

Les traitements de seconde ligne des CBNPC, hors addiction oncogénique

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Liens d'intérêt



Amgen, Astellas, Astra Zénéca, Bayer, BMS, I.P. Bocuse, Boehringer-Ingelheim, Chugai, Daichy, P Fabre Oncologie, Lilly, Merck, Merrimack, MSD, Novartis, Pfizer, Roche, Sandoz, Taiho, Takéda

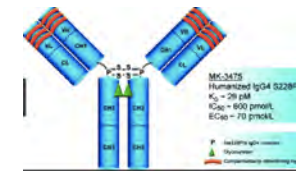
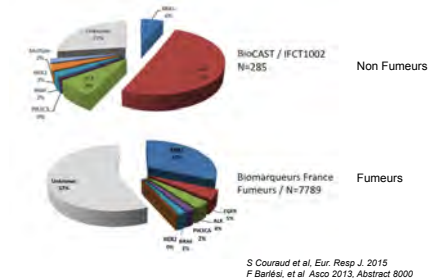
CBNPC de stade IV

Traitements de première lignes en 2018

15 – 20 %: thérapies ciblées

15-20 % : Pembrolizumab (PDL-1 > 50 %)

60-70 %: chimiothérapie

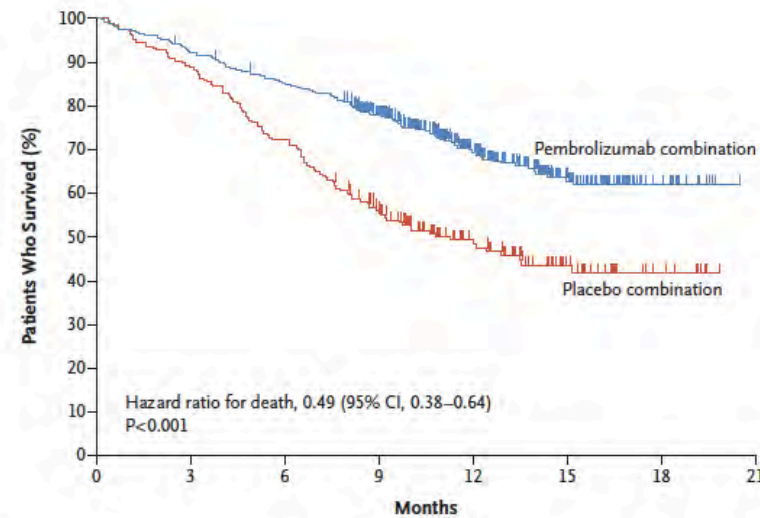


CBNPC de stade IV

Chimiothérapie
+
Pembrolizumab

Nouveau standard??

A Overall Survival



No. at Risk

Pembrolizumab combination	410	377	347	278	163	71	18	0
Placebo combination	206	183	149	104	59	25	8	0

CBNPC de stade IV L2

Quel traitement après une première ligne d'IO ?

Chimiothérapie à base de sels de platine

Association IO + Chimiothérapie ??

Poursuite IO + Traitement local d'un site évolutif ??

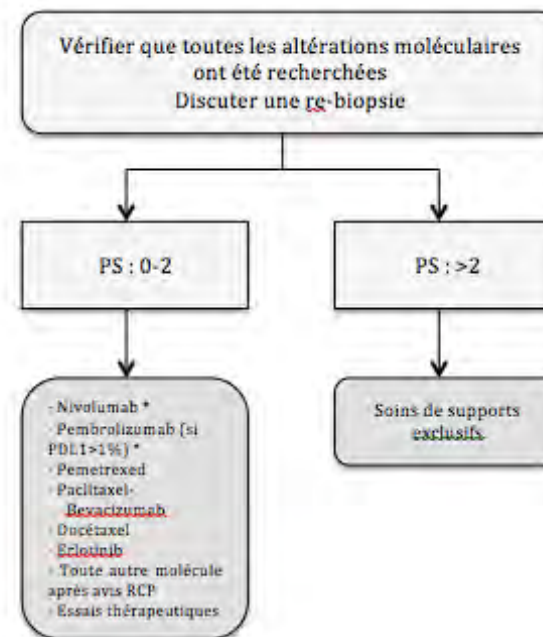
Quel traitement après une association IO + CT???

Combo : PDL1 + Anti CTLA4? Ou autre association??

CT seule?

CBNPC de stade IV L2

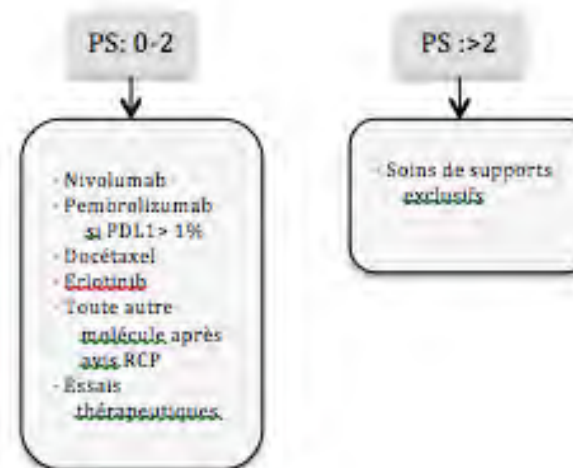
CBNPC non épidermoïde



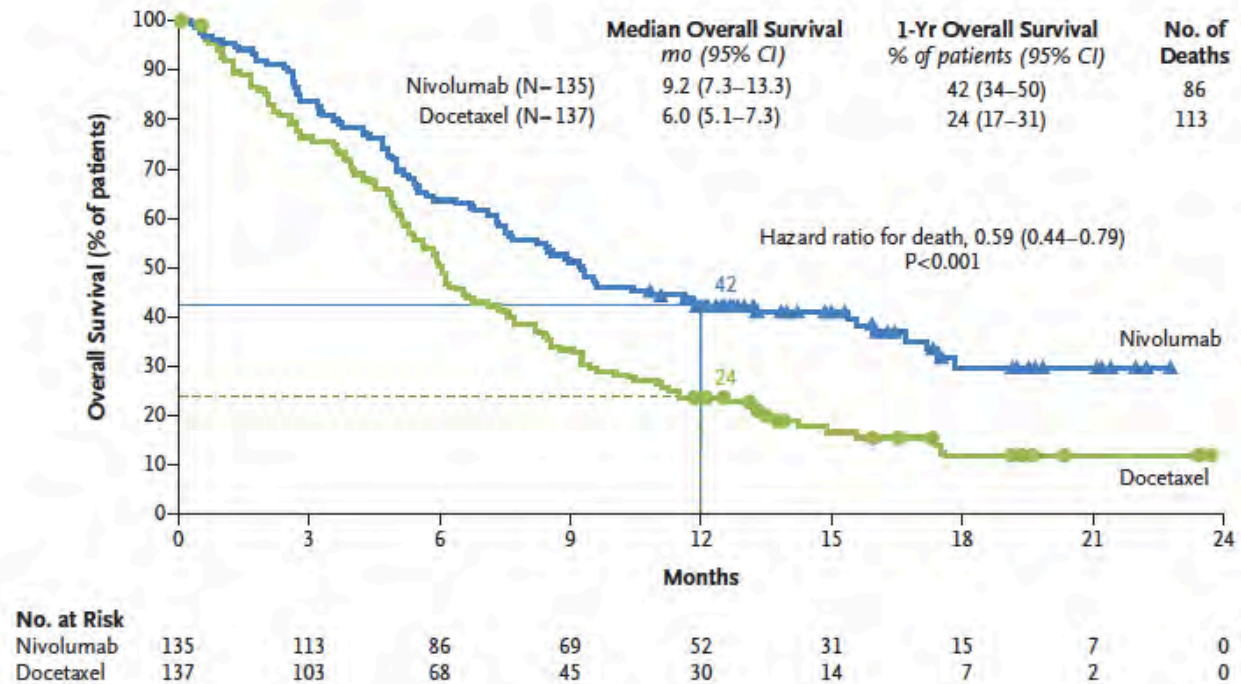
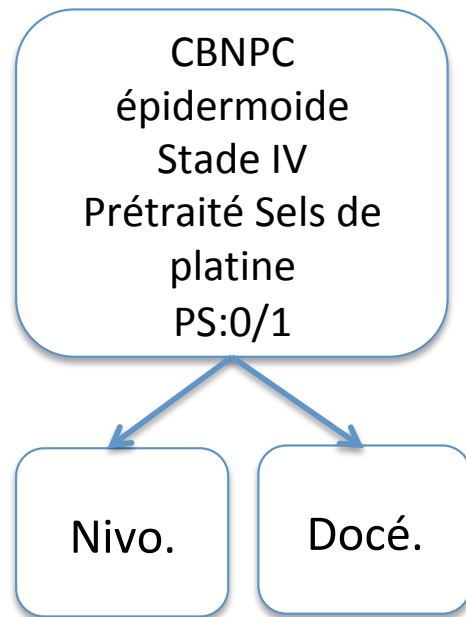
* si immunothérapie non utilisée en première ligne.

CBNPC de stade IV L2

CBNPC épidermoïdes

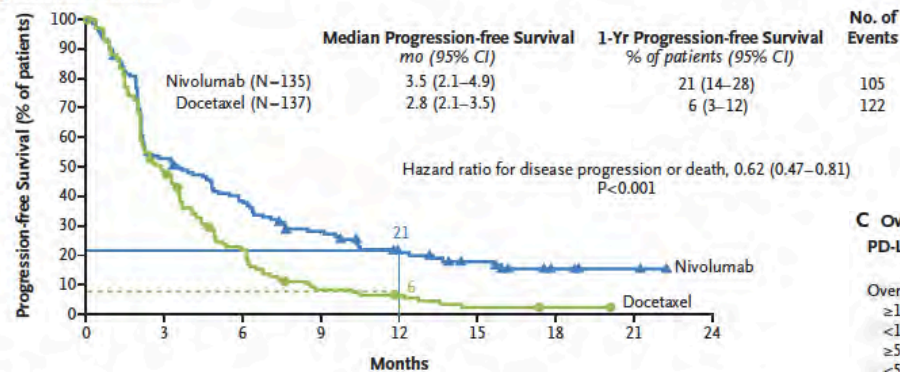


CBNPC de stade IV L2. Epi



CBNPC de stade IV L2 Epi

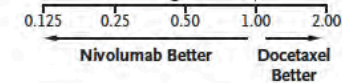
B Progression-free Survival



No. at Risk	0	3	6	9	12	15	18	21	24
Nivolumab	135	68	48	33	21	15	6	2	0
Docetaxel	137	62	26	9	6	2	1	0	0

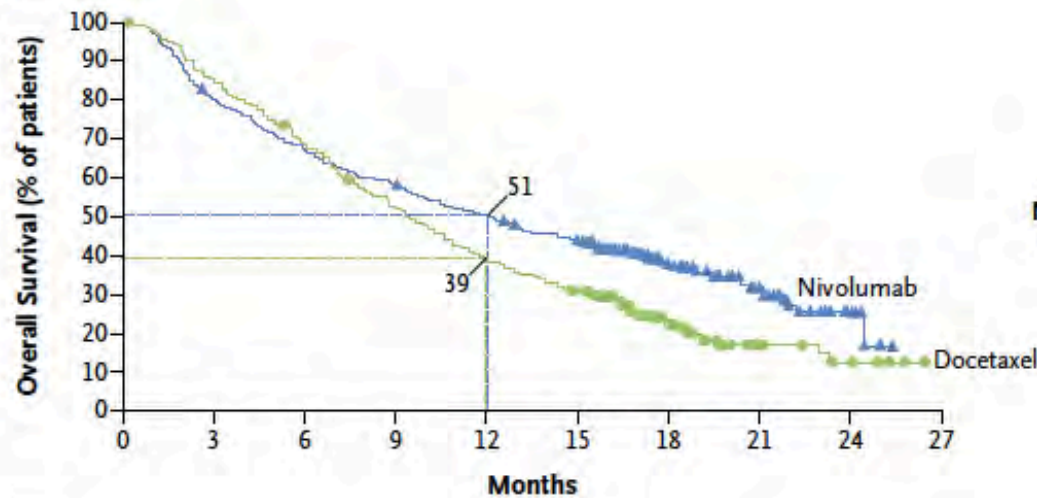
C Overall and Progression-free Survival According to PD-L1 Expression Level

PD-L1 Expression Level	Nivolumab no. of patients	Docetaxel no. of patients	Unstratified Hazard Ratio (95% CI)
Overall survival			
≥1%	63	56	0.69 (0.45–1.05)
<1%	54	52	0.58 (0.37–0.92)
≥5%	42	39	0.53 (0.31–0.89)
<5%	75	69	0.70 (0.47–1.02)
≥10%	36	33	0.50 (0.28–0.89)
<10%	81	75	0.70 (0.48–1.01)
Not quantifiable at baseline	18	29	0.39 (0.19–0.82)
Progression-free survival			
≥1%	63	56	0.67 (0.44–1.01)
<1%	54	52	0.66 (0.43–1.00)
≥5%	42	39	0.54 (0.32–0.90)
<5%	75	69	0.75 (0.52–1.08)
≥10%	36	33	0.58 (0.33–1.02)
<10%	81	75	0.70 (0.49–0.99)
Not quantifiable at baseline	18	29	0.45 (0.23–0.89)



CBNPC de stade IV L2 Non épi

A Overall Survival

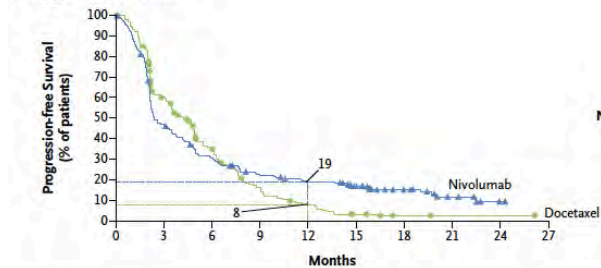


	No. of Deaths/ Total No. of Patients	Median Overall Survival (95% CI) <i>mo</i>	1-Yr Overall Survival Rate (95% CI) <i>%</i>
Nivolumab	190/292	12.2 (9.7–15.0)	51 (45–56)
Docetaxel	223/290	9.4 (8.1–10.7)	39 (33–45)

Hazard ratio for death, 0.73 (96% CI, 0.59–0.89)
P=0.002

CBNPC de stade IV L2 Non Epi.

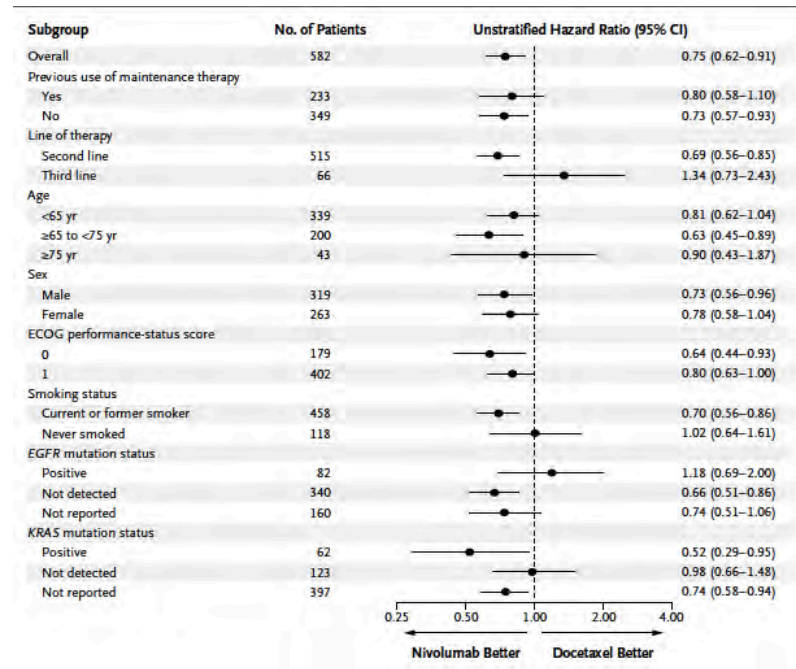
C Progression-free Survival



	No. of Events/ Total No. of Patients	Median Progression-free Survival (95% CI) mo	1-Yr Progression-free Rate (95% CI) %
Nivolumab	234/292	2.3 (2.2-3.3)	19 (14-23)
Docetaxel	245/290	4.2 (3.5-4.9)	8 (5-12)

Hazard ratio for disease progression or death, 0.92 (95% CI, 0.77-1.11); P=0.39

No. at Risk	0	3	6	9	12	15	18	21	24	27
Nivolumab	292	128	82	58	46	35	17	7	2	0
Docetaxel	290	156	87	38	18	6	2	1	1	0

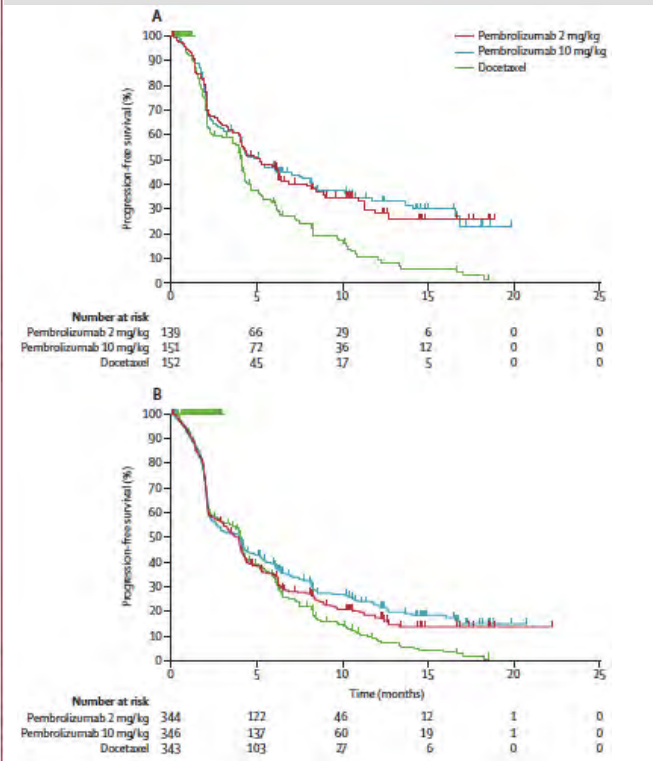
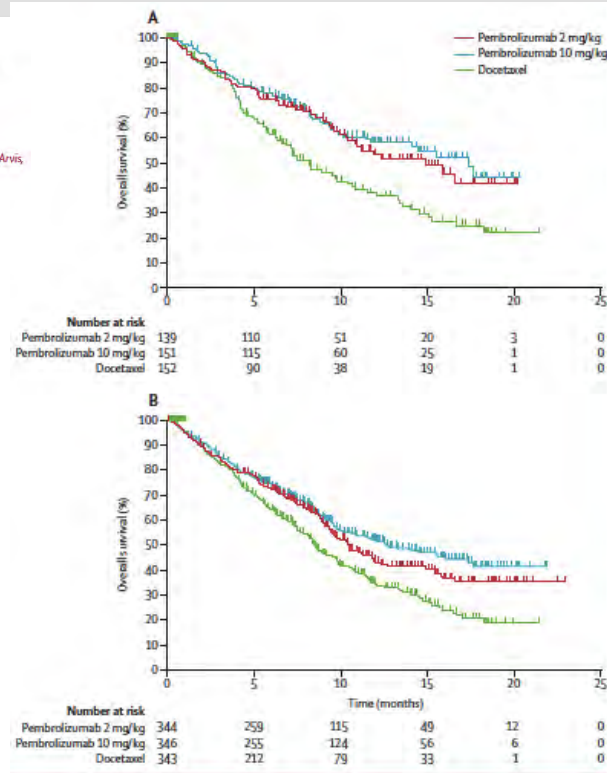


CBNPC de stade IV L2

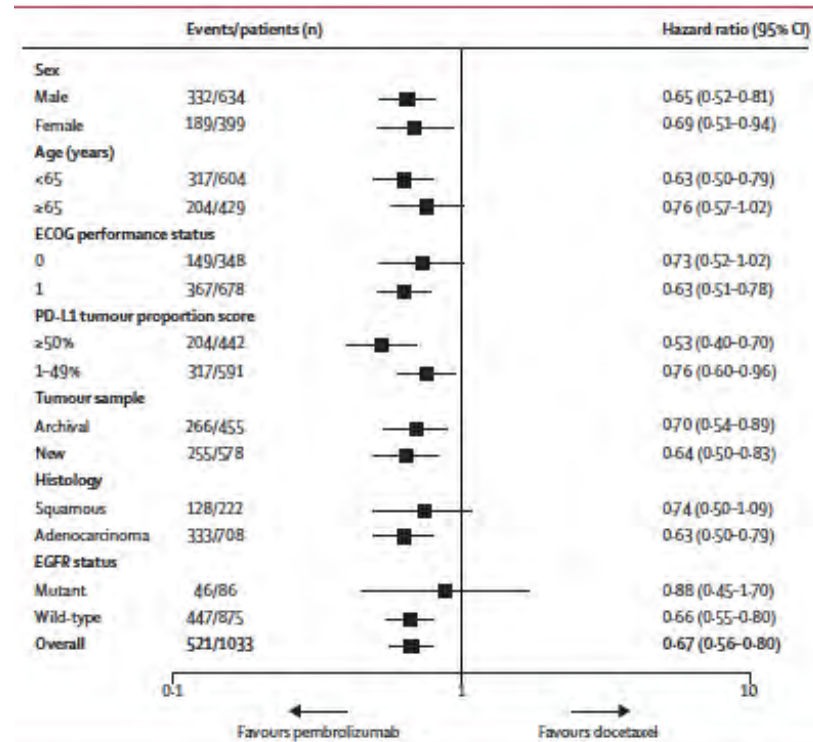
Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial

Roy S Herbst, Paul Baas, Dong-Wan Kim, Enriqueta Felip, José L Pérez-Gracia, Ji-Youn Han, Julian Molina, Joo-Hang Kim, Catherine Dubos Arvis, Myung-Ju Ahn, Margarita Majem, Mary J Fidler, Gilberto de Castro Jr, Marcelo Garrido, Gregory M Lubiniecki, Yue Shenbu, Ellie Im, Maria Dalled-Filhart, Edward B Garon

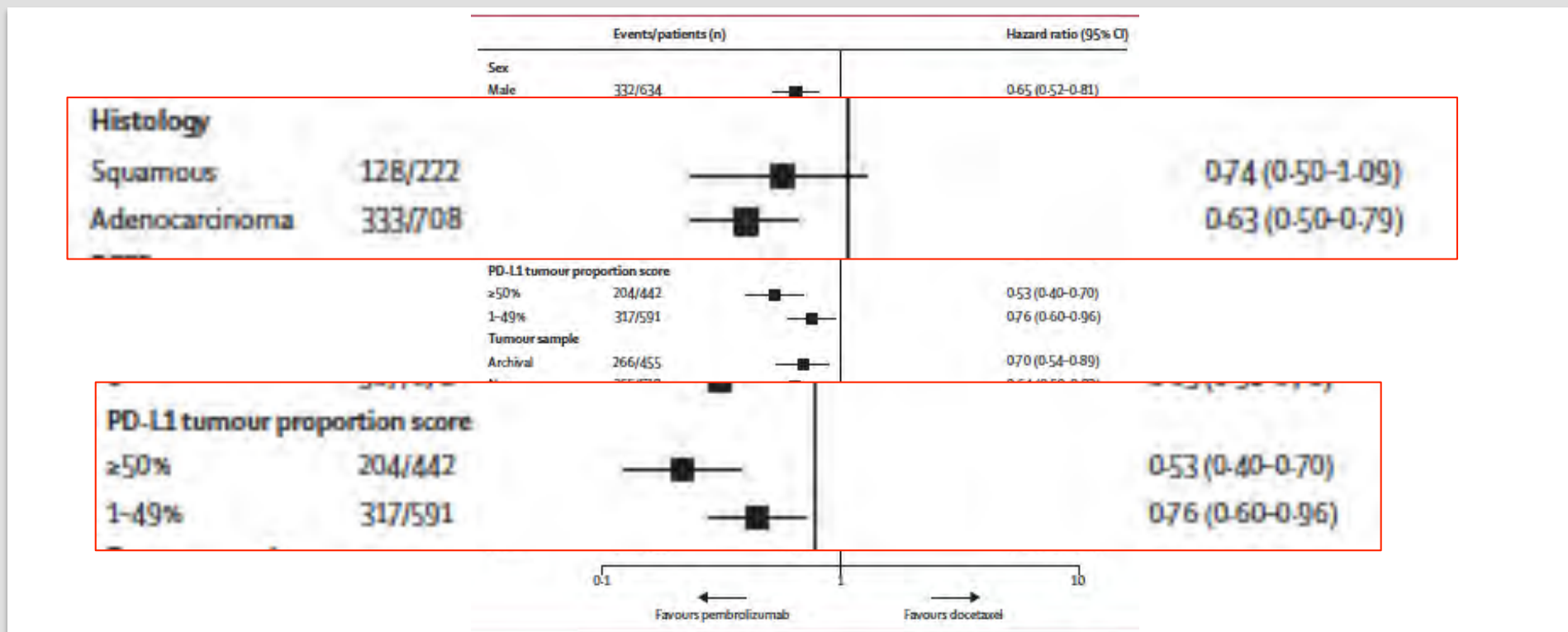
CBNPC toute histologie
L1 par sels de platine
PS: 0/1
1034 patients
PDL1 > 0%



CBNPC de stade IV L2



CBNPC de stade IV L2



CBNPC de stade IV L2

Phase III OAK study design

Locally Advanced or Metastatic NSCLC

- 1–2 prior lines of chemo including at least 1 platinum based
 - Any PD-L1 status
- N = 1,225 enrolled^a

Stratification factors

- PD-L1 expression
- Histology
- Prior chemotherapy regimens

R 1:1

Atezolizumab
1200 mg IV q3w

PD or loss of clinical benefit

Docetaxel
75 mg/m² q3w

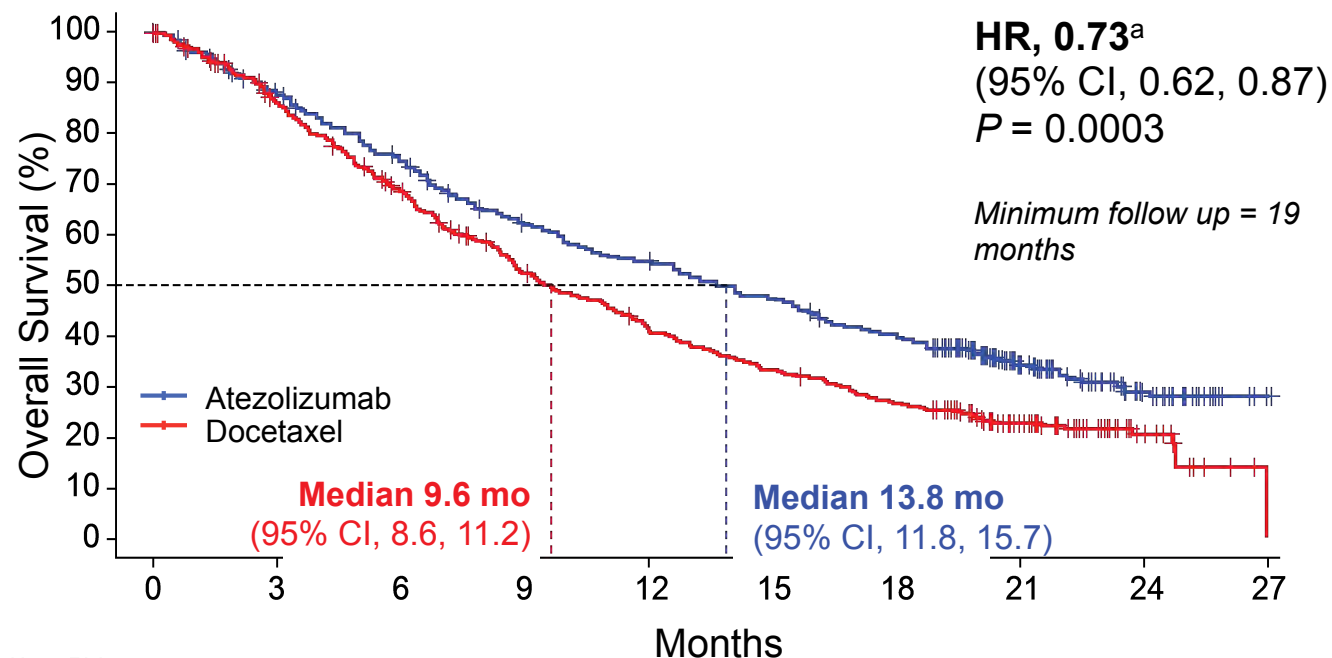
PD

Primary Endpoints (first 850 enrolled patients):

- OS in the ITT population
- OS in patients with PD-L1 expression on $\geq 1\%$ TC or IC

Secondary Endpoints: ORR, PFS, DoR, Safety

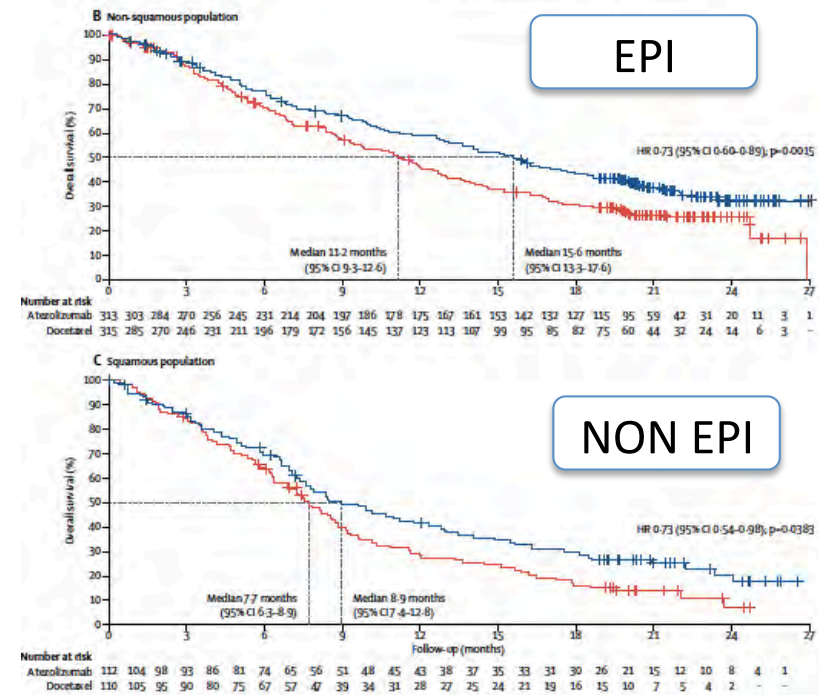
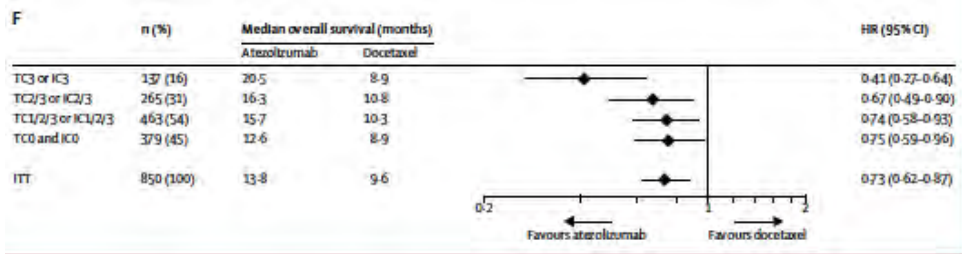
CBNPC de stade IV L2



No. at Risk	0	3	6	9	12	15	18	21	24	27																		
Atezolizumab	425	407	382	363	342	326	305	279	260	248	234	223	218	205	198	188	175	163	157	141	116	74	54	41	28	15	4	1
Docetaxel	425	390	365	336	311	286	263	236	219	195	179	168	151	140	132	123	116	104	98	90	70	51	37	28	16	6	3	

