



## Clinical trial results:

### "Effectiveness of leech therapy in treatment of chronic low back pain - a randomised controlled clinical study"

#### Summary

EudraCT number	2011-004393-28
Trial protocol	DE
Global end of trial date	31 December 2017

#### Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

#### Trial information

##### Trial identification

Sponsor protocol code	06-2011
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##### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	Charité - University Hospital of Berlin
Sponsor organisation address	Charitéplatz 1, Berlin, Germany, 10117
Public contact	Abteilung für Naturheilkunde , Charité Universitätsmedizin Berlin, 49 3080505691, naturheilkunde@immanuel.de
Scientific contact	Abteilung für Naturheilkunde , Charité Universitätsmedizin Berlin, 49 3080505691, naturheilkunde@immanuel.de

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:

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**Results analysis stage**

Analysis stage	Final
Date of interim/final analysis	31 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 February 2016
Global end of trial reached?	Yes
Global end of trial date	31 December 2017
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

Main objective of the trial:

Changes in the VAS (100mm) pain score 7 days after leech treatment

Protection of trial subjects:

This proof-of-concept study was planned, approved, and conducted as a two-center, open, nonblinded, randomized controlled clinical trial. Formally a pharmaceutical trial, it was carried out according to the requirements of the German Medicines Act and the Ordinance on the Implementation of Good Clinical Practice in the Conduct of Clinical Trials on Medicinal Products for Use in Humans (GCP-V).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects****Subjects enrolled per country**

Country: Number of subjects enrolled	Germany: 44
Worldwide total number of subjects	44
EEA total number of subjects	44

Notes:

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**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)	40
From 65 to 84 years	4
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Official approval to conduct the study was granted on 12 July 2012. The first patient was recruited in May 2013

### Pre-assignment

Screening details:

Telephone screening (n = 103)

– Declined participation

(n = 10)

– Inclusion/exclusion criteria not fulfilled (n = 24)

Preinclusion examination by physician (n = 69)

– Inclusion/exclusion criteria not fulfilled (n = 17)

Randomization (n = 52)

### Period 1

Period 1 title	Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Leech therapy

Arm description:

The leech therapy comprised a single local application of four to seven leeches in an area 3 to 15 cm from the spinal column at the level of vertebrae L1 to S3. Following careful examination of each participant's back by the study physician, the leeches were preferentially applied at points of maximal pressure sensitivity and at zones of hardened and/or swollen connective tissue. No two leeches were placed closer than 5 cm to each other in any direction, and there were a maximum of four leeches per square decimeter. The number of leeches used depended on the area of the participant's lower back and on the extent of the zones classed as requiring treatment.

Arm type	Experimental
Investigational medicinal product name	Hirudo verbana
Investigational medicinal product code	SUB14106MIG
Other name	
Pharmaceutical forms	Not assigned
Routes of administration	Intradermal use

Dosage and administration details:

area 3 to 15 cm from the spinal column at the level of vertebrae L1 to S3. The control treatment comprised one 60-min session of exercise therapy each week for 4 weeks.

<b>Arm title</b>	back exercise school
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Arm description:

The control intervention was a 4-week course of exercise treatment with one 60-min session each week. The exercise consisted of aerobic training in the form of Nordic walking plus various back exercises in small groups under the supervision of a physiotherapist.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

<b>Number of subjects in period 1</b>	Leech therapy	back exercise school
Started	25	19
Completed	23	13
Not completed	2	6
Adverse event, non-fatal	-	2
Loss of interest	-	2
Protocol deviation	2	2

## Baseline characteristics

### Reporting groups

Reporting group title	Leech therapy
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Reporting group description:

The leech therapy comprised a single local application of four to seven leeches in an area 3 to 15 cm from the spinal column at the level of vertebrae L1 to S3. Following careful examination of each participant's back by the study physician, the leeches were preferentially applied at points of maximal pressure sensitivity and at zones of hardened and/or swollen connective tissue. No two leeches were placed closer than 5 cm to each other in any direction, and there were a maximum of four leeches per square decimeter. The number of leeches used depended on the area of the participant's lower back and on the extent of the zones classed as requiring treatment.

Reporting group title	back exercise school
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Reporting group description:

The control intervention was a 4-week course of exercise treatment with one 60-min session each week. The exercise consisted of aerobic training in the form of Nordic walking plus various back exercises in small groups under the supervision of a physiotherapist.

Reporting group values	Leech therapy	back exercise school	Total
Number of subjects	25	19	44
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	59.29 ± 6.99	56.53 ± 7.8	-
Gender categorical Units: Subjects			
Female	22	18	40
Male	3	1	4
BMI Units: kg/m <sup>2</sup> arithmetic mean standard deviation	27.69 ± 5	25.53 ± 5.2	-
Duration of pain Units: years arithmetic mean standard deviation	13.29 ± 14.01	11.18 ± 9.4	-
Expectations			
Related to the effect of the allocated treatment on a 5-point Likert scale			
Units: Scale arithmetic mean standard deviation	4.00 ± 0.71	3.57 ± 1.06	-
Height Units: cm arithmetic mean standard deviation	169.86 ± 9.92	168.53 ± 8.4	-
Weight Units: kg			

arithmetic mean	79.94	72.52	
standard deviation	± 15.9	± 15.7	-

## End points

### End points reporting groups

Reporting group title	Leech therapy
Reporting group description: The leech therapy comprised a single local application of four to seven leeches in an area 3 to 15 cm from the spinal column at the level of vertebrae L1 to S3. Following careful examination of each participant's back by the study physician, the leeches were preferentially applied at points of maximal pressure sensitivity and at zones of hardened and/or swollen connective tissue. No two leeches were placed closer than 5 cm to each other in any direction, and there were a maximum of four leeches per square decimeter. The number of leeches used depended on the area of the participant's lower back and on the extent of the zones classed as requiring treatment.	
Reporting group title	back exercise school
Reporting group description: The control intervention was a 4-week course of exercise treatment with one 60-min session each week. The exercise consisted of aerobic training in the form of Nordic walking plus various back exercises in small groups under the supervision of a physiotherapist.	

### Primary: VAS: pain

End point title	VAS: pain
End point description: 100-mm visual analog scale	
End point type	Primary
End point timeframe: 28 Days	

End point values	Leech therapy	back exercise school		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	19		
Units: Scale				
arithmetic mean (standard deviation)				
Day 0	61.2 (± 15.6)	61.5 (± 14.7)		
Day 28 ± 3	33.1 (± 22.4)	59.7 (± 16.7)		

Attachments (see zip file)	Course of primary outcome measure/VASpain.docx
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### Statistical analyses

Statistical analysis title	Pain reduction over time
Statistical analysis description: For the primary outcome measure of VAS pain reduction, a univariate covariance analysis model (ANCOVA) was used in the framework of the general linear model (SAS procedure PROC GLM) in which the outcome measure was modeled as a function of group membership (classified, fixed factor on two levels), the	

baseline value (linear, fixed covariate), and the participant's expectations (ordinal, fixed factor on five levels).

Comparison groups	Leech therapy v back exercise school
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	$\leq 0.05$
Method	ANCOVA

## Secondary: VAS: global impairment

End point title	VAS: global impairment
End point description:	
End point type	Secondary
End point timeframe:	
28 Days	

End point values	Leech therapy	back exercise school		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	19		
Units: Scale				
arithmetic mean (standard deviation)				
Day 0	59.6 ( $\pm$ 18.0)	54.4 ( $\pm$ 24.5)		
Day 28 $\pm$ 3	31.7 ( $\pm$ 23.8)	51.0 ( $\pm$ 17.6)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change of the Roland–Morris Disability Questionnaire

End point title	Change of the Roland–Morris Disability Questionnaire
End point description:	
RMDQ	
End point type	Secondary
End point timeframe:	
56 Days	



End point values	Leech therapy	back exercise school		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	19		
Units: Score				
arithmetic mean (standard deviation)				
Day 0	12.6 (± 4.3)	12.2 (± 5.4)		
Day 28 ± 3	6.7 (± 4.7)	11.6 (± 5.4)		
Day 56 ± 5	5.6 (± 4.1)	15.3 (± 8.1)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change of the FFbH-R

End point title	Change of the FFbH-R
End point description:	Funktionsfragebogen Hannover für Rückenschmerzen, FFbH-R
End point type	Secondary
End point timeframe:	56 Days

End point values	Leech therapy	back exercise school		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	19		
Units: Score				
arithmetic mean (standard deviation)				
Day 0	58.88 (± 16.8)	75.7 (± 13.9)		
Day 28 ± 3	74.7 (± 15.8)	56.1 (± 16.9)		
Day 56 ± 5	75.7 (± 13.9)	56.9 (± 19.0)		

