Lung Cancer UPDATES
WCLC HIGHLIGHTS
06 - 09 SEPTIEMBRE 2025
Barcelona, Spain

Iniciativa científica de:
GECP lung cancer research

Cáncer de pulmón no microcítico localmente avanzado

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Disclosures

- ***Advisory / Consultancy :*** *AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, MSD, Novartis, Roche, Takeda, Pfizer, Janseng-Cilag*

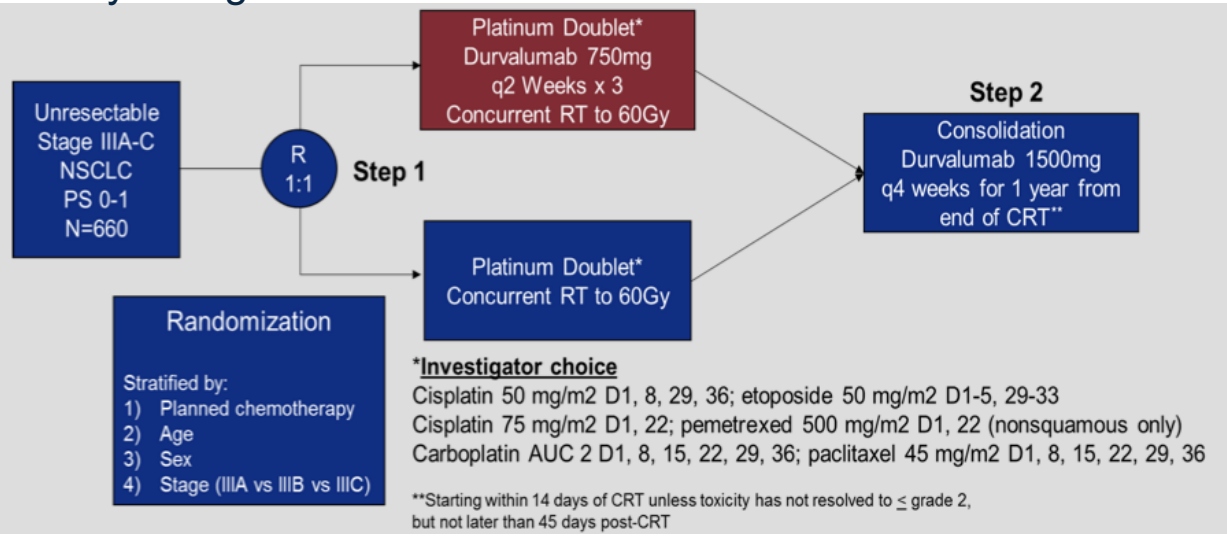
- ***Speaker Bureau / Expert testimony****: AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, MSD, Novartis, Pfizer, Roche, Takeda, Pierre-Fabre, Regeneron*

- ***Travel / Accommodation / Expenses*** *:Bristol-Myers Squibb, Pfizer, Roche, Takeda, Astra Zeneca*

Locally Advanced NSCLC

ECOG-ACRIN EA5181: Phase 3 Trial of Concurrent and Consolidative Durvalumab vs Consolidation Durvalumab Alone for Unresectable Stage III NSCLC

Sutdy Design



Baseline Characteristics

	ChemoRT/IO, N= 335	ChemoRT, N= 327	TOTAL
SEX- MALE	60.6%	60.6%	60.6%
AGE –Median(range)	67.4(37.6-86.7)	66.82(39.1-89.4)	67.1(37.6-89.4)
RACE			
White	85.7%	91.1%	88.4%
Black	10.1%	6.4%	8.3%
STAGE			
IIIA	166 (49.6%)	169 (51.7%)	335 (50.6%)
IIIB	141 (42.1%)	134 (41.0%)	275 (41.5%)
IIIC	26 (7.8%)	22 (6.7%)	48 (7.3%)
HISTOLOGY			
Adenocarcinoma	159 (47.3%)	164 (50.2%)	323 (48.7%)
Squamous Cell ca	133 (39.6%)	121 (37.0%)	254 (38.3%)
SMOKING			
Current	128 (38.2%)	136 (41.6%)	264 (39.9%)
Former	185 (55.2%)	168 (51.4%)	353 (53.3%)
Never	22 (6.6%)	23 (7.0%)	45 (6.8%)
CHEMOTHERAPY			
Carboplatin/paclitaxel	82.4%	82.5%	82.5%

