



## Clinical trial results: Worms for immune regulation of multiple sclerosis Summary

EudraCT number	2008-005008-24
Trial protocol	GB
Global end of trial date	18 January 2016

### Results information

Result version number	v1 (current)
This version publication date	17 February 2018
First version publication date	17 February 2018

### Trial information

#### Trial identification

Sponsor protocol code	08126
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01470521
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	University of Nottingham
Sponsor organisation address	Derby Rd, Nottingham, United Kingdom, NG7 2UH
Public contact	Clinical Neurology, University of Nottingham, 0115 8231443, cris.constantinescu@nottingham.ac.uk
Scientific contact	Clinical Neurology, University of Nottingham, 0115 8231443, cris.constantinescu@nottingham.ac.uk

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	21 July 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 January 2016
Global end of trial reached?	Yes
Global end of trial date	18 January 2016
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Whether controlled parasitic infection with *N. americanus* (25 larvae per patient) reduces the cumulative number of gadolinium enhancing (Gd+) lesions, new T2 lesions, and enlarging T2 lesions in MS at month 9 in comparison to baseline and placebo.

Protection of trial subjects:

Minimal pain and distress (blood samples and MRI) in this trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 September 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 71
Worldwide total number of subjects	71
EEA total number of subjects	71

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)	71
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Recruitment from NUH clinical database

### Pre-assignment

Screening details:

73 screened. 2 screening failures. Inclusion: RR or SP MS, untreated. Exclusion: pregnant or planned pregnancy, younger than 18 or older than 65, comorbidities, anaemia, prior evidence of parasitic infection.

### Period 1

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

### Arms

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

Arm description:

Patients treated with *Necator americanus*

Arm type	Experimental
Investigational medicinal product name	<i>Necator americanus</i> larvae
Investigational medicinal product code	3057
Other name	
Pharmaceutical forms	Concentrate for cutaneous solution
Routes of administration	Cutaneous use

Dosage and administration details:

25 larvae, single dose, in water solution, applied by patch applied to skin.

<b>Arm title</b>	Placebo
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Arm description:

Patients receiving no treatment

Arm type	Placebo
Investigational medicinal product name	placebo patch
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous patch
Routes of administration	Cutaneous use

Dosage and administration details:

Administered to arm

<b>Number of subjects in period 1</b>	Treated	Placebo
Started	35	36
Completed	35	36

## Baseline characteristics

### Reporting groups

Reporting group title	Treated
Reporting group description: Patients treated with <i>Necator americanus</i>	
Reporting group title	Placebo
Reporting group description: Patients receiving no treatment	

Reporting group values	Treated	Placebo	Total
Number of subjects	35	36	71
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	35	36	71
From 65-84 years	0	0	0
85 years and over	0	0	0
Adults (18-65 years)	0	0	0
Gender categorical			
Units: Subjects			
Female	25	26	51
Male	10	10	20
disease type			
RRMS or SPMS			
Units: Subjects			
RRMS	31	27	58
SPMS	4	9	13

## End points

### End points reporting groups

Reporting group title	Treated
Reporting group description:	
Patients treated with Necator americanus	
Reporting group title	Placebo
Reporting group description:	
Patients receiving no treatment	

### Primary: MRI disease activity

End point title	MRI disease activity
End point description:	
Total number of new, enlarging, and enhancing lesions	
End point type	Primary
End point timeframe:	
Visit 1 to Visit 13	

End point values	Treated	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31 <sup>[1]</sup>	33 <sup>[2]</sup>		
Units: Lesions	31	33		

Notes:

[1] - Those with 2, or less, missing MRI

[2] - Those with 2, or less, missing MRI

<b>Attachments (see zip file)</b>	Lesion dot plot.png
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### Statistical analyses

<b>Statistical analysis title</b>	Primary
Statistical analysis description:	
Comparison of lesion counts: treated v placebo	
Comparison groups	Treated v Placebo
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority <sup>[3]</sup>
P-value	< 0.27 <sup>[4]</sup>
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median difference (final values)
Point estimate	0

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**Confidence interval**

level	95 %
sides	2-sided
lower limit	-2
upper limit	0

**Notes:**

[3] - Hypothesis: there are there fewer new lesions in the treated than placebo group.