CBNPC de stade IV L2

Effacité pour tout niveau d'expression de PDL1 TC et IC



CBNPC de stade IV L2

CBNPC de
stade IIIB/IV

Progression après 1^{ère}
ligne à base de sel de
platine

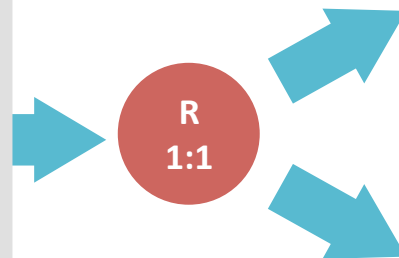
Analyse des patients

(PD-L1+):
N=529
(≥1% cellules tumorales)

patients:
N=792

Stratification:

- Tumeurs PD-L1+ vs PD-L1-
- Epidermoïde vs non-épidermoïde



Avelumab
10 mg/kg / 2 sem

PD-L1+: n=264
Tous patients: n=396

Traitement jusqu'à
progression, toxicité ou retrait
du consentement

Docetaxel
75 mg/m² / 3 sem

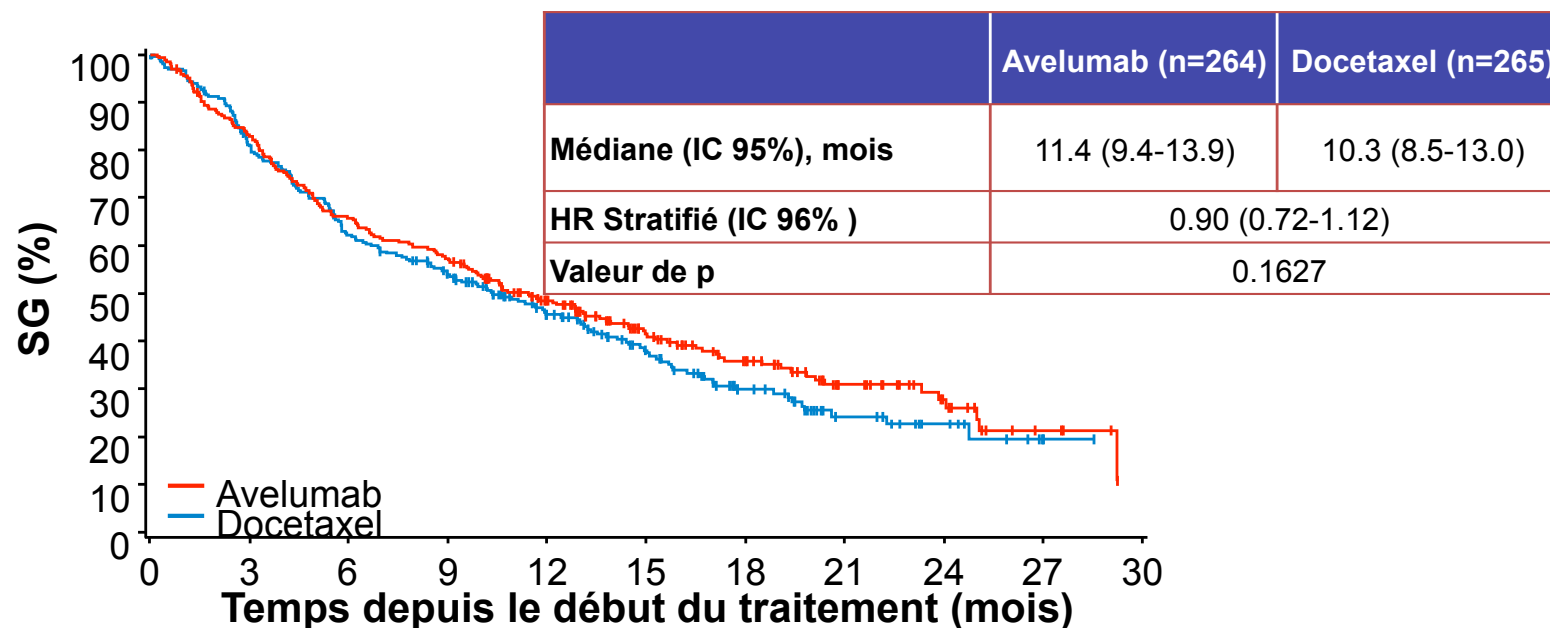
PD-L1+: n=265
Tous patients : n=396

Objectif principal:
SG
(population PD-L1+)

Objectif secondaire :
SG (tous patients),
Meilleure réponse, SSP,
Qdv, Tolérance

CBNPC de stade IV L2

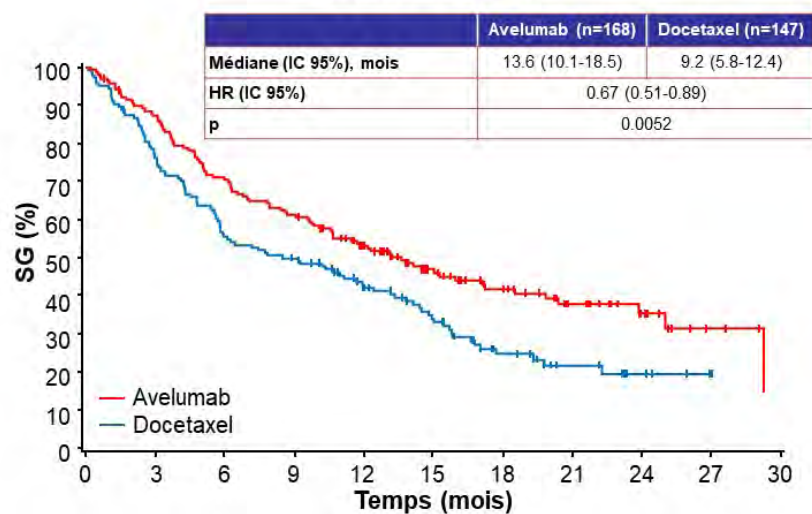
SG dans la population PD-L1+ ($\geq 1\%$)



Avelumab	264	218	172	150	109	73	52	29	16	5	0
Docetaxel	265	210	160	132	94	65	38	18	10	2	0

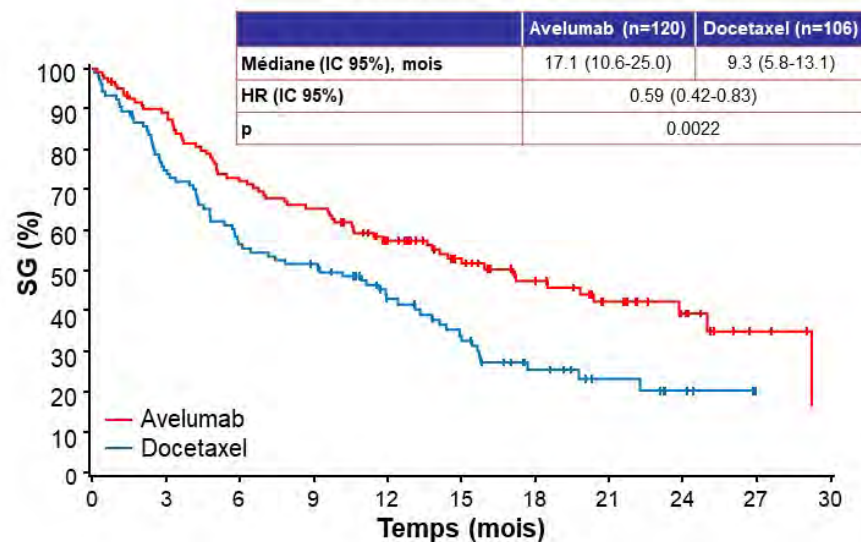
CBNPC de stade IV L2

≥50% PD-L1+



Avelumab	168	145	117	102	76	52	38	23	12	4	0
Docetaxel	147	110	80	71	50	37	20	11	6	1	0

≥80% PD-L1+



Avelumab	120	105	85	77	59	43	31	21	12	4	0
Docetaxel	106	77	58	52	35	26	14	8	4	0	0

Avelumab

- ▶ 10 mois MS du Docétaxel
- ▶ 36 % de cross over dans le bras Docétaxel
- ▶ Critères d'inclusion

	Docétaxel	Pemetrexed	Paclitaxel+ bevacizumab	Docétaxel+ nindétanib	Docétaxel+ ramucirumab	Erlotinib	Afatinib
Dose	75 mg/m2 J1/21	500 mg/m2 J1/21	Paclitaxel 90 mg/m2 J1,8 et 15 Bevacizumab 10 mg/kg J1 et 15 / 28 jours	Docétaxel 75 mg/m2 J1/21 Nindétanib 200mgx2/J J2-22	Docétaxel 75 mg/m2 Ramucirumab 10mg/kg J1/21	150 mg/j	40 mg/j
Phase III	Vs placebo	Vs Docétaxel	Vs Docetaxel	Vs Docétaxel	Vs Docétaxel	Vs placebo	Vs Erlotinib
Histologie	Toutes	Toutes	Adénocarcinome	Toutes	Toutes	Epidermoïde	Epidermoïde
Résultats	N=272 SG :9,2 vs 6 m* (HR : 0,62) SSP :3,5 vs 2,8 m* (HR : 0,62) RO : 20 vs 9 % Tox G3-4 : 8 vs 56%	N= 571 SG :8,3 vs 7,9 m SSP :2,9 vs 2,9 m RO : 9,1 vs 8,8% Toxicités moindres avec le Pemetrexed	N= 166 SG : 9,9 vs 10,8 m SSP : 5,4 vs 3,9 m* (HR 0,62) RO : 22,5 vs 5,5 % * Toxicités : Moindre neutropénie Plus neuropathie	N=1314 SG 12,6 vs 10,3 * (ADK) (HR 0,83) SSP 3,7 vs 2,4 m* (HR 0,83) RO : 4,4 vs 3,3 % Toxicités: augmentées avec nindétanib	N= 1253 SG 10,5 vs 9,1 m* (HR 0,86) SSP :3,4 vs 2,7 m* (HR :0,79) RO : 23 vs 14% * Toxicités : augmentation neutropénie	N= 731 SG : 6,7 vs 4,7 m* (HR :0,70) SSP :2,2 vs 1,8 m* (HR :0,61) RO : 8,9 vs 0,7 %* Toxicités : attendues avec erlotinib	N=795 SG : 7,9 vs 6,8 m* (HR 0,81) SSP: 2,6 vs 1,9 m* (HR : 0,81) RO : 6 vs 3% Toxicités : identiques
Commentaire		Etude de non infériorité	En 2° ou 3° ligne. Cross over autorisé 1° ligne avec bévacizumab autorisée	Pas de remboursement dans cette indication	Pas de remboursement dans cette indication		AMM obtenu mais pas de remboursement dans cette indication

CBNPC de stade IV L2

	Nivolumab	Pembrolizumab	Atézolizumab	Durvalumab	Avélumab
Type d'anticorps	Anti PD1 IgG4	Anti PD1 IgG4	Anti PDL1 IgG1 modifiée	Anti PDL1 IgG1 modifiée	Anti PDL1 IgG1
Dose recommandée (CBNPC)	3 mg/kg / 14 j 240 mg / 14 j	2 mg/kg / 21 j 200 mg / 21 j	1200 mg / 21 j	10 mg/kg / 14 j (Adjuvant stade III)	10 mg/kg / 14 j
Test expression PDL1	Dako 28-8	Dako 22C3	Ventana SP142	Ventana SP 263	Dako 73-10

Les Questions ???

