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STATISTICAL ANALYSIS PLAN

EVOLUS-CLIN201

A Phase II Multi-Center, Prospective, Randomized, Double Blind, Active-Controlled, Single Treatment, Increasing Dose Trial to Study the Safety and Duration of Effect of 40U of PrabotulinumtoxinA-xvfs in Adult Subjects for Treatment of Moderate-to-Severe Glabellar Lines

Version v1.1
31-MAY-2023

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ABBREVIATIONS

AE	Adverse Event
BLA	Biologic License Application
BP	Blood Pressure
CFR	U. S. Code of Federal Regulations
CI	Confidence Interval
CRA	Clinical Research Associate
CRO	Clinical Research Organization
ECG	Electrocardiogram
ET	Early Termination
eCRF	electronic Case Report Form
FDA	Food and Drug Administration
GCP	Good Clinical Practices
GAIS	Global Aesthetic Improvement Scale
GLS	Glabellar Line Scale (0=none, 1=mild, 2=moderate, 3=severe)
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IND	Investigational New Drug
IP	Investigational Product
IRB	Institutional Review Board
ITT	Intent-to-Treat
PI	Principal Investigator
PP	Per protocol
SAE	Serious Adverse Event
SAFT	Safety
SAP	Statistical Analysis Plan
SMMP	Safety and Medical Monitoring Plan
SOC	System Organ Class
SSS	Subject Satisfaction Scale
TRAE	Treatment Related Adverse Event
UADR	Unanticipated Adverse Drug Reaction
ULN	Upper Limit of Normal
UPT	Urine Pregnancy Test
US	United States

1. INTRODUCTION

This Statistical Analysis Plan (SAP) gives a comprehensive and detailed description of statistical techniques to be used for study EVOLUS-CLIN201. The purpose of this SAP is to ensure the credibility of the study findings by pre-specifying the statistical approaches for the analysis of study data prior to database lock. This SAP provides additional details concerning the statistical analyses outlined in the protocol. Whenever differences exist in descriptions or explanations provided in the protocol and SAP, the SAP prevails.

1.1. Background

Botulinum toxin type A, now manufactured by several pharmaceutical/biotechnology companies, has been approved for the temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult subjects.

The clinical study designs that have supported the New Drug Applications for these products have generally followed the same pattern in that they were all multicenter, randomized, double-blind, placebo-controlled studies that assessed the efficacy of the product to reduce the severity of glabellar lines at 30 days following injection of the targeted glabellar muscles.

More recently, botulinum toxins approved in the US have investigated the effect of increasing dose on duration of effect. In this clinical investigation, the dose of prabotulinumtoxinA will be increased and the safety and duration of effect will be studied.

1.2. Rationale for Study

PrabotulinumtoxinA, using a total dose of 20 Units (i.e., 4 Units injected into five sites of the glabellar complex muscles), has been approved by the FDA for the treatment of moderate to severe glabellar lines. The current study will explore the safety and effectiveness of injecting 40 Units of prabotulinumtoxinA into the glabella and determine if the duration of effect of prabotulinumtoxinA 40 Units is superior to that of prabotulinumtoxinA 20 Units.

Exploratory analyses will determine if the duration of effect of prabotulinumtoxinA 40 Units is superior to that of onabotulinumtoxinA 20 Units, as well as if the duration of effect of prabotulinumtoxinA 20 Units is superior to that of onabotulinumtoxinA 20 Units.

1.3. Statistical Hypothesis

The general form of duration of effect hypotheses will be:

H_o: $\beta = 0$
H_A: $\beta < 0$

where exp(β) is the hazard ratio (experimental treatment / comparator treatment) for loss of effect. The study is not powered for formal hypothesis testing and any analyses presented will be for interpretation purposes only.

1.4. Study Objectives

The primary objectives of this study are to demonstrate the safety and duration of effect of 40U of prabotulinumtoxinA-xvfs in providing temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugators and/or procerus muscle activity in adult subjects.

2. OVERVIEW OF STUDY DESIGN

2.1. Study Design

This is a multicenter, prospective, randomized, double-blind, active-controlled, single-treatment, increasing dose design.

Approximately 150 subjects will be randomized 1:1:1, to either 20U onabotulinumtoxinA, 20U prabotulinumtoxinA-xvfs, or 40U prabotulinumtoxinA-xvfs. Subjects with moderate or severe glabellar lines at maximum frown on the 4-point validated Glabellar Line Scale (*GLS, 0=none, 1= mild, 2=moderate, 3=severe*), as judged by the investigator and the subject, will be eligible.

Safety and effectiveness will be assessed on days 3, 7, and 30, then every 30 days up to 365 days or until the subject has returned to Baseline as assessed by the Investigator, at which point the subject will exit the study. Please refer to Table 1 below for visit specifics.

Duration of effect will be estimated by Kaplan-Meier analysis and will be based on the number of days from Treatment Day (Baseline) to the day that GLS severity (Investigator assessment) at maximum frown returns to the Baseline value (i.e., the treatment will be considered to remain effective for the amount of time during which GLS severity at maximum frown has not returned to Baseline severity).

The Evaluating Investigator (i.e., Blinded Investigator) will be responsible for managing the subject, monitor for related and unrelated adverse effects, and carrying out the evaluations. Injections of study drug will be performed by an "Unblinded Injector" (i.e., physician or nurse practitioner not responsible for subject follow-up).

2.2. Study Population

The full list of inclusion and exclusion criteria can be found in the Study Protocol.

2.3. Primary Endpoint

The primary effectiveness endpoint will be duration of effect, defined as the number of days from Treatment Day (Baseline) to the day that GLS severity (Investigator assessment) at maximum frown returns to the Baseline value. The treatment will be considered to remain effective for the amount of time during which GLS severity at maximum frown has not returned to Baseline severity. Duration of effect will be estimated by Kaplan–Meier analysis.

Although the trial is not powered for inferential analysis, this will be the most influential outcome in the overall assessment of the effectiveness of prabotulinumtoxinA 40 Units, compared to prabotulinumtoxinA 20 Units, in treating moderate to severe glabellar lines.

TABLE 1. SCHEDULE OF EVENTS AND PROCEDURES

Visit Number	V1 [1] Screening	V2 [1]	V3	V4 (phone f/u)	V5 to V15 [2]	V16 [3] (or Final Visit, or ET)	Unscheduled Visit [11]
Day/Week/Month	**≤ 14D**	**Tx Day**	**48Hr**	**D7**	**D30 to D330** **Monthly Visits**	**D365**	
Visit Windows	--	--	--	±1 Day	D30 ±3D, ≥D60 ±7D	±14D	
Assessment and Procedures							
Informed Consent	X						
Inc/Excl Criteria	X						
Demographics, Med Hx	X						
Randomization to Study Tx [4]		X					
Effectiveness - Investigator							
Glabellar Line Scale [5]	X	X	X		X	X	X
Global Aesthetic Improvement			X		X	X	X
Effectiveness - Subject							
Glabellar Line Scale [5]	X	X	X		X	X	X
7-Day Subject Diary		X →					
Global Aesthetic Improvement			X		X	X	X
Subject Satisfaction Score			X		X	X	X
Clinical Interview [6]					D30 only	X	X
Safety Evaluations							
Directed Questionnaire [7]	X		X		X	X	X
Directed Review of Systems	X		X		X	X	X
Vital Signs [8]	X		X		X	X	X
Physical Exam [9]	X		X		X	X	X
UPT (as applicable)	X	X				X	
Clinical Laboratory Tests [10]	X					X	X
ECG	X					X	X
Safety Assessment Phone Call				X			
Brow Area Photography	X	X	X		X	X	X
Concomitant Medications	X	X	X	X	X	X	X
AE Assessment		X	X	X	X	X	X

1. Screening and treatment visit can take place the same day, at the discretion of the investigator
2. Subjects will be followed monthly until their Glabellar Line Scale score is back to Baseline (Investigator assessment)
3. Subject exits study once their Glabellar Line Scale Score has returned to Baseline (Investigator assessment)
4. IP may be administered same day as Screening
5. Glabellar Line Scale at Maximum Frown, 0=none, 1=mild, 2=moderate, 3=severe
6. Clinical Interview Questions
   - What did you like about the treatment (clinically or other feedback)?
   - What did you dislike about the treatment (clinically or other feedback)?
   - If treated with botulinum toxin before this study, which treatment did you prefer, the study treatment or the previous treatment?
7. Directed Questionnaire: Have you noticed any problems with speaking, swallowing, or breathing? Have you had any headaches, eyelid or eyebrow drooping?
8. Blood pressure, heart rate, respiration rate
9. Physical exam to be based on the Investigator judgment as a response to the Medical History, Questionnaire, Review of Systems, and any other relevant information. Neurological exam includes extraocular movement, cranial nerve and muscle weakness assessment
10. Clinical Laboratory Tests:
    - Hematology: Hemoglobin, Hematocrit, RBC, WBC, WBC differential, Platelets
    - Serum: ALP, BUN, Creatinine, ALT, AST, Alb, total protein, UA, Glucose, Na, K, Cl, Ca, anti-botulinum toxin antibodies
    - Urinalysis: Specific Gravity, pH, Protein, Glucose, WBC, Blood
11. Unscheduled Visit: May occur at any time during the study to complete missed study procedures, assess AEs, or assess ongoing unresolved drug-related AEs after study exit. During a visit, some or all of the safety and effectiveness evaluations may be performed.

