ISRCTN16962255 https://doi.org/10.1186/ISRCTN16962255

Use of ARA 290 for the treatment of diabetic macular oedema

Submission date 09/06/2015	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 25/06/2015	**Overall study status** Completed	
Last Edited 04/07/2024	**Condition category** Eye Diseases	

Plain English summary of protocol

Background and study aims
Diabetic retinopathy is the most common cause of sight loss in people of working age. Sight loss occurs in diabetes because of diabetic macular oedema (DMO) and/or proliferative diabetic retinopathy (PDR) - both are complications of diabetes in the eye. In DMO, fluid accumulates in the macula, the area responsible for our central sight. As the fluid accumulates, the sight drops. The current treatments for DMO include laser and “anti-VEGF” drugs (VEFF stands for vascular endothelial growth factor). Anti-VEGF drugs have been very helpful in the treatment of DMO. However, they need to be given by an injection into the eye. An ophthalmologist (eye specialist) or a specialist nurse (a nurse trained for this purpose) needs to treat patients with DMO in the hospital. Patients require injections every four weeks during the first months of treatment and long term treatment is required. Not all patients respond to anti-VEGFs: in 40 - 50% of patients the sight does not improve despite these injections. Because many patients with DMO have DMO in both eyes, injections need to be given in both eyes to many patients.
There is a clear need to develop new treatments for people with DMO. ARA 290 is a drug that has anti-inflammatory properties and has an effect in preventing the death of cells. As inflammation is known to play a role in the occurrence of DMO, ARA 290 could potentially be helpful in treating patients with this condition. The aim of the study is to find out if ARA 290 helps drying the fluid in DMO.

Who can participate?
Adult patients with diabetic retinopathy and centre involving DMO with central retinal thickness of > 400 microns.

What does the study involve?
Participants will have to a subcutaneous injection of 4mg of ARA290 at home for a period of 12 weeks. Ie they will give themselves an injection under the skin in the left or right thigh. If they are unable to inject into either thigh, they can inject under the skin of the abdomen.They will be monitored with a follow up visit every four weeks until the end of the treatment and will undergo a series of tests at the beginning, during and at the end of the treatment.

What are the possible benefits and risks of participating?
This is an initial study and a larger one will be required to provide confirmation.

If this treatment is successful, the health service may benefit from a reduction of the demands on health care services and patients may benefit from the following: one injection given can treat both eyes at once ; reduced risks associated with injections; the injection is administered subcutaneously (under the skin) rather than in the eye which may be a more pleasant treatment. These potential benefits would last only whilst participants are in the study. ARA290 is a relatively new drug. The most common side effect observed after its administration has been headaches. A fluorescein test is carried out before and after the treatment period. For this test, the dye (fluorescein) is injected into a vein in the arm from where it will travel to the eye. Photographs are taken as the dye goes through the blood vessels in the eye, which allows us to determine whether the blood vessels in the eye are less “leaky” after the treatment and whether there is good circulation of blood through the retina. This dye test is often done in people with diabetic retinopathy and DMO; the risks associated with it are mild (mild: nausea may occur in 7 out of 100 patients and vomiting in 1 out of 100 patients; moderate: a skin rash may occur in 1 out of 100 patients) or rare (bronchospasm and laryngeal oedema which can be treated successfully).

Where is the study run from?
Belfast Health & Social Care Trust, Northern Ireland (UK)

When is the study starting and how long is it expected to run for?
May 2015 to May 2016

Who is funding the study?
This is an investigator led study funded by Araim Pharmaceuticals Ltd (UK).