▶ IO en 2° ligne ou en 3° ligne ?

▶ Y a t'il une différence entre les IO??

IMMUNOTHERAPIE : L2 OU Lx ?



Exclusive systemic tt	N=319 (75%)		
Single agent chemotherapy	n=210 (49 %)	Docetaxel	61 (14%)
		Gemcitabine	64 (15%)
		Paclitaxel +/- bevacizumab	38 (9%)
		Vinorelbine	24 (6%)
		Pemetrexed	20 (5%)
		Other	3 (1%)
Platin-based doublet	n=35 (8%)	Platin-Paclitaxel	21 (5%)
		Other	14 (3%)
Targeted therapy	n=57 (13%)	Erlotinib	43 (10%)
		Other	14 (3%)
Nivolumab rechallenge	n=15 (4%)		
Other/unknown systemic tt	n=2 (0.5%)		
Surgery +/- radiotherapy +/- systemic tt	N=100 (24%)		
Unknown tt	N=7 (2%)		

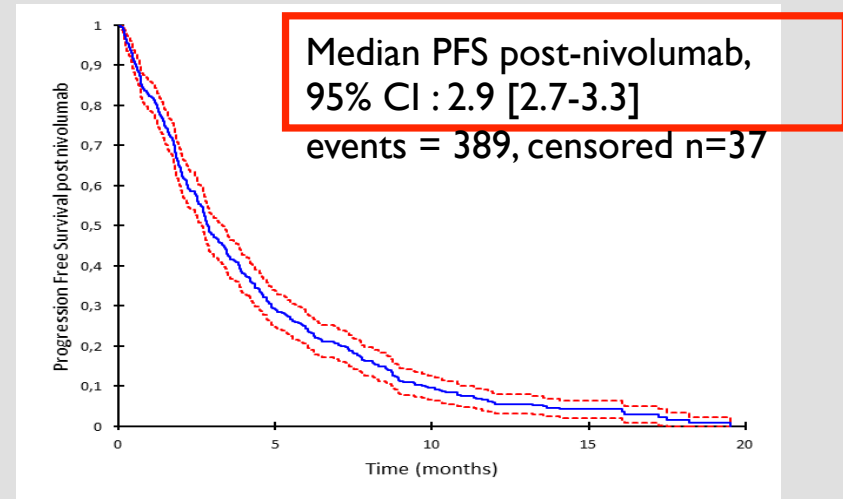
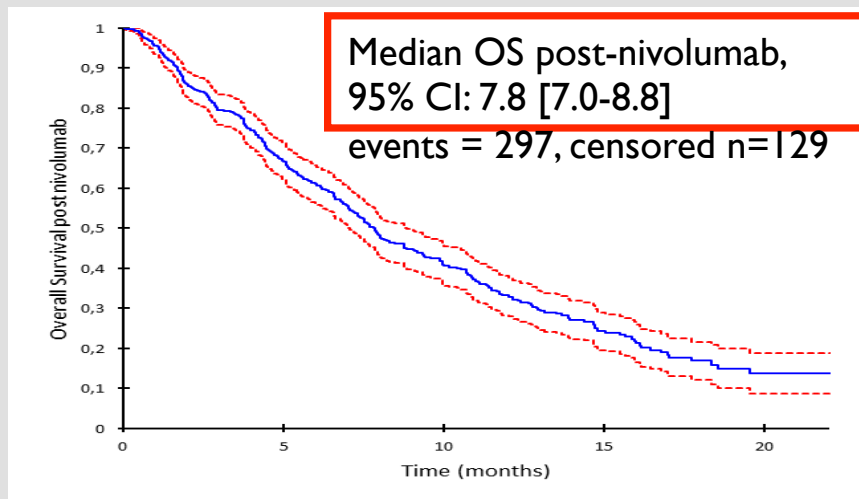
9371 - N. Girard et al.

IFCT - 1502 CLINIVO: Real - life experience with nivolumab in 600 patients (pts) with advanced Non - Small Cell Lung Cancer (NSCLC).



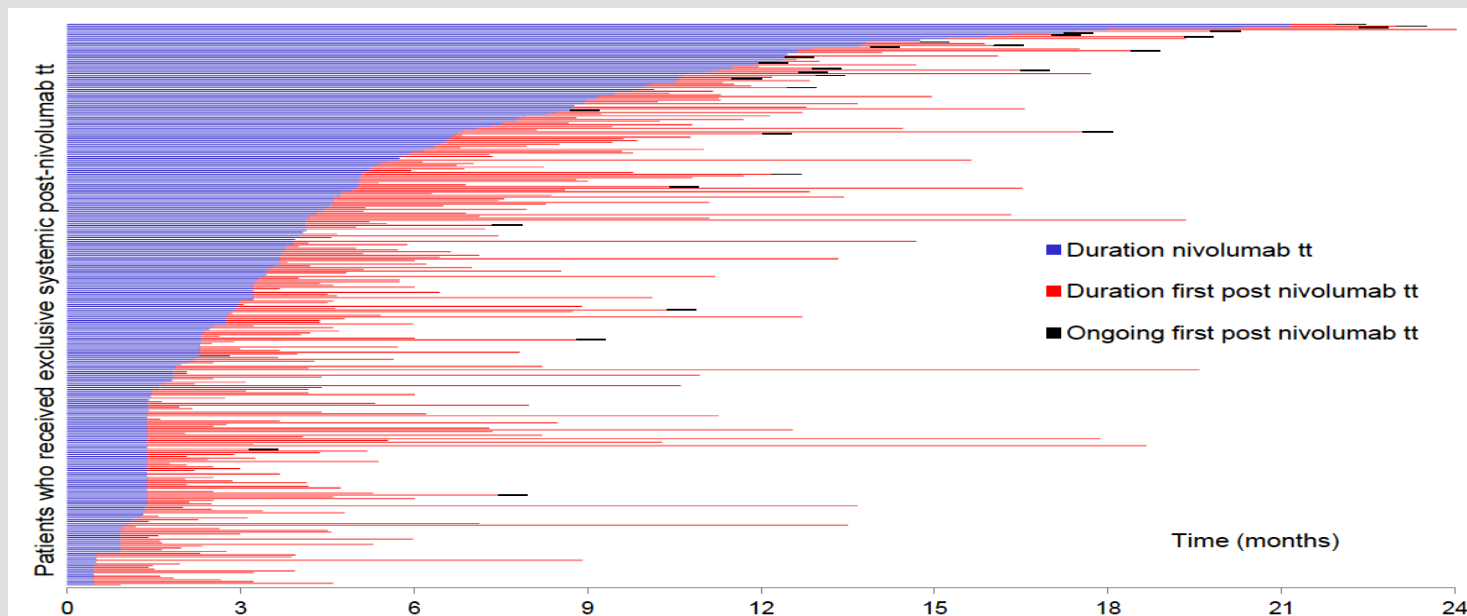
IMMUNOTHERAPIE : L2 OU Lx ?

- Best response to first post-nivolumab systemic tt (n=319) was: ORR=16.2 %; SD=42.3%; PD=41.5%.



IMMUNOTHERAPIE : L2 OU Lx??

Duration of nivolumab and first post-nivolumab treatment



CBNPC de stade IV

NOMBREUSES REVUES SYSTEMATIQUES ET « META-ANALYSES »

N TOMOHIRO et al	The Oncologist 2017
PM ELLIS et al	Clin Lung Cancer 2017
M KHAN et al	Medicine 2018
F PASSIGLIA et al	Int J Cancer 2018
P CREQUIT et al	BMC Médecine 2017
X ARMOIRY et al	Plos One 2018

Table 1. Characteristics of included studies.

