Lung Cancer UPDATES
ASCO HIGHLIGTHS
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Chicago, USA

Iniciativa científica de:
GECP
lung cancer research

Cáncer de pulmón no microcítico: Enfermedad Precoz

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Iniciativa científica de: GECP lung cancer research

CPNM: Contexto **adyuvante**

LBA3: 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, Masahiro Tsuboi, Tom John, Terufumi Kato, Margarita Majem, Christian Grohé, Jie Wang, Jonathan W. Goldman, Shun Lu, Wu-Chou Su, Filippo de Marinis, Frances A. Shepherd, Ki Hyeong Lee, Nhieu Le, Arunee Dechaphunkul, Dariusz M. Kowalski, Lynne Poole, Marta Stachowiak, Yuri Rukazenkov, Yi-Long Wu

ADAURA Phase III study design

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

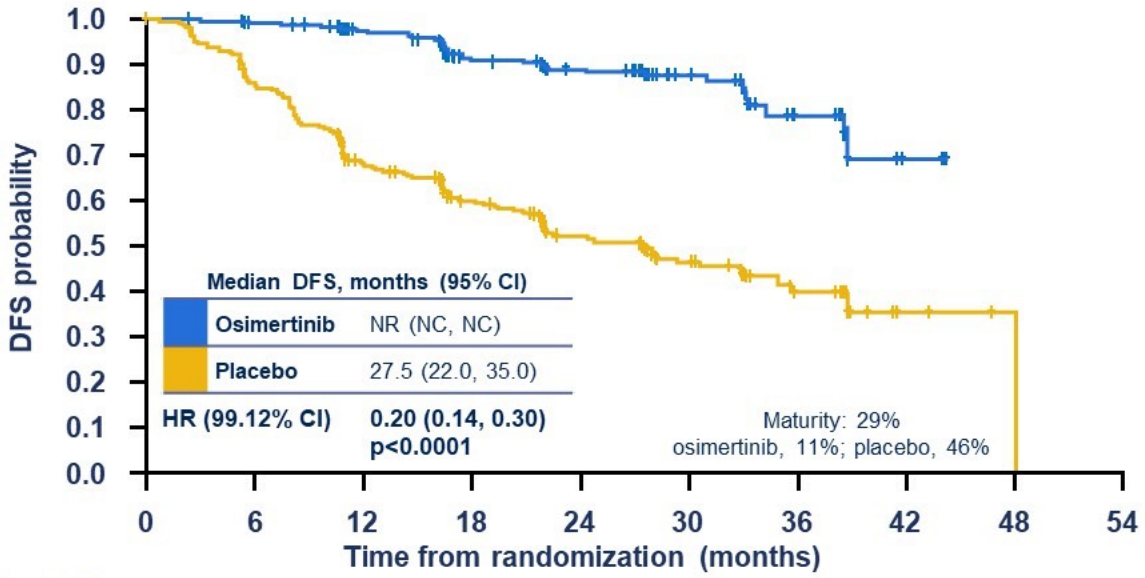
Endpoints
- **Primary endpoint:** DFS by investigator assessment in stage II–IIIA patients
- **Key secondary endpoints:** DFS in the overall population (stage IB–IIIA), landmark DFS rates, OS, safety, health-related quality of life

Adjuvant osimertinib has significantly improved DFS

- Adjuvant osimertinib demonstrated highly statistically significant[1,2] and clinically meaningful improvement in DFS in completely resected EGFRm NSCLC vs placebo in both the primary (stage II–IIIA) and overall (IB–IIIA) populations, along with a tolerable safety profile[1–4]

ADAURA primary DFS analysis[1,2] (stage IB–IIIA)*

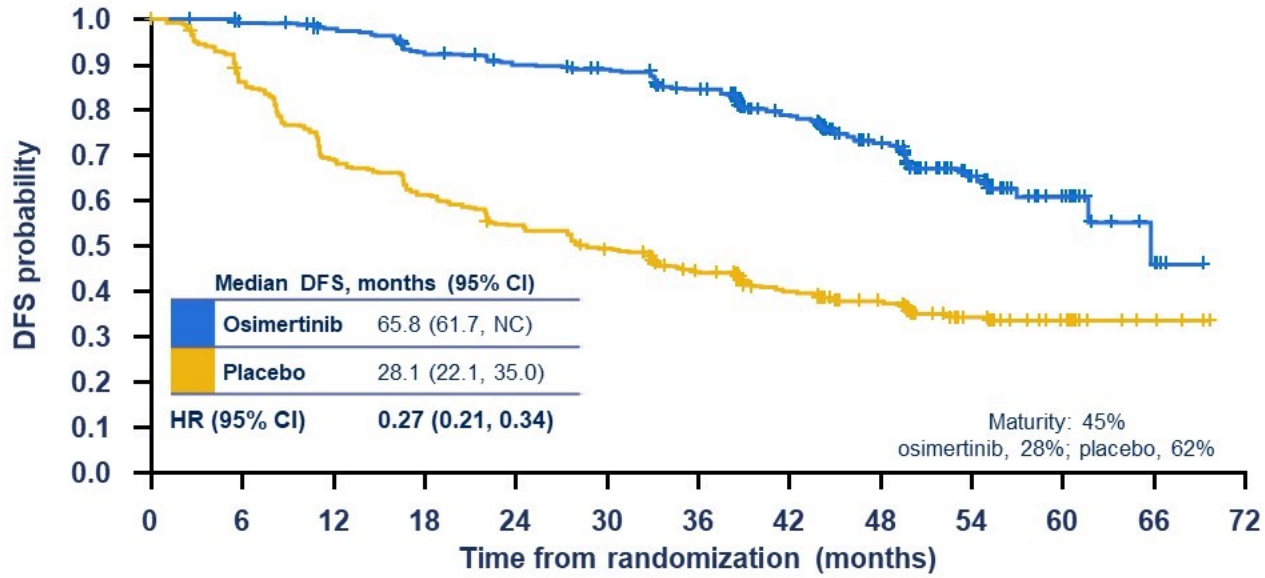
NEJM October 2020



No. at risk										
Osimertinib	339	313	272	208	138	74	27	5	0	-
Placebo	343	287	207	148	88	53	20	3	1	0

ADAURA updated DFS analysis[3,4] (stage IB–IIIA)†

JCO January 2023



No. at risk													
Osimertinib	339	316	307	289	278	270	249	201	139	73	33	5	0
Placebo	343	288	230	205	181	162	137	115	84	48	25	4	0

