A confirmatory, prospective, open-label, multi-centre phase 3 study to evaluate diagnostic performance of 89Zirconium-labelled girentuximab (89Zr-TLX250) to non-invasively detect clear cell renal cell carcinoma (ccRCC) by positron emission tomography/CT (PET/CT) imaging in patients with indeterminate renal masses (ZIRCON study)

Published: 19-11-2018
Last updated: 12-04-2024

Primary Objective:To evaluate sensitivity and specificity of qualitative assessment of PET/CT imaging with 89Zr-TLX250 to non-invasively detect ccRCC in patients with indeterminate renal masses, using histology as standard of truth.Secondary...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Renal and urinary tract neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON52858

Source
ToetsingOnline

Brief title
ZIRCON study

Condition

- Renal and urinary tract neoplasms malignant and unspecified

Synonym
clear cell renal carcinoma - kidney cancer

Research involving
Human

Sponsors and support

Primary sponsor: TELIX International Pty Ltd - Françoise Bruyère
Source(s) of monetary or material Support: Sponsor of the study (TELIX)

Intervention

Keyword: 89Zirconium-labelled girentuximab, clear cell renal cell carcinoma (ccRCC), Girentuximab, Positron Emission Tomography

Outcome measures

Primary outcome

Sensitivity and Specificity of 89Zr-TLX250 PET/CT imaging to detect ccRCC

Secondary outcome

- Further test performance parameters

- Standardized uptake value (SUV)

- Inter-reader variability

- Safety

- Exploratory Variable

Study description

Background summary

In this research a new promising image-forming technique is applied. Here a PET (Positron Emission Tomography) scan and CT (computer tomography) scan is made

after administration of an imaging agent. This image-forming agent (89Zr-girentuximab) consists of girentuximab coupled to a small amount of a radioactive substance (zirconium-89).

Girentuximab is an antibody (a substance that can bind to other substances in the human body, eg proteins). Research in thousands of patients has shown that after administration, girentuximab binds to a protein which is common in a form of kidney cancer that often occurs; the clear cell renal cell carcinoma.
With the aid of a PET / CT scan, 89Zr-girentuximab can be visualized and thus also the tumor and / or possible metastases. Only in the case of clear cell renal cell carcinoma will the tumor be visible on the scan. Moreover, it appears that if the tumor is not visible, there is a big chance that the abnormality is benign or that it is a less aggressive form of kidney cancer.

In previous research girentuximab has been linked to zirconium-89 (89Zr-girentuximab) and administered in more than 40 patients. The results of this study have shown that the product can be safely used as an imaging agent for the detection of clear cell renal cell carcinoma.

It is now important to examine 89Zr-girentuximab in a larger number of patients to determine whether the drug can correctly demonstrate whether it is a clear cell renal cell carcinoma. The aim of this research is therefore to determine whether it is possible to correctly determine the nature of the established or suspected cancer in the kidneys after administration of 89Zr-girentuximab.

If the study is successful, it could prevent the need for a biopsy or unnecessary surgery for a benign tumor.

Study objective

Primary Objective:
To evaluate sensitivity and specificity of qualitative assessment of PET/CT imaging with 89Zr-TLX250 to non-invasively detect ccRCC in patients with indeterminate renal masses, using histology as standard of truth.

Secondary Objectives:
1 & 2. To determine sensitivity (1) and specificity (2) of 89Zr-TLX250 PET/CT imaging to detect ccRCC in the subgroup of patients with indeterminate renal masses of <= 4 cm in largest diameter (cT1a)
3. To identify a standardized uptake value (SUV) cut-off for 89Zr TLX250, suitable to discriminate ccRCC from non-ccRCC
4. To determine inter-reader variability of diagnostic assessments of 89Zr-TLX250 PET/CT images, when performed by multiple readers
5 & 6. To determine inter-reader (5) and intra-reader (6) variability of diagnostic assessments of 89Zr-TLX250 PET/CT images.
7. To establish safety and tolerability of 89Zr-TLX250 in patients with inderterminate renal masses.

8. To evaluate sensivity and specificity of 89Zr-TLX250 PET/CT imaging to detect ccRCC in patients with IRMs <= 3cm, IRMs <= 2cm and Bosniak 3 and 4 lesions.

Study design

This will be a confirmatory, prospective, open-label, multi-centre phase 3 study to evaluate sensitivity and specificity of 89Zr-TLX250 PET/CT imaging to non-invasively detect clear cell renal cell cancer (ccRCC) in adult patients with indeterminate renal masses (IRM), scheduled for partial or total nephrectomy.

Study burden and risks

- The use of an intravenous infusion for administration of the IP and laboratory blooddraw may be accompanied by a mild bruising and in rare cases with a transient inflammation of the vessel wall. After the initial irritation following the insertion of the cannula the blooddraw can ussually performed painless and without significant irritation
- There is a small to moderate chance of discomfort associated with lying in a scanner (eg back pain
as a result of lying still)
- There is an additional risk of developing stochastic effects after exposure to ionizing
radiation. Because the amount of radiation used in this study falls into the clinical-diagnostic range, the chance is considered very small.
- There is a chance of developing an allergic reaction for the IMP or one of the components. Because allergic reactions have never been seen in various preclinical and clinical studies this chance is considered very small.

The burden and risks associated with study participation are described in detail in the Patient Information Leaflet.

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

- Male or female >= 18 years of age
- Imaging evidence of a single indeterminate renal mass of <= 7 cm in largest diameter (tumour stage cT1), on standard of care imaging, based on national standards, not older than 90 days on Day 0, but performed before any screening procedure.
- Scheduled for lesion resection as part of regular diagnostic work-up within 90 days from planned 89Zr-TLX250 administration.
- Sufficient life expectancy to justify nephrectomy.
- Consent to practise highly effective contraception until a minimum of 42 days after 89Zr-TLX250 administration.

Exclusion criteria

- A biopsy procedure only (rather than partial or total nephrectomy) planned for histological species delineation of IRM
- Renal mass known to be a metastasis of another primary tumour.
- Active non-renal malignancy requiring therapy during the time frame of the study participation.
- Chemotherapy, radiotherapy, or immunotherapy within 4 weeks prior to the planned administration of 89Zr -TLX250 or continuing adverse effects (> grade 1) from such therapy (Common Terminology Criteria for Adverse Events [CTCAE] version 5.0).
- Planned antineoplastic therapies (for the period between administration of

89Zr-TLX250 and imaging).
- Exposure to murine or chimeric antibodies within the last 5 years.
- Previous administration of any radionuclide within 10 half-lives of the same
- Serious non-malignant disease
- Known hypersensitivity to girentuximab or DFO (desferoxamine)
- Renal insufficiency with GFR <= 45 mL/min/ 1.73 m²

Study design

Design

Study phase:	3
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-09-2019
Enrollment:	45
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	89Zr-TLX250
Generic name:	Zr89-girentuximab

Ethics review

Approved WMO

Date:	19-11-2018
Application type:	First submission
Review commission:	METC NedMec

Approved WMO Date:	10-04-2019
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	16-05-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-05-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-08-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-09-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-01-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-01-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-06-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-07-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	02-09-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-09-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-07-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-07-2022
Application type:	Amendment
Review commission:	METC NedMec

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	EUCTR2018-002773-21-NL
ClinicalTrials.gov	NCT03849118
CCMO	NL67645.031.18