15th CONGRESS on Lung CANCER

MADRID

23&24 November 2023

#15CongressGECP

Fundación GECP lung cancer research

Stage III NSCLC: Moving beyond concurrent CT-RT and consolidation IT

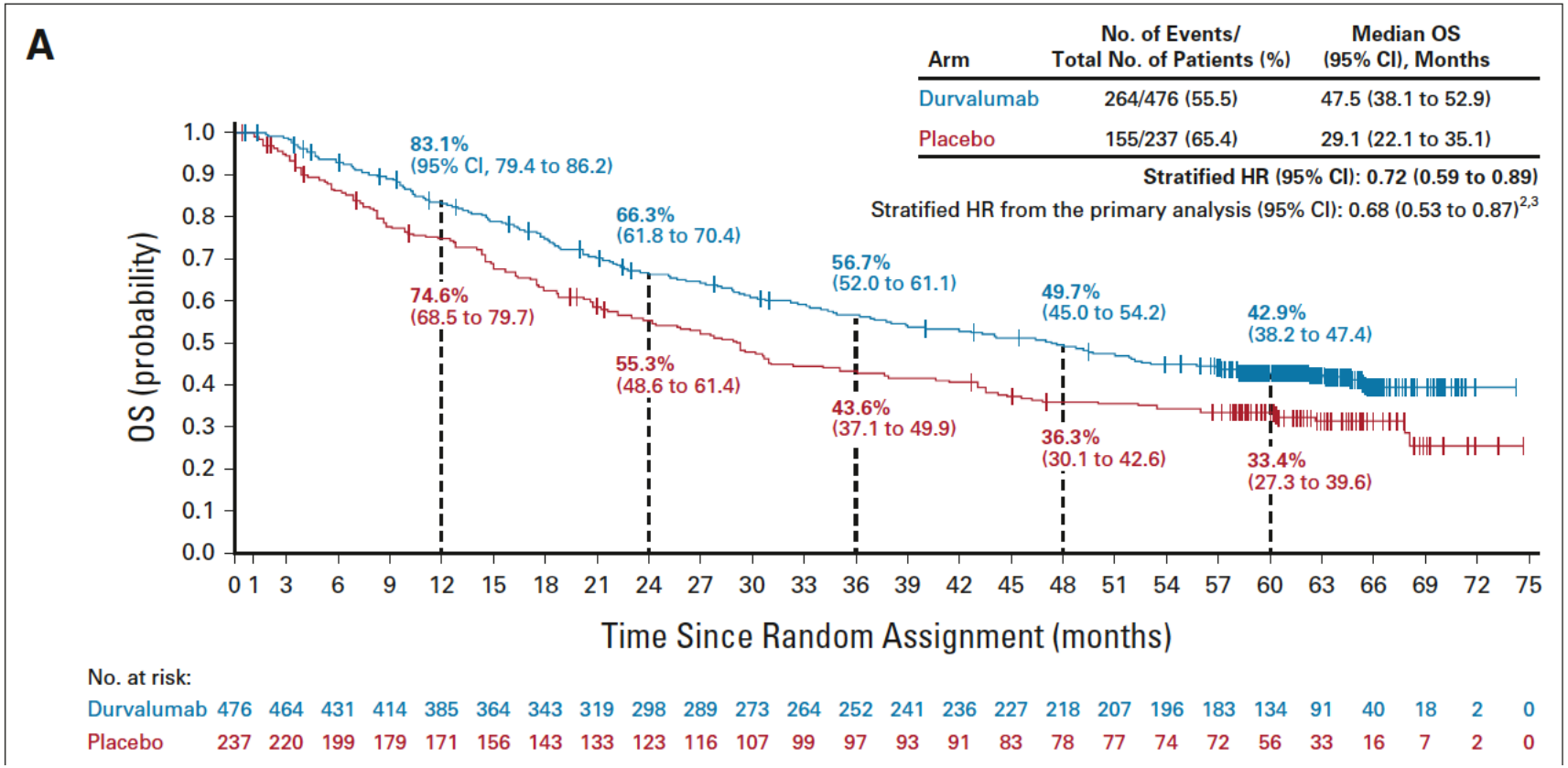
Dra Reyes Bernabé

HOSPITAL VIRGEN DEL ROCIO

CONFLICTOS DE INTERÉS

- Consultant or Advisory Role: Astra Zeneca, Roche, BMS, Lilly, MSD, Takeda, Sanofi, Janssen
- Research Funding: Roche
- Speaking: Astra Zeneca, Roche, BMS, Lilly, MSD, Takeda, Sanofi, Janssen

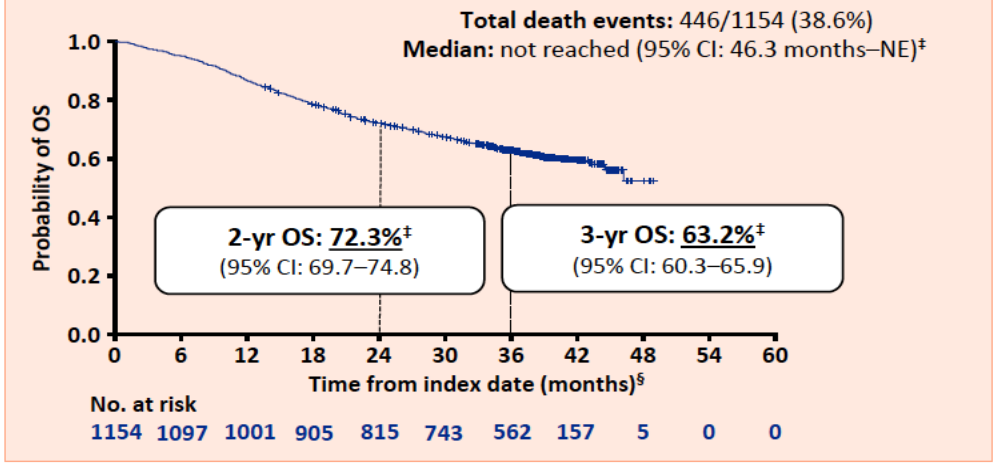
Five-Year Survival Outcomes From the PACIFIC Trial: Durvalumab After Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer



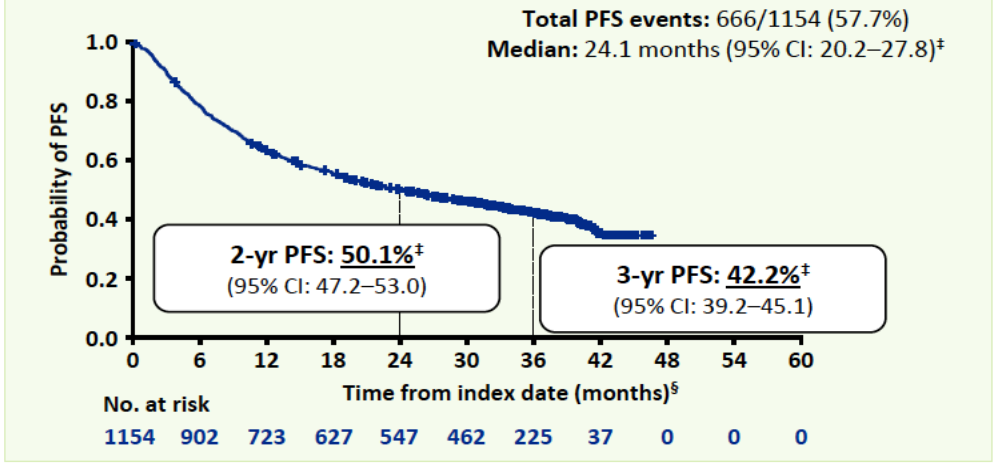
Spigel, JCO 2022, 40:12

Outcomes in the full analysis set (N=1154)

Overall survival*



Investigator-assessed PFS*†

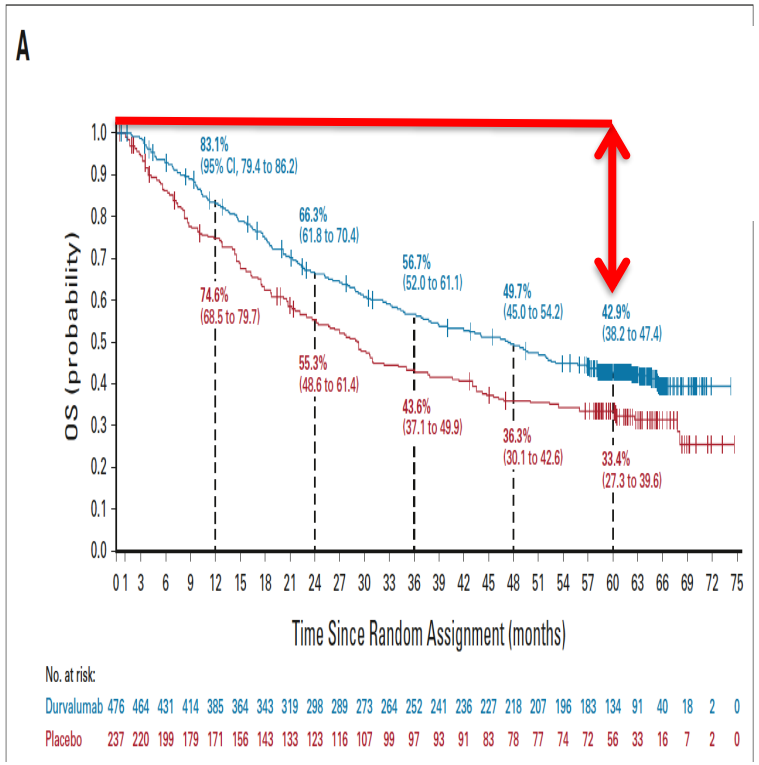


- As reported previously,[1] PACIFIC-R data continue to provide evidence for the effectiveness of consolidation durvalumab after CRT in a large, diverse, real-world population, consistent with findings from the pivotal, phase 3 PACIFIC trial[2-4]
  - These outcomes support the continued use of consolidation durvalumab after CRT (the 'PACIFIC regimen') as a global SoC for patients with unresectable stage III NSCLC

CI, confidence interval; CRT, chemoradiotherapy; EAP, early access programme; NE, not estimable; NSCLC, non-small-cell lung cancer; OS, overall survival; PFS, progression-free survival; SoC, standard of care; yr, year

*Analyses are based on the 3rd chart extraction from PACIFIC-R (end date: Nov 30, 2021; reported previously[1]); the median follow-up duration in patients censored at the end of data extraction was 38.7 months (range: 13.6–49.0). †Because of the real-world nature of PACIFIC-R, progression could be documented by either radiological evaluation (per Response Evaluation Criteria in Solid Tumors [RECIST] v1.1) or the investigator's clinical judgment (depending on local practice). ‡Calculated using the Kaplan–Meier method. §The PACIFIC-R index date is the date that durvalumab was initiated within the EAP.[1]Girard N et al., Oral Presentation 580. Presented at ESMO IO 2022; [2]Antonia SJ et al., N Engl J Med 2018;379:2342–50; [3]Antonia SJ et al., N Engl J Med 2017;377:1919–29; [4]Spigel DR et al., J Clin Oncol 2022;40:1301–11

PERO… ¿CUÁLES SON NUESTROS PROBLEMAS?

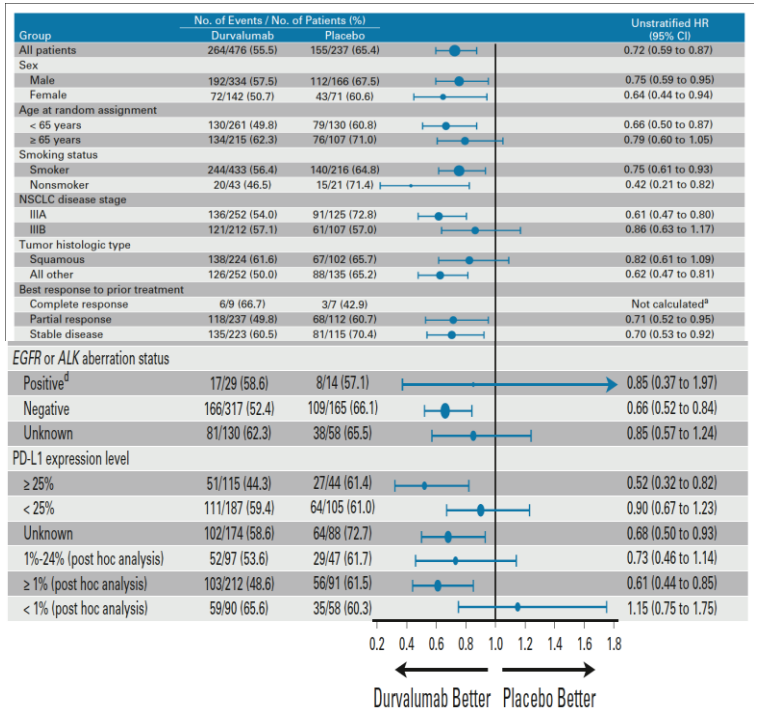


1) PACIENTES QUE NO SE BENEFICIAN DEL PACIFIC : 57%

2) PACIENTES QUE NO PUEDEN/DEBEN RECIBIR ESQUEMA PACIFIC

- PACIENTES QUE NO PUEDEN RECIBIR CONCOMITANCIA
- PACIENTES CON TUMORES PDL1< 1%
- PACIENTES CON MUTACIONES DRIVER

3) FALTA DE BIOMARCADORES



Spigel, JCO 2022, 40:12

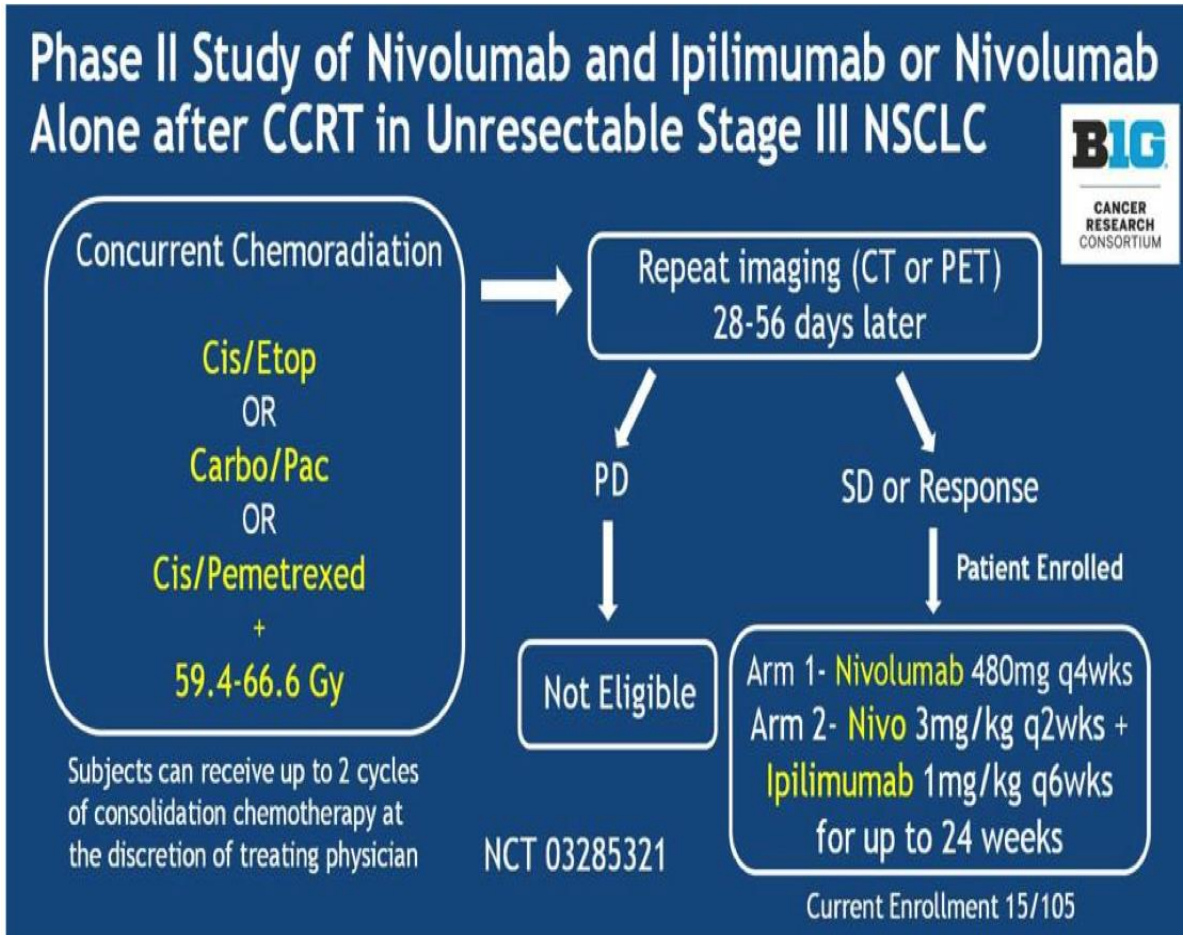
NUEVAS ESTRATEGIAS EN EL ESTADIO III IRRESECABLE

1. Intensification of the consolidation phase post-CRT
2. Integration of immunotherapy with CRT + consolidation
3. Induction with CT-IO (or IO alone) followed by CRT and subsequent maintenance
4. Sequential CT→RT + consolidation with inmunotherapy
5. RT+ consolidation with inmunotherapy
6. Biomarkers: ctDNA

Intensification of the consolidation phase post-CRT

Intensification of the consolidation phase post-CRT

BTCRC LUN 16–081: FASE II. n:105 PACIENTES



KEY RESULTS:

- At the time of analysis, **efficacy and safety** were reported, including for the primary endpoint of PFS[3, 4]

Table 3: Efficacy outcomes in BTCRC-LUN16-081[3]

Efficacy outcome	NIVO (n = 52)	NIVO + IPI (n = 47)
Median PFS, months (95% CI)	25.8 (23.0–NR)	25.4 (25.0–NR)
18-month PFS rate, % (95% CI)	64.0 (53.8–72.6)[a]	67.7 (57.6–75.9)[b]
Median OS, months (95% CI)	NR (NR–NR)	NR (28.1–NR)
18-month OS rate, % (95% CI)	82.8 (69.5–90.7)	85.7 (72.3–92.9)
24-month OS rate, % (95% CI)	78.2 (63.9–87.3)	80.8 (66.1–89.6)

Abbreviations: CCRT, concurrent chemoradiotherapy; CI, confidence interval; IPI, ipilimumab; NIVO, nivolumab; NR, not reached; OS, overall survival; PFS, progression-free survival.
Table adapted from Durm et al., WCLC, 2022.
[a]$P < 0.1$ vs historical control of CCRT alone.
[b]$P < 0.1$ vs historical control of CCRT followed by durvalumab.

