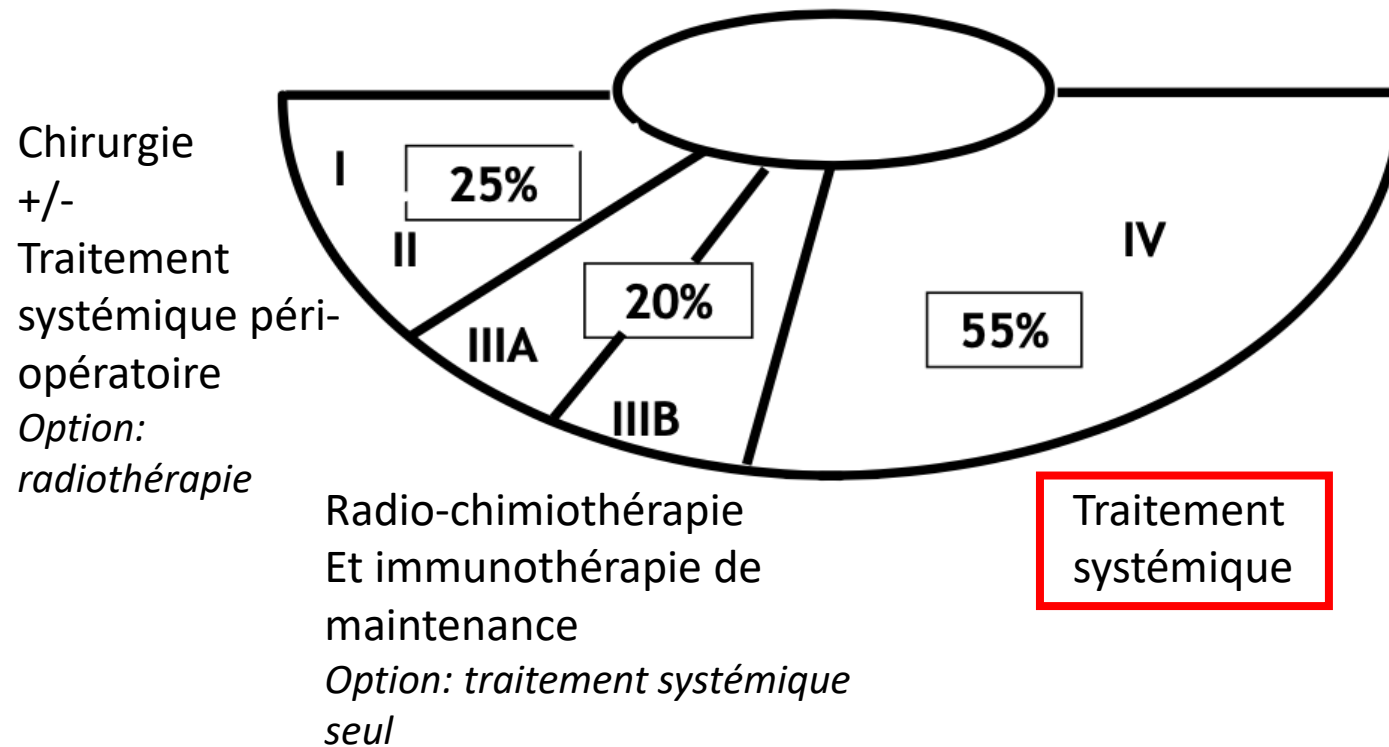


Cancers bronchiques non à petites cellules métastatique sans addiction oncogénique – Prise en charge chez le sujet âgé

