PDS Biotechnology

Statistical Analysis Plan

Sponsor Name: PDS Biotechnology Corp

Protocol Number: VERSATILE-002 (PDS0101-HNC-201)
Protocol Title: A Phase 2, Open-Label, Multi-Center Study of PDS0101 (R-DOTAP [Versamune®] + HPVmix) and Pembrolizumab (KEYTRUDA®) Combination Immunotherapy in Subjects with Recurrent and/or Metastatic Head and Neck Cancer and High-Risk Human Papillomavirus-16 (HPV16) Infection

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Revision History

Version #	Date (DD-Mmm-YYYY)	Document Owner	Revision Summary
Version 1.0	02-May-2022	[redacted]	Finalized version.
Version 2.0	21-Jul-2023	[redacted]	Finalized version.
Version 3.0	19-Nov-2024	[redacted]	• Administrative updates • Additional analyses/outputs for ITT and mITT populations • Clarification of the rules to the confirmed BOR analysis • Inclusion of Durable Response Rate at 6 and 12 months • Definition of duration of stable disease
Version 4.0	ddMMMyyyy	[redacted]	• Administrative updates • Clarified ITT population definition

I confirm that I have reviewed this document and agree with the content.

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1. Glossary of Abbreviations

Abbreviation	Description
AE	Adverse event
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical
BMI	Body Mass index
BOR	Best overall response
BUN	Blood urea nitrogen
cBOR	Best overall response based on confirmed CR or confirmed PR
CD4	Cluster of Differentiation 4
CD8	Cluster of Differentiation 8
CI	Confidence Interval
COVID-19	Coronavirus Disease 2019
CPI	Checkpoint inhibitor
CPS	Combined positive score
CR	Complete response
CRF	Case report form
CTMS	Clinical Trial Management System
DCR	Disease Control Rate
DLT	Dose-limiting toxicity
DMC	Data Monitoring Committee
DOR	Duration of response
DRESS	Drug Rash with Eosinophilia and Systemic Symptom
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
EFF	Efficacy analysis population
EU	European Union
FT3	Free Triiodothyronine
FT4	Free thyroxine
HIV	Human Immunodeficiency Virus
HLA	Human leukocyte antigen

Abbreviation	Description
HNSCC	Head and Neck Cancer also Head and Neck Squamous Carcinoma Cancer
HPV	Human Papilloma Virus
HPV-16	Human Papilloma Virus-16
ICH	International Council for Harmonization
IHC	Immunohistochemistry
INR	International normalized ratio
IRT	Interactive Response Technology
ITT	Intent-to-Treat population
IV	Intravenous
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified Intent-to-Treat
N/A	Not Applicable
NE	Not Evaluable
NCI-CTCAE	National Cancer Institute – Common Terminology Criteria for Adverse Events
ORR	Objective response rate
OS	Overall survival
PBMC	Peripheral Blood Mononuclear Cells
PD-L1	Programmed cell death ligand 1
PFS	Progression free survival
PR	Partial response
PT	Preferred Term
PTT	Partial Thromboplastin Time
Q3W	Every three weeks
QTc	Corrected QT Interval
R-DOTAP	R-enantiomer of 1,2-dioleoyl-3-trimethylammonium-propane chloride
RECIST	Response evaluation criteria in solid tumors
SAE	Serious Adverse Event
SAF	Safety analysis population
SAP	Statistical Analysis Plan
SC	Subcutaneous
SD	Stable Disease

Abbreviation	Description
SI	Standard International System of Units
SJS	Stevens-Johnson Syndrome
SOC	System organ class
SOP	Standard operating procedure
T1DM	Type 1 Diabetes Mellitus
T3	Triiodothyronine
TEAE	Treatment-emergent adverse event
TEN	Toxic Epidermal Necrolysis
TFL	Table, Figure and Listing
TPS	Tumor proportion score
TSH	Thyroid stimulating hormone
uBOR	Best overall response based on observed CR or observed PR, also referred to unconfirmed best overall response
UK	United Kingdom
WHODD	World Health Organization - Drug Dictionary

2. Purpose

The purpose of this statistical analysis plan (SAP) is to ensure that the data listings, summary tables and figures which will be produced, and the statistical methodologies that will be used, are complete and appropriate to allow valid conclusions regarding the study objectives.

This SAP is adhering to the proper regulatory guidelines and the most recent International Council for Harmonization (ICH) guidelines. This SAP is consistent with the most recent version of the Protocol (Version 4.1 Amendment 5.0 dated October 10th, 2022) and will be updated as necessary with subsequent protocol amendments.

In the event that a discrepancy is found between the descriptions in the statistical section of the protocol and this document, the description in this document supersedes the description in the statistical section of the protocol.

The Sponsor plans to finalize this SAP prior to database lock. If any changes occur after SAP finalization, the deviations will be documented in a Reviewer Guide and/or in a note to file.

2.1. Responsibilities

The Sponsor or designee will perform the statistical analyses and are responsible for the production and quality control of all tables, figures and listings (TFLs).

2.2. Timings of Final Analyses

The primary analysis of safety and efficacy is planned after all subjects complete the final study visit or terminate early from the study and all relevant study data have been processed and integrated into the final locked database.

2.3. Timing of Interim Analyses

An independent data monitoring committee (DMC) will review descriptive summaries of accumulating safety, subject disposition, and efficacy data (futility) according to a pre-specified schedule defined in the DMC charter Section 12. Additional ad-hoc DMC meeting and analysis could be requested by DMC as needed. The following is a brief summary of the planned interim analyses for DMC, and description in detail of analysis scope can be found in the DMC charter.

1) Milestone interim analysis:
   - Milestone 1: Lead-in Safety Cohort Review
   - Milestone 2: Stage 1 futility analysis per Simon's 2-stage design
   - Milestone 3: Stage 2 futility analysis per Simon's 2-stage design

2) General safety data review interim analysis – Every 4 to 5 months

3. Study Objectives

3.1. Primary Objective

- To assess the preliminary activity of the combination of pembrolizumab (KEYTRUDA®) and PDS0101 in checkpoint inhibitor (CPI) naïve or refractory subjects with recurrent and/or metastatic head and neck squamous cell carcinoma (HNSCC) and high-risk human papilloma virus-16 (HPV-16) infection as measured by confirmed Best Overall Response (cBOR).

3.2. Secondary Objectives

In both CPI naïve and CPI refractory subjects:

- Assess Progression-Free Survival (PFS) per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1.
- Assess overall survival (OS).
- Assess safety and tolerability of the combination of pembrolizumab and PDS0101.

3.3. Exploratory Objectives

- Duration of Response (DOR) for all subjects seen at time of disease progression or Cycle 35.
- Evaluate anti-HPV-16 E6 and E7 immune responses elicited by treatment with pembrolizumab and PDS0101 using IsoPlexis Functional Proteomics at Days 85 (Cycle 5) and 253 (Cycle 13), compared to baseline.

3.4. Brief Description

This is a Phase 2, open-label, single-arm, non-randomized study of a combination of pembrolizumab and PDS0101 in HPV-16 DNA positive subjects with recurrent and/or metastatic HNSCC to be conducted at multiple centers in the United States, the United Kingdom (UK) and the European Union (EU).

The study is designed to evaluate the safety and efficacy of pembrolizumab and PDS0101 when administered in combination. Subjects will be enrolled into either the CPI naïve group or the CPI refractory group, and up to 95 subjects in total (54 CPI naïve subjects and 41 CPI refractory subjects) will be enrolled in the order in which they are screened and meet eligibility criteria utilizing a Simon's 2-Stage Optimum Design which is described in Section 3.6 of this SAP.

A regimen of pembrolizumab (200 mg) and PDS0101 (3.0 mg R-enantiomer of 1,2-dioleoyl-3-trimethylammonium-propane chloride (R-DOTAP [Versamune®]) and 2.7 mg HPV16 mix) will be administered every 3 weeks (Q3W) for the first 4 Cycles: intravenous (IV) infusion of pembrolizumab followed by subcutaneous (SC) injections of PDS0101 on Days 1 (Cycle 1), 22 (Cycle 2), 43 (Cycle 3), and 64 (Cycle 4). The fifth and final PDS0101 injection will be administered again on Day 232 (6 months after the 4th vaccination, Cycle 12 of pembrolizumab).

Pembrolizumab administration will continue every 3 weeks from study start (Day 1, Cycle 1) until unacceptable toxicity or disease progression. Subjects without disease progression will be treated for up to 35 Cycles.

For each subject, this study will include a pre-screening period between Week -6 and -4, screening period during Days -28 to -1, a treatment period during Days 1 to 715 (up to 35 cycles), a safety follow-up period of 30 days (Days 715 to 745), and a survival follow-up phase. The duration for an individual subject's participation in the study during the treatment phase will be up to approximately 24 months (35 cycles + 30-day follow-up), excluding screening. Once a subject discontinues study drug treatment, the subject enters the overall survival follow-up phase until death, withdrawal of consent, or the end of the study, whichever occurs first.

A lead-in cohort of 12 subjects will be enrolled to assess safety of the combination of pembrolizumab with PDS0101. There will be a pause in enrollment after the 12th subject is deemed eligible for treatment until the DMC provides their recommendations of the safety of the study combination treatment. Accrual will resume after the recommendation of the DMC regarding safety, dose regimen, and possible subsequent cohorts.

These initial 12 subjects will be monitored through three weeks after the first administration of pembrolizumab and PDS0101 for any signs of dose-limiting toxicity (DLT). At the end of the assessment period (Cycle 1/21 days; Day 1 to 21), the DMC will assess the DLTs and safety of the combination treatment. The DMC may elect to assess a second cohort of 12 subjects depending on the data from the first 12 subjects.

Subjects that experience a DLT related to PDS0101 (possibly/probably/definitely related) may continue with a dose reduction of PDS0101 or be discontinued. For dose reduction, subjects will be administered only 1 injection of 0.5 mL of PDS0101 (1.5 mg R-DOTAP with 1.35 mg HPV16 mix) per vaccination SC into the upper anterior arm. PDS0101 administration will be halted upon any further unacceptable toxicity of the combination that includes a reduced dose of PDS0101 (Protocol Section 7.1).