Primary endpoint – OS intention to treat population;
25% reduction in OS HR

Secondary endpoint –PFS, toxicity, ORRs, and Recurrence patterns

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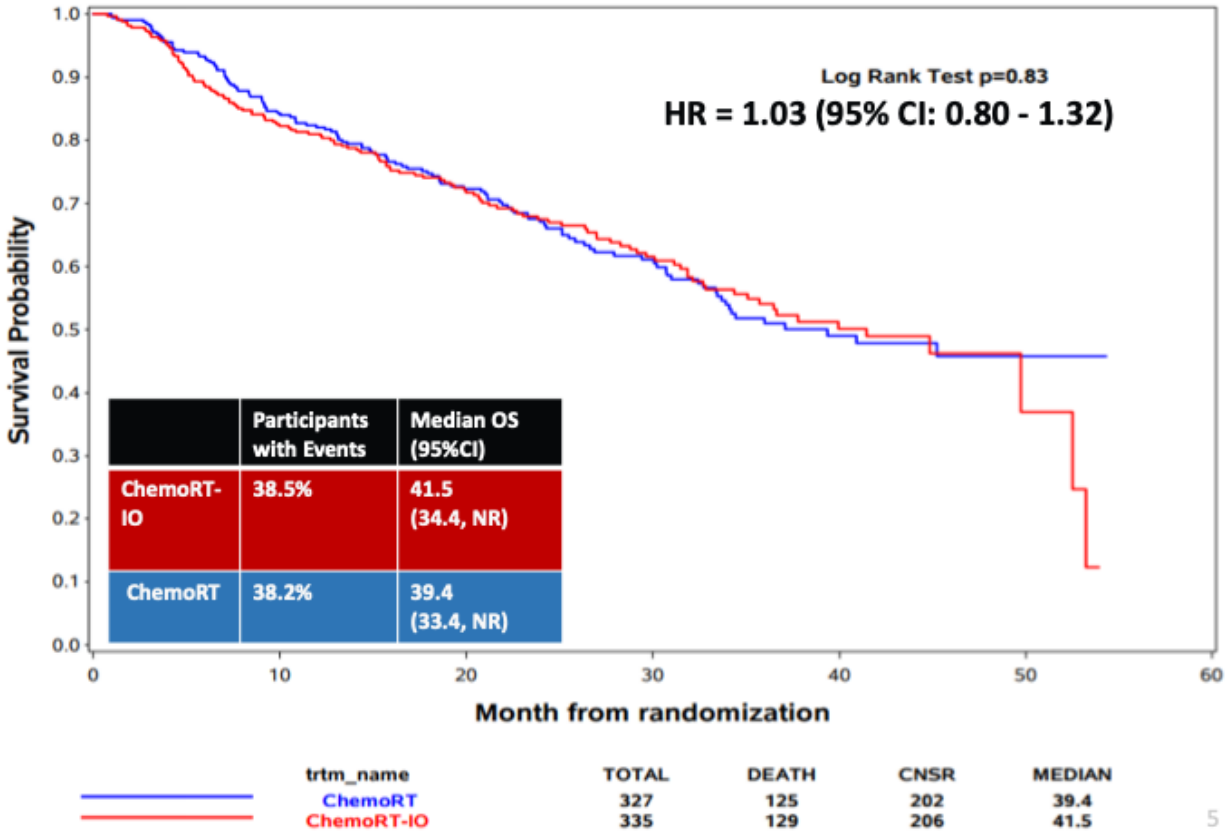
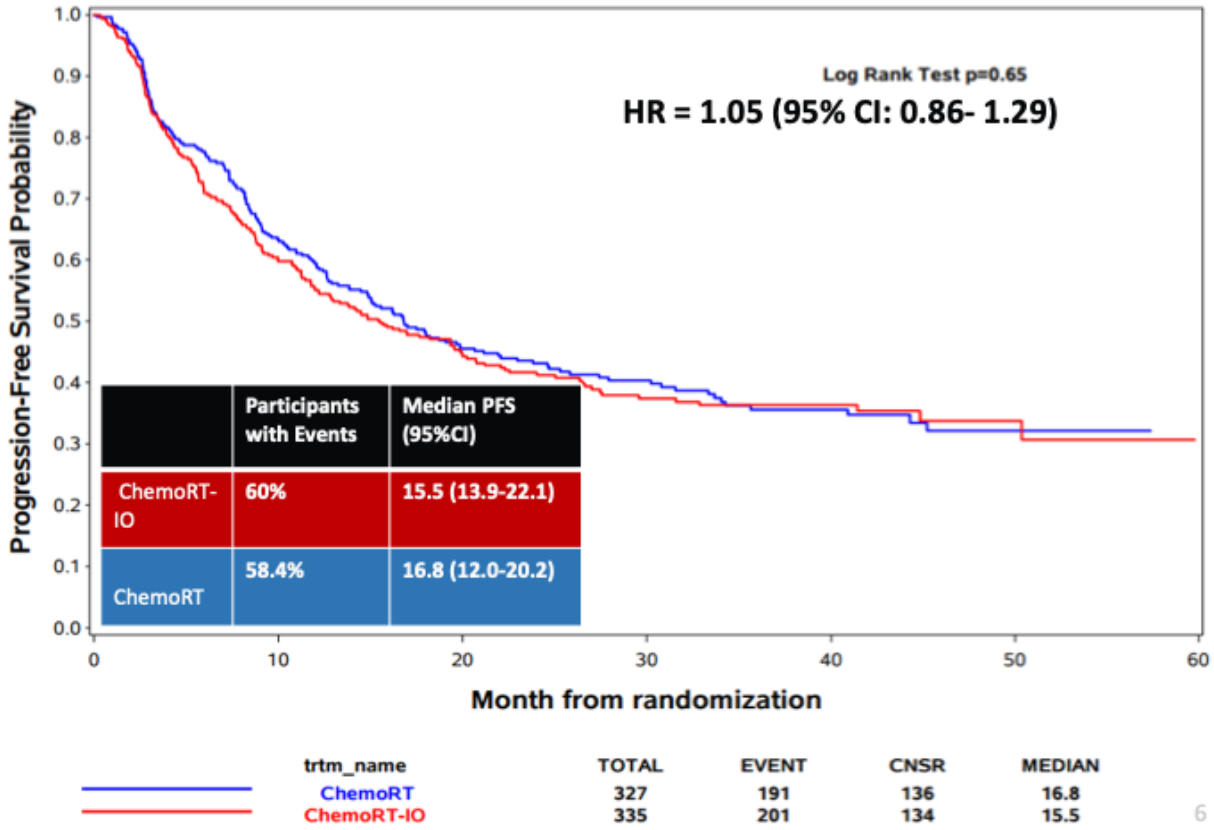
Overall Survival



