Stade III : immunothérapie de consolidation pour tous ?

Dr Charles RICORDEL

Date 15/12/2023

17ème réunion clinico-pathologique en oncologie thoracique

CONFLITS D'INTÉRÊT

Invitations & hospitalité

LVL médical ouest, Lilly France SAS, Novartis Pharma SAS, MSD France, Boehringer Ingelheim France, Pfizer SAS, Chugai Pharma, Roche SAS, AstraZeneca

Subventions de recherche

Roche, Novartis

Interventions rémunérées / non rémunérées

MSD France, Boerhinger Ingelheim France, AstraZeneca, Takeda, Sanofi

CONTEXTE

Stade III

Résécabilité ?

CONTEXTE

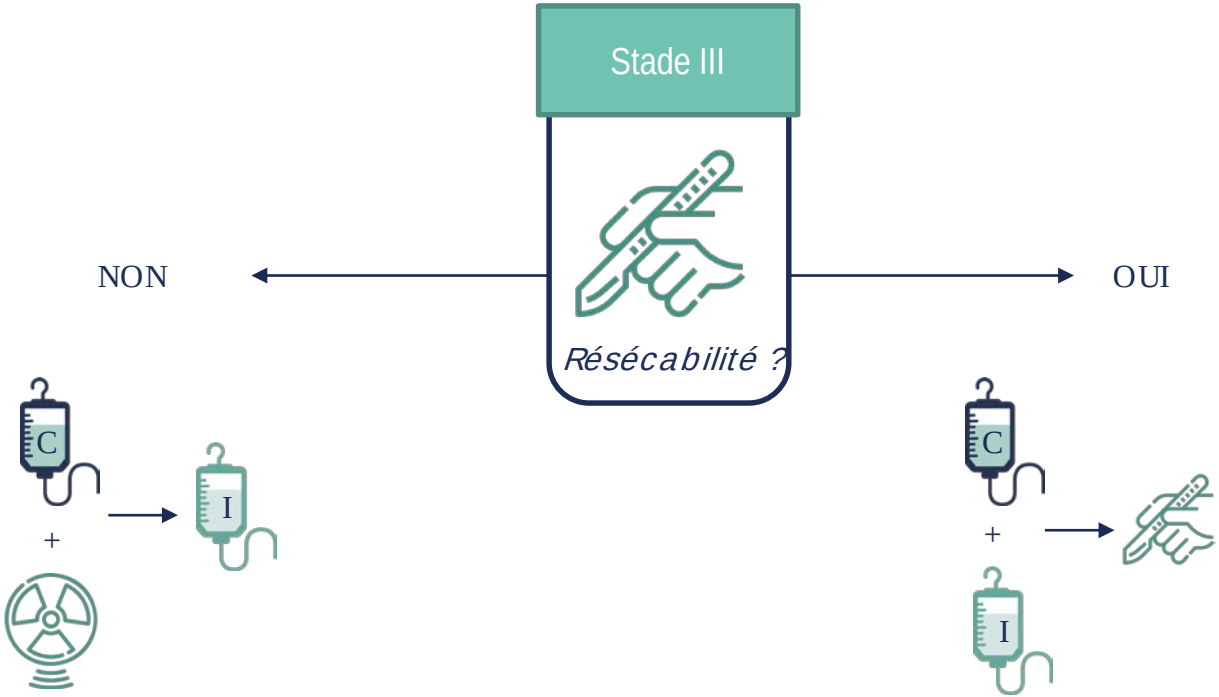
EORTC- Lung Cancer Group Initiative on a consensual definition of stage III NSCLC resectability

	N0	N1	N2 single (non-bulky)	N2 multi (non-bulky)	N2 Bulky$	N2 invasive	N3
T1- T2			RESECTABLE	POTENTIALLY RESECTABLE*	?	UNRESECTABLE	UNRESECTABLE
T3 size / satellite /invasion		RESECTABLE	RESECTABLE	POTENTIALLY RESECTABLE*	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE
T4 size /satellite	RESECTABLE	RESECTABLE	RESECTABLE	POTENTIALLY RESECTABLE*	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE
T4 invasion	POTENTIALLY RESECTABLE	POTENTIALLY RESECTABLE	POTENTIALLY RESECTABLE	POTENTIALLY RESECTABLE*	UNRESECTABLE	UNRESECTABLE	UNRESECTABLE

* Exact number of N2 stations not defined

$ lymph nodes with short axis diameter >2,5- 3cm

CONTEXTE


Stade III
NON
Résécabilité ?
OUI
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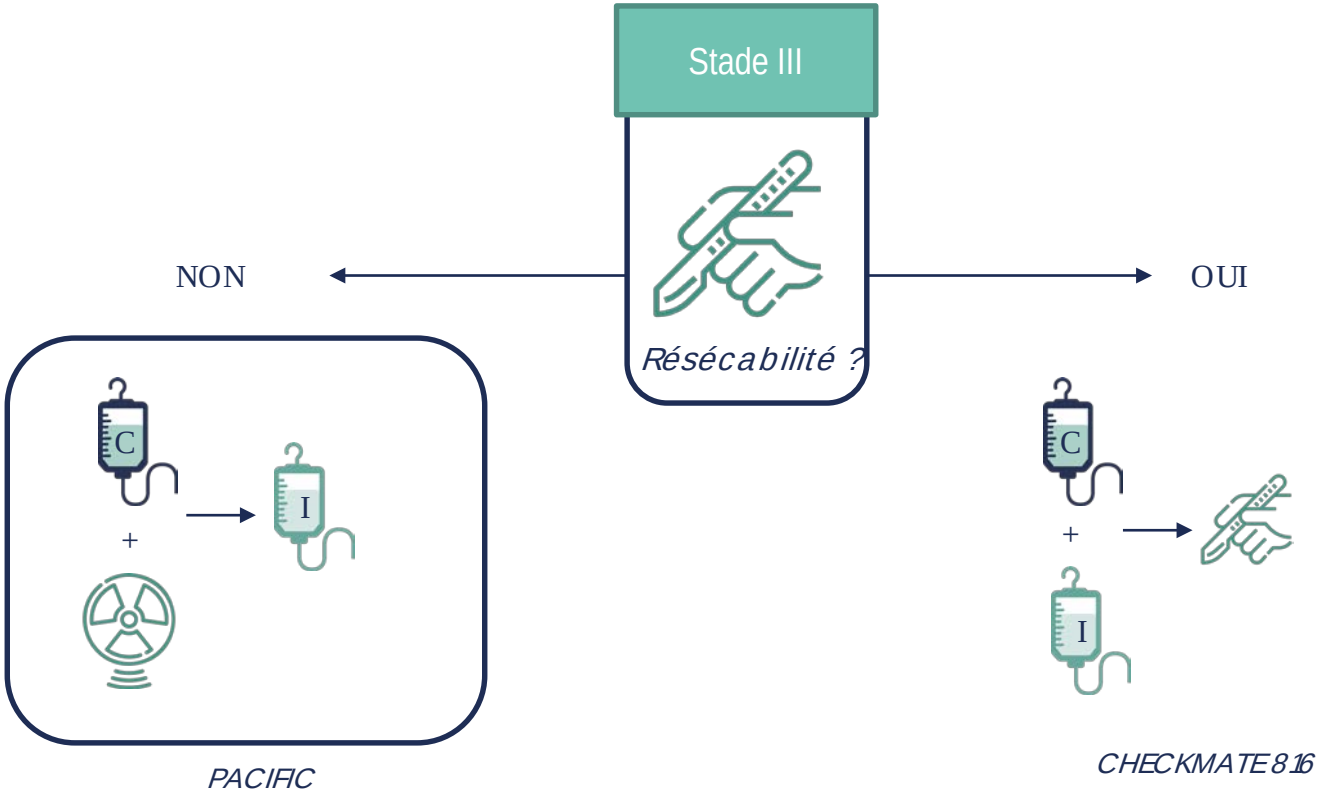
PACIFIC
CHECKMATE 816 (PD-L1≥1%)

CONTEXTE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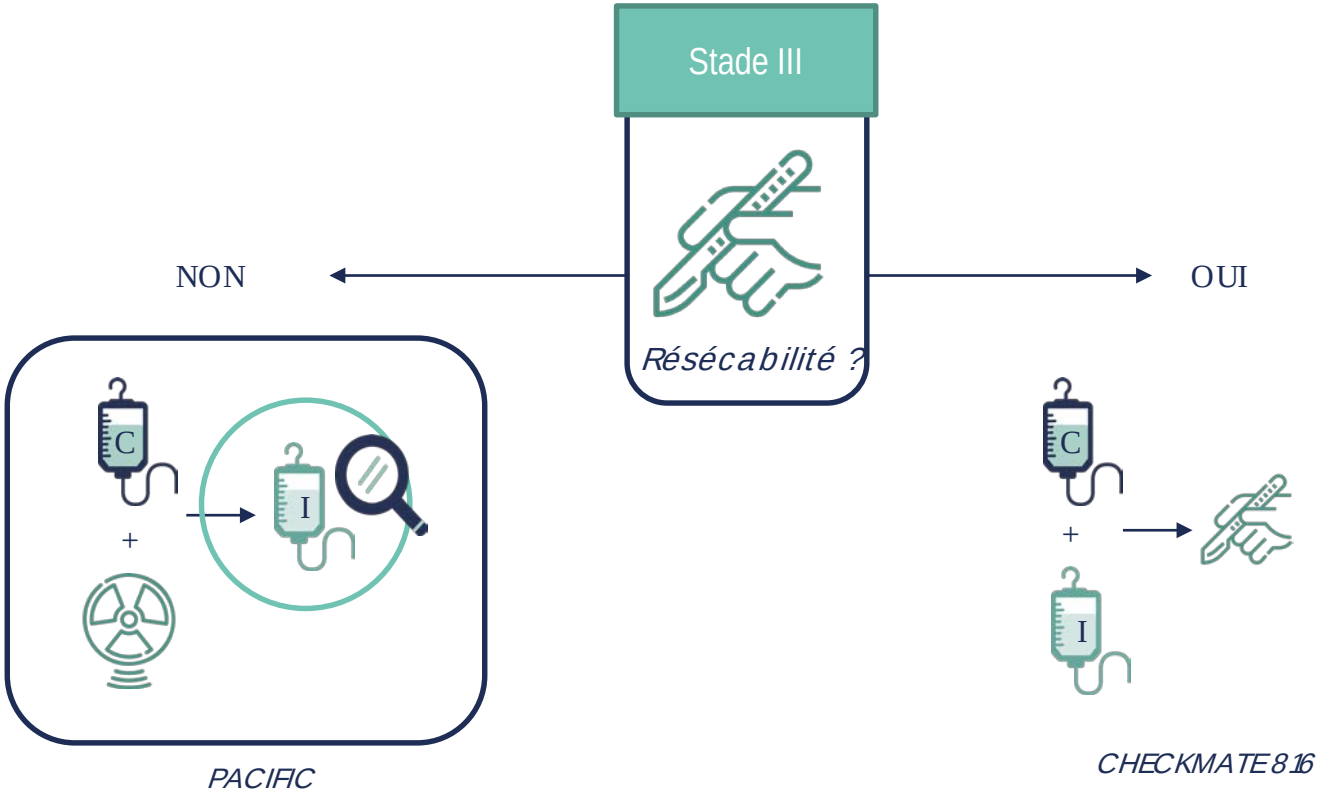
Stade III
Résécabilité ?
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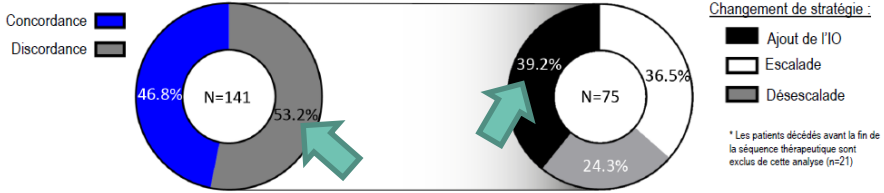
CHECKMATE 816 (PD-L1≥1%)

GFPC- OBSTINATE

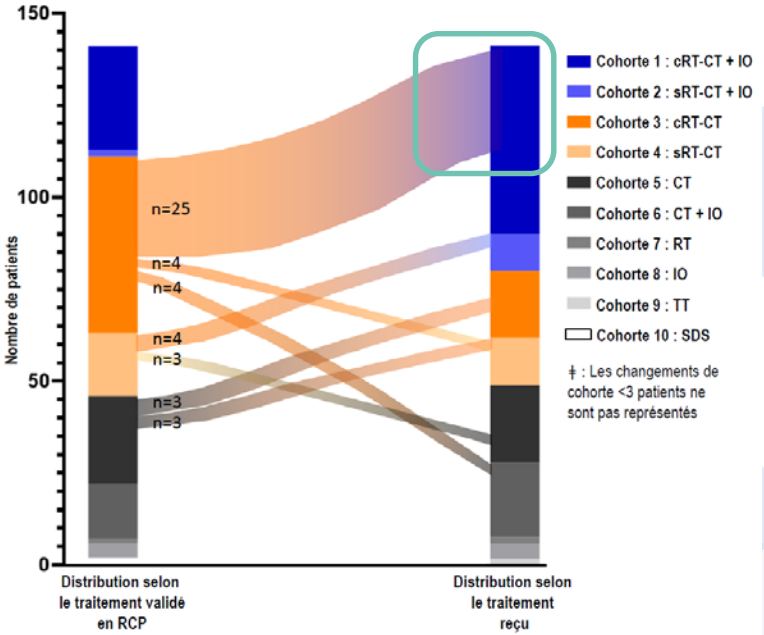
- *Stratégie retenue en RCP vs Traitements reçus*

- Etude **observationnelle** prospective multicentrique Stade III non-résécable
- Objectif principal : évaluation de la **QdV**
- **Inclusions terminées** (>150 patients dans les cohortes d'intérêt)
- Importance du **suivi longitudinal** des patients et de leur données de QdV

► **Concordance entre la stratégie validée en RCP et le traitement reçu (n=141*)**

