CANCEROPOLE EST 2025

LES NOUVEAUTÉS EN IMMUNOTHÉRAPIE DANS LE CANCER BRONCHIQUE

DR LUCILE PABST

UNITÉ D'ONCOLOGIE THORACIQUE

CHRU DE STRASBOURG

UMR1260 - INSERM

CBPC

- LOCALEMENT AVANCÉ
- MÉTASTATIQUE

CBNPC

- LOCALISÉ
- LOCALEMENT AVANCÉ – NON RÉSÉCABLE
- MÉTASTATIQUE

LE CANCER BRONCHIQUE À PETITES CELLULES

CBPC LOCALEMENT AVANCÉ : ADRIATIC

- Stage I–III LS-SCLC (stage I/II inoperable)
- WHO PS 0 or 1
- Had not progressed following cCRT*
- PCI* permitted before randomisation

N=730

R†

Stratified by:
Disease stage (I/II vs III)
PCI (yes vs no)

- **Durvalumab** N=264
- **Placebo** N=266
- **Durvalumab + tremelimumab** N=200

Treatment until investigator-determined PD or intolerable toxicity, or for a **maximum of 24 months**

Dual primary endpoints:
- D vs P
  - PFS,‡ OS

Key secondary endpoints:
- D+T vs P
  - PFS,‡ OS

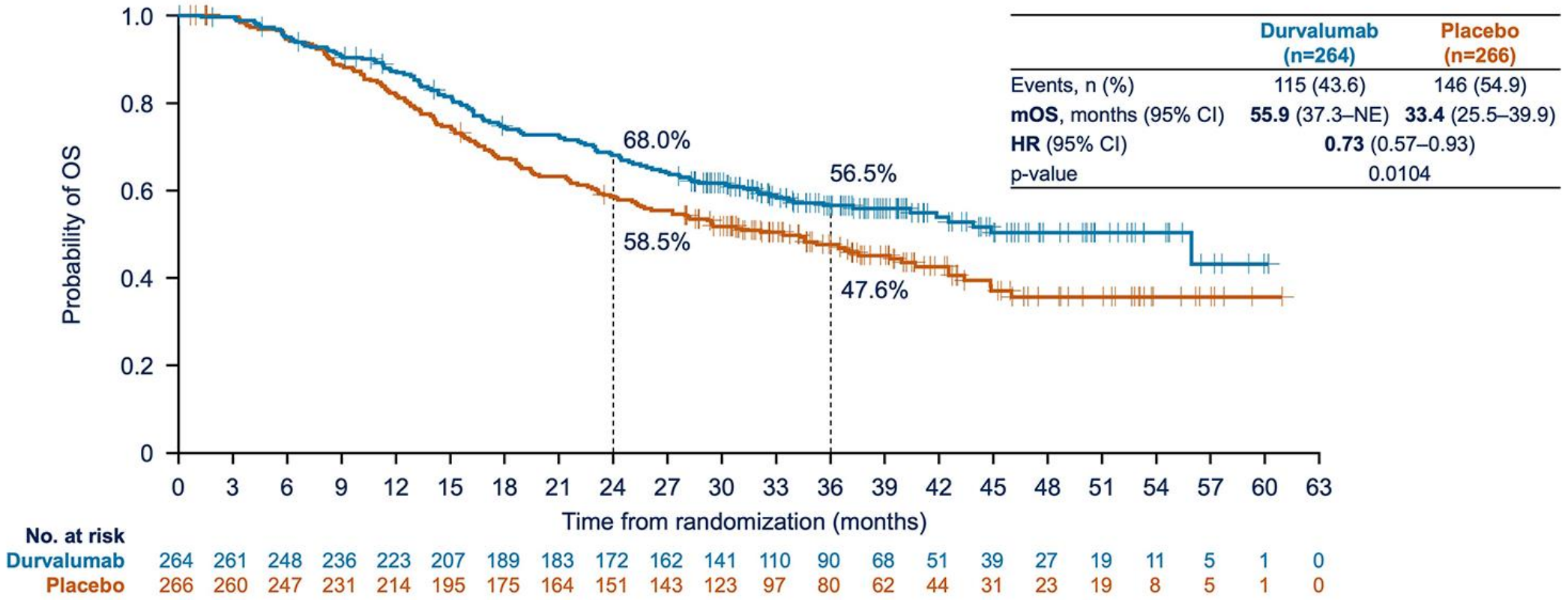
Other secondary endpoints:
- PFS/OS landmarks, safety

PCI/cCRT components (in line with standards of care)*
- PCI delivered before randomisation, as clinically indicated
- Four cycles of platinum (cisplatin or carboplatin) and etoposide (three permitted†)
- RT: 60–66 Gy QD over 6 weeks or 45 Gy BID over 3 weeks‡

ITT population	Durvalumab (n = 264)	Placebo (n = 266)
Received PCI, %	54	54
Carboplatin / cisplatin CT,§ %	34 / 66	33 / 67
BID / QD thoracic RT, %	26 / 74	30 / 70

Spigel et al, ASCO 2024

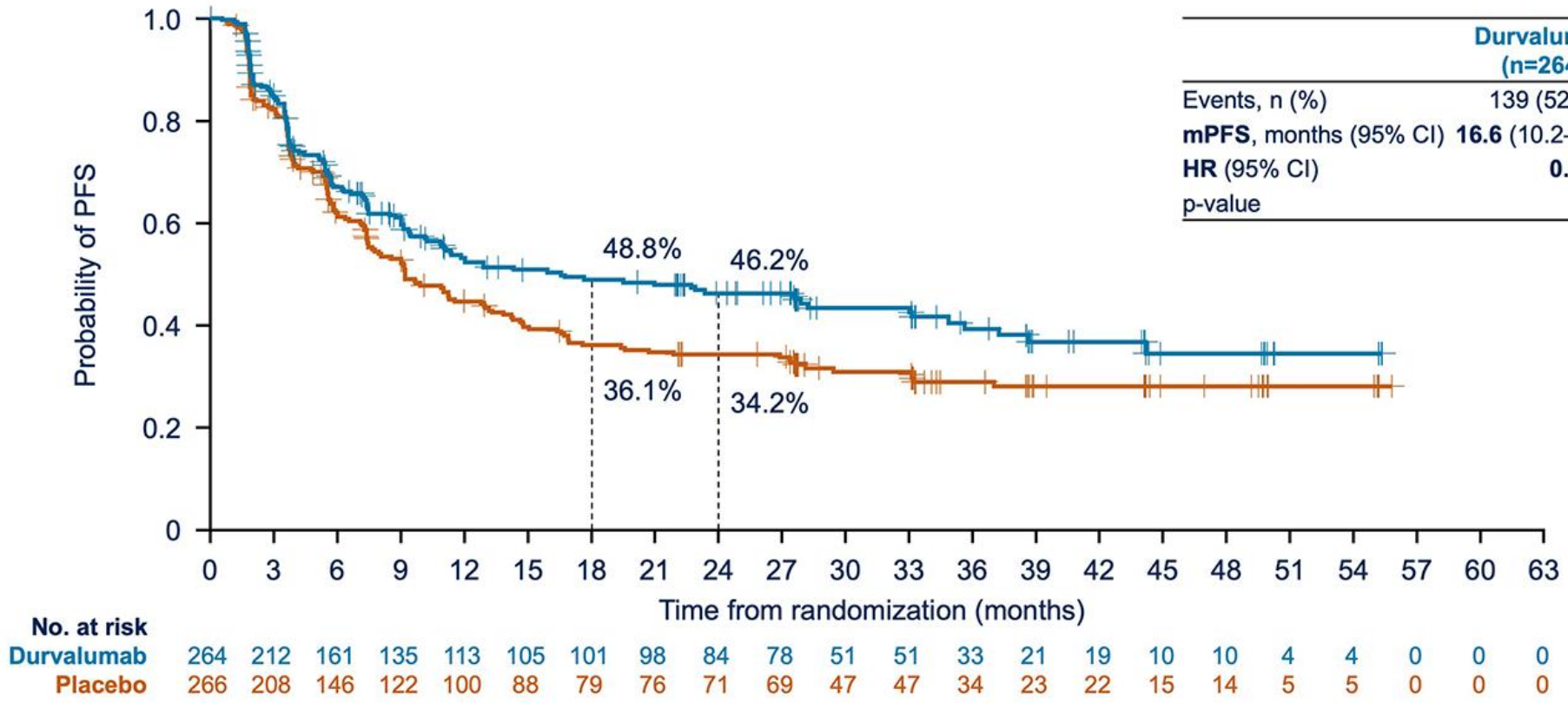
CBPC LOCALEMENT AVANCÉ : ADRIATIC



	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	115 (43.6)	146 (54.9)
mOS, months (95% CI)	**55.9** (37.3–NE)	**33.4** (25.5–39.9)
HR (95% CI)	**0.73** (0.57–0.93)	
p-value	0.0104	

Spigel et al, ASCO 2024

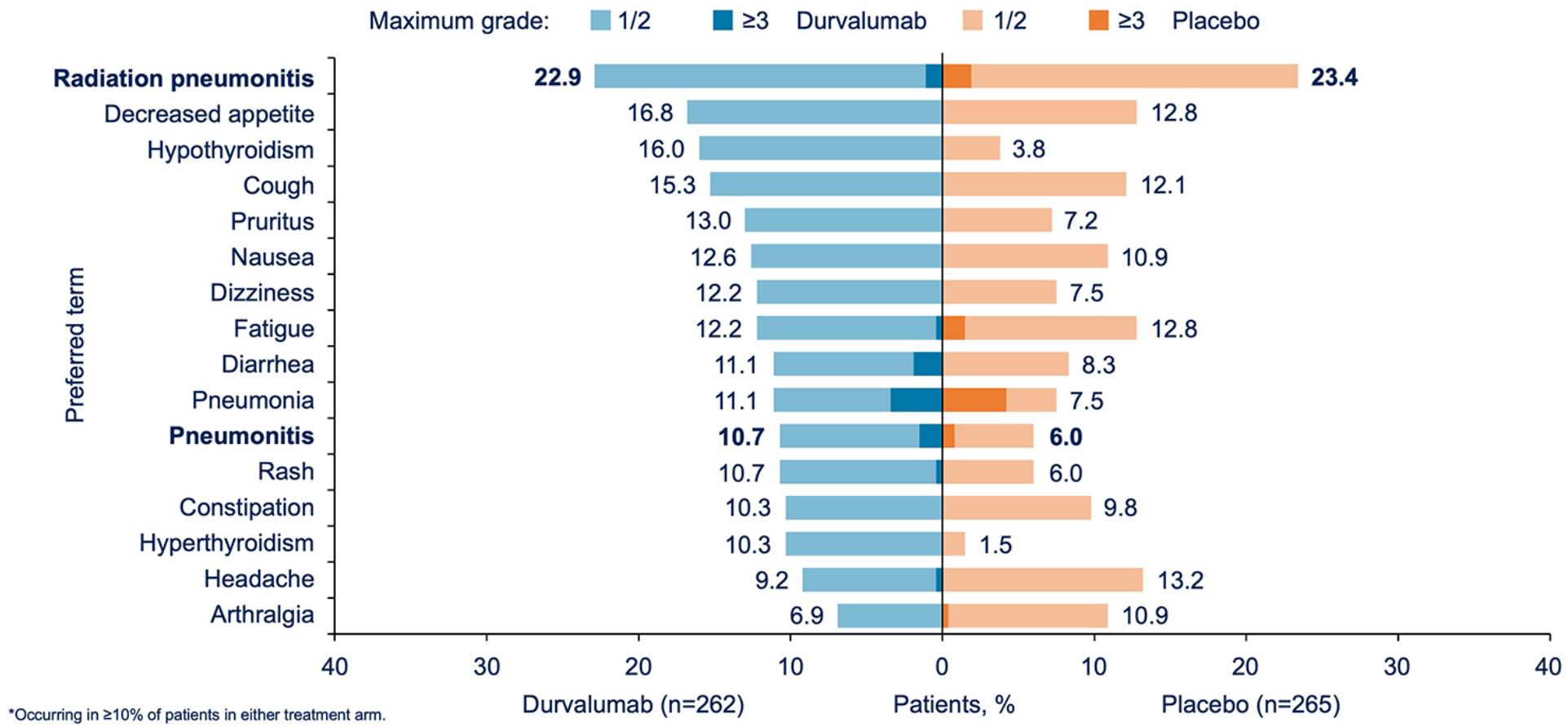
CBPC LOCALEMENT AVANCÉ : ADRIATIC



	Durvalumab (n=264)	Placebo (n=266)
Events, n (%)	139 (52.7)	169 (63.5)
mPFS, months (95% CI)	**16.6** (10.2–28.2)	**9.2** (7.4–12.9)
HR (95% CI)	**0.76** (0.61–0.95)	
p-value	0.0161	

Spigel et al, ASCO 2024

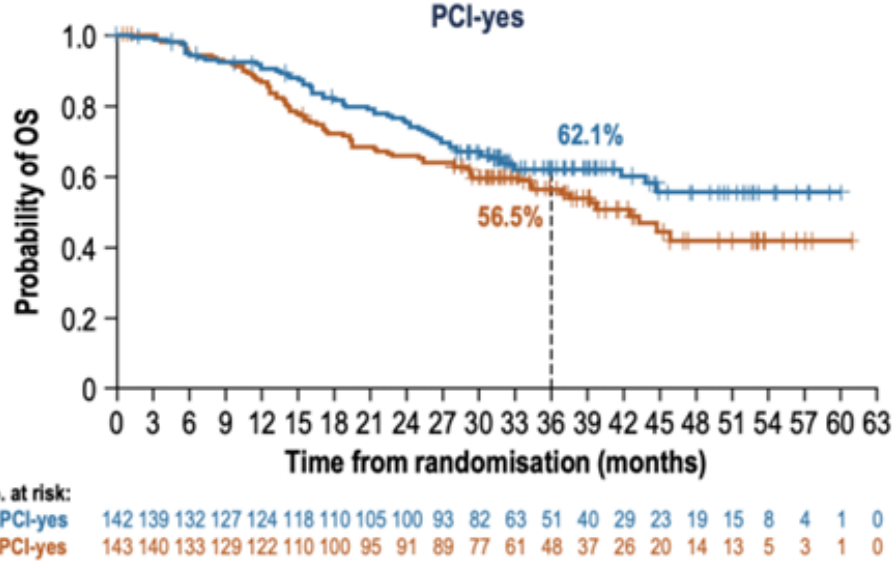
CBPC LOCALEMENT AVANCÉ : ADRIATIC

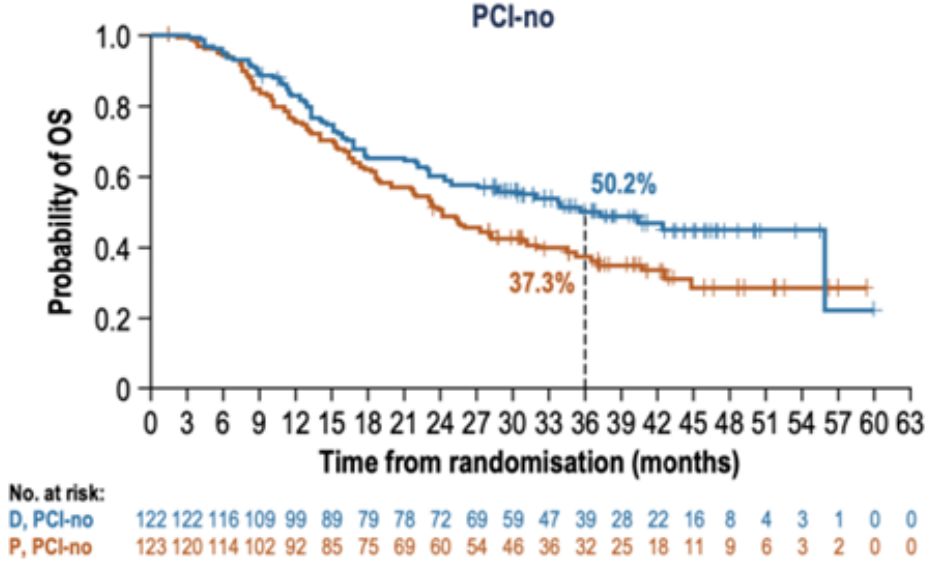


Spigel et al, ASCO 2024

CBPC LOCALEMENT AVANCÉ : ADRIATIC

	PCI-yes		PCI-no		ITT	
	D (n = 142)	P (n = 143)	D (n = 122)	P (n = 123)	D (n = 264)	P (n = 266)
Median OS (95% CI), months	NR (43.9–NE)	42.5 (33.4–NE)	37.3 (24.3–NE)	24.1 (18.8–31.1)	55.9 (37.3–NE)	33.4 (25.5–39.9)
3-year OS, %	62.1	56.5	50.2	37.3	56.5	47.6
HR (95% CI)	0.75 (0.52–1.07)*		0.71 (0.51–0.99)*		0.73 (0.57–0.93)†	
Multivariable HR (95% CI)	0.72 (0.50–1.03)‡		0.73 (0.52–1.02)‡		–	



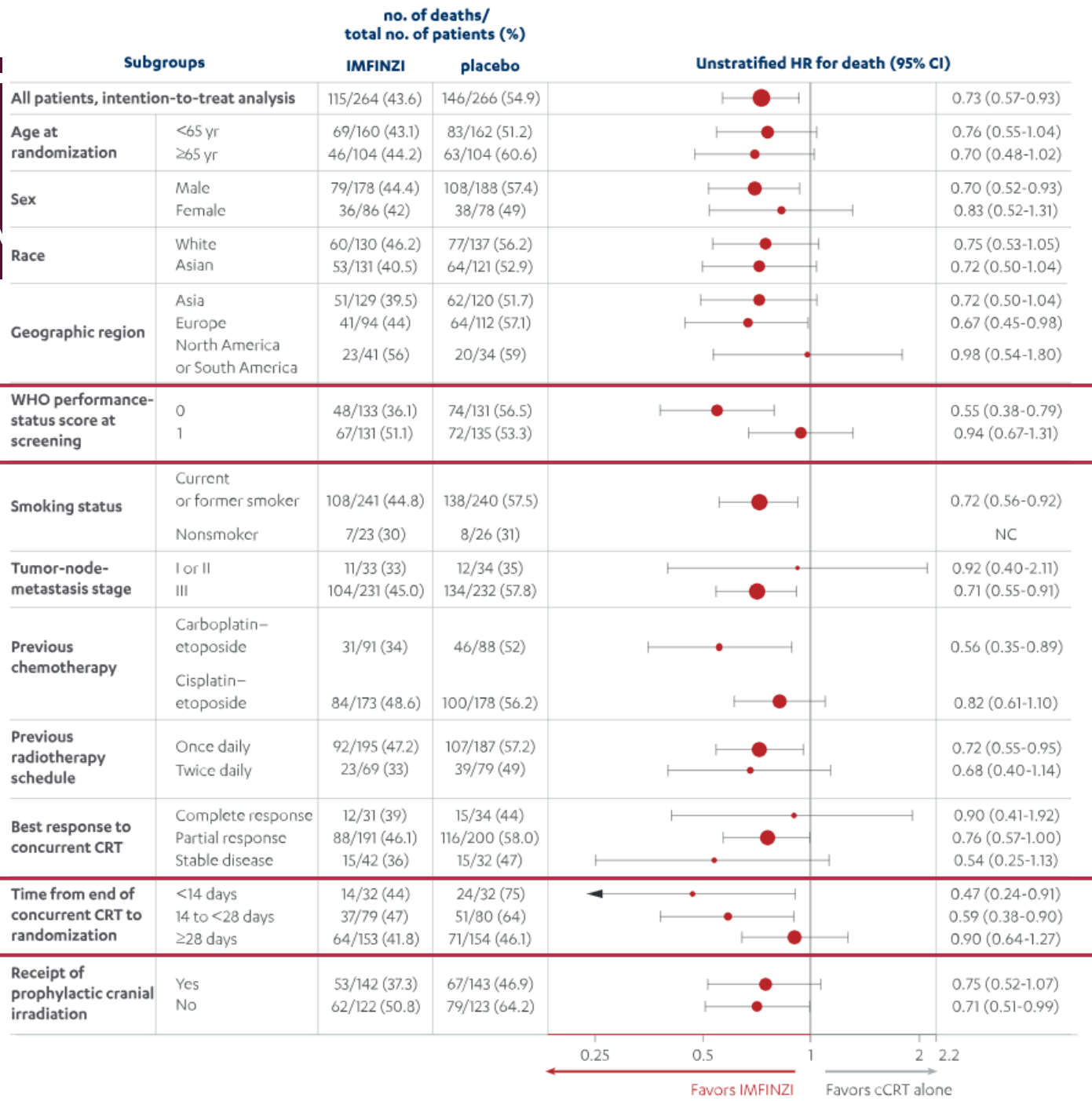


CI, confidence interval; NE, not estimable; NR, not reached; yr, year.

