PHMB 0.08% in the management of Acanthamoeba keratitis

Case series from the Ophthalmology Clinic of Messina

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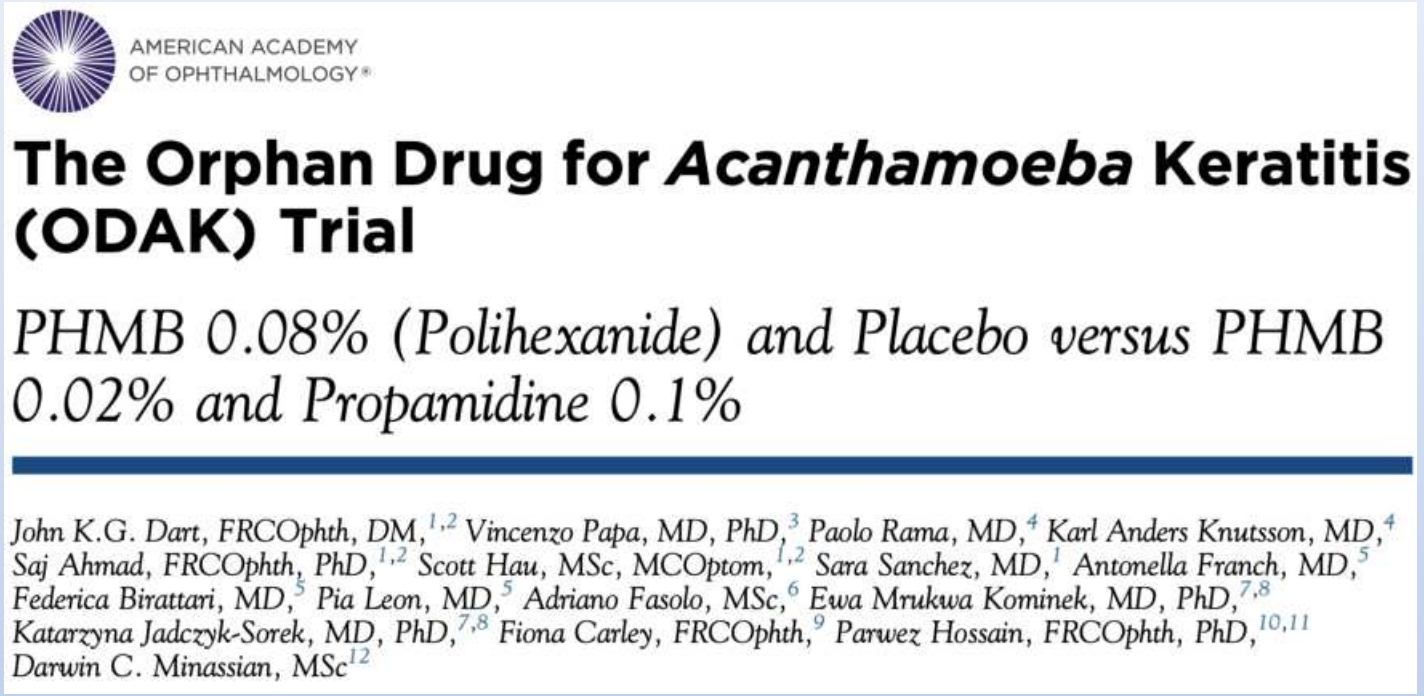
The ODAK (Orphan Drug for *Acanthamoeba* keratitis) trial

The ultimate step forward to the FIRST approved product for the treatment of *Acanthamoeba* keratitis.

Dart JK et al. 2023, Ophthalmology


AMERICAN ACADEMY OF OPHTHALMOLOGY®

The Orphan Drug for *Acanthamoeba* Keratitis (ODAK) Trial

PHMB 0.08% (Polihexanide) and Placebo versus PHMB 0.02% and Propamidine 0.1%

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ODAK Trial: study outline

Aim of the study	To evaluate the **clinical efficacy** of polihexanide (PHMB) 0.8 mg/ml (0.08%) in a comparative clinical trial *vs.* active control
Why PHMB 0.08%	**Highest safe dose** tested in healthy volunteers (Papa et al. - BJO 2020)
Choice of the comparator	The combination of PHMB 0.02% plus a diamidine (propamidine or hexamidine) is the **most used available treatment** in both the EU and US for the medical treatment of *Acanthamoeba* keratitis (Kaufman & Tu - Ocul Surf 2022)
Statistical hypothesis:	Monotherapy with PHMB 0.08% superior (or at least non inferior) of the combination treatment
Sample size required:	n=116 (α 0.05; β 80%; δ 20%)
Primary outcome	**Clinical resolution*** within 12 months from starting treatment, after 1 month off-therapy (confirmed at 3 months)

* Absence of corneal inflammation, conjunctival inflammation, limbitis, scleritis, anterior chamber inflammation. No surgery and relapse

ODAK Trial: protocol

Patients naïve with confirmed diagnosis of AK (clinical AND IVCM findings)

Randomization 1:1

- **PHMB 0.08% PLUS placebo** — **n = 69**
- **PHMB 0.02% PLUS propamidine 0.1%** — **n = 66 (65?)**

Intensive phase (19 days) daytime only → **Continuation phase (until resolution)** → **STOP ALL treatments** → **Follow-Up Off of therapy**

Treatment

5 d (0 – 5) | 7 d (6 – 12) | 7 d (13 – 19) | From d 20 to max 1 yr

16x/day → 8x/day → 6x/day → 4x/day

Study visits

Day 7 | *Day 14* | *Day 21* | *Day 30* | *→ every 30 days until resolution*

1 drop of each solution daytime only

30 days

PRIMARY END POINT

90 days

END OF STUDY

ClinicalTrials.gov NCT03274895

ODAK trial: clinical resolution

Full analysis set (FAS)		Univariate analysis		Multivariate* analysis
	All (n)	Cured (n)	Cured (%) (95% CI)	Cured (%) (95%CI)
PHMB 0.08% + placebo	**66**	**56**	**84.8% (73.9–92.5)**	**86.7%** (79.5–93.8)
PHMB 0.02% + propamidine 0.1%	61	54	88.5% (77.8–95.3)	86.6% (79.1–94.0)
Combined	127	110	86.6% (79.4-92.0)	86.6% (81.3-91.9)
Difference in proportion resolved (p-value)			**-0.037 (0.544)**	**0.001 (0.980)**

Primary endpoint met:

PHMB 0.08% at least not inferior of best available treatment

*Risk factors adjusted: age; AK stage; days delay in diagnosis; study site; prior drugs used (steroids, antibiotics, antivirals)

Use of PHMB 0.08% in clinical practice

- In November 2022, SIFI SpA activated in Italy a **compassionate use program** for the early access to PHMB 0.08%.
- The program was approved by the Italian Medicines Agency (**AIFA**)
- Nominal request (**individual patient)** approved by the local **Ethics Committee**

- **82 patients** distributed in 29 centers entered in the program according to data updated to March 2024.

Source: SIFI SpA (March 2024)

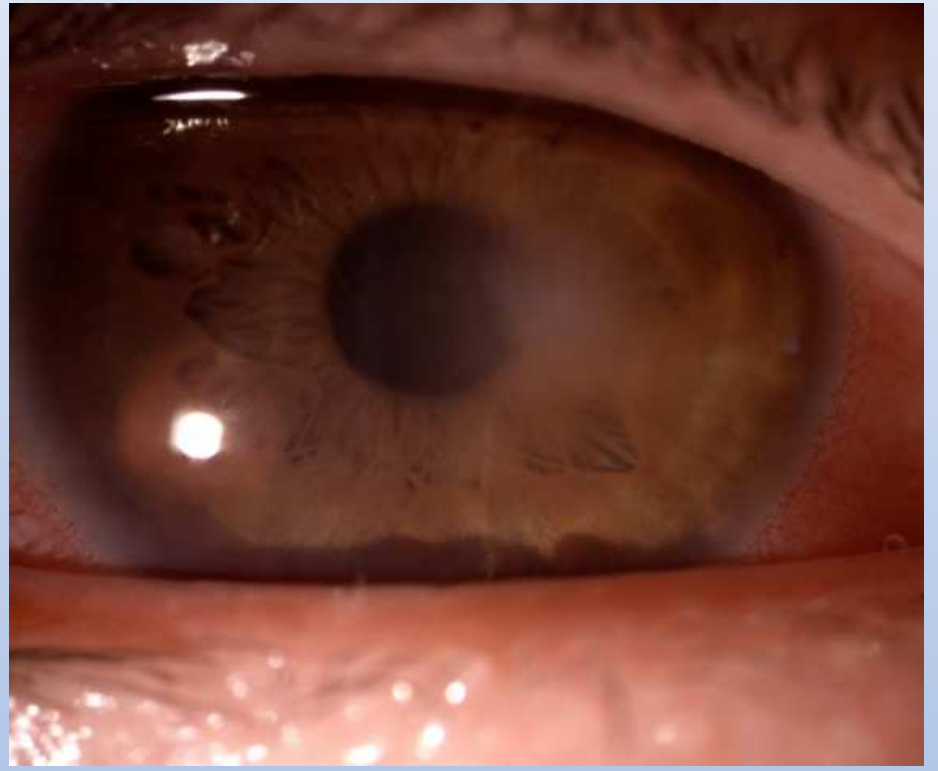
Our experience:

