16.1.9 Documentation of statistical methods

- Statistical Analysis Plan – Version 1 – 18 December 2018
- Table Shells – 18 December 2018
- Listing Shells –18 December 2018
- Figure Shells – 18 December 2018
- Biostatistics File Note – Additional Analysis of ACQ5 – 27 April 2020

Statistical Analysis Plan

Study Number: ANB020-004

Placebo-Controlled Proof of Concept Study to Investigate ANB020 Activity in Adult Patients with Severe Eosinophilic Asthma

Author: [redacted]
Version Number: 1.0
Date: 18Dec2018

Statistical Analysis Plan Signature Page

Statistical Analysis Plan V1.0 (Dated 18Dec2018) for Protocol ANB020-004.

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Position:			
Company:	IQVIA™		

Upon review of this document, the undersigned approves this version of the Statistical Analysis Plan, authorizing that the content is acceptable for the reporting of this study.

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Modification History

Unique Identifier for this Version	Date of the Document Version	Author	Significant Changes from Previous Authorized Version
Draft 0.1	07 Nov 2017	[redacted]	Not Applicable – First Version
Draft 0.2	21 Nov 2017		Resolved comments from internal review
Draft 0.2	15 Feb 2018		Resolved comments from SBR and PK
Draft 0.3	27 Feb 2018		Resolved comments from MW
Draft 0.4	28 Nov 2018		Finalization prior to database lock and unblinding

Table of Contents

List of Abbreviations and Definitions of Terms

Abbreviation	Definition
ACQ=-7	Asthma Control Questionnaire
ADA	Anti-drug Antibodies
AE	Adverse event
ANCOVA	Analysis of covariance
AUC	Area under the concentration-time curve
AUC0-inf	Area under the concentration-time curve from time zero (predose) extrapolated to infinite time
AUC0-last	area under the concentration-time curve from time zero (predose) to time of last quantifiable concentration
bec	blood eosinophil count
BLQ	Below the lower limit of quantitation
BMI	Body mass index
BP	Blood pressure
CGIC	Clinical Global Impression of Change
CI	Confidence interval
CL	Systemic clearance following intravenous dosing
C_{max}	Maximum observed concentration
CV	Coefficient of variation
ECG	Electrocardiogram
eCRF	Electronic case report form
EOS	End of Study

eos	eosinophil
EoT	End of Treatment
ET	Early Termination
FeNO	Fractional exhaled nitric oxide
FEV1	Forced expiratory volume in 1 second
FSH	Follicle stimulating hormone
gCV	Geometric coefficient of variation
Gmean	Geometric mean
HR	Heart rate
ICH	International Council for Harmonisation
IFN-γ	Interferon-gamma
IgE	Immunoglobulin E
IL	Interleukin
IP	Investigational product
IV	Intravenous(ly)
λ_z	Apparent terminal rate constant
LLOQ	Lower limit of quantitation
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	Mixed-model repeated measures
n	Sample size or number of observations
PD	Pharmacodynamic(s)
PGIC	Patient Global Impression of Change

PK	Pharmacokinetic(s)
R_{sq}	Coefficient of determination
SABA	short-acting beta-agonists
SAE	Serious adverse event
SAP	Statistical analysis plan
SAS	Statistical analysis system
SD	Standard deviation
SI	System International
TEAE	Treatment emergent adverse event
$t_{1/2}$	Apparent terminal half-life
t_{max}	Time to maximum observed concentration
V_{SS}	Volume of distribution at steady state following intravenous dosing
V_Z	Volume of distribution during terminal phase
WBC	White blood cell
WHO DD	World Health Organization Drug Dictionary
WOCBP	Women of childbearing potential

1. INTRODUCTION

This document describes the statistical analyses to be performed and data presentations to be produced for this phase 2a, randomized, double-blind, placebo-controlled, study to assess the effects of a single 300 mg/100 mL intravenous (IV) dose of ANB020 (etokimab) compared to placebo in adult patients with severe eosinophilic asthma.

The purpose of this statistical analysis plan (SAP) is to ensure the credibility of the study findings by specifying the rules and conventions to be used in the presentation and analysis of efficacy, safety, pharmacokinetics (PK), and pharmacodynamics (PD) data prior to database lock and unblinding of treatment groups at the individual level. It also describes how the data are to be summarized and analyzed.

This SAP has been developed based on the International Council for Harmonization (ICH) E3 and E9 Guidelines and in reference to the following document:

Protocol Anaptys ANB020-004 Amendment 4 dated 31 Oct 2018.

Any changes to the planned analysis, after database lock/ unblinding, will be described in an amendment to the SAP.

2. STUDY OBJECTIVES

2.1. PRIMARY OBJECTIVES

To measure the reduction of eosinophils (blood eosinophil count [bec or eos])[from Baseline (Day 1 pre-dose) to Day 22 in adult severe eosinophilic asthma patients administered with ANB020.

To assess the safety and tolerability of a single, IV dose of ANB020 compared to placebo in adult patients with severe eosinophilic asthma.

2.2. SECONDARY OBJECTIVES

To measure the reduction of eosinophils (blood eosinophil count) from Baseline (Day 1 pre-dose) to the End of Study (EOS) visit (Day 127) in adult severe eosinophilic asthma patients administered with ANB020.

To assess the change from Baseline in the clinic forced expiratory volume in 1 second (FEV_1) from Baseline (Day 1 pre-dose) to the EOS visit (Day 127).

To assess the change from Baseline in the fractional exhaled nitric oxide (FeNO) in the breath from Baseline (Day 1 pre-dose) to the EOS visit (Day 127).

To assess the PD activity of ANB020 on ex vivo induced interferon-gamma (IFN-γ) levels.

To test for any immunogenicity to ANB020.

To describe the PK of ANB020 following a single, IV dose in adult patients with severe eosinophilic asthma.

2.3. EXPLORATORY OBJECTIVES

To assess the effect of ANB020 on circulating serum cytokines.

To assess the activity of ANB020 after a single, IV dose on clinical scores such as the Asthma Control Questionnaire (ACQ-7), Patient Global Impression of Change (PGIC), and the Clinical Global Impression of Change (CGIC).

To assess the effect of ANB020 on the asthma symptoms, change in standard of care treatment, and rescue medication (short-acting beta-agonists [SABA]) usage.

To assess the effect of ANB020 on immunoglobulin E (IgE) levels.

3. STUDY DESIGN`

This is a proof of concept study designed to assess the effects of a single 300 mg/100 mL IV dose of ANB020 compared to placebo in adult patients with severe eosinophilic asthma. This study will also assess the safety and tolerability of ANB020 in adult patients with severe eosinophilic asthma.

The screening visit will be conducted 7 to 14 days before Day 1. After obtaining the informed consent from the patients; medical history, concomitant medications, vital signs, physical examination, FeNO measurement, spirometry to determine FEV1, and laboratory tests will be performed at the screening visit.

Eligible patients will be randomized in a 1:1 ratio to receive ANB020 or placebo on Day 1. Specific study assessments and safety laboratory tests will be performed. Blood samples to determine the eosinophil count, ex vivo induced IFN-γ levels, anti-drug antibodies (ADA), serum cytokines, and serial samples for PK analysis will be collected.

All patients will be followed up for 18 weeks. Patients will return to the study center for study

assessments on Day 2, 8, 22, 36, 64, 85, and 106 and will be contacted via telephone by study staff on Day 50 and 57. The EOS visit will be on Day 127 (Week 18) at the study center. All patients will undergo the FeNO and FEV_1 (spirometry) tests at each study center visit. An ACQ-7 will be completed by all patients at each study center visit (except Day 2) and the patient diary must be completed on a daily and weekly basis. The Investigator will rate the patient's response using the CGIC scale and the patients will be asked to rate the degree of change in the overall asthma status using the PGIC scale (part of the diary card). During the follow-up period, assessments including vital signs, safety laboratory testing, eosinophil count, PK, and pharmacodynamic analysis will be performed at specified time points.

Sample Size:

The number of patients enrolled is not based on statistical power considerations. All patients who discontinue the study prior to completing the Day 36 study assessments will be replaced. Patients who are withdrawn from the study after Day 36 will not be replaced. A total of approximately 24 patients will be randomized in a 1:1 ratio to receive ANB020 or placebo.

Randomization:

On Day 1, eligible patients will be assigned sequential randomization numbers, based on a randomization schedule, to receive one IV dose of either ANB020 (300 mg/100 mL) or placebo (0.9% sodium chloride [100 mL]) in a 1:1 ratio.

Study Treatments:

Investigational medicinal product is a single IV infusion of ANB020 300 mg/100mL.

Comparator (placebo) is a single IV infusion of 100 mL sterile normal saline (0.9% NaCl)

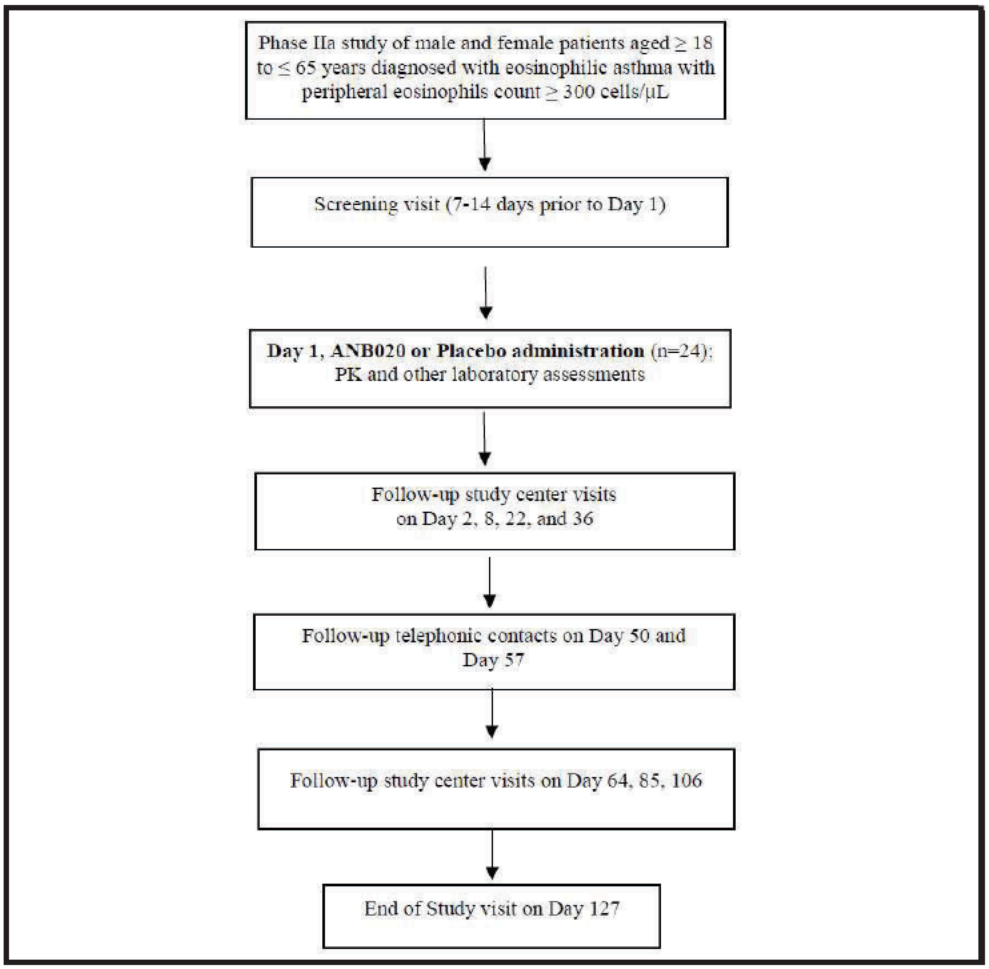
Infusions will be administered over 1 hour.

Blinding:

This is a randomized, double-blind, placebo-controlled study with limited access to the randomization code. The Sponsor, Investigators, and patients will be blinded to treatment assignment of ANB020 or placebo.

A schematic of the study design is included as Figure 1:

Figure 1: Schematic of Study Design



3.1. SCHEDULE OF EVENTS

The schedule of events can be found in Section 4.1, Table 4.1 of the protocol.

3.2. CHANGES TO ANALYSIS FROM PROTOCOL

An intermediate analysis has been planned for this study after Day 36 and Day 64. However, no changes in the endpoints were made.

4. PLANNED ANALYSIS

This SAP describes the methodology for intermediate analysis data cut times and final analyses.

4.1. DATA MONITORING COMMITTEE (DMC)

No DMC is planned of this study.

4.2. INTERIM ANALYSIS

No interim analysis is planned for this study. However, an intermediate analysis has been planned for this study after the last subject complete visit Day 36 and Day 64 where a limited number of unblinded safety data listings will be generated and the same will be reviewed by a restricted group. The restricted group will only include Randomizer/Unblinded Bios and one designated person from AnaptysBio. No Statistical analysis or alpha adjustment will be done for this purpose.

4.3. FINAL ANALYSIS

The final statistical analysis identified in this SAP will be performed by the IQVIA Biostatistics department following sponsor authorization of this SAP, determination of the analysis populations, database lock and unblinding of treatment.

Analysis of the PK of ANB020 will be the responsibility of the clinical pharmacokineticist (PK analyst) at IQVIA. The PD analysis, PK/PD summaries, data listings, and PK/PD figures will be the responsibility of the ECD biostatistician at IQVIA.

5. ANALYSIS SETS

Agreement and authorization of patients included/excluded from each analysis set will be obtained prior to the database lock of the study. The patients and observations excluded from analysis sets, and the reason for the exclusions, will be described in the clinical study report (CSR).

Pharmacokinetic data will be reviewed in a 2-stage process:

First stage (before unblinding): no concentrations or PK parameters will be included. Data are to be evaluated on a case-by-case basis whether the subject should be excluded from the PK analysis set before the concentration results are disclosed.

Second stage (after unblinding): data with concentration results will be reviewed. The PK analysis set defined prior to concentration results disclosure will be confirmed or updated.

The following analysis sets will be used:

5.1. ALL PATIENTS SCREENED [SCR]

Patients who have signed the informed consent form and have been screened.

5.2. RANDOMIZED ANALYSIS SET [RND]

All patients who have been allocated to a randomized treatment arm, regardless of whether they received the planned treatment or not. Patients in this set will be analyzed in the respective randomized treatment arm.

5.3. FULL ANALYSIS SET [FAS]

All patients who have received ANB020 or placebo and have at least one post-baseline blood eosinophils count assessment (Day 2). The full analysis set will be used for all efficacy analyses. Patients will be analyzed according to their randomized treatment.

5.4. SAFETY ANALYSIS SET [SAF]

All patients who have received ANB020 or placebo. The safety analysis set will be used for all safety analyses. Patients will be analyzed according to the actual treatment received.

5.5. PHARMACOKINETIC ANALYSIS SET [PK]

All patients who have received ANB020 and have at least one post-dose serum concentration data value available for ANB020 without any events or protocol deviation deemed to affect PK assessments. The PK analysis set will be used for all PK analyses.

Allocation of subjects to the PK population and all protocol deviations will be fully documented in the BDR report.

5.6. PHARMACODYNAMIC ANALYSIS SET [PD]

All patients who have received ANB020 or placebo and provide at least one evaluable post-dose PD measurement without any events or protocol deviation deemed to affect PD assessment. The PD analysis set will be used for all PD analyses.

Allocation of subjects to the PD population and all protocol deviations will be fully documented in the BDR report.

6. GENERAL CONSIDERATIONS

All clinical data from the internal database, and immunogenicity, PD and PK data from an external database will be provided as raw datasets with validated values. Summaries will be presented by treatment and overall as appropriate.

Listings will be presented for all patients available in the data transfer received from data management.

Data from patients excluded from an analysis set will be included in the data listings, but not in the summaries.

Coding of adverse events (AEs) and medical history will be done by Medical Dictionary for Regulatory Activities (MedDRA) directory version 19.1 (or higher) and medications data by the World Health Organization (WHO)-drug dictionary dated Dec2016 (or higher) by IQVIA™.

The following descriptive statistics will be presented in summary tables for non-PK/PD data:

Continuous variables: summarized by treatment groups using number of observations (n), mean, standard deviation (SD), minimum, median, and maximum.

Categorical variables: summarized by treatment groups using frequency tables [frequencies (n) and percentages (%)]. Percentages will be based on the total category count excluding the missing category, if not otherwise mentioned. Missing category with zero count will not be presented.

In general, for non-PK/PD data, the number of decimal places displayed for each statistic will be determined as follows:

Mean and median: 1 more than the number of decimal places allotted in the raw data received from data management.

SD: 2 more than the number of decimal places allotted in the raw data.

Minimum and maximum: equal to the number of decimal places allotted in the raw data.

Percentages: All percentages between 0 and 100 will be rounded to one decimal unless there is a need to report more than one decimal for percentages.

Reference ranges will be reported to the same number of decimal places displayed by the laboratory.

P-values and confidence intervals (CIs), if any, will be reported to four decimal places. P-values less than 0.0001 will be presented as “<0.0001” and p-value greater than 0.9999 will be presented as “1.0000”.

The following descriptive statistics will be presented in summary tables for PK/PD data:

PK concentrations and PD variables will be summarized by treatment group and nominal time point using n, mean, SD, coefficient of variation (CV), minimum, median, and maximum. For PK concentrations (and PD variables, if applicable), the number of observations ≥ lower limit of quantitation (LLOQ) will also be included. For PD variables, the 95% confidence interval (CI) for the mean will also be included. The CV will not be presented for change from baseline PD data.

Pharmacokinetic summaries will be presented for all patients in the PK analysis set as defined in Section 5.5. Similarly, PD summaries will be presented for all patients in the PD analysis set as defined in Section 5.6. Data from patients excluded from an analysis set will be included in the data listings, but not in the summaries

PK parameters except for t_{max} will be summarized by treatment group using n, mean, SD, coefficient of variation (CV), minimum, median, maximum, geometric mean, and geometric CV% (gCV), where gCV is defined as $100 \cdot \sqrt{(\exp(s^2)-1)}$ where 's' is the SD of the data on a log scale. The parameter t_{max} will be summarized using n, minimum, median, and maximum only.

For PK/PD data, the data will be rounded as follows:

Pharmacokinetic concentration and PD dependent variable data will be reported and analyzed with the same precision as the source data regardless of how many significant figures or decimals the data carry. Percentages (e.g., change from baseline) will be reported with 1 decimal place. Pharmacokinetic parameters will be rounded for reporting purposes both in the summary tables and by-subject listings. For the calculation of descriptive statistics and the statistical analysis, the rounded parameter values as presented in the data listings will be used. For most derived PK parameters, 3 significant figures will be used as the standard rounding procedure, with the following exceptions:

Parameters directly derived from source data (e.g., maximum concentration in serum [C_{max}]) will be reported and analysed with the same precision as the source data.

Parameters derived from actual elapsed sample collection times (e.g., time of maximum concentration [t_{max}]) will be reported in hours with 2 decimal places.

For PK/PD data, reporting of mean (arithmetic or geometric), SD, median, and CI on the mean will carry 1 more significant figure/decimal place than the source data, according to the precision method used for source data. Minimum and maximum will carry the same number of significant figures/decimal

places as the source data. The geometric LS mean ratios and bounds of their CIs will be reported with 2 decimal places, and coefficients of variation (CV and gCV) will be reported to 1 decimal place.

6.1. Reference Start Date and Study Day

The reference start date is defined as the day of the dose administration of study treatment (Day 1), and will appear in every listing where an assessment date or event date appears.

The study day will be calculated from the study treatment start date and will be used to show start/stop day of assessments and events.

If the date of the event is on or after the reference date then:

Study Day = (date of event – reference date) + 1

If the date of the event is prior to the reference date then:

Study Day = (date of event – reference date)

If the event date is partial or missing, Study Day, and any corresponding durations will appear missing for that partial date in the listings.

Refer to Appendix 1 for more details.

6.2. Baseline

The pre-dose measurement taken prior to ANB020 or placebo administration at randomization [Day 1], i.e. reference start date, will be considered as baseline. For all safety variables, baseline will be last non-missing measurement taken prior to reference start date (including unscheduled assessments or retests).

If the pre-dose measurement and the reference start date coincide, that measurement will be considered baseline.

6.3. Retests, Unscheduled Visits and Early Termination Data

Listings will include scheduled, unscheduled, retest and early termination data.

For by-visit summaries, data recorded at the nominal visit will be presented. Unscheduled measurements will not to be included in by-visit summaries but may contribute to the baseline value.

6.4. WINDOWING CONVENTIONS

Not applicable.

6.5. STATISTICAL TESTS

All tests of treatment effects will be conducted at a 2-sided alpha level of 0.05, or with 2-sided 95% CIs.

6.6. COMMON CALCULATIONS

For continuous measurements, change from baseline will be calculated as:

Test Value at scheduled Visit X – Baseline Value

Ratio to baseline will be calculated for pharmacodynamic endpoints as:

Test Value (post baseline) / Baseline Value

6.7. SOFTWARE VERSION

Non-compartmental analysis of PK data for final or any interim analysis, and descriptive statistics and graphics for any interim PK analysis, will be performed using Phoenix WinNonlin® 6.4 or higher (Certara, L.P., Princeton, New Jersey, USA). All other analyses, statistics, and graphics (including PK/PD) will be conducted using Statistical Analysis System (SAS) System® Version 9.4 or higher (SAS-Institute, Cary, North Carolina, USA).

7. STATISTICAL CONSIDERATIONS

7.1. ADJUSTMENTS FOR COVARIATES AND FACTORS TO BE INCLUDED IN ANALYSES

The change from baseline on Day 22 of peripheral eosinophil count will be compared between ANB020 and placebo using a mixed-model repeated measures (MMRM) analysis with treatment, visit of measurement, and treatment by visit interaction as fixed effects and baseline eosinophil count and baseline by visit interaction as a covariate.

7.2. MULTICENTER STUDIES

There are a total 7 centers from United Kingdom (3) and USA (4) included in this study.

7.3. MISSING DATA

For non-PK/PD data, no imputations will be performed on missing data. Partial dates will be imputed as per Appendix 1. Missing PK or PD data will be handled as described in Section 19 or Section 20.

7.4. MULTIPLE COMPARISONS/ MULTIPLICITY

Not applicable.

7.5. EXAMINATION OF SUBGROUPS

No subgroups analysis will be performed for this study.

