Les scoops en cancérologie thoracique

Vendredi 26 janvier 2026

Palais de la Bourse, Bordeaux

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Liens d’intérêts

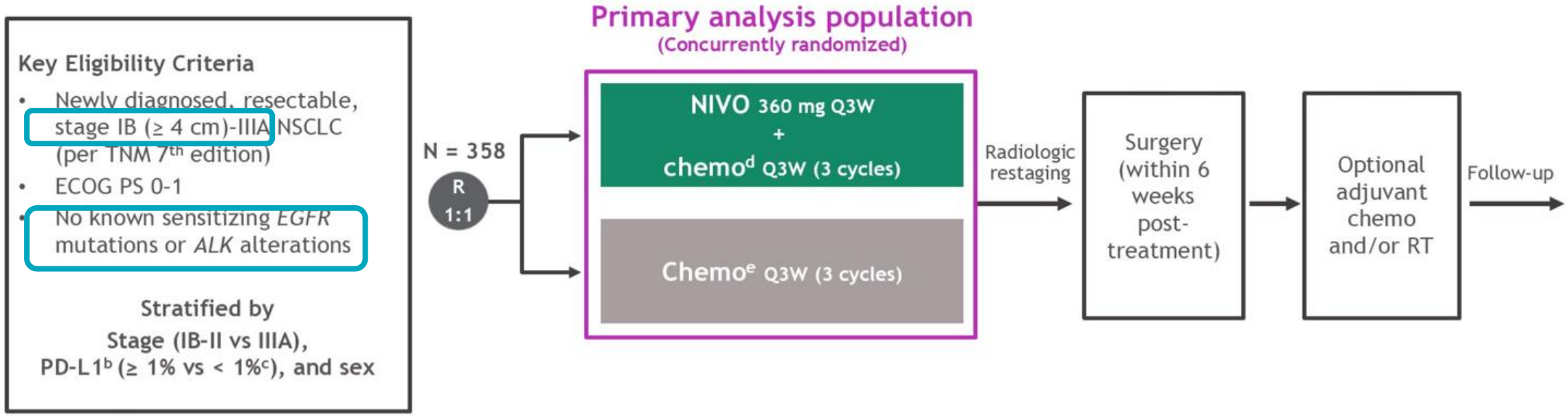
- Honoraires/interventions: MSD, Astrazeneca, Johnson & Johnson, Roche, Lilly, Abbvie, Amgen
- Boards: Amgen, Astrazeneca, BMS, Johnson & Johnson, Takeda, Lilly, Regeneron
- Financements/Prise en charge: MSD, Johnson & Johnson, Pfizer, Sanofi, Astrazeneca, Takeda

Focus sur…

- Amélioration de la survie globale des patients CBNPC traités par chimiothérapie immunothérapie néo adjuvante
  - → ASCO2025: résultats d'OS de CHECKMATE-816
- L'intensification en première ligne dans le CBNPC EGFR muté
  - →WCLC2025: résultats d'OS de FLAURA-2
- Le tarlatamab comme nouveau standard dans le carcinome bronchique à petites cellules
  - →ASCO2025: résultats de Dellphi-304

Confirmation d'un STANDARD en néo adjuvant dans le CBNPC

CHECKMATE-816: Design



Minimum/median follow-up: 59.9/68.4 months

Primary endpoints
- pCR by BIPR
- EFS by BICR

Key secondary endpoints
- OS
- MPR by BIPR
- TTDM

Exploratory analyses
- OS by pCR, ctDNA clearance
- Lung cancer-specific survival

Forde P.M. et al. Abstract LBA8000 ASCO 2025

Confirmation d'un STANDARD en néo adjuvant dans le CBNPC

CHECKMATE-816: caractéristiques des patients

Characteristic	Nivolumab plus Chemotherapy (N=179)	Chemotherapy Alone (N=179)
Age		
Median (range) — yr	64 (41–82)	65 (34–84)
Distribution — no. (%)		
<65 yr	93 (52.0)	83 (46.4)
≥65 yr	86 (48.0)	96 (53.6)
Sex — no. (%)		
Male	128 (71.5)	127 (70.9)
Female	51 (28.5)	52 (29.1)
Geographic region — no. (%)		
North America	41 (22.9)	50 (27.9)
Europe	41 (22.9)	25 (14.0)
Asia	85 (47.5)	92 (51.4)
Rest of the world*	12 (6.7)	12 (6.7)
ECOG performance-status score — no. (%)†		
0	124 (69.3)	117 (65.4)
1	55 (30.7)	62 (34.6)
Disease stage — no. (%)‡		
IB or II	65 (36.3)	62 (34.6)
IIIA	113 (63.1)	115 (64.2)
Histologic type of tumor — no. (%)		
Squamous	87 (48.6)	95 (53.1)
Nonsquamous	92 (51.4)	84 (46.9)

Characteristic	Nivolumab plus Chemotherapy (N=179)	Chemotherapy Alone (N=179)
Smoking status — no. (%)§		
Never smoked	19 (10.6)	20 (11.2)
Current or former smoker	160 (89.4)	158 (88.3)
PD-L1 expression level — no. (%)¶		
Could not be evaluated	12 (6.7)	13 (7.3)
<1%	78 (43.6)	77 (43.0)
≥1%	89 (49.7)	89 (49.7)
1–49%	51 (28.5)	47 (26.3)
≥50%	38 (21.2)	42 (23.5)
Tumor mutational burden — no. (%)‖		
Could not be evaluated or was not reported	91 (50.8)	89 (49.7)
<12.3 mutations per megabase	49 (27.4)	53 (29.6)
≥12.3 mutations per megabase	39 (21.8)	37 (20.7)
Type of platinum therapy — no. (%)		
Cisplatin	124 (69.3)	134 (74.9)
Carboplatin	39 (21.8)	33 (18.4)

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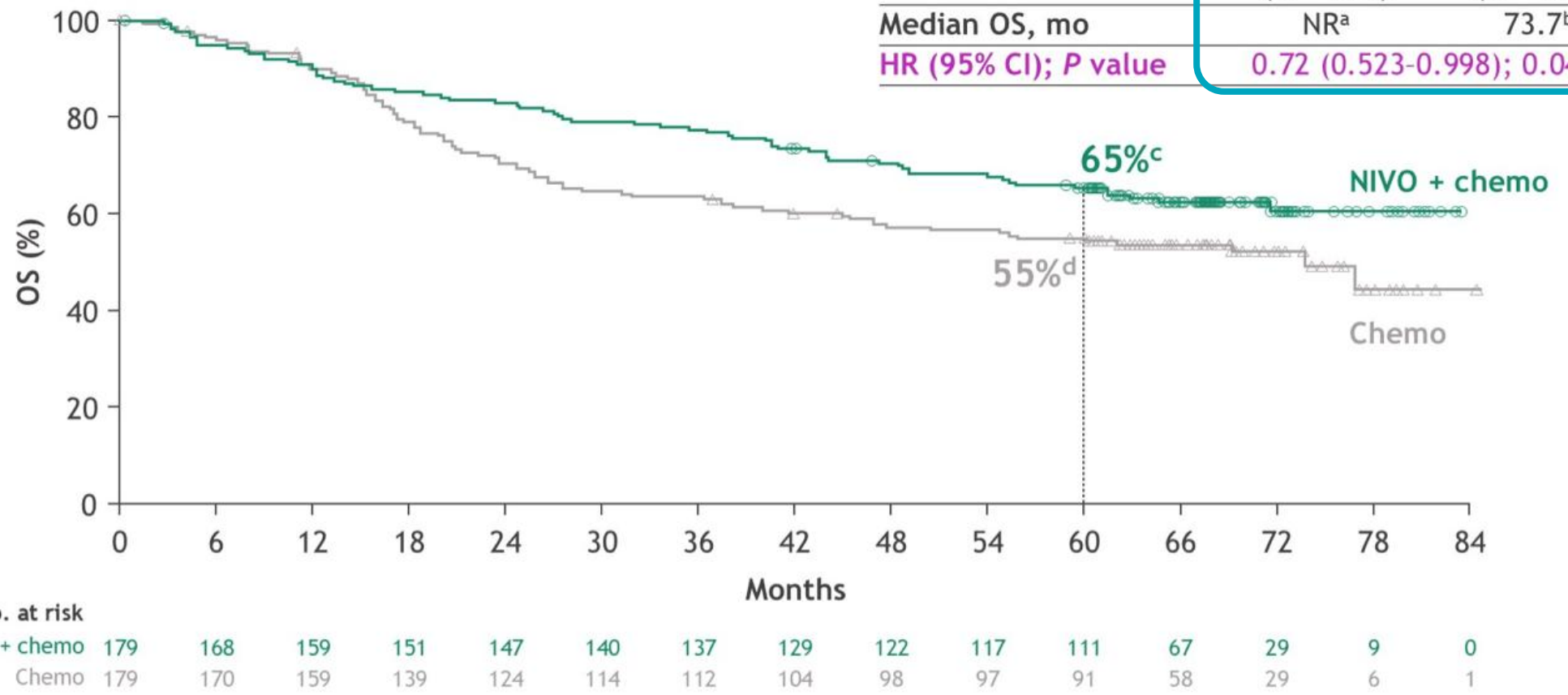
Confirmation d'un STANDARD en néo adjuvant dans le CBNPC

CHECKMATE-816: données de SURVIE GLOBALE

	NIVO + chemo (n = 179)	Chemo (n = 179)
Median OS, mo	NR[a]	73.7[b]
HR (95% CI); *P* value	0.72 (0.523-0.998); 0.0479	



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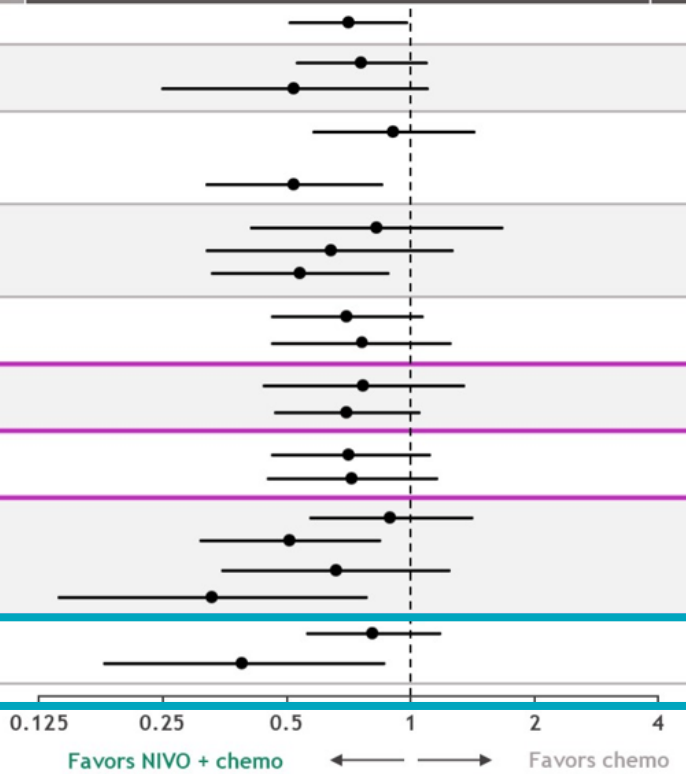
Confirmation d'un STANDARD en néo adjuvant dans le CBNPC

CHECKMATE-816: Analyse de sous groupes pour la survie globale

	Median OS, mo		Unstratified HR (95% CI)	Unstratified HR
	NIVO + chemo (n = 179)	Chemo (n = 179)		
Overall (N = 358)	NR	73.7		0.71
Male (n = 255)	NR	61.8		0.76
Female (n = 103)	NR	NR		0.52
White (n = 169)	NR	73.7		0.91
Black or African American (n = 7)	NR	20.9		
Asian (n = 179)	NR	76.8		0.52
North America (n = 91)	NR	73.7		0.83
Europe (n = 66)	NR	38.3		0.64
Asia (n = 177)	NR	76.8		0.54
ECOG PS 0 (n = 241)	NR	76.8		0.70
ECOG PS 1 (n = 117)	71.6	45.3		0.76
Stage IB-II (n = 126)	NR	76.8		0.77
Stage IIIA (n = 229)	NR	73.7		0.70
Squamous (n = 182)	NR	73.7		0.71
Nonsquamous (n = 176)	NR	NR		0.72
PD-L1 < 1% (n = 155)	NR	61.8		0.89
PD-L1 ≥ 1% (n = 178)	NR	73.7		0.51
PD-L1 1%-49% (n = 98)	NR	73.7		0.66
PD-L1 ≥ 50% (n = 80)	NR	76.8		0.33
Cisplatin (n = 258)	NR	76.8		0.81
Carboplatin (n = 72)	NR	37.2		0.39



Minimum/median follow-up: 59.9/68.4 months.
HRs were NC if there was an insufficient number of events (< 10 per arm).

