

**Clinical trial results:****Clinical assessment of the tissue distribution of [18F]FMISO, INJ SOL after intravenous injection in patients with malignancy****Summary**

EudraCT number	2011-000839-84
Trial protocol	CZ
Global end of trial date	20 June 2014

Results information

Result version number	v1 (current)
This version publication date	29 August 2021
First version publication date	29 August 2021

Trial information**Trial identification**

Sponsor protocol code	FMISO/2011/II
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	RadioMedic s.r.o.
Sponsor organisation address	Husinec-Řež 289, Řež, Czechia, 250 68
Public contact	Publicly available information service for professionals VPOIS, RadioMedic s.r.o., +420 725015370, verejnost@radiomedic.cz
Scientific contact	Publicly available information service for professionals VPOIS, RadioMedic s.r.o., +420 725015370, verejnost@radiomedic.cz

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	05 January 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 June 2014
Global end of trial reached?	Yes
Global end of trial date	20 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the clinical trial is to confirm the accumulation of [18F]FMISO, INJ SOL in squamous cell tumors, in accordance with the results of non-clinical studies and published data, and thus to prove the diagnostic potential of [18F]FMISO, INJ SOL in nuclear medicine. Furthermore, the trial aims to verify whether the administered radioactivity is sufficient to obtain well evaluable PET images under given conditions. The trial should also confirm that parenteral administration of [18F]FMISO, INJ SOL does not cause any adverse drug reactions, including allergic reactions.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles of Good Clinical Practice (GCP) and the Declaration of Helsinki. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. The study was regularly monitored by the Sponsor.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 July 2013
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	Czechia: 16
Worldwide total number of subjects	16
EEA total number of subjects	16

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)	6
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening performed by a medical doctor according to the inclusion and exclusion criteria.

Main screening criteria:

Squamous cell carcinoma confirmed by 18F-FDG PET and histologic examination

18F-FDG PET examination performed within 28 days

Laboratory blood test (CBC, serum creatinine, urea, HCG pregnancy test) and urinalysis

Period 1

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

Arms

Arm title	[18F]FMISO PET
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	[18F]FMISO, INJ SOL
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Single dose administration, 4.5 MBq/kg (maximal dose 550 MBq) of [18F]FMISO, INJ SOL 2-3 hours prior to PET scan

Number of subjects in period 1	[18F]FMISO PET
Started	16
Completed	15
Not completed	1
reclassification of histological findings	1

Baseline characteristics

Reporting groups

Reporting group title	Overall trial
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Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	16	16	
Age categorical Units: Subjects			
Adults (18-64 years)	6	6	
From 65-84 years	10	10	
Gender categorical Units: Subjects			
Female	13	13	
Male	3	3	

Subject analysis sets

Subject analysis set title	Full analysis set
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Subject analysis set type	Full analysis
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Subject analysis set description:

Includes all patients who entered the study.

Reporting group values	Full analysis set		
Number of subjects	16		
Age categorical Units: Subjects			
Adults (18-64 years)	6		
From 65-84 years	10		
Gender categorical Units: Subjects			
Female	13		
Male	3		

End points

End points reporting groups

Reporting group title	[18F]FMISO PET
Reporting group description:	-
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	Includes all patients who entered the study.

Primary: Efficacy - Accumulation of [18F]FMISO, INJ SOL in the tumor

End point title	Efficacy - Accumulation of [18F]FMISO, INJ SOL in the tumor ^[1]
End point description:	PET scan was performed 2-3 hours after [18F]FMISO, INJ SOL administration with subsequent semi-quantitative evaluation of [18F]FMISO accumulation using the maximal standardized uptake value (SUVmax) in the region of interest (ROI). The SUVmax values ranged from 2.4 to 5.9 and confirmed accumulation of [18F]FMISO in squamous cell tumors.
End point type	Primary
End point timeframe:	- evaluation of individual results for each single patient within 48 hours after [18F]FMISO, INJ SOL PET scan - statistical processing of results (descriptive statistics only) after the end of trial

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: Single arm study, only descriptive statistics were performed for this endpoint.

End point values	Full analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: SUVmax				
arithmetic mean (standard deviation)	3.71 (\pm 1.08)			

Statistical analyses

No statistical analyses for this end point

Secondary: Comparison of [18F]FMISO, INJ SOL and 18F-FDG accumulation

End point title	Comparison of [18F]FMISO, INJ SOL and 18F-FDG accumulation
End point description:	For each patient 18F-FDG PET scan was performed on the same device using the same procedure within 28 days prior to [18F]FMISO, INJ SOL PET scan. Semi-quantitative evaluation based on ratio of maximal standardized uptake value (SUVmax) in the region of interest (ROI) of [18F]FMISO, INJ SOL and 18F-FDG was performed. The differences in SUVmax values between FMISO and FDG reflect a different mechanism of accumulation.
End point type	Secondary
End point timeframe:	- evaluation of individual results for each single patient within 48 hours after [18F]FMISO, INJ SOL PET scan

End point values	Full analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: ratio of SUVmax FDG/FMISO				
arithmetic mean (standard deviation)	5.56 (\pm 2.72)			

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of changes in physiological functions in relation to [18F]FMISO, INJ SOL administration

End point title	Evaluation of changes in physiological functions in relation to [18F]FMISO, INJ SOL administration
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End point description:

Evaluation of changes in physiological functions in relation to [18F]FMISO, INJ SOL administration included measurement of systolic and diastolic blood pressure and heart rate before and after application. Changes in patients' subjective feelings were also monitored. The observed changes in function were not clinically significant and no patient reported a change in subjective feelings associated with the clinical trial.

End point type	Secondary
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End point timeframe:

- evaluation of acute changes within 2 hours after examination
 - statistical processing of results (descriptive statistics only) after the end of trial
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End point values	Full analysis set			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: HRbefore-HRafter (bpm)				
arithmetic mean (standard deviation)	1.93 (\pm 6.81)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Adverse events recorded from clinical trial enrollment (signing an informed consent) until hospital discharge.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: [¹⁸F]FMISO is a radiolabeled imaging agent used in such low chemical doses that do not exhibit clinically and/or analytically noticeable pharmacodynamic effects. Chemical amount of FMISO in single injection dose of [¹⁸F]FMISO with administrated activity 400MBq is approximately $1,5 \cdot 10^{-9}$ g.

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

None reported