STATISTICAL ANALYSIS PLAN

AN OPEN-LABEL, PHASE II STUDY TO EVALUATE SCB01A IN PATIENTS WITH RECURRENT OR METASTATIC SQUAMOUS CELL HEAD AND NECK CANCER WHO HAVE RECEIVED PLATINUM-BASED TREATMENT

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SAP APPROVAL

By my signature, I confirm that this SAP has been approved for use on the SCB01A-21 study:

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1.Introduction

The following Statistical Analysis Plan (SAP) provides the outline for the statistical analysis of the data from SCB01A-21 study. This SAP is based on the study protocol version 3.0 (dated on 25Jul2016).

The planned analyses identified in this SAP may be included in clinical study reports (CSRs), regulatory submissions, or future manuscripts. Also, post hoc analyses not necessarily identified in this SAP may be performed to further examine study data. Any post hoc, or unplanned, exploratory analyses performed will be clearly identified as such in the final CSR.

Note: This study was designed to have two phases, namely run-in phase I (dose escalation phase) and phase II. This study was terminated early in run-in phase I, with eight (8) subjects screened and five (5) subjects enrolled. There was no recruitment for phase II. In light of the small number of subjects enrolled in this study, the SAP will focus on safety data analysis. Efficacy data will be conducted only if there are enough subjects/events, as appropriate, for the analysis methods.

2.Project Overview

2.1.Description of Overall Study Design and Plan

This is an open-label, phase II study to evaluate SCB01A in patients with recurrent or metastatic squamous cell head and neck cancer, who have received platinum-based treatment. This study was designed with two phases: one run-in phase I (dose escalation phase) and one continuation phase (phase II).

Run-in Phase I (Dose Escalation Phase)

The run-in phase I was to determine the optimal dose for SCB01A to be used in phase II. In the phase I, dose-escalation was involved, in which successive cohorts of three subjects would receive escalating doses of SCB01A until 24 mg/m^2. Dose escalation assessment would be based on tolerability observed during 3 cycles of treatment. An Optimal Dose would be agreed upon.

Dose level was initiated at 3.25 mg/m^2 (Dose 1) in the first cohort, and could be escalated to 12 mg/m^2 (Dose 2), 18 mg/m^2 (Dose 3) and 24 mg/m^2 (Dose 4) by an up and down approach. Briefly, at each dose level, if 1 of the three subjects experienced a dose limiting toxicity (DLT) during the first 3 cycles of SCB01A treatment, an additional three subjects will be enrolled at the same dose level. If 0/6 or 1/6 i.e ≤1 of subjects experienced DLT at the given dose level, the dose of the subsequent cohort would be increased to the next level, then this process would continue until >1/6 of subjects experienced DLT at certain dose level or the maximum dose in this protocol, 24 mg/m^2 (Dose 4) was reached. This process could continue at a reduced dose level, if >1/6 of subjects experienced DLT at a higher dose level. The reduced dose levels potentially to be tested were specified in the protocol as 10 mg/ m^2 (Dose 1a), 5 mg/m^2 (Dose 0a), 15 mg/m^2 (Dose 2a), and 21mg/m^2 (Dose 3a).

When the study was terminated in run-in phase I, subjects were recruited only for cohorts of 3.25 mg/m^2 (Dose 1) and 12 mg/m^2 (Dose 2).

Phase II

In the phase II of the study additional subjects would be enrolled to evaluate the Optimal Dose as established by review of the safety committee.

The phase II followed a Simon's optimal two-stage design to test the disease control rate (including complete response, partial response and stable disease) in subjects treated with SCB01A was at least 25% (alternative hypothesis). In the first stage of phase II, a total of 13 subjects would be enrolled at the optimal dose level, including those already enrolled at the optimal dose level from Run-in Phase I. If 1 or fewer patient was observed with disease control response in the stage 1 of phase II, then the study would be stopped for futility, with disease control rate concluded to be less than or equal to 10% (null hypothesis). Otherwise, the phase II would enter into its stage 2, in which an additional 21 subjects would be enrolled at the optimal dose level. If 6 or more subjects were observed with disease control response out of the 34 subjects enrolled (13 + 21) in the stage 2, the disease control rate in subjects treated with SCB01A would be concluded to be at least 25%. Otherwise, the disease control rate in subjects treated with SCB01A would be concluded to be less than or equal to 10%, and further investigation of the investigational treatment was not warranted.

The study was terminated without any recruitment for phase II.

Subjects would receive the recommended dose of mono-therapy of SCB01A for 9 weeks (3 weeks*3 cycles) or until disease progression, intolerable toxicity, consent withdrawal or death, whichever occurs first. DLT and safety would be followed in each phase of study. Pharmacokinetic (PK) would be performed on subjects enrolled in the run-in phase, with PK blood samples taken immediately pre-infusion then at 2, 3, 4, 6, 10, 21 and 24 hours after the start of infusion on Days 1 and 8 of Cycles 1, 2 and 3. Bioanalytical measurements and health outcome data (EORTC QLQ-C30 and EORTC QLQ-H&N35) were to be collected. Tumor response would be assessed by using computerized tomography (CT) or MRI scans according to RECIST v1.1 at baseline, and every 3 cycles prior to the next cycle until progression of the disease.

2.2.Objectives

Run-in Phase I (Dose Escalation Phase)

Primary objective:

- To determine the optimal dose for 3 cycles of i.v. administration of SCB01A on Days 1 and 8 of each cycle in a 3-week cycle

Secondary Objective:

- To evaluate the safety and toxicity for 3 cycles of i.v. administration of SCB01A on Days 1 and 8 of each cycle in a 3-week cycle
- To assess the PK profile of SCB01A of subjects in the run-in phase.

Phase II

Primary Objective:

- To assess the disease control rate (DCR) at the end of the 9th week (3 cycles, each cycle consists of 21 days) after treatment with SCB01A, according to the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1.

Secondary Objectives:

- To assess the overall survival (OS) rate at 36 weeks after first treatment with SCB01A in subjects with recurrent or metastatic squamous cell head and neck cancer who have previously been treated with platinum therapy.

- To assess the progression-free survival (PFS)
- To assess health outcomes using patient-reported European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30) and EORTC QLQ H&N35 questionnaires.
- To assess biomarkers relevant to the efficacy and mechanism of action of SCB01A.
- To explore the possible association between biomarkers and clinical outcomes

2.3.Study Endpoints

Safety

- Hematology, clinical chemistry, coagulation factors and urinalysis laboratory data changes
- AE/SAE incidence
- Physical examination results changes
- Vital sign changes
- Electrocardiogram (ECG) (including PR, QRS, QT, QTc, and RR intervals) results

Efficacy

- Disease Control Rate (DCR) is defined as the percentage of subjects who have achieved complete response (CR), partial response (PR) and stable disease (SD) at Week 9 after first treatment, according to RECIST v1.1.
- Progression-free Survival (PFS) is defined as the time from the start of treatment up to the date of first progression based on RECIST v1.1, second primary malignancy or death from any cause, whichever occurs first.
- Overall survival (OS) rate at Week 36 is defined as the percentage of subjects who are still alive at 36 weeks after first treatment with SCB01A.
- Health outcomes assessment using patient-reported EORTC QLQ-C30 and QLQ-H&N35 questionnaires.

