STATISTICAL ANALYSIS PLAN

PROTOCOL NO: NCIG-006

Randomized, Double Blind, Placebo-Controlled Trial of the Safety and Efficacy of HORIZANT® (Gabapentin Enacarbil) Extended-Release Tablets for the Treatment of Alcohol Use Disorder

Protocol Version No.: 5.0 **Version Date:** 18Aug2016

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Version Number 2.0

Date: 22 August 2016

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Table of Contents

List of Tables

List of Listings

List of Figures

1. ABBREVIATIONS

Abbreviation	Definition
ACQ-SR-R	Alcohol Craving Scale – Short Form
AE	Adverse event
AICc	Akaike Information Criterion corrected for finite samples
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
AUC	Area under the concentration time curve
AUD	Alcohol Use Disorder
BAC	Blood alcohol concentration
BAI	Beck Anxiety Inventory
BDI-II	Beck Depression Inventory-II
BID	Twice daily
BIS	Barratt Impulsiveness Scale
CFR	Code of Federal Regulations
CI	Confidence interval
CIWA-AR	Clinical Institute Withdrawal Assessment for Alcohol-revised
CrCl	Creatinine clearance
C-SSRS	Columbia-Suicide Severity Rating Scale
CTCAE	Common terminology criteria for adverse events
dL	Deciliter
DNA	Deoxyribonucleic acid
DSM-5	Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition
DSMB	Data and Safety Monitoring Board
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
EDMS	Electronic Data Management System
EOS	End of study
F	Fahrenheit
FDA	Food and Drug Administration
g	Gram
GCP	Good Clinical Practice
GGT	Gamma-glutamyl transferase
hr	Hour
ICH	International Conference on Harmonization
IRB	Institutional Review Board
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
µg	Microgram
min	Minutes

Abbreviation	Definition
MINI	MINI Neuropsychiatric Interview
mITT	Modified intention-to-treat
mL	Milliliter
mm	Millimeter
NHDD	No heavy drinking days
NIAAA	National Institutes on Alcohol Abuse and Alcoholism
oz	Ounce
PD	Pharmacodynamic
PEth	Phosphatidylethanol
PK	Pharmacokinetic
POMS	Profile of Mood State
PSNHDD	Percentage of subjects with no heavy drinking days
PSQI	Pittsburg Sleep Quality Index
PT	Preferred term
RNA	Ribonucleic acid
ROC	Receiver Operator Curve
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Standard deviation
SDU	Standard drinking unit
SOC	System Organ Class
THC	Tetrahydrocannabinol
TLFB	Timeline followback
ULN	Upper limit of normal
WHO	World Health Organization

2. INTRODUCTION

This statistical analysis plan (SAP) for Protocol No. NCIG-006, "Randomized, Double Blind, Placebo-Controlled Trial of the Safety and Efficacy of HORIZANT® (Gabapentin Enacarbil) Extended-Release Tablets for the Treatment of Alcohol Use Disorder" describes and expands upon the analytical plan presented in the protocol.

This document contains all planned analyses, reasons and justifications for these analyses for all study data with the exception of the pharmacokinetics data. The population pharmacokinetic/pharmacodynamic (PK/PD) analysis will be described in a separate population PK/PD analysis plan that will be authored and performed by XenoPort, Inc. This plan also includes sample tables, figures, and listings that will be populated. The SAP will follow the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines as indicated in Topic E3 (Structure and Content of Clinical Study Reports), Topic E8 (General Considerations for Clinical Trials) and Topic E9 (Statistical Principles for Clinical Trials). The structure and content of the SAP provides sufficient detail to meet the requirements identified by the FDA and ICH.

The following sources were used in preparation of this SAP:

- Protocol # NCIG-006, Protocol Version No.: 3.0; Version Date: 18 May 2015
- ICH Guidance Topics E9, E3 and E8

3. PROTOCOL SUMMARY

3.1. Study Objectives

3.1.1. Primary

The primary objective of the study is to compare the efficacy of HORIZANT (gabapentin enacarbil) Extended-Release Tablets 600 mg twice daily (BID) with matched placebo on the primary alcohol consumption outcome endpoint, percentage of subjects with no heavy drinking days (PSNHDD) during the last 4 weeks of treatment, among patients with Alcohol Use Disorder (AUD). PSNHDD will also be analyzed during other time periods (i.e., the last 8, 12, 16, 20, and 24 weeks of the maintenance period) in exploratory analyses (see 9.11.4).

3.1.2. Secondary

Secondary objectives are separated into two categories: key secondary and supportive secondary. The key secondary objective is to compare HORIZANT to placebo on the percentage of subjects abstinent from alcohol during the last 4 weeks of treatment. The supportive secondary study objectives are to assess other treatment benefits including: reduction in other alcohol consumption endpoints, alcohol-related craving and consequences, mood, sleep quality, smoking quantity and frequency, and safety.

3.2. Study Design

This study is a double-blind, randomized, placebo-controlled, parallel group, multi-site study designed to assess the efficacy of HORIZANT Extended-Release Tablets compared with placebo to reduce drinking in 346 subjects (173 in each group) who report 4 or more Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition (DSM-5™) symptoms of AUD and who meet the drinking criteria outlined hereafter. This study will be conducted at 10 clinical sites. If eligible for the study, subjects will be randomized using a stratified permuted block randomization procedure with "clinical site" as the stratification variable in an approximate 1:1 ratio (targeting 173 subjects per group) to receive either HORIZANT Extended-Release Tablets or placebo for 26 weeks (1 week escalation; 24 weeks maintenance; 1 week taper).

Subjects will be seen in the clinic at screening, at randomization and 11 other times during the study. During the Week 1 dose escalation period (midway through the week) and during the maintenance period (Weeks 2 to 25), subjects will be contacted once per week by telephone at non-clinic visit weeks to encourage study drug compliance and to assess withdrawal, adverse events (AEs), and concomitant medications. A final follow-up telephone interview will occur during Weeks 28 to 29 (1 to 2 weeks after the end of dosing).

An overview of the study design is provided in **Figure 1**. Study assessments and procedures will be performed at the visits and time points outlined in the Schedule of Assessments (**Table 1**).

Figure 1: Overview of Study Design

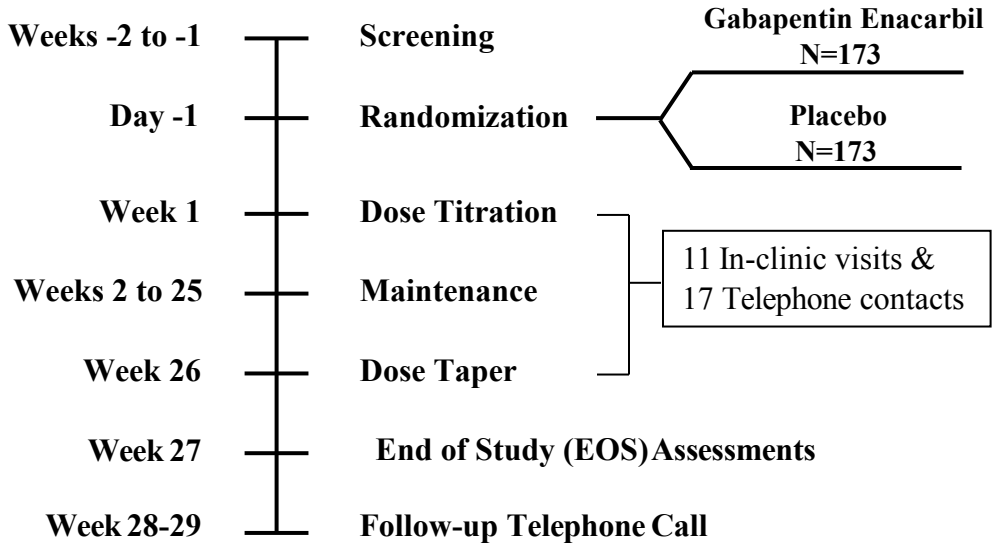


Table 1: Schedule of Assessments

	Screen		Ti-trate	Maintenance																		Taper		Safety Follow-up
Clinic Visit #	**0**	**1**		**2**		**3**		**4**		**5**		**6**		**7**		**8**		**9**		**10**		**11**	**12**	
Study Week	**-2 to -1**	**Day -1**	**1**	**2**	**Mid week 2 & 3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13 - 15**	**16**	**17-19**	**20**	**21-23**	**24**	**25**	**26**	**EOS[a] /27**	**28-29**
Informed Consent	X																							
Alcohol Breathalyzer	X	X		X		X		X		X		X		X		X		X		X		X	X	
Urine Drug Screen[b]	X	X		X		X		X		X		X		X		X		X		X		X	X	
Locator Form	X																							
Demographics	X																							
Medical History	X	X																						
Physical Exam	X	X																					X	
MINI V 7.0	X																					X[c]		
Clinical Chemistry[d]	X					X				X				X		X		X		X		X	X	
Vital Signs[e]	X	X				X				X				X		X		X		X		X	X	
ECG	X																						X	
Prior and Concomitant Meds	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
CIWA-AR	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Eligibility Checklist	X	X																						
Blood for DNA Genomics Testing[f]		X																						
Blood for RNA Expression Testing		X																		X				
Blood for PK/Medication Compliance[g]														X				X		X				
Blood spot for PEth		X																				X		
Drug compliance/ accountability				X		X		X		X		X		X		X		X		X		X	X	

	Screen		Ti-trate	Maintenance																		Taper		Safety Follow-up
Clinic Visit #	**0**	**1**		**2**		**3**		**4**		**5**		**6**		**7**		**8**		**9**		**10**		**11**	**12**	
Study Week	**-2 to -1**	**Day -1**	**1**	**2**	**Mid week 2 & 3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13 - 15**	**16**	**17-19**	**20**	**21-23**	**24**	**25**	**26**	**EOS[a] /27**	**28-29**
Pregnancy Test + birth control	X	X				X				X				X		X		X		X			X	
Weight	X															X							X	
Drinking Goal		X																						
AEs	X[h]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
C-SSRS		X		X		X		X		X		X		X	14	X	18	X	22	X		X	X	
RANDOMIZATION		X																						
Brief Telephone Interview[i]			X		X		X		X		X		X		X		X		X		X			
Take Control		X		X		X		X		X		X		X		X		X		X		X		
Exit Interview																							X	
Treatment Referral																							X	
Follow-Up Telephone Interview			7																					X
Final Subject Disposition																								X
Subject Reported Outcomes																								
Family History of Alcohol Problems		X																						
BIS		X																				X		
ImBIBe		X				X				X				X		X		X		X		X		
TLFB	X	X		X		X		X		X		X		X		X		X		X		X	X	
Drinking question[j]				X		X		X		X		X		X		X		X		X		X	X	
ACQ-SR-R		X		X		X		X		X		X		X		X		X		X		X		
Fagerström Test for Nicotine Dependence		X																						
Smoking quantity/frequency		X		X		X		X		X		X		X		X		X		X		X	X	

	Screen		Ti-trate	Maintenance																		Taper		Safety Follow-up
Clinic Visit #	**0**	**1**		**2**		**3**		**4**		**5**		**6**		**7**		**8**		**9**		**10**		**11**	**12**	
Study Week	**-2 to -1**	**Day -1**	**1**	**2**	**Mid week 2 & 3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13 - 15**	**16**	**17-19**	**20**	**21-23**	**24**	**25**	**26**	**EOS[a] /27**	**28-29**
PSQI		X				X				X				X		X		X		X		X		
BAI		X				X				X				X		X		X		X		X		
BDI-II		X				X				X				X		X		X		X		X		
POMS		X				X				X				X		X		X		X		X		
Other Services Used for Alcohol Use Problems		X				X				X				X		X		X		X			X	

[a]EOS=end of study. These assessments are to be done at Week 27 or if the subject discontinues early and agrees to a final clinic visit.
[b]Test for opioids, cocaine, amphetamines, methamphetamine, tetrahydrocannabinol (THC), buprenorphine, methadone or benzodiazepines.
[c]Only the AUD module is performed at Week 26.
[d]Aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, creatinine, and gamma glutamyltransferase (GGT).
[e]Sitting blood pressure and heart rate.
[f]Only for subjects who consent to provide this sample.
[g]For each subject, blood collections should be scheduled at different times relative to the morning dose at these 3 clinic visits.
[h]Only serious adverse events (SAEs) will be reported from the time of signing informed consent until the first dose of investigational product administration. Thereafter, AEs and SAEs will be reported for the duration of the study.
[i]AEs, concomitant medications, CIWA-AR, and drug compliance reminder.
[j]Only asked to subjects who are no longer participating in clinic visits and not willing to providing TLFB drinking data.

3.3. Study Endpoints

3.3.1. Primary Efficacy Endpoint

The primary efficacy endpoint examines the hypothesis that HORIZANT Extended-Release Tablets will increase the percentage of subjects with no heavy drinking days (PSNHDD) compared to placebo during the last 4 weeks of maintenance period of treatment (Study Weeks 22-25). A "heavy drinking day" is 4 or more drinks per drinking day for women and 5 or more drinks per drinking day for men. PSNHDD will also be analyzed during other time periods (i.e., the last 8, 12, 16, 20, and 24 weeks of the maintenance period) in exploratory analyses (see 9.11.4). In all of these analyses, a different "grace peiod" is being explored.

3.3.2. Secondary Efficacy Endpoints

Secondary endpoints will be analyzed over the last 4 weeks of the maintenance phase of treatment.

1. Percentage of subjects abstinent from alcohol (key secondary endpoint)
2. Percentage of subjects with a World Health Organization (WHO) drinking risk category decrease of:
    a. at least 1-level
    b. at least 2-levels
3. Percentage of days abstinent per week
4. Percentage of heavy drinking days per week
5. Weekly mean number of drinks per week
6. Weekly mean drinks per drinking day
7. Cigarettes per week among smokers
8. Alcohol craving score [Alcohol Craving Scale – Short Form (ACQ-SR-R)]
9. Alcohol related consequences (ImBIBe) score
10. Pittsburg Sleep Quality Index (PSQI) score
11. Beck Anxiety Inventory (BAI) score
12. Beck Depression Inventory Scale – II (BDI-II) score

3.3.3. Safety Endpoints

1. Vital signs
2. Blood chemistries
3. Urine drug screen results
4. Blood alcohol concentration (BAC) by breathalyzer
5. AEs

6. Electrocardiogram (ECG) results
7. Clinical Institute of Withdrawal – Alcohol Revised (CIWA-AR) scores
8. Profile of Moods States (POMS) scores
9. Frequency of subjects with suicidal ideation at any time during the treatment period – Columbia-Suicide Severity Rating Scale (C-SSRS)

3.3.4. Compliance

Compliance will be assessed by self report of compliance with investigational products and gabapentin plasma levels. Compliance will be calculated as the percentage of medication taken as prescribed.

3.3.5. Pharmacokinetics

A population PK/PD analysis will be performed using gabapentin plasma levels determined from blood samples collected at Weeks 12, 20, and 24 from subjects in the HORIZANT Extended-Release Tablets group. There will be a separate population PK/PD SAP that addresses this analysis.

3.3.6 Exploratory Endpoints

1. Percentage of subjects abstinent from smoking
2. Number of symptoms observed in the MINI AUD scale
3. Blood PEth levels
4. PSNHDD, percentage subjects abstinent from alcohol, percentage of subjects with a WHO- 1-level decrease, and WHO 2-level decrease in alcohol consumption on a weekly and monthly basis, and across all grace periods, with and without imputation (exclusive of the primary endpoint)
5. All secondary endpoints with imputation
6. Moderators of PSNHDD during Weeks 22-25

4. DEFINITION OF ANALYSIS SETS

The study analysis populations will consist of the following:

Modified Intention-to-Treat (mITT) Analysis Set: The mITT set is defined as subjects randomized to participate in the study who took at least one dose of investigational product.

