

ASCO GI Update: The Impact of the Matterhorn Clinical Trial on the Management of Gastric Cancer



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Medicine Foundation.

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Competing Interests

SJK has served a consultant/advisory role for Bristol Myers Squibb, Merck, Astellas, Daiichi-Sankyo, Natera, Novartis, AstraZeneca, Mersana, Beigene, Gilead, Elevation Oncology, EsoBiotec, Eisai, Taiho, Boehringer-Ingelheim, and I-Mab, Signet Therapeutics.

SJK reports research support (institutional) from AstraZeneca, I-Mab, Arcus Biosciences, Mersana, Parabilis, the Torrey Coast Foundation, the Degregorio Foundation, the Gastric Cancer Foundation, Debbie's Dream Foundation, NIH/NCI, StandUp2Cancer, AACR.

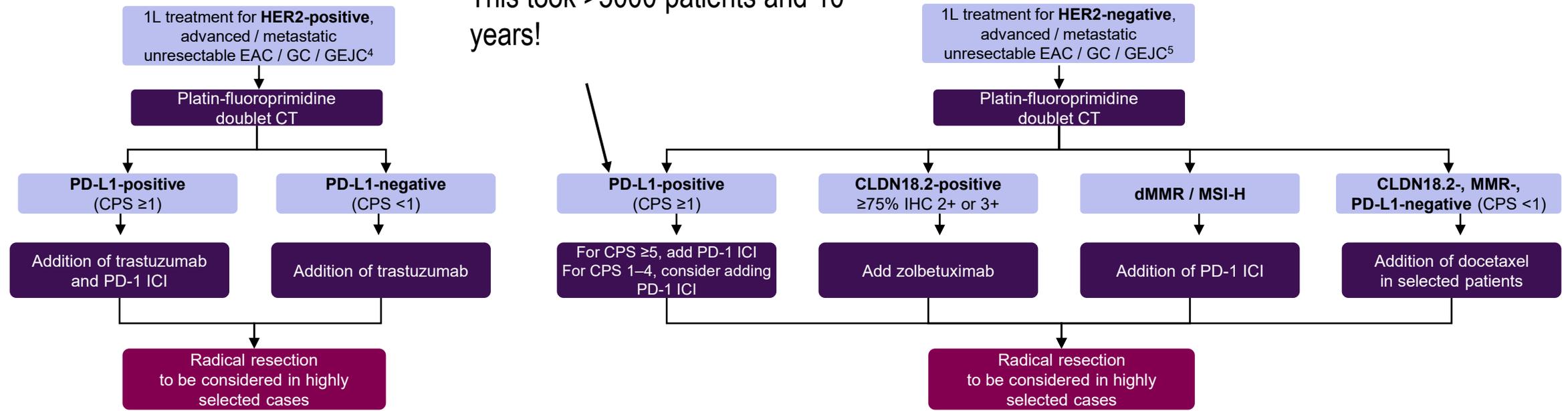
SJK serves (uncompensated) on the NCCN guidelines for gastric and esophageal cancers and the medical advisory board for Debbie's Dream Foundation.



Biomarker expression guides treatment decision-making for advanced unresectable GC / GEJC

- **Gastroesophageal cancers**, such as GC and GEJC, are often detected at an advanced stage of disease, with high mortality rates¹⁻³
- The treatment of locally advanced, unresectable or metastatic GC / GEJC depends on the biomarker profile of the patient⁴⁻⁸

This took >5000 patients and 10 years!



Adapted from the ESMO Living Guidelines

1L, first-line; CLDN 18.2, Claudin 18.2; CPS, combined positive score; CT, chemotherapy; dMMR, deficient mismatch repair; EAC, oesophageal adenocarcinoma; GC, gastric cancer; GEJC, gastroesophageal junction cancer; HER2, human epidermal growth factor receptor; ICI, immune checkpoint inhibitor; IHC, immunohistochemistry; MMR, mismatch repair; MSI-H, microsatellite instability high; PD-1, programmed cell death-1; PD-L1, programmed cell death ligand-1.

1. Xiao H, et al. *BMC Cancer* 2023;23:186. 2. NIH. Cancer Stat Facts: Stomach Cancer. <https://seer.cancer.gov/statfacts/html/stomach.html>. Accessed 7 April, 2025.

3. NIH. Cancer Stat Facts: Esophageal Cancer. <https://seer.cancer.gov/statfacts/html/esoph.html>. Accessed 7 April, 2025. 4. ESMO Gastric Cancer Living Guideline. First-line HER2-positive. v1.4 - September 2024. <https://www.esmo.org/guidelines/living-guidelines/esmo-living-guideline-gastric-cancer/metastatic-disease/first-line-for-her2-positive>. Accessed 14 August 2025. 5. ESMO Gastric Cancer Living Guideline. First-line HER2-negative. v1.4 - September 2024. <https://www.esmo.org/guidelines/living-guidelines/esmo-living-guideline-gastric-cancer/metastatic-disease/first-line-for-her2-negative>. Accessed 14 August 2025. 6. Shitara K, et al. *ESMO Open* 2024;9:102226. 7. NCCN Guidelines. Gastric Cancer. v2.2025. https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed 16 April 2025. 8. NCCN Guidelines. Esophageal and Esophagogastric Junction Cancers. v2.2025. https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf. Accessed 16 April 2025.



Global guidelines recommend molecular testing to guide treatment decisions in advanced GC / GEJC



Guideline recommendations: molecular testing practices¹⁻⁷

Biomarker		HER2				PD-L1			MSI / MMR			CLDN18.2		
Guidelines		NCCN	ESMO	Pan-Asian	ASCO	NCCN	ESMO	Pan-Asian	NCCN	ESMO	Pan-Asian	NCCN	ESMO	Pan-Asian
Who	All newly diagnosed								✓	✓	✓			
	Locally advanced, recurrent or metastatic	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	†
When	At diagnosis	✓				✓			✓	✓	✓		✓	
	Before 1L		✓	✓	✓		✓	✓						†
	Before 2L / intent to treat	*												†
How		NCCN: IHC / ISH / PCR is preferred initially, followed by NGS if appropriate ^{1,2}				NCCN: IHC of a minimum 100 tumour cells			PCR / NGS (MSI) and IHC (MMR)			IHC		

*Repeat biomarker testing may be considered at clinical or radiologic progression of advanced or metastatic disease. †Recommended if available.

1L, first-line; 2L, second-line; AE, adverse event; CLDN18.2, Claudin 18.2; ESMO, European Society for Medical Oncology; GC, gastric cancer; GEJC, gastroesophageal junction cancer;

HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, *in situ* hybridisation; MMR, mismatch repair; MSI, microsatellite instability; NCCN, National Comprehensive Cancer Network; NGS, next-generation sequencing; PCR, polymerase chain reaction; PD-L1, programmed cell death ligand-1.

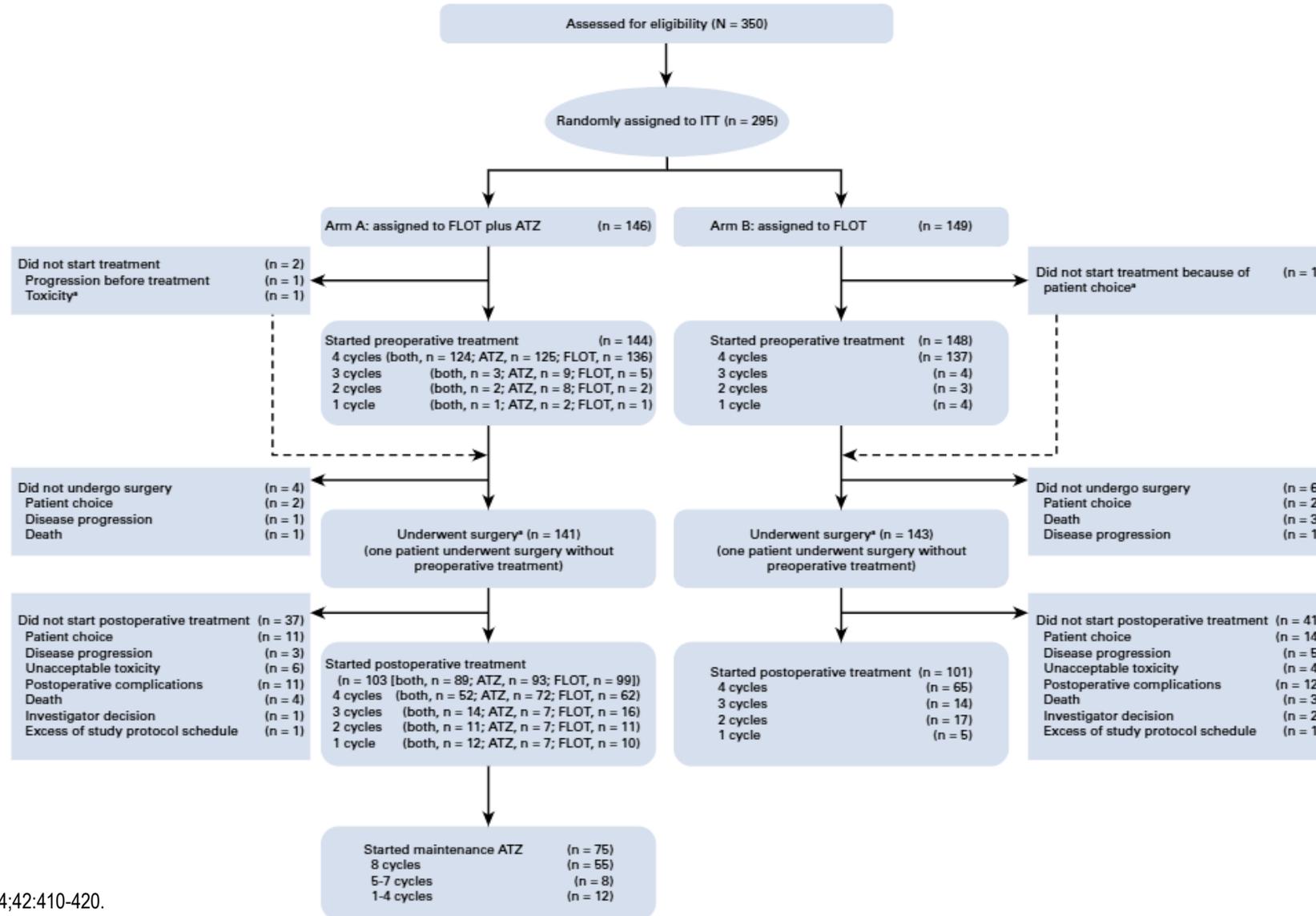
1. NCCN Guidelines. Gastric Cancer. v2.2025. https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf. Accessed 16 April 2025. 2. NCCN Guidelines. Esophageal and Esophagogastric Junction Cancers. v2.2025.

https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf. Accessed 16 April 2025. 3. Lordick F, et al. Ann Oncol 2022;33:1005–1020. 4. Obermannová R, et al. Ann Oncol 2025;10:104134. 5. Shitara K, et al. ESMO Open

2024;9:102226. 6. Shah MA, et al. J Clin Oncol 2023;41:1470–1491. 7. Bartley AN, et al. J Clin Oncol 2017;35:446-464.



Phase II/III DANTE/IKF-s633 Trial: Perioperative Atezolizumab Plus Fluorouracil, Leucovorin, Oxaliplatin, and Docetaxel for Resectable Esophagogastric Cancer



DANTE Results

- Surgical morbidity (A, 45%; B, 42%) and 60-day mortality (A, 3%; B, 2%) were comparable between arms. Downstaging favored arm A versus arm B (ypT0, 23% v 15% [one-sided $P = .044$]; ypT0-T2, 61% v 48% [one-sided $P = .015$]; ypN0, 68% v 54% [one-sided $P = .012$]).
- Histopathologic complete regression rates (pathologic complete response or TRG1a) were higher after FLOT plus ATZ (A, 24%; B, 15%; one-sided $P = .032$), and the difference was more pronounced in the PD-L1 CPS ≥ 10 (A, 33%; B, 12%) and MSI (A, 63%; B, 27%) subpopulations. Complete margin-free (R0) resection rates were relatively high in both arms (A, 96%; B, 95%).
- The incidence and severity of adverse events were similar in both groups.

