TGF-β And PDL-1 inhibition with Bintrafusp alfa in Esophageal Squamous Cell carcinoma combined with chemoradiation TheRapY (TAPESTRY)

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This study has been transitioned to CTIS with ID 2023-503312-32-00 check the CTIS register for the current data. Possibly, outcomes of treatment of irresectable squamous cell carcinoma of the esophagus can be improved by adding bintrafusp alfa to...

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

Summary

ID

NL-OMON52872

Source
ToetsingOnline

Brief title
TAPESTRY

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal neoplasms malignant and unspecified

Synonym
esophageal squamous cell carcinoma, esophagus cancer

Research involving
Human

Sponsors and support

Primary sponsor: Medische oncologie
Source(s) of monetary or material Support: Health Holland,Merck

Intervention

Keyword: definitive chemoradiation, feasability, inhibition, PDL-1 inhibition, TGF-&beta

Outcome measures

Primary outcome

The primary endpoint is feasibility defined as percentage of patients that complets at least two of the three planned cylces of bintrafusp alfa. Patients that do not complete treatment with bintrafusp alfa for reasons other than toxicity will be replaced and not included in the analysis of the primary end point.

Secondary outcome

Secondary endpoints are:

- Incidence and severity of toxicity defined according to CTCAE v5 and Radiation Oncology Group (RTOG) criteria.

- Safety of Bintrafusp alfa in combination with chemoradiotherapy

- Percentage completion of chemotherapy and radiation treatment.

- Percentage withdrawal rate from chemoradiation due to bintrafusp alfa related complications

- Infield locoregional progression free survival.

- Any progression free survival.

- 1*year progression free survival.

- Overall survival.

- Quality of life, measured by EORTC QLQ C3070 and the EORTC OG2571, and

dysphagia adapted from Mellow and Pinkas.72

Exploratory endpoints are:

- Potential biomarker development based on assessment of tumour and duodenal

biopsies, faeces and blood samples.

- Other patient reported outcome measures (PROMs), including but not limited to

anxiety and depression, worry of cancer progression and work productivity.

Study description

Background summary

The prognosis of irresectable esophageal cancer is poor, despite the possibility of curative treatment with definitive chemoradiotherapy. Outcomes of treatment can possibly be improved by adding certain forms of immunetherapy, such as bintrafusp alfa, a combined TGF-beta and PD-L1 inhibitor, to the treatment. In this study we investigate whether this is feasible.

Study objective

This study has been transitioned to CTIS with ID 2023-503312-32-00 check the CTIS register for the current data.

Possibly, outcomes of treatment of irresectable squamous cell carcinoma of the esophagus can be improved by adding bintrafusp alfa to treatment with definitive chemoradiotherapy. As a first step we aim to know whether the addition of bintrafusp alfa is feasible. That is, we want to know how the treatment is tolerated and whether the treatment can be given as scheduled.

Study design

This is a non-randomized feasibility study on treatment of esophageal cancer with the combination of bintrafusp alfa and chemoradiotherapy (carboplatin, paclitaxel and radiation).

Intervention

Bintrafusp alfa is added to the standard therapy on day 1, 22 and 43 of treatment.

Study burden and risks

Administration of bintrafusp alfa prolongs the visit twice with ca. 90 minutes, once the patient visits the hospital for administration of bintrafusp alfa alone (also ca. 90 minutes)

In some cases, both taking of blood samples as well as the insertion of an infusion needle may be painful and cause bruising.

In rare cases, the additional gastroduodenoscopy can result in perforation or bleeding.

Finally, a patient can have side effects of the study medication. The most common side effects of bintrafusp alfa are: fatigue, low blood pressure, cutaneous reactions, and diarrhea. Because bintrafusp alfa enhances the immunesystem, specific side effects can occur which have to do with an immune response directed against one's own body. This can manifest itself as a skin reaction, but also as a too slow or too fast-acting thyroid, auto-immune inflammation of the lungs or as adrenal insufficiency. Finally, a (transient) reaction during or shortly after infusion of bintrafusp alfa is possible.

