Clinical trial results:
Treatment of chronic subdural hematoma by corticosteroids : a prospective randomized study

Summary

EudraCT number	2015-000927-96
Trial protocol	FR
Global end of trial date	20 March 2019

Results information

Result version number	v1 (current)
This version publication date	12 January 2024
First version publication date	12 January 2024

Trial information

Trial identification

Sponsor protocol code	SUCRE

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02650609
WHO universal trial number (UTN)	-
Other trial identifiers	SUCRE: Morandi SUCRE

Notes:

Sponsors

Sponsor organisation name	CHU de Rennes
Sponsor organisation address	2 rue Henri Le Guilloux, Rennes, France, 35000
Public contact	Ganivet, CHU of Rennes, 33 299282555, anne.ganivet@chu-rennes.fr
Scientific contact	Ganivet, CHU of Rennes, 33 299282555, anne.ganivet@chu-rennes.fr

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 March 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 March 2019
Global end of trial reached?	Yes
Global end of trial date	20 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To show that a treatment with methylprednisolone can decrease the need for surgical treatment in patients with chronic subdural hematoma without clinical or radiological signs of severity

Protection of trial subjects:

An independent Data and Safety Monitoring Board will be constituted at the beginning of the study with 5
members who are not involved in the study, including a neurosurgeon, a neurologist, a pharmacologist, a
methodologist, and a statistician.
In order to prematurely stop the study in case of efficacy, two interim analyses are planned. These analyses
will be performed on the primary endpoint but will also evaluate safety data in order to rapidly detect any
unexpected serious adverse events due to the absence of systematic surgical treatment or to corticosteroids.
The Data and Safety Monitoring Board will meet after each interim analysis and at the end of the study. It
can also meet on request of the coordinating investigator or the methodologist if serious adverse events or
results which can jeopardize the existence of the protocol occur.
The Data and Safety Monitoring Board will propose to stop the study if the interim statistical analyses reache significance or if it appears that study continuation would be contrary to ethics rules (occurrence of
serious adverse events, publication of trial results providing the answer to the question...).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 198
Worldwide total number of subjects	198
EEA total number of subjects	198

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)	38
From 65 to 84 years	123
85 years and over	37

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The screening phase will take place during the hospitalisation or the consultation during which the diagnosis
of CSDH will be confirmed

Period 1

Period 1 title	Baseline V1 (D0)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Blinding implementation details:

This study is double-blind. Active treatment and placebo will be identical and prepared in capsules by the PPRIGO platform at Brest University Hospital

Arms

Are arms mutually exclusive?	Yes
Arm title	Methylprednisolone

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Methylprednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

Capsules will be administered orally in the morning, during breakfast with a glass of water.
Dose is adapted according to the weight of the patient (1mg/kg):
- <60 kg: 3 pills of 16 mg/day
- 60-80kg: 4 pills of 16 mg/day
- >80kg: 5 pills of 16 mg/day
The duration of the treatment is 21 days. No progressive decrease of treatment dose is necessary because
treatment duration is less than one month.
The duration of treatment was choosen to avoid the necessity of progressive decrease of treatment dose and
is supported by the pathophysiology of the CSDH formation (inflammatory process supposed to be maximal
at 2 to 3 weeks).

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

Active treatment and placebo will be identical

Number of subjects in period 1	Methylprednisolone	Placebo
Started	99	99
Completed	99	99

Period 2	
Period 2 title	Follow-up visits
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Methylprednisolone

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Methylprednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

Capsules will be administered orally in the morning, during breakfast with a glass of water.
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treatment duration is less than one month.
The duration of treatment was choosen to avoid the necessity of progressive decrease of treatment dose and
is supported by the pathophysiology of the CSDH formation (inflammatory process supposed to be maximal
at 2 to 3 weeks).

Arm title	Placebo

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

Active treatment and placebo will be identical

Number of subjects in period 2	Methylprednisolone	Placebo
Started	99	99
Completed	99	99

Period 3	
Period 3 title	Day 7
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Methylprednisolone

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Methylprednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

Capsules will be administered orally in the morning, during breakfast with a glass of water.
Dose is adapted according to the weight of the patient (1mg/kg):
- <60 kg: 3 pills of 16 mg/day
- 60-80kg: 4 pills of 16 mg/day
- >80kg: 5 pills of 16 mg/day
The duration of the treatment is 21 days. No progressive decrease of treatment dose is necessary because
treatment duration is less than one month.
The duration of treatment was choosen to avoid the necessity of progressive decrease of treatment dose and
is supported by the pathophysiology of the CSDH formation (inflammatory process supposed to be maximal
at 2 to 3 weeks).

Arm title	Placebo

Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

Active treatment and placebo will be identical

Number of subjects in period 3	Methylprednisolone	Placebo
Started	99	99
Completed	99	99

Period 4	
Period 4 title	Day 14
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms	
Are arms mutually exclusive?	Yes
Arm title	Methylprednisolone

Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Methylprednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

Capsules will be administered orally in the morning, during breakfast with a glass of water.
Dose is adapted according to the weight of the patient (1mg/kg):
- <60 kg: 3 pills of 16 mg/day
- 60-80kg: 4 pills of 16 mg/day
- >80kg: 5 pills of 16 mg/day

The duration of the treatment is 21 days. No progressive decrease of treatment dose is necessary because
treatment duration is less than one month.
The duration of treatment was choosen to avoid the necessity of progressive decrease of treatment dose and
is supported by the pathophysiology of the CSDH formation (inflammatory process supposed to be maximal
at 2 to 3 weeks).