Evaluable Analysis Set: The evaluable analysis set is defined as those subjects randomized to the study who took at least 80% of the prescribed dose of tablets during the maintenance period (Weeks 2 - 25) and did not have a major protocol violation.

The analysis of the primary and secondary efficacy endpoints will be conducted on both the mITT and evaluable analysis sets. Exploratory analyses will be performed on the mITT analysis set, unless otherwise specified. Safety analyses will be conducted on the mITT analysis set.

5. ASSSESSMENT AND JUSTIFICATION OF STUDY ENDPOINTS

5.1. Alcohol Consumption Endpoints

5.1.1. Daily Quantity of Alcohol Consumption

Drinking will be assessed using the TLFB methodology and Form 90 structured assessment pattern chart. The TLFB is a semi-structured interview that provides estimates of the daily quantity of alcohol consumption during specified time periods. It uses a calendar prompt and a number of other memory aids (e.g., holidays, payday, and other personally relevant dates) to facilitate accurate recall of drinking or other drug use during the target period. The procedure has been widely used in clinical and research contexts. It has demonstrated adequate levels of reliability and validity when administered as an in-person interview, over the telephone, and when administered via computer (Carey-1997, Sobell et al-1988, Sobell et al-1996).

If a subject is withdrawn from the study early and is no longer participating in clinic visits or providing TLFB drinking data but is willing to be contacted by phone at the week most proximal to dropout, then they will be asked about any drinking and heavy drinking during the time since last contact. Phone calls will continue until the end of the treatment period, as deemed acceptable by the patient. The two questions cover whether the subject had any heavy drinking days or drinking days during the period covered.

5.1.2. Drinking Days

A drinking day is one calendar day in which the subject reported any alcohol consumption (i.e., > 0 standard drinking units [SDUs]). A standard drink contains approximately 0.6 fluid ounces (oz) of pure alcohol. The data given by the subjects on amount and type of alcoholic beverage(s) consumed will be converted to SDUs. Standard drink unit definitions are provided in **Table 2**.

Table 2: Standard Drink Unit Definitions

For Beer (~ 5% alcohol), the approximate number of SDUs in: • 12 oz = 1.0 • 16 oz = 1.3 • 22 oz = 2.0 • 40 oz = 3.3 For malt liquor (~ 7% alcohol), the approximate number of SDUs in**:** • 12 oz = 1.4 • 16 oz = 1.9 • 22 oz = 2.6 • 40 oz = 4.7
For table wine (~ 12% alcohol), the approximate number of SDUs in: • 750 mL bottle = 25oz = 5.0 • 5 oz glass = 1.0 • 10 oz glass = 2.0

Table 2: Standard Drink Unit Definitions (Continued)

For 80 proof spirits (~ 40% alcohol), or hard liquor, the approximate number of SDUs in: • 1.5 oz (mixed drink) = 1.0 • 16 oz (pint) = 11.0 • 25 oz (a fifth)= 17.0 • 1.75 L (59 oz) = 39.0

5.1.3. Heavy Drinking Day

A heavy drinking day is defined as a day with 5 or more drinks (SDUs) for males and 4 or more drinks (SDUs) for females.

5.1.4. Days at Risk

If a subject is being treated at an inpatient facility, is incarcerated, or otherwise under confinement, the days spent in under these conditions is considered a reduction in the days at risk for drinking and is deducted from the denominator in calculations of rates of drinking days.

5.1.5. Percentage of Subjects with No Heavy Drinking Days and Percentage of Subjects Abstinent from Alcohol

The percentage of subjects with no heavy drinking days is the number of subjects that have no heavy drinking days during the period of interest divided by the number of subjects with at least one day of non-missing drinking data during the period of interest, multiplied by 100.

The percentage of subjects abstinent from alcohol is calculated similarly, except the numerator is the number of subjects that have no drinking days during the period of interest.

5.1.6. Weekly Percentage of Heavy Drinking Days and Weekly Percentage of Days Abstinent

Weekly percentage of heavy drinking days is the number of heavy drinking days in a 7-day period divided by 7 then multiplied by 100. The TLFB permits capturing data in a subsequent visit if a visit is missed; however, if fewer than 7 days are observed then the denominator is the number of days observed in the 7-day period. At least 3 days in a week must be observed; otherwise, the week is considered missing.

Weekly percentage of days abstinent is similarly calculated by using the number of days abstinent instead of the number of heavy drinking days.

5.1.7. Weekly Mean Number of Drinks and Weekly Mean Number of Drinks per Drinking Day

Weekly mean number of drinks is the sum of SDUs calculated to the tenths over 7 calendar days divided by the number of days with non-missing data. The quotient is multiplied by 7. At least 3 days in a week must be observed; otherwise, the week is considered missing.

Weekly mean number of drinks per drinking days utilizes the same numerator, and the denominator is the number of days with greater than 0 SDUs. Weeks where all days within the week are abstinent are assigned a value of 0 for weekly drinks per drinking day.

5.1.8. World Health Organization Drinking Risk Categorical Scale

The WHO has developed a drinking risk categorical scale that can be used in a responder analysis approach to assess clinically relevant decreases in alcohol consumption (Aubin et al-2015). Two dichotomous endpoints will be analyzed: WHO 1-level and WHO 2-level decrease in alcohol consumption. The WHO 1-level and 2-level decrease endpoints are the percentage of subjects experiencing at least a 1-level or 2-level decrease in WHO levels of alcohol consumption, respectively, from the level at baseline (the period including the 28 days before screening) to the level during the last 4 weeks of the maintenance phase (Study Weeks 22-25). The WHO levels of average alcohol consumption per day are as follows:

	Males	**Females**
Low Risk	1 to 40g	1 to 20g
Medium Risk	41 to 60g	21 to 40g
High Risk	61 to 100g	41 to 60g
Very High Risk	101+g	61+g

where 14g = 1 SDU (WHO-2000). In computing the alcohol consumption level, average drinks per day will be used, computed as the sum of all drinking in the 28 day period divided by the number of days with non-missing drinking data in that period. Abstinent subjects will be included in a separate "Abstinent" category. A subject must have at least 1 week of data during the last 4 weeks of the maintenance phase to be considered non-missing.

5.2. Alcohol-Related Craving, Consequences, and Withdrawal

Alcohol-related craving is measured using the ACQ-SR-R scale and alcohol-related consequences are measured using the ImBIBe and CIWA-AR scales.

The ACQ-SR-R contains 12-items adapted from the 47-item ACQ-NOW developed by Singleton et al (1994) to assess craving for alcohol among alcohol users in the current context (right now). There are 4 subscale scores for compulsivity, expectancy, purposefulness and emotionality. Each subscale has 3 items with each item having a 1 to 7 raw score (from strongly disagree to strongly agree). A subscale score is obtained by summing the raw scores for the 3 items and dividing by 3. Items 3, 8, and 11 are reverse keyed. A general craving index is derived by summing all items and dividing by 12. If an item is missing, then the number of items is reduced by the number missing, and the sum is only the sum of the answered items. At least 10 items must be endorsed for the general craving index of ACQ-SR-R to be considered non-missing (i.e., scored). Any subscale with a missing item will be considered missing.

ImBIBe is a 15-item questionnaire in which the subject responds on a 5-point scale responses to questions on the consequences of alcohol use. This scale was adapted from the Drinker Inventory of Consequences questionnaire based on FDA recommendations on patient reported outcomes (Miller & Tonigen-1995). The total score is the sum of the individual item scores. In order to account for missing items, the sum is the sum of the responses times 15 divided by the number of items endorsed.

The CIWA-AR modified telephone version is an adaptation for telephone administration of the CIWA-AR a brief 10-item measure used to provide a quantitative index of the severity of the alcohol withdrawal syndrome (Sullivan et al-1989). The CIWA-AR has been used both in clinical and research applications and has demonstrated both reliability and validity (Sellers et al-1992, Stuppaeck et al-1994). The total score is the sum of the individual item scores. Since this is an interview scale, no missing items are anticipated. A score ≥ 10 is considered an indication that the subject is undergoing alcohol withdrawal.

5.3. Mood

Mood will be measured with the POMS, BDI-II, and BAI.

The POMS measures dimensions of affect or mood (McNair and Heuchert-2005). It consists of 65 adjectives to which the subject responds according to a 5-point scale ranging from "not at all (0)" to "extremely (5)." Six subscale scores will be computed for items grouped as follows: Tension-Anxiety, Depression-Dejection, Anger-Hostility, Vigor-Activity, Fatigue-Inertia, and Confusion-Bewilderment. A Total Mood Disturbance score will also be computed which consists of the sum of Tension-Anxiety, Depression-Dejection, Anger-Hostility, Fatigue-Inertia, and Confusion-Bewilderment scores then subtracting the Vigor-Activity subscale score. A missing value within a subscale will be replaced by the average score of the answered items within the subscale; if 2 or more items within a subscale are missing then the entire subscale is missing (Macefield et al-2010).

The BDI-II is a 21-item multiple choice questionnaire that is used for measuring the severity of depression (Beck et al-1966). Each item is scored on a scale value of 0 to 3. The BDI-II score is computed by summing all items. If fewer than 4 items are missing, then the missing items are replaced by the average value of the answered items, rounded to the nearest whole number (Lipps et al-2010). If 4 or more items are missing then the BDI-II is not scored. The standardized cutoffs for depression severity are:

0–13: minimal depression

14–19: mild depression

20–28: moderate depression

29–63: severe depression

The BAI consists of 21 questions about how the subject has been feeling in the last week, expressed as common symptoms of anxiety (such as numbness and tingling, sweating not due to heat, and fear of the worst happening). This inventory was designed to minimize the overlap with depression scales (Beck et al-1988). Missing responses to items will be treated the same as the BDI-II. Each question has the same set of four possible answer choices. These are:

Not at all. (0 points)

Mildly: It did not bother me much. (1 point)

Moderately: It was very unpleasant, but I could stand it. (2 points)

Severely: I could barely stand it. (3 points)

The BAI score is computed by summing all items. The standardized cutoffs for anxiety severity are:

0-7: minimal level of anxiety

8-15: mild anxiety

16-25: moderate anxiety

26-63: severe anxiety

5.4. Sleep Quality

Sleep quality will be measured using the PSQI. The PSQI is a 19-item questionnaire with 6 subscales (subjective sleep quality, sleep latency, sleep duration, habitual sleep disturbances, use of sleep medication and day time dysfunction) (Buysse et al-1989). Each subscale is rated from 0 to 3 with the higher scores reflecting more severe sleep complaints. The addition of all the scores permits an analysis of the subject's overall sleep experience in the past 30 days. The lower the overall score, the better the person sleeps. The scale and scoring instructions from Buysse et al-1989 are provided in Appendix A. A score ≥ 5 is indictive of a sleep disturbance. If any of the items is missing, then the entire form is missing (i.e, overall score and subscale scores) for that evaluation (PSQI website).

5.5. Alcohol Use Disorder (MINI Version 7 – DSM5)

The AUD module of the MINI specifies the severity of AUD into 3 categories based on the total number of symptoms to which the subject is coded "Yes" as follows:

Mild = 2 to 3 symptoms

Moderate = 4 to 5 symptoms

Severe = 6 or more symptoms

Subjects must have at least 4 symptoms to be eligible to participate in the study. The total number of symptoms being scored is 11. No imputation for missing values will be used.

5.6. Smokers and Cigarettes per Week

A quantity frequency interview at baseline and during treatment will include two questions to assess cigarette smoking behavior: 1) Over the past week, on how many days did you smoke cigarettes?, 2) On the days you smoked during the past week, how many cigarettes did you smoke on average?. At baseline subjects that answer "0" to question #1 are considered non-smokers for the study. Cigarettes per week is the answer to question #1 multiplied by the answer to question #2. No imputation for missing values will be used.

6. HYPOTHESES TO BE TESTED

6.1. Primary Efficacy Endpoint

It is hypothesized that HORIZANT Extended-Release Tablets, as compared to placebo, will increase the PSNHDD during Study Weeks 22 to 25 (last 4 weeks of the maintenance period). This hypothesis will be explored using other time periods (see 9.11.4).

6.2. Secondary Efficacy Endpoints

Over the last 4 weeks of the maintenance period, it is hypothesized that the HORIZANT Extended-Release Tablets group, as compared to the placebo group, will:

1. Increase the percentage of subjects abstinent from alcohol (key secondary endpoint)
2. Increase the percentage of subjects with a WHO drinking risk category decrease of::
    a. at least 1-level
    b. at least 2-levels
3. Increase the percentage of days abstinent per week
4. Decrease the percentage of heavy drinking days per week
5. Decease the weekly mean number of drinks per week
6. Decrease the weekly mean drinks per drinking day
7. Decrease the cigarettes per week among smokers
8. Decrease the alcohol craving score (ACQ-SR-R) per visit
9. Decrease the alcohol related consequences (ImBIBe) score per visit
10. Decrease PSQI score
11. Decrease the BAI score
12. Decrease the BDI-II score

6.3 Exploratory Efficacy Endpoints

The following exploratory endpoints will be examined to generate hypotheses or perform sensitivity analyses for hypotheses that the HORIZANT Extended-Release Tablets group, as compared to the placebo group, will:

1. Increase the percentage of subjects abstinent from smoking in subjects that were smokers at the start of the study
2. Decrease the number of symptoms observed in the MINI AUD scale
3. Decrease the blood PEth levels
4. Increase the PSNHDD, percentage of subjets abstinent from alcohol, percentage of subjects with a WHO- 1-level decrease, and a WHO 2-level decrease in alcohol consumption on a weekly and monthly basis, and across all grace periods, with and without imputation (exclusive of the primary endpoint)

5. Change all secondary endpoints, with imputation, in the direction listed in Section 6.2
6. Have a greater treatment effect on the primary endpoint during Weeks 22-25, among moderators suggestive of alcohol withdrawal and increased severity of alcohol use disorder.

7. SAMPLE SIZE CONSIDERATIONS

The sample size was based on a conservative approach to the results of the randomized, placebo-controlled trial reported by Mason et al (2014). Mason et al (2014) found an effect size for PSNHDD of odds ratio = 2.8 (Cohen's h = 0.48). However, this study was a single site trial and single site trials are known to have greater effect sizes than multi-site trials (Feinn and Kranzler, 2005). Taking a conservative approach, we assumed a smaller effect size for the current multi-site trial, an odds ratio = 2.5; (Cohen's h=.34, that occurs given a placebo PSNHDD during Study Weeks 22-25 of 13% and an active study drug PSNHDD of 27%). To achieve 91% power for this trial, given a two-tailed alpha of 0.05, then a sample size of 173 per group (346 total) is needed (Fleiss et al-2003). The estimates of 13% and 27% for placebo and gabapentin, respectively, assumes 15% of the randomized subjects in each treatment group will dropout prior to or during the last 4 weeks of the Maintenance Period, and consequently, these dropouts will be imputed as subjects with heavy drinking days (i.e., treatment failures).

8. DATA QUALITY ASSURANCE

Data quality assurance will start with training of clinical investigative staff on data collection and assessment procedures including a Manual of Operations that describes what data to collect and procedures for completion of eCRFs. Completed eCRFs will be reviewed by Fast-Track Drugs and Biologics clinical monitors on a regular basis throughout the trial by comparison against the source documents.

All study data will come from the eCRFs and no other source data. eCRFs for this study were created using an electronic data management system (EDMS) based on Merge eClinicalOS. eCRFs were created using an established data dictionary for each variable including the field name, field type, field attributes, and coding for variables. Range checks, alpha-numeric requirements, and null/not null parameters were programmed as applicable. The back end database application is Oracle. Data entered into the EDMS system will be reviewed by Fast-Track clinical monitors and data managers. If incomplete or inaccurate data are found, the data will be queried in the system for site staff to address. The site will resolve data inconsistencies and errors using the EDMS with full audit trail of corrections being maintained within the system. Corrections and changes to the data will be reviewed by Fast-Track clinical monitors and data managers.

Additional edit checks will be written to detect anomalies in the database. These checks will address inconsistencies (within visits, across visits), invalid/unusual values, missing values, and protocol violations. Edit checking will be validated on test data or actual clinical trial data. In addition to programmed edit checks, quality control examination of data will also be performed on reviews of data listings.

9. STATISTICAL CONSIDERATIONS

9.1. General Considerations

For descriptive purposes, dichotomous and categorical variables will be presented as number of observations and percentages; continuous variables will be given as means, standard deviations (SD), median, miniumum (min) and maximum(max). Statistical tests will be two-tailed at a 0.05 Type I error rate. P-values for the primary and secondary endpoints of < 0.05 will be considered statistically significant. Endpoint data will also be screened for outliers and skewness. Appropriate non-parametric tests will be used to compare treatment groups on continuous baseline characteristics that are not normally distributed. Continuous endpoint data that are not normally distributed will be transformed using either a square root, logarithmic, or inverse transformation, the selection of which is determined by skewness and kurtosis statistics with values closest to zero. Cohen's d will be used to calculate the effect size for means and Cohen's h will be used to calculate the effect size for proportions. Odds ratios will be provided for all dichotomous outcomes and coverted to Cohen's d when appropriate. Descriptive statistics – mean, SD, median, min and max – of all endpoint data will be provided for each assement point or summarized at each week for drinking endpoints. All data will be presented in listings.

9.2. Participant Accountability and Protocol Deviations

A summary will be prepared to show dropouts/retention over time in each group, along with the reason for early termination. The number of missing observations will be presented between groups. Protocol deviations will be presented as summaries by type of deviation.

9.3. Demographics and Other Baseline Characteristics

Summaries of the characteristics of the subjects in each of the study groups at baseline will be prepared for the mITT, and evaluable analysis sets. Demographic characteristics (e.g., age, gender, race, ethnicity, marital status, employment, and education) and other baseline characteristics including Family History of Alcohol Problems, Barratt Impulsiveness scale (BIS), mood scales (e.g., Beck Anxiety Inventory (BAI), Beck Depression Inventory – II (BDI-II), Profile of Mood States (POMS) total and subscale scores), Pittsburg Sleep Quality Index (PSQI), and drinking goal (multiple choices and dichotomized total abstinence or not total abstinence) will be summarized by treatment group for the mITT and evaluable subjects.

Baseline drinking parameters in the 28-days prior to the start of screening, age started drinking regularly, medical treatments for drinking in the past year, and other services used for alcohol problems in the past 4 weeks prior to consent will be summarized by treatment group for the mITT subjects. The number and percentage of subjects with mild, moderate and severe symptoms of AUD and summary statistics for total number of symptoms will also be presented.

Nicotine dependence will be assessed using the modified Fagerstrom Test for Nicotine Dependence with responses to each question will be presented. A summary nicotine dependence score will be tabulated. The quantity of cigarettes smoked per week in the week prior to randomization will be presented for those subjects who reported any smoking. The numbers and percentages of subjects who test positive for THC will also be presented.

Baseline drinking-associated consequences (CIWA-AR and ImBIBe scores) and drinking-associated-craving (ACQ-SR-R) total score and subscales will be summarized in the tables.

Continuous variables will be summarized using means, standard deviations, medians, min, and maximum values. Categorical variables will be summarized using counts and percentages.

The comparability among the treatment groups with respect to the demographic and baseline variables will be evaluated by appropriate statistical methods. These will include t-tests for continuous variables, chi-square tests for categorical variables, and Fisher's exact test for binary variables. If a continuous variable is skewed, then the Wilcoxon rank sum test will be used on the raw data or a t-test on an appropriately transformed variable.

9.4. Efficacy Analysis

9.4.1. Primary Analysis of the Primary Efficacy Endpoint

The primary analysis of the primary efficacy endpoint will be conducted via a fully covaried logistic regression of PSNHDD during Study Weeks 22 to 25 (last 4 weeks of the maintenance period on the mITT population). The Wald statistic from the fully covaried logistic regression will be used to test for treatment differences. A two-tailed p-value < 0.05 will be considered statistically significant. A bar graph will present the results. Exploratory analyses will examine other timeframes beyond the last 4 weeks (see Section 9.11.4).

9.4.2. Covariate Adjustment for the Primary Analysis of the Primary Efficacy Endpoint

The logistic regression model will include treatment group, clinical site, pre-randomization drinking goal (abstinence versus not abstinent), and baseline percent heavy drinking days. Clinical site was deemed a covariate because it was chosen as a stratification variable to account for between site variability in outcome. Prior to conducting the logistic regression, a blinded analysis of site by treatment group by PSNHDD outcome will be performed to determine if every site has an outcome. Clinical sites with fewer than 3 events will be be combined for the purpose of conducting the logistic regression. The subject's pre-randomization goal for drinking outcome has been observed in prior studies as a predictor of reducing the frequency of heavy drinking days and will be included in this study as a dichotomized covariate. Baseline drinking is a strong predictor of drinking outcome, and thus will be included as a covariate. Since all subjects will have at least one heavy drinking day at baseline (thus preclusing the possibility of between subject variability on baseline PSNHDD), it was not possible to use baseline PSNHDD as a covariate of PSNHDD outcome. Thus, baseline percent heavy drinking days was chosen to be the covariate as a near-analgous measure of PSNHDD outcome.

9.4.3. Analysis of the Secondary Efficacy Endpoints

Secondary efficacy endpoints will also be analyzed based on data collected during the last 4 weeks of the maintenance period (Weeks 22 through 25), including TLFB and other questionnaire data assessed at Week 26 that reflect data collected during this period.

In general, every continuous secondary efficacy endpoint is analyzed using a repeated measures mixed effects model where subjects are random effects; factors and covariates are fixed effects. The analyses will be performed using SAS PROC MIXED procedure with the categorical or

dichotomous fixed effects variable having values ordered per the data. The information criterion is requested from every mixed effects model. Subjects are treated as a class variable and not continuous. The week (Weeks 22 through 25), treatment group, and clinical site are also treated as class variables.

The primary analysis model for all continuous endpoints is:

- Appropriately transformed endpoint = treatment + week + treatment*week + clinical site + baseline equivalent of endpoint + other covariates (identified in Section 9.4.4)

This model will also be created for the untransformed endpoint. The solution statement from SAS PROC MIXED is requested to provide the solution for the fixed effects parameters. A REPEATED statement specifies that values are repeated each week and subjects are nested within treatment group. The covariance structure is specified.

The selection of the covariance structure is performed using a simple repeated mixed effects model that includes treatment group as the only fixed effect and subject nested within treatment group as the only random effect. The covariance structure for each continuous secondary endpoint is selected from autoregressive, compound symmetry, Toeplitz, and unstructured. The Akaike Information Criterion (AICc) corrected for a finite sample is obtained from each of the four models for the four possible covariance structures to determine model fit. The smallest (minimum) AICc associated with one of the covariance structurs is selected and the difference for each of the other three covariance structurs is calculated. A graph is produced of the model fit statistics and relative difference for the four possible covariance structures. The graphs across the continuous endpoints are compared to determine which covariance structure will be selected for all continuous endpoints or if one or more models need different covariance structures.

Results based on the primary analysis model and the model of the untransformed endpoint will be presented in tabular form. The overall least squares means and least square means for each time point along with the 95% confidence intervals will be presented for the untransformed endpoint only, while two-tailed p-values and Cohen's d will be presented for both the untransformed and transformed data. Inference and Cohen's d will be based upon the results using appropriately transformed data. Graphs of all secondary endpoints will be produced.

9.4.3.1. Key Secondary Endpoint: Percentage of Subjects Abstinent

Percentage of subjects abstinent during Weeks 22 to 25 is the key secondary endpoint. The analysis will be performed as indicated in Section 9.4.4 and the two-tailed p-value from the fully covaried logistic regression will be evaluated if and only if the primary endpoint (PSNHDD) is statistically significant ($p<0.05$ [Section 9.4.1]). The testing procedure utilizes the serial gatekeeping methodology (Dmitrienko and Tamhane 2009). The key secondary endpoint can only be evaluated for statistical significance after the primary endpoint has been identified as statistically significant. In this situation, percentage of subjects abstinent will be evaluated using the Wald statistic from the logistic regression model at $p<0.05$ after PSNHDD is found to have $p<0.05$. If PSNHDD is not statistically significant at the 0.05 level then no significance testing of percentage of subjects abstinent will be performed. This analysis will be performed on mITT subjects with a drinking day imputed for missing data. However, if drinking data are missing by TLFB, but the subject reports any drinking during Weeks 22 to 25 using the Drinking Question

eCRF, then the subject will be considered not abstinent. An analysis of percent subjects abstinent without imputation for missing data will be performed as an exploratory analysis

9.4.3.2. Secondary Drinking Endpoints

Percentage of days abstinent per week, percentage of heavy drinking days per week, weekly mean number of drinks per week, and weekly mean number of drinks per drinking day will be analyzed using the mixed effects model specified in Section 9.4.3. Covariates for these models will be identified as in Section 9.4.4.

Percentage of subjects with a WHO 1-level decrease, and WHO 2-level decrease in alcohol consumption risk category will be analyzed during the last 4 weeks of the maintenance period (Weeks 22 through 25) using the same logistic regression model method and contingency table as defined for the primary endpoint in Sections 9.4.1 and 9.4.2. Covariates for these models will be identified as in Section 9.4.4.

9.4.3.3. Alcohol Consequences and Craving Scales

The ImBIBe and ACQ-SR-R scales are assessed at Study Weeks 24 and 26 which will be used for the secondary endpoints. Mixed effects models as stated in Section 9.4.3 will be generated for the total score for each of these scales and for the 4 subscales for the ACQ-SR-R. Covariates for these models will be identified as in Section 9.4.4.

9.4.3.4. Smoking Quantity

The mean number of cigarettes smoked in the past week is measured at Study Weeks 24 and 26. The sample is the mITT subjects who smoked at baseline. The data will be analyzed as described in Section 9.4.3. Covariates for this endpoint will be identified in Section 9.4.4.

9.4.3.5. Depression, Anxiety, and Sleep Scales

The BDI-II total score, BAI total score, and PSQI total score (and subscale scores) are continuous variables. The secondary endpoints for the BDI-II, BAI, and PSQI subscales are assessed at Study Weeks 24 and 26. The data will be analyzed as described in Section 9.4.3. Covariates for these models will be identified as in Section 9.4.4.

9.4.4. Covariate Adjustment for the Analysis of Secondary Efficacy Endpoints

Covariates for continuous secondary efficacy endpoints include the baseline equivalent of the endpoint, clinical site, treatment, time and the treatment by time interaction. Additional covariates for the secondary efficacy endpoints may include baseline characteristics with a theoretical and/or empirical basis for a relationship with a particular secondary endpoint. Such characteristics may include, but are not limited to, drinking goal (total abstinence versus less than total abstinence), age, years of regular drinking (age minus age first started drinking alcohol regularly), baseline alcohol craving scale total score. Prior to the unblinding of the data, matrices of correlations between these baseline characteristics and each of the secondary efficacy endpoints, pooled across blinded treatment assignment, will be produced (using Pearson for continuous variables, Spearman for categorical outcomes). Selection of baseline variables to include as covariates in the models will be based on consideration of the following criteria: at least modest correlation with outcome (i.e., $r \geq 0.20$), and clinical expertise. Each endpoint may

have a unique set of covariates. Care is taken to only select a limited number of covariates such that the models are not over fitted.

Covariates for the dichotomous secondary endpoints, percentage of subjects abstinent, WHO 1-level risk category decrease, and WHO 2-level risk category decrease in alcohol consumption, will be the same as those used for the primary endpoint PSNHDD as described in Section 9.4.2. Fewer covariates for the logistic regression may be used depending upon the number of events. If the number of events permits the inclusion of a baseline drinking covariate, the percentage of days abstinent will be used as the covariate for the percent subjects abstinent endpoint; however, no baseline drinking covariate will be employed for the endpoint, percent subjects with a WHO decrease in alcohol consumption, as this endpoint already adjusts for baseline drinking in its calculation.

9.5. Handling of Missing Data

9.5.1. Primary Analysis of the Primary Efficacy Endpoint

The primary efficacy analysis of the PSNHDD endpoint will use all mITT subjects and will employ imputation for missing drinking data such that any subject with any missing drinking data during the evaluation period for this endpoint will be imputed as a subject with a heavy drinking day.

Prior to the subject dropping out of the study, every attempt will be made to continue to collect TLFB data; however, if the subject does not want to participate in the collection of the TLFB they will be asked to participate in a periodic follow-up phone call to collect a summary of drinking information.If the subject agrees to be contact then they will be asked about any drinking and heavy drinking during the time since last contact. Phone calls will continue until the end of the treatment period, as deemed acceptable by the patient. The two questions cover whether the subject had any heavy drinking days or drinking days during the period covered. This summary drinking data will be used for the primary endpoint.

If the subject does not agree to participate with phone contact thus no summary drinking data nor TLFB data is available then imputation as indicated above will be used.

9.5.2. Analysis of the Secondary Efficacy Endpoints

The primary efficacy analysis of the percentage of subjects abstinent endpoint will use all mITT subjects and will employ imputation for missing drinking data such that any subject with any missing drinking data during the evaluation period for this endpoint will be imputed as a subject with a drinking day. Analyses of supportive secondary efficacy endpoints will use all mITT subjects with no imputation for missing data. Analyses will also be performed in evaluable subjects.

9.6. Safety Analysis

9.6.1. Adverse Events

AEs will be coded using the most recent version of the Medical Dictionary for Regulatory Activities (MedDRA) and will be grouped by system, organ, and class (SOC) and preferred term (PT) designation. The severity, frequency, and relationship of AEs to investigational product will

be presented by SOC and PT groupings. Listings of each individual AE including start date, stop date, severity, relationship, outcome, and duration will be provided. Each AE (based on PT) will be counted once only for a given study subject. If the same AE occurred on multiple occasions, the highest severity will be assumed. Thus, study subjects are not counted multiple times in a given numerator in the calculation of frequencies for a specific AE. C-SSRS reports of suicidality or suicidal ideation will be reported as AEs and analyzed as AEs if the investigator determines after an interview with the subject, that the responses are consistent with suicidal ideation or attempt.

9.6.2. Clinical Laboratory and Point of Care Tests

For clinical laboratory data, descriptive statistics will be generated for all tests performed at screening and at each clinic visit. If a laboratory analysis is repeated, the last measurement performed prior to the clinic visit will be used in the summary statistics for that clinic visit. If an unscheduled clinical laboratory visit occurs prior to a scheduled visit that is missed due to dropout, then the unscheduled visit will be used in the summary statistics for the missed scheduled clinical visit. If an unscheduled clinical laboratory visit occurs between two scheduled clinical visits, then the data from the unscheduled visit only be presented in the listings and not in summary statistics. In addition, at each post-randomization clinic visit descriptive statistics for change from baseline will be generated. Laboratory values will be plotted as mean ± standard error over time. All laboratory measurements will be presented in the listings.

Number and percentage of positive urine drug tests and pregnancy tests for screening visits and all treatment and follow-up visits will be tabulated. Results of all urine drug tests and pregnancy tests will be presented in the listings. The percentage of subjects with a positive urine drug test at any time post start of treatment will also be presented by test type and treatment group.

9.6.3. Vital Signs, ECG, and Body Weight

Vital signs will be presented as summary statistics and change from baseline. The percentage of ECG results considered abnormal and clinically significant will be provided. Body weight will be presented as summary statistics and change from screening. Vital signs, ECG results, and weight measurements for all visits will be presented in the listings.

