Statistical Analysis Report

Evaluation of a chlorhexidine mouthwash for the eradication of asymptomatic pharyngeal Neisseria gonorrhoeae infection (Mouthwash N. gonorrhoeae - MoNg Study)

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1. Introduction

This report presents the interim analysis for the "Evaluation of a chlorhexidine mouthwash for the eradication of asymptomatic pharyngeal Neisseria gonorrhoeae infection (Mouthwash N. gonorrhoeae - MoNg)" study.

The purpose of this study is to assess if there a pharyngeal NG infection could be eradicated after 6 days of chlorhexidine mouthwash and gargling (MWG). The study conduct is described in the study protocol (ITM201902) and in the European Union Drug Regulating Authorities Clinical Trials Database (EudraCT 2019-003604-12).

This is a single arm pilot study of men who have sex with men (MSM) with a diagnosis of asymptomatic gonococcal pharyngeal infection who present to the HIV/STI Outpatient Clinic of the ITM.

A total of 100 asymptomatic MSM with a culture positive pharyngeal NG mono-infection (not in the other anatomical sites) was initially calculated in order to obtain at least 20 participants to assess efficacy. No randomization was done in the study, as all participants received the same treatment.

2. Study design and objectives

Primary Objective

The primary objective of this study is to assess if MWG with chlorhexidine 0.2% x 60 seconds twice a day for six days is able to eradicate pharyngeal NG based on culture conversion by day 7 (range 6-8 days).

Secondary Objectives

1. Assess if there is a decline in NG bacterial load over time under treatment with MWG with chlorhexidine.
2. Assess the time to culture negativity under treatment with MWG with chlorhexidine
3. Assess if MWG with chlorhexidine 0.2% x 60 seconds twice a day for six days is able to eradicate pharyngeal NG based on NAAT conversion by day 14 (range 13-15 days).
4. Assess if MWG with chlorhexidine 0.2% x 60 seconds twice a day for six days is able to eradicate pharyngeal NG based on culture negativity by day 14 (range 13-15 days).
5. Assess if MWG with chlorhexidine 0.2% x 60 seconds twice a day for six days results in changes in pharyngeal microbiome and resistome before versus 14 days (range 13-15 days) after the start of chlorhexidine MWG therapy.

Safety Objective

Assess the safety of the use of MWG with chlorhexidine 0.2% twice a day for 6 days

3. Summary of Statistical Methods and Data sources

Statistical analyses were performed on the locked final data, extracted on the 22-March-2021 following the Statistical Analysis Plan (SAP) which was finalized on 08-March-2021.

The data of the study come from:

1. The clinical study database
2. The computer-assisted self-interviewing (CASI) questionnaire at the study planned visits

The clinical study database contains general information on the subjects, eligibility, laboratory, STI history, medication and safety among others. The CASI questionnaire contains information on number of sexual partners, condom use, antibiotic intake, STI diagnoses.

4. Description of study population

4.1. Subject accounting

A total of the 6 participants were enrolled in the study, 3 of who had a negative NG lab result at day 1 and were exited from the study. The remaining 3 subjects had a positive NG result at day 7. The detailed patient accounting is explained in **Error! Reference source not found.**.

Table 1: Patient Accounting

	Total
Enrolled in the study	6
Did not complete day 7	3 (50 %)
- Negative NG at day 1	3
Completed day 7	3 (50 %)

4.2. Description of study population

A description of recorded demographic characteristics for the 6 recruited subjects. Continuous characteristics are presented as medians with interquartile ranges and categorical characteristics as counts and percentages (Table 2).

Table 2: Baseline Characteristics

	Total n (%)
N	6
Age (yr): median (IQR)	35.5 (31.25 - 40.5)
Main partner	3 (50)
Number of sex partners (last month)	1 (1 - 1.75)
Mouthwash use (last 14 days)	0 (0)
Antibiotic use (last 14 days)	0 (0)

4.3. Efficacy analysis

Efficacy analysis will only include endpoints until visit at day 7. The results are presented as counts and percentages together with two-sided Wilson's confidence intervals (Table 3).

Table 3: Summary of Primary and Secondary Efficacy Analysis Results

	n/N; % (95 % CI)
Negative pharyngeal NG culture (day 7) / tests + symptomatic	0/3; 0 (0 – 56.1)
Negative pharyngeal NG culture (day 7) / tests + any reason	0/3; 0 (0 – 56.1)

4.4. Safety analysis

No adverse events or other mouth related complaints have been reported during the study.