PARIS 2022 ESMO congress

# PRODIGE 59 - DURIGAST trial: A randomised phase II study evaluating FOLFIRI plus Durvalumab and FOLFIRI plus Durvalumab plus tremelimumab in second-line treatment of patients with advanced gastric or gastro-oesophageal junction adenocarcinoma.

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# DECLARATION OF INTERESTS

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Laetitia Dahan:
Farid El Hajbi: None
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Pascal Artru
Christophe Louvet: MSD, Roche, Servier, Amgen

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# Introduction

- Immune checkpoint inhibitors (ICI) in combination with chemotherapy have demonstrated their efficacy as first-line treatment of in advanced gastric/gastro-oesphageal junction (GEJ) with PD-L1 combined positive score (CPS) ≥5.

- Efficacy of 2nd line chemotherapy in advanced gastric/GEJ adenocarcinoma remains limited and based on paclitaxel, ramucirumab, irinotecan alone and/or combined with 5FU.

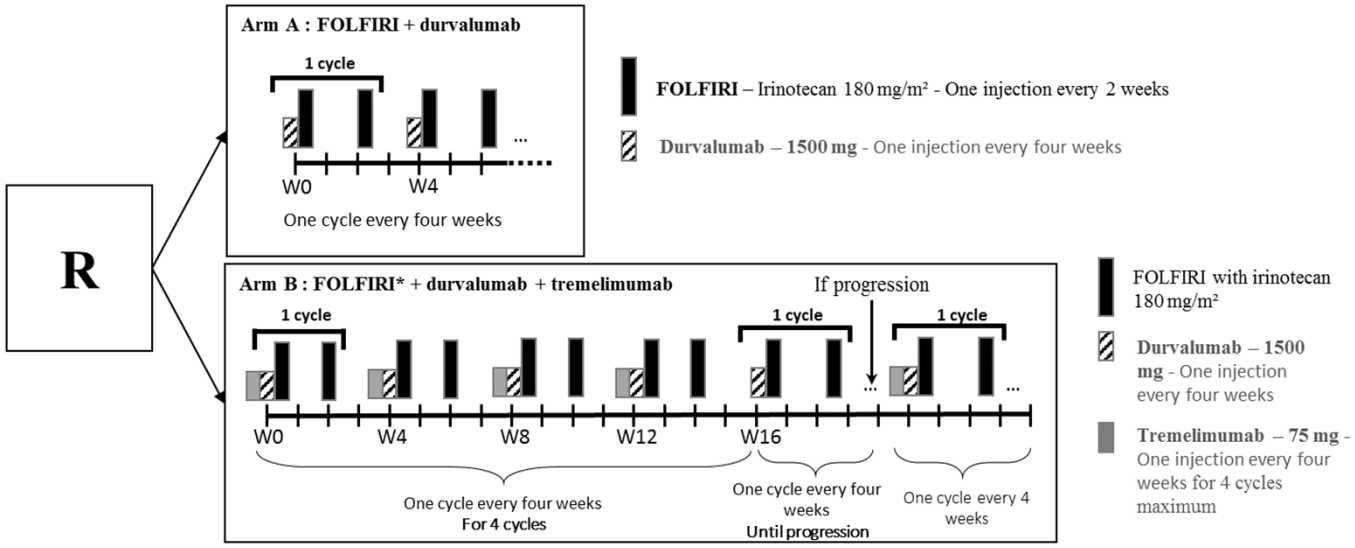
- Efficacy of ICIs alone as 2nd line treatment of advanced gastric/GEJ adenocarcinoma is limited.

- No study has evaluated the efficacy of two ICIs combined with chemotherapy in the treatment of advanced gastric/GEJ adenocarcinoma.

# Patients and methods

- DURIGAST - PRODIGE 59 is a randomized, multicenter, phase II study evaluating the safety and efficacy of the combination of FOLFIRI plus durvalumab (anti-PD-L1) (FD) versus FOLFIRI plus durvalumab and tremelimumab (anti-CTLA-4) (FDT) in second-line of advanced gastric/GEJ adenocarcinoma.

Key eligibility criteria:
- advanced gastric/GEJ adenocarcinoma.
- platinum-based first-line chemotherapy.
- ECOG PS 0 or 1.
- No prior ICI.




- The primary endpoint is PFS at 4 months (H1: 70% and H0: 50%).

