



## Clinical trial results: Triple therapy in early active rheumatoid arthritis Summary

EudraCT number	2004-002006-30
Trial protocol	GB
Global end of trial date	06 June 2006

### Results information

Result version number	v1 (current)
This version publication date	05 April 2019
First version publication date	05 April 2019

### Trial information

#### Trial identification

Sponsor protocol code	RN02RH001
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#### Additional study identifiers

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

Notes:

### Sponsors

Sponsor organisation name	NHS Greater Glasgow and Clyde
Sponsor organisation address	West Glasgow Ambulatory Care Hospital, Dalnair Street, Glasgow, United Kingdom, G3 8SW
Public contact	Dr M. Travers, NHS Greater Glasgow and Clyde, 0044 141 232 1813, Maureen.travers@ggc.scot.nhs.uk
Scientific contact	Dr Duncan Porter , NHS Greater Glasgow and Clyde, 0044 141 452 6176 , 0044 141 452 6176, duncan.porter@ggc.scot.nhs.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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	01 March 2006
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 March 2006
Global end of trial reached?	Yes
Global end of trial date	06 June 2006
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

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Main objective of the trial:

The aim of the trial is to test the hypothesis that improved, sustained disease control (with acceptable toxicity) will result from early triple therapy with methotrexate, hydroxychloroquine and sulphasalazine. The specific research questions that will be addressed are:

1) Does early triple therapy in the treatment of early active rheumatoid arthritis confer significant benefits in terms of disease control when compared to a 'step up' strategy for the use of disease modifying drug therapy?

Protection of trial subjects:

As part of the study patients required to attend hospital visits and investigations which could be above those considered to be standard care. The visit schedule and the number and type of investigations were fully explained to the the patient verbally and in writing via the patient information sheet to ensure patients were fully aware what was entailed in the prior to them consenting into the study. The patient information sheet also fully explained the design of the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2002
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	United Kingdom: 96
Worldwide total number of subjects	96
EEA total number of subjects	96

Notes:

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**Subjects enrolled per age group**

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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)	96
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

A total of 263 were screened between 01/02/2003 and 01/03/2005. Of these 96 patients were enrolled in the study.

### Pre-assignment

Screening details:

A total of 263 patients with newly diagnosed rheumatoid arthritis screened

### Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

### Arms

Are arms mutually exclusive?	Yes
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<b>Arm title</b>	step up group
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled injector, Tablet
Routes of administration	Oral use, Subcutaneous use

Dosage and administration details:

7.5mg / week escalating to max 25 mg / week

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

Dosage and administration details:

500 mg daily, increasing weekly to target dose 40 mg/kg/week) (or max tolerated dose)

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

Dosage and administration details:

400 mg / day

<b>Arm title</b>	Triple therapy
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Arm description: -

Arm type	Experimental
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Investigational medicinal product name	Methotrexate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Suspension for injection in pre-filled injector
Routes of administration	Oral use, Subcutaneous use
Dosage and administration details:	
7.5 mg / week dose escalated to max 25mg / week	
Investigational medicinal product name	Sulphasalazine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
1g / day escalating to 40mg / kg per day	
Investigational medicinal product name	hydroxychloroquine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
200mg / day	

<b>Number of subjects in period 1</b>	step up group	Triple therapy
Started	47	49
Completed	44	47
Not completed	3	2
Adverse event, serious fatal	-	1
Lost to follow-up	3	1

## Baseline characteristics

### Reporting groups

Reporting group title

Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	96	96	
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)	96	96	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	74	74	
Male	22	22	

## End points

### End points reporting groups

Reporting group title	step up group
Reporting group description: -	
Reporting group title	Triple therapy
Reporting group description: -	

### Primary: Mean change in disease activity score 28

End point title	Mean change in disease activity score 28 <sup>[1]</sup>
End point description:	

End point type	Primary
End point timeframe:	
0 - 12 months	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Uploader not involved in the trial and not aware of the details of the statistical analysis performed

End point values	step up group	Triple therapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	47		
Units: Mean change				
number (not applicable)	-4.0	-3.3		

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

01/09/2002 - 06/06/2006

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	17
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### Reporting groups

Reporting group title	SAEs
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Reporting group description:

All

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No Non Serious Adverse Events collected

Serious adverse events	SAEs		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 96 (10.42%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic renal cell carcinoma			
subjects affected / exposed <sup>[2]</sup>	1 / 1 (100.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Investigations			
Galstones, ERCP and sphincterectomy			
subjects affected / exposed <sup>[3]</sup>	1 / 1 (100.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Intertrochanteric fracture Left Hip			
subjects affected / exposed <sup>[4]</sup>	1 / 1 (100.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oesophageal rupture			



subjects affected / exposed <sup>[5]</sup>	1 / 1 (100.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Possible TIA			
subjects affected / exposed <sup>[6]</sup>	1 / 1 (100.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Congestive cardiac failure			
subjects affected / exposed <sup>[7]</sup>	1 / 1 (100.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachycardia			
subjects affected / exposed <sup>[8]</sup>	1 / 1 (100.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial Infection			
subjects affected / exposed <sup>[9]</sup>	1 / 1 (100.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed <sup>[10]</sup>	1 / 1 (100.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
dyspepsia			
subjects affected / exposed <sup>[11]</sup>	1 / 1 (100.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Fractured Humerus			

subjects affected / exposed <sup>[12]</sup>	1 / 1 (100.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Thoracic Herpes Zoster			
subjects affected / exposed <sup>[13]</sup>	1 / 1 (100.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Notes:

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: No Non Serious Adverse Events collected

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: No Non Serious Adverse Events collected

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: No Non Serious Adverse Events collected

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: No Non Serious Adverse Events collected

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: No Non Serious Adverse Events collected

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: No Non Serious Adverse Events collected

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: No Non Serious Adverse Events collected

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: No Non Serious Adverse Events collected

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: No Non Serious Adverse Events collected

[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: No Non Serious Adverse Events collected

[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: No Non Serious Adverse Events collected

[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: No Non Serious Adverse Events collected

Frequency threshold for reporting non-serious adverse events: 0 %

<b>Non-serious adverse events</b>	SAEs		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 96 (0.00%)		



## **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