Clinical trial results:
A Phase I/IIa study to evaluate safety, biodistribution, dosimetry and preliminary diagnostic performance of 68Ga-NeoBOMB1 in patients with advanced TKI-treated GIST using positron-emission tomography/computer tomography (PET/CT).

Summary

EudraCT number	2016-002053-38
Trial protocol	AT
Global end of trial date	09 April 2019

Results information

Result version number	v1 (current)
This version publication date	23 May 2020
First version publication date	23 May 2020
Summary attachment (see zip file)	Study Synopsis (MITIGATE_StudySynopsis_ Protocol_v1.1_20160718.pdf)

Trial information

Trial identification

Sponsor protocol code	MITIGATE-NeoBOMB1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02931929
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Medical University Innsbruck
Sponsor organisation address	Anichstraße 35, Innsbruck, Austria, 6020
Public contact	Department of nuclear medicine, Medical University Innsbruck, +43 51250422651, irene.virgolini@i-med.ac.at
Scientific contact	Department of nuclear medicine, Medical University Innsbruck, +43 51250422651, irene.virgolini@i-med.ac.at

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	18 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 May 2018
Global end of trial reached?	Yes
Global end of trial date	09 April 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Phase I part:
- Safety, tolerability
- Human pharmacokinetics and dosimetry data to determine the organ doses and to identify potentially dose-limiting critical organs through PBPK modelling

Phase I/IIa part:
- Safety, tolerability
- Preliminary targeting properties of 68Ga-NeoBOMB1 in advanced, GRP positive GIST tumours.

Protection of trial subjects:

Patients received a PET-Scan with Tracerapplication, blood and urine samples were taken, 3 times ECG and pregnancy tests in WOCBP

Background therapy:

Diagnostic CT + contrast agent, Low-dose whole-body CT

Evidence for comparator: -

Actual start date of recruitment	28 November 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 9
Worldwide total number of subjects	9
EEA total number of subjects	9

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	5
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Due to a very low incidence and prevalence as well as pre-determined imaging schedules in local patients with known GIST diagnosis, recruitment was very difficult throughout the study. Recruitment was supported by Mannheim Medical University, a specialized European centre for GIST which contributed 5 patients to the study.

Pre-assignment

Screening details:

All subjects have gastrointestinal stromal tumours, previously or currently under TKI treatment, including at least 50% TKI-resistant patients. The screening examinations must be performed between 1 and 28 days before being enrolled in the study. Overall, 9 participants were screened and enrolled in this study.

Period 1

Period 1 title	overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Tracer Application NeoBOMB1

Arm description:

68Ga-NeoBOMB1 imaging will be performed using 3D PET/CT Three-dimensional PET will be used to investigate 68Ga-NeoBOMB1 biodistribution in detail. PET/CT will be used to (a) demonstrate 68Ga-NeoBOMB1 binding inside or in proximity to the structural tumour lesion, as observed on CT (tumour targeting), and (b) to provide attenuation correction and partial
volume correction data for the PET measurements. Image transfer and processing will be performed per Image.

Arm type	Experimental
Investigational medicinal product name	Kit for the preparation of 68Ga-NeoBOMB1
Investigational medicinal product code	436047
Other name	GalliaPharm
Pharmaceutical forms	Radionuclide generator
Routes of administration	Intravenous use

Dosage and administration details:

Patients received a single injection of 68Ga-NeoBOMB1 at 3 MBq/ kg body weight (with a minimum of 150 and a maximum of 250 MBq)

Number of subjects in period 1	Tracer Application NeoBOMB1
Started	9
Completed	9

Baseline characteristics

Reporting groups	
Reporting group title	overall study
Reporting group description:	
All treated patients	

Reporting group values	overall study	Total	
Number of subjects	9	9	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	5	5	
From 65-84 years	4	4	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	64.4		
standard deviation	± 11.2	-	
Gender categorical Units: Subjects			
Female	6	6	
Male	3	3	

End points

End points reporting groups

Reporting group title	Tracer Application NeoBOMB1

Reporting group description:

68Ga-NeoBOMB1 imaging will be performed using 3D PET/CT Three-dimensional PET will be used to investigate 68Ga-NeoBOMB1 biodistribution in detail. PET/CT will be used to (a) demonstrate 68Ga-NeoBOMB1 binding inside or in proximity to the structural tumour lesion, as observed on CT (tumour targeting), and (b) to provide attenuation correction and partial
volume correction data for the PET measurements. Image transfer and processing will be performed per Image.

