Néo-adjuvant versus adjuvant, entre les deux mon cœur balance :

news en 2022 mais que choisir?

GHT LEMAN MONT-BLANC GROUPE HOSPITALIER DE TERRITOIRE

CHAL CENTRE HOSPITALIER ALPES LÉMAN

Liens d'intérêts

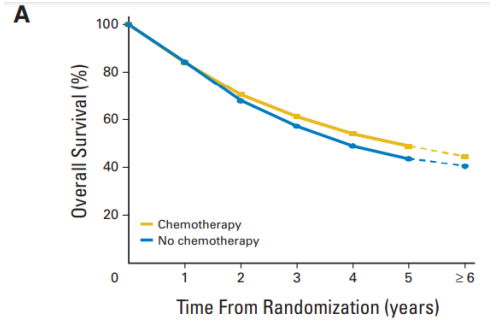
- Participations Boards
  - BMS
  - Novartis
  - Sanofi
- Interventions
  - BMS
  - GSK
  - Sanofi
  - Cheisi
  - Novartis
  - Astra Zeneca
  - Menarini
- Financements congrès
  - Elivie
  - Pfizer

Historique

Stade	Survie à 5 ans IASLC
IB	68%
IIA	60%
IIB	53%
IIIA	36%

Historique

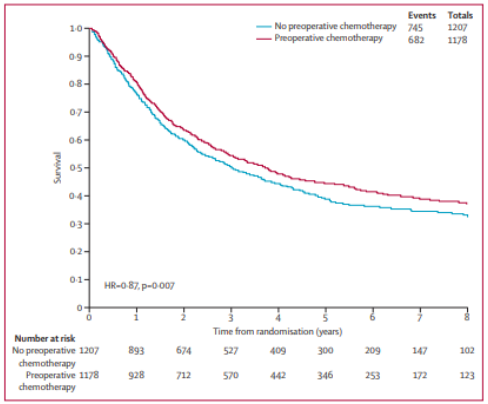
- Chimiothérapie adjuvante: Lung Adjuvant Cisplatin Evaluation: A Pooled Analysis by the LACE Collaborative Group 2008



Deaths / person years by period	Years 0-3	Years 4-5	Years ≥ 6
Control	966 / 5,155	239 / 1,668	49 / 720
Chemotherapy	857 / 5,181	203 / 1,817	76 / 790

+ 5,4% à 5 ans

- Preoperative chemotherapy for non-small-cell lung cancer: a systematic review and meta-analysis of individual participant data Collaborative Group 2014



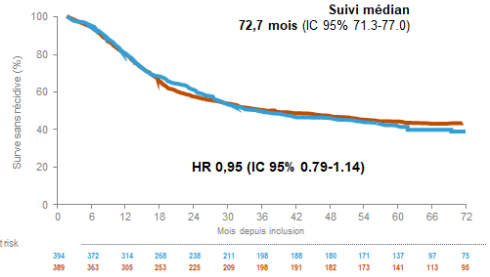
+ 5% à 5 ans

Pemetrexed Cisplatine / Navelbine Cisplatine Adjuvant non épidermoïde: Étude JIPANG actualisation ESMO 2022

SSR et Survie globale : Suivi 5 ans

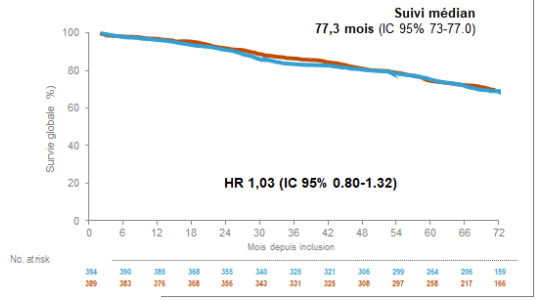
SSR évalué par investigateurs

	VNR+CDDP (n=394)	PEM+CDDP (n=389)
Nbre d'évènements	236	220
SSR médiane (IC 95%)	37.5 mois (28.9-52.6)	43.4 mois (29.0-59.7)
SSR à 3 ans (IC 95%)	51.0% (49.5-74.9%)	51.6% (46.5-56.4%)
SSR à 5 ans (IC 95%)	42.6% (37.7-47.5%)	44.9% (39.8-49.8%)



Survie globale

	VNR+CDDP (n=394)	PEM+CDDP (n=389)
Nbre d'évènements	119	123
SG médiane (IC 95%)	Non atteinte (NA-NA)	Non atteinte (NA-NA)
Survie à 3 ans (IC 95%)	84.1% (80.0-87.3%)	87.0% (83.2-90.0%)
Survie à 5 ans (IC 95%)	75.6% (71.0-79.6%)	75.0% (70.3-79.0%)



Safety overview

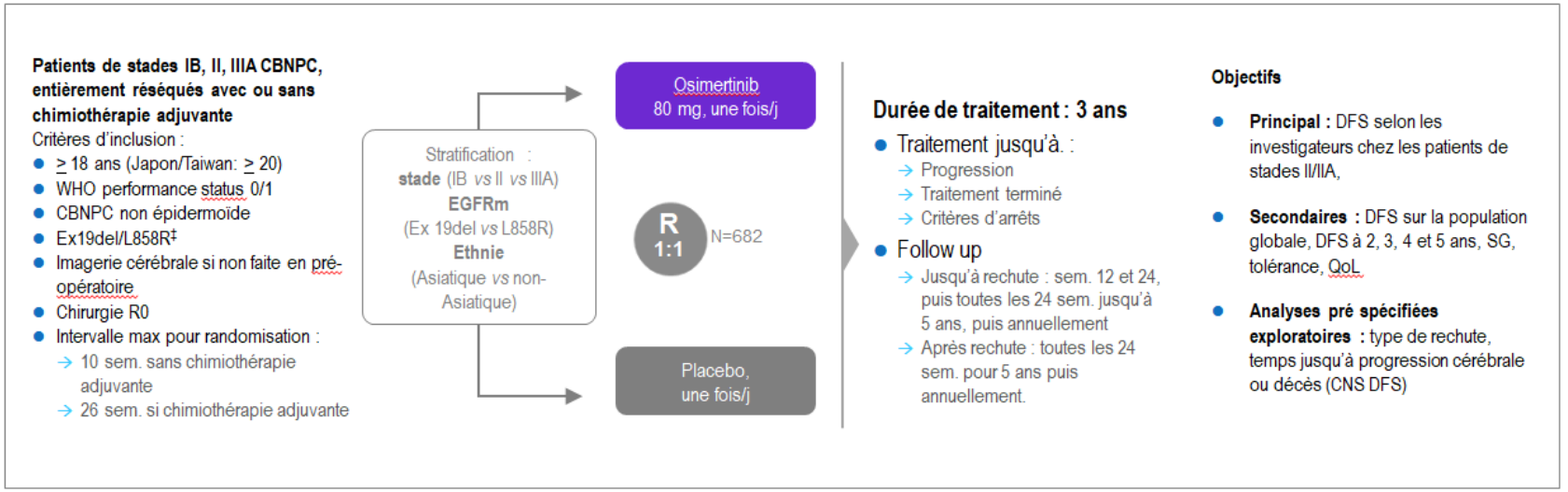
	VNR+CDDP N=396	(%)	PEM+CDDP N=392	(%)
Treatment-related AEs	396	(100)	391	(99.7)
Serious AEs	47	(11.9)	19	(4.8)
Grade 3-5*	354	(89.4)	186	(47.4)
Hematological AEs*	324	(81.8)	97	(24.7)
Non-hematological AEs	135	(34.1)	122	(31.1)
Led to death	1	(0.3)	1	(0.3)
Led to discontinuation*	93	(23.5)	37	(9.5)

AEs: adverse events
*in eligible population

*p<0.001 (chi-square test)

