An open label Phase I PET imaging study to investigate the bio-distribution and tumor uptake of [89Zr]Zr-BI 765063 and [89Zr]Zr-BI 770371 in patients with head and neck squamous cell carcinoma, non-small cell lung cancer or melanoma who are treated with ezabenlimab

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This study has been transitioned to CTIS with ID 2024-514034-20-00 check the CTIS register for the current data. The primary objective is to estimate the average relative change from baseline in tumoruptake of [89Zr]Zr-BI 765063 (arm A) or [89Zr]Zr-...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON51904

Source
ToetsingOnline

Brief title
To test uptake of BI765063/BI770371 when given with ezobenlimab in cancers

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym

Head and neck cancer, lung cancer, skincancer

Research involving
Human

Sponsors and support

Primary sponsor: IQVIA RDS Netherlands B.V.
Source(s) of monetary or material Support: De opdrachtgever Boehringer Ingelheim

Intervention

Keyword: Biodistribution, HNSCC, Melanoma, NSCLC, PET

Outcome measures

Primary outcome

Relative change from baseline (Cycle 1, up to Day 7) of peak Standardized

Uptake Values (SUVs) of [89Zr]Zr-BI 765063 (arm A) or [89Zr]Zr-BI 770371 (arm

B) in up to five target lesions at post BI 765063 (arm A) or BI 770371 (arm B)

treatment scanning time points (Cycle 2, up to Day 7).

Secondary outcome

There is no secondary endpoint in this trial.

Study description

Background summary

This research focuses on two ways in which tumors defend themselves against the body's immune system. The tumors contain proteins that give a 'don't find me' and 'don't eat me' signal. These signals ensure that the immune system cannot find or attack the tumor cells. The immune system normally makes sure that the white blood cells clear out the cancer cells.

The proteins we are looking at in this study are PD-L1 and CD47. PD-L1 transmits the 'don't find me' signal. CD47 transmits 'don't eat me' signal. Both proteins are on the surface of the tumor cell.

The investigational drug ezabenlimab blocks the 'don't find me' signal. This

means the immune system can still find the tumor cells. The research drugs BI 765063 and BI 770371 have been developed to block the 'don't eat me' signal. This allows the immune system to "eat" the cancer cells. By combining both drugs, we hope that the cancer will be treated better than when the drugs are given separately.

See protocol section 1.

Study objective

This study has been transitioned to CTIS with ID 2024-514034-20-00 check the CTIS register for the current data.

The primary objective is to estimate the average relative change from baseline in tumor
uptake of [89Zr]Zr-BI 765063 (arm A) or [89Zr]Zr-BI 770371 (arm B) upon treatment with BI 765063 (arm A) or BI 770371 (arm B).

Study design

This is a Phase I, open label, non-randomized bio-distribution trial to be conducted in one specialized center. The trial is divided in 2 parts as described in Figure 3.1:1 and will be conducted in a staggered approach.

Intervention

Intravenous administration of:

[89Zr]Zr- BI 765063: Once 20mL (6 mg research drug)
BI 765063: Recommended dose for expansion (RDE) of FIH trial, administered every 3 weeks (q3w).
BI 754091: 240 mg q3w
[89Zr]Zr- BI 770371: Once 20mL (6 mg research drug)
BI 770371: Recommended dose for expansion (RDE) of FIH trial, administered every 3 weeks (q3w).

Study burden and risks

Considering the medical need for the development of a better tolerated and more effective treatment for patients with advanced and/or metastatic malignancies, the anticipated benefit of BI 765063 (arm A) or BI 770371 (arm B) and ezabenlimab is considered favourable for patients with advanced cancers and outweighs the potential risks

See section 1.4 of the protocol

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) prior to any trial-specific procedures 2. Male or female aged >= 18 years (no upper limit of age) at the time of ICF signature 3. Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 4. Life expectancy of at least 3 months 5. For Arm A, only patients with a SIRPα polymorphism V1/V1 will be eligible; SIRPα polymorphism will be assessed in blood sampling (patient DNA) in a central laboratory; V1 allele is understood to include V1 and potential V1-like alleles. If, at a later time, V1/V2 heterozygous patients are considered for inclusion in this Arm of the trial, these patients will require to be centrally confirmed with at least one V1 allele. 6. Patients with histologically or cytologically documented advanced/metastatic primary or recurrent HNSCC, melanoma, NSCLC who failed or are not eligible to standard therapy 7. Patients

