



Clinical trial results:

RETREAT(F) (REmoval of Treatment for patients in REmission in psoriatic ArThritis – Feasibility study). A randomised controlled trial to compare withdrawal of therapy versus continuing therapy in low disease states in psoriatic arthritis – feasibility study, RCT Arm

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2012-003736-23 |
| Trial protocol | GB |
| Global end of trial date | 02 December 2013 |

Results information

| | |
|-----------------------------------|---|
| Result version number | v1 (current) |
| This version publication date | 06 March 2020 |
| First version publication date | 06 March 2020 |
| Summary attachment (see zip file) | Retreat AE Tables (retreat AE tables.pdf) RETREAT publication (RETREAT_ClinRheum_2015.pdf) |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | RR11/9229 |
|-----------------------|-----------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | University of Leeds |
| Sponsor organisation address | Worsley Building, Leeds, United Kingdom, LS2 9JT |
| Public contact | Dr P Helliwell, University for Leeds, 0113 3923064, p.helliwell@leeds.ac.uk |
| Scientific contact | Dr P Helliwell, University for Leeds, 0113 3923064, p.helliwell@leeds.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 | 02 December 2013 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 02 December 2013 |
| Global end of trial reached? | Yes |
| Global end of trial date | 02 December 2013 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

For this feasibility study we wish to know the proportion of eligible patients who are willing to undergo treatment withdrawal and the proportion remaining in minimal disease at the end of the study period. Within the three month treatment withdrawal period, a minimal disease activity (MDA) score of 5 or more (achievement of the minimal disease activity criteria) will be used to confirm continuing low disease activity. A person not achieving the MDA criteria at any of the monthly assessment time points will be deemed to be experiencing a flare of their disease. The proportion of patients who flare will also be used to inform the full study.

Protection of trial subjects:

All information collected during the course of the trial will be kept strictly confidential. Information will be held securely on paper and electronically will comply with all aspects of the Data Protection Act 1998. An Independent Trial Steering Group (TSG) will meet before the start of patient recruitment and just after the last patient has been reviewed at the three month visit. The study will be reviewed by a data monitoring and ethics committee (DMEC).

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 03 December 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: 17 |
| Worldwide total number of subjects | 17 |
| EEA total number of subjects | 17 |

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) | 14 |
| From 65 to 84 years | 3 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

All patients which met the inclusion criteria were invited to attend an initial screening visit where consent was obtained. Patients were recruited from outpatient clinics in the UK. at baseline a full assessment was undertaken and the patient was randomized at a ratio of 2:1 in favor of the withdrawal arm.

Pre-assignment

Screening details:

Participants attended an initial screening visit (visit 0) where consent was obtained; a clinical assessment was undertaken; and MDA was confirmed utilizing the MDA criteria.

Period 1

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

Blinding implementation details:

N/A

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|----------------|
| Arm title | Withdrawal Arm |
|------------------|----------------|

Arm description:

Patients randomized to drug withdrawal will undergo a phased withdrawal of medication where the last treatment added will be the first treatment withdrawn. Drugs will be withdrawn to doses routinely administered. Treatment will be withdrawn in a stepwise fashion phasing out and stopping over three months. Participants will be reviewed in clinic on 4 occasions 1 month apart (after screening) to manage treatment changes and monitor withdrawal response using the MDA criteria above. It is anticipated that the majority of patients will be taking TNF inhibitors at enrolment and up to one third will be taking methotrexate alone.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Methotrexate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

step-wise reduction of 2.5 mg per week until cessation

| | |
|--|---------------|
| Investigational medicinal product name | Sulfasalazine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

dose halved for 6 weeks and then stopped

| | |
|--|-------------|
| Investigational medicinal product name | Leflunomide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

dose halved for 6 weeks and then stopped

| | |
|--|---------------------|
| Investigational medicinal product name | Cyclosporin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details: dose halved for 6 weeks and then stopped | |
| Investigational medicinal product name | Etanercept |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: week 0, 2, 4, 8 | |
| Investigational medicinal product name | Infliximab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: week 8 or 10 | |
| Investigational medicinal product name | Adalimumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: week 0, 4, 8 | |
| Investigational medicinal product name | Golimumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intravenous use |
| Dosage and administration details: week 6 | |
| Arm title | Standard Care Arm |
| Arm description: Patients in this group will continue with their current therapy for the duration of the study. However, the treating clinician will be free to change their treatment if clinically indicated to do so (e.g., escalate treatment doses if patient is relapsing or decrease/change treatment if there are side-effects). Patients in this group will be seen at the same intervals as the intervention arm. | |
| Arm type | Control |
| Investigational medicinal product name | Methotrexate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: step-wise reduction of 2.5 mg per week until cessation | |
| Investigational medicinal product name | Sulfasalazine |
| Investigational medicinal product code | |
| Other name | |