9.6.4. CIWA-AR Scores

The number and percentage of subjects who reported CIWA-AR scores ≥ 10 at any time after the start of dosing will be presented.

9.6.5. Profile of Mood States

The POMS has 6 subscales and total disturbance score. Each subscale and summary score are continuous data and will be analyzed over the entire maintenance period using the same repeated measures mixed effects model as specified in Section 9.4.3. Treatment group, clinical site, study week, the treatment group by study week interaction, and baseline value of the subscale or summary score will be the only covariates in the mixed effects models for this endpoint. The entire maintenance period will be used for this endpoint. No imputation will be utilized for this safety endpoint.

9.7. Drug Exposure and Retention Analyses

Drug exposure will be presented for both groups as the mean number of tablets taken per week by subject self report during the entire treatment phase, mean total exposure over the entire maintenance period, and number of days that at least one dose was taken over the maintenance period. Self-reported compliance with HORIZANT Extended-Release Tablets will be compared against plasma samples having detectable levels of gabapentin by using 2 x 2 contingency tables. In addition, the percentage of subjects discontinuing medication and a listing of the reasons for discontinuation will be provided.

9.8. Other Services Used Analysis

Weekly days of attendance at self-help meetings or other professional service providers to help reduce/quit drinking will be presented as summary statistics by treatment group. All other services used data will be presented in the listings.

9.9. Blood Alcohol Content

The number and percent of subjects at any clinic visit that have a BAC > 0 will be tabulated. All BAC measurements will be presented in the listings.

9.10. PK Analysis

Plasma levels of gabapentin will be presented as descriptive statistics including mean, SD, coefficient of variation, geometric mean, 95% CI, minimum and maximum levels and mean ± SD will be presented graphically over time. Population PK analyses will be conducted in accordance with a separate PK/PD SAP.

9.11. Exploratory Analyses

9.11.1. Exploratory Endpoint: Percentage of Subjects Abstinent from Smoking

The percentage of subjects abstinent from smoking is the number of subjects that have consumed no cigarettes per week during the weeks included in period of interest divided by the number of subjects with at least one week of non-missing smoking data during the period of interest, multiplied by 100. This endpoint will be analyzed only among subjects who smoked at baseline. Analysis will include two treatment time periods of interest: during the last 4 weeks of the maintenance period and over the entire maintenance period. The analysis will follow the plan in Section 9.4.1.The covariate selection plan will follow the plan in Section 9.4.2; however, if the number of events permits the inclusion of a baseline smoking covariate, the mean number of cigarettes smoked per week will be used. All analyses of this endpoint will be conducted on both a nonimputed and imputed endpoint. Imputation will proceed such that any subject with any missing cigarettes per week data during the evaluation periods for this endpoint will be imputed as a smoker.

9.11.2. Exploratory Endpoint: MINI AUD Number of Symptoms

The MINI AUD total number of symptoms at Week 26 (covering the last 4 weeks of the maintenance period) will be modeled using analysis of covariance with the following variables

included in the model: treatment group, clinical site, and baseline MINI AUD total number of symptoms. No imputation will be performed.

9.11.3. Exploratory Endpoint: Blood PEth Levels

Blood PEth levels are measured at baseline and Week 26. Analysis of Week 26 blood PEth levels will be modeled using analysis of covariance with the following variables included in the model: treatment group, clinical site, and baseline blood PEth level. No imputation will be performed for this analysis.

The proportion of positive samples [a test result > 8 ng/mL - the lower limit of quantitation (LLOQ) of the test] at Week 26 data will be modeled using logistic regression with treatment group, clinical site, and baseline PEth level as covariates provided there are sufficient events. No imputation will be performed for this analysis.

9.11.4. Primary and Secondary Endpoints With or Without Imputation over Different Study Periods

Treatment group differences will be analyzed on a weekly and monthly basis for the imputed and nonimputed versions of the following three dichotomous drinking endpoints: PSNHDD, percentage of subjects abstinent from alcohol, percentage of subjects with a WHO 1-level decrease, and a WHO 2-level decrease in alcohol consumption. These analyses will use 2x2 contingency table. The Wald statistic from the fully covaried logistic regression will be used to test for treatment group differences. The adjusted prevalence rates are obtained from the logistic regression model. These rates along with the SD, 95% CI, difference between adjusted prevalence rates for the treatment groups, and Cohen's h. Graphs will present the weekly and monthly prevalence rates. These three dichotomous endpoints (both imputed and nonimputed) will further be analyzed by grace period, over: Weeks 22-25 (last 4 weeks), Weeks 18-25 (last 8 weeks), Weeks 14-25 (last 12 weeks), Weeks 10-25 (last 16 weeks), Weeks 6-25 (last 20 weeks) and Weeks 2-25 (last 24 weeks; i.e., entire maintenance phase) using 2x2 contngency tables. The Wald statistic from the fully covaried logistic regression will be used to test for treatment group differences. Graphs of the prevalence rates will be presented over the grace periods.

Covariates used in the exploratory analyses of these endpoints may be excluded if there are insufficient numbers of events. The imputation of PSNHDD and percentage of subjects abstinent from alcohol will proceed such that subjects with missing endpoint data will considered treatment failures. Since the WHO 1-level and WHO 2-level decrease in alcohol consumption utilizes average drinks per day in its calculation, multiple imputation (described below) will be used to impute weekly drinks per day data prior to computing this endpoint. The last 4 weeks (Weeks 22-25) for these three endpoints will be analyzed within the evaluable analysis set using imputed data for PSNHDD and non-imputed data for Percentage of Subjects abstinent from alcohol and WHO 1-level and WHO 2-level decrease in alcohol consumption.

Continuous secondary endpoints will be imputed via multiple imputation analyzed over the last 4 weeks of the maintenance period, and both imputed and nonimputed endpoints will be analyzed over the entire maintenance period, using repeated measures mixed effects described in Section 9.4 and using the same covariates selected for the primary analyses of these endpoints. Graphs will present the least squares means of the untransformed endpoints without imputation. The multiple imputation method for handling missing data will use the mITT population and will

replace each missing value with a set of "m" plausible values that represent the uncertainty about the right value to impute (Hopke et al-2001, Rubin-1976, Rubin-1996, Schafer-1997). The data are assumed to have monotone missingness, and the regression method will be used.The same variables used in the mixed effects model will be included in the multiple imputation models with the addition of time-related variables such as the values of the endpoint prior to dropout. The "m" imputed datasets each will be analyzed using mixed effects models then SAS PROC MIANALYZE will be used to combine the parameter estimates.

9.11.5. Moderators of Drinking Outcomes

A number of variables will be tested as potential moderators of the medication treatment effect on the imputed PSNHDD primary endpoint. The time period of interest is the last 4 weeks of the maintenance period (Weeks 22-25). The models identified in Section 9.4 will be amended to include the potential moderator variable and the moderator by treatment group interaction. For the logistic regression models of PSNHDD, two covariates may need to be dropped from the final model of Section 9.4.2 to accommodate the moderator variable and interaction term. To aid with interpretation, continuous moderator variables will be dichotomized based on clinically accepted levels available from the literature. In the event a clinically meaningful cutoff is not available, receiver operator curves (ROC) (Harris-2010, Lambert and Lipkovich-2008) will be used. In all approaches, an appropriate cutoff will be one that ensures a suffient sample size in all resultant subgroups. The potential moderator variables that will be examined include measures suggestive of alcohol withdrawal (i.e., withdrawal question on the MINI for alcohol use disorder, BAI, BDI-II, PSQI total score, POMS total and subscales, ACQ-SR-R total score, and number of days abstinent prior to randomization), severity of alcohol use disorder (i.e., drinks per week [28 days prescreen] and years of regular drinking), reducer status (change in baseline drinks per day), alcohol-related treatment goal (total abstinence vs. less than total abstinence), Barratt Impulsiveness Scale score, total dose of medication taken, and baseline smoking status.

10. VALIDATION OF PROGRAMMING CODE

All SAS codes used to generate tables and listings will be validated and reviewed before being finalized. The validation process will be used to determine that the numbers are produced by a statistically valid method and that the execution of the computations is correct. Qualified personnel who have not previously been involved in the production of the original programming codes will perform the validation procedures. Methods of validation include independent programming and comparison to data listings. Tables will be reviewed for accuracy, consistency with this plan, consistency within tables, and consistency with corresponding output. Once validation is complete, a quality control reviewer will perform a final review of the documents for accuracy and consistency. Upon completion of validation and quality review procedures, all documentation will be collected and filed in the study documentation files at Fast-Track.

11. REFERENCES

Aubin HJ, Reimer J, Nutt DJ, Bladstrom A, Torup L, Francois C, Chick J. Clinical relevance of as-needed treatment with nalmefene in alcohol dependent patients. Eur Addict Res. 2015;21:160–68.

Beck AT, Steer RA, Ball R, Ranieri W. Comparison of Beck Depression Inventories -IA and -II in psychiatric outpatients. J Personality Assess. 1966;67: 588-97.

Beck AT, Epstein N, Brown G, Steer RA. "An inventory for measuring clinical anxiety: Psychometric properties. J Consult Clinical Psych. 1988;56:893-897.

Buysse, D. J., Reynolds, C. F., 3rd, Monk, T. H., et al. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989;28:193-213.

Carey KB. Reliability and validity of the time-line follow-back interview among psychiatric outpatients: a preliminary report. Psych Addic Behav. 1997;11, 26-33.

Dmitrienko A, Tamhane AC . Gatekeeping procedures in clinical trials. Multiple Testing Problems in Pharmaceutical Statistics. Dmitrienko, A., Tamhane, A.C., Bretz, F. (editors). Chapman and Hall/CRC Press, New York. 2009.

Feinn R, Kranzler HR. Does effect size in naltrexone trials for alcohol dependence differ for single-site vs. multi-center studies? Alcohol Clin Exp Res. 2005;29:963-988.

Fleiss JL, Levin B., Paik MC. Statistical Methods for Rates and Proportions. Third Edition. John Wiley & Sons. New York. 2003.

Harris K. ROC Hard? No, ROC made easy. *Proc 2010 SAS Global Forum*. http://support.sas.com/resources/.../proceedings10/222-2010.pdf

Hopke PK, Liu C, Rubin DB. Multiple imputation for multivariate data with missing and below-threshold measurements: time-series concentrations of pollutants in the Arctic. Biometrics. 2001;57:22-33.

Lambert J, Lipkovich I. A Macro For Getting More Out Of Your ROC Curve." *Proc 2008 SAS Global Forum*. http://www2.sas.com/proceedings/forum2008/231-2008.pdf

Lipps GE, Lowe GA, De La Haye W, Longman-Mills S, Clarke TR, Banton EM, Bain B. Validation of the Beck Depression Inventory II in HIV-positive patients. West Ind Med J 2010;59:374-379.

Macefield RC, Metcalfe C, Lane JA, Donovan JL, Avery KNL, Blazeby JM, Down L, Neal DE, Hamdy FC, Vedhara K. Impact of prostate cance testing: evaluation of the emotional consequences of a negative biopsy result. Br J Cancer 2010;102:1335-1340.

Mason BJ, Light JM, Williams LD, Drobes DJ. Proof-of-concept human laboratory study for protracted abstinence in alcohol dependence: Effects of gabapentin. Addict Biol. 2009;14:73-83.

Mason BJ, Quello S, Goodell V, Shadan F. Gabapentin treatment for alcohol dependence. JAMA. 2014;174:70-77.

McNair DM, Heuchert JWP. Profile of Mood States (POMS) Multi-Health Systems, Tonawanda, NY. 2005.

Miller WR, Tonigan JS. The Drinker Inventory of Consequences (DrInC): an instrument for assessing adverse consequences of alcohol abuse. In Mattson, M. E., and Marshall, L. A. (Eds.) NIAAA Project MATCH Monograph Series, Vol. 4. Rockville, MD: National Institute on Alcohol Abuse and Alcoholism. 1995.

Peduzzi P, Concato J, Kemper E, Holford TR, Feinstein AR. A simulation study of the number of events per variable in logistic regression analysis. 1996;49:1373-1379.

Rubin DB. Inference and Missing Data. Biometrika. 1976;63:581–592.

Rubin DB. Multiple Imputation After 18+ Years. J Amer Statistical Assoc. 1996;91:473–489.

Schafer JL. Analysis of Incomplete Multivariate Data, New York: Chapman and Hall. 1997.

Sellers EM, Sullivan JT, Somer G, Sykora K. Characterization of DSM-III-R criteria for uncomplicated alcohol withdrawal: proposal for a diagnostic inventory and revised withdrawal scale. In Naranjo, C. A. and Sellers, E. M. (Eds.) Novel pharmacological interventions for alcoholism. New York (pp. 369-71). 1992.

Singleton EG, Tiffany, ST, Henningfield JE. Development and validation of a new questionnaire to assess craving for alcohol. In: Harris LS (ed) *Problems of Drug Dependence, 1994; Proceedings of the 56th Annual Scientific Meeting, The College on Problems of Drug Dependence, Inc*. National Institute of Drug Abuse Research Monograph Series. Vol. 153. Rockville, MD 1995. p. 289.

Sobell LC, Sobell MB, Leo GI, Cancilla A. Reliability of a timeline method: assessing normal drinkers' reports of recent drinking and a comparative evaluation across several populations. Br J Addict. 1988;83:393-402.

Sobell LC, Brown J, Leo GI, Sobell MB. The reliability of the Alcohol Timeline Followback when administered by telephone and by computer. Drug Alcohol Depend 1996;42:49-54.

Stuppaeck CH, Barnas C, Falk M, Guenther V, Hummer M, Oberbauer H, Pycha R, Whitworth AB, Fleischhacker WW. Assessment of the alcohol withdrawal syndrome--validity and reliability of the translated and modified Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-A). Addiction. 1994;89:1287-92.

Sullivan JT, Sykora K, Schneiderman J, Naranjo CA, Sellers EM. Assessment of alcohol withdrawal: the revised clinical institute withdrawal assessment for alcohol scale (CIWA-AR). Br J Addict. 1989;84:1353-7.

World Health Organization (WHO): International Guide for Monitoring Alcohol Consumption and Related Harm. Geneva, WHO, 2000. Available at: http://whqlibdoc.who.int/hq/2000/who_msd_msb_00.4.pdf.

12. TABLE, LISTING, AND FIGURE SHELLS

12.1. Tables

12.1.1. Subject Disposition, Participation, Compliance

Table 1: Subject Disposition - All Randomized Subjects

	Treatment Group			
	Placebo (N=xx) n (%)	HORIZANT (N=xx) n (%)	Total (N=xxx) n (%)	p-value[1]
Number of Subjects Randomized not Receiving Study Drug	x (xx.x%)	x (xx.x%)	x (xx.x%)	
Number of mITT Subjects	xx (xx.x%)	xx (xx.x%)	xxx (xx.x%)	0.xxx
Number of Completed Subjects	xx (xx.x%)	xx (xx.x%)	xxx (xx.x%)	0.xxx
Number of Evaluable Subjects	xx (xx.x%)	xx (xx.x%)	xxx (xx.x%)	0.xxx
Number of Subjects Discontinuing Medication, Remain in Study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Number of Subjects Discontinuing Medication, Drop out of Study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Reason for Any Discontinuation				
Lost to follow up	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Died	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Logistical or practical reasons	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Lack of perceived efficacy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Absent from the protocol due to confinement in a controlled environment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Other reason	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

Notes: A subject might have more than one reason for discontinuation. .

[1] p-value from chi-square test (c), and Fisher's exact test for binary (f)

Programmer Notes: The discontinuation reasons are as given on the CRF. Include only the reasons actually used for the subjects in the study. If a subject discontinued, but the specific reason is missing, include 'Missing' as a row in the table. Use the order of discontinuation reasons as presented on the CRF page.