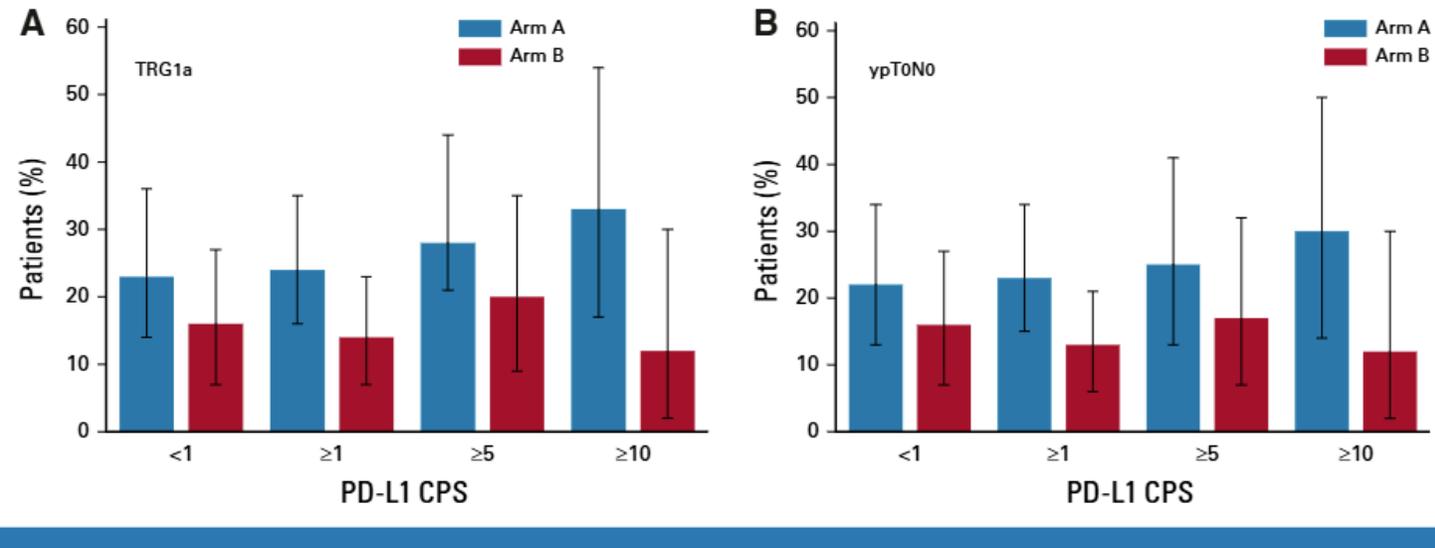
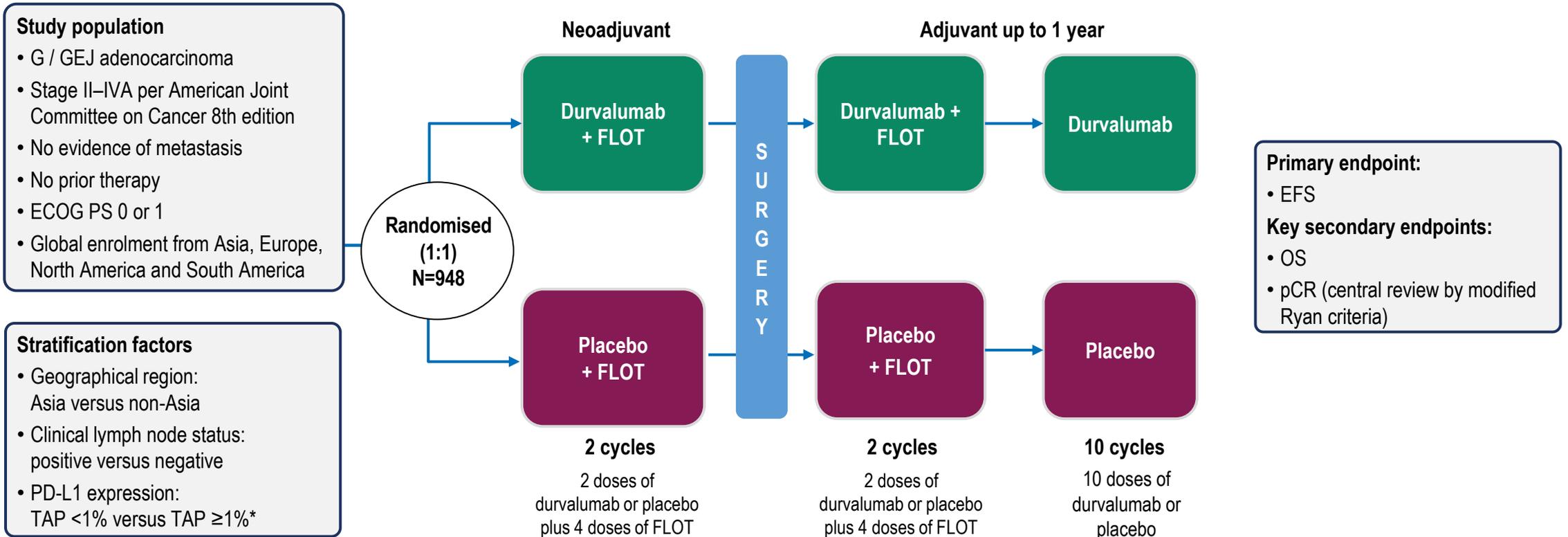


FIG 2. Outcomes by PD-L1 CPS. (A) Complete pathologic regression (TRG1a) and (B) ypT0N0 stage rates with 95% CI on the basis of PD-L1 CPS are shown for arm A and arm B. CPS, combined positive score.

MATTERHORN study design^{1,2}

MATTERHORN is a global, Phase 3, randomised, double-blind, placebo-controlled study



*Measured by immunohistochemistry using VENTANA PD-L1 (SP263) Companion Diagnostic Assay (Roche Diagnostics; investigational use only) and recorded at randomisation on the Interactive Response Technology System, Randomisation and Trial Supply Management, Electronic Case Report Form or from external vendor data from samples collected on or before randomisation. FLOT: 5-fluorouracil 2600 mg/m², leucovorin 200 mg/m², oxaliplatin 85 mg/m², docetaxel 50 mg/m², on Days 1 and 15 Q4W, 4 doses (2 cycles) pre- and post-operative; durvalumab: 1500 mg on Day 1 Q4W, 2 doses (2 cycles) of durvalumab or placebo pre- and post-operative, followed by 10 doses of post-operative durvalumab or placebo monotherapy. Participants underwent surgery 4–8 weeks after last dose of neoadjuvant therapy. Adjuvant therapy began 4–12 weeks post-surgery. Durvalumab or placebo monotherapy may be continued if post-operative FLOT is discontinued due to toxicity.

ECOG, Eastern Cooperative Oncology Group; EFS, event-free survival; FLOT, 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; G / GEJ, gastric / gastroesophageal junction; OS, overall survival; pCR, pathological complete response; PD-L1, programmed cell death ligand-1; PS, performance status; Q4W, every 4 weeks; TAP, tumour area positivity.

1. Janjigian YY, et al. *N Engl J Med* 2025;393:217–230. 2. Janjigian YY, et al. Presented at: ASCO Congress; 30 May–3 June 2025; Chicago, IL. Oral presentation LBA5.

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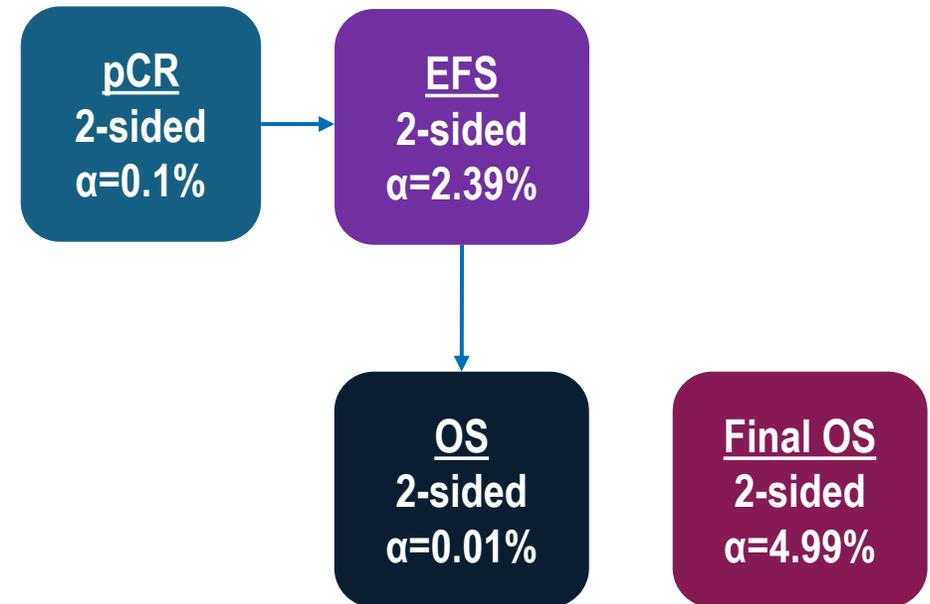
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Statistical considerations¹⁻³

- pCR (data cut-off: 01 February 2023)*: assessed after all patients were randomised and either underwent surgery or were deemed ineligible; results were final³
- EFS (data cut-off: 20 December 2024)*: triggered at 41% maturity (n=385 events), results were final; OS[†]: tested at EFS analysis with a minimal α -spend of 0.01% (34% maturity)
- Final OS (data cut-off: 01 September 2025): tested using the remaining α of 4.99%; results shown here

Multiple testing procedure



*An overall 5% α (2-sided) was initially split between the pCR analysis (0.1%) and EFS analysis (4.9%); given the pCR analysis was positive, the α of 0.1% for pCR was recycled to the EFS analysis. At the EFS analysis, an α of 0.01% was allocated to OS.

[†]Only tested if EFS was statistically significant.

EFS, event-free survival; OS, overall survival; pCR, pathological complete response.

1. Janjigian YY, et al. *N Engl J Med* 2025;393:217–230. 2. Janjigian YY, et al. Presented at: ASCO Congress; 30 May–3 June 2025; Chicago, IL. Oral presentation LBA5. 3. Janjigian YY, et al. *Ann Oncol* 2023;34:S1315–S1316. Abs LBA73.

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Baseline characteristics

		Central pathology analysis set*		ypN evaluable analysis set†	
		Durvalumab + FLOT (n=385)	Placebo + FLOT (n=372)	Durvalumab + FLOT (n=411)	Placebo + FLOT (n=400)
Median age, years (range)		61.0 (27–84)	63.0 (29–81)	61.0 (27–84)	62.0 (29–81)
Sex, n (%)	Male	264 (68.6)	286 (76.9)	286 (69.6)	304 (76.0)
Geographical region, n (%)	Non-Asia	310 (80.5)	293 (78.8)	336 (81.8)	319 (79.8)
	Asia	75 (19.5)	79 (21.2)	75 (18.2)	81 (20.3)
ECOG PS, n (%)	0 (normal activity)	275 (71.4)	291 (78.2)	292 (71.0)	313 (78.3)
	1 (restricted activity)	110 (28.6)	81 (21.8)	119 (29.0)	87 (21.8)
Site of tumour, n (%)	Gastric	255 (66.2)	244 (65.6)	275 (66.9)	265 (66.3)
	GEJ	130 (33.8)	128 (34.4)	136 (33.1)	135 (33.8)
Primary tumour stage, n (%)	T4	93 (24.2)	91 (24.5)	95 (23.1)	97 (24.3)
	Non-T4	292 (75.8)	281 (75.5)	316 (76.9)	303 (75.8)
Clinical lymph node status, n (%)	N+	264 (68.6)	260 (69.9)	284 (69.1)	280 (70.0)
PD-L1 expression by TAP, n (%)	<1%	38 (9.9)	36 (9.7)	40 (9.7)	39 (9.8)
	≥1%	347 (90.1)	336 (90.3)	371 (90.3)	361 (90.3)
Histology type (investigator assessed), n (%)	Intestinal	195 (50.6)	193 (51.9)	212 (51.6)	207 (51.8)
	Diffuse	102 (26.5)	91 (24.5)	107 (26.0)	100 (25.0)
	Unspecified adenocarcinoma or mixed / other	88 (22.9)	88 (23.7)	92 (22.4)	93 (23.3)
MSI status, n (%)	MSI-high	18 (4.7)	21 (5.6)	17 (4.1)	21 (5.3)
	Not-MSI-high	251 (65.2)	253 (68.0)	270 (65.7)	272 (68.0)
	Not evaluable / missing	116 (30.1)	98 (26.3)	124 (30.2)	107 (26.8)

*Participants who completed surgery with samples that were evaluable for modified Ryan scoring by central assessment. †Participants who completed surgery with samples that were evaluable for nodal involvement by investigator assessment.