Who is the main contact?
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Clinical Trials Information System (CTIS)
2015-001940-12

Protocol serial number
14166NL-AS

Study information

Scientific Title
A Phase II Clinical Trial on the use of ARA 290 for the treatment of Diabetic Macular Oedema

Acronym
ARA 290-DMO

Study objectives
The hypothesis tested is that ARA 290, when administered subcutaneously at 4mg on a daily basis for 12 weeks, due to its anti-inflammatory, anti-apoptotic and neuroprotective effects, will be of therapeutic value in patients with diabetes mellitus and diabetic macular oedema.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. South Central –Berkshire Research Ethics Committee, 14/03/2016, ref: 16/SC/0089
2. Scotland A Research Ethics Committee, 23/03/2016, ref: 16/SS/0048
3. Office for Research Ethics Northern Ireland (ORECNI), 21/10/2015

Primary study design
Interventional

Study design
Prospective open-label interventional single-centre investigator-led Phase II study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Diabetic macular oedema (DMO)

Interventions
The patient will be required to self administer a subcutaneous injection of ARA 290 in their own home, at a dose of 4 mg daily for a period of 12 weeks. The patient will be monitored carefully with a follow up visit every four weeks until the end of the 12 week trial treatment. If the patient responds to the treatment and the retina is seen to be dried at the 12 week visit, the treatment will stop and a further visit will be arranged at week 16 to see whether the effect of the treatment lasts even when the treatment has been stopped.

Dosing regime: Weeks 1 - 12. 4 mg ARA 290 injected subcutaneously on a daily basis.

Baseline: Medical history; vital signs; ETDRS BCVA; Schirmer test; SD-OCT; Wide angle fundus photographs and fluorescein angiography (FFA); Microperimetry; Bloods; Urine collection; C-SSRS; EQ-5D-5L; NEI VFQ-25.
Weeks 4 & 8 (+/-7days): Vital signs; ETDRS BCVA; SD-OCT; Record of adverse events; C-SSRS.
Week 12 (+/-7days): vital signs; ETDRS BCVA; Schirmer test; SD-OCT; Wide angle fundus photographs and fluorescein angiography (FFA); Microperimetry; Record of AEs; Bloods; Urine collection; C-SSRS; EQ-5D-5L; NEI VFQ-25.
Week 16 (if applicable): vital signs; ETDRS BCVA; Schirmer test; SD-OCT; Microperimetry; Bloods; Urine collection; C-SSRS; EQ-5D-5L; NEI VFQ-25.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
ARA 290 (cibinetide)

Primary outcome(s)
Primary outcome measures as of 20/01/2017:
Best corrected distance visual acuity is measured using Early Treatment Diabetic Retinopathy Study (ETDRS) charts at baseline, weeks 4, 8 and 12 (+ or - 7 days). If at week 12 the retina is dry, a further visit will be arranged at week 16 to measure BCVA.

Original primary outcome measure:
Changes from baseline to week 12 (+ or - 7 days) in best corrected distance visual acuity

Key secondary outcome(s)
Secondary outcome measures as of 20/01/2017:
1. Central subfield thickness is measured using spectral domain optical coherence tomography (SD-OCT) at baseline, weeks 4, 8 and week 12 (+ or - 7 days)
2. Central retinal sensitivity is measured using “macular microperimetry” at baseline and week 12 (+ or - 7 days)
3. Retinal perfusion is measured using wide angle fundus fluorescein angiography (FFA) at baseline and week 12 (+ or - 7 days)
4. Tear production is measured using Schirmer test at baseline and week 12 (+ or - 7 days) and week 16 if applicable
5. Patient reported outcomes are measured using “EQ-5D 5L and NEI VFQ-25 at baseline and week 12 (+ or - 7 days)
6. ARA 290 antibodies are measured using “blood sample at baseline and week 12 (+ or - 7 days)

and week 16 if the macular oedema resolved at week 12
7. Adverse events are assessed by the PI or designee who will ask at each visit (weeks 4, 8, 12 (and week 16 if applicable) if the patient has experienced any AEs. In addition the patient will be telephoned at week 2 and asked if they have experienced any AEs and again 4 weeks post study drug termination)