Immune monitoring assessments will be performed prior to the first study combination treatment (baseline), and on Days 85 (Cycle 5, 21 days following vaccination #4) and 253 (Cycle 13, 21 days following final vaccination #5).

3.5. Subject Selection

Inclusion criteria for the study is detailed in Protocol Section 8.1 and exclusion criteria for the study is detailed in Protocol Section 8.2.

3.6. Determination of Sample Size

Statistical assumptions used to determine sample size for this study are developed based on the KEYNOTE-048 study results (Burtness et al. 2019). The KEYNOTE-048 study enrolled 301 HNSCC subjects with combined positive score (CPS) ≥1 in the Pembrolizumab monotherapy arm and observed an objective response rate (ORR) of 19.1% (90% Confidence Intervals [CI]: 15.1%, 23.6%).

The study will enroll CPI naïve and CPI refractory subjects and so a separate sample size is calculated for each group. For CPI naïve subjects, it is expected that the combination therapy will yield 1.7 times increase in ORR over monotherapy (70% increase in ORR), thus the expected ORR for combination therapy is approximately 32.5% in CPI naïve subjects. For CPI refractory subjects, we anticipate a lower ORR since these subjects have already experienced progression or recurrence after treatment with CPIs. Given this consideration, the CPI naïve and CPI refractory groups will be examined separately as described below.

CPI Naïve

A Simon's 2-Stage Optimum Design (Simon, 1989) will be used to determine the enrollment for the CPI naïve subjects. Setting the type I error rate to 5% (alpha=0.05), and the power to 80%, we will test the true objective response rate (ORR) of 17% (null hypothesis) versus the alternative ORR of 33% (alternative hypothesis) for CPI naïve subjects.

We will enroll 17 subjects in the first stage. If 3 or fewer responses (complete response [CR] or partial response [PR]) are observed after 17 subjects in Stage 1 have been on the study for at least 6 months (Cycle 10), the study may be stopped for futility, or regulatory agency feedback will be incorporated per Sponsor's discretion. If 4 or more responses are observed, the study will enroll an additional 37 subjects for a total of 54 subjects. At the completion of the second stage, the combination of PDS0101 with pembrolizumab will be considered efficacious if at least 14 responses have been observed out of the 54 subjects enrolled. If 13 or fewer responses are observed after 54 subjects have been on the study for at least 6 months (Cycle 10), the study may be stopped for futility, or regulatory agency feedback will be incorporated per Sponsor's discretion.

CPI Refractory

A Simon's 2-Stage Optimum Design will be used to determine the enrollment for the CPI refractory subjects. Setting the type I error rate to 5% (alpha=0.05), and the power to 90%, we will test the true ORR of 5% (null hypothesis) versus the alternative ORR of 20% (alternative hypothesis) for CPI refractory subjects.

We will enroll 21 subjects in the first stage. If 1 or 0 responses (CR or PR) are observed after 21 subjects have been on the study for at least 6 months (Cycle 10), the study may be stopped for futility, or regulatory agency feedback will be incorporated per Sponsor's discretion. If 2 or more responses are observed, the study will enroll an additional 20 subjects for a total of 41 subjects. At the completion of the second stage, the combination of PDS0101 with pembrolizumab will be considered efficacious if at least 5 responses have been observed out of the 41 subjects enrolled. If 4 or fewer responses are observed after 41 subjects have been on the study for at least 6 months (Cycle 10), the study may be stopped for futility or regulatory agency feedback will be incorporated per Sponsor's discretion.

The following table summarizes the assumptions of the Simon's 2-Stage Design for the enrollment of the CPI naïve and CPI refractory subjects:

Table 1 - Simon's 2-Stage Optimum Design Assumptions

CPI Group	Alpha Beta	Response Probability of Poor Drug (P0)	Response Probability of Good Drug (P1)	Total Sample Size	Sample Size at Stage 1	Sample Size at Stage 2	Stop if Stage 1 Response ≤	Reject Treatment if Total Responses ≤
CPI naïve	Alpha=0.05, Beta=0.20 (power=80%)	17%	33%	54	17	37	3	13
CPI Refractory	Alpha=0.05, Beta=0.10 (power=90%)	5%	20%	41	21	20	1	4

Thus, if significant efficacy were observed in both groups at completion of stage 1 of enrollment, expansion to a total of 95 subjects would be allowed. These sample size and power estimations were performed using PASS 2020, v20.0.1.

3.7. Treatment Assignment & Blinding

Since the study is an open-label, one-armed study, there is no blinding regarding the treatment. Study drug treatment will be managed using an Interactive Response Technology (IRT) system that will provide medication identifications for each component of the investigational product at each visit for each eligible subject.

3.8. Administration of Study Medication

The combination treatment of pembrolizumab and PDS0101 to be used in this study are outlined below in Table 2. Details of study treatment are described in Section 9.1 of the Protocol.

Table 2 - Study Treatments

Study Treatment Name	Dosage Formulation	Unit Dose Strength(s)	Dosage Level(s)	Route of Admin-istration	Regimen/ Treatment Phase/ Vaccination Regimen	Sourcing
Pembrolizumab (MK-3475)	Solution for infusion	100 mg/vial	200 mg Q3W	IV infusion	Day 1 of each Cycle (3-week Cycles) up to 35 Cycles	Provided by PDS Biotech
PDS0101 (R-DOTAP [Versamune®])	Solution for subcutaneous injection	3.0 mg	3.0 mg	SC injection	Days 1, 22, 43, 64 and 232 (Cycles 1-4 & 12)	Provided by PDS Biotech
PDS0101 (HPVmix)	Solution for subcutaneous injection	2.7 mg	2.7 mg	SC injection	Days 1, 22, 43, 64 and 232 (Cycles 1-4 & 12)	Provided by PDS Biotech

3.9. Study Procedures and Flowchart

Study procedures/assessments and the schedule of procedures/assessments is also detailed in Protocol Section 10.

4. Endpoints

4.1. Primary Efficacy Endpoint

- The primary efficacy endpoint will be the best overall response (BOR) of confirmed complete response (CR) or confirmed partial response (PR) per RECIST 1.1 of the combination of pembrolizumab and PDS0101.

4.2. Secondary Efficacy Endpoints

- PFS per RECIST 1.1 in all subjects at 9, 12 and 24 months.
- OS in all subjects in 9, 12, and 24 months.

4.3. Exploratory Efficacy Endpoints

- Duration of response (DOR) for all subjects who demonstrated best overall response based on confirmed CR or confirmed PR (cBOR).
- Disease control rate (DCR) for all subjects who demonstrated cBOR of CR, PR or SD.
- Duration of stable disease for subjects with cBOR of SD.
- Change from Baseline in anti-HPV16 E6 and E7 immune responses elicited by treatment with pembrolizumab and PDS0101 using IsoPlexis Functional Proteomics at Days 85 (Cycle 5) and 253 (Cycle 13).
- Subgroup analysis by programmed cell death ligand 1 (PD-L1) expression levels (CPS <1, CPS 1 – 19, CPS ≥20, CPS ≥1) for the following clinical outcomes:
    - BOR, DOR, DCR, PFS, OS

4.4. Safety and Exposure Endpoints

- Extent of Exposure
- Adverse Events
    - Incidence of treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (SAEs), PDS0101 related TEAEs and combination treatment related TEAEs.
- Laboratory Assessments (hematology, chemistry, urinalysis)
    - Observed values and change from baseline values
- Vital Sign Assessments (blood pressure, respiratory rate, pulse rate, body temperature, oxygen saturation, weight)
    - Observed values and change from baseline values
- Electrocardiogram (ECG)
    - Observed values and change from baseline values

5. Analysis Populations

5.1. Screened Population

The screened population will include all subjects with signed informed consent. Unless specified otherwise, this set will be used for subject enrollment listings and a disposition summary.

5.2. Safety Analysis Population (SAF)

The Safety Analysis Population includes all subjects who have received at least 1 dose of study drug (PDS0101 or pembrolizumab). This SAF population will be used to summarize all safety and tolerability assessments.

5.3. Intent-to-Treat Population (ITT)

The ITT population includes all subjects who meet eligibility criteria, have received at least 1 dose of study drug (PDS0101 or pembrolizumab) and have characterized PD-L1 expression. For CPI naïve group, a CPS ≥ 1 confirmed by central laboratory or local laboratory using the FDA approved Dako PD-L1 immunohistochemistry (IHC) 22C3 PharmDx assay is required. For CPI refractory group, ITT population only PD-L1 characterization is required. This ITT population will be used to summarize demographics and baseline characteristics, and secondary efficacy analysis of overall survival.

5.4. Modified Intent-to-Treat Population (mITT) / Efficacy Analysis Population (EFF)

The Modified Intent-to-Treat subjects are all those from the ITT and who have ≥ 1 assessment of overall tumor response following the initial dose of combination treatment (pembrolizumab plus PDS0101). This will be the primary population for efficacy assessment and it is referred to as the Efficacy Analysis Population in the protocol.

There is an exception rule for the mITT population. A subject will be included in the mITT population if the subject received the initial dose of combination treatment and died before the first imaging assessment. For efficacy analysis, this subject will be a non-responder and time from the initial dose of treatment to death will be used for time to event analyses of PFS and OS.

In the event of over enrollment, only the planned numbers of subjects by the end of each stage will be included in the mITT population for efficacy analysis sorted by their dates of the first dose of study drug.

5.5. Subject Group

This study has 2 distinguished subject groups at the time of enrollment, namely CPI naïve vs CPI refractory. This definition will come directly from the response to the question of “Is this patient CPI naïve or CPI refractory” for each subject.

Within each analysis population (SAF, ITT and mITT), data summary will be displayed for study overall and by each subject group.

