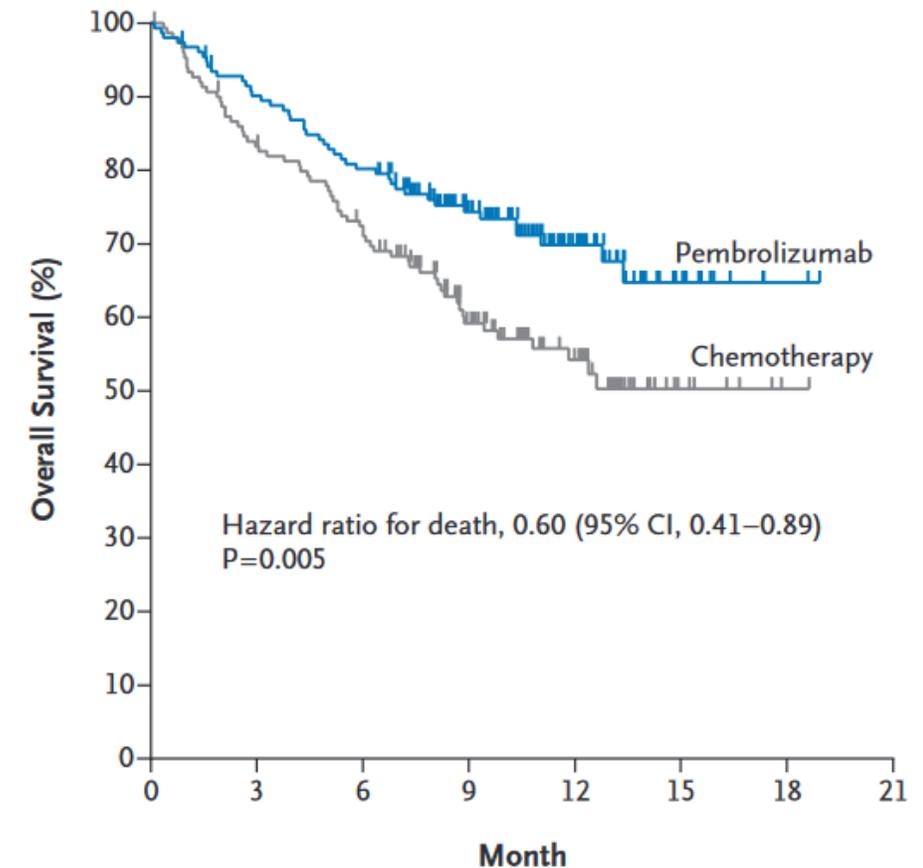


Relation entre le tabagisme et l'efficacité de l'immunothérapie en cancérologie thoracique

Eléonore SIMON



- Cancer bronchique 1^{ère} cause de mortalité
- Immunothérapie = standard thérapeutique



No. at Risk	0	3	6	9	12	15	18	21
Pembrolizumab	154	136	121	82	39	11	2	0
Chemotherapy	151	123	106	64	34	7	1	0

- Tabac facteur de risque principal
- Risques du tabagisme en per-opératoire et péri-radiothérapie

