STATISTICAL ANALYSIS PLAN

Date of Plan: October 31, 2022

Based on Protocol Version:

Amendment 1, 18 Jan 2018
Amendment 2, 10 Jul 2018
Amendment 3, 28 Feb 2019
Amendment 3.1, 28 Feb 2019
Amendment 4, 30 Apr 2020
Amendment 5, 26 Mar 2021
Amendment 6, 04 May 2021
Amendment 7, 15 Sep 2021

STUDY DRUG: DSP-0509

STUDY NUMBER: BBI-DSP-0509-101

STUDY TITLE:

A First-in-Human Phase 1/2 Trial to Determine the Safety and the Pharmacokinetic Profile of DSP-0509, a Synthetic Toll-Like Receptor 7 (TLR-7) Agonist, Administered as Monotherapy and in Combination with Pembrolizumab in Adult Patients with Advanced Solid Tumors

Sponsor:

Sumitomo Pharma Oncology Inc.
84 Waterford Drive
Marlborough, MA 01752

USA

This study is being conducted in compliance with good clinical practice, including the archiving of essential documents.

SIGNATURE PAGE

Author:

[redacted] _____

Data Science, Sumitomo Pharma Oncology, Inc. Date

Approved by:

[redacted] _____

Data Science, Sumitomo Pharma Oncology, Inc. Date

[redacted] _____

Clinical Development, Sumitomo Pharma Oncology, Inc. Date

Table of Contents

LIST OF ABBREVIATIONS

Abbreviation or specialist term	Explanation
ADI	Actual Dose Intensity
AE	Adverse Event
BLRM	Bayesian logistic regression model
BMI	Body Mass Index
BOR	Best Overall Response
CR	Complete Response
CTCAE	Common Terminology Criteria for Adverse Events
DLT	Dose-limiting Toxicity
DOR	Duration of Response
ECG	Electrocardiogram
ECHO	Echocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	electronic Case Report Form
EOS	End of Study
EOT	End of Treatment
ES	Efficacy Set
FAS	Full Analysis Set
HNSCC	Head and Neck Squamous Cell Carcinoma
IDI	Intended Dose Intensity
iPR	immune Partial Response
iRECIST	immune-related Response Evaluation Criteria in Solid Tumors
MedDRA	Medical Dictionary for Regulatory Activities
MTD	Maximum Tolerated Dose
MUGA	Multigated Acquisition Scan
NCI	National Cancer Institute
ORR	Objective Response Rate
PT	Preferred Term
RDI	Relative Dose Intensity
RECIST	Response Evaluation Criteria in Solid Tumors
RP2D	Recommended Phase 2 dose
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SMPO	Sumitomo Pharma Oncology, Inc
SOC	System Organ Class
SS	Safety Set
Std Dev	Standard Deviation
TEAE	Treatment-Emergent Adverse Event
TTP	Time-to-Progression
WHO	World Health Organization

1. STUDY CONDUCT

In August 2022, Sumitomo Pharma Oncology, Inc (SMPO) decided to terminate this study and no new patients were enrolled after that decision was made. SMPO also decided to conclude this study with a synoptic CSR focusing on safety, and no efficacy analysis will be conducted.

At the time of study termination, there were no patients enrolled in the dose expansion cohort, nor any Japanese patients enrolled in any cohorts. This Statistical Analysis Plan (SAP) only applies to all patients included in this study for the dose escalation cohorts (Arm A of Monotherapy: DSP-0509 and Arm B of Combination therapy: DSP-0509 + pembrolizumab).

All statistical programs employed in the analysis, data reporting and statistical outputs will be validated by the Biostatistician/Programmer in charge of the study.

