

# Traitements péri-opératoire / radio-chimiothérapie concomitante

Vendredi 21/10/2025

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**Angoulême**

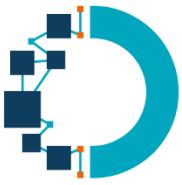
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**Pr THUMEREL, CHU Bordeaux**

**Dr GARCIA, CHU Poitiers**

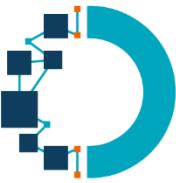
**Dr DENIZOT, CHU Limoges**

5<sup>ème</sup> rencontre oncologie thoracique de Nouvelle Aquitaine



## Liens d'intérêts

- MT: Aucun
- CG: Aucun
- AD: Aucun

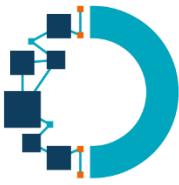


# Evolution classification TNM

## TNM8 – Stade III

- **N1 – Atteinte N+ péri bronchique et/ou hilaire homolatérale**
- **N2 – Atteinte N médiastinale homolatérale et/ou sous carénaire**
- **N3 – Atteinte N controlatérale et/ou sus-claviculaire**

	N0	N1	N2	N3
T1a	IA-1	IIB	IIIA	IIIB
T1b	IA-2	IIB	IIIA	IIIB
T1c	IA-3	IIB	IIIA	IIIB
T2a	IB	IIB	IIIA	IIIB
T2b	IIA	IIB	IIIA	IIIB
T3	IIB	IIIA	IIIB	IIIC
T4	IIIA	IIIA	IIIB	IIIC

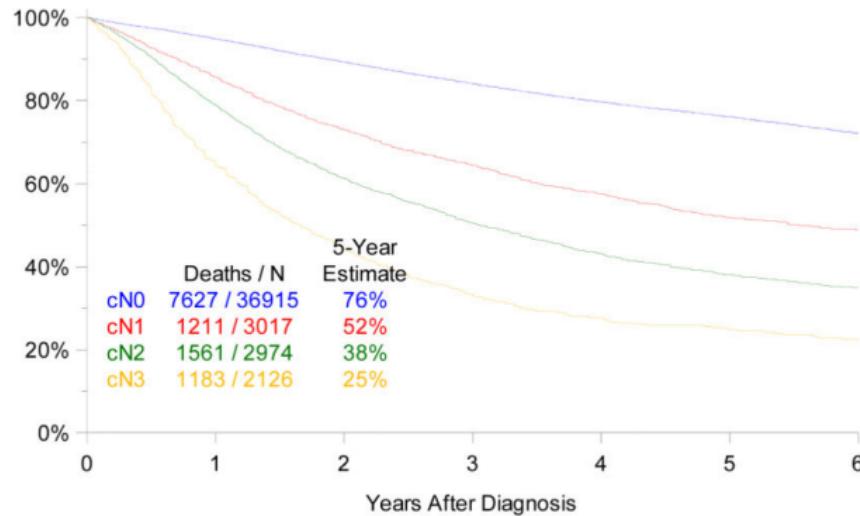


# Evolution classification TNM

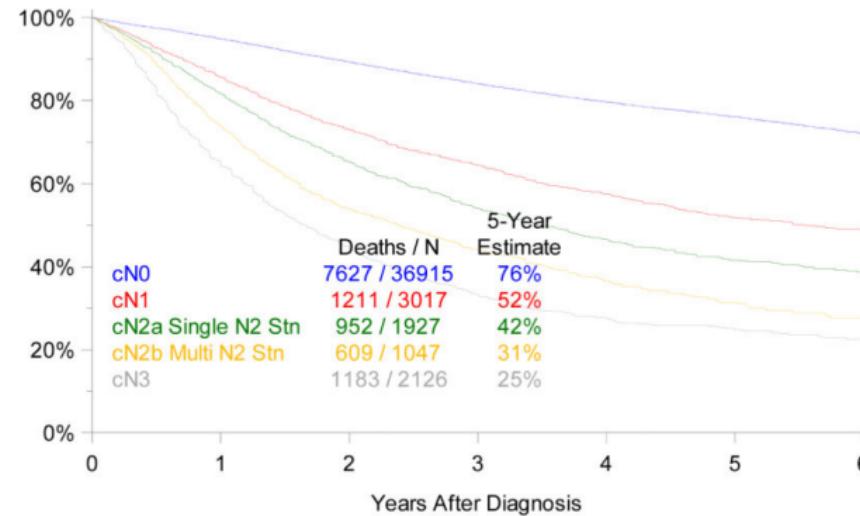
**Analyse IASLC sur 87 000 patients**

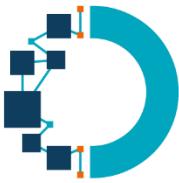
- **Population N2 hétérogène**

a1) Current 8th edition cN



a2) Proposed 9th edition cN



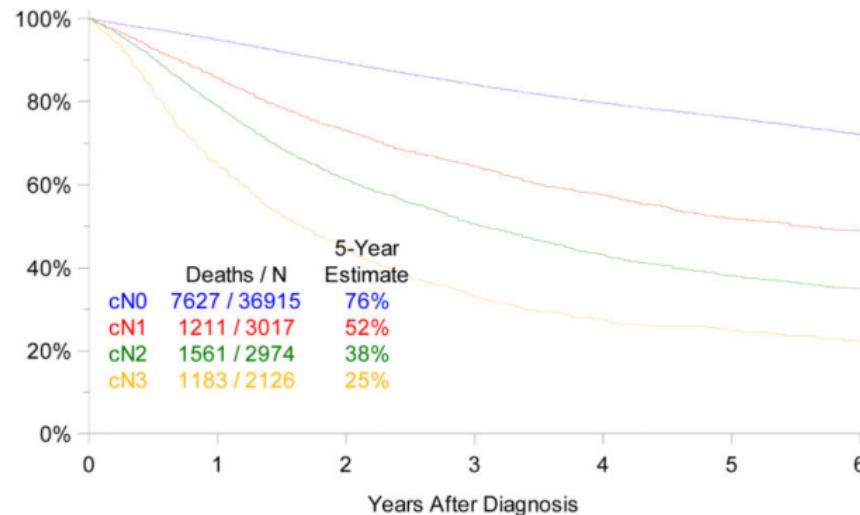


# Evolution classification TNM

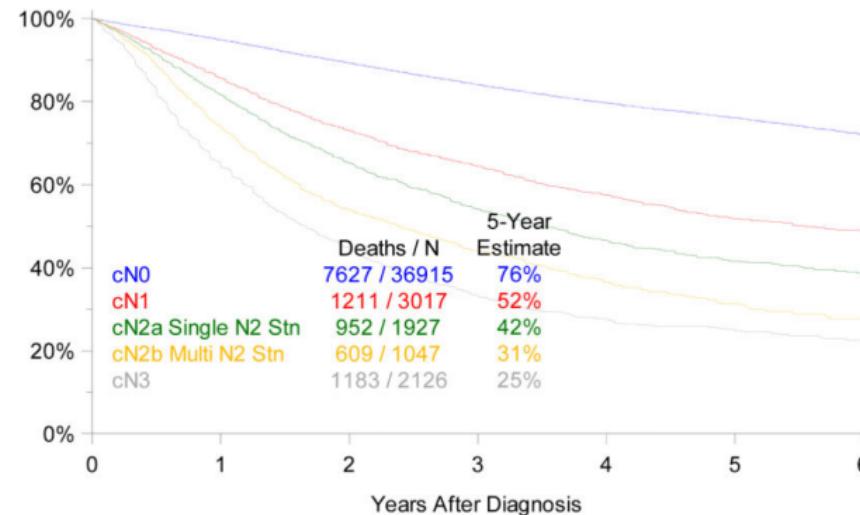
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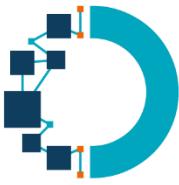
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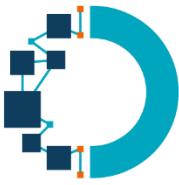
a2) Proposed 9th edition cN





# Evolution classification TNM

	TNM8				TNM 9				
	N0	N1	N2	N3	N0	N1	N2a	N2b	N3
T1a	IA-1	IIB	IIIA	IIIB	IA-1	IIA	IIB	IIIA	IIIB
T1b	IA-2	IIB	IIIA	IIIB	IA-2	IIA	IIB	IIIA	IIIB
T1c	IA-3	IIB	IIIA	IIIB	IA-3	IIA	IIB	IIIA	IIIB
T2a	IB	IIB	IIIA	IIIB	IB	IIB	IIIA	IIIB	IIIB
T2b	IIA	IIB	IIIA	IIIB	IIA	IIB	IIIA	IIIB	IIIB
T3	IIB	IIIA	IIIB	IIIC	IIB	IIIA	IIIA	IIIB	IIIC
T4	IIIA	IIIA	IIIB	IIIC	IIIA	IIIA	IIIB	IIIB	IIIC



# Evolution classification TNM

	TNM8				TNM 9				
	N0	N1	N2	N3	N0	N1	N2a	N2b	N3
T1a	IA-1	IIB	IIIA	IIIB	IA-1	IIA	IIB	IIIA	IIIB
T1b	IA-2	IIB	IIIA	IIIB	IA-2	IIA	IIB	IIIA	IIIB
T1c	IA-3	IIB	IIIA	IIIB	IA-3	IIA	IIB	IIIA	IIIB
T2a	IB	IIB	IIIA	IIIB	IB	IIB	IIIA	IIIB	IIIB
T2b	IIA	IIB	IIIA	IIIB	IIA	IIB	IIIA	IIIB	IIIB
T3	IIB	IIIA	IIIB	IIIC	IIB	IIIA	IIIA	IIIB	IIIC
T4	IIIA	IIIA	IIIB	IIIC	IIIA	IIIA	IIIB	IIIB	IIIC



# Evolution classification TNM

## N2 hétérogène

- N2 occulte de découverte fortuite
- N2 unisite ( N2a)
- N2 multisite (N2b)
- N2 invasif avec atteinte des organes a proximité

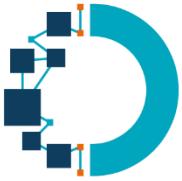


# Définition de résectabilité

	N0	N1	N2 SINGLE (non-bulky, non-invasive)	N2 MULTI (non-bulky, non-invasive)	N2 BULKY <sup>11</sup>	N2 INVASIVE	N3
T1-2	NOT STAGE III DISEASE	NOT STAGE III DISEASE	RESECTABLE	POTENTIALLY RESECTABLE*	UNCLEAR	UNRESECTABLE	UNRESECTABLE
T3 size / satellite / invasion	NOT STAGE III DISEASE	RESECTABLE	RESECTABLE	POTENTIALLY RESECTABLE*	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE
T4 size / satellite	RESECTABLE	RESECTABLE	RESECTABLE	POTENTIALLY RESECTABLE*	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE
T4 invasion	POTENTIALLY RESECTABLE <sup>5</sup>	POTENTIALLY RESECTABLE <sup>5</sup>	POTENTIALLY RESECTABLE <sup>5</sup>	POTENTIALLY RESECTABLE*	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE

\*Multiple station N2: case-by-case discussion; the exact number of nodes/stations cannot be defined

<sup>11</sup>Bulky N2: lymph nodes with a short-axis diameter >2.5-3 cm; in specific situations of *highly selected patients*, including those patients in multidisciplinary trials with surgery as local therapy can be discussed



# QUIZ CAS CLINIQUES

Traitement péri-opératoire / radio-chimiothérapie concomitante



1

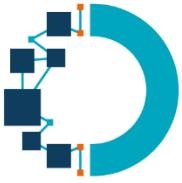
Allez sur [wooclap.com](https://wooclap.com)

2

Entrez le code d'événement dans le bandeau supérieur

Code d'événement  
**NSAADQ**





## 1er cas clinique

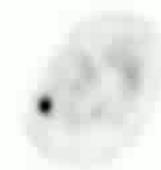
- Patiente de 65 ans
- Pas d'antécédent. Pas de traitement habituel
- Tabagisme sevré il y a 1 an estimé à 30PA
- Expectorations hémoptoïques font découvrir une lésion lobaire moyenne .
- **Adénocarcinome PDL1 - 15% sans addiction oncogénique**
- Un TEP Scanner est réalisé
- Imagerie cérébrale normale

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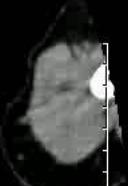
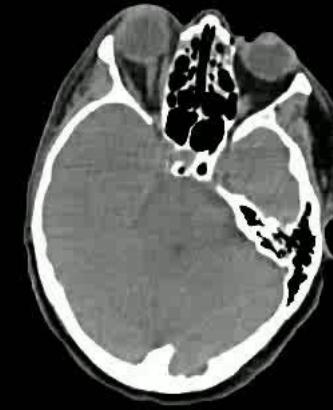
A



200 mm

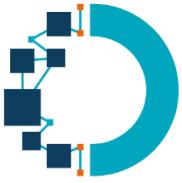
P

A



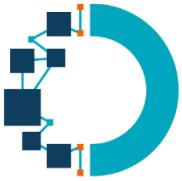
160 mm

P



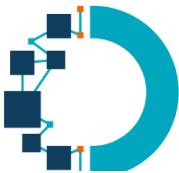
# Prise en charge?

- 1) Traitement de 1ere ligne par chimio-immunothérapie
- 2) Radio chimiothérapie concomitante puis immunothérapie de consolidation
- 3) Radio chimiothérapie séquentielle puis immunothérapie de consolidation
- 4) Traitement néoadjuvant par chimio immunothérapie puis chirurgie
- 5) Prise en charge chirurgicale première



# Prise en charge?

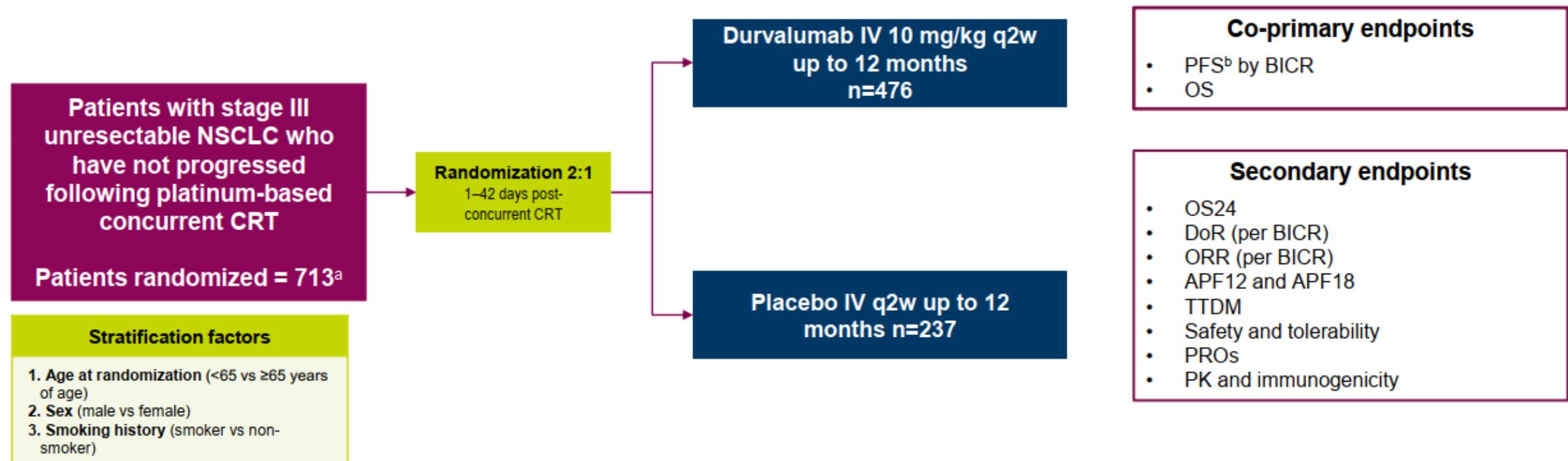
- 1) Traitement de 1ere ligne par chimio-immunothérapie
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# Etude PACIFIC

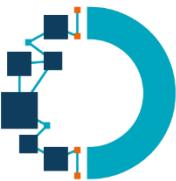
## PACIFIC Study: Trial Design

Phase III, randomized, double-blind, placebo-controlled, multicenter, global study<sup>1,2,3</sup>

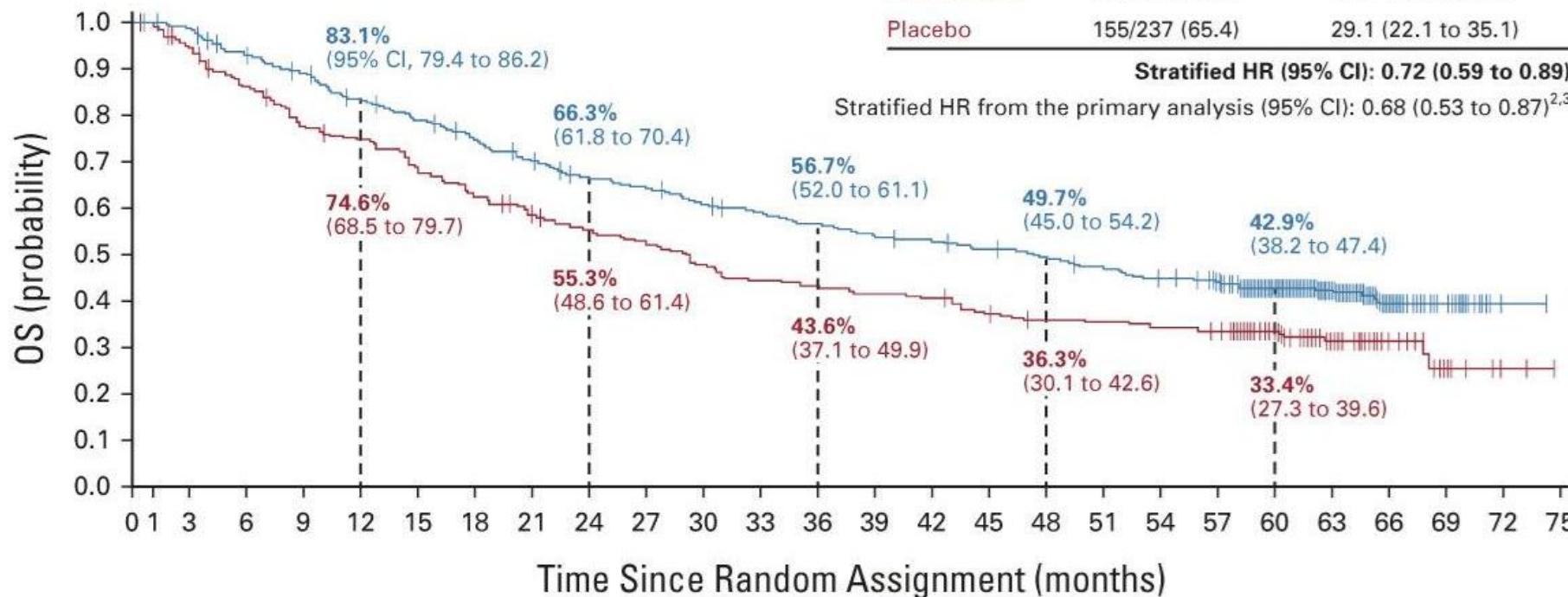


**Table 1.** Baseline Characteristics, Stratification Factors, and Prior Therapy in the Intention-to-Treat Population.\*

Characteristic	Durvalumab (N = 476)	Placebo (N = 237)	Total (N = 713)
Age — yr			
Median	64	64	64
Range	31–84	23–90	23–90
Sex — no. (%)			
Male	334 (70.2)	166 (70.0)	500 (70.1)
Female	142 (29.8)	71 (30.0)	213 (29.9)
Race — no. (%)†			
White	337 (70.8)	157 (66.2)	494 (69.3)
Black	12 (2.5)	2 (0.8)	14 (2.0)
Asian	120 (25.2)	72 (30.4)	192 (26.9)
Disease stage — no. (%)			
IIIA	252 (52.9)	125 (52.7)	377 (52.9)
IIIB	212 (44.5)	107 (45.1)	319 (44.7)
Other‡	12 (2.5)	5 (2.1)	17 (2.4)
WHO performance-status score — no. (%)§			
0	234 (49.2)	114 (48.1)	348 (48.8)
1	240 (50.4)	122 (51.5)	362 (50.8)
Tumor histologic type — no. (%)			
Squamous	224 (47.1)	102 (43.0)	326 (45.7)
Nonsquamous	252 (52.9)	135 (57.0)	387 (54.3)
Smoking status — no. (%)			
Current smoker	79 (16.6)	38 (16.0)	117 (16.4)
Former smoker	354 (74.4)	178 (75.1)	532 (74.6)
Never smoked	43 (9.0)	21 (8.9)	64 (9.0)
Previous radiotherapy — no. (%)¶			
<54 Gy	3 (0.6)	0	3 (0.4)
≥54 to ≤66 Gy	442 (92.9)	217 (91.6)	659 (92.4)
>66 to ≤74 Gy	30 (6.3)	19 (8.0)	49 (6.9)
Previous chemotherapy — no. (%)			
Induction	123 (25.8)	68 (28.7)	191 (26.8)
Concurrent with radiation therapy	475 (99.8)	236 (99.6)	711 (99.7)
Best response to previous chemoradiotherapy — no. (%)			
Complete response	9 (1.9)	7 (3.0)	16 (2.2)
Partial response	232 (48.7)	111 (46.8)	343 (48.1)
Stable disease	222 (46.6)	114 (48.1)	336 (47.1)

