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| Study Title:  The Burden of Atypical Hemolytic Uremic Syndrome and The Clinical  Characteristics of Patients in Egyptian Hospitals  A Multicenter, Observational, Retrospective Cohort Study in Egypt  Study Name: REACH-Egypt Study  Study Number: D928BR00001 |

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List of abbreviations and definition of terms

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| **Abbreviation** | **Definition** |
| aHUS | Atypical Hemolytic Uremic Syndrome |
| AKI | Acute Kidney Injury |
| IQR | Interquartile Range |
| OS | Overall Survival Rate |
| SAP | Statistical Analysis Plan |
| SD | Standard Deviation |
| TMA | Thrombotic Microangiopathy |

# Document History

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| **Version** | **Author** | **Title** | **Date** | **Description** |
| Draft V0.1 | Abeer Mahmoud | BS2 | 27-Nov-2024 |  |
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# Overview and study plan

This statistical analysis plan (SAP) provides a comprehensive and detailed description of strategy and statistical technique to be used for the analysis of data for study REACH-EGYPT (Study code: D928BR00001)

## Study design

A multicenter, observational, non-interventional, retrospective, national study of medical records of patients with TMA from at least five sites across Egypt. To describe their demographic and clinical characteristics, documented clinical manifestations of TMA, and the resulting complications of aHUS.

### Inclusion Criteria:

**To be eligible for this trial, patients must meet all of the following criteria:**

Patients must fulfill all the following inclusion criteria to be included in the study:

* Male or female patients aged one month or older who have been diagnosed with TMA between 01-Jan-2010 and 31-Dec-2023.

### Exclusion Criteria

**Patients with any of the following criteria will not be eligible to participate in the study:**

None. All records of patients with TMA will be screened for aHUS diagnosis

## Study Objectives

### Primary objectives

* To describe demographic and clinical characteristics of patients with aHUS.
* To describe the clinical manifestations of TMA and long-term complications of aHUS

### Secondary objectives

* To estimate the prevalence of patients diagnosed with aHUS among the total number of patients with TMA in the participating hospitals
* To describe treatment patterns and clinical outcomes of current treatment in patients with aHUS.

### Exploratory objectives

NA

## Study Endpoints

### Primary Endpoints

Primary outcomes will be assessed for all patients diagnosed with TMA including patients with aHUS as a subgroup.

Analysis will include:

1. Demographic and clinical characteristics of patients with aHUS.

o Duration between TMA diagnosis and the first manifestation

o Duration between aHUS diagnosis and the first manifestation

o Duration between the first aHUS treatment initiation and aHUS diagnosis

1. TMA manifestations as hematologic and renal events, and extra-renal events due to aHUS.

### Secondary Endpoints

1. The prevalence of patients will be calculated as follows:
2. Types and Number of Therapies: Counts and percentages of each therapy type.
3. Clinical outcomes of current treatment (at 3 months and 12 months after treatment initiation if available):

* Overall Survival Rate (OS):

Kaplan-Meier survival analysis will be used to estimate OS at specified time points (3- and 12-months post-treatment initiation).

* ESRD-Free Survival Rate:

Like OS, will be calculated using Kaplan-Meier analysis, where the event is reaching ESRD.

* Complete TMA Response and Time to Complete TMA Response:

Proportion Achieving TMA Response: Calculate the proportion of patients achieving a complete TMA response.

Time to TMA Response: For patients achieving a response, calculate the time to response using Kaplan-Meier

Censoring Time to event endpoints is defined from the date of first Treatment initiation. If the subject did not have an event, the time to event will be censored at the last contact date

* Dialysis requirement status

The percentage of patients requiring dialysis will be described at each follow-up point (3 and 12 months).

1. Changes in estimated glomerular filtration rate (eGFR), creatinine (Cr), platelets, lactate dehydrogenase (LDH), and hemoglobin (Hgb) from baseline (at the start of the current treatment) as well as at 3- and 12-months post-initiation (if data are available) will be summarized using descriptive statistics, specifically mean and standard deviation (SD) for normally distributed data or median and interquartile range (IQR) for non-normally distributed data.