8. OUTPUT PRESENTATIONS

The templates provided with this SAP describe the presentations for this study and the format and content of the summary tables, figures and listings to be provided by IQVIA Biostatistics.

All visit assessments will be presented according to the nominal visit name.

9. DISPOSITION AND WITHDRAWALS

All patients who provide informed consent will be accounted for.

Data collected in Early Termination (ET) and End of Study (EOS) pages in the electronic Case Report Form (eCRF) will be used to present disposition and withdrawal results. Frequency table will be provided for:

Number of patients screened per Informed Consent.

Number of patients eligible at screening.

Number of screen failures (from EoS page).

Number of patients in the Randomized Analysis Set (patients who are assigned treatment).

Number of patients randomized at day 1.

Number of patients willing to participate at Day 1.

Number of patients in the Safety Analysis Set (patients administered the treatment).

Number of patients in the Full Analysis Set.

Number of patients in the Pharmacokinetic Analysis Set.

Number of patients in the Pharmacodynamic Analysis Set.

Number of patients who completed the study (from EoS page).

Number of patients who Completed the Study assessments till Day 36.

Number of patients who discontinued/withdrew the study (from EoT page).

Primary reason for discontinuation (from EoT page).

A listing will be presented with the following details.

screen failure (Yes/No)?

Willing to Participate at Day 1

assigned treatment

completed study (Yes/No)?

If not completed the study, then reason for end of treatment.

10. DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Demographic data and other baseline characteristics will be presented for the SAF. No statistical testing will be carried out for demographic or other baseline characteristics.

Summary statistics will be provided for:

Age (years) - calculated relative to date of informed consent

Weight (kg) as collected on the Vital Signs Screening eCRF

Height (cm) as collected on the Vital Signs Screening eCRF

BMI (kg/m^2) as collected on the Vital Signs Screening eCRF

Frequency tables will be provided for:

Gender

Women of child bearing potential

Race

Ethnicity

A listing for patient demographic data and other baseline characteristics will be presented.

11. PROTOCOL DEVIATIONS

All protocol deviations observed during study conduct will be captured in Clinical Trial Management System (CTMS).

The Investigator and Sponsor will review the protocol violation records from CTMS and provide confirmation on the categorization of violations as major/ critical/ minor.

Major protocol deviations or events include changes to the procedures that may impact the quality of the data or any circumstances that can alter the evaluation of the PK or PD data. Examples include, but may not be limited to, sample processing errors that lead to inaccurate bioanalytical results, incomplete dose administered, incomplete PK or PD profile collected, and use of disallowed concomitant medication thought to affect PK or PD. In the case of a major protocol deviation or event, the corresponding PK or PD data collected will be excluded from the summaries and statistical analyses, yet will be reported in the study result listings.

A list of major protocol deviations that could significantly affect study assessments will be provided. The incidence of each protocol violation will be listed. A frequency table for major protocol violations will be provided for Safety Analysis Set. Major protocol deviations or events that impact the quality of the PK and/or PD data will be listed only.

If a patient refuses blood collection for PK analysis, this will not be considered a protocol violation as the PK analysis is a secondary objective.

12. MEDICAL HISTORY

The frequency and percentage will be provided for medical history findings summarized by system organ class (SOC), preferred terms (PT) and report term for the SAF. Medical history will be coded using version 20.0 (or higher) of MedDRA.

Patients experiencing multiple events within the same SOC will only be counted once within that SOC and multiple PTs within the same SOC will only be counted once for each unique PT within the SOC.

Summary tables will be table sorted in descending order of SOC and descending order of PT within SOC.

Percentages will be sorted by decreasing frequency of SOC and PT within SOC for overall. Events will be mentioned as "Uncoded" if they are not coded yet.

A listing of medical history diagnosis with all details will be presented.

13. CONCOMITANT ILLNESSES

Medical history that are ongoing at the screening will be coded using version 20.0 (or higher) of MedDRA and presented similar to medical history.

The frequency and percentage will be provided summarized by SOC and PT for the SAF.

Patients experiencing multiple events within the same SOC will only be counted once within that SOC and multiple PTs within the same SOC will only be counted once for each unique PT within the SOC.

Percentages will be sorted by decreasing frequency of SOC and PT within SOC for overall. Events will be mentioned as "Uncoded" if they are not coded yet.

A listing of ongoing medical illnesses with all details will be presented along with medical history conditions.

14. CONCOMITANT MEDICATIONS

A frequency table will be provided for prior and concomitant medications and will be summarized by SOC and PT for the SAF. Medications will be coded using WHO drug dictionary version Dec 2016.

Patients with multiple usage of the same medication within the same SOC and PT will only be counted once within that level.

Percentages will be sorted by decreasing frequency of SOC and PT for overall. Medications will be mentioned as "Uncoded" if they are not coded yet.

See Appendix 1 for handling of partial dates for medications. If it is not possible to define a medication as prior or concomitant, the medication will be classified by the worst case; i.e. concomitant.

'Prior' medications are medications which started and stopped prior to the administration of study drug.

'Concomitant' medications are medications which:

started prior to, on or after the administration of study drug,

AND ended on or after the date of administration of study drug or were ongoing at the end of the study.

A listing for medication with all details will be presented for the SAF.

15. Study Treatment Exposure

A listing of study drug exposure will be presented, with details of start date & time and end date & time of infusion and total volume administered as well as reason if <100 ml was infused. Data from IP Administration eCRF page will be used to generate the summary table and listing.

16. Study Treatment Compliance

Overall compliance is expected as the study treatment is being administered at the clinic, however no summary will be provided for compliance.

17. Efficacy Outcomes

17.1. Primary Endpoints

17.1.1. Primary Efficacy Endpoint

Not applicable.

17.1.2. Primary Pharmacodynamic Endpoint

Reduction of peripheral eosinophil count from Baseline (Day 1) to Day 22

17.1.2.1. Analysis of Primary Pharmacodynamic Endpoint

Pharmacodynamic analysis will be carried out for the PD Analysis Set. For analysis of primary PD endpoint, refer to Section 20 for details.

17.2. SECONDARY ENDPOINTS

17.2.1. SECONDARY EFFICACY ENDPOINTS

Change in FEV_1 (Litres) from Baseline (Day 1) to the EOS visit (Day 127)

Change in FeNO (ppb) from Baseline (Day 1) to the EOS visit (Day 127)

17.2.1.1. Analysis of Secondary Efficacy Endpoints

The null hypothesis for the secondary efficacy analysis is:

H0: There is no difference in change from baseline on day 127 (for FEV_1 and FeNO) between ANB020 and placebo.

Vs the alternative:

H1: There is a difference in change from baseline on day 127 (for FEV_1 and FeNO) between ANB020 and placebo.

The analysis of the secondary efficacy endpoints will be carried out for the FAS population.

Day1 pre-bronchodilator spirometry assessment will be considered as the baseline.

The actual and change from baseline (Day 1) to the EOS visit (Day 127) for FEV1 and FeNO will be summarized using descriptive statistics by treatment groups at all time points where assessment is done. Change from baseline will be evaluated where possible.

Change from baseline for FEV_1 and FeNO will be compared between ANB020 and placebo using an analysis of covariance (ANCOVA) with treatment as fixed effect and baseline result as covariate and patient as a random effect. An unstructured covariance matrix will be used. If the model fails to converge, then an appropriate covariance matrix [e.g. compound symmetric (CS), CHS, AR] will be selected based on the Akaike Information Criteria (AIC). For AIC, a lower value will imply a better fit.

The following statistics will be presented:

Treatment Least Square Mean (LSM)

Treatment LSM difference

Standard error of treatment LSM difference

95% confidence interval (CI)

P-value for the difference

A supportive analyses will be performed using an MMRM analysis. The model includes terms for treatment, time point of measurement, and treatment by time point interaction as fixed effects and baseline value and baseline*time point as covariate. At each visit day, model-based LSMs for the treatment effects, 95% CIs, and p-values will be calculated for within and between treatment comparisons.

Patient-wise data listings will be provided.

17.2.2. SECONDARY PHARMACOKINETIC ENDPOINTS

Maximum observed concentration (C_{max})

Time to maximum observed concentration (t_{max})

Area under the concentration-time curve in serum from time zero (pre-dose) extrapolated to infinite time [$AUC_{(0\text{-}inf)}$]

Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration [$AUC_{(0\text{-}last)}$]

Systemic clearance (CL)

Apparent terminal rate constant (λ_z)

Apparent terminal half-life ($t_{1/2}$)

Volume of distribution during terminal phase (V_Z)

Volume of distribution at steady state following intravenous dosing (V_{SS})

17.2.2.1. Analysis of Secondary Pharmacokinetic Endpoints

For analysis of secondary PK endpoints, refer to Section 19 for details.

17.2.3. SECONDARY PHARMACODYNAMIC ENDPOINTS

Reduction of peripheral eosinophil count from Baseline (Day 1) to EOS visit (Day 127)

Whole blood ex vivo induced IFN-γ levels

17.2.3.1. Analysis of Secondary Pharmacodynamic Endpoints

For analysis of secondary PD endpoints, refer to Section 20 for details.

17.3. EXPLORATORY ENDPOINTS

17.3.1. EXPLORATORY EFFICACY ENDPOINTS

Clinical scores for ACQ-7 (Screening, Day 1, 8, 22, 36, 64, 85, 106, and EOS), PGIC (throughout the study), and CGIC (Day 2, 8, 22, 36, 64, 85, 106, and EOS)

Patient diary data of asthma symptoms, change in standard of care treatment, and rescue medication (SABA) usage (collected throughout the study)

Reduction of IgE levels from Baseline (Day 1) to the EOS visit (Day 127)

17.3.1.1. Analysis of Exploratory Endpoints

The FAS will be used for the exploratory efficacy analysis.

Total ACQ-7 will be calculated as sum of all individual scores for each patient at each visit.

Symptoms will be scored on a scale of 0 to 6 with 6 being the worst case. ACQ-7 will be missing if any individual score is missing.

The actual and change from baseline for ACQ, PGIC, CGIC, and IgE levels will be summarized using appropriate descriptive statistics by treatment groups at all time points where assessment is done. Change from baseline will be evaluated where possible.

PGIC and CGIC scores will be collected during the study for an overall response to the treatment where a score of 1 implies “Very much improved” and a score of 7 implies “Very much worse”.

Applicable diary assessments, e.g. frequency of asthma symptoms (wheezing, cough, shortness of breath, chest tightness, etc.) experienced during the week, number of patients receiving rescue medication, and number of patients who have change in SOC treatment will be summarized using appropriate descriptive statistics.

Applicable exploratory endpoints analyses will be performed same as secondary efficacy analyses. Clinical Global Impression of Change Scale (CGIC Scores) and Patient Global Impression of Change (Summary of PGIC Scores) will be analysed using Cochran–Mantel–Haenszel test at each visit by row-

mean-score-difference test using ridit scores to compare ANB020 vs placebo. Patient-wise data listings will be provided.

17.3.2. EXPLORATORY PHARMACODYNAMICS ENDPOINTS

Circulating cytokines including, but not limited to interleukin IL-4, IL-5, , IL-13, IL-33, and sST2 at day 1, 2, 8, 22, 36, 64, and EOS.

17.3.2.1. Analysis of Exploratory Pharmacodynamic Endpoints

For analysis of exploratory PD endpoints, refer to Section 20 for details.

18. SAFETY OUTCOMES

Safety analyses will be based on the SAF.

The following are the safety and tolerability endpoints:

- Assessment of Adverse Events (AEs)/ Serious Adverse Events (SAEs)
- Physical examination
- Vital signs
- Clinical safety laboratory tests
- Electrocardiograms
- Number of asthma exacerbations
- Assessment of immunogenicity (ADA status)

There will be no statistical comparisons between the treatment groups for safety data.

18.1. ADVERSE EVENTS

AEs will be coded using MedDRA version 19.1.

Treatment emergent adverse events (TEAEs) are defined as AEs that started or worsened in severity on or after the date and time of the study drug infusion.

Non-treatment emergent adverse event (Non-TEAE) will be defined as any AE that started on or after the date of informed consent and before the administration of study drug.

AEs with missing start dates will be considered treatment-emergent. AEs with missing stop dates or

with stop dates after the end of the study date will be considered to have been ongoing at the end of the study.

The severity of AEs will be characterized as “mild, moderate, severe” according to the following definitions:

Mild events are usually transient and do not interfere with the patient’s daily activities

Moderate events introduce a low level of inconvenience or concern to the patient and may interfere with daily activities

Severe events interrupt the patient’s usual daily activity

Missing severity will be assumed to be the worst severity case i.e. ‘severe’; however, in the listing, it will be displayed as missing.

The causal relationship between the study drug and the AE will be characterized as “Unrelated, Unlikely, Possible, Probable, and Unknown (unable to judge)”.

The summaries will be presented as “Related” versus “Not Related”.

Categories “Unrelated” and “Unlikely” will be mapped to “Not Related”, while the categories “Possible”, “Probable” and “Unknown” will be mapped to “Related”.

Missing relationship will be assumed to be the worst severity case i.e. ‘Related; however, in the listing, it will be displayed as missing.

An overview of adverse event along with the number and percentage of patients experiencing TEAEs, for each treatment group will be provided.

If patient has multiple TEAEs by severity and/or multiple relationship with study drug, worst case severity and the worst-case relationship to the study drug will used for overview tabulation.

For TEAE by final outcome, if a patient has multiple TEAEs with different outcomes, worst case will be considered, where ‘Fatal’ being the worst.

For Action Taken with the Drug, patient can be counted in more than one categories.

The following summary tables will be provided by SOC and PT for each treatment group and overall:

- Number of patients with at least one TEAE
- Number of patients with at least one serious TEAE

- Number of patients with at least one TEAE by severity
- Number of patients with at least one TEAE by relationship to study drug
- Number of patients with at least one TEAE leading to permanent discontinuation of study drug
- Number of patients with at least one TEAE leading to interruption of study drug
- Number of patients with at least one TEAE leading to patient withdrawal from study
- Number of patients with at least one TEAE leading to death
- Number of patients with non-TEAE

If an AE occurs more than once, the patient will be counted only once per SOC and once per PT within each SOC. If a patient reports a TEAE more than once within a SOC/PT, the AE with the worst-case severity will be used in the corresponding severity summaries and the worst-case relationship to the study drug will be used in the corresponding relationship summaries.

Percentages will be calculated relative to the total number of patients in the SAF. The summaries will be sorted by descending frequencies of SOC and descending frequencies of PT with in SOC.

Listings will be provided for TEAEs, Serious TEAEs, TEAEs leading to discontinuation from study or from IP, and TEAEs leading to death for the SAF.

18.2. DEATHS

The number of patients with at least one TEAE leading to death will be summarized as described above.

18.3. LABORATORY EVALUATIONS

The following tests will be conducted throughout the study under laboratory evaluations:

Hematology (Hematocrit, Packed Cell Volume [PCV], Hemoglobin, MCH, MCH concentration, MCV, Platelet count, RBC, WBC [absolute], Basophils [absolute and %], Eosinophils [absolute and %], Monocytes [absolute and %], Neutrophils [absolute and %], Lymphocytes [absolute and %], Immunoglobulins [IgA, IgG, IgM, IgE, IgD])

Clinical Chemistry (ALT, Albumin, ALP, AST, Bicarbonate, Bilirubin [Total], Bilirubin [Direct-if total is elevated], Calcium, Chloride, C-reactive Protein (CRP), Creatinine, GGT, Glucose, Potassium, Phosphate [Inorganic], Protein [Total], Sodium, Troponin, Urea, hCG [WOCBP])

Urinalysis (Bilirubin, Blood, Glucose, Ketones, Leukocytes, Nitrates, pH, Protein, Specific gravity, and Urobilinogen)

The following tests were conducted only at screening:

Virology (Hepatitis B Surface Antigen, Hepatitis C Antibody, HIV Antibodies)

TB (QuantiFERON TB Gold test)

Drugs of Abuse

FSH

Urine Pregnancy-dipstick (prior to IP administration on Day 1)

The actual and change from baseline values at scheduled assessment for each laboratory parameter will be summarized using appropriate descriptive statistics by treatment groups and all available visits.

Frequency count and percentages will be provided for categorical variables.

The following summaries also will be provided for laboratory data:

Incidence of abnormal values according to normal range criteria

Normal, Abnormal NCS and Abnormal CS by test

Shift table for laboratory test parameters from baseline will be summarized at each visit. Percentages will be based on the number of patients in the SAF population with data at baseline and the visit of interest.

Hematology and clinical chemistry data will be reported in System International (SI) units.

18.4. ECG EVALUATIONS

A standard 12-lead ECG will be performed at screening and EOS visits. The following ECG parameters will be summarized:

Heart Rate (bpm)

PR Interval (msec)

QRS Interval (msec)

QT Interval (msec)

QTc Interval (msec)

QTcF (msec) {based on Fridericia formula}

The actual and change from baseline values for the above parameters will be summarized using descriptive statistics (n, mean, standard deviation, median, and range) by treatment groups and all available visits.

The overall assessment of ECG will be summarized using frequency and percentage of the following indications:

Normal

Abnormal, Not Clinically Significant (ANCS)

Abnormal, Clinically Significant (ACS)

A listing of ECG parameters and of the overall assessment will be provided.

18.4.1. ECG SPECIFIC DERIVATION

Fridericia's Correction (msec)

$$QTcF\ (\text{msec}) = \frac{QT\ (ms)}{\sqrt[3]{RR\ (ms)/1000}}$$

18.4.2. ECG MARKEDLY ABNORMAL CRITERIA

Absolute values of the QT interval will be classified as:

≥450 msec

≥480 msec

≥500 msec

Since, there are different ranges for QTcF between the males and females, we will summarise the QTcF by gender as defined below:

Absolute values of the QT interval as: Males: 431- 450 msec; Female: 451- 470 msec.

Abnormal values of the QT interval as: Males: > 450 msec Females: > 470 msec.

The change from Baseline of QT interval will be classified as:

>30 msec increase from baseline

>60 msec increase from baseline

18.5. VITAL SIGNS

The following Vital Signs measurements will be reported for this study:

Blood Pressure - systolic and diastolic (mmHg)

Respiratory Rate (resp/min)

Pulse Rate (breaths/min)

Temperature (^{0}C)

The actual and change from baseline values for the above parameters will be summarized using descriptive statistics (n, mean, standard deviation, median, and range) by treatment groups and all available visits.

A listing of the above parameters will be provided.

18.6. PHYSICAL EXAMINATION

The physical examination includes evaluation of general appearance, head, eyes, ears, nose, and throat, and the pulmonary, cardiovascular, gastrointestinal, renal/genito-urological, endocrine (including thyroid), musculoskeletal/spinal, lymphatic, and dermatologic systems.

The physical examination will be conducted at screening and EOS.

The frequency and percentage of patients with normal, abnormal CS, and abnormal NCS assessments will be summarized by body system and treatment group at each available visit.

A listings of physical examination findings will be provided.

18.7. OTHER SAFETY ASSESSMENTS (NUMBER OF ASTHMA EXACERBATIONS)

Number of asthma exacerbations will be summarized using frequency count and percentage for the SAF.

Time (in days) from randomization to the first asthma exacerbation will be used as a supportive variable

and will be calculated as follows:

Start date of first asthma exacerbation − Date of randomization + 1

The time to first asthma exacerbation for patients who do not experience an asthma exacerbation during the period till end of study will be censored at the date of their last visit, or at the time point after which an exacerbation could not be assessed (for lost to follow-up patients).

Time to first asthma exacerbation will be analyzed to explore the extent to which treatment delays the time to first exacerbation compared with placebo. A cox proportional hazard model will be deployed by using treatment group as a class variable and number of exacerbations in the study as covariates. Results of the analysis will be summarized as hazard ratios and 95% confidence intervals (CIs) comparing ANB020 with placebo.

Time to first asthma exacerbation will be displayed graphically using a Kaplan-Meier plot.

The median time to event will be summarized by treatment groups, if there is sufficient uncensored data available to calculate these median values.

18.8. Other Safety Assessments (Immunogenicity)

Blood samples will be taken for ADA analysis at day 1, 8, 36, 85, 106, and 127/ET.

Titer values will be summarized by treatment using appropriate descriptive statistics. The frequency and percentage of patients with categorical result assessments will be summarized by treatment groups at each available visit and time points.

19. Pharmacokinetic Outcomes

The PK parameters will be derived using non-compartmental methods. The actual elapsed sampling times will be used in the PK parameter calculations, except any interim analysis will use nominal sampling times.

The PK analysis set will be used for PK analysis.

Patient listings of PK sampling dates and times and all concentration-time data for each treatment will be presented.

Concentration data of ANB020 will be summarized by treatment and nominal time point, as described in Section 6. Concentrations below the lower limit of quantitation

(BLQ) will be treated as zero for calculation of descriptive statistics. If the calculated mean concentration is BLQ, the mean value will be reported as BLQ and the SD and CV will be reported as not determined (ND). Missing data will not be inputted, except any missing pre-dose concentrations will be assigned a value of zero for calculation PK parameters. If 1 or more concentrations at a given time point are missing, they will be reported as missing and will be omitted from the calculation of descriptive statistics.

Plots of the mean (±SD) plasma concentration-time profile for ANB020 will be presented by nominal sampling time on linear and semi-logarithmic scales. Individual concentration-time data will be listed and plotted by actual sampling times on linear and semi-logarithmic scales.

For the calculation of PK parameters, concentrations that are BLQ will be assigned a value of zero if they precede quantifiable samples prior to t_{max}. Any anomalous concentration values observed at pre-dose will be identified in the study report and will be used for the computation of PK parameters if the anomalous value is not greater than 5% of C_{max}. If the anomalous value is greater than 5% of C_{max}, the PK parameters for the given patient will be included in listings but excluded from summary presentations and analyses. Following C_{max}, BLQ values embedded between 2 quantifiable data points will be treated as missing. Trailing BLQ values (BLQ values after the last quantifiable concentration) will be set to zero. If consecutive BLQ concentrations are followed by quantifiable concentrations in the terminal portion of the concentration curve, these quantified values will be excluded from the PK analysis by setting them to missing.