2. INTRODUCTION

This SAP details the planned methodology for summarizing data collected in the clinical study conducted under Sumitomo Pharma Oncology, Inc., protocol BBI-DSP-0509-101, and for comparing outcomes between cohorts of patients receiving various dosages of DSP-0509. The most current protocol amendment 7.2 (dated 17 Mar 2022) was developed to include Japanese patients. Since no Japanese patients were enrolled, this SAP is based on study protocol Amendment 7 (dated 15 Sep 2021). Additionally, the study protocol is a companion document to this SAP, thus aspects in the protocol unrelated to statistical issues (eg, patient eligibility criteria and descriptions of clinical materials) are not repeated here.

2.1. Study Design

This is a Phase 1 dose-escalation study (with 2 treatment arms) with a Phase 2 dose expansion to evaluate the safety, pharmacokinetics (PK), pharmacodynamics, and preliminary antitumor activity of DSP-0509 given alone or in combination with pembrolizumab in patients with advanced solid tumors.

Monotherapy Arm

- Arm A: Dose escalation, Phase 1

Combination Arms

- Arm B: Dose escalation (patients with advanced solid tumor with primary or acquired resistance to immune checkpoint inhibitors [ICIs]), Phase 1
- Arm C: Dose expansion (patients with Head and Neck Squamous Cell Carcinoma [HNSCC] with primary or acquired resistance to ICIs), Phase 2

Monotherapy Arm A: The primary objective of Monotherapy Arm A is to determine the maximum tolerated dose (MTD) or recommended Phase 2 dose (RP2D) of DSP-0509 when administered as a single agent. Dose escalation uses a Bayesian logistic regression model (BLRM) approach. DSP-0509 will be administered on Day 1 and then every 2 weeks thereafter until discontinuation.

Combination Therapy Arm B: The primary objective of Combination Arm B is to determine the RP2D of DSP-0509 when administered in combination with pembrolizumab. Dose escalation is guided by the BLRM approach. Combination Arm B will enroll patients with advanced solid tumors that are (a) metastatic or unresectable, and recurrent and/or refractory to available therapy, (b) a condition for which pembrolizumab is an approved treatment, and (c) in patients who have shown either primary or acquired resistance to an ICI. Dose escalation of DSP-0509 in combination with 400 mg pembrolizumab every 6 weeks (q6w) will start at the same dose of DSP-0509 as the highest (not exceeding the MTD) level tested in the combination regimen with 200 mg pembrolizumab every 3 weeks (q3w). Upon completion of the DLT evaluation period for the first DSP-0509 dose level tested in combination with 400 mg pembrolizumab q6w in newly enrolled patients, if this dose level is found not to exceed the MTD, any ongoing patients receiving DSP-0509 in combination with 200 mg pembrolizumab q3w will be allowed, at the investigator's discretion, to transition to the 400 mg pembrolizumab q6w regimen, while maintaining the originally assigned DSP-0509 dose level.

Combination Therapy Arm C: The primary objective of Combination Arm C is to determine the Objective Response Rate (ORR) of DSP-0509 when administered in combination with pembrolizumab. Combination Arm C will enroll patients with HNSCC tumors that are (a) metastatic or unresectable, and recurrent and/or refractory to available therapy, (b) in patients who have been treated with pembrolizumab or other PD 1 or PD-L1 inhibitors in monotherapy, and (c) in patients who have subsequently shown either primary or acquired resistance to ICIs.

DSP-0509 will be administered on Day 1 and q2w thereafter until discontinued. Pembrolizumab will be administered on Day 1 and q6w thereafter until discontinued.

2.2. Study Objectives and Endpoints

Complete details on how endpoints are calculated within treatment groups are presented in the subsections below.