[4] - Two tailed. Unfortunately there were many ties (zero detectable MRI activity) particularly in the treated group. Ultimately this has impaired the power of the planned analysis.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Visit 1 to visit 13.

Adverse event reporting additional description:

Self reporting

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	2016
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### Reporting groups

Reporting group title	Treated
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Reporting group description:

Patients treated with Necator americanus

Reporting group title	Placebo
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Reporting group description:

Patients receiving no treatment

<b>Serious adverse events</b>	Treated	Placebo	
<b>Total subjects affected by serious adverse events</b>			
subjects affected / exposed	2 / 35 (5.71%)	4 / 36 (11.11%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
<b>Surgical and medical procedures</b>			
<b>Hysterectomy</b>			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Thyroidectomy</b>			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Nervous system disorders</b>			
<b>Brain hypoxia</b>			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
<b>Pregnancy, puerperium and perinatal conditions</b>			

Pregnancy			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Multiple sclerosis relapse			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Allergy to synthetic fabric			
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Diabetes mellitus			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 35 (0.00%)	2 / 36 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

<b>Non-serious adverse events</b>	Treated	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 35 (100.00%)	33 / 36 (91.67%)	
Cardiac disorders			
Chest pain			
subjects affected / exposed	2 / 35 (5.71%)	0 / 36 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1	6 / 36 (16.67%) 6	
Dizziness subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0	2 / 36 (5.56%) 2	
General disorders and administration site conditions reaction at plaster site subjects affected / exposed occurrences (all)	29 / 35 (82.86%) 29	10 / 36 (27.78%) 10	
hay fever subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1	3 / 36 (8.33%) 3	
Immune system disorders Multiple sclerosis relapse subjects affected / exposed occurrences (all)	4 / 35 (11.43%) 4	9 / 36 (25.00%) 9	
Ear and labyrinth disorders Ear infection subjects affected / exposed occurrences (all)	0 / 35 (0.00%) 0	3 / 36 (8.33%) 3	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	9 / 35 (25.71%) 9	9 / 36 (25.00%) 9	
Abdominal discomfort subjects affected / exposed occurrences (all)	8 / 35 (22.86%) 8	6 / 36 (16.67%) 6	
Gastroenteritis subjects affected / exposed occurrences (all)	4 / 35 (11.43%) 4	5 / 36 (13.89%) 5	
Constipation subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1	3 / 36 (8.33%) 3	
Nausea			

subjects affected / exposed occurrences (all)	3 / 35 (8.57%) 3	0 / 36 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract infection subjects affected / exposed occurrences (all)	16 / 35 (45.71%) 16	18 / 36 (50.00%) 18	
Lower respiratory tract infection subjects affected / exposed occurrences (all)	3 / 35 (8.57%) 3	3 / 36 (8.33%) 3	
Cough subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2	2 / 36 (5.56%) 2	
Skin and subcutaneous tissue disorders			
Rash subjects affected / exposed occurrences (all)	3 / 35 (8.57%) 3	3 / 36 (8.33%) 3	
Pain of skin subjects affected / exposed occurrences (all)	1 / 35 (2.86%) 1	2 / 36 (5.56%) 2	
Renal and urinary disorders			
Urinary tract infection subjects affected / exposed occurrences (all)	7 / 35 (20.00%) 7	6 / 36 (16.67%) 6	
Psychiatric disorders			
Depression subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2	1 / 36 (2.78%) 1	
Musculoskeletal and connective tissue disorders			
Pain in extremity subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2	7 / 36 (19.44%) 7	
Back pain subjects affected / exposed occurrences (all)	3 / 35 (8.57%) 3	2 / 36 (5.56%) 2	
Nasopharyngitis			

subjects affected / exposed occurrences (all)	3 / 35 (8.57%) 3	2 / 36 (5.56%) 2	
Infections and infestations Tooth abscess subjects affected / exposed occurrences (all)	3 / 35 (8.57%) 3	3 / 36 (8.33%) 3	

## **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**

None reported