Study Title: Effectiveness of an integrated program for the prevention of rheumatic heart disease in endemic regions: an incomplete stepped wedge cluster randomized trial

Short title: PREVENT

Phase of the trial:

CTA Number: ET-CT-0044

Protocol No.

Version No.

National Principal Investigator (NPI): Abraha Hailu Weldegerima, MD

Trial Site: Mekelle

Sponsor: Insel Gruppe AG, Inselspital Bern, Universitätsklinik für Kardiologie

Ethics Approval date:

Submission Date to EFDA: June 18, 2024

EFDA Status of trial (Approval or Rejection): Closed **Date:** Dec 28, 2024

Study Rationale

Timely detection and treatment of Group A beta-hemolytic streptococcal infections (GAHBS) pharyngitis among children represents an effective target for primary prevention of Rheumatic heart disease (RHD). To study different approaches to reduce the burden of RHD include primary and secondary antibiotic prevention.

General objective / Study aims

The overall objective of the present study is to evaluate the effectiveness of an integrated, school-based program for the prevention of RHD in regions with an endemic pattern of RHD compared to standard of care (control phases) using a cluster randomized design.

Primary objectives

Objective

To quantify the reduction of the prevalence of definite or borderline RHD according to the criteria of the WHF after implementation of an integrated, school-based awareness and prevention program.

Outcome measures

The reduction in prevalence of definite or borderline RHD according to the WHF criteria[1] as assessed by systematic echocardiographic screening in experimental and control phases.

Secondary Objectives and Outcome Measures

Objective

(1) to assess gender differences in the incidence of GABHS pharyngitis as assessed by RADT, the incidence of ARF according to the modified Jones criteria, and the incidence of definite or borderline RHD according to the criteria of the WHF; (2) to evaluate the cost-effectiveness of the integrated awareness and prevention program; (3) to investigate attitudes of students, parents and teachers towards the intervention over time; and (4) to evaluate the social and gender equity in access to and compliance with the integrated awareness and prevention program.

Outcome measures

be (1) gender differences in the incidence of GABHS pharyngitis as assessed by RADT, in the incidence of ARF according to the modified Jones criteria, and in the incidence of definite or borderline RHD according to the WHF criteria; (2) the costs for the prevention of one case of latent RHD; (3) attitudes of students, parents, and teachers towards the intervention over time as assessed by a 7-item Likert scale at the end of every school year; and (4) social and gender equity in access to and compliance with the RHD prevention program.

Study Design

An incomplete stepped wedge cluster randomized trial

Study Population

The study population consists of children 5 to 16 years of age attending randomly selected schools in Lusaka (Zambia), Mekelle (Ethiopia) and Kathmandu (Nepal).

Eligibility Criteria

Inclusion Criteria:

- Age 5-16 years
- Attending a randomly selected school at one of the three study sites.

Exclusion criteria:

- Children / parent / legal representative not providing informed consent to participate
- Children not attending one of the selected schools.

Study Duration

Not Specified

Investigational Medicinal Product

NA

Intervention (s)

Formulation : NA

Dose : NA

Route of administration : NA

Other interventions

Sample size

A total number of 18 schools (clusters) will be randomized in an incomplete stepped wedge cluster randomization design, with an expected number of 300-400 children per school with independent echocardiographic RHD assessment. School sizes are expected to vary between 200 and 500 children and an attempt will be made to measure all children (if consented) currently attending the school at the end of the school year.

Evaluator's Risk/Benefit Assessment:

EFDA has not received a response from the applicant to further request over twelve months. We therefore consider the application CLOSED.