A Randomized, Double-blind, Placebo-controlled, Phase III Study of Neoadjuvant-Adjuvant Durvalumab and FLOT Chemotherapy Followed by Adjuvant Durvalumab or Placebo in Patients with Resectable Gastric and Gastroesophageal Cancer (GC/GEJC) (MATTERHORN)

Published: 20-10-2020
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This study has been transitioned to CTIS with ID 2023-507338-26-00 check the CTIS register for the current data. Primary objective:To compare Arm A relative to Arm B on event-free survival (EFS)Key secondary objectives:- To compare Arm A relative to...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Interventional

Summary

ID

NL-OMON55260

Source
ToetsingOnline

Brief title
MATTERHORN

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC

Synonym
gastric and gastroesophageal Junction Cancer, gastric or gastroesophageal junction adenocarcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: opdrachtgever / sponsor: AstraZeneca

Intervention

Keyword: Durvalumab, FLOT, Gastric cancer, Gastroesophageal cancer

Outcome measures

Primary outcome

The primary objective of the study is to confirm the superiority of Arm A

compared to Arm B in terms of event-free survival (EFS) as assessed according

to RECIST 1.1 per blinded independent central review (BICR) and/or locally by

pathology testing in patients with resectable GC/GEJC.

Endpoint/variable of the primary objective:

EFS is defined as the time from randomization to the following, according to

RECIST 1.1 per BICR assessment and/or locally by pathology testing:

1) Progression that precludes surgery or requires

non-protocol therapy

2) Local or distant recurrence or progression

of disease

3) death due to any cause

Secondary outcome

Endpoint/variable of the key secondary objectives:

- OS: Overall survival is length of time from randomization until the date of death due to any cause.

- pCR: the pCR rate is defined as the proportion of patients who have no residual viable tumor in the resected specimens and as determined by pathology review.

Study description

Background summary

Neoadjuvant-adjuvant or adjuvant alone chemotherapy are a standard component of resectable gastric cancer and gastroesophageal junction cancer (GC/GEJC) treatment. The currently recommended chemotherapies have had a positive impact on the survival of patients with resectable GC/GEJC; however, the recurrence rate within 5 years after surgery remains high and the 5-year overall survival (OS) rate remains poor, especially in Western countries. Therefore, there is a significant unmet medical need in resectable GC/GEJC and a novel therapy is globally required.

The combination of immune checkpoint inhibitors (PD-L1/PD-1) and platinum-based chemotherapy has shown significant anti-tumor activity in multiple tumor types and has become a standard of care in first-line NSCLC. Durvalumab is a human monoclonal antibody (mAb) of the IgG immunoglobulin G (IgG) 1* subclass that inhibits binding of PD-L1 to PD-1 and cluster of differentiation (CD)80. It is considered that the combination of durvalumab with neoadjuvant-adjuvant FLOT chemotherapy (fluorouracil [5-FU] + leucovorin + oxaliplatin + docetaxel), commonly used in Western countries, may result in a significant improvement in clinical outcomes in patients with resectable GC/GEJC.

Therefore, this study will evaluate neoadjuvant-adjuvant treatment with durvalumab in combination with FLOT (Arm A) compared to placebo in combination with FLOT (Arm B) in patients with resectable GC/GEJC.

Study objective

This study has been transitioned to CTIS with ID 2023-507338-26-00 check the CTIS register

for the current data.

Primary objective:
To compare Arm A relative to Arm B on event-free survival (EFS)

Key secondary objectives:
- To compare Arm A relative to Arm B on overall survival (OS)
- To compare Arm A relative to Arm B on pathological complete response (pCR) rate

Study design

This is a randomized, double-blind, placebo-controlled, multicenter, global Phase III study to assess the efficacy and safety of neoadjuvant-adjuvant durvalumab in combination with FLOT chemotherapy followed by adjuvant durvalumab monotherapy in patients with resectable GC/GEJC (ie, radical-surgery eligible; >T2 N0-3 M0 or T0-4 N1-3 M0, per AJCC 8th edition).

