An open-label, Phase I study to assess safety, tolerability, radiation dosimetry, and imaging properties of 89Zr-labelled girentuximab (89Zr-girentuximab) for in vivo detection of clear cell renal carcinoma (CCRC) by positron emission tomography (PET) using different PET imaging methodologies.

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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-OMON44583

Source
ToetsingOnline

Brief title
89Zr-girentuximab dosimetry in CCRC study * ZIR-DOSE

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.
Source(s) of monetary or material Support: Industrie

Intervention

Keyword: clear cell renal carcinoma, dosimetry, girentuximab, positron emission tomography

Outcome measures

Primary outcome

The primary objective of this study will be to evaluate clinical safety and

tolerability of 89Zr-girentuximab.

Secondary outcome

- To determine the whole body radiation dosimetry of 89Zr-girentuximab in

patients with suspected CCRC

- To assess diagnostic image quality of 89Zr-girentuximab using a

time-of-flight PET (TOF-PET) compared a conventional PET (C-PET reconstruction)

- To assess diagnostic image quality of 89Zr-girentuximab using a 37 MBq (1

mCi) activity dose and different acquisition durations (5, 10, 15 vs. 20 min)

- To establish activity dose and recommended acquisition modalities for further

clinical development

Study description

Background summary

Distinct advantages of immunoPET as compared to immunoSPECT are the superior resolution, the short acquisition time for whole-body 3D images, and the potential for quantitative analysis of tumor targeting. Clinical immuno*PET trials with 89Zr*labeled monoclonal antibodies (mAbs) have been performed or are ongoing with at least 15 MAbs, including most of the FDA approved MAbs. 89Zr*immuno*PET has become an integrated part of the MAb development programs of several of the world-leading pharmaceutical and biotech companies. Girentuximab can be stably labeled with the PET radionuclide Zirconium- 89 (Zr-89; 89Zr) and in preclinical studies the in vivo distribution of 89Zr-girentuximab was shown to be identical to that of 111In-girentuximab. In addition, due to prolonged trapping of the radiolabel in the tumor and simultaneous washout from normal tissues, PET imaging with 89Zr-girentuximab was shown to be superior to 124I-girentuximab. Combining the superior characteristics of PET with the use of the residualizing 89Zr radionuclide are major steps forward in the development of this imaging biomarker.

Study objective

The identification of RCC is crucial for planning possible surgery and treatment. The aim of this study is to investigate the safety, tolerability, radiation dosimetry, as well as the diagnostic performance of 89Zr-girentuximab PET/CT in patients with suspected CCRC. The results of this study will be used to pave the way for further studies with 89Zr-girentuximab as a PET/CT imaging agent which was shown to have higher diagnostic resolution 124I-girentuximab in animal studies due to prolonged trapping of the radiolabel in the tumor and simultaneous washout from normal tissues. It is anticipated to develop 89Zr-girentuximab as an improved imaging agent for CCRC.

Study design

This will be an exploratory, open-label, Phase I study to evaluate safety, tolerability, whole body dosimetry, and imaging properties of 89Zr-girentuximab, when image acquisition is made using different PET reconstruction methods, namely time-of-flight (TOF-PET) and conventional (PET) reconstruction, in order to estimate a possible impact of variable scanner technology on image quality variability in a planned multi-centre study. In addition, different acquisition durations (5 *20 min) will be explored using an activity dose of 37 mBq (1 mCi), in order to establish, whether acquisition time has an impact on diagnostic performance.

Study burden and risks

Given the well-known safety and tolerability of radiolabelled girentuximab and the low doses used in this study, no harmful effects can be anticipated, and

the results of this study may contribute to the development of 89Zr-girentuximab as an improved imaging agent for CCRC. Although highly unlikely, 89Zr-girentuximab may cause allergic-type reactions. The study centres are well equipped to treat allergic/anaphylactic reactions.

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

All patients must meet all of the following criteria:;- Written informed consent
- Male or female >50 years of age
- Clinical suspicion of CCRC, based on incidental imaging evidence of a renal mass, requiring further diagnostic work-up (incidentalomas), or patients with established diagnosis of CCRC requiring staging
- Life expectancy of at least 6 months

- Consent to practise contraception until end of study (7 days after 89Zr-girentuximab injection)

Exclusion criteria

A patient will be excluded from participation in the trial if one or more of the following criteria are met:;- Known hypersensitivity to girentuximab
- Known uncontrolled hyperthyreoidism
- Exposure to any experimental diagnostic or therapeutic drug within 30 days from the date of planned administration of 89Zr-girentuximab
- Exposure to any radiopharmaceutical within 30 days (corresponding to 8 half-lives of 89Zr) prior to the administration of 89Zr-girentuximab.
- Ongoing toxicity grade 2 from previous standard or investigational therapies (Common Terminology Criteria for Adverse Events [CTCAE] version 4.03)
- Planned (for the period between injection of 89Zr-girentuximab and imaging) antineoplastic therapies
- Established renal cell carcinomas of other histological entities than CCRC
- Known brain metastases
- Serious non-malignant disease (e.g. psychiatric, infectious, autoimmune or metabolic), that may interfere with the objectives of the study or with the safety or compliance of the subject, as judged by the investigator
- Pregnant or breast-feeding women. Female patients of childbearing potential or male patients with female partners of childbearing potential, unless willing to practice full and true sexual abstinence or being surgically/permanently sterile or with a history of hysterectomy for women, not willing to practice effective contraception by using: a non-oral, injected or implanted non-oestrogen progesterone based hormonal method, male condom, vaginal diaphragm, cervical cap, intrauterine device, during the study period and within a period of 28 days (corresponding to 8 half-lives of 89Zr) after receiving study drug.
11. Subjects not able to declare meaningful informed consent on their own (e.g. with legal guardian for mental disorders)

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-06-2018
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Zr89-girentuximab
Generic name:	Zr89-girentuximab

Ethics review

Approved WMO Date:	15-01-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-04-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-07-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2017-004769-28-NL
CCMO	NL64206.091.17