Novedades y Claves en Cáncer de Pulmón 2022

Enfermedad localizada y localmente avanzada

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PHARMACEUTICAL COMPANIES OF Johnson&Johnson

Organizado por:

GECP lung cancer research

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CONTENIDO

A) Enfermedad localizada

B) Enfermedad localmente avanzada: potencialmente resecable e irresecable

C) Biomarcadores

Organizado por:

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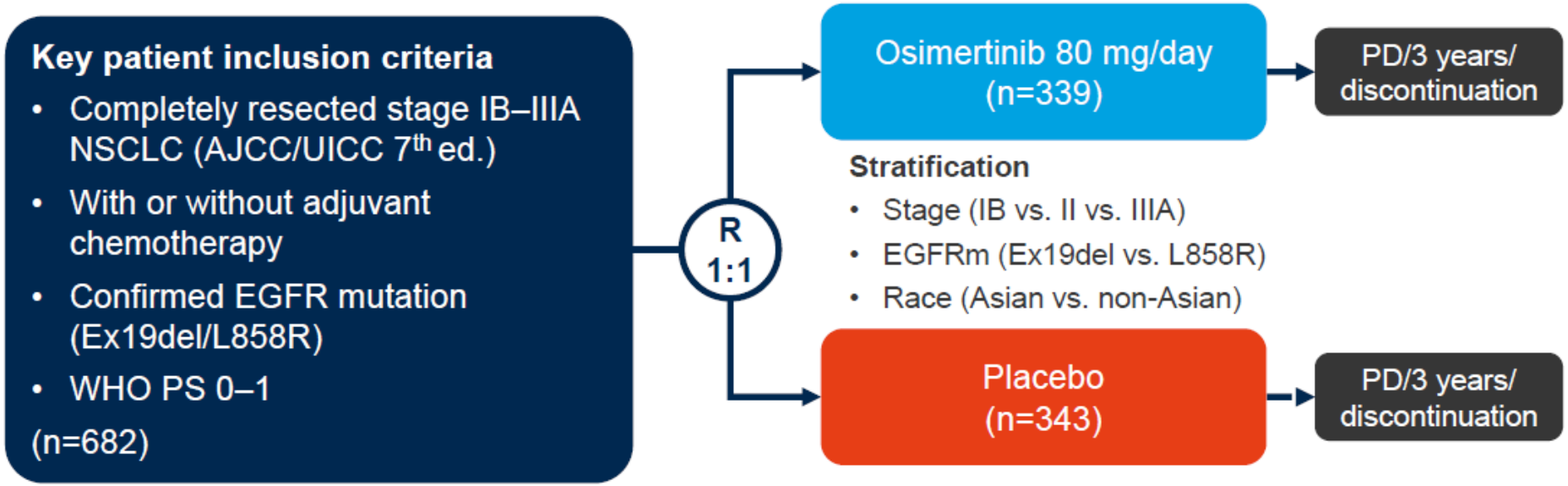
LBA47: Osimertinib as adjuvant therapy in patients with resected EGFR-mutated stage IB-IIIA non-small cell lung cancer: updated results from ADAURA

- **Study objective**
  - To evaluate the updated efficacy and safety of adjuvant osimertinib in patients with resected EGFR-mutated NSCLC in the ADAURA study



Primary endpoint

- DFS (in stage II/IIIA)

Secondary endpoints

- DFS (overall population[a]), OS, HRQoL, safety

[a]Stage IB, II and IIIA

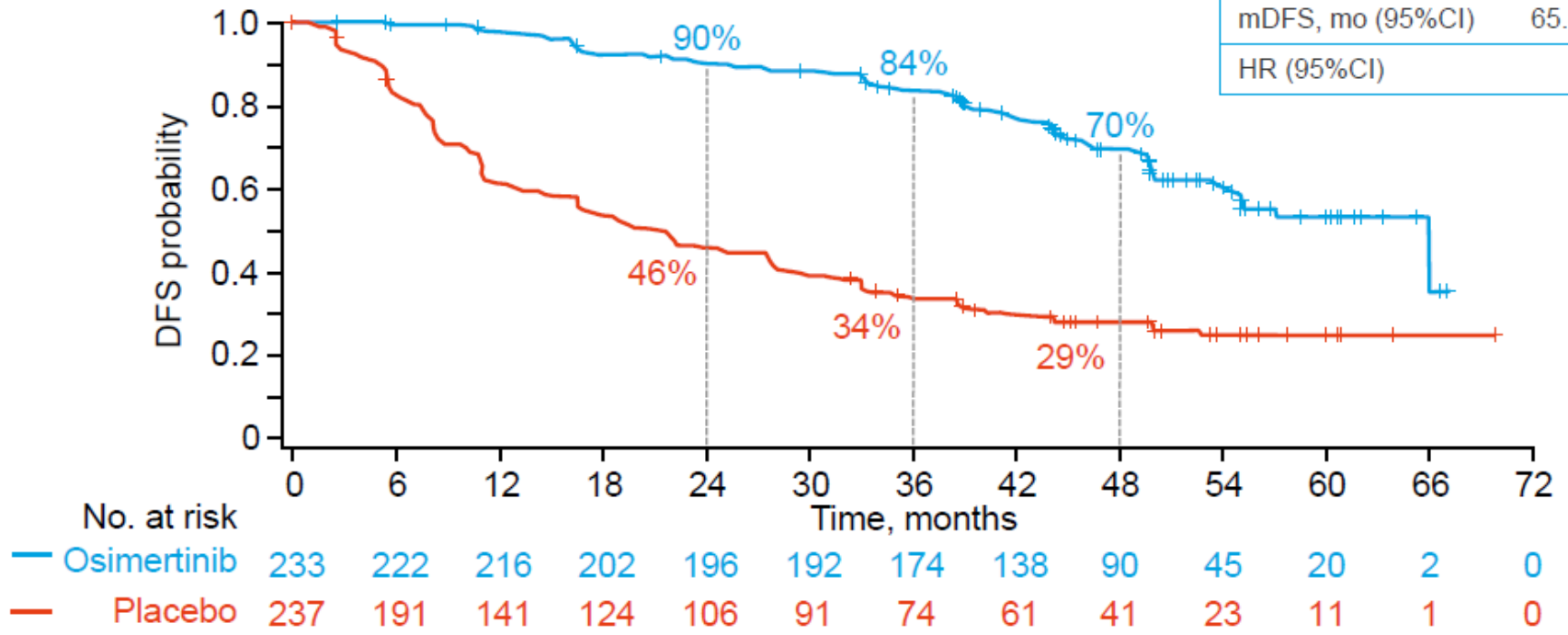
Tsuboi M, et al. Ann Oncol 2022;33(suppl):Abstr LBA47

Organizado por: GECP lung cancer research

Key results

Disease-free survival in stage II/IIIA patients

	Osimertinib (n=233)	Placebo (n=237)
mDFS, mo (95%CI)	65.8 (54.4, NC)	21.9 (16.6, 27.5)
HR (95%CI)	0.23 (0.18, 0.30)	



– In the overall population, mDFS was 65.8 mo (95%CI 61.7, NC) and 28.1 mo (95%CI 22.1, 35.0) in the osimertinib and placebo arms, respectively (HR 0.27 [95%CI 0.21, 0.34])

Tsuboi M, et al. Ann Oncol 2022;33(suppl):Abstr LBA47

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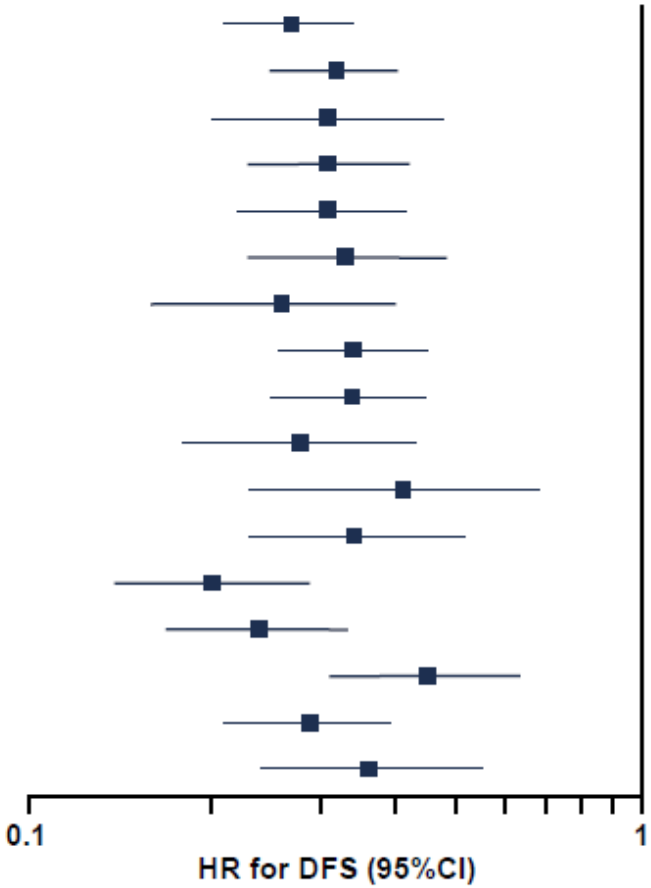
DFS across subgroups in the overall population