Primary: Human pharmakokinetics

End point title	Human pharmakokinetics[1]

End point description:

Generation of decay corrected time activity curves from 68Ga-NeoBOMB1 PET/CT images in normal organs, tumour lesions. Quantification of urinary excretion of 68Ga-NeoBOMB1
Calculation of half-life of 68Ga-NeoBOMB1 in blood

End point type	Primary

End point timeframe:

Day 0

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses have been done due to small number of participants

End point values	Tracer Application NeoBOMB1			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: mSv/ MBq				
arithmetic mean (standard deviation)				
urinary excretion of 68Ga-NeoBOMB1	26 (± 5)			
half-life of 68Ga-NeoBOMB1 in blood	41 (± 15)			
half-life of 68Ga-NeoBOMB1 in serum	35 (± 8)			

Statistical analyses

No statistical analyses for this end point

Primary: Safety & tolerability

End point title	Safety & tolerability[2]

End point description:

Tolerability and safety of the administration of 68Ga-NeoBOMB1 in a diagnostic dose
Last follow-up visit (visit 3) for previous participant in first 3 participants

End point type	Primary

End point timeframe:

Day 0- Day 8

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statisitcal analyses have been done due to small number of participants

End point values	Tracer Application NeoBOMB1			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: SAEs/ AES				
number (not applicable)				
Number of SAEs	0			
Number of AEs	6			

Statistical analyses

No statistical analyses for this end point

Primary: Dosimetry

End point title	Dosimetry[3]

End point description:

Generation of non-decay-corrected time activity curves and residence times from 68Ga-NeoBOMB1 PET/CT images in normal organs, tumour lesions
Calculation of absorbed doses and effective whole body dose of 68Ga-NeoBOMB1, also by PBPK modelling of 68Ga-NeoBOMB1

End point type	Primary

End point timeframe:

Day 0- Day 5

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses have been done due to small number of participants

End point values	Tracer Application NeoBOMB1			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: mSv/ MBq				
arithmetic mean (standard deviation)				
effective whole body dose of 68Ga-NeoBOMB1	0.0287 (± 0.0063)			

Statistical analyses

No statistical analyses for this end point

Primary: Preliminary targeting properties

End point title	Preliminary targeting properties[4]

End point description:

Description of 68Ga-NeoBOMB1 accumulation in tumour lesion (number of lesions, SUV value per lesion) and comparison with known tumour lesions.
Comparison of tumour targeting with immunhistopathology (at least in Phase I/IIa patients)

End point type	Primary

End point timeframe:

Day0- Day5

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses have been done due to small number of participants

End point values	Tracer Application NeoBOMB1			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Ga-NeoBOMB1				
number (not applicable)				
Positive imaging finding for primary lesion	2			
Positive imaging finding for liver metastases	4			
Positive imaging finding for other metastases	2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 28.11.2016-09.04.2019	
Assessment type	Systematic
Dictionary used	
Dictionary name	CTCAE
Dictionary version	4.03
Reporting groups	
Reporting group title	Adverse events

Reporting group description: -

Serious adverse events	Adverse events		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Adverse events		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 9 (33.33%)		
Blood and lymphatic system disorders			
Neutophila			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Leukocytosis			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
Alterations of aPTT and PT			
subjects affected / exposed	1 / 9 (11.11%)		
occurrences (all)	1		
General disorders and administration site conditions			

Nightly sweats subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 2		
Renal and urinary disorders Leukocyturia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		
Metabolism and nutrition disorders Hypophosphatemia subjects affected / exposed occurrences (all)	1 / 9 (11.11%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

As we were limited by the EU FP7 project, we had to stop recriutment before we achieved including 12 patients into the study.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30775647

http://www.ncbi.nlm.nih.gov/pubmed/29137110

http://www.ncbi.nlm.nih.gov/pubmed/27754750

http://www.ncbi.nlm.nih.gov/pubmed/27493272