Health outcomes assessment

- EORTC QLQ-C30
- EORTC QLQ-H&N35

Pharmacokinetic

PK concentration:

- Plasma concentration of SCB01A at the sampling time

PK parameters:

- AUC_{0-t}: area under the plasma concentration-time curve from time zero to time t
- AUC_{0-inf}: plasma concentration-time curve from time zero to infinite time
- C_{max}: maximum plasma concentration
- T_{max}: maximum concentration
- CL: clearance
- Vd: volume of distribution

- $t_{1/2}$: half-life
- Kel: elimination constant
- MRT: mean residence time

Bioanalytical measurement

- Circulating endothelial cells (CEC), vascular endothelial growth factor (VEGF) and circulating endothelial progenitor (CEP) cells

- Tumor micro vessel density and blood flow by dynamic contrast-enhanced MRI (DCE-MRI) at baseline and 6 hours after the infusion of the drug on C1D1

- Human Papillomavirus (HPV) status (expression of p16 by immunohistochemistry [IHC]) at baseline

2.4.Sample Size

Run-in Phase I (Dose Escalation Phase)

No formal statistical calculation of sample size was conducted for run-in phase I (dose escalation phase). This was a standard 3 + 3 up/down dose escalation design. The sample size was empirical. The small numbers per cohort in this phase were not intended for statistical hypotheses. Only five (5) subjects were recruited in run-in phase I when the trial was terminated.

Phase II

The sample size in phase II was based on Simon's optimal two-stage design to test that the disease control rate in subjects treated with SCB01A was less than or equal to 10% (null hypothesis), or at least 25% (alternative hypothesis), with a significance level of 0.10 (one-sided) and power of 80%. As mentioned above, in stage 1 of phase II, 13 subjects would be needed, and 21 subjects would be needed in stage 2 of phase II, with a total of 34 subjects (13 + 21) needed in phase II. There was no recruitment for phase II.

2.5.Randomization and Assignment of Subjects to Treatment Groups

This is an open label study, and no randomization is applicable.

3.Statistical Considerations

Data will be handled and processed according to the sponsor's representative (Novotech (Australia) Pty Ltd) Standard Operating Procedures (SOPs), which are written based on the principles of Good Clinical Practice (GCP).

All data collected on the eCRFs will be presented in the data listings and will be listed and sorted by subject number and visit, where applicable. All summaries will present the data by SCB01A dose level (cohort) and overall (total enrolled subjects), as applicable. Patient data will be separated via cohort and presented for enrolled subjects.

Unless otherwise stated, the following statistical approaches will be taken:

- Continuous variables: Descriptive statistics will include the number of non-missing values (N), mean, standard deviation (SD), median, minimum, maximum.
- Categorical variables: Descriptive statistics will include frequency counts and percentages per category. Percentages will be rounded to one decimal place, with the denominator being the number of subjects in the relevant population with non-missing data, unless otherwise specified.
- Imputation: No missing data will be imputed generally.
- Pharmacokinetic (PK) data: For PK data the arithmetic mean, standard deviation (SD), median, minimum, maximum, geometric mean and coefficient of variation (CV%) values will be presented.
- Confidence intervals (CIs): CIs will be two-sided and will use 95% confidence levels unless specified otherwise.
- Baseline: Baseline values will be defined as the last non-missing observation for each subject prior to the dosing of study medication (i.e. start of infusion on Cycle 1, Day 1).
- Repeat assessments: Repeat assessments will be included in summary presentations (Tables). Only the original values will be used in summary presentations. All repeat assessments captured in the Electronic Data Capture (EDC) system will be presented in the data listings.

Continuous variables will be reported to the same precision as the source data. Derived variables will be reported using the same precision to the value(s) from which they were derived. For the reporting of descriptive statistics, the mean (95% CI) and median will be reported to 1 decimal place more than the source data; the minimum, and the maximum values will be presented to the same precision as the source data; and standard deviation will be reported to 2 decimal places more than the source data. Rounding is not allowed in the middle of the calculation. It only takes place at the last step to report the final result. Post-dose time points/visits will be calculated relative to start time of infusion on Day 1. Study day will be defined as assessment day minus dosing day +1.

Analysis will conducted for run-in phase I only. The dose levels (cohorts) will be referred to in the text, tables and listings as follows,

- 3.25 mg/m^2 (Dose 1)
- 12 mg/m^2 (Dose 2)
- Total

4.Analysis Populations

The protocol pre-specified the analysis populations of Full Analysis Set, Per-protocol, Safety and PK. However, this study was terminated early with only five (5) subjects enrolled, thus the analysis populations were modified accordingly as follows.

Furthermore, any additional analysis populations not identified in the SAP will be identified in the final CSR as post hoc analyses. This may include the addition of additional study populations or subgroups of interest.

- Full Analysis Set (FAS): The FAS consists of all subjects enrolled in the run-in phase. This population will be used for the listing and summary of efficacy, health outcome, and bioanalytical measurement data.

- Safety population: The safety population will consist of all subjects who received at least one dose of SCB01A. All safety, treatment exposure, demographic and baseline characteristic data will be listed and summarized using the Safety Population

- PK population: The PK population will consist of all subjects who received at least one dose of SCB01A with sufficient post-dose bio-samples collected for PK profile characterization. PK analysis will be conducted using the PK Population.

5.Subject Disposition

All subjects who provide informed consent and are enrolled will be accounted for in this study. Subject disposition will be summarized using the Safety Population.

By-subject data listings for subject disposition will be generated, including informed consent date, phase, completion status, date completed, date discontinued and reason for discontinuation from the study, if applicable.

The number of subjects enrolled, as well as the number and percentage of subjects completing the study, and withdrawn from the study will be presented by dose levels and overall. The reason for discontinuation will also be summarized for all subjects who do not complete the study.

6.Protocol Deviations

In case protocol deviations are reported, protocol deviations will be presented for each subject in the by-subject data listings.

Prior to database lock, all protocol deviations will be reviewed by medical monitors and assigned a category (see below).