Data cut-off: 20 December 2024

ECOG, Eastern Cooperative Oncology Group; FLOT, 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; GEJ, gastroesophageal junction; MSI, microsatellite instability; PD-L1, programmed cell death ligand-1; PS, performance status; TAP, tumour area positivity; TTD, time to deterioration; ypN, pathological nodal status.

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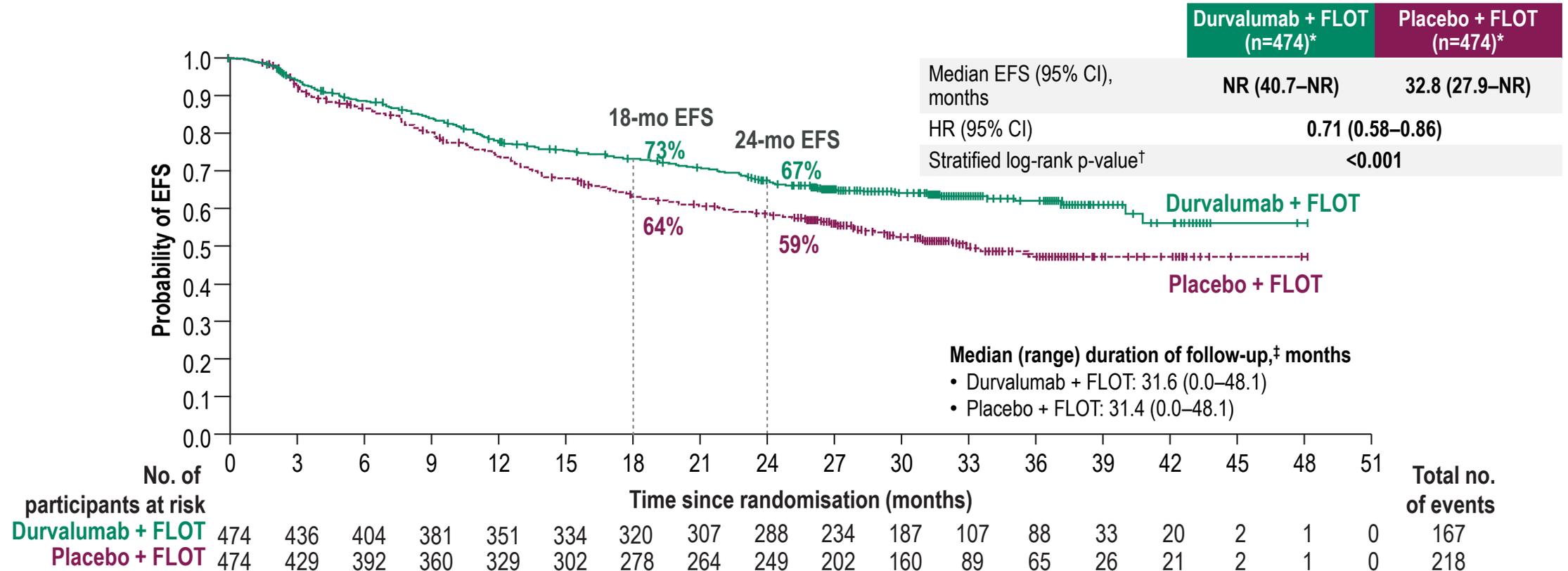
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Primary endpoint of EFS¹

A statistically significant improvement in EFS was observed with durvalumab + FLOT versus placebo + FLOT



*Full analysis set (all randomised participants, regardless of treatment received). [†]The threshold of significance for this analysis was 0.0239. [‡]In censored participants.

Events were defined as the earliest of RECIST v1.1 events, non-RECIST v1.1 events or deaths due to any cause. Analysis was based on BICR assessments and / or locally by pathology testing if clinically required. The HR and its CI were estimated from a Cox proportional hazards model, adjusted for geographical region, clinical lymph node status and PD-L1 expression. The CI for the HR was calculated using a profile likelihood approach. The 2-sided p-value was calculated using a stratified log-rank test adjusted for geographical region, clinical lymph node status and PD-L1 expression.

BICR, blinded independent central review; CI, confidence interval; EFS, event-free survival; FLOT, 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; HR, hazard ratio; mo, month; NR, not reached; PD-L1, programmed cell death ligand-1; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1.

1. Janjigian YY, et al. *N Engl J Med* 2025;393:217–230.

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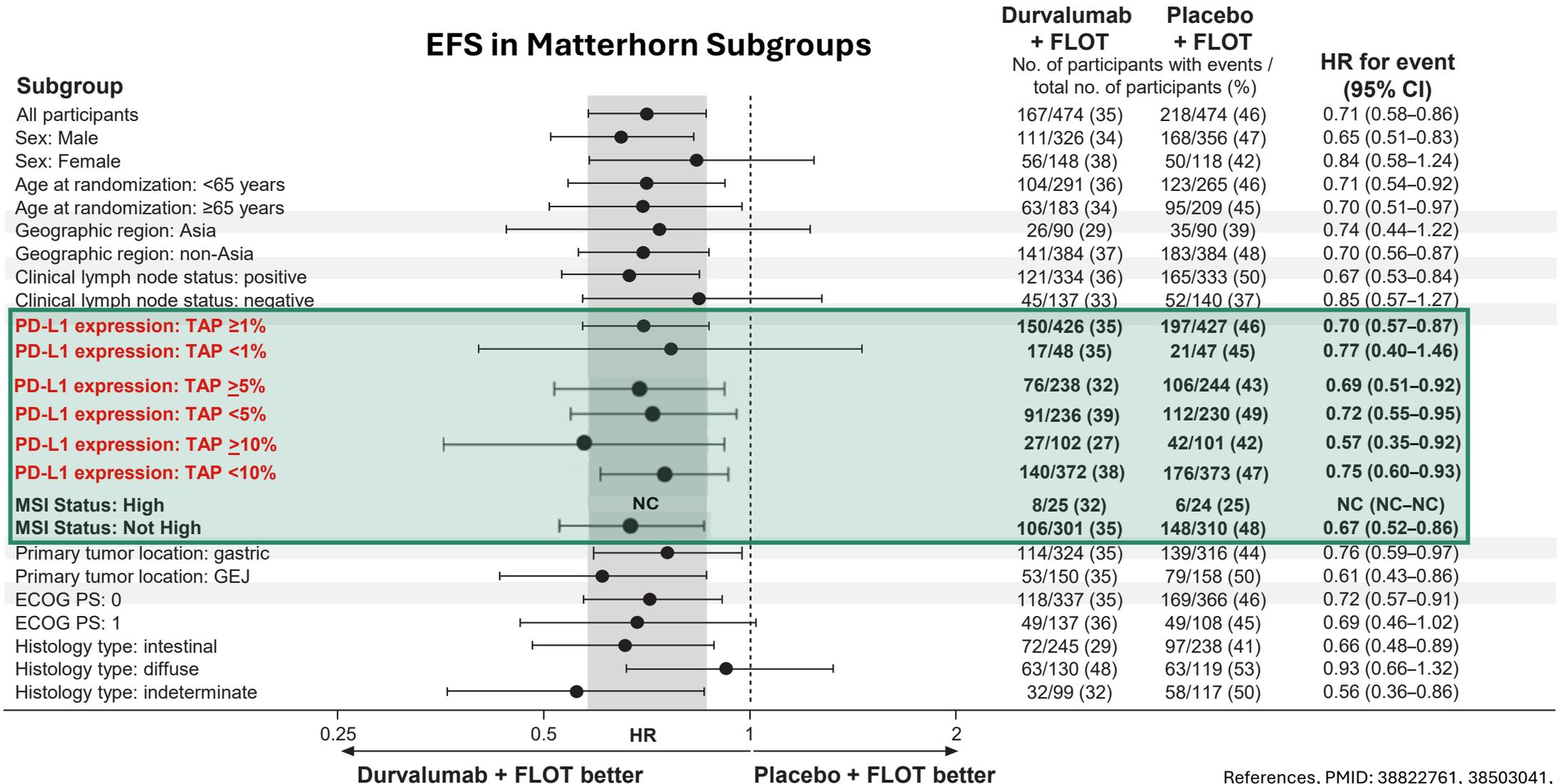
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Patient Subgroups

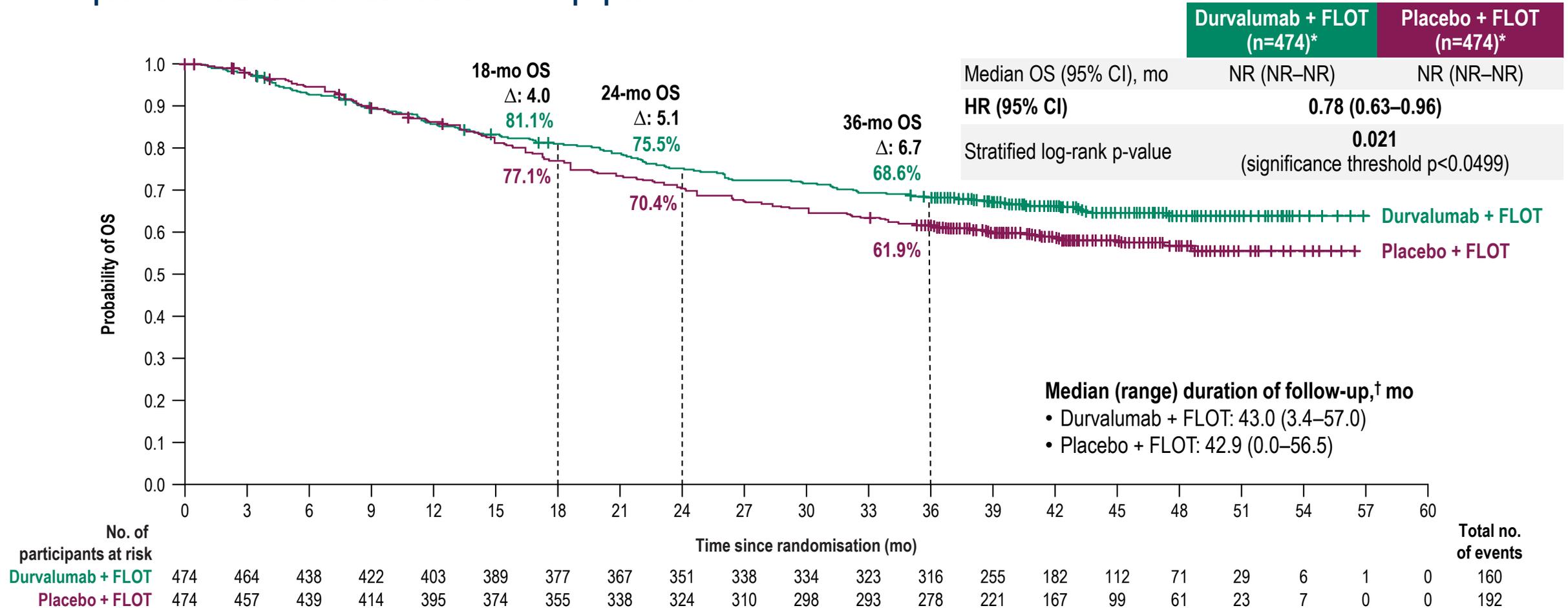
EFS in Matterhorn Subgroups



References, PMID: 38822761, 38503041, 40373876

Final OS

Durvalumab + FLOT demonstrated a statistically significant and clinically meaningful improvement in OS versus placebo + FLOT in the intention to treat population



*Intention to treat analysis set (all randomised participants, regardless of treatment received). †In censored participants. Data cut-off: 01 September 2025. OS maturity: 37.1%. Events were defined as time from randomisation until the date of death due to any cause. The HR and its CI were estimated from a Cox proportional hazards model, adjusted for geographic region, clinical lymph node status, and PD-L1 expression status. The CI for the HR was calculated using a profile likelihood approach. An HR <1 favours durvalumab + FLOT. The two-sided p-value was calculated using a stratified log-rank test adjusting for geographic region, clinical lymph node status, and PD-L1 expression status. CI, confidence interval; FLOT, 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; HR, hazard ratio; mo, month; NR, not reached; OS, overall survival; PD-L1, programmed cell death ligand-1.