Emeline ORILLARD
5 Avril 2024

Métastatique

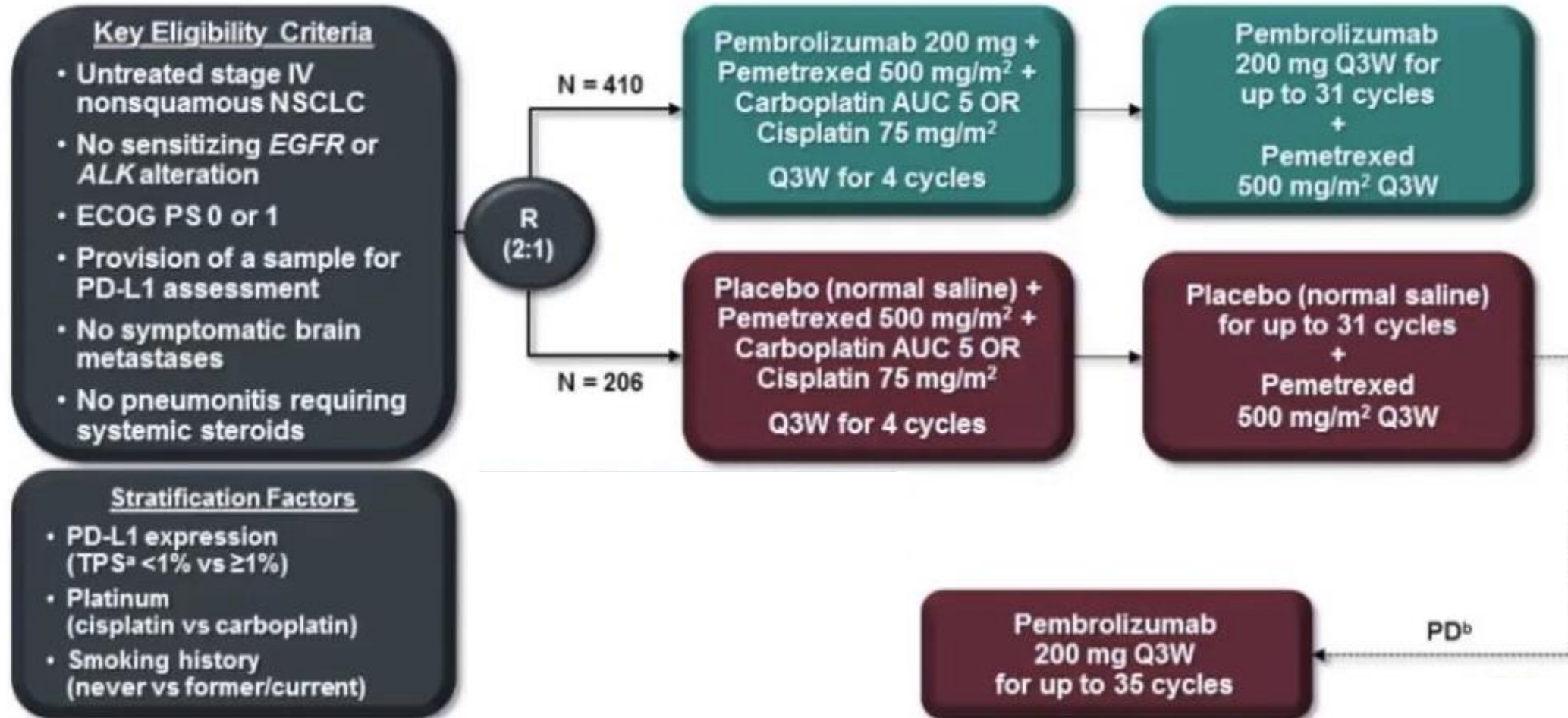


Métastatique ou localement avancé non irradiable

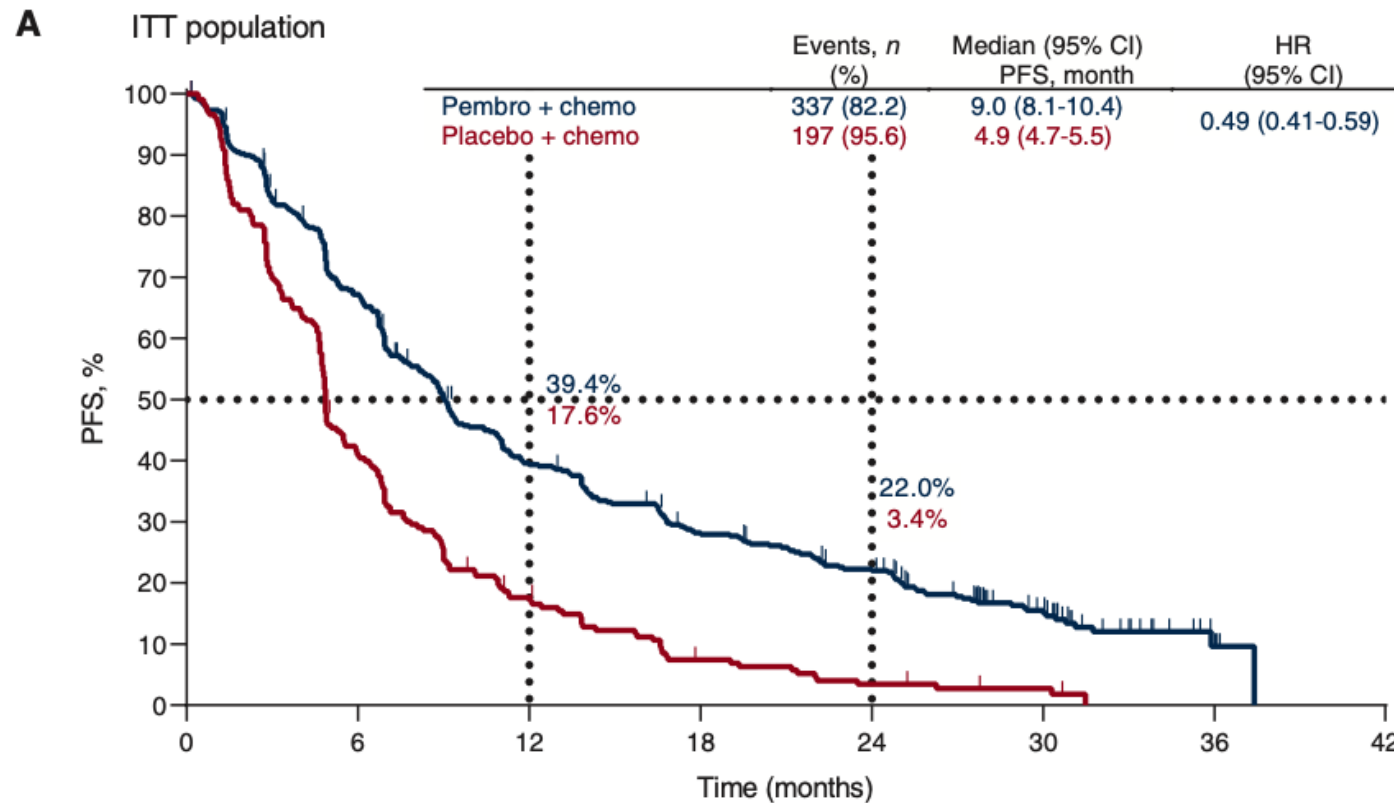
En 2024: dépend de

- l'histologie
- la présence d'addiction oncogénique
- PD-L1
- Performans status

CBNPC non épidermoïde, sans addiction, quel que soit le statut PD-L1

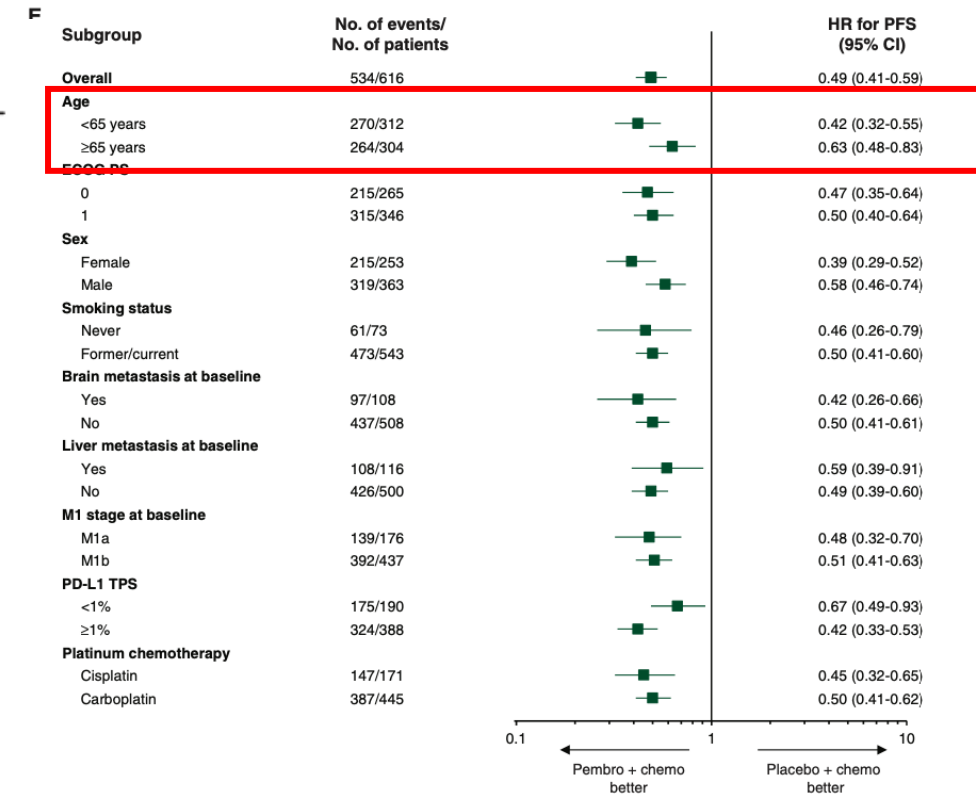


CBNPC non épidermoïde, sans addiction, quel que soit le statut PD-L1



No. at risk:

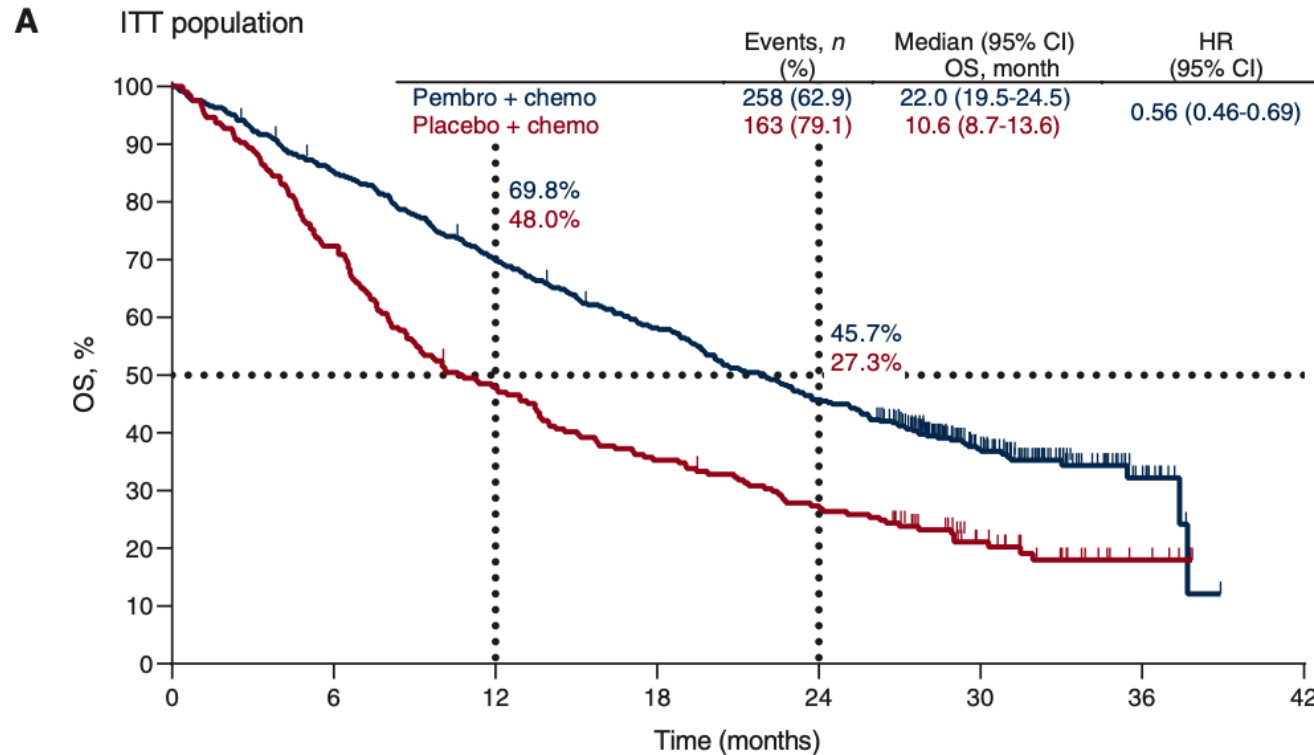
	0	6	12	18	24	30	36	42
Pembro + chemo	410	270	154	107	80	32	2	0
Placebo + chemo	206	83	33	13	6	3	0	0



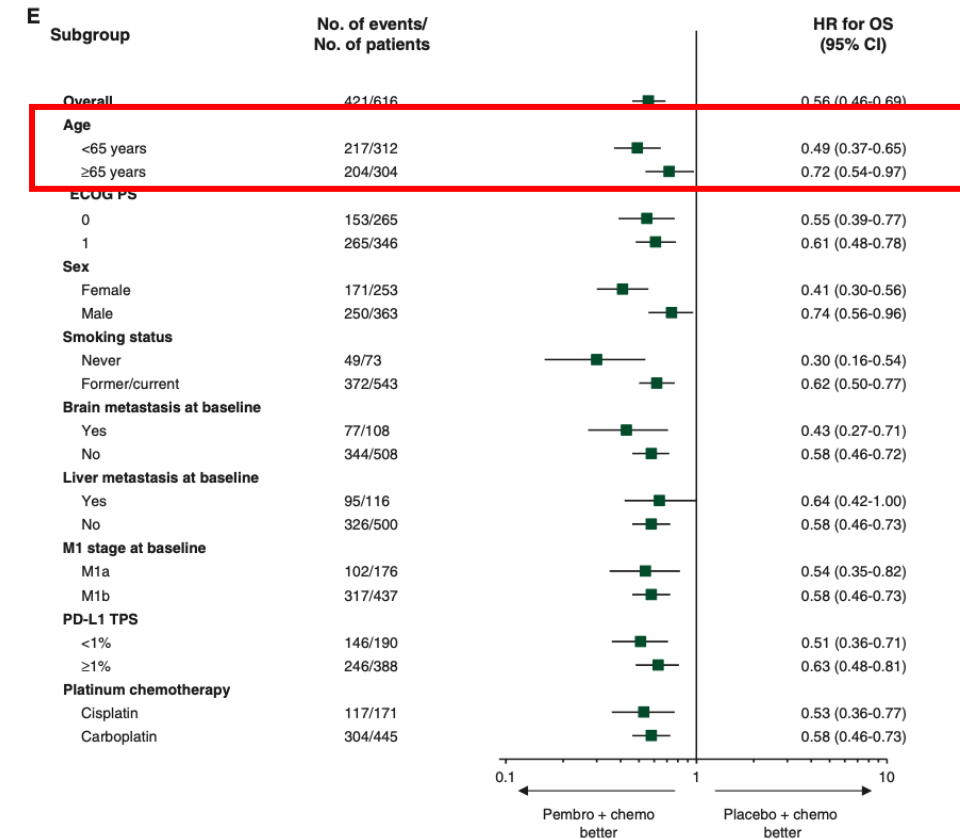
Keynote 189, Gandhi et al NEJM 2018

Rodríguez-Abreu et al. Annals of Oncology 2021 (final analysis)

CBNPC non épidermoïde, sans addiction, quel que soit le statut PD-L1



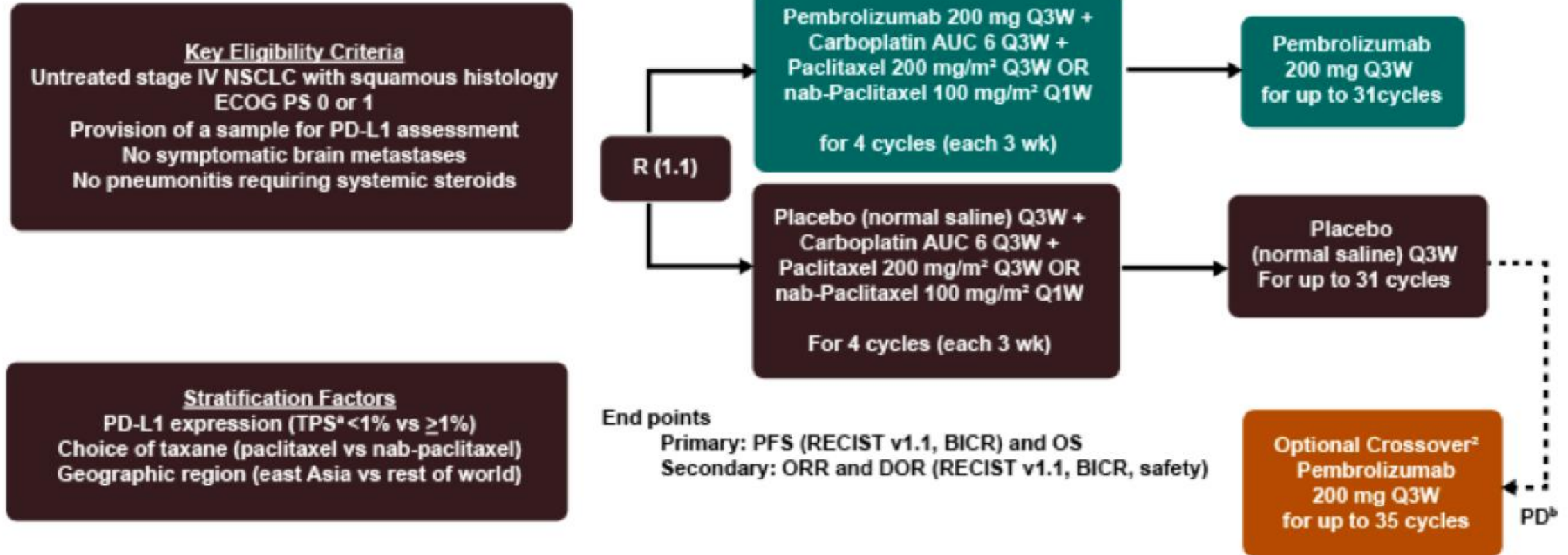
No. at risk:	0	6	12	18	24	30	36	42
Pembro + chemo	410	347	283	234	184	86	12	0
Placebo + chemo	206	149	98	72	55	25	5	0