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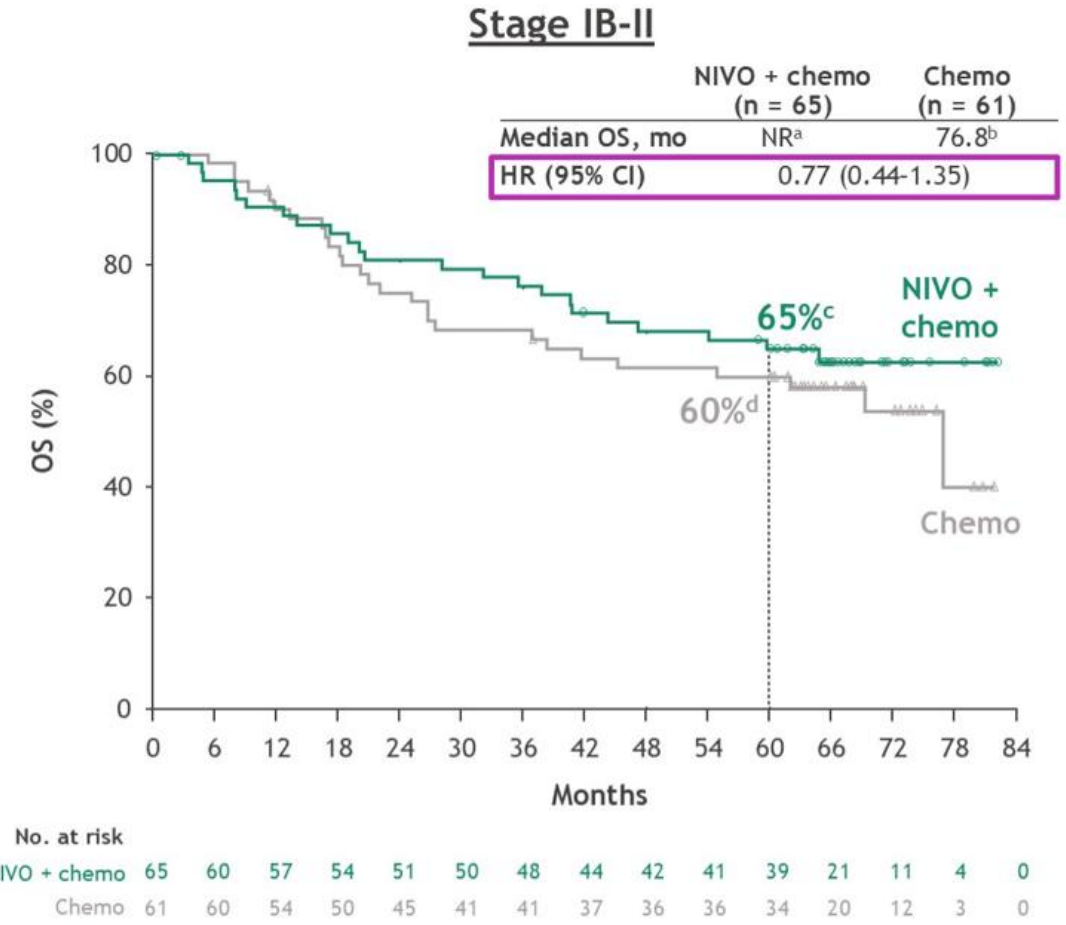
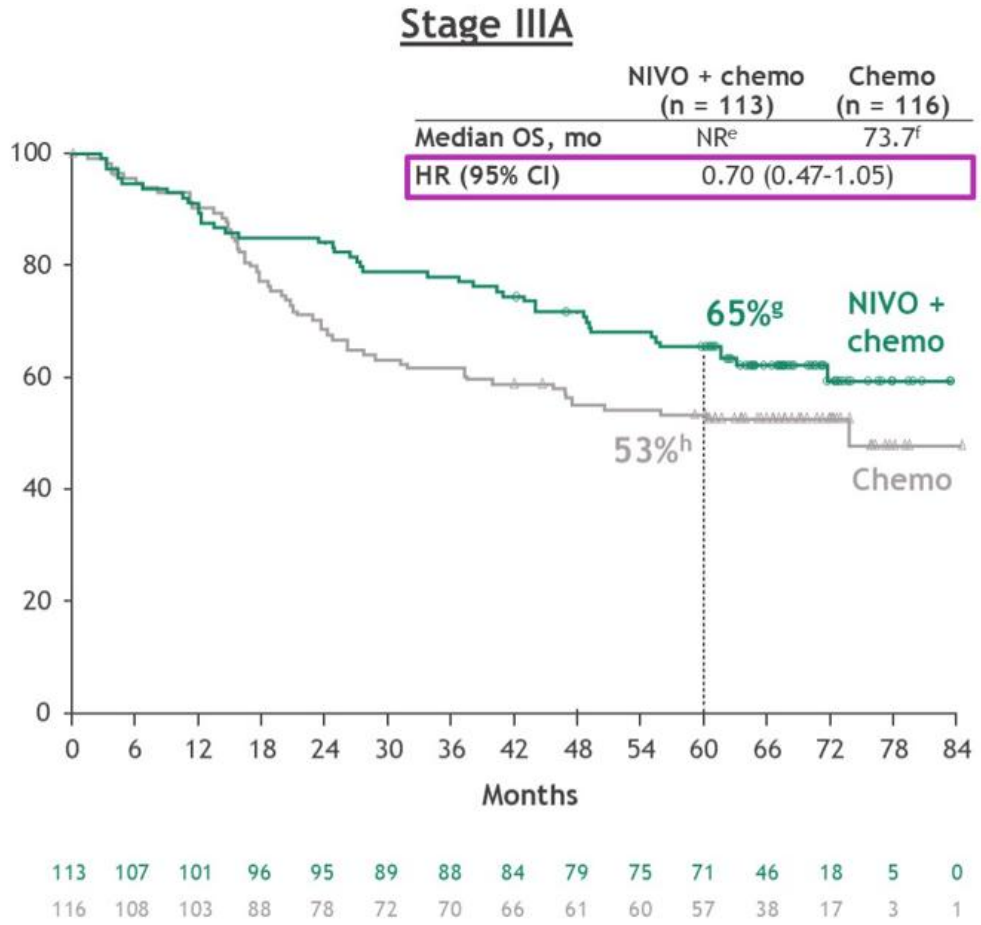
Confirmation d'un STANDARD en néo adjuvant dans le CBNPC

CHECKMATE-816: Survie globale selon le stade





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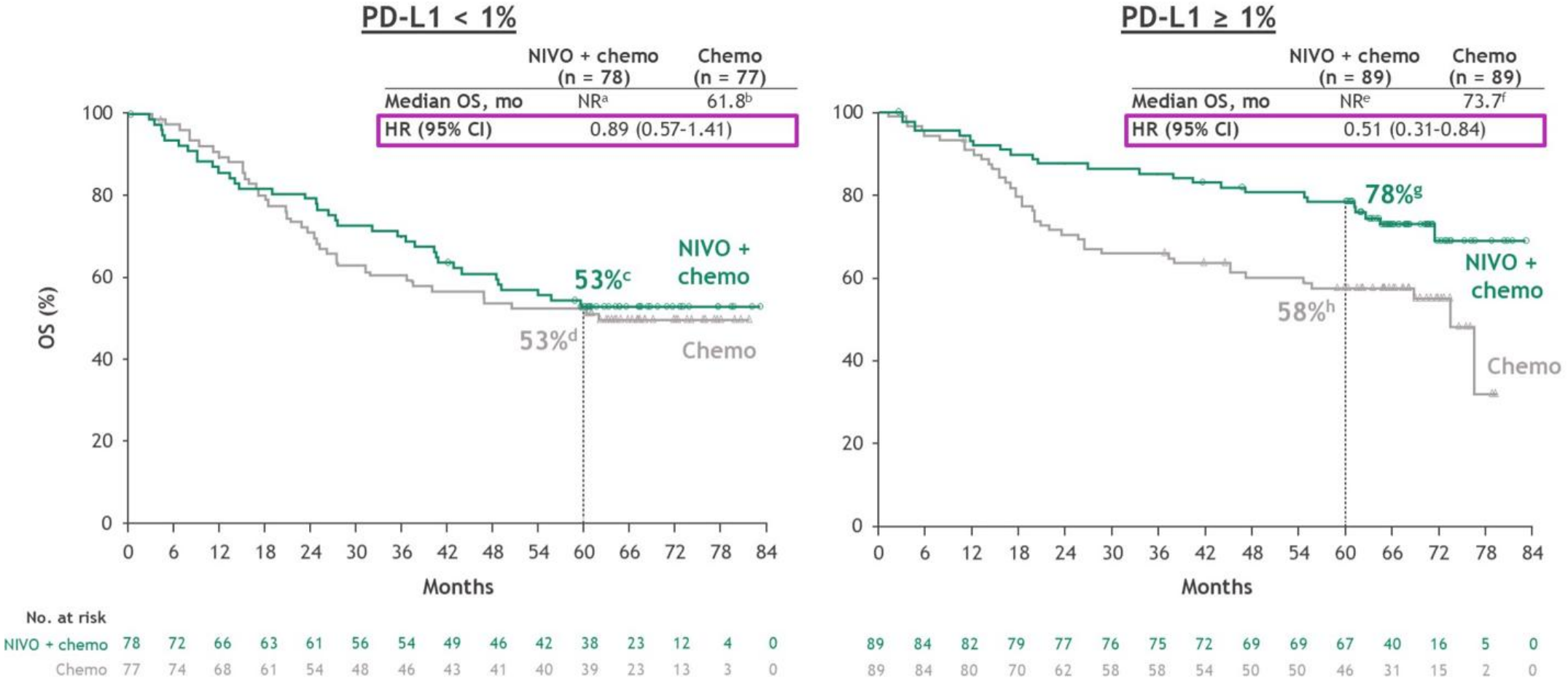
Confirmation d'un STANDARD en néo adjuvant dans le CBNPC