The following PK parameters will be computed for ANB020, if data permits:

C_{max}	Maximum concentration in serum (µg/mL), obtained directly from the observed concentration versus time data.
t_{max}	Time of maximum concentration (h), obtained directly from the observed concentration versus time data.
$AUC_{(0\text{-inf})}$	Area under the concentration-time curve in serum from time zero (pre-dose) extrapolated to infinite time (h·µg/mL), calculated by linear up/log down trapezoidal summation and extrapolated to infinity by addition of the last quantifiable concentration divided by the apparent terminal rate constant: $AUC_{(0\text{-last})} + C_{last}/\lambda_z$.

$AUC_{(0\text{-last})}$	Area under the serum concentration-time curve from time zero to the time of the last quantifiable concentration (h·µg/mL), calculated by linear up/log down trapezoidal summation.
CL	Systemic clearance (L/h), calculated as dose/ $AUC_{0\text{-inf}}$.
λ_z	Apparent terminal rate constant (1/h), determined by linear regression of the terminal points of the log-linear concentration-time curve.
$t_{1/2}$	Apparent terminal half-life (h), determined as ($\ln 2/\lambda_z$).
Vz	Volume of distribution (L) during terminal phase, estimated by dividing the systemic clearance by λ_z.
V_{SS}	Volume of distribution at steady state following intravenous dosing (L), calculated as $[([AUMC_{last} + ([t_{last}*C_{last}]/\lambda z) + C_{last}/\lambda z^2]/ AUC_{(0\text{-inf})}) - TI/2]*CL$, where $AUMC_{last}$ is the area under the moment curve from the time of dosing to C_{last}, t_{last} is the time of C_{la}st, and TI is infusion duration.

The following ANB020 PK parameters will be calculated for diagnostic purposes and listed, but will not be summarized:

λ_z_lower	The start time (h) of the interval of the log-linear regression to determine λ_z and $t_{1/2}$.
λ_z_upper	The end time (h) of the interval of the log-linear regression to determine λ_z and $t_{1/2}$.
$t_{1/2}$, Interval	The time interval (h) of the log-linear regression to determine λ_z and $t_{1/2}$, calculated as λ_z_upper − λ_z_lower.
$t_{1/2}$, N	Number of data points included in the log-linear regression analysis used to calculate λ_z and $t_{1/2}$. A minimum of 3 data points is required.
R_{sq}	Coefficient of determination for calculation of λ_z. A minimum of 3 data points (excluding C_{max}) will be used for determination of the terminal linear

	phase of the concentration-time profile. If the Rsq is less than 0.800 then λ_z, $t_{1/2}$, $AUC_{(0\text{-inf})}$, CL, V_Z, and V_{SS} will be listed but not included in summary presentations or analyses.
$\%AUC_{ex}$	Percentage of $AUC_{(0\text{-inf})}$ obtained by extrapolation, calculated as $[(C_{last}/\lambda_z)/AUC_{(0\text{-inf})}\times 100]$. If the extrapolated area is greater than 20.0% of $AUC_{(0\text{-inf})}$, then $AUC_{(0\text{-inf})}$, CL, V_Z, and V_{SS} will be listed but not included in summary presentations or analyses.

The PK parameters will be summarized by treatment as described in Section 6.

PHARMACODYNAMIC OUTCOMES

20. The PD analysis set will be used for PD analysis. The PD endpoints are:

Eosinophil count

Cytokines: IL-4, IL-5, IL-13, IL-33, and sST2

Ex-vivo induced IFN- γ

Observed, change from baseline, and ratio to baseline for all PD endpoints will be summarized by treatment and nominal time point using descriptive statistics as described in Section **6.** Values that are BLQ will be treated as ½ LLOQ for calculation of descriptive statistics and change from baseline. If the calculated mean is BLQ, the mean value will be reported as BLQ and the SD and CV will be reported as not determined (ND). Missing data will not be imputed. If 1 or more values at a given time point are missing, they will be reported as missing and will be omitted from the calculation of descriptive statistics and change from baseline. If the pre-dose value is missing for baseline, the screening value, if available, will be used as the baseline.

For comparison of the primary PD endpoint between the two treatments, change from baseline in peripheral eosinophil count for each post-dose time point will be analyzed by an MMRM analysis with fixed terms for treatment, time point of measurement, and treatment by time point interaction, baseline eosinophil count as a covariate, and a repeated time point effect within a subject. An unstructured covariance matrix will be used with subject as the experimental unit. If the model fails to converge, then

appropriate covariance matrix (e.g., compound symmetric) will be selected based on AIC. The same model will be used to compare the overall average between the treatment groups. All tests of treatment effects will be conducted at a 2-sided alpha level of 0.05 or with 2-sided 95% CIs. The following statistics will be presented:

Treatment LSM

SE of LS Mean

95% CI for LS mean

Treatment LSM difference

SE of LS Mean Difference

95% CI for LSM treatment difference

P-value for comparison of ANB020 versus placebo

For secondary and exploratory endpoints (ex vivo induced IFN-γ and serum cytokines), comparison between ANB020 and placebo will be performed using a similar MMRM analysis as described above for primary PD endpoint.

Ratio to baseline values may be used where change from baseline analysis does not meet analysis assumptions. Suitable transformations (e.g., log) may be applied upon such parameters as appropriate to meet the analysis assumptions.

Plots of the mean (±95% CI) observed and change from baseline versus time profiles for PD endpoints will be presented by nominal sampling time on a linear scale.

Plots of observed PD endpoints versus ANB020 concentration will be presented for coinciding nominal time points.

A listing of PD blood sample collection date and times will be provided.

21. INTERIM/INTERMEDIATE ANALYSIS

No interim analysis is planned for the study. However, there will be two unblinded intermediate analysis will be performed once all patients complete the day 36 assessments and again once all patients complete the day 64 assessments. The following 2 data cuts will be provided for data review to unblinded statistician.

D. 36 time point:

- Safety labs (hematology/chem)
- FEV1
- FeNO
- Safety (AE/SAEs)

D.64 time point:

- Safety labs (hematology/chem)
- FEV1
- FeNO
- Safety (AE/SAEs)
- Demographics (Sex/Age)

22. GENETIC ANALYSIS

Not applicable.

23. DATA NOT SUMMARIZED OR PRESENTED

The unscheduled visits will not be summarized but listed.

24. REFERENCES

Protocol amendment 4 dated 31Oct2018

Annotated study book version 9 dated 22May2018

APPENDIX 1. PARTIAL DATE CONVENTIONS

Imputed dates will NOT be presented in the listings.

Algorithm for Treatment Emergence of Adverse Events:

START DATE	STOP DATE	ACTION
Known	Known	If start date < study med start date, then not TEAE If start date ≥ study med start date, then TEAE
	Partial	If start date < study med start date, then not TEAE If start date ≥ study med start date, then TEAE

START DATE	STOP DATE	ACTION
	Missing	If start date < study med start date, then not TEAE If start date ≥ study med start date, then TEAE
Partial, but known components show that it cannot be on or after study med start date	Known	Not TEAE
	Partial	Not TEAE
	Missing	Not TEAE
Partial, could be on or after study med start date	Known	If stop date ≥ study med start date, then TEAE
	Partial	Impute stop date as latest possible date (i.e. last day of month if day unknown or 31st December if day and month are unknown), then: If stop date < study med start date, then not TEAE If stop date ≥ study med start date, then TEAE
	Missing	Assumed TEAE
Missing	Known	If stop date < study med start date, then not TEAE If stop date ≥ study med start date, then TEAE
	Partial	Impute stop date as latest possible date (i.e. last day of month if day unknown or 31st December if day and month are unknown), then: If stop date < study med start date, then not TEAE If stop date ≥ study med start date, then TEAE
	Missing	Assumed TEAE

Algorithm for Prior / Concomitant Medications:

START DATE	STOP DATE	ACTION
Known	Known	If stop date < study med start date, assign as prior If stop date >= study med start date assign as concomitant
	Partial	Impute stop date as latest possible date (i.e. last day of month if day unknown or 31st December if day and month are unknown), then: If stop date < study med start date, assign as prior If stop date ≥ study med start date, assign as concomitant
	Missing	If stop date is missing, it could never be assumed a prior medication, assign as concomitant
Partial	Known	Impute start date as earliest possible date (i.e. first day of month if day unknown or 1st January if day and month are unknown), then: If stop date < study med start date, assign as prior If stop date ≥ study med start date, assign as concomitant

START DATE	STOP DATE	ACTION
	Partial	Impute start date as earliest possible date (i.e. first day of month if day unknown or 1st January if day and month are unknown) and impute stop date as latest possible date (i.e. last day of month if day unknown or 31st December if day and month are unknown), then: If stop date < study med start date, assign as prior If stop date >= study med start date, assign as concomitant
	Missing	If stop date is missing, it could never be assumed a prior medication, assign as concomitant
Missing	Known	If stop date < study med start date, assign as prior If stop date >= study med start date, assign as concomitant
	Partial	Impute stop date as latest possible date (i.e. last day of month if day unknown or 31st December if day and month are unknown), then: If stop date < study med start date, assign as prior If stop date >= study med start date, assign as concomitant
	Missing	Assumed concomitant

APPENDIX 2. PROGRAMMING CONVENTIONS FOR OUTPUTS

IQVIA Output Conventions

Outputs will be presented according to the following Global Bios > Processes > GBIOS Processes -

Implementation Guidelines and Templates > General Guidelines and Templates > Output Conventions

Dates & Times

Depending on data available, dates and times will take the form yyyy-mm-ddThh:mm:ss

Spelling Format

English UK

Presentation of Treatment Groups

For outputs, treatment groups will be represented as follows and in that order

Treatment Group	For Tables, Listings and Graphs	Treatment Number
ANB020	Dummy1	1
Placebo	Dummy2	2

Presentation of Visits

For outputs, visits will be represented as follows and in that order:

Long Name (default)	Short Name	Visit Number
Screening (Day 0)	Scr	1
Baseline (Day 1)	BL	2
Day 2	Day002	3
Day 8, week 1	Day008	4
Day 22, week 3	Day022	5
Day 36, week 5	Day036	6
Day 64, week 9	Day064	7
Day 85, week 12	Day085	8
Day 106, week 15	Day106	9
Day 127, week 18 (EOS/ET)	EOS	10

For outputs, visits for PK/PD will be represented as follows and in that order:

Visit	PK	Ex vivo induced INF-γ	ADA	Cytokines
Day 1	Pre-dose (-0.5 hours) 0.5 hours post SOI EOI EOI+3 hours EOI+6 hours	Pre-dose (-0.5 hours)	Pre-dose (-0.5 hours)	Pre-dose (-0.5 hours)
Day 2	24 hours post SOI	-	-	24 hours post SOI
Day 8, week 1	168 hours post SOI	168 hours post SOI	168 hours post SOI	168 hours post SOI
Day 22, week 3	504 hours post SOI	-	-	504 hours post SOI
Day 36, week 5	840 hours post SOI	840 hours post SOI	840 hours post SOI	840 hours post SOI
Day 64, week 9	1512 hours post SOI	-	-	1512 hours post SOI
Day 85, week 12	-	2016 hours post SOI	2016 hours post SOI	-
Day 106, week 15	-	2520 hours post SOI	2520 hours post SOI	-
Day 127, week 18 (EOS/ET)		3024 hours post SOI	3024 hours post SOI	3024 hours post SOI

Listings

All listings will be ordered by the following:

center-subject ID

randomized treatment group (or treatment received if it's a safety output), first by active dose and then by placebo

date (where applicable).

APPENDIX 3. SAMPLE SAS CODE

SAS CODE FOR ANCOVA

```
PROC MIXED DATA=<data_set_name>;
CLASS trt usubjid;
MODEL chg = trt base/ ddfm=kr;
LSMEANS trt / alpha = 0.05;
ESTIMATE "Test versus placebo" trt -1 1 / cl;
Random trt / subject=usubjid type=UN;
RUN;
```

Where,
trt = treatment group (ANB020 and placebo), usubjid=patient
base=Baseline and chg= change from baseline

SAS CODE FOR MMRM

```
PROC MIXED DATA=<data_set_name> alpha=0.05;
CLASS trt usubjid avisitn;
MODEL chg = trt visit trt*visit base base*trt / solution ddfm=kr;
LSMEANS trt  avisitn  trt*visit / diff cl;
ESTIMATE "Test versus placebo" trt -1 1 / cl;
REPEATED avisitn/ subject=usubjid type=UN;
RUN;
```

Where,
trt = treatment group (ANB020 and placebo), usubjid=patient, avisitn=visit
base=Baseline and chg= change from baseline

SAS CODE FOR CMH TEST

```
PROC Freq data=<data_set_name>;
By visit;
Where trt in ('ANB020' 'Placebo');
Tables trt*score/cmh score=ridit nocol nopercent;
```

Ods Output cmh=cmh5 (where= (AltHypothesis= “Row Mean Scores Differ”));
RUN;
Where, trt = treatment group (ANB020 and placebo)

SAS CODE FOR A COX PROPORTIONAL HAZARD MODEL

PROC PHREG data=<data_set_name>;
CLASS trt (ref class trt (placebo first); =first);
MODEL time*censor (0) = number of exacerbations/rl;
Assess var= (number of exacerbations)/resample;
hazardratios trt;
RUN;
Where, trt = treatment group (ANB020 and placebo)

SAS CODE FOR KAPLAN-MEIER PLOT

PROC LIFETEST data=<data_set_name> noprint;
TIME time*censor (0);
STRATA trt;
RUN;
Where, trt = treatment group (ANB020 and placebo), time=visit.

QUINTILES

Document Approval Signature(s)

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TABLE SHELLS

Placebo-Controlled Proof of Concept Study to Investigate ANB020 Activity in Adult Patients with Severe Eosinophilic Asthma

Study No. ANB020-004

Output Templates Signature Page

Table Shells V1 0 (Dated 18Dec2018) for Protocol ANB020-004

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Position:			
Company:	IQVIA™		

Upon review of this document, the undersigned approves this version of the Output Templates, authorizing that the content is acceptable for the reporting of this study.

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Modification History

Unique Identifier for this Version	Date of the Document Version	Author	Significant Changes from Previous Authorized Version
Draft 0.1	04 Dec 2017	[redacted]	Not Applicable - First Draft
Draft 0.2	07 Dec 2017		Resolved comments from internal review
Draft 0.3	03 Dec 2018		Resolved comments from Sponsor review

Table of Contents

Table 14.1.1.1
Patient Disposition – All Patients Screened

Category	ANB020 (N=XX) n (%)	Placebo (N=XX) n (%)	Total (N=xx) n (%)
Patients Screened[1]	-	-	xx
Patients Eligible at Screening	-	-	xx
Screen Failures	-	-	xx
Patients in Randomized Analysis Set	xx	xx	xx
Patients Willing to Participate at Day 1	xx	xx	xx
Patients in Safety Analysis Set	xx (xx.x)	xx (xx.x)	xx (xx.x)
Patients in Full Analysis Set	xx (xx.x)	xx (xx.x)	xx (xx.x)
Patients in Pharmacokinetic Analysis Set	xx (xx.x)	xx (xx.x)	xx (xx.x)
Patients in Pharmacodynamic Analysis Set	xx (xx.x)	xx (xx.x)	xx (xx.x)
Patients who Completed the Study	xx (xx.x)	xx (xx.x)	xx (xx.x)
Patients who Completed the Study assessments till Day 36	xx (xx.x)	xx (xx.x)	xx (xx.x)
Patients who Discontinued the Study	xx (xx.x)	xx (xx.x)	xx (xx.x)
Reason for Discontinuation			
Adverse Event	xx (xx.x)	xx (xx.x)	xx (xx.x)
Screen Failure			
Death	xx (xx.x)	xx (xx.x)	xx (xx.x)
Lost follow up	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subject withdrawl consent	xx (xx.x)	xx (xx.x)	xx (xx.x)
Physical Decision	xx (xx.x)	xx (xx.x)	xx (xx.x)
----------	----------		
Lack of compliance of protocol	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	xx (xx.x)	xx (xx.x)	xx (xx.x)

Source: Listing 16.2.1.1, 16.2.3.1.1
Note:
- [1] – Patients who provided informed consent
- N is the number of patients within each treatment group in the Randomized Analysis Set.
- Percentages are based on the number of randomized patients in the respective treatment arm (N).
- Percentage for reason for discontinuation is based on number of patients who discontinued the study.

Programming Note (not part of table): Add missing row where necessary.

Table 14.1.2.1
Protocol Deviations – Randomized Analysis Set

Deviations/Violations	ANB020 (N=XX) n (%)	Placebo (N=XX) n (%)	Total (N=XX) n (%)
Patients with major protocol deviations	xx (xx.x)	xx (xx.x)	xx (xx.x)
Patients with category 1 deviation	xx (xx.x)	xx (xx.x)	xx (xx.x)
Patients with category 2 deviation	xx (xx.x)	xx (xx.x)	xx (xx.x)

Source: Listing 16 2.2.1
Note:
- N is the number of patients within each treatment group in the Randomized Analysis Set.
- Percentages are based on the number of randomized patients in the respective treatment arm (N).
- Patients with multiple protocol deviations within the same category are counted only once under that category.

Table 14.1.3.1
Demographic Characteristics – Safety Analysis Set

Characteristic	Statistics	ANB020 (N=XX)	Placebo (N=XX)	Total (N=XX)
Age (years)	n	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx
Gender	n (%)			
Male		xx (xx.x)	xx (xx.x)	xx (xx.x)
Female		xx (xx.x)	xx (xx.x)	xx (xx.x)
Child Bearing Potential Females	n (%)			
Yes		xx (xx.x)	xx (xx.x)	xx (xx.x)
No		xx (xx.x)	xx (xx.x)	xx (xx.x)
If Not Child Bearing Potential,	n (%)			
<Categories>		xx (xx.x)	xx (xx.x)	xx (xx.x)
Race	n (%)			
<Categories>		xx (xx.x)	xx (xx.x)	xx (xx.x)
Ethnicity	n (%)			
<Categories>		xx (xx.x)	xx (xx.x)	xx (xx.x)
Weight (kg)	--------			
Height (cm)	--------			
BMI (kg/m^2)	--------			

Source: Listing 16 2.4.2
Note: BMI – Body Mass Index , Age is calculated relative to informed consent date
- N is the number of patients within each treatment group in the Safety Analysis Set Percentages are based on the number of patients in the respective treatment arm (N).

Programming Note (not part of table):
- Present descriptive statistics similar to age for weight, height and BMI, Present descriptive statistics similar to gender for race and ethnicity.

Table 14.1.3.2
Other Baseline Characteristics – Safety Analysis Set

Characteristic	Statistics	ANB020 (N=XX)	Placebo (N=XX)	Total (N=XX)
Drugs of Abuse				
Sample Collected?	n (%)			
Yes		xx (xx.x)	xx (xx.x)	xx (xx.x)
Positive		xx (xx.x)	xx (xx.x)	xx (xx.x)
Negative		xx (xx.x)	xx (xx.x)	xx (xx.x)
No		xx (xx.x)	xx (xx.x)	xx (xx.x)
Quantiferon Gold Test [1]				
Blood Sample Collected?	n (%)			
Yes		xx (xx.x)	xx (xx.x)	xx (xx.x)
Positive		xx (xx.x)	xx (xx.x)	xx (xx.x)
Negative		xx (xx.x)	xx (xx.x)	xx (xx.x)
No		xx (xx.x)	xx (xx.x)	xx (xx.x)
Virology				
Blood Sample Collected?	n (%)			
Yes		xx (xx.x)	xx (xx.x)	xx (xx.x)
No		xx (xx.x)	xx (xx.x)	xx (xx.x)
If Yes,				
Hepatitis B Surface Antigen	n (%)			
Positive		xx (xx.x)	xx (xx.x)	xx (xx.x)
Negative		xx (xx.x)	xx (xx.x)	xx (xx.x)
Not Done		xx (xx.x)	xx (xx.x)	xx (xx.x)
Hepatitis C Antibody	n (%)			
<Categories>		xx (xx.x)	xx (xx.x)	xx (xx.x)
HIV Antibody	n (%)			
<Categories>		xx (xx.x)	xx (xx.x)	xx (xx.x)

Table 14.1.3.2
Other Baseline Characteristics – Safety Analysis Set

Characteristic	Statistics	ANB020 (N=XX)	Placebo (N=XX)	Total (N=XX)

Source: Listing 16.2.4.5, 16.2.4.6, 16.2.4.7
Note:
- N is the number of patients within each treatment group in the Safety Analysis Set. Percentages are based on the number of patients in the respective treatment arm (N).
- [1] – Test for Tuberculosis

Programming Note (not part of table): Add missing row where applicable. *This table can be modified as per the data requirement.*

Table 14.1.4.1
Medical History – Safety Analysis Set

System Organ Class Preferred Term Report Term	ANB020 (N=XX) n (%)	Placebo (N=XX) n (%)	Total (N=XX) n (%)
System Organ Class 1			
Preferred Term1	xx (xx x)	xx (xx.x)	xx (xx.x)
Preferred Term2	xx (xx x)	xx (xx.x)	xx (xx.x)
----------	xx (xx x)	xx (xx.x)	xx (xx.x)
System Organ Class 2			
Preferred Term1	xx (xx x)	xx (xx.x)	xx (xx.x)
Preferred Term2	xx (xx x)	xx (xx.x)	xx (xx.x)
----------	xx (xx x)	xx (xx.x)	xx (xx.x)

Source: Listing 16 2.4.3
Note:
- N is the number of patients within each treatment group in the Safety Analysis Set.
- Patients experiencing multiple events within the same SOC or PT are counted only once under those categories.
- Percentages are based on the number of patients in the respective treatment arm (N).

Programming Note (not part of table): Number and percentage (%) of patients with Medical History, sorted by decreasing frequency of system organ class and preferred term in total column. Mention “Uncoded” if there are any terms which are not coded yet.

Table 14.1.5.1
Prior Medications – Safety Analysis Set

System Organ Class Preferred Term	ANB020 (N=XX) n (%)	Placebo (N=XX) n (%)	Total (N=XX) n (%)
Number of Patients with at least one Prior Medication	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
----------			
	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2			

Source: Listing 16 2.4.4
Note:
- N is the number of patients within each treatment group in Safety Analysis Set.
- Medications are coded using WHO Drug Dictionary Dec 2016.
- Patients experiencing multiple events within the same SOC or PT are counted only once under those categories.
- Percentages are based on number of patients within each treatment group under Safety Analysis Set (N).
- Only the patients with prior medications are summarized. 'Prior' medications are medications which started and stopped prior to the administration of study drug.

