A multi-centre, open-label, single-arm, dose-finding phase I/II study to evaluate safety, tolerability, dosing schedule, and preliminary efficacy of carrier-added 4-L-[131I]iodo-phenylalanine (131I-IPA), administered as single or repetitive injections in patients with recurrent glioblastoma multiforme (GBM), concomitantly to 2nd line external radiation therapy (XRT) - IPAX-1Study

Published: 05-03-2019
Last updated: 09-04-2024

Primary objectiveTo assess the safety and tolerability of intravenous 131I-IPA administered concomitantly to 2nd line XRT in recurrent GBMSecondary objectives:- To assess the maximum tolerated dose (MTD) of 131I -IPA administered concomitantly to...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Nervous system neoplasms malignant and unspecified NEC
Study type	Interventional

Summary

ID

NL-OMON49405

Source
ToetsingOnline

Brief title
131I-IPA-TLX-101-001

Condition

- Nervous system neoplasms malignant and unspecified NEC

Synonym
Brain cancer, GMB

Research involving
Human

Sponsors and support

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

Intervention

Keyword: IPAX-1Study, open-label, Phase II, recurrent glioblastoma multiforme

Outcome measures

Primary outcome

EOS will be 12 months after 1st 131I-IPA infusion, or earlier, if progression

is diagnosed on imaging.

Secondary outcome

- To assess the maximum tolerated dose (MTD) of 131I-IPA administered

concomitantly to 2nd line XRT in recurrent GBM

- To evaluate the feasibility of a fractionated administration of 131IIPA

- To evaluate the radiation absorbed dose to tumour from 131I-IPA

- To explore the antineoplastic effect of 131I-IPA + XRT combination therapy

- To explore a possible influence of MGMT promoter methylation status on the

biological response to 131I-IPA + XRT combination therapy

- To explore the occurrence and frequency of pseudo-progression (PsPD) in

response to 131I-IPA + XRT combination therapy

- To explore the cognitive function before, during and after therapy

Study description

Background summary

Cancer cells have a considerably larger nutrient consumption than non-malignant cells. This is also the case for malignant gliomas which show a higher uptake of amino acids in comparison with normal brain tissue. The uptake typically increases with the malignancy grade, and is particularly high in GBM. Amino acid transporter proteins actively transport amino acids across the blood-brain barrier (BBB) into tumour cells. Thus, they are prime targets for radio-imaging and targeted radiotherapy of gliomas in general and for GBM in particular.

4-iodo-L-phenylalanine (IPA) is a derivative of the naturally occurring essential amino acid L- phenylalanine, containing an iodine atom in position 4 (para-position) of the phenyl ring. Due to its mode of beta decay, 131I is known to cause mutation and death in cells that it penetrates, and other cells up to several millimetres away, making it an ideal candidate for imaging and treating inoperable GBM lesions. In addition to this physical effect, an intrinsic cytostatic effect on GBM cells of IPA was demonstrated in pre-clinical studies, as well as a radio-sensitising activity, synergistic to both, the intramolecular radiolabel, and external field radiation therapy (XRT).

(see also study protocol chapter 1.1 Background, page 26)

Study objective

Primary objective
To assess the safety and tolerability of intravenous 131I-IPA administered concomitantly to 2nd line XRT in recurrent GBM

Secondary objectives:
- To assess the maximum tolerated dose (MTD) of 131I -IPA administered concomitantly to 2nd line XRT in recurrent GBM
- To evaluate the feasibility of a fractionated administration of 131IIPA
- To evaluate the radiation absorbed dose to tumour from 131I-IPA
- To explore the antineoplastic effect of 131I-IPA + XRT combination therapy
- To explore a possible influence of MGMT promoter methylation status on the biological response to 131I-IPA + XRT combination therapy
- To explore the occurrence and frequency of pseudo-progression (PsPD) in response to 131I-IPA + XRT combination therapy
- To explore the cognitive function before, during and after therapy

Study design

Open-label, single-arm, randomised, parallel-group, multicentre dose-finding study.

Intervention

IV administration of [131I]-L-4-iodophenylalanine
(see the information provided in section J)

Study burden and risks

A physical examination, including measurement of bloodpressure, heartrate, temperature, weight and an ECG, collection of blood- and urine samples and completion of two questionnaires will take place at screening, treatment visits and end of study visit. In addition CT and MRI scans will be performed at several visits. Depending on the treatment group, SPECT imaging and whole body planar imaging will be done.
During study visits, the patient will be asked about his wellbeing and potential adverse events. The patient will need to follow guidelines after radiation for 7 days. The study patient may experience adverse reactions related to radiation therapy.

The Patient Information Leaflet & Informed Consent Form provides information on the possible adverse events and other inconveniences in chapter 4

The study protocol contains a chapter on risks and benefit: chapter 1.3 Benefit-Risk Assessment, page 26.

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

- Previously confirmed histological diagnosis of GBM, with current clinical or imaging evidence for first recurrence according to modified RANO criteria (2017). History of GBM standard therapy (debulking surgery, followed by radio-chemotherapy (50-60 Gy in 2 Gy fractions, temozolomide).
- Interval since end of 1st line XRT >=6 months
- Amino acid-based molecular imaging (preferably 18F-FET-PETor 11Cmethionine, as institutionally established) indicating pathologically increased amino acid uptake inside or in the vicinity of the tumour clearly discernible from background activity.

Exclusion criteria

- Primary XRT dose >60 Gy
- Doses to organs at risk defined by Yasar and .Tugrul (2005) exceeded or reached by prior radiation therapy; e.g. cumulative total dose on the optical chiasm >54 Gy for 2 Gy/fraction, alpha/beta=2
- Multifocal distant recurrence, defined as tumour lesion outside the primary XRT field, as evidenced by amino acid-based PET imaging
- Prior treatment with brachytherapy
- Prior treatment with bevacizumab

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-08-2020
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	[131I]-L-4-iodophenylalanine
Generic name:	[131I]-L-4-iodophenylalanine

Ethics review

Approved WMO Date:	05-03-2019
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	09-07-2019
Application type:	First submission
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	09-01-2020
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van

	Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	10-04-2020
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)
Approved WMO Date:	06-07-2020
Application type:	Amendment
Review commission:	PTC Stichting het Nederlands Kanker Instituut - Antoni van Leeuwenhoekziekenhuis (Amsterdam)

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
Other	03849
EudraCT	EUCTR2018-002262-39-NL
CCMO	NL69050.031.19

Study results

Date completed:	14-07-2021
Actual enrolment:	2

Summary results
Trial is onging in other countries