Patients treated with PHMB 0.08% in our Clinic

- 3 Patients initially treated with PHMB 0.02% and subsequently switched to 0.08%
- 1 Patient treated from the beginning with PHMB 0.08%

With the addition of the following standard topical therapy:

- Voriconazole 1%
- Fluoroquinolones
- Antiseptics
- Mydriatics
- Artificial tears



Patient 1, F 48 yo (monthly contact lenses)

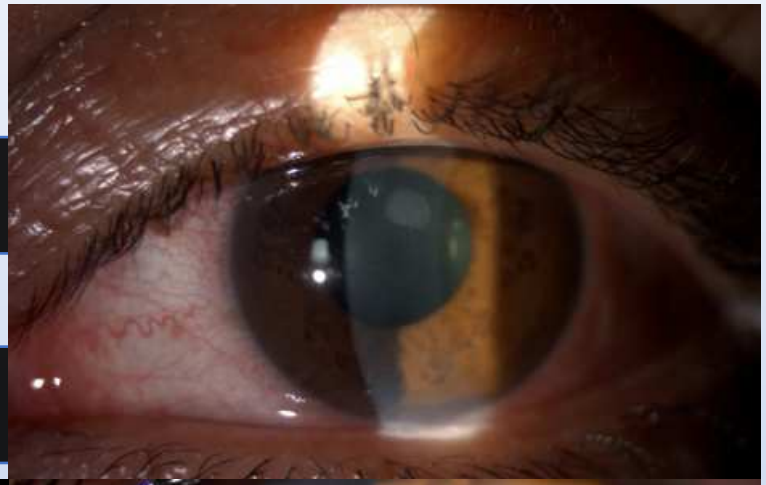
July, 2023 (confocal microscopy+)

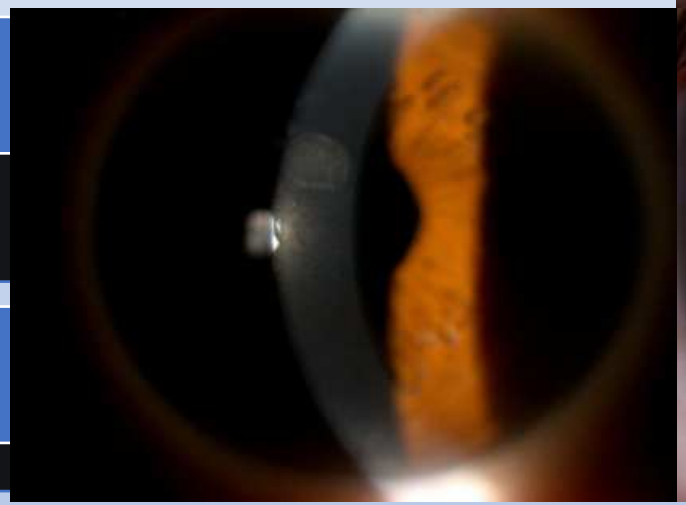
BCVA 0.5

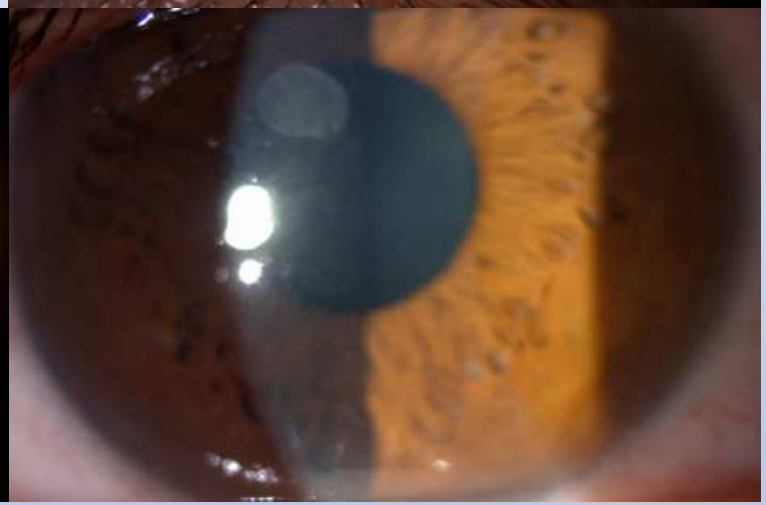
Switched after 3 weeks (CE)

