Clinical trial results:
Efficacy and Safety of gadoPIClenol for CenTral NervoUs System (CNS) Magnetic REsonance Imaging (MRI) (PICTURE trial)

Summary

EudraCT number	2018-003988-54
Trial protocol	FR BE DE HU ES IT
Global end of trial date	11 September 2020

Results information

Result version number	v1 (current)
This version publication date	25 November 2021
First version publication date	25 November 2021

Trial information

Trial identification

Sponsor protocol code	GDX-44-010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03996447
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Guerbet
Sponsor organisation address	B.P. 57400, CdG Cedex, France, 95943
Public contact	Jing Hao, MD, Guerbet, +33 (0)1 45 91 51 76 , jing.hao@guerbet.com
Scientific contact	Jing Hao, MD, Guerbet, +33 (0)1 45 91 51 76 , jing.hao@guerbet.com

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	23 March 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 September 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To demonstrate the superiority of gadopiclenol-enhanced MRI at 0.05 mmol/kg body weight compared to unenhanced MRI for patient referred for contrast-enhanced MRI of CNS, in terms of 3 lesion visualization co-primary criteria using the patient as his/her own control.
- To demonstrate the non-inferiority of gadopiclenol at 0.05 mmol/kg compared to gadobutrol at 0.1 mmol/kg in terms of 3 lesion visualization co-primary criteria for patient referred for contrast-enhanced MRI of CNS.

Protection of trial subjects:

This trial has been conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, that are consistent with Good Clinical Practice (GCP) according to International Conference on Harmonisation (ICH) guidelines and with the applicable regional/local regulations of the country in which the trial was conducted.
The safety of subjects was assessed over 1 day follow-up period after each MRI visit, for vital signs, injection site tolerance, clinical laboratory parameters and monitoring of adverse events.
For patients enrolled in France: a safety follow-up contact between 7 and 14 days after the last IMP injection was performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 April 2019
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	United States: 46
Country: Number of subjects enrolled	Taiwan: 4
Country: Number of subjects enrolled	Korea, Republic of: 13
Country: Number of subjects enrolled	Mexico: 17
Country: Number of subjects enrolled	Poland: 29
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	France: 6
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Hungary: 104
Country: Number of subjects enrolled	Italy: 23
Worldwide total number of subjects	256
EEA total number of subjects	176

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)	164
From 65 to 84 years	92
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	260[1]
Number of subjects completed	256

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Screen failure: 4

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number of patients presented in the Pre-assignment period (260) is the number of screened patients. Among these patients, 256 were randomized.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Arm title	Overall population

Arm description:

All patients who received at least one injection of one of the 2 contrast agents.

Arm type	Experimental
Investigational medicinal product name	gadopiclenol
Investigational medicinal product code	
Other name	P03277
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

single intravenous bolus injection at 0.05 mmol/kg.
The recommended injection rate was 2 mL/second followed by a saline flush via manual injection or power injector.

Investigational medicinal product name	gadobutrol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Single intravenous bolus injection at 0.1 mmol/kg.
The recommended injection rate was 2 mL/second followed by a saline flush via manual injection or power injector.

Number of subjects in period 1	Overall population
Started	256
Completed	242
Not completed	14
Adverse event other than COVID-19	4
Consent withdrawn by subject	4
COVID-19 pandemic preventing protocol follow-up	3
Inclusion/non-inclusion criteria not met/met	1
Other reason	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial (overall period)

Reporting group description: -

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	256	256	
Age categorical Units: Subjects			
18-64 years	164	164	
≥ 65 years	92	92	
Age continuous Units: years			
arithmetic mean	57.2		
standard deviation	± 13.8	-	
Gender categorical Units: Subjects			
Female	137	137	
Male	119	119	

End points

End points reporting groups

Reporting group title	Overall population
Reporting group description:	
All patients who received at least one injection of one of the 2 contrast agents.	
Subject analysis set title	FAS1 Paired images
Subject analysis set type	Full analysis
Subject analysis set description:	
Full analysis set 1 (FAS1): all patients who have both Pre and Paired images with gadopiclenol assessable for primary criteria 1 for at least one matching lesion for at least one off-site reader	
Subject analysis set title	FAS1 Pre images
Subject analysis set type	Full analysis
Subject analysis set description:	
Full analysis set 1 (FAS1): all patients who have both Pre and Paired images with gadopiclenol assessable for primary criteria 1 for at least one matching lesion for at least one off-site reader	
Subject analysis set title	PPS2 Gadopiclenol
Subject analysis set type	Per protocol
Subject analysis set description:	
Per-Protocol Set 2 (PPS2): all patients from Full Analysis Set 2 (FAS 2) who have no major protocol deviations for primary criteria 2 FAS 2: all patients who have Paired images for both gadopiclenol and gadobutrol assessable for primary criteria 2 for at least one matching lesion for at least one off-site reader	
Subject analysis set title	PPS2 Gadobutrol
Subject analysis set type	Per protocol
Subject analysis set description:	
Per-Protocol Set 2 (PPS2): all patients from Full Analysis Set 2 (FAS 2) who have no major protocol deviations for primary criteria 2 FAS 2: all patients who have Paired images for both gadopiclenol and gadobutrol assessable for primary criteria 2 for at least one matching lesion for at least one off-site reader	

