

Supplementary information: ctDNA clearance and outcomes for resectable lung cancer from NeoCOAST-2

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Institutional review board and ethics committee approvals

The study protocol, protocol amendments, informed consent form, investigator brochure and other relevant documents were reviewed and approved by the Institutional Review Boards and Ethics Committees at each participating center, as follows. Belgium, UZ Leuven. Canada: McGill University Health Centre; Centre hospitalier de l'Université de Montréal; Alberta Health Services Cross Cancer Institute. France: CHU de Bordeaux Hopital Saint André; Centre Hospitalier de Cornouaille; CHU Dupuytren; Hopital Foch; CHU Rouen Hopital; Hopital d'Instruction des Armées Sainte Anne; Centre Hospitalier D'Avignon Hopital Henri Duffaut Médecine Interne Onco-Hématolo. Hungary: Bacs-Kiskun Varmegyei Oktataskorhaz; Tudogyogyintezet Torokbalint; Fejér Varmegyei Szent György Egyetemi Oktató Kórház; Szent Bor bala Korhaz. Ireland: University Hospital Galway; Mater Misericordiae Hospital. Italy: Regina Elena; Istituto Nazionale dei Tumori; Istituti Fisioterapici Ospitalieri (IFO); Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS); Ospedale San Gerardo – ASST di Monza, IRCCS; Istituto Clinico Humanitas Rozzano, IRCCS; Istituto Oncologico Veneto, IRCCS; Ospedale S.Maria della Misericordia; AO di Perugia S.C. Oncologia Medica; Ospedale Policlinico San Martino, IRCCS; SO di Cisanello; AOU Pisana; AOU Careggi UO Radioterapia; Ospedale Niguarda; ASST Grande Ospedale Metropolitano Niguarda; ASST Spedali Civili di Brescia. Portugal: Hospital da Luz; Centro Hospitalar e Universitário Lisboa Central Hospital Santo António dos Capuchos; Instituto Português Oncologia Francisco Gentil do Porto; Instituto Português de Oncologia de Lisboa Francisco Gentil. South Korea: Asan Medical Center; Seoul National University Hospital Department of Internal; The Catholic University of Korea; St. Vincent's Hospital Oncology; CHA Bundang Medical Center; CHA University; Inje University Haeundae Paik Hospital. Spain: Hospital Teresa Herrera (CHUAC); Hospital Universitario Puerta De Hierro De Majadahonda; H.U.M. de Terrassa; H.U. Sant Joan de Reus; Hospital Clínico San Carlos; H. Clínico de Valencia; Hospital Universitario Virgen De La Macarena; Hospital Regional Universitario de Málaga; Hospital Clinic De Barcelona; Fundacion Jimenez Diaz; Hospital General Universitario De Alicante. Taiwan: National Cheng Kung University Hospital; Taipei Medical University Shuang Ho Hospital Pulmonology. Turkey: Goztepe Prof. Dr. Suleyman Yalcin Sehir Hastanesi Tibbi Onkoloji. United States: MD Anderson Cancer Center; Cleveland

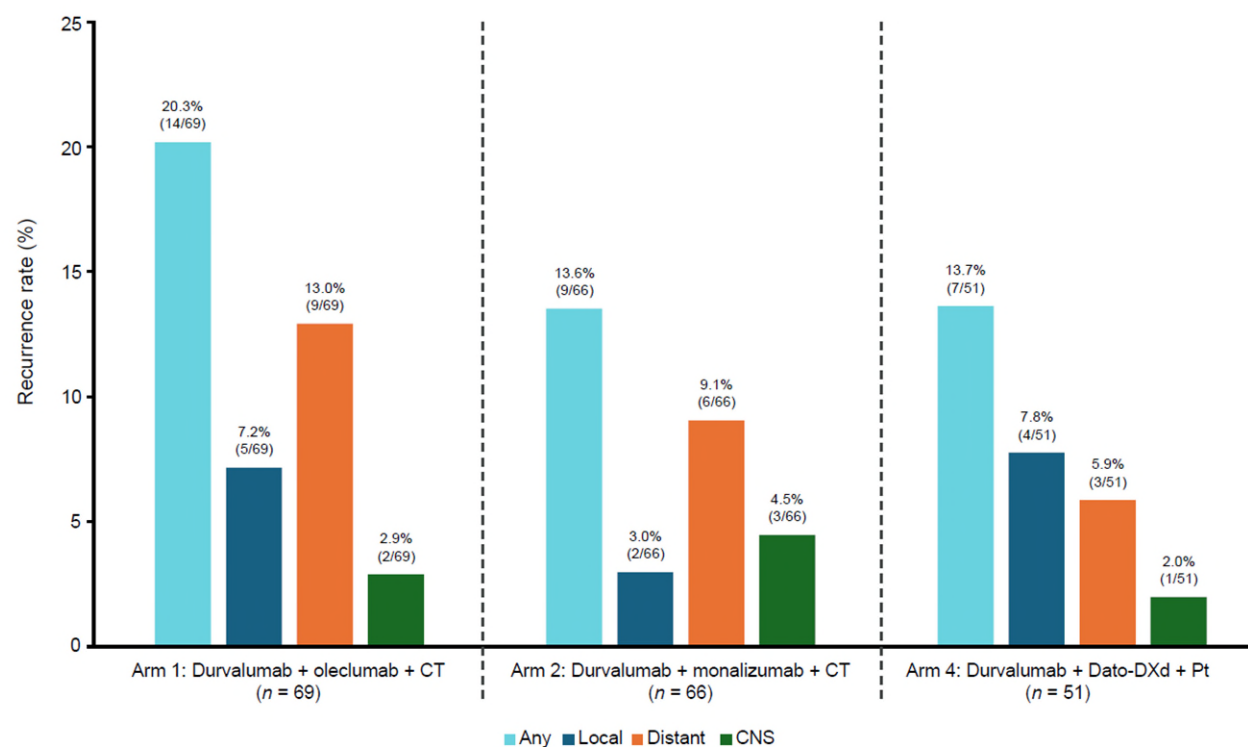
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Clinic Medical Oncology/Hematology; John Hopkins Medicine
Hematology/oncology; US Oncology Virginia Cancer Specialists, P.C. (VCS);
Cleveland Clinic Florida Martin Health.

Supplementary Figure 1 | Rates of local, distant and CNS recurrence.

Data are presented amongst all patients in the mITT who underwent surgical resection at the data cut-off (25 March 2026).

