A Phase 2 non-randomized, open-label, multi-cohort, multi-center study assessing the clinical benefit of SAR444245 (THOR-707) combined with other anticancer therapies for the treatment of participants with advanced and metastatic gastrointestinal cancer

Published: 27-10-2021
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Main objective:English To determine the antitumor activity of SAR444245 in combination with other anticancer therapiesSecondary objectives: English - To assess the safety of SAR444245 when combined with other anticancer therapies- To assess other...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON52360

Source
ToetsingOnline

Brief title
ACT16902

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
gastrointestinal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Genzyme Europe BV
Source(s) of monetary or material Support: Genzyme Europe B.V.

Intervention

Keyword: Clinical benefit, Gastrointestinal cancer, Open label, Phase 2

Outcome measures

Primary outcome

To determine the antitumor activity of SAR444245 in combination with other anticancer therapies.

Objective response rate (ORR) defined as the proportion of participants who have a confirmed complete response (CR) or partial response (PR) determined by Investigator per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1

Secondary outcome

To assess the safety of SAR444245 in combination with other anticancer therapies

To assess other indicators of antitumor activity

To assess the pharmacokinetics of SAR444245 in combination with other anticancer therapies

To assess the immunogenicity of SAR444245

Study description

Background summary

The proposed study aims to establish proof-of-concept that combining the non-alpha-IL2 SAR444245 with other anticancer therapies will result in a significant increase in the percentage of participants experiencing an objective response in the setting of various advanced gastrointestinal cancers.

Study objective

Main objective:
English To determine the antitumor activity of SAR444245 in combination with other anticancer therapies

Secondary objectives: English - To assess the safety of SAR444245 when combined with other anticancer therapies
- To assess other indicators of antitumor activity
- To assess the pharmacokinetics of SAR444245 when given in combination with other anticancer therapies
- To assess the immunogenicity of SAR444245

Study design

This is a Phase 2, multi-cohort, un-controlled, non-randomized, open-label, multi-center study assessing the antitumor activity and safety of SAR444245 combined with other anticancer therapies in participants with advanced or metastatic gastrointestinal cancer.

This study is developed as a master protocol in order to accelerate the investigation of SAR444245 with various anticancer therapies by identifying early efficacy signals. This design is with the flexibility to open new treatment cohorts as new treatment combinations become available and close existing treatment arms that demonstrate minimal clinical activity or unacceptable toxicity.

Intervention

The duration of the study for a participant will include:
-Screening Period: up to 28 days
-Treatment Period: enrolled participants will receive continuous treatment until progressive disease (PD), unacceptable adverse event (AE) or other full permanent discontinuation criteria; or completion of Cycle 35 (if applicable).1 cycle = 21 days.
-End of Treatment and Follow-up: End of Treatment Visit will occur 30 days ±7

days from last IMP administration or prior to initiation of further therapy, whichever comes first.
-Participants who move into the Survival Phone Call Follow-Up Period will be contacted by telephone every 3 months ±14 days to assess for survival status.

Investigational medicinal products: SAR444245, pembrolizumab and cetuximab.
• Formulation: sterile liquid for injection
• Route of administration: intravenous (IV) infusion
• Dose regimen: SAR444245 (24 µg/kg), pembrolizumab (200 mg), cetuximab (400 mg/m2 infused over 120 minutes followed by 250 mg/m2 infused over 60 minutes for all subsequent doses

Study burden and risks

Risks related to blood draws and side effects of the study drug.

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

Main protocol:
-Participant must be >=18 years of age (or country's legal age of majority if >18 years), at the time of signing the informed consent.
-Capable of giving signed informed consent
-Females are eligible to participate if they are not pregnant or breastfeeding, not a woman of childbearing potential (WOCBP) or are a WOCBP that agrees:
- to use approved contraception method and submit to regular pregnancy testing prior to treatment and for at least 120 days after discontinuing study treatment
- and to refrain from donating or cryopreserving eggs for 120 days after discontinuing study treatment.
- Males are eligible to participate if they agree to refrain from donating or cryopreserving sperm, and either abstain from heterosexual intercourse OR use approved contraception during study treatment and for at least 3 days after discontinuing study treatment.

Sub-study01:
-Histologically or cytologically confirmed diagnosis of advanced unresectable or metastatic esophageal cancer of the squamous cell carcinoma subtype
-MSI status: Participants must have either unknown MSI status or if MSI status is known, participants must have non-MSI-H disease to be eligible.
-Prior anticancer therapy: Participants should have received at least one but no more than 2 prior lines of treatment, including an anti-PD-1/PDL-1 containing regimen and have progressed after a primary or secondary resistance to an anti-PD-1/PDL-1.

-Sub-study02:
-Histologically or cytologically confirmed diagnosis of advanced unresectable or metastatic gastric cancer or Siewert Type 2 & 3 GEJ.
-PD-L1 expression using CPS as determined at local laboratory with an approved test
-MSI status: Participants must have MSI status known, determined locally and must have non-MSI-H disease to be eligible.
-HER2/neu status: Participants with unknown HER2/neu status must have their HER2/neu status determined locally. Participants with HER2/neu negative are eligible. Participants with HER2/neu positive tumors must have documentation of disease progression on treatment containing trastuzumab to be eligible.
-Prior anticancer therapy: Participants could be anti-PD-1/PDL-1 naïve (cohort B1 and B2) or have received an anti-PD-1/PDL-1 before (cohort B3)

Participants (all sub-studies) must have at least one measurable lesion.
Mandatory baseline biopsy for the first 20 participants to enroll in substudy01

and sub-study02 .

Exclusion criteria

- Eastern Cooperative Oncology Group (ECOG) performance status of >=2
- Predicted life expectancy <=3 months
- Poor organ function
- Active brain metastases or leptomeningeal disease.
- History of allogenic or solid organ transplant.
- Last administration of prior antitumor therapy or any investigational treatment within 28 days or less than 5 times the half-life, whichever is shorter; major surgery within 28 days prior to first IMP administration
- Comorbidity requiring corticosteroid therapy
-History of pneumonitis, interstitial lung disease, HIV infection, uncontrolled hepatitis B infection,
- Antibiotic use (excluding topical antibiotics) <=14 days prior to first dose of IMP
- Severe or unstable cardiac condition within 6 months prior to starting study treatment
- Active, known, or suspected autoimmune disease that has required systemic treatment in the past 2 years
- Known second malignancy either progressing or requiring active treatment within the
last 3 years
- Participants with baseline SpO2 <=92% (without oxygen therapy).
- Participant has received prior IL2-based anticancer treatment.
- Participants on sub-study02 cohort B1 and B2 or sub-study 04 - cohort D1 with prior treatment with an agent that blocks the PD-1/PD-L1 pathway.
- Receipt of a live-virus vaccination within 28 days of planned treatment start. Seasonal flu vaccines that do not contain live virus are permitted

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	27-05-2022
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Pembrolizumab
Generic name:	Keytruda
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	27-10-2021
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-05-2022
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	30-01-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-02-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	21-04-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-05-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-12-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-12-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2021-002181-41-NL
CCMO	NL78461.100.21
Other	U1111-1251-4981