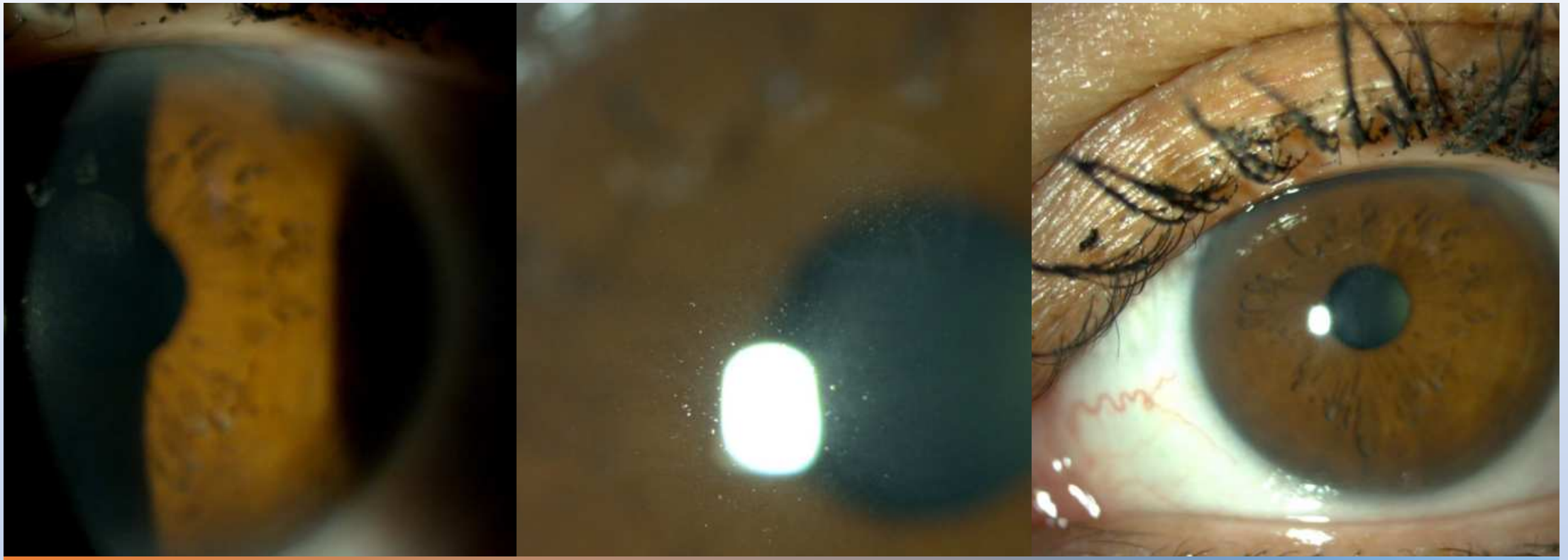
- To PHMB 0.08% Protocol

BCVA 1.0 after 1 month





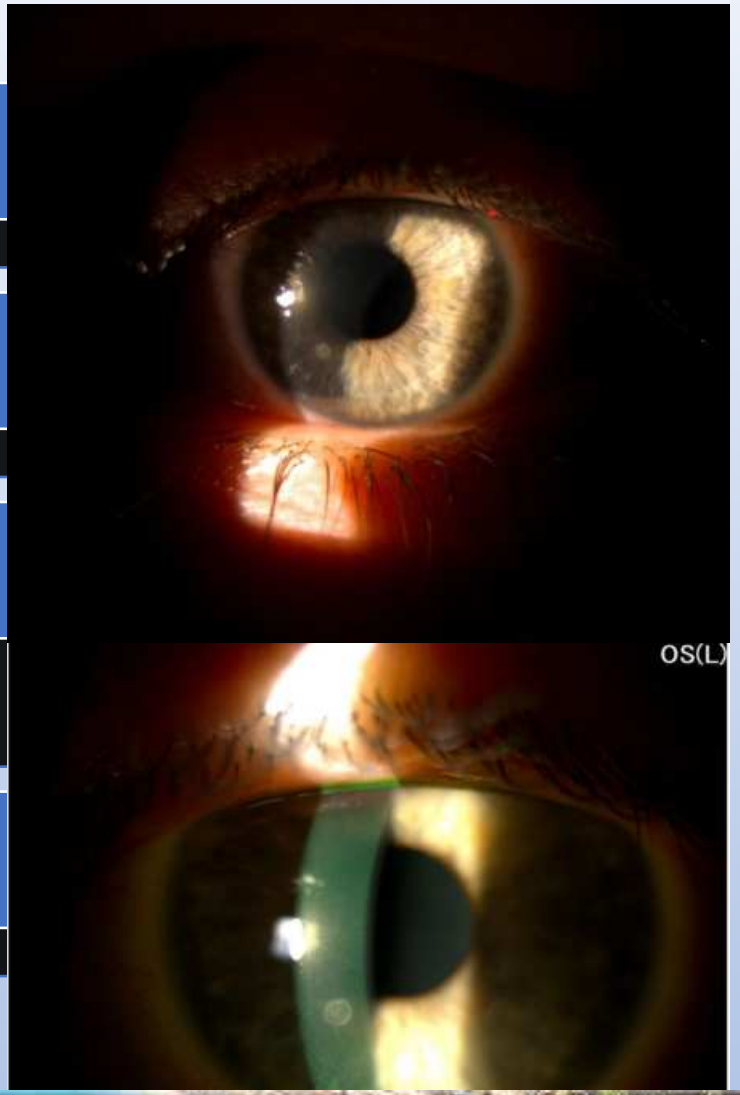


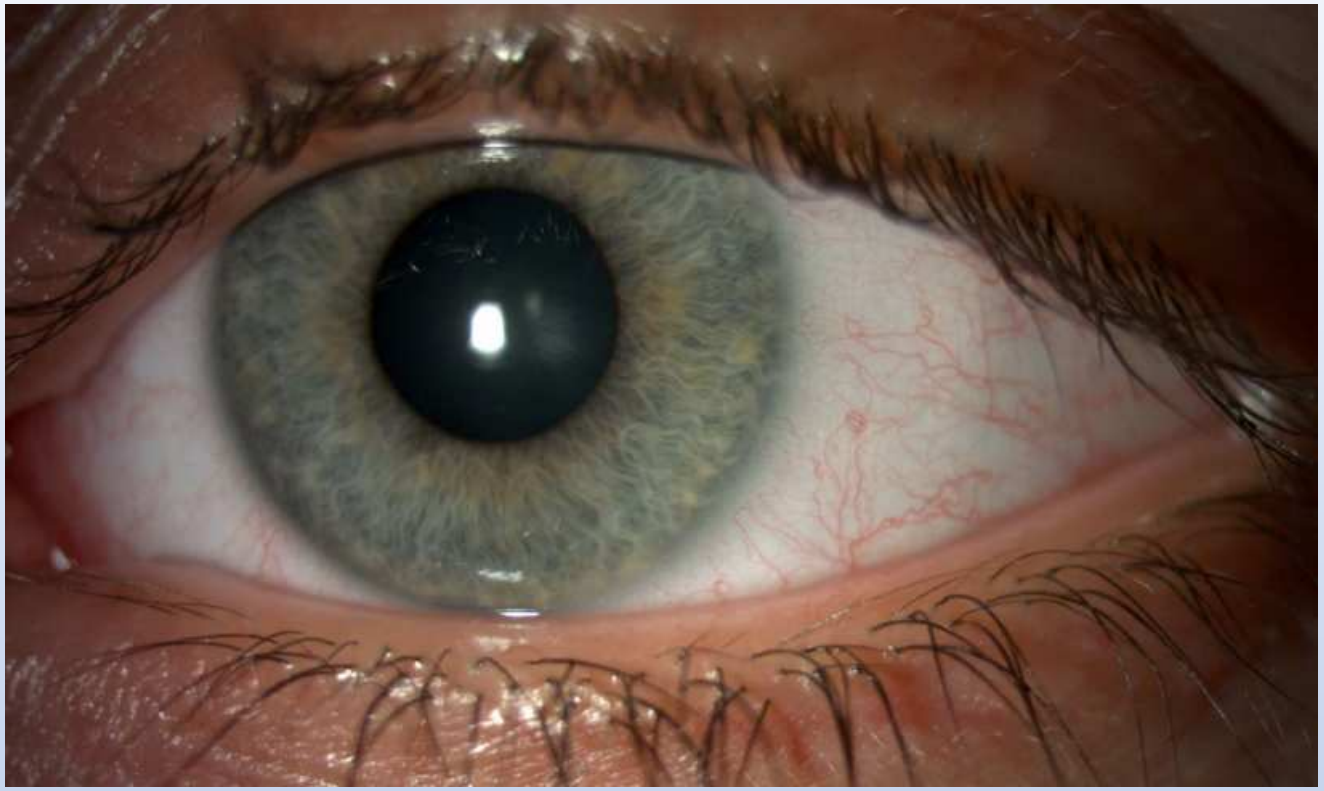


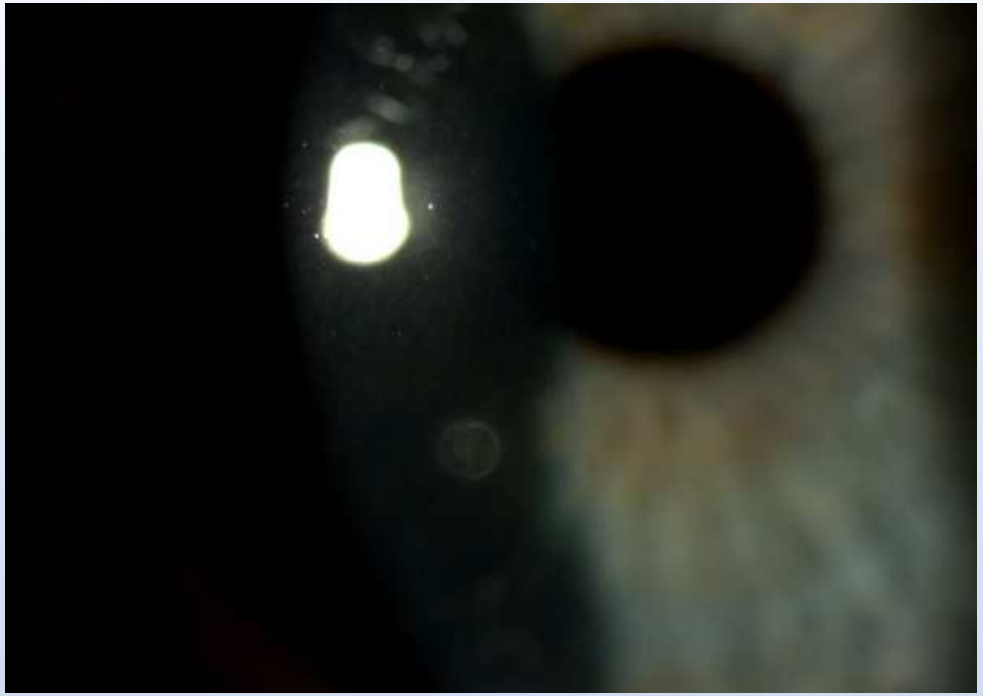
Results after 8 months

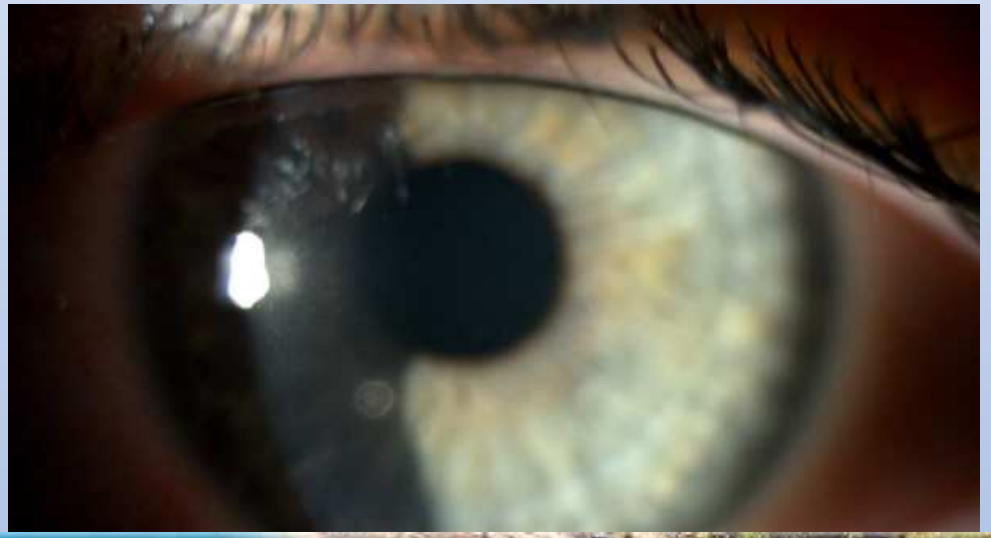
Patient 2, F 23 yo (daily contact lenses)

- July, 2023 (confocal microscopy+)