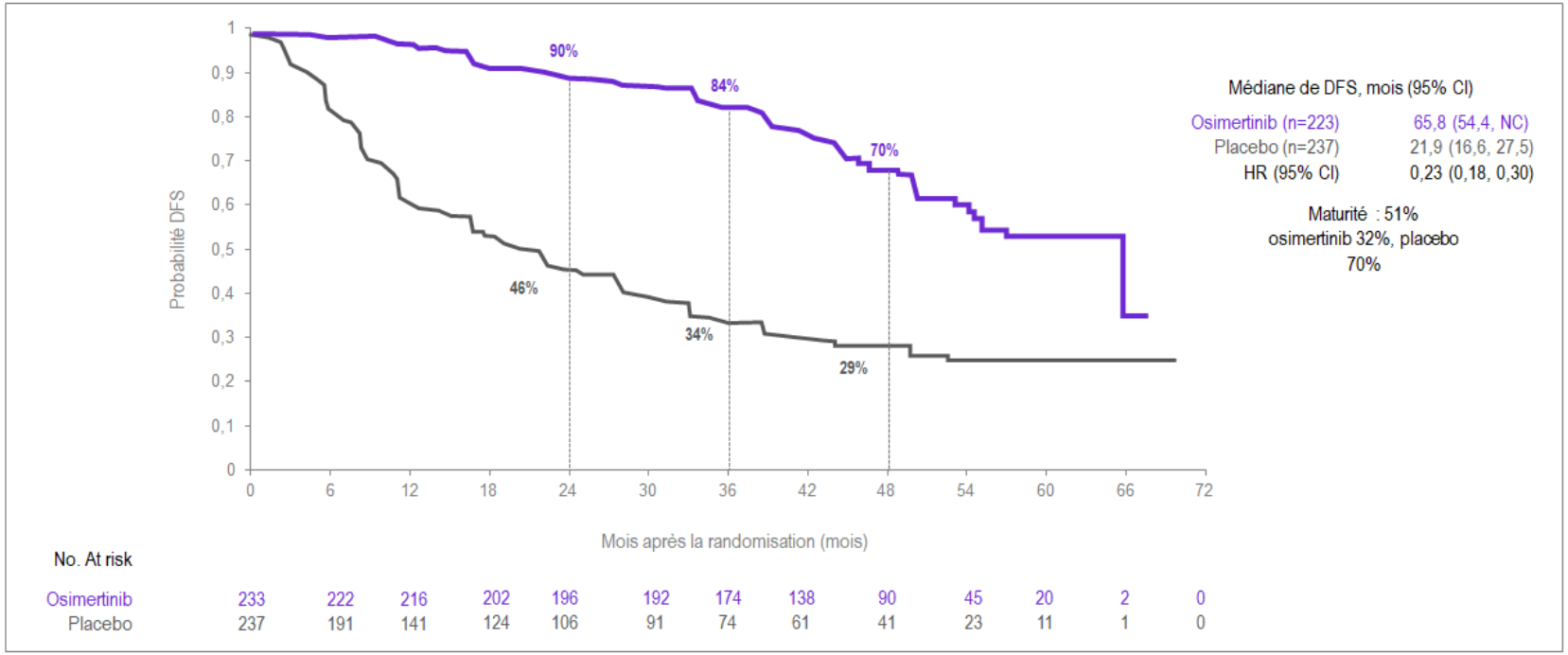
LES NOUVEAUTÉS EN ADJUVANT

ADAURA

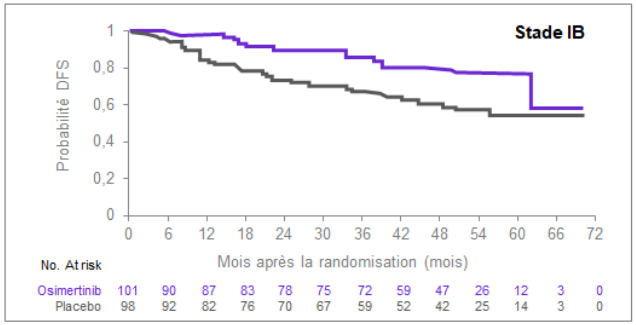

Patients de stades IB, II, IIIA CBNPC, entièrement réséqués avec ou sans chimiothérapie adjuvante
Critères d'inclusion :
≥ 18 ans (Japon/Taiwan: ≥ 20)
WHO performance status 0/1
CBNPC non épidermoïde
Ex19del/L858R‡
Imagerie cérébrale si non faite en pré-opératoire
Chirurgie R0
Intervalle max pour randomisation :
→ 10 sem. sans chimiothérapie adjuvante
→ 26 sem. si chimiothérapie adjuvante
Stratification :
stade (IB vs II vs IIIA)
EGFRm
(Ex 19del vs L858R)
Ethnie
(Asiatique vs non-Asiatique)
Osimertinib
80 mg, une fois/j
R
1:1
N=682
Placebo,
une fois/j
Durée de traitement : 3 ans
Traitement jusqu'à. :
→ Progression
→ Traitement terminé
→ Critères d'arrêts
Follow up
→ Jusqu'à rechute : sem. 12 et 24, puis toutes les 24 sem. jusqu'à 5 ans, puis annuellement
→ Après rechute : toutes les 24 sem. pour 5 ans puis annuellement.
Objectifs
Principal : DFS selon les investigateurs chez les patients de stades II/IIA,
Secondaires : DFS sur la population globale, DFS à 2, 3, 4 et 5 ans, SG, tolérance, QoL
Analyses pré spécifiées exploratoires : type de rechute, temps jusqu'à progression cérébrale ou décès (CNS DFS)

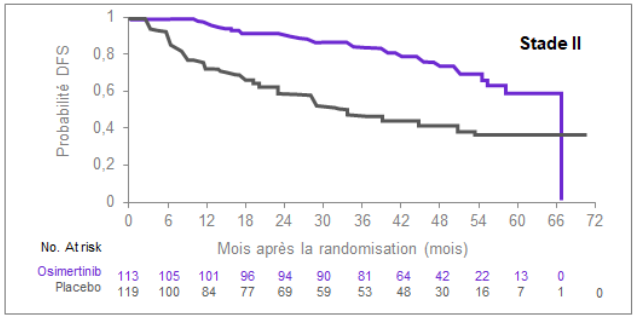
ADAURA actualisation ESMO 2022 M Tsuboi

Objectif principal : DFS actualisée dans les stades II/IIIA

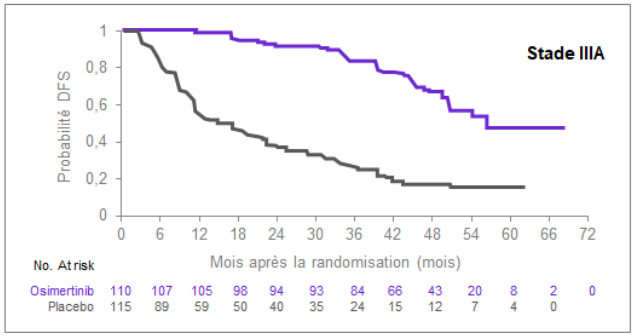


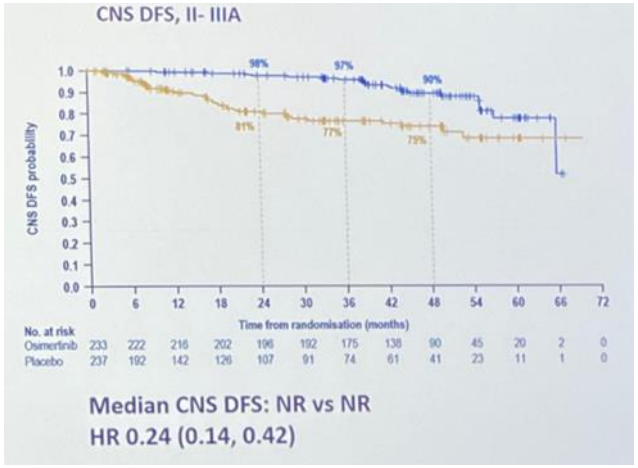
DFS actualisée par stades (AJCC/UICC 8ème Edition)





	Stade IB	Stade II	Stade IIIA
DFS taux à 4 ans, % (95% CI)			
Osimertinib	80 (69, 87)	75 (65, 83)	66 (55, 75)
Placebo	60 (49, 69)	43 (34, 52)	16 (10, 24)
Tous HR I (IC 95%)	0.44 (0,25 - 0,76)	0.33 (0,21 - 0,50)	0.22 (0,15 - 0,31)





Tolérance

Résumé de la tolérance

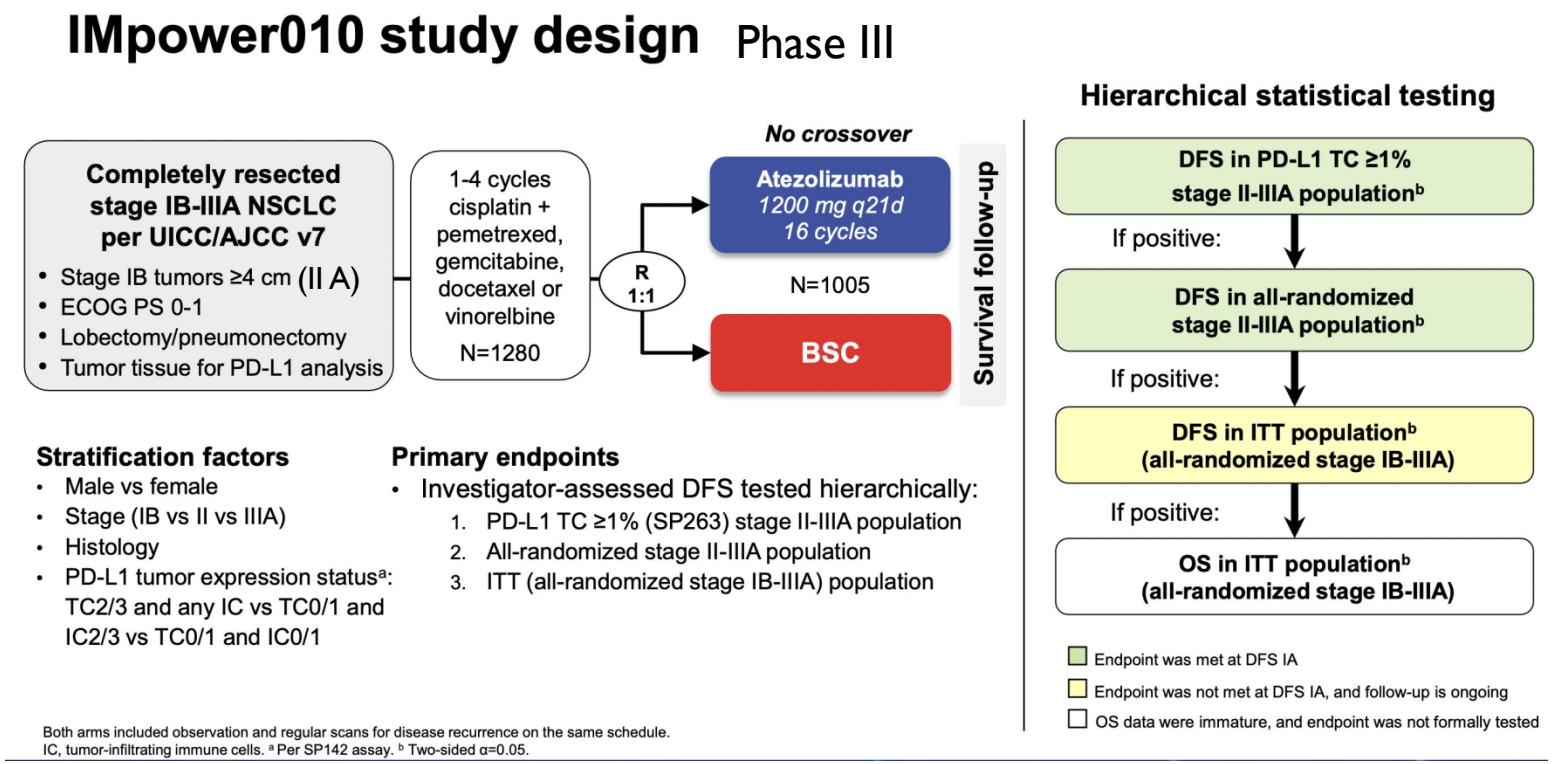
- Patients ayant complété les 3 ans de traitement: osimertinib n=222 (66%), placebo n = 139 (41%)
- Médiane de durée d'exposition : osimertinib : 35,8 mois (intervalle 0 - 38), placebo : 25,1 mois (intervalle 0 -39)

