TaiMed Biologics, Inc.

Protocol TMB-311
NCT02707861

A Phase 3, Multicenter, Expanded Access Study of Ibalizumab Plus an Optimized Background Regimen (OBR) in Treatment-Experienced Patients Infected With Multi-Drug Resistant (MDR) HIV-1

Statistical Analysis Plan

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Final Version 3

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1. Introduction

This document outlines the planned statistical analyses for data collected within the scope of the TaiMed ibalizumab protocol TMB-311, entitled "A Phase 3, Multicenter, Expanded Access Study of Ibalizumab Plus an Optimized Background Regimen (OBR) in Treatment-Experienced Patients Infected With Multi-Drug Resistant (MDR) HIV-1". This statistical analysis plan (SAP) applies to the most recent version of the study protocol (dated 11 December 2017) and will be updated as necessary if future protocol amendments warrant an update to the manner of analysis. This document was prepared in accordance with the International Conference on Harmonisation (ICH) Guideline E3: Structure and Content of Clinical Study Reports [1].

2. Study Overview

2.1. Study Design

This Phase 3 multicenter study will evaluate safety and tolerability of ibalizumab in HIV positive patients with MDR HIV infection. Eligible patients will include those currently receiving ibalizumab under a TaiMed-sponsored or Investigator-INDprotocol, and treatment-experienced patients with no history of ibalizumab treatment who are on a failing regimen, or who have failed and are off treatment. Patients will be enrolled in one of two Cohorts. Cohort 1 consists of patients currently receiving ibalizumab via other TaiMed-sponsored or Investigator-IND (compassionate use) protocols. These patients will continue their current dosage of ibalizumab (800 mg every 2 weeks or 2000 mg every 4 weeks). Cohort 2 consists of patients initiating ibalizumab. These patients will receive a 2000 mg loading dose at Baseline/Day 0 followed by 800 mg maintenance doses every 2 weeks.

For Cohort 1, screening procedures and Day 0 procedures are scheduled for the same day. Patients who qualify for entry into Cohort 1 of this study who are currently receiving 800 mg ibalizumab every 2 weeks will have physical and laboratory measures performed and receive the first on-study dose of ibalizumab at Screening/Day 0. These patients will return to the clinic on Day 14 and every 2 weeks thereafter through the remainder of participation in the study (up to 144 weeks) for study drug administration (800 mg) and effectiveness and safety evaluations. Patients who are discontinued or who withdraw from the study prematurely will be asked to return for an Early Withdrawal visit to have all assessments detailed in the Schedule of Events for that visit performed.

Patients who qualify for entry into Cohort 1 of this study who are currently receiving 2000 mg ibalizumab every 4 weeks will have physical and laboratory measures performed, and receive the first on-study dose of ibalizumab at Screening/Day 0. These patients will return to the clinic at Week 4 and every 4 weeks thereafter through the remainder of participation in the study (up to 144 weeks) for study drug administration (2000 mg) and effectiveness and safety evaluations. Patients who are discontinued or who withdraw from the study prematurely will be asked to return for

an Early Withdrawal visit to have all assessments detailed in the Schedule of Events for that visit performed.

For Cohort 2, patients will complete all screening procedures during the six weeks before Baseline/Day 0. Successful screening results will allow the patients to proceed to the Baseline/ Day 0 Visit, where they will initiate the selected OBR in addition to undergoing physical and laboratory measures. At this visit patients will also receive the loading dose of the study medication (2000 mg). Patients will return to the clinic on Day 7 for effectiveness and safety evaluations, and on Day 14 and every two weeks thereafter through the remainder of participation in the study (up to 144 weeks) for study drug administration (800 mg) and effectiveness and safety evaluations. Patients who are discontinued or who withdraw from the study prematurely will be asked to return for an Early Withdrawal visit to have all assessments detailed in the Schedule of Events for that visit performed.

All patients who complete Week 144 or end of study (EOS) visit will return for a follow-up visit at Week 150. Patients may be discontinued from the study at the patient's request or if the patient becomes pregnant, at investigator request, for a protocol violation, for treatment-related serious or intolerable adverse events (AEs), for toxicity (defined as two consecutive laboratory results, at least 14 days apart, with a CD4+ T-cell count below 200 cells/mm3 that also represents a 50% reduction from the Baseline CD4+ T-cell count), or for virologic failure. Virologic failure is defined as two consecutive measurements beginning at Week 24 or later if less than a 0.5 log10 decline from the Baseline viral load.

2.2. Study Objectives

2.2.1. Primary

The primary objectives of this study are to:

Cohort 1

- Continue to provide ibalizumab to patients currently receiving ibalizumab treatment under Investigator-sponsored INDs or TaiMed-sponsored protocols
- Demonstrate the safety and tolerability of ibalizumab in HIV positive patients with MDR HIV infection

Cohort 2

- Provide access to ibalizumab for qualifying MDR HIV-1 infected patients with limited treatment options
- Demonstrate the safety, efficacy, and tolerability of ibalizumab in HIV positive patients with MDR HIV infection

2.2.2. Secondary

The secondary objectives of this study are to:

- Demonstrate the antiviral activity of ibalizumab in HIV positive patients with MDR HIV infection
- Characterize HIV-1 sensitivity/susceptibility changes associated with protocol-defined virologic failure after ibalizumab administration in combination with OBR
- Determine the presence and significance of anti-ibalizumab antibodies associated with protocol-defined virologic failure after ibalizumab administration, if any (immunogenicity of ibalizumab)

2.3. Study Drug Dosage and Administration

The investigational product, ibalizumab, is a humanized IgG4 monoclonal antibody (MAb) administered via intravenous (IV) infusion. Patients will be enrolled in one of two Cohorts (Cohort 1 and Cohort 2). Cohort 1 patients will continue their current dosage of ibalizumab (800 mg every 2 weeks or 2000 mg every 4 weeks). Cohort 2 patients will receive a 2000 mg loading dose at Baseline/Day 0 followed by 800 mg maintenance doses every 2 weeks.

Patients receiving ibalizumab under Investigator-IND protocols, who will enroll into Cohort 1 of this study, are currently being supplied with ibalizumab vials containing a 1.2 mL injection volume and 180 mg ibalizumab per vial. For this study, these patients will continue receiving ibalizumab in this vial configuration until that supply of drug product is exhausted, at which time they will be switched to the drug product with a 1.33 mL injection volume and 200 mg ibalizumab per vial.

Patients receiving ibalizumab in study TMB-301, who will enroll into Cohort 1 of this study, and patients initiating ibalizumab in Cohort 2 will receive only vials with a 1.33 mL injection volume and 200 mg ibalizumab per vial. During this study, it will be very important to ensure that all drug supplies are clearly labeled and segregated by vial configuration to prevent confusion.

In addition to the study drug, all patients will receive an OBR, which is a standard–of-care regimen selected by the investigator based upon treatment history and the results of recent viral resistance testing. For patients enrolling into Cohort 2, previous resistance testing done within 6 months prior to Screening must demonstrate that the patient's viral isolate is sensitive/susceptible to a minimum of one of the agents selected for the OBR. The patient must be willing and able to take at least one of the agents to which their virus is sensitive/susceptible as part of the OBR.

2.4. Procedures

2.4.1. Patient Identification

Once consent is obtained and study eligibility has been determined, a patient will be enrolled into the study and will be assigned a Participant Identification (PID) number. The 5-digit PID number will consist of a 2-digit site number and a 3-digit sequential patient number. If a patient in Cohort 2 is a screen failure, the PID number will not be reassigned.

2.4.2. Randomization

This will be an open-label, non-randomized study.

2.4.3. Blinding/Unblinding

There will be no blinding/unblinding considerations for this open-label, non-randomized study.

2.4.4. Replacement

Patients who withdraw or otherwise discontinue the study prematurely will not be replaced.

3. Statistical Analysis Considerations

3.1. Sample Size

Anticipated enrollment is approximately 100 patients from approximately 50 sites in North America; however, the numbers of participating patients and sites will not be limited and may exceed 100 patients.

3.2. Analysis Populations

3.2.1. Intent-to-Treat (ITT) Population

The ITT population is defined as all patients enrolled into the TMB-311 study. The ITT Analysis Population will be used for the patient disposition, demographic and physical characteristics, and efficacy analyses.

If there are ITT patients who do not receive at least one complete dose of study drug, then a modified ITT (mITT) Analysis Population will be used for a supportive effectiveness analysis.

3.2.2. Safety (SAF) Population

All patients who receive at least one partial dose of study drug will be included in the SAF Population. Patients will be analyzed according to the treatment they actually received. The SAF Population will be used for the safety analyses.