Table 2: Exposure to Investigational Products – mITT Subjects

	Placebo						HORIZANT						
Period	**N**	**Mean**	**SD**	**Med**	**Min**	**Max**	**n**	**Mean**	**SD**	**Med**	**Min**	**Max**	**p-value[1]**
Escalation													
Dose[2]													
Week 1	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Maintenance (Weeks 2-25)													
Total Dose	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Dose per Day	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Dose													
Week 2	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 3	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 4	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 5	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 6	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 7	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 8	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 9	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 10	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 11	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 12	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 13	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 14	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 15	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 16	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 17	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 18	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 19	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 20	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 21	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 22	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 23	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 24	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 25	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Taper													
Dose													
Week 26	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx

	Placebo						HORIZANT						
Period	**N**	**Mean**	**SD**	**Med**	**Min**	**Max**	**n**	**Mean**	**SD**	**Med**	**Min**	**Max**	**p-value[1]**
Overall (Weeks 1-26)													
Total dose	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Total dose per day	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx

[1] p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w).

[2] Dose is expressed in number of capsules of HORIZANT or placebo.

Table 3: Exposure to Investigational Products – Evaluable Subjects

Same as Table 2 only using Evaluable subjects.

Table 4: Drug Compliance – mITT Subjects

	Placebo						HORIZANT						
Period	**n**	**Mean**	**SD**	**Med**	**Min**	**Max**	**n**	**Mean**	**SD**	**Med**	**Min**	**Max**	**p-value[1]**
Escalation													
Compliance[2]													
Week 1	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Maintenance (Weeks 2-25)													
Compliance													
Total Dose	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 2	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 3	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 4	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 5	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 6	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 7	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 8	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 9	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 10	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 11	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 12	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 13	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 14	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 15	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 16	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 17	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 18	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 19	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx

	Placebo						HORIZANT						
Period	**n**	**Mean**	**SD**	**Med**	**Min**	**Max**	**n**	**Mean**	**SD**	**Med**	**Min**	**Max**	**p-value[1]**
Week 20	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 21	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 22	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 23	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 24	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Week 25	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Taper													
Compliance													
Week 26	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx
Overall (Weeks 1-26)													
Compliance													
Total dose	xx	xx.x	xx.x	xx.x	xx.x	xx.x	xx	xx.x	xx.x	xx.x	xx.x	xx.x	0.xxx

[1] p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w).
[2] Compliance is expressed in number of capsules of HORIZANT or placebo.

Table 5: Drug Compliance – Evaluable Subjects

Same as Table 4 only using evaluable subjects.

Table 6: Summary of HORIZANT Blood Levels – HORIZANT Group (mITT Subjects)

								95% CI	
Study Week	**N**	**Mean**	**SD**	**% CV[1]**	**Min**	**Max**	**GeoMean**	**Upper CI**	**Lower CI**
12	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
20	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
24	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

[1]CV=Coefficient of variation

Table 7: Summary of HORIZANT Blood Levels – HORIZANT Group (Evaluable Subjects)

Same as Table 6 only using evaluable subjects.

Table 8: Self Report of HORIZANT Use (within 24 hours prior to PK sample) Versus Positive Gabapentin Blood Level – mITT Subjects

		Pill Count Indicates Drug Taken		
Timing	**Blood Level Indicates Drug Taken[1]**	**Yes**	**No**	**p-value**
Week 12				
	Yes	xx (xx.x%)	xx (xx.x%)	x.xxx
	No	xx (xx.x%)	xx (xx.x%)	
Week 20				
	Yes	xx (xx.x%)	xx (xx.x%)	x.xxx
	No	xx (xx.x%)	xx (xx.x%)	
Week 24				
	Yes	xx (xx.x%)	xx (xx.x%)	x.xxx
	No	xx (xx.x%)	xx (xx.x%)	
Overall				
	Yes	xx (xx.x%)	xx (xx.x%)	x.xxx
	No	xx (xx.x%)	xx (xx.x%)	

[1]Blood level of ≥80 ng/mL (lower limit of quantitation) indicates drug taken

Table 9: Self Report of HORIZANT Use (within 24 hours prior to PK sample) Versus Positive Gabapentin Blood Level – Evaluable Subjects

Same as Table 8 only using evaluable subjects.

Table 10: Exit Interview – mITT Subjects

Question	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
What medication do you believe you were taking?				0.xxx
Placebo	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Active	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Both Active & Placebo	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
No Idea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Missing	xx	xx	xx	
Why did you answer above?				0.xxx
Had side effects	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Had no side effects	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Staff treated me different	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
No improvement	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Had improvement	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Had a hunch	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
I just felt different	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Missing	xx	xx	xx	
Do you feel the medication helped you to reduce drinking?				0.xxx
Very Much	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Much	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Moderately	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
A little	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Not at all	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Missing	xx	xx	xx	
How would you describe your experience taking the medication?				0.xxx
Experienced no unwanted side effects and benefited	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Experienced some unwanted side effects but benefited	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Experienced a lot unwanted side effects but benefited	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Experienced no unwanted side effects but did not benefit	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Experienced some unwanted side effects and did not benefit	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Experienced a lot of unwanted side effects and did not benefit	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Missing	xx	xx	xx	

Question	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
If a friend were in need of help for a drinking problem, would you recommend taking the medication to him/her?				0.xxx
Yes, definitely	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Yes, generally	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Neither yes nor no	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
No, not really	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
No, definitely not	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Missing	xx	Xx	xx	
If you were to need treatment in the future, would you choose to take the medication again?				0.xxx
Definitely yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Probably yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Maybe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Probably not	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Definitely not	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Missing	xx	Xx	xx	
How much do you think of yourself as wanting to please other people (people pleaser)?				0.xxx
More than average	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Average	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Less than average	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Missing	xx	Xx	xx	

[1] p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w) - chi-square test for categorical variables (c).

Table 11: Exit Interview – Evaluable Subjects

Same as Table 10 only using evaluable subjects.

Table 12: Dropouts by Treatment Group and Week – mITT Subjects

	Placebo (N=xx)			HORIZANT (N=xx)			
Study Week[2]	**n**	**Cumulative n**	**Cumulative %**	**n**	**Cumulative n**	**Cumulative %**	**p-value[1]**
Week 1	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 2	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 3	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 4	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 5	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 6	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 7	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 8	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 9	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 10	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 11	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 12	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 13	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 14	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 15	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 16	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 17	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 18	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 19	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 20	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 21	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 22	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 23	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 24	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 25	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 26	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx
Week 27	xx	xx	xx.x%	xx	xx	xx.x%	0.xxx

[1] Fisher's exact test

[2]Subjects are considered dropouts when they stop providing TLFB and other data. Subjects that discontinue study drug but provide data are not considered dropouts.

Table 13: Dropouts by Treatment Group and Week – Evaluable Subjects

Same as Table 12 only using evaluable subjects.

Table 14: Number and Percent of Subjects Using Summary Drinking Questions after Discontinuing TLFB – mITT Subjects

	Placebo		HORIZANT		
Study Week	**n**	**%**	**n**	**%**	**p-value[1]**
Week 3	xx	xx.x%	xx	xx.x%	0.xxx
Week 4	xx	xx.x%	xx	xx.x%	0.xxx
Week 5	xx	xx.x%	xx	xx.x%	0.xxx
Week 6	xx	xx.x%	xx	xx.x%	0.xxx
Week 7	xx	xx.x%	xx	xx.x%	0.xxx
Week 8	xx	xx.x%	xx	xx.x%	0.xxx
Week 9	xx	xx.x%	xx	xx.x%	0.xxx
Week 10	xx	xx.x%	xx	xx.x%	0.xxx
Week 11	xx	xx.x%	xx	xx.x%	0.xxx
Week 12	xx	xx.x%	xx	xx.x%	0.xxx
Week 13	xx	xx.x%	xx	xx.x%	0.xxx
Week 14	xx	xx.x%	xx	xx.x%	0.xxx
Week 15	xx	xx.x%	xx	xx.x%	0.xxx
Week 16	xx	xx.x%	xx	xx.x%	0.xxx
Week 17	xx	xx.x%	xx	xx.x%	0.xxx
Week 18	xx	xx.x%	xx	xx.x%	0.xxx
Week 19	xx	xx.x%	xx	xx.x%	0.xxx
Week 20	xx	xx.x%	xx	xx.x%	0.xxx
Week 21	xx	xx.x%	xx	xx.x%	0.xxx
Week 22	xx	xx.x%	xx	xx.x%	0.xxx
Week 23	xx	xx.x%	xx	xx.x%	0.xxx
Week 24	xx	xx.x%	xx	xx.x%	0.xxx
Week 25	xx	xx.x%	xx	xx.x%	0.xxx
Week 26	xx	xx.x%	xx	xx.x%	0.xxx
Week 27	xx	xx.x%	xx	xx.x%	0.xxx
Overall	xx	xx.x%	xx	xx.x%	0.xxx

[1]Fisher's exact test

Note only rows with values above 0 will be presented

Table 15: Number and Percent of Subjects Using Summary Drinking Questions after Discontinuing TLFB – Evaluable Subjects

Same as Table 14 only using evaluable subjects.

12.1.2. Demographic and Baseline Characteristics

Table 16: Demographic Characteristics - mITT Subjects

Characteristic	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
Age (years)				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Gender				0.xxx
N				
Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Race				0.xxx
N	xx	xx	xx	
White	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
African-American or Black	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Native Hawaiian or Other Pacific Islander	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
American Indian or Alaskan Native	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Ethnicity				0.xxx
N	xx	xx	xx	
Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Not Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Race/Ethnicity				0.xxx
N	xx	xx	xx	
White	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Black	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Hispanic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

1 p-value from chi-square test (c), t-test for continuous data, and Fisher's exact test for binary categories (f)

Table 16: Demographic and Baseline Characteristics - mITT Subjects (Continued)

Characteristic	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
Education (years)				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Education				0.xxx
≤ High School	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
> High School	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Marital Status				0.xxx
Legally Married	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Living with Partner / Cohabitating	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Widowed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Separated	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Divorced	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Never Married	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Marital Status				0.xxx
Married	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Not Married	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Employment				0.xxx
Full-time > 35 hrs /week	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Part-time regular	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Part-time irregular	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Student	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Military Service	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Unemployed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Retired/Disabled	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Homemaker	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
In controlled environment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Employment				0.xxx
Employed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Unemployed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

Table 17: Demographic Characteristics - Evaluable Subjects

Same as Table 16 only using evaluable subjects.

Table 18: Psychiatric Baseline Characteristics – mITT Subjects

Characteristic	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
BIS First Order Factors				
Attention				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Motor				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Self Control				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Cognitive Complexity				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	

Characteristic	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
Perseverance				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Cognitive Instability				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
BIS Second-order Factors				
Attentional				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Motor				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	

Characteristic	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
Non planning				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
BAI				
N	xx	xx	xx	0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Range			(xx-xx)	
Minimal anxiety	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Mild anxiety	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Moderate anxiety	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Severe anxiety	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
BDI-II				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Minimal depression	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Mild depression	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Moderate depression	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Severe depression	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

Characteristic	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
DSM-5 Disorders				
Depression	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Suicidality	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Manic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Hypomanic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Bipolar	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Panic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Agoraphobia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Social Phobia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Obsessive Compulsive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Posttraumatic Stress	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Substance Abuse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Psychotic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Mood	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Anorexia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Bulemia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Binge-eating	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Generalized Anxiety	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Medical Organic	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Antisocial Personality	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

1 p-value from chi-square test (c), t-test (t), and Fisher's exact test for binary categories (f)

Table 19: Psychiatric Baseline Characteristics – Evaluable Subjects

Same as Table 18 only using evaluable subjects.

Table 20: Baseline POMS – mITT Subjects

Characteristic	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
Tension-Anxiety				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Depression-Dejection				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Anger-Hostility				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Fatigue-Inertia				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	

Characteristic	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
Confusion-Bewilderment				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Vigor-Activity				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Total Mood Disturbance				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	

Note: 1 p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w)

Table 21: Baseline POMS – Evaluable Subjects

Same as Table 20 only using evaluable subjects.

Table 22: Baseline PSQI – mITT Subjects

Characteristic	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
Sleep Quality				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Sleep Latency				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Sleep Duration				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Sleep Disturbance				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	

Characteristic	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
Use of Sleep Medication				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Daytime Dysfunction				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	
Overall Sleep Experience				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx-xx)	

Note: 1 p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w)

Table 23: Baseline PSQI – Evaluable Subjects

Same as Table 22 only using evaluable subjects.

Table 24: Drinking-related Behavior and Characteristics – mITT Subjects

Characteristic	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
Family Members with History of Alcohol Problems				0.xxx
None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Father	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Mother	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
1 Sibling	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
>1 Sibling	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
1 Child	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
>1 Child	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Parental History of Alcohol Problems				0.xxx
Father and/or Mother	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Drinking Goal (n, %)				0.xxx
Controlled Use	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Temporary Abstinence	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Occasional Drinking	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Total Abstinence with Slip	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Total Abstinence	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
No Goal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Abstinence Goal				0.xxx
<Total Abstinence	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Total Abstinence	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Motivation to Reach Goal				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx – xx)	
Confidence to Reach Goal				
N	xx	xx	xx	0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx – xx)	

Characteristic	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
AUD Symptom Severity				0.xxx
Moderate (4 or 5 symptoms)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Severe (6 or more symptoms)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
AUD Number of Symptoms				0.xxx
4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
5	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
6	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
7	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
8	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
9	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
10	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
11	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
AUD Number of Symptoms (continuous)				0.xxx
N	xx	xx	xx	
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Age First Started Drinking Regularly (years)				
N	xx	xx	xx	0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Number Lifetime Hospitalizations to Reduce/Quit Drinking				
N	xx	xx	xx	0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	

Characteristic	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
Number Lifetime Hospitalizations for Illness/ Injuries due to Drinking				
N	xx	xx	xx	0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Number Outpatient Visits to Reduce/Quit Drinking in Last 12 Months				
N	xx	xx	xx	0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Number Lifetime Medical Detoxifications				
N	xx	xx	xx	0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Past Year Number of Support Group Meetings				
N	xx	xx	xx	0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xxx.xx	xxx.xx	xxx.xx	
Median	xx	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	

Note: Percentages are based on the number of non-missing values in each variable.
[1] p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w) - chi-square test for categorical variables (c) – Fisher's exact test for dichotomous variables (f)

Table 25: Drinking-related Behavior and Characteristics – Evaluable Subjects

Same subjects as Table 24 only using evaluable subjects.

Table 26: Baseline Drinking by TLFB – mITT Subjects

Parameter	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
Drinks/Week (Pre-screening Days -1 to -28)				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Minimum	xx.x	xx.x	xx.x	
Maximum	xx.x	xx.x	xx.x	
Drinks/Week (7 Days Prior to Randomization)				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Minimum	xx.x	xx.x	xx.x	
Maximum	xx.x	xx.x	xx.x	
Drinks/Week (Percent Change Pre-screening Days -1 to -28 to 7 Days Prior to Randomization)				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Minimum	xx.x	xx.x	xx.x	
Maximum	xx.x	xx.x	xx.x	
Drinks/Drinking Day (Pre-screening Days -1 to -28)				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Minimum	xx.x	xx.x	xx.x	
Maximum	xx.x	xx.x	xx.x	
Drinks/Drinking Day (7Days Prior to Randomization)				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Minimum	xx.x	xx.x	xx.x	
Maximum	xx.x	xx.x	xx.x	

Parameter	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
Drinks/Drinking Day (Percent Change Pre-screening Days -1 to -28 to 7 Days Prior to Randomization)				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Minimum	xx.x	xx.x	xx.x	
Maximum	xx.x	xx.x	xx.x	
Percentage of Heavy Drinking Days (Pre-screening Days -1 to -28)				0.xxx
Mean	xx.x%	xx.x%	xx.x%	
SD	xx.x%	xx.x%	xx.x%	
Median	xx.x%	xx.x%	xx.x%	
Minimum	xx.x%	xx.x%	xx.x%	
Maximum	xx.x%	xx.x%	xx.x%	
Percentage Days Abstinent (Pre-screening Days -1 to -28)				0.xxx
Mean	xx.x%	xx.x%	xx.x%	
SD	xx.x%	xx.x%	xx.x%	
Median	xx.x%	xx.x%	xx.x%	
Minimum	xx.x%	xx.x%	xx.x%	
Maximum	xx.x%	xx.x%	xx.x%	
WHO Risk Level				0.xxx
High Risk	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Very High Risk	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

Note: Percentages are based on the number of non-missing values in each variable.
[1] p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w) - chi-square test for categorical variables (c)

Table 27: Baseline Drinking by TLFB – Evaluable Subjects

Same as Table 26 only using evaluable subjects.

Table 28: Baseline Alcohol-Related Craving, Consequences, and Withdrawal – mITT Subjects

Parameter	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
ACQ-SR-R				
Total Score				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx.x – xx.x)	
Compulsivity				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx.x – xx.x)	
Expectancy				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx.x – xx.x)	
Purposefulness				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx.x – xx.x)	
Emotionality				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Min-Max	(xx-xx)	(xx-xx)	(xx-xx)	
Scale Min-Max			(xx.x – xx.x)	

Parameter	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
ImBIBe				
Total Score				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Minimum	xx.x	xx.x	xx.x	
Maximum	xx.x	xx.x	xx.x	
Scale Min-Max			(xx.x – xx.x)	
CIWA-AR				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Minimum	xx.x	xx.x	xx.x	
Maximum	xx.x	xx.x	xx.x	
Scale Min-Max			(xx.x – xx.x)	
Withdrawal Symptoms (CIWA ≥ 10)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx

Note: 1 p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w); chi-squared test for symptoms (c)

Programmer's note: Place the parenthesis and character after each p-value to denote the test

Table 29: Baseline Alcohol-Related Craving, Consequences, and Withdrawal – Evaluable Subjects

Same as Table 28 only using evaluable subjects.

Table 30: Baseline Other Substance Use – mITT Subjects

Parameter	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
Fagerstrom Test for Nicotine Dependence				
How often do you smoke?				
Not at all	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Occasionally	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Daily	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
How soon upon waking smoke?				0.xxx
<= 5 min	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
6-30 min	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
31-60 min	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
After 1 hr	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Difficult to refrain from smoking?				0.xxx
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Which cigarette do you hate to give up the most?				0.xxx
First morning	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
All others	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
How many cigarettes per day?				0.xxx
10 or less	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
11-20	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
21-30	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
31 or more	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Smoke more frequently during 1st hours of waking?				0.xxx
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Do you smoke if you are ill and in bed?				0.xxx
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

Parameter	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
Nicotine Dependence Score				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Minimum	xx.x	xx.x	xx.x	
Maximum	xx.x	xx.x	xx.x	
Days Smoked in the Past Week				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Minimum	xx.x	xx.x	xx.x	
Maximum	xx.x	xx.x	xx.x	
Average Cigarettes Smoked Per Week				0.xxx
Mean	xx.x	xx.x	xx.x	
SD	xx.x	xx.x	xx.x	
Median	xx.x	xx.x	xx.x	
Minimum	xx.x	xx.x	xx.x	
Maximum	xx.x	xx.x	xx.x	
THC				0.xxx
Negative	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	
Positive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	

Note: Percentages are based on the number of non-missing values in each variable. [1] p-value from t-test for continuous variables (t) – skewed continuous data uses the Wilcoxon rank-sum test (w) - chi-square test for categorical (c), Fisher's exact test for binary variables (f)
Programmer's note: Place the parenthesis and character after each p-value to denote the test

Table 31: Baseline Other Substance Use – Evaluable Subjects

Same as Table 30 only using evaluable subjects.

12.1.3. Primary Efficacy Endpoint

Table 32: Subjects with No Heavy Drinking Days (mITT) – Full Model, Logistic Regression, Weeks 22-25, with Imputation[a]

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's h	OR	95% CI	
									Upper CI	Lower CI
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	Overall	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Site	1	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Site	2..10	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Cov		x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx

[a]Missing day imputed as a heavy drinking day

Table 33: Subjects with No Heavy Drinking Days (Evaluable) – Full Model, Logistic Regression, Weeks 22-25, with Imputation

Same as Table 32 only using evaluable subjects.

12.1.4. Secondary Efficacy Endpoints

Table 34: Percent Subjects Abstinent from Alcohol (mITT) – Weeks 22-25, With Imputation[a]

	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)
Completely Abstinent			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[a] Missing data imputed as a drinking day

Table 35: Subjects Abstinent from Alcohol (mITT) – Full Model, Logistic Regression, Weeks 22-25, With Imputation[a]

									95% CI	
Parameter		**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > Chi-Square**	**Cohen's h**	**OR**	**Upper CI**	**Lower CI**
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	Overall	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Site	1	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Site	2..10	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Cov		x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx

[a] Missing data imputed as a drinking day

Table 36: Percent Subjects Abstinent from Alcohol (Evaluable) – Weeks 22-25, With Imputation[a]

Same as Table 36 only using evaluable subjects.

Table 37: Subjects Abstinent from Alcohol (Evaluable) – Full Model, Logistic Regression, Weeks 22-25, with Imputation[a]

Same as Table 37 only using evaluable subjects.

Table 38: WHO Shift Baseline to Weeks 22-25, No Imputation

Baseline Category	Week 22-25 Category[a] mITT Subjects				
	Abstinent n (%)	Low Risk n (%)	Medium Risk n (%)	High Risk n (%)	Very High Risk n (%)
High Risk					
Very High Risk					

[a] Percent is based upon row denominator (eg # subjects with High Risk at baseline)

Same table for Horizant subjects only

Same table for Placebo subjects only

Table 39: WHO 1-Level Decrease in Alcohol Consumption (mITT) – Weeks 22-25, No Imputation

	Placebo (N=xx)	**HORIZANT (N=xx)**	**Total (N=xxx)**
WHO 1-Level Decrease			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 40: WHO 1-Level Decrease in Alcohol Consumption (mITT) – Full Model, Logistic Regression, Weeks 22-25, No Imputation

Parameter		**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > Chi-Square**	**Cohen's h**	**OR**	**95% CI**	
									Upper CI	**Lower CI**
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	Overall	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's h	OR	95% CI	
									Upper CI	Lower CI
Site	1	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Site	2..10	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Cov		x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx

Table 41: WHO 1-Level Decrease in Alcohol Consumption (Evaluable) – Weeks 22-25, No Imputation

Same as Table 39 only using evaluable subjects.

Table 42: WHO 1-Level Decrease in Alcohol Consumption (Evaluable) – Full Model, Logistic Regression, Weeks 22-25, No Imputation

Same as Table 40 only using evaluable subjects.

Table 43: WHO 2-Level Decrease in Alcohol Consumption (mITT) – Weeks 22-25, No Imputation

	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)
WHO 2-Level Decrease			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 44: WHO 2-Level Decrease in Alcohol Consumption (mITT) – Full Model, Logistic Regression, Weeks 22-25, No Imputation

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's h	OR	95% CI	
									Upper CI	Lower CI
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	Overall	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Site	1	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Site	2..10	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Cov		x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx

Table 45: WHO 2-Level Decrease in Alcohol Consumption (Evaluable) – Weeks 22-25, No Imputation

Same as Table 43 only using evaluable subjects.

Table 46: WHO 2-Level Decrease in Alcohol Consumption (Evaluable) – Full Model, Logistic Regression, Weeks 22-25, No Imputation

Same as Table 44 only using evaluable subjects.

Table 47: Percentage of Days Abstinent per Week (mITT) -- Full Model, Mixed Effects, Transformed, Weeks 22-25 , No Imputation

Type III Wald Tests

Parameter	Num DF	Den DF	F Value	p-value
ARM	1	xxx	xxx.xx	0.xxx
Week	3	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
Cov	x	xxx	xxx.xx	0.xxx
ARM*Week	3	xxx	xxx.xx	0.xxx

Least Squares Means

				95% CI				Untransformed		Transformed	
Arm	Week	Estimate	SE	Lower CI	Upper CI	Difference	SE	p-value	Cohen's d	p-value	Cohen's d
HORIZANT	22	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	22	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	23	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	23	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	24	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	24	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	25	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	25	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx						

Table 48: Percentage of Days Abstinent per Week (Evaluable) -- Full Model, Mixed Effects, Transformed, Weeks 22-25, No Imputation

Same as Table 47 only using evaluable subjects.

Table 49: Percentage of Days Abstinent per Week (mITT) – Untransformed, Weeks 2-25, No Imputation

	HORIZANT						Placebo					
Study Week	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**
2	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
5	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
7	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
9	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
11	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
12	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
14	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
15	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
16	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
17	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
18	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
19	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
20	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
21	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
22	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
23	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
24	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
25	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Table 50: Percentage of Days Abstinent per Week (Evaluable) – Untransformed, Weeks 2-25, No Imputation

Same as Table 49 only using evaluable subjects.

Table 51: Percentage of Heavy Drinking Days per Week (mITT) – Full Model, Mixed Effects, Transformed, Weeks 22-25, No Imputation

Type III Wald Tests

Parameter	Num DF	Den DF	F Value	p-value
ARM	1	xxx	xxx.xx	0.xxx
Week	3	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
Cov	x	xxx	xxx.xx	0.xxx
ARM*Week	3	xxx	xxx.xx	0.xxx

Least Squares Means

				95% CI				Untransformed		Transformed	
Arm	Week	Estimate	SE	Lower CI	Upper CI	Difference	SE	p-value	Cohen's d	p-value	Cohen's d
HORIZANT	22	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	22	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	23	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	23	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	24	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	24	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	25	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	25	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx						

Table 52: Percentage of Heavy Drinking Days per Week (Evaluable) – Full Model, Mixed Effects, Transformed, Weeks 22-25, No Imputation

Same as Table 51 only with evaluable subjects.

Table 53: Percentage of Heavy Drinking Days per Week (mITT) – Untransformed, Weeks 2-25, No Imputation

	HORIZANT						Placebo					
Study Week	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**
2	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
5	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
7	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
9	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
11	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
12	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
14	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
15	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
16	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
17	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
18	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
19	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
20	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
21	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
22	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
23	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
24	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
25	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Table 54: Percentage of Heavy Drinking Days per Week (Evaluable) – Untransformed, Weeks 2-25, No Imputation

Same as Table 53 only using evaluable subjects.

Table 55: Drinks per Week (mITT) – Full Model, Mixed Effects, Transformed, Weeks 22-25, No Imputation

Type III Wald Tests

Parameter	Num DF	Den DF	F Value	p-value
ARM	1	xxx	xxx.xx	0.xxx
Week	3	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
Cov	x	xxx	xxx.xx	0.xxx
ARM*Week	3	xxx	xxx.xx	0.xxx

Least Squares Means

				95% CI				Untransformed		Transformed	
Arm	Week	Estimate	SE	Lower CI	Upper CI	Difference	SE	p-value	Cohen's d	p-value	Cohen's d
HORIZANT	22	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	22	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	23	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	23	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	24	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	24	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	25	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	25	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx						

Table 56: Drinks per Week (Evaluable) – Full Model, Mixed Effects, Transformed, Weeks 22-25, No Imputation

Same as Table 55 only using evaluable subjects.

Table 57: Drinks per Week (mITT) – Untransformed, Weeks 2-25, No Imputation

	HORIZANT						Placebo					
Study Week	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**
2	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
5	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
7	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
9	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
11	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
12	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
14	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
15	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
16	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
17	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
18	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
19	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
20	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
21	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
22	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
23	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
24	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
25	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Table 58: Drinks per Week (Evaluable) – Untransformed, Weeks 2-25, No Imputation

Same as Table 57 only using evaluable subjects.

Table 59: Drinks per Drinking Day (mITT) – Full Model, Mixed Effects, Transformed, Weeks 22-25, No Imputation

Type III Wald Tests

Parameter	Num DF	Den DF	F Value	p-value
ARM	1	xxx	xxx.xx	0.xxx
Week	3	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
Cov	x	xxx	xxx.xx	0.xxx
ARM*Week	3	xxx	xxx.xx	0.xxx

Least Squares Means

				95% CI				Untransformed		Transformed	
Arm	Week	Estimate	SE	Lower CI	Upper CI	Difference	SE	p-value	Cohen's d	p-value	Cohen's d
HORIZANT	22	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	22	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	23	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	23	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	24	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	24	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	25	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	25	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx						

Table 60: Drinks per Drinking Day (Evaluable) – Full Model, Mixed Effects, Transformed, Weeks 22-25, No Imputation

Same as Table 59 only using evaluable subjects.

Table 61: Drinks per Drinking Day (mITT) – Untransformed, Weeks 2-25, No Imputation

	HORIZANT						Placebo					
Study Week	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**
2	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
3	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
5	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
7	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
9	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
11	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
12	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
13	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
14	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
15	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
16	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
17	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
18	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
19	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
20	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
21	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
22	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
23	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
24	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
25	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Table 62: Drinks per Drinking Day (Evaluable) – Untransformed, Weeks 2-25, No Imputation

Same as Table 61 only using evaluable subjects.

Table 63: ACQ-SR-R Score (mITT) – Full Model, Mixed Effects, Transformed, Weeks 24 + 26 (covering last 4 weeks of maintenance phase), No Imputation

Type III Wald Tests

Parameter	Num DF	Den DF	F Value	p-value
ARM	1	xxx	xxx.xx	0.xxx
Week	1	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
Cov	X	xxx	xxx.xx	0.xxx
ARM*Week	1	xxx	xxx.xx	0.xxx

Least Squares Means

				95% CI				Untransformed		Transformed	
Arm	Week	Estimate	SE	Lower CI	Upper CI	Difference	SE	p-value	Cohen's d	p-value	Cohen's d
HORIZANT	24	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	24	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	26	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	26	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx						

Table 64: ACQ-SR-R Score (Evaluable) – Full Model, Mixed Effects, Transformed, Weeks 24 + 26 (covering last 4 weeks of maintenance phase), No Imputation

Same as Table 63 only using evaluable subjects.

Table 65: ACQ-SR-R Score (mITT) – Untransformed, Each Evaluation During Maintenance Period, No Imputation

	HORIZANT						Placebo					
Study Week	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**
2	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
12	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
16	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
20	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
24	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
26	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Table 66: ACQ-SR-R Score (Evaluable) – Untransfomed, Each Evaluation During Maintenance Period, No Imputation

Same as Table 65 only using evaluable subjects.

Table 67: ImBIBe Score (mITT) – Full Model, Mixed Effects, Transformed, Weeks 24 + 26 (covering last 4 weeks of maintenance phase), No Imputation

Type III Wald Tests

Parameter	Num DF	Den DF	F Value	p-value
ARM	1	xxx	xxx.xx	0.xxx
Week	1	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
Cov	X	xxx	xxx.xx	0.xxx
ARM*Week	1	xxx	xxx.xx	0.xxx

Least Squares Means

				95% CI				Untransformed		Transformed	
Arm	Week	Estimate	SE	Lower CI	Upper CI	Difference	SE	p-value	Cohen's d	p-value	Cohen's d
HORIZANT	24	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	24	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	26	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	26	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx						

Table 68: ImBIBe Score (Evaluable) – Full Model, Mixed Effects, Transformed, Weeks 24 + 26 (covering last 4 weeks of maintenance phase), No Imputation

Same as Table 67 only using evaluable subjects.

