Study Title: A Phase 2a Open-label Study to Investigate Safety and Tolerability (including the MTD), Efficacy, Pharmacokinetics, Pharmacodynamics and Immunogenicity of MT-3724 in Combination with Gemcitabine and Oxaliplatin in Subjects with Relapsed or Refractory B-Cell Non-Hodgkin Lymphoma

Molecular Templates (MTEM) Study No: MT-3724_NHL_002
Syne qua non Ltd Study No: MES20001

Statistical Analysis Plan

Version: Final 1.0

Date: 25th March 2021

Author

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04/01/2021 15:50:54 UTC
[redacted] (Signer)

NCT Number: NCT03488251
This NCT number has been applied to the document
for the purposes of posting on clinicaltrials.gov

Modification History

Version	Change History	Reason	Date
1.0	First Version	N/A	25MAR2021

Contents

LIST OF ABBREVIATIONS

AE	Adverse Event
BMI	Body Mass Index
BOR	Best Objective Response
BP	Blood Pressure
BSA	Body Surface Area
CI	Confidence Interval
CLS	Capillary Leak Syndrome
CRF	Case Report Form
CR	Complete Response
CRS	Cytokine Release Syndrome
CSR	Clinical Study Report
DCR	Disease Control Rate
DLT	Dose Limiting Toxicities
DOR	Duration of Response
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
IRR	Infusion-related Reaction
LVEF	Left Ventricular Ejection Fraction
LYRIC	Lymphoma Response to Immunomodulatory Therapy Criteria
MedDRA	Medical Dictionary for Regulatory Activities
MTD	Maximum Tolerated Dose
MTEM	Molecular Templates
NCI CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events
NHL	Non-Hodgkin Lymphoma
NYHA	New York Heart Association
ORR	Objective Response Rate
PDy	Pharmacodynamics
PD	Progressive Disease
PDC	Protocol Deviation Criteria
PFS	Progression-free Survival
PK	Pharmacokinetics
PR	Partial Response
PT	Preferred Term

QW	Once a week
RDI	Relative Dose Intensity
SAE	Serious Adverse Event
SAF	Safety Population
SAP	Statistical Analysis Plan
SD	Stable Disease
SIRS	Systemic Inflammatory Response Syndrome
SOC	System Organ Class
TEAE	Treatment Emergent Adverse Event
TIW	Three times a week
WHO Drug	World Health Organization Drug Dictionary

1 INTRODUCTION

This document details the statistical analysis of the data that will be performed for the MTEM study: MT-3724_NHL_002 titled “A Phase 2a Open-label Study to Investigate Safety and Tolerability (including the MTD), Efficacy, Pharmacokinetics, Pharmacodynamics and Immunogenicity of MT-3724 in Combination with Gemcitabine and Oxaliplatin in Subjects with Relapsed or Refractory B-Cell Non-Hodgkin Lymphoma”.

The study was to be completed in two sequential parts (Part 1 and Part 2). At the time of writing this Statistical Analysis Plan (SAP), a study decision has been taken to close Part 1 and not open Part 2 of the study. This decision was taken February 2021 due to lack of adequate manufacturing lot material at this time. At the time of closing the study, 8 subjects had been recruited into the first dosing cohort.

The proposed analysis is based on the contents of the Final Version of the protocol Amendment 2.0 dated 12-Sep-19 (V3.0), Amendment 1.0 dated 14-Jan-19 (V2.0) and Version 1.0 dated 29-Mar-18.

The purpose of this SAP is to provide details of the statistical analyses required for an abbreviated Clinical Study Report (CSR). This will comprise a full safety profile of MT-3724 and limited efficacy data. Other data collected as outlined in the protocol – pharmacokinetic data, pharmacodynamic data and immunological data – does not fall within the scope of this SAP. Analysis of this data will be described in a separate analysis plan, not produced by SQN.

The table, listing and figure shells are supplied in a separate document.

