Les scoops de l'ASCO 2023 en Oncologie Thoracique

Mardi 20 juin 2023

WEBINAIRE

Dr Sophie Cousin

3ème Post-ASCO en Nouvelle Aquitaine

Liens d'intérêts

- Boards: BMS, Astrazeneca, Takeda, Sanofi, Novartis, Abbvie, MSD
- Réunions/oratrice: MSD, Astrazeneca, Takeda, BMS
- Participation congrès: Astrazeneca, MSD, Takeda, Pfizer, Pharmamar

CBNPC: péri opératoire, Keynote-671

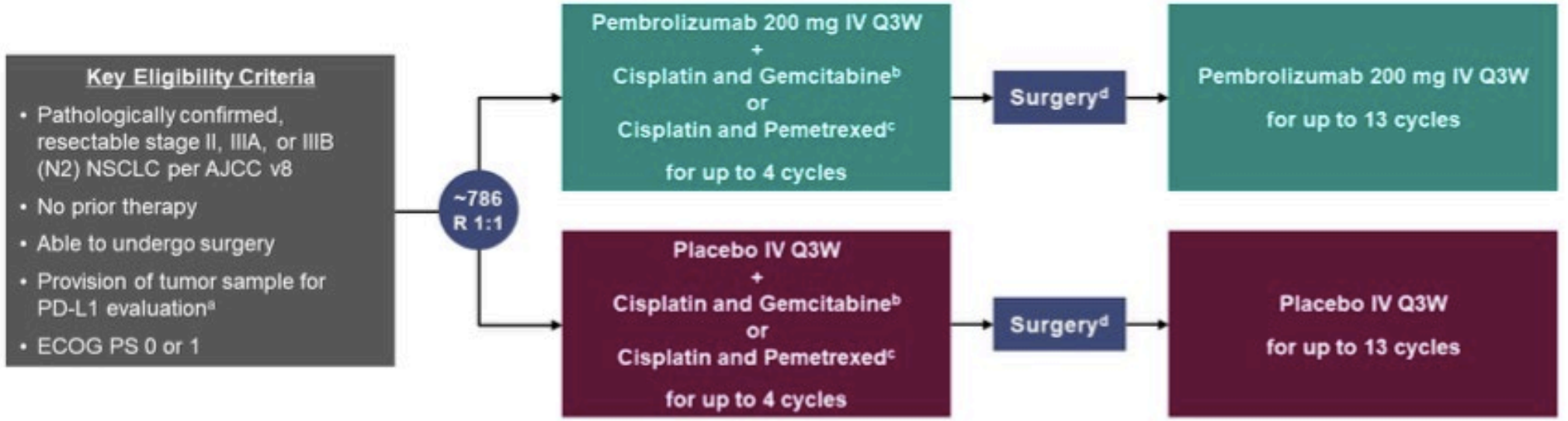
KEYNOTE-671: Randomized, Double-Blind, Phase 3 Study of Pembrolizumab or Placebo plus Platinum-Based Chemotherapy Followed by Resection and Pembrolizumab or Placebo for Early-Stage NSCLC

Heather Wakelee,[1] Moishe Liberman,[2] Terufumi Kato,[3] Masahiro Tsuboi,[4] Se-Hoon Lee,[5] Shugeng Gao,[6] Ke-Neng Chen,[7] Christophe Dooms,[8] Margarita Majem,[9] Ekkehard Eigendorff,[10] Gastón L Martinengo,[11] Olivier Bylicki,[12] Delvys Rodríguez-Abreu,[13] Jamie Chaft,[14] Silvia Novello,[15] Jing Yang,[16] Steven M Keller,[16] Ayman Samkari,[16] Jonathan D Spicer,[17] on behalf the KEYNOTE-671 Investigators

[1]Stanford University School of Medicine/Stanford Cancer Institute, Stanford, CA, USA; [2]Centre Hospitalier de Universite to Montréal (CHUM), Montréal, QC, Canada; [3]Kanagawa Cancer Center, Yokohama, Japan; [4]National Cancer Center Hospital East, Kashiwa, Japan; [5]Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; [6]National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [7]Beijing Cancer Hospital, Peking University, Beijing, China; [8]University Hospitals Leuven, Leuven, Belgium; [9]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [10]Zentralklinik Bad Berka, Bad Berka, Germany; [11]Sanatorio Parque, Córdoba, Argentina; [12]HIA Sainte-Anne, Toulon, France; [13]Hospital Universitario Insular de Gran Canaria, Universidad de Las Palmas de Gran Canaria, Las Palmas de Gran Canaria, Spain; [14]Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, New York, NY, USA; [15]Department of Oncology, University of Turin, A.O.U. San Luigi Gonzaga di Orbassano, Turin, Italy; [16]Merck & Co. Inc., Rahway, NJ, USA; [17]McGill University Health Centre, Montréal, QC, Canada

Design: Keynote-671

Etude de phase III, randomisée, en double aveugle



Stratification Factors

- Disease stage (II vs III)
- PD-L1 TPS[a] (<50% vs ≥50%)
- Histology (squamous vs nonsquamous)
- Geographic region (east Asia vs not east Asia)

Dual primary end points: EFS per investigator review and OS

Key secondary end points: mPR and pCR per blinded, independent pathology review, and safety

[a] Assessed at a central laboratory using PD-L1 IHC 22C3 pharmDx. [b] Cisplatin 75 mg/m² IV Q3W + gemcitabine 1000 mg/m² IV on days 1 and 8 Q3W was permitted for squamous histology only. [c] Cisplatin 75 mg/m² IV Q3W + pemetrexed 500 mg/m² IV Q3W was permitted for nonsquamous histology only. [d] Radiotherapy was to be administered to participants with microscopic positive margins, gross residual disease, or extracapsular nodal extension following surgery and to participants who did not undergo planned surgery for any reason other than local progression or metastatic disease. ClinicalTrials.gov identifier: NCT03425643.

Caractéristiques des patients

	Pembro Arm (N = 397)	Placebo Arm (N = 400)
Median age (range), years	63 (26-83)	64 (35-81)
Male	279 (70.3%)	284 (71.0%)
Race		
American Indian or Alaska Native	1 (0.3%)	0
Asian	124 (31.2%)	125 (31.3%)
Black or African American	6 (1.5%)	10 (2.5%)
Multiple	3 (0.8%)	10 (2.5%)
White	250 (63.0%)	239 (59.8%)
Missing data	13 (3.3%)	16 (4.0%)
Geographic region		
East Asia	123 (31.0%)	121 (30.3%)
Not east Asia	274 (69.0%)	279 (69.8%)
ECOG PS		
0	253 (63.7%)	246 (61.5%)
1	144 (36.3%)	154 (38.5%)
Histology		
Nonsquamous	226 (56.9%)	227 (56.8%)
Squamous	171 (43.1%)	173 (43.3%)