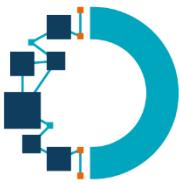


# Etude PACIFIC



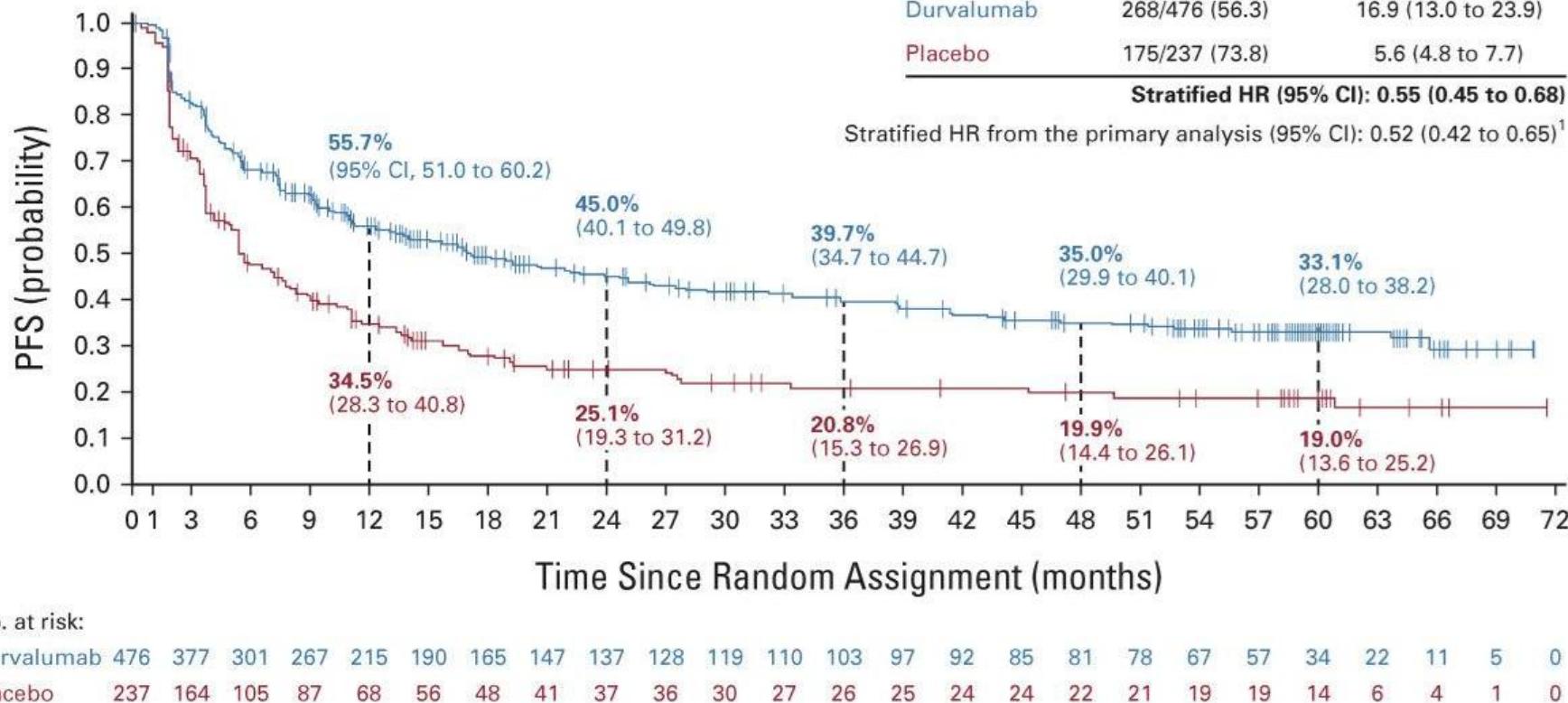
No. at risk:

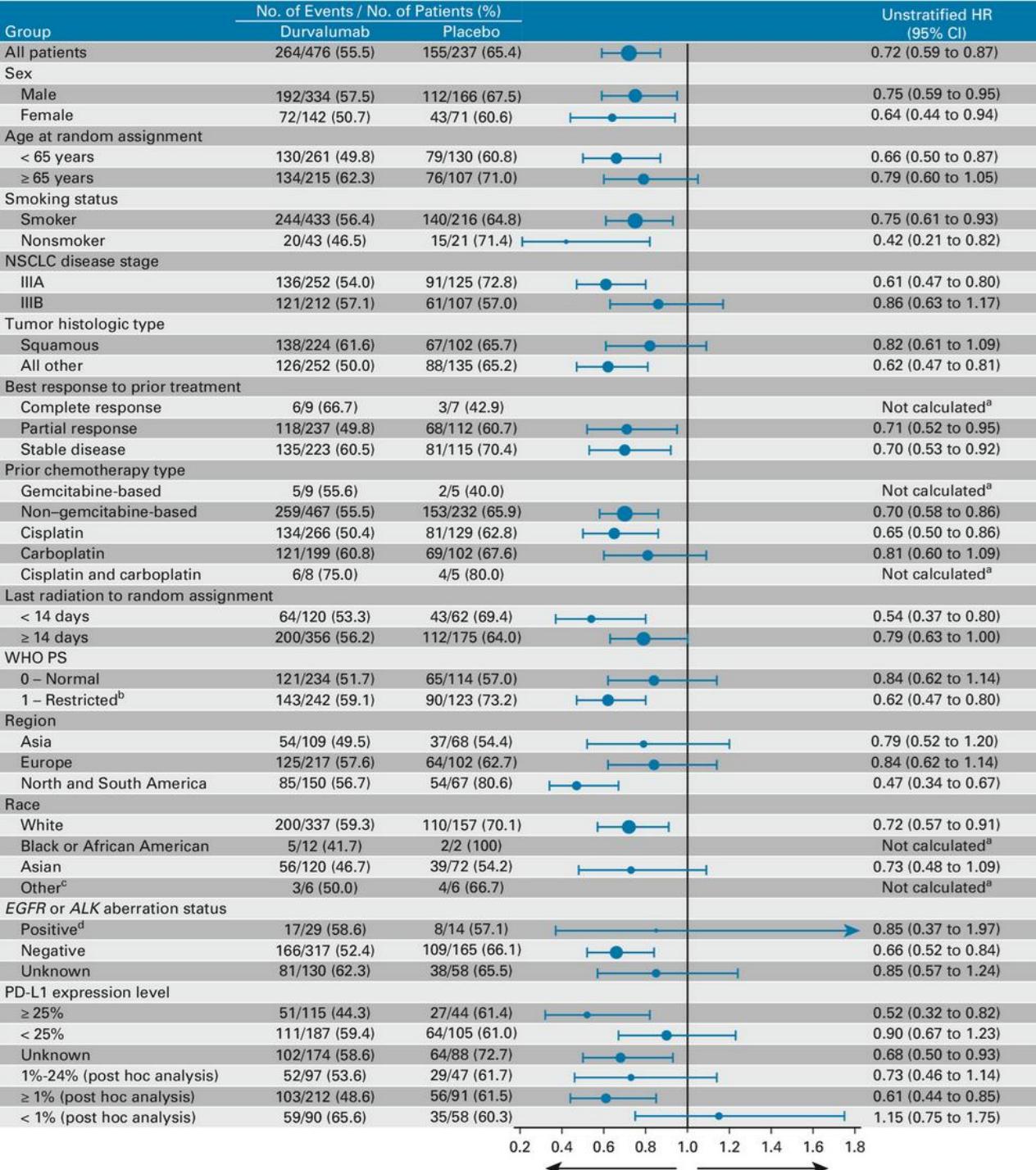
Durvalumab	476	464	431	414	385	364	343	319	298	289	273	264	252	241	236	227	218	207	196	183	134	91	40	18	2	0
Placebo	237	220	199	179	171	156	143	133	123	116	107	99	97	93	91	83	78	77	74	72	56	33	16	7	2	0



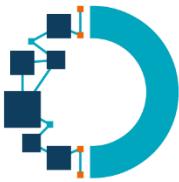
# Etude PACIFIC

B



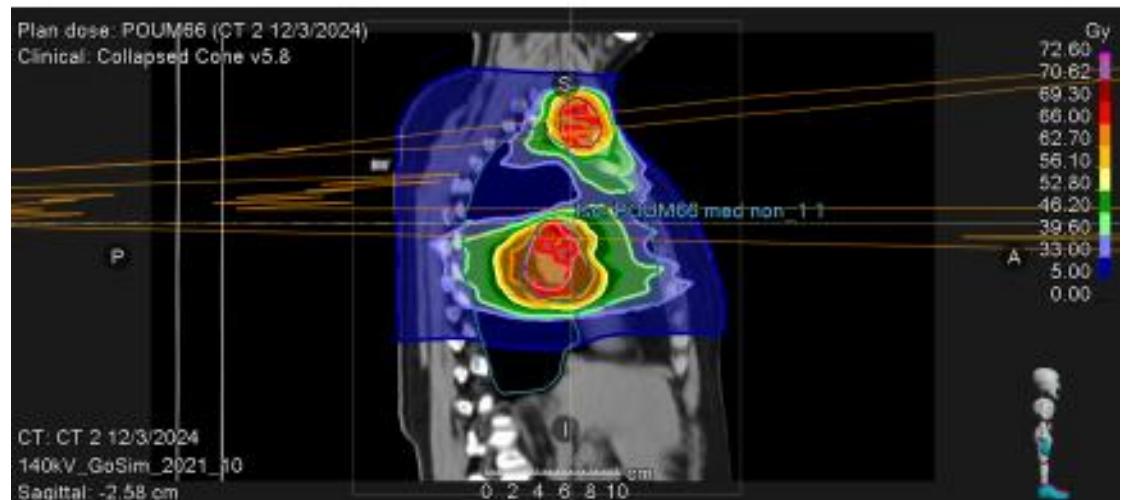
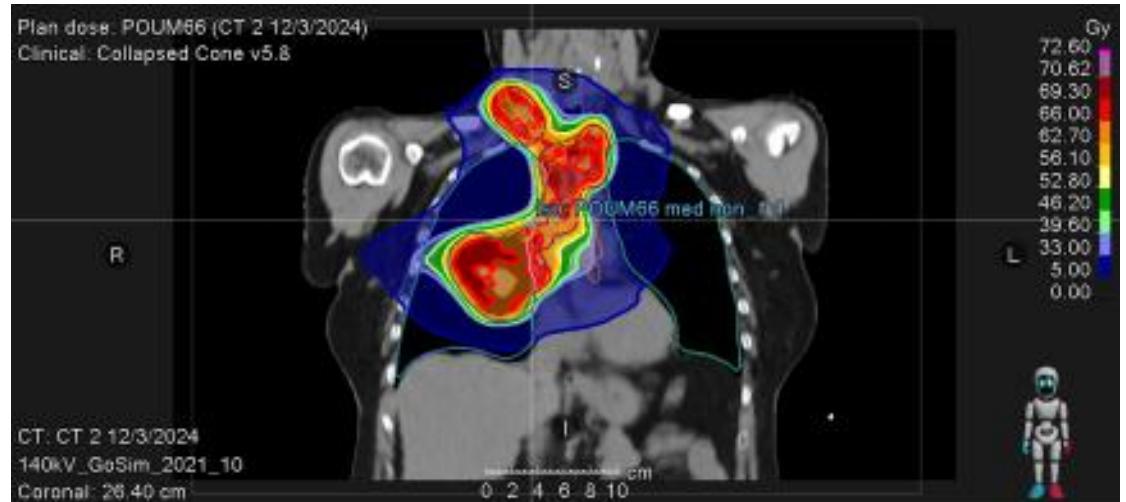


Pas de données de survie en fonction du stade IIIA ou IIIB



# Etude PACIFIC

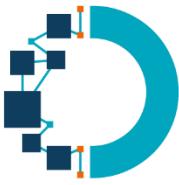
- Radio-chimiothérapie
- Cisplatine-Navelbine
- 66 Gy en 33 séances (~6 semaines de traitement)
- DURVALUMAB entretien (12 mois)





# Cas clinique M. A

- Patient 69 ans
- ATCD : Sd dépressif, dyslipidémie
- Retraité mécanicien avec exposition à l'amiante, tabagisme 80 PA actif
- Scanner systématique : lésion LID 10mm sans dissémination ganglionnaire
- TEP : Lésion LID SUV à 5 et ADP aire 4R SUV à 10
- IRM cérébrale normale

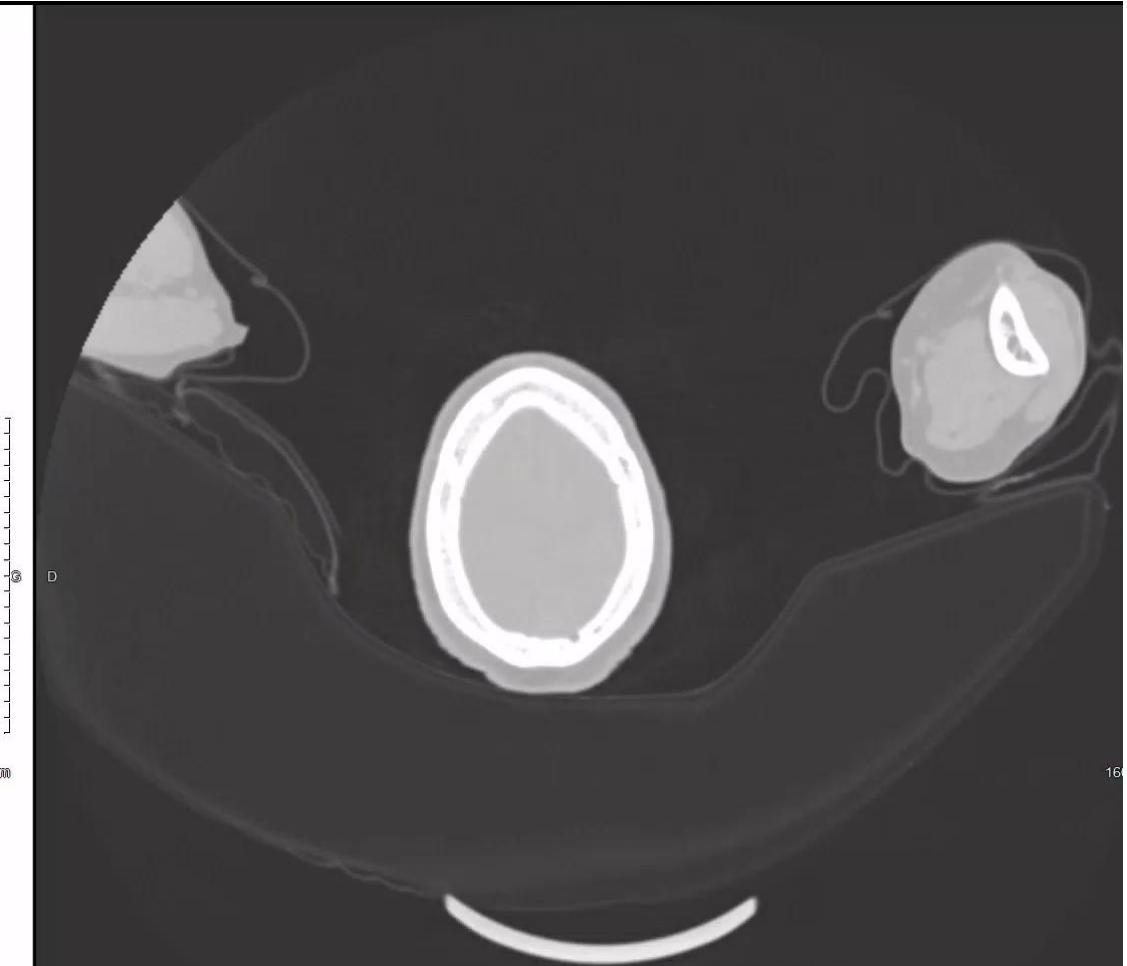
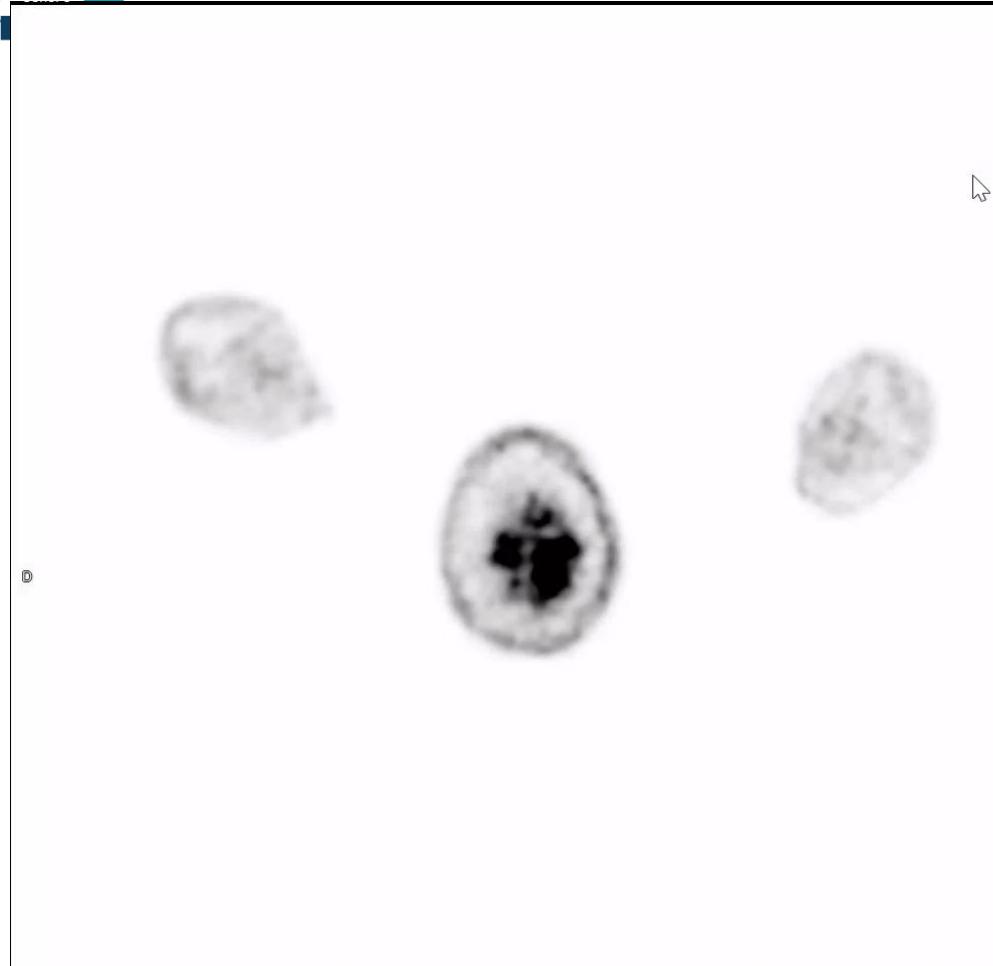


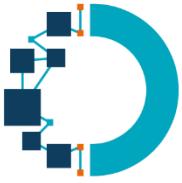
## Cas clinique M. A

- EBUS : Positive en 4R : Adénocarcinome PDL1 80%
  - Reste des ADP négatives (hile droit et aire 7)
- EFR OK



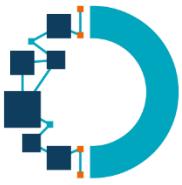
## Cas clinique M. A





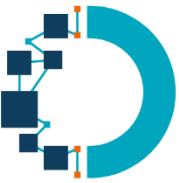
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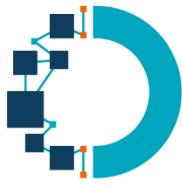
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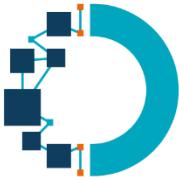
## Cas clinique M. A

- Chimio immunothérapie néo adjuvante patr 3 cures de CARBOPLATINE PACLITAXEL NIVOLUMAB
- TEP de réévaluation : régression quasi complète de l'ADP 4R et régression minime du nodule LID
- Lobectomie inférieure droite : ADK pulmonaire de 14 mm LID ypT1bN0 (20% de cellules viables)
- Curage négatif



## Liens d'intérêts

- Aucun



# Pièce opératoire post traitement néo adjuvant... Une situation particulière

- **Objectif supplémentaire** : évaluation de la réponse pathologique (RP) = % de tumeur viable
  - Evaluation standardisée, identique selon les traitements
  - Evaluer l'efficacité du traitement

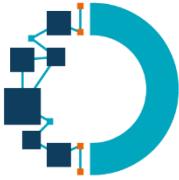
REVIEW ARTICLE



## IASLC Multidisciplinary Recommendations for Pathologic Assessment of Lung Cancer Resection Specimens After Neoadjuvant Therapy

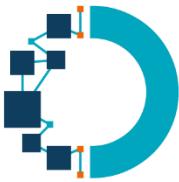


William D. Travis, MD,<sup>a,\*</sup> Sanja Dacic, MD,<sup>b</sup> Ignacio Wistuba, MD,<sup>c</sup>  
Lynette Sholl, MD,<sup>d</sup> Prasad Adusumilli, MD,<sup>e</sup> Lukas Bubendorf, MD,<sup>f</sup> Paul Bunn, MD,<sup>g</sup>  
Tina Cascone, MD, PhD,<sup>h</sup> Jamie Chaft, MD,<sup>i</sup> Gang Chen, MD,<sup>j</sup> Teh-Ying Chou, MD,<sup>k</sup>  
Wendy Cooper, MD,<sup>l</sup> Jeremy J. Erasmus, MD,<sup>m</sup> Carlos Gil Ferreira, MD,<sup>n</sup>  
Jin-Mo Goo, MD,<sup>o</sup> John Heymach, MD, PhD,<sup>p</sup> Fred R. Hirsch, MD,<sup>p</sup>  
Hidehito Horinouchi, MD,<sup>q</sup> Keith Kerr, MD,<sup>r</sup> Mark Kris, MD,<sup>i</sup> Deepali Jain, MD,<sup>s</sup>  
Young T. Kim, MD,<sup>t</sup> Fernando Lopez-Rios, MD,<sup>u</sup> Shun Lu, MD,<sup>v</sup>



