Perioperative Durvalumab Plus FLOT Demonstrates Significant Survival Benefit in Resectable G/GEJ Adenocarcinoma

American Medical Journal

The publication of this infographic has been supported by AstraZeneca.

Oncol AMJ. 2026; https://doi.org/10.33590/oncolamj/2H42YL49

1. INTRODUCTION

Globally, G/GEJ adenocarcinomas are among the leading causes of cancer-related deaths.[1]

In locally advanced resectable disease, surgery and perioperative FLOT is the primary treatment approach, but recurrence is common.[1]

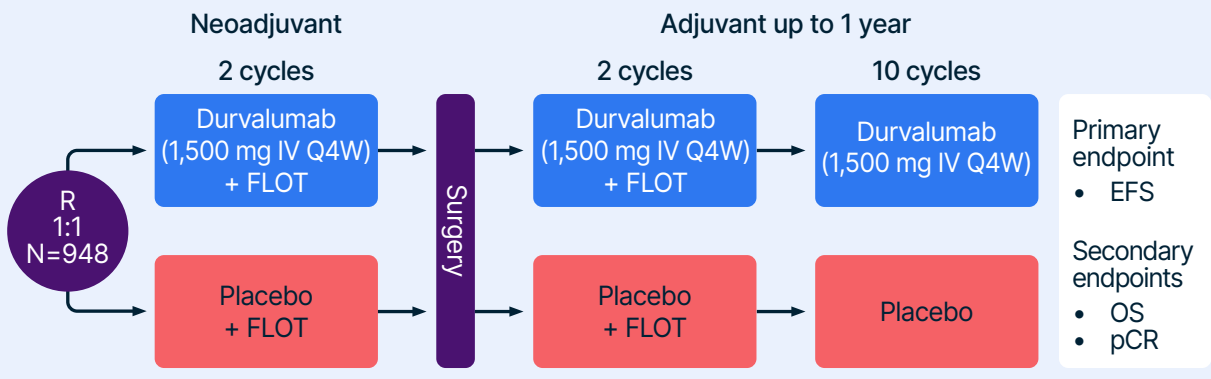
Durvalumab is an anti-PD-L1 antibody, approved for the treatment of a range of solid tumors.[1]

MATTERHORN trial data show that, compared to placebo + perioperative FLOT, perioperative durvalumab + FLOT:

- Significantly improved EFS and OS overall, with a generally consistent OS treatment effect across PD-L1 TAP subgroups and FLOT dosing flexibility.[1-3]
- Did not delay surgical management or increase SAEs.[1,4]

MATTERHORN Study Design[1]

A global, Phase III, randomized, double-blind, placebo-controlled study



FLOT dose/component flexibility was allowed in accordance with local standard clinical practice.

Study population

- G/GEJ adenocarcinoma
- Stage II–IVa
- No evidence of metastasis
- No prior therapy
- ECOG PS 0 or 1
- Global enrollment in Asia, Europe, and North and South America

2. RESULTS

When comparing durvalumab + FLOT to placebo + FLOT, the results of the MATTERHORN trial showed:

Statistically significant improvements in OS (HR: 0.78; 95% CI: 0.63–0.96; p=0.021). At 36 months, OS was 68.6% in the durvalumab group and 61.9% in the placebo group.[2]

Consistent benefit observed in most key subgroups[a] including:

- PD-L1 status by TAP score (TAP ≥1%: HR: 0.79; 95% CI: 0.63–0.99; TAP <1%: HR: 0.79; 95% CI: 0.41–1.50).[1,2]
- Histology type (diffuse: HR: 0.98; 95% CI: 0.68–1.40; indeterminate: HR: 0.61; 95% CI: 0.38–0.96).[2]

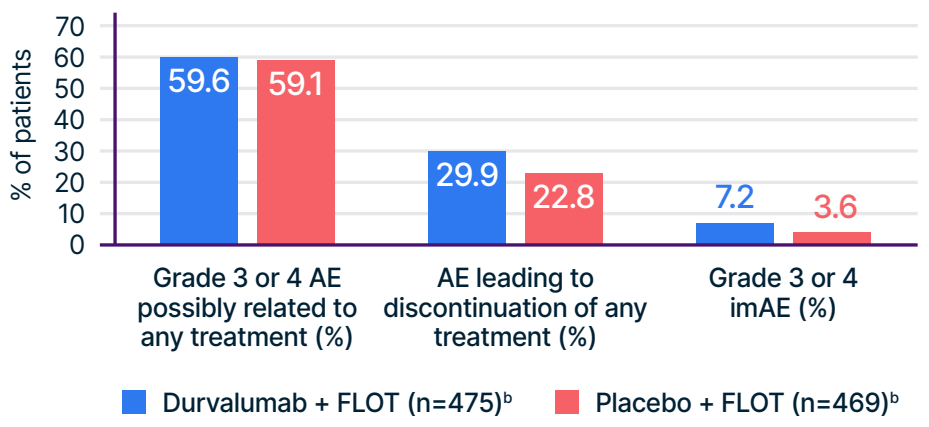
[a]The OS subgroup analysis was not powered to show differences between or within individual subgroups.