CHECKMATE-816: Survie globale selon le statut PD-L1



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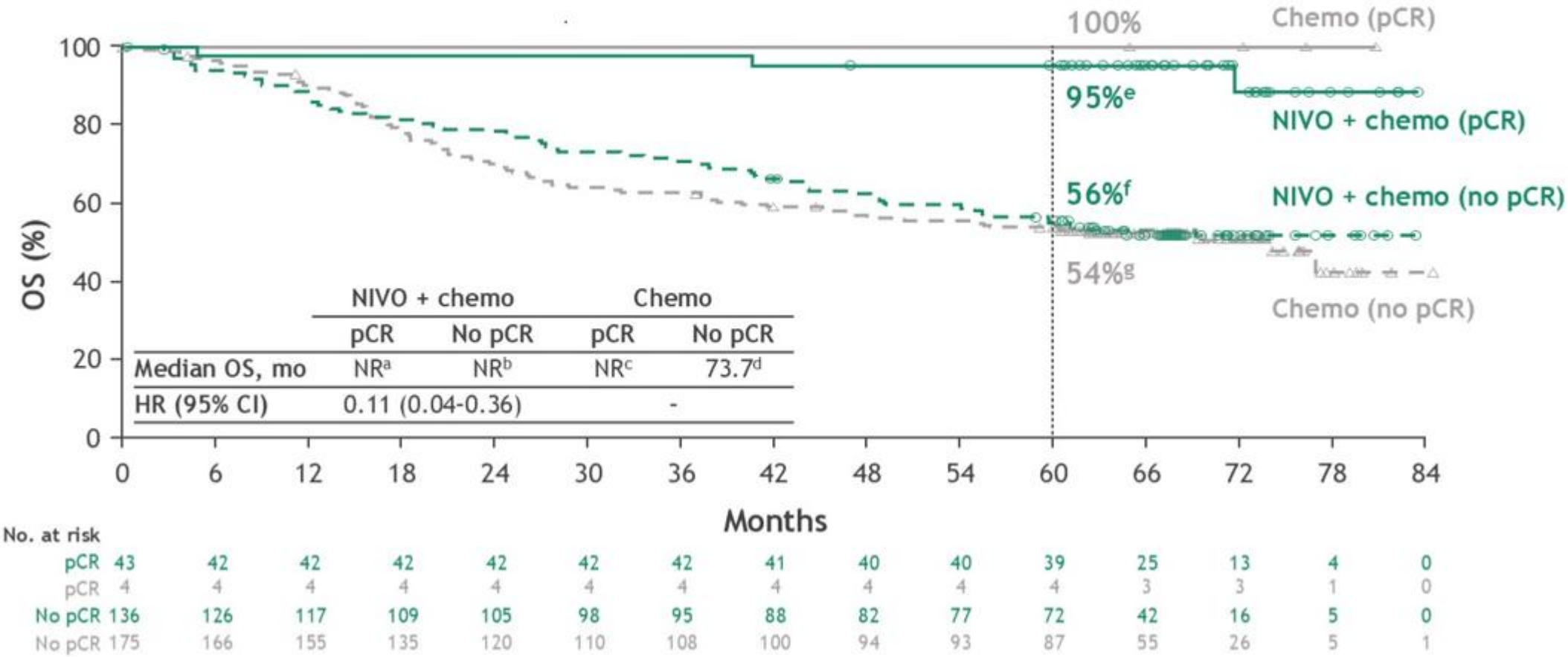
CHECKMATE-816: survie globale selon la réponse pathologique



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Confirmation d'un STANDARD en néo adjuvant dans le CBNPC

CHECKMATE-816: Pas de nouveau signal concernant la tolérance

Patients, n (%)	NIVO + chemo (n = 176)		Chemo (n = 176)	
	Any grade	Grade 3-4	Any grade	Grade 3-4
All AEs[b]	165 (94)	76 (43)	173 (98)	79 (45)
TRAEs[b]	147 (84)	63 (36)	159 (90)	67 (38)
All AEs leading to discontinuation[b]	18 (10)	10 (6)	20 (11)	7 (4)
TRAEs leading to discontinuation[b]	18 (10)	10 (6)	17 (10)	6 (3)
All SAEs[b]	30 (17)	19 (11)	24 (14)	17 (10)
Treatment-related SAEs[b]	21 (12)	15 (8)	18 (10)	14 (8)
Surgery-related AEs[c]	67 (45)	17 (11)	66 (49)	20 (15)
Treatment-related deaths[d]	0		3 (2)[e]	

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CHECKMATE-816

IMPLICATION

Importance de la biologie moléculaire et du staging N

- Se poser la question d'un traitement néo adjuvant si:
  - Tumeur ≥ 4 cm
  - N+ extirpable
  - = tumeur à haut risque de récidive
- Nécessité d'obtenir:
  - Statut **PD-L1**
  - Statut **EGFR** et **ALK**

AURA

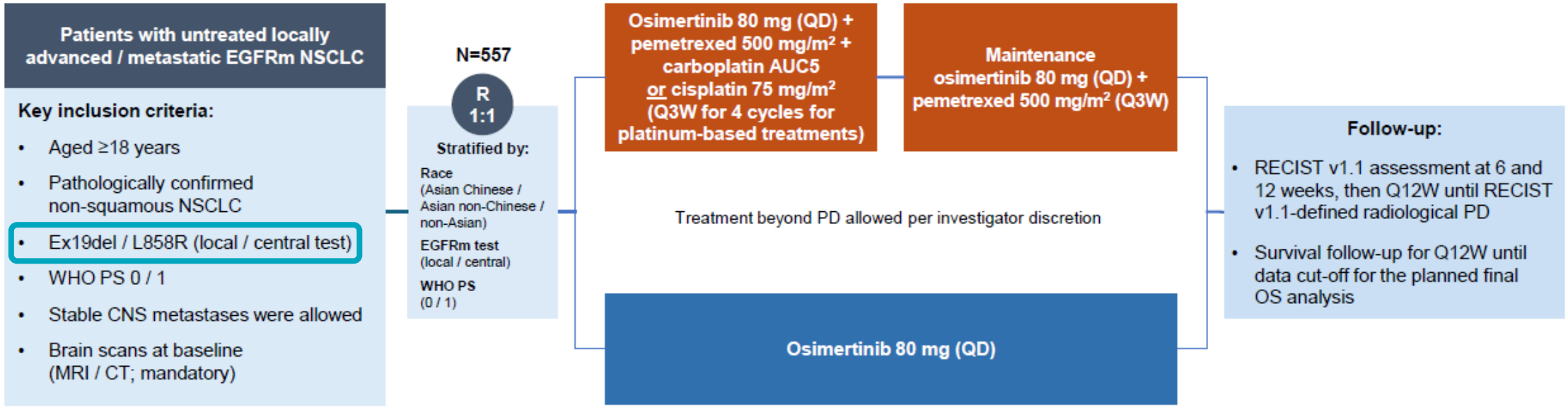
Recommandation
Chez les patients PD-L1≥1% sans mutation de l'*EGFR* ni de réarrangement d'*ALK* de stade II à IIIB (tumeurs résécables jugées à haut risque de récidive), un traitement néoadjuvant par 3 cycles d'immunochimiothérapie- est accessible en accès précoce : -quelle que soit l'histologie par carboplatine AUC 5 ou 6 + paclitaxel (150 ou 200 mg/m²) + nivolumab 360mg -pour les carcinomes épidermoïdes par cisplatine (75 mg/m²) + gemcitabine (1000 ou 1250 mg/m²) + nivolumab 360mg. -pour les carcinomes non-épidermoïdes : sel de platine + pemetrexed (500 mg/m²) + nivolumab 360mg

L'intensification en 1ère ligne chez les patients EGFR (mutations communes) mutés

FLAURA-2: Design

Median PFS, months (95% CI)	
Osi + CTx	**25.5** (24.7, NC)
Osi mono	**16.7** (14.1, 21.3)

HR:0,62 (IC95%: 0,49-0,69 p<0,001)



- **Primary endpoint:** Investigator-assessed PFS (RECIST v1.1)[1]
- **Secondary endpoints included:** OS, TFST, DoR, DCR, PFS2, TSST, HRQoL

OS was a key secondary endpoint*

Final OS analysis performed at 57% maturity

Planchard D. et al. WCLC 2025

L'intensification en 1ière ligne chez les patients EGFR (mutations communes) mutés

FLAURA-2: Caractéristiques des patients

Characteristic, %*	Osi + CTx (n=279)	Osi mono (n=278)
Sex: male / female	38 / 62	39 / 61
Age: median (range), years	61 (26–83)	62 (30–85)
Race: Asian Chinese / Asian non-Chinese / non-Asian / missing†	25 / 39 / 35 / <1	25 / 38 / 36 / 1
WHO PS: 0 / 1‡	37 / 62	37 / 63
Smoking status: never / current / former	67 / 1 / 31	65 / 1 / 33
Histology: adenocarcinoma / adenosquamous / other	99 / 1 / 1	99 / 0 / 1
EGFR mutation type: Ex19del / L858R§	61 / 38	60 / 38
Locally advanced / metastatic	5 / 95	3 / 97
CNS metastases present at baseline	42	40
Baseline tumour size: median (range), mm	57 (10–284)	57 (11–221)