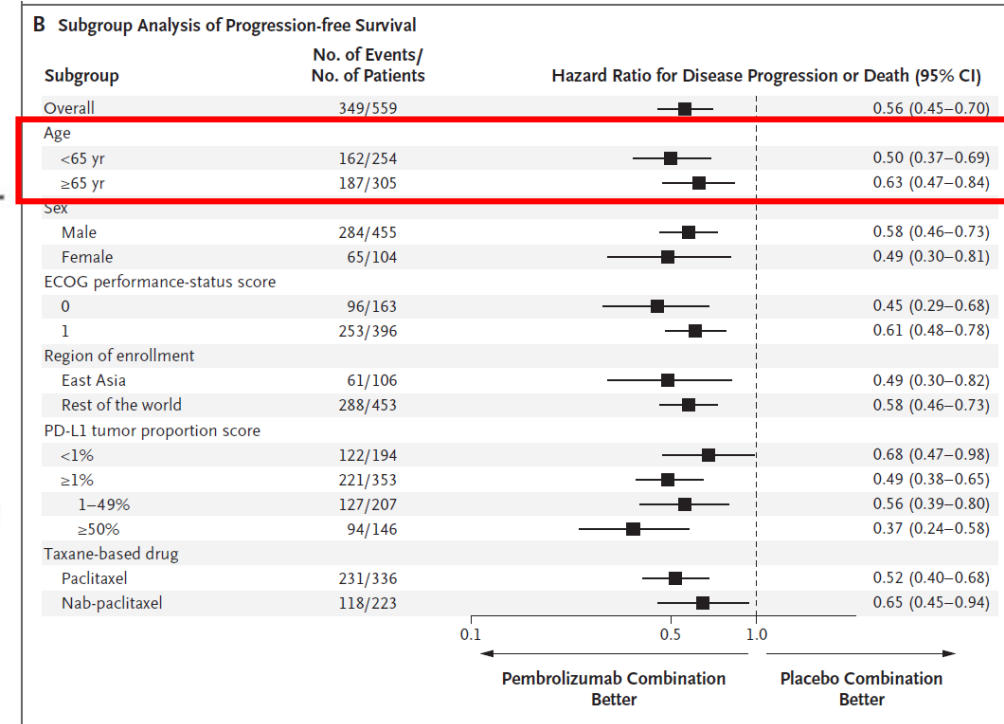
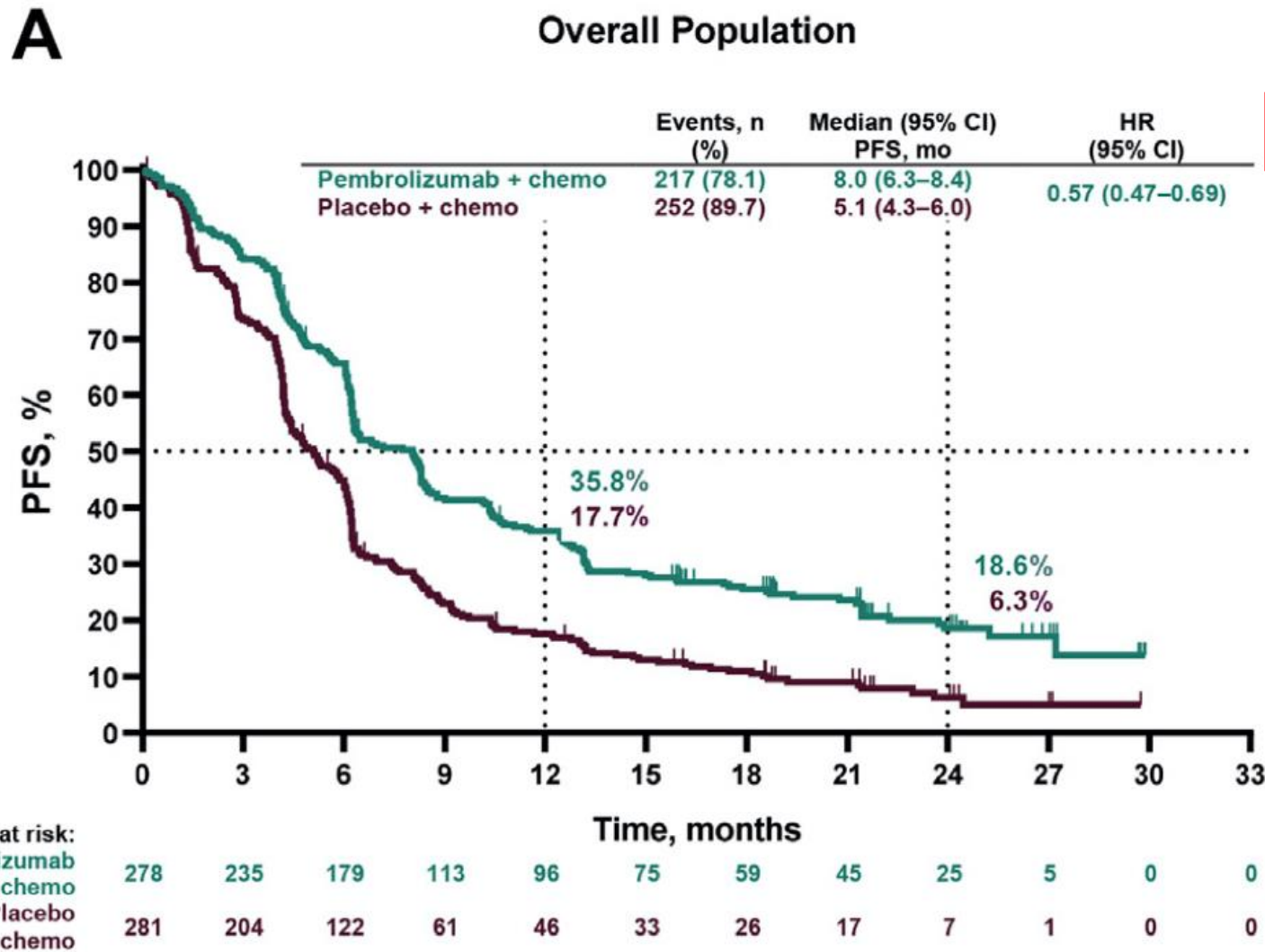
Keynote 189, Gandhi et al NEJM 2018

Rodríguez-Abreu et al. Annals of Oncology 2021 (final analysis)

CBNPC épidermoïde, sans addiction, quel que soit le statut PD-L1

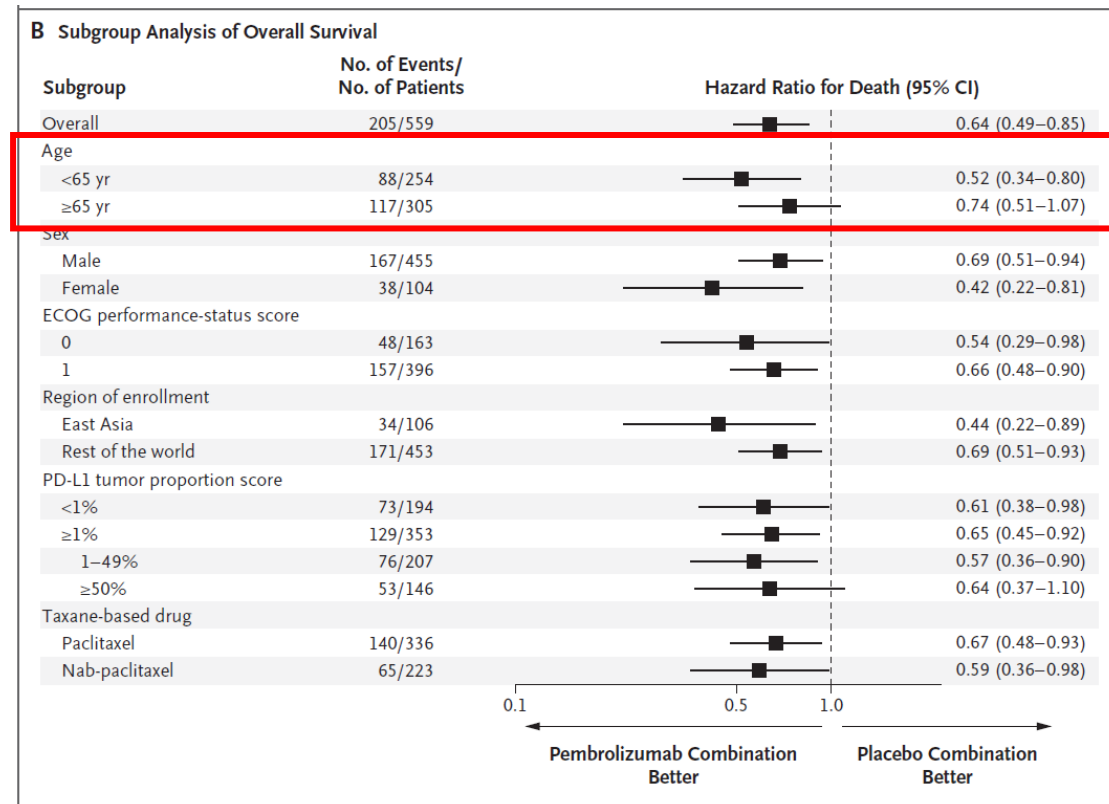
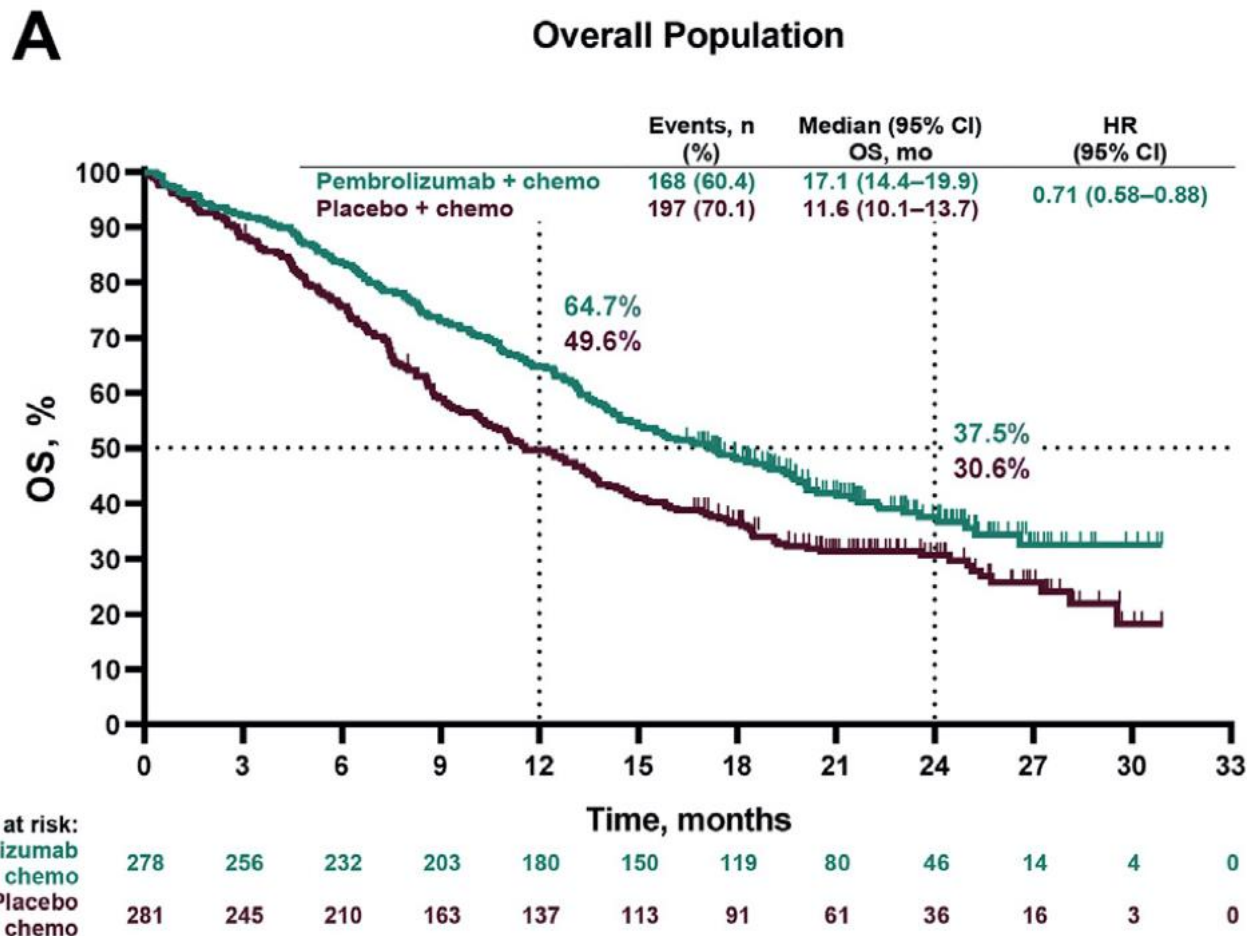