6. General Aspects for Statistical Analysis

6.1. General Methods

- Unless otherwise specified, summaries will be presented for each subject group (CPI naïve group, CPI refractory group) as well as overall.
- Continuous variables will be summarized using the number of observations (n), mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized using number of observations (n), frequency, and percentages of subjects.
- All relevant subject data will be included in listings. All subjects entered into the database will be included in subject data listings.
- Decimal Places – The following rules will be followed with regards to the number of decimal places and presentation of data in the tables and listings:
  - Present original observed values in listings
  - For any derived values from the observed values, add one more decimal digit
  - For any sub-derived values (derived from derived values), add two more decimal digits to the original observed values.
- Statistical analyses will be carried out by using SAS Version 9.4 or higher. Any deviations from the planned analysis as described in the SAP will be justified and recorded in the clinical study report.
- If multiple assessments are present at a given time point or visit for a single parameter, the earliest value recorded will be presented in the summary tables.

6.2. Key Definitions

6.2.1. Definition of Baseline

Unless otherwise stated, the last observed (non-missing) measurement (including unscheduled measurements) prior to the first dose of study drug (earliest of PDS0101 or pembrolizumab) will be considered the baseline measurement.

6.2.2. Study Day Calculations for Reporting Purposes

The following conventions will be used to calculate study drug day for reporting purposes:

- Study Day xx = date of measurement/observation – first dose date + 1; if date of measurement/observation is on or after the first dose date
- Study Day xx = date of measurement/observation – first dose date; if date of measurement / observation is prior to the first dose date
- Study Day 1 is the first dose date; no Day 0 is defined for this study

6.3. Missing Data

Unless specified in the specific section in this SAP, missing data will not be imputed.

Subjects with no imaging or tumor measurements at any timepoint, or with two consecutive missing imaging/efficacy assessments generating two not evaluable (NE) timepoints will be considered treatment failures.

For analyses of overall survival, subjects who are lost to follow-up will be censored at the last known date of contact and will be censored at Day 1 if there are no post-baseline visits.

For analyses of PFS, subjects without documented PD who are lost to follow-up will be censored at the last known date of tumor assessment and will be censored at Day 1 if there are no post-baseline visits.

Any adverse events (AEs) with missing or partially missing onset dates will be grouped into treatment-emergent AEs (TEAEs), unless a partially missing AE end date occurs before treatment administration in which case it will not be considered as a TEAE. AEs with missing causality will be counted as definitely related to PDS0101 (or related for the PDS0101 and/or pembrolizumab summaries described in Section 9.3) for each preferred term (PT) and system organ class (SOC) unless the subject has another AE of the same PT or SOC with non-missing causality. AEs with missing severity will be counted as grade 3 for each PT or SOC summarized unless the subject has another AE of the same PT or SOC with non-missing severity. The listings will present the original missing values.

Prior or concomitant medications with incomplete start dates will be handled as follows for the sole purpose of determining whether a non-study medication is a prior or concomitant medication:

- If the start/stop date of a medication is partially missing, the date will be compared as far as possible with the date of the start of administration of study drug.
    - The medication will be assumed to be concomitant if it cannot be definitively shown that the stop date is before the start of administration of study drug.
    - The medication will be assumed to be prior if it cannot be definitively shown that the start date is after the start of administration of study drug (unless the stop date can be definitively shown to be after the start of study drug administration in which case it will be considered concomitant).
- If the start and stop dates are both completely missing, a medication will be considered prior and concomitant.

The original partial or missing date will be shown in listings of all non-study medications and adverse events.

6.4. Visit Windows

There will be no derivation for visit windows in terms of summary of assessments. Nominal visits as indicated in the schedule of procedures will be used for TFLs.

6.5. Pooling of Centers

All data/subjects across all centers will be pooled in data presentation. Selective analysis will be carried out stratified by region if warranted.

7. Demographic, Other Baseline Characteristics and Medication

7.1. Subject Disposition and Withdrawals

Subject disposition will be presented for the screened population, and will include the following:

1) The number of subjects screened
2) The number (%, denominator is number of subjects screened) of subjects who failed screening
3) The number (%, denominator is number of subjects screened) of subjects in the safety analysis population
4) The number (%, denominator is number of subjects screened) of subjects in the ITT population
5) The number (%, denominator is number of subjects screened) of subjects in the mITT population
6) The number (%, denominator is ITT population) of subjects continuing on the study
7) The number (%, denominator is ITT population) of subjects who completed the study
8) The number (%, denominator is ITT population) of subjects who discontinued from the study and the primary reason for discontinuation
9) The number (%, denominator is ITT population) of subjects continuing on PDS0101 treatment
10) The number (%, denominator is ITT population) of subjects who discontinued from PDS0101 treatment and the primary reason for discontinuation
11) The number (%, denominator is ITT population) of subjects continuing on pembrolizumab treatment
12) The number (%, denominator is ITT population) of subjects who discontinued from pembrolizumab treatment and the primary reason for discontinuation

The summary will be performed for the screened subjects by CPI naïve, CPI refractory, and CPI missing (as there could be screen failure subjects with a missing CPI classification). The denominators for the percentage calculation will be listed in the footnote of subject disposition table.

Subjects' completion/discontinuation status will be listed, including subject identifier, date of completion/early discontinuation and, for those who discontinued the study and each treatment discontinued including the specific reason(s) for discontinuation.

A subject listing of analysis populations and reasons for exclusion from each analysis population will be provided.

The inclusion/exclusion criteria for the subjects who fail screening will be listed for the screened population.

7.2. Demographic and Other Baseline Characteristics

Demographic and baseline characteristics of the Safety Analysis Population, ITT population and mITT population will be summarized with descriptive statistics including n, mean, standard deviation, median, minimum, and maximum for numeric variables and frequency and percentage for categorical variables.

- Demographics include age (years), gender, childbearing potential for females, ethnicity, race, height (cm), weight (kg), and body mass index (BMI) kg/m^2.

  Height (in cm) = height (in inches) * 2.54

  Weight (in kg) = weight (in lbs) * 0.4536

  BMI (kg/m^2) = Weight(kg)/[Height$(m)^2$]

- Other baseline characteristics include
    - Eastern Cooperative Oncology Group (ECOG) performance score (0, 1)
    - Human Immunodeficiency Virus (HIV) test results (negative, positive)
    - Vitamin D – 25(OH)D results at baseline.

7.3. Protocol Deviations

Protocol deviations may be identified during Study Monitoring Visits (via source data verification for example) or after the fact, such as the site's reply to a data query that confirms that the protocol was not followed. For this project, collection of protocol deviations will be managed in the [redacted] by the Site Monitor or Central Monitor during site visits or contacts. Protocol deviations will be reviewed by the Sponsor, classified as major or minor deviations, and approved prior to database lock.

Protocol deviations are summarized descriptively for subjects in the ITT and mITT Population with at least 1 protocol deviation and subjects with at least 1 protocol deviation related to Coronavirus Disease 2019 (COVID-19). Protocol deviations will also be summarized by deviation category (such as prohibited concomitant medication, inclusion or exclusion criteria, etc.). Protocol deviations related to COVID-19 will be summarized similarly.

Protocol deviation data will be listed for the ITT population. Protocol deviations related to COVID-19 will also be listed for the ITT population.

7.4. Medical and Surgical History and Concomitant Diseases

A summary table of the number and percentage of subjects by medical history SOC and PT will be produced for subjects in the ITT population. Previous and concurrent diseases/conditions will be sorted alphabetically by SOC and PT using the Medical Dictionary for Regulatory Activities (MedDRA) coding dictionary, version 23.1 or higher. For the summary tables, a subject may appear more than once if he/she has more than one medical/surgical history coded under different SOC categories. However, the subject will be counted only once in the summarization category.

All medical and surgical history data will be listed for the ITT population.

7.5. Other Baseline Characteristics

7.5.1. Prior HNSCC Therapies

Prior HNSCC therapy data includes medication/therapy, radiation therapy, whether medication/therapy was immunologic and related information.

A summary table for the ITT and mITT population will be prepared for prior HNSCC therapy; this summary will include

1) Number (%) subjects received prior HNSCC chemotherapy
2) Number (%) subjects received prior HNSCC radiation therapy
3) Number (%) subjects received prior HNSCC immunotherapy

4) Number (%) subjects by total number of lines/regimens received. Subjects who did not receive any prior immunologic therapy will be included in the category of '0'.

5) Number (%) of subjects by reason therapy ended within each line of therapy

Prior HNSCC therapy data will be listed for the ITT population.

7.5.2. Historical and Cytologically Confirmed Disease

CRF page for historical disease data includes date of HNSCC diagnosis and active brain metastases and/or carcinomatosis meningitis status and related information. Cytological confirmed disease data includes HPV-16 DNA genotyping, biomarker analysis data (PD-L1 Expression Level) and related information.

A summary table for the ITT and mITT population based on this page of CRF will be prepared, including

1) Age at time of HNSCC diagnosis, defined as (date of HNSCC diagnosis - date of birth + 1) / 365.25 then truncated to complete years.

2) Time (months) since the date of HNSCC diagnosis to the first dose of study drug, defined as (study day 1 visit date – date of HNSCC diagnosis) / 30.4167 then rounded to the first decimal point.

3) Number (%) subjects with active brain metastases and/or carcinomatosis (Y/N)

4) Number (%) subjects with HPV16 DNA genotyping samples collected (Y/N)

5) Number (%) subjects with HPV16 positivity confirmed by local lab (Y/N)

6) Number (%) subjects with HPV16 positivity confirmed by central lab (Y/N)

7) Number (%) subjects with Biomarker analysis by local lab, by central lab, by local or central lab (Y/N)

8) Number (%) subjects for each PD-L1 Expression level (CPS <1, CPS 1-19, CPS ≥20). PD-L1 expression level will be defined based on the CPS results from central lab if available, otherwise local lab CPS results will be used to define CPS subset. A category of CPS ≥1 will also be displayed in the summary; this category includes the pooled subjects from (CPS 1-19) and (CPS ≥20) subsets.

9) Number (%) subjects with PD-L1 Expression level confirmed by the central lab (Y/N).

Historical and cytologically confirmed disease data will be listed for the ITT population.

7.5.3. ECOG Performance Score

ECOG performance score, assessed at screening, will be listed for the ITT and mITT population. A summary of this data will be included in the table of 'Demographics and Baseline Characteristics'.

7.5.4. Human Leukocyte Antigen (HLA)

HLA typing, assessed by a central laboratory at screening, will be listed for the ITT population. A summary of this data will be included in the table of 'Demographics and Baseline Characteristics'.