A protocol deviation is defined as any intentional or unintentional change to, or noncompliance with, the approved protocol procedures or requirements. Deviations may result from the action or inaction of the patient, investigator, or site staff. All deviations will be tracked and should be reported to (Institutional Review Board) IRBs in accordance with their reporting policy. Examples of deviations include, but are not limited to:

- Failure to adhere to study exclusion and inclusion criteria;
- Failure to comply with dispensing or dosing requirements;
- Use of medications, food, drink, herbal remedies, or supplements that are specifically prohibited in the protocol;
- Missed or out-of-window visits;
- Drug dosing not administered within the time frame specified in the protocol;
- Failure to adhere to test requirements, including vital signs, laboratory tests, physical examinations, blood draws, medical history, etc. – either tests not done, incorrect tests done, or not done within the time frame specified in the protocol;
- Procedural deviations such as incorrect storage of study drug, failure to update the ICF when new risks become known, failure to obtain IRB/EC approvals for the protocol and ICF revisions.

7.Demographic and Baseline Information

Demographic and baseline body measurements will be summarized using the Safety Population.

7.1.Demographics

Demographic data, including age, gender, race, ethnicity, weight, height, BMI, smoking status, number of years discontinued smoking, number of years smoked, and number of smokes per day will be summarized by dose level (cohort) and overall. A by-subject data listing for demographic characteristics will be generated.

7.2.Medical history and cancer history

Past medical history will be coded using the Medical Dictionary for Regulatory Activities, MedDRA® Version 19.1 or above. Medical history data, including the MedDRA codes, will be presented in the by-subject data listings.

Cancer history including date of initial diagnosis, type of cancer diagnosis, date for diagnosis of recurrent, differentiate grading of tumor, date for diagnosis of metastasis, and metastatic sites will be listed for each subject. Betel nut use status will be listed.

7.3.Inclusion/Exclusion Criteria

Inclusion/exclusion eligibility criteria information, including any criteria not met, will be listed for each subject.

7.4.Serum Pregnancy Test

A serum beta-HCG test for women of childbearing potential will be performed ≤ 14 days prior to the first dose of study treatment. Child-bearing potential (yes/no), and pregnancy test dates and results will be included in the by-subject data listings.

7.5.Human Papillomavirus (HPV) Status

Data for Human Papillomavirus (HPV) status at screening will be listed for each subject.

7.6.Nerve Conduction Velocity

Nerve conduction velocity would be performed for all patients at baseline and then during the trial only if grade 2 or above neurological symptoms experienced by the patient after receiving treatment with SCB01A. Baseline nerve conduction velocity will be summarized by NCI grade and the data will be listed as well.

8.Study Drug Administration

Study drug administration results will be presented using the Safety Population. Study drug is the administration of SCB01A. The dosing was scheduled as 3 cycles of I.V. administration of SCB01A on Days 1 and 8 of each cycle in a 3-week cycle.

A by-subject data listing will be generated for study drug administration. This listing will include date, start time, end time of administration, dose on schedule/delay (including reason for delay and days of delay), dose level, and actual dose given for SCB01A.

Dose delay, days of delay, dose omission will be summarised by dose level (cohort) and overall and by treatment cycle/day. Dose omission is defined as the missed dosing for a scheduled treatment cycle/day before early withdrawal or end of treatment. Study drug discontinuation and reason for premature study drug discontinuation will be summarised as well. Date and reason of early study drug discontinuation will be listed as well.

Body surface area (BSA) was calculated for dosing purpose, BSA will be summarised descriptively and listed for each subject.

9.Safety

Statistical methods for the safety analyses will be primarily descriptive in nature. Each dose level (cohort) will be summarized separately. No formal statistical comparisons of SCB01A dose levels will be made.

Safety endpoints include in the analysis are AEs, concomitant medications, clinical laboratory assessments (hematology, clinical chemistry, coagulation, and urinalysis), vital signs, physical examination, and 12-lead ECG. Safety endpoints will be analyzed using the Safety Population.

9.1.Adverse Events

Adverse events (AEs) will be coded using the Medical Dictionary for Regulatory Activities (MedDRA®, Version 19.1 or higher), and data will be summarized by System Organ Class (SOC) and Preferred Term (PT). The number and percent of subjects reporting each AE will be summarized for each dose level (cohort) and overall. A subject with two or more AEs within the same level of summarization (i.e., SOC or PT) will be counted only once in that level using the most severe (i.e., highest severity/grade) event or most related (for the relationship to study drug table). Percentages will be based on the number of subjects in the Safety Population within each dose level (cohort). The number of AEs reported will also be presented.

Treatment-emergent AEs (TEAEs) are defined as pre-treatment existing conditions that worsen after study drug administration, or events that occur during the course of the study during or after administration of study drug. Only TEAEs will be included in the AE summary tables which will present data by dose level (cohort). The cohorts to be included in each table are listed in section 3. In the case of a missing AE start date or stop date, the most conservative approach will be followed to classify AE into TEAE.

An overall summary of AEs will be produced including the number of TEAEs; the number and % of subjects reporting at least one: TEAE, serious TEAE, Dose Limiting Toxicity (DLT), grade 3 or higher TEAE, TEAE related to study treatment (possibly, probably, or definitely related), serious TEAE related to study treatment, grade 3 or higher TEAE related to the study drug, TEAEs by maximum severity and TEAEs by maximum relationship.

Additional AE tables will be generated as follows:

- TEAEs by SOC and PT
- Study Medication Related TEAEs by SOC and PT
- TEAEs by (Maximum) Severity
- TEAEs by (Maximum) Relationship to Study Medication
- Grade 3 or Higher TEAE by SOC and PT
- Treatment Emergent SAEs
- Study Medication Related SAEs by SOC and PT
- Dose Limiting Toxicity (DLT) by SOC and PT
- TEAEs Leading to Study Medication Permanently Discontinued
- TEAEs Leading to Study Medication Interrupted
- TEAEs Leading to Death
- Duration from Last Dosing to the Start of TEAE (days of each TEAE since its immediate last dosing)

A by-subject AE data listing, including verbatim term, MedDRA SOC and PT, severity, outcome and relationship to study treatment, will be provided. A separate listing will be generated for SAEs.

9.2.Concomitant medication

Concomitant medications will be coded using World Health Organization Drug Dictionary (WHO-DD, September 2016 or higher). Concomitant medications are medications taken at least once after the start of first study-drug administration. Medications stopped prior to the day of the start of first study-drug administration will not be considered concomitant medication. The prior medication will not be summarized, but they will be listed along with concomitant medications. Only concomitant medications will be summarized.

Individual data listings will be presented for each subject and summarized by WHO-DD Anatomical Therapeutic Chemical (ATC) anatomical group, and preferred term using frequency counts and percentages. Subjects who take the same medication more than once will be counted only once for that preferred term.

Follow-up visits were scheduled after end of treatment or early withdrawal visit with regards to cancer radiation therapy, cancer systemic therapy, or cancer surgery. These treatments, if any, will be listed separately.

