



## 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 |
|-----------------------|-----------|

#### 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,<br>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,<br>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:

## Results analysis stage

|                                                      |               |
|------------------------------------------------------|---------------|
| 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:

## General information about the trial

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:

## Population of trial subjects

### 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:

### 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) | 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 |
|------------------------------|-----|

|                  |               |
|------------------|---------------|
| <b>Arm title</b> | step up group |
|------------------|---------------|

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 |
|------------------|----------------|

Arm description: -

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|                                                 |                                                         |
|-------------------------------------------------|---------------------------------------------------------|
| 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<br>(gestational age < 37 wks) | 0             | 0     |  |
| Newborns (0-27 days)                                  | 0             | 0     |  |
| Infants and toddlers (28 days-23<br>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 |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |    |
|--------------------|----|
| Dictionary version | 17 |
|--------------------|----|

### Reporting groups

|                       |      |
|-----------------------|------|
| Reporting group title | SAEs |
|-----------------------|------|

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           |  |  |
| <b>Infections and infestations</b><br><b>Thoracic Herpes Zoster</b><br>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