Table 1. Primary objectives and endpoints

Primary Objectives	Endpoints
Monotherapy Arm A - Dose Escalation (Phase 1):	
To determine the safety, tolerability, and maximum tolerated dose (MTD) of DSP-0509 administered intravenously (IV) as a single agent in patients with advanced solid tumors To identify a recommended Phase 2 dose (RP2D) of DSP-0509 monotherapy for patients with advanced solid tumors.	Incidence of dose-limiting toxicities (DLTs) within the first 6 weeks of dosing Incidence and severity of treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) using National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) Incidence of dose interruption, dose reduction, and dose intensity Changes in clinical laboratory values (hematology, clinical chemistry, urinalysis), electrocardiogram (ECG) parameters, multigated acquisition (MUGA) scan/echocardiograms (ECHO) parameters
Combination Arm B - Dose Escalation (Phase 1):	
To determine the safety, tolerability, and MTD of DSP-0509 administered IV in combination with pembrolizumab for patients with advanced solid tumors who have shown primary or acquired resistance to immune checkpoint inhibitors (ICIs) To identify an RP2D of DSP-0509 when given in combination with pembrolizumab for such patients	Incidence of DLTs within the first 6 weeks of dosing Incidence and severity of TEAEs and SAEs using NCI CTCAE Incidence of dose interruption, dose reduction, and dose intensity Changes in clinical laboratory values (hematology, clinical chemistry, urinalysis), ECG parameters, MUGA scan/ECHO parameters
Combination Arm C – Dose Expansion (Phase 2):	
To evaluate the preliminary antitumor activity of DSP-0509 in combination with pembrolizumab in patients with HNSCC who have shown primary or acquired resistance to ICIs	Objective response rate (ORR), as assessed by Response Evaluation Criteria in Solid Tumors (RECIST), v1.1 and by Immune RECIST (iRECIST, modified RECIST for immunotherapy studies)

Safety Assessments:

Adverse events (AEs) will be collected from the time the patient signs informed consent to the End of Study (EOS) visit scheduled for 30 days after the last dose of study drug. AEs will be assessed according to NCI CTCAE v5.0. Additional safety assessments will include MUGA scans, ECHO, 12 lead ECGs, chest x-rays, vital signs, clinical laboratory tests, and ocular examinations (slit lamp, fundoscopy, visual field testing).

Efficacy Assessments:

SMPO decided to terminate this study with a synoptic CSR focusing on safety, and no efficacy analysis will be conducted.

3. ANALYSIS SET

Full Analysis Set

The Full Analysis Set (FAS) in this study consists of all patients who entered the study and received one dose of study treatment (DSP-0509 or pembrolizumab).

Safety Set

The safety set (SS) is the same as the FAS. Safety analysis set will be used for all safety related analyses such as AE, concomitant medication, laboratory tests, and vital signs and drug exposure evaluation.

Dose-Limiting Toxicity (DLT) Set

The DLT population will consist of all patients who met the prespecified criteria for being evaluable for DLT detailed in the following.

The DLT period for dose-escalation review is from Study Days 1 through 42. During this period, treated patients will be monitored closely for AEs in general and for DLTs in particular.

A patient will be considered evaluable for DLT if observed for 42 days following the first dose of DSP-0509 in monotherapy and with pembrolizumab in combination. Patients discontinued during the DLT period due to DLTs are considered as evaluable for DLT.

Patients who do not meet the above criteria will be considered non-evaluable for DLT and may be replaced to provide sufficient evaluable patients to fully assess a given dose level.

4. STATISTICAL METHODOLOGY AND STATISTICAL ANALYSES

At the time of study termination, there were no patients enrolled in the dose expansion cohort, nor any Japanese patients enrolled in any cohorts. This SAP only applies to all patients included in this study.

Statistical analyses will be descriptive in nature; no formal statistical hypothesis testing will be performed. Statistical analyses will be carried out by using SAS Version 9.4 or higher. Whilst every effort has been made to pre-specify all analyses in this SAP, if any additional exploratory analyses are found to be necessary, the analyses and the reasons for them will be detailed in the clinical study report (CSR).

4.1. Statistical Methods and Analytical Considerations

4.1.1. Statistical Methods

This section describes analysis issues that relate to all or some of the analysis sections that follow. It describes general guidelines for analysis as well as the following.