*Subgroup HRs and CIs calculated using an unstratified Cox proportional hazards model.
†ITT HR and CIs calculated using a Cox proportional hazards model stratified by receipt of PCI.
‡Multivariable analysis interaction p-value 0.96.

Spigel et al, ASCO 2024

CBPC LOCALEN



Subgroups		no. of deaths/ total no. of patients (%) IMFINZI	placebo	Unstratified HR for death (95% CI)
All patients, intention-to-treat analysis		115/264 (43.6)	146/266 (54.9)	0.73 (0.57-0.93)
Age at randomization	<65 yr	69/160 (43.1)	83/162 (51.2)	0.76 (0.55-1.04)
	≥65 yr	46/104 (44.2)	63/104 (60.6)	0.70 (0.48-1.02)
Sex	Male	79/178 (44.4)	108/188 (57.4)	0.70 (0.52-0.93)
	Female	36/86 (42)	38/78 (49)	0.83 (0.52-1.31)
Race	White	60/130 (46.2)	77/137 (56.2)	0.75 (0.53-1.05)
	Asian	53/131 (40.5)	64/121 (52.9)	0.72 (0.50-1.04)
Geographic region	Asia	51/129 (39.5)	62/120 (51.7)	0.72 (0.50-1.04)
	Europe	41/94 (44)	64/112 (57.1)	0.67 (0.45-0.98)
	North America or South America	23/41 (56)	20/34 (59)	0.98 (0.54-1.80)
WHO performance-status score at screening	0	48/133 (36.1)	74/131 (56.5)	0.55 (0.38-0.79)
	1	67/131 (51.1)	72/135 (53.3)	0.94 (0.67-1.31)
Smoking status	Current or former smoker	108/241 (44.8)	138/240 (57.5)	0.72 (0.56-0.92)
	Nonsmoker	7/23 (30)	8/26 (31)	NC
Tumor-node-metastasis stage	I or II	11/33 (33)	12/34 (35)	0.92 (0.40-2.11)
	III	104/231 (45.0)	134/232 (57.8)	0.71 (0.55-0.91)
Previous chemotherapy	Carboplatin–etoposide	31/91 (34)	46/88 (52)	0.56 (0.35-0.89)
	Cisplatin–etoposide	84/173 (48.6)	100/178 (56.2)	0.82 (0.61-1.10)
Previous radiotherapy schedule	Once daily	92/195 (47.2)	107/187 (57.2)	0.72 (0.55-0.95)
	Twice daily	23/69 (33)	39/79 (49)	0.68 (0.40-1.14)
Best response to concurrent CRT	Complete response	12/31 (39)	15/34 (44)	0.90 (0.41-1.92)
	Partial response	88/191 (46.1)	116/200 (58.0)	0.76 (0.57-1.00)
	Stable disease	15/42 (36)	15/32 (47)	0.54 (0.25-1.13)
Time from end of concurrent CRT to randomization	<14 days	14/32 (44)	24/32 (75)	0.47 (0.24-0.91)
	14 to <28 days	37/79 (47)	51/80 (64)	0.59 (0.38-0.90)
	≥28 days	64/153 (41.8)	71/154 (46.1)	0.90 (0.64-1.27)
Receipt of prophylactic cranial irradiation	Yes	53/142 (37.3)	67/143 (46.9)	0.75 (0.52-1.07)
	No	62/122 (50.8)	79/123 (64.2)	0.71 (0.51-0.99)

Spigel et al, ASCO 2024

CBPC MÉTASTATIQUE : BMS 986012

A randomized, open-label phase 2 study of BMS-986012 (anti-Fuc-GM1) + NIVO + chemo as first-line therapy for ES-SCLC

Key eligibility criteria
- Age ≥ 18 years
- Histologically/cytologically confirmed ES-SCLC[a]
- No prior systemic therapy/ newly diagnosed
- ≥ 1 measurable lesion
- ECOG PS (0/1)

Stratification
- Liver metastases (yes/no)
- ECOG PS (0/1)

R 1:1

Induction
4 cycles (1 cycle = 21 days)

Maintenance
≤ 2 years or until progression, unacceptable toxicity, or death

- BMS-986012 420 mg + NIVO 360 mg IV Q3W + chemo[b] → BMS-986012 560 mg + NIVO 480 mg IV Q4W
- NIVO 360 mg IV Q3W + chemo[b] → NIVO 480 mg IV Q4W

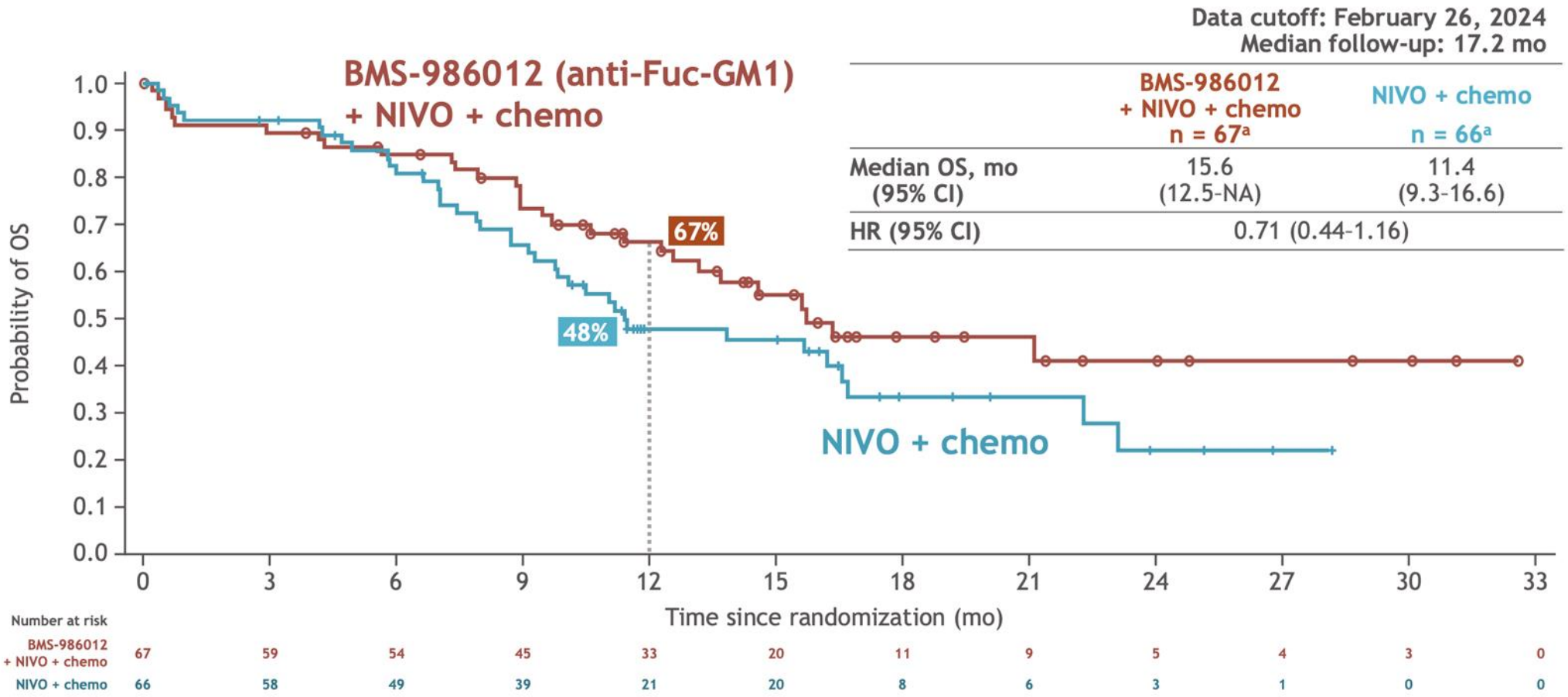
Primary endpoints
- Safety
- PFS by BICR (per RECIST v1.1)

Secondary endpoints
- OS
- ORR, DOR and TTR by BICR (per RECIST v1.1)
- PFS by investigator (per RECIST v1.1)
- Immunogenicity

Ad hoc exploratory endpoint
- OS by baseline brain metastases

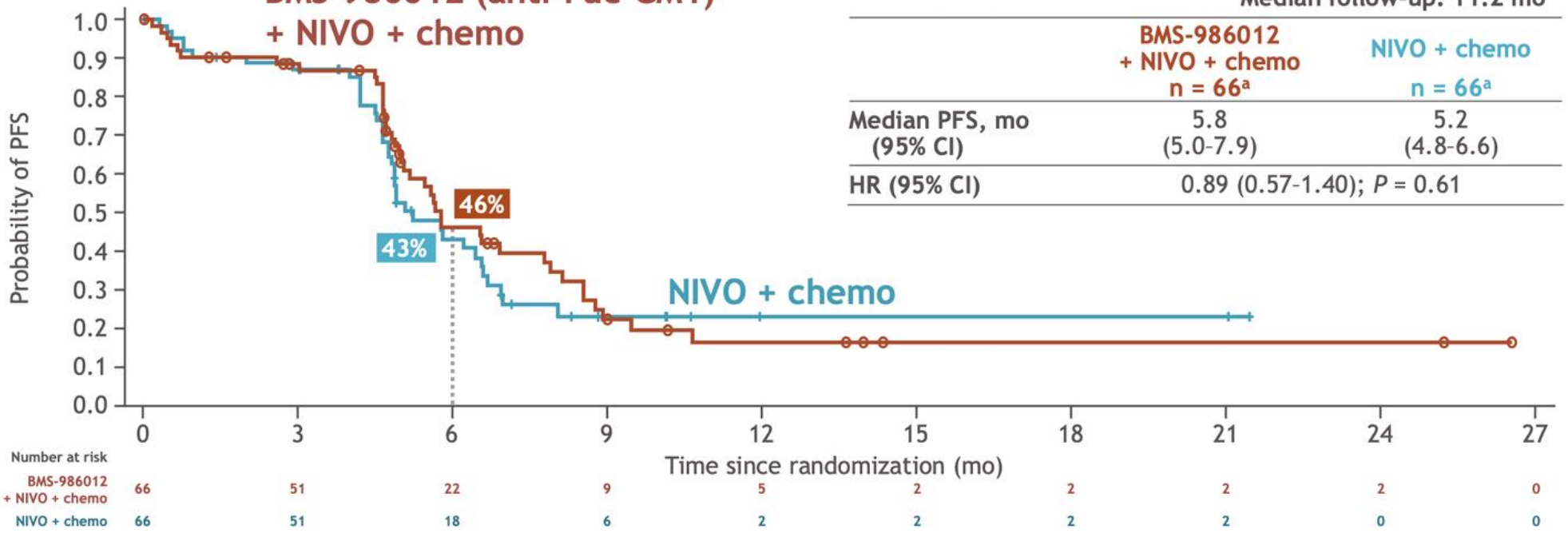
- The prespecified interim analysis took place when ~75% of PFS information was available: data cutoff August 28, 2023
- An additional analysis took place after longer follow-up to a allow a more meaningful assessment of OS: data cutoff February 26, 2024

CBPC MÉTASTATIQUE : BMS 986012



	BMS-986012 + NIVO + chemo n = 67[a]	NIVO + chemo n = 66[a]
Median OS, mo (95% CI)	15.6 (12.5-NA)	11.4 (9.3-16.6)
HR (95% CI)	0.71 (0.44-1.16)	

CBPC MÉTASTATIQUE : BMS 986012



Interim analysis (data cutoff: August 28, 2023)
Median follow-up: 11.2 mo

	BMS-986012 + NIVO + chemo n = 66[a]	NIVO + chemo n = 66[a]
Median PFS, mo (95% CI)	5.8 (5.0-7.9)	5.2 (4.8-6.6)
HR (95% CI)	0.89 (0.57-1.40); *P* = 0.61	

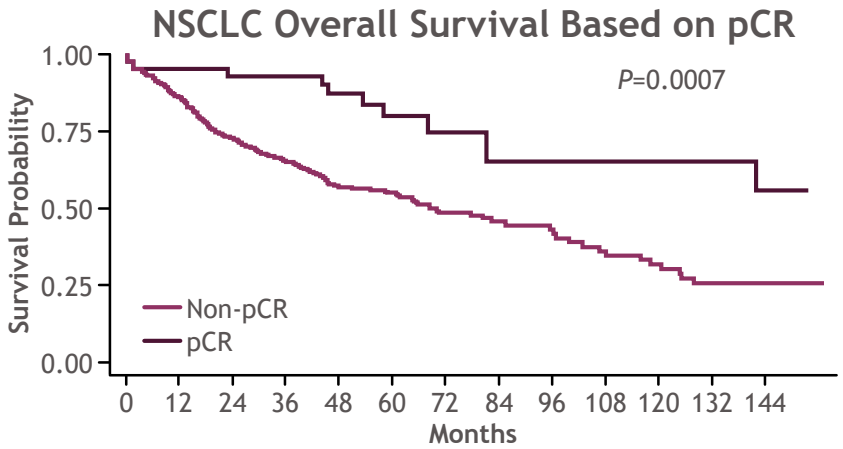
- At the later February 2024 data cutoff (median follow-up of 17.2 mo), median PFS was 5.8 mo (95% CI, 5.0-7.9) with **BMS-986012 + NIVO + chemo** vs 5.1 mo (95% CI, 4.8-6.6) with **NIVO + chemo**, HR 0.81 (95% CI, 0.53-1.23, *P* = 0.32)
  - The 12-month PFS rate was 22% (95% CI, 12-33) with **BMS-986012 + NIVO + chemo** vs 19% (95% CI, 9-31) with **NIVO + chemo**

LE CANCER BRONCHIQUE NON À PETITES CELLULES

CBNPC localisé

CBNPC LOCALISÉ

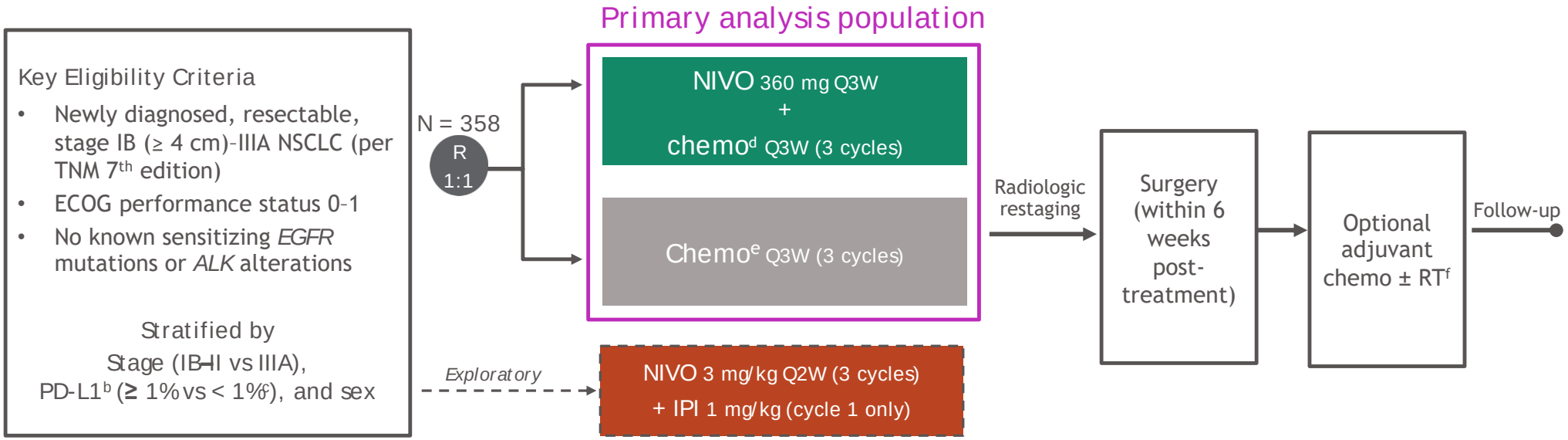
Approches		Critères
Néoadjuvant	R → Traitement → Chirurgie	EFS, pCR, MPR, OS
Adjuvant	Chirurgie → R → Traitement	DFS, OS
Péri-operatoire	R → Traitement → Chirurgie → Traitement	EFS, pCR, MPR, OS



Mouillet G et al. J Thorac Oncol 2012;7(5):841-849.

- IMMUNOTHERAPIE **NEOADJUVANTE**

CBNPC LOCALISÉ : CHECKMATE 816



Primary endpoints
- pCR by BIPR
- EFS by BICR

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

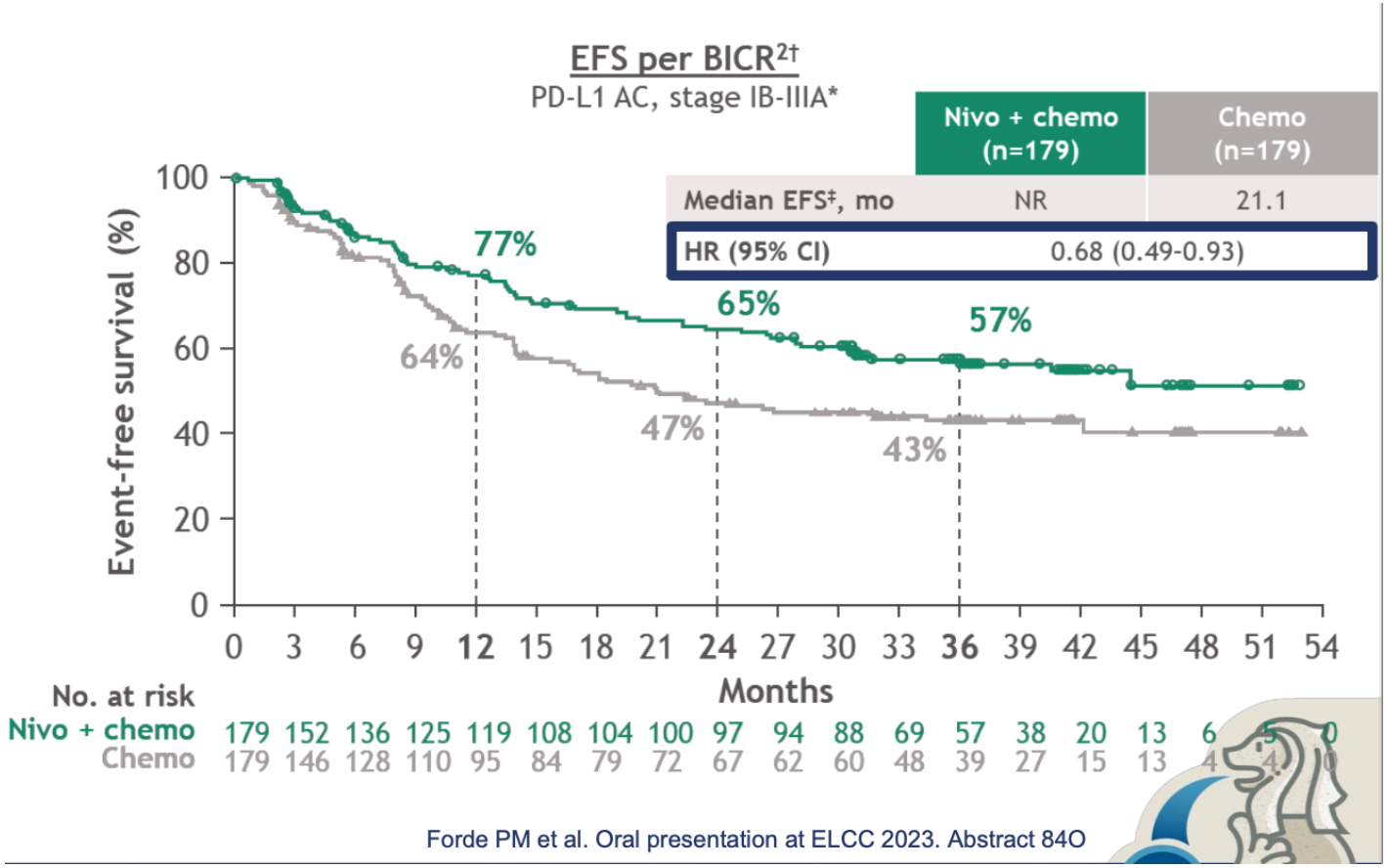
Exploratory endpoints
- ORR by BICR
- Predictive biomarkers (PD-L1, TMB, ctDNA[g])

