

# Traitements de 1e ligne des CBNPC métastatiques sans addiction oncogénique

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Boulogne-Billancourt



## Liens d'intérêt

### *Honoraria / advisory board :*

Amgen, AstraZeneca, Boehringer-Ingelheim, Bristol-Myers-Squibb, Janssen, Lilly, MSD, Novartis, Oncodesign, Roche, Sanofi, Takeda

### *Research grants (institution) :*

AstraZeneca, Bristol-Myers-Squibb, Roche

# TRAITEMENTS DE 1<sup>E</sup> LIGNE

## ***Éléments décisionnaires préliminaires :***

*Âge*

*PS*

*Comorbidités / comédications*

## ***Traitement « historique » de référence :***

***Sel de platine +***

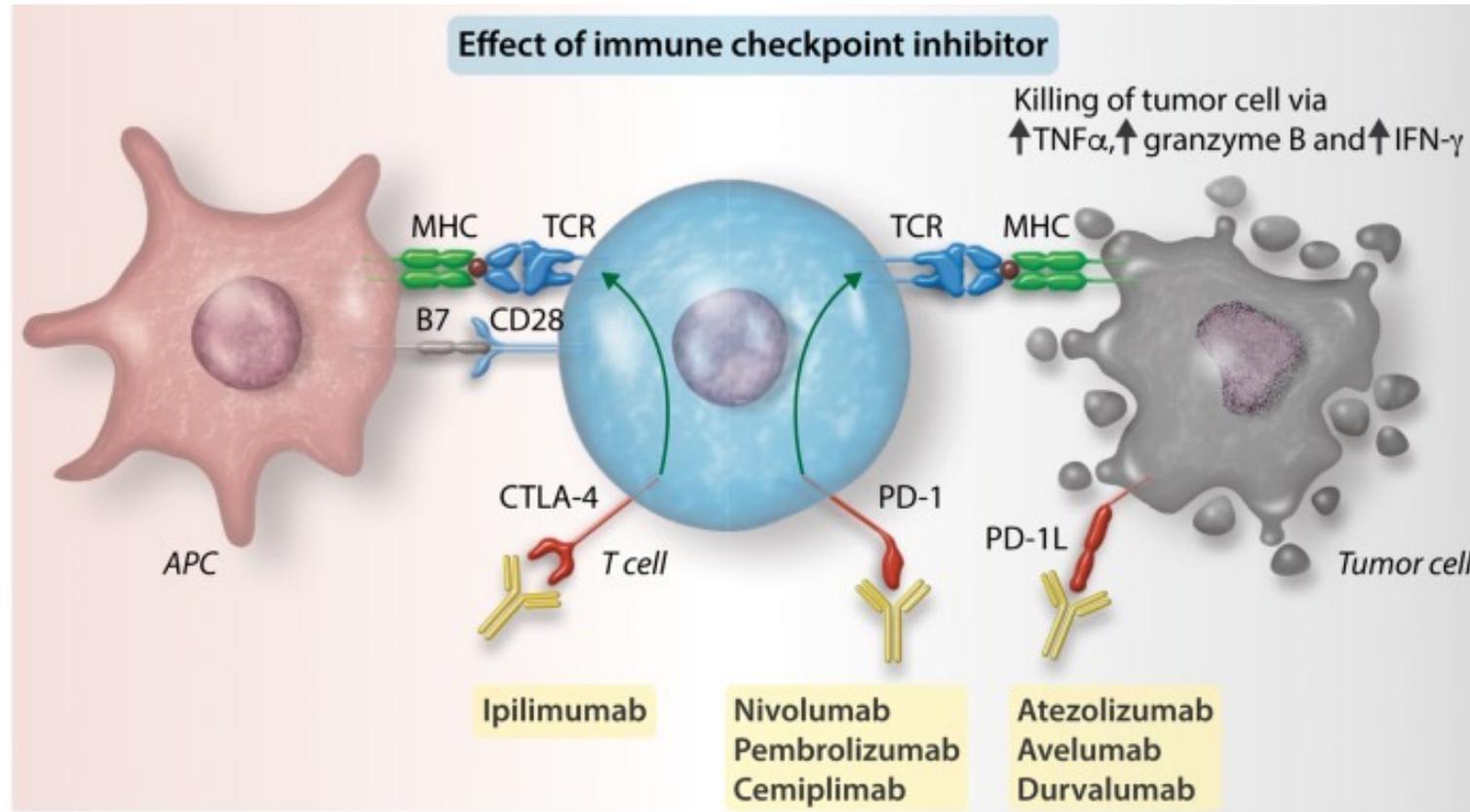
*Taxanes (paclitaxel, docetaxel)*

*Pemetrexed (non-épidermoïdes), avec maintenance au décours*

*Gemcitabine*

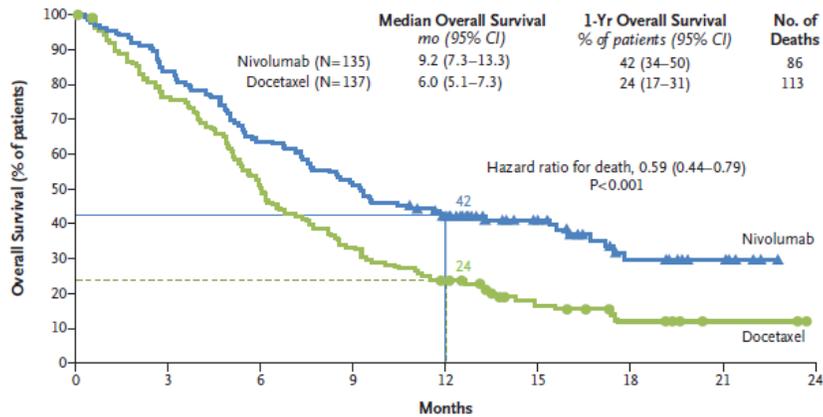
***Jusqu'en 2015 : SG ≈10-16 mois***

# Inhibiteurs des point de contrôle immunitaires (ICIs)



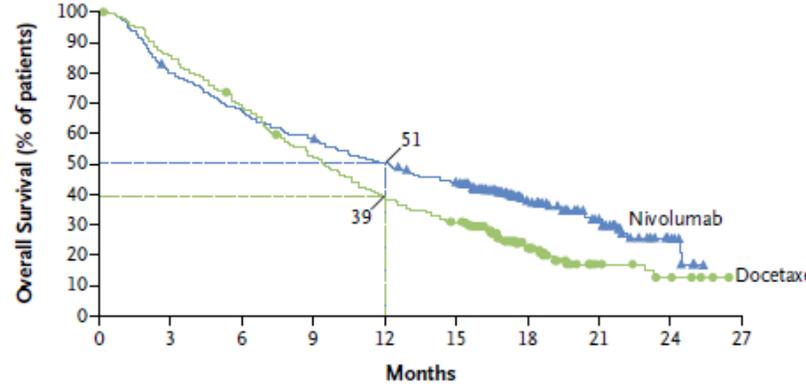
# 2015 : arrivée de l'immunothérapie en L2

## Nivolumab - épidermoïdes



No. at Risk	0	3	6	9	12	15	18	21	24
Nivolumab	135	113	86	69	52	31	15	7	0
Docetaxel	137	103	68	45	30	14	7	2	0

## Nivolumab - non-épidermoïdes

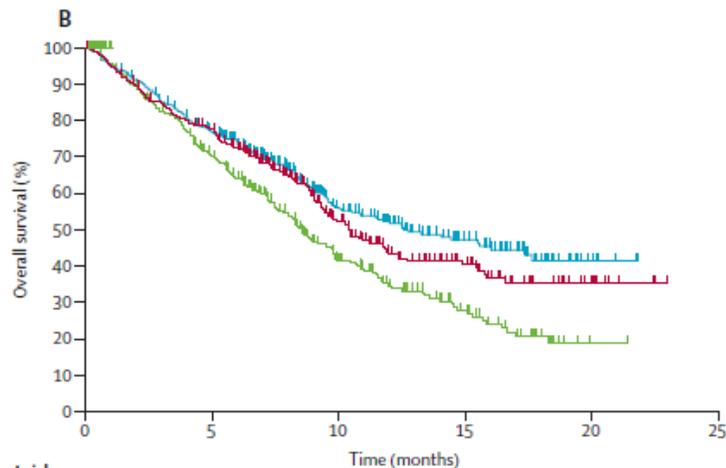


	No. of Deaths/ Total No. of Patients	Median Overall Survival (95% CI) mo	1-Yr Overall Survival Rate (95% CI) %
Nivolumab	190/292	12.2 (9.7-15.0)	51 (45-56)
Docetaxel	223/290	9.4 (8.1-10.7)	39 (33-45)

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

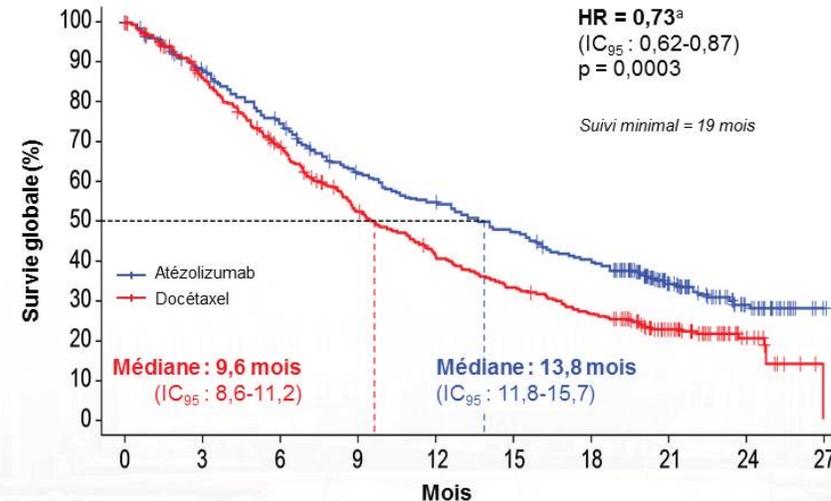
No. at Risk	0	3	6	9	12	15	18	21	24	27
Nivolumab	292	232	194	169	146	123	62	32	9	0
Docetaxel	290	244	194	150	111	88	34	10	5	0

## Pembrolizumab - PDL1 ≥ 1%



Number at risk	0	5	10	15	20	25
Pembrolizumab 2 mg/kg	344	259	115	49	12	0
Pembrolizumab 10 mg/kg	346	255	124	56	6	0
Docetaxel	343	212	79	33	1	0

## Atezolizumab



Patients à risque	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	26	16	6	3	

**Brahmer et al. NEJM 2015;**  
**Borghaei et al. NEJM 2015 ;**  
**Herbst et al. Lancet 2015**  
**Rittmeyer et al. Lancet 2017**

# TRAITEMENTS DE 1<sup>E</sup> LIGNE

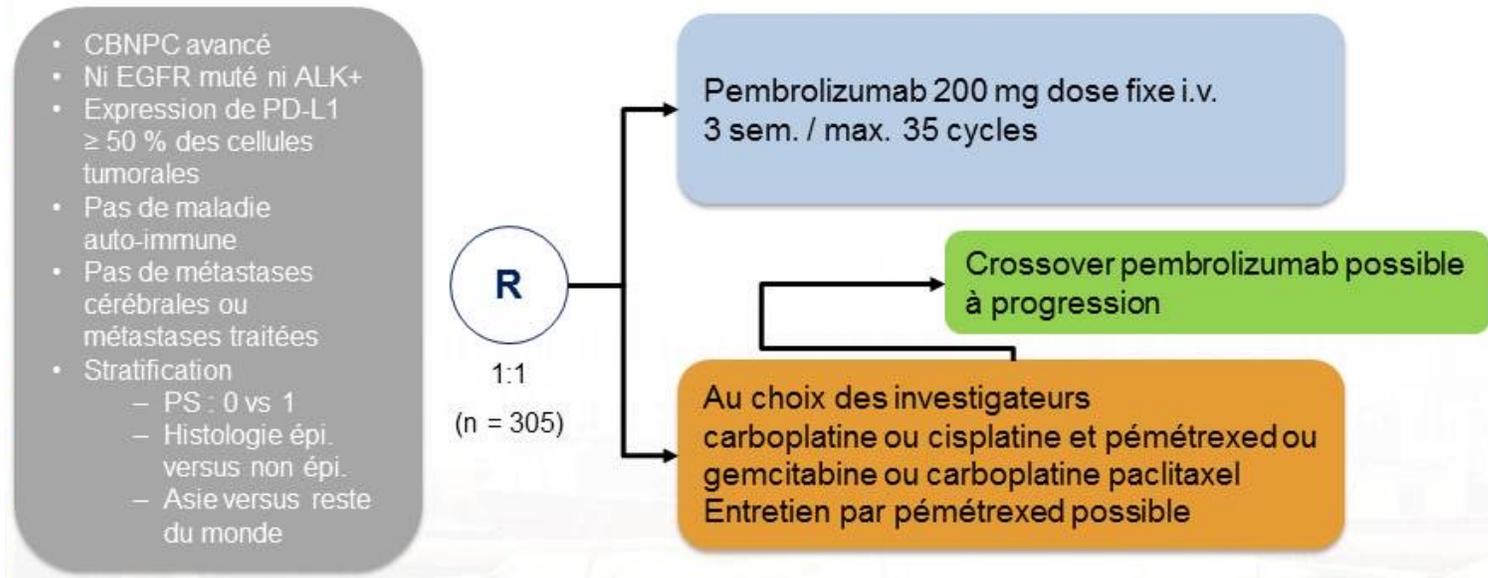
Stratégies à base d'immunothérapie

IMMUNOTHERAPIE SEULE

Populations particulières

# Pembrolizumab versus Chemotherapy for PD-L1-Positive Non-Small-Cell Lung Cancer

Martin Reck, M.D., Ph.D., Delvys Rodríguez-Abreu, M.D.,  
Andrew G. Robinson, M.D., Rina Hui, M.B., B.S., Ph.D., Tibor Csőszi, M.D.,  
Andrea Fülöp, M.D., Maya Gottfried, M.D., Nir Peled, M.D., Ph.D.,  
Ali Tafreshi, M.D., Sinead Cuffe, M.D., Mary O'Brien, M.D., Suman Rao, M.D.,  
Katsuyuki Hotta, M.D., Ph.D., Melanie A. Leiby, Ph.D., Gregory M. Lubiniecki, M.D.,  
Yue Shentu, Ph.D., Reshma Rangwala, M.D., Ph.D., and Julie R. Brahmer, M.D.,  
for the KEYNOTE-024 Investigators\*

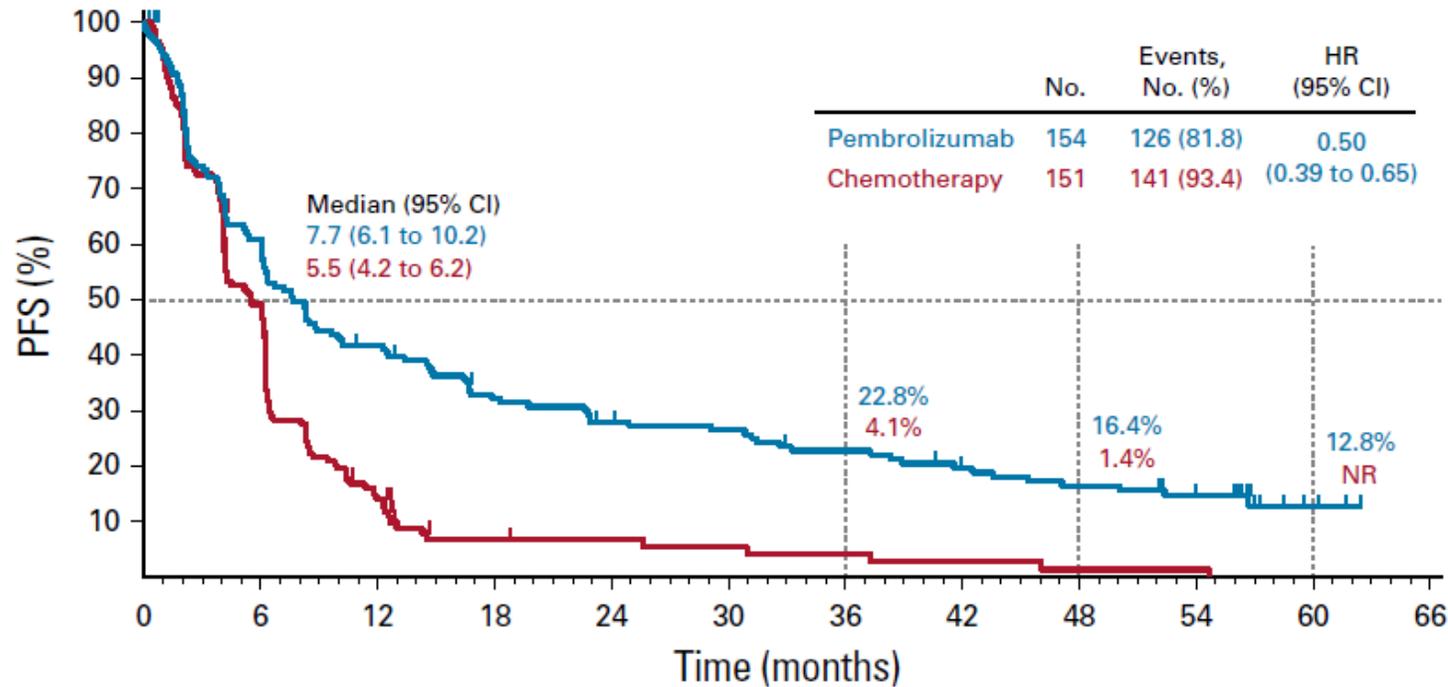


**Objectif principal : SSP (ICR)**

Objectifs secondaires : SG, ORR, toxicité

Objectif exploratoire : durée de la réponse

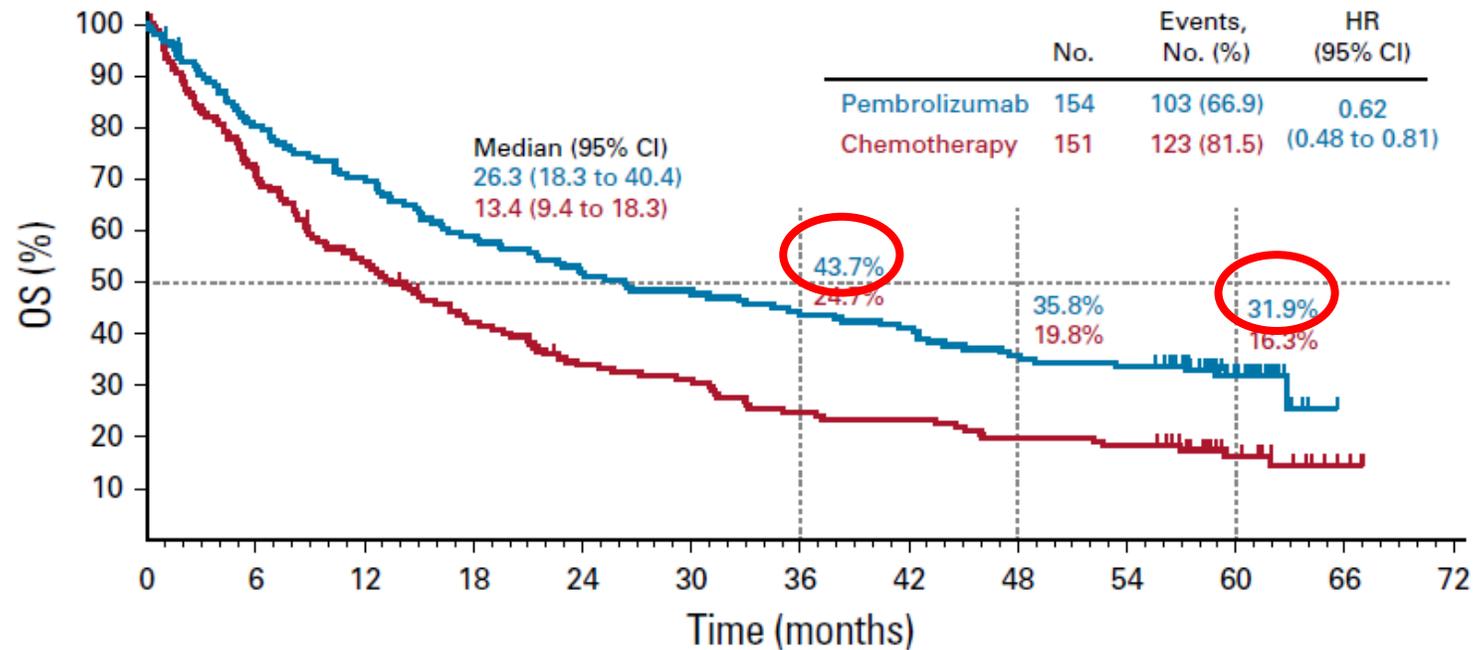
# KN-024 – Survie sans progression



No. at risk:

Pembrolizumab	154	92	62	46	38	36	30	24	20	15	3	0
Chemotherapy	151	73	20	6	5	4	3	2	1	1	0	0

# KN-024 – Survie globale

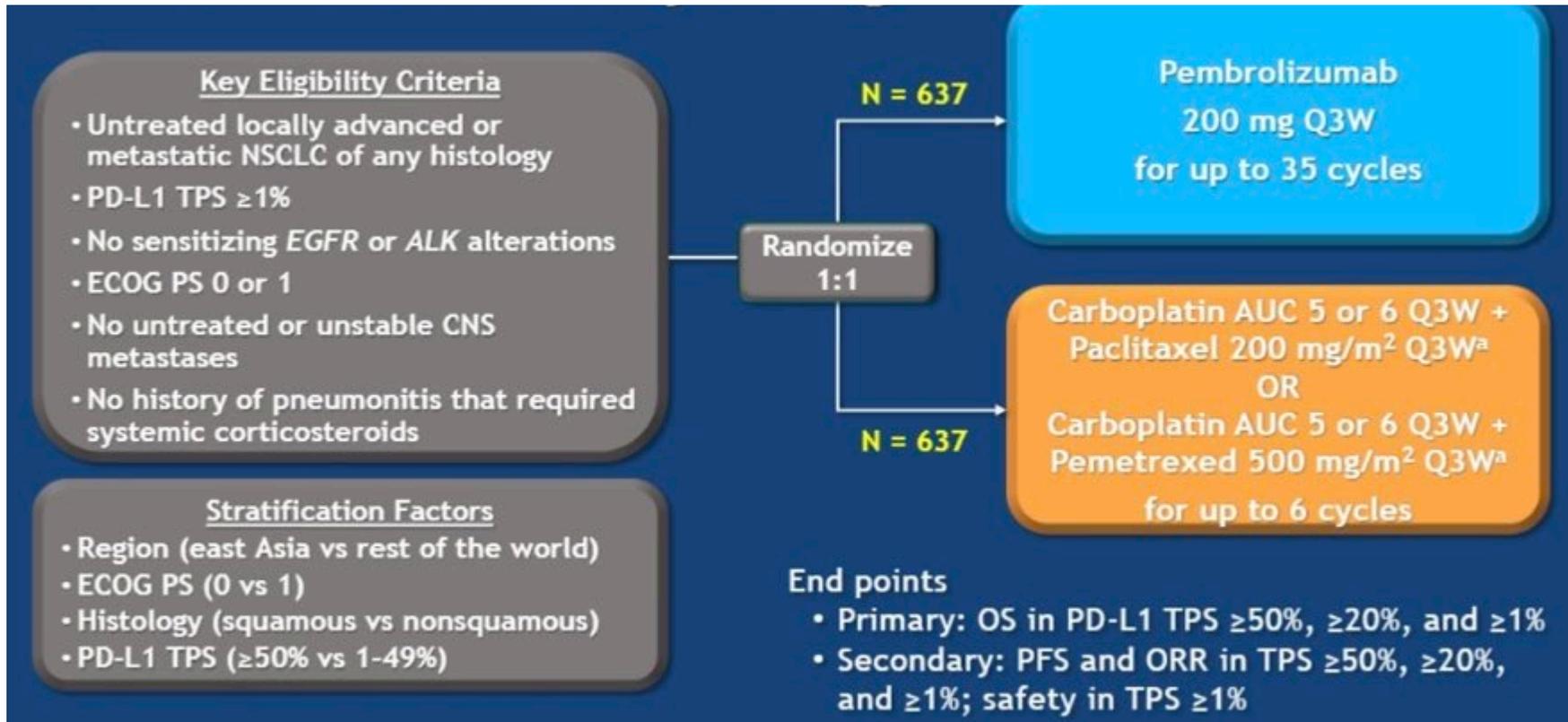


No. at risk:

Pembrolizumab	154	121	106	89	78	73	66	62	54	51	20	0	0
Chemotherapy	151	108	80	61	48	44	35	33	28	26	13	3	0

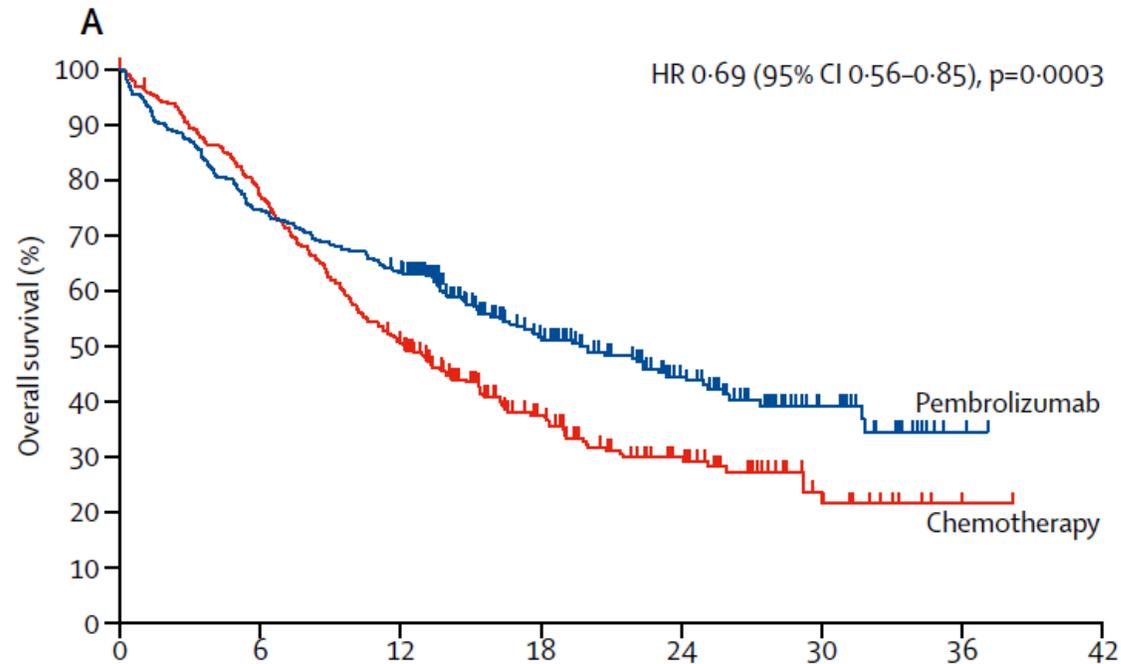
# Pembrolizumab versus chemotherapy for previously untreated, PD-L1-expressing, locally advanced or metastatic non-small-cell lung cancer (KEYNOTE-042): a randomised, open-label, controlled, phase 3 trial

Tony S K Mok, Yi-Long Wu, Iveta Kudaba, Dariusz M Kowalski, Byoung Chul Cho, Hande Z Turna, Gilberto Castro Jr, Vichien Srimuninnimit, Konstantin K Laktionov, Igor Bondarenko, Kaoru Kubota, Gregory M Lubiniecki, Jin Zhang, Debra Kush, Gilberto Lopes, for the KEYNOTE-042 Investigators\*

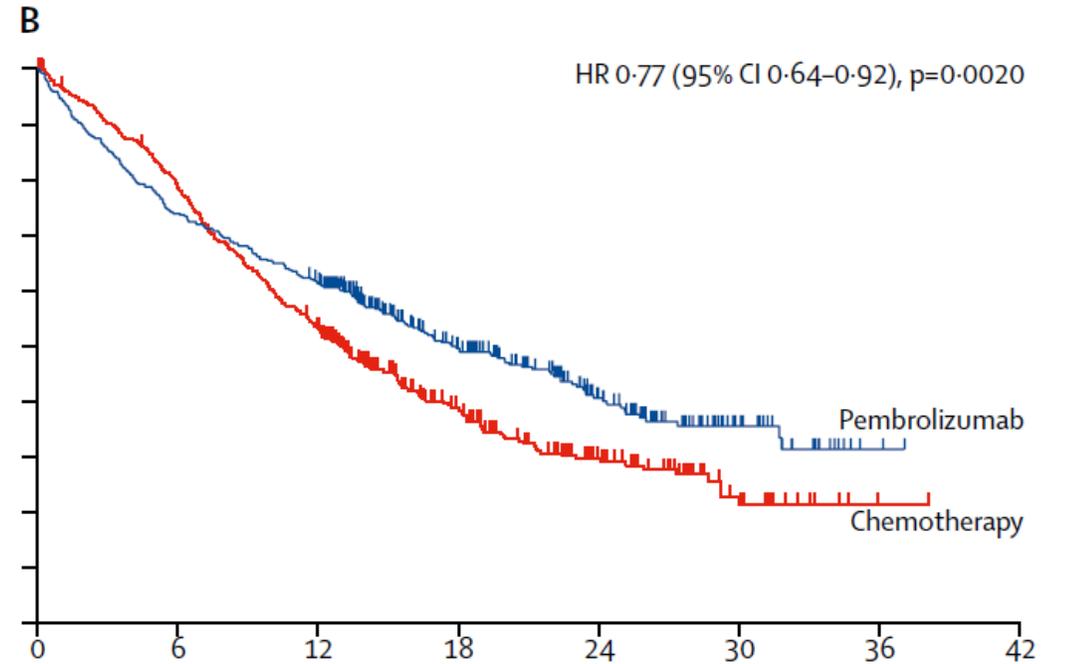


# KN-042 - Survie globale

PD-L1 $\geq$ 50%



PD-L1 $\geq$ 20%

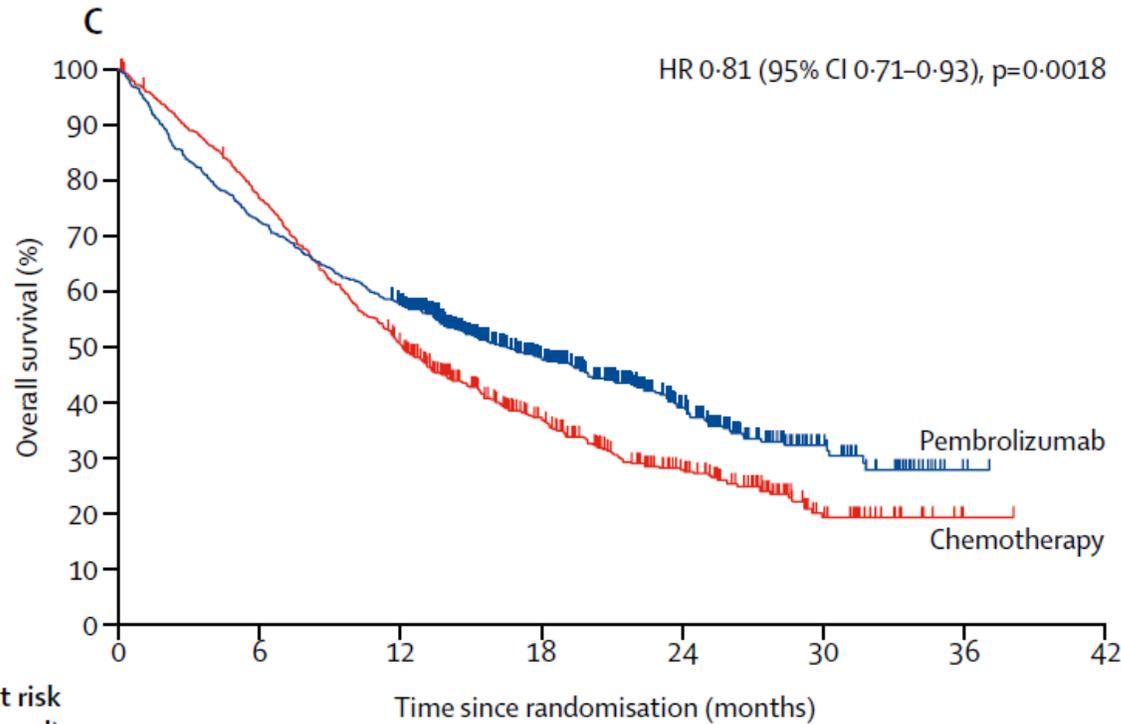


Number at risk  
(censored)

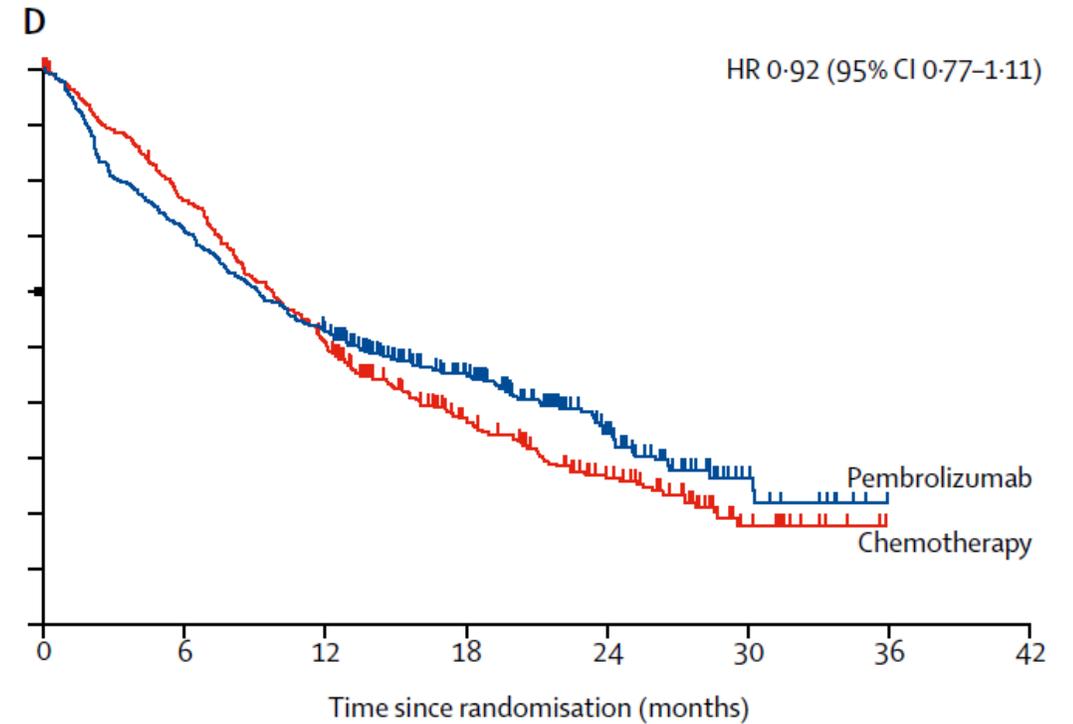
	0	6	12	18	24	30	36	42	0	6	12	18	24	30	36	42
Pembrolizumab group	299 (0)	224 (0)	189 (1)	107 (55)	59 (91)	22 (122)	2 (140)	0 (142)	413 (0)	305 (0)	251 (2)	144 (70)	73 (120)	24 (161)	2 (181)	0 (183)
Chemotherapy group	300 (0)	231 (2)	149 (4)	75 (46)	40 (67)	11 (90)	1 (100)	0 (101)	405 (0)	313 (6)	210 (8)	106 (64)	53 (94)	14 (125)	1 (138)	0 (139)

# KN-042 - Survie globale

PD-L1 $\geq$ 1%



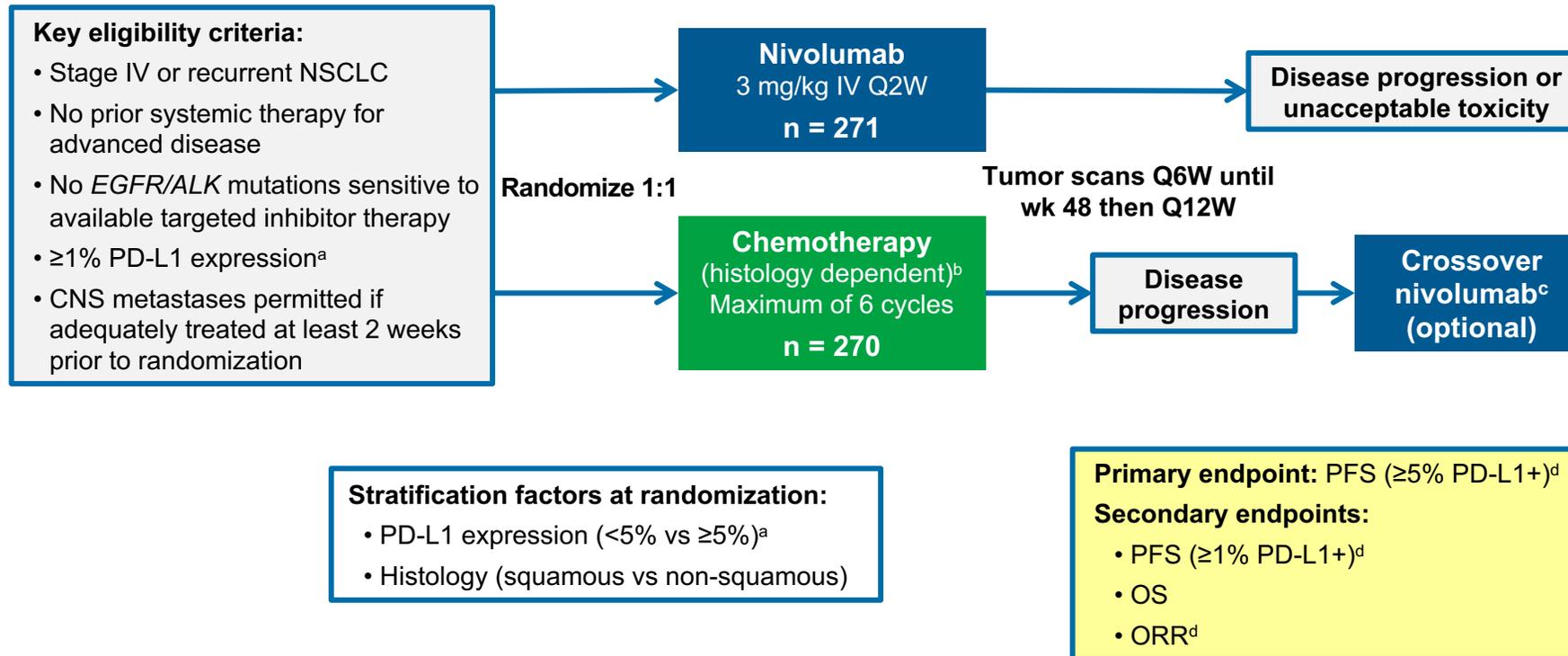
PD-L1 1-49%



	0	6	12	18	24	30	36	42	0	6	12	18	24	30	36	42	
<b>Number at risk (censored)</b>																	
Pembrolizumab group	637 (0)	463 (0)	365 (3)	214 (104)	112 (174)	35 (235)	2 (264)	0 (266)	338 (0)	239 (0)	176 (2)	107 (49)	53 (83)	13 (113)	0 (124)	0 (124)	
Chemotherapy group	637 (0)	485 (6)	316 (10)	166 (88)	88 (128)	24 (175)	1 (198)	0 (199)	337 (0)	254 (4)	167 (6)	91 (42)	48 (61)	13 (85)	0 (98)	0 (98)	

# First-Line Nivolumab in Stage IV or Recurrent Non–Small-Cell Lung Cancer

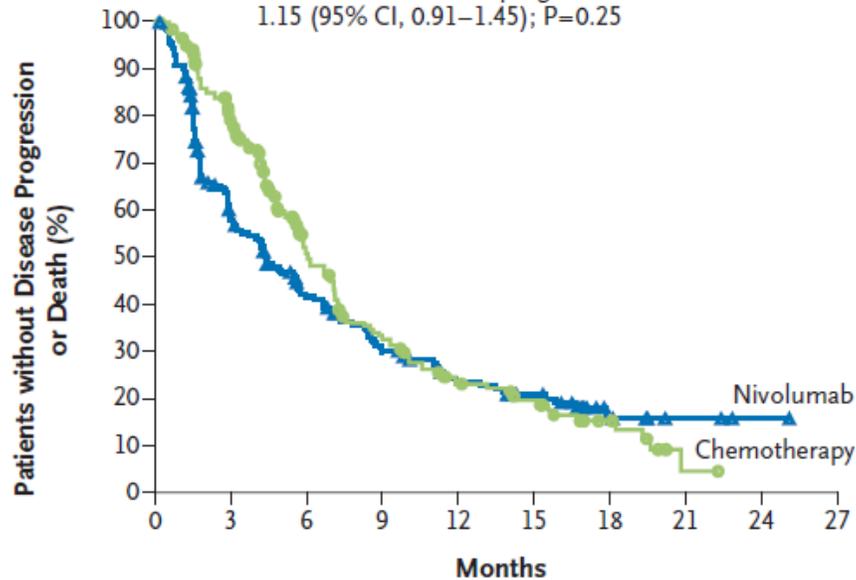
D.P. Carbone, M. Reck, L. Paz-Ares, B. Creelan, L. Horn, M. Steins, E. Felip, M.M. van den Heuvel, T.-E. Ciuleanu, F. Badin, N. Ready, T.J.N. Hiltermann, S. Nair, R. Juergens, S. Peters, E. Minenza, J.M. Wrangle, D. Rodriguez-Abreu, H. Borghaei, G.R. Blumenschein, Jr., L.C. Villaruz, L. Havel, J. Krejci, J. Corral Jaime, H. Chang, W.J. Geese, P. Bhagvatheeswaran, A.C. Chen, and M.A. Socinski, for the CheckMate 026 Investigators\*



# CM-026 – population PD-L1 $\geq 5\%$

	Median Progression-free Survival (95% CI) <i>mo</i>	1-Yr Progression-free Survival Rate %
Nivolumab (N=211)	4.2 (3.0–5.6)	24
Chemotherapy (N=212)	5.9 (5.4–6.9)	23

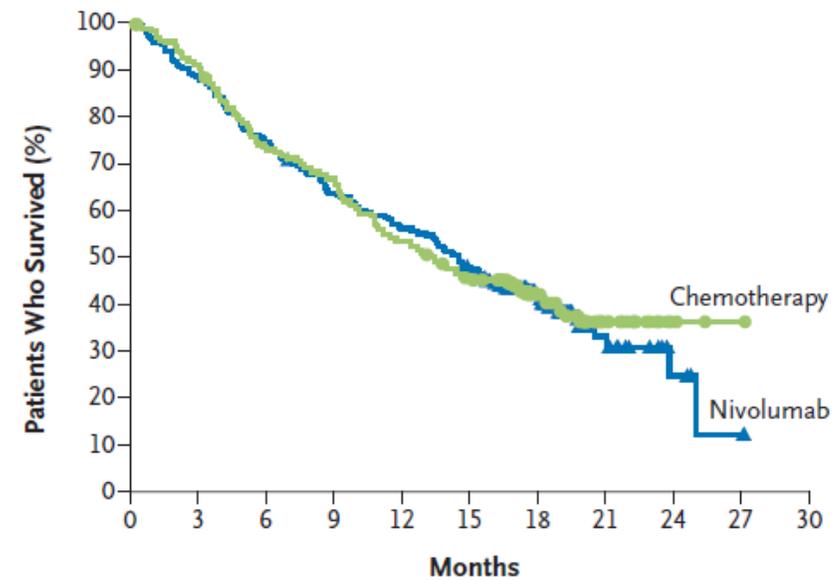
Hazard ratio for disease progression or death, 1.15 (95% CI, 0.91–1.45); P=0.25



No. at Risk	0	3	6	9	12	15	18	21	24	27
Nivolumab	211	104	71	49	35	24	6	3	1	0
Chemotherapy	212	144	74	47	28	21	8	1	0	0

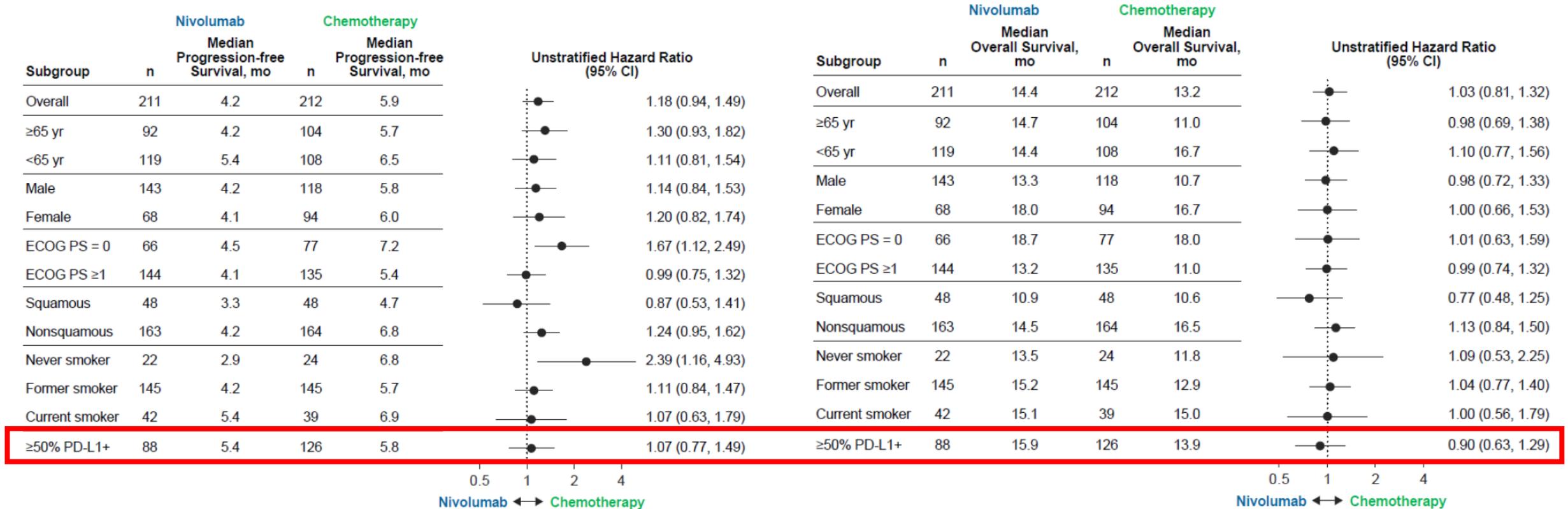
	Median Overall Survival (95% CI) <i>mo</i>	1-Yr Overall Survival Rate %
Nivolumab (N=211)	14.4 (11.7–17.4)	56
Chemotherapy (N=212)	13.2 (10.7–17.1)	54

Hazard ratio for death, 1.02 (95% CI, 0.80–1.30)



No. at Risk	0	3	6	9	12	15	18	21	24	27	30
Nivolumab	211	186	156	133	118	98	49	14	4	0	0
Chemotherapy	212	186	153	137	112	91	50	15	3	1	0