7.5.5. HIV Test

HIV test results, assessed by a local laboratory at screening, will be listed for the ITT population.

7.5.6. HPV16 Test

HPV16 test results, assessed by a central laboratory at screening, will be listed for the ITT population. Number (%) patients with HPV16 positivity results confirmed by the central lab will be included in the summary table for 'Historical and Cytologically Confirmed Disease'.

7.5.7. PD-L1 CPS Results

PD-L1 CPS results, assessed by a central laboratory at screening, will be listed for the ITT and mITT population. CPS from local lab will also be displayed. Number (%) subjects for each PL-L1 expression level and number (%) subjects with the central lab PD-L1 expression level will be included in the summary table for 'Historical and Cytologically Confirmed Disease'.

7.6. Prior and Concomitant Medications

All prior and concomitant medications will be classified using the Anatomical Therapeutic Chemical (ATC) classification and preferred drug names from the World Health Organization Drug Dictionary (WHODD), version GLOBAL B3-Sep 2020 or later. Prior and concomitant medications will be listed by subject for the ITT population, and an identifier will be included to show if a medication is prior and/or concomitant.

Summaries of medications will be presented in tabular form using the ATC Level 3 term (ATC3) as an upper classification and the preferred drug name as a lower classification level. All medications will be summarized overall and sorted by descending counts in the upper classification term and the lower classification term within the upper. The summary will consist of the frequency and percentage of subjects who used the medication at least once. For each subject, the medication will be counted only once within the upper classification level and only once within the lower classification level.

7.6.1. Prior Medications

Medications will be considered prior if started and stopped before the first study treatment dose date. A medication with an incomplete start/stop date will be handled as described in SAP Section 6.3 solely to determine if the medication is prior or concomitant.

Prior medications will be summarized for the ITT and mITT population.

7.6.2. Concomitant Medications

Medications started prior to first dose of study treatment and continuing beyond the first dose of study treatment as well as those medications started on or after the first dose of study treatment will be considered concomitant medications. All medications marked as ongoing are considered concomitant medications. A medication with an incomplete start/stop date will be handled as described in SAP Section 6.3 solely to determine if the medication is prior or concomitant.

Concomitant medications will be summarized and listed for the ITT population.

8. Efficacy

Efficacy analysis will be provided on the mITT population unless specified otherwise. All analyses will be provided by CPI status group (Naïve or Refractory) and study overall; an ITT subject who did not have any tumor assessment post treatment will be excluded from mITT analysis set unless this subject died before the first tumor assessment (see Section 5.3). mITT subjects with missing efficacy assessments (i.e., who died before first tumor assessment) will be treatment failures. Unless otherwise specified, the mITT population will be used for the presentation of subject listings for all efficacy endpoints in this study.

8.1. Primary Efficacy Endpoint and Analyses

The primary efficacy endpoint will be the BOR based on confirmed CR or confirmed PR per RECIST v1.1. This BOR, therefore, is referred to as the confirmed BOR (cBOR) to differentiate it from the BOR that CR confirmation or PR confirmation is not required (that is, BOR is determined from observed CR or observed PR; and it is referred to as the unconfirmed BOR (uBOR)). Subjects achieved cBOR will also be referenced as the treatment responders.

To confirm CR and to confirm PR the criteria stated in the RECIST v1.1 guidance document Table 3 (Eisenhauer et al, 2009) will be used.

Table 3 – Best overall responses when confirmation of CR and PR required.

Overall response First time point	Overall response Subsequent time point	BEST overall response (Confirmed BOR)
CR	CR	CR
CR	PR	SD, PD or PR[a]
CR	SD	SD provided minimum criteria for SD duration met, otherwise, PD
CR	PD	SD provided minimum criteria for SD duration met, otherwise, PD
CR	NE	SD provided minimum criteria for SD duration met, otherwise, NE
PR	CR	PR
PR	PR	PR
PR	SD	SD
PR	PD	SD provided minimum criteria for SD duration met, otherwise, PD
PR	NE	SD provided minimum criteria for SD duration met, otherwise, NE
NE	NE	NE

Source: RECIST v1.1 Table 3.
CR = complete response; PR = partial response; SD = stable disease; PD = progressive disease; NE = inevaluable.
[a] if a CR is truly met at first time point, then any disease seen at a subsequent time point, even disease meeting PR criteria relative to baseline, makes the disease PD at that point (since disease must have reappeared after CR). Best response would depend on whether minimum duration for SD was met. However, sometimes 'CR' may be claimed when subsequent scans suggest small lesions where likely still present and in fact the patient had PR, not CR at the first time point. Under these circumstances, the original CR should be changed to PR and the best response is PR.

The minimum criteria for SD duration are 6 weeks (42 days) for this study. The duration of SD will be the elapsed days from study day 1 to the date when the first PD is observed or to the date when the last SD is reported if no PD.

The following special rules will apply to the confirmed BOR analysis:

1) If a subject has only 1 scan and the observed overall response in this 1 scan is either a CR or PR, the subject will be listed as NE for the confirmed BOR analysis.

2) If a subject has only one observed PR and the subject had a SD before this PR, this subject will be classified as SD for the confirmed BOR analysis. That is, RECIST Table 3 (row #8) identified a subject with PR->SD outcome as a SD, this rule is to expand the situation to (SD->PR) as a SD for the confirmed BOR analysis.

3) Subjects died post dosing but before the any post dosing scheduled scan will be classified as NE for the confirmed BOR analysis.

4) If a subject observes one or more NE between the initial PR or CR and the confirmation visit (PR→NE→PR or CR→NE→CR), this subject will be classified as having a confirmed PR/CR for the confirmed BOR analysis.

Since tumor response images will be assessed by both the local reading (investigator assessment) and central reading, cBOR will be determined twice: once per central imaging assessment and once per investigator imaging assessment. Tumor assessment data listings per central imaging assessment and per investigator assessment will include the target lesion data, non-target lesion data, and new lesion data and a flag showing discordance between the investigator assessment and the central imaging assessment; If there is discordance between the investigator assessment and the central imaging assessment, summary based on the central imaging assessment and an additional summary per the investigator assessment will be prepared and discussed in the final study report.

cBOR will be summarized twice per the mITT population: one based on the central imaging assessment; the second based on the investigator assessment. A second sensitivity analysis of cBOR will be performed on the ITT population: all subjects irrespective of whether they have undergone a tumor assessment or not will be included in the denominator in this analysis. Subjects with missing efficacy assessments will be treatment failures and will be included in the category of NE. This second sensitivity analysis will be based on the central imaging assessment only.

Summary tables for cBOR will include number and percent of subjects in the following each response category: cBOR of CR, PR, SD, PD, and NE. Number and percentage of responders (subjects who achieved cBOR of CR or PR) and durable response rate at 6- and 12-months will also be presented. Using the Clopper-Pearson method an exact 2-sided 90% CIs and an exact 2-sided 95% CIs will be provided.

Classification for uBOR, cBOR, and SD duration derived from central imaging assessment and investigator imaging assessment for each subject will be listed for the mITT population.

8.2. Secondary Efficacy Endpoints and Analyses

Secondary Efficacy Endpoints:

- PFS per RECIST 1.1 in all mITT subjects. Rate of PFS will be estimated at 9, 12 and 24 months.

- OS in all subjects in all ITT subjects. Rate of OS will be estimated at 9, 12, and 24 months.

8.2.1. Progression-Free Survival

PFS is defined as the time from start of study treatment, until documented disease progression or death (by any cause, in the absence of progression). For the primary analysis of PFS, the progression date will be the earliest of:

a. objectively documented per RECIST v1.1 criteria,
b. clinical PD is reported at treatment discontinuation, or
c. date of death (of any cause). Death is always considered as a confirmed PD event.

Those subjects who are still alive and without disease progression (i.e., progression-free subjects) will be censored at the last date of tumor assessment. Subjects with no post baseline assessment will be censored at Day 1.

The primary analysis for PFS endpoint will be the analysis per central imaging assessment on the mITT population. There are 3 planned PFS sensitivity analyses: 1) PFS analysis per investigator assessment on the mITT population, 2) PFS analysis per central imaging assessment on the ITT population, and 3) PFS analysis per investigator assessment on the ITT population. Non-mITT subjects will be excluded from the primary analysis and the first sensitivity analysis.

PFS analysis summary tables will include estimates of time to PFS and 95% CI of estimates per Kaplan-Meier time-to-event methodology at 75%, 50%, and 25% percentiles and will be reported in months. Estimates of PFS rate at 9 months (270 days) 12 months (365 days), and 24 months (730 days), and the associated 2-sided 95% CIs will be calculated using Product-Limit methodology. Kaplan-Meier survival curves for PFS will also be presented.

8.2.2. Overall Survival

OS is defined as the time from start of study treatment, until death (by any cause). Subjects alive or those lost to follow-up are censored at the last known date of contact, for OS analysis. Subjects who have received study drug but without any post-baseline visits or assessments will be censored at Day 1.

OS analysis summary table will include estimates of OS and 95% CIs of estimates per Kaplan-Meier time-to-event methodology at 75%, 50%, and 25% percentiles and will be reported in months. Estimates of OS rate at 9 months (270 days), 12 months (365 days), and 24 months (730 days), and the associated 2-sided 95% CIs will be calculated using Product-Limit methodology. Kaplan-Meier survival curves for OS will also be presented. OS analysis will be evaluated using the ITT population. As a sensitivity analysis, OS analysis using mITT population will also be performed.

Swimmer plots of OS and PFS will be generated based on central imaging assessment and investigator assessment using ITT and mITT populations.

8.3. Exploratory Endpoints and Analyses

Exploratory Analyses:

- Evaluation of DOR for all subjects who demonstrated CR or PR (i.e., treatment responders).
- Disease control rate (DCR) defined as the percentage of subjects who demonstrated CR, PR or SD

- Evaluation of anti-HPV-16 E6 and E7 immune responses elicited by treatment with pembrolizumab and PDS0101 using IsoPlexis Functional Proteomics at Days 85 (Cycle 5) and 253 (Cycle 13) compared with baseline.

- Subgroup analysis by PD-L1 expression levels for the following clinical outcomes: BOR, DCR, DOR, PFS, and OS.

- Subgroup analysis by ECOG status and Prior Treatment for the following clinical outcomes: BOR, DCR, DOR, PFS, and OS.

8.3.1. Duration of Response/Duration of Stable Disease

Duration of response (DOR) will be determined for all subjects who demonstrated CR or PR per cBOR (i.e., treatment responders). This endpoint does not apply to subjects who did not achieve cBOR (CR or PR); hence, they will be excluded from this analysis.

DOR is calculated as the time from the earliest date of documented CR or PR (whichever is the first record) until documented the date of disease progression or death (by any cause, in the absence of progression). For those who achieve cBOR (CR or PR) and are progression-free subjects, the DOR is censored at the last tumor assessment date following the earliest date of documented CR or PR. Estimates of DOR and 95% CIs of estimates will be obtained from Kaplan-Meier time-to-event methodology at 75%, 50%, and 25% percentiles and will be reported in months.

Duration of stable disease is calculated for subjects with confirmed best overall response as stable disease, which is defined as the time from the start of study treatment until disease progression or death for subjects who have experienced disease progression or death, or the time from the start of study treatment until the last tumor assessment for subjects who have not experienced disease progression or death. Descriptive statistics will be provided for duration of stable disease along with the numbers and percentages of subjects with stable disease duration greater than or equal to 42 days, which is the minimum stable disease duration for CR and PR confirmation.

Time to response, duration of response and duration of stable disease will be summarized twice per mITT population: once based on the central imaging assessment and once per investigator assessment. Subject data will be listed along with other derived efficacy variables for the mITT population.

8.3.2. Disease Control Rate

Disease control rate is defined as the percentage of subjects who have demonstrated CR, PR or SD based on confirmed best overall responses. Duration of disease control rate at 6- and 12- months will also be provided. Results will be summarized based on both investigator and central imaging assessments. Exact 2-sided CIs at both 90% and 95% confidence levels will be provided using Clopper-Pearson method.

8.3.3. Visual Presentation of Treatment Response

Treatment response in all mITT population will be visually displayed as

- A swimmer lane plot of time on study treatment and time to confirmed best overall response (CR, PR, SD, PD, NE)
- A stem plot of time to response (presenting time for only subjects with response of CR or PR) and time to progression (presenting time for only subjects with disease progression)

Two sets of figures will be generated, using central imaging assessments and investigator assessments respectively.

8.3.4. Change in Sum of the Longest Diameters of Target Lesions

Percent change from baseline in the sum of the longest diameters of target lesions will be determined. When a target lesion becomes 'too small to measure', the RECIST (v1.1) guidelines provided the following suggestion:

"Target lesions that become 'too small to measure': While on study, all lesions (nodal and non-nodal) recorded at baseline should have their actual measurements recorded at each subsequent evaluation, even when very small (e.g., 2mm). However, sometimes lesions or lymph nodes which are recorded as target lesions at baseline become so faint on CT scan that the radiologist may not feel comfortable assigning an exact measure and may report them as being 'too small to measure'. When this occurs, it is important that a value be recorded on the case report form. If it is the opinion of the radiologist that the lesion has likely disappeared, the measurement should be recorded as 0mm. If the lesion is believed to be present and is faintly seen but too small to measure, a default value of 5mm should be assigned (Note: It is less likely that this rule will be used for lymph nodes since they usually have a definable size when normal and are frequently surrounded by fat such as in the retroperitoneum; however, if a lymph node is believed to be present and is faintly seen but too small to measure, a default value of 5mm should be assigned in this circumstance as well). This default value is derived from the 5mm CT slice thickness (but should not be changed with varying CT slice thickness). The measurement of these lesions is potentially non-reproducible, therefore providing this default value will prevent false responses or progressions based upon measurement error. To reiterate, however, if the radiologist is able to provide an actual measure, that should be recorded, even if it is below 5mm." (Section 4.3.2)

Based on this suggestion, when post-baseline sum of the longest diameters of target lesions is missing due to 'no longer measurable' this missing data will be treated as '0'. For the purpose of the analysis, If a subject's target lesion overall response is a CR at a visit and sum of the longest diameter of target lesions at this visit has a missing value, the missing value will be interpreted as '0'. That is, this subject will have -100% change from baseline at this visit for this analysis.

Percent change from baseline in the sum of the longest diameters of target lesions will be presented visually. The following plots will be presented for the mITT population:

- A waterfall plot of best percentage change from baseline in sum of diameters of target lesions, where best percent change is defined as the biggest reduction (or smallest increase if no reduction was achieved) in the sum of the longest diameters of target lesions observed in the study. The color presentation will be determined by the cBOR classification of the subject.
    - Note: any subjects with missing data for percent change from baseline will be removed. A footnote will be added to document it.
- A spider plot of percent change in sum of diameters of target lesions from baseline during the course study. Line colors will be determined by the cBOR classification of the subject.

8.3.5. Efficacy Endpoint Subgroup Analysis

1. Efficacy endpoints BOR, DOR, DCR, PFS, and OS will also be presented for the following subgroups: PD-L1 expression level: PD-L1 expression level will be assessed at screening as a CPS and as a TPS.
    - Subjects will be grouped into the following 3 subgroups based on their CPS

- CPS <1, CPS 1 - 19, or CPS ≥20.
- Note: In summary tables a column with header (CPS ≥1) will also be displayed; this column will include pooled data from subjects in the (CPS 1- 19) subset and subjects in the (CPS ≥20) subset.

The subgroup analysis will follow the same approach as the overall analysis described in previous Sections (8.1, 8.2 and 8.3). Those analyses are exploratory objectives of the study (see Section 3.3).

8.3.6. IsoPlexis Functional Proteomics

Summaries of anti-HPV-16 E6 and E7 immune responses elicited by treatment with pembrolizumab and PDS0101 using IsoPlexis Functional Proteomics will be handled another vendor, hence, this set of data analysis will not be covered by this SAP.

9. Safety and Exposure

The Safety Analysis Population will be used for summaries of safety analyses and for safety listings, unless otherwise specified. Safety and tolerability will be assessed on the basis of AE reports, clinical laboratory data, vital signs, ECG parameters, physical examinations, extent of exposure and compliance with study drug use, post-vaccine contact surveys and subject vaccine diary results.

9.1. Extent of Exposure

Extent of exposure will be summarized using Safety Analysis, ITT and mITT populations. The total number of doses of PDS0101, number and percentage of subjects with any dose reduction of PDS0101, number and percentage of subjects with any dose of PDS0101 withheld and the total number of doses of PDS0101 withheld, total number of doses of pembrolizumab, number and percentage of subjects with any dose of pembrolizumab withheld and the total number of doses of pembrolizumab withheld, treatment duration (in months), and cumulative actual dose (mg) of PDS0101 and pembrolizumab will be descriptively summarized and listed for all subjects in the safety population. The total number of doses will also be summarized by categories of at least 1 dose to the category of at least 5 or more doses of PDS0101 or at least 10 or more doses of pembrolizumab. Administration of PDS0101 and pembrolizumab, including missed doses and the corresponding reasons if available, will be listed for the safety population.

PDS0101 duration (months) = (Date of the last dose of PDS0101 - Date of the first dose of PDS0101 + 1) / 30.4167

Pembrolizumab duration (months) = (Date of the last dose of pembrolizumab - Date of the first dose of pembrolizumab + 1) / 30.4167

Cumulative actual dose (mg) = sum of actual doses received (PDS0101 or pembrolizumab)

9.2. Treatment Compliance

The number of completely missed doses of PDS0101 and pembrolizumab will be calculated based on the case report form (CRF) responses to whether any dose of PDS0101 or pembrolizumab were administered at a scheduled administration visit. The number and percentage of subjects with at least one missing dose of PDS0101, and the number and percentage of subjects with at least one missing dose of pembrolizumab will be summarized for the safety population. The total number of missed doses of PDS0101 and pembrolizumab will be descriptively summarized and listed for the SAF population.

9.3. Adverse Events

AEs will be coded using the MedDRA dictionary Version 23.1 or higher and will be graded using National Cancer Institute – Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 5.0.

AEs are pre-specified into 4 categories:

1) PDS0101 injection site reaction
2) Pembrolizumab injection site extravasation
3) Pembrolizumab infusion related reaction
4) Other

On the AE page of eCRF, the investigator will provide his/her assessment of causality for each AE (regardless AE category) separately for each study drug as follows:

1) Relationship to PDS0101: unrelated, possibly related, probably related, definitely related.

   An AE is considered PDS0101 related if the response to this question is possibly related, or probably related, or definitely related.

2) Relationship to Pembrolizumab: unrelated, possibly related, probably related, definitely related

   An AE is considered Pembrolizumab related if the response to this question is possibly related, or probably related, or definitely related.

The response to above 2 questions will be used together to determine the causality to the combination treatment. That is, an AE is considered combination treatment related if the AE is either PDS0101 related or Pembrolizumab related, including the following three scenarios: related to both PDS0101 and Pembrolizumab, related to PDS0101 but unrelated to Pembrolizumab, related to Pembrolizumab but unrelated to PDS0101. An investigator will also determine if an AE is of clinical interest.

Immune-related AEs (irAEs) are the AEs associated with pembrolizumab exposure or pembrolizumab combination exposure that represent an immunologic etiology. These irAEs may occur shortly after the first dose or several months after the last dose of pembrolizumab treatment and may affect more than one body system simultaneously. irAEs will include but not limited to those events identified in Table 4 with severity grade ≥ 2 (with the exception for type 1 diabetes mellitus or hyperglycemia or exfoliative dermatologic conditions). The final irAE list from the study will be identified by manual review of the AE dataset prior to database lock. irAEs will be summarized by PT and displayed in a separate listing.

Table 4 – irAEs Categories

Pneumonitis
Diarrhea / Colitis
AST or ALT elevation or Increased Bilirubin
Type 1 diabetes mellitus (T1DM)[1] or Hyperglycemia
Hypophysitis
Hyperthyroidism
Hypothyroidism
Nephritis: grading according to increased creatinine or acute kidney injury
Neurological Toxicities
Myocarditis
Exfoliative Dermatologic Conditions (Suspected or confirmed SJS, TEN, or DRESS)[2]

All Other irAEs include but not limited to encephalitis, vasculitis and sclerosing cholangitis, and other clinically important irAEs.

