

# Statistical Analysis Plan

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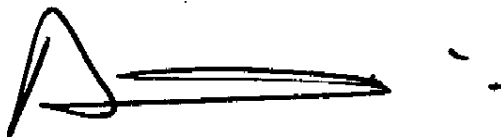
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**Abbreviations**

HIV	Human Immunodeficiency Virus
CNS	Central Nervous System
CSF	Cerebrospinal Fluid
ARV	Antirretroviral
TAF	Tenofovir Alafenamide Fumarate
FTC	Emtricitabine
ART	Antirretroviral Treatment
PK	Pharmacokinetics
PD	Pharmacodynamics

## Table of contents

1. Introduction .....	5
2. Study Design .....	5
3. Aims and Objectives .....	5
4. Outcomes .....	6
5. Population to be analyzed.....	6
6. Analyses.....	6
7. Missing data .....	6

## 1. Introduction

The aim of this project is to assess doravirine concentrations in CSF and to estimate penetration into the CNS and to evaluate antiviral activity of a combination of Doravirine+FTC/TAF in CSF in people live with HIV.

This statistical analysis plan (SAP) will give more detailed descriptions of the endpoints in the study and the corresponding analyses.

## 2. Study Design

Study subjects will be selected from the routine control visits in the outpatient clinic of the HIV and STD Unit at the Bellvitge University Hospital. Asymptomatic, HIV-1 infected individuals and be on stable ART continuously or  $\geq 3$  consecutive months and Plasma HIV-1 RNA at  $< 40$  copies/mL for at least 3 months will be recruited.

This is Pilot study, Phase III, prospective, open label, single arm, single center. Study patients will receive one tablet of Doravirine 100 mg administered in combination with FTC and TAF (Descovy®).

Clinic visits will be performed at 3 time points: baseline, week 4 and week 8, only in w4 HIV-1 RNA concentration and Doravirine CSF concentration will be assessed.

### 2.1 Sample Size.

Fifteen individuals will be included in the study. This is a pilot study designed to obtain information about Doravirine concentrations and HIV viral suppression in CSF. The study design is similar to other studies evaluating ARV PK and PD in this compartment.

## 3. Aims and Objectives

This study will address these unknowns and provide additional evidence for the scientific rationale for the use of Doravirine in treatment and prevention of HIV associated neurocognitive disorders.

## 4. Outcomes

- Total and unbound Doravirine concentrations in cerebrospinal fluid in HIV-1 infected individual receiving ART with TAF/FTC+Doravirine.
- Total Doravirine concentrations in blood plasma.
- Doravirine CSF/plasma ratio.
- HIV-1 RNA in cerebrospinal fluid.
- HIV-1 RNA in blood plasma.

### 4.1 Safety outcomes

#### Adverse events

Adverse events are reported at each clinic visit.

#### Concomitant medications

Usage of medications during study period will be recorded.

## 5. Population to be analyzed

### Per Protocol (PP)

All randomised study subjects completing the whole study period (complete cases). For a specific analysis, study subjects with missing data on any of the variables in the model will be excluded from the analysis.

## 6. Analyses

All outcomes will be presented using descriptive statistics; normally distributed data by the mean and standard deviation (SD) and skewed distributions by the median and interquartile range (IQR). Binary and categorical variables will be presented using counts and percentages. SAS 9.4 will be used for all statistical analysis.

The primary analysis will determine the Doravirine concentration in CSF and blood plasma, and the HIV-1 viral load in CSF and blood plasma.

## 7. Missing data

Subjects with missing data will be excluded for the analysis.