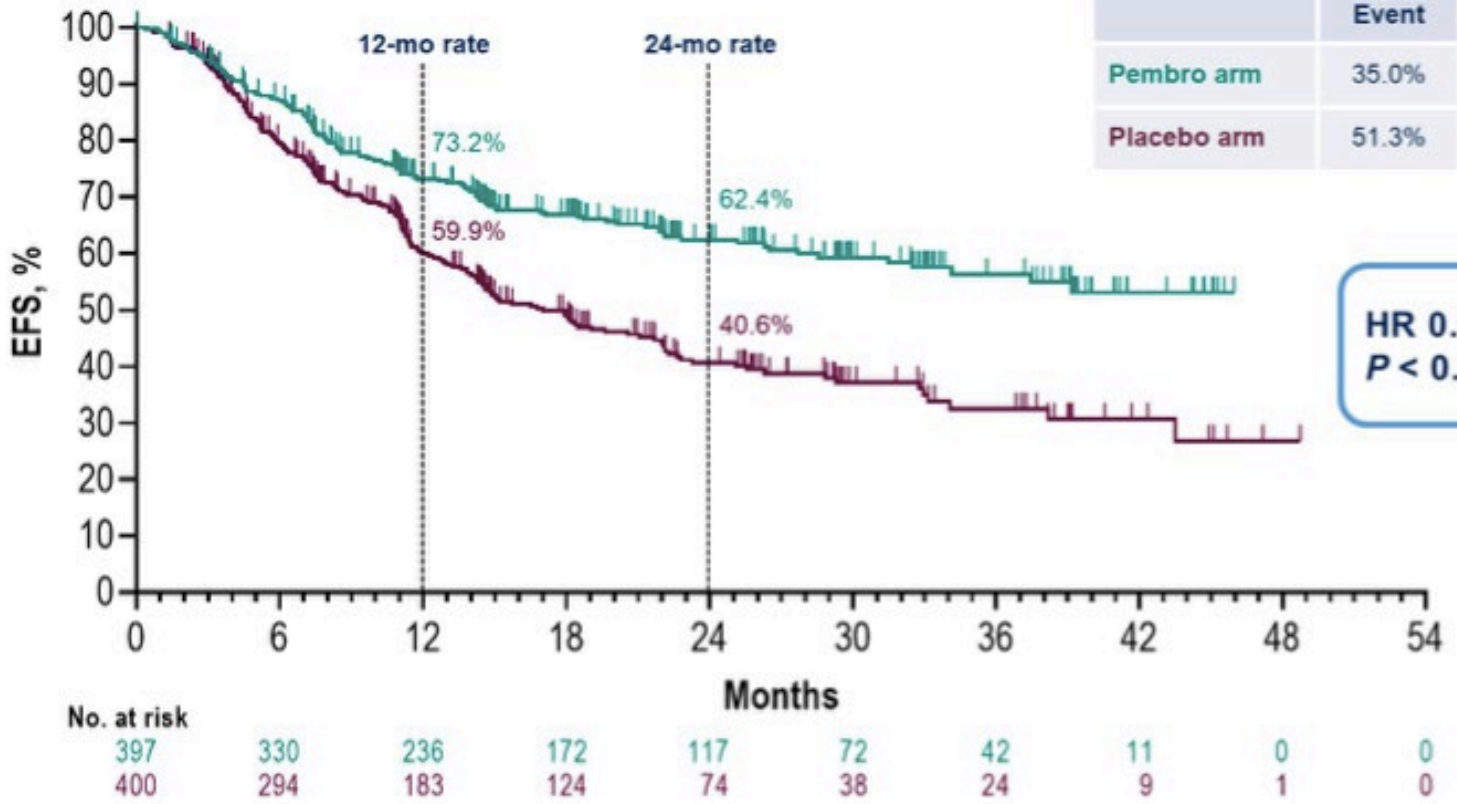
	Pembro Arm (N = 397)	Placebo Arm (N = 400)
Smoking status		
Current	96 (24.2%)	103 (25.8%)
Former	247 (62.2%)	250 (62.5%)
Never	54 (13.6%)	47 (11.8%)
Disease stage at baseline (per AJCC v8)		
II	118 (29.7%)	121 (30.3%)
IIIA	217 (54.7%)	225 (56.3%)
IIIB	62 (15.6%)	54 (13.5%)
pN status		
N0	148 (37.3%)	142 (35.5%)
N1	81 (20.4%)	71 (17.8%)
N2	168 (42.3%)	187 (46.8%)
PD-L1 TPS		
≥50%	132 (33.2%)	134 (33.5%)
1-49%	127 (32.0%)	115 (28.8%)
<1%	138 (34.8%)	151 (37.8%)
Known *EGFR* mutation[a]	14 (3.5%)	19 (4.8%)
Known *ALK* translocation[a]	12 (3.0%)	9 (2.3%)

[a] *EGFR* mutation and *ALK* translocation status were tested locally per investigator discretion. *EGFR* status was unknown in 272 (68.5%) participants in the pembro arm and 254 (63.5%) in the placebo arm; *ALK* status was unknown in 281 (70.8%) and 258 (64.5%), respectively. Data cutoff date for IA1: July 29, 2022.

Données de chirurgie

	Pembro Arm N = 325	Placebo Arm N = 317
In-Study Surgery[a]		
Resected	320 (98.5%)	302 (95.3%)
Complete - R0	299 (92.0%)	267 (84.2%)
Incomplete - R1	17 (5.2%)	31 (9.8%)
Incomplete - R2	4 (1.2%)	4 (1.3%)
Unresected	5 (1.5%)	15 (4.7%)
Surgical procedure		
Lobectomy	256 (78.8%)	238 (75.1%)
Pneumonectomy	37 (11.4%)	39 (12.3%)
Bilobectomy	26 (8.0%)	26 (8.2%)
Exploratory thoracotomy	4 (1.2%)	13 (4.1%)
Other	2 (0.6%)[b]	1 (0.3%)[c]
30-day all-cause mortality	6 (1.8%)[d]	2 (0.6%)[e]

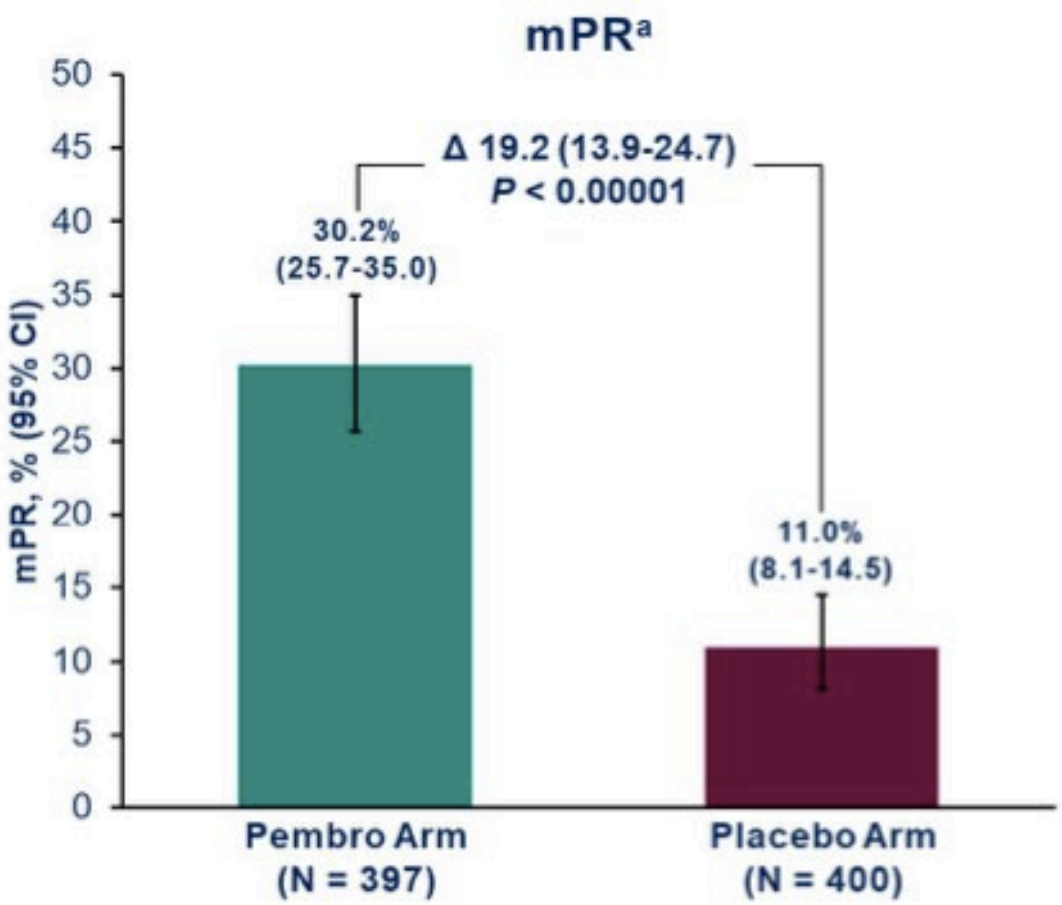
Survie sans événement (EFS)