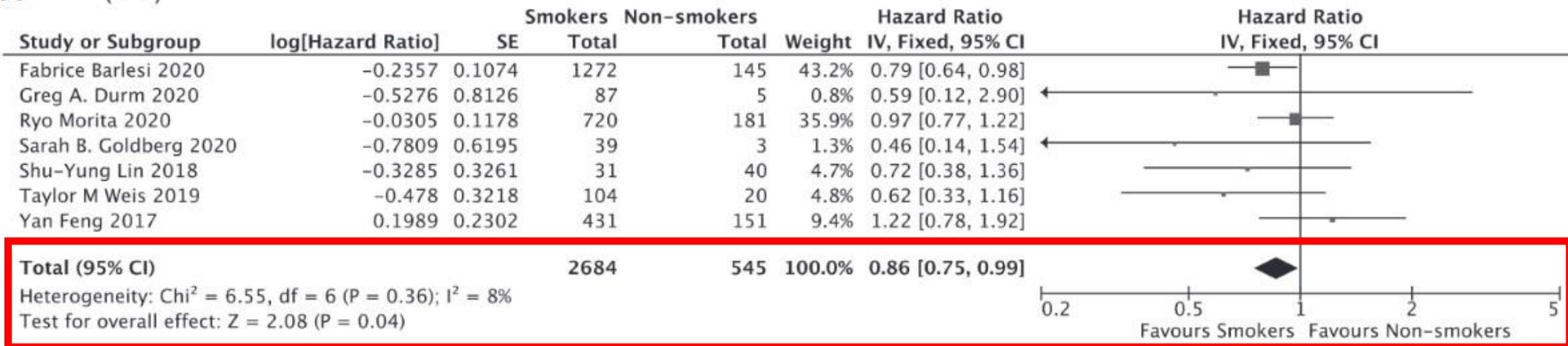
Effets du Tabagisme sur l'immunothérapie?

Objectif principal: Corréler le statut tabagique et l'efficacité des inhibiteurs checkpoints immunitaires (ICI) dans le cancer bronchique non à petites cellules (CBNPC)

ICI Monothérapie

CBNPC stade IV

A HR (OS)



ICI Monothérapie

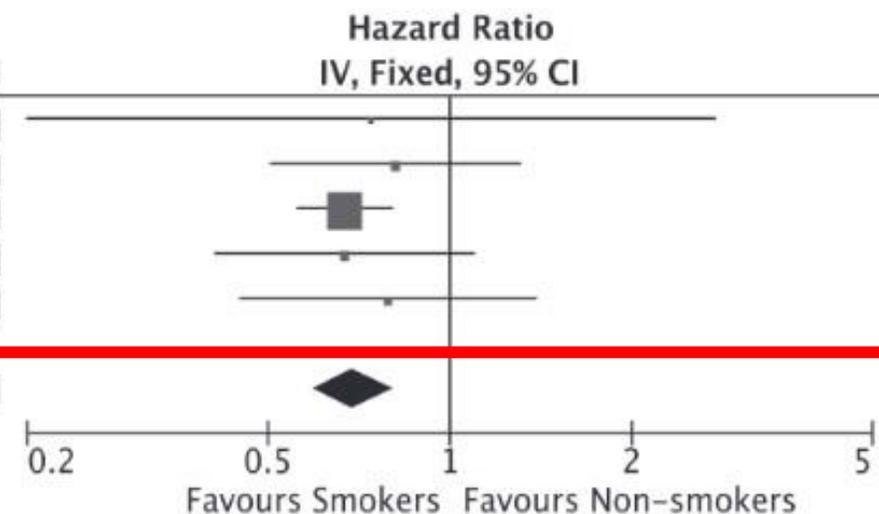
CBNPC stade IV

B HR (PFS)

Study or Subgroup	log[Hazard Ratio]	SE	Smokers	Non-smokers	Weight	Hazard Ratio
			Total	Total		IV, Fixed, 95% CI
Greg A. Durm 2020	-0.3011	0.6675	87	5	1.3%	0.74 [0.20, 2.74]
Minjiang Chen 2020	-0.207	0.2419	57	40	10.2%	0.81 [0.51, 1.31]
Ryo Morita 2020	-0.4005	0.0915	720	181	71.6%	0.67 [0.56, 0.80]
Shu-Yung Lin 2018	-0.4005	0.2506	31	40	9.5%	0.67 [0.41, 1.09]
Taylor M Weis 2019	-0.2357	0.2871	104	20	7.3%	0.79 [0.45, 1.39]
Total (95% CI)			999	286	100.0%	0.69 [0.60, 0.81]

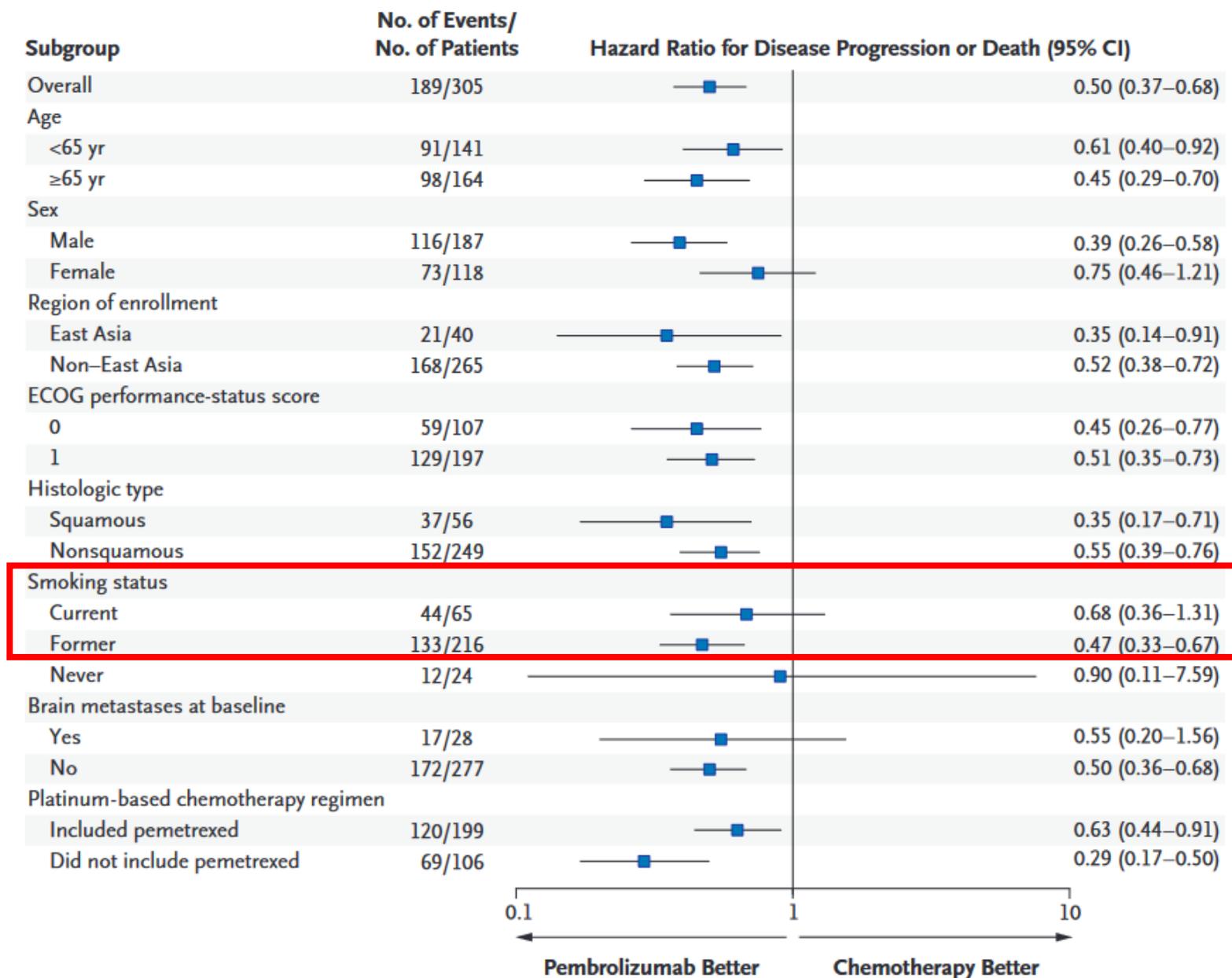
Heterogeneity: $\text{Chi}^2 = 0.81$, $\text{df} = 4$ ($P = 0.94$); $I^2 = 0\%$