Primary: lesion visualization criteria for gadopiclenol-enhanced MRI compared to unenhanced MRI (off-site read)

End point title	lesion visualization criteria for gadopiclenol-enhanced MRI compared to unenhanced MRI (off-site read)
End point description:	
The lesion visualization criteria were based on 3 co-primary criteria: border delineation, internal morphology and degree of contrast enhancement, assessed on the images acquired during the MRI performed with gadopiclenol. Data presented are the differences in mean of scores for border delineation, internal morphology and degree of contrast enhancement.	
End point type	Primary
End point timeframe:	
1 day procedure	

End point values	FAS1 Paired images	FAS1 Pre images		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	239	239		
Units: None				
least squares mean (standard error)				
Border delineation - Reader 1	3.90 (± 0.02)	2.08 (± 0.02)		

Border delineation - Reader 2	3.64 (± 0.04)	1.74 (± 0.04)		
Border delineation - Reader 3	3.97 (± 0.03)	2.61 (± 0.03)		
Internal morphology - Reader 1	3.92 (± 0.03)	1.66 (± 0.03)		
Internal morphology - Reader 2	3.65 (± 0.03)	1.88 (± 0.03)		
Internal morphology - Reader 3	3.97 (± 0.04)	2.01 (± 0.04)		
Degree of contrast enhancement - Reader 1	3.77 (± 0.03)	1.00 (± 0.03)		
Degree of contrast enhancement - Reader 2	3.58 (± 0.03)	1.00 (± 0.03)		
Degree of contrast enhancement - Reader 3	3.90 (± 0.02)	1.00 (± 0.02)		

Statistical analyses

Statistical analysis title	Border delineation - Reader 1
Statistical analysis description:	
The Null hypothesis is rejected if the difference [“Paired” scores mean – “Pre” scores mean] is significantly different from zero with a type 1 error set at 0.025.	
Comparison groups	FAS1 Paired images v FAS1 Pre images
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	1.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.76
upper limit	1.88
Variability estimate	Standard error of the mean
Dispersion value	0.03

Statistical analysis title	Border delineation - Reader 2
Statistical analysis description:	
The Null hypothesis is rejected if the difference [“Paired” scores mean – “Pre” scores mean] is significantly different from zero with a type 1 error set at 0.025.	
Comparison groups	FAS1 Paired images v FAS1 Pre images
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	1.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.81
upper limit	2
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	Border delineation - Reader 3

Statistical analysis description:

The Null hypothesis is rejected if the difference [“Paired” scores mean – “Pre” scores mean] is significantly different from zero with a type 1 error set at 0.025.

Comparison groups	FAS1 Paired images v FAS1 Pre images
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	1.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.29
upper limit	1.44
Variability estimate	Standard error of the mean
Dispersion value	0.04

Statistical analysis title	Internal morphology - Reader 1

Statistical analysis description:

The Null hypothesis is rejected if the difference [“Paired” scores mean – “Pre” scores mean] is significantly different from zero with a type 1 error set at 0.025.

Comparison groups	FAS1 Paired images v FAS1 Pre images
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	2.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.2
upper limit	2.33

Variability estimate	Standard error of the mean
Dispersion value	0.03

Statistical analysis title	Internal morphology - Reader 2

Statistical analysis description:

The Null hypothesis is rejected if the difference [“Paired” scores mean – “Pre” scores mean] is significantly different from zero with a type 1 error set at 0.025.

Comparison groups	FAS1 Paired images v FAS1 Pre images
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	1.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.69
upper limit	1.85
Variability estimate	Standard error of the mean
Dispersion value	0.04

Statistical analysis title	Internal morphology - Reader 3

Statistical analysis description:

The Null hypothesis is rejected if the difference [“Paired” scores mean – “Pre” scores mean] is significantly different from zero with a type 1 error set at 0.025.

