16th CONGRESS Lung ON CANCER

BARCELONA 27 / 28 NOVEMBER 2025

GECP lung cancer research

INDUCTION TREATMENT PREVIOUSLY TO RT/CT

Dra. Virginia Calvo de Juan, MD, PhD

Hospital Universitario Puerta de Hierro Majadahonda, Madrid

DISCLOSURE

- **Employment:** H. Universitario Puerta de Hierro Majadahonda, Madrid
- **Consultant or Advisory Role:** Roche, AstraZeneca, MSD, BMS, Takeda, Regeneron, AMGEN, GSK, Boehringer Ingelheim, J&J, BeOne. Pierre Fabre
- **Stock Ownership:** none
- **Research Funding:** Roche
- **Speaking:** Roche, AstraZeneca, MSD, BMS, Takeda, Regeneron, AMGEN, Pfizer, J&J, BeOne, Pierre Fabre
- **Grant support:** none
- **Other:** none

OUTLINE

- Introduction
  - PACIFIC
- Beyond PACIFIC:
  - Intensification during chemoradiotherapy
  - Intensification after chemoradiotherapy
  - **Intensification before chemoradiotherapy**
- Can we convert borderline/unresectable in resectable?
- Conclusions

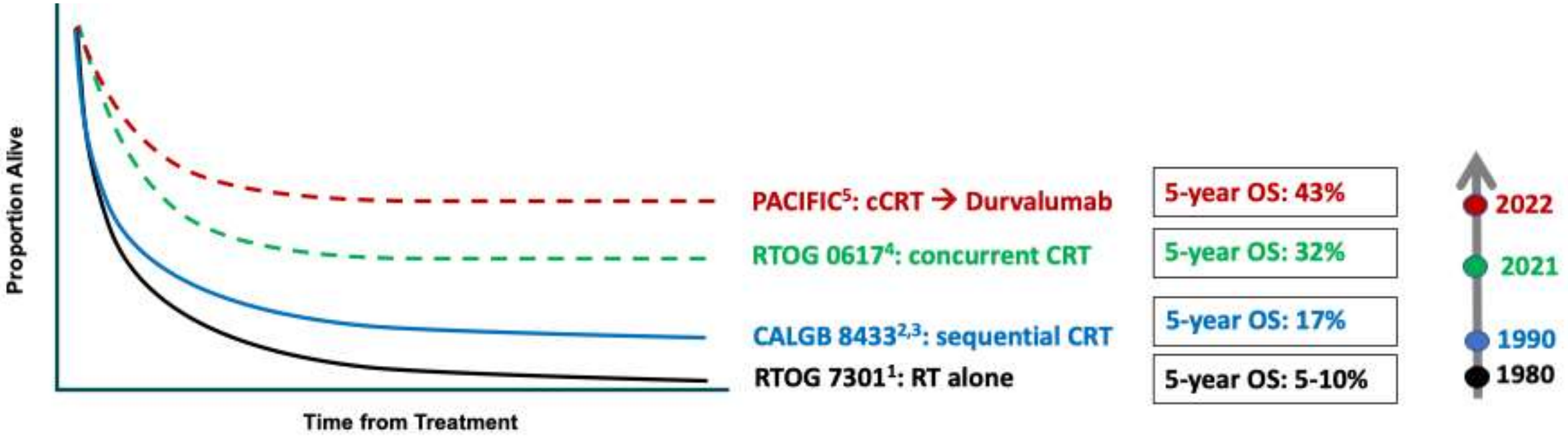
INTRODUCTION

- NSCLC accounts for 80–85% of all lung cancer cases[1]
- Approximately 20–35% of NSCLC cases will be diagnosed as stage III[2]
- Locally advanced NSCLC is a highly heterogeneous disease
- Multidisciplinary discussion is mandatory to define tumor operability as well as best treatment approaches: characteristics of the disease, local expertise, patient´s comorbidities and preferences
- Several trials have compared the treatment with cCRT versus exclusive RT[3,4] indicating that the cCRT contributes a clear improvement in survival
- 2018: PACIFIC trial[5] established definitive cCRT followed by a 1-year durvalumab consolidation
- However, patient remain at a high risk of disease progression, with 1-year PFS rate of only ≃ 50%
- Given the significant benefit of neoadjuvant chemo-immunotherapy in resectable NSCLC, induction with immunotherapy with or without chemotherapy may provide more survival benefit for initially unresectable stage III NSCLC

1.Siegel RL, et al. Cancer statistics, 2024. CA Cancer J Clin 2024;74:12-49; 2.Aupérin A, et al. J Clin Oncol. 2010;28(13):2181-90
3.Schaake-Koning C. et al, N Engl J Med 1992;326:524-30; 4.Jeremic B. et al, J Clin Oncol 1995;15:452-8; 5.Antonia S.J. et al, N Engl J Med. 2017;377:1919-29

INTRODUCTION

RAISING THE BAR IN UNRESECTABLE STAGE III NSCLC



1.Perez CA, et al. Cancer 1982;50(6):1091-9; 2.Dilman RO, et al. N Engl J Med 1990; 3.Dilman RO, et al. JNCI 1996;88(17):1210-5; 4.Bradley JD, et al. J Clin Oncol. 2020;38(7):706-14; 5.Spigel DR, et al. J Clin Oncol 2022;40(12):1301-11

INTRODUCTION: PACIFIC TRIAL

- Unresectable, Stage III NSCLC without progression after definitive platinum-based cCRT (≥2 cycles)
- 18 years or older
- WHO PS score 0 or 1
- If available, archived pre-cCRT tumor tissue for PD-L1 testing*

All-comers population (i.e. irrespective of PD-L1 status)

N=713 randomized

1–42 days post-cCRT

R

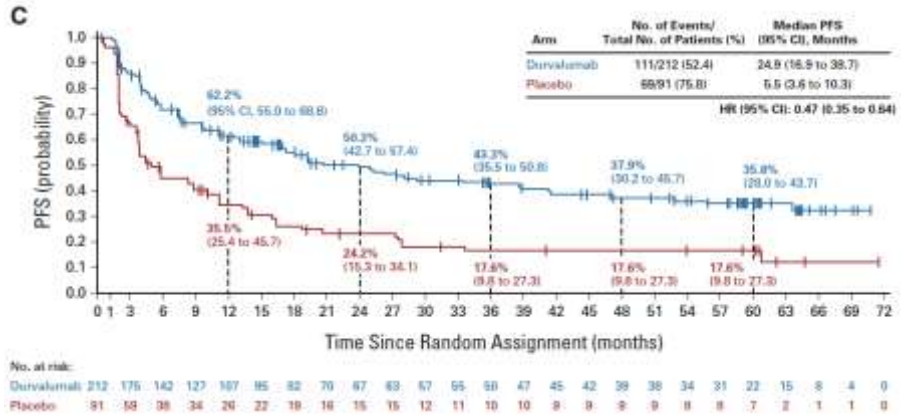
Durvalumab 10 mg/kg q2w for up to 12 months N=476

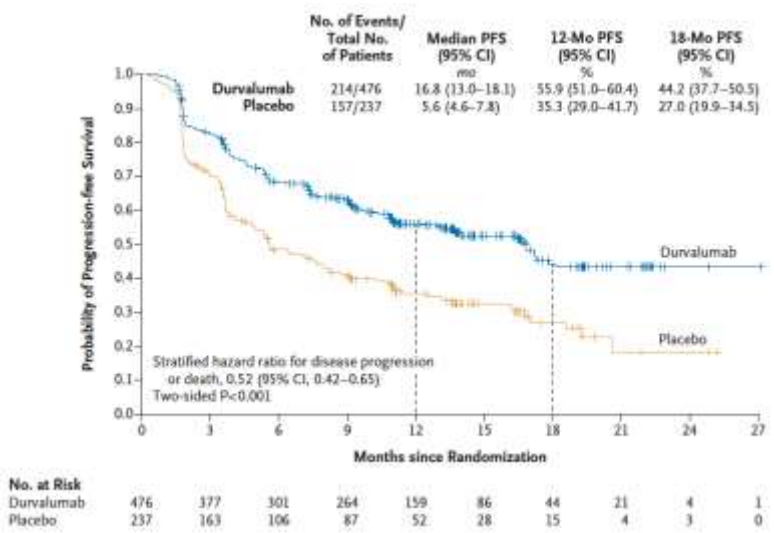
2:1 randomization, stratified by age, sex, and smoking history

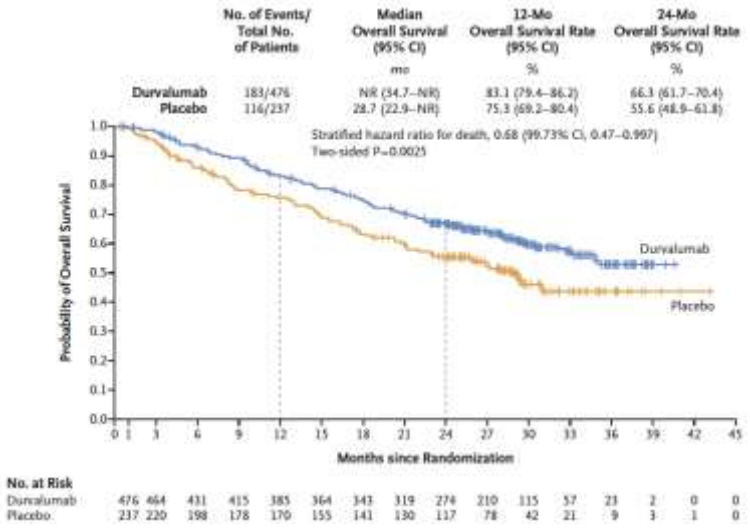
Placebo 10 mg/kg q2w for up to 12 months N=237

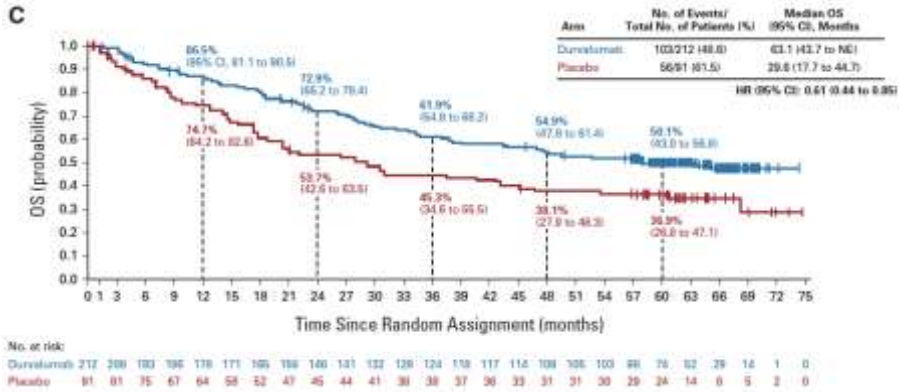
Primary endpoints
- PFS by BICR using RECIST v1.1†
- OS

Key secondary endpoints
- ORR, DoR and TTDM by BICR
- PFS2 by investigator
- Safety
- PROs









Antonia SJ, et al. N Engl J Med. 2017;377(20):1919-29; Antonia SJ, et al. N Engl J Med. 2018;379(24):2342-50; Spigel DR, et al. J Clin Oncol. 2022;40(12):1301-11

BEYOND PACIFIC

IO Consolidation Intensification cCRT → IO + IO	IO concurrent with cCRT IO + cCRT → IO	IO-CT Induction prior to cCRT IO+/-CT → cCRT → IO
• **COAST (Phase II)**	• **PACIFIC-2 (Phase III)**	• **AFT-16 (Phase II)**
• **LUN16-081 (Phase II)**	• **CheckMate-73L (Phase III)**	• **APOLO (Phase II)**
• PACIFIC 8 (Phase III)	• **EA5181 (Phase III)**	• **PACIFIC-BRAZIL (Phase II)**
• PACIFIC 9 (Phase III)	• **KEYNOTE-799 (Phase II)**	• **GASTO-1091 (Phase II)**
• SKYSCRAPER-03 (Phase III)	• **NICHOLAS (Phase II)**	• AFT-57 (Phase II)
• CheckMate-73L (Phase III)	• **DETERRED (Phase II)**	• DEDALUS (Phase II)
• MPLALC (Phase II)	• **CRUISER (Phase II)**	• BRIDGE (Phase II)
	• KEYLIN-012 (Phase III)	
	• KEYVIBE-006 (Phase III)	
	• NCT05386888 (Phase II)	

Adapted from Delcuratolo MD, et al. Cancer Treat Rev 2025;135:102918

INTENSIFICATION BEFORE CHEMORADIOTHERAPY

Study	Treatment	N	mPFS (months)	1-y PFS rate	mOS (months)	1-y OS rate	AEs G>3	Pneumonitis G>3	Discontinuation
AFT-16	Atezo → cCRT	62	30	69%	NR	87%	48%	6.4%	19.4%
APOLO	Atezo + CT → cCRT	38	20.8	68.4%	NR	86.8%	73.7%	NA	18%
PACIFIC-BRAZIL	Durva + CT → cCRT + Durva	49	NR	68.1%	NR	81.2%	82%	14%	NA (14% death)
GASTO-1091	Nivo + CT → cCRT	86	NR	72.6%	NR	NA	21% (non-haematological)	3.5%	NA

IO-CT induction prior to cCRT: phase II studies, with promising but preliminary activity and tolerable profile