Patient data will be grouped for summarization within each dose level and each cohort (Monotherapy Arm A: DSP-0509 and Combination Arm B: DSP-0509 + pembrolizumab) of the dose-escalation phase. Details of dose levels are listed in the following.

Dose escalation for monotherapy Arm A

- A1. DSP-0509 at 0.3 mg, 3 minutes, q1w
- A2. DSP-0509 at 1.0 mg, 3 minutes, q1w
- A3. DSP-0509 at 1.5 mg, 3 minutes, q1w
- A4. DSP-0509 at 1.5 mg, 10 minutes, q2w
- A5. DSP-0509 at 2.4 mg, 10 minutes, q2w
- A6. DSP-0509 at 3.5 mg, 10 minutes, q2w

Dose escalation for combination therapy Arm B

- B1. DSP-0509 at 0.3 mg 10 minutes, q1w + pembrolizumab (200 mg, q3w)
- B2. DSP-0509 at 0.3 mg, 10 minutes, q2w + pembrolizumab (200 mg, q3w)
- B3. DSP-0509 at 1.0 mg, 10 minutes, q2w + pembrolizumab (200 mg, q3w)
- B4. DSP-0509 at 1.0 mg, 10 minutes, q2w + pembrolizumab (400 mg, q6w)

Baseline will be defined as the last evaluable/non-missing observation/assessment prior to the first dose of study drug. For patients ongoing at the time of analysis, the last dose date will be considered the date of the most recent study visit in the database for that patient where a dose of study drug was recorded.

Adverse events will be graded by the Investigator based on the National Cancer Institute (NCI) CTCAE, Version 5.0, and will be coded for summarization using the Medical Dictionary for Regulatory Activities (MedDRA® Version 21.0 or higher). Concomitant medications will be coded using the World Health Organization (WHO) Drug Dictionary (Enhanced + Herbal B3 March 2018).

Tabulations will be produced for appropriate demographic, baseline, and safety parameters. Continuous variables will be summarized by reporting the number of observations, mean, standard deviation (Std Dev), median, minimum, and maximum. Categorical variables will be summarized using the number and

percentage of patients within a particular category, where the denominator is the number of non-missing values for the variable at the given time point (unless otherwise specified).

Means and medians will be presented to 1 more decimal place than the recorded data. The Std Devs will be presented to 2 more decimal places than the recorded data. Confidence intervals about a parameter estimate will be presented using the same number of decimal places as the parameter estimate.

By-patient data listings will be produced for data collected on the electronic Case Report Forms (eCRFs) throughout the study (eg, labs). All data listings that contain an evaluation date will contain a relative study day (Study Day). Pre-treatment and on-treatment study days are numbered relative to the day of the first dose of study medication, which is designated as Day 1. The preceding day is Day -1, the day before that is Day -2, etc.

In general, the listings will be sorted by study arm, dose level, patient number, and assessment date (and time) if applicable.

If a patient has multiple assessments (eg, multiple laboratory results) at a given time point (planned, repeat, and unscheduled), only the earliest non-missing value will be included in summary tables unless specified otherwise. The other values will be included in the listings, but not the summary table.

4.1.2. Visit Windows

All data will be tabulated per the nominal visit as recorded on the eCRF, even if the assessment is outside of the visit window. Unless otherwise stated in the analysis sections below, unscheduled visits will be included in data listings only.

4.1.3. Handling of Dropouts and Missing Data

In general, missing values will not be replaced by imputed values unless indicated otherwise.

The following general rules will be used for AEs:

- If the start day is missing but the start month and year are complete, an AE will be excluded as being treatment-emergent only if the start month/year of the AE is before the month/year of study drug administration or if the stop date/time of the event is before study drug administration.
- If the start day and month are missing but the start year is complete, an AE will be excluded as being treatment-emergent only if the start year of the AE is before the year of study drug administration or if the stop date/time of the event is before study drug administration.
- If the start date is completely missing, an AE will be considered treatment-emergent unless the stop date is before study drug administration.
- If the relationship to study treatment is missing, then that AE will be assumed to be related to treatment.