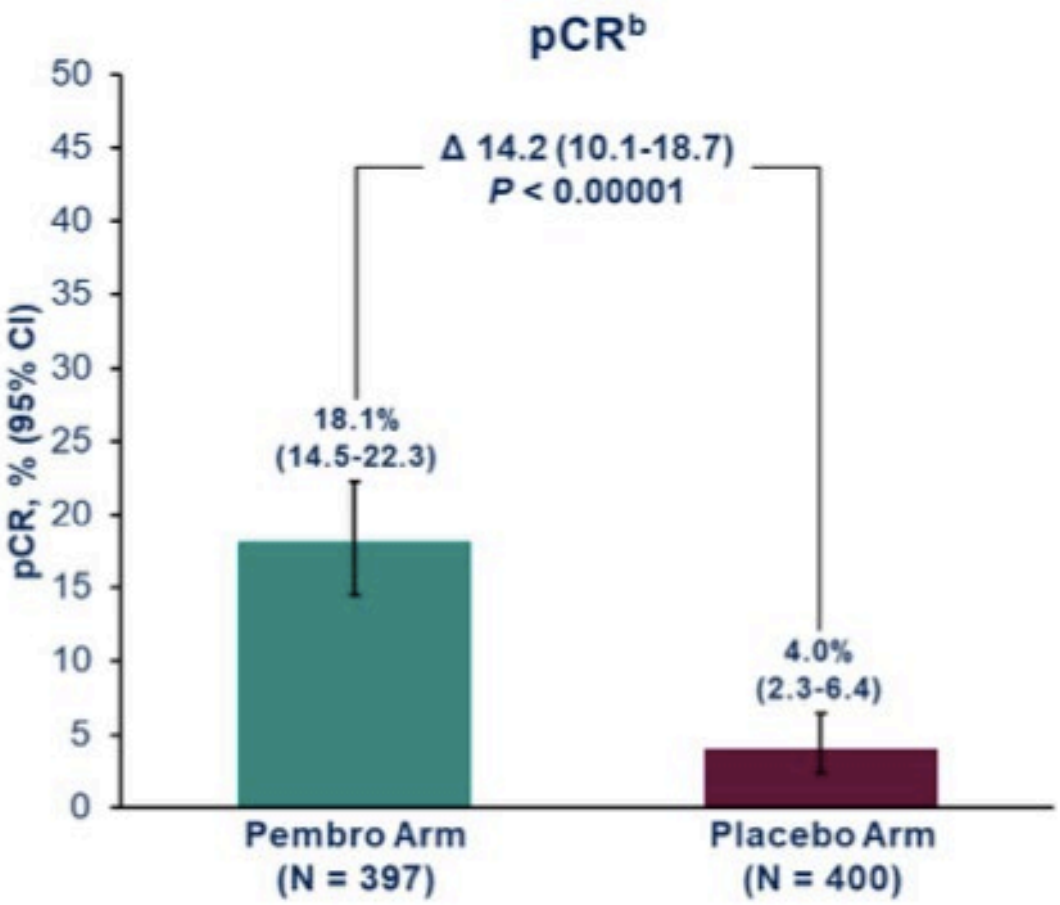


	Pts w/ Event	Median (95% CI), mo
Pembro arm	35.0%	NR (34.1-NR)
Placebo arm	51.3%	17.0 (14.3-22.0)

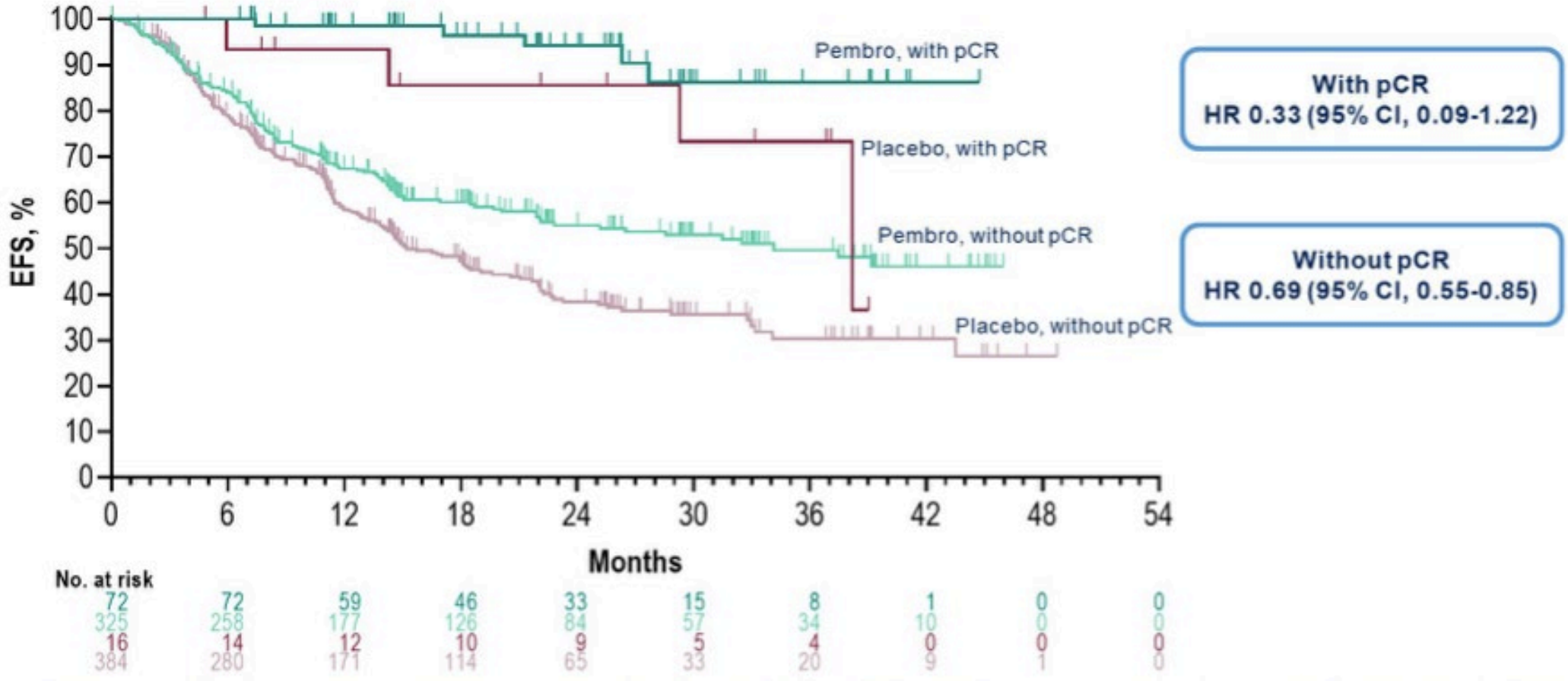
HR 0.58 (95% CI, 0.46-0.72)
***P* < 0.00001**

Réponse pathologique





EFS selon la réponse pathologique complète



Temps d'exposition et tolérance

	Pembro Arm (n = 396)	Placebo Arm (n = 399)
Exposure		
Days on pembro or placebo, median (range)	332 days (1-567)	315 days (1-596)
No. pembro or placebo administrations, median (range)	12 (1-17)	10 (1-17)
Treatment-related AEs[a]	383 (96.7%)	379 (95.0%)
Grade 3-5	178 (44.9%)	149 (37.3%)
Serious	70 (17.7%)	57 (14.3%)
Led to death	4 (1.0%)[b]	3 (0.8%)[c]
Led to discontinuation of all study treatment	50 (12.6%)	21 (5.3%)
Immune-mediated AEs and infusion reactions	100 (25.3%)	42 (10.5%)
Grade 3-5	23 (5.8%)	6 (1.5%)
Serious	21 (5.3%)	6 (1.5%)
Led to death	1 (0.3%)[d]	0
Led to discontinuation of all study treatment	20 (5.1%)	3 (0.8%)

Données de survie d'ADAURA

Overall survival analysis from the ADAURA trial of adjuvant osimertinib in patients with resected EGFR-mutated (EGFRm) stage IB–IIIA non-small cell lung cancer (NSCLC)

Roy S. Herbst[1], Masahiro Tsuboi[2], Thomas John[3], Terufumi Kato[4], Margarita Majem[5], Christian Grohé[6], Jie Wang[7], Jonathan Goldman[8], Shun Lu[9], Wu-Chou Su[10], Filippo de Marinis[11], Frances A. Shepherd[12], Ki Hyeong Lee[13], Nhieu Thi Le[14], Arunee Dechaphunkul[15], Dariusz Kowalski[16], Lynne Poole[17], Marta Stachowiak[18], Yuri Rukazenkov[19], Yi-Long Wu[20]

[1]Medical Oncology, Yale School of Medicine and Yale Cancer Center, New Haven, CT, USA; [2]Department of Thoracic Surgery and Oncology, National Cancer Center Hospital East, Kashiwa, Japan; [3]Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia; Sir Peter MacCallum Department of Oncology, The University of Melbourne, Melbourne, Australia; [4]Department of Thoracic Oncology, Kanagawa Cancer Center, Yokohama, Japan; [5]Department of Medical Oncology, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [6]Klinik für Pneumologie - Evangelische Lungenklinik Berlin Buch, Berlin, Germany; [7]Cancer Hospital, Chinese Academy of Medical Sciences, Beijing, China; [8]David Geffen School of Medicine at University of California Los Angeles, Los Angeles, CA, USA; [9]Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China; [10]Department of Oncology, National Cheng Kung University, Tainan, Taiwan; [11]Thoracic Oncology Division, European Institute of Oncology (IEO), IRCCS, Milan, Italy; [12]Department of Medical Oncology and Hematology, University Health Network, Princess Margaret Cancer Centre, Toronto, Ontario, Canada; [13]Department of Internal Medicine, Chungbuk National University Hospital, Cheongju, Republic of Korea; [14]Ho Chi Minh City Oncology Hospital, Binh Thanh District, Ho Chi Minh City, Vietnam; [15]Department of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand; [16]Department of Lung Cancer and Thoracic Tumours, Maria Sklodowska-Curie National Research Institute of Oncology, Warsaw, Poland; [17]Oncology Biometrics, AstraZeneca, Cambridge, UK; [18]Late Oncology Research & Development, AstraZeneca, Warsaw, Poland; [19]Oncology Research & Development, AstraZeneca, Cambridge, UK; [20]Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou, China

ADAURA

Etude de phase III, randomisée, en double aveugle

Patients with completely resected stage* IB, II, IIIA NSCLC, with or without adjuvant chemotherapy†

Key inclusion criteria:
- ≥18 years (Japan / Taiwan: ≥20)
- WHO performance status 0 / 1
- Confirmed primary non-squamous NSCLC Ex19del / L858R‡
- Brain imaging, if not completed pre-operatively
- Complete resection with negative margins§
- Maximum interval between surgery and randomization:
  - 10 weeks without adjuvant chemotherapy
  - 26 weeks with adjuvant chemotherapy

Stratification by:
Stage (IB vs II vs IIIA)
EGFRm (Ex19del vs L858R)
Race (Asian vs non-Asian)

Randomization 1:1 (N=682)

- **Osimertinib 80 mg, once daily**
- **Placebo, once daily**

Planned treatment duration:
3 years

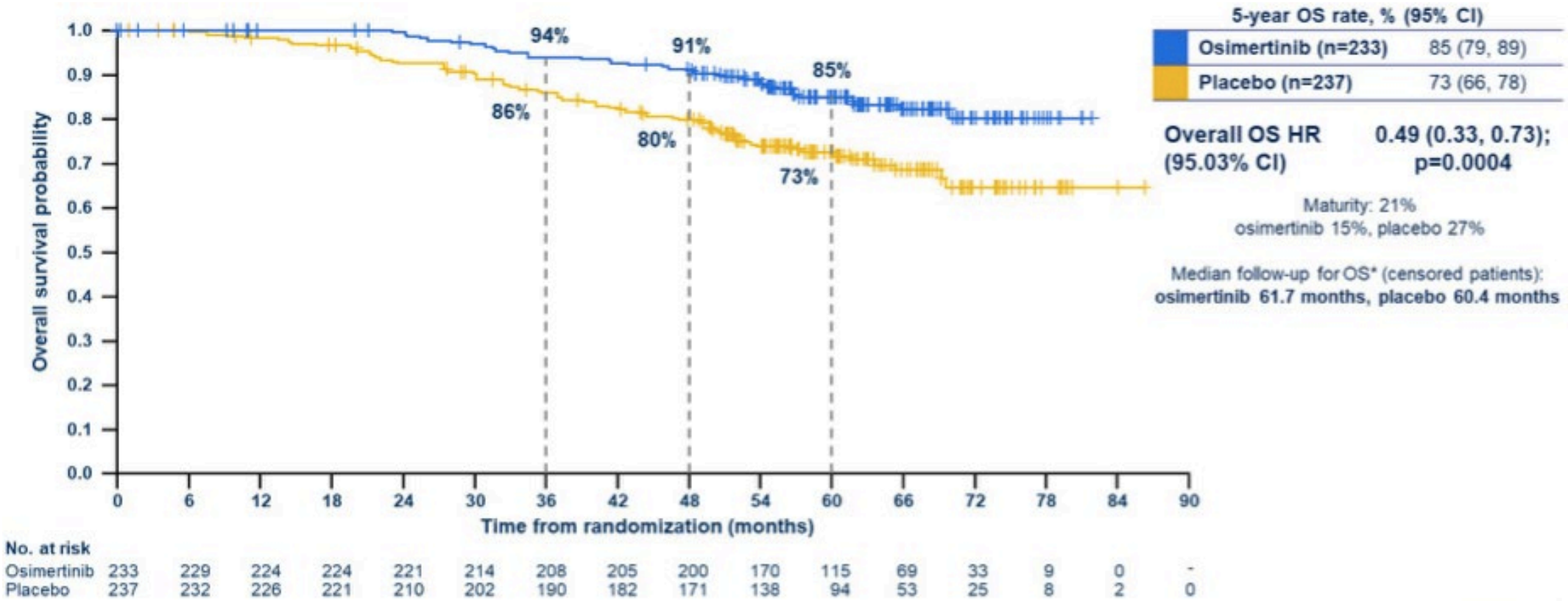
Treatment continued until:
- Disease recurrence
- Treatment completion
- Discontinuation criterion met

Follow-up:
- Until recurrence: Week 12 and 24, then every 24 weeks to 5 years, then yearly
- After recurrence: every 24 weeks for 5 years, then yearly

Endpoints
- **Primary endpoint:** DFS by investigator assessment in stage II–IIIA patients
- **Key secondary endpoints:** DFS in the overall population (stage IB–IIIA), landmark DFS rates, OS, safety, health-related quality of life

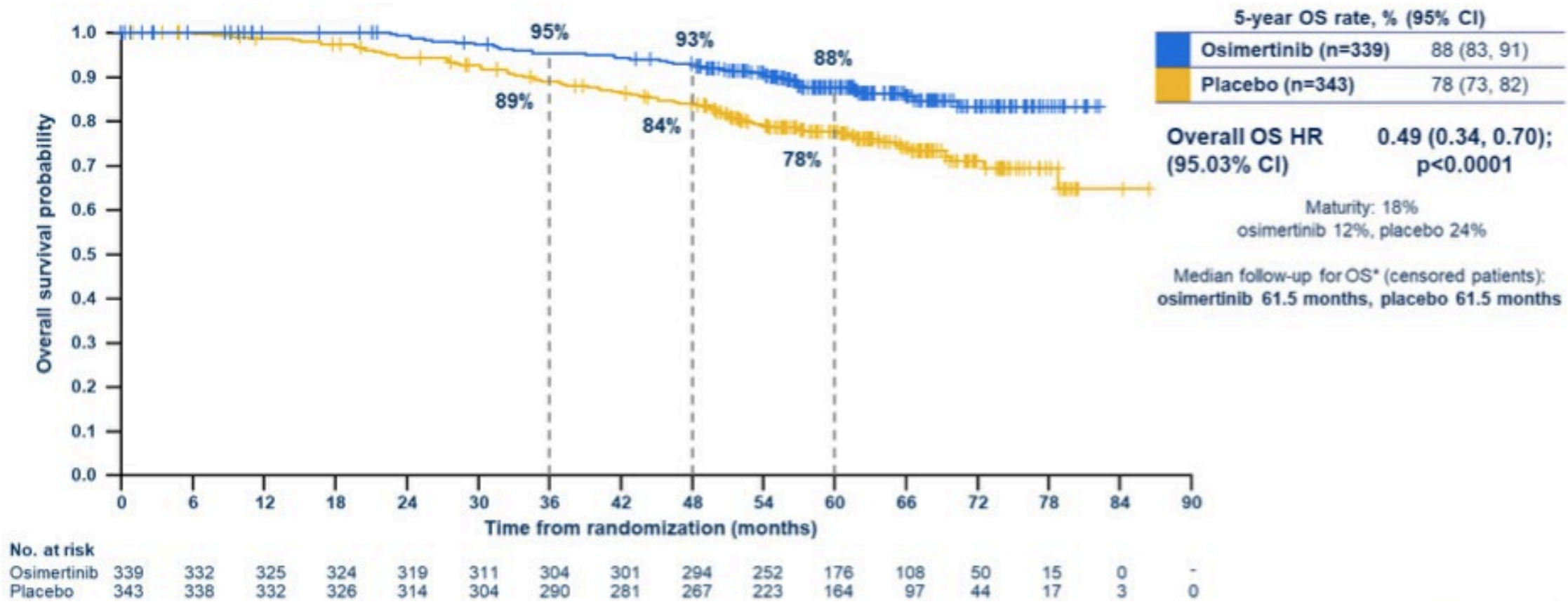
Données de survie globale dans les stades II/IIIA