# Patients characteristics

| Variables | All patients n=92 | Folfiri + Durvalumab n=47 | Folfiri + Durvalumab + Tremelimumab n=45 |
|---|---|---|---|
| **Age (years, mean [range])** | 60.0 [24.7-83.3] | 59.9 [28.2-83.3] | 60.2 [24.7-82.6] |
| **Female (n, %)** | 28 (30.4%) | 14 (29.8%) | 14 (31.1%) |
| **ECOG performance status (n, %)*** ** | | | |
| **0** | 31 (33.7%) | 11 (23.4%) | 20 (44.4%) |
| **1** | 61 (66.3%) | 36 (76.6%) | 25 (55.6%) |
| **Primary tumour site (n, %)** | | | |
| **Gastro-esophageal junction** | **49 (53.3%)** | **27 (57.4%)** | **22 (48.9%)** |
| **Stomach** | 43 (46.7%) | 20 (42.6%) | 23 (51.1%) |
| **Tumour subtype (Lauren classification) (n, %)** | | | |
| **Intestinal type** | **46 (50.0%)** | 22 (46.8%) | 24 (53.3%) |
| **Diffuse type** | 36 (39.1%) | 20 (42.6%) | 16 (35.6%) |
| **Others/Unknown** | 10 (10.9%) | 5 (10.6%) | 5 (11.1%) |
| **Delay of metastatic disease (n, %)** | | | |
| **Metachronous** | 32 (34.8%) | 17 (36.2%) | 15 (33.3%) |
| **Synchronous** | **60 (65.2%)** | **30 (63.8%)** | **30 (66.7%)** |
| **Site of metastases (n, %)** | | | |
| **Liver** | **37 (40.2%)** | **19 (40.4%)** | **18 (40.0%)** |
| **Lung** | 18 (19.6%) | 9 (19.1%) | 9 (20.0%) |
| **Peritoneal carcinomatosis** | **33 (35.9%)** | **16 (34.0%)** | **16 (34.0%)** |
| **Lymph nodes** | **36 (39.1%)** | **19 (40.4%)** | **17 (37.8%)** |

# Safety

- At the time of analysis, 6 pts in FD and 12 pts in FDT were still under treatment.
- In each arm we observed 47.8% of grade 3-5 adverse events related to treatment.

| | Folfiri + Durvalumab n=46 | | Folfiri + Durvalumab + Tremelimumab n=46 | |
|---|---|---|---|---|
| | **Grade 1-2** | **Grade 3-4-5** | **Grade 1-2** | **Grade 3-4-5** |
| **Patients with at least one adverse event** | **43 (93.5%)** | **22 (47.8%)** | **42 (91.3%)** | **22 (47.8%)** |
| **Endocrine disorders** | **4 (8.7%)** | **-** | **10 (21.7%)** | **-** |
| Hyperthyroidism | 1 (2.2%) | - | 8 (17.4%) | - |
| Hypothyroidism | 3 (6.5%) | - | 5 (10.9%) | - |
| **Gastrointestinal disorders** | **37 (80.4%)** | **5 (10.9%)** | **40 (87.0%)** | **11 (23.9%)** |
| Diarrhea | 23 (50.0%) | 1 (2.2%) | 30 (65.2%) | 5 (10.9%) |
| Colitis | - | 2 (4.3%) | - | - |
| Vomiting | 12 (26.1%) | 3 (6.5%) | 14 (30.4%) | 1 (2.2%) |
| **Investigations** | **30 (65.2%)** | **10 (21.7%)** | **29 (63.0%)** | **14 (30.4%)** |
| AST/ALT increase | 6 (13.0%) | - | 7 (15.2%) | - |
| Neutrophil decrease | 14 (30.4%) | 7 (15.2%) | 9 (19.6%) | 11 (23.9%) |
| Lymphocyte decrease | 10 (21.7%) | 1 (2.2%) | 14 (30.4%) | 2 (4.3%) |

