A Phase 1a/1b, Multi-Centre, Open-Label, Dose-Escalation and Dose-Expansion Study in Patients with Solid Tumour Malignancies to Evaluate GEH200520 Injection / GEH200521 (18F) Injection Safety and Tolerability, Positron Emission Tomography Imaging, Pharmacokinetics, and Changes in Imaging after Treatment

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This study has been transitioned to CTIS with ID 2024-515218-42-00 check the CTIS register for the current data. The primary, secondary and exploratory objectives of the study are as follows:Part APrimary:• To evaluate the safety and tolerability of...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON53493

Source
ToetsingOnline

Brief title
GEH200520/GEH200521(18F) used for PET scans in patients with solid tumors

Condition

- Other condition

Synonym
head and neck SCC, PET scan bij solid tumors

Health condition

irresectable or metastatic solid tumour or a local and resectable head and neck squamous cell carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: GE Healthcare Ltd.
Source(s) of monetary or material Support: Industry: GE Healthcare Ltd.

Intervention

Keyword: GEH200520 injection/GEH200521 (18F), PET scans, solid tumour malignancies

Outcome measures

Primary outcome

Part A

Primary:

• The incidence and severity of AEs per National Cancer Institute*s Common

Terminology Criteria for Adverse Events (NCI CTCAE version 5.0) based on the

causality to the IMP.

Part B

Primary:

• Comparison of GEH200521 (18F) Injection uptake between longitudinal PET

scans.

Secondary outcome

Part A

Secondary:

• Assessment of the dosimetry estimates and cumulated activity by source region and by entire body including whole blood and excreted urine at timepoints up to 6 hours post-administration of GEH200521 (18F) Injection.

• Assessment of qualitative and quantitative uptake of GEH200521 (18F) Injection in images, including signal to background ratios and uptake in regions of interest.

• Determination of GEH200520 Injection optimal dose will be based on totality of evidence captured during Part A assessments such as safety and tolerability, imaging quality, and PK profile.

• The PK parameters assessed for GEH200520 Injection and GEH200521 (18F) Injection combined concentrations will be:

o Area under the curve (AUC)

o Maximum serum concentration (Cmax)

o CL

o V

o t1/2

• Assessment of AEs/serious AEs (SAEs)/AEs of special interest (AESIs) and changes in physical examination, laboratory variables, ECG, and vital signs between baseline and the end of study.

• Incidence of treatment-induced ADA responses following administration of

GEH200520 Injection with GEH200521 (18F) Injection and the impact of ADA on safety profile of IMPs.

Part B

Secondary:

• AEs/SAEs/AESIs, physical examination, laboratory variables, ECG, vital signs.

• Evaluate inter- and intra-subject variability in biodistribution and tumour uptake of GEH200521 (18F) Injection, including normal tissue distribution.

• Evaluate the uptake of GEH200521 (18F) Injection versus sample biopsy/lesion findings, when available, across inter- and intra-subject populations.

• Assess changes in tumour uptake of GEH200521 (18F) Injection in comparison to CT RECIST v1.1 criteria and/or [18F]-FDG scans, when available.

• The following PK parameters will be assessed for GEH200520 Injection and GEH200521 (18F) Injection combined concentrations:

o AUC

o Cmax

o CL

o V

o t1/2

• Incidence of treatment-induced ADA responses following administration of GEH200520 Injection with GEH200521 (18F) Injection and the impact of ADA on safety and PK.

Study description

Background summary

The body*s immune system identifies and destroys cancer cells. However, tumours have the capability to alter functioning of the immune system which enables cancer cells to escape the immune system and grow without the body being able to identify and destroy the tumor. Immunotherapy is group of drugs that prevent the tumour to develop mechanisms to escape the immune system. People react differently to the immunotherapy, some have good response and the tumour decreases in size while other people might not have such a beneficial effect. Therefore, identifying people who are more likely to respond to treatment is critical for management of patients. The study drug we develop should enable identification of people who are more likely to respond to treatment.