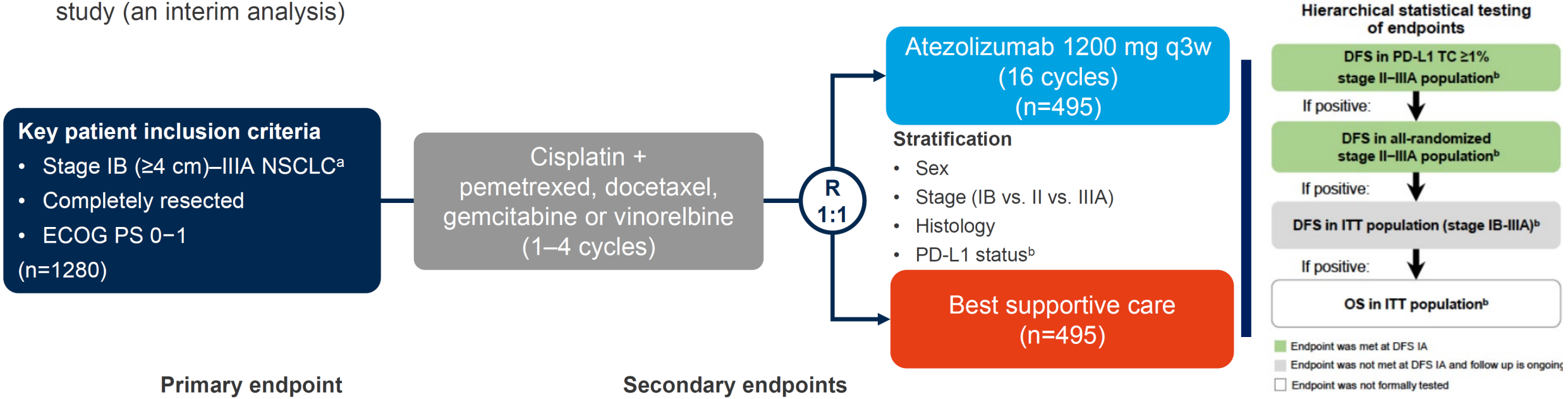


		HR	95%CI
Overall (n=682)	Stratified log-rank	0.27	0.21, 0.34
	Unadjusted Cox PH	0.32	0.25, 0.40
Sex	Male (n=204)	0.31	0.20, 0.48
	Female (n=478)	0.31	0.23, 0.42
Age	<65 years (n=380)	0.31	0.22, 0.42
	≥65 years (n=302)	0.33	0.23, 0.48
Smoking history	Yes (n=194)	0.26	0.16, 0.40
	No (n=488)	0.34	0.26, 0.45
Race	Asian (n=434)	0.34	0.25, 0.45
	Non-Asian (n=248)	0.28	0.18, 0.43
Stage	IB (n=212)	0.41	0.23, 0.69
	II (n=236)	0.34	0.23, 0.52
	IIIA (n=234)	0.20	0.14, 0.29
EGFR mutation	Ex19Del (n=378)	0.24	0.17, 0.33
	L858R (n=304)	0.45	0.31, 0.64
Adjuvant chemotherapy	Yes (n=410)	0.29	0.21, 0.39
	No (n=272)	0.36	0.24, 0.55

Tsuboi M, et al. Ann Oncol 2022;33(suppl):Abstr LBA47

PL03.09: IMpower010: Overall Survival Interim Analysis of a Phase III study of Atezolizumab vs Best Supportive Care in resected NSCLC

- **Study objective**
  - To evaluate the efficacy and safety of atezolizumab in patients with resected NSCLC in the IMpower010 study (an interim analysis)



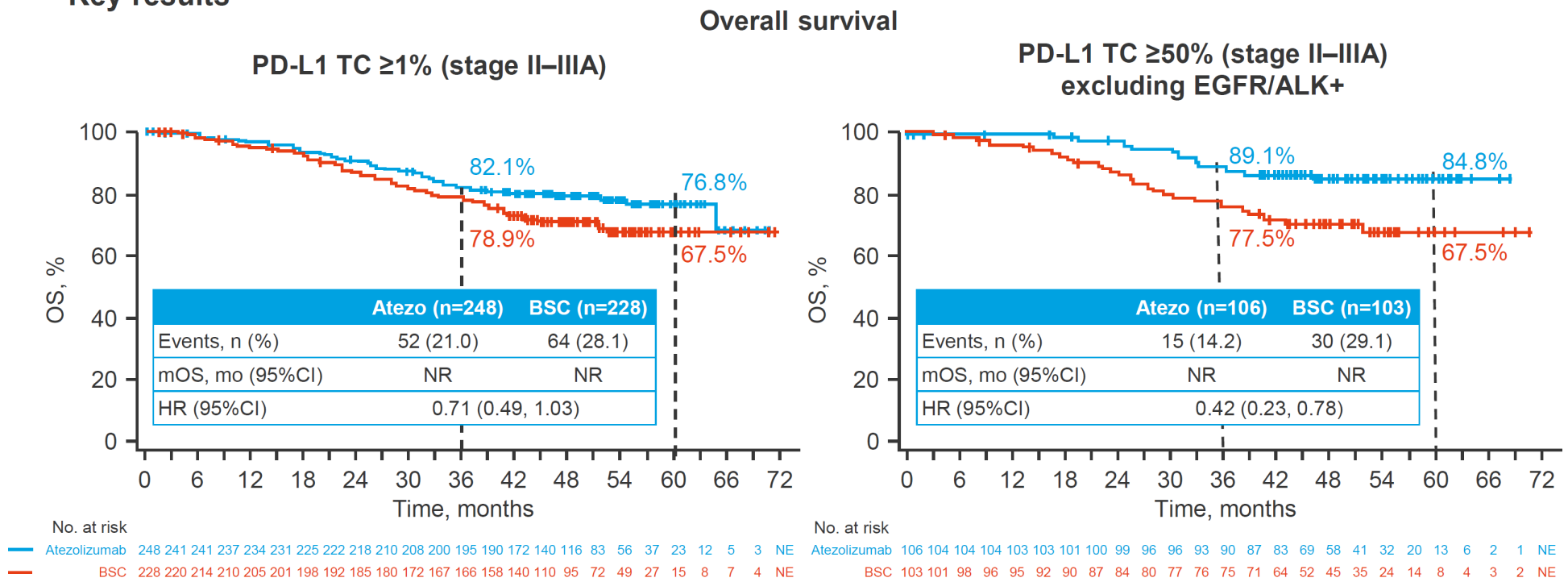
Primary endpoint
- DFS

Secondary endpoints
- OS, safety

[a]Per American Joint Committee on Cancer (AJCC) cancer staging manual, 7th edition;
[b]TC2/3 and any IC vs. TC0/1 and IC2/3 vs. TC0/1 and IC0/1

Felip E, et al. J Thorac Oncol 2022;17(suppl):Abstr PL03.09

- **Key results**



Felip E, et al. J Thorac Oncol 2022;17(suppl):Abstr PL03.09

In patients with resected stage II–IIIA NSCLC with PD-L1 TC ≥1%, at an interim analysis, atezolizumab demonstrated a trend for improved OS and there were no new safety signals observed

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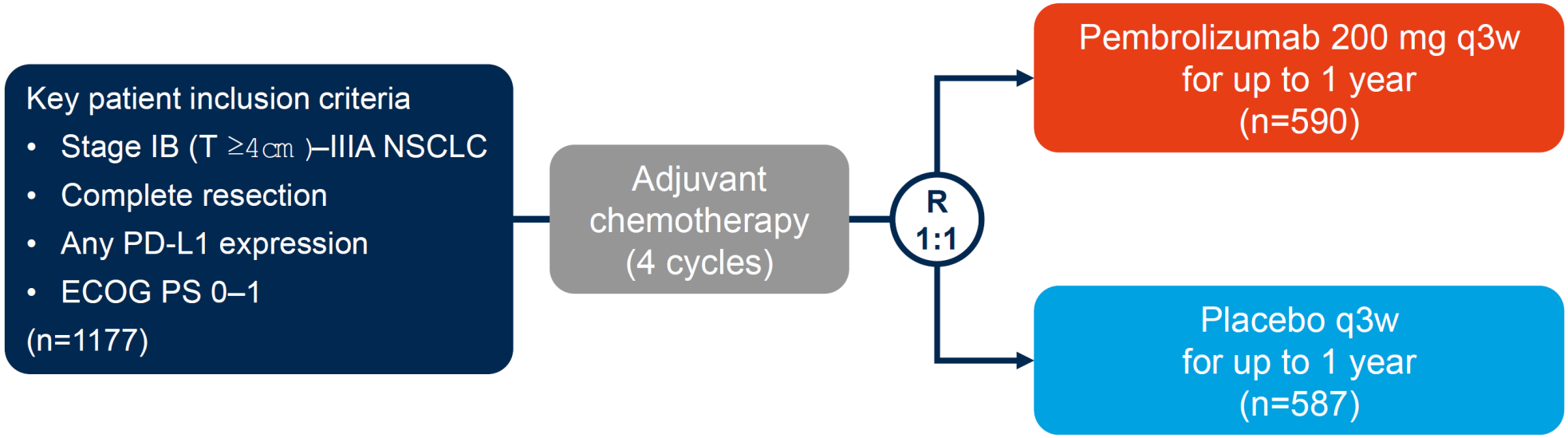
930MO: Pembrolizumab vs placebo in completely resected stage IB-IIIA NSCLC: subgroup analysis according to PD-L1 of PEARLS/KEYNOTE091

- **Study objective**
  - To evaluate the efficacy and safety of adjuvant pembrolizumab in patients with completely resected early stage NSCLC in the PEARLS/KEYNOTE-091 study



Primary endpoint

- DFS (overall population), DFS (PD-L1 TPS ≥50%)