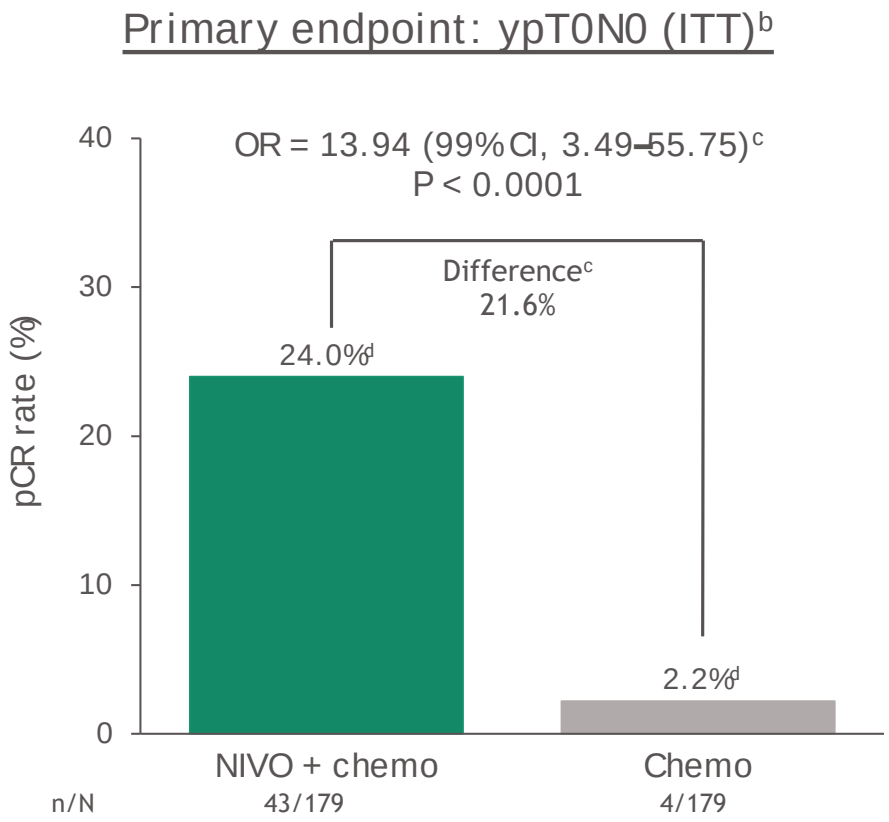
Database lock: September 16, 2020; minimum follow-up: 7.6 mo for NIVO + chemo and chemo arms.

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

Spicer et al. ASCO 2021

CBNPC LOCALISÉ : CHECKMATE 816

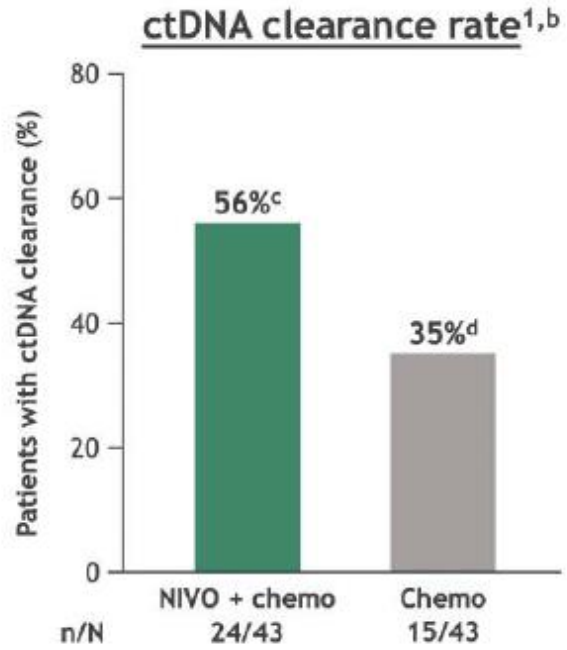


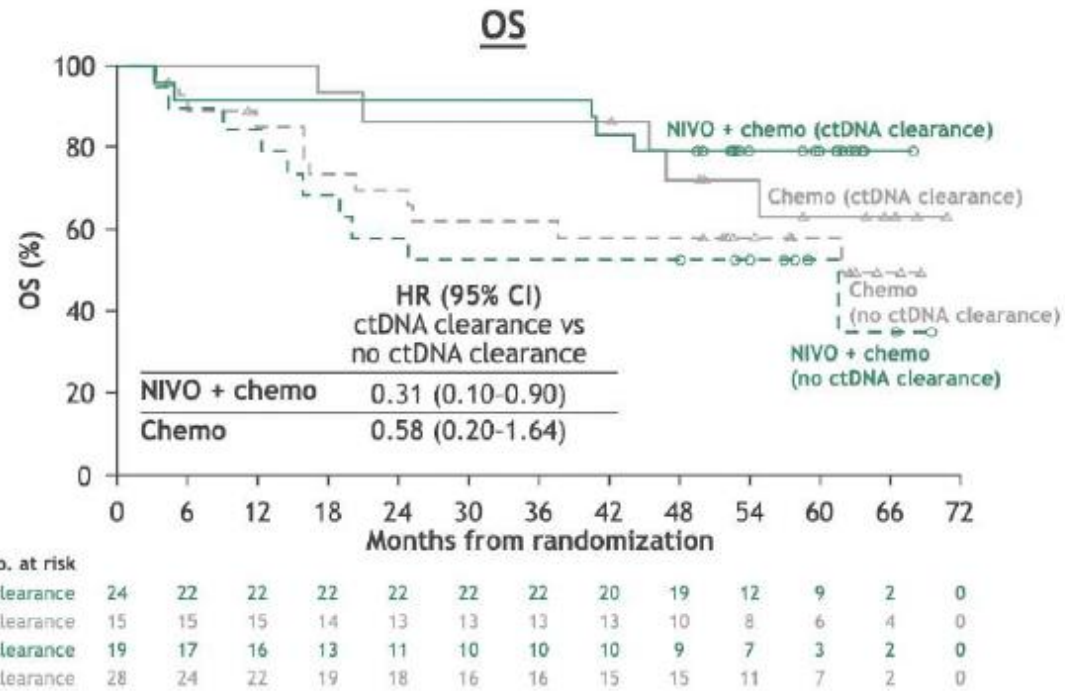


Spicer et al. ASCO 2021

CBNPC LOCALISÉ : CHECKMATE 816

- Among concurrently randomized patients, 89 (25%) had evaluable ctDNA levels, and 86 (24%) had detectable ctDNA levels at baseline[1,a]

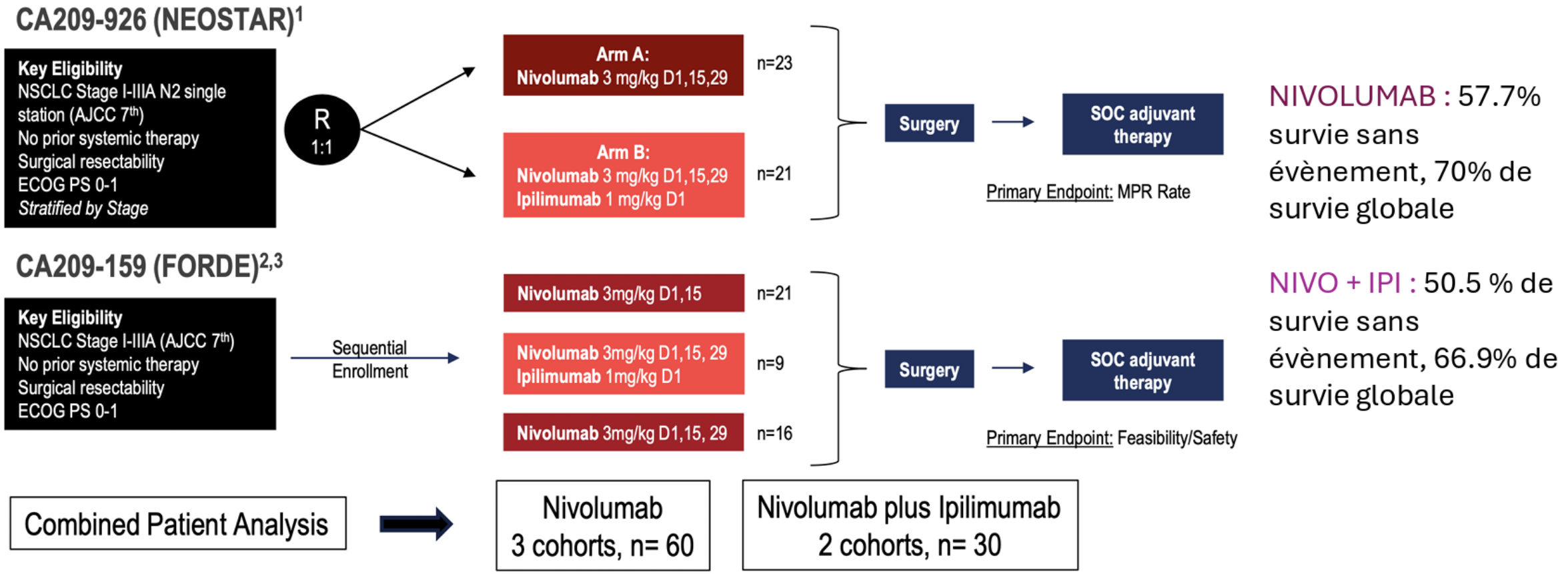




Minimum/median follow-up, 49.1/57.6 months.

Spicer et al. ASCO 2021

CBNPC LOCALISÉ : NEOSTAR & FORDE



NIVOLUMAB : 57.7% survie sans évènement, 70% de survie globale

NIVO + IPI : 50.5 % de survie sans évènement, 66.9% de survie globale

1. Cascone et al. Nat Med 2021; 2. Forde et al. N Engl J Med 2018; 3. Reuss et al. J Immunother Cancer 2020

Reuss et al, ESMO24

CBNPC LOCALISÉ : NEOSTAR & FORDE

Pathologic Response Rates

	MPR (95% CI)	pCR (95% CI)
Nivo (n=60)	28.1% (17.4, 42.1)	8.3% (3.5, 18.5)
Nivo plus Ipi (n=30)	33.3% (19.0, 51.7)	26.7% (13.9, 45.0)
TOTAL (n=90)	30.0% (21.5, 40.2)	13.5% (6.6, 25.7)

