Oncologie thoracique

Post ESMO 2019

Dr Sophie Cousin

Institut Bergonié

Plan: 2 sujets abordés

A- Données de survie de l'Osimertinib en première ligne dans les carcinomes bronchiques non à petites cellules métastatiques avec mutation activatrice de l'EGFR (FLAURA)

B- Données en première ligne dans les carcinomes bronchiques non à petites cellules métastatiques: Checkmate 227, IMpower110

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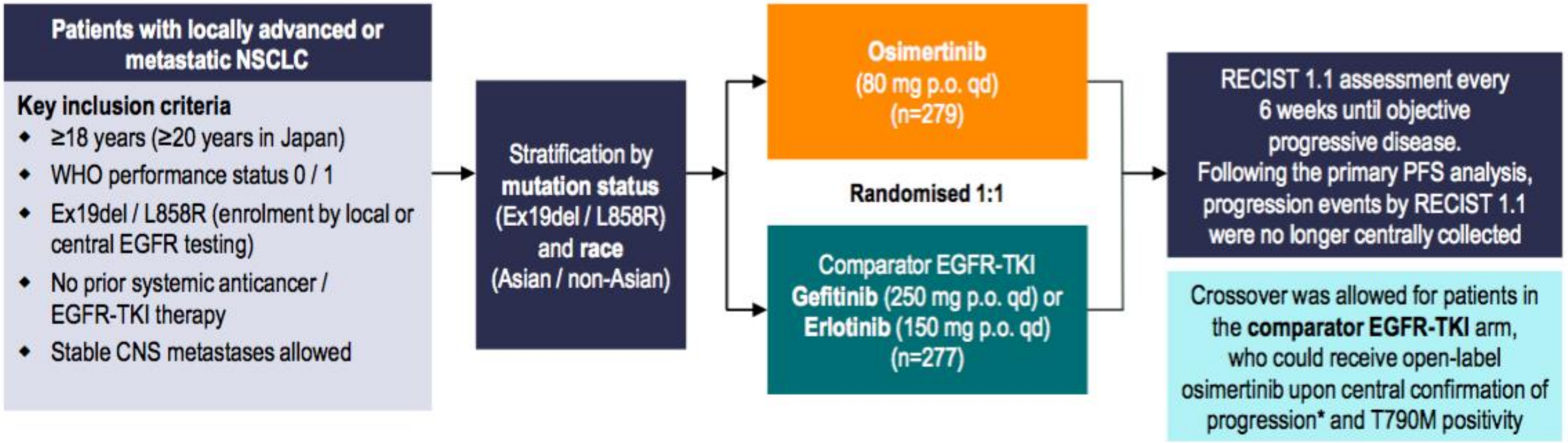
Données de survie globale de l'étude FLAURA

OSIMERTINIB VS COMPARATOR EGFR-TKI AS FIRST-LINE TREATMENT FOR EGFRm ADVANCED NSCLC (FLAURA): FINAL OVERALL SURVIVAL ANALYSIS

Suresh S Ramalingam[1], Jhanelle E Gray[2], Yuichiro Ohe[3], Byoung Chul Cho[4], Johan Vansteenkiste[5], Caicun Zhou[6], Thanyanan Reungwetwattana[7], Ying Cheng[8], Busayamas Chewaskulyong[9], Riyaz Shah[10], Ki Hyeong Lee[11], Parneet Cheema[12], Marcello Tiseo[13], Thomas John[14], Meng-Chih Lin[15], Fumio Imamura[16], Rachel Hodge[17], Yuri Rukazenkov[17], Jean-Charles Soria[18,19], David Planchard[19]

Design de l'étude:



Survie globale: Objectif secondaire

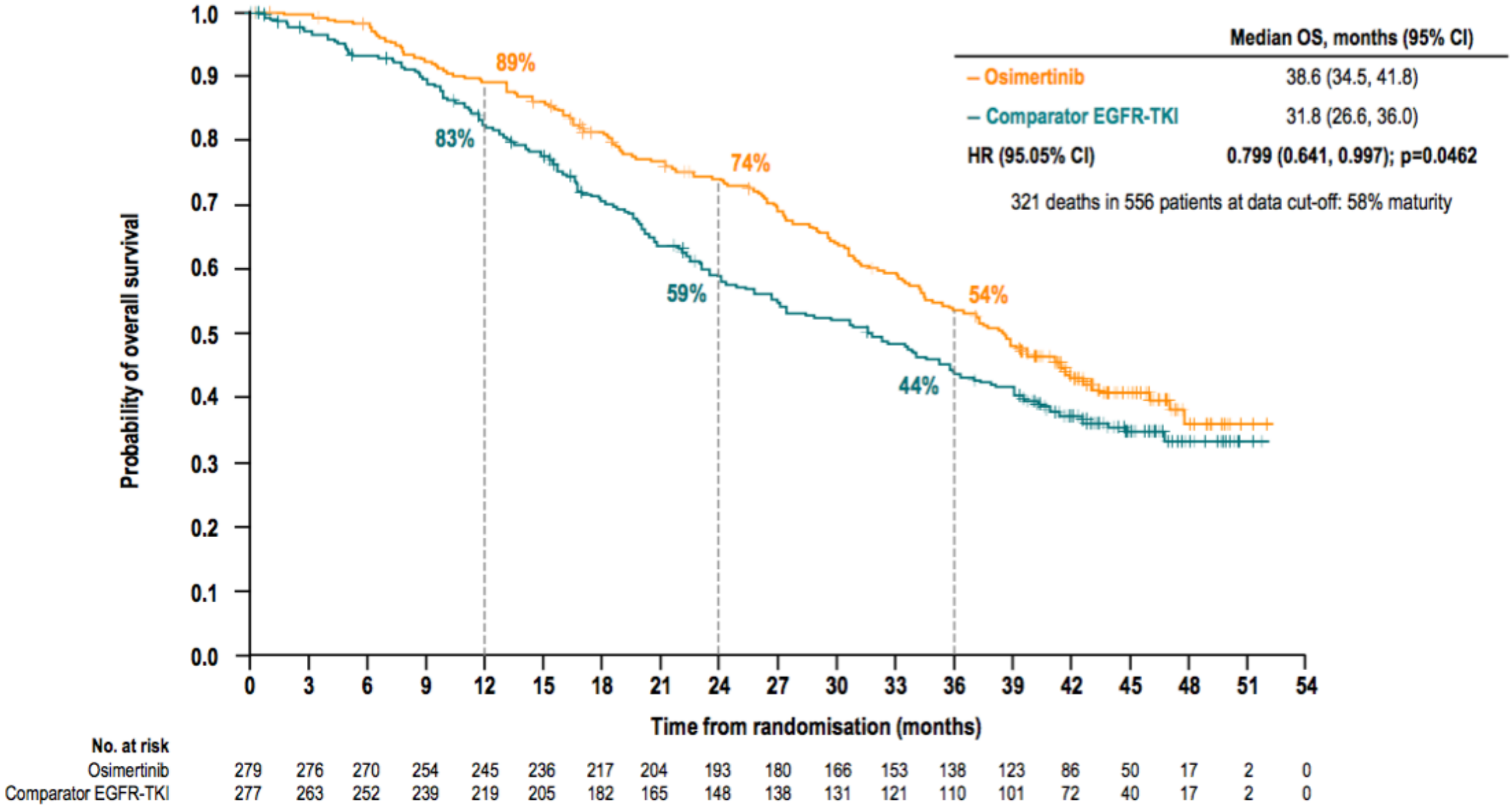
Objectifs I: PFS (pour rappel)

- PFS: **18. 9** mois vs **10.2** mois,
- HR= **0.46** (0.37 - 0.57), **p< 0.001**

Caractéristiques des patients:

Characteristic, %	Osimertinib (n=279)	Comparator EGFR-TKI (n=277)
Sex: male / female	36 / 64	38 / 62
Age, median (range), years	64 (26–85)	64 (35–93)
Race: Asian / non-Asian	62 / 38	62 / 38
Smoking status: never / ever	65 / 35	63 / 37
CNS metastases at study entry	19	23
WHO performance status: 0 / 1	40 / 60	42 / 58
Overall disease classification: metastatic / advanced	95 / 5	95 / 5
Histology: adenocarcinoma / other	99 / 1	98 / 2
EGFR mutation at randomisation: Ex19del / L858R	63 / 37	63 / 37

Résultats de survie globale:



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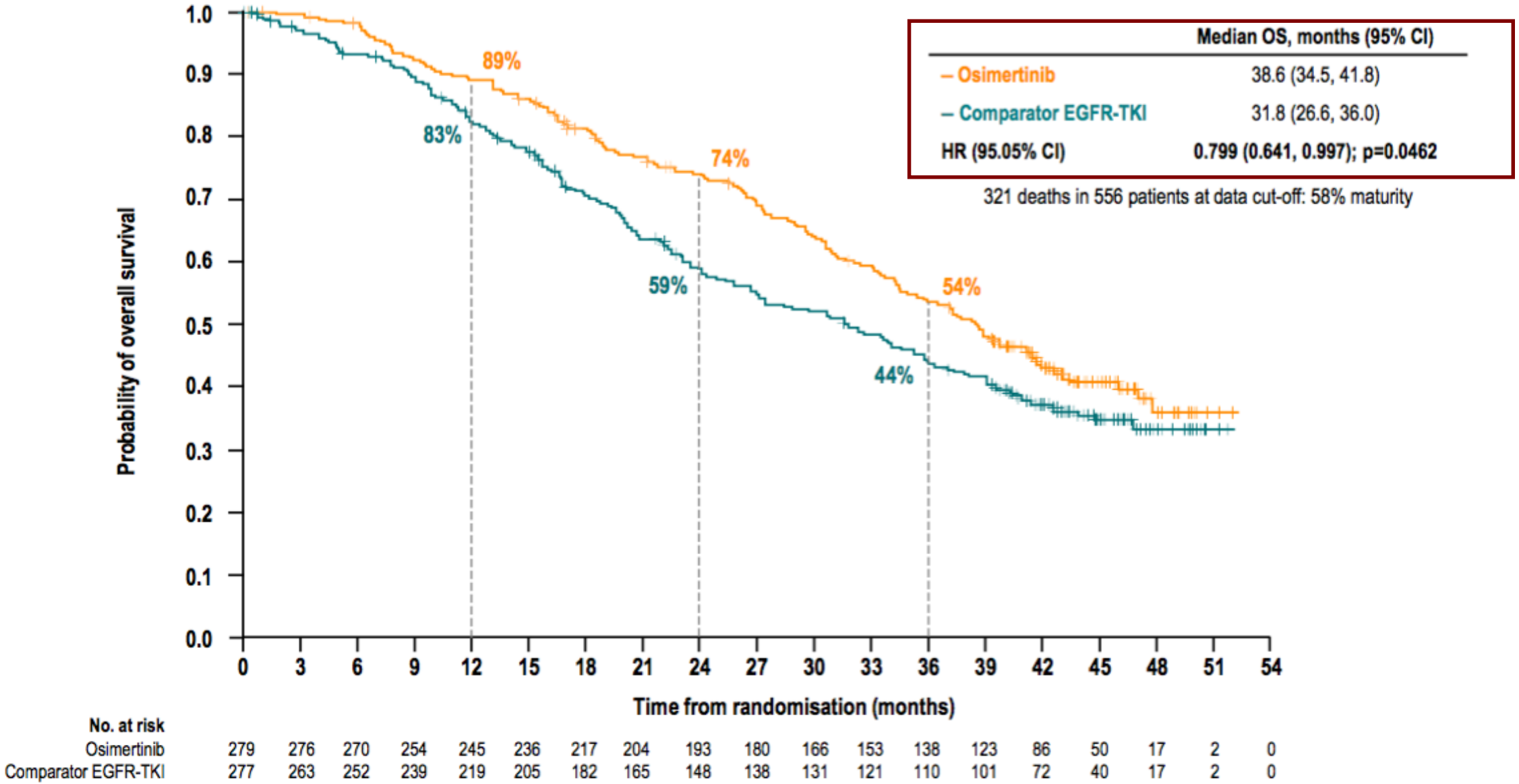
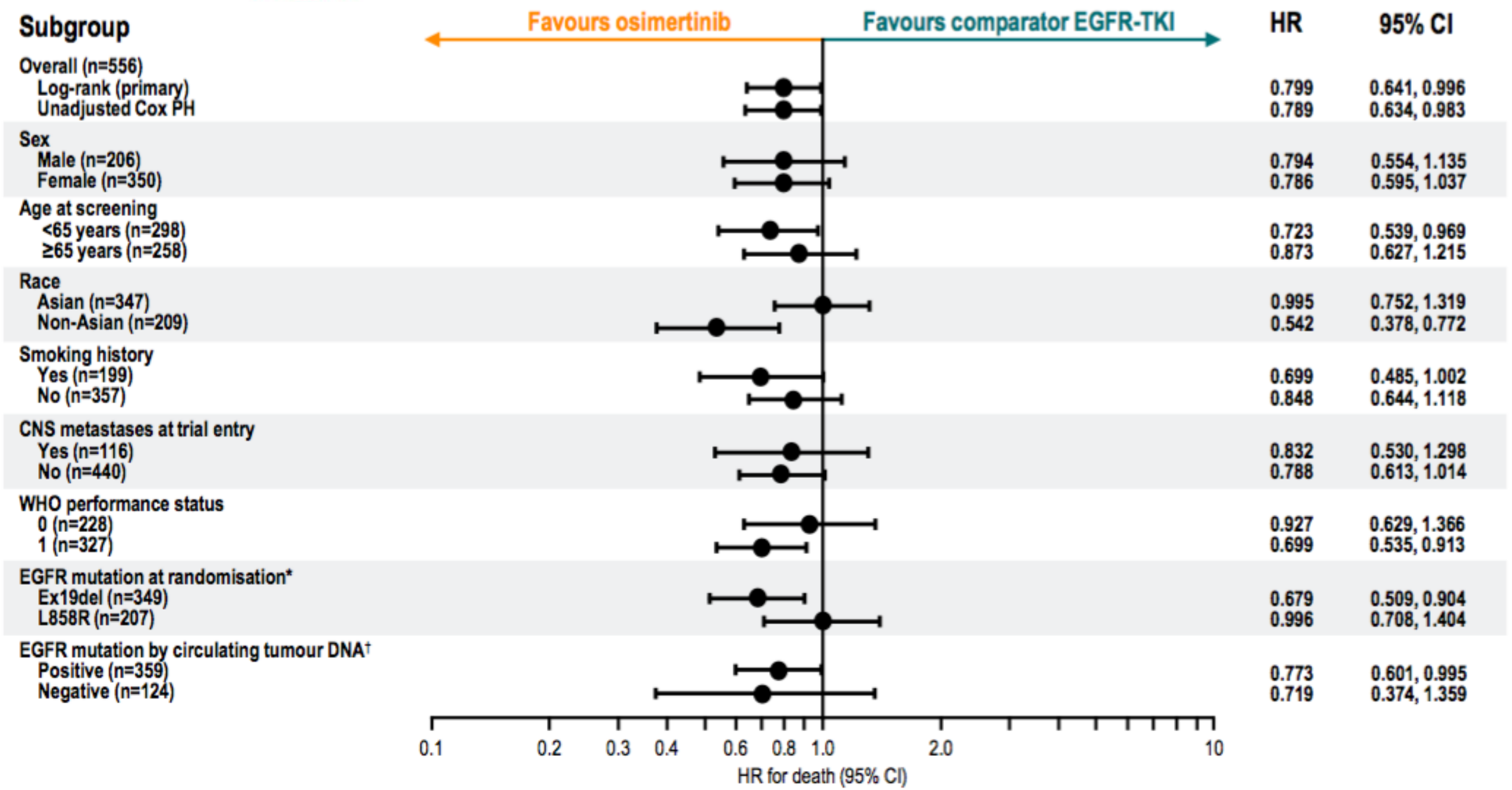
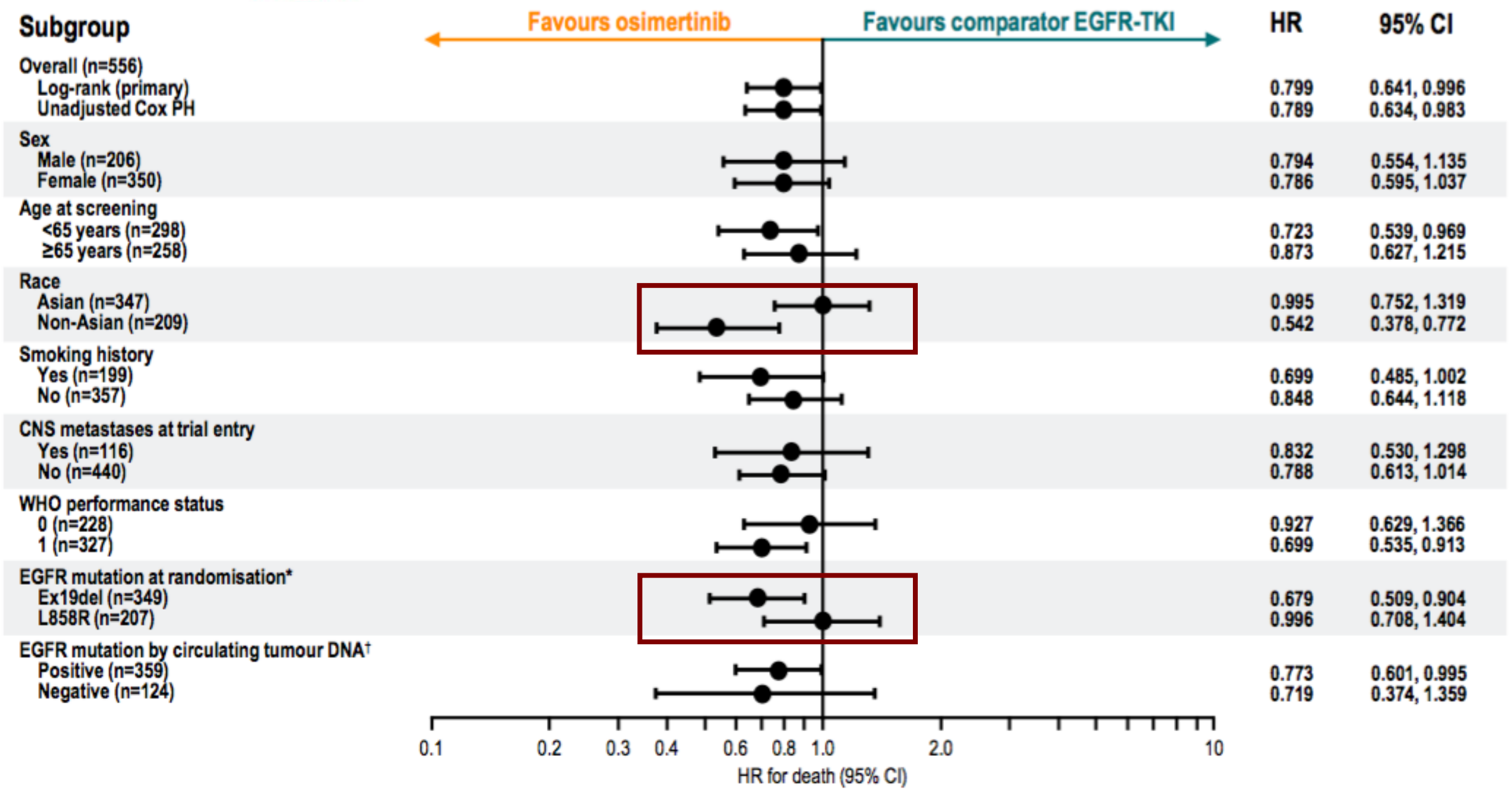



Subgroup
Favours osimertinib
Favours comparator EGFR-TKI
HR
95% CI
Overall (n=556)
Log-rank (primary) 0.799 0.641, 0.996
Unadjusted Cox PH 0.789 0.634, 0.983
Sex
Male (n=206) 0.794 0.554, 1.135
Female (n=350) 0.786 0.595, 1.037
Age at screening
<65 years (n=298) 0.723 0.539, 0.969
≥65 years (n=258) 0.873 0.627, 1.215
Race
Asian (n=347) 0.995 0.752, 1.319
Non-Asian (n=209) 0.542 0.378, 0.772
Smoking history
Yes (n=199) 0.699 0.485, 1.002
No (n=357) 0.848 0.644, 1.118
CNS metastases at trial entry
Yes (n=116) 0.832 0.530, 1.298
No (n=440) 0.788 0.613, 1.014
WHO performance status
0 (n=228) 0.927 0.629, 1.366
1 (n=327) 0.699 0.535, 0.913
EGFR mutation at randomisation*
Ex19del (n=349) 0.679 0.509, 0.904
L858R (n=207) 0.996 0.708, 1.404
EGFR mutation by circulating tumour DNA†
Positive (n=359) 0.773 0.601, 0.995
Negative (n=124) 0.719 0.374, 1.359
0.1
0.2
0.3
0.4
0.6
0.8
1.0
2.0
10
HR for death (95% CI)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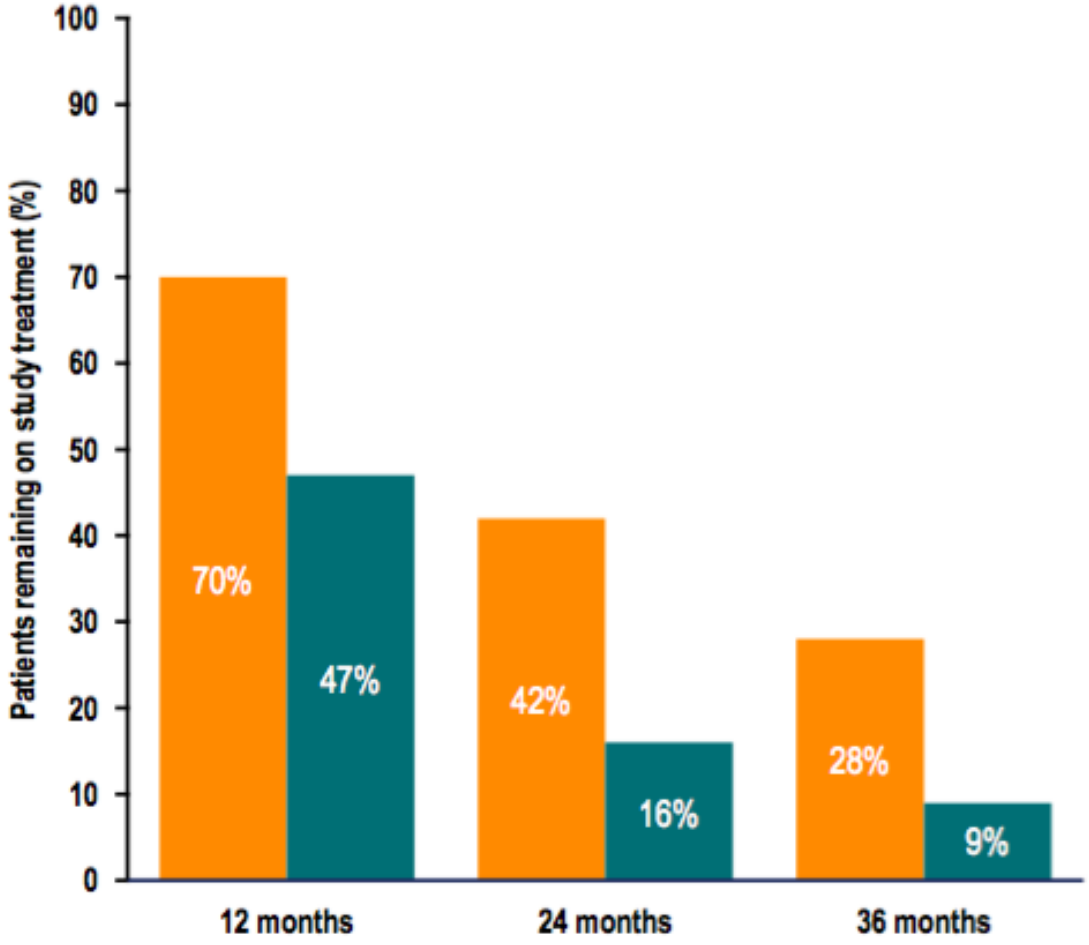
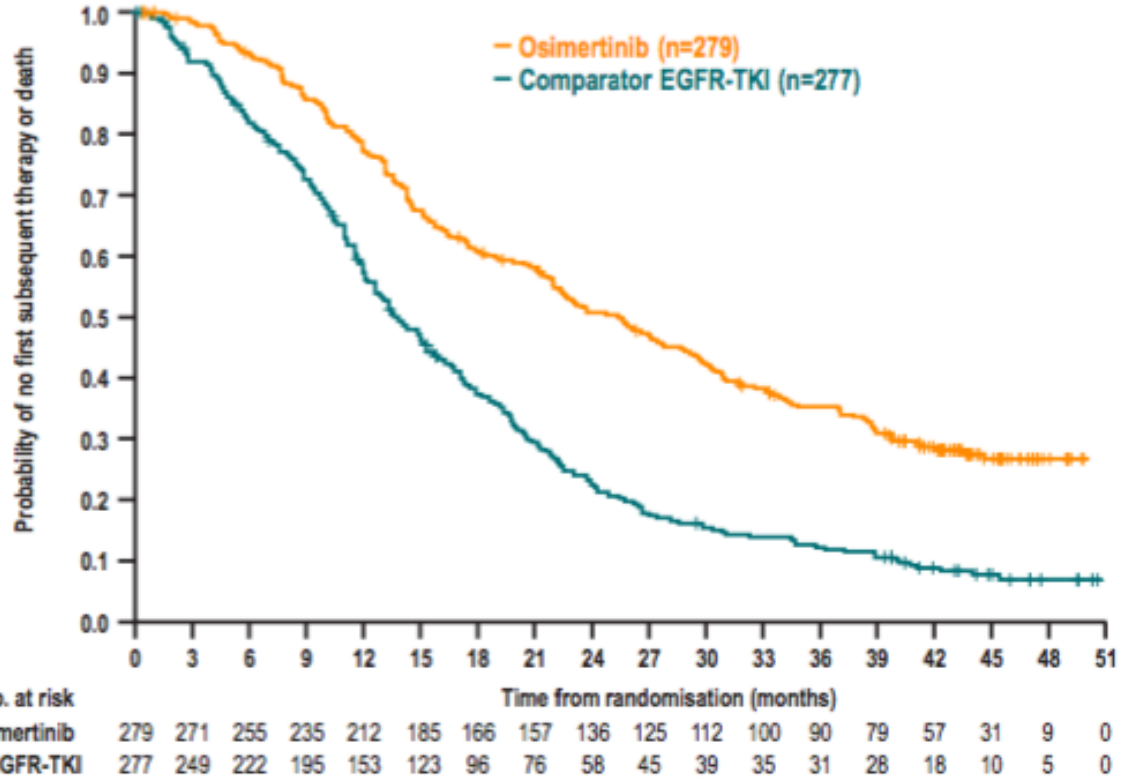
HR for death (95% CI)

Patients remaining on study treatment

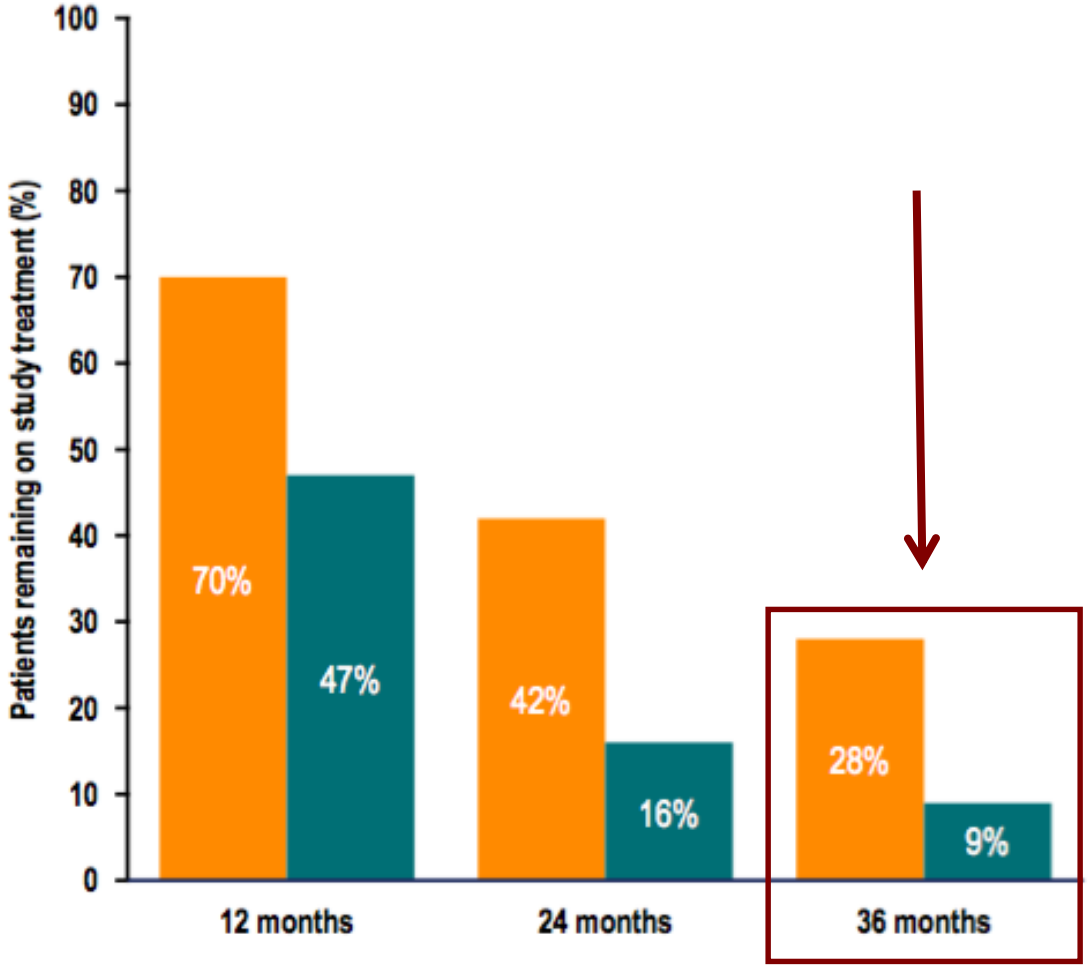


Time to first subsequent treatment*



Time to first subsequent therapy or death	Events	Median, months (95% CI)
Osimertinib	194	25.5 (22.0, 29.1)
Comparator EGFR-TKI	242	13.7 (12.3, 15.7)
HR (95% CI)		0.478 (0.393, 0.581) p<0.0001

Patients remaining on study treatment



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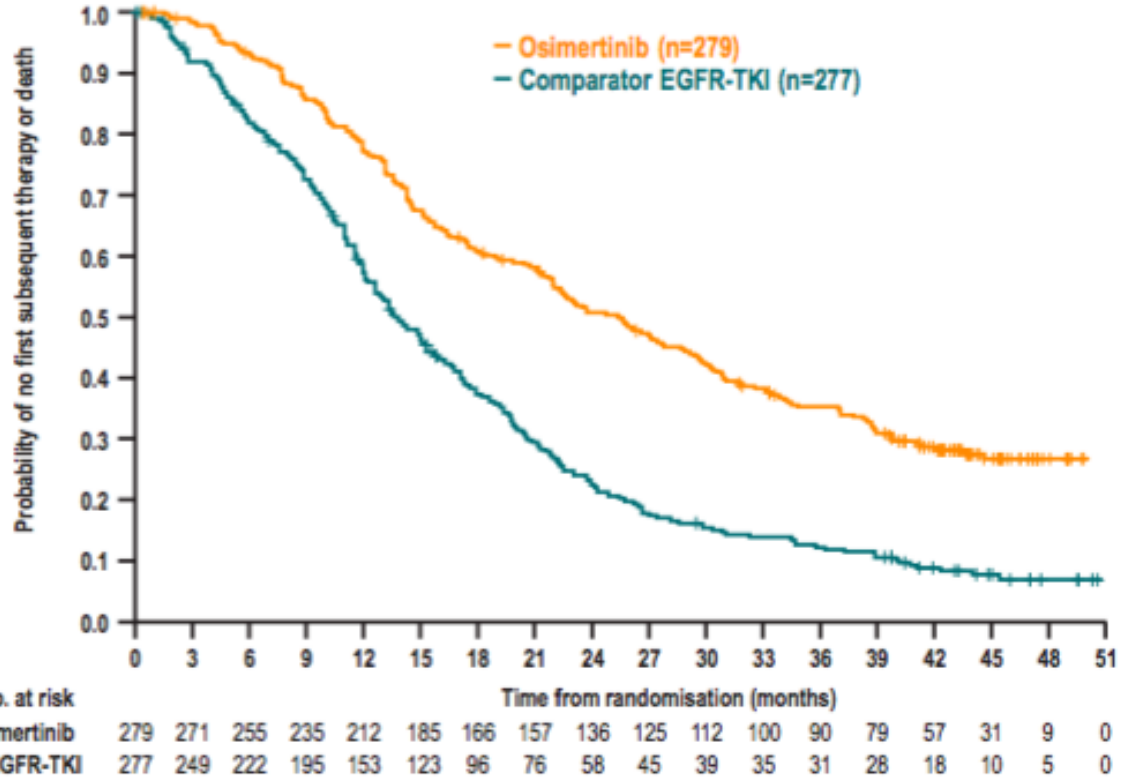

No. at risk																	
Osimertinib	279	271	255	235	212	185	166	157	136	125	112	100	90	79	57	31	9	0
Comparator EGFR-TKI	277	249	222	195	153	123	96	76	58	45	39	35	31	28	18	10	5	0

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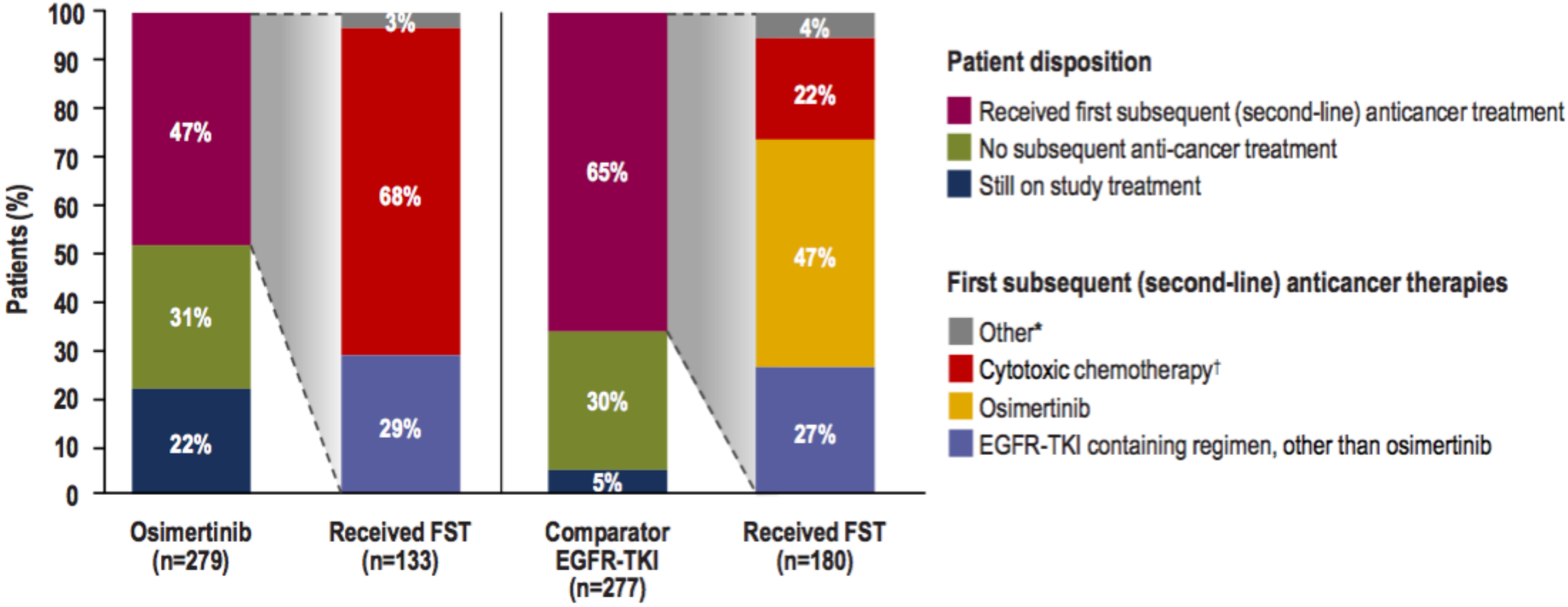
Deuxième ligne après progression:

31% dans le bras Osimertinib et 30% dans le bras TKI G1 ne reçoivent pas de 2nd ligne.