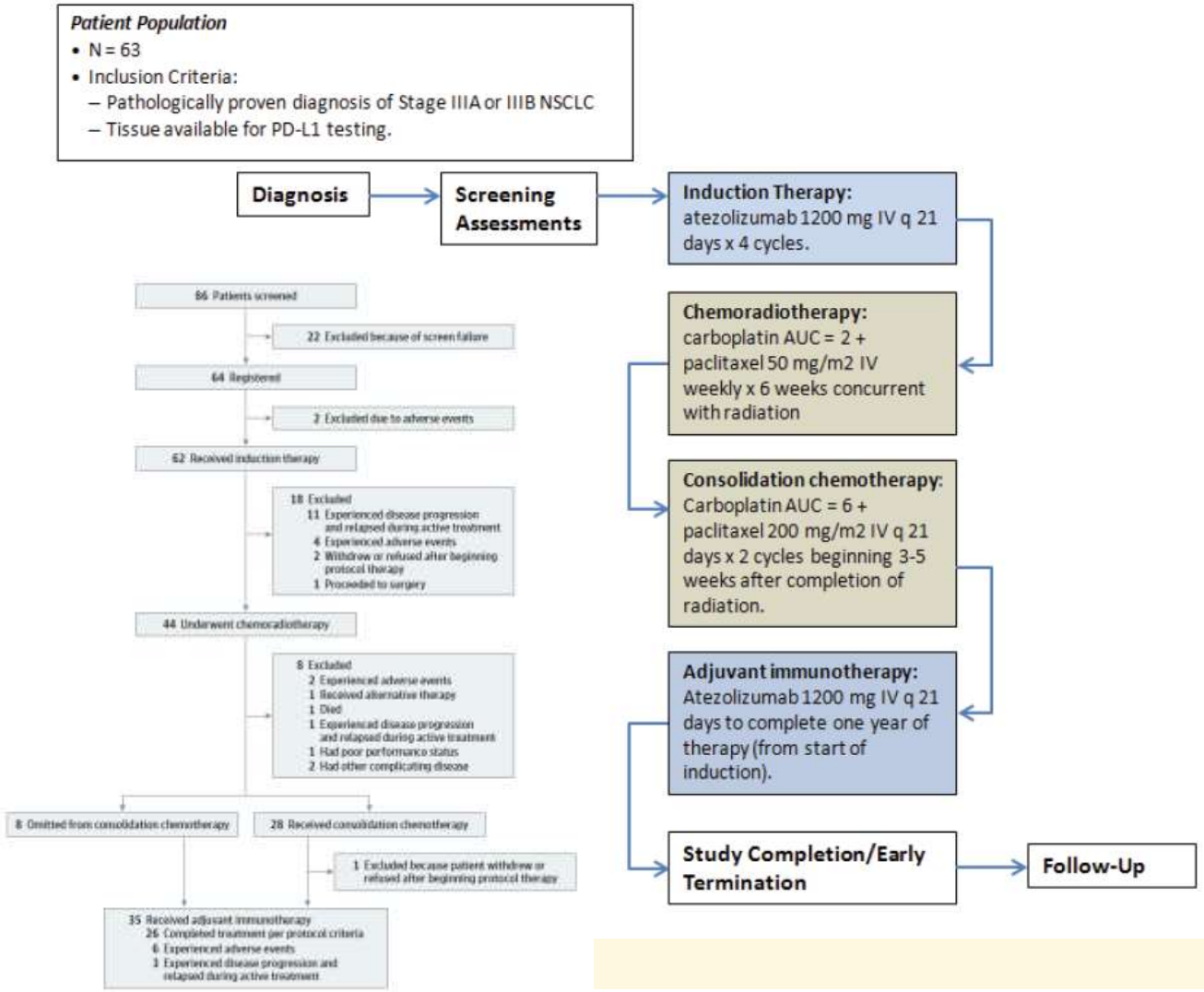
Ross HL, et al. JAMA Oncol 2024; Provencio M, et al. WCLC 2024; Qiu, et al. ASCO 2024; William N William Jr, et al. WCLC 2024

AFT-16

JAMA Oncology | Original Investigation

Atezolizumab Before and After Chemoradiation for Unresectable Stage III Non-Small Cell Lung Cancer
A Phase II Nonrandomized Controlled Trial

Helen J. Ross, MD; David Kozono, MD, PhD; Xiaofei F. Wang, PhD; James John Urbanic, MD;



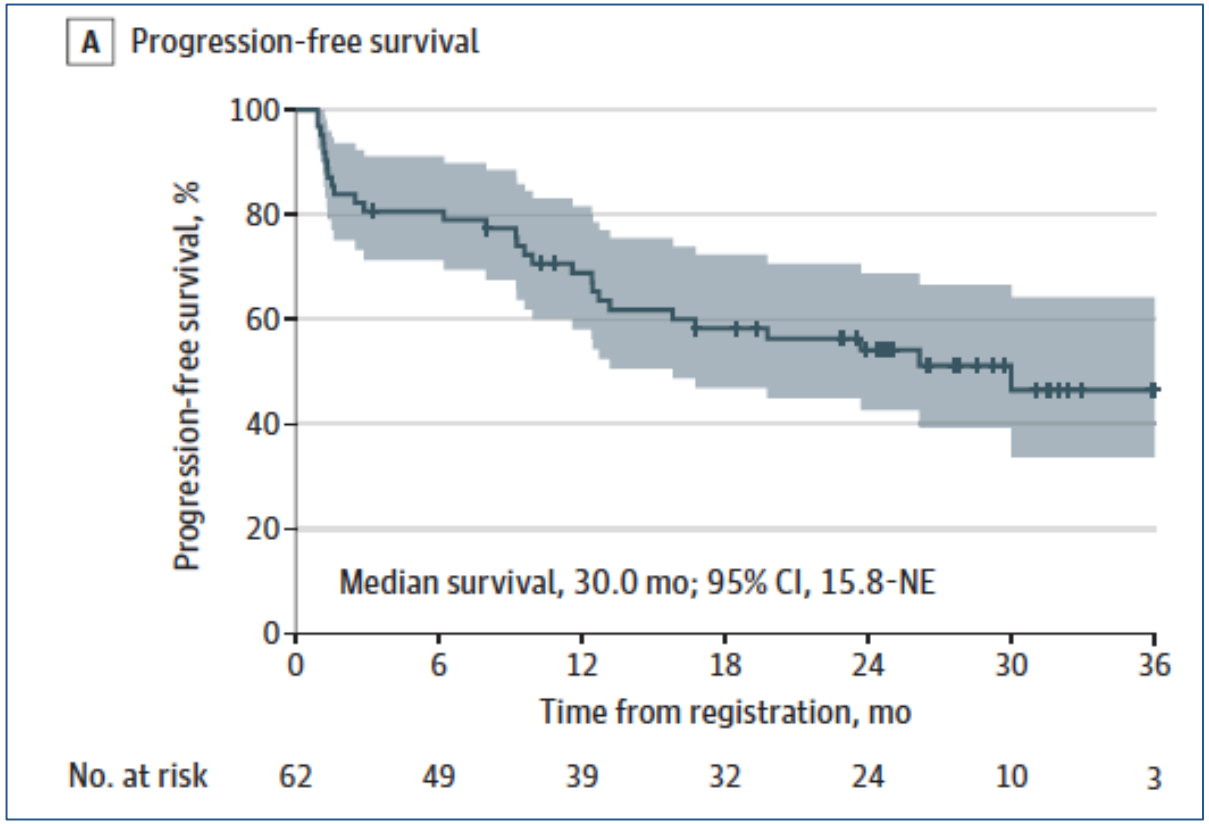
- The primary end point was **DCR at 12 weeks:**

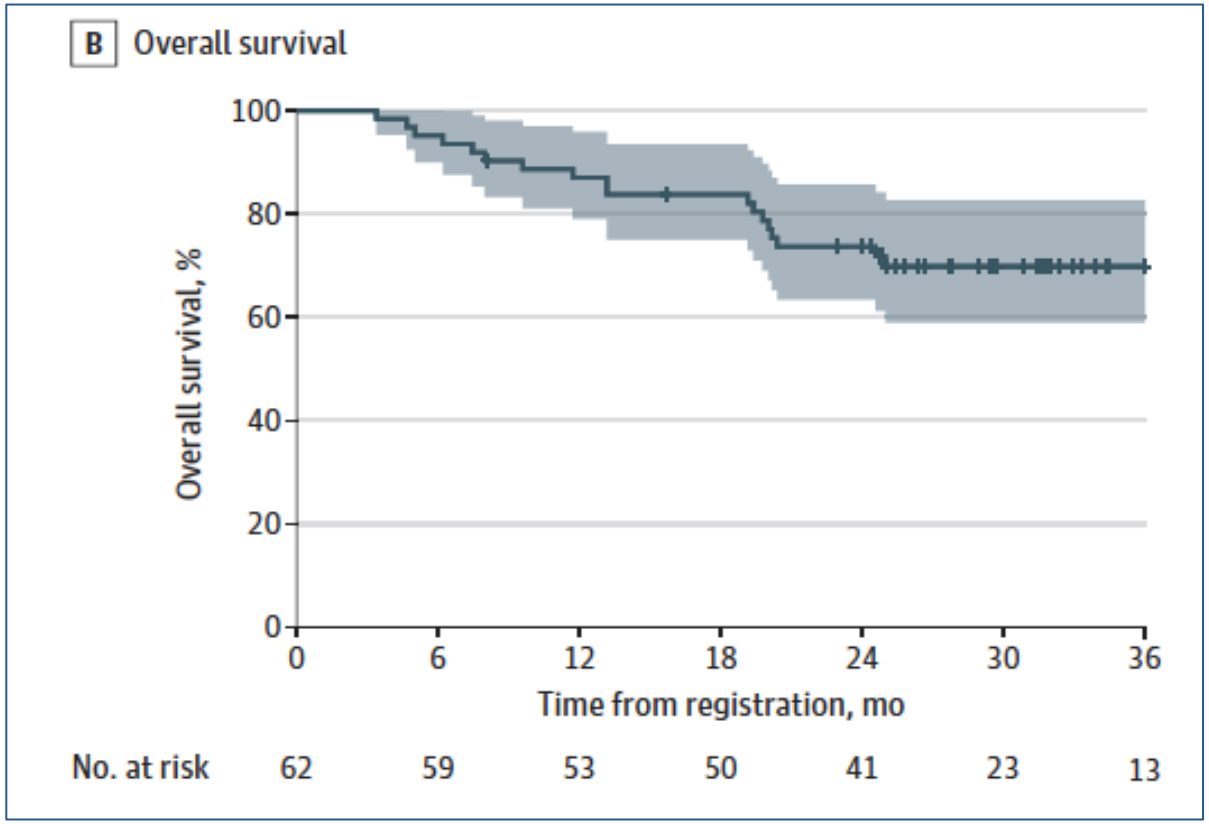
- The **DCR after 12 weeks** of neoadjuvant atezolizumab was **74.2%** (80% CI, 65.7%-81.4%; 95% CI, 61.5%-84.5%)
  - Partial response: 17 participants (27.4%)
  - Stable disease: 29 participants (46.8%)

- The DCR after 6 weeks was similar at 77.4%(80%
- CI, 69.2%-84.3%; 95% CI, 65.0%-87.1%)

Ross HJ, et al. JAMA Oncol 2024;10(9):1212-9

AFT-16: Atezolizumab before and after chemoradiation for unresectable stage III Non-Small Cell Lung Cancer





mPFS: 30 months (95% CI 15.8 months-NR)

1-year PFS: 69%

mOS: NR

1-year OS: 87%

Ross HJ, et al. JAMA Oncol 2024;10(9):1212-9

AFT-16: Atezolizumab before and after chemoradiation for unresectable stage III Non-Small Cell Lung Cancer

Adverse event	No. (%)		
	Grade 3	Grade 4	Grade 5
Aspartate aminotransferase increased	0	1 (1.6)	0
Colitis	3 (4.8)	0	0
Dyspnea	5 (8.1)	2 (3.2)	0
Esophagitis	3 (4.8)	0	0
Fever	4 (6.5)	0	0
Guillain-Barré syndrome	0	1 (1.6)	0
Hyperglycemia	3 (4.8)	0	0
Hypertension	5 (8.1)	0	0
Hyponatremia	4 (6.5)	0	0
Hypotension	0	1 (1.6)	0
Hypoxia	3 (4.8)	0	0
Infusion-related reaction	3 (4.8)	0	0
Lung infection	9 (14.5)	0	0