9.3.Laboratory

9.3.1.Laboratory Parameters

Hematology Parameters
- WBC
- Neutrophils
- Lymphocytes
- Monocytes
- Eosinophils
- Basophils
- Red blood cell (RBC)
- Hematocrit (Hct)
- Hemoglobin
- Mean corpuscular volume (MCV)
- Mean corpuscular hemoglobin (MCH)
- Mean corpuscular haemoglobin concentration (MCHC),
- Platelet count

Chemistry Parameters

- Blood urea nitrogen (BUN)
- Creatinine
- AST
- ALT
- ALP
- Total Bilirubin
- Albumin
- Calcium
- Glucose
- Uric Acid
- Potassium
- Total creatine kinase (Ck) (if total Ck is above the ULN for the laboratory, Troponin-T or Troponin-I will be determined)
- Gamma-glutamyl transferase (GGT)
- Total cholesterol
- High-density lipoprotein (HDL)
- Low-density lipoprotein (LDL)
- Triglycerides (TG)
- Amylase
- Lipase

Coagulation Parameters

- Prothrombin Time
- INR

Urinalysis Parameters

- Specific gravity
- pH
- Protein
- Glucose
- Leucocytes
- Erythrocyte
- Nitrite
- Ketone body
- Urobilinogen
- Bilirubin
- RBC
- WBC
- Hyaline
- Cast
- CAOX
- Crystal
- AMOR
- Mucus

9.3.2.Biostatistical methods

All hematology, chemistry and coagulation parameters will be summarized using descriptive statistics for each dose level (cohort) for all time points assessed, including change from baseline (last pre-dose value) for all post-dose assessments. All continuous parameters will be summarized using the units reported from the laboratory.

Urinalysis will be summarised as categorical data by using frequency and percentage, as appropriate, except for specific gravity and pH which will be treated as continuous data.

Subjects with abnormal laboratory values will be summarized for each laboratory parameter by study visit and by dose cohort. The frequency counts and percentages of subjects with laboratory value out of reference range (low/high) and their clinical significance (if any data) will be summarized. Shift tables from Cycle 1, Day 1 (pre-dose) to all follow-up visits will also be generated for each chemistry laboratory parameter with values of Within Normal Limits (WNL), High, and Low used for the shift categories.

All laboratory data will be included in the by-subject data listings. Laboratory values will be compared to normal range of the single local laboratory and values that fall outside of the normal ranges will be flagged as: H (High) and L (Low) in the data listings.

9.4.Vital Signs

9.4.1.Vital Sign Parameters

- Heart Rate (beats/min)
- Systolic Blood Pressure (SBP) (mmHg)
- Diastolic Blood Pressure (DBP) (mmHg)
- Respiratory rate (breaths/minute)
- Body Temperature (°C)

9.4.2.Biostatistical methods

All vital sign parameters will be summarized using descriptive statistics for each dose level and overall for all time points assessed, including change from baseline (last pre-dose value) for all post-dose assessments. Pre-dosing vital sign on Cycle1, Day 1 will be used as baseline data. If the baseline value is missing, then the data from Screening will be used as baseline data.

9.5.Physical examination

9.5.1.Body Systems Assessed

- General Appearance
- Dermatologic
- HEENT (Head, Eyes, Ears, Nose and Throat)
- Respiratory
- Cardiovascular
- Musculoskeletal
- Gastrointestinal

- Abdomen/Pelvic
- Neurological
- Other

For abnormal result of physical examination:

- Abnormal NCS (Not Clinically Significant)
- Abnormal CS (Clinically Significant)

9.5.2.Biostatistical methods

Physical examination will be summarized by study visit and treatment cohort. The frequency counts and percentages of subjects with different physical examination results and their clinical significance (for abnormal) will be summarized.

By-subject data listings will be generated for the physical examination data, including the Investigator assessment of clinical significance for abnormal findings, for all time points assessed.

9.6.12-lead ECG

9.6.1.ECG Parameters

- Ventricular Rate (beats/min)
- PR interval (msec)
- QRS duration (msec)
- QT interval (msec)
- QTc interval (msec)
- RR interval (msec)
- Overall interpretation of 12-lead ECG:
    - Normal
    - Abnormal NCS (Not Clinically Significant)
    - Abnormal CS (Clinically Significant)

9.6.2.Biostatistical methods

Descriptive statistics will be calculated for ventricular rate, PR interval, QRS duration, QT interval, QTc interval, and RR interval, including change from baseline (last pre-dose value on Cycle 1, Day 1) for each dose level (cohort) for all time points assessed. If triplicate ECG parameters are available, the average of the triplicate ECG parameters will be used. Unscheduled visits will be excluded from summary tables. However, the findings from the unscheduled will be listed.

In addition, the overall interpretation of 12-lead ECG results will be classified using frequency counts and percentages for the categories of Normal, Abnormal - Not Clinically Significant (NCS) and Abnormal - Clinically Significant (CS) for each treatment group for all time points assessed.

All ECG data will be presented in the by-subject data listings.

10.Efficacy

Statistical methods for the efficacy analyses will be primarily descriptive in nature, due to small number of subjects enrolled. Each dose level (cohort) and overall group will be summarized separately. No formal statistical comparisons of SCB01A dose levels will be made.

Efficacy endpoints include in the analysis are DCR, PFS, and OS. Efficacy endpoints will be analyzed using the Full Analysis Set. For PFS and OS, if there is no event reported (progression or death), their survival functions can not be estimated. Thus, only simple descriptive statistics will be provided.

When confidence interval (CI) is estimated, both 90% CI and 95% CI will be provided for DCR. For other endpoints, only 95% CI will be provided.

10.1.Tumor Response and Disease Control Rate

Tumor assessments were made based upon the RECIST criteria (Response Evaluation Criteria in Solid Tumors version 1.1). Tumor assessments were scheduled at baseline, and every 3 cycles prior to next cycle until progression of disease. For this analysis purpose, tumor response evaluation at Week 9 (Cycle 4, Day 1) or end of treatment/early termination will be pooled and used as the best overall response from start of dosing up to Week 9.

For the analysis of tumor response, a summary table presenting the number and proportion of responders (DC) and non-responders (non-DC) in each dose level, together with the two-sided 90% and 95% confidence intervals for response rates will be produced. The proportion and the corresponding 90% and 95% confidence interval for each of the response categories (CR, PR, SD, PD, and unevaluable) by dose level will also be presented. The confidence interval will be based on Pearson-Clopper exact CI.

The details of target lesions, non-target lesion, and new lesions (if any) will be listed for each subject.

10.2.Progression-free Survival and Overall Survival

Progression-free Survival (PFS) is defined as the time from the start of treatment up to the date of first progression based on RECIST v1.1, second primary malignancy or death from any cause, whichever occurs first. Patients without progression or death will be censored at the last disease assessment date.

Overall survival (OS) is defined as the time from the start of treatment up to the date of death, regardless of causes. Patients without death will be censored at the last follow up date.

