| GlaxoSmithKline | **Statistical Analysis Plan** |
|---|---|
| **Detailed Title:** | A Phase I, open-label study to evaluate the long-term immunogenicity of the gp120-NefTat/AS01B vaccine administered in HIV-1 uninfected subjects |
| **eTrack study number and Abbreviated Title** | 201606 (PRO-HIV-013 EXT:002) |
| **Scope:** | All data pertaining to the above study. |
| **Date of Statistical Analysis Plan** | Final: 03 September 2018 |
| **Co-ordinating author:** | PPD (Lead statistician)<br>PPD (Lead statistician) |
| **Reviewed by:** | PPD (Clinical and Epidemiology Project Lead)PPD (Clinical Research Development Lead)PPD (Director, Biostat & Stat Prog)PPD (Lead Statistical Analyst), PPD (Lead Statistical Analyst)PPD (Scientific Writer), PPD (Lead Scientific Writer)PPD (Regulatory Affairs)PPD (SERM Physician)PPD (CLS Clinical Read-Out Team Leader)PPD (Public disclosure representative) |
| **Approved by:** | PPD (Clinical Research Development Lead)PPD (Lead Statistician)PPD (Lead Scientific Writer)PPD (Lead Statistical Analyst) |

*APP 9000058193 Statistical Analysis Plan Template ( Effective date: 14 April 2017)*

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# LIST OF ABBREVIATIONS

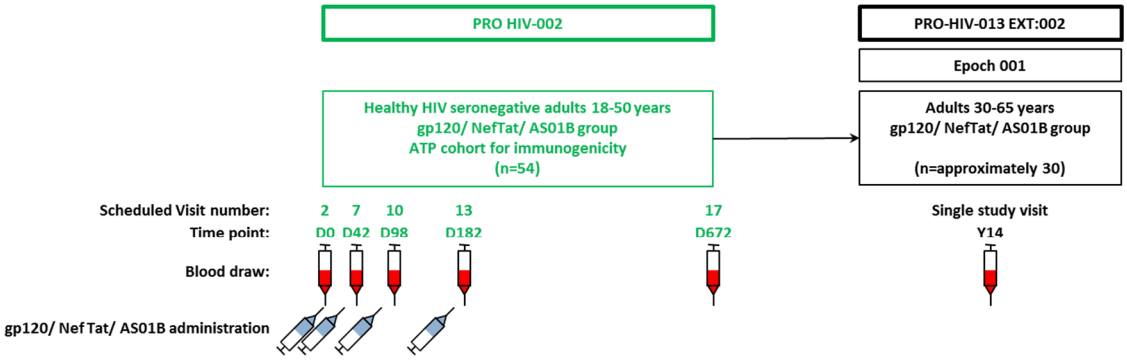
| | |
|---|---|
| AE | Adverse event |
| CI | Confidence Interval |
| CMI | cell-mediated immunity |
| CRF | Case Report Form |
| CTRS | Clinical Trial Registry Summary |
| eCRF | Electronic Case Report Form |
| EoS | End of study |
| ES | Exposed Set |
| GMT | Geometric mean antibody titer |
| GSK | GlaxoSmithKline |
| ICS | intracellular cytokine staining assays |
| LL | Lower Limit of the confidence interval |
| MedDRA | Medical Dictionary for Regulatory Activities |
| N.A. | Not Applicable |
| PBMC | Peripheral blood mononuclear cells |
| PCD | Primary completion Date |
| PD | Protocol Deviation |
| PP | Per Protocol |
| SAE | Serious adverse event |
| SAP | Statistical Analysis Plan |
| SD | Standard Deviation |
| SR | Study Report |
| TFL | Tables Figures and Listings |
| TOC | Table of Content |
| UL | Upper Limit of the confidence interval |

# 1. DOCUMENT HISTORY

| Date | Description | Protocol Version |
|---|---|---|
| 03 September 2018 | first version | Final: 12-JUL-2017 |

# 2. STUDY DESIGN

**Figure 1 Schematic representation of the study design**




D: Day, Y: Year

This study will only invite subjects from PRO HIV-002 Group 3 who received 4 doses of gp120/NefTat/ASO1B at PRO HIV-002 D0, D28, D84, and D168.

Y14 biological samples will be tested in addition to historical PRO-HIV-002 biological samples of selected time points

- Experimental design: Phase I, open-label, descriptive, mono-centric, and uncontrolled study with one single group. This study will consist of a single sample collection visit.
- Duration of the study: 1 day (single study visit) for each subject
  - Epoch 001: Prospective data collection at single study visit that will occur approximately 14 years post vaccination
- Primary completion Date (PCD): Year 14
- End of Study (EoS): Last reading results released for all subjects from Year 14 single study visit
- Study group and epoch foreseen in the study:

| Study Groups | Number of subjects | Age (Min - Max) | Epochs |
|---|---|---|---|
| | | | Epoch 001 |
| Group 1 | Approximately 30 | 30 years - 65 years | x |

- Control: uncontrolled
- Vaccination schedule: Not applicable
- Treatment allocation: Not applicable
- Blinding of study epochs:

| Study Epochs | Study Groups | Blinding |
|---|---|---|
| Epoch 001 | Group 1 | Open |

- Sampling schedule:
  - Blood samples will be collected from all subjects during the single study visit to assess humoral immunity and cell-mediated immunity (CMI).
  - Retrospective serum samples from subjects in study PRO HIV-002 at Day (D)0, D182, and D672 time points will be re-tested for humoral immunity using exploratory humoral assays.
  - Retrospective PBMC samples from subjects in study PRO HIV-002 at D0, D98, and D672 time points will be re-tested for CMI responses using intracellular cytokine staining (ICS) assays.
- Type of study: extension of protocol PRO HIV-002 (732461)
- Data collection: Electronic Case Report Form (eCRF)
- Safety monitoring: Not applicable

# 3. OBJECTIVES

## 3.1. Primary objective

- To assess the persistence of immune responses approximately 14 years after administration of the gp120-NefTat/AS01B vaccine candidate, in terms of anti-V1V2 binding antibody response by Binding Antibody Multiplex Assay (BAMA) versus historical time points in study PRO-HIV-002.