For partial dates of medications, the following approach will be taken:

- If the start day is missing but the start month and year are complete, a medication will be excluded as being concomitant only if the start month/year of the medication is before the month/year of study drug administration and if the stop date (either full date, month and year if missing day, or year if missing month and day) is before study drug administration.
- If the start day and month are missing but the start year is complete, a medication will be excluded as concomitant only if the start year of the medication is before the year of study drug administration and if the stop date (either: full date, month and year if missing day, or year if missing month and day) is before study drug administration.

For cancer, surgical, or medical history, a date of first diagnosis with incomplete dates will be considered as:

- Day is missing then day is set to the first day of the month;
- Day is missing and month is missing then date will be set to 01 January;
- Complete date is missing then will be set to missing.

4.2. Patient Characteristics

4.2.1. Patient Disposition

All patients who provide informed consent will be accounted for in this study. Disposition information for all patients will be provided in patient listings.

Patient disposition will be presented by dose level and overall for Monotherapy Arm A, Combination Arm B, and for Arm A and Arm B combined. Tabulation will include the number of patients screened, number (%) of patient's screen failed, number (%) of patients included in various analysis sets (FAS, SS and DLT set), as well as the number (%) of patients discontinuing study treatment and the reason for treatment discontinuation. In addition, this table will summarize the number of patients discontinuing the study and the primary reason for study discontinuation.

Patients excluded from the various analysis sets will be listed by dose level.

4.2.2. Protocol Deviations

Protocol deviation data will not be summarized or listed.

4.2.3. Demographic and Baseline Characteristics

Summaries of baseline characteristics will be statistics that are appropriate for continuous (eg, age, height, weight) and categorical (eg, sex, race, ethnicity) variables. Separate summaries may be produced for the safety and per-protocol patient populations. Patient age in years on the date of enrollment will be calculated by dividing the number of days since birth (Day 1) by 365.25 and rounded down to the nearest integer.

The following variables will be listed and summarized using both continuous and categorical descriptive statistics:

- Age (years)
- Age group (< 65 years and ≥ 65 years)
- Gender
- Ethnicity
- Race
- Height (cm)
- Weight (kg)
- BMI (kg/m^2)

4.2.4. Non-Cancer Related Medical/Surgical History

Medical/Surgical History as recorded at screening will be listed by system organ class (SOC) and preferred term (PT), and sorted alphabetically by SOC and by decreasing frequency of PT within each SOC using MedDRA coding dictionary version 21.0 or later in the summary table. Medical history events ongoing at the time of informed consent will be included.

Medical/surgical history data listings will be sorted by study arm, dose level, patient ID, onset date, end date, SOC, and PT.

4.2.5. Cancer History

Cancer history will be collected as a baseline characteristic. The smoking history, primary cancer type, time since initial cancer diagnosis in days, time since most recent relapse/progression, histological grade, predominant histology, stage at initial diagnosis, stage at time of study entry, and staging system will be listed by study arms and dose level.

4.2.6. Prior and Concomitant Medications

Prior medications will be defined as any medication taken prior to the first dose of study drug.

Concomitant medications are defined as any medication taken on or after the first dose of study drug. Medications with a start date prior to the first dose of DSP-0509 and an end date after the first dose of DSP-0509 (or ongoing) will be classified as both a prior medication and a concomitant medication.

Medications missing both start and stop dates, having a start date prior to the first dose of study drug and a missing stop date or having a stop date on or after the last dose of study drug and a missing start date will be counted as a concomitant medication.

Prior and concomitant medications will be coded using the WHO Drug Dictionary (Enhanced + Herbal B3 March 2018), and patient incidence will be listed by Anatomic Therapeutic Class (ATC) level 2 term (ATC2) and preferred term, by study arms and dose level using the safety set.

All prior, concomitant, and post medications will be included in a by-patient data listing.