- BCVA 0.9
- Switched after 3 weeks (CE)
  - To PHMB 0.08% protocol
- BCVA 1.0 after 1 month









Results after 6 months
(BCVA 1.0)

Patient 3, M 45 yo (daily contact lenses)

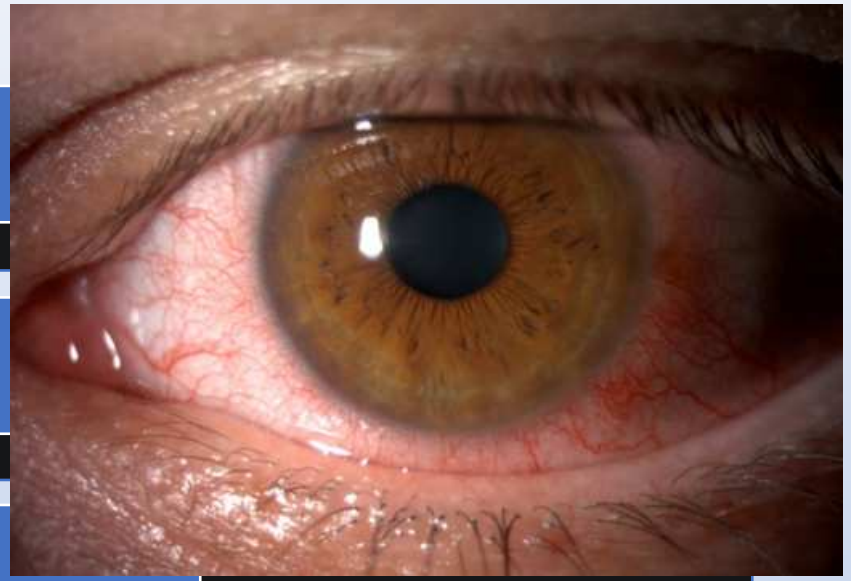
September 2023 (confocal microscopy+)

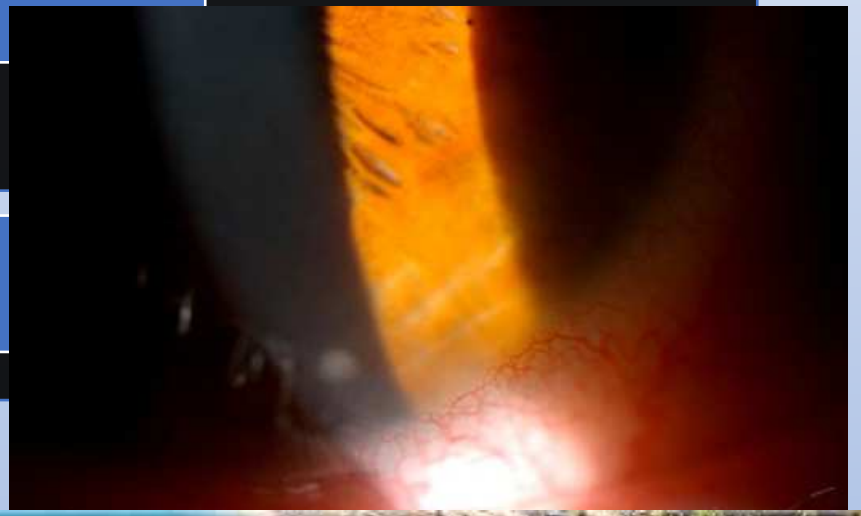
BCVA 1.0

Switched after two weeks (CE)

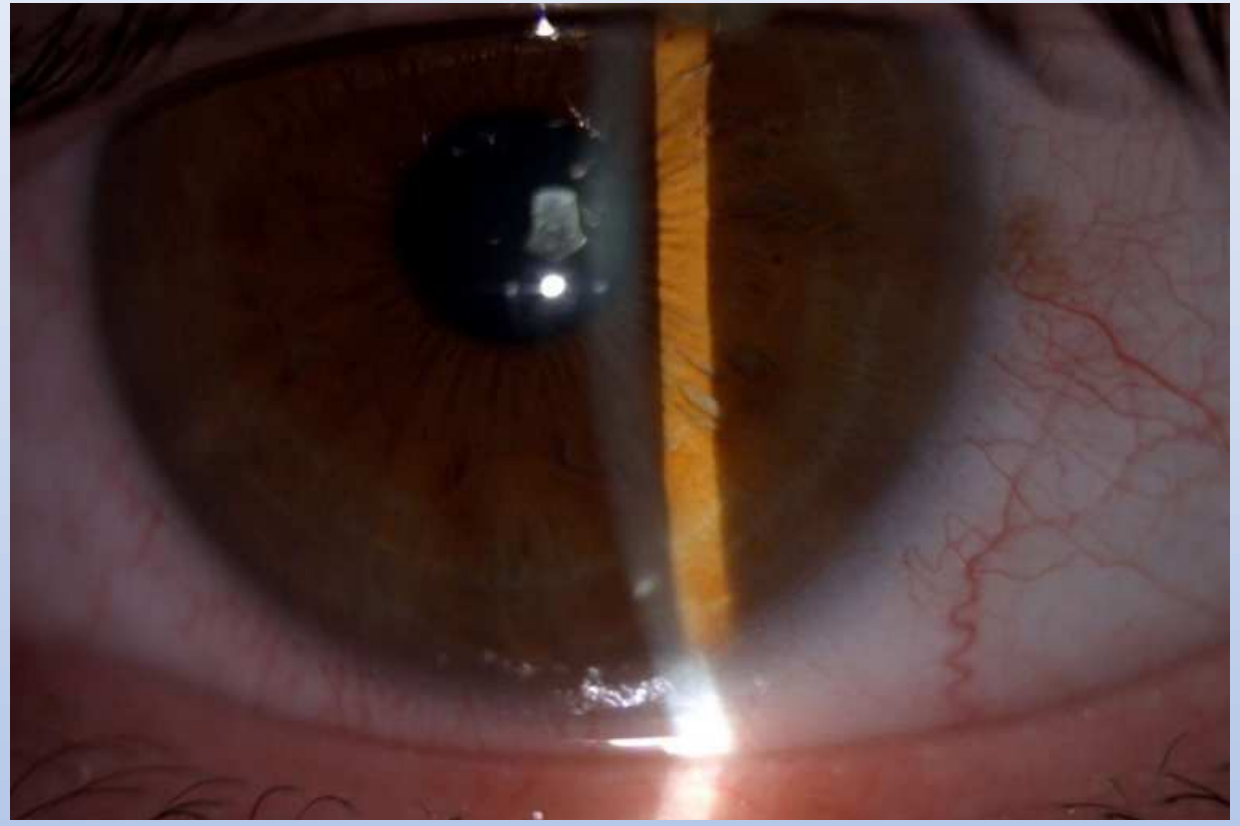
- Protocol PHMB 0.08%

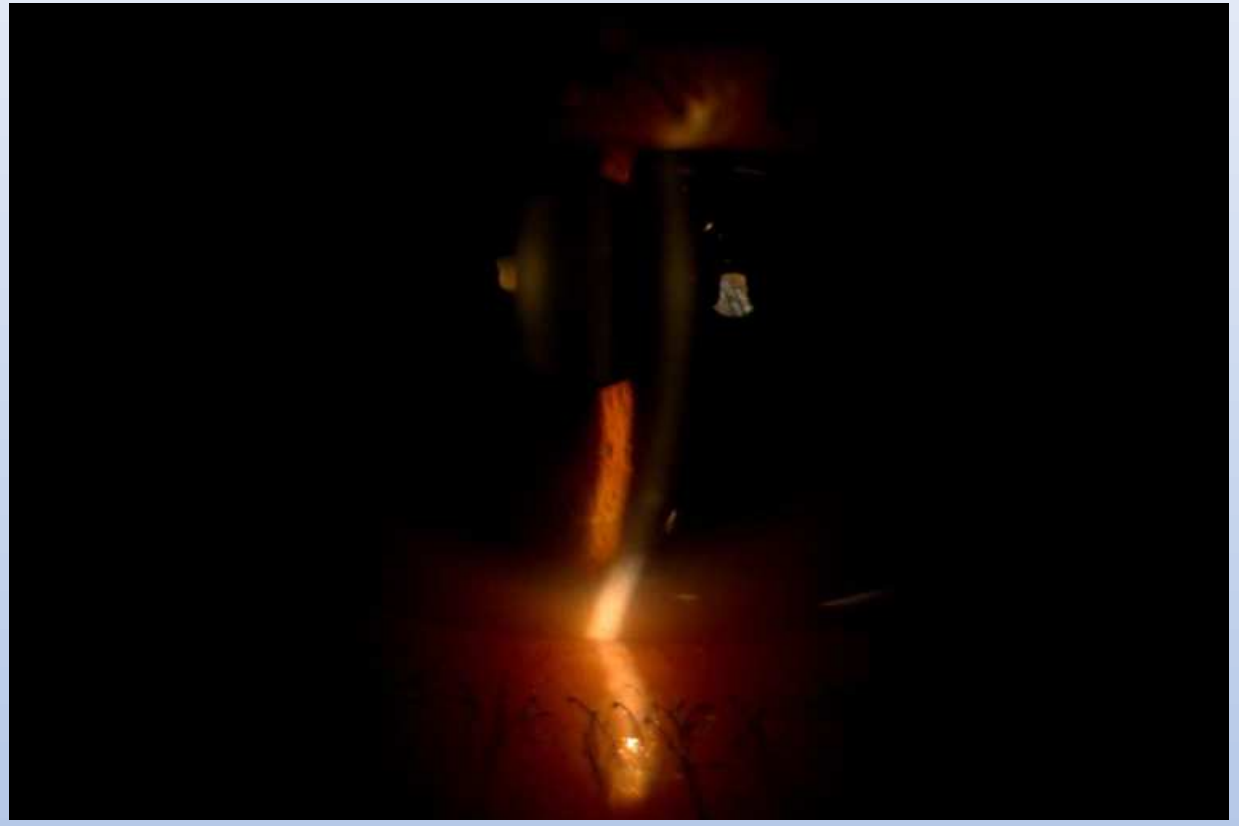
Stable BCVA after treatment





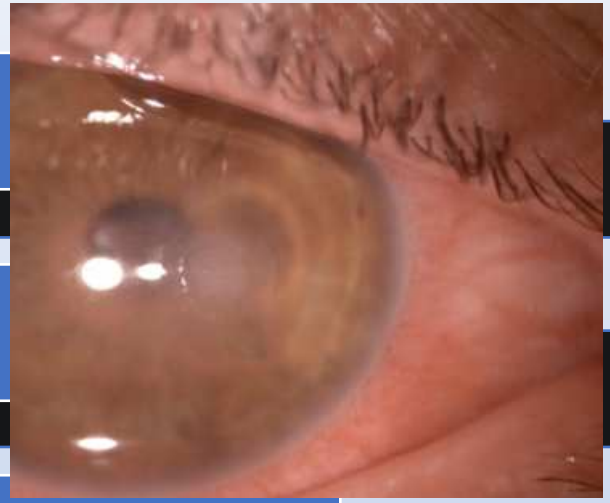
Results after 1 month

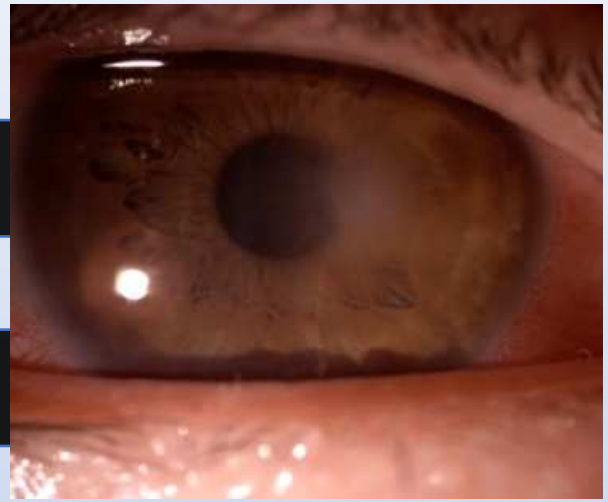




Patient 4, M 45 yo (monthly contact lenses)

November 2023 (confocal microscopy+)