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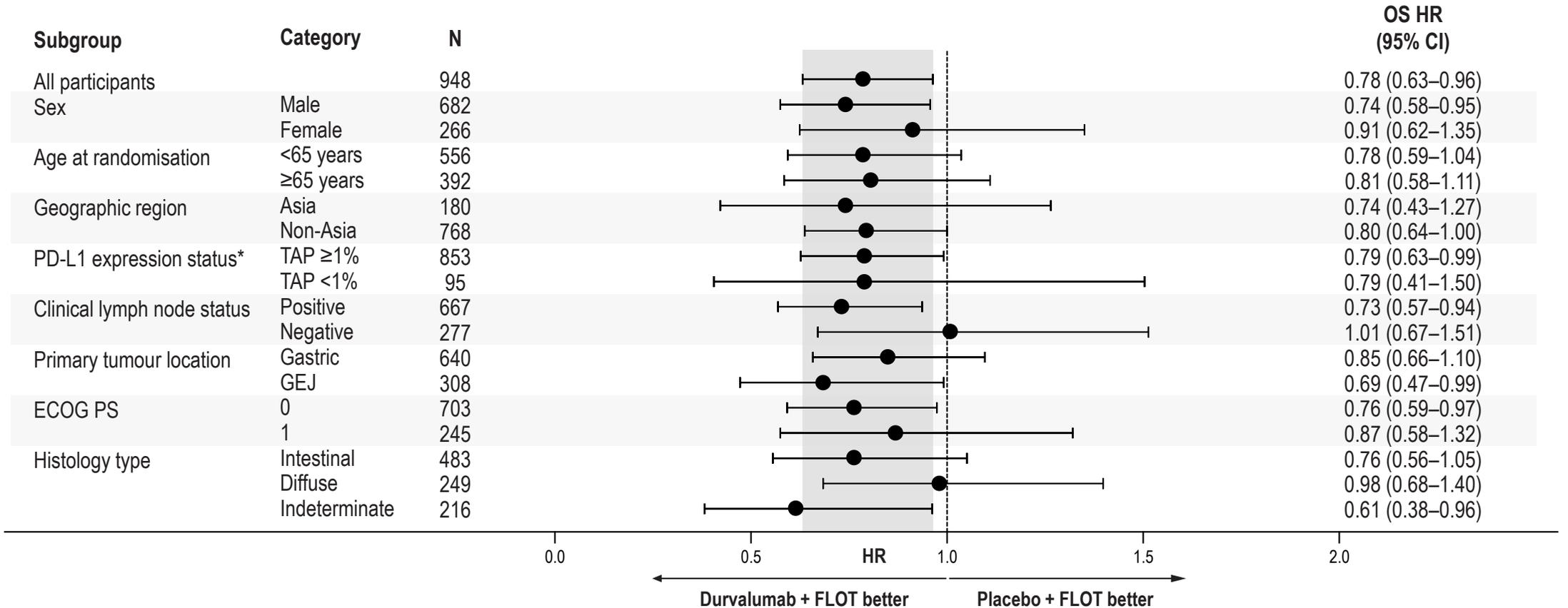
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OS in key subgroups

A consistent benefit in OS was observed with durvalumab + FLOT versus placebo + FLOT in most key subgroups



*Measured by immunohistochemistry using VENTANA PD-L1 (SP263) Companion Diagnostic Assay (Roche Diagnostics; investigational use only) and recorded at randomisation on the Interactive Response Technology System, Randomisation and Trial Supply Management, Electronic Case Report Form or from external vendor data from samples collected on or before randomisation. Participants provided a tumour tissue sample at screening to determine PD-L1 status using the TAP scoring method.

Data cut-off: 01 September 2025. The analysis was performed using a Cox proportional hazards model with treatment as the only covariate. An HR <1 favours durvalumab + FLOT. The CI was calculated using a profile likelihood approach. The grey band represents the 95% CI for the intention to treat HR. CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; FLOT, 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; GEJ, gastroesophageal junction; HR, hazard ratio; OS, overall survival; PD-L1, programmed cell death ligand-1; TAP, Tumour Area Positivity.

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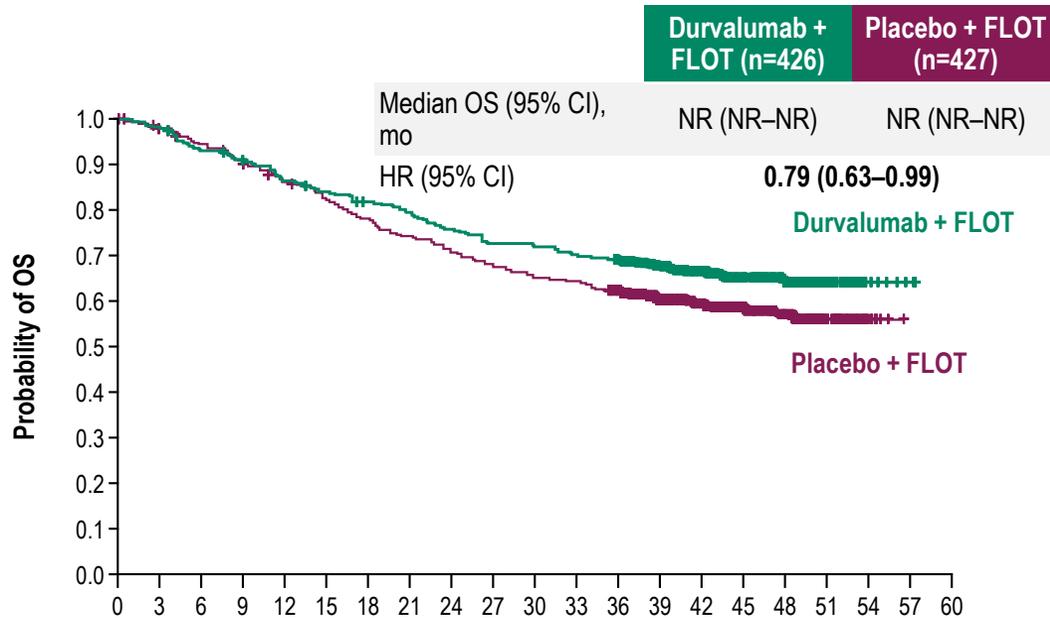
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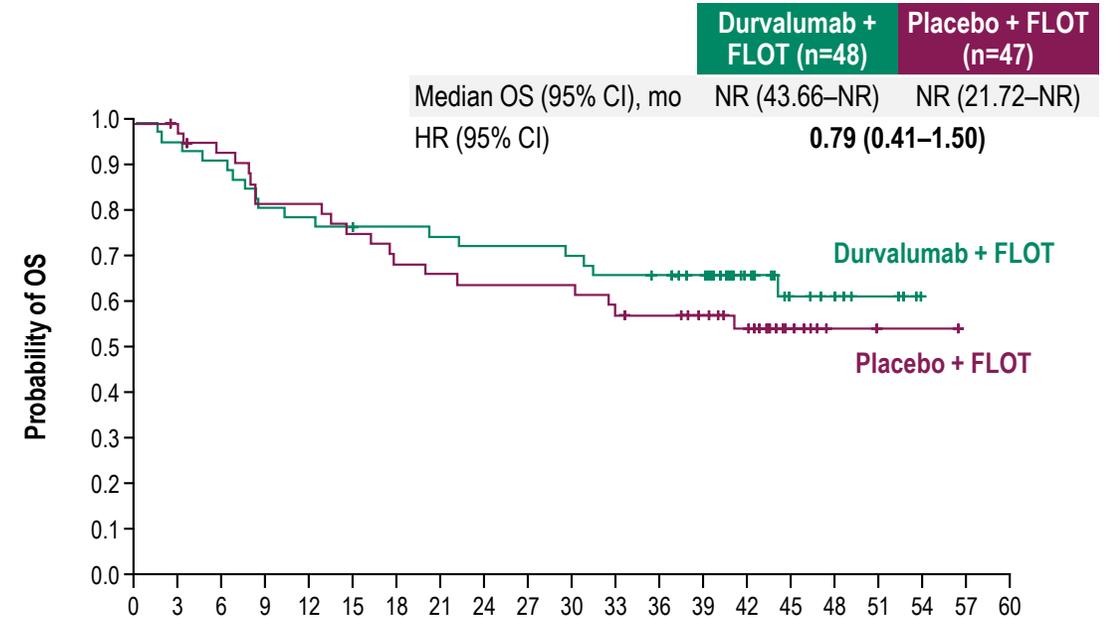
OS by PD-L1 status

OS was improved with durvalumab + FLOT versus placebo + FLOT regardless of PD-L1 status

PD-L1 TAP $\geq 1\%^*$



PD-L1 TAP $< 1\%^*$



	Time since randomisation (mo)																Total no. of events					
No. of participants at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	
Durvalumab + FLOT	426	418	394	383	365	353	341	332	317	304	301	292	286	229	165	101	64	25	6	1	0	143
Placebo + FLOT	427	412	397	377	358	340	324	308	295	281	270	267	253	200	152	91	59	22	6	0	0	172

	Time since randomisation (mo)																Total no. of events					
No. of participants at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	
Durvalumab + FLOT	48	46	44	39	38	36	36	35	34	34	33	31	30	26	17	11	7	4	0	0	0	17
Placebo + FLOT	47	45	42	37	37	34	31	30	29	29	28	26	25	21	15	8	2	1	1	0	0	20

*Measured by immunohistochemistry using VENTANA PD-L1 (SP263) Companion Diagnostic Assay (Roche Diagnostics; investigational use only) and recorded at randomisation on the Interactive Response Technology System, Randomisation and Trial Supply Management, Electronic Case Report Form or from external vendor data from samples collected on or before randomisation. Participants provided a tumour tissue sample at screening to determine PD-L1 status using the TAP scoring method. Data cut-off: 01 September 2025. The HR and its CI were estimated from a Cox proportional hazards model. The CI for the HR was calculated using a profile likelihood approach. CI, confidence interval; FLOT, 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; HR, hazard ratio; NR, not reached; OS, overall survival; PD-L1, programmed cell death ligand-1; TAP, Tumour Area Positivity.

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Pathological and nodal assessments

- Pathological response was assessed centrally in participants who completed surgery with samples that were evaluable for modified Ryan scoring by central assessment (N=757)
 - **pCR:** modified Ryan score 0 (125 participants [16.5%])
 - **Non-pCR:** modified Ryan score 1, 2 and 3 (632 participants [83.5%])
 - **MPR:** modified Ryan score 0 and 1 (195 participants [25.8%])
 - **Any pathological response:** modified Ryan score 0, 1 and 2 (659 participants [87.1%])
- Nodal staging status was assessed locally in participants who completed surgery with samples that were evaluable for nodal involvement by investigator assessment (N=811)
 - **ypN-:** no nodal involvement (418 participants [51.5%])
 - **ypN+:** nodal involvement (393 participants [48.5%])

Modified Ryan score ¹	Response	Description
0	Complete response	No viable cancer cells
1	Near complete response	Single cells or rare small groups of cancer cells
2	Partial response	Residual cancer with evident tumour regression, but more than single cells or rare small groups of cancer cells
3	Poor or no response	Extensive residual cancer with no evident tumour regression

Data cut-off: 20 December 2024.