2 STUDY OBJECTIVES AND DESIGN

2.1 Study Objectives

The primary objective of the study is to determine the safety and tolerability [including the maximum tolerated dose (MTD)] of MT-3724 in combination with gemcitabine and oxaliplatin in subjects with relapsed or refractory B-Cell Non-Hodgkin Lymphoma (NHL).

The secondary objectives of the study are:

- Characterize the pharmacokinetics (PK) of MT-3724 in combination with gemcitabine and oxaliplatin in subjects with relapsed or refractory B-Cell NHL.
- Assess the pharmacodynamics (PDy) of MT-3724 in combination with gemcitabine and oxaliplatin in subjects with relapsed or refractory B-Cell NHL.
- Assess the immunogenicity of MT-3724 in combination with gemcitabine and oxaliplatin in subjects with relapsed or refractory B-Cell NHL.
- Assess the tumor response to MT-3724 in combination with gemcitabine and oxaliplatin in subjects with relapsed or refractory B-Cell NHL.

The first three of these secondary objectives fall outside the scope of the analysis documented in this SAP.

2.2 Study Estimands

As the primary objective of this study is to determine the safety and tolerability of MT-3724 in combination with gemcitabine and oxaliplatin and the planned summaries are all descriptive in nature, the estimand framework (per the ICH E9 (R1) addendum) will not be implemented.

2.3 Study Endpoints

The study endpoints are as follows. Note that the terms ‘endpoint’ and ‘variable’ may be used interchangeably throughout this SAP to refer to the measurement of interest:

The primary analysis will be a comprehensive evaluation of adverse events (AEs) and serious adverse events (SAEs) and other safety variables, detailed below:

- The type, incidence, severity, timing, seriousness, relatedness and outcome of adverse events.
- Incidence of dose limiting toxicities (DLTs) and treatment-emergent adverse events (TEAEs) that led to treatment modification.
- Recording of Infusion related reactions (IRR), cytokine release syndrome (CRS) and capillary leak syndrome (CLS).
- Results of vital sign assessment (blood pressure, heart rate and body temperature).
- Results of electrocardiogram (ECG) assessment.
- Results of clinical chemistry, hematology, coagulation, and urinalysis tests.
- Changes in physical examination.
- Need for concomitant medications.

The secondary endpoints associated with the secondary objective of assessing the tumor response to MT-3724 in combination with gemcitabine and oxaliplatin in subjects with relapsed or refractory B-Cell NHL are as follows:

- Objective tumor response at each time point.
- Best objective response (BOR).
- The objective response rate (ORR).
- Disease control rate (DCR).
- Duration of response (DOR).
- Progression-free survival (PFS).

Other secondary endpoints will not be covered in this SAP.

3 SAMPLE SIZE

This is an exploratory Phase 2a study, so a formal power calculation was not deemed necessary to justify the sample size. Up to 24 subjects were planned to be enrolled in Part 1, dependent on the number of dose cohorts needed to identify the MTD of MT-3724 in combination with gemcitabine and oxaliplatin in Part 1.

4 INTERIM ANALYSIS

No interim statistical analysis was planned as part of this study.

Informal statistical analyses could be performed at the sponsor's discretion at any time during the study. These analyses would be performed without an interim data base lock for the purposes of the Investigator's Brochure update, safety reports to the health authorities (e.g. Development Safety Update Report) and meetings with health authorities for internal decisions.

In addition, data from individual subjects and cohorts were reviewed without formal statistical analysis on an ongoing basis during the study (e.g. to support the dose escalation decisions in Part 1).

5 ANALYSIS PLAN

5.1 General

Summary statistics for continuous variables will consist of number of non-missing observations (n), mean, standard deviation, minimum, median and maximum, unless specified otherwise. The precision of these variables is defined in the table, figure and listing shells document.

For categorical variables the number and percentage of subjects in each category will be presented, based on the number of subjects in the analysis set. For tumor response, this will be based on the number of subjects with a non-missing best overall response assessment.

5.2 General Derivations

This section provides details of general derivations. Derivations specific to the parameter of interest are detailed within the specific SAP section. Some example text is given below:

- Definition of baseline

For safety endpoints, baseline is defined as the last non-missing value (including scheduled and unscheduled assessments) prior to the subject receiving study treatment.