3. SUBJECT NUMBERING, RANDOMIZATION AND BLINDING

3.1. Subject Numbering

All subjects will receive a 3-digit subject number, starting at 001. Subject numbers will be assigned at site level and in ascending order and will be coupled with the site identification number for unique identification of each subject. Subjects withdrawn from the study will retain their subject number; new subjects will be allocated a new subject number.

Subjects who do not meet eligibility criteria will be deemed screen failures. Screen Failures will not be entered in the eCRF. However, these subjects may be re-screened at a later date.

3.2. Subject Randomization

At Visit 2/Treatment Day, subjects will be randomized (1:1:1 ratio) to treatment with either 20U onabotulinumtoxinA, 20U prabotulinumtoxinA-xvfs, or 40U prabotulinumtoxinA-xvfs.

Subjects will be randomized using a blocked randomization scheme that will be stratified by the following factors:

- Baseline GLS: moderate vs. severe
- Age group: ≤65 vs. >65 within each stratum
- Gender: female vs male

3.3. Blinding

To maintain study blind, the "Unblinded Injector" (i.e., physician or nurse practitioner not responsible for subject follow-up) will have access to the Randomization Schedule, be aware of treatment assignment, will prepare syringes of reconstituted IP, and will administer injections of study drug to study subjects.

3.4. Unblinding

The study blind will be broken only after all data are verified, entered into the database and validated, and the database is locked.

4. STUDY TREATMENT

Subjects will be treated either with the study drug 40U of prabotulinumtoxinA or one of the two controls; 20U of prabotulinumtoxinA or 20U of onabotulinumtoxinA.

The reconstitution and syringe preparations will be done in a double-blinded fashion.

4.1. Concomitant Medications

All treatment/procedures received by the subject within 14 days prior to Visit 2 (Treatment Day) and throughout the treatment period, including the name of the treatment/procedure, must be recorded in the eCRF with start date, stop date, dosage, frequency and indication, if applicable.

5. STUDY EVALUATIONS

5.1. Effectiveness Assessments

5.1.1. Glabellar Lines Scale (GLS)

The severity of glabellar lines at "maximum frown" will be assessed by both the Investigator (Blinded Evaluator) and subjects using the validated 4-point GLS as per Table 2.

Table 2. GLS at Maximum Frown

Grade	Score	Description
None	**0**	No lines
Mild	**1**	Line seen, not sharp
Moderate	**2**	Line sharper, deep, may see heaping of skin
Severe	**3**	Deeper line, heaping of skin, skin may be opposed

5.1.2. Global Aesthetic Improvement Scale (GAIS)

GAIS will be assessed by both the Investigator (Blinded Evaluator) and subjects using the 5-grade scale as per Table 3.

Table 3. GAIS

Grade	Score	Description
Much Improved	**2**	Marked improvement in appearance
Improved	**1**	Improved in appearance, but would like more
No Change	**0**	The appearance is essentially the same as the original condition
Worse	**-1**	The appearance is worse than the original condition
Much Worse	**-2**	The appearance is much worse that the original condition

5.1.3. Subject Satisfaction Scale (SSS)

SSS will be assessed by the subject using the following 5-grade scale as detailed in Table 4.

Table 4. Subject Satisfaction Scale

Grade	Score	Description
Very Satisfied	**2**	I am very satisfied with the treatment
Satisfied	**1**	I am satisfied with the treatment
Indifferent	**0**	I am indifferent with the treatment
Unsatisfied	**-1**	I am unsatisfied with the treatment
Very Unsatisfied	**-2**	I am very unsatisfied with the treatment

Clinical Interview (Day 30, Final Visit/Early Termination, and Unscheduled Visit)

5.1.4. Clinical Interview (Day 30, Final Visit/Early Termination, and Unscheduled Visit)

Subject opinion regarding study treatment will be assessed through a clinical interview employing the following questions:

- What did you like about the treatment (clinically or other feedback)?
- What did you dislike about the treatment (clinically or other feedback)?
- If treated with botulinum toxin before this study, which treatment did you prefer, the study treatment or the previous treatment?

5.1.5. 7-Day Subject Diary

In the morning of the day after study treatment, subjects will be issued a 7-day electronic subject diary that will assess subjects' opinion regarding onset of study treatment effect. Subjects will respond "Yes" or "No" to the following question: "*Since being injected, have you noticed any effect on the appearance of your glabellar lines?*"

6. SAFETY ASSESSMENTS

6.1. Directed Questionnaire

The following questions will be asked looking for signs of local or distant botulinum toxin spread and to set a baseline:

- Have you noticed any problems with speaking, swallowing, or breathing?
- Have you had any headaches, eyelid or eyebrow drooping?

6.2. Directed Review of Systems

Directed Review of Systems will include review of the following systems: Head and Neck, Respiratory, Cardiovascular, Neurological, Musculoskeletal, Dermatological.

6.3. Vital Signs

Blood pressure (systolic, diastolic), respiratory rate, and heart rate will be recorded.

6.4. Physical Exam

Based on the response to the medical history, directed questions, directed reviews of systems, inclusion and exclusion criteria, an appropriate physical examination will be conducted by the Investigator. The neurological examination should include extraocular movement, cranial nerve and muscular weakness assessments. This exam will also establish a baseline for the subject.

6.5. Urine Pregnancy Test

UPTs will be conducted at Screening (Visit 1), Visit 2 (if applicable) and end of study. Pregnancies will be recorded using the Unanticipated Problems Reporting Form and are not be considered AEs.

6.6. Clinical Safety Laboratory Tests

The clinical laboratory data consist of blood analysis (including hematology, clinical chemistry, and urinalysis) will be conducted as per the visit schedule. Clinically significant results (Investigator opinion) will be reported as AEs.

The following tests will be performed:

- Hematology: hemoglobin, hematocrit, red blood cell count, white blood cell count, neutrophils, lymphocytes, monocytes, eosinophils, basophils, platelet count
- Chemistry: alkaline phosphate, urea nitrogen, creatinine, ALT, AST, albumin, total protein, uric acid, glucose, sodium, potassium, chloride, calcium
- Urinalysis: specific gravity, pH, protein, glucose, leukocytes, occult blood
- Botulinum antibodies

6.7. 12-Lead ECG

12-lead ECGs will be at Screening and at the final study visit and will include heart rate, PR, QRS, QT, and QTc. ECG results will be interpreted by as Normal, Abnormal; not clinically significant (NCS), or Abnormal; clinically significant (CS). If Abnormal, details will be provided, and "Abnormal Clinically Significant" results (Investigator opinion) will be reported as AEs."

6.8. Concomitant Medications

All treatment/procedures received by the subject within 14 days prior to study treatment and

throughout the treatment period, including the name of the treatment/procedure, must be recorded in the eCRF with end dates, if applicable.

6.9. Adverse Events

The Blinded Investigator will assess for all types of AEs and will record details of seriousness, severity, duration, and action taken with the study IP, and relationship to the IP. AEs will be reported from the time of consent until the final visit.

Treatment-Related AEs will be followed until the event has resolved or stabilized or until follow-up is no longer possible or the PI deems it unnecessary.

6.9.1. Causality Assessment

The Blinded Investigator will assign the causality assessment according to his/her clinical experience and the subject's description of the event. The Sponsor will be responsible for the final causality judgment. The causal relationship should be classified according to the following criteria (not all variables need to be present to be indicative of relationship to the treatment):

Definitely related:
- The temporal sequence of AE onset relative to study treatment is reasonable.
- The AE is more likely explained by study treatment than by another cause.
- The AE shows a pattern consistent with previous knowledge of study treatment.

Probably related:
- The temporal sequence of AE onset relative to study treatment is reasonable.
- The AE is more likely explained by the study treatment than by another cause.

Possibly related:
- The temporal sequence of AE onset relative to study treatment is reasonable.
- The AE could have been due to another equally likely cause.

Probably not related:
- There is another more likely cause of the AE.

Definitely not related:
- The temporal sequence of AE onset relative to study treatment is not reasonable.
- There is another obvious cause of the AE.

6.9.2. Severity Assessment

For all types of AEs, the Blinded Investigator will determine the severity classification based on his/her clinical experience and by using the following definitions of severity:

- **Mild:** Symptoms are barely noticeable or do not make the subject uncomfortable. The AE does not influence performance or functioning. Prescription drugs are not ordinarily needed for relief of symptom(s).
- **Moderate:** Symptoms are of sufficient severity to make the subject uncomfortable. Performance of daily activities is influenced. Treatment of symptom(s) with prescription drugs or therapies may be needed.
- **Severe:** Symptoms are of sufficient severity to cause the subject severe discomfort. Performance of daily activities is compromised. Treatment for symptom(s) with prescription drugs or therapies may be needed.

The maximal severity for the AE will be recorded, even if the AE presented as being less severe at some point during the event.

Adverse Events of Special Interest (AESI) Reporting

6.9.3. Adverse Events of Special Interest (AESI) Reporting

AESI are important medical events that may be consistent with botulinum toxin effects, such as:

- Swallowing or breathing difficulties
- Asthenia
- Generalized muscle weakness
- Diplopia
- Dysphagia
- Dysphonia
- Dysarthria

6.9.4. Unexpected Adverse Drug Reaction (UADR) Reporting

A UADR is a treatment-related adverse reaction where the nature or severity is not consistent with the applicable product information in the Investigator's Brochure. An AE will be considered as a UADR if it is a treatment-related event not associated with the following Expected Adverse Drug Reactions:

- Headache
- Facial paresis (eyelid ptosis, brow ptosis)
- Blepharospasm
- Injection site pain
- Injection site hematoma
- Injection site reaction
- Eyelid edema
- Nausea

7. STATISTICAL METHODS

7.1. Primary Effectiveness Endpoint

The primary effectiveness endpoint will be duration of effect (regardless of responder status), defined as the number of days from Treatment Day (Baseline) to the day that GLS severity (Investigator assessment) at maximum frown returns to the Baseline value. Although the trial is not powered for inferential analysis, this will be the most influential outcome in the overall assessment of the effectiveness of prabotulinumtoxinA 40 Units, compared to prabotulinumtoxinA 20 Units, in treating moderate to severe glabellar lines. Analysis will be performed using the modified Intent-To-Treat (mITT) population and regardless of responder status.

Duration of effect will be described by Kaplan-Meier curves and the respective median times with associated 2-sided 95% confidence interval (CI) for each treatment group. Statistical analyses of treatment group differences will be done using Cox proportional hazards regression with time to return to Baseline as the dependent variable, treatment group as the independent variable, and age, gender, and Baseline GLS score (Investigator assessment) at maximum frown as covariates.

Statistical significance will be established at the 0.025 level with one-sided hypothesis testing.

7.2. Secondary Effectiveness Endpoints

Secondary effectiveness endpoints will be used to provide additional analyses regarding duration of effect of prabotulinumtoxinA 40U, prabotulinumtoxinA 20U, and onabotulinumtoxinA 20U. As duration of effect outcomes, secondary effectiveness endpoints will be assessed as described above for the primary endpoint. The mITT population will be used for summaries and comparisons. Secondary endpoints, in order of importance, will be:

1. Duration of effect (PraB vs. OnaB only, regardless of responder status), defined as the number of days from Treatment Day (Baseline) to the day that GLS severity (Investigator assessment) at maximum frown returns to the Baseline value.
2. Duration of effect (all treatment groups, regardless of responder status), defined as the number of days from Treatment Day (Baseline) to the day that GLS severity (subject assessment) at maximum frown returns to the Baseline value.
3. Duration of effect (all treatment groups) in GAIS responders (score of 2 or 1 at Day 30) as assessed by Investigator.
4. Duration of effect (all treatment groups) in GAIS responders (score of 2 or 1 at Day 30) as assessed by subject.
5. Duration of effect (all treatment groups) in SSS responders (score of 2 or 1 at Day 30) as assessed by subjects.

7.3. Exploratory Effectiveness Endpoints

Exploratory effectiveness endpoints will be evaluated for signals of effectiveness to explore whether any should be elevated in importance for subsequent trials. These endpoints will be assessed using either logistic regression (for binary endpoints) or survival analysis-type methods as described above. Comparisons will be made between all treatment groups. Chi-square tests of association or Fisher's exact tests will be used to compare treatment group differences in proportion of subjects returning to Baseline at each time point in the study. Exploratory endpoints will be:

1. Duration of effect for GLS responders, defined as the number of days from Treatment Day (Baseline) to the day that GLS severity at maximum frown returns to the Baseline value. Analyses will be conducted for Investigator and subject assessments of GLS. Various responder definitions will be tested (1-Point, 2-Point and 3-Point responders at any time during the study; GLS Score of 0 or 1 at any time during the study; 1-Point responders at Day 30).
2. Time to loss of GLS responder status, with responder being defined as a GLS score of 0 or 1 at any point during the study. Analyses will be conducted for Investigator and subject assessments of GLS.
3. GLS responder rates (Investigator assessments) at each study visit. Various responder definitions will be tested (1-Point, 2-Point and 3-Point responders; GLS Score of 0 or 1; GLS Score 0 or 1 **&** ≥2-Point improvement; GLS Score 0 or 1 **&** ≥2-Point improvement **&** Investigator GLS = subject GLS).
4. GLS responder rates (Subject assessments) at each study visit. Various responder definitions will be tested (1-Point, 2-Point and 3-Point responders; GLS Score of 0 or 1).
5. GAIS response (score of 2 or 1) as assessed by Investigator and subject at each visit.
6. SSS response (score of 2 or 1) as assessed by subjects at each visit.
7. Onset of effect as assessed by subjects through the 7-Day Subject Diary.

7.4. Safety Endpoint

Safety endpoints will include incidence of treatment-emergent and treatment-related AEs and changes from Baseline in ECG parameters, safety laboratory parameters, physical exams, and vital signs. The SAFT Population will be used for descriptive summaries of the safety endpoints.

7.4.1. Adverse Events (AEs)

AEs will be coded to system organ class (SOC) and preferred term (PT) using the Medical Dictionary for Regulatory Activities (MedDRA). The number and percentage (incidence) of subjects reporting an AE and the number of AEs will be summarized. A treatment-emergent AE will be defined as AEs that started at or after the first injection.

The following AE incidence tables will be provided for treatment-emergent AEs:

- AE Profile Overview
- Treatment-Emergent AEs by SOC and PT
- Treatment-Related AEs by SOC and PT
- Treatment-Emergent SAEs by SOC and PT
- Treatment-Related SAEs by SOC and PT
- Unexpected Adverse Drug Reactions by SOC and PT
- Adverse Events of Special Interest by SOC and PT

Treatment-related AEs will be defined as possibly, probably, or definitely related. Two-sided Wilson 95% confidence intervals will be calculated for the overall incidence of AEs and SAEs.

7.4.2. Laboratory Variables

The number and percentage of subjects with a clinically significant laboratory abnormality (Investigator opinion) will be summarized for each laboratory test with available normal ranges.

Descriptive statistics will be used to summarize observed values and changes from Baseline. Shift tables and other tabular and graphical methods may be used to present results for laboratory tests of interest. Listings will be provided with flags indicating clinically significant abnormalities.

7.4.3. Vital Signs

The number and percentage of subjects with a clinically significant vital sign abnormality (Investigator opinion) will be summarized for each parameter; percentages will be based on subjects with non-missing values.

Descriptive statistics will be used to summarize observed values and changes from Baseline. Tabular and graphical methods may be used to present results for parameters of interest. Listings will be provided with flags indicating clinically significant abnormalities.

7.4.4. 12-Lead ECGs

The number and percentage of subjects with a clinically significant ECG abnormality (Investigator opinion) will be summarized for each parameter; percentages will be based on subjects with non-missing values.

Descriptive statistics will be used to summarize results and changes from Baseline. Tabular and graphical methods may be used to present results for parameters of interest. Listings will be provided with flags indicating clinically significant abnormalities.

7.5. Analysis Populations

Three analysis populations are defined: Modified Intent-to-Treat (mITT) Population, Per Protocol (PP) Population, and Safety (SAFT) Population. All analysis populations will be defined and determined prior to database closure and unblinding for the final analysis.

Modified Intent-to-Treat Population

7.5.1. Modified Intent-to-Treat Population

The mITT Population is defined as all subjects who were randomized, received their injection of IP, and have at least one post-dosing assessment for the primary effectiveness endpoint. The ITT principle will be followed in that subjects in the mITT population will be analyzed according to the treatment assigned as per the randomization schedule. The mITT Population will be the primary population used for effectiveness analyses of primary, secondary, tertiary, and exploratory effectiveness endpoints.

7.5.2. Per-Protocol Population

The PP Population is defined as treated subjects who complete the entire study up to the final visit with no protocol deviations that could affect effectiveness assessments. The decision whether a protocol violation/deviation is relevant for the exclusion of subjects from the PP Population will be made in a data review meeting prior to breaking the study blind. The PP Population will be used for supportive effectiveness analyses.