Statistically significant improvements in EFS. At 24 months, 67.4% of the participants in the durvalumab and 58.5% of those in the placebo group remained event free (HR: 0.71; 95% CI: 0.58–0.86; p<0.001).[1]

EFS benefits were seen among participants with any degree of pathological response (HR: 0.60; 95% CI: 0.46–0.79).[2,3]

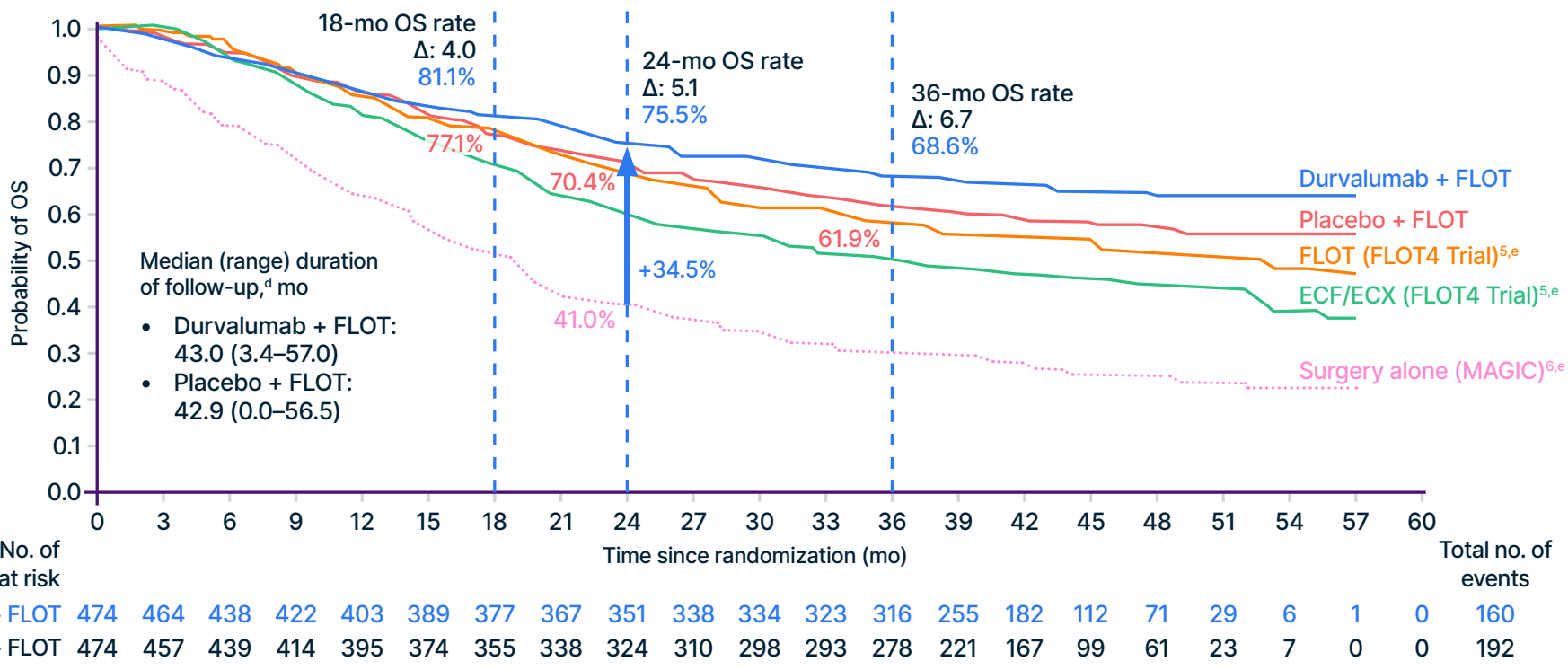
- DFS benefit was seen in those with R0 resection (24-month DFS: 75% with durvalumab + FLOT vs 66% with placebo + FLOT; HR: 0.70; 95% CI: 0.53–0.93; p=0.012).[1]

The safety profile was consistent with the known profiles of each medicine.[1]



[b]Safety analysis set: patients who received at least one dose of study treatment. One patient in the placebo + FLOT group received a single dose of durvalumab and is included in the durvalumab + FLOT group.