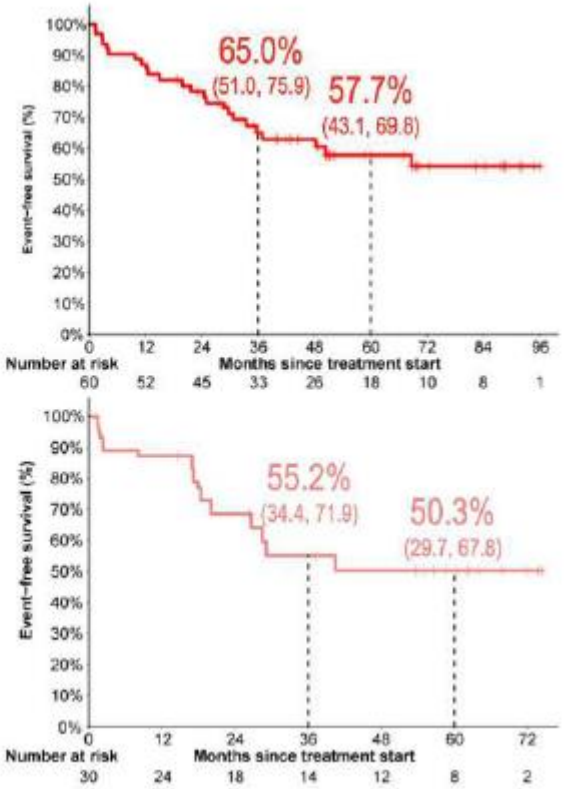
Nivo n=60

Median f/u 68.4mo

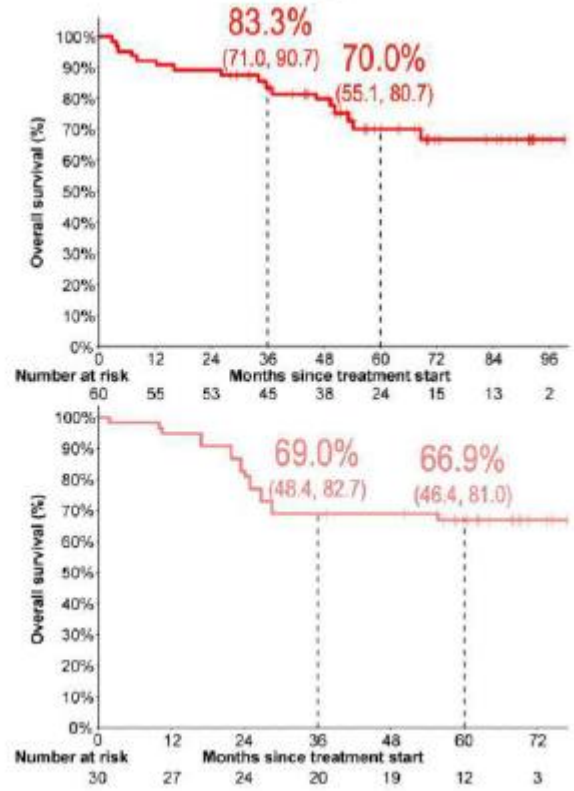
Nivo plus Ipi n=30

Median f/u 62.1mo

EFS

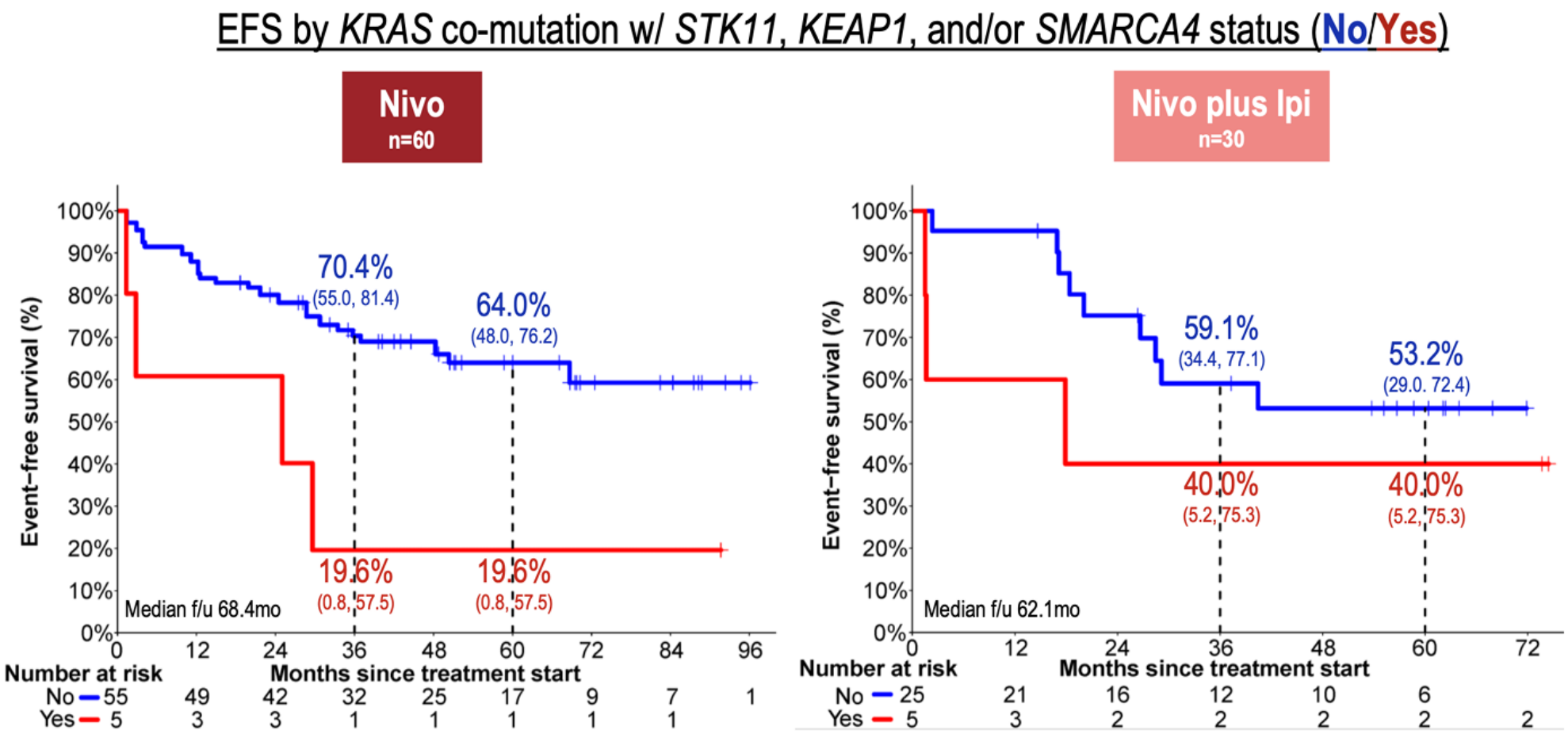


OS



Reuss et al, ESMO24

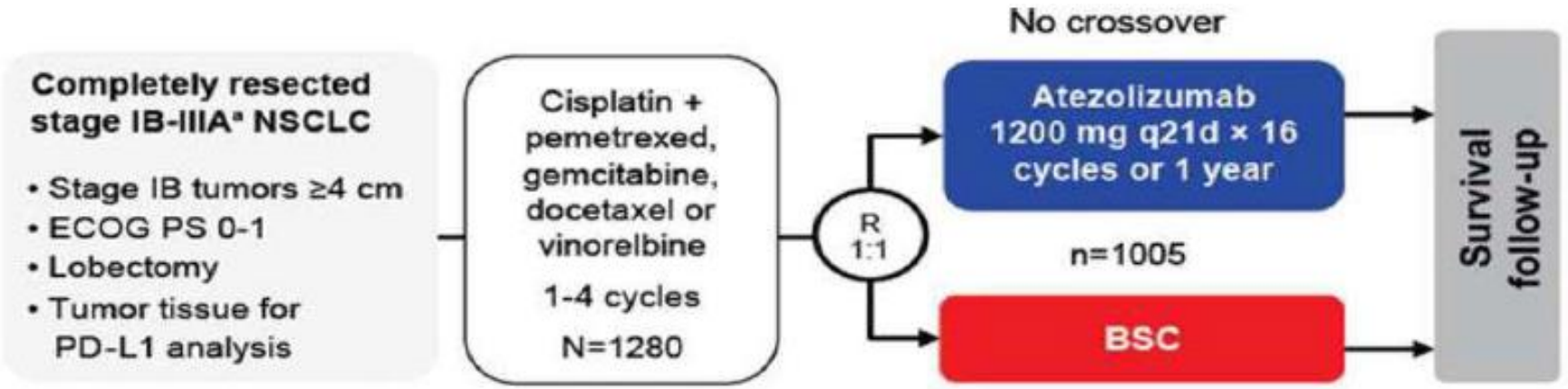
CBNPC LOCALISÉ : NEOSTAR & FORDE



Reuss et al, ESMO24

- IMMUNOTHERAPIE **ADJUVANTE**

CBNPC LOCALISÉ : IMPOWER 010



Stratification factors
• Sex | Disease stage | Histology | PD-L1 status

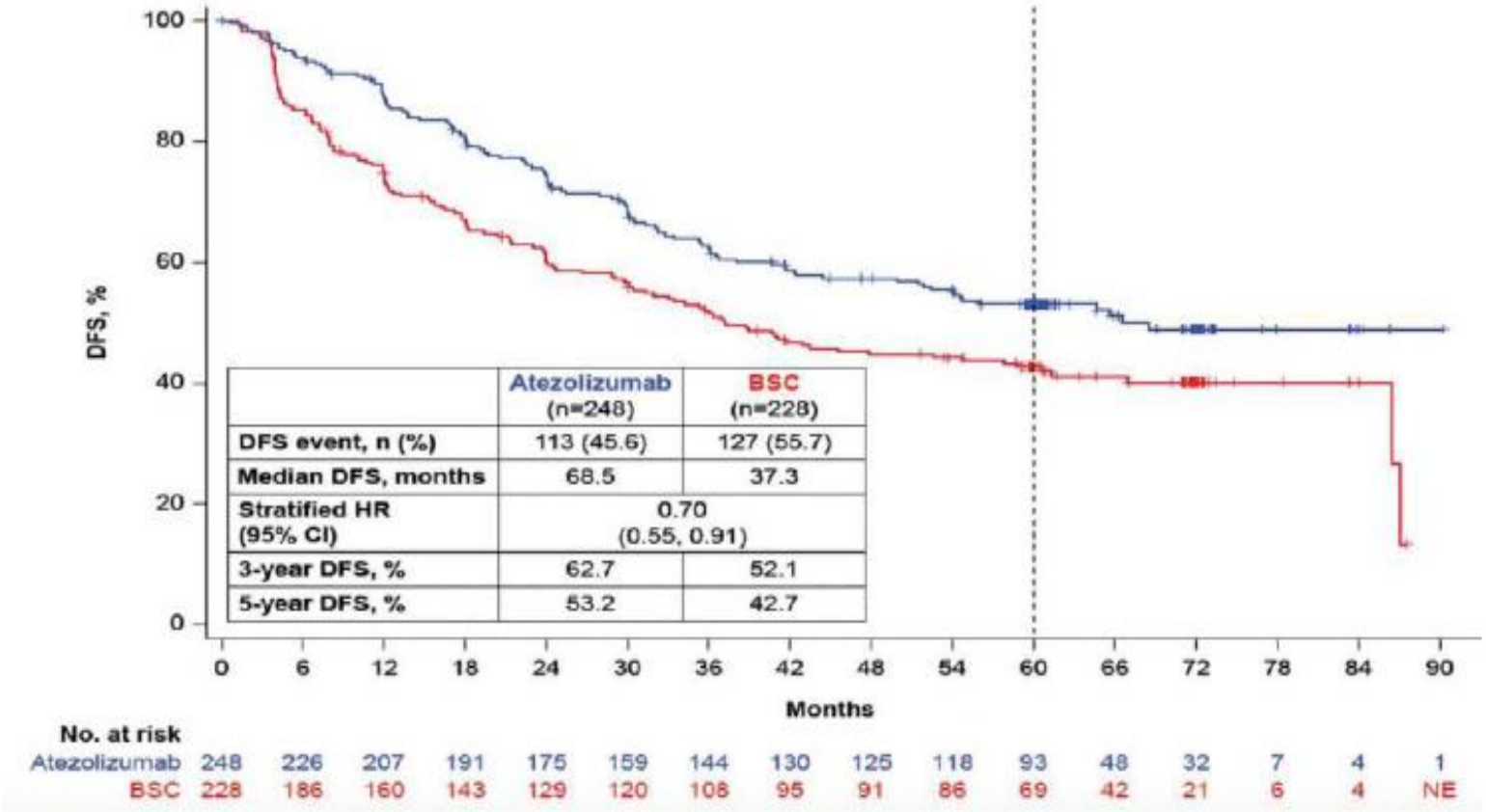
Primary endpoint
• Investigator-assessed DFS tested hierarchically

Key secondary endpoints
• OS in ITT | DFS in PD-L1 TC ≥50% stage II-IIIA | 3- and 5-year DFS

Wakelee et al, ASCO24

CBNPC LOCALISÉ : IMPOWER 010

Figure 2. DFS in the stage II-IIIA PD-L1 TC ≥1% population

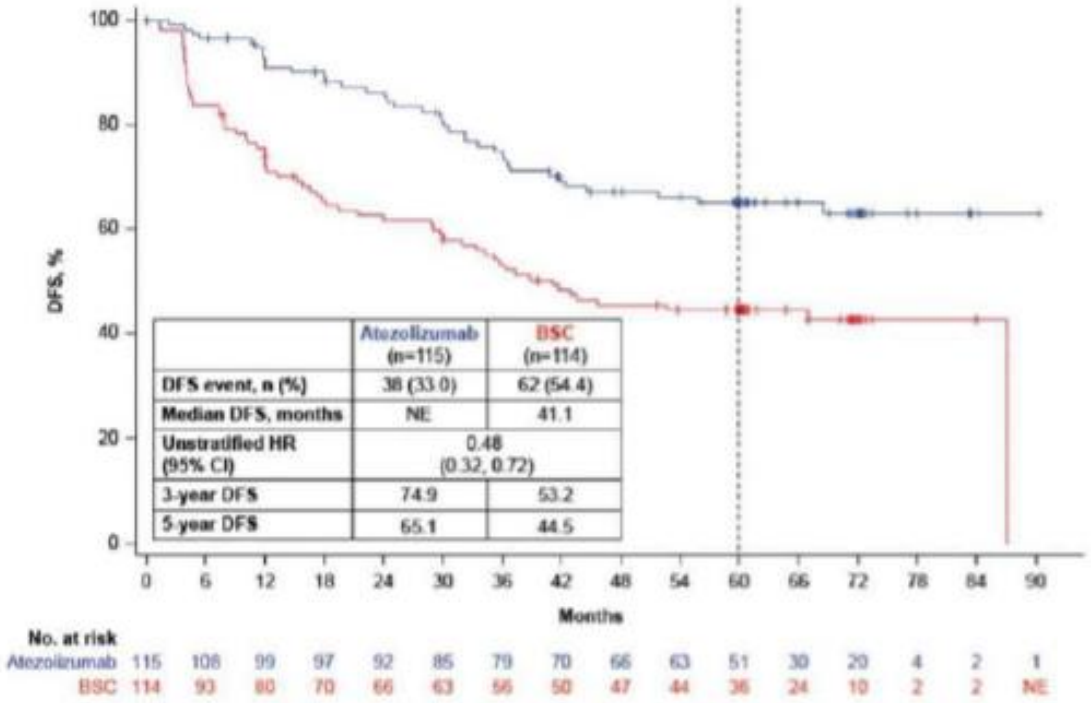


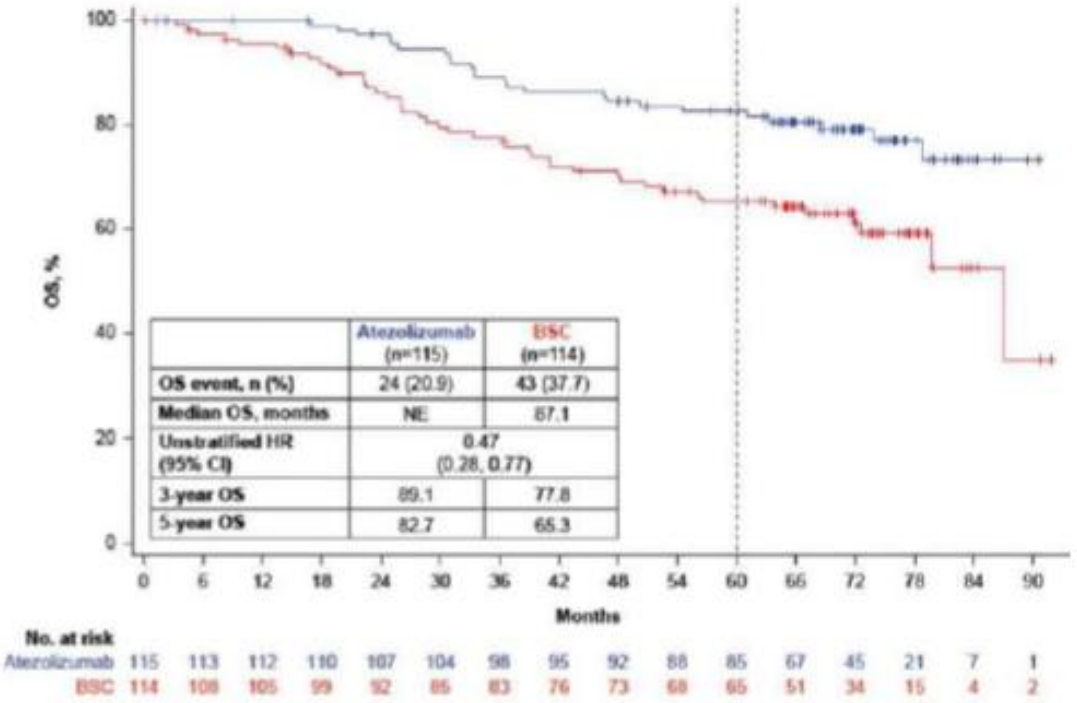
	Atezolizumab (n=248)	BSC (n=228)
DFS event, n (%)	113 (45.6)	127 (55.7)
Median DFS, months	68.5	37.3
Stratified HR (95% CI)	0.70 (0.55, 0.91)	
3-year DFS, %	62.7	52.1
5-year DFS, %	53.2	42.7

Wakelee et al, ASCO24

CBNPC LOCALISÉ : IMPOWER 010

Figure 5. DFS and OS in the stage II-IIIA PD-L1 TC ≥50% population

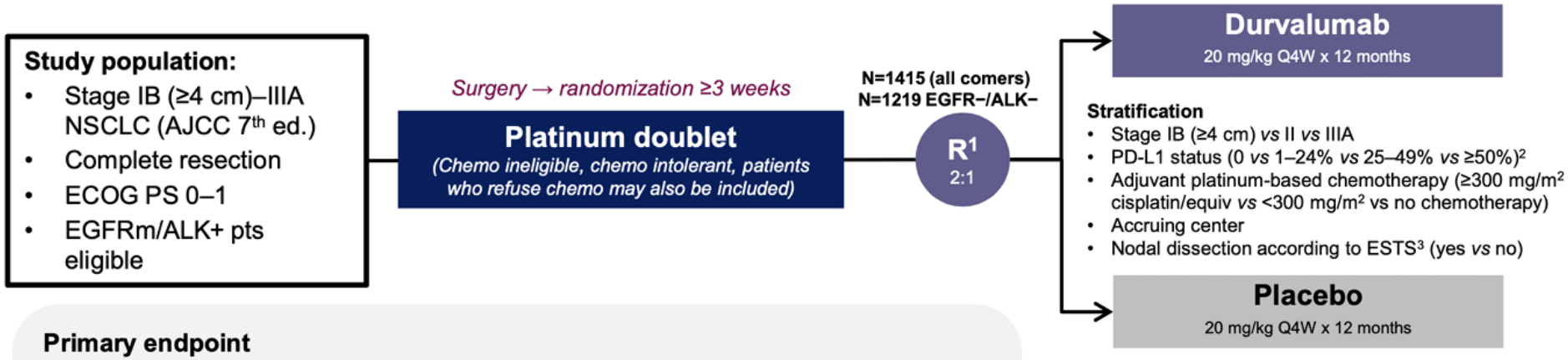




Wakelee et al, ASCO24

CBNPC LOCALISÉ : CCTG BR.31

CCTG BR.31 Trial Design



Primary endpoint

- DFS[4] (Investigator Assessed) in patients with PD-L1 TC ≥25% and EGFR−/ALK−

Key secondary endpoints

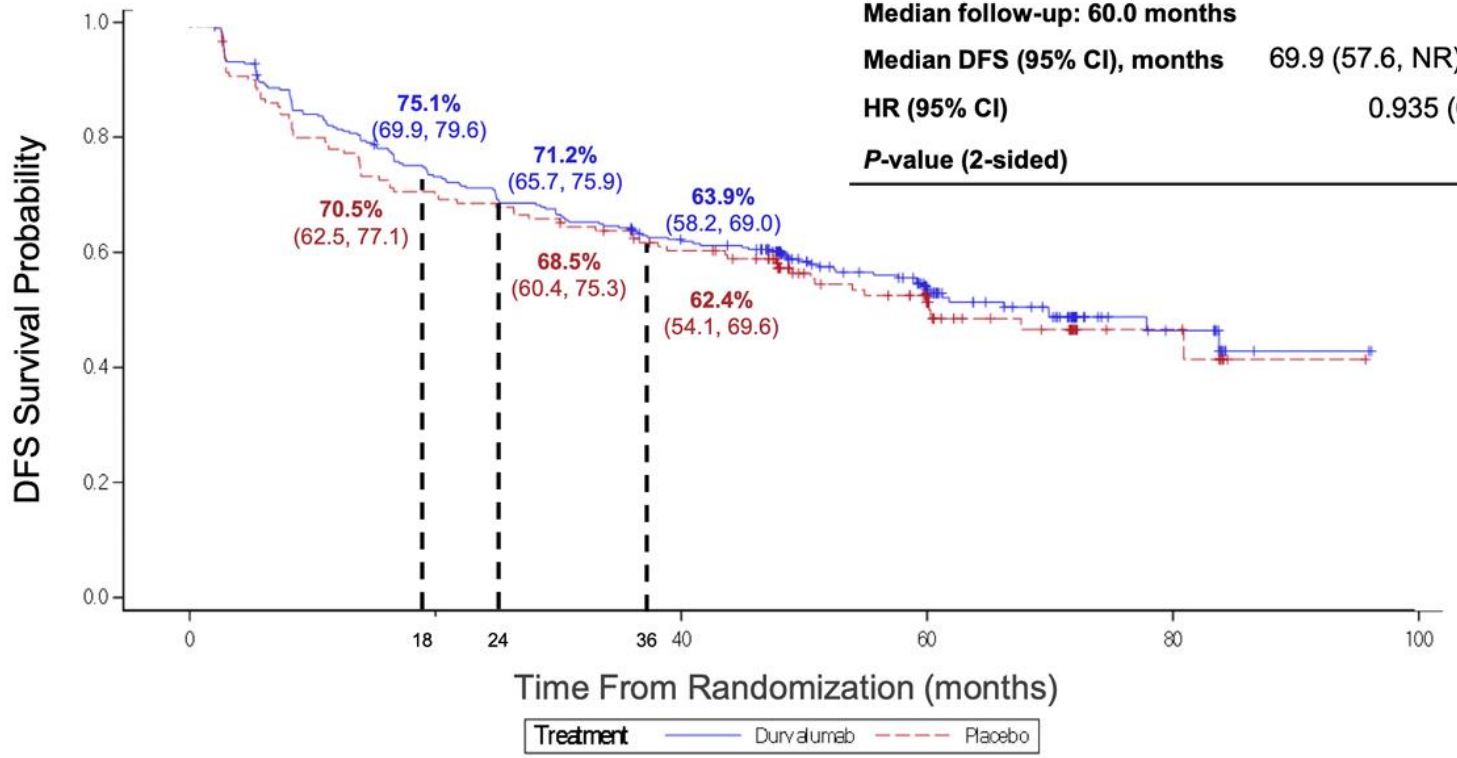
- DFS in patients with:
  - PD-L1 TC ≥1% and EGFR−/ALK−
  - All PD-L1 TC ≥25%
  - All randomized patients
  - PD-L1 all comers and EGFR−/ALK−
  - All PD-L1 TC ≥1%
- OS (six patient subpopulations)
- AEs
- QoL

Goss et al, ESMO24

CBNPC LOCALISÉ : CCTG BR.31

DFS in PD-L1≥25% EGFR−/ALK−

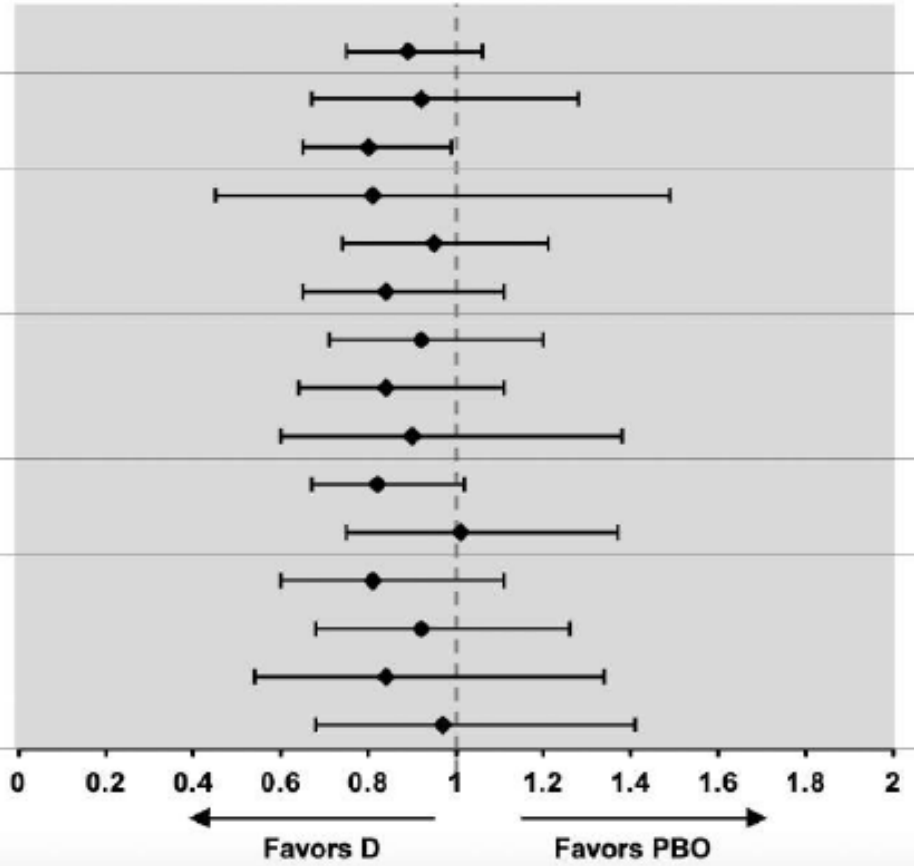
	D arm n=316	PBO arm n=161
Median follow-up: 60.0 months		
Median DFS (95% CI), months	69.9 (57.6, NR)	60.2 (47.7, NR)
HR (95% CI)	0.935 (0.706, 1.247)	
***P*-value (2-sided)**	0.642	