Arm title	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

Active treatment and placebo will be identical

Number of subjects in period 4	Methylprednisolone	Placebo
Started	99	99
Completed	99	99

Period 5	
Period 5 title	Day 21
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Methylprednisolone
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Methylprednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

Capsules will be administered orally in the morning, during breakfast with a glass of water.
Dose is adapted according to the weight of the patient (1mg/kg):
- <60 kg: 3 pills of 16 mg/day
- 60-80kg: 4 pills of 16 mg/day
- >80kg: 5 pills of 16 mg/day
The duration of the treatment is 21 days. No progressive decrease of treatment dose is necessary because
treatment duration is less than one month.
The duration of treatment was choosen to avoid the necessity of progressive decrease of treatment dose and
is supported by the pathophysiology of the CSDH formation (inflammatory process supposed to be maximal

at 2 to 3 weeks).

Arm title	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

Active treatment and placebo will be identical

Number of subjects in period 5	Methylprednisolone	Placebo
Started	99	99
Completed	99	99

Period 6	
Period 6 title	Month 1
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Methylprednisolone
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Methylprednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

Capsules will be administered orally in the morning, during breakfast with a glass of water.
Dose is adapted according to the weight of the patient (1mg/kg):
- <60 kg: 3 pills of 16 mg/day
- 60-80kg: 4 pills of 16 mg/day

- >80kg: 5 pills of 16 mg/day
The duration of the treatment is 21 days. No progressive decrease of treatment dose is necessary because
treatment duration is less than one month.
The duration of treatment was choosen to avoid the necessity of progressive decrease of treatment dose and
is supported by the pathophysiology of the CSDH formation (inflammatory process supposed to be maximal
at 2 to 3 weeks).

Arm title	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

Active treatment and placebo will be identical

Number of subjects in period 6	Methylprednisolone	Placebo
Started	99	99
Completed	99	99

Period 7

Period 7 title	Month 3
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Methylprednisolone
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Methylprednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

Capsules will be administered orally in the morning, during breakfast with a glass of water.
Dose is adapted according to the weight of the patient (1mg/kg):

- <60 kg: 3 pills of 16 mg/day
- 60-80kg: 4 pills of 16 mg/day
- >80kg: 5 pills of 16 mg/day
The duration of the treatment is 21 days. No progressive decrease of treatment dose is necessary because
treatment duration is less than one month.
The duration of treatment was choosen to avoid the necessity of progressive decrease of treatment dose and
is supported by the pathophysiology of the CSDH formation (inflammatory process supposed to be maximal
at 2 to 3 weeks).

Arm title	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

Active treatment and placebo will be identical

Number of subjects in period 7	Methylprednisolone	Placebo
Started	99	99
Completed	99	99

Period 8	
Period 8 title	Month 6
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Methylprednisolone
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Methylprednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

Capsules will be administered orally in the morning, during breakfast with a glass of water.
Dose is adapted according to the weight of the patient (1mg/kg):
- <60 kg: 3 pills of 16 mg/day
- 60-80kg: 4 pills of 16 mg/day
- >80kg: 5 pills of 16 mg/day
The duration of the treatment is 21 days. No progressive decrease of treatment dose is necessary because
treatment duration is less than one month.
The duration of treatment was choosen to avoid the necessity of progressive decrease of treatment dose and
is supported by the pathophysiology of the CSDH formation (inflammatory process supposed to be maximal
at 2 to 3 weeks).

Arm title	Placebo
Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Pillules
Routes of administration	Oral use

Dosage and administration details:

Active treatment and placebo will be identical

Number of subjects in period 8	Methylprednisolone	Placebo
Started	99	99
Completed	99	99

Baseline characteristics

Reporting groups	
Reporting group title	Methylprednisolone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Methylprednisolone	Placebo	Total
Number of subjects	99	99	198
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	73.86	73.92	
standard deviation	± 13.87	± 11.86	-
Gender categorical Units: Subjects			
Female	23	28	51
Male	76	71	147

End points

End points reporting groups

Reporting group title	Methylprednisolone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Methylprednisolone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Methylprednisolone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Methylprednisolone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Methylprednisolone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Methylprednisolone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Methylprednisolone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Methylprednisolone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Methylprednisolone
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Delay of occurrence of surgical treatment

End point title	Delay of occurrence of surgical treatment

End point description:

The primary evaluation criterion is the delay of occurrence of surgical treatment (censored criteria) of the
CSDH at one month

End point type	Primary

End point timeframe:

during the month following the diagnosis of CSDH (Chronic subdural hematomas)

End point values	Methylprednisolone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	99		
Units: day	4	12		

Statistical analyses

Statistical analysis title	Survival probability
Statistical analysis description: Survival probability at 30 days	
Comparison groups	Methylprednisolone v Placebo
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0313
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.96

Secondary: Time to surgical treatment during the first 6 months (censored criteria)

End point title	Time to surgical treatment during the first 6 months (censored criteria)
End point description:	
End point type	Secondary
End point timeframe: At 180 days	

End point values	Methylprednisolone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	99		
Units: days	10	18		

Statistical analyses

Statistical analysis title	Survival probability
Comparison groups	Methylprednisolone v Placebo
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0864
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.24
upper limit	1.12

Secondary: SF12: Quality of life assessed by the SF12 scale - PCS

End point title	SF12: Quality of life assessed by the SF12 scale - PCS
End point description:	
End point type	Secondary
End point timeframe:	
At 1, 3 and 6 months	

End point values	Methylprednisolone	Placebo	Methylprednisolone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	85	83	84
Units: unit(s)				
arithmetic mean (standard deviation)	43.46 (± 8.48)	45.40 (± 7.54)	47.58 (± 8.29)	46.34 (± 8.94)

End point values	Methylprednisolone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	75		
Units: unit(s)				
arithmetic mean (standard deviation)	47.6 (± 8.4)	48.10 (± 7.97)		