3.3. Data Handling

3.3.1. Measurement Times

The nominal visit time point entered on the electronic case report forms (eCRFs) will be used. Patients are asked to adhere to the following visit schedule (with windows in parentheses):

- For Cohort 1 patients, Screening and Day 0 (first on-study administration of ibalizumab) are scheduled for the same day.
- For Cohort 2 patients, the Screening will occur 1 to 6 weeks prior to Day 0.
- For Cohort 2, Day 7 (+/- 1 day) serves as the time point at which the antiviral activity of ibalizumab will be assessed to address the primary effectiveness objective.
- For all Cohorts, Day 14 (+/- 1 day) and Week 4 (+/- 2 days) through Week 144/EOS Visit (+/- 2 days) from the Day 0 date (Visit Week will depend on the dosing schedule per Cohort 1 or 2; please refer to the Schedule of Visits Tables 3.1-3.6 in the study protocol).

3.3.2. Clinical Laboratory Data Handling Conventions

If a patient has multiple results in the clinical laboratory data for the Screening visit, only the last result prior to the first dose of study drug will be included in the analysis. If a patient has multiple results (retests) for subsequent visits, the retest results will only be included in the analysis if the patient does not have a value recorded for the original assessment at the given visit.

3.3.3. Baseline Values

For patients in Cohort 1 who were enrolled in the TMB-202 or TMB-301 studies, Baseline values for TMB-311 are defined as the values recorded for the Baseline visit in the previous study. For patients in Cohort 1 who were not enrolled in the TMB-202 or TMB-301 studies as well as for patients in Cohort 2, Baseline is defined as the last assessment prior to their first dose of study drug on the TMB-311 Day 0 visit.

3.3.4. Missing Data Conventions

Cohort 2 patients with missing data at Day 0 will use the Screening visit value as their Day 0 result. Similarly, patients with missing data at Screening will use the Day 0 visit value as their Screening result. No Screening or Day 0 data will be imputed for Cohort 1 patients.

Unless otherwise specified, missing data for subsequent visits will be considered missing at random and will not be imputed. If necessary, imputation of partial dates may be performed during the data analysis and will be documented (e.g., missing month=July; missing day=15).

The **Missing Equals Failure (MEF)** imputation technique will be applied to the viral load measures ($\log_{10}$ copies/mL and copies/mL) only. If a viral load measurement is missing at any scheduled visit, the value will be replaced with the baseline viral load measurement. Also, all visits after a confirmed virologic failure will be imputed as failures (replaced with the baseline measurement) for all study visits even if the patient discontinued early.

The Last Observation Carried Forward (LOCF) imputation technique will be applied to the CD4+ T-Cell Counts ($cells/mm^3$) only. If a CD4+ T-Cell Count is missing at any scheduled visit, the value will be replaced with the most recent previous non-missing value.

3.4. Statistical Methods

3.4.1. General Overview and Plan of Analysis

The data collected are intended primarily for clinical review and interpretation. The analysis of study data will be primarily descriptive, with emphasis on tabular and graphical displays. Descriptive statistics will be used to guide decisions as to the clinical relevance of findings. Unless otherwise stated, p-values will be determined only if they appear to be warranted from the summary statistics.

All results will be displayed in the following patient groupings:

1) Cohort 1 TMB-301 rollover patients;
2) Cohort 1 TMB-202 rollover patients in the 800mg dose group;
3) Cohort 1 TMB-202 rollover patients in the 2000mg dose group;
4) Cohort 2 patients;
5) Total – includes all patients from 1-4.

The two patients who were formerly enrolled in the investigator-sponsored IND (compassionate use) studies will be included in listings only.

For continuous data, descriptive statistics will be presented as number of patients (n), mean, standard deviation, median, minimum and maximum. For categorical data, the frequency and percentage of patients in each category will be presented. Percentages will be based on non-missing data unless otherwise specified.

Data will be described and analyzed using the SAS System Version 9 (SAS Institute Inc., Cary, NC, SAS System). Individual patient data will be presented in patient data listings.

3.4.2. Hypothesis Testing

This study is designed to evaluate the safety and efficacy of ibalizumab in treatment-experienced patients infected with multi-drug resistant HIV-1. No formal statistical hypothesis testing is planned for the study. [Note: Hypothesis testing may be performed as additional/exploratory analyses (see Section 4.6)].

4. Statistical Analysis

4.1. Patient Disposition

The number of patients in the ITT and SAF Populations will be tabulated.

Study completion data will be summarized for all enrolled patients. The number and percent of patients who complete treatment; discontinue study medication prematurely; or discontinue the study prematurely will be tabulated. The primary reason for premature discontinuation of study medication and/or discontinuation from study participation will be tabulated. Any additional reason(s) for premature discontinuation of study medication will also be tabulated. A listing of all enrolled patients will be provided.

4.2. Demographic and Physical Characteristics

Summary statistics will be presented for demographic and other Baseline characteristics for the ITT Population. Tabulations for age, sex, ethnicity (Hispanic/Latino, Neither Hispanic nor Latino, Unknown), and race (American Indian/Alaska Native, Asian, Black/African American, Native Hawaiian/Other Pacific Islander, White, Unknown, or Other) will be presented. Age (years) will be calculated as the integer part of [(date of screening - date of birth + 1)/365.25]. Baseline physical characteristics, such as height (cm) and weight (kg), will also be summarized.

A listing of demographic and Baseline characteristics will be presented, as well as a listing of medical history.

4.3. Analysis of Safety and Tolerability

Safety and tolerability will be assessed by both clinical and laboratory examinations. Summary statistics will be presented by AEs; hematology and chemistry; vital signs, changes from Baseline, and clinically significant findings; and abnormal physical examination findings in the SAF Population. Clinical laboratory values outside the normal ranges will be flagged in patient data listings. Non-numeric data will be presented in patient data listings, but will not be tabulated.

4.3.1. Extent of Study Drug Exposure

Summary statistics will be presented for the cumulative dose (mg) and duration of treatment received by the patients in the SAF Population. Duration of treatment will be represented as number of days from first dose of study drug. For Cohort 1 patients, the date of their first dose of study drug in the previous study will be used. Corresponding listings will also be generated for study drug administration and OBR adherence.

4.3.2. AEs

All AEs will be coded, using MedDRA dictionary version 17.0. The use of another version will not be considered a violation of the SAP, nor require an amendment to the plan. All summary tables will be based on coded preferred terms (PTs), instead of verbatim terms. The only exception being all rashes are combined into one category named RASHES. The categories and definitions of severity and causal relationship for all AEs, including the criteria for which an AE is to be classified as "serious," are as described in the protocol (Section 8).

A treatment-emergent AE (TEAE) is defined as any event not present before exposure to study drug or any event already present that worsens in either intensity or frequency following exposure to study drug. AEs with missing start dates, but with stop dates either overlapping into the dosing period or missing, will be considered TEAEs. A TEAE with missing severity or relationship will be considered severe or related, respectively.

The overall incidence of TEAEs will be summarized for all patients in the SAF Population. The number and percentage of patients having the following will be tabulated:

- TEAE
- Serious TEAE
- TEAE leading to discontinuation
- TEAE with outcome of death
- TEAE related to study drug (definitely, probably, or possibly)

- Severe TEAE
- Class C TEAE per the Centers for Disease Control and Prevention (CDC) Classification System for HIV Infection

The overall incidence of TEAEs will also be summarized by System Organ Class (SOC), and by SOC and PT. The number and percentage of patients reporting an event, as well as the number of events reported by the patients will be tabulated. The incidence of serious TEAEs and TEAEs leading to study discontinuation (if any) will be summarized in the same manner. If there are multiple occurrences of the same TEAE within any SOC or PT for the same patient, only the first occurrence will be counted.

The incidence of TEAEs by severity/grade (mild, moderate, severe, or potentially life-threatening) and by relationship to study drug (unrelated, possibly related, probably related, and definitely related), and the incidence of SAEs by relationship to study drug, will also be summarized.

All other AEs will be classified as non-TEAEs and identified in listings only. Serious TEAEs, TEAEs leading to study discontinuation, and TEAEs with an outcome of death will be presented in separate listings, if needed.

These tables will be repeated for patients receiving an investigational agent [Fostemsavir (BMS-068), Cabotegravir, or PRO140] as a concomitant medication versus those patients who did not receive an investigational agent.

4.3.3. Clinical Laboratory Parameters

Summary statistics will be presented for laboratory measurements (hematology and chemistry) overall for all patients in the SAF Population. Urinalysis results will be presented in a listing. The following analytes will be tabulated/listed:

- **Hematology**: complete white blood cell count with differential, hemoglobin, hematocrit, and platelets.
- **Serum chemistry profile**: albumin, alkaline phosphatase, alanine aminotransferase (ALT), amylase, aspartate aminotransferase (AST), blood urea nitrogen, calcium, chloride, creatine phosphokinase, creatinine, direct bilirubin, gamma glutamyl transferase, glucose, lactate dehydrogenase, lipase, lipid profile (total cholesterol, high-density lipoprotein, low-density lipoprotein, and triglycerides), magnesium, phosphorus, potassium, sodium, total bilirubin, total protein, and uric acid. In addition, eGFR will be presented using the following formula: $eGFR = 1.86 \times [Creatinine/88.4]^{-1.154} \times [Age]^{-0.203} \times [0.742 \text{ if female}] \times [1.210 \text{ if Black}]$.

Urinalysis results will be presented in a data listing and will include results from microscopic testing only. Pregnancy test, Serum Follicle-Stimulating Hormone (FSH) test, Hepatitis Serology, C-reactive Protein, and Viral Resistance Testing will also be presented in a data listing only.

Normal ranges for the laboratory parameters will be provided by the laboratory that performed the assessments. All normal ranges will be standardized and results will be reported in standard units. The tables will include summary statistics for the Baseline assessments and the changes from Baseline to each subsequent time point of measurement. A listing of patients with abnormal (i.e., outside normal range) laboratory assessments will also be presented.

Potentially Clinically Significant (PCS) criteria may be applied to laboratory parameters as clinically indicated, and if applied, will be summarized as described above. PCS is defined as a laboratory value that is lower or higher than a laboratory's normal range limits.

Note: Electronic clinical laboratory data will be received at Westat. Data reconciliation will be performed to resolve any discrepancies with the Oracle database. Details of data receipt will be described in the Data Receipt Plan.

4.3.4. Vital Signs

Summary statistics for vital signs and weight will be presented overall for all patients in the SAF Population for all scheduled visits. Actual values and changes from Baseline will be summarized for all visits where collected.

4.3.5. Physical Examination Findings

Physical examination findings at each scheduled visit will be summarized overall for all patients in the SAF Population. The number and percent of patients with abnormal findings by body system will be tabulated.

4.3.6. Medications

All prescriptions or over-the-counter medications continued at the start of the trial or started during the trial, and different from the study drug will be recorded. All of these medications will be coded, using WHO Drug Dictionary (March 2014). The use of another version will not be considered a violation of the SAP, nor require an amendment to the plan. Both the coded terms and verbatim terms will be presented in data listings for:

- Concomitant procedures (procedures are not coded)

- Previous and Concomitant medications
- OBR medications
- ART medications

4.4. Efficacy

As described in section 3.3.3 of this document, the MEF technique will be applied to the efficacy analyses with regard to imputing missing viral load results as applicable. Note: Prior to calculating change from Baseline in viral load, the log10 value of each measurement will be calculated and will be rounded to one decimal point.

4.5.1. Primary Efficacy Endpoint

Per the protocol, the primary efficacy endpoint for the Cohort 2 patients is defined as the proportion of patients achieving a ≥ 0.5 $\log_{10}$ decrease in viral load from Baseline at Day 7 on study drug. A 95% confidence interval around the observed rate will be presented. This endpoint will be presented for all Cohort 2 patients, as well as stratified by:

1) Sex (Male vs Female)
2) Age (<50 vs $\geq$ 50)
3) Race (Caucasian, Asian, and Other)

The primary efficacy endpoint will not be analyzed for the TMB-301 and TMB-202 rollover patients, as they did not have dosing or viral load measurements at Day 7 on study drug in the TMB-311 study.

4.5.2. Secondary Efficacy Endpoints

Although the TMB-311 protocol indicates the secondary efficacy endpoints would only be performed for the Cohort 2 patients, for completeness all secondary efficacy endpoints will be assessed for all patients in all cohorts at applicable visits.

4.5.2.1 HIV-1 RNA levels (copies/mL)

The frequency and proportion of patients achieving RNA levels < 50 copies/mL and < 400 copies/mL along with 95% confidence intervals around the observed rate will be presented at all key visits [Day 7 (Cohort 2 only), and Weeks 24, 48, 72, 96, 120, and 144/EOS] where assessed.

Summary statistics for the actual and change from Baseline of RNA levels will be presented for at all visits where assessed.

4.5.2.2 Viral Load (log_{10} copies/mL)

The frequency and proportion of patients achieving a ≥ 0.5 log_{10} and ≥ 1.0 log_{10} decrease from Baseline in viral load along with 95% confidence intervals will be performed at all key visits [Day 7 (Cohort 2 only), and Weeks 24, 48, 72, 96, 120, and 144/EOS] where assessed. The mean change from Baseline at all assessment time points will be presented.

These tables will be repeated for patients receiving an investigational agent [Fostemsavir (BMS-068), Cabotegravir, or PRO140] as a concomitant medication versus those patients who did not receive an investigational agent.

4.5.2.3 Virologic Outcome

<u>Snapshot Approach</u>
Virologic outcome will be assigned for each patient at each key visit after Week 12 [Weeks 24, 48, 72, 96, 120, and 144/EOS], per the snapshot approach, using the following standard categories:

1=Virologic success (≥0.5 log10 decline from Baseline in viral load)
2a=(<0.5 log_{10} copies/mL drop from Baseline in viral load)
2b=Discontinued efficacy portion of study because of virologic failure (may still continue safety)
2c=Discontinued because of other reasons and the drop from baseline in viral load at the time of discontinuation was <0.5 log_{10} copies/mL
2d=OBR changed
3a=Discontinued because of AE or death
3b=Discontinued because of other reasons and the drop from baseline in viral load at the time of discontinuation was >=0.5 log_{10} copies/mL
3c=Missing data during the window but on study

<u>Other Virologic Outcomes</u>
Other virologic outcomes will also be defined as follows:

Failure to achieve/maintain response:
Patient does not have ≥0.5 log_{10} decline from baseline (BL) by Week 12 on study drug OR patient has a 0.5 log_{10} decline from BL prior to Week 12 but fails to maintain the 0.5 log_{10} decline from BL and does not have a ≥1 log10 increase from nadir on any two consecutive scheduled efficacy assessments after achieving the ≥0.5 log_{10} decline from BL.

Rebound:
Patient has a ≥0.5 log10 decline from BL by Week 12 but viral load remains >=50 copies (not suppressed), followed by ≥1 log_{10} increase from nadir at two consecutive scheduled visits any time after achieving the ≥0.5 log_{10} decline from BL.

Breakthrough:
Patient has suppressed viral load (< 50 copies) at any time after primary endpoint followed by ≥200 copies at two consecutive scheduled efficacy assessments.

Suboptimal Response:
Patient has a ≥0.5 log_{10} decline but does not suppress (<50 copies) at any time after primary endpoint and does not have a ≥1 log_{10} increase from nadir on any two consecutive scheduled efficacy assessments after achieving the ≥0.5 log_{10} decline from BL.

Virologic Suppression:
Patient has a ≥0.5 log_{10} decline and does suppress (<50 copies) at any time after primary endpoint and does not have a ≥1 log_{10} increase from nadir on any two consecutive scheduled efficacy assessments after achieving the ≥0.5 log_{10} decline from BL.

A table summarizing virologic outcome at the each key visit after Week 12 [Weeks 24, 48, 72, 96, 120, and 144/EOS] according to the above categories will be provided. A listing indicating the virologic outcome for each patient will be included.

4.5.2.4 CD4+ T-Cell Counts

Summary statistics will be presented for CD4+ T-cell count and change from Baseline in CD4+ T-cell count at the each key visit after Week 12 [Weeks 24, 48, 72, 96, 120, and 144/EOS].

CD4+ T-Cell Counts for all patients at all assessed visits will also be presented in a data listing. The listing will include a column indicating whether or not the patient met the definition of toxicity (2 consecutive laboratory results, at least 14 days apart, with a CD4+ T-cell count below

200 cells/mm^3 that also represents a 50% reduction from the Baseline CD4+ T-cell count).

4.5.3. Graphical Displays

In addition to the tables and listings described above, the following graphical displays of efficacy endpoints will also be included:

- Proportion of patients achieving a ≥ 0.5 $\log_{10}$ decrease from Baseline in viral load at all scheduled visits;
- Proportion of patients achieving a ≥ 1.0 $\log_{10}$ decrease from Baseline in viral load at all scheduled visits;
- Proportion of patients achieving RNA levels < 50 copies/mL at all scheduled visits;
- Proportion of patients achieving RNA levels < 400 copies/mL at each study visit;
- Mean (+/- SE) RNA levels (copies/mL) at all scheduled visits;
- Mean (+/- SE) change from Baseline in RNA levels (copies/mL) at all scheduled visits;
- Mean (+/- SE) CD4+ cell count (cells/mm^3) at all scheduled visits;
- Mean (+/- SE) change from Baseline in CD4+ T-cell count (cells/mm^3) at all scheduled visits.

4.6. Exploratory/Other Analyses

Summaries of viral resistance test results, immunogenicity results, and other virology results will be presented, prepared by TaiMed.