For efficacy endpoints, baseline scan is defined as the scan performed at screening or within 28 days before the start treatment if an existing scan of the same lesion(s) is available.

- Incomplete dates

For calculation purposes, incomplete dates will be completed using worst case. Further details are detailed in the relevant sections as required.

- Non-numeric values

In the case where a variable is recorded as “>x”, “≥x”, “<x” or “≤x”, if a numeric value is needed for analysis purposes, then a value of x will be taken. Where a range of values is quoted the midpoint of the range will be taken.

- Methods for handling withdrawals and missing data

Missing data will not be imputed.

5.3 Analysis Sets

The following analysis populations are defined for this study.

The **Enrolled Set** includes all subjects who passed screening irrespective of whether they received the study treatment.

The **Safety Population** (SAF) consists of all subjects who received at least one dose of any study drug (either MT-3724, or gemcitabine or oxaliplatin). Subjects will be analyzed according to the treatment actually taken. The SAF will be used for the primary statistical analysis of safety endpoints.

The **DLT evaluable Population** consists of SAF subjects who either experienced DLT or had completed at least one cycle of treatment.

The **Efficacy Population** consists of all subjects in the SAF who have an evaluable baseline tumor assessment, and have at least one evaluable post-baseline tumor assessment or have experienced disease progression (including death). The efficacy population will be used for the efficacy endpoints, although all efficacy data will still be listed using the SAF.

The protocol also lists other analysis populations which are not required for the analysis detailed in this SAP.

The Analysis Set Planning form indicates which analysis sets require individual subject assignments to be listed for review and agreement prior to final analysis, as well as the timing of the reviews. Where analysis sets do not require review of individual subject assignments, the definitions are considered sufficient to determine the subjects included within these analysis sets without listing and review.

5.4 Data presentations

There is only one dosing cohort included in the analysis, however this will be split into 2 dosing regimens. All data will be summarized in tabular form by regimen and overall using the treatment labels:

- Cohort 1A (10 µg/kg/dose)
- Cohort 1B (10 µg/kg/dose)
- Total

Cohort 1A is defined as MT-3724 at 10 µg/kg/dose three times a week (TIW) with concomitant chemotherapy for the first two 4-week cycles followed by MT-3724 once a week (QW) thereafter, per protocol versions 1-2. Cohort 1B is defined as MT-3724 at 10 µg/kg/dose TIW for two weeks prior to starting chemotherapy for the first 6-week cycle and QW dosing of MT-3724 thereafter, per protocol version 3.

Eligibility and analysis set listings will be based on the enrolled set and all other listings will be based on the SAF set.

Listings will be sorted by regimen, subject number and date/time of assessment.

Graphical presentations of the data may also be provided where appropriate.

5.5 Disposition of subjects

The number and percentage of all subjects enrolled, included in the SAF, DLT evaluable and Efficacy Population, who completed the study and prematurely discontinued the study, study duration and treatment duration will be summarized. The number and percentage of subjects will be summarized by their reasons for withdrawal from the study. Study duration will be derived as the number of days between Day 1 (date of first administration of study treatment) and the date of study completion or the date of early study withdrawal. Treatment duration will be derived as the number of days between first administration of study drug and the date of the last administration of study drug.

Eligibility for each of the analysis sets along with reasons for exclusion will be listed. Study completion/withdrawal data will be listed. The version of protocol under which the subject was enrolled will be listed.

5.6 Protocol Deviations

Prior to database lock, MTEM may review the individual deviations to confirm that important protocol deviations have been captured correctly as indicated in the protocol deviation criteria (PDC) form. Important protocol deviations are a subset of protocol deviations that may significantly impact the completeness, accuracy and/or reliability of the study data or that may significantly affect a subject's rights, safety or well-being.

Only important protocol deviations, as specified in the PDC form, will be included in the statistical outputs.

Details of all important protocol deviations (date, deviation group, deviation category and specific details) will be listed.