EI toutes causes *, n (%)	Osimertinib (nn=337)	Placebo (n=343)
EI tous	330 (98)	309 (90)
EI Grade ≥3	79 (23)	48 (14)
EI entrainant le décès	1 (<1)	2 (1)
AE sévère	68 (20)	47 (14)
EI conduisant à l'arrêt temporaire du traitement	43 (13)	9 (3)
EI conduisant à une reduction de dose	42 (12)	3 (1)
EI conduisant à l'arret définitif du traitement	91 (27)	43 (13)
EI , possiblement lié au traitement, n (%)	**Osimertinib (nn=337)**	**Placebo (n=343)**
Tous EI	308 (91)	199 (58)
EI Grade > 3	36 (11)	7 (2)
EI entrainant le décés	0	0
EI severe	10 (3)	2 (1)

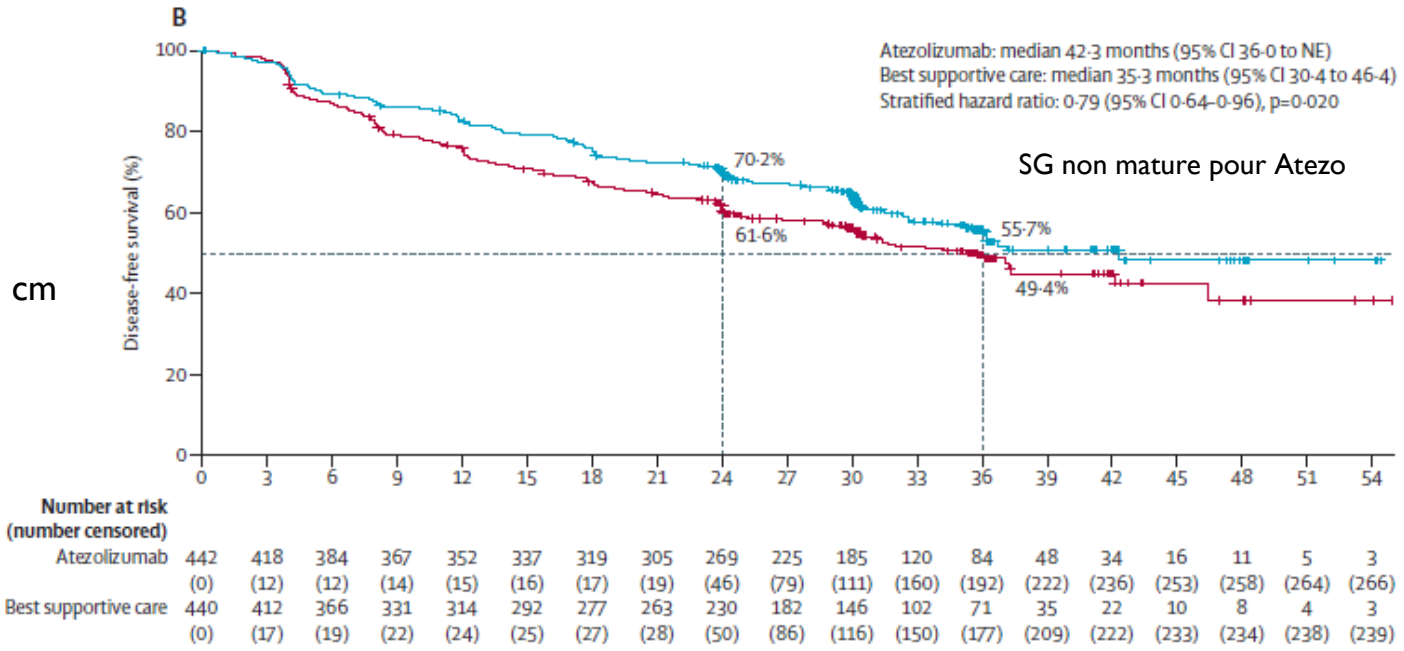
ADAURA

- Guérison ou décalage ?
- Les rechutes sont elles sensibles à Osimertinib ?

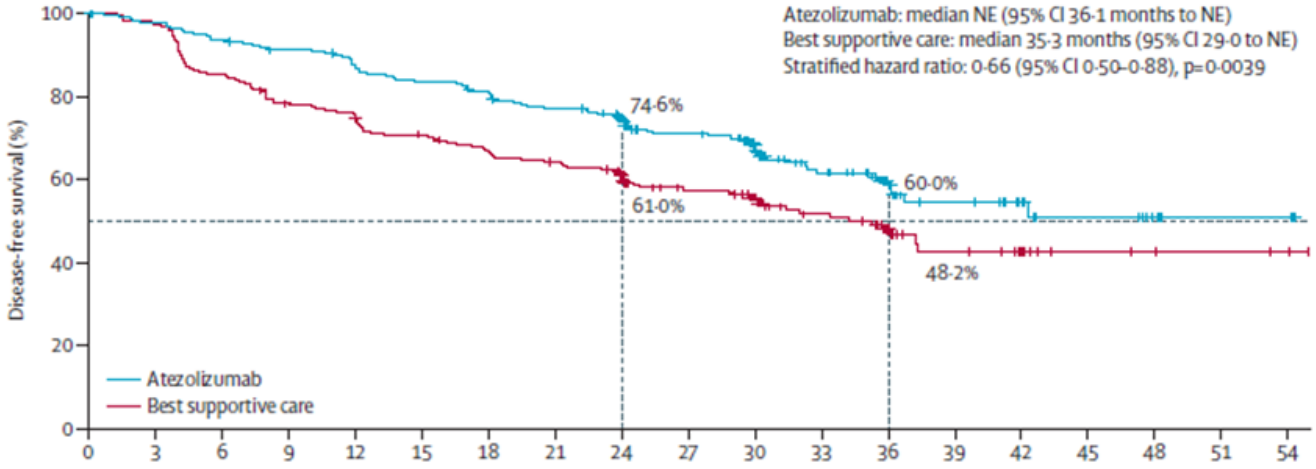
Immunothérapie post opératoire



Tous PDL1
Stade II ≥5 cm
à IIIA

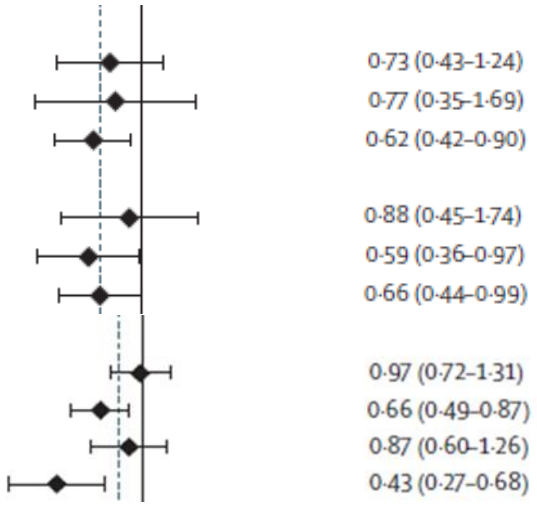


PDL1 > 1%
Stade II ≥5 cm
à IIIA



Atezolizumab adjuvant stade II-IIIA

Stage					
IIA	85/161	NE (36·1–NE)	76/161	NE (29·7–NE)	0·73 (0·43–1·24)
IIB	46/83	NE (35·3–NE)	37/83	NE (32·0–NE)	0·77 (0·35–1·69)
IIIA	117/232	42·3 (30·5–NE)	115/232	26·7 (18·0–35·3)	0·62 (0·42–0·90)
Regional lymph node stage (pN)					
N0	60/106	36·7 (35·5–NE)	46/106	NE (32·0–NE)	0·88 (0·45–1·74)
N1	100/194	NE (NE–NE)	94/194	NE (30·4–NE)	0·59 (0·36–0·97)
N2	88/176	32·3 (24·2–NE)	88/176	21·3 (15·7–31·4)	0·66 (0·44–0·99)
PD-L1 status by SP263					
TC <1%	181/383	36·1 (30·2–NE)	202/383	37·0 (28·6–NE)	0·97 (0·72–1·31)
TC ≥1%	248/476	NE (36·1–NE)	228/476	35·3 (29·0–NE)	0·66 (0·49–0·87)
TC 1–49%	133/247	32·8 (29·4–NE)	114/247	31·4 (24·0–NE)	0·87 (0·60–1·26)
TC ≥50%	115/229	NE (42·3–NE)	114/229	35·7 (29·7–NE)	0·43 (0·27–0·68)