5. References

1. Center for Drug Evaluation and Research, Food and Drug Administration, U.S. Department of Health and Human Services. (2013, June). *Guidance for industry: Human immunodeficiency virus-1 infection: Developing antiretroviral drugs for treatment*. Retrieved from http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/guidances/ucm355239.htm.

2. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. (1995, November 30). *ICH E3: Structure and content of clinical study reports.* Retrieved from http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html.

6. Proposed Summary Listings and Tables

ATTACHMENT
TaiMed Biologics, Inc.

Protocol TMB-311

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an Optimized Background Regimen (OBR) in Treatment-Experienced Patients Infected With Multi-Drug Resistant (MDR) HIV-1

Mock Statistical Listings

November 9, 2017
Final Version 2

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Notes Applicable to All Listings

General Programming Notes:

1. There are a few listings that might fit as they are or might have to be split once we see the output with actual data.
2. All listings should start with and be sorted by Patient ID (concatenation of site number and patient number)and then visit date as appropriate.
3. If columns with specific text should be widened due to the amount of text, it is up to the programmer's discretion. However, please keep to the industry standard margin of 1 inch on bottom and sides and 1.25 inches on the top. Font is Courier New 8 point.
4. For all dates used, character format dates to capture partial dates. Use dashes where a month or day is missing. If entire date is missing just leave blank. i.e., – JAN2011 or 01—2011.
5. If a programming note appears on the mock listing indicating that the footnote should appear only on the first page, this means the first page of output contains all footnotes and ONLY footnotes. All subsequent pages contain data with one footnote that says "Refer to page 1 for footnotes".
6. Some of the mock tables display numbers rather than x's. The numbers are meaningless and are for example only. Where visit names are displayed in tables, these are examples as well. Correct visit names for the TMB-311 study should be displayed in the actual output.
7. Each listing should include all applicable data, even if only a subset of the full set of treatment groups is displayed in the mocks. And unlike the tables and graphs, the listings should also include the 2 PI-IND rollover patients.
8. Sort each listing by Treatment and then Patient ID where applicable.

Listing 16.2.1.1

Patient Disposition

Treatment	Patient ID	Screened	ITT Population [1]	SAF Population [2]
C1:301/800mg	311-XX-XXX	YES	YES	YES
C1:202/800mg	311-XX-XXX	YES	YES	YES
C1:202/2000mg	311-XX-XXX	YES	YES	YES
C2:800mg	311-XX-XXX	YES	YES	YES

[1]Intent-to-Treat (ITT) Population consists of all patients enrolled into the study.
[2]Safety (SAF) Population consists of patients receiving at least one partial dose of study drug.

Programming note: Add the mITT population if analyst decides it is needed later.

Listing 16.2.1.2
Study Discontinuation

Treatment	Patient ID	Study Discontinuation Date	Date of Last Treatment	Completed Study Treatment	Reason for Treatment Discontinuation	Completed Study	Reason for Study Discontinuation	Death Date
C2:800mg	311-XX-XXX	20161101	20161004	NO	CONSENT WITHDRAWN OR VOLUNTARY WITHDRAWAL	NO	CONSENT WITHDRAWN OR VOLUNTARY WITHDRAWAL	
C2:800mg	311-XX-XXX	20160920	20160823	NO	ADVERSE EVENT-SEVERE DRUG RASH AND FEVER OF 1 WEEK.	NO	ADVERSE EVENT-SEVERE DRUG RASH AND FEVER OF 1 WEEK.	
C1:202/2000mg	311-XX-XXX	20160517	20160421	NO	INVESTIGATORS DECISION-INVESTIGATORS DECISION	NO	INVESTIGATORS DECISION-LACK OF CLINICAL PROGRESSION	
C2:800mg	311-XX-XXX	20161101	20160810	NO	INVESTIGATORS DECISION-SUBJECT NEVER CAME TO FOLOOW UP VISIT BECAUSE NEVER RECOVERED FROM PCP	NO	INVESTIGATORS DECISION-SUBJECT NEVER CAME TO F/UP VISIT BECAUSE NEVER RECOVERED FROM PNEUMONIA	
C1:301/800mg	311-XX-XXX	20160728	20160728	NO	CONSENT WITHDRAWN OR VOLUNTARY WITHDRAWAL	NO	CONSENT WITHDRAWN OR VOLUNTARY WITHDRAWAL	
C1:202/800mg	311-XX-XXX	20161004	20160720	NO	ADVERSE EVENT-SUBJECT DECEASED AS RESULT OF TRAUMA DURING ACCIDENTAL FALL	NO	ADVERSE EVENT-SUBJECT DECEASED AS RESULT OF TRAUMA DURING ACCIDENTAL FALL	20161001

Listing 16.2.2.1
Text of Inclusion and Exclusion

Criterion Type	Criterion Number	Criterion Text
Inclusion	1	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
	2	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
	…	
	9	
Exclusion	1	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx
	2	
	…	
	12	

Listing 16.2.2.2
Protocol Violations

Treatment	Patient ID	Visit	Protocol Violation Code	Details of Violation	Approval Obtained	Date of Approval
C1:202/800mg	311-XX-XXX	XXXXXX	XXX	XXXXXXXXXXX	Yes/No	DDMONYYYY
C1:202/2000mg	311-XX-XXX	XXXXXX	XXX	XXXXXXXXXX	Yes/No	DDMONYYYY

Listing 16.2.2.3
Protocol Deviations

Treatment	Patient ID	Visit	Protocol Deviation Code	Details of Deviation	Approval Obtained	Date of Approval
C1:202/2000mg	311-XX-XXX	XXXXXX	XXX	XXXXXXXXXX	Yes/No	DDMONYYYY
C2:800mg	311-XX-XXX	XXXXXX	XXX	XXXXXXXXXX	Yes/No	DDMONYYYY

Listing 16.2.2.4
Inclusion/Exclusion Criteria Violations/Deviations

Treatment	Patient ID	Date of Informed Consent	Time of Informed Consent (hh:mm)	Subject be Enrolled in Study	Criterion Type and Number [1]	Approval Obtained	Date of Approval
C1:301/800mg	311-XX-XXX	DDMONYYYY	XX:XX	Yes/No	EXC XXX/INC XXX	Yes/No	DDMONYYYY
C1:202/800mg	311-XX-XXX	DDMONYYYY	XX:XX	Yes/No	EXC XXX/INC XXX	Yes/No	DDMONYYYY

[1]Refer to Listing 16.2.2.1 for text.

Listing 16.2.4.1.1

Demographic Characteristics

Treatment	Patient ID	Date of Birth	Age (years) [1]	Ethnicity	Race	Sex
C1:301/800mg	311-XX-XXX	1962-01-22	54	NOT HISPANIC OR LATINO	BLACK OR AFRICAN AMERICAN	M
C1:202/800mg	311-XX-XXX	1954-11-26	61	NOT HISPANIC OR LATINO	WHITE	M
C2:800mg	311-XX-XXX	1988-02-11	28	NOT HISPANIC OR LATINO	BLACK OR AFRICAN AMERICAN	M
C1:2000mg	311-XX-XXX	1960-12-16	55	HISPANIC OR LATINO	UNKNOWN	M
C1:301/800mg	311-XX-XXX	1962-11-15	53	NOT HISPANIC OR LATINO	WHITE	M
C2:800mg	311-XX-XXX	1966-04-21	50	NOT HISPANIC OR LATINO	WHITE	M

[1] Age = Age at Screening.

Listing 16.2.4.1.2
Demographic Characteristics
Screen Failures

Treatment	Patient ID	Date of Birth	Age (years) [1]	Ethnicity	Race	Sex
SCREEN FAILURE	311-XX-XXX	1962-01-22	54	NOT HISPANIC OR LATINO	BLACK OR AFRICAN AMERICAN	M
SCREEN FAILURE	311-XX-XXX	1954-11-26	61	NOT HISPANIC OR LATINO	WHITE	M
SCREEN FAILURE	311-XX-XXX	1988-02-11	28	NOT HISPANIC OR LATINO	BLACK OR AFRICAN AMERICAN	M
SCREEN FAILURE	311-XX-XXX	1960-12-16	55	HISPANIC OR LATINO	UNKNOWN	M
SCREEN FAILURE	311-XX-XXX	1962-11-15	53	NOT HISPANIC OR LATINO	WHITE	M
SCREEN FAILURE	311-XX-XXX	1966-04-21	50	NOT HISPANIC OR LATINO	WHITE	M

[1] Age = Age at Screening.

