# Circadian variations in cytokines and the effect of timed release tablet prednisone in rheumatoid arthritis

Submission date Recruitment status Prospectively registered 16/08/2007 No longer recruiting [ ] Protocol [ ] Statistical analysis plan Registration date Overall study status 04/10/2007 Completed [X] Results [ ] Individual participant data Last Edited Condition category Musculoskeletal Diseases 18/01/2012

# Plain English summary of protocol

Not provided at time of registration

## Contact information

#### Type(s)

Scientific

#### Contact name

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# Additional identifiers

Protocol serial number ME/2005/2073

# Study information

Scientific Title

#### Study objectives

Rheumatoid Arthritis (RA) is a systemic, inflammatory condition causing joint pain and swelling, disability, and psychological distress.

To document overnight variations of serum pro-inflammatory and anti-inflammatory cytokines in 12 volunteers with rheumatoid arthritis on one night before and one night during treatment with a Timed Release Tablet (TRT) containing 5 mg prednisone, and to relate blood cytokine levels to biogenic amines and the hormones of the hypothalamic-pituitary-adrenal axis.

#### Ethics approval required

Old ethics approval format

#### Ethics approval(s)

Approval received from the North Somerset and South Bristol Research Ethics Committee (REC) on the 28th November 2005 (ref: 054/Q2006/185).

#### Study design

Non-randomised, non-controlled interventional single centre study of patients before and after two weeks treatment with night time prednisone

#### Primary study design

Interventional

#### Study type(s)

Treatment

#### Health condition(s) or problem(s) studied

Rheumatoid Arthritis (RA)

#### **Interventions**

The study uses a delayed (timed) release formulation of prednisone which will release the full dose of the active drug during sleep after a lag time of 4 hours, allowing the patient to take the medication at a convenient point in time, namely at 22:00 hours +/- 30 minutes.

Intervention: Timed-Release Tablet (TRT) prednisone 5 mg, one tablet taken at 22.00 each evening for 12 - 16 nights (depending on the convenience of the final study night for the patient). There is no study follow-up after the end of medication.

#### Intervention Type

Drug

#### Phase

**Not Specified** 

## Drug/device/biological/vaccine name(s)

Prednisone

## Primary outcome(s)

Changes in overnight pattern of plasma cortisol and interleukin-6 concentrations, determined at baseline and two weeks.

#### Key secondary outcome(s))

Standard assessment tools will be used to assess the state of the patient's arthritis. These assessments will be:

- 1. Swollen and tender joint counts
- 2. Pain (visual analogue scale)
- 3. Morning stiffness (minutes)
- 4. Patient's opinion of condition
- 5. Clinician's opinion of condition
- 6. Health Assessment Questionnaire
- 7. The Multidimensional Assessment of Fatigue scale
- 8. Hospital Anxiety and Depression Scale

The secondary outcome measures are determined at baseline and two weeks.

#### Completion date

14/06/2008

# **Eligibility**

#### Key inclusion criteria

- 1. Have rheumatoid arthritis by the criteria of the American College of Rheumatology
- 2. Are over 50 but less than 80 years old
- 3. Have active disease as evidenced by:
- 3.1. Three or more swollen joints
- 3.2. Three or more tender joints
- 3.3. Morning stiffness at least 45 minutes
- 3.4. Pain at least 30 mm on a 100 mm Visual Analogue Scale (VAS)
- 3.5. Erythrocyte Sedimentation Rate (ESR) at least 29 mm in first hour or C-Reactive Protein (CRP) at least 15 mg/L
- 4. Stable Disease-Modifying Anti-Rheumatic Drug (DMARD) therapy (or no therapy) for at least 28 days
- 5. Stable Non-Steroidal Anti-Inflammatory Drug (NSAID)/analgesic therapy for at least seven days

It is anticipated that the ratio of female to male patients will be approximately 2:1, in accordance with the pattern of disease occurrence. To be safe, we will invite women of childbearing potential to take part in the study only if they are using contraception.

#### Participant type(s)

Patient

#### Healthy volunteers allowed

No

#### Age group

Senior

#### Sex

Αll

#### Key exclusion criteria

- 1. Pregnancy and lactation
- 2. Participation in a clinical trial within the past 30 days
- 3. Presence of contraindication of corticosteroids
- 4. Known hypersensitivity to prednisone/prednisolone
- 5. Parenteral treatment with corticosteroids or crystalloid injection into joints within the past three months
- 6. Other diseases which require corticoid treatments
- 7. Inflammatory diseases, such as Irritable Bowel Disease (IBD), Colitis, Crohn's Disease, Asthma
- 8. Other auto-immune diseases
- 9. Cancer
- 10. Infections, treatment with antibiotics within the past six weeks
- 11. Requirement of non-permitted concomitant medication
- 12. Consumption of benzodiazepines, antidepressants, antipsychotic drugs, antihistaminic drugs
- 13. Tumour Necrotising Factor alpha (TNFα) inhibitors
- 14. Working shift employee
- 15. Jet lag
- 16. Significant renal disease (creatinine greater than 150 µmol/L)
- 17. Significant hepatic impairment

#### Date of first enrolment

15/06/2006

#### Date of final enrolment

14/06/2008

## Locations

#### Countries of recruitment

United Kingdom

England

# Study participating centre Academic Rheumatology Unit

Bristol United Kingdom BS2 8HW

# Sponsor information

#### Organisation

United Bristol Healthcare NHS Trust (UK)

#### **ROR**

https://ror.org/04nm1cv11

# Funder(s)

## Funder type

Industry

#### **Funder Name**

Nitec Pharma AG (Switzerland)

# **Results and Publications**

Individual participant data (IPD) sharing plan

## IPD sharing plan summary

Not provided at time of registration

## **Study outputs**

Output type	Details	Date created Date added	d Peer reviewed?	? Patient-facing?
Results article	results	01/04/2010	Yes	No
Participant information sheet	Participant information sheet	11/11/2025 11/11/2025	5 No	Yes