[1] New onset T1DM or Grade 3 or 4 hyperglycemia associated with evidence of β-cell failure
[2] SJS=Stevens-Johnson Syndrome; TEN=Toxic Epidermal Necrolysis; DRESS=Drug Rash with Eosinophilia and Systemic Symptom

All AEs will be listed by subject for the safety population. The following listings of AEs will be provided:

1) All AEs
2) Injection site reactions
3) AEs with an outcome of death
4) SAEs
5) AEs related to PDS0101
6) AEs related to combination treatment
7) AEs leading to permanent discontinuation of either PDS0101 or pembrolizumab
8) DLTs
9) AEs of clinical interest (detailed definition in Protocol Section 12.6.4)
10) irAEs

TEAEs are AEs that start after the first study treatment, or if present at baseline, have worsened in severity after the first study treatment, through the follow-up safety visit. If any AEs with missing or partially missing onset dates, these AEs will be grouped into TEAEs unless the partially missing end date is before treatment administration in which case it will not be considered as a TEAE.

Only TEAEs will be included in summary tables. Summaries for AEs will be presented for the SAF population. An overall summary table of TEAEs will be produced for the following categories:

- Any TEAEs
- PDS0101 related TEAEs
- Combination treatment related TEAEs
- Treatment-emergent SAEs
- PDS0101 related SAEs
- Combination treatment related SAEs
- TEAEs with an outcome of death
- TEAEs leading to permanent discontinuation of study-drug (presenting those leading to permanent discontinuation of either PDS0101 or pembrolizumab; those leading to permanent discontinuation of PDS0101; and those leading to permanent discontinuation of pembrolizumab)
- TEAEs of clinical interest
- DLTs during Cycle 1 of combination treatment with pembrolizumab and PDS0101
- DLTs during Cycle 1 leading to a dose reduction of PDS0101
- Injection site reactions
- Injection site reactions of Grade 1
- Injection site reactions of Grade 2
- Injection site reactions of Grade 3 or greater

The incidence of TEAEs will be summarized by SOC and PT. Frequency count (of events) and the number and percentage of unique subjects reporting a specified TEAE will be tabulated. For the number of unique subjects reporting a TEAE, if a subject reported more than one AE that is coded to the same SOC or PT, the subject will be counted only once for that specific SOC or PT.

The following summaries of TEAEs will be provided:

1. All TEAEs by SOC and PT
2. All TEAEs by SOC, PT and maximum severity (Grade 1, 2, 3, 4, 5)
3. All TEAEs by strongest causality relationship (unrelated, possibly related, probably related, definitely related) to PDS0101 by SOC and PT
4. All TEAEs by causality relationship (unrelated, related) to combination treatment by SOC and PT
5. PDS0101 related TEAEs by SOC and PT
6. Combination treatment related TEAEs by SOC and PT
7. PDS0101 related TEAEs by SOC, PT and maximum severity (Grade 1, 2, 3, 4, 5)
8. Combination treatment related TEAEs by SOC, PT and maximum severity (Grade 1, 2, 3, 4, 5)
9. All Serious TEAEs by SOC and PT
10. PDS0101 related serious TEAEs by SOC and PT
11. Combination treatment related serious TEAEs by SOC and PT
12. DLTs by SOC and PT
13. TEAEs of clinical interest by SOC and PT
14. TEAEs by decreasing incidence (incidence ≥10%) by PT
15. Immune-related AEs by PT

Please note the following imputation rules

1) For TEAEs presented by relationship to study treatment(s), the strongest relationship to study treatment(s) during the study will be presented for each subject if coded to the same SOC or PT. For TEAEs presented by severity (see Protocol Section 12.6.7 for severity grading scales), the worst severity (grade=mild, grade=moderate, or grade=severe) during the study will be presented for each subject if coded to the same SOC or PT.

9.4. Laboratory Evaluations

A central lab will be used to assess the cluster of differentiation 4 (CD4), cluster of differentiation 8 (CD8), and the ratios of CD4 vs CD8 (CD4/CD8) via peripheral blood mononuclear cells (PBMC) per the schedule of procedures (Cycles 1, 5, and 13). A descriptive summary table and a data listing will be provided for these parameters on the SAF population.

The following laboratory assessments will be performed per the schedule of procedures. All samples will be analyzed at local laboratories unless otherwise specified. Parameters will be standardized according to the International System of Units (SI) prior to summarization.

- Hematology: Hemoglobin, hematocrit, red blood cell count, platelet count, white blood cell count with differential [including basophils (% and absolute count), eosinophils (% and absolute count), lymphocytes (% and absolute count), monocytes (% and absolute count), and neutrophils (% and absolute count)]

- Chemistry: Alkaline phosphatase, alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin (total), blood urea nitrogen (BUN), creatinine phosphokinase, creatinine, sodium, potassium, calcium, phosphorus, magnesium, glucose, albumin, and total protein

- Coagulation at screening/Week 0, Day 1 only: international normalized ratio (INR), partial thromboplastin time (PTT), active partial thromboplastin time, prothrombin time, and fibrinogen

- Urinalysis: dipstick determinations of protein, hematuria, and glucose. If abnormal (presence of protein, hematuria, or glucose ≥ 1+), a microscopic examination will be performed.

- Microscopic Urinalysis if indicated: red blood cells, white blood cells, epithelial cells, microorganisms, casts, and crystals
- Pregnancy tests (urine) will be conducted for Women of childbearing potential
- Thyroid Function: Triiodothyronine (T3), Free Triiodothyronine (FT3), Free Thyroxine (FT4), and Thyroid stimulating hormone (TSH)
- Vitamin D – 25(OH)D at Week 0, Day 1 only

Baseline and all scheduled post-baseline assessments, as well as the change from baseline, will be summarized for the clinical laboratory tests in hematology, chemistry and thyroid function using descriptive statistics. Box plots over time (i.e., study cycle), presenting mean and percentiles (25th percentile, median, and 75th percentile) of lab tests' values for absolute lymphocyte counts and selected serum chemistry parameters (AST, ALT, bilirubin, glucose, BUN, and creatinine) will be produced.

The clinical grade (low/normal/high) is calculated based on values below the normal range (low), within the normal range (normal), or above the normal range (high) for a specified parameter. The clinical grade and shift from baseline to end of study assessments will be provided in a summary table for hematology and chemistry, and assessments not done, or assessments with missing normal range will be summarized in a missing/not done category. Any clinically significant findings will be recorded as medical history (if at screening) or as an AE (if after first dose of treatment).

Summaries for laboratory evaluations will be presented for the SAF population. Separate listings will be produced for each laboratory test group for the SAF population.

9.5. Vital Signs

The following vital signs will be assessed per the schedule of procedures: systolic blood pressure (mmHg), diastolic blood pressure (mmHg), pulse (bpm), respiratory rate (breaths/min), and temperature (°C).

Following the first vaccination of PDS0101, subjects will have vital signs and symptoms monitored for 1 hours and measurements taken with the subject seated at 0-, 15-, 30-, 60-minutes post-study combination treatment with a ± 5-minute window allowed. If no significant immediate AEs are identified with the first vaccination, subjects will be monitored for 15 minutes with subsequent vaccinations 2 through 5 and measurements will be taken with the subject seated at 0- and 15-minutes post-study combination treatment with a ± 5-minute window allowed.

Baseline and all scheduled post-baseline assessments, as well as the change from baseline, will be summarized for vital signs using descriptive statistics for the SAF population. All vital signs data will be listed for the SAF population.

9.6. ECG

12-Lead ECG will be collected for every subject at baseline once eligibility is confirmed and after each study combination treatment (Cycles 1, 2, 3, 4, and 12) as part of the safety monitoring and to document the effect of the study combination treatment on corrected QT (QTc) intervals. Results will include ventricular rate, PR interval, QRS duration, QRS axis, QTc (corrected using Fridericia formula), ST segment (None observed, Elevation, or Depression), T Wave (None Observed or Inversion), and investigator assessment of overall ECG interpretation (Normal, Abnormal and Not Clinically Significant, and Abnormal and Clinically Significant) and any abnormal findings.

Baseline and all scheduled post-baseline assessments, as well as the change from baseline, will be summarized for numeric ECG results using descriptive statistics for the SAF population. The overall ECG interpretation and shift from baseline to end of study assessments will be provided in a summary table for the SAF population, and assessments not done, or missing will be summarized in a missing/not done category. All ECG data will be listed for the SAF population.

9.7. Other Safety Assessments

9.7.1. Physical Examination

Full physical examination will be performed at screening (including cardiorespiratory, abdominal, basic neurological, and skin exam [e.g., rashes, discoloration]). Subsequent physical examinations will be targeted and include a general assessment, cardiac, pulmonary, and previous injection site assessments; blood pressure, pulse, respiration rate, temperature, weight (at screening and study discharge only) with subject seated, and height (at screening only) will also be recorded.

No formal data summary or data listing will be provided for physical examination since any clinically significant event post-treatment allocation should be recorded as an AE (see Protocol Section 12.3).

9.7.2. Post-Vaccine Contact

Study staff will contact and survey each subject via phone call or e-mail at least 24 hours after, but within 72 hours of study combination treatment at Day 1 (Week 0), Day 22 (Week 3), Day 43 (Week 6), Day 64 (Week 9) and Day 232 (Week 33) (Cycles 1, 2, 3, 4 and 12). Refer to Protocol Appendix C Post Vaccine Contact for more details.

The objective of those post-vaccine contact is to collect post treatment adverse events and concomitant medications. Hence, all findings from those contacts should be recorded as an AE or concomitant medication accordingly. Therefore, the post-vaccine contact status data will not be formally summarized. A data listing will be prepared for the SAF population subjects.

10. Futility Analyses

For the purpose of futility analysis, the best overall response will be based on the investigator's assessment. When central imaging assessment becomes available, the assessments between the investigator and the central imaging will be compared; any discordance will be documented and impact on the futility results will be assessed and documented.

