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Can deep phenotyping using retinal images predict response to intravitreal aflibercept therapy in patients with neovascular age-related macular degeneration?

Submission date
27/06/2019

Recruitment status
No longer recruiting

Registration date
27/08/2019

Overall study status
Completed

Last Edited
17/09/2024

Condition category
Eye Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Regular injections of the drug aflibercept into the eye are the most common treatment option for neovascular (wet) age related macular degeneration (AMD) in the UK. Aflibercept treatment typically begins with three injections given at monthly intervals (loading dose), followed by regular review for up to and often beyond 2 years. It is clear that some patients respond to very well after the first three injections, with the retina being completely “dry” (that is without any retinal fluid in the subfoveal area). If the retina is completely dry, it is unlikely additional treatment can improve the visual outcome. In previous studies, it was suggested that these good responders account for about 35-40% of all patients in clinical trials. Recent data suggests that it might be as high as 50% as patients are now presenting earlier to retinal clinics. However, at present, it is impossible to predict the good responders to aflibercept treatment in order to provide patients with better information at the start of treatment. The aim of this study is to use artificial intelligence to evaluate markers of response. The accuracy of artificial intelligence to identify markers of response on optical coherence tomography (OCT) and OCT angiography (OCTA) will be compared to human graders.

Who can participate?
Patients aged 50 to 100 with new onset wet AMD being treated with the loading doses of aflibercept

What does the study involve?
The OCT and OCTA scans done to assess response to aflibercept treatment are collected and analysed by retinal specialists as well as by artificial intelligence.

What are the possible benefits and risks of participating?
The study may not be of benefit to the participant but it will provide better information to

retinal specialists for the future management of patients. There is no risk to the participants as these tests are routinely done in the management of patients with AMD having treatment with aflibercept.

Where is the study run from?
Moorfields Eye Hospital (UK)

When is the study starting and how long is it expected to run for?
July 2019 to June 2022 (updated 14/04/2021, previously: December 2021)

Who is funding the study?
Boehringer Ingelheim

Who is the main contact?
Prof. Sobha Sivaprasad
sobha.sivaprasad@nhs.net

Contact information

Type(s)
Scientific

Contact name
Prof Sobha Sivaprasad

ORCID ID
https://orcid.org/0000-0001-8952-0659

Contact details
NIHR Moorfields Biomedical Research Centre
Moorfields Eye Hospital & UCL Institute of Ophthalmology
162 City Road
London
United Kingdom
EC1V 2PD
+44 (0)7817886759
sobha.sivaprasad@nhs.net

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
SIVS1045

Study information

Scientific Title
Can deep phenotyping using retinal images predict response to intravitreal aflibercept therapy in patients with neovascular age-related macular degeneration?

Acronym
PRECISE

Study objectives
Can artificial intelligence predict treatment response with aflibercept for neovascular age-related macular degeneration better than human graders?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/09/2019, London – Stanmore REC (Health Research Authority, Ground Floor, NRES /HRA, Skipton House, SE1 6LH, UK; Email: nrescommittee.london-stanmore@nhs.net), REC Ref: 19/LO/1385

Study design
Diagnostic accuracy study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Wet age-related macular degeneration

Interventions
The OCT and OCTA images taken at baseline and various time points until after the third aflibercept injection for wet AMD will be evaluated by retinal specialists and artificial intelligence to develop a prognostic model to define response to treatment. The total duration of observation is up to 20 weeks post first aflibercept injection.
Duration of follow-up is also up to a maximum of 20 weeks.

Intervention Type
Other

Primary outcome(s)
Diagnostic accuracy of artificial intelligence over human graders in assessing the response of loading phase of intravitreal aflibercept injections for wet age-related macular degeneration

Key secondary outcome(s))
1. The analyses will be repeated excluding patients who appeared in the training set and the primary validation set
2. Performance of the AI will be evaluated using higher-quality images with no media opacity (eg, cataracts) as noted by professional graders

3. AUC subgroups will be computed stratified by age and sex, smoking or medical history
4. The analysis will be repeated by calculating the AUC, sensitivity, and specificity of the AI and the proportion of concordant and discordant eyes on the external validation datasets, compared with the reference standards

Completion date
30/06/2022

Eligibility

Key inclusion criteria
Inclusion criteria for both retrospective and prospective parts:
1. Adults who are ≥ 50 years and ≤ 100 years
2. Treatment naïve neovascular AMD at baseline
3. Media clarity, pupillary dilation and patient cooperation for adequate imaging
4. Ability to give informed consent

Inclusion criteria for retrospective part only in addition to the above:
1. Have received 3 loading injections of intravitreal aflibercept therapy at monthly intervals as per standard care
2. Review up to 10 weeks after the 3rd loading dose with or without injection at this visit
3. Had Heidelberg OCT at least at baseline and after the loading phase but ideally 4 Heidelberg OCTs for the 4 visits
4. Heidelberg OCTA images if available for baseline and any visit thereafter (2nd, 3rd or 4th visit) provided there is a baseline OCTA (optional criteria)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
2128

Key exclusion criteria
1. Co-existent ocular disease: any other ocular condition that, in the opinion of the investigator, might affect or alter visual acuity during the course of the study
2. Any patient who has opted out of their information being used for research nationally or locally at any site

Date of first enrolment
01/12/2019

Date of final enrolment
01/12/2021

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Moorfields Eye Hospital
162 City Road
London
United Kingdom
EC1V 2PD

Sponsor information

Organisation
Moorfields Eye Hospital

ROR
https://ror.org/03tb37539

Funder(s)

Funder type
Industry

Funder Name
Boehringer Ingelheim

Alternative Name(s)
Boehringer Ingelheim Pharmaceuticals, Inc., Boehringer Ingelheim International GmbH, BI, BIPI

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

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	PRECISE Study Report 1	20/04/2023	17/07/2023	Yes	No
Results article	PRECISE study report 3: baseline characteristics in patients with and without early residual fluid	15/12/2023	17/09/2024	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 2.1	24/02/2021	16/08/2022	No	No