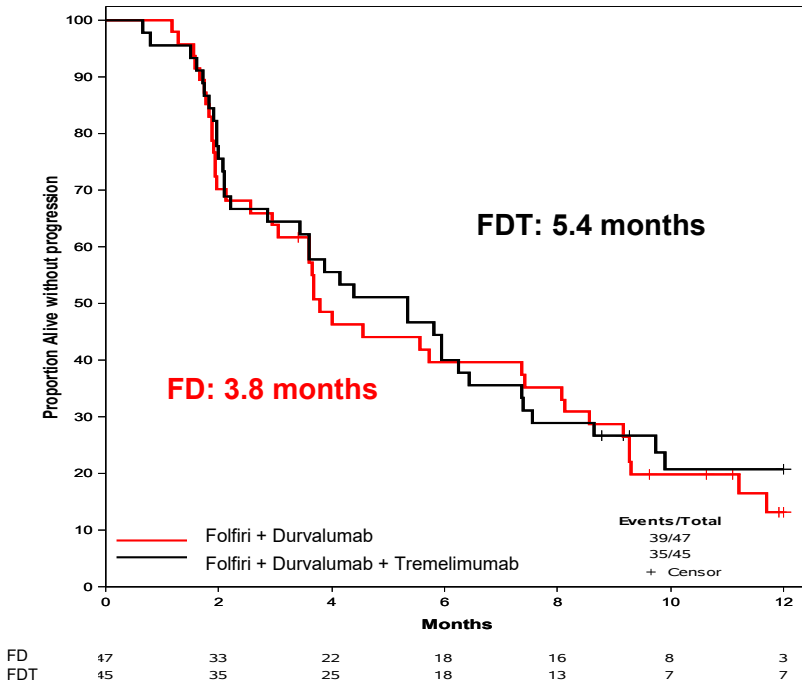
# Survival results

| | Folfiri + Durvalumab | FOLFIRI + durvalumab + tremelimumab |
|---|---|---|
| PFS at 4 months [90% CI] | **44.7% [32.2-57.7]** | **55.6% [42.3-68.3]** |
| Disease contol rate | 67.4% | 68.9% |
| Median duration of response | 5.1 months | 4.3 months |

- The primary endpoint is not meet (PFS at 4 months inferior to 70%).
- A remarkable disease control over 12 months was observed in FDT arm (n=7, 15.2%) as compared FD arm (n=2, 4.3%).

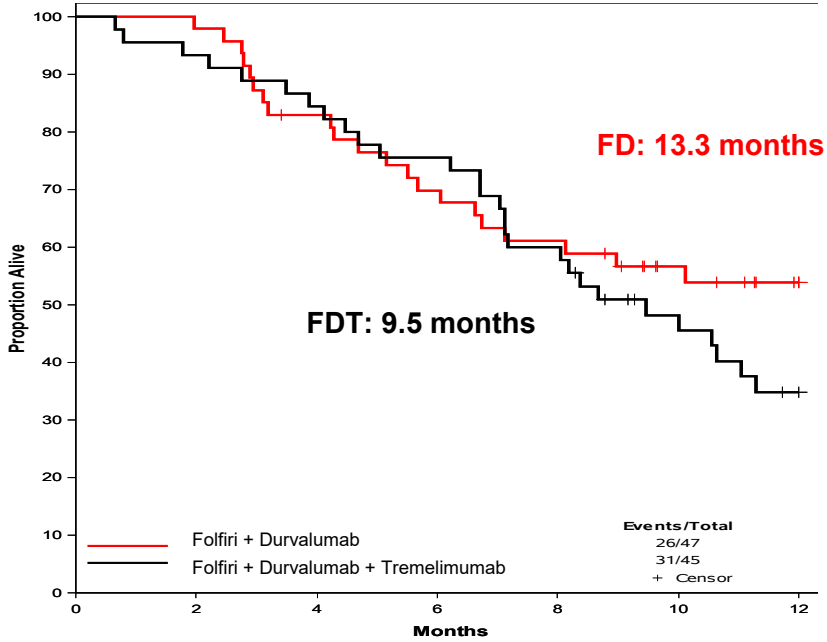
# Survival curves

## Progression-free survival




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| FD | 47 | 33 | 22 | 18 | 16 | 8 | 3 |
| FDT | 45 | 35 | 25 | 18 | 13 | 7 | 7 |

## Overall survival




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| FD | 47 | 46 | 38 | 32 | 28 | 20 | 13 |
| FDT | 45 | 42 | 38 | 34 | 27 | 18 | 12 |

# Conclusion - Discussion

- Acceptable safety profile of two immune checkpoint inhibitors plus FOLFIRI in 2nd line treatment for advanced gastric/GEJ adenocarcinoma.
- Primary endpoint was not meet but both arms demonstrated a clinically relevant PFS and OS never before achieved with chemotherapy alone.

- Both combinations seem to be very active in ≈30% of patients with an OS superior to 12 months.
- Ancillary studies are ongoing to identify predictive biomarkers of efficacy (PD-L1 status, immune scores, tumour mutation burden and microbiota).

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