Statistical Analysis Plan: Mock-up Tables and Figures

Version 3.0, 14DEC2018

Protocol Number: SCB01A-22

An Open-Label, Phase II Study to Evaluate the Efficacy and Safety of SCB01A in Subjects with Recurrent or Metastatic Squamous Cell Head and Neck Cancer Who Have Failed Platinum-Based Treatment

Protocol version: 1.0 /19-Dec-2016
Sponsor: SynCore Biotechnology Co., Ltd.

Table of Contents

1 Statistical Changes from Study Protocol

The statistical analysis methods will follow study protocol version 1.0, 19DEC2016, exceptions and clarifications are described below:

1.1 PK Analysis

Pharmocokinetics Sampling will be bio-analyzed, and PK Parameters will be calculated by Protech Pharmaservices Corporation. All PK and PK parameter data will be provided to sponsor directly, no data handling, data listing nor statistical analysis on such data will be done by A2 Healthcare.

> 8.6. PK Analysis
>
> The blood samples will be assayed for SCB01A and PK parameters (maximum plasma concentration [Cmax], clearance [CL], volume of distribution [Vd], half-life [t1/2], elimination constant [Kel], mean residence time [MRT] and time to maximum concentration [Tmax]) will be determined and presented graphically and descriptively (as appropriate).

1.2 Objective response rate (ORR) Definition

ORR is defined as the percentage of subjects who have achieved confirmed CR and PR during treatment phase, according to RECIST v1.1. Not-confirmed CR or PR, or withdraw for DLT are counted as non-responder. There are 5 subjects who are not evaluated due to clinical disease progression or AE/SAE. Tumor non-evaluable subjects are tend to be treatment failure and will also be counted as non-responder (Not Evaluable for Response), instead of counted as missing.

> **Criteria for Evaluation:**
> **Efficacy measurements:**
>
> - ORR is defined as the percentage of subjects who have achieved confirmed CR and PR during treatment phase, according to RECIST v1.1. Not-confirmed CR or PR, or withdraw for DLT are counted as non-responder.

2 Mock-up Tables and Figures

The Mock-up “TABLES and FIGURES” is planned according to ICH E3, in which relevant CSR section is 14. The words shadowed below are to be adjusted or repeated upon real data, or just for notification.

For all statistical analyses tables, the descriptive statistics will be displayed on maximum treatment dose level and overall.

Columns {Label, Max. Dose Levels, Total} will be included with the analyzed population specified. In the mock table below, only the Label with one treatment column were presented to show the descriptive/inferential statistics to be displayed in the final tabulation.

The DSMB, composed of medical monitors (physicians experienced in oncology studies) and at least one statistician. Their responsibilities are to review and evaluate the data for safety, study conduct and progress, and make recommendations concerning the continuation, modification, or termination of study. Serial assessments of PK results also may be taken into account for safety evaluation. A neurologist will be invited to join DSMB meeting as a consultant when neurotoxicity occurred.
The document review or meeting of DSMB will be held when the following scenarios:

- *A subject is not recovered from Grade 2 neurotoxicity over three weeks;*
- *A subject revealed Grade 3 or above neurotoxicity;*
- *After 10 evaluable subjects finished the study in Stage I*

Note:

(1) Site ID:

Site ID	Site Name
1	Taipei Medical University Hospital (TMUH)
2	National Cheng Kung University Hospital (NCKUH)
3	Taipei Veterans General Hospital (TVGH)
4	Taipei Medical University Shuang Ho Hospital (TMUSHH)

(2) Study subjects will be categorized into the following populations for analysis:

- Intention-to-treat (ITT) population: The ITT population consists of all subjects enrolled in the study and received at least one study treatment.
- Per-protocol (PP) population: The PP population will consist of all subjects who
  (1) withdraw from study for DLT, or
  (2) completed at least 3 cycles of study treatment regimen, have measurable baseline disease and, at least, one post-baseline RECIST assessment (PD, SD, PR or CR). Subjects with a major protocol deviation or AE, deemed by the Medical Monitor to have an impact on the study endpoints, will be excluded from the PP population.
- PK population: The PK population will consist of all subjects in stage I who received, at least, one dose of 24 mg/m^2 of SCB01A with sufficient post-dose bio-samples collected for PK profile characterization.

(3) Maximum treatment dose level

Level 1 (12 mg/m^2)	Level 1a (9 mg/m^2)	Level 1b (7 mg/m^2)
Level 2 (18 mg/m^2)	Level 2a (15 mg/m^2)	Level 2b (12 mg/m^2)
Level 3 (24 mg/m^2)	Level 3a (20 mg/m^2)	Level 3b (16 mg/m^2)

(4) For Visit Name, C(c) denotes cycle (c), D(d) denotes day (d)