5.7 Background and Demographic Characteristics

5.7.1 Demography

Demographic characteristics (age, gender, ethnicity and race), and body measurements (height, weight, Body mass index (BMI) Body Surface Area (BSA)) collected at Screening will be summarized.

Height will be summarized in centimeters. If collected in inches the following conversion with be applied:

Height (cm) = Height (in) x 2.54

Age is calculated in years from the date of first administration of study treatment, unless age has been entered directly into the case report form (CRF).

All subject demographic data including informed consent will be listed.

5.7.2 Smoking and Alcohol Consumption History

All smoking and alcohol consumption history collected at screening will be listed.

5.7.3 Medical History

Medical history events will be coded using the MedDRA dictionary version 23.0. The version used will be indicated in the data listing. Medical history data will be listed only.

5.7.4 Prior NHL Systemic Therapy and Radiotherapy

Prior NHL systemic therapy and radiotherapy will be collected as separate categories and all prior therapy data will be listed.

5.7.5 Histological NHL Diagnosis

NHL histology confirmed by biopsy, organ and date of confirmation will be listed. This information can be found in the following locations of the CRF:

	Cohort 1A		Cohort 1B	
Reported Variable	**CRF Page**	**CRF Variable**	**CRF Page**	**CRF Variable**
NHL histology confirmation by biopsy	Disease Diagnostic – NHL Diagnosis	NHL relapse histology confirmation by biopsy	Disease Diagnostic - Histological NHL Diagnosis	NHL relapse/refractory CD20 positive histology confirmation by biopsy
Organ	Disease Diagnostic – NHL Diagnosis	Organ, specify	Disease Diagnostic - Histological NHL Diagnosis	Organ specify
Date of histology confirmation	Disease Diagnostic – NHL Diagnosis	Date of histology confirmation	Disease Diagnostic - Histological NHL Diagnosis	Date of CD-20 histology confirmation

5.7.6 Initial B-Cell NHL Diagnosis

Details of initial diagnosis will be listed including NHL type, histological grade, Ann Arbor staging and grade (International Prognostic Index or Follicular Lymphoma-specific International Prognostic Index) where collected.

5.7.7 Current B-Cell NHL Diagnosis

Details of current diagnosis at screening will be listed including current diagnosis, date of current relapse, Ann Arbor staging and current grade at screening (International Prognostic Index or Follicular Lymphoma-specific International Prognostic Index) and genetic abnormalities.

5.8 Prior and Concomitant Medications

Medications will be coded using the latest World Health Organization Drug dictionary (WHO Drug) version B2 Enhanced MAR2017. The version used will be indicated in the listings.

Prior medications are defined as those that started and ended prior to the first administration of study treatment. Medications that are ongoing at the first administration of study treatment or started after time of first administration will be deemed to be concomitant medications. If medication dates are incomplete and it is not clear whether the medication was concomitant, it will be assumed to be concomitant.

Medication data will be listed only, where concomitant medications will be flagged.

5.9 Administration of Study treatment and Exposure

The number of cycles of MT-3724 started, number of cycles completed, number of dose interruptions, number of delays, number of dose reductions, the total drug received and the total amount of drug received and total duration of exposure (calculated as date of last infusion of MT-3724 – date of first infusion of MT-3724 + 1) will be summarized. Summaries will be repeated for gemcitabine administration and oxaliplatin administration, but omitting number of cycles started and completed.

Drug interruptions and delays are identified from the ‘reason study drug was not given per protocol’ field on the relevant study drug administration page of the CRF. Dose reductions are identified from the question ‘was study drug given at the planned dose?’, where the answer is ‘no’ and reason is ‘reduction in dose’.

Total amount of drug received will be measured in µg and summed over all visits. If the entire dose was delivered then total dose prepared will be used in the calculation, otherwise , the total amount at the visit will be derived as the total dose prepared divided by 100 and multiplied by the total volume infused.

Total drug received will be measured in µg/kg and is calculated as the total amount of drug received for each subject divided by the most recent weight collected for the subject.