Secondary endpoints

- DFS (PD-L1 TPS ≥1%), OS, safety

Peters S, et al. Ann Oncol 2022;33(suppl):Abstr 930MO

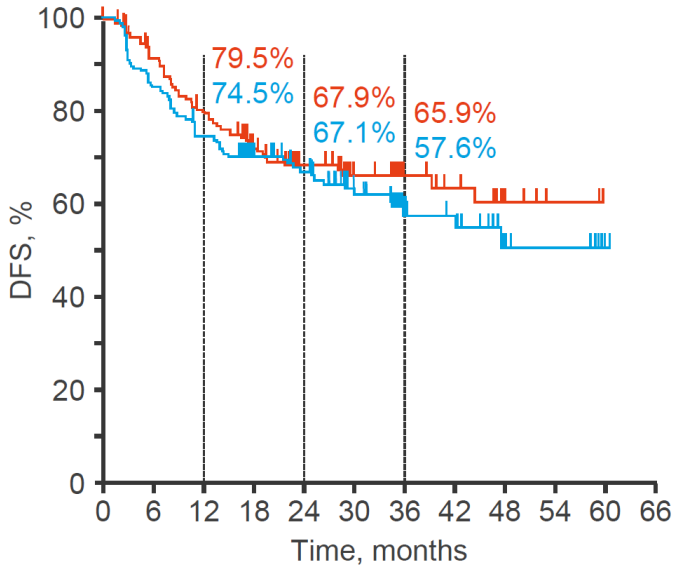
Organizado por: GECP lung cancer research

- **Key results**

DFS: Pembrolizumab vs. placebo by PD-L1 TPS

TPS ≥50%

	Pembrolizumab (n=168)	Placebo (n=165)
mDFS, mo (95%CI)	NR (44.3, NR)	NR (35.8, NR)
HR (95%CI); p-value	0.82 (0.57, 1.18); 0.14	

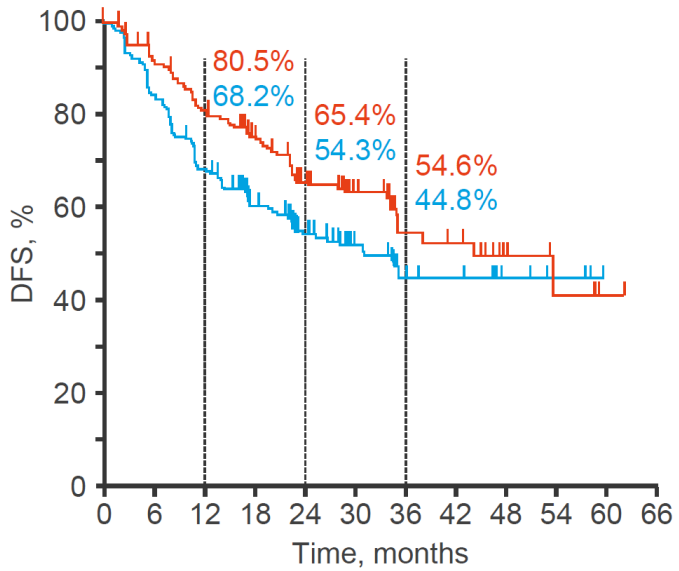


No. at risk

Pembrolizumab	168	145	126	99	69	50	26	22	7	4	0	0
Placebo	165	140	121	100	75	54	28	22	8	6	1	0

TPS 1–49%

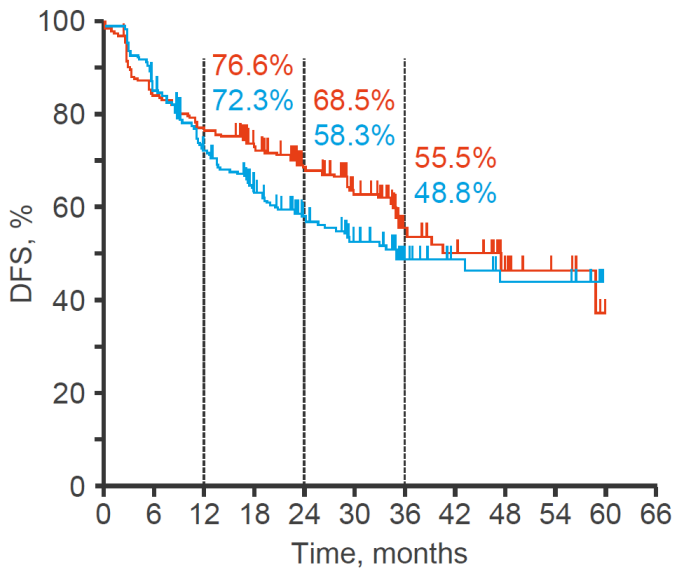
	Pembrolizumab (n=189)	Placebo (n=190)
mDFS, mo (95%CI)	44.2 (34.9, NR)	31.3 (22.5, NR)
HR (95%CI)	0.67 (0.48, 0.92)	



	189	158	137	113	84	61	22	20	9	5	1	0
	190	159	128	97	75	45	15	12	5	3	0	0

TPS <1%

	Pembrolizumab (n=233)	Placebo (n=232)
mDFS, mo (95%CI)	47.4 (35.0, NR)	34.9 (22.5, NR
HR (95%CI)	0.78 (0.58, 1.03)	



	233	190	171	146	111	74	34	28	12	7	0	0
	232	194	160	129	91	61	29	23	9	9	0	0

Peters S, et al. Ann Oncol 2022;33(suppl):Abstr 930MO

anizado por:

In patients with completely resected early stage NSCLC, pembrolizumab demonstrated benefit in DFS in overall population- but not in all PD-L1 expression subgroups. Safety profile was similar across the subgroups

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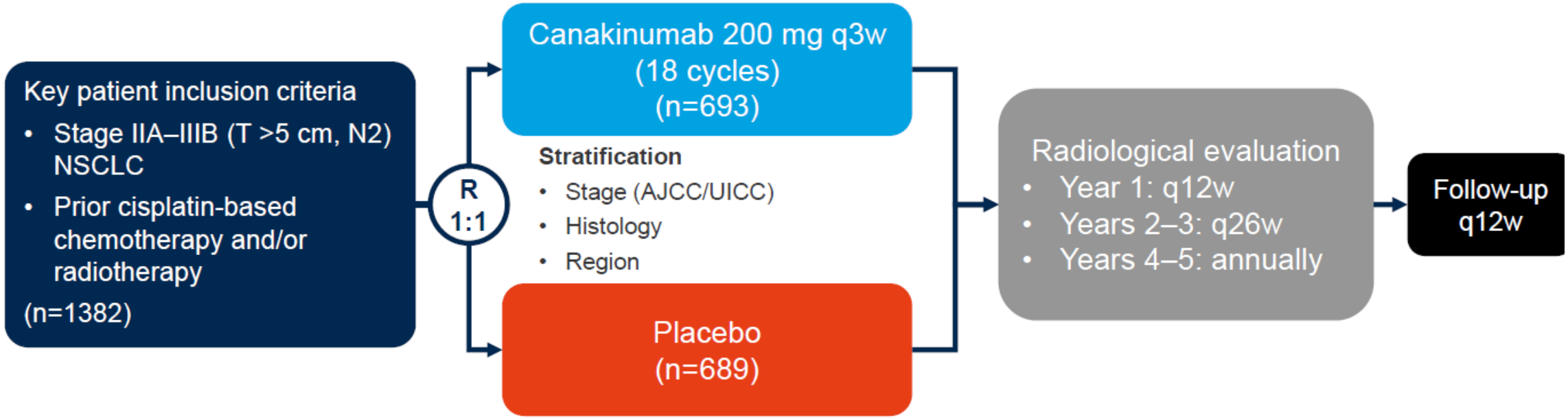
LBA49: CANOPY-A: Phase 3 study of canakimumab as adjuvant therapy in patients with completly resected non-small cell lung cancer

- **Study objective**
  - To evaluate the efficacy and safety of canakinumab in patients with completely resected NSCLC in the CANOPY-A study