CBNPC épidermoïde, sans addiction, quel que soit le statut PD-L1



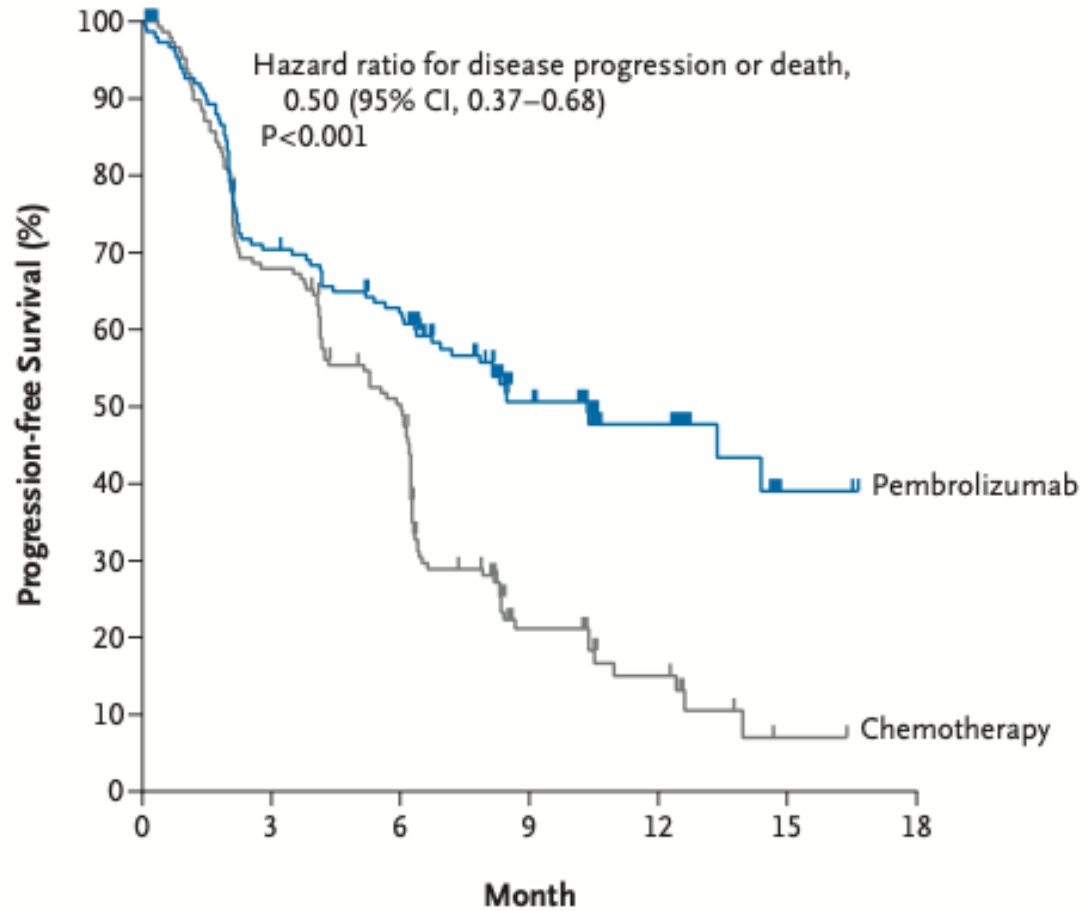
Keynote 407, Paz Ares et al NEJM 2018
 Paz Ares et al, JTO 2020 (final analysis)

CBNPC épidermoïde, sans addiction, quel que soit le statut PD-L1



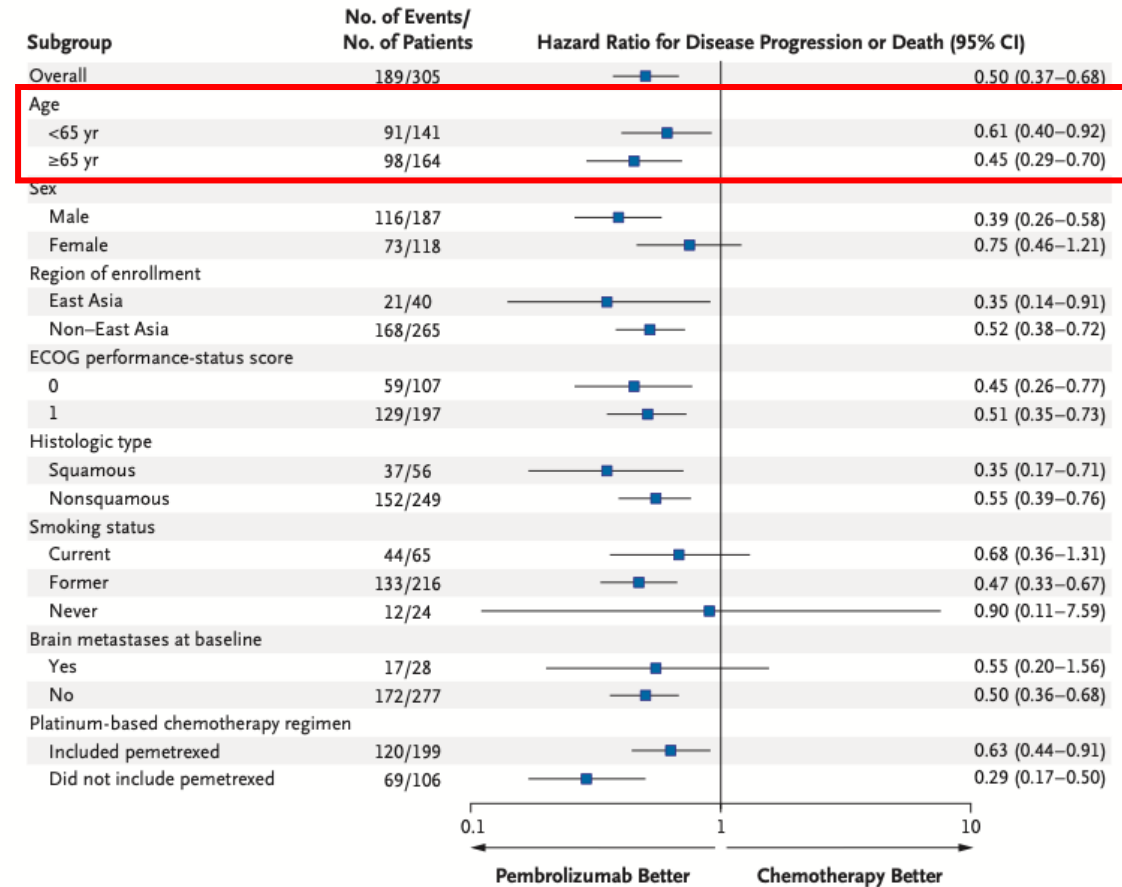
Keynote 407, Paz Ares et al NEJM 2018
 Paz Ares et al, JTO 2020 (final analysis)