| | |
|--|---------------------|
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: dose halved for 6 weeks and then stopped | |
| Investigational medicinal product name | Leflunomide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: dose halved for 6 weeks and then stopped | |
| Investigational medicinal product name | Cyclosporin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |
| Dosage and administration details: dose halved for 6 weeks and then stopped | |
| Investigational medicinal product name | Etanercept |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: week 0, 2, 4, 8 | |
| Investigational medicinal product name | Infliximab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: week 8 or 10 | |
| Investigational medicinal product name | Adalimumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Subcutaneous use |
| Dosage and administration details: week 0, 4, 8 | |
| Investigational medicinal product name | Golimumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intravenous use |
| Dosage and administration details: week 6 | |

| Number of subjects in period 1 | Withdrawal Arm | Standard Care Arm |
|---------------------------------------|----------------|-------------------|
| Started | 11 | 6 |
| Completed | 11 | 6 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|----------------|
| Reporting group title | Withdrawal Arm |
|-----------------------|----------------|

Reporting group description:

Patients randomized to drug withdrawal will undergo a phased withdrawal of medication where the last treatment added will be the first treatment withdrawn. Drugs will be withdrawn to doses routinely administered. Treatment will be withdrawn in a stepwise fashion phasing out and stopping over three months. Participants will be reviewed in clinic on 4 occasions 1 month apart (after screening) to manage treatment changes and monitor withdrawal response using the MDA criteria above. It is anticipated that the majority of patients will be taking TNF inhibitors at enrolment and up to one third will be taking methotrexate alone.

| | |
|-----------------------|-------------------|
| Reporting group title | Standard Care Arm |
|-----------------------|-------------------|

Reporting group description:

Patients in this group will continue with their current therapy for the duration of the study. However, the treating clinician will be free to change their treatment if clinically indicated to do so (e.g., escalate treatment doses if patient is relapsing or decrease/change treatment if there are side-effects). Patients in this group will be seen at the same intervals as the intervention arm.

| Reporting group values | Withdrawal Arm | Standard Care Arm | Total |
|--|----------------|-------------------|-------|
| Number of subjects | 11 | 6 | 17 |
| 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) | 8 | 6 | 14 |
| From 65-84 years | 3 | 0 | 3 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 5 | 2 | 7 |
| Male | 6 | 4 | 10 |

End points

End points reporting groups

| | |
|---|-------------------|
| Reporting group title | Withdrawal Arm |
| Reporting group description: Patients randomized to drug withdrawal will undergo a phased withdrawal of medication where the last treatment added will be the first treatment withdrawn. Drugs will be withdrawn to doses routinely administered. Treatment will be withdrawn in a stepwise fashion phasing out and stopping over three months. Participants will be reviewed in clinic on 4 occasions 1 month apart (after screening) to manage treatment changes and monitor withdrawal response using the MDA criteria above. It is anticipated that the majority of patients will be taking TNF inhibitors at enrolment and up to one third will be taking methotrexate alone. | |
| Reporting group title | Standard Care Arm |
| Reporting group description: Patients in this group will continue with their current therapy for the duration of the study. However, the treating clinician will be free to change their treatment if clinically indicated to do so (e.g., escalate treatment doses if patient is relapsing or decrease/change treatment if there are side-effects). Patients in this group will be seen at the same intervals as the intervention arm. | |

Primary: Overall Flare Status

| | |
|--|-------------------------------------|
| End point title | Overall Flare Status ^[1] |
| End point description: Actual number of patients who experienced a flare are captured, though expressed in percentage from in the attached publication. | |
| End point type | Primary |
| End point timeframe: The trial Primary endpoint was to determine how controlled withdrawal of trial treatment impacted on flare rates compared to standard treatment in patients with stable low disease activity psoratic RA, to see if remission can be sustained. | |
| 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: Please see attached publication for all exploratory statistical analysis's performed in the trial. | |

| End point values | Withdrawal Arm | Standard Care Arm | | |
|-------------------------------------|-----------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 11 | 6 | | |
| Units: No of Patients who relapsed. | 6 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

AEs will be collected for all patients from randomisation until the last dose of treatment with a protocol IMP. AEs will be evaluated for duration and intensity according to the NCRI Common Toxicity Criteria.

Adverse event reporting additional description:

Information about AEs, whether volunteered by the patient, discovered by the investigator questioning or detected through physical examination, laboratory test or other investigation will be collected and recorded on the CRF.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|-------|
| Dictionary name | CTCAE |
|-----------------|-------|

| | |
|--------------------|-----|
| Dictionary version | 4.0 |
|--------------------|-----|

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

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 Serious Adverse Events were recorded on the trial. For details of all adverse events, please see the attached document, retreat AE tables.pdf

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 21 December 2012 | MHRA CTA application amended to update the supply arrangements of two of the IMP's, as the research team requested to use generic hospital stock instead of the previous agreed supplier |

Notes:

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.

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|-----|
| N/A |
|-----|

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/25644584>