Test for overall effect: $Z = 4.74$ ($P < 0.00001$)



ICI Monothérapie

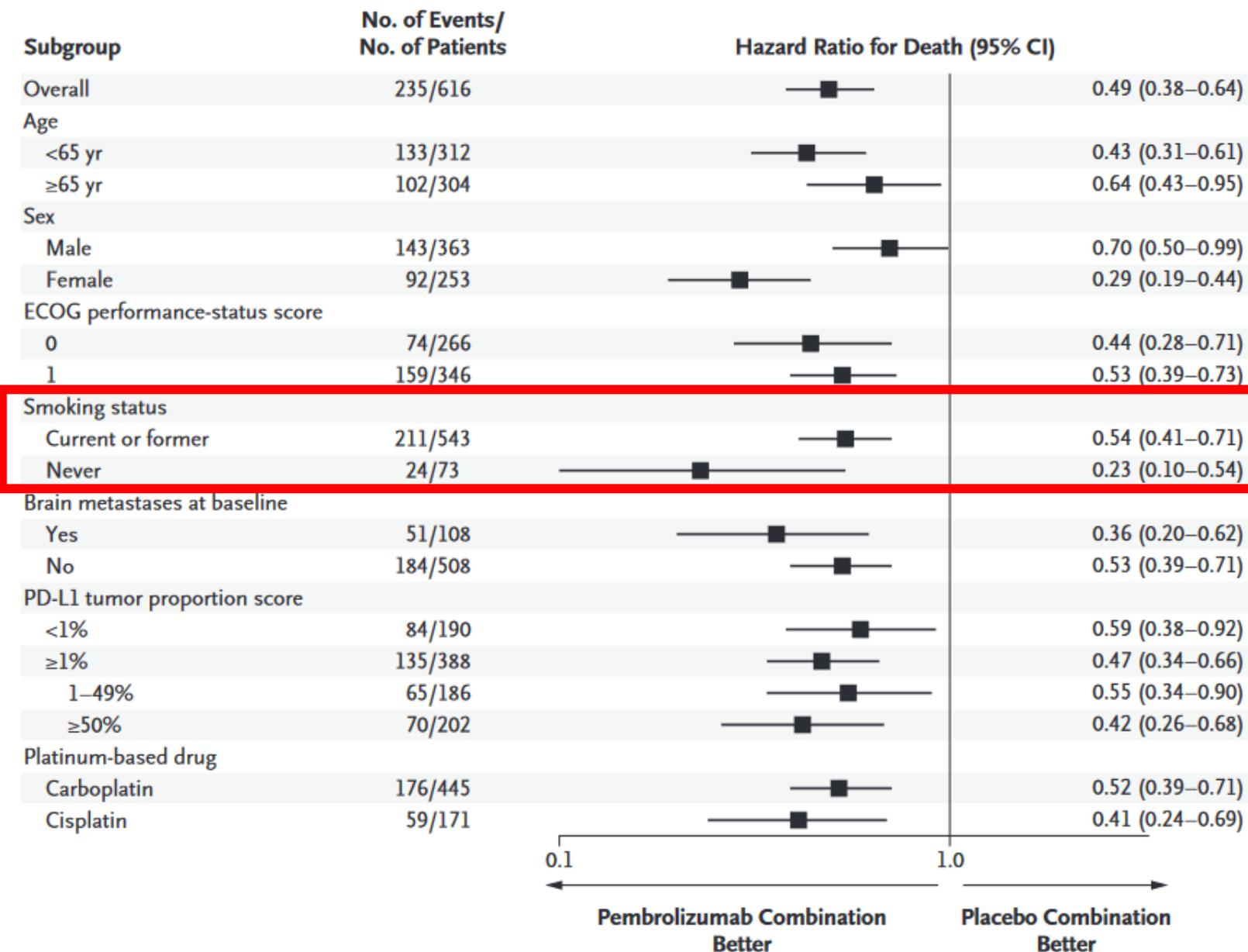
Sevrés vs Actifs



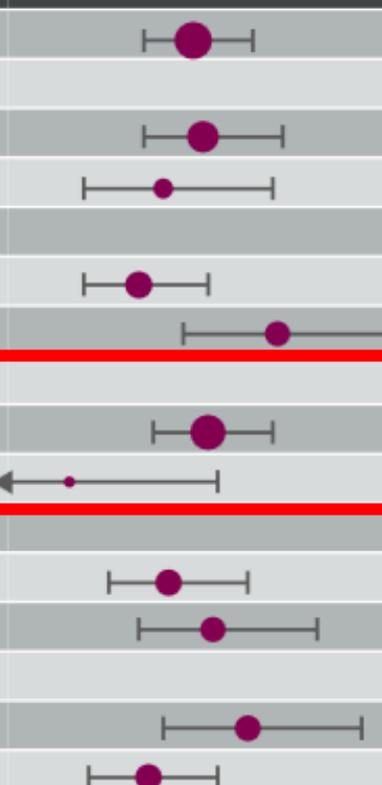
Chimiothérapie + ICI

CBNPC stade IV

B Subgroup Analysis of Overall Survival



Stade non métastatique : CBNPC localement avancé

	No. of events / No. of patients (%)			Unstratified HR (95% CI)
	Durvalumab	Placebo		
All patients	266/476 (55.9%)	174/237 (73.4%)		0.58 (0.48–0.70)
Sex				
Male	192/334 (57.5%)	121/166 (72.9%)		0.60 (0.48–0.76)
Female	74/142 (52.1%)	53/71 (74.6%)		0.52 (0.36–0.74)
Age at randomization				
<65 years	137/261 (52.5%)	98/130 (75.4%)		0.47 (0.36–0.61)
≥65 years	129/215 (60.0%)	76/107 (71.0%)		0.75 (0.56–0.99)
Smoking status				
Smoker	244/433 (56.4%)	157/216 (72.7%)		0.61 (0.50–0.74)
Nonsmoker	22/43 (51.2%)	17/21 (81.0%)		0.33 (0.17–0.63)
NSCLC disease stage				
Stage IIIA	130/252 (51.6%)	93/125 (74.4%)		0.53 (0.41–0.69)
Stage IIIB	130/212 (61.3%)	78/107 (72.9%)		0.62 (0.47–0.83)
Tumor histologic type				
Squamous histology	138/224 (61.6%)	74/102 (72.5%)		0.69 (0.52–0.92)
All other histology	128/252 (50.8%)	100/135 (74.1%)		0.49 (0.37–0.63)