Tout CBNPC, sans addiction, PD-L1 > 50%



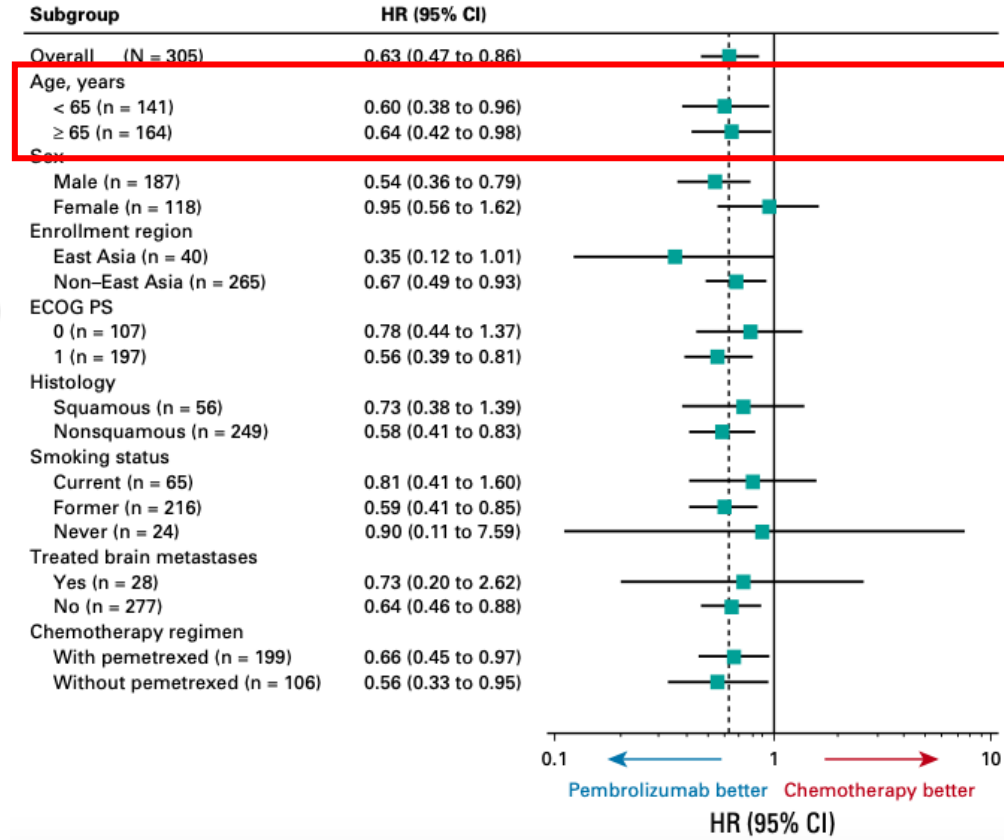
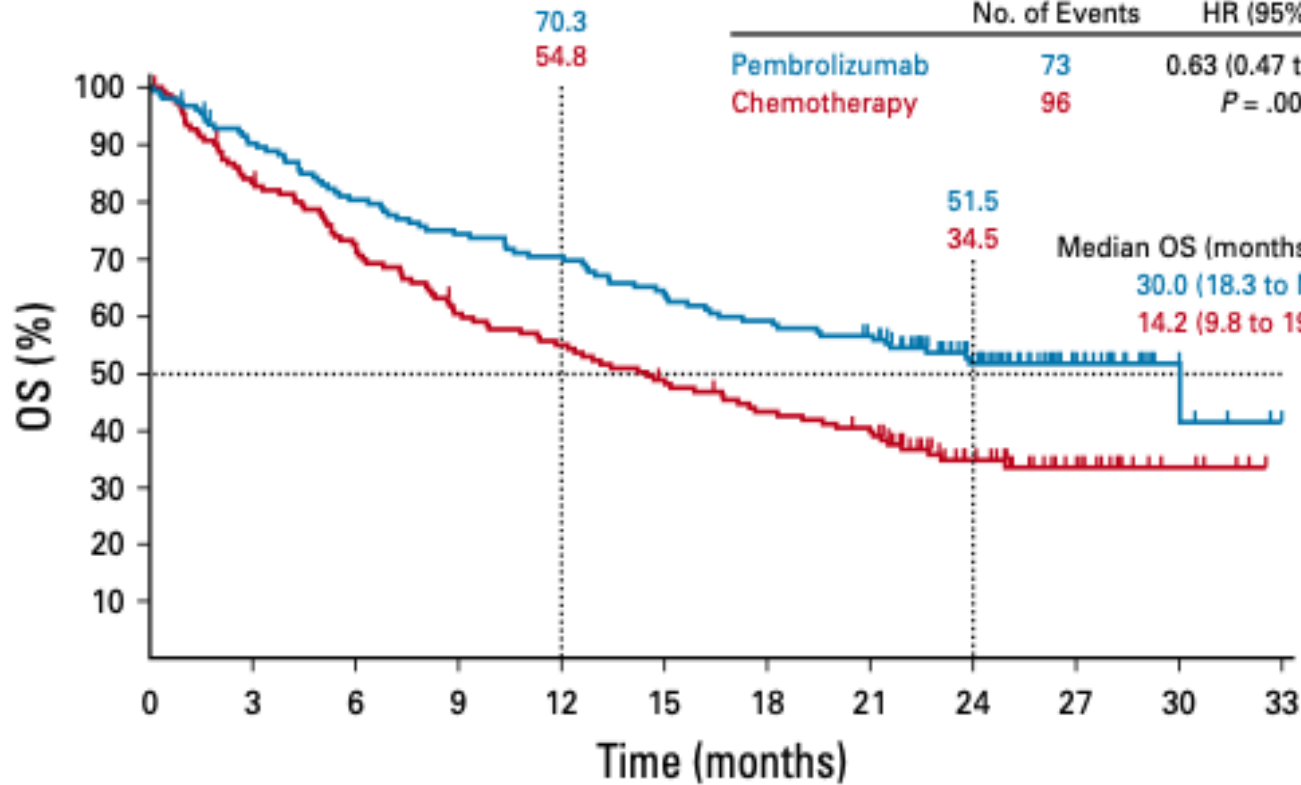
No. at Risk

	0	3	6	9	12	15	18
Pembrolizumab	154	104	89	44	22	3	1
Chemotherapy	151	99	70	18	9	1	0



Tout CBNPC, sans addiction, PD-L1 > 50%

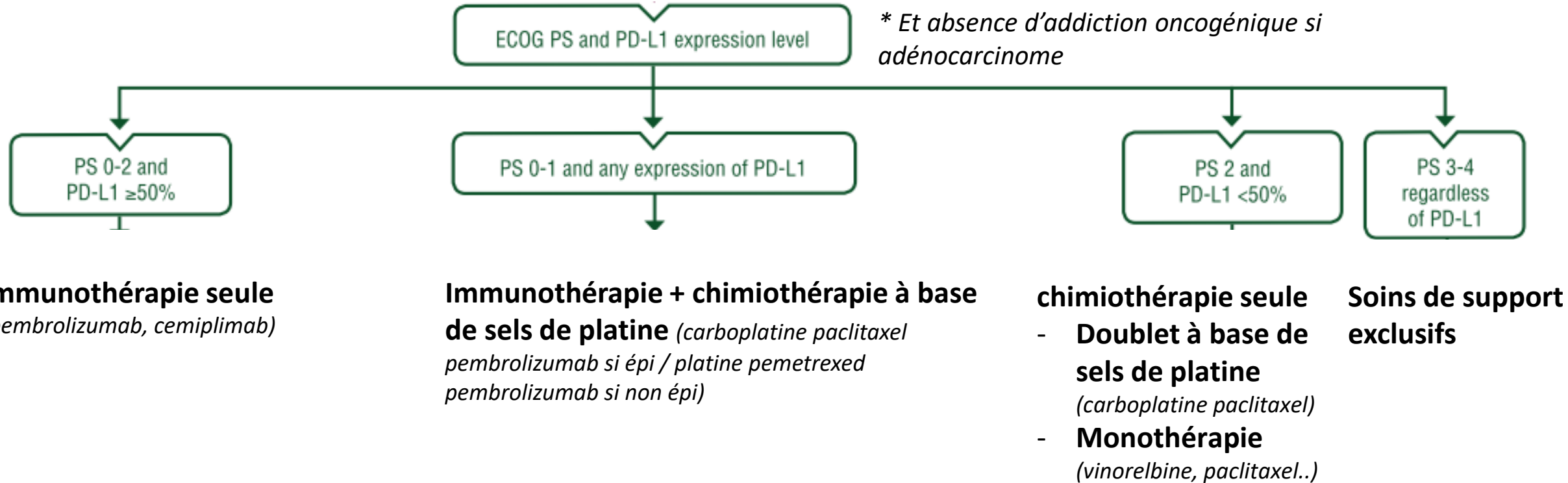
A



No. at risk:

	0	3	6	9	12	15	18	21	24	27	30	33
Pembrolizumab	154	136	121	112	106	96	89	83	52	22	5	0
Chemotherapy	151	123	107	88	80	70	61	55	31	16	5	0

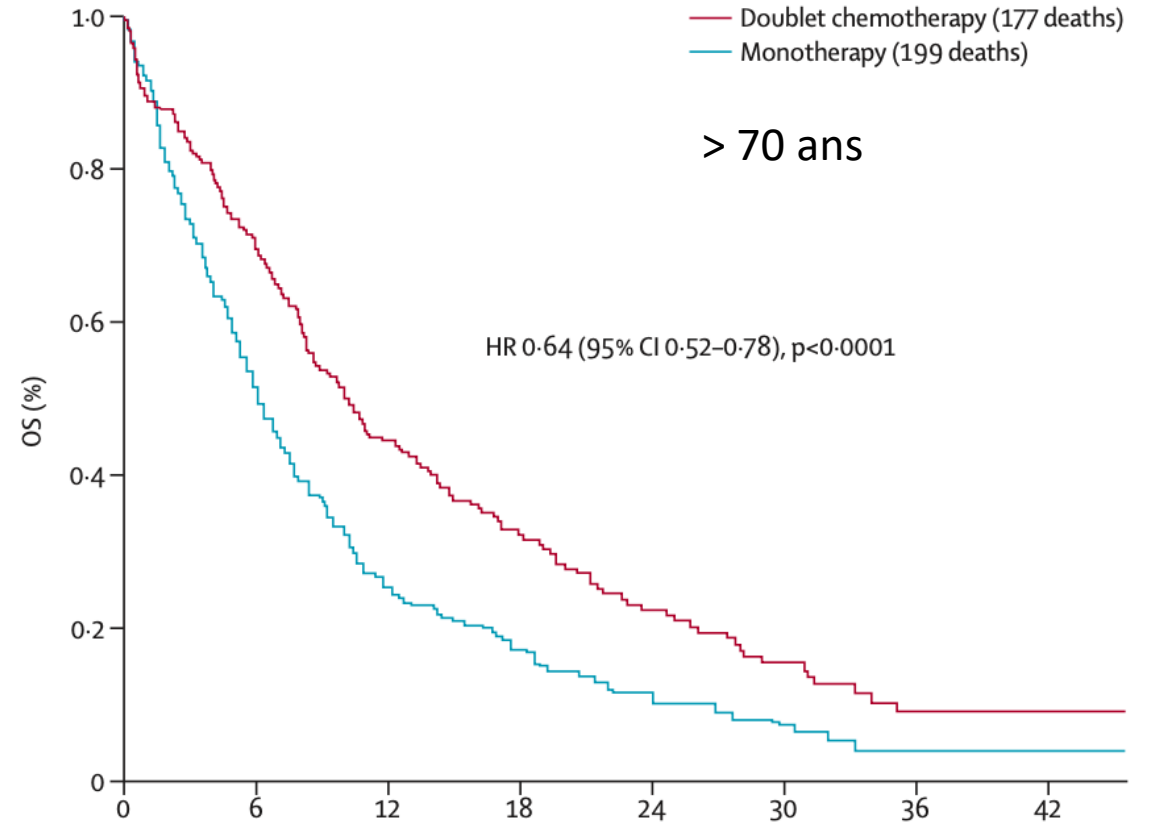
Que fait-on?



Et l'âge dans tout ça?

Age médian au diagnostic
71 ans

Avant 2019 : Carboplatine paclitaxel hebdomadaire

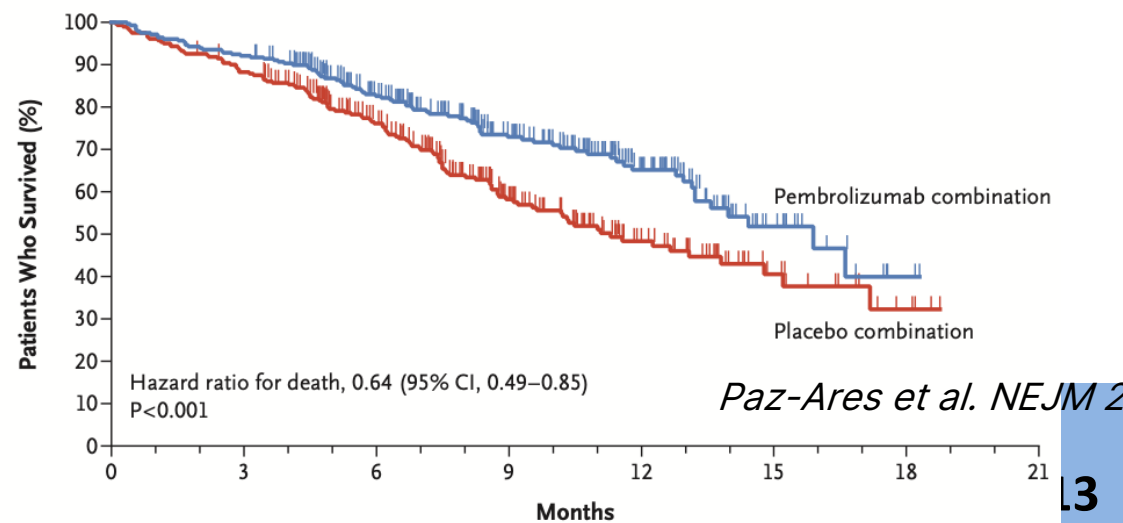
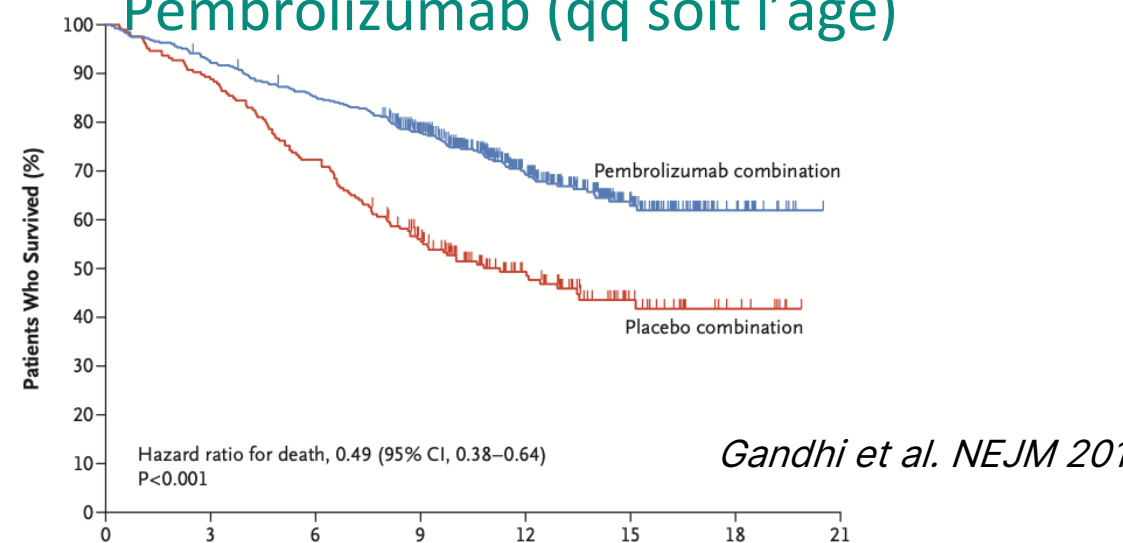