For MT-3724, relative dose intensity (RDI) up to the last actual day of dosing will also be summarized. RDI is defined as follows:

RDI = 100%*(actual cumulative dose/planned cumulative dose)

Actual dose at each visit is the total amount of drug received, derived as detailed above. At the first dosing visit, if planned dose administered is ‘Yes’ then planned dose is equal to actual dose, otherwise planned dose will be the dose administered multiplied by the subject’s most recent weight, rounded to the nearest 10. Once a subject’s dose has been reduced, it cannot be increased again per protocol, therefore at subsequent dosing visits, the planned dose will be equal to the previous dose

administered. If dosing is delayed at a dosing visit, planned dose will remain at the last dose administered until the next dose is given and actual dose will be 0. If for any reason a planned dosing visit has not been entered into the database, this will not be included in the calculation of RDI.

Planned dosing visits for subjects in Cohort 1A are as follows:

In Cycles 1 and 2, MT-3724 should be administered on Days 1, 3, 5, 8, 10 and 12. In Cycle 3 and beyond, MT-3724 should be administered on Days 1, 8, 15 and 22. All cycles are 28 days in length.

Planned dosing visits for subjects in Cohort 1B are as follows:

In Cycle 1, MT-3724 should be administered on Days 1, 3, 5, 8, 10, 12, 15, 22, 29 and 36. In Cycle 2 and beyond, MT-3724 should be administered on Days 1, 8, 15 and 22. Cycle 1 is 42 days in length and all other cycles are 28 days in length.

Information in the listing will include total dose of MT-3724, gemcitabine and oxaliplatin administered, start and stop times, duration of infusion, any delays, interruptions or missed doses, and duration of interruption (where applicable).

Infusions are expected during the CRF defined visits. If a dose is delayed, the investigator has discretion to make up that infusion within 2 days. Any infusions administered and recorded at unscheduled visits will be mapped to the expected infusion visit for summary purposes.

5.10 EFFICACY EVALUATION

5.10.1 Primary Analysis

The primary endpoints of this study are safety related and therefore there are no primary efficacy endpoints.

5.10.2 Secondary Analyses

A secondary analysis of efficacy to evaluate response to MT-3724 in combination with gemcitabine and oxaliplatin will be performed in this trial. The efficacy parameters of interest are ORR, BOR, DCR, DOR and PFS. Investigator assessed overall response will be used for all analyses.

All efficacy analyses will be performed in the efficacy population.

5.10.2.1 Objective Response Rate

The ORR measures the proportion of subjects with a reduction in tumor size (Partial Response (PR) or Complete Response (CR)) using the five-point scale per the Lugano Classification for Lymphoma, adjusted according to LYRIC (lymphoma response to immunomodulatory therapy criteria)[1]. An overview of LYRIC is presented in the protocol appendix D. The ORR representing clinically significant clinical benefit in the study will comprise the Lugano Score 1, 2 or 3, or the CR, or PR. The number and percentage of subjects with clinically significant results will be presented, alongside the exact 95% confidence interval (CI) for the percentage.

The best objective response will also be summarized. Subjects who experience disease progression before undergoing the first tumor assessment will be added to the disease progression stratum.

5.10.2.2 Disease Control Rate

The DCR will be defined as the percentage of subjects with objective response of CR, PR or stable disease (SD) defined as SD for 3 months or longer from the baseline scan. The DCR will be summarized descriptively by regimen and overall, alongside exact 95% CIs.

5.10.2.3 Duration of Response

All subjects achieving clinically significant clinical benefit according to the response criteria (Lugano Score 1, 2, 3 or CR or PR or stable disease for at least 3 months) will be included in the analysis of the DOR. For subjects who met the criteria of having stable disease for at least 3 months from baseline, DOR is defined as the time from first documented stable disease to the actual date of disease progression or death. For other subjects, DOR is defined as the time from the first documented complete or partial response (achieved after the date of exposure to MT-3724) to the actual date of disease progression or death.