Comparison groups	FAS1 Paired images v FAS1 Pre images
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	1.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.85
upper limit	2.06
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	Degree of contrast enhancement - Reader 1

Statistical analysis description:

The Null hypothesis is rejected if the difference ["Paired" scores mean – "Pre" scores mean] is significantly different from zero with a type 1 error set at 0.025.

Comparison groups	FAS1 Paired images v FAS1 Pre images
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	2.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.69
upper limit	2.85
Variability estimate	Standard error of the mean
Dispersion value	0.04

Statistical analysis title	Degree of contrast enhancement - Reader 2

Statistical analysis description:

The Null hypothesis is rejected if the difference ["Paired" scores mean – "Pre" scores mean] is significantly different from zero with a type 1 error set at 0.025.

Comparison groups	FAS1 Paired images v FAS1 Pre images
Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	2.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.49
upper limit	2.67
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	Degree of contrast enhancement - Reader 3
Comparison groups	FAS1 Paired images v FAS1 Pre images

Number of subjects included in analysis	478
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.84
upper limit	2.95
Variability estimate	Standard error of the mean
Dispersion value	0.03

Primary: Lesion visualization criteria for gadopiclenol compared to gadobutrol (off-site read)

End point title	Lesion visualization criteria for gadopiclenol compared to gadobutrol (off-site read)

End point description:

The lesion visualization criteria were based on 3 co-primary criteria: border delineation, internal morphology and degree of contrast enhancement, assessed on the images acquired during the MRI performed with gadopiclenol and those performed with gadobutrol.
Data presented are the differences in mean of scores for border delineation, internal morphology and degree of contrast enhancement.

End point type	Primary

End point timeframe:

Data from two different MRI (with gadopiclenol and gadobutrol) performed at an interval of 2 to 14 days

End point values	PPS2 Gadopiclenol	PPS2 Gadobutrol		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	236	236		
Units: None				
least squares mean (standard error)				
Border delineation - Reader 1	3.91 (± 0.02)	3.93 (± 0.02)		
Border delineation - Reader 2	3.64 (± 0.04)	3.60 (± 0.04)		
Border delineation - Reader 3	3.97 (± 0.01)	3.95 (± 0.01)		
Internal morphology - Reader 1	3.93 (± 0.02)	3.93 (± 0.02)		
Internal morphology - Reader 2	3.64 (± 0.04)	3.62 (± 0.04)		
Internal morphology - Reader 3	3.97 (± 0.02)	3.92 (± 0.02)		
Degree of contrast enhancement - Reader 1	3.78 (± 0.04)	3.77 (± 0.04)		
Degree of contrast enhancement - Reader 2	3.57 (± 0.04)	3.52 (± 0.04)		
Degree of contrast enhancement - Reader 3	3.89 (± 0.03)	3.81 (± 0.03)		

Statistical analyses

Statistical analysis title	Border delineation - Reader 1

Statistical analysis description:

The Null hypothesis is rejected if the 2-sided 95% Confidence Interval (CI) for the difference [gadopiclenol scores mean – gadobutrol scores mean] had its lower limit above -0.35

Comparison groups	PPS2 Gadopiclenol v PPS2 Gadobutrol
Number of subjects included in analysis	472
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.06
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Border delineation - Reader 2

Statistical analysis description:

The Null hypothesis is rejected if the 2-sided 95% Confidence Interval (CI) for the difference [gadopiclenol scores mean – gadobutrol scores mean] had its lower limit above -0.35

Comparison groups	PPS2 Gadopiclenol v PPS2 Gadobutrol
Number of subjects included in analysis	472
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.11
Variability estimate	Standard error of the mean
Dispersion value	0.04

Statistical analysis title	Border delineation - Reader 3

Statistical analysis description:

The Null hypothesis is rejected if the 2-sided 95% Confidence Interval (CI) for the difference [gadopiclenol scores mean – gadobutrol scores mean] had its lower limit above -0.35

Comparison groups	PPS2 Gadopiclenol v PPS2 Gadobutrol
Number of subjects included in analysis	472
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Internal morphology - Reader 1

Statistical analysis description:

The Null hypothesis is rejected if the 2-sided 95% Confidence Interval (CI) for the difference [gadopiclenol scores mean – gadobutrol scores mean] had its lower limit above -0.35

Comparison groups	PPS2 Gadopiclenol v PPS2 Gadobutrol
Number of subjects included in analysis	472
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Internal morphology - Reader 2

Statistical analysis description:

The Null hypothesis is rejected if the 2-sided 95% Confidence Interval (CI) for the difference [gadopiclenol scores mean – gadobutrol scores mean] had its lower limit above -0.35