Programming Note (not part of table): Number and percentage (%) of patients with prior medications, sorted by descending order of frequency in total column. Add"Uncoded" if any events are not coded yet.
Programming Note (not part of table): Similar table will be generated as follows:

Table 14.1.5.2
Concomitant Medications – Safety Analysis Set

Tables 14.1.5.2 will be summarized only for patients having atleast one concomitant medication.

Source: Listing 16.2.4.4 Programming note: All the above footnotes should be there except the one in yellow. Instead of that the following footnote should be used:
Only the patients with concomitant medications are summarized. Concomitant' medications are medications which started prior to, on or after the administration of study drug and ended on or after the date of administration of study drug or were ongoing at the end of the study

Table 14 1 6 1
Study Drug Exposure – Safety Analysis Set

Charateristic	Statistics	ANB020 (N=XX) n (%)	Placebo (N=XX) n (%)	Total (N=XX) n (%)
Total Volume Administered (ml)	n	xx	xx	xx
	Mean (SD)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)
	Median	xx x	xx x	xx x
	Min, Max	xx, xx	xx, xx	xx, xx

Source: Listing 16 2 5 1
Note:
- N is the number of patients within each treatment group in Safety Analysis Set
-

Table 14 4 2 1 1
Eosinophil Counts (unit) – Pharmacodynamic Analysis Set

Visit	Statistics	ANB020 (N=XX)			Placebo (N=XX)		
		Observed	Change from Baseline	Ratio to baseline	Observed	Change from Baseline	Ratio to baseline
Screening	n	xx	-	-	xx	-	-
	Mean (SD)	xx x (xx xx)	-	-	xx x (xx xx)	-	-
	CV (%)	xx x	-		xx x	-	-
	95% CI	(xx xxxx, xx xxxx)	-	-	(xx xxxx, xx xxxx)	-	-
	Median	xx x	-	-	xx x	-	-
	Min, Max	xx, xx	-	-	xx, xx	-	-
Baseline	n	xx	-	-	xx	-	-
	Mean (SD)	xx x (xx xx)	-	-	xx x (xx xx)	-	-
	CV (%)	xx x	-	-	xx x	-	-
	95% CI	(xx xxxx, xx xxxx)	-	-	(xx xxxx, xx xxxx)	-	-
	Median	xx x	-	-	xx x	-	-
	Min, Max	xx, xx	-	-	xx, xx	-	-
Day 2	n	xx	xx	xx	xx	xx	xx
	Mean (SD)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)
	CV (%)	xx x	-	xx x	xx x	-	xx x
	95% CI	(xx xxxx, xx xxxx)	(xx xxxx, xx xxxx)	(xx xxxx, xx xxxx)	(xx xxxx, xx xxxx)	(xx xxxx, xx xxxx)	(xx xxxx, xx xxxx)
	Median	xx x	xx x	xx x	xx x	xx x	xx x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
<Visits>							

Source: Listing 16.2.9.2

Note: CI = Confidence Interval, CV = coefficient of variation, Max = maximum, Min = minimum, SD = Standard Deviation.

- N is the number of patients within each treatment group inFull Analysis Set
- Baseline will be last non-missing measurement taken prior to reference start date (including unscheduled assessments or retests)

Programming Note: Continue this table for all available visits and respective change from baseline.

Table 14 4 2 1 2
Primary Pharmacodynamic Endpoint: Change from Baseline in Peripheral Eosinophil Count (cells/μL) on Day 22 – Pharmacodynamic Analysis Set

Statistic	ANB020 (N=XX)	Placebo (N=XX)
N	xx	xx
LS Mean	xxx.xx	xxx.xx
SE of LS Mean	xx.xxx	xx.xxx
95% CI	[xxx.xx, xxx.xx]	[xxx.xx, xxx.xx]
LS Mean Difference (ANB020 – Placebo)	xx.xx	
SE of LS Mean Difference	xx.xx	
95% CI for LS Mean Difference	[xx.xx, xx.xx]	
P-value	x.xxxx	

Source: Listing 16 2 9 2
Note:
- LS: Least Squares; SE: Standard Error; CI: Confidence Interval; MMRM: Mixed Model for Repeated Measures;
- n is the number of subjects with non-missing values
- N is the number of subjects within each treatment group under Full Analysis Set
- P-value is obtained using an MMRM model with treatment, visit, treatment*visit as fixed effects and baseline eosinophil count

Programming Note: Refer SAP for Model

Table 14 4 2 1 3
Whole Blood Ex-vivo induced IFN- γ (pg/mL) – Pharmacodynamic Analysis Set

Analyte (unit)	Visit	Nominal Time Point	Statistics	ANB020 (N=XX)			Placebo (N=XX)		
				Observed	Change from Baseline	Ratio to baseline	Observed	Change from Baseline	Ratio to baseline
INF-y (pg/mL)	Baseline	Pre-dose (-0 5 hours)	n	xx	-	-	xx	-	-
			Mean (SD)	xx x (xx xx)	-	-	xx x (xx xx)	-	-
			CV (%)	xx x	-	-	-	xx x	-
			95% CI	(xx xxxx, xx xxxx)	-	-	(xx xxxx, xx xxxx)	-	-
			Median	xx x	-	-	xx x	-	-
			Min, Max	xx, xx	-	-	xx, xx	-	-
	Day 8	168 hours post SOI	n	xx	xx	xx	xx	xx	xx
			Mean (SD)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)
			CV (%)	xx x	-	xx x	-	xx x	xx x
			95% CI	(xx xxxx, xx xxxx)	(xx xxxx, xx xxxx)	(xx xxxx, xx xxxx)	(xx xxxx, xx xxxx)	(xx xxxx, xx xxxx)	(xx xxxx, xx xxxx)
			Median	xx x	xx x	xx x	xx x	xx x	xx x
			Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
	<visits>	<time points>							

Source: Listing 16 2 9 3
Note:
- SOI – Start of Infusion, CI = Confidence Interval, SD = Standard deviation CV = coefficient of variation, Max = maximum, Min = minimum,
- Baseline will be last non-missing measurement taken prior to reference start date (including unscheduled assessments or retests)
- N is the number of patients within each treatment group in Full Analysis Set

Programming Note (not part of table): Continue the table for all ex vivo analytes in whole blood at all available visits and respective time points

Table 14 4 2 2 1
Secondary Pharmacodynamic Endpoint: Change from Baseline in Peripheral Eosinophil Count (cells/μL) on Day 127/ET – Pharmacodynamic Analysis Set

Statistic	ANB020 (N=XX)	Placebo (N=XX)
n	xx	xx
LS Mean	xxx.xx	xxx.xx
SE of LS Mean	xx.xxx	xx.xxx
95% CI	[xxx.xx, xxx.xx]	[xxx.xx, xxx.xx]
LS Mean Difference (ANB020 – Placebo)	xx.xx	
SE of LS Mean Difference	xx.xx	
95% CI for LS Mean Difference	[xx.xx, xx.xx]	
P-value	x.xxxx	

Source: Listing 16 2 9 2
Note:
- LS: Least Squares; SE: Standard Error; CI: Confidence Interval; MMRM: Mixed Model for Repeated Measures;
- n is the number of subjects with non-missing values
- N is the number of subjects within each treatment group under Full Analysis Set

P-value is obtained using an MMRM model with treatment, visit, treatment*visit as fixed effects and baseline eosinophil count

Table 14 4 2 2 2
Secondary Pharmacodynamic Endpoint: Change from Baseline in Whole Blood Ex-vivo induced IFN-γ (pg/ml) on Day 127/ET – Pharmacodynamic Analysis Set

Statistic	ANB020 (N=XX)	Placebo (N=XX)
n	xx	xx
LS Mean	xxx xx	xxx xx
SE of LS Mean	xx xxx	xx xxx
95% CI	[xxx xx, xxx xx]	[xxx xx, xxx xx]
LS Mean Difference (ANB020 – Placebo)	xx xx	
SE of LS Mean Difference	xx xx	
95% CI for LS Mean Difference	[xx xx, xx xx]	
P-value	x xxxx	

Source: Listing 16 2 9 3
Note:
- LS: Least Squares; SE: Standard Error; CI: Confidence Interval; MMRM: Mixed Model for Repeated Measures;
- n is the number of subjects with non-missing values
- N is the number of subjects within each treatment group under Full Analysis Set

P-value is obtained using an MMRM model with treatment, visit, treatment*visit as fixed effects and baseline eosinophil count

Table 14 4 2 3 1
Serum Cytokines(pg/mL) – Pharmacodynamic Analysis Set

Parameter	Visit	Nominal Time Point	Statistics	ANB020 (N=XX)			Placebo (N=XX)		
				Observed	Change from Baseline	Ratio to baseline	Observed	Change from Baseline	Ratio to baseline
IL-4	Baseline	Pre-dose (-0 5 hours)	n	xx	-	-	xx	-	-
			Mean (SD)	xx x (xx xx)	-	-	xx x (xx xx)	-	-
			95% CI	(xx xxxx, xx xxxx)	-	-	(xx xxxx, xx xxxx)	-	-
			Median	xx x	-	-	xx x	-	-
			Min, Max	xx, xx	-	-	xx, xx	-	-

Table 14 4 2 3 1
Serum Cytokines(pg/mL) – Pharmacodynamic Analysis Set

Parameter	Visit	Nominal Time Point	Statistics	ANB020 (N=XX)			Placebo (N=XX)		
				Observed	Change from Baseline	Ratio to baseline	Observed	Change from Baseline	Ratio to baseline
						-			-
	Day 2	24 hours post SOI	n	xx	xx		xx	xx	
			Mean (SD)	xx x (xx xx)	xx x (xx xx)	xx	xx x (xx xx)	xx x (xx xx)	xx
			95% CI	(xx xxxx, xx xxxx)	(xx xxxx, xx xxxx)	xx x (xx xx)	(xx xxxx, xx xxxx)	(xx xxxx, xx xxxx)	xx x (xx xx)
			Median	xx x	xx x	xx x	xx x	xx x	xx x
			Min, Max	xx, xx	xx, xx	(xx xxxx, xx xxxx)	xx, xx	xx, xx	(xx xxxx, xx xxxx)
	<visits>	<time points>							
<Parameters>									

Source: Listing 16 2 9 1
Note:
- SOI – Start of Infusion
- Baseline is defined as the the pre-dose measurement taken prior to ANB020 or placebo administration at randomization [Day 1], i e reference start date

Programming Note (not part of table): Continue the table for all serum cytokines at all available visits and respective time points

Table 14 4 2 3 2
Exploratory Pharmacodynamic Endpoint: Change from Baseline in Serum Cytokines(pg/mL) on Day 127/ET – Pharmacodynamic Analysis Set

Analyte (unit) Statistic	ANB020 (N=XX)	Placebo (N=XX)
IL-4 (pg/mL)		
n	xx	xx
LS Mean	xxx.xx	xxx.xx
SE of LS Mean	xx.xxx	xx.xxx
95% CI	[xxx.xx, xxx.xx]	[xxx.xx, xxx.xx]
LS Mean Difference (ANB020 – Placebo)	xx.xx	
SE of LS Mean Difference	xx.xx	
95% CI for LS Mean Difference	[xx.xx, xx.xx]	
P-value	x.xxxx	

Source: Listing 16 2 9 1
Note:
- LS: Least Squares; SE: Standard Error; CI: Confidence Interval;
- n is the number of subjects with non-missing values
- N is the number of subjects within each treatment group under Full Analysis Set
- P-value is obtained using mixed-effect ANCOVA model with treatment as fixed effect and baseline result as covariate and patient as a random effect
-

Programming Note: Refer SAP for Model Continue the table for all other parameters of Cytokines *This table can be modified as per the data requirement*

Table 14 2 1 1
Spriometry (FEV_1) – Full Analysis Set

Parameter	Visit	Statistics	ANB020 (N=XX)		Placebo (N=XX)	
			Observed	Change from Baseline	Observed	Change from Baseline
Predicted FEV_1 (L)	Screening	n	xx	-	xx	-
		Mean (SD)	xx x (xx xx)	-	xx x (xx xx)	-
		95% CI	(xx xxxx, xx xxxx)	-	(xx xxxx, xx xxxx)	-
		Median	xx x	-	xx x	-
		Min, Max	xx, xx	-	xx, xx	-
	Baseline (Pre-Bronchodilator)	n	xx	-	xx	-
		Mean (SD)	xx x (xx xx)	-	xx x (xx xx)	-
		95% CI	(xx xxxx, xx xxxx)	-	(xx xxxx, xx xxxx)	-
		Median	xx x	-	xx x	-
		Min, Max	xx, xx	-	xx, xx	-
	Post-Bronchodilator	n	xx	-	xx	-
		Mean (SD)	xx x (xx xx)	-	xx x (xx xx)	-
		95% CI	(xx xxxx, xx xxxx)	-	(xx xxxx, xx xxxx)	-
		Median	xx x	-	xx x	-
		Min, Max	xx, xx	-	xx, xx	-
	<Visits>	--------				
Actual FEV_1(L)	<Visits>					
FEV_1 % Predicted	<Visits>	--------				

Source: Listing 16.2.6.2

Note: FEV1 = Forced expiratory volume in 1 second, CI = Confidence Interval, SD = Standard deviation.

- N is the number of patients within each treatment group under Full Analysis Set
-
- Day1 pre-bronchodilator spirometry assessment will be considered as the baseline

Programming Note: Continue this table for all available visits and respective change from baseline for FEV1

Table 14 2 1 2
Secondary Efficacy Endpoint: Change in FEV1 (Litres) from Baseline to Day 127 – Full Analysis Set

Statistic	ANB020 (N=XX)	Placebo (N=XX)
n	xx	xx
LS Mean	xxx.xx	xxx.xx
SE of LS Mean	xx.xxx	xx.xxx
95% CI	[xxx.xx, xxx.xx]	[xxx.xx, xxx.xx]
LS Mean Difference (ANB020 – Placebo)	xx.xx	
SE of LS Mean Difference	xx.xx	
95% CI for LS Mean Difference	[xx.xx, xx.xx]	
P-value	x.xxxx	

Source: Listing 16.2.6.2

Note:
- LS: Least Squares; SE: Standard Error; CI: Confidence Interval;
- n is the number of subjects with non-missing values
- N is the number of subjects within each treatment group under Full Analysis Set
- P-value is obtained using mixed-effect ANCOVA model with treatment as fixed effect and baseline result as covariate and patient as a random effect

- Similar table will be generated for FeNO as following:

Table 14 2 2 1
Fractional Exhaled Nitric Oxide (FeNO) (in ppb) Test – Full Analysis Set

*Source listing for Table 14.2.1 is **16.2.6.1***

Table 14 2 2 2
Secondary Efficacy Endpoint: Change in Fractional Exhaled Nitric Oxide(FeNO) (in ppb) from Baseline to Day 127 – Full Analysis Set

Table 14 2 1 3
Secondary Efficacy Endpoint: Change in FEV1 (Litres) from Baseline – Supportive Analysis – Full Analysis Set

Visit	Statistic	ANB020 (N=XX)	Placebo (N=XX)
Day 2	n	xx	xx
	LS Mean	xxx.xx	xxx.xx
	SE of LS Mean	xx.xxx	xx.xxx
	95% CI	[xxx.xx, xxx.xx]	[xxx.xx, xxx.xx]
	LS Mean Difference (ANB020 – Placebo)	xx.xx	
	SE of LS Mean Difference	xx.xx	
	95% CI for LS Mean Difference	[xx.xx, xx.xx]	
	P-value	x.xxxx	
Day 8	n	xx	xx
	LS Mean	xxx.xx	xxx.xx
	SE of LS Mean	xx.xxx	xx.xxx
	95% CI	[xxx.xx, xxx.xx]	[xxx.xx, xxx.xx]
	LS Mean Difference (ANB020 – Placebo)	xx.xx	
	SE of LS Mean Difference	xx.xx	
	95% CI for LS Mean Difference	[xx.xx, xx.xx]	
	P-value	x.xxxx	
[ETC…]			

Source: Listing 16.2.6.2

Note:
- LS: Least Squares; SE: Standard Error; CI: Confidence Interval; MMRM: Mixed Model for Repeated Measures;
- n is the number of subjects with non-missing values
- N is the number of subjects within each treatment group under Full Analysis Set
- P-value is obtained using MMRM model with treatment, visit, treatment*visit as fixed effects and baseline and baseline*visit as covariates

- Similar table will be generated for FeNO as following:

Table 14 2 2 3
Secondary Efficacy Endpoint: Change in FeNO (ppb) from Baseline to Day 127– Supportive Analysis – Full Analysis Set

Table 14 2 3 1
Asthma Control Questionnaire (Summary of Scores) – Full Analysis Set

Visit	Statistics	ANB020 (N=XX)		Placebo (N=XX)	
		Observed	Change from Baseline	Observed	Change from Baseline
Screening	n	xx	-	xx	-
	Mean (SD)	xx x (xx xx)	-	xx x (xx xx)	-
	95% CI	(xx xxxx, xx xxxx)	-	(xx xxxx, xx xxxx)	-
	Median	xx x	-	xx x	-
	Min, Max	xx, xx	-	xx, xx	-
Baseline	n	xx	-	xx	-
	Mean (SD)	xx x (xx xx)	-	xx x (xx xx)	-
	95% CI	(xx xxxx, xx xxxx)	-	(xx xxxx, xx xxxx)	-
	Median	xx x	-	xx x	-
	Min, Max	xx, xx	-	xx, xx	-
Day 8	n	xx	xx	xx	xx
	Mean (SD)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)
	95% CI	(xx xxxx, xx xxxx)	(xx xxxx, xx xxxx)	(xx xxxx, xx xxxx)	(xx xxxx, xx xxxx)
	Median	xx x	xx x	xx x	xx x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
<Visits>					

Source: Listing 16.2.6.3

Note:

- N is the number of patients within each treatment group under Full Analysis Set
- Baseline will be last non-missing measurement taken prior to reference start date (including unscheduled assessments or retests)
- Total ACQ will be calculated as sum of all individual scores for each patient at each visit
- If any individual score is missing , the ACQ for that visit will also be missing

Programming Note: Continue this table for all available visits and respective change from baseline

Table 14 2 3 2
Exploratory Efficacy Endpoint: Change in ACQ from Baseline to Day 127 – Full Analysis Set

Statistic	ANB020 (N=XX)	Placebo (N=XX)
n	xx	xx
LS Mean	xxx.xx	xxx.xx
SE of LS Mean	xx.xxx	xx.xxx
95% CI	[xxx.xx, xxx.xx]	[xxx.xx, xxx.xx]
LS Mean Difference (ANB020 – Placebo)	xx.xx	
SE of LS Mean Difference	xx.xx	
95% CI for LS Mean Difference	[xx.xx, xx.xx]	
P-value	x.xxxx	

Source: Listing 16.2.6.3

Note:
- LS: Least Squares; SE: Standard Error; CI: Confidence Interval;
- n is the number of subjects with non-missing values
- N is the number of subjects within each treatment group under Full Analysis Set
- P-value is obtained using mixed-effect ANCOVA model with treatment as fixed effect and baseline result as covariate and patient as a random effect

Table 14 2 4 1
Patient Global Impression of Change (PGIC Scores) – Full Analysis Set

Visit	Category	ANB020 (N=XX)	Placebo (N=XX)
Screening	Very much improved	xx (xx x)	xx (xx x)
	Much improved	xx (xx x)	xx (xx x)
	Minimally Improved	xx (xx x)	xx (xx x)
	No changes	xx (xx x)	xx (xx x)
	Minimally worse	xx (xx x)	xx (xx x)
	Much worse	xx (xx x)	xx (xx x)
	Very much worse	xx (xx x)	xx (xx x)
	Row mean score differences(a)	x xxx	x xxx
Baseline	Very much improved	xx (xx x)	xx (xx x)
	Much improved	xx (xx x)	xx (xx x)
	Minimally Improved	xx (xx x)	xx (xx x)
	No changes	xx (xx x)	xx (xx x)
	Minimally worse	xx (xx x)	xx (xx x)
	Much worse	xx (xx x)	xx (xx x)
	Very much worse	xx (xx x)	xx (xx x)
	Row mean score differences(a)	x xxx	x xxx
Day 8	Very much improved	xx (xx x)	xx (xx x)
	Much improved	xx (xx x)	xx (xx x)
	Minimally Improved	xx (xx x)	xx (xx x)
	No changes	xx (xx x)	xx (xx x)
	Minimally worse	xx (xx x)	xx (xx x)
	Much worse	xx (xx x)	xx (xx x)
	Very much worse	xx (xx x)	xx (xx x)
	Row mean score differences(a)	x xxx	x xxx

<Visits>

Source: Listing 16 2 6 4
Note:
- N is the number of patients within each treatment group in Full Analysis Set
- Percentages are based on number of patients within each treatment group under Full Analysis Set (N)
CMH- Cochran–Mantel–Haenszel test;
(a) Row mean scores differences obtained from the CMH test comparing ANB020 vs Placebo
Programming Note (not part of table): Similar table will be generated for CGIC as follows:

Table 14 2 4 2
Asthma Symptoms (Patient Diary) – Full Analysis Set

Characteristic	Visit	Statistics	ANB020 (N=XX)	Placebo (N=XX)	Total (N=XX)
Number of Patients needed to use Rescue Inhaler	<Visits>	n (%)	xx (xx x)	xx (xx x)	xx (xx x)
Number of Patients needed to use Rescue Medication	<Visits>	n (%)	xx (xx x)	xx (xx x)	xx (xx x)
Number of Patients Experiencing					
Wheezing	<Visits>	n (%)	xx (xx x)	xx (xx x)	xx (xx x)
Cough	<Visits>	n (%)	xx (xx x)	xx (xx x)	xx (xx x)
Shortness of Breath	<Visits>	n (%)	xx (xx x)	xx (xx x)	xx (xx x)
Chest Tightness	<Visits>	n (%)	xx (xx x)	xx (xx x)	xx (xx x)
Others	<Visits>	n (%)	xx (xx x)	xx (xx x)	xx (xx x)
Number of Patients who Changed Any of their Prescribed Long Term Controller Medicine	<Visits>	n (%)	xx (xx x)	xx (xx x)	xx (xx x)
Number of Patients Rating the Study Treatment as					
<Categories>	<Visits>	n (%)	xx (xx x)	xx (xx x)	xx (xx x)
Number of Patients who Rating the Level of Satisfaction With the Side Effects Related to the Study Treatment as					
<Categories>	<Visits>	n (%)	xx (xx x)	xx (xx x)	xx (xx x)

Table 14 2 4 2
Asthma Symptoms (Patient Diary) – Full Analysis Set

Characteristic	Visit	Statistics	ANB020 (N=XX)	Placebo (N=XX)	Total (N=XX)

Source: Listing 16.2.6.4

Note:

- N is the number of patients within each treatment group under Full Analysis Set
- Baseline will be last non-missing measurement taken prior to reference start date (including unscheduled assessments or retests)

Percentages are based on number of patients within each treatment group under Full Analysis Set (N).Programming Note: Continue this table for all available visits.