Patients will be randomized in a 1:1 ratio to each of the following treatment arms:
- Treatment Arm A: durvalumab 1500 mg on Day 1 + FLOT on Days 1 and 15 Q4W for 4 cycles (2 cycles neoadjuvant + 2 cycles adjuvant) followed by durvalumab 1500 mg on Day 1 Q4W for 10 additional cycles
- Treatment Arm B: placebo on Day 1 + FLOT on Days 1 and 15 Q4W for 4 cycles (2 cycles neoadjuvant + 2 cycles adjuvant) followed by placebo on Day 1 Q4W for 10 additional cycles

Intervention

Patients will be randomized in a 1:1 ratio to each of the following treatment arms:

- Treatment Arm A: durvalumab 1500 mg on Day 1 + FLOT on Days 1 and 15 Q4W for 4 cycles (2 cycles neoadjuvant + 2 cycles adjuvant) followed by durvalumab 1500 mg on Day 1 Q4W for 10 additional cycles
- Treatment Arm B: placebo on Day 1 + FLOT on Days 1 and 15 Q4W for 4 cycles (2 cycles neoadjuvant + 2 cycles adjuvant) followed by placebo on Day 1 Q4W for 10 additional cycles

Patients will be stratified according to:
- geographic region (Asia vs non-Asia)
- clinical lymph node status (positive vs negative)
- PD-L1 expression status (TIP >=1% vs TIP <1%)

Tumor sample should be collected during screening to determine the PD-L1

expression status.

Study burden and risks

Patients are subject to the following assessments throughout the study:
- Anamnesis (at screening, including medical history)
- Physical examination
- ECOG performance status
- Vital functions (blood pressure, heart rate, body temperature and respiratory rhythm)
- Body weight measurement
- CT/MRI scan
- ECG
- blood - and urine examination
- questionnaires (in hospital using a tablet) (EORTC QLQ-C30, EORTC QLQ-STO22, EORTC IL38, EQ-5D-5L, PRO-CTCAE, PGIC, PGIS,
PGI-TT).
- pregnancy test when applicable
- AE/SAE assessment
- IP administration
- biopsy (new biopsy or <3 months old)

The side effects of durvalumab can range from mild to severe or in some cases even life-threatening. Conditions have been built into the study to identify as early as possible the side effects that can be serious.

Very common (seen in more than 1 in 10 people):
Fatigue/tiredness, diarrhea, rash/dry itchy skin, liver problems, nausea, vomiting and abdominal pain, oedema, upper respiratory tract infections, decreased appetite, shortness of breath, cough, pain in muscles and joints, fever.

Common (seen in more than 1 in 100 people):
Pneumonitis, colitis, low or high thyroid (hypothyroidism or hyperthyroidism), kidney injury, nervous system problems, infusion related reactions and allergic reactions, pneumonia, influenza, hoarse voice, painful urination, night sweats, oral thrush, dental infections, soft tissue infections.

Moreover, the study procedures could also have risks:
- pain or bruises through collection of blood/tumor biopsy
- rash through ECG stickers
- health risks through radiation of CT-scan/MRI

Contacts

Public
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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Patients with histologically documented gastric or gastroesophageal junction adenocarcinoma with resectable disease (Stage II or higher per AJCC 8th edition).
- Patients must have undergo radical surgery.
- No prior anti-cancer therapy for the current malignancy.
- World Health Organization (WHO)/ECOG PS of 0 or 1 at enrollment
- Adequate organ and marrow function
- Availability of tumor sample prior to study entry
- Must have a life expectancy of at least 24 weeks

Exclusion criteria

- Patients with peritoneal dissemination or distant metastasis
- Patients with adenosquamous cell carcinoma, squamous cell carcinoma, or GI stromal tumor
- History of allogeneic organ transplantation.
- Contra-indication to any of the study drugs
- Current or prior use of immunosuppressive medication within 14 days before the first dose of durvalumab.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-06-2021
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	5-Fluorouracil
Generic name:	5-Fluorouracil
Registration:	Yes - NL outside intended use
Product type:	Medicine

Brand name:	Eloxatin
Generic name:	Oxaliplatin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Imfinzi
Generic name:	Durvalumab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Leucovorin
Generic name:	Folinic acid
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Taxotere
Generic name:	Docetaxel
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	20-10-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-01-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-01-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-05-2021

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-01-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-12-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-01-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2023-507338-26-00
EudraCT	EUCTR2019-001555-40-NL
CCMO	NL75180.056.20
Other	volgt