Post ESMO 2024

ACTUALITES EN ONCOLOGIE THORACIQUE

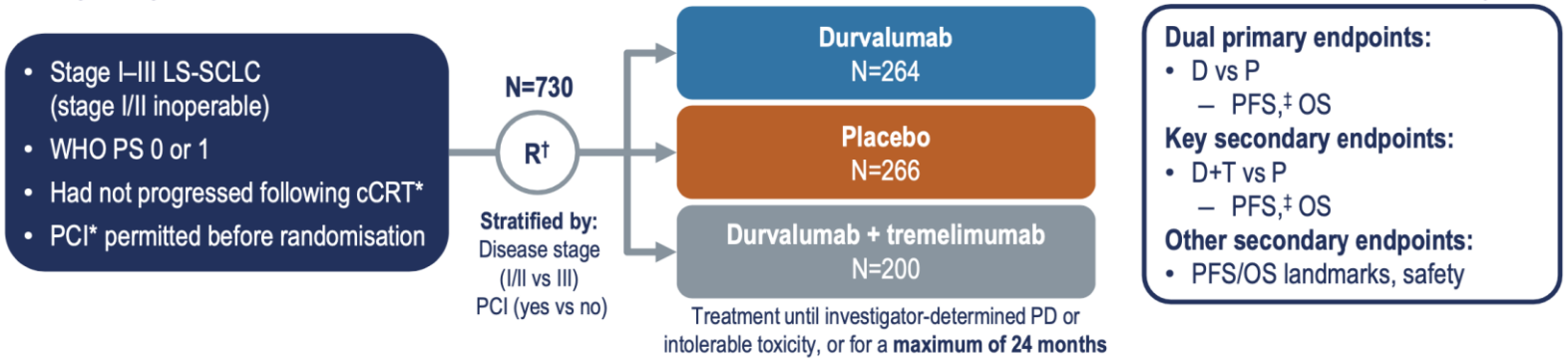
Dr Déborah LAMY - Dr Thomas COLLOT

Plan

CBPC	• Localement avancé • Métastatique
CBNPC sans driver	• Localisé • Métastatique
CBNPC avec driver	• EGFR • ALK • KRAS • BRAF

CBPC – localement avancé : ADRIATIC

Ongoing, randomised, double-blind, placebo-controlled, multicentre, international study



PCI/cCRT components (in line with standards of care)*

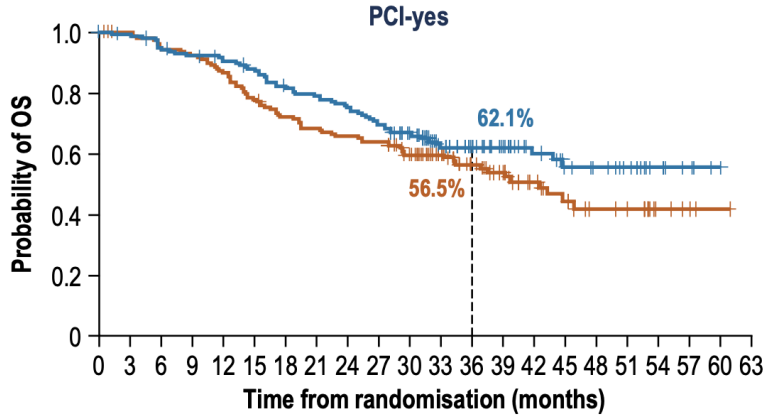
- PCI delivered before randomisation, as clinically indicated
- Four cycles of platinum (cisplatin or carboplatin) and etoposide (three permitted†)
- RT: 60–66 Gy QD over 6 weeks or 45 Gy BID over 3 weeks‡

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

CBPC – localement avancé : ADRIATIC

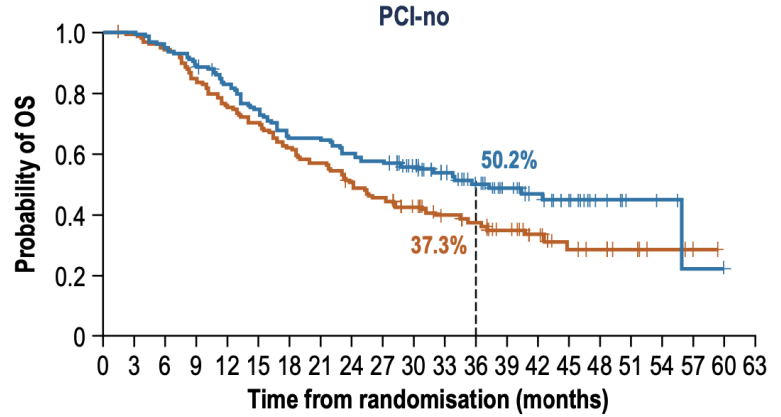
PCI-yes and PCI-no subgroups – OS

	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)‡		–	



No. at risk:

D, PCI-yes	142	139	132	127	124	118	110	105	100	93	82	63	51	40	29	23	19	15	8	4	1	0
P, PCI-yes	143	140	133	129	122	110	100	95	91	89	77	61	48	37	26	20	14	13	5	3	1	0



No. at risk:

D, PCI-no	122	122	116	109	99	89	79	78	72	69	59	47	39	28	22	16	8	4	3	1	0	0
P, PCI-no	123	120	114	102	92	85	75	69	60	54	46	36	32	25	18	11	9	6	3	2	0	0

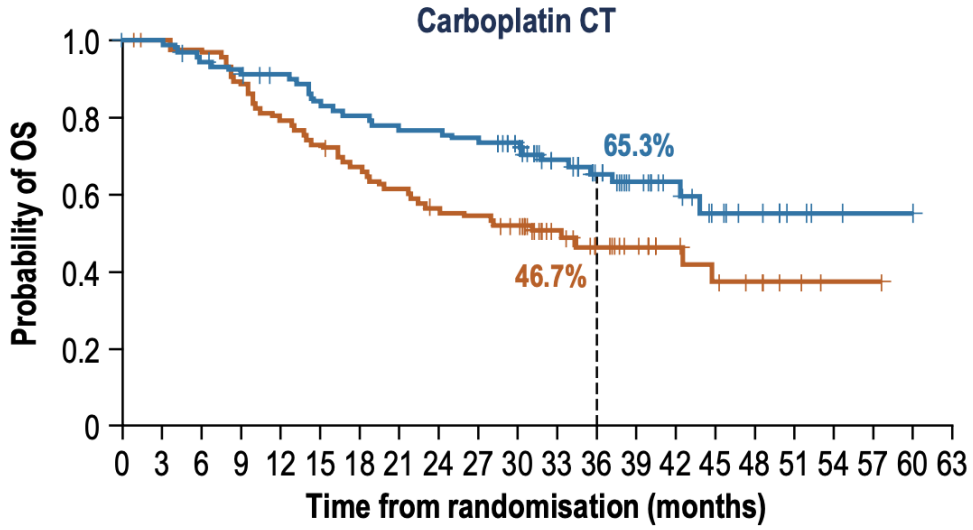
*Subgroup HRs and CIs calculated using an unstratified Cox proportional hazards model.
†ITT HR and CIs calculated using a Cox proportional hazards model stratified by receipt of PCI.
‡Multivariable analysis interaction p-value 0.96.

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

ADRIATIC : CARBOPLATINE VS CISPLATINE

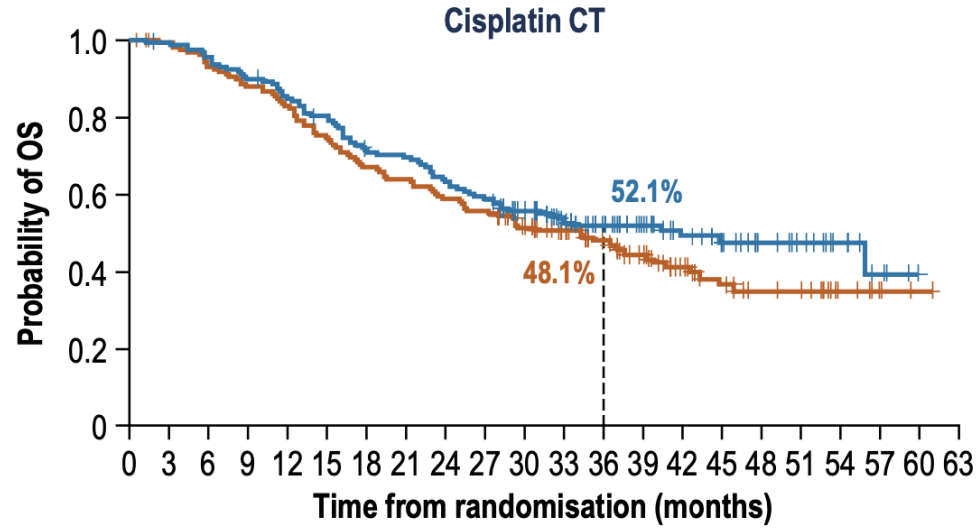
Survie Globale

	Carboplatin CT		Cisplatin CT		ITT	
	D (n = 91)	P (n = 88)	D (n = 173)	P (n = 178)	D (n = 264)	P (n = 266)
Median OS (95% CI), months	NR (42.5–NE)	33.4 (21.7–NE)	41.9 (27.7–NE)	34.3 (25.4–40.7)	55.9 (37.3–NE)	33.4 (25.5–39.9)
3-year OS, %	65.3	46.7	52.1	48.1	56.5	47.6
HR (95% CI)	0.56 (0.35–0.89)*		0.82 (0.61–1.10)*		0.73 (0.57–0.93)†	
Multivariable HR (95% CI)	0.55 (0.35–0.87)‡		0.81 (0.60–1.08)‡		–	



No. at risk:

D, carboplatin	91	90	84	81	77	71	68	66	65	63	55	40	32	23	17	11	8	4	2	1	1	0
P, carboplatin	88	86	84	77	69	63	57	52	47	45	41	28	22	16	11	8	6	3	1	1	0	0