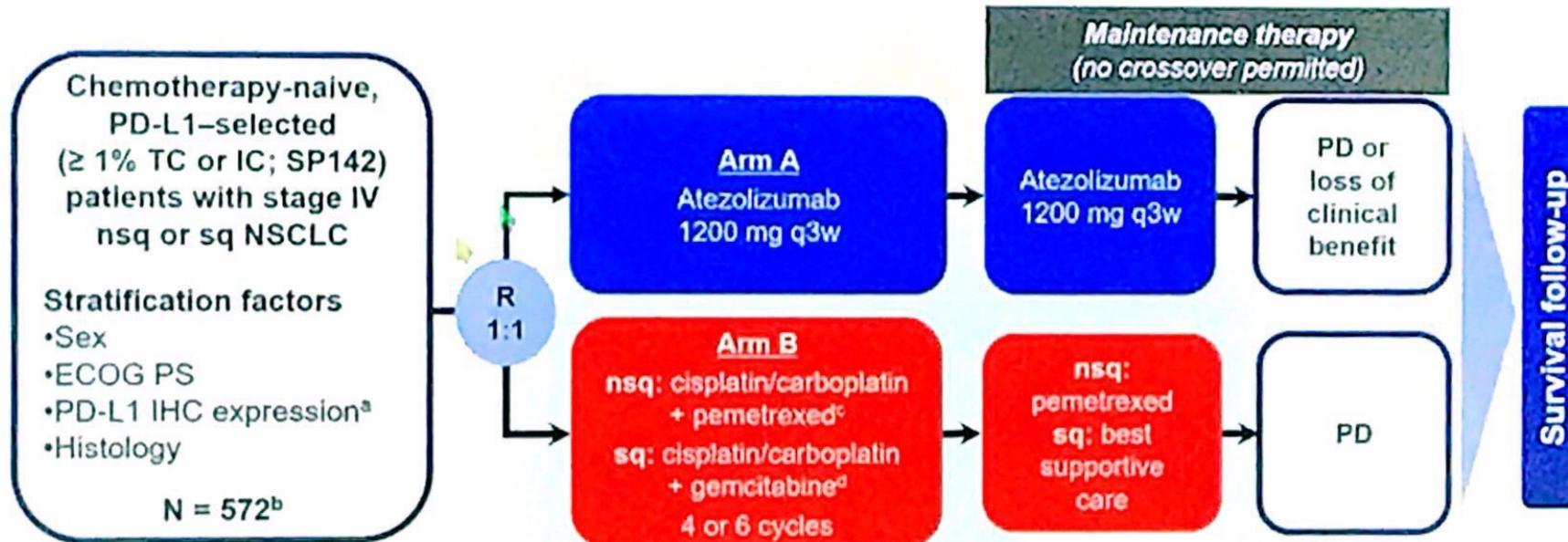
# CM-026 – population PD-L1 ≥5%



# Atezolizumab for First-Line Treatment of PD-L1–Selected Patients with NSCLC

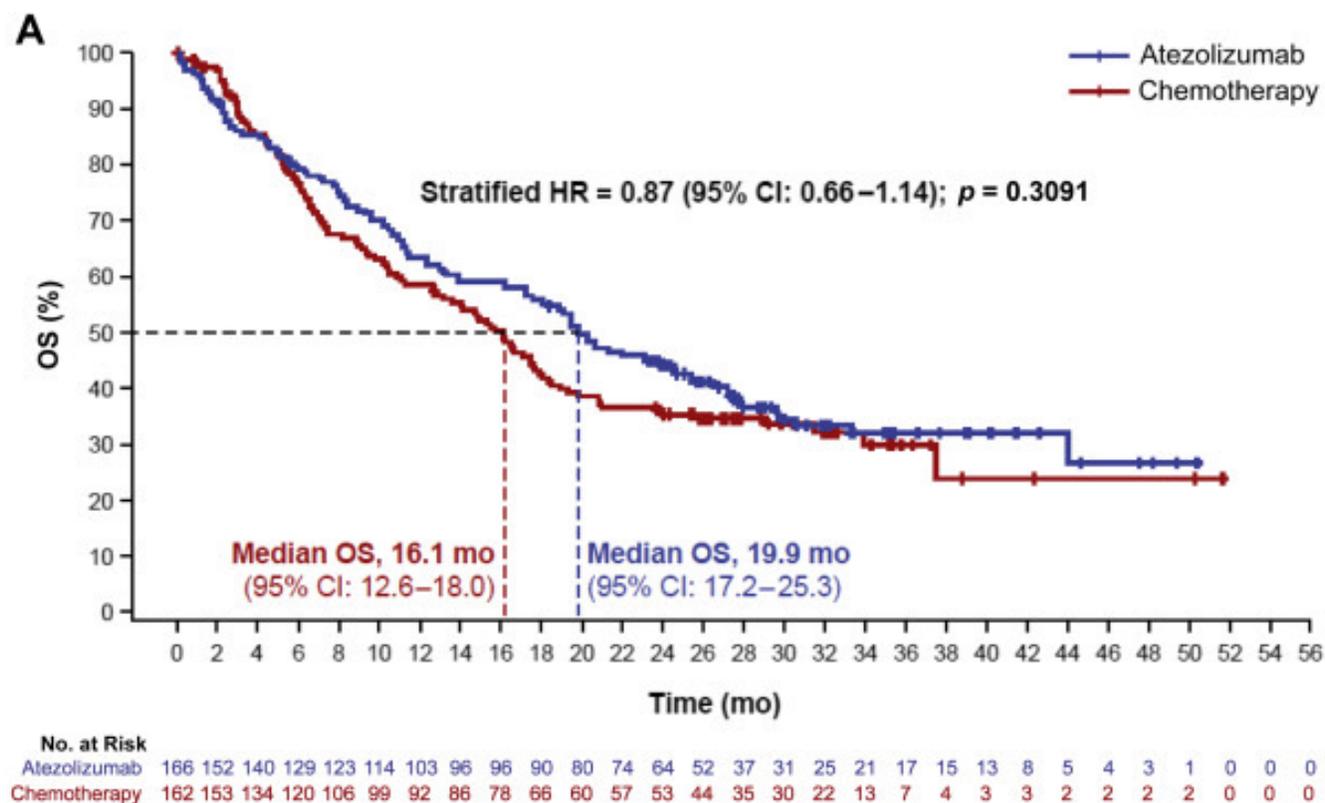
Roy S. Herbst, M.D., Ph.D., Giuseppe Giaccone, M.D., Ph.D.,  
Filippo de Marinis, M.D., Niels Reinmuth, M.D., Alain Vergnenegre, M.D.,  
Carlos H. Barrios, M.D., Masahiro Morise, M.D., Enriqueta Felip, M.D.,  
Zoran Andric, M.D., Sarayut Geater, M.D., Mustafa Özgüroğlu, M.D.,  
Wei Zou, Ph.D., Alan Sandler, M.D., Ida Enquist, Ph.D.,  
Kimberly Komatsubara, M.D., Yu Deng, Ph.D., Hiroshi Kuriki, M.Sc.,  
Xiaohui Wen, M.D., Mark McClelland, Ph.D., Simonetta Mocci, M.D., Ph.D.,  
Jacek Jassem, M.D., Ph.D., and David R. Spigel, M.D.

*ImPOWER-110*



# ImPOWER-110 : résultats actualisés

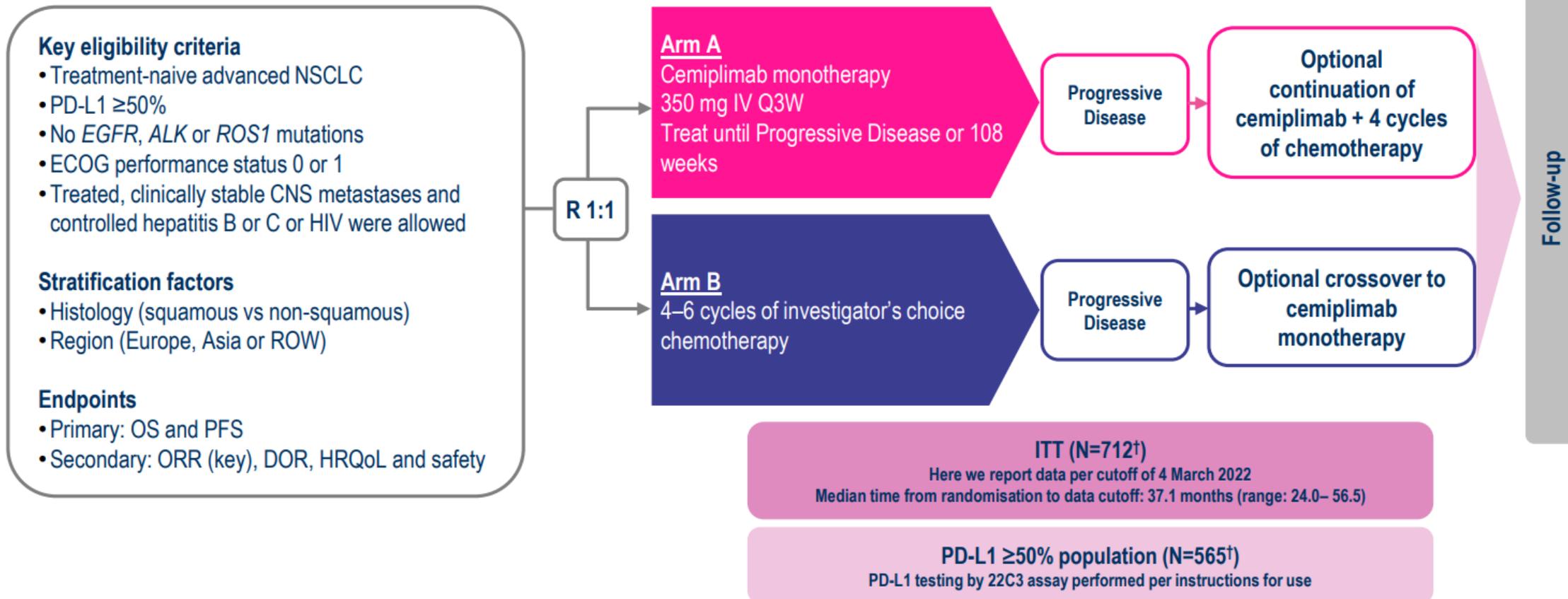
## High-intermediate PDL1



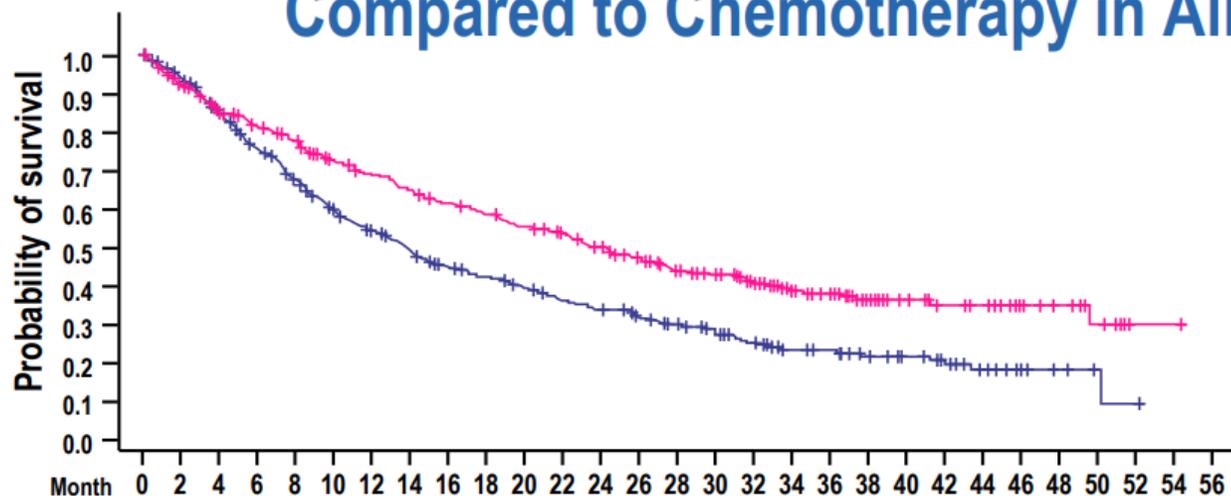
Analyses hiérarchiques pour l'OS  
→ Pas de possibilité d'analyses  
du groupe tout PDL1

Analyses actualisées pour les PDL1 élevés :  
HR= 0,76 (95% CI 0,54-1,09)  
médiane = 20,2 versus 14,7 mois

# EMPOWER-Lung 1 Study Design – 3-Year Outcomes

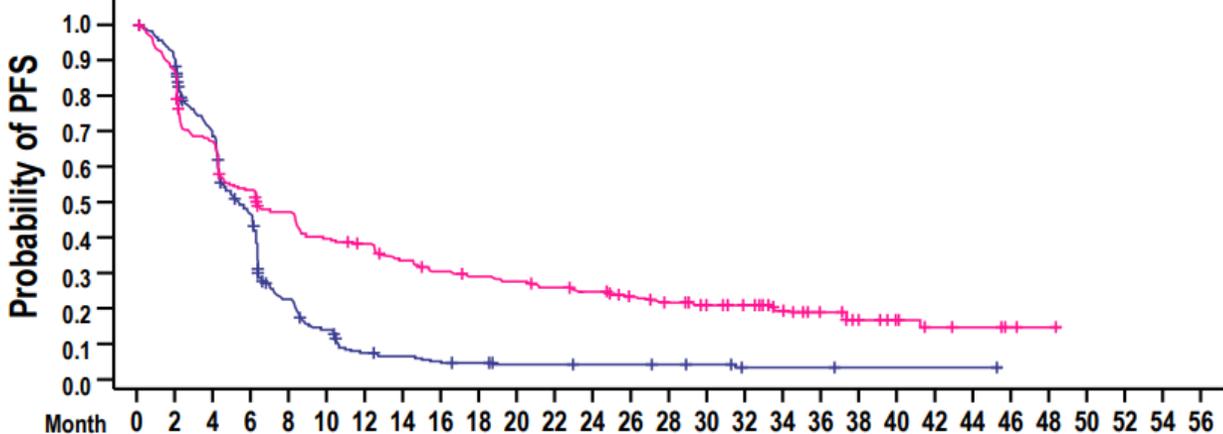


# At 3-Year Follow-up Cemiplimab Produced Significantly Longer OS and PFS Compared to Chemotherapy in All Randomized Patients



Patients at risk

Month	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52	54	56
Cemiplimab	357	321	286	269	254	229	215	202	190	179	169	159	147	130	110	103	88	63	52	36	29	23	21	13	10	6	1	1	0
Chemotherapy	355	318	278	242	211	182	160	143	126	117	106	95	88	78	69	60	51	39	35	29	22	17	11	6	4	2	1	0	0



Patients at risk

Month	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52	54	56
Cemiplimab	357	295	229	183	158	134	128	110	98	93	88	82	77	69	60	52	43	29	20	12	9	6	5	2	1	0	0	0	0
Chemotherapy	355	296	222	147	67	41	21	17	13	12	8	8	7	7	6	5	2	2	2	1	1	1	1	0	0	0	0	0	0

## ITT: 3-year outcomes

	Patients, n	Median OS, months
Cemiplimab	357	23.4 (95% CI, 19.4, 27.4)
Chemotherapy	355	13.7 (95% CI, 11.2, 16.2)
		<b>HR, 0.63 (95% CI, 0.52–0.77); P=0.0001</b>

## ITT: 3-year outcomes

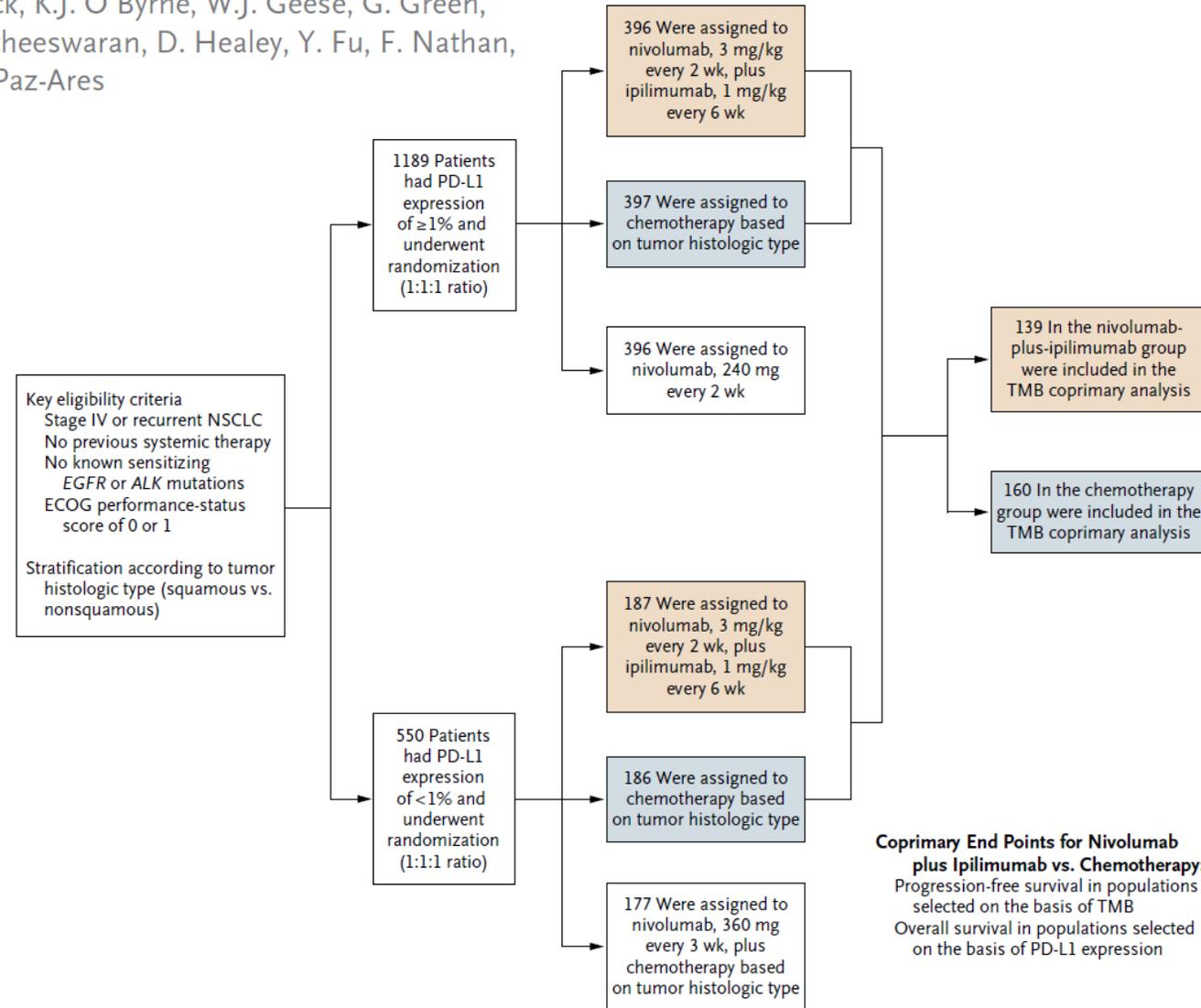
	Patients, n	Median PFS, months
Cemiplimab	357	6.3 (95% CI, 4.6, 8.3)
Chemotherapy	355	5.3 (95% CI, 4.3, 6.0)
		<b>HR, 0.56 (95% CI, 0.47, 0.67); P=0.0001</b>

CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; OS, overall survival; PFS, progression free survival

Data cutoff date: 4 March 2022

# Nivolumab plus Ipilimumab in Lung Cancer with a High Tumor Mutational Burden

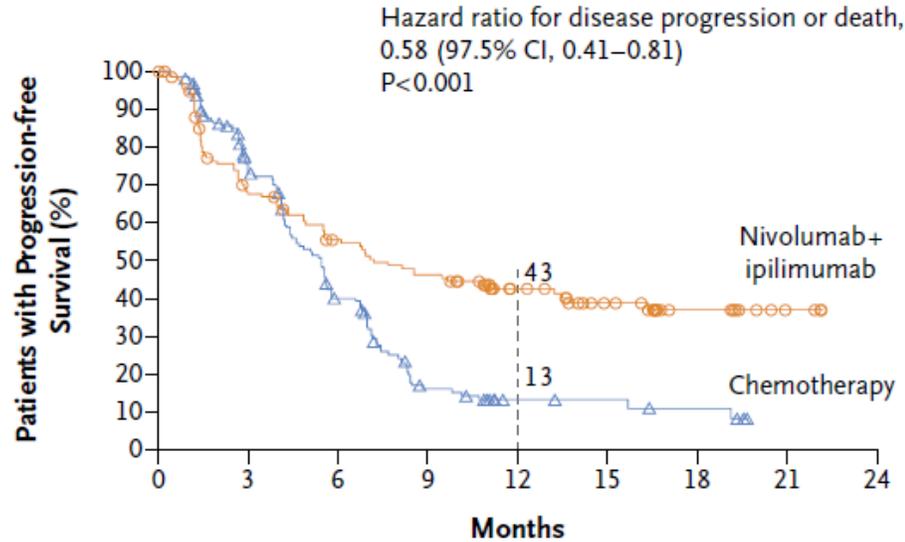
M.D. Hellmann, T.-E. Ciuleanu, A. Pluzanski, J.S. Lee, G.A. Otterson, C. Audigier-Valette, E. Minenza, H. Linardou, S. Burgers, P. Salman, H. Borghaei, S.S. Ramalingam, J. Brahmer, M. Reck, K.J. O'Byrne, W.J. Geese, G. Green, H. Chang, J. Szustakowski, P. Bhagavatheeswaran, D. Healey, Y. Fu, F. Nathan, and L. Paz-Ares



# CM-227 : critères de jugement principaux

TMB haut

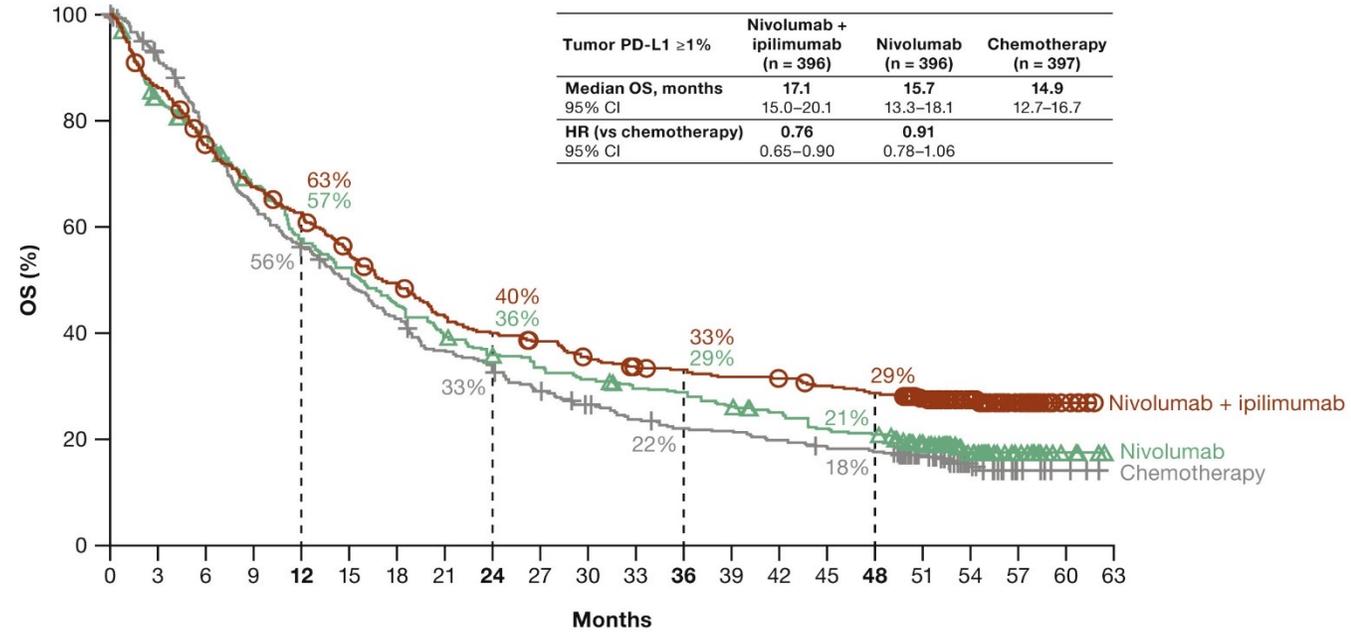
A Progression-free Survival



No. at Risk	0	3	6	9	12	15	18	21	24
Nivolumab + ipilimumab	139	85	66	55	36	24	11	3	0
Chemotherapy	160	103	51	17	7	6	4	0	0