Stade non métastatique : CBNPC opéré en néoadjuvant

Subgroup	No. of Patients	Median Event-free Survival (95% CI)		Unstratified Hazard Ratio for Disease Progression, Disease Recurrence, or Death (95% CI)
		Nivolumab plus chemotherapy (N=179) mo	Chemotherapy alone (N=179) mo	
Overall	358	31.6 (30.2–NR)	20.8 (14.0–26.7)	0.63 (0.45–0.87)
Age				
<65 yr	176	NR (31.6–NR)	20.8 (14.0–NR)	0.57 (0.35–0.93)
≥65 yr	182	30.2 (23.4–NR)	18.4 (10.6–31.8)	0.70 (0.45–1.08)
Sex				
Male	255	30.6 (20.0–NR)	16.9 (13.8–24.9)	0.68 (0.47–0.98)
Female	103	NR (30.5–NR)	31.8 (13.9–NR)	0.46 (0.22–0.96)
Geographic region				
North America	91	NR (25.1–NR)	NR (12.8–NR)	0.78 (0.38–1.62)
Europe	66	31.6 (13.4–NR)	21.1 (10.2–NR)	0.80 (0.36–1.77)
Asia	177	NR (30.2–NR)	16.5 (10.8–22.7)	0.45 (0.29–0.71)
ECOG performance-status score				
0	241	NR (30.2–NR)	22.7 (16.6–NR)	0.61 (0.41–0.91)
1	117	30.5 (14.6–NR)	14.0 (9.8–26.2)	0.71 (0.41–1.21)
Disease stage at baseline				
IB or II	127	NR (27.8–NR)	NR (16.8–NR)	0.87 (0.48–1.56)
IIIA	228	31.6 (26.6–NR)	15.7 (10.8–22.7)	0.54 (0.37–0.80)
Histologic type of tumor				
Squamous	182	30.6 (20.0–NR)	22.7 (11.5–NR)	0.77 (0.49–1.22)
Nonsquamous	176	NR (27.8–NR)	19.6 (13.8–26.2)	0.50 (0.32–0.79)
Smoking status				
Current or former smoker	318	31.6 (30.2–NR)	22.4 (15.7–NR)	0.68 (0.48–0.96)
Never smoked	39	NR (5.6–NR)	10.4 (7.7–20.8)	0.33 (0.13–0.87)

- ICI monothérapie bénéfique chez fumeurs (sevrés > actifs)
 - Association ICI + CT bénéfique > chez non-fumeurs
 - ICI stades précoces et localement avancés bénéfique > chez non-fumeurs
- > Place du sevrage chez patients atteints d'un CBNPC traités par ICI*