HR: 0.49 (0.33 – 0.73), p=0.0004



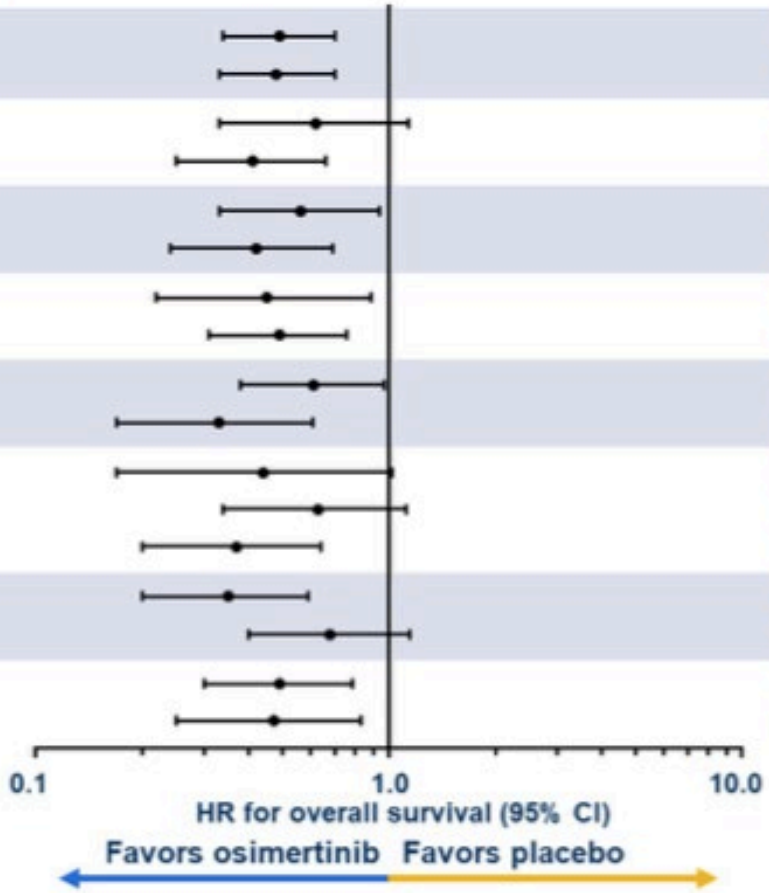
Données de survie globale dans les stades IB/II/IIIA

HR= 0.49 (0.34 – 0.70), p<0.0001



Analyse de sous groupes

Subgroup		No. of events / patients	HR	95% CI
Overall (N=682)	Stratified log-rank	124 / 682	0.49	0.34, 0.70
	Unadjusted Cox PH	124 / 682	0.48	0.33, 0.70
Sex	Male	42 / 204	0.62	0.33, 1.13
	Female	82 / 478	0.41	0.25, 0.66
Age	<65 years	60 / 380	0.56	0.33, 0.94
	≥65 years	64 / 302	0.42	0.24, 0.69
Smoking history	Yes	34 / 194	0.45	0.22, 0.89
	No	90 / 488	0.49	0.31, 0.76
Race	Asian	73 / 434	0.61	0.38, 0.97
	Non-Asian	51 / 248	0.33	0.17, 0.61
Stage*	IB	24 / 212	0.44	0.17, 1.02
	II	46 / 236	0.63	0.34, 1.12
	IIIA	54 / 234	0.37	0.20, 0.64
EGFR mutation	Ex19del	65 / 378	0.35	0.20, 0.59
	L858R	59 / 304	0.68	0.40, 1.14
Adjuvant chemotherapy	Yes	74 / 410	0.49	0.30, 0.79
	No	50 / 272	0.47	0.25, 0.83



Traitements subséquents systémiques reçus

Subsequent treatments, n (%)	Osimertinib (n=339)	Placebo (n=343)
Patients who received subsequent anti-cancer treatment*	76 (22)	184 (54)
EGFR-TKIs	58 (76)	162 (88)
Osimertinib	31 (41)	79 (43)
Other EGFR-TKIs	28 (37)	114 (62)
Chemotherapy	20 (26)	46 (25)
Radiotherapy	30 (39)	53 (29)
Other anti-cancer treatments	12 (16)	29 (16)

Un TKI anti EGFR a été le traitement le plus fréquemment proposé à la rechute

Mésothéliome: CCTG IND.227

ISTITUTO NAZIONALE TUMORI IRCCS – Fondazione Pascale

Canadian Cancer Trials Group / Groupe canadien des essais sur le cancer

IFCT Intergroupe Francophone de Cancérologie Thoracique

CCTG IND.227: A Randomized Phase 3 Study of Chemotherapy *versus* Chemotherapy plus Pembrolizumab in Treatment–Naive Pleural Mesothelioma

A Collaboration of

The Canadian Cancer Trials Group (CCTG)

The National Cancer Institute of Naples (NCIN) and

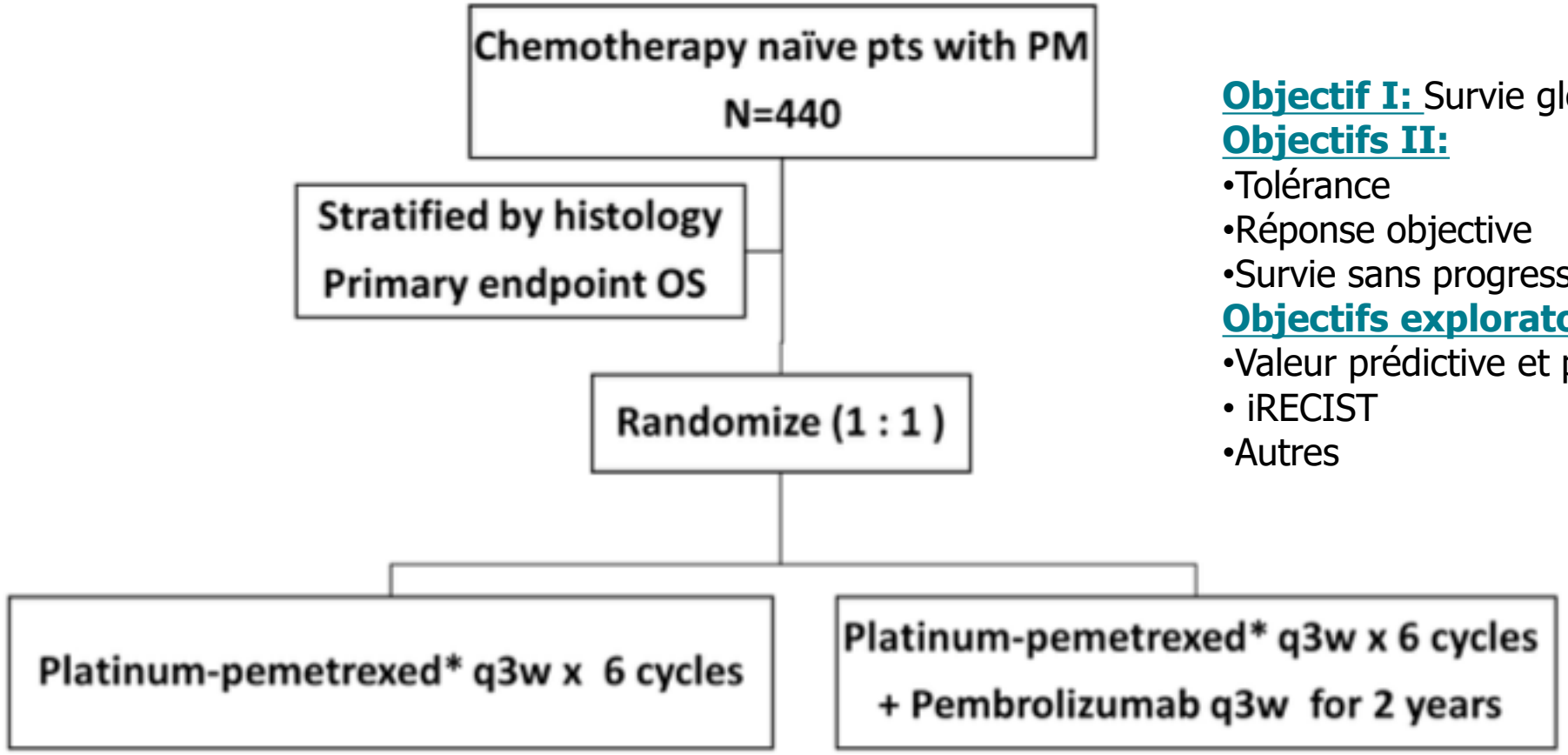
The French Cooperative Thoracic Intergroup (IFCT)

Quincy Chu, Maria Carmela Piccirillo, Laurent Greillier, Federica Grosso, Giuseppe Lo Russo, Marie Florescu, Manlio Mencoboni, Penelope Bradbury, Alessandro Morabito, Fabiana Letizia Cecere, Sara Delfanti, Arnaud Scherpereel, Myriam Locatelli-Sanchez, Gerard Zalcman, David Dawe, Joana Sederias, Scott Laurie, Christopher Lee, Wei Tu, Lesley Seymour

Canadian Cancer Trials Group / Groupe canadien des essais sur le cancer

Design: CCTG IND.227

Etude de phase III, randomisée, en ouvert



Objectif I: Survie globale (OS)

Objectifs II:

- Tolérance
- Réponse objective
- Survie sans progression (PFS)

Objectifs exploratoires:

- Valeur prédictive et pronostique de PD-L1
- iRECIST
- Autres

* Cisplatine 75mg/m^2 ou carboplatine AUC5 ou 6 – pemetrexed 500mg/m^2

Caractéristiques des patients (1)

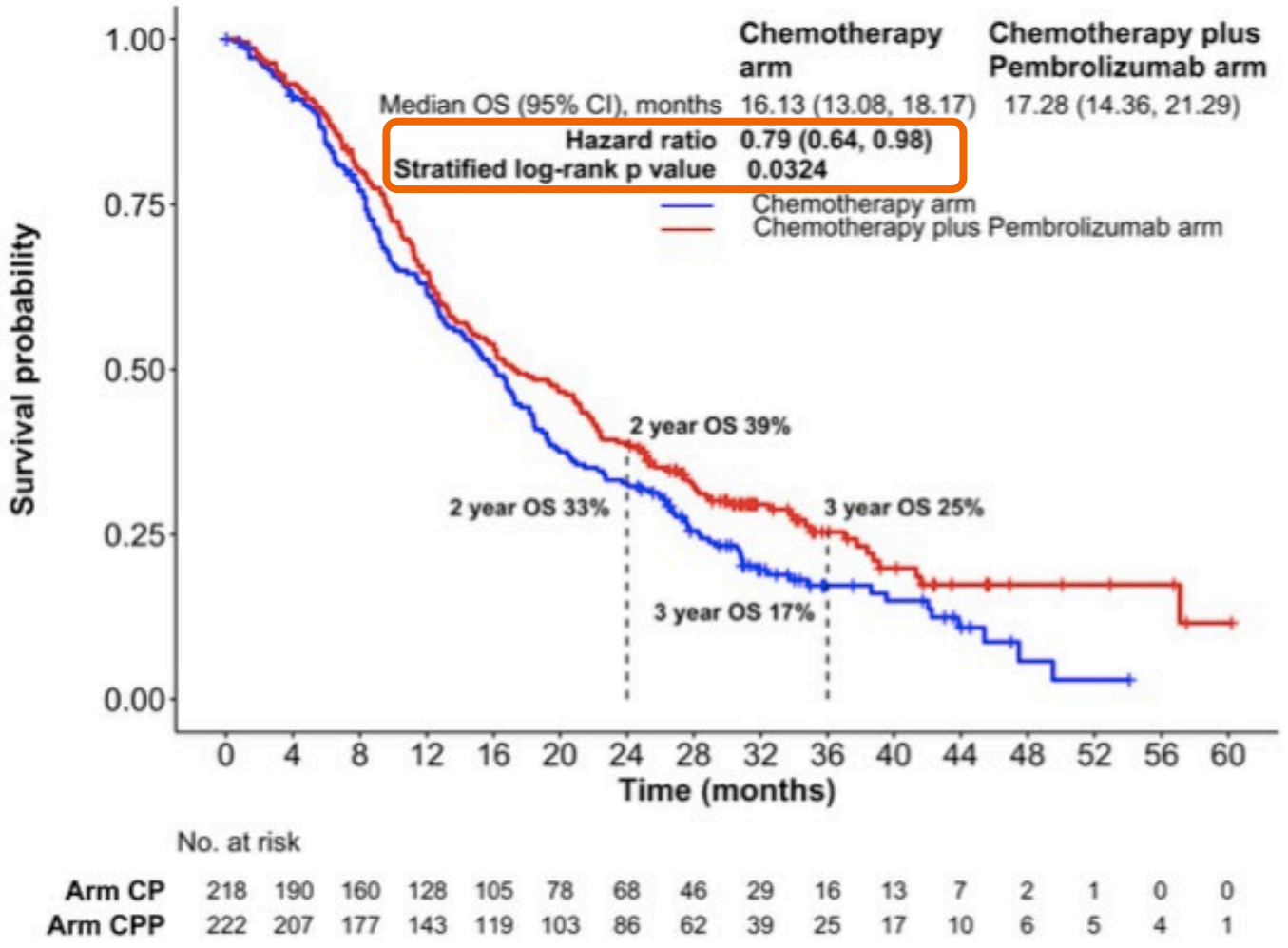
Patient Characteristic		CP N=218 N (%)	CPP N=222 N (%)
Sex	Female Male	50 (23) 168 (77)	57 (26) 165 (74)
Ethnicity	White Other Unknown or not reported	172 (79) 1 (1) 45 (21)	175 (79) 1 (1) 46 (21)
Age	Median Age (Range)	71 (28-88)	71 (33-87)
ECOG PS	0 1	105 (48) 113 (52)	101 (46) 121 (55)
Prior Asbestos Exposure	No Yes	87 (40) 130 (60)*	98 (44) 124 (56)
Prior Smoking History		116 (53)	129 (58)

Caractéristiques des patients (2)

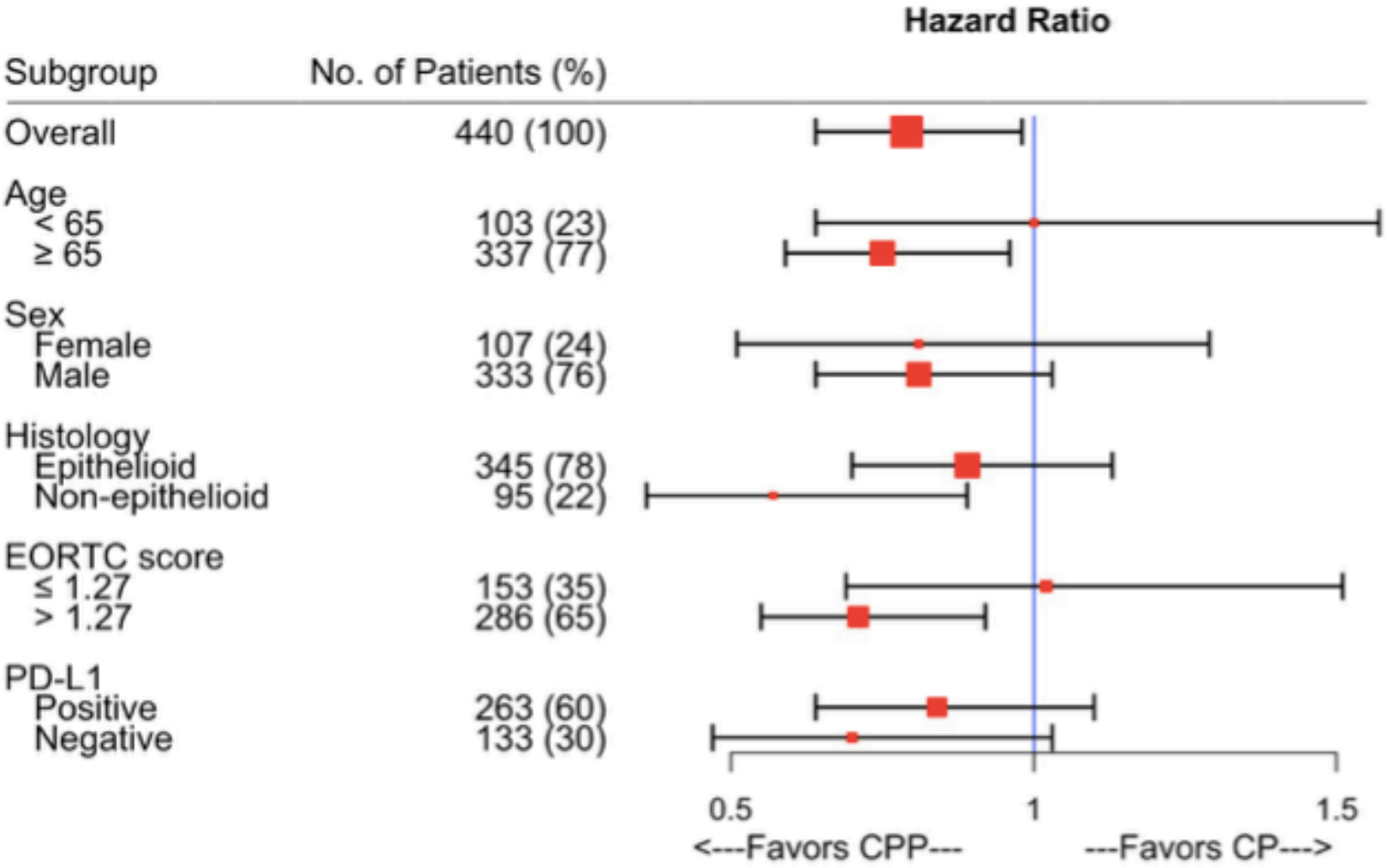
Patient Characteristic		CP N=218 N (%)	CPP N=222 N (%)
Histological subtypes[1]	Epithelioid Mixed/biphasic Sarcomatoid Other	168 (77) 27 (12) 21 (10) 2 (1)	174 (78) 35 (16) 10 (5) 3 (1)
PD-L1[2] ≥ 1 cut off	Positive Negative Unknown Not Done	132 (61) 63 (29) 6 (3) 17 (8)	131 (59) 70 (32) 7 (3) 14 (6)
EORTC Prognostic[3] Score	≤1.27 >1.27 Unknown	76 (35) 141 (65) 1 (0)	77 (35) 145 (65) 0

Résultats: survie globale

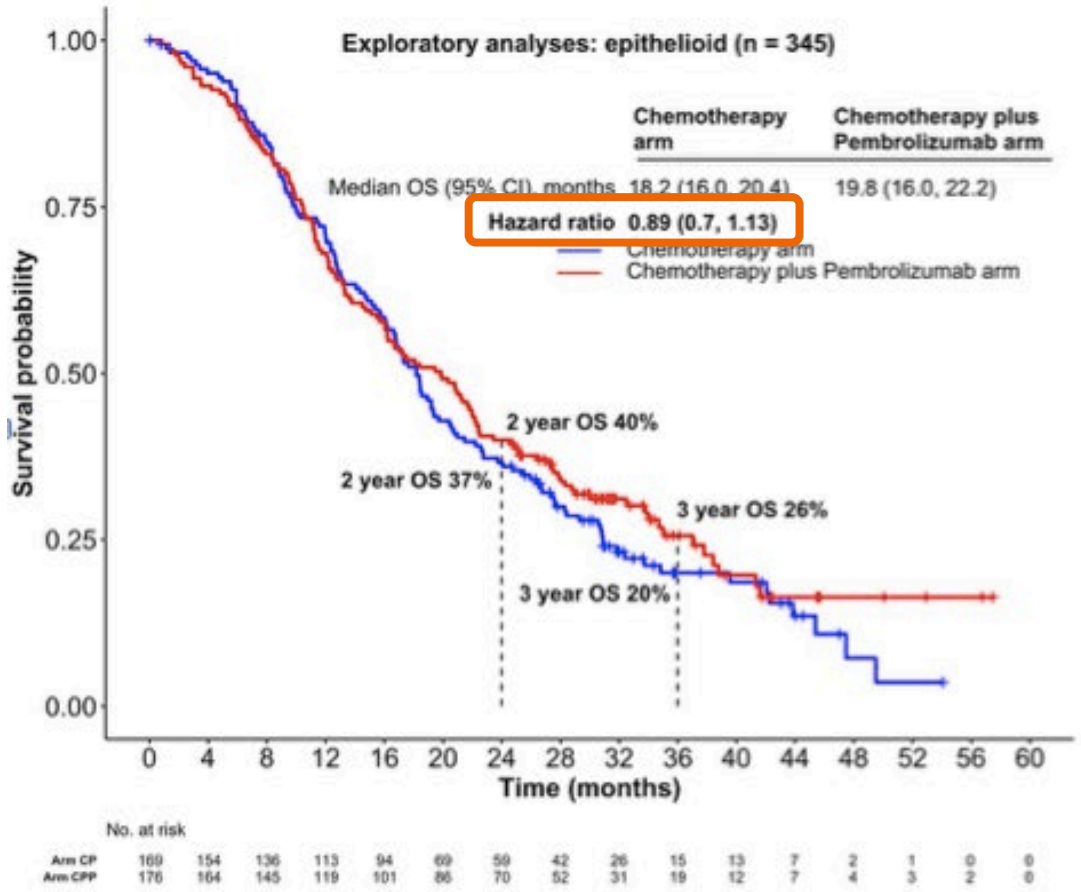
Etude positive sur son objectif principal