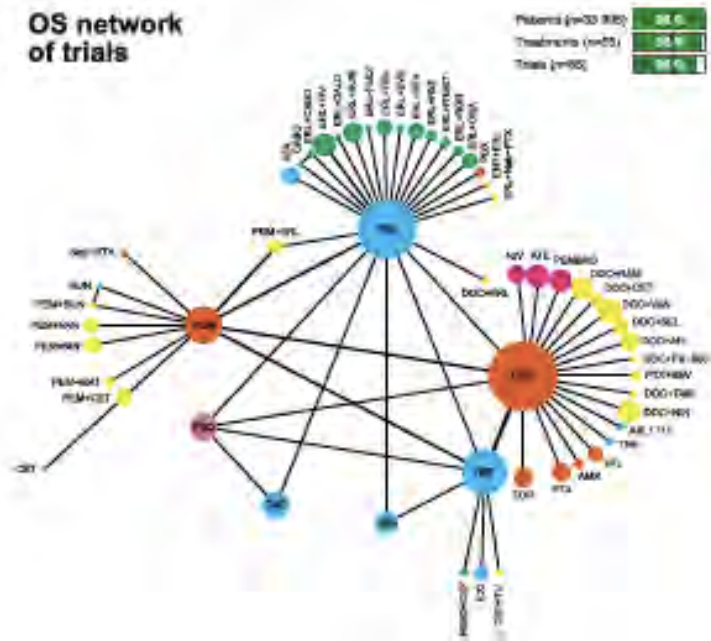
Variables (n (%)) unless stated	REVEL		EUSM-EUSG 1		CHECKMATE 017		CHECKMATE 057		Hanna		KEYNOTE-019		POPULAR		TAYLOR		USAC		Van Looij 8		Karamitsis et al. (2016)	
	RAM + DOC (n = 628)	PBO + DOC (n = 625)	SOB + DOC (n = 635)	PBO + DOC (n = 639)	SOB (n = 133)	DOC (n = 137)	NTV (n = 292)	DOC (n = 298)	PMB (n = 283)	DOC (n = 288)	Platinu (n = 344)	DOC (n = 343)	ATEZ (n = 145)	DOC (n = 145)	ERL (n = 119)	DOC (n = 119)	ATEZ (n = 121)	DOC (n = 121)	AFA (n = 395)	ERL (n = 397)	PMB (n = 146)	ERL (n = 146)
Age, years (median, range)	62 (21–85)	61 (25–86)	60 (53–67)	60 (54–66)	62 (39–85)	64 (42–84)	61 (37–84)	64 (21–85)	59 (23–84)	57 (28–87)	65 (56– 69)	62 (56–69)	62 (42–81)	62 (36–84)	66 (40–81)	67 (37–83)	65 (37–82)	64 (34–83)	65 (36–84)	64 (35–86)	66 (42–66)	67 (37–81)
Male sex	619 (67)	613 (68)	676 (73)	679 (73)	141 (82)	97 (71)	334 (52)	366 (58)	194 (68.6)	117 (75.2)	212 (62)	209 (61)	93 (64)	76 (53)	77 (77)	73 (66)	261 (64)	259 (64)	335 (84)	331 (83)	138 (93.1)	135 (92.3)
White	526 (64)	549 (61)	533 (61)	538 (60)	122 (86)	136 (93)	267 (93)	266 (92)	NA	NA	246 (72)	251 (73)	NA	NA	166 (95)	166 (99)	362 (71)	296 (70)	312 (78)	311 (78)	NA	NA
Asian	74 (12)	80 (14)	150 (18)	150 (18)	4 (3)	2 (1)	9 (3)	8 (3)			73 (21)	72 (21)	NA	NA	1 (1)	1 (1)	85 (20)	95 (22)	86 (21)	86 (22)	NA	NA
Black	17 (3)	18 (2)	41 (5)	41 (5)	8 (6)	2 (1)	7 (2)	9 (3)			13 (4)	7 (2)	NA	NA	0	0	5 (1)	11 (3)	NA	NA	NA	NA
PS-0	267 (33)	199 (22)	187 (21)	189 (21)	23 (16)	37 (27)	66 (23)	65 (22)	253 (88.5)	292 (187.8)	412 (100)	416 (100)	46 (32)	45 (32)	32 (60)	33 (60)	237 (36)	180 (39)	126 (32)	134 (34)	37 (22.3)	60 (26.3)
PS-1	425 (67)	425 (68)	447 (71)	479 (74)	106 (75)	100 (73)	208 (77)	194 (67)			229 (67)	224 (65)	96 (66)	97 (68)	68 (64)	59 (45)	229 (64)	265 (62)	269 (68)	262 (66)	98 (33)	104 (62.7)
Current and former smoker	148 (18)	145 (17)	190 (22)	198 (23)	121 (86)	129 (94)	231 (79)	227 (78)	NA	NA	279 (81)	269 (78)	117 (81)	113 (80)	99 (81)	68 (77)	243 (60)	313 (63)	361 (91)	362 (92)	128 (77.1)	124 (74.7)
Never smoker	180 (17)	181 (21)	189 (22)	184 (21)	69 (7)	7 (3)	58 (20)	60 (21)			63 (18)	63 (20)	27 (20)	29 (20)	19 (17)	38 (27)	64 (20)	72 (17)	26 (7)	18 (5)	24 (18.3)	28 (17.5)
Stage IIB or inclusion	0	0	188 (22)	186 (22)	29 (21)	24 (18)	28 (17)	24 (8)	71 (25.1)	73 (23.3)	na	na	NA	NA	NA	NA	NA	NA	48 (12)	48 (12)	19 (13.6)	12 (7.2)
Stage IV or inclusion	628 (100)	625 (100)	399 (46)	408 (48)	180 (78)	112 (82)	272 (93)	266 (92)	112 (39.6)	131 (74.7)	na	na	NA	NA	NA	NA	NA	NA	349 (88)	343 (87)	117 (86.6)	134 (92.9)
Non- squamous	465 (74)	447 (72)	547 (63)	532 (61)	0	0	292 (100)	280 (100)	154 (54.6)	142 (88.3)	240 (70)	240 (70)	95 (66)	95 (68)	78 (77.3)	87 (78)	113 (28)	113 (28)	17 (4)	13 (4)	136 (93.1)	127 (86.5)
Squamous	157 (23)	178 (27)	270 (42)	279 (42)	189 (100)	117 (86)	0	0	78 (27.4)	91 (32.3)	70 (22)	66 (19)	49 (34)	68 (49)	31 (26.4)	29 (26)	112 (28)	109 (26)	381 (96)	362 (92)	36 (22.7)	39 (23.8)
Prior platinum- based therapy	603 (96)	602 (96)	638 (97)	636 (98)	153 (100)	158 (100)	293 (100)	280 (100)	263 (92.6)	239 (159)	na	na	NA	NA	109 (100)	110 (100)	425 (100)	425 (100)	368 (100)	397 (100)	346 (100)	366 (100)
Prior-line biologically targeted therapy	58 (14)	53 (15)	27 (3)	23 (3)	1 (1)	2 (1)	na	na	0	0	na	na	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Prior immunologic treatment	133 (21)	141 (23)	NA	NA	NA	NA	112 (42)	111 (39)	NA	NA	na	na	148 (100)	143 (100)	109 (100)	109 (100)	NA	NA	NA	NA	NA	NA
Previous tissue	153 (24)	152 (24)	NA	NA	64 (46)	46 (34)	na	na	71 (25.8)	80 (27.3)	na	na	NA	NA	0 (0)	0 (0)	NA	NA	NA	NA	NA	NA
ECR0 Wild type	287 (36)	197 (32)	NA	NA	NA	NA	na	na	NA	NA	293 (85)	294 (86)	NA	NA	109 (100)	110 (100)	218 (75)	218 (75)	NA	NA	57 (42)	53 (36)
ECR0 delmut	15 (2)	16 (3)	NA	NA	NA	NA	44 (16)	38 (13)			28 (8)	28 (8)	11 (8)	11 (8)	0	0	42 (10)	43 (10)	NA	NA	24 (18)	14 (10)
Unknown or missing	499 (81)	496 (80)	NA	NA	NA	NA	na	na			23 (7)	21 (7)	NA	NA	0	0	63 (15)	72 (17)	NA	NA	NA	NA
1 prior therapy	628 (100)	625 (100)	653 (100)	659 (100)	183 (100)	117 (86)	292 (100)	280 (100)	263 (100)	239 (100)	243 (71)	233 (68)	95 (66)	96 (67)	Unknown unknown	unknown	420 (75%)	520 (75%)	109 (100)	102 (100)	101 (69.8)	103 (69.8)
2 prior therapies	0	0	0	0	0	0	0	0	0	0	66 (19)	75 (22)	11 (8)	17 (12)			109 (25%)	100 (23%)	0	0	45 (33.2)	77 (48.4)

<https://doi.org/10.1371/journal.pone.0199575.t001>

Armoiry X, Tsertsvadze A, Connock M, Royle P, Melendez-Torres GJ, et al. (2018) Comparative efficacy and safety of licensed treatments for previously treated non-small cell lung cancer: A systematic review and network meta-analysis. PLOS ONE 13(7): e0199575. <https://doi.org/10.1371/journal.pone.0199575>
<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0199575>

CBNPC de stade IV L2

OS network of trials



SAE network of trials

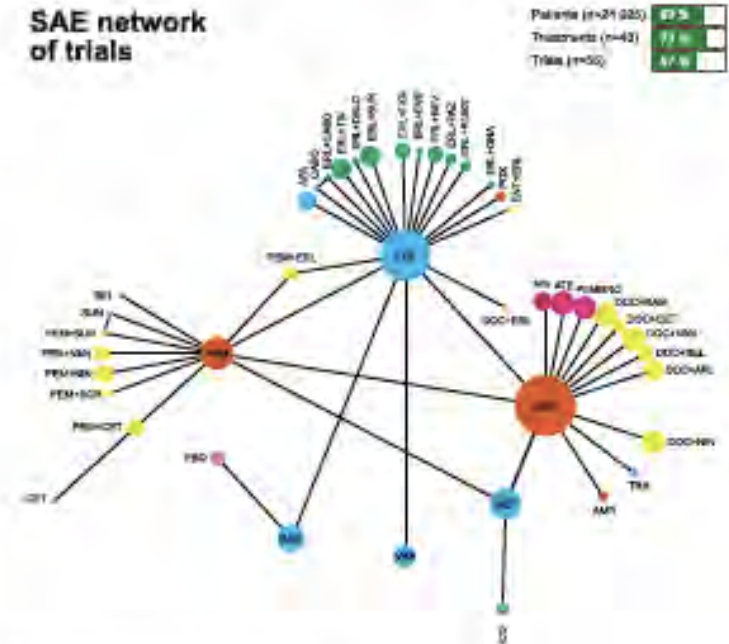


Fig. 3 (See legend on next page.)

CBNPC de stade IV L2

Docetaxel	0.53 (0.26-1.09)	0.45 (0.19-1.16)	0.76 (0.56-1.06)	1.02 (0.68-1.47)	0.97 (0.59-1.59)	1.03 (0.72-1.48)
1.03 (0.92-1.17)	Pemetrexed	0.85 (0.44-1.71)	1.43 (0.69-2.88)	1.90 (0.80-4.30)	1.82 (0.75-4.38)	1.94 (0.67-4.33)
1.01 (0.89-1.16)	0.98 (0.84-1.13)	Erlotinib	1.67 (0.65-4.10)	2.23 (0.81-5.83)	2.14 (0.74-5.91)	2.26 (0.83-5.85)
1.04 (0.94-1.14)	1.00 (0.88-1.14)	1.02 (0.90-1.16)	saquinavir	1.34 (0.79-2.14)	1.28 (0.70-2.27)	1.37 (0.83-2.14)
0.69 (0.56-0.83)	0.67 (0.52-0.83)	0.68 (0.53-0.86)	0.66 (0.53-0.83)	irinotecan	0.95 (0.52-1.81)	1.01 (0.61-1.75)
0.71 (0.56-0.90)	0.69 (0.53-0.89)	0.70 (0.54-0.92)	0.68 (0.53-0.88)	1.03 (0.77-1.40)	Pemetrexed	1.06 (0.58-1.96)
0.73 (0.62-0.87)	0.71 (0.57-0.87)	0.72 (0.58-0.88)	0.70 (0.58-0.85)	1.06 (0.82-1.37)	1.03 (0.77-1.36)	irinotecan

Efficacité

Effets secondaires

CBNPC de stade IV L2

Docetaxel	1.10 (0.72-1.73)	1.24 (0.76-2.08)	1.45 (0.97-2.15)	2.02 (0.98-4.27)	2.15 (0.80-5.67)	1.01 (0.49-2.07)
1.04 (0.87-1.24)	Remplacé	1.13 (0.69-1.83)	1.32 (0.82-2.03)	1.84 (0.78-4.29)	1.96 (0.65-5.54)	0.91 (0.39-2.07)
1.06 (0.87-1.29)	1.02 (0.83-1.27)	1.11 (0.70-1.88)	1.17 (0.70-1.88)	1.63 (0.67-3.96)	1.74 (0.57-5.08)	0.81 (0.34-1.92)
1.03 (0.88-1.20)	0.99 (0.83-1.18)	0.97 (0.79-1.18)	1.39 (0.61-3.29)	1.48 (0.51-4.28)	1.48 (0.51-4.28)	0.69 (0.31-1.59)
0.78 (0.59-1.02)	0.75 (0.54-1.03)	0.74 (0.52-1.02)	0.76 (0.55-1.03)	1.06 (0.31-3.53)	1.06 (0.31-3.53)	0.50 (0.18-1.36)
0.88 (0.61-1.26)	0.85 (0.57-1.26)	0.83 (0.55-1.25)	0.85 (0.58-1.27)	1.13 (0.72-1.79)	1.13 (0.72-1.79)	0.47 (0.14-1.57)
0.95 (0.73-1.23)	0.91 (0.66-1.25)	0.89 (0.64-1.23)	0.92 (0.68-1.25)	1.21 (0.83-1.79)	1.07 (0.69-1.68)	1.07 (0.69-1.68)

SSP

RO

CBNPC de stade IV L2

Le meilleur taux de réponse
23 % vs 14 %

La meilleure survie sans
progression..