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de Marseille | **ap.**
hm

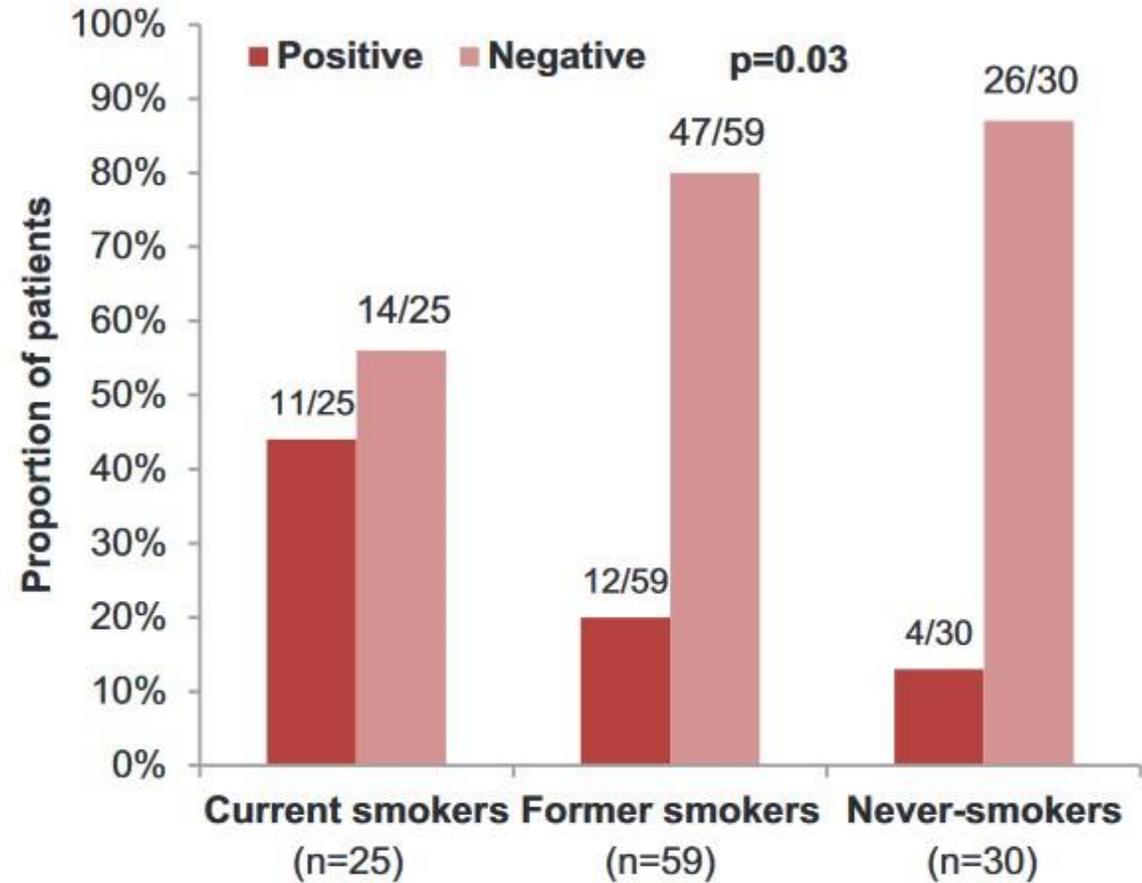
MERCI



PDL1

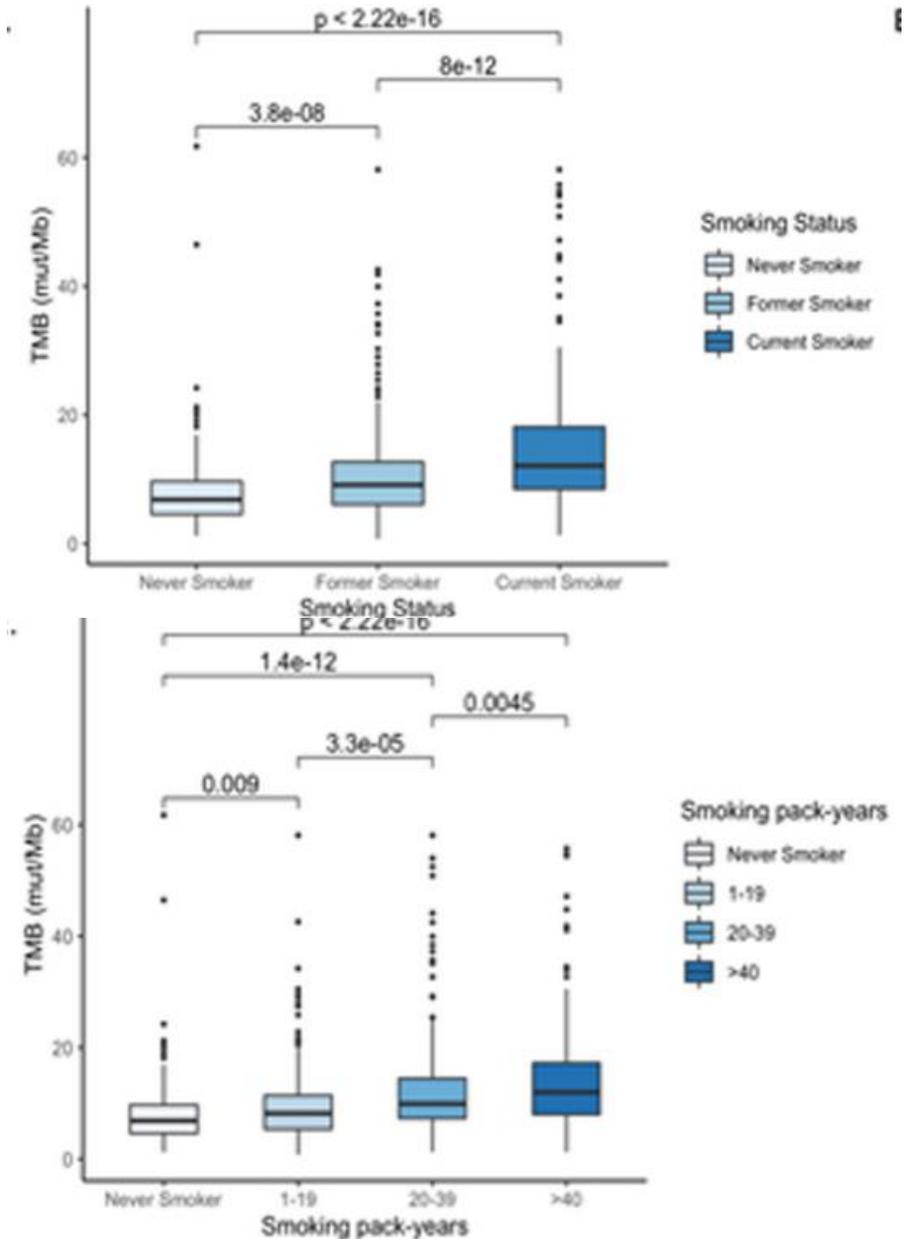
- + Fumeurs
- Corrélié au PA

A



TMB

- + Fumeurs
- Corrélation avec PA controversée
- Histologie et addiction oncogénique > variabilité relation TMB/tabac



Stade non métastatique CBNPC opéré en adjuvant

A

	Atezolizumab group		Best supportive care group		Hazard ratio (95% CI)
	Events/patients, n/N	Median DFS (95% CI), months	Events/patients, n/N	Median DFS (95% CI), months	
Age					
<65 years	156/287	NE (36.0-NE)	131/287	34.2 (29.7-NE)	0.67 (0.46-0.96)
≥65 years	92/189	42.3 (32.3-NE)	97/189	36.0 (23.0-NE)	0.64 (0.41-1.01)
Sex					
Male	171/318	NE (36.7-NE)	147/318	36.0 (29.0-NE)	0.69 (0.48-0.99)
Female	77/158	NE (31.3-NE)	81/158	30.1 (23.9-37.3)	0.61 (0.38-0.97)
Race					
White	162/328	NE (36.1-NE)	166/328	35.3 (29.7-NE)	0.63 (0.45-0.89)
Asian	78/134	42.3 (30.5-NE)	56/134	31.4 (18.0-NE)	0.63 (0.37-1.06)