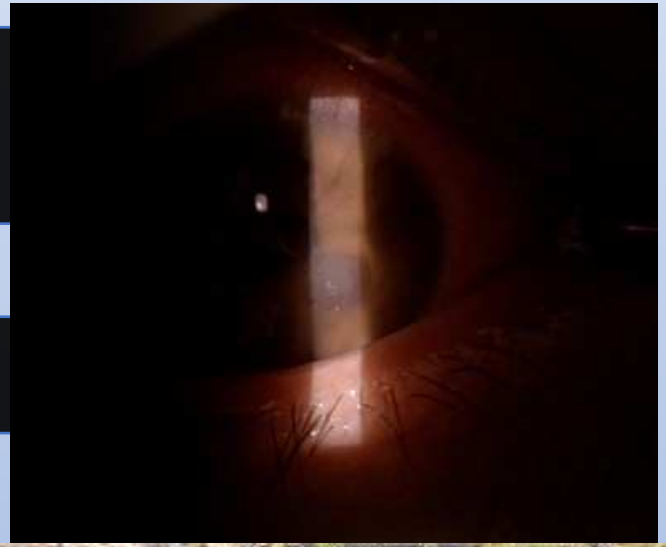




BCVA 0.3

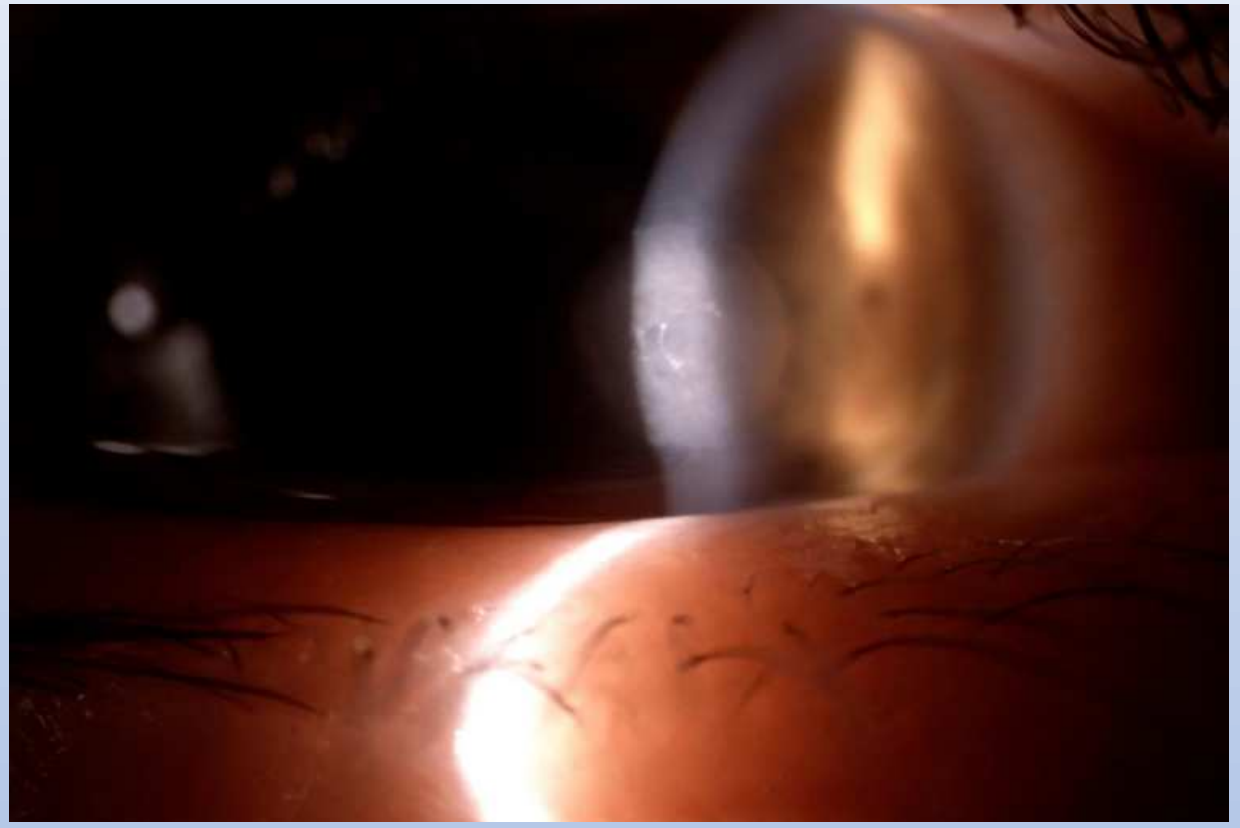
Treated with protocol 0.08% from the beginning