Table 14 2 5 1
Clinical Global Impression of Change Scale (CGIC Scores) – Full Analysis Set

Source: Listing 16 2 6 5

Table 14 2 6 1
Exploratory Endpoint: Reduction from Baseline in IgE levels(Unit) on Day 127/ET – Full Analysis Set

Statistic	ANB020 (N=XX)	Placebo (N=XX)
n	xx	xx
LS Mean	xxx.xx	xxx.xx
SE of LS Mean	xx.xxx	xx.xxx
95% CI	[xxx.xx, xxx.xx]	[xxx.xx, xxx.xx]
LS Mean Difference (ANB020 – Placebo)	xx.xx	
SE of LS Mean Difference	xx.xx	
95% CI for LS Mean Difference	[xx.xx, xx.xx]	
P-value	x.xxxx	

Source: Listing 16.2.8.5

Note:
- LS: Least Squares; SE: Standard Error; CI: Confidence Interval;
- n is the number of subjects with non-missing values
- N is the number of subjects within each treatment group under Full Analysis Set
- P-value is obtained using mixed-effect ANCOVA model with treatment as fixed effect and baseline result as covariate and patient as a random effect

Programming Note: Refer SAP for Model *This table can be modified as per the data requirement*

Table 14 4 1 1 1
Serum Concentration(ug/mL) of ANB020 – Pharmacokinetic Analysis Set

Visit	Nominal Time Point	Statistics	ANB020 (N=XX)
Baseline	Pre-dose (-0 5 hours)	n, LLOQ (n)	xx, xx
		Mean (SD)	xx x (xx xx)
		CV	xx x
		Median (Min, Max)	xx x (xx, xx)
	0 5 hours post SOI	n, LLOQ (n)	xx, xx
		Mean (SD)	xx x (xx xx)
		CV	xx x
		Median (Min, Max)	xx x (xx, xx)
	EOI	----------	
	EOI+3 hours	----------	
Day 2	24 hours post SOI	----------	
Day 8	168 hours post SOI	----------	
Day 22	504 hours post SOI	----------	
Day 36	840 hours post SOI	----------	
Day 64	1512 houirs post SOI	----------	

Source: Listing 16 2 5 2
Note:
- LLOQ(n)=number of observations ≥lower limit of quantification
- SOI – Start of Infusion, EOI – End of Infusion

Programming Note (not part of table): Use all relevant visits and time points

Table 14 4 1 2 1
Pharmacokinetic Parameters of ANB020 – Pharmacokinetic Analysis Set

Parameter	Statistics	ANB020 (N=XX)
C_{max}	N, LLQ(n)	xx, xx
	Mean (SD)	xx x (xx xx)
	CV	xx x
	Median (Min, Max)	xx x (xx, xx)
	Gmean (gCV)	xx x (xx xx)
t_{max}	n	xx
	Median	xx xx
	Min, Max	xx, xx

Source: Listing 16 2 5 3
Programming Note (not part of table): Continue this for all other estimated non-diagnostic parameters, if any

Table 14 3 1 1
Overview of Adverse Events – Safety Analysis Set

Characteristic	ANB020 (N=XX) n (%)	Placebo (N=XX) n (%)	Total (N=XX) n (%)
Overall TEAEs	xx	xx	xx
Overall Non-TEAEs	xx	xx	xx
Patients with at least one			
TEAE	xx (xx x)	xx (xx x)	xx (xx x)
Serious TEAE	xx (xx x)	xx (xx x)	xx (xx x)
Severe TEAE	xx (xx x)	xx (xx x)	xx (xx x)
Related TEAE	xx (xx x)	xx (xx x)	xx (xx x)
Non-TEAE	xx (xx x)	xx (xx x)	xx (xx x)
Patients with TEAE by Severity			
< Categories >	xx (xx x)	xx (xx x)	xx (xx x)
Patients with TEAE by Final Outcome			
< Categories >	xx (xx x)	xx (xx x)	xx (xx x)
Action Taken with the Study Drug for Patients with TEAE			
< Categories >	xx (xx x)	xx (xx x)	xx (xx x)
Patients with TEAE with Relationship to Study Drug			
< Categories >	xx (xx x)	xx (xx x)	xx (xx x)
Patients with TEAE with Seriousness Criteria			
< Categories >	xx (xx x)	xx (xx x)	xx (xx x)
Patients Discontinued from the Study Due to TEAE	xx (xx x)	xx (xx x)	xx (xx x)

Table 14 3 1 1
Overview of Adverse Events – Safety Analysis Set

Characteristic	ANB020 (N=XX) n (%)	Placebo (N=XX) n (%)	Total (N=XX) n (%)

Source: Listing 16 2 7 1, 14 3 2 1, 14 3 2 2, 14 3 2 3
Note:
- N is the number of patients within each treatment group under Safety Analysis Set, Percentages are based on number of patients within each treatment group under Safety Analysis Set (N)
- Adverse Event terms are coded using MedDRA version 19 1, Patients experiencing multiple events are counted only once within the treatment group
- If patient has multiple TEAEs by severity and/or multiple relationship with study drug, worst case severity and the worst case relationship to the study drug will used for overview tabulation
- AE- Adverse Event, TEAE- Treatment Emergent Adverse Events
- Treatment emergent adverse events (TEAEs) are defined as AEs that started or worsened in severity on or after the date and time of the study drug infusion

Programming Note (not part of table): For count of TEAEs, use the coded term (preferred term)

Table 14 3 1 2
TEAE by System Organ Class and Preferred Term – Safety Analysis Set

System Organ Class Preferred Term Verbatim Term	ANB020 (N=XX) n (%)	Placebo (N=XX) n (%)	Total (N=XX) n (%)
Number of Patients with at least one TEAE	xx (xx x)	xx (xx x)	xx (xx x)

Table 14 3 1 2
TEAE by System Organ Class and Preferred Term – Safety Analysis Set

System Organ Class Preferred Term Verbatim Term	ANB020 (N=XX) n (%)	Placebo (N=XX) n (%)	Total (N=XX) n (%)
System Organ Class 1	xx (xx x)	xx (xx x)	xx (xx x)
Preferred Term 1	xx (xx x)	xx (xx x)	xx (xx x)
Preferred Term 2	xx (xx x)	xx (xx x)	xx (xx x)

System Organ Class 2	xx (xx x)	xx (xx x)	xx (xx x)
Preferred Term 1	xx (xx x)	xx (xx x)	xx (xx x)

Source: Listing 16 2 7 1, 14 3 2 1, 14 3 2 2, 14 3 2 3
Note:
- N is the number of patients within each treatment group under Safety Analysis Set
- Percentages are based on number of patients within each treatment group under Safety Analysis Set (N)
- Adverse Event terms are coded using System Organ Class and Preferred term using using latest version of MedDRA
- Patients experiencing multiple events within the same SOC or PT are counted only once under those categories

Programming Note (not part of table):
- Table will be sorted in decreasing frequency of system organ class and preferred term of total column Include "Uncoded" if events are not coded
  A subject can have one or more preferred terms reported under a given system organ class
- Similar tables will be generated for Safety Analysis Set as follows:

Table 14 3 1 2 1 TEAEs by Preferred Term – Safety Analysis Set

Table 14 3 1 3 TEAEs Leading to Discontinuation of Patient from the Study by System Organ Class and Preferred Term – Safety Analysis Set

Table 14 3 1 4 TEAEs Leading to Interruption of Study Drug by System Organ Class and Preferred Term – Safety Analysis Set

Table 14 3 1 5
TEAEs by Severity, System Organ Class and Preferred Term – Safety Analysis Set

System Organ Class Preferred Term Verbatim Term	ANB020 (N=XX)			Placebo (N=XX)		
	Mild	Moderate	Severe	Mild	Moderate	Severe
Number of Patients with at least one TEAE by Severity	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)
System Organ Class 1	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)
Preferred Term 1	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)
Preferred Term 2	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)
System Organ Class 2	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)
Preferred Term 1	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)

Source: Listing 16 2 7 1, 14 3 2 1, 14 3 2 2, 14 3 2 3
Note:
- N is the number of patients within each treatment group under Safety Analysis Set
- Percentages are based on number of patients within each treatment group under Safety Analysis Set (N)
- Adverse Event terms are coded using System Organ Class and Preferred term using using latest version of MedDRA
- Patients experiencing multiple events within the same SOC or preferred term are counted only once under those categories
- Patients experiencing the same event with different severity level are counted under the most severe occurrence

Programming Note (not part of table):
- Table will be sorted in decreasing frequency of system organ class and preferred term of total column Include "Uncoded" if events are not coded
- A subject can have one or more preferred terms reported under a given system organ class

Table 14 3 1 5
TEAEs by Severity, System Organ Class and Preferred Term – Safety Analysis Set

System Organ Class Preferred Term Verbatim Term	Total (N=XX) Mild	Moderate	Severe
Number of Patients with at least one TEAE by Severity	xx (xx x)	xx (xx x)	xx (xx x)
System Organ Class 1	xx (xx x)	xx (xx x)	xx (xx x)
Preferred Term 1	xx (xx x)	xx (xx x)	xx (xx x)
Preferred Term 2	xx (xx x)	xx (xx x)	xx (xx x)
System Organ Class 2	xx (xx x)	xx (xx x)	xx (xx x)
Preferred Term 1	xx (xx x)	xx (xx x)	xx (xx x)

Source: Listing 16 2 7 1, 14 3 2 1, 14 3 2 2, 14 3 2 3
Note:
- N is the number of patients within each treatment group under Safety Analysis Set
- Percentages are based on number of patients within each treatment group under Safety Analysis Set (N)
- Adverse Event terms are coded using System Organ Class and Preferred term using using latest version of MedDRA
- Patients experiencing multiple events within the same SOC or preferred term are counted only once under those categories
- Patients experiencing the same event with different severity level are counted under the most severe occurrence

Programming Note (not part of table):
- Table will be sorted in decreasing frequency of system organ class and preferred term of total column Include "Uncoded" if events are not coded
- A subject can have one or more preferred terms reported under a given system organ class

Table 14 3 1 6
TEAEs by Relationship to Study Drug, System Organ Class and Preferred Term – Safety Analysis Set

System Organ Class Preferred Term Verbatim Term	ANB020 (N=XX)		Placebo (N=XX)		Total (N=XX)	
	Related	Not Related	Related	Not Related	Related	Not Related
Number of Patients with at least one TEAE by Relationship	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)
System Organ Class 1	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)
Preferred Term 1	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)
Preferred Term 2	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)
System Organ Class 2	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)
Preferred Term 1	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)

Source: Listing 16 2 7 1, 14 3 2 1, 14 3 2 2, 14 3 2 3Note:
- N is the number of patients within each treatment group under Safety Analysis Set
- Percentages are based on number of patients within each treatment group under Safety Analysis Set (N)
- Adverse Event terms are coded using System Organ Class and Preferred term using using latest version of MedDRA
- Patients experiencing multiple events within the same SOC or preferred term are counted only once under those categories
- Patients experiencing the same event with different relationship level are counted under the worst degree of relationship
- AEs with relationship in ("Possible", "Probable" and "Unknown") are mapped to "Related", else to "Unrelated"

Programming Note (not part of table):
- Table will be sorted in decreasing frequency of system organ class and preferred term of total column Include "Uncoded" if events are not coded
- A subject can have one or more preferred terms reported under a given system organ class

Table 14 3 1 7 Serious TEAEs by System Organ Class and Preferred Term – Safety Analysis Set

Table 14 3 1 8 TEAEs Leading to Death by System Organ Class and Preferred Term – Safety Analysis Set

Table 14 3 1 9 Non TEAEs by System Organ Class and Preferred Term – Safety Analysis Set

Table 14 3 4 1
Potential Clinically Significant Laboratory Assessments (Hematology) – Safety Analysis Set

Parameter	Visit	Potential Clinical Significance Status	ANB020 (N=XX)	Placebo (N=XX)	Total (N=XX)
Parameter 1	<Visits>	Normal	xx (xx x)	xx (xx x)	xx (xx x)
		Abnormal NCS	xx (xx x)	xx (xx x)	xx (xx x)
		Abnormal CS	xx (xx x)	xx (xx x)	xx (xx x)
		Missing	xx (xx x)	xx (xx x)	xx (xx x)
Parameter 2	<Visits>	Normal	xx (xx x)	xx (xx x)	xx (xx x)
		Abnormal NCS	xx (xx x)	xx (xx x)	xx (xx x)
----------		Abnormal CS	xx (xx x)	xx (xx x)	xx (xx x)
		Missing	xx (xx x)	xx (xx x)	xx (xx x)

Source: Listing 14 3 4 1
Note:
- N is the number of patients within each treatment group under Safety Analysis Set
- Baseline will be last non-missing measurement taken prior to reference start date (including unscheduled assessments or retests)
- Percentages are based on number of patients within each treatment group under Safety Analysis Set (N)
- NCS – Not Clinically Significant, CS – Clinically Significant

Programming Note (not part of table):
- Use all relevant visits and parameters
- Similar tables will be generated for Safety Analysis Set as follows:

Table 14 3 4 2 Potential Clinically Significant Laboratory Assessments (Clinical Chemistry) – Safety Analysis Set

Table 14 3 4 3 Potential Clinically Significant Laboratory Assessments (Urinalysis) – Safety Analysis Set

Table 14 3 4 4
Summary of Potentially Clinically Significant ECG Parameters – Safety Analysis Set

Category	Visit	ANB020 (N=XX)	Placebo (N=XX)	Total (N=XX)
Normal	Screening	xx (xx x)	xx (xx x)	xx (xx x)
Abnormal, NCS		xx (xx x)	xx (xx x)	xx (xx x)
Abnormal, CS		xx (xx x)	xx (xx x)	xx (xx x)
Normal	End of study	xx (xx x)	xx (xx x)	xx (xx x)
Abnormal, NCS		xx (xx x)	xx (xx x)	xx (xx x)
Abnormal, CS		xx (xx x)	xx (xx x)	xx (xx x)

Source: Listing 16 2 8 2
Note:
CS- Clinically Significant; NCS- Not Clinically Significant
N is the number of patients under Safety Analysis Set
Percentages are based on N

Table 14 3 5 1
Pregnancy Test – Safety Analysis Set

	Visit	Characteristic	Result	Statistics	ANB020 (N=XX)	Placebo (N=XX)	Total (N=XX)
Urine Pregnancy Test	Baseline	Test Performed	Yes	n (%)	xx (xx x)	xx (xx x)	xx (xx x)
			No		xx (xx x)	xx (xx x)	xx (xx x)
		Outcome	Positive	n (%)	xx (xx x)	xx (xx x)	xx (xx x)
			Negative		xx (xx x)	xx (xx x)	xx (xx x)
Serum Pregnancy Test	Screening	Test Performed	Yes	n (%)	xx (xx x)	xx (xx x)	xx (xx x)
			No		xx (xx x)	xx (xx x)	xx (xx x)
		Outcome	Positive	n (%)	xx (xx x)	xx (xx x)	xx (xx x)
			Negative		xx (xx x)	xx (xx x)	xx (xx x)
	<Visits>	----------					

Source: Listing 16 2 4 2, 16 2 8 1
Note:
- N is the number of female patients within each treatment group in the Safety Analysis Set
- Percentages are based on the number of female patients in respective treatment arm (N)
- Above test are conducted only for women of child bearing potential

Programming Note (not part of table): Add missing row where applicable *This table can be modified as per the data requirement.*

Table 14 3 5 2
Laboratory Parameters (Hematology) – Safety Analysis Set

			ANB020 (N=XX)		Placebo (N=XX)		Total (N = XX)	
Parameter (Unit)	Visit	Statistics	Actual	Change from Baseline	Actual	Change from Baseline	Actual	Change from Baseline
Parameter 1	Baseline	n	xx	-	xx	-	xx	-
		Mean (SD)	xx x (xx xx)	-	xx x (xx xx)	-	xx x (xx xx)	-
		Median	xx x	-	xx x	-	xx x	-
		Min, Max	xx, xx	-	xx, xx	-	xx, xx	-
	<Visits>	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)
		Median	xx x	xx x	xx x	xx x	xx x	xx x
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

Parameter 2	----------							

Table 14 3 5 2
Laboratory Parameters (Hematology) – Safety Analysis Set

			ANB020 (N=XX)		Placebo (N=XX)		Total (N = XX)	
Parameter (Unit)	Visit	Statistics	Actual	Change from Baseline	Actual	Change from Baseline	Actual	Change from Baseline

Source: Listing 14 3 4 1
Note:
- N is the number of patients within each treatment group under Safety Analysis Set
-
- Baseline will be last non-missing measurement taken prior to reference start date (including unscheduled assessments or retests),
- Unit is SI unit

Programming Note (not part of table):
- Provide appropriate discreptives for urinalysis Use all relevant visits
- Similar tables will be generated for Safety Analysis Set as follows:

Table 14 3 5 3
Laboratory Parameters (Clinical Chemistry) – Safety Analysis Set

Table 14 3 5 4
Laboratory Parameters (Urinalysis) – Safety Analysis Set

Table 14 3 5 5
Shifts from Baseline in Clinical Laboratory Results – Safety Analysis Set

			Post Baseline Assessments									
			ANB020 (N=XX)					Placebo (N=XX)				
Laboratory Category Parameter (Unit)	Visit	Baseline Assessment	Low	Normal	High	Total	Missing	Low	Normal	High	Total	Missing
Hematology												
Parameter 1	Day 1	Low	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)
		Normal	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)
		High	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)
		Total	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)
		Missing	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)	xx (xx x)
	Day 2											

Parameter 2	------											

Source: Listing 14 3 4 1
Note:
- N is the number of patients within each treatment group under Safety Analysis Set
- Baseline will be last non-missing measurement taken prior to reference start date (including unscheduled assessments or retests), Unit is SI unitPercentages are based on the number of patients in the SAF with data at Baseline and the visit of interest

Programming Note (not part of table): Present all the parameters in Hematology, Clinical Chemistry and Urinalysis Use all relevant visits

Table 14 3 5 6
12-Lead ECG – Safety Analysis Set

Parameter (Unit)	Visit	Statistics	ANB020 (N=XX) Actual	ANB020 (N=XX) Change from Baseline	Placebo (N=XX) Actual	Placebo (N=XX) Change from Baseline	Total (N=XX) Actual	Total (N=XX) Change from Baseline
Heart Rate (bpm)	Baseline	n	xx	-	xx	-	xx	-
		Mean (SD)	xx x (xx xx)	-	xx x (xx xx)	-	xx x (xx xx)	-
		Median	xx x	-	xx x	-	xx x	-
		Min, Max	xx, xx	-	xx, xx	-	xx, xx	-
	End of Study	n	xx	xx	xx	xx	xx	xx
		Mean (SD)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)	xx x (xx xx)
		Median	xx x	xx x	xx x	xx x	xx x	xx x
		Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
PR Interval (msec)	----------							
QRS Interval (msec)	----------							
QT Interval (msec)	----------							
QTc Interval (msec)	----------							
QTcF (msec)	----------							

Source: Listing 16 2 8 2
Note:
- N is the number of patients within each treatment group under Safety Analysis Set
- Baseline will be last non-missing measurement taken prior to reference start date (including unscheduled assessments or retests)

Programming Note (not part of table): Continue the table for all parameters and all available visits

Table 14 3 5 7
Summary of QT Changes from Baseline to Last Observation – Safety Analysis Set

Category	ANB020 (N=XX)	Placebo (N=XX)	Total (N=XX)
Mean change [a] in QT Interval (msec) from baseline	xx (xx x)	xx (xx x)	xx (xx x)
	xx (xx x)	xx (xx x)	xx (xx x)
Number (%) of patients reaching a value in QT Interval			
Males:			
.....			
Females:			
.....			
Total			
>450 (msec)	xx (xx x)	xx (xx x)	xx (xx x)
>480 (msec)	xx (xx x)	xx (xx x)	xx (xx x)
>500 (msec)	xx (xx x)	xx (xx x)	xx (xx x)
Number (%) of patients experiencing an increase in QT Interval	xx (xx x)	xx (xx x)	xx (xx x)
>30 (msec)	xx (xx x)	xx (xx x)	xx (xx x)
>60 (msec)	xx (xx x)	xx (xx x)	xx (xx x)
Number (%) of patients experiencing a decrease in QT Interval			
>30 (msec)			
>60 (msec)			
Mean change [a] in QTcF Interval (msec) from baseline			
Number (%) of patients reaching a value in QTcF Interval			
>450 (msec)			
>480 (msec)			
>500 (msec)			

Source: Listing 16 2 8 2
Note:
QTcF = Fridericia's correction for QT;
N is the number of patients under Safety Analysis Set
Baseline will be last non-missing measurement taken prior to reference start date (including unscheduled assessments or retests)
[a] Change from baseline to last observation

Programming note: Please refer SAP for the male and female reference ranges

Table 14 3 5 8
Vital Signs – Safety Analysis Set

			ANB020 (N=XX)		Placebo (N=XX)		Total (N=XX)	
Parameter (Unit)	Visit	Statistics	Actual	Change from Baseline	Actual	Change from Baseline	Actual	Change from Baseline
Pulse Rate (bpm)	<Visits>	n	xx	-	xx	-	xx	-
		Mean (SD)	xx x (xx xx)	-	xx x (xx xx)	-	xx x (xx xx)	-
		Median	xx x	-	xx x	-	xx x	-
		Min, Max	xx, xx	-	xx, xx	-	xx, xx	-
Respiratory Rate (resp/min)	<Visits>							
Body Temperature (°C)	<Visits>							
Systolic Blood Pressure (mmHg)	<Visits>							
Diastolic Blood Pressure (mmHg)	<Visits>							