Docétaxel-Ramucirumab

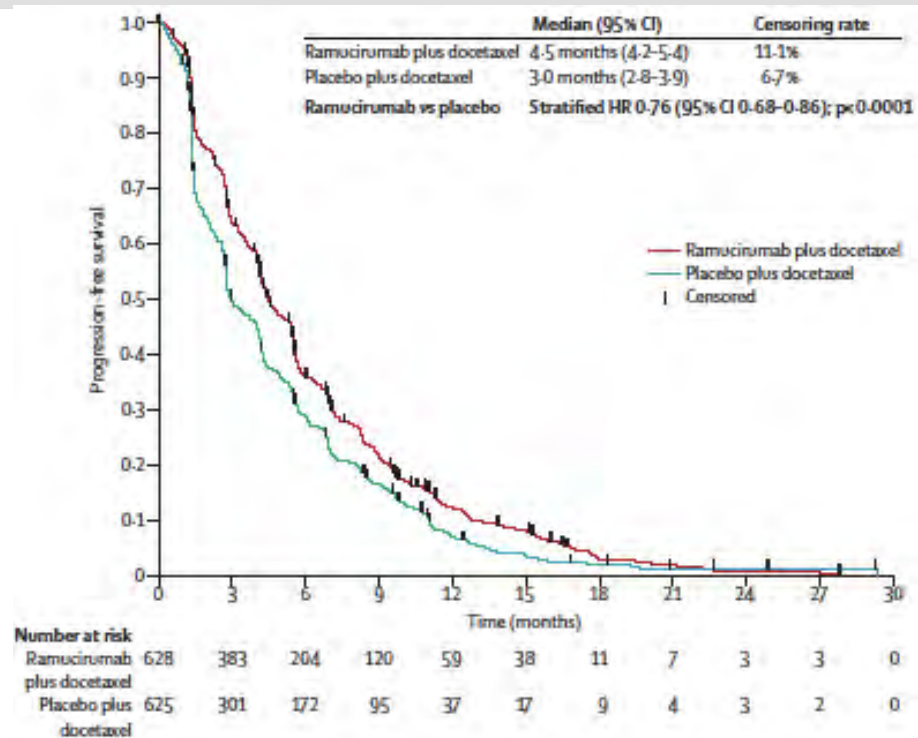
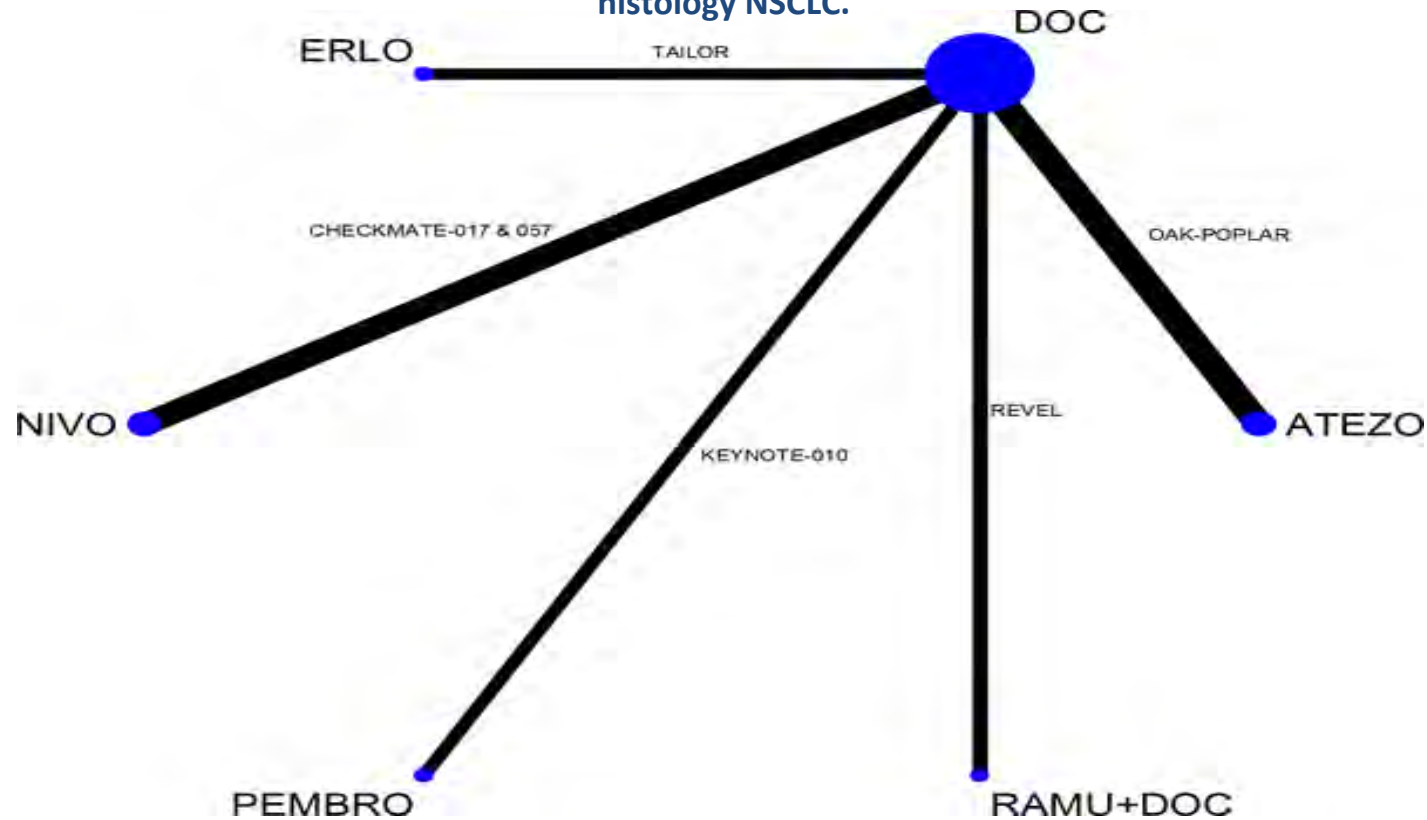
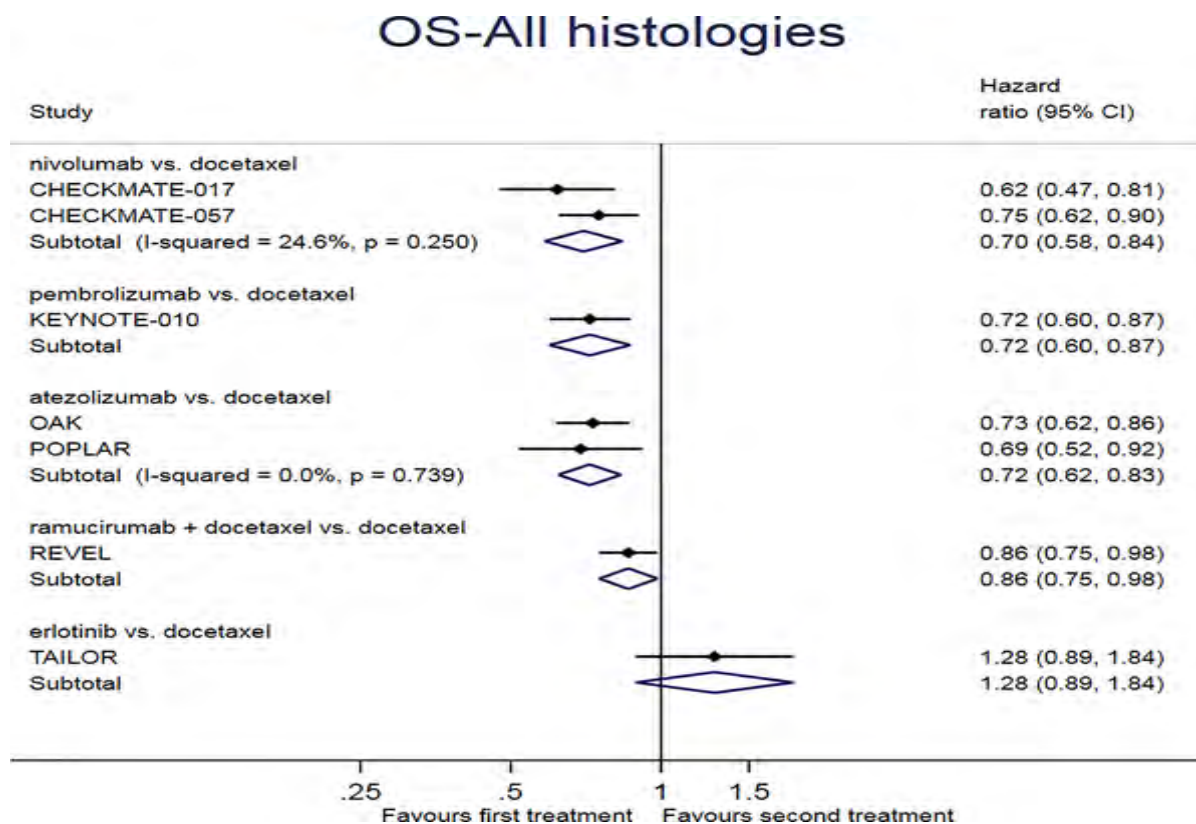


Fig 2. Network of studies comparing effectiveness (OS, PFS) and safety (grade 3–5 drug-related AE) outcomes in all-histology NSCLC.



Armoiry X, Tsertsvadze A, Connock M, Royle P, Melendez-Torres GJ, et al. (2018) Comparative efficacy and safety of licensed treatments for previously treated non-small cell lung cancer: A systematic review and network meta-analysis. PLOS ONE 13(7): e0199575. <https://doi.org/10.1371/journal.pone.0199575>
<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0199575>

Fig 3. Pairwise meta-analyses, OS in all-histology NSCLC.



Armoiry X, Tsertsvadze A, Connock M, Royle P, Melendez-Torres GJ, et al. (2018) Comparative efficacy and safety of licensed treatments for previously treated non-small cell lung cancer: A systematic review and network meta-analysis. PLOS ONE 13(7): e0199575. <https://doi.org/10.1371/journal.pone.0199575>
<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0199575>

Table 2. Network meta-analyses: PFS, OS, grade 3–5 AE in all-histology NSCLC.