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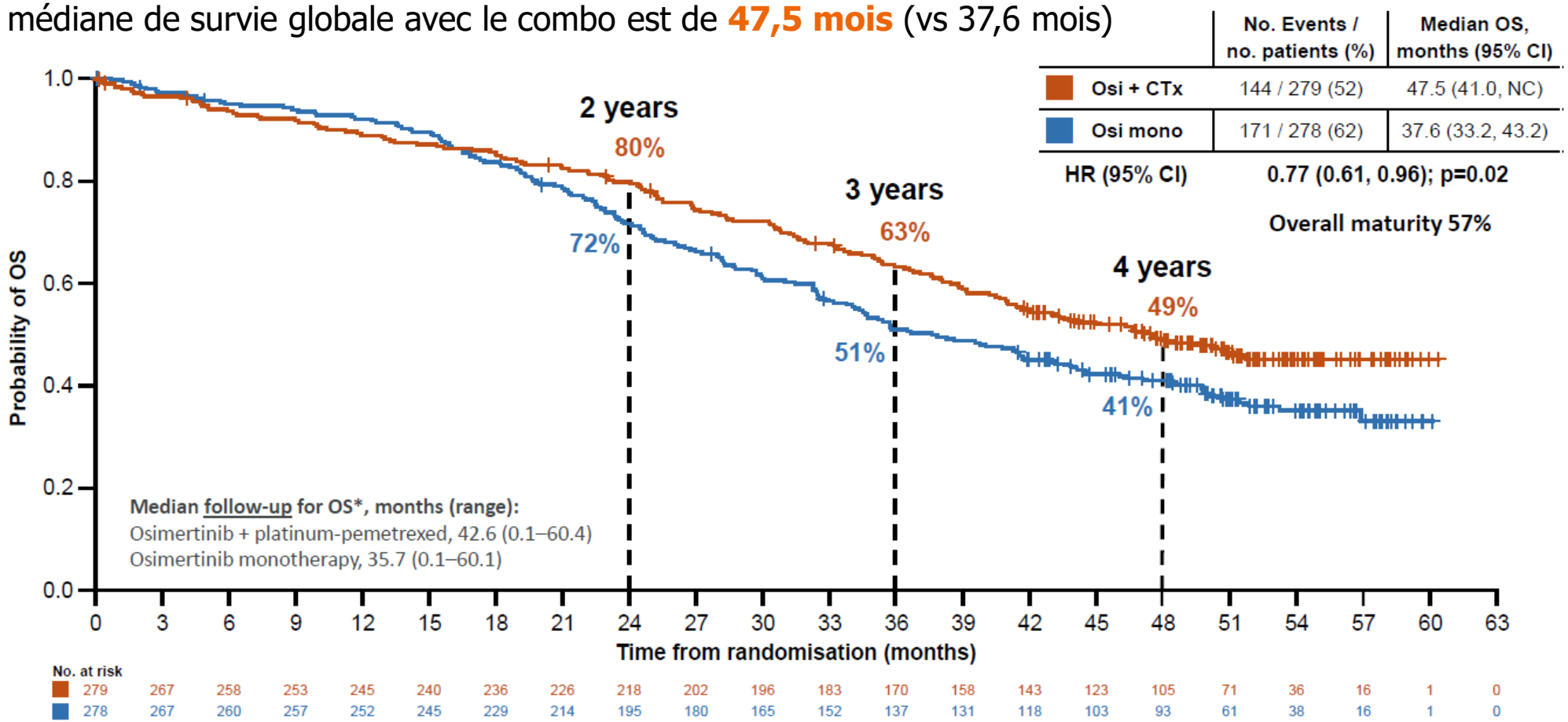
L'intensification en 1ère ligne chez les patients EGFR (mutations communes) mutés

FLAURA-2: données de survie globale

La médiane de survie globale avec le combo est de **47,5 mois** (vs 37,6 mois)



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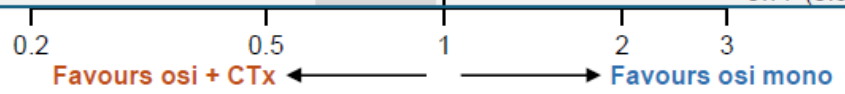
L'intensification en 1ère ligne chez les patients EGFR (mutations communes) mutés

FLAURA-2: analyse de sous groupes pour la survie globale

Subgroup*		Osi + CTx (Events / patients)	Osi mono (Events / patients)	HR (95% CI)
All patients	Stratified log-rank	144 / 279	171 / 278	0.77 (0.61, 0.96)
	Unadjusted Cox PH	144 / 279	171 / 278	0.76 (0.61, 0.95)
Sex	Male	65 / 106	72 / 109	0.84 (0.60, 1.17)
	Female	79 / 173	99 / 169	0.71 (0.53, 0.96)
Race†	Asian Chinese	34 / 71	39 / 69	0.76 (0.48, 1.20)
	Asian non-Chinese	65 / 107	66 / 107	1.00 (0.71, 1.40)
	Non-Asian	45 / 101	66 / 102	0.56 (0.39, 0.82)
EGFR mutation test method	Central	65 / 121	73 / 119	0.81 (0.58, 1.14)
	Local	79 / 158	98 / 159	0.73 (0.54, 0.98)
Age at screening	<65 years	80 / 174	95 / 166	0.71 (0.53, 0.95)
	≥65 years	64 / 105	76 / 112	0.87 (0.63, 1.22)
Smoking history	Yes	52 / 91	60 / 97	0.83 (0.57, 1.20)
	No	92 / 188	111 / 181	0.73 (0.55, 0.96)
EGFR mutation type‡	Ex19del	78 / 172	95 / 169	0.76 (0.56, 1.02)
	L858R	66 / 106	74 / 107	0.76 (0.55, 1.07)
WHO PS	0	47 / 101	55 / 102	0.82 (0.55, 1.20)
	1	97 / 178	116 / 176	0.73 (0.56, 0.96)
CNS mets at baseline	Yes	71 / 116	79 / 110	0.72 (0.52, 0.99)
	No	73 / 163	92 / 168	0.77 (0.57, 1.05)



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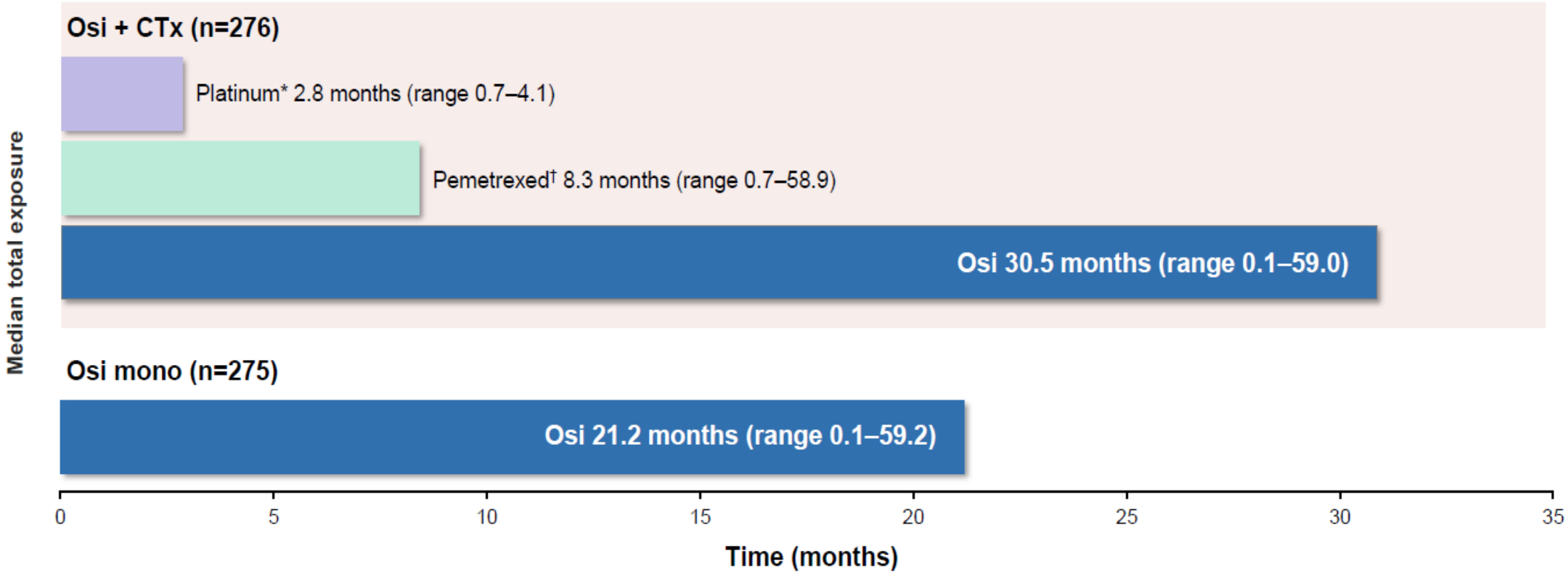
L'intensification en 1ère ligne chez les patients EGFR (mutations communes) mutés

FLAURA-2: Durée d'exposition aux traitements



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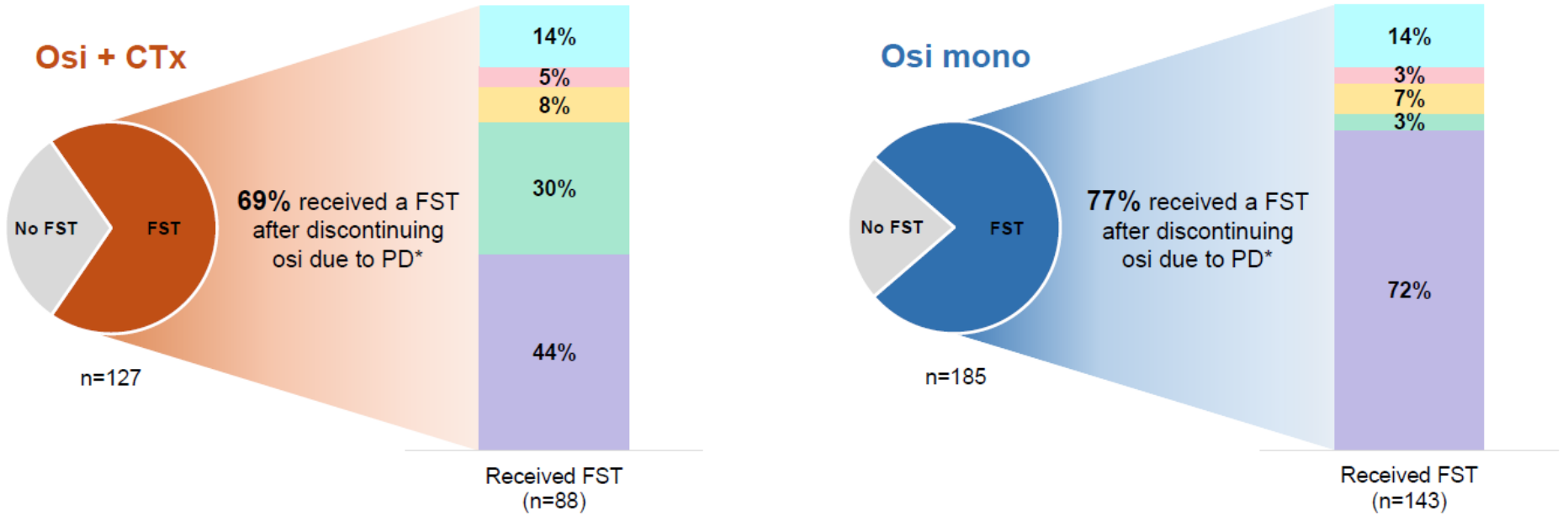
L'intensification en 1ère ligne chez les patients EGFR (mutations communes) mutés

FLAURA-2: traitements subséquents

La chimiothérapie est le traitement subséquent le + fréquemment donné (74%) post combo. 44% sont des rechallenges en platine

Le bénéfice en SG est observé malgré le fait que le traitement subséquent le + fréquemment donné est la chimio à base de platine



Subsequent treatment was per investigator choice

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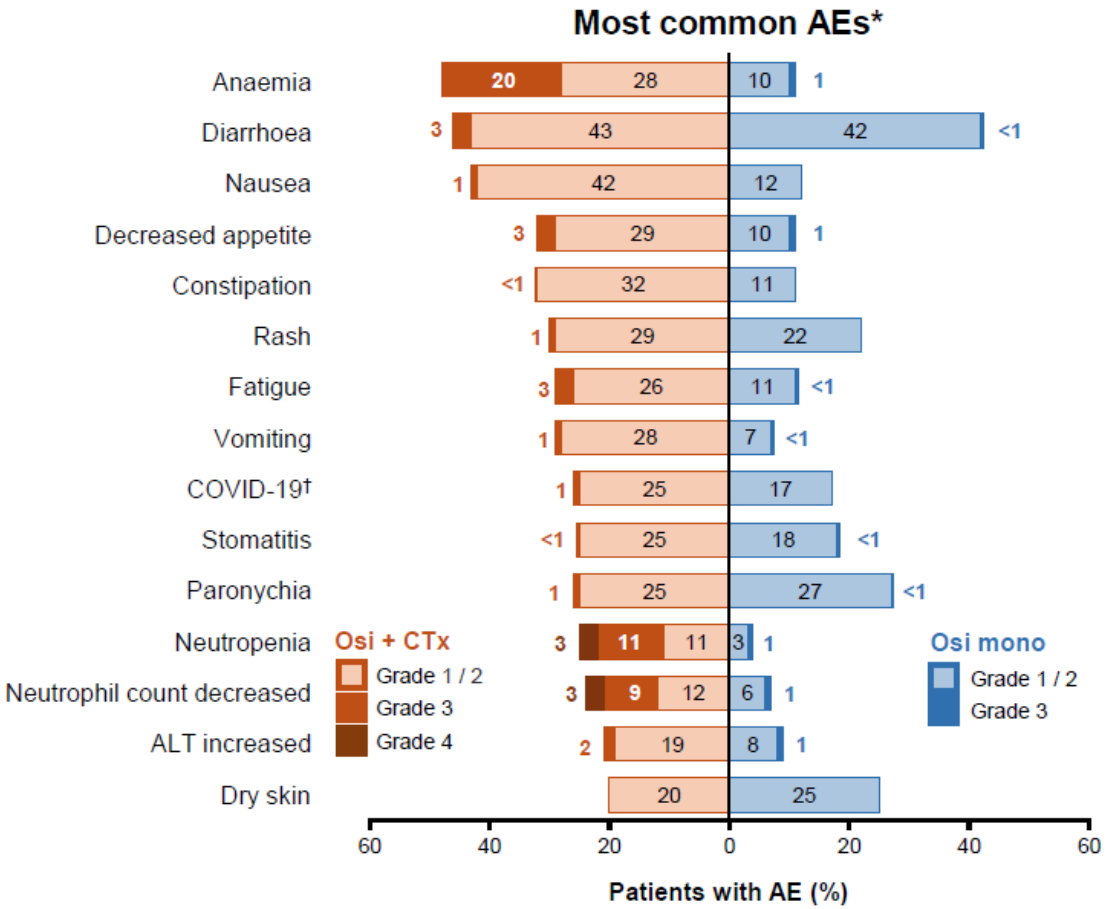
L'intensification en 1ère ligne chez les patients EGFR (mutations communes) mutés

FLAURA-2: Données de tolérance



Pas de nouveau signal de toxicité

Une toxicité bien sur accrue bras combo

AE summary	Osi + CTx (n=276)	Osi mono (n=275)
AE any cause, n (%)		
Any grade	276 (100)	269 (98)
Grade ≥3	193 (70)	94 (34)
Serious	126 (46)	75 (27)
Outcome of death	22 (8)	10 (4)
Considered possibly related to treatment	5 (2)	2 (1)
Leading to discontinuation of osi	34 (12)	20 (7)
Leading to discontinuation of pemetrexed	137 (50)	NA
Leading to discontinuation of platinum	46 (17)	NA

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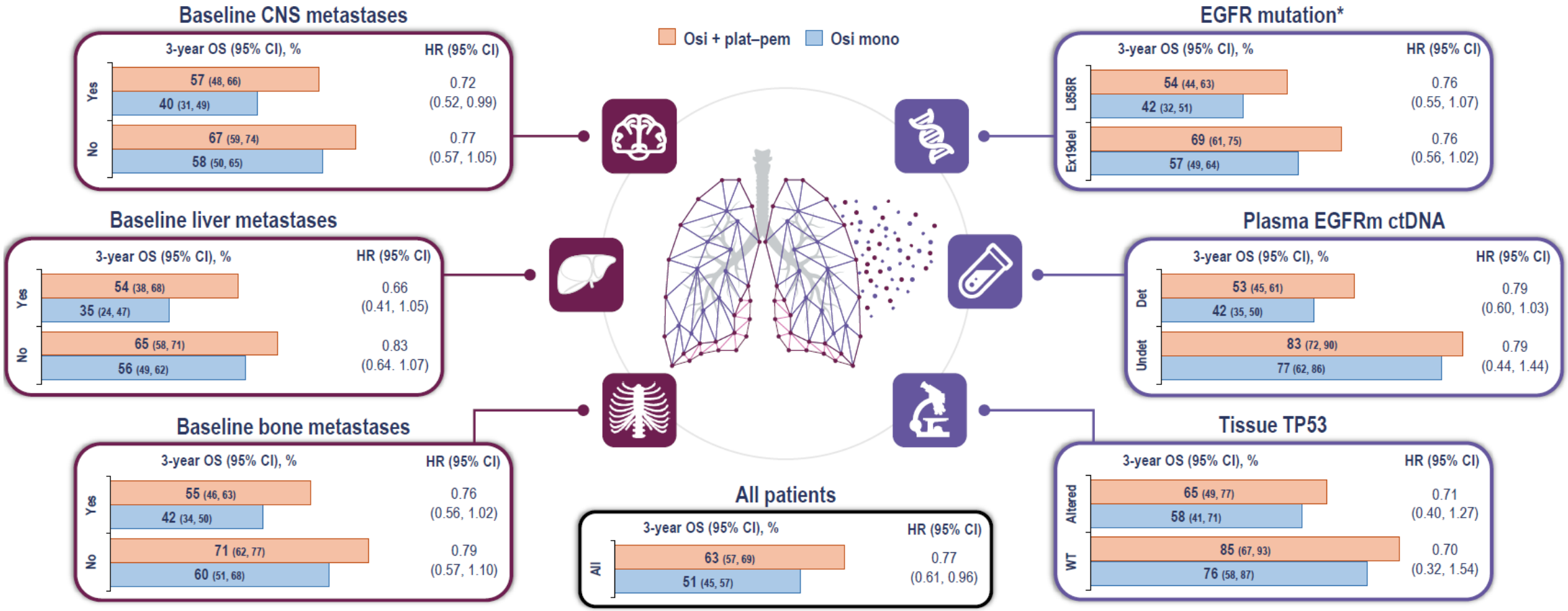
L'intensification en 1ère ligne chez les patients EGFR (mutations communes) mutés

FLAURA-2: Rappels des résultats sur les populations d'intérêt



Janne ESMO 2025; NEJM 2025

L'intensification en 1ère ligne chez les patients EGFR (mutations communes) mutés

FLAURA-2: Quelle conclusion?

- Devient un **nouveau standard** de traitement
- La question est de savoir chez qui nous ne souhaitons/pouvons pas intensifier:
  - Population âgée?
  - Patients fragiles?
  - Patients refusant la chimio

Quid dans AURA 2026?

OPTION : Dans les carcinomes non-épidermoïdes avec mutation classique de l'*EGFR* (Del19 et L858R), de PS 0-1, une association sels de platine (Cisplatine 75mg/m² ou Carboplatine AUC 5) – pemetrexed (500mg/m²) – osimertinib (80mg/j) suivie d'une maintenance par pemetrexed-osimertinib dispose d'une AMM mais n'est pas remboursé à la date de rédaction. Le bénéfice est plus important chez les patients avec des métastases cérébrales et les PS1.

OPTION : L'association Lazertinib-Amivantamab en première ligne, sera une option à considérer dès qu'elle sera disponible en France, chez les patients avec mutation classique de l'*EGFR* (Del19 et L858R), de PS 0-1. Une thrombo-prophylaxie de 4 mois est indiquée en association. Il est conseillé d'être très attentif à la tolérance, notamment cutané, de cette association.

Un nouveau standard en deuxième ligne dans le carcinome bronchique à petites cellules

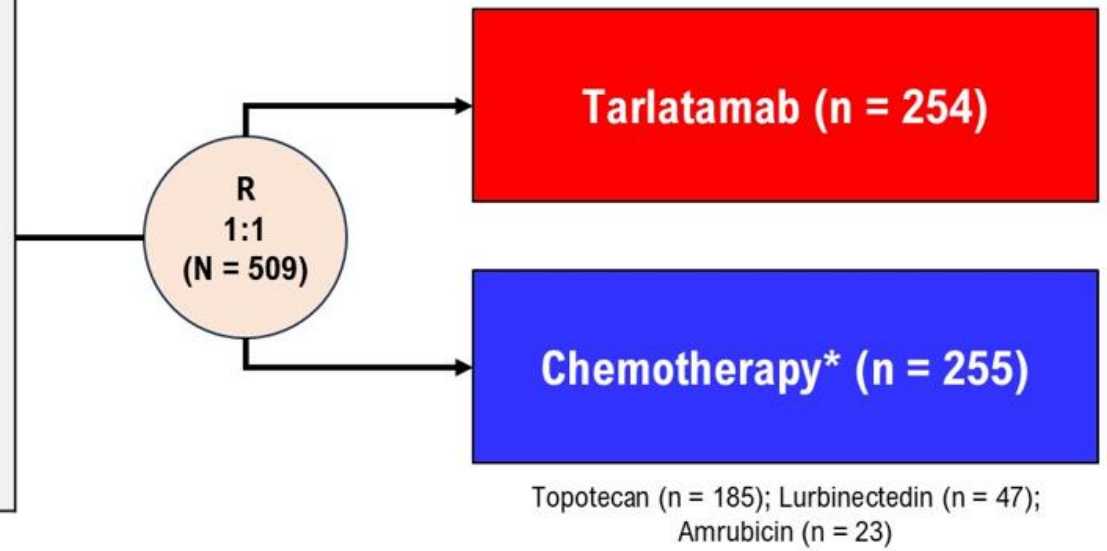
Dellphi-304: design

Key inclusion criteria

- Histologically or cytologically confirmed SCLC
- Progression after 1L platinum-based chemotherapy +/- anti-PD-(L)1
- ECOG PS 0 or 1
- Asymptomatic, treated or untreated brain metastases

Randomization stratified by

- Prior anti-PD-(L)1 exposure (yes/no)
- Chemotherapy-free interval (< 90 days vs ≥ 90 to < 180 days vs ≥ 180 days)
- Presence of (previous/current) brain metastases (yes/no)
- Intended chemotherapy (topotecan/amrubicin vs lurbinectedin)



Primary Endpoint: Overall survival
Key Secondary Endpoints: Progression-free survival, patient-reported outcomes
Other Secondary Endpoints: Objective response, disease control, duration of response, safety

*Topotecan was used in all countries except Japan, lurbinectedin in Australia, Canada, Republic of Korea, Singapore and the United States, and amrubicin in Japan.
1L, first-line; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **PD-(L)1**, programmed death (ligand)-1; **R**, randomization; **SCLC**, small cell lung cancer.

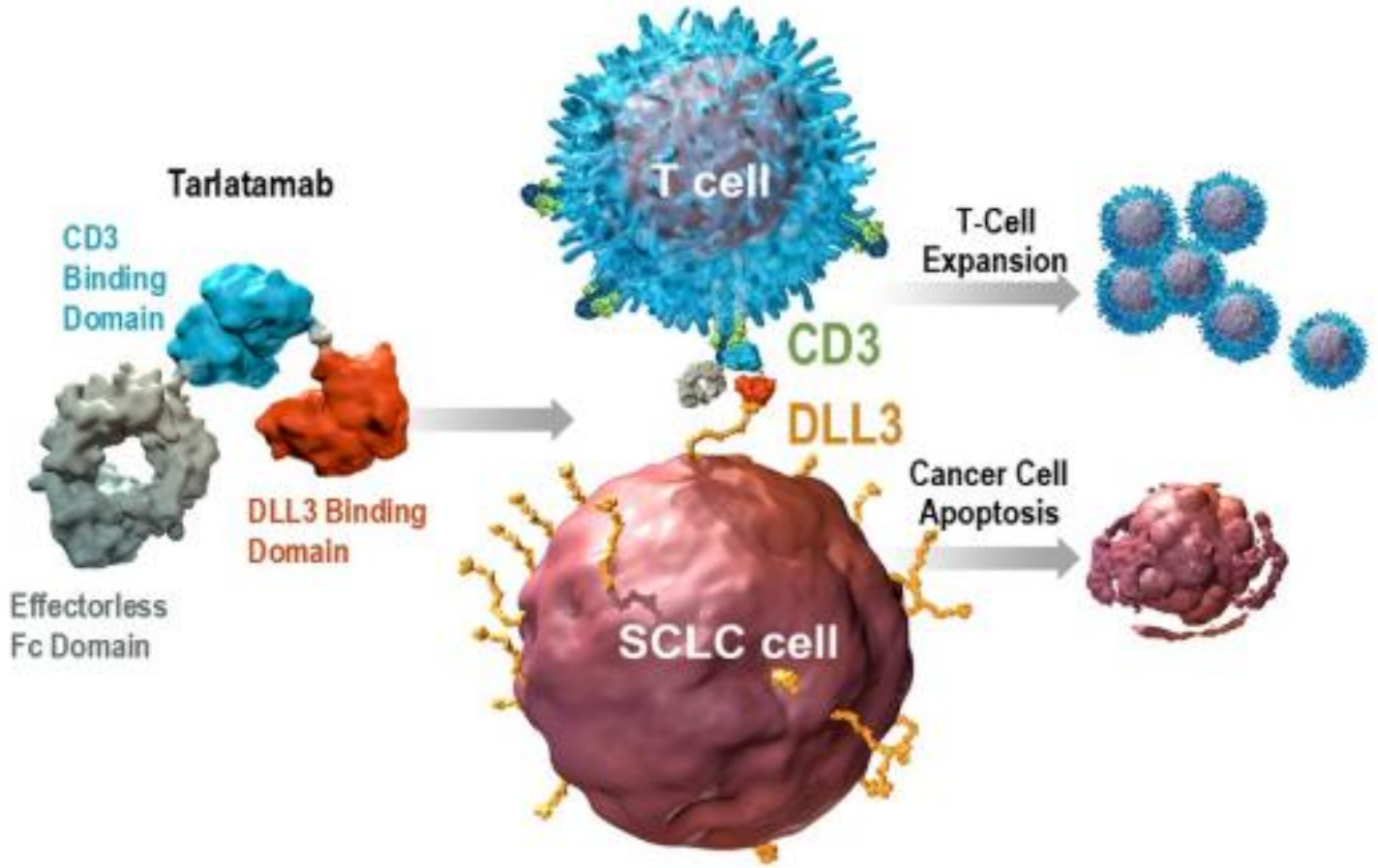
Rudin C.M. et al. ASCO 2025

Un nouveau standard en deuxième ligne dans le carcinome bronchique à petites cellules

Dellphi-304: la molécule

Tarlatamab

= BiTE



Un nouveau standard en deuxième ligne dans le carcinome bronchique à petites cellules

Dellphi-304: caractéristiques des patients

	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Median age, years (range)	64 (20 – 86)	66 (26 – 84)
Male / Female, %	72 / 28	66 / 34
Race Asian / Black / White, %	38 / 1 / 60	42 / 1 / 55
Smoking history Current or former smokers / Never smokers, %	91 / 9	88 / 12
ECOG performance status, 0 / 1, %	33 / 67	31 / 68
Prior anti-PD-(L)1 therapy, %	71	71
Prior radiotherapy for current malignancy*, %	63	63
Chemotherapy-free interval,%		
< 90 days	43	45
≥ 90 to < 180 days	33	31
≥ 180 days	24	25
Presence of brain / liver metastases, %	44 / 33	45 / 37
DLL3 expression, %, (n/N†)	95 (207/217)	93 (198/214)

*Includes patients who received radiotherapy for brain metastases; †Number of patients with DLL3 expression (n) among patients with evaluable tumor tissue sample (N).
DLL3, delta-like ligand 3; **ECOG,** Eastern Cooperative Oncology Group; **PD-(L)1,** programmed death (ligand)-1.

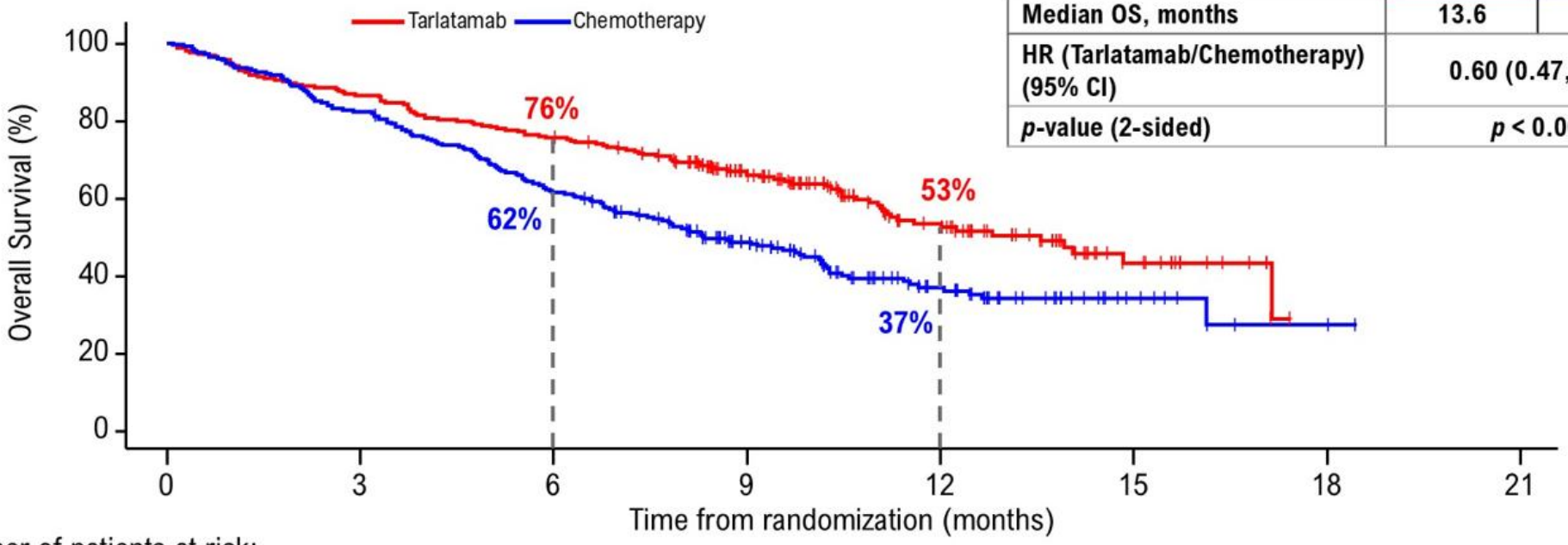
Rudin C.M. et al. ASCO 2025

Un nouveau standard en deuxième ligne dans le carcinome bronchique à petites cellules

Dellphi-304: données de survie globale

La survie globale est de **13,6 mois** dans le bras tarlatamab vs **8,3 mois** dans le bras contrôle

	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Median OS, months	13.6	8.3
HR (Tarlatamab/Chemotherapy) (95% CI)	0.60 (0.47, 0.77)	
p-value (2-sided)	*p* < 0.001	



Number of patients at risk:

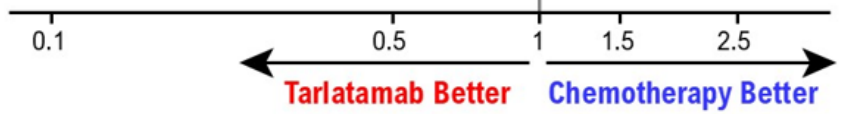
Tarlatamab	254	220	192	131	60	17	0
Chemotherapy	255	210	156	97	42	9	2	0

Rudin C.M. et al. ASCO 2025

Un nouveau standard en deuxième ligne dans le carcinome bronchique à petites cellules

Dellphi-304: Analyse de sous groupes

Subgroup	Tarlatamab (no. of patients)	Chemotherapy (no. of patients)	Hazard Ratio for Death (95% CI)
Age			
< 65 years	129	115	0.57 (0.40, 0.81)
≥ 65 years	125	140	0.67 (0.48, 0.94)
Sex			
Male	182	169	0.70 (0.53, 0.93)
Female	72	86	0.43 (0.26, 0.72)
Race			
White	152	139	0.51 (0.37, 0.70)
Asian	97	107	0.75 (0.50, 1.11)
Prior anti-PD-(L)1 exposure			
Yes	180	180	0.61 (0.45, 0.82)
No	74	75	0.65 (0.42, 1.03)
Chemotherapy-free interval			
< 90 days	109	114	0.60 (0.43, 0.84)
≥ 90 days	145	141	[illegible]
≥ 90 to <180 days	85	78	0.71 (0.46, 1.10)
≥ 180 days	60	63	0.54 (0.29, 1.03)
Presence (previous or current) of brain metastases			
Yes	113	115	0.45 (0.31, 0.65)
No	141	140	0.81 (0.58, 1.13)
Liver metastases			
Yes	84	95	0.82 (0.57, 1.18)
No	170	160	0.54 (0.39, 0.75)
Chemotherapy			
Topotecan/Amrubicin	209	208	0.57 (0.44, 0.75)
Lurbinectedin	45	47	0.81 (0.46, 1.44)



Hazard ratios and 95% CIs were estimated using the Cox proportional hazards model.
PD-(L)1, programmed cell death (ligand)-1.

