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Optimised treatment for pre-existing diabetic macular oedema during cataract surgery

Submission date
08/01/2021

Recruitment status
No longer recruiting

Registration date
25/01/2021

Overall study status
Completed

Last Edited
25/01/2021

Condition category
Ear, Nose and Throat

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Diabetic macular oedema (DME) is one of the major causes of visual-threatening diabetic retinopathy (VTDR) globally. In Hong Kong, it is the commonest cause of VTDR, which affects 1 in every 11 diabetic patients. Diabetes also predisposes patients to cataracts, and DME with cataract is linked to worse vision loss.

Cataract surgery can lead to inflammation and worsening of DME. Progression of DME following cataract surgery, causing worsened vision, is a profound disappointment for patients who have initial high expectations for visual improvement after the operation. On the other hand, deferring cataract surgery until DME is adequately treated leads to prolonged visual impairment and complications from cataracts.

The aim of this research is to determine the most effective and safe treatment to control cataract surgery-induced inflammation and to prevent further disintegration of the blood-retinal barrier in DME, in order to achieve the best outcomes for the vision of patients. The clinical trial will compare two drugs for treating pre-existing DME with cataract surgery for safety and effectiveness over 12 months. The extended evaluations over 24 months will establish an important database for long-term real-world outcomes of DME treatment following cataract extraction.

Furthermore, the trial will investigate the relationship of changes to the small blood vessels of the eye with clinical outcomes and treatment responses. These changes will be assessed using optical coherence tomography angiography (OCTA), a method of imaging to assess the blood vessels of the eye. It is hoped that this study will provide reliable OCTA metrics that can be used for clinical decision-making to provide individualised and cost-effective management of DME with cataract.

Who can participate?
Adults with type 2 diabetes and visually significant cataract requiring surgery and centre-involving DME at the time of study enrolment. Written consent is also needed for participation.

What does the study involve?
Participants will be randomly allocated to one of two groups and will receive either treatment with an intravitreal injection of 2.0 mg aflibercept or a 0.7 mg dexamethasone implant.

Participants will be assessed monthly for 12 months and will receive any additional retreatment as and when required (indicated by predefined criteria) during this period. OCTA will be used for the assessment of changes to the blood vessels in the eye.

In the second year, patients will be evaluated for real-world treatment outcomes. The study will be completed after a total of 24 months.

What are the possible benefits and risks of participating?
It is hoped that this study will provide information on the best management of concurrent DME with cataract and to alleviate the long-term treatment burden of this chronic condition.
Patients will be closely monitored. Care and retreatment will be provided promptly in case one of the retreatment criteria is met. This clinical trial will not impose extra risk on patients on top of the risks of cataract surgery and intravitreal injection.

Where is the study run from?
The study is being run by the Department of Ophthalmology and Visual Sciences, the Chinese University of Hong Kong, and involves 3 hospitals and 1 eye centre in Hong Kong.

When is the study starting and how long is it expected to run for?
From November 2020 to December 2024.

Who is funding the study?
General Research Fund, University Grants Committee (Hong Kong)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
RGC GRF Application 14104821

Study information

Scientific Title
Optimised treatment for pre-existing Diabetic Macular oEdema during CATaract surgery – a randomised controlled trial (ODMECAT)

Acronym
ODMECAT

Study objectives
1. Head-to-head clinical trial for comparison of intravitreal injection of aflibercept with dexamethasone implant at the time of cataract surgery followed by pro re nata (PRN) retreatment according to predefined criteria will reveal the difference in efficacy and treatment frequency between these two therapies in reducing inflammatory insult to the eye following cataract surgery and further breakdown of the compromised blood-retinal barrier in Diabetic Macular Oedema (DME).
2. Objective evaluation and quantification of diabetic macular ischemia by Optical Coherence Tomography Angiography (OCTA) is associated with clinical outcomes and treatment prognosis following cataract surgery.
3. Clinical trial provides data from subjects under circumscribed conditions including predetermined retreatment criteria. Real-world data accounts for pragmatic circumstances that may influence treatment adherence. Retaining the rigor of clinical trial investigations for real-world treatment end-point allows outcome evaluations without compromising study duration, validity, and relevance of results.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Pending, Kowloon Central Cluster Research Ethics Committee/Kowloon East Cluster Research Ethics Committee, Hong Kong Hospital Authority
2. Pending, New Territories East Cluster Research Ethics Committee, Hong Kong Hospital Authority

