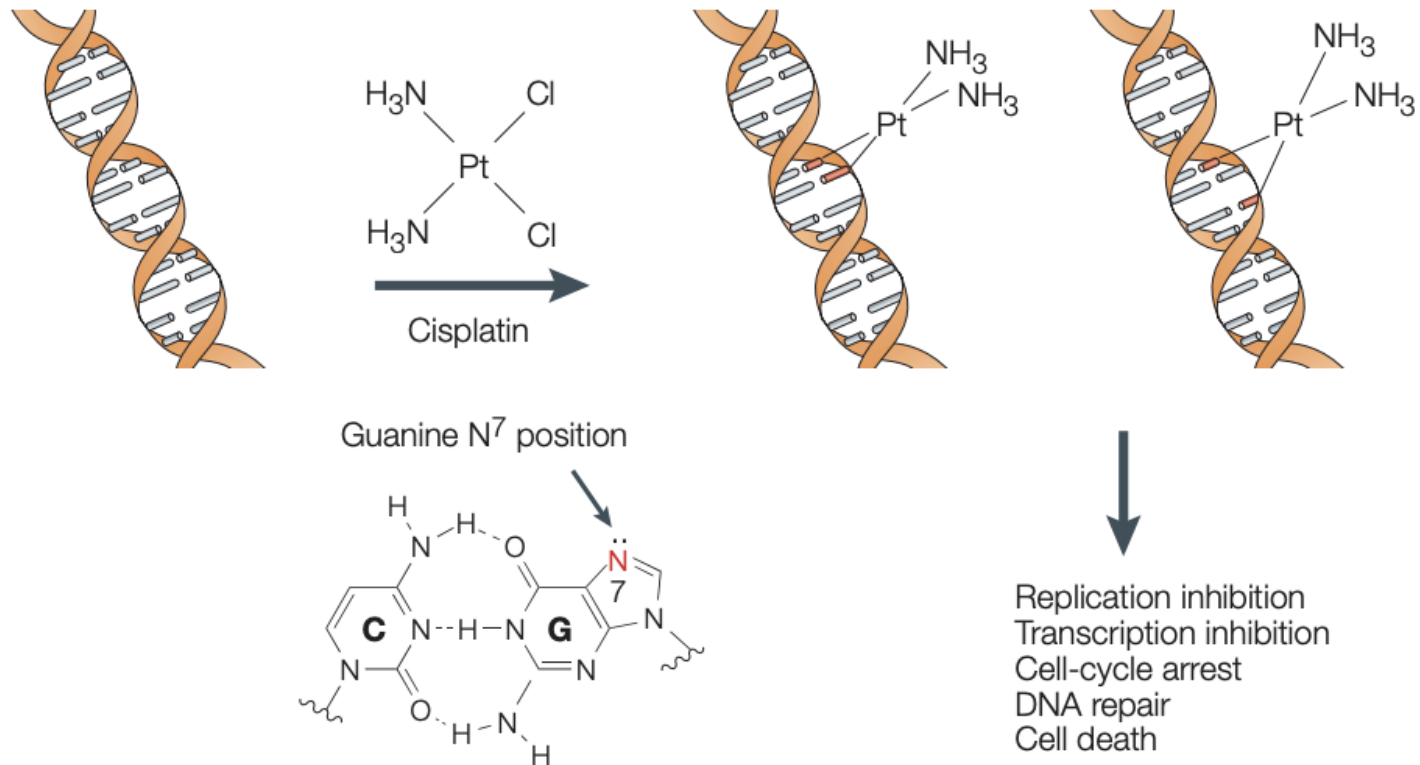
LEVEL 4

Case series; case control study (diagnostic studies); poor reference standard; analyses with no sensitivity analyses.

LEVEL 5 (lower quality of evidence)

Expert opinion.

All roads lead to Platinum doublets in NSCLC : similar survival, choice driven by tolerance



Dong Wang et al. – Nature review 2005

Kelland, L et al. – Nature reviews cancer 2007