4.2.7. Concomitant Procedures

A listing will be created to present the relevant information on concomitant procedures, including the procedure name, date, relationship with the disease, and reason for the procedure.

4.2.8. Prior Cancer Therapies

Prior cancer therapies will be listed separately from other prior and concomitant medications. The classification of the cancer therapies includes regimen number, drug name, best response, and reason for stopping captured on the Prior Cancer Therapy eCRF page.

The listing will be ordered by study arm, dose level, patient ID, and the start date of the therapy.

4.2.9. Prior Cancer Surgery

Prior cancer surgeries will be listed separately from other prior and concomitant procedures. It will include surgery description, and type of procedures. The listing will be ordered by study arm, dose level, patient ID, and the date of surgery.

4.2.10. Prior Radiation Therapies

Prior radiation therapies will be listed separately from other prior and concomitant therapies. The classification of the radiation therapies includes therapy received, anatomic site, total dose received, and settings captured on the Prior Radiation Therapy eCRF page.

The listing will be ordered by study arm, dose level, patient ID, and the start date of the therapy.

4.3. Study Drug Exposure

Study drug exposure will be presented by dose level and overall, for Monotherapy Arm A and Combination therapy Arm B.

The total cumulative dose (mg) received and the duration of exposure will be summarized, where duration of exposure will be calculated as:

Duration of Exposure (weeks) = (Last dose date – first dose date + 1) / 7.

Treatment compliance of DSP-0509 will be presented for the induction phase and the maintenance phase of the treatment. Compliance in terms of actual dose intensity (ADI) and relative dose intensity (RDI) will be calculated as follows:

Actual Dose Intensity: The ADI is based on the dose (mg) taken by the patient and the duration of exposure (weeks) during the induction phase or the maintenance phase and given as:

ADI (mg/week) = Total dose (mg) received/duration (weeks) of exposure during the induction phase or maintenance phase.

Intended Dose Intensity (IDI): The IDI is based on the dose level assigned to the patient and the dose schedule. During the induction phase, IDI will be equal to the assigned dose level as the dose schedule is q1w. During the maintenance phase, IDI will be one-half, one-third or one-six of the assigned dose level, corresponding to the q2w, q3w or q6w dose schedule.

Relative Dose Intensity: The RDI (%) is based on the ADI and the RDI given as follows: RDI (%) = ADI/IDI * 100.

Dose exposure data will be also provided by a data listing ordered by study arm, dose level, patient ID, and the study day.

4.4. Efficacy Analysis

No efficacy analysis will be conducted.

Tumor response assessment by iRECIST/RECIST, targeted/non-target/new lesion assessment by RECIST will be listed in settings captured on the eCRF page.

4.5. Safety Analysis

The primary objective for this study is to determine the safety, tolerability, and MTD of DSP-0509. All safety analyses will be performed using the Safety Set, unless otherwise specified. Relevant data supporting safety analyses will be listed by patient within DSP-0509 dose.

4.5.1. Adverse Events

Adverse events will be graded according to the NCI CTCAE Version 5.0 coded using the MedDRA coding system, version 21.0, and displayed in tables and data listings by MedDRA SOC and PT.

Analyses of AEs will be performed for those events that are considered treatment-emergent, where treatment-emergent adverse event (TEAE) is defined as any condition that occurs after administration of the first dose of study drug or that is present at baseline but worsens in intensity after the first dose of study drug.

If the start date of an AE is partially or completely missing, the date will be compared as far as possible with the date of the start of administration of study drug. The AE will be assumed to be treatment-emergent if it cannot be definitively shown that the AE did not occur or worsen during the treatment-emergent period (worst case approach).

Adverse events are summarized via patient incidence rates; therefore, in any tabulation, a patient contributes only once to the count for a given SOC or PT (ie, the most related occurrence or the most intense occurrence). Missing relationship will be considered related to study drug.