Attachments (see zip file)	CHART_SF12-PCS_SUCRE.JPG

Statistical analyses

Statistical analysis title	Visit
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANOVA

Statistical analysis title	Group
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8002
Method	ANOVA

Statistical analysis title	Visit*Group
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0732
Method	ANOVA

Secondary: SF12: Quality of life assessed by the SF12 scale - MCS

End point title	SF12: Quality of life assessed by the SF12 scale - MCS

End point description:

End point type	Secondary

End point timeframe:

At 1, 3 and 6 months

End point values	Methylprednisolone	Placebo	Methylprednisolone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	85	83	84
Units: unit(s)				
arithmetic mean (standard deviation)	47.27 (± 10.93)	48.28 (± 10.89)	49.32 (± 9.70)	51.34 (± 9.15)

End point values	Methylprednisolone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	75		
Units: unit(s)				
arithmetic mean (standard deviation)	50.73 (± 9.03)	50.44 (± 9.87)		

Attachments (see zip file)	CHART_SF12-MCS_SUCRE.JPG

Statistical analyses

Statistical analysis title	Visit
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANOVA

Statistical analysis title	Group
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3861
Method	ANOVA

Statistical analysis title	Visit*Group
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	490
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2982
Method	ANOVA

Secondary: Rate of surgical treatment of the CSDH

End point title	Rate of surgical treatment of the CSDH

End point description:

End point type	Secondary

End point timeframe:

At 1, 3 and 6 months

End point values	Methylprednisolone	Placebo	Methylprednisolone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	96	93	90	92
Units: %	4	12	9	17

End point values	Methylprednisolone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	87		
Units: %	10	18		

Statistical analyses

Statistical analysis title	M1
Comparison groups	Methylprednisolone v Placebo
Number of subjects included in analysis	189
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.031
Method	Chi-squared

Statistical analysis title	M3
Comparison groups	Methylprednisolone v Placebo
Number of subjects included in analysis	182
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1022
Method	Chi-squared

Statistical analysis title	M6
Comparison groups	Methylprednisolone v Placebo

Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1057
Method	Chi-squared

Secondary: Functional scales: daily living (IADL)

End point title	Functional scales: daily living (IADL)

End point description:

End point type	Secondary

End point timeframe:

At 1, 3 and 6 months

End point values	Methylprednisolone	Placebo	Methylprednisolone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	88	87	82	83
Units: unit(s)				
arithmetic mean (standard deviation)	6.68 (± 2.03)	6.85 (± 1.85)	7.01 (± 1.65)	7.0 (± 1.70)

End point values	Methylprednisolone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	75		
Units: unit(s)				
arithmetic mean (standard deviation)	6.91 (± 1.74)	7.28 (± 1.57)		

Statistical analyses

Statistical analysis title	Visit
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	493
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0483
Method	ANOVA

	Group

Statistical analysis title	
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	493
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5519
Method	ANOVA

Statistical analysis title	Visit*Group
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	493
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1678
Method	ANOVA

Secondary: Functional scales: cognitive (MMSE)	
End point title	Functional scales: cognitive (MMSE)
End point description:	
End point type	Secondary
End point timeframe:	
At 1, 3 and 6 months	

End point values	Methylprednisolone	Placebo	Methylprednisolone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86	86	83	82
Units: unit(s)				
arithmetic mean (standard deviation)	26.58 (± 3.5)	27.33 (± 3.2)	27.01 (± 3.4)	27.61 (± 2.96)

End point values	Methylprednisolone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	75		
Units: unit(s)				
arithmetic mean (standard deviation)	27.28 (± 3.19)	27.2 (± 3.31)		

Statistical analyses

Statistical analysis title	Visit
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANOVA

Statistical analysis title	Group
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2349
Method	ANOVA

Statistical analysis title	Visit*Group
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.302
Method	ANOVA

Secondary: Functional scales: modified Rankin Scale (mRs)	
End point title	Functional scales: modified Rankin Scale (mRs)
End point description:	

End point type	Secondary
End point timeframe:	
At 1, 3 and 6 months	

End point values	Methylprednisolone	Placebo	Methylprednisolone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	90	87	85	85
Units: unit(s)				
arithmetic mean (standard deviation)	0.83 (± 1.10)	0.82 (± 1.04)	0.55 (± 0.92)	0.53 (± 0.87)

End point values	Methylprednisolone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	75		
Units: unit(s)				
arithmetic mean (standard deviation)	0.35 (± 0.82)	0.28 (± 0.71)		

Statistical analyses

Statistical analysis title	Visit
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANOVA

Statistical analysis title	Group
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8494
Method	ANOVA

Statistical analysis title	Visit*Group
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo

Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8655
Method	ANOVA

Secondary: Plasma sodium

End point title	Plasma sodium

End point description:

End point type	Secondary

End point timeframe:

At day 0, 7, 14, and 21 and at 1-month

End point values	Methylprednisolone	Placebo	Methylprednisolone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	85	86	89	85
Units: mmol/L				
arithmetic mean (standard deviation)	139.24 (± 3.13)	139.65 (± 3.06)	139.49 (± 3.52)	139.89 (± 3.34)

End point values	Methylprednisolone	Placebo	Methylprednisolone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	84	85	80	81
Units: mmol/L				
arithmetic mean (standard deviation)	138.75 (± 3.96)	139.91 (± 3.57)	139.03 (± 3.59)	140.99 (± 2.77)

End point values	Methylprednisolone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	74		
Units: mmol/L				
arithmetic mean (standard deviation)	139.33 (± 3.77)	140.33 (± 3.10)		

Statistical analyses

Statistical analysis title	Visit
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	818
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0031
Method	ANOVA

Statistical analysis title	Group
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	818
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0405
Method	ANOVA

Statistical analysis title	Visit*Group
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	818
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0009
Method	ANOVA