Table 69: ImBIBe Score (mITT) – Untransformed, Each Evaluation During Maintenance Period, No Imputation

	HORIZANT						Placebo					
Study Week	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**
4	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
12	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
16	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
20	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
24	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
26	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Table 70: ImBIBe Score (Evaluable) – Untransformed, Each Evaluation During Maintenance Period, No Imputation

Same as Table 69 only using evaluable subjects.

Table 71: Mean Cigarettes Smoked (mITT) – Full Model, Mixed Effects, Transformed, Weeks 24 + 26 (covering last 4 weeks of maintenance phase), No Imputation

Type III Wald Tests

Parameter	Num DF	Den DF	F Value	p-value
ARM	1	xxx	xxx.xx	0.xxx
Week	1	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
Cov	X	xxx	xxx.xx	0.xxx
ARM*Week	1	xxx	xxx.xx	0.xxx

Least Squares Means

				95% CI				Untransformed		Transformed	
Arm	Week	Estimate	SE	Lower CI	Upper CI	Difference	SE	p-value	Cohen's d	p-value	Cohen's d
HORIZANT	24	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	24	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	26	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	26	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx						

Table 72: Mean Cigarettes Smoked (Evaluable) – Full Model, Mixed Effects, Transformed, Weeks 24 + 26 (covering last 4 weeks of maintenance phase), No Imputation

Same as Table 71 only using evaluable subjects.

Table 73: Mean Cigarettes Smoked (mITT) – Untransformed, Each Evaluation During Maintenance Period, No Imputation

	HORIZANT						Placebo					
Study Week	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**
2	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
4	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
6	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
10	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
12	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
16	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
20	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
24	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
26	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Table 74: Mean Cigarettes Smoked (Evaluable) – Untransformed, Each Evaluation During Maintenance Period, No Imputation

Same as Table 73 only using evaluable subjects.

Table 75: PSQI Score (mITT) – Full Model, Mixed Effects, Transformed, Weeks 24 + 26 (covering last 4 weeks of maintenance phase), No Imputation

Type III Wald Tests

Parameter	Num DF	Den DF	F Value	p-value
ARM	1	xxx	xxx.xx	0.xxx
Week	1	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
Cov	x	xxx	xxx.xx	0.xxx
ARM*Week	1	xxx	xxx.xx	0.xxx

Least Squares Means

				95% CI				Untransformed		Transformed	
Arm	Week	Estimate	SE	Lower CI	Upper CI	Difference	SE	p-value	Cohen's d	p-value	Cohen's d
HORIZANT	24	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	24	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	26	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	26	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx						

Table 76: PSQI Score (Evaluable) – Full Model, Mixed Effects, Transformed, Weeks 24 + 26 (covering last 4 weeks of maintenance phase), No Imputation

Same as Table 75 using only evaluable subjects.

Table 77: PSQI Score (mITT) – Untransformed, Each Evaluation During Maintenance Period, No Imputation

	HORIZANT						Placebo					
Study Week	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**	**N**	**Mean**	**SD**	**Median**	**Min**	**Max**
4	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
12	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
16	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
20	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
24	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
26	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Table 78: PSQI Score (Evaluable) – Untransformed, Each Evaluation During Maintenance Period, No Imputation

Same as Table 77 using only evaluable subjects.

Table 79: PSQI Sleep Quality Score (mITT) – Full Model, Mixed Effects, Transformed, Weeks 24 + 26 (covering last 4 weeks of maintenance phase), No Imputation

Same method as Table 75.

Table 110: BDI-II Score (Evaluable) – Untransformed, Each Evaluation During Maintenance Period, No Imputation

12.1.5. Safety Analyses

Table 111: Overall Summary of Adverse Events – mITT Subjects

Disposition	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]
Subjects reporting at least one Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Subjects reporting at least one Severe Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Subjects reporting at least one Treatment−Related[2] Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Subjects reporting at least one Treatment−Related Severe Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Subjects reporting at least one Serious Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Subjects reporting at least one Treatment−Related Serious Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Subjects who Discontinued Medication due to an Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx
Subjects who Died due to an Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx

[1] p-value from chi-square test (c), unless a row has fewer than 5 in a cell then Fisher's exact test (f)
[2] Treatment related is defined as an adverse event that is possibly, probably, or definitely related to treatment

Table 112: Number and Percentage of Subjects with Adverse Events - mITT Subjects

MedDRA System Organ Class/ Preferred Term	Placebo (N=xx)	HORIZANT (N=xx)	p-value[1]
- Any Adverse Events -	xx (xx.x%)	xx (xx.x%)	0.xxx
SOC			
- Overall -	xx (xx.x%)	xx (xx.x%)	0.xxx
Preferred term 1	xx (xx.x%)	xx (xx.x%)	
Preferred term 2	xx (xx.x%)	xx (xx.x%)	

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term.
[1] Fisher's exact test
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 113: Summary of Subjects with Adverse Events by Severity and Relationship – HORIZANT

		Number of Subjects (%) (N=x)										
		Mild		Moderate		Severe		Life-threatening		All Grades		
SOC	MedDRA PT	R	NR	R	NR	R	NR	R	NR	R	NR	R + NR
		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Notes: Events are counted once per subject at the highest severity grade and closest relationship to the investigational product. R= related to investigational product (possibly, probably, definitely). NR = not related to investigational product (unrelated, unlikely).

Table 114: Summary of Subjects with Adverse Events by Severity and Relationship – Placebo

		Number of Subjects (%) (N=x)										
		Mild		Moderate		Severe		Life-threatening		All Grades		
SOC	MedDRA PT	R	NR	R	NR	R	NR	R	NR	R	NR	R + NR
		xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Notes: Events are counted once per subject at the highest severity grade and closest relationship to the investigational product. R= related to investigational product (possibly, probably, definitely). NR = not related to investigational product (unrelated, unlikely).

Table 115: Number and Percentage of Subjects with Adverse Events by Maximum Severity - mITT Subjects

MedDRA SOC/ Preferred Term	Placebo (N=xx)				HORIZANT (N=xx)			
	Mild	Moderate	Severe	Life-threatening	Mild	Moderate	Severe	Life-threatening
- Any Adverse Events - SOC	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
- Overall -	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
Preferred term 1	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
Preferred term 2	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term.
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 116: Number and Percentage of Subjects Adverse Events by Relatedness - mITT Subjects

MedDRA SOC/ Preferred Term	Placebo (n=xx)		HORIZANT (n=xx)	
	Related[1]	Not-Related[2]	Related	Not-Related
SOC	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
- Overall -				
Preferred term 1	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
Preferred term 2	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)

[1]Related are possibly, probably or definitely related to investigational product

[2] Not Related to investigational product (not related or unlikely)

Table 117: Number and Percentage of Subjects with Treatment-Related Adverse Events by Maximum Severity- mITT Subjects

MedDRA SOC/ Preferred Term	Placebo (N=xx)				HORIZANT (N=xx)			
	Mild	Moderate	Severe	Life-threatening	Mild	Moderate	Severe	Life-threatening
SOC	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
- Overall -								
Preferred term 1	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)
Preferred term 2	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)	nn (xx.x%)

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term.
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 118: Number and Percentage of Subjects with Adverse Events Occurring in >= 5% - mITT Subjects

MedDRA SOC/ Preferred Term	Placebo (N=xx)	HORIZANT (N=xx)	p-value[1]
SOC	nn (xx.x%)	nn (xx.x%)	0.xxx
- Overall -			
Preferred term 1	nn (xx.x%)	nn (xx.x%)	0.xxx
Preferred term 2	nn (xx.x%)	nn (xx.x%)	0.xxx

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term. At least 5% occurring in either arm to be included in the table.
1 Fisher's Exact test
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 119: Number and Percentage of Subjects with Adverse Events Leading to Discontinuation of Study - mITT Subjects

MedDRA SOC/ Preferred Term	Placebo (N=xx)	HORIZANT (N=xx)
SOC	nn (xx.x%)	nn (xx.x%)
- Overall -		
Preferred term 1	nn (xx.x%)	nn (xx.x%)
Preferred term 2	nn (xx.x%)	nn (xx.x%)
	nn (xx.x%)	nn (xx.x%)
	nn (xx.x%)	nn (xx.x%)
	nn (xx.x%)	nn (xx.x%)
	nn (xx.x%)	nn (xx.x%)

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term.
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 120: Number and Percentage of Subjects with Adverse Events Leading to Discontinuation of Study Medication – mITT Subjects

MedDRA SOC/ Preferred Term	Placebo (N=xx)	HORIZANT (N=xx)
SOC	nn (xx.x%)	nn (xx.x%)
- Overall -		
Preferred term 1	nn (xx.x%)	nn (xx.x%)
Preferred term 2	nn (xx.x%)	nn (xx.x%)
	nn (xx.x%)	nn (xx.x%)
	nn (xx.x%)	nn (xx.x%)
	nn (xx.x%)	nn (xx.x%)
	nn (xx.x%)	nn (xx.x%)

Notes: Percentages are based on the total number of subjects, as given in the column heading.
Multiple occurrences of a specific adverse event for a subject are counted once in the frequency for the adverse event. Likewise, multiple occurrences of adverse events within a specific preferred term for a subject are counted once in the frequency for the preferred term.
Programmer's Notes: Order System Organ Class alphabetically and preferred term alphabetically within System Organ Class.

Table 121: Number and Percentage of Subjects with Somnolence or Dizziness AEs that Started on a Drinking Day – mITT Subjects

Adverse Event	Placebo (N=xx)	HORIZANT (N=xx)
Somnolence	nn (xx.x%)	nn (xx.x%)
Dizziness	nn (xx.x%)	nn (xx.x%)

Table 122: CIWA-AR Score ≥ 10 at Least Once During Treatment – mITT Subjects

	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)	p-value[1]	Cohen's h	Odds Ratio	95% CI OR Lower CI	95% CI OR Upper CI
CIWA-AR Score >= 10								
Never	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)					
At Least Once	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	0.xxx	0.xx	xx.xxx	xx.xxx	xx.xxx

1 Chi-squared test

Table 123: Summary of Vital Signs and Body Weights – mITT Subjects

Parameter	N	Mean	SD	Med	Max	Min
Vital Sign (units)						
Screening						
Placebo	xx	xx.x	xx.x	xx.x	xx.x	xx.x
HORIZANT	xx	xx.x	xx.x	xx.x	xx.x	xx.x
Week 4						
Placebo	xx	xx.x	xx.x	xx.x	xx.x	xx.x
HORIZANT	xx	xx.x	xx.x	xx.x	xx.x	xx.x
Change from baseline						
Placebo	xx	xx.x	xx.x	xx.x	xx.x	xx.x
HORIZANT	xx	xx.x	xx.x	xx.x	xx.x	xx.x
Weeks 8, 12, 16, 20, 24, 26, 27						

Programmers note: vital signs include pulse rate, systolic blood pressure, and diastolic blood pressure. Body weight (kg) will also be presented.

Table 124: Summary of Other Services Used During Treatment Period – mITT Subjects

Services	Placebo (N=xx)	HORIZANT (N=xx)	p-value[1]
Self Help Meetings			0.xxx
N	xx	xx	
Mean	xx.x	xx.x	
SD	xxx.xx	xxx.xx	
Median	xx	xx	
Min-Max	(xx-xx)	(xx-xx)	
Have you visited another health professional to get help reducing drinking?			
N	Xx	xx	
Yes n (%)	xx (xx)	xx (xx)	
Type of Professional			
A	xx (xx)	xx (xx)	
B	xx (xx)	xx (xx)	
C	xx (xx)	xx (xx)	
Other	xx (xx)	xx (xx)	

Programmer note: categorize type of professional for those categories reaching 5%

Table 125: Summary of ECG Results - mITT Subjects

Result	Placebo (N=xx)	HORIZANT (N=xx)
Screening		
Normal	nn (xx.x%)	nn (xx.x%)
Abnormal, Not Clinically Significant	nn (xx.x%)	nn (xx.x%)
Abnormal, Clinically Significant	nn (xx.x%)	nn (xx.x%)
Week 27		
Normal	nn (xx.x%)	nn (xx.x%)
Abnormal, Not Clinically Significant	nn (xx.x%)	nn (xx.x%)
Abnormal, Clinically Significant	nn (xx.x%)	nn (xx.x%)

Table 126: Summary of Blood Chemistries – mITT Subjects

	Placebo						HORIZANT					
Test	**N**	**Mean**	**SD**	**Med**	**Min**	**Max**	**N**	**Mean**	**SD**	**Med**	**Min**	**Max**
Test Name (units)												
Screening												
Week 4												
Change from baseline												
Weeks 8, 12, 16, 20, 24, 26, 27												

Programmers note: table will include creatinine, ALT, AST, total bilirubin, and GGT.

Table 127: Summary of Positive Urine Drug Tests, Preganancy Test or BAC > 0.000 Any Time During the Study– mITT Subjects

	Number (% Positive)	
Test	**Placebo**	**HORIZANT**
THC	xx (xx%)	xx (xx%)
Cocaine	xx (xx%)	xx (xx%)
Opioids	xx (xx%)	xx (xx%)
Methamphetamine	xx (xx%)	xx (xx%)
Amphetamine	xx (xx%)	xx (xx%)
Benzodiazapines	xx (xx%)	xx (xx%)
Buprenorphine	xx (xx%)	xx (xx%)
Methadone	xx (xx%)	xx (xx%)
Pregnancy	xx (xx%)	xx (xx%)
BAC > 0.000	xx (xx%)	xx (xx%)

Table 128: POMS Total Mood Disturbance Score (mITT) -- Full Model, Mixed Effects, Transformed, Entire Maintenance Period, No Imputation

Type III Wald Tests

Parameter	Num DF	Den DF	F Value	p-value
ARM	1	xxx	xxx.xx	0.xxx
Week	6	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
Baseline Total Score	x	xxx	xxx.xx	0.xxx
ARM*Week	6	xxx	xxx.xx	0.xxx

Least Squares Means

				95% CI				Untransformed		Transformed	
Arm	Week	Estimate	SE	Lower CI	Upper CI	Difference	SE	p-value	Cohen's d	p-value	Cohen's d
HORIZANT	4	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	4	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	8	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	8	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	12	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	12	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	16	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	16	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	20	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	20	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	24	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	24	xx.xx	0.xxx	0.xxx	0.xxx						

				95% CI				Untransformed		Transformed	
Arm	Week	Estimate	SE	Lower CI	Upper CI	Difference	SE	p-value	Cohen's d	p-value	Cohen's d
HORIZANT	27	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	27	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx						

Table 129: POMS Total Mood Disturbance Score (mITT) --Untransformed, Each Evaluation During Maintenance Period, No Imputation

	HORIZANT						Placebo					
Study Week	N	Mean	SD	Median	Min	Max	N	Mean	SD	Median	Min	Max
4	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
8	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
12	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
16	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
20	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
24	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx
26	xx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xxx

Table 130: POMS Tension-Anxiety Score (mITT) -- Full Model, Mixed Effects, Transformed, Entire Maintenance Period, No Imputation

Table 131: POMS Tension-Anxiety Score (mITT) -- Untransformed, Each Evaluation During Maintenance Period, No Imputation

Table 132: POMS Anger-Hostility Score (mITT) -- Full Model, Mixed Effects, Transformed, Entire Maintenance Period, No Imputation

Table 141: POMS Depression-Dejection Score (mITT) -- Untransformed, Each Evaluation During Maintenance Period, No Imputation

Table 142: Frequency of Subjects with Suicidal Ideation Any Time During the Study – mITT Subjects

Number of Subjects Reporting Suicidal Ideation by C-SSRS (%)		
Placebo (N=xx)	**HORIZANT (N=xx)**	**p-value**
xx (xx.x%)	xx (xx.x%)	0.xxx
xx (xx.x%)	xx (xx.x%)	