> *Duration of response = Date of progression/death or censoring – Date of 1st objective response (except for subjects having SD for at least 3 months, which will use first documented SD) + 1*

Duration of response will only be calculated for the subset of subjects who have an objective response or SD for at least 3 months. Subjects who do not meet the criteria for progression or death by the time of analysis will be censored at their last evaluable disease assessment and their first response will be noted as ongoing.

DOR will be listed.

5.10.2.4 Progression-free Survival

PFS will be defined as the time from the start of treatment with MT-3724 on Cycle 1 Day 1 to the date of disease progression or death from any cause. Subjects who have not progressed or died at the time of analysis will be censored at the date of their last tumor assessment.

PFS (days) = Date of progression/death or censoring – Date of 1st infusion + 1

If a subject has no evaluable assessments or does not have baseline data they will be censored at Day 1.

PFS will be listed.

5.10.2.5 Tumor Lesion Assessment

All tumor lesion assessment details including sum of perpendicular diameters and change from baseline will be listed for all subjects in the SAF.

5.11 SAFETY EVALUATION

5.11.1 Tolerability

The tolerability of MT-3724 in combination with gemcitabine and oxaliplatin will be assessed based on AEs, DLTs, clinical laboratory evaluation and other safety evaluations (vital signs, ECG, physical examination).

5.11.2 Adverse Events

AEs will be coded using the MedDRA dictionary version 23.0. The version used will be indicated in the data summaries and listings.

Treatment-emergent adverse events (TEAEs) and treatment-emergent serious adverse events (TESAEs) will be reported from the time of start of first infusion of study drug until the end of the short-term follow-up visit or start of new therapy for NHL whichever occurs earlier. TEAEs/TESAEs are defined as those AEs/SAEs that occurred or worsened at or after the start of the first infusion of the study drug. An AE/SAE that occurred or worsened after last dose of study drug is TEAE/TESAE only if it happened before the initiation of alternative therapy or safety follow up (SFU), whichever is earlier. If adverse event dates are incomplete and it is not clear whether the adverse event was treatment-emergent, it will be assumed to be treatment-emergent.

A treatment-related TEAE is defined as a TEAE that is possibly, probably or definitely related to the study treatment. If the TEAE has a missing relationship it is assumed to be related to the study treatment for analysis purposes.

The CTCAE v 5.0 will be used for grading the severity of AEs. For missing severity, no imputation will be made.

A summary table will present the following:

- TEAEs (events and subjects).
- Serious TEAEs (events and subjects).
- TEAEs by relationship to study treatment and the pooled study treatment related category (events and subjects)
- TEAEs leading to dose interruption of MT-3724 (related and non-related; and subjects only)
- TEAEs leading to dose delay of MT-3724 (related and non-related; subjects only)
- TEAEs leading to dose reduction of MT-3724 (related and non-related; subjects only)
- TEAEs leading to discontinuation (related and non-related; subjects only)
- TEAEs by severity (CTC grade) (events and subjects).
- DLTs (events and subjects)
- CLS TEAEs (events and subjects)
- CRS TEAEs (events and subjects)
- IRR TEAEs (events and subjects)
- TEAEs leading to death (subjects only).

In the above summaries, if a subject experienced more than one TEAE, the subject will be counted once using the most related event for the “by relationship to study treatment” and “related to study treatment” summaries and at the worst severity for the

"by severity" summary. All percentages presented will be based on the number of subjects in the SAF, except for DLTs which will be based on the number of subjects in the DLT evaluable population.

The following tables will be presented:

1. TEAEs by system Organ Class (SOC) and Preferred Term (PT).
2. TEAEs by SOC, PT and maximum CTC grade.
3. TEAEs by SOC, PT and relationship to investigational product (MT-3724) and the pooled related categories (related/unrelated).

For all of the above, SOC and PT will be presented in decreasing frequency of the total number of subjects with TEAEs.

Further details of the above four tables are given below:

1. If a subject experienced more than one TEAE, the subject will be counted once for each SOC and once for each PT.
2. If a subject experienced more than one TEAE, the subject will be counted once for each SOC and once for each PT at the worst CTC grade.
3. If a subject experienced more than one TEAE, the subject will be counted once for each SOC and once for each PT using the most related event.

