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Zhongshan angle-closure prevention (ZAP) study

Submission date 16/01/2008	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 06/05/2008	**Overall study status** Completed	
Last Edited 30/05/2023	**Condition category** Eye Diseases	

Plain English summary of protocol

Current plain English summary as of 17/01/2022:
Background and study aims
Glaucoma is the leading cause of irreversible blindness. Primary angle closure glaucoma (PACG) is the more severe of the two major types of glaucoma. If you have healthy eyes, the fluid in your eye drains away through drainage channels. In some people the eye is shaped differently and the drainage area is very narrow (narrow drainage angles). Under certain circumstances the drain can completely close off, so your eye pressure increases, injuring your optic nerve and damaging your vision. This is considered an attack of angle closure glaucoma. Laser peripheral iridotomy (LPI) is the first-line treatment for PACG. LPI uses a laser beam to create a small hole in your iris, unblocking the drainage channels. LPI is also very effective at preventing symptoms developing in the unaffected eye of patients who have suffered the condition in the other eye. However, so far no conclusions can be drawn regarding the use of prophylactic (preventative) LPI in persons with narrow drainage angles and without any symptoms or signs of active glaucoma. To determine the case for performing prophylactic LPI for all people with narrow angles (1 in 5 Chinese women over the age of 60 fall into this category), it is important to identify how many people with narrow angles will eventually suffer acute symptoms or develop glaucoma. Equally, it is important to know if LPI will reduce this risk, and whether there is any significant adverse risk associated with early LPI treatment. This study aims to assess whether LPI is safe and effective at preventing the development of primary angle closure in high-risk angle-closure patients. The study also specifically aims to answer the question of whether there are any particular features that help to predict who will go on to develop angle closure.

Who can participate?
Guangzhou city residents aged 50 to 70 with narrow drainage angles.

What does the study involve?
The right and left eyes of each participant are randomly allocated to LPI treatment or current standard treatment only. Both treated and untreated eyes are examined on follow-up visits after 2 weeks, 6 months, 18 months, 36 months, 54 months and 72 months.

What are the possible benefits and risks of participating?
Participants will obtain regular and careful medical support from a qualified team of medical experts. There are no obvious risks in participating in this study.

Where is the study run from?
University College London (UK).

When is the study starting and how long is it expected to run for?
March 2008 to February 2017. Patient re-examination commencing 2022 (12+ year follow-up)

Who is funding the study?
1. Fight for Sight (UK)
2. Sun Yat-sen University (China)
3. Wilmer Eye Institute (USA).
4. Ministry of Education of the People's Republic of China (China)
5. National Natural Science Foundation of China (China)
6. The State Key Laboratory, Zhongshan Ophthalmic Center & SunYat-Sen University (China)

Who is the main contact?
1. Prof. Paul J Foster (p.foster@ucl.ac.uk)
2. Prof. Mingguang He (mingguang_he@yahoo.com)
3. Prof. David S Friedman (david_friedman@meei.harvard.edu)

Previous plain English summary:
Background and study aims
Glaucoma is the leading cause of irreversible blindness. Primary angle closure glaucoma (PACG) is the more severe of the two major types of glaucoma. If you have healthy eyes, the fluid in your eye drains away through drainage channels. In some people the eye is shaped differently and the drainage area is very narrow (narrow drainage angles). Under certain circumstances the drain can completely close off, so your eye pressure increases, injuring your optic nerve and damaging your vision. This is considered an attack of angle closure glaucoma. Laser peripheral iridotomy (LPI) is the first-line treatment for PACG. LPI uses a laser beam to create a small hole in your iris, unblocking the drainage channels. LPI is also very effective at preventing symptoms developing in the unaffected eye of patients who have suffered the condition in the other eye. However, so far no conclusions can be drawn regarding the use of prophylactic (preventative) LPI in persons with narrow drainage angles and without any symptoms or signs of active glaucoma. To determine the case for performing prophylactic LPI for all people with narrow angles (1 in 5 Chinese women over the age of 60 fall into this category), it is important to identify how many people with narrow angles will eventually suffer acute symptoms or develop glaucoma. Equally, it is important to know if LPI will reduce this risk, and whether there is any significant adverse risk associated with early LPI treatment. This study aims to assess whether LPI is safe and effective at preventing the development of primary angle closure in high-risk angle-closure patients. The study also specifically aims to answer the question of whether there are any particular features that help to predict who will go on to develop angle closure.