Primary endpoint

- DFS

Secondary endpoints

- OS, LCSS, safety

Garon EB, et al. Ann Oncol 2022;33(suppl):Abstr LBA49

Organizado por:
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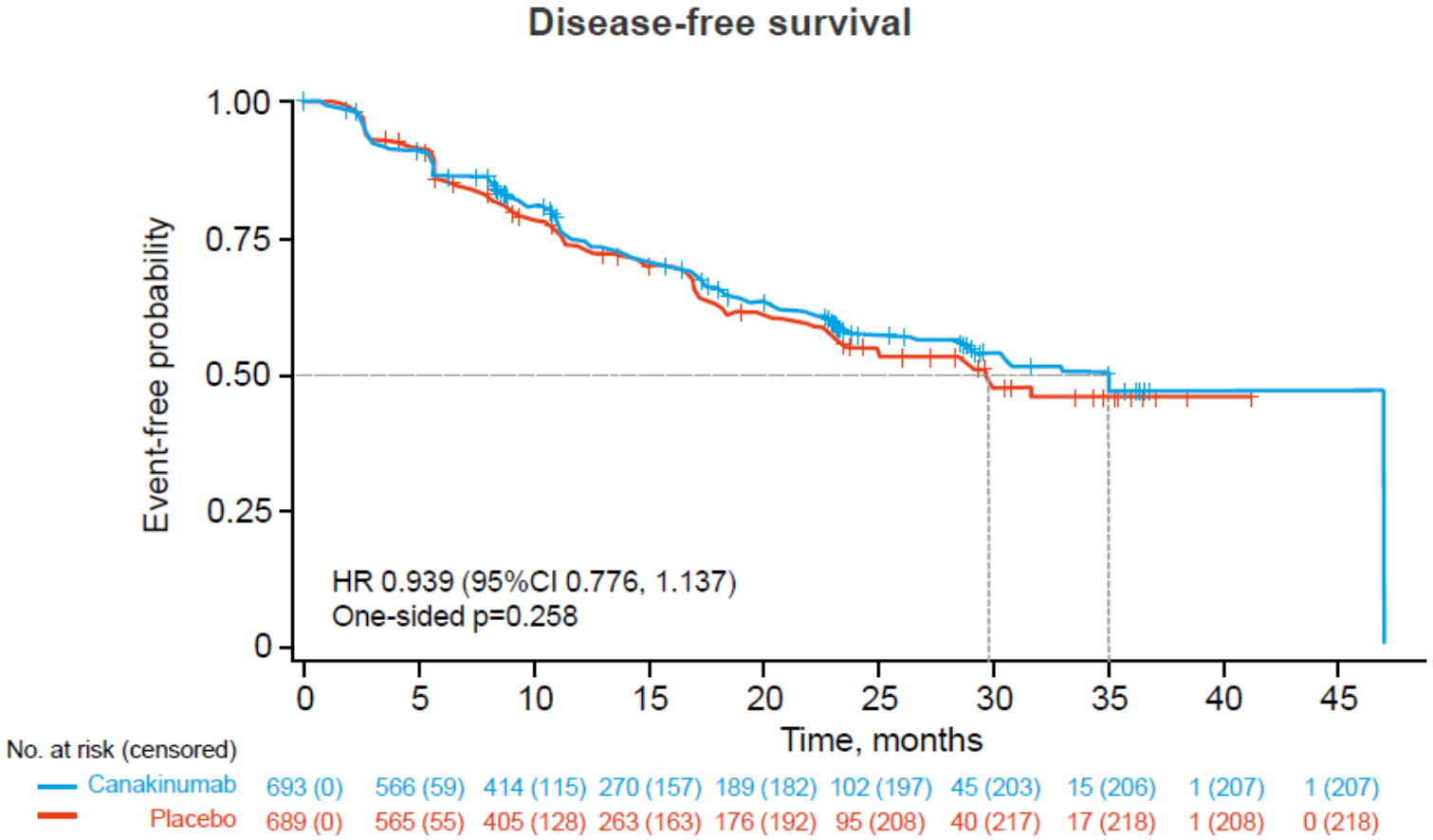
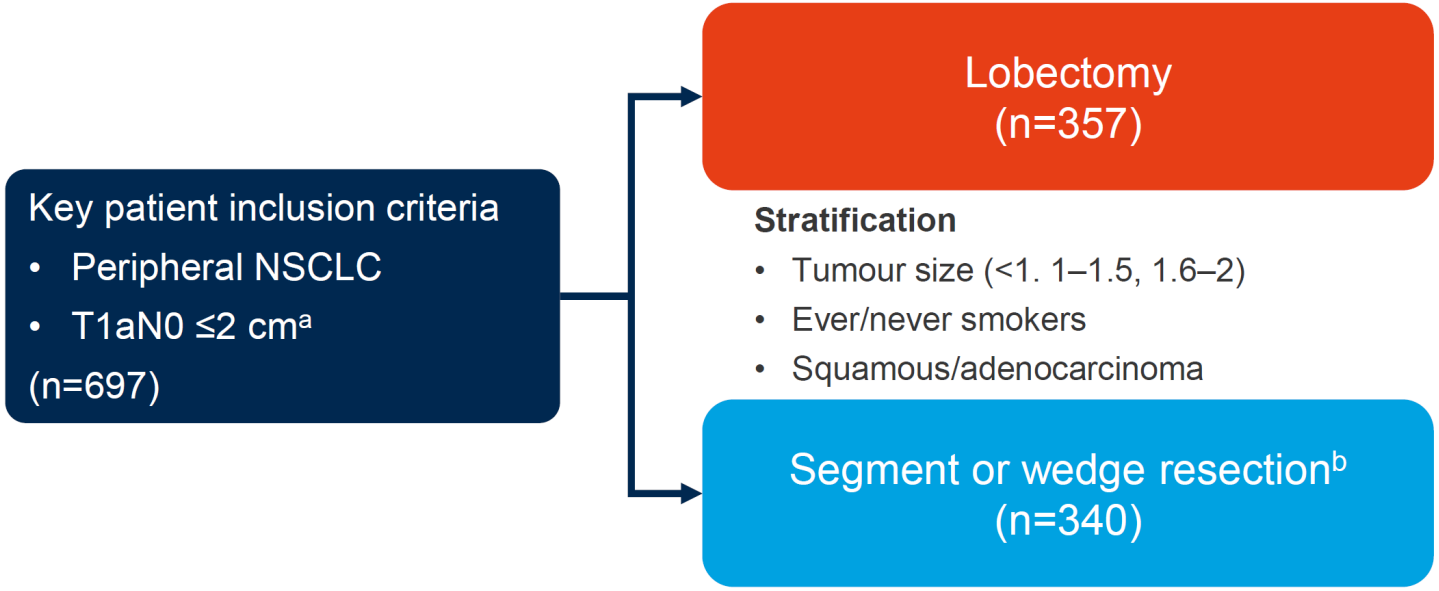
- **Key results**



Garon EB, et al. Ann Oncol 2022;33(suppl):Abstr LBA49

PL 03.06: Lobar or sub-lobar resection for peripheral clinical stage IA=2cm in NSCLC. CALGB 140503 [Alliance]

- **Study objective**
  - To evaluate the efficacy of lobar or sub-lobar resection in patients with peripheral clinical stage IA ≤2 cm NSCLC in the CALGB 140503 study



Primary endpoint

- DFS

Secondary endpoints

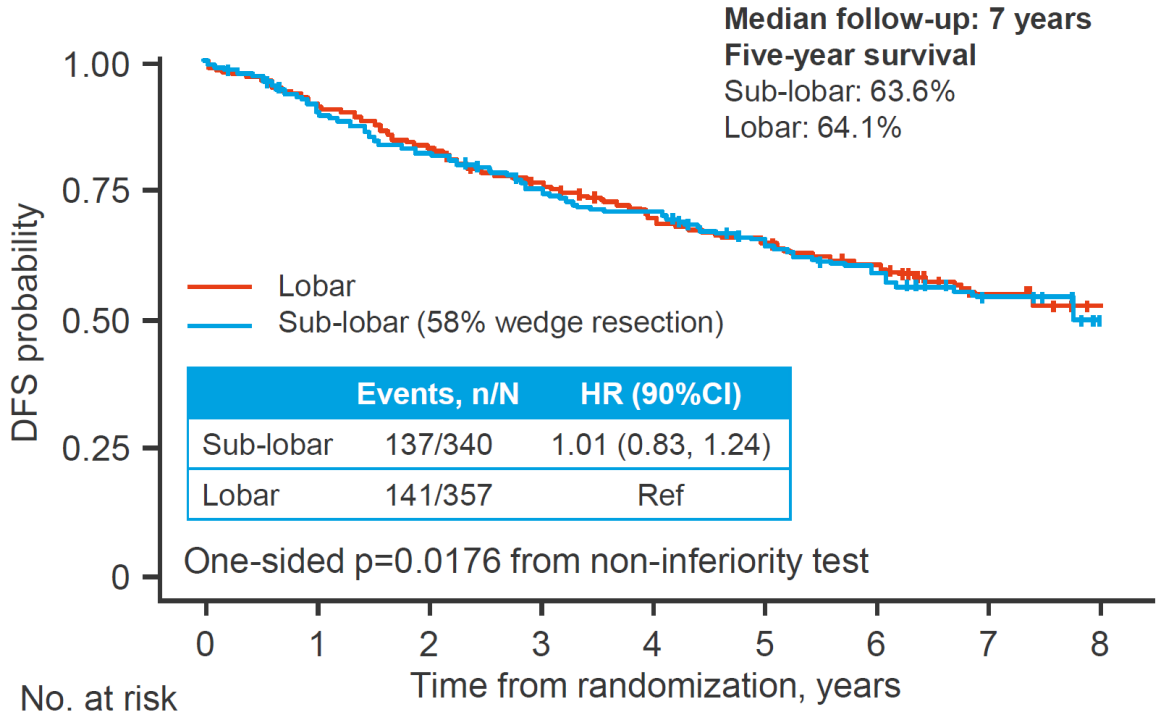
- OS, PFS, recurrence

[a]Mediastinal nodal staging was mandatory to confirm lymph nodes status;
[b]depending on investigator's choice

Altorki NK, et al. J Thorac Oncol 2022;17(suppl):Abstr PL03.06

- **Key results**

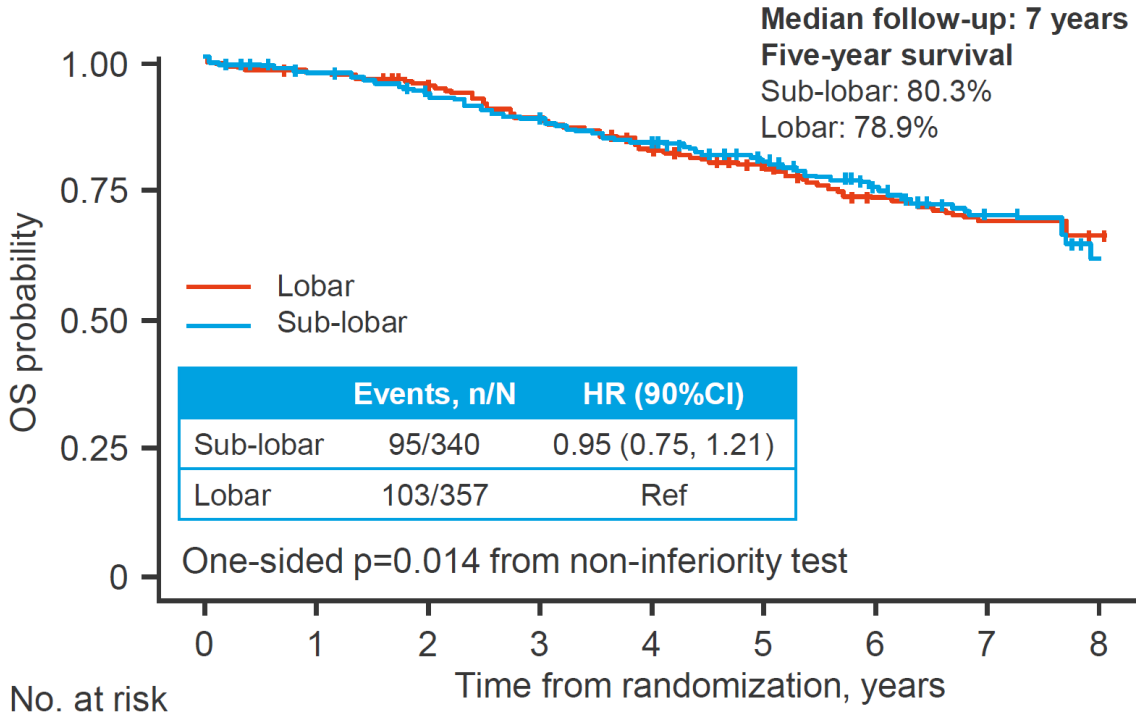
Disease-free survival



No. at risk

Lobar	357	310	276	246	209	175	132	80	5
Sub-lobar	340	291	254	222	201	172	123	78	6