Progression Free Survival



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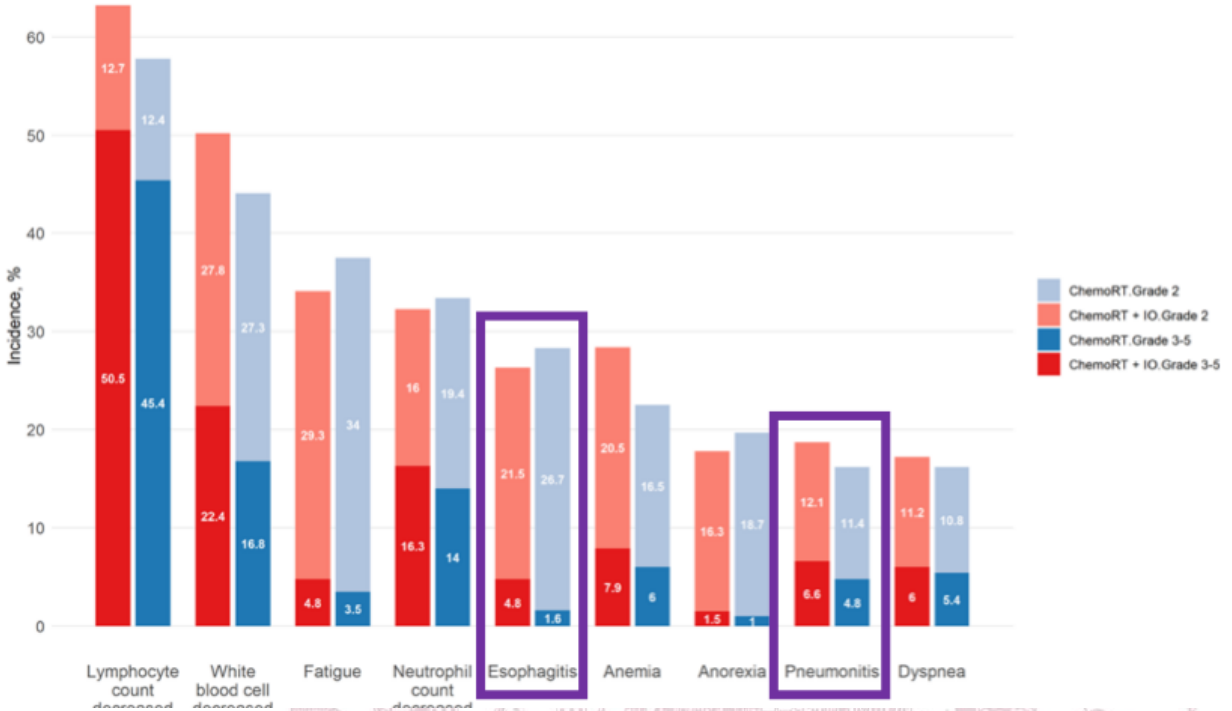
Adverse Events

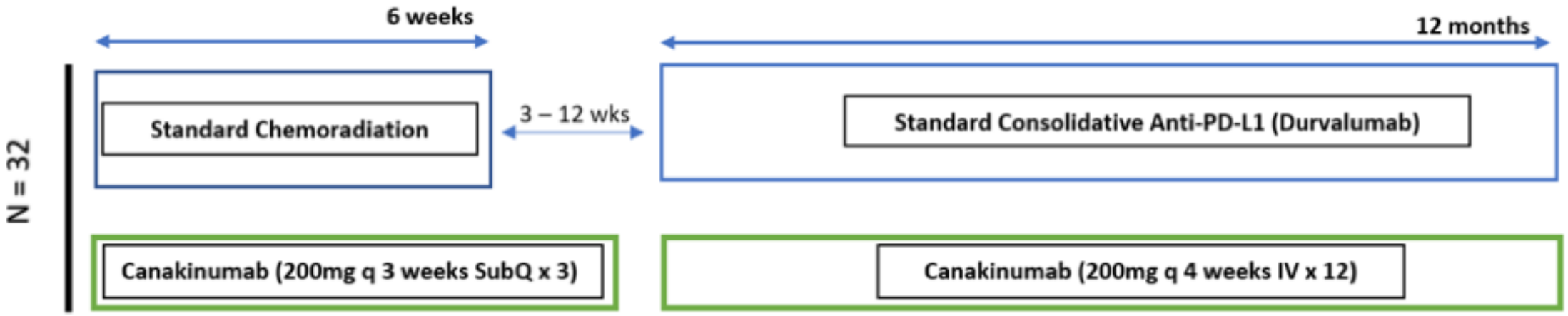
Treatment-Related Adverse Events	ChemoRT-IO (N=331)	ChemoRT (N=315)	P-VALUE
Pulmonary Events – STEP1			
Grade 2-5	188(56.8%)	166 (52.7%)	p = 0.98
Grade 3-5	30(9.1%)	19(6.0%)	p = 0.18
Cardiac Events –STEP 1			
Grade 2-5	67(20.2%)	52(16.5%)	P = 0.52
Grade 3-5	31(9.4%)	26(8.3%)	P = 0.39
Adverse Events, grade 3-4 –STEPS 1 & 2	224 (67.7%)	196 (62.2%)	P=0.16
Grade 5 events- STEPS 1 & 2	12 (3.6%)	11 (3.5%)	P = 1
Treatment Discontinuation – ADVERSE EVENTS STEPS - 1 & 2	63 (19.0%)	52 (16.5%)	P = 0.41



