Clinical trial results:
Effects of Montelukast on neuroinflammation in Parkinson's Disease. An open-label single-center trial.

Summary

EudraCT number	2020-000148-76
Trial protocol	SE
Global end of trial date	07 July 2022

Results information

Result version number	v1 (current)
This version publication date	01 May 2023
First version publication date	01 May 2023

Trial information

Trial identification

Sponsor protocol code	3.0

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Academic Specialist Center
Sponsor organisation address	Solnavägen 1E, Stockholm, Sweden, 11365
Public contact	Academic Specialist Center, Stockholm Health Care Services, 0046 812367300,
Scientific contact	Academic Specialist Center, Stockholm Health Care Services, 0046 812367300,

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	01 January 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 July 2022
Global end of trial reached?	Yes
Global end of trial date	07 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Safety and tolerability of Montelukast treatment in Parkinson's disease.

Protection of trial subjects:

Study subjects were treated with Montelukast, an approved drug for 12 weeks. Dosage was higher than in regular clinical practice. Adverse events were closely monitored. Other examinations did not differ from regular clinical practice for patients with Parkinson's disease.

Background therapy:

Regular dopaminergic treatment for Parkinson's disease.

Evidence for comparator: -

Actual start date of recruitment	09 February 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

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)	7
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Candidates for the trial will be patients followed at the Academic Specialist Centre, Stockholm, a highly specialized outpatient clinic for parkinsonian disorders. More than 600 patients with PD are treated at the Academic Specialist Centrum.

Pre-assignment

Screening details:

Patients will be screened using the history of their Parkinson's disease, supported by any available clinical correspondence according to usual standard of care.
Participants will be considered eligible for enrolment in this trial if they fulfil all the inclusion criteria and none of the exclusion criteria.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

All participants received Montelukast treatment.

Arms

Arm title	Baseline

Arm description:

Only one arm. 40 mg of Montelukast daily.

Arm type	Experimental
Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	Singulair
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

2 tabletts of 10 mg Montelukast were taken by the subject at morning and evening for a total daily dose of 40 mg.

Number of subjects in period 1	Baseline
Started	15
Completed	15

Period 2

Period 2 title	12 weeks
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	12 weeks of Montelukast

Arm description:

Only one arm. 40 mg of Montelukast daily.

Arm type	Experimental
Investigational medicinal product name	Montelukast
Investigational medicinal product code	
Other name	Singulair
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

2 tabletts of 10 mg Montelukast were taken by the subject at morning and evening for a total daily dose of 40 mg.

Number of subjects in period 2	12 weeks of Montelukast
Started	15
Completed	15

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	15	15	
Age categorical Units: Subjects			
Adults (18-64 years)	7	7	
From 65-84 years	8	8	
Age continuous Units: years			
median	65		
inter-quartile range (Q1-Q3)	63 to 69	-	
Gender categorical Units: Subjects			
Female	8	8	
Male	7	7	

End points

End points reporting groups

Reporting group title	Baseline
Reporting group description:	
Only one arm. 40 mg of Montelukast daily.	
Reporting group title	12 weeks of Montelukast
Reporting group description:	
Only one arm. 40 mg of Montelukast daily.	

Primary: • Safety and tolerability of Montelukast in PD patients

End point title	• Safety and tolerability of Montelukast in PD patients[1]
End point description:	
End point type	Primary
End point timeframe:	
Between baseline and 12 weeks of treatment	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Primary endpoint was safety and tolerability. All participants finished the trial. No meaningful statistical analysis can be made from the count of adverse events since there is no control group.

End point values	Baseline	12 weeks of Montelukast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: Adverse events	0	10		

Attachments (see zip file)	Adverse events.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: • Microglia activation in the brain measured as measured by [11C]PBR28 PET

End point title	• Microglia activation in the brain measured as measured by [11C]PBR28 PET
End point description:	
Pooled grey matter binding of TSPO PET before and after treatment.	
End point type	Secondary
End point timeframe:	
Between baseline and 12 weeks of treatment	

End point values	Baseline	12 weeks of Montelukast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: Mean Vt				
arithmetic mean (standard deviation)	4.25 (± 2.0)	4.17 (± 1.44)		

Statistical analyses

Statistical analysis title	Paired t-test
Comparison groups	12 weeks of Montelukast v Baseline
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8 [2]
Method	t-test, 2-sided

Notes:

[2] - Non significant.