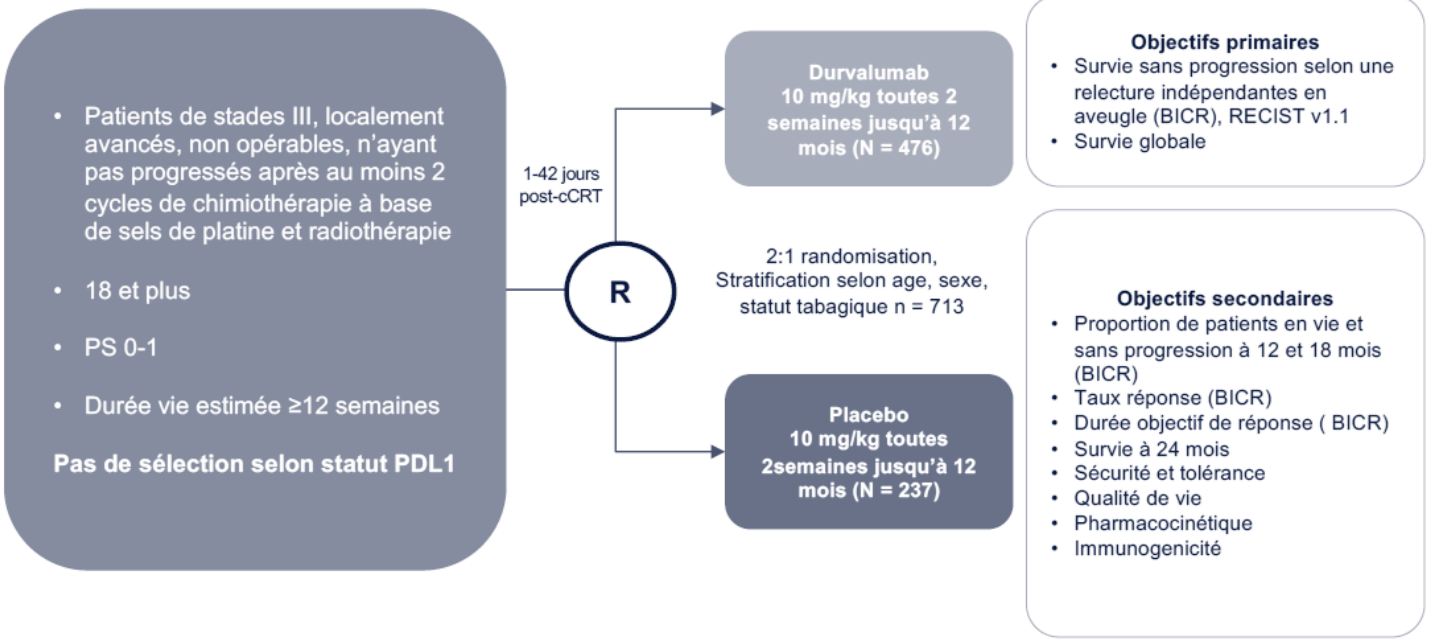


► **Distribution des cohortes en fonction de la stratégie proposée en RCP et le traitement reçu : (n= 141) ǂ**



PACIFIC

Design



Antonia, NEJM, 2017

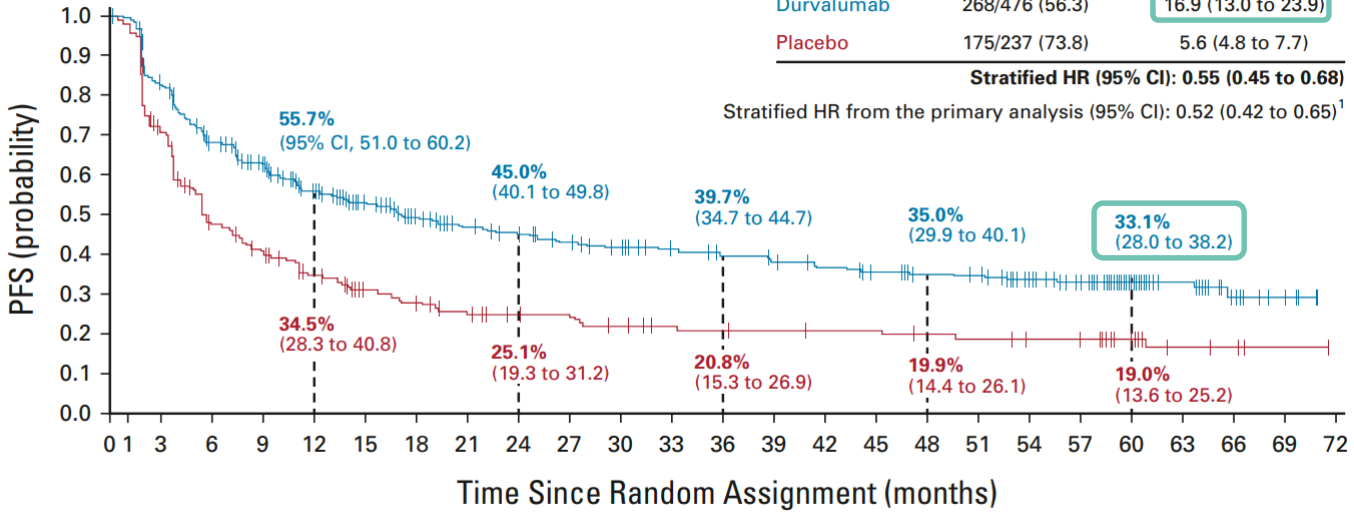
PACIFIC

- *PFS à 5 ans*

Arm	No. of Events/ Total No. of Patients (%)	Median PFS (95% CI), Months
Durvalumab	268/476 (56.3)	16.9 (13.0 to 23.9)
Placebo	175/237 (73.8)	5.6 (4.8 to 7.7)

Stratified HR (95% CI): 0.55 (0.45 to 0.68)

Stratified HR from the primary analysis (95% CI): 0.52 (0.42 to 0.65)[1]



No. at risk:

Durvalumab	476	377	301	267	215	190	165	147	137	128	119	110	103	97	92	85	81	78	67	57	34	22	11	5	0
Placebo	237	164	105	87	68	56	48	41	37	36	30	27	26	25	24	24	22	21	19	19	14	6	4	1	0

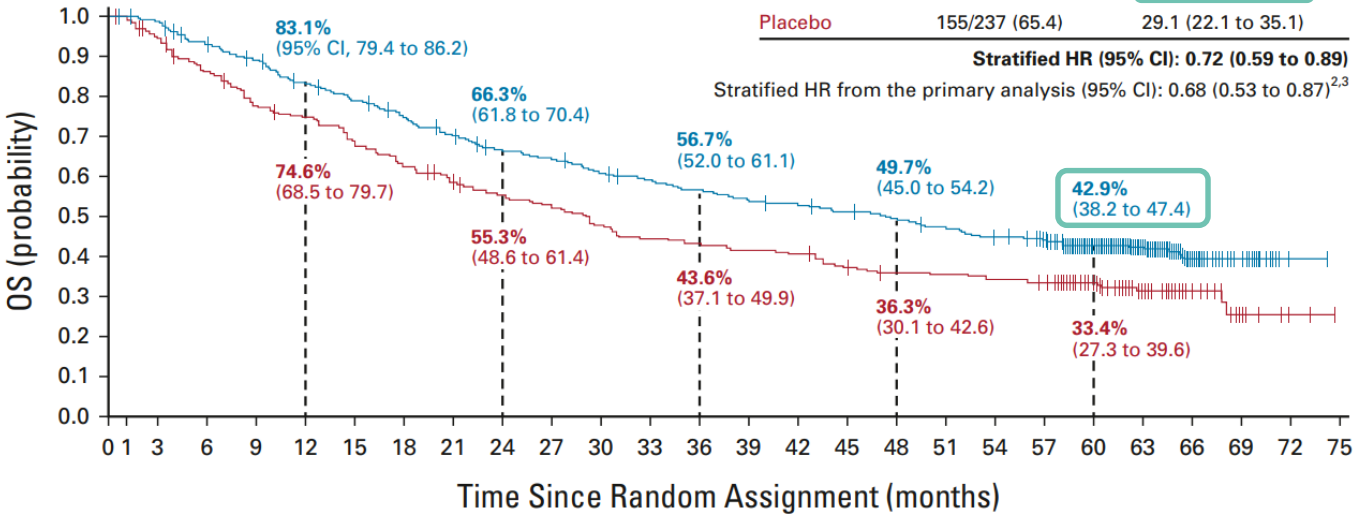
PACIFIC

- *Survie globale à 5 ans*

Arm	No. of Events/ Total No. of Patients (%)	Median OS (95% CI), Months
Durvalumab	264/476 (55.5)	47.5 (38.1 to 52.9)
Placebo	155/237 (65.4)	29.1 (22.1 to 35.1)

Stratified HR (95% CI): 0.72 (0.59 to 0.89)

Stratified HR from the primary analysis (95% CI): 0.68 (0.53 to 0.87)[2,3]

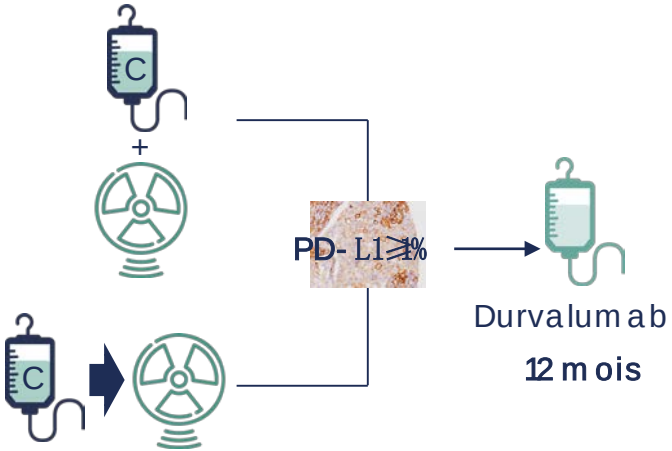


No. at risk:

Durvalumab	476	464	431	414	385	364	343	319	298	289	273	264	252	241	236	227	218	207	196	183	134	91	40	18	2	0
Placebo	237	220	199	179	171	156	143	133	123	116	107	99	97	93	91	83	78	77	74	72	56	33	16	7	2	0

PACIFIC

AMM européenne du durvalumab ou IMFINZI®
« En monothérapie pour le traitement du cancer bronchique non à petites cellules (CBNPC) localement avancé, non opérable, chez les adultes dont les tumeurs expriment PD-L1 ≥ 1% des cellules tumorales et dont la maladie n'a pas progressé après une chimioradiothérapie à base de platine »



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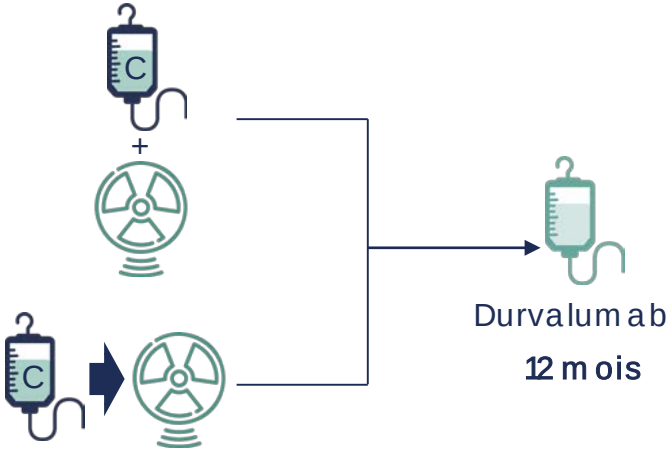
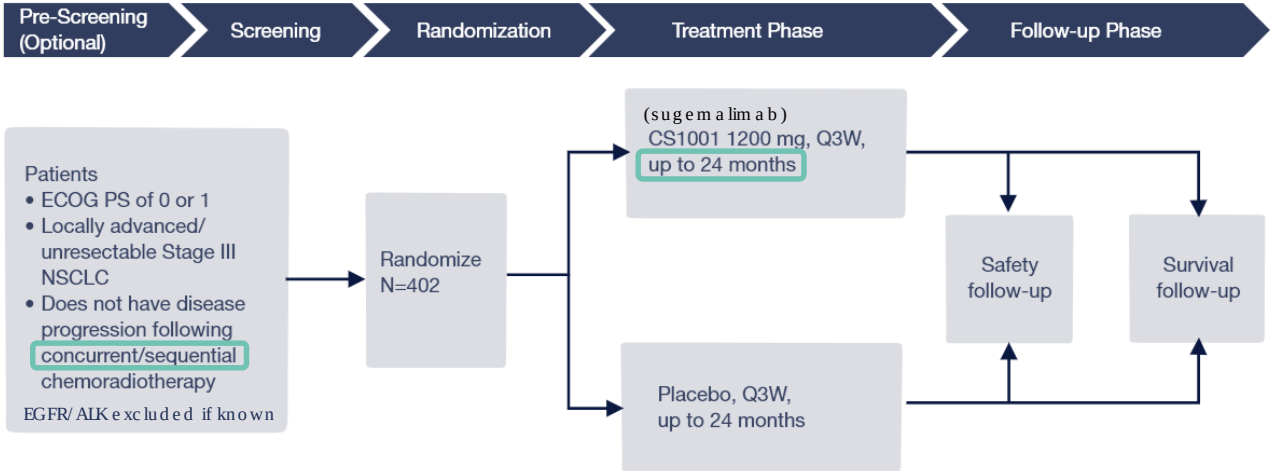


« Traitement des patients adultes atteints d'un cancer bronchique non à petites cellules (CBNPC) localement avancé non opérable et dont la maladie n'a pas progressé après une chimioradiothérapie à base de platine, en cas d'expression tumorale de PD-L1 < 1% ou dans le cas où ce statut est recherché mais le résultat de ce marqueur n'est pas exploitable (statut inconnu). »