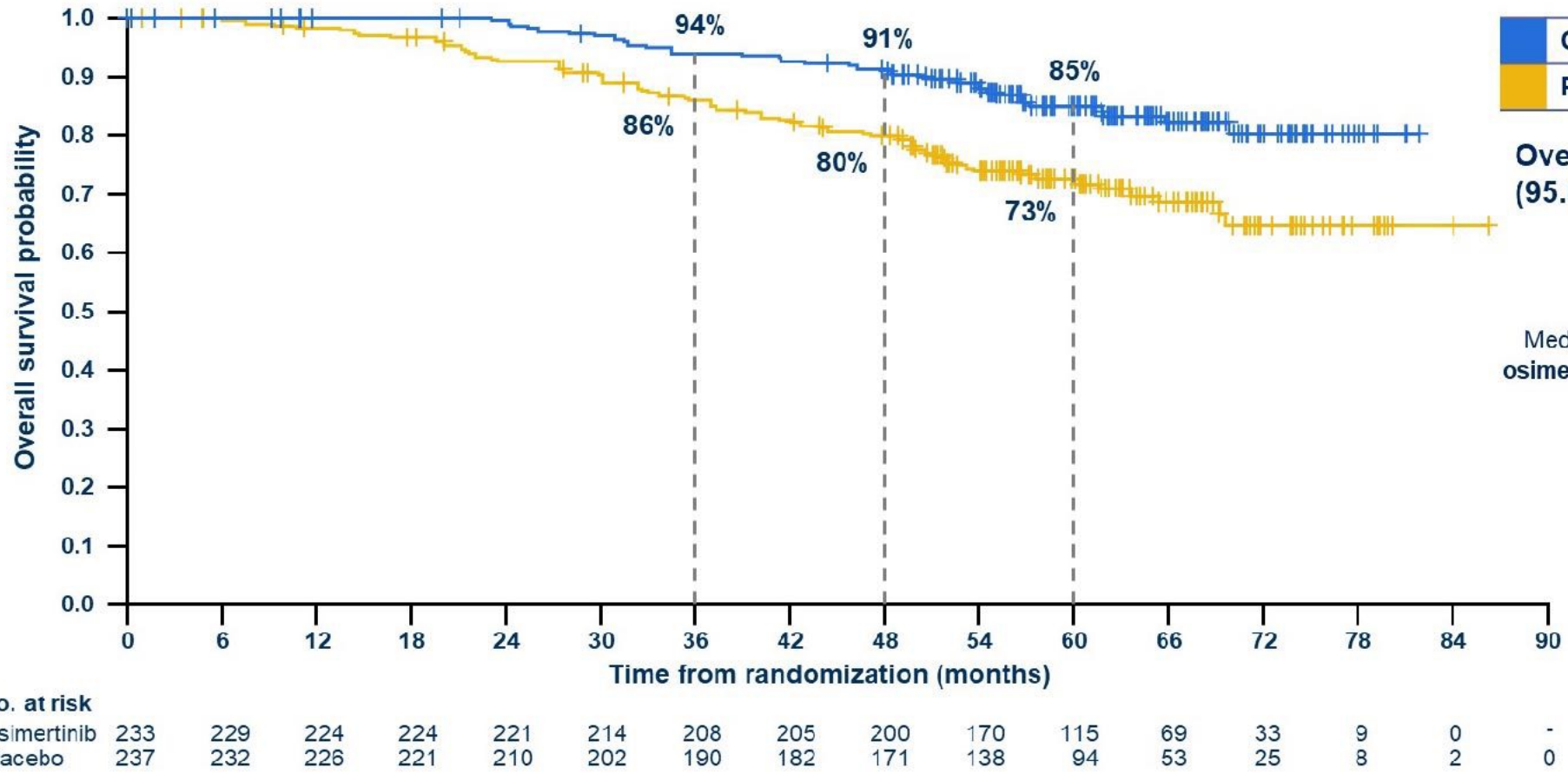
*Data cut-off: January 17, 2020. †Data cut-off: April 11, 2022.

1. Wu et al. N Engl J Med 2020;383:1711–1723; 2. Herbst et al. J Clin Oncol 2020;38(Suppl 18): abstract / oral LBA5; 3. Herbst et al. J Clin Oncol 2023;41:1830–1840; 4. Tsuboi et al. Ann Oncol 2022;33(Suppl 7): abstract / oral LBA47.

CI, confidence interval; DFS, disease-free survival; EGFRm, epidermal growth factor receptor-mutated; HR, hazard ratio; NC, not calculable; NR, not reached; NSCLC, non-small cell lung cancer

Overall survival: patients with stage II / IIIA disease

- Adjuvant osimertinib demonstrated a statistically and clinically significant improvement in OS vs placebo in the primary population of stage II–IIIA disease



No. at risk																
Osimertinib	233	229	224	224	221	214	208	205	200	170	115	69	33	9	0	-
Placebo	237	232	226	221	210	202	190	182	171	138	94	53	25	8	2	0

5-year OS rate, % (95% CI)	
Osimertinib (n=233)	85 (79, 89)
Placebo (n=237)	73 (66, 78)

Overall OS HR (95.03% CI) **0.49 (0.33, 0.73); p=0.0004**

Maturity: 21%
osimertinib 15%, placebo 27%

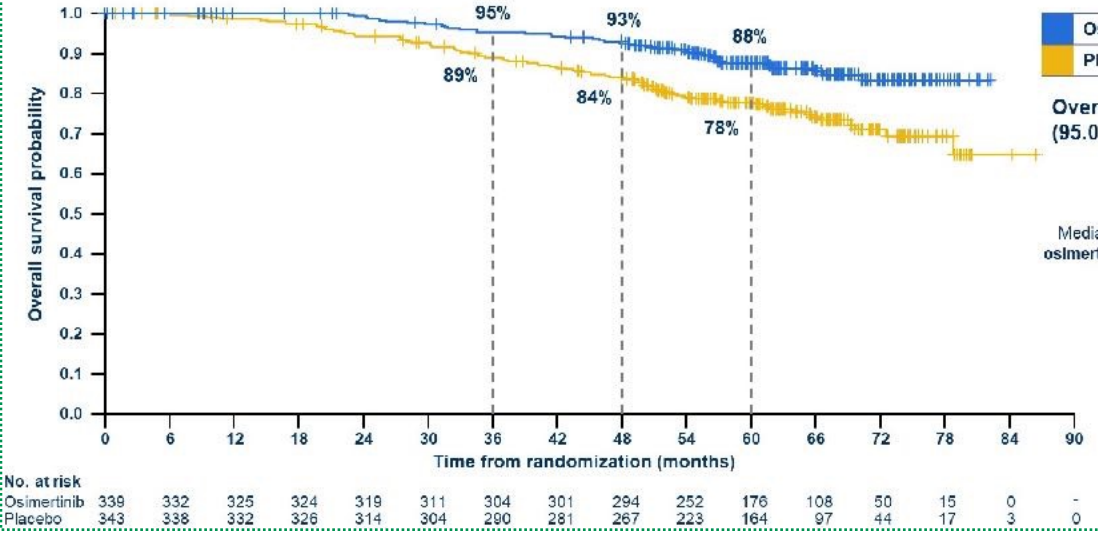
Median follow-up for OS* (censored patients):
osimertinib 61.7 months, placebo 60.4 months

Data cut-off: January 27, 2023.
Tick marks indicate censored data. Alpha allocation of 0.0497. *Median follow-up for OS (all patients): osimertinib 59.9 months, placebo 56.2 months.

CI, confidence interval; HR, hazard ratio; OS, overall survival

Overall survival: patients with stage IB / II / IIIA disease

- Adjuvant osimertinib demonstrated a statistically and clinically significant improvement in OS vs placebo in the overall population of stage IB–IIIA disease



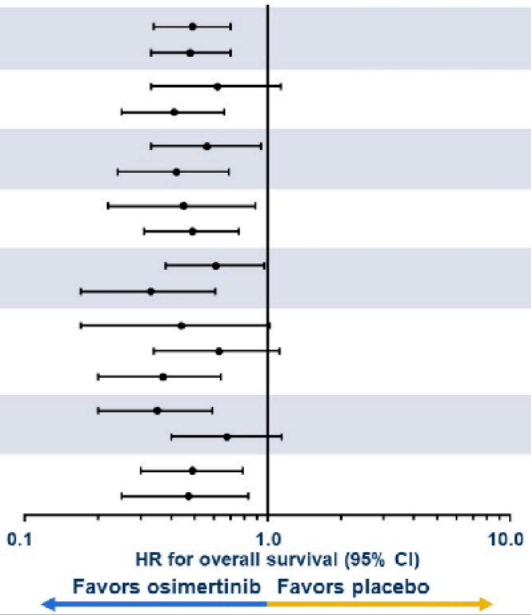
5-year OS rate, % (95% CI)	
Osimertinib (n=339)	88 (83, 91)
Placebo (n=343)	78 (73, 82)

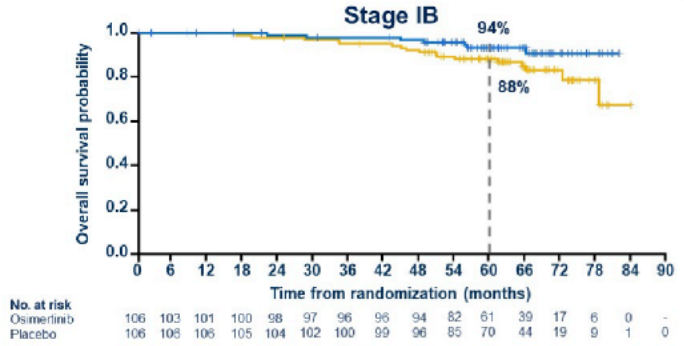
Overall OS HR (95.03% CI) 0.49 (0.34, 0.70); p<0.0001