A

PD-L1≥1%



Number of patients at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63
Nivolumab + ipilimumab	396	341	295	264	244	212	190	165	153	145	132	124	121	116	114	108	103	84	58	23	5	0
Nivolumab	396	330	299	265	220	201	176	153	139	129	119	112	108	98	91	80	76	61	31	15	4	0
Chemotherapy	397	358	306	250	218	190	166	141	126	112	98	87	80	78	72	66	63	46	24	7	3	0

**Pas de prise en charge en France**

# TRAITEMENTS DE 1<sup>E</sup> LIGNE

Stratégies à base d'immunothérapie

IMMUNOTHERAPIE SEULE

si PD-L1 $\geq$ 50%

→ pembrolizumab

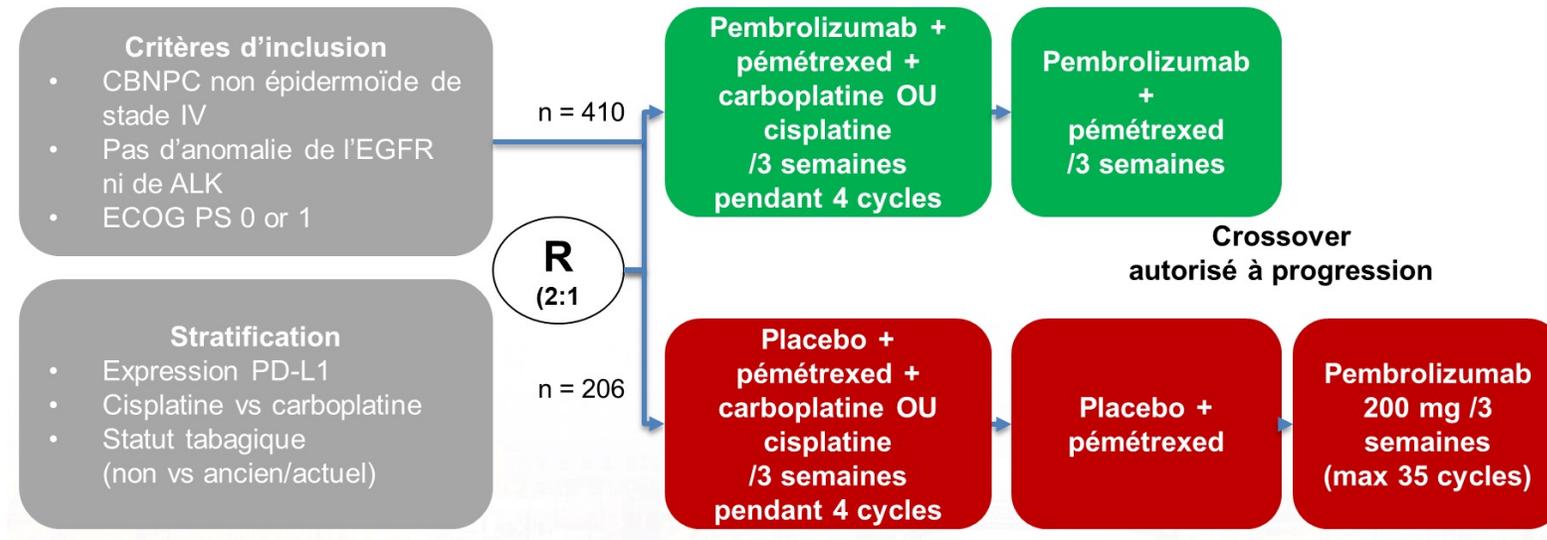
→ cemiplimab

IMMUNOTHERAPIE +  
CHIMIOOTHERAPIE

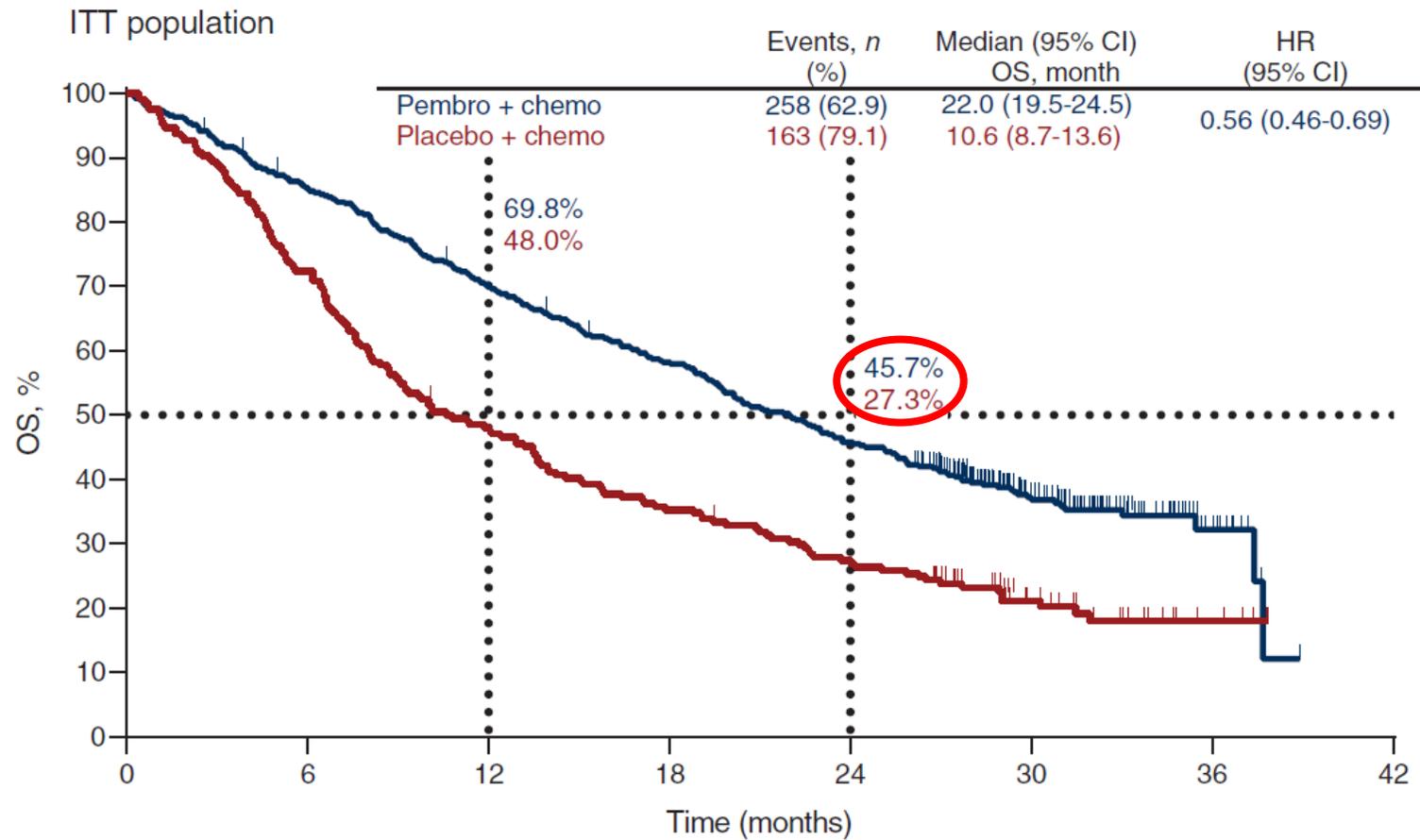
Populations particulières

# Pembrolizumab plus Chemotherapy in Metastatic Non–Small-Cell Lung Cancer

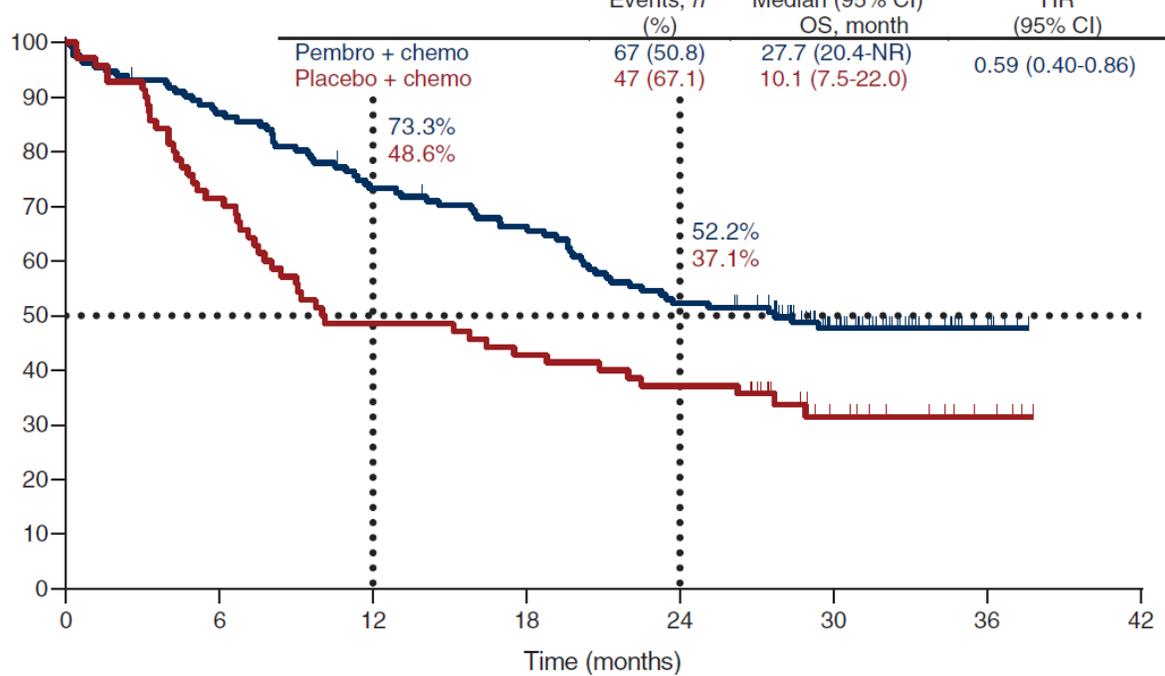
L. Gandhi, D. Rodríguez-Abreu, S. Gadgeel, E. Esteban, E. Felip,  
F. De Angelis, M. Domine, P. Clingan, M.J. Hochmair, S.F. Powell, S.Y.-S. Cheng,  
H.G. Bischoff, N. Peled, F. Grossi, R.R. Jennens, M. Reck, R. Hui, E.B. Garon,  
M. Boyer, B. Rubio-Viqueira, S. Novello, T. Kurata, J.E. Gray, J. Vida, Z. Wei,  
J. Yang, H. Raftopoulos, M.C. Pietanza, and M.C. Garassino,  
for the KEYNOTE-189 Investigators\*



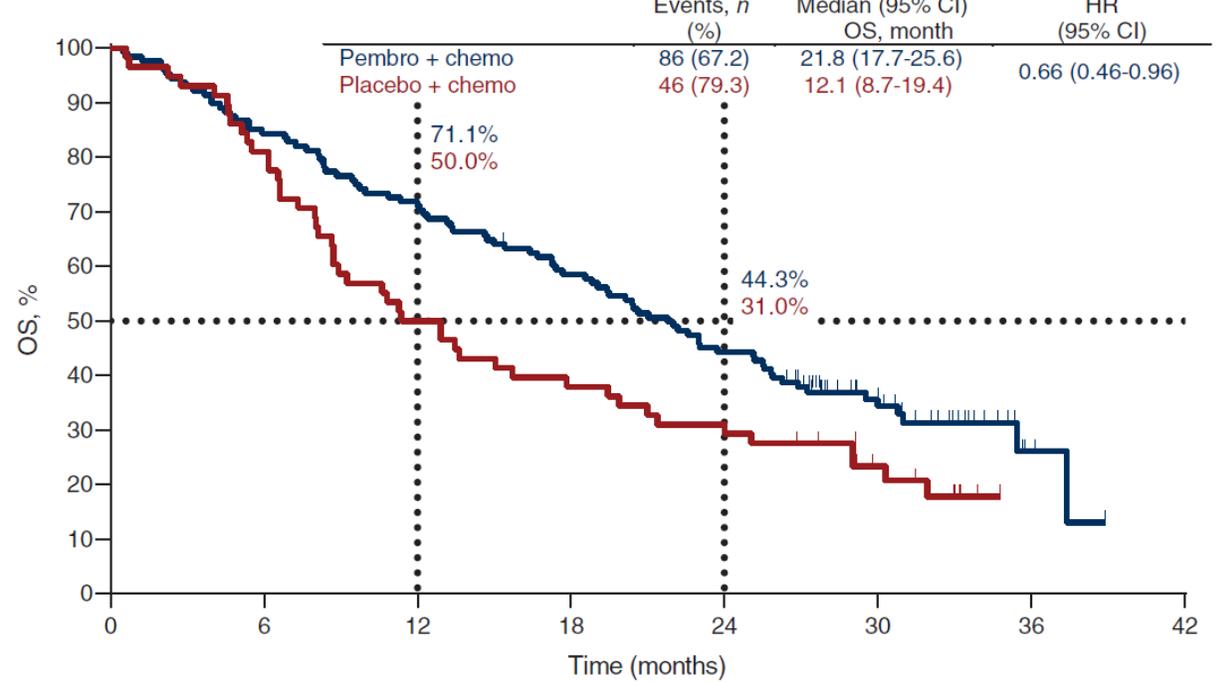
# KN-189 - survie globale



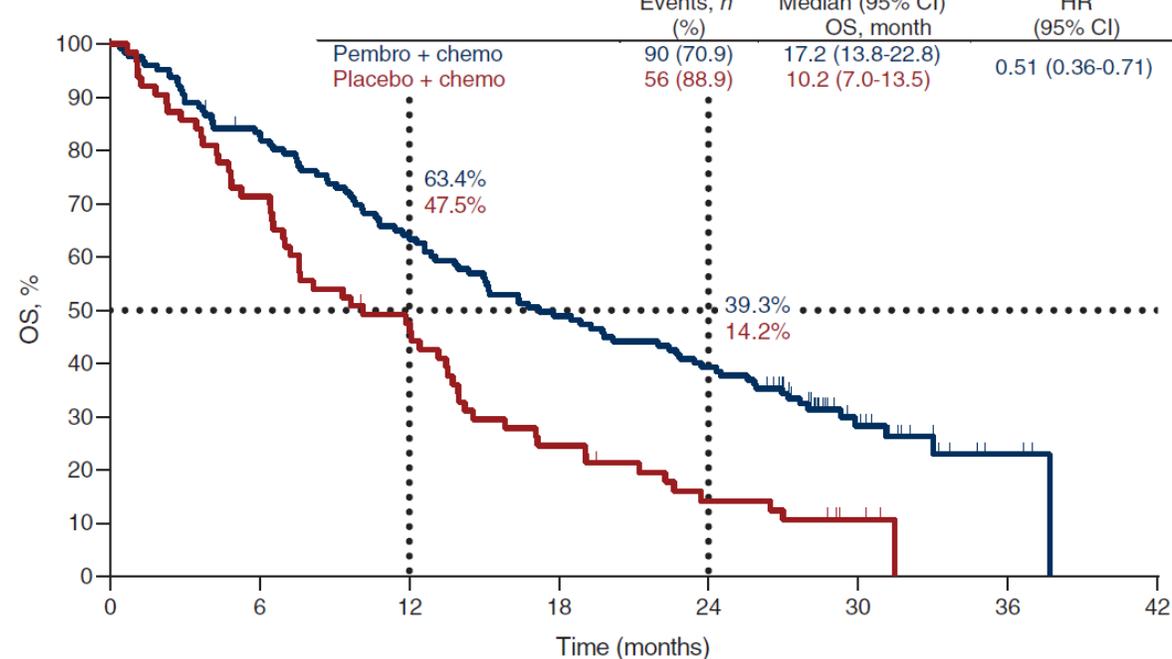
PD-L1 TPS  $\geq 50\%$



PD-L1 TPS 1%-49%

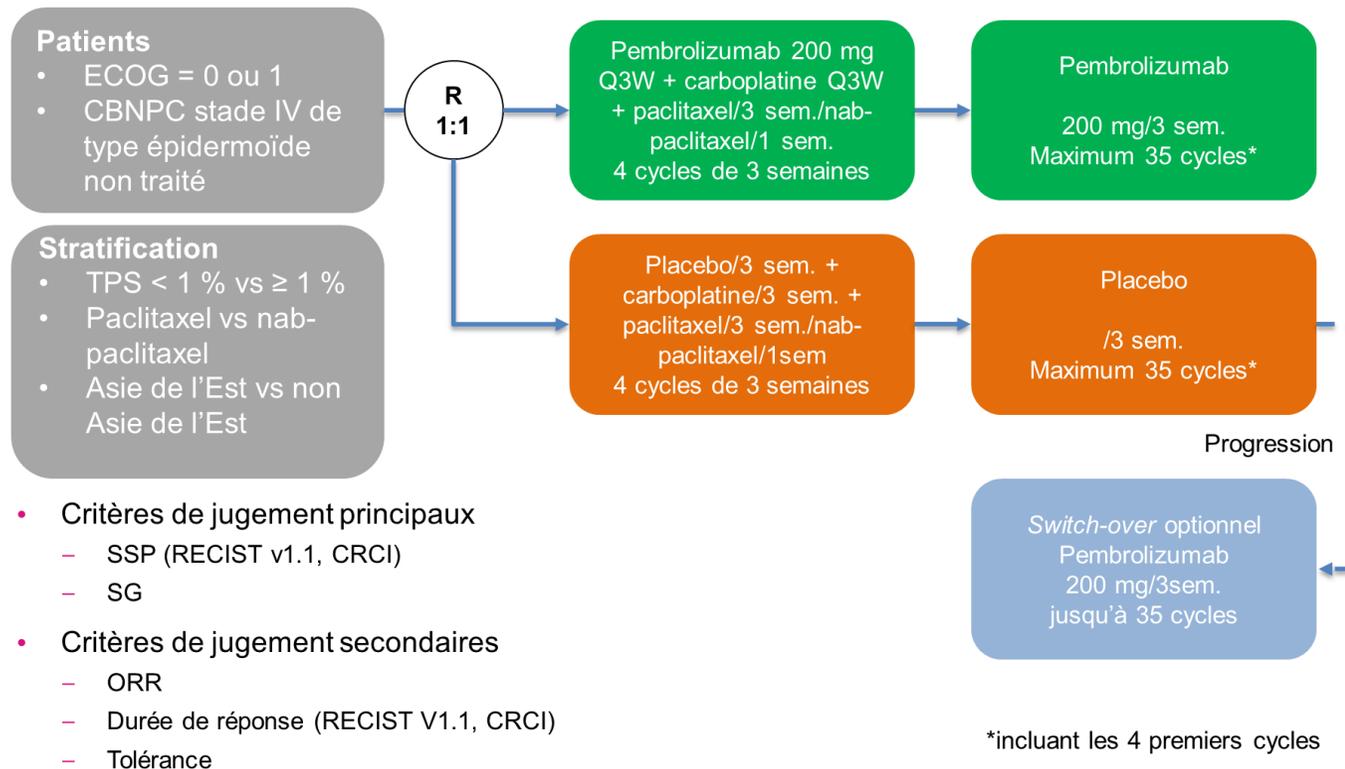


PD-L1 TPS <1%

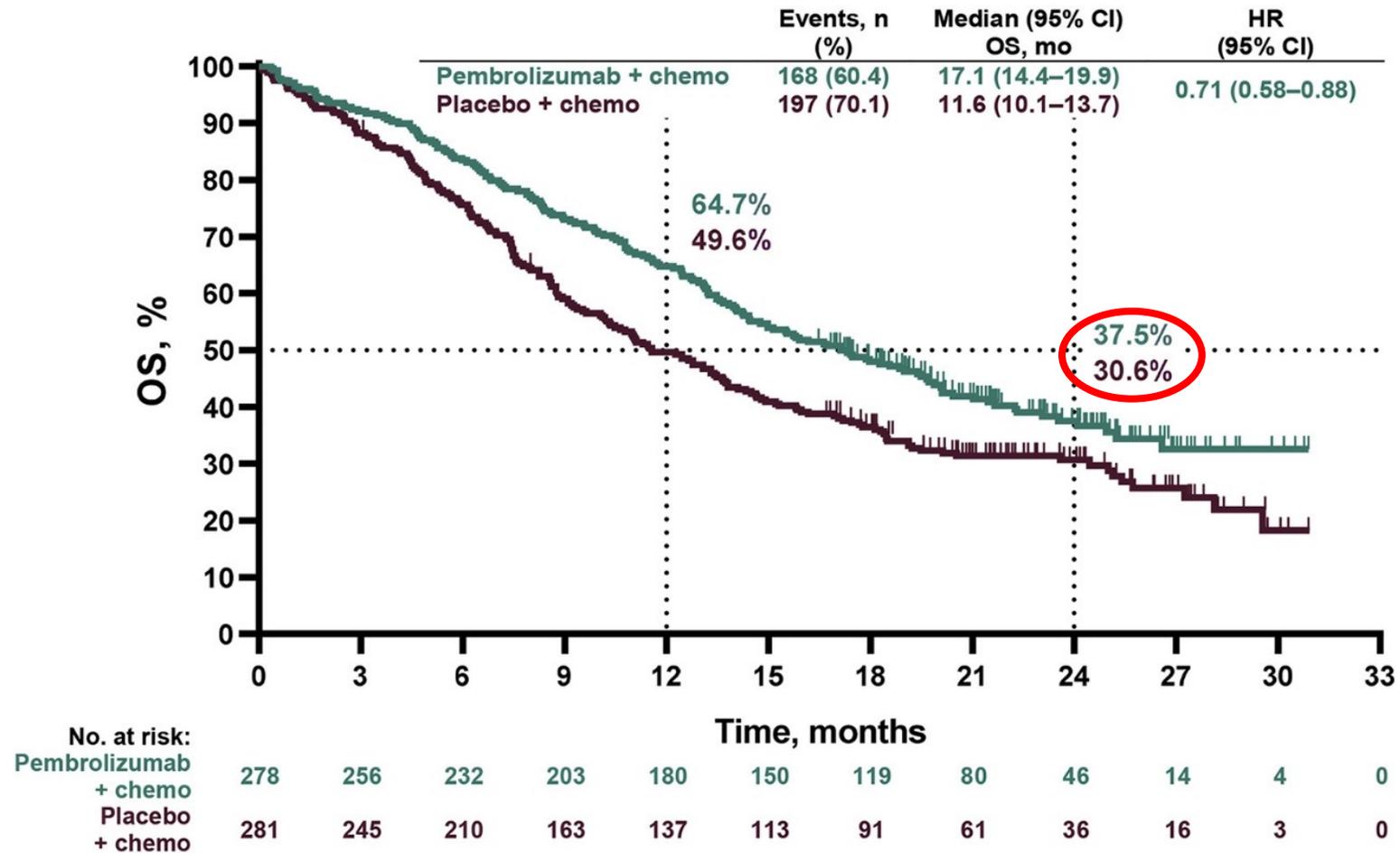


# Pembrolizumab plus Chemotherapy for Squamous Non–Small-Cell Lung Cancer

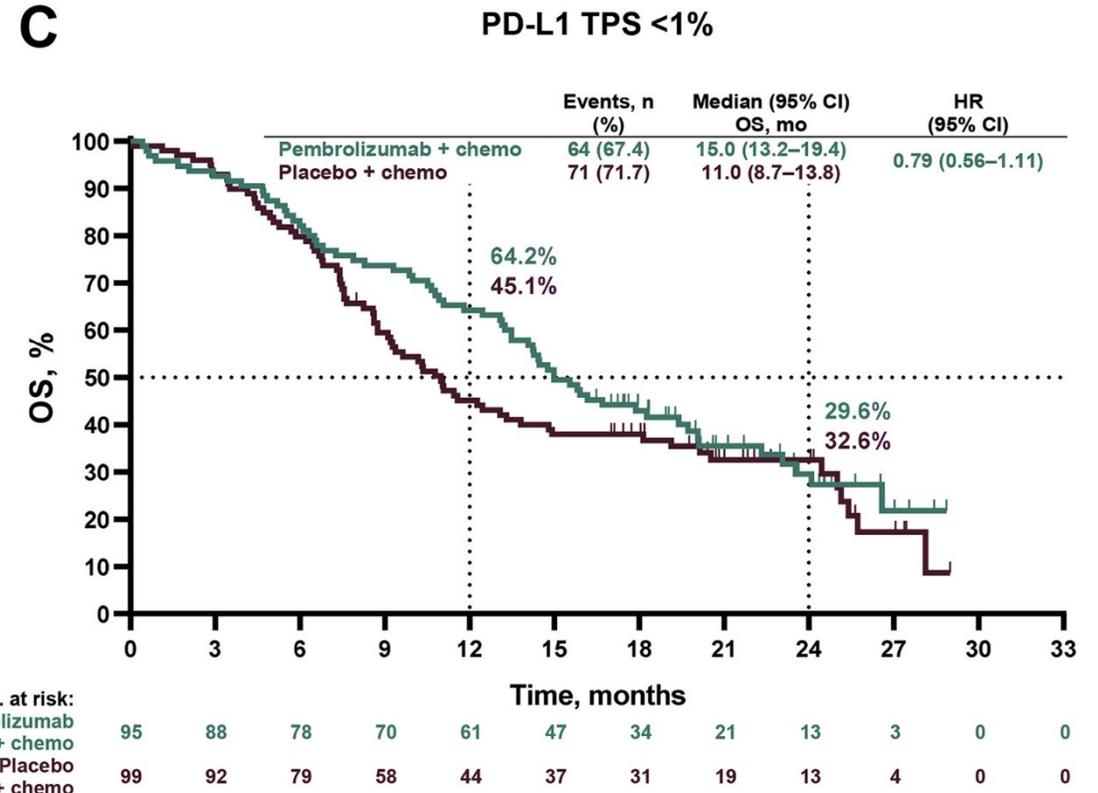
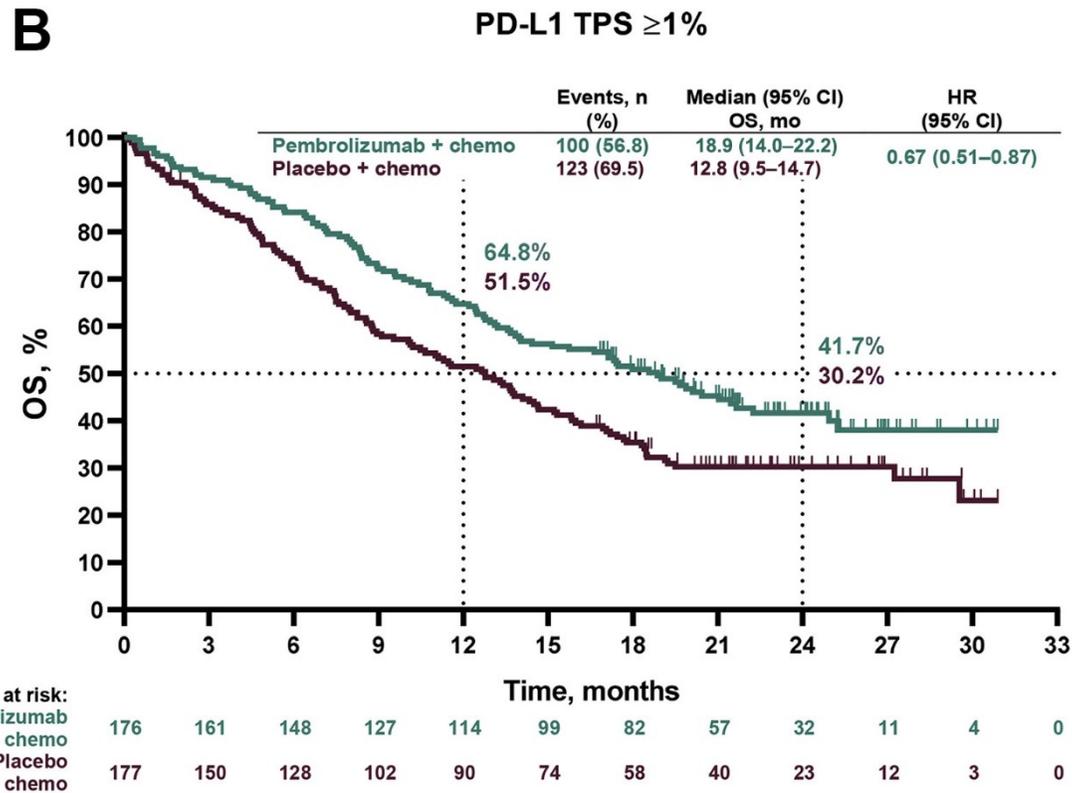
L. Paz-Ares, A. Luft, D. Vicente, A. Tafreshi, M. Gümüş, J. Mazières, B. Hermes, F. Çay Şenler, T. Csőszi, A. Fülöp, J. Rodríguez-Cid, J. Wilson, S. Sugawara, T. Kato, K.H. Lee, Y. Cheng, S. Novello, B. Halmos, X. Li, G.M. Lubiniecki, B. Piperdi, and D.M. Kowalski, for the KEYNOTE-407 Investigators\*



# KN-407 - survie globale



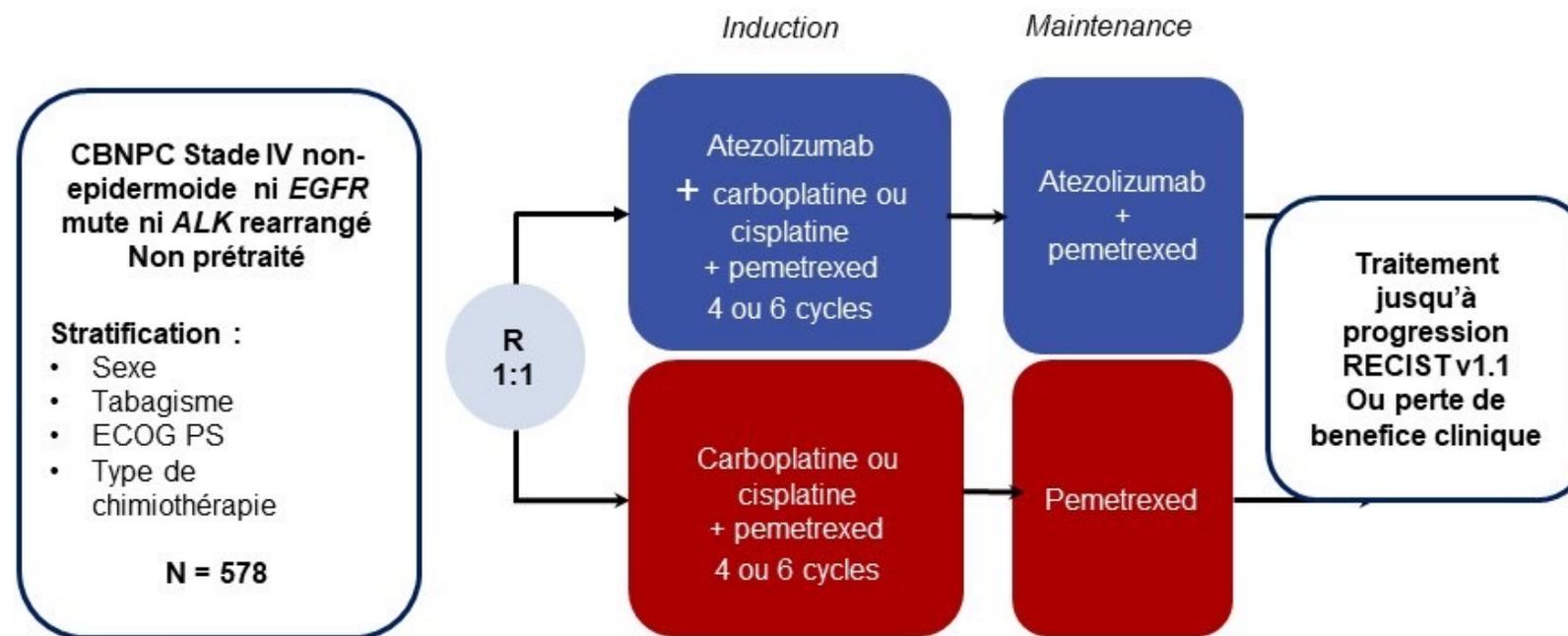
# KN-407 - survie globale



# Atezolizumab Plus Chemotherapy for First-Line Treatment of Nonsquamous NSCLC: Results From the Randomized Phase 3 IMpower132 Trial

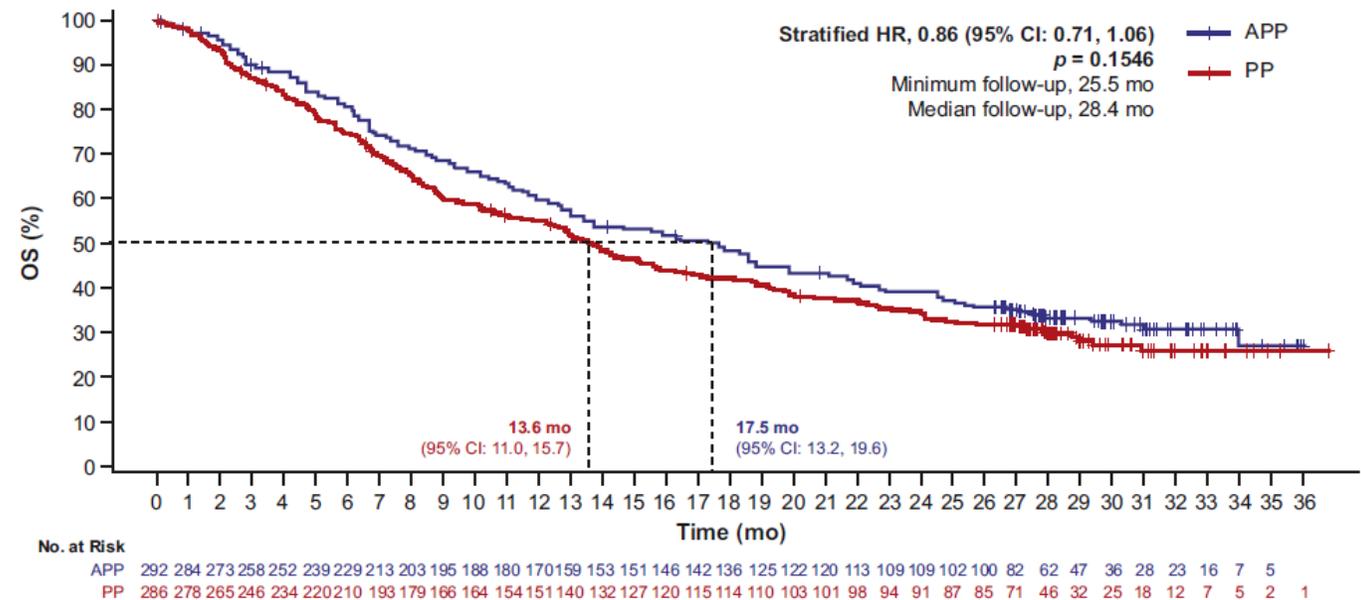
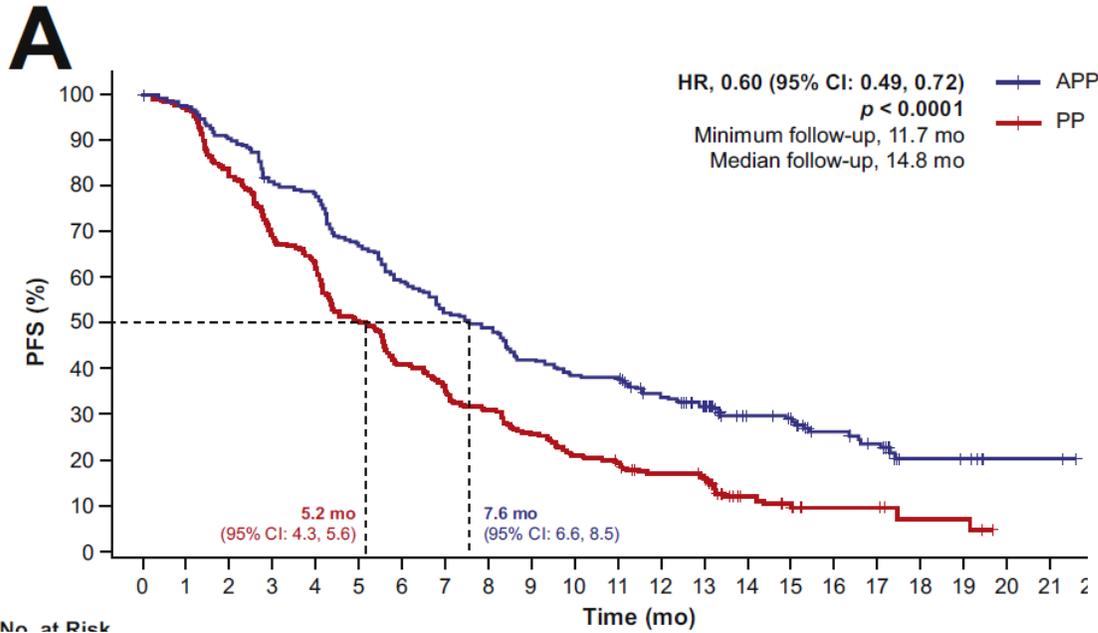


Makoto Nishio, MD, PhD,<sup>a,\*</sup> Fabrice Barlesi, MD, PhD,<sup>b,c</sup> Howard West, MD,<sup>d</sup> Simon Ball, PhD,<sup>e</sup> Rodolfo Bordoni, MD,<sup>f</sup> Manuel Cobo, MD,<sup>g</sup> Pascale Dubray Longeras, MD,<sup>h</sup> Jerome Goldschmidt Jr., MD,<sup>i</sup> Silvia Novello, MD, PhD,<sup>j</sup> Francisco Orlandi, MD,<sup>k</sup> Rachel E. Sanborn, MD,<sup>l</sup> Zsuzsanna Szalai, PhD,<sup>m</sup> Grigoriy Ursol, PhD,<sup>n</sup> Diana Mendus, PhD,<sup>o</sup> Lijia Wang, PhD,<sup>o</sup> Xiaohui Wen, MD,<sup>o</sup> Mark McClelland, PhD,<sup>o</sup> Tien Hoang, MD,<sup>o</sup> See Phan, MD,<sup>o</sup> Mark A. Socinski, MD<sup>p</sup>



- Objectifs principaux: SSP et SG selon les investigateurs

# ImPower-132 – survie sans progression & survie globale



# EMPOWER-Lung 3 (Part 2) Study Design (NCT03409614)

**Background:** Cemiplimab (a high-affinity, fully human anti-PD-1) is approved as first-line monotherapy for advanced NSCLC with PD-L1  $\geq 50\%$  (EMPOWER-Lung 1 Study<sup>1</sup>)

## Key eligibility criteria

- Treatment-naive advanced NSCLC (non-squamous and squamous histology; Stage IIIb/c<sup>†</sup>, IV)
- Any PD-L1 expression
- No *EGFR*, *ALK*, or *ROS1* mutations
- ECOG PS 0 or 1
- Treated, clinically stable CNS metastases <sup>‡</sup>

## Stratification factors

- PD-L1 expression:  $<1\%$  vs  $1-49\%$  vs  $\geq 50\%$
- Histology: non-squamous vs squamous

## Endpoints

- Primary: OS
- Key secondary: PFS and ORR
- Additional secondary: DOR, BOR, safety, and PRO

R 2:1

## Arm A

Cemiplimab 350 mg Q3W + investigator's choice platinum-doublet chemo Q3W for 4 cycles<sup>§</sup>

PD or 108 weeks

## Arm B

Placebo Q3W + investigator's choice platinum-doublet chemo Q3W for 4 cycles<sup>§</sup>

PD or 108 weeks

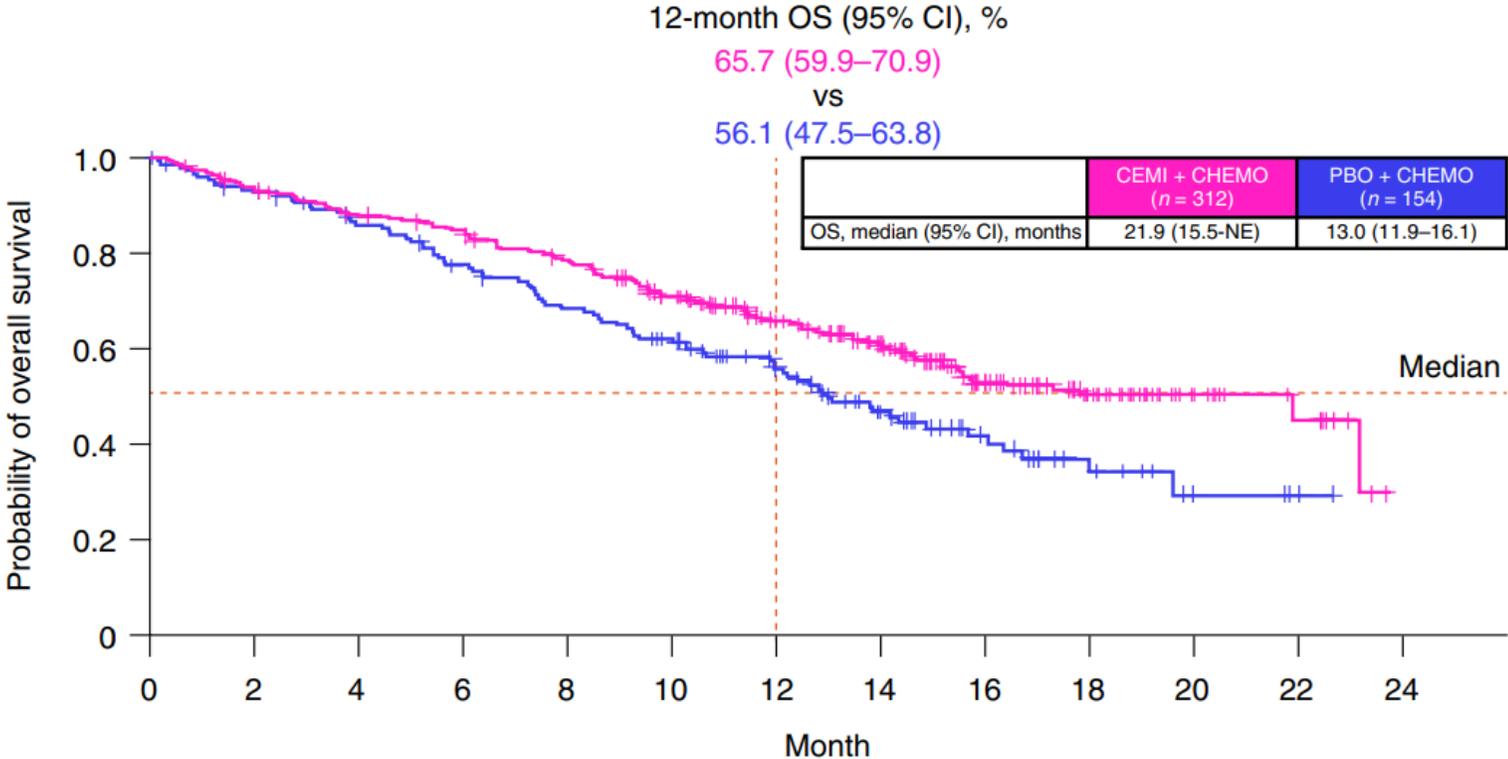
Follow-up

**N=466**

Two interim analyses were prespecified per protocol  
Second interim analysis (14 June 2021) presented here

# EMPOWER-Lung 3 – survie globale

**a**



No. at risk:

	0	2	4	6	8	10	12	14	16	18	20	22	24
Cemiplimab + chemo (n = 312)	312	289	269	256	233	199	162	131	86	52	18	8	0
Placebo + chemo (n = 154)	154	141	126	112	98	85	65	46	26	14	5	2	0

# First-line nivolumab plus ipilimumab combined with two cycles of chemotherapy in patients with non-small-cell lung cancer (CheckMate 9LA): an international, randomised, open-label, phase 3 trial

*Luis Paz-Ares, Tudor-Eliade Ciuleanu, Manuel Cobo, Michael Schenker, Bogdan Zurawski, Juliana Menezes, Eduardo Richardet, Jaafar Bennouna, Enriqueta Felip, Oscar Juan-Vidal, Aurelia Alexandru, Hiroshi Sakai, Alejo Lingua, Pamela Salman, Pierre-Jean Souquet, Pedro De Marchi, Claudio Martin, Maurice Pérol, Arnaud Scherpereel, Shun Lu, Thomas John, David P Carbone, Stephanie Meadows-Shropshire, Shruti Agrawal, Abderrahim Oukessou, Jinchun Yan, Martin Reck*

*Lancet Oncol 2021*

## First-line nivolumab plus ipilimumab with two cycles of chemotherapy versus chemotherapy alone (four cycles) in advanced non-small-cell lung cancer: CheckMate 9LA 2-year update

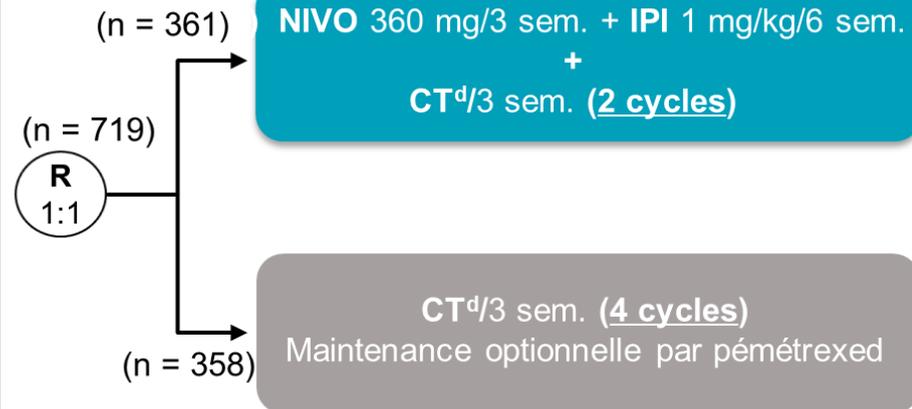
M. Reck<sup>1\*</sup>, T.-E. Ciuleanu<sup>2</sup>, M. Cobo<sup>3</sup>, M. Schenker<sup>4</sup>, B. Zurawski<sup>5</sup>, J. Menezes<sup>6</sup>, E. Richardet<sup>7</sup>, J. Bennouna<sup>8</sup>, E. Felip<sup>9</sup>, O. Juan-Vidal<sup>10</sup>, A. Alexandru<sup>11</sup>, H. Sakai<sup>12</sup>, A. Lingua<sup>13</sup>, F. Reyes<sup>14</sup>, P.-J. Souquet<sup>15</sup>, P. De Marchi<sup>16†</sup>, C. Martin<sup>17</sup>, M. Pérol<sup>18</sup>, A. Scherpereel<sup>19</sup>, S. Lu<sup>20</sup>, L. Paz-Ares<sup>21</sup>, D. P. Carbone<sup>22</sup>, A. Memaj<sup>23</sup>, S. Marimuthu<sup>23</sup>, X. Zhang<sup>23</sup>, P. Tran<sup>23</sup> & T. John<sup>24</sup>

# Design

## Principaux critères d'éligibilité

- CBNPC de stade IV ou en rechute
- Pas de traitement systémique antérieur
- Pas de mutation activatrice de l'EGFR ou de réarrangement connu d'ALK
- ECOG PS 0-1

**Stratification :**  
PD-L1<sup>b</sup> (< 1%<sup>c</sup> vs ≥ 1%),  
sexe et histologie (SQ vs NSQ)



Jusqu'à progression, toxicité inacceptable ou 2 ans de traitement pour l'immunothérapie

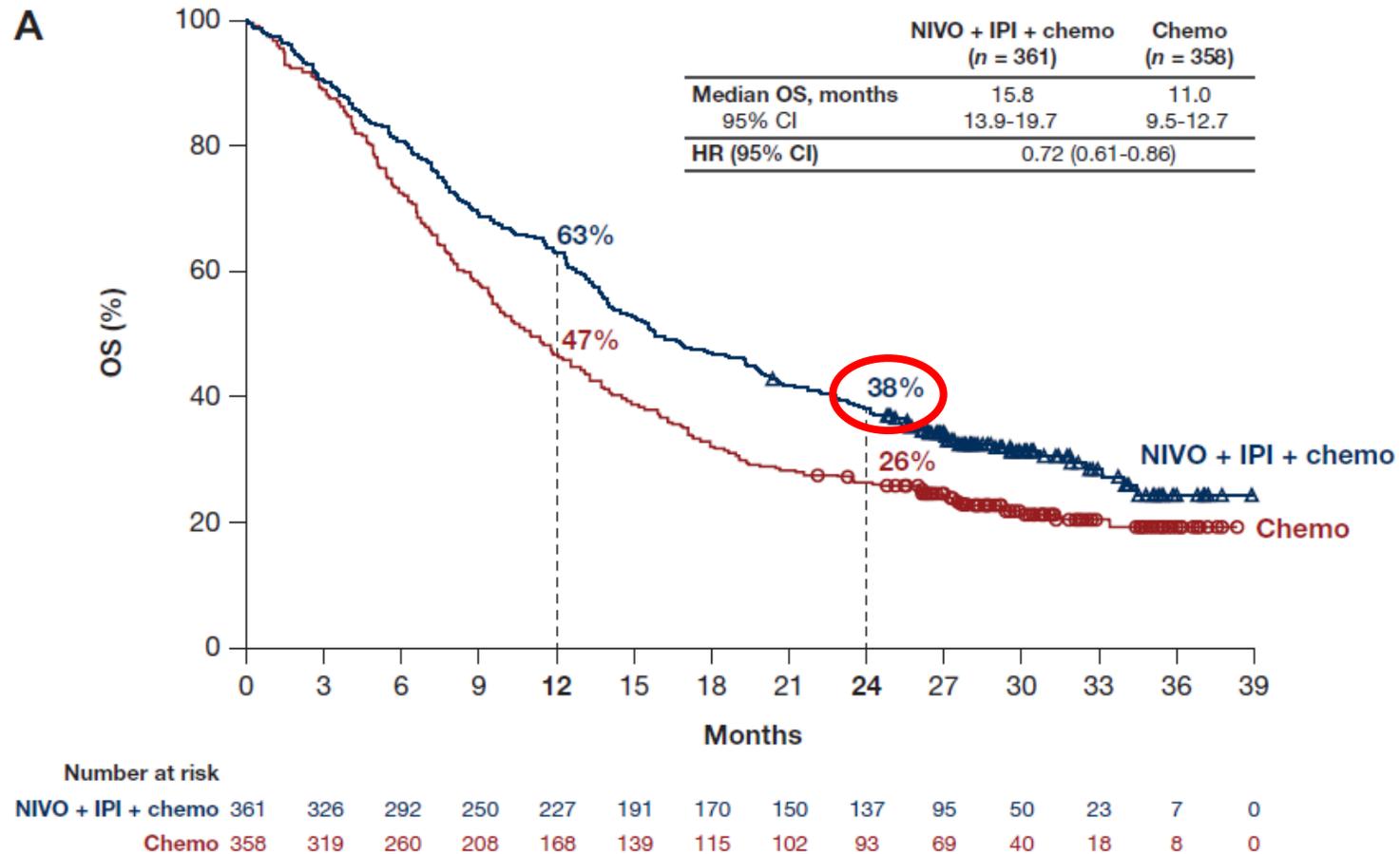
## Critère principal

- SG

## Critères secondaires

- SSP (comité de revue indépendant)
- Taux de RO (comité de revue indépendant)
- Efficacité en fonction de l'expression de PD-L1

# CM-9LA – Survie globale

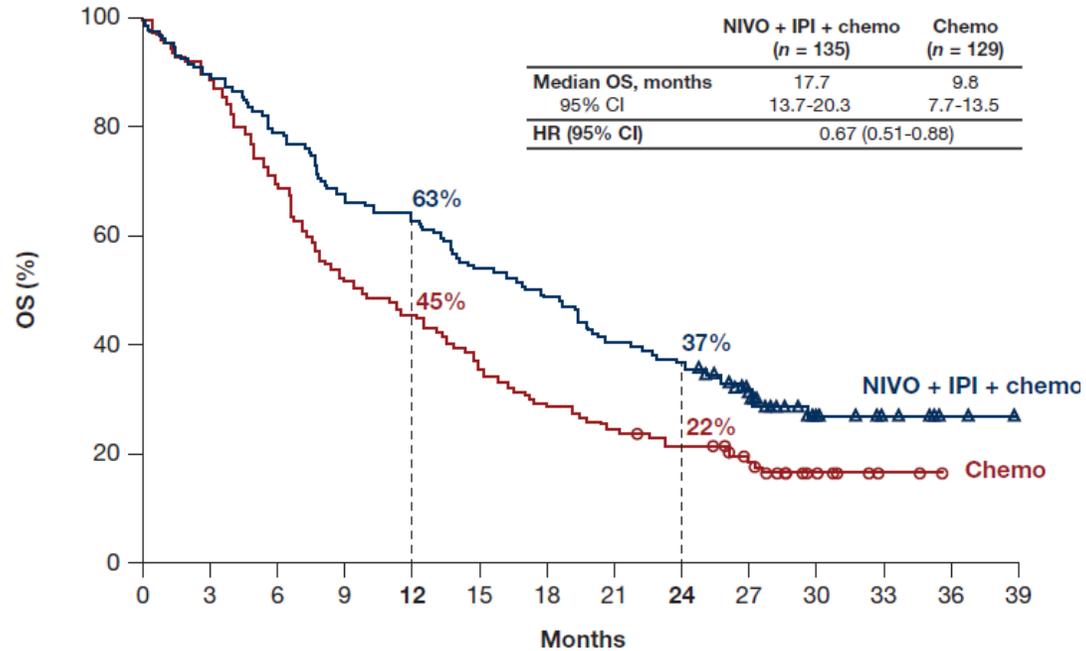


# CM-9LA – Survie globale

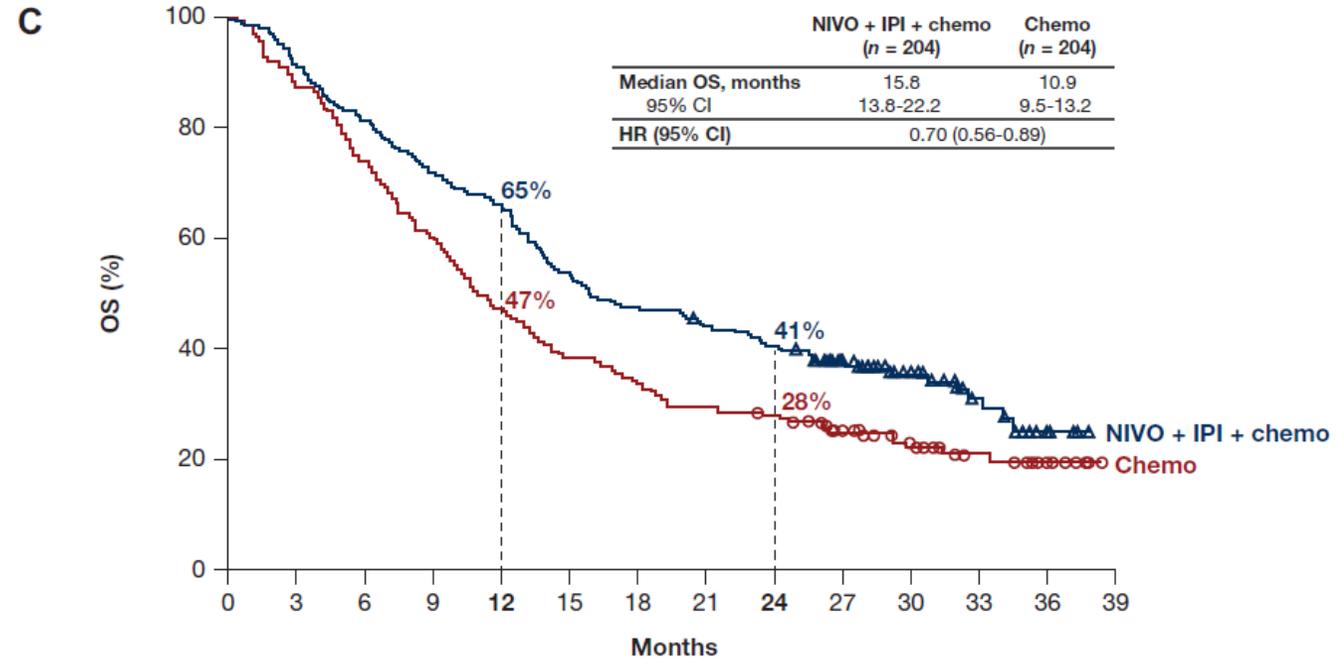
## PDL1 négatif

## PDL1 ≥1%

B



C

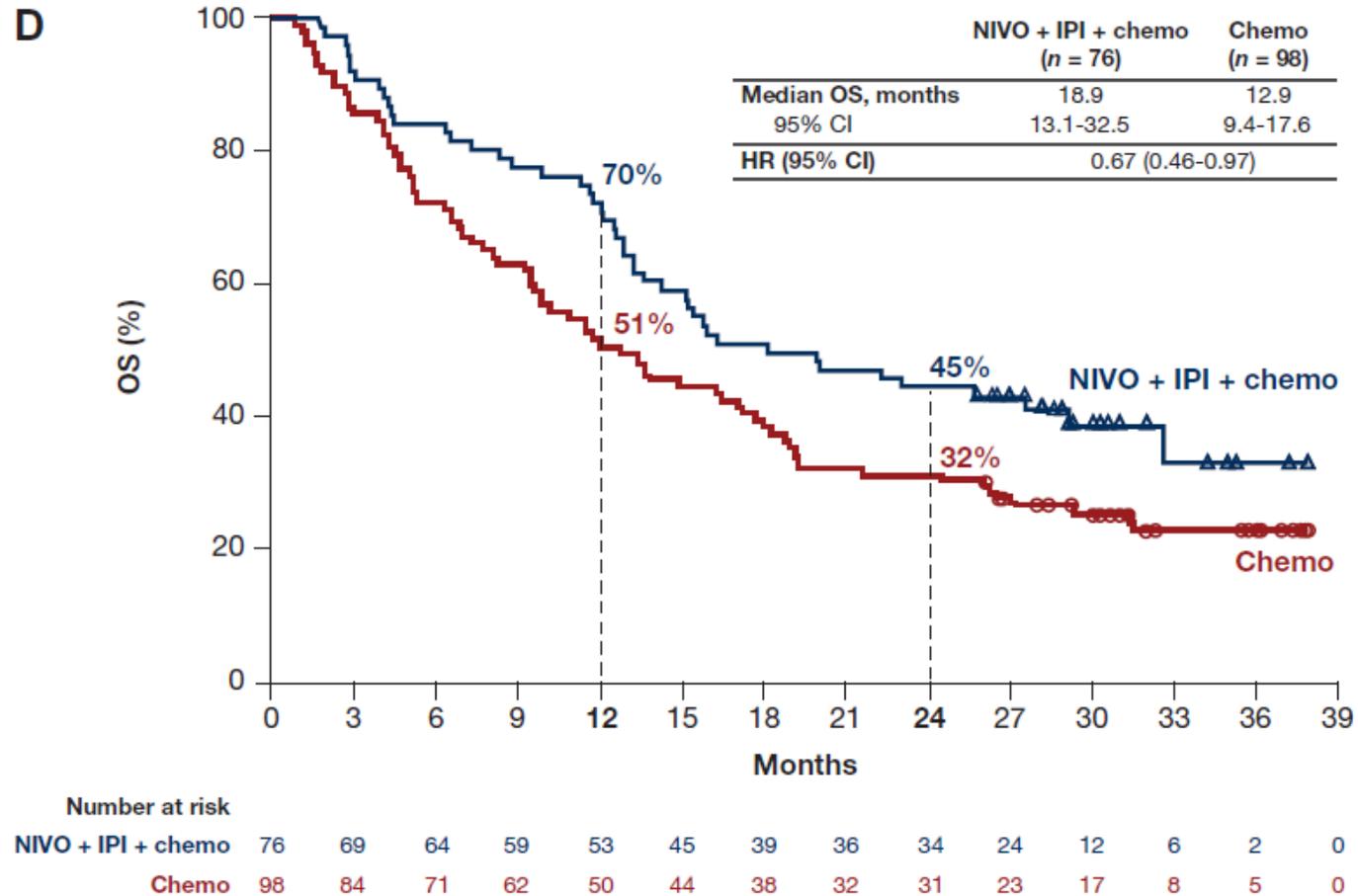


Number at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39
NIVO + IPI + chemo	135	120	107	90	85	73	66	55	50	31	13	6	2	0
Chemo	129	116	90	68	58	47	37	32	27	21	7	2	0	0

Number at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39
NIVO + IPI + chemo	204	186	166	147	133	109	97	89	82	60	35	17	5	0
Chemo	204	179	151	122	96	79	68	60	56	42	29	14	8	0

# CM-9LA – Survie globale

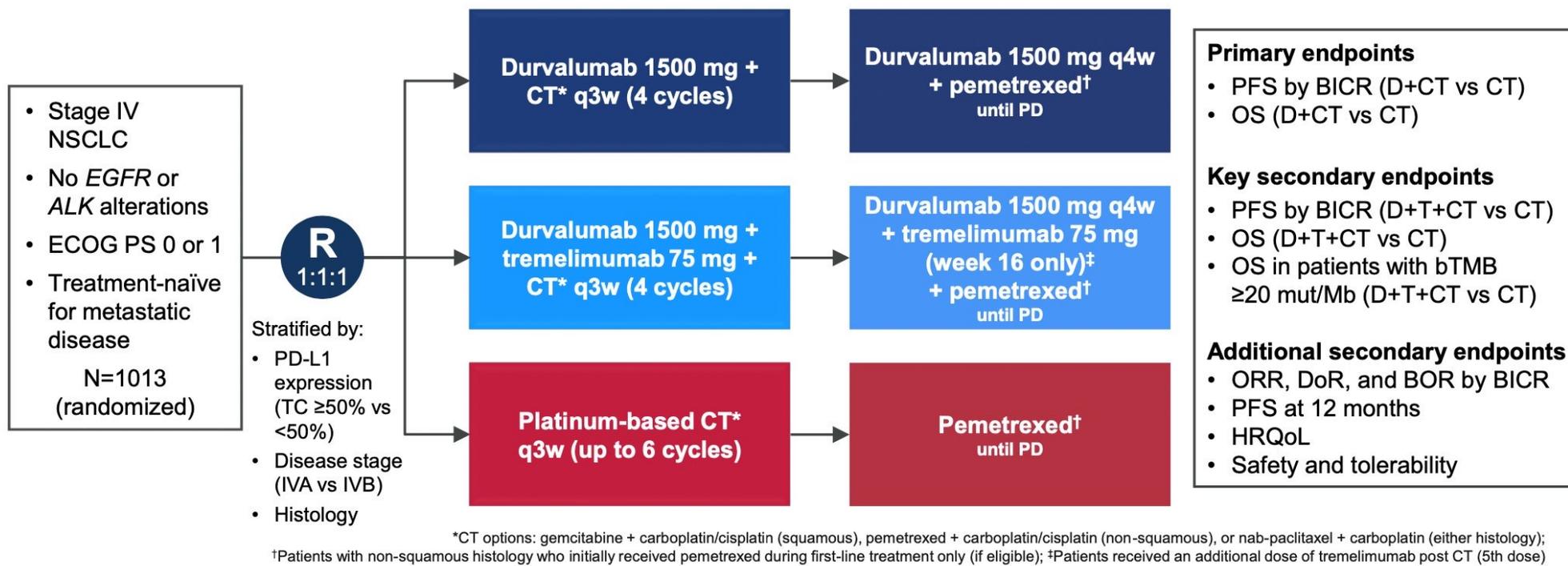
**PDL1 ≥50%**



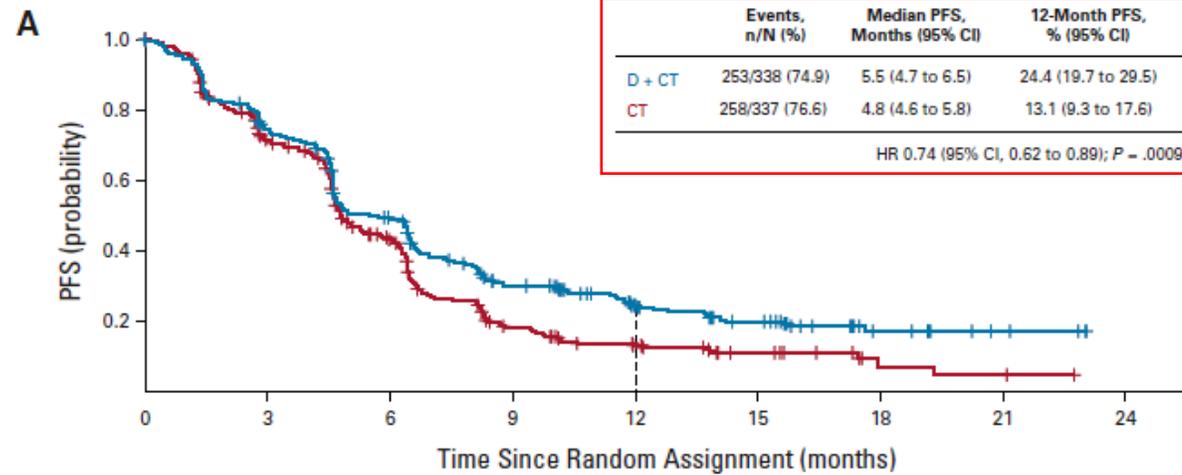
# Essai POSEIDON

## POSEIDON Study Design

Phase 3, global, randomized, open-label, multicenter study



# Objectifs principaux



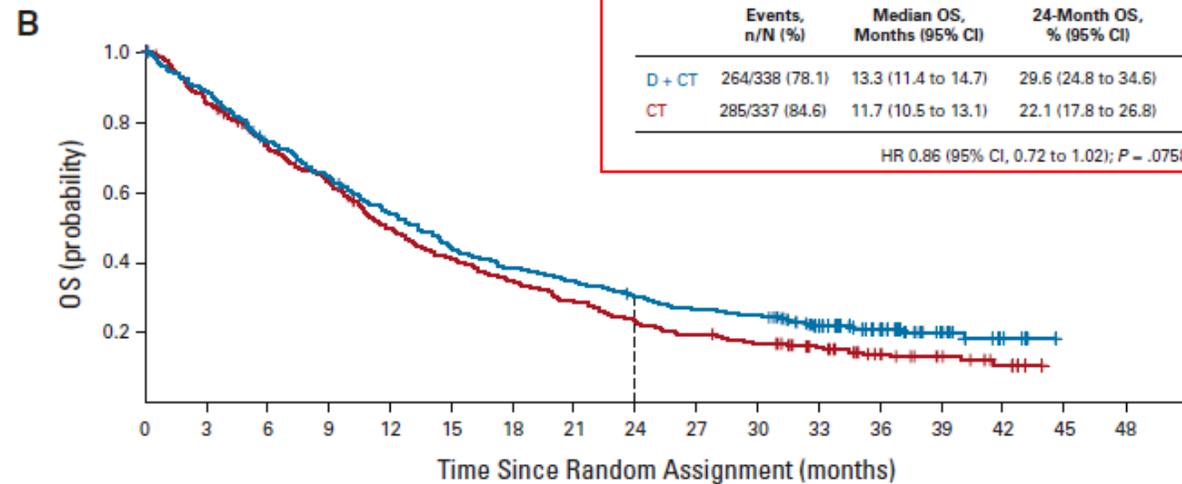
No. at risk:

D + CT

CT

338	246	158	88	53	35	11	4	0
337	219	121	43	23	12	3	2	0

Suivi médian: 35 mois (OS)  
et 10 mois (PFS)



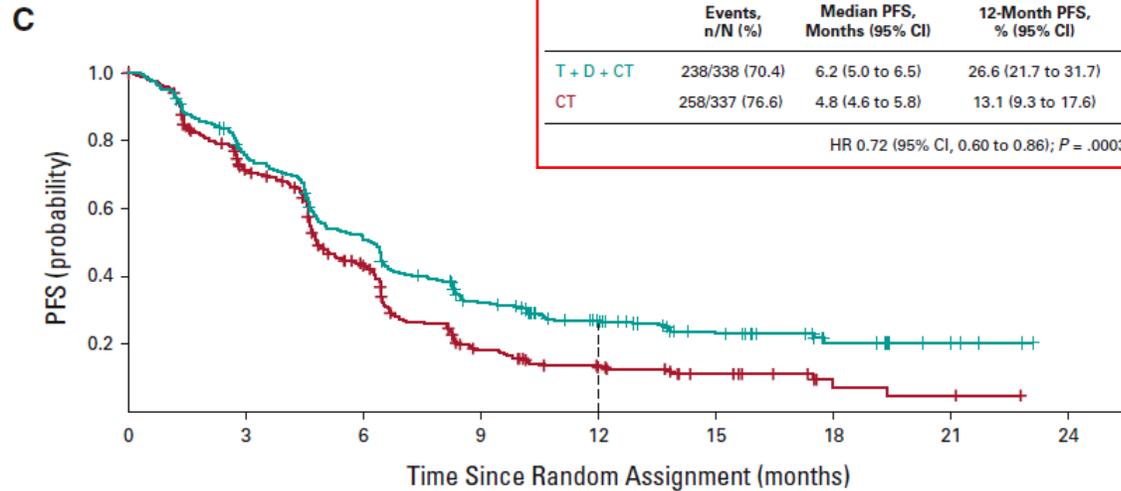
No. at risk:

D + CT

CT

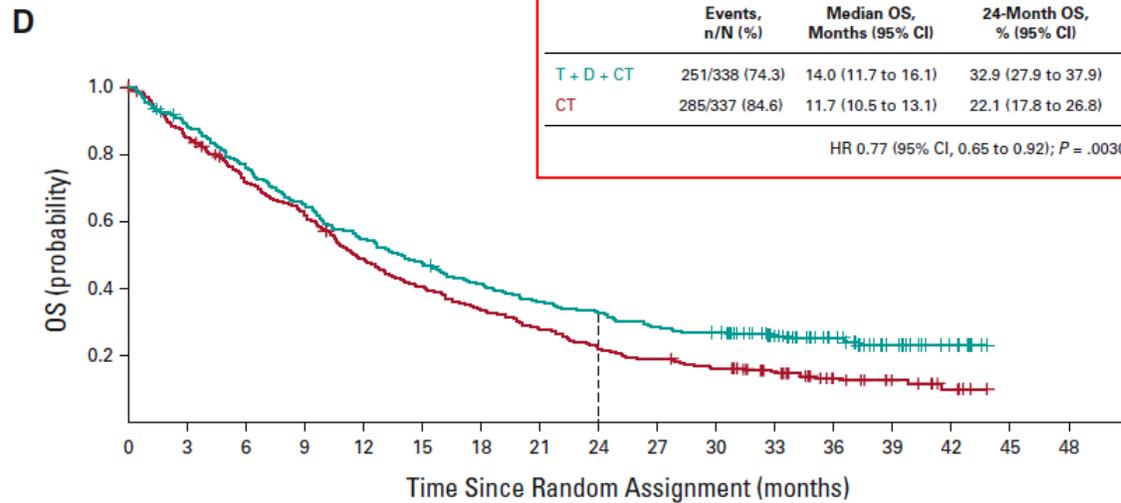
338	296	247	212	176	142	126	112	97	85	81	51	33	15	5	0	0
337	284	236	204	160	132	111	91	72	62	52	38	21	13	6	0	0