Durvalumab + FLOT improves OS vs SoC FLOT and surgery[c] | 2006–2025: Achievements in 19 years of perioperative treatment[2]



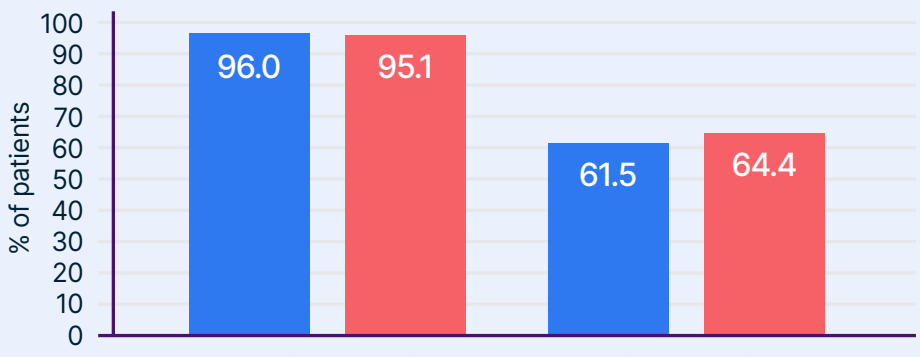
[c]Intention-to-treat analysis set (all randomized participants, regardless of treatment received).
[d]In censored participants.
[e]FLOT4 and MAGIC curves shown for historical context; cross-trial comparisons are illustrative and not head-to-head.

Data cut-off: September 1st, 2025. OS maturity: 37.1%. Events were defined as time from randomization 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.

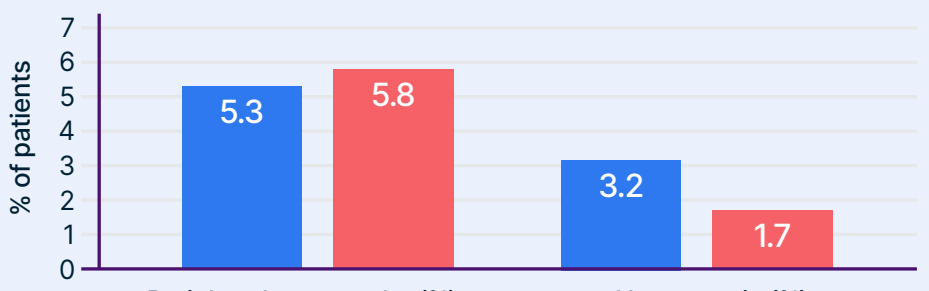
3. FLOT FLEXIBILITY

MATTERHORN allowed FLOT dose/component flexibility in accordance with local standard clinical practice. Participants could continue durvalumab, including as monotherapy, if FLOT or FLOT component was discontinued or modified for reasons other than disease progression or recurrence.[1,3]

Patients who completed all planned FLOT doses[3]



The most common AEs causing FLOT discontinuation were peripheral neuropathy and neutropenia[3]



EFS benefit was seen with durvalumab + FLOT vs placebo + FLOT regardless of FLOT completion status (patients who completed all FLOT cycles: HR: 0.68; 95% CI: 0.49–0.94; patients who discontinued all FLOT: HR: 0.72; 95% CI: 0.55–0.95).[2,3]

[f]Safety analysis set (patients who received at least one dose of study treatment); one patient in the placebo + FLOT arm received a single dose of durvalumab and is, therefore, included in the durvalumab + FLOT arm for the safety analysis.[3]

4. SURGICAL OUTCOMES

Crucially, durvalumab + FLOT did not impact the surgical journey, compared to placebo + FLOT.[1]

There was an EFS benefit with durvalumab + FLOT vs placebo + FLOT regardless of:
- tumor location (GC: HR: 0.70; 95% CI: 0.52–0.94; GEJC: HR: 0.64; 95% CI: 0.43–0.95);[4]
- resection margin (R0: HR: 0.67; 95% CI: 0.51–0.86; R1: HR: 0.58; 95% CI: 0.28–1.19);[4]
- lymphadenectomy type (D1: HR: 0.75; 95% CI: 0.33–1.70; D2/D3: HR: 0.67; 95% CI: 0.52–0.86).[4]