Visit No.	**Visit Name**	**Visit Code**	**Planned Visit Day**
0	Screening Visit	SV	-28 ~ -1
1.01	Cycle 1 Day 1	C1D1	1
1.08	Cycle 1 Day 8	C1D8	7±1 days after C1D1
1.15	Cycle 1 Day 15	C1D15	14±2 days after C1D1
[c].01	Cycle [c] Day 1	C[c]D1	21±1 days after C[k]1D1 [k]=[c]-1
[c].08	Cycle [c] Day 8	C[c]D8	7±1 days after C[c]D1
[c].15	Cycle [c] Day 15, **[c]=1, 2, 3 only**	C[c]D15	14±2 days after C[c]D1
	End of Treatment (EOT) / Early Withdrawal (EW)	EOT / EW	EOT: 21±2 days after C[k]1D1 or 14±2 days after C[k]1D8, [k]=[c]-1 EW: after the last treatment dose
99.1	Follow-Up Visit 1 (FU1)	FU1	21±3 after EOT/EW
99.2	Follow-Up Visit 2 (FU2)	FU2	21±3 after FU1-W3

Visit No.	Visit Name	Visit Code	Planned Visit Day
99.3	Follow-Up Visit 3 (FU3)	FU3	21±3 after FU2-W6
99. [F]	Follow-Up Visit [F] (FU[F])	FU[F]	Every 9 weeks ±7 days
66.[x][x]	Unscheduled Visit (UV)	UV	

[c]: cycle number where [c]≥2, [F]: assigned sequentially from 4, [x][x]: assigned sequentially from 01

(5) Full term for 'Protocol Deviation Code':

Code	Full Term
	<To be added upon real data in final tabulation>

(6) Clinical description of severity for CTCAE Term:

CTCAE Term	Clinical description
Tachycardia	Heart rate > 100 bpm
Bradycardia	Heart rate < 60 bpm
Hypertension Grade ≥1	SBP > 120 or DBP > 80 mmHg
Hypertension Grade ≥2	SBP > 140 or DBP > 90 mmHg
Hypertension Grade ≥3	SBP > 160 or DBP > 100 mmHg
Hypotension	SBP < 90 or DBP < 60 mmHg
Fever Grade ≥1	Temperature ≥ 38 degree C
Fever Grade ≥3	Temperature ≥ 40 degree C
Hypothermia Grade ≥2	temperature ≤ 35 degree C
Hypothermia Grade ≥3	temperature ≤ 32 degree C
Tachypnea	respiratory rate > 20 breaths/min
Bradypnea	respiratory rate < 12 breaths/min
QTc Prolonged Grade ≥ 1	QTc ≥ 450 msec
QTc Prolonged Grade ≥ 3	QTc ≥ 501 msec

(7) For clinical relevant

CS : abnormal and clinically significant
NCS: abnormal but not clinically significant
LLN: lower limit of normal range
ULN: upper limit of normal range

(8) Abbreviations of statistics

N: number of non-missing values
Missing: number of missing values
Mean: mean of values
SD: standard deviation of values
Q1: 25% quartile of values
Q3: 25% quartile of values
Median: median of values
IQR: inter-quartile-range (IQR=Q3-Q1)
Min: minimum of values
Max: maximum of values
CI: confidence interval
LS-mean: least-square mean
ANOVA: analysis of variance
ANCOVA: analysis of covariance
CHISQ: Chi-Square test
CMH: Cochran-Mantel-Haenszel test adjusted by stratification
CMH[G]: CMH for General Association
CMH[D]: CMH for Row Mean Scores Differ
FISHER: Fisher's exact test
KW: Kruskal-Wallis test
MHCHISQ: Mantel-Haenszel chi-square test on given scores
T: two sample t test
W: Wilcoxon Rank-sum Test
Diff.: difference

3 Change From Preceding Version of Statistical Analysis Plan

3.1 SAP 2.0: Progression Free Survival (PFS) Estimation

For Progression Free Survival, missing data will be estimated as the time from treatment onset date to date of last implementation of radiological image assessment +1 or estimated as '1' if no post-treatment tumor assessment available. Estimating missing data as censored on Day 1 shall be rather conservative than omitting the missing ones.

6.1. Efficacy Measurements

Subjects will be considered evaluable for tumor assessment in this study if they fulfill the criteria for evaluation according to RECIST v1.1, i.e., those subjects who undergo a baseline disease assessment within 4 weeks of treatment initiation, and who undergo at least 1 disease assessment on study (the following should be revised if revision in corresponding part in synopsis is accepted) .

- PFS is defined as the time from the start of treatment up to the date of first progression based on RECIST v1.1 or the date of death, whichever comes first.

3.2 SAP 3.0: Response Evaluation

There are 5 subjects who are not evaluated due to clinical disease progression or AE/SAE. The subjects will be counted as 'Not Evaluable for Response' if no any post-treatment radiological image assessments. Each patient will be assigned one of the following categories:

1. Complete response
2. Partial response
3. Stable disease
4. Progression disease
5. Not Evaluable for Response.

14 TABLES AND FIGURES

14.1 DEMOGRAPHIC DATA AND BASELINE CHARACTERISTICS

14.1.1 Screen Failures and Subject Disposition by Study Site

Population: All Screened Subjects / Eligible Subjects

Characteristics	Study Site
.All Screened Subjects *(multiple-selection)*	
N	XXX
Eligible Subjects	XXX (XXX.X%)
Screening Failures	XXX (XXX.X%)
~INC01	XXX (XXX.X%)
~INC02	XXX (XXX.X%)
~INC03	XXX (XXX.X%)
~EXC01	XXX (XXX.X%)
~EXC02	XXX (XXX.X%)
~EXC03	XXX (XXX.X%)
. Eligible Subject *(multiple-selection)*	
N	XXX
~ ITT	XXX (XXX.X%)
~ PP	XXX (XXX.X%)
~ Non-PP	XXX (XXX.X%)
~ <Reason 1>	XXX (XXX.X%)
~ <Reason 2>	XXX (XXX.X%)
...	XXX (XXX.X%)
~ Non-ITT	XXX (XXX.X%)

14.1.2 Study Visits, Study Termination, Subject Disposition and Protocol Deviation

Population: ITT Population

Characteristics	Max. Dose Level
. Study Termination	
N	XXX
Study Completed	XXX (XXX.X%)
Prematurely Discontinued	XXX (XXX.X%)
~ Withdrew consent	XXX (XXX.X%)
~ AE	XXX (XXX.X%)
…	XXX (XXX.X%)
. Study visits completed *(multiple-selection)*	
N	XXX
Screening Visit (SV)	XXX (XXX.X%)
Cycle 1 Day 1 (C1D1)	XXX (XXX.X%)
Cycle 1 Day 8 (C1D8)	XXX (XXX.X%)
Cycle 1 Day 15 (C1D15)	XXX (XXX.X%)
Cycle [c] Day 1 (C[c]D1)	XXX (XXX.X%)
Cycle [c] Day 8 (C[c]D8)	XXX (XXX.X%)
Cycle [c] Day 15 (C[c]D15)	XXX (XXX.X%)
End of Treatment (EOT) /Early Withdrawal (EW)	XXX (XXX.X%)
Toxicity Follow-Up Visit (TFU)	XXX (XXX.X%)

Characteristics	Max. Dose Level
. Study Duration [days]	
N (Missing)	XXX (XXX)
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX
.Population *(multiple-selection)*	
N	XXX
~ PP	XXX (XXX.X%)
~ Non-PP	XXX (XXX.X%)
~ <Reason 1>	XXX (XXX.X%)
~ <Reason 2>	XXX (XXX.X%)
...	
.Protocol Deviation *(multiple-selection)*	
N	XXX
~ Major Protocol Deviation	XXX (XXX.X%)
~ <Reason 1>	XXX (XXX.X%)
~ <Reason 2>	XXX (XXX.X%)
...	XXX (XXX.X%)
~ Minor Protocol Deviation	XXX (XXX.X%)
~ <Reason 1>	XXX (XXX.X%)
~ <Reason 2>	XXX (XXX.X%)
...	XXX (XXX.X%)

Study Duration [days] = End Date of Treatment Phase - Visit 0, or alternatively as the last visit date - Visit 0

14.1.3 Demographic Data, Smoking Status and Betelnut Consumption

Population: ITT Population

Characteristics	Max. Dose Level
.Study Site	
N	XXX
Site 01: TMUH	XXX (XXX.X%)
Site 02: NCKUH	XXX (XXX.X%)
Site 03: TVGH	XXX (XXX.X%)
Site 04: TMUSHH	XXX (XXX.X%)
. Variable, including Age [Y/O], Body Weight [kg], Body Height [cm], BMI [kg/m^2]	
N (Missing)	XXX (XXX)
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX
. Gender	
N (Missing)	XXX (XXX)
Male	XXX (XXX.X%)
Female	XXX (XXX.X%)
. Race	
N (Missing)	XXX (XXX)

Characteristics	Max. Dose Level
Aboriginal	XXX (XXX.X%)
Asian	XXX (XXX.X%)
Black /African American	XXX (XXX.X%)
Torres Strait Islander	XXX (XXX.X%)
White or Caucasian	XXX (XXX.X%)
Other	XXX (XXX.X%)
. Ethnicity	
N (Missing)	XXX (XXX)
Hispanic or Latino	XXX (XXX.X%)
Not Hispanic/Latino	XXX (XXX.X%)
. Smoking Status	
N (Missing)	XXX (XXX)
Never Smoked	XXX (XXX.X%)
Former Smoker	XXX (XXX.X%)
Current Smoker	XXX (XXX.X%)
. Betelnut Consumption	
N (Missing)	XXX (XXX)
Never Took Betelnut	XXX (XXX.X%)
Former Taker	XXX (XXX.X%)
Current Taker	XXX (XXX.X%)

Age [Y/O] = year of informed consent – year of birth
BMI [kg/m^2] = Body Weight [kg]/(Body Height [cm]/100)^2

14.1.4 Head and Neck Squamous Cell Carcinoma History & Tumor Staging

Population: ITT Population

Characteristics	Max. Dose Level
. Disease Duration [Years]	
N (Missing)	XXX (XXX)
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX
. Disease Status *(multiple-selection)*	
N (Missing)	XXX (XXX)
Recurrence	XXX (XXX.X%)
Disease Progression	XXX (XXX.X%)
Metastasis	XXX (XXX.X%)
. Histological grade	
N (Missing)	XXX (XXX)
Cannot be assessed	XXX (XXX.X%)
Undifferentiated	XXX (XXX.X%)
Poorly differentiated	XXX (XXX.X%)
Moderate differentiated	XXX (XXX.X%)
Well differentiated	XXX (XXX.X%)
. Metastatic sites *(multiple-selection)*	
N (Missing)	XXX (XXX)

Characteristics	Max. Dose Level
Lymph	XXX (XXX.X%)
Mediastinum	XXX (XXX.X%)
Bone	XXX (XXX.X%)
Bone Marrow	XXX (XXX.X%)
Adrenal	XXX (XXX.X%)
Nodes Lung	XXX (XXX.X%)
Liver	XXX (XXX.X%)
Skin	XXX (XXX.X%)
Chest Wall	XXX (XXX.X%)
CNS	XXX (XXX.X%)
Other	XXX (XXX.X%)
. Tumor Stage	
N (Missing)	XXX (XXX)
Stage I	XXX (XXX.X%)
Stage II	XXX (XXX.X%)
Stage III	XXX (XXX.X%)
Stage IVa	XXX (XXX.X%)
Stage IVb	XXX (XXX.X%)

Disease Duration [years] = (date of screening visit – earliest onset date of initial diagnosis with histological or cytological confirmation)/365.25, missing day is estimated as 15, missing month is estimated as Jul-01

14.1.5 General Medical History

Population: ITT Population

Characteristics	Max. Dose Level
.Medical History *(multiple-selection)*	
N	XXX
At least one below	XXX (XXX.X%)
~ Ophthalmologic	XXX (XXX.X%)
~ Ear, Nose, Throat, Mouth	XXX (XXX.X%)
~ Cardiovascular	XXX (XXX.X%)
~ Cerebrovascular	XXX (XXX.X%)
…	…
.Current Condition *(multiple-selection)*	
N	XXX
At least one below	XXX (XXX.X%)
~ Ophthalmologic	XXX (XXX.X%)
~ Ear, Nose, Throat, Mouth	XXX (XXX.X%)
~ Cardiovascular	XXX (XXX.X%)
~ Cerebrovascular	XXX (XXX.X%)
…	…

Current condition lists the medical histories that are ongoing or with end date ≥ date of visit 0

14.1.6 Study Drug Administration

Population: ITT Population

Characteristics	Max. Dose Level
. Treatment Exposure [cycles], Maximum Unit Dose Level [mg/m^2], Maximum Unit Dose [mg], Cumulated Dose Level [mg/m^2], Cumulated Dose [mg], Mean Cycle Dose Level [mg/m^2/cycle], Mean Cycle Dose [mg/cycle]	

Characteristics	Max. Dose Level
N (Missing)	XXX (XXX)
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX

For Treatment Exposure, completion of Day 1 and Day 8 is counted as 1 cycle, and Day 1 only is counted as 0.5 cycle.

14.2 EFFICACY DATA

By stage analysis, no Overall of both stages will be presented if only stage I data are available.

14.2.1 Objective Response Rate

Population: ITT / PP Population

Characteristics	Max. Dose Level
--Stage: Overall, Stage I, Stage II	
--Population: ITT, PP	
Best Response	
N (Missing)	XXX (XXX)
CR	XXX (XXX.X%)
PR	XXX (XXX.X%)
ORR (CR + PR)	XXX (XXX.X%)
SD	XXX (XXX.X%)
PD	XXX (XXX.X%)
Not Evaluable for Response	XXX (XXX.X%)
95% CI of ORR (WI)	XXX-XXXb
. Any PD for Target Lesions	
. Any PD for Non-Target Lesions	
. Any PD for Overall Response	
N (Missing)	XXX (XXX)
Yes	XXX (XXX.X%)
No	XXX (XXX.X%)
Progression Free Survival [days], Overall Survival[days]	
N (Missing)	XXX (XXX)
Censored No.	XXX (XXX%)
Observed No.	XXX (XXX%)
Q1 [95% CI]	XXX [XX~XX]
Median [95% CI]	XXX [XX~XX]
Q3 [95% CI]	XXX [XX~XX]

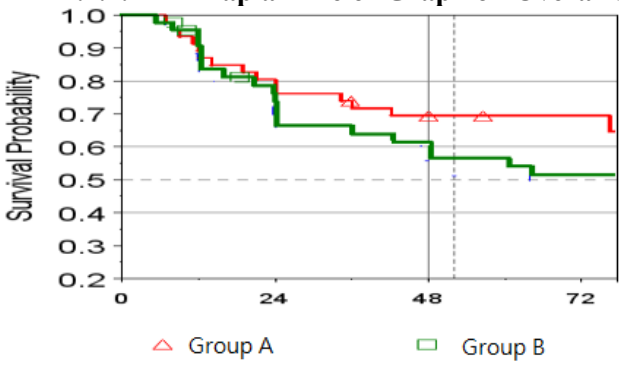
For CI (WI, within group), b denotes exact CI of binomial proportion of # using binomial test
Progression Free Survival [days] = Date of PD / death – treatment onset date + 1, or date of Last Implementation of Radiological Image Assessment – treatment onset date + 1, or estimated as '1' if no post-treatment tumor assessment available.
Overall Survival[days] = Date of death – treatment onset date +1, or last known alive date – treatment onset date +1