CNS, central nervous system; CT, platinum doublet chemotherapy; mITT, modified intention-to-treat; Pt, single-agent platinum chemotherapy.



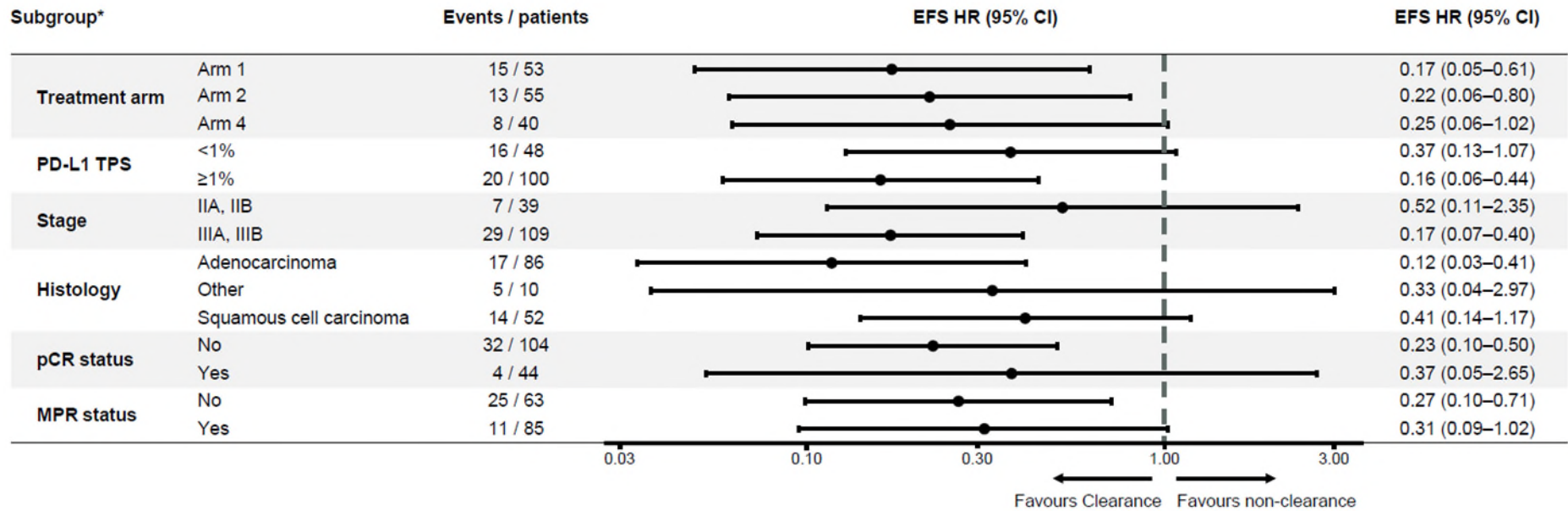
Supplementary Figure 2 | Subgroup analysis of the association between ctDNA clearance at neoadjuvant C3D1 and EFS.

Descriptive forest plot showing EFS based on ctDNA clearance at neoadjuvant C3D1 amongst relevant subgroups of the neoadjuvant C3D1 ctDNA clearance-evaluable population. For each data bar, the dot represents the EFS HR while the whiskers represent the 95% CI. HRs < 1 indicate lower risk of an EFS event amongst patients with ctDNA clearance versus those without. The vertical dashed line represents a HR of 1.00. Data cut-off was 25 March 2026.

*For subgroups other than treatment arm, patients from Arms 1, 2, and 4 are pooled.

C3D1, Cycle 3 Day 1; ctDNA, circulating tumour DNA; EFS, event-free survival; pCR, pathological complete response; MPR, major pathological response; PD-L1, programmed cell death ligand-1; TPS, tumour proportion score

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Supplementary Figure 3 | Clinical outcomes by ctDNA trajectory amongst patients evaluable for ctDNA at both pre-surgical and post-surgical timepoints.