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3. Prof. David S Friedman (david.friedman@jhu.edu)

Contact information

Type(s)
Scientific

Contact name
Dr Paul Foster

Contact details
University College London
Institute of Ophthalmology
11-43 Bath Street
London
United Kingdom
EC1V 9EL
+44 (0)20 7608 6899
p.foster@ucl.ac.uk

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
1

Study information

Scientific Title
A randomised controlled trial of prevention of angle-closure glaucoma in China

Acronym
ZAP

Study objectives
That laser iridotomy helps to prevent primary angle-closure (a major risk factor for glaucoma) in Chinese adults aged 50 years and older.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Current ethics approval as of 17/01/2022:
1. Ethical Review Board of Zhongshan Ophthalmic Centre (China), November 2002
2. London School of Hygiene and Tropical Medicine (UK), 17/03/2008, ref: 5267
Extension study:
1. Zhongshan Ophthalmic Centre (China), 28/01/2016, ref: Zhongshan Ophthalmic Center Medical Ethical Committee [2007] No.12
2. London School of Hygiene and Tropical Medicine (UK), 05/03/2011, ref: A240 5267
Extended Follow-up Study:
Approved 01/11/2021, Zhongshan Ophthalmic Center Medical Ethical Committee (Zhongshan Ophthalmic Centre, China)

Previous ethics approval:
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Study design
Single-centre randomised controlled trial (not masked)

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Available in Chinese with English translation upon request

Health condition(s) or problem(s) studied
Angle-closure glaucoma

Interventions
Current intervention as of 17/01/2022:
The right and left eyes of each participant will be randomly allocated to the intervention treatment or no treatment (control).

Intervention treatment: Laser peripheral iridotomy (LPI) by sequential argon then Nd:YAG laser. Duration of the laser treatment is about 5 minutes.
Control: No intervention (current standard treatment only)

Each participant will be examined at baseline, 2 weeks, 6, 18, 30 and 42 months.

Each participant will be further examined at 54 and 72 months after LPI.

Re-examination to assess visual function, supplementary surgery (i.e. cataract surgery), and to document any differences in risk factor profile for glaucomatous loss of vision (intraocular pressure, peripheral anterior synechiae) between treated and untreated eyes at 12+ from intervention.

Previous intervention:
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Intervention treatment: Laser peripheral iridotomy (LPI) by sequential argon then Nd:YAG laser. Duration of the laser treatment is about 5 minutes.
Control: No intervention (current standard treatment only)

Each participant will be examined at baseline, 2 weeks, 6, 18, 30 and 42 months.

Added 20/09/2016:
Each participant will be further examined at 54 and 72 months after LPI.

Intervention Type
Procedure/Surgery

Primary outcome measure
The following will be assessed on each of the scheduled follow-up (6, 18, 30 and 42 months):
1. Raised intraocular pressure (either with or without symptoms). Intraocular pressure greater than 24 mmHg verified on two consecutive measurements on separate days. These patients will be further identified as having open, partially-closed or completely closed angles on dark room gonioscopy and anterior segment optical coherence tomography (AS-OCT).
2. Peripheral anterior synechiae
3. Glaucomatous optic neuropathy

If participants are felt to have met a failure criterion, they are re-assessed (by examination with one of the senior investigators) within the next 2 weeks to confirm. The failure will then be classified as having occurred at 6, 18, 30 or 42 months (end of the study).

Added 20/09/2016:
Outcomes will also be assessed at 54 and 72 months.
If participants are felt to have met a failure criterion, they are re-assessed (by examination with one of the senior investigators) within the next 2 weeks to confirm. The failure will then be classified as having occurred at 54 or 72 months (end of the study).

Secondary outcome measures
The following will be assessed on each of the scheduled follow-up (6, 18, 30 and 42 months):
1. Specular microscopy measures of corneal endothelial cell loss
2. Formation of lens opacity
3. Anterior segment optical coherence tomography measures (qualitative and quantitative) of ocular anterior segment anatomy
4. Digital iris photograph measures of iris
5. Ultrasound biomicroscopy measurements of ocular anterior segment anatomy
If participants are felt to have met a failure criterion, we will re-assess (by examination with one of the senior investigators) within the next 2 weeks to confirm. The failure will then be classified as having occurred at 6, 18, 30 or 42 months (end of the study).

