An open label, randomized Phase II study of BI 754091 alone or in combination with BI 836880 in patients with chemotherapy resistant, unresectable, metastatic squamous cell carcinoma of the anal canal

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Gastrointestinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON49049

Source
ToetsingOnline

Brief title
A study of BI 754091 and with BI 836880 in pt with anal cancer

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
metastatic squamous cell carcinoma of the anal canal; anal cancer

Research involving

Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: De opdrachtgever Boehringer Ingelheim

Intervention

Keyword: anal canal, BI 754091, BI 836880, squamous cell carcinoma

Outcome measures

Primary outcome

Objective response (OR)

See protocol section 2.1.2

Secondary outcome

Duration of objective response (DoR)

Progression-free survival (PFS)

Overall survival (OS)

Disease control (DC)

Adverse events (AEs) from the time of treatment initiation until the end of the

Residual Effect Period (REP).

Drug related AEs from the time of treatment initiation until the end of the REP.

Drug related AEs leading to dose reduction of BI 836880 and/or discontinuation

of study treatment (i.e. both trial drugs).

See protocol 2.1.3

Study description

Background summary

Anal cancer is a very rare type of malignancy. There is a significant unmet medical need for treatment of patients with chemotherapy resistant, unresectable, metastatic squamous cell carcinoma of the anal canal (SCCA). There is no approved standard of care (SOC) by FDA or other health authorities for patients in this setting. However, according to guidelines, e.g. the most current version of the US NCCN Guidelines (Version 1.2020) for anal cancer, single agent nivolumab and pembrolizumab are considered as treatment options for patients with metastatic anal cancer who have progressed on firstline chemotherapy. However, further studies of PD-1/PD-L1 inhibitors are necessary and ongoing.

See protocol chapter 1.

Study objective

The objective of this trial is to assess anti-tumour activity of BI 754091 as a monotherapy and of BI 754091 in combination with BI 836880 in patients with unresectable or metastatic squamous cell carcinoma of the anal canal who progressed on or after chemotherapy.

Study design

An internationational, open-label, two-arm randomized, parallel group, multi-centre Phase II study.

See protocol section 3.1 for further details.

Intervention

BI 754091 and BI 836880 will be administered every 3 weeks as two separate consecutive intravenous infusions.

Study burden and risks

This trial is for patients with no therapy options of proven efficacy, or who are not amenable to standard therapies. The investigational agents, BI 754091 as a monotherapy and the BI 754091 and BI 836880 combination treatment, have been tested in previous and ongoing clinical trials. There are several immune checkpoint inhibitors and also several antiangiogenic agents already approved to treat cancer. However, there is no approved treatment for the patient population selected for this clinical trial.

Based on the mode of action of BI 754091 and BI 836880, published and internal preclinical data and available clinical data, it is expected that both treatments arms, i.e. monotherapy with BI 754091 and the combination treatment (BI 754091 + BI 836880), will show antitumour efficacy and result in a clinically meaningful in response.

Both, BI 754091 and BI 836880 are currently tested in clinical trials and have been administered only to a limited number of patients. Accordingly, both trial drugs and also the combination of the two trial drugs may have risks that are not yet known.

See protocol sections 1.4.1 and 1.4.2

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) Signed and dated written Informed Consent Form (ICF) in accordance with ICH-GCP and local legislation prior to admission to the trial.
2) Patients *18 years of age or over the legal age of consent in countries where that
is greater than 18 years at the time of signature of the ICF.
3) Patients must have histologically or cytologically documented surgically unresectable
locally-advanced or metastatic SCCA.
4) Patients with loco-regional anal cancer as initial diagnosis must have unresectable
progressive locally advanced or metastatic SCCA after failure of at least one line (but
not more than two lines) of previous systemic treatment unless ineligible for or intolerant to this systemic therapy.
Note 1: the primary treatment (chemoradiotherapy) for loco-regional disease is not
considered as a previous line of systemic treatment
Note 2: If palliative radiotherapy was given, this radiotherapy must have been completed at least 30 days prior to the start of the trial treatment and lesions previously receiving palliative radiotherapy must not be selected as target lesions for
RECIST 1.1 evaluation during this trial.
Patients with metastatic anal cancer as initial diagnosis (no prior treatment for
loco-regional cancer) must have failed one line of previous systemic treatment (chemotherapy ± radiotherapy) for the metastatic anal cancer unless ineligible for or
intolerant to this systemic treatment. (Patients with metastatic anal cancer as initial
diagnosis who have received two or more lines of systemic treatment for the metastatic
anal cancer are not eligible for the study.)
5) All patients must have at least one measurable lesion according to RECIST v1.1
criteria.
6) Eastern Cooperative Oncology Group performance status [ECOG, R01-0787] score 0 to 1
7) All patients must be willing to undergo blood testing for human immunodeficiency
virus (HIV) presence in the blood if not tested within the past 6 months prior to
signature of ICF for this trial.
For patients confirmed as HIV positive, all of the following (a-d) applies:
a) CD4+ count * 250 cells/*L

b) Undetectable viral load (local lab assessment)
c) Must be currently receiving Highly Active Antiretroviral Therapy
d) A HIV/Infectious Diseases specialist must be consulted or patient must be under
the care of the HIV/Infectious Diseases specialist
8) Patients must be willing to allow PD-L1 status assessment by one of following options.
Preference is given to fresh tumour biopsy sample collection at baseline before receiving first trial medication. In case a fresh tumour biopsy cannot be obtained (e.g.
inaccessible lesions or patient safety concern), archival tissue will be requested. If
neither is available any previous historical information regarding PD-L1 status should
be collected via eCRF. Exceptions may be considered after consultation with and approval by the Sponsor.
9) Male or female patients. Women of childbearing potential (WOCBP)1 and men able to
father a child must be ready and able to use highly effective methods of birth control
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per ICH M3 (R2) that result in a low failure rate of less than 1% per year when used
consistently and correctly, for the entire duration of the trial treatment intake and for 6
months after the end of the trial treatment. A list of contraception methods meeting
these criteria is provided in the patient information. For further detail refer to Section
4.2.2.3 and FlowChart

Exclusion criteria

- Current or prior treatment with any systemic anti-cancer therapy or any investigational product (or device) either within 28 days or less than 5 half-lives (whichever is shorter) before start of trial treatment.
- Major injuries and/or surgery or bone fracture within 4 weeks of start of treatment, or planned surgical procedures during the trial period.
- Significant cardiovascular/cerebrovascular diseases (i.e. uncontrolled hypertension, unstable angina, history of infarction within past 6 months,

congestive heart failure > NYHA II).
- Known inherited predisposition to bleeding or to thrombosis in the opinion of the investigator.
- History of severe hemorrhagic or thromboembolic event in the past 12 months (excluding central venous catheter thrombosis and peripheral deep vein thrombosis).
- Patients who require full-dose anticoagulation (according to local guidelines). No Vitamin K antagonist and other anticoagulation allowed; LMWH and acetylsalicylic acid (ASA) allowed only for prevention not for curative treatment.
- Prior treatment with anti-PD-1, anti-PD-L1, or anti CTLA-4 treatment
- Prior treatment with any antiangiogenic agent (e.g. bevacizumab, cediranib, aflibercept, vandetanib, XL-184, sunitinib, etc.)
- Further criteria apply.

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:	Will not start
Enrollment:	3
Type:	Anticipated

Ethics review

Approved WMO

Date:	15-07-2020
Application type:	First submission

Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	07-10-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	EUCTR2019-004749-33-NL
CCMO	NL73401.041.20