## Définition de la « réponse pathologique »

- CPR (« complete pathological response ») (ypT0N0) : absence de tumeur viable sur l'ensemble du lit tumoral pulmonaire + ganglions lymphatiques
- MPR (« major pathological response ») :  $\leq 10\%$  tumeur viable
- PNR (pathological non response) :  $\geq 90\%$  tumeur viable

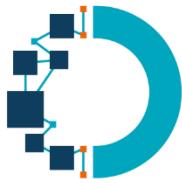


## En pratique... Avant l'anapath

- Eléments nécessaires pour l'évaluation de la RP ++ :
  - Traitement néoadjuvant ? Type ?
  - ATCD spécifique (tuberculose, pneumopathie...)
  - Imagerie **avant** et **après** le traitement néoadjuvant :
    - Localisation + nombre de tumeur + taille du lit tumoral post traitement
    - Présence + nombre + localisation de ganglion métastatique
    - Réponse RECIST : réponse partielle – complète, stable, ou progression

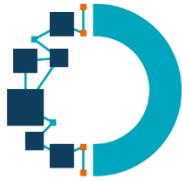
Modification de la PEC  
macroscopique

Corrélation réponse radiologique –  
thérapeutique - histologique



## En pratique... Avant l'anapath

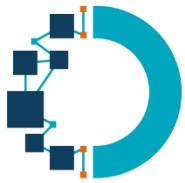
- Nécessité résultat d'analyse :
  - IHC PDL1 (score TPS) et ALK
  - analyse moléculaire NGS ++/ technique ciblée (EGFR)



## En pratique...

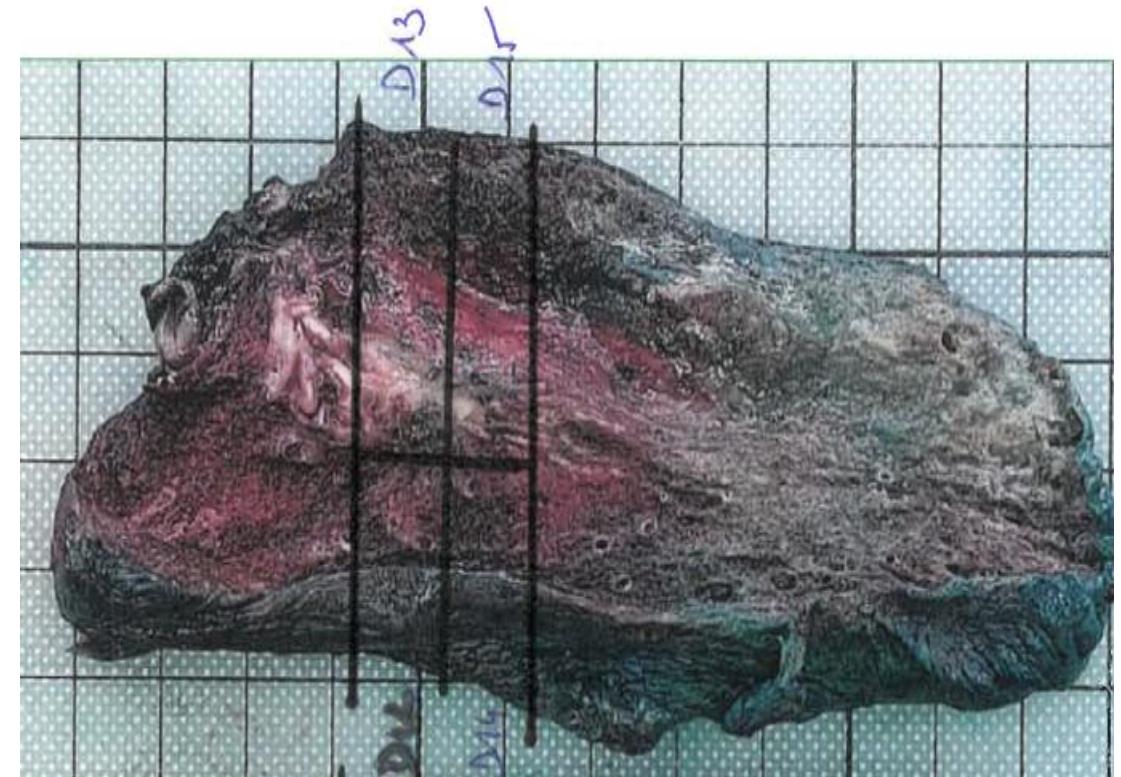
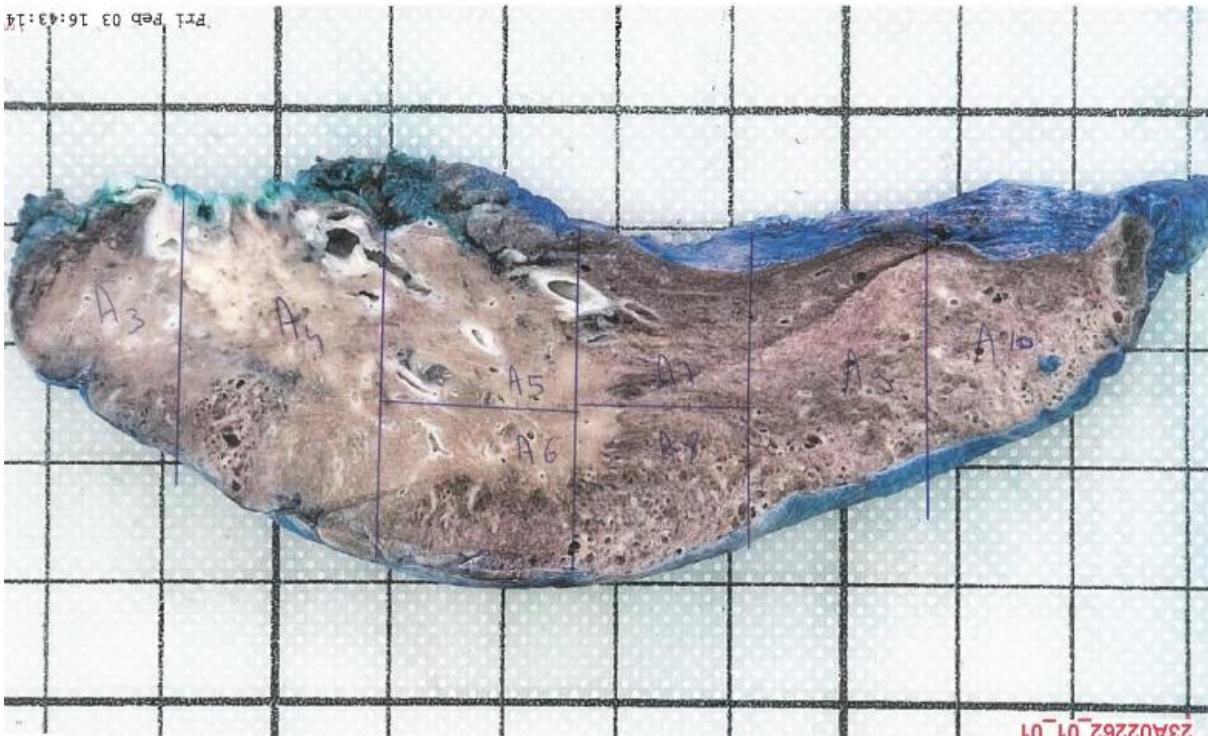
### Durant l'anapath : étape de macroscopie

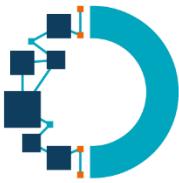
- Etape de macroscopie :
  - Repérage du lit tumoral + description + évaluer limite exérèse
  - Attention au remaniements non tumoraux pouvant fausser la taille (pneumopathie péri tumorale ++)
  - Echantillonnage avec cartographie du lit tumoral



# En pratique...

## Durant l'anapath : étape de macroscopie

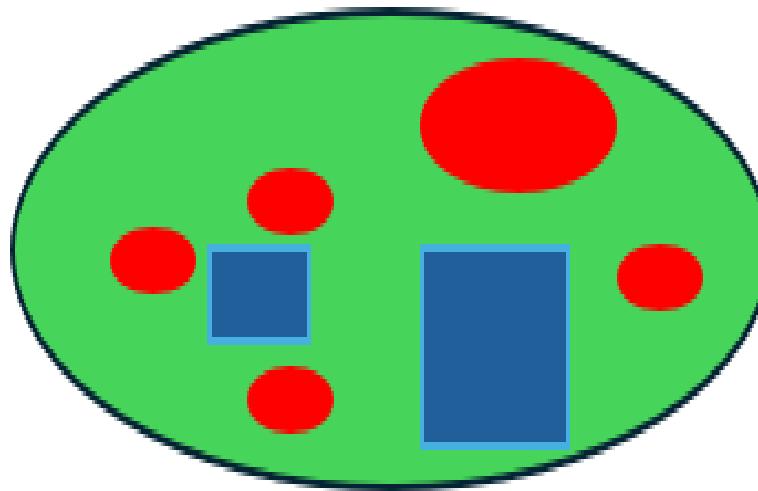




## En pratique...

### Durant l'anapath : étape de microscopie

- Identification des 3 composantes du lit tumoral

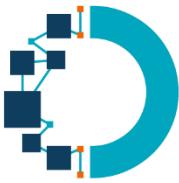


Tumeur viable (%)

Nécrose (%)

Stroma fibro-inflammatoire (%)

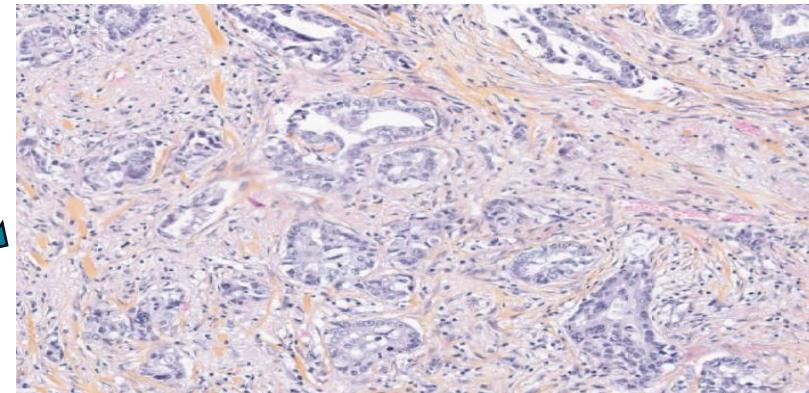
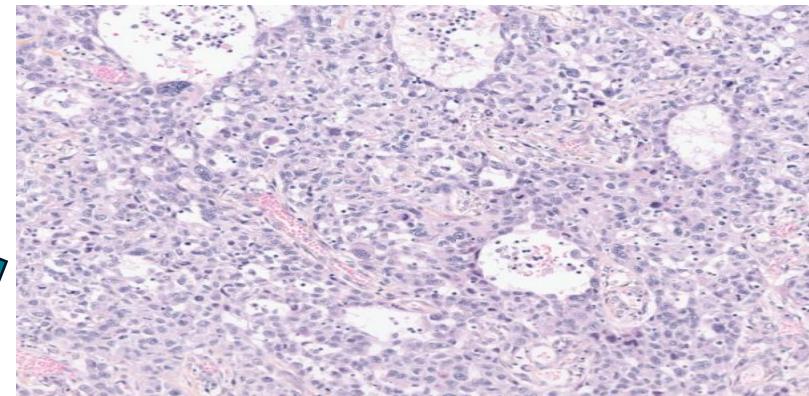
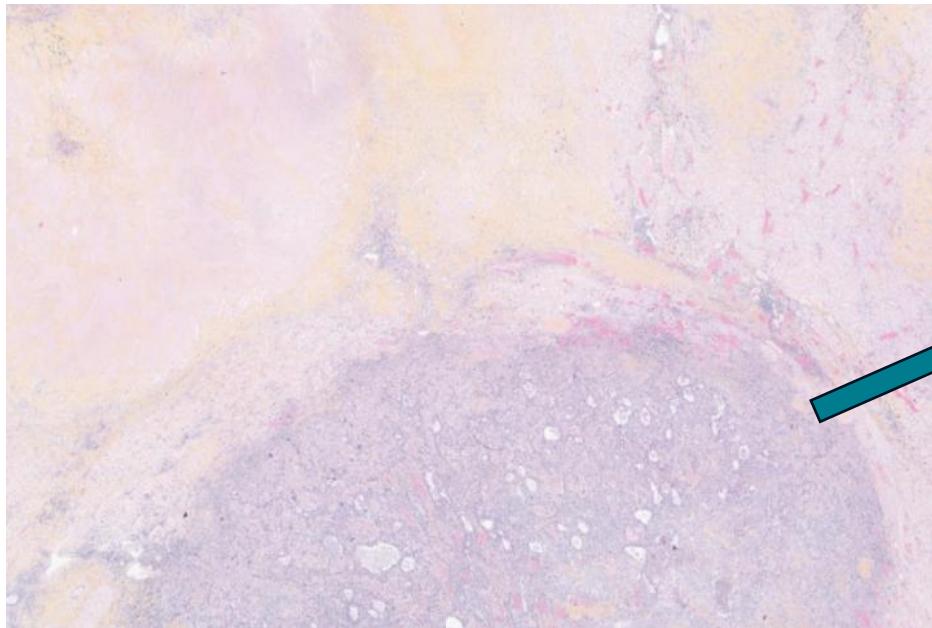
Lit tumoral =  
 $T + N + S = 100 \%$

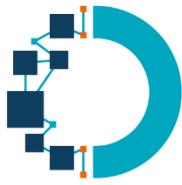


## En pratique...

### Durant l'anapath : étape de microscopie

**% reliquat tumoral viable + % nécrose + % tissu inflammatoire**  
= 100 %

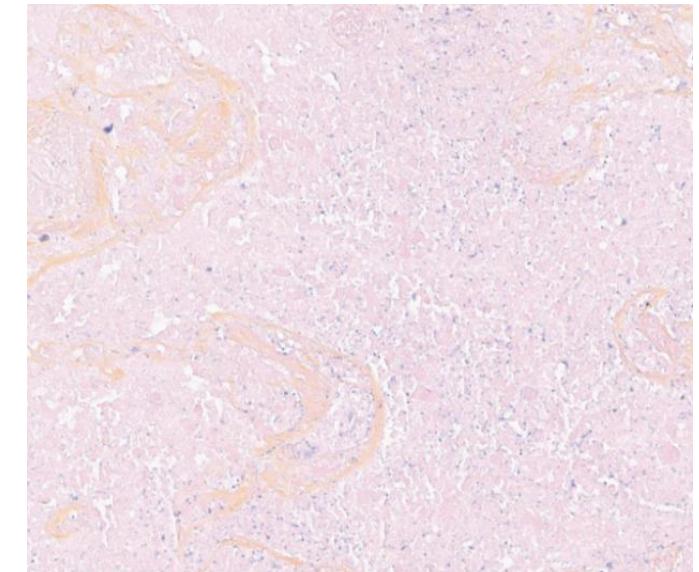
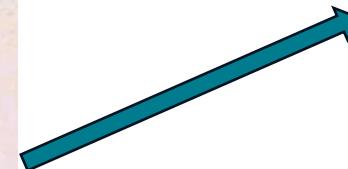
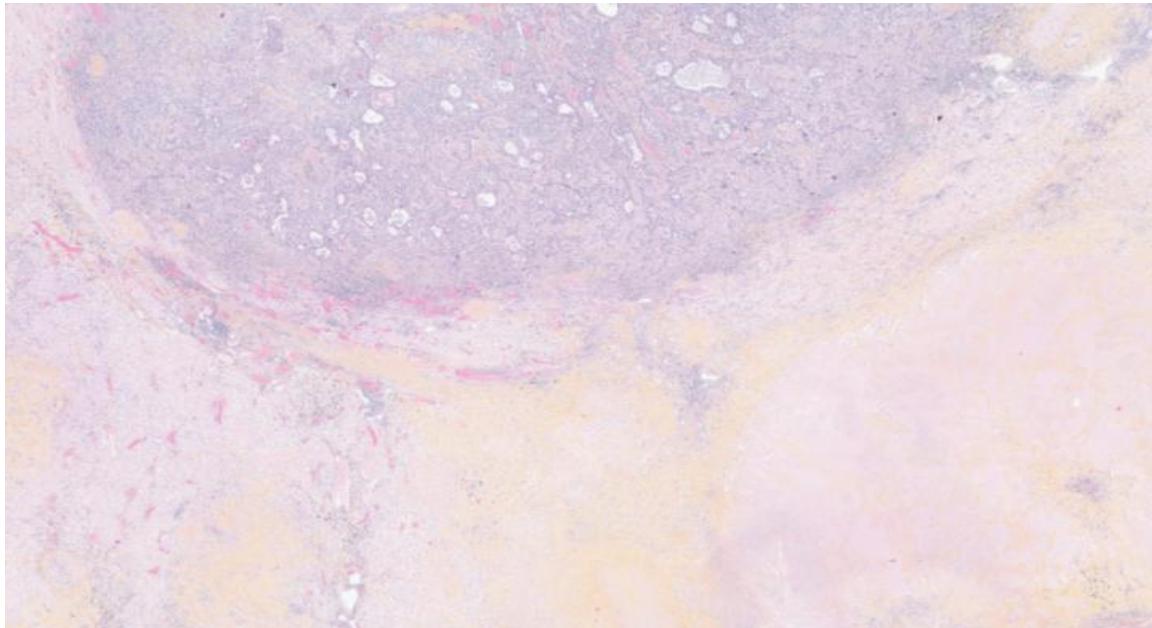


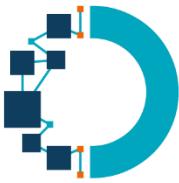


## En pratique...

### Durant l'anapath : étape de microscopie

% reliquat tumoral viable + **% nécrose** + % tissu inflammatoire  
= 100 %

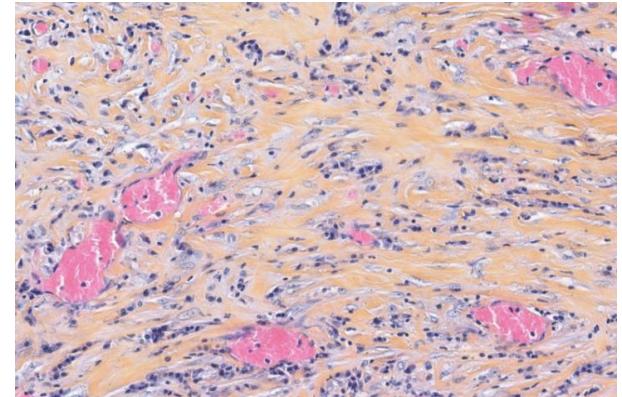
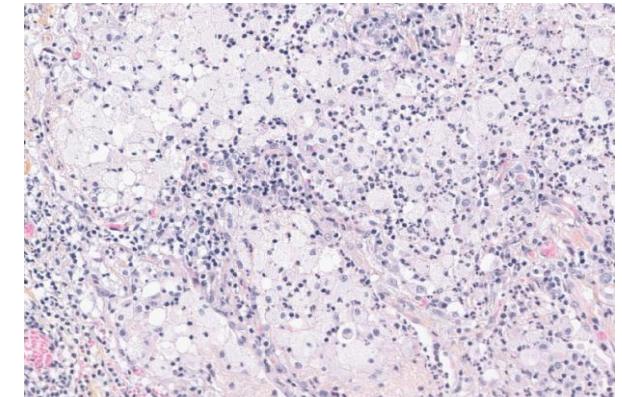
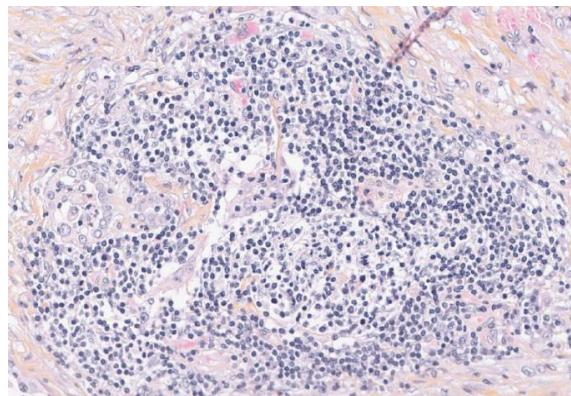
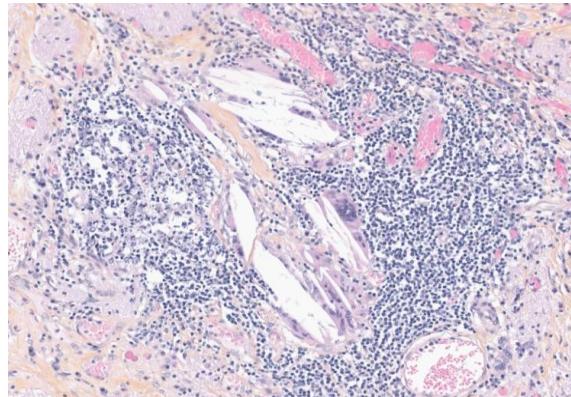


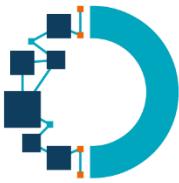


## En pratique...

### Durant l'anapath : étape de microscopie

% reliquat tumoral viable + % nécrose + **% tissu fibro-inflammatoire** = 100 %

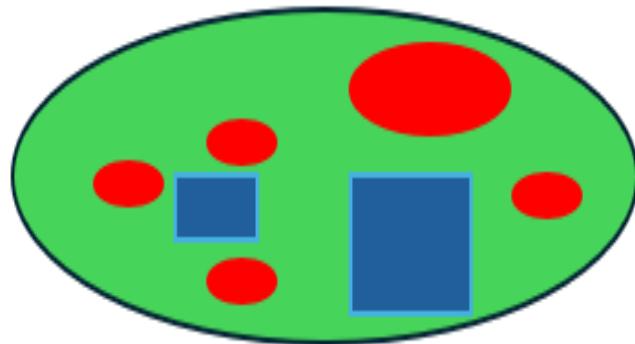




## En pratique...

### Durant l'anapath : étape de microscopie

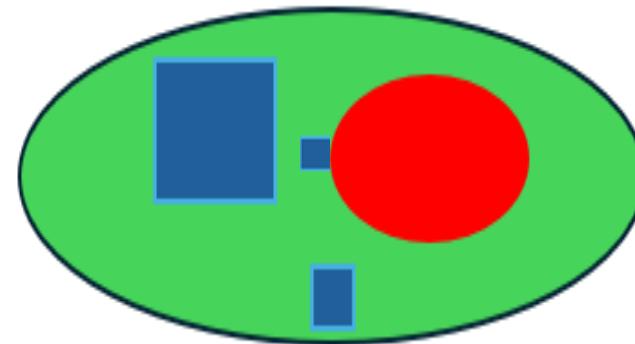
- Mais difficulté d'interprétation....