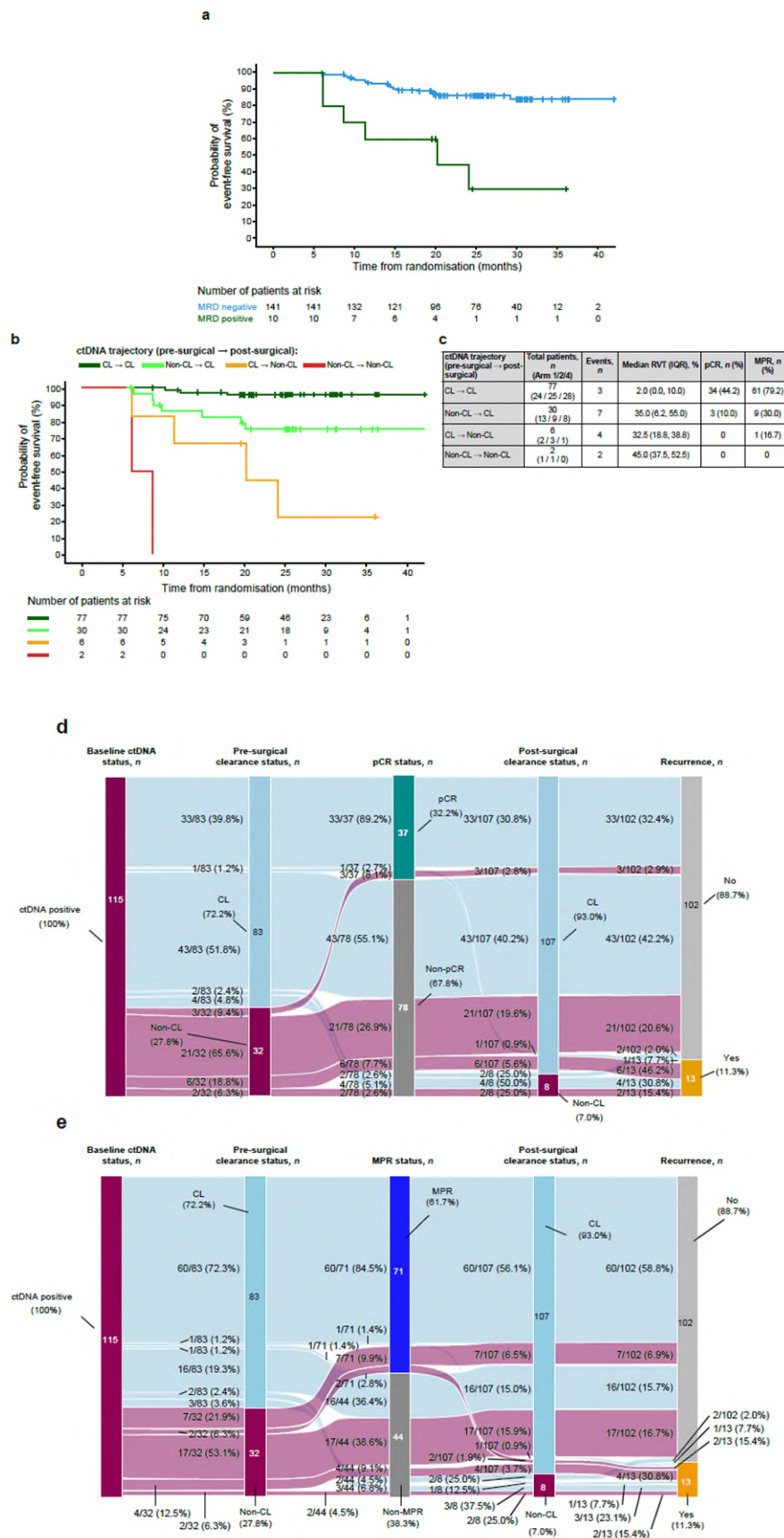
a. Kaplan–Meier plot of EFS by ctDNA detected (MRD+) versus ctDNA undetected (MRD-) after surgery (pre-dose adjuvant C1D1) irrespective of baseline or pre-surgery ctDNA status. **b.** Kaplan–Meier plot of EFS by ctDNA trajectory based on clearance status at the pre-surgical visit and after surgery (pre-dose adjuvant C1D1). Cox regression undetected versus detected at adjuvant C1D1 HR 0.16; 95% CI = 0.06–0.40) **c.** EFS events, median %RVT, and pathological responses by ctDNA trajectory. **d and e.** Sankey diagram showing ctDNA clearance status at pre-surgery, pCR status (d) and MPR status (e), post-surgical ctDNA clearance status, and recurrence. The population for the analysis in b–e ($N = 115$) began with the $N = 154$ patients who were pre-surgical clearance evaluable, detailed in Extended Data Fig. 2, and were subset to those also adjuvant C1D1 clearance evaluable. Of the 154 patients, 39/154 were non-evaluable (34/39 missing adjuvant C1D1 sample, and 5/39 not evaluable at adjuvant C1D1 per on-treatment clearance definitions). Of these 39 patients (not depicted), the breakdown with pCR outcomes was as follows: for baseline undetected ($n = 6$ total), six had pre-surgical non-clearance (one pCR, five no pCR). For baseline detected ($n = 33$ total), 17 had pre-surgical non-clearance (one pCR, 16 non-pCR) and 16 had pre-surgical clearance (seven pCR, nine non-pCR). The breakdown with MPR outcomes were as follows: for baseline undetected ($n = 6$ total), six had pre-surgical non-clearance (two MPR, four non-MPR). For baseline detected ($n = 33$ total), 17 had pre-surgical non-clearance (four MPR, 13 non-MPR) and 16 had pre-surgical clearance (11 MPR, five non-MPR). Twelve of the 39 unevaluable patients had recurrence; the pathological responses for patients with recurrence were as follows: 0/12 with pCR and 3/12 with MPR. Of those with recurrence and MPR: one had presurgical ctDNA clearance, and two did not; of those with non-MPR: one had presurgical clearance, and eight did not). An additional 36 patients were evaluable for MRD status (a) but not depicted in panels b–e due to 5/36 patients who were evaluable at the pre-surgical timepoint but not evaluable at adjuvant C1D1, 5/36 patients who were evaluable at adjuvant C1D1 but not at the pre-surgical timepoint, and 26/36 not evaluable for both. Of these 36, 34/36 (94.4%) were MRD-negative and 2/36 (5.6%) were MRD-positive. Recurrence occurred in 8 of these 36 patients; all 8 patients who recurred were MRD-negative and clearance

non-evaluable. Pathological responses were as follows: 0/8 with pCR and 2/8 with MPR.

In (c), of 16 EFS events presented, 13 disease recurrences are represented in the Sankey diagrams (d and e); the remaining events were 3 non-cancer related deaths (2 in the ctDNA clearance-to-clearance group, 1 in the ctDNA non-clearance-to-clearance group).

Analyses were grouped across arms and carried out (a) amongst patients with pre-dose adjuvant C1D1 ctDNA result and b–e amongst patients evaluable for ctDNA at both pre-surgery and after surgery. Data cut-off was 25 March 2026.

C1D1, cycle 1 day 1; ctDNA, circulating tumour DNA; CL, clearance; EFS, event-free survival; HR, hazard ratio; MPR, major pathological response; MRD, molecular residual disease; pCR, pathological complete response; RVT, residual viable tumour



Supplementary Table 1 | Patient demographics, baseline disease characteristics, pathological responses and event-free survival for the mITT population and ctDNA-evaluable populations.