14.2.1.1 Kaplan-Meier Graph on Progression Free Survival (ITT)

14.2.1.2 Kaplan-Meier Graph on Progression Free Survival (PP)

14.2.1.3 Kaplan-Meier Graph on Overall Survival (ITT)

14.2.1.4 Kaplan-Meier Graph on Overall Survival (PP)



14.3 SAFETY DATA

14.3.1 Treatment Emergent Adverse Events – Subject Based Analyses

14.3.1.1 Treatment Emergent AEs – Subjects with AEs

14.3.1.2 Treatment Emergent AEs – Subjects with DLTs

Population: ITT Population

Characteristics	Max. Dose Level
. By MedDRA SOC and Preferred Term	
N	XXX
At least one below	XXX (XXX.X%)
<MedDRA Body System1>	XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX (XXX.X%)
<MedDRA Body System2>	XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX (XXX.X%)

For each MedDRA SOC or Preferred Term, Subject with multiple events are counted as one incidence.

14.3.1.3 Treatment Emergent AEs – Subjects with Grade ≥3 AEs

Population: ITT Population

Characteristics	Max. Dose Level
. By MedDRA SOC and Preferred Term	
N	XXX

Characteristics	Max. Dose Level
At least one below	XXX (XXX.X%)
<MedDRA Body System1>	XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX (XXX.X%)
Grade ≥ 4	XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX (XXX.X%)
Grade ≥ 4	XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX (XXX.X%)
<MedDRA Body System2>	XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX (XXX.X%)

Grade ≥ 4 AEs will be listed additionally if any

14.3.1.4 Treatment Emergent AEs – Subject with Treatment Related AEs

Population: ITT Population

Characteristics	Max. Dose Level
. By MedDRA SOC and Preferred Term	
N	XXX
At least one below	XXX (XXX.X%)
<MedDRA Body System1>	XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX (XXX.X%)
<MedDRA Body System2>	XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX (XXX.X%)

Treatment Related is defined as Definitely Related, Probable Related, or Possibly Related

14.3.1.5 Treatment Emergent AEs – Subject with Treatment Modified AEs

Population: ITT Population

Characteristics	Max. Dose Level
. The Action Taken by MedDRA SOC and Preferred Term	
N	XXX
At least one below	XXX (XXX.X%)
<MedDRA Body System1>	XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX (XXX.X%)
~ Treatment Infusion Interrupted	XXX (XXX.X%)
~ Treatment Omitted	XXX (XXX.X%)
~ Dose Reduced	XXX (XXX.X%)
~ Treatment Discontinued	XXX (XXX.X%)
<MedDRA Body System2>	XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX (XXX.X%)
~ Treatment Infusion Interrupted	XXX (XXX.X%)
~ Treatment Omitted	XXX (XXX.X%)
~ Dose Reduced	XXX (XXX.X%)
~ Treatment Discontinued	XXX (XXX.X%)

14.3.1.6 Treatment Emergent AEs – Subjects with SAEs

Population: ITT Population

Characteristics	Max. Dose Level
. By MedDRA SOC and Preferred Term	
N	XXX
At least one below	XXX (XXX.X%)
<MedDRA Body System1>	XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX (XXX.X%)
~ Requires or Prolongs Hospitalization	XXX (XXX.X%)
~ Death	XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX (XXX.X%)
~ Requires or Prolongs Hospitalization	XXX (XXX.X%)
~ Death	XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX (XXX.X%)
~ Requires or Prolongs Hospitalization	XXX (XXX.X%)
~ Death	XXX (XXX.X%)
<MedDRA Body System2>	XXX (XXX.X%)
~ <MedDRA Preferred Term 1>	XXX (XXX.X%)
~ Requires or Prolongs Hospitalization	XXX (XXX.X%)
~ Death	XXX (XXX.X%)
~ <MedDRA Preferred Term 2>	XXX (XXX.X%)
~ Requires or Prolongs Hospitalization	XXX (XXX.X%)
~ Death	XXX (XXX.X%)
~ <MedDRA Preferred Term 3>	XXX (XXX.X%)
~ Requires or Prolongs Hospitalization	XXX (XXX.X%)
~ Death	XXX (XXX.X%)