Study design

Multicenter interventional randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Diabetic Macular Oedema in type 2 diabetic patients with visually significant cataract

Interventions
Eligible patients will be enrolled in the study after signing the informed consent form (ICF). Patients will be assessed for medical and ophthalmic history, HbA1c levels, blood pressure, Best Corrected Visual Acuity (BCVA),
Intraocular Pressure (IOP), ophthalmic examination with slit lamp, and fundoscopy. The cataract status will be graded by the Lens Opacities Classification System III (LOC III). Colour fundus photography, Optical Coherence Tomography (OCT line-scan), and optical coherence tomography angiography (OCTA) examinations of the macula will be performed. A quality of life questionnaire (NEI VFQ-25) will be administered.

During baseline visit (up to 2 weeks or on the same day prior to cataract surgery), eligible patients will be randomised by a computer programme to receive either intravitreal aflibercept 2.0mg (Group A) or dexamethasone 0.7mg implant (Group B) injection at a 1:1 ratio.

Patients will receive the first intravitreal injection according to their randomised group immediately following cataract surgery in the operating theatre. In the event of complicated cataract surgery where there is rupture of the posterior capsule or loss of vitreous, the patient will be withdrawn from the study without injection of study medication.
As a routine, the dressing will remain intact until postoperative day 1 before starting to apply chloramphenicol 0.5% and dexamethasone 0.1% eye drops six times daily and tapered over 4 weeks.

At each monthly follow-up visit (until 12 months), patients will be assessed on BCVA, IOP, ophthalmic examination, OCT (line-scan) and OCTA. Color fundus photographs will be taken at 3-month intervals. NEI VFQ-25 questionnaire will be administered at month 12.

PRN retreatment (between 2 to 12 months, and at least 1 month since last intravitreal aflibercept injection or 4 months since last intravitreal dexamethasone injection) will be considered if either one of the following criteria is met when compared with prior visit :
1. Increase in CMT by ≥50 μm
2. BCVA decrease by ≥5 letters

There will be an extended evaluation of real-world outcomes between 13 and 24 months. Patients will be referred back to their usual healthcare providers for continuity of care. Clinic visit intervals and any form of treatment including injections of any types of intravitreal anti-VEGF, corticosteroids, and macular photocoagulation, thereby, will be provided at the discrete of their attending ophthalmologists. These patients will have additional visits to the research clinic at 3-month intervals (at 15, 18, 21, and 24 months). Electronic medical records will be assessed for updates on medical, ophthalmic, and treatment histories. BCVA, IOP, ophthalmic examination, OCT (line-scans), OCTA, and color fundus photographs will be performed according

to the same investigational protocol as previous trial visits. NEI VFQ-25 questionnaire will be administered at month 24.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
aflibercept (EYLEA® 2.0 mg injection), dexamethasone (OZURDEX® 0.7mg intravitreal implant)

Primary outcome(s)
1. Mean change in Best Corrected Visual Acuity (BCVA) measured using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity charts monthly between baseline and 12 months