- Survie sans progression PDL1 ≥ 50%
  - A 24 mois Atezo: 87% / BSC 63,6%
  - A 36 mois Atezo 75,1% / BSC 50,4%
- Survie globale PDL1 ≥ 50% non mature
  - A 36 mois Atezo 89% / BSC 77,5%

Tolérance

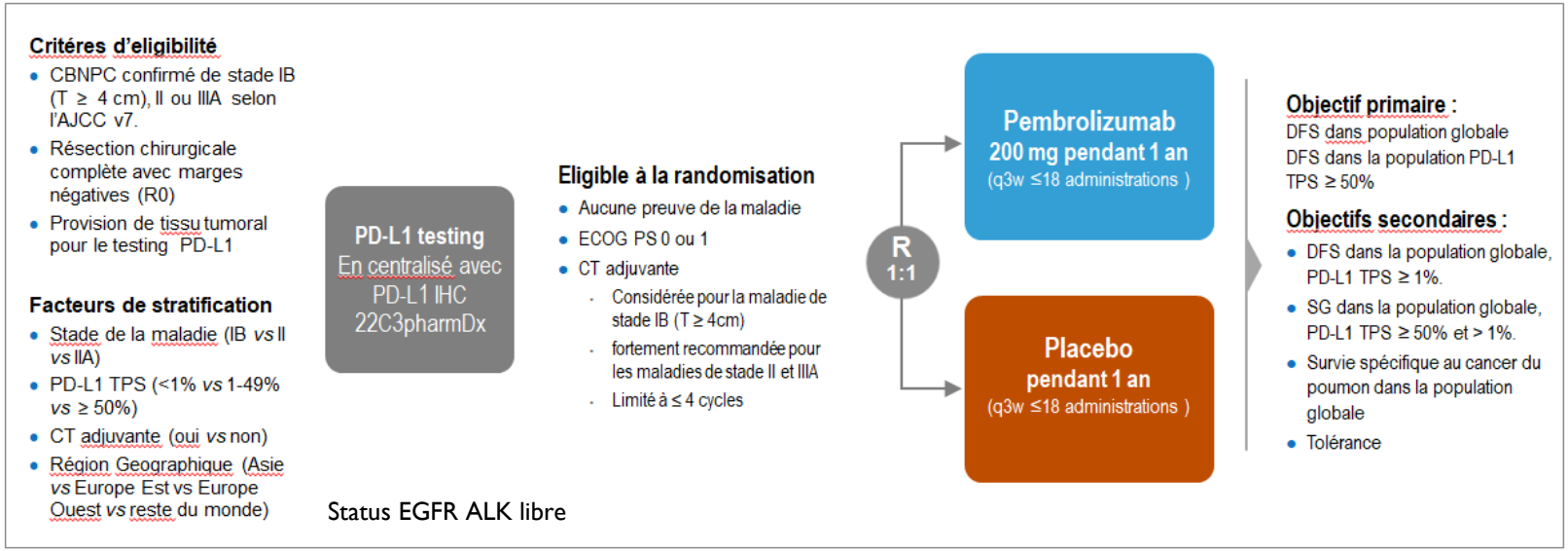
	Atezolizumab group (n=495)	Best supportive care group (n=495)
Adverse event		
Any grade	459 (93%)	350 (71%)
Grade 3–4	108 (22%)	57 (12%)
Serious	87 (18%)	42 (8%)
Grade 5	8 (2%)*	3 (1%)†
Led to dose interruption of atezolizumab	142 (29%)	..
Led to atezolizumab discontinuation	90 (18%)	..
Immune-mediated adverse events		
Any grade	256 (52%)	47 (9%)
Grade 3–4	39 (8%)	3 (1%)
Required the use of systemic corticosteroids‡	60 (12%)	4 (1%)
Led to discontinuation	52 (11%)	0

Data are n (%). *Interstitial lung disease, multiple organ dysfunction syndrome, myocarditis, and acute myeloid leukaemia (all four events related to atezolizumab), and pneumothorax, cerebrovascular accident, arrhythmia, and acute cardiac failure. †Pneumonia; pulmonary embolism; and cardiac tamponade and septic shock in the same patient. ‡Atezolizumab-related.

Table 2: **Safety summary in the safety evaluable population**

PEARLS/KEYNOTE-091 Essai randomisé de phase III Pembrolizumab en situation adjuvante

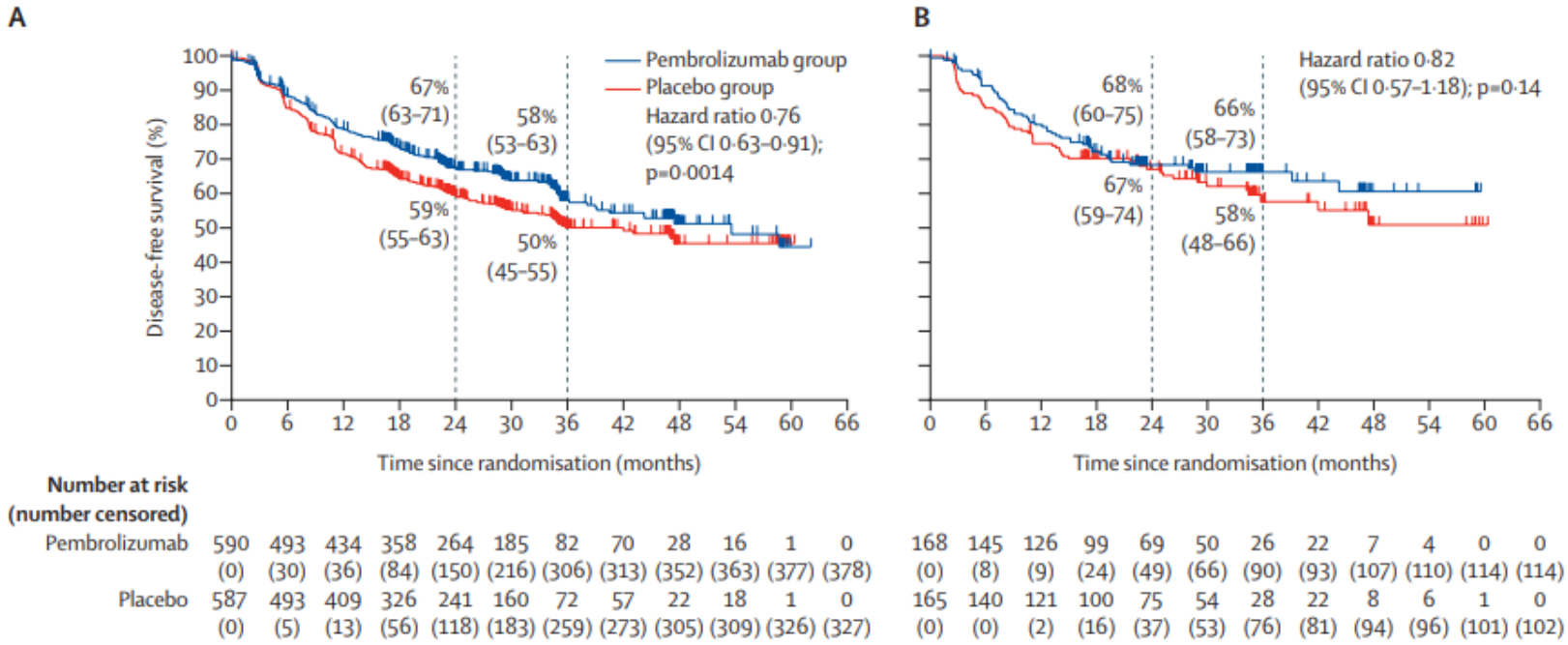
Lancet Oncol 2022 Published Online September 12, 2022



Received adjuvant chemotherapy				
No	84 (14%)	83 (14%)	25 (15%)	24 (15%)
Yes†	506 (86%)	504 (86%)	143 (85%)	141 (85%)
1–2 cycles	35 (6%)	32 (5%)	8 (5%)	8 (5%)
3–4 cycles	471 (80%)	472 (80%)	135 (80%)	133 (81%)

Tous PDL1

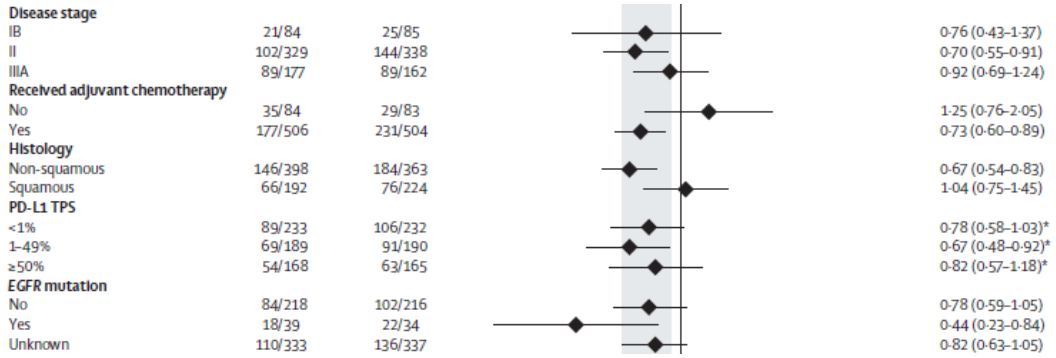
PDL1 ≥ 50%



Number at risk (number censored)