Listing 16.2.4.2
Medical History

Treatment	Patient ID	Medical Condition/Surgery	Start Date	Stop Date
C1:301/800mg	311-XX-XXX	XXXXXXXXXXXXX	DDMONYYYY	DDMONYYYY or ONGOING
C2:800mg	311-XX-XXX	XXXXXXXXXXXXX	DDMONYYYY	DDMONYYYY or ONGOING

Listing 16.2.5.1
Study Drug Administration

Treatment	Patient ID	Visit	Visit Date	Dose (mg)	Start Time of Infusion (hh:mm)	Stop Time of Infusion (hh:mm)	Infusion Site	Infusion Side	Starting Volume (ml)	Ending Volume (ml)	Was entire dose delivered?	Reason if No or Interrupted
C1:301/800mg	311-XX-XXX	XXXXXXX	DDMONYYYY	2000/800	XX:XX	XX:XX	Cephalic Vein/Other Vein	Left/ Right	XXX	XXX	Yes/No/Yes w/ Interruption	XXXXXXXXXX
		XXXXXXX	DDMONYYYY	2000/800	XX:XX	XX:XX	Cephalic Vein/Other Vein	Left/ Right	XXX	XXX	Yes/No/Yes w/ Interruption	
C2:800mg	311-XX-XXX	XXXXXXX	DDMONYYYY	2000/800	XX:XX	XX:XX	Cephalic Vein/Other Vein	Left/ Right	XXX	XXX	Yes/No/Yes w/ Interruption	XXXXXXXXXX

Listing 16.2.5.2
ART Exposure

Treatment	Patient ID	Medication	Standardized Medication Name [1]	Indication	Start Date	Stop Date	Dose	Unit	Route	Frequency
C1:202/2000 mg	311-XX-XXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	DDMONYYYY	DDMONYYYY Or ONGOING	XXXX	XXXX	XXXXX	XX
C2:800mg	311-XX-XXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	DDMONYYYY	DDMONYYYY Or ONGOING	XXXX	XXXX	XXXXX	XX

[1]Medications were coded with WHO Drug Dictionary Version March,2014.

Listing 16.2.5.3
Previous and Concomitant Medications

Treatment	Patient ID	Medication	Standardized Medication Name [1]	Indication	Start Date	Stop Date	Dose	Unit	Route	Frequency
					DDMONYYYY	DDMONYYYY				
C1:202/800 mg	311-XX-XXX	XXXXXXXX	XXXXXXXX	XXXXXXXX		Or ONGOING	XXXX	XXXX	XXXXX	XX
						DDMONYYYY				
C2:800mg	311-XX-XXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	DDMONYYYY	Or ONGOING	XXXX	XXXX	XXXXX	XX

[1]Medications were coded with WHO Drug Dictionary Version March, 2014.

Listing 16.2.5.4
Concomitant Procedures

Treatment	Patient ID	Procedure	Procedure Date	Reason
C1:301/800mg	**311-XX-XXX**	**XXXXXXXX**	**DDMONYYYY**	**XXXXXXXX**
		XXXXXXXX		
C2:800mg	**311-XX-XXX**		**DDMONYYYY**	**XXXXXXXX**

Listing 16.2.5.5
Optimized Background Regimen (OBR)

Treatment	Patient ID	Medication	Standardized Medication Name [1]	Indication	Start Date	Stop Date	Dose	Unit	Route	Frequency	Reason for Change
C1:301/800mg	311-XX-XXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	DDMONYYYY	DDMONYYYY Or ONGOING	XXXX	XXXX	XXXXX	XX	XXX
C2:800mg	311-XX-XXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	DDMONYYYY	DDMONYYYY Or ONGOING	XXXX	XXXX	XXXXX	XX	XXX

[1]Medications were coded with WHO Drug Dictionary Version March, 2014.

Listing 16.2.5.6
Optimized Background Regimen (OBR) Adherence

Treatment	Patient ID	Visit	Visit Date	Has the patient taken all required doses of OBR since the last visit?	If No Explain
C1:202/800mg	311-XX-XXX	XXXXX	DDMONYYYY	YES/NO	XXXXXXXXXXXX
C1:202/2000mg	311-XX-XXX	XXXX	DDMONYYYY	YES/NO	XXXXXXXXXXXX

Listing 16.2.6.1
Post-Injection Observation

Treatment	Patient ID	Visit	Visit Date	Observed After Study Drug	Start Time of Observation (hh:mm)	End Time of Observation (hh:mm)	Comments
C1:301/800mg	311-XX-XXX	XXX	DDMONYYYY	YES/NO	XX:XX	XX:XX	XXXXXXXXXXXXXXXX
C2:800mg	311-XX-XXX	XXX	DDMONYYYY	YES/NO	XX:XX	XX:XX	XXXXXXXXXXXXXXXX

Listing 16.2.6.2
CD4+ Cell Count (cells/mm^3)

				Unimputed Original Values			Imputed with LOCF [5]	
Treatment	Patient ID	Visit [1]	Visit Date (Study Day)	CD4+ Cell Count (cells/mm^3) [2]	CD4+ Cell Count Change from Baseline (%) [3]	Toxicity [4]	CD4+ Cell Count (cells/mm^3) [2]	CD4+ Cell Count Change from Baseline (%) [3]
C1:301/800mg	311-XX-XXX	XXXXXXX	DDMONYYYY (XX)	XXX*	XXXX	XXXX	XXX*	XXXX
C2:800mg	311-XX-XXX	XXXXXXX	DDMONYYYY (XX)	XXX	XXXX	XXXX	XXX	XXXX

[1] EOS=End of Study visit conducted at Week 174 (for TMB-301 rollovers)/Week 150 (for all other patients).

[2]*=below 200 cells/mm^3

[3]Calculated as (visit value – baseline)/baseline*100%

[4]Toxicity is defined as 2 consecutive laboratory results, at least 14 days apart, with a CD4+ cell count below 200 cells/mm3 that also represents a 50% reduction from the baseline CD4+ cell count.

[5] Missing values are imputed using the Last Observation Carried Forward (LOCF) method.e

Listing 16.2.6.5
Viral Load

Treatment	Patient ID	Visit [2]	Visit Date (Study Day)	Treatment Date (Study Day) [3]	Unimputed Original Values: Viral Load (log10 cp/mL)	Unimputed Original Values: Chg from Baseline (log10 cp/mL)	Unimputed Original Values: HIV-1 RNA (cp/mL) [5]	Imputed with MEF [4]: Viral Load (log10 cp/mL)	Imputed with MEF [4]: Chg from Baseline (log10 cp/mL)	Imputed with MEF [4]: HIV-1 RNA (cp/mL) [5]
C1:301/800mg	311-XX-XXX	DAY 0	2016-08-22	2016-08-10 (159)	1.0		TND**	1.0		TND**
		DAY 14					4.9	0.0		73700
		WEEK 12					4.9	0.0		73700
		WEEK 16					4.9	0.0		73700
		WEEK 12	2016-11-14 (84)	2016-10-31 (245)	1.3	-3.6	TD**	1.3	-3.6	TD**
		WEEK 20					4.9	0.0		73700
		WEEK 24					4.9	0.0		73700
		WEEK 24	2017-02-06 (168)	2017-01-23 (329)	1.0	-3.9	TND**	1.0	-3.9	TND**
	311-XX-XXX	DAY 0	2016-09-07	2016-08-24 (154)	1.3		TD**	1.3		TD**
		DAY 14					3.8	0.0		6530
		WEEK 12					3.8	0.0		6530
		WEEK 16					3.8	0.0		6530
		WEEK 12	2016-12-01 (352)	2016-11-17 (513)	1.0	-2.8	TND**	1.0	-2.8	TND**
		WEEK 20					3.8	0.0		6530
		WEEK 24					3.8	0.0		6530
		WEEK 24	2017-02-23 (436)	2017-02-10 (598)	1.0	-2.8	TND**	1.0	-2.8	TND**

[1] EOS=End of Study visit conducted at Week 174 (for TMB-301 rollovers)/Week 150 (for all other patients).
[2] Visits are assigned based on study day using the windows defined in the statistical analysis plan.
[3] Last treatment prior to viral load measurement.
[4] Viral Load results are imputed based on MEF (Missing Equals Failure). This means null viral load results are replaced with the baseline value such that Change from Baseline=0 and the result is a failure. Also all records following a CONFIRMED virologic failure are set to failure.
[5] *=below 400 copies/mL; **=below 50 copies/mL. HIV-1 RNA level results below level of quantitation are coded as target detected (TD) or target not detected (TND).

(Continued)

Listing 16.2.6.6
Virologic Outcome Parameters

At EOS

Treatment	Patient ID	Visit [1]	Visit Date (Study Day)	Virologic Outcome [2]	Virologic Failure [3]	Virologic Success [4]
C1:301/800mg	311-XX-XXX	XXXXXXX	DDMONYYYY (XX)	XX	XXXXXXX	XXXXXXX
C2:800mg	311-XX-XXX	XXXXXXX	DDMONYYYY (XX)	XX	XXXXXXX	XXXXXXX

[1]Visits are assigned based on study day using the windows defined in the statistical analysis plan.

