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Dear Participant,

Greetings!

You have been diagnosed with "high myopia (HM)," and we cordially invite you to participate in a research study titled " Effect of Intraocular Pressure Reduction on Progressive High Myopia (PHM study): a Randomized Controlled Trial". The purpose of this informed consent form is to provide you with comprehensive research information, enabling you to make an informed decision regarding your participation in this trial. We kindly request you to read this document attentively and direct any inquiries to the responsible researchers.

Please note that participation in this study is entirely voluntary. The research protocol has undergone rigorous review and approval by the Ethics Committee of Zhongshan Ophthalmic Center, Sun Yat-sen University, ensuring compliance with ethical standards for conducting clinical research.

1. Why is this study being conducted?

HM, particularly pathological myopia, can lead to various severe complications that significantly impact visual function. The axial elongation of the eye in adult patients with HM is a risk factor for the progression of pathological myopia. Therefore, finding ways to delay the continuous axial elongation in adult patients with HM has become a pressing clinical issue. Research indicates that lowering intraocular pressure (IOP) serves as a protective factor against axial elongation in adult patients with high myopia. Animal experiments and our previous small-scale retrospective study have shown that localized IOP reduction can effectively slow down the progression of HM. However, there is currently a lack of robust clinical randomized controlled trials providing substantial evidence in this regard. Hence, it is imperative to conduct this research to establish a strong foundation for determining treatment strategies for patients with progressive high myopia (PHM).

2. Who is eligible to participate in this study?

Inclusion criteria

1. Age ≥18 years and ≤65 years.

2. Diagnosed with HM: spherical equivalent ≤-6.00 diopters or axial length ≥26.5 mm.

3. Diagnosed with PHM: axial elongation ≥0.05mm in the past 6 months or ≥0.1mm in the past 12 months.

4. IOP: ≥10 mmHg and ≤21mmHg on at least 2 visits using Goldmann applanation tonometry with correction for the dependence of the IOP-reading on corneal thickness.

5. Best corrected visual acuity (BCVA) ≥6/12, ability to undergo axial length measurement, fundus

photography, optical coherence tomography (OCT), and complete visual field examination.

Exclusion criteria

1. Patients who have been using IOP-lowering medications within the last year.
2. Allergy to any kind of IOP-lowering eyedrops.
3. Presence of serious fundus pathologies like proliferative diabetic retinopathy, retinal detachment, central retinal artery occlusion, etc.
4. Presence of chronic, recurrent, or severe ocular inflammatory lesions such as chronic or recurrent uveitis.
5. Significant corneal or iris lesions, severe cataract affecting fundus examination, or patients with only one eye.
6. Intraocular surgery or laser treatment within the last year, such as cataract surgery.
7. With a history of previous refractive surgery or prior treatment for myopia-related conditions (e.g., orthokeratology lens wear, low-intensity red light therapy, or low-concentration atropine treatment).
8. Presence of other serious systemic diseases (e.g., hypertension, heart disease, diabetes, rheumatic immune system disease) that hinder long-term follow-up and eye treatment.
9. Pregnancy, lactation, or plans to have children during the follow-up period.

In this study, only one eye per eligible participant will be included. If both eyes meet the inclusion criteria, the eye with a higher rate of axial elongation, a worse mean perimetric deviation (MD) value, and a worse BCVA will be selected.

3. How is the study conducted?

Once you are diagnosed with PHM, we will provide you with the above explanation. If you agree to participate in this study, we will proceed with the following research procedures after you have signed this informed consent form. These procedures involve collecting your research data and relevant examination results as specified in the research protocol. The study process is as follows:

1) Informed consent and screening for eligibility, with medication washout if necessary.
2) The study physician will select the appropriate eye for research observation based on the requirements of the research protocol and the patient's individual circumstances.

3) Randomization: Participants will be randomly assigned in a 1:1 ratio to either the intraocular pressure-lowering medication group or the control group (no medication).

Participants assigned to the intervention group will receive medical IOP-lowering therapy for a duration of 12 months or until they reach the endpoint**.** Only the study eye will receive medication in the enrolled participants. The preferred medication for reducing IOP is Xalacom® eye drop (Pfizer Inc., New York, NY, USA), a fixed latanoprost and timolol combination.

The treatment protocol will involve the instillation of a single drop of prostaglandin ophthalmic solution in the study eye once daily in the evening for medications such as Xalacom. To ensure the standardisation of medication usage among participants, subjects will be provided with medication logbooks, which will be collected and recorded by the investigators during the study visits.

Control group

Participants assigned to the control group will be followed up for 12 months or until they reach the endpoint without medical IOP-lowering therapy.

- Medication Administration:

Xalacom: One drop once daily at 22:00 (±1 hour), with lacrimal sac compression for one minute after administration.

- Medication Follow-up Duration: 1 year (Participants are required to complete three visits within one year, scheduled at approximately 1 month (±1 week), 6 months (±2 weeks), and 12 months (±4 weeks) respectively).
- Follow-up Examinations: Visual acuity (uncorrected visual acuity, BCVA), computerized auto-refraction, Goldmann tonometry, central corneal thickness, axial length, visual field, fundus photography, OCT examination, quality of life questionnaire, etc.

Throughout the study, we will closely monitor any changes in your condition and make necessary adjustments to the follow-up plan in order to ensure your rights and safety.

4. What is required to participate in the study?

1) Understand the details of this study and voluntarily agree to participate.

2) Adhere to the medication regimen (for the IOP-lowering medication group) and follow-up visits as specified in the protocol. Provide accurate information regarding medication response and changes in your condition.

5. Impact on daily life by participating in the study

1) You may experience inconvenience due to the study visits and examinations. Additionally, some tests may cause discomfort. If you have any concerns or questions about the examinations and procedures during the study, you can consult the research physician.

2) During the study period, please consult your research physician before using any new prescription medications to avoid conflicts.

3) To ensure your safety and the validity of the study results, you will not be able to participate in any other clinical studies involving medications or medical devices during the study.

6. Potential benefits of participating in the study:

Participation in the study will not directly benefit the participants. However, as part of the study, you will receive close follow-up for one year, and the study-related costs, such as the IOP-lowering medication and examinations, will be provided free of charge. This allows for timely detection and treatment of disease progression or other complications. The application of the study results may contribute to improving treatment recommendations for controlling axial elongation in HM.

7. Risks of participating in the study

1) Risks if enrolled in the IOP-lowering medication group:

- The medication used in this study for lowering IOP is a commonly used glaucoma medication approved by the regulatory authority. Known local and systemic adverse reactions are rare and include eye redness, eyelid pigmentation, eyelash growth, and medication allergies, which are detailed in the drug's package insert.

- Low IOP: During the first week after administering the medication, the participants' IOP will be monitored. If low IOP or other related conditions occur, dose reduction or discontinuation of the medication will be implemented. However, based on previous studies, even when the IOP of normal-tension glaucoma patients is lowered to 30% of baseline, excessively low IOP has not been observed. Therefore, this risk is extremely low.

2) Risks if enrolled in the control group:

- The control group in this study does not receive medication. Only a small number of highly myopic participants may have suspected glaucoma, and there is a possibility of worsening of the suspected glaucoma condition during the follow-up. If the examination reveals suspected glaucoma and there is progression of visual field defects during the follow-up, the study will be terminated, and participants will receive further glaucoma-related treatment according to clinical guidelines. The visit intervals in this study are 3-6 months, during which any potential progression would be mild and manageable.

3) Risks associated with HM itself:

- This study focuses on individuals with HM. In the natural course of HM, retinal pathologies associated with high myopia such as chorioretinal atrophy, retinal tears, macular holes, retinal detachment, and choroidal neovascularization may occur. Therefore, before enrollment, participants will undergo a detailed dilated fundus examination to exclude individuals at high risk of developing severe complications in the short term. These individuals will be referred to relevant clinical departments for further diagnosis and treatment. If a participant experiences severe retinal complications, such as retinal detachment, during the follow-up period, and it is determined to be unrelated to the medication, the participant will be responsible for the related treatment costs, and the participant will be provided with convenient access to medical care. At the same time, the participant will discontinue the study.

4) Risks associated with examinations:

- Risks associated with the examination instruments: All the ophthalmic examinations used in this study have been widely used in clinical practice and do not pose adverse effects on participants. The Goldmann tonometry examination involves contact with the cornea, but with skilled technicians performing precise operations and strict disinfection protocols, the risk is minimized.

- Risks associated with examination medications: The study requires the use of compound tropicamide eye drops for pupil dilation, which is a commonly used mydriatic in clinical practice. Due to pupil dilation, participants may experience blurred vision and mild photosensitivity, which naturally resolves within 4-5 hours. After this examination, participants should avoid engaging in activities such as driving that require visual acuity for about half a day. In rare cases, localized reactions such as allergic conjunctivitis or eyelid inflammation may occur. Therefore, before administering the medication, participants' medical history and allergies will be thoroughly assessed and explained to minimize the occurrence of risks.

8. What happens if harm occurs during participation in the study?

Except for unforeseeable circumstances, this study will not cause harm to the participants. The researchers will provide insurance services to the participants involved in the clinical study, as required by Good Clinical Practice (GCP), to protect their rights and interests in participating in the study. Compensation for any harm related to the clinical research will be carried out in accordance with applicable laws and regulations in China.

9. Is personal information kept confidential?

Yes. Your medical records (medical history, examination results, etc.) will be securely stored at the hospital where you receive treatment. The doctor will record the examination results in your medical records. Researchers, ethics committees, and regulatory authorities will be allowed to access your medical records. Any public reports regarding the results of this study will not disclose your personal identity. We will make every effort to protect the privacy of your personal medical information within the limits permitted by law.

10. Is participation in this study mandatory?

Participation in this study is completely voluntary, and it is entirely up to your discretion whether to participate. You have the right to refuse to participate in this study or withdraw from the study at any time without affecting your relationship with the doctor or any other medical or personal interests.

If you decide to withdraw from this study, please inform your research doctor in advance. If you experience any abnormal symptoms during the study, please inform your research doctor or study staff.

For your best interests, the research doctor may suspend your participation in this study at any time if: 1) continuing the study may be detrimental to you, 2) you need treatment that is prohibited by this study, 3) you fail to follow instructions, or 4) the study is terminated.

11. What should I do now?

Whether or not to participate in this study is a decision for you (and your family) to make. Before making a decision to participate in the study, please ask your doctor any questions you may have.T hank you for reading the above information. If you decide to participate in this study, please inform your doctor, who will arrange all the necessary matters related to the study. Please keep this information for your reference.

Contact number for the Ethics Committee of Sun Yat-sen Eye Center, Sun Yat-sen University: 020-66610729.

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Consent Statement:

I have read the above information regarding this study and have had the opportunity to discuss it with the doctor and ask questions. All the questions I have raised have been satisfactorily answered.

I am aware of the risks and benefits associated with participating in this study. I understand that participation is voluntary and confirm that I have had sufficient time to consider it. Furthermore, I understand that:

- I can consult the doctor for additional information at any time.
- I can withdraw from this study at any time without discrimination or retaliation, and my medical treatment and rights will not be affected.
- I also understand that if I withdraw from the study, I should inform the doctor about changes in my medical condition and complete the necessary physical and laboratory examinations, as this would be beneficial to the overall study.
- If I require any other medication treatment due to changes in my medical condition, I will either seek the doctor's advice in advance or truthfully inform the doctor afterward.
- I agree that regulatory authorities, ethics committees, or representatives of the sponsor may access my research data.

Finally, I have decided to consent to participate in this study and commit to following the medical advice to the best of my ability.

Signature of Participant (or Guardian)：_____ Date: _____

Contact Phone Number：_____

I confirm that I have explained the details of this trial to the patient, including their rights and the potential benefits and risks involved.

Signature of Researcher：_____ Date: _____

Contact Phone Number：_____