Overall survival



No. at risk

Lobar	357	337	322	297	270	240	192	142	14
Sub-lobar	340	320	298	276	258	236	185	127	19

Altorki NK, et al. J Thorac Oncol 2022;17(suppl):Abstr PL03.06

In patients with peripheral clinical stage IA ≤2 cm NSCLC, sub-lobar resection was not inferior to lobectomy in terms of survival (DFS and OS) and had similar rates of recurrence

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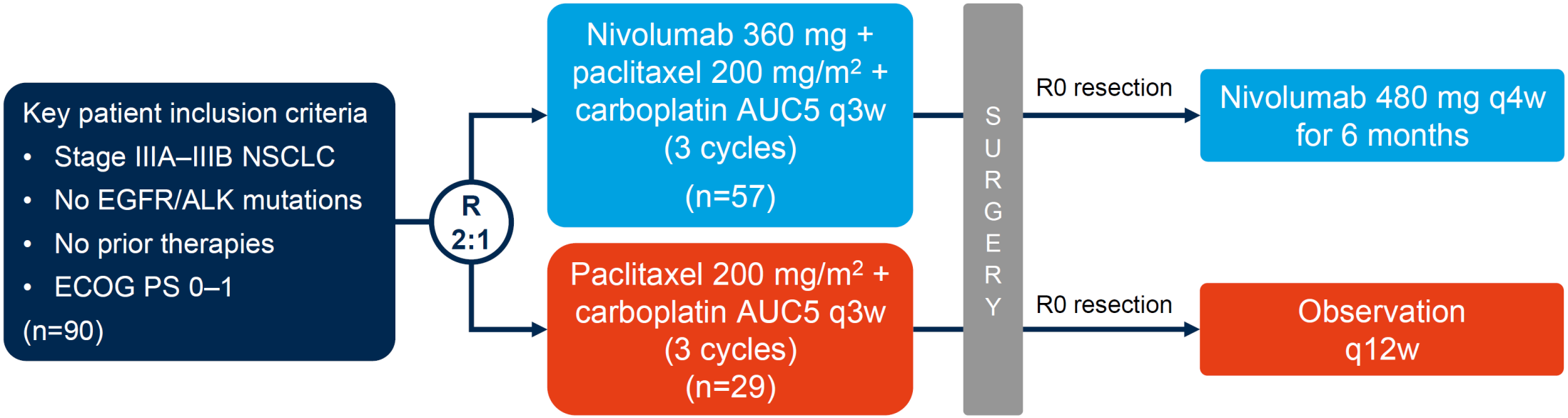
A) Enfermedad localizada

B) Enfermedad localmente avanzada: potencialmente resecable e irresecable

C) Biomarcadores

8501: Phase 2 NADIM II trial: Nivolumab + ChT vs ChT as neoadjuvant treatment for resectable stage IIIA-B NSCLC: pathological complete response (pCR)

- **Study objective**
  - To evaluate the efficacy and safety of neoadjuvant nivolumab + chemotherapy in patients with resectable stage IIIA–IIIB NSCLC in the phase 2 NADIM II trial



Primary endpoint

- pCR[a]

Secondary endpoints

- MPR[b], OS, PFS, ORR, biomarkers, safety

[a]Defined as 0% viable tumor cells in resected lung and lymph nodes;
[b]defined as ≤10% residual viable tumor cells in resected lung and lymph nodes

Provencio-Pulla M, et al. J Clin Oncol 2022;40(suppl):Abstr 8501

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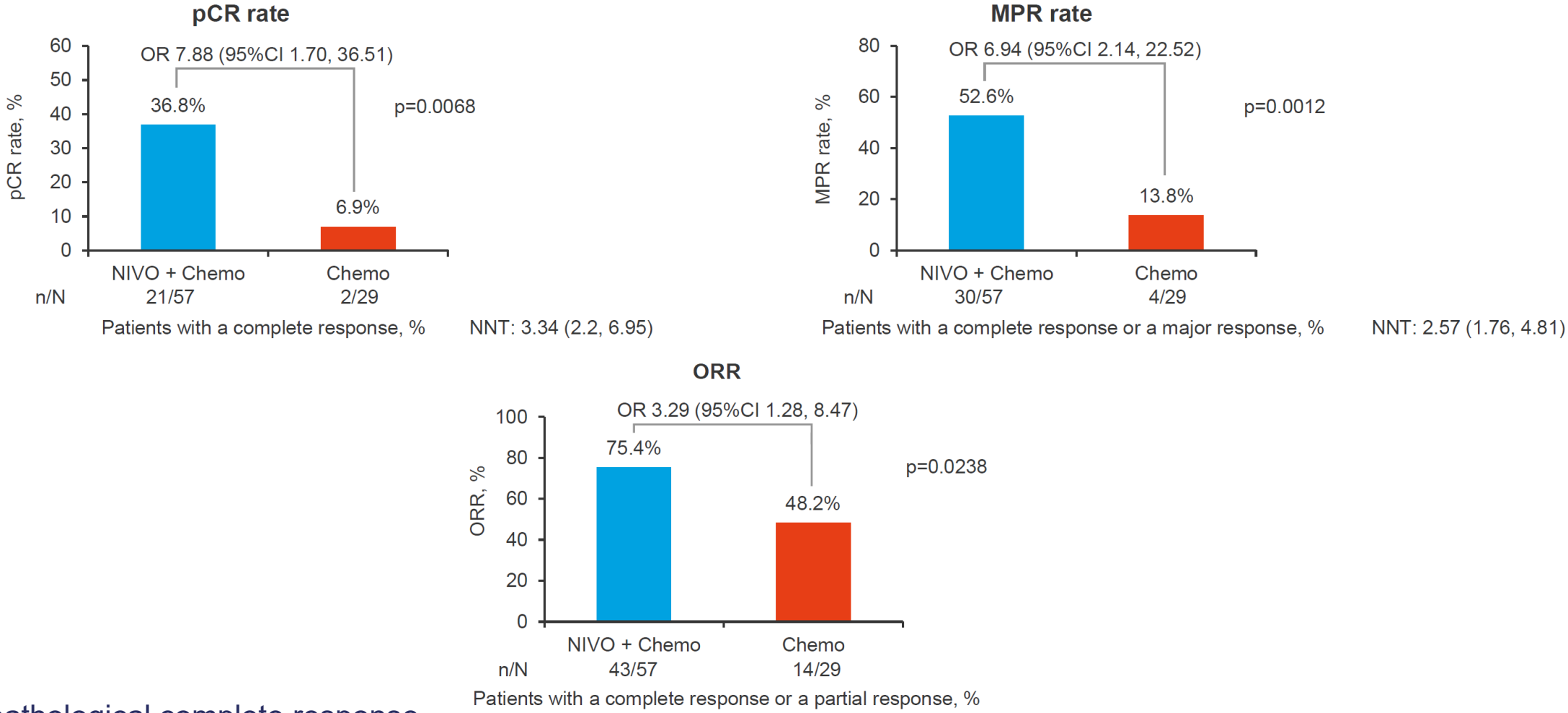
- **Key results**