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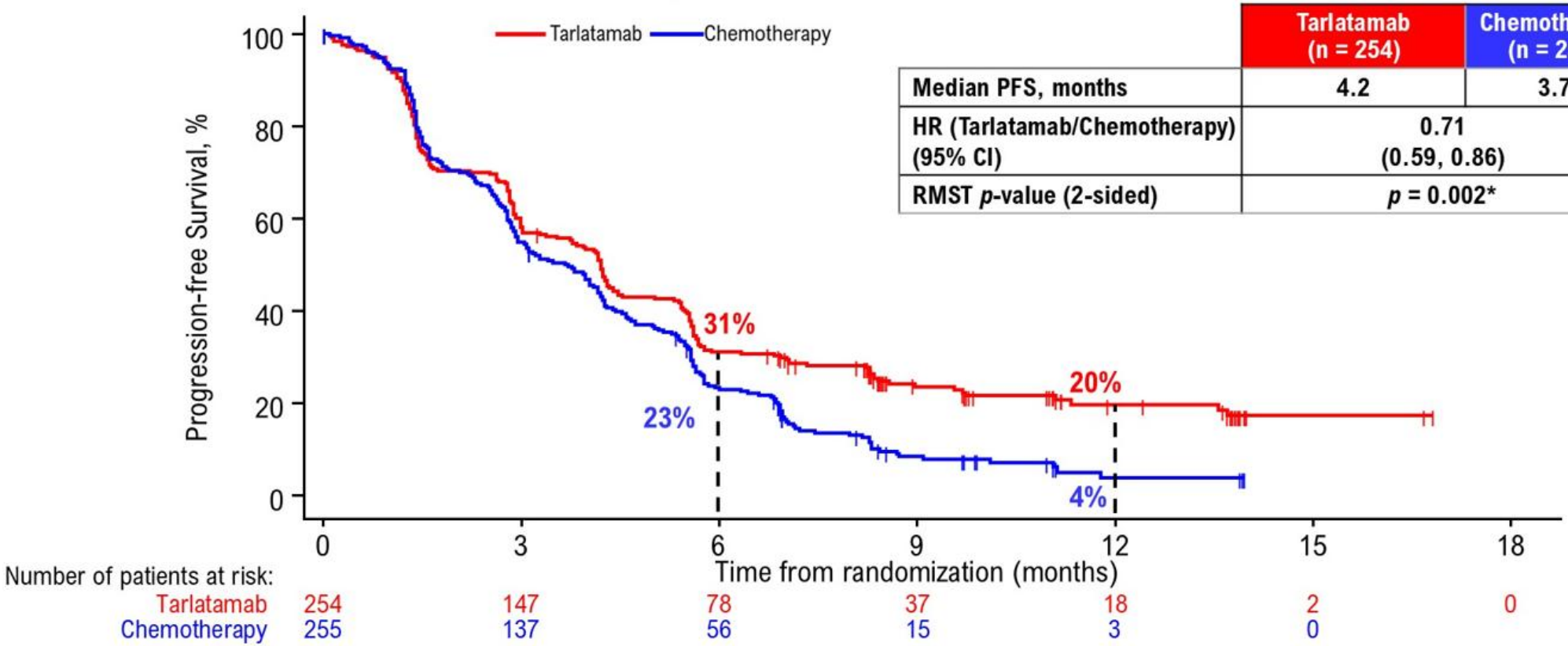
Dellphi-304: données de survie sans progression



	Tarlatamab (n = 254)	Chemotherapy (n = 255)
Median PFS, months	4.2	3.7
HR (Tarlatamab/Chemotherapy) (95% CI)	0.71 (0.59, 0.86)	
RMST *p*-value (2-sided)	*p* = 0.002*	

Median follow-up time: 11.0 months for the tarlatamab and the chemotherapy group. *The restricted mean PFS time in the tarlatamab and the chemotherapy group was 5.3 months and 4.3 months at 12 months respectively, resulting in statistically significant improvement of the tarlatamab group over the chemotherapy group.
HR: hazard ratio; **PFS**, progression-free survival.

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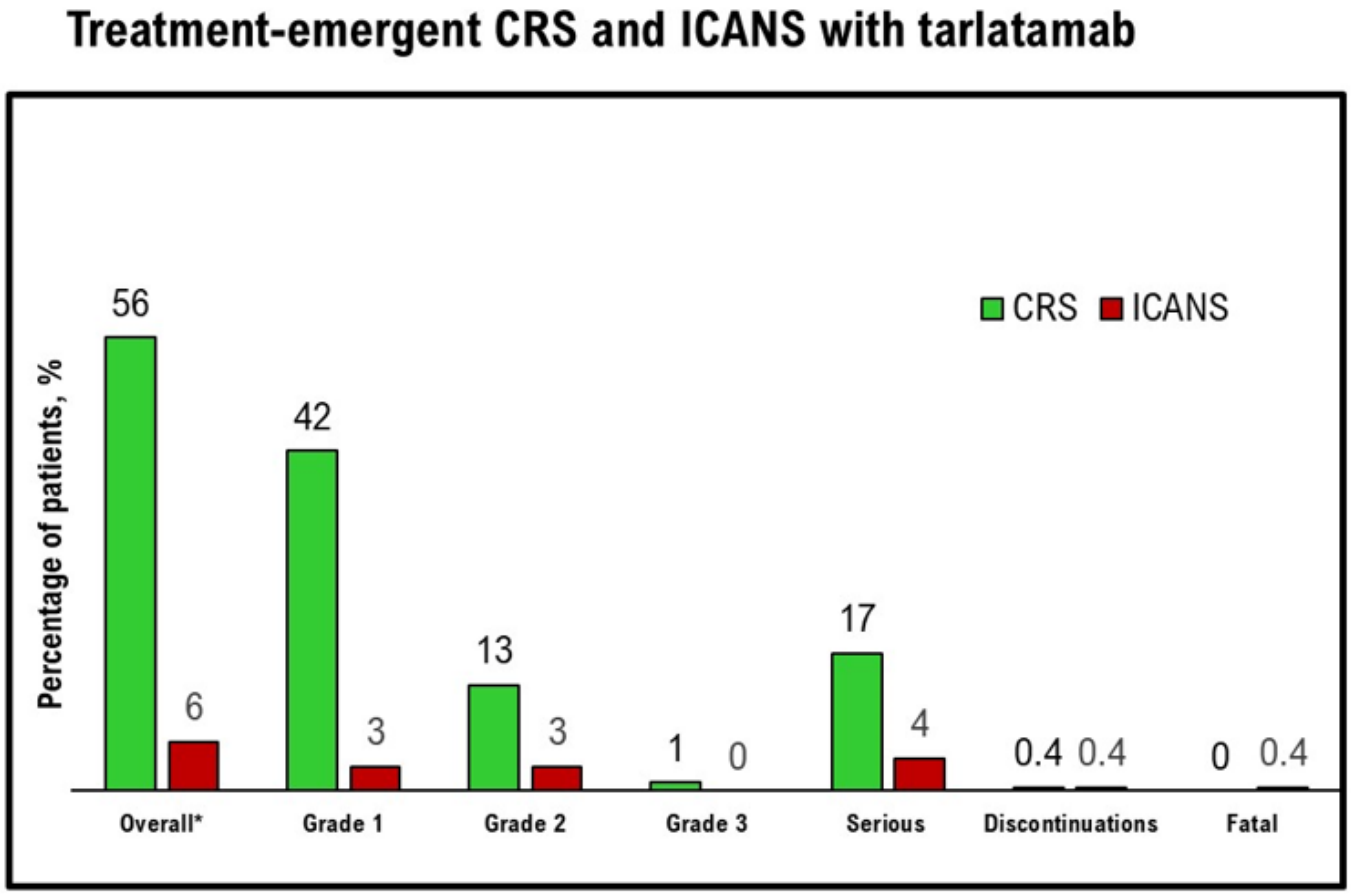
Dellphi-304: tolérance

Meilleur profil de tolérance que le bras chimiothérapie

	Tarlatamab (n = 252)*	Chemotherapy (n = 244)*
Median duration of treatment, months, (range)	4.2 (< 1–17)	2.5 (< 1–15)
All grade, TEAEs, n (%)	249 (99)	243 (100)
All grade, TRAEs n (%)	235 (93)	223 (91)
Grade ≥ 3 TRAEs, n (%)	67 (27)	152 (62)
Serious TRAEs, n (%)	70 (28)	75 (31)
TRAEs leading to dose interruption and/or dose reduction, n (%)	48 (19)	134 (55)
TRAEs leading to discontinuation, n (%)	7 (3)	15 (6)
Treatment-related grade 5 events†, n (%)	1 (0.4)	4 (2)



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Un nouveau standard en deuxième ligne dans le carcinome bronchique à petites cellules

Dellphi-304: implications

- Tarlatamab devient **le standard** en deuxième ligne dans le carcinome bronchique à petites cellules
- Pas d'accès à l'heure de cette présentation
- Se former aux toxicités particulières de la molécule
  - CRS
  - ICANS
  - (Dysgueusie)

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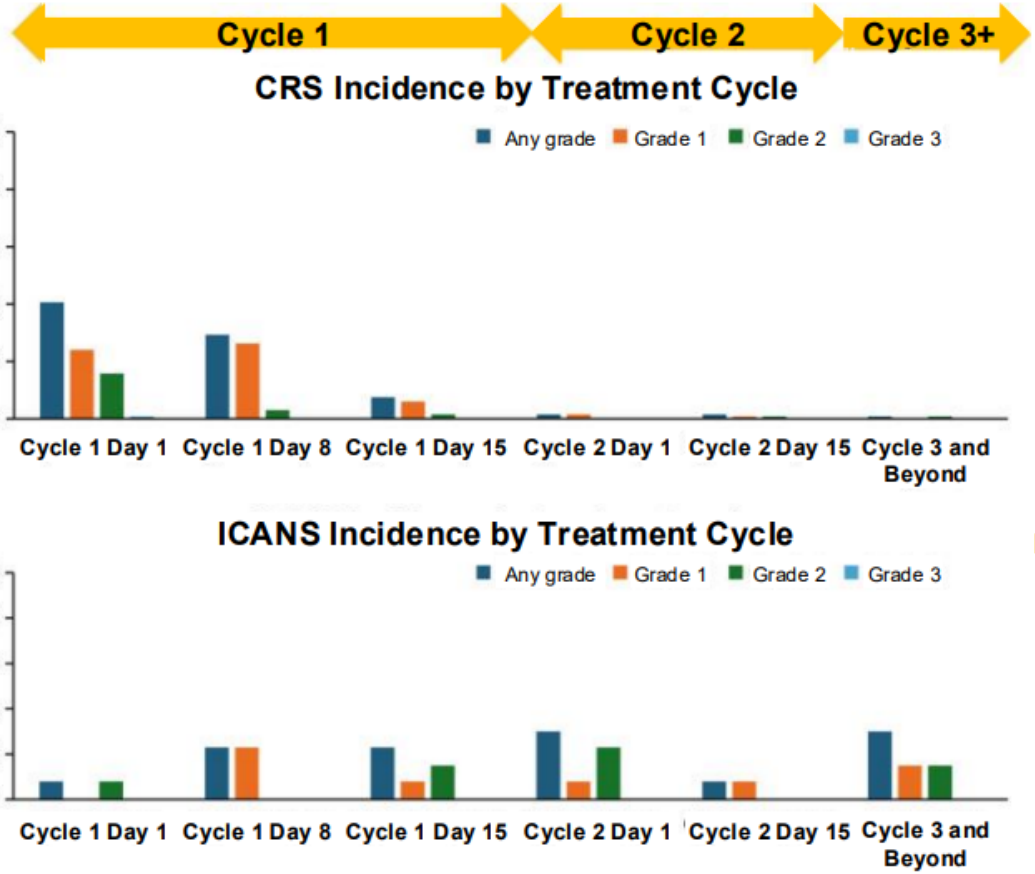
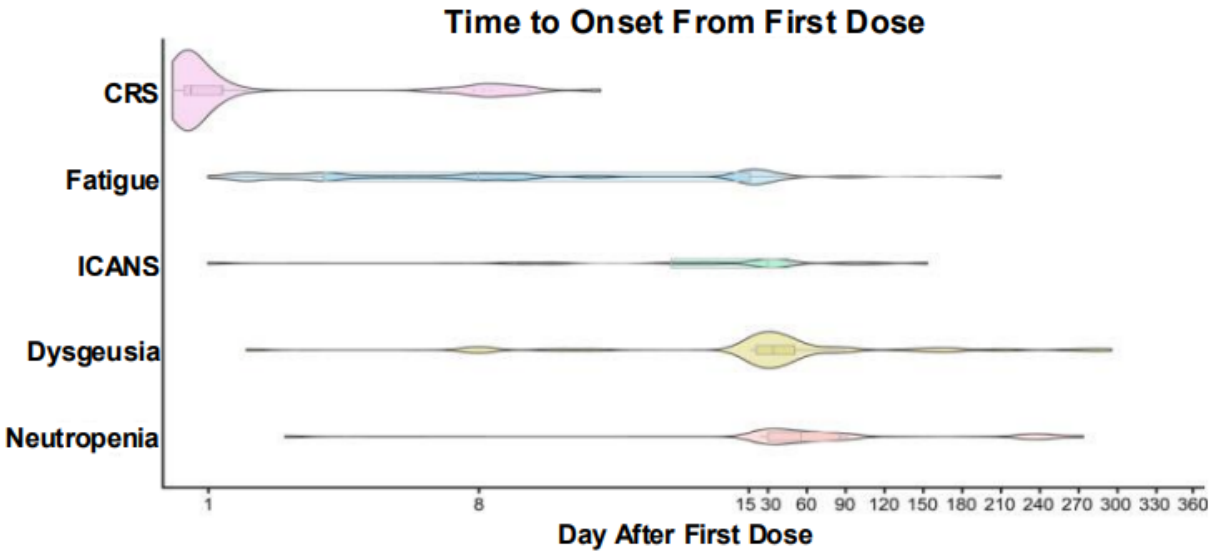
PEC des toxicités du tarlatamab