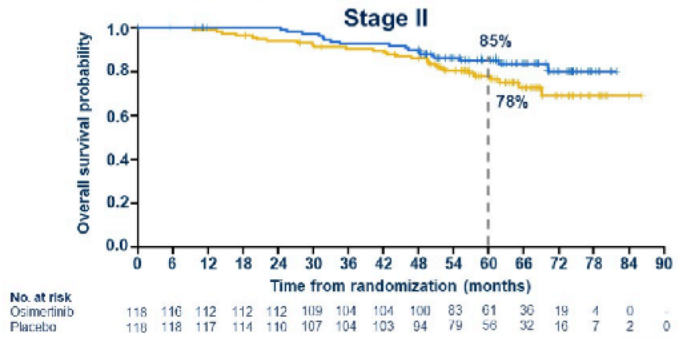
Maturity: 18%
osimertinib 12%, placebo 24%

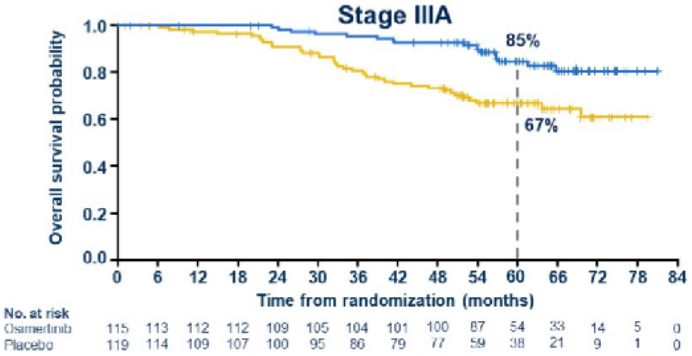
Median follow-up for OS* (censored patients):
osimertinib 61.5 months, placebo 61.5 months

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

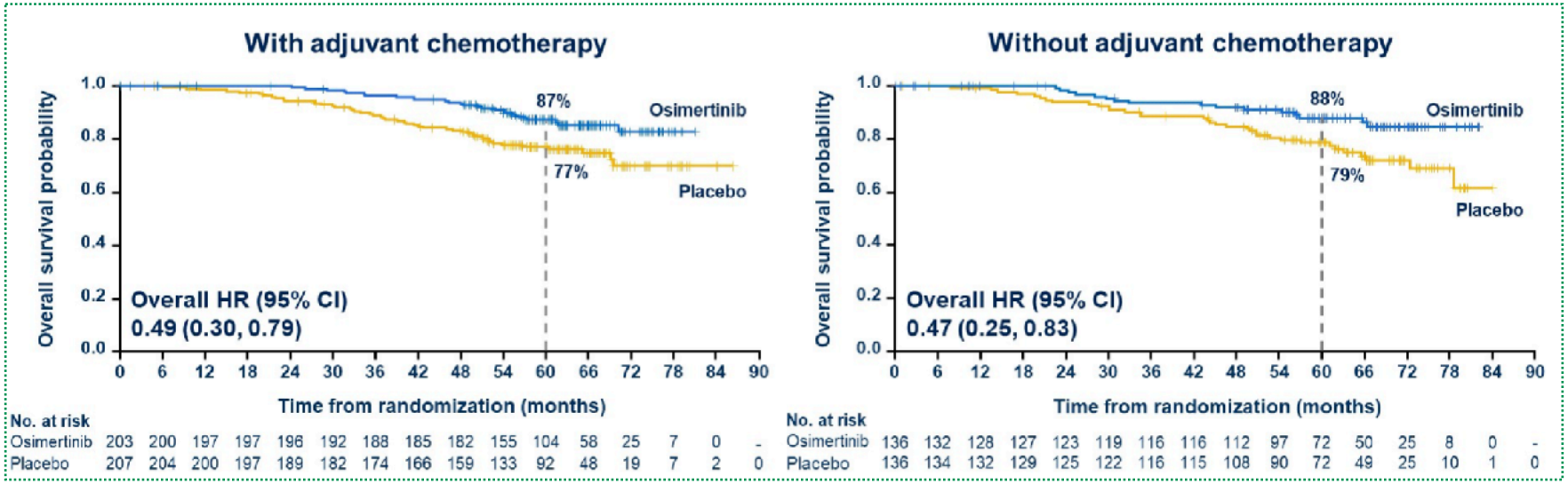








5 year OS rate, % (95% CI)	Stage IB	Stage II	Stage IIIA
Osimertinib	94 (86, 97)	85 (77, 91)	85 (76, 91)
Placebo	88 (80, 93)	78 (69, 85)	67 (57, 75)
Overall HR (95% CI)	0.44 (0.17, 1.02)	0.63 (0.34, 1.12)	0.37 (0.20, 0.64)



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)

AE, any cause*, n (%)	Osimertinib (n=337)	Placebo (n=343)
Any AE	330 (98)	309 (90)
Any AE Grade ≥3	79 (23)	48 (14)
Any AE leading to death	1 (<1)	2 (1)
Any serious AE	68 (20)	47 (14)
Any AE leading to discontinuation	43 (13)	9 (3)
Any AE leading to dose reduction	42 (12)	3 (1)
Any AE leading to dose interruption	91 (27)	43 (13)
AE, possibly causally related*†, n (%)		
Any AE	308 (91)	199 (58)
Any AE Grade ≥3	36 (11)	7 (2)
Any AE leading to death	0	0
Any serious AE	10 (3)	2 (1)

ADAURA is the first global Phase III study to demonstrate statistically significant and clinically meaningful OS benefit with targeted treatment in this patient population, reinforcing adjuvant osimertinib as the standard of care for patients with resected EGFRm stage IB-IIIA NSCLC

Iniciativa científica de: GECP lung cancer research

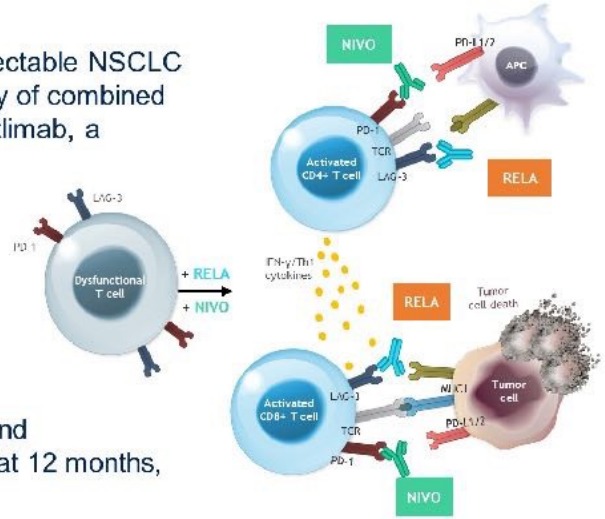
CPNM: Contexto **neoadyuvante**

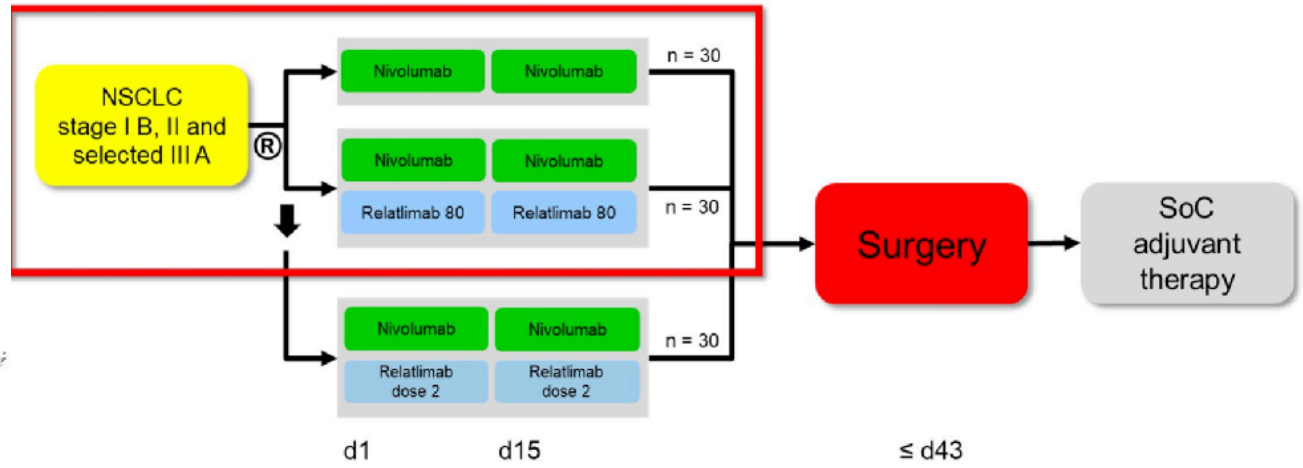
#8500: Surgical outcomes of patients with resectable non-small-cell lung cancer receiving neoadjuvant immunotherapy with nivolumab plus relatlimab or nivolumab: Findings from the prospective, randomized, multicentric phase II study NEOpredict-Lung

Clemens Aigner, Bert Du Pont, Koen Hartemink, Marcel Wiesweg, Michel Vanbockrijck, Kaid Darwiche, Balazs Hegedus, Alexander Schramm, Hubertus Hautzel, Brigitte Maes, Dirk Theegarten, Hans-Ulrich Schildhaus, Paul Baas, Kristof Cuppens, Martin H. Schuler, Till Plönes

Study design

- Randomized phase II study in patients with resectable NSCLC exploring the feasibility, safety and early efficacy of combined preoperative treatment with nivolumab and relatlimab, a monoclonal antibody targeting LAG-3
- Reference arm with nivolumab monotherapy
- Primary study endpoint: Feasibility of curatively intended surgery within 43 days (continuously assessed)
- Secondary endpoints (selected): Radiological and histopathological response rates, DFS and OS at 12 months, safety, R0 resection rate





Características basales

	Nivolumab (240 mg)	Nivolumab (240 mg)/Relatlimab (80 mg)
n (female, male)	30 (15, 15)	30 (13, 17)
Age (median, range)	65 (43-78) years	67 (44-81) years
Histology		
▪ Adenocarcinoma	13	15
▪ Squamous cell carcinoma	10	9
▪ Adenosquamous	2	2
▪ Other	5	4
UICC stage (8th edition)		
▪ I B	9	10
▪ II A	6	1
▪ II B	11	16
▪ III A	3	3
▪ III B	1	0
PD-L1 status [TPS]		
▪ < 1%	6	8
▪ 1-49%	14	15
▪ ≥ 50%	10	7

	Nivolumab (240 mg)	Nivolumab (240 mg)/Relatlimab (80 mg)
Central tumor location	50%	45%
R0 resection	n=57 (unexpected pleural carcinosis n=2, R1 n=1) 95% ITT 98.3% curatively resected population	
Resection		
• Lobectomy	23	24
• Bilobectomy	2	1
• Sleeve lobectomy	5	4
• Lobectomy + Segmentectomy	0	1
▪ VATS	60%	63.3%
▪ Thoracotomy	40%	36.6%
▪ Conversion	n=3	n=2

Abordaje quirúrgico

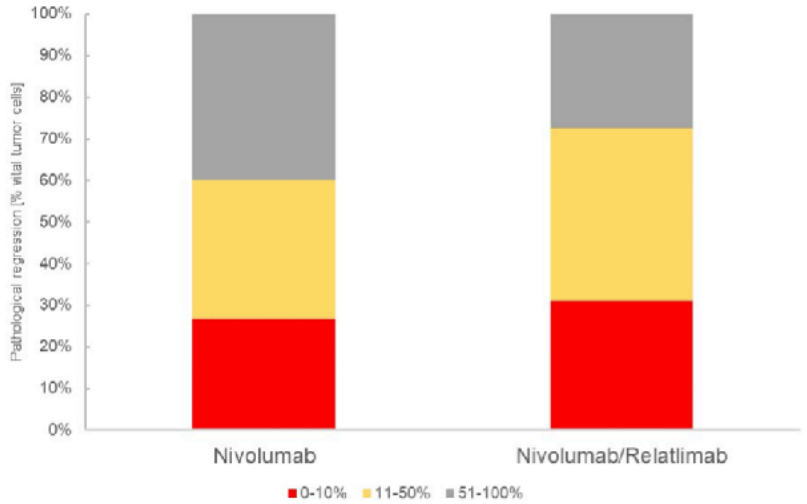
Complicaciones perioperatorias

Complication	Nivolumab (240 mg)	Nivolumab (240 mg)/Relatlimab (80 mg)
Intraoperative	1 (3%) - conversion due to bleeding	1 (3%) - conversion due to bleeding
Revision	2 (7%) - empyema, PAL	1 (3%) - middle lobe torsion
Pulmonary embolism	1 (3%)	0
Atrial fibrillation	3 (10%)	0
Prolonged air leak	1 (3%)	3 (10%)
Chest wall hematoma	0	1 (3%)
Middle lobe atelectasis	0	1 (3%)
Pleural effusion	1 (3%)	1 (3%)
Stridor	1 (3%)	0
Pneumothorax	1 (3%)	0
Atelectasis	0	1 (3%)

Efectos adversos IO

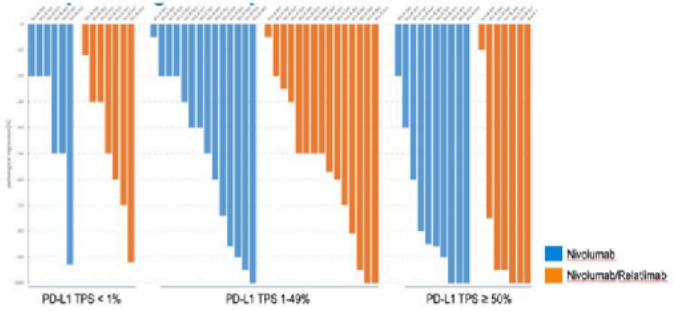
	Nivolumab (240 mg)		Nivolumab (240 mg)/ Relatlimab (80 mg)	
	all	grade ≥ 3	all	grade ≥ 3
Anemia	2 (7%)	-	-	-
Atrial fibrillation	1 (3%)	1 (3%)	-	-
Hyperthyroidism	5 (17%)	1 (3%)	4 (13%)	-
Hypothyroidism	2 (7%)	-	3 (10%)	-
Gastrointestinal	1 (3%)	-	2 (7%)	-
Hepatic	1 (3%)	1 (3%)	1 (3%)	1 (3%)
Proteinuria	1 (3%)	-	-	-
Pneumonitis	-	-	2 (7%)	-
Chills/fever	2 (3%)	-	-	-
Rash	1 (3%)	-	-	-