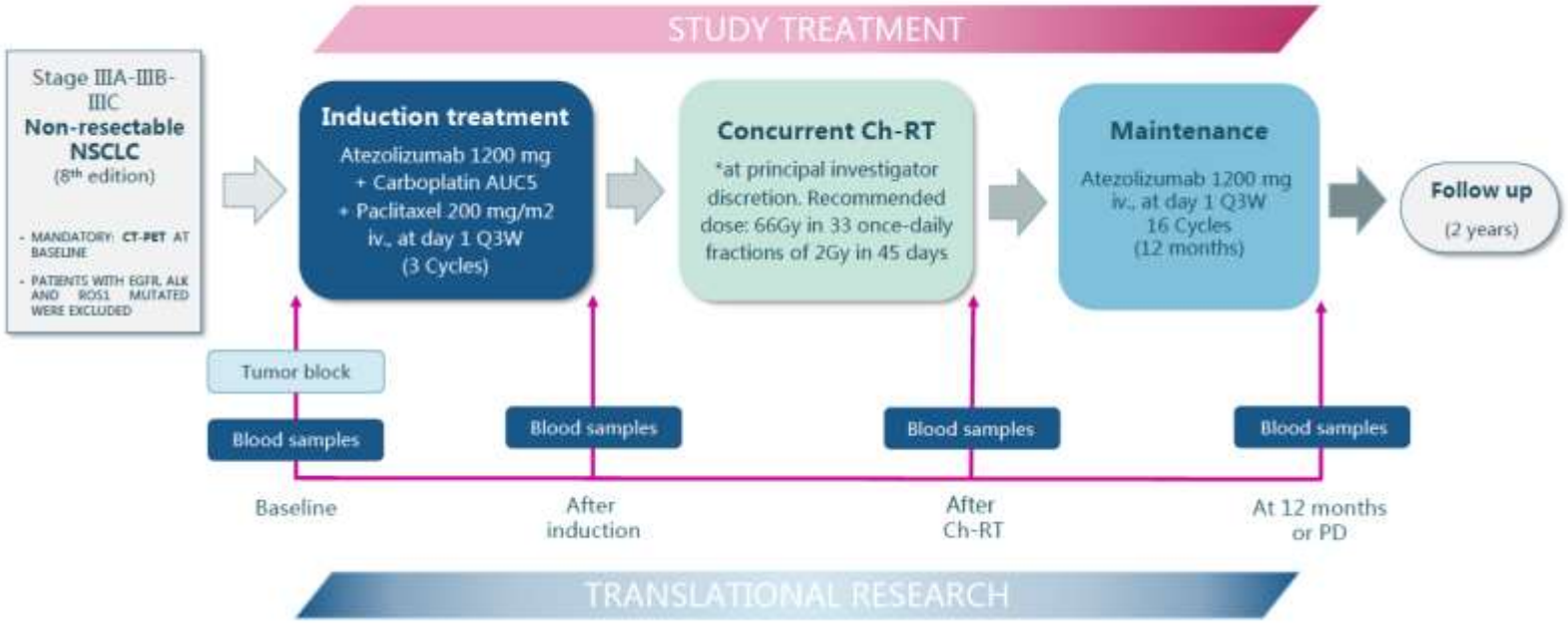
6.4%

Adverse event	No. (%)		
	Grade 3	Grade 4	Grade 5
Lymphocyte count decreased	9 (14.5)	8 (12.9)	0
Neutrophil count decreased	7 (11.3)	1 (1.6)	0
Pericardial effusion	0	1 (1.6)	0
Platelet count decreased	2 (3.2)	2 (3.2)	0
Pneumonitis	3 (4.8)	0	1 (1.6)
Respiratory failure	0	1 (1.6)	0
Sepsis	0	3 (4.8)	1 (1.6)
Thromboembolic event	4 (6.5)	0	0
Treatment-related secondary malignant neoplasm	0	1 (1.6)	0
Upper respiratory infection	1 (1.6)	1 (1.6)	0
Ventricular tachycardia	0	1 (1.6)	0
Vomiting	3 (4.8)	0	0
White blood cell count decreased	7 (11.3)	2 (3.2)	0

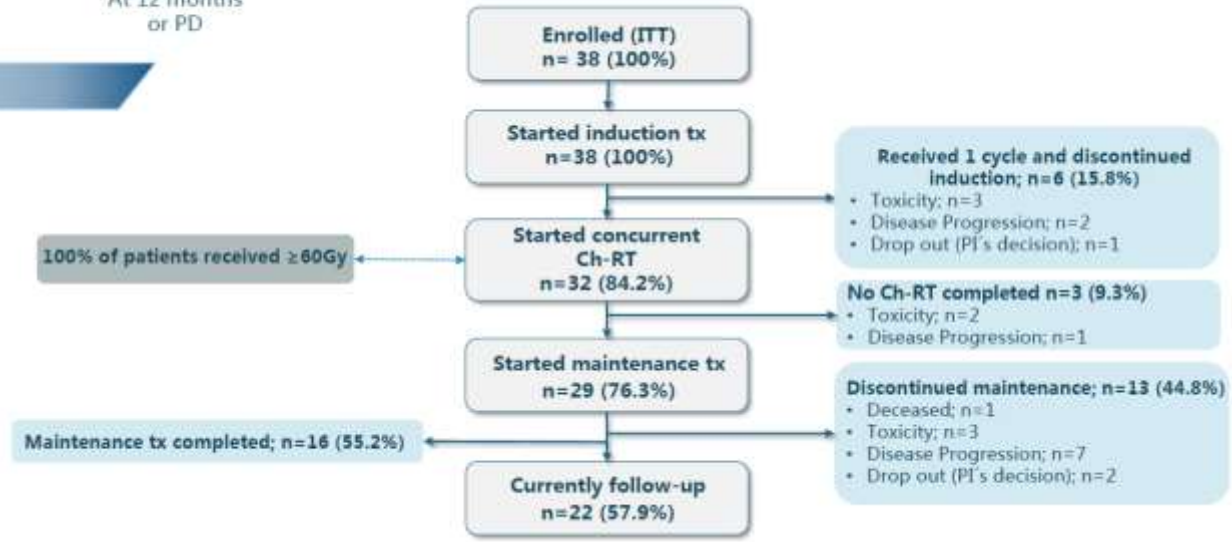
- 17 patients (27.4%) experienced grade 3 or higher immune-related adverse events, including 1 with grade 5 pneumonitis and 1 with grade 4 Guillain-Barré syndrome
- 30 patients (48.4%) experienced grade 3 or higher treatment-related adverse events

Ross HJ, et al. JAMA Oncol 2024;10(9):1212-9

APOLO: Atezolizumab + induction chemotherapy (Ch) + chemo-radiotherapy (Ch-RT) and atezolizumab maintenance in non-resectable stage III NSCLC

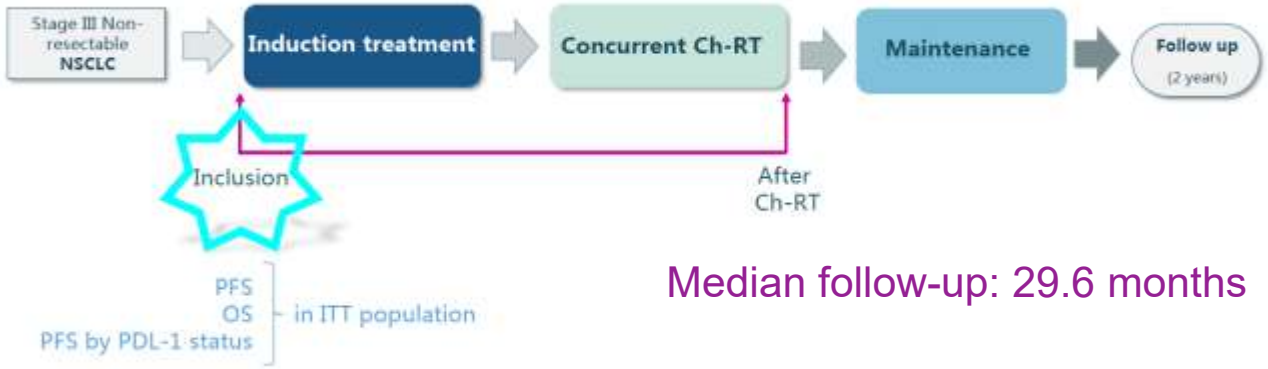


- **Primary endpoint:** PFS rate at 12 months
- **Secondary endpoints:** PFS-PACIFIC related at 12 months, PFS rate at 24 months, OS rate at 12 and 24 months, ORR, sites of first failure, safety and tolerability, others: ctDNA

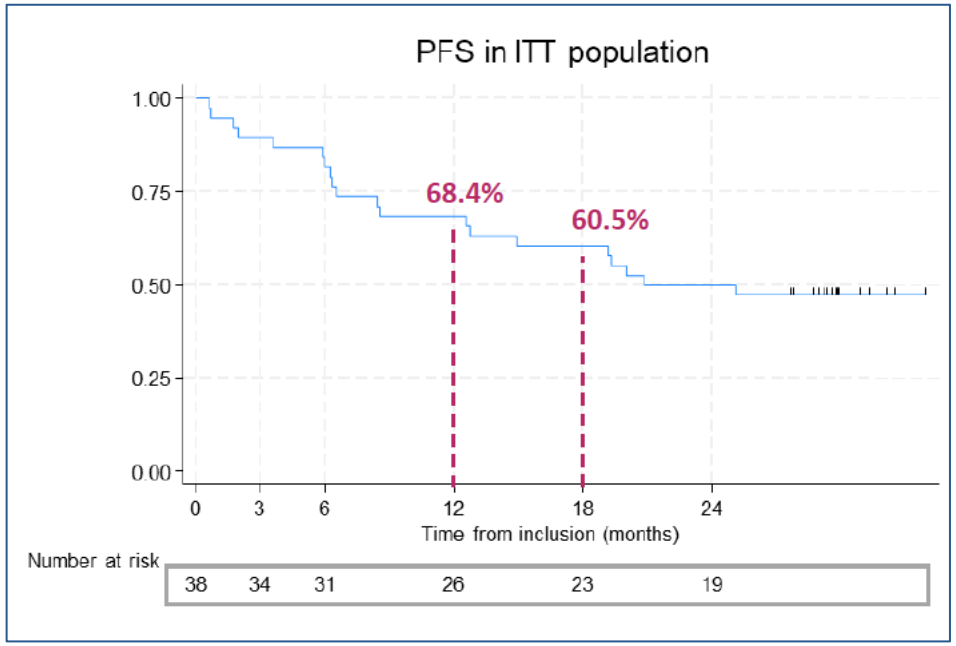


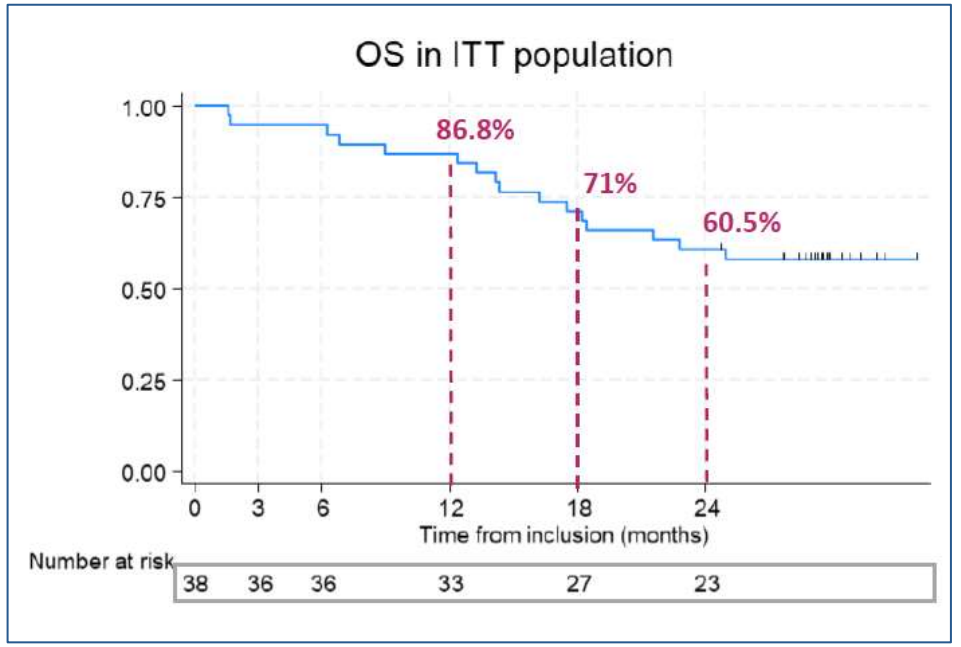
Provencio M, et al. WCLC 2024; J Thorac Oncol 2024;19:S37

APOLO



Median follow-up: 29.6 months





mPFS: 20.8 months (95% CI, 12.6-NR)

1-year PFS: 68.4% (95% CI, 51.1-80.6%)

18-months PFS: 60.5% (95% CI, 43.3-74%)

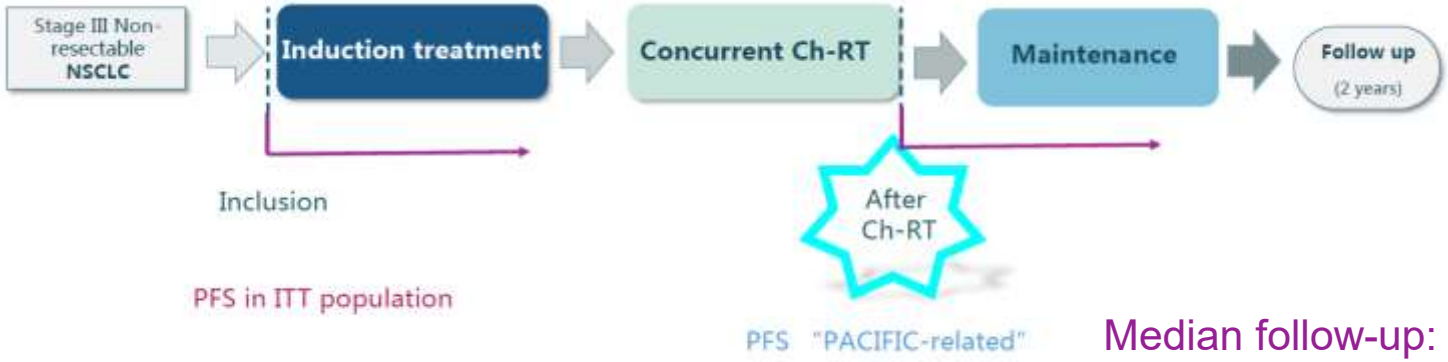
mOS: NR

1-year OS: 86.8% (95% CI, 71.2-94.3%)