Secondary: Plasma potassium

End point title	Plasma potassium

End point description:

End point type	Secondary

End point timeframe:

At 0, 7, 14 and 21 days and Month 1

End point values	Methylprednisolone	Placebo	Methylprednisolone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	85	85	89	85
Units: mmol/L				
arithmetic mean (standard deviation)	4.16 (± 0.37)	4.15 (± 0.46)	4.26 (± 0.5)	4.46 (± 0.54)

End point values	Methylprednisolone	Placebo	Methylprednisolone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	84	85	80	80
Units: mmol/L				
arithmetic mean (standard deviation)	4.45 (± 0.57)	4.56 (± 0.54)	4.44 (± 0.48)	4.49 (± 0.47)

End point values	Methylprednisolone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	74		
Units: mmol/L				
arithmetic mean (standard deviation)	4.35 (± 0.40)	4.42 (± 0.40)		

Statistical analyses

Statistical analysis title	Visit
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	816
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANOVA

Statistical analysis title	Group
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	816
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1712
Method	ANOVA

Statistical analysis title	Visit*Group
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	816
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1649
Method	ANOVA

Secondary: Fasting glucose

End point title	Fasting glucose

End point description:

End point type	Secondary

End point timeframe:

At 0, 7, 14 and 21 days and Month 1

End point values	Methylprednisolone	Placebo	Methylprednisolone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	80	81	87	84
Units: g/l				
arithmetic mean (standard deviation)	1.02 (± 0.20)	0.95 (± 0.12)	0.92 (± 0.23)	0.96 (± 0.12)

End point values	Methylprednisolone	Placebo	Methylprednisolone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	82	84	77	81
Units: g/l				
arithmetic mean (standard deviation)	0.91 (± 0.24)	0.95 (± 0.12)	0.90 (± 0.25)	0.94 (± 0.11)

End point values	Methylprednisolone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	71		
Units: g/l				
arithmetic mean (standard deviation)	1.01 (± 0.25)	0.95 (± 0.14)		

Statistical analyses

Statistical analysis title	Visit
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	794
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANOVA

Statistical analysis title	Group
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	794
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0273
Method	ANOVA

Statistical analysis title	Visit*Group
Comparison groups	Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo v Methylprednisolone v Placebo
Number of subjects included in analysis	794
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANOVA

Secondary: Survival

End point title	Survival

End point description:

End point type	Secondary

End point timeframe:

At 6 months

End point values	Methylprednisolone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	99	99		
Units: Day	2	1		

Statistical analyses

Statistical analysis title	Survival probability
Comparison groups	Methylprednisolone v Placebo
Number of subjects included in analysis	198
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5679
Method	Logrank

Secondary: Radiological improvement

End point title	Radiological improvement

End point description:

End point type	Secondary

End point timeframe:

At 1, 3 and 6 months

End point values	Methylprednisolone	Placebo	Methylprednisolone	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	92	91	89	88
Units: %	79	71	75	80

End point values	Methylprednisolone	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	81		
Units: %	58	65		

Statistical analyses

Statistical analysis title	M1
Comparison groups	Methylprednisolone v Placebo
Number of subjects included in analysis	183
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1674
Method	Chi-squared

Statistical analysis title	M3
Comparison groups	Methylprednisolone v Placebo
Number of subjects included in analysis	177
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1807
Method	Chi-squared

Statistical analysis title	M6
Comparison groups	Methylprednisolone v Placebo
Number of subjects included in analysis	161
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2471
Method	Chi-squared

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From 24/06/2016 to 20/03/2019	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	Methylprednisolone at M6

Reporting group description:

Methylprednisolone is administered orally with one administration in the morning during breakfast with water. Dose is adapted according to the weight of the patient (1mg/kg):
<60 kg : 3 pills of 16 mg/day
60-80kg : 4 pills of 16 mg/day
>80kg : 5 pills of 16 mg/day
Treatment is prescribed for 3 weeks with a sudden stop without decrease.

Reporting group title	Placebo at M6
Reporting group description: -	
Reporting group title	Methylprednisolone at M2
Reporting group description: -	
Reporting group title	Placebo at M2

Reporting group description: -

Serious adverse events	Methylprednisolone at M6	Placebo at M6	Methylprednisolone at M2
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 95 (17.89%)	10 / 94 (10.64%)	15 / 95 (15.79%)
number of deaths (all causes)	0	2	2
number of deaths resulting from adverse events	0	2	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic neoplasm			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Vascular disorders			
Venous thrombosis	Additional description: Venous thrombosis / Pulmonary embolism		
subjects affected / exposed	1 / 95 (1.05%)	2 / 94 (2.13%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Hypertension			

subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	1 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Subdural haematoma evacuation			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palliative care			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial appendage closure	Additional description: "Left atrial appendage occlusion"		
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fall			
subjects affected / exposed	3 / 95 (3.16%)	5 / 94 (5.32%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 4	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Asthenia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Condition aggravated			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	2 / 95 (2.11%)	0 / 94 (0.00%)	2 / 95 (2.11%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1