pCR: pathological complete response
MPR: Major pathologic response

Provencio-Pulla M, et al. J Clin Oncol 2022;40(suppl):Abstr 8501

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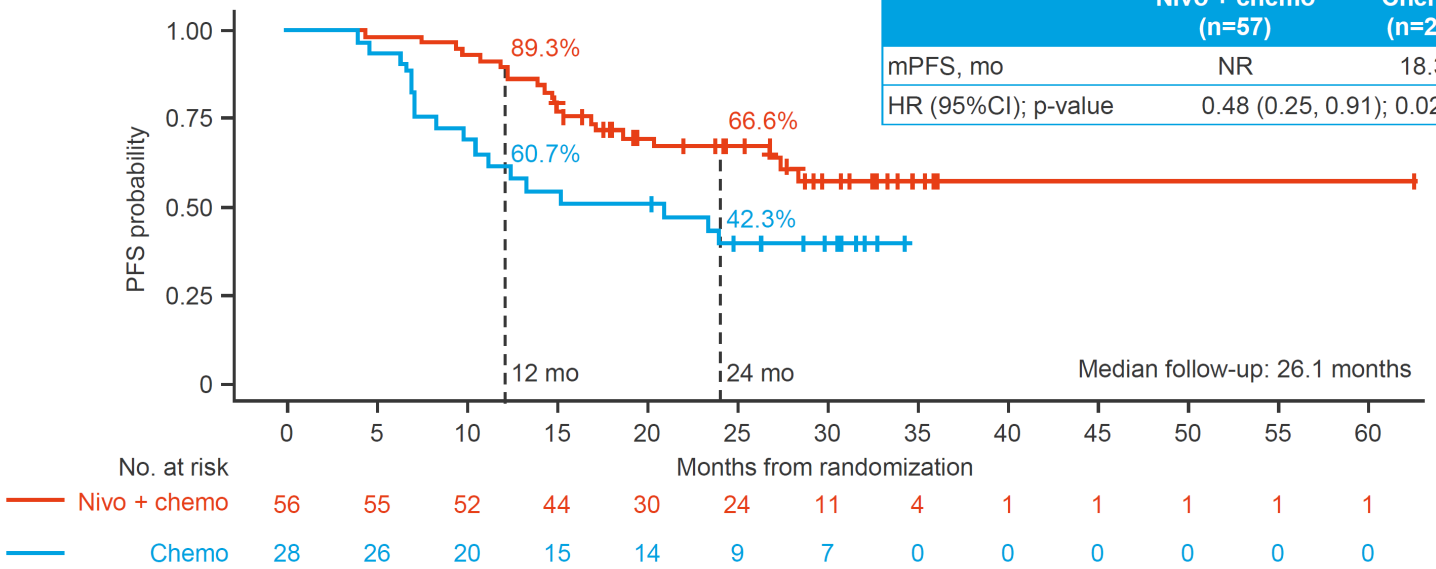
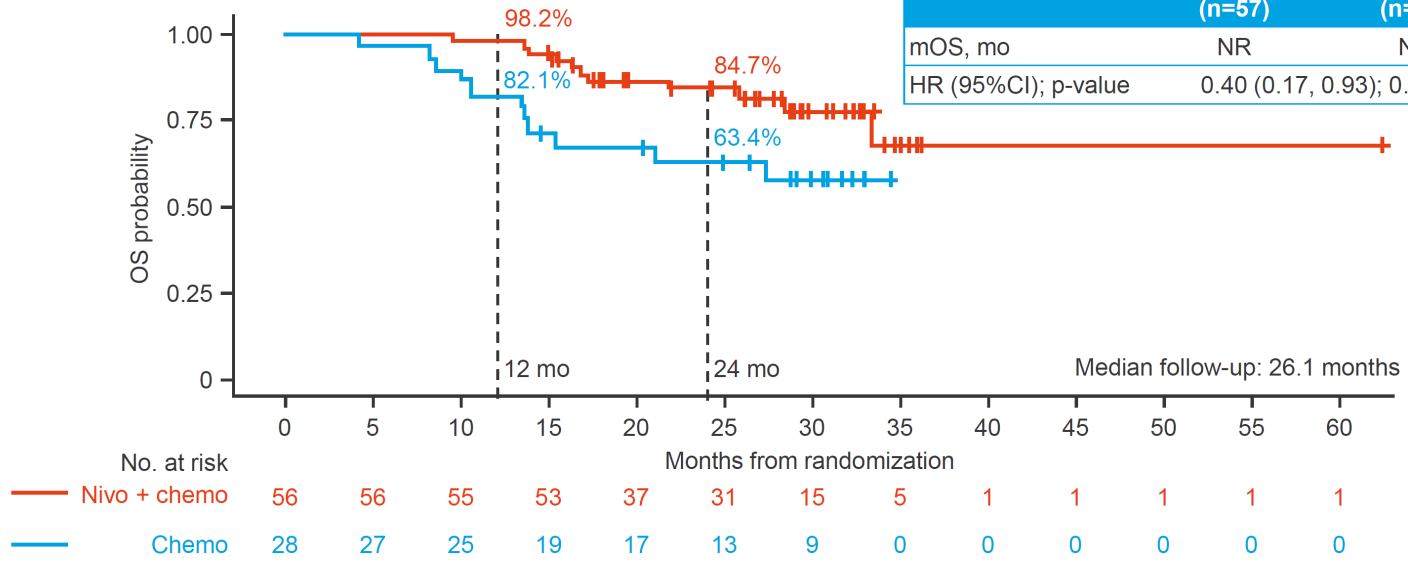
Progression-free survival (ITT)



	Nivo + chemo (n=57)	Chemo (n=29)
mPFS, mo	NR	18.3
HR (95%CI); p-value	0.48 (0.25, 0.91); 0.025	

Overall survival (ITT)



	Nivo + chemo (n=57)	Chemo (n=29)
mOS, mo	NR	NR
HR (95%CI); p-value	0.40 (0.17, 0.93); 0.034	

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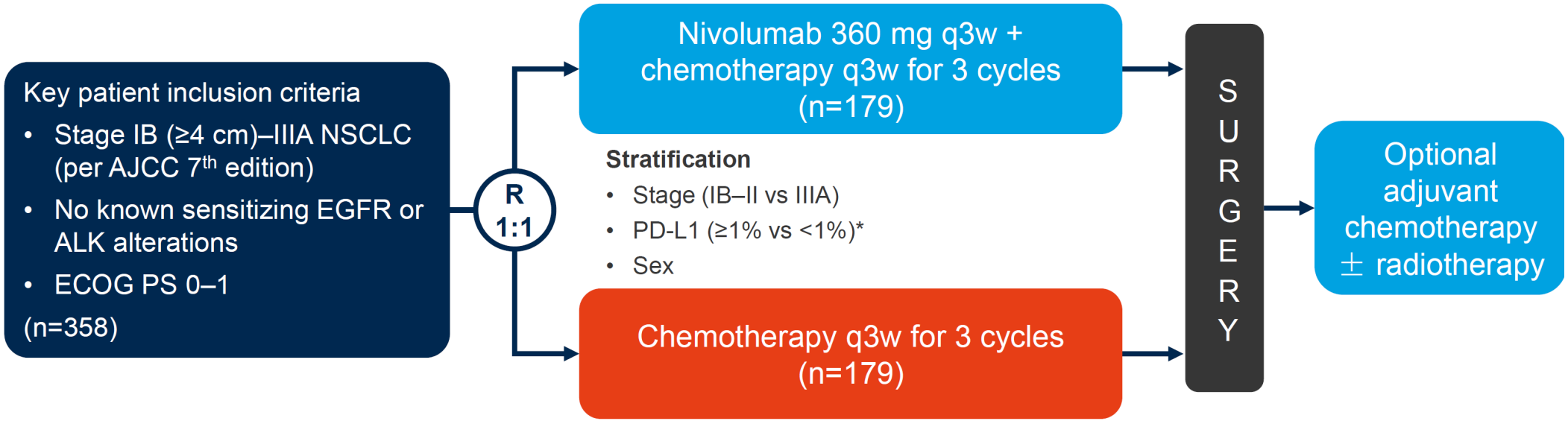
Provencio M, et al. J Thorac Oncol 2022;17(suppl):Abstr PL03.12

Surgical outcomes	Nivo + chemo (n=57)	Chemotherapy (n=29)
R0, n (%)	49 (92.5)	13 (65.0)
OR (95%CI); p-value	6.60 (1.67, 26.02); 0.007	
Definitive surgery[a], %	93.0	69.0
OR (95%CI); p-value	5.96 (1.65, 21.56); 0.008	
Downstaging, n (%) Yes No	 37 (69.8) 16 (30.2)	 8 (40.0) 12 (60.0)
Downstaging rate, %	69.8	40.0
OR (95%CI); p-value	3.47 (1.19, 10.1); 0.04	

In patients with potentially resectable stage IIIA-B NSCLC, neoadjuvant nivolumab + ChT provided promising antitumor activity, survival, and showed a manageable safety profile.

LBA8511: CheckMate 816: Neodajuvant nivolumab + platinum doublet chemo vs chemo for resectable (IB-IIIA) NSCLC: Pathological response and event-free survival

- **Study objective**
  - To evaluate the association between pathological regression and EFS for neoadjuvant nivolumab + platinum-doublet chemotherapy in patients with resectable stage IB–IIIA NSCLC in the CheckMate 816 trial



Primary endpoints

- pCR (0% viable tumor cells in lung and lymph nodes), EFS (BICR)

Secondary endpoints

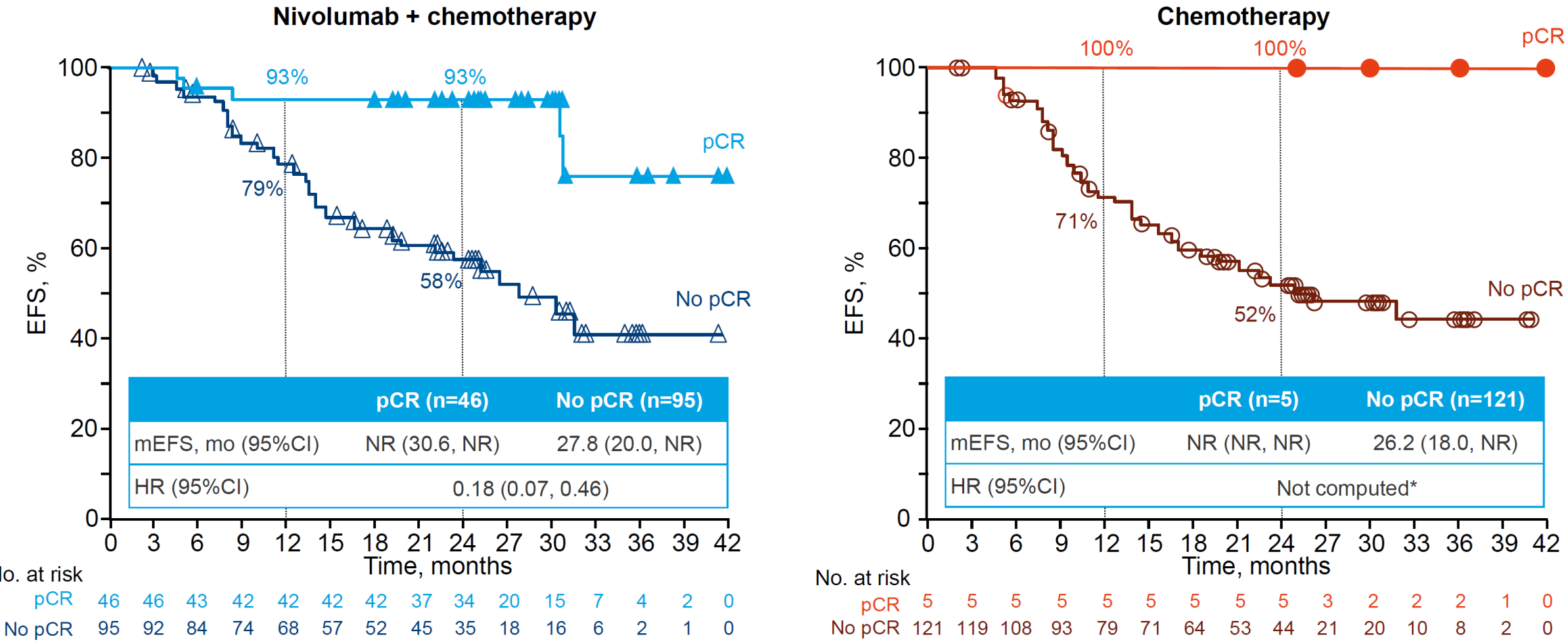
- MPR, OS, time to death or distant metastases, safety

*Determined by the PD-L1 28-8 pharmDx assay

Provencio-Pulla M, et al. J Clin Oncol 2022;40(suppl):Abstr LBA8511

- **Key results**

Event-free survival by pCR status



*Too few patients with pCR

Provencio-Pulla M, et al. J Clin Oncol 2022;40(suppl):Abstr LBA8511

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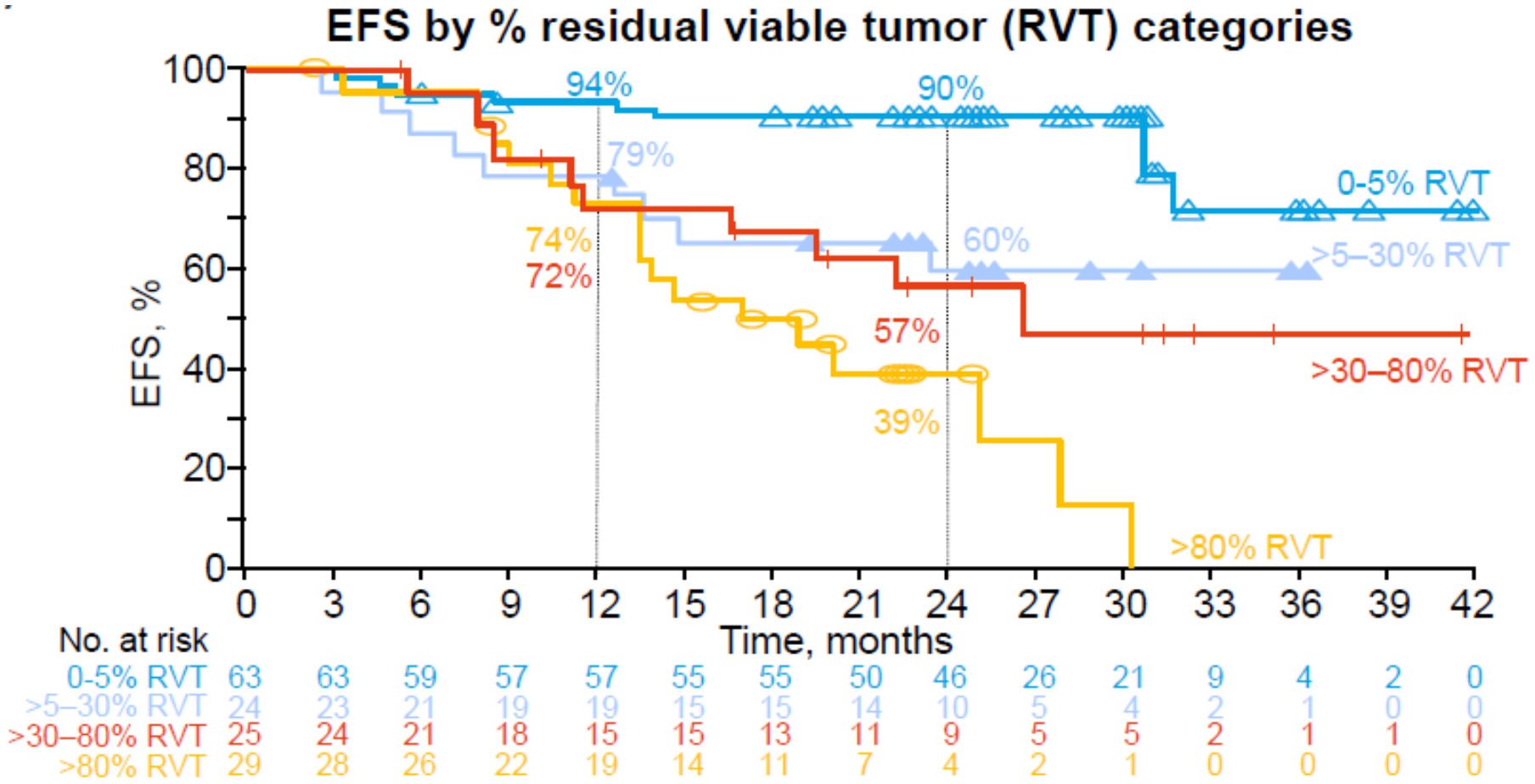

RVT	mEFS, mo (95% CI)
0.5%	NR (31.6, NR)
>5–30%	NR (13.6, NR)
>30–80%	26.6 (11.6, NR)
>80%	18.9 (13.4, 27.8)

RVT: Residual Viable Tumor

Organizado por:
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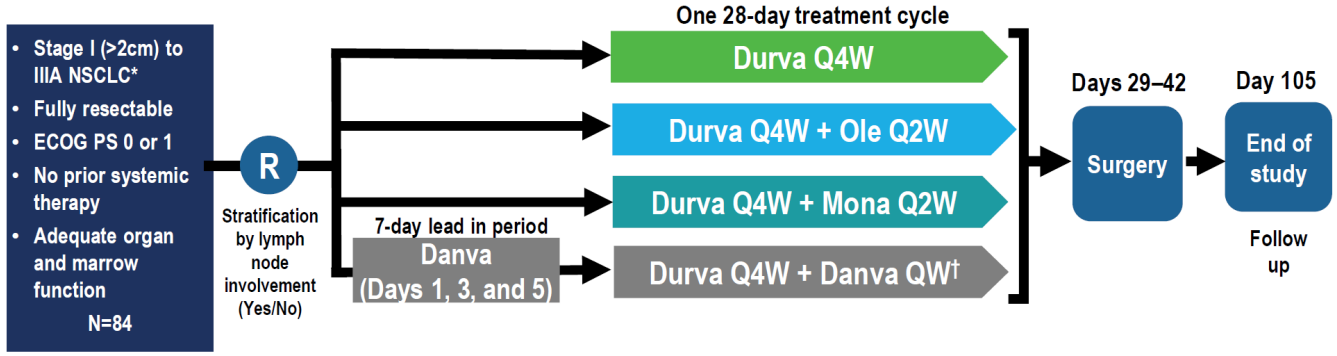
NeoCOAST: Neoadjuvant durvalumab +/– novel agents in resectable, early-stage (I [>2cm] to IIIA) NSCLC



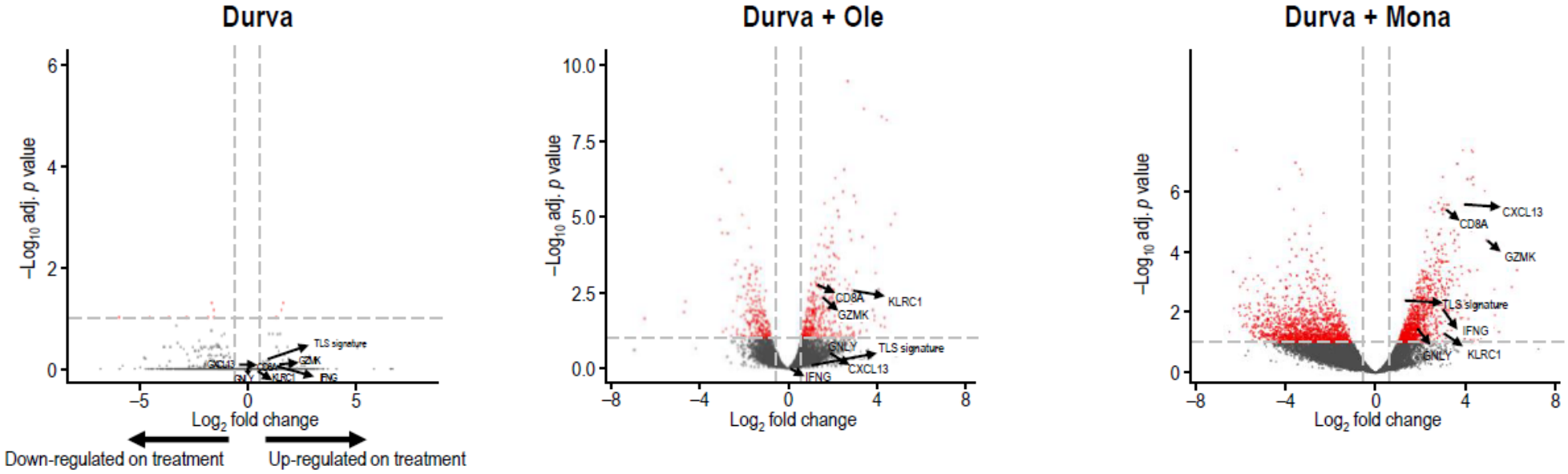
	Durva (n=27)	Durva + Ole (n=21)	Durva + Mona (n=20)	Durva + Danva (n=16)
Overall MPR (n/N, %)	3/27 (11%)	4/21 (19%)	6/20 (30%)	5/16 (31%)
PD-L1+	0/6 (0%)	2/5 (40%)	3/6 (50%)	0/2 (0%)
PD-L1–	0/3 (0%)	1/6 (16.7%)	0/2 (0%)	0/5 (0%)
PD-L1 NE	3/18 (17%)	1/10 (10%)	3/12 (25%)	5/9 (56%)

- Primary endpoint: MPR rate (proportion of patients with ≤10% residual viable tumour cells in resected tumour specimen and sampled nodes at surgery) per investigator assessment.
- A **single cycle of** neoadjuvant durva combined with ole, mona, or danva produced numerically improved MPR rates (19–31.3%) compared with durva alone (11.1%).[1]
- MPR was associated with baseline tumour PD-L1 expression in durva + ole and durva + mona arms.

*Per American Joint Committee on Cancer Staging, 8th edition. †Danvatirsen arm was stopped early as the program was discontinued.
ctDNA, circulating tumour DNA; ECOG, Eastern Cooperative Oncology Group; MPR, major pathological response; NE, not evaluable; NSCLC, non-small-cell lung cancer; PD-L1, programmed cell death ligand-1; PS, performance status; Q4W, once every 4 weeks; Q2W, once every 2 weeks; QW, every week; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1; TMB, tumour mutational burden.

1. Cascone T, et al. AACR 2022 (presentation CT011).

Evaluation of gene expression between tumours pre-therapy and at surgery reveals signatures of intratumoural immune activation



- Whole transcriptome RNA-sequencing was performed from tumour tissue collected pre-therapy and at surgery for all patients, where both samples were available.
- Expression of genes and gene signatures associated with NK cells (*KLRC1*, *GNLY*), CD8 T cells (*CD8A*, *GZMK*), cytotoxicity (*IFNG*, *GZMK*), tertiary lymphoid structures, and lymphocyte recruitment (*CXCL13*) demonstrated greater increases with durva + ole and durva + mona, than with durva alone.

Patients with major pathological response out of total sample pairs: durva, 0/4; durva + ole, 1/5; durva + mona, 2/4.
NK, natural killer; TLS, tertiary lymphoid structures.

A) Enfermedad localizada

B) Enfermedad localmente avanzada: potencialmente resecable e irresecable

C) Biomarcadores

933MO: Longitudinal monitoring of circultaing tumor DNA from plasma in patients with curative resected stage IA-IIIA EGFR mutant NSCLC

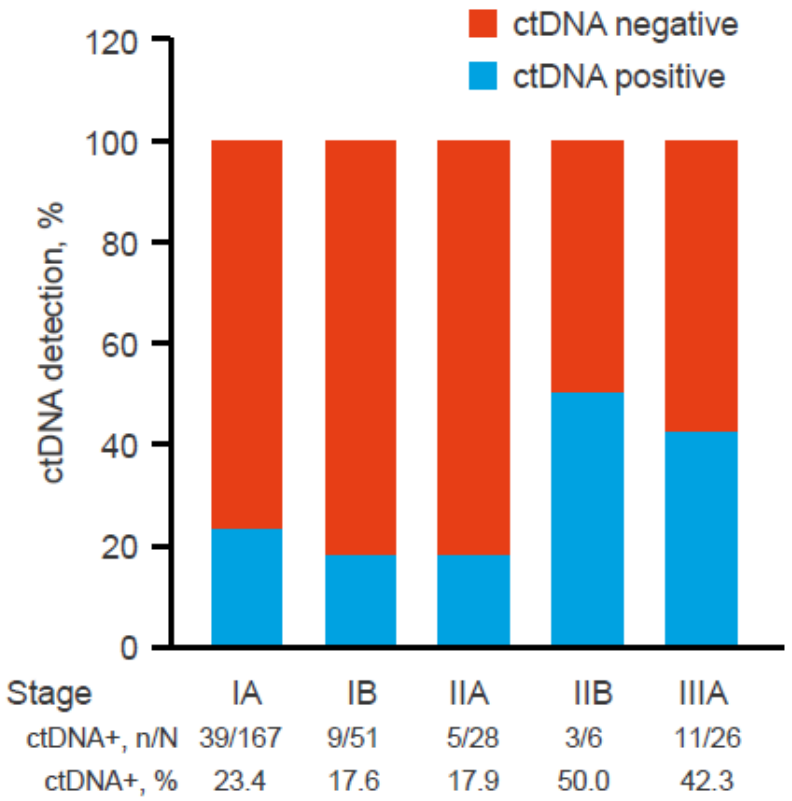
- **Study objective**
  - To assess the role of longitudinal monitoring of ctDNA in patients with resected stage IA–IIIA EGFR-mutant NSCLC

- **Methods**
  - Between August 2015 and October 2017, ctDNA samples (droplet digital PCR; BioRad) were collected from eligible patients with stage IA–IIIA NSCLC and Del19 or L859R alternations
  - ctDNA samples were analysed before surgery, 4 weeks after surgery, and at regular intervals for the next 5 years or until radiological recurrence (first year: every 3 months; second year: every 4 months; third year: every 6 months; year 4 and 5: once a year)

Ahn M-J, et al. Ann Oncol 2022;33(suppl):Abstr 933MO

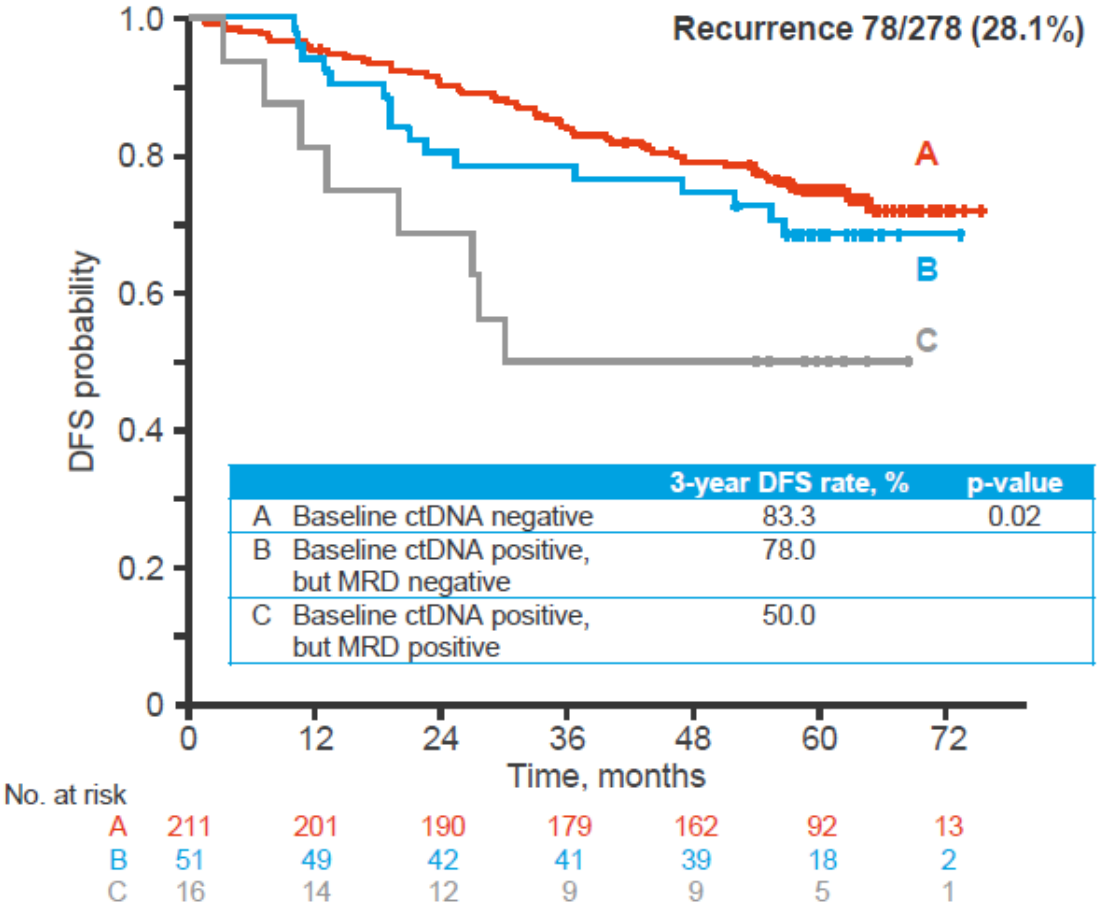
- **Key results**

Baseline ctDNA detection rate



Stage	IA	IB	IIA	IIB	IIIA
ctDNA+, n/N	39/167	9/51	5/28	3/6	11/26
ctDNA+, %	23.4	17.6	17.9	50.0	42.3

DFS by ctDNA status



		3-year DFS rate, %	p-value
A	Baseline ctDNA negative	83.3	0.02
B	Baseline ctDNA positive, but MRD negative	78.0	
C	Baseline ctDNA positive, but MRD positive	50.0	

No. at risk							
A	211	201	190	179	162	92	13
B	51	49	42	41	39	18	2
C	16	14	12	9	9	5	1

Ahn M-J, et al. Ann Oncol 2022;33(suppl):Abstr 933MO

In patients with resected stage IA-IIIA EGFR-mutant NSCLC, baseline ctDNA may be predictive of DFS

Take-home messages

-En estadíos IA <2cm periféricos, la resección sublobar/segmentectomía debe considerarse como tratamiento quirúrgico estándar

-Se confirma el beneficio en SLE a 4 años para osimertinib adyuvante EII-IIIA en *EGFRm,* a la espera de los datos en OS

-Se confirma el beneficio en SLE para atezolizumab adyuvante en EII-IIIA en PD-L1 ≥ 1% – aprobado para la EMA en los PD-L1 ≥ 50%. Tendencia a mejorar la OS con atezolizumab adyuvante, que incrementa con la expresión de PD-L1

-Se confirma el papel de la combinación de quimio-inmunoterapia neoadyuvante en ensayos clínicos randomizados (NADIM II, CheckMate 816). Nuevo estándar de tratamiento para enfermedad potencialmente resecable

-El papel de la biopsia líquida en enfermedad localmente avanzada sigue siendo un reto

Gracias por vuestra atención

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