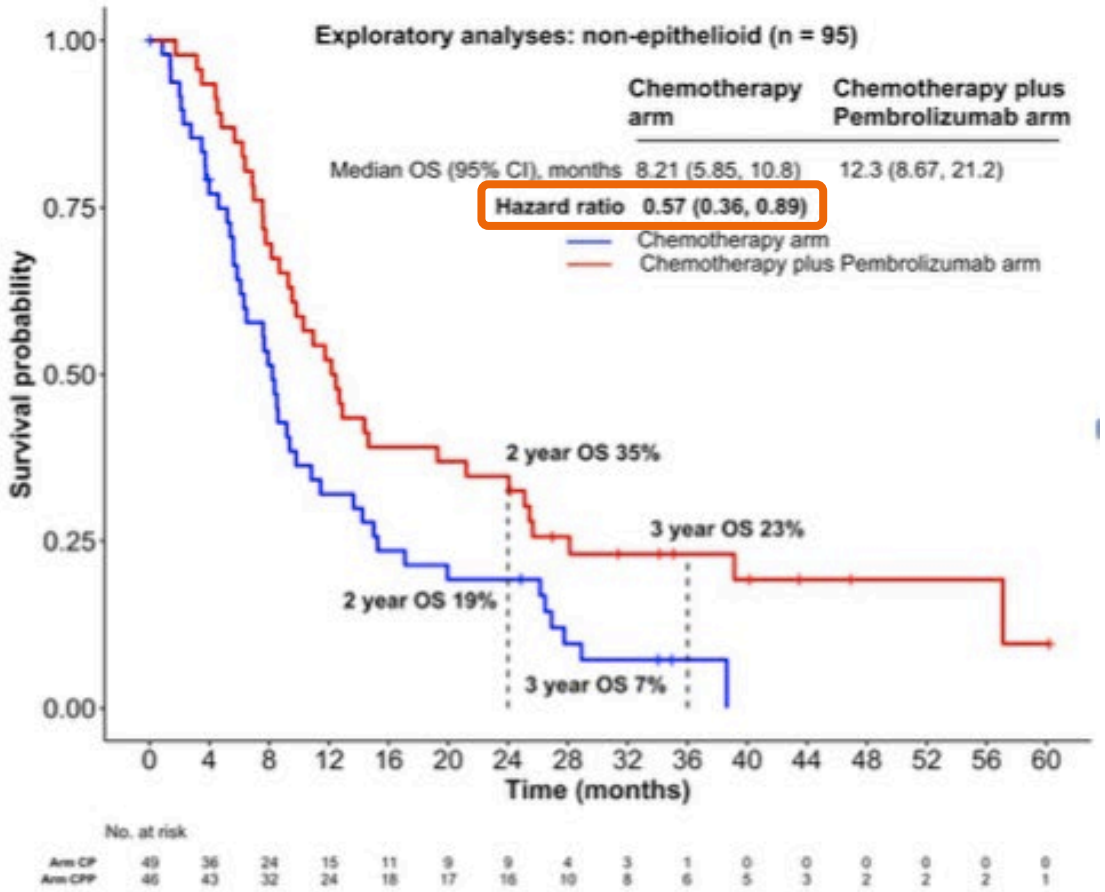


Analyse de sous groupe



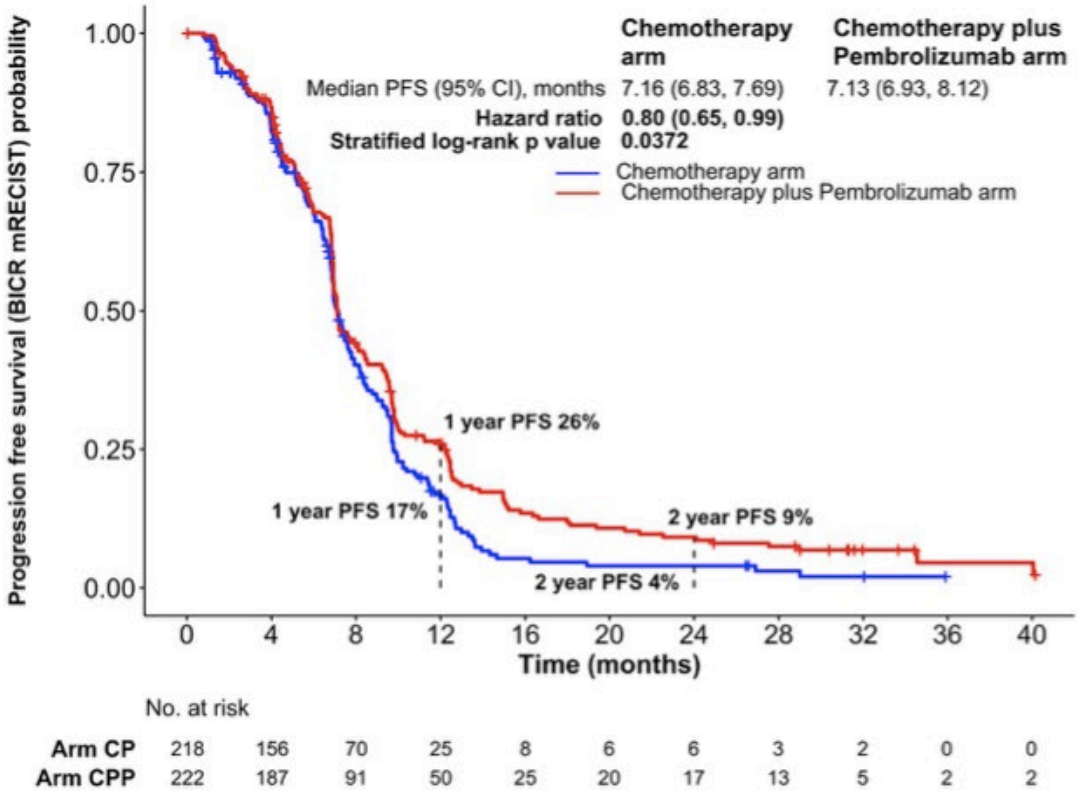
Bénéfice seulement chez les non épithélioïdes





Autres résultats:

PFS:



Données de réponse objective:

Response		CP (N=218)	CPP (N=222)	P-value
Complete Response		0	2 (1%)	P< 0.0001
Partial Response		83 (38%)	136 (61%)	
Stable disease/non-CR/PD		103 (47%)	70 (32%)	
Disease Progression		11 (5%)	9 (4%)	
Response could not be assigned	Total	21 (10%)	5 (2%)	
	Never treated/WOC[1]	7 (3%)	0	
	Other reasons[2]	9 (4%)	3 (1%)	
	No baseline images uploaded	5 (2%)	2 (1%)	
Duration of CR/PR (mths)	Median (95% CI)	5.5m (4.2-6)	5.8m (5.5-7)	P=0.185
	Range	0.03, 25.1	0.03, 38.9	

Pas de nouveau signal de toxicité

Adverse Event	CP (n = 211)			CPP (n = 222)		
	Grade[2] 1-2	Grade 3	Grade 4 [3]	Grade 1-2	Grade 3	Grade 4[3]
Any	141 (67%)	31 (15%)	1(<1%)	138 (65%)	50 (23%)	10 (5%)
Nausea	93 (44%)	2 (1%)	0	99 (45%)	10 (5%)	0
Fatigue	100 (47%)	12 (6%)	0	97 (44%)	15 (7%)	0
Diarrhea	**18 (9%)**	**3(1%)**	**0**	**48 (22%)**	**3 (1%)**	**0**
Mucositis oral	32 (15%)	2 (1%)	0	42 (19%)	0	0
Vomiting	29 (14%)	2 (1%)	0	40 (18%)	3 (1%)	0
Anorexia	36 (17%)	2 (1%)	0	38 (17%)	0	0
Constipation	27 (13%)	0	0	36 (16%)	0	0
Pruritus	**7 (3%)**	**0**	**0**	**33 (15%)**	**0**	**0**
Rash maculo-papular	**14 (7%)**	**1 (<1%)**	**0**	**28 (13%)**	**2 (1%)**	**0**
Dysgeusia	27 (13%)	0	0	26 (12%)	0	0
Watering eyes	14 (7%)	0	0	26 (12%)	0	0
Peripheral sensory neuropathy	17 (8%)	0	0	24 (11%)	0	0
Anemia	0	0	0	0	4 (2%)	1 (<1%)
Febrile neutropenia	**0**	**2 (1%)**	**0**	**0**	**8 (4%)**	**3 (1%)**

Brèves

- Etude NeoTORCH: bénéfice en terme d'EFS, mPR, cPR de l'ajout du toripalimab avec chimio à base de platine versus chimio seule suivi d'une maintenance dans les CBNPC stade III résecables

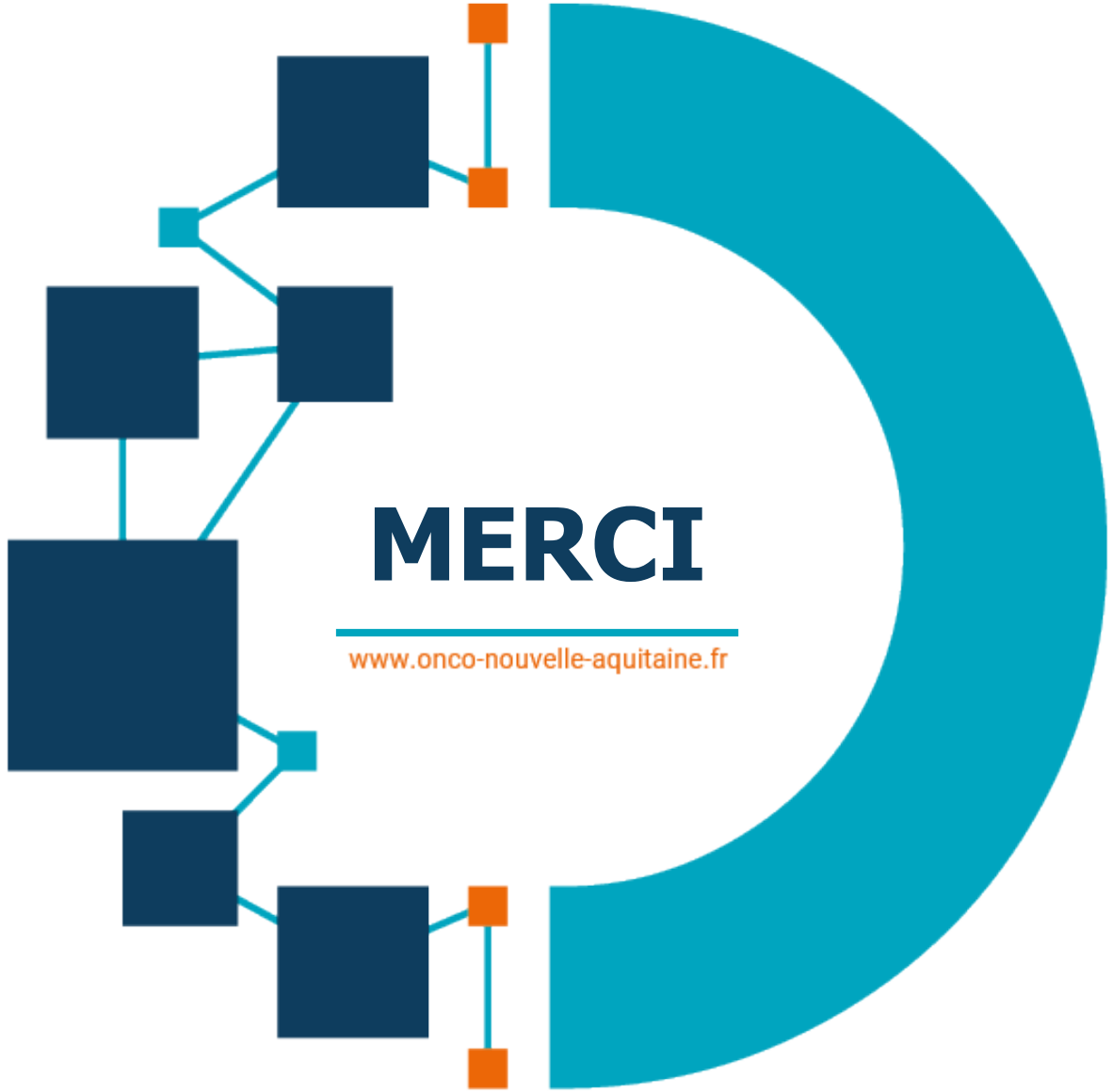
- Keynote-789: Pas de bénéfice à l'ajout du Pembrolizumab à une chimiothérapie à base de platine dans les CBNPC, EGFR muté, TKI résistants

En conclusion

- Confirmation d'un changement de pratique: chimiothérapie+ IO pré opératoire dans le CBNPC, mais quid de la place de l'IO adjuvante?

- Première étude avec un bénéfice en survie globale en adjuvant d'un TKI (Osimertinib): Etude ADAURA

- Combo chimiothérapie + Pembrolizumab dans le mésothéliome en première ligne: Quelle place par rapport au Nivo+ Ipi?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www.onco-nouvelle-aquitaine.fr