GEMSTONE-301

- *Design*

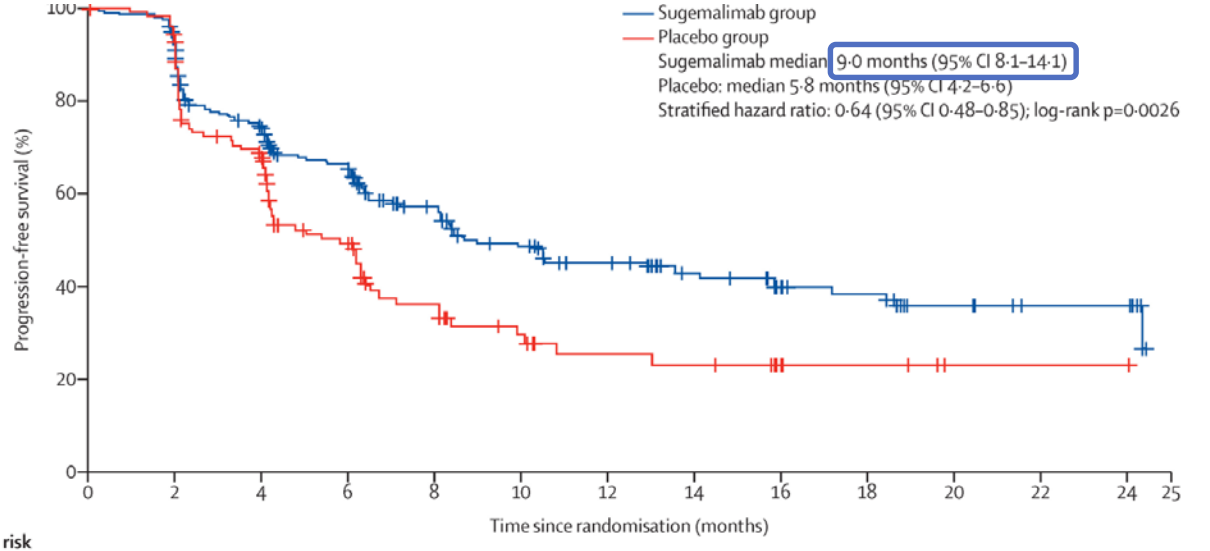


Primary objective	PFS assessed by investigator
Secondary objectives	OS, PFS assessed by BICR, ORR, DoR, and TTDM
	Safety and tolerability
	Pharmacokinetics (PK) and immunogenicity of CS1001
Exploratory objectives	Correlation between PD-L1 expression with CS1001 Correlation between TMB level with CS1001

Zhou, Transl Lung Cancer Res. 2020

GEMSTONE-301

- *SSP (BICR)*

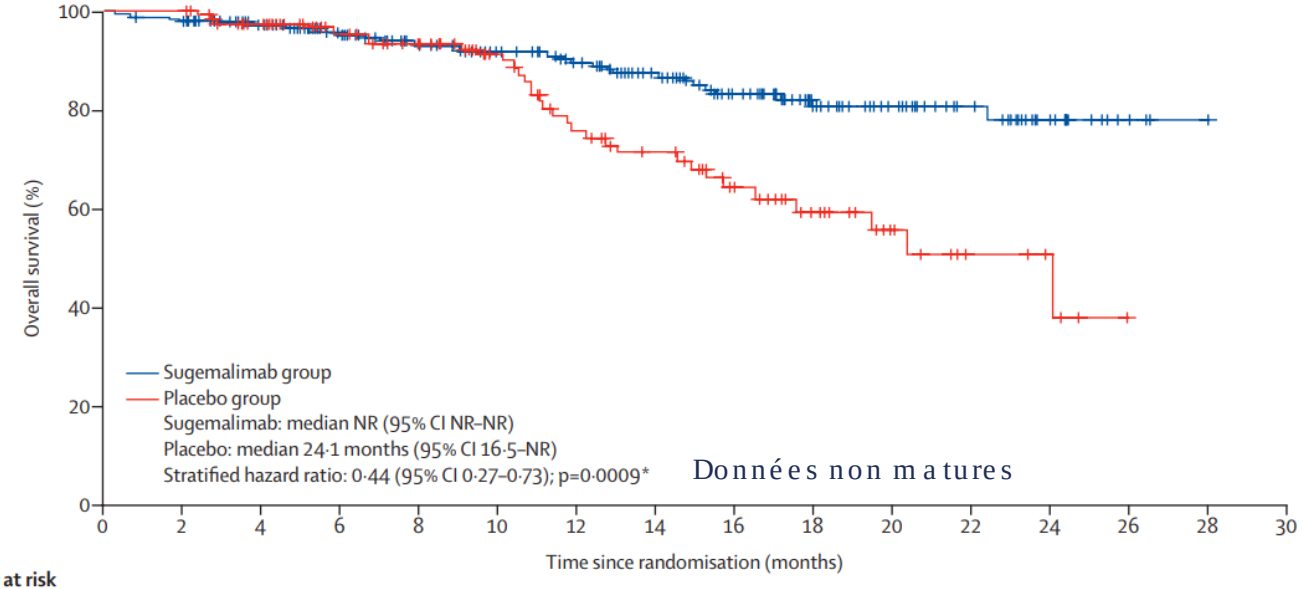


Number at risk (number censored)													
Sugemalimab group	255 (0)	225 (10)	162 (32)	130 (48)	96 (65)	76 (71)	63 (79)	48 (91)	35 (101)	30 (105)	20 (113)	11 (122)	11 (122) 0 (132)
Placebo group	126 (0)	115 (4)	77 (12)	46 (23)	25 (34)	16 (39)	11 (42)	10 (42)	6 (46)	4 (48)	1 (51)	1 (51)	1 (51) 0 (52)

Zhou, Transl Lung Cancer Res. 2020

GEMSTONE-301

- *OS*

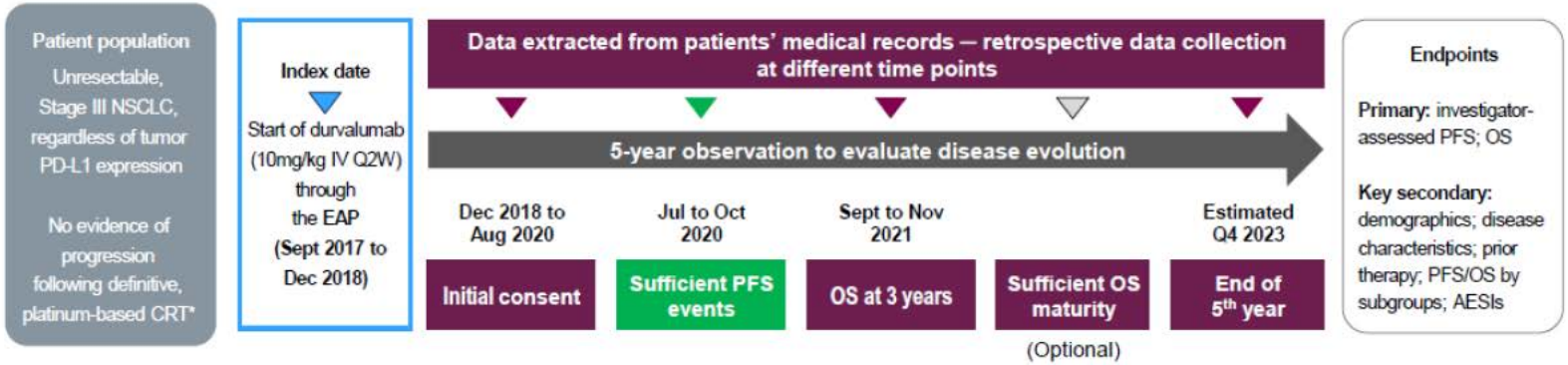


Number at risk (number censored)																
Sugemalimab group	255 (0)	249 (1)	221 (27)	189 (56)	165 (75)	149 (88)	136 (98)	114 (117)	84 (142)	62 (163)	45 (179)	31 (193)	17 (206)	4 (219)	1 (222)	0 (223)
Placebo group	126 (0)	126 (0)	112 (11)	95 (26)	85 (34)	69 (48)	53 (53)	44 (59)	31 (68)	21 (76)	12 (84)	6 (89)	4 (91)	0 (94)	0 (94)	0 (94)

Zhou, Lancet Oncol, 2022

PACIFIC- R

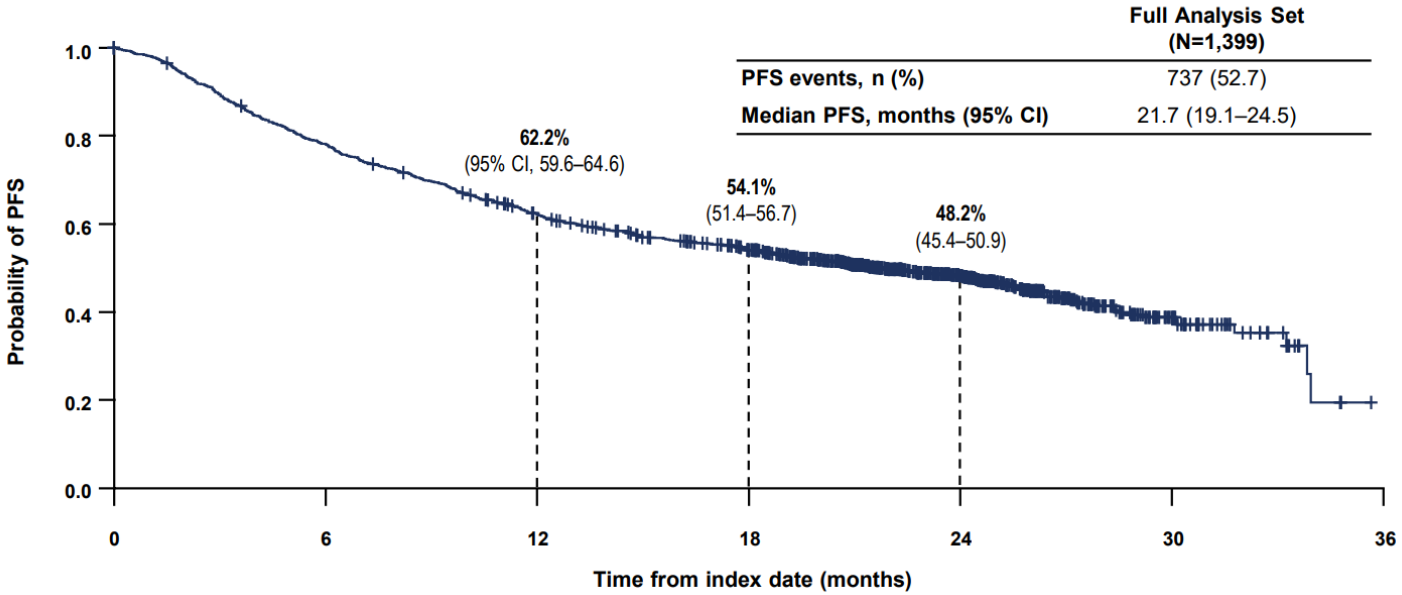
- *Design*



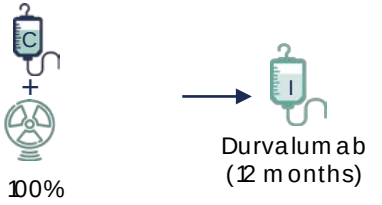
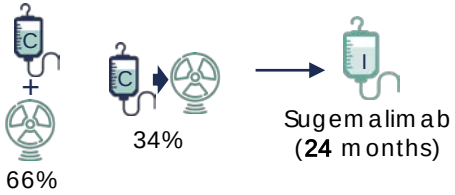
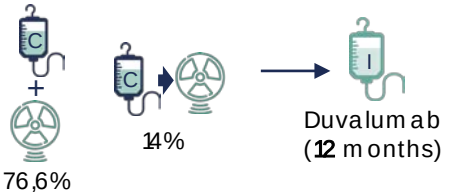
- *Etude internationale observationnelle : 1399 patients (290 centres et 11 pays)*

PACIFIC- R

- *SSP évalué par investigateur*

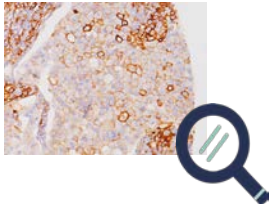


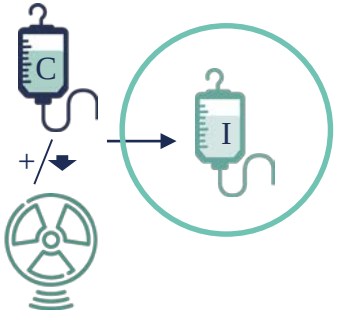
PACIFIC	55,7%	45%

		mPFS	PFS 1y	PFS 2y
PACIFIC		16,9	55,7%	45%
GEMSTONE-301		9,0	45,4%	-
PACIFIC-R		21,7	62,2%	48,2%

CONTEXTE

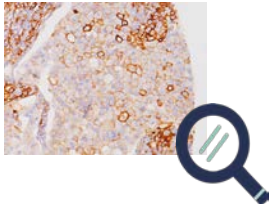
Statut PD- L1





CONTEXTE

Statut PD- L1



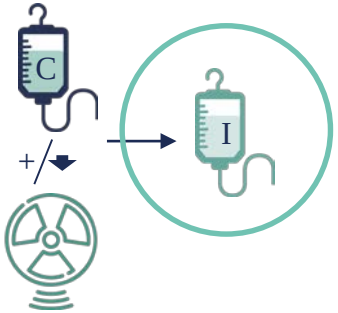


Schéma de radiothérapie

CONTEXTE

Stade III

Statut PD- L1

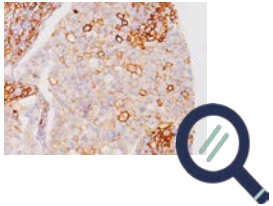
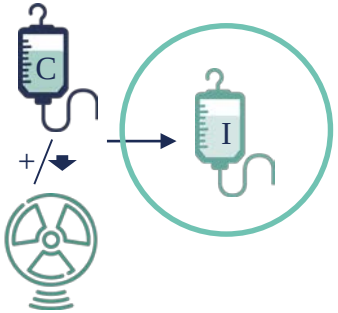


Schéma de radiothérapie

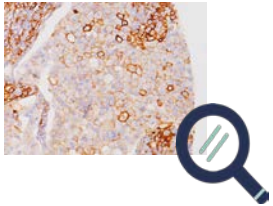


Addiction oncogénique activable

CONTEXTE

Stade III

Statut PD- L1



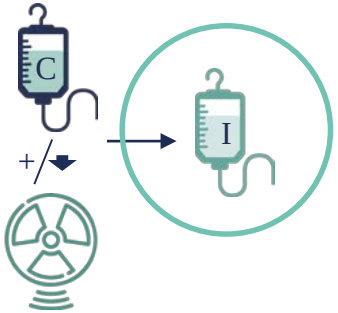


Schéma de radiothérapie

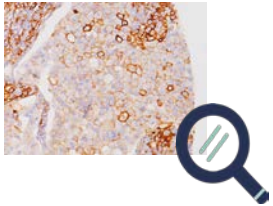
Addiction oncogénique activable

Timing idéal pour l'immunothérapie

CONTEXTE

Stade III

Statut PD- L1



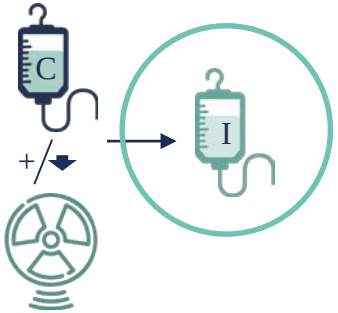


Schéma de radiothérapie

Addiction oncogénique activable

Timing idéal pour l'immunothérapie

Statut PD-L1

- *Influence du statut PD-L1 évalué par TCS*
  - Cas d'un stade IIIAN2 non résécable
  - Statut PD-L1 élevé
  - Quel influence sur une proposition de RT-CT puis IO ?

Pas de différence de profil de répondant (taille de centre, lieu d'exercice, expérience)

PACIFIC

Statut PD- L1

- *Analyse en sous-groupe*

- Recherche du statut PD-L1 non obligatoire
- Statut inconnu pour **37%** des patients de la cohorte

GEMSTONE-301

Statut PD-L1

- *Caractéristiques des patients*

	Sugemalimab group (n=255)	Placebo group (n=126)
Sex		
Male	236 (93%)	115 (91%)
Female	19 (7%)	11 (9%)
Age, years		
Median	61 (56–65)	60 (55–65)
<65	182 (71%)	94 (75%)
≥65	73 (29%)	32 (25%)
Smoking history		
Never smoked	42 (16%)	16 (13%)
Former or current smoker	213 (84%)	110 (87%)
Eastern Cooperative Oncology Group performance status		
0	78 (31%)	38 (30%)
1	177 (69%)	88 (70%)
Chemoradiotherapy type		
Sequential	86 (34%)	41 (33%)
Concurrent	169 (66%)	85 (67%)
Radiotherapy dose		
<60 Gy	43 (17%)	20 (16%)
≥60 Gy	212 (83%)	106 (84%)
Disease stage		
IIIA	74 (29%)	32 (25%)
IIIB	146 (57%)	65 (52%)
IIIC	33 (13%)	28 (22%)
Other	2 (1%)	1 (1%)
Tumour histological type		
Squamous cell carcinoma	177 (69%)	86 (68%)
Non-squamous cell carcinoma	76 (30%)	40 (32%)
Missing data	2 (1%)	0
Previous platinum treatment*		
Cisplatin	130 (51%)	61 (48%)
Carboplatin	82 (32%)	47 (37%)
Nedaplatin	56 (22%)	20 (16%)
Best response to chemoradiotherapy		
Complete response	4 (2%)	2 (2%)
Partial response	172 (67%)	77 (61%)
Stable disease	79 (31%)	47 (37%)
PD-L1 expression†		
<1%	51 (20%)	29 (23%)
≥1%	72 (28%)	23 (18%)
Missing	132 (52%)	74 (59%)

Data are median (IQR) or n (%). *Some patients had more than one type of platinum treatment. †Assessment of baseline PD-L1 expression was not mandatory for study enrolment, therefore PD-L1 status was missing for more than half of the randomly assigned patients.

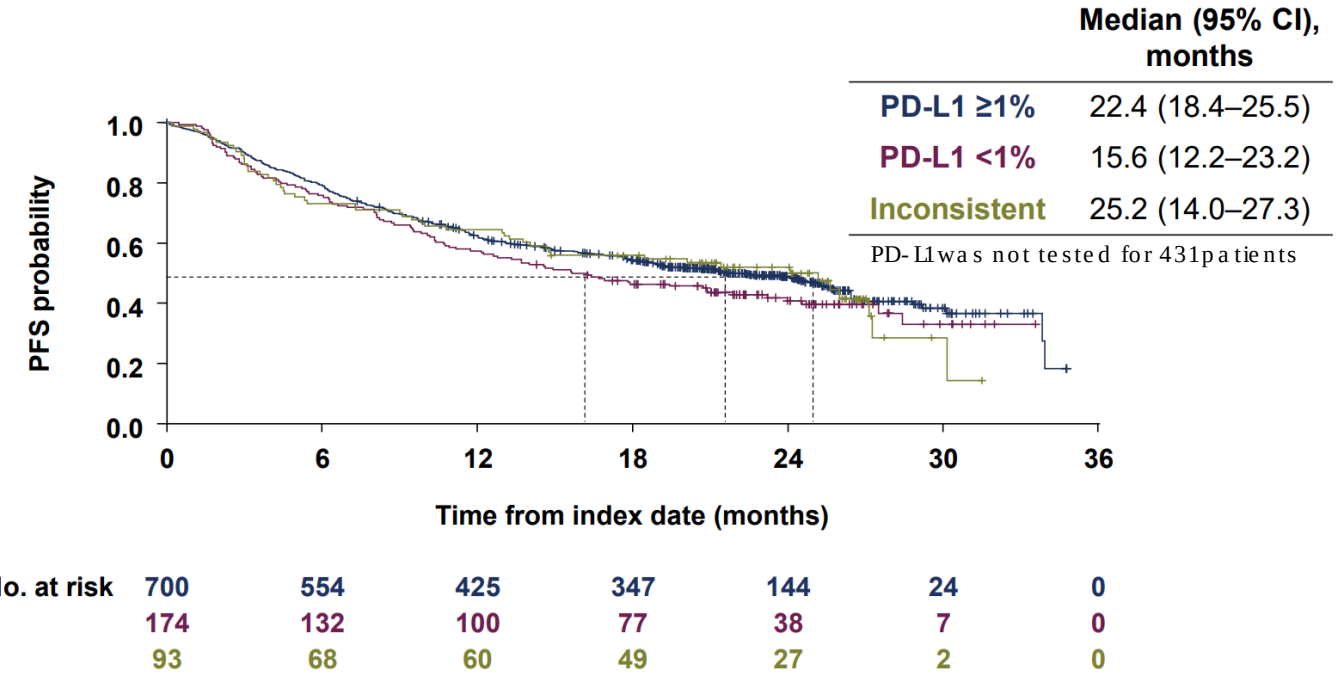
Table 1: **Baseline characteristics of patients in the intention-to-treat population**

- Statut inconnu pour **>50%** des patients de la cohorte
- Aucune analyse en sous groupe communiquée sur PD-L1 (objectif exploratoire pourtant)

PACIFIC- R

Statut PD- L1

- *Analyses en sous- groupes*



PACIFIC- R

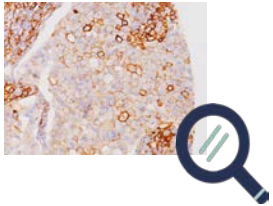
		Median RwPFS		RwPFS rate, %		
		Months	95% CI	12 Months	18 Months	24 Months
Smoking status (at EAP inclusion)						
Current smoker	n = 456	21.6	17.7–26.9	62.9	53.8	49.0
Former smoker	n = 832	23.0	19.4–25.5	62.5	55.0	49.1
Never smoker	n = 111	17.4	11.7–22.6	56.6	48.0	37.4
Timing of durvalumab initiation relative to the end of radiotherapy						
≤42 days	n = 411	25.7	18.4–NE	62.0	55.5	51.5
>42 days	n = 954	20.8	18.6–24.2	62.3	53.8	47.1
>3 months	n = 197	22.6	16.7–26.5	67.9	55.3	48.3
>6 months	n = 13	NE	5.0–NE	61.5	53.8	53.8
PD-L1 status						
PD-L1 ≥1%	n = 700	22.4	18.4–25.5	62.4	54.4	48.9
PD-L1 <1%	n = 174	15.6	12.2–23.2	57.5	46.4	40.9
PD-L1 inconsistent[a]	n = 93	25.2	14.0–27.3	64.5	55.9	52.0
Oncogenic aberration status (reported at Stage III diagnosis)						
Any known aberration[b]	n = 185	20.9	13.9–25.8	60.8	52.0	44.7
KRAS mutated	n = 113	24.2	17.8–NE	66.3	59.1	50.8
EGFR mutated	n = 46	11.1	8.8–24.0	47.8	41.3	35.5

PD- L1was not tested for 431patients

CONTEXTE

Stade III

Statut PD- L1



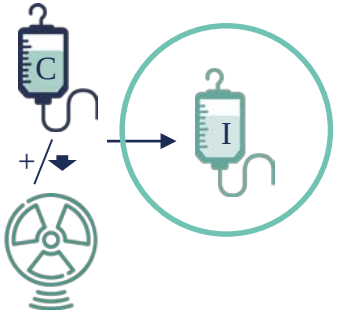


Schéma de radiothérapie

Addiction oncogénique activable

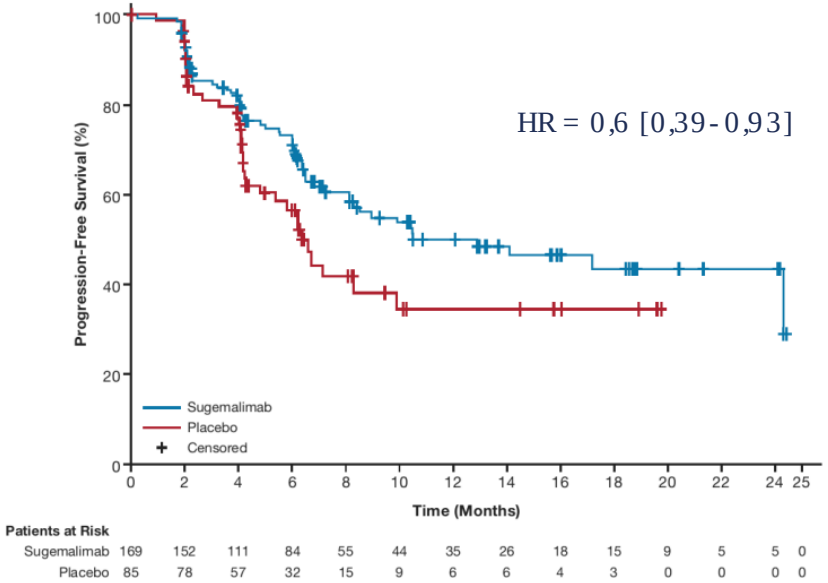
Timing idéal pour l'immunothérapie

GEMSTONE-301

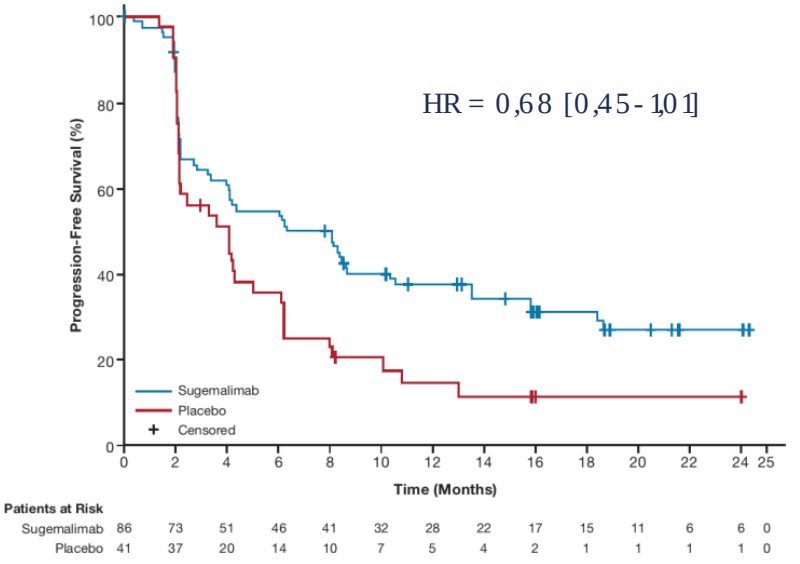
Schéma de RT-CT

- *SSP (BICR)*

cCT-RT préalable



sCT-RT préalable



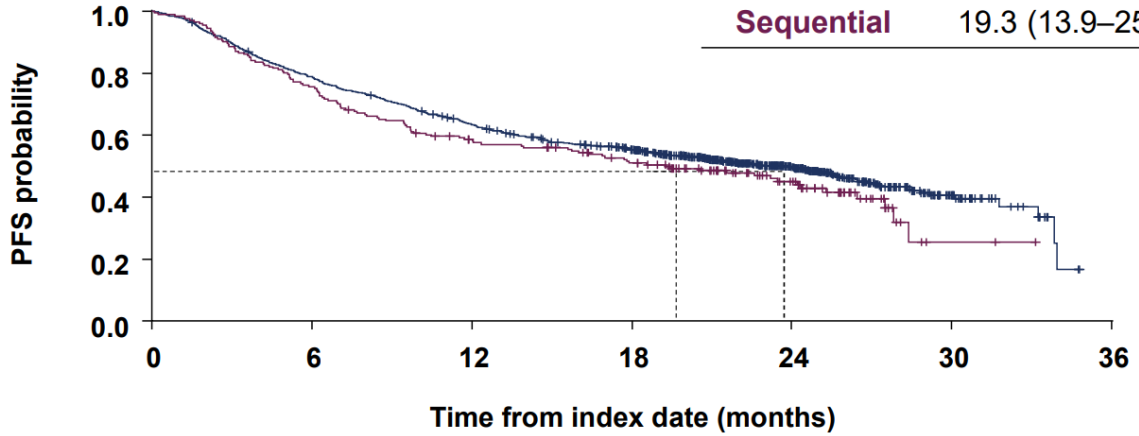
Zhou, Transl Lung Cancer Res. 2020

PACIFIC- R

Schéma de RT- CT

- *Analyses en sous- groupes*

	Median (95% CI), months
Concurrent	23.7 (20.1–25.8)
Sequential	19.3 (13.9–25.3)