Respuesta histopatológica



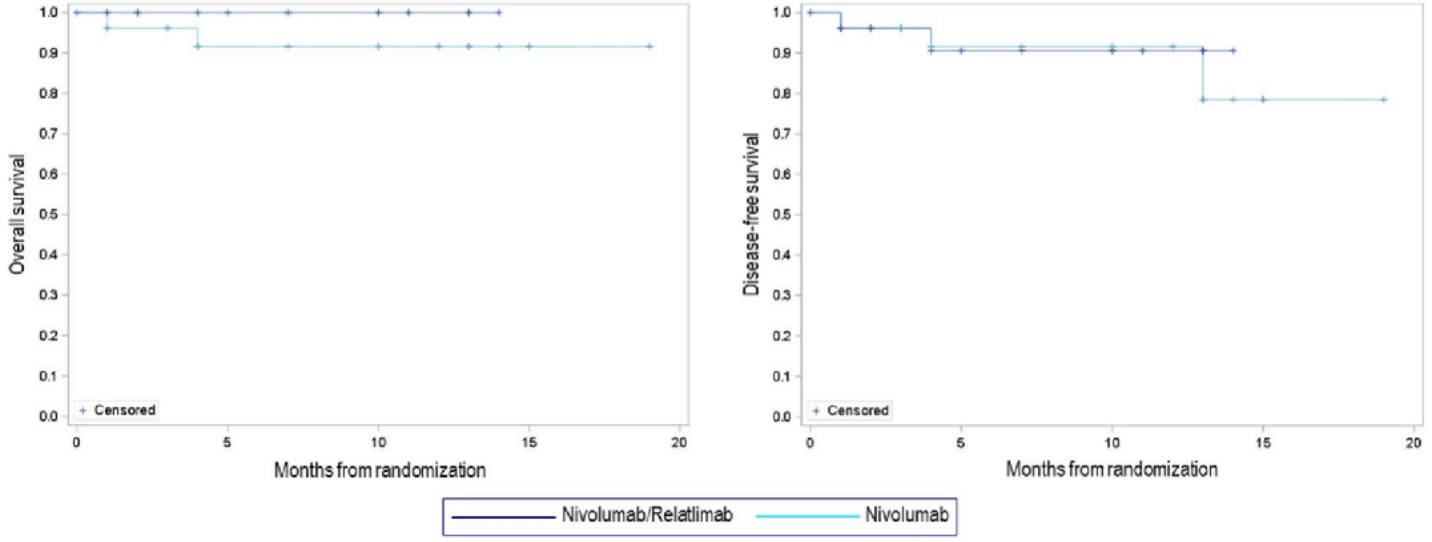
Protocol definition: Vital tumor cells

0-10%	major pathological response
11-50%	pathological response
51-100%	no pathological response



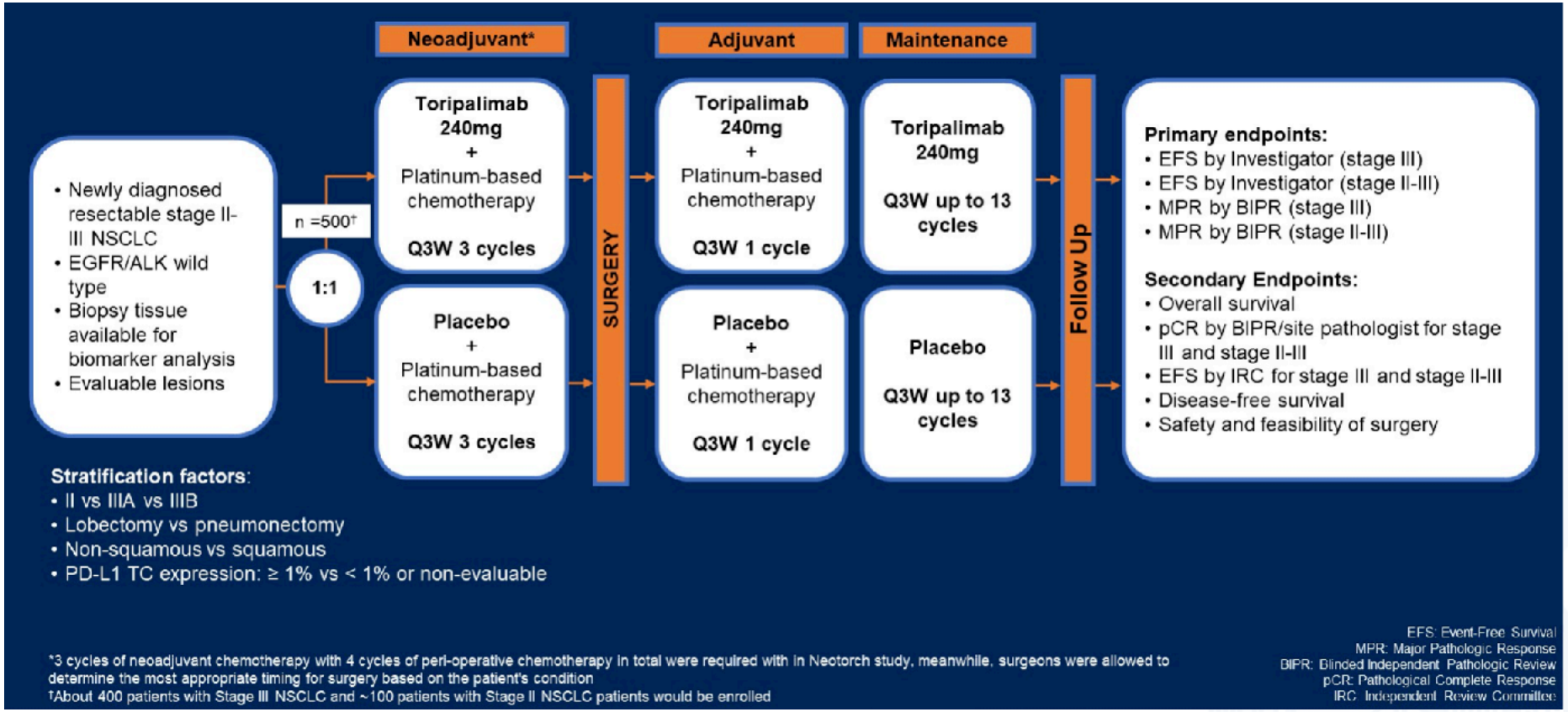
	pCR	MPR
Nivolumab	13.3%	27%
Nivolumab + Relatlimab	16.7%	30%

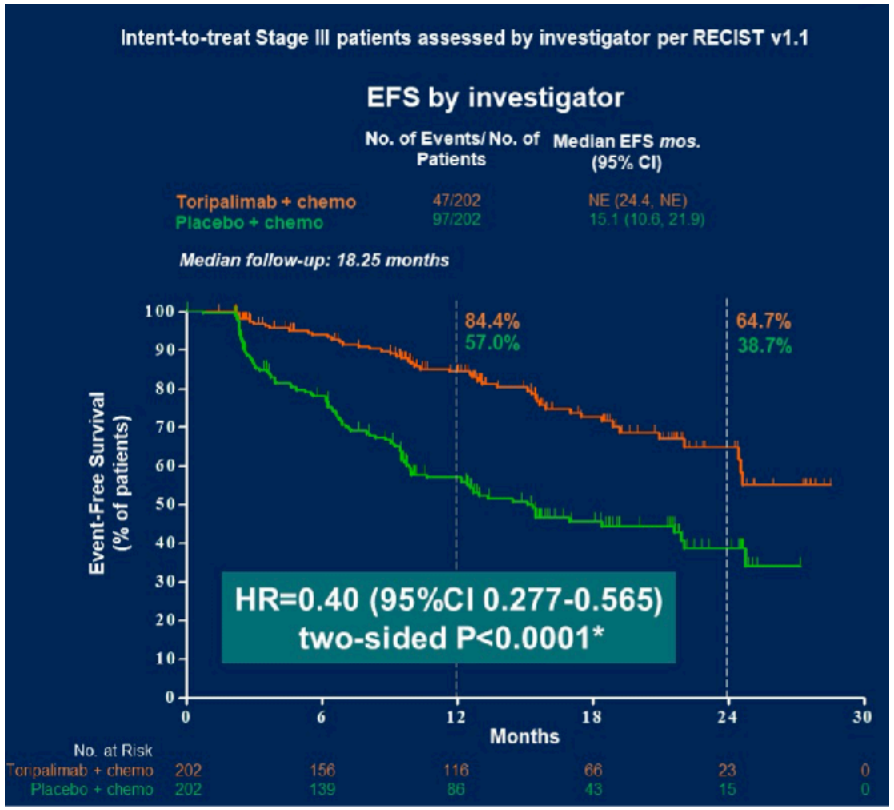
	Nivolumab (240 mg)	Nivolumab (240 mg)/Relatlimab (80 mg)
30 day mortality	0%	0%
Adjuvant therapy (guideline based according to pathological staging)	n=14	n=14
12 months OS	96 % (95% CI: 83-99%)	
12 months DFS	91% (95% CI: 78-97%)	