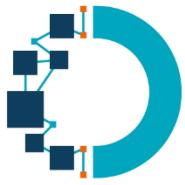
Tumeur viable (%)

Nécrose (%)

Stroma fibro-inflammatoire (%)



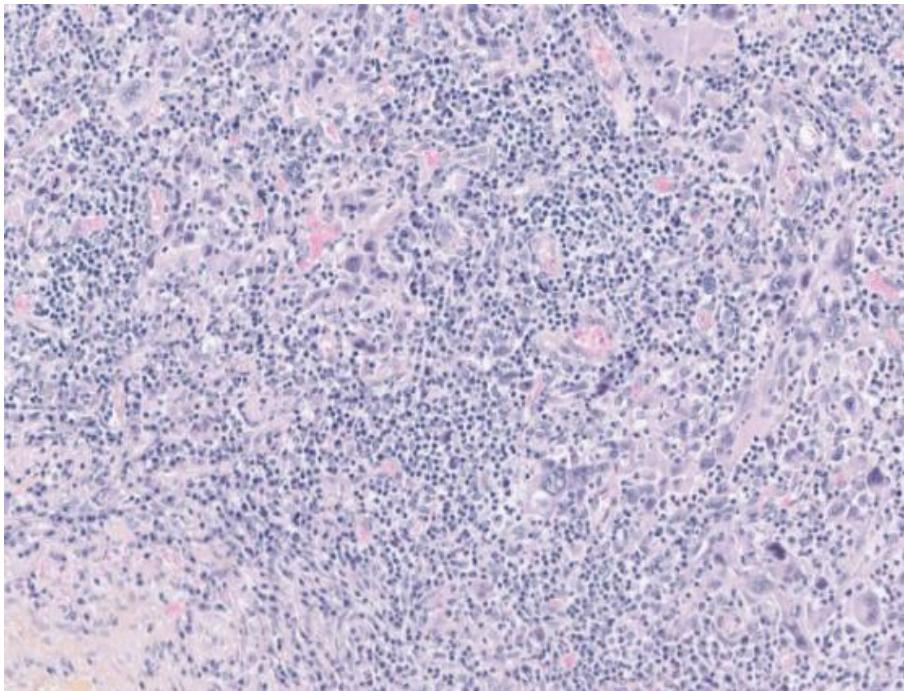
- Caractère fragmenté
- Imbrication des différents contingents entre eux

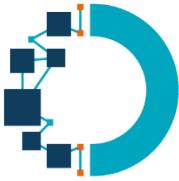


## En pratique...

### Durant l'anapath : étape de microscopie

- Mais difficulté d'interprétation....

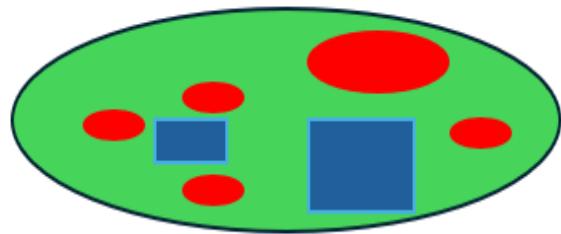




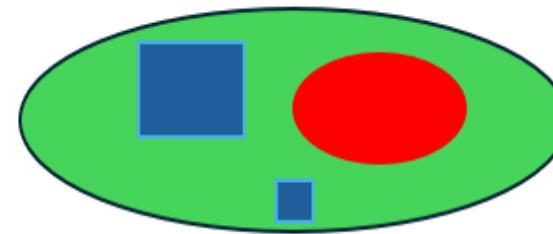
## En pratique...

### Durant l'anapath : étape de microscopie

- Mais difficulté d'interprétation....

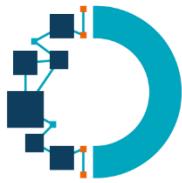


Tumeur viable (%)  
Nécrose (%)  
Stroma fibro-inflammatoire (%)



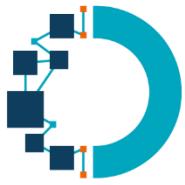
**Evaluation sur chaque lame, moyenne sur l'ensemble des lames**

- 1 évaluation / tumeur
- Extension/qualité d'exérèse : ne tenir compte que de la tumeur viable
- Approche identique sur les ganglions



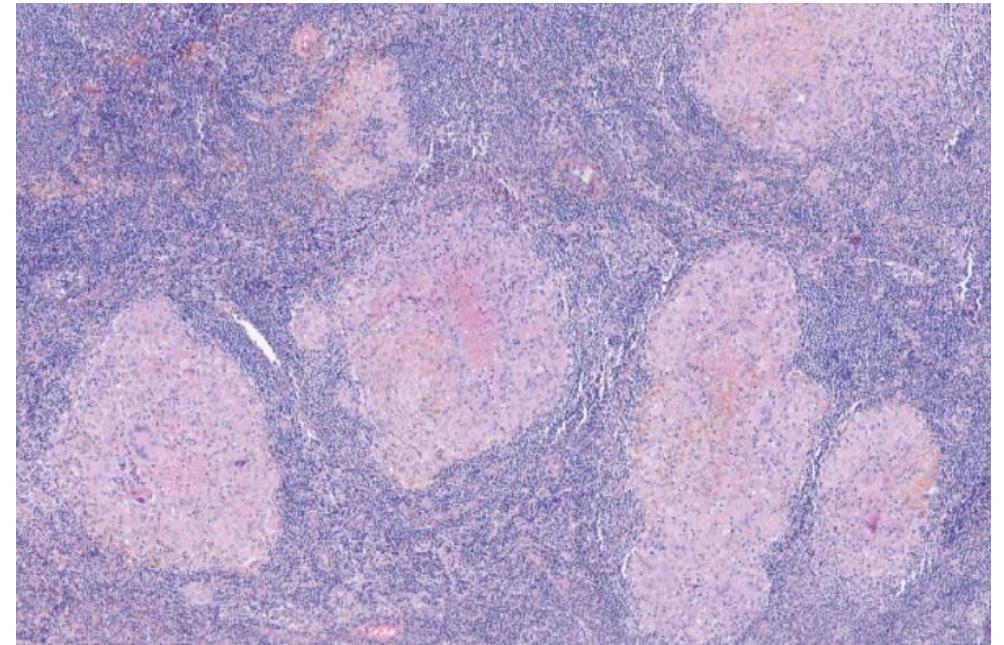
# Différence de réponse histologique en fonction des traitements néoadjuvants

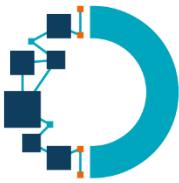
- Absence d'aspect histopathologique pathognomonique
- Remaniements fibro-inflammatoires ++ après IT
  - ✓ Fibrose élastique proliférative
  - ✓ Néovascularisation
  - ✓ Inflammation : lymphocytaire (TIL), structure lymphoïde tertiaire, empreinte cristaux cholestérol



# Cas de discordance réponse histologique - imagerique

- Remaniements fibro-inflammatoires (traitement IT ++)
- Granulome épithélioïde et giganto cellulaire
- ....

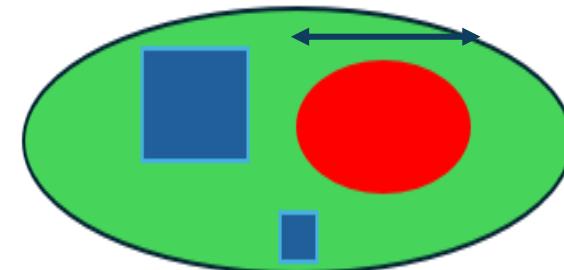
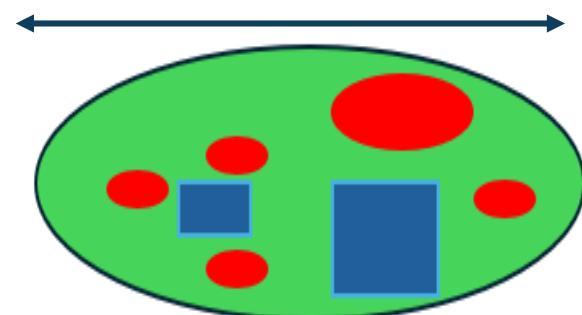




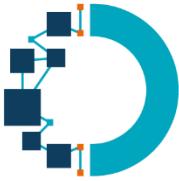
# Quid de la détermination du ypT ?

- ypT = taille de la tumeur et non du lit tumoral
- Difficulté :
  - Fragmentation de la tumeur au sein de remaniements post thérapeutiques ++
  - Pas de réel consensus

Taille du lit tumoral  
x % tumeur viable

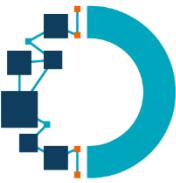


Mesure grand  
axe tumoral



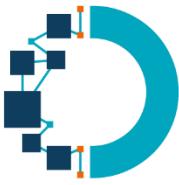
## Synthèse

- **Objectif complémentaire** : évaluation de la réponse pathologique
- Indication du contexte de traitement néo-adjuvant ++
- Evaluation composante stromale, nécrose, tumorale
- Subjectivité ++
- Manque de consensus officiel
- Standardisation (reproductibilité mais peu spécifique en fonction type tumoral ou TTT)



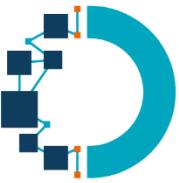
# Bibliographie

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- Cotrell T R et al. Pathologic features of response to neoadjuvant anti-PD-1 in resected non-small-cell lung carcinoma: a proposal for quantitative immune-related pathologic response criteria (irPRC). *Ann oncol* 2018
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- Saqi A, Leslie KO, Moreira AL, Lantuejoul S, Shu CA, Rizvi NA, Sonett JR, Tajima K, Sun SW, Gitlitz BJ, Colby TV. Assessing Pathologic Response in Resected Lung Cancers: Current Standards, Proposal for a Novel Pathologic Response Calculator Tool, and Challenges in Practice. *JTO Clin Res Rep.* 2022
- Qu Y, Emoto K, Eguchi T, Aly RG, Zheng H, Chaft JE, Tan KS, Jones DR, Kris MG, Adusumilli PS, Travis WD. Pathologic Assessment After Neoadjuvant Chemotherapy for NSCLC: Importance and Implications of Distinguishing Adenocarcinoma From Squamous Cell Carcinoma. *J Thorac Oncol.* 2019
- EPU poumon, mai 2025, Pr S. LANTUEJOUL, Dr N. POTE, Dr A. MANSUET LUPO, Pr D. DAMOTTE, Dr V. HOFMAN, Dr N. PITON, Dr N. MACAGNO, Dr I. ROUQUETTE



# Traitements néo-adjuvant

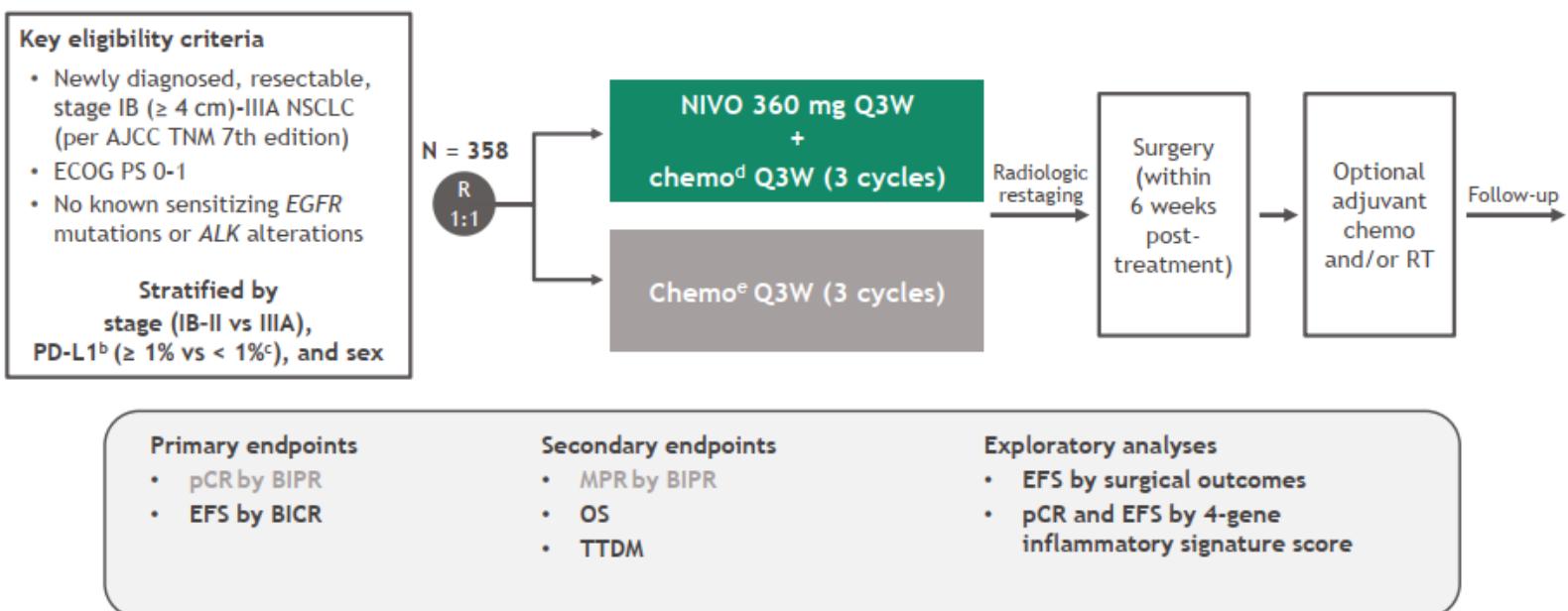
- **Néoadjuvant seul**
- **CHECKMATE-816**
- **Péri-opératoire**
- **KEYNOTE-671**
- **CHECKMATE 77T**
- **AEGEAN**

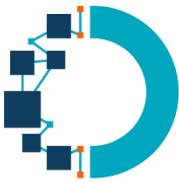


# CHECKMATE-816

- 358 patients
- Stade IB au IIIA TNM7  
EGFR/ALK négatif
- Tout PDL-1

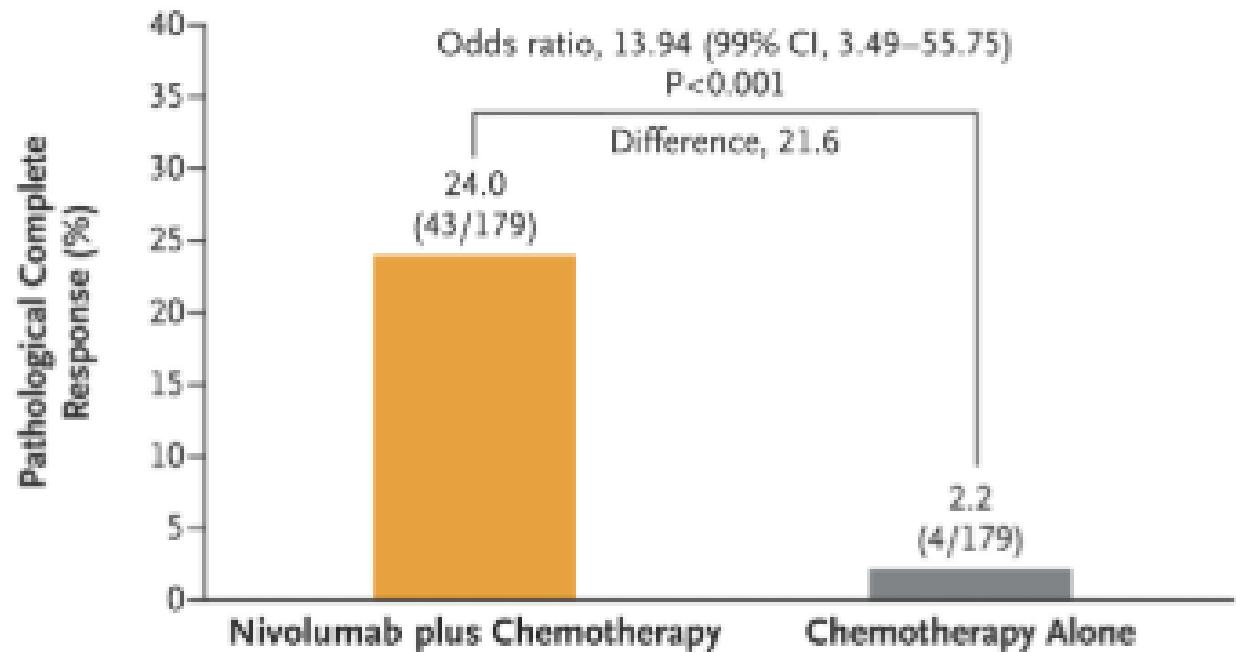
## CheckMate 816 study design<sup>a</sup>

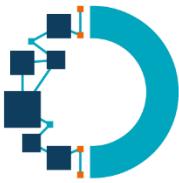




# CHECKMATE-816

- Meilleure réponse pathologique complète
- Meilleure réponse pathologique majeure