Locally Advanced NSCLC

Phase I/II Trial of Canakinumab with Chemoradiation & Durvalumab in Unresected Stage III Non-Small Cell Lung Cancer

Study Design



Key Eligibility:

- Stage IIIA-C NSCLC
- Fit for concurrent chemoradiation therapy
- Candidate for durvalumab consolidation

Primary Endpoint: 2-year Progression-Free Survival

- Hypothesis: Improvement from the historical 2- year PFS rate of 46% (PACIFIC) to a 2-year PFS of 64%.
- Tested using a one-sided CI based on KM method with a 10% type 1 error (positive trial = lower bound of 90% CI > 46% at 2-years)

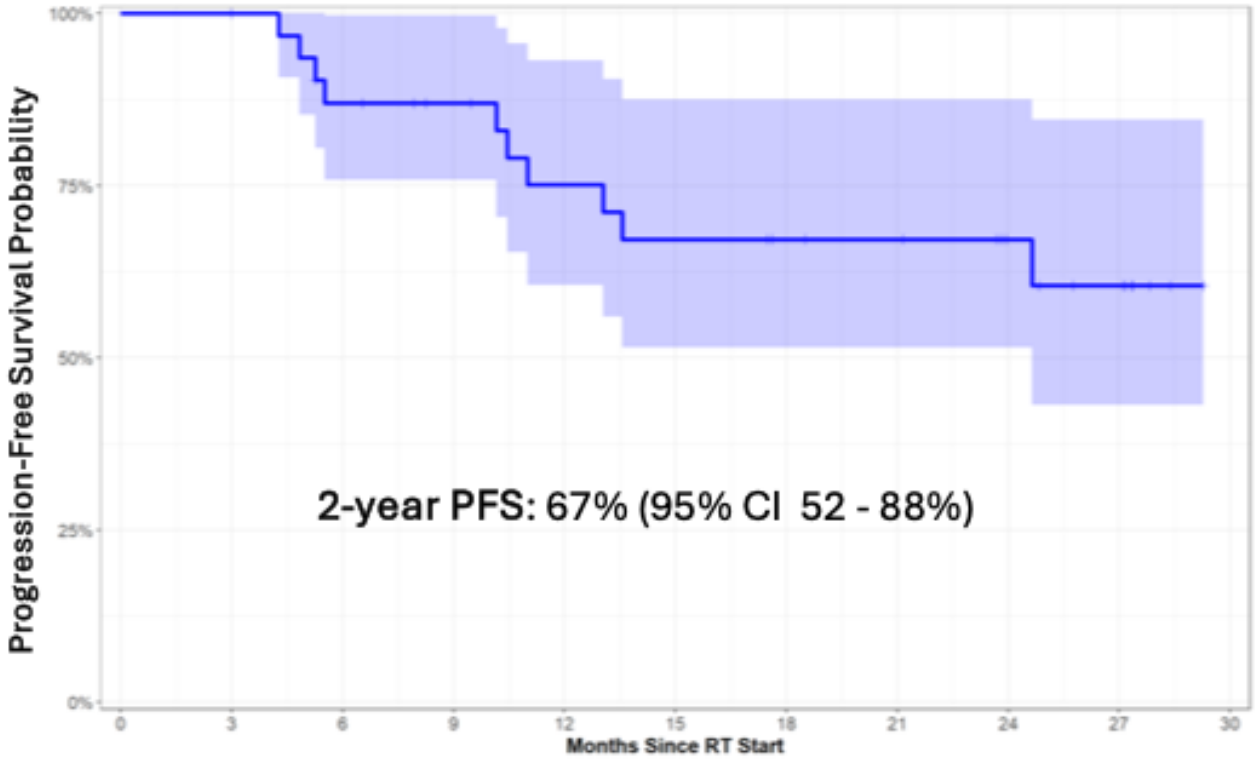
Secondary Endpoints: 2-year overall survival, Rate of pneumonitis, Objective response rate per RECIST 1.1