Source: Listing 16 2 8 3
Note:
- N is the number of patients within each treatment group under Safety Analysis Set
- Baseline will be last non-missing measurement taken prior to reference start date (including unscheduled assessments or retests)

Programming Note (not part of table): Continue the table for all parameters and all available visits

Table 14 3 5 9
Physical Examination – Safety Analysis Set

Parameter	Visit	Category	ANB020 (N=XX) n (%)	Placebo (N=XX) n (%)	Total (N=XX) n (%)
General appearance	Baseline	Normal	xx (xx x)	xx (xx x)	xx (xx x)
		Abnormal, NCS	xx (xx x)	xx (xx x)	xx (xx x)
		Abnormal, CS	xx (xx x)	xx (xx x)	xx (xx x)
		Not Done	xx (xx x)	xx (xx x)	xx (xx x)
	EOS	Normal	xx (xx x)	xx (xx x)	xx (xx x)
		Abnormal, NCS	xx (xx x)	xx (xx x)	xx (xx x)
		Abnormal, CS	xx (xx x)	xx (xx x)	xx (xx x)
		Not Done	xx (xx x)	xx (xx x)	xx (xx x)

Source: Listing 16 2 8 4
Note:
- N is the number of patients within each treatment group under Safety Analysis Set
- Percentages are based on number of patients within each treatment group under Safety Analysis Set (N)
- NCS – Not Clinically Significant, CS – Clinically Significant

Programming Note (not part of table): Continue the table for all other parameters and all available visits May need to add "Missing" row if response is not available for some patients

Table 14 3 5 10
Other Safety Assessments (Number of Exacerbations) – Full Analysis Set

Characteristic	Statistics	ANB020 (N=XX)	Placebo (N=XX)	Hazard Ratio	P-value
Number of Patients with Exacerbatiuons	n (%)	xx (xx x)	xx (xx x)		-
Total Number of Exacerbations	E	xx	xx		-
Time to First Asthma Exacerbation[1] (Days)	n	xx	xx		-
	Mean (SD)	xx x (xx xx)	xx x (xx xx)		
	Median	xx x	xx x		
	Min, Max	xx, xx	xx, xx		
Number of Censored Patients	n (%)	xx (xx x)	xx (xx x)		
	Median (95% CI)	xx x (xx x, xx x)	xx x (xx x, xx x)		
	1st Quartile (95% CI)	xx x (xx x, xx x)	xx x (xx x, xx x)		
	3rd Quartile (95% CI)	xx x (xx x, xx x)	xx x (xx x, xx x)		0 xxxx

Source: Listing 16 2 6 6

Note:

- N is the number of patients within each treatment group under Full Analysis Set
- [1] - Time (in days) from randomization to the first asthma exacerbation = Start date of first asthma exacerbation − Date of randomization + 1
- The time to first asthma exacerbation for patients who have not experienced an asthma exacerbation during the period till end of study have been censored at the date of their last visit, or at the time point after which an exacerbation could not be assessed (for lost to follow-up patients)
- The quartiles and confidence intervals are estimated based on the Kaplan-Meier estimation method
- Hazard ratio and P-value are computed based on cox-proportional hazard model

Programming Note: Continue this table for all available visits and categories

Table 14 3 5 11

Other Safety Assessments (Immunogenicity - ADA) – Safety Analysis Set

Visit	Result	(N=xx) n(%)	Summary of Titre values Mean(SD),Median
Day 1	Positive	xx (xx x)	xx xx (xx xxx), xx xx
	Negative	xx (xx x)	
Day 11	Positive	xx (xx x)	
	Negative	xx (xx x)	
Day 64	Positive	xx (xx x)	xx xx (xx xxx), xx xx
	Negative	xx (xx x)	
Day 120	Positive	xx (xx x)	xx xx (xx xxx), xx xx
	Negative	xx (xx x)	
End of Study	Positive	xx (xx x)	xx xx (xx xxx), xx xx
	Negative	xx (xx x)	

Source: Listing 16 2 8 5

N is the number of patients under Safety Analysis Set

Programming Note (not part of table): Continue the table for all other parameters of in whole blood at all available visits and respective time points

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LISTING SHELLS

Placebo-Controlled Proof of Concept Study to Investigate ANB020 Activity in Adult Patients with Severe Eosinophilic Asthma

Study No. ANB020-004

OUTPUT TEMPLATES SIGNATURE PAGE

Listing Shells V 1.0 (Dated 18Dec2018) for Protocol ANB020-004.

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Modification History

Unique Identifier for this Version	Date of the Document Version	Author	Significant Changes from Previous Authorized Version
Draft 0.1	04 Dec 2017	[redacted]	Not Applicable - First Draft
Draft 0.2	07 Dec 2017		Resolved comments from internal review
Draft 0.3	03 Dec 2018		Resolved comments from Sponsor review

Table of Contents

Listing 16.2.1.1
Patient Disposition - All Patients Screened

Patient No.	Treatment	Age/Gender	Eligible at Screening	Willing to Participate at Day 1	Patient Discontinued Study	Date of Discontinuation	Date of Last Dose	Primary Reason for Discontinuation	Patient Completed the Study	If No, Provide the Primary Reason	Date of Completion
XXX	XXX	32/Male	Yes	Yes	Yes	DDMMMYYYY	DDMMMYYYY	xxxxx	No	xxxxx	
XXX	XXX	31/Female	Yes	Yes	No	-	DDMMMYYYY	-	Yes	-	DDMMMYYYY
XXX	XXX	28/Female									
…											

Programming Note (not part of table): Sort by treatment, patient number.

Listing 16 2.2.1
Protocol Deviation - All Patients Screened

Patient No.	Treatment	Age/Gender	Significance	Deviation Date	Deviation Category	Deviation Description	Lead to Patient Exclusion from PK Population	Lead to Patient Exclusion from PD Population
XXX	XXX	32/Male	Major	DDMMMYYYY	xxxxxxx	xxxxxxxxxxxxx	Yes	No
XXX	XXX	31/Female	Major	DDMMMYYYY	xxxxxxx	xxxxxxxxxxxxx	xx	xx
XXX	XXX	28/Female						
……								

Programming Note (not part of table): Sort by treatment, patient number.

Listing 16.2.3.1 1
Analysis Sets - All Patients Screened

Patient No.	Treatment	Age/Gender	Randomized Analysis Set [RND]	Administered the Treatment	Full Analysis Set (FAS)	Safety Analysis Set (SAF)	Pharmacodynamic Analysis Set (PD)	Pharmacokinetic Analysis Set (PK)
XXX	XXX	32/Male	Yes	Yes	Yes	Yes	Yes	Yes
XXX	XXX	31/Female	Yes	Yes	No	Yes	No	No
XXX	XXX	28/Female	Yes	No	No	No	No	No
…….								

Programming Note (not part of table): Sort by treatment, patient number.

Listing 16.2.4 1.1
Inclusion Criteria - All Patients Screened

Patient No.	Treatment	Age/Gender	INC1	INC2	INC3	INC4	……..	INC11
XXX	XXX	32/Male	Yes	Yes	Yes	Yes		Yes
XXX	XXX	31/Female	Yes	Yes	No	Yes		No
XXX	XXX	28/Female	Yes	No	No	No		No
…….								

Programming Note (not part of table): Sort by treatment, patient number. If columns do not fit in the one page, move to next page with unique columns patient no., treatment, age and gender.

Listing 16.2.4.1.2
Exclusion Criteria - All Patients Screened

Patient No.	Treatment	Age/Gender	EXC1	EXC2	EXC3	EXC4	……..	EXC20
XXX	XXX	32/Male	Yes	Yes	Yes	Yes		Yes
XXX	XXX	31/Female	Yes	Yes	No	Yes		No
XXX	XXX	28/Female	Yes	No	No	No		No
…								

Programming Note (not part of table): Sort by treatment, patient number. If columns do not fit in the one page, move to next page with unique columns patient no., treatment, age and gender

Listing 16.2.4.2
Demography and Other baseline Characteristics - Safety Analysis Set

Patient No./ Treatment	Age/ Gender	Race/ If Other, Specify	Ethnicity/ If Other, Specify	Weight (kg)	Height (cm)	BMI (kg/m^2)	If Female, then WOCBP	If Not WOCBP, then Specify	Urine Pregnancy Test Performed[1]/ If No, Specify	Date and Time of Urine Pregnancy Test	Result
XXX/ XXX/	32/ Male	Asian	xxxxxx	xx.xx	xx.xx	xx.xx	-	-	-	-	-
XXX/ XXX/	31/ Female	Other: xxxx	Other: xxxx	xx.xx	xx.xx	xx.xx	Yes	-	Yes	DDMMMYYYYT HH:MM	Negative
XXX/ XXX/	28/ Female	xxxxxx	xxxxxx	xx.xx	xx.xx	xx.xx	No	Other: xxxx	No: xxxx	-	-
…											

Note:
- WOCBP: Women of Child Bearing Potential.
- [1] – Urine pregnancy test is performed only for WOCBP Patients.
- Age: (Date of Informed Consent - Date of Birth +1)/365 25
- Demographic details such as weight, height and BMI will be based on Screening visit.

Programming Note (not part of table): Sort by treatment, patient number.

Listing 16.2.4.3
Medical History - Safety Analysis Set

Patient No./ Treatment	Age/Gender	Primary System Organ Class	Preferred Term	Reported Term	Start Date/ End Date	Currently taking medication?
XXX/ XXX/	32/Male	Xxxxx	xxxx	xxxxx	DDMMMYYY/ DDMMMYYY	No
XXX/ XXX/	31/Female	Xxxxx	xxxxx	xxxxx	DDMMMYYY	Yes
XXX/ XXX/	28/Female	Xxxxxx				

Note: Medical History Conditions were coded using MedDRA Dictionary, Version 19.1.

Programming Note (not part of table): Sort by treatment, patient number.

Listing 16.2.4.4
Prior and Concomitant Medication - Safety Analysis Set

Patient No./ Treatment	Age/ Gender	Medication Name Reported/ Preferred Term	Prior or Concomitant	Medication Considered as a Standard of Care for the Treatment of Asthma	Start Date/Study Day	End Date/ Ongoing/Study Day	Dose (Unit)	Route/ Frequency	Indication/ Specify
XXX/ XXX/	32/ Male	xxxxx/ xxxx	Concomitant	Yes	DDMMMYYYY/xx	Ongoing	xx (xxx)	xxxx	xxxxxx/ xxxxxxxxx
XXX/ XXX/	31/ Female	xxxxx/ xxxx	Prior	No	DDMMMYYYY/xx	DDMMMYYYY/xx	xx (xxx)	xxxx	xxxxxx/ xxxxxxxxx
XXX/ XXX/	28/ Female	xxxxx/ xxxx							
……..									

Note:
- WHO-DD: World Health Organization-Drug Dictionary.
- Prior medication: Medications which started and stopped prior to the administration of study drug.
- Concomitant medication: Medications which started prior to, on or after the administration of study drug and ended on or after the date of administration of study drug or were ongoing at the end of the study
- If Date of assessment ≥ Reference Start Date then Study Day= (Date of assessment – Reference start date) +1, else Study Day= Date of assessment – Reference start date.
- Prior Medications were coded using WHO Drug Dictionary, Version DDMMMYYYY

Programming Note (not part of table): Sort by treatment, patient number.

Listing 16.2.4.5
Virology at Screening - Safety Analysis Set

Patient No./ Treatment	Age/ Gender	Blood Sample Collected for Virology	If No, Specify	Date of Sample Collection	Hepatitis B Surface Antigen/ If Not Done, Specify	Hepatitis C Antibody/ If Not Done, Specify	HIV Antibody/ If Not Done, Specify
XXX/ XXX/	32/ Male	Yes		DDMMMYYYY	Negative	Negative	Negative
XXX/ XXX/	32/ Male	Yes		DDMMMYYYY	Not Done/ xxxxxxxx	Negative	Negative
XXX/ XXX/	31/ Female	No	xxxxxx				

Programming Note (not part of table): Sort by treatment and patient number.

Listing 16.2.4.6
TB Screening - Safety Analysis Set

Patient No / Treatment	Age/ Gender	Was a blood sample collected for quantiferon gold test?	If No, Specify reason	Date of sample collection	Result
XXX/ XXX/ XXX/ X	32/ Male	Yes		DDMMMYYYY	Negative
XXX/ XXX/ XXX/ X	31/ Female	No	xxxx		
XXX/ XXX/ XXX/ x …	28/ Female	Yes		DDMMMYYYY	Positvie

Note:
- TB: Tuberculosis

Programming Note (not part of table): Sort by treatment and patient number.

Listing 16.2.4.7
Drugs of Abuse - Safety Analysis Set

Patient No./ Treatment	Age/ Gender	Was a Sample Collected for Drugs of Abuse?	If No, Specify Reason	Date of Sample Collection	Result	If Positive , Specify
XXX/ XXX/ XXX/ X	32/ Male	Yes	-	DDMMMYYYY	Negative	
XXX/ XXX/ XXX/ X	31/ Female	No	xxxx			

XXX/ XXX/ XXX/ x …	28/ Female	Yes	-	DDMMMYYYY	Positvie	xxxx

Programming Note (not part of table): Sort by treatment and patient number.

Listing 16 2.5.1
Study Drug Exposure - Safety Analysis Set

Patient No./ Treatment	Age/ Gender	IP Administered via IV	Dose Start Date and Time	Dose End Date and Time	Total Volume Administered (ml)	Specify Reason if Total Volume Administered is <100 ml
XXX/ XXX/	32/ Male	xxxxx/ xxxx	DDMMMYYYY/ HH:MM	DDMMMYYYY/ HH:MM	xxx	xxxxxxx
XXX/ XXX/	31/ Female	xxxxx/ xxxx	DDMMMYYYY/ HH:MM	DDMMMYYYY/ HH:MM	xxx	-
XXX/ XXX/	28/ Female	xxxxx/ xxxx				
…						

Note:
IP – Investigational Product
IV – Intravenous

Programming Note (not part of table): Sort by treatment, patient number.

Listing 16.2.5.2
Individual ANB020 Pharmacokinetic Sampling Times and Concentrations by Time Point
Safety Analysis Set

Patient No.	Visit	Blood sample collected for PK analysis	If no, specify reason	Dose Date/ Time	Nominal Time point	Sample Date/ Time	Collection Actual Elapsed Time (h)	Deviation (h:min) (derived)	Concentration (µg/mL)	Comment
XXX	Day 1	Yes		DDMMMYYYY/ HH:MM	Pre-dose (-0.5 hours)	DDMMMYYYY/HH:MM	xx.xx	HH:MM	xxxx	
		Yes			0.5 hours post SOI	DDMMMYYYY/HH:MM	xx.xx	HH:MM	xxxx	
		Yes			EOI	DDMMMYYYY/HH:MM	xx.xx	HH:MM	xxxx	
		Yes			EOI+3 hours	DDMMMYYYY/HH:MM	xx.xx	HH:MM	xxxx	
XXX	Day 2	No	xxxxxx	DDMMMYYYY/ HH:MM	24 hours post SOI					
…										

BLQ = below lower limit of quantitation (LLOQ). LLOQ = xxx µg/mL.
Programming Note (not part of table) Sort by patient number, visit, nominal time. Present all the visits , including unscheduled/early termination..

Listing 16.2.5.3
Individual ANB020 Pharmacokinetic Parameters Following ANB020 Treatment
Safety Analysis Set

Patient No.	Cmax (ug/mL)	tmax (h)	AUC(0-inf) (h*ug/mL)	AUC(0-last) (h*ug/mL)	t1/2 (h)	Lambda_z (1/h)	CL (L/h)	Vz (L)	Vss (L)
XXX	xxxx	xxxx							
XXX	xxxx	xxxx							
XXX	xxxx	xxxx							
…									

Programming Note (not part of table) Sort by patient number.

Listing 16.2 5.3
Individual Diagnostic ANB020 Pharmacokinetic Parameters Following ANB020 Treatment
Safety Analysis Set

Patient No.	Lambda-z_lower (h)	Lambda-z_upper (h)	t1/2, Interval (h)	t1/2, N	Rsq	%AUCex
XXX						
XXX						
XXX						
…						

Note(s): Lambda_z_lower = the start time of the interval of the log-linear regression to determine lambda_z and t1/2; Lambda_z_upper = the end time of the interval of the log-linear regression to determine lambda_z and t1/2; ND = not determined; Rsq = coefficient of determination for calculation of lambda_z; t1/2, Interval = the time interval in the terminal phase used to determine lambda_z; t1/2, N = number of observations included in calculation of lambda_z; %AUCex = percentage of AUC(0-inf) extrapolated.

Programming Note (not part of table) Sort by patient number.

Listing 16.2.6.1
Fractional Exhaled Nitric Oxide Test - Full Analysis Set

Patient No./ Treatment	Age/ Gender	Visit	Fractional Exhaled Nitric Oxide Test Performed	Date and Time of Test/ Study Day	Measurement of FeNO (in ppb)	Change from Baseline
XXX/ XXX/	32/ Male	Screening	Yes	DDMMMYYYYTHH:MM/ xx	xxx	-
		Baseline	Yes	DDMMMYYYYTHH:MM/ xx	xxx	-
		Day 2	Yes	DDMMMYYYYTHH:MM/ xx	xxx	xxx
		Day 8	Yes	DDMMMYYYYTHH:MM/ xx	xxx	xxx
		…				
XXX/ XXX/	31/ Female	Screening	Yes	DDMMMYYYYTHH:MM/ xx	xxx	
		…				
…….						

Note:

- FeNO: Fractional Exhaled Nitric Oxide.
- Baseline is defined as the pre-dose measurement taken prior to ANB020 or placebo administration at randomization [Day 1], i.e. reference start date. If the pre-dose measurement and the reference start date coincide, that measurement will be considered baseline.
- If Date of assessment ≥ Reference Start Date then Study Day= (Date of assessment – Reference start date) +1,
  else Study Day= Date of assessment – Reference start date.

Programming Note (not part of table): Sort by treatment, patient number and visit.

Listing 16.2.6.2
Spirometry - Full Analysis Set

Patient No./ Treatment	Age/ Gender	Visit	Date of Spirometry or Peak Flow/ Study Day	Predicted FEV_1 (L)	Change from Baseline Predicted FEV_1 (L)	Actual FEV_1 (L)	Change from Baseline Actual FEV_1 (L)	FEV_1 % Predicted	Change from Baseline Predicted FEV_1 %	Bronchodilator Administered on Day 1/ Time of Administration
XXX/ XXX/	32/ Male	Screening	DDMMMYYYYTHH:MM / xx	xxx		xxx		xxx		-
		Baseline Pre Bronchodilator	DDMMMYYYYTHH:MM/ xx	xxx		xxx		xxx		-
		Post Bronchodilator	DDMMMYYYYTHH:MM/ xx	xxx		xxx		xxx		Yes/ HH:MM
		Day 2	DDMMMYYYYTHH:MM / xx	xxx	xxx	xxx	xxx	xxx	xxx	-
		Day 8	DDMMMYYYYTHH:MM / xx	xxx	xxx	xxx	xxx	xxx	xxx	-
		……								
……..										

Note:

- FEV1: Forced Expiratory Volume in 1 second.
- Day1 pre-bronchodilator spirometry assessment will be considered as the baseline.
- Post Bronchodilator readingis captured only at Day 1. For all other study center visits, only pre-bronchodilator spirometry has been performed
- If Date of assessment ≥ Reference Start Date then Study Day= (Date of assessment – Reference start date) +1, else Study Day= Date of assessment – Reference start date.

Listing 16 2.6.3
Asthma Control Questionnaire - Full Analysis Set

Patient No./ Treatment	Age/ Gender	Visit	ACQ Completed	Questions	Result	Change from Baseline
XXX/ XXX/	32/ Male	Screening	Yes	On average, during the past week, how often were you woken by your asthma during the night?	1	
				On average, during the past week, how bad were your asthma symptoms when you woke up in the morning?	0	
				…		
				On average, during the past week, how many puffs/inhalations of short-acting bronchodilator (eg. Ventolin/Bricanyl) have you used each day?	6	
				Total ACQ Score	xx	-
				FEV1 % predicted	xx	
		Baseline	Yes	On average, during the past week, how often were you woken by your asthma during the night?	1	
				…		
				Total Score	xx	
				FEV1 % predicted	xx	
		Day 8	Yes	On average, during the past week, how often were you woken by your asthma during the night?	1	
				……..		
				Total ACQ Score	xx	xx
				FEV1 % predicted	xx	
		<Visits>				
…….						

Note:

- ACQ: Asthma Control Questionnaire.
- Baseline is defined as the pre-dose measurement taken prior to ANB020 or placebo administration at randomization [Day 1], i.e. reference start date. If the pre-dose measurement and the reference start date coincide, that measurement will be considered baseline.
- Total ACQ has been calculated as sum of all individual scores for each patient at each visit. ACQ will be missing if any individual score is missing.

Listing 16.2.6.4
Patient Diary - Full Analysis Set

Patient No./ Treatment	Age/ Gender	Visit	Date of First Diary Entry/ Date of Last Diary Entry/ Study Days	Need to Use Rescue Inhaler	If Yes, Total Number of Puffs/ Total Number of Days the Rescue inhaler Used	Description of the Change Related to Asthma[a]	Experiencing any Symptom/ If Others, Specify	Change in any of the Prescribed Medicine/ Specify	Rate of Study Treatment	Level of Satisfaction with the Side Effects Related to Study Treatment
XXX/ XXX/	32/ Male	Screening	DDMMMYYYY/ DDMMMYYYY/ xx/xx	No	-	2	Other/ xxxx	No	Good	Good
		Baseline	DDMMMYYYY/ DDMMMYYYY/ xx/xx	Yes	xx/ xx	2	Cough	Yes/ xxxx	Fair	Good
		<Visits>								
…….										

Note:
- Study day is calculated for both first and last diary entry date.
  If Date of assessment ≥ Reference Start Date then Study Day= (Date of assessment – Reference start date) +1, else Study Day= Date of assessment – Reference start date.
- [a]: 1=Very much improved, 2= Much improved, 3=Minimally improved, 4=No changes, 5=Minimally worse, 6=Much worse, 7=Very much worse.