	Arm 1 Durvalumab + oleclumab + CT (N = 74)				Arm 2 Durvalumab + monalizumab + CT (N = 70)				Arm 4 Durvalumab + Dato-DXd + Pt (N = 54)			
	mITT Durvalumab + oleclumab + CT (N = 74)	ctDNA evaluable at baseline (n = 72)	ctDNA clearance evaluable at neoadjuvant C3D1 (n = 53)	ctDNA clearance evaluable at pre-surgical assessment (n = 56)	mITT Durvalumab + monalizumab + CT (N = 70)	ctDNA evaluable at neoadjuvant baseline (n = 69)	ctDNA clearance evaluable at C3D1 (n = 55)	ctDNA clearance evaluable at pre-surgical assessment (n = 54)	mITT Durvalumab + Dato-DXd + Pt (N = 54)	ctDNA evaluable at baseline (n = 54)	ctDNA clearance evaluable at neoadjuvant C3D1 (n = 40)	ctDNA clearance evaluable at pre-surgical assessment (n = 44)
Age												
Median (range), years	66.5 (30–79)	67.0 (30–79)	66.0 (30–79)	66.5 (30–79)	66.0 (48–83)	66.0 (48–83)	66.0 (48–79)	66.0 (48–79)	65.0 (38–81)	65.0 (38–81)	66.0 (38–81)	65.5 (38–81)
<65 years, n (%)	28 (37.8)	27 (37.5)	23 (43.4)	22 (39.3)	30 (42.9)	29 (42.0)	23 (41.8)	22 (40.7)	25 (46.3)	25 (46.3)	17 (42.5)	20 (45.5)
≥65 years, n (%)	46 (62.2)	45 (62.5)	30 (56.6)	34 (60.7)	40 (57.1)	40 (58.0)	32 (58.2)	32 (59.3)	29 (53.7)	29 (53.7)	23 (57.5)	24 (54.5)
Sex, n (%)												
Female	28 (37.8)	27 (37.5)	16 (30.2)	17 (30.4)	28 (40.0)	27 (39.1)	21 (38.2)	17 (31.5)	22 (40.7)	22 (40.7)	16 (40.0)	19 (43.2)
Male	46 (62.2)	45 (62.5)	37 (69.8)	39 (69.6)	42 (60.0)	42 (60.9)	34 (61.8)	37 (68.5)	32 (59.3)	32 (59.3)	24 (60.0)	25 (56.8)
Smoking status, n (%)												
Current	15 (20.3)	14 (19.4)	12 (22.6)	12 (21.4)	22 (31.4)	21 (30.4)	15 (27.3)	14 (25.9)	15 (27.8)	15 (27.8)	9 (22.5)	11 (25.0)
Former	55 (74.3)	55 (76.4)	39 (73.6)	41 (73.2)	46 (65.7)	46 (66.7)	38 (69.1)	39 (72.2)	36 (66.7)	36 (66.7)	29 (72.5)	31 (70.5)
Never	4 (5.4)	3 (4.2)	2 (3.8)	3 (5.4)	2 (2.9)	2 (2.9)	2 (3.6)	1 (1.9)	3 (5.6)	3 (5.5)	2 (5.0)	2 (4.5)

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	Arm 1 Durvalumab + oleclumab + CT (N = 74)				Arm 2 Durvalumab + monalizumab + CT (N = 70)				Arm 4 Durvalumab + Dato-DXd + Pt (N = 54)			
	mITT Durvalumab + oleclumab + CT (N = 74)	ctDNA evaluable at baseline (n = 72)	ctDNA clearance evaluable at neoadjuvant C3D1 (n = 53)	ctDNA clearance evaluable at pre-surgical assessment (n = 56)	mITT Durvalumab + monalizumab + CT (N = 70)	ctDNA evaluable at neoadjuvant baseline (n = 69)	ctDNA clearance evaluable at C3D1 (n = 55)	ctDNA clearance evaluable at pre-surgical assessment (n = 54)	mITT Durvalumab + Dato-DXd + Pt (N = 54)	ctDNA evaluable at baseline (n = 54)	ctDNA clearance evaluable at neoadjuvant C3D1 (n = 40)	ctDNA clearance evaluable at pre-surgical assessment (n = 44)
Race, n (%)												
Asian	7 (9.5)	7 (9.7)	6 (11.3)	6 (10.7)	5 (7.1)	5 (7.2)	4 (7.3)	3 (5.6)	5 (9.3)	5 (9.3)	4 (10.0)	4 (9.1)
Black or African American	1 (1.4)	1 (1.4)	0	1 (1.8)	0	0	0	0	0	0	0	0
White	46 (62.2)	44 (61.1)	33 (62.3)	34 (60.7)	42 (60.0)	41 (59.4)	33 (60.0)	33 (61.1)	37 (68.5)	37 (68.5)	29 (72.5)	31 (70.5)
Not reported	20 (27.0)	20 (27.8)	14 (26.4)	15 (26.8)	23 (32.9)	23 (33.3)	18 (32.7)	18 (33.3)	12 (22.2)	12 (22.2)	7 (17.5)	9 (20.5)
ECOG PS, n (%)[*]												
0	45 (61.6)	45 (63.4)	33 (63.5)	37 (67.3)	48 (68.6)	47 (68.1)	36 (65.5)	35 (64.8)	35 (64.8)	35 (64.8)	26 (65.0)	29 (65.9)
1	28 (38.4)	26 (36.6)	19 (36.5)	18 (32.7)	22 (31.4)	22 (31.9)	19 (34.5)	19 (35.2)	19 (35.2)	19 (35.2)	14 (35.0)	15 (34.1)
Missing	1	1	1	1	0	0	0	0	0	0	0	0
PD-L1 TPS, n (%)[†]												
<1%	25 (33.8)	25 (34.7)	17 (32.1)	17 (30.4)	29 (41.4)	29 (42.0)	22 (40.0)	23 (42.6)	16 (29.6)	16 (29.6)	10 (25.0)	10 (22.7)
≥1%	49 (66.2)	47 (65.3)	36 (67.9)	39 (69.6)	41 (58.6)	40 (58.0)	33 (60.0)	31 (57.4)	38 (70.4)	38 (70.4)	30 (75.0)	34 (77.3)
1–49%	20 (27.0)	19 (26.4)	17 (32.1)	17 (30.4)	17 (24.3)	17 (24.6)	13 (23.6)	12 (22.2)	22 (40.7)	22 (40.7)	18 (45.0)	20 (45.5)
≥50%	29 (39.2)	28 (38.9)	19 (35.8)	22 (39.3)	24 (34.3)	23 (33.3)	20 (36.4)	19 (35.2)	16 (29.6)	16 (29.6)	12 (30.0)	14 (31.8)