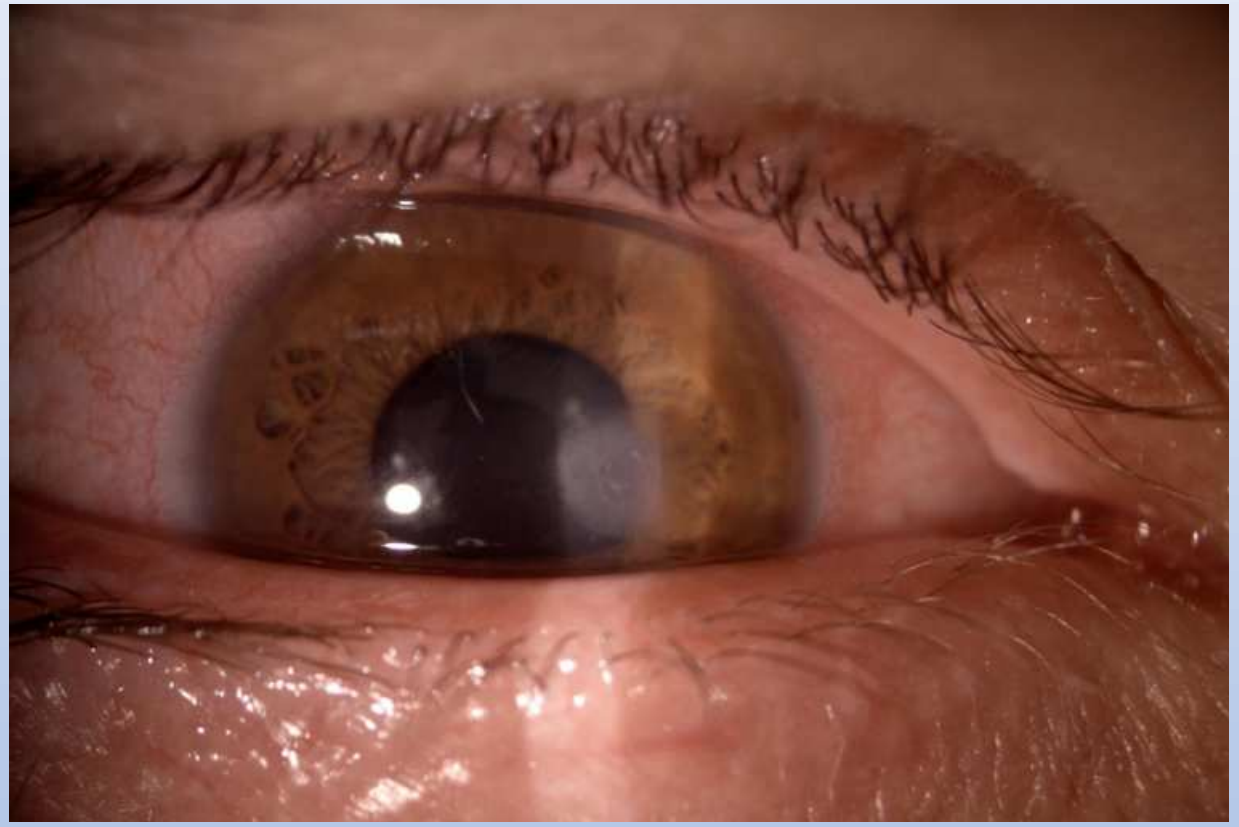
- Protocol PHMB 0.08%



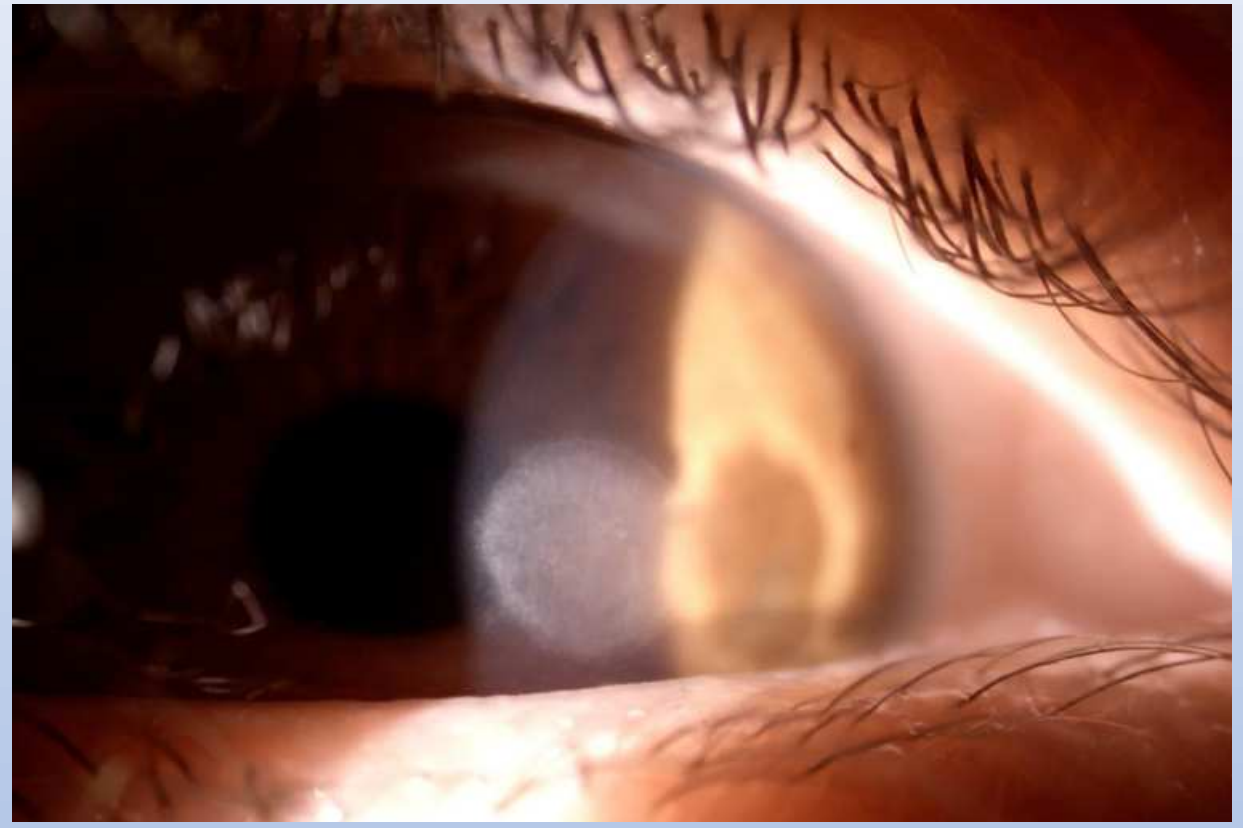
Final BCVA 1.0

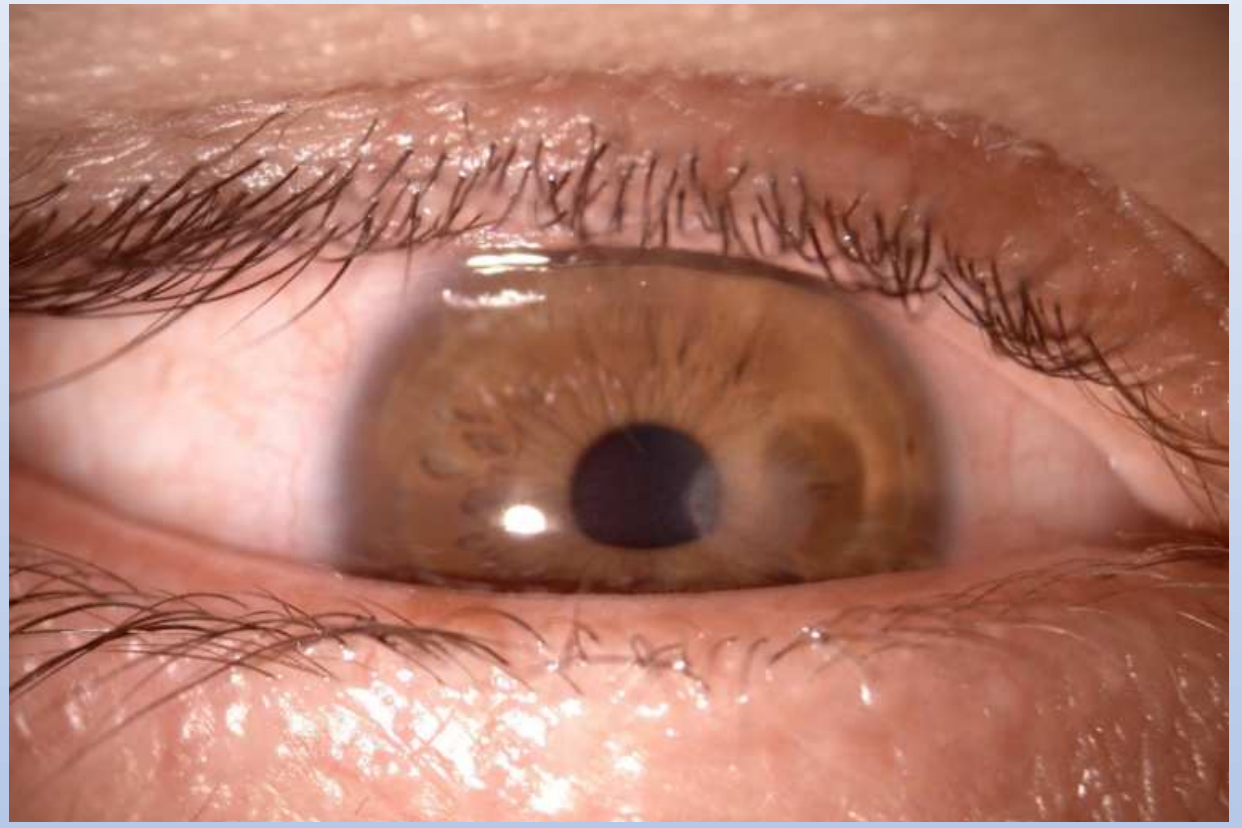
After 7 days



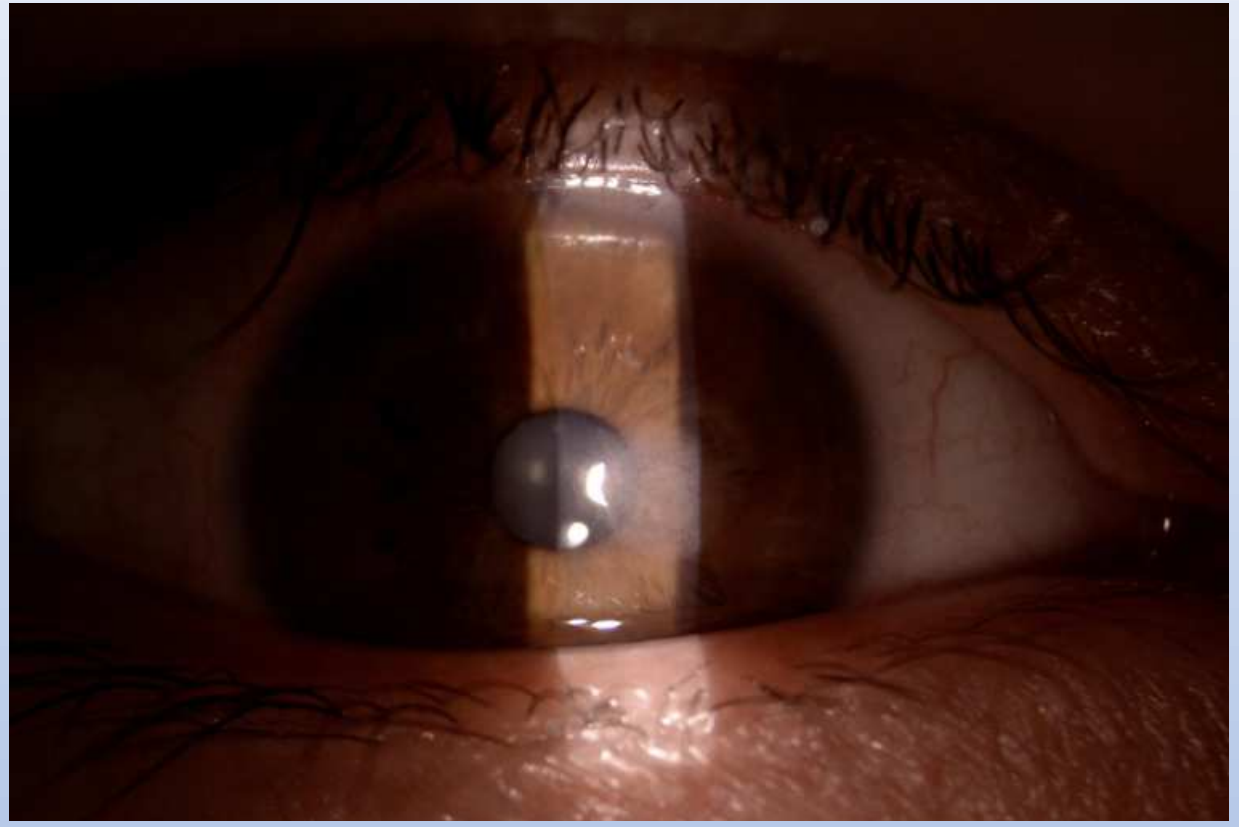


After 1 month



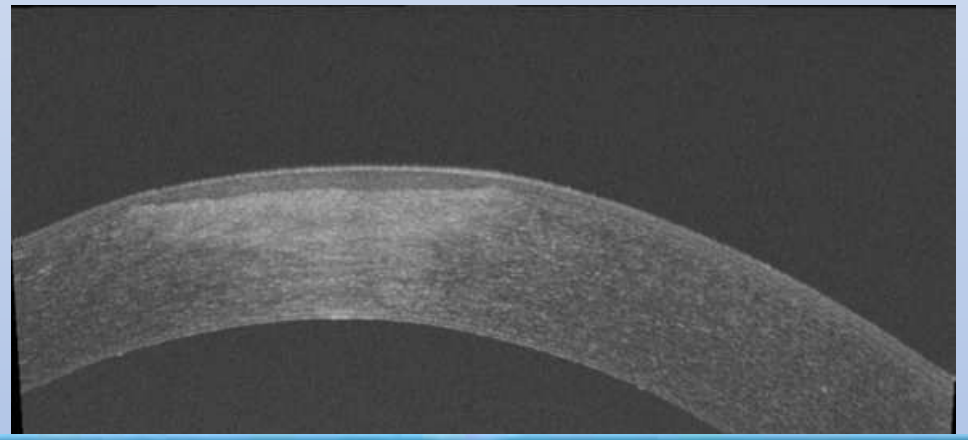


After 2 months

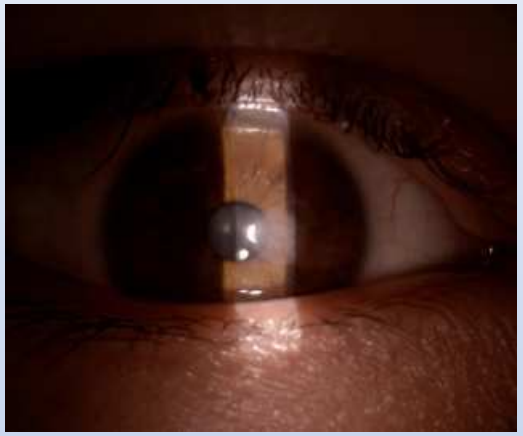


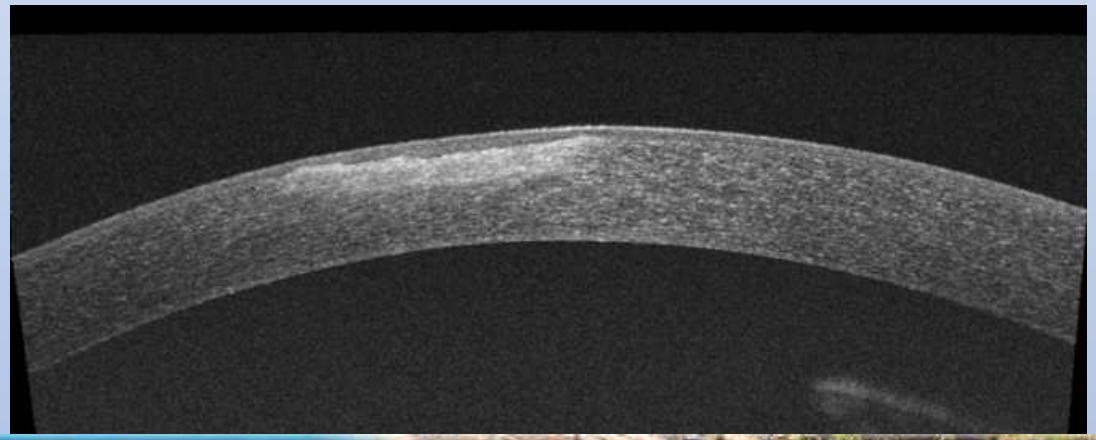
OCT findings

Before treatment

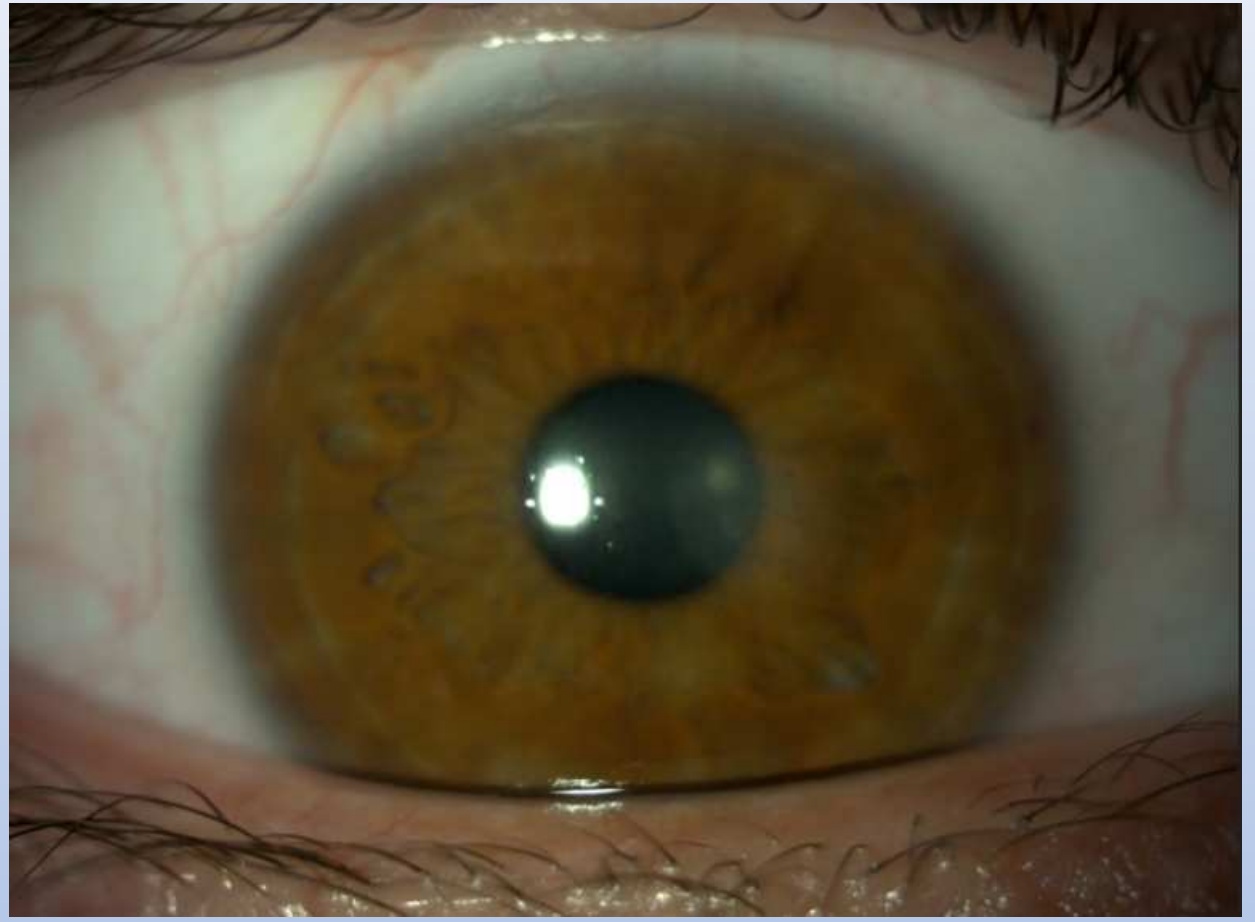


2 Months after treatment





30 days after discontinuing AAT at the slit lamp:



Take home messages

The ODAK trial has brought a novel and evidence-based protocol for the treatment of patients with *Acanthamoeba* keratitis with a GMP compliant product containing 0.08% PHMB.

Results obtained in the ODAK trial can be reproduced also in a clinical practice setting

PHMB 0,08% **was approved by the European Commission on August 22, 2024**, making it the first **'first in class'** drug for the treatment of Acanthamoeba keratitis and establishing a new therapeutic standard.

The positive results obtained from our case series further support the effectiveness of PHMB 0.08% as a therapeutic option, confirming its potential in the treatment of Acanthamoeba keratitis in real-world clinical settings

Grazie per l’attenzione