Clinical trial results:
Pharmaco-EEG for Montelukast. Can we detect neural changes during medication with Montelukast in the EEG?

Summary

EudraCT number	2016-003061-25
Trial protocol	AT
Global end of trial date	30 January 2019

Results information

Result version number	v1 (current)
This version publication date	02 January 2020
First version publication date	02 January 2020

Trial information

Trial identification

Sponsor protocol code	MPEEG_2

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Department of Neurology, Christian Doppler Medical Center, Paracelsus Medical University Salzburg
Sponsor organisation address	Ignaz-Harrer-Str. 79, Salzburg, Austria, 5020
Public contact	Principal Investigator, Department of Neurology, Christian Doppler Medical Center, Paracelsus Medical University Salzburg, w.staffen@salk.at
Scientific contact	Principal Investigator, Department of Neurology, Christian Doppler Medical Center, Paracelsus Medical University Salzburg, w.staffen@salk.at

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	11 December 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 January 2019
Global end of trial reached?	Yes
Global end of trial date	30 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

We aimed to examine effects of Montelukast on brain activity.

Protection of trial subjects:

Participants were treated with Montelukast per indication, the trial added only examination with psychological tests and the electroencephalogram. Both of these examinations are free of distress and pain.

Background therapy:

No background therapy was used.

Evidence for comparator:

No comparators were used.

Actual start date of recruitment	02 January 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 13
Worldwide total number of subjects	13
EEA total number of subjects	13

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)	10
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from begin of trial until 8 weeks before end of trial by Pulmonologists in Salzburg.

Pre-assignment

Screening details:

When a pulmonologist in Salzburg prescribed Montelukast to the patient, he informed the patient in written and oral form about the trial. If the patient was interested, he/she could choose whether he would give the doctor the informed consent to forward his contact information to the study team or whether he would like to contact the study team.

Period 1

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

Blinding implementation details:

No blinding was implemented. Patients received treatment according to indication.

Arms

Arm title	All participants

Arm description:

There was only one arm in the study.

Arm type	Observation
Investigational medicinal product name	Singulair
Investigational medicinal product code	PR1
Other name	Montelukast
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Treatment is not specified by the protocol; the medical doctor decides on the treatment. The trial observed cognitive/brain changes during this treatment over 8 weeks. Treatment is likely to be continued after participation of the patient in this trial.

Number of subjects in period 1	All participants
Started	13
Completed	13

Period 2

Period 2 title	overall trial - 8 weeks follow-up
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

No blinding was done.

Arms

Arm title	All participants

Arm description:

There was only one arm in the study.

Arm type	Observation
Investigational medicinal product name	Singulair
Investigational medicinal product code	PR1
Other name	Montelukast
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Treatment is not specified by the protocol; the medical doctor decides on the treatment. The trial observed cognitive/brain changes during this treatment over 8 weeks. Treatment is likely to be continued after participation of the patient in this trial.

Number of subjects in period 2	All participants
Started	13
Completed	12
Not completed	1
Consent withdrawn by subject	1

Baseline characteristics

Reporting groups	
Reporting group title	overall trial - baseline

Reporting group description: -

Reporting group values	overall trial - baseline	Total	
Number of subjects	13	13	
Age categorical Units: Subjects			
Adults (18-64 years)	8	8	
From 65-84 years	5	5	
Age continuous Units: years			
arithmetic mean	53.38		
full range (min-max)	20 to 73	-	
Gender categorical Units: Subjects			
Female	10	10	
Male	3	3	
Handedness Units: Subjects			
right	13	13	
left	0	0	

End points

End points reporting groups	
Reporting group title	All participants
Reporting group description:	
There was only one arm in the study.	
Reporting group title	All participants
Reporting group description:	
There was only one arm in the study.	