[2]Per the Snapshot Approach:

1=Virologic success (=0.5 log copies/mL drop from Baseline in viral load)

2a=(<0.5 log copies/mL drop from Baseline in viral load)

2b=Discontinued because of virologic failure

2c=Discontinued because of other reasons and drop from baseline in viral load at the time of discontinuation was <0.5 log copies/mL

2d=OBR changed

3a=Discontinued because of AE or death

3b=Discontinued because of other reasons and drop from baseline in viral load at the time of discontinuation was >=0.5 log copies/mL

3c=Missing data during the window but on study

[3] Failure to achieve/maintain response=Patient does not have >=0.5 log10 decline from baseline(BL) by Week 12 on study drug OR patient has a 0.5 log10 decline from BL prior to Week 12 but fails to maintain the 0.5 log10 decline from BL with a <1 log10 increase from nadir on any two consecutive scheduled efficacy assessments after Week 12.

Rebound=Patient has a >=0.5 log10 decline from BL by Week 12 that is maintained but viral load remains >=50 copies (not suppressed), followed by >=1 log10 increase from nadir at two consecutive scheduled visits any time after the primary endpoint.

Breakthrough=Patient has suppressed viral load (< 50 copies) at any time after primary endpoint followed by >=200 copies at two consecutive scheduled efficacy assessments.
[4]Suboptimal Response=Patient has a 0.5 log10 decline but does not suppress (<50 copies) at any time after primary endpoint;
Virologic Suppression=Patient has a 0.5 log10 decline and does suppress (<50 copies) at any time after primary endpoint

Programming note: **See footnotes (values to the left of the =) to indicate what values will be displayed in the listing.**

Listing 16.2.6.7
Patients with Virologic Failure

Treatment	**Patient ID**	Visit	Visit Date	Viral Load (log_{10} copies/mL)	Change from Baseline
C1:301/800mg	311-XX-XXX	XXX	DDMONYYYY	XXX	XXX
C1:800 MG	311-XX-XXX	XXX	DDMONYYYY	XXX	XXX

Note: Virologic failure is defined as two consecutive measurements of less than a 0.5 log_{10} decline from the Baseline viral load. For the Cohort 2 and TMB-301 rollover patients, virologic failure will not be assessed prior to 24 weeks on study drug. For the TMB-202 rollover patients, virologic failure will not be assessed prior to the start of the TMB-311 study period.

Listing 16.2.7.1
Adverse Events

Treatment	Patient ID	System Organ Class	Preferred Term[1]	Adverse Event Verbatim	TEAE [2]	Start Date (Study Day)	Stop Date (Study Day)	Sev. /Grade [3]	SAE	Caus. [4]	Action Taken [5]	Outcm. [6]	Class C AE
C1:301/800mg	311-XX-XXX	MUSCULOSKELETAL AND CONNECTIVE TISSUE	ARTHRALGIA	MILD PAIN (DUE TO FALL AT	Y	20160923 (283)	20161010 (300)	1	N	0	0	1	
C2:800mg	311-XX-XXX	NERVOUS SYSTEM DISORDERS	HEADACHE	WORSENING HEADACHES	Y	20160516 (3)	20160524 (11)	2	N	0	0	1	
		INVESTIGATIONS	BREATH SOUNDS ABNORMAL	DECREASED BREATH SOUNDS	Y	20160520 (7)	20160609 (27)	1	N	0	0	1	
C1:202/2000mg	311-XX-XXX	RENAL AND URINARY DISORDERS	POLLAKIURIA	URINARY FREQUENCY	Y	20161005 (208)		2	N	0	1	3	
C1:202/800mg	311-XX-XXX	SKIN AND SUBCUTANEOUS TISSUE DISORDERS	RASH MACULO-PAPU-LAR	MACULOPAPULAR RASH ON EXTREMITIES	Y	20170119 (349)	20170214 (375)	2	N	1	1	1	

[1] Adverse events are coded using MedDRA Version 17.0.
[2] A treatment-emergent AE (TEAE) is defined as any event not present before exposure to study drug or any event already present that worsens in either intensity or frequency following exposure to study drug. AEs with missing start dates, but with stop dates either overlapping into the dosing period or missing, will be considered TEAEs
[3] Severity/Grade: 1=Mild, 2=Moderate, 3=Severe, 4=Potentially Life Threatening, 5=Death
[4] Causality: 0=Unrelated, 1=Possible, 2=Probable, 3=Definite
[5] Action Taken: 0=None, 1=Medication Given, 2=Non-Medication Therapy, 3=Suspended Study Drug, 4=Permanently Discontinued Study Drug, 99=Other
[6] Outcome: 1=Resolved, 2=Resolved w/sequelae, 3=Ongoing, 4=Worsened, 5=Death, 7=Chronic/Stable, 98=Unknown

Listing 16.2.7.2
Serious Adverse Events

Treatment	Patient ID	System Organ Class	Preferred Term[1]	Adverse Event Verbatim	TEAE [2]	Start Date (Study Day)	Stop Date (Study Day)	Sev. /Grade [3]	SAE	Caus. [4]	Action Taken [5]	Outcm. [6]	Class C AE
C2:800mg	311-XX-XXX	INVESTIGATIONS	BLOOD POTASSIUM DECREASED	LOW SERUM POTASSIUM	Y	20161116 (187)	20161118 (189)	3	Y	0	1,99	1	
C1:301/800mg	311-XX-XXX	INFECTIONS AND INFESTATIONS	CELLULITIS	FACE CELLULITIS	Y	20161017 (153)	20161101 (168)	2	Y	0	1,99	7	
C1:202/2000mg	311-XX-XXX	NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	TONSIL CANCER METASTATIC	METASTATIC SQUAMOUS CELL CARCINOMA OF THE RIGHT TONSIL	Y	20161130 (190)		4	Y	0	0	3	
C1:202/800mg	311-XX-XXX	NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	TONSIL CANCER METASTATIC	METASTATIC SQUAMOUS CELL CARCINOMA OF THE RIGHT TONSIL	Y	20170203 (255)	20170204 (256)	4	Y	0	1	4	
		NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	TONSIL CANCER METASTATIC	METASTATIC SQUAMOUS CELL CARCINOMA OF THE RIGHT	Y	20170205 (257)	20170205 (257)	5	Y	0	1	5	

[1] Adverse events are coded using MedDRA Version 17.0.
[2] A treatment-emergent AE (TEAE) is defined as any event not present before exposure to study drug or any event already present that worsens in either intensity or frequency following exposure to study drug. AEs with missing start dates, but with stop dates either overlapping into the dosing period or missing, will be considered TEAEs.
[3] Severity/Grade: 1=Mild, 2=Moderate, 3=Severe, 4=Potentially Life Threatening, 5=Death
[4] Causality: 0=Unrelated, 1=Possible, 2=Probable, 3=Definite
[5] Action Taken: 0=None, 1=Medication Given, 2=Non-Medication Therapy, 3=Suspended Study Drug, 4=Permanently Discontinued Study Drug, 99=Other
[6] Outcome: 1=Resolved, 2=Resolved w/sequelae, 3=Ongoing, 4=Worsened, 5=Death, 7=Chronic/Stable, 98=Unknown

Listing 16.2.7.3
Adverse Events Leading to Study Discontinuation or Death

Treatment	Patient ID	System Organ Class	Preferred Term[1]	Adverse Event Verbatim	TEAE [2]	Start Date (Study Day)	Stop Date (Study Day)	Sev. /Grade [3]	SAE	Caus. [4]	Action Taken [5]	Outcm. [6]	Class C AE
C1:2000mg	311-XX-XXX	NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	TONSIL CANCER METASTATIC	METASTATIC SQUAMOUS CELL CARCINOMA OF THE RIGHT TONSIL	Y	20170205 (257)	20170205 (257)	5	Y	0	1	5	
C1:301/800mg	311-XX-XXX	GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	PYREXIA	FEVER	Y	20160830 (7)	20160901 (9)	3	N	1	1,4	1	
C2:800mg	311-XX-XXX	INFECTIONS AND INFESTATIONS	SEPSIS	SEPSIS SECONDARY TO NEUTROPENIA	Y	20160901 (93)	20161114 (167)	5	Y	0	1,4	5	YES
C1:202/800mg	311-XX-XXX	INJURY, POISONING AND PROCEDURAL COMPLICATIONS	INJURY	TRAUMA FROM FALL	Y	20161001 (157)	20161001 (157)	5	Y	0	4	5	