The analysis of PFS and OS is based on the survivor function, which is the probability to survive or, more generally, to stay event-free beyond a certain point in time. The survival function is estimated by the Kaplan-Meier method. The survival function will be summarized for 25th percentile, median, and 75th percentile and their 95% confidence intervals. For OS, survival rate at Week 36 will be reported, based on the survival function, if this estimate is available. The plot of Kaplan-Meier estimates for the dose levels will be presented. If there is no event reported (progression or death), only simple descriptive statistics will be provided.

11.Health Outcome and ECOG-PS

Statistical methods for the health outcome analyses will be primarily descriptive in nature. Each dose level (cohort) will be summarized separately. No formal statistical comparisons of SCB01A dose levels will be made.

Patients would complete the EORTC QLQ-C30 and QLQ-H&N35 questionnaires at screening and before study drug administered, except Cycle 1, Day1. The questionnaire consists of 65 questions that help determine the health outcome of the patients. Health outcome endpoints will be analyzed using the Full Analysis Set.

Analysis of Eastern Cooperative Oncology Group Performance Status (ECOG-PS) will be provided as well.

11.1.EORTC QLQ-C30

The EORTC quality of life questionnaire (QLQ) is an integrated system for assessing the health-related quality of life (QoL) of cancer patients participating in international cancer trials. The QLQ-C30 (version 3.0, 30 questions) is composed of both multi-item scales and single-item measures. According to the EORTC QLQ-C30 scoring manual, these questions are grouped into five functional scales, three symptom scales, a global health status/QoL scale and six single items. The 30 questions of the QLQ-C30 are numbered 1 to 30 and the grouping is summarized as follows.

Grouping of the EORTC QLQ-C30 Questionnaire

Description of Sub-scores	Number of Questions	Question Number in CRF	Range*
Global Health Status/QoL			
Global health status/QoL	2	29, 30	6
Functional Scales			3
Physical functioning	5	1 to 5	3
Role functioning	2	6, 7	3
Emotional functioning	4	21 to 24	3
Cognitive functioning	2	20, 25	3
Social functioning	2	26, 27	3
Symptom Scales /Items			
Fatigue	3	10, 12, 18	3
Nausea and Vomiting	2	14, 15	3
Pain	2	9, 19	3
Dyspnoea	1	8	3
Insomnia	1	11	3
Appetite loss	1	13	3
Constipation	1	16	3
Diarrhoea	1	17	3
Financial difficulties	1	28	3

* Difference between the highest and the lowest possible answer to a question

The computation of the scores for each scale based on the questions assigned to it will be completed in several steps and will follow the scoring procedure given in the manual. The individual steps are briefly outlined below.

Calculation of the Raw Score

A Raw Score (RS) is calculated by averaging the answers given for all items I_1, I_2, …, I_n included in a scale according to the formula

$$RS = (I_1 + I_2 + \ldots, I_n) / n$$

where I_i is the answer to the question I (i=1,…,n) and n denotes the total number of questions in the scale to be analyzed.

As an example, the RS for the functional scale "Physical Functioning" is calculated by adding up all the answers a patient gives to questions 1 to 5 and subsequently dividing the result by 5. The RS for the functional scale "Role Functioning" is similarly obtained be averaging the two scores the patient selects for questions 6 and 7.

Standardization

As specified in the manual, the Raw Scores are subsequently standardized for each of the functional scales, symptom scales /items and global health status/QoL to a value between 0 and 100. For all functional scales of the QLQ-C30 the linear transformation applied is

$$S = \left\{1 - \frac{(RS - 1)}{range}\right\} \times 100 .$$

For the symptom scales/items and the global health status formulae/QoL the linear transformation is

$$S = \{(RS - 1)/range\} \times 100 .$$

The range is the difference between the possible maximum and minimum response a patient can select for each scale.

Handling of Missing Values

The psychometrically validated method according to the EORTC manual will be used to handle cases where some questions belonging to a symptom scale, functional scale or global health status are not answered. If at least half of the items from the scale have been answered, the missing items are imputed and will have values equal to the average of those items which are present for that respondent. Otherwise, the raw score of the scale is set to missing.

Interpretation

The scores S computed according to formulae above have the following interpretation:

- a high score for a **functional scale** represents a high / healthy level of functioning
- a high score for the **global health status/QoL** represents a high QoL
- a high score for a **symptom scale/item** represents a high level of symptomatology / problems

Biostatistical methods

The assessment of EORTC QLQ-C30 conducted at screening is regarded as the baseline assessment, as it is taken prior to dosing. Quality of life data will be summarised descriptively. Global health status/QoL, each functional scale, and each symptom scale/item
will be summarized using descriptive statistics for each dose level for all time points assessed, including change from baseline for all post-dose assessments. Plots of mean values and 95% confidence intervals by dose level over time will be provided for each scale or item.

11.2.EORTC QLQ-H&N35

The QLQ-H&N35 is used among a wide range of patients with head & neck cancer, varying in disease stage and treatment modality. There are 35 questions assessing symptoms and side effects of treatment, social function and body image/sexuality. The questions are grouped into seven multi-item scales that assess pain, swallowing, senses (taste and smell), speech, social eating, social contact and sexuality. There are also eleven single items. The 35 questions of the QLQ-STO22 are numbered 31 to 65 and the grouping is summarized as follows.

Grouping of the EORTC QLQ-H&N35 Questionnaire

Description of Sub-scores	Number of Questions	Question Number in CRF	Range*
Symptom Scales / Items			
Pain	4	31, 32, 33, 34	3
Swallowing	4	35, 36, 37, 38	3
Senses problems	2	43, 44	3
Speech problems	3	46, 53, 54	3
Trouble with social eating	4	49, 50, 51, 52	3
Trouble with social contact	5	48, 55, 56, 57, 58	3
Less sexuality	2	59, 60	3
Teeth	1	39	3
Opening mouth	1	40	3
Dry mouth	1	41	3
Sticky saliva	1	42	3
Coughing	1	45	3
Felt ill	1	47	3
Pain killers	1	61	1
Nutritional supplements	1	62	1
Feeding tube	1	63	1
Weight loss	1	64	1
Weight gain	1	65	1

* Difference between the highest and the lowest possible answer to a question

The principle for scoring the scales is the same as for the EORTC QLQ-C30 questionnaire symptom scales/items, as described above.

- Estimate the average of the items that contribute to the scale to obtain the Raw Score
- Use a linear transformation to standardize the raw score, so that scores range from 0 to 100; a high score represents a higher (“worse”) level of symptoms

Biostatistical Methods

The assessment of EORTC QLQ-H&N35 conducted at screening is regarded as the baseline assessment, as it is taken prior to dosing. Quality of life data will be summarised descriptively. Each symptom scale/item will be summarized using descriptive statistics for each dose level for all time points assessed, including change from baseline for all post-dose assessments. Plots of mean values and 95% confidence intervals by dose level over time will be provided for each scale or item.