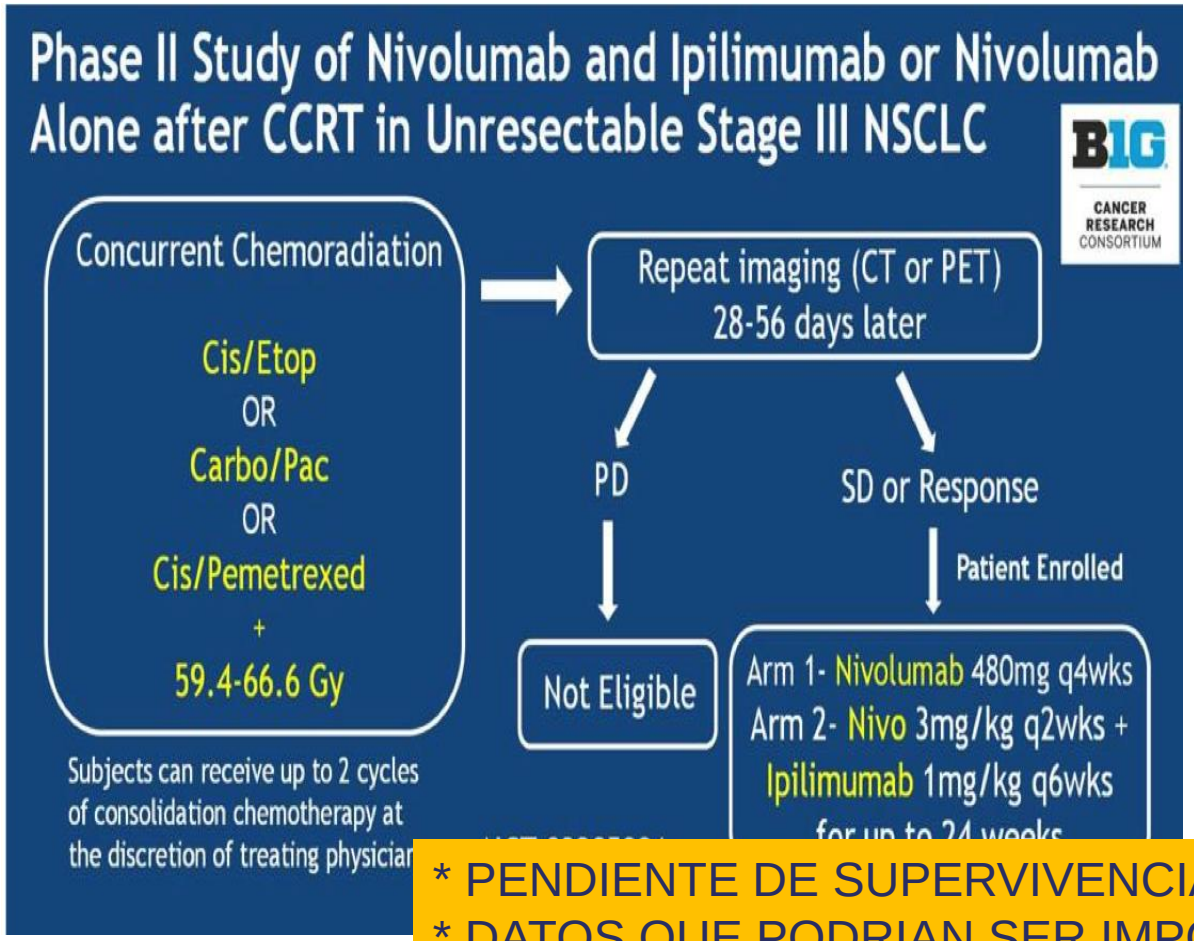
Table 4: Safety in BTCRC-LUN16-081[3]

Outcome, n (%)	NIVO (n = 54)	NIVO + IPI (n = 51)
Any TRAE	39 (72.2)	41 (80.4)
Grade ≥ 3 TRAEs	10 (18.5)	14 (27.5)

J Clin Oncol. 2022;40(suppl 16):8509–8509.

Intensification of the consolidation phase post-CRT

BTCRC LUN 16–081: FASE II. n:105 PACIENTES



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* PENDIENTE DE SUPERVIVENCIA GLOBAL
* DATOS QUE PODRIAN SER IMPORTANTES:
  - POBLACIÓN PDL1: NEGATIVOS
  - DURACIÓN DE MANTENIMIENTO 6 MESES

J Clin Oncol. 2022;40(suppl 16):8509–8509.

SKYSCRAPER-03:phase III study of tiragolumab + atezolizumab versus durvalumab after platinum-based chemoradiotherapy in unresectable stage III NSCLC

Actual study start date: 2020
Estimated primary completion date: 2024

- **Stage III unresectable NSCLC**
- **Without progression after platinum-based cCRT (≥2 cycles)**
- **Known PD-L1 status**
- **ECOG PS 0–1**
- ***EGFR/ALK* WT**

N=800*

Randomised within 1–42 days after last dose of cCRT

R 1:1

Tiragolumab 840mg i.v. q4w + atezolizumab 1,680mg i.v. q4w for 13 cycles (12 months)

Durvalumab 10mg/kg i.v. q2w or 1500mg i.v. q4w on 28-day cycle for 13 cycles (12 months)

Primary endpoint:
- Independent review facility-assessed PFS

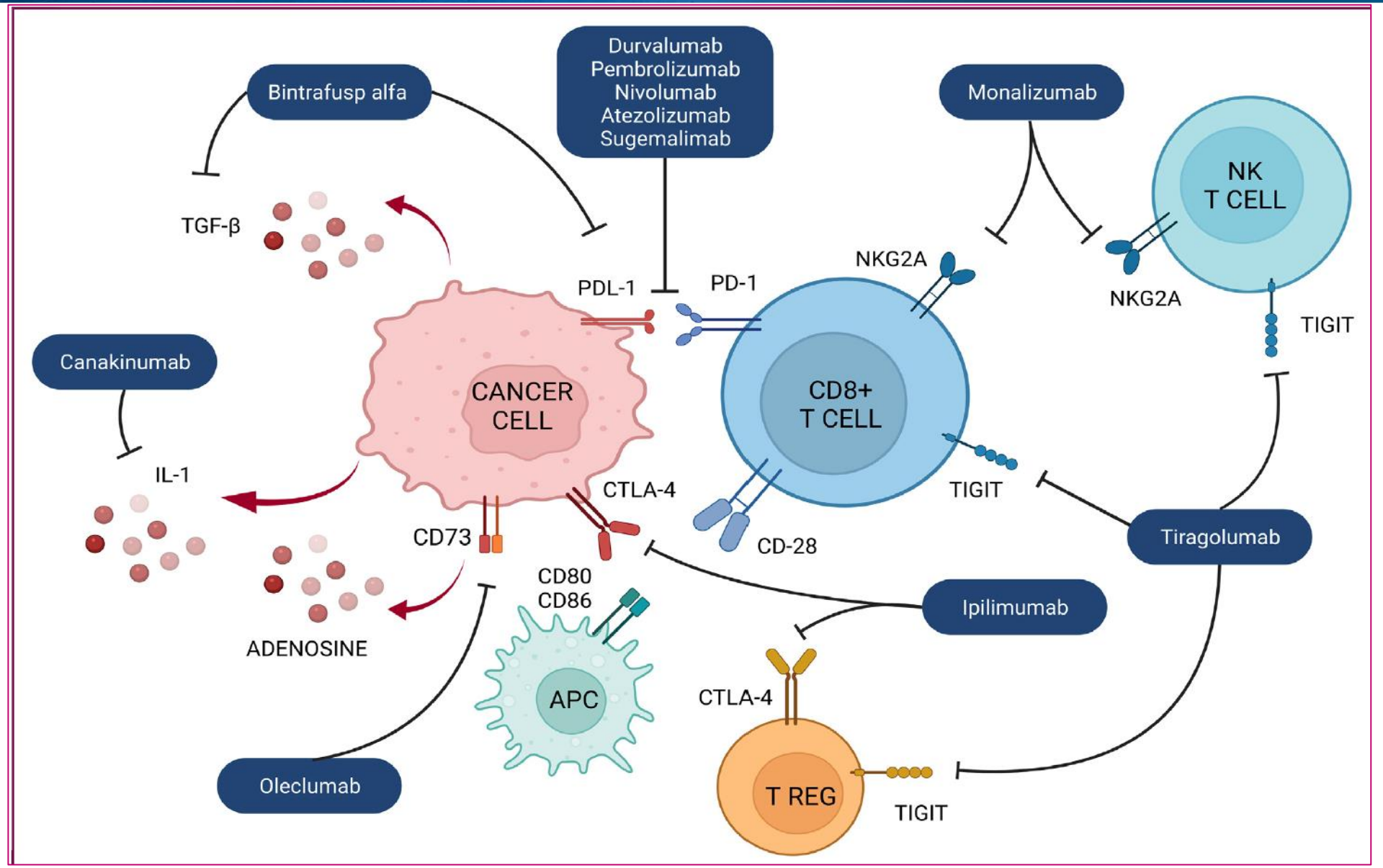
Key secondary endpoints:
- OS, ORR, DOR, PFS & OS rates, TTDM, PROs, safety

Stratification factors:
- PD-L1 status
- ECOG PS
- Staging
- Histology

*Includes safety run-in: 24 patients (12 per arm) who have completed first 2 full cycles