MPR, major pathological response; pCR, pathological complete response; ypN, pathological nodal status.

1. College of American Pathologists. Protocol for the examination of specimens from patients with carcinoma of the stomach. <https://documents.cap.org/protocols/cp-giupper-stomach-20-4100.pdf>. Accessed 11 September 2025.

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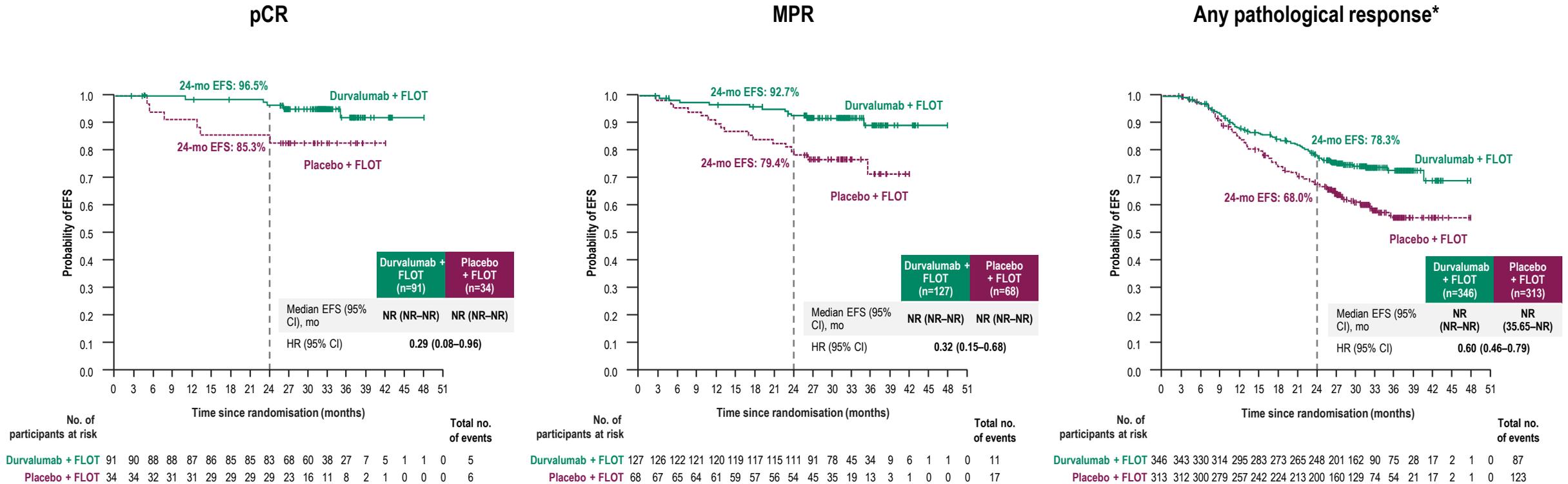
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Pathological response and EFS

EFS was improved with durvalumab + FLOT versus placebo + FLOT among participants with any degree of pathological response



*Among participants who completed surgery with samples that were evaluable for modified Ryan scoring by central assessment, the rate of participants who achieved any pathological response was 89.9% in the durvalumab + FLOT arm and 84.1% in the placebo + FLOT arm. Data cut-off: 20 December 2024. pCR is defined as modified Ryan score of 0; MPR is defined as modified Ryan score of 0 and 1; any pathological response is defined as modified Ryan score 0, 1, and 2. Events were defined as the earliest of RECIST v1.1 events, non-RECIST v1.1 events or deaths due to any cause. Analysis was based on BICR assessments and / or locally by pathology testing if clinically required. The HR and its CI were estimated from a Cox proportional hazards model. The CI for the HR was calculated using a profile likelihood approach. BICR, blinded independent central review; CI, confidence interval; EFS, event-free survival; FLOT, 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; HR, hazard ratio; mo, month; MPR, major pathological response; NR, not reached; pCR, pathological complete response; RECIST v1.1, Response Evaluation Criteria for Solid Tumors version 1.1.

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Nodal staging assessment by investigator

The rate of participants who achieved ypN- was higher in those receiving durvalumab + FLOT versus placebo + FLOT

	Durvalumab + FLOT (n=411)*	Placebo + FLOT (n=400)*
ypN staging at surgery, n (%)	411 (100.0)	400 (100.0)
Total N-	239 (58.2)	179 (44.8)
Downstaged to N-	148 (36.0)	112 (28.0)
Persistent N-	89 (21.7)	67 (16.8)
Total N+ (persistent or upstaged)	171 (41.6)	220 (55.0)

*Participants who completed surgery with samples that were evaluable for nodal involvement by investigator assessment.
Data cut-off: 20 December 2024.
FLOT, 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; ypN, pathological nodal status.

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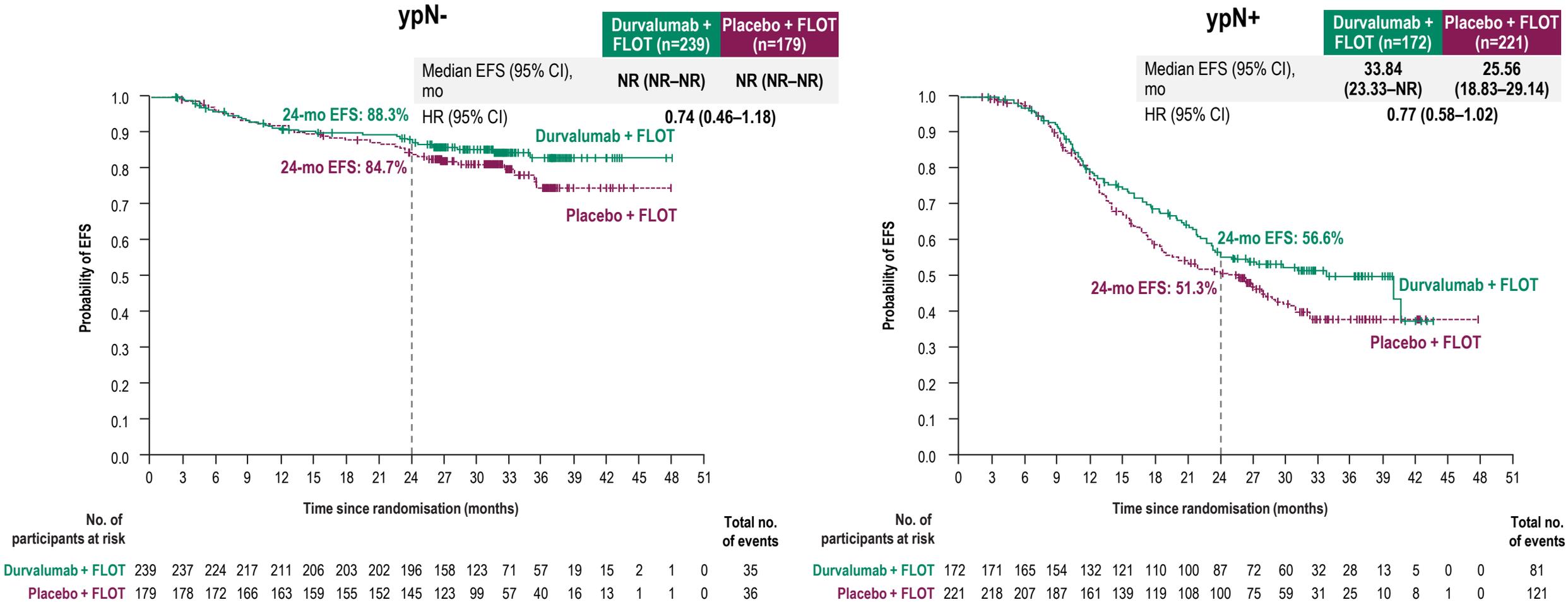
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Nodal staging and EFS

EFS was improved with durvalumab + FLOT versus placebo + FLOT, regardless of ypN status



Data cut-off: 20 December 2024. Events were defined as the earliest of RECIST v1.1 events, non-RECIST v1.1 events or deaths due to any cause. Analysis was based on BICR assessments and / or locally by pathology testing if clinically required. The HR and its CI were estimated from a Cox proportional hazards model. The CI for the HR was calculated using a profile likelihood approach.

BICR, blinded independent central review; CI, confidence interval; EFS, event-free survival; FLOT, 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; HR, hazard ratio; mo, month; NR, not reached; RECIST v1.1, Response Evaluation Criteria for Solid Tumors version 1.1; ypN, pathological nodal status.

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New Data at ASCO GI 2026

- 1. Surgical Specifics
- 2. Dose Intensity from Chemo



MATTERHORN exploratory analysis poster presentation at ASCO GI 2026

Poster 353

Surgical journey for participants in the MATTERHORN trial: a global, randomized, Phase 3 study of durvalumab plus 5-fluorouracil, leucovorin, oxaliplatin and docetaxel (FLOT) in resectable gastric / gastroesophageal junction (GEJ) adenocarcinoma

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Rates of treatment, surgery, and resection margin^{1,2}

The rates of participants who **attempted / completed surgery, type of surgery, rates of R0, R1, and R2 resection, and extent of nodal dissection** were comparable between treatment arms

	Durvalumab + FLOT (n=474)*	Placebo + FLOT (n=474)*
Received any neoadjuvant treatment, n (%)	474 (100)	470 (99.2)
Completed durvalumab or placebo	458 (96.6)	449 (94.7)
Completed all FLOT	448 (94.5)	437 (92.2)
Attempted surgery, n (%)	431 (90.9)	428 (90.3)
Completed surgery, n (%)	412 (86.9)	400 (84.4)
Type of surgery[†], n (%)		
Distal gastrectomy	38 (8.0)	38 (8.0)
Subtotal gastrectomy	79 (16.7)	72 (15.2)
Total gastrectomy	168 (35.4)	166 (35.0)
Gastroesophagectomy	127 (26.8)	124 (26.2)
Surgery attempted but not completed, n (%)	19 (4.0)	28 (5.9)
Did not undergo surgery, n (%)	43 (9.1)	46 (9.7)
Resection margin[‡], n (%)		
R0	377 (91.5)	369 (92.3)
R1 [†]	23 (5.6)	21 (5.3)
R2 [†]	11 (2.7)	10 (2.5)
Type of lymphadenectomy, n (%)		
D1	36 (8.7)	26 (6.5)
D2 / D3	375 (91.0)	373 (93.3)
Missing	1 (0.2)	1 (0.3)
Received any adjuvant treatment, n (%)	364 (76.8)	352 (74.3)
Completed durvalumab or placebo	248 (52.3)	245 (51.7)
Completed all FLOT	229 (48.3)	245 (51.7)

Data cutoff: December 20, 2024.

*ITT analysis set (all randomized participants, regardless of treatment received). †Data not reported in Janjigian YY, et al. *N Engl J Med* 2025.2 ‡Among participants who completed surgery.

FLOT, 5-fluorouracil, leucovorin, oxaliplatin, and docetaxel; ITT, intention to treat.

1. Janjigian YY, et al. *N Engl J Med* 2025;393:217–230. 2. Molena D, et al. Presented at ASCO GI 2026; 8–10 January, San Francisco, CA, USA. Abstract # 353.



SAEs* possibly related to surgery and surgical mortality rates were comparable between the two arms

	Durvalumab + FLOT (n=475) [†]	Placebo + FLOT (n=469) [†]
Participants with any SAE possibly related to surgery, n (%)	61 (12.8)	61 (13.0)
Infections and infestations	14 (2.9)	14 (3.0)
Pneumonia	3 (0.6)	2 (0.4)
Pneumonia aspiration	2 (0.4)	3 (0.6)
Respiratory, thoracic, and mediastinal disorders	5 (1.1)	6 (1.3)
Gastrointestinal disorders	24 (5.1)	25 (5.3)
Ileus	5 (1.1)	1 (0.2)
Intestinal obstruction	1 (0.2)	4 (0.9)
Injury, poisoning, and procedural complications	17 (3.6)	20 (4.3)
Anastomotic leak	3 (0.6)	0
Failure to anastomose	1 (0.2)	5 (1.1)
Gastrointestinal anastomotic leak	7 (1.5)	3 (0.6)
Surgical mortality, n (%)	Durvalumab + FLOT (n=413)[‡]	Placebo + FLOT (n=399)[‡]
Death at any time after the surgery	97 (23.5)	119 (29.8)
Death within 30 days after the surgery	5 (1.2)	6 (1.5)
Death within 60 days after the surgery	10 (2.4)	6 (1.5)
Death within 90 days after the surgery	13 (3.1)	8 (2.0)

Data cutoff: December 20, 2024. Participants with multiple causally related SAEs counted once for each SOC / PT.