Study objective

This study has been transitioned to CTIS with ID 2024-515218-42-00 check the CTIS register for the current data.

The primary, secondary and exploratory objectives of the study are as follows:
Part A
Primary:
• To evaluate the safety and tolerability of the different GEH200520 Injection mass doses and a fixed dose of GEH200521 (18F) Injection when administered together in patients with solid tumour malignancies.
Secondary:
• To evaluate the radiation dosimetry of a fixed dose of GEH200521 (18F) Injection when administered with the different GEH200520 Injection mass doses.
• To evaluate the optimal imaging time window for GEH200521 (18F) Injection PET imaging when administered with different GEH200520 Injection mass doses.
• To determine the appropriate mass dose of GEH200520 Injection for administration with GEH200521 (18F) Injection to achieve an acceptable PET image quality.
• To characterise the PK properties of total protein (GEH200520 and [18F]GEH200521 combined) following administration of different GEH200520 Injection mass doses with a fixed dose of GEH200521 (18F) Injection.
• To assess changes in physical examination, laboratory variables, ECG, and vital signs following administration of the different GEH200520 Injection mass doses with a fixed dose of GEH200521 (18F) Injection.
• To assess immunogenicity after a single injection of the different GEH200520 Injection mass doses administered with a fixed dose of GEH200521 (18F) Injection.
Exploratory:
• To assess changes in selected biomarkers and compare biomarkers to tracer uptake characteristics following administration of the different GEH200520

Injection mass doses with a fixed dose of GEH200521 (18F) Injection.
Part B
Primary:
• To evaluate the time-course changes in GEH200521 (18F) Injection uptake after ICI treatment cycles compared to baseline.
Secondary:
• To evaluate the safety and tolerability of multiple administrations of GEH200520 Injection with GEH200521 (18F) Injection.
• To assess the biodistribution and tumour uptake of GEH200521 (18F) Injection with the optimal GEH200520 Injection dose determined in Part A.
• To compare tumour GEH200521 (18F) Injection uptake with immune cell CD8+ expression from a biopsy sample/resected lesion when available.
• To compare changes in tumour GEH200521 (18F) Injection uptake with changes in CT image assessment, according to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1, and/or [18F]-fluorodeoxyglucose (FDG) scans, when available.
• To assess changes in physical examination, laboratory variables, ECG, and vital signs following administration of GEH200520 Injection with GEH200521 (18F) Injection.
• To characterise the PK properties of total protein (GEH200520 and [18F]GEH200521 combined) following administration of GEH200520 Injection with GEH200521 (18F) Injection.
• To compare immunogenicity after multiple administrations of GEH200520 Injection with GEH200521 (18F) Injection.
Exploratory:
• To assess changes in selected biomarkers and compare biomarkers to tracer uptake characteristics following administration of GEH200520 Injection with GEH200521 (18F) Injection.

Study design

This is a Phase 1a/1b, multicentre, open-label, study to assess GEH200520 Injection / GEH200521 (18F) Injection safety and tolerability, PET imaging, PK, and changes in imaging after ICI treatment in subjects with solid tumour malignancies.
Two investigational medicinal products (IMPs) will be administered in this study: a non-radiolabelled IMP, GEH200520 Injection, and a radiolabelled IMP, GEH200521 (18F) Injection. GEH200521 (18F) Injection is composed of aluminium [18F] fluoride ([18F]AlF) chelated to the non-radiolabelled RESCA-VHH protein component, GEH200520.

The study consists of 2 parts:
• In Part A, subjects will receive one administration of GEH200520 Injection followed by one administration of GEH200521 (18F) Injection at a single imaging visit. The main objectives include dose escalation, assessments of safety and tolerability, dosimetry, PK, and anti-drug antibodies (ADA) for the different doses of GEH200520 Injection, administered together with a fixed dose of GEH200521 (18F) Injection, in subjects with solid tumour malignancies. A total

of 14 subjects are estimated to be enrolled in Part A at 1 study site.
• In Part B, subjects will receive one administration of GEH200520 Injection followed by one administration of GEH200521 (18F) Injection at 3 separate imaging visits using the optimal dose of GEH200520 Injection identified in Part A and a fixed dose of GEH200521 (18F) Injection. The main objectives include assessments of the changes in tracer uptake after ICI treatment, safety and tolerability, PK, and ADA. A total of 36 subjects are estimated to be enrolled in Part B at up to 2 study sites.