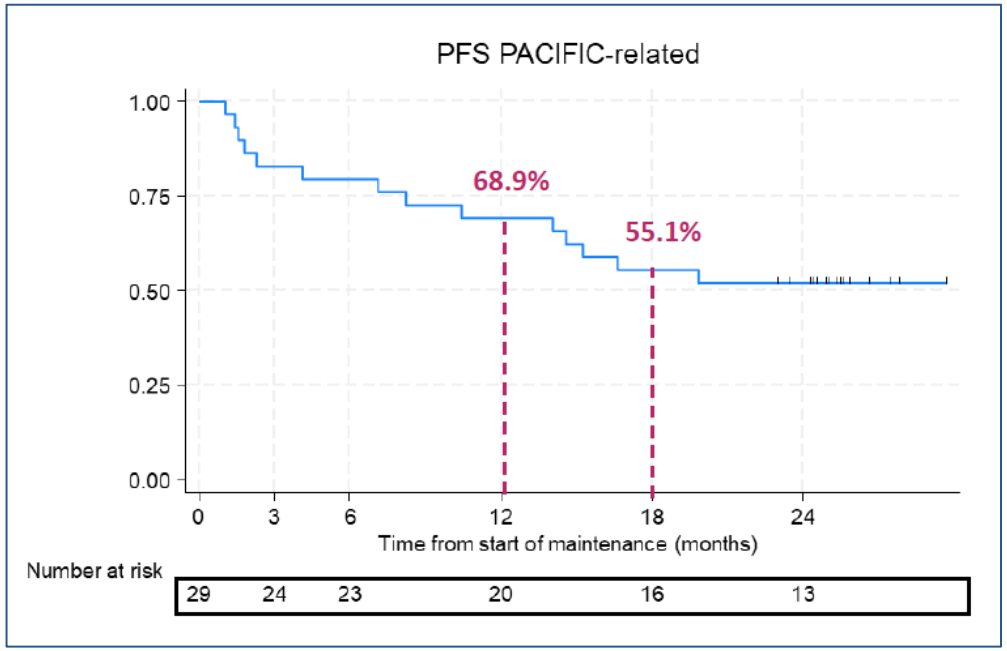
2-year OS: 60.5% (95% CI, 43.3-74%)

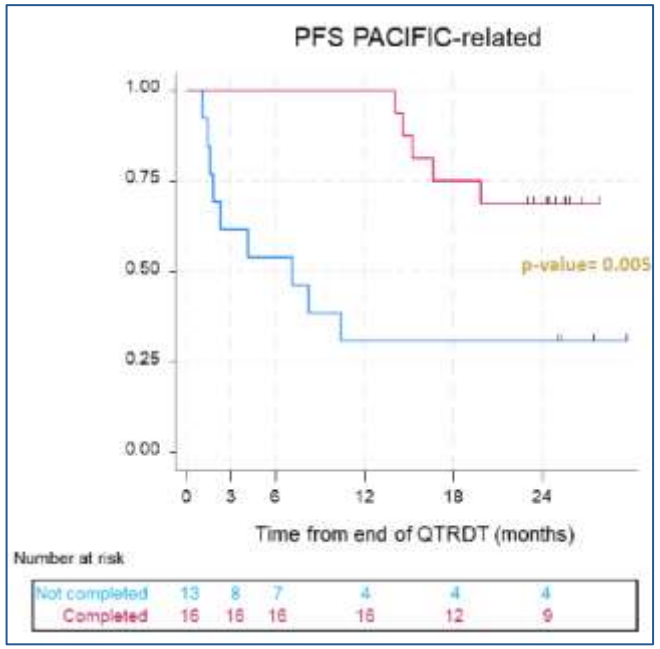
Provencio M, et al. WCLC 2024; J Thorac Oncol 2024;19:S37

APOLO



Median follow-up: 29.6 months





	12 m (95%CI)	18 m (95%CI)	24 m (95%CI)
Maintenance tx Completed	100%	75% (46.3-89.8)	68.7% (40.4-85.6)
Maintenance tx Not Completed	30.7% (9.5-55.4)	30.7% (9.5-55.4)	30.7% (9.5-55.4)

1-year PFS: 68.9% (95% CI, 48.8-82.4%)

18-months PFS: 55.1% (95% CI, 35.6-71%)

Provencio M, et al. WCLC 2024; J Thorac Oncol 2024;19:S37

APOLO: Atezolizumab + induction chemotherapy (Ch) + chemo-radiotherapy (Ch-RT) and atezolizumab maintenance in non-resectable stage III NSCLC

Induction tx (n= 38) Total events = 350	Atezolizumab Related			Carboplatin Related			Paclitaxel Related		
	Any Grade	Grade 1-2	Grade 3-4	Any Grade	Grade 1-2	Grade 3-4	Any Grade	Grade 1-2	Grade 3-4
	number of patients with TRAE (%)								
Any TRAE*	26 (68.4)	24 (63.2)	6 (15.8)	34 (89.5)	32 (84.2)	9 (23.7)	36 (94.7)	34 (89.5)	9 (23.7)
TRAEs leading to discontinuation of tx	3 (7.9)	0	3 (7.9)	2 (5.2)	0	2 (5.2)	2 (5.2)	0	2 (5.2)
Serious TRAEs	1 (2.6)	0	1 (2.6)	5 (13.1)	0	5 (13.1)	5 (13.1)	0	5 (13.1)
Treatment-related deaths	0			0			0		

*Treatment Related Adverse Events with an incidence of ≥10%

Conc Ch-RT tx (n= 38) Total events = 95	Chemotherapy Related			Radiotherapy Related		
	Any Grade	Grade 1-2	Grade 3-4	Any Grade	Grade 1-2	Grade 3-4
	number of patients with TRAE (%)					
Any TRAE*	11 (28.9)	9 (23.7)	6 (15.8)	23 (60.5)	21 (55.2)	4 (10.5)
TRAEs leading to discontinuation of tx	1 (2.6)	0	1 (2.6)	2 (5.2)	1 (2.6)	1 (2.6)
Serious TRAEs	1 (2.6)	0	1 (2.6)	2 (5.2)	0	2 (5.2)
Treatment-related deaths	0			0		

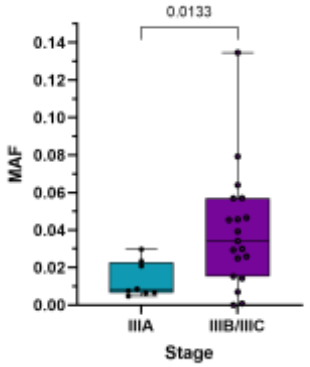
*Treatment Related Adverse Events with an incidence of ≥10%

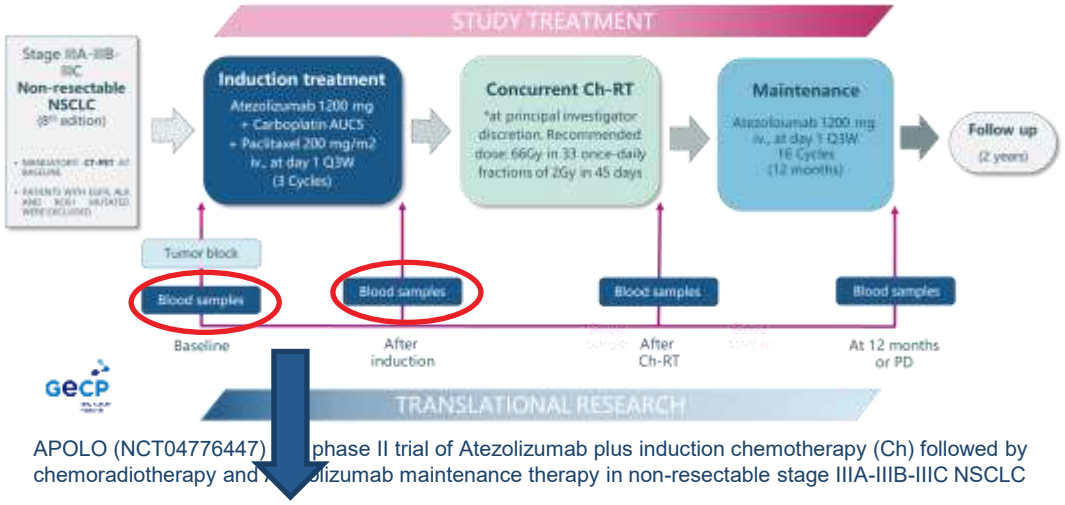
Maintenance tx (n = 38) Total events = 39	Atezolizumab Related		
	Any Grade	Grade 1-2	Grade 3-4
	number of patients with TRAE (%)		
Any TRAE*	17 (44.7)	15 (39.5)	3 (7.9)
TRAEs leading to discontinuation of tx	2 (5.2)	1 (2.6)	1 (2.6)
Serious TRAEs	1 (2.6)	0	1 (2.6)
Treatment-related deaths	0		

*Treatment Related Adverse Events with an incidence of ≥10%

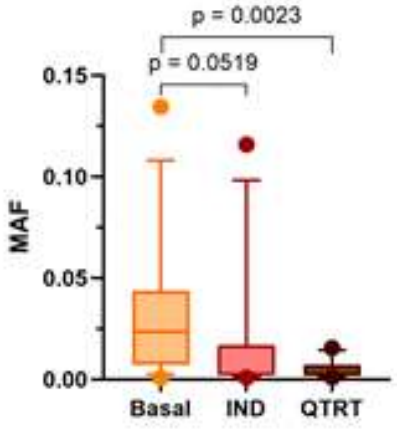
Provencio M, et al. WCLC 2024; J Thorac Oncol 2024;19:S37

APOLO: Atezolizumab + induction chemotherapy (Ch) + chemo-radiotherapy (Ch-RT) and atezolizumab maintenance in non-resectable stage III NSCLC

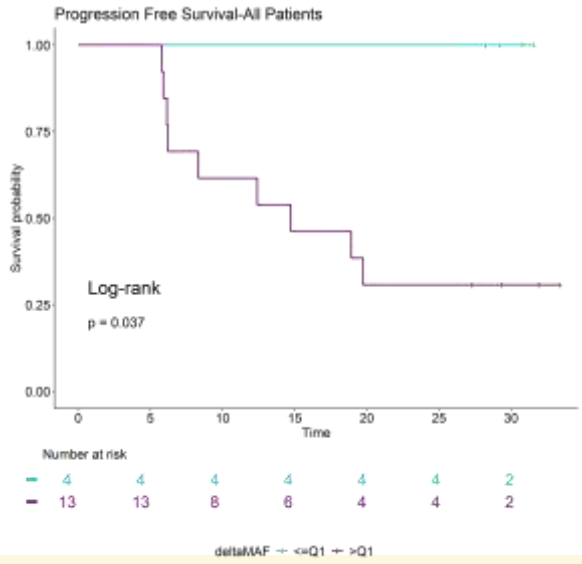


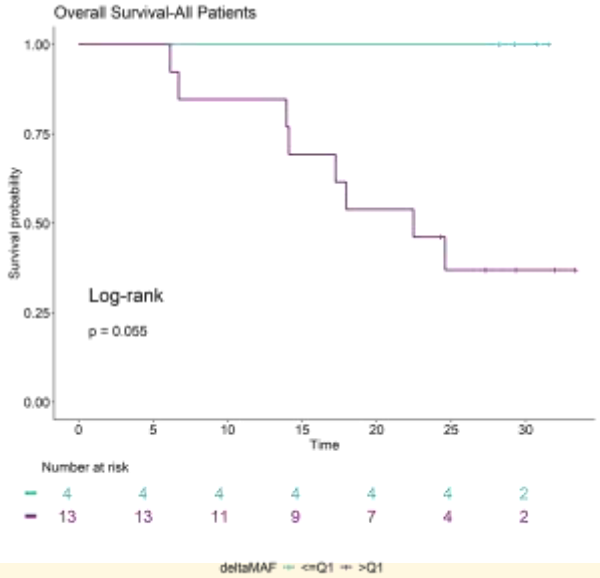


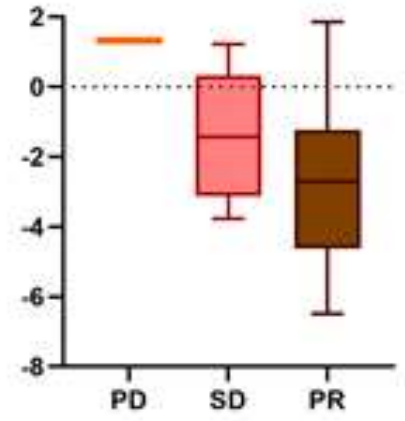
APOLO (NCT04776447) phase II trial of Atezolizumab plus induction chemotherapy (Ch) followed by chemoradiotherapy and atezolizumab maintenance therapy in non-resectable stage IIIA-IIIB-IIIC NSCLC



- None of the patients who exhibited a reduction of at least 93% (upper quartile) in ctDNA levels died or experienced disease progression







Provencio et al. Nature Comunication in press

Provencio M, et al. WCLC 2024; J Thorac Oncol 2024;19:S37

PACIFIC-BRAZIL (LACOG 2218): intensified chemo-immuno-radiotherapy with durvalumab for stage III NSCLCs: a single arm phase II study

- **Phase 2, single-arm, multi-center (8 Brazilian research sites) study conducted through LACOG (NCT04230408)**

ELIGIBILITY CRITERIA

- ✓ Non-small cell lung cancer
- ✓ Stage III (TNM 8th ed.)†
- ✓ PS 0-1
- ✓ FEV1 ≥ 1.2 liters/second (or ≥ 50% predicted value)
- ✓ Predicted lung V20 <35%, cardiac V50 ≤25%
- ✓ No previous local or systemic therapy

N= 49

INDUCTION CHEMO-IMMUNOTHERAPY

Carboplatin AUC 6 IV+
Paclitaxel 200mg/m² IV+
Durvalumab 1500mg/m² IV q3w for 2 cycles

CONCURRENT CHEMO-IMMUNO-RADIOTHERAPY

Carboplatin AUC 2 IV weekly for 6 weeks +
Paclitaxel 50 mg/m² IV weekly for 6 weeks +
Durvalumab 1500mg/m² q3w for 2 cycles +
Intensity-modulated radiation therapy to 60 Gy in 30 fractions over 6 weeks‡

CONSOLIDATION IMMUNOTHERAPY

Durvalumab 1500mg/m² IV q4w for 12 cycles

PRIMARY ENDPOINT:	**12-month progression-free survival**
SECONDARY ENDPOINTS:	Overall survival, overall response rate, duration of response, patterns of failure, efficacy (iRECIST as opposed to RECIST version 1.1), toxicity (CTCAE version 5)
EXPLORATORY ENDPOINTS:	Predictive biomarkers of response/survival

†PET-CT was mandatory, invasive mediastinal staging was strongly encouraged. ‡Image guided radiation therapy (IGRT) was strongly encouraged.

William WN, et al. WCLC 2024; J Thorac Oncol 2024;19:S37-8

PACIFIC-BRAZIL (LACOG 2218): intensified chemo-immuno-radiotherapy with durvalumab for stage III NSCLCs: a single arm phase II study

Demographic and disease characteristics	All Patients (N=49)
Age, in years — median (range)	67 (48 – 83)
Sex	
Female	28 (57%)
Male	21 (43%)
Race or ethnic group	
White	25 (51%)
Black/Mixed	21 (43%)
Other	3 (6%)
Smoking status at diagnosis	
Current/Former smoker	41 (84%)
Never	8 (16%)
Histology	
Squamous	18 (37%)
Non-squamous†	31 (63%)
Disease stage (TNM 8th ed.)‡	
IIB	1 (2%)
IIIA	26 (53%)
IIIB	18 (37%)
IIIC	4 (8%)

†29 adenocarcinomas, 2 not otherwise specified. ‡23 patients (47%) underwent invasive mediastinal staging

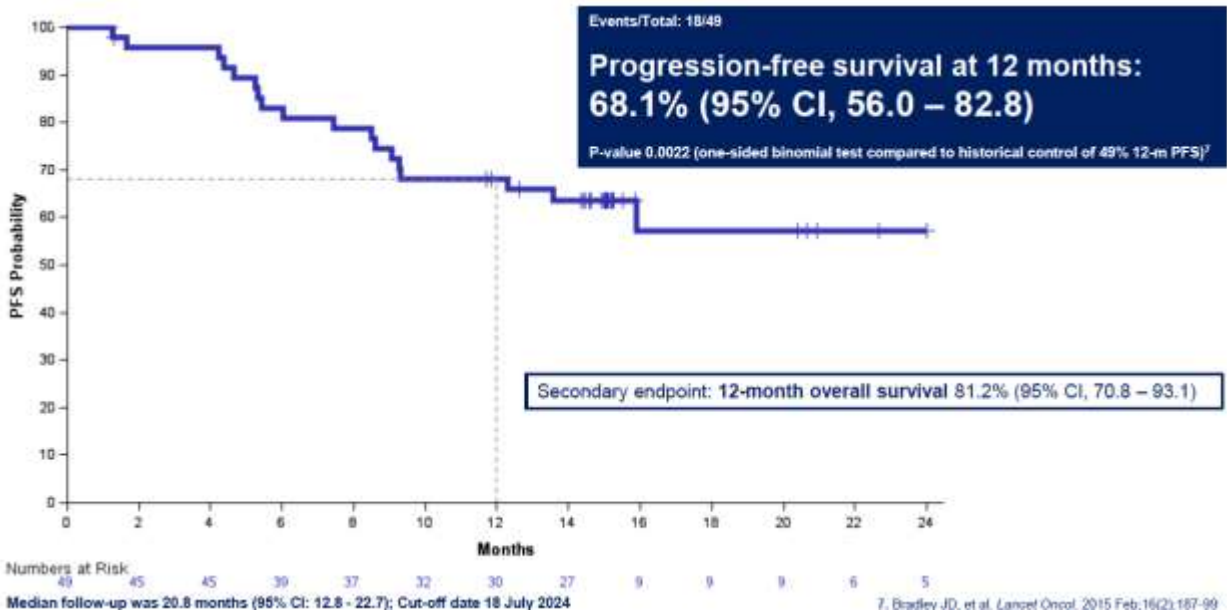
Radiotherapy was given to >59 Gy in 93.4% of patients who initiated concurrent chemo-immuno-radiotherapy

Tumor characteristics	All Patients (N=49)
Primary tumor T	
T1c	2 (4%)
T2a	8 (16%)
T2b	3 (6%)
T3	10 (20%)
T4	26 (53%)
Regional lymph nodes	
N0	7 (14%)
N1	5 (10%)
N2	28 (57%)
N3	9 (18%)

William WN, et al. WCLC 2024; J Thorac Oncol 2024;19:S37-8

PACIFIC-BRAZIL (LACOG 2218): intensified chemo-immuno-radiotherapy with durvalumab for stage III NSCLCs: a single arm phase II study

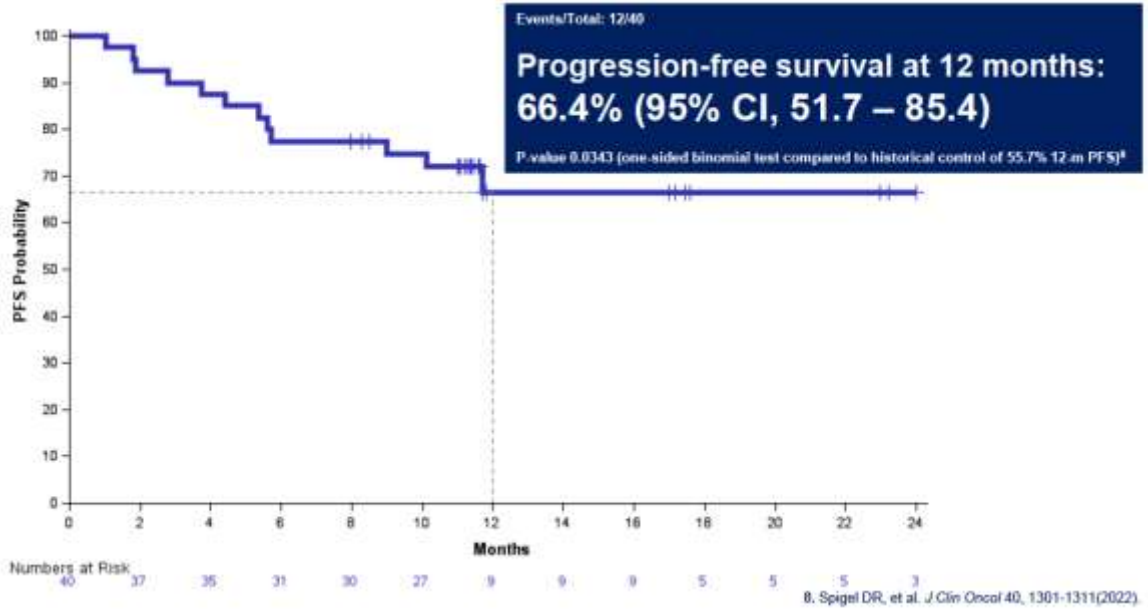
Progression-free survival from treatment initiation



Median follow-up was 20.8 months (95% CI: 12.8 - 22.7); Cut-off date 18 July 2024

7. Bradley JD, et al. *Lancet Oncol*. 2015 Feb;16(2):187-99

Progression-free survival from consolidation immunotherapy



8. Spigel DR, et al. *J Clin Oncol* 40, 1301-1311(2022).

William WN, et al. WCLC 2024; J Thorac Oncol 2024;19:S37-8

PACIFIC-BRAZIL (LACOG 2218): intensified chemo-immuno-radiotherapy with durvalumab for stage III NSCLCs: a single arm phase II study

Adverse Event[†]	Overall N=49		Induction Chemo-immunotherapy N=49		Concurrent Chemo-immuno-radiotherapy N=46[a]		Consolidation immunotherapy N=40[b]	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any	48 (98%)	40 (82%)	46 (94%)	12 (25%)	46 (94%)	32 (65%)	33 (67%)	10 (20%)
Occurred in >20% of patients[c]								
Neutropenia	33 (67%)	16 (33%)	3 (6%)	2 (4%)	31 (67%)	15 (33%)	5 (13%)	0
Anaemia	32 (65%)	9 (18%)	10 (20%)	1 (2%)	29 (59%)	8 (17%)	11 (28%)	0
Fatigue	26 (53%)	2 (4%)	16 (33%)	1 (2%)	16 (35%)	1 (2%)	4 (10%)	0
Lymphopenia	21 (43%)	16 (33%)	3 (6%)	0	21 (46%)	16 (35%)	10 (25%)	2 (5%)
Nausea	20 (41%)	0	17 (35%)	0	11 (24%)	0	2 (5%)	0
Thrombocytopenia	20 (41%)	0	1 (2%)	0	20 (44%)	0	0	0
Alopecia	19 (39%)	1 (2%)	17 (35%)	1 (2%)	3 (7%)	0	0	0
Leukopenia	19 (39%)	7 (14%)	1 (2%)	1 (2%)	18 (39%)	6 (13%)	0	0
Odynophagia	14 (29%)	0	0	0	14 (30%)	0	1 (3%)	0
Pain	13 (27%)	1 (2%)	12 (25%)	1 (2%)	2 (4%)	0	0	0
Pneumonitis	13 (27%)	7 (14%)	2 (4%)	1 (2%)	2 (4%)	2 (4%)	9 (23%)	4 (10%)
Constipation	12 (25%)	1 (2%)	6 (12%)	0	8 (17%)	1 (2%)	0	0
Cough	12 (25%)	0	0	0	10 (22%)	0	2 (5%)	0
Paraesthesia	11 (22%)	0	9 (18%)	0	3 (7%)	0	2 (5%)	0
Vomiting	11 (22%)	1 (2%)	6 (12%)	0	9 (20%)	1 (2%)	1 (3%)	0
Diarrhoea	10 (20%)	2 (4%)	8 (16%)	1 (2%)	2 (4%)	0	1 (3%)	1 (3%)
Neuropathy peripheral	10 (20%)	0	7 (14%)	0	3 (7%)	0	1 (3%)	0

[†] Highest grade per patient. If patient experiences the same adverse event more than once during different treatment phases, such adverse event is computed once per phase and once overall (highest grade)

[a] 3 patients did not start concurrent chemo-immuno-radiotherapy. [b] 6 patients did not start consolidation immunotherapy. [c] Overall

There were 7 (14%) grade 5 events (2 related, 5 unrelated to treatment) during the concurrent (3) or consolidation (3) phases: pneumonia (3), COVID-19 (2), sepsis (1), pneumonitis (1)

William WN, et al. WCLC 2024; J Thorac Oncol 2024;19:S37-8

GASTO-1091: a phase II randomized trial evaluating consolidative nivolumab in locally advanced NSCLC post neoadjuvant nivolumab plus chemotherapy and concurrent chemoradiotherapy (CA209-7AL)

Randomized, phase 2 trial

Key eligibility criteria
- Unresectable, stage III NSCLC (per AJCC 8th edition)
- No prior anti-cancer treatment
- age 18 to 75 years
- ECOG 0-1

NIVO 360 mg Q3W + Chemo[b] Q3W (2 cycles) → Split-Course Hypo-RT (54~64Gy) + Concurrent chemo[c] (weekly) → R 1:1 → NIVO 360 mg Q3W (1 year) / Observation (1 year) → Follow-up

Stratified by age, sex, smoking history and EGFR mutation status

Primary endpoint
- PFS

Secondary endpoints
- OS
- ORR
- Safety
- QOL

Exploratory analyses
- Cytokine levels in plasma
- Peripheral lymphocyte subsets

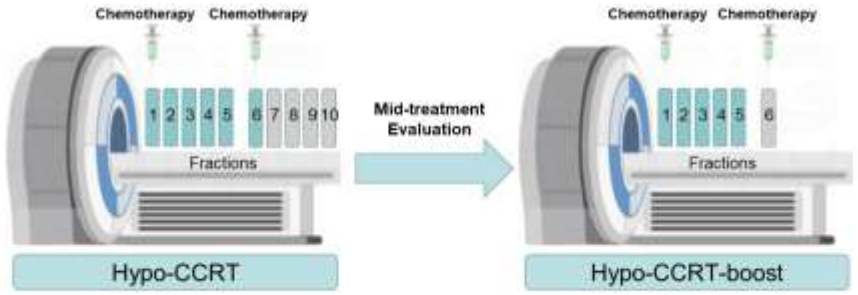
[a] NCT04085250 , [b,c] docetaxel plus cisplatin

- **Hypo-CCRT and hypo-CCRT-boost** [1,2]

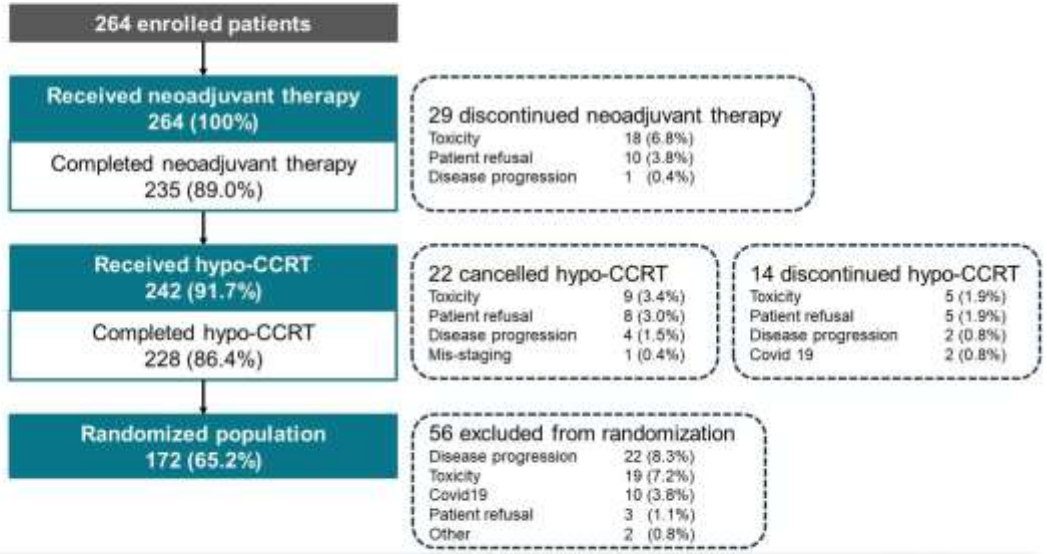
  Hypo-CCRT: 40Gy/10fr or 30Gy/6fr; Hypo-CCRT-boost: 24~30Gy/6fr; Total dose: 60~64Gy

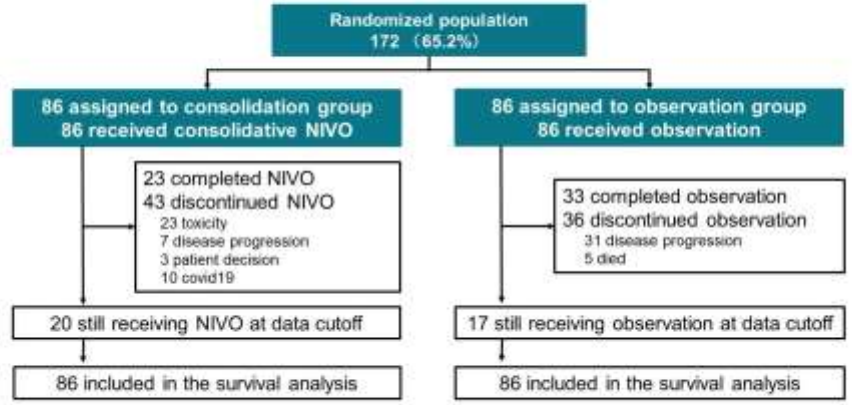
- **Concurrent chemotherapy**

  Docetaxel 25 mg/ m², d1 plus cisplatin 25 mg/ m², d1, every week



[1] Hui Liu et al. *Int J Radiat Oncol Biol Phys.* 2023;117(2):387-395; [2] Bo Qiu et al. *Clin Cancer Res.* 2024 Apr 23.

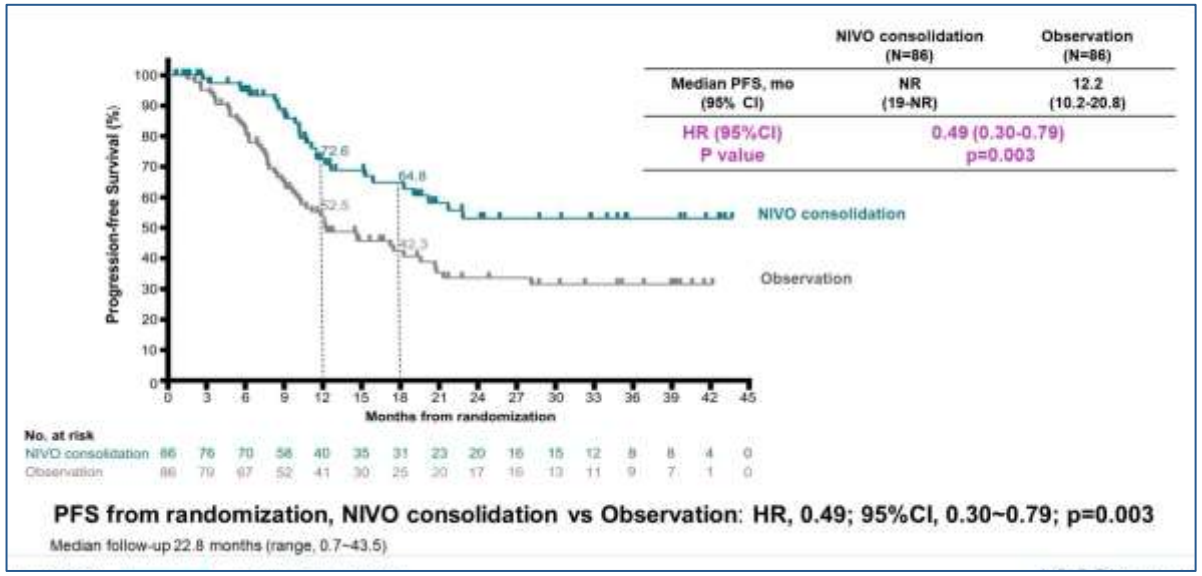




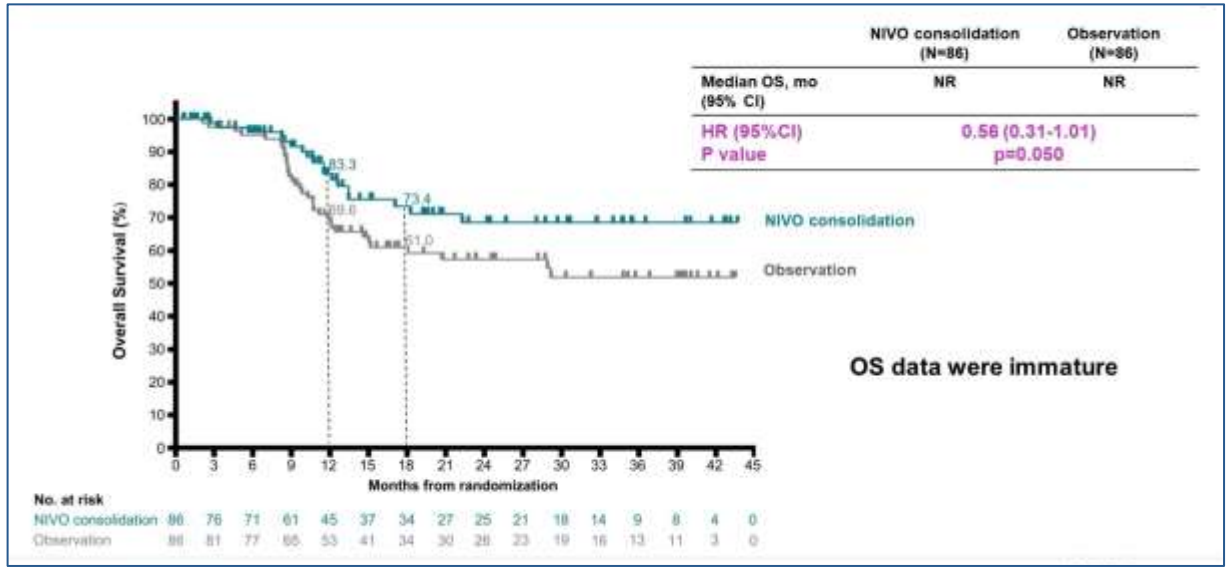
Liu H, et al. ASCO 2024

GASTO-1091: a phase II randomized trial evaluating consolidative nivolumab in locally advanced NSCLC post neoadjuvant nivolumab plus chemotherapy and concurrent chemoradiotherapy (CA209-7AL)

PFS (NIVO Consolidation vs Observation)



OS with NIVO Consolidation vs Observation



Liu H, et al. ASCO 2024

GASTO-1091: a phase II randomized trial evaluating consolidative nivolumab in locally advanced NSCLC post neoadjuvant nivolumab plus chemotherapy and concurrent chemoradiotherapy (CA209-7AL)

Adverse Event	Number of patients (percent)	
Led to discontinuation of neoadjuvant therapy	19 (7.2%)	
	Any Grade	Grade 3 or 4
All	259 (98.1%)	120 (45.5%)
Lymphopenia	214 (81.1%)	93 (35.2%)
Neutrophil count decreased	35 (13.3%)	26 (9.9%)
Leukopenia	41 (15.5%)	19 (7.2%)
Platelet count decreased	37 (14.0%)	13 (4.9%)
Diarrhea	55 (20.8%)	11 (4.2%)
Hyponatremia	116 (43.9%)	10 (3.8%)
Pneumonitis	11 (4.2%)	3 (1.1%)
Vomiting	23 (8.7%)	3 (1.1%)
Aspartate aminotransferase increased	31 (11.7%)	3 (1.1%)
Alanine aminotransferase increased	57 (21.6%)	2 (0.8%)
Dyspnea	19 (7.2%)	2 (0.8%)
Fever	21 (8.0%)	2 (0.8%)
Hemoglobin decreased	170 (64.4%)	1 (0.4%)
Anorexia	75 (28.4%)	1 (0.4%)
Nausea	19 (7.2%)	1 (0.4%)
Rash	17 (6.4%)	1 (0.4%)
Fatigue	17 (6.4%)	1 (0.4%)

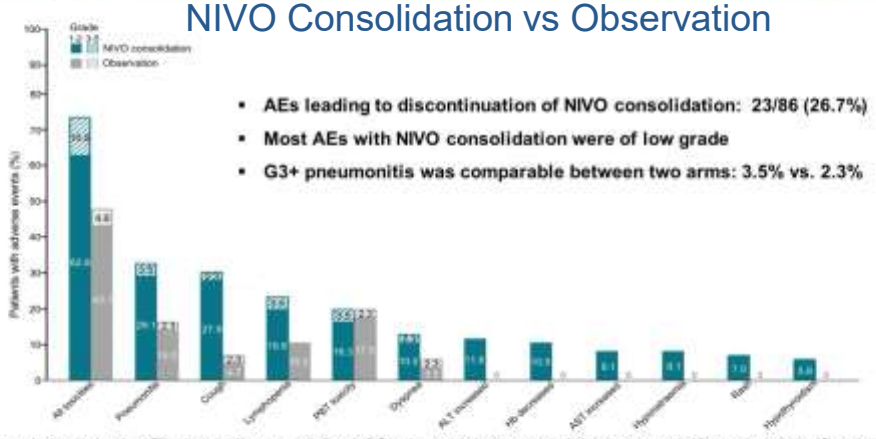
Neoadjuvant period

Adverse Event	Number of patients (percent)	
Led to discontinuation of hypo-CCRT	5 (2.1%)	
	Any Grade	Grade 3 or 4
All	238 (98.3%)	99 (40.9%)
Lymphopenia	218 (90.1%)	89 (36.8%)
Esophagitis	42 (17.4%)	8 (3.3%)
Pneumonitis	132 (54.5%)	6 (2.5%)
Dyspnea	38 (15.7%)	5 (2.1%)
Aspartate aminotransferase increased	29 (12.0%)	5 (2.1%)
Alanine aminotransferase increased	24 (9.9%)	4 (1.7%)
Leukopenia	88 (36.4%)	4 (1.7%)
Cough	74 (30.6%)	3 (1.2%)
Neutrophil count decreased	24 (22.3%)	3 (1.2%)
Hemoglobin decreased	100 (41.3%)	2 (0.8%)
Anorexia	45 (18.6%)	0

Pneumonitis: G2+, 9.9%; G3~4, 2.5%

Split-course Hypo-CCRT period

NIVO Consolidation vs Observation



Liu H, et al. ASCO 2024

BEYOND PACIFIC

IO Consolidation Intensification cCRT → IO + IO	IO concurrent with cCRT IO + cCRT → IO	IO-CT Induction prior to cCRT IO+/-CT → cCRT → IO
• **COAST (Phase II)**	• **PACIFIC-2 (Phase III)**	• **AFT-16 (Phase II)**
• **LUN16-081 (Phase II)**	• **CheckMate-73L (Phase III)**	• **APOLO (Phase II)**
• PACIFIC 8 (Phase III)	• **EA5181 (Phase III)**	• **PACIFIC-BRAZIL (Phase II)**
• PACIFIC 9 (Phase III)	• **KEYNOTE-799 (Phase II)**	• **GASTO-1091 (Phase II)**
• SKYSCRAPER-03 (Phase III)	• **NICHOLAS (Phase II)**	• AFT-57 (Phase II)
• CheckMate-73L (Phase III)	• **DETERRED (Phase II)**	• DEDALUS (Phase II)
• MPLALC (Phase II)	• **CRUISER (Phase II)**	• BRIDGE (Phase II)
	• KEYLIN-012 (Phase III)	
	• KEYVIBE-006 (Phase III)	
	• NCT05386888 (Phase II)	

Adapted from Delcuratolo MD, et al. Cancer Treat Rev 2025;135:102918

ONGOING PHASE II/III IN UNRESECTABLE STAGE III NSCLC: INDUCTION CHEMO-IMMUNOTHERAPY

NCT number (name)	Phase	Treatment arms	N	Primary endpoints	Status
NCT05798663 (AFT-57)	II	ArmA: Atezolizumab - cCRT+Atezolizumab - Atezolizumab ArmB: Atezolizumab+Tiragolumab - cCRT+Atezolizumab - Atezolizumab+Tiragolumab ArmC: Atezolizumab+Tiragolumab - cCRT+Atezolizumab+Tiragolumba - Atezolizumab+Tiragolumab	178	PFS	Recruiting
NCT05128630 (DEDALUS)	II	Durvalumab+CT - Durvalumab+HypoRT - Durvalumab	45	Safety	Recruiting

Delcuratolo MD, et al. Cancer Treat Rev 2025;135:102918; Filippi AR, et al. ESMO OPEN 2024;9:102704

CAN WE CONVERT BORDERLINE/UNRESECTABLE IN RESECTABLE?

Clinical Study	Treatment Regimen	N (%) (Surgery)	ORR	pCR	MPR	mEFS (months)	1-y EFS
Wu et al 2024	SHR1701 + CT → Surgery/RT	27/107 (25%)	74%	26%	44%	N.R	80%
Ricciuti et al 2025	IO + CT → Surgery	84/112 (75%)	67.5%	29%	42%	52.6	81%
Wang et al 2025	IO + CT → Surgery/RT	79/113 (70%)	N.A	32%	56%	N.R	82.3%
Yi et al 2025	IO +/- CT → Surgery	47/100 (47%)	54%	38%	61.7%	30	78.5%
Liu et al WCLC 2025	Tislelizumab + CT → Surgery/RT	10/13 (77%)	100%	60%	90%	N.A	N.A

IO-CT conversion strategy under investigation in clinical trials (more than 30 studies ongoing)

Wu, et al. Cancer Cell 2024; Ricciuti B, et al. JAMA Oncol 2025;11(7):735-741; Wang, et al. Clin Lung Cancer 2025; Yi, et al. Nature Comm 2025; Liu, WCLC 2025

PANDA-1: Tislelizumab plus chemotherapy followed by surgery or radiotherapy and adjuvant tislelizumab in unresectable stage III NSCLC

Inclusion Criteria
- Histologically confirmed stage III NSCLC (per AJCC 8th edition), deemed initially unresectable based on at least one of the following criteria as assessed by MDT:
  (1) T4 tumors invade vital organ* precluding R0 resection
  (2) multi-station/bulky N2 metastases
  (3) N3 metastases
- No prior systemic therapy
- ECOG PS 0-1
- Without known EGFR/ALK mutation

N=55

Induction therapy

Tislelizumab 200 mg d1
+
Nab-paclitaxel 260 mg/m² d1
+
Cisplatin 75 mg/m² or carboplatin AUC 5 d1,
Q3W for 2-4 cycles

MDT**

Local therapy

Definitive Surgery

Definitive RT±Chemo

Adjuvant therapy

Tislelizumab±chemo Q3W for 17 cycles#

Or until PD or unacceptable toxicity

Tislelizumab Q3W for 17 cycles

Primary endpoint:
- 1-year EFS rate (assessed in radical treatment analysis set)

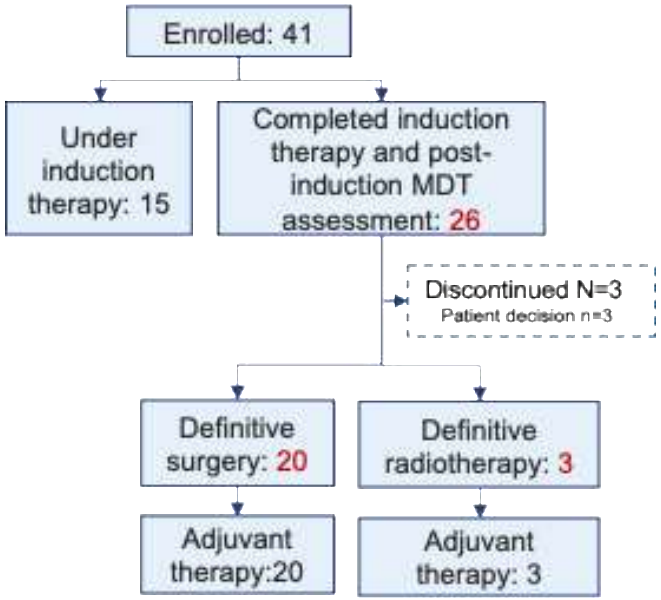
Secondary endpoints:
- EFS, OS, TTDM, TTLR, ORR, DCR, clinical downstaging rate, and surgery rate (based on safety analysis set and and radical treatment analysis set)
- R0 resection rate, pCR, MPR, and pathological downstaging rate (based on surgery analysis set)
- Safety (based on safety analysis set)

Analysis set:
- **Safety analysis set:** includes all patients who received at least one dose of any study drug.
- **Radical treatment analysis set:** includes all patients who underwent surgery or radiotherapy after completing induction therapy.
- **Surgery analysis set:** includes all patients who underwent surgical resection after completing induction therapy.

*Lesions invading vital organs, including diaphragm, mediastinum, major blood vessels, trachea, recurrent laryngeal nerve, esophagus, or satellite nodules in the different lobe of the primary tumor.
**The resectability of the lesions will be re-evaluated by MDT after two cycles of induction therapy and each subsequent induction cycle.
Postoperative radiotherapy is allowed for patients with ypN2+ or ypN3+ after surgery, at the discretion of investigator.

➢ Treatment Status

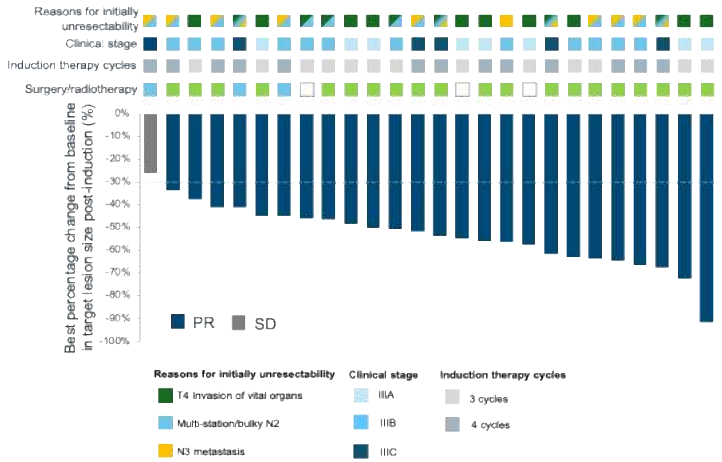
- As of Jul 11, 2025, **41** patients were enrolled.
- **26** patients have completed post-induction MDT assessment.



Liu J, et al. WCLC 2025

PANDA-1: Tislelizumab plus chemotherapy followed by surgery or radiotherapy and adjuvant tislelizumab in unresectable stage III NSCLC

96.2% patients achieved tumor response post-induction, with a markedly high surgery conversion rate

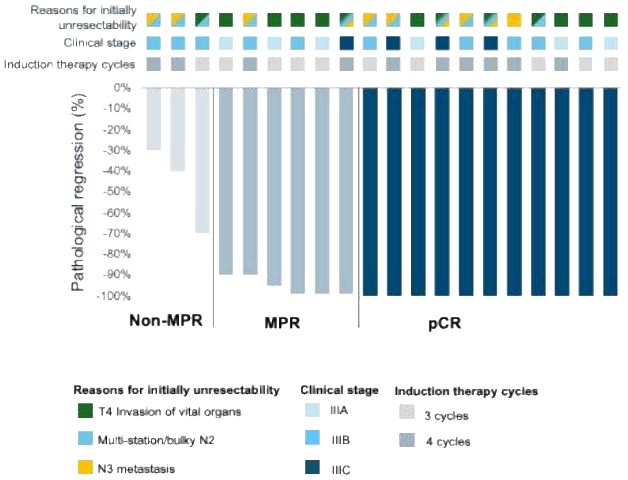


Among 26 patients who completed induction therapy and post-induction MDT assessment:

- **ORR was 96.2%** (25/26).
- **Surgery conversion rate** was **76.9%** (20/26).

	Surgical patients (N=20)
R0 resection rate*, n (%)	20 (100%)
Surgical approach, n(%)	
Minimally invasive	14 (70%)
Thoracotomy	6 (30%)
Minimally invasive to thoracotomy	0
Type of surgery, n(%)	
Lobectomy	20 (100%)

High pCR and MPR rates were attained in surgical patients



Among 20 patients who underwent surgery:

- **pCR** and **MPR rates** were **55.0%** and **85.0%**, respectively.
- pCR and MPR in patients receiving 3 cycles and those receiving 4 cycles of induction therapy were summarized in the below table.

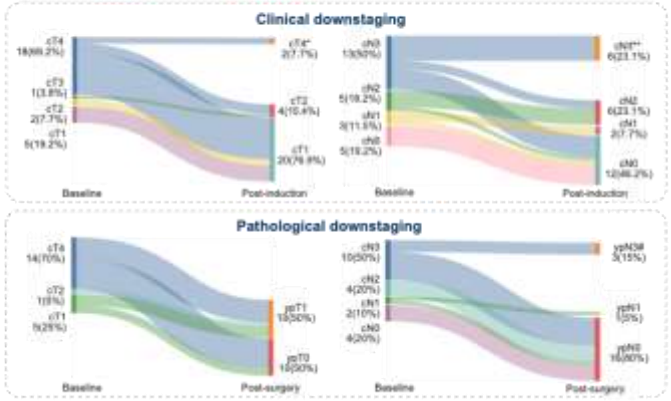
	Surgical patients (n=20)	Cycles of induction therapy	
		3 cycles (n=10)	4 cycles (n=10)
pCR, n (%)	11 (**55.0%**)	5 (50.0%)	6 (60.0%)
MPR, n (%)	17 (**85.0%**)	9 (90.0%)	8 (80.0%)

Promising clinical and pathological downstaging was observed

- Clinical and pathological downstaging occurred in **84.6%** (22/26) and **90.0%** (18/20) of patients.

	Patients completed post-induction MDT assessment (n=26)
Clinical downstaging rate, n (%)	**84.6% (22/26)**
T downstaging	73.1% (19/26)
cT4→<cT4	n=3
cT4→<cT3	n=13
cT3→<cT2	n=1
cT2→<cT1	n=2
N downstaging	34.6% (9/26)
cN3→<cN2	n=2
cN3→<cN0	n=5
cN2→<cN0	n=1
cN1→<cN0	n=1

	Surgical patients (n=20)
Pathological downstaging rate, n (%)	**90.0% (18/20)**
T downstaging	85.0% (17/20)
cT4→ypT1	n=6
cT4→ypT0	n=6
cT3→ypT1	n=1
cT1→ypT0	n=2
N downstaging	60.0% (12/20)
cN3→ypN0	n=7
cN2→ypN0	n=4
cN1→ypN0	n=1



*1 pt underwent radiotherapy; 1 pt with significant tumor shrinkage post induction therapy, despite vascular invasion, the difficulty of surgery was greatly reduced, thus underwent surgery.
**3 pts underwent radiotherapy, 2 pts underwent primary tumor resection and regional N3 lymph node dissection, 1 pt received primary tumor and N2 lymph node radical resection+N3 radiotherapy. # Postoperative radiotherapy was given to these 3 pts.

- Grade ≥3 TRAEs occurred in 18 (43.9%) patients, with the majority being hematological toxicities.
- No TRAEs resulted in treatment discontinuation or death.
- No surgery cancellations due to TRAEs.

Liu J, et al. WCLC 2025

MDT-BRIDGE

BERLIN 2025 ESMO congress

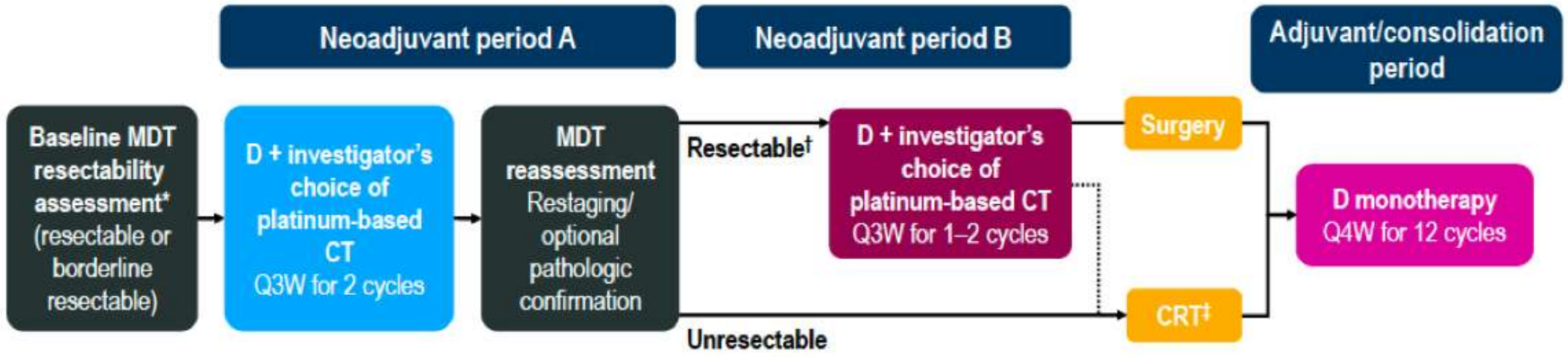
Neoadjuvant durvalumab + chemotherapy followed by either surgery and adjuvant durvalumab or chemoradiotherapy and consolidation durvalumab in patients with resectable or borderline resectable stage IIB–IIIB NSCLC: interim analysis of the phase 2 MDT-BRIDGE study