Goss et al, ESMO24

CBNPC LOCALISÉ : CCTG BR.31

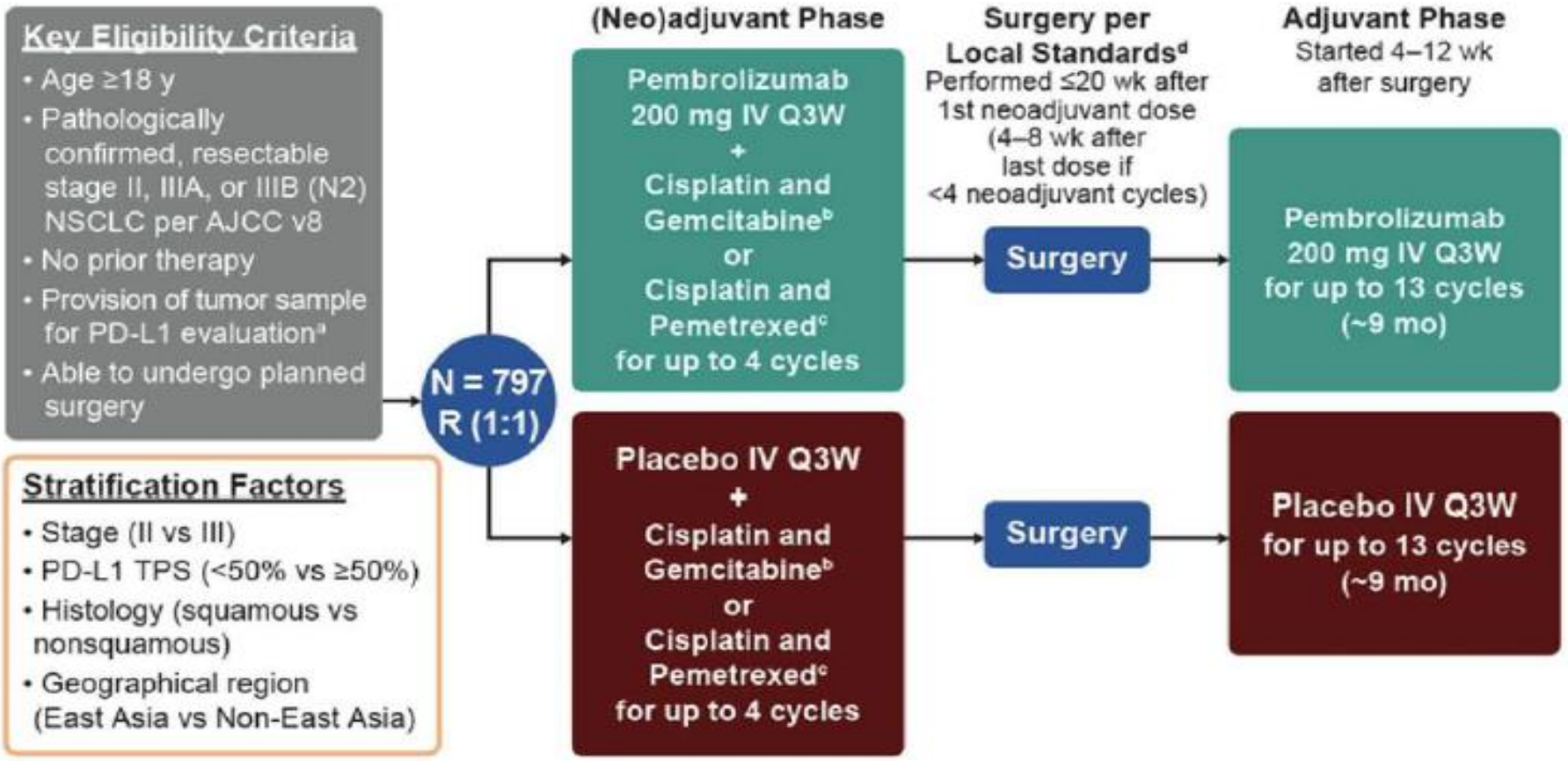
Category	Subgroup	HR (95% CI)	N events / patients (%) D arm	N events / patients (%) PBO arm
All EGFR−/ALK−		0.89 (0.75, 1.06)	377/815 (46.3)	197/404 (48.8)
Histology[1]	Squamous	0.92 (0.67, 1.28)	99/232 (42.7)	61/142 (43.0)
	Non-squamous	0.80 (0.65, 0.99)	262/540 (48.5)	134/245 (54.7)
Disease stage (IWRS)	Stage IB	0.81 (0.45, 1.49)	31/70 (44.3)	17/36 (47.2)
	Stage II	0.95 (0.74, 1.21)	197/443 (44.5)	97/209 (46.4)
	Stage IIIA	0.84 (0.65, 1.11)	149/302 (49.3)	83/159 (52.2)
Chemotherapy (IWRS)	≥300 mg/m²	0.92 (0.71, 1.20)	165/372 (44.4)	85/183 (46.4)
	<300 mg/m²	0.84 (0.64, 1.11)	145/316 (45.9)	79/156 (50.6)
	No chemotherapy	0.90 (0.60, 1.38)	67/127 (52.8)	33/65 (50.8)
Nodal sampling (IWRS)	Yes	0.82 (0.67, 1.02)	239/520 (46.0)	131/255 (51.4)
	No	1.01 (0.75, 1.37)	131/282 (46.5)	65/143 (45.5)
PD-L1 status (Rescored)[2]	<1%	0.81 (0.60, 1.11)	115/261 (44.1)	60/119 (50.4)
	1–24%	0.92 (0.68, 1.26)	120/237 (50.6)	64/121 (52.9)
	25–49%	0.84 (0.54, 1.34)	51/100 (51.0)	29/52 (55.8)
	≥50%	0.97 (0.68, 1.41)	91/217 (41.9)	44/112 (39.3)



Goss et al, ESMO24

IMMUNOTHERAPIE PERIOPERATOIRE

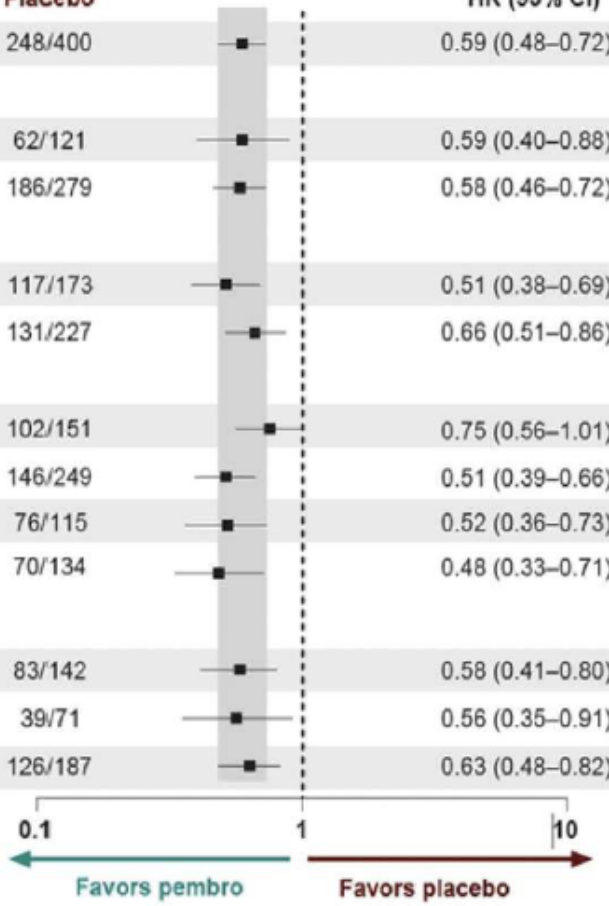
CBNPC LOCALISÉ : KEYNOTE 671

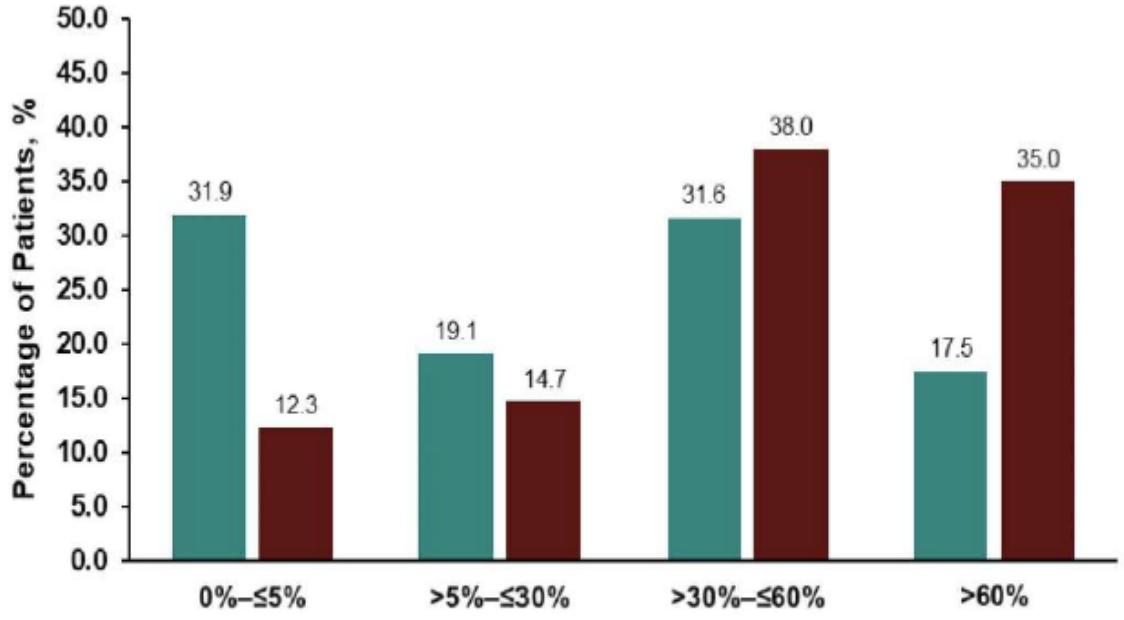


Garassino et al, ESMO24

CBNPC LOCALISÉ : KEYNOTE 671

	No. of Events/No. of Patients		
	Pembro	Placebo	HR (95% CI)
Overall	174/397	248/400	0.59 (0.48–0.72)
Stage at baseline			
Stage II	40/118	62/121	0.59 (0.40–0.88)
Stage III	134/279	186/279	0.58 (0.46–0.72)
Histology			
Squamous	72/171	117/173	0.51 (0.38–0.69)
Nonsquamous	102/226	131/227	0.66 (0.51–0.86)
PD-L1 TPS status			
TPS <1%	78/138	102/151	0.75 (0.56–1.01)
TPS ≥1%	96/259	146/249	0.51 (0.39–0.66)
TPS 1%–49%	55/127	76/115	0.52 (0.36–0.73)
TPS ≥50%	41/132	70/134	0.48 (0.33–0.71)
N status at baseline[a]			
N0	59/148	83/142	0.58 (0.41–0.80)
N1	29/81	39/71	0.56 (0.35–0.91)
N2	86/168	126/187	0.63 (0.48–0.82)





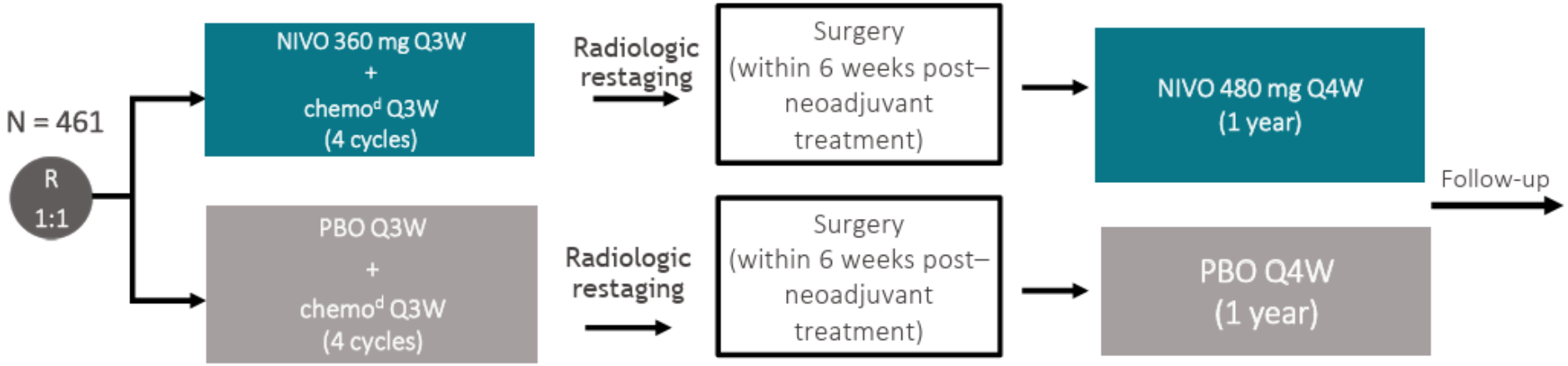
	n	Median %RVT (IQR), %
Pembro Arm	320	29.5 (1.0–56.0)
Placebo Arm	300	52.0 (29.0–68.0)

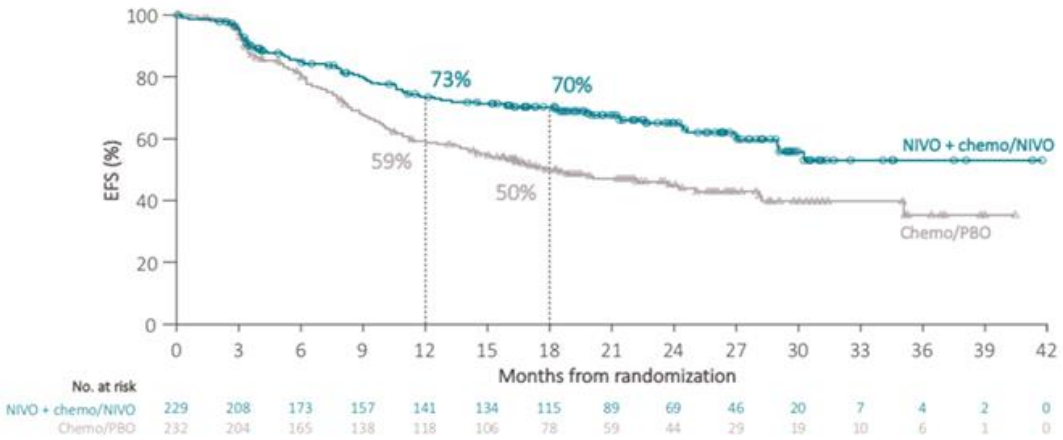
Garassino et al, ESMO24
Jones et al, WCLC24

CBNPC LOCALISÉ : CHECKMATE 77T

Key eligibility criteria

- Resectable, stage IIA (> 4 cm)–IIIB (N2) NSCLC (per AJCC 8th edition)
- No prior systemic anti-cancer treatment
- ECOG PS 0–1
- No *EGFR* mutation/known *ALK* alterations[b]



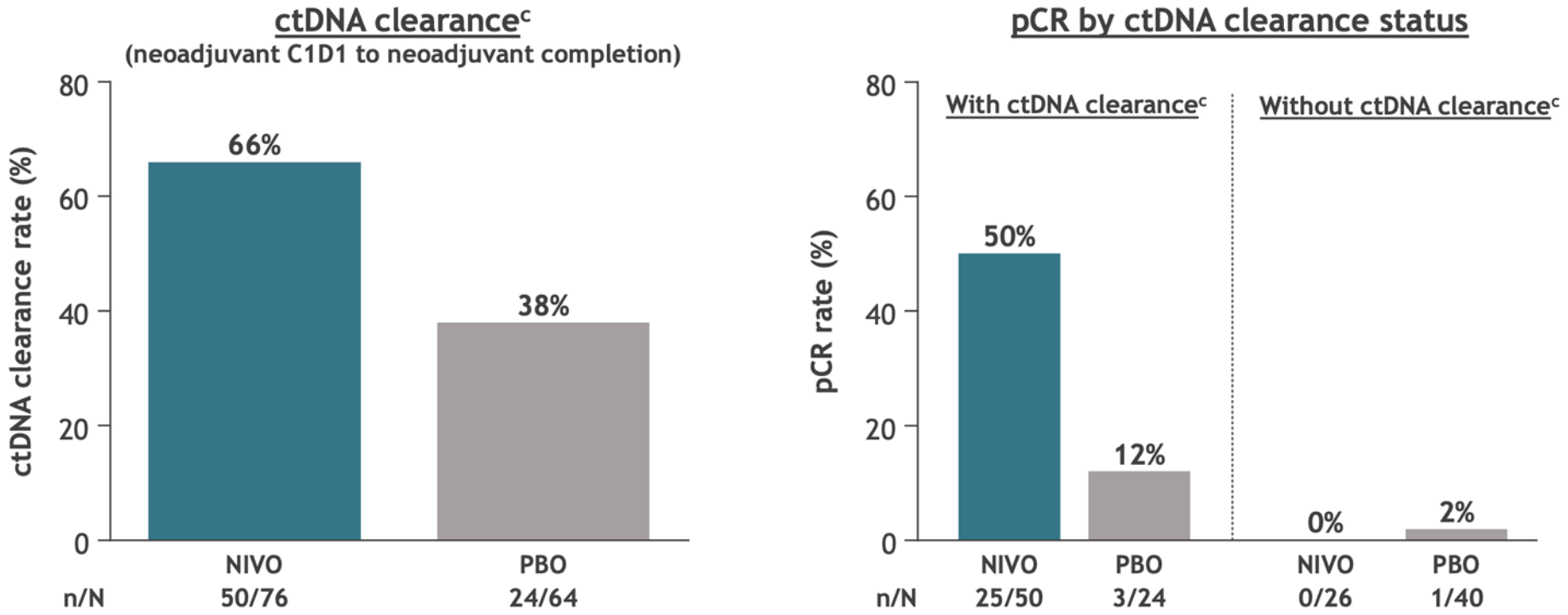


	NIVO + chemo/NIVO (n = 229)	Chemo/PBO (n = 232)
Median EFS, mo (95% CI)	NR (28.9–NR)	18.4 (13.6–28.1)
HR (97.36% CI)[b]	0.58 (0.42–0.81)	
***P* value**	0.00025	

Spicer et al, Esmo24

CBNPC LOCALISÉ : CHECKMATE 77T

Augmentation de la survie sans évènements à **40 mois groupe expérimental** versus **17 mois groupe contrôle**

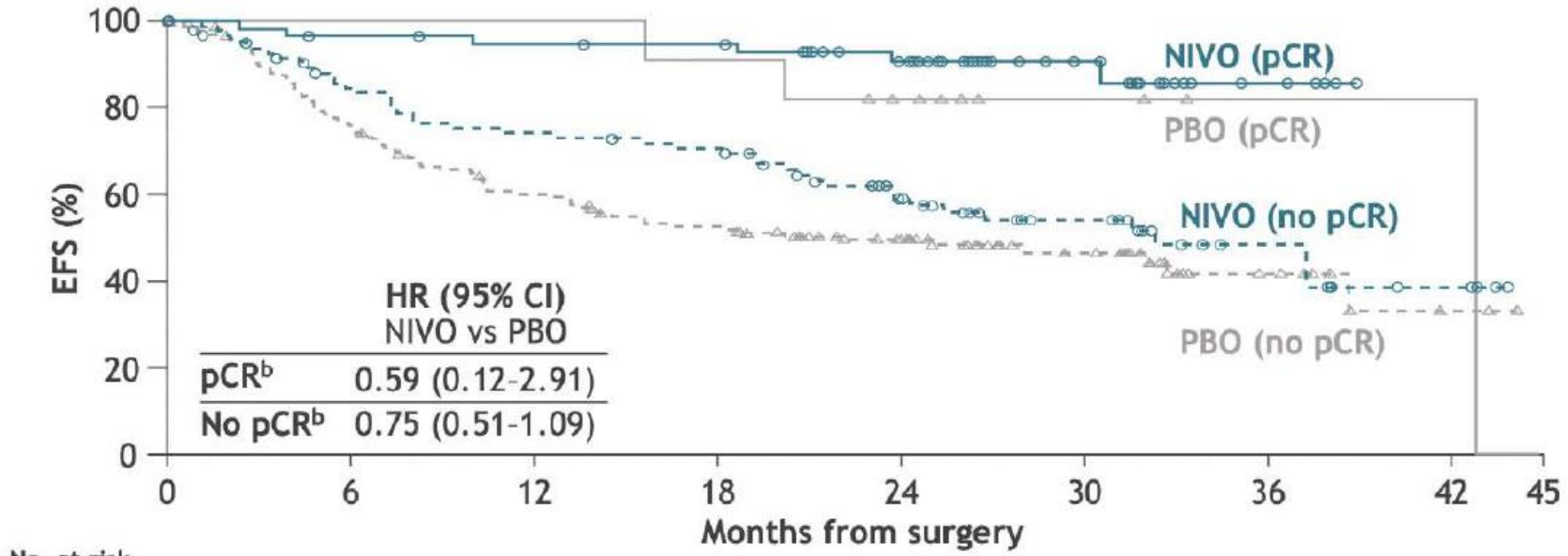


- Among patients with ctDNA clearance, the EFS HR was 0.38 (95% CI, 0.16-0.88); 2-year EFS rates were 81% (NIVO) vs 58% (PBO)
- Among patients without ctDNA clearance, the EFS HR was 0.74 (95% CI, 0.39-1.42); 2-year EFS rates were 50% (NIVO) vs 31% (PBO)