Intervention

Investigational Medicinal Product:
GEH200520 Injection
For Part A, subjects will receive a single administration of GEH200520 Injection at a mass dose of 1, 2, 4, 8, and 12 or 15 mg.
For Part B, GEH200520 Injection will be administered on 3 separate imaging days at a single mass dose as determined from the Part A results.
GEH200520 Injection will be administered as a single intravenous (IV) bolus injection; it is recommended to be injected slowly at a rate up to a maximum of 2 mL/min followed by a 10 mL saline flush (as required based on Investigator judgment).

GEH200521 (18F) Injection:
For Part A, subjects will receive a single administration of between 110 and 185 ±10% MBq GEH200521 (18F) Injection.
For Part B, subjects will receive a single administration of between 110 and 185 ±10% MBq GEH200521 (18F) Injection on 3 separate imaging days.

When scanning using a conventional PET scanner the target dose is 185 MBq ±10%. Total-body PET scanners have a longer axial field-of-view and can scan the head to thighs simultaneously; due to the increased detection sensitivity of this scanner, the target dose when scanning using a total-body system is 110 MBq ±10%.

GEH200521 (18F) Injection will be administered 2 to 4 minutes after GEH200520 Injection as a single IV bolus injection; it is recommended to be injected slowly over a period of up to 60 seconds followed by a 10 mL saline flush (as required based on Investigator judgment).
Comparator Imaging:

GEH200521 (18F) Injection uptake will be compared to CT images, when available, and changes in uptake in response to therapy will be compared to RECIST v1.1 criteria. Where other SoC images, such as [18F]-FDG scans, are available, they will also be used for comparison with GEH200521 (18F) Injection PET imaging.

Study burden and risks

The new study drugs have never been used in humans before. However, they have been tested in a laboratory and also on animals and no safety concern was identified during those studies.

Patients are closely monitored, and extra attention is paid to possible allergic reactions.

A patient may feel anxiety when lying in the PET scanner. This is also taken into account, and the patient is well prepared for this.

Contacts

Public
GE Healthcare Ltd.

Pollards Wood, Chalfont St Giles -
Buckinghamshire HP8 4SP
GB
Scientific
GE Healthcare Ltd.

Pollards Wood, Chalfont St Giles -
Buckinghamshire HP8 4SP
GB

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

(1) The subject is able and willing to comply with all study procedures as

described in the protocol, including the imaging day pre-visit requirements, and has read, signed, and dated an informed consent form prior to any study procedures being performed.
(2) The subject is male or female, >=18 years of age.
(3) Subject has a body mass index (BMI) >=18 and <=30 kg/m2.
(4) Subject has a life expectancy >=12 weeks.
(5) Subject has Eastern Cooperative Oncology Group (ECOG) performance status 0-1.
(6) Subject has an irresectable or metastatic solid tumour or a local and resectable head and neck squamous cell carcinoma.
(7) Subject is eligible for ICI treatment.
(8) Subject has at least 1 measurable tumour lesion documented on CT/magnetic resonance imaging (MRI) RECIST v1.1 during the last 12 months. Previously irradiated lesions should not count as target lesions.
(9) Subject has a tumour lesion(s) of which a biopsy can safely be obtained according to standard clinical care procedures.
(10) Subject is male, or a female who is either surgically sterile (has had a documented bilateral oophorectomy and/or documented hysterectomy), postmenopausal (cessation of menses for more than 1 year), or non-lactating, or if of childbearing potential the results of a serum or urine human chorionic gonadotropin pregnancy test, at screening and on the day of IMP administration (with the result known before IMP administration), must be negative. Women of childbearing potential and males who are sexually active with a partner of childbearing potential must use adequate contraception from Screening until 30 days after IMP administration. Such methods include: hormonal contraception including oral contraceptives; intrauterine device; intrauterine hormone-releasing system; bilateral tubal occlusion; vasectomised partner; sexual abstinence; adequate barrier method with spermicide (e.g., diaphragm, condom).