Key secondary outcome(s))
1. Any treatment-related adverse events measured from ophthalmic investigation and examination and/or clinical notes between baseline and 12 months
2. Number of injections measured from clinical notes or injection records between baseline and 12 months
3. Central Macular Thickness (CMT) measured using Spectral domain (SD) OCT (Spectralis; Heidelberg Engineering, Heidelberg, Germany) monthly between baseline and 12 months
4. Optical Coherence Tomography Angiography (OCTA) metrics at Superficial Capillary Plexus (SCP) and Deep Capillary Plexus (DCP) measured using OCTA monthly between baseline and 12 months:
4.1. Vessel density
4.2. Foveal Avascular Zone (FAZ) area
4.3. FAZ circularity
4.4. Fractal dimension
5. Patient-reported outcomes using the 25-item National Eye Institute Visual Function Questionnaire (NEI VFQ-25) quality of life questionnaire at baseline and 12 months
6. Types of treatment received measured from electronic medical records at 15, 18, 21, and 24 months
7. Frequency of treatments received measured from electronic medical records at 15, 18, 21, and 24 months
8. Best Corrected Visual Acuity (BCVA) measured using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity charts at 15, 18, 21, and 24 months
9. CMT measured using Spectral domain (SD) OCT (Spectralis; Heidelberg Engineering, Heidelberg, Germany) at 15, 18, 21, and 24 months
10. OCTA metrics at SCP and DCP measured using OCTA monthly at 15, 18, 21, and 24 months:
10.1. Vessel density
10.2. Foveal Avascular Zone (FAZ) area
10.3. FAZ circularity
10.4. Fractal dimension
11. Patient-reported outcomes using the NEI VFQ-25 questionnaire at 24 months

Completion date
31/12/2024

Eligibility

Key inclusion criteria
1. Aged ≥18 years
2. Type 2 diabetes mellitus
3. Visually significant cataract requiring surgery
4. Centre-involving DME at the time of study enrolment
5. Written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. History of intravitreal injection of anti-Vascular Endothelial Growth Factor (anti-VEGF) within 1 month, steroids within 3 months, or macular focal/grid laser within 3 months, prior to cataract surgery
2. Macular oedema from causes other than diabetic maculopathy
3. Proliferative diabetic retinopathy requiring treatment, media opacities which affect fundus examination or Optical Coherence Tomography (OCT) measurements at baseline, or known significant macular ischemia demonstrated on fluorescein angiography or OCTA
4. Pre-existing glaucoma at the time of enrolment or previous history of steroid response (Intraocular Pressure (IOP) elevation >35 mmHg following steroid treatment)
5. Ocular disorders in the study eye at the time of enrollment that may confound interpretation of study results and compromise visual acuity (including retinal detachment, age-related macular degeneration, pathologic myopia, lamellar macular hole, and epiretinal membrane of the macula)
6. History of hypersensitivity to any intravitreal drugs
7. History of stroke or myocardial infarction within the 6 months prior to the screening visit
8. Pregnant or lactating

Date of first enrolment
01/01/2022

Date of final enrolment
30/09/2022

Locations

Countries of recruitment
Hong Kong

Study participating centre
Hong Kong Eye Hospital
147K Argyle Street
Kowloon
Hong Kong
Hong Kong
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Study participating centre
The Chinese University of Hong Kong (CUHK) Eye Centre
3/F, Hong Kong Eye Hospital
147K Argyle Street
Kowloon
Hong Kong
Hong Kong
-

Study participating centre
Prince of Wales Hospital
30-32 Ngan Shing Street
Shatin
New Territories
Hong Kong
Hong Kong
-

Study participating centre
Alice Ho Miu Ling Nethersole Hospital
11 Chuen On Road
Tai Po
New Territories
Hong Kong
Hong Kong
-

Sponsor information

Organisation
Chinese University of Hong Kong

ROR
https://ror.org/00t33hh48

Funder(s)

Funder type
University/education

Funder Name
University Grants Committee

Alternative Name(s)
The University Grants Committee, , UGC

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
Hong Kong

Results and Publications

Individual participant data (IPD) sharing plan
Participant-level data will be available on request. Individual participant data the underlies the results reported in this article, after deidentification (texts, tables, figures, and appendices), will be shared. Study protocol will also be available. Data will be shared with investigators whose proposed use of the data, for individual participant data meta-analysis, has been approved by an independent review committee identified for this purpose. Data will be available beginning 9 months and ending 36 months following article publication. Data sharing proposals should be directed to dannyng@cuhk.edu.hk. To gain access, requestors will need to sign a data access agreement.

IPD sharing plan summary
Available on request