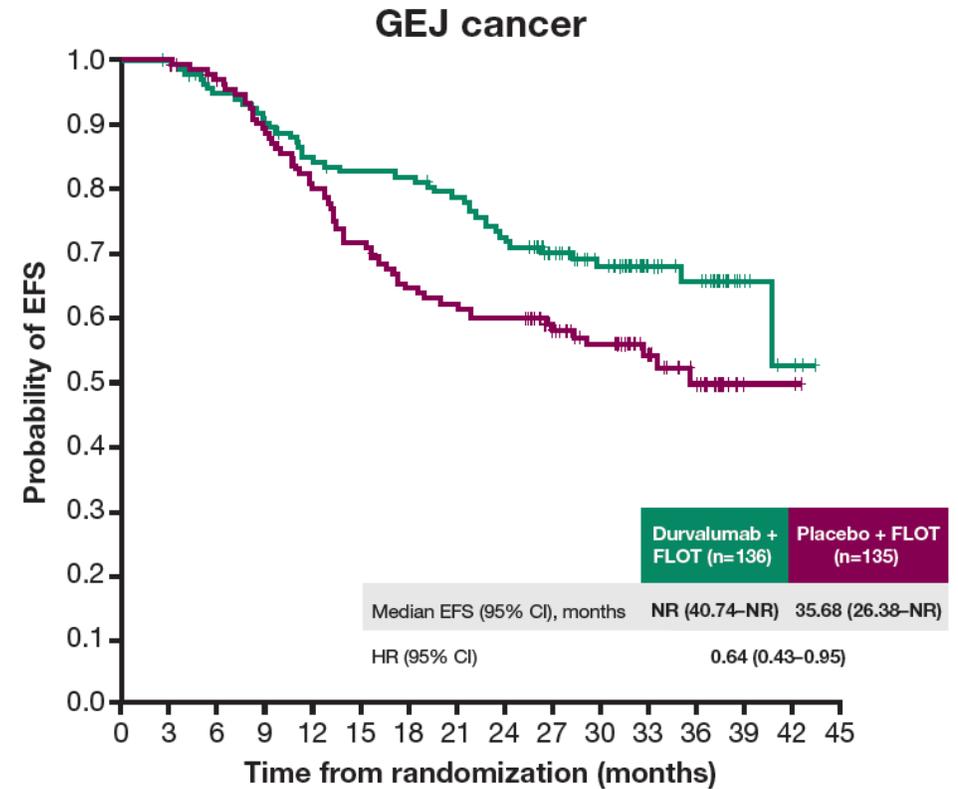
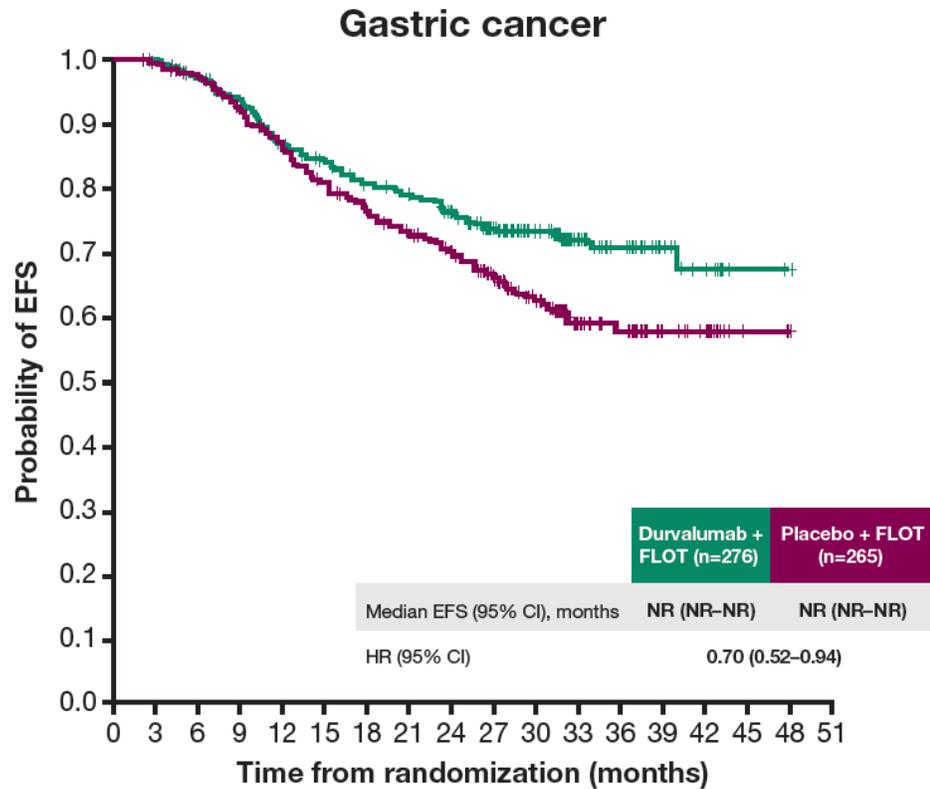
*Includes SOCs occurring in ≥1% participants and PTs occurring in ≥0.6% participants in either treatment arm. [†]Safety analysis set (participants who received at least one dose of study treatment); one participant in the placebo + FLOT group received a single dose of durvalumab and is, therefore, included in the durvalumab + FLOT group for the safety analysis. [‡]Participants in the safety analysis set who completed surgery.

FLOT, 5-fluorouracil, leucovorin, oxaliplatin and docetaxel; PT, Preferred Term; SAE, serious adverse event; SOC, System Organ Class.

1. Molena D, et al. Presented at ASCO GI 2026; 8–10 January, San Francisco, CA, USA. Abstract # 353.



EFS benefit was observed with durvalumab + FLOT regardless of tumor location



	No. of participants at risk																Total no. of events		
	276	275	264	252	232	220	207	201	190	153	121	69	58	25	17	2	1	0	74
Durvalumab + FLOT	276	275	264	252	232	220	207	201	190	153	121	69	58	25	17	2	1	0	74
Placebo + FLOT	265	262	253	237	221	206	192	181	169	137	107	57	46	23	19	2	1	0	98

	No. of participants at risk																Total no. of events
	136	134	125	119	111	107	106	101	93	77	62	34	27	7	3	0	43
Durvalumab + FLOT	136	134	125	119	111	107	106	101	93	77	62	34	27	7	3	0	43
Placebo + FLOT	135	134	126	116	103	92	82	79	76	61	51	31	19	3	2	0	59

Data cutoff: December 20, 2024.

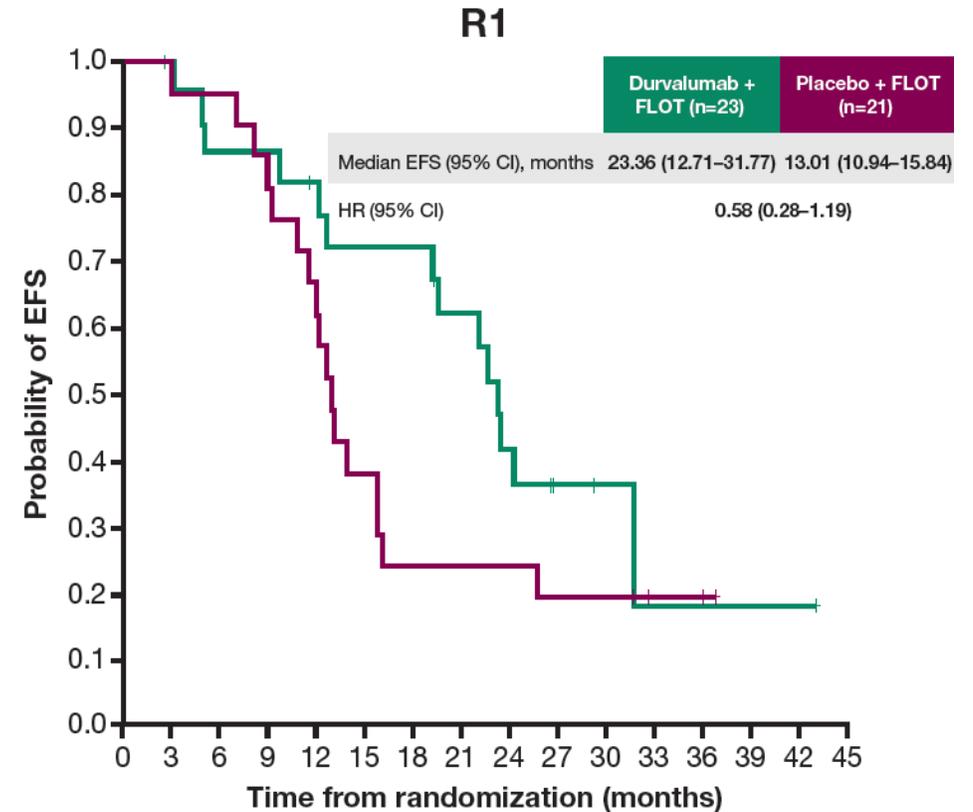
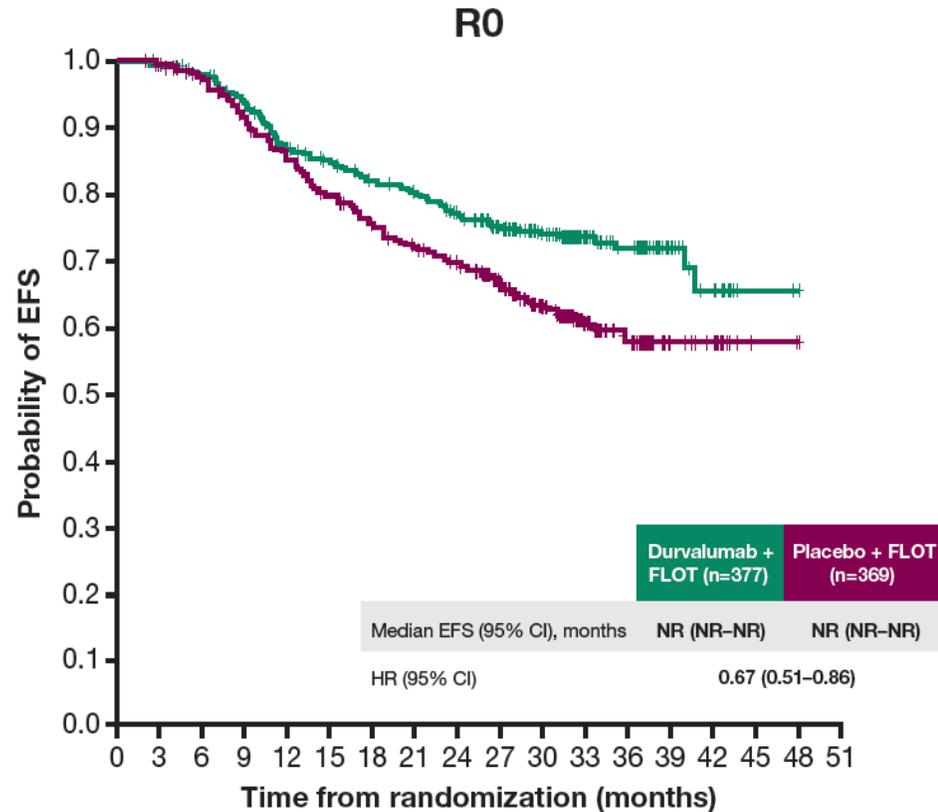
ITT analysis set (all randomized participants, regardless of treatment received).