Primary: EEG-characteristics - brainrate	
End point title	EEG-characteristics - brainrate
End point description:	
Differences in EEG characteristics (brainrate) between baseline (before treatment) and follow up (after 8 weeks of treatment).	
End point type	Primary
End point timeframe:	
from baseline to after 8 weeks of treatment	

End point values	All participants	All participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	7		
Units: brainrate				
arithmetic mean (standard deviation)	7.766 (± 0.3475)	8.0798 (± 0.3248)		

Statistical analyses

Statistical analysis title	EEG brainrate comparison
Comparison groups	All participants v All participants
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	= 0.0313 [2]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Point estimate	-0.3138
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.73
upper limit	0.1

Variability estimate	Standard deviation
Dispersion value	0.25

Notes:

[1] - pre- to post treatment comparison

[2] - signed rank=1

Primary: EEG characteristics - Hjorth activity

End point title	EEG characteristics - Hjorth activity

End point description:

End point type	Primary

End point timeframe:

baseline to after 8 weeks of treatment

End point values	All participants	All participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	7		
Units: activity				
arithmetic mean (standard deviation)	127.8879 (± 41.9411)	126.1421 (± 124.5285)		

Statistical analyses

Statistical analysis title	EEG Hjorth activity comparison
Comparison groups	All participants v All participants
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	= 0.375 [4]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Point estimate	1.7458
Confidence interval	
level	90 %
sides	2-sided
lower limit	-219.07
upper limit	222.57
Variability estimate	Standard deviation
Dispersion value	134.24

Notes:

[3] - pre- to post treatment comparison

[4] - signed rank=20

Primary: EEG characteristics - Hjorth mobility

End point title	EEG characteristics - Hjorth mobility

End point description:

End point type	Primary

End point timeframe:
baseline to after 8 weeks of treatment

End point values	All participants	All participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	7		
Units: mobility index				
arithmetic mean (standard deviation)	0.6128 (± 0.1385)	0.6379 (± 0.1078)		

Statistical analyses

Statistical analysis title	EEG Hjorth mobility comparison
Comparison groups	All participants v All participants
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	other[5]
P-value	= 0.4688 [6]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Point estimate	-0.0252
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.1558
upper limit	0.1055
Variability estimate	Standard deviation
Dispersion value	0.0794

Notes:
[5] - pre- to post treatment comparison
[6] - signed rank=9

Primary: EEG characteristics: alpha power

End point title	EEG characteristics: alpha power

End point description:

End point type	Primary

End point timeframe:
baseline to after 8 weeks of treatment

End point values	All participants	All participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	7		
Units: micro Volt				
arithmetic mean (standard deviation)	44.8017 (± 22.5384)	66.7682 (± 91.2418)		

Statistical analyses

Statistical analysis title	EEG alpha power comparison
Comparison groups	All participants v All participants
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	other[7]
P-value	= 0.9375 [8]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Point estimate	-21.97
Confidence interval	
level	90 %
sides	2-sided
lower limit	-174.54
upper limit	130.61
Variability estimate	Standard deviation
Dispersion value	92.75

Notes:

[7] - pre- to post treatment comparison

[8] - signed rank=15

Secondary: Psychological tests - Epitrack

End point title	Psychological tests - Epitrack

End point description:

Epitrack is a cognitive test battery, the score indicates perfomance in memory and attention.

End point type	Secondary

End point timeframe:

after 8 weeks of treatment

End point values	All participants	All participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: score				
arithmetic mean (standard deviation)	35.4615 (± 3.5435)	37 (± 3.6056)		

Statistical analyses

Statistical analysis title	Epitrack cognitive changes
Statistical analysis description: Analyze change on Epitrack test	
Comparison groups	All participants v All participants
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other[9]
P-value	= 0.1816 [10]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Point estimate	-1.25
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.0138
upper limit	3.5138
Variability estimate	Standard deviation
Dispersion value	2.8959

Notes:
[9] - pre- to post treatment comparison
[10] - signed rank=13.5

Secondary: Psychological tests - VLMT-learning

End point title	Psychological tests - VLMT-learning
End point description:	
End point type	Secondary
End point timeframe: before and after 8 weeks of treatment	