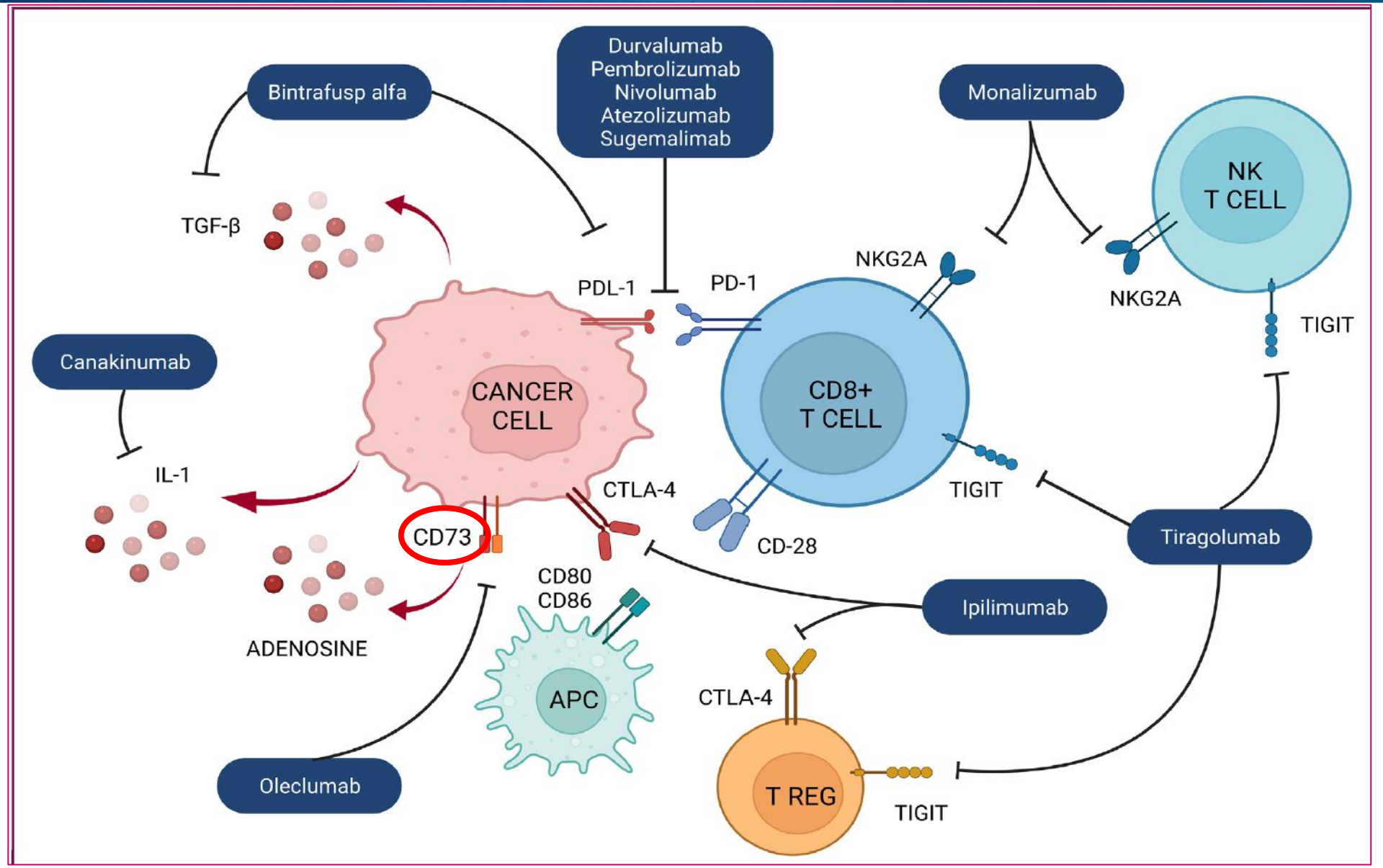
NCT04513925

OTRAS COMBINACIONES…



Cortiula, Ann Oncol 2022

OTRAS COMBINACIONES…



Cortiula, Ann Oncol 2022

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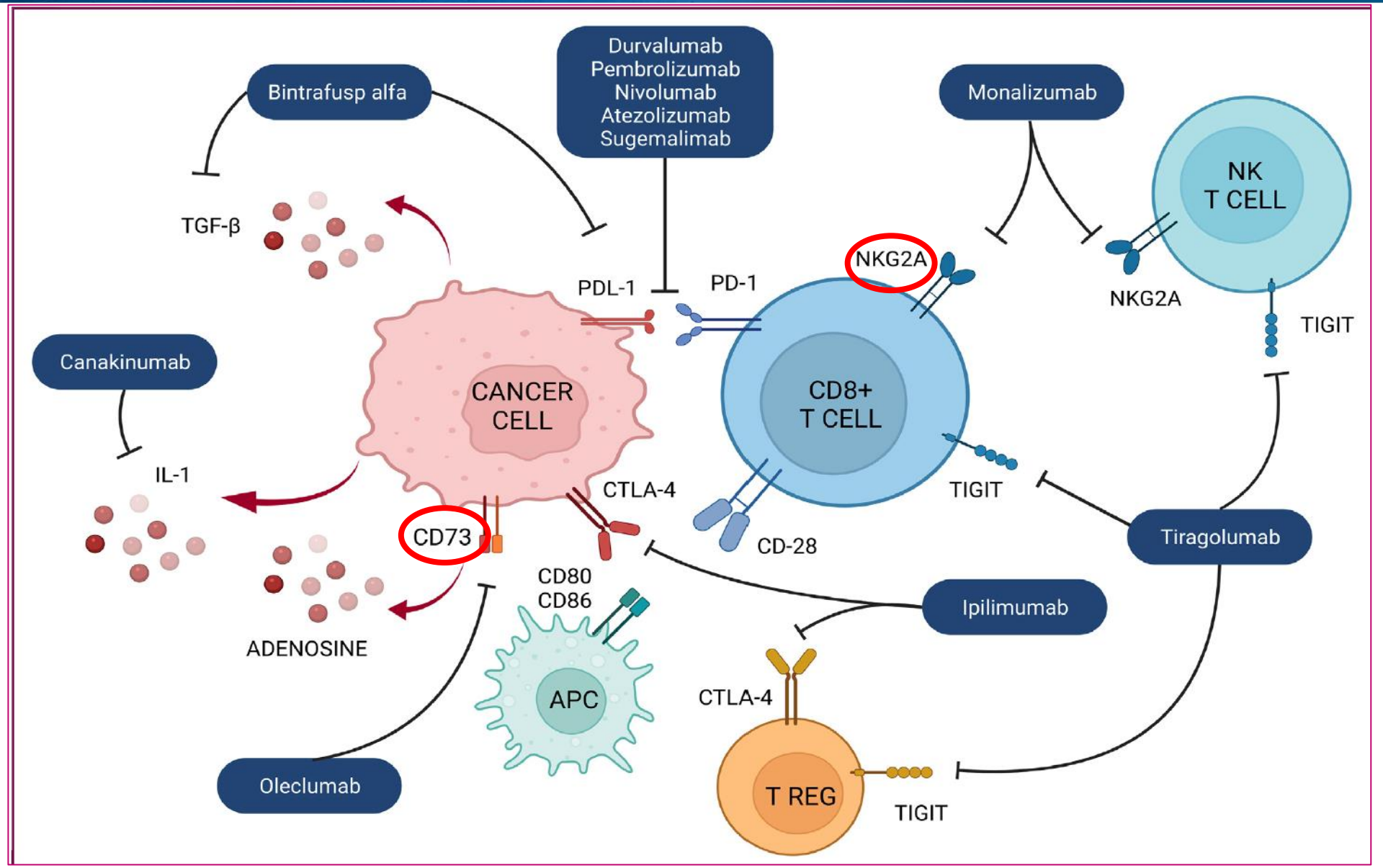
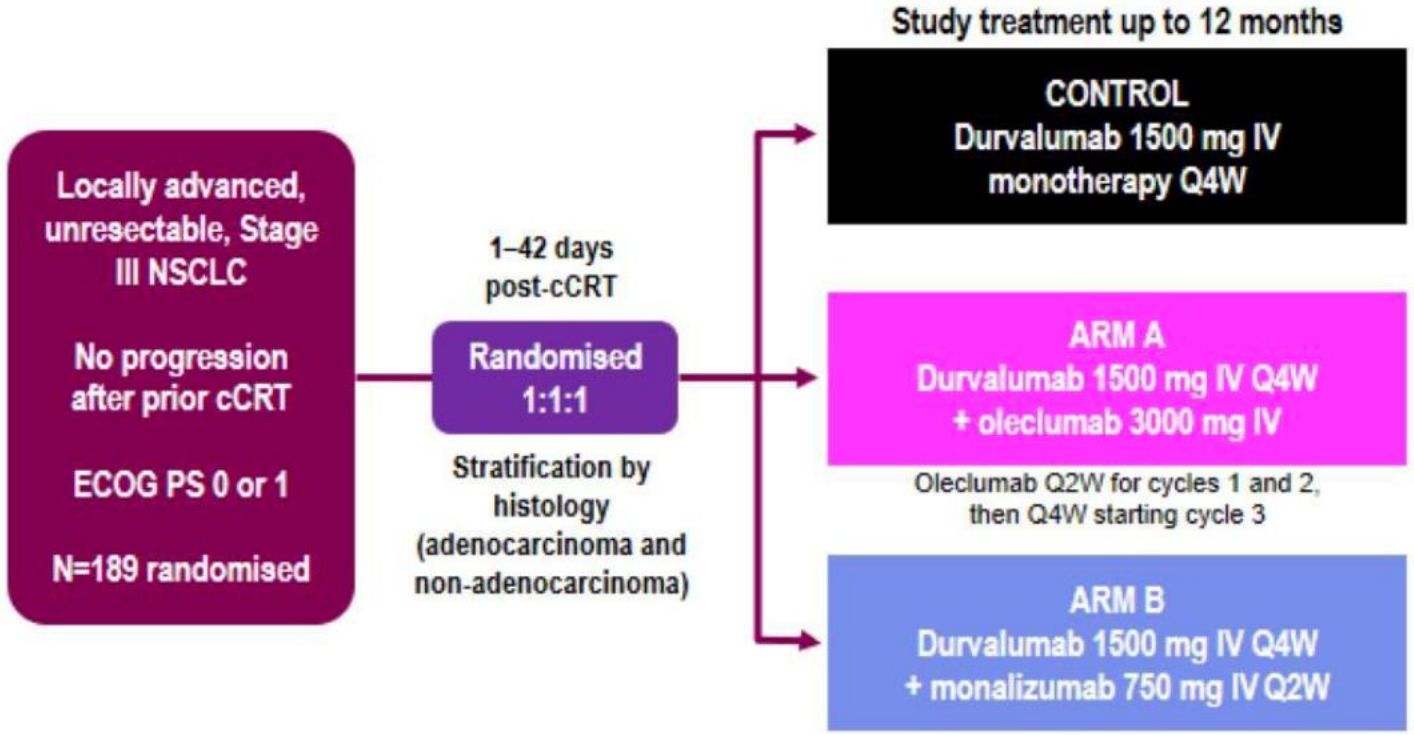


Cortiula, Ann Oncol 2022

COAST: Phase 2, randomised open-label study



Primary Endpoint
- ORR by investigator assessment (RECIST v1.1)

Secondary Endpoints
- Safety
- DoR
- DCR
- PFS by investigator assessment (RECIST v1.1)
- OS
- PK
- Immunogenicity

- A planned sample size of 60 patients per arm was designed to provide acceptable precision in estimating antitumour activities in an early phase setting
- Between Jan 2019 and Jul 2020, 189 patients were randomised of whom 186 received D (n=66), D+O (n=59) or D+M (n=61)
- As of 17 May 2021, all patients had a minimum of 10 months potential follow-up and the median actual follow-up was 11.5 months (range, 0.4–23.4; all patients)

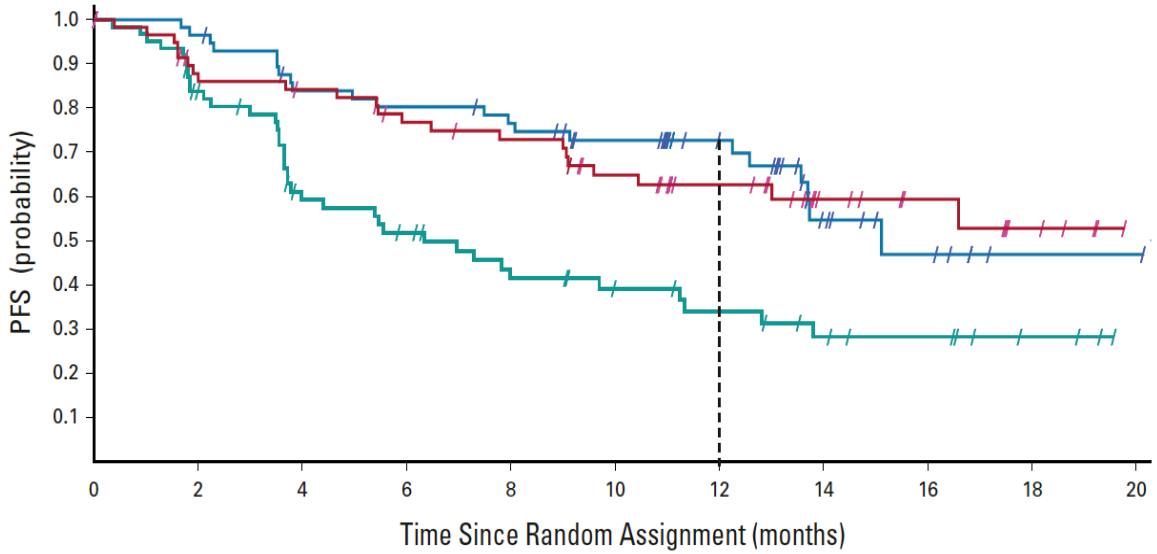
Antitumour activity by investigator assessment
(interim analysis; ITT population)

Antitumour activity	D (N=67)	D+O (N=60)	D+M (N=62)
Confirmed ORR (95% CI),[b] %	**17.9 (9.6, 29.2)**	**30.0 (18.8, 43.2)**	**35.5 (23.7, 48.7)**
[n]	[12]	[18]	[22]
Confirmed + unconfirmed ORR (95% CI),[b] %	**25.4 (15.5, 37.5)**	**38.3 (26.1, 51.8)**	**37.1 (25.2, 50.3)**
[n]	[17]	[23]	[23]
ORR odds ratio (95% CI)[a,b]	–	**1.83 (0.80, 4.20)**	**1.77 (0.77, 4.11)**
Objective responses by RECIST,[a] n (%)			
CR	2 (3.0)	1 (1.7)	3 (4.8)
PR	15 (22.4)	22 (36.7)	20 (32.3)
SD	27 (40.3)	25 (41.7)	27 (43.5)
PD	15 (22.4)	7 (11.7)	7 (11.3)
NE	8 (11.9)	5 (8.3)	4 (6.5)
DCR at 16 weeks (95% CI),[a,c] %	**58.2 (45.5, 70.2)**	**81.7 (69.6, 90.5)**	**77.4 (65.0, 87.1)**
[n]	[39]	[49]	[48]
Median DoR (95% CI),[a] months	**NR (2.3, NA)**	**12.9 (6.7, NA)**	**NR (9.0, NA)**
Range	0.0+, 17.5+	0.0+, 16.9+	1.9+, 18.4+

Data cutoff: 17 May 2021 (median follow-up of 11.5 months; range, 0.4–23.4)

PFS by investigator assessment (interim analysis; ITT population)

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:

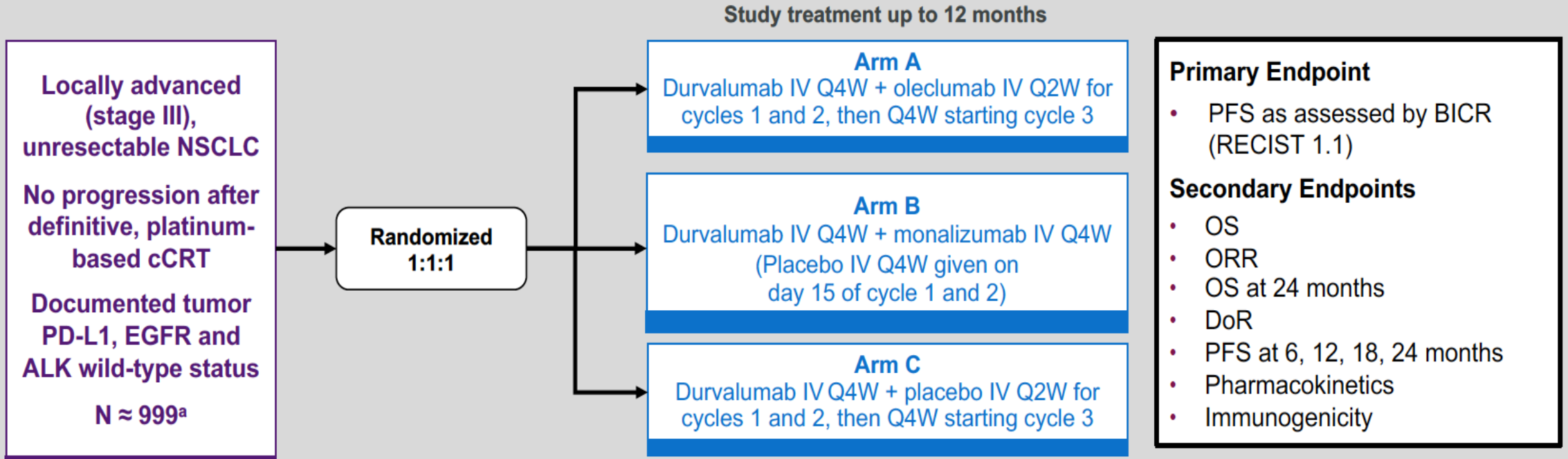
Durvalumab + monalizumab	62	55	46	44	41	35	25	11	6	1	1
Durvalumab + oleclumab	60	49	46	40	37	30	22	13	9	5	0
Durvalumab	67	50	32	27	20	16	13	9	7	3	0

Characteristic[a]	Durvalumab (n = 67)	Durvalumab + Oleclumab (n = 60)	Durvalumab + Monalizumab (n = 62)
Median age, years (range)	66.0 (46-81)	65.0 (37-83)	65.0 (44-87)
Male, %	67.2	70.0	67.7
Race, No. (%)[b]			
American Indian or Alaska Native	0	1 (1.7)	0
Asian	5 (7.7)	4 (6.8)	5 (8.1)
Black or African American	1 (1.5)	5 (8.5)	2 (3.2)
Native Hawaiian or Other Pacific Islander	1 (1.5)	0	0
White	57 (87.7)	47 (79.7)	55 (88.7)
Other	1 (1.5)	2 (3.4)	0
ECOG PS, No. (%)[b]			
0	30 (45.5)	33 (55.9)	27 (44.3)
1	36 (54.5)	26 (44.1)	34 (55.7)
Ever smoked, No. (%)	63 (94.0)	54 (90.0)	59 (95.2)
Histology, No. (%)			
Squamous	30 (44.8)	24 (40.0)	27 (43.5)
Nonsquamous	37 (55.2)	36 (60.0)	35 (56.5)
Disease stage at study entry, No. (%)			
IIIA	27 (40.3)	27 (45.0)	32 (51.6)
IIIB	34 (50.7)	29 (48.3)	27 (43.5)
IIIC	6 (9.0)	4 (6.7)	3 (4.8)
PD-L1 status, No. (%)[c]			
TC ≥ 1%	30 (44.8)	23 (38.3)	20 (32.3)
TC < 1%	16 (23.9)	7 (11.7)	12 (19.4)
Unknown	21 (31.3)	30 (50.0)	30 (48.4)
Prior RT dose, Gy, No. (%)			
54-66	62 (92.5)	54 (90.0)	57 (91.9)
> 66	5 (7.5)	6 (10.0)	5 (8.1)
Time from last RT to random assignment, days, No. (%)			
< 14	9 (13.4)	4 (6.7)	6 (9.7)
14-28	27 (40.3)	27 (45.0)	30 (48.4)
29-42	31 (46.3)	29 (48.3)	26 (41.9)
Prior platinum-based CT, No. (%)[d]			
Cisplatin	23 (34.3)	28 (46.7)	15 (24.2)
Carboplatin	43 (64.2)	28 (46.7)	44 (71.0)

Herbst, JCO April 24, 2022

PACIFIC-9

Phase III, randomized, double-blind, placebo-controlled multicenter study

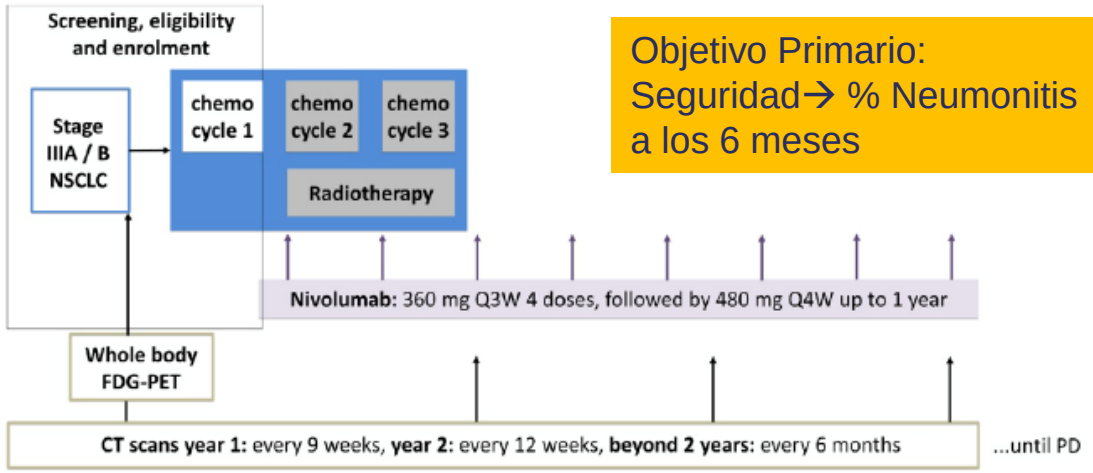


Study NCT05221840. Clinicaltrials.gov website

Integration of immunotherapy with CRT + consolidation

ESTUDIO NICOLAS (NCT02434081)

NICOLAS (NCT02434081) is a single-arm phase II trial assessing the safety and efficacy of the administration of nivolumab consolidation to standard first-line chemo-RT in unresectable locally advanced stage IIIA/B NSCLC.



Objetivo Primario: Seguridad→ % Neumonitis a los 6 meses

Methods

Statistical Considerations

Primary endpoint:

- Pneumonitis-free rate of grade ≥3 (CTCAE V4.0) observed any time during 6 months post radiotherapy.