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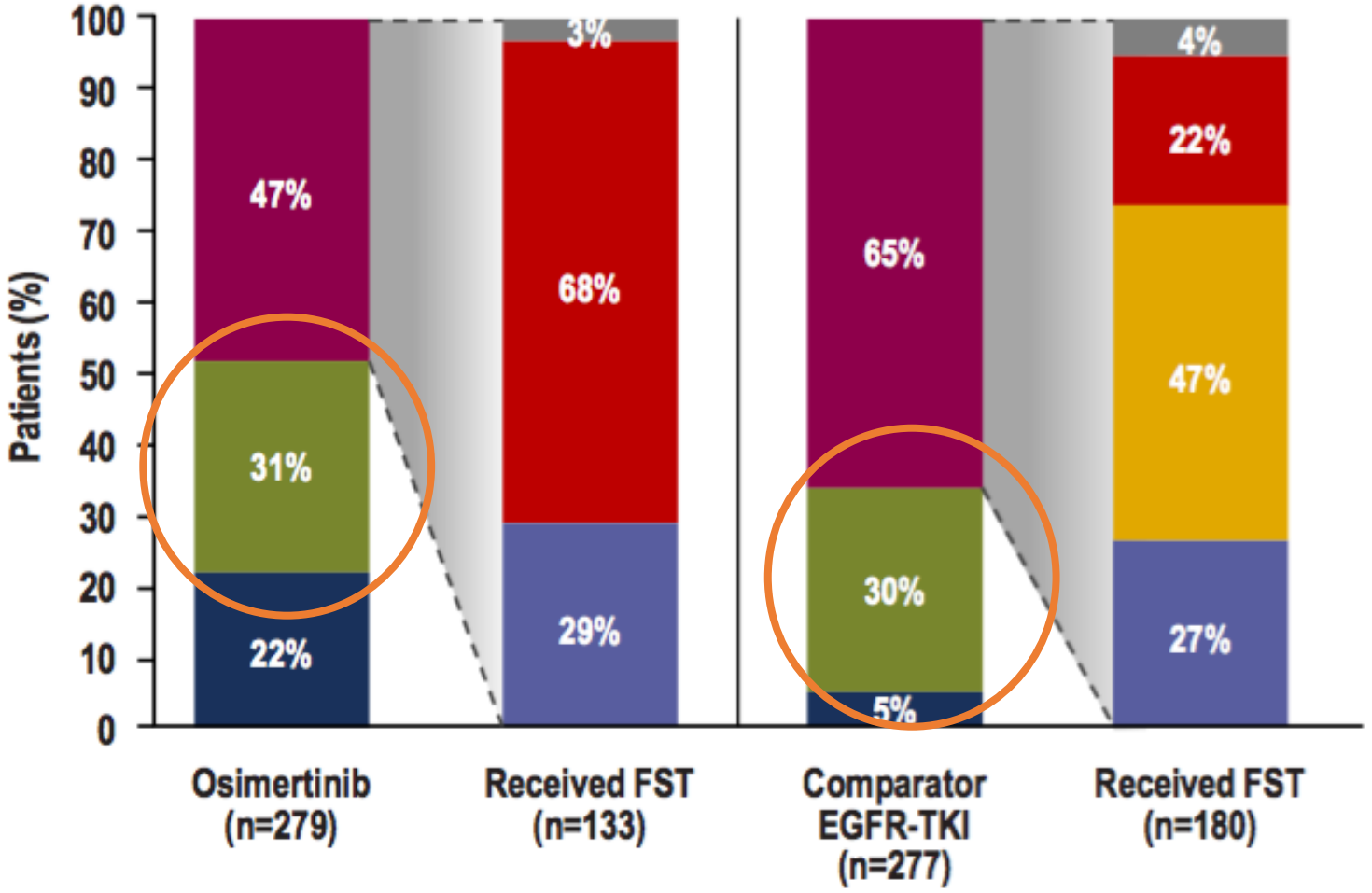

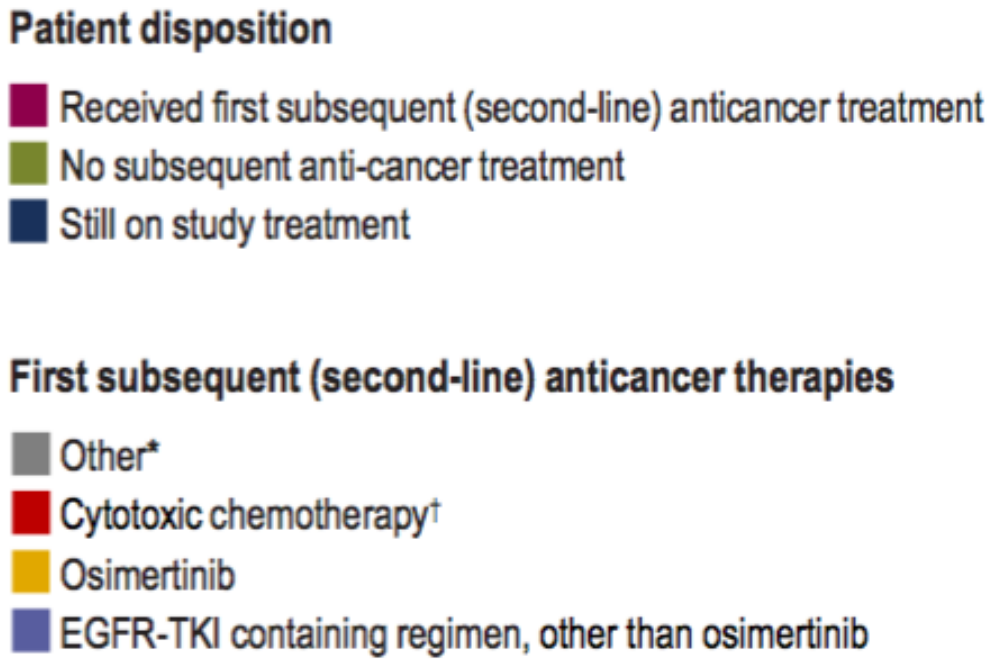

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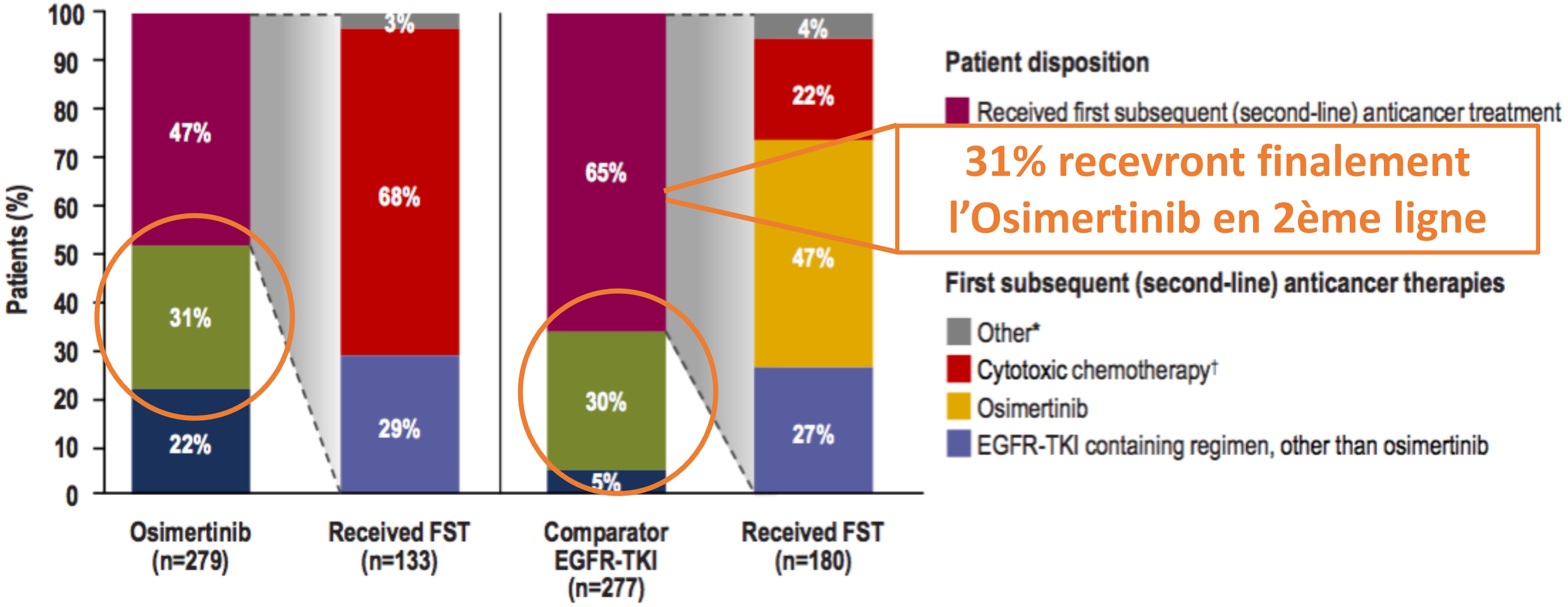
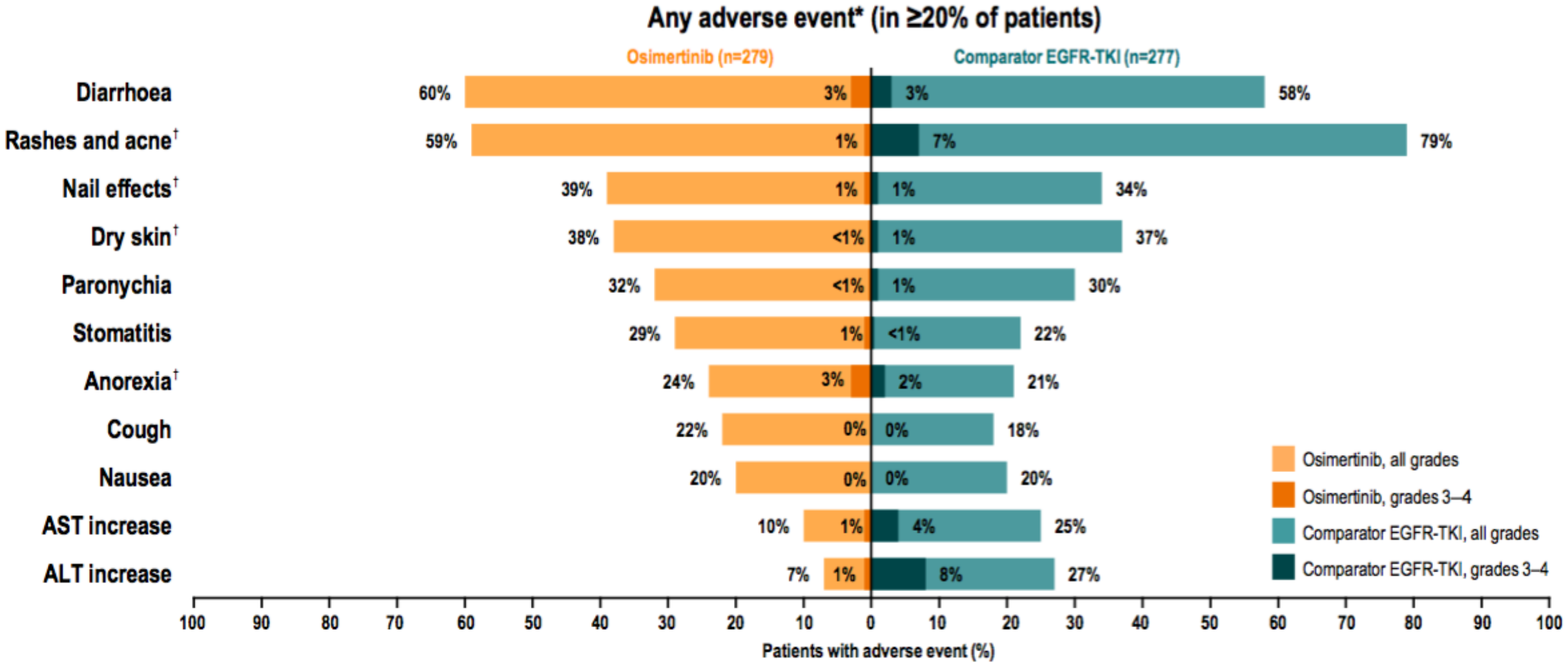


Données de tolérance:

Temps médian d'exposition 20.7 mois vs 11.5 mois pour le bras standard

G≥3: **18%** pour l'Osimertinib vs **29%** pour bras standard



Conclusion

→ 6,8 mois de survie en plus

→ Moins de toxicités grade 3

→A 3 ans: toujours 28% des patients sous traitement versus 9%

Confirmation du statut de « standard » de l'Osimertinib dans les carcinomes bronchiques non à petites cellules avancés ou métastatiques avec mutation activatrice de l'EGFR en première ligne

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NOUVELLE-AQUITAINE
Réseau Régional de Cancérologie

IO seul, Combo IO+IO ou Combo chimio + IO en première ligne dans le mCBNPC?