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	miTT Durvalumab + oleclumab + CT (N = 74)	ctDNA evaluable at baseline (n = 72)	ctDNA clearance evaluable at neoadjuvant C3D1 (n = 53)	ctDNA clearance evaluable at pre-surgical assessment (n = 56)	miTT Durvalumab + monalizumab + CT (N = 70)	ctDNA evaluable at neoadjuvant baseline (n = 69)	ctDNA clearance evaluable at C3D1 (n = 55)	ctDNA clearance evaluable at pre-surgical assessment (n = 54)	miTT Durvalumab + Dato-DXd + Pt (N = 54)	ctDNA evaluable at baseline (n = 54)	ctDNA clearance evaluable at neoadjuvant C3D1 (n = 40)	ctDNA clearance evaluable at pre-surgical assessment (n = 44)
Planned platinum agent, n (%)												
Cisplatin	21 (28.4)	19 (26.4)	15 (28.3)	16 (28.6)	15 (21.4)	15 (21.7)	14 (25.5)	13 (24.1)	7 (13.0)	7 (13.0)	5 (12.5)	6 (13.7)
Carboplatin	53 (71.6)	53 (73.6)	38 (71.7)	40 (71.4)	55 (78.6)	54 (78.3)	41 (74.5)	41 (75.9)	47 (87.0)	47 (87.0)	35 (87.5)	38 (86.3)
Primary tumour, n (%)[†]												
T1	1 (1.4)	1 (1.4)	1 (1.9)	1 (1.8)	3 (4.3)	3 (4.3)	3 (5.5)	2 (3.7)	0	0	0	0
T1a	0	0	0	0	0	0	0	0	0	0	0	0
T1b	3 (4.1)	3 (4.2)	2 (3.8)	2 (3.6)	5 (7.1)	5 (7.2)	3 (5.5)	2 (3.7)	2 (3.7)	2 (3.7)	1 (2.5)	1 (2.3)
T1c	4 (5.4)	4 (5.5)	3 (5.7)	4 (7.1)	2 (2.9)	2 (2.9)	2 (3.6)	2 (3.7)	5 (9.3)	5 (9.3)	2 (5.0)	3 (6.8)
T2	7 (9.5)	7 (9.7)	5 (9.4)	5 (8.9)	5 (7.1)	4 (5.8)	4 (7.3)	3 (5.5)	3 (5.6)	3 (5.5)	3 (7.5)	3 (6.8)
T2a	3 (4.1)	3 (4.2)	3 (5.7)	3 (5.4)	2 (2.9)	2 (2.9)	2 (3.6)	2 (3.7)	2 (3.7)	2 (3.7)	2 (5.0)	2 (4.5)
T2b	12 (16.2)	10 (13.9)	7 (13.2)	7 (12.5)	13 (18.6)	13 (18.8)	10 (18.2)	11 (20.4)	10 (18.5)	10 (18.5)	8 (20.0)	9 (20.5)
T3	27 (36.5)	27 (37.5)	19 (35.8)	21 (37.5)	22 (31.4)	22 (31.9)	15 (27.3)	16 (29.6)	18 (33.3)	18 (33.3)	14 (35.0)	15 (34.1)
T4	17 (23.0)	17 (23.6)	13 (24.5)	13 (23.2)	18 (25.7)	18 (26.1)	16 (29.1)	16 (29.6)	14 (25.9)	14 (25.9)	10 (25.0)	11 (25.0)
Regional lymph nodes, n (%)[§]												
N0	27 (36.5)	26 (36.1)	20 (37.7)	21 (37.5)	23 (32.9)	23 (33.3)	15 (27.3)	17 (31.5)	17 (31.5)	17 (31.5)	11 (27.5)	11 (25.0)

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	mITT Durvalumab + oleclumab + CT (N = 74)	ctDNA evaluatable at baseline (n = 72)	ctDNA clearance evaluatable at neoadjuvant C3D1 (n = 53)	ctDNA clearance evaluatable at pre-surgical assessment (n = 56)	mITT Durvalumab + monalizumab + CT (N = 70)	ctDNA evaluatable at neoadjuvant baseline (n = 69)	ctDNA clearance evaluatable at C3D1 (n = 55)	ctDNA clearance evaluatable at pre-surgical assessment (n = 54)	mITT Durvalumab + Dato-DXd + Pt (N = 54)	ctDNA evaluatable at baseline (n = 54)	ctDNA clearance evaluatable at neoadjuvant C3D1 (n = 40)	ctDNA clearance evaluatable at pre-surgical assessment (n = 44)
N1	15 (20.3)	15 (20.8)	9 (17.0)	9 (16.1)	20 (28.6)	20 (29.0)	19 (34.5)	19 (35.2)	10 (18.5)	10 (18.5)	7 (17.5)	9 (20.5)
N2	32 (43.2)	31 (43.1)	24 (45.3)	26 (46.4)	27 (38.6)	26 (37.7)	21 (38.2)	18 (33.3)	27 (50.0)	27 (50.0)	22 (55.0)	24 (54.5)
Single station	21 (28.4)	20 (27.8)	15 (28.3)	17 (30.4)	17 (24.3)	17 (24.6)	14 (25.5)	12 (22.2)	18 (33.3)	18 (33.3)	15 (37.5)	17 (38.6)
Multi station	11 (14.9)	11 (15.3)	9 (17.0)	9 (16.1)	10 (14.3)	9 (13.0)	7 (12.7)	6 (11.1)	9 (16.7)	9 (16.7)	7 (17.5)	7 (15.9)
Distant metastases, n (%)												
M0	74 (100)	72 (100)	53 (100)	56 (100)	70 (100)	69 (100)	55 (100)	54 (100)	54 (100)	54 (100)	40 (100)	44 (100)
Stage, n (%)^{II}												
Ila	8 (10.8)	7 (9.7)	5 (9.4)	5 (8.9)	9 (12.9)	9 (13.0)	6 (10.9)	7 (13.0)	2 (3.7)	2 (3.7)	2 (5.0)	2 (4.5)
Iib	13 (17.6)	13 (18.1)	10 (18.9)	11 (19.6)	15 (21.4)	15 (21.7)	11 (20.0)	12 (22.2)	13 (24.1)	13 (24.1)	7 (17.5)	9 (20.5)
IIla	39 (52.7)	38 (52.8)	27 (50.9)	28 (50.0)	34 (48.6)	33 (47.8)	29 (52.7)	26 (48.1)	28 (51.9)	28 (51.9)	21 (52.5)	22 (50.0)
IIlb	14 (18.9)	14 (19.4)	11 (20.8)	12 (21.4)	12 (17.1)	12 (17.4)	9 (16.4)	9 (16.7)	11 (20.4)	11 (20.4)	10 (25.0)	11 (25.0)
Histology, n (%)												
Squamous cell	23 (31.1)	23 (31.9)	21 (39.6)	21 (37.5)	19 (27.1)	19 (27.5)	16 (29.1)	18 (33.3)	17 (31.5)	17 (31.5)	15 (37.5)	16 (36.4)
Adenocarcinoma	49 (66.2)	47 (65.3)	31 (58.5)	34 (60.7)	46 (65.7)	45 (65.2)	34 (61.8)	32 (59.3)	33 (61.1)	33 (61.1)	21 (52.5)	24 (54.5)
Other ^{II}	2 (2.7)	2 (2.8)	1 (1.9)	1 (1.8)	5 (7.1)	5 (7.2)	5 (9.1)	4 (7.4)	4 (7.4)	4 (7.4)	4 (10.0)	4 (9.1)

	Arm 1 Durvalumab + oleclumab + CT (N = 74)				Arm 2 Durvalumab + monalizumab + CT (N = 70)				Arm 4 Durvalumab + Dato-DXd + Pt (N = 54)			
	mITT Durvalumab + oleclumab + CT (N = 74)	ctDNA evaluab at baseline (n = 72)	ctDNA clearance evaluab at neoadjuvant C3D1 (n = 53)	ctDNA clearance evaluab at pre-surgical assessment (n = 56)	mITT Durvalumab + monalizumab + CT (N = 70)	ctDNA evaluab at neoadjuvant baseline (n = 69)	ctDNA clearance evaluab at C3D1 (n = 55)	ctDNA clearance evaluab at pre-surgical assessment (n = 54)	mITT Durvalumab + Dato-DXd + Pt (N = 54)	ctDNA evaluab at baseline (n = 54)	ctDNA clearance evaluab at neoadjuvant C3D1 (n = 40)	ctDNA clearance evaluab at pre-surgical assessment (n = 44)
Pathological response rates, n/N (%)												
pCR	15/74 (20.3)	15/72 (20.8)	13/53 (24.5)	14/56 (25.0)	18/70 (25.7)	18/69 (26.1)	15/55 (27.3)	15/54 (27.8)	19/54 (35.2)	19/54 (35.2)	16/40 (40.0)	17/44 (38.6)
MPR	31/74 (41.9)	31/72 (43.1)	27/53 (50.9)	28/56 (50.0)	35/70 (50.0)	35/69 (50.7)	30/55 (54.5)	30/54 (55.6)	34/54 (63.0)	34/54 (63.0)	28/40 (70.0)	30/44 (68.2)
EFS rates at 24 months, % (95% CI)												
	70.5 (57.9–80.0)	69.8 (57.0–79.4)	69.5 (54.5–80.4)	69.5 (55.0–80.2)	75.7 (63.4–84.4)	75.7 (63.3–84.4)	77.3 (63.4–86.4)	76.7 (62.5–86.1)	77.9 (62.4–87.6)	77.9 (62.4–87.6)	79.6 (61.6–89.8)	81.6 (64.9–90.8)

Data presented for patients in the mITT population, comprising all randomised patients with confirmed NSCLC histology who received at least one dose of any study treatment at the data cut-off (EFS: 25 March 2026; all other values 14 October 2025), and the ctDNA-evaluab population, which includes all patients in the mITT population who had at least one sample processed at the data cut-off. *Percentages were calculated with the number of patients with reported performance status as the denominator. †For PD-L1, central testing results were used where available, otherwise local results were used. ‡T1–T4 refers to the size and extent of the primary tumour, with T1 indicating a smaller tumour and T4 indicating a larger, more advanced tumour. §N0–N2 refers to the extent of lymph node involvement in the TNM staging system. ¶The stages were described by the International Association for the Study of Lung Cancer 2020. ¶mITT population; Arm 1: carcinoma, type not determined (n = 2); Arm 2: carcinoma, type not determined (n = 1), other (n = 4); Arm 4: carcinoma, type not determined (n = 1), large cell carcinoma (n = 2), other (n = 1)⁴.

C3D1, Cycle 3 Day 1; CI, confidence interval; CT, platinum-doublet chemotherapy; ctDNA, circulating tumour DNA; Dato-DXd, datopotamab deruxtecan; ECOG PS, Eastern Cooperative Oncology Group performance status; EFS, event-free survival; mITT, modified intention-to-treat; MPR, major pathological response; NSCLC, non-small cell lung cancer; pCR, pathological complete response; Pt, single-agent platinum chemotherapy; TNM, tumour node metastasis; TPS, tumour proportion score.

Supplementary Table 2 | Exposure to study treatment in the neoadjuvant and adjuvant study periods.

	Arm 1 Durvalumab + oleclumab + CT (N = 74)		Arm 2 Durvalumab + monalizumab + CT (N = 71)		Arm 4 Durvalumab + Dato-DXd + Pt (N = 54)	
	Neoadjuvant period (n = 74)	Adjuvant period (n = 57)	Neoadjuvant period (n = 71)	Adjuvant period (n = 53)	Neoadjuvant period (n = 54)	Adjuvant period (n = 47)
Median number of cycles (range)	4.0 (1–4)	12.0 (1–12)	4.0 (1–4)	12.0 (1–12)	4.0 (2–4)	12.0 (1–12)
Cumulative number of cycles, n						
≥1	74 (100)	56 (98.2)	71 (100)	53 (100)	54 (100)	47 (100)
≥2	72 (97.3)	55 (96.5)	64 (90.1)	50 (94.3)	54 (100)	46 (97.9)
≥3	65 (87.8)	53 (93.0)	60 (84.5)	48 (90.6)	50 (92.6)	44 (93.6)
≥4	55 (74.3)	51 (89.5)	54 (76.1)	46 (86.8)	40 (74.1)	44 (93.6)
≥5	NA	51 (89.5)	NA	44 (83.0)	NA	44 (93.6)
≥6	NA	49 (86.0)	NA	43 (81.1)	NA	41 (87.2)
≥7	NA	49 (86.0)	NA	43 (81.1)	NA	37 (78.7)
≥8	NA	47 (82.5)	NA	42 (79.2)	NA	36 (76.6)
≥9	NA	44 (77.2)	NA	41 (77.4)	NA	35 (74.5)

NeoCOAST-2 ctDNA manuscript – supplementary information

≥10	NA	43 (75.4)	NA	40 (75.5)	NA	35 (74.5)
≥11	NA	39 (68.4)	NA	37 (69.8)	NA	35 (74.5)
12	NA	32 (56.1)	NA	28 (52.8)	NA	28 (59.6)

Data presented for patients in the safety population, which comprised all patients who were randomised and received at least one dose of any study treatment at the data cut-off (14 October 2025). CT, platinum-doublet chemotherapy; Dato-DXd, datopotamab deruxtecan; NA, not applicable; Pt, single-agent platinum chemotherapy.

Supplementary Table 3 | EFS rates in PD-L1 TPS, tumour histology, pCR, and MPR subgroups.

	24-month EFS rate, % (95% CI)		
	Arm 1 Durvalumab + oleclumab + CT (N = 74)	Arm 2 Durvalumab + monalizumab + CT (N = 70)	Arm 4 Durvalumab + Dato-DXd + Pt (N = 54)
All patients	70.5 (57.9–80.0)	75.7 (63.4–84.4)	77.9 (62.4–87.6)
PD-L1 TPS			
<1%	58.2 (35.9–75.2) <i>n</i> = 26	66.5 (45.4–81.0) <i>n</i> = 28	64.3 (32.4–84.1) <i>n</i> = 16
≥1%	77.3 (61.7–87.2) <i>n</i> = 48	82.0 (65.8–91.0) <i>n</i> = 42	83.4 (64.2–92.9) <i>n</i> = 38
1–49%	73.3 (46.8–88.1) <i>n</i> = 20	77.0 (49.6–90.7) <i>n</i> = 19	76.8 (48.1–90.9) <i>n</i> = 22
≥50%	80.6 (59.3–91.5) <i>n</i> = 28	85.9 (62.4–95.2) <i>n</i> = 23	92.3 (56.6–98.9) <i>n</i> = 16
Tumour histology			

Squamous cell carcinoma	68.4 (44.7–83.6) <i>n</i> = 23	66.8 (40.3–83.6) <i>n</i> = 19	81.3 (41.5–95.2) <i>n</i> = 17
Non-squamous cell carcinoma	71.6 (56.0–82.6) <i>n</i> = 51	79.1 (64.5–88.2) <i>n</i> = 51	76.5 (58.2–87.6) <i>n</i> = 37
Pathological response			
pCR	84.6 (51.2–95.9) <i>n</i> = 15	94.4 (66.6–99.2) <i>n</i> = 18	92.9 (59.1–99.0) <i>n</i> = 19
Non-pCR	67.0 (52.6–77.9) <i>n</i> = 59	69.1 (54.0–80.1) <i>n</i> = 52	69.4 (48.8–83.0) <i>n</i> = 35
MPR	89.4 (70.6–96.5) <i>n</i> = 31	82.3 (64.7–91.6) <i>n</i> = 35	85.4 (65.0–94.4) <i>n</i> = 34
Non-MPR	56.7 (39.5–70.7) <i>n</i> = 43	68.6 (49.4–81.8) <i>n</i> = 35	63.5 (35.9–81.8) <i>n</i> = 20

Data are presented for patients in the mITT population, comprising all randomised patients with confirmed NSCLC histology who received at least one dose of any study treatment at the data cut-off (25 March 2026). Patients with EFS events per arm at data cut-off were as follows: Arm 1: *n* = 20; Arm 2: *n* = 17; Arm 4: *n* = 11. CT, platinum-doublet chemotherapy; Dato-DXd, datopotamab deruxtecan; EFS, event-free survival; mITT, modified intention-to-treat; MPR, major pathological response; NSCLC, non-small cell

lung cancer; pCR, pathological complete response; PD-L1, programmed death-ligand 1; Pt, single-agent platinum chemotherapy; TPS, tumour proportion score.

Supplementary Table 4 | Sites of disease recurrence and time to recurrence across Arms 1, 2 and 4.

	Recurrence, n (%)	Median TTR, months (min–max)
Arm 1: Durvalumab + oleclumab + CT (N = 69)		
Any recurrence	14 (20.3)	8.3 (1.3–16.6)
Local	5 (7.2)	8.3 (3.3–13.8)
Lung	4 (5.8)	8.3 (3.3–13.8)
Lymph node	1 (1.4)	11.0 (11.0–11.0)
Distant	9 (13.0)	5.4 (1.3–16.6)
Lung	3 (4.3)	11.3 (5.4–16.6)
Other	3 (4.3)	8.2 (2.9–11.1)
Brain/CNS	2 (2.9)	1.4 (1.3–1.4)
Bone	1 (1.4)	1.5 (1.5–1.5)
Liver	1 (1.4)	8.2 (8.2–8.2)
Lymph node	1 (1.4)	2.9 (2.9–2.9)

Pleura	1 (1.4)	5.4 (5.4–5.4)
Arm 2: Durvalumab + monalizumab + CT (N = 66)		
Any recurrence*	9 (13.6)	11.0 (1.2–26.0)
Local	2 (3.0)	4.7 (3.9–5.4)
Lymph node	2 (3.0)	4.7 (3.9–5.4)
Lung	1 (1.5)	3.9 (3.9–3.9)
Distant	6 (9.1)	13.4 (1.2–26.0)
Brain/CNS	3 (4.5)	16.3 (1.2–26.0)
Lung	2 (3.0)	6.5 (1.2–11.8)
Liver	1 (1.5)	14.9 (14.9–14.9)
Lymph node	1 (1.5)	11.8 (11.8–11.8)
Other	1 (1.5)	1.2 (1.2–1.2)
Pleura	1 (1.5)	11.0 (11.0–11.0)
Lung	1 (1.5)	2.8 (2.8–2.8)
Arm 4: Durvalumab + Dato-DXd + Pt (N = 51)		

Any recurrence	7 (13.7)	8.3 (3.0–20.5)
Local	4 (7.8)	16.6 (3.0–20.5)
Lymph node	3 (5.9)	16.6 (3.0–20.5)
Lung	2 (3.9)	9.8 (3.0–16.6)
Distant	3 (5.9)	5.6 (5.1–8.3)
Lung	2 (3.9)	6.7 (5.1–8.3)
Brain/CNS	1 (2.0)	5.6 (5.6–5.6)
Other	1 (2.0)	5.6 (5.6–5.6)
Pleura	1 (2.0)	5.1 (5.1–5.1)
Overall (<i>N</i> = 186)		
Any recurrence	30 (16.1)	8.3 (1.2–26.0)
Local	11 (5.9)	8.3 (3.0–20.5)
Lung	7 (3.8)	8.3 (3.0–16.6)
Lymph node	6 (3.2)	8.2 (3.0–20.5)
Distant	18 (9.7)	8.3 (1.2–26.0)
Lung	7 (3.8)	8.3 (1.2–16.6)

NeoCOAST-2 ctDNA manuscript – supplementary information

Brain/CNS	6 (3.2)	3.5 (1.2–26.0)
Other	5 (2.7)	5.6 (1.2–11.1)
Pleura	3 (1.6)	5.4 (5.1–11.0)
Liver	2 (1.1)	11.6 (8.2–14.9)
Lymph node	2 (1.1)	7.4 (2.9–11.8)
Bone	1 (0.5)	1.5 (1.5–1.5)

Data are presented per arm and overall amongst all patients in the mITT who underwent surgical resection at the data cut-off (25 March 2026). *One patient had undetermined local or distant recurrence. CNS, central nervous system; CT, platinum-doublet chemotherapy; Dato-DXd, datopotamab deruxtecan; Pt, single-agent platinum chemotherapy; TTR, time to recurrence.

Supplementary Table 5 | ctDNA clearance status at neoadjuvant C3D1 by PD-L1 TPS status across arms.

	PD-L1 TPS				
	<1 %	≥1%	1–49%	≥50%	Total
Arm 1: Durvalumab + oleclumab + CT					
n	17	36	17	19	53
Clearance, n (%)	8 (47.1)	19 (52.8)	7 (41.2)	12 (63.2)	27 (50.9)
Non-clearance, n (%)	9 (52.9)	17 (47.2)	10 (58.8)	7 (36.8)	26 (49.1)
Arm 2: Durvalumab + monalizumab + CT					
n	22	33	13	20	55
Clearance, n (%)	9 (40.9)	21 (63.6)	9 (69.2)	12 (60.0)	30 (54.5)
Non-clearance, n (%)	13 (59.1)	12 (36.4)	4 (30.8)	8 (40.0)	25 (45.5)
Arm 4: Durvalumab + Dato-DXd + Pt					
n	10	30	18	12	40
Clearance, n (%)	6 (60.0)	23 (76.7)	14 (77.8)	9 (75.0)	29 (72.5)
Non-clearance, n (%)	4 (40.0)	7 (23.3)	4 (22.2)	3 (25.0)	11 (27.5)

Data are presented for patients in the neoadjuvant C3D1 ctDNA clearance-evaluable population, comprising all randomised patients with confirmed NSCLC histology who received at least one dose of any study treatment at the data cut-off (14 October 2025). Percentages are based on the number of patients in the corresponding arm and PD-L1 TPS subgroup. C3D1, cycle 3 day 1;

CT, platinum-doublet chemotherapy; ctDNA, circulating tumour DNA; Dato-DXd, datopotamab deruxtecan; mITT, modified intention-to-treat; PD-L1, programmed death-ligand 1; Pt, single-agent platinum chemotherapy; TPS, tumour proportion score.

Supplementary Table 6 | Safety summary during the neoadjuvant period according to ctDNA clearance status.

<i>n</i> (%)	Arm 1 Durvalumab + oleclumab + CT (<i>N</i> = 65)			Arm 2 Durvalumab + monalizumab + CT (<i>N</i> = 62)			Arm 4 Durvalumab + Dato-DXd + Pt (<i>N</i> = 48)		
	Clearance at C3D1 (<i>n</i> = 27)	Non-clearance at C3D1 (<i>n</i> = 26)	ctDNA non-evaluable at C3D1 (<i>n</i> = 12)	Clearance at C3D1 (<i>n</i> = 30)	Non-clearance at C3D1 (<i>n</i> = 25)	ctDNA non-evaluable at C3D1 (<i>n</i> = 7)	Clearance at C3D1 (<i>n</i> = 29)	Non-clearance at C3D1 (<i>n</i> = 11)	ctDNA non-evaluable at C3D1 (<i>n</i> = 8)
Any TEAE	27 (100)	26 (100)	12 (100.0)	30 (100)	25 (100)	7 (100)	29 (100)	10 (90.9)	8 (100)
Any AE possibly related to any investigational treatment or chemotherapy*	26 (96.3)	26 (100)	12 (100.0)	28 (93.3)	24 (96.0)	7 (100)	28 (96.6)	10 (90.9)	7 (87.5)
Grade ≥3 TEAE	7 (25.9)	13 (50.0)	3 (25.0)	11 (36.7)	10 (40.0)	3 (42.9)	9 (31.0)	3 (27.3)	1 (12.5)
Any grade ≥3 possibly related to any investigational treatment or chemotherapy*	6 (22.2)	12 (46.2)	2 (16.7)	9 (30.0)	6 (24.0)	2 (28.6)	7 (24.1)	1 (9.1)	0
AE leading to omission of any investigational treatment or chemotherapy	3 (11.1)	4 (15.4)	1 (8.3)	4 (13.3)	2 (8.0)	0	5 (17.2)	1 (9.1)	0
AE leading to dose reduction of any	3 (11.1)	4 (15.4)	1 (8.3)	5 (16.7)	6 (24.0)	1 (14.3)	7 (24.1)	4 (36.4)	2 (25.0)

NeoCOAST-2 ctDNA manuscript – supplementary information

n (%)	Arm 1 Durvalumab + oleclumab + CT (N = 65)			Arm 2 Durvalumab + monalizumab + CT (N = 62)			Arm 4 Durvalumab + Dato-DXd + Pt (N = 48)		
	Clearance at C3D1 (n = 27)	Non-clearance at C3D1 (n = 26)	ctDNA non-evaluable at C3D1 (n = 12)	Clearance at C3D1 (n = 30)	Non-clearance at C3D1 (n = 25)	ctDNA non-evaluable at C3D1 (n = 7)	Clearance at C3D1 (n = 29)	Non-clearance at C3D1 (n = 11)	ctDNA non-evaluable at C3D1 (n = 8)
investigational treatment or chemotherapy									
AE leading to discontinuation of any investigational treatment or chemotherapy	2 (7.4)	3 (11.5)	2 (16.7)	3 (10.0)	6 (24.0)	1 (14.3)	5 (17.2)	1 (9.1)	1 (12.5)
Any SAE	1 (3.7)	6 (23.1)	1 (8.3)	0	5 (20.0)	2 (28.6)	7 (24.1)	2 (18.2)	0
SAE with the outcome of death	0	0	0	0	0	0	0	0	0

Data presented for patients in the safety population, which comprised all patients who were randomised and received at least one dose of any study treatment at the data cut-off (14 October 2025). Overall N represents the number of patients per treatment group with non-missing ctDNA clearance data at neoadjuvant C3D1. Percentages are based on the number of patients in the corresponding treatment and ctDNA clearance category. *Related AEs defined as a reasonable possibility that the AE was caused

by treatment as assessed by investigator. AE, adverse event; C3D1, cycle 3 day 1; CT, platinum-doublet chemotherapy; ctDNA, circulating tumour DNA; Dato-DXd, datopotamab deruxtecan; Pt, single-agent platinum chemotherapy; SAE, serious AE; TEAE, treatment-emergent AE.