Key secondary endpoint:

- 1-year progression-free survival

Other secondary endpoints:

- Time to first pneumonitis event of grade ≥ 3
- Objective response rate
- Time to treatment failure
- Overall survival
- Adverse events - Toxicity

Safety evaluation:

➢ ***Interim safety analysis, n=21:***
Pneumonitis-free rate of grade ≥3 at 3 months post-RT
Assumption: 70% of events occur within the 3 months
(O'Brien-Fleming approach)
Success rule: NO events

➢ ***Primary safety evaluation, n=41***
(if safety not proven at interim):
Pneumonitis-free rate of grade ≥3 at 6 months post-RT
H_0: $\pi_0 \leq 67\%$ vs H_1: $\pi_1 > 85\%$
(1-sided alpha=5%, power=83%)
Success rule: up to 8 events

Hierarchical design: IF safety proven →
- Efficacy evaluation: 1-year PFS, n=74
H_0: $PFS_0 \leq 45\%$ vs H_1: $PFS_1 > 60\%$
(1-sided alpha=5%, power=83%)

Table 2: Safety in NICOLAS (N = 77)[2]

Outcome	Related to RT	Related to NIVO[a]
Any TRAE, n (%[b])	168 (21.5)	249 (31.9)
Grade ≥ 3 TRAEs, n	32	44
Leading to death, n	2	7
Leading to permanent discontinuation, n	6	16[c]
Pneumonitis grade ≥ 3, n (%)	9 (11.7)[d]	
1-year time to first pneumonitis of grade ≥ 3, % (95% CI)[e]	87.0 (76.4–93.0)[f]	

Efficacy outcome	NIVO + CCRT (n = 74; primary efficacy cohort)[a]
1-year PFS rate, % (95% CI)	50.0 (39.9–60.1); *P* = 0.23

Efficacy outcome	NIVO + CCRT (n = 74; primary efficacy cohort)[a]
	NIVO + CCRT (N = 79; full CCRT cohort)
Median OS, months (95% CI)[b]	38.8 (26.8–NR)
1-year OS rate, % (95% CI)	75.7 (64.6–83.7)
2-year OS rate, % (95% CI)	63.7 (51.9–73.4)
ORR, % (95% CI)	73.4 (62.3–82.7)
Complete response, n (%)	5 (6.3)
Partial response, n (%)	53 (67.1)
DOR, months (95% CI)	11.0 (8.6–20.7)
Observed treatment failure, n (%)	58 (73.4)
1-year TTF, % (95% CI)	41.8 (30.8–52.3)

Lung Cancer 133 (2019) 83–87

PHASE II: DETERRED TRIAL

DETERRED Schema

Part 1 (N=10)

Concurrent ChemoRadiation* → Consolidation Chemo** + Atezolizumab IV Q3weeks x 2 cycles → Atezolizumab IV Q3weeks for 1 year

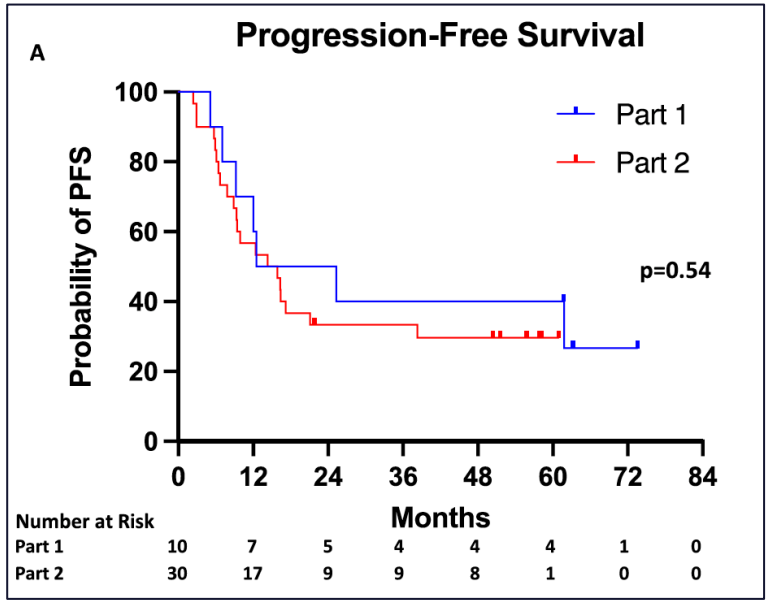
If no concerning toxicities

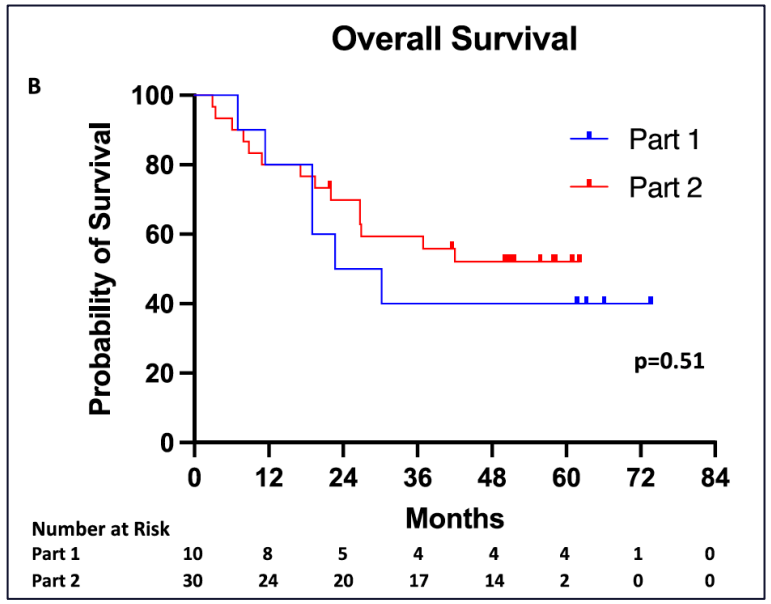
Atezolizumab = 1200 mg

Part 2 (N=30)

Concurrent ChemoRadiation* + Atezolizumab IV Q3weeks → Consolidation Chemo** + Atezolizumab IV Q3weeks x 2 cycles → Atezolizumab IV Q3weeks for 1 year

*weekly carboplatin AUC 2.0 and paclitaxel 50 mg/m² concurrent with radiation (60-66 Gy/30-33 fx)
**carboplatin AUC 6.0 and paclitaxel 200 mg/m² IV Q3 weeks for 2 cycles

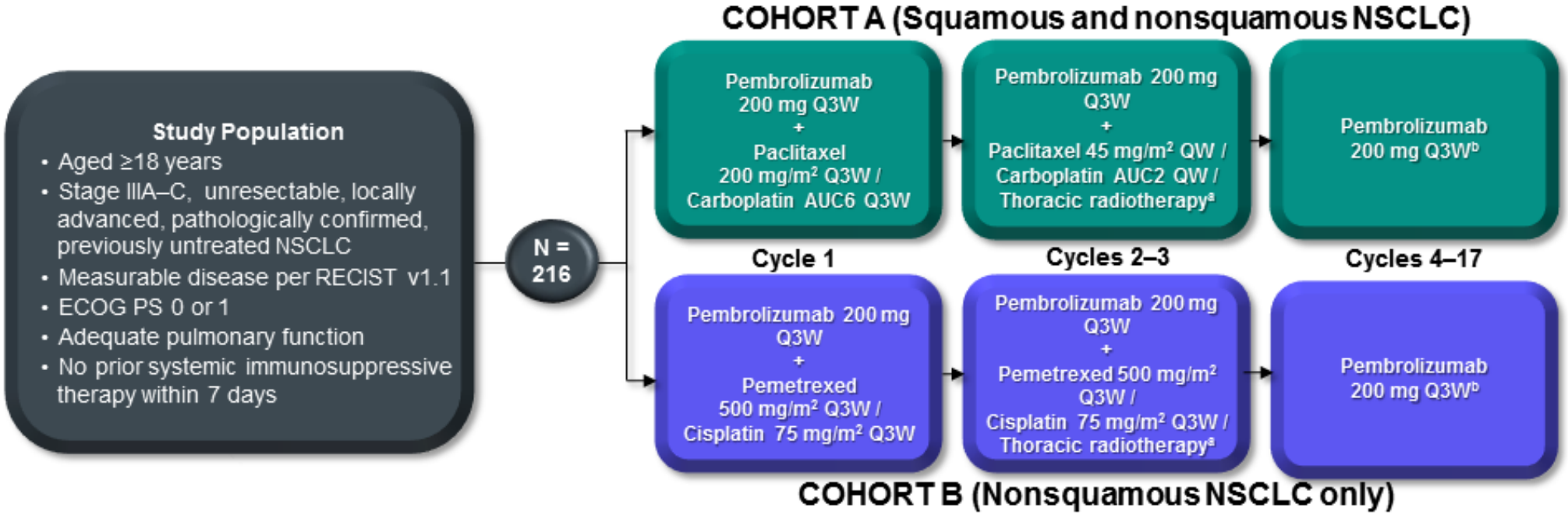




Lung Cancer 174 (2022) 112–117

M Reck. WCLC 2021.

KEYNOTE-799 (NCT03631784)



Primary Objectives

- ORR per RECIST version 1.1 by BICR
- Percentage of patients who develop grade ≥3 pneumonitis

Secondary Objectives

- PFS, OS, safety

Statistical Analysis Details

- Efficacy assessed in all patients with first study dose before or on October 31, 2019 (PE population)
- Safety assessed in all patients in the as-treated population

BICR, blinded, independent central review; PE, primary efficacy.

[a]60 Gy in 30 daily 2-Gy fractions. [b]Treatment will continue until cycle 17 is completed or until documented disease progression, unacceptable AEs, intercurrent illness that prevents further administration of treatment, or study withdrawal. Pembrolizumab therapy will be discontinued permanently in patients who develop grade ≥3 or recurrent grade 2 pneumonitis.

Two Years Update: Keynote 799

M Reck. WCLC 2021.

Baseline Characteristics

Characteristics	Cohort A[a] n = 112[b]	Cohort B[c] As-treated population n = 101	Cohort B[c] Primary efficacy population n = 61
Age, median (range), y	66.0 (46–90)	64.0 (35–81)	64.0 (45–78)
Men	76 (67.9)	62 (61.4)	36 (59.0)
ECOG PS 1	61 (54.5)	44 (43.6)	29 (47.5)
Histology			
Squamous	73 (65.2)	0	0
Nonsquamous	39 (34.8)	101 (100)	61 (100)
Former/current smoker	106 (94.6)	96 (95.0)	59 (96.7)
PD-L1 TPS			
≥1%	66 (58.9)	40 (39.6)	26 (42.6)
<1%	21 (18.8)	28 (27.7)	17 (27.9)
Unknown/not evaluable	25 (22.3)	33 (32.7)	18 (29.5)

TPS, tumor proportion score. Data listed as n (%) unless otherwise noted.
[a]Squamous and nonsquamous. [b]As-treated and primary efficacy populations were the same for cohort A. [c]Nonsquamous only.
Data cutoff: July 30, 2020.

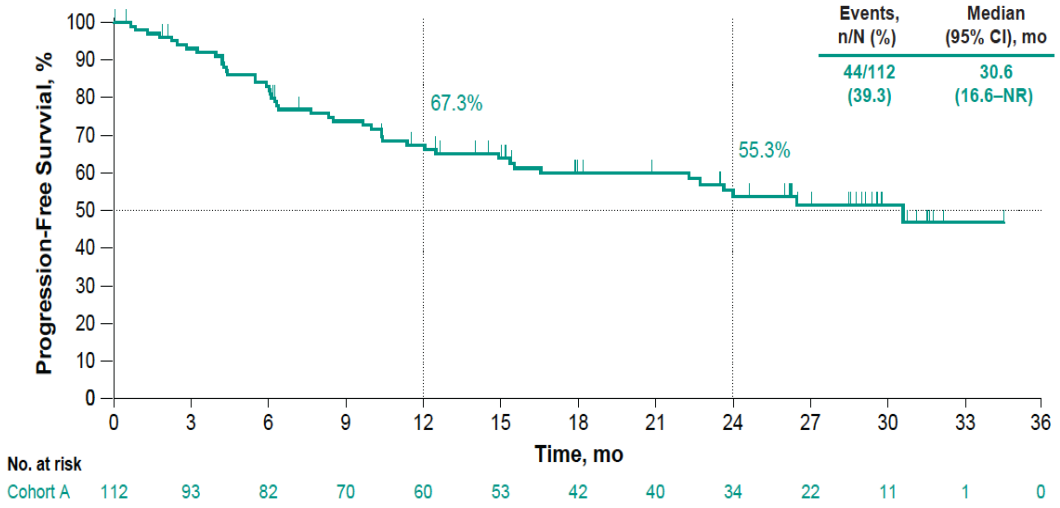
Table 3: ORR (95% CI) in the as-treated population and key patient subgroups

Subgroup	Cohort A[a] (n = 112)	Cohort B[b] (n = 102)
Overall population	**71.4 (62.1–79.6)[c]**	**75.5 (66.0–83.5)[d]**
Age		
<65 years	75.5 (61.1–86.7)	74.1 (60.3–85.0)
≥65 years	68.3 (55.3–79.4)	77.1 (62.7–88.0)
Sex		
Female	75.0 (57.8–87.9)	75.0 (58.8–87.3)
Male	69.7 (58.1–79.8)	75.8 (63.3–85.8)
Race		
White	74.2 (63.8–82.9)	79.7 (68.8–88.2)
All others	56.3 (29.9–80.2)	71.4 (41.9–91.6)
Region		
USA	56.5 (34.5–76.8)	81.8 (48.2–97.7)
All others	75.3 (65.0–83.8)	74.7 (64.5–83.3)
Cancer stage		
IIIA	73.2 (57.1–85.8)	76.9 (60.7–88.9)
IIIB	73.0 (60.3–83.4)	73.8 (58.0–86.1)
IIIC	50.0 (15.7–84.3)	76.2 (52.8–91.8)
Histology		
Squamous	72.0 (60.4–81.8)	N/A
Nonsquamous	70.3 (53.0–84.1)	75.5 (66.0–83.5)
ECOG PS		
0	74.5 (60.4–85.7)	73.7 (60.3–84.5)
1	68.9 (55.7–80.1)	77.8 (62.9–88.8)
PD-L1 TPS		
<1%	66.7 (43.0–85.4)	78.6 (59.0–91.7)
≥1%	77.3 (65.3–86.7)	72.5 (56.1–85.4)

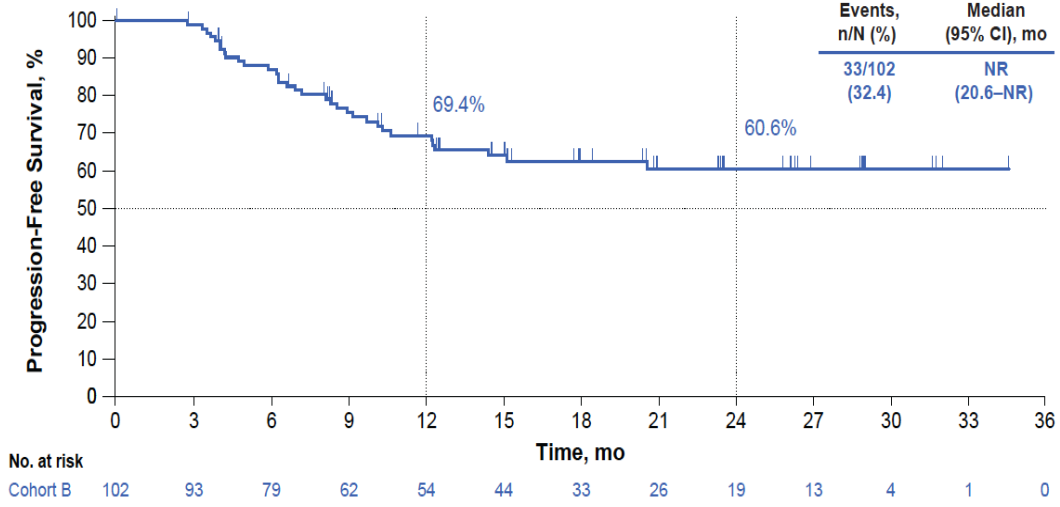
AE, n (%)	Cohort A[a] (n = 112)	Cohort B[b] (n = 102)
Grade ≥3 pneumonitis[c]	9 (8.0)	7 (6.9)
Treatment-related AEs	105 (93.8)	99 (97.1)
Grade 3–5	72 (64.3)	52 (51.0)
Occurring in >10% of patients in either cohort		
Neutropenia	18 (16.1)	10 (9.8)
Anemia	12 (10.7)	4 (3.9)
Led to death	4 (3.6)[d]	1 (1.0)[e]
Led to discontinuation of any treatment component	38 (33.9)	21 (20.6)
Immune-mediated AEs and infusion reactions[f]	58 (51.8)	46 (45.1)
Grade 3–5	18 (16.1)	9 (8.8)
Occurring in >5% of patients in either cohort		
Pneumonitis	7 (6.3)	6 (5.9)
Led to death	4 (3.6)[d]	1 (1.0)[e]
Led to discontinuation of any treatment component	21 (18.8)	12 (11.8)

Two Years Updte: Keynote 799

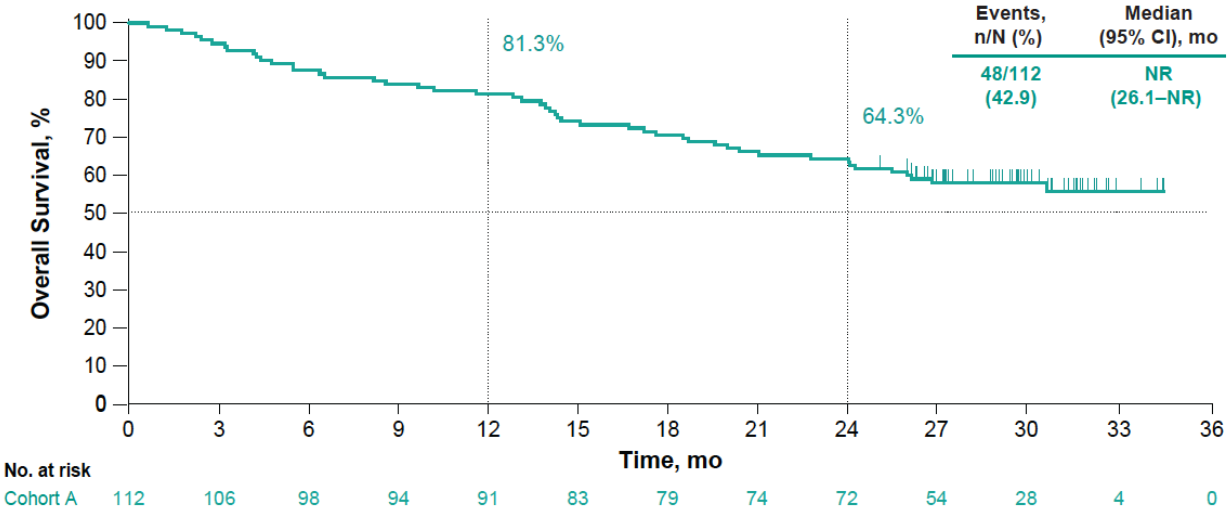
A. Cohort A (squamous and nonsquamous histology)