Secondary: Changes in clinical rating scales

End point title	Changes in clinical rating scales
End point description:	
Changes in MDS-UPDRS part 1-4, MoCA, BDI, NMSQuest, PDQ-39.	
End point type	Secondary
End point timeframe:	
Between baseline and 12 weeks.	

End point values	Baseline	12 weeks of Montelukast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: mean score				
arithmetic mean (standard deviation)				
MDS-UPDRS 1	7.20 (± 4.55)	4.87 (± 3.46)		
MDS-UPDRS 2	6.87 (± 6.14)	5.20 (± 4.38)		
MDS-UPDRS 3	17.33 (± 17.33)	14.53 (± 8.53)		
MDS-UPDRS 4	1.73 (± 1.44)	1.60 (± 1.3)		
MoCA	28.33 (± 1.23)	29.07 (± 1.10)		
BDI	5.93 (± 4.95)	4.67 (± 3.56)		
NMSQuest	5.13 (± 3.93)	5.27 (± 3.26)		
PDQ-39	9.76 (± 8.86)	7.95 (± 7.16)		

Statistical analyses

Statistical analysis title	MoCA
Statistical analysis description: Before and after treatment	
Comparison groups	12 weeks of Montelukast v Baseline
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.021
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	NMSQuest
Statistical analysis description: Before and after treatment.	
Comparison groups	12 weeks of Montelukast v Baseline
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.685
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	PDQ-39
Statistical analysis description: Before and after treatment	
Comparison groups	12 weeks of Montelukast v Baseline
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.053
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	MDS-UPDRS part 1
Statistical analysis description: Before and after treatment	
Comparison groups	12 weeks of Montelukast v Baseline

Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	t-test, 2-sided

Statistical analysis title	MDS-UPDRS part 2
Statistical analysis description: Before and after treatment.	
Comparison groups	12 weeks of Montelukast v Baseline
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.015
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	MDS-UPDRS Part 3
Statistical analysis description: Before and after treatment.	
Comparison groups	12 weeks of Montelukast v Baseline
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.024
Method	t-test, 2-sided

Statistical analysis title	MDS-UPDRS Part 4
Statistical analysis description: Before and after treatment.	
Comparison groups	12 weeks of Montelukast v Baseline
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.758
Method	t-test, 2-sided

Statistical analysis title	BDI
Statistical analysis description: Before and after treatment.	
Comparison groups	12 weeks of Montelukast v Baseline

Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.038
Method	Wilcoxon (Mann-Whitney)

Secondary: Montelukast levels in plasma and CSF

End point title	Montelukast levels in plasma and CSF

End point description:

End point type	Secondary

End point timeframe:

Between baseline and 12-weeks of treatment.

End point values	Baseline	12 weeks of Montelukast		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	13		
Units: ng/l				
arithmetic mean (standard deviation)				
Plasma	0 (± 0)	1621.26 (± 361.11)		
CSF	0 (± 0)	3.66 (± 1.31)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Telephone inquiry two weeks after baseline, 4 week follow-up visit, 6 week telephone inquiry, 9 week telephone inquiry and lastly at 12 week final visit.

Assessment type	Systematic

Dictionary used

Dictionary name	Bioportal MedDRA
Dictionary version	2022AB

Reporting groups

Reporting group title	All participants

Reporting group description:

Only one arm in the study. All exposed to trial treatment.

Serious adverse events	All participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 15 (6.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Vascular disorders			
Pulmonary embolism	Additional description: 1 patient got an pulmonary embolism after immobilisation post-op. It was not deemed connected to IMP. The condition resolved with anti-coagulant therapy.		
subjects affected / exposed	1 / 15 (6.67%)		
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	All participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 15 (60.00%)		
Injury, poisoning and procedural complications			
Catheter site hematoma	Additional description: From arterial catheter placed for PET examination		
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Surgical and medical procedures			

Lumbar puncture headache			
subjects affected / exposed	4 / 15 (26.67%)		
occurrences (all)	4		
Nervous system disorders			
Tremor	Additional description: Worsening of Parkinsonian tremor.		
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Gastrointestinal disorders			
Stools loose			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	3		
Psychiatric disorders			
Fatigue			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Musculoskeletal stiffness			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	1		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Small sample size of 15 patients. No control group. Short treatment period. The primary endpoint was reached however and we plan a larger RCT based on these results.

Notes: