# A Randomized, Double - Masked, Placebo - Controlled Study of PRM - 151 in the Prevention of Postoperative Scarring in Glaucoma Patients Following Primary Trabeculectomy.

Published: 15-06-2010
Last updated: 02-05-2024

Primary: To assess the effects of PRM-151 compared to placebo on the success of trabeculectomy by reducing post-surgical scarring in glaucoma patients who have undergone primary trabeculectomy, evaluated at day 120.Secondary: To assess the safety...

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Glaucoma and ocular hypertension |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON34925

**Source**
ToetsingOnline

**Brief title**
PRM-151 Trabulectomy Scarring prevention V1

### Condition

- Glaucoma and ocular hypertension

**Synonym**
Prevention of Scarring after Glaucoma (Ocular hypertension) Surgery

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Promedior Inc.
**Source(s) of monetary or material Support:** Promedior Inc.

## Intervention

**Keyword:** Glaucoma Patients, Postoperative scarring, PRM 151, Trabuculectomy

## Outcome measures

### Primary outcome

The main co-primary endpoints of the study upon which the efficacy conclusions will be based are the following:

1. Successful IOP control (either qualified or unqualified) at day 120.

Successful IOP control is defined as unqualified when IOP was between 6 and 18 mmHg or a 25% reduction from the pre-surgical IOP without medication and qualified when IOP-lowering therapies are required to maintain IOP at that level.

2. Bleb scarring at day 120, as assessed by OCT.

3. Vascularity of the peripheral, non-bleb conjunctiva at day 120 as assessed by the Moorfields bleb grading scale.

4. Comparison of mean decrease from baseline in IOP at day 120

The primary analysis will be based on the following null hypotheses:

1. There is no difference for the proportion of subjects with successful IOP control at day 120 between PRM-151 and placebo.

2. There is no difference for the distribution of bleb scarring at day 120

between PRM-151 and placebo.

3. There is no difference for the distribution of vascularity of the peripheral, non-bleb conjunctiva at day 120 between PRM-151 and placebo.

4. There is no difference for the mean decrease in IOP at day 120 between PRM-151 and placebo.

The proportions of subjects with successful IOP control at day 120, the distributions of bleb scarring at day 120 and the distributions of the vascularity of the peripheral, non-bleb conjunctivas at day 120 will be compared between PRM-151 and placebo by Fisher's exact test. The mean decrease in IOP at day 120 will be compared between PRM-151 and placebo by two sample t-test.

**Secondary outcome**

Secondary efficacy endpoints include the primary efficacy endpoints assessed at all other timepoints, percent change from baseline in IOP, trabeculectomy failure rate, the mean number of IOP-lowering medications taken per subject, and the other parameters assessed by Moorfields bleb grading system.

The baseline for IOP will be the IOP measured at the time of the decision to perform the surgery.

Subjects will be randomized within each stratum in a 1:1 ratio to placebo or PRM-151. The primary analysis will be based on the intent-to-treat (ITT) analysis set, which will include all randomized, treated subjects who receive at least one injection of test article. The last-observation-carried-forward (LOCF) imputation will be implemented for those subjects with missing efficacy values, who are prematurely discontinued, or have undergone rescue procedures.

Secondary analyses include the analyses for co-primary endpoints at all timepoints. In addition, a stratified analysis will be performed using a Cochran-Mantel-Haenszel (CMH) test (age and baseline IOP as stratification factors) for IOP control, bleb scarring and vascularity of the peripheral, non-bleb conjunctiva. For the mean decrease in IOP, an Analysis of Covariance (ANCOVA) model will be used to include the stratification factors age and baseline IOP as covariates. Bleb scarring and the vascularity of the peripheral, non-bleb conjunctiva will be also analyzed as continuous variables.

# Study description

### Background summary

SAP (Serum Amyloid P) is a naturally occurring protein that circulates in the bloodstream and plays a crucial role in regulating wound healing. SAP's role is to regulate the activity of innate immune cells including monocyte-derived cells (fibrocytes, macrophages, dendritic cells) and myofibroblasts. The innate responses to injury can result in excess collagen production and scarring. This excess collagen production is an unwanted effect at surgical sites or in response to injury in a solid organ. Studies conducted show that maintaining an elevated level of SAP in the blood or locally at the site of injury can prevent production of excess scarring and the progression of fibrosis.

### Study objective

Primary: To assess the effects of PRM-151 compared to placebo on the success of trabeculectomy by reducing post-surgical scarring in glaucoma patients who have undergone primary trabeculectomy, evaluated at day 120.
Secondary: To assess the safety and tolerability of PRM-151 administered as a subconjunctival injection in glaucoma patients who have undergone primary trabeculectomy.

### Study design

This is a multicenter, randomized, double-masked, placebo-controlled 120-day study of PRM-151 administered as a subconjunctival injection to patients undergoing primary trabeculectomy followed by an investigator-masked, 240- day

extension.

**Intervention**

Subjects will be randomly assigned to one of two treatment arms:
A: PRM-151 2 mg will be administered as a subconjunctival injection at the end of surgery on day 1 followed by an additional injection of PRM-151 2 mg administered as a subconjunctival injection on days 2, 3, 5 and 9 post-surgery.

B: Placebo will be administered as a subconjunctival injection at the end of surgery on day 1 followed by an additional injection of placebo administered as a subconjunctival injection on days 2, 3, 5 and 9 post-surgery.

**Study burden and risks**

Each subject will participate in the study for approximately 1 year. Participation will include a screening evaluation within 30 days before initial test article administration on day 1, 1 visit following surgery and 12 follow up visits during the year post-surgery. Following surgery, patients will be evaluated on days 2, 3, 5, 9, 14, 21, 30, 60, 90 and 120 for the double-masked phase, and on days 180 and 360 for the investigator- masked extension.
Time input visits: screening: half a day - 1 day. 1 visit after surgery: 1 - 3 hours and 12 follow up visits until 1 year after surgery 2 - 4 hours.
Total: appr. 7 - 8 days.

Risks:
In a study of healthy volunteers, the following were common side effects: headache and fatigue. It is unknown whether the subject will experience these side effects or not. There is a possibility that an allergic reaction to the medication can occur. This could require prescribtion of additional medications to treat this condition.

PRM-151 is a protein and the possibility of an allergic drug reaction does exist. Early signs and symptoms of anaphylaxis can include urticaria, rhinitis, conjunctivitis, abdominal pain, vomiting and diarrhea.

Subconjunctival injections: The possible side effects and discomforts of having an injection under the conjunctiva include the possibility of pain or bruising at the site of the injection; and rarely, infection at the site of the injection.

Eye examinations: The risks and discomforts of eye examinations are similar to those of eye examinations the subject may have had in the past. For example, dilating drops or anesthetic drops may sting when they are first into your eyes. Dilation of your pupils may cause some temporary glare and blurring of vision. The drops could cause an allergic reaction, and, if they are

contaminated, they could cause an infection. This problem is rare.

Slit-lamp photography: The camera flash is bright and may cause temporary discomfort due to aversion for light.

Tonometry (Measuring the pressure inside the eyes): The instrument used to measure the pressure of the eye, could scratch the outside of your eye.

Visual Field and OCT: There are no risks or side effects assocatied with these tests.

Blood draw: There is minimal risk from routine blood drawing, but slight pain or discomfort during this procedure is common. The side effects from blood drawing procedures may include the following: discomfort, bleeding or bruising where the needle enters the body, and in rare cases, fainting, scarring, or infection.

## Contacts

**Public**
Promedior Inc.

371 Phoenixville Pike
Malvern, PA 19355
US
**Scientific**
Promedior Inc.

371 Phoenixville Pike
Malvern, PA 19355
US

## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

Inclusion Criteria
General
1. Men or women of nonchildbearing potential (WONCBP) aged 18 years and older at screening.
WONCBP may be included if they are either surgically sterile (hysterectomy and/or oophorectomy) or postmenopausal for >=1 year (with follicle stimulating hormone [FSH] >=38 mIU/mL) and must have a negative pregnancy test result at screening. Women who are surgically sterile must provide documentation of the procedure by an operative report or by ultrasound. Sexually active men must agree to use a medically acceptable form of contraception from day 1 to 12 weeks after the last dose of test article.
2. Diagnosis of chronic angle-closure glaucoma or open-angle glaucoma, phakic or pseudophakic, with visual field or optic disc changes characteristic of glaucoma. For pseudophakic glaucoma patients, the cataract surgery performed was with phacoemulsification and through a corneal incision.
3. Suitable candidate for trabeculectomy in the study eye which the physician deems as medically necessary.

## Exclusion criteria

Exclusion Criteria
Medical History
1. Diagnosis of glaucoma other than chronic angle-closure glaucoma or open-angle glaucoma (ie., uveitic, traumatic or neovascular glaucoma).
2. Any previous ocular surgeries in the study eye involving the upper conjunctiva and sclera.
3. History of laser surgeries in the study eye within 90 days before day 1.
4. Presence or history of any disease that could affect wound healing.
5. Any asymmetric abnormality of the anterior segment which requires additional intervention (surgery or medication).
6. Any abnormality other than glaucoma in the study eye that could affect tonometry.
7. Presence or history of uveitis within 10 years or any other ocular infection or inflammation within 14 days before day 1.
8. Presence or history of any abnormality or disorder that could interfere with the study procedure or prevent the successful completion of the study.
9. Clear corneal phacoemulsification performed within 90 days before day 1.
10. Any significant unstable cardiovascular, hepatic, renal, respiratory, gastrointestinal, endocrine, immunologic, dermatologic, hematologic, neurologic, or psychiatric disease.
11. Any surgical or medical condition that may interfere with the absorption, distribution, metabolism, or excretion of the test article or the assessment of the effect of the test article.

12. History of drug abuse or alcohol abuse within 1 year before screening that may interfere with the subject*s ability to comply with the protocol requirements.
Physical and Laboratory Findings
13. Conjunctival scarring precluding a trabeculectomy.
14. Vitreous in the anterior chamber.
15. Proliferative retinopathy.
16. Abnormality preventing reliable applanation tonometry in each eye.
Allergies and Adverse Drug Reactions
17. History of drug anaphylaxis to any of the test articles used in this study.
Prohibited Treatments
18. Hemodialysis.
19. Use of any anti-scarring ophthalmologic agents within 90 days before day 1.
20. Use of antimetabolites or systemic steroids within 90 days before day 1.
21. Treatment with cancer chemotherapy within 30 days before day 1.
22. Use of any investigational drug within 30 days before day 1.

# Study design

## Design

| | |
|---|---|
| Study phase: | 2 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Prevention |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 21-02-2011 |
| Enrollment: | 20 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |

| | |
|---|---|
| Brand name: | NVT |
| Generic name: | PRM-151 |

## Ethics review

| | |
|---|---|
| Approved WMO Date: | 15-06-2010 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 16-08-2010 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 19-10-2010 |
| Application type: | First submission |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 14-03-2011 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 12-07-2011 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |
| Approved WMO Date: | 28-09-2012 |
| Application type: | Amendment |
| Review commission: | CMO regio Arnhem-Nijmegen (Nijmegen) |

## Study registrations

### Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EudraCT | EUCTR2009-017859-98-NL |
| ClinicalTrials.gov | NCT01064817 |
| CCMO | NL31350.091.10 |