A Phase II Open-Label, Multi-Center Study of MEDI4736 Evaluated as Single Agent or in Combination with Tremelimumab in Patients with Metastatic Pancreatic Ductal Adenocarcinoma

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To determine the efficacy and safety of MEDI4736 evaluated as a single agent or in combination with tremelimumab in patients with metastatic pancreatic ductal adenocarcinoma (PDAC) whose disease has progressed on 5-FU-containing or gemcitabine-...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Exocrine pancreas conditions
Study type	Interventional

Summary

ID

NL-OMON42744

Source
ToetsingOnline

Brief title
ALPS

Condition

- Exocrine pancreas conditions

Synonym
Pancreatic cancer

Research involving

Human

Sponsors and support

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

Intervention

Keyword: MEDI4736, Pancreatic cancer, Tremelimumab

Outcome measures

Primary outcome

To assess the efficacy of MEDI4736 monotherapy and MEDI4736 + tremelimumab combination therapy in terms of ORR according to RECIST1:1

Secondary outcome

To further assess the efficacy of the combination of MEDI4736 and tremelimumab and MEDI4736 alone in terms of DoR, DCR, PFS, PFS3, PFS6, OS, OS6, and OS12

To investigate the immunogenicity of MEDI4736 monotherapy and MEDI4736 + tremelimumab combination therapy

To assess the PK of MEDI4736 monotherapy and MEDI4736 + tremelimumab combination therapy

To assess the safety and tolerability profile of MEDI4736 monotherapy and MEDI4736 + tremelimumab combination therapy

Study description

Background summary

Pancreatic ductal adenocarcinoma (PDAC), which accounts for more than 90% of all pancreatic tumors, is a malignancy with an extremely poor prognosis, as shown by a 1-year survival rate of around 18% for all stages of the disease and an estimated 5-year survival rate of less than 5%. The low survival rates associated with PDAC primarily reflect the fact that tumors progress rapidly with few specific symptoms and are thus at an advanced stage at diagnosis in most patients (almost 80% of patients at diagnosis; Hidalgo et al 2015).
The poor prognosis reflects the limited treatment options available, highlighting the need for the development of newer therapeutic options. Very few patients with truly localized disease can be cured by surgery.
This study will utilize an open-label design due to the different treatment administration schedules and treatment durations.

1.MEDI4736 monotherapy

2.MEDI4736 + tremelimumab combination therapy

In this study the efficacy and safety of MEDI4736 evaluated as single agent or in combination with tremelimumab in patients with metastatic PDAC. MEDI4736 is a human mAb of the immunoglobulin G 1 kappa subclass that inhibits the binding of PD-L1 and tremelimumab is a mAB which binds to the cytotoxic T-lymphocyte-associated protein 4 (CTLA-4). Both PD-L1 and CTLA-4 proteins play a role in the suppression on the immune system which the tumor uses in order to escape the immune system. The proposed treatments may have the potential to provide meaningful clinical benefit by generating durable clinical responses, thereby improving quality of life (QoL) and potentially extending survival.

Study objective

To determine the efficacy and safety of MEDI4736 evaluated as a single agent or in combination with tremelimumab in patients with metastatic pancreatic ductal adenocarcinoma (PDAC) whose disease has progressed on 5-FU-containing or gemcitabine-containing first-line therapy.

Study design

This is a Phase II, open-label, multi-center study to determine the efficacy and safety of MEDI4736 evaluated as single agent or in combination with tremelimumab in patients with metastatic pancreatic ductal adenocarcinoma (PDAC) whose disease has progressed on
5-FU-containing or gemcitabine-containing first-line chemotherapy.

The patients will be randomized in a 1:1 ratio to receive treatment with

- MEDI4736 monotherapy
- MEDI4736 + tremelimumab combination therapy

Intervention

MEDI4736 monotherapy:

1,5 g MEDI4736 via IV infusion every 4 weeks for up to 12 months (up to 13 doses)

MEDI4736 and tremelimumab combination therapy:

1,5 g MEDI4736 by IV infusion every 4 weeks and 75 mg tremelimumab by IV infusion every 4 weeks starting at week 0 (up to 4 doses), followed by 1,5 g MEDI4736 monotherapy by IV infusion every 4 weeks (starting at week 16) to complete a total of 12 months of therapy (up to a total of 9 additional doses)

Study burden and risks

On several days during the study patients will undergo the following assessments: - anamnesis (at screening also medical history) - physical examination - WHO performance status - vital signs (blood pressure, pulse, respiratory rate, temperature) - length - weight - CT or MRI scan - ECG - blood and urine assessments - tumor biopsy (if applicable) - pregnancy test

Related side effects reported in subjects receiving MEDI4736 alone are: fatigue, nausea, diarrhea, decreased appetite, rash, vomiting, itchiness, difficulty breathing, fever, low thyroid, increased liver enzymes, cough, muscle pain, stomach pain, dizziness.

Related and serious side effects reported in subjects receiving MEDI4736 alone are: Blockage in the urinary tract, fluid in the space surrounding the lung and inflammation of the lung, increase in calcium in the blood, joint pain, worsening of cancer, spinal cord swelling, increase in liver enzymes and blockage of the tract between the liver and small intestine, irregular heart beat or rhythm, chest pain and fluid in the abdomen, dehydration, disorder in the blood vessels of the organs, swelling of the tumor, lack of muscle control during walking or picking up objects.

Related side effects reported in subjects receiving MEDI4736 and tremelimumab together are: fatigue, diarrhea, high level of amylase, high level of ALT, itching, decreased appetite, low level of TSH, high level of AST, inflammation of the large intestine, rash, high level of lipase.

Related and serious side effects reported in at least 2 subjects receiving MEDI4736 and tremelimumab together are: diarrhea, inflammation of the large intestine, inflammation of the lung, high level of AST, high level of ALT, high level of amylase.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1.Histologically or cytologically confirmed metastatic PDAC, no more than 1 prior chemotherapy regimen
2. ECOG 0 or 1
3. At least 1 lesion, not previously irradiated, that can be accurately measured at baseline as *10 mm in the longest diameter (except lymph nodes, which must have short axis *15 mm) with computed tomography (CT) or magnetic resonance imaging (MRI) scan

and that is suitable for accurate repeated measurements

Exclusion criteria

1.Any concurrent chemotherapy, IP, biologic, or hormonal therapy for cancer treatment.
2. History of leptomeningeal carcinomatosis
3. Ascites requiring intervention
4. Brain metastases or spinal cord compression.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-01-2016
Enrollment:	14
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	n.v.t.
Generic name:	durvalumab
Product type:	Medicine
Brand name:	n.v.t.
Generic name:	tremelimumab

Ethics review

Approved WMO Date:	28-09-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-12-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-02-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-02-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-04-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-07-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-08-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-03-2017

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-03-2017
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
EudraCT	EUCTR2015-002001-11-NL
ClinicalTrials.gov	NCT02558894
CCMO	NL54436.018.15