Clinical trial results:
Neurophysiological assessment of the effect of Sativex (THC/CBD oromucosal spray) as add-on to treat spasticity following stroke

Summary

EudraCT number	2016-001034-10
Trial protocol	IT
Global end of trial date	20 February 2020

Results information

Result version number	v1 (current)
This version publication date	26 April 2020
First version publication date	26 April 2020

Trial information

Trial identification

Sponsor protocol code	SativexStroke

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	IRCCS Ospedale Policlinico San Martino
Sponsor organisation address	Largo Rosanna Benzi 10, Genova, Italy, 16132
Public contact	UO Epidemiologia Clinica, IRCCS Ospedale Policlinico San Martino, +39 0105558477,
Scientific contact	UO Epidemiologia Clinica, IRCCS Ospedale Policlinico San Martino, +39 0105558477,

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

Notes:

General information about the trial

Main objective of the trial:

To assess if Sativex is able to reduce spasticity in chronic stroke patients

Protection of trial subjects:

N/A

Background therapy:

Background therapy shall remain the same during the trial period. Other cannabinoid-derived compounds are not permitted.

Evidence for comparator: -

Actual start date of recruitment	02 May 2018
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	Italy: 41
Worldwide total number of subjects	41
EEA total number of subjects	41

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)	19
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Planned recruitment was 50 stroke survivors between May 2018 and May 2020 in Italy.

Pre-assignment

Screening details:

Stroke survivors with spasticity in at least one muscle segment (Modified Ashworth Scale of at least 1) will be screened. Botulinum toxin treatment washout of at least 4 months is required, while concomitant antispastic drugs can be continued keeping dosage unaltered throughout the trial period.

Period 1

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

Blinding implementation details:

All subjects will be treated with both active drug and placebo with a crossover design.

Arms

Arm title	Experimental

Arm description:

Sativex, crossover phase 1

Arm type	Experimental
Investigational medicinal product name	Sativex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal spray
Routes of administration	Transmucosal use

Dosage and administration details:

Oromucosal self administration with gradual increase up to 12 sprays/day

Number of subjects in period 1	Experimental
Started	41
Completed	37
Not completed	4
Consent withdrawn by subject	2
Adverse event, non-fatal	2

Period 2	
Period 2 title	Phase 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Arm title	Experimental 2

Arm description:

Sativex, crossover second phase

Arm type	Experimental
Investigational medicinal product name	Sativex
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oromucosal spray
Routes of administration	Transmucosal use

Dosage and administration details:

Oromucosal self administration with gradual increase up to 12 sprays/day

Number of subjects in period 2	Experimental 2
Started	37
Completed	34
Not completed	3
Consent withdrawn by subject	1
Adverse event, non-fatal	2

Baseline characteristics

Reporting groups	
Reporting group title	Phase 1
Reporting group description:	
41 stroke survivors were recruited	

Reporting group values	Phase 1	Total	
Number of subjects	41	41	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	19	19	
From 65-84 years	22	22	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	10	10	
Male	31	31	

Subject analysis sets	
Subject analysis set title	Intention-to-treat
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
94 patients were screened, 41 signed informed consent and started the trial	

Reporting group values	Intention-to-treat		
Number of subjects	41		
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)	19		
From 65-84 years	22		
85 years and over	0		

Gender categorical Units: Subjects			
Female	10		
Male	31		

End points

End points reporting groups

Reporting group title	Experimental
Reporting group description: Sativex, crossover phase 1	
Reporting group title	Experimental 2
Reporting group description: Sativex, crossover second phase	
Subject analysis set title	Intention-to-treat
Subject analysis set type	Intention-to-treat
Subject analysis set description: 94 patients were screened, 41 signed informed consent and started the trial	

Primary: Spasticity assessment

End point title	Spasticity assessment
End point description: The co-primary endpoints of the study will be to assess the effect of the tested treatment on muscle spasticity assessed with the stretch reflex and the 0-10 numeric rating scale for spasticity (NRS)	
End point type	Primary
End point timeframe: Primary endpoint ware assessed 4 times: at baseline (T0), at the end of phase 1 (T1), at the beginning of phase 2 (T2) and at the end of phase 2 (T3)	

End point values	Experimental	Experimental 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	34		
Units: Numeric rating scale	37	34		

Statistical analyses

Statistical analysis title	Primary endpoints analysis
Statistical analysis description: Primary endpoints will be compared between phase 1 baseline (T0) versus phase 1 end (T1) and phase 2 baseline (T2) versus phase 2 end (T3) with respect to experimental/placebo conditions. Quantitative endpoint (stretch reflex) will be compared using a paired t-test. Semi-quantitative data (NRS) will be compared using a non-parametric test (Wilcoxon signed rank)	
Comparison groups	Experimental v Experimental 2
Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)

Notes:

[1] - In a crossover design patients taking active drug in period 1 are compared to placebo in period 2 and viceversa

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Study period (about 2 and a half months per patient)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	none
Dictionary version	0

Reporting groups	
Reporting group title	Period 1
Reporting group description: -	
Reporting group title	Period 2
Reporting group description: -	

Serious adverse events	Period 1	Period 2	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 41 (0.00%)	2 / 37 (5.41%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Seizure	Additional description: First epileptic seizure (probably unrelated to study drug)		
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 41 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0.05 %

Non-serious adverse events	Period 1	Period 2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 41 (48.78%)	21 / 37 (56.76%)	
Nervous system disorders			

Dizziness subjects affected / exposed occurrences (all) Balance disorder subjects affected / exposed occurrences (all)	8 / 41 (19.51%) 8 4 / 41 (9.76%) 4	10 / 37 (27.03%) 10 8 / 37 (21.62%) 8	
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	2 / 41 (4.88%) 2	4 / 37 (10.81%) 4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28882919