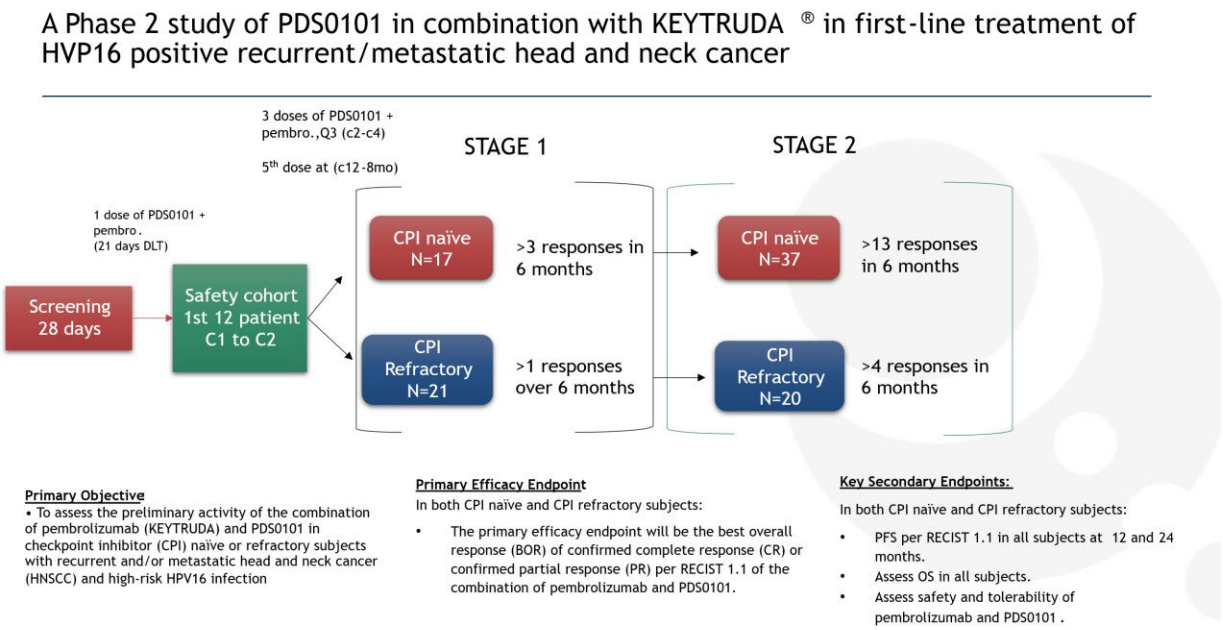
Per the Simon's 2-Stage Design, futility analyses are incorporated at Stage 1 and Stage 2 for both CPI naïve and CPI refractory groups to guard against an unacceptably low ORR (of confirmed CR or PR). For each CPI group, the null hypothesis (H0) that the true response rate (P) is P0 (P0 = 0.17 for CPI naïve, P0 = 0.05 for CPI refractory) will be tested against a one-sided alternative response rate P1 (P1 = 0.33 for CPI naïve, P1 = 0.2 for CPI refractory):

H0: P = P0
Ha: P = P1 (where P1 > P0)

In the first stage, n1 subjects will be accrued (n1 = 17 for CPI naïve, n1 = 21 for CPI refractory). If there are r1 or fewer responses in these n1 subjects (r1 = 3 for CPI naïve, r1 = 1 for CPI refractory) after being on the study for at least 6 months (Cycle 10), the study may be stopped for futility or regulatory agency feedback will be incorporated per Sponsor's discretion. Otherwise, n - n1 additional subjects will be accrued for a total of n subjects (n - n1 = 37 for CPI naïve, n - n1 = 20 for CPI refractory leading to n = 54 for CPI naïve, and n = 41 for CPI refractory). The null hypothesis (H0) will be rejected if r2 + 1 or more responses (r2 + 1 = 14 for CPI naïve, r2 + 1 = 4 for CPI refractory) are observed in the n patients after being on the study for at least 6 months (Cycle 10), and the study may be stopped for futility or regulatory agency feedback will be incorporated per Sponsor's discretion.

The overall study design through the end of the Simon's 2-Stage Design is presented in Figure 1.

Figure 1 - Overall Study Design Through the End of the Simon's 2-Stage Design



A summary table of BOR following initial treatment will be utilized to assess futility at each milestone of the Simon's 2-Stage Design. The summary table of BOR will display the number and percentage of subjects in the mITT population for the CPI naïve and CPI refractory group with a response of CR or PR based on an investigator assessment. Exact 90% CIs will be estimated for subjects who achieve CR or PR using the Clopper-Pearson method. The futility assessment will compare the BOR summary table to the target number of responders at each stage as defined in the Simon's 2-Stage Design rules (i.e., r1 and r2).

The timings of the meetings to assess futility will be determined by the earliest outcome of the scenario described below:

1. Stage 1 is ready to proceed into Stage 2 prior to enrolling the total sample size
   - 4 responses in CPI naïve population (r1 + 1)
   - 2 responses in CPI refractory population (r1 + 1)
2. Stage 1 has completed enrolling and treatment time
   - 17 CPI naïve subjects at 6 months (n1)
   - 21 CPI refractory subjects at 6 months (n1)
3. Stage 2 has exceeded total responses needed (r2 + 1)
4. Stage 2 has completed enrollment and treatment

11. Changes from Analysis Planned in Protocol

Analyses described in this SAP reflect the analyses planned in the most recent protocol.

12. Reference List

1. Simon R. Optimal two-stage designs for phase II clinical trials. Control Clin Trials. 1989;10(1):1-10.
2. Burtness B, Harrington KJ, Greil R, Soulières D, Tahara M, de Castro G Jr, Psyrri A, Basté N, Neupane P, Bratland Å, Fuereder T, Hughes BGM, Mesía R, Ngamphaiboon N, Rordorf T, Wan Ishak WZ, Hong RL, González Mendoza R, Roy A, Zhang Y, Gumuscu B, Cheng JD, Jin F, Rischin D; KEYNOTE-048 Investigators. Pembrolizumab alone or with chemotherapy versus cetuximab with chemotherapy for recurrent or metastatic squamous cell carcinoma of the head and neck (KEYNOTE-048): a randomised, open-label, phase 3 study. Lancet. 2019 Nov 23;394(10212):1915-1928. doi: 10.1016/S0140-6736(19)32591-7. Epub 2019 Nov 1. Erratum in: Lancet. 2020 Jan 25;395(10220):272. Erratum in: Lancet. 2020 Feb 22;395(10224):564. Erratum in: Lancet. 2021 Jun 12;397(10291):2252. PMID: 31679945.
3. Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, Dancey J, Arbuck S, Gwyther S, Mooney M, Rubinstein L, Shankar L, Dodd L, Kaplan R, Lacombe D, Verweij J. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer. 2009 Jan;45(2):228-47. doi: 10.1016/j.ejca.2008.10.026. PMID: 19097774.

13. Programming Considerations

All tables, figures, listings (TFLs), and statistical analyses will be generated using SAS for Windows, Release 9.4 (SAS Institute Inc., Cary, NC, USA). Computer-generated table, listing and figure output will adhere to the following specifications.

13.1. General Considerations

- One SAS program can create several outputs.
- One output file can contain several outputs.
- Output files will be delivered in Word format.
- Numbering of TFLs will follow International Council for Harmonization (ICH) E3 guidance

13.2. Table, Listing, and Figure Format

13.2.1. General

- All TFLs will be produced in landscape format on American letter size, unless otherwise specified.
- All TFLs will be produced using the Times New Roman font, size 9, which is an acceptable point size for the Regulatory Authorities.
- The data displays for all TFLs will have a minimum blank 1-inch margin on the top and bottom of the output, and minimum blank 0.7-inch margin on the left and right sides of the output.
- Headers and footers for figures will be in Times New Roman font, size 9, which is an acceptable point size for the Regulatory Authorities.
- Legends will be used for all figures with more than 1 variable, group, or item displayed.
- Tables and listings will be in black and white (no color), unless otherwise specified. Figures may use color.
- Specialized text styles, such as bolding, italics, borders, shading, and superscripted and subscripted text, will not be used in the TFLs, unless otherwise specified. On some occasions, superscripts 1, 2, or 3 may be used (see below).
- Only standard keyboard characters will be used in the TFLs. Special characters, such as non-printable control characters, printer-specific, or font-specific characters, will not be used. Hexadecimal-derived characters will be used, where possible, if they are appropriate to help display math symbols (e.g., μ). Certain subscripts and superscripts (e.g., cm2, Cmax) will be employed on a case-by-case basis.
- Mixed case will be used for all titles, footnotes, column headers, and programmer-supplied formats, as appropriate.

13.2.2. Headers

- All output should have the following header at the top left of each page:

- PDS Biotechnology Corp
- Protocol: PDS0101-HNC-201

- All outputs should have the following header at the top right of each page:
  - Database Date/Analysis: <date>/<Draft/Final Run>
  - Page n of N. TFLs are internally paginated in relation to the total length (i.e., the page number should appear sequentially as page n of N, where N is the total number of pages in the table).
- The date when the output was generated should appear along with the program name and file path as a footer on each page.

13.2.3. Display Titles

- Each TFL are identified by the designation and a numeral. (i.e., Table 14.1.1). ICH E3 numbering is strongly recommended, but sponsor preferences are obtained before final determination A decimal system (x.y and x.y.z) are used to identify TFLs with related contents. The title is centered. The analysis population are identified on the line immediately following the title. The title and table designation are single spaced. A solid line spanning the margins will separate the display titles from the TFL.
- Column headers. There will be 1 blank line between the last title and the solid line.

Table x.y.z
First Line of Title
Second Line of Title if Needed
ITT Analysis Population

13.2.4. Column Headers

- Column headings are displayed immediately below the solid line described above in initial upper-case characters.
- In the case of efficacy tables, the variable (or characteristic) column will be on the far left followed by the treatment group columns and total column (if applicable). P-values may be presented under the total column or in separate p-value column (if applicable). Within-treatment comparisons may have p-values presented in a row beneath the summary statistics for that treatment.
- For numeric variables, include “unit” in column or row heading when appropriate.
- Analysis population sizes will be presented for each treatment group in the column heading as (N=xx) (or in the row headings, if applicable). This is distinct from the ‘n’ used for the descriptive statistics representing the number of subjects in the analysis population.