Pembrolizumab	590	493	434	358	264	185	82	70	28	16	1	0	168	145	126	99	69	50	26	22	7	4	0	0
	(0)	(30)	(36)	(84)	(150)	(216)	(306)	(313)	(352)	(363)	(377)	(378)	(0)	(8)	(9)	(24)	(49)	(66)	(90)	(93)	(107)	(110)	(114)	(114)
Placebo	587	493	409	326	241	160	72	57	22	18	1	0	165	140	121	100	75	54	28	22	8	6	1	0
	(0)	(5)	(13)	(56)	(118)	(183)	(259)	(273)	(305)	(309)	(326)	(327)	(0)	(0)	(2)	(16)	(37)	(53)	(76)	(81)	(94)	(96)	(101)	(102)

SSP médiane Pembro 53,6 mois / 42 mois PCB (suivi médian 35,6 mois)
PDL1 > 50% SSP non atteinte
SG non mature



EI immunologiques

	Pembrolizumab group (n=580)				Placebo group (n=581)			
	Grade 1–2	Grade 3	Grade 4	Grade 5	Grade 1–2	Grade 3	Grade 4	Grade 5
Any event	180 (31%)	38 (7%)	6 (1%)	2 (<1%)	64 (11%)	11 (2%)	0	0
Hypothyroidism	119 (21%)	1 (<1%)	0	0	27 (5%)	0	0	0
Hyperthyroidism	61 (11%)	1 (<1%)	0	0	17 (3%)	0	0	0
Pneumonitis	32 (6%)	6 (1%)	2 (<1%)	0	13 (2%)	4 (1%)	0	0
Severe skin reactions	5 (1%)	11 (2%)	0	0	2 (<1%)	2 (<1%)	0	0
Colitis	10 (2%)	4 (1%)	0	0	4 (1%)	1 (<1%)	0	0
Adrenal insufficiency	6 (1%)	4 (1%)	0	0	0	0	0	0
Hepatitis	1 (<1%)	5 (1%)	4 (1%)	0	2 (<1%)	2 (<1%)	0	0
Hypophysitis	4 (1%)	3 (1%)	0	0	0	0	0	0
Thyroiditis	6 (1%)	0	0	0	1 (<1%)	0	0	0
Infusion reactions	5 (1%)	0	0	0	4 (1%)	0	0	0
Myocarditis	1 (<1%)	2 (<1%)	0	2 (<1%)	0	1 (<1%)	0	0
Nephritis	4 (1%)	0	0	0	0	0	0	0
Pancreatitis	2 (<1%)	0	0	0	1 (<1%)	1 (<1%)	0	0
Myositis	1 (<1%)	0	0	0	0	0	0	0
Sarcoidosis	0	1 (<1%)	0	0	0	0	0	0
Type 1 diabetes	0	1 (<1%)	0	0	0	0	0	0
Vasculitis	0	1 (<1%)	0	0	0	0	0	0

Data are n (%). Potentially immune-mediated adverse events and infusion reactions were based on a list of terms prepared by the sponsor and were considered regardless of attribution to trial treatment by the investigator. In addition to the specific preferred terms listed, related terms were included.

***Table 3*: Potentially immune-mediated adverse events and infusion reactions of any incidence in the safety population**

Ph Romand Les incontournables en cancérologie 2022

Etudes phases III adjuvant

	Stade	Protocole CT	IO/TKi	Objectif principal
IMPOWER 10	IB-IIIA (7è)	1-4 cycles Cis + Pem, Gem, Doc, Nav	Atezo	SSP
ANVIL	IB-IIIA (7è)	CT Rt autorisée	Nivo	SSP, SG
PEARLS	IB-IIIA (7è)	CT optio	Pembro	SSP
BR 31	IB-IIIA (7è)	CT optio	Durva	SSP
ALCHEMIST IO	IB-IIIA	CT optio	Pembro	SSP, SG
CANOPY A	IB-IIIA IIIB	CT optio	Canakinumab	SSP
NADIM A	IB-IIIA	Carbo-Pac	CT-Nivo/Nivo/CT	SSP
ALCHEMIST CT-IO	IB-IIIA (7è)	1-4 cycles Carbo ou Cis + Pem, Gem, Pac	CT-Pembro puis Pembro/PCB	SSP, SG
ALINA (ALK)	IB (4 cm) IIIA	4 cycles Cis + Pem, Gem, Vino	Alectinib 24 mois / CT	SSP

LES PROGRÈS EN NEO-ADJUVANT

CheckMate 816 association néoadjuvante nivolumab + chimiothérapie CBNPC résécables

CheckMate 816 study design[a,1]

Key eligibility criteria

- Newly diagnosed, resectable, stage IB (≥ 4 cm)-IIIA NSCLC (IIA) (per TNM 7th edition)
- ECOG PS 0-1
- No known sensitizing *EGFR* mutations or *ALK* alterations

Stratified by stage (IB/II vs IIIA), PD-L1[b] (≥ 1% vs < 1%[c]), and sex

N = 358 → R 1:1

- **NIVO 360 mg Q3W + chemo[d] Q3W (3 cycles)**
- **Chemo[e] Q3W (3 cycles)**

→ Radiologic restaging → Surgery (within 6 weeks post-treatment) → Optional adjuvant chemo ± RT → Follow-up

Primary endpoints	Key secondary endpoints	Key exploratory endpoints included
• pCR by BIPR	• MPR by BIPR	• ORR by BICR
• EFS by BICR	• OS	• **Feasibility of surgery; peri- and post-operative surgery-related AEs**
	• Time to death or distant metastases	

Database lock: September 16, 2020; minimum follow-up: 7.6 months for NIVO + chemo and chemo arms.

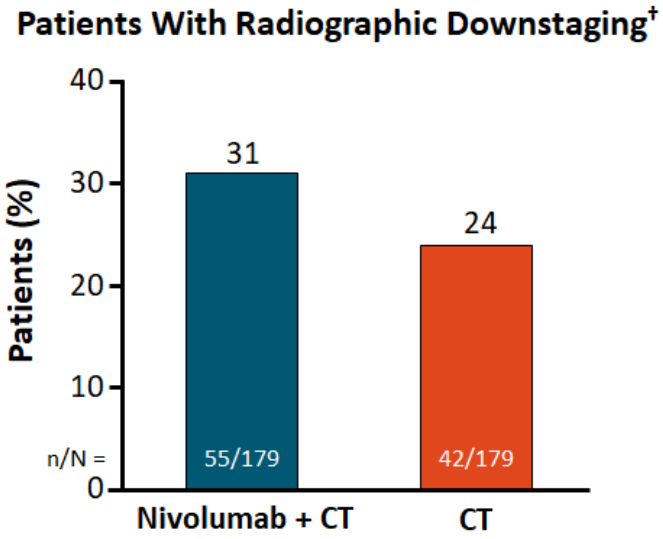
[a]NCT02998528; this study included an exploratory arm: NIVO 3 mg/kg Q2W (3 cycles) + ipilimumab 1 mg/kg (cycle 1 only). Data from this arm are not included in this presentation; [b]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako); [c]Included patients with PD-L1 expression status not evaluable and indeterminate; [d]NSQ: pemetrexed + cisplatin or paclitaxel + carboplatin; SQ: gemcitabine + cisplatin or paclitaxel + carboplatin; [e]Vinorelbine + cisplatin, docetaxel + cisplatin, gemcitabine + cisplatin (SQ only), pemetrexed + cisplatin (NSQ only), or paclitaxel + carboplatin.

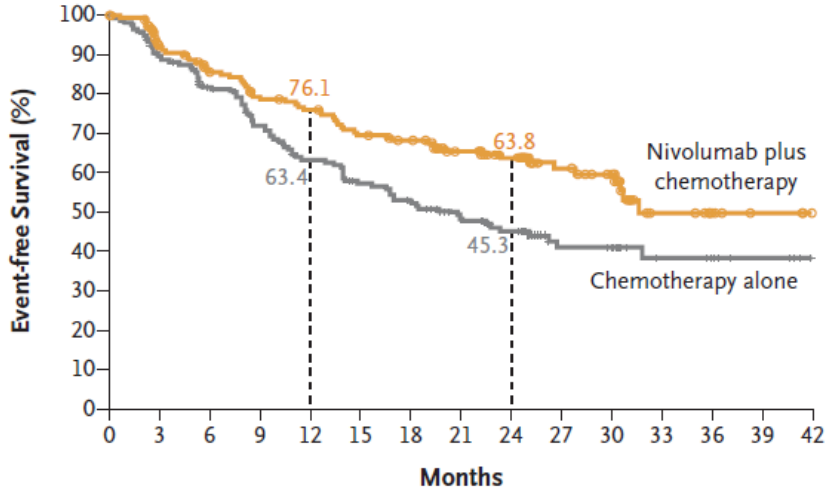
1. Forde PM, et al. Oral presentation at the AACR Annual Meeting; April 8-10, 2021; virtual. Abstract 5218.

Disease stage — no. (%)‡		
IB or II	65 (36.3)	62 (34.6)
IIIA	113 (63.1)	115 (64.2)

Réponse radiologique

Patients, n (%)	Nivolumab + CT (n = 179)	CT (n = 179)
ORR,* n (%) [95% CI]	96 (54) [46-61]	67 (37) [30-45]
Best overall response		
▪ CR	1 (1)	3 (2)
▪ PR	95 (53)	64 (36)
▪ SD	70 (39)	88 (49)
▪ PD	8 (4)	11 (6)
▪ Not evaluable	1 (1)	1 (1)
▪ Not reported	4 (2)	12 (7)





	No. of Patients	Median Event-free Survival (95% CI) *mo*
Nivolumab plus Chemotherapy	179	31.6 (30.2–NR)
Chemotherapy Alone	179	20.8 (14.0–26.7)

Hazard ratio for disease progression, disease recurrence, or death, 0.63 (97.38% CI, 0.43–0.91)
P=0.005

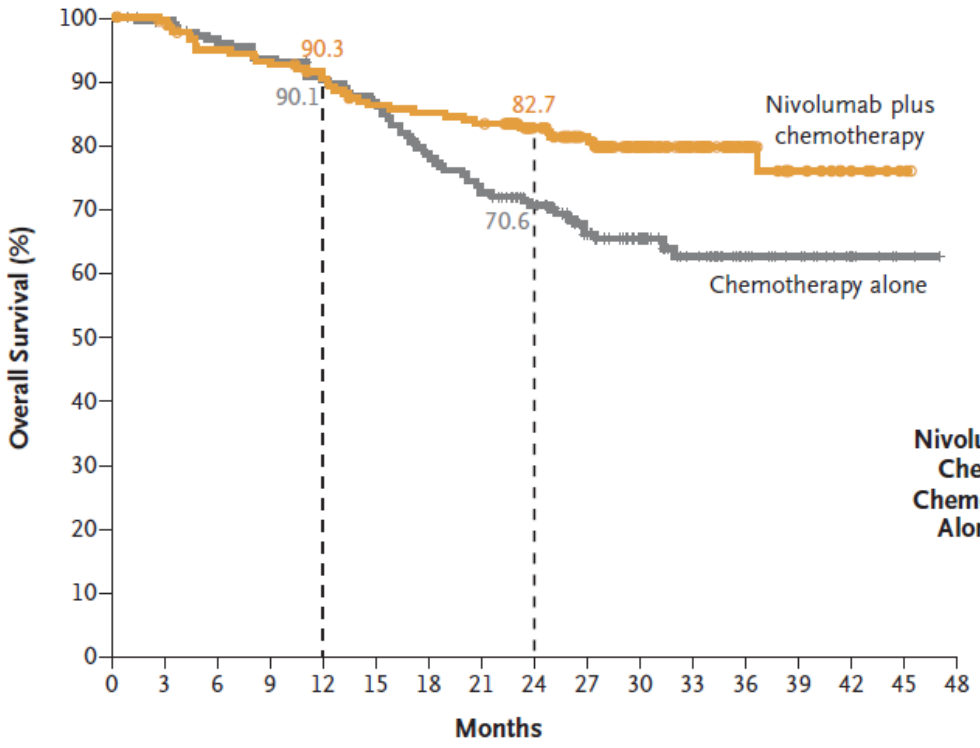
No. at Risk

Nivolumab plus chemotherapy	179	151	136	124	118	107	102	87	74	41	34	13	6	3	0
Chemotherapy alone	179	144	126	109	94	83	75	61	52	26	24	13	11	4	0

Suivi médian 31,6 mois)

Disease stage at baseline				
IB or II	127	NR (27.8–NR)	NR (16.8–NR)	0.87 (0.48–1.56)
IIIA	228	31.6 (26.6–NR)	15.7 (10.8–22.7)	0.54 (0.37–0.80)
Histologic type of tumor				
Squamous	182	30.6 (20.0–NR)	22.7 (11.5–NR)	0.77 (0.49–1.22)
Nonsquamous	176	NR (27.8–NR)	19.6 (13.8–26.2)	0.50 (0.32–0.79)
PD-L1 expression level				
<1%	155	25.1 (14.6–NR)	18.4 (13.9–26.2)	0.85 (0.54–1.32)
≥1%	178	NR (NR–NR)	21.1 (11.5–NR)	0.41 (0.24–0.70)
1–49%	98	NR (27.8–NR)	26.7 (11.5–NR)	0.58 (0.30–1.12)
≥50%	80	NR (NR–NR)	19.6 (8.2–NR)	0.24 (0.10–0.61)

CT + Nivo



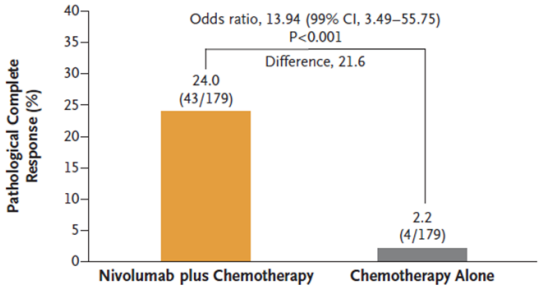
	No. of Patients	Median Overall Survival (95% CI) *mo*
Nivolumab plus Chemotherapy	179	NR (NR–NR)
Chemotherapy Alone	179	NR (NR–NR)

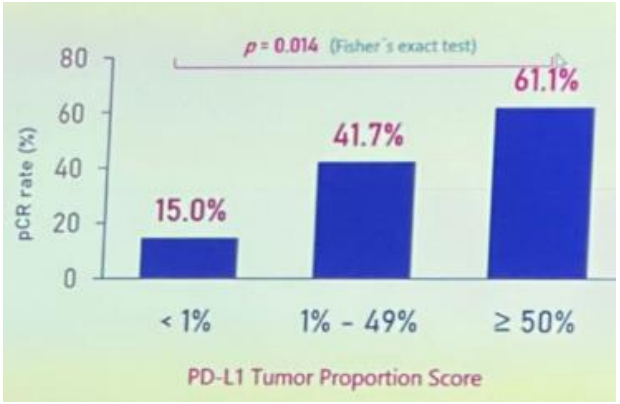
Hazard ratio for death, 0.57
(99.67% CI, 0.30–1.07)
P=0.008

No. at Risk

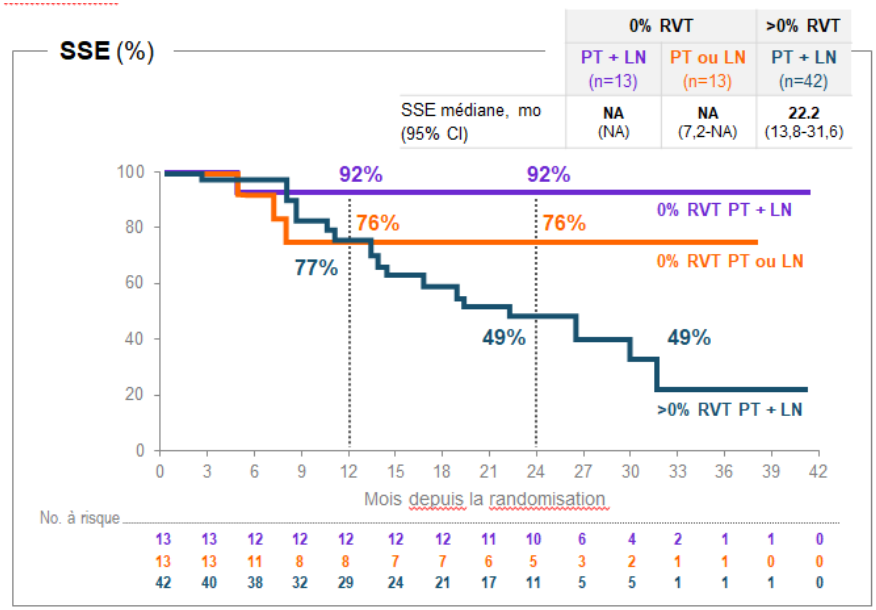
Nivolumab plus chemotherapy	179	176	166	163	156	148	146	143	122	101	72	48	26	16	7	3	0
Chemotherapy alone	179	172	165	161	154	148	133	123	108	80	59	41	24	16	7	2	0

Réponse pathologique





Réponse pathologique complète



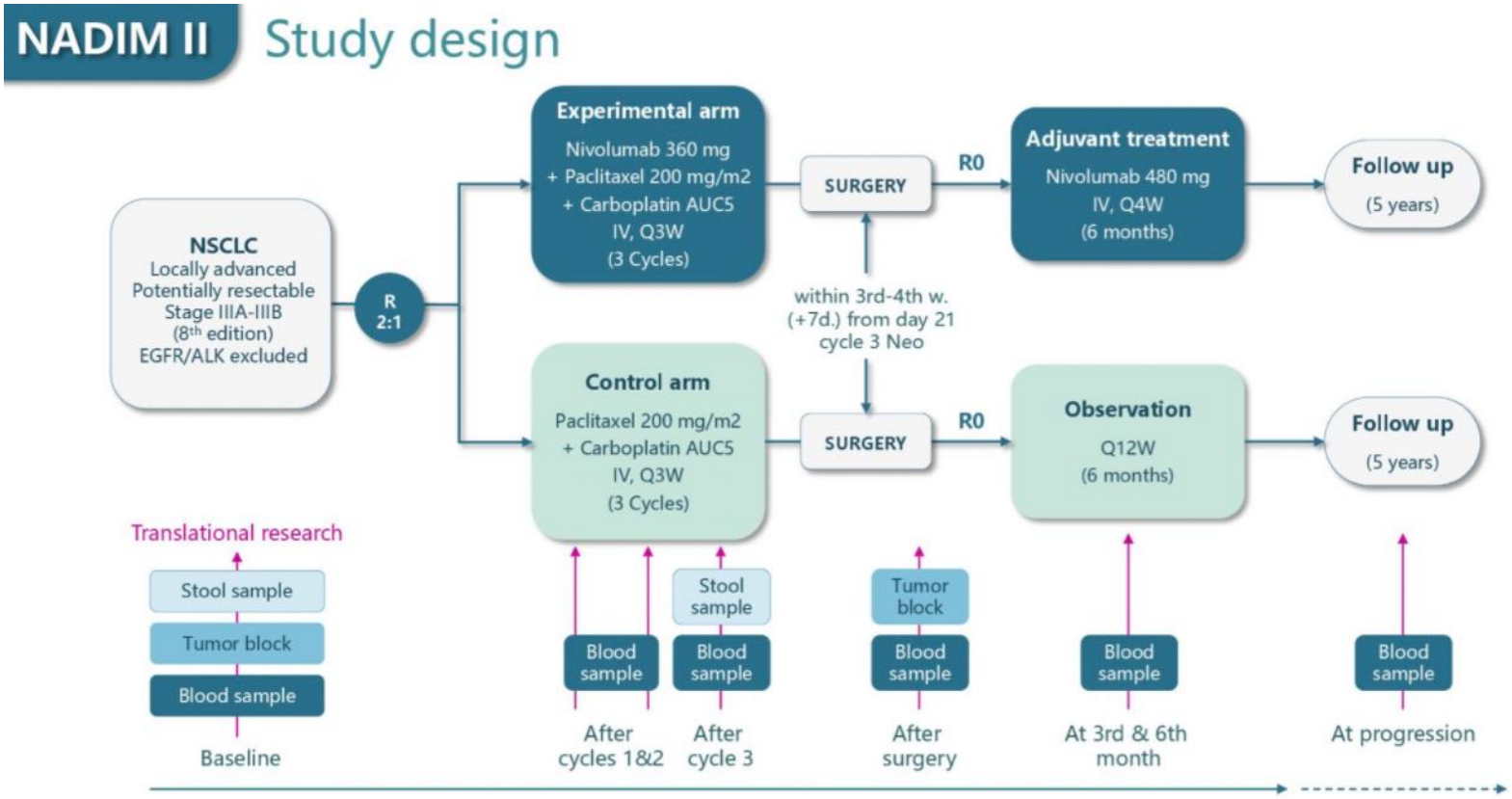
Réponse pathologique et pronostic

Tolérance

Table 2. Adverse Events.*

Event	Nivolumab plus Chemotherapy (N = 176)		Chemotherapy Alone (N = 176)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Adverse events of any cause — no. (%)†				
All	163 (92.6)	72 (40.9)	171 (97.2)	77 (43.8)
Leading to discontinuation of treatment	18 (10.2)	10 (5.7)	20 (11.4)	7 (4.0)
Serious	30 (17.0)	19 (10.8)	24 (13.6)	17 (9.7)
Treatment-related adverse events — no. (%)†				
All	145 (82.4)	59 (33.5)	156 (88.6)	65 (36.9)
Leading to discontinuation of treatment	18 (10.2)	10 (5.7)	17 (9.7)	6 (3.4)
Serious	21 (11.9)	15 (8.5)	18 (10.2)	14 (8.0)
Death‡	0	—	3 (1.7)	—
Surgery-related adverse events — no./total no. (%)§	62/149 (41.6)	17/149 (11.4)	63/135 (46.7)	20/135 (14.8)

NADIM II phase II



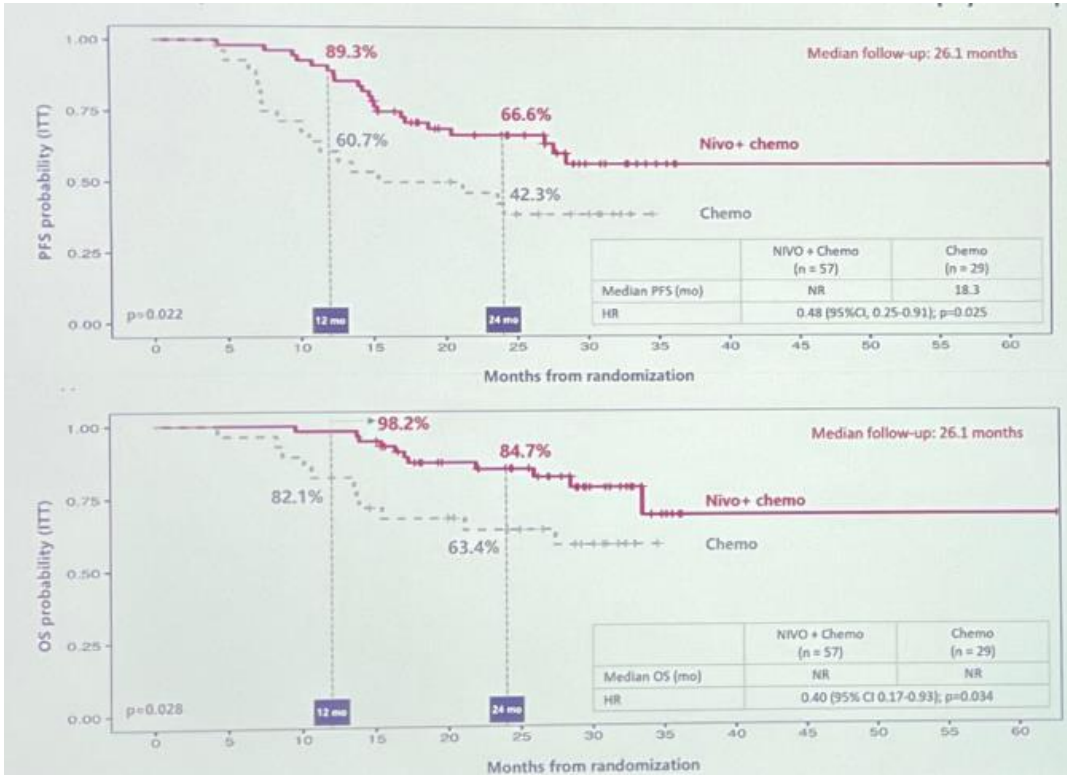
Critère principal: réponse complète pathologique

90 pts, 87 analysés

Résultats préliminaires réponse ESMO 2022

	NIVO+ chemo (n=53)	Chemo (n=20)	P value
pCR	36.8	6.9	0.0068
ORR	75.4%	48.2%	0.023
MPR	52.6%	13.8%	0.0012
Definitive surgery	93.0%	69.0%	0.00807
Down staging	69.8%	40%	0.04

Données WCLC 2022

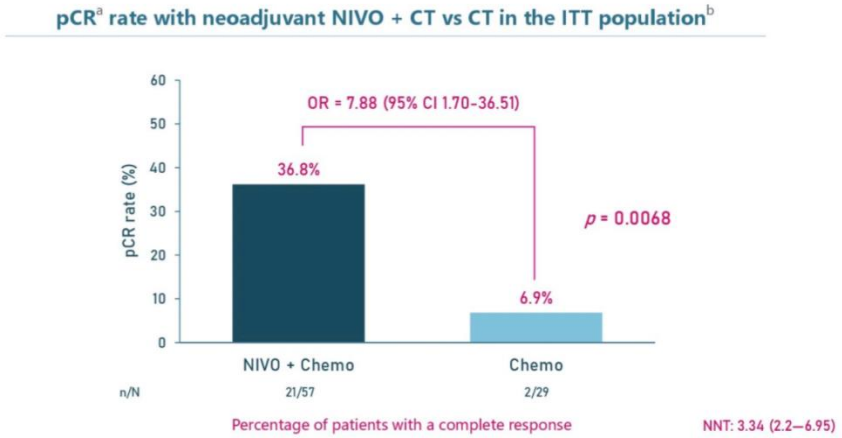


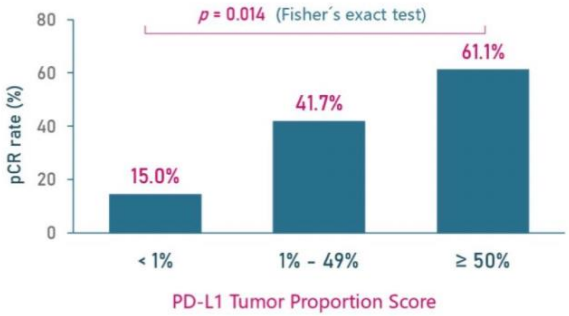
Progression free survival
18.3 months → NR
HR 0.48 (0.25-0.91)

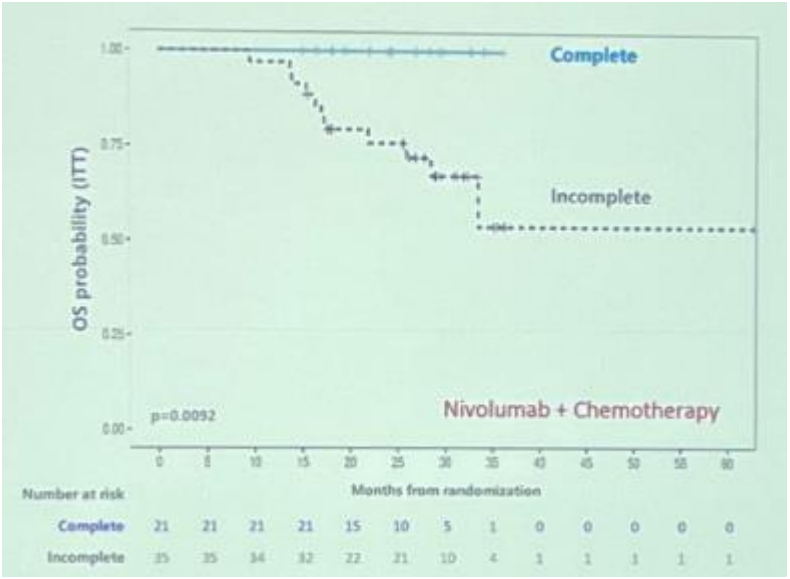
24 Month overall survival
63.4% → 84.7%
Median NR, HR 0.4 (0.17-0.93)

Provencio et al. IASLC WCLC 2022, PL03.12

Résultats préliminaires 2022
Réponse pathologique







Etudes phase III en néo-adjuvant

	Stade	IO	CT	Adjuvant IO	Objectif principal
CheckMate 816	IB IIIA (7è)	+/- Nivo	3 cycles (Pem/cis Pac/carb Gem/cis)	non	RC patho SSP
Keynote 671	IB IIIA (8è)	+/- Pembro	4 cycles (Pem/cis gem/cis)	13 cylces Pembro	SSP, SG
IMPOWER 030	IB IIIA (8è)	+/- Atezo	4 cycles (Pem/cis Pem/carb Pac/carb Gem/cis)	16 cycles Atezo	SSP
AEGEAN	IB IIIA (8è)	+/- Durva	4 cycles (Pem/cis Pem/carb Pac/carb Gem/cis)	12 cycles Durva/4s	SSP
ChekMate 77T	IB IIIA (8è)	+/- Nivo	4 cycles (Pem/cis Pem/carb Pac/carb Doc/cis Gem/cis)	Nivo ou PCB 1 an	SSP
Neo ADAURA	II IIB N2	Osimertinib	Osi seul/ Osi + 3 cycles (Cis ou carbo/Pem Pac/carb)/CT	non	R majeure patho

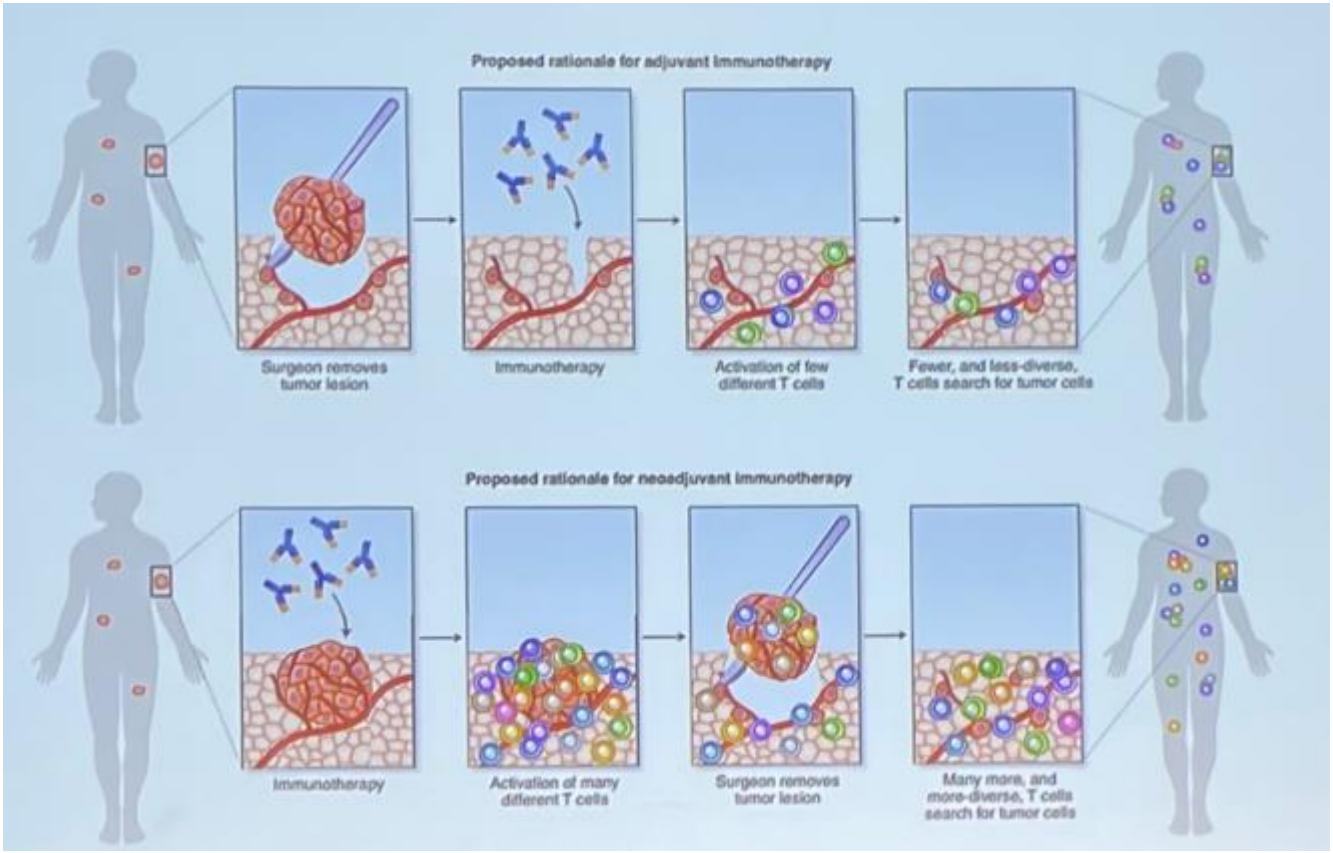
Immunothérapie

NEO-ADJUVANT OU ADJUVANT OU LES DEUX ?

Débat

- Néo-adjuvant
  - Améliore résecabilité et R0 ?
  - Evite chirurgie inutile chez les progresseurs rapides
  - Permet de préparer le patient (bilan cardio-vasculaire, réhabilitation, nutrition…)
  - Evaluation de la réponse radiologique et pathologique et du pronostic
  - Meilleur adhérence (70% en adj)
  - Contrôle micro-métastases
  - Amélioration SSP et SG
- Adjuvant
  - Stadification précise pTNM R
  - Pas de délai chirurgical
  - Evite les EI pré-chirurgicaux
  - Pas de complication per ou post-opératoire liée au traitement néo-adjuvant (adhérences ganglions)
  - Intervention sans preuve histologique
  - Permet des traitements plus longs
  - Calendrier plus souple
  - Contrôle micro-métastases
  - Amélioration SSP et SG

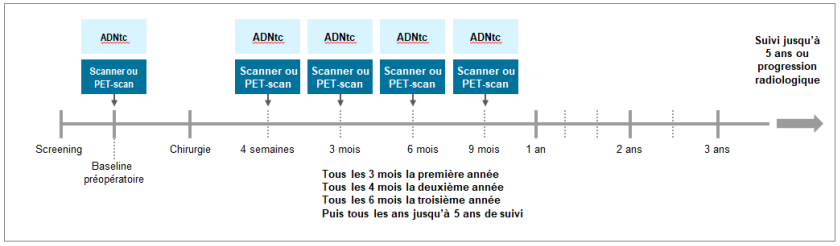
Immunothérapie pré ou post-opératoire

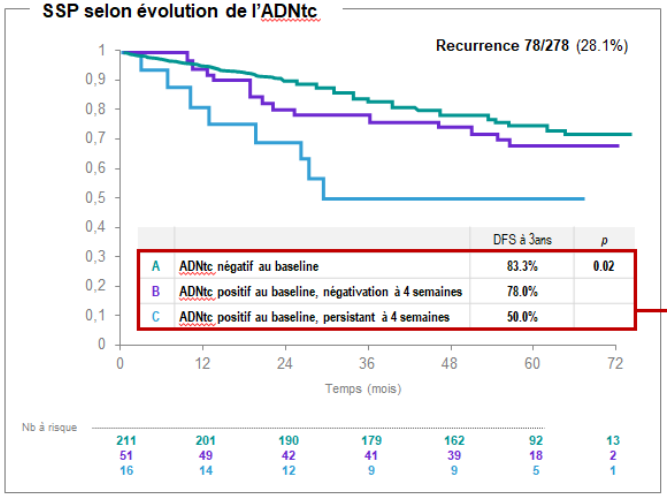


Valeur pronostic de l'ADN tumorale circulante post opératoire (MJ Ahn ESMO 2022)

Population de l'étude

- Entre août 2015 et octobre 2017
- Patients en résection complète d'un CBNPC avec mutation *EGFR* classique de stade stage IA-IIIA (AJCC 7ème édition)
- Suivi radiologique par scanner TAP ou TEP, avec monitoring longitudinal de l'ADN tumoral circulant par ddPCR





En conclusion

- Des standards en péri-opératoire
  - Chimiothérapie adjuvante stades II et III
  - Osimertinib adjuvant EGFR muté stade IB > 3cm à III
- Des futurs « incontournables »?
  - Atezolizumab PDL1 > 50% stade ≥ II en adjuvant (AMM EMA)
  - CT IO Nivolumab néo-adjuvant PDL1 > 1% stade ≥ II
- Traitements à la carte ?
  - Age et comorbidités
  - Néoadjuvant tumeur en limite de résecabilité
  - En fonction mutations, PDL1
  - En fonction réponse pathologique
  - En fonction ADN tumoral circulant post opératoire