with at least one measurable lesion are allowed as per RECIST v1.1 8. Patient must have at least one PET imageable and evaluable tumor lesion with a diameter of at least 20 mm 9. Patients must agree to on-treatment tumor biopsies (optional for first 3 patients in Part 1). 10. Adequate biological parameters defined as: • absolute neutrophil count (ANC) >= 1.5 x 109/L • hemoglobin (Hb) level >= 9 g/dL (without recent red blood cell transfusion within 2 weeks prior to study entry) • platelet count >= 100 x 109/L • total bilirubin level <= 1.5 x Upper Limit Normal (ULN), except for patients with Gilbert's syndrome from whom total bilirubin < 3.0 x ULN or direct bilirubin < 1.5 x ULN is authorized • aspartate transaminase (AST) and alanine transaminase (ALT) <= 2.5x ULN • serum creatinine <= 1.5 x ULN or creatinine clearance > 50 mL/min (Chronic Kidney Disease Epidemiology [CKD-EPI] CKD-epi formula) • INR <= 1.5 (except if patient treated with anti-vitamin K); anticoagulation with anti-vitamin K and low molecular weight heparin [LMWH] is allowed 11. Prior major treatment-related surgery completed at least 28 days before study drug administration 12. Interval of at least 28 days or 5 half-lives (whichever is shorter) since the last chemotherapy, approved immunotherapy, biological or investigational therapy, radiation or tyrosine kinase inhibitor (TKI) therapy (e.g., sunitinib, sorafenib) must have elapsed before the first study drug administration(s) (on C1D1) and all toxicities related to previous anticancer therapies have resolved to normal value or <= Grade 1 prior to the study treatment administration (on C1D1), except alopecia 13. Male or female patients. Women of childbearing potential (WOCBP) and men able to father a child must agree to use highly effective methods of contraception (i.e. one that results in a less than 1% per year failure rate when used consistently and correctly), prior to study entry, during the study and for 5 months after the last dose of study drug. A list of contraception methods meeting these criteria is provided in the patient information. The requirement of contraception does not apply to women of no childbearing potential and men not able to father a child, but they must have an evidence of such at screening. 14. Females of childbearing potential must have a serum negative pregnancy test within 7 days prior to first administration. Females who are postmenopausal for at least 1 year (defined as more than 12 months since last menses) or are surgically sterilized do not require this test 15. Capable of understanding and complying with protocol requirements.

Exclusion criteria

1. Patients with symptomatic/active central nervous system (CNS) metastases; patients with previously treated brain metastases are eligible if there is no evidence of progression for at least 28 days before the first study treatment administration, as ascertained by clinical examination and brain imaging (MRI or CT) during the screening period 2. Other tumor location necessitating an urgent therapeutic intervention (e.g., palliative care, surgery or radiation therapy, such as spinal cord compression, other compressive mass, uncontrolled

painful lesion, bone fracture) 3. Presence of other active invasive cancers other than the one treated in this trial within 5 years prior to screening (or less, pending discussion with sponsor), except appropriately treated basal cell carcinoma of the skin, or in situ carcinoma of uterine cervix, or other local tumors considered cured by local treatment 4. Patients with active autoimmune disease or a documented history of autoimmune disease, that requires systemic treatment (i.e. corticosteroids or immunosuppressive drugs); except patients with vitiligo, resolved childhood asthma/atopy, alopecia, or any chronic skin condition that does not require systemic therapy, patients with autoimmune-related hypothyroidism on a stable dose of thyroid replacement hormone and/or controlled Type 1 diabetes mellitus on a stable insulin regimen may be eligible 5. Known severe infusion related reactions to monoclonal antibodies (Grade >= 3 NCI-CTCAE v5.0) and patients removed from previous anti-PD-1 or anti-PD-L1 therapy because of a severe or life-threatening immune-related adverse event (irAE) (Grade >= 3 NCI-CTCAE v5.0); 6. Patients receiving systemic treatment with any immunosuppressive medication within one-week prior to treatment start with SIRPa antibody (BI 765063 or BI 770371) and ezabenlimb; steroids of max. 10 mg prednisolone equivalent per day are allowed, topical and inhaled steroids are not considered as immunosuppressive 7. Patients who have interstitial lung disease or active, non-infectious pneumonitis. 8. Patients with uncontrolled disease-related metabolic disorders (e.g., hypercalcemia, SIADH) or uncontrolled diabetes 9. Patients with uncontrolled congestive heart failure defined as New York Heart Association (NYHA) class III or IV, uncontrolled hypertension, unstable heart disease (e.g., coronary artery disease with unstable angina or myocardial infarction within 6 months before study treatment administration) 10. Patients with significant ECG abnormalities defined as any cardiac dysrhythmia (> Grade 2) (i.e., significant ventricular arrhythmia as persistent ventricular tachycardia and/or ventricular fibrillation; severe conduction disorders as atrio-ventricular block 2 and 3, sino-atrial block) or baseline QT/QTc interval >480 milliseconds (ms) 11. Patients with significant chronic liver disease (e.g., significant fibrosis, known cirrhosis) or active HBV or HCV infection; if HbsAg positive, an effective antiviral treatment to prevent hepatitis B reactivation is recommended 12. Patients with known Human Immunodeficiency Virus (HIV) infection or patients with an active infection requiring specific anti-infective therapy until all signs of infection have resolved, and this within 2 weeks prior to the first study treatment administration 13. Women who are breastfeeding. Women who are breastfeeding can be enrolled if they stop breastfeeding. In this case, the patient will not be permitted to resume breastfeeding even after discontinuation of study treatment. 14. Patients whose medical, psychological including alcohol or drug abuse, or surgical conditions are unstable and may affect the study completion and/or compliance and/or the ability to give informed consent.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-03-2022
Enrollment:	22
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Ezabenlimab
Generic name:	N/A

Ethics review

Approved WMO Date:	07-07-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-10-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-08-2022
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-11-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-12-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-02-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-08-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-12-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-06-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-07-2024
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	CTIS2024-514034-20-00
EudraCT	EUCTR2021-001063-25-NL
CCMO	NL77950.029.21
Other	Nog niet bekend