Inflammation			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Chest pain			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcoholism			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcohol withdrawal syndrome			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Craniocerebral injury			
subjects affected / exposed	1 / 95 (1.05%)	2 / 94 (2.13%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accidental overdose			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medication error			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcohol poisoning			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax traumatic			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prescribed overdose			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Supraventricular tachycardia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Headache			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	6 / 95 (6.32%)	2 / 94 (2.13%)	3 / 95 (3.16%)
occurrences causally related to treatment / all	0 / 6	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	2 / 95 (2.11%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VIIth nerve injury	Additional description: "VIIth nerve paralysis"		
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aphasia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sensorimotor disorder			

subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Dementia with Lewy bodies			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Normochromic normocytic anaemia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Rectal haemorrhage			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			

subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia strangulated			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Intestinal obstruction			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Hiatus hernia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenocortical insufficiency acute			
subjects affected / exposed	3 / 95 (3.16%)	0 / 94 (0.00%)	3 / 95 (3.16%)
occurrences causally related to treatment / all	3 / 3	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glucocorticoid deficiency			
subjects affected / exposed	2 / 95 (2.11%)	1 / 94 (1.06%)	2 / 95 (2.11%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Neck pain			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung diffusion disorder	Additional description: Lung infection		
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Urinary tract infection			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Bronchopneumopathy	Additional description: Bronchopneumonia		
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			

subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus	Additional description: "Diabetes"		
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo at M2		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 94 (5.32%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic neoplasm			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Venous thrombosis	Additional description: Venous thrombosis / Pulmonary embolism		

subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Subdural haematoma evacuation				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Palliative care				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial appendage closure	Additional description: "Left atrial appendage occlusion"			
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Fall				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Asthenia				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Condition aggravated				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

General physical health deterioration				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inflammation				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Prostatitis				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Agitation				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hallucination				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Alcoholism				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Alcohol withdrawal syndrome				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Femur fracture				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Craniocerebral injury				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Accidental overdose				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Medication error				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal fracture				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Alcohol poisoning				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Subdural haematoma				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Traumatic intracranial haemorrhage				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax traumatic				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prescribed overdose				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial fibrillation				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardio-respiratory arrest				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				

subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Headache				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
VIIth nerve injury	Additional description: "VIIth nerve paralysis"			
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cognitive disorder				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aphasia				

subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sensorimotor disorder				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subarachnoid haemorrhage				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dementia with Lewy bodies				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Thrombocytopenia				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anaemia				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Normochromic normocytic anaemia				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Rectal haemorrhage				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophagitis				

subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia strangulated				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hiatus hernia				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Urinary retention				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute kidney injury				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Adrenocortical insufficiency acute				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Glucocorticoid deficiency				

subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung diffusion disorder	Additional description: Lung infection		
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchopneumopathy	Additional description: Bronchopneumonia		
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetes mellitus	Additional description: "Diabetes"		
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gout			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperkalaemia			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Methylprednisolone at M6	Placebo at M6	Methylprednisolone at M2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 95 (50.53%)	36 / 94 (38.30%)	43 / 95 (45.26%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Parathyroid tumour benign			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Salivary gland neoplasm			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0

Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Meningioma			
subjects affected / exposed	0 / 95 (0.00%)	2 / 94 (2.13%)	0 / 95 (0.00%)
occurrences (all)	0	2	0
Metastatic neoplasm			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Venous thrombosis	Additional description: Venous thrombosis / Pulmonary embolism		
subjects affected / exposed	2 / 95 (2.11%)	2 / 94 (2.13%)	1 / 95 (1.05%)
occurrences (all)	3	2	2
Hypertension			
subjects affected / exposed	4 / 95 (4.21%)	3 / 94 (3.19%)	1 / 95 (1.05%)
occurrences (all)	4	3	1
Haematoma			
subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	1 / 95 (1.05%)
occurrences (all)	1	1	1
Microangiopathy			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	2	0
Surgical and medical procedures			
Subdural haematoma evacuation			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Palliative care			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Rehabilitation therapy			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Left atrial appendage closure implant			

subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Cataract operation			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Prostate ablation			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Weight increased			
subjects affected / exposed	3 / 95 (3.16%)	1 / 94 (1.06%)	3 / 95 (3.16%)
occurrences (all)	3	1	3
Hypokalaemia			
subjects affected / exposed	2 / 95 (2.11%)	2 / 94 (2.13%)	2 / 95 (2.11%)
occurrences (all)	2	2	2
Oedema peripheral			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Diabetes mellitus	Additional description: "Diabetes"		
subjects affected / exposed	2 / 95 (2.11%)	0 / 94 (0.00%)	2 / 95 (2.11%)
occurrences (all)	2	0	2
Hyperglycaemia			
subjects affected / exposed	8 / 95 (8.42%)	6 / 94 (6.38%)	8 / 95 (8.42%)
occurrences (all)	8	6	8
Gout			
subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	1	1	0
Hyperthermia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Asthenia			
subjects affected / exposed	7 / 95 (7.37%)	6 / 94 (6.38%)	7 / 95 (7.37%)
occurrences (all)	7	6	7
Fatigue			

subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Gait disturbance			
subjects affected / exposed	2 / 95 (2.11%)	2 / 94 (2.13%)	1 / 95 (1.05%)
occurrences (all)	2	3	1
Condition aggravated			
subjects affected / exposed	2 / 95 (2.11%)	0 / 94 (0.00%)	2 / 95 (2.11%)
occurrences (all)	2	0	2
General physical health deterioration			
subjects affected / exposed	2 / 95 (2.11%)	3 / 94 (3.19%)	2 / 95 (2.11%)
occurrences (all)	2	3	2
Influenza like illness			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Walking disability	Additional description: Abasia		
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Inflammation			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Prostatitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Erectile dysfunction			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			