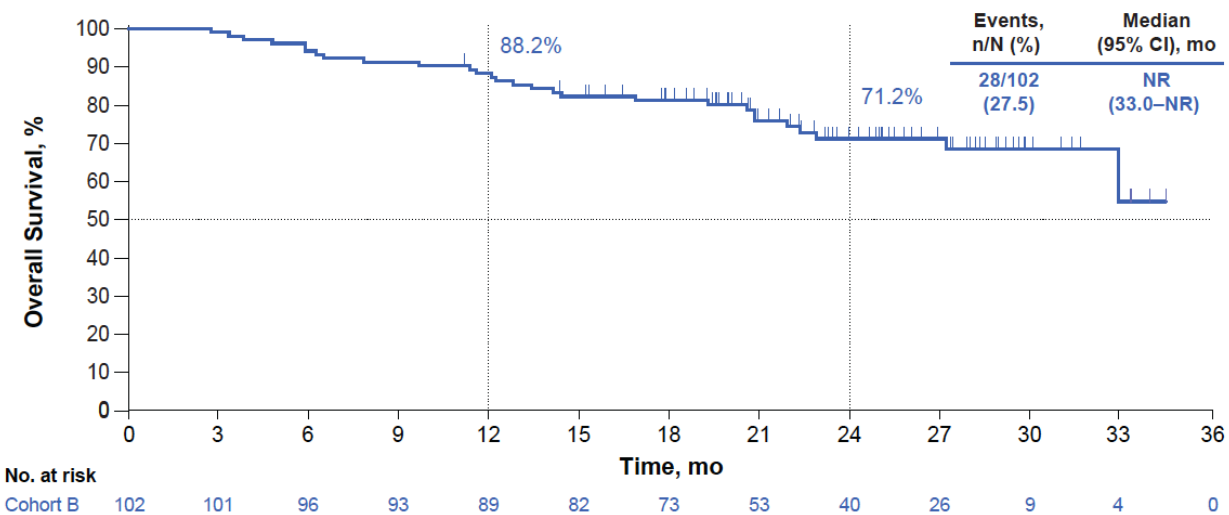
B. Cohort B (nonsquamous histology only)



A. Cohort A (squamous and nonsquamous histology)



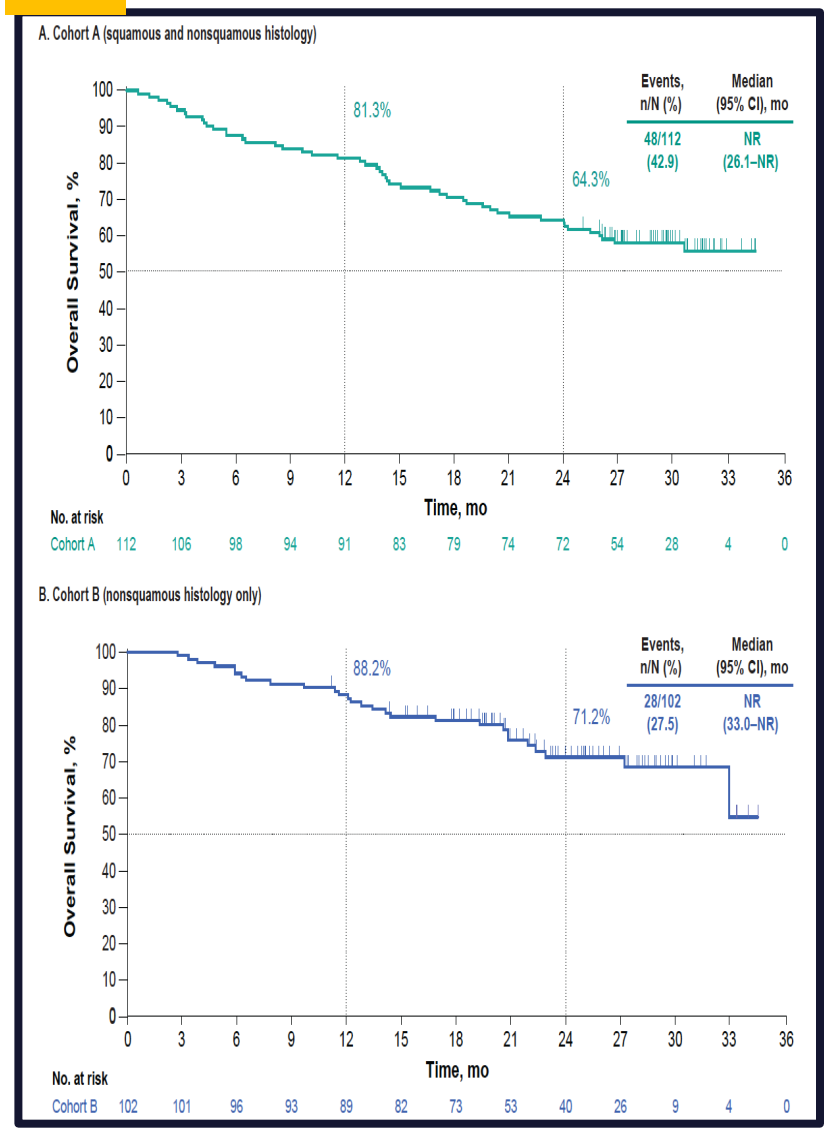
B. Cohort B (nonsquamous histology only)



Reck, ASCO 2022

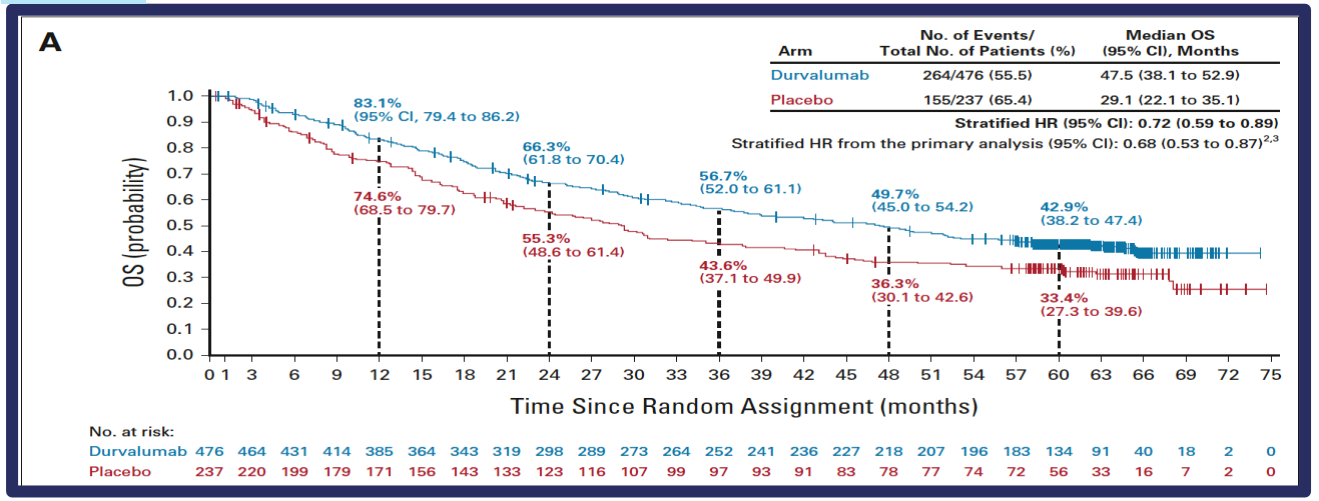
Two Years Updte: Keynote 799

KN799



Reck, ASCO 2022

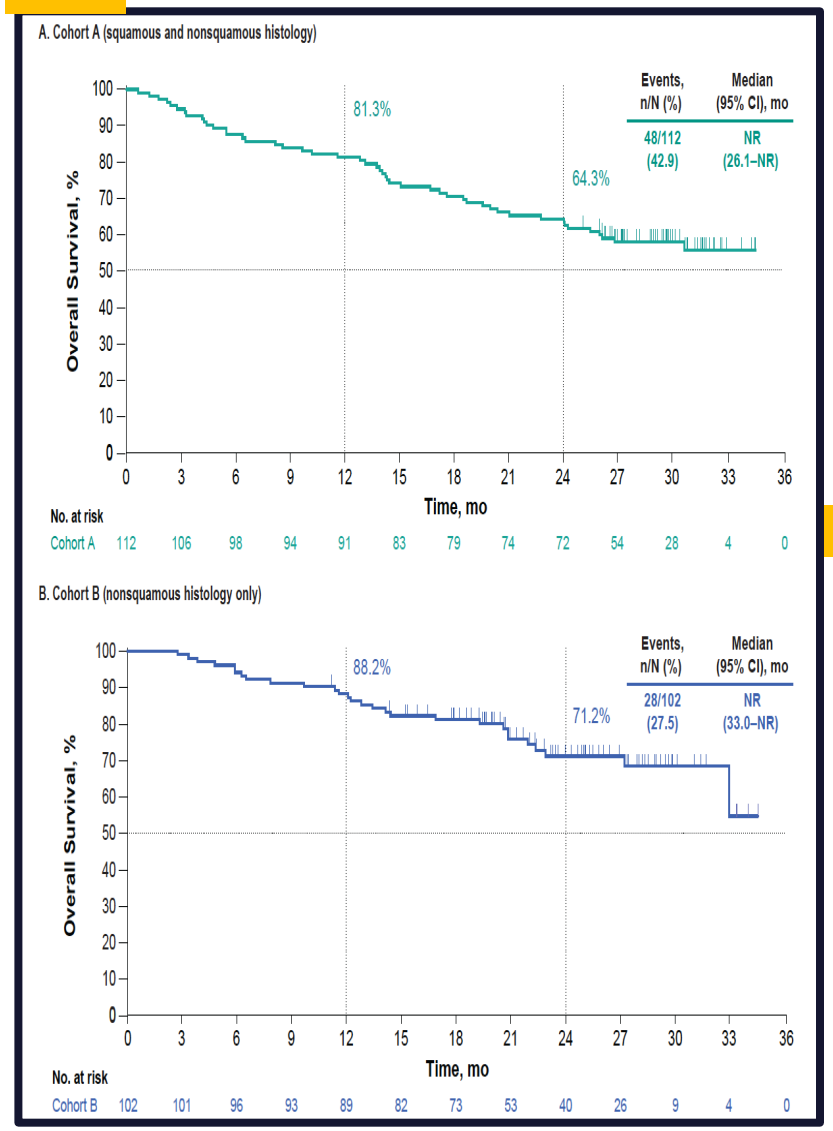
PACIFIC



Paz-Ares, Ann Oncol 2020,31:6

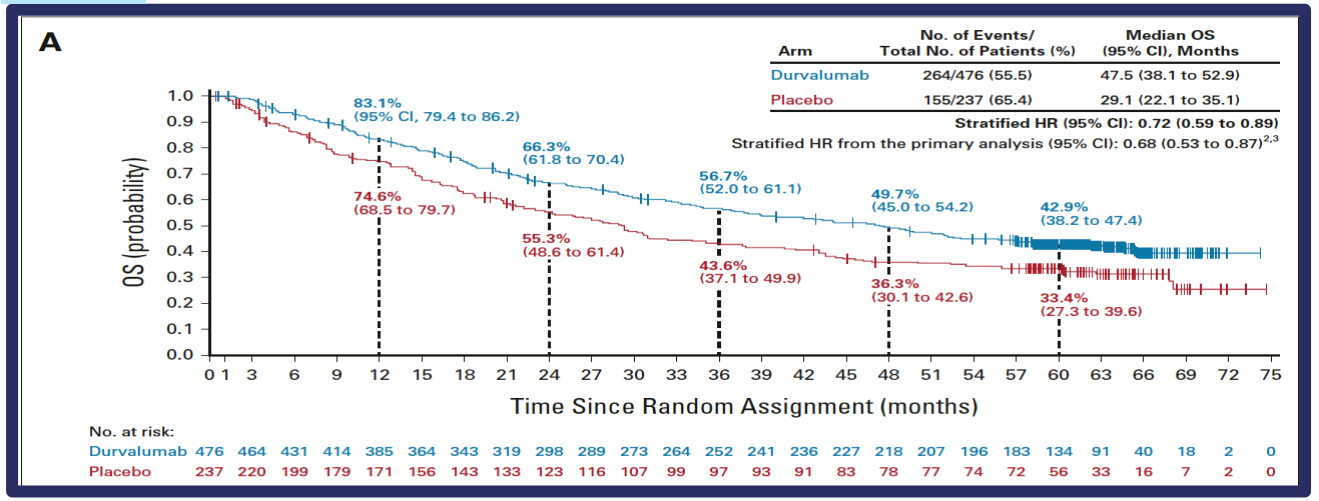
Two Years Updte: Keynote 799

KN799



Reck, ASCO 2022

PACIFIC



KN799

atient Demographics and Baseline Characteristics
ients as Treated

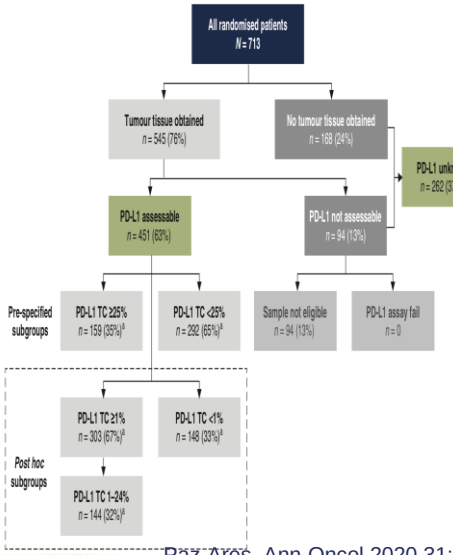
No pérdida peso >10%

Characteristic	No. (%)[a] Cohort A (n = 112)	Cohort B (n = 102)
Sex		
Men	76 (67.9)	62 (60.8)
Women	36 (32.1)	40 (39.2)
Age, median (range), y	66.0 (46-90)	64.0 (35-81)
Region of enrollment[b]		
East Asia	13 (11.6)	10 (9.8)
Non-East Asia	99 (88.4)	92 (90.2)
Smoking status		
Never	6 (5.4)	5 (4.9)
Former	75 (67.0)	65 (63.7)
Current	31 (27.7)	32 (31.4)
Tumor histologic type		
Squamous	73 (65.2)	NA
Nonsquamous	39 (34.8)	102 (100)
ECOG performance status		
0	51 (45.5)	57 (55.9)
1	61 (54.5)	45 (44.1)
Disease stage		
IIIA	41 (36.6)	39 (38.2)
IIIB	63 (56.3)	42 (41.2)
IIIC	8 (7.1)	21 (20.6)
PD-L1 status		
TPS<1%	21 (18.8)	28 (27.5)
TPS≥1%	66 (58.9)	40 (39.2)
Not evaluable[c]	6 (5.4)	2 (2.0)
Unknown[d]	19 (17.0)	32 (31.4)

PACIFIC

Table 1. Baseline Characteristics, Stratification Factors, and Prior Therapy in the Intention-to-Treat Population.*

Characteristic	Durvalumab (N=476)	Placebo (N=237)	Total (N=713)
Age — yr			
Median	64	64	64
Range	31–84	23–90	
Sex — no. (%)			
Male	334 (70.2)	166 (70.0)	
Female	142 (29.8)	71 (30.0)	
Race — no. (%)†			
White	337 (70.8)	157 (66.2)	
Black	12 (2.5)	2 (0.8)	
Asian	120 (25.2)	72 (30.4)	
Disease stage — no. (%)			
IIIA	252 (52.9)	125 (52.7)	
IIIB	212 (44.5)	107 (45.1)	
Other‡	12 (2.5)	5 (2.1)	
WHO performance-status score — no. (%)§			
0	234 (49.2)	114 (48.1)	
1	240 (50.4)	122 (51.5)	
Tumor histologic type — no. (%)			
Squamous	224 (47.1)	102 (43.0)	
Nonsquamous	252 (52.9)	135 (57.0)	
Smoking status — no. (%)			
Current smoker	79 (16.6)	38 (16.0)	
Former smoker	354 (74.4)	178 (75.1)	
Never smoked	43 (9.0)	21 (8.9)	
Previous radiotherapy — no. (%)¶			
<54 Gy	3 (0.6)	0	
≥54 to ≤66 Gy	442 (92.9)	217 (91.6)	
>66 to ≤74 Gy	30 (6.3)	19 (8.0)	
Previous chemotherapy — no. (%)‖			
Induction	123 (25.8)	68 (28.7)	
Concurrent with radiation therapy	475 (99.8)	236 (99.6)	
Best response to previous chemoradiotherapy — no. (%)			
Complete response	9 (1.9)	7 (3.0)	
Partial response	232 (48.7)	111 (46.8)	
Stable disease	222 (46.6)	114 (48.1)	336 (47.1)