Number at risk		Duration (months)							
	0	6	12	18	24	30	36	42	
Doublet	225	160	92	52	32	19	7	2	
Monotherapy	226	117	54	25	15	8	2	2	

Et l'âge dans tout ça?

Age médian au diagnostic
71 ans

A partir de 2019 : Extension AMM du Pembrolizumab (qq soit l'âge)



Et l'âge dans tout ça?

**Faut-il intensifier une bi-chimiothérapie
à base de sels de platine avec une
immunothérapie chez les sujets âgés ?**



Et l'âge dans tout ça?

Méthode de la revue

Essais contrôlés
randomisés
CBNPC avancé
(métastatique, ou
localement avancé non
irradiable)
Incluant des sujets de
+ de 65 ans

Chimiothérapie +/-
bevacizumab +
immunothérapie

Chimiothérapie +/-
bevacizumab

Objectifs primaires :

- Survie globale *
- Effets indésirables liés au traitement *

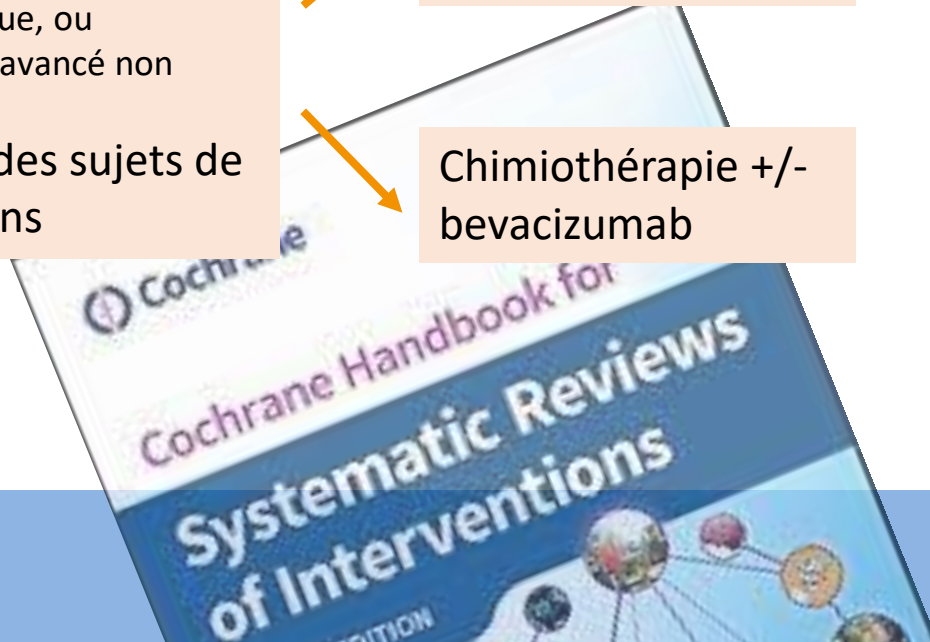
Objectifs secondaires:

- Survie sans progression *
- Taux de réponse objective *
- Temps à réponse *
- Durée de réponse *
- Qualité de vie *

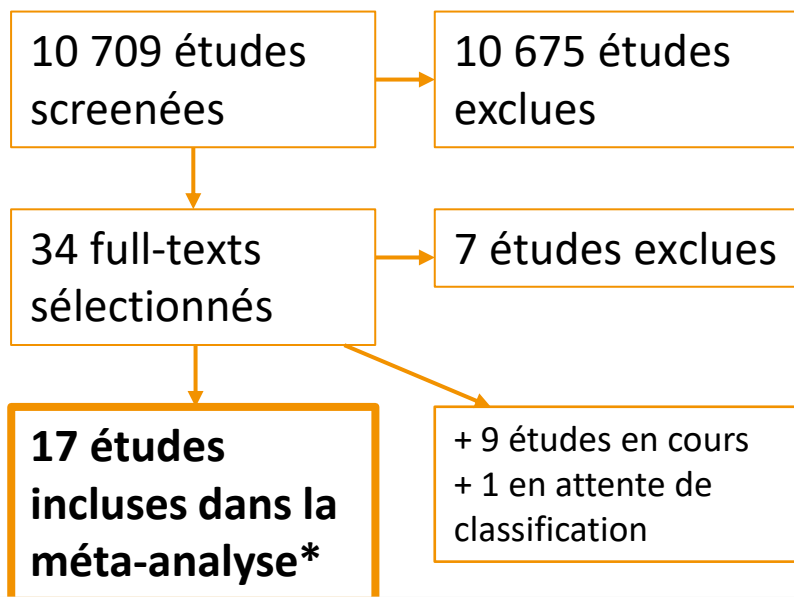
*Par classe d'âge : > 65 ans / 65 à 75 ans / > 75 ans

Analyses en sous-groupe :

- Performans status (0 et 1 vs 2)
- Paramètres gériatriques (échelle G-8, Charlson index, ADLs, IADLs).



Et l'âge dans tout ça?



* 12 incluait des patients de + de 75 ans

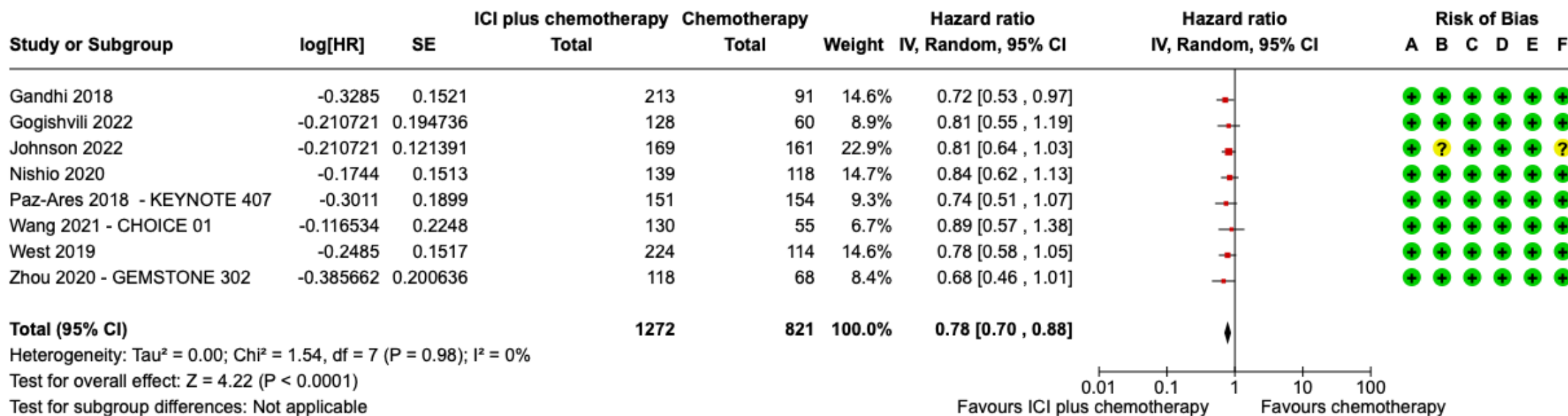


Etudes incluses (n = 4276 (46%) pts inclus de + de 65 ans)	
KEYNOTE 189 (Gandhi 2018): Platine Pemetrexed +/- Pembrolizumab	RATIONALE 304 (Lu 2021): Platine Pemetrexed +/- Tislelizumab
KEYNOTE 407 (Paz-Ares 2018): Carboplatine Paclitaxel +/- Pembrolizumab	RATIONALE 307 (Wang 2021): Carboplatine Paclitaxel +/- Tislelizumab
Checkmate 9LA (Paz-Ares 2021): Platine Paclitaxel ou pemetrexed +/- Nivolumab et Ipilimumab	GOVINDAN 2017: Carboplatine Paclitaxel +/- Ipilimumab
GEMSTONE 302 (Zhou 2020): Carboplatine Paclitaxel ou pemetrexed +/- Sugemalimab	Camel (Zhou 2021): Carboplatine Pemetrexed +/- Camrelizumab
IMPOWER 130 (West 2019): Carboplatine nab-paclitaxel +/- Atezolizumab	Camel-sq (Ren 2021): Carboplatine paclitaxel +/- camrelizumab
IMPOWER 131 (Jotte 2020): Carboplatine nab-paclitaxel +/- Atezolizumab	POSEIDON (Johnson 2022): Platine nab-paclitaxel ou gemcitabine +/- Durvalumab +/- Tremelimumab
IMPOWER 132 (Nishio 2020): Platine pemetrexed +/- Atezolizumab	CHOICE-01 (Wang 2021): Carboplatine Nab-paclitaxel ou Cisplatine pemetrexed +/- Toripalimab
IMPOWER 150 (Socinski 2018): Carboplatine paclitaxel bevacizumab +/- Atezolizumab	EMPOWER-Lung-3 (Goghishvili 2022): platine pemetrexed ou paclitaxel +/- Cemiplimab
TASUKI-52 (Sugawara 2021): Carboplatine paclitaxel bevacizumab +/- Nivolumab	

Et l'âge dans tout ça?