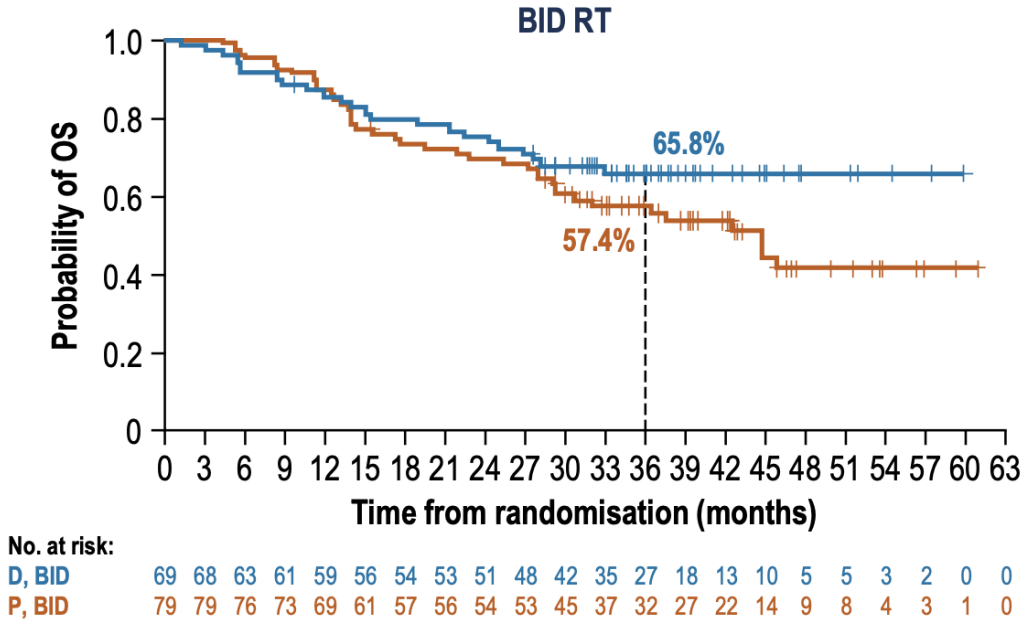
No. at risk:

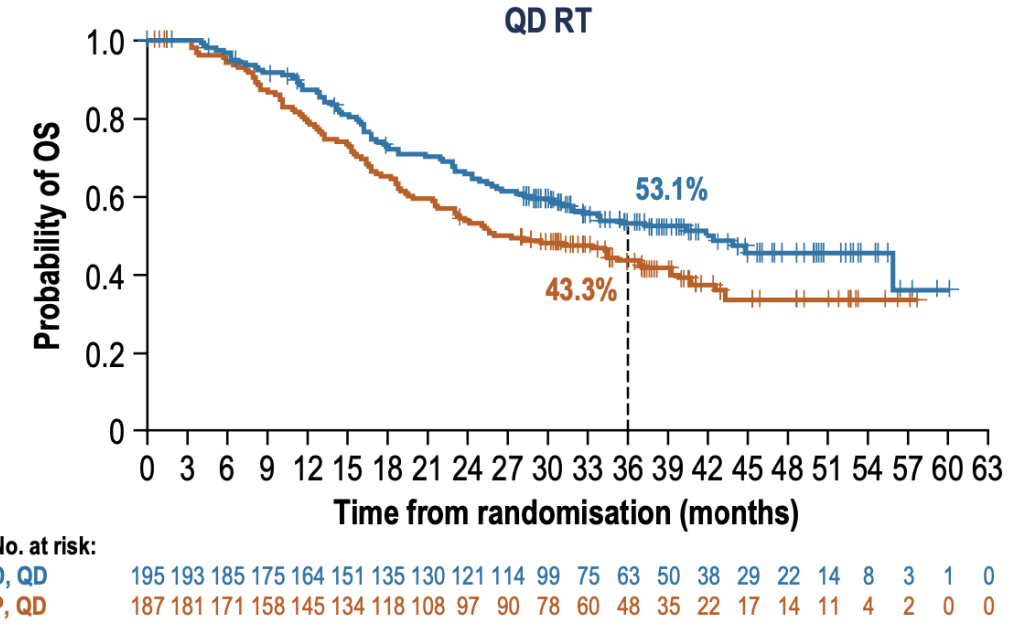
D, cisplatin	173	171	164	155	146	136	121	117	107	99	86	70	58	45	34	28	19	15	9	4	0	0
P, cisplatin	178	174	163	154	145	132	118	112	104	98	82	69	58	46	33	23	17	16	7	4	1	0

ADRIATIC : Bifractionné VS monofractionné

Survie globale

	BID RT		QD RT		ITT	
	D (n = 69)	P (n = 79)	D (n = 195)	P (n = 187)	D (n = 264)	P (n = 266)
Median OS (95% CI), months	NR (NE–NE)	44.8 (29.4–NE)	41.9 (32.0–NE)	26.1 (21.7–36.8)	55.9 (37.3–NE)	33.4 (25.5–39.9)
3-year OS, %	65.8	57.4	53.1	43.3	56.5	47.6
HR (95% CI)	0.68 (0.40–1.14)*		0.72 (0.55–0.96)*		0.73 (0.57–0.93)†	
Multivariable HR (95% CI)	0.71 (0.42–1.18)‡		0.73 (0.55–0.96)‡		–	





Plan

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CBNP avec driver	• EGFR • ALK • KRAS • BRAF

CBPC – Métastatique : BMS 986012

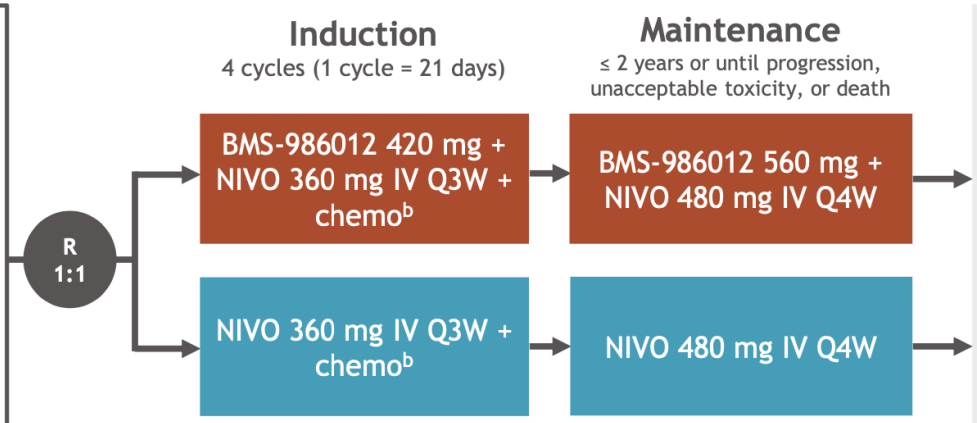
Anti FUC-GM1 + CT + NIVOLUMAB

Study design

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)



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

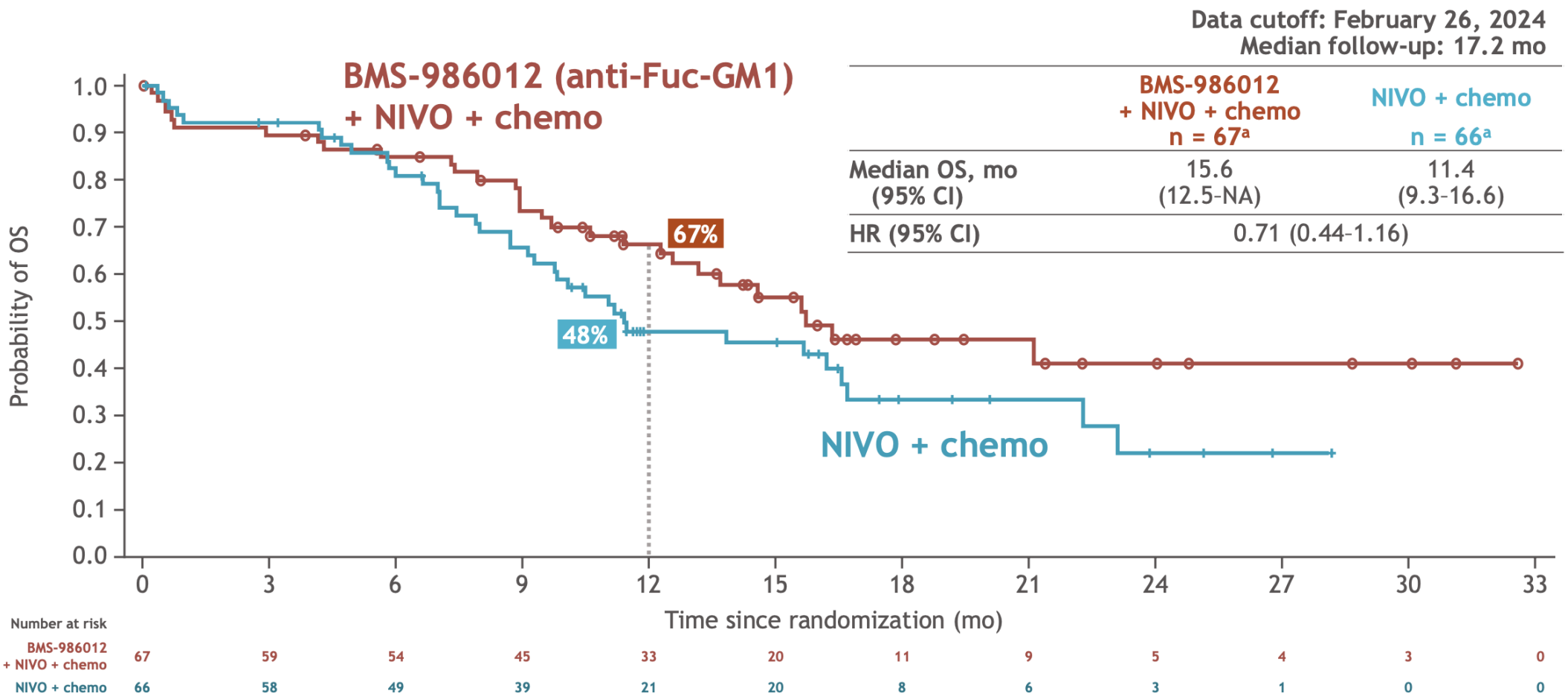
Secondary endpoints
- OS
- ORR, DOR and TTR by BICR (per RECIST v1.1)
- PFS by investigator (per RECIST v1.1)
- Immunogenicity