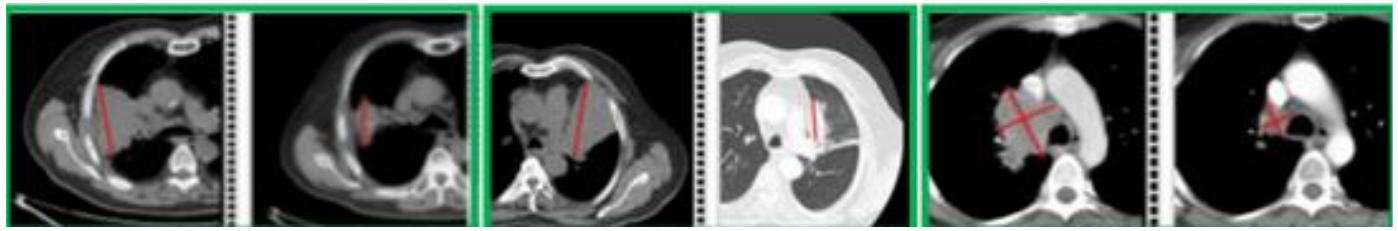
Locally Advanced NSCLC

Phase I/II Trial of Canakinumab with Chemoradiation & Durvalumab in Unresected Stage III Non-Small Cell Lung Cancer

GECP lung cancer research

Eficacy





Primary endpoint met (2-year PFS 67%)

- ORR on first scan post cCRT + canakinumab:
  74% (95% CI 55 – 88%)
  48% with ≥ 50% reduction in target lesions

- Confirmed ORR at any time point on study:
  81% (95% CI 63 – 93%)

Safety:
- No canakinumab treatment-related deaths
- Grade 3-4 canakinumab-related toxicities
- Mostly during cCRT phase of treatment:
  Neutropenia (n=4), Lymphopenia (n=1), Febrile neutropenia (n=1), G4 neutropenia (n=1)
- During durvalumab consolidation:
  Lung infection (n=1), Fatigue (n=1), Hypertension (n=1)

Locally Advanced NSCLC

Preliminary results of the Phase I LuCa-MERIT-1 trial: An advanced NSCLC pt cohort treated with BNT116 + cemiplimab post CRT

BNT116 is an investigational mRNA-LPX cancer immunotherapy utilizing mRNA-encoded tumor antigens (CLDN6, KK-LC-1, MAGE-A3, MAGE-A4, MAGE-C1, PRAME) frequently expressed in NSCLC

Patients

Key inclusion

- Unresectable Stage III NSCLC
- cCRT shortly before entering the trial
- Able to tolerate anti-PD-1
- ECOG PS 0 to 2

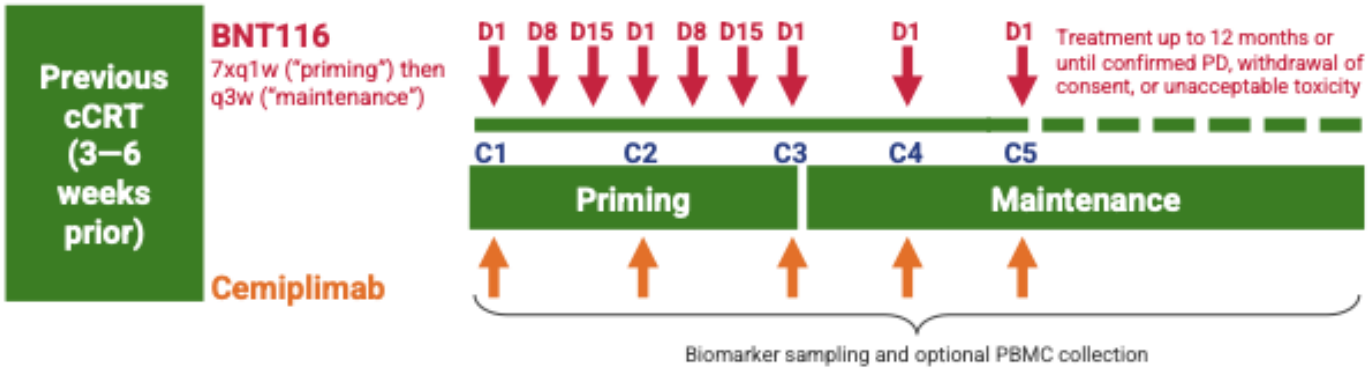
Key exclusion

- Prior systemic therapy or radiation therapy except for CRT
- Progressive disease after CRT

Endpoints (selected)

Primary	Safety and tolerability
Secondary	Clinical activity: EFS, OS
Exploratory	Predictive and pharmacodynamic biomarkers

Treatment schedule



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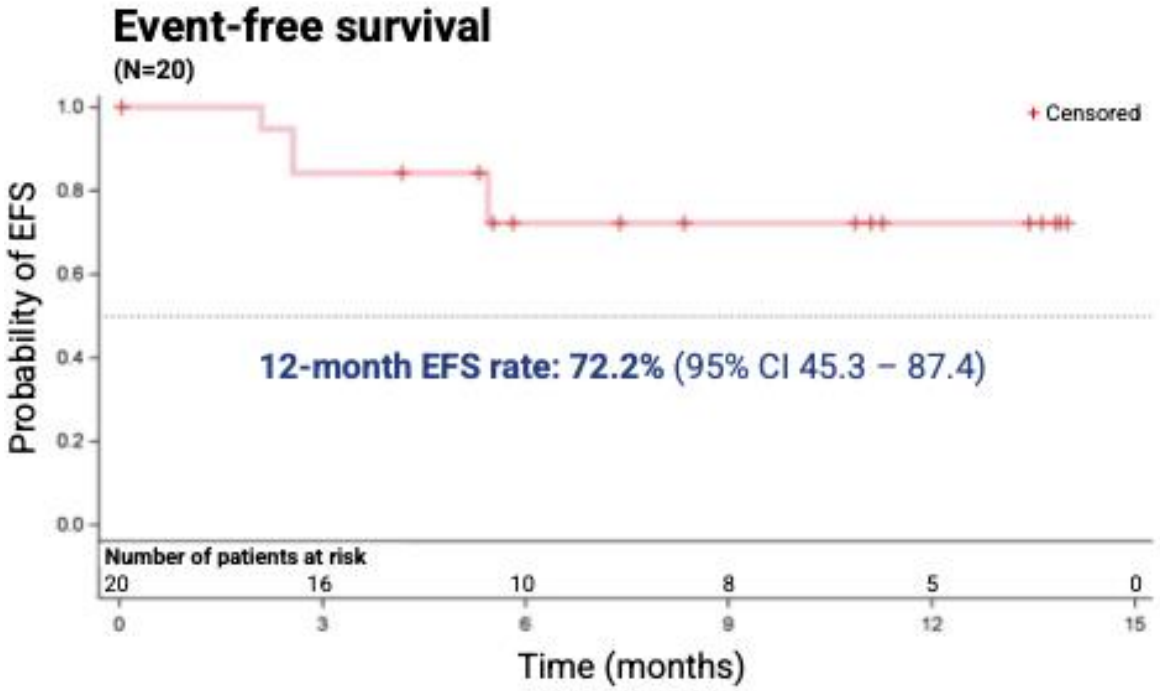