Spicer et al, Esmo24

CBNPC LOCALISÉ : CHECKMATE 77T

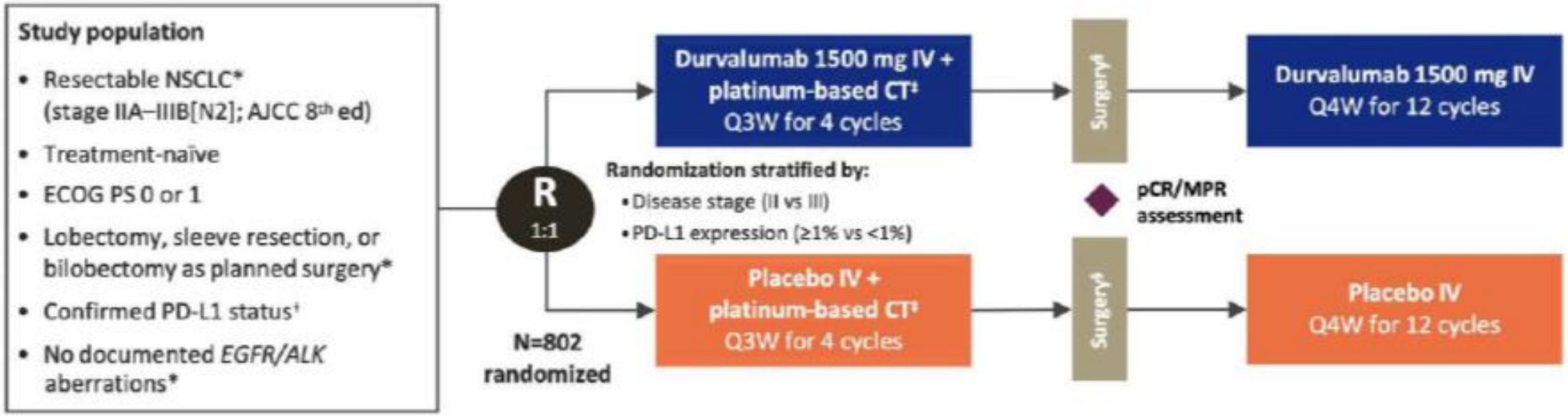
Landmark EFS from definitive surgery[a] by pCR status



No. at risk									
pCR	58	54	52	51	40	19	5	0	0
pCR	11	11	11	10	7	3	1	1	0
No pCR	98	74	65	61	40	26	10	4	0
No pCR	148	109	84	71	50	27	9	2	0

Spicer et al, Esmo24

CBNPC LOCALISÉ : AEGAN (ANALYSE INTERMÉDIAIRE)



Efficacy analyses were performed in the mITT population (or its resected subpopulation), which excluded patients with documented EGFR/ALK aberrations¶

Primary endpoints: pCR, evaluated centrally (IASLC 2020[1]), and EFS per BICR (RECIST v1.1)

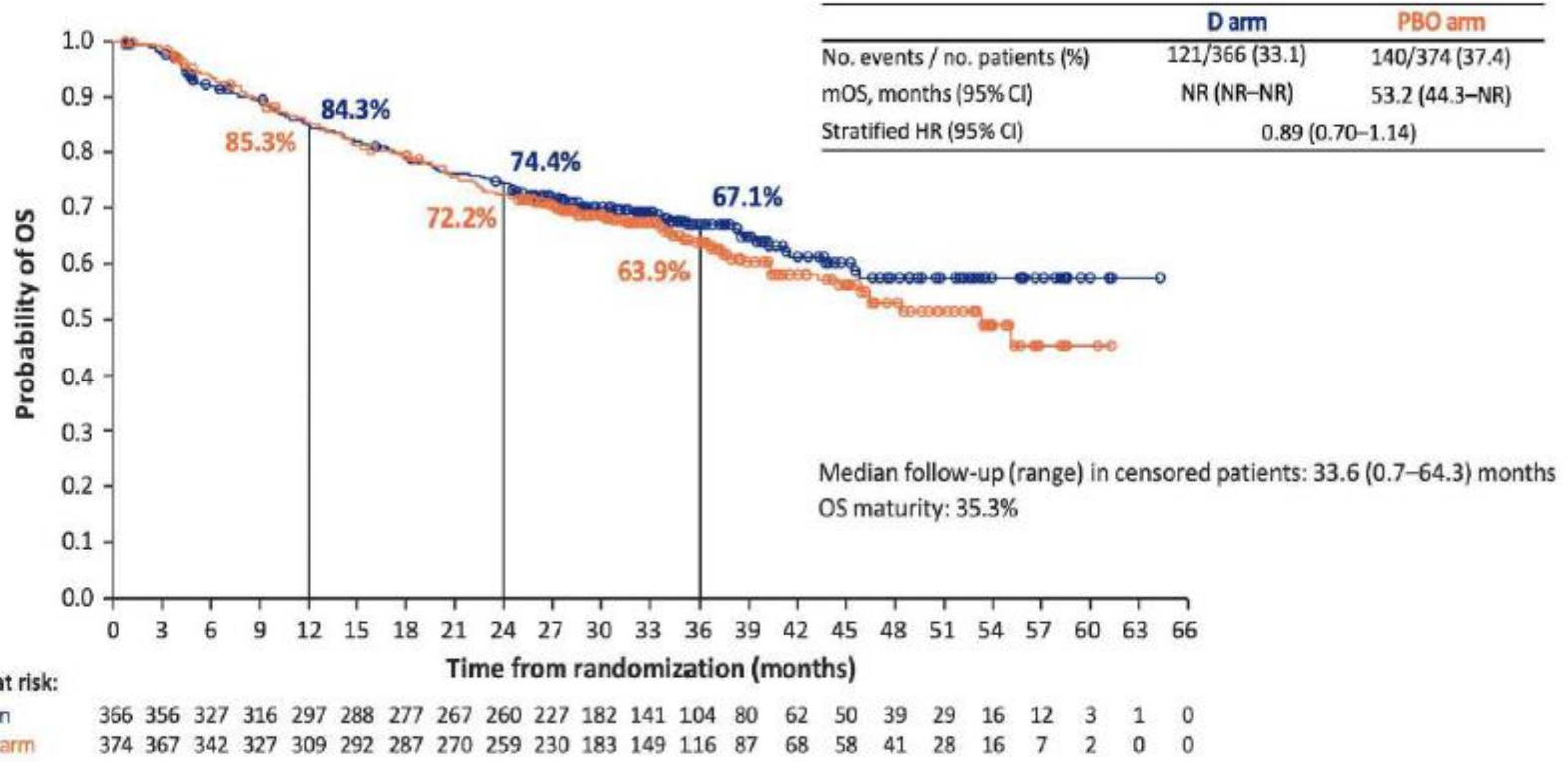
Key secondary endpoints: MPR, evaluated centrally (IASLC 2020[1]), DFS per BICR (RECIST v1.1) in the resected subpopulation, and OS

	EFS interim analysis #1	EFS interim analysis #2 (reported here)
Data cutoff	November 10, 2022	May 10, 2024
Median EFS follow-up	11.7 months (censored patients)	25.9 months (censored patients)
Data maturity	31.9%	39.1%

Heymach et al. WCLC24

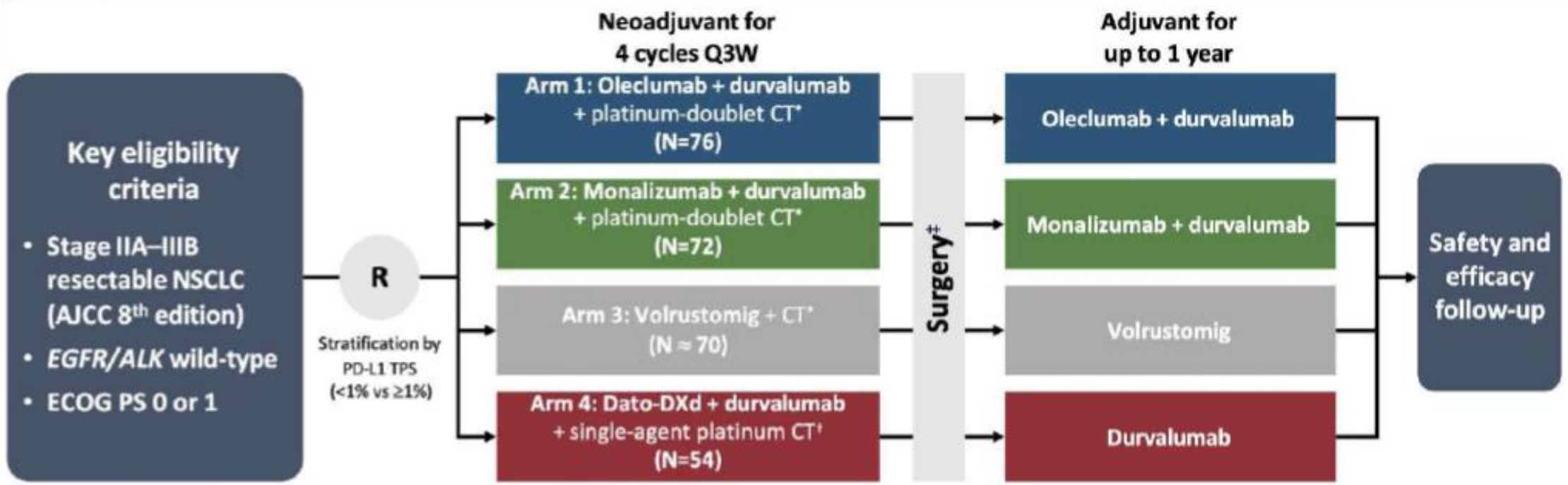
CBNPC LOCALISÉ : AEGAN (ANALYSE INTERMÉDIAIRE)

- Based on 35% maturity, an OS trend favoring the durvalumab arm was observed



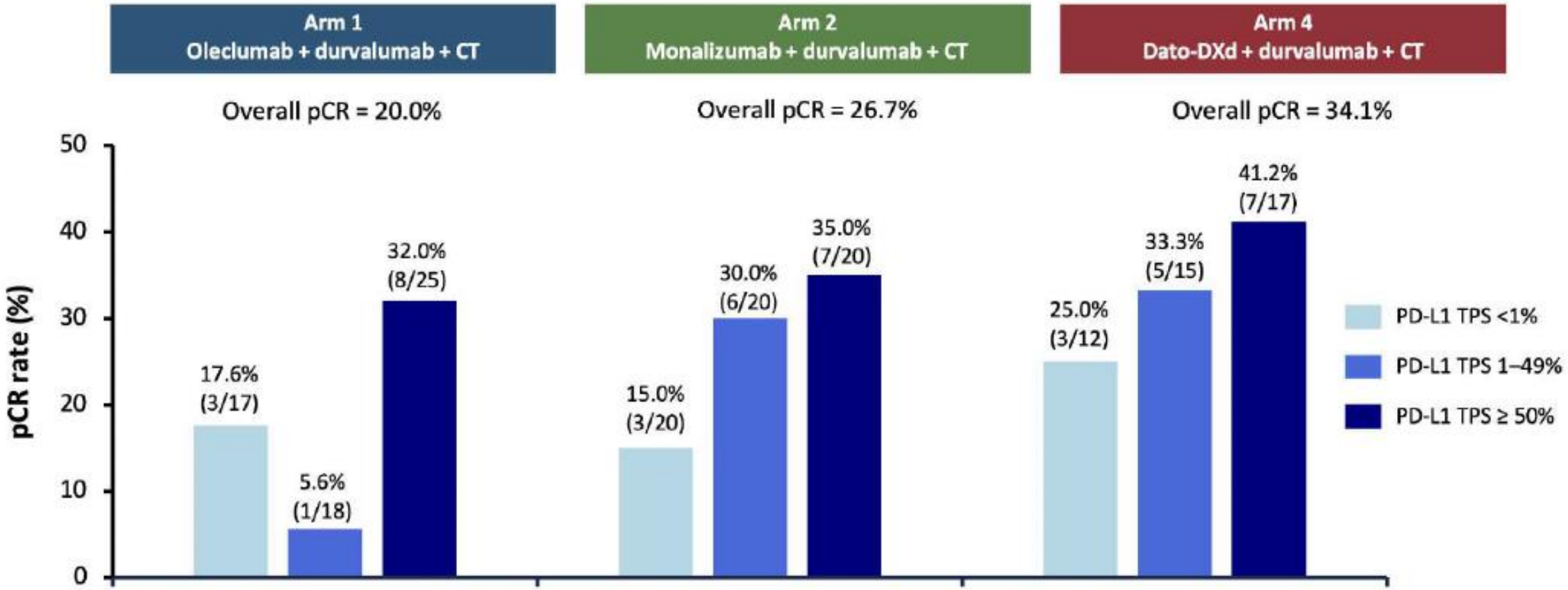
Heymach et al. WCLC24

CBNPC LOCALISÉ : NOUVELLES MOLÉCULES (NEOCOAST)



Cascone et al. WCLC24

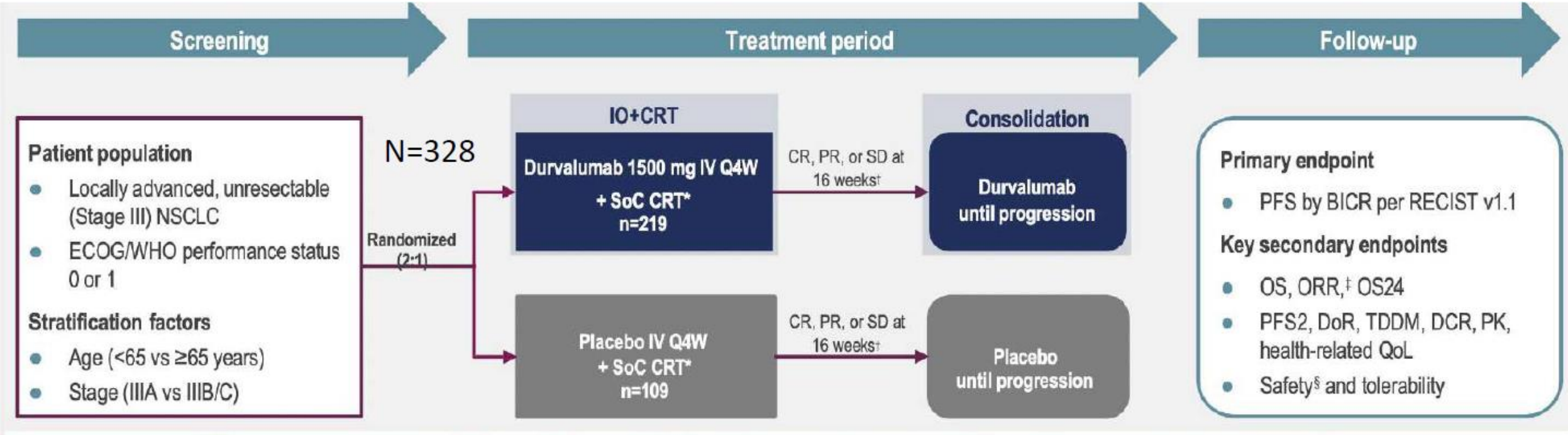
CBNPC LOCALISÉ : NOUVELLES MOLÉCULES (NEOCOAST)



Cascone et al. WCLC24

CBNPC
non résécable

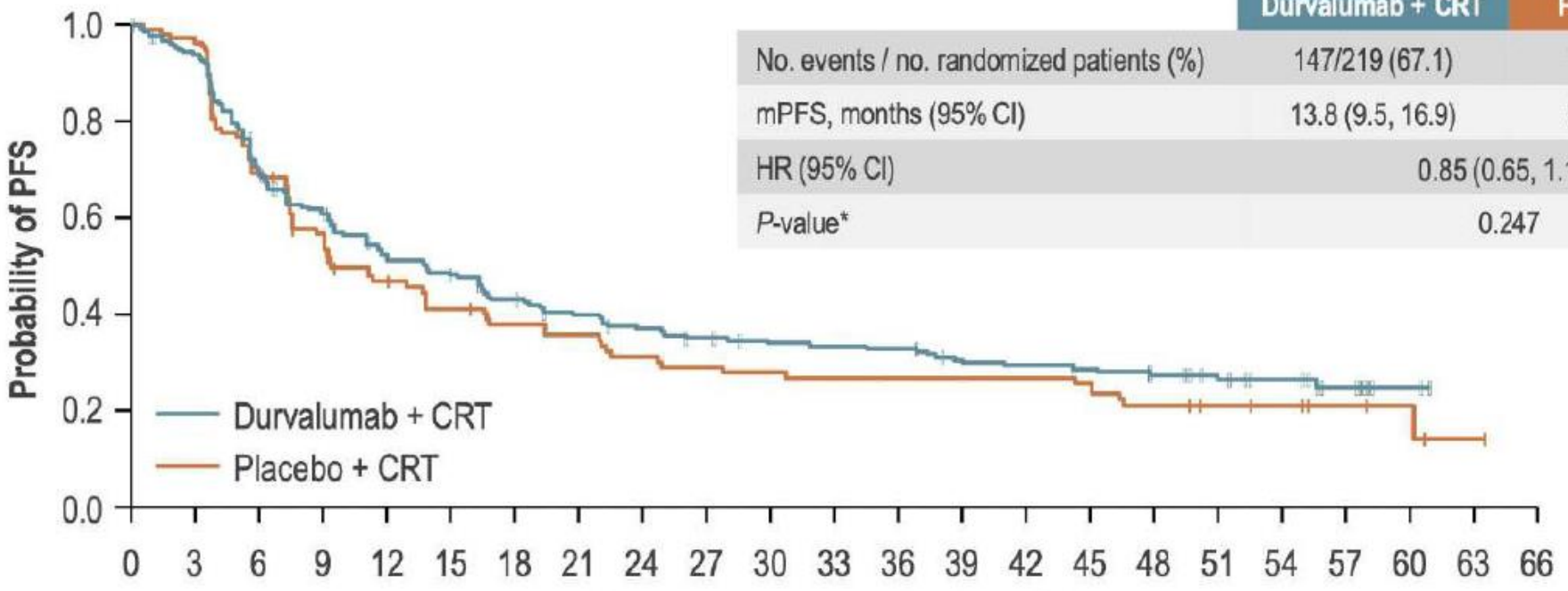
CBNPC NON RÉSÉCABLE : PACIFIC 2



Bradley et al, ELCC 2024

CBNPC NON RÉSÉCABLE : PACIFIC 2

	Durvalumab + CRT	Placebo + CRT
No. events / no. randomized patients (%)	147/219 (67.1)	80/109 (73.4)
mPFS, months (95% CI)	13.8 (9.5, 16.9)	9.4 (7.5, 16.6)
HR (95% CI)	0.85 (0.65, 1.12)	
P-value*	0.247	