That is the question

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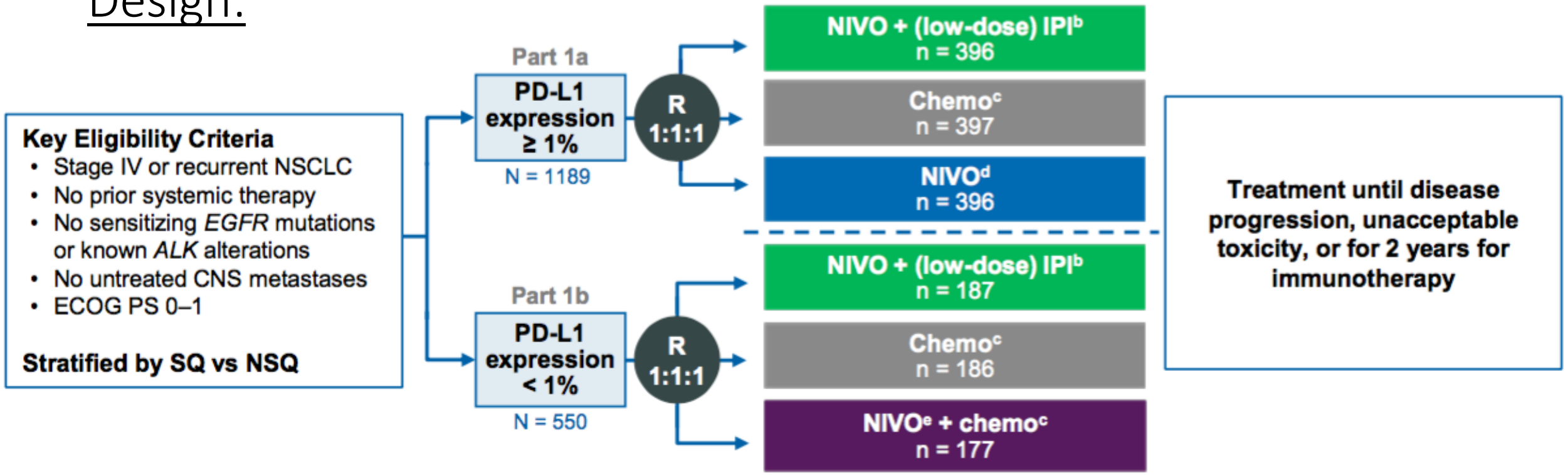
Checkmate 227 part 1: données de survie globale si PD-L1≥ 1+ du bras Ipilimumab+Nivolumab vs chimiothérapie

Nivolumab + Low-Dose Ipilimumab Versus Platinum-Doublet Chemotherapy as First-Line Treatment for Advanced Non-Small Cell Lung Cancer: CheckMate 227 Part 1 Final Analysis

Solange Peters,[1] Suresh Ramalingam,[2] Luis Paz-Ares,[3] Reyes Bernabe Caro,[4] Bogdan Zurawski,[5] Sang-We Kim,[6] Aurelia Alexandru,[7] Lorena Lupinacci,[8] Emmanuel de la Mora Jimenez,[9] Hiroshi Sakai,[10] István Albert,[11] Alain Vergnenegre,[12] Martin Reck,[13] Hossein Borghaei,[14] Julie R. Brahmer,[15] Kenneth O'Byrne,[16] William J. Geese,[17] Prabhu Bhagavatheeswaran,[17] Faith E. Nathan,[17] Matthew D. Hellmann[18]

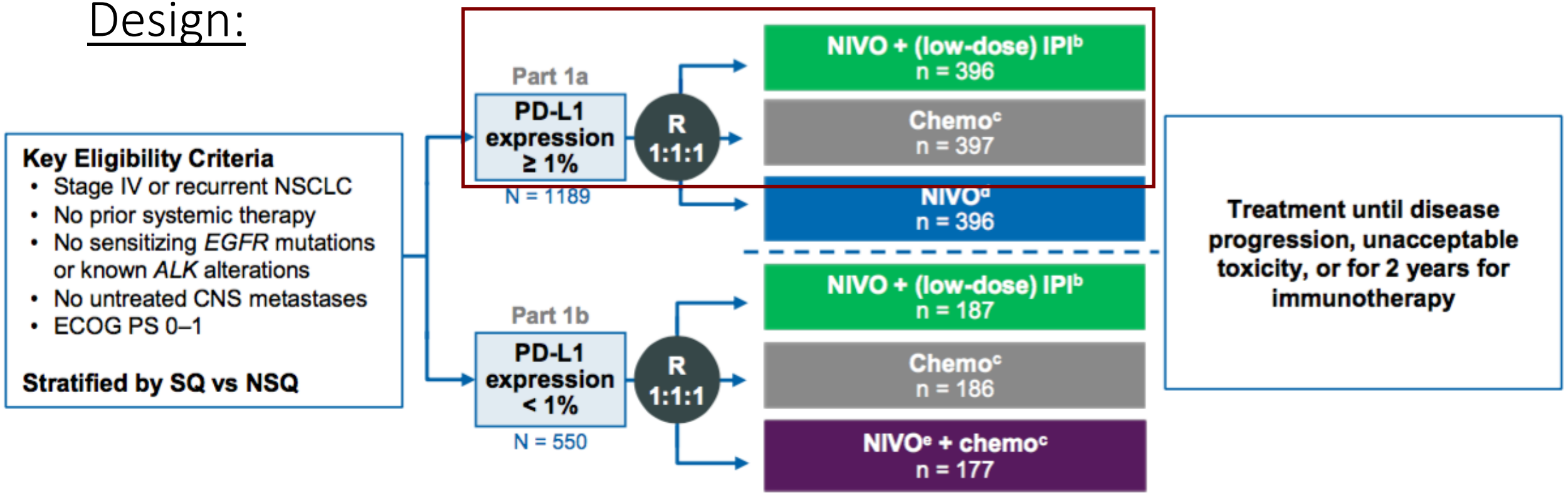
Design:



Independent co-primary endpoints: NIVO + IPI vs chemo
- PFS in high TMB (≥10 mut/Mb) population[f]
- OS in PD-L1 ≥ 1% population[g]

Secondary endpoints (PD-L1 hierarchy):
- PFS: **NIVO + chemo vs chemo** in PD-L1 < 1%
- OS: **NIVO + chemo vs chemo** in PD-L1 < 1%
- OS: **NIVO vs chemo** in PD-L1 ≥ 50%

Design:



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Secondary endpoints (PD-L1 hierarchy):
- PFS: **NIVO + chemo vs chemo** in PD-L1 < 1%
- OS: **NIVO + chemo vs chemo** in PD-L1 < 1%
- OS: **NIVO vs chemo** in PD-L1 ≥ 50%

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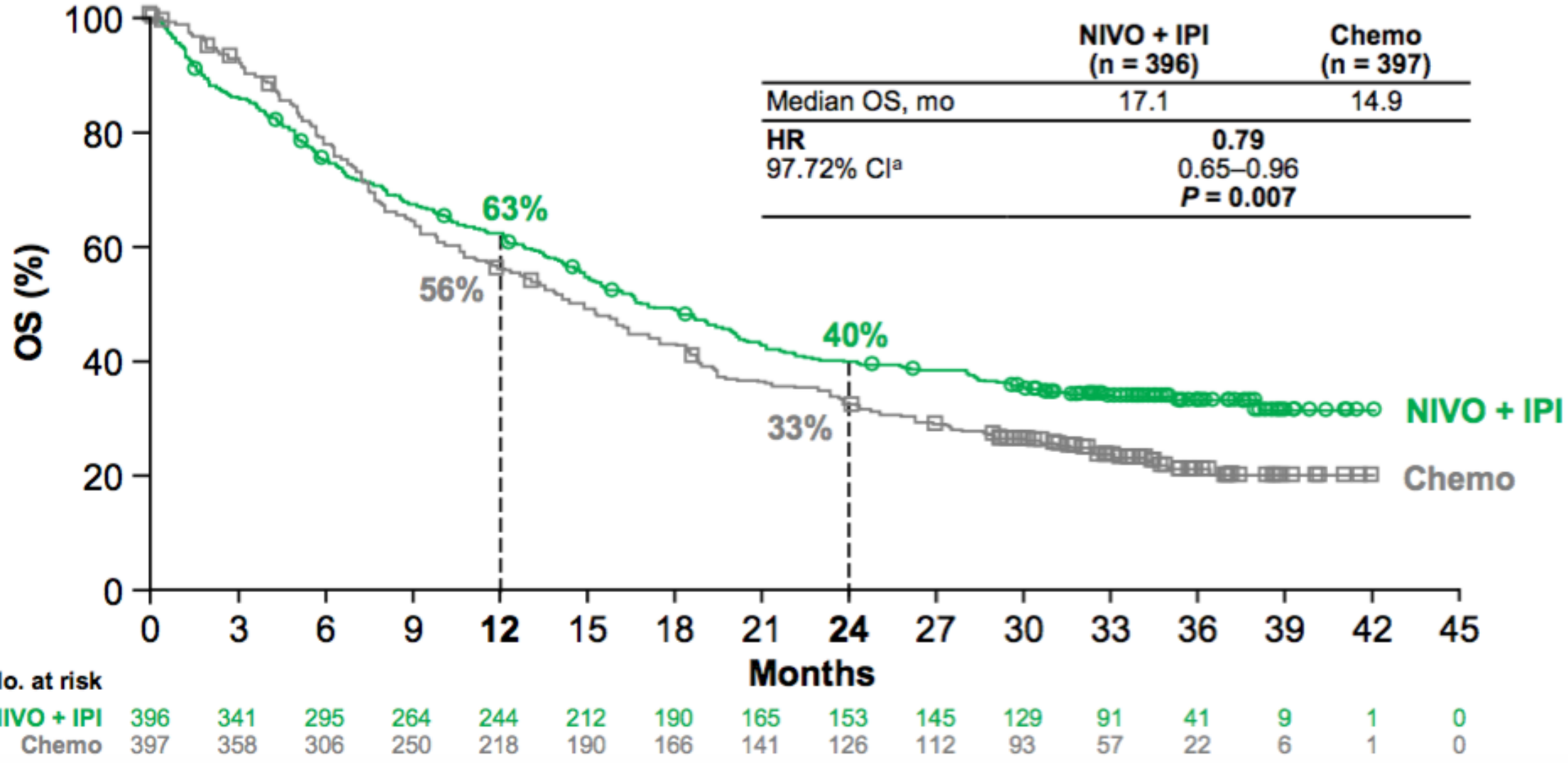
Caractéristiques des patients:

	All randomized (PD-L1 < 1% + PD-L1 ≥ 1%)		PD-L1 ≥ 1%
	NIVO + IPI (n = 583)	Chemo (n = 583)	NIVO (n = 396)
Median age, years (range)	64 (26–87)	64 (29–87)	64 (27–85)
Female, %	33	34	31
ECOG PS,[a] %			
0 / 1	35 / 65	33 / 66	36 / 64
Smoking status,[b] %			
Current / former smoker	85	86	86
Never smoker	14	13	13
Histology,[c] %			
Squamous / non-squamous	28 / 72	28 / 72	30 / 70
Metastases, %			
Bone	28	26	27
Liver	21	22	23
CNS	11	9	11
Tumor PD-L1 expression, %			
< 1%	32	32	NA
≥ 1%	68	68	100
1–49%	33	35	46
≥ 50%	35	33	54
Tissue TMB, %			
Evaluable	57	59	58
≥ 10 mut/Mb	42	46	45
< 10 mut/Mb	58	54	55