13.2.5. Body of the Data Display

13.2.5.1. General Conventions

Data in columns of a table or listing are formatted as follows:

- Alphanumeric values are left-justified;
- Numeric values are center-justified

13.2.5.2. Table Conventions

- Units will be included where available
- If the categories of a parameter are ordered, then all categories between the maximum and minimum category are presented in the table, even if n=0 for all treatment groups in a given category that is between the minimum and maximum level for that parameter. For example, the frequency distribution for symptom severity would appear as:

Severity Rating	N
severe	0
moderate	8
mild	3

Where percentages are presented in these tables, zero percentages will not be presented and so counts of 0 will be presented as 0 and not as 0 (0%).

- If the categories are not ordered (e.g., Medical History, Reasons for Discontinuation from the Study, etc.), then only those categories for which there is at least 1 subject represented in 1 or more groups are included.
- An Unknown or Missing category are added to each parameter for which information is not available for 1 or more subjects.
- Unless otherwise specified, the estimated mean, median, and IQR for a set of values are printed out to 1 more significant digit than the original values, and standard deviations are printed out to 2 more significant digits than the original values. The minimum, maximum, and range should report the same significant digits as the original values. For example, for systolic blood pressure:

N	XX
Mean	XXX.X
Std Dev	X.XX
Median	XXX.X
IQR	XXX.X
Minimum	XXX
Maximum	XXX
Range	XXX

- P-values are output in the format: “0.xxx”, where xxx is the value rounded to 3 decimal places. Every p-value less than 0.001 will be presented as <0.001. If the p-value are less than 0.0001, then present as <0.0001. If the p-value is returned as >0.999, then present as >0.999
- Percentage values are printed to one decimal place, in parentheses with no spaces, one space after the count (e.g., 7 (12.8%), 13 (5.4%)). Pre-determine how to display values that round down to 0.0. A common convention is to display as '<0.1', or as appropriate with additional decimal

places. Unless otherwise noted, for all percentages, the number of subjects in the analysis population for the treatment group who have an observation will be the denominator. Percentages after zero counts should not be displayed and percentages equating to 100% are presented as 100%, without decimal places.

- Tabular display of data for medical history, prior/concomitant medications, and all tabular displays of adverse event data are presented by the body system, treatment class, or SOC with the highest occurrence in the active treatment group in decreasing order, assuming all terms are coded. Within the body system, drug class and SOC, medical history (by preferred term), drugs (by ATC3 code), and adverse events (by preferred term) are displayed in decreasing order. If incidence for more than 1 term is identical, they should then be sorted alphabetically. Missing descriptive statistics or p-values which cannot be estimated are reported as "-".

- The percentage of subjects is normally calculated as a proportion of the number of subjects assessed in the relevant treatment group (or overall) for the analysis population presented. However, careful consideration is required in many instances due to the complicated nature of selecting the denominator, usually the appropriate number of subjects exposed. Describe details of this in footnotes or programming notes.

- For categorical summaries (number and percentage of subjects) where a subject can be included in more than one category, describe in a footnote or programming note if the subject is included in the summary statistics for all relevant categories or just 1 category and the criteria for selecting the criteria.

- Where a category with a subheading (such as system organ class) has to be split over more than one page, output the subheading followed by "(cont.)" at the top of each subsequent page. The overall summary statistics for the subheading should only be output on the first relevant page.

13.2.5.3. Listing Conventions

- Listings will be sorted for presentation in order of treatment groups as above, subject number, visit/collection day, and visit/collection time.

- Missing data are represented on subject listings as either a hyphen ("-") with a corresponding footnote ("- = unknown or not evaluated"), or as "N/A", with the footnote "N/A = not applicable", whichever is appropriate.

- Dates are printed in SAS DATE9.format ("ddMMMyyyy": 01JUL2000). Missing portions of dates are represented on subject listings as dashes ("JUL2000" or "2000"). Dates that are missing because they are not applicable for the subject are output as "N/A", unless otherwise specified.

- All observed time values are to be presented using a 24-hour clock HH:MM or HH:MM:SS format (e.g., 11:26:45, or 11:26). Time will only be reported if it was measured as part of the study.

13.2.5.4. Figure Conventions

- Unless otherwise specified, for all figures, study visits will be displayed on the X-axis and endpoint (e.g., treatment mean change from Baseline) values will be displayed on the Y-axis.

13.2.6. Footnotes

- A solid line and 1 blank row spanning the margins will separate the body of the data display from the footnotes.
- All footnotes will be left justified with single-line spacing immediately below the solid line underneath the data display.
- Footnotes should always begin with “Note:” if an informational footnote, or 1, 2, 3, etc. if a reference footnote. Each new footnote should start on a new line, where possible.
- Subject specific footnotes are avoided, where possible.
- Footnotes will be used sparingly and add value to the table, figure, or listing. If more than six lines of footnotes are planned, then a cover page is strongly recommended to be used to display footnotes, and only those essential to comprehension of the data will be repeated on each page.
- The last 2 lines of the footnote section will be a standard source line that indicates the name of the program used to produce the data display, date the program was run, and the listing source (i.e., the 2nd to last line would say ‘Reference Listing: 16.x.y.z’ and the last line would say ‘P:\PDS Biotechnology\PDS0101-HNC-201\Biostats\Programs\TLFs\t-xxxx.sas ddMMMyyyy HH:MM’).

14. Quality Control

All SAS programs that create outputs or supporting analysis datasets will be validated by a second statistical programmer or biostatistician. At a minimum, validation of programs will consist of a review of the program log, review of output or dataset format and structure, and independent confirmatory programming to verify output results or dataset content. Additionally, all outputs will undergo a review by a senior level team member before finalization.

The content of the source data will be reviewed on an ongoing basis by project statistical programmers and statisticians. Data will be checked for missing values, invalid records, and extreme outliers through defensive programming applications, analysis-based edit checks, and other programmatic testing procedures. All findings will be forwarded to the project data manager for appropriate action and resolution.

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16.2.4.3.7	PD-L1 CPS Results Intent-to-Treat Population
16.2.4.3.8	PD-L1 CPS Results Intent-to-Treat Population
16.2.4.4	Prior and Concomitant Medications Intent-to-Treat Population
16.2.4.5	Prior and Concomitant Procedures Intent-to-Treat Population
16.2.5.1.1	PDS0101 Administration Safety Analysis Population
16.2.5.1.2	Pembrolizumab Administration Safety Analysis Population
16.2.5.2.1	PDS0101 Extent of Exposure, Duration and Missed Doses Safety Analysis Population
16.2.5.2.2	Pembrolizumab Extent of Exposure, Duration and Missed Doses Safety Analysis Population
16.2.6.1.1	Overall Tumor Response Based on Central Imaging Assessment Per RECIST v1.1 Modified Intent-to-Treat Population
16.2.6.1.2	Overall Tumor Response Based on Investigator Assessment Per RECIST v1.1 Modified Intent-to-Treat Population
16.2.6.1.3	Target Lesions – Central Imaging Assessment Modified Intent-to-Treat Population
16.2.6.1.4	Target Lesions – Investigator Assessment Modified Intent-to-Treat Population

Listing Number	Title and Population
16.2.6.1.5	Non-Target Lesions – Central Imaging Assessment Modified Intent-to-Treat Population
16.2.6.1.6	Non-Target Lesions – Investigator Assessment Modified Intent-to-Treat Population
16.2.6.1.7	New Lesions – Central Imaging Assessment Modified Intent-to-Treat Population
16.2.6.1.8	New Lesions – Investigator Assessment Modified Intent-to-Treat Population
16.2.6.2.1.1	Subjects Best Response and Progression-Free Survival Based on Central Imaging Assessment Per RECIST v1.1 Modified Intent-to-Treat Population
16.2.6.2.1.2	Subjects Best Response and Progression-Free Survival Based on Investigator Assessment Per RECIST v1.1 Modified Intent-to-Treat Population
16.2.6.2.2	Overall Survival Intent-to-Treat Population
16.2.6.3	Time to Response and Duration of Response Based on Central Imaging Assessment Per RECIST v1.1 Modified Intent-to-Treat Population
16.2.7.1	Adverse Events Safety Analysis Population
16.2.7.2	Injection Site Reactions Safety Analysis Population
16.2.7.3	Adverse Events with an Outcome of Death Safety Analysis Population
16.2.7.4	Serious Adverse Events Safety Analysis Population
16.2.7.5	Adverse Events Related to PDS0101 Safety Analysis Population
16.2.7.6	Adverse Events Related to Combination Treatment Safety Analysis Population
16.2.7.7	Adverse Events Leading to Permanent Discontinuation of Either Pembrolizumab or PDS0101 Safety Analysis Population
16.2.7.8	Dose-Limiting Toxicities (DLTs) Safety Analysis Population
16.2.7.9	Adverse Events of Clinical Interest Safety Analysis Population
16.2.7.10	Immune-Related Adverse Events Safety Analysis Population
16.2.8.1.1	Hematology Safety Analysis Population
16.2.8.1.2	Chemistry Safety Analysis Population
16.2.8.1.3	Coagulation Safety Analysis Population
16.2.8.1.4	Urinalysis Safety Analysis Population
16.2.8.1.5	Pregnancy Test Results Safety Analysis Population
16.2.8.1.6	Thyroid Function Safety Analysis Population
16.2.8.1.7	Vitamin D - 25(OH)D Safety Analysis Population

Listing Number	Title and Population
16.2.8.1.8	CD4, CD8 and CD4/CD8 Results via PBMC Safety Analysis Population
16.2.8.2.1	Vital Signs Safety Analysis Population
16.2.8.2.2	Electrocardiogram (ECG) Results Safety Analysis Population
16.2.8.2.3	Post-Vaccine Contact Survey Safety Analysis Population

18. Appendix 1: Topline and DMC Results

Topline outputs as well as outputs for the DMC will be presented by CPI group (CPI naïve and CPI refractory) and overall. A list of DMC outputs is provided in the DMC charter.