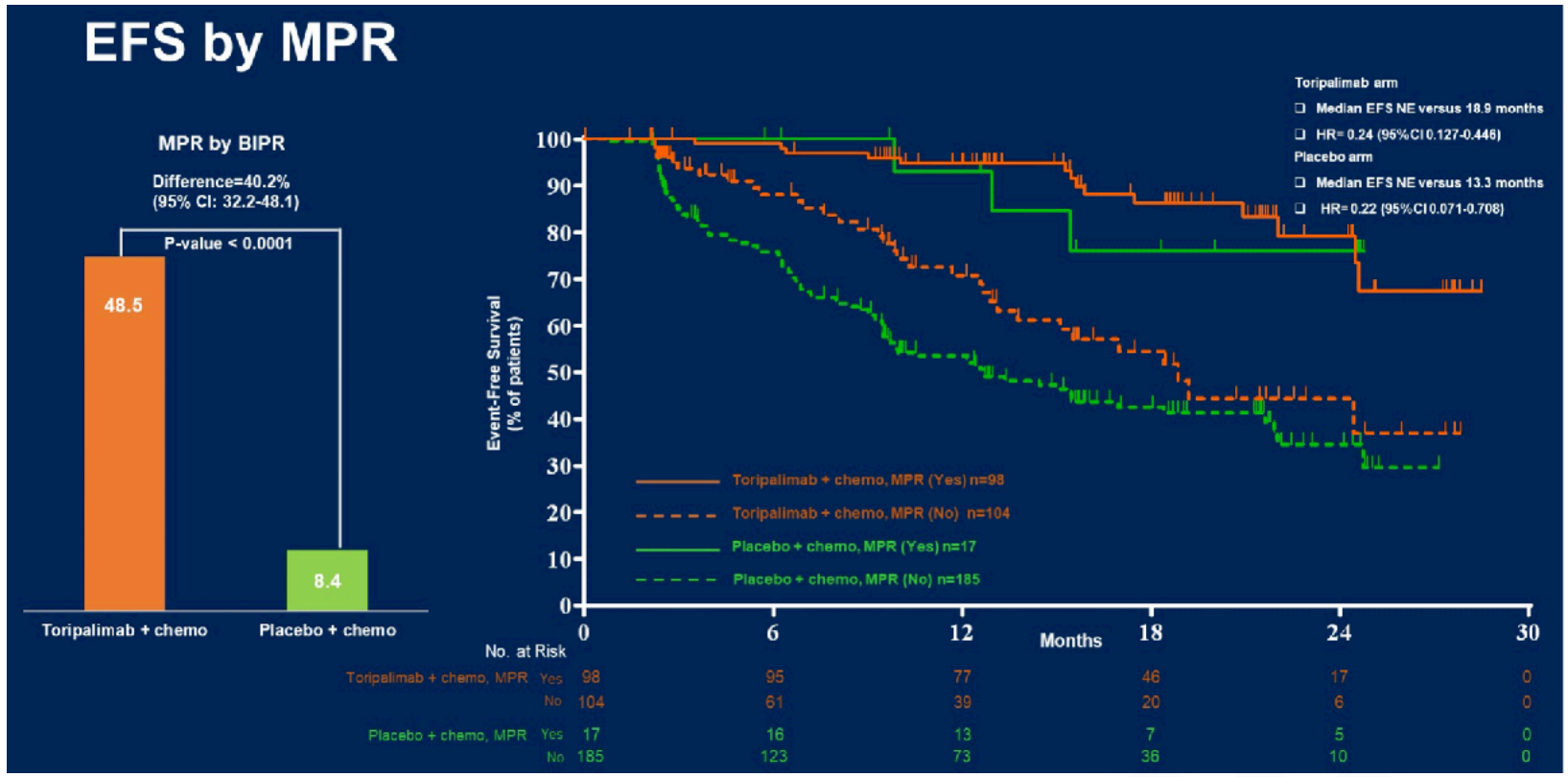


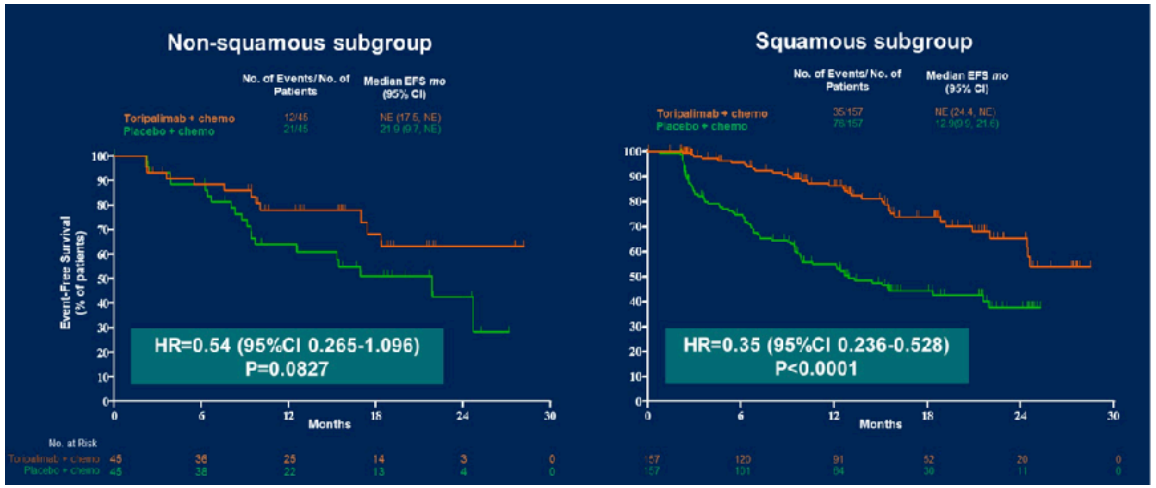
#8501: Perioperative toripalimab + platinum-doublet chemotherapy vs chemotherapy in resectable stage II/III non-small cell lung cancer (NSCLC): Interim event-free survival (EFS) analysis of the phase III NEOTORCH study

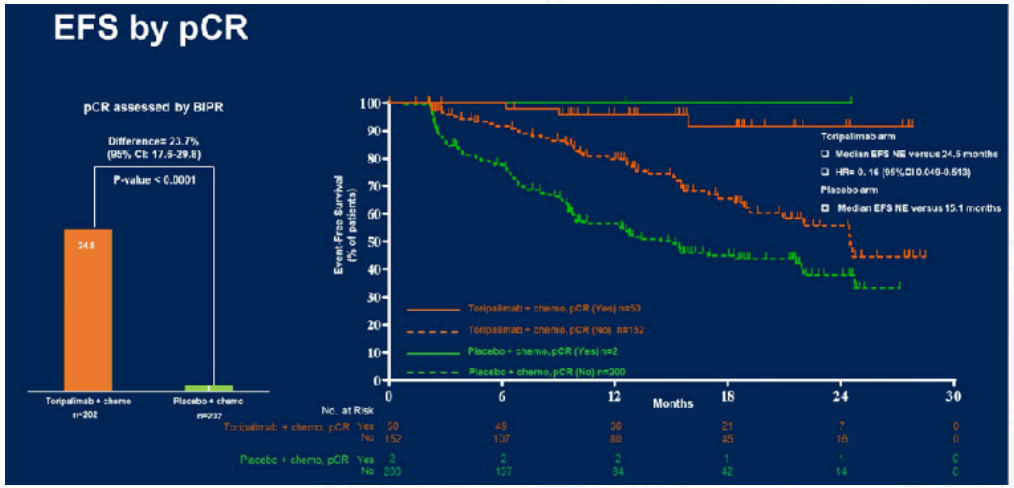
Shun Lu, Lin Wu, Wei Zhang, Peng Zhang, Wenxiang Wang, Wentao Fang, Wenqun Xing, Qixun Chen, Jiandong Mei, Lin Yang, Lijie Tan, Xiaohong Sun, Shidong Xu, Xiaohua Hu, Guohua Yu, Dongliang Yu, Jinlu Shan, Nong Yang, Yuping Chen, Hui Tian