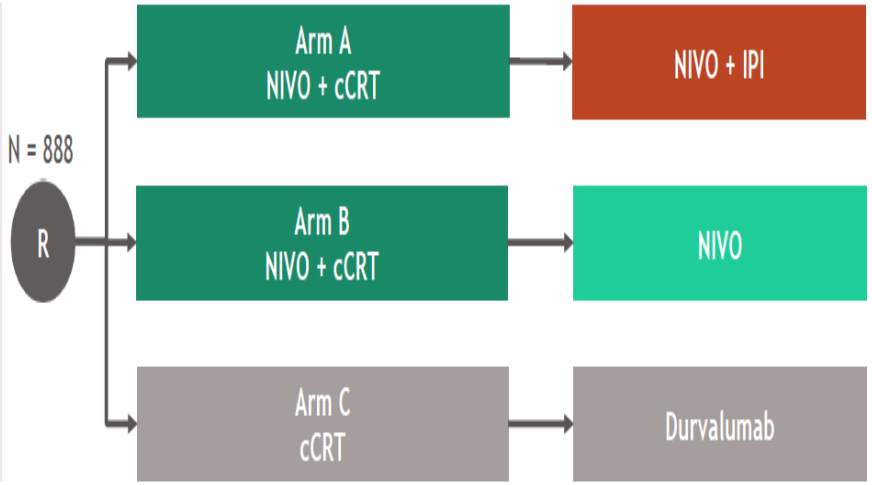
Paz-Ares, Ann Oncol 2020,31:6

Phase 3 trial of NIVO + cCRT followed by NIVO ± IPI vs cCRT followed by durvalumab in untreated, locally advanced NSCLC (CheckMate 73L) (CA209-73L / NCT04026412)[1,2]

Phase 3 trial

Select eligibility criteria

- Histologically confirmed, locally advanced (stage IIIA-IIIC[a]) NSCLC
- Newly diagnosed and treatment-naive
- ECOG PS 0-1
- No active infection requiring systemic therapy ≤ 14 days prior to randomization
- No history of organ or tissue transplant that required systemic immune suppressive agents
- No prior thoracic radiotherapy



Purpose

- To compare the effectiveness of NIVO + cCRT followed by NIVO + IPI versus cCRT followed by durvalumab in patients with untreated, locally advanced NSCLC

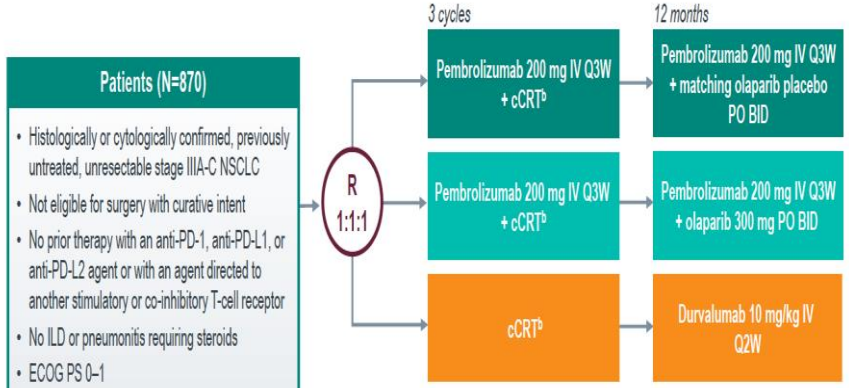
Primary endpoint

- PFS (Arms A vs C)

Secondary endpoints

- OS (Arms A vs C)
- PFS and OS (Arms B vs C)
- ORR, DOR, and TTR
- Time to death or distant metastases
- Safety
- PROs

KEYLYNK-012: Phase 3, Double-blind, Placebo-controlled Study of Pembrolizumab + Concurrent CRT Followed by Pembrolizumab ± Olaparib in Patients With Unresectable, Locally Advanced, Stage III NSCLC



Stratification Factors[a]

- Stage (IIIA vs IIIB/IIIC)
- Tumor histology (SQ vs NSQ)
- PD-L1 expression (TPS <50% vs ≥50%)
- Geographic region (East Asia vs North America/Western Europe/UK vs Other)

Primary End Points

- PFS[c]
- OS

Secondary End Points

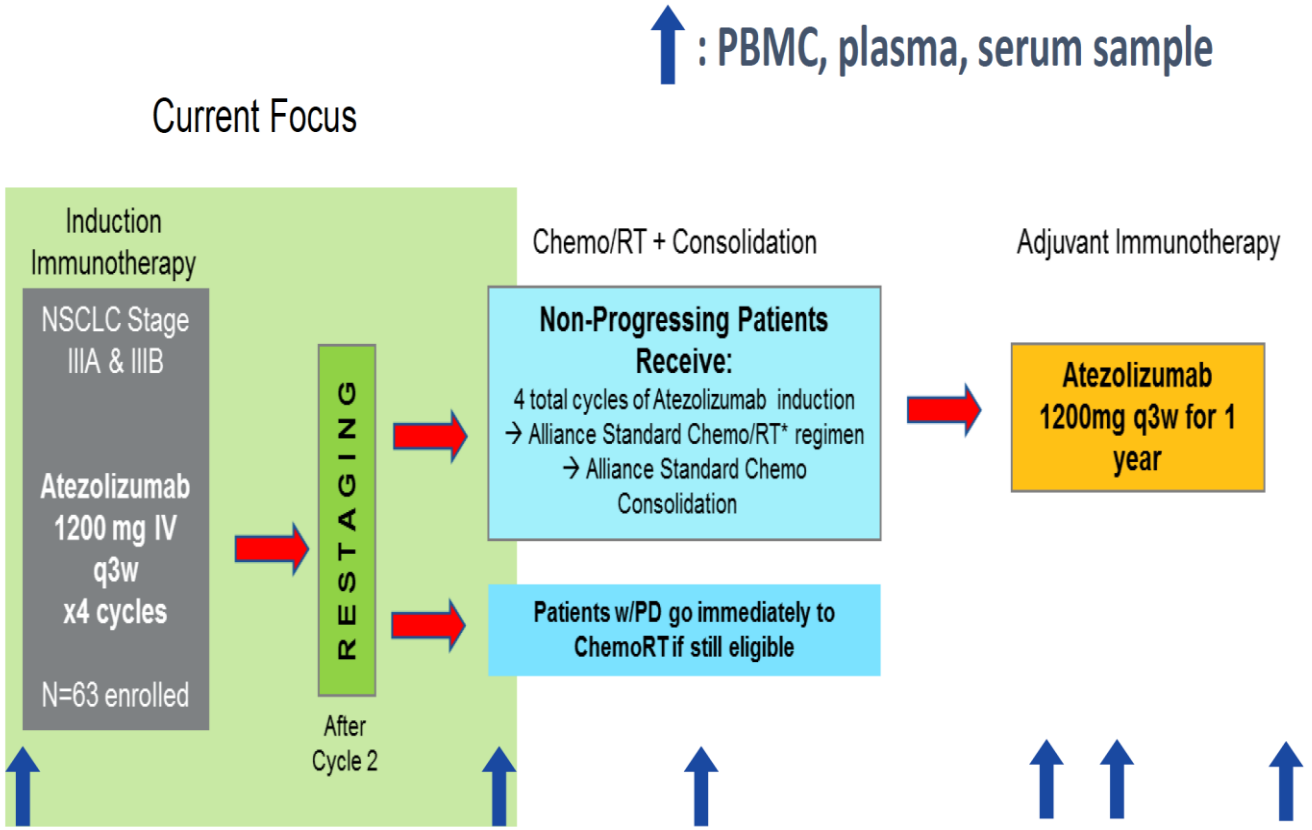
- Safety
- ORR[c]
- DOR[c]
- HRQoL

Exploratory End Points

- Assess ctDNA and its correlation with efficacy end points
- Identify molecular biomarkers of response, safety, and activity
- Efficacy outcomes by PD-L1 levels
- Efficacy by iRECIST (investigator assessement)
- PFS2 (per RECIST v1.1 by investigator assessement), TFST, and TSST
- Characterize health utility for use in economic models

Induction with CT-IO (or IO alone) followed by CRT and subsequent maintenance

AFT16 Study Design

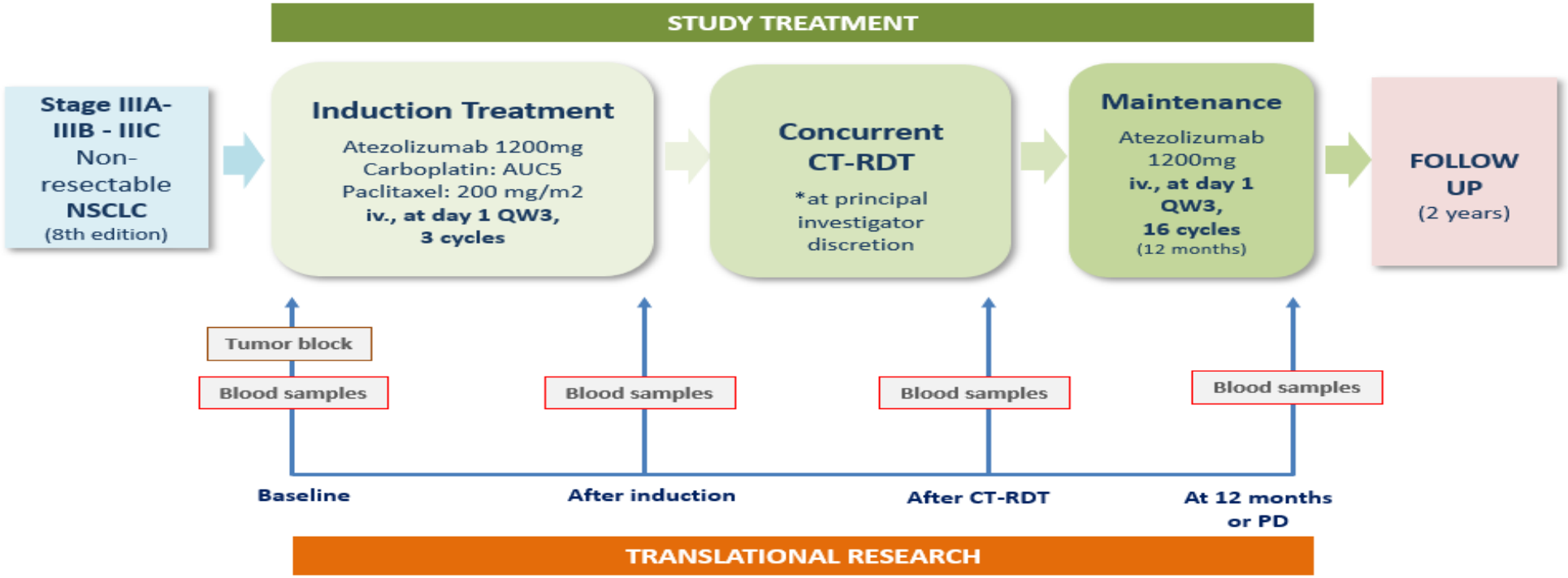


	DATOS DISPONIBLES
OBJETIVO PRIMARIO	Control enfermedad tras la inducción con atezolizumab
Mediana PFS	23.7 months (95% CI 13.2 months-NR),
PFS 1 año	66% (95% CI 55% to 79%)
PFS 18 meses	57% (95% CI 45% to 71%),
PFS a los 12 meses de terminar QT+RT	78%* (PACIFIC PFS 12m 55%) * Pacientes muy seleccionados

Ross H. ASCO 2021;Cortiula, Ann Oncol 2022

Estudio APOLO

- **Pharma Partner:** Hoffmann-La Roche
- **Protocol code:** GECP 20/08 (ML42787)
- **Population:** non-resectable stage IIIA-IIIB-IIIC non-small cell lung cancer patients
- **Design:** Open-label, non-randomized, phase II multi-centre controlled clinical trial



¿Por qué la desescalada?

1.- Porque no siempre más es mejor
2.- Porque hay pacientes que no se benefician (p.ej driver)
3.- Porque hay pacientes que tienen toxicidades graves
4.- Porque la duración y los intervalos de los ciclos de la inmunoterapia de consolidación es arbitraria
5.- Porque hay pacientes que no pueden recibir esquemas de QT+RT o QT+IO+RT concomitante

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¿Cómo lo hacemos?....

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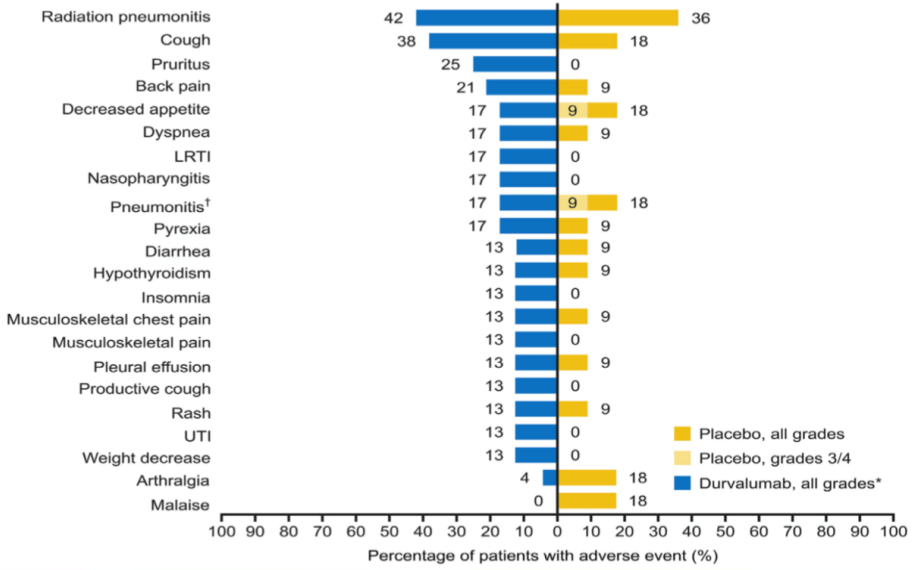
¿Cómo lo hacemos?....

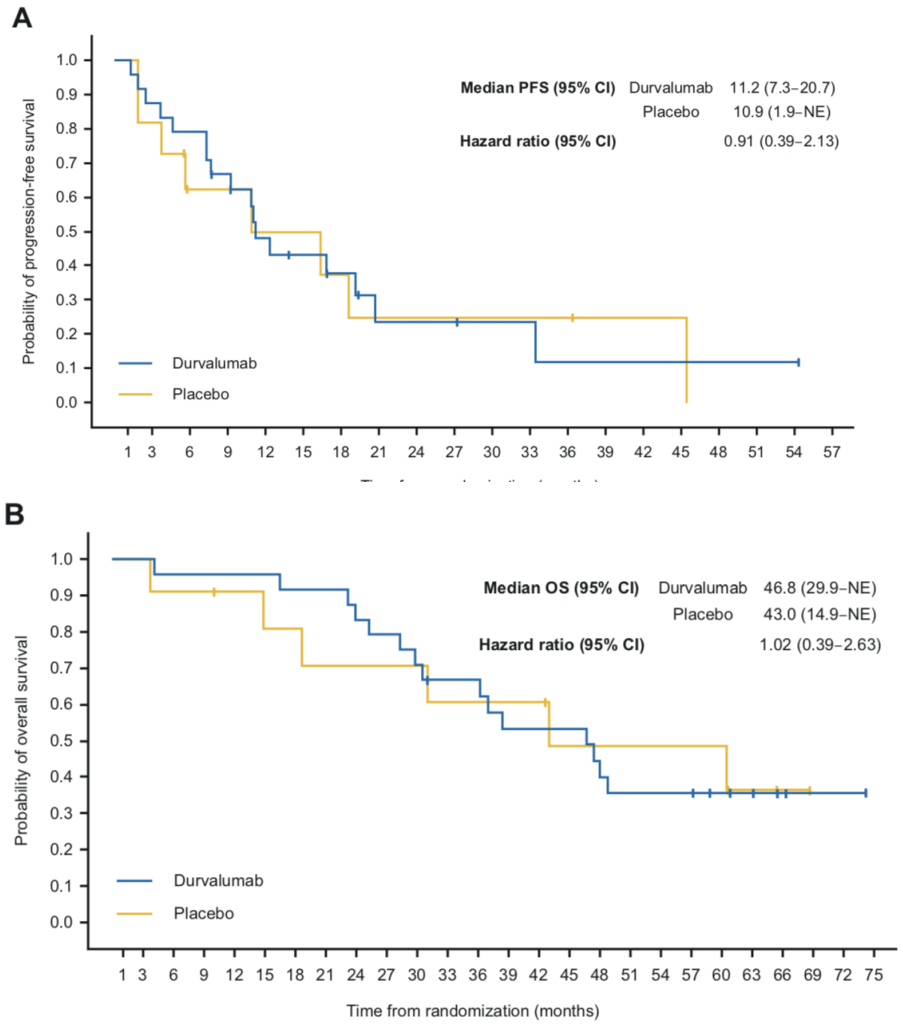
PACIENTE + BIOMARCADORES

Brief Report: Durvalumab After Chemoradiotherapy in Unresectable Stage III EGFR-Mutant NSCLC: A Post Hoc Subgroup Analysis From PACIFIC

Table 1. Baseline Demographics and Characteristics for the PACIFIC *EGFR*m Subgroup