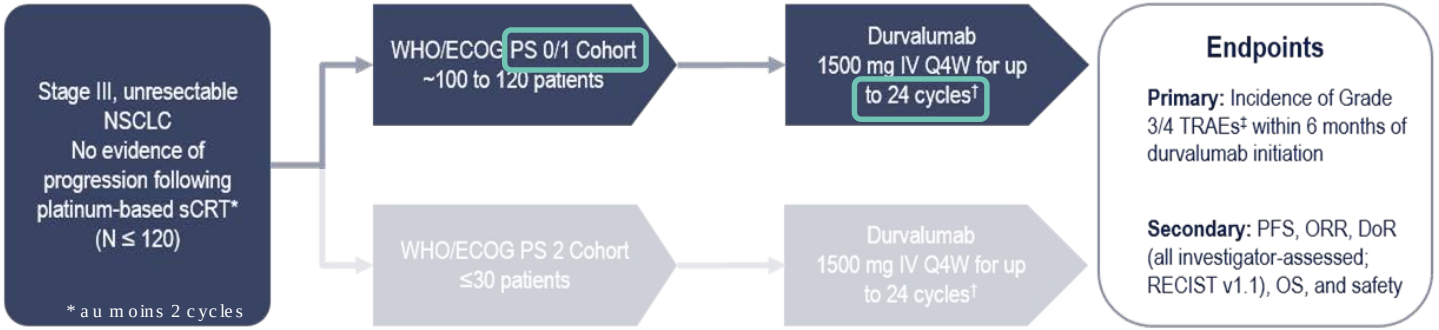


No. at risk							
	1071	843	672	549	245	41	0
	201	152	112	91	45	2	0

PACIFIC- 6

Schéma de RT- CT

- *Design (phase 2)*



- Incidence of AEs (CTCAE v4.03), and the ORR, were summarised with descriptive statistics
- PFS and OS were analysed by Kaplan–Meier method (to estimate medians, 12-month rates and associated 95% CIs)

PACIFIC- 6

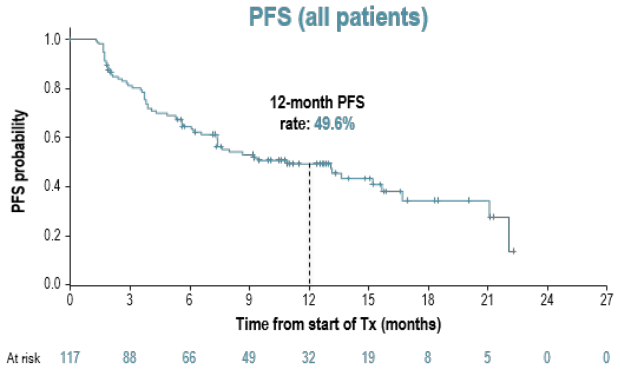
- *Population*

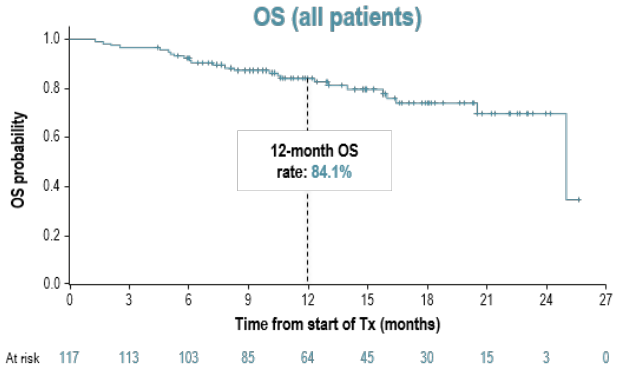
Table 1. Baseline Patient and Disease Characteristics

Characteristic	ECOG PS 0 or 1 (n = 114)
Median age (range), y	68.0 (39-85)
Age group, n (%)	
<65 y	39 (34.2)
≥65 y	75 (65.8)
≥75 y	20 (17.5)
Sex, n (%)	
Men	71 (62.3)
Women	43 (37.7)
Race, n (%)	
White	101 (88.6)
Unknown	13 (11.4)
Smoking history, n (%)	
Never smoker	9 (7.9)
Former smoker	73 (64.0)
Current smoker	32 (28.1)
ECOG PS, n (%)	
0	47 (41.2)
1	67 (58.8)
2	0
Histologic type, n (%)	
Adenocarcinoma	63 (55.3)
Squamous cell	42 (36.8)
Other	9 (7.9)
Disease stage at baseline, n (%)	
IA	1 (0.9)
IIIA	44 (38.6)
IIIB	58 (50.9)
IIIC	11 (9.6)
PD-L1 expression on TCs, n (%)	
<1%	34 (29.8)
≥1%	33 (28.9)
Missing	47 (41.2)

PACIFIC- 6

- *Données de survie*





Endpoint		All patients (N = 117)*	PS 0/1 cohort (n = 114)†
PFS	Median, months (95% CI)	10.9 (7.3–15.6)	13.1 (7.4–16.7)
	12-month rate, % (95% CI)	49.6 (39.5–58.9)	50.1 (39.9–59.5)
OS	Median, months (95% CI)	25.0 (25.0–NC)	25.0 (25.0–NC)
	12-month rate, % (95% CI)	84.1 (75.6–89.9)	84.6 (76.0–90.3)
Confirmed ORR	n (%)	20 (17.1)‡	20 (17.5)‡
	[95% CI]§	[11.1–25.8]	[11.4–26.4]

CONTEXTE

Stade III

Statut PD- L1

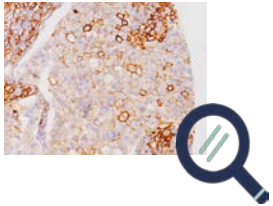
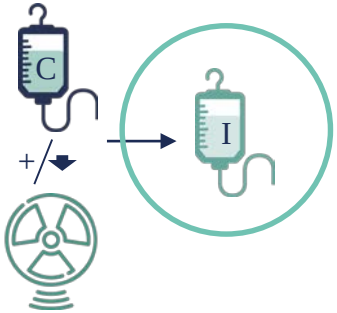


Schéma de radiothérapie



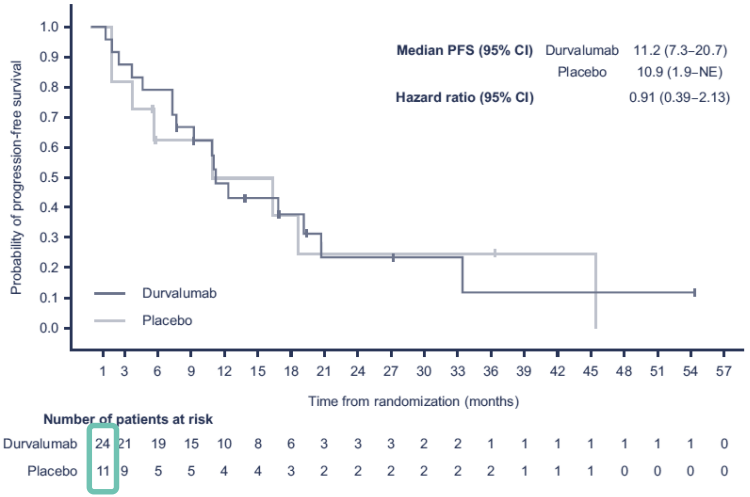
Addiction oncogénique activable

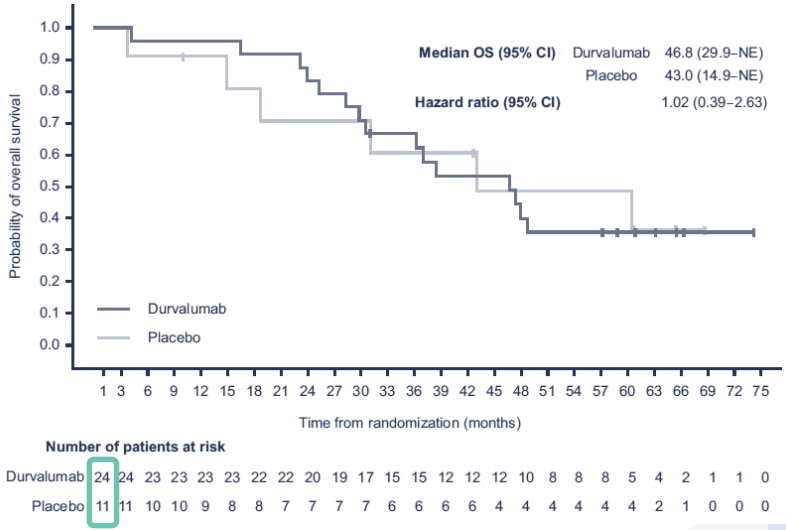
Timing idéal pour l'immunothérapie

PACIFIC

Patients avec mutation EGFR

- *Analyse post-hoc*





PACIFIC- R

Patients avec mutation EGFR

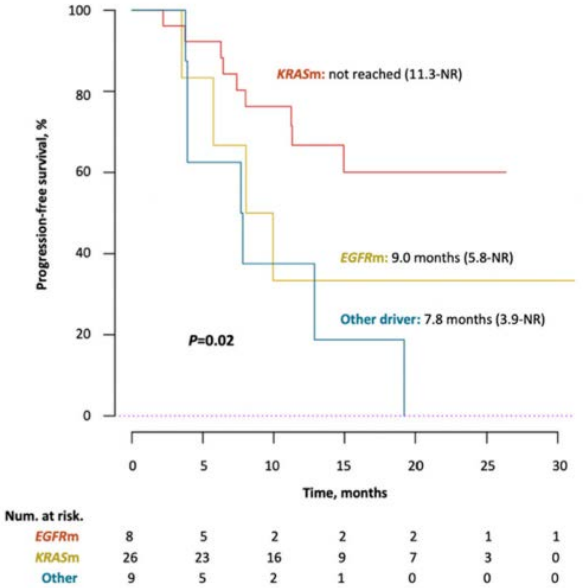
		Median RwPFS		RwPFS rate, %		
		Months	95% CI	12 Months	18 Months	24 Months
Smoking status (at EAP inclusion)						
Current smoker	n = 456	21.6	17.7–26.9	62.9	53.8	49.0
Former smoker	n = 832	23.0	19.4–25.5	62.5	55.0	49.1
Never smoker	n = 111	17.4	11.7–22.6	56.6	48.0	37.4
Timing of durvalumab initiation relative to the end of radiotherapy						
≤42 days	n = 411	25.7	18.4–NE	62.0	55.5	51.5
>42 days	n = 954	20.8	18.6–24.2	62.3	53.8	47.1
>3 months	n = 197	22.6	16.7–26.5	67.9	55.3	48.3
>6 months	n = 13	NE	5.0–NE	61.5	53.8	53.8
PD-L1 status						
PD-L1 ≥1%	n = 700	22.4	18.4–25.5	62.4	54.4	48.9
PD-L1 <1%	n = 174	15.6	12.2–23.2	57.5	46.4	40.9
PD-L1 inconsistent[a]	n = 93	25.2	14.0–27.3	64.5	55.9	52.0
Oncogenic aberration status (reported at Stage III diagnosis)						
Any known aberration[b]	n = 185	20.9	13.9–25.8	60.8	52.0	44.7
KRAS mutated	n = 113	24.2	17.8–NE	66.3	59.1	50.8
EGFR mutated	n = 46	11.1	8.8–24.0	47.8	41.3	35.5

Etudes rétrospectives

Patients avec mutation EGFR

Original Research

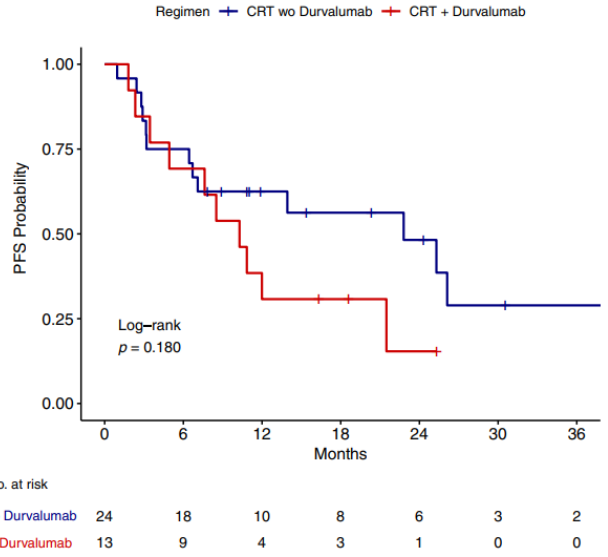
Durvalumab consolidation in patients with unresectable stage III non-small cell lung cancer with driver genomic alterations



ORIGINAL ARTICLE

Durvalumab for Stage III *EGFR*-Mutated NSCLC After Definitive Chemoradiotherapy

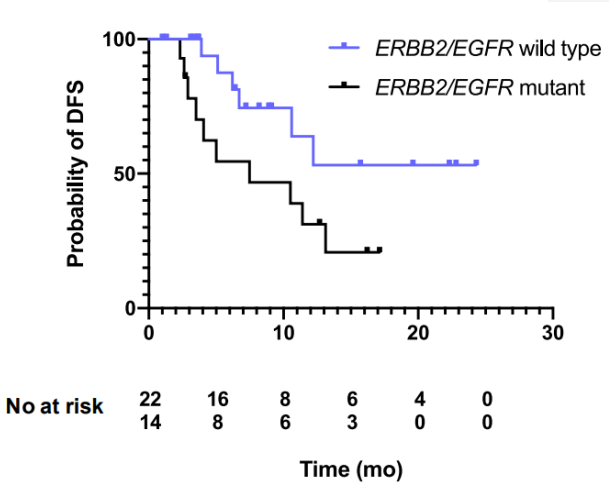
IASLC



BRIEF REPORT

Role of Consolidation Durvalumab in Patients With *EGFR*- and *HER2*-Mutant Unresectable Stage III NSCLC

IASLC



Riudavets, EJC 2022; Aredo, JTO, 2021; Hellyers, JTO, 2021

Guidelines ESMO

Patients avec mutation EGFR

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

ESMO expert consensus statements on the management of *EGFR* mutant non-small-cell lung cancer

9: In patients with *EGFR*-mutant inoperable stage III NSCLC, undergoing curative-intent chemoradiotherapy, what is the role of consolidation ICI therapy?