Dyspnoea			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Lung disorder			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Interstitial lung disease			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	11 / 95 (11.58%)	1 / 94 (1.06%)	9 / 95 (9.47%)
occurrences (all)	11	1	9
Anxiety			
subjects affected / exposed	2 / 95 (2.11%)	2 / 94 (2.13%)	1 / 95 (1.05%)
occurrences (all)	2	2	1
Nervousness			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Confusional state			
subjects affected / exposed	4 / 95 (4.21%)	1 / 94 (1.06%)	4 / 95 (4.21%)
occurrences (all)	4	2	4
Depression			
subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	1 / 95 (1.05%)
occurrences (all)	1	1	1
Depressed mood			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Persecutory delusion			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Hallucination			

subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	1 / 95 (1.05%)
occurrences (all)	1	1	1
Euphoric mood			
subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	1 / 95 (1.05%)
occurrences (all)	1	1	1
Irritability			
subjects affected / exposed	2 / 95 (2.11%)	0 / 94 (0.00%)	2 / 95 (2.11%)
occurrences (all)	2	0	2
Affective disorder			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Apathy			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Abnormal behaviour			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Sleep disorder			
subjects affected / exposed	20 / 95 (21.05%)	5 / 94 (5.32%)	20 / 95 (21.05%)
occurrences (all)	21	5	21
Delirium tremens			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Alcoholism			
subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	1 / 95 (1.05%)
occurrences (all)	1	1	1
Withdrawal syndrome			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Alcohol abuse			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Alcohol withdrawal syndrome			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Investigations			

Weight decreased			
subjects affected / exposed	3 / 95 (3.16%)	2 / 94 (2.13%)	3 / 95 (3.16%)
occurrences (all)	3	2	3
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	5 / 95 (5.26%)	11 / 94 (11.70%)	2 / 95 (2.11%)
occurrences (all)	6	12	2
Femur fracture			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Rib fracture			
subjects affected / exposed	0 / 95 (0.00%)	2 / 94 (2.13%)	0 / 95 (0.00%)
occurrences (all)	0	2	0
Craniocerebral injury			
subjects affected / exposed	1 / 95 (1.05%)	7 / 94 (7.45%)	1 / 95 (1.05%)
occurrences (all)	2	7	1
Accidental overdose			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Medication error			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Myocardial necrosis marker increased			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Foot fracture			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Spinal fracture			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Alcohol poisoning			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Subdural haematoma			

subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Pneumothorax traumatic			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Wound			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Limb injury			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Skin wound			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Prescribed overdose			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Congenital, familial and genetic disorders			
Huntington's disease			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrioventricular block			
subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	1 / 95 (1.05%)
occurrences (all)	1	1	1
Atrial fibrillation			
subjects affected / exposed	2 / 95 (2.11%)	0 / 94 (0.00%)	2 / 95 (2.11%)
occurrences (all)	2	0	2
Cardio-respiratory arrest			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Palpitations			

subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Tachycardia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Supraventricular tachycardia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Angina unstable			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Cardiac failure			
subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 95 (13.68%)	16 / 94 (17.02%)	11 / 95 (11.58%)
occurrences (all)	13	18	11
Memory impairment			
subjects affected / exposed	4 / 95 (4.21%)	2 / 94 (2.13%)	2 / 95 (2.11%)
occurrences (all)	4	2	2
Epilepsy			
subjects affected / exposed	7 / 95 (7.37%)	4 / 94 (4.26%)	4 / 95 (4.21%)
occurrences (all)	8	4	4
Cerebral haemorrhage			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Cerebrovascular accident			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Ischaemic stroke			
subjects affected / exposed	3 / 95 (3.16%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	4	0	1
VIth nerve paralysis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1

Cognitive disorder			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Dyskinesia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Movement disorder			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Hemiparesis			
subjects affected / exposed	0 / 95 (0.00%)	3 / 94 (3.19%)	0 / 95 (0.00%)
occurrences (all)	0	4	0
Tremor			
subjects affected / exposed	2 / 95 (2.11%)	2 / 94 (2.13%)	2 / 95 (2.11%)
occurrences (all)	2	2	2
Balance disorder			
subjects affected / exposed	4 / 95 (4.21%)	3 / 94 (3.19%)	4 / 95 (4.21%)
occurrences (all)	4	3	4
Cerebellar syndrome			
subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	1 / 95 (1.05%)
occurrences (all)	1	1	1
Aphasia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Right hemisphere deficit syndrome			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	1 / 95 (1.05%)
occurrences (all)	1	1	1
Psychomotor skills impaired			
subjects affected / exposed	0 / 95 (0.00%)	2 / 94 (2.13%)	0 / 95 (0.00%)
occurrences (all)	0	2	0
Clonus			
subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	1	1	0

Dizziness			
subjects affected / exposed	7 / 95 (7.37%)	7 / 94 (7.45%)	3 / 95 (3.16%)
occurrences (all)	7	7	3
Dizziness postural			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Paraesthesia			
subjects affected / exposed	2 / 95 (2.11%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	2	0	1
Speech disorder			
subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	1 / 95 (1.05%)
occurrences (all)	1	1	1
Sensorimotor disorder			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Dementia with Lewy bodies			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Cogwheel rigidity			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Hyperreflexia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Dysgraphia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Restless legs syndrome			
subjects affected / exposed	0 / 95 (0.00%)	2 / 94 (2.13%)	0 / 95 (0.00%)
occurrences (all)	0	2	0