11.3.Eastern Cooperative Oncology Group Performance Status (ECOG-PS)

ECOG-PS will be treated as continuous data, and will be summarised descriptively for each dose level for all time points assessed, including change from baseline for all post-dose assessments. ECOG-PS will be listed for all subjects.

12.Pharmacokinetics (PK)

PK analyses will be conducted with the PK Population. PK analysis of SCB01A plasma concentration-time data will be performed using validated PK software (Phoenix WinNonlin version 6.3 or higher), by a standard non-compartmental model. The actual plasma sampling times from the CRF database, i.e., the elapsed time of the blood sampling time from the dosing time, will be used for PK analysis. The PK blood samples would be taken immediately pre-infusion then at 2, 3, 4, 6, 10, 21 and 24 hours after the start of infusion on Days 1 and 8 of Cycles 1, 2 and 3

12.1.Definition of variables

Whenever possible, the PK parameters listed below will be calculated for each subject based on the plasma concentrations of SCB01A according to the model independent approach.

SCB01A Plasma, Day 1 and Day 8 of each Cycle

AUC_{0-t}	The area under the plasma concentration-time curve, from time 0 (time of dosing) to the last time point with measurable analyte concentration, calculated by the log-linear trapezoidal method.
AUC_{0-inf}	The area under the plasma concentration-time curve from time 0 extrapolated to infinity. AUC_{0-inf} is calculated as the sum of AUC_{0-t} plus the ratio of the last measurable plasma concentration to the elimination rate constant (λz).
C_{max}	Maximum observed concentration.
T_{max}	The first time when C_{max} is observed
CL	Apparent clearance calculated as Dose/AUC_{0-inf}.
Vd	Apparent total volume of distribution at the terminal phase, calculated as Dose/(Kel × AUC_{0-inf}).
$t_{½}$	Apparent terminal elimination half-life of medication, calculated as 0.693/λz.
Kel:	The apparent first-order terminal elimination rate constant, calculated by linear least-squares regression analysis the terminal log-linear phase of the plasma concentration vs. time curves using at least 3 time points.
MRT	mean residence time

12.2.Biostatistical methods

SCB01A plasma concentrations will be listed by subject, dose level, and nominal (scheduled) sampling time. SCB01A concentrations will be summarized by dose level and nominal sampling time for the PK Analysis Population. Plasma concentrations that are below the limit of quantitation (BLQ) will be set to 0 for calculation of summary statistics for concentration data at each time point, except geometric statistics (geometric mean and geometric CV%). For the

calculation of the geometric statistics they will be treated as equal to the Lower Limit of Quantification (LLQ). Missing values will be omitted from the calculation of descriptive statistics.

The actual blood sampling dates and times relative to dosing time will be listed by study group (dose level), subject and nominal sampling time, with time deviation calculated, for all subjects with available plasma concentration data, including subjects excluded from the PK Analysis Population.

Figures of individual plasma concentration vs. actual time profiles for SCB01A will be produced on both linear and semi-log scales for the PK Analysis Population. Mean and median plasma blood concentration vs. nominal time curves for all dose levels in the PK Analysis Population will be plotted together on both linear and semi-log scales for SCB01A.

Pharmacokinetic parameters for each dose level will be calculated from the concentrations of SCB01A measured in pre-dose and post-dose plasma samples. Actual collection time will be used in the calculation of plasma PK parameters. For the calculation of the PK parameters, all plasma concentrations that are BLQ prior to the first measurable concentration will be set to zero. The BLQ values that are between measurable concentrations will be set to missing. The BLQ values that occur at the end of the profile (after the last quantifiable concentration) will be set to missing and will not be used for the estimation of parameter values.

For each dose level, descriptive statistics will be provided for the PK parameters. Summary tabulations will display the number of observations, mean, SD, CV%, median, minimum and maximum. Geometric means and geometric CV% will be calculated for AUCs and C_{max}. PK parameters will be displayed by dose levels. AUC_{0-t}, AUC_{0-inf}, and C_{max} will also be presented in scatter plots by treatment.

13.Bioanalytical Measurement

Exploratory research would be performed to analyze relevant biomarkers.

- Biomarkers analysis would be performed on patients enrolled in the run-in phase including circulating endothelial cells (CEC), vascular endothelial growth factor (VEGF) and circulating endothelial progenitor (CEP) cells
- Tumor micro vessel density and blood flow by dynamic contrast-enhanced MRI (DCE-MRI) will be performed in patients with identified sites which be selected by the sponsor at both baseline and 6 hours after the infusion of the drug on Cycle 1, Day 1. Analysis of DCE-MRI data might not be covered by this SAP.

Depending on the availability of biomarker data (CEC, VEGF and CEP), these data will be summarised descriptively by dose level and overall. These data will be listed as well for all subjects.

14.Handling of Missing Data

Missing values will not be imputed.

15.Changes to the Planned Analysis

Any changes to the analyses outlined in the approved SAP will be detailed in the Clinical Study Report (CSR).

16.Interim and Final Analysis

16.1.Interim Analyses

An interim statistical analysis was planned following the completion of stage 1, Phase II. However, this study was terminated in run-in phase I.

16.2.Final Analysis (End of Study)

The final end of study analysis, post the data base lock, will be based on the final version of the SAP.

17.Software

The following software will be used to perform the statistical analyses: SAS® Version 9.2 or higher (SAS Institute, Cary, North Carolina, USA)