14.3.2 Clinical Relevance of Laboratory Assessment – Hematology

14.3.2.1 Clinical Relevance of Hematology – Item 1

14.3.2.2 Clinical Relevance of Hematology – Item 2

14.3.2.3 …

14.3.3 Clinical Relevance of Laboratory Assessment – Biochemistry

14.3.3.1 Clinical Relevance of Biochemistry – Item 1

14.3.3.2 Clinical Relevance of Biochemistry – Item 2

14.3.3.3 …

14.3.4 Clinical Relevance of Laboratory Assessment – Coagulation

14.3.4.1 Clinical Relevance of Coagulation – Item 1

14.3.4.2 Clinical Relevance of Coagulation – Item 2

14.3.4.3 …

14.3.5 Clinical Relevance of Laboratory Assessment – Urinalysis

14.3.5.1 Clinical Relevance of Urinalysis – Item 1

14.3.5.2 Clinical Relevance of Urinalysis – Item 2

14.3.5.3 …

Population: ITT Population

Characteristics	Max. Dose Level
The Worst Clinical Relevance of Baseline Laboratory	
(Baseline visits are Screening Visit, Cycle 1 Day 1)	
N	XXX
Normal	XXX (XXX.X%)
NCS	XXX (XXX.X%)
CS	XXX (XXX.X%)
The Worst Clinical Relevance of Post-Baseline Laboratory	
(Excluding Baseline Visits)	
N	XXX
Normal	XXX (XXX.X%)
NCS	XXX (XXX.X%)
CS	XXX (XXX.X%)
The Worst Clinical Relevance Change from Baseline to Post-Baseline	
N (Missing)	XXX (XXX)
Relieved: CS to Normal / NCS	XXX (XXX.X%)
Unchanged	XXX (XXX.X%)
Worsened: Normal / NCS to CS	XXX (XXX.X%)

Unchanged: Normal to Normal, NCS to NCS, Normal to NCS, NCS to Normal
Baseline visits are Screening Visit, Cycle 1 Day 1
The Worst Clinical Relevance of Baseline : Compare the data in the two Baseline visits and list the worst one
Worst: CS > NCS > Normal

14.3.6 Toxicity Grade of Laboratory Assessment – Hematology

14.3.6.1 Toxicity Grade of Hematology – Item 1

14.3.6.2 Toxicity Grade of Hematology – Item 2

14.3.6.3 …

14.3.7 Toxicity Grade of Laboratory Assessment – Biochemistry

14.3.7.1 Toxicity Grade of Biochemistry – Item 1

14.3.7.2 Toxicity Grade of Biochemistry – Item 2

14.3.7.3 …

14.3.8 Toxicity Grade of Laboratory Assessment – Coagulation

14.3.8.1 Toxicity Grade of Coagulation – Item 1

14.3.8.2 Toxicity Grade of Coagulation – Item 2

14.3.8.3 …

14.3.9 Toxicity Grade of Laboratory Assessment –Urinalysis

14.3.9.1 Toxicity Grade of Urinalysis – Item 1

14.3.9.2 Toxicity Grade of Urinalysis – Item 2

14.3.9.3 …

Population: ITT Population

Characteristics	Max. Dose Level
The Worst Toxicity Grade of Baseline Laboratory	
(Baseline visits are Screening Visit, Cycle 1 Day 1)	
N	XXX
Grade 0	XXX (XXX.X%)
Grade 1	XXX (XXX.X%)
Grade 2	XXX (XXX.X%)
Grade 3	XXX (XXX.X%)
…	…
The Worst Toxicity Grade of Post-Baseline Laboratory	
(Excluding Baseline Visits)	
N	XXX
Grade 0	XXX (XXX.X%)
Grade 1	XXX (XXX.X%)
Grade 2	XXX (XXX.X%)
Grade 3	XXX (XXX.X%)
…	…
The Worst Toxicity Grade Change: Post-Baseline - Baseline	
N	XXX
Grade +3	XXX (XXX.X%)
Grade +2	XXX (XXX.X%)
Grade +1	XXX (XXX.X%)
Grade 0	XXX (XXX.X%)
Grade -1	XXX (XXX.X%)
Grade -2	XXX (XXX.X%)
…	…
Visits with Toxicity Grade Change ≥ Grade +3	

Characteristics	Max. Dose Level
N	XXX
Cycle 1 Day 1	XXX (XXX.X%)
Cycle 1 Day 8	XXX (XXX.X%)
Cycle 1 Day 15	XXX (XXX.X%)
…	…

Baseline visits are Screening Visit, Cycle 1 Day 1
The Worst Clinical Relevance of Baseline : Compare the data in the two Baseline visits and list the worst one
Worst: Grade 5 > Grade 4 > Grade 3 > Grade 2 > Grade 1 > Grade 0

14.3.10 Vital Signs, Body Weight and ECOG Performance Status

14.3.10.1 Heart Rate [bpm]

14.3.10.2 Systolic Blood Pressure and Diastolic Blood Pressure [mmHg]

14.3.10.3 Temperature [Degree C]

14.3.10.4 Respiratory Rate [breaths/min]

14.3.10.5 Weight [kg]

Population: ITT Population

Characteristics	Max. Dose Level
Baseline Value *(Baseline is Cycle 1 Day 1(Pre-IV Infusion) or alternatively as Screening Visit if Cycle 1 Day 1 data is not available)*	
N	XXX
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX
Vital Signs Abnormalities at Baseline Visits *(multiple-selection)* *(Baseline is Cycle 1 Day 1 (Pre-IV Infusion) or alternatively as Screening Visit if Cycle 1 Day 1 data is not available)*	
N	XXX
At least one below	XXX (XXX.X%)
Tachycardia	XXX (XXX.X%)
Bradycardia	XXX (XXX.X%)
Hypertension Grade ≥1	XXX (XXX.X%)
Hypertension Grade ≥2	XXX (XXX.X%)
Hypertension Grade ≥3	XXX (XXX.X%)
Hypotension	XXX (XXX.X%)
Fever Grade ≥1	XXX (XXX.X%)
Fever Grade ≥3	XXX (XXX.X%)
Hypothermia Grade ≥2	XXX (XXX.X%)
Hypothermia Grade ≥3	XXX (XXX.X%)
Tachypnea	XXX (XXX.X%)
Bradypnea	
Vital Signs Abnormalities at Post-Baseline Visits *(multiple-selection)* *(Excluding Baseline Visits)*	
N	XXX