Added 20/09/2016:
Outcomes will also be assessed at 54 and 72 months.
If participants are felt to have met a failure criterion, they are re-assessed (by examination with one of the senior investigators) within the next 2 weeks to confirm. The failure will then be classified as having occurred at 54 or 72 months (end of the study).

Overall study start date
01/03/2008

Completion date
28/02/2017

Eligibility

Key inclusion criteria
1. Anatomically narrow drainage angles in the anterior segment of the eye
2. No evidence of primary angle-closure (high pressure or peripheral anterior synechiae)
3. Aged greater than or equal to 50 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
50 Years

Sex

Both

Target number of participants
1,100

Key exclusion criteria
1. Inability or unwillingness to give informed consent
2. Raised intraocular pressure, peripheral anterior synechiae or glaucomatous optic neuropathy
3. Previous intraocular surgery

Date of first enrolment
01/09/2008

Date of final enrolment
22/10/2010

Locations

Countries of recruitment
Australia

China

England

United Kingdom

United States of America

Study participating centre
UCL Institute of Ophthalmology & Moorfields Eye Hospital
11-43 Bath Street
London
United Kingdom
EC1V 9EL

Study participating centre
Centre for Eye Research Australia (CERA)
Royal Victorian Eye and Ear Hospital
Peter Howson Wing
Level 7, 32 Gisborne Street
East Melbourne
Melbourne
Australia
3002

Study participating centre
Massachusetts Eye and Ear Infirmary
243 Charles St
Boston
United States of America
02114

Study participating centre
Zhongshan Ophthalmic Center
#54 Xian Lie South Road
State Key Laboratory of Ophthalmology
Clinical Research Center
Sun Yat-Sen University
Guangzhou
China
510080

Sponsor information

Organisation
University College London (UK)

Sponsor details
Gower Street
London
England
United Kingdom
WC1E 6BT
+44 (0)20 7608 6854
h.jones@ucl.ac.uk

Sponsor type
University/education

Website
http://www.ucl.ac.uk/

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type

Government

Funder Name
Fight for Sight UK

Alternative Name(s)
Fight for Sight

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Funder Name
Sun Yat-sen University

Alternative Name(s)
SYSU

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
China

Funder Name
Ministry of Education of the People's Republic of China

Alternative Name(s)
, Министерство образования Китайской Народной Республики, , Bildungsministerium der Volksrepublik China, Ministry of Education of China, Ministry of Education, The People's Republic of China, Ministry of Education of the Central People's Government, State Education Commission, MOE

Funding Body Type
Government organisation

Funding Body Subtype

National government

Location
China

Funder Name
National Natural Science Foundation of China

Alternative Name(s)
Chinese National Science Foundation, Natural Science Foundation of China, National Science Foundation of China, NNSF of China, NSF of China, , National Nature Science Foundation of China, Guójiā Zìrán Kēxué Jījīn Wěiyuánhuì, NSFC, NNSF, NNSFC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
China

Funder Name
Wilmer Eye Institute

Funder Name
The State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center

Results and Publications

Publication and dissemination plan
Current publication and dissemination plan as of 17/01/2022:
The main findings of the ZAP study were published in The Lancet in 2019 and presented at academic conferences. A range of publications dealing with clinical features of treated and untreated patients have been published by the same authors (He, Foster, Friedman). An extended follow-up is underway in 2022, with a view to publish in 2023

Previous publication and dissemination plan:
The main findings of the ZAP study will be published in peer-reviewed journals before the end of 2017 and presented at academic conferences.

Intention to publish date
31/03/2019

Individual participant data (IPD) sharing plan

Current individual participant data (IPD) sharing statement as of 17/01/2022:
The datasets generated and/or analysed during the current study are available from Prof. Paul Foster (p.foster@ucl.ac.uk), Prof Friedman (david_friedman@meei.harvard.edu), and Prof. Mingguang He (mingguang.he@unimelb.edu.au; mingguang_he@yahoo.com) on reasonable request.

Previous individual participant data (IPD) sharing statement:
The datasets generated and/or analysed during the current study are available from Prof. Paul Foster (p.foster@ucl.ac.uk) and Prof. Mingguang He (mingguang.he@unimelb.edu.au; mingguang_he@yahoo.com) on reasonable request.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Visual symptoms	01/07/2012		Yes	No
Results article	results	20/04/2019		Yes	No
Results article	Cataract progression	02/05/2022	03/05/2022	Yes	No
Results article	Iris volume change	26/05/2023	30/05/2023	Yes	No