### Exploratory Endpoints

NA

## Study Safety

NA

## Determination of sample size

Due to the descriptive nature of the study, no formal sample size is considered. It is planned to enroll 200 patients*.*

## Study plan

A multicenter, observational, non-interventional, retrospective, national study of medical records of patients with TMA from at least five sites across Egypt. To describe their demographic and clinical characteristics, documented clinical manifestations of TMA, and the resulting

complications of aHUS.

## Modifications from the protocol

NA*.*

## Modifications from the approved statistical analysis plan

NA*.*

# collected data

## Site questionnaire

NA

## Screening log

NA*.*

## Patient data

NA

# general Statistical approach

Descriptive analysis for quantitative data will include mean, and standard deviation (SD) for normally distributed variables. When normal distribution is not met, the median and interquartile range (IQR) will be used. For qualitative categorical variables,

# Analysis of Site questionnaire

## Analysis variables

NA

## Analysis population

NA

## Statistical methods

NA

# Analysis of patient data

## Analysis variables

*Insert CRF with highlighted critical variable.*

## Analysis population(s)

Patients diagnosed with TMA between 01-Jan-2010 and 31-Dec-2023 regardless of administered treatment. Medical records of all patients fulfilling the eligibility criteria will be collected.

### Eligible patient population:

Patients diagnosed with TMA between 01-Jan-2010 and 31-Dec-2023 regardless of administered treatment. Medical records of all patients fulfilling the eligibility criteria will be collected.

### Other population (to be adapted)

NA

## Statistical methods

All analysis variables will be described according to the methods defined in this section for the description of continuous and categorical variables.

### Disposition of patients

A diagram will be provided in the statistical analysis report

### Analyses of baseline characteristics

• Demographic and clinical characteristics of patients with aHUS.

o Duration between TMA diagnosis and the first manifestation

o Duration between aHUS diagnosis and the first manifestation

o Duration between the first aHUS treatment initiation and aHUS diagnosis

• TMA manifestations as hematologic and renal events, and extra-renal events due to aHUS.

### Analyses of evaluation variables

#### **Analysis of main evaluation variable(s)**

- Continuous variables will be described as median, interquartile range (IQR) and

categorical variables will be presented as frequency and percentages

#### **Analyses of secondary evaluation variables**

* The proportion of patients diagnosed with aHUS will be divided by the total number of

patients with TMA in the participating hospitals as of 31st December 2023.

* Continuous variables will be described as median, interquartile range (IQR) and

categorical variables will be presented as frequency and percentages. Rates will be

described as both fractions and percentages.

#### **Analysis of Exploratory evaluation variables**

NA

#### **Analysis of Safety evaluation variables**

NA

# Data handling conventions

## Data handling conventions for site questionnaire

NA

## Data handling conventions for patient data

* The duration between TMA diagnosis and the first manifestation will be calculated as follows:

Duration in months =First Manifestation Date−TMA Diagnosis Date /30.4

* Duration between aHUS diagnosis and the first manifestation will be calculated as follows:

Duration in month=First Manifestation Date−AHUS Diagnosis Date /30.4

* Duration between the first aHUS treatment initiation and aHUS diagnosis will be calculated as follows:

Duration in month= Date of the 1st treatment initiation −AHUS Diagnosis Date /30.4

* Duration of treatment will be calculated as follows:
* Duration of treatment in months = End date of treatment – start date of treatment /30.4

Time to Complete TMA Response is calculated as follows:

Duration to Response (months)= Date of complete TMA response −Treatment Initiation Date/30.4

## Missing data

Missing data will not be imputed – a complete case analysis approach will be used.

# Interim analysis

NA

# Software documentation

All summaries and statistical analyses will be generated using R version 4.2.3 or higher.