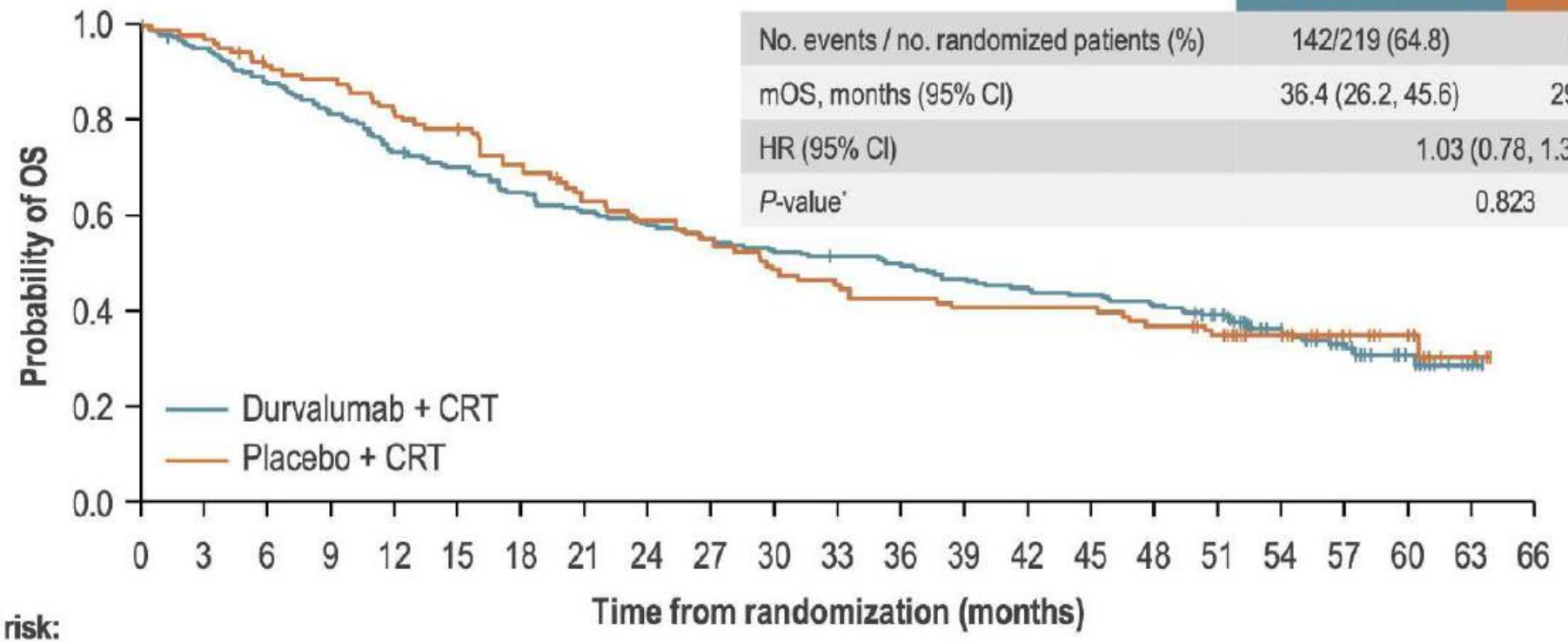


No. at risk:																							
Durvalumab + CRT	219	199	145	124	102	94	83	75	69	64	60	59	58	50	49	47	43	28	24	10	2	0	0
Placebo + CRT	109	104	72	58	44	38	34	32	28	26	25	24	24	24	24	23	19	15	12	7	3	1	0

Bradley et al, ELCC 2024

CBNPC NON RÉSÉCABLE : PACIFIC 2

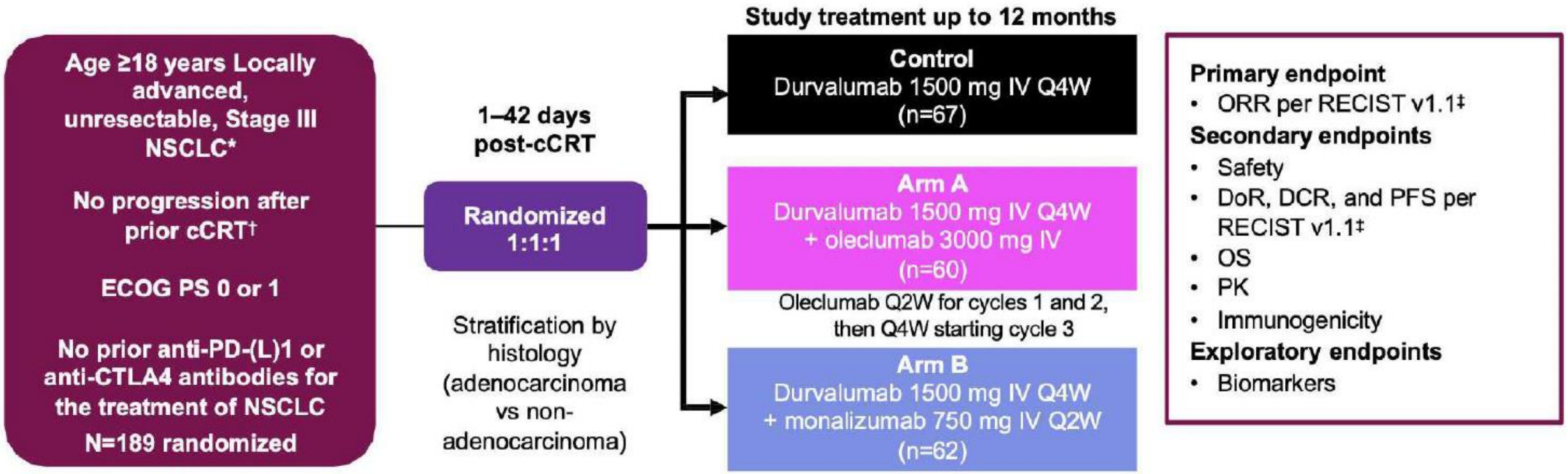
	Durvalumab + CRT	Placebo + CRT
No. events / no. randomized patients (%)	142/219 (64.8)	69/109 (63.3)
mOS, months (95% CI)	36.4 (26.2, 45.6)	29.5 (23.2, 45.1)
HR (95% CI)	1.03 (0.78, 1.39)	
P-value*	0.823	



No. at risk:																							
Durvalumab + CRT	219	207	191	177	160	152	141	132	126	120	114	111	107	100	95	94	89	75	49	31	15	1	0
Placebo + CRT	109	106	98	95	87	83	75	66	62	57	51	47	45	43	43	43	39	35	27	17	9	2	0

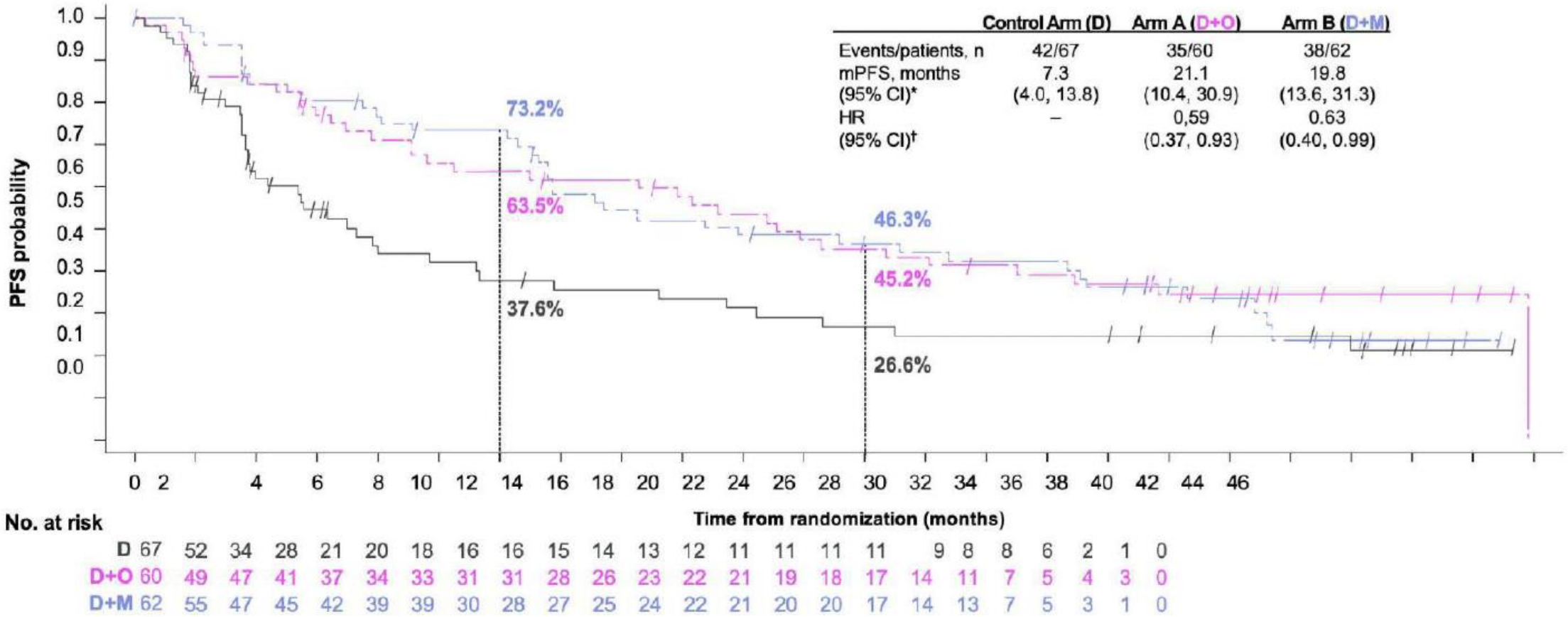
Bradley et al, ELCC 2024

CBNPC NON RÉSÉCABLE : COAST



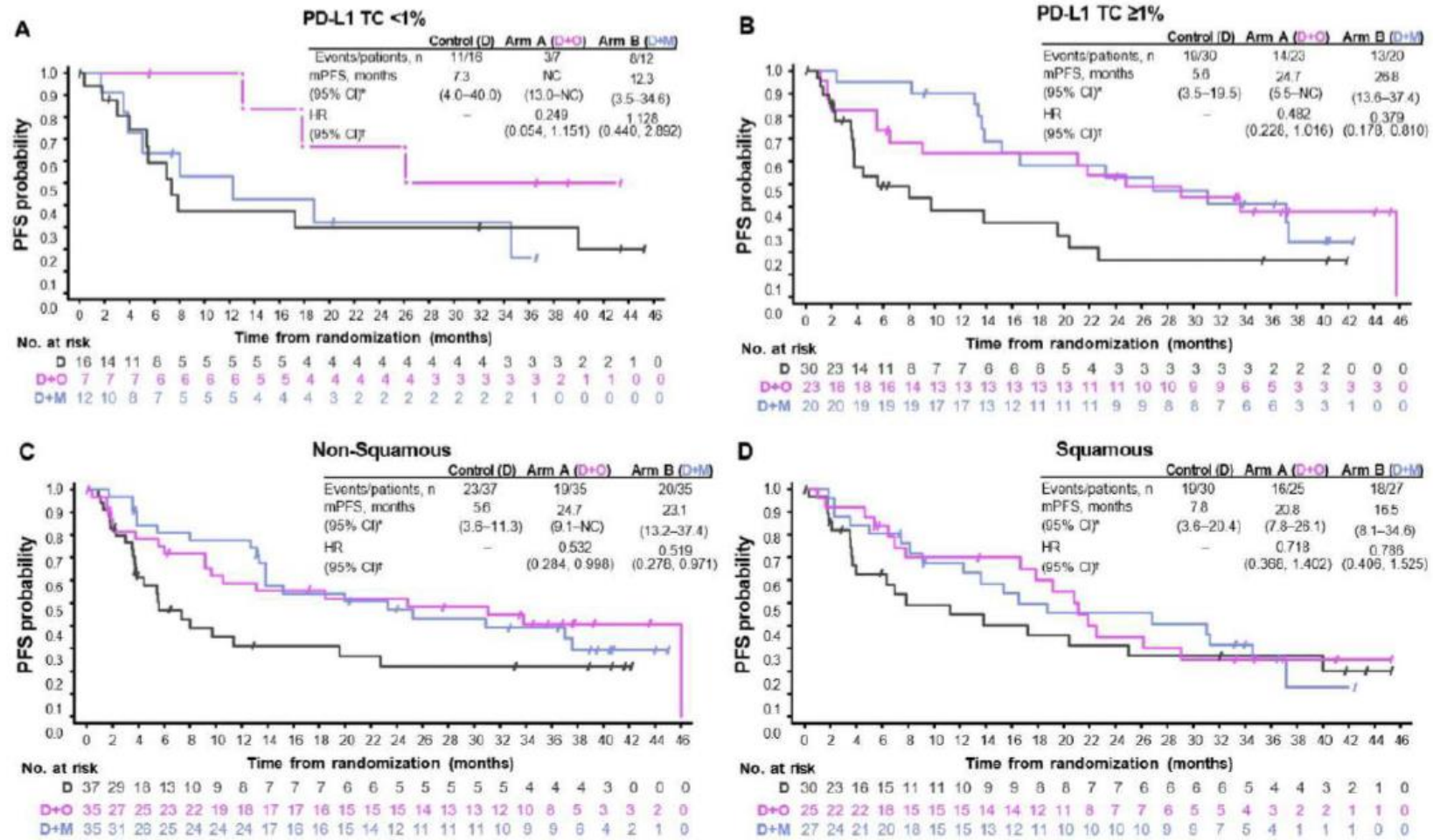
Aggarwal et al, ASCO 2024

CBNPC NON RÉSÉCABLE : COAST



Aggarwal et al, ASCO 2024

CBNPC NON RÉSÉCABLE : COAST

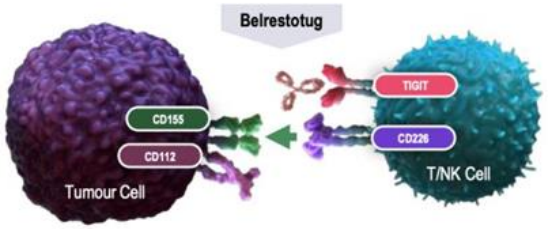


Aggarwal et al, ASCO 2024

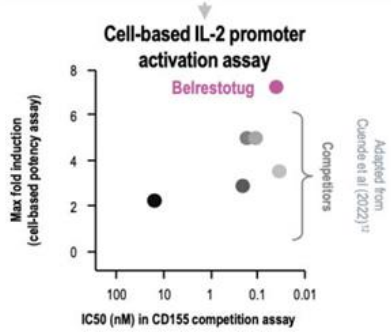
CBNPC métastatique

CBNPC MÉTASTATIQUE : GALAXIES LUNG 201

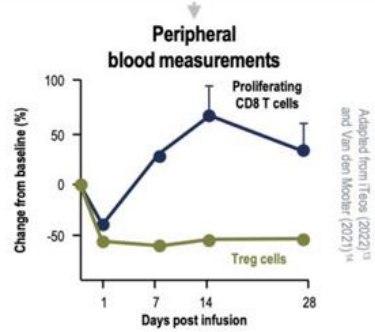
Belrestotug is an **Fcγ-receptor enabled mAb**[10,11] with two key mechanisms of action



Belrestotug demonstrated **higher potency** relative to other anti-TIGIT mAbs[12]



Belrestotug treatment leads to increases in proliferating CD8+ T-cells and a **marked reduction in Tregs** in patients[13,14]



Key Eligibility Criteria:

- Previously untreated, unresectable, locally advanced/metastatic NSCLC
- PD-L1 high (TPS ≥50%; determined locally or centrally by DAKO 22C3 or VENTANA SP263 assay)
- EGFR/ALK wild-type, no actionable driver mutations
- Current or former smoker
- Asymptomatic and treated brain metastases are eligible

R

Stratification: Squamous vs non-squamous

Substudy 1

- Pembrolizumab 200 mg Q3W
- Dostarlimab 500 mg Q3W
- A: Belrestotug 100 mg + dostarlimab 500 mg Q3W
- B: Belrestotug 400 mg + dostarlimab 500 mg Q3W
- C: Belrestotug 1000 mg + dostarlimab 500 mg Q3W

Substudy 2

- Belrestotug + dostarlimab + nelistotug[2] Q3W

Substudies to be added by amendment

Study initiation timeline

Primary Endpoint:

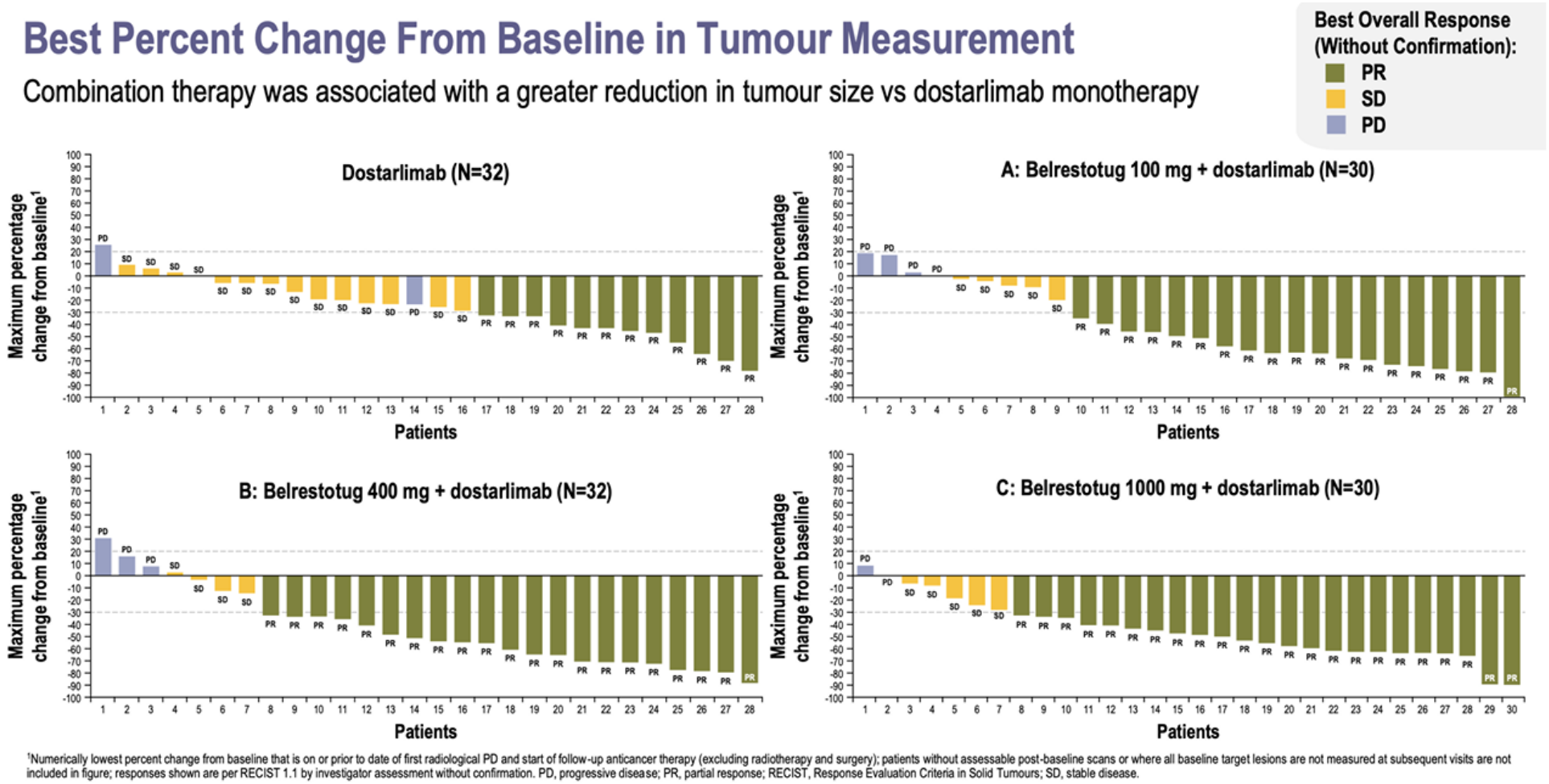
ORR per RECIST 1.1 by investigator assessment

Key Secondary Endpoints:

- PFS
- OS
- DoR
- Safety
- PK
- ADA

CBNPC MÉTASTATIQUE : GALAXIES LUNG 201

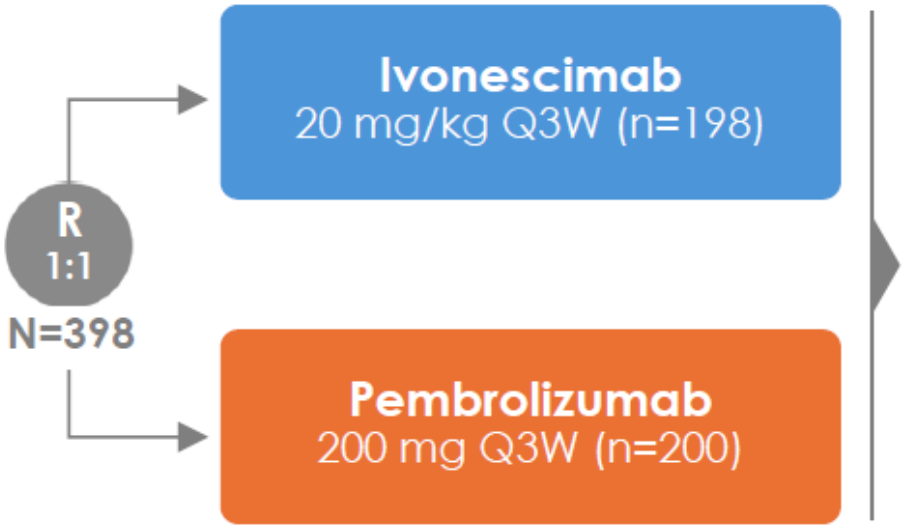
Taux de réponse objective :
➢ 28.1 % groupe DOSTARLIMAB seul
➢ Environ 60% pour toutes les autres combinaisons anti TIGIT + DOSTARLIMAB



CBNPC MÉTASTATIQUE : HARMONI-2 (AKT 112-303)

Patient population

- CBNPC stade IIIB-IV
- Naïfs de traitement systémique
- Absence de mutation EGFR ou rearrangement ALK
- ECOG PS 0 or 1
- PD-L1 TPS ≥1%



Traitement jusqu'à absence de bénéfice clinique, toxicité inacceptable ou jusqu'à 24 mois

Strafication

- Stade Clinique (IIIB/C vs IV)
- Histologie (SQ vs non-SQ)
- PD-L1 TPS (≥50% vs 1-49%)

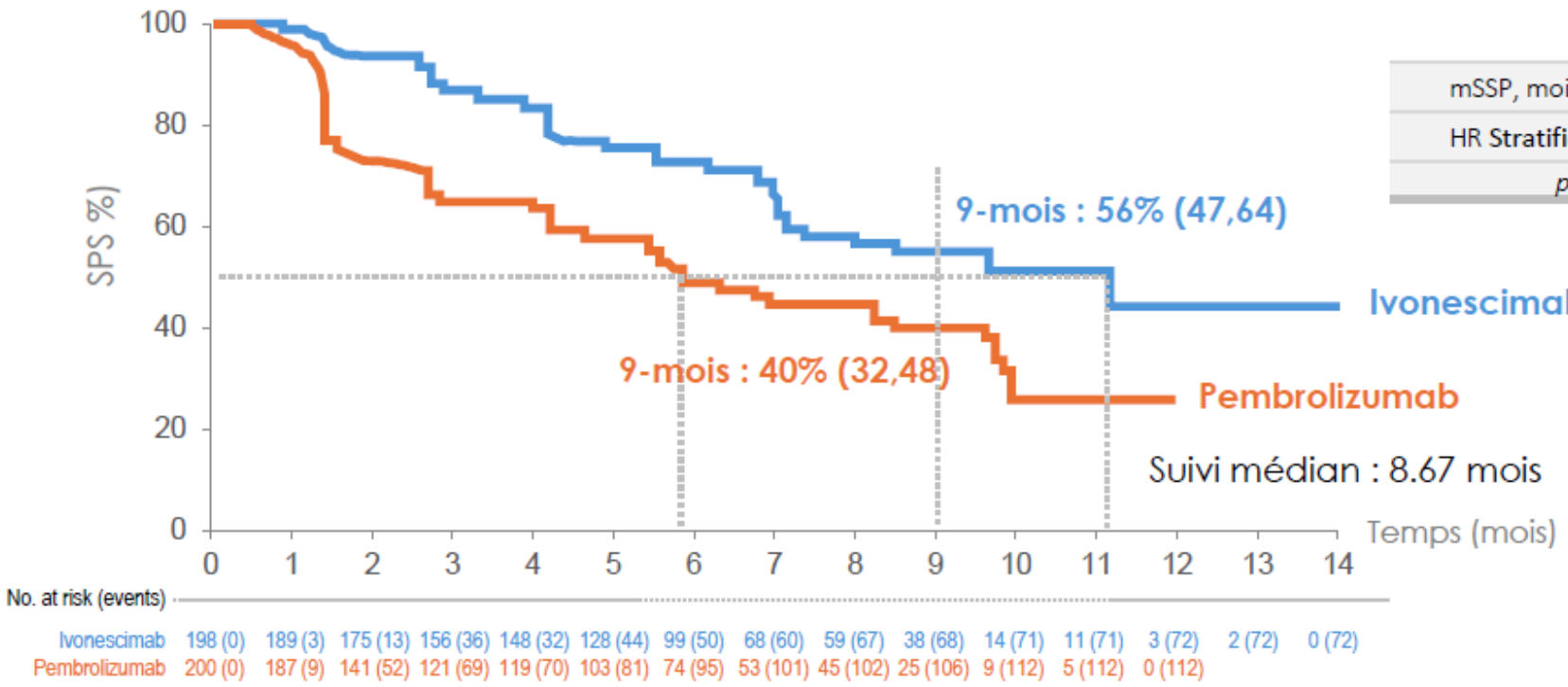
Critères de jugement

- Principal : SSP par revue indépendante par RECIST v1.1
- Secondaires : SG, SSP par investigateurs, ORR, DoR, TTR et tolérance
- Exploratoire : QoL (qualité de vie)

Zhou et al, WCLC 2024

CBNPC MÉTASTATIQUE : HARMONI-2 (AKT 112-303)

Objectif principal: SSP par revue indépendante



	Ivonescimab (n=198)	Pembrolizumab (n=200)
mSSP, mois (IC95%)	11,14 (7,33- NE)	5,82 (5,03-8,21)
HR Stratifié (IC95%)	0.51 (0.38, 0.69)	
p	<0,0001	

Zhou et al, WCLC 2024

LES NOUVEAUTÉS À SUIVRE

LES ADC ANTI TROP 2

Key eligibility criteria
- Histologically confirmed ES-SCLC
- Disease progression after no more than 1 prior line of platinum-based chemo and anti–PD-(L)-1 therapy
- Measurable disease per RECIST v1.1
- ECOG PS 0–1
- Stable, treated brain metastases allowed[a]

→ **ES-SCLC cohort** (N = 43)

sacituzumab govitecan

→ **SG 10 mg/kg** IV on D1 and D8 21-day cycles (until PD or unacceptable toxicity)

→ **Survival follow-up**

Primary end points
- ORR (INV[b])

Secondary end points
- DOR, CBR, PFS (INV[b])
- ORR, DOR, CBR, PFS (BICR[b])
- OS
- Safety

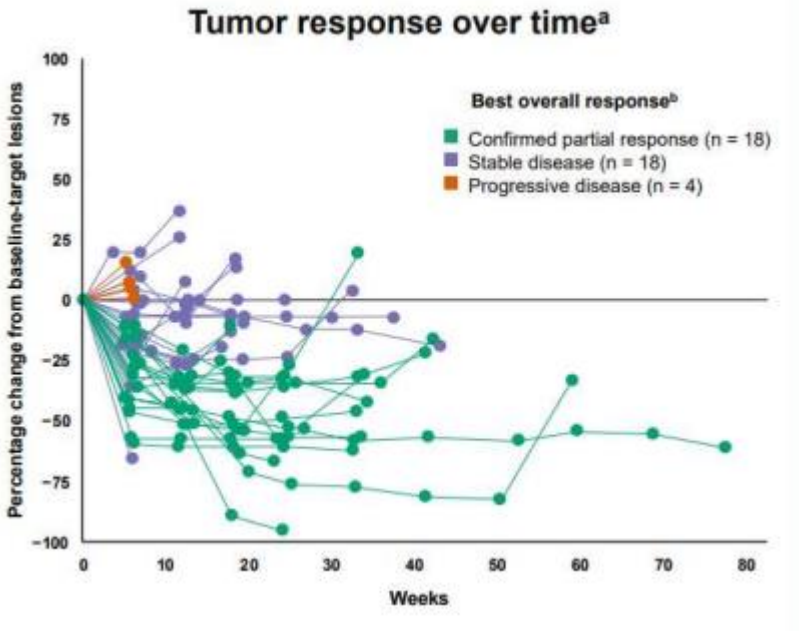
- At data cutoff (8 March 2024), median follow-up was 12.3 (range, 8.1–20.1) months

Best response to last prior anti-cancer therapy, n (%)[d]	
CR/PR	24 (55.8)
SD/PD	16 (37.2)

Chemotherapy-free interval, n (%)[b]	
<90 days (platinum-resistant)	20 (46.5)
≥90 days (platinum-sensitive)	23 (53.5)

Dowlati et al. WCLC 2024, Dowlati et al. JTO 2025

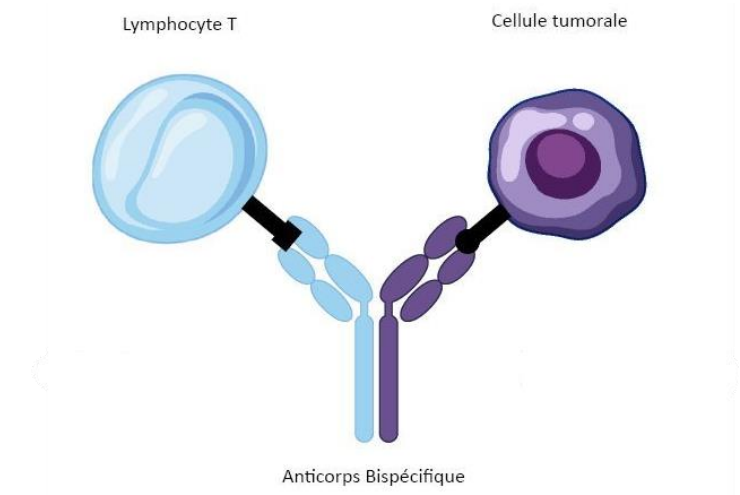
LES ADC ANTI TROP 2

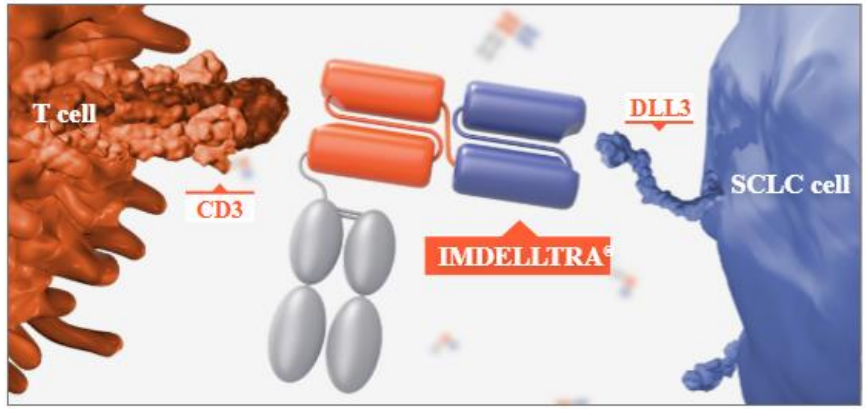


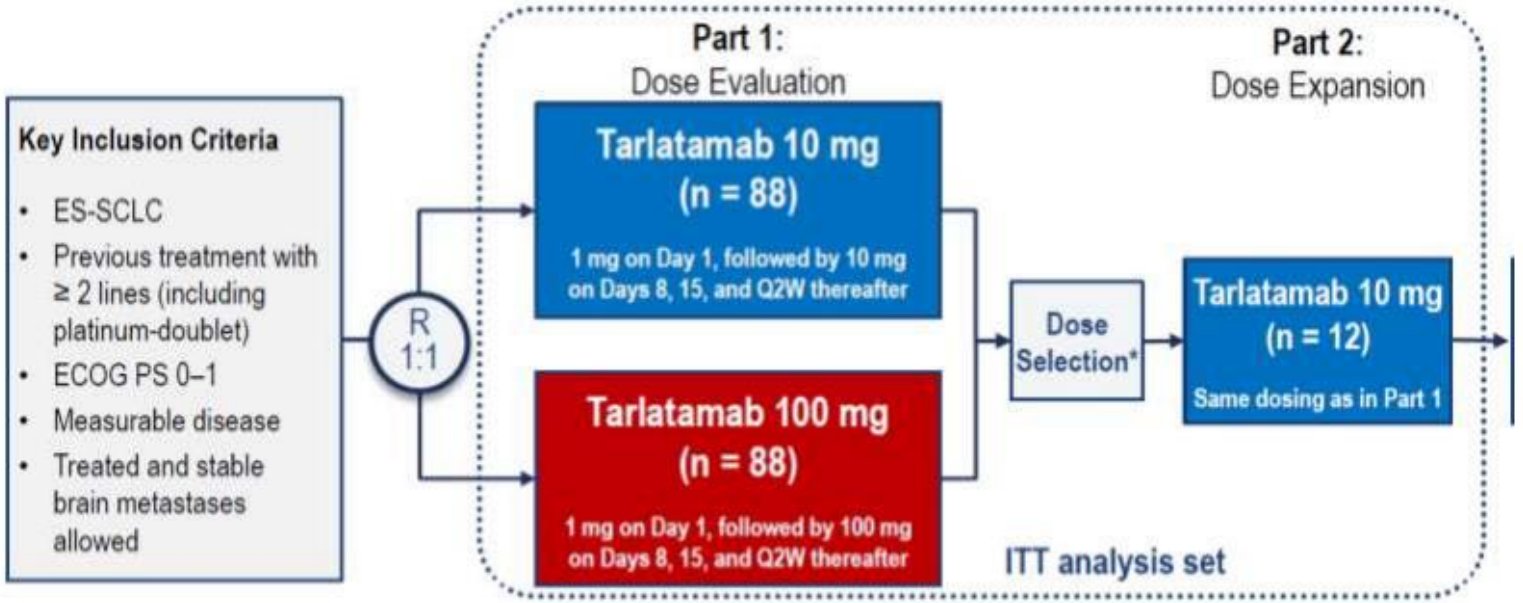
Efficacy[a]	Platinum resistant (CTFI <90 days) (n = 20)	Platinum sensitive (CTFI ≥90 days) (n = 23)
ORR, % (95% CI)	**35.0 (15.4–59.2)**	**47.8 (26.8–69.4)**
BOR, n (%)		
Confirmed PR	7 (35.0)	11 (47.8)
SD	7 (35.0)	11 (47.8)
PD	4 (20.0)	0
Not assessed[b]	2 (10.0)	1 (4.3)
DCR (confirmed PR + SD), % (95% CI)	70.0 (45.7–88.1)	95.7 (78.1–99.9)
CBR (confirmed PR + SD for ≥6 months), % (95% CI)	40.0 (19.1–63.9)	56.5 (34.5–76.8)
Median DOR, months (95% CI)[c,d]	6.3 (1.5–6.9)	4.4 (3.0–NR)
DOR rate at 6 months, % (95% CI)[c]	57.1 (17.2–83.7)	41.6 (13.1–68.4)
Median PFS, months (95% CI)[c]	3.8 (1.4–7.6)	5.0 (4.1–7.4)
Median OS, months (95% CI)[c]	6.6 (4.7–17.7)	14.7 (7.7–NR)

Dowlati et al. WCLC 2024, Dowlati et al. JTO 2025

LES ANTICORPS BI SPÉCIFIQUES : ANTI DLL3

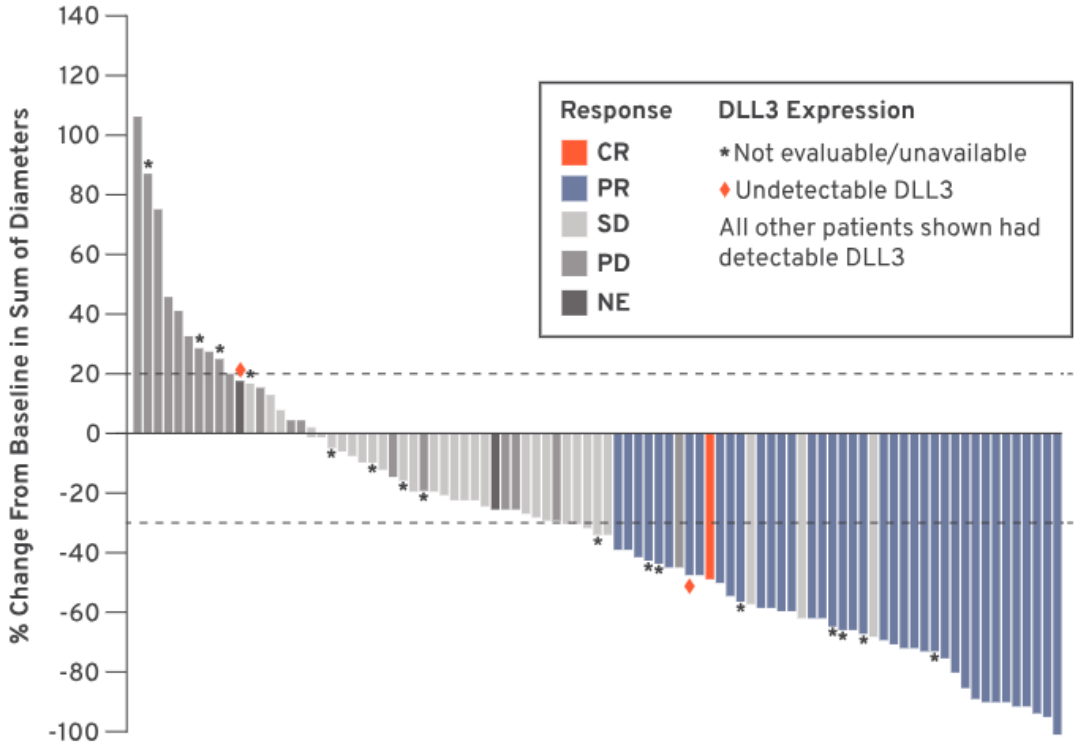


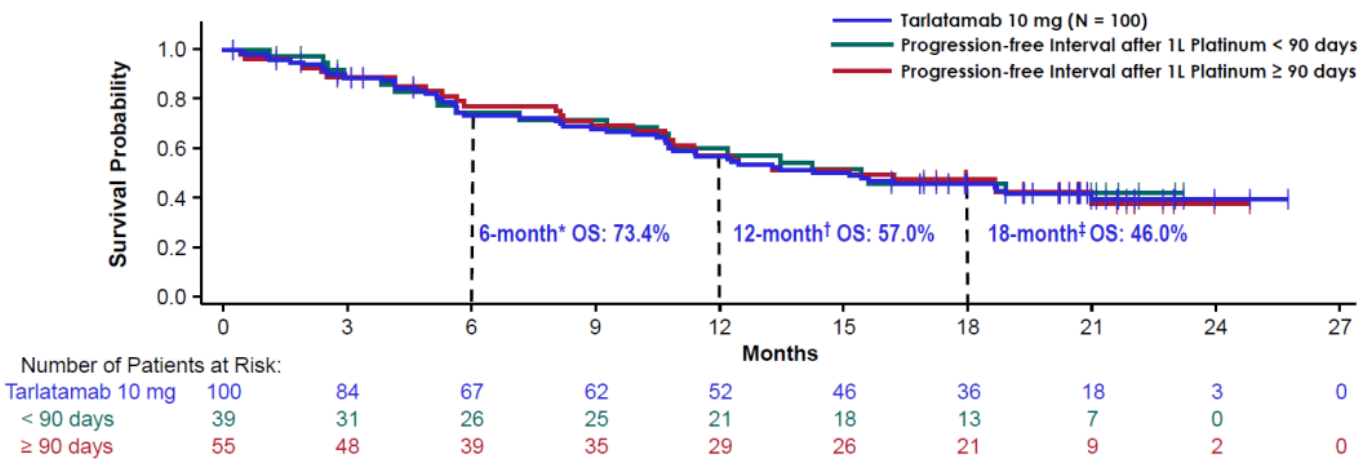




https://www.imdelltrahcp.com/
Ahn et al. NEJM 2023

LES ANTICORPS BI SPÉCIFIQUES : ANTI DLL3





Ahn et al. NEJM 2023, Sands WCLC 2024

LES ANTICORPS BI SPÉCIFIQUES : ANTI DLL3

SG à 9 mois de la maintenance : 89%

Médiane de SSP (après maintenance) : 5,6 mois

Lau WCLC 2024

MERCI POUR VOTRE ATTENTION