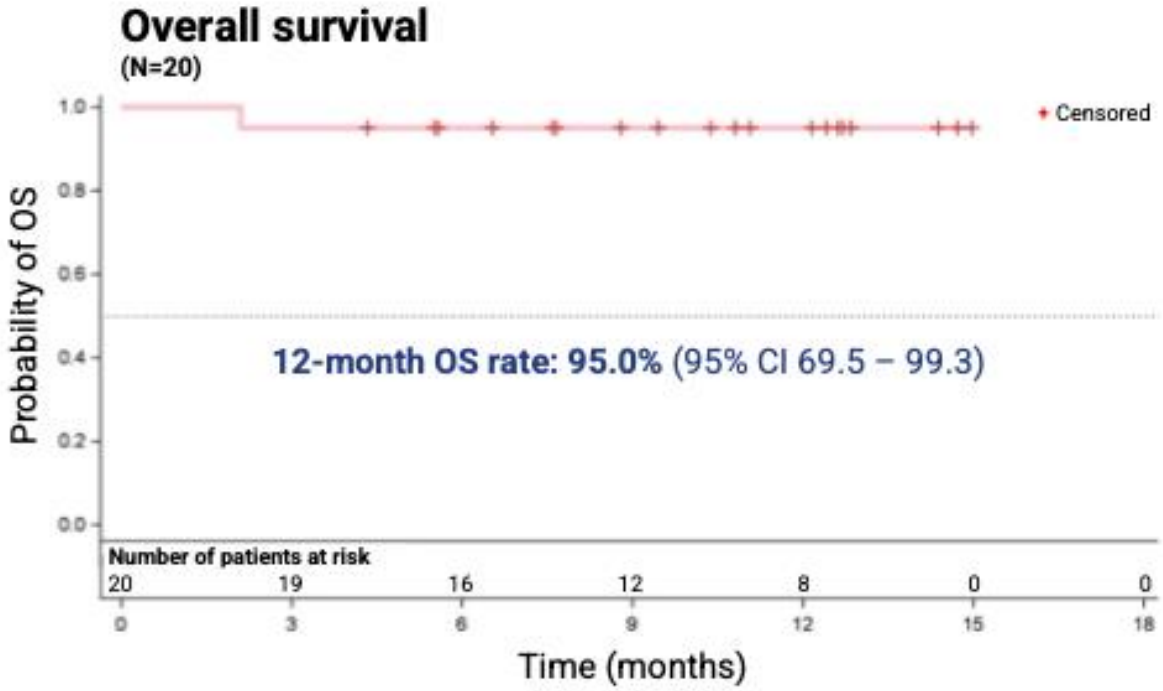

- Median follow-up 10.6 months (range 2 – 15 months).
- Tumor control was observed in most patients.

To wrap up

1. In patients with unresectable Stage III disease, the addition of concomitant durvalumab during chemoradiation did not demonstrate a significant benefit in overall survival (OS) or progression-free survival (PFS).

2. New drugs are currently under study to improve the limited benefit observed with current treatments.