OS comparisons (Findings are expressed as HR (95% CI), use of random-effects model.							
Drug	SUCRA	Nivo	Atezo	Pembro	Ramu+Doc	Doc	Erlo
Nivo	0.82		0.98 (0.79,1.21)	0.98 (0.77,1.25)	0.82 (0.67,1.00)	0.71 (0.61,0.82)	0.55 (0.37,0.82)
Atezo	0.77			1.00 (0.79,1.27)	0.84 (0.69,1.02)	0.72 (0.62,0.83)	0.56 (0.38,0.83)
Pembro	0.77				0.84 (0.67,1.05)	0.72 (0.60,0.87)	0.56 (0.37,0.85)
Ramu+Doc	0.42					0.86 (0.75,0.98)	0.67 (0.46,0.99)
Doc	0.18						0.78 (0.54,1.12)
Erlo	0.02						
PFS comparisons (Findings expressed as HR (95% CI), use of random-effects model.							
Drug	SUCRA	Ramu+Doc	Nivo	Pembro	Atezo	Doc	Erlo
Ramu+Doc	0.84		0.98 (0.68,1.41)	0.86 (0.58,1.29)	0.80 (0.57,1.14)	0.76 (0.58,0.99)	0.55 (0.35,0.88)
Nivo	0.81			0.88 (0.60,1.29)	0.82 (0.59,1.13)	0.77 (0.61,0.99)	0.56 (0.36,0.88)
Pembro	0.57				0.93 (0.64,1.35)	0.88 (0.65,1.18)	0.64 (0.39,1.03)
Atezo	0.45					0.95 (0.76,1.18)	0.69 (0.44,1.06)
Doc	0.31						0.72 (0.50,1.06)
Erlo	0.02						
Grade 3–5 AE comparisons (Findings are expressed as RR (95% CI), use of random-effects model.							
Drug	SUCRA	Nivo	Atezo	Pembro	Erlo	Doc	Ramu+Doc
Nivo	1		0.55 (0.38,0.79)	0.52 (0.34,0.81)	0.46 (0.29,0.72)	0.18 (0.14,0.25)	0.17 (0.12,0.23)
Atezo	0.68			0.95 (0.66,1.38)	0.83 (0.55,1.23)	0.34 (0.28,0.41)	0.31 (0.25,0.38)
Pembro	0.63				0.87 (0.54,1.39)	0.35 (0.26,0.48)	0.32 (0.23,0.44)
Erlo	0.49					0.41 (0.29,0.58)	0.37 (0.26,0.53)
Doc	0.2						0.91 (0.85,0.97)
Ramu+Doc	0						

Note: The table must be read as the drug on the column against the drug on the row. For example the PFS HR of ramucirumab+docetaxel against nivolumab is 0.98 (95%CI 0.68, 1.41).

<https://doi.org/10.1371/journal.pone.0199575.t002>

Armoiry X, Tsertsvadze A, Connock M, Royle P, Melendez-Torres GJ, et al. (2018) Comparative efficacy and safety of licensed treatments for previously treated non-small cell lung cancer: A systematic review and network meta-analysis. PLOS ONE 13(7): e0199575. <https://doi.org/10.1371/journal.pone.0199575>
<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0199575>

CBNPC de stade IV L2

SUCRA (surface under cumulative Ranking Curve) :

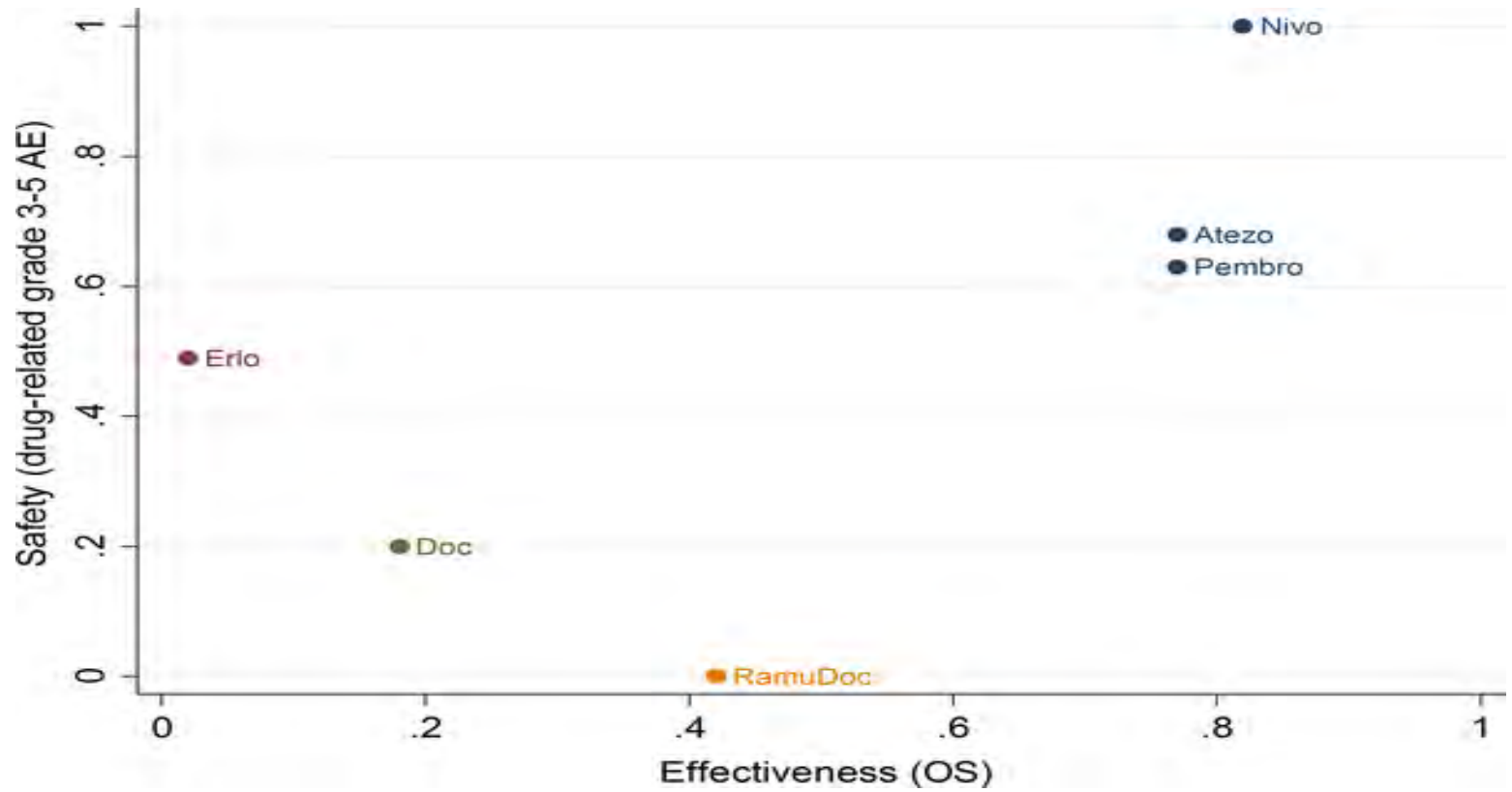
Epidermoïde

Nivo > ? Mais faible nombre d'épi dans certaines études

Non épidermoïde

Nivo = Pembro = Atézo > Pem > Ninde+ Doc, = Ramu+Doc > Doc

Fig 4. Clustered ranking plot on effectiveness (OS) and safety (grade 3–5 drug-related AE) both expressed as SUCRAS.



Armoiry X, Tsertsvadze A, Connock M, Royle P, Melendez-Torres GJ, et al. (2018) Comparative efficacy and safety of licensed treatments for previously treated non-small cell lung cancer: A systematic review and network meta-analysis. PLOS ONE 13(7): e0199575. <https://doi.org/10.1371/journal.pone.0199575>
<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0199575>

CBNPC de stade IV L2

MOINS D'EFFETS SECONDAIRES G3-G4-G5 avec le Nivolumab vs Pembro ou Atézo???
MEME TAUX D'EFFETS SECONDAIRES G1-G5 entre les 3 IO...

BIAIS: 1 visite médicale J1 – J15 – J29 – J43 – bilan vers J 55

 1 visite médicale J1 – J22 – J43 – bilan vers J 60

Importance de la surveillance médicale, notamment au début du traitement

Symptômes IMMUCARE (saisie hebdomadaire)
 Dermatologie (C.H. LYON SUD)



Choix de l'établissement Choix du formulaire **Saisie du formulaire**

Evaluez chaque semaine les effets indésirables liés à votre traitement par immunothérapie. Vos réponses seront transmises à la salle de soins.

EVALUEZ VOS SYMPTOMES

- **Fatigue**

0 1 2 3

Pas de fatigue
- **Maux de tête**

0 1 2 3

Pas de mal de tête
- **Essoufflement**

0 1 2 3 4

Pas d'essoufflement
- **Nausées, vomissements**

0 1 2 3 4

Pas de nausée ni de vomissement
- **Eruption cutanée**

0 1 2 3 4

Pas d'éruption
- **Diarrhée**

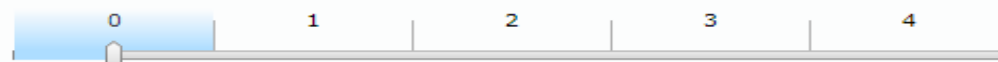
0 1 2 3 4

Pas de diarrhée



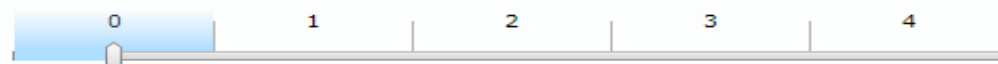
Suite

● **Perte d'appétit**



Pas de perte d'appétit

● **Fièvre**



Pas de fièvre

● **Fourmillements des extrémités**



Pas de fourmillement

● **Douleur**



Pas de douleur

● **Trouble visuel**



Aucun trouble visuel

● Quel est votre poids ? (kg)

● Souhaitez-vous nous signaler autre chose, être rappelé ?

En cas d'urgence, n'utilisez pas cette zone : contactez le SAMU en composant le 15.

Précédent

Valider

CBNPC de stade IV L2

Nivolumab: 1053 € les 100mg: 240 mg/14 jours: 7581,6 Euros pour 6 semaines

Pembrolizumab: 2672 € les 100 mg soit par 6 semaines 10 688 Euros

Atézolizumab??

Nivolumab 1 HJ de plus, 1 VSL, 1 bio / 6 semaines que Pembrolizumab = moins de 3100 Euros.... .

CBNPC de stade IV L2



MERCI POUR ATTENTION



Université Claude Bernard  Lyon 1