Region					
Asia-Pacific	75/129	42.3 (30.5-NE)	54/129	31.4 (18.3-NE)	0.63 (0.37-1.09)
Europe and the Middle East	145/289	NE (36.1-NE)	144/289	35.3 (29.7-NE)	0.64 (0.45-0.93)
North America	28/57	NE (24.1-NE)	29/57	35.7 (23.9-NE)	0.79 (0.34-1.80)
ECOG performance status					
0	140/265	NE (35.5-NE)	125/265	30.4 (24.0-37.3)	0.57 (0.40-0.83)
1	107/200	36.7 (26.0-NE)	102/200	NE (28.8-NE)	0.70 (0.51-1.22)
Tobacco use history					
Never	51/92	31.3 (29.4-36.1)	41/92	20.5 (12.2-37.2)	0.63 (0.37-1.10)
Previous	163/309	NE (42.3-NE)	146/309	35.3 (26.7-NE)	0.54 (0.37-0.78)
Current	34/75	36.7 (27.9-NE)	41/75	NE (34.2-NE)	1.24 (0.58-2.64)
Histology					
Squamous	96/181	NE (36.1-NE)	85/181	NE (32.0-NE)	0.78 (0.47-1.29)
Non-squamous	152/295	42.3 (35.5-NE)	143/295	30.1 (23.0-37.2)	0.60 (0.42-0.84)
Stage					
IIA	85/161	NE (36.1-NE)	76/161	NE (29.7-NE)	0.73 (0.43-1.24)
IIB	46/83	NE (35.3-NE)	37/83	NE (32.0-NE)	0.77 (0.35-1.69)
IIIA	117/232	42.3 (30.5-NE)	115/232	26.7 (18.0-35.3)	0.62 (0.42-0.90)