CI, confidence interval; EFS, event-free survival; FLOT, 5-fluorouracil, leucovorin, oxaliplatin, and docetaxel; GEJ, gastroesophageal junction; HR, hazard ratio; ITT, intention to treat; NR, not reached.

1. Molena D, et al. Presented at ASCO GI 2026; 8-10 January, San Francisco, CA, USA. Abstract # 353.



EFS benefit was observed with durvalumab + FLOT regardless of resection margin



	No. of participants at risk																Total no. of events		
	377	375	363	345	319	305	291	283	268	223	179	100	82	30	18	2	1	0	
Durvalumab + FLOT	377	375	363	345	319	305	291	283	268	223	179	100	82	30	18	2	1	0	98
Placebo + FLOT	369	365	349	325	301	282	262	249	236	190	151	85	63	26	21	2	1	0	135

	No. of participants at risk																Total no. of events		
	23	22	19	19	17	15	15	12	8	3	2	1	1	1	1	0	0	0	
Durvalumab + FLOT	23	22	19	19	17	15	15	12	8	3	2	1	1	1	1	0	0	0	14
Placebo + FLOT	21	21	20	18	14	8	5	5	5	4	4	2	2	0	0	0	0	0	17

Data cutoff: December 20, 2024.

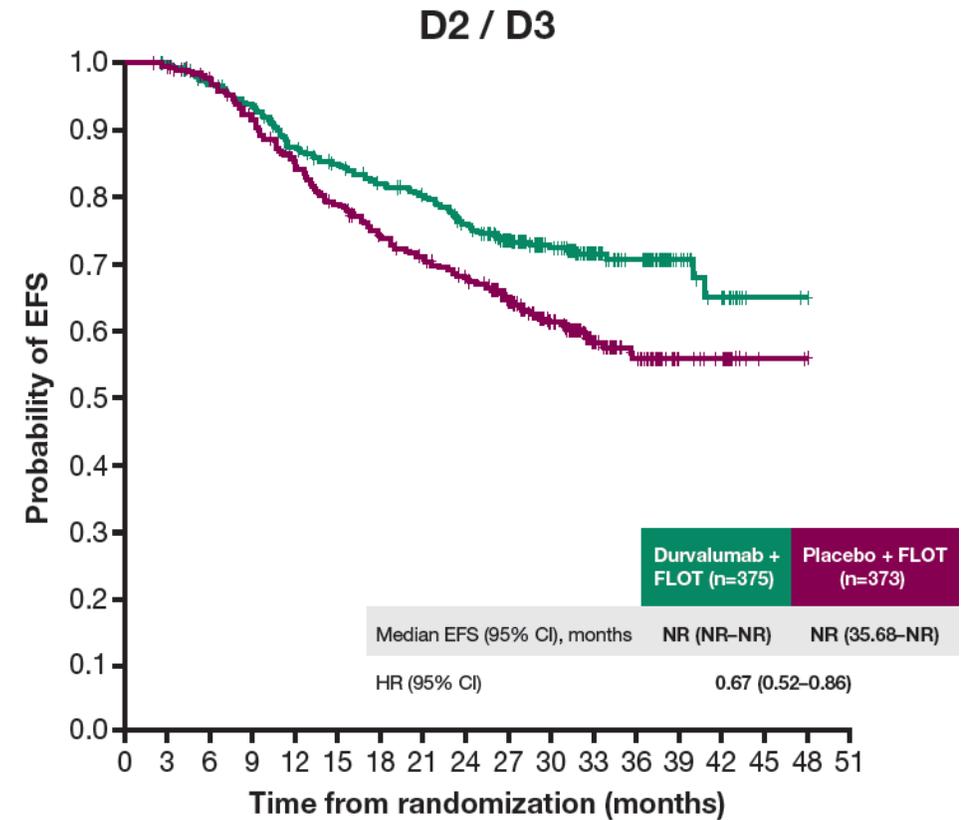
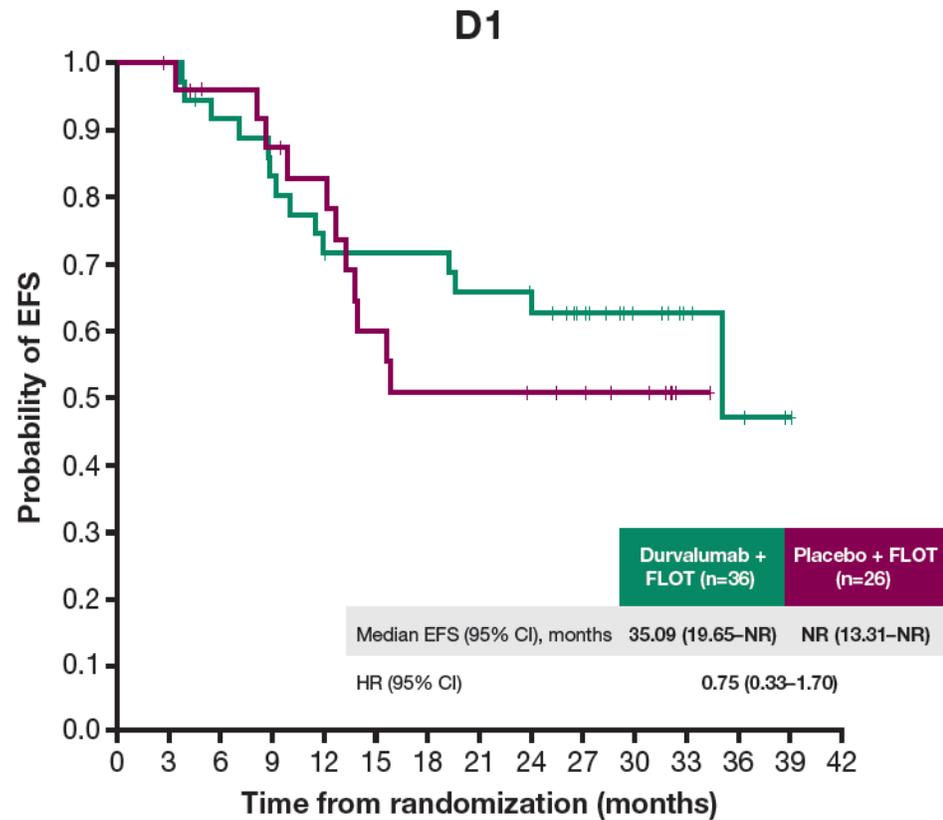
ITT analysis set (all randomized participants, regardless of treatment received).

CI, confidence interval; EFS, event-free survival; FLOT, 5-fluorouracil, leucovorin, oxaliplatin, and docetaxel; GEJ, gastroesophageal junction; HR, hazard ratio; ITT, intention to treat; NR, not reached.

1. Molena D, et al. Presented at ASCO GI 2026; 8-10 January, San Francisco, CA, USA. Abstract # 353



EFS benefit was observed with durvalumab + FLOT regardless of lymphadenectomy type



	No. of participants at risk													Total no. of events		
	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	
Durvalumab + FLOT	36	36	32	29	26	24	24	22	21	16	10	5	3	1	0	14
Placebo + FLOT	26	25	22	20	18	13	11	11	10	9	7	1	0	0	0	11

	No. of participants at risk																			Total no. of events
	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51		
Durvalumab + FLOT	375	372	356	341	316	302	288	279	261	213	172	97	81	30	20	2	1	0	103	
Placebo + FLOT	373	370	356	332	305	284	263	249	235	189	151	87	65	26	21	2	1	0	145	

Data cutoff: December 20, 2024.

ITT analysis set (all randomized participants, regardless of treatment received).

CI, confidence interval; EFS, event-free survival; FLOT, 5-fluorouracil, leucovorin, oxaliplatin, and docetaxel; GEJ, gastroesophageal junction; HR, hazard ratio; ITT, intention to treat; NR, not reached.

1. Molena D, et al. Presented at ASCO GI 2026; 8–10 January, San Francisco, CA, USA. Abstract # 353



Conclusions and key takeaways

- In participants with resectable GC/GEJC in MATTERHORN, the surgical journey did not differ with durvalumab + FLOT versus placebo + FLOT
- The addition of durvalumab to FLOT did not delay surgery or initiation of adjuvant treatment versus placebo + FLOT
- The rates of surgery completion, R0 resection, and the extent of nodal dissection were similar between treatment arms
- SAEs and mortality rates following surgery were comparable between treatment arms
- EFS benefit was observed with the addition of durvalumab to FLOT, regardless of tumor location, resection margin, or lymphadenectomy type
- Results of this analysis support the use of durvalumab + FLOT as a new global SoC for the treatment of locoregional resectable GC/GEJC



Number of FLOT cycles received were similar in both arms of MATTERHORN

Median number of FLOT cycles received in both treatment arms was 4.0 in both neoadjuvant and adjuvant periods

	Durvalumab + FLOT (n=475)*	Placebo + FLOT (n=469)*
Number of neoadjuvant FLOT cycles (Days 1 and 15), n (%)		
Cycle 1 Day 1	475 (100)	469 (100)
Cycle 1 Day 15	469 (98.7)	459 (97.9)
Cycle 2 Day 1	462 (97.3)	452 (96.4)
Cycle 2 Day 15	456 (96.0)	446 (95.1)
Number who received ≥1 adjuvant FLOT cycle	n=354	n=345
Number of adjuvant FLOT cycles (Days 1 and 15), n (%)		
Cycle 3 Day 1	354 (74.5)	345 (73.6)
Cycle 3 Day 15	341 (71.8)	333 (71.0)
Cycle 4 Day 1	318 (66.9)	319 (68.0)
Cycle 4 Day 15	292 (61.5)	302 (64.4)

Rows are cumulative and participants are included if they have taken treatment up to that number of cycles. If a cycle was prolonged due to toxicity, this was counted as 1 cycle. **A cycle was counted if treatment was started, even if the full dose was not delivered.**

*Safety analysis set (participants who received ≥1 dose of study treatment); one participant in the placebo + FLOT arm received a single dose of durvalumab and is, therefore, included in the durvalumab + FLOT arm for the safety analysis.

FLOT, 5-fluorouracil, leucovorin, oxaliplatin, and docetaxel.
Smyth E, et al. Presented at ASCO GI 2026; 8–10 January, San Francisco, CA, USA. Abstract # 343.



FLOT component discontinuation due to AEs by treatment period was comparable between the two arms

Overall rate of discontinuation of **at least one FLOT component** due to AEs:

- 25.5% in the **durvalumab + FLOT arm**
- 20.3% in the **placebo + FLOT arm**

	Neoadjuvant		Adjuvant		Overall	
	Durvalumab + FLOT (n=475)*	Placebo + FLOT (n=469)*	Durvalumab + FLOT (n=365)*	Placebo + FLOT (n=351)*	Durvalumab + FLOT (n=475)*	Placebo + FLOT (n=469)*
≥1 FLOT component discontinuation due to AEs,† n (%)	31 (6.5)	36 (7.7)	78 (21.4)	53 (15.1)	121 (25.5)	95 (20.3)
5-fluorouracil	13 (2.7)	11 (2.3)	40 (11.0)	28 (8.0)	64 (13.5)	42 (9.0)
Oxaliplatin	27 (5.7)	30 (6.4)	70 (19.2)	41 (11.7)	112 (23.6)	81 (17.3)
Docetaxel	21 (4.4)	25 (5.3)	48 (13.2)	30 (8.5)	80 (16.8)	59 (12.6)

- Overall rates of discontinuation for each FLOT component due to AEs were similar between arms
- The most commonly discontinued FLOT component was oxaliplatin in both the neoadjuvant period and the adjuvant period

*Safety analysis set (participants who received ≥1 dose of study treatment); one participant in the placebo + FLOT arm received a single dose of durvalumab and is, therefore, included in the durvalumab + FLOT arm for the safety analysis. †Includes discontinuations of 5-fluorouracil, leucovorin, oxaliplatin, and docetaxel.