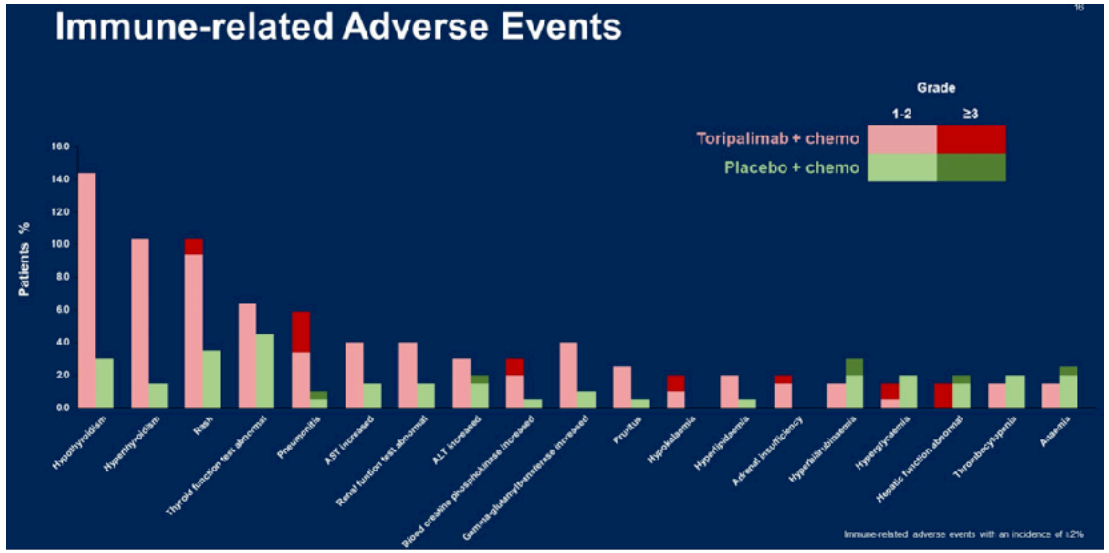






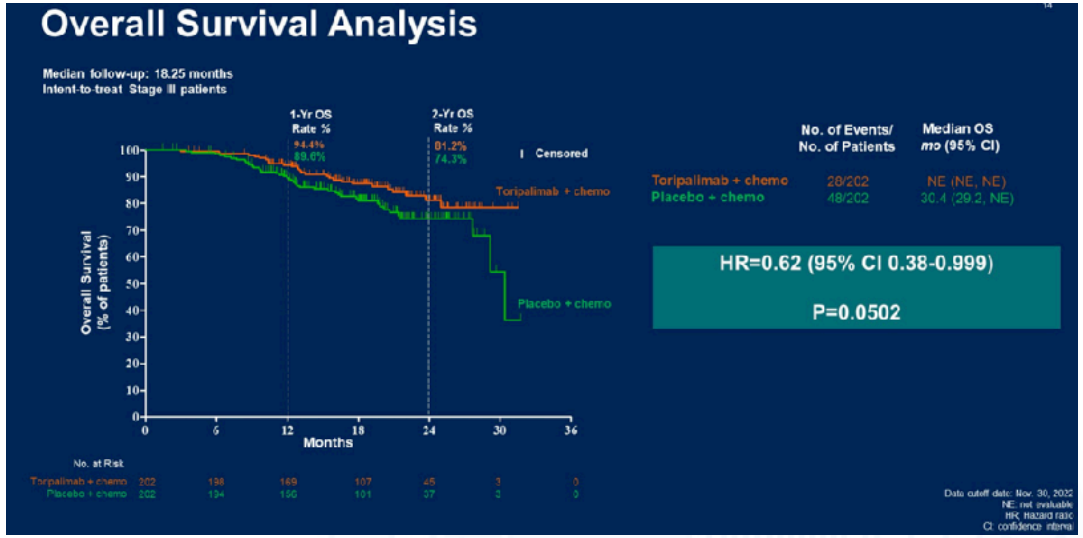
#8501: Perioperative toripalimab + platinum-doublet chemotherapy vs chemotherapy in resectable stage II/III non-small cell lung cancer (NSCLC): Interim event-free survival (EFS) analysis of the phase III NEOTORCH study

Adverse Event Category n (%)	Toripalimab + chemo n = 202	Placebo + chemo n = 202
Any TEAEs	201(99.5)	199 (98.5)
Any TEAEs Grade ≥3	128 (63.4)	109 (54.0)
Any SAEs	82 (40.6)	57 (28.2)
Any TEAEs leading to death Related to toripalimab/placebo	6 (3.0) 1(0.5)	4 (2.0) 0(0.0)
Any TEAEs leading to interruption of toripalimab/placebo	57 (28.2)	29 (14.4)
Any TEAEs leading to discontinuation of toripalimab/placebo	19 (9.4)	15 (7.4)
Any Investigator-determined irAEs	85 (42.1)	46 (22.8)
Grade ≥3 irAEs	24 (11.9)	6 (3.0)
Any infusion-related reactions	7 (3.5)	13 (6.4)



Surgery-related Postoperative Adverse Events

n (%)	Toripalimab + chemo n = 166	Placebo + chemo n = 148
Any AEs	124 (74.4%)	104 (70.3%)
Grade ≥3 AEs	36 (21.7%)	30 (20.3%)
Any AEs leading to discontinuation of toripalimab/placebo	3 (1.8%)	4 (2.7%)
Any AEs leading to interruption of toripalimab/placebo	11 (6.6%)	2 (1.4%)
Any AEs leading to Death	0	2 (1.4%)



The results from Neotorch study, as well as other studies, indicated that perioperative immunotherapy plus chemotherapy should be a standard of care for stage III NSCLC patients

#8509: Pembrolizumab and ramucirumab neoadjuvant therapy for PD-L1-positive stage IB-IIIA lung cancer (EAST ENERGY)

Keiju Aokage, Yoshihisa Shimada, Kiyotaka Yoh, Masashi Wakabayashi, Miki Fukutani, Hideki Furuya, Kotaro Nomura, Tomohiro Miyoshi, Kenta Tane, Joji Samejima, Shogo Kumagai, Shohei Koyama, Hiroyoshi Nishikawa, Tetsuro Taki, Takuo Hayashi, Jun Matsubayashi, Genichiro Ishii, Norihiko Ikeda, Masahiro Tsuboi

Iniciativa científica de: GECP lung cancer research

Trial Design: RAM+Pembro, neoadjuvant, single arm Phase II

SR-1224 / I4T-JE-O030 P.I. Tsuboi M.

Key eligibility criteria
- Resectable clinical stage IB-IIIA NSCLC (UICC/AJCC ver.8)
- Age ≥20
- ECOG PS 0-1
- PD-L1 ≥ 1% (22C3)
- Adequate organ function

Ramucirumab 10mg/kg
Pembrolizumab 200 mg
Q3W, 2cycles

→ **SURGERY** (lobectomy, bi-lobectomy, or pneumonectomy with LND)

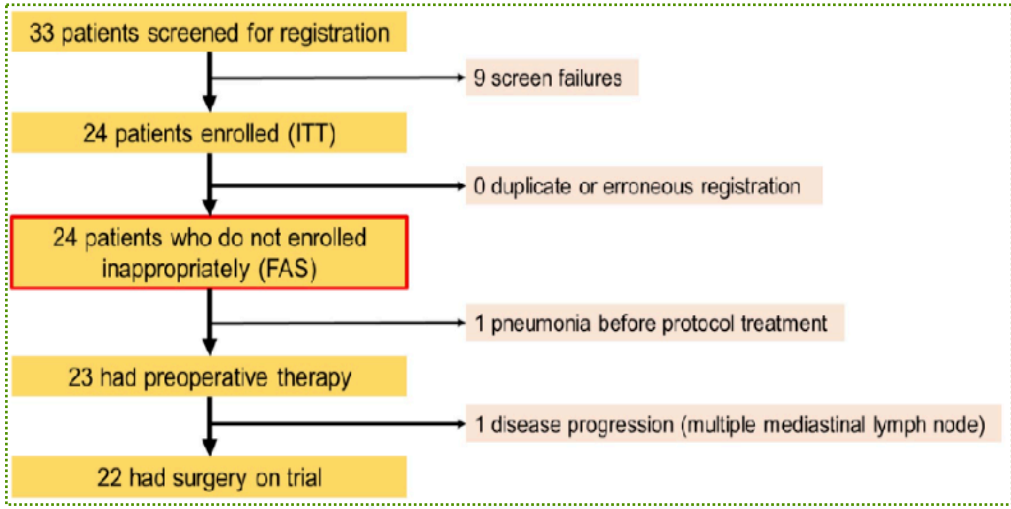
→ Optional therapy at physician's discretion

within 4 to 8 weeks after last dose

Trial design:
- **Phase:** 2
- **Design:** Single arm, open label
- **Enrollment duration:** 2.5 years
- **Primary Endpoint:** Major pathologic response (MPR) rate by blind independent central pathology review (BIPR)
- **Secondary Endpoint:** pCR rate, R0 rate, ORR, RFS, OS in the different PD-L1 status, toxicity and immunological change as TR

Statistical Consideration:
- Sample size: **24** (expected and threshold MPR rate of 45% and 20%, one-sided alpha error of 5% and power of 80%)
- If there are ≥ **9** patients with MPR (MPR rate ≥ 37.5%) among 24 patients the primary endpoint will be met.

Study locations
- National Cancer Center Hospital EAST
- Tokyo Medical University Hospital

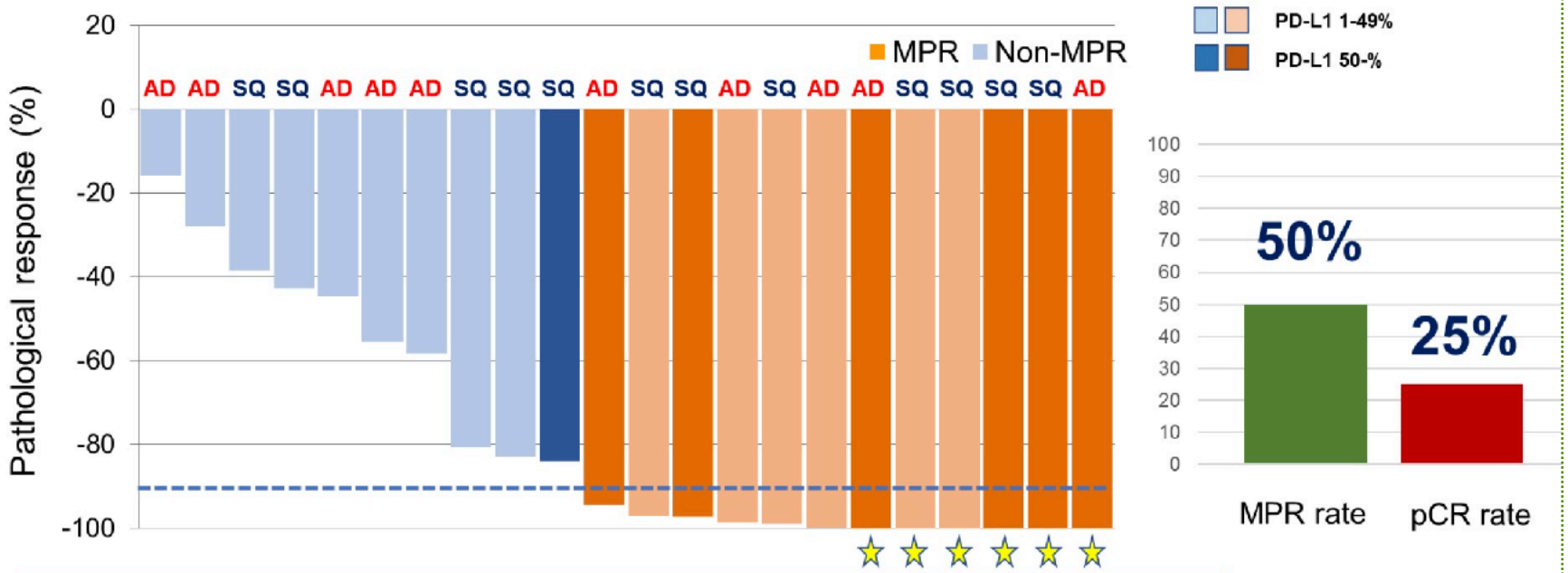


Characteristics	NSCLC, PD-L1 ≥ 1% FAS (N=24)
Age, median (range), y	75 (50-78)
Sex (M / F)	18 / 6
ECOG-PS 0 / 1	23 / 1
Current / former smoker / Never	1 / 18 / 5
Clinical stage IB / IIA / IIB /IIIA	1 / 4 / 9 / 10
Clinical N status N0 / N1/ N2	12 / 9 / 3
Pathological type (Sq / Ad)	12 / 12
PD-L1 status (22C3) 1-49% / ≥ 50%	15 / 9

Characteristics	NSCLC, PD-L1 ≥ 1% Operation (N=22)
Surgery	
segmentectomy / lobectomy / bi-lobectomy	1 / 20 / 1
Bronchoplasty	3 (13.6%)
R0 resection	21 (95.4%)
Pathological stage 0/IA /IB/IIA/IIB/IIIA/IIIB	4 / 8 / 2 / 2 / 3 / 2 / 1
Pathological N status N0/N1/N2/N3	17 / 3 / 1 /1

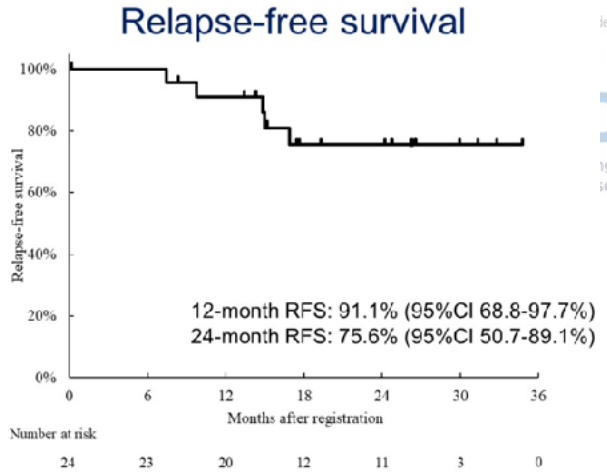
Resection rate	22/24 (91.7%)
Complete resection rate	21/24 (87.5%)

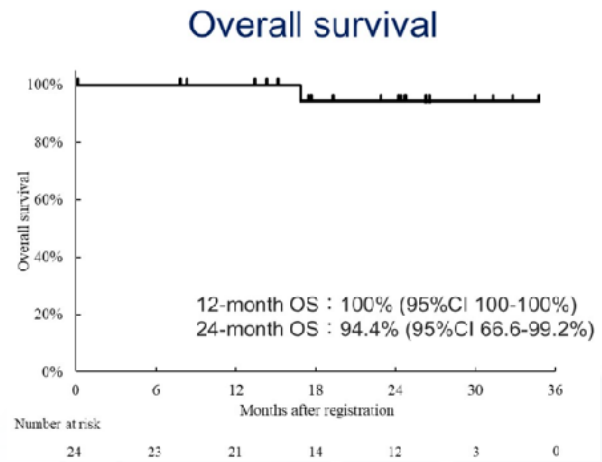
Results: Efficacy (FAS 24 cases including unresected 2 cases)



MPR rate: 12/24 = 50.0% (90%CI 31.9-68.1) (95%CI 29.1-70.9)

☆"Star" = pCR





Overall safety summary (n=23*)	TEAE	TRAE
All grade	23 / 23 (100%)	23 / 23 (100%)
Grade 3	8 / 23 (34.8%)	7 / 23 (30.4%)
Grade 4	0	0
Death related to AE (grade 5)	0	0
Serious AE	5 / 23 (21.7%)	5/ 23 (21.7%)
Patients who postponed or discontinued treatment due to AEs	2 / 23 (8.7%)**	2 / 23 (8.7%)**

A novel combination of ICIs and antiangiogenic agents as preoperative therapy was highly efficacious and well tolerated in PD-L1-positive resectable NSCLC

Conclusiones

Iniciativa científica de:
GECP
lung cancer research