Résultats – Survie globale

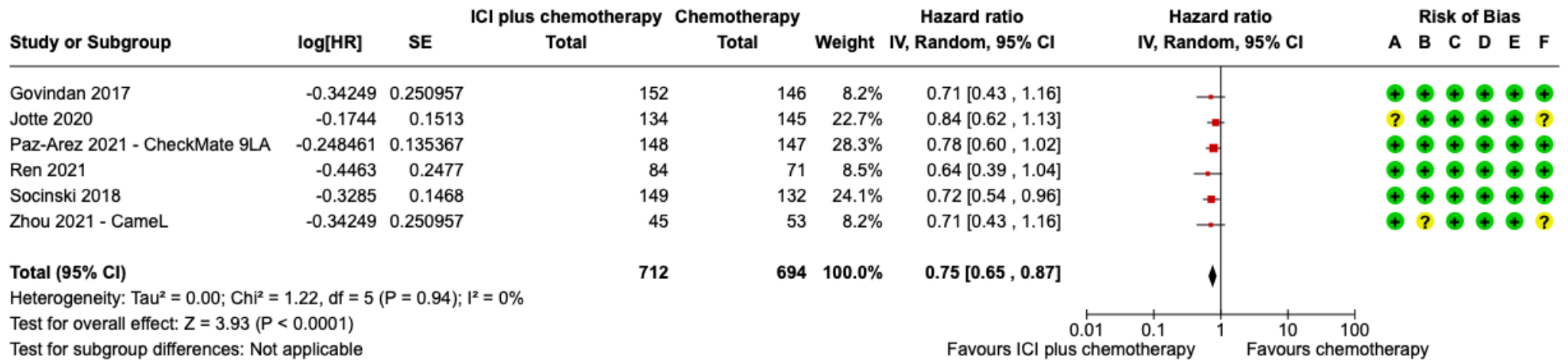
65 et +



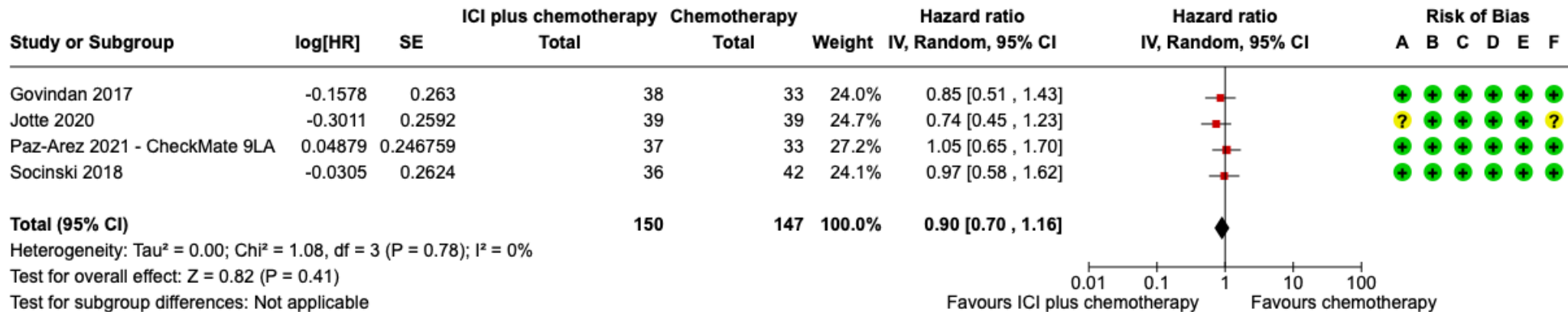
Et l'âge dans tout ça?

Résultats – Survie globale

65 – 75
(36% des sujets inclus)



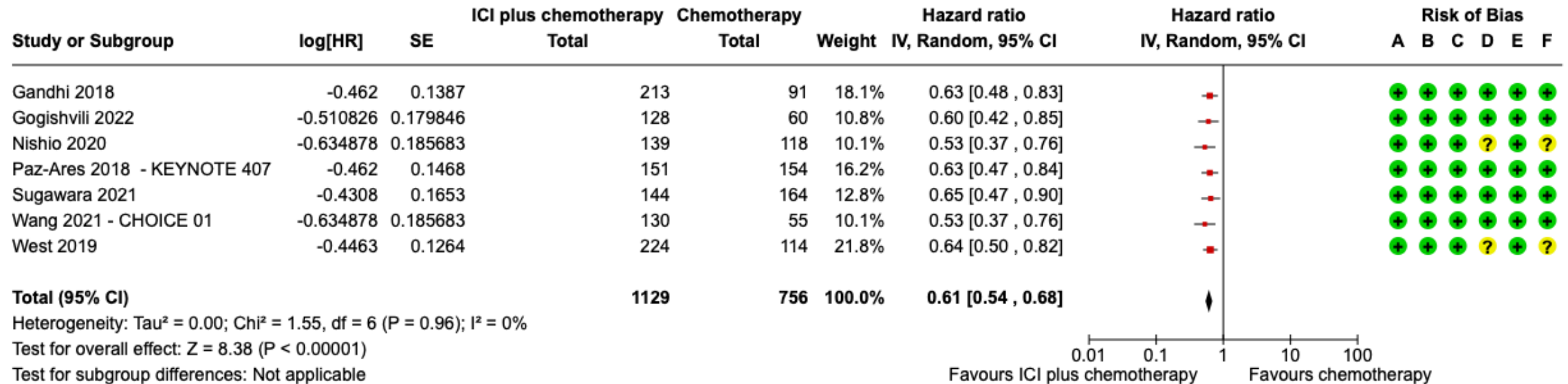
75 et +
(<10% des sujets inclus)



Et l'âge dans tout ça?

Résultats - SSP

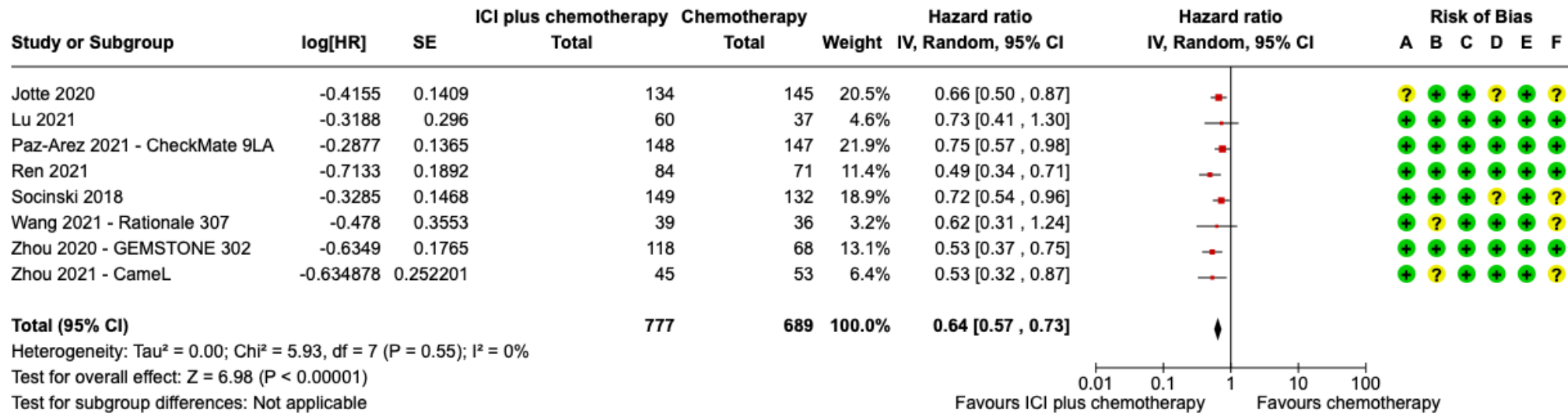
65 et +



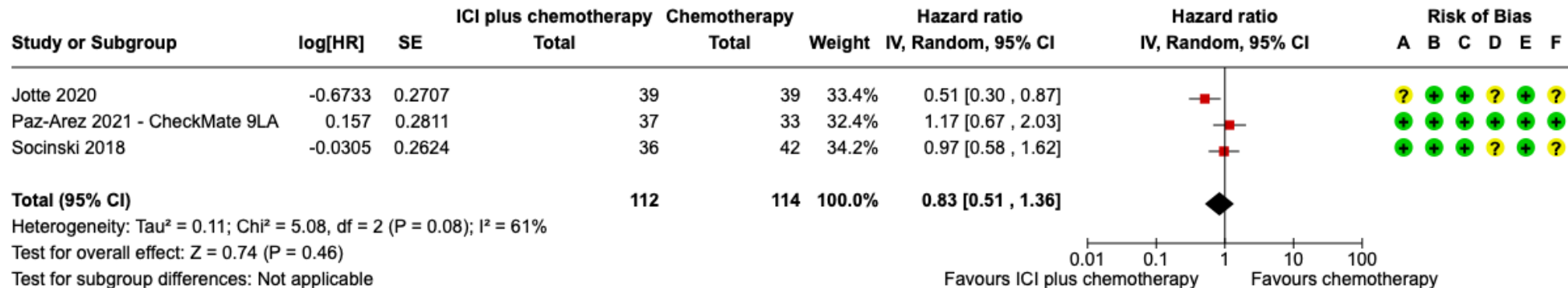
Et l'âge dans tout ça?

Résultats - SSP

65 – 75
(36% des sujets inclus)



75 et +
(<10% des sujets inclus)



Et l'âge dans tout ça?



Outcomes	N° of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)
OS - Age ≥ 65 years (at any time points)	2093 (8 studies)	Moderate ⊕⊕⊕○ ¹	HR 0.78 (0.70 to 0.88)
PFS - Age 65 ≥ years (at any time points)	1885 (7 studies)	Moderate ⊕⊕⊕○ ¹	HR 0.61 (0.54 to 0.68)

46% des patients inclus

Outcomes	N° of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)
OS - Age ≥ 65 to ≤ 75 years (at any time points)	1406 (6 studies)	Moderate ⊕⊕⊕○ ¹	HR 0.75 (0.65 to 0.87)
PFS - Age ≥ 65 to ≤ 75 years (at any time points)	1466 (8 studies)	Moderate ⊕⊕⊕○ ¹	HR 0.64 (0.57 to 0.73)

36% des patients inclus

Outcomes	N° of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)
OS - Age ≥ 75 years (at any time points)	297 (4 studies)	Low ⊕⊕○○ ^{1,2}	HR 0.90 (0.70 to 1.16)
PFS - Age ≥ 75 years (at any time points)	226 (3 studies)	Very low ⊕○○○ ^{1,2,3}	HR 0.83 (0.51 to 1.36)

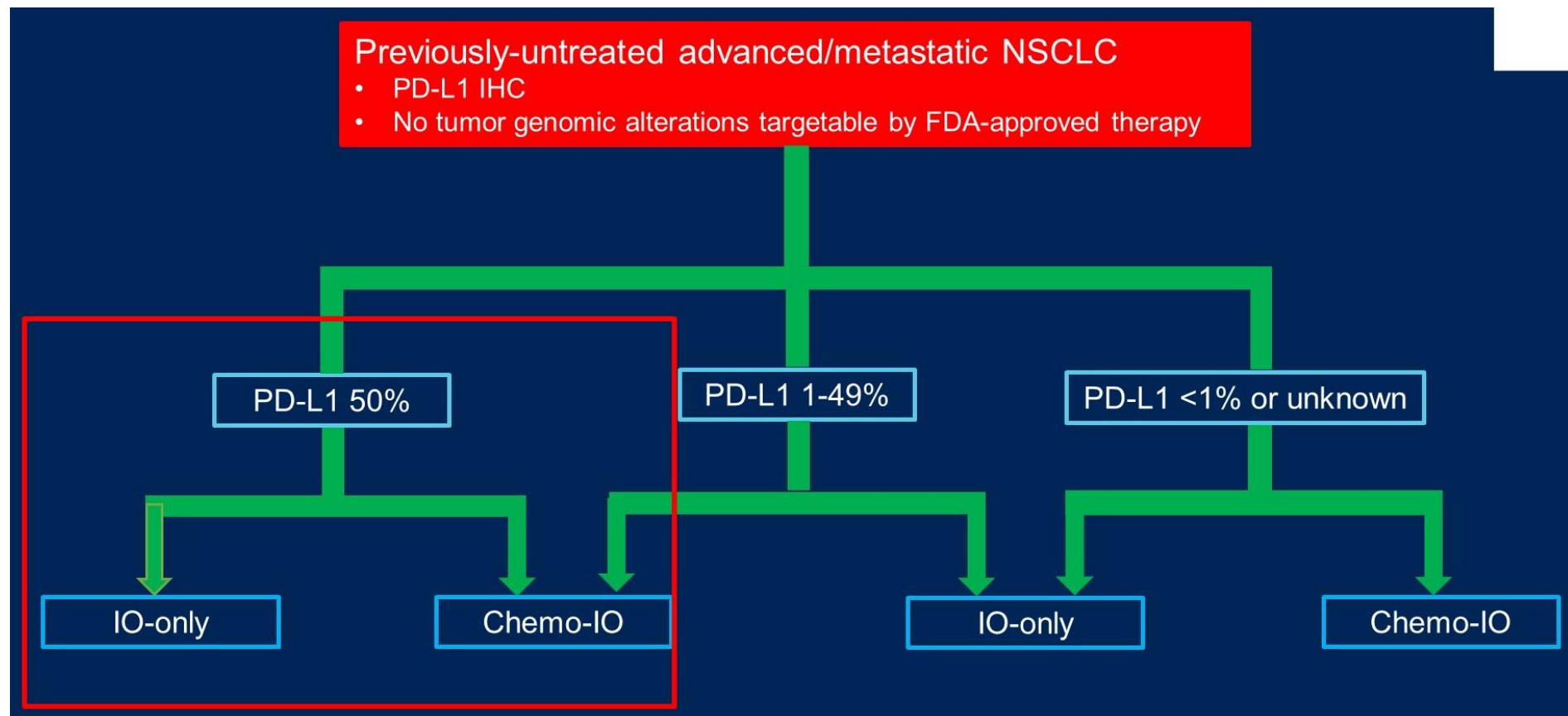
10% des patients inclus

Outcomes of anti-PD-(L)1 therapy with or without chemotherapy (chemo) for first-line (1L) treatment of advanced non-small cell lung cancer (NSCLC) with PD-L1 score $\geq 50\%$: FDA Pooled Analysis

Oladimeji Akinboro¹, Jonathon Vallejo¹, Erica Nakajima¹, Yi Ren¹, Pallavi Mishra-Kalyani¹, Erin Larkins¹, Paz Vellanki¹, Nicole Drezner¹, Mathieu Luckson¹, Shenghui Tang¹, Martha Donoghue^{1,2}, Richard Pazdur^{1,2}, Julia A. Beaver^{1,2}, Harpreet Singh^{1,2}

¹Center for Drug Evaluation and Research, U.S. Food and Drug Administration

²Oncology Center of Excellence, U.S. Food and Drug Administration



Pooled Analysis Population

- Advanced NSCLC
- PD-L1 TPS $\geq 50\%$
 - Excluded staining by tumor-infiltrating immune cells
- No sensitizing *EGFR* mutations or *ALK* alterations
- Clinical trial supported FDA approval of IO-based regimen

Chemo-IO

Exploratory Primary Outcome measure

- OS

Other exploratory outcome measures

- PFS
- ORR

Sub-group analyses

- Age (yrs): *<65 vs 65-75 vs ≥ 75*
- ECOG PS: *0 vs. ≥ 1*
- Smoking history: *Never vs. Ever*

IO-only

Chemo-IO Trials		IO-only Trials	
Trial	Investigational Regimen	Trial	Investigational Regimen
KEYNOTE-021*	Pembrolizumab + Chemo**	CheckMate 026	Nivolumab**
KEYNOTE-189	Pembrolizumab + Chemo**	KEYNOTE-024	Pembrolizumab**
KEYNOTE-407	Pembrolizumab + Chemo**	KEYNOTE-042	Pembrolizumab**
IMpower150	Atezolizumab + Bevacizumab + Chemo***	IMpower110	Atezolizumab**
IMpower130	Atezolizumab + Chemo**	CheckMate 227	Nivolumab + Ipilimumab**
CheckMate-9LA	Nivolumab + Ipilimumab + Chemo**	EMPOWER-Lung 1	Cemiplimab**

Demographic and baseline characteristics

		Chemo-IO (N=455)	IO alone (N=1,298)	Chemo (N=1,436)	Overall (N=3,189)
Age	Median, years	65	64	64	64
	<65 years, %	49	53	50	51
	65-74 years, %	41	36	39	38
	≥75 years, %	10	11	11	11
Sex	Female	37	29	31	31
Race	White, %	91	77	80	80
	Black, %	1	1	2	1
	Asian, %	8	20	16	16
Smoking history	Ever smoked, %	87	89	88	89
ECOG PS	≥1, %	59	68	67	66
Histology	Non-squamous, %	78	69	68	70

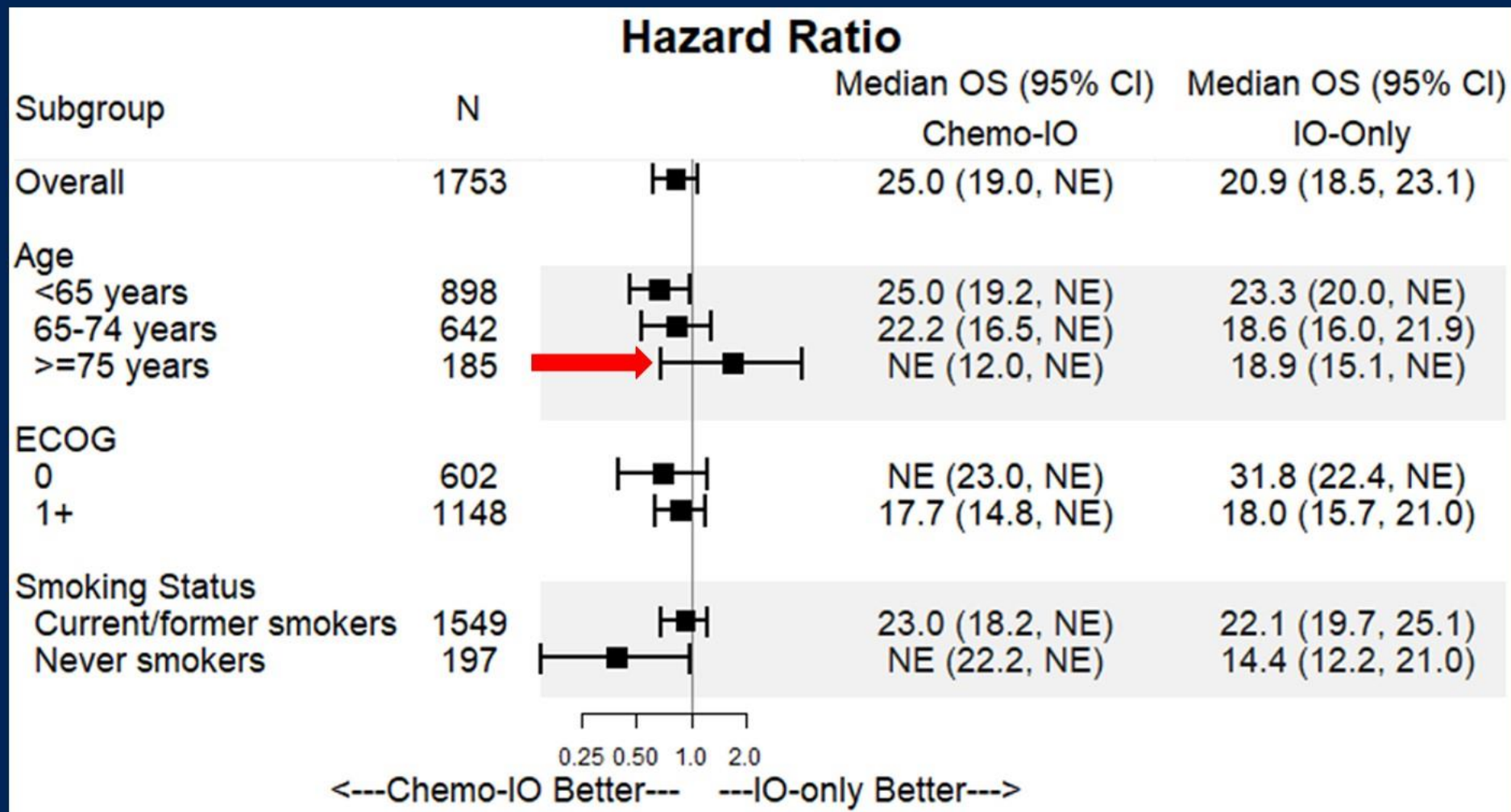
Abbreviations: Chemo-IO=platinum-based doublet chemotherapy plus immunotherapy; ECOG PS=Eastern Cooperative Oncology Group Performance Status; IO=immunotherapy; N=number.

Exploratory OS, PFS, and ORR: NSCLC PD-L1 $\geq 50\%$

	Chemo-IO (N=455)	IO-alone (N=1,298)
OS		
Median, months (95% CI)	25.0 (19.0, NE)	20.9 (18.5, 23.1)
HR (95% CI)	0.82 (0.62, 1.08)	
PFS		
Median, months (95% CI)	9.6 (8.4, 11.1)	7.1 (6.3, 8.3)
HR (95% CI)	0.69 (0.55, 0.87)	
ORR		
% (95% CI)	61 (56, 66)	43 (41, 46)
Odds ratio	1.2 (1.1, 1.3)	

Abbreviations: Chemo-IO=platinum-based doublet chemotherapy plus immunotherapy; CI=confidence interval; HR=hazards ratio; IO=immunotherapy; N=number; NSCLC=non-small-cell lung cancer; NE=not estimable; ORR=objective response rate; OS=overall survival; PD-L1=programmed death ligand-1; PFS=progression-free survival.

OS in NSCLC PD-L1 $\geq 50\%$ in selected subgroups



Abbreviations: Chemo-IO= platinum-based doublet chemotherapy plus immunotherapy; CI=confidence interval; ECOG=Eastern Cooperative Oncology Group Performance Status; IO=immunotherapy; NE=not estimable; NSCLC=non-small-cell lung cancer; OS=overall survival; PD-L1=programmed death ligand-1.

Au delà de la 1ère ligne?

Immunothérapie si non pré exposé

Chimiothérapie:

Docetaxel

Gemcitabine

Paclitaxel

Pemetrexed (non épi)

Conclusion

Chez le sujet âgé :

Aujourd'hui pas de recommandation spécifique, mais :

- PD-L1 > 50% : **privilégier immunothérapie**
- Quel que soit le PD-L1 : peut-être pas de nécessité d'intensifier le traitement:
carboplatine paclitaxel hebdomadaire : intérêt de l'évaluation onco-gériatrique +++
- Au delà de la 1ere ligne: chimiothérapie ou immunothérapie, selon évaluation onco-gériatrique

Je vous remercie pour votre attention

Emeline ORILLARD
eorillard@chu-besancon.fr