7.5.3. Safety Population

The SAFT Population will be used for safety analysis and will consist of all randomized subjects who received treatment with the IP and will be analyzed as per treatment received. The SAFT population will be the primary population for safety analyses.

7.6. Sample Size Considerations

This study is not powered for inferential analyses. Approximately 150 subjects will be randomized to the study, 50 subjects in each of the three treatment arms; 20U onabotulinumtoxinA, 20U prabotulinumtoxinA and 40U prabotulinumtoxinA. Assuming 50 subjects per treatment group, exponential distributions for failure and censoring times, a median duration of effect of 4 months in the reference group, and an annual censoring rate of 10%, the study will have 80% power to detect a hazard ratio of 0.47 based on a one-sided hypothesis test of the primary effectiveness endpoint with alpha = 0.025. As such, it is the opinion of the study Sponsor that 50 subjects per group (total sample size n=150) will be sufficient to address the objectives of this study.

7.7. General Considerations

Data will be listed by subject number. Data will be summarized by treatment and study visit, where applicable. For categorical parameters, the number and percentage of subjects/observations in each category will be presented; percentages will be based on the number of subjects in the relevant analysis population in each treatment group. For continuous parameters, descriptive statistics will include n (number of subjects or observations), mean, standard deviation, median, and range. A full description of the statistical methods planned for this study will be provided in the Statistical Analysis Plan (SAP). All programs for data output and analyses will be written in SAS version 9.4 or higher (SAS Institute, Inc., Cary, NC).

Missing Values: For the mITT analysis of primary, secondary, tertiary, and exploratory duration of effectiveness endpoints, in the case of a missed visit, subjects will be considered to have returned to Baseline if they are confirmed to have returned to Baseline at the next non-missed visit. Subjects will be considered to have to have returned to Baseline if they fail to attend 2 consecutive visits or drop out of the study. For missing observations for exploratory endpoints other than duration of effect data will be analyzed as observed without imputation.

Discontinuation and Drop-Outs: Dropouts will not be replaced. Subject disposition will summarize the number of subjects who were randomized and who discontinued from the study (including reasons for discontinuation).

Interim Analysis: An interim analysis will be conducted when >90% of subjects have completed Visit 8 (Day 120) to evaluate response to exposure (efficacy, duration) and adverse events. For assessment of the primary effectiveness endpoint, 95% CIs will be presented but statistical analyses will not be conducted and a statistical penalty for the final analysis will not be employed. While data by treatment group will be presented, individual subjects will not be unblinded.

Poolability of Investigative Sites: Data from all investigative sites will be pooled based on the assumption of clinical comparability: the same protocol will be used for all sites, all sites will be monitored for protocol compliance, and the same data collection instrument and methodology will be used across all sites.

APPENDIX A: STATISTICAL TABLES

14.1 Subject Disposition

Table 14.1.1 Enrollment

Site	Screened	Screen Failures	Randomized	PP	ITT	SAFT
01	xx	xx	xx	xx	xx	xx
02	xx	xx	xx	xx	xx	xx
03	xx	xx	xx	xx	xx	xx
04	xx	xx	xx	xx	xx	xx
05	xx	xx	xx	xx	xx	xx
All sites	xx	xx	xx	xx	xx	xx

Number of subjects

Table 14.1.2 Subject Discontinuations with Primary Reason

Study Exit		PraB 40 (n = xx)	OnaB 20 (n = xx)	PraB 20 (n = xx)
Completion of Study	N	xx	xx	xx
	Completed up to return to BL	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Primary Reason for d/c* prior to return to BL	N	xx (xx.x%)	xx	xx
	Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Lost to follow- up	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Withdrew consent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Protocol violation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Investigator Decision		xx (xx.x%)	xx (xx.x%)
	Other		xx (xx.x%)	xx (xx.x%)

Number of subjects (% in parenthesis). *d/c= discontinuation

Table 14.1.3 Listing of Subject Discontinuations

Subject Number	Treatment Group	Gender*	Age	Last Visit	Primary Reason for Discontinuation
##-###	PraB 40	M/F	xx	V#	xxxxxxxxxxxxxxxxxx
##-###	PraB 20	M/F	xx	V#	xxxxxxxxxxxxxxxxxx
##-###	OnaB 20	M/F	xx	V#	xxxxxxxxxxxxxxxxxx
##-###	OnaB 20	M/F	xx	V#	xxxxxxxxxxxxxxxxxx
##-###	PraB 40	M/F	xx	V#	xxxxxxxxxxxxxxxxxx
##-###	PraB 20	M/F	xx	V#	xxxxxxxxxxxxxxxxxx
##-###	PraB 40	M/F	xx	V#	xxxxxxxxxxxxxxxxxx
##-###	OnaB 20	M/F	xx	V#	xxxxxxxxxxxxxxxxxx

M=Male, F=Female

Table 14.1.4 Subject Disposition per Visit

Disposition of Subjects at each Study Visit	PraB 40 (n = xx)	OnaB 20 (n = xx)	PraB 20 (n = xx)
N	xx	xx	xx
V1 (screening)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
V2 (pre-Tx)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
V3 (48hr)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
V4 (D7; phone f/u)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
V5 (D30)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
V6 (D60)	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%)
V16 (D365)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Number of subjects (% in parenthesis)

Table 14.1.5 Study Dates

FPFV	LPFV	LPLV	Enrollment Duration	Study Duration
dd-mmm-yyyy	dd-mmm-yyyy	dd-mmm-yyyy	xxx	xxx

FPFV= First Patient First Visit, LPFV= Last Patient First Visit, LPLV= Last Patient Last Visit. Enrollment duration=FPFV-LPFV+1, Study duration=FPFV-LPLV+1

14.2 Demographic, Con-Med, Study Treatment Details

14.2.1 Demographics

Table 14.2.1.1 Demographics

Demographics		PraB 40 (n = xx)	OnaB 20 (n = xx)	PraB 20 (n = xx)
Age	N	xx	xx	xx
	Mean ± SD	xx.x ± xx.x [xx.x,xx.x]	xx.x ± xx.x [xx.x,xx.x]	xx.x ± xx.x [xx.x,xx.x]
	Median (P25, P75)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	Min, Max	xx, xx	xx, xx	xx, xx
	Missing values	xx	xx	xx
BMI	N	xx	xx	xx
	Mean ± SD	xx.x ± xx.x [xx.x,xx.x]	xx.x ± xx.x [xx.x,xx.x]	xx.x ± xx.x [xx.x,xx.x]
	Median (P25, P75)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	Min, Max	xx, xx	xx, xx	xx, xx
	Missing values	xx	xx	xx
Gender	N	xx	xx	xx
	Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Missing values	xx	xx	xx
Race	N	xx	xx	xx
	American Indian or Alaska Native	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Black or African American	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Caucasian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Hawaiian / Pacific Islander	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Missing values	xx	xx	xx
Ethnicity	N	xx	xx	xx
	Hispanic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Non-Hispanic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Missing values	xx	xx	xx
Baseline GLS	N	xx	xx	xx
	Mean ± SD	xx.x ± xx.x [xx.x,xx.x]	xx.x ± xx.x [xx.x,xx.x]	xx.x ± xx.x [xx.x,xx.x]
	Median (P25, P75)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	Moderate (2)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Severe (3)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

95% CI [xx.x,xx.x], Mean ± standard deviation. Number of subjects (% in parenthesis).

14.2.2 Inclusion / Exclusion Criteria

Table 14.2.2.1 Inclusion Criteria

Inclusion Criteria		(n = xx)
Inclusion 1	No	xx (xx.x%)
	Yes	xx (xx.x%)
Inclusion 2	No	xx (xx.x%)
	Yes	xx (xx.x%)
Inclusion 3	No	xx (xx.x%)
	Yes	xx (xx.x%)
…	No	xx (xx.x%)
	Yes	xx (xx.x%)
…	No	xx (xx.x%)
	Yes	xx (xx.x%)
Inclusion 6	No	xx (xx.x%)
	Yes	xx (xx.x%)

Number of subjects (% in parenthesis).

Table 14.2.2.2 Exclusion Criteria

Exclusion Criteria		(n = xx)
Exclusion 1	No	xx (xx.x%)
	Yes	xx (xx.x%)
Exclusion 2	No	xx (xx.x%)
	Yes	xx (xx.x%)
Exclusion 3	No	xx (xx.x%)
	Yes	xx (xx.x%)
…	No	xx (xx.x%)
	Yes	xx (xx.x%)
…	No	xx (xx.x%)
	Yes	xx (xx.x%)
…	No	xx (xx.x%)
	Yes	xx (xx.x%)
Exclusion 22	No	xx (xx.x%)
	Yes	xx (xx.x%)

Number of subjects (% in parenthesis).