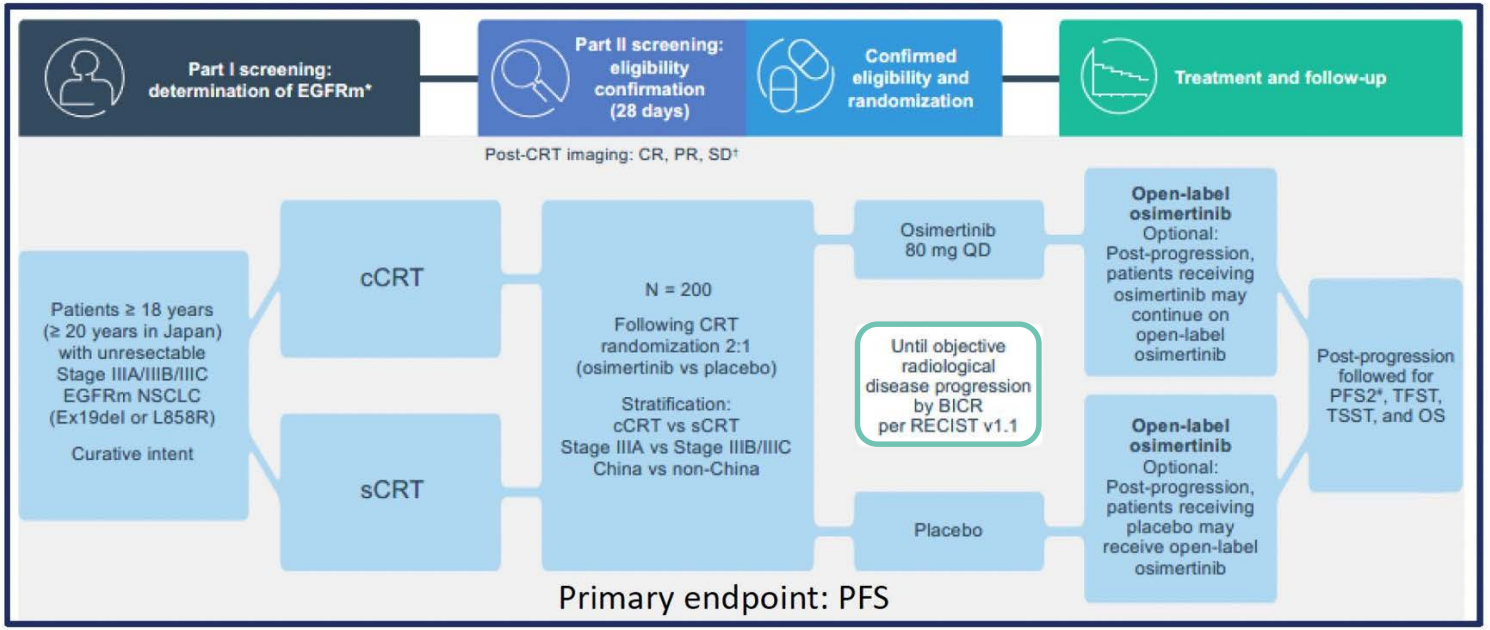
STATEMENT: In *EGFR*-positive disease, the use of consolidation ICI therapy after curative-intent chemoradiotherapy (CT-RT), is not recommended [I,C].

Riudavets, EJC 2022; Aredo, JTO, 2021; Hellyers, JTO, 2021

Perspectives

Patients avec mutation EGFR

- *Etude LAURA*



NB : étude comparable en cours avec l'aumolertinib

Lu, Clin Lung Can, 2021

CONTEXTE

Stade III

Statut PD- L1

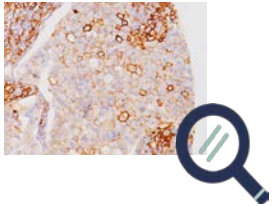
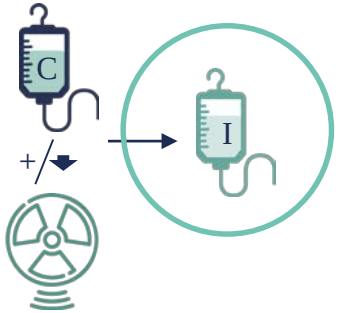


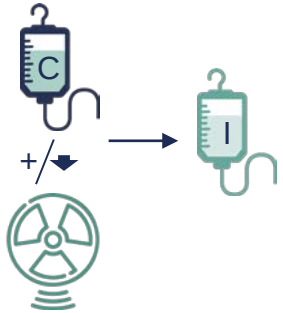
Schéma de radiothérapie

Addiction oncogénique activable



Timing idéal pour l'immunothérapie

Quel timing pour l'immunothérapie ?



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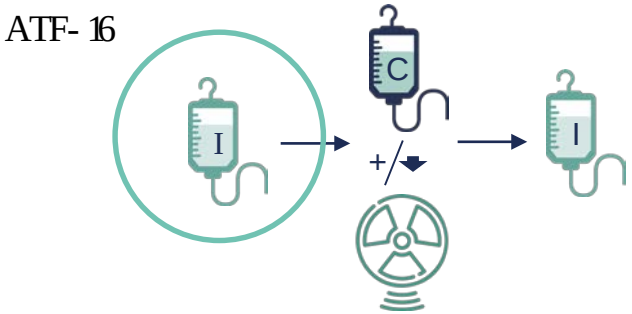

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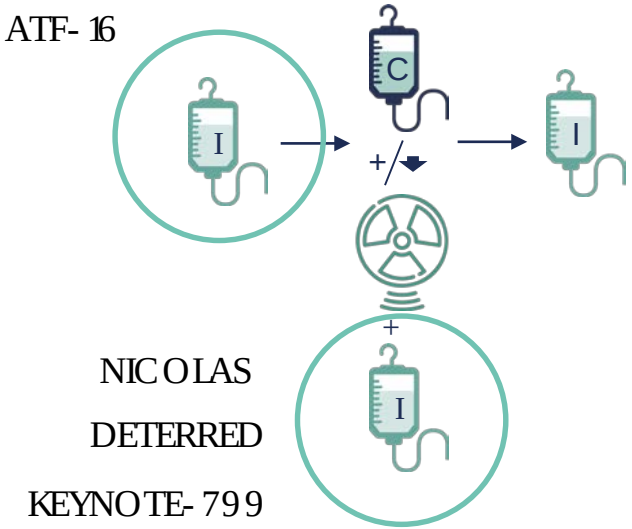

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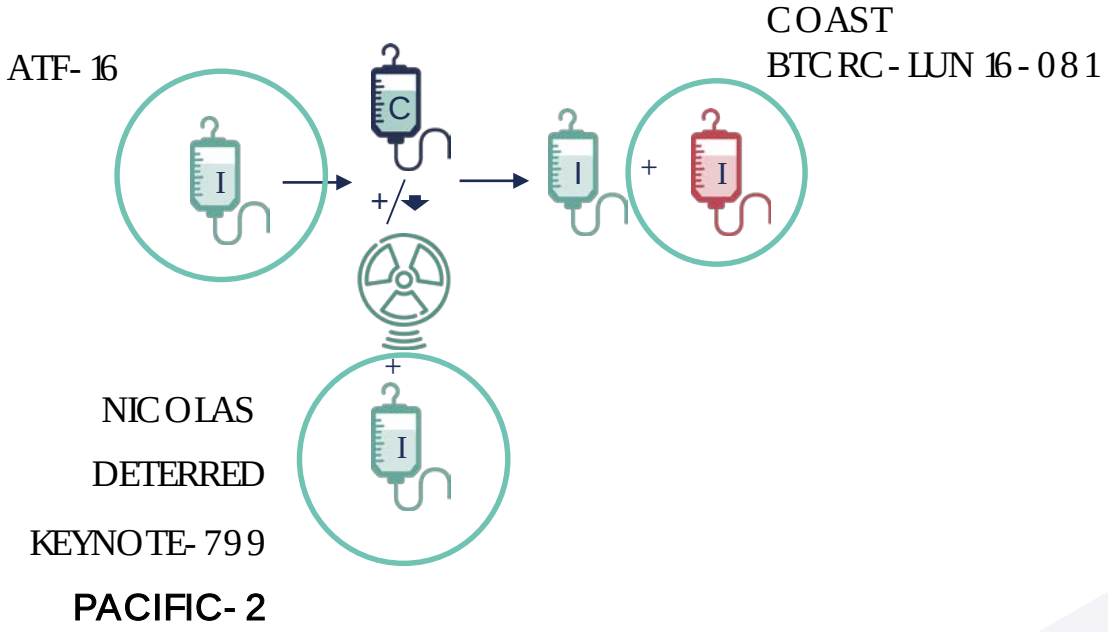
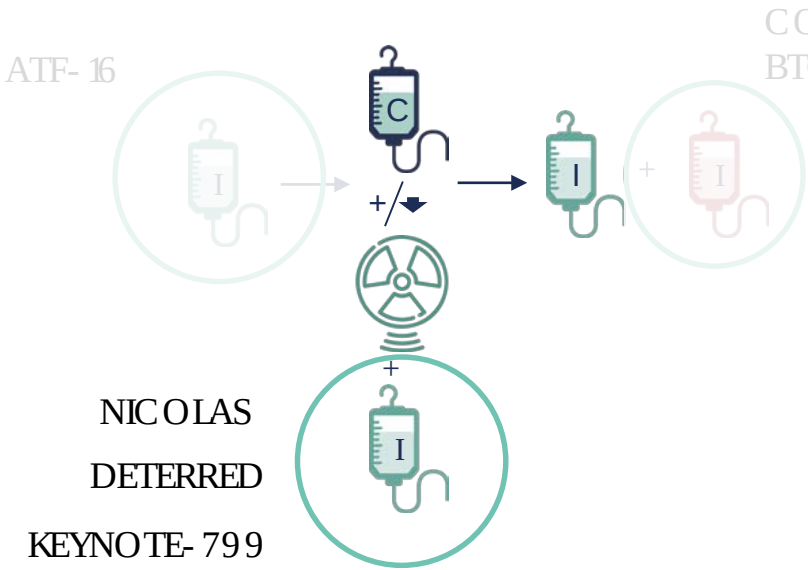


Quel timing pour l'immunothérapie ?



NICOLAS

DETERRED

KEYNOTE-799

PACIFIC-2

Immunothérapie concomitante

	Phase	m PFS	m OS	Pn G3	Notes
NICOLAS nivolumab	II	12,7	38,8	10,3%	- cRTCT ou sRT-CT
DETERRED atezolizumab	II	Part 2 : 13,2	NR	16%	- Part 2 : triplet cRT-CT-IO
KEYNOTE-199 pembrolizumab	II	A : 30,6 B : NR	NR	7,5%	- Cohorte A = SQ+NSQ - Cohorte B = NSQ - **Exclusion si ↓ poids >10% sur 3 mois**

Immunothérapie concomitante

	Phase	m PFS	m OS	Pn G3	Notes
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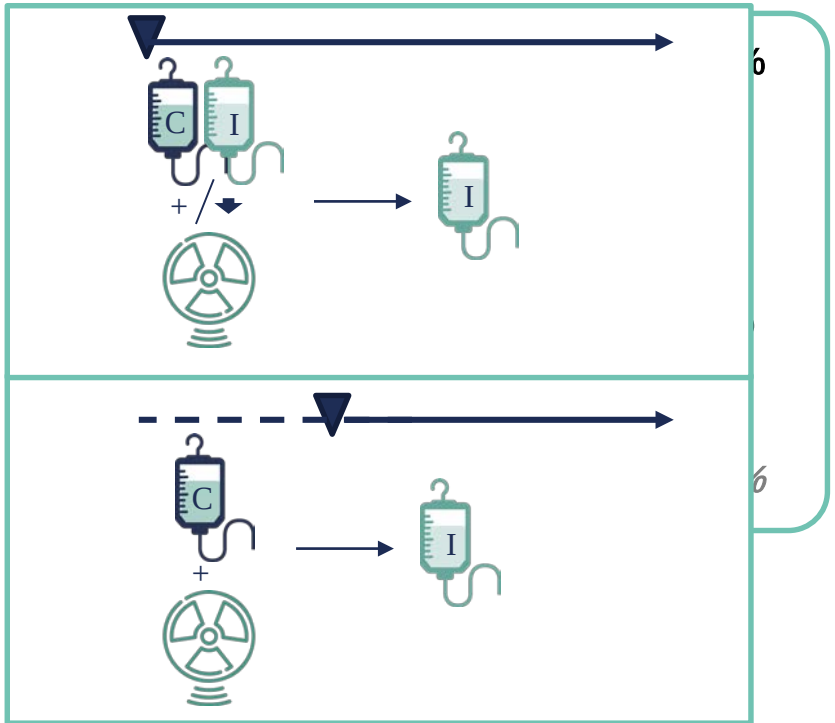
DETERRED atezolizumab	II	Part 2 : 13,2	NR	16%	- Part 2 : triplet cRT-CT-IO
KEYNOTE-199 pembrolizumab	II	A : 30,6 B : NR	NR	7,5%	- Cohorte A = SQ+NSQ - Cohorte B = NSQ - **Exclusion si ↓ poids >10% sur 3 mois**
PACIFIC *durvalumab*	*III*	*16,9*	*47,5*	*3,4%*	

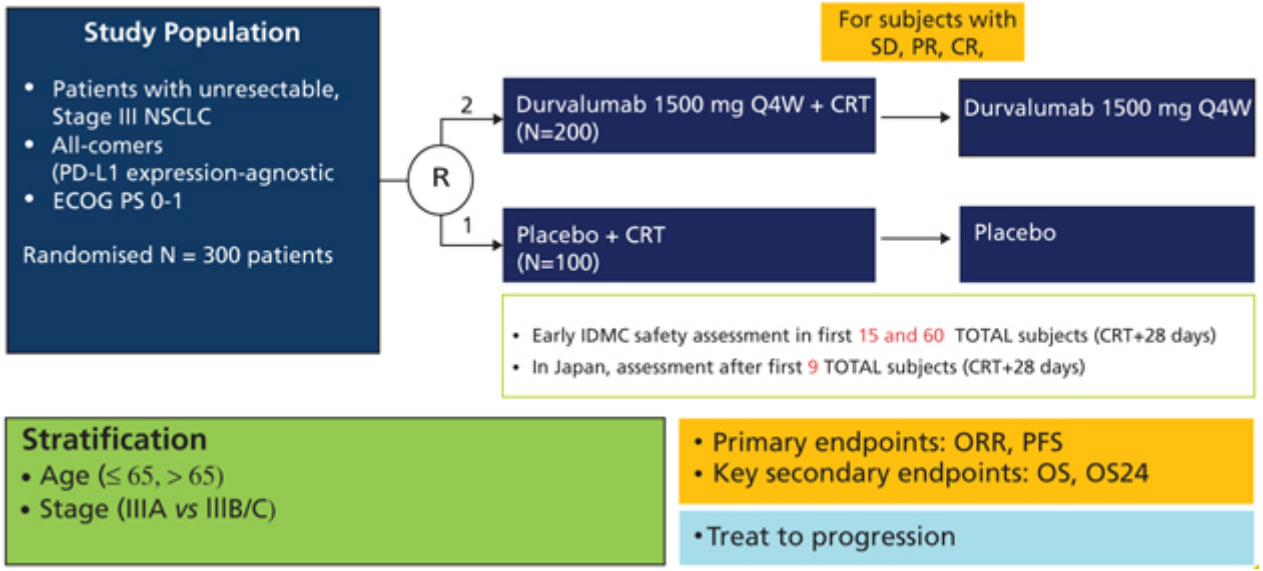
Immunothérapie concomitante

	Phase	m PFS	m OS	Pn G3	Notes
NICOLAS nivolumab	II			%	- cRTCT ou sRT-CT
DETERRED atezolizumab	II				- Part 2 : triplet cRT-CT-IO
KEYNOTE-199 pembrolizumab	II				- Cohorte A = SQ+NSQ - Cohorte B = NSQ - **Exclusion si ↓ poids >10% sur 3 mois**
PACIFIC *durvalumab*	*III*			*%*	



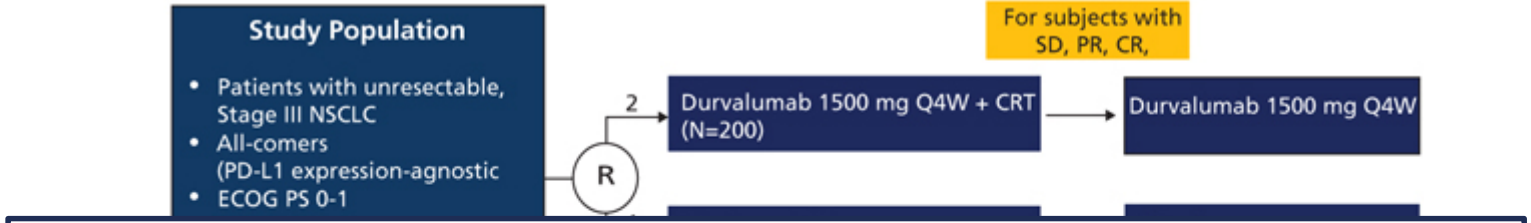
PACIFIC- 2

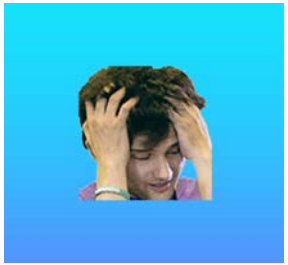
- *Design*



PACIFIC- 2

- *Design*





Update on PACIFIC-2 Phase III trial of Imfinzi concurrently administered with platinum-based chemoradiotherapy in unresectable, Stage III non-small cell lung cancer

PUBLISHED
14 November 2023

The PACIFIC-2 Phase III trial for *Imfinzi* (durvalumab) concurrently administered with chemoradiotherapy (CRT) did not achieve statistical significance for the primary endpoint of progression-free survival (PFS) versus CRT alone for the treatment of patients with unresectable, Stage III non-small cell lung cancer (NSCLC).

PACIFIC- 2

- *Design*

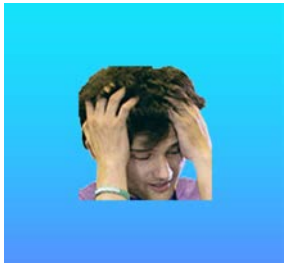
Study Population

- Patients with unresectable, Stage III NSCLC
- All-comers (PD-L1 expression-agnostic
- ECOG PS 0-1

R

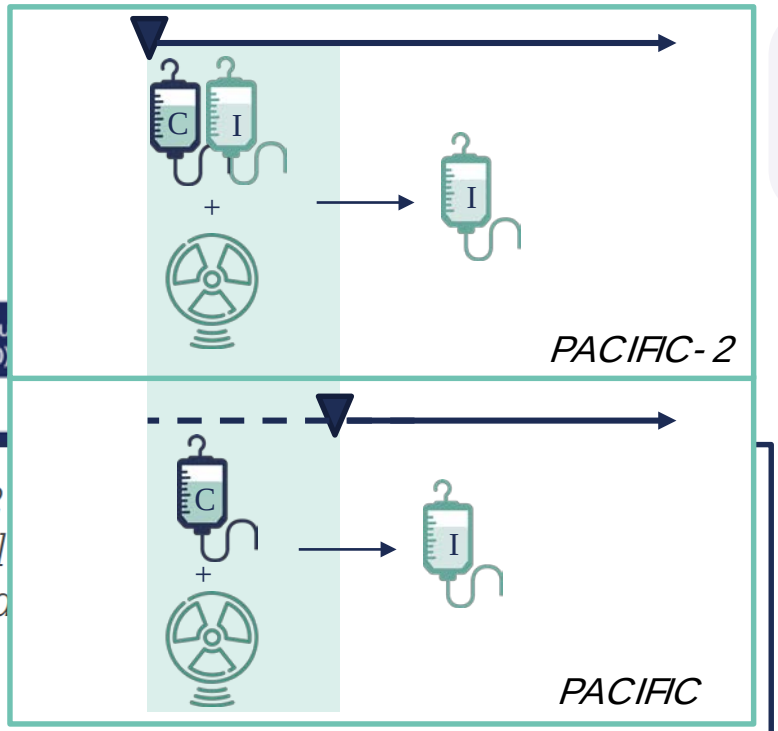
2

Durvalu
(N=200)



Update on PACIFIC-2
administered with pl
unresectable, Sta

PUBLISHED
14 November 2023



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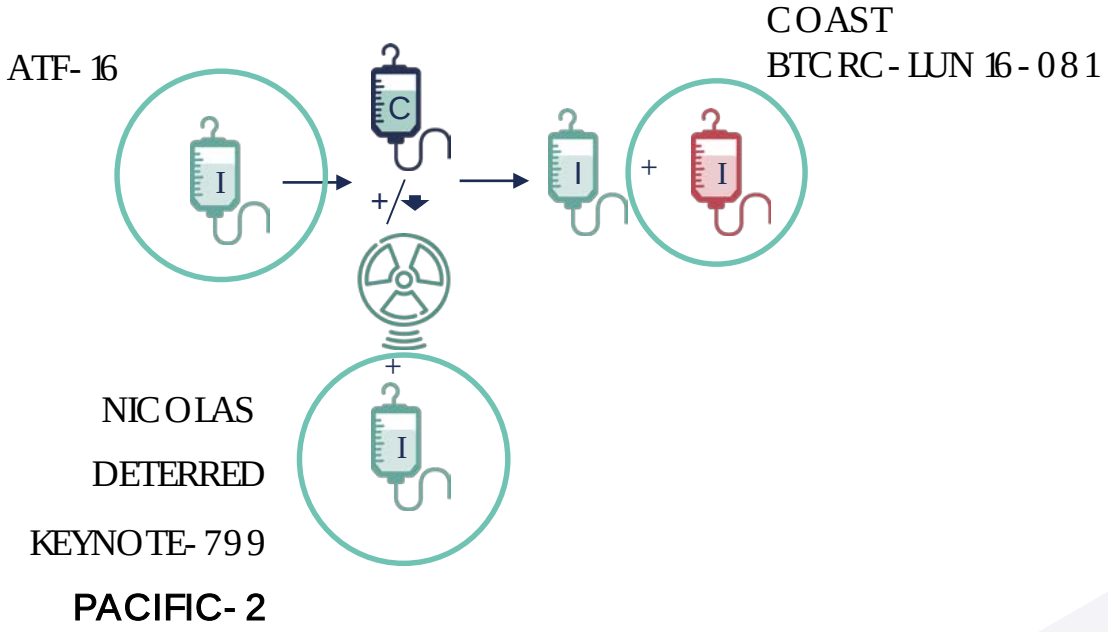
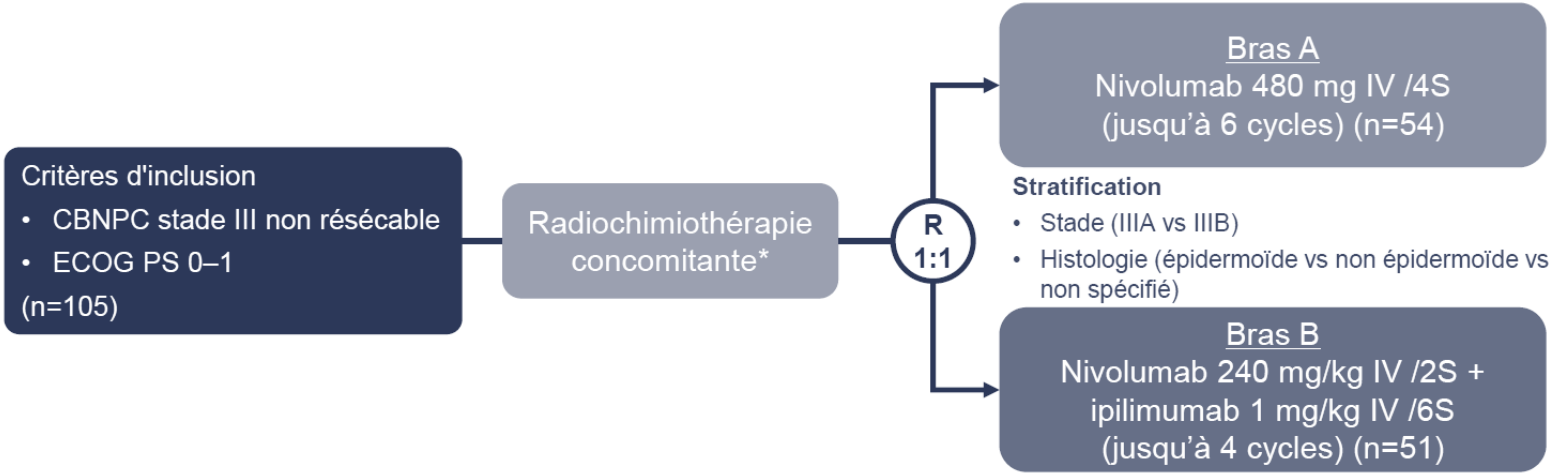
Quel timing pour l'immunothérapie ?



Combinaison d'immunothérapie

- *BTCRC LUN 16-081: design*



Critère principal

- SSP à 18 mois

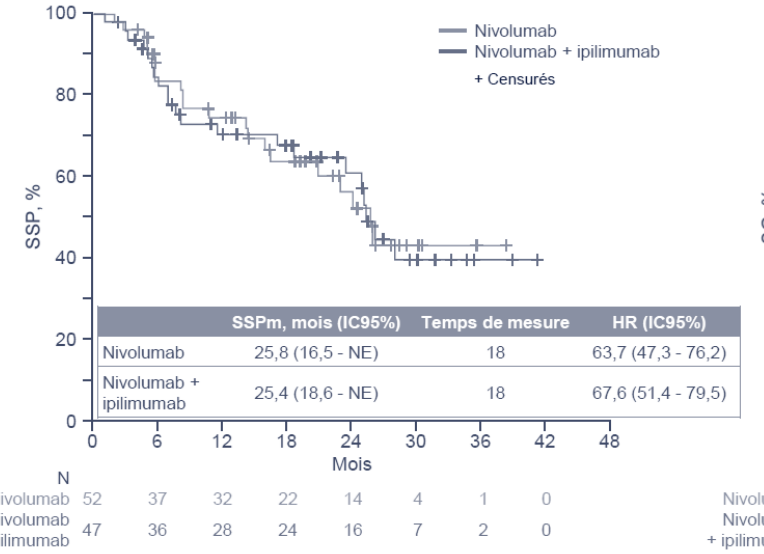
Critères secondaires

- Délai jusqu'à métastases à distance, SG, tolérance

Combinaison d'immunothérapie

- *BTCRC LUN 16-081 : résultats*

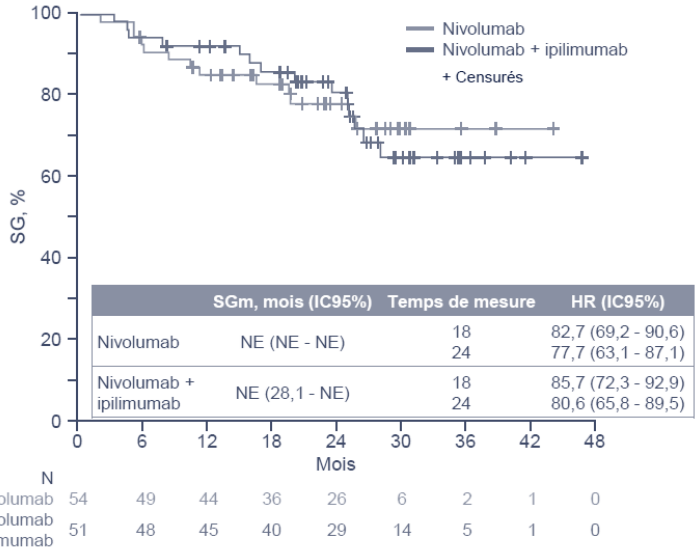
Survie sans progression



	SSPm, mois (IC95%)	Temps de mesure	HR (IC95%)
Nivolumab	25,8 (16,5 - NE)	18	63,7 (47,3 - 76,2)
Nivolumab + ipilimumab	25,4 (18,6 - NE)	18	67,6 (51,4 - 79,5)