Comparison groups	PPS2 Gadopiclenol v PPS2 Gadobutrol
Number of subjects included in analysis	472
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.03

Statistical analysis title	Internal morphology - Reader 3

Statistical analysis description:

The Null hypothesis is rejected if the 2-sided 95% Confidence Interval (CI) for the difference [gadopiclenol scores mean – gadobutrol scores mean] had its lower limit above -0.35

Comparison groups	PPS2 Gadopiclenol v PPS2 Gadobutrol
Number of subjects included in analysis	472
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	0.08
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Degree of contrast enhancement - Reader 1

Statistical analysis description:

The Null hypothesis is rejected if the 2-sided 95% Confidence Interval (CI) for the difference [gadopiclenol scores mean – gadobutrol scores mean] had its lower limit above -0.35

Comparison groups	PPS2 Gadopiclenol v PPS2 Gadobutrol

Number of subjects included in analysis	472
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.07
Variability estimate	Standard error of the mean
Dispersion value	0.03

Statistical analysis title	Degree of contrast enhancement - Reader 2

Statistical analysis description:

The Null hypothesis is rejected if the 2-sided 95% Confidence Interval (CI) for the difference [gadopiclenol scores mean – gadobutrol scores mean] had its lower limit above -0.35

Comparison groups	PPS2 Gadopiclenol v PPS2 Gadobutrol
Number of subjects included in analysis	472
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.12
Variability estimate	Standard error of the mean
Dispersion value	0.04

Notes:

[1] - The Null hypothesis is rejected if the 2-sided 95% Confidence Interval (CI) for the difference [gadopiclenol scores mean – gadobutrol scores mean] had its lower limit above -0.35

Statistical analysis title	Degree of contrast enhancement - Reader 3

Statistical analysis description:

The Null hypothesis is rejected if the 2-sided 95% Confidence Interval (CI) for the difference [gadopiclenol scores mean – gadobutrol scores mean] had its lower limit above -0.35

Comparison groups	PPS2 Gadopiclenol v PPS2 Gadobutrol

Number of subjects included in analysis	472
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	0.15
Variability estimate	Standard error of the mean
Dispersion value	0.03

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded from informed consent signature up to one day after the second MRI. For patients enrolled in France: a safety follow-up contact between 7 and 14 days after the last IMP injection was performed.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Safety Set - Gadopiclenol

Reporting group description:

All patients having received at least one injection of gadopiclenol regardless of the quantity

Reporting group title	Safety Set - Gadobutrol

Reporting group description:

All patients having received at least one injection of gadobutrol regardless of the quantity

Serious adverse events	Safety Set - Gadopiclenol	Safety Set - Gadobutrol	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 247 (0.00%)	1 / 245 (0.41%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
General physical health deterioration	Additional description: Worsening General Condition Leading To Fatal Respiratory Failure Not related to contrast		
subjects affected / exposed	0 / 247 (0.00%)	1 / 245 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Safety Set - Gadopiclenol	Safety Set - Gadobutrol	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 247 (14.57%)	42 / 245 (17.14%)	
Vascular disorders			
Pallor			

subjects affected / exposed	1 / 247 (0.40%)	0 / 245 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	5 / 247 (2.02%)	5 / 245 (2.04%)	
occurrences (all)	5	5	
Injection site bruising			
subjects affected / exposed	3 / 247 (1.21%)	3 / 245 (1.22%)	
occurrences (all)	3	3	
Injection site erythema			
subjects affected / exposed	1 / 247 (0.40%)	3 / 245 (1.22%)	
occurrences (all)	1	3	
Injection site coldness			
subjects affected / exposed	2 / 247 (0.81%)	1 / 245 (0.41%)	
occurrences (all)	2	1	
Injection site warmth			
subjects affected / exposed	1 / 247 (0.40%)	2 / 245 (0.82%)	
occurrences (all)	1	2	
Injection site haematoma			
subjects affected / exposed	1 / 247 (0.40%)	1 / 245 (0.41%)	
occurrences (all)	1	1	
Injection site haemorrhage			
subjects affected / exposed	0 / 247 (0.00%)	2 / 245 (0.82%)	
occurrences (all)	0	2	
Injection site paraesthesia			
subjects affected / exposed	1 / 247 (0.40%)	1 / 245 (0.41%)	
occurrences (all)	1	1	
Vessel puncture site haemorrhage			
subjects affected / exposed	0 / 247 (0.00%)	2 / 245 (0.82%)	
occurrences (all)	0	5	
Asthenia			
subjects affected / exposed	0 / 247 (0.00%)	1 / 245 (0.41%)	
occurrences (all)	0	1	
Drug ineffective			

subjects affected / exposed	1 / 247 (0.40%)	0 / 245 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	1 / 247 (0.40%)	0 / 245 (0.00%)	
occurrences (all)	1	0	
Feeling hot			
subjects affected / exposed	1 / 247 (0.40%)	0 / 245 (0.00%)	
occurrences (all)	1	0	
Injection site discomfort			
subjects affected / exposed	1 / 247 (0.40%)	0 / 245 (0.00%)	
occurrences (all)	1	0	
Injection site extravasation			
subjects affected / exposed	0 / 247 (0.00%)	1 / 245 (0.41%)	
occurrences (all)	0	1	
Injection site hypoaesthesia			
subjects affected / exposed	0 / 247 (0.00%)	1 / 245 (0.41%)	
occurrences (all)	0	1	
Injection site oedema			
subjects affected / exposed	1 / 247 (0.40%)	0 / 245 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	1 / 247 (0.40%)	0 / 245 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 247 (0.00%)	1 / 245 (0.41%)	
occurrences (all)	0	1	
Psychiatric disorders			
Claustrophobia			
subjects affected / exposed	1 / 247 (0.40%)	0 / 245 (0.00%)	
occurrences (all)	1	0	
Sleep disorder			
subjects affected / exposed	0 / 247 (0.00%)	1 / 245 (0.41%)	
occurrences (all)	0	1	
Investigations			

Blood creatinine increased			
subjects affected / exposed	1 / 247 (0.40%)	5 / 245 (2.04%)	
occurrences (all)	1	5	
Blood phosphorus decreased			
subjects affected / exposed	1 / 247 (0.40%)	0 / 245 (0.00%)	
occurrences (all)	1	0	
Neutrophil count increased			
subjects affected / exposed	1 / 247 (0.40%)	0 / 245 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Incorrect dose administered			
subjects affected / exposed	2 / 247 (0.81%)	1 / 245 (0.41%)	
occurrences (all)	2	1	
Cardiac disorders			
Tachycardia			
subjects affected / exposed	1 / 247 (0.40%)	0 / 245 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 247 (0.81%)	5 / 245 (2.04%)	
occurrences (all)	2	5	
Dizziness			
subjects affected / exposed	5 / 247 (2.02%)	1 / 245 (0.41%)	
occurrences (all)	5	1	
Dysgeusia			
subjects affected / exposed	1 / 247 (0.40%)	2 / 245 (0.82%)	
occurrences (all)	1	2	
Partial seizures			
subjects affected / exposed	1 / 247 (0.40%)	2 / 245 (0.82%)	
occurrences (all)	1	2	
Blood and lymphatic system disorders			
Anaemia macrocytic			
subjects affected / exposed	0 / 247 (0.00%)	1 / 245 (0.41%)	
occurrences (all)	0	1	
Eye disorders			

Scleral haemorrhage			
subjects affected / exposed	0 / 247 (0.00%)	1 / 245 (0.41%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 247 (1.62%)	1 / 245 (0.41%)	
occurrences (all)	4	1	
Paraesthesia oral			
subjects affected / exposed	1 / 247 (0.40%)	0 / 245 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	0 / 247 (0.00%)	1 / 245 (0.41%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	1 / 247 (0.40%)	1 / 245 (0.41%)	
occurrences (all)	1	1	
Erythema			
subjects affected / exposed	1 / 247 (0.40%)	1 / 245 (0.41%)	
occurrences (all)	1	1	
Ecchymosis			
subjects affected / exposed	0 / 247 (0.00%)	1 / 245 (0.41%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	0 / 247 (0.00%)	1 / 245 (0.41%)	
occurrences (all)	0	1	
Rash macular			
subjects affected / exposed	0 / 247 (0.00%)	1 / 245 (0.41%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Groin pain			
subjects affected / exposed	0 / 247 (0.00%)	1 / 245 (0.41%)	
occurrences (all)	0	1	
Myofascial pain syndrome			
subjects affected / exposed	1 / 247 (0.40%)	0 / 245 (0.00%)	
occurrences (all)	1	0	

Pain in extremity subjects affected / exposed occurrences (all)	1 / 247 (0.40%) 1	0 / 245 (0.00%) 0	
Infections and infestations Sinusitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 247 (0.40%) 1 1 / 247 (0.40%) 1	0 / 245 (0.00%) 0 0 / 245 (0.00%) 0	
Metabolism and nutrition disorders Hypoglycaemia subjects affected / exposed occurrences (all)	1 / 247 (0.40%) 1	0 / 245 (0.00%) 0	

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