18.Tables

No.	Title	Analysis Population	Table to be Generated
	Disposition and Baseline Data		
14.1.1.1	Summary of Disposition and Analysis Populations	Safety	Y
14.1.1.2	Summary of Demographics	Safety	Y
14.1.1.3	Summary of Baseline Never Conduction Velocity by NCI Grade	Safety	
	Efficacy		
14.2.1.1	Summary of Tumor Response and Disease Control Rate	FAS	Y
14.2.1.2	Summary of Progression-free Survival	FAS	Y
14.2.1.3	Summary of Overall Survival	FAS	Y
	Health Outcome		
14.2.2.1	Summary of EORTC QLQ-C30 (Version 3.0) Over Time	FAS	Y
14.2.2.2	Summary of EORTC QLQ-H&N35 Over Time	FAS	Y
14.2.2.3	Summary of Eastern Cooperative Oncology Group Performance Status (ECOG-PS)	FAS	
	PK		
14.2.3.1	Summary of Plasma Concentrations of SCB01A by Dose Level	PK	Y
14.2.3.2	Summary of Plasma Pharmacokinetic Parameters of SCB01A by Dose Level and Treatment Cycle/Day	PK	Y
	Biomarker		
14.2.4.1	Summary of Biomarker Data (if available)	FAS	
	Study Treatment		
14.3.1.1	Summary of Dose Delay, Dose Omission and Early Study Drug Discontinuation	Safety	
14.3.1.2	Summary of Body Surface Area (BSA, m^2)	Safety	
	Adverse Events		
14.3.2.1	Overall Summary of Treatment Emergent Adverse Events	Safety	Y
14.3.2.2	Summary of Treatment Emergent Adverse Events by SOC (System Organ Class) and PT (Preferred Term)	Safety	Y
14.3.2.3	Summary of Related Treatment Emergent Adverse Events by SOC (System Organ Class) and PT (Preferred Term)	Safety	Y
14.3.2.4	Summary of Treatment Emergent Adverse Events by Maximum Severity	Safety	
14.3.2.5	Summary of Treatment Emergent Adverse Events by Maximum Relationship to Study Medication	Safety	
14.3.2.6	Summary of Grade 3 or Higher Treatment Emergent Adverse Events by SOC (System Organ Class) and PT (Preferred Term)	Safety	
14.3.2.7	Summary of Treatment Emergent Serious Adverse Events by SOC (System Organ Class) and PT (Preferred Term)	Safety	Y
14.3.2.8	Summary of Related Treatment Emergent Serious Adverse Events by SOC (System Organ Class) and PT (Preferred Term)	Safety	
14.3.2.9	Summary of Dose Limiting Toxicity (DLT) by SOC (System Organ Class) and PT (Preferred Term)	Safety	Y

No.	Title	Analysis Population	Table to be Generated
14.3.2.10	Summary of Treatment Emergent Adverse Events Leading to Study Medication Permanently Discontinued	Safety	
14.3.2.11	Summary of Treatment Emergent Adverse Events Leading to Study Medication Interrupted	Safety	
14.3.2.12	Summary of Treatment Emergent Adverse Events Leading to Death	Safety	
14.3.2.13	Summary of Duration from Last Dosing to the Start of Treatment Emergent Adverse Events	Safety	Y
	Concomitant Medications		
14.3.3.1	Summary of Concomitant Medications	Safety	Y
	Laboratory		
14.3.4.1	Laboratory - Hematology: Summary and Change from Baseline	Safety	Y
14.3.4.2	Laboratory - Chemistry: Summary and Change from Baseline	Safety	Y
14.3.4.3	Laboratory - Coagulation: Summary and Change from Baseline	Safety	Y
14.3.4.4	Laboratory - Urinalysis: Summary and Clinical Significance	Safety	Y
14.3.4.5	Laboratory - Hematology: Out of Range and Clinical Significance	Safety	Y
14.3.4.6	Laboratory - Chemistry: Out of Range and Clinical Significance	Safety	Y
14.3.4.7	Laboratory - Coagulation: Out of Range and Clinical Significance	Safety	Y
14.3.4.8	Laboratory – Hematology: Shift Table	Safety	
14.3.4.9	Laboratory - Chemistry: Shift Table	Safety	
14.3.4.10	Laboratory - Coagulation: Shift Table	Safety	
	Vital Signs		
14.3.5.1	Summary of Vital Signs	Safety	Y
	Physical Examination		
14.3.6.1	Summary of Physical Examination	Safety	
	ECG		
14.3.7.1	Summary of ECG Values	Safety	Y
14.3.7.2	Summary of ECG Findings	Safety	Y

Due to limitation of available data, only those tables marked as 'Y' will be generated.

19.Listings

No.	Title	Analysis Population	Listing to be Generated
	Disposition and Baseline Data		
16.2.1.1	Listing of Enrolment, Informed Consent and Disposition	Safety	Y
16.2.2.1	Listing of Protocol Deviations	Safety	
16.2.3.1	Listing of Analysis Populations	Safety	Y
16.2.4.1	Listing of Demographics	Safety	Y
16.2.4.2	Listing of Medical History	Safety	Y
16.2.4.3	Listing of Cancer History	Safety	Y
16.2.4.4	Listing of Betel Nut Use Status	Safety	Y
16.2.4.5	Listing of Inclusion/Exclusions Criteria	Safety	Y
16.2.4.6	Listing of Serum Pregnancy Test – Females Only	Safety	
16.2.4.7	Listing of Human Papillomavirus (HPV) Status	Safety	
16.2.4.8	Listing of Never Conduction Velocity	Safety	
	Study Treatment		
16.2.5.1	Listing of Study Drug Administration	Safety	Y
16.2.5.2	Listing of Early Study Drug Discontinuation	Safety	Y
16.2.5.3	Listing of Body Surface Area (BSA)	Safety	
	Concomitant Medications		
16.2.5.4	Listing of Concomitant and Prior Medications	Safety	Y
16.2.5.5	Listing of Cancer-Radiation Therapy	Safety	Y
16.2.5.6	Listing of Cancer-Systemic Therapy	Safety	Y
16.2.5.7	Listing of Cancer-Surgery	Safety	Y
	Efficacy		
16.2.6.1	Listing of Target Lesions	FAS	Y
16.2.6.2	Listing of Non-Target Lesions	FAS	Y
16.2.6.3	Listing of Tumor Response Evaluation (Based on RECIST)	FAS	Y
16.2.6.4	Listing of Survival Status	FAS	Y
16.2.6.5	Listing of EORTC QLQ-C30	FAS	Y
16.2.6.6	Listing of EORTC QLQ-H&N35	FAS	Y
16.2.6.7	Listing of Eastern Cooperative Oncology Group Performance Status (ECOG-PS)	FAS	Y
	PK		
16.2.6.8	Listing of Individual SCB01A Plasma Concentration Data	PK	Y
16.2.6.9	Listing of Individual SCB01A Plasma Pharmacokinetic Parameters by Treatment Cycle/Day	PK	Y
	Biomarker		
16.2.6.10	Listing of Biomarker Data (if available)	FAS	
	Adverse Events		
16.2.7.1	Listing of Adverse Events	Safety	Y
16.2.7.2	Listing of Serious Adverse Events	Safety	Y
16.2.7.3	Listing of Dose Limiting Toxicity (DLT)	Safety	
16.2.7.4	Listing of Adverse Events Leading to Study Medication Permanently Discontinued or Interrupted	Safety	
	Laboratory		
16.2.8.1	Listing of Haematology	Safety	Y

No.	Title	Analysis Population	Listing to be Generated
16.2.8.2	Listing of Biochemistry	Safety	Y
16.2.8.3	Listing of Coagulation	Safety	Y
16.2.8.4	Listing of Urinalysis	Safety	Y
	Vital Signs		
16.2.9.1	Listing of Vital Signs	Safety	Y
	Physical Examination		
16.2.10.1	Listing of Physical Examination	Safety	Y
	ECG		
16.2.11.1	Listing of ECG Values and Findings	Safety	Y

Due to limitation of available data, only those listings marked as 'Y' will be generated.

