Combined Immunosuppression and Radiotherapy in Thyroid Eye Disease

Submission date Recruitment status Prospectively registered 25/01/2006 No longer recruiting [X] Protocol [] Statistical analysis plan Registration date Overall study status 01/02/2006 Completed [X] Results Individual participant data **Last Edited** Condition category 14/02/2018 **Eve Diseases**

Plain English summary of protocol

Not provided at time of registration

Study website

http://www.cirted.org

Contact information

Type(s)

Scientific

Contact name

Mr Richard Lee

Contact details

Department of Clinical Sciences Bristol Eye Hospital Lower Maudlin street Bristol United Kingdom BS1 2LX

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

N/A

Study information

Scientific Title

Combined Immunosuppression and Radiotherapy in Thyroid Eye Disease

Acronym

CIRTED

Study objectives

Primary hypotheses:

To test the following hypotheses in patients being treated with prednisolone for active Thyroid Eye Disease (TED):

- 1. Radiotherapy (compared with placebo) induces early remission and reduces long-term disease severity
- 2. Combined systemic immunosuppression with oral azathioprine (compared with placebo) reduces long-term disease severity

Secondary hypotheses:

- 1. To test the hypothesis that patients being treated with prednisolone for active TED, using radiotherapy and combined systemic immunosuppression with oral azathioprine, can improve patient-centred outcomes and quality of life scores
- 2. To validate the use of a new TED specific quality of life score in the UK population
- 3. To improve understanding of the extent and type of psychosocial distress experienced by TED patients
- 4. To conduct an economic evaluation of the cost of TED and its treatment to patients, the NHS and Society
- 5. To compare treatments using health-economic analysis
- 6. To report the safety and tolerability of combined systemic immunosuppression with oral azathioprine in TED patients

Ethics approval required

Old ethics approval format

Ethics approval(s)

Central & South Bristol Research Ethics Committe (reference: 05/Q2006/62), approval gained 5th May 2005 (amendment to inclusion and exclusion criteria approved on the 2nd June 2006).

Study design

Factorial randomised controlled trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Not specified

Study type(s)

Treatment

Participant information sheet

Patient information can be found at: http://www.cirted.org/patients.htm

Health condition(s) or problem(s) studied

Thyroid Eye Disease (TED)

Interventions

All the patients receive six months of oral prednisolone and then are randomly assigned to receive one of the following interventions:

- 1. Radiotherapy and azathioprine
- 2. Radiotherapy and placebo
- 3. Azathioprine and placebo
- 4. Control: placebo and placebo

Intervention Type

Drug

Phase

Not Specified

Drug/device/biological/vaccine name(s)

Azathioprine

Primary outcome measure

Primary:

- 1. Binary composite clinical outcome measure
- 2. Ophthalmopathy index

Co-primary outcome measure:

1. Clinical activity score

Secondary outcome measures

- 1. Total Eye Score (TES)
- 2. Hospital Anxiety and Depression Scale (HADS) score
- 3. Derriford Appearance scale-short form score
- 4. Graves Ophthalmopathy Quality of Life (GO-QoL) score
- 5. World Health Organisation Brief Quality of Life (WHOQoL) assessment score
- 6. Open-ended responses to interview questions
- 7. Health economic measures

Overall study start date

01/01/2006

Completion date

01/12/2008

Eligibility

Key inclusion criteria

- 1. Mourits' Clinical Activity Score more than or equal to four (worst eye) or more than two (worst eye) with a history of proptosis (defined as either subjective unilateral proptosis confirmed by asymmetry in exophthalmometry of more than 2 mm or subjective bilateral proptosis) or motility restriction (defined as intermittent, inconstant or constant diplopia grade) which is less than six months long
- 2. Past or present history of abnormal Thyroid Gland Function (TGF) or a clinical diagnosis of TED made and confirmed by more than two muscle involvement on Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) scan plus a history of recent onset motility restriction and/or proptosis

Participant type(s)

Patient

Age group

Adult

Sex

Both

Target number of participants

100

Key exclusion criteria

- 1. Age less than 20 or greater than 75 years
- 2. Optic neuropathy
- 3. Mourits Clinical Activity Score more than four without proptosis or motility restriction
- 4. Pre-existing glaucoma with a characteristic optic disc appearance and associated visual field defect
- 5. Use of radioiodine within the last three months
- 6. Pre-existing diabetes mellitus (not simply steroid-induced disease from recent therapy)
- 7. Previous adverse event associated with, or contraindication to, either prednisolone or azathioprine
- 8. Within six months of pregnancy, women planning pregnancy
- 9. Lactation
- 10. Haemoglobin concentration, total white cell count or platelet count below the local laboratory's reference range
- 11. Low, intermediate or high Thiopurine Methyltransferase (TPMT) activity
- 12. Lymphocyte count less than $0.8 \times 10^9/l$
- 13. Abnormal renal function (assessed by urea and creatinine levels above the local laboratorys reference range)
- 14. Abnormal liver function, specifically: bilirubin, alanine aminotransferase or alkaline phosphatase concentrations above the local laboratorys reference range
- 15. Malignant or pre-malignant (dysplastic) condition within the past five years
- 16. Previous tuberculosis
- 17. Shingles within the past three months
- 18. Human Immunodeficiency Virus (HIV)/Acquired Immune Deficiency Syndrome (AIDS)
- 19. Concurrent use of:
- a. Other immunosuppressive or cytotoxic agents

b. Allopurinol20. Live vaccines within the past three months21. Previous orbital irradiation

Date of first enrolment 01/01/2006

Date of final enrolment 01/12/2008

Locations

Countries of recruitment England

United Kingdom

Study participating centre
Department of Clinical Sciences
Bristol
United Kingdom
BS1 2LX

Sponsor information

Organisation

University of Bristol (UK)

Sponsor details

Research & Enterprise Development Senate House Tyndall Avenue Bristol England United Kingdom BS8 1TH

Sponsor type

University/education

ROR

https://ror.org/0524sp257

Funder(s)

Funder type

Research organisation

Funder Name

The National Eye Research Centre, Bristol (UK)

Funder Name

Special trustees of Moorfields Eye Hospital (UK)

Funder Name

The Charitable Trusts for the United Bristol Hospitals (UK)

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

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	Peer reviewed?	Patient-facing?
Protocol article	protocol	31/01/2008		Yes	No
Results article	results	01/04/2018		Yes	No