Adverse event data will be listed in full and this will also include a treatment emergent flag, the time of onset and cessation of event relative to first dosing of study treatment and duration of AE.

Serious TEAEs (including a treatment-emergent flag) and pre-treatment AEs will also be listed.

MTEM will review all AEs recorded in the database and flag which are considered DLTs. This list will be provided to SQN prior to database lock.

5.12 Capillary Leak Syndrome, Systemic Inflammatory Response Syndrome (SIRS)/Cytokine Release Syndrome and Infusion Related Reaction Symptoms

Any CLS, SIRS/CRS and IRR symptoms recorded will be listed.

5.13 Clinical Laboratory Evaluation

All laboratory results included in version 5.0 of CTCAE will be graded according to the NCI CTCAE v5.0 severity grade. Frequencies of worst severity grade observed during treatment will be displayed in a shift from baseline table by regimen and overall.

Hematology and clinical chemistry results and changes from baseline over time will be summarized by regimen and overall. Frequencies of values below, within and above the normal reference ranges will also be summarized over time.

Urinalysis results (Normal, Abnormal Clinically Significant, Abnormal Not Clinically Significant) will be summarized over time. The results will be summarized by subject counts and percentage for each category.

If a repeat laboratory sample was drawn for a visit, the values from the repeat sample will be used for summary and analysis purposes.

Hematology, clinical chemistry and urinalysis data (including microscopy data) will be listed separately including change from baseline and reference ranges flagging all out of range values.

Other laboratory data will be listed separately including HbA1c, coagulation (activated partial thromboplastin time and international normalized ratio or prothrombin time), thyroid function (TSH and FT4), serum cytokines, histamine, complement, immunoglobulins, and serology (if applicable).

5.14 Vital Signs

Observed values and change from baseline for each vital signs parameter (heart rate, temperature, systolic blood pressure, diastolic blood pressure) will be summarized by regimen and overall.

In addition, 'substantial' changes from baseline will be categorized as follows: change from baseline in systolic/diastolic blood pressure (BP) (systolic BP [<-40 mmHg, >+40 mmHg], diastolic BP [<-20 mmHg, >+20 mmHg]) and heart rate [<-30 bpm, >+30 bpm].

All vital sign data will be listed including change from baseline and flags for substantial changes from baseline, reference ranges flagging all out of range values.

Reference ranges for vitals signs are given in the table below:

Vital Sign	**Normal Value**
Heart Rate	60-100 beats/minute
Temperature	96-100.4 (36.6 to 38C)
Systolic Blood Pressure	95-140 mm Hg
Diastolic Blood Pressure	60-90 mm Hg

5.15 Electrocardiography

For ECG data recorded on continuous scales, if more than one value is recorded per assessment, the mean value will be presented. For overall interpretation if more than one value is recorded per assessment, then the most severe of the respective readings will be taken.

ECG observed values and change from baseline by parameter (unit), will be summarized over time.

All ECG results will be listed including change from baseline values and overall interpretation.

Parameters will be presented in the same order as the CRF.

5.16 Physical Examination

Individual subject physical examination data will be listed.

5.17 Eastern Cooperative Oncology Group (ECOG)

Individual subject ECOG data will be listed.

5.18 New York Heart Association (NYHA) Function Classification

Individual subject NYHA data will be listed.

5.19 Left Ventricular Ejection Fraction (LVEF)

Individual LVEF data will be listed.

5.20 Pregnancy test

Pregnancy test details will be listed.

5.21 References

1. Cheson BD, et al. Recommendations for initial evaluation, staging and response assessment of Hodgkin and Non-Hodgkin Lymphoma. The Lugano Classification. J Clin Oncol. 2014;32:3059-67.