Listing 16.2.6.5
Clinical Global Impression of Change Scale - Full Analysis Set

Patient No./ Treatment	Age/ Gender	Visit	CGIC Performed/ If No, Specify Reason	Date of Assessment/ Study Day	Description of the Change in Patient's Overall Asthma Symptom [a]	Any Asthma Exacerbations Occurred Since the Past Week	Type of cercerbation
XXX/ XXX/	32/ Male	Day 2	No/ xxxx	-	-	-	-
		Day 8	Yes	DDMMMYYYY/ xx	4	Yes	Inpatient hospitalization due to asthma (>24hrs)
		<Visits>					
XXX/ XXX/	31/ Female	Day 2	Yes	DDMMMYYYY/ xx	2	No	-
		<Visits>					
……							

Note:
- CGIC: Clinical Global Impression of Change Scale.
- [a]: 1=Very much improved, 2= Much improved, 3=Minimally improved, 4=No changes, 5=Minimally worse, 6=Much worse, 7=Very much worse
- If Date of assessment ≥ Reference Start Date then Study Day= (Date of assessment – Reference start date) +1, else Study Day= Date of assessment – Reference start date.

Programming Note (not part of table): Sort by treatment, patient number and visit.

Listing 16.2.6.6
Time to first asthma exacerbation - Full Analysis Set

Patient No./ Treatment	Date of Randomization	Date of first Exacerbation	Time of first Exacerbation	Censored
XXX/ XXX/	DDMMMYYYY	DDMMMYYYY	xxxx	Yes
XXX/ XXX/	DDMMMYYYY	DDMMMYYYY	xxxx	No
.....				

Programming Note (not part of table): Sort by treatment, patient number and visit.

Listing 16.2.6.7
Rescue Medication - Safety Analysis Set

Patient No./ Treatment	Age/ Gender	Medication Name	Start Date/ Study Day	End Date/ Study Day/ Ongoing	Dose (Unit)	Frequency	Route	Indication
XXX/ XXX/	32/ Male	xxxxx	DDMMMYYYY/ xx	DDMMMYYYY/ xx	xx (xx)	xxxxx	xxxxx	xxxxx
		xxxxx	DDMMMYYYY/ xx	Ongoing	xx (xx)	xxxxx	xxxxx	xxxxx
XXX/ XXX/	31/ Female	xxxxx	DDMMMYYYY/ xx	DDMMMYYYY/ xx	xx (xx)	xxxxx	xxxxx	xxxxx
		…….						
……..								

Note:
- If Date of assessment ≥ Reference Start Date then Study Day= (Date of assessment – Reference start date) +1, else Study Day= Date of assessment – Reference start date.

Programming Note (not part of table): Sort by treatment, patient number, and start date.

Listing 16.2.7.1
Adverse Event - Safety Analysis Set

Patient No./ Treatment	Age/ Gender	System Organ Class/ Preferred Term/Verbatim Term	Start Date/ Study Day	End Date/ Study Day	Did AE Occur Prior to the Start of IP?	Severity	TEAE	Final Outcome	Action taken with the Study Drug	Relationship to Study Drug	Serious/ Criteria[a]	Did the AE Cause the Patient to Discontinue from the Study?	Was Patient Treated for AE?
XXX/ XXX/	32/ Male	xx/xx/xx	DDMMMY YYY/ xx	DDMMMY YYY/ xx	No	Severe	Yes	Recovered	Dose interrupted	Unlikely	Yes/ XXX	Yes	No
XXX/ XXX/	31/ Female	xx/xx/xx	DDMMMY YYY/ xx	DDMMMY YYY/ xx	Yes	Mild	No	Fatal	Drug permanently discontinued	Possible	Yes/ XXX	Yes	Yes
…													

Note:
- [a]: If SAE led to death, then date of death and primary/ secondary cause of death are provided; if required hospitalization, then date of admission and date of discharge are provided.
- If Date of assessment ≥ Reference Start Date then Study Day= (Date of assessment – Reference start date) +1,, else Study Day= Date of assessment – Reference start date.
- TEAE: Treatment emergent adverse event is defined as AE that started or worsened in severity on or after the date and time of the study drug infusion.

Programming Note (not part of table): Sort by treatment, patient number, and start date.

Listing 14.3 2.1
Treatment Emergent Adverse Events Leading to Deaths - Safety Analysis Set

Programming Note: Repeat the same template of Listing 16.2.7.1. Remove the column "Final Outcome"

Listing 14.3 2.2
Serious Treatment Emergent Adverse Event - Safety Analysis Set

Programming Note: Repeat the same template of Listing 16.2.7.1. Remove the column "Serious/Criteria".

Listing 14.3 2.3
Treatment Emergent Adverse Events Leading to Discontinuation from Study or of IP - Safety Analysis Set

Programming Note: Repeat the same template of Listing 16.2.7.1. Remove the column "Did the AE cause the Patient to discontinue from the study and Action taken with the Study Drug".

Listing 14.3.4.1
Clinically Significant Laboratory Results - Safety Analysis Set

Patient No./ Treatment	Age/ Gender	Test	Blood Sample Collected / If No, Specify	Parameter	Visit	Date of Sample Collection/ Study Day	Result[a]	Unit	Reference Range	Change from Baseline
XXX/ XXX/	32/ Male	Hematology	Yes	Hemoglobin	Screening	DDMMMYYYY/ xx	xxxx	xx	(xx-yy)	-
					Baseline	DDMMMYYYY/ xx	xxxx	xx	(xx-yy)	-
					Day 2	DDMMMYYYY/ xx	xxxx	xx	(xx-yy)	xx
					Day 8	DDMMMYYYY/ xx	xxxx	xx	(xx-yy)	xx
					……					
					EOS	DDMMMYYYY/ xx	xxxx	xx	(xx-yy)	xx

Listing 14.3.4.1
Clinically Significant Laboratory Results - Safety Analysis Set

Patient No./ Treatment	Age/ Gender	Test	Blood Sample Collected / If No, Specify	Parameter	Visit	Date of Sample Collection/ Study Day	Result[a]	Unit	Reference Range	Change from Baseline
				<Parameters>	<Visits>	……..				
		Clinical Chemistry	Yes	<Parameters>	<Visits>	DDMMMYYYY/ xx	xxxx	xx	(xx,xx)	-
…….										

Note:

- [a]:The high (H) or low (L) values are only flagged.
- Baseline will be last non-missing measurement taken prior to reference start date (including unscheduled assessments or retests).
- If Date of assessment ≥ Reference Start Date then Study Day= (Date of assessment – Reference start date) +1, else Study Day= Date of assessment – Reference start date.

Listing 16.2.8.1
Serum Pregnancy Test - Safety Analysis Set

Patient No./ Treatment	Age/ Gender	Visit	Test Performed	If No, Specify	Date of Pregnancy Test/ Study Day	Result
XXX/ XXX/	32/ Female	Screening	Yes	-	DDMMMYYYY/ xx	Negative
		<Visits>				
XXX/ XXX/	32/ Female	Screening	Yes	-	DDMMMYYYY/ xx	Negative
		<Visits>				
XXX/ XXX/	31/ Female	Screening	No	xxxx	-	-
		<Visits>				

Note:
- If Date of assessment ≥ Reference Start Date then Study Day= (Date of assessment – Reference start date) +1, else Study Day= Date of assessment – Reference start date.
- The listings consists only of female patients in SAF population.

Programming Note (not part of table): Sort by treatment, patient number and visit.

Listing 16.2.8.2
Electrocardiogram Results - Safety Analysis Set

Patient No./ Treatment	Age/ Gender	ECG Performed	Test (Unit)	Visit	Date of Assessment/ (Study Day	Results	Change from Baseline	If Abnormal CS, Details
XXX/ XXX/	32/ Female	Yes	Heart Rate (bpm)	Screening	DDMMMYYYY/ xx	xx	-	-
				EOS	DDMMMYYYY/ xx	xx	xx	-
			<Parameters>					
			Overall Result	Screening	DDMMMYYYY/ xx	Normal	-	
				EOS	DDMMMYYYY/ xx	Abnormal CS	-	xxxxxxxx

Listing 16.2.8.2
Electrocardiogram Results - Safety Analysis Set

Patient No./ Treatment	Age/ Gender	ECG Performed	Test (Unit)	Visit	Date of Assessment/ (Study Day	Results	Change from Baseline	If Abnormal CS, Details
XXX/ XXX/ …….	31/ Female	No	<Parameters>	<Visits>				

Note:
- Baseline will be last non-missing measurement taken prior to reference start date (including unscheduled assessments or retests).
- If Date of assessment ≥ Reference Start Date then Study Day= (Date of assessment – Reference start date) +1, else Study Day= Date of assessment – Reference start date.
- CS: Clinically Significant, NCS: Not Clinically Significant

Programming Note (not part of table): Sort by treatment, patient number and visit.

Listing 16.2.8.3
Vital Signs - Safety Analysis Set

Patient No./ Treatment	Age/ Gender	Vital Signs Collected	Parameter	Unit	Visit	Date of Assessment/ Study Day	Result	Change from Baseline
XXX/ XXX/	32/ Female	Yes	Pulse Rate	xx	Screening	DDMMMYYYY/ xx	xxxx	-
					Baseline	DDMMMYYYY/ xx	xxxx	-
					Day 2	DDMMMYYYY/ xx	xxxx	xx
					……..			
					EOS	DDMMMYYYY/ xx	xxxx	xx
			<Parameters>	xx	<Visits>	…….		
XXX/ XXX/ ……	31/ Female	Yes	<Parameters>	xx	<Visits>	…….		

Note:
- Baseline will be last non-missing measurement taken prior to reference start date (including unscheduled assessments or retests).
- If Date of assessment ≥ Reference Start Date then Study Day= (Date of assessment – Reference start date) +1, else Study Day= Date of assessment – Reference start date.

Programming Note (not part of table): Sort by treatment, patient number and visit.

Listing 16.2.8.4
Physical Examination - Safety Analysis Set

Patient No./ Treatment	Age/ Gender	Physical Examination Performed	Body System	Visit	Date of Examination/ Study Day	Result	If Abnormal, clinically significant, specify
XXX/ XXX/	32/ Female	Yes	General Appearance	Screening	DDMMMYYYY/ xx	Normal	-
				EOS	DDMMMYYYY/ xx	Normal	-
						…	
			HEENT (head, eyes, ears, nose, throat)	Screening	DDMMMYYYY/ xx	Abnormal CS	xxxx
				EOS	DDMMMYYYY/ xx	Normal	-
			<Body Systems>				
XXX/ XXX/ ……..	31/ Female	No	<Body Systems>	<Visits>	…….		-

Note:
- Baseline will be last non-missing measurement taken prior to reference start date (including unscheduled assessments or retests).
- If Date of assessment ≥ Reference Start Date then Study Day= (Date of assessment – Reference start date) +1, else Study Day= Date of assessment – Reference start date.
- CS: Clinically Significant, NCS: Not Clinically Significant

Programming Note (not part of table): Sort by treatment, patient number and visit.

Listing 16 2.8.5
Anti-Drug Antibody Assessment - Safety Analysis Set

Patient No./ Treatment	Age/ Gender	Serum Sample Collected/ If No, Specify	Visit	Date and Time of Sample Collection/ Study Day	Result	Titer
XXX/	32/	Yes	Baseline	DDMMMYYYY/ HH:MM/ xx	Positive	-
XXX/	Male					
		Yes	Day 8	DDMMMYYYY/ HH:MM/ xx	Negative	xx
			Day 36	DDMMMYYYY/ HH:MM/ xx	Positive	xx
			……			
			<Visits>	DDMMMYYYY/ HH:MM/ xx	Negative	-
……						

Note:
- If Date of assessment ≥ Reference Start Date then Study Day= (Date of assessment – Reference start date) +1, else Study Day= Date of assessment – Reference start date.
- Baseline will be last non-missing measurement taken prior to reference start date (including unscheduled assessments or retests).

Programming Note (not part of table): Sort by treatment, patient number and visit.Present for all available visits.

Listing 16.2.9.1
Cytokines Assessment
Safety Analysis Set

Treatment	Patient No.	Visit	Sample Date/Time	IL-4 (pg/mL)			IL-5 (pg/mL)			IL-13 (pg/mL)			IL-33 (pg/mL)			sST2 (pg/mL)		
				Obs	CFB	RTB	Obs	CFB	RTB	Obs	CFB	RTB	Obs	CFB	RTB	Obs	CFB	RTB
Placebo	XXX	Day 1	DDMMMYYYY/ HH:MM	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx
		Day 2	DDMMMYYYY/ HH:MM	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx
ANB020	XXX	Day 1	DDMMMYYYY/ HH:MM	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx	Xxxx
	…																	

BLQ = below lower limit of quantitation (LLOQ); CFB = change from baseline; IL = Interleukin; Obs = observed; RTB = ratio to baseline.
LLOQ: IL-4 = xxx pg/mL; IL-5 = xxx pg/mL; IL-13 = xxx pg/mL; IL-33 = xxx pg/mL; sST2 = xxx pg/mL.
Note: For summary and analysis purposes BLQ values were considered as 1/2 * LLOQ.

Programming Note (not part of table) Sort by treatment, patient number, visit. Present all visits.

Listing 16.2.9.2
Eosinophil Assessment
Safety Analysis Set

Treatment	Patient No.	Visit	Blood sample collected for eosinophils	If no, specify	Sample Date/Time	Eosinophils (unit)		
						Observed	CFB	RTB
Placebo	XXX	Day 1	Yes		DDMMMYYYY/ HH:MM	Xxxx	Xxxx	Xxxx
		Day 2	No	xxxxxx				
ANB020	XXX	Day 1	Yes		DDMMMYYYY/ HH:MM	Xxxx	Xxxx	Xxxx
	…							

BLQ = below lower limit of quantitation (LLOQ); CFB = change from baseline. RTB = ratio to baseline.
LLOQ: xxx <units>.
Note: For summary and analysis purposes BLQ values were considered as 1/2 * LLOQ.

Programming Note (not part of table) Sort by patient number, visit. Present all visits.

Listing 16.2.9.3
Ex-vivo induced IFN-y assessment
Safety Analysis Set

Treatment	Patient No.	Visit	Blood sample collected for ex-vivo induced IFN-y analysis	If no, specify	Date and time of sample collection	Observed (units)	Change from Baseline (units)	Ratio to baseline
Placebo	XXX	Day 1	Yes		DDMMMYYYY/ HH:MM	xxxx	xxxx	xxxx
		Day 127	Yes		DDMMMYYYY/ HH:MM	xxxx	xxxx	xxxx
ANB020	XXX	Day 1	Yes		DDMMMYYYY/ HH:MM	xxxx	xxxx	xxxx
		Day 127	No		DDMMMYYYY/ HH:MM	xxxx	xxxx	xxxx

BLQ = below lower limit of quantitation (LLOQ).
LLOQ = xxx <unit>.
Note: For summary and analysis purposes BLQ values will be considered as 1/2 * LLOQ.
Programming Note (not part of table) Sort by treatment, patient number, visit. Present all visits.

Listing 16.2.9.4
Patient Screening Summary - All Patients Screened

Patient No.	Age/Gender	Date and Time of IC	Confirmed Informed Consent at Day 1/If No, Specify	Patient Randomized/ Date	Randomization No.	Assigned Treatment	Administered the Treatment
XXX	32/Male	DDMMMYYYYTHH:MM	Yes	Yes/ DDMMYYYY	xx	Yes	Yes
XXX	31/Female	DDMMMYYYYTHH:MM	Yes	-	-	-	Screen Failure
XXX	28/Female	DDMMMYYYYTHH:MM	No: xxxx	-	-	-	Subject Withdrew Consent
------							

Note:
- IC: Informed Consent.

Programming Note (not part of table): Sort by treatment, patient number.

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FIGURE SHELLS

Placebo-Controlled Proof of Concept Study to Investigate ANB020 Activity in Adult Patients with Severe Eosinophilic Asthma

Study No. ANB020-004

Output Templates Signature Page

Figure Shells V1 0 (Dated 18Dec2018) for Protocol ANB020-004

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Modification History

Unique Identifier for this Version	Date of the Document Version	Author	Significant Changes from Previous Authorized Version
Draft 0 1	04 Dec 2017	[redacted]	Not Applicable - First Draft
Draft 0 2	07 Dec 2017		Resolved comments from internal review
Draft 0 3	03 Dec 2018		Resolved comments from sponsor review

Table of Contents

Figure 14 2 1 1
Kaplan-Meier plot of Time to first asthma exacerbation – Full Analysis Set

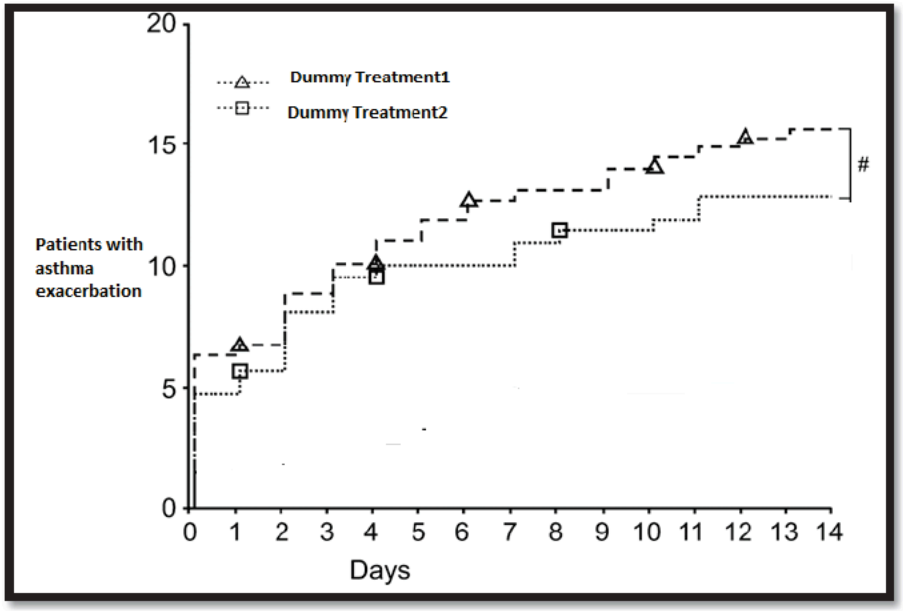
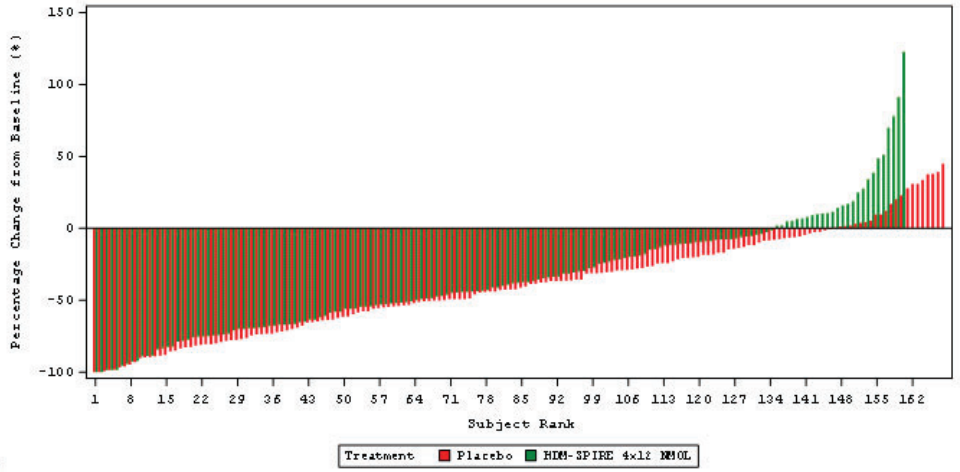


Figure 14 4 2 1
Waterfall plot: Change from Baseline in Peripheral Eosinophil Count on Day 22 – Pharmacodynamic Analysis Set



Programming Note: This is graph is only for representation purpose Y axis should have the % change from baseline, X-axis should have the treatments

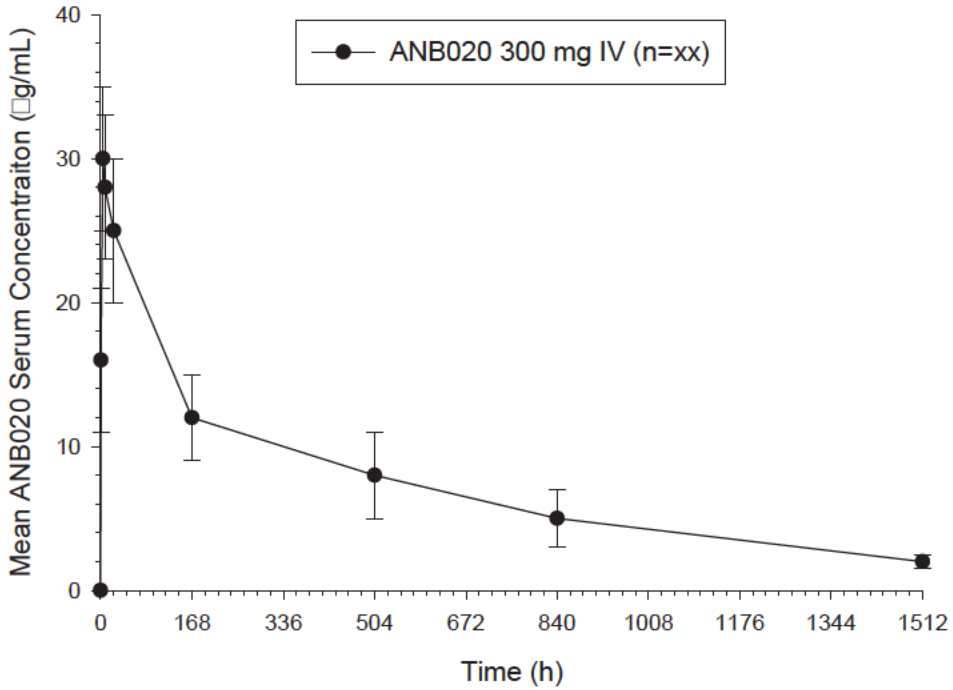
Figure 14 4 2 2
Waterfall plot: Change from Baseline in Peripheral Eosinophil Count on Day 127/ET – Pharmacodynamic Analysis Set

Programming note: The abive layout should be followed

Figure 14 4 1 1

Mean (±SD) Serum Concentration Time Profile of ANB020 for IV infusion – Safety Analysis Set