Original secondary outcome measures:
Changes from baseline to week 12 (+ or - 7 days) in:
1. Central subfield thickness
2. Central retinal sensitivity
3. Retinal perfusion
4. Tear production
5. Patient reported outcomes
6. Inflammatory markers
7. Carbamylated and glycosylated albumin
8. ARA 290 antibodies
9. Adverse events
10. Best corrected distance visual acuity
11. Central subfield retinal thickness
12. Retinal perfusion, as determined by fundus fluorescein angiography
13. Macular function, as determined by macular microperimetry
14. Patient reported outcomes
15. Tear production as determined by the Schirmer test
16. Anti-ARA 290 antibodies and inflammatory biomarkers

Completion date
31/10/2017

Eligibility

Key inclusion criteria
1. Patients with diabetic retinopathy and centre involving DMO with a central subfield thickness of > 400 microns, as determined using SD-OCT
2. >= 18 years of age
3. Clear media and naïve to previous treatments for DMO

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
9

Key exclusion criteria
Exclusion criteria as of 08/12/2016:
1. Macular oedema related to other retinal disease
2. Hazy media that prevents adequate retinal imaging
3. Allergy to fluorescein
4. Previous treatments for DMO
5. DMO with central subfield thickness of < 400 microns
6. Patients on systemic or topical steroids
7. Use of erythropoiesis stimulating agents within the two months prior to screening or during the trial
8. Treated with any other investigational medication or device within 60 days
9. Pregnant women, women who have not yet reached the menopause (no menses for ≥ 12 months without an alternative medical cause) who test positive for pregnancy or who are unwilling to take a pregnancy test prior to trial entry or are unwilling to undertake adequate precautions to prevent pregnancy for the duration of the trial.
10. Men who have a female partner and who are unwilling to undertake adequate precautions to prevent pregnancy for the duration of the trial.
11. Female patients who are breastfeeding
12. Active proliferative diabetic retinopathy (PDR) requiring treatment.
13. Patients with other eye diseases besides DR
14. Patients who are unable or unwilling to commit to the study schedule of events
15. Serious illness that is likely to affect the patient's ability to complete the study

Any patient showing a clinically significant improvement between the initial screening and presenting for the first screening/baseline visit may no longer be eligible for the study and will be recorded as a screen failure and will not be entered on to the study.

Original exclusion criteria:
1. Macular oedema related to other retinal disease
2. Hazy media that prevents adequate retinal imaging
3. Allergy to fluorescein
4. Previous treatments for DMO
5. DMO with central subfield thickness of < 400 microns
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8. Treated with any other investigational medication or device within 60 days
9. Pregnant women, women who have not yet reached the menopause (no menses for ≥ 12 months without an alternative medical cause) who test positive for pregnancy, are unwilling to take a pregnancy test prior to trial entry or are unwilling to undertake adequate precautions to prevent pregnancy for the duration of the trial.
10. Female patients who are breastfeeding
11. Active proliferative diabetic retinopathy (PDR) requiring treatment.
12. Patients with other eye diseases besides diabetic retinopathy
13. Patients who are unable or unwilling to commit to the study schedule of events

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Date of first enrolment
01/09/2015

Date of final enrolment
01/01/2017

Locations

Countries of recruitment
United Kingdom

Northern Ireland

Study participating centre
Belfast Health & Social Care Trust (BHSCT)
Belfast
United Kingdom
BT9 7AB

Sponsor information

Organisation
Belfast Health & Social Care Trust (UK)

ROR
https://ror.org/02tdmfk69

Funder(s)

Funder type
Industry

Funder Name
Araim Pharmaceuticals Ltd

Results and Publications

Individual participant data (IPD) sharing plan

The current 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		14/07/2020	04/07/2024	Yes	No
Basic results				No	No
HRA research summary			28/06/2023	No	No
HRA research summary			28/06/2023	No	No
Protocol file	version 4.0	06/07/2017	06/10/2022	No	No