[1] Adverse events are coded using MedDRA Version 17.0.
[2] A treatment-emergent AE (TEAE) is defined as any event not present before exposure to study drug or any event already present that worsens in either intensity or frequency following exposure to study drug. AEs with missing start dates, but with stop dates either overlapping into the dosing period or missing, will be considered TEAEs
[3] Severity/Grade: 1=Mild, 2=Moderate, 3=Severe, 4=Potentially Life Threatening, 5=Death
[4] Causality: 0=Unrelated, 1=Possible, 2=Probable, 3=Definite
[5] Action Taken: 0=None, 1=Medication Given, 2=Non-Medication Therapy, 3=Suspended Study Drug, 4=Permanently Discontinued Study Drug, 99=Other
[6] Outcome: 1=Resolved, 2=Resolved w/sequelae, 3=Ongoing, 4=Worsened, 5=Death, 7=Chronic/Stable, 98=Unknown

Listing 16.2.8.1.1
Clinical Laboratory Test
Hematology

Treatment	Patient ID	Visit [1]	Date of Sample (Study Day)	Test	Result (L/H)[2]	Unit	Lower Limit of Normal	Upper Limit of Normal	Potentially Clinically Significant[3]
C1:301/800mg	311-XX-XXX	XXXXXXXXX	2016-03-04 (-172)	Basophils	0	10^9/L	0	0.2	
				Basophils/Total Cells	0	%	0	2	
				Eosinophils	0.02	10^9/L	0	0.57	
				Eosinophils/Total Cells	1	%	0	6.8	
				Hematocrit	0.31(L)	Proport-	0.39	0.54	YES
C1:800mg	311-XX-XXX	XXXXXXXXX	2016-11-14 (84)	Hemoglobin	106(L)	g/L	127	181	YES
				Leukocytes	1.62(L)	10^9/L	3.8	10.7	YES
				Lymphocytes	0.6(L)	10^9/L	0.91	4.28	YES
				Lymphocytes/Total Cells	37	%	15.4	48.5	
				Monocytes	0.16	10^9/L	0.12	0.92	
				Monocytes/Total Cells	10	%	2.6	10.1	
				Neutrophils	0.84(L)	10^9/L	1.96	7.23	YES
				Neutrophils/Total Cells	52	%	40.5	75	
				Platelets	278	10^9/L	140	400	
C1:2000mg	311-XX-XXX	XXXXXXXXX	2016-11-14 (84)	Basophils	0.08	10^9/L	0	0.2	
				Basophils/Total Cells	2.3(H)	%	0	2	YES
				Eosinophils	0.19	10^9/L	0	0.57	
				Eosinophils/Total Cells	5.5	%	0	6.8	
				Hematocrit	0.39	Proport-	0.39	0.54	
C2:800mg	311-XX-XXX	XXXXXXXXX	2016-11-14 (84)	Hemoglobin	128	g/L	127	181	
				Leukocytes	3.47(L)	10^9/L	3.8	10.7	YES
				Lymphocytes	1.49	10^9/L	0.91	4.28	
				Lymphocytes/Total Cells	43	%	15.4	48.5	
				Monocytes	0.34	10^9/L	0.12	0.92	
				Monocytes/Total Cells	9.7	%	2.6	10.1	
				Neutrophils	1.37(L)	10^9/L	1.96	7.23	YES
				Neutrophils/Total Cells	39.5(L)	%	40.5	75	YES
				Platelets	250	10^9/L	140	400	

[1] For TMB301 Rollovers, BASELINE is the value recorded on Day 7 of the TMB-301 study. For TMB202 Rollovers, BASELINE is the value recorded on Day 0 of the TMB-202 study. Lab samples were not collected at the TMB-311 Screening for the Cohort 1 patients. EOS=End of Study visit conducted at Week 96.
[2] L = Below lower limit of normal; H = Above upper limit of normal.
[3] Potentially Clinically Significant is defined as having a result either below the lower limit of normal or above the upper limit of normal.

Listing 16.2.8.1.2
Clinical Laboratory Test
Chemistry

Treatment	Patient ID	Visit [1]	Date of Sample (Study Day)	Test	Result (L/H)[2]	Unit	Lower Limit of Normal	Upper Limit of Normal	Potentially Clinically Significant[3]
C1:301/800mg	311-XX-XXX	XXXXXXX	2016-03-04 (-172)	Alanine Aminotransferase	21	U/L	6	43	
				Albumin	36	g/L	33	49	
				Alkaline Phosphatase	100	U/L	35	131	
				Amylase	167(H)	U/L	28	120	YES
C1:202/800mg	311-XX-XXX	XXXXXXX	2016-11-14 (84)	Alanine Aminotransferase	18	U/L	6	43	
				Albumin	38	g/L	33	49	
				Alkaline Phosphatase	131	U/L	35	131	
				Amylase	158(H)	U/L	28	120	YES
				Aspartate Aminotransferase	20	U/L	11	36	
C1:202/2000mg	311-XX-XXX	XXXXXXXX	2016-03-04 (-172)	Alanine Aminotransferase	21	U/L	6	43	
				Albumin	36	g/L	33	49	
				Alkaline Phosphatase	100	U/L	35	131	
				Amylase	167(H)	U/L	28	120	YES
C2:800mg	311-XX-XXX	XXXXXXX	2016-11-14 (84)	Alanine Aminotransferase	18	U/L	6	43	
				Albumin	38	g/L	33	49	
				Alkaline Phosphatase	131	U/L	35	131	
				Amylase	158(H)	U/L	28	120	YES
				Aspartate Aminotransferase	20	U/L	11	36	

[1] For TMB301 Rollovers, BASELINE is the value recorded on Day 7 of the TMB-301 study. For TMB202 Rollovers, BASELINE is the value recorded on Day 0 of the TMB-202 study. Lab samples were not collected at the TMB-311 Screening for the Cohort 1 patients. EOS=End of Study visit conducted at Week 96.
[2] L = Below lower limit of normal; H = Above upper limit of normal.
[3] Potentially Clinically Significant is defined as having a result either below the lower limit of normal or above the upper limit of normal.

Listing 16.2.8.1.3
Clinical Laboratory Test
Urinalysis

Treatment	Patient ID	Visit	Date of Sample (Study Day)	Test	Unit	Result
C1:301/800mg	311-XX-XXX	XXXXXXXX	2016-03-04 (-172)	Calcium Oxalate Crystals		Present
				Hyaline Casts	/LPF	2
				Sediment Examination		Positive
		XXXXXXXX	2016-11-14 (84)	Sediment Examination		Positive
		XXXXXXXX	2017-02-06 (168)	Sediment Examination		Positive
C1:202/800mg	311-XX-XXX	XXXXXXXX	2016-03-16 (92)	Mucous Threads		Present
		XXXXXXXX	2016-03-23 (99)	Calcium Oxalate Crystals		Present
				Sediment Examination		Positive
		XXXXXXXX	2017-02-23 (436)	Amorphous Crystals		Present
				Sediment Examination		Positive
C2:800mg	311-XX-XXX	XXXXXXXX	2016-04-07 (-37)	Sediment Examination		Positive
		XXXXXXXX	2016-05-13 (0)	Sediment Examination		Positive
		XXXXXXXX	2016-05-20 (7)	Hyaline Casts	/LPF	2
				Sediment Examination		Positive
C1:202/2000mg	311-XX-XXX	XXXXXXXX	2016-03-11 (0)	Sediment Examination		Negative
		XXXXXXXX	2016-06-03 (84)	Calcium Oxalate Crystals		Present
				Mucous Threads		Present
				Sediment Examination		Positive
		XXXXXXXX	2016-08-25 (167)	Sediment Examination		Negative

EOS=End of Study visit conducted at Week 96.

Listing 16.2.8.1.4
Abnormal Laboratory Results

Treatment	Patient ID	Visit [1]	Date of Sample (Study Day)	Category	Test	Result (L/H)[2]	Unit	Lower Limit of Normal	Upper Limit of Normal	Potentially Clinically Significant[3]
C1:301/800mg	311-XX-XXXX	XXXXXXXXX	2016-03-04 (-172)	CHEMISTRY	Amylase	167(H)	U/L	28	120	YES
					Direct Bilirubin	1(L)	umol/L	2	7	YES
				HEMATOLOGY	Hematocrit	0.31(L)	Proportion of 1	0.39	0.54	YES
					Hemoglobin	106(L)	g/L	127	181	YES
					Leukocytes	1.62(L)	10^9/L	3.8	10.7	YES
					Lymphocytes	0.6(L)	10^9/L	0.91	4.28	YES
					Neutrophils	0.84(L)	10^9/L	1.96	7.23	YES
C1:202/800mg	311-XX-XXX	XXXXXXXXX	2016-11-14 (84)	CHEMISTRY	Amylase	158(H)	U/L	28	120	YES
					Bilirubin	1.5(L)	umol/L	3	21	YES
					Direct Bilirubin	1(L)	umol/L	2	7	YES
				HEMATOLOGY	Basophils/Total Cells	2.3(H)	%	0	2	YES
					Leukocytes	3.47(L)	10^9/L	3.8	10.7	YES
					Neutrophils	1.37(L)	10^9/L	1.96	7.23	YES
					Neutrophils/Total Cells	39.5(L)	%	40.5	75	YES
C1:202/2000mg	311-XX-XXX	XXXXXXXXX	2017-02-06 (168)	CHEMISTRY	Amylase	133(H)	U/L	28	120	YES
					Direct Bilirubin	1(L)	umol/L	2	7	YES
				HEMATOLOGY	Hematocrit	0.37(L)	Proportion of 1	0.39	0.54	YES
					Hemoglobin	124(L)	g/L	127	181	YES
C2:800mg	311-XX-XXX	XXXXXXXXX	2016-03-23 (99)	CHEMISTRY	Alanine Aminotransferase	68(H)	U/L	6	43	YES
					Aspartate Aminotransferase	59(H)	U/L	11	36	YES
					Cholesterol	3.03(L)	mmol/L	4.53	7.71	YES
					Creatine Kinase	393(H)	U/L	39	308	YES