End point values	All participants	All participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	8		
Units: score				
arithmetic mean (standard deviation)	54.36 (± 9.33)	56.13 (± 8.75)		

Statistical analyses

Statistical analysis title	VLMT-learning comparison pre- to post-treatment
Comparison groups	All participants v All participants

Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	other[11]
P-value	= 0.25 [12]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Point estimate	-3.25
Confidence interval	
level	90 %
sides	2-sided
lower limit	-12.42
upper limit	5.92
Variability estimate	Standard deviation
Dispersion value	5.57

Notes:

[11] - pre- to post-treatment comparison

[12] - signed rand=6.5

Secondary: Psychological tests - VLMT-consolidation

End point title	Psychological tests - VLMT-consolidation

End point description:

End point type	Secondary

End point timeframe:

baseline to 8 weeks after treatment

End point values	All participants	All participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: score				
arithmetic mean (standard deviation)	40.56 (± 8.38)	38.50 (± 8.97)		

Statistical analyses

Statistical analysis title	VLMT-consolidation comparison
Comparison groups	All participants v All participants
Number of subjects included in analysis	17
Analysis specification	Pre-specified
Analysis type	other[13]
P-value	= 1 [14]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Point estimate	-0.25

Confidence interval	
level	90 %
sides	2-sided
lower limit	-16.5998
upper limit	16.0998
Variability estimate	Standard deviation
Dispersion value	9.94

Notes:
[13] - coparison pre- to post-treatment
[14] - signed rank=10

Secondary: Psychological tests - VLMT- recognition

End point title	Psychological tests - VLMT- recognition

End point description:

End point type	Secondary

End point timeframe:
baseline to after 8 weeks of treatment

End point values	All participants	All participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	8		
Units: score				
arithmetic mean (standard deviation)	43.88 (± 11.23)	43.38 (± 15.46)		

Statistical analyses

Statistical analysis title	VLMT-recognition comparison
Comparison groups	All participants v All participants
Number of subjects included in analysis	16
Analysis specification	Pre-specified
Analysis type	other[15]
P-value	= 1 [16]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Point estimate	0.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-12.39
upper limit	13.39
Variability estimate	Standard deviation
Dispersion value	7.84

Notes:
[15] - pre- to post treatment comparison
[16] - signed rank=14

Secondary: EEG-paradigm - Wordpair learning

End point title	EEG-paradigm - Wordpair learning

End point description:

End point type	Secondary

End point timeframe:
baseline to 8 weeks post treatment

End point values	All participants	All participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: number of words remembered				
arithmetic mean (standard deviation)	22.1 (± 10.514)	23.2 (± 13.1386)		

Statistical analyses

Statistical analysis title	Wordpair learning comparison
Comparison groups	All participants v All participants
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	other[17]
P-value	= 0.9698 [18]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Point estimate	1.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.2246
upper limit	1.9754
Variability estimate	Standard deviation
Dispersion value	5.3219

Notes:
[17] - pre- to post treatment comparison
[18] - ranksum: 104, z-value -0.0378

Secondary: EEG-paradigm - virtual reality task

End point title	EEG-paradigm - virtual reality task

End point description:

End point type	Secondary

End point timeframe:
baseline to after 8 weeks of treatment

End point values	All participants	All participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: remembered items				
arithmetic mean (standard deviation)	40.625 (± 9.5647)	42.1429 (± 13.1739)		

Statistical analyses

Statistical analysis title	Virtual reality task comparison
Comparison groups	All participants v All participants
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other[19]
P-value	= 0.5801 [20]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Point estimate	1.25
Confidence interval	
level	90 %
sides	2-sided
lower limit	-11.8
upper limit	14.3
Variability estimate	Standard deviation
Dispersion value	7.93