AEs leading to FLOT discontinuation by treatment period

	Neoadjuvant		Adjuvant		Overall	
	Durvalumab + FLOT (n=475)*	Placebo + FLOT (n=469)*	Durvalumab + FLOT (n=365)*	Placebo + FLOT (n=351)*	Durvalumab + FLOT (n=475)*	Placebo + FLOT (n=469)*
≥1 FLOT component discontinuation due to AEs,[†] n (%)	31 (6.5)	36 (7.7)	78 (21.4)	53 (15.1)	121 (25.5)	95 (20.3)
Peripheral neuropathy [‡]	14 (2.9)	16 (3.4)	7 (1.9)	5 (1.4)	25 (5.3)	27 (5.8)
Neutropenia [§]	1 (0.2)	1 (0.2)	10 (2.7)	7 (2.0)	15 (3.2)	8 (1.7)
Infusion-related reaction	1 (0.2)	0	12 (3.3)	5 (1.4)	13 (2.7)	5 (1.1)
Hypersensitivity	2 (0.4)	1 (0.2)	9 (2.5)	6 (1.7)	11 (2.3)	7 (1.5)

- Overall, there were higher FLOT discontinuation rates due to AEs in the adjuvant than the neoadjuvant period
- The most common AEs causing FLOT discontinuation were peripheral neuropathy and neutropenia

AEs shown are those occurring in ≥2% of participants in either arm overall.

*Safety analysis set (participants who received ≥1 dose of study treatment); one participant in the placebo + FLOT arm received a single dose of durvalumab and is, therefore, included in the durvalumab + FLOT arm for the safety analysis.

[†]Includes discontinuations of 5-fluorouracil, leucovorin, oxaliplatin, and docetaxel.

[‡]Grouped term includes the PTs peripheral sensory neuropathy, neuropathy peripheral, and paresthesia.

[§]Grouped term includes the PTs neutropenia and neutrophil count decreased.

^{||}Grouped term includes the PTs hypersensitivity and drug hypersensitivity.



AEs leading to FLOT discontinuation by FLOT component

- The most commonly discontinued FLOT component due to AEs was oxaliplatin
- The most common AEs causing FLOT component discontinuation were:
 - Neutropenia for 5-fluorouracil and docetaxel
 - Peripheral neuropathy for oxaliplatin

	5-fluorouracil		Oxaliplatin		Docetaxel	
	Durvalumab + FLOT (n=475)*	Placebo + FLOT (n=469)*	Durvalumab + FLOT (n=475)*	Placebo + FLOT (n=469)*	Durvalumab + FLOT (n=475)*	Placebo + FLOT (n=469)*
FLOT component discontinuation due to any AE, n (%)	64 (13.5)	42 (9.0)	112 (23.6)	81 (17.3)	80 (16.8)	59 (12.6)
Peripheral neuropathy [†]	2 (0.4)	1 (0.2)	24 (5.1)	27 (5.8)	11 (2.3)	7 (1.5)
Neutropenia [‡]	11 (2.3)	5 (1.1)	12 (2.5)	5 (1.1)	14 (2.9)	8 (1.7)
Infusion-related reaction	1 (0.2)	1 (0.2)	11 (2.3)	5 (1.1)	4 (0.8)	1 (0.2)
Hypersensitivity [§]	2 (0.4)	2 (0.4)	10 (2.1)	5 (1.1)	2 (0.4)	0

*Safety analysis set (participants who received ≥ 1 dose of study treatment); one participant in the placebo + FLOT arm received a single dose of durvalumab and is, therefore, included in the durvalumab + FLOT arm for the safety analysis.

[†]Grouped term includes the PTs peripheral sensory neuropathy, neuropathy peripheral, and paresthesia.

[‡]Grouped term includes the PTs neutropenia and neutrophil count decreased.

[§]Grouped term includes the PTs hypersensitivity and drug hypersensitivity.



AEs leading to FLOT discontinuation by component

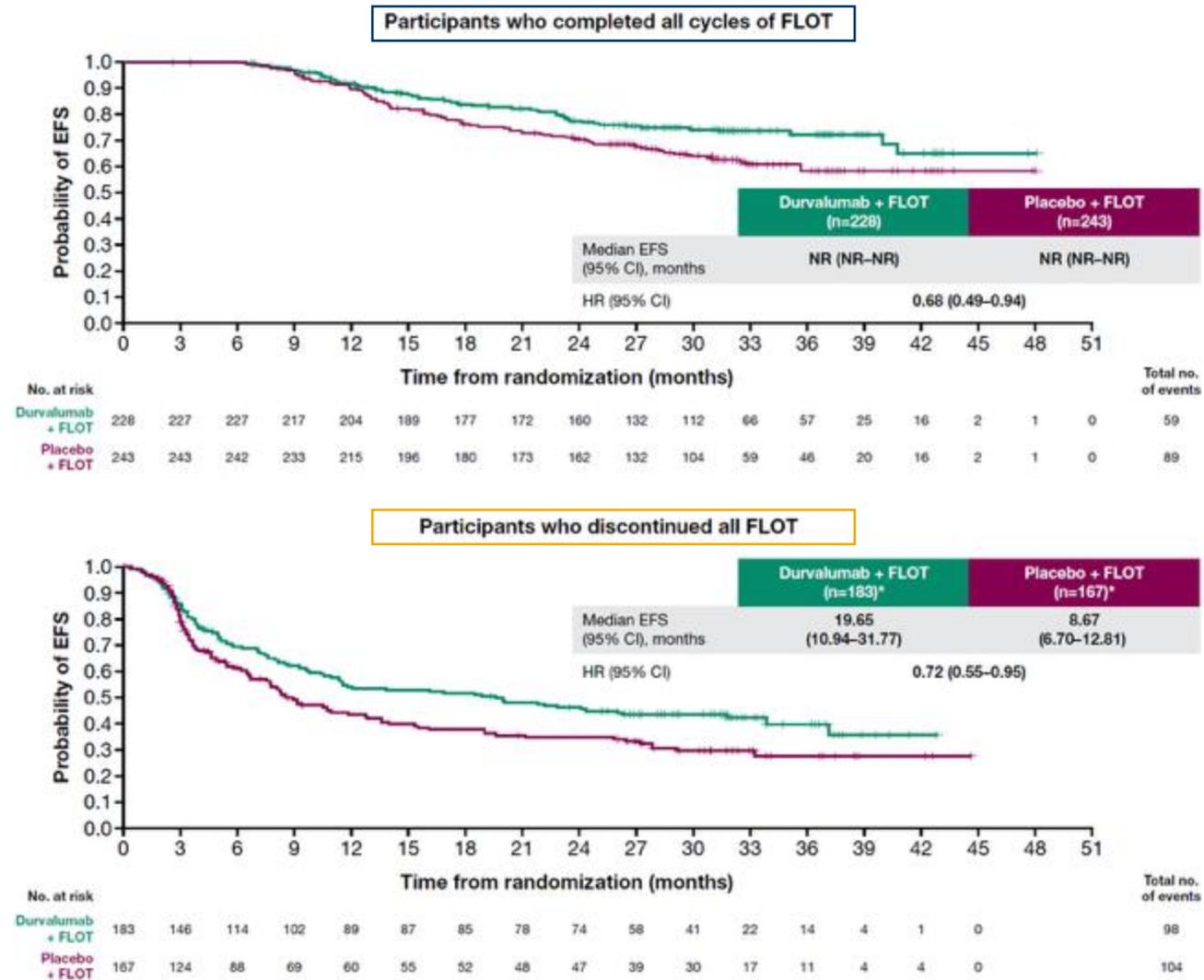
The most common AEs causing FLOT component discontinuation were:

- Neutropenia for 5-FU and docetaxel
- Peripheral neuropathy for oxaliplatin

	5-FU		Oxaliplatin		Docetaxel	
	Durvalumab + FLOT (n=475)	Placebo + FLOT (n=469)	Durvalumab + FLOT (n=475)	Placebo + FLOT (n=469)	Durvalumab + FLOT (n=475)	Placebo + FLOT (n=469)
Discontinuation due to AE, n (%)	64 (13.5)	42 (9.0)	112 (23.6)	81 (17.3)	80 (16.8)	59 (12.6)
Neutropenia	11 (2.3)	5 (1.1)	12 (2.5)	5 (1.1)	13 (2.7)	5 (1.1)
Diarrhea	5 (1.1)	4 (0.9)	5 (1.1)	4 (0.9)	5 (1.1)	6 (1.3)
Fatigue	6 (1.3)	1 (0.2)	5 (1.1)	1 (0.2)	6 (1.3)	1 (0.2)
Nausea	5 (1.1)	1 (0.2)	5 (1.1)	2 (0.4)	5 (1.1)	1 (0.2)
Neuropathy peripheral	0	0	9 (1.9)	8 (1.7)	5 (1.1)	2 (0.4)
Asthenia	4 (0.8)	1 (0.2)	5 (1.1)	2 (0.4)	5 (1.1)	3 (0.6)
Peripheral sensory neuropathy	2 (0.4)	0	11 (2.3)	16 (3.4)	4 (0.8)	3 (0.6)
Infusion-related reaction	1 (0.2)	1 (0.2)	11 (2.3)	5 (1.1)	4 (0.8)	1 (0.2)
Drug hypersensitivity	1 (0.2)	1 (0.2)	5 (1.1)	4 (0.9)	1 (0.2)	0
Hypersensitivity	1 (0.2)	1 (0.2)	5 (1.1)	1 (0.2)	1 (0.2)	0



EFS was improved with durvalumab + FLOT versus placebo + FLOT, regardless of FLOT completion status



Analyses performed in the intention-to-treat analysis set (all randomized participants, regardless of treatment received). HRs show durvalumab + FLOT versus placebo + FLOT, with an HR <1 favoring durvalumab + FLOT.

*Includes 62 participants in the durvalumab + FLOT arm and 70 participants in the placebo + FLOT arm who did not complete surgery. †In participants who discontinued 1, 2, or 3 of the 4 FLOT components.

CI, confidence interval; EFS, event-free survival; FLOT, 5-fluorouracil, leucovorin, oxaliplatin, and docetaxel; HR, hazard ratio; NR, not reached.

Smyth E, et al. Presented at ASCO GI 2026; 8–10 January, San Francisco, CA, USA. Abstract # 343.



EFS was improved with durvalumab + FLOT versus placebo + FLOT, regardless of FLOT completion status

FLOT discontinuation and EFS

	Durvalumab + FLOT (n=474)	Placebo + FLOT (n=470)	EFS HR (95% CI)
Discontinued any FLOT components, n (%)	246 (51.9)	227 (48.3)	0.68 (0.53–0.88)
Discontinued 1 FLOT component, n (%)	47 (9.9)	45 (9.6)	
Discontinued 2 FLOT components, n (%)	15 (3.2)	15 (3.2)	0.35 (0.16–0.71) [†]
Discontinued 3 FLOT components, n (%)	1 (0.2)	0	
Discontinued all FLOT, n (%)	183 (38.6)	167 (35.5)	0.72 (0.55–0.95)

Analyses performed in the intention-to-treat analysis set (all randomized participants, regardless of treatment received). HRs show durvalumab + FLOT versus placebo + FLOT, with an HR <1 favoring durvalumab + FLOT.

*Includes 62 participants in the durvalumab + FLOT arm and 70 participants in the placebo + FLOT arm who did not complete surgery. †In participants who discontinued 1, 2, or 3 of the 4 FLOT components.

CI, confidence interval; EFS, event-free survival; FLOT, 5-fluorouracil, leucovorin, oxaliplatin, and docetaxel; HR, hazard ratio; NR, not reached.

Smyth E, et al. Presented at ASCO GI 2026; 8–10 January, San Francisco, CA, USA. Abstract # 343.



Conclusions

- The addition of durvalumab to FLOT did not impact the ability to receive FLOT
 - No new safety signals were identified based on this analysis
- EFS was improved with durvalumab + FLOT versus placebo + FLOT, regardless of FLOT completion status; however, MATTERHORN was designed for participants to receive the full perioperative FLOT regimen
- The results of this exploratory analysis support the use of durvalumab + FLOT as a new global standard of care for patients with localized gastric and gastroesophageal junction adenocarcinoma



MATTERHORN Will Teach Us More