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PEC des toxicités du tarlatamab

Recommandations d'administration et surveillance

Dosage and Scheduling of Tarlatamab

Schedule	Day	Dose	Administration	Recommended Monitoring
Step-up dosing schedule cycle 1	Day 1[a]	Step-up dose[a]: 1 mg	Administer tarlatamab as a 1-hour intravenous infusion in an appropriate healthcare setting	• Monitor patients from the start of infusion for 22-24 h on cycle day 1 and cycle 1 day 8 in an appropriate healthcare setting • Recommend that patients remain within 1 h of an appropriate healthcare setting for a total of 48 h from the start of the infusion, accompanied by a care partner
	Day 8[a]	10 mg[a]		• Observe patients for 6-8 h post infusion[b]
	Day 15	10 mg		• Observe patients for 6-8 h post infusion[b]
Cycle 2	Day 1 & 15	10 mg		• Observe patients for 3-4 h post infusion[b]
Cycles 3 & 4	Day 1 & 15	10 mg		• Observe patients for 2 h • post infusion[b]
Cycle 5 & subsequent infusions	Day 1 &15	10 mg		

Concomitant Medications for Tarlatamab Administration

- **Day 1 & 8:** 8 mg of dexamethasone intravenously (or equivalent) within 1 h prior to tarlatamab administration
- **Day 1, 8 & 15:** 1 L of normal saline intravenously over 4-5 h immediately after completion of tarlatamab infusion

- Step-up dosing schedule reduces the incidence and severity of CRS
- After step-up dosing schedule, administer tarlatamab biweekly (every 2 weeks) until disease progression or unacceptable toxicity
- Concomitant medications can also reduce the risk of CRS

Prise en charge du CRS

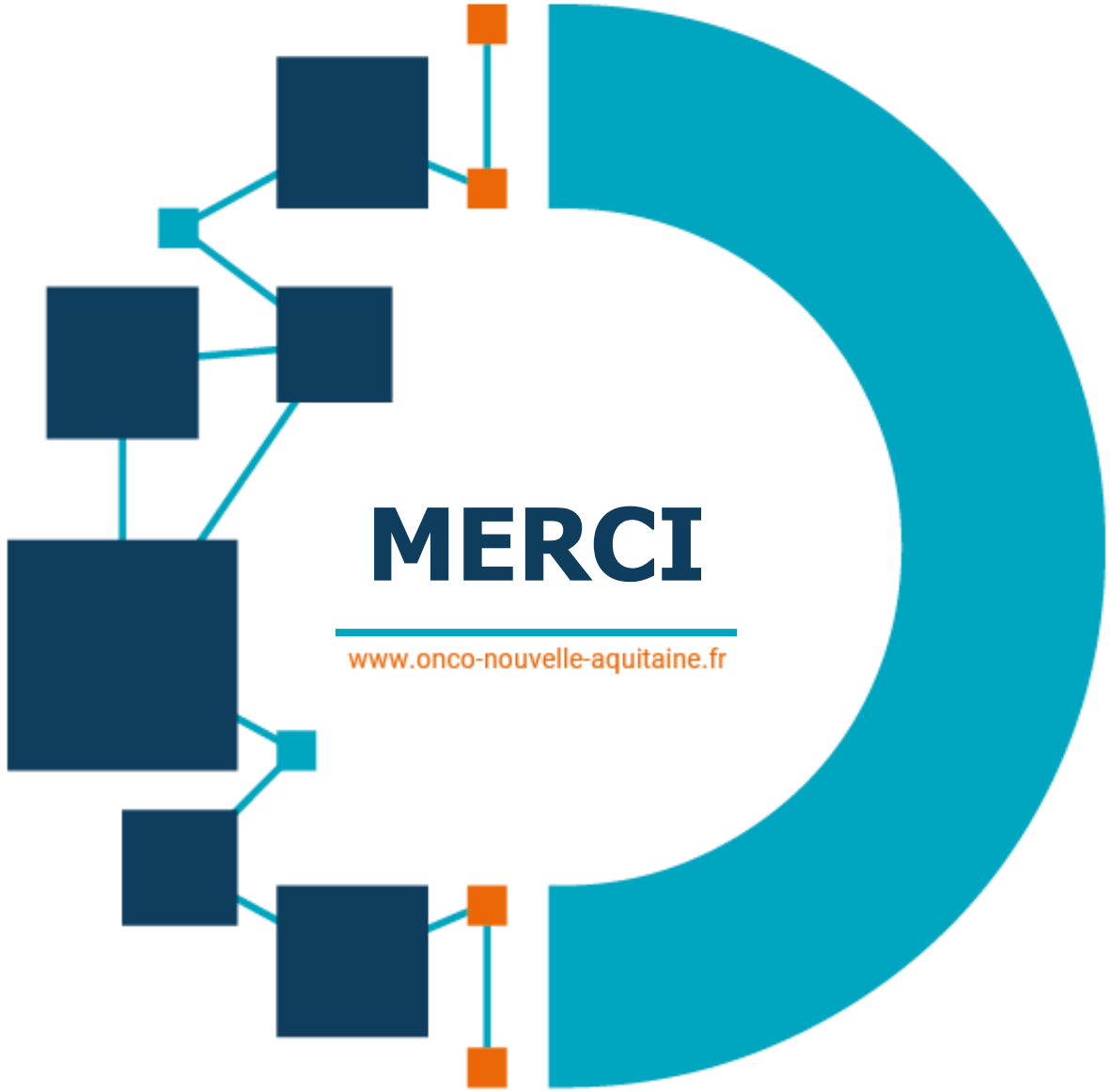
Grade	Defining Symptoms
Grade 1	Symptoms require symptomatic treatment only (eg, fever ≥100.4°F without hypotension or hypoxia)
Grade 2	Symptoms require and respond to moderate intervention • Fever ≥100.4°F • Hypotension not requiring vasopressors ***AND/OR*** • Hypoxia requiring low-flow nasal cannula or blow-by
Grade 3	Severe symptoms defined as temperature ≥100.4°F with: • Hemodynamic instability requiring a vasopressor (with or without vasopressin) ***OR*** • Worsening hypoxia or respiratory distress requiring high-flow nasal cannula (>6 L/min oxygen) or face mask
Grade 4	Life-threatening symptoms defined as temperature ≥100.4°F with: • Hemodynamic instability requiring multiple vasopressors (excluding vasopressin) • Worsening hypoxia or respiratory distress despite oxygen administration requiring positive pressure (eg, CPAP, BiPAP, intubation, and mechanical ventilation

Grade[a]	Management Strategies[a]	Dosage Modifications
Grade 1	• Symptomatic treatment (eg, acetaminophen) for fever	• Withhold tarlatamab until event resolves, then resume at the next scheduled dose
Grade 2	• Recommend hospitalization for a minimum of 24 h with cardiac telemetry and pulse oximetry • Administer symptomatic treatment (eg, acetaminophen) for fever • Administer supplemental oxygen and IV fluids when indicated • Consider dexamethasone[b] (or equivalent) 8 mg IV • Consider tocilizumab (or equivalent) • When resuming treatment at the next planned dose, monitor patients from the start of the infusion for 22 to 24 h in an appropriate healthcare setting	• Withhold tarlatamab until event resolves, then resume at the next scheduled dose
Grade 3	In addition to grade 2 treatment • Recommend intensive monitoring (eg, ICU care) • Administer dexamethasone[b] (or equivalent) 8 mg IV every 8 h up to 3 doses • Vasopressor support as needed • Recommend tocilizumab (or equivalent) • Prior to the next dose, administer concomitant medications • When resuming treatment at the next planned dose, monitor patients from the start of the tarlatamab infusion for 22 to 24 h in an appropriate healthcare setting	• Withhold tarlatamab until the event resolves, then resume at the next scheduled dose • For recurrent grade 3 events, permanently discontinued tarlatamab
Grade 4	• ICU care • Per grade 3 treatment • Recommend tocilizumab (or equivalent)	• Permanently discontinue tarlatamab

Pharmacist's Role in CRS: Monitor for drug interactions. Tarlatamab causes transient release of cytokines that may suppress CYP450 enzymes and result in an increased exposure of concomitant CYP substrates during and up to 14 d after occurrence of CRS

Prise en charge des ICANS

Grade[a]	Management Strategies	Dosage Modifications
Grade 1	• Supportive care	• Withhold tarlatamab until ICANS resolves, then resume at the next scheduled dose
Grade 2	• Supportive care. • Dexamethasone[b] (or equivalent) 10 mg IV. Can repeat every 6 h or methylprednisolone 1 mg/kg IV every 12 h if symptoms worsen • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management • Monitor patients for 22 to 24 h following the next dose of tarlatamab	• Withhold tarlatamab until ICANS resolves, then resume at the next scheduled dose
Grade 3	• Recommend intensive monitoring (eg, ICU care) • Consider mechanical ventilation for airway protection; dexamethasone[b] (or equivalent) 10 mg IV every 6 h or methylprednisolone 1 mg/kg IV every 12 h • Consider repeat neuroimaging (CT or MRI) every 2-3 d if patient has persistent Grade ≥3 neurotoxicity • Monitor patients for 22 to 24 h following the next dose of tarlatamab	• Withhold tarlatamab until the ICANS resolves, then resume at the next scheduled dose • If there is no improvement to grade ≤ 1 within 7 d or grade 3 toxicity reoccurs within 7 d of reinitiation, permanently discontinue tarlatamab • For recurrent grade 3 events, permanently discontinue
Grade 4	• ICU care • Consider mechanical ventilation for airway protection • High dose corticosteroids	• Permanently discontinue tarlatamab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