Notes:
[19] - pre- to post treatment comparison
[20] - signed rank 46.5

Secondary: Psychological tests - TAP phasic alertness

End point title	Psychological tests - TAP phasic alertness

End point description:

End point type	Secondary

End point timeframe:
baseline to after 8 weeks of treatment

End point values	All participants	All participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: T-value				
arithmetic mean (standard deviation)	45.77 (± 9.27)	45.92 (± 5.48)		

Statistical analyses

Statistical analysis title	TAP comparison
Comparison groups	All participants v All participants
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other[21]
P-value	= 0.9531 [22]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Point estimate	-0.17
Confidence interval	
level	90 %
sides	2-sided
lower limit	-14.42
upper limit	14.09
Variability estimate	Standard deviation
Dispersion value	8.67

Notes:

[21] - comparison of baseline to after 8 weeks of treatment

[22] - signed rank=38

Secondary: Psychological tests - FPZ

End point title	Psychological tests - FPZ

End point description:

End point type	Secondary

End point timeframe:

Baseline to after 8 weeks of treatment.

End point values	All participants	All participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	12		
Units: score				
arithmetic mean (standard deviation)	220.98 (± 37.89)	219.98 (± 34.24)		

Statistical analyses

Statistical analysis title	FPZ pre- to post treatment comparison
Comparison groups	All participants v All participants
Number of subjects included in analysis	25
Analysis specification	Pre-specified
Analysis type	other[23]
P-value	= 0.6904 [24]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Point estimate	3.8367
Confidence interval	
level	90 %
sides	2-sided
lower limit	-31.67
upper limit	39.35
Variability estimate	Standard deviation
Dispersion value	21.586

Notes:

[23] - pre- to post treatment comparison

[24] - signed rank=44.5

Secondary: Psychological tests - HADS depression

End point title	Psychological tests - HADS depression

End point description:

End point type	Secondary

End point timeframe:

baseline to after 8 weeks of treatment

End point values	All participants	All participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	11		
Units: T-value				
arithmetic mean (standard deviation)	49.75 (± 9.17)	49.74 (± 12.63)		

Statistical analyses

Statistical analysis title	HADS depression comparison

Statistical analysis description:

Pre- to post treatment comparison of depression scores

Comparison groups	All participants v All participants

Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6563 [25]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Point estimate	0.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-7.67
upper limit	8.07
Variability estimate	Standard deviation
Dispersion value	4.78

Notes:
[25] - signed rank =17

Secondary: Psychological tests - HADS anxiety

End point title	Psychological tests - HADS anxiety

End point description:

End point type	Secondary

End point timeframe:
baseline to after 8 weeks of treatment

End point values	All participants	All participants		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	11		
Units: T-value				
arithmetic mean (standard deviation)	47.26 (± 12.87)	44.65 (± 12.22)		

Statistical analyses

Statistical analysis title	HADS anxiety comparison
Comparison groups	All participants v All participants
Number of subjects included in analysis	24
Analysis specification	Pre-specified
Analysis type	other[26]
P-value	= 0.5781 [27]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)
Point estimate	1.68

Confidence interval	
level	90 %
sides	2-sided
lower limit	-12.08
upper limit	15.45
Variability estimate	Standard deviation
Dispersion value	8.37

Notes:

[26] - comparison of baseline to after 8 weeks of treatment

[27] - signed rank=22.5

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Begin of trial until end of trial.	
Adverse event reporting additional description:	
Participants were informed upon inclusion to immediately inform the medical doctor or the study team about adverse events.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups	
Reporting group title	All participants
Reporting group description:	
There was only one arm in the study.	

Serious adverse events	All participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	All participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 13 (7.69%)		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
General disorders and administration site conditions			
Agitation	Additional description: SOC: Behavioral disorders		
subjects affected / exposed	1 / 13 (7.69%)		
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.

Because recruitment was rather difficult, even after extending the trial two years resulted in a low number of subjects (12 instead of the aim of N=24). The analysis is thus likely underpowered.

Notes: