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BIMAtoprost eye drops in thyroid eye disease

Submission date
07/02/2014

Recruitment status
No longer recruiting

Registration date
14/03/2014

Overall study status
Completed

Last Edited
09/08/2019

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered

[_] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims
Thyroid eye disease (TED) is a chronic disfiguring and debilitating disease of the eyes which can lead to sight loss in severe cases. Patients with TED often have characteristic eyeball protrusion (proptosis) due to increased fat accumulation behind the eye. The discomfort and changes in appearance of the eyes is a source of severe psychological distress and reduced quality of life in many patients. Current treatments for TED are unsatisfactory and established nonsurgical therapies which specifically reduce proptosis are lacking. Reduced eyelid protrusion has recently been reported as a side effect of the use of prostaglandin analogue eye drops such as Bimatoprost (PGF2alpha) in the routine treatment of glaucoma and we have data showing inhibition of fat cells by Bimatoprost. Hence PGF2alpha eye drops potentially represent a simple, non-invasive low-toxicity alternative to surgery in TED. However, no clinical trials of Bimatoprost have been conducted in TED to date. The aim of this study is to determine whether Bimatoprost eye drops are effective in reducing proptosis and thus improving quality of life in patients with TED.

Who can participate?
Men and women aged 18 years and older from the TED clinic at the University Hospital Wales (Cardiff & Vale University Health Board). Only participants with stable, late, inactive thyroid eye disease will be enrolled. The clinic is a regional referral centre for the treatment and study of TED and is run by a multidisciplinary team of ophthalmologists, endocrinologists, and orthoptists with expertise in TED.

What does the study involve?
Following informed consent, you will be randomly allocated to use Bimatoprost or placebo (dummy) eye drops daily for three months, after which you will not use eye drops for two months, before switching to the opposite treatment in the final three months of the study. Patients will be followed up at one further visit 2 months later. You will be enrolled in the study for 10 months in total. There are six visits: before the start of the study, random allocation and four follow-up visits. You will be asked to complete quality of life questionnaires and a health economic questionnaire at each of the follow-up visits. Eye tests will be carried out before the start of the study and at follow-up visits.

What are the possible benefits and risks of participating?
If the treatment you are receiving is found to be better than the current standard treatment

then you will benefit from participating in this study. Otherwise, taking part may not be of direct benefit to you. It should, however, help us to provide better care for patients with Thyroid Eye Disease in the future. Note that all participants will receive the active treatment at one stage of the study. The most common side effects after using Bimatoprost eye drops are an itching sensation in the eyes and/or eye redness. This was reported in about 4% of patients. Bimatoprost may cause other less common side effects which typically occur on the skin close to where it is applied, or in the eyes. These include skin darkening, longer or thicker eyelashes, dryness of the eyes and redness of the eyelids. Any eyelid skin darkening or eye lash thickening /elongation are expected to reverse after several weeks to months after stopping the eye drops. Bimatoprost use may also cause increased brown pigmentation (reported in about 1% of patients) of the coloured part of the eye known as iris which may be permanent. Bimatoprost eye drops have been in routine long-term clinical use in glaucoma for 12 years, and will be used in this study at the same dose as in glaucoma therapy. Drug formulations containing Bimatoprost have been in regular use for glaucoma for some time, and Bimatoprost preparations are available over the counter for cosmetic application, thus their safety is well established.

Where is the study run from?
University Hospital of Wales, Cardiff & Vale University Health Board, UK.

When is the study starting and how long is it expected to run for?
It is expected that recruitment will start in May 2014. You will be enrolled on the study for 10 months; however, it is expected that the study will run until February 2016 to complete data analysis.

Who is funding the study?
Research for Patient and Public Benefit Wales, part of National Institute for Social Care & Health Research (NISCHR), UK.

Who is the main contact?
Professor Colin Dayan
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2014-000540-15

IRAS number

ClinicalTrials.gov number
NCT02059655

Secondary identifying numbers
SPON1266-14

Study information

Scientific Title
Prostaglandin F2-alpha eye drops (BIMAtoprost) in thyroid eye disease: a randomised controlled double blind crossover trial

Acronym
BIMA

Study objectives
We hypothesise that topical treatment with Bimatoprost may reduce orbital tissue volume in noninflamed orbits and thereby improve quality of life in patients with thyroid eye disease (TED).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Wales REC 3, initial approval obtained on 21/03/2014, REC reference: 14/WA/0081, substantial amendment 1 on 17/06/2014

Study design
Randomised placebo-controlled double-blind crossover design

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Graves' eye disease

Interventions
Bimatoprost or placebo eye drops (daily application) for three months followed by a two-month drug washout period before switching to the opposite treatment in the final three months of study.

1 drop daily for 3 months (placebo or Bimatoprost)
Stop treatment for following 2 months
1 drop daily for following 3 months (cross over to either placebo or Bimatoprost)
Patients will be followed up at one further visit 2 months later

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure
Change in proptosis measurement; reduction of 2 mm or more would be regarded as clinically relevant. Measured at all visits (baseline, 2, 3, 4, 5). Measured by exophthalmometry readings by Hertel exophthalmometer.

Secondary outcome measures
1. Change in quality of life scores: measured at visits 1, 2, 3, 4, 5. Measured by EUGOGO GO-Quality of Life and EQ-5D-5L Health Questionnaire
2. Side effects: measured at visits 2, 3, 4, 5. Standardised questionnaire in the form of a patient diary log. Patients will be requested to record any side effects in their diary
3. Change in intraocular pressure: measured at visits baseline, 2, 3, 4, 5. Measured by Goldmann Applanation Tonometer
4. Health economic cost: measured at visits 1, 2, 3, 4, 5. Measured by Client Service Receipt Inventory (CSRI)

Overall study start date
05/12/2012

Completion date
15/04/2016

Eligibility

Key inclusion criteria
1. Stable TED with no reported change in proptosis for at least 6 months
2. Clinical activity score <3
3. Proptosis (subjective unilateral proptosis confirmed by asymmetry in exophthalmometry of >2 mm OR greater than 20 mm on exophthalmometry measurement in one eye)
4. Euthyroid (FT3 and FT4 in the reference range)
5. If female, must be using a reliable form of contraception during the trial, e.g. oral contraceptive and condom, intrauterine device (IUD) and condom, diaphragm with spermicide and condom

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
31

Total final enrolment
31

Key exclusion criteria
1. Age <18 years
2. Dysthyroid optic neuropathy unless previously treated
3. Pregnancy or lactation
4. Previous corneal herpes simplex infection
5. On therapy for glaucoma or intraocular hypertension
6. Less than 6 months from prior steroid use
7. Aphakia, pseudophakia with torn posterior lens capsule or anterior chamber lenses
8. Patient with risk factors for cystoid macular oedema, iritis or uveitis
9. Severe asthma (risk of severe allergic reaction to medication).
10. Previous allergy to Bimatoprost or preservative

Date of first enrolment
20/11/2014

Date of final enrolment
12/02/2015

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Institute of Molecular & Experimental Medicine
Cardiff
United Kingdom
CF14 4XW

Sponsor information

Organisation
Cardiff University (UK)

Sponsor details
Research, Innovation & Enterprise Services (RIES)
MacKenzie House
30-36 Newport Road
Cardiff
Wales
United Kingdom
CF24 0DE

Sponsor type
University/education

Website
http://www.cf.ac.uk/racdv/resgov/index.html

ROR
https://ror.org/03kk7td41

Funder(s)

Funder type
Government

Funder Name
National Institute for Social Care & Health Research (Welsh Assembly Government) (UK)
RFPPB20121015

Results and Publications

Publication and dissemination plan
It is intended that the results of the study will be reported and disseminated at local and international conferences and in peer-reviewed scientific journals.

Intention to publish date
31/12/2018

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/04/2019	13/06/2019	Yes	No
Basic results			09/08/2019	No	No
HRA research summary			28/06/2023	No	No