[1] For TMB301 Rollovers, BASELINE is the value recorded on Day 7 of the TMB-301 study. For TMB202 Rollovers, BASELINE is the value recorded on Day 0 of the TMB-202 study. Lab samples were not collected at the TMB-311 Screening for the Cohort 1 patients. EOS=End of Study visit conducted at Week 96.
[2] L = Below lower limit of normal; H = Above upper limit of normal.
[3] Potentially Clinically Significant is defined as having a result either below the lower limit of normal or above the upper limit of normal.

Listing 16.2.8.1.5
Other Laboratory Results

Treatment	Patient ID	Visit [1]	Date of Sample (Study Day)	Category	Test	Result (L/H)[2]	Unit	Lower Limit of Normal	Upper Limit of Normal	Potentially Clinically Significant[3]
C1:301/800mg	311-XX-XXXX	XXXXXXXXX	2016-03-04 (-172)	CHEMISTRY	Amylase	167(H)	U/L	28	120	YES
					Direct Bilirubin	1(L)	umol/L	2	7	YES
				HEMATOLOGY	Hematocrit	0.31(L)	Proportion of 1	0.39	0.54	YES
					Hemoglobin	106(L)	g/L	127	181	YES
					Leukocytes	1.62(L)	10^9/L	3.8	10.7	YES
					Lymphocytes	0.6(L)	10^9/L	0.91	4.28	YES
					Neutrophils	0.84(L)	10^9/L	1.96	7.23	YES
C1:202/800mg	311-XX-XXX	XXXXXXXXX	2016-11-14 (84)	CHEMISTRY	Amylase	158(H)	U/L	28	120	YES
					Bilirubin	1.5(L)	umol/L	3	21	YES
					Direct Bilirubin	1(L)	umol/L	2	7	YES
C1:202/2000mg	311-XX-XXX	XXXXXXXXX	2017-02-06 (168)	CHEMISTRY	Amylase	133(H)	U/L	28	120	YES
					Direct Bilirubin	1(L)	umol/L	2	7	YES
				HEMATOLOGY	Hematocrit	0.37(L)	Proportion of 1	0.39	0.54	YES

[1] For TMB301 Rollovers, BASELINE is the value recorded on Day 7 of the TMB-301 study. For TMB202 Rollovers, BASELINE is the value recorded on Day 0 of the TMB-202 study. Lab samples were not collected at the TMB-311 Screening for the Cohort 1 patients. EOS=End of Study visit conducted at Week 96.
[2] L = Below lower limit of normal; H = Above upper limit of normal.
[3] Potentially Clinically Significant is defined as having a result either below the lower limit of normal or above the upper limit of normal.

Listing 16.2.8.2
Viral Resistance Testing

Treatment	Patient ID	Visit	Visit Date	Test Type	Reverse Transcriptase (Resistance)	Protease (Resistance)	Integrase Genese (Resistance)	Trop-ism	Entry Inhibitors (Resistance)		
									Ibal-izumab	Mara-viroc	Enfu-virt-ide
C1:301/800mg	311-xx-xxx	SCREENING	2015-09-08	Geno	Abacavir (Y) Stavudine (P) Tenofovir (Y) Zidovudine (P) Delavirdine (N) Didanosine (Y) Efavirenz (N)	Atazanavir (ATV) (N) Tipranavir (P) Atazanavir (ATV/r) (P) Darunavir (Y) Fosamprenavir (P)	Dolutegravir (Y) Elvitegravir (Y) Raltegravir (Y)	DM	Y	Y	Y
				Pheno	Abacavir (Y) Stavudine (Y) Tenofovir (Y) Zidovudine (Y) Delavirdine (N) Didanosine (Y) Efavirenz (N)	Atazanavir (ATV) (Y) Tipranavir (Y) Atazanavir (ATV/r) (Y) Darunavir (Y) Fosamprenavir (Y)	Dolutegravir (Y) Elvitegravir (Y) Raltegravir (Y)				
		WEEK 9	2015-11-03	Geno	Abacavir (P) Stavudine (N)	Atazanavir (ATV) (N) Tipranavir (P)	Dolutegravir (Y)	DM	N	Y	Y

[1] EOS=End of Study visit conducted at Week 96.
[2] Note: Abbreviations for Resistance: Y = Sensitive, P = Partially Sensitive, N = Resistant

(Continued)

Listing 16.2.8.3
Vital Signs

Treatment	Patient ID	Visit	Visit Date	Scheduled Time Point	Time (hh:mm)	Height (cm) [2]	Weight (kg) [2]	Temp. (C) [2]	Rate (bpm) [2]	Resp. Rate (breaths/min) [2]	Systolic Blood Pressure (mmHg) [2]	Diastolic Blood Pressure (mmHg) [2]
C1:301/800mg	311-XX-XXX	SCREENING	2015-08-04			170	69	36.5	62	16	129	85
		DAY 0	2015-08-31				69	36.9	81	16	108	68
		DAY 7	2015-09-08	PRE-INFUSION	10:45			36.9	74	15	127	76
			2015-09-08	POST-INFUSION	12:00			36.8	76	16	110	69
		DAY 21	2015-09-22	PRE-INFUSION	10:00			36.9	82	15	103	68
			2015-09-22	POST-INFUSION	11:05			36.8	80	15	115	72
		WEEK 5	2015-10-06	PRE-INFUSION	10:40			36.4*	67	16	126	83
			2015-10-06	POST-INFUSION	11:40			36.8	76	15	122	72
		WEEK 7	2015-10-19	PRE-INFUSION	11:20			38.9*	117*	15	123	72
			2015-10-19	POST-INFUSION	12:15			37.1	108	15	124	72
		WEEK 19	2016-01-14	PRE-INFUSION	12:45			36.8	79	16	108	65
			2016-01-14	POST-INFUSION	13:25			36.7	78	16	109	70
C1:202/800mg	311-XX-XXX	SCREENING	2015-08-05			179	83	36.6	69	15	124	85

[1]EOS=End of Study visit conducted at Week 96.
[2]*Denotes Potentially Clinically Significant Vital Signs outside of these ranges: Temperature: 36.44-37.22 C; Pulse: 60-110 BPM; Respiration rate: 12-20 breaths per minute; Blood Pressure: Systolic 100-140 mmHg; Diastolic 60-90 mmHg

Listing 16.2.8.4
Physical Examinations

Treatment	Patient ID	Visit	Visit Date	Performed at Visit	Body System [1]	Status (Details)
C1:301/800mg	311-XX-XXX	Screening	DDMONYYYY	Yes/No	HEENT	Normal/Abnormal/Not Done
					Cardiovascular	XXX
					Musculoskeletal	XXX
					Lymphatic	XXX
					Respiratory	XXX
					Gastrointestinal	XXX
					Skin	XXX
					Neurological	
					Additional PE Findings	

C1:202/800mg	**311-XX-XXX**	**Day 0**	**DDMONYYYY**	**Yes/No**	**Cardiovascular**	**Normal/Abnormal/Not Done**
					Lymphatic	**XXX**
					Respiratory	**XXX**
					Abdomen	**XXX**
					Extremities	**XXX**
					Neurological	**XXX**
					Additional PE Findings	**XXX**

[1]A complete physical examination is performed only at <list correct visits>. An abbreviated physical examination is performed at other visits.

Listing 16.2.9
Extent of Treatment Exposure

Treatment	Patient ID	Start Date of Ibalizumab	Last Date of Ibalizumab*	Years on Ibalizumab
C1:301/800mg	311-XX-XXX	04MAR2016	21FEB2017	1.0
C1:202/800mg	311-XX-XXX	23MAR2016	23FEB2017	0.9
C1:202/2000mg	311-XX-XXX	16JUN2015	10FEB2017	1.7
C2:800mg	311-XX-XXX	19AUG2015	15FEB2017	1.5

*Last Dose recorded prior to the Data Cutoff Date.