N								
Nivolumab	52	37	32	22	14	4	1	0
Nivolumab + ipilimumab	47	36	28	24	16	7	2	0

Survie globale



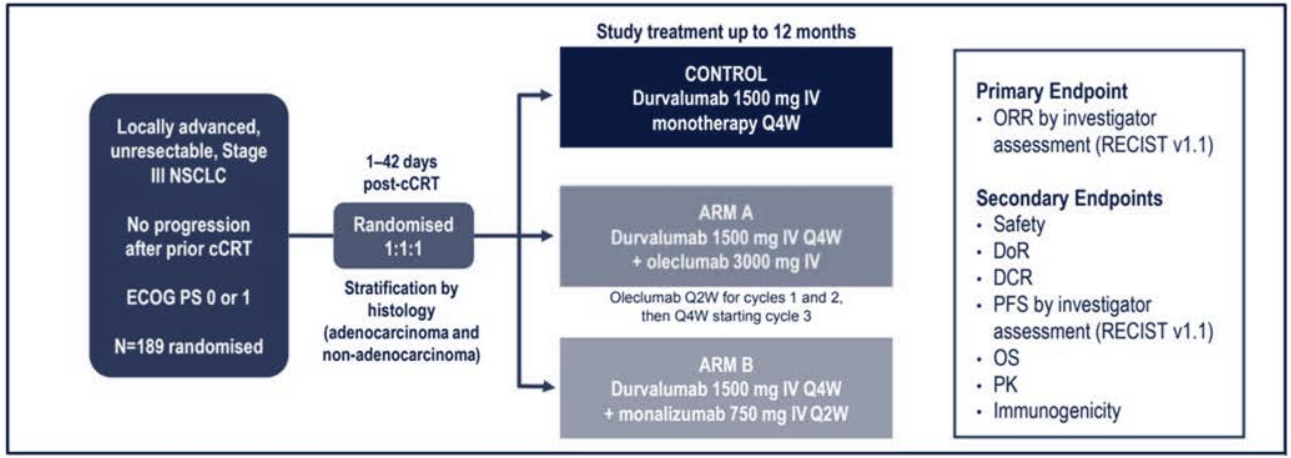
	SGm, mois (IC95%)	Temps de mesure	HR (IC95%)
Nivolumab	NE (NE - NE)	18 24	82,7 (69,2 - 90,6) 77,7 (63,1 - 87,1)
Nivolumab + ipilimumab	NE (28,1 - NE)	18 24	85,7 (72,3 - 92,9) 80,6 (65,8 - 89,5)

N								
Nivolumab	54	49	44	36	26	6	2	1	0
Nivolumab + ipilimumab	51	48	45	40	29	14	5	1	0

EILTs, n (%)	Nivolumab (n=54)	Nivolumab + ipilimumab (n=51)
Total	39 (72,2)	41 (80,4)
EILTs grade ≥3	10 (18,5)	14 (27,5)

Combinaison d'immunothérapie

- *COAST : design*

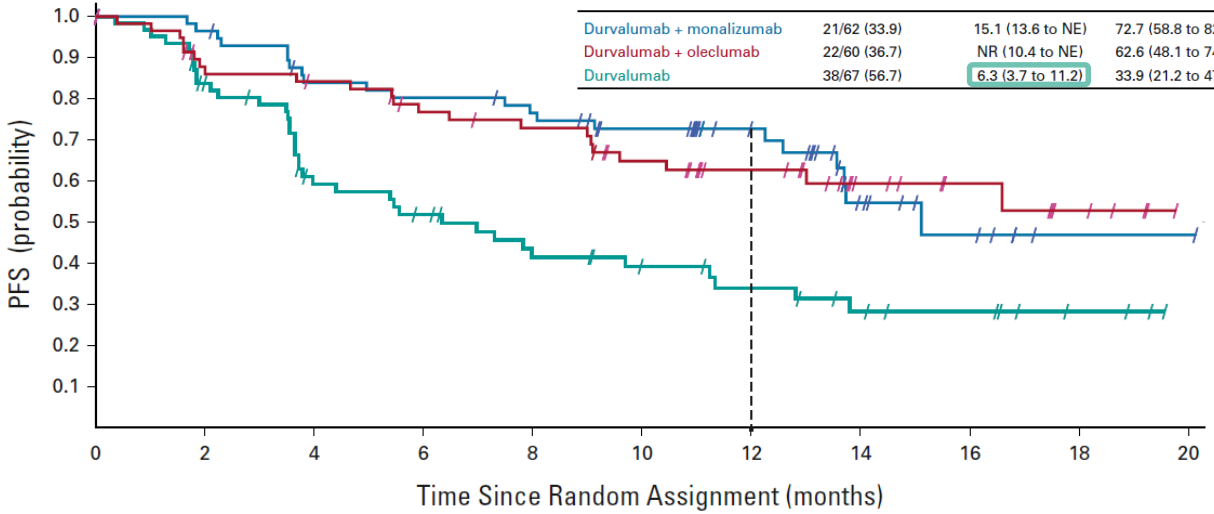


- *Oleclumab : anti-CD73 (inhibition de la disponibilité de l'adénosine dans le microenvironnement tumorale)*
- *Monalizumab : anti-NKG2A (inhibition de l'anergie des cellules NK)*

Combinaison d'immunothérapie

- *Résultats (PFS – obj secondaire)*

Treatment Arm	No. of Events/ Total No. of Patients (%)	Median PFS, Months (95% CI)[a]	12-Month PFS Rate, % (95% CI)	HR, % (95% CI)[b,c]
Durvalumab + monalizumab	21/62 (33.9)	15.1 (13.6 to NE)	72.7 (58.8 to 82.6)	0.42 (0.24 to 0.72)
Durvalumab + oleclumab	22/60 (36.7)	NR (10.4 to NE)	62.6 (48.1 to 74.2)	0.44 (0.26 to 0.75)
Durvalumab	38/67 (56.7)	6.3 (3.7 to 11.2)	33.9 (21.2 to 47.1)	–



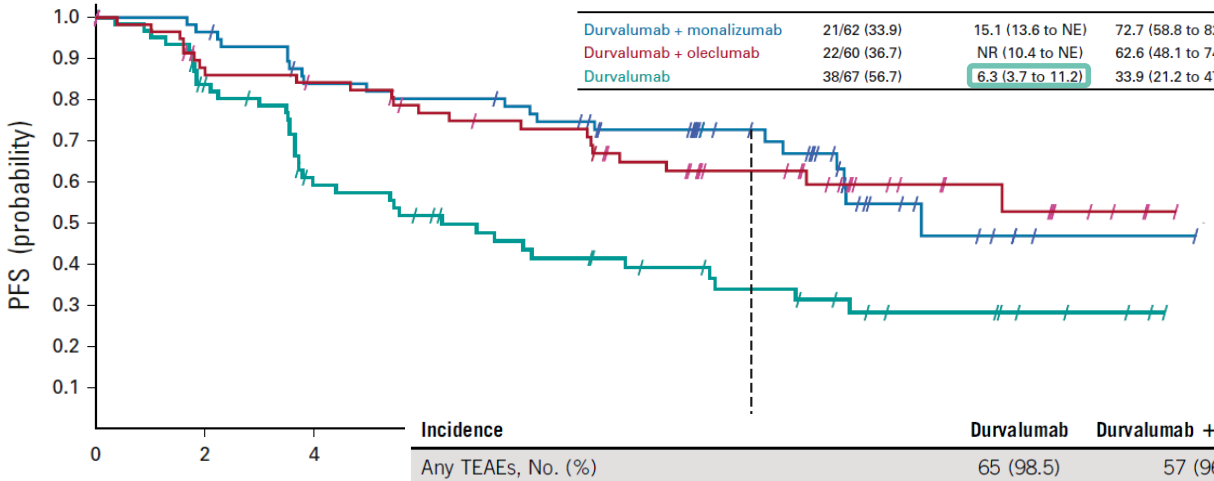
No. at risk:											
Durvalumab + monalizumab	62	55	46	44	41	35	25	11	6	1	1
Durvalumab + oleclumab	60	49	46	40	37	30	22	13	9	5	0
Durvalumab	67	50	32	27	20	16	13	9	7	3	0

Herbst, JCO, 2022

Combinaison d'immunothérapie

- *Résultats (PFS – obj secondaire)*

Treatment Arm	No. of Events/ Total No. of Patients (%)	Median PFS, Months (95% CI)[a]	12-Month PFS Rate, % (95% CI)	HR, % (95% CI)[b,c]
Durvalumab + monalizumab	21/62 (33.9)	15.1 (13.6 to NE)	72.7 (58.8 to 82.6)	0.42 (0.24 to 0.72)
Durvalumab + oleclumab	22/60 (36.7)	NR (10.4 to NE)	62.6 (48.1 to 74.2)	0.44 (0.26 to 0.75)
Durvalumab	38/67 (56.7)	6.3 (3.7 to 11.2)	33.9 (21.2 to 47.1)	–



No. at risk:

Durvalumab + monalizumab	62	55	46
Durvalumab + oleclumab	60	49	46
Durvalumab	67	50	32

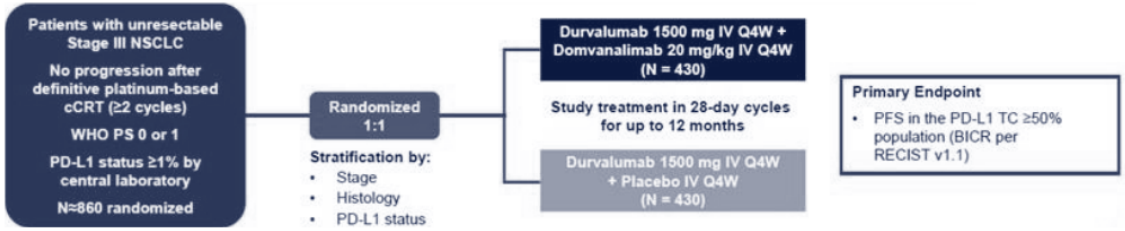
Incidence	Durvalumab	Durvalumab + Oleclumab	Durvalumab + Monalizumab
Any TEAEs, No. (%)	65 (98.5)	57 (96.6)	61 (100)
Grade ≥ 3 TEAEs, No. (%)	26 (39.4)	24 (40.7)	17 (27.9)
Study drug-related AEs, No. (%)	49 (74.2)	46 (78.0)	50 (82.0)
Study drug-related SAEs, No. (%)	6 (9.1)	7 (11.9)	5 (8.2)
TEAEs leading to treatment discontinuation, No. (%)	11 (16.7)	9 (15.3)	9 (14.8)

Combinaison d'immunothérapie

- *Phases 3 a suivre …*

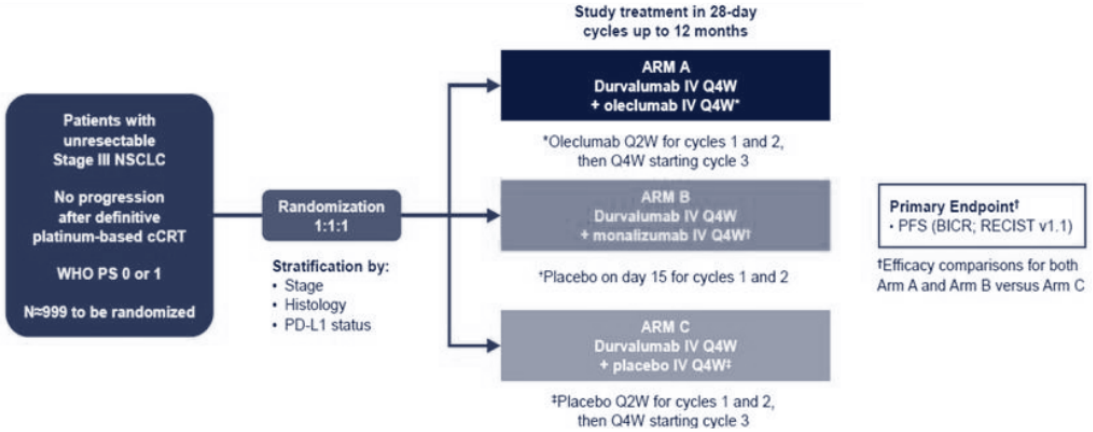
PACIFIC-8

Anti-TIGIT

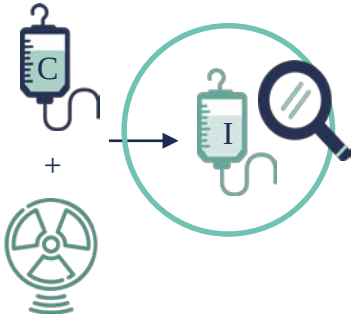


PACIFIC-9

Anti-CD73
Anti-NKG2A



CONCLUSION



- *Immunothérapie de consolidation pout tous ?*

- Quelque soit le statut PD-L1? **OUI**

- Quelque soit les modalités de RT-CT? **OUI**

- Chez les patients avec mutation EGFR? **NON**
  (et autres drivers du non-fumeur?)

- Quel perspectives : → RT-CT-IO conco ? **Incertain…**
  → Combinaison d'immunothérapie ? **Phase 3 à suivre…**
  → Place pour une désescalade ? **Essai académique**
  (1an d'IO pour tous ? CT pour tous ?)

Merci