14.2.3 Medical / Surgical History

Table 14.2.3.1 Medical / Surgical History

Medical / Surgical History	PraB 40 (n = xx)	OnaB 20 (n = xx)	PraB 20 (n = xx)
1. Blood and lymphatic system disorders	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
2. Cardiac/Vascular disorders	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
3. Eye/Ear and labyrinth disorders	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
4. Endocrine disorders	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
5. Gastrointestinal/Hepatobiliary disorders	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
6. Gen.disorders and administration site conditions	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
7. Immune system disorders	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
8. Infections and infestations	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
9. Injury, poisoning and procedural complications	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
10. Metabolism and nutrition disorders	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
11. Musculoskel. and connective tissue disorders	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
12. Neoplasms benign, malignant and unspecified	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
13. Nervous system disorders	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
14. Psychiatric disorders	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
15. Renal and urinary disorders	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
16. Reproductive system and breast disorders	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
17. Resp., thoracic and mediastinal disorders	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
18. Skin and subcutaneous tissue disorders	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
19. Surgical and medical procedures	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
20. Allergies	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
21. Other	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]

Number of subjects (% in parenthesis).
95% CI [xx.x,xx.x]

14.2.4 Concomitant Medications/Treatment

Table 14.2.4.1 Concomitant Medications/Treatment

Concomitant Medication/Treatment	PraB 40 (n = xx)	OnaB 20 (n = xx)	PraB 20 (n = xx)
xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]
xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]	xx (xx.x%) [xx.x,xx.x]

Number of subjects (% in parenthesis).
95% CI [xx.x,xx.x]

14.3 Efficacy Response Data

14.3.1 Primary Effectiveness Endpoint - Duration of Effect

Table 14.3.1.1 Duration of Effect (Investigator; Regardless of Responder Status; PraB 40 vs PraB 20)

GLS (Investigator) Duration of Effect *(Return to Baseline GLS score)*	**PraB 40** **(n = xx)**	**PraB 20** **(n = xx)**
Subject Status, n (%)		
Returned to BL (event)	xx (xx%)	xx (xx%)
Censored	xx (xx%)	xx (xx%)
Kaplan-Meier Estimates for Return to BL		
1st Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
Median, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
3rd Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
Adjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)	
Stratified Log-Rank p-value	p<x.xxxx	
Unadjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)	
Unstratified Log-Rank p-value	p<x.xxxx	

Data for all subjects regardless of Responder status

Duration of effect in days, calculated from Visit 2 (Treatment Day) to when subject returns to Baseline GLS score

Responder = At least 1-Point improvement in GLS (max frown)

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14.3.2 Secondary Effectiveness Endpoints – Duration of Effect

Table 14.3.2.1 Duration of Effect (Investigator; Regardless of Responder Status; PraB vs OnaB)

GLS (Investigator) Duration of Effect *(Return to Baseline GLS score)*	**PraB 40** **(n = xx)**	**OnaB 20** **(n = xx)**	**PraB 20** **(n = xx)**	**OnaB 20** **(n = xx)**
Subject Status, n (%)				
Returned to BL (event)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Censored	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Kaplan-Meier Estimates for Return to BL				
1st Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Median, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
3rd Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Adjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Stratified Log-Rank p-value	p<x.xxxx		p<x.xxxx	
Unadjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Unstratified Log-Rank p-value	p<x.xxxx		p<x.xxxx	

Data for all subjects regardless of Responder status

Duration of effect in days, calculated from Visit 2 (Treatment Day) to when subject returns to Baseline GLS score

Responder = At least 1-Point improvement in GLS (max frown)

Table 14.3.2.2 Duration of Effect (Subject; Regardless of Responder Status)

GLS (Subject) Duration of Effect *(Return to Baseline GLS score)*	**PraB 40** **(n = xx)**	**PraB 20** **(n = xx)**	**PraB 40** **(n = xx)**	**OnaB 20** **(n = xx)**	**PraB 20** **(n = xx)**	**OnaB 20** **(n = xx)**
Subject Status, n (%)						
Returned to BL (event)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Censored	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Kaplan-Meier Estimates for Return to BL						
1st Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Median, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
3rd Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Adjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Stratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	
Unadjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Unstratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	

Data for all subjects regardless of Responder status

Duration of effect in days, calculated from Visit 2 (Treatment Day) to when subject returns to Baseline GLS score

Responder = At least 1-Point improvement in GLS (max frown)

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Table 14.3.2.3 Duration of Effect for GAIS Responders (Investigator; Score of 2 or 1 at Day 30)

GAIS (Investigator) Duration of Effect *(Return to Baseline GAIS score)*	**PraB 40** **(n = xx)**	**PraB 20** **(n = xx)**	**PraB 40** **(n = xx)**	**OnaB 20** **(n = xx)**	**PraB 20** **(n = xx)**	**OnaB 20** **(n = xx)**
Subject Status, n (%)						
Returned to BL (event)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Censored	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Kaplan-Meier Estimates for Return to BL						
1st Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Median, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
3rd Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Adjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Stratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	
Unadjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Unstratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	

Data for subjects deemed Responder on or before Visit 5 (Day 30)

Duration of effect in days, calculated from Visit 2 (Treatment Day) to when subject returns to Baseline GAIS score

Responder = GAIS score of 2 or 1

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Table 14.3.2.4 Duration of Effect for GAIS Responders (Subject; Score of 2 or 1 at Day 30)

GAIS (Subject) Duration of Effect *(Return to Baseline GAIS score)*	**PraB 40** **(n = xx)**	**PraB 20** **(n = xx)**	**PraB 40** **(n = xx)**	**OnaB 20** **(n = xx)**	**PraB 20** **(n = xx)**	**OnaB 20** **(n = xx)**
Subject Status, n (%)						
Returned to BL (event)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Censored	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Kaplan-Meier Estimates for Return to BL						
1st Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Median, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
3rd Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Adjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Stratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	
Unadjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Unstratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	

Data for subjects deemed Responder on or before Visit 5 (Day 30)

Duration of effect in days, calculated from Visit 2 (Treatment Day) to when subject returns to Baseline GAIS score

Responder = GAIS score of 2 or 1

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Table 14.3.2.5 Duration of Effect for SSS Responders (Subject; Score of 2 or 1 at Day 30)

SSS (Subject) Duration of Effect *(Return to Baseline SSS score)*	**PraB 40** **(n = xx)**	**PraB 20** **(n = xx)**	**PraB 40** **(n = xx)**	**OnaB 20** **(n = xx)**	**PraB 20** **(n = xx)**	**OnaB 20** **(n = xx)**
Subject Status, n (%)						
Returned to BL (event)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Censored	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Kaplan-Meier Estimates for Return to BL						
1st Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Median, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
3rd Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Adjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Stratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	
Unadjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Unstratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	

Data for subjects deemed Responder on or before Visit 5 (Day 30)

Duration of effect in days, calculated from Visit 2 (Treatment Day) to when subject returns to Baseline SSS score

Responder = SSS score of 2 or 1

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14.3.3 Exploratory Effectiveness Endpoints

14.3.3.1 Duration of Effect for GLS Responders - Investigator

Table 14.3.3.1.1 Duration of Effect for GLS Responders (Investigator; 1-Point Responders at any Point During the Study)

GLS (Investigator) Duration of Effect *(Return to Baseline GLS score)*	**PraB 40** **(n = xx)**	**PraB 20** **(n = xx)**	**PraB 40** **(n = xx)**	**OnaB 20** **(n = xx)**	**PraB 20** **(n = xx)**	**OnaB 20** **(n = xx)**
Subject Status, n (%)						
Returned to BL (event)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Censored	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Kaplan-Meier Estimates for Return to BL						
1st Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Median, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
3rd Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Adjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Stratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	
Unadjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Unstratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	

Data for subjects deemed Responder at any point during the study

Duration of effect in days, calculated from Visit 2 (Treatment Day) to when subject returns to Baseline GLS score

Responder = At least 1-Point improvement in GLS (max frown)

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Table 14.3.3.1.2 Duration of Effect for GLS Responders (Investigator; 2-Point Responders at any Point During the Study)

GLS (Investigator) Duration of Effect *(Return to Baseline GLS score)*	**PraB 40** **(n = xx)**	**PraB 20** **(n = xx)**	**PraB 40** **(n = xx)**	**OnaB 20** **(n = xx)**	**PraB 20** **(n = xx)**	**OnaB 20** **(n = xx)**
Subject Status, n (%)						
Returned to BL (event)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Censored	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Kaplan-Meier Estimates for Return to BL						
1st Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Median, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
3rd Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Adjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Stratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	
Unadjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Unstratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	

Data for subjects deemed Responder at any point during the study

Duration of effect in days, calculated from Visit 2 (Treatment Day) to when subject returns to Baseline GLS score

Responder = At least 2-Point improvement in GLS (max frown)