5.22 Changes from the Protocol Planned Analysis

- Enrolled Analysis Set has been defined in the SAP and will be used to summarize analysis sets.
- DLT evaluable population has been defined in the SAP and will be used to summarize DLTs.
- Efficacy analyses will be performed in the Efficacy Population, rather than the SAF since both an evaluable baseline and post-baseline assessment are required.
- Additional efficacy endpoints have been added:
    - Progression free survival as defined by the interval from receiving the first dose of MT-3724 to documented disease progression or death.
    - Subjects with stable disease for at least 3 months will be added to the clinical benefit group for duration of response.
- Due to limited data included in the abbreviated CSR, the following endpoints will not be summarized:
    - The incidence of TEAEs leading to dose interruption, dose delay, dose reduction, permanent discontinuation, IRR, CRS and CLS by treatment group, SOC and PT.
    - Laboratory results by treatment group using absolute values and change from baseline and incidence of laboratory data outside of the reference range.
    - The overall results of the physical examination.

- Results of vital signs over time.
- Overall interpretation of ECG results.
- Prior and concomitant medications.

Document History

SignNow E-Signature Audit Log

All dates expressed in MM/DD/YYYY (US)

Document name: MT-3724 GEMOX MES20001 Statistical Analysis Plan v1.0
Document created: 04/01/2021 15:41:38
Document pages: 19
Document ID: 24c7fe8afb5c4245925d0064b13d62b39e4eab88
Document Sent: 04/01/2021 15:47:05 UTC
Document Status: Signed
04/01/2021 16:12:36UTC

Sender: [redacted]
Signers: [redacted]
[redacted]

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Client	Event	By	Server Time	Client Time	IP Address
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SignNow Web Application	Viewed the Document	[redacted]	04/01/2021 15:42:26 pm UTC	04/01/2021 15:42:26 pm UTC	62.232.1.93
SignNow Web Application	Document Saved	[redacted]	04/01/2021 15:45:04 pm UTC	04/01/2021 15:45:04 pm UTC	62.232.1.93
SignNow Web Application	Signer Authentication Success	[redacted]	04/01/2021 15:50:25 pm UTC	04/01/2021 15:50:31 pm UTC	108.49.23.33
SignNow Web Application	Viewed the Document	[redacted]	04/01/2021 15:50:40 pm UTC	04/01/2021 15:50:47 pm UTC	108.49.23.33
SignNow Web Application	Signed the Document, Signature ID: df9aaaf3bce54434a501	[redacted]	04/01/2021 15:50:54 pm UTC	04/01/2021 15:51:01 pm UTC	108.49.23.33
SignNow Web Application	Document Saved	[redacted]	04/01/2021 15:50:55 pm UTC	04/01/2021 15:51:01 pm UTC	108.49.23.33
SignNow Web Application	Signer Authentication Success	[redacted]	04/01/2021 16:12:03 pm UTC	04/01/2021 16:12:00 pm UTC	68.132.189.171
SignNow Web Application	Viewed the Document	[redacted]	04/01/2021 16:12:27 pm UTC	04/01/2021 16:12:25 pm UTC	68.132.189.171
SignNow Web Application	Signed the Document, Signature ID: c24777299352450ca6a6	[redacted]	04/01/2021 16:12:36 pm UTC	04/01/2021 16:12:33 pm UTC	68.132.189.171
SignNow Web Application	Document Saved	[redacted]	04/01/2021 16:12:36 pm UTC	04/01/2021 16:12:33 pm UTC	68.132.189.171
SignNow Web Application	Signer Authentication Success	[redacted]	04/06/2021 07:46:19 am UTC	04/06/2021 07:46:18 am UTC	62.232.1.93
SignNow Web Application	Viewed the Document	[redacted]	04/06/2021 07:46:40 am UTC	04/06/2021 07:46:39 am UTC	62.232.1.93
SignNow Web Application	Signed the Document, Signature ID: 705da245d6d747c7a5d1	[redacted]	04/06/2021 07:47:02 am UTC	04/06/2021 07:47:00 am UTC	62.232.1.93
SignNow Web Application	Added a Text	[redacted]	04/06/2021 07:47:02 am UTC	04/06/2021 07:47:00 am UTC	62.232.1.93
SignNow Web Application	Document Saved	[redacted]	04/06/2021 07:47:02 am UTC	04/06/2021 07:47:00 am UTC	62.232.1.93