<b>Attachments (see zip file)</b>	Course of secondary primary outcome measure daily /FFbH-R.
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### Statistical analyses

No statistical analyses for this end point

### Secondary: Change of the General quality of life: physical health

End point title	Change of the General quality of life: physical health
End point description:	measured using the Short-Form Health Survey 36 [SF-36]
End point type	Secondary

End point timeframe:

56 Days

End point values	Leech therapy	back exercise school		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	19		
Units: Score				
arithmetic mean (standard deviation)				
Day 0	33.1 (± 9.7)	33.8 (± 7.1)		
Day 28 ± 3	42.6 (± 8.7)	36.1 (± 9.2)		
Day 56 ± 5	43.3 (± 8.4)	30.5 (± 11.7)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change of the General quality of life: mental health

End point title Change of the General quality of life: mental health

End point description:

End point type Secondary

End point timeframe:

56 Days

End point values	Leech therapy	back exercise school		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	19		
Units: Score				
arithmetic mean (standard deviation)				
Day 0	46.5 (± 9.8)	46.3 (± 12.3)		
Day 28 ± 3	48.1 (± 10.0)	47.9 (± 14.1)		
Day 56 ± 5	50.3 (± 11.3)	45.4 (± 18.6)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change of the mood

End point title Change of the mood

End point description: the Center for Epidemiological Studies Depression Scale [CES-D] to measure mood	
End point type	Secondary
End point timeframe: 56 Days	

End point values	Leech therapy	back exercise school		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	19		
Units: Scale				
arithmetic mean (standard deviation)				
Day 0	17.1 (± 8.8)	17.6 (± 10.3)		
Day 28 ± 3	13.1 (± 8.6)	17.5 (± 10.9)		
Day 56 ± 5	11.9 (± 10.7)	19.4 (± 16.9)		

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change of the Perception of pain: affective pain perception

End point title	Change of the Perception of pain: affective pain perception
End point description: Perception of pain (using the Pain Perception Scale [Schmerzempfindungsskala, SES])	
End point type	Secondary
End point timeframe: 56 Days	

End point values	Leech therapy	back exercise school		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	19		
Units: Scale				
arithmetic mean (standard deviation)				
Day 0	30.5 (± 9.6)	28.6 (± 7.8)		
Day 28 ± 3	22.0 (± 6.7)	24.2 (± 4.9)		
Day 56 ± 5	19.9 (± 5.3)	23.7 (± 6.9)		

### Statistical analyses

No statistical analyses for this end point

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**Secondary: Change of the Perception of pain: sensory pain**

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End point title	Change of the Perception of pain: sensory pain
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End point description:

End point type	Secondary
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End point timeframe:

56 Days

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End point values	Leech therapy	back excercise school		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	19		
Units: Scale				
arithmetic mean (standard deviation)				
Day 0	17.1 (± 5.5)	17.5 (± 4.5)		
Day 28 ± 3	13.7 (± 4.2)	17.1 (± 3.9)		
Day 56 ± 5	12.9 (± 3.1)	17.5 (± 5.9)		

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**Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

56 Days

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	Own
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Dictionary version	1
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### Reporting groups

Reporting group title	Leech therapy
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Reporting group description: -

Reporting group title	back school group
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Reporting group description: -

Serious adverse events	Leech therapy	back school group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)	0 / 19 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Leech therapy	back school group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 25 (36.00%)	7 / 19 (36.84%)	
Nervous system disorders			
migraine			
subjects affected / exposed	0 / 25 (0.00%)	1 / 19 (5.26%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
suspected biliary colic			
subjects affected / exposed	1 / 25 (4.00%)	0 / 19 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
more intense itching on more than 3 days			

subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2	0 / 19 (0.00%) 0	
Musculoskeletal and connective tissue disorders increased back pain subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	5 / 19 (26.32%) 5	
Product issues prolonged continuation of bleeding up to 24 h subjects affected / exposed occurrences (all)	3 / 25 (12.00%) 3	0 / 19 (0.00%) 0	
Additional description: with our anemia			
Infections and infestations influenza-like illness, cystitis subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2	1 / 19 (5.26%) 1	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### 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.

prolonged bleeding, makes effective blinding practically impossible. The absence of blinding means that the size of the nonspecific effect cannot be measured accurately. the low number of cases in the trial, the possible selection bias.
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Notes:

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/30636672>