Dysarthria			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	1	1	0
Radicular pain			
subjects affected / exposed	2 / 95 (2.11%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	2	0	0
Cerebral atrophy			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Subdural hygroma			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
White matter lesion			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Anaemia			
subjects affected / exposed	0 / 95 (0.00%)	2 / 94 (2.13%)	0 / 95 (0.00%)
occurrences (all)	0	2	0
Normochromic normocytic anaemia			
subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	1 / 95 (1.05%)
occurrences (all)	1	1	1
Thrombocytopenia			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	1 / 95 (1.05%)
occurrences (all)	1	1	1
Tympanic membrane perforation			

subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Tinnitus			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Ocular hypertension			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Exophthalmos			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Visual impairment			
subjects affected / exposed	2 / 95 (2.11%)	0 / 94 (0.00%)	2 / 95 (2.11%)
occurrences (all)	2	0	2
Keratitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Retinal haemorrhage			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Eyelid oedema			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Ocular hyperaemia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Asthenopia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed	2 / 95 (2.11%)	1 / 94 (1.06%)	1 / 95 (1.05%)
occurrences (all)	2	1	1
Faeces soft			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Abdominal pain			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	3 / 95 (3.16%)	0 / 94 (0.00%)	3 / 95 (3.16%)
occurrences (all)	3	0	3
Vomiting			
subjects affected / exposed	3 / 95 (3.16%)	0 / 94 (0.00%)	3 / 95 (3.16%)
occurrences (all)	3	0	3
Stomatitis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Inguinal hernia strangulated			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Constipation			
subjects affected / exposed	3 / 95 (3.16%)	0 / 94 (0.00%)	3 / 95 (3.16%)
occurrences (all)	3	0	3
Intestinal obstruction			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Lip disorder			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Lip oedema			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Hiatus hernia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Umbilical hernia			

subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Dental alveolar anomaly			
subjects affected / exposed	2 / 95 (2.11%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	2	1	0
Dental cyst			
subjects affected / exposed	2 / 95 (2.11%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	2	1	0
Rectal haemorrhage			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Oesophagitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Dermatitis diaper			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Drug eruption			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Erythema			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 95 (0.00%)	2 / 94 (2.13%)	0 / 95 (0.00%)
occurrences (all)	0	2	0
Rash			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Decubitus ulcer			
subjects affected / exposed	0 / 95 (0.00%)	2 / 94 (2.13%)	0 / 95 (0.00%)
occurrences (all)	0	2	0

Acne			
subjects affected / exposed	2 / 95 (2.11%)	1 / 94 (1.06%)	1 / 95 (1.05%)
occurrences (all)	2	1	1
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Renal failure			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Urinary retention			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Acute kidney injury			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Hyperadrenocorticism			
subjects affected / exposed	2 / 95 (2.11%)	3 / 94 (3.19%)	2 / 95 (2.11%)
occurrences (all)	2	3	2
Glucocorticoid deficiency			
subjects affected / exposed	7 / 95 (7.37%)	1 / 94 (1.06%)	7 / 95 (7.37%)
occurrences (all)	7	1	7
Adrenocortical insufficiency acute			
subjects affected / exposed	3 / 95 (3.16%)	0 / 94 (0.00%)	3 / 95 (3.16%)
occurrences (all)	3	0	3
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 95 (2.11%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	2	0	0
Myalgia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Muscle atrophy			
subjects affected / exposed	2 / 95 (2.11%)	0 / 94 (0.00%)	2 / 95 (2.11%)
occurrences (all)	2	0	2

Muscle spasms			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	2	0	2
Back pain			
subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	1	1	0
Neck pain			
subjects affected / exposed	3 / 95 (3.16%)	1 / 94 (1.06%)	2 / 95 (2.11%)
occurrences (all)	4	1	2
Polyarthritis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Periarthritis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Tooth abscess			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Wound infection			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Bronchitis			
subjects affected / exposed	2 / 95 (2.11%)	3 / 94 (3.19%)	1 / 95 (1.05%)
occurrences (all)	2	3	1
Nasopharyngitis			
subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	1	1	0
Sinusitis			

subjects affected / exposed	0 / 95 (0.00%)	3 / 94 (3.19%)	0 / 95 (0.00%)
occurrences (all)	0	3	0
Urinary tract infection			
subjects affected / exposed	2 / 95 (2.11%)	2 / 94 (2.13%)	2 / 95 (2.11%)
occurrences (all)	2	2	2
Nasal herpes			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Ophthalmic herpes simplex			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Acarodermatitis			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Bronchopneumopathy	Additional description: + Bronchopneumonia		
subjects affected / exposed	2 / 95 (2.11%)	0 / 94 (0.00%)	2 / 95 (2.11%)
occurrences (all)	2	0	2
Septic shock			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Cat scratch disease			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Diverticulitis			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	0 / 95 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Hyperphagia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1

Sodium retention			
subjects affected / exposed	1 / 95 (1.05%)	1 / 94 (1.06%)	1 / 95 (1.05%)
occurrences (all)	1	1	1
Malnutrition			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0
Hypercalcaemia			
subjects affected / exposed	1 / 95 (1.05%)	0 / 94 (0.00%)	1 / 95 (1.05%)
occurrences (all)	1	0	1
Hyperkalaemia			
subjects affected / exposed	10 / 95 (10.53%)	8 / 94 (8.51%)	10 / 95 (10.53%)
occurrences (all)	10	8	10
Hyponatraemia			
subjects affected / exposed	2 / 95 (2.11%)	2 / 94 (2.13%)	2 / 95 (2.11%)
occurrences (all)	3	2	3
Hypoglycaemia			
subjects affected / exposed	4 / 95 (4.21%)	1 / 94 (1.06%)	4 / 95 (4.21%)
occurrences (all)	4	3	4
Vitamin D deficiency			
subjects affected / exposed	0 / 95 (0.00%)	1 / 94 (1.06%)	0 / 95 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Placebo at M2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 94 (27.66%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Parathyroid tumour benign			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Salivary gland neoplasm			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Chronic lymphocytic leukaemia			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Meningioma			

subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Metastatic neoplasm			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Venous thrombosis	Additional description: Venous thrombosis / Pulmonary embolism		
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Haematoma			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Microangiopathy			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			
Subdural haematoma evacuation			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Palliative care			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Rehabilitation therapy			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Left atrial appendage closure implant			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Cataract operation			

subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Prostate ablation			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Weight increased			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Oedema peripheral			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Diabetes mellitus	Additional description: "Diabetes"		
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	6 / 94 (6.38%)		
occurrences (all)	6		
Gout			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Hyperthermia			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Asthenia			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Fatigue			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Gait disturbance			

subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	2		
Condition aggravated			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
General physical health deterioration			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Influenza like illness			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Walking disability	Additional description: Abasia		
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Inflammation			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Prostatitis			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Erectile dysfunction			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Lung disorder			

subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Interstitial lung disease			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Sleep apnoea syndrome			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Anxiety			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Nervousness			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Confusional state			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Depressed mood			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Persecutory delusion			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Hallucination			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Euphoric mood			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		