Martin Reck,[1] Nicolas Girard,[2] Ernest Nadal,[3] Carl M. Gay,[4] Andrew R. Filippi,[5] Linda W. Martin,[6] Cordula Petersen,[7] David A. Cairns,[8] Benoit Rioch,[9] Ilaria Attili,[10] Rosa Alvarez Alvarez,[11] Arnaud Boyer,[12] Margarita Majem,[13] Andrew Robinson,[14] Eva-Lotte Buchwalder,[15] Matteo Giaj Levra,[16] Lei Li,[17] Ignacio Diaz Perez,[18] Nehdi Georgopoulos,[19] Jonathan Spicer[20]

Global, phase 2, non-randomized study (NCT05925530)

Key inclusion criteria and study requirements

- Aged ≥18 years
- Previously untreated and pathologically confirmed, resectable or borderline resectable, stage IIB–IIIB NSCLC (per AJCC 8th edition[2])
- *EGFR*/*ALK*wt (per local test)
- WHO/ECOG PS 0–1
- At least 1 target lesion not previously irradiated
- Pre-operative RT not allowed



Primary endpoint

- Resection rate, defined as proportion of all patients who underwent definitive surgery

Secondary endpoints

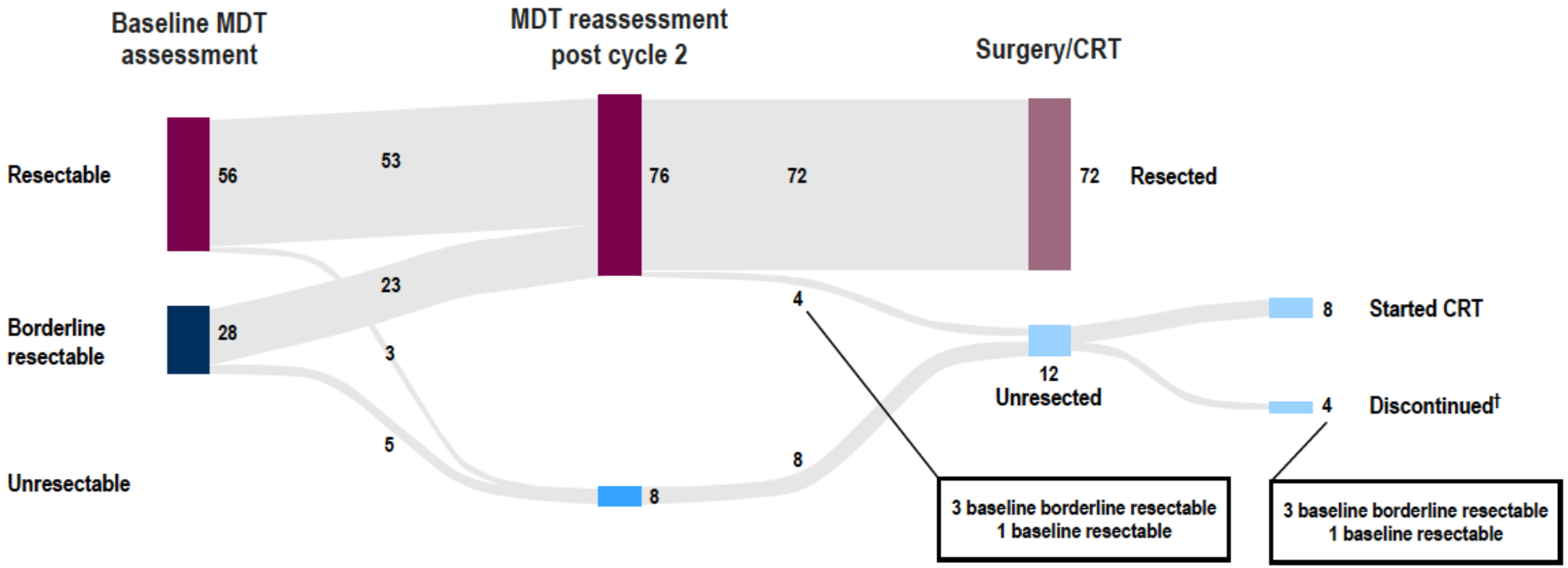
- Resection rate in patients deemed resectable/borderline resectable at baseline
- Surgical outcomes in patients who underwent surgery
- ORR in patients deemed resectable/unresectable at reassessment
- pCR in patients deemed resectable at reassessment
- Safety

- This planned interim analysis (DCO 8 May 2025) was conducted in the subset with sufficient follow-up, defined as patients who have had the opportunity to be followed up for 6 months or undergo definitive surgery, including patients who discontinued the study for any reason or died (**efficacy subset, N=84**)
- Safety was analysed in all patients who had received ≥1 dose of study treatment at the time of the DCO (**safety population, N=131**)

Reck M, et al. LBA65. ESMO 2025; Reck M, et al. Clin Lung Cancer 2024;25(6):587-93.e3

Change in resectability and local treatment received (efficacy subset*)

Most patients deemed borderline resectable at baseline were reassessed as resectable after 2 cycles

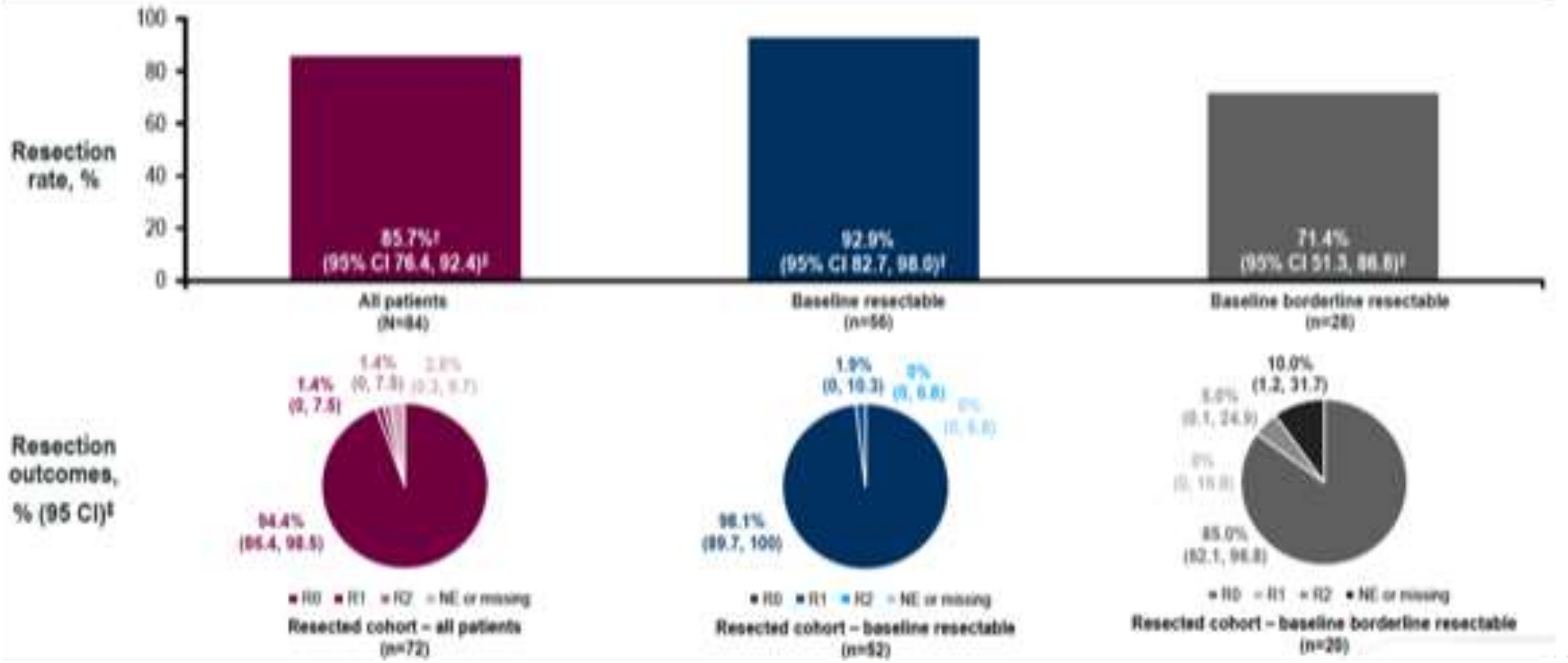


95.2% had either surgery or CRT after neoadjuvant D + CT

Reck M, et al. LBA65. ESMO 2025; Reck M, et al. Clin Lung Cancer 2024;25(6):587-93.e3

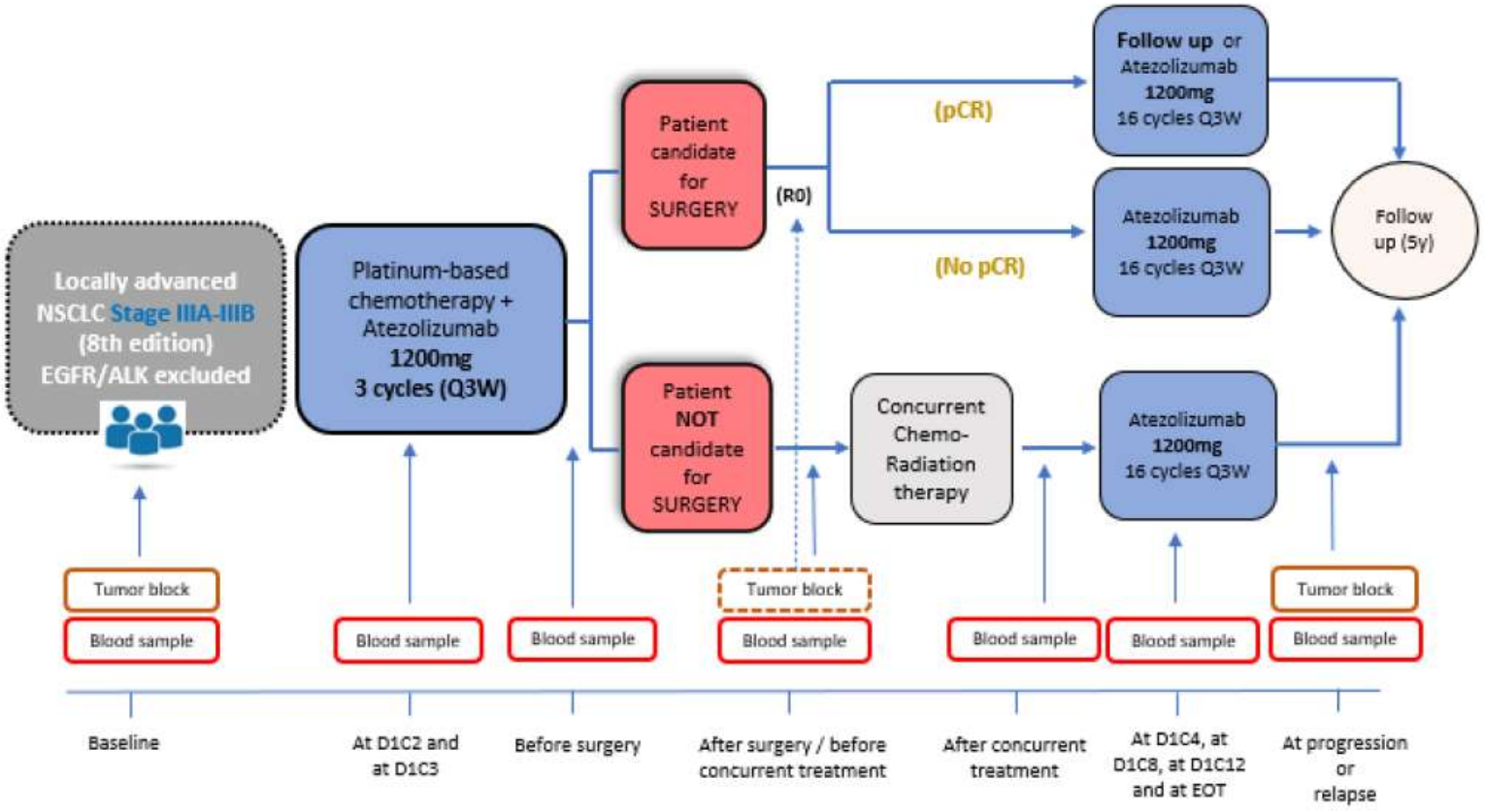
Resection rates and outcomes (efficacy subset*)

Overall resection rate: 85.7%
The majority of patients had R0 resection: 94.4%



Reck M, et al. LBA65. ESMO 2025; Reck M, et al. Clin Lung Cancer 2024;25(6):587-93.e3

ATHENEA: phase II clinical trial of chemotherapy + atezolizumab for stage IIIA and IIIB non-small cell lung cancer followed by atezolizumab as adjuvant treatment after surgery and atezolizumab as maintenance treatment for non-resected patients after chemoradiotherapy



GECP 23/02 (ML45372)

CONCLUSIONS

- PACIFIC regimen remains standard in stage III unresectable NSCLC
- Intensifications strategies in different moments are being evaluated with interesting results
- It seems reasonable to explore new research avenues to assess whether a chemo-immunotherapy induction approach may be superior to Ch-RT + consolidation immunotherapy
- Promising preliminary evidence for IO-CT induction prior to cCRT
- We may be able to convert unresectable in resectable using perioperative strategies

16th CONGRESS Lung ON CANCER

BARCELONA 27 / 28 NOVEMBER 2025

THANK YOU

GECP lung cancer research