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

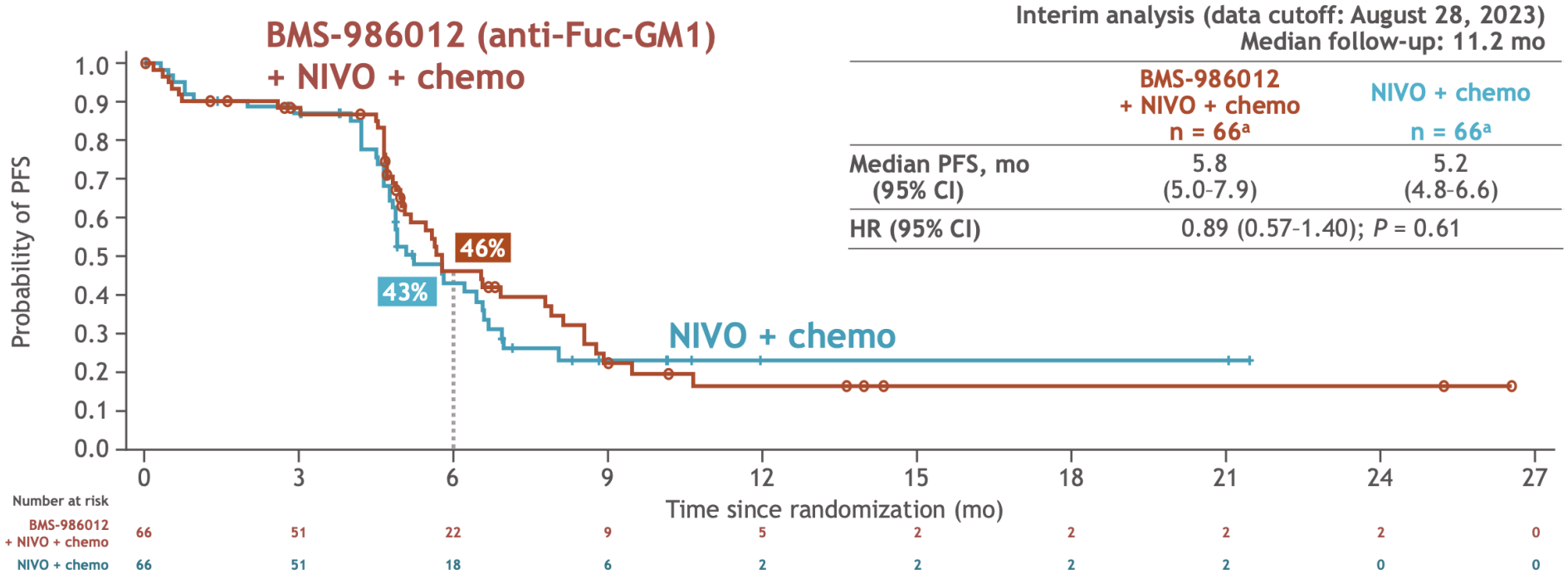
Anti FUC-GM1 + CT + NIVOLUMAB - Survie globale



	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

Anti FUC-GM1 + CT + NIVOLUMAB – Survie sans progression



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

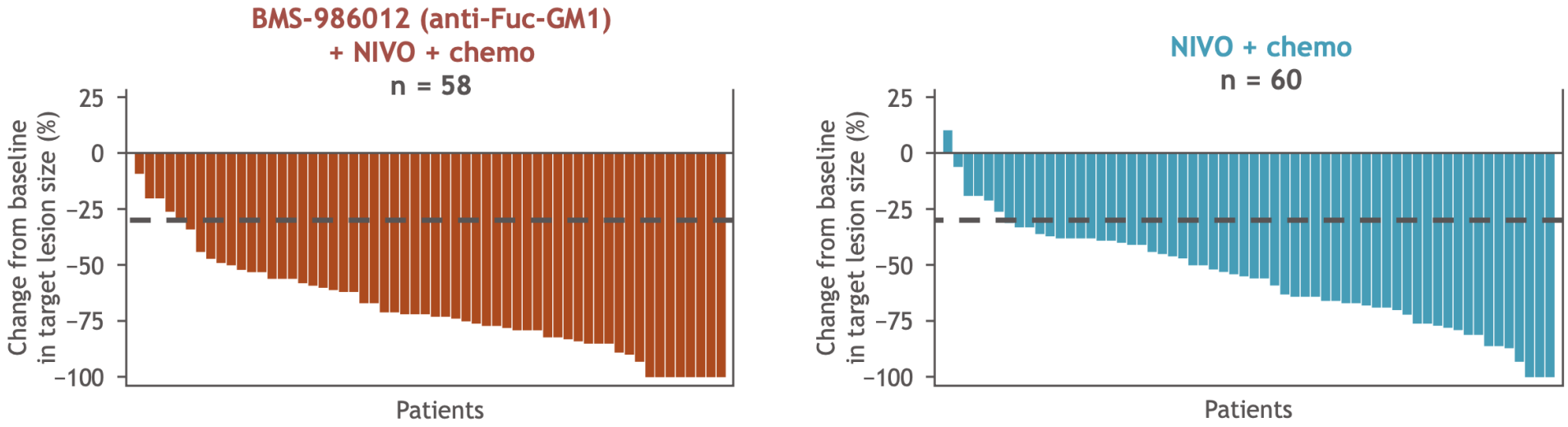
	BMS-986012 + NIVO + chemo n = 66[a]	NIVO + chemo n = 66[a]
Median PFS, mo (95% CI)	5.8 (5.0-7.9)	5.2 (4.8-6.6)
HR (95% CI)	0.89 (0.57-1.40); *P* = 0.61	

- 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**

CBPC – Métastatique : BMS 986012

Profondeur de la réponse

Depth of response and time to response



- Median time to response[a] was 1.5 mo (range 1.3–3.0) with **BMS-986012 (anti-Fuc-GM1) + NIVO + chemo** and 1.6 mo (range 1.2–5.2) with **NIVO + chemo**

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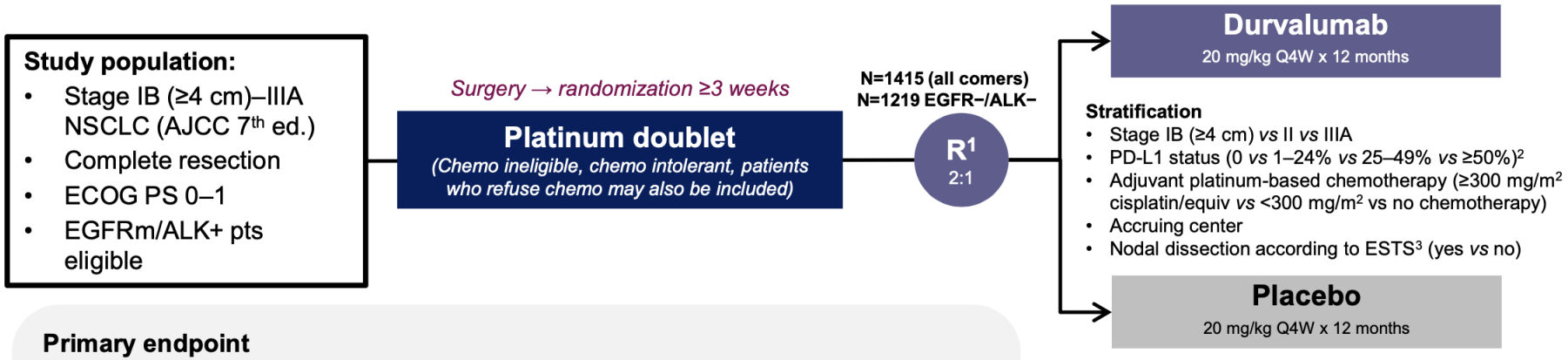
CBNPC localisé : CCTG BR31

Schéma de l'étude : DURVALUMAB en adjuvant (après CT)

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

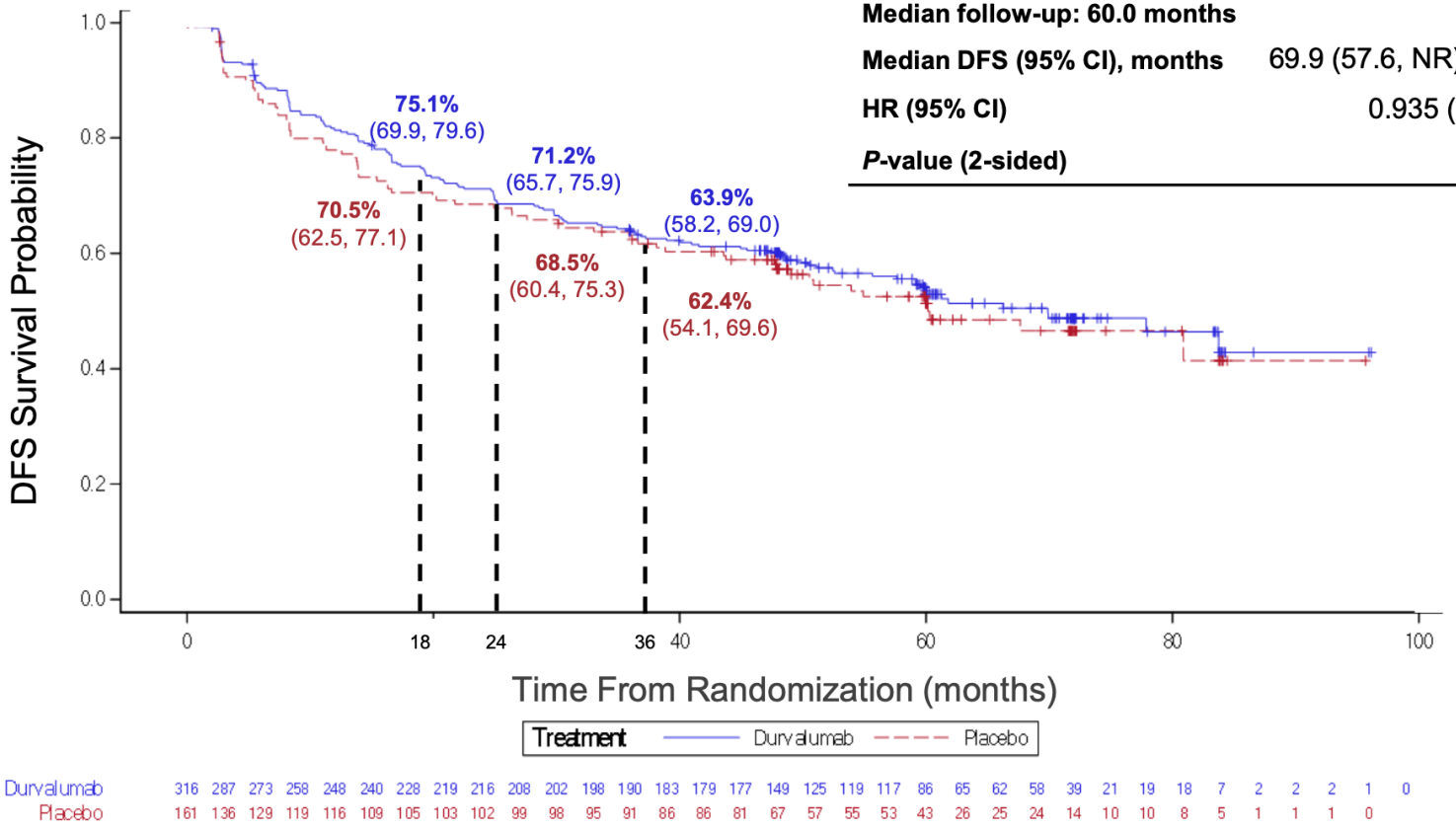
Today, we will present the final DFS analysis from three EGFR−/ALK− populations

CBNPC localisé : CCTG BR31 (durvalumab adjuvant)

Survie sans maladie PDL1 ≥ 25%, EGFR - ALK -

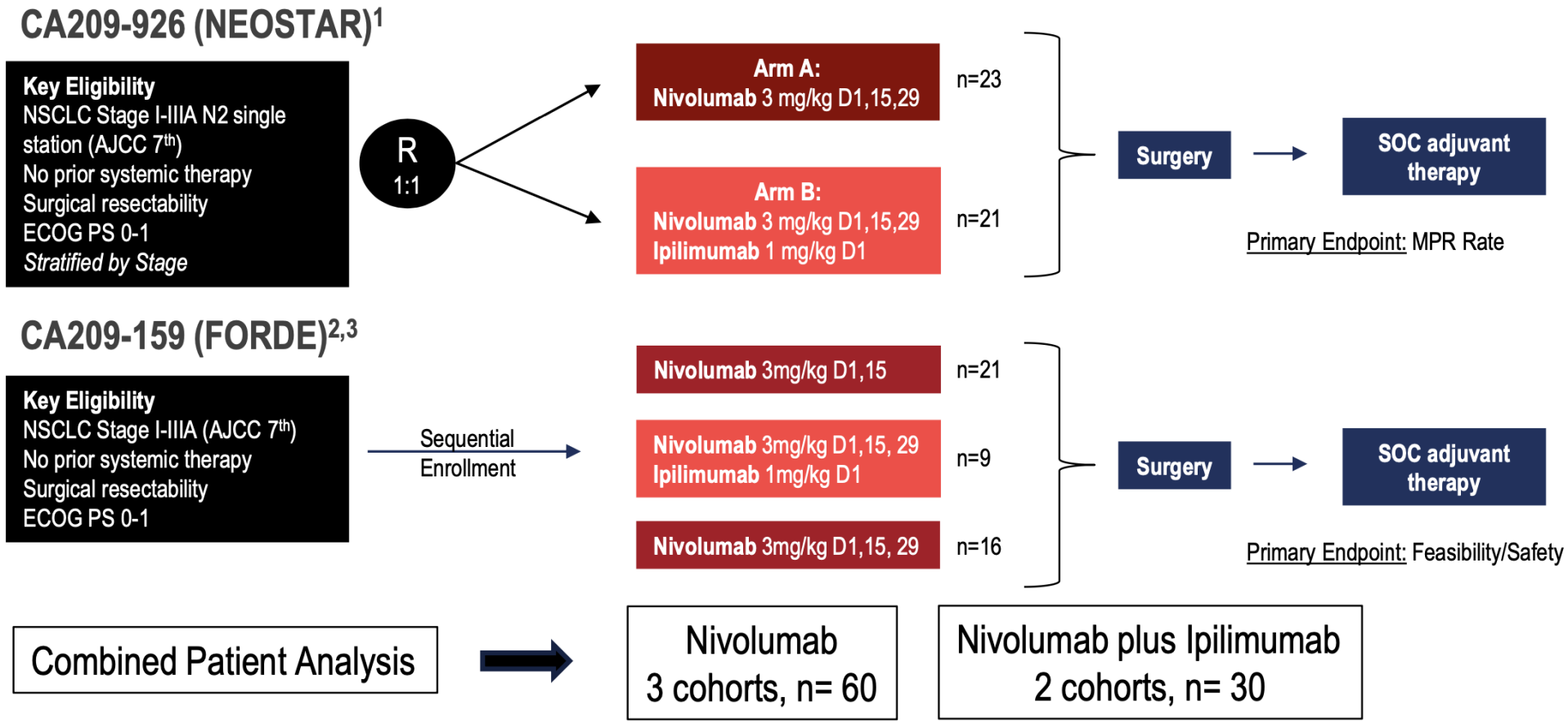
DFS in PD-L1≥25% EGFR−/ALK−

	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	



CBNPC localisé : NEOSTAR and CA209-159

Résultats de survie combinés à 5 ans



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

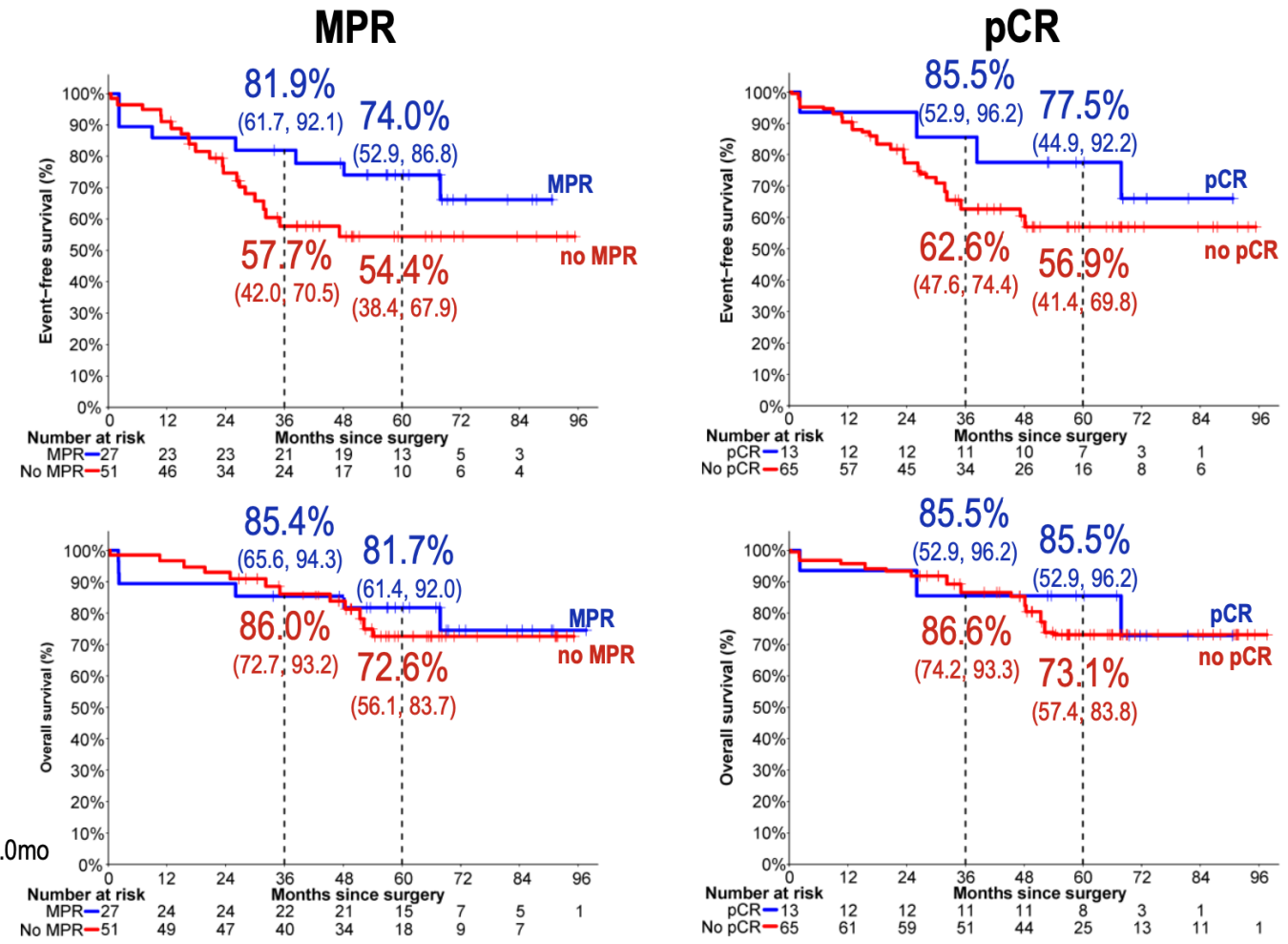
CBNPC localisé : NEOSTAR et CA209-159

Données de survie selon le taux de réponse pathologique

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)

Landmark EFS and OS by pathologic response status for whole study population



Median f/u 65.0mo

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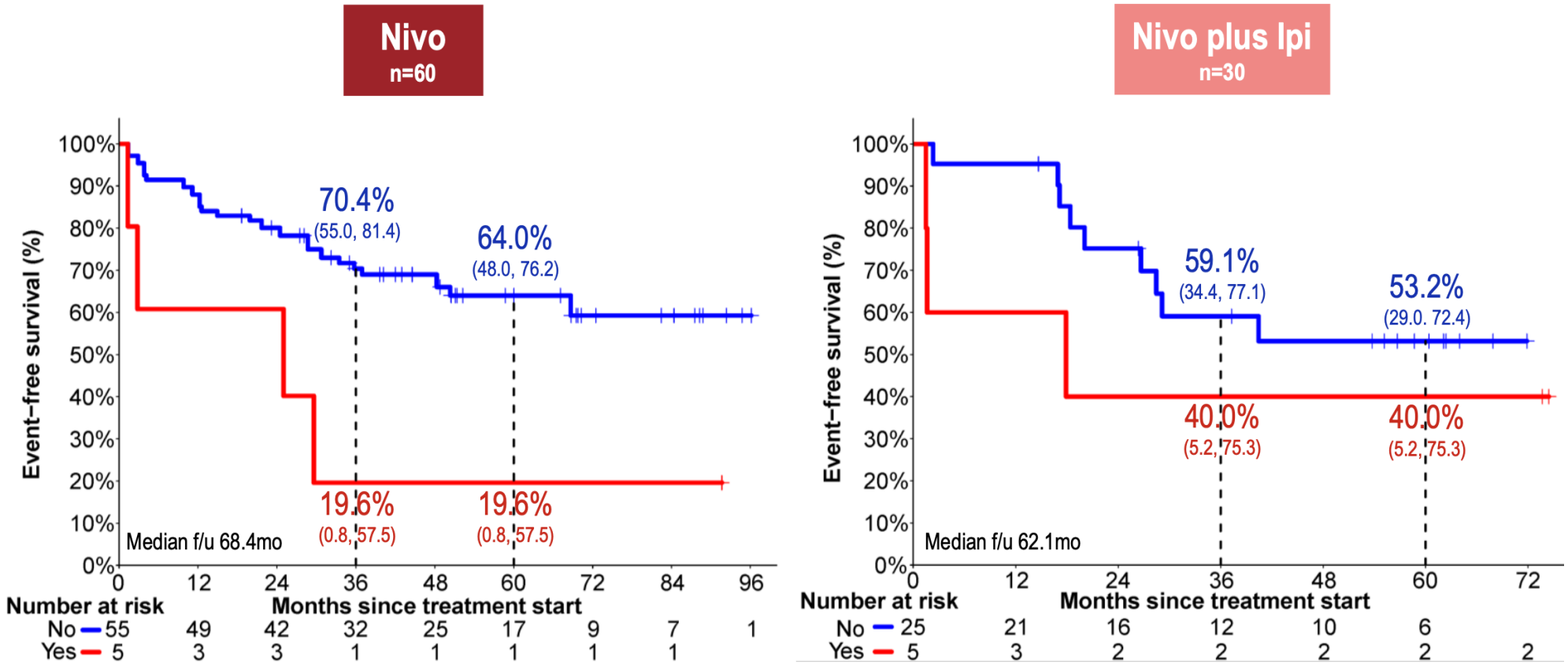
Joshua E. Reuss

CBNPC localisé : NEOSTAR et CA209-159

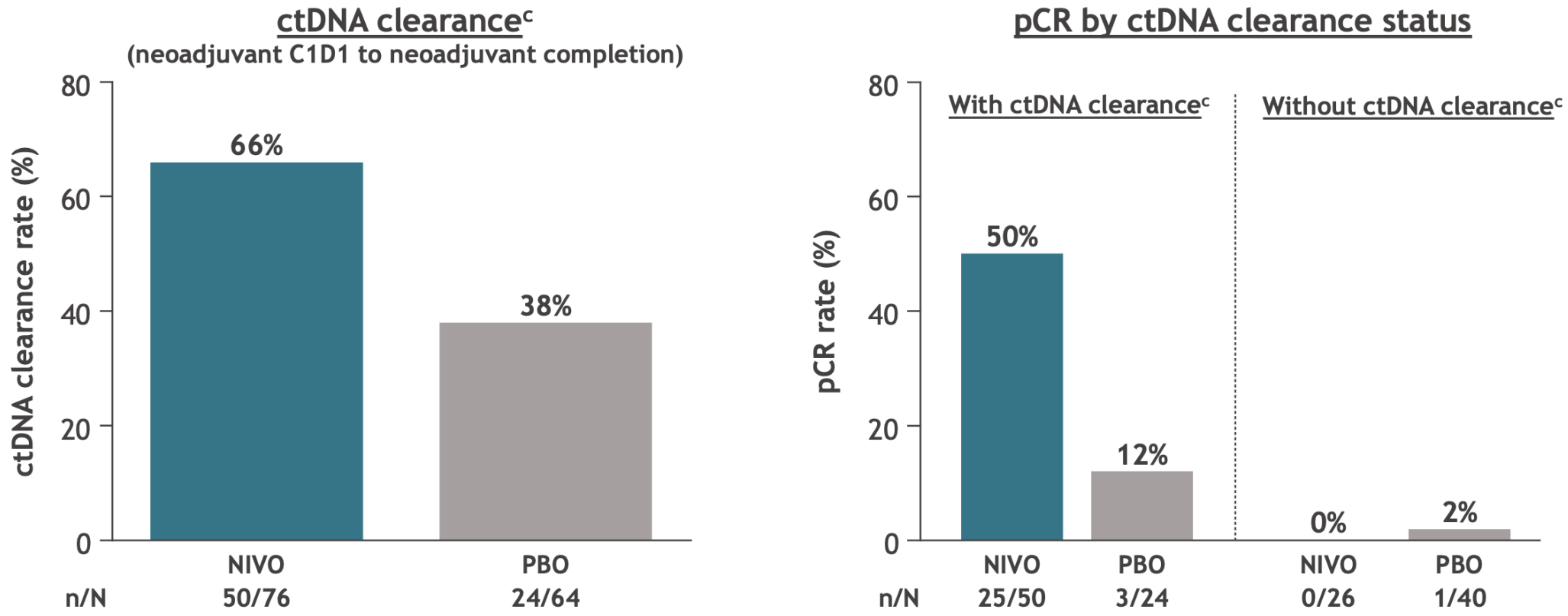
selon le statut moléculaire



CBNPC localisé : CHECKMATE 77T

NIVOLUMAB péri-opératoire versus placebo : exploratory analyses

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)

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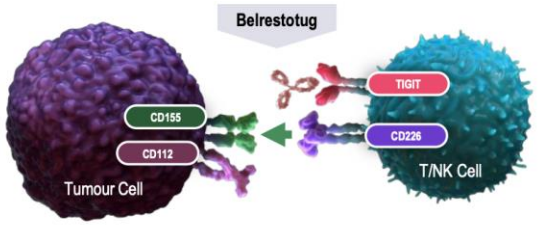
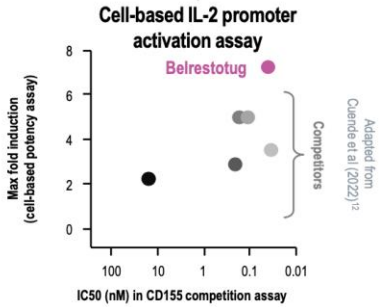
CBNPC métastatique: GALAXIES Lung 201

Belrestotug (anti TIGIT)+ Dostarlimab (anti PD1)

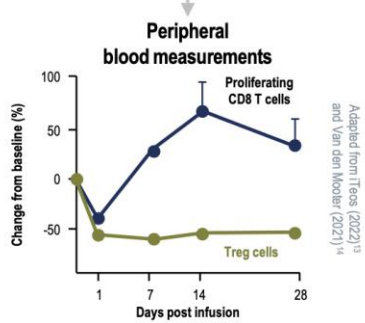
Belrestotug is an **Fcγ-receptor enabled mAb**[10,11] with two key mechanisms of action



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

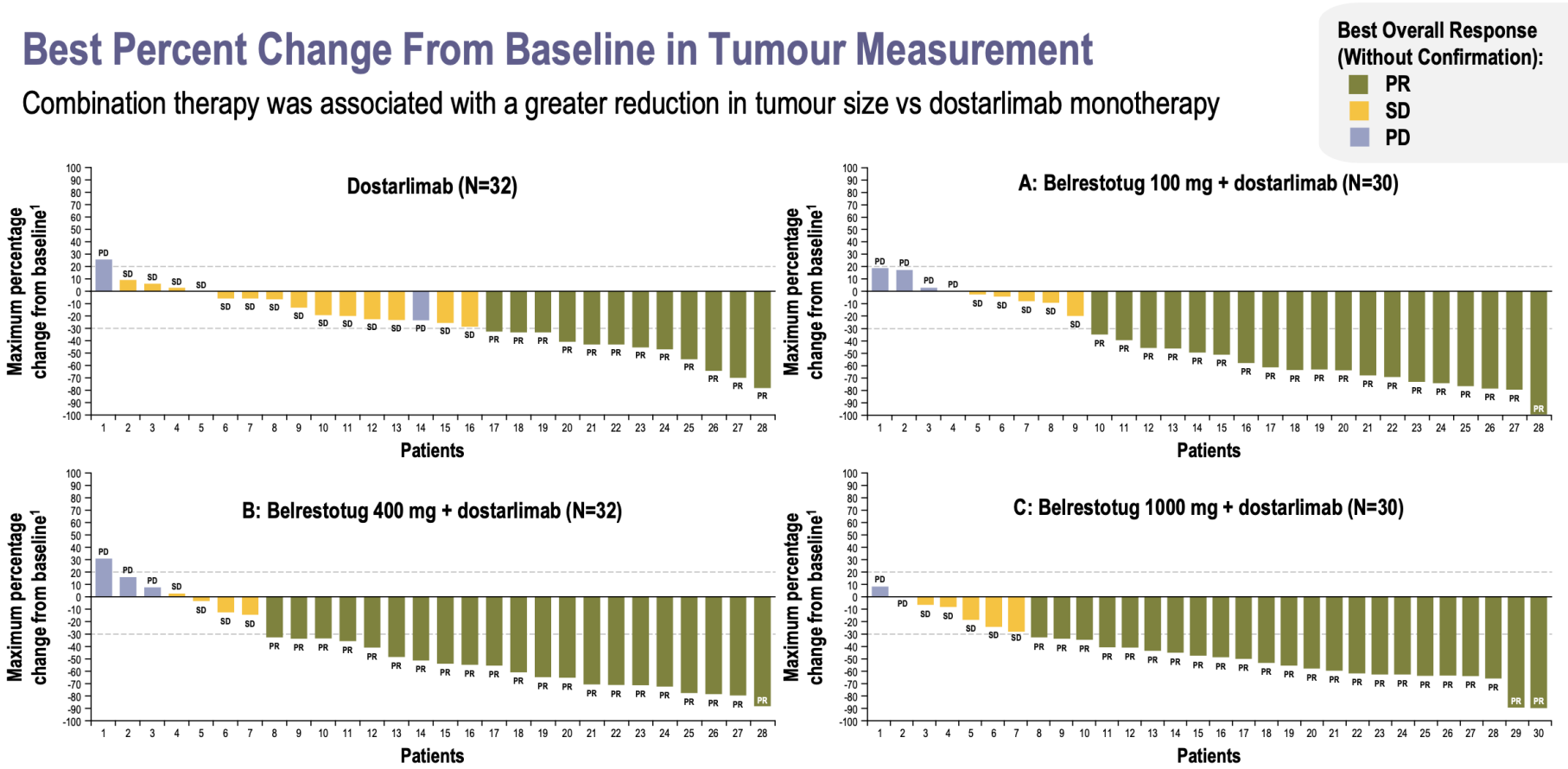
Belrestotug (anti TIGIT)+ Dostarlimab (anti PD1)

Taux de réponse objective :

- 28.1 % groupe DOSTARLIMAB seul
- Environ 60% pour toutes les autres combinaisons anti TIGIT + DOSTARLIMAB

Best Percent Change From Baseline in Tumour Measurement

Combination therapy was associated with a greater reduction in tumour size vs dostarlimab monotherapy

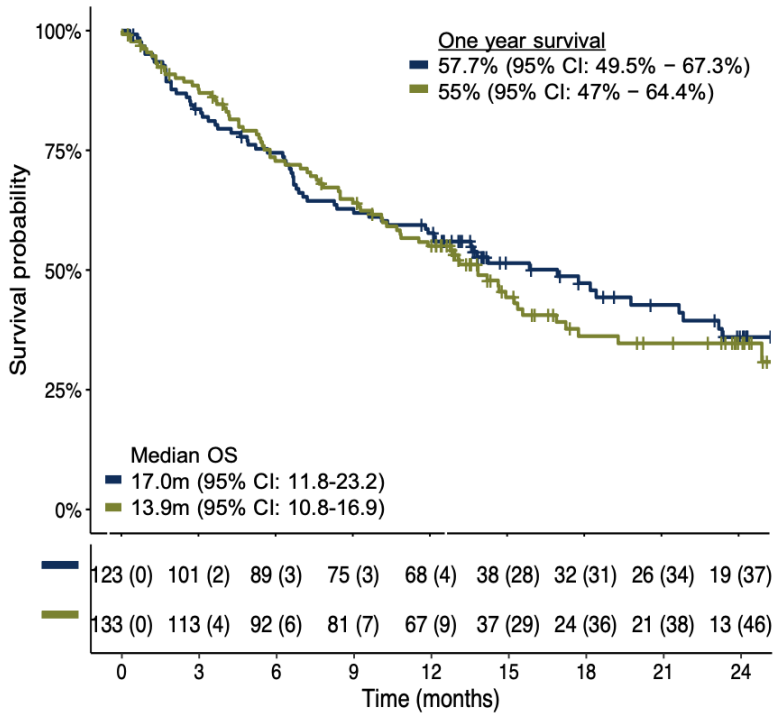


[1]Numerically lowest percent change from baseline that is on or prior to date of first radiological PD and start of follow-up anticancer therapy (excluding radiotherapy and surgery); patients without assessable post-baseline scans or where all baseline target lesions are not measured at subsequent visits are not included in figure; responses shown are per RECIST 1.1 by investigator assessment without confirmation. PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumours; SD, stable disease.

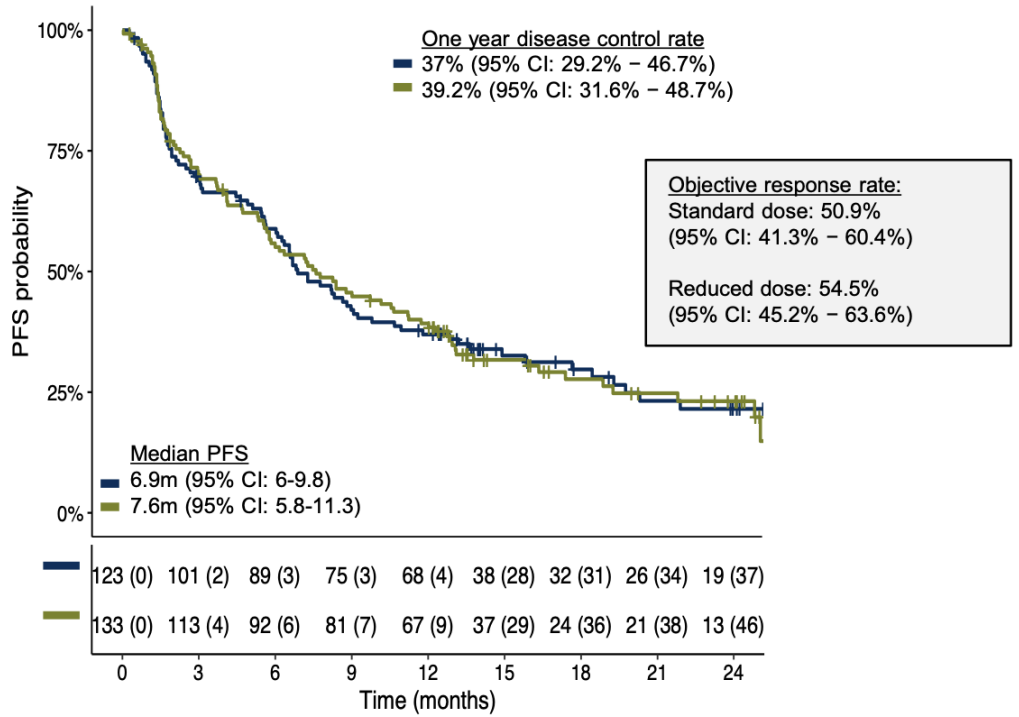
CBNPC métastatique : DEDICATION-1

Désescalade de dose PEMBROLIZUMAB : 100mg/3 sem ou 300 mg/6 sem

Overall survival



Progression free survival



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Standard dose

Reduced dose

DEDICATION

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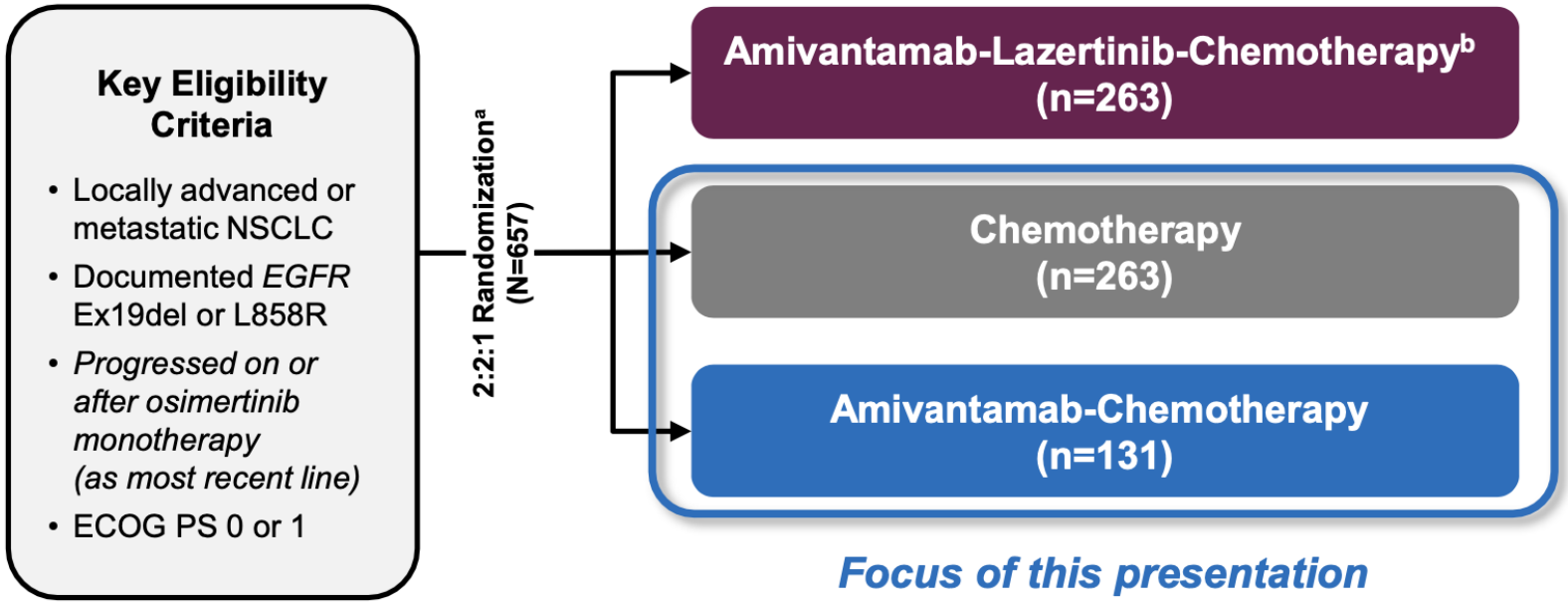
EGFR + : MARIPOSA 2 – 18 mois de suivi

Amivantanab + chimiothérapie en L2

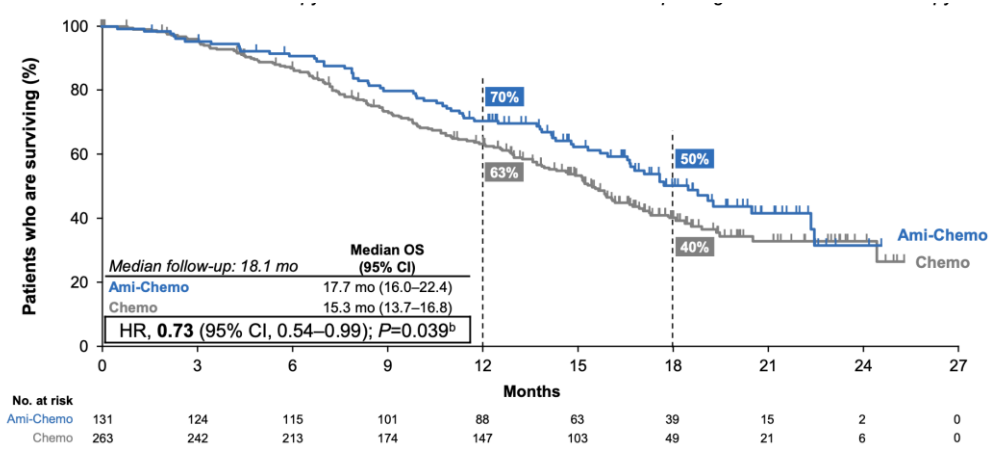


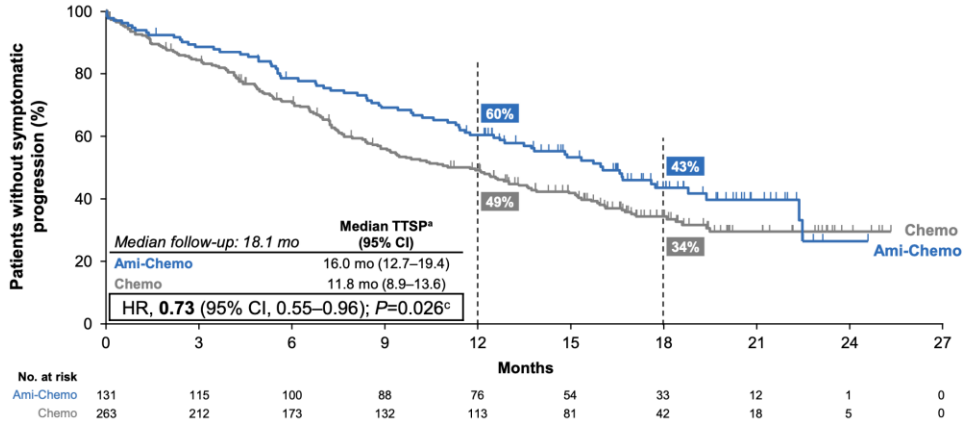
Secondary/Exploratory Efficacy Endpoints Reported:

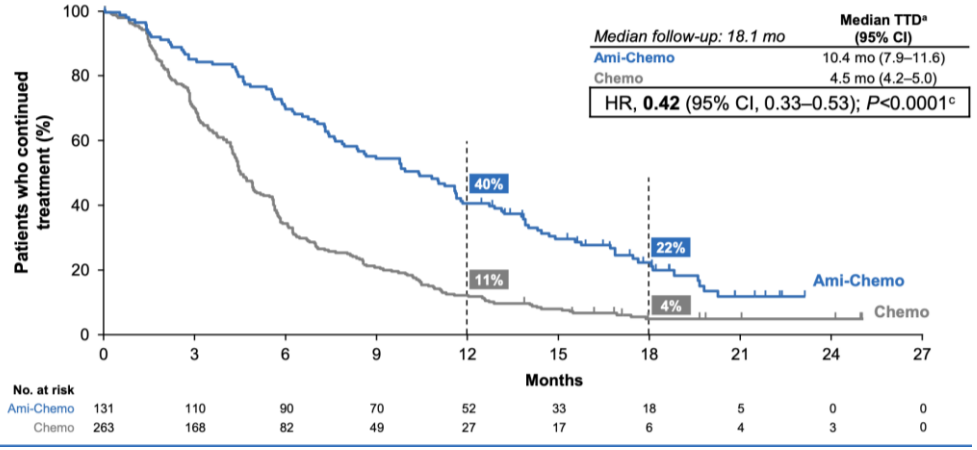
- Overall survival (OS)
- Time to symptomatic progression (TTSP)
- Time to treatment discontinuation (TTD)
- Time to subsequent therapy (TTST)
- PFS after first subsequent therapy (PFS2)

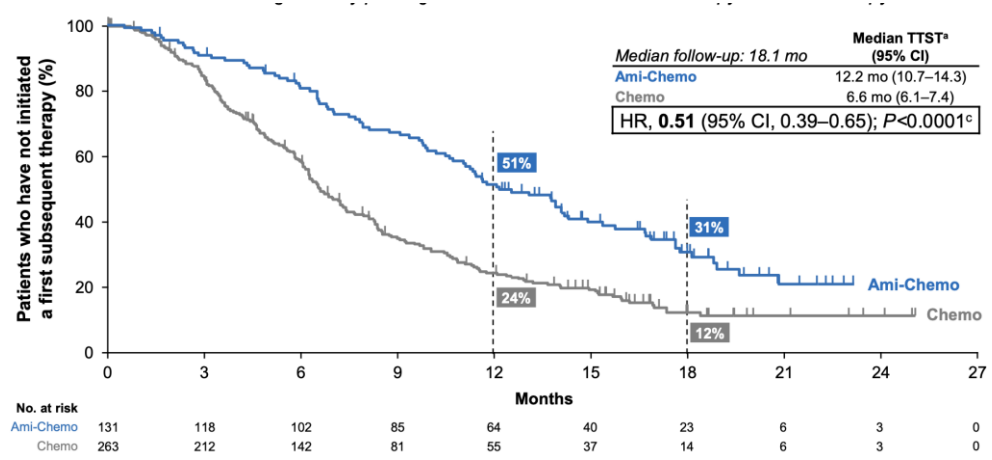
EGFR + : MARIPOSA 2 – 18 mois de suivi

Amivantamab + chimiothérapie en L2









EGFR avec ins ex 20 : REZILIENT

Zipalertinib dans CBNPC avec insertion exon 20 EGFR, après AMIVANTAMAB

Statistics, n (%) [95% CI]	Ami only (n=18)	Ami + other ex20ins (n=12)	Total (N=30)
Confirmed ORR	9 (50.0) [26.0–74.0]	3 (25.0) [5.5–57.2]	12 (40.0) [22.7–59.4]
CR	1 (5.6) [0.1–27.3]	0	1 (3.3) [0.1–17.2]
PR	8 (44.4) [21.5–69.2]	3 (25.0) [5.5–57.2]	11 (36.7) [19.9–56.1]
SD	7 (38.9) [17.3–64.3]	8 (66.7) [34.9–90.1]	15 (50.0) [31.3–68.7]
DCR (CR+PR+SD)	16 (88.9) [65.3–98.6]	11 (91.7) [61.5–99.8]	27 (90.0) [73.5–97.9]

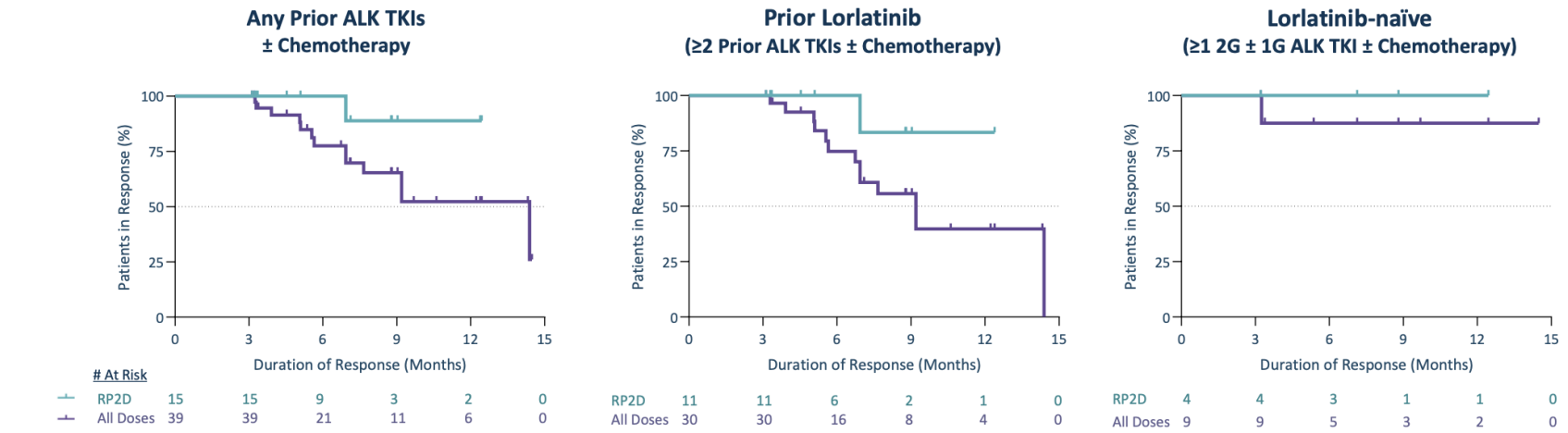
Médiane PFS : 9.7 mois

Plan

CBPC	• Localement avancé • Métastatique
CBNPC sans driver	• Localisé • Métastatique
CBNPC avec driver	• EGFR • ALK • KRAS • BRAF

CBNPC ALK + : ALKOV-1 (NVL 655)

Durable Tumor Response:
Previously Treated Patients with ALK+ NSCLC



NSCLC Response-Evaluable	All Dose Levels	RP2D	All Dose Levels	RP2D	All Dose Levels	RP2D
Median DOR, m (95% CI)	**14.4** (6.9, NE)	**Not Reached** (6.9, NE)	**9.2** (6.9, NE)	**Not Reached** (6.9, NE)	**Not Reached** (3.3, NE)	**Not Reached** (NE, NE)
DOR ≥ 6 m [a] (95% CI)	**78%** (58, 89)	**100%** (100, 100)	**75%** (52, 88)	**100%** (100, 100)	**88%** (39, 98)	**100%** (100, 100)

Plan

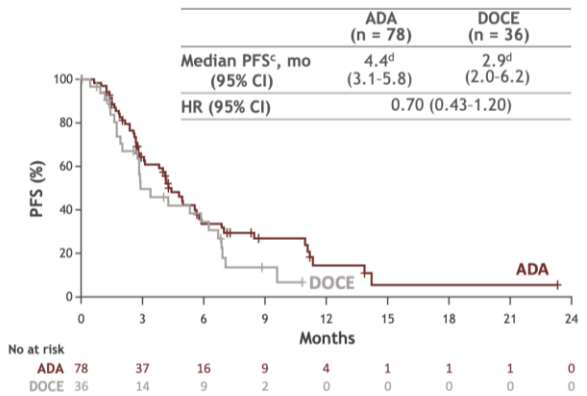
CBPC	• Localement avancé • Métastatique
CBNPC sans driver	• Localisé • Métastatique
CBNPC avec driver	• EGFR • ALK • KRAS • BRAF

CBNPC KRAS G12C : KRYSTAL 12
Adagrasib versus docetaxel

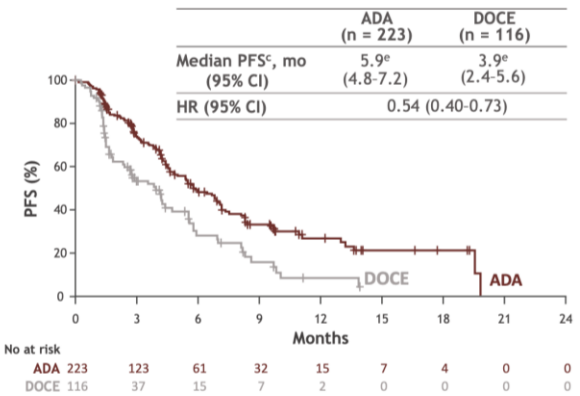
Amélioration PFS en faveur de l'ADAGRASIB (HR 0.58)
Réponse cérébrale : 40% ADAGRASIB versus 11% DOCETAXEL

Patients, n (%)	With baseline brain metastases		Without baseline brain metastases		All randomized	
	ADA (n = 77)	DOCE (n = 35)	ADA (n = 221)	DOCE (n = 105)	ADA (n = 298)	DOCE (n = 140)
All TRAEs	72 (94)	30 (86)	208 (94)	91 (87)	280 (94)	121 (86)
TRAEs leading to discontinuation	5 (7)	6 (17)	18 (8)	14 (13)	23 (8)	20 (14)
TRAEs leading to dose reduction	36 (47)	12 (34)	107 (48)	21 (20)	143 (48)	33 (24)
TRAEs leading to dose interruption	39 (51)	4 (11)	138 (62)	22 (21)	177 (59)	26 (19)
Treatment-related SAEs	13 (17)	8 (23)	49 (22)	15 (14)	62 (21)	23 (16)
Treatment-related deaths	0	1 (3)[c]	4 (2)[d]	0	4 (1)	1 (< 1)

Patients with baseline brain metastases



Patients without baseline brain metastases



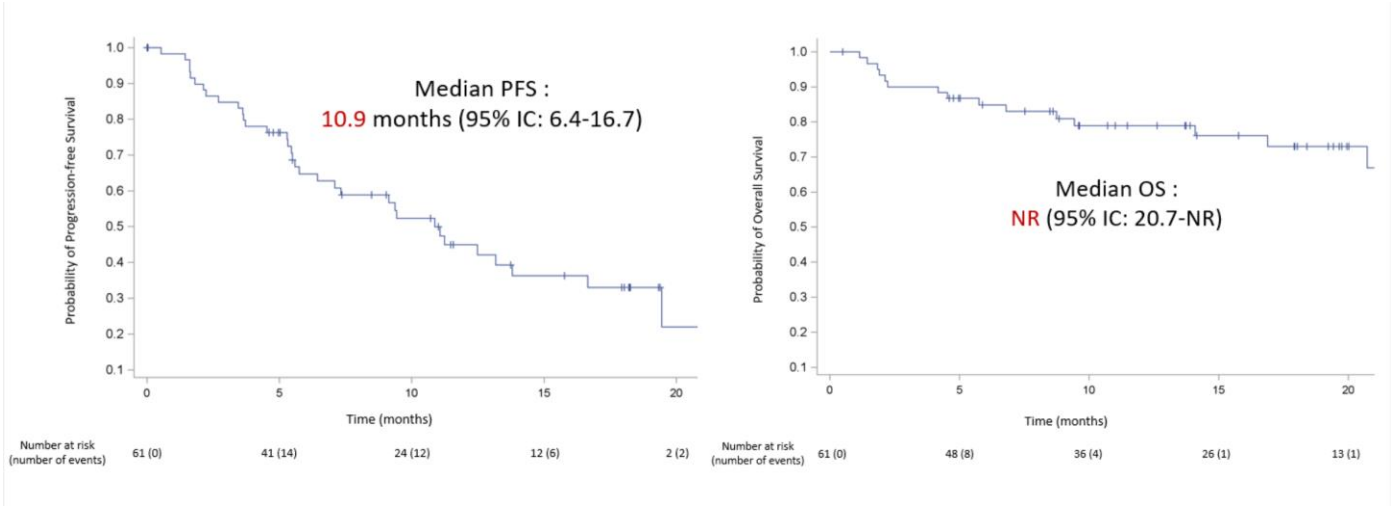
- ORR was higher in the ADA vs DOCE arm in patients with (26.9% vs 2.8%) and without (33.6% vs 11.2%) baseline brain metastases
- Median DOR[f] was higher in the ADA vs DOCE arm in patients with (7.4 vs 5.4 mo) and without (8.3 vs 5.4 mo) baseline brain metastases

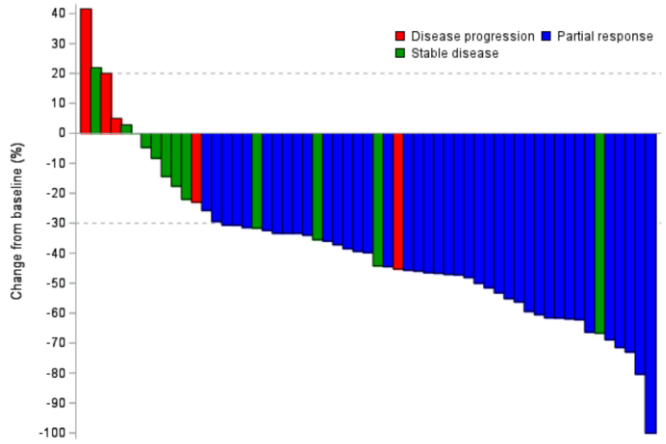
Plan

CBPC	• Localement avancé • Métastatique
CBNPC sans driver	• Localisé • Métastatique
CBNPC avec driver	• EGFR • ALK • KRAS • BRAF

CBNPC BRAF V600E : ENCOBRAF

encorafenib + binimetinib en première ligne





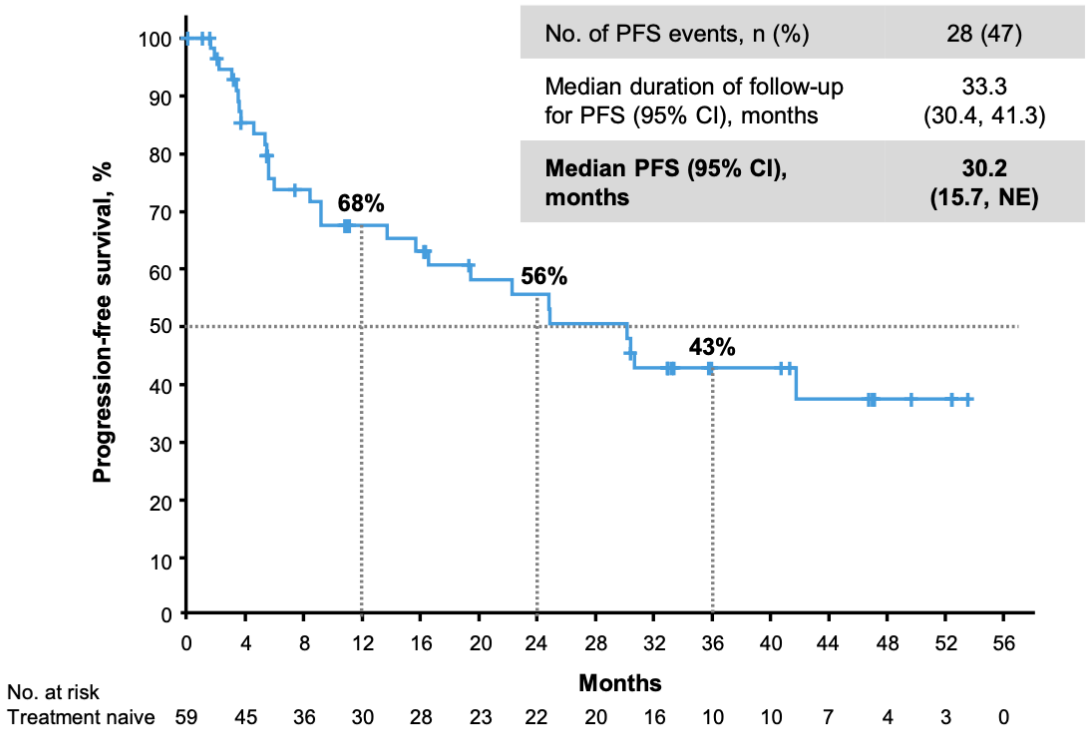
	Cohorte A (n=61)
Overall response confirmed, n (%) [95% CI]	**40 (65.6%)** [53.7% - 77.5%]
Partial response, n (%)	40 (65.6%)
Stable disease, n (%)	12 (19.7%)
Progressive disease, n (%)	5 (8.2%)
Not evaluable*, n (%)	4 (6.6%)
DOR, median [95% CI], months	**13 months** [9.1-NR]
DCR , % [95% CI]	**85.2%** [76.3% - 94.1%]

* 4 patients were not evaluable

CBNPC BRAF V600E : PHAROS

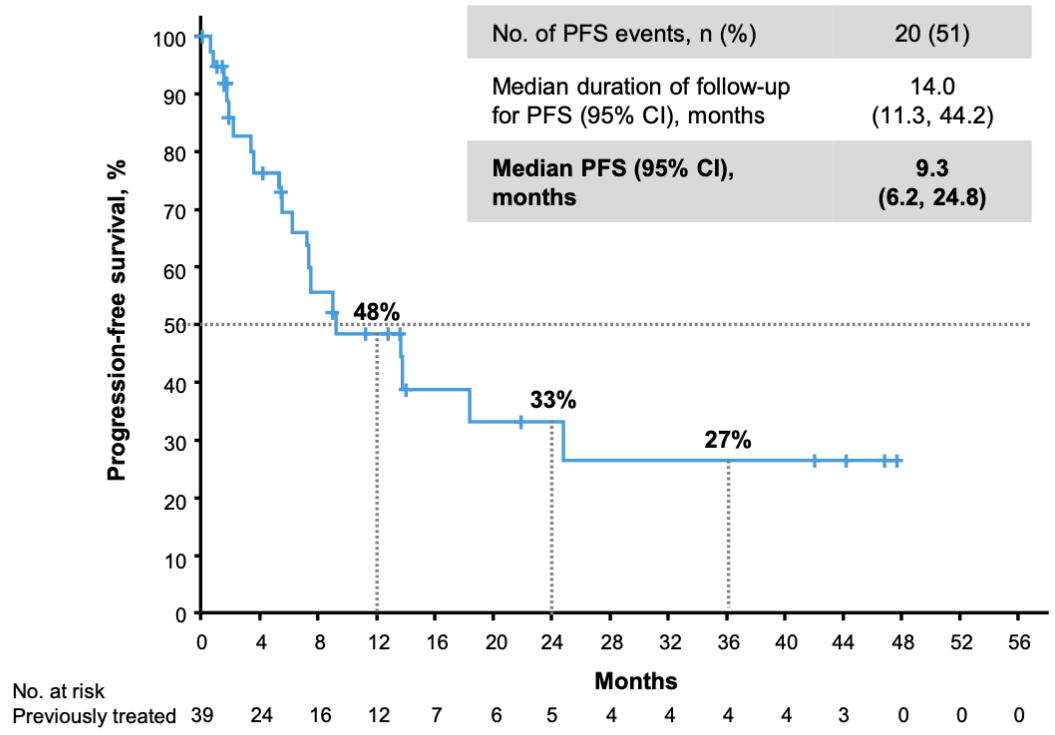
encorafenib + binimetinib en première et deuxième ligne

Treatment naive (n=59)



No. of PFS events, n (%)	28 (47)
Median duration of follow-up for PFS (95% CI), months	33.3 (30.4, 41.3)
Median PFS (95% CI), months	**30.2 (15.7, NE)**

Previously treated (n=39)



No. of PFS events, n (%)	20 (51)
Median duration of follow-up for PFS (95% CI), months	14.0 (11.3, 44.2)
Median PFS (95% CI), months	**9.3 (6.2, 24.8)**

Post ESMO Oncologie thoracique

Merci pour votre attention