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Table 14.3.3.1.3 Duration of Effect for GLS Responders (Investigator; 3-Point Responders at any Point During the Study)

GLS (Investigator) Duration of Effect *(Return to Baseline GLS score)*	**PraB 40** **(n = xx)**	**PraB 20** **(n = xx)**	**PraB 40** **(n = xx)**	**OnaB 20** **(n = xx)**	**PraB 20** **(n = xx)**	**OnaB 20** **(n = xx)**
Subject Status, n (%)						
Returned to BL (event)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Censored	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Kaplan-Meier Estimates for Return to BL						
1st Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Median, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
3rd Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Adjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Stratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	
Unadjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Unstratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	

Data for subjects deemed Responder at any point during the study

Duration of effect in days, calculated from Visit 2 (Treatment Day) to when subject returns to Baseline GLS score

Responder = At least 3-Point improvement in GLS (max frown)

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Table 14.3.3.1.4 Duration of Effect for GLS Responders (Investigator; GLS Score of 0 or 1 at any Point During the Study)

GLS (Investigator) Duration of Effect *(Return to Baseline GLS score)*	**PraB 40** **(n = xx)**	**PraB 20** **(n = xx)**	**PraB 40** **(n = xx)**	**OnaB 20** **(n = xx)**	**PraB 20** **(n = xx)**	**OnaB 20** **(n = xx)**
Subject Status, n (%)						
Returned to BL (event)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Censored	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Kaplan-Meier Estimates for Return to BL						
1st Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Median, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
3rd Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Adjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Stratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	
Unadjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Unstratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	

Data for subjects deemed Responder at any point during the study

Duration of effect in days, calculated from Visit 2 (Treatment Day) to when subject returns to Baseline GLS score

Responder = GLS Score of 0 or 1

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Table 14.3.3.1.5 Duration of Effect for GLS Responders (Investigator; 1-Point Responders at Day 30)

GLS (Investigator) Duration of Effect *(Return to Baseline GLS score)*	**PraB 40** **(n = xx)**	**PraB 20** **(n = xx)**	**PraB 40** **(n = xx)**	**OnaB 20** **(n = xx)**	**PraB 20** **(n = xx)**	**OnaB 20** **(n = xx)**
Subject Status, n (%)						
Returned to BL (event)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Censored	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Kaplan-Meier Estimates for Return to BL						
1st Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Median, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
3rd Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Adjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Stratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	
Unadjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Unstratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	

Data for subjects deemed Responder at Visit 5 (Day 30)

Duration of effect in days, calculated from Visit 2 (Treatment Day) to when subject returns to Baseline GLS score

Responder = At least 1-Point improvement in GLS (max frown).

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Table 14.3.3.1.6 Time to Loss of GLS Responder Status (Investigator; Score of 0 or 1 at any Point During the Study)

GLS (Investigator) Duration of Effect *(Return to Score 2 or higher)*	**PraB 40** **(n = xx)**	**PraB 20** **(n = xx)**	**PraB 40** **(n = xx)**	**OnaB 20** **(n = xx)**	**PraB 20** **(n = xx)**	**OnaB 20** **(n = xx)**
Subject Status, n (%)						
Returned to BL (event)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Censored	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Kaplan-Meier Estimates for Return to BL						
1st Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Median, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
3rd Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Adjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Stratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	
Unadjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Unstratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	

Data for subjects deemed Responder at any point during the study

Time to Loss of Responder Status = Days from Treatment to first returning back to Score 2 or higher, after achieving Score 0 or 1

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14.3.3.2 Duration of Effect for GLS Responders - Subject

Table 14.3.3.2.1 Duration of Effect for GLS Responders (Subject; 1-Point Responders at any Point During the Study)

GLS (Subject) Duration of Effect *(Return to Baseline GLS score)*	**PraB 40** **(n = xx)**	**PraB 20** **(n = xx)**	**PraB 40** **(n = xx)**	**OnaB 20** **(n = xx)**	**PraB 20** **(n = xx)**	**OnaB 20** **(n = xx)**
Subject Status, n (%)						
Returned to BL (event)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Censored	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Kaplan-Meier Estimates for Return to BL						
1st Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Median, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
3rd Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Adjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Stratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	
Unadjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Unstratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	

Data for subjects deemed Responder at any point during the study

Duration of effect in days, calculated from Visit 2 (Treatment Day) to when subject returns to Baseline GLS score

Responder = At least 1-Point improvement in GLS (max frown)

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Table 14.3.3.2.2 Duration of Effect for GLS Responders (Subject; 2-Point Responders at any Point During the Study)

GLS (Subject) Duration of Effect *(Return to Baseline GLS score)*	**PraB 40** **(n = xx)**	**PraB 20** **(n = xx)**	**PraB 40** **(n = xx)**	**OnaB 20** **(n = xx)**	**PraB 20** **(n = xx)**	**OnaB 20** **(n = xx)**
Subject Status, n (%)						
Returned to BL (event)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Censored	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Kaplan-Meier Estimates for Return to BL						
1st Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Median, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
3rd Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Adjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Stratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	
Unadjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Unstratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	

Data for subjects deemed Responder at any point during the study

Duration of effect in days, calculated from Visit 2 (Treatment Day) to when subject returns to Baseline GLS score

Responder = At least 2-Point improvement in GLS (max frown)

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Table 14.3.3.2.3 Duration of Effect for GLS Responders (Subject; 3-Point Responders at any Point During the Study)

GLS (Subject) Duration of Effect *(Return to Baseline GLS score)*	**PraB 40** **(n = xx)**	**PraB 20** **(n = xx)**	**PraB 40** **(n = xx)**	**OnaB 20** **(n = xx)**	**PraB 20** **(n = xx)**	**OnaB 20** **(n = xx)**
Subject Status, n (%)						
Returned to BL (event)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Censored	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Kaplan-Meier Estimates for Return to BL						
1st Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Median, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
3rd Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Adjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Stratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	
Unadjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Unstratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	

Data for subjects deemed Responder at any point during the study

Duration of effect in days, calculated from Visit 2 (Treatment Day) to when subject returns to Baseline GLS score

Responder = At least 3-Point improvement in GLS (max frown)

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Table 14.3.3.2.4 Duration of Effect for GLS Responders (Subject; Score of 0 or 1 at any Point During the Study)

GLS (Subject) Duration of Effect *(Return to Baseline GLS score)*	**PraB 40** **(n = xx)**	**PraB 20** **(n = xx)**	**PraB 40** **(n = xx)**	**OnaB 20** **(n = xx)**	**PraB 20** **(n = xx)**	**OnaB 20** **(n = xx)**
Subject Status, n (%)						
Returned to BL (event)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Censored	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Kaplan-Meier Estimates for Return to BL						
1st Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Median, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
3rd Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Adjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Stratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	
Unadjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Unstratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	

Data for subjects deemed Responder at any point during the study

Duration of effect in days, calculated from Visit 2 (Treatment Day) to when subject returns to Baseline GLS score

Responder = GLS Score of 0 or 1.

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Table 14.3.3.2.5 Duration of Effect for GLS Responders (Subject; 1-Point Responders at Day 30)

GLS (Subject) Duration of Effect *(Return to Baseline GLS score)*	**PraB 40** **(n = xx)**	**PraB 20** **(n = xx)**	**PraB 40** **(n = xx)**	**OnaB 20** **(n = xx)**	**PraB 20** **(n = xx)**	**OnaB 20** **(n = xx)**
Subject Status, n (%)						
Returned to BL (event)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Censored	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Kaplan-Meier Estimates for Return to BL						
1st Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Median, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
3rd Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Adjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Stratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	
Unadjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Unstratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	

Data for subjects deemed Responder at Visit 5 (Day 30)

Duration of effect in days, calculated from Visit 2 (Treatment Day) to when subject returns to Baseline GLS score

Responder = At least 1-Point improvement in GLS (max frown).