Demographic or Characteristic	Durvalumab (n = 24)	Placebo (n = 11)	Total (N = 35)
Age (y): median (range)	65 (42-83)	69 (57-90)	67 (42-90)
Sex: male/female, n (%)	13 (54)/11 (46)	8 (73)/3 (27)	21 (60)/14 (40)
Race: Asian/non-Asian, n (%)	15 (63)/9 (38)[c]	6 (55)/5 (45)	21 (60)/14 (40)
Disease stage[a] IIIA/IIIB, n (%)	11 (46)/13 (54)	7 (64)/4 (36)	18 (51)/17 (49)
WHO PS: 0/1, n (%)	13 (54)/11 (46)	7 (64)/4 (36)	20 (57)/15 (43)
Tumor history: Squamous/nonsquamous	3 (13)/21 (88)[c]	1 (9)/10 (91)	4 (11)/31 (89)
Smoking history Yes/no, n (%)	13 (54)/11 (46)	5 (45)/6 (55)	18 (51)/17 (49)
Best response to previous CRT: CR/PR/stable disease, n (%)	0/11 (46)/13 (54)	0/4 (36)/7 (64)	0/15 (43)/20 (57)
Positive *EGFR* mutation status: exon 19 del/L858R/other,[b] n (%)	10 (42)/6 (25)/8 (33)	3 (27)/5 (45)/3 (27)[c]	13 (37)/11 (31)/11 (31)[c]
PD-L1 status ≥25%/<25%/unknown, n (%)	4 (17)/16 (67)/4 (17)[c]	3 (27)/4 (36)/4 (36)[c]	7 (20)/20 (57)/8 (23)
Primary tumor stage T1a-b/T2a-b/T3/T4, n (%)	6 (25)/9 (38)/4 (17)/5 (21)[c]	2 (18)/6 (55)/1 (9)/2 (18)	8 (23)/15 (43)/5 (14)/7 (20)
Regional lymph nodes N0/N2/N3, n (%)	2 (8)/10 (42)/12 (50)	1 (9)/7 (64)/3 (27)	3 (9)/17 (49)/15 (43)[c]
Previous induction chemotherapy, n (%)	2 (8)	4 (36)	6 (17)

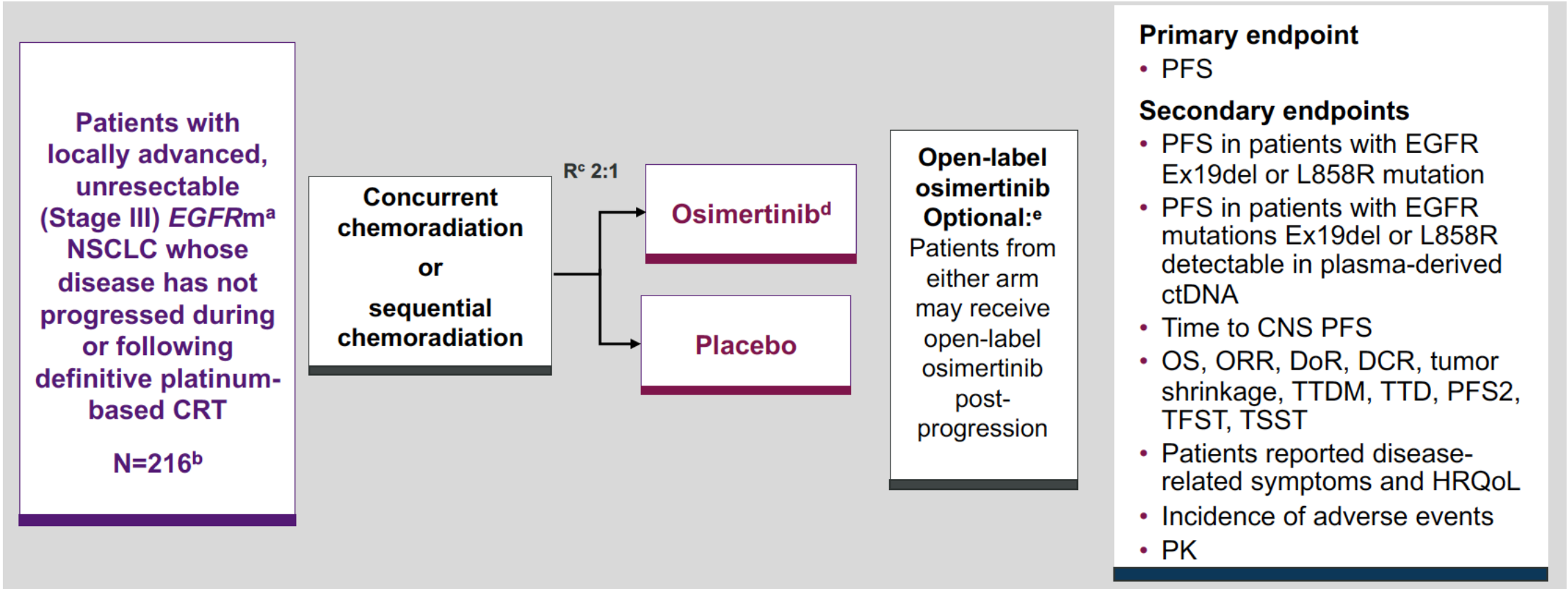




Naidoo, JTO 2023: 18, 5: 657–663

LAURA

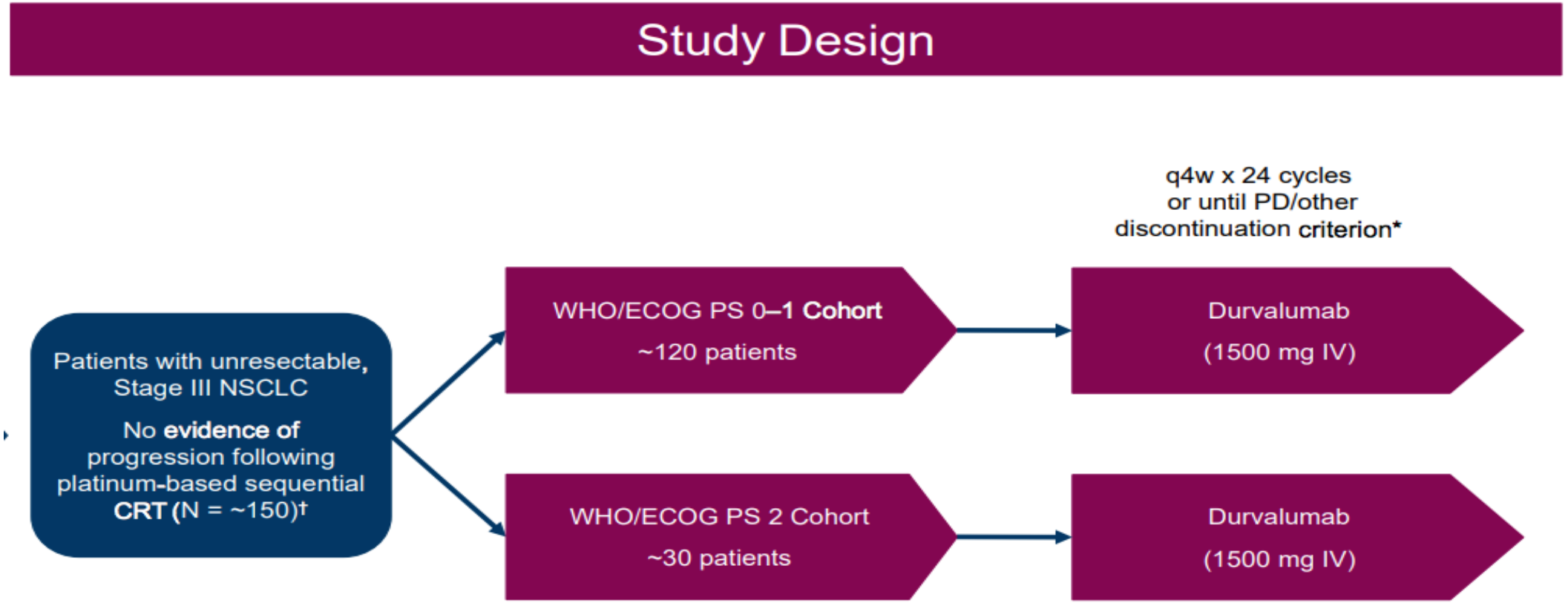
Phase III, double-blind, randomized, placebo-controlled trial



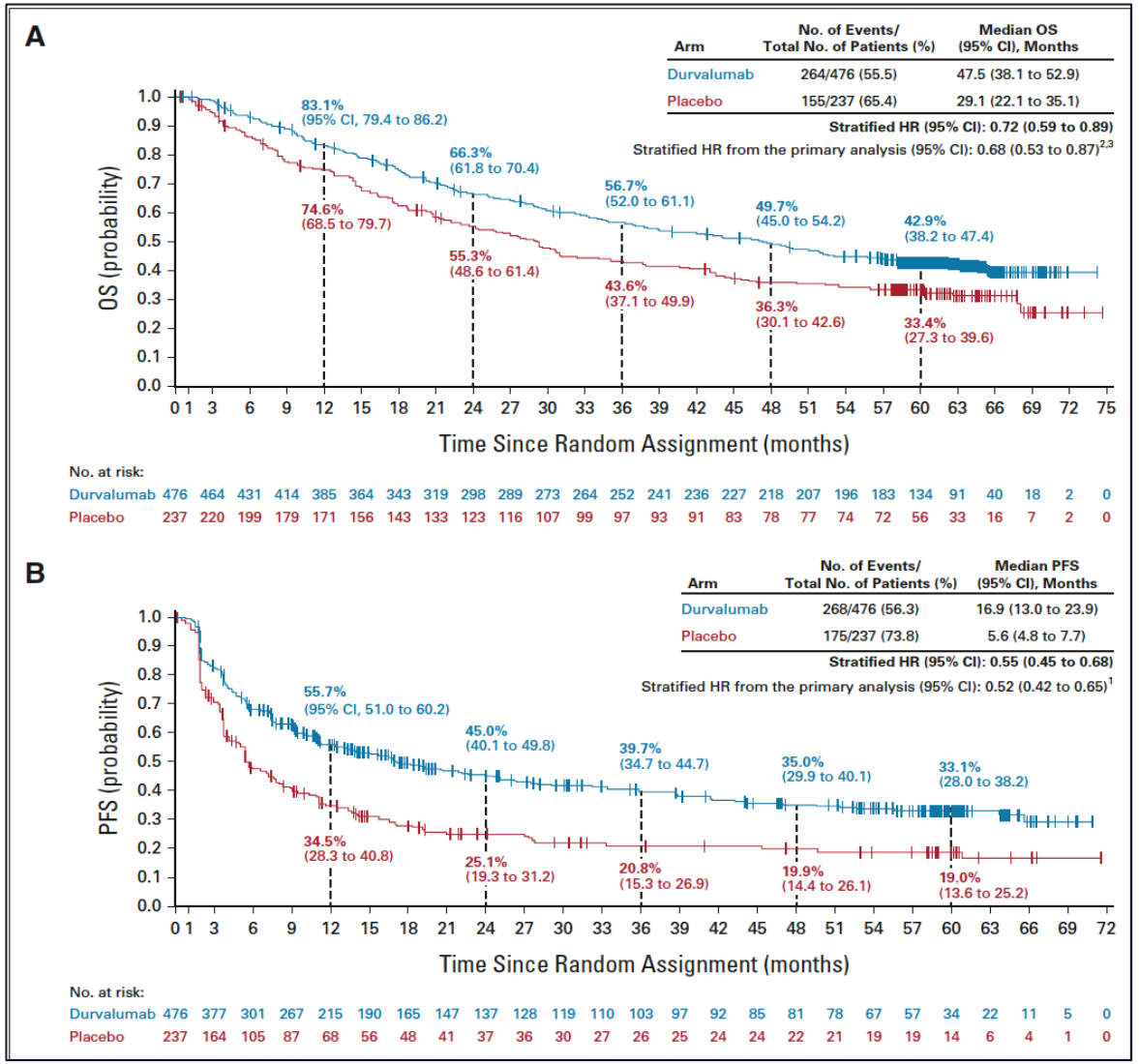
Study NCT03521154. ClinicalTrials.gov website

Durvalumab After Sequential Chemoradiotherapy in Stage III, Unresectable NSCLC: The Phase 2 PACIFIC-6 Trial

PACIFIC-6: A Phase 2 study of durvalumab following sequential chemoradiotherapy in patients with Stage III, unresectable NSCLC



Five-Year Survival Outcomes From the PACIFIC Trial: Durvalumab After Chemoradiotherapy in Stage III Non–Small-Cell Lung Cancer



J Clin Oncol 40:1301-1311

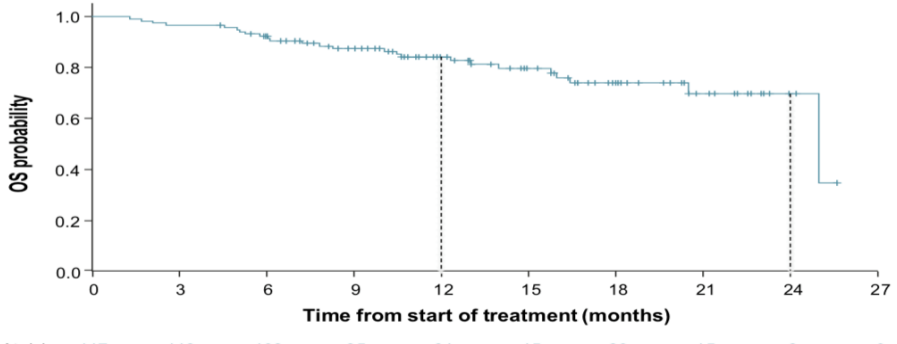
ORIGINAL ARTICLE

IASLC

Durvalumab After Sequential Chemoradiotherapy in Stage III, Unresectable NSCLC: The Phase 2 PACIFIC-6 Trial

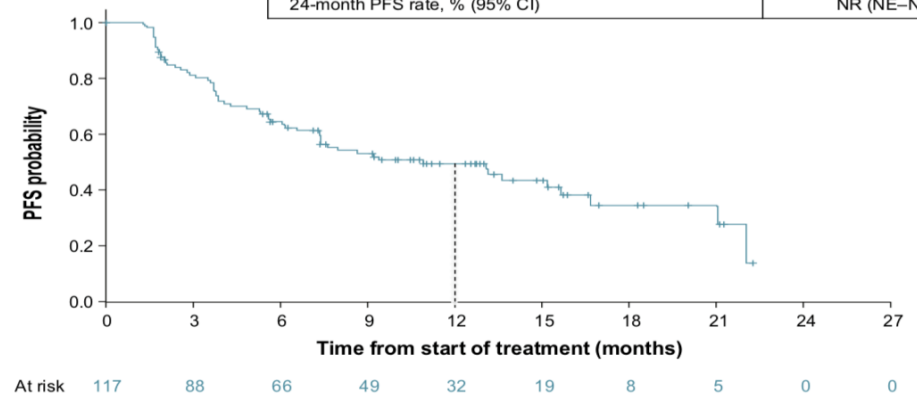
B

	All patients (N = 117)
Deaths, n (%)	25 (21.4)
Median OS, months (95% CI)	25.0 (25.0–NE)
12-month OS rate, % (95% CI)	84.1 (75.6–89.9)
24-month OS rate, % (95% CI)	69.8 (55.8–80.2)



A

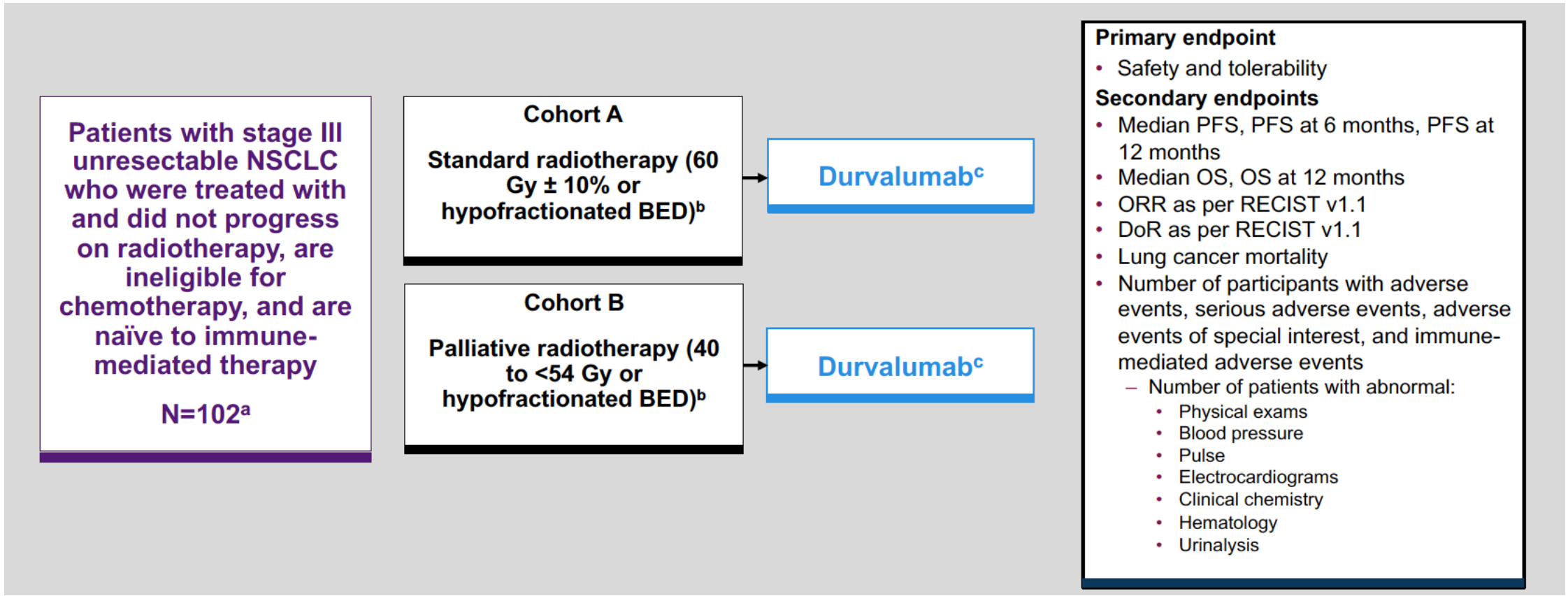
	All patients (N = 117)
Total progression events, n (%)	61 (52.1)
Median PFS, months (95% CI)	10.9 (7.3–15.6)
12-month PFS rate, % (95% CI)	49.6 (39.5–58.9)
24-month PFS rate, % (95% CI)	NR (NE–NE)



J Thorac Oncol 2022 Aug 9;S1556-0864

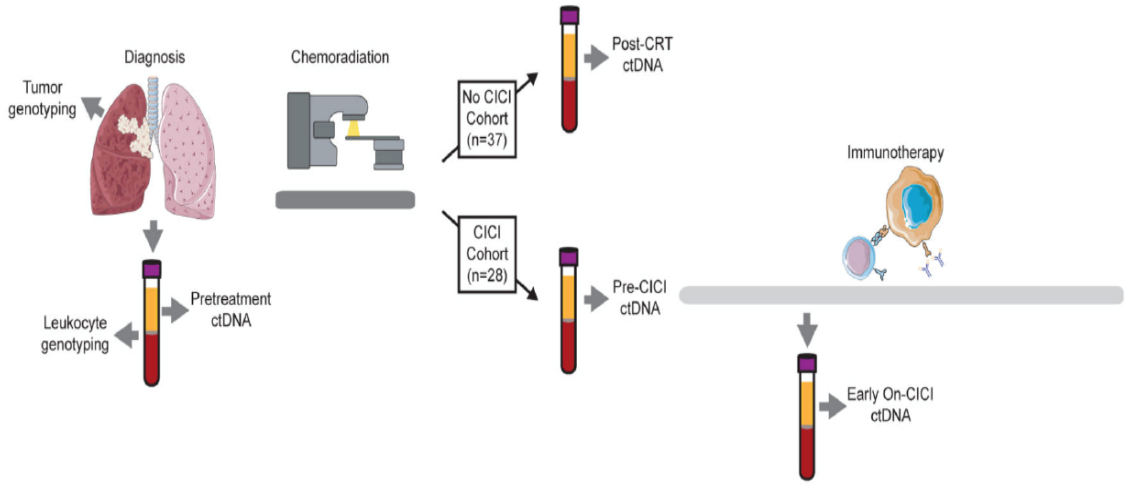
DUART

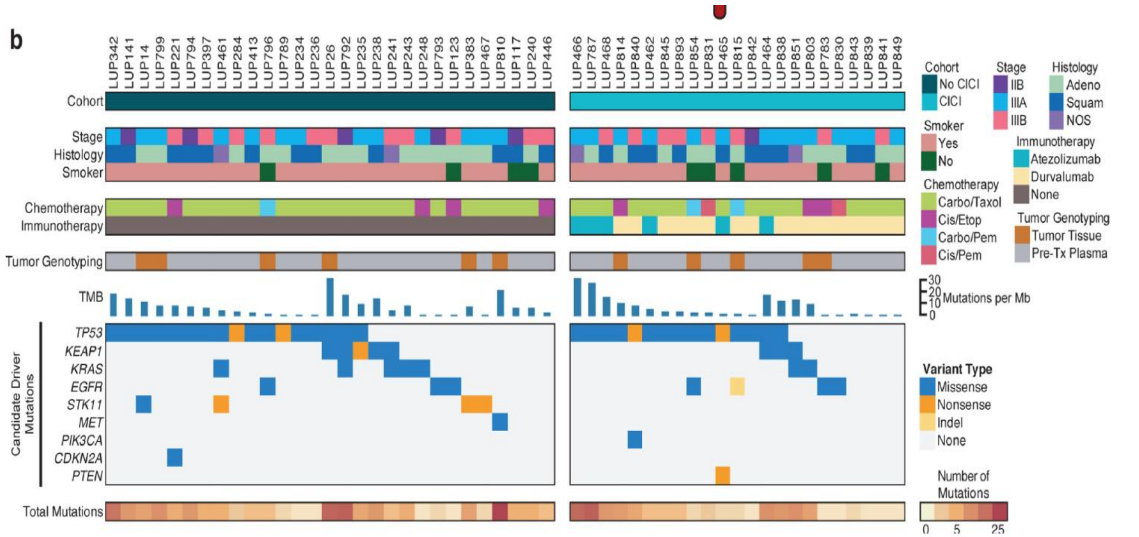
Phase II, open-label, single-arm study



Study NCT04249362. ClinicalTrials.gov website

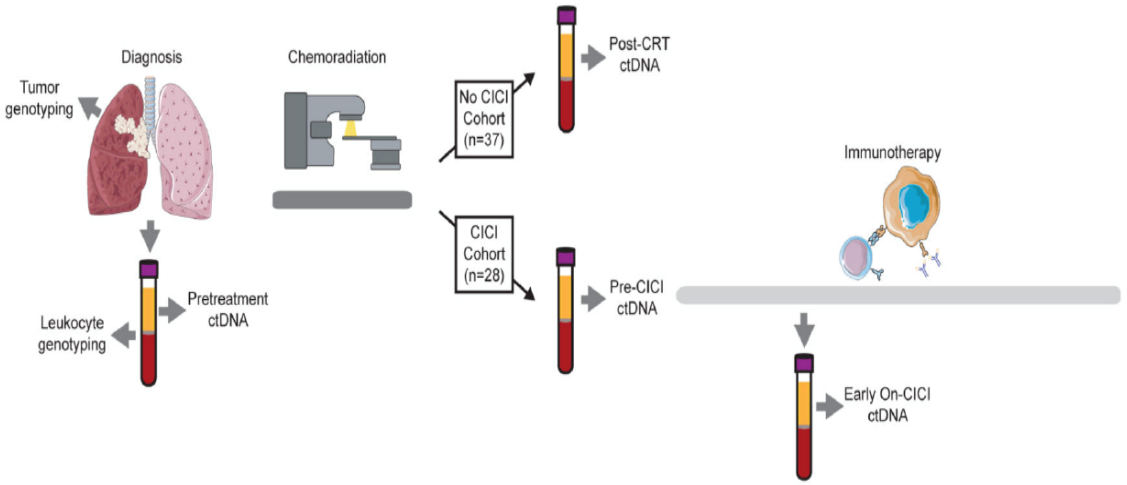
CIRCULATING TUMOR DNA

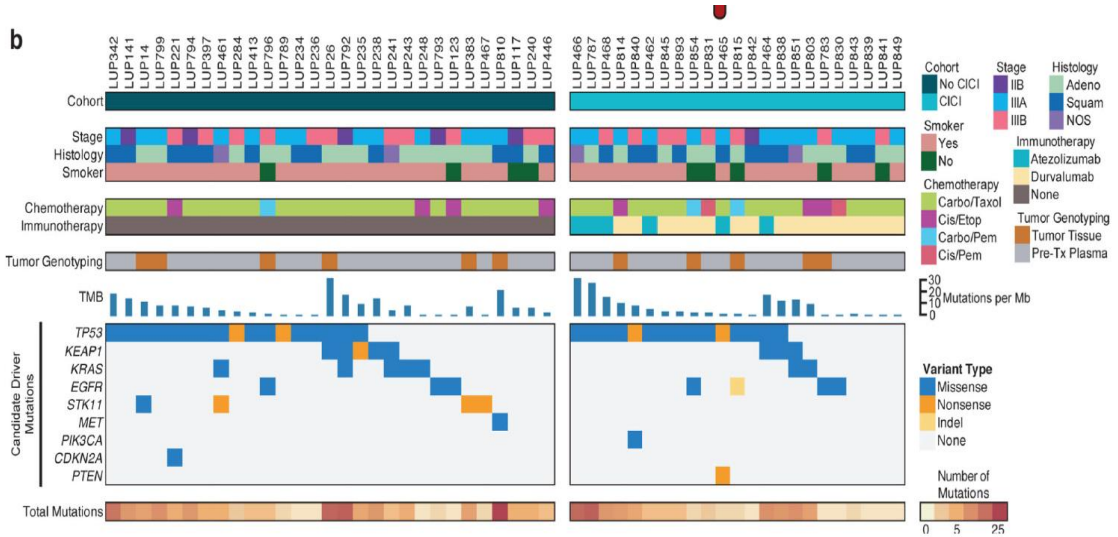


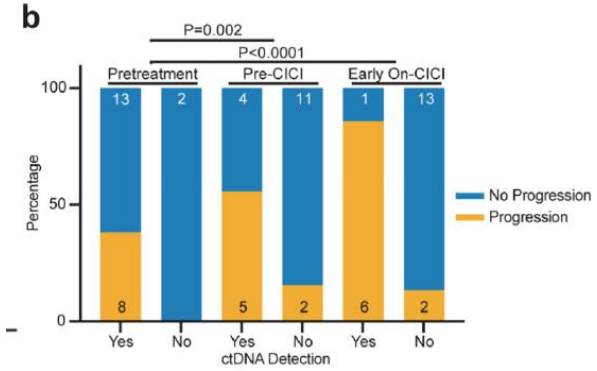


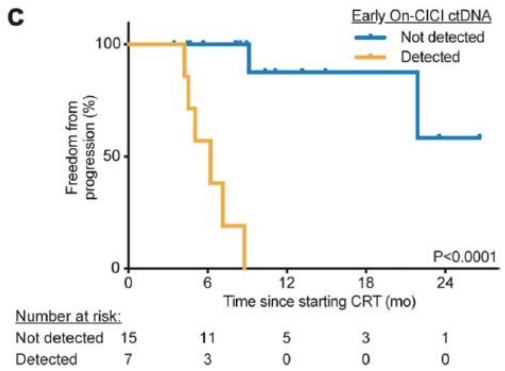
Nat Cancer. 2020 February ; 1(2): 176–183.

CIRCULATING TUMOR DNA









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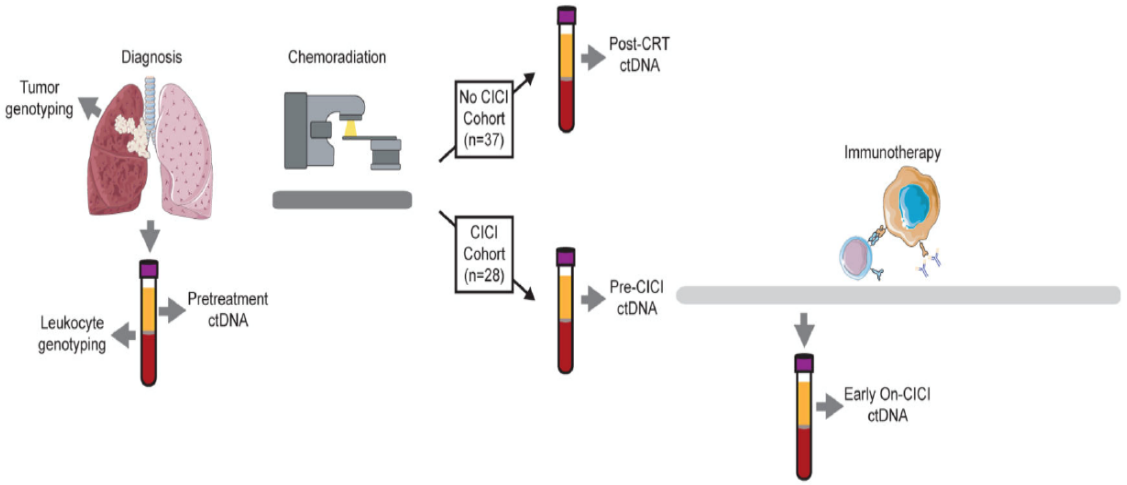
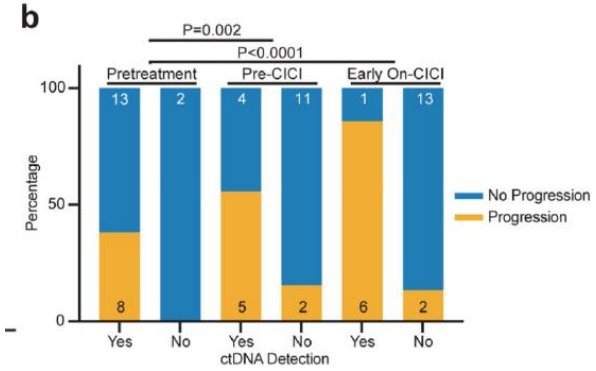
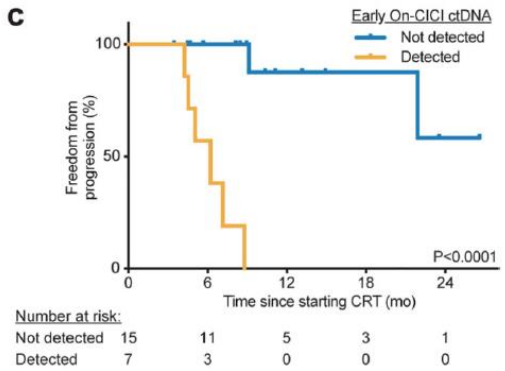
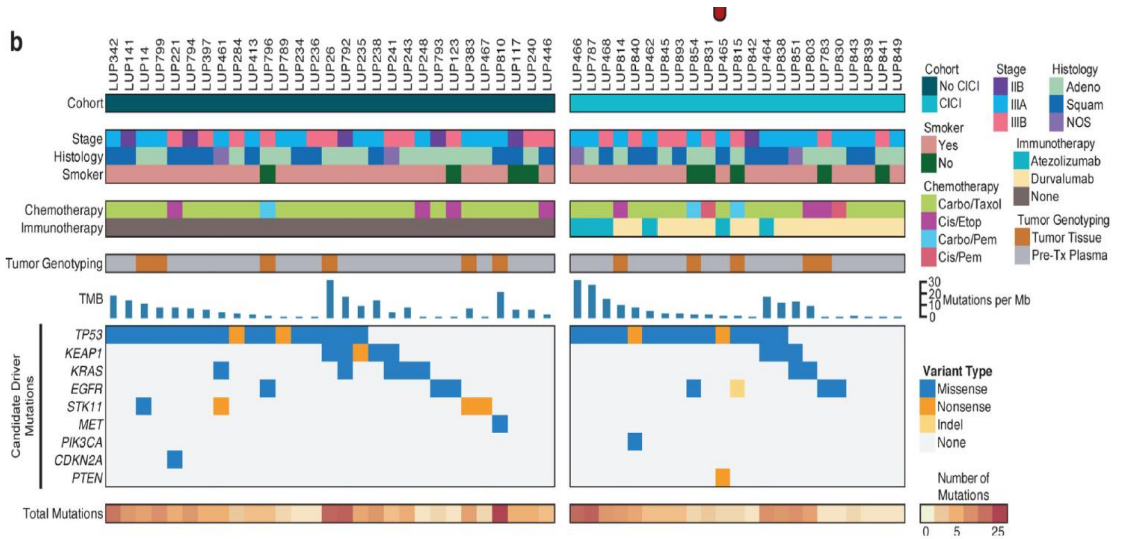
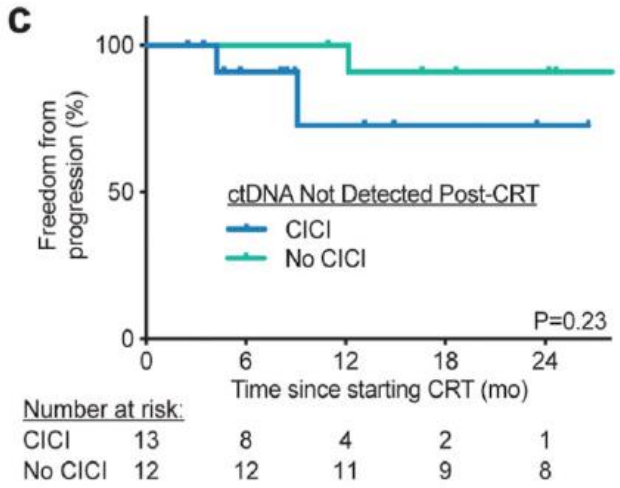
CIRCULATING TUMOR DNA

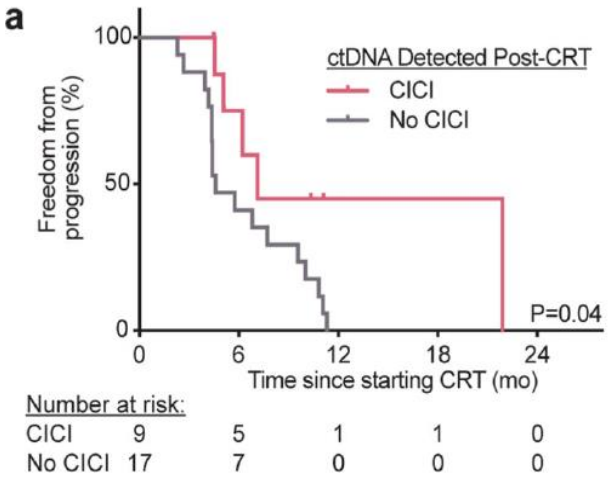












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En resumen…

1.- PACIFIC nos ha aportado un cambio en la supervivencia de los pacientes estadios III irresecables pero… no en todos

2.- Necesitamos nuevas estrategias para los diferentes subgrupos de tratamiento

3.- Deberíamos centrar los estudios mas que en añadir diferentes terapias o en repetir los mismos EC con cada medicamento, en buscar nuevos biomarcadores para personalizar bien los tratamientos

4.- La detección de driver y el ctDNA podrían ser biomarcadores muy prometedores


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