SUMMARY EVALUATION REPORT TEMPLATE

Study Title: Cluster randomised controlled trial of a complex intervention package to reduce blindness from severe microbial keratitis in Uganda.

NDA CTA Number: CTA 0235

Protocol No. Not provided

Version No. 2 **Date:** 12/07/2022

National Principal Investigator (NPI): Dr. Simon Arunga

Institution /Trial Site: Mbarara University and Referral Hospital Eye Center, Lower circle road, Mbarara

Sponsor: London School of Hygiene and Tropical Medicine

REC of record: MUST REC **REC reference number:** MUST-2021-62

UNCST reference number: HS1814ES

NDA Date of Approval: 14th March 2023

Study background and Rationale

Sight-loss from severe microbial keratitis (MK) in Low- and Medium-Income Countries results from a combination of adverse factors: eye injuries, limited awareness, TEM use, delayed presentation, limited health-worker training, few available treatments.

In Uganda, most patients first present to a primary health centre (PHC), where care is provided by health workers with limited eye training, who may struggle to recognize this serious problem and have few treatment options to offer. Patients are sometimes referred urgently to regional eye units. However, there is often further delay (median 2 weeks) before patients travel to the eye unit and start definitive intensive treatment. Sometimes due to the failure to recognize this problem at the PHCs, referral advice is never given to the patients who may then resort to try other things like TEM making the situation worse.

Therefore, reducing blindness from MK will require a complex intervention package approach that simultaneously addresses these challenges, to prevent MK becoming severe. The key elements are preventing harm and reducing delay in starting effective intense antimicrobial treatment.

General objective / Study aims

To determine if a complex intervention package delivered at the Primary Health Centres (PHCs) including early recognition, prompt chlorhexidine 0.2% treatment and rapid referral can result in reduced rates of blindness from severe MK at three months.	

Primary Objectives and Outcome Measures

To determine if a complex intervention package delivered at the Primary Health Centres, including early recognition, prompt chlorhexidine 0.2% treatment and rapid referral can result in reduced rates of blindness from severe MK at three months, compared to the standard of care.

The primary outcome will be the proportion of people who are blind (vision less than 3/60) in the affected eye at three months, compared by arm.

Secondary Objectives and Outcome Measures

To determine whether there is a difference between the complex intervention pack at PHCs and the control standard of care in terms of secondary outcomes:

1. Scar/infiltrate size at 3 months, slit lamp examination by ophthalmologists (trial certified).

2. Perforation and / or therapeutic corneal transplant (TPK) by three months, slit lamp examination by ophthalmologists.

3. Diagnostic accuracy in primary care

4. Time between symptom onset and presenting to primary care facility

5. Adherence to and time taken to attend referral at eye hospital

6. Quality of life questionnaires: EQ-5D, WHO/PBD-VF20, WHOQOL-BREF

7. Cost effectiveness analysis

Study Design

This is a prospective, single-masked, parallel group, two-arm cluster randomised controlled trial (cRCT), in Uganda.

Study Population

The study will be conducted in Ntungamo and Isingiro districts in South Western Uganda

Eligibility Criteria

Inclusion Criteria:

Corneal abrasion characterized by corneal epithelial ulceration seen on fluorescein staining but no corneal infiltrate.

OR

• Acute Microbial Keratitis characterized by:

o Corneal epithelial ulceration

o Corneal stromal infiltrate

o Acute inflammation: e.g. conjunctival injection, anterior chamber inflammatory cells, hypopyon

Exclusion criteria:

• Unwilling to participate in trial or attend for follow-up

• <18 years

• Pregnancy or breast feeding

• No light perception in the affected eye

• Fellow eye visual acuity <6/60

• Known allergy to study medication (including preservatives)

• Previous penetrating keratoplasty in the affected eye

- Bilateral corneal ulcers
- Nationals of another country

Study Duration

The anticipated overall project duration is about 2 years. The fieldwork will take about one year

Investigational Medicinal Product

Chlorhexidine 0.2% ophthalmic solution (chlorhexidine gluconate 2mg)

Study Arms

Two arm study:

Arm I: Offer an early interventional package including smartphone-based triage system for MK, prompt treatment with g-chlorhexidine digluconate 0.2% eye drops, early facilitated referral to the eye hospital.

Arm II: Offer “standard of care” for MK.

Sample size

200 eligible participants

Evaluator’s Risk/Benefit Assessment:

The current information provided on the investigational product is sufficient to justify the proposed clinical trial. The potential benefits of conducting the trial are considered to outweigh the risks involved, provided that the study is carried out in accordance

with the approved protocol, applicable local regulatory standards, ethical standards derived from the Declaration of Helsinki and the principles of Good Clinical Practice