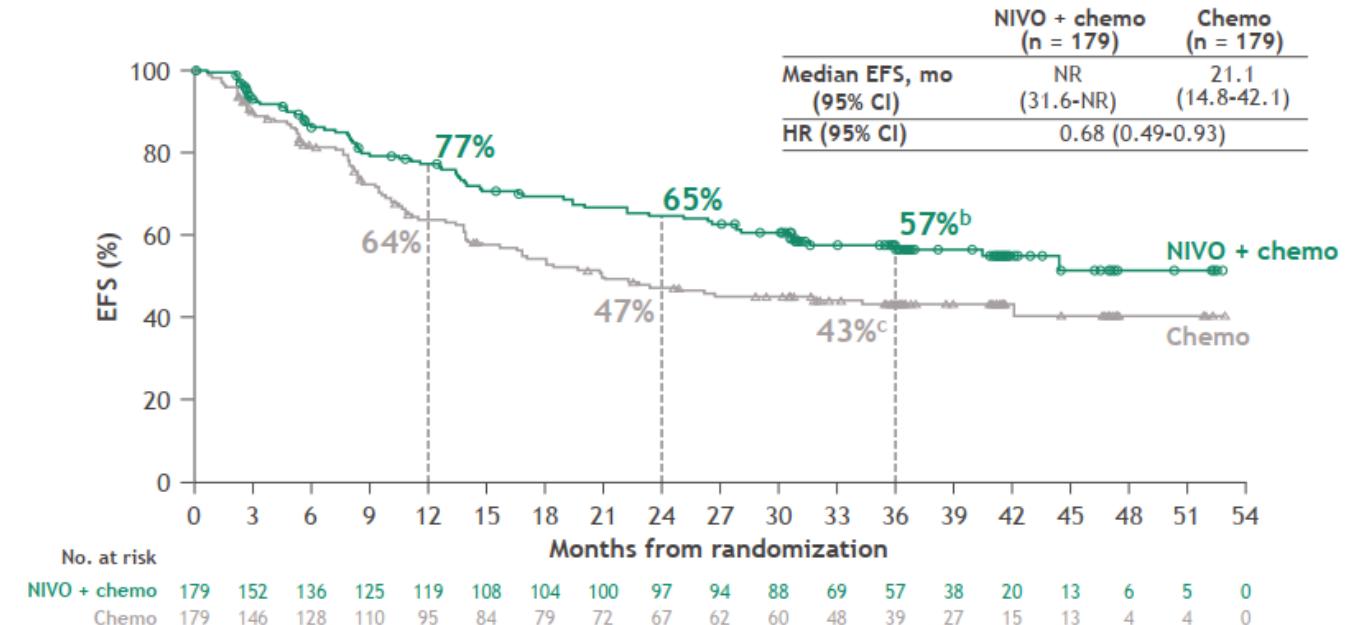


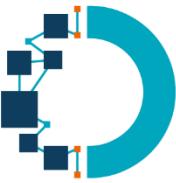


# CHECKMATE-816

- Meilleure survie sans évènement

## EFS with neoadjuvant NIVO + chemo vs chemo: 3-year update<sup>a</sup>



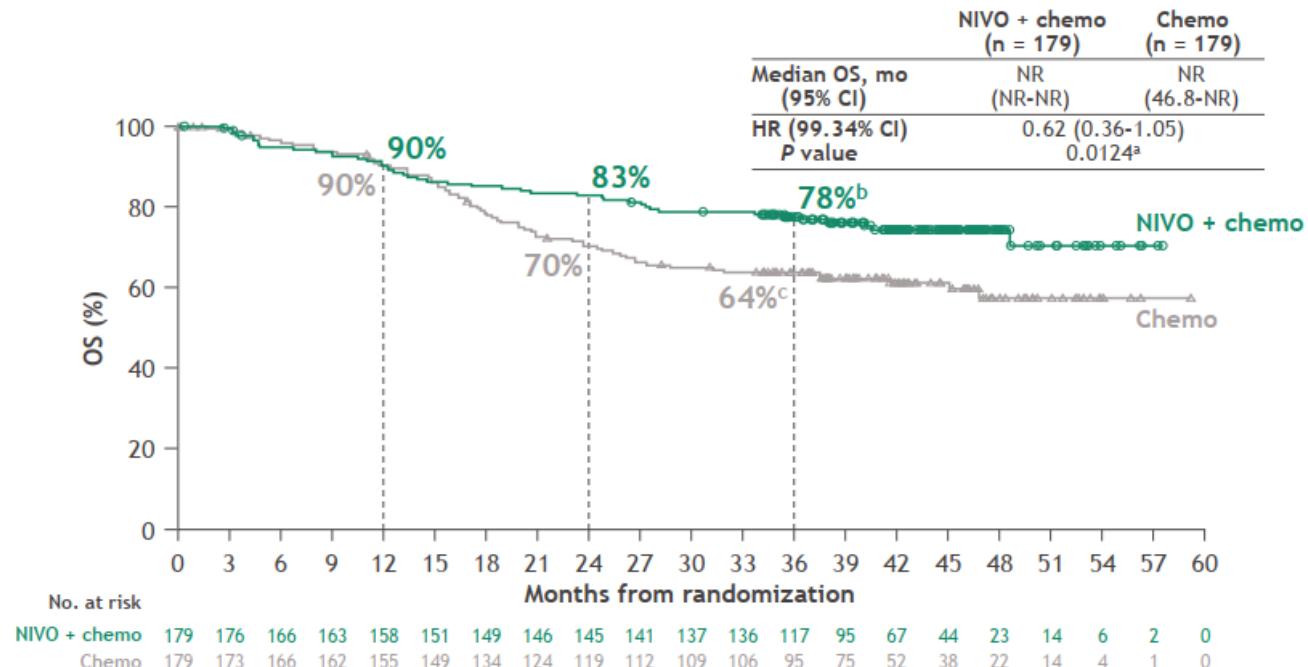


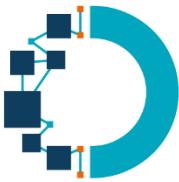
# CHECKMATE-816

CheckMate 816: 3-y efficacy/safety update and biomarker analysis

## OS with neoadjuvant NIVO + chemo vs chemo: 3-year update

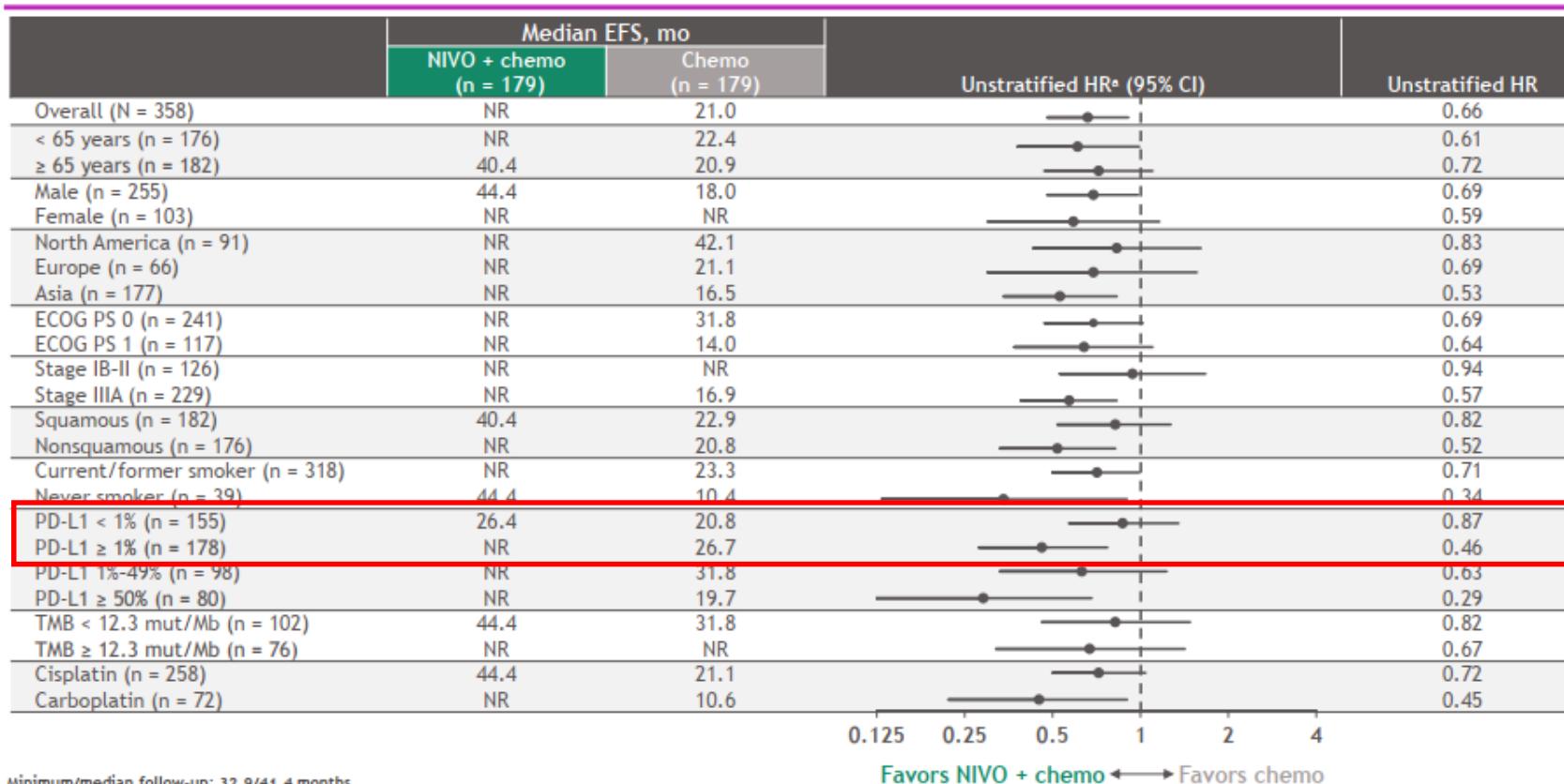
- Meilleure survie globale

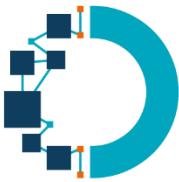




# CHECKMATE-816

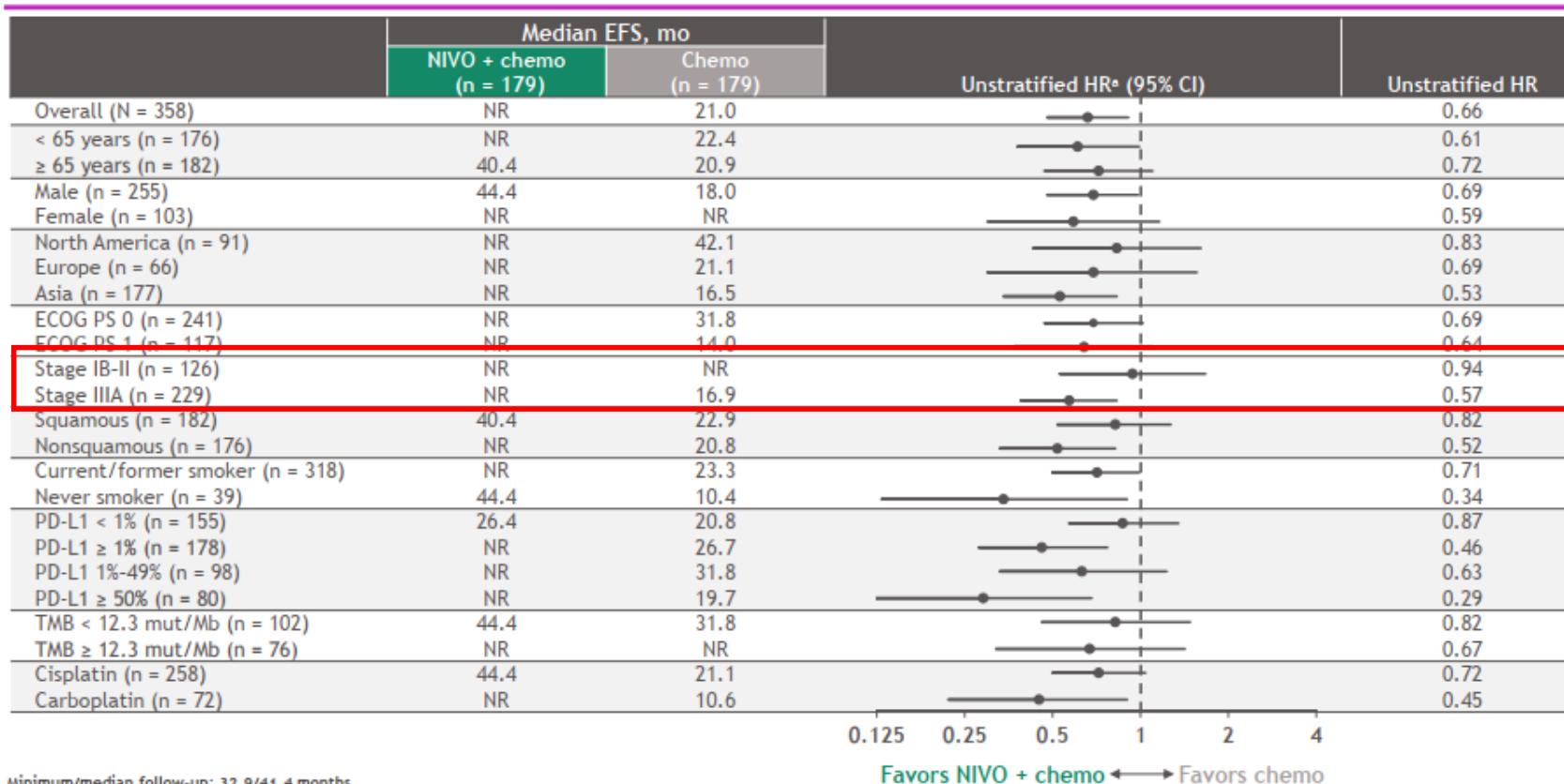
## EFS<sup>a</sup> subgroup analysis: 3-year update





# CHECKMATE-816

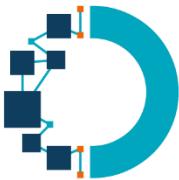
## EFS<sup>a</sup> subgroup analysis: 3-year update





## CHECKMATE-816

- 2023 Nivolumab : « en association à une chimiothérapie à base de sels de platine dans le traitement néoadjuvant des patients atteints d'un CBNPC résécable à haut risque de récidive, dont les tumeurs expriment **PD-L1 au seuil  $\geq 1\%$**  et dont les tumeurs ne présentent pas de mutation sensibilisante de l'EGFR connue, ni de translocation ALK connue »



# Définition de résectabilité

	N0	N1	N2 SINGLE (non-bulky, non-invasive)	N2 MULTI (non-bulky, non-invasive)	N2 BULKY <sup>11</sup>	N2 INVASIVE	N3
T1-2	NOT STAGE III DISEASE	NOT STAGE III DISEASE	RESECTABLE	POTENTIALLY RESECTABLE*	UNCLEAR	UNRESECTABLE	UNRESECTABLE
T3 size / satellite / invasion	NOT STAGE III DISEASE	RESECTABLE	RESECTABLE	POTENTIALLY RESECTABLE*	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE
T4 size / satellite	RESECTABLE	RESECTABLE	RESECTABLE	POTENTIALLY RESECTABLE*	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE
T4 invasion	POTENTIALLY RESECTABLE <sup>5</sup>	POTENTIALLY RESECTABLE <sup>5</sup>	POTENTIALLY RESECTABLE <sup>5</sup>	POTENTIALLY RESECTABLE*	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE

\*Multiple station N2: case-by-case discussion; the exact number of nodes/stations cannot be defined

<sup>11</sup>Bulky N2: lymph nodes with a short-axis diameter >2.5-3 cm; in specific situations of *highly selected patients*, including those patients in multidisciplinary trials with surgery as local therapy can be discussed



# Définition de résectabilité

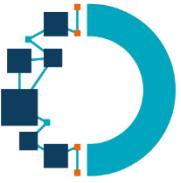
	N0	N1	N2 SINGLE (non-bulky, non-invasive)	N2 MULTI (non-bulky, non-invasive)	N2 BULKY <sup>1</sup>	N2 INVASIVE	N3
T1-2	NOT STAGE III DISEASE	NOT STAGE III DISEASE		POTENTIALLY RESECTABLE*			
T3 size / satellite / invasion	NOT STAGE III DISEASE			POTENTIALLY RESECTABLE*			
T4 size / satellite				POTENTIALLY RESECTABLE*			
T4 invasion	POTENTIALLY RESECTABLE <sup>§</sup>	POTENTIALLY RESECTABLE <sup>§</sup>	POTENTIALLY RESECTABLE <sup>§</sup>	POTENTIALLY RESECTABLE <sup>§</sup>			

**CHECKMATE816**  
PDL 1  $\geq 1\%$

**PACIFIC**

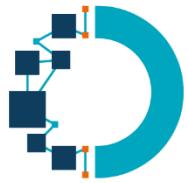
\*Multiple station N2: case-by-case discussion; the exact number of nodes/stations cannot be defined

<sup>1</sup>Bulky N2: lymph nodes with a short-axis diameter  $>2.5-3$  cm; in specific situations of *highly selected patients*, including those patients in multidisciplinary trials with surgery as local therapy can be discussed



## Cas clinique de Mme D S

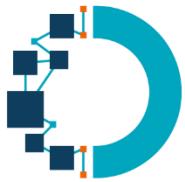
- Femme de 51 ans
- syndrome de Pierre Marie, tabac actif 35PA,
- Tumeur pulmonaire du LID diagnostiquée
- **Adenocarcinome lépidique TTF1+, PDL 1 à 0% muté KRAS G12D par ponction**
- EFR normales



## Mme D S

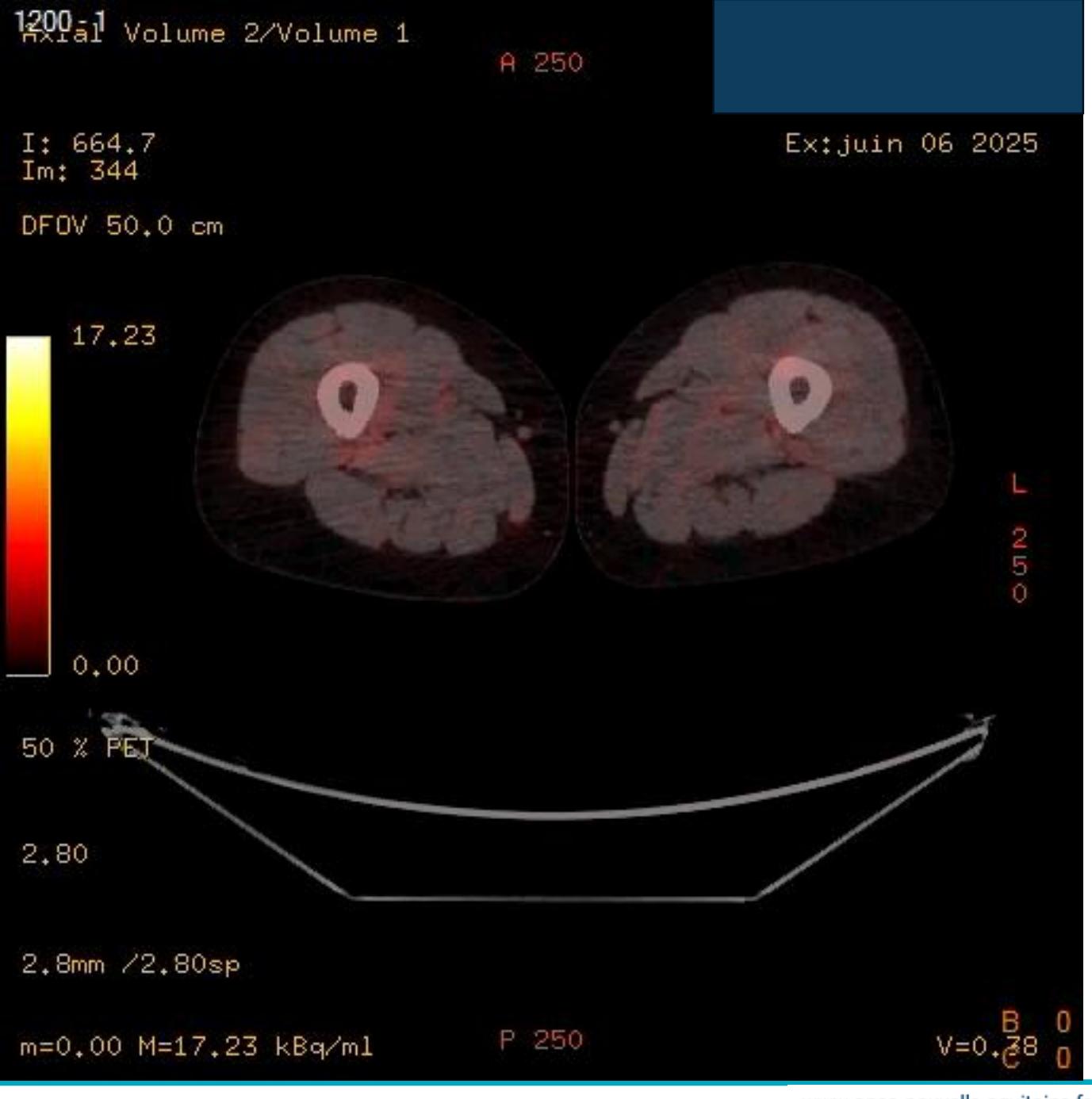
- Suite

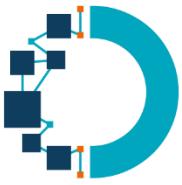




# Mme DS

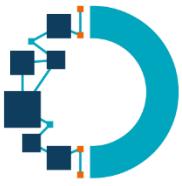
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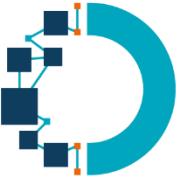


# Prise en charge ?

- 1) Radio chimiothérapie concomitante puis immunothérapie de consolidation
- 2) Radio chimiothérapie séquentielle puis immunothérapie de consolidation
- 3) Traitement néoadjuvant par chimio immunothérapie puis chirurgie
- 4) Prise en charge chirurgicale première

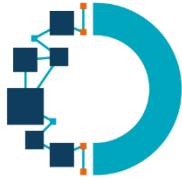


- RCP le 7/5/25
- Tumeur classée cT2aN1M0, stade IIB, SUV masse 37mm à 19,5 N1 10mm à 3,8 non prouvé



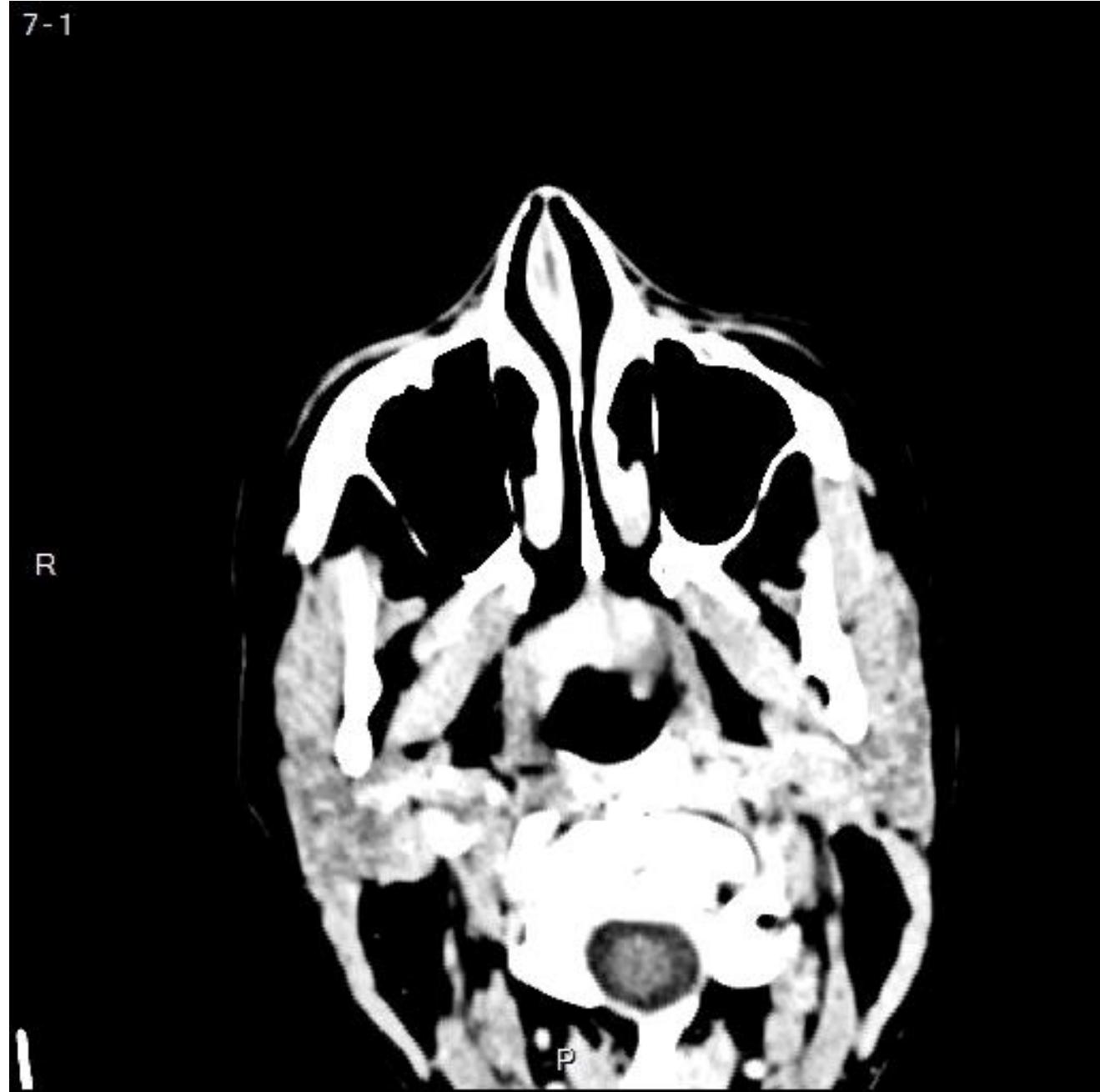
## Mme D S

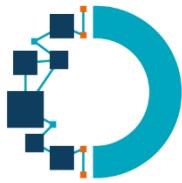
- Cs oncologique le 21/5/25: relecture PDL 1 à 0% confirmant pas de CT-Immuno possible, patiente souhaite une chirurgie d'emblée puis ttt adjuvant si nécessaire.
- Nouveau TEP le 6/6/25: masse 55mm à 22,3 de SUV, N1 à 6,3 SUV isolé.
- Cs chir le 26/6/25 pour bloc le 07/07/25 soit à 2 mois de l'avis initial: pneumonectomie Dt sur infiltration gglionnaire
- Anapath pTNM: ADK invasif micropapillaire peu différencié, STAS +, marges ok, pas d'embols, pT3N2R0, N1 en RC et N2 positif en RC en 2D et 4D, PDL1 à 10%



## Mme D S

- Cs oncologique le 28/8/25: à 7 semaine de la chirurgie douleur sternale atypique, OMS 1, Pierre Marie idem
- TDM de réévaluation : extension Crane, poumon G, sternum +/- foie



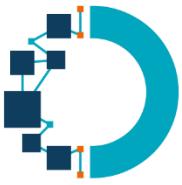


**Mme D S**

- Indication posée de chimio-immunothérapie commencée le 01/09/25
- Réévaluation TDM 09/10/2025: RAS crane, -23% recist poumon G, stable sur l'os, pas de nouvelle lésion.



- Caractère central et N1
  - Doit faire reconsidérer cN2 potentiel
  - Pensez stadification du N pour diminuer le upstaging néfaste pour tt le monde: EBUS, EUS, M°
  - Resécabilité du N1?
  - Nouveau statut PDL1 ?
  - Délai
- Intérêt à faire relire la ponction pour changement de statut PDL ? Pas de nouvelle biopsie pour PDL 1 qui passe de 0 préop à 10% postop



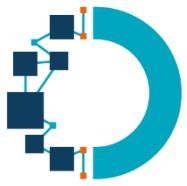
## Mme D S

- Résécabilité:
  - Intérêt du chirurgien !
  - Honnêteté du chirurgien?
  - Attention pneumonectomie (même si toutes ne DCD pas en postop)
  - Savoir faire des EBUS et M°
- Confirmation de l'intérêt du ttt systémique néoadj. Quid de faire accepter ce ttt comme sélection des bons candidats aux ttt locaux?



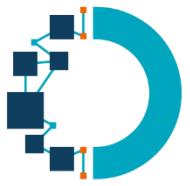
## Cas clinique Mme C C

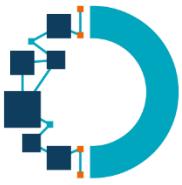
- Bilan de toux et AEG, non fumeuse, TDM 01/07/25: masse pulmonaire LSD cT2bN2
- EFR 11/07: supranormale
- F°15/07: RAS
- TEP 17/07: cT2bN2bMx puis M0
- Ponction 07/2025: ADK, ALKneg, PDL1 à 4%, muté EGFR L858R Ex21
- EBUS 23/08: confirmation 4D+, 10bilat et 7 neg



**Mme**  
**Suite**

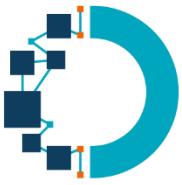






# Prise en charge?

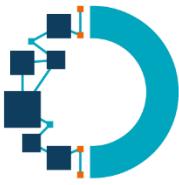
- 1) Radio chimiothérapie concomitante puis immunothérapie de consolidation
- 2) Traitement néoadjuvant par chimio immunothérapie puis chirurgie
- 3) Prise en charge chirurgicale première
- 4) Traitement de 1ere ligne métastatique...



# Mme CCC

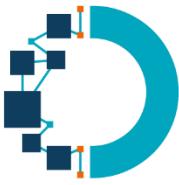
## Suite

- RCP CHU Bordeaux le 03/09/25: CT-immuno néoadjuvante hors AMM mais...
- Réévaluation à 2 cycles :
  - Si bonne réponse: 3ème cycle puis chir
  - Si mauvaise réponse : pas de chir à voir RT-CT conco ou autre



## Mme C C Suite

- Réévaluation avant ttt le 16/09 par TEP (2 mois du précédent):  
Lésion classée cT2bN2bM1c (surrénales et ADP hile coeliaque)



# Mme C Suite

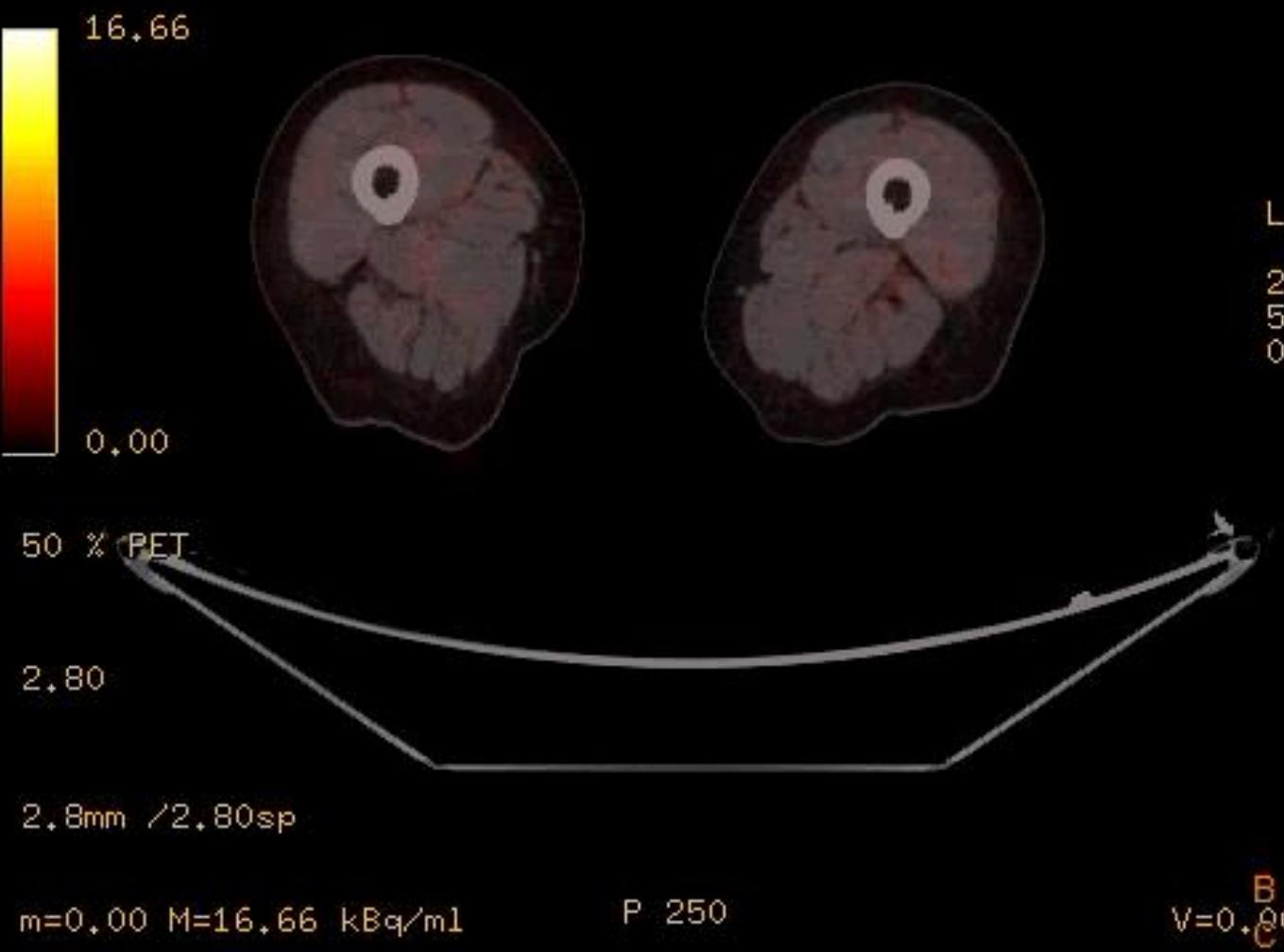
1200-1  
Axial Volume 2/Volume 1

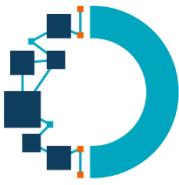
COESNON CATHERINE

A 250

I: 687.3  
Im: 293  
DFOV 50,0 cm

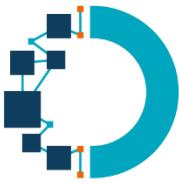
Ex:sept. 16 2025





# Prise en charge?

- 1) Poursuite de la chimio immunothérapie car seulement 2 cures
- 2) Traitement par TKI type OSIMERTINIB



# Prise en charge?

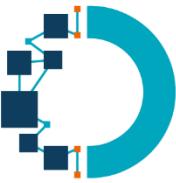
- 1) Poursuite de la chimio immunothérapie car seulement 2 cures
- 2) **Traitement par TKI type OSIMERTINIB**



# Mme C C

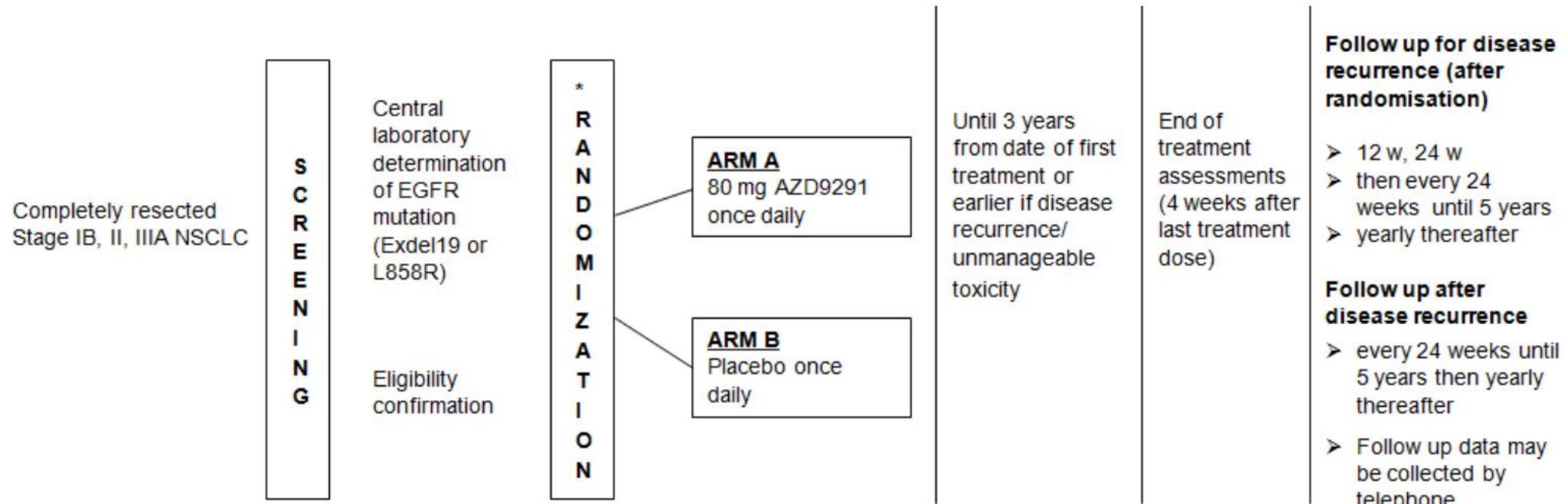
## Discussion

- Réévaluation TEP moins de 1,5-2mois:
  - valable pour tt le monde (onco ici mais chir ou RT aussi)
  - Cinétique tumorale souvent intéressante !
- Se tenir au courant des essais en cours
- Interactions EGFR muté sensibles TKI et Immuno
- Le bulky N2 est il un pb pour resecabilité après néoadj?



# Focus EGFR stade III

## ADAURA TRIAL

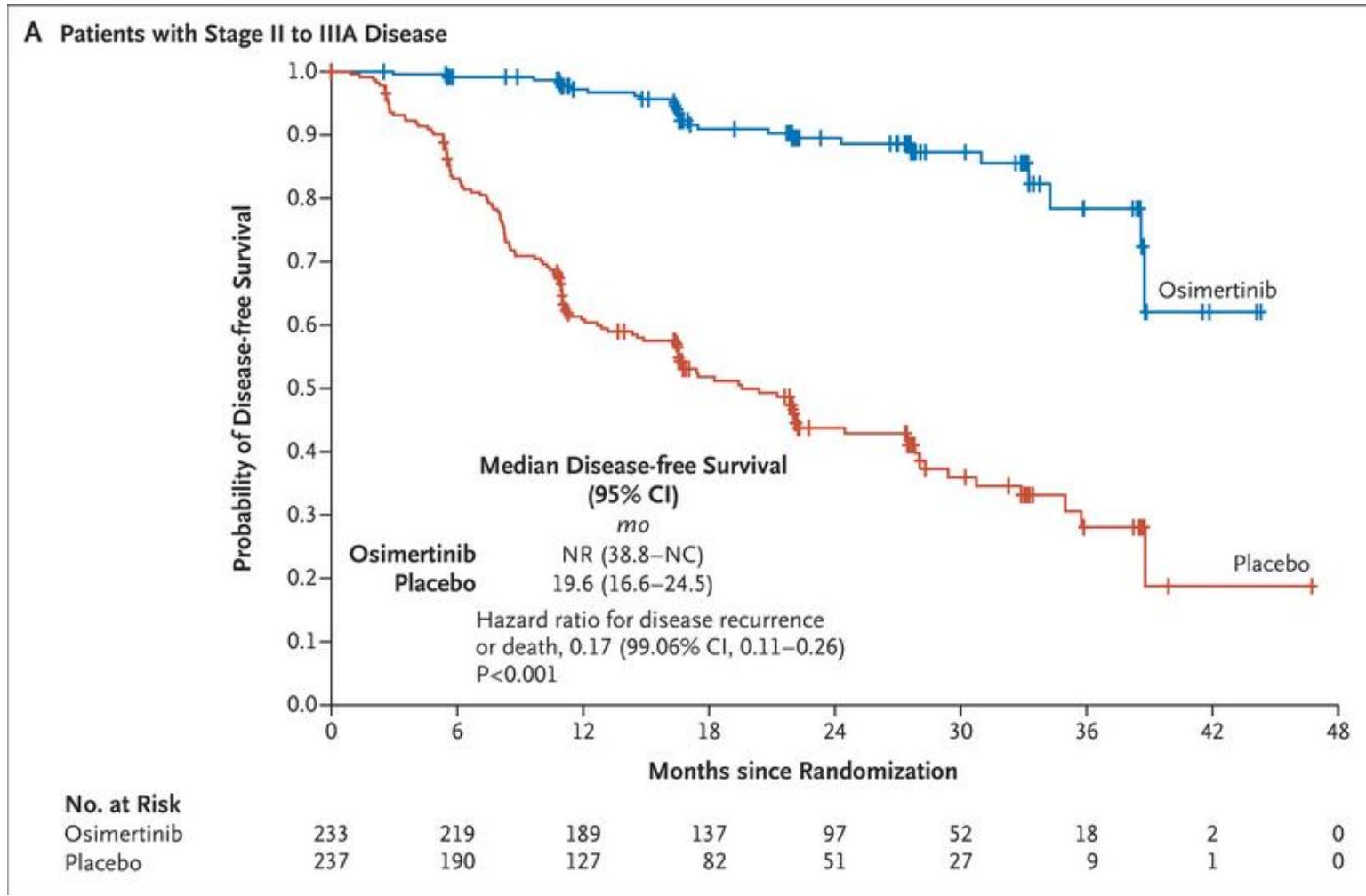


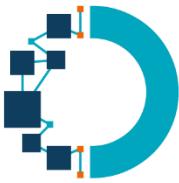
Herbst RS, Wu YL, John T, et al. Adjuvant Osimertinib for Resected EGFR-Mutated Stage IB-IIIA Non-Small-Cell Lung Cancer: Updated Results From the Phase III Randomized ADAURA Trial. *J Clin Oncol*. 2023



# Focus EGFR stade III

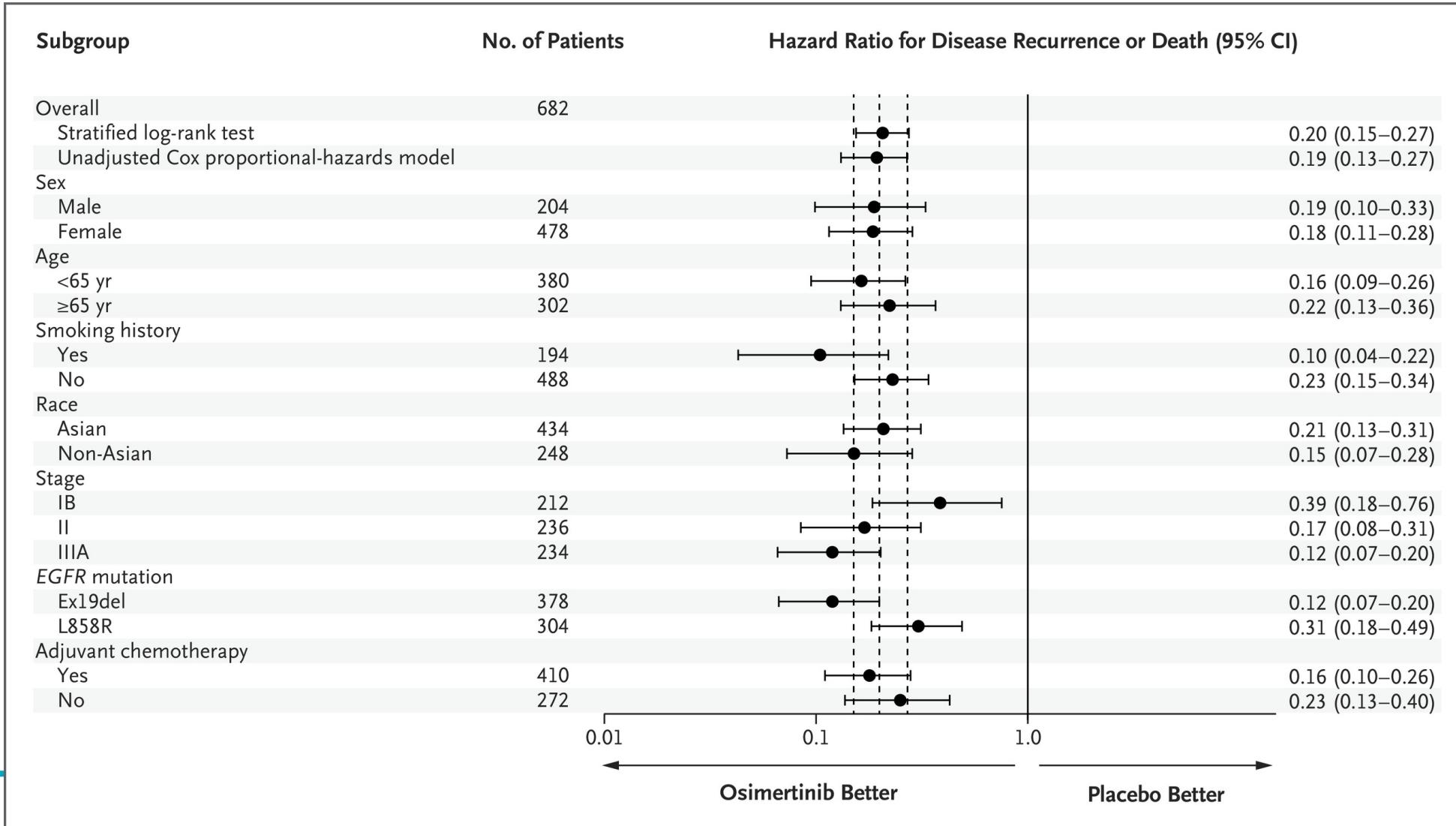
## ADAURA TRIAL

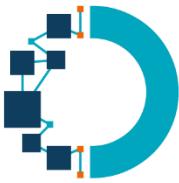




# Focus EGFR stade III

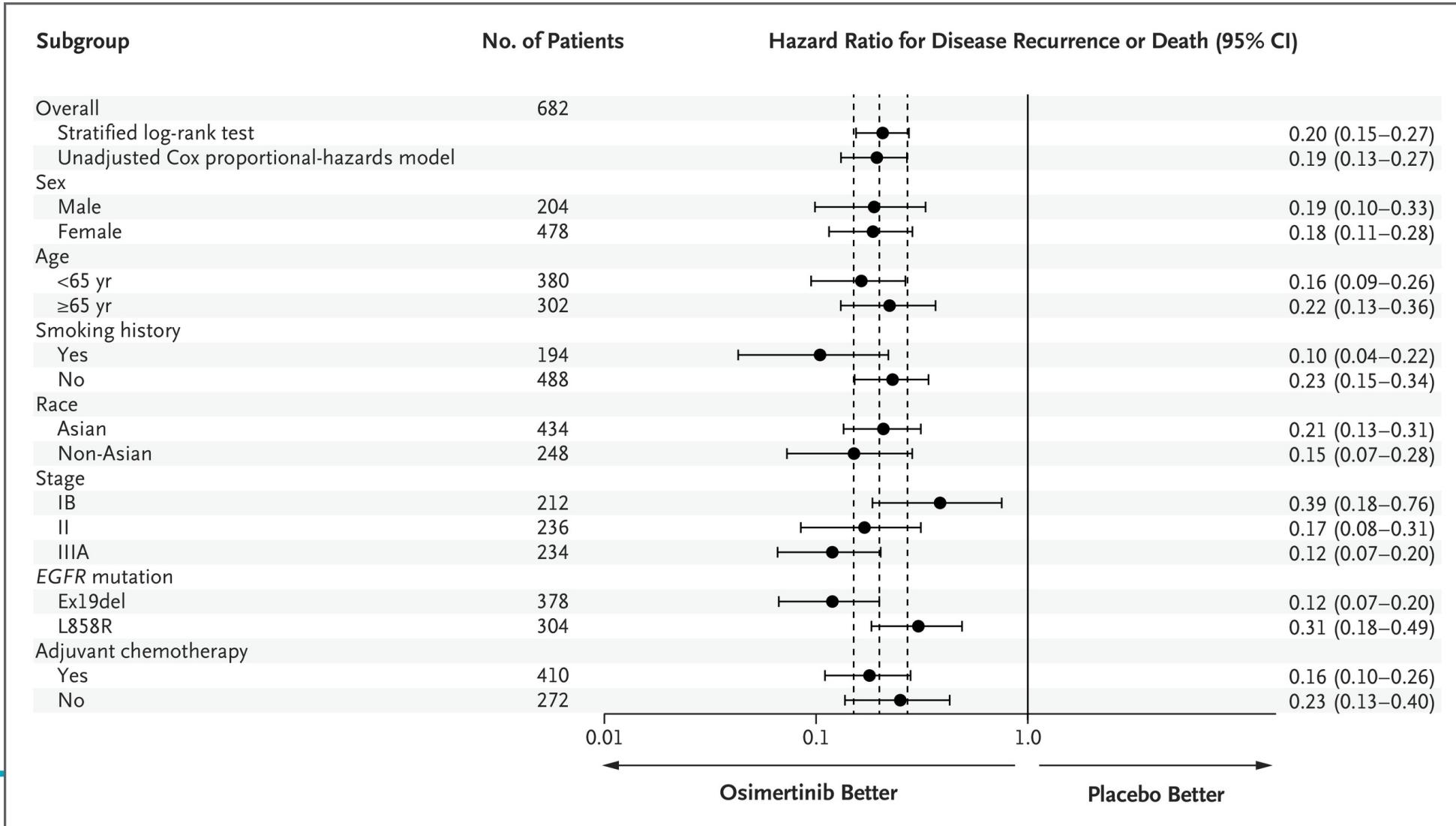
## ADAURA TRIAL

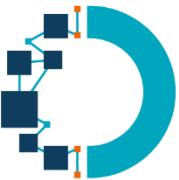




# Focus EGFR stade III

## ADAURA TRIAL

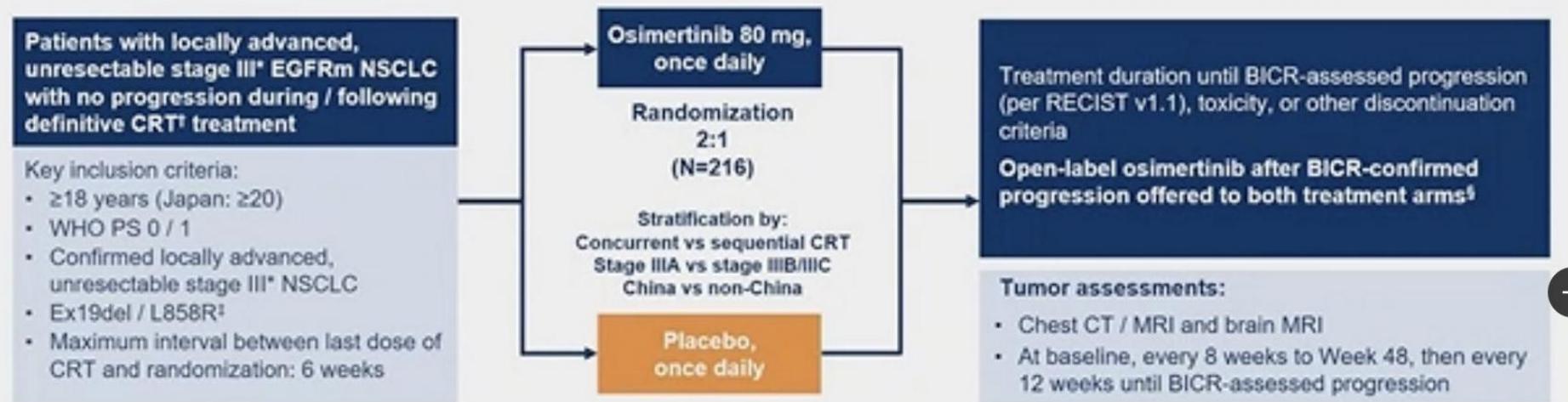




# Focus EGFR stade III

## LAURA TRIAL

## LAURA Phase 3 double-blind study design



## Endpoints

- Primary endpoint: PFS assessed by BICR per RECIST v1.1 (sensitivity analysis: PFS by investigator assessment)
  - Secondary endpoints included: OS, CNS PFS, safety

\*According to AJCC (UICC) staging (7<sup>th</sup> edition).  
†Concurrent or sequential CRT comprising  $\geq 2$  cycles of platinum-based chemotherapy (at 5 doses of weekly platinum-based chemotherapy) and a total dose of radiation of 60 Gy ± 10%.

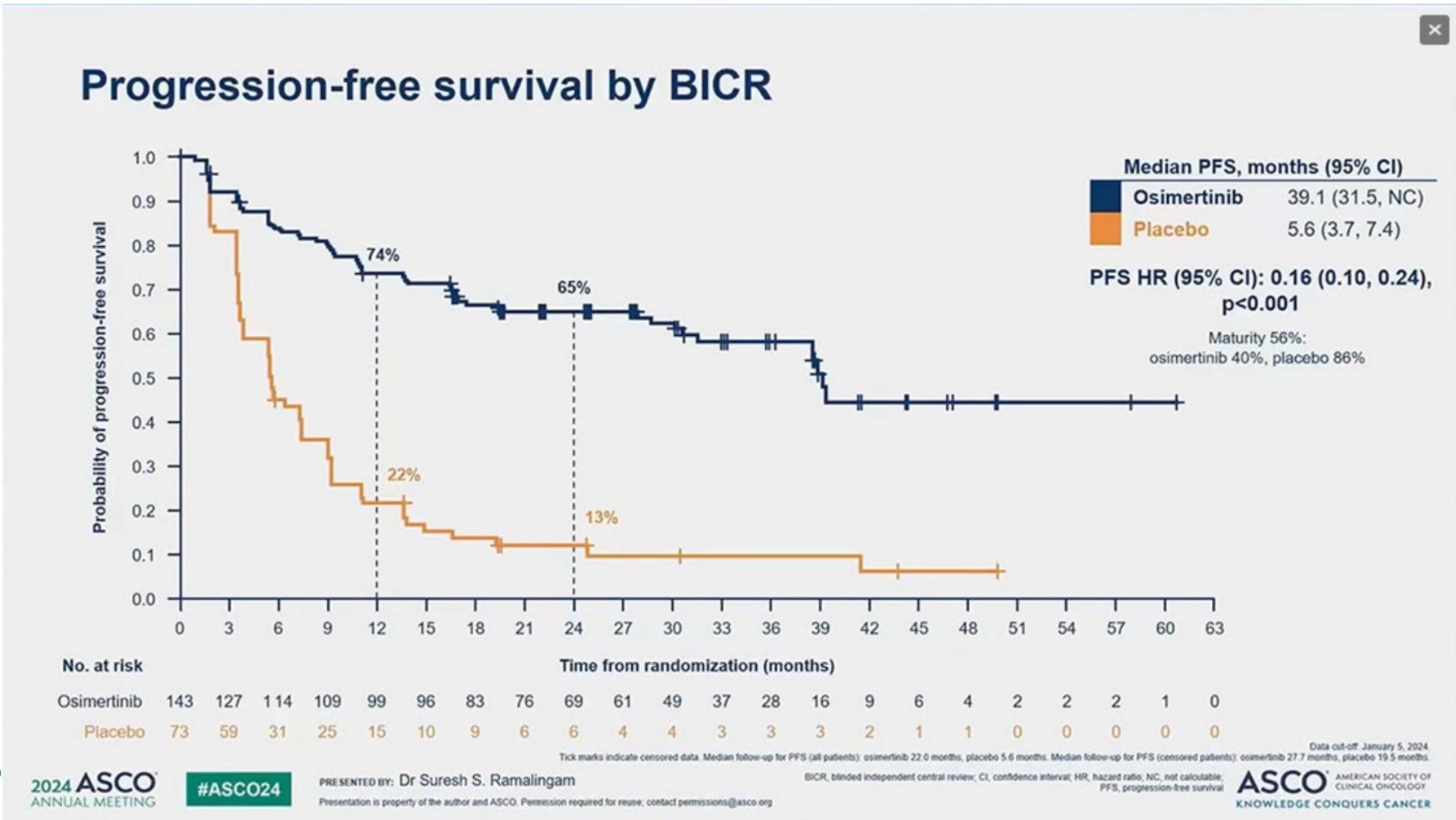
Committee on Cancer, BCR, Winkler Independent Clinical Review, CLIA, Clinical Laboratory Improvement Amendments, CT, computer tomography, CT, computed tomography, ESRD, end-stage renal disease, hemodialysis, hemodialysis-associated infection, FRS, Food and Drug Administration, fMRI, magnetic resonance imaging (MRI), National Institutes of Health, NIH, overall survival, PFS, progression-free survival, RECIST, Response Evaluation Criteria in Solid Tumors.

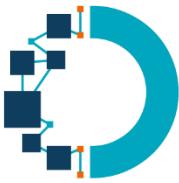
AMERICAN SOCIETY OF  
CLINICAL ONCOLOGY  
KNOWLEDGE CONQUERS CANCER



# Focus EGFR grade III

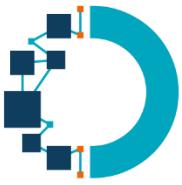
## LAURA TRIAL





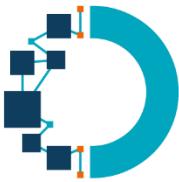
## Focus EGFR stade III

- Patients exclus de l'ensemble des essais de néo-adjuvant et de péri opératoire (sauf Keynote 671, très faible effectif)
- Seuls essais fortement positifs : ADAURA après chir pour tous stades et LAURA après RT CT pour stades III



## Quid des N2-multisite

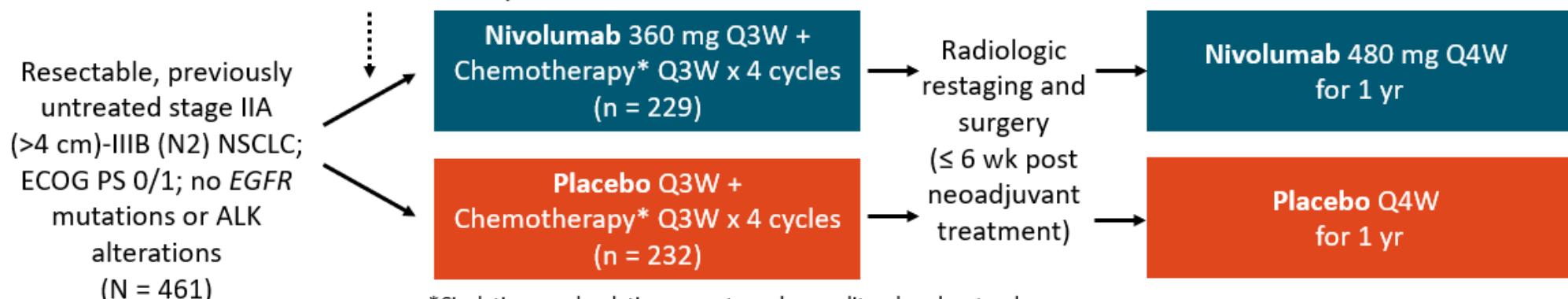
- Checkmate-816 : Aucune information concernant le N2 ( Utilisation du TNM7 qui ne fait pas cette distinction )



# CHECKMATE-77T

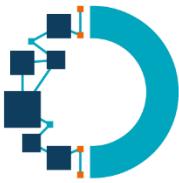
- Global randomized, double-blind phase III trial

*Stratified by histology (nonsquamous vs squamous), stage (II vs III), PD-L1 status ( $\geq 1\%$  vs  $< 1\%$  vs NE/indeterminate)*



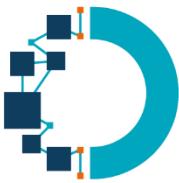
\*Cisplatin or carboplatin + pemetrexed or paclitaxel or docetaxel.

- **Primary endpoint:** EFS by BICR
- **Secondary endpoints:** pCR by BIPR, MPR by BIPR, OS, safety
- **Exploratory analyses:** EFS by pCR/MPR, EFS by adjuvant treatment



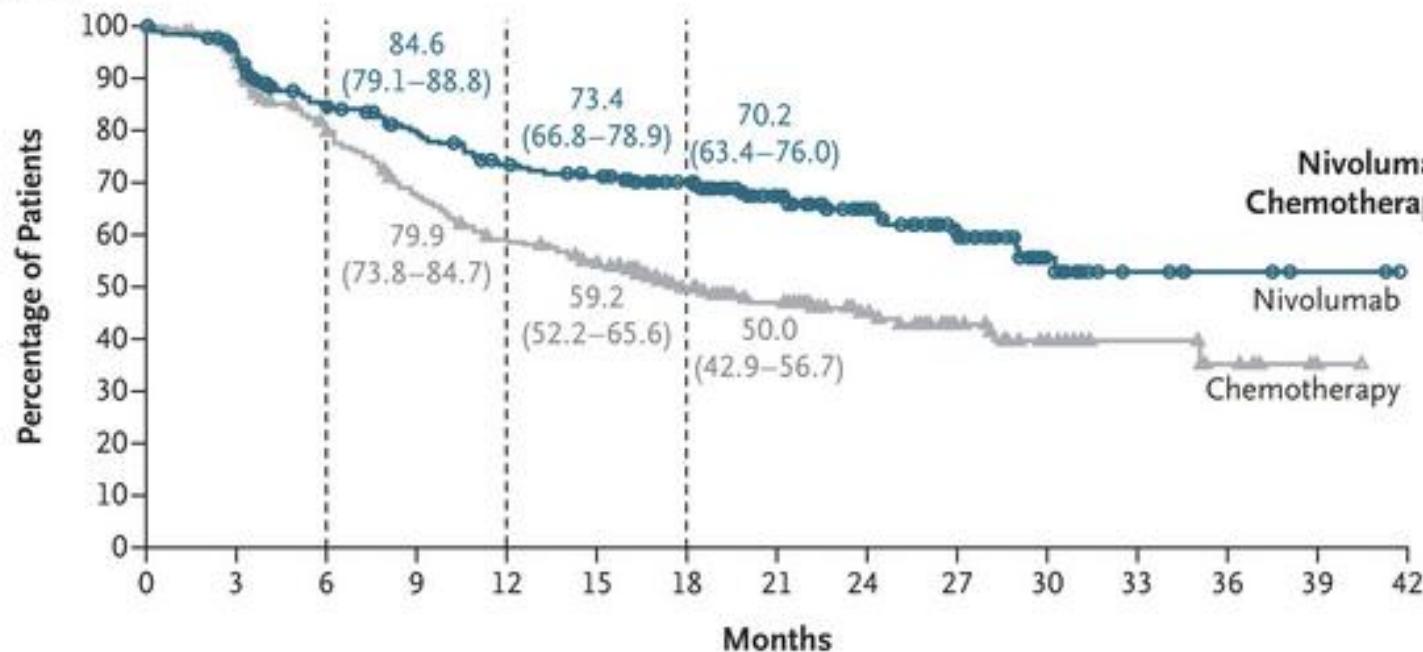
# CHECKMATE-77T

Characteristic	Nivolumab (N=229)	Chemotherapy (N=232)
Disease stage — no. (%)¶		
IIA to IIB	81 (35.4)	81 (34.9)
IIIA to IIIB	146 (63.8)	149 (64.2)
Node stage — no. (%)		
N0	80 (34.9)	87 (37.5)
N1	56 (24.5)	52 (22.4)
N2	91 (39.7)	91 (39.2)
Single-station	59 (25.8)	53 (22.8)
Multistation	31 (13.5)	38 (16.4)
Tumor histology — no. (%)		
Squamous	116 (50.7)	118 (50.9)**
Nonsquamous	113 (49.3)	114 (49.1)



# CHECKMATE-77T

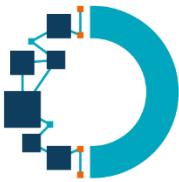
## A Event-free Survival



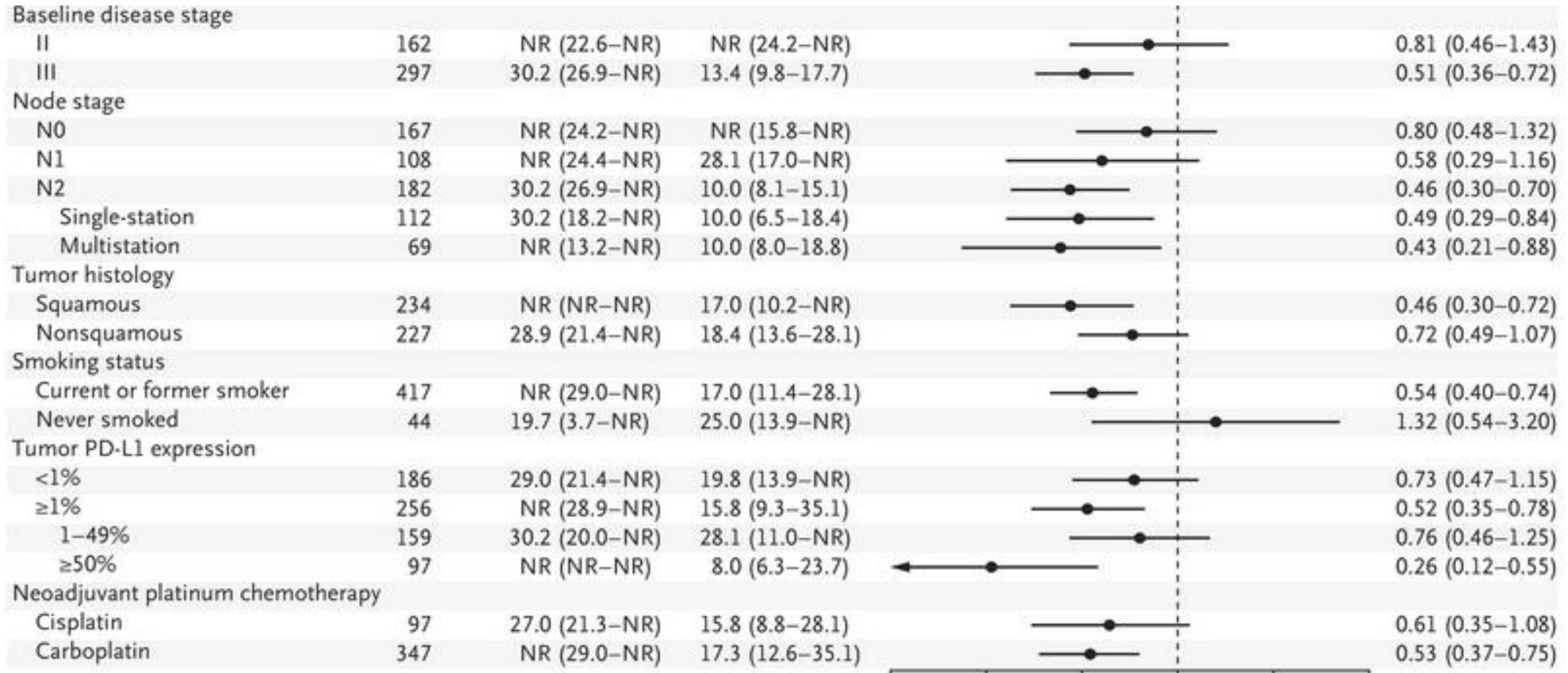
No. of Patients	Median Event-free Survival (95% CI) mo
229	NR (28.9-NR)
232	18.4 (13.6-28.1)
Hazard ratio for disease progression or death, 0.58 (97.36% CI, 0.42-0.81)	
P<0.001	

## No. at Risk

Nivolumab	229	208	173	157	141	134	115	89	69	46	20	7	4	2	0
Chemotherapy	232	204	165	138	118	106	78	59	44	29	19	10	6	1	0



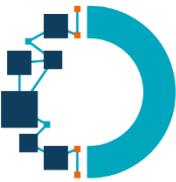
# CHECKMATE-77T



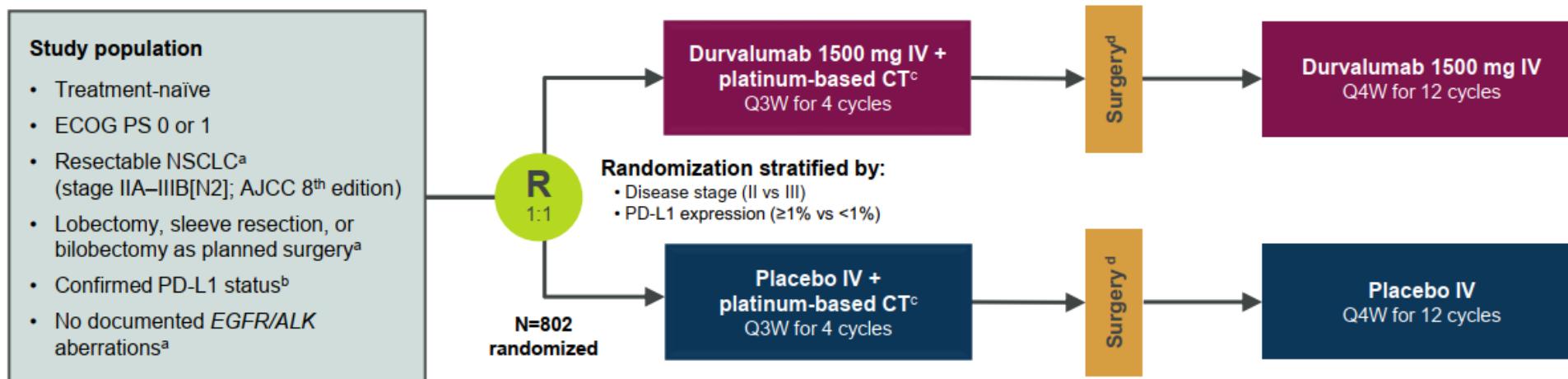
Tina Cascone et al., for the CheckMate 77T Investigators N Engl J Med 2024;390:1756-1769

Nivolumab  
Better

Chemotherapy  
Better



## AEGEAN: Study Design



**Endpoints:** All efficacy analyses performed on a modified population that excludes patients with documented EGFR/ALK aberrations<sup>e</sup>

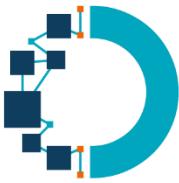
**Primary:**

- pCR by central lab (per IASLC 2020)
- EFS using BICR (per RECIST v1.1)

**Key secondary:**

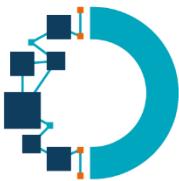
- MPR by central lab (per IASLC 2020)
- DFS using BICR (per RECIST v1.1)
- OS

John V. Heymach, et al. N Engl J Med 2023;389:1672-1684



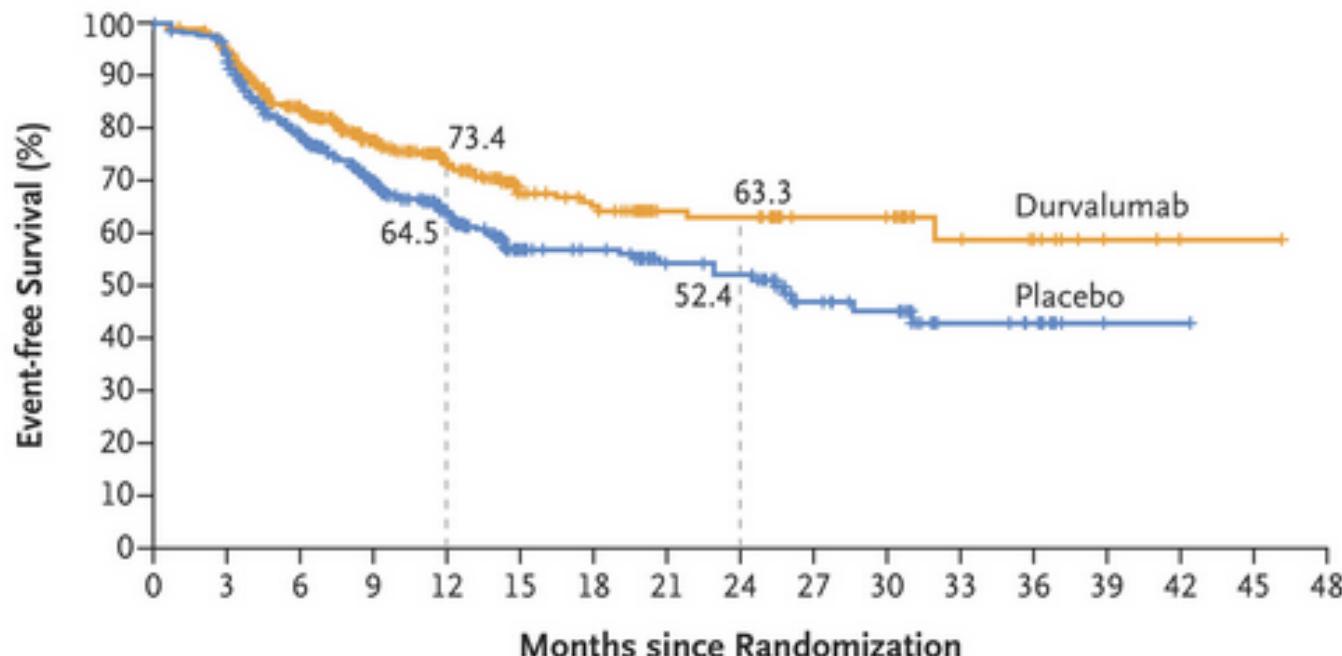
# AEGEAN

Characteristic†	Durvalumab Group (N=366)	Placebo Group (N=374)
Disease stage — no. (%)¶		
II	104 (28.4)	110 (29.4)
IIIA	173 (47.3)	165 (44.1)
IIIB	88 (24.0)	98 (26.2)
TNM classification, primary tumor — no. (%)		
T1	44 (12.0)	43 (11.5)
T2	97 (26.5)	108 (28.9)
T3	128 (35.0)	129 (34.5)
T4	97 (26.5)	94 (25.1)
TNM stage, regional lymph nodes — no. (%)		
N0	110 (30.1)	102 (27.3)
N1	75 (20.5)	87 (23.3)
N2	181 (49.5)	185 (49.5)
Single-station	141 (38.5)	132 (35.3)
Multistation	34 (9.3)	40 (10.7)



# AEGEAN

## A Event-free Survival

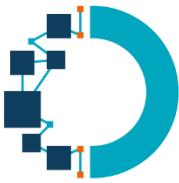


	No. of Events/ No. of Patients	Median Event-free Survival (95%CI) mo
Durvalumab	98/366 (26.8)	NR (31.9–NR)
Placebo	138/374 (36.9)	25.9 (18.9–NR)

Stratified hazard ratio for disease progression, recurrence, or death, 0.68 (95% CI, 0.53–0.88)  
P=0.004 by stratified log-rank test

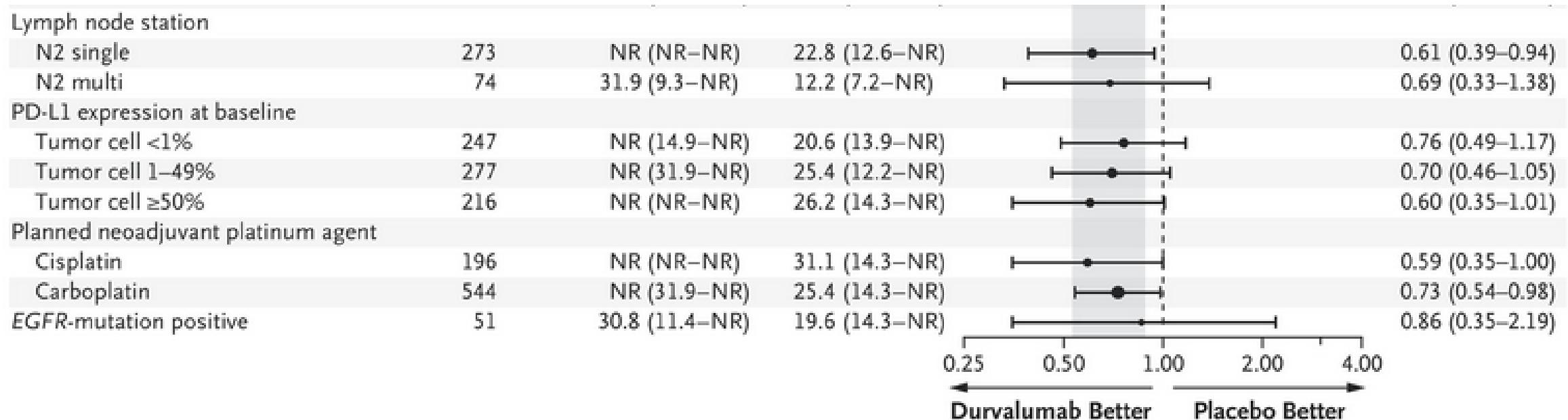
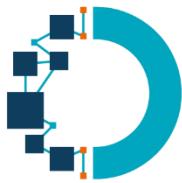
## No. at Risk

Durvalumab	366	336	271	194	140	90	78	50	49	31	30	14	11	3	1	1	0
Placebo	374	339	257	184	136	82	74	53	50	30	25	16	13	1	1	0	0



## B Subgroup Analysis

Subgroup	No. of Patients	Median Event-free Survival (95% CI)		Hazard Ratio for Disease Progression, Recurrence, or Death (95% CI)
		Durvalumab mo	Placebo mo	
All patients	740	NR (31.9–NR)	25.9 (18.9–NR)	0.68 (0.53–0.88)
Age at randomization				
<65 yr	358	NR (NR–NR)	NR (18.9–NR)	0.71 (0.47–1.04)
≥65 yr	382	NR (17.9–NR)	24.5 (13.6–31.1)	0.69 (0.48–0.97)
Sex				
Male	530	NR (31.9–NR)	22.9 (14.3–31.1)	0.61 (0.44–0.82)
Female	210	NR (17.5–NR)	NR (13.6–NR)	0.95 (0.58–1.56)
ECOG performance-status score				
0	506	NR (31.9–NR)	25.4 (14.3–NR)	0.65 (0.47–0.89)
1	234	NR (21.8–NR)	25.9 (14.3–NR)	0.78 (0.49–1.22)
Race				
Asian	307	NR (NR–NR)	25.4 (13.9–NR)	0.60 (0.40–0.90)
Non-Asian	433	31.9 (21.8–NR)	26.2 (14.3–NR)	0.76 (0.54–1.06)
Geographic region				
Asia	305	NR (NR–NR)	22.9 (13.9–NR)	0.62 (0.41–0.93)
Europe	281	31.9 (31.9–NR)	NR (14.3–NR)	0.75 (0.49–1.14)
North America	86	NR (21.8–NR)	24.5 (10.0–NR)	0.69 (0.27–1.62)
South America	68	16.5 (13.0–NR)	11.0 (7.1–NR)	0.71 (0.33–1.53)
Smoking status				
Current smoker	190	NR (NR–NR)	14.3 (8.1–NR)	0.48 (0.28–0.80)
Former smoker	443	NR (31.9–NR)	25.9 (19.5–NR)	0.79 (0.57–1.10)
Never smoked	107	NR (NR–NR)	24.5 (14.3–NR)	0.76 (0.35–1.58)
Histologic features				
Squamous	360	NR (31.9–NR)	26.2 (13.0–NR)	0.71 (0.49–1.03)
Nonsquamous	375	NR (NR–NR)	25.4 (14.3–NR)	0.69 (0.48–0.99)
Disease stage				
II	214	NR (NR–NR)	31.1 (25.4–NR)	0.76 (0.43–1.34)
IIIA	338	NR (NR–NR)	19.5 (11.7–NR)	0.57 (0.39–0.83)
IIIB	186	31.9 (11.7–NR)	18.9 (11.8–NR)	0.83 (0.52–1.32)





# Définition de résectabilité

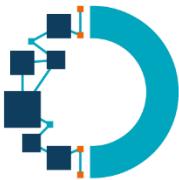
	N0	N1	N2 SINGLE (non-bulky, non-invasive)	N2 MULTI (non-bulky, non-invasive)	N2 BULKY <sup>1</sup>	N2 INVASIVE	N3
T1-2	NOT STAGE III DISEASE	NOT STAGE III DISEASE		POTENTIALLY RESECTABLE*			
T3 size / satellite / invasion	NOT STAGE III DISEASE			POTENTIALLY RESECTABLE*			
T4 size / satellite				POTENTIALLY RESECTABLE*			
T4 invasion	POTENTIALLY RESECTABLE <sup>§</sup>	POTENTIALLY RESECTABLE <sup>§</sup>	POTENTIALLY RESECTABLE <sup>§</sup>	POTENTIALLY RESECTABLE <sup>§</sup>			

CHECKMATE816  
PDL 1  $\geq 1\%$

PACIFIC

\*Multiple station N2: case-by-case discussion; the exact number of nodes/stations cannot be defined

<sup>1</sup>Bulky N2: lymph nodes with a short-axis diameter  $>2.5-3$  cm; in specific situations of *highly selected patients*, including those patients in multidisciplinary trials with surgery as local therapy can be discussed



# Définition de résectabilité

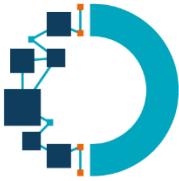
	N0	N1	N2 SINGLE (non-bulky, non-invasive)	N2 MULTI (non-bulky, non-invasive)	N2 BULKY <sup>1</sup>	N2 INVASIVE	N3
T1-2	NOT STAGE III DISEASE	NOT STAGE III DISEASE					
T3 size / satellite / invasion	NOT STAGE III DISEASE						
T4 size / satellite							
T4 invasion							

**CHECKMATE816**  
PDL 1  $\geq 1\%$

**PACIFIC**

\*Multiple station N2: case-by-case discussion; the exact number of nodes/stations cannot be defined

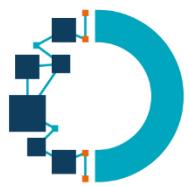
<sup>1</sup>Bulky N2: lymph nodes with a short-axis diameter  $>2.5-3$  cm; in specific situations of *highly selected patients*, including those patients in multidisciplinary trials with surgery as local therapy can be discussed

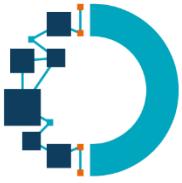


# Cas clinique de Mr F S

## Façon RMM ou EPP

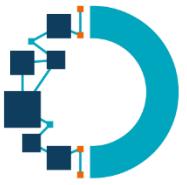
- Homme 80 ans, crachats hémoptoïques 04/2024, opacité LM connue depuis 09/2023
  - Hypothyroïdie supplémentée, varices, tabac jeune
  - VEMS 93%, pas de DLCO
- F° 11/09/24: atypies ADK dans LM
- Ponction LID 12/11/24: ADK , PDL 1 à 5%, ALK-, muté BRAF V600E
- RCP 20/11/24: lésion classée cT4N0M0 du LID , LM pas forcément retenue car foyer DDB historique, proposition de chirurgie





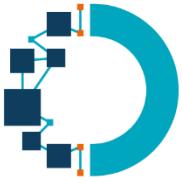
## Mr F S Suite

- Cs chir le 25/11/24: chir prévue le 20/12 finalement reportée pour DLCO effondrée, réhabilitation, transplantation ...
- Chir le 01/04/25: bilobectomy inf sans pb , atélectasie partielle LM et masse LID
- Anapath: ADK acineux double LM et LID de 8 et 9cm , STAS +, embols+, pT4N2R0 (N2 en 8 et 3)
- Pas de ttt adjuvant (âge et compliance)
- TDM 09/2025: nodule LSD para-scissural...



# Mr F Suite





# Mr F S

## Discussion

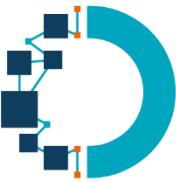
- Impact du bronchiolo sur indication néoadjuvant ?
- Impact mutation BRAF V600E?
- En fait double T4 (taille LID et 2 nodules dans 2 lobes différents)
- Pourquoi pas d'EBUS ou M°?



# Mr F S

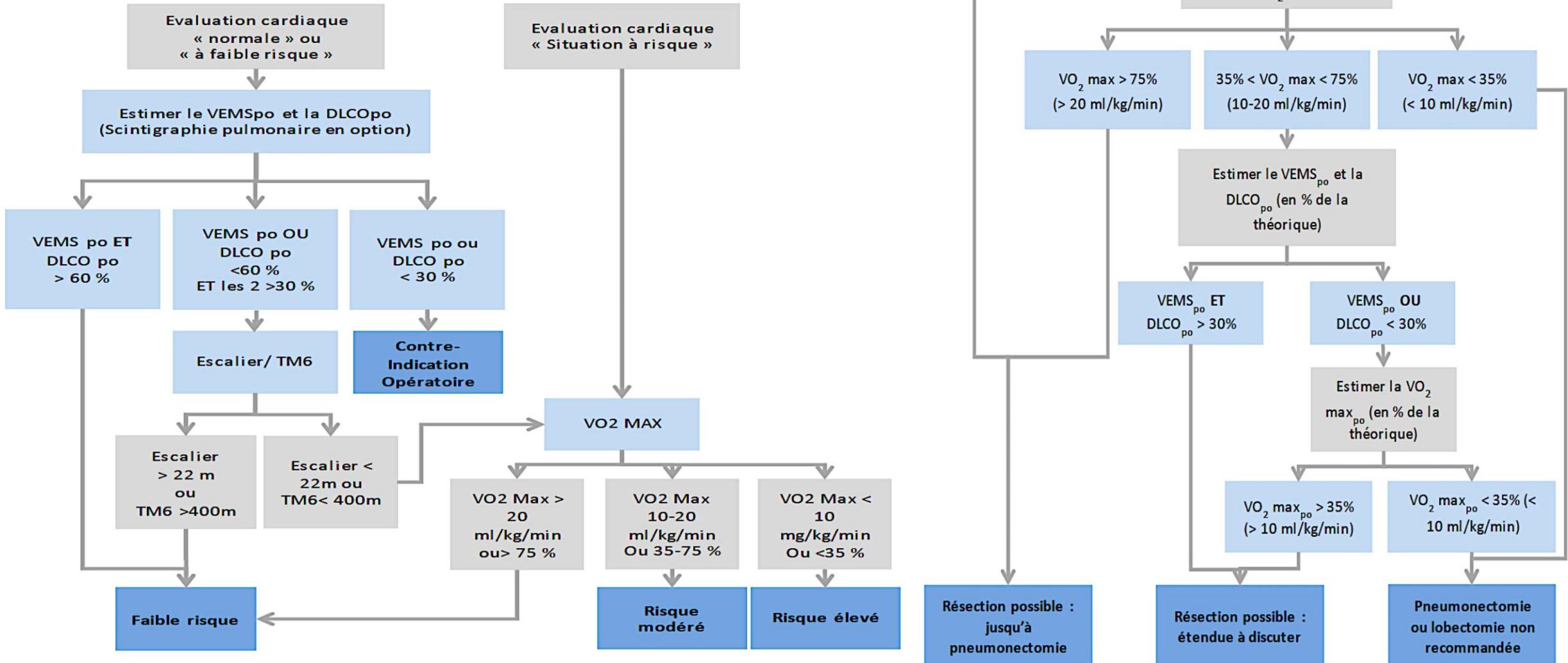
## Discussion

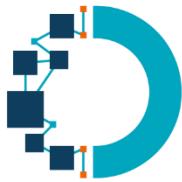
- Ne pas tenir compte de la DLCO: effet shunt du bronchiolo ! Perte de 4 mois ici.
- Compliance des patients:
  - Perte de temps diagnostique
  - Comment faire accepter le systémique quand nécessaire?
  - Comment expliquer que la chirurgie interviendra après?
  - Age : pb pour systémique? Pour le chir?



# Synthèse

## Bilan opérabilité respiratoire



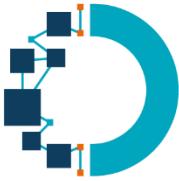


# Synthèse

## Bilan opérabilité cardiaque

Facteurs de risque	Score
Créatinine > 176 µMoles/l	1
Cardiopathie ischémique	1,5
Maladie cérébro-vasculaire	1,5
Pneumonectomie envisagée	1,5
<i>Interprétation :</i>	
<i>Valeur du score</i>	<i>Mortalité post-opératoire</i>
<i>Score = 0 (A)</i>	<i>1.5%</i>
<i>Score 1 à 1,5 (B)</i>	<i>5.8%</i>
<i>Score &gt;1,5-2,5 (C)</i>	<i>9%</i>
<i>Score &gt;2,5 (D)</i>	<i>23%</i>

- Penser Epreuve de stress cardio effort ou pharmaco si FDR +:
  - Chir pulm tjs valable
  - Idm
  - Insulinothérapie
  - AVC
  - I renale
- +/- >60ans, jamais exploré

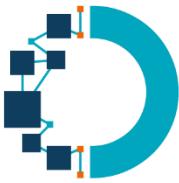


# Synthèse

## Reco staging ganglionnaire : EBUS, M°, EUS

- Tumeur pulmonaire avec un médiastin PATHOLOGIQUE (adp petit diamètre  $\geq 10\text{mm}$  et/ou hyperfixation en TEP)
- Médiastin NORMAL et tumeur avec les caractéristiques suivantes :
  - Plus grand axe  $\geq 30\text{ mm}$
  - Localisation centrale
  - Faible captation du traceur sur le TEP

De Leyn et al. ESTS guidelines. Trans Lung Cancer Res 2014; Vilman et al. ESGE ERS ESTS guidelines 2015



# Synthèse

## Chirurgie et CT-Immuno

- Checkmate 816= Moins de conversion que séries précédentes et durée opératoire plus courte dans le groupe immuno-chimio
- Taux de complication similaire