## 3.2. Secondary objectives

- To assess the persistence of immune responses approximately 14 years after administration of the gp120-NefTat/AS01B vaccine candidate, in terms of HIV-1 specific CD4+ T cell and CD8+ T cell responses versus historical time points in study PRO-HIV-002.
- To assess the persistence of immune responses approximately 14 years after administration of the gp120-NefTat/AS01B vaccine candidate, in terms of anti-gp120 antibody response by BAMA versus historical time points in study PRO-HIV-002.

Based on the outcome of the primary responses, other exploratory investigations may be performed on stored samples (sera and peripheral blood mononuclear cells [PBMCs]) to better characterize the effect of vaccination on other immunologic parameters, such as antibody function, memory B cells, or other read-outs that might be available at the time of the analysis.

# 4. ENDPOINTS

## 4.1. Primary endpoint

- Seropositivity status and anti-V1V2 (IgG, IgG1, IgG2, IgG3, and IgG4) binding antibody concentration as measured by BAMA at Y14, and at historical time points of study PRO HIV-002 (D0, D182, and D672).

Testing of samples for PRO HIV-002 time points will depend on availability of samples.

## 4.2. Secondary endpoints

- Magnitude, responder status, cytokine co-expression profile of HIV-1 specific CD4+ T cell and CD8+ T cell responses as assessed by ICS assay at Y14, and at historical time points of study PRO HIV-002 (D0, D98, and D672).
- Seropositivity status and anti-gp120 (IgG, IgG1, IgG2, IgG3, and IgG4) binding antibody concentration as measured by BAMA at Y14, and at historical time points of study PRO HIV-002 (D0, D182, and D672).

Testing of samples for PRO HIV-002 time points will depend on availability of samples.

Additional investigations, such as additional CMI parameters, memory B cell phenotypes and antibody function may be performed based on study results and availability of samples.

# 5. ANALYSIS SETS

## 5.1. Definition

Note that in order to align to ICH and CDISC terminology the Total Cohort has been renamed Exposed Set (ES).

### 5.1.1. All enrolled subjects

The “All enrolled subjects” set will include all enrolled subjects with recorded data.

### 5.1.2. Exposed Set

The ES will include all subjects who signed the informed consent and provided a blood sample.

### 5.1.3. Per-protocol cohort for analysis of immunogenicity

The PP cohort for immunogenicity analysis will include all subjects from the ES:

- who meet all eligibility criteria,
- who present a negative HIV-RNA test at Y14.

Subjects eliminated from the PP cohort for immunogenicity analysis will have their results reported as line listings.

## 5.2. Criteria for eliminating data from Analysis Sets

Elimination codes are used to identify subjects to be eliminated from analysis. Detail is provided below for each sets.

### 5.2.1. Elimination from Exposed Set (ES)

Code 900 (invalid informed consent or fraud data) and code 1020 (Blood sample for immunogenicity tests [humoral and CMI] not available) will be used for identifying subjects eliminated from ES.

### 5.2.2. Elimination from Per-protocol (PP) cohort for immunogenicity analysis

#### 5.2.2.1. Excluded subjects

A subject will be excluded from the PP cohort for immunogenicity analysis under the following conditions

| Code | Decode => Condition under which the code is used |
|---|---|
| 900 | Invalid informed consent or fraud data |
| 1020 | Blood samples for immunogenicity tests (humoral and CMI) not available |
| 2010 | Protocol violation (inclusion/exclusion criteria) => ineligible subject:<br>• A subject who has not received at least three doses of the gp120-NefTat/AS01B vaccine candidate in GSK Biologicals-sponsored PRO HIV-002 study<br>• Other considerations as stated in section 4.2 – 4.3 in the protocol |
| 2020 | Initially HIV status positive or unknown => HIV-RNA result at Y14 positive or missing |
| 2100 | Serological results not available post-vaccination => all tests are missing at Y14 |
| 2120 | Obvious incoherence or abnormality or error in data =>BS result available while BS not taken |

## 5.3. Important protocol deviation not leading to elimination from per-protocol cohort

NA

# 6. STATISTICAL ANALYSES

Note that standard data derivation rule and stat methods are described in Annex 1 and will not be repeated below.

## 6.1. Demography

### 6.1.1. Analysis of demographics/baseline characteristics planned in the protocol

For the ES and for the PP cohort for immunogenicity analysis, demographic data (age at vaccination in years, age at Y14 visit of this current LTFU study in years, gender and race) will be summarized using descriptive statistics:

- Frequency tables for gender and race.
- Mean, median, standard error for age.

### 6.1.2. Additional considerations

- Age at vaccination will be computed as the difference between the date of dose 1 administration in primary PRO HIV-002 study and the date of birth collected in that primary study (full date collected while only year of birth is collected in the current study). Age at Y14 visit in the study will be computed as the difference between the date of Y14 visit and the date of birth from study 002. The ages will be expressed in years.
- Summary statistics (Mean, median, standard error ) of height and weight at the time of dose 1 administration will also be tabulated
- For a given subject and a given demographic variable, missing measurements will not be replaced unless they can be found in the primary PRO HIV-002 study.

## 6.2. Exposure

### 6.2.1. Analysis of exposure planned in the protocol

Not applicable

### 6.2.2. Additional considerations

Not applicable

## 6.3. Efficacy/Effectiveness

### 6.3.1. Analysis of efficacy planned in the protocol

Not applicable

### 6.3.2. Additional considerations

Not applicable

## 6.4. Immunogenicity

### 6.4.1. Analysis of immunogenicity planned in the protocol

The primary analysis will be performed on the PP cohort for immunogenicity analysis and, if the percentage of vaccinated subjects with serological results excluded from the PP cohort for immunogenicity analysis is at least 20%, a second analysis will be performed on the Exposed Set.

**For the humoral immune response**

For anti-V1V2 and anti-gp120 (IgG, IgG1, IgG2, IgG3, and IgG4) antibody concentrations (by BAMA), at each time point [PRE(D0), PIV(D182), PIV(D672), PIV(Y14)] where such information is available:

- Seropositivity rates with 95%CIs will be tabulated.
- Geometric mean concentrations (GMCs) with 95% CIs will be tabulated and presented graphically.
- Geometric mean of ratios (GMR) of antibody concentrations at each post-vaccination time point [PIV(D182), PIV(D672), PIV(Y14)] over pre-vaccination [PRE(D0)] will be tabulated with 95% CI.
- Antibody concentrations post-vaccination will also be presented using reverse cumulative curves.

**For the cell-mediated immune response**

The following parameters will be summarised using descriptive statistics (N, GM, min, Q1, median, Q3, max) at each time point [PRE(D0), PIII(D98), PIV(D672), PIV(Y14)] where CMI results are available:

- Frequency of HIV-1 specific CD4+/CD8+ T-cells expressing **at least two markers** among CD40L, IL-2, TNF-α and IFN-γ as measured by ICS using PBMCs.
- Frequency of HIV-1 specific CD4+/CD8+ T-cells expressing **at least one marker** among CD40L, IL-2, TNF-α and IFN-γ as measured by ICS using PBMCs.

- Geometric mean ratios (GMR) of frequency of HIV-1 specific CD4+/CD8+ T-cells expressing **at least two markers** among CD40L, IL-2, TNF-α and IFN-γ at each post-vaccination time point [PIII(D98), PIV(D672), PIV(Y14)] over pre-vaccination (D0) will be tabulated with 95% CI.
- Vaccine response rates for HIV-1-specific CD4+ T-cells expressing **at least two markers** among CD40L, IL-2, TNF-α and IFN-γ.

Note: HIV-1-specific CD4+/CD8+ T-cells will be obtained by stimulating the PBMC samples with gp120.

### 6.4.2. Additional considerations

**For the humoral immune response**

- A seronegative subject will be defined as a subject whose antibody titer/concentration is below the cut-off value of the assay. A seropositive subject is a subject whose antibody titer/concentration is greater than or equal to the cut-off value of the assay.
- Anti-gp140 (IgG, IgG1, IgG2, IgG3, and IgG4) antibody concentrations will also be measured (by BAMA). At each time point [PRE(D0), PIV(D182), PIV(D672), PIV(Y14)] where such information is available:
  - Seropositivity rates with 95%CIs will be tabulated.
  - Geometric mean concentrations (GMCs) with 95% CIs will be tabulated and presented graphically.
- After the review of the data obtained from the primary and secondary objectives, the parties involved (GSK study team and Duke Human Vaccine Institute performing the lab testing) will provide a go/no-go decision on whether to evaluate the quality of anti-V1V2 and anti-gp120 antibody responses by biolayer interferometry (BLI) or BAMA avidity index. If applicable an additional analysis request will be developed to describe the statistical analyses of those endpoints.

- List of HIV strains that might be tested:

| **gp70 V1V2 Breadth Panel** | | |
|---|---|---|
| **Analyte Name** | **Clade** | **Country of Origin** |
| gp70-191084_B7 V1V2 | A | Uganda |
| gp70_B.CaseA_V1_V2 | B | USA |
| gp70-RHPA4259.7 V1V2 | B | USA |
| gp70-62357.14 V1V2 | B | USA |
| gp70-700010058 V1V2 | B | USA |
| gp70-TT31P.2F10.2792 V1V2 | B | Trinidad/Tobago |
| gp70-BF1266_431a_V1V2 | C | Malawi |
| gp70-7060101641 V1V2 | C | South Africa |
| gp70-96ZM651.02 V1v2 | C | Zambia |
| gp70-001428.2.42 V1V2 | C | India |
| gp70-CAP210.2.00.E8 V1V2 | C | South Africa |
| gp70-TV1.21 V1V2 | C | South Africa |
| gp70-Ce1086_B2 V1V2 | C | Malawi |
| gp70-CM244.ec1 V1V2 | CRF01_AE | Thailand |
| gp70-C2101.c01_V1V2 | CRF01_AE | Thailand |
| gp70-BJOX002000.03.2 V1V2 | CRF07-BC | China |
| **gp120 Breadth Panel** | | |
| **Analyte Name** | **Clade** | **Country of Origin** |
| 1086C_D7gp120.avi/293F | C | Malawi |
| 51802_D11gp120.avi/293F | A1 | Kenya |
| BORI_D11gp120.avi/293F | B | USA |
| TT31P.2792_D11gp120.avi/293F | B | Trinidad |
| B.6240_D11gp120/293F | B | USA |
| A244 D11gp120_avi | CRF01-AE | Thailand |
| 254008_D11gp120.avi/293F | CRF01-AE | Thailand |
| CNE20_D11gp120.avi/293F | CRF07-BC | China(Xinjiang) |
| BJOX002_D11gp120.avi/293F | CRF07-BC | China (Beijing) |
| **gp140 Breadth Panel** | | |
| **Analyte Name** | **Clade** | **Country of Origin** |
| 9004S.gp140C.avi | A1 | Uganda |
| RHPA4259_C7.gp140C.avi | B | USA |
| SC42261_gp140.avi/293F | B | Trinidad |
| WITO4160.gp140C.avi | B | USA |
| BF1266_gp140C.avi/293F | C | Malawi |
| 1086C gp140C_avi | C | Malawi |
| C.CH505TF_gp140/293F | C | Malawi |
| AE.01.con_env03 gp140CF_avi | Consensus AE | n/a |

**For the cell-mediated immune response**

- Raw data available in the database (events/per million of cells) will be divided by 10 000 in order to express the results in percentage (%) in the output tables/graphs.
- The frequency of antigen-specific CD4+ or CD8+ T-cells producing at least 2 cytokines for each individual subject is calculated as the difference between the frequency of CD4+ or CD8+ T-cells producing at least 2 cytokines, upon in vitro stimulation with the antigen (induction condition) minus the frequency of CD4+ or CD8+ T-cells producing at least 2 cytokines upon in vitro stimulation in medium only (background condition).

$$Freq^{2+}_{Induction} = \frac{n^{2+}_{Induction} - n^{2+}_{Backgroung}}{10\ 000}$$

$n^{2+}_{Induction}$ = Number of antigen – specific CD4+/CD8+ T-cells (per million of cells) expressing at least 2 cytokines

$n^{2+}_{Background}$ = Number of CD4+/CD8+ T-cells (per million of cells) expressing at least 2 cytokines in the medium only

Values less than or equal to zero will be set to 1 for the purpose of geometric mean and standard deviation calculation and graphical representation.

Similar calculations will be used to estimate the frequency of HIV-1 specific CD4+/CD8+ T-cells expressing at least one marker.

- Co-expression profile of the HIV-1 specific CD4+ T-cells of each combination of the 4 markers (CD40L, IL-2, TNF-a and IFN-g) will be presented graphically
- Vaccine response rates for HIV-1- specific CD4+ T-cells expressing **at least two markers** among CD40L, IL-2, TNF-α and IFN-γ with responders will be defined as subjects with:
  - a 2-fold increase as compared to the cut-off (=354, limit of quantification [LOQ] of the assay), for subjects with pre-vaccination frequency below the cut-off;
  - at least 2-fold increase as compared to pre-vaccination frequency, for subjects with pre-vaccination frequency above the cut-off.

  Other definitions of the CMI vaccine response might be explored during the current analysis or after.

## 6.5. Analysis of safety

### 6.5.1. Analysis of safety planned in the protocol

For the Exposed Set, a detailed description of SAEs considered by the investigator to be related to study participation or concurrent GSK medication/product will be provided.

### 6.5.2. Additional considerations

#### 6.5.2.1. Unsolicited Adverse Events

Only SAEs related to study participation or to a concurrent GSK medication/product will be collected and recorded from the time the subject consents to participate in the study (i.e., ICF signature) until the subject is discharged from the study. The original verbatim terms used by investigators to identify adverse events in the CRFs will be mapped to preferred terms using the MedDRA dictionary. A listing of the SAEs reported during the study will be provided. It will include all relevant collected information (intensity, duration,…) as well as the MedDRA terms.

#### 6.5.2.2. Concomitant Medication

Medications will be coded using the GSKDRUG dictionary. A listing of the concomitant medications reported during the study will be provided.

# 7. ANALYSIS INTERPRETATION

All analyses are descriptive. The use of these descriptive analyses should be limited to supportive analysis of confirmatory analyses or hypothesis generation.

# 8. CONDUCT OF ANALYSES

## 8.1. Sequence of analyses

| **Description** | **Analysis ID** | **Disclosure Purpose (CTRS=public posting, SR=study report, internal)** | **Dry run review needed (Yes/No)** | ***Study Headline Summary (SHS)*requiring expedited communication to upper management (Yes/No)** | **Reference for TFL** |
|---|---|---|---|---|---|
| Final | E1_01 | CTRS and Study Report | Yes | Yes | All tables from TFL |

## 8.2. Statistical considerations for interim analyses

Not applicable

# 9. CHANGES FROM PLANNED ANALYSES

None

# 10. LIST OF FINAL REPORT TABLES, LISTINGS AND FIGURES

The TFL TOC provides the list of tables/listings and figures needed for the study report. It also identifies the tables eligible for each analyses and their role (synopsis, in-text, post-text, SHS, CTRS,…). Note that all TFL aimed to be included as post-text are noted as post-text even if these are tabulation of individual data such as listing of SAE. The post-text material contains all source material for the study report and accordingly a post-text table may be redundant with an in-text table.

The following group name will be used in the TFLs, to be in line with the T-domains:

| Group order in tables | Group label in tables | Group definition for footnote | Pooled Groups label in tables | Pooled definition for footnote |
|---|---|---|---|---|
| 1 | Group 1 | gp120-NefTat/AS01B vaccine | NA | NA |

NA=Not applicable

# 11. ANNEX 1 STANDARD DATA DERIVATION RULE AND STATISTICAL METHODS

## 11.1. Statistical Method References

The exact two-sided 95% CIs for a proportion within a group will be the Clopper-Pearson exact CI [Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of binomial. *Biometrika*. 1934;26:404-413].

## 11.2. Standard data derivation

### 11.2.1. Date derivation

- SAS date derived from a character date: In case day is missing, 15 is used. In case day & month are missing, 30 June is used.
- Duration: Duration of an event is expressed in days. It is the number of days between the start & the stop dates + 1. Therefore duration is 1 day for an event starting & ending on the same day.

### 11.2.2. Demography

- Age: Age at the reference activity, computed as the number of units between the date of birth and the reference activity. Note that due to incomplete date, the derived age may be incorrect by 1 year. This may lead to apparent inconsistency between the derived age and the eligibility criteria.

### 11.2.3. Immunogenicity

- For a given subject and given immunogenicity measurement, missing or non-evaluable measurements will not be replaced. Therefore, an analysis will exclude subjects with missing or non-evaluable measurements.
- The Geometric Mean Concentrations/Titres (GMC/Ts) calculations are performed by taking the anti-log of the mean of the log titre transformations. Antibody titres below the cut-off of the assay will be given an arbitrary value of half the cut-off of the assay for the purpose of GMT calculation. The cut-off value will be defined by the laboratory before the analysis.
- A seronegative subject is a subject whose antibody titre is below the cut-off value of the assay. A seropositive subject is a subject whose antibody titre is greater than or equal to the cut-off value of the assay.
- All CI computed will be two-sided 95% CI.

### 11.2.4. Number of decimals displayed

The following decimal description from the decision rules will be used for the demography, immunogenicity.

| Display Table | Parameters | Number of decimal digits |
|---|---|---|
| Demographic characteristics | Mean, median age | 1 |
| Demographic characteristics | SD (age) | 1 |
| Immunogenicity | Ratio of GMT/C | 2 |
| All summaries | % of count, including LL & UL of CI | 1 |

# 12. ANNEX 2: STUDY SPECIFIC MOCK TFL

The following mock TFLs will be used.

The title and footnote are for illustration purpose and will be adapted to the study specificity as indicated in the TFL TOC.

Note that there may be few changes between the study specific SAP mock TFL and the final TFLs. These editorial/minor changes will not lead to a SAP amendment.

## Template 1 Study population (All enrolled subjects)

| | Group 1 |
|---|---|
| **Number of subjects** | |
| Planned, N | |
| Enrolled, N | |
| Included in the Exposed set, N | |
| Completed n (%) | |
| **Demographics** | |
| N (Exposed set) | |
| Females: Males | |
| Mean Age (at Y14 visit), years (SD) | |
| Median Age (at Y14 visit), years (minimum, maximum) | |
| <Most frequent category of race>, n (%) | |
| <Second most frequent category of race>, n (%) | |
| <Third most frequent category of race>, n (%) | |

Group 1 = gp120-NefTat/AS01B vaccine
SD - Standard Deviation

## Template 2 Number of subjects by country (All enrolled subjects)

| | Group 1 | |
|---|---|---|
| **Country** | n | % |
| | | |
| All | | |

Group 1 = gp120-NefTat/AS01B vaccine
n = number of subjects for a given country or for all country
All = sum of all subjects
% = n/All x 100

## Template 3 Summary of important protocol deviations leading to elimination from Exposed Set and Per Protocol Cohort for immunogenicity analysis (All enrolled subjects)

| | | | Group 1 N = | | |
|---|---|---|---|---|---|
| **Characteristics** | **Category** | **Subcategory** | **n*** | **n** | **%** |
| Important PD leading to elimination from Exposed Set | Any | Any | | | |
| | Invalid informed consent or fraud data (code 900) | <each subcategory> | | | |
| | Blood samples for immunogenicity tests (humoral and CMI) not available (code 1020) | <each subcategory> | | | |
| Important PD leading to elimination from Per Protocol Cohort for immunogenicity analysis | Any | Any | | | |
| | Protocol violation (inclusion/exclusion criteria) (code 2010) | <each subcategory> | | | |
| | Initially HIV status positive or unknown (code 2020) | <each subcategory> | | | |
| | Serological results not available post-vaccination (code 2100) | <each subcategory> | | | |
| | Obvious incoherence or abnormality or error in data (code 2120) | <each subcategory> | | | |

Group 1 = gp120-NefTat/AS01B vaccine
N = number of enrolled subjects
n* = number of important protocol deviations in the specified category and subcategory
n = number of subjects with at least one important protocol deviations in the specified category and subcategory
%= (n/N)*100
Note: A subject may have multiple important protocol deviations

## Template 4 Summary of demographic characteristics (Per Protocol Cohort for immunogenicity analysis)

| | Group 1 N=XXXX | |
|---|---|---|
| | **Value or n** | **%** |
| **Age in years at Dose 1 of HIV vaccine** | | |
| N with data | xxx | |
| Mean | xxx.x | |
| SD | xxx.x | |
| Median | xxx.x | |
| Minimum | xxx | |
| Maximum | xxx | |
| **Age in years at Y14 visit** | | |
| N with data | xxx | |
| Mean | xxx.x | |
| SD | xxx.x | |
| Median | xxx.x | |
| Minimum | xxx | |
| Maximum | xxx | |
| **Gender** | | |
| Female | xxx | xx.x |
| Male | xxx | xx.x |
| **Geographic Ancestry** | | |
| <EACH GEOGRAPHIC ANCESTRY> | xxx | xx.x |
| … | xxx | xx.x |
| **Height (cm) at Dose 1 of HIV vaccine** | | |
| N with data | xxx | |
| Mean | xxx.x | |
| SD | xxx.x | |
| Median | xxx.x | |
| Minimum | xxx | |
| Maximum | xxx | |
| **Weight (kg) at Dose 1 of HIV vaccine** | | |
| N with data | xxx | |
| Mean | xxx.x | |
| SD | xxx.x | |
| Median | xxx.x | |
| Minimum | xxx | |
| Maximum | xxx | |

Group 1 = gp120-NefTat/AS01B vaccine
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
N with data = number of subjects with documentation of the corresponding data
SD = standard deviation

## Template 5 Minimum and maximum activity dates (Exposed Set)

| Activity number | Activity Description | Minimum date | Maximum date |
|---|---|---|---|
| 10 | VISIT 1(Y14) | | |

## Template 6 Number of enrolled subjects by age category (All enrolled subjects)

| | Group 1 N=XXXX | |
|---|---|---|
| | Value or n | % |
| **Age category** | | |
| In utero | xxx | xx.x |
| Preterm new-born infants (gestational age < 37 wks) | xxx | xx.x |
| New-borns (0-27 days) | xxx | xx.x |
| Infants and toddlers (28 days-23 months) | xxx | xx.x |
| Children (2-11 years) | xxx | xx.x |
| Adolescents (12-17 years) | xxx | xx.x |
| Adults (18-64 years) | xxx | xx.x |
| From 65-84 years | xxx | xx.x |
| 85 years and over | xxx | xx.x |
| Missing | xxx | xx.x |

Group 1 = gp120-NefTat/AS01B vaccine
N = total number of subjects
n/% = number / percentage of subjects in a given category

**Template 7 Percentage of subjects with anti-gp120 IgG antibody titres previously measured in PRO-HIV-002 study greater than or equal to 1474 EL.U/ML and GMCs with 95% CI in subjects vaccinated in PRO-HIV-002 study with or without a Y14 follow-up visit (ATP cohort for immunogenicity analysis in PRO-HIV-002 study)**

| FU status | Timing | N | ≥ 1474 EL.U/ML | | | | GMC | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | n | % | 95% CI | | Value | 95% CI | |
| | | | | | LL | UL | | LL | UL |
| With Y14 FU | PRE(D0) | | | | | | | | |
| | PI(D28) | | | | | | | | |
| | PII(D42) | | | | | | | | |
| | PII(D84) | | | | | | | | |
| | PIII(D98) | | | | | | | | |
| | PIII(D168) | | | | | | | | |
| | PIV(D182) | | | | | | | | |
| | PIV(D196) | | | | | | | | |
| | PIV(D336) | | | | | | | | |
| | PIV(D504) | | | | | | | | |
| | PIV(D672) | | | | | | | | |
| Without Y14 FU | PRE(D0) | | | | | | | | |
| | PI(D28) | | | | | | | | |
| | PII(D42) | | | | | | | | |
| | PII(D84) | | | | | | | | |
| | PIII(D98) | | | | | | | | |
| | PIII(D168) | | | | | | | | |
| | PIV(D182) | | | | | | | | |
| | PIV(D196) | | | | | | | | |
| | PIV(D336) | | | | | | | | |
| | PIV(D504) | | | | | | | | |
| | PIV(D672) | | | | | | | | |

With Y14 FU = Subjects who received gp120-NefTat/AS01B vaccine in PRO-HIV-002 study and came back at the Y14 visit

Without Y14 FU = Subjects who received gp120-NefTat/AS01B vaccine in PRO-HIV-002 study and did not come back at the Y14 visit

GMT = geometric mean antibody titre calculated on all subjects

N = number of subjects with available results

n/% = number/percentage of subjects with titre within the specified range

95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit

PRE(D0) = Prevaccination, PI(D28) = Post Dose I (Day 28), PII(D42) = Post Dose II (Day 42), PII(D84) = Post Dose II (Month 3), PIII(D98) = Post Dose III (Day 98), PIII(D168) = Post Dose III (Month 6), PIV(D182) = Post Dose IV (Day 182), PIV(D196) = Post Dose IV (Month 7), PIV(D336) = Post Dose IV (Month 12), PIV(D504) = Post Dose IV (Month 18), PIV(D672) = Post Dose IV (Month 24)

## Template 8 Percentage of subjects with anti-V1V2 Total IgG antibody titres greater than or equal to the <*cut-off*> MFI and GMTs with 95% CI (Per Protocol Cohort for immunogenicity analysis)

| HIV Strain | Group | Timing | N | ≥ <*cut-off*> | | | | GMT | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | n | % | 95% CI | | Value | 95% CI | |
| | | | | | | LL | UL | | LL | UL |
| <*each HIV strain*> | Group 1 | PRE (D0) | | | | | | | | |
| | | PIV (D182) | | | | | | | | |
| | | PIV (D672) | | | | | | | | |
| | | PIV (Y14) | | | | | | | | |

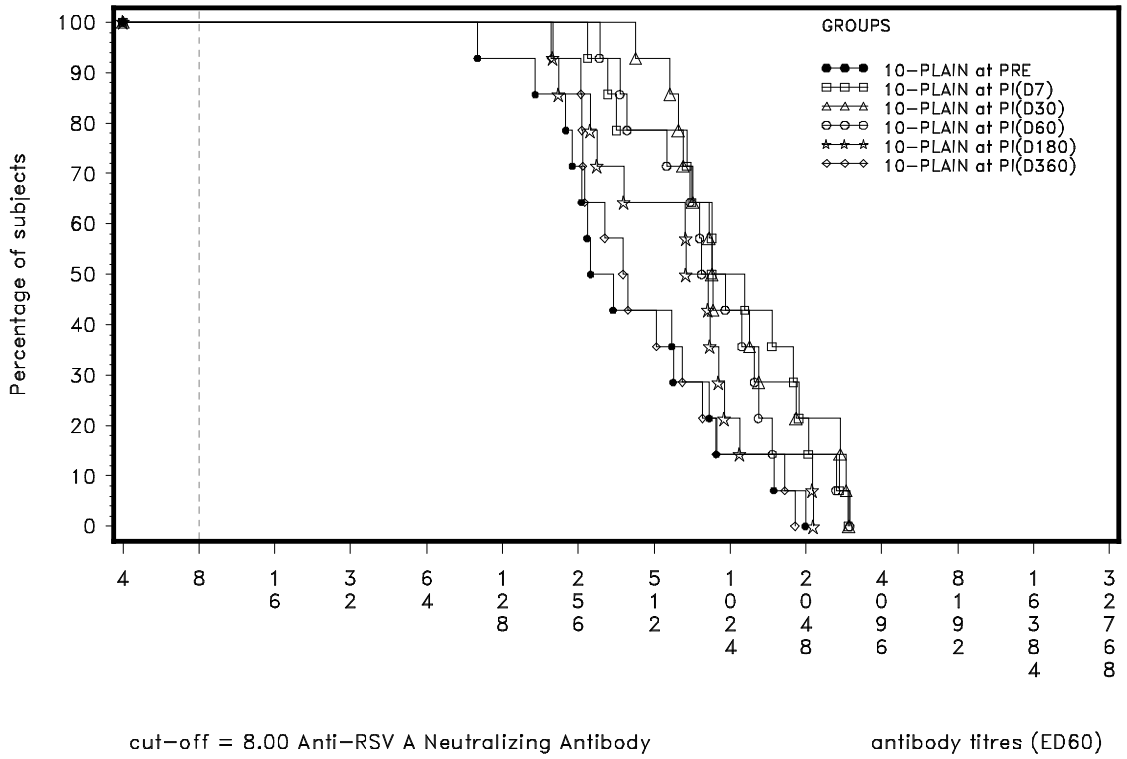
Group 1 = gp120-NefTat/AS01B vaccine
GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with titre within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE (D0) = Prevaccination
PIV (D182) = Post Dose IV (Day 182),
PIV (D672) = Post Dose IV (Month 24)
PIV (Y14) = Post Dose IV (Year 14)

## Template 9 Geometric mean of the individual ratio of anti-V1V2 Total IgG and IgG subclasses antibody titers at each post-vaccination timepoint compared to pre-vaccination with 95% CI (Per Protocol Cohort for immunogenicity analysis)

| | | | | | | | | GMT ratio | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 95% CI | |
| HIV Strain | Group | Test | N | Time point description | GMT | Time point description | GMT | Ratio order | Value | LL | UL |
| <each HIV strain> | Group 1 | Total IgG | | PIV (D182) | | PRE (D0) | | PIV (D182)/ PRE (D0) | | | |
| | | | | PIV (D672) | | PRE (D0) | | PIV (D672)/ PRE (D0) | | | |
| | | | | PIV (Y14) | | PRE (D0) | | PIV (Y14)/ PRE (D0) | | | |
| | | IgG1 | | PIV (D182) | | PRE (D0) | | PIV (D182)/ PRE (D0) | | | |
| | | | | PIV (D672) | | PRE (D0) | | PIV (D672)/ PRE (D0) | | | |
| | | | | PIV (Y14) | | PRE (D0) | | PIV (Y14)/ PRE (D0) | | | |
| | | IgG2 | | PIV (D182) | | PRE (D0) | | PIV (D182)/ PRE (D0) | | | |
| | | | | PIV (D672) | | PRE (D0) | | PIV (D672)/ PRE (D0) | | | |
| | | | | PIV (Y14) | | PRE (D0) | | PIV (Y14)/ PRE (D0) | | | |
| | | IgG3 | | PIV (D182) | | PRE (D0) | | PIV (D182)/ PRE (D0) | | | |
| | | | | PIV (D672) | | PRE (D0) | | PIV (D672)/ PRE (D0) | | | |
| | | | | PIV (Y14) | | PRE (D0) | | PIV (Y14)/ PRE (D0) | | | |
| | | IgG4 | | PIV (D182) | | PRE (D0) | | PIV (D182)/ PRE (D0) | | | |
| | | | | PIV (D672) | | PRE (D0) | | PIV (D672)/ PRE (D0) | | | |
| | | | | PIV (Y14) | | PRE (D0) | | PIV (Y14)/ PRE (D0) | | | |

Group 1 = gp120-NefTat/AS01B vaccine
GMT = geometric mean antibody titer
N = Number of subjects with available results at the two considered time points
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE (D0) = Prevaccination
PIV (D182) = Post Dose IV (Day 182),
PIV (D672) = Post Dose IV (Month 24)
PIV (Y14) = Post Dose IV (Year 14)

**Template 10 Reverse cumulative distribution curve of <HIV Strain> anti-V1V2 Total IgG antibody titres at post vaccination time-points (Per Protocol Cohort for immunogenicity analysis)**




Group 1 = gp120-NefTat/AS01B vaccine
PRE (D0) = Prevaccination
PIV (D182) = Post Dose IV (Day 182),
PIV (D672) = Post Dose IV (Month 24)
PIV (Y14) = Post Dose IV (Year 14)

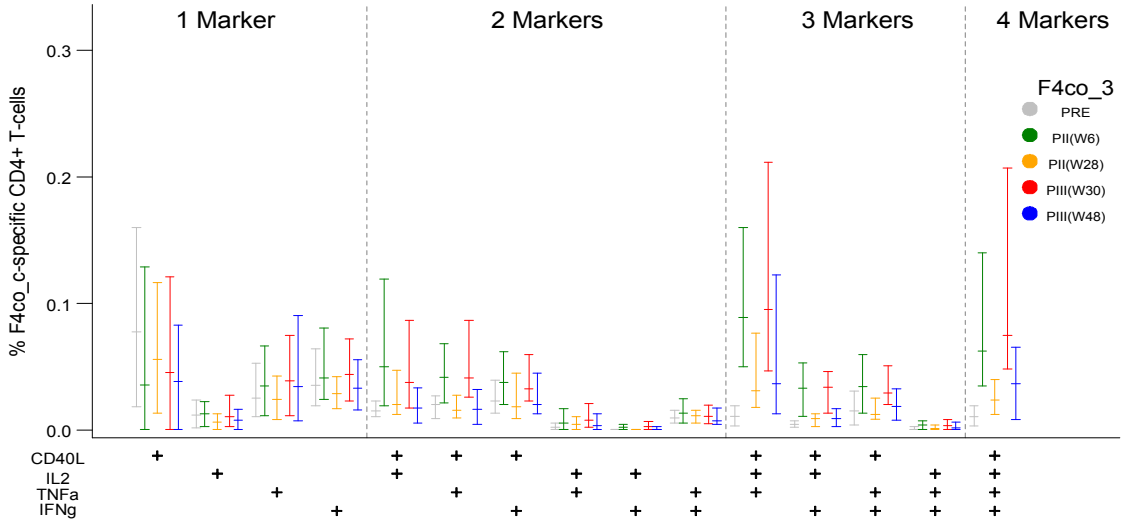
Note: This graph is provided as an example. A similar graph will be prepared for each assay/HIV straincomparing the values at PRE (D0), PIV(D182), PIV(D672) and PIV(Y14) (4 RCCs in each graph)

**Template 11 Descriptive statistics of the frequency of HIV-1 specific CD4+ T-cells expressing at least two markers at Day 0, Day 98, Month 24 and Year 14 (Per Protocol Cohort for immunogenicity analysis)**

| Immune marker | Group | Timing | N | Nmiss | Mean | SD | Min | Q1 | Median | Q3 | Max |
|---|---|---|---|---|---|---|---|---|---|---|---|
| CD4+ T-cells expressing at least two markers | Group 1 | PRE (D0) | | | | | | | | | |
| | | PIII (D98) | | | | | | | | | |
| | | PIV (D672) | | | | | | | | | |
| | | PIV (Y14) | | | | | | | | | |

Group 1 = gp120-NefTat/AS01B vaccine
N = number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1,Q3 = First and third quartiles
Min/Max = Minimum/Maximum
PRE (D0) = Prevaccination
PIII (D98) = Post Dose III (Day 98),
PIV (D672) = Post Dose IV (Month 24)
PIV (Y14) = Post Dose IV (Year 14)

**Template 12 Co-expression profile of the HIV-1 specific CD4+ T-cells of each combination of the 4 markers: CD40L, IL-2, TNF-a and IFN-g (Per Protocol Cohort for immunogenicity analysis)**




Note: This graph is given as an example. Template will be adapted to display Q1-Median-Q3 for each combination of markers (CD40L, IL-2, TNF-a and IFN-g →15 combinations) for each timepoint: PRE (D0), PIII (D98), PIV (D672) and PIV (Y14).

## Template 13 Geometric mean of the individual ratio of frequency of HIV-1 specific CD4+ T-cells expressing at least two markers at each post-vaccination timepoint compared to pre-vaccination with 95% CI (Per Protocol Cohort for immunogenicity analysis)

| | | GM of ratio | | | |
|---|---|---|---|---|---|
| | | | | 95% CI | |
| **Group** | **Ratio order** | **N** | **Value** | **LL** | **UL** |
| Group 1 | PIII (D98)/ PRE (D0) | | | | |
| | PIV (D672)/ PRE (D0) | | | | |
| | PIV (Y14)/ PRE (D0) | | | | |

Group 1 = gp120-NefTat/AS01B vaccine
GM = geometric mean
N = Number of subjects with available results at the two considered time points
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE (D0) = Pre-vaccination
PIII (D98) = Post Dose III (Day 98),
PIV (D672) = Post Dose IV (Month 24)
PIV (Y14) = Post Dose IV (Year 14)

## Template 14 Vaccine response rates for HIV-1- specific CD4+ T-cells expressing at least two markers among CD40L, IL-2, TNF-α and IFN-γ at Day 98, Day 672 and Year 14 (Per Protocol Cohort for immunogenicity analysis)

| | | | | Vaccine response | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | 95% CI | |
| **Test description** | **Group** | **Post-vaccination timing** | **Pre-vaccination category** | **N** | **n** | **%** | **LL** | **UL** |
| HIV-1- specific CD4+ T-cells expressing at least two markers | Group 1 | PIII (D98) | frequency <354 | | | | | |
| | | | frequency >=354 | | | | | |
| | | | Total | | | | | |
| | | PIV (D672) | frequency <354 | | | | | |
| | | | frequency >=354 | | | | | |
| | | | Total | | | | | |
| | | PIV (Y14) | frequency <354 | | | | | |
| | | | frequency >=354 | | | | | |
| | | | Total | | | | | |

Group 1 = gp120-NefTat/AS01B vaccine
Vaccine response defined as :
For subjects with pre-vaccination frequency < 354: post-vaccination frequency ≥ 708 (2-fold increase as compared to the cut-off)
For subjects with pre-vaccination frequency ≥ 354: post-vaccination frequency ≥ 2-fold increase as compared to pre-vaccination frequency
N = number of subjects with both pre- and post-vaccination results available
n/% = number/percentage of responders
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PIII (D98) = Post Dose III (Day 98),
PIV (D672) = Post Dose IV (Month 24)
PIV (Y14) = Post Dose IV (Year 14)

## Template 15 Listing of SAEs that are causally related to study participation or concurrent GSK medication/product (All enrolled subjects)

| Group | Sub. No. | Gender | Country | Race | Age at onset (Year) | Verbatim | Preferred Term |
|---|---|---|---|---|---|---|---|
| Group 1 | xxxxxx | zzz | zzz | Zzz | Xx | zzz | zzz |

| Group | Sub. No. | Primary System Organ Class | Medical visit type | Duration | Intensity | Causality | Outcome |
|---|---|---|---|---|---|---|---|
| Group 1 | xxxxxx | zzz | Zzz | x | zzz | zzz | zzz |

Group 1 = gp120-NefTat/AS01B vaccine

## Template 16 Number (%) of subjects with serious adverse events during the study period including number of events reported (All enrolled subjects)

| | | | Group 1 N=XXXX | | |
|---|---|---|---|---|---|
| Type of Event | Primary System Organ Class (CODE) | Preferred Term (CODE) | n* | n | % |
| SAE | | At least one symptom | xxx | xxx | xx.x |
| | <each SOC (SOC code)> | <each PT (PT code)> | xxx | xxx | xx.x |
| | … | … | xxx | xxx | xx.x |
| Related SAE | | At least one symptom | xxx | xxx | xx.x |
| | <each SOC (SOC code)> | <each PT (PT code)> | xxx | xxx | xx.x |
| | … | … | xxx | xxx | xx.x |
| Fatal SAE | | At least one symptom | xxx | xxx | xx.x |
| | <each SOC (SOC code)> | <each PT (PT code)> | xxx | xxx | xx.x |
| | … | … | xxx | xxx | xx.x |
| Related Fatal SAE | | At least one symptom | xxx | xxx | xx.x |
| | <each SOC (SOC code)> | <each PT (PT code)> | xxx | xxx | xx.x |
| | … | … | xxx | xxx | xx.x |

Group 1 = gp120-NefTat/AS01B vaccine
N = number of subjects with administered dose
n/% = number/percentage of subjects reporting the symptom at least once
n* = Number of events reported
Related = assessed by the investigator as related