20.Figures

No.	Title	Analysis Population	Figures to be Generated
	Efficacy		
14.2.1.1	Kaplan-Meier Curve of Progression-free Survival	FAS	Y
14.2.1.2	Kaplan-Meier Curve of Overall Survival	FAS	Y
	Health Outcome		
14.2.2.1a	Plot of Mean Global Health Status Score/QoL with 95% Confidence Interval Over Time (EORTC QLQ-C30)	FAS	Y
14.2.2.1b	Plot of Mean Physical Functioning Score with 95% Confidence Interval Over Time (EORTC QLQ-C30)	FAS	
14.2.2.1c	Plot of Mean Role Functioning Score with 95% Confidence Interval Over Time (EORTC QLQ-C30)	FAS	
14.2.2.1d	Plot of Mean Emotional Functioning Score with 95% Confidence Interval Over Time (EORTC QLQ-C30)	FAS	
14.2.2.1e	Plot of Mean Cognitive Functioning Score with 95% Confidence Interval Over Time (EORTC QLQ-C30)	FAS	
14.2.2.1f	Plot of Mean Social Functioning Score with 95% Confidence Interval Over Time (EORTC QLQ-C30)	FAS	
14.2.2.1g	Plot of Mean Fatigue Score with 95% Confidence Interval Over Time (EORTC QLQ-C30)	FAS	
14.2.2.1h	Plot of Mean Nausea and Vomiting Score with 95% Confidence Interval Over Time (EORTC QLQ-C30)	FAS	
14.2.2.1i	Plot of Mean Pain Score with 95% Confidence Interval Over Time (EORTC QLQ-C30)	FAS	
14.2.2.1j	Plot of Mean Dyspnoea Score with 95% Confidence Interval Over Time (EORTC QLQ-C30)	FAS	
14.2.2.1k	Plot of Mean Insomnia Score with 95% Confidence Interval Over Time (EORTC QLQ-C30)	FAS	
14.2.2.1l	Plot of Mean Appetite Loss Score with 95% Confidence Interval Over Time (EORTC QLQ-C30)	FAS	
14.2.2.1m	Plot of Mean Constipation Score with 95% Confidence Interval Over Time (EORTC QLQ-C30)	FAS	
14.2.2.1n	Plot of Mean Diarrhoea Score with 95% Confidence Interval Over Time (EORTC QLQ-C30)	FAS	
14.2.2.1o	Plot of Mean Financial Difficulties Score with 95% Confidence Interval Over Time (EORTC QLQ-C30)	FAS	
14.2.2.2a	Plot of Mean Pain Score with 95% Confidence Interval Over Time (EORTC QLQ-H&N35)	FAS	
14.2.2.2b	Plot of Mean Swallowing Score with 95% Confidence Interval Over Time (EORTC QLQ-H&N35)	FAS	
14.2.2.2c	Plot of Mean Senses Problems Score with 95% Confidence Interval Over Time (EORTC QLQ- H&N35)	FAS	
14.2.2.2d	Plot of Mean Speech Problems Score with 95% Confidence Interval Over Time (EORTC QLQ-H&N35)	FAS	
14.2.2.2e	Plot of Mean Trouble with Social Eating Score with 95% Confidence Interval Over Time (EORTC QLQ-H&N35)	FAS	
14.2.2.2f	Plot of Mean Trouble with Social Contact Score with 95% Confidence Interval Over Time (EORTC QLQ-H&N35)	FAS	

No.	Title	Analysis Population	Figures to be Generated
14.2.2.2g	Plot of Mean Less Sexuality Score with 95% Confidence Interval Over Time (EORTC QLQ-H&N35)	FAS	
14.2.2.2h	Plot of Mean Teeth Score with 95% Confidence Interval Over Time (EORTC QLQ-H&N35)	FAS	
14.2.2.2i	Plot of Mean Opening Mouth Score with 95% Confidence Interval Over Time (EORTC QLQ-H&N35)	FAS	
14.2.2.2j	Plot of Mean Dry Mouth Score with 95% Confidence Interval Over Time (EORTC QLQ-H&N35)	FAS	
14.2.2.2k	Plot of Mean Sticky Saliva Score with 95% Confidence Interval Over Time (EORTC QLQ-H&N35)	FAS	
14.2.2.2l	Plot of Mean Coughing Score with 95% Confidence Interval Over Time (EORTC QLQ-H&N35)	FAS	
14.2.2.2m	Plot of Mean Felt Ill Score with 95% Confidence Interval Over Time (EORTC QLQ-H&N35)	FAS	
14.2.2.2n	Plot of Mean Pain Killers Score with 95% Confidence Interval Over Time (EORTC QLQ-H&N35)	FAS	
14.2.2.2o	Plot of Mean Nutritional Supplements Score with 95% Confidence Interval Over Time (EORTC QLQ-H&N35)	FAS	
14.2.2.2p	Plot of Mean Feeding Tube Score with 95% Confidence Interval Over Time (EORTC QLQ-H&N35)	FAS	
14.2.2.2q	Plot of Mean Weight Loss Score with 95% Confidence Interval Over Time (EORTC QLQ-H&N35)	FAS	
14.2.2.2r	Plot of Mean Weight Gain Score with 95% Confidence Interval Over Time (EORTC QLQ-H&N35)	FAS	
	PK		
14.2.3.1a	Mean (+SD) Plasma Concentrations of SCB01A Over Time by Dose Level (Linear Scale)	PK	
14.2.3.1b	Mean (+SD) Plasma Concentrations of SCB01A Over Time by Dose Level (Semilogarithmic Scale)	PK	Y
14.2.3.2a	Median Plasma Concentrations of SCB01A Over Time by Dose Level (Linear Scale)	PK	
14.2.3.2b	Median Plasma Concentrations of SCB01A Over Time by Dose Level (Semilogarithmic Scale)	PK	
14.2.3.3a	Individual Plasma Concentrations of SCB01A Over Time (Linear Scale)	PK	
14.2.3.3b	Individual Plasma Concentrations of SCB01A Over Time (Semilogarithmic Scale)	PK	Y
14.2.3.4a	Scatterplot of Individual and Mean Plasma AUC_{0-t} of SCB01A versus Dose Level by Treatment Cycle/Day	PK	
14.2.3.4b	Scatterplot of Individual and Mean Plasma AUC_{0-inf} of SCB01A versus Dose Level by Treatment Cycle/Day	PK	
14.2.3.4c	Scatterplot of Individual and Mean Plasma C_{max} of SCB01A versus Dose Level by Treatment Cycle/Day	PK	

Due to limitation of available data, only those figures marked as 'Y' will be generated.

21.References

1) SCB01A-21 Clinical Study Protocol, Version 3.0, 25Jul2016