Durvalumab + FLOT

90.9%
of patients attempted surgery[1]

86.9% of patients completed surgery[1] → 91.5% of patients who completed surgery had R0 resection[1]

10.1% of patients experienced delayed surgery[g]

Placebo + FLOT

90.3%
of patients attempted surgery[1]

84.4% of patients completed surgery[1] → 92.3% of patients who completed surgery had R0 resection[1]

10.8% of patients experienced delayed surgery[g]

Higher pCR and near-pCR rates were observed with durvalumab + FLOT than with placebo + FLOT.[1]

SAE and mortality rates were similar across both arms.[1,4]

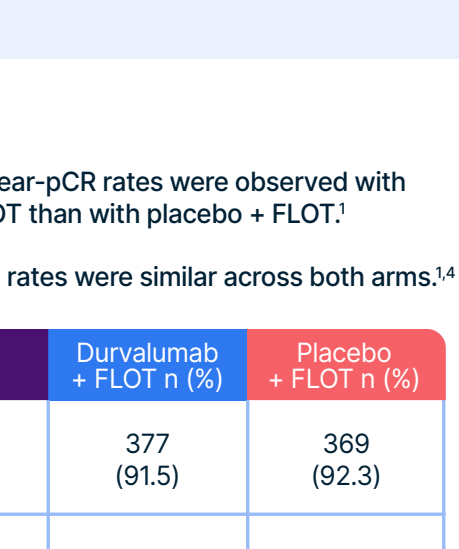
Outcome	Durvalumab + FLOT n (%)	Placebo + FLOT n (%)
R0 resection rates[h]	377 (91.5)	369 (92.3)
Patients undergoing D2/D3 lymphadenectomy[h]	375 (91.0)	373 (93.3)
Any SAE possibly related to surgery[i]	61 (12.8)	61 (13.0)
Death within 90 days of surgery[j]	13 (3.1)	8 (2.0)

[g]Delay defined as surgery occurring more than 8 weeks after the final dose of neoadjuvant treatment.
[h]Percentages are of participants who completed surgery (durvalumab + FLOT: n=412; placebo + FLOT: n=400).
[i]Percentages are of the safety analysis set (participants who received at least one dose of study treatment; durvalumab + FLOT: n=475; placebo + FLOT: n=469). 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.
[j]Percentages are of participants in the safety analysis set who completed surgery (durvalumab + FLOT: n=413; placebo + FLOT: n=399).

5. CONCLUSION

Results from the MATTERHORN trial demonstrate that adding durvalumab to perioperative FLOT significantly improves OS and EFS in patients with G/GEJ adenocarcinoma, without increasing surgical risk or SAEs.[1]

- **Benefits were consistent across clinically relevant subgroups, including PD-L1 status and histology type.[1-3]**
- **The addition of durvalumab to FLOT did not impact the surgical journey; EFS benefit seen regardless of FLOT completion status.[3]**
- **Together, these findings support perioperative durvalumab + FLOT as a potential new SoC for patients with resectable G/GEJ adenocarcinoma.**



Abbreviations:

AE: adverse event; D1: dissection level 1; D2: dissection level 2; D3: dissection level 3; DFS: disease-free survival; ECF/ECX: epirubicin, cisplatin, 5-fluorouracil/epirubicin, cisplatin, capecitabine; ECOG PS: Eastern Cooperative Oncology Group Performance Status; EFS: event-free survival; FLOT: fluorouracil, leucovorin, oxaliplatin, and docetaxel; GC: gastric cancer; GEJC: gastroesophageal junction cancer; G/GEJ: gastric/gastroesophageal junction; HR: hazard ratio; imAE: immune-mediated adverse event; mo: months; OS: overall survival; pCR: pathologic complete response; PD-L1: programmed death-ligand 1; Q4W: every 4 weeks; R0: no residual tumor; R1: microscopic residual tumor; SAE: serious adverse event; SoC: standard of care; TAP: tumor area positivity; vs: versus.

References:

1. Janjigian YY et al. N Engl J Med. 2025;393(3):217-30.
2. Tabernero J et al. Abstract LBA81. ESMO Congress, October 17-21, 2025.
3. Smyth E et al. Abstract 343. ASCO Gastrointestinal Cancers Symposium, January 8-10, 2026.
4. Molena D et al. Abstract 353. ASCO Gastrointestinal Cancers Symposium, January 8-10, 2026.
5. Al-Batran SE et al. Lancet. 2019;393(10184):1948-57.
6. Cunningham D et al. N Engl J Med. 2006;355(1):11-20.