Clinical trial results:
CRPS-potilaiden aivomuutosten korjaantuminen hoidon myötä

Summary

EudraCT number	2010-024558-12
Trial protocol	FI
Global end of trial date	06 May 2014

Results information

Result version number	v1 (current)
This version publication date	26 December 2024
First version publication date	26 December 2024

Trial information

Trial identification

Sponsor protocol code	CRPS-1-2011-2014

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Aalto University, Department of Neuroscience and Biomedical Engineering
Sponsor organisation address	Aalto University School of Science, P.O. Box 12200, Finland, FI-00076 AALTO
Public contact	Academic coordinator, Aalto University, Department of Neuroscience and Biomedical Engineering, +358 947001,
Scientific contact	Academic coordinator, Aalto University, Department of Neuroscience and Biomedical Engineering, +358 947001,
Sponsor organisation name	HUS, Pain Clinic
Sponsor organisation address	PL 612, Helsinki, Finland, 00029 HUS
Public contact	Nurse Manager, HUS, Pain Clinic, +358 94711,
Scientific contact	Nurse Manager, HUS, Pain Clinic, +358 94711,

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	30 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 May 2014
Global end of trial reached?	Yes
Global end of trial date	06 May 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial is to explore the alterations in brain function and structure and the effect of trial treatment on these changes and patient symptoms.

Protection of trial subjects:

Trial subjects were informed of study protocol including medication and imaging procedures and that they are able to terminate the study or any test at any point without a need to explain their decision. Patients were informed of the possible side effects and they were instructed to keep a diary and inform research personel on any possible side effects. If any side effects were to occur, they would be taken care of accordingly. The suitability of study medicines for the subjects were handled by participant exclusion criteria. The medication was initiated by increasing the dosage slowly to minimize side-effects. All the stimuli applied in this study were painless and harmless.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 2011
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	Finland: 10
Worldwide total number of subjects	10
EEA total number of subjects	10

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	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The patients were recruited mainly from the Pain Clinic of the Helsinki University Hospital and from two other Hospitals at the Uusimaa district.

Pre-assignment

Screening details:

Inclusion criteria were age from 18 to 65, CRPS type 1 in the upper limb for at least 6 months, and during the past week the maximum intensity of pain more than 4 on a 11-point numeric rating scale. Exclusion criteria were major psychiatric or neurological diseases and alcohol or drug abuse by self-report. No previous use of memantine was allowed.

Pre-assignment period milestones

Number of subjects started	10
Number of subjects completed	10

Period 1

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

Arms

Arm title	Medication

Arm description:

12-week integrated, interdisciplinary therapy, consisted of pharmacological, psychological and physiotherapeutic treatment. Pharmacological treatment included combination of morphine and memantine medication.

Arm type	Experimental
Investigational medicinal product name	MORPHINE HYDROCHLORIDE TRIHYDRATE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

First, the patients started with oral morphine 10 mg daily and increased the dose every 3 days to 10 mg three times a day, if tolerated. After 12 weeks, medication was discontinued.

Investigational medicinal product name	MEMANTINE HYDROCHLORIDE
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

First, the patients started with oral morphine 10 mg daily and increased the dose every 3 days to 10 mg three times a day, if tolerated. After a week, oral memantine 5 mg daily was added and the dose was every 3 days increased up to 40 mg per day, if tolerated. Patients used medication altogether 12 weeks, after which they discontinued the medication.

Number of subjects in period 1	Medication
Started	10
Completed	10

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	10	10	
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			
median	49		
full range (min-max)	43 to 57	-	
Gender categorical Units: Subjects			
Female	10	10	
Male	0	0	

Subject analysis sets

Subject analysis set title	Symptom reduction and improved function in chronic CRPS type 1
Subject analysis set type	Full analysis

Subject analysis set description:

The patients were recruited mainly from the Pain Clinic of the Helsinki University Hospital and from two other Hospitals at the Uusimaa district as part of a larger CRPS study which included MRI and video experiments [16], [17], [18], [19]. Inclusion criteria were age from 18 to 65, CRPS type 1 (Budapest criteria [1]) in the upper limb for at least 6 months, and during the past week the maximum intensity of pain more than four on a 11-point numeric rating scale (NRS 0–10, 0=no pain, 10=extreme pain). Exclusion criteria were major psychiatric or neurological diseases and alcohol or drug abuse by self-report. Additionally, no previous use of memantine, which was part of the study medication, was allowed and mild opioids were tapered down before study medication.

Reporting group values	Symptom reduction and improved function in chronic CRPS type 1		
Number of subjects	10		

Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
median	49		
full range (min-max)	43 to 57		
Gender categorical Units: Subjects			
Female	10		
Male	0		

End points

End points reporting groups

Reporting group title	Medication

Reporting group description:

12-week integrated, interdisciplinary therapy, consisted of pharmacological, psychological and physiotherapeutic treatment. Pharmacological treatment included combination of morphine and memantine medication.

Subject analysis set title	Symptom reduction and improved function in chronic CRPS type 1
Subject analysis set type	Full analysis

Subject analysis set description:

The patients were recruited mainly from the Pain Clinic of the Helsinki University Hospital and from two other Hospitals at the Uusimaa district as part of a larger CRPS study which included MRI and video experiments [16], [17], [18], [19]. Inclusion criteria were age from 18 to 65, CRPS type 1 (Budapest criteria [1]) in the upper limb for at least 6 months, and during the past week the maximum intensity of pain more than four on a 11-point numeric rating scale (NRS 0–10, 0=no pain, 10=extreme pain). Exclusion criteria were major psychiatric or neurological diseases and alcohol or drug abuse by self-report. Additionally, no previous use of memantine, which was part of the study medication, was allowed and mild opioids were tapered down before study medication.

Primary: CRPS symptom count

End point title	CRPS symptom count

End point description:

For CRPS symptom count, patients reported on a questionnaire with dichotomous scale (0=no, 1=yes) the presence of the following symptoms of the affected limb: hyperalgesia, allodynia, swelling, abnormal sweating, movement restriction, weakness, tremor, dystonic postures, trophic changes in skin, nails, or hair, differences in temperature or color, or changes in color.

End point type	Primary

End point timeframe:

Pre- and post-intervention.

End point values	Medication	Symptom reduction and improved function in chronic CRPS type 1		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	10	10		
Units: Symptoms	10	10		

Statistical analyses

Statistical analysis title	CRPS symptom count

Statistical analysis description:

To summarize effects of the intervention, we combined data from the motor tests, pain ratings, and psychological questionnaires into a single subject-wise index. First, change in each was transformed to a categorical variable of 1, 0 or −1, representing improvement, no change, or deterioration respectively. Then the subject-wise index was calculated as the mean of these categorical variables. The indices were tested in the group statistics against 0 with a one-sample Wilcoxon signed-rank test.

Comparison groups	Medication v Symptom reduction and improved function in chronic CRPS type 1
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	> 0.05
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During intervention.

Adverse event reporting additional description:

None of the patients were able to complete the pharmacological intervention quite as planned. In all patients, the dose or duration of study medication had to be diminished due to side-effects. Overall, patients reported 9.5±3.3 (mean±SD; range 6–15) different adverse events with a mean severity of 3.3±1.3 (1–9; NRS-11).

Assessment type	Systematic

Dictionary used

Dictionary name	No dictionary
Dictionary version	0

Reporting groups

Reporting group title	All subjects

Reporting group description:

All subjects receiving medication.

Serious adverse events	All subjects		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 10 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	All subjects		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	9 / 10 (90.00%)		
occurrences (all)	9		
Sleepiness			
subjects affected / exposed	9 / 10 (90.00%)		
occurrences (all)	9		
Headache			

subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	10		
speech problem			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Memory impairment			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Speech problems			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Eye disorders			
Visual impairment			
subjects affected / exposed	8 / 10 (80.00%)		
occurrences (all)	8		
Dry eye			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Photophobia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	10		
Nausea			
subjects affected / exposed	9 / 10 (90.00%)		
occurrences (all)	9		
Vomiting			
subjects affected / exposed	5 / 10 (50.00%)		
occurrences (all)	5		
pain	Additional description: stomach pain		
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Dry mouth			

subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
swallowing problems			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Taste disorder			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	4 / 10 (40.00%)		
occurrences (all)	4		
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Agitation			
subjects affected / exposed	1 / 10 (10.00%)		
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

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/30789827