Characteristics	Max. Dose Level
At least one below	XXX (XXX.X%)
Tachycardia	XXX (XXX.X%)
Bradycardia	XXX (XXX.X%)
Hypertension Grade ≥1	XXX (XXX.X%)
Hypertension Grade ≥2	XXX (XXX.X%)
Hypertension Grade ≥3	XXX (XXX.X%)
Hypotension	XXX (XXX.X%)
Fever Grade ≥1	XXX (XXX.X%)
Fever Grade ≥3	XXX (XXX.X%)
Hypothermia Grade ≥2	XXX (XXX.X%)
Hypothermia Grade ≥3	XXX (XXX.X%)
Tachypnea	XXX (XXX.X%)
Bradypnea	
Vital Signs Significant Change from Baseline to Post-Baseline Visits *(multiple-selection)*	
N	XXX
At least one below	XXX (XXX.X%)
Non-Tachycardia to Tachycardia	XXX (XXX.X%)
~ Cycle 1 Day 1	XXX (XXX.X%)
~ Cycle 1 Day 8	XXX (XXX.X%)
~ Cycle 1 Day 15	XXX (XXX.X%)
…	XXX (XXX.X%)
Non-Bradycardia to Bradycardia	
Non-Hypertension Grade<2 to Hypertension Grade ≥2	
Hypertension Grade <3 to Hypertension Grade ≥3	
Non-Hypotension to Hypotension	
Non-Fever Grade=0 to Fever Grade ≥1	
Non-Fever Grade<3 to Fever Grade ≥3	
Non-Hypothermia Grade<2 to Hypothermia Grade≥2	
Non-Hypothermia Grade<3 to Hypothermia Grade≥3	
Non-Tachypnea to Tachypnea	
Non-Bradypnea to Bradypnea	
<The same layout as above>	

Baseline is Cycle 1 Day 1 (Pre-IV Infusion) or alternatively as Screening Visit if Cycle 1 Day 1 data is not available.

14.3.10.6 ECOG Performance Status

Population: ITT Population

Characteristics	Max. Dose Level
The Worst ECOG Performance Status at Baseline Visits *(multiple-selection)*	
(Baseline visits are Screening Visit, Cycle 1 Day 1)	
N	XXX
ECOG ≥1	XXX (XXX.X%)
ECOG ≥2	XXX (XXX.X%)
ECOG ≥3	XXX (XXX.X%)
…	XXX (XXX.X%)
The Worst ECOG Performance Status at Post-Baseline Visits *(multiple-selection)*	
(Excluding Baseline Visits)	
N	XXX

Characteristics	Max. Dose Level
ECOG ≥1	XXX (XXX.X%)
ECOG ≥2	XXX (XXX.X%)
ECOG ≥3	XXX (XXX.X%)
…	XXX (XXX.X%)
The Worst ECOG Performance Status Change from Baseline to Post-Baseline Visits *(multiple-selection)*	
N	XXX
At least one below	XXX
ECOG <1 to ECOG ≥1	XXX (XXX.X%)
Cycle 1 Day 1	XXX (XXX.X%)
Cycle 1 Day 8	XXX (XXX.X%)
Cycle 1 Day 15	XXX (XXX.X%)
…	
ECOG <2 to ECOG ≥2	XXX (XXX.X%)
Cycle 1 Day 1	XXX (XXX.X%)
Cycle 1 Day 8	XXX (XXX.X%)
Cycle 1 Day 15	XXX (XXX.X%)
…	

Baseline visits are Screening Visit, Cycle 1 Day 1
The Worst Clinical Relevance of Baseline : Compare the data in the two Baseline visits and list the worst one
Worst: Grade 5 > Grade 4 > Grade 3 > Grade 2 > Grade 1 > Grade 0

14.3.11 Nerve Conduction Velocity Examination

14.3.11.1 Neurosensory Result

14.3.11.2 Neuromotor Result

<Use the layout for 14.3.2 Clinical Relevance of Laboratory Assessment – Hematology>

14.3.12 Electrocardiogram (ECG, EKG)

14.3.12.1 Electrocardiogram - Overall Interpretation

<Use the layout for 14.3.2 Clinical Relevance of Laboratory Assessment – Hematology>

14.3.12.2 Electrocardiogram - PR Interval [msec]

14.3.12.3 Electrocardiogram - QRS Interval [msec]

14.3.12.4 Electrocardiogram - QTc Interval [msec]

Population: ITT Population

Characteristics	Max. Dose Level
Baseline Value *(Baseline is Cycle 1 Day 1 (Pre-IV Infusion) or alternatively as Screening Visit if Cycle 1 Day 1 data is not available)*	
N	XXX
Mean (SD)	XXX (XXX)
Median (IQR)	XXX (XXX)
Q1~Q3	XXX~XXX
Min~Max	XXX~XXX
ECG Abnormalities at Baseline Visits *(multiple-selection)* *(Baseline is Cycle 1 Day 1 (Pre-IV Infusion) or alternatively as Screening Visit if Cycle 1 Day 1 data is not available)*	

Characteristics	Max. Dose Level
N	XXX
QTc Prolonged Grade ≥ 1	XXX (XXX.X%)
QTc Prolonged Grade ≥ 3	XXX (XXX.X%)
ECG Abnormalities at Post-Baseline Visits *(multiple-selection)* *(Excluding Baseline Visits)*	
N	XXX
QTc Prolonged Grade ≥ 1	XXX (XXX.X%)
QTc Prolonged Grade ≥ 3	XXX (XXX.X%)
ECG Significant Change from Baseline to Post-Baseline Visits *(multiple-selection)*	
N	XXX
At least one below	XXX
QTc Prolonged Grade < 1 to Grade ≥ 1	XXX (XXX.X%)
~ Cycle 1 Day 1	XXX (XXX.X%)
~ Cycle 1 Day 8	XXX (XXX.X%)
~ Cycle 1 Day 15	XXX (XXX.X%)
…	
QTc Prolonged Grade < 3 to Grade ≥ 3	XXX (XXX.X%)
~ Cycle 1 Day 1	XXX (XXX.X%)
~ Cycle 1 Day 8	XXX (XXX.X%)
~ Cycle 1 Day 15	XXX (XXX.X%)
…	

Baseline is Cycle 1 Day 1 (Pre-IV Infusion) or alternatively as Screening Visit if Cycle 1 Day 1 data is not available.

14.3.13 Physical Examination

14.3.13.1 Physical Examination – All Abnormalities

Population: ITT Population

Characteristics	Max. Dose Level
The Worst Physical Abnormalities at Baseline *(Baseline visits are Screening Visit, Cycle 1 Day 1)*	
N (Missing)	XXX (XXX)
At least one below	XXX (XXX.X%)
~ <Body System 1>	XXX (XXX.X%)
~ <Body System 2>	XXX (XXX.X%)
~ <Body System 3>	XXX (XXX.X%)
~ <Body System 4>	XXX (XXX.X%)
…	XXX (XXX.X%)
The Worst Physical Abnormalities at Post-Baseline *(Excluding Baseline Visits)*	
N (Missing)	XXX (XXX)
At least one below	XXX (XXX.X%)
~ <Body System 1>	XXX (XXX.X%)
~ <Body System 2>	XXX (XXX.X%)
~ <Body System 3>	XXX (XXX.X%)
~ <Body System 4>	XXX (XXX.X%)
…	XXX (XXX.X%)

Characteristics	Max. Dose Level
Transition of the Worst Physical Abnormalities from Baseline to Post-Baseline (Normal to NCS / CS**)**	
N (Missing)	XXX (XXX)
At least one below	XXX (XXX.X%)
~ <Body System 1>	XXX (XXX.X%)
~ <Body System 2>	XXX (XXX.X%)
~ <Body System 3>	XXX (XXX.X%)
~ <Body System 4>	XXX (XXX.X%)
…	XXX (XXX.X%)

The Worst Clinical Relevance of Baseline : Compare the data in the two Baseline visits and list the worst one
Worst: CS > NCS > Normal

14.3.13.2 Physical Examination – Clinical Significant (CS) Abnormalities

Population: ITT Population

Characteristics	Max. Dose Level
The Worst CS Physical Abnormalities at Baseline	
(Baseline visits are Screening Visit, Cycle 1 Day 1)	
N (Missing)	XXX (XXX)
At least one below	XXX (XXX.X%)
~ <Body System 1>	XXX (XXX.X%)
~ <Body System 2>	XXX (XXX.X%)
~ <Body System 3>	XXX (XXX.X%)
~ <Body System 4>	XXX (XXX.X%)
…	XXX (XXX.X%)
The Worst CS Physical Abnormalities at Post-Baseline	
(Excluding Baseline Visits)	
N (Missing)	XXX (XXX)
At least one below	XXX (XXX.X%)
~ <Body System 1>	XXX (XXX.X%)
~ <Body System 2>	XXX (XXX.X%)
~ <Body System 3>	XXX (XXX.X%)
~ <Body System 4>	XXX (XXX.X%)
…	XXX (XXX.X%)
Transition of the Worst CS Physical Abnormalities from Baseline to Post-Baseline (Normal/NCS to CS**)**	
N (Missing)	XXX (XXX)
At least one below	XXX (XXX.X%)
~ <Body System 1>	XXX (XXX.X%)
~ <Body System 2>	XXX (XXX.X%)
~ <Body System 3>	XXX (XXX.X%)
~ <Body System 4>	XXX (XXX.X%)
…	XXX (XXX.X%)

The Worst Clinical Relevance of Baseline : Compare the data in the two Baseline visits and list the worst one
Worst: CS > NCS > Normal