# Objectifs secondaires « clés »



No. at risk:

T + D + CT	338	243	161	94	56	32	13	5	0
CT	337	219	121	43	23	12	3	2	0



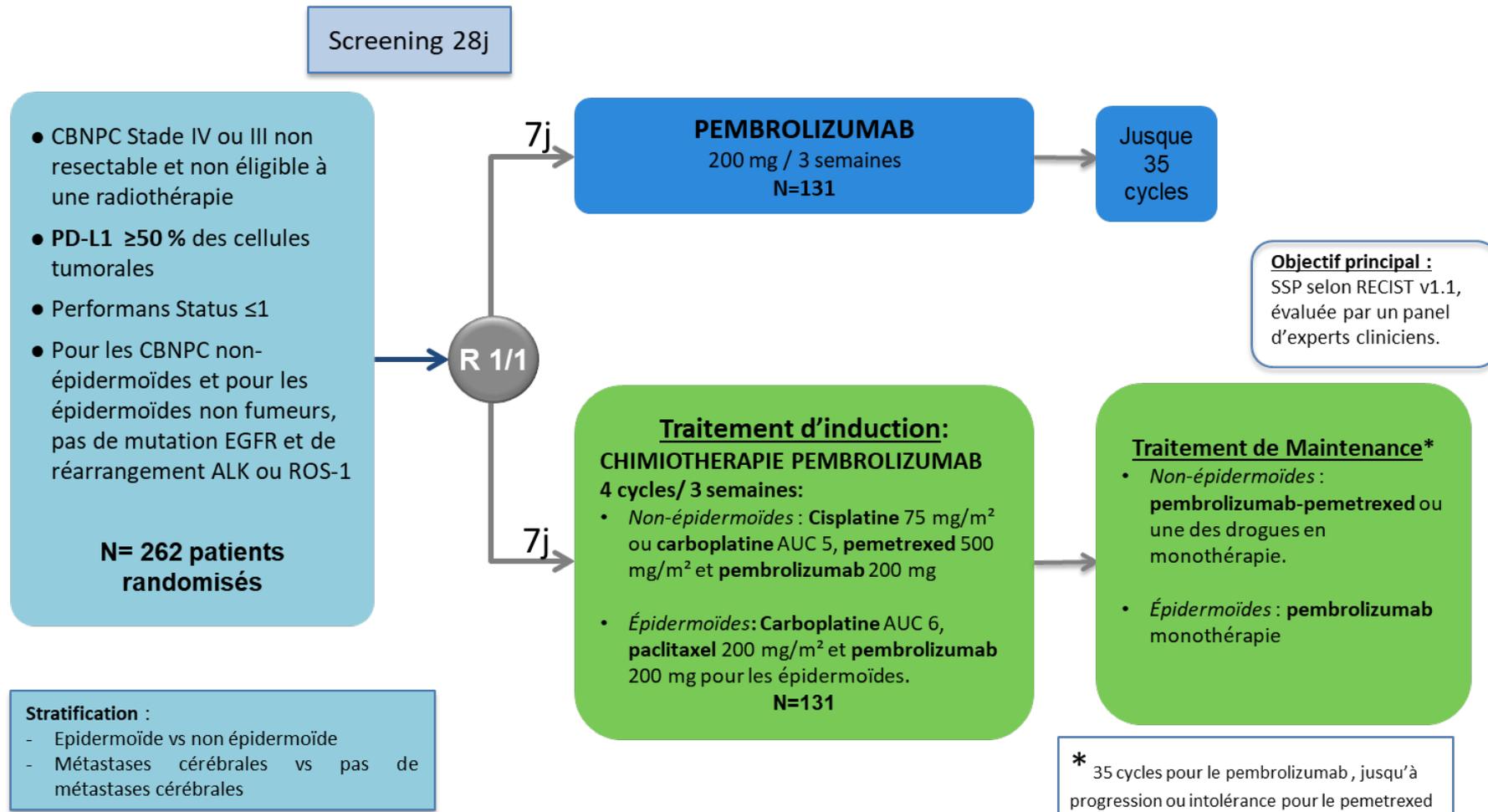
No. at risk:

T + D + CT	338	298	256	217	183	159	137	120	109	95	88	64	41	20	9	0	0
CT	337	284	236	204	160	132	111	91	72	62	52	38	21	13	6	0	0

	POSEIDON			Checkmate-9LA			EMPOWER-Lung 3	Keynote-189	Keynote-407	EMPOWER-Lung 3
protocole testé	durvalumab + tremelimumab + 4 cures de CT			nivolumab + ipilimumab + 2 cures de CT			Cemiplimab + ipilimumab + 2 cures de CT	pembrolizumab + CT	pembrolizumab + CT	cemiplimab + CT
type histologique	tout	non-épidermoïde	épidermoïde	tout	non-épidermoïde	épidermoïde	tout	non-épidermoïde	épidermoïde	tout
<b>tout PDL1</b>										
HR (OS)	0,77 (0,72-1,02)	0,70 (0,56-0,87)	0,88 (0,68-1,16)	0,72 (0,61-0,86)	0,78 (0,63-0,96)	0,63 (0,47-0,85)	0,62 (0,44-0,86)	0,56 (0,49-0,69)	0,71 (0,58-0,88)	0,71 (0,53-0,93)
%OS à 2 ans	32,9%	41,4%	18,1%	38%	40%	35%	NA	45,7%	37,5%	NA
<b>PDL1≥1%</b>	NA	NA	NA							NA
HR (OS)				0,70 (0,59-0,89)	0,71 (0,53-0,95)	0,70 (0,48-1,01)		0,63 (0,48-0,81)	0,67 (0,51-0,87)	
%OS à 2 ans				41%	42%	38%		48,3%	41,70%	
<b>PDL1≥50%</b>	NA	NA	NA							
HR (OS)				0,67 (0,46-0,97)	-	-		0,59 (0,40-0,86)	0,79 (0,52-1,21)	0,61 (0,37-1,02)
%OS à 2 ans				45%	-	-		52,2%	-	NA
<b>PDL1 1-49%</b>	NA	NA	NA							
HR (OS)				NA	NA	NA		0,66 (0,46-0,96)		0,52 (0,32-0,83)
%OS à 2 ans				NA	NA	NA		44,3%		NA
<b>PDL1&lt;1%</b>	NA	NA	NA							
HR (OS)				0,67 (0,51-0,88)	0,75 (0,54-1,04)	0,48 (0,28-0,81)	0,65 (0,40-1,05)	0,51 (0,36-0,71)	0,79 (0,56-1,11)	1,01 (0,63-1,60)
%OS à 2 ans				37%	38%	33%		39,3%	29,6%	NA
<b>toxicités liées au traitement grade 3-5</b>	51,8%	<b>Autres essais négatifs (SG) :</b> Atezo+CT (ImPOWER-132) Durva+CT (POSEIDON)		48%	-	-		52,3%	56,5%	43,6%

# PDL1 ≥50% : essai GFPC PERSEE

PI: Dr Renaud DESCOURT, Dr Chantal DECROISSETTE



# TRAITEMENTS DE 1<sup>E</sup> LIGNE

Stratégies à base d'immunothérapie

IMMUNOTHERAPIE SEULE  
si PD-L1 $\geq$ 50%  
→ pembrolizumab  
→ cemiplimab

IMMUNOTHERAPIE + CHIMIOOTHERAPIE

→ Pembrolizumab + CT

Populations particulières

**Sujets âgés**

**PS 2**



# Efficacy of PD-1 & PD-L1 inhibitors in older adults: a meta-analysis

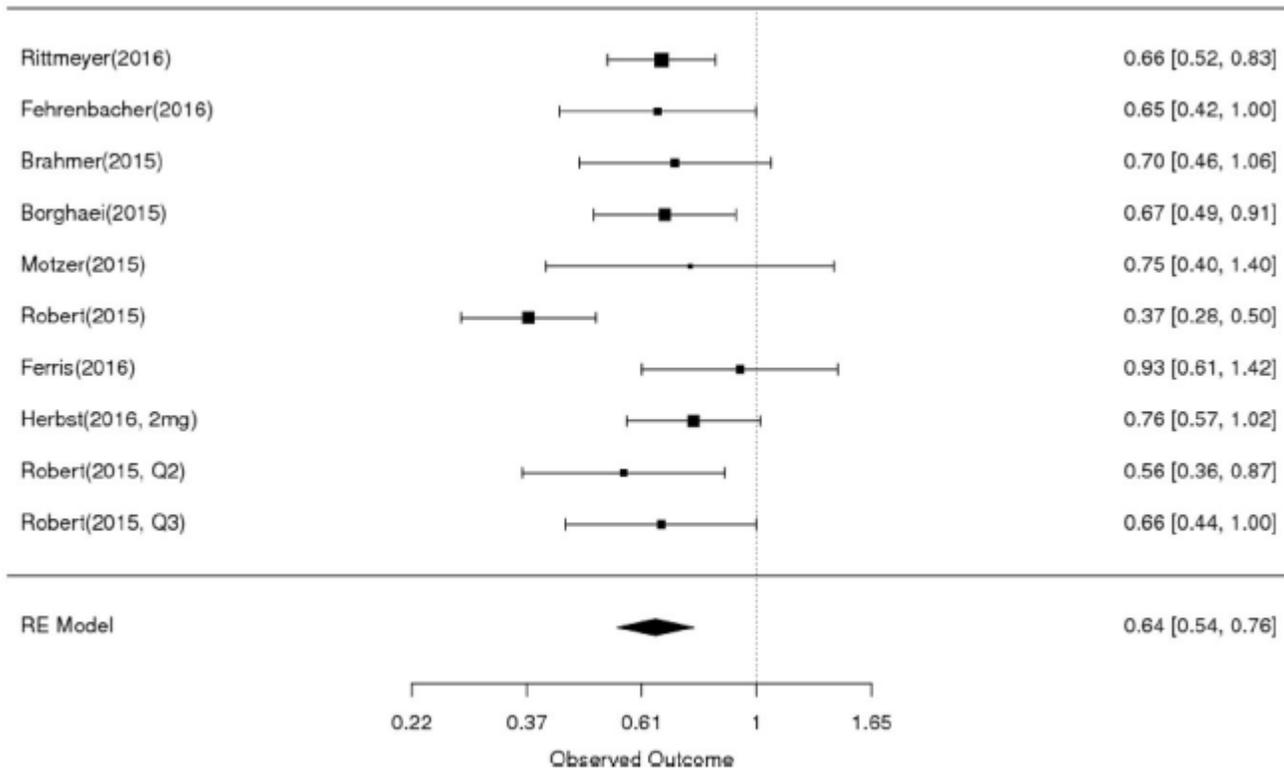
Rawad Elias<sup>1</sup>, Anita Giobbie-Hurder<sup>2</sup>, Nadine Jackson McCleary<sup>3</sup>, Patrick Ott<sup>3</sup>, F. Stephen Hodi<sup>3</sup> and Osama Rahma<sup>3\*</sup>

	Study Name	Drug	Phase	Malignancy	First line	Arm 1	Arm 2	Arm 3	Patient number	Age median	Age range	Age mean	n (%) < 65 y	n (%) ≥ 65 y
Rittmeyer 2016 [33]	OAK	Atezolizumab	3	NSCLC	N	Atezolizumab 1200 mg Q 3 W	Docetaxel 75 mg/m <sup>2</sup> Q 3 W		850	64	33–85	63	453 (53)	397 (47)
Fehrenbacher 2016 [26, 34]	POPLAR	Atezolizumab	2	NSCLC	N	Atezolizumab 1200 mg Q 3 W	Docetaxel 75 mg/m <sup>2</sup> Q 3 W		287	62	36–84	61.5	174 (61)	113 (39)
Brahmer 2015 [5]	Checkmate-017	Nivolumab	3	S-NSCLC	N	Nivolumab 3 mg/kg Q 2 W	Docetaxel 75 mg/m <sup>2</sup> Q 3 W		272	63	39–85	63	152 (56)	120 (44)
Borghaei 2015 [6]	Checkmate-057	Nivolumab	3	NS-NSCLC	N	Nivolumab 3 mg/kg Q 2 W	Docetaxel 75 mg/m <sup>2</sup> Q 3 W		582	62	21–85	NR	339 (58)	243 (42)
Motzer 2015 [4]	Checkmate-025	Nivolumab	3	RCC	N	Nivolumab 3 mg/kg Q 2 W	Everolimus 10 mg daily		821	62	18–88	61.3	497 (61)	324 (39)
Robert 01–2015 [29]	Checkmate-066	Nivolumab	3	Melanoma	Y	Nivolumab 3 mg/kg Q 2 W	Dacarbazine 1000 mg/m <sup>2</sup> Q 3 W		418	65	18–87	62.7	200 (48)	218 (52)
Ferris 2016 [2]	Checkmate-141	Nivolumab	3	H&N	N	Nivolumab 3 mg/kg Q 2 W	Chemotherapy		361	60	28–83	59.1	248 (69)	113 (31)
Herbst 2016 [8]	Keynote-010	Pembrolizumab	2/3	NSCLC	N	Pembrolizumab 2 mg/kg Q 3 W	Pembrolizumab 10 mg/kg Q 3 W	Docetaxel 75 mg/m <sup>2</sup> Q 3 W	1033	NR	NR	62	604 (58)	429 (42)
Robert 06–2015 [9]	Keynote-006	Pembrolizumab	3	Melanoma	N	Pembrolizumab 10 mg/kg Q 2 W	Pembrolizumab 10 mg/kg Q 3 W	Ipilimumab 3 mg/kg Q 3 W	834	NR	NR	60.3	467 (56)	367 (44)

n=5458

# Survie globale

**≥ 65 ans**

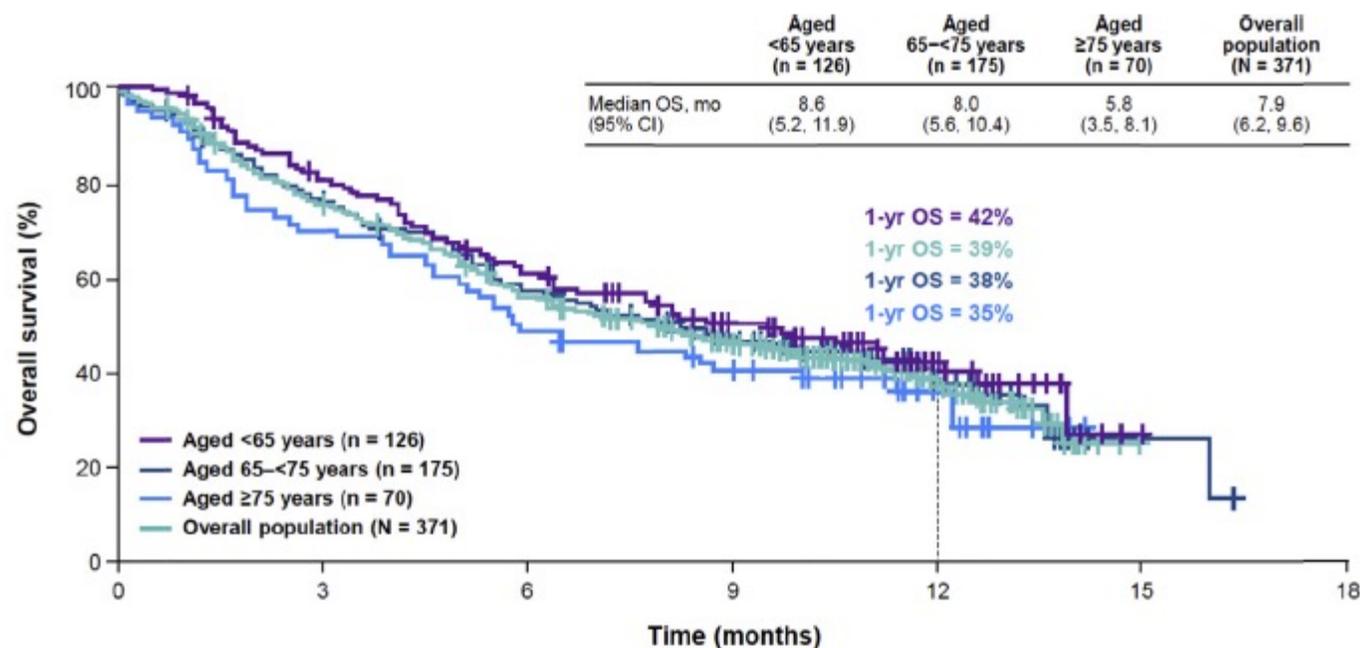


**Table 2** Summary of HR for OS by Age

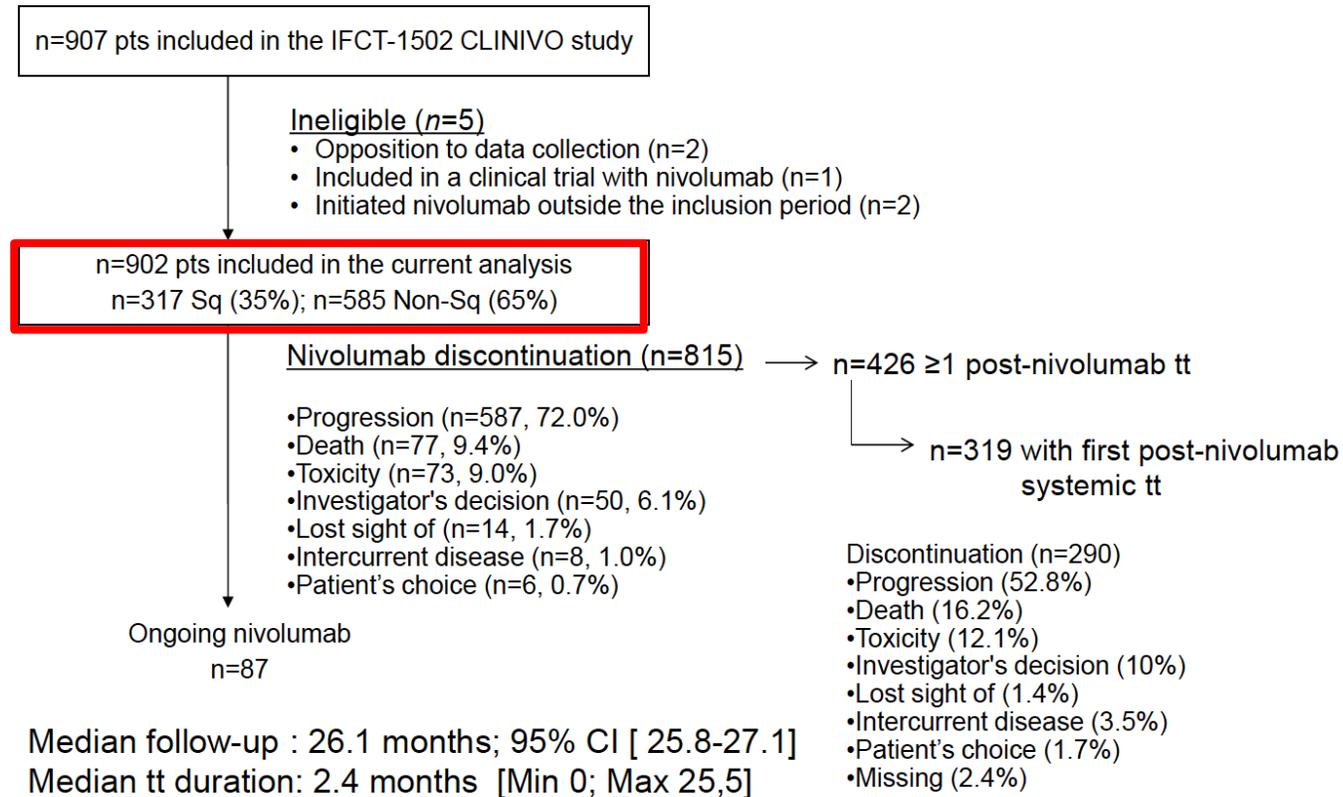
Age	HR (95% CI)
Age < 65 years	0.68 (0.61 to 0.75)
Age ≥ 65 years	0.64 (0.54 to 0.76)

# Use of nivolumab in elderly patients with advanced squamous non–small-cell lung cancer: results from the Italian cohort of an expanded access programme

Characteristics	Univariate, HR (95% CI)	Multivariate, HR (95% CI)
Gender (male versus female)	1.67 (1.05–2.64) p = 0.03	
Age ( $\geq 75$ versus 65–<75)	1.15 (0.82–1.61) p = 0.42	
Smoking habits (current/former versus never)	1.68 (0.86–3.30) p = 0.13	
Brain mets (yes versus no)	1.08 (0.55–2.11) p = 0.83	
Liver mets (yes versus no)	1.59 (1.09–2.33) p = 0.02	1.53 (1.05–2.79) p = 0.03
Bone mets (yes versus no)	2.06 (1.49–2.83) p < 0.0001	2.03 (1.47–2.79) p < 0.0001
ECOG PS (2 versus 0–1)	1.69 (0.94–3.05) p = 0.08	
Previous therapies ( $\geq 2$ versus 1)	0.80 (0.59–1.09) p = 0.15	



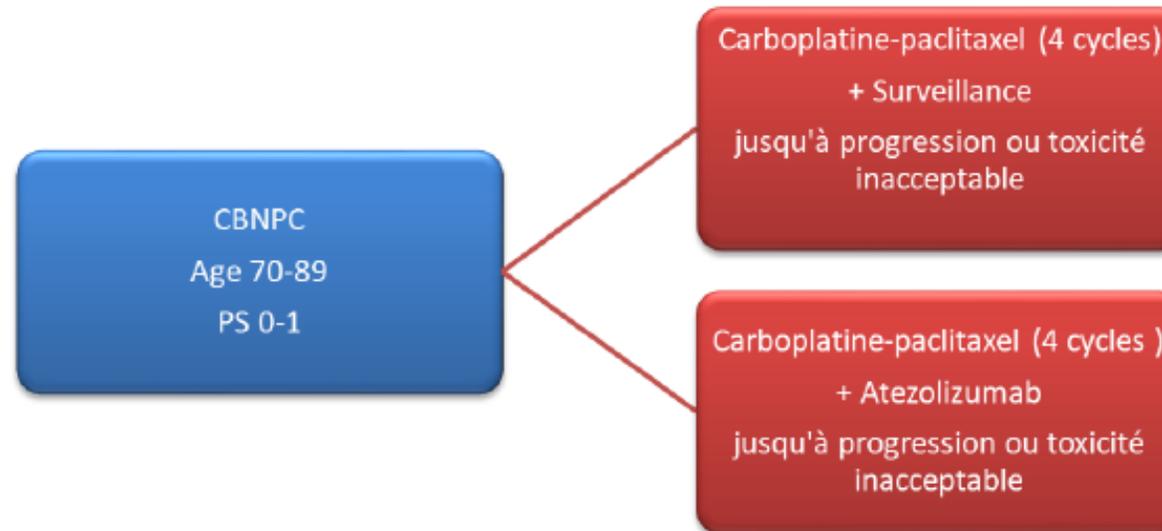
# IFCT-1502 CLINIVO



Gender, **age at initiation of nivolumab**, smoking history, TNM stage, histology were not associated with OS.

# Essai en cours : IFCT-1805 ELDERLY

*PI: Pr Elisabeth QUOIX, Pr Céline MASCAUX*



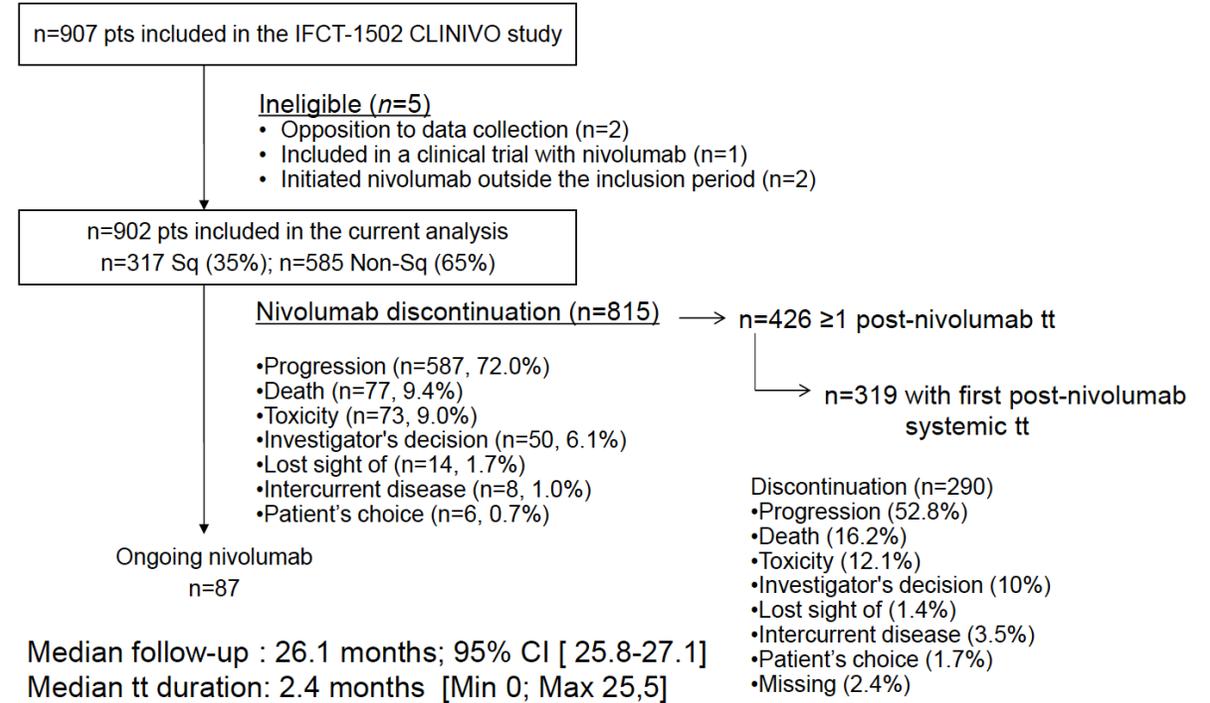
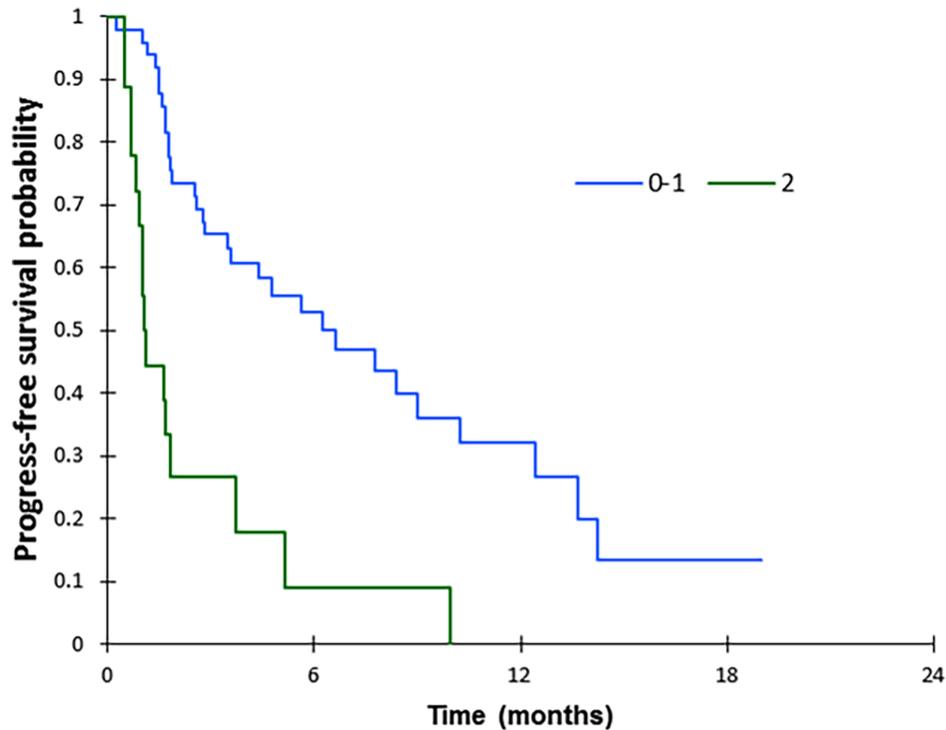
**CJP : SG**

Facteur de stratification :

- Histologie (épidermoïde vs non épidermoïde)
- Age (70-79 vs 80-89 ans)
- Expression de PD-L1 (0 vs  $\geq 1$  vs inconnu)

# PS 2

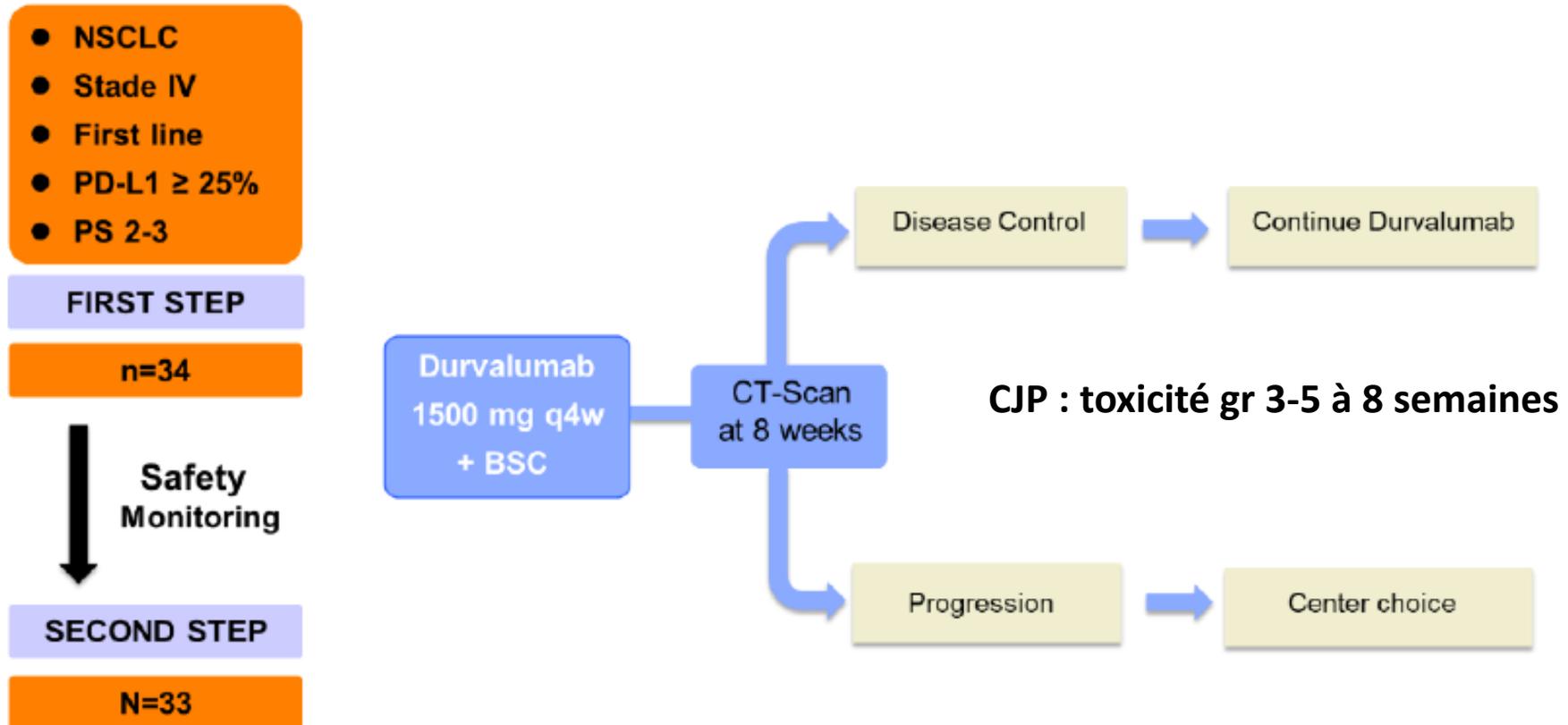
**Etude bicentrique retrospective, nivolumab (n=67)**



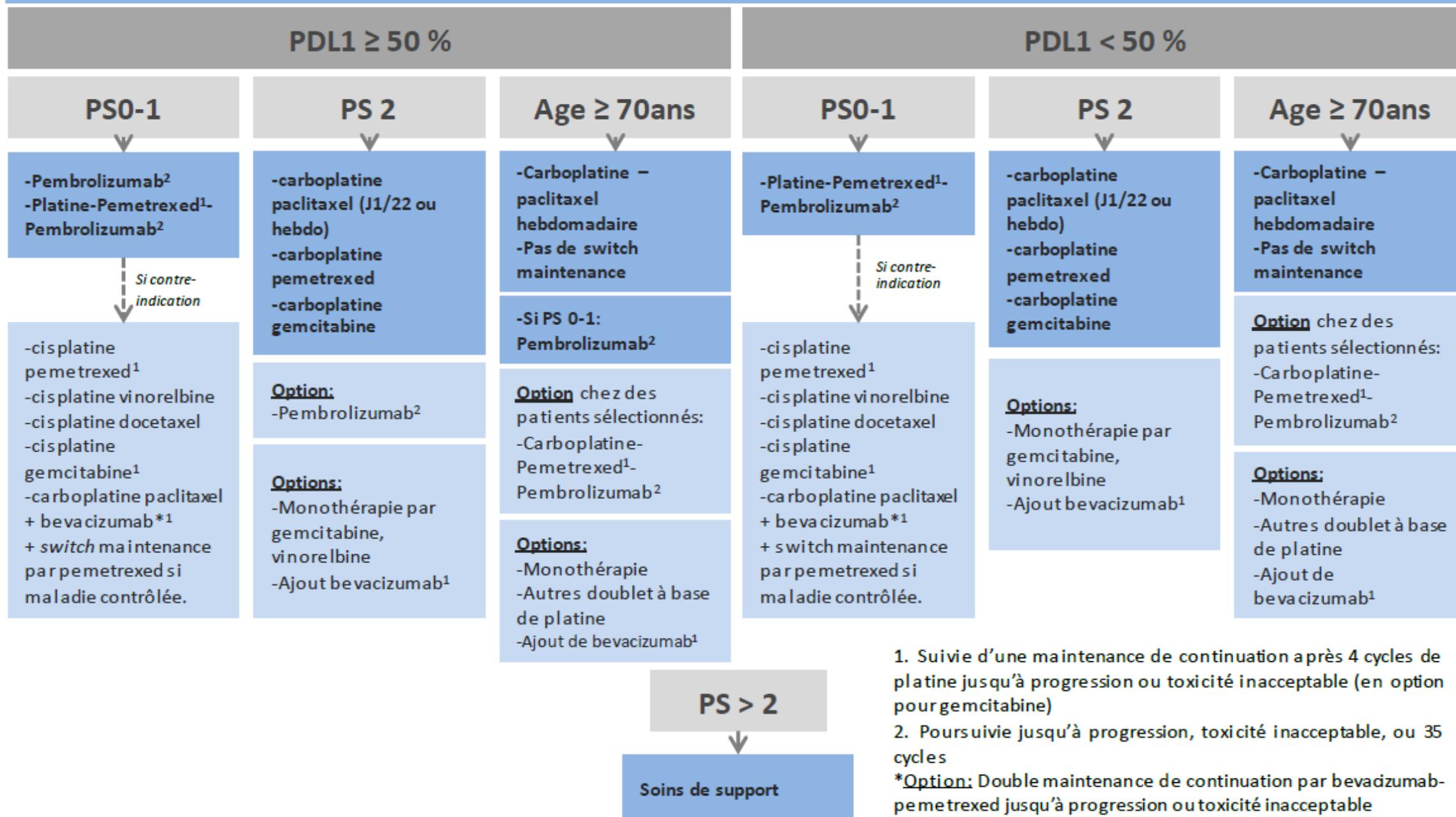
Characteristics	Univariate analysis			Multivariate analysis (n=889)		
	HR	95% CI	p	HR	95% CI	p
<b>ECOG PS</b>						
≥2 (vs 0/1)	2.24	1.85-2.72	<0.0001	2.21	1.82-2.69	<0.0001
<b>Brain metastasis</b>						
Yes (vs No)	1.39	1.15-1.68	0.001	1.38	1.15-1.67	0.0007

# Essai en cours : IFCT-1802 SAVIMMUNE

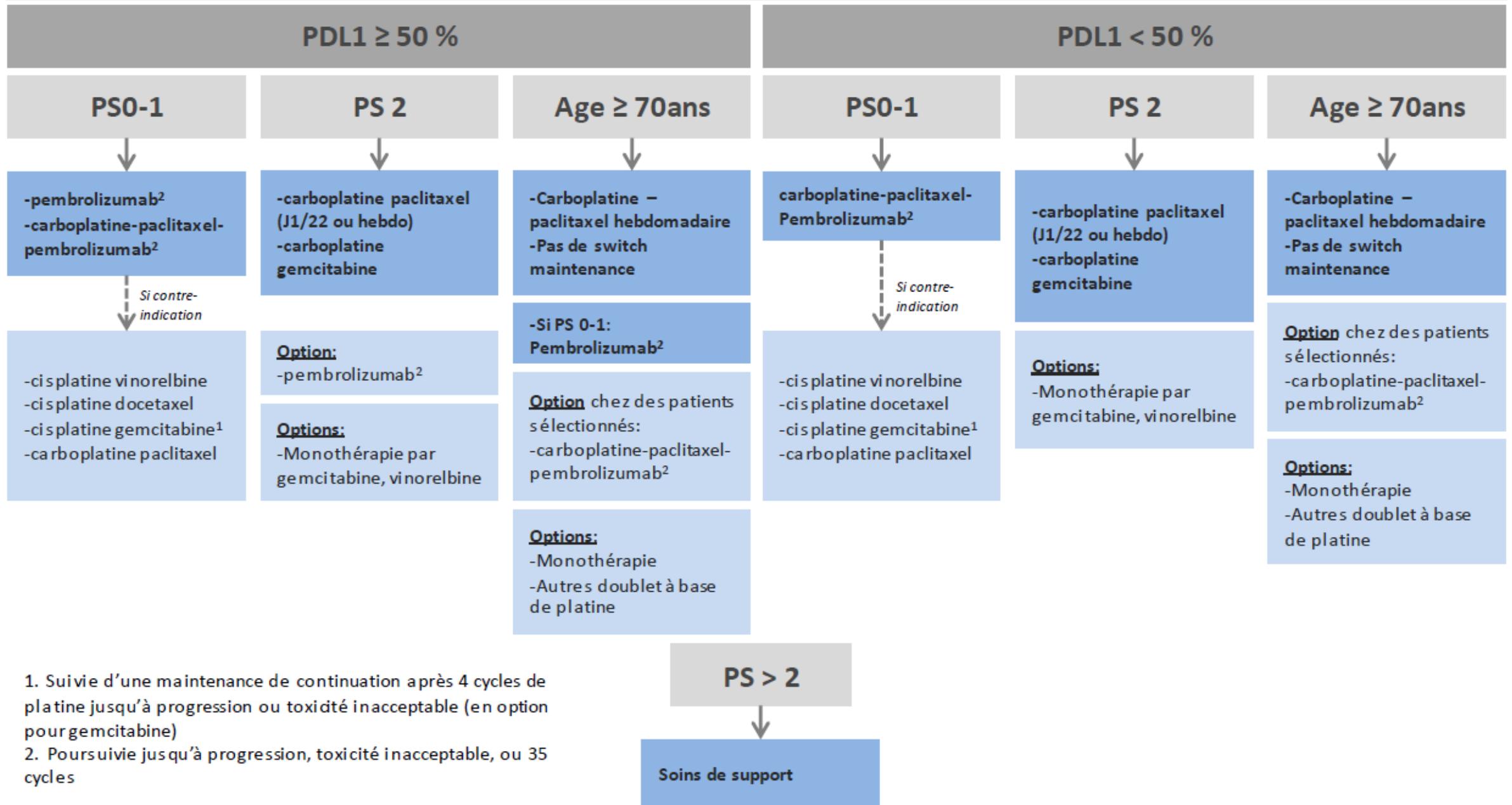
PI: Dr Valérie GOUNANT, Dr Michael DURUISSEAUX



# CANCERS NON-EPIDERMOÏDES DE STADE cIV SANS altération ciblable



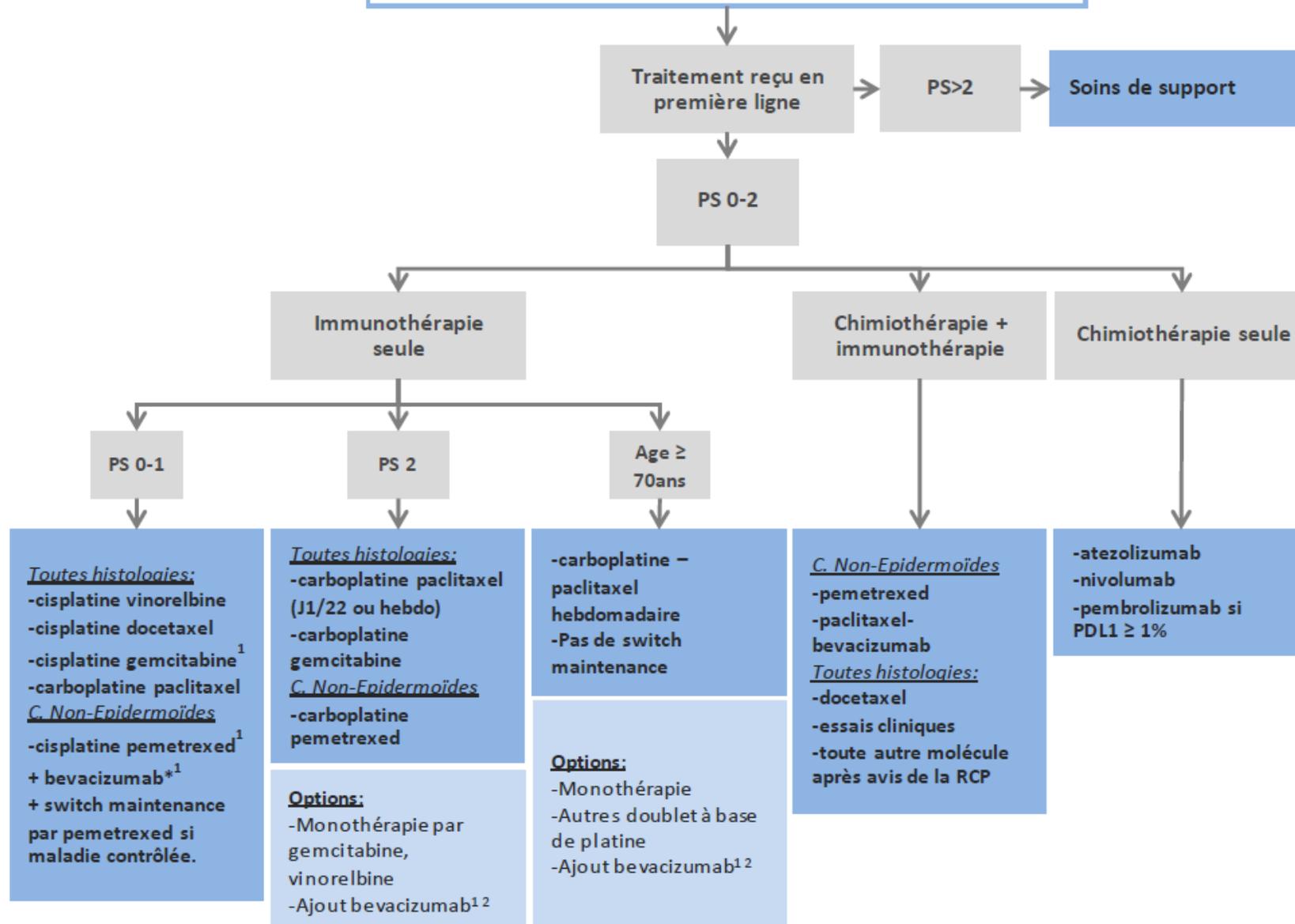
# CANCERS EPIDERMOÏDES DE STADE cIV SANS altération ciblable



1. Suivie d'une maintenance de continuation après 4 cycles de platine jusqu'à progression ou toxicité inacceptable (en option pour gemcitabine)

2. Poursuivie jusqu'à progression, toxicité inacceptable, ou 35 cycles

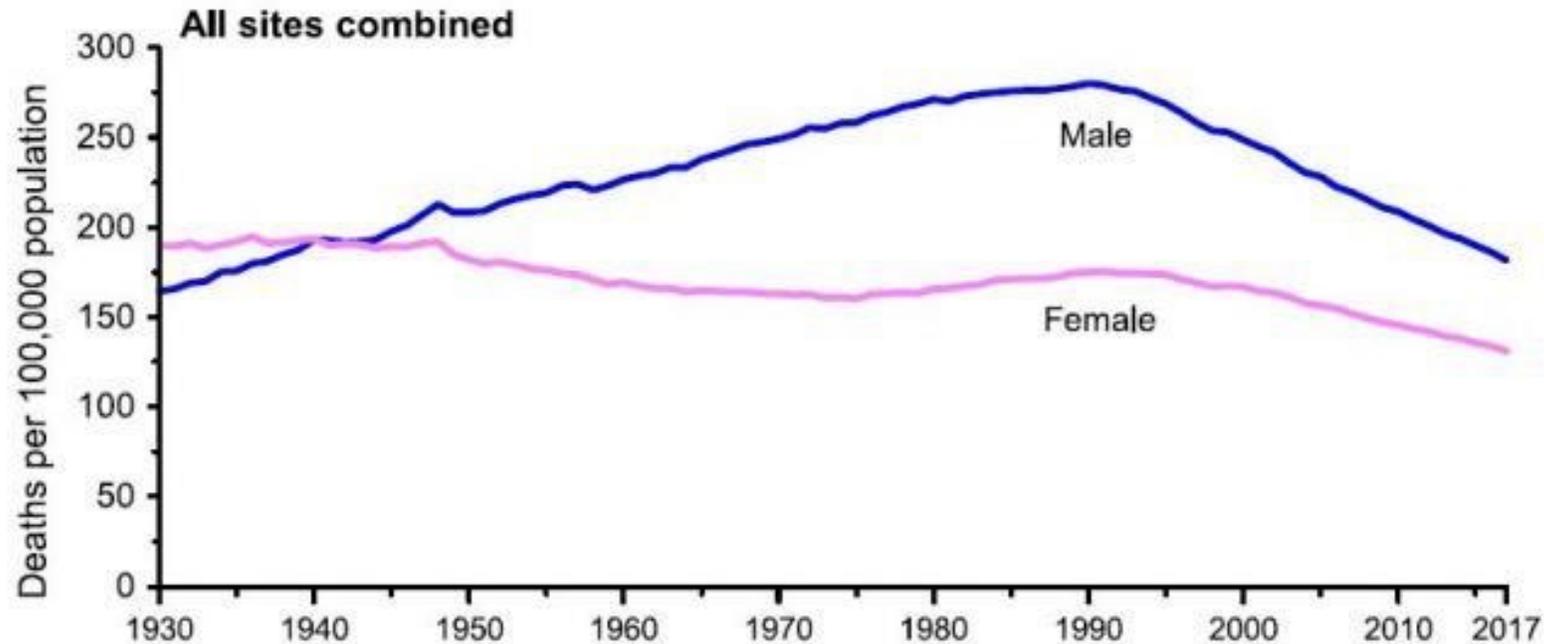
## SECONDE LIGNE CBNPC DE STADE cIV



# Conclusion

La « bonne » nouvelle de 2020

Réduction de la mortalité par cancer bronchique chez les hommes et les femmes (aux USA)



**Diagnostic plus précoce  
Traitements plus efficaces**