Irritability			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Affective disorder			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Apathy			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Abnormal behaviour			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Sleep disorder			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Delirium tremens			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Alcoholism			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Withdrawal syndrome			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Alcohol abuse			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Investigations			
Weight decreased			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			

Fall				
subjects affected / exposed	2 / 94 (2.13%)			
occurrences (all)	2			
Femur fracture				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences (all)	1			
Rib fracture				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences (all)	1			
Craniocerebral injury				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Accidental overdose				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Medication error				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences (all)	1			
Myocardial necrosis marker increased				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Foot fracture				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Spinal fracture				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Alcohol poisoning				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Subdural haematoma				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Traumatic intracranial haemorrhage				

subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Pneumothorax traumatic			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Wound			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Limb injury			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Skin wound			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Prescribed overdose			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Congenital, familial and genetic disorders			
Huntington's disease			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Atrioventricular block			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Atrial fibrillation			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Cardio-respiratory arrest			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Tachycardia			

subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Supraventricular tachycardia			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Angina unstable			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Cardiac failure			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 94 (8.51%)		
occurrences (all)	9		
Memory impairment			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Epilepsy			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Cerebral haemorrhage			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Cerebrovascular accident			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Ischaemic stroke			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
VIth nerve paralysis			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Cognitive disorder			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		

Dyskinesia				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Movement disorder				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences (all)	1			
Hemiparesis				
subjects affected / exposed	3 / 94 (3.19%)			
occurrences (all)	3			
Tremor				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences (all)	1			
Balance disorder				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences (all)	1			
Cerebellar syndrome				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Aphasia				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Right hemisphere deficit syndrome				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences (all)	1			
Somnolence				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences (all)	1			
Psychomotor skills impaired				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences (all)	1			
Clonus				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences (all)	1			
Dizziness				
subjects affected / exposed	4 / 94 (4.26%)			
occurrences (all)	4			

Dizziness postural				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Paraesthesia				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Speech disorder				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences (all)	1			
Sensorimotor disorder				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Subarachnoid haemorrhage				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Dementia with Lewy bodies				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Cogwheel rigidity				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Hyperreflexia				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Dysgraphia				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Syncope				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Restless legs syndrome				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Dysarthria				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			

Sciatica			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Radicular pain			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Cerebral atrophy			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Subdural hygroma			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
White matter lesion			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Anaemia			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Normochromic normocytic anaemia			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Tympanic membrane perforation			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Tinnitus			

subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Eye disorders			
Ocular hypertension			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Exophthalmos			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Visual impairment			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Keratitis			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Retinal haemorrhage			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Eyelid oedema			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Ocular hyperaemia			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Asthenopia			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Faeces soft			

subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Abdominal pain				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Nausea				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Vomiting				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Stomatitis				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Inguinal hernia strangulated				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Constipation				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Intestinal obstruction				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Lip disorder				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences (all)	1			
Lip oedema				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Hiatus hernia				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Umbilical hernia				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences (all)	0			
Dental alveolar anomaly				

subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Dental cyst			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Rectal haemorrhage			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Oesophagitis			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Dermatitis diaper			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Drug eruption			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Decubitus ulcer			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Acne			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		

Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Renal failure			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Urinary retention			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Acute kidney injury			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Hyperadrenocorticism			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Glucocorticoid deficiency			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Adrenocortical insufficiency acute			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Muscle atrophy			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		

Back pain			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Polyarthritis			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Periarthritis			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Tooth abscess			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Wound infection			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Bronchitis			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Urinary tract infection			

subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Nasal herpes			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Ophthalmic herpes simplex			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Acarodermatitis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Bronchopneumopathy	Additional description: + Bronchopneumonia		
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Septic shock			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Cat scratch disease			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Diverticulitis			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Hyperphagia			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Sodium retention			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		

Malnutrition subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		
Hypercalcaemia subjects affected / exposed occurrences (all)	0 / 94 (0.00%) 0		
Hyperkalaemia subjects affected / exposed occurrences (all)	8 / 94 (8.51%) 8		
Hyponatraemia subjects affected / exposed occurrences (all)	2 / 94 (2.13%) 2		
Hypoglycaemia subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 3		
Vitamin D deficiency subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 January 2016	- Addition of a non-inclusion criteria: diabetic patient - Correction of the inclusion criteria: no clinical sign of severity (Glasgow scale > 12, motor deficit ≥ 4/5) - Update of the list of investigators (modification of an investigator and a location) - Change of research director
25 August 2017	- Update of the Investigational Drug File (addition of an appeal procedure for manufacture of the experimental treatment and modification of the size of the capsules) - Update of the list of investigators (modification of principal investigators and closure of centers)
27 April 2018	Changes: - Increase in the inclusion period and the duration of the study. - Update of the list of investigators (modification of principal investigators and closure of centers) Rationale: - 174/202 patients are included today (27/04/2018). The end date of inclusions is scheduled for 24/06/2018. In order to reach the necessary number of subjects, we want to increase the inclusion period by 4 months. i.e. until 24/10/2018. The end of the study will also be extended to 24/10/2019. - The principal investigators are modified for 2 centers and one center is closed for lack of inclusions.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28583162