Contacts

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Selecteer

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Histologically proven squamous cell carcinoma of the esophagus or gastro esophageal junction.
- Surgically irresectable (T1-T4a, N0 or N+, M0), as determined by Endoscopic Ultra Sound (EUS), PET scan and diagnostic CT scan of neck, thorax and abdomen. Patients with M1 disease solely on the basis of supraclavicular metastasis are eligible. Patients with resectable tumors refusing radical surgery or inoperable patients due to comorbidity are eligible.
- Locoregional recurrences without distant metastasis after surgery alone or endoscopical resection
- Locoregional recurrences without distant metastasis after neoadjuvant chemoradiation + resection or definitive chemoradiation outside the previously irradiated area, provided that full dose of radiation can safely be delivered.
- Tumors that cannot be passed with an endoscope for endoscopic ultrasound are eligible if all other criteria are fulfilled.
- If the tumor extends below the gastroesophageal (GE) junction into the proximal stomach, the bulk of the tumor must involve the esophagus or GE junction.
- Age >= 18.
- ECOG performance status 0-2
- Adequate hematological, renal and hepatic functions.
- Written, voluntary informed consent
- Patients must be accessible to management and follow-up in the treatment center

Exclusion criteria

- Past or current history of malignancy other than entry diagnosis interfering

with prognosis of esophageal cancer.
- Patient with tracheo-esophageal fistula or extension into the mucosal layer of the trachea, highly at risk to develop fistula. Thus, tumor extension to the trachea is allowed, but not through the trachea.
- Patient with aortal involvement with high risk of bleeding or developing a fistula.
- Patients with pathological lymph nodes at both supraclavicular and truncus coeliacus level.
- Pregnancy (positive serum pregnancy test), planning to become pregnant, and lactation.
- Patient (male or female) in the reproductive age is not willing to use highly effective methods of contraception (per institutional standard) during treatment and for 6 months (male or female) after the end of treatment.
- Previous chemotherapy, radiation and/or treatment with checkpoint inhibitors for the currently present esophageal tumor.
- Previous chemotherapy and/or treatment with targeted agents and/or checkpoint inhibitors for other forms of cancer within the last six months.
- Previous radiation to the mediastinum precluding full dose radiation of the currently present esophageal tumor.
- Presence of an esophageal stent.
- History of bleeding diathesis or major bleeding event (grade >= 2) in the month prior to first dose of trial treatment.
- Current use of direct oral anticoagulants or coumarins.
- Clinically significant cardiovascular disease precluding safe treatment with chemoradiation.
- Evidence of pulmonary fibrosis and/or clinically significant impairment of lung function precluding safe treatment with chemoradiation. In case of doubt about pulmonary function, a lung function test should be performed and, in case of abnormalities, discussed with the principle investigator.
- Serious underlying medical condition which would impair the ability of the patient to receive the planned treatment, including prior allergic reactions to drugs containing cremophor, such as teniposide or cyclosporine.
- Mental status that would prohibit the understanding and giving of informed consent.
- Inadequate caloric- and/or fluid intake despite consultation of a dietician and/or tube feeding.
- Has an active autoimmune disease that has required systemic treatment in past 2 years (i.e. with use of disease modifying agents, corticosteroids, or immunosuppressive drugs). Replacement therapy (e.g., thyroxine for patients with a history of autoimmune-related hypothyroidism, insulin for patients with type 1 diabetes mellitus, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is not considered a form of systemic treatment. Patients with vitiligo with dermatological manifestations only are eligible to enter the study.
- Diagnosis of HIV unless stable on antiretroviral therapy for at least 4 weeks, no evidence of multi-drug resistance, viral load of < 400 copies/ml and CD4+ T-cells >= 350 cells/µl.

- Active HBV/HCV. Participants on a stable dose of antiviral therapy with HBV/HCV viral load below the limit of quantification are eligible.
- A diagnosis of immunodeficiency or is receiving systemic steroid therapy (>10 mg/day prednisone or equivalent) or any other form of immunosuppressive therapy within 7 days prior to the first dose of trial treatment.
- Evidence of interstitial lung disease or active, non-infectious pneumonitis.
- An active infection requiring systemic therapy, which has not resolved 3 days (simple infection such as cystitis) to 7 days (severe infection such as pyelonephritis) prior to the first dose of trial treatment.
- Administration of a live vaccine within 30 days prior to the first dose of trial treatment. Seasonal flu vaccines that do not contain a live virus are permitted.
- Patients with prior allogeneic stem cell or solid organ transplantation.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-12-2020
Enrollment:	67
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	bintrafusp alfa
Generic name:	bintrafusp alfa
Product type:	Medicine
Brand name:	Carboplatin

Generic name:	Carboplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Paclitaxel
Generic name:	Paclitaxel
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	10-07-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-10-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-01-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-02-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-05-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-05-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-11-2021

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-01-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-04-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-04-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-04-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	CTIS2023-503312-32-00
EudraCT	EUCTR202000207936-NL
CCMO	NL73750.018.20