Exclusion criteria

(1) Subject is unable to undergo all procedures in the study and/or is unable to remain still and tolerate the imaging procedure.
(2) Subject has 12-lead ECG significant findings during screening, per Investigator*s assessment.
(3) Subject is not stable due to medical condition or therapy that, in the opinion of the Investigator, could compromise subject safety or protocol objectives.
(4) Subject has active autoimmune disease or a documented history of autoimmune disease or syndrome that requires systemic steroids or immunosuppressive agents.
(5) Subject has a confirmed active COVID-19 infection.
(6) Subject has serious non-malignant disease or conditions that, in the opinion of the Investigator, could compromise subject safety or protocol objectives.

(7) Subject has B or T cell lymphoma.
(8) Subject has brain or bone-marrow metastasis that, in the opinion of the Investigator, could compromise subject safety or protocol objectives.
(9) Subject has signs or symptoms of systemic infection within 2 weeks prior to imaging day.
(10) Subject has history of severe allergic, anaphylactic, or other hypersensitivity reactions to chimeric or humanised antibodies or fusion proteins or known allergy to the study IMP ingredients and/or the proposed ICI therapy.
(11) Subject has any other diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates the use of the ICI treatment, or that may affect the interpretation of the results or render the subject at high risk from complications.
(12) Subject has laboratory values of:
I. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) greater than 3 times the upper limit of normal (ULN) or greater than 5 times the ULN in case of liver metastases.
II. Bilirubin >3.0 x ULN
III. Creatinine clearance <45 mL/min/1.73 m2
IV. Leukocyte count <3,500/mm3
V. Platelet count <100,000/µL
(13) Subject has any safety laboratory test results (clinical chemistry, haematology, and urinalysis) that, in the opinion of the Investigator, could compromise subject safety or protocol objectives.
(14) Subject has had any major surgery within 4 weeks prior to enrolment or major surgery is scheduled during the study, with the exception of procedures that are part of the study site IIS.
(15) Subject has been enrolled in another interventional clinical study within the 30 days before screening for this study, except for the study site IIS.
(16) Subject is pregnant or planning to become pregnant or is lactating.
(17) Subject has a history of alcohol or drug abuse within the last year.
(18) Subject has had treatment with systemic immunostimulatory agents (including but not limited to interferons [IFNs] or interleukin-2 [IL-2]) within 6 weeks or 5 half-lives of the drug, whichever is shorter, prior to dosing with the IMP.
(19) Subject has had treatment with systemic immunosuppressive medications (including but not limited to prednisone, cyclophosphamide, azathioprine, methotrexate, thalidomide, and anti-tumour necrosis factor agents) within 2 weeks prior to dosing with the IMP.
(20) Subject has received acute, low-dose, systemic immunosuppressant medications (e.g., a one-time dose of dexamethasone for nausea) that, in the opinion of the Investigator, could compromise protocol objectives.
(21) Subject has used systemic corticosteroids to treat inflammatory or autoimmune symptoms within 15 days or other immunosuppressive drugs within 30 days prior to screening. Inhaled and topical corticosteroids are permitted.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	27-01-2023
Enrollment:	50
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	GEH200520
Generic name:	GEH200520
Product type:	Medicine
Brand name:	GEH200521 (18F)
Generic name:	GEH200521 (18F)

Ethics review

Approved WMO Date:	07-04-2022
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-11-2022
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO Date:	20-09-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-11-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-12-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-02-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	CTIS2024-515218-42-00
EudraCT	EUCTR2022-000246-16-NL
CCMO	NL80931.042.22