<< Insert KM Curve >>

Table 14.3.3.2.6 Time to Loss of GLS Responder Status (Subject; Score of 0 or 1 at any Point During the Study)

GLS (Subject) Duration of Effect *(Return to Score 2 or higher)*	**PraB 40** **(n = xx)**	**PraB 20** **(n = xx)**	**PraB 40** **(n = xx)**	**OnaB 20** **(n = xx)**	**PraB 20** **(n = xx)**	**OnaB 20** **(n = xx)**
Subject Status, n (%)						
Returned to BL (event)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Censored	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Kaplan-Meier Estimates for Return to BL						
1st Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Median, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
3rd Quartile, (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Adjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Stratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	
Unadjusted Hazard Ratio (95% CI)	x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)		x.xx (x.xx, x.xx)	
Unstratified Log-Rank p-value	p<x.xxxx		p<x.xxxx		p<x.xxxx	

Data for subjects deemed Responder at any point during the study

Time to Loss of Responder Status = Days from Treatment to first returning back to Score 2 or higher, after achieving Score 0 or 1

14.3.3.3 GLS Responder Rates

Table 14.3.3.3.1 GLS Responder Rates (Investigator)

GLS Responder Rate Investigator		PraB 40 (n = xx)	PraB 20 (n = xx)	OnaB 20 (n = xx)	P-value / OR		
					PraB-40 vs. PraB-20	PraB-40 vs. OnaB-20	PraB-20 vs. OnaB-20
V3 (48hrs)	N	xx	xx	xx			
≥1-Point	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
≥2-Point	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
≥3-Point	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
Score 0 or 1	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
Score 0 or 1 **&** ≥2-Point improvement	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
Score 0 or 1 **&** ≥2-Point improvement **&** Inv. GLS = subject GLS	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
….	N	xx	xx	xx			
≥1-Point	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
≥2-Point	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
≥3-Point	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
……..	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx

95% CI [xx.x,xx.x]

<< Insert graphs for each Responder type >>

Table 14.3.3.3.2 GLS Responder Rates (Subject)

GLS Responder Rate Subject		PraB 40 (n = xx)	PraB 20 (n = xx)	OnaB 20 (n = xx)	P-value / OR PraB-40 vs. PraB-20	 PraB-40 vs. OnaB-20	 PraB-20 vs. OnaB-20
V3 (48hrs)	N	xx	xx	xx			
≥1-Point	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
≥2-Point	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
≥3-Point	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
Score 0 or 1	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
….	N	xx	xx	xx			
≥1-Point	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
≥2-Point	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
≥3-Point	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
Score 0 or 1	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx

95% CI [xx.x,xx.x]

<< Insert graphs for each Responder type >>

14.3.3.4 GAIS Responder Rates

Table 14.3.3.4.1 GAIS Responder Rates (Investigator)

GAIS Responder Rate Investigator		PraB 40 (n = xx)	PraB 20 (n = xx)	OnaB 20 (n = xx)	P-value PraB-40 vs. PraB-20	P-value PraB-40 vs. OnaB-20	P-value PraB-20 vs. OnaB-20
V3 (48hrs)	N	xx	xx	xx			
Score 2 or 1	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
V5 (D30)	N	xx	xx	xx			
Score 2 or 1	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
….	N	xx	xx	xx			
Score 2 or 1	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx

95% CI [xx.x,xx.x]

<< Insert graph>>

Table 14.3.3.4.2 GAIS Responder Rates (Subject)

GAIS Responder Rate Subject		PraB 40 (n = xx)	PraB 20 (n = xx)	OnaB 20 (n = xx)	P-value PraB-40 vs. PraB-20	P-value PraB-40 vs. OnaB-20	P-value PraB-20 vs. OnaB-20
V3 (48hrs)	N	xx	xx	xx			
Score 2 or 1	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
V5 (D30)	N	xx	xx	xx			
Score 2 or 1	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
….	N	xx	xx	xx			
Score 2 or 1	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx

95% CI [xx.x,xx.x]

<< Insert graph>>

14.3.3.5 SSS Responder Rates

Table 14.3.3.5.1 SSS Responder Rates (Subject)

SSS Responder Rate Subject		PraB 40 (n = xx)	PraB 20 (n = xx)	OnaB 20 (n = xx)	P-value PraB-40 vs. PraB-20	P-value PraB-40 vs. OnaB-20	P-value PraB-20 vs. OnaB-20
V3 (48hrs)	N	xx	xx	xx			
Score 2 or 1	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
V5 (D30)	N	xx	xx	xx			
Score 2 or 1	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx
….	N	xx	xx	xx			
Score 2 or 1	Percent, CI 95%	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	xx.x% [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx

95% CI [xx.x,xx.x]

<< Insert graph>>

14.3.3.6 Onset of Effect

Table 14.3.3.6.1 Onset of Effect (Subject)

Onset of Effect (Days)		PraB 40 (n = xx)	PraB 20 (n = xx)	OnaB 20 (n = xx)	P-value PraB-40 vs. PraB-20	P-value PraB-40 vs. OnaB-20	P-value PraB-20 vs. OnaB-20
Onset	N	xx	xx	xx			
	Days, CI 95%	x.x ± x.x [xx.x, xx.x]	x.x ± x.x [xx.x, xx.x]	x.x ± x.x [xx.x, xx.x]	x.xxxx	x.xxxx	x.xxxx
	OR (95% CI)				x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)	x.xxxx (xx.x, xx.x)
	OR (p-value)				x.xxxx	x.xxxx	x.xxxx

95% CI [xx.x,xx.x]

Based on 7-day subject diary

<< Insert graph>>

14.4 Safety Data

14.4.1 Adverse Events

Table 14.4.1.1 Adverse Event Profile Overview

Adverse Events – All Subjects		PraB 40 (n = xx)	PraB 20 (n = xx)	OnaB 20 (n = xx)
Participants with any TEAE[a]	Participants	xx (xx.x%) [xx.x, xx.x]	xx (xx.x%) [xx.x, xx.x]	xx (xx.x%) [xx.x, xx.x]
	Events	xxx	xxx	xxx
	Events/Participants	xxx	xxx	xxx
Participants with any TRAE[b]	Participants	xx (xx.x%) [xx.x, xx.x]	xx (xx.x%) [xx.x, xx.x]	xx (xx.x%) [xx.x, xx.x]
	Events	xxx	xxx	xxx
	Events/Participants	xxx	xxx	xxx
Participants with SAE[c]	Participants	xx (xx.x%) [xx.x, xx.x]	xx (xx.x%) [xx.x, xx.x]	xx (xx.x%) [xx.x, xx.x]
	Events	xxx	xxx	xxx
	Events/Participants	xxx	xxx	xxx
Participants with any TRSAE[d]	Participants	x (xx.x%) [xx.x, xx.x]	xx (xx.x%) [xx.x, xx.x]	xx (xx.x%) [xx.x, xx.x]
	Events	xxx	xxx	xxx
	Events/Participants	xxx	xxx	xxx
Participants with UADR[e]	Participants	xx (xx.x%) [xx.x, xx.x]	xx (xx.x%) [xx.x, xx.x]	xx (xx.x%) [xx.x, xx.x]
	Events	xxx	xxx	xxx
	Events/Participants	xxx	xxx	xxx
Participants with AESI[f]	Participants	xx (xx.x%) [xx.x, xx.x]	xx (xx.x%) [xx.x, xx.x]	xx (xx.x%) [xx.x, xx.x]
	Events	xxx	xxx	xxx
	Events/Participants	xxx	xxx	xxx

95% CI [xx.x, xx.x]. [a]TEAE= Treatment-Emergent AE. [b]TRAE= Treatment-Related AE. [c]SAE= Serious AE. [d]TRSAE= Treatment-Related SAE. [e]UADR= Unexpected Adverse Drug Reaction. [f]AESI= Adverse Effect of Special Interest. Number of Participants (% in parenthesis).

Table 14.4.1.2 Treatment-Emergent Adverse Events Sorted by SOC and PT

		PraB 40 (n = xx)		PraB 20 (n = xx)		OnaB 20 (n = xx)	
SOC	**PT**	**Participants**	**Events**	**Participants**	**Events**	**Participants**	**Events**
Any TEAE		xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
XXXXXXX		xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
	XXXXXXX	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
XXXXXXX		xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
	XXXXXXX	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx

95% CI [xx.x, xx.x] Number of Participants (% in parenthesis).

Table 14.4.1.3 Treatment-Related Adverse Events Sorted by SOC and PT

		PraB 40 (n = xx)		PraB 20 (n = xx)		OnaB 20 (n = xx)	
SOC	**PT**	**Participants**	**Events**	**Participants**	**Events**	**Participants**	**Events**
Any TRAE		xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
XXXXXXX		xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
	XXXXXXX	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
XXXXXXX		xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
	XXXXXXX	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx

95% CI [xx.x, xx.x] Number of Participants (% in parenthesis).

Table 14.4.1.4 Treatment-Emergent Serious Adverse Events Sorted by SOC and PT

		PraB 40 (n = xx)		PraB 20 (n = xx)		OnaB 20 (n = xx)	
SOC	**PT**	**Participants**	**Events**	**Participants**	**Events**	**Participants**	**Events**
Any TESAE		xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
XXXXXXX		xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
	XXXXXXX	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
XXXXXXX		xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
	XXXXXXX	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx

95% CI [xx.x, xx.x] Number of Participants (% in parenthesis).

Table 14.4.1.5 Treatment-Related Serious Adverse Events Sorted by SOC and PT

		PraB 40 (n = xx)		PraB 20 (n = xx)		OnaB 20 (n = xx)	
SOC	**PT**	**Participants**	**Events**	**Participants**	**Events**	**Participants**	**Events**
Any TRSAE		xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
XXXXXXX		xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
	XXXXXXX	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
XXXXXXX		xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
	XXXXXXX	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx

95% CI [xx.x, xx.x] Number of Participants (% in parenthesis).

