MATTERHORN: Efficacy and safety of neoadjuvant-adjuvant durvalumab and FLOT chemotherapy in resectable gastric and gastroesophageal junction cancer – a randomised, double-blind, placebo-controlled, Phase 3 study

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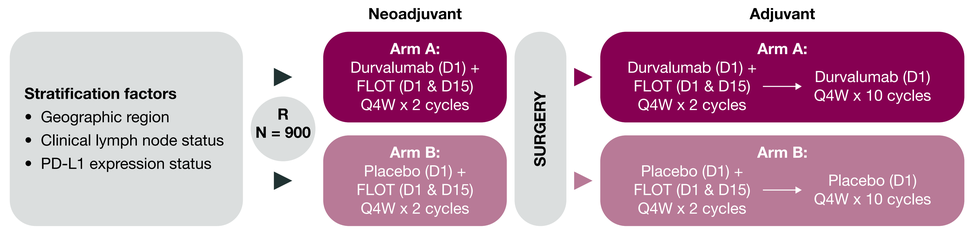
Introduction

- Gastric cancer and gastroesophageal junction cancer (GC/GEJC) are the 5th most common cancer types, and the 4th leading cause of cancer-related deaths worldwide[1]
- Standard of care for resectable GC/GEJC in Western countries includes neoadjuvant-adjuvant 5-fluorouracil, leucovorin, oxaliplatin, and docetaxel (FLOT) chemotherapy combined with surgery, and lymph node dissection for some regions of the world.[2,3] While in East Asian countries, the current strategy is surgery followed by adjuvant chemotherapy, with perioperative chemotherapy being increasingly used[4]
- Although treatment advances have improved survival, the recurrence rate remains high and 5-year overall survival (OS) is poor for patients with resectable GC/GEJC[5,6]
- Cytotoxic chemotherapy can promote antitumour immunity[7]
- Therefore, the combination of an immune checkpoint inhibitor, such as durvalumab (anti-programmed cell death ligand-1 [PD-L1] antibody) with cytotoxic chemotherapy may result in increased efficacy[7,8]
- These data support the evaluation of durvalumab combined with FLOT chemotherapy for the treatment of patients with resectable GC/GEJC

Methods

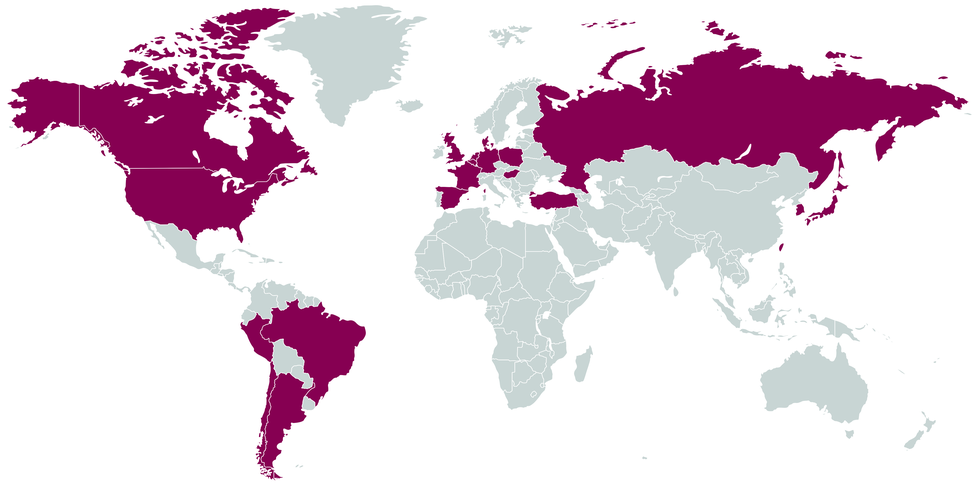
- **MATTERHORN (NCT04592913)** is a multicentre, global, Phase 3, randomised, double-blind, placebo-controlled study to evaluate neoadjuvant-adjuvant durvalumab and FLOT chemotherapy in patients with resectable GC/GEJC
- Approximately 900 patients with histologically confirmed, Stage II or higher, resectable GC/GEJC not previously treated with anticancer therapy will be randomised to Arm A or Arm B

MATTERHORN study design: Patients diagnosed with histologically confirmed, Stage II or higher, resectable GC/GEJC not previously treated with anticancer therapy



FLOT: 5-fluorouracil 2600 mg/m² + leucovorin 200 mg/m² + oxaliplatin 85 mg/m² + docetaxel 50 mg/m² on Days 1 and 15 Q4W
Durvalumab: 1500 mg on Day 1 Q4W

There are currently 20 countries and regions participating in the MATTERHORN study



Key inclusion criteria

- Age ⩾18 years (⩾20 years in Japan)
- Histologically confirmed, Stage II or higher, resectable GC/GEJC not previously treated with anticancer therapy
- Complete surgical resection of the primary tumour must be achievable
- WHO/ECOG PS 0 or 1
- Adequate organ and marrow function
- Availability of tumour sample prior to study entry

Key exclusion criteria

- Any prior immune-mediated therapy
- Peritoneal dissemination or distant metastasis
- (Adeno)squamous cell carcinoma or gastrointestinal stromal tumour
- Any concurrent chemotherapy, investigational product, biologic or hormonal therapy for cancer treatment
- Contraindication to any of the study drugs

Study endpoints

1°
- Event-free survival for Arm A versus Arm B

2°
- OS
- Pathological complete response
- Safety and tolerability profile of both arms

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Abbreviations

D, Day; ECOG, Eastern Cooperative Oncology Group; FLOT, 5-fluorouracil, leucovorin, oxaliplatin, and docetaxel; GC, gastric cancer; GEJC, gastroesophageal junction cancer; OS, overall survival; PD-L1, programmed cell death ligand-1; PS, performance status; Q4W, once every 4 weeks; WHO, World Health Organization

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For more details on MATTERHORN, please visit https://clinicaltrials.gov/ct2/show/NCT04592913

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