Linear Scale



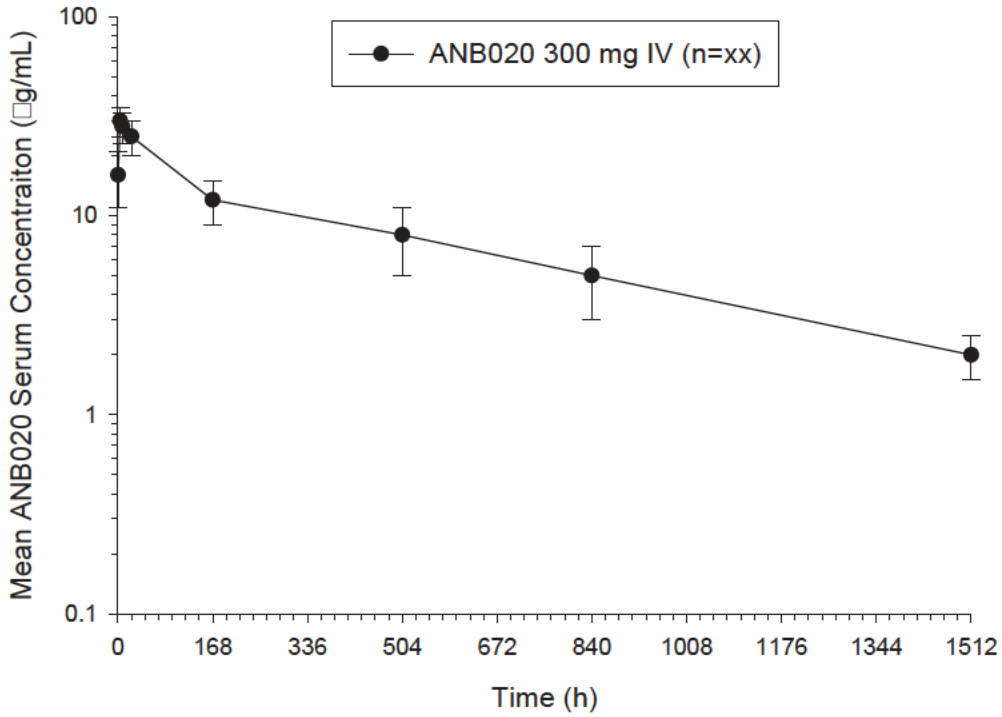
End of infusion (EOI) was approximately 1 hour after the start of infusion and is plotted as 1 hour

SD = standard deviation

<Note: Plot is for example. Actual plot will have x- and y-axes and time points modified according to actual study data.>

Figure 14 4 1 1 (Cont'd)
Mean (±SD) Serum Concentration Time Profile of ANB020 for IV infusion – Pharmacokinetic Analysis Set

Semi-logarithmic scale



End of infusion (EOI) was approximately 1 hour after the start of infusion and is plotted as 1 hour

SD = standard deviation

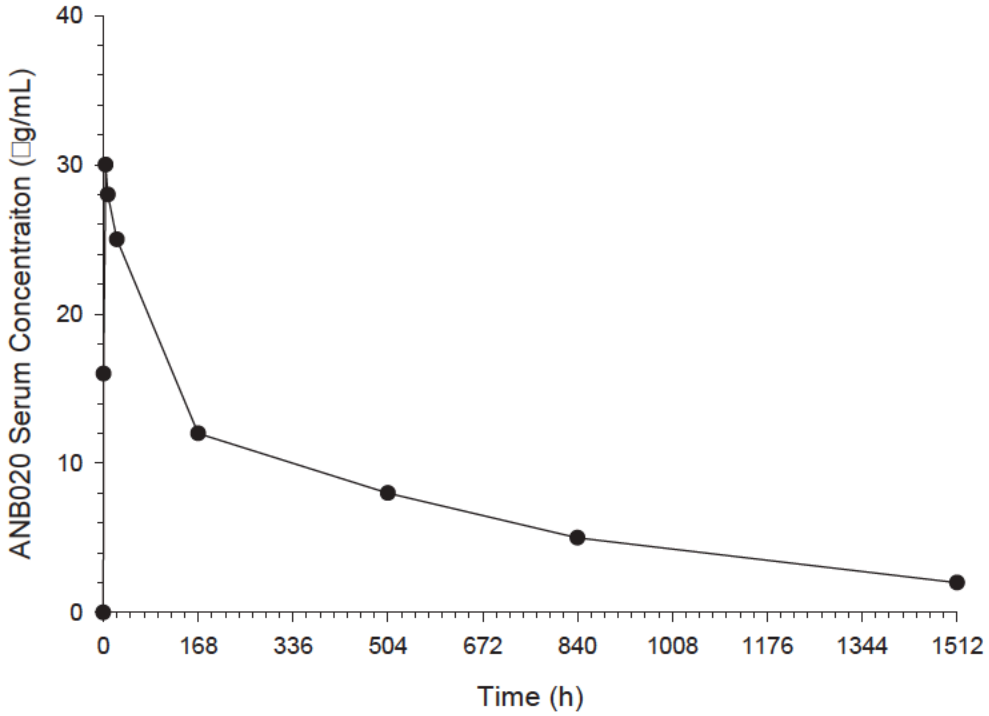
<Note: Plot is for example. Actual plot will have x- and y-axes and time points modified according to actual study data.>

Figure 14 4 1 2

Individual Serum Concentration Time Profile of ANB020 for IV infusion – Safety Analysis Set

Patient 1

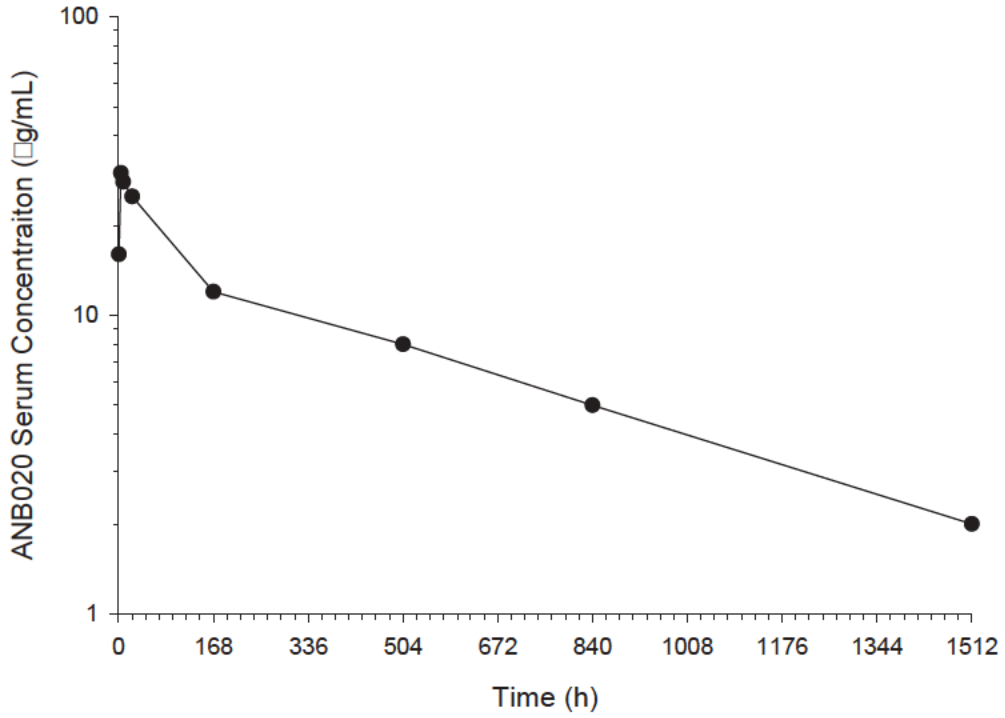
Linear Scale



<Programming Note: Present all the patients. A linear and semi-log plot will be prepared for each subject >
<Note: Plot is for example. Actual plot will have x- and y-axes and time points modified according to actual study data.>

Figure 14 4 1 2 (Cont'd)
Individual Serum Concentration Time Profile of ANB020 for IV infusion – Safety Analysis Set
Patient 1

Semi-logarithmic scale

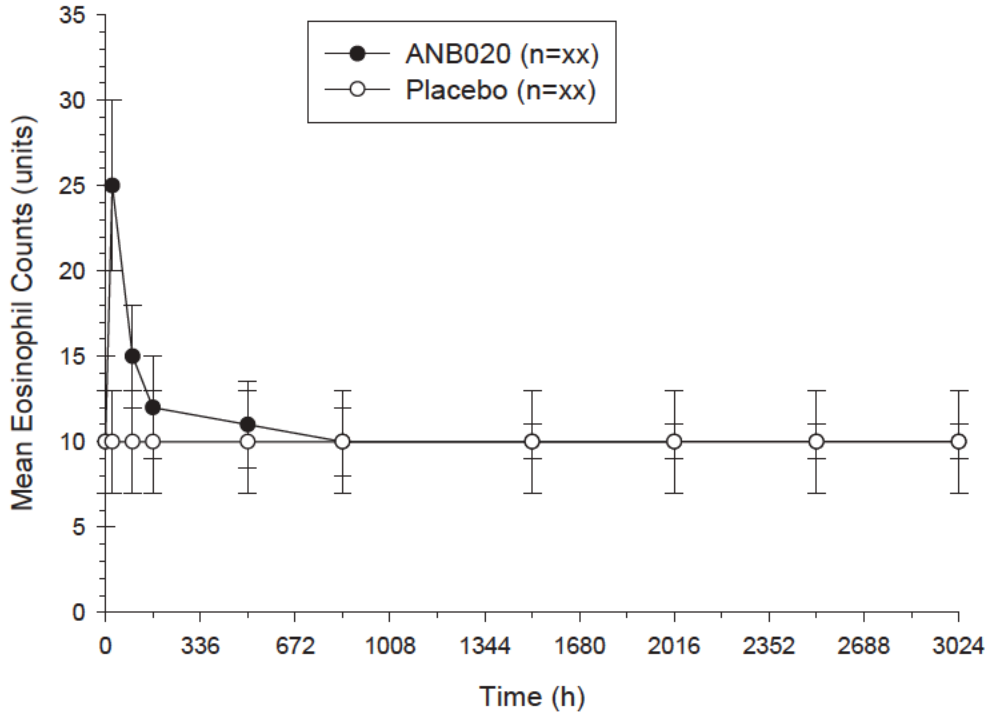


<Programming Note: Present all the patients. A linear and semi-log plot will be prepared for each subject >

<Note: Plot is for example. Actual plot will have x- and y-axes and time points modified according to actual study data.>

Figure 14 4 2 1

Mean (±95% CI) Eosinophil Count-time Profiles – Pharmacodynamic Analysis Set



CI = confidence interval

<Note: Plot is for example Actual plot will have x- and y-axes and time points modified according to actual study data >

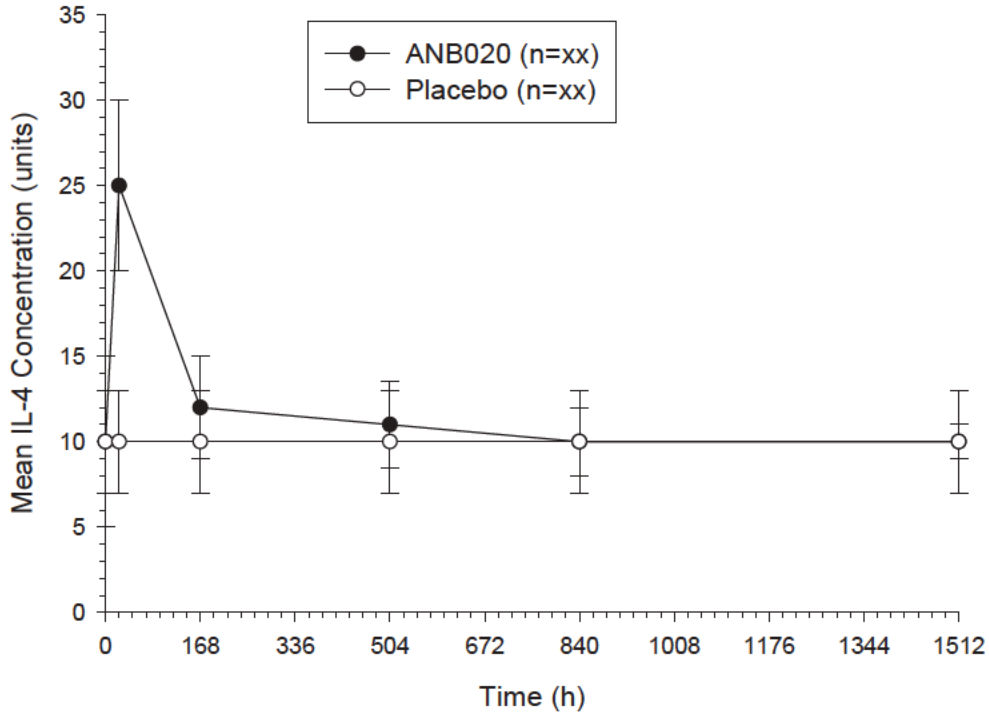
Figure 14 4 2 2

Mean (±95% CI) Change from Baseline Eosinophil Count-time Profiles – Pharmacodynamic Analysis Set

A plot similar to Figure 14 4 2 1 will be presented for change from baseline values

Figure 14 4 2 3

Mean (±95% CI) Concentration-time Profiles for Serum Cytokines – Pharmacodynamic Analysis Set



CI = confidence interval

<Programming Note: Present for all cytokines analytes with units Analytes: IL-4, IL-5, IL-13, IL-33, and sST2 >

<Note: Plot is for example Actual plot will have x- and y-axes and time points modified according to actual study data

Figure 14 4 2 4

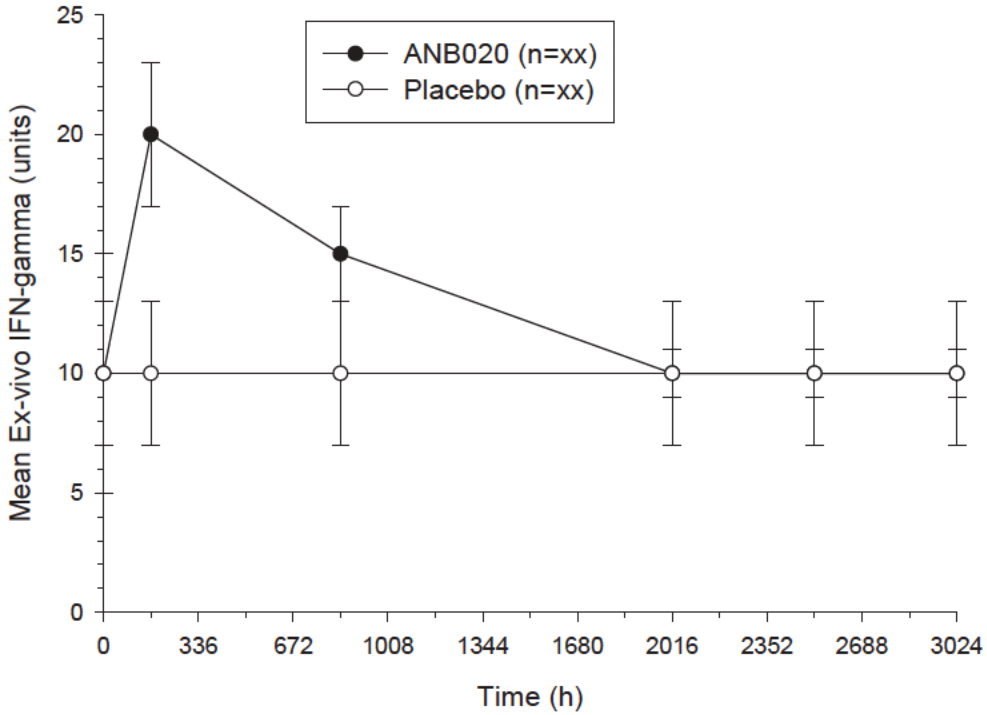
Mean (±95% CI) Change from Baseline Concentration-time Profiles for Serum Cytokines – Pharmacodynamic Analysis Set

A plot similar to Figure 14 4 2 3 will be presented for change from baseline values

<Programming Note: Present for all cytokines analytes with units Analytes: IL-4, IL-5, IL-13, IL-33, and sST2 >

Figure 14 4 2 5

Mean (±95% CI) for Ex-vivo IFN-gamma – Pharmacodynamic Analysis Set



CI = confidence interval

Figure 14 4 2 6

Mean (±95% CI) Change from Baseline for Ex-vivo IFN-gamma – Pharmacodynamic Analysis Set

A plot similar to Figure 14 4 2 5 will be presented for change from baseline values

Figure 14 4 2 7

Scatter Plot of Observed Eosinophil Count versus Serum ANB020 Concentration – Pharmacodynamic Analysis Set

Figure 14 4 2 8

Scatter Plot of Observed Serum Cytokine Levels versus Serum ANB020 Concentration – Pharmacodynamic Analysis Set

Note: All available cytokines will be presented on separate plots

Figure 14 4 2 9

Scatter Plot of Observed Ex-vivo IFN-gamma Levels versus Serum ANB020 Concentration – Pharmacodynamic Analysis Set

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Section A

Customer:	AnaptysBio, Inc.
Project Code:	CYA74392
Protocol Number:	ANB020-004
Title of Note:	Additional analyses outside the scope of final SAP (Version Date: 18DEC2018)

Section B

DESCRIPTION:

Background
The note-to-file (NTF) is intended to document the additional analyses that are outside the scope of the final SAP dated 18DEC2018.

Objective
The objective of the additional analysis is to assess the reduction in asthma control questionnaire (ACQ) 5 score relative to the scheduled study time points including day 8, 22, 36, 64, 85, 106 and end of study (EOS) visit.

Endpoint
The endpoint of the additional analysis is ACQ-5 score and its percent change from baseline relative to scheduled study time points.

Analysis Set
Full analysis set (FAS), as defined in the SAP dated 18DEC2018, will be used for the analysis.

Analysis Method
The analyses will be performed descriptively using n (number of subjects with non-missing values), mean, standard deviation (SD), median, minimum and maximum as summary statistics. Additionally, 95% confidence interval (CI) for mean will also be provided.

The above mentioned summary statistics and 95% CI's for mean using classical method will be provided for both observed and percent change from baseline relative to different scheduled visits for ACQ-5 score. Summaries for screening and baseline will be provided for the observed values only.

Number of subjects within each treatment group under FAS (N) will also be reported along with summary statistics for the analysis.

A line plot for mean (± SD) percent change from baseline for ACQ-5 score will be provided for each of the treatment groups against the applicable scheduled study visits.

A listing detailing the individual ACQ component scores along with ACQ-5 score will be presented for each visit of data collection along with demographic characteristics such as age and gender for each subject as applicable.

Derivation
ACQ-5 score will be derived by summing the 5 individual scores, as described in Table 1, and utilizing the average for each subject at each applicable visit. A percentage of change from baseline was then assessed.

Symptoms will be scored on a scale of 0 to 6 with 6 being the worst case. ACQ-5 will be missing if any individual score is missing.

Table 1: Individual components and corresponding responses for calculating ACQ-5 score

Individual item	Response
1. On average, during the past week, how often were you **woken by your asthma** during the night?	0 Never 1 Hardly ever 2 A few times 3 Several times

	4 Many times 5 A great many times 6 Unable to sleep because of asthma
2. On average, during the past week, how **bad were your asthma symptoms when you woke up** in the morning?	0 No symptoms 1 Very mild symptoms 2 Mild symptoms 3 Moderate symptoms 4 Quite severe symptoms 5 Severe symptoms 6 Very severe symptoms
3. In general, during the past week, how **limited were you in your activities** because of your asthma?	0 Not limited at all 1 Very slightly limited 2 Slightly limited 3 Moderately limited 4 Very limited 5 Extremely limited 6 Totally limited
4. In general, during the past week, how much **shortness of breath** did you experience because of your asthma?	0 None 1 A very little 2 A little 3 A moderate amount 4 Quite a lot 5 A great deal 6 A very great deal
5. In general, during the past week, how much of the time did you wheeze?	0 None 1 1-2 puffs/inhalations most days 2 3-4 puffs/inhalations most days 3 5-8 puffs/inhalations most days 4 9-12 puffs/inhalations most days 5 13-16 puffs/inhalations most days 6 More than 16 puffs/inhalations most days

Further action required:

List of outputs

Below is the list of outputs that will be produced for the proposed analysis on ACQ-5.

Table 1: Asthma Control Questionnaire (Summary of Scores for ACQ-5) - Full Analysis Set
Listing 1: Asthma Control Questionnaire (ACQ-5) - Full Analysis Set
Figure 1: Mean (±SD) % change from baseline of ACQ-5 score by visit

Programming Note:

One ADaM dataset "ADQS_AD" will be created by modifying the program of already existing dataset "ADQS". "ADQS_AD" will have all the variables as in "ADQS" with only below mentioned additional information under "**Programing logic for "ADQS_AD"**".

The newly created outputs and dataset mentioned in this NTF and their programs will be stored in the respective study folders as in the main analysis for this project.

Programing logic for "ADQS_AD":

If ACQ-5 individual item are non-missing, then populate
PARAM="ACQ5 Score";
PARAMCD="ACQ5";
AVAL=5 Average of 5 individual ACQ-5 items if all the individual items are non-missing; else set the value of AVAL to missing if at least one individual item score is missing.
PARAMN=9; PARCAT2="Asthma Control Questionnaire";
AVALC=character result of AVAL;
ABLFL= "Y" (for baseline value, else populate as blank);
BASE=Populate the baseline value;
BASEC=Character result of BASE;
CHG=Post baseline - Baseline;
PCHG= [(Post baseline - Baseline)*100]/Baseline if non-zero baseline (BASE ne 0); else set the value of PCHG to missing if BASE = 0;

Section C

AUTHOR:

Signature (Print Name): [redacted] **Signature (Sign):** _____

Job Title: [redacted] **Date:** _____

Reviewer:

Signature (Print Name): [redacted] **Signature (Sign):** _____

Job Title: [redacted] **Date:** _____

Approver:

Signature (Print Name):	[redacted]	**Signature (Sign):**	
Job Title:	[redacted] AnaptysBio, Inc	**Date:**	