Table 14.4.1.6 Unexpected Adverse Drug Reactions Sorted by SOC and PT

		PraB 40 (n = xx)		PraB 20 (n = xx)		OnaB 20 (n = xx)	
SOC	**PT**	**Participants**	**Events**	**Participants**	**Events**	**Participants**	**Events**
Any UADR		xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
XXXXXXX		xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
	XXXXXXX	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
XXXXXXX		xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
	XXXXXXX	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx

95% CI [xx.x, xx.x] Number of Participants (% in parenthesis).

Table 14.4.1.7 Adverse Events of Special Interest Sorted by SOC and PT

		PraB 40 (n = xx)		PraB 20 (n = xx)		OnaB 20 (n = xx)	
SOC	**PT**	**Participants**	**Events**	**Participants**	**Events**	**Participants**	**Events**
Any AESI		xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
XXXXXXX		xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
	XXXXXXX	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
XXXXXXX		xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx
	XXXXXXX	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx	xx (xx.x%) [xx.x, xx.x]	xx

95% CI [xx.x, xx.x] Number of Participants (% in parenthesis).

14.4.2 Shift Tables

Table 14.4.2.1 Safety Laboratory Shift Tables

Parameter: e.g., Hemoglobin												
	PraB 40 (n = xx) Baseline				**PraB 20 (n = xx) Baseline**				**OnaB 20 (n = xx) Baseline**			
Timepoint	Low	Normal	High	Total	Low	Normal	High	Total	Low	Normal	High	Total
Final Visit												
Low	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Normal	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
High	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Total	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)

Shift from Baseline
(x.x%) = proportion of subjects

Table 14.4.2.2 ECG Shift Tables

Parameter: e.g., PR Interval												
	PraB 40 (n = xx) Baseline				**PraB 20 (n = xx) Baseline**				**OnaB 20 (n = xx) Baseline**			
Timepoint	Normal	Abnormal (NCS)	Abnormal (CS)	Total	Normal	Abnormal (NCS)	Abnormal (CS)	Total	Normal	Abnormal (NCS)	Abnormal (CS)	Total
Final Visit												
Normal	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Abnormal (NCS)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Abnormal (CS)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Total	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)

Shift from Baseline
(x.x%) = proportion of subjects

Table 14.4.2.3 Physical Exam Shift Tables

Parameter: e.g., Respiratory System												
	PraB 40 (n = xx) Baseline				**PraB 20 (n = xx) Baseline**				**OnaB 20 (n = xx) Baseline**			
Timepoint	Normal	Abnormal (NCS)	Abnormal (CS)	Total	Normal	Abnormal (NCS)	Abnormal (CS)	Total	Normal	Abnormal (NCS)	Abnormal (CS)	Total
V3 (48hr)												
Normal	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Abnormal (NCS)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Abnormal (CS)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Total	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
V5 (D30)												
Normal	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Abnormal (NCS)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Abnormal (CS)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Total	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
….												
Normal	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Abnormal (NCS)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Abnormal (CS)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Total	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
V16 (D365)												
Normal	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Abnormal (NCS)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Abnormal (CS)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Total	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)

Shift from Baseline
(x.x%) = proportion of subjects

14.4.3 Directed Review of Systems

Table 14.4.3.1 Directed Review of Systems

Parameter: e.g., Head and Neck												
	PraB 40 (n = xx) Baseline				**PraB 20 (n = xx) Baseline**				**OnaB 20 (n = xx) Baseline**			
Timepoint	Normal	Abnormal (NCS)	Abnormal (CS)	Total	Normal	Abnormal (NCS)	Abnormal (CS)	Total	Normal	Abnormal (NCS)	Abnormal (CS)	Total
V3 (48hr)												
Normal	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Abnormal (NCS)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Abnormal (CS)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Total	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
V5 (D30)												
Normal	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Abnormal (NCS)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Abnormal (CS)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Total	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
….												
Normal	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Abnormal (NCS)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Abnormal (CS)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Total	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
V16 (D365)												
Normal	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Abnormal (NCS)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Abnormal (CS)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Total	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)

Shift from Baseline
(x.x%) = proportion of subjects

14.4.4 Vital Signs

Table 14.4.4.1 Vital Signs - SBP

V1 (BL)	PraB 40 (n = xx)	PraB 20 (n = xx)	OnaB 20 (n = xx)
V1 (BL)	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x
SBP (mean ± SD)	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x
V3 (48hr)			
SBP (mean ± SD)	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x
Δ from BL	xx.x ± xx.x	xx.x ± xx.x	xx.x ± xx.x
….			
SBP (mean ± SD)	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x
Δ from BL	xx.x ± xx.x	xx.x ± xx.x	xx.x ± xx.x
Normal	xx (x.x%)	xx (x.x%)	xx (x.x%)

Table 14.4.4.2 Vital Signs - DBP

V1 (BL)	PraB 40 (n = xx)	PraB 20 (n = xx)	OnaB 20 (n = xx)
V1 (BL)	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x
DBP (mean ± SD)	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x
V3 (48hr)			
DBP (mean ± SD)	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x
Δ from BL	xx.x ± xx.x	xx.x ± xx.x	xx.x ± xx.x
….			
DBP (mean ± SD)	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x
Δ from BL	xx.x ± xx.x	xx.x ± xx.x	xx.x ± xx.x
Normal	xx (x.x%)	xx (x.x%)	xx (x.x%)

Table 14.4.4.3 Vital Signs - HR

V1 (BL)	PraB 40 (n = xx)	PraB 20 (n = xx)	OnaB 20 (n = xx)
V1 (BL)	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x
HR (mean ± SD)	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x
V3 (48hr)			
HR (mean ± SD)	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x
Δ from BL	xx.x ± xx.x	xx.x ± xx.x	xx.x ± xx.x
….			
HR (mean ± SD)	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x
Δ from BL	xx.x ± xx.x	xx.x ± xx.x	xx.x ± xx.x
Normal	xx (x.x%)	xx (x.x%)	xx (x.x%)

Table 14.4.4.4 Vital Signs – Respiratory Rate (RR)

V1 (BL)	PraB 40 (n = xx)	PraB 20 (n = xx)	OnaB 20 (n = xx)
V1 (BL)	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x
RR (mean ± SD)	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x
V3 (48hr)			
RR (mean ± SD)	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x
Δ from BL	xx.x ± xx.x	xx.x ± xx.x	xx.x ± xx.x
….			
RR (mean ± SD)	xxx.x ± xx.x	xxx.x ± xx.x	xxx.x ± xx.x
Δ from BL	xx.x ± xx.x	xx.x ± xx.x	xx.x ± xx.x
Normal	xx (x.x%)	xx (x.x%)	xx (x.x%)

14.4.5 Vital Signs

Table 14.4.5.1 Directed Questionnaire

	PraB 40 (n = xx)		PraB 20 (n = xx)		OnaB 20 (n = xx)	
V1 (BL)	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**
Speaking	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Swallowing	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Breathing	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Headaches	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Eyelid Drooping	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Eyebrow Drooping	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
V3 (48hr)						
Speaking	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Swallowing	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Breathing	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Headaches	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Eyelid Drooping	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Eyebrow Drooping	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
V5 (D30)						
Speaking	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Swallowing	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Breathing	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Headaches	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Eyelid Drooping	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Eyebrow Drooping	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
…..						
Speaking	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Swallowing	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Breathing	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Headaches	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Eyelid Drooping	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)
Eyebrow Drooping	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)	xx (x.x%)

Shift from Baseline
(x.x%) = proportion of subjects

14.4.6 Antitoxin Antibodies

Table 14.4.6.1 Presence of Antibodies

	PraB 40 (n = xx)		PraB 20 (n = xx)		OnaB 20 (n = xx)	
	Yes	**No**	**Yes**	**No**	**Yes**	**No**
V1 (BL)	n=xx xx (x.x%)	xx (x.x%)	n=xx xx (x.x%)	xx (x.x%)	n=xx xx (x.x%)	xx (x.x%)
V3 (48hr)	n=xx xx (x.x%)	xx (x.x%)	n=xx xx (x.x%)	xx (x.x%)	n=xx xx (x.x%)	xx (x.x%)
V5 (D30	n=xx xx (x.x%)	xx (x.x%)	n=xx xx (x.x%)	xx (x.x%)	n=xx xx (x.x%)	xx (x.x%)
V6 (D60)	n=xx xx (x.x%)	xx (x.x%)	n=xx xx (x.x%)	xx (x.x%)	n=xx xx (x.x%)	xx (x.x%)
…..	n=xx xx (x.x%)	xx (x.x%)	n=xx xx (x.x%)	xx (x.x%)	n=xx xx (x.x%)	xx (x.x%)

xx (x.x%) = number of subjects (proportion of subjects)