An overall summary of the number and percentage of patients reporting TEAEs, treatment-related TEAEs, serious TEAEs, treatment-related serious TEAEs, Grade 3 (or worse) TEAEs, AEs considered to be DLTs, TEAEs leading to dose withdrawal, and fatal TEAEs will be presented. An AE will be considered as treatment-related if it is possibly, probably, or definitely related to the study treatment.

TEAE incidence summary tables will be produced and will include:

- Overall summary of TEAEs
- TEAEs by SOC and PT
- Serious TEAEs by SOC and PT
- DSP-0509-related TEAEs by SOC and PT
- DSP-0509-related serious TEAEs by SOC and PT
- TEAE with toxicity Grade 3 or higher by SOC and PT

The summaries presenting incidence of AEs by SOC and PT will be ordered by overall descending frequency of SOC and then, within an SOC, by overall descending frequency of PT for the overall patients.

No formal hypothesis-testing analysis of AE incidence rates will be performed. All AEs occurring on-study will be provided in data listings. By-patient listings also will be provided for the following: DLTs, DSP-0509-related AEs, SAEs, DSP-0509-related SAEs, AEs leading to DSP-0509 discontinuation, and AEs leading to death.

4.5.2. COVID-19

Patients who have tested positive for COVID-19 are identified and relevant information collected. Any patient-reported illness of COVID-19 during the study is recorded as an AE. COVID-19 test results will be reported separately in a listing in parameters captured on eCRF page.

4.5.3. Physical Examination

Physical examinations will be conducted according to the Schedule of Assessments. A physical examination will include examination of the skin; head, eyes, ears, nose, throat (HEENT); chest including the lungs and the heart; abdomen; neurologic, and extremities and areas of major lymph node chains. Physical examination results will be reported in a physical examination listing.

4.5.4. Vital Signs

Vital signs will include systolic and diastolic blood pressures, pulse, respiratory rate, temperature, and weight.

Body temperature will be summarized in °C. If body temperature is recorded as °F, then temperature will be converted to °C as follows:

Temperature (°C) = (5/9) x [Temperature (°F) - 32]

A listing of vital signs results will be presented for all Safety Set patients.

4.5.5. Electrocardiogram

A 12-lead ECG will be obtained in triplicate during the study. Electrocardiogram data will be provided in a by-patient listing.

4.5.6. Laboratory Parameters

All summaries of hematology and chemistry will be based on the results of Standard International (SI) system of units. Summary tables for hematology and chemistry laboratory variables will include the descriptive statistics for results in SI units and the corresponding change from baseline for all continuous variables by visit.

All laboratory results in SI units will be presented in data listings. Tests will be listed in alphabetical order within their respective panels (hematology, clinical chemistry). Abnormal values will be flagged.

Urinalysis, coagulation, pregnancy testing, and serology testing data will be listed only.

4.5.7. Evaluation of Eastern Cooperative Oncology Group (ECOG) Performance Status

The actual value of ECOG performance status score and change from baseline to each visit will be descriptively summarized as a continuous variable by visit. A by-patient listing of all ECOG results will be listed by treatment group and dose level.

4.5.8. Echocardiogram/Multigated Acquisition (MUGA) Scan

Echocardiogram and MUGA results including left ventricular ejection fraction (LVEF) (%) will be presented in a by-patient listing.

4.5.9. Chest X-rays

Chest x-rays will be performed at screening to rule out pulmonary disorders and assess patient's eligibility as described in the Schedules of Assessments. Chest x-rays can be performed during the study at the Investigator's discretion on an as-needed basis. Chest x-ray data will be presented in a by-patient listing.

4.5.10. Ocular Examinations

Ocular examinations, including slit lamp examinations, visual field testing, and fundoscopy will be performed by a qualified ophthalmologist at Screening, Day 29, and the EOT visit as described in the Schedules of Assessments to monitor for potential ophthalmological toxicity. Ocular examinations data will be presented in a by-patient listing.