Données de survie globale: IPI+NIVO vs chimio si **PD-L1 ≥ 1%**:



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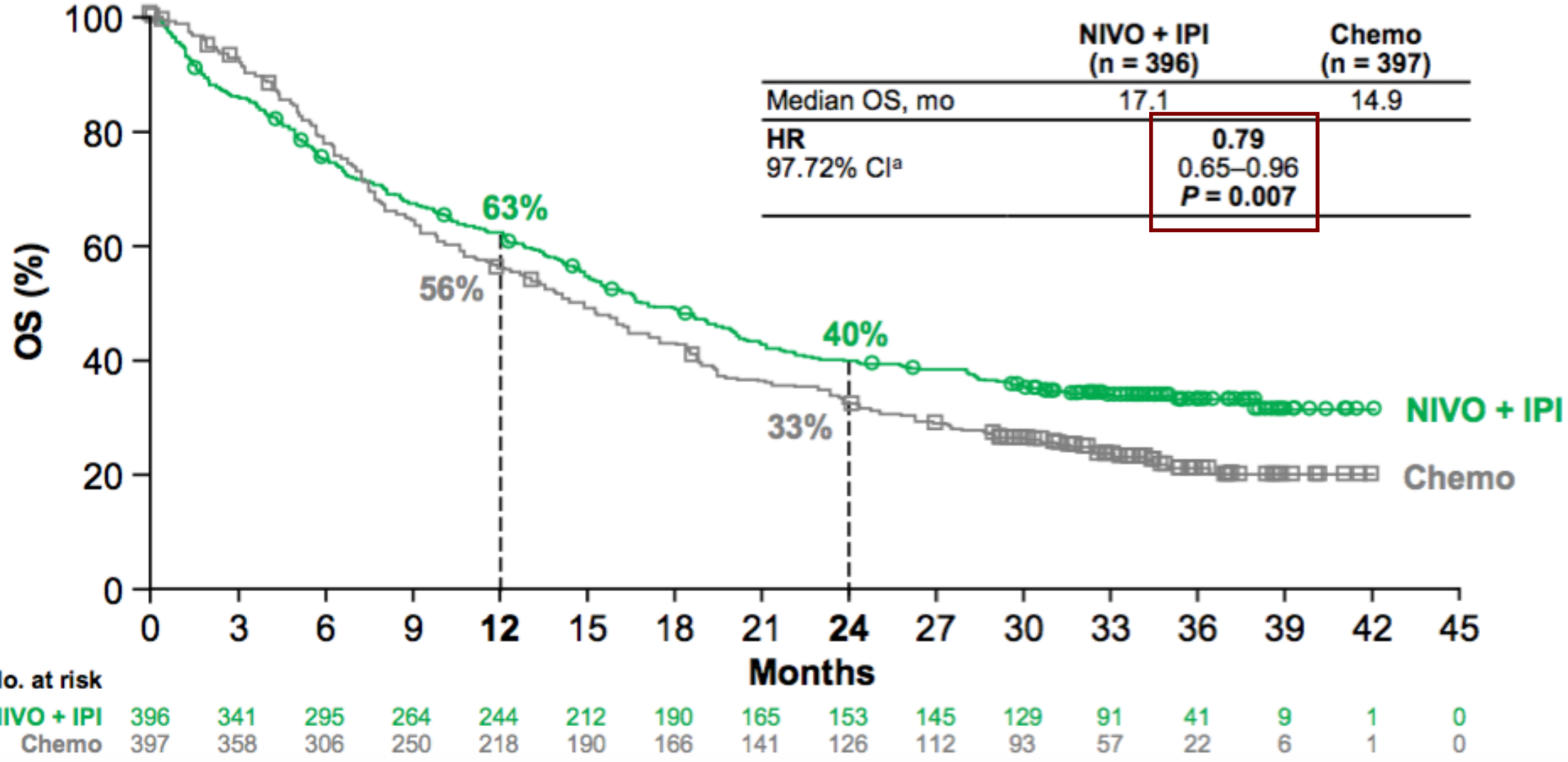

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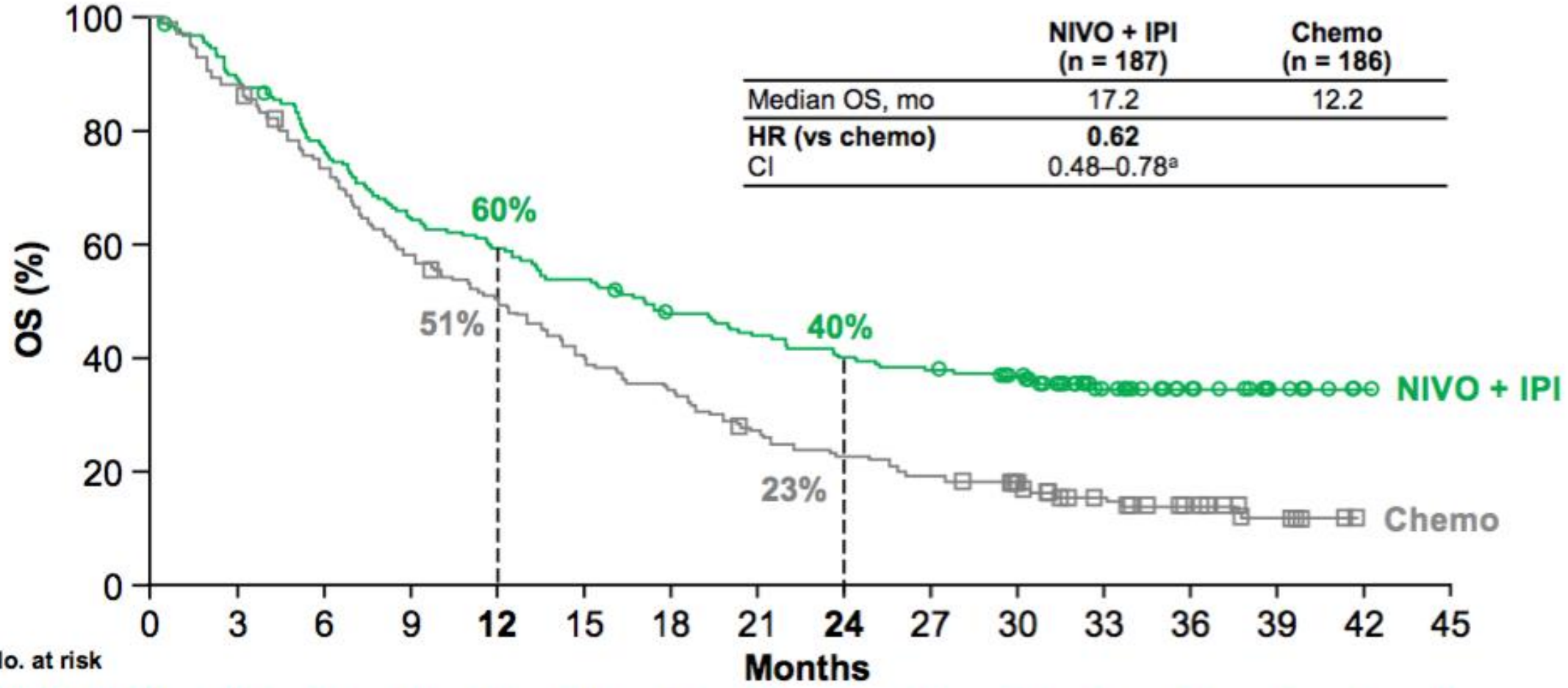
Données de survie globale: IPI+NIVO vs chimio si **PD-L1 ≤ 1%**:

	NIVO + IPI (n = 187)	Chemo (n = 186)
Median OS, mo	17.2	12.2
HR (vs chemo)	**0.62**	
CI	0.48–0.78[a]	



No. at risk																
NIVO + IPI	187	165	142	120	110	100	87	80	73	69	59	34	19	8	2	0
Chemo	186	164	135	107	92	74	62	49	41	35	29	19	12	5	0	0

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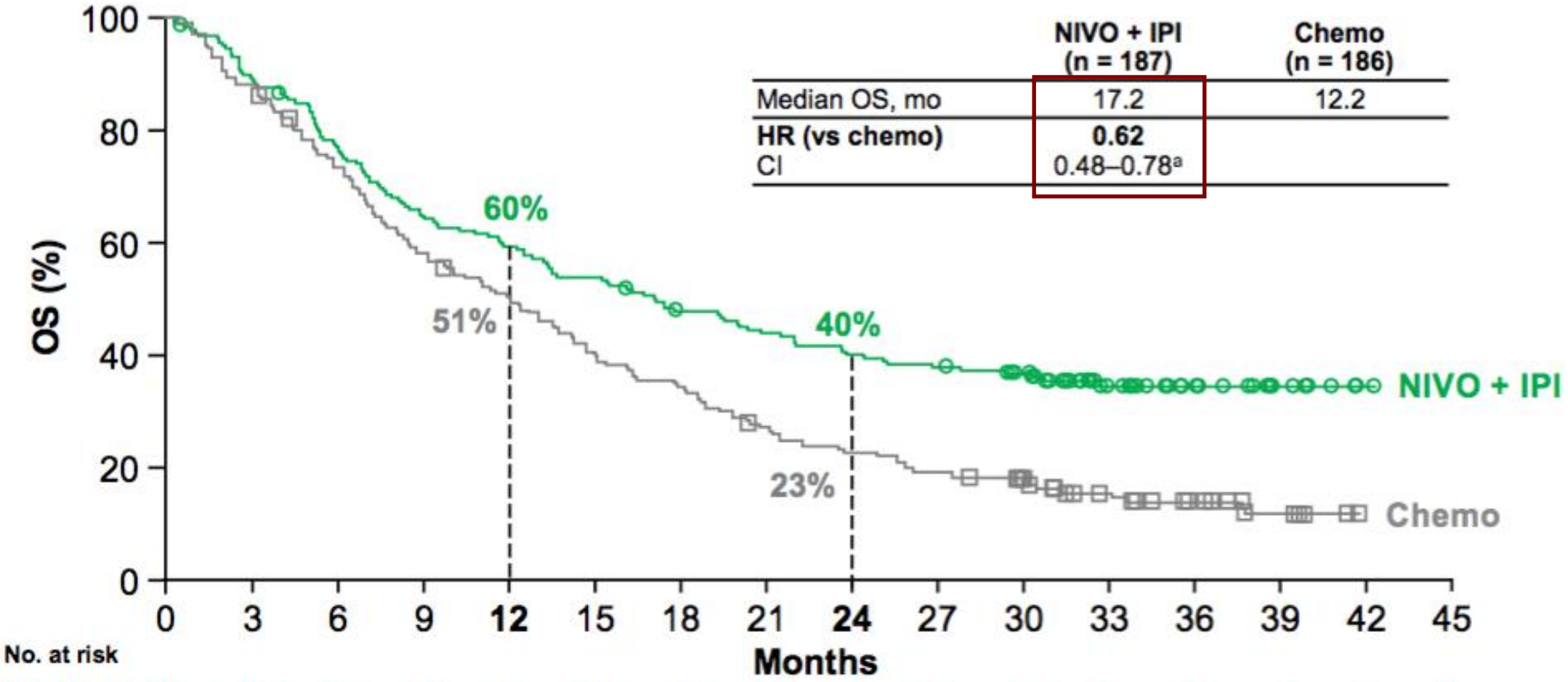
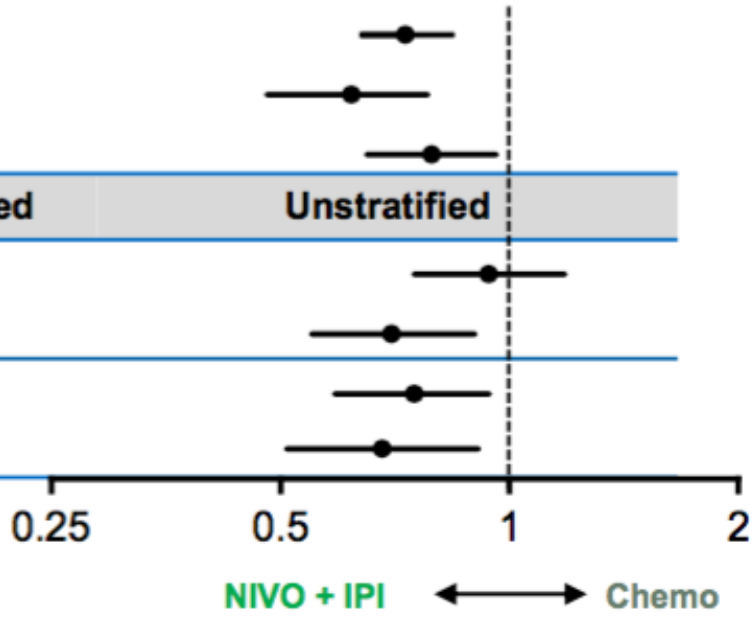


Analyses par sous groupes:

		Median OS, months		HR	HR (95% CI)
		NIVO + IPI n = 583	Chemo n = 583		
Randomized groups				**Stratified**	**Stratified**
PD-L1	All randomized (N = 1166)	17.1	13.9	0.73	
	PD-L1 < 1% (n = 373)	17.2	12.2	0.62	
	PD-L1 ≥ 1% (n = 793)	17.1	14.9	0.79[a]	
Additional exploratory subgroups analyses[b,c]				**Unstratified**	**Unstratified**
PD-L1	1–49% (n = 396)	15.1	15.1	0.94	
	≥ 50% (n = 397)	21.2	14.0	0.70	
TMB[d] (mut/Mb)	low, < 10 (n = 380)	16.2	12.6	0.75	
	high, ≥ 10 (n = 299)	23.0	16.4	0.68	



Le bénéfice en survie globale observé chez les PD-L1≥ 1% est enrichi par les PD-L1 ≥ 50%

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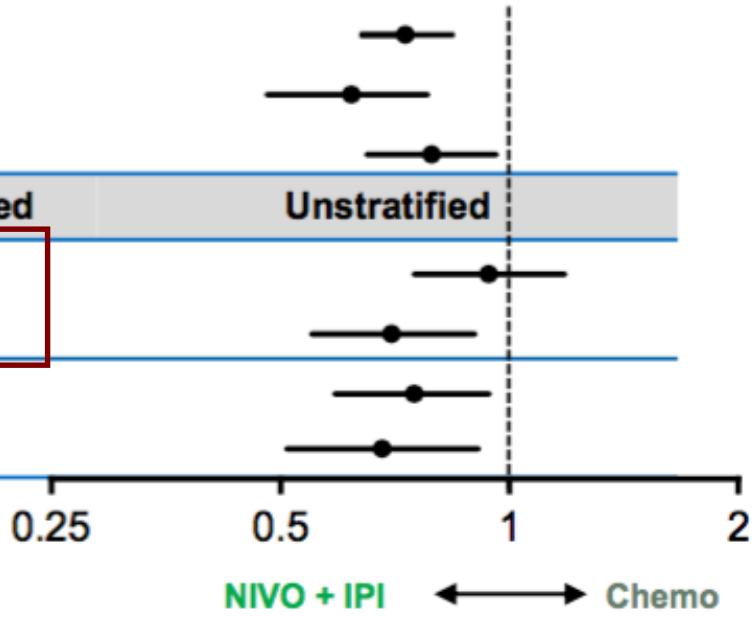

Le bénéfice en survie globale observé chez les PD-L1≥ 1% est enrichi par les PD-L1 ≥ 50%

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A propos de la toxicité:

TRAE,[a] %	NIVO + IPI (n = 576)		Chemo (n = 570)		NIVO[b] (n = 391)	
	Any grade	Grade 3–4	Any grade	Grade 3–4	Any grade	Grade 3–4
Any TRAE	77	33	82	36	66	19
TRAE leading to discontinuation[c]	18	12	9	5	12	7
Most frequent TRAEs (≥ 15%)						
Diarrhea	17	2	10	1	12	< 1
Rash	17	2	5	0	11	1
Fatigue	14	2	19	1	11	< 1
Decreased appetite	13	1	20	1	7	0
Nausea	10	< 1	36	2	6	< 1
Anemia	4	1	33	12	3	< 1
Constipation	4	0	15	< 1	2	0
Neutropenia	< 1	0	17	10	< 1	0
Treatment-related deaths[d]	1		1		< 1	

Toxicité du combo IO non négligeable: 33% de toxicités de haut grade pour NIVO+IPI vs 36% pour le bras chimio (19% dans le bras NIVO)

A propos de la toxicité:

TRAE,[a] %	NIVO + IPI (n = 576)		Chemo (n = 570)		NIVO[b] (n = 391)	
	Any grade	Grade 3–4	Any grade	Grade 3–4	Any grade	Grade 3–4
Any TRAE	77	33	82	36	66	19
TRAE leading to discontinuation[c]	18	12	9	5	12	7
Most frequent TRAEs (≥ 15%)						
Diarrhea	17	2	10	1	12	< 1
Rash	17	2	5	0	11	1
Fatigue	14	2	19	1	11	< 1
Decreased appetite	13	1	20	1	7	0
Nausea	10	< 1	36	2	6	< 1
Anemia	4	1	33	12	3	< 1
Constipation	4	0	15	< 1	2	0
Neutropenia	< 1	0	17	10	< 1	0
Treatment-related deaths[d]	1		1		< 1	

Toxicité du combo IO non négligeable: 33% de toxicités de haut grade pour NIVO+IPI vs 36% pour le bras chimio (19% dans le bras NIVO)

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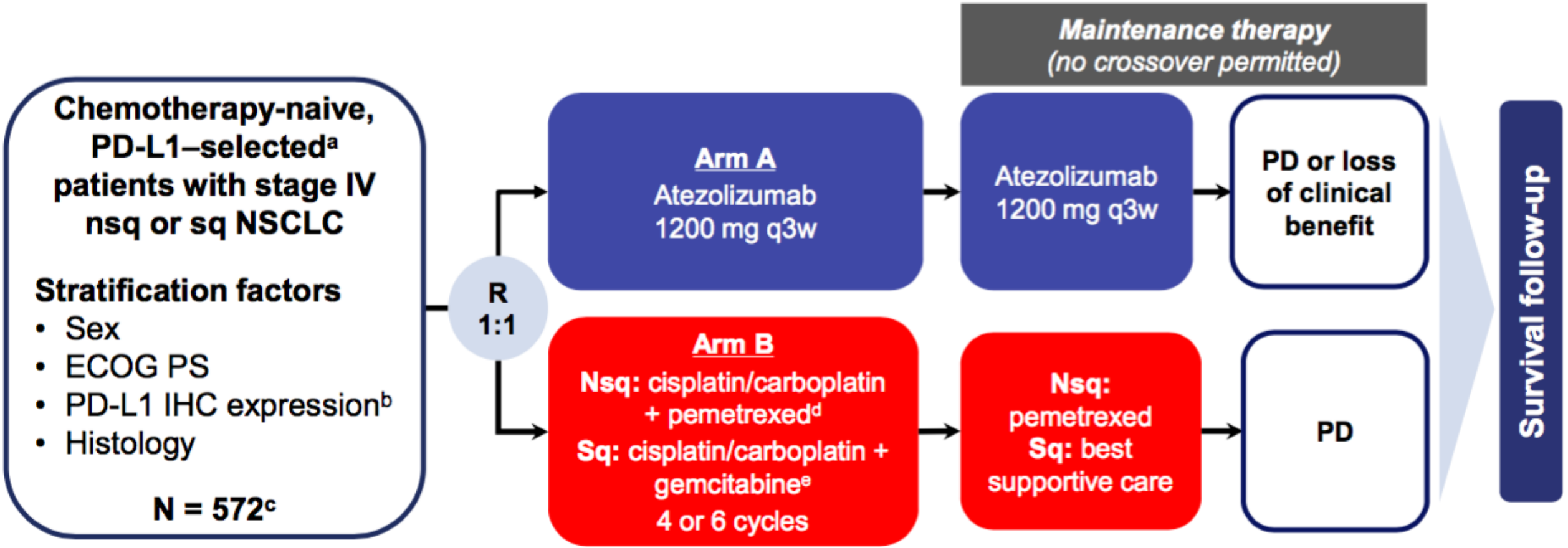
IMpower110

IMpower110: Interim OS Analysis of a Phase III Study of Atezolizumab (atezo) vs Platinum-Based Chemotherapy (chemo) as 1L Treatment (tx) in PD-L1–selected NSCLC

David R Spigel,[1] Filippo De Marinis,[2] Giuseppe Giaccone,[3] Niels Reinmuth,[4] Alain Vergnenegre,[5] Carlos Henrique Barrios,[6] Masahiro Morise,[7] Enriqueta Felip,[8] Zoran Andric,[9] Sarayut Geater,[10] Mustafa Özgüroğlu,[11] Simonetta Mocci,[12] Mark McCleland,[12] Ida Enquist,[12] Kim Komatsubara,[12] Yu Deng,[12] Hiroshi Kuriki,[12] Xiaohui Wen,[12] Jacek Jassem,[13] Roy S Herbst[14]

Design:



Objectif primaire: Survie globale des tumeurs WT (sans addiction oncogénique)

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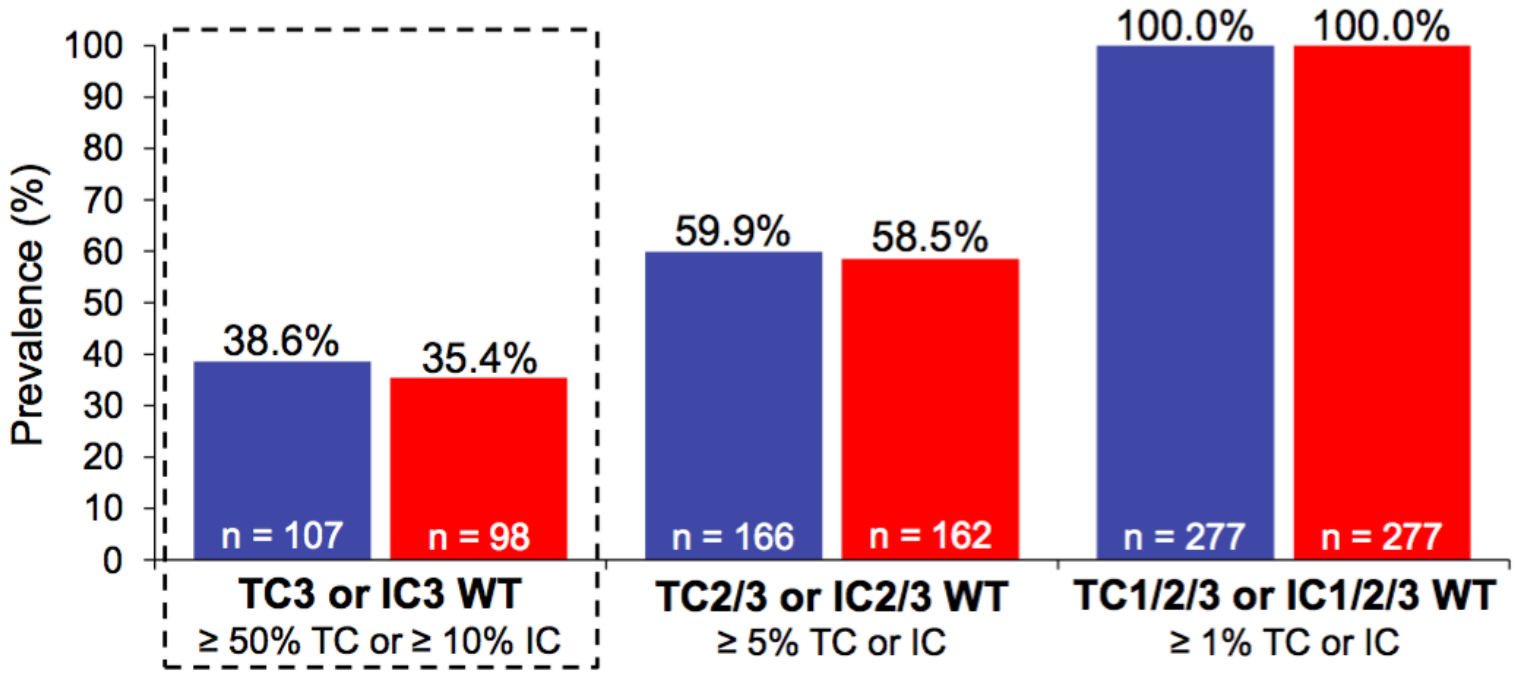
Caractéristiques des patients:

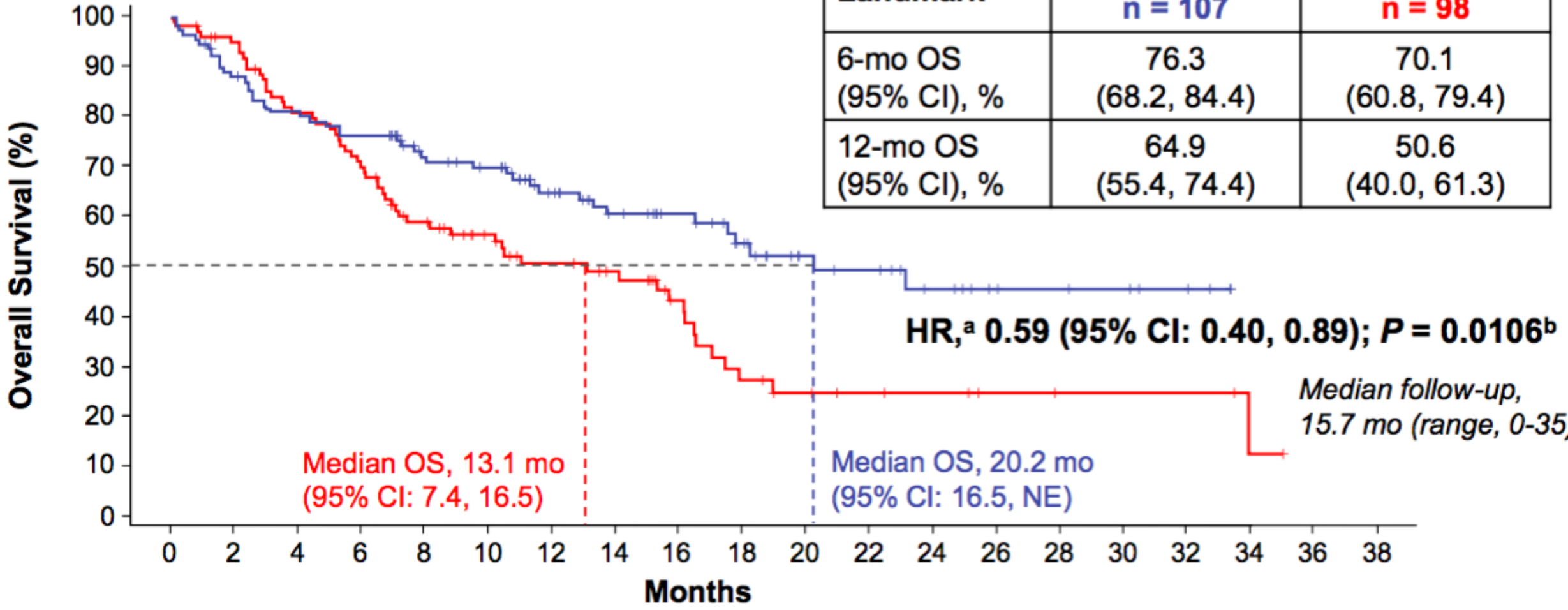
Characteristic	TC1/2/3 or IC1/2/3 WT		TC3 or IC3 WT	
n (%)	Arm A (atezo) n = 277	Arm B (chemo) n = 277	Arm A (atezo) n = 107	Arm B (chemo) n = 98
Age < 65 y	143 (51.6)	134 (48.4)	59 (55.1)	43 (43.9)
Male	196 (70.8)	193 (69.7)	79 (73.8)	64 (65.3)
White	227 (81.9)	240 (86.6)	87 (81.3)	82 (83.7)
Asian	45 (16.2)	30 (10.8)	20 (18.7)	15 (15.3)
Never used tobacco	37 (13.4)	35 (12.6)	9 (8.4)	15 (15.3)
Non-squamous histology	192 (69.3)	193 (69.7)	80 (74.8)	75 (76.5)
ECOG PS 0	97 (35.0)	102 (36.8)	35 (32.7)	38 (38.8)



Prévalence de l'expression de PD-L1

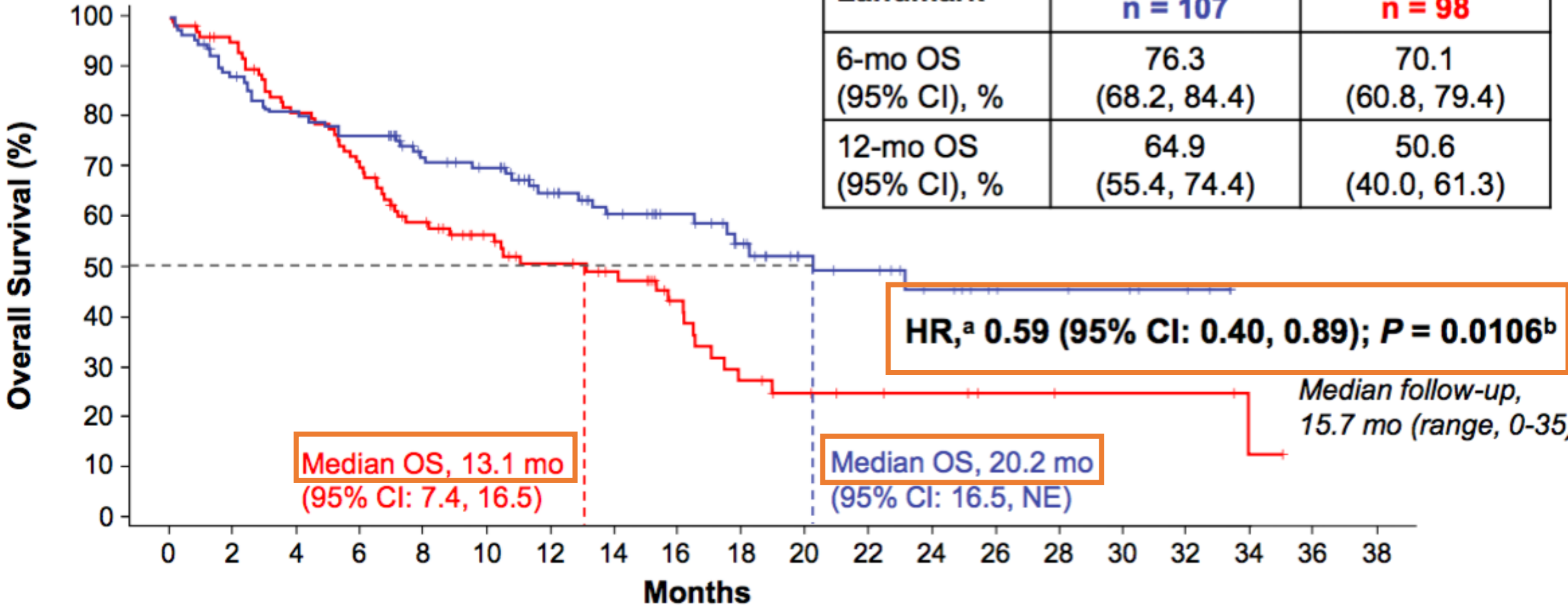
Données de survie globale si TC3 ou IC3

Landmark	Arm A (atezo) n = 107	Arm B (chemo) n = 98
6-mo OS (95% CI), %	76.3 (68.2, 84.4)	70.1 (60.8, 79.4)
12-mo OS (95% CI), %	64.9 (55.4, 74.4)	50.6 (40.0, 61.3)



Données de survie globale si TC3 ou IC3

Landmark	Arm A (atezo) n = 107	Arm B (chemo) n = 98
6-mo OS (95% CI), %	76.3 (68.2, 84.4)	70.1 (60.8, 79.4)
12-mo OS (95% CI), %	64.9 (55.4, 74.4)	50.6 (40.0, 61.3)

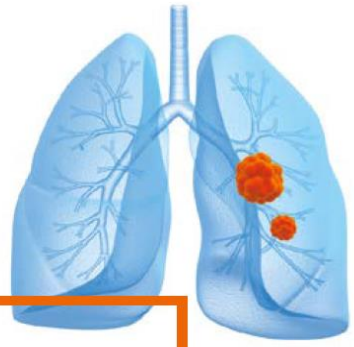


Conclusion

A- Confirmation de la place de l'Osimertinib comme standard en première ligne dans les mCBNPC mutés EGFR (Chez les non asiatiques…)

B- Choix de la première ligne dans le carcinome bronchique non à petites cellules avancé sans addiction??? **Pas si facile**

- Immunothérapie seule (Pembrolizumab/Atezolizumab) dans les > 50% ou TC3/IC3? →Quid des Hyperprogresseurs?
- PD-L1< 1%: Nivo+Ipi fait match égal avec le combo chimio +IO →toxicités différentes, quid du prix?
- PD-L1 entre 1 et 49%: seul le combo IO + chimio a démontré une différence statistiquement significative → Pas vraiment de match



onco NOUVELLE-AQUITAINE
Réseau Régional de Cancérologie

Guide multidisciplinaire de bonnes pratiques pour la prise en charge des petits prélèvements de tumeurs broncho-pulmonaires

Avec la participation de H. BEGUERET, G. BRAS, N. BRAZZALOTTO, F. CHOMY, L. DIGUE, A. HOURSIANGOU, F. LAURENT, J-P. MERLIO et I. SOUBEYRAN

<u>But:</u> optimisation de la réalisation et de l'utilisation des petits prélèvements tumoraux et donc améliorer la prise en charge des patients

Onglet pour chaque professionnel

Messages clairs communs

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Réseau Régional de Cancérologie

Merci de votre attention

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Données comparées aux données d'anti PD1/PD-L1 en monothérapie si PD-L1≥50% et 1-49%

Trial	N[a]	Population	IMP	PDL1 Stratum	OS HR (95%CI)	TRAEs G3/4[a]	% discontinuation[a]
CM227[1]	1,166	All histologies	Nivo-Ipi	≥50% 1-49%	0.70 (0.55-0.90) 0.94 (0.75-1.18)	33%	12%
			Nivo	≥1%	0.88 (0.75-1.04)	19.4%	7.4%
KN024[2]	305	All histologies	Pembro	≥50%	0.63 (0.47-0.86)	26.6%	7.1%
KN042[3]	1,274	All histologies	Pembro	≥50% 1-49%	0.69 (0.56-0.85) 0.92 (0.77-1.11)	18%	9%
IMP110[4]	572	All histologies	Atezo	TC3 or IC3	0.59 (0.40-0.89)	12.9%	6.3%

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Données comparées aux données pembro+ chimio si PD-L1≥50% et 1-49%:

Trial	N[a]	Population	IMP	PDL1 Stratum	OS HR (95%CI)	TRAEs G3/4[a]	% discontinuation[a]
CM227[1]	1,166	All histologies	Nivo-Ipi	≥50% 1-49%	0.70 (0.55-0.90) 0.94 (0.75-1.18)	33%	12%
			Nivo	≥1%	0.88 (0.75-1.04)	19.4%	7.2%
KN189[4]	616	Non-squamous	Pembro + Plat-Pem	≥50% 1-49%	0.42 (0.26-0.68) 0.55 (0.34-0.90)	NR	11.9%
KN407[5]	559	Squamous	Pembro + Carbo-Tax / (nab)Tax	≥50% 1-49%	0.64 (0.37-1.10) 0.57 (0.36-0.90)	NR	12.2%

Données comparées aux données de Pembro+ chimio si PD-L1 < 1%:

Trial	N[a]	Population	IMP	PDL1 Stratum	OS HR (95%CI)	TRAEs G3/4[a]	% discontinuation[a]
CM227[1]	1,166	All histologies	Nivo-Ipi	<1%	0.62 (0.48-0.78)	33%	12%
			Nivo-Chemo[b]	<1%	0.78 (0.60-1.02)	56%	7.6%
KN189[2]	616	Non-squamous	Pembro + Plat/Pem	<1%	0.59 (0.38-0.92)	NR	11.9%
KN407[3]	559	Squamous	Pembro + Carbo-Tax / (nab)Tax	<1%	0.61 (0.38-0.98)	NR	12.2%