Table 143: Summary of Concomitant Medication Use – mITT Subjects

	Number of Subjects (%)	
Medication Name	**Placebo (N=xx)**	**HORIZANT (N=xx)**
Medication Name #1	xx (xx.x%)	xx (xx.x%)
Medication Name #2	xx (xx.x%)	xx (xx.x%)

12.1.6. Exploratory Analyses

12.1.6.1. No Heavy Drinking Days by Week, Month and Grace Periods

Table 144: Percentage of Subjects No Heavy Drinking Days (mITT) – Weeks 22-25, with Imputation[a]

	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)
No Heavy Drinking Days			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[a]Missing day imputed as a heavy drinking day

Table 145: Percentage of Subjects No Heavy Drinking Days Weeks 22-25 – No Imputation (mITT)

	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)
No Heavy Drinking Days			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 146: Percentage of Subjects with No Heavy Drinking Days Weeks 22-25 – Full Model No Imputation Logistic Regression (mITT)

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's h	OR	95% CI	
									Upper CI	Lower CI
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's h	OR	95% CI	
									Upper CI	Lower CI
Site	Overall	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Site	1	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Site	2..10	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Cov		x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx

Table 147: Percentage of Subjects No Heavy Drinking Days Weekly with Imputation[a] (mITT)

	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)
WK 2 Heavy Drinking Days			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Repeat for all weeks			

Repeated for weeks 3-25

[a]Missing day imputed as a heavy drinking day

Table 148: Summary of Percentage of Subjects No Heavy Drinking Days (mITT) – Full Model, Weekly, with Imputation[a]

Model Week[b]	Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's h	OR	95% CI Upper CI	95% CI Lower CI
2	Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
3	Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
4 … 25	Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx

[a]Missing day is imputed as a heavy drinking day. [b] Separate models are created for each week only the treatment arm results are presented in the summary table. All models have the same factors, only the week is different

Adjusted Prevalence Estimates[1]

Arm	Week	Estimate	SE	95% CI Lower CI	95% CI Upper CI	Difference	SE	p-value	Cohen's h
HORIZANT	2	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	2	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	3	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	3	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	4	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	4	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	5	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	5	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	6	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	6	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	7	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	7	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	8	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	8	xx.xx	0.xxx	0.xxx	0.xxx				

				95% CI					
Arm	**Week**	**Estimate**	**SE**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's h**
HORIZANT	9	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	9	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	10	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	10	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	11	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	11	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	12	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	12	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	13	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	13	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	14	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	14	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	15	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	15	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	16	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	16	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	17	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	17	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	18	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	18	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	19	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	19	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	20	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	20	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	21	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	21	xx.xx	0.xxx	0.xxx	0.xxx				

				95% CI					
Arm	**Week**	**Estimate**	**SE**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's h**
HORIZANT	22	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	22	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	23	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	23	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	24	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	24	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	25	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	25	xx.xx	0.xxx	0.xxx	0.xxx				

[1]The adjusted prevalence rates are obtained from the weekly logistic regression models.

Table 149: Percentage of Subjects No Heavy Drinking Days Weekly No Imputation (mITT)

	Placebo (N=xx)	**HORIZANT (N=xx)**	**Total (N=xxx)**
WK 2 Heavy Drinking Days			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Repeat for all weeks			

Repeated for weeks 3-25

Table 150: Summary of Percentage of Subjects No Heavy Drinking Days (mITT) – Full Model, Weekly, No Imputation

Same as Table 137 without imputation

Table 151: Percentage of Subjects No Heavy Drinking Days Monthly with Imputation[a] (mITT)

	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)
Mo 1 Heavy Drinking Days			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mo 2 Heavy Drinking Days			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Repeat for all months			

Repeated for months 3-6

[a]Missing day imputed as a heavy drinking day

Table 152: Summary of Percentage of Subjects No Heavy Drinking Days (mITT) – Full Model, Monthly, with Imputation[a]

Model Month[b]	Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's h	OR	95% CI	
										Upper CI	Lower CI
1	Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
2	Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
3	Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
4	Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
5	Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
6	Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx

[a]Missing day imputed as a heavy drinking day; [b] Separate models are created for each month; only the treatment arm results are presented in the summary table. All models have the same factors; only the month is different.

Adjusted Prevalence Estimates[1]

Arm	Month	Estimate	SE	95% CI		Difference	SE	p-value	Cohen's h
				Lower CI	Upper CI				
HORIZANT	1	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	1	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	2	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	2	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	3	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	3	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	4	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	4	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	5	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	5	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	6	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	6	xx.xx	0.xxx	0.xxx	0.xxx				

[1]The adjusted prevalence rates are obtained from the monthly logistic regression models

Table 153: Percentage of Subjects No Heavy Drinking Days Monthly No Imputation (mITT)

	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)
Mo 1 Heavy Drinking Days			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mo 2 Heavy Drinking Days			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Repeat for all months			

Table 154: Summary of Percentage of Subjects No Heavy Drinking Days (mITT) – Full Model, Monthly, No Imputation

Same as table 141 no imputation.

Table 155: Percentage of Subjects No Heavy Drinking Days - Weeks 18-25 with Imputation[a] (last 8 weeks)(mITT)

	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)
Heavy Drinking Days			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[a]Missing day imputed as a heavy drinking day

Table 156: Subjects with No Heavy Drinking Days (mITT) – Logistic Regression, Weeks 18-25 (last 8 weeks) , with Imputation[a]

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's h	OR	95% CI	
									Upper CI	Lower CI
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	Overall	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Site	1	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Site	2..10	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Cov		x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx

[a]Missing day imputed as a heavy drinking day

Table 157: Percentage of Subjects No Heavy Drinking Days - Weeks 18-25 No Imputation (last 8 weeks) (mITT)

Same as Table 148 no imputation.

Table 158: Subjects with No Heavy Drinking Days (mITT) – Logistic Regression, Weeks 18-25 (last 8 weeks) , No Imputation

Same as Table 149 no imputation.

Table 159: Percentage of Subjects No Heavy Drinking Days - Weeks 14-25 with Imputation[a] (last 12 weeks) (mITT)

Table 160: Subjects with No Heavy Drinking Days (mITT) – Logistic Regression, Weeks 14-25 (last 12 weeks) , with Imputation[a]

Table 161: Percentage of Subjects No Heavy Drinking Days - Weeks 14-25 No Imputation (last 12 weeks) (mITT)

Table 162: Subjects with No Heavy Drinking Days (mITT) – Logistic Regression, Weeks 14-25 (last 12 weeks) , No Imputation

Table 163: Percentage of Subjects No Heavy Drinking Days - Weeks 10-25 (last 16 weeks) with Imputation[a] (mITT)

12.1.6.2. Abstinent from Alcohol by Week, Month, and Grace Period

Table 175: Percentage of Subjects Abstinent from Alcohol Weeks 22-25 with Imputation[a] (mITT)

	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)
Completely Abstinent			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[a]Missing day imputed as a drinking day

Table 176: Subjects Abstinent from Alcohol (mITT) – Logistic Regression, Weeks 22-25, with Imputation[a]

								95% CI	
Parameter		**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > Chi-Square**	**Cohen's h**	**OR**	**Upper CI**	**Lower CI**
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	Overall	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Site	1	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Site	2..10	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Cov		x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx

[a]Missing day imputed as a drinking day

Table 177: Percentage of Subjects Abstinent from Alcohol Weekly with Imputation[a] (mITT)

	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)
WK 2 Drinking Days			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Repeat for all weeks			

[a]Missing day imputed as a drinking day

Repeated for weeks 3-25

Table 178: Summary of Subjects Abstinent from Alcohol (mITT) – Logistic Regression, Weekly, with Imputation[a]

Model Week[b]	Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's h	OR	95% CI Upper CI	95% CI Lower CI
2	Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
3	Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
4 … 25	Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx

[a]Missing day imputed as a drinking day, [b] Separate models are created for each week; only the treatment arm results are presented in the summary table. All models have the same factors; only the week is different.

Adjusted Abstinence Estimates[1]

Arm	Week	Estimate	SE	95% CI Lower CI	95% CI Upper CI	Difference	SE	p-value	Cohen's h
HORIZANT	2	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	2	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	3	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	3	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	4	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	4	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	5	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	5	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	6	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	6	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	7	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	7	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	8	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	8	xx.xx	0.xxx	0.xxx	0.xxx				

				95% CI					
Arm	**Week**	**Estimate**	**SE**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's h**
HORIZANT	9	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	9	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	10	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	10	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	11	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	11	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	12	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	12	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	13	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	13	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	14	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	14	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	15	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	15	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	16	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	16	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	17	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	17	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	18	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	18	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	19	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	19	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	20	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	20	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	21	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	21	xx.xx	0.xxx	0.xxx	0.xxx				

				95% CI					
Arm	**Week**	**Estimate**	**SE**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's h**
HORIZANT	22	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	22	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	23	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	23	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	24	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	24	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	25	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	25	xx.xx	0.xxx	0.xxx	0.xxx				

[1]The adjusted prevalence rates are obtained from the weekly logistic regression models.

Table 179: Percentage of Subjects Abstinent from Alcohol Weekly No Imputation (mITT)

Table 180: Summary of Subjects Abstinent from Alcohol (mITT) – Logistic Regression, Weekly, No Imputation

Table 181: Percentage of Subjects Abstinent Monthly with Imputation[a] (mITT)

	Placebo (N=xx)	**HORIZANT (N=xx)**	**Total (N=xxx)**
Mo 1 Drinking Days			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mo 2 Drinking Days			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Repeat for all months			

Repeated for months 3-6

[a]Missing day imputed as a drinking day.

Table 182: Summary of Subjects Abstinent from Alcohol (mITT) – Logistic Regression, Monthly, With Imputation[a]

Table 183: Percentage of Subjects Abstinent from Alcohol Monthly No Imputation (mITT)

Table 184: Summary of Subjects Abstinent from Alcohol (mITT) – Logistic Regression, Weekly, No Imputation

Table 185: Percentage of Subjects Abstinent from Alcohol - Weeks 18-25 with Imputation[a] (last 8 weeks) (mITT)

	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)
Drinking Days			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[a]Missing day imputed as a drinking day.

Table 186: Subjects Abstinent from Alcohol (mITT) – Logistic Regression, Weeks 18-25 (last 8 weeks), with Imputation[a]

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's h	OR	95% CI	
									Upper CI	Lower CI
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	Overall	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Site	1	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Site	2..10	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Cov		x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx

[a]Missing imputed as a drinking day.

12.1.6.3. WHO Drinking Grade Shifts by Week, Month, and Grace Period

Table 205: WHO Shift Baseline to Weeks 22-25, With Imputation[a] (mITT)

Baseline Category	Week 22-25 Category[b]				
	Abstinent N (%)	Low Risk n (%)	Medium Risk n (%)	High Risk n (%)	Very High Risk n (%)
High Risk					
Very High Risk					

[a] Multiple imputation for missing weeks

[b] Percent is based upon row denominator (eg # subjects with High Risk at baseline)

Same table for Horizant only subjects

Same table for Placebo only subjects

Table 206: WHO 1-Level Decrease in Alcohol Consumption Weeks 22-25 With Imputation[a] (mITT)

	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)
WHO 1-Level Decrease			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[a] Multiple imputation for missing weeks

Table 207: WHO 1-Level Decrease in Alcohol Consumption (mITT) – Logistic Regression, Weeks 22-25, With Imputation[a]

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's h	OR	95% CI Upper CI	95% CI Lower CI
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's h	OR	95% CI	
									Upper CI	Lower CI
Site	Overall	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Site	1	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Site	2..10	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Cov		x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx

[a] Multiple imputation for missing weeks

Table 208: WHO 2-Level Decrease in Alcohol Consumption Weeks 22-25 With Imputation[a] (mITT)

	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)
WHO 2-Level Decrease			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[a] Multiple imputation for missing weeks

Table 209: WHO 2-Level Decrease in Alcohol Consumption (mITT) – Logistic Regression, Weeks 22-25, With Imputation[a]

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's h	OR	95% CI	
									Upper CI	Lower CI
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	Overall	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Site	1	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Site	2..10	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx

Parameter	DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's h	OR	95% CI	
								Upper CI	Lower CI
Cov	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx

[a] Multiple imputation for missing weeks

Table 210: WHO Shift Baseline to Weekly Time Period, with Imputation[a] (mITT)

Baseline Category	Week 2 Category[b]				
	Abstinent n (%)	Low Risk n (%)	Medium Risk n (%)	High Risk n (%)	Very High Risk n (%)
High Risk					
Very High Risk					

Repeat for each week

[a] Multiple imputation model used to impute missing weeks.

[b] Percent is based upon row denominator (eg # subjects with High Risk at baseline)

Same table for Horizant only subjects

Same table for Placebo only subjects

Table 211: Percentage of Subjects WHO 1-Level Decrease in Alcohol Consumption Weekly with Imputation[a] (mITT)

	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)
WK 2 WHO 1-Level Decrease			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Repeat for all weeks

[a]Multiple imputation model used to impute missing weeks.

Table 212: Summary of WHO 1-Level Decrease in Alcohol Consumption (mITT) – Logistic Regression, Weekly, with Imputation[a]

Model Week[b]	Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's h	OR	95% CI	
										Upper CI	Lower CI
2	Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
3	Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
4 … 25	Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx

[a]Missing day imputed as a drinking day, [b] Separate models are created for each week; only the treatment arm results are presented in the summary table. All models have the same factors; only the week is different.

Adjusted Prevalence Estimates[1]

Arm	Week	Estimate	SE	95% CI		Difference	SE	p-value	Cohen's h
				Lower CI	Upper CI				
HORIZANT	2	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	2	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	3	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	3	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	4	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	4	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	5	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	5	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	6	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	6	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	7	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx

				95% CI					
Arm	**Week**	**Estimate**	**SE**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's h**
Placebo	7	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	8	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	8	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	9	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	9	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	10	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	10	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	11	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	11	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	12	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	12	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	13	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	13	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	14	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	14	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	15	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	15	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	16	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	16	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	17	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	17	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	18	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	18	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	19	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	19	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	20	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx

				95% CI					
Arm	**Week**	**Estimate**	**SE**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's h**
Placebo	20	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	21	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	21	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	22	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	22	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	23	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	23	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	24	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	24	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	25	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	25	xx.xx	0.xxx	0.xxx	0.xxx				

[1]Prevalence estimates are obtained from the weekly logistic regression models.

Table 213: Percentage of Subjects WHO 2-Level Decrease in Alcohol Consumption Weekly with Imputation[a] (mITT)

	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)
WK 2 WHO 2-Level Decrease			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Repeat for all weeks			

[a]Multiple imputation model used to impute missing weeks.

Table 214: Summary of WHO 2-Level Decrease in Alcohol Consumption (mITT) – Logistic Regression, Weekly, with Imputation[a]

Model Week[b]	Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's h	OR	95% CI	
										Upper CI	Lower CI
2	Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
3	Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
4 … 25	Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx

[a]Missing day imputed as a drinking day, [b] Separate models are created for each week; only the treatment arm results are presented in the summary table. All models have the same factors; only the week is different.

Adjusted Prevalence Estimates[1]

Arm	Week	Estimate	SE	95% CI		Difference	SE	p-value	Cohen's h
				Lower CI	Upper CI				
HORIZANT	2	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx

				95% CI					
Arm	**Week**	**Estimate**	**SE**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's h**
Placebo	2	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	3	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	3	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	4	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	4	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	5	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	5	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	6	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	6	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	7	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	7	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	8	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	8	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	9	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	9	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	10	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	10	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	11	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	11	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	12	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	12	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	13	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	13	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	14	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	14	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	15	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx

				95% CI					
Arm	**Week**	**Estimate**	**SE**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's h**
Placebo	15	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	16	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	16	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	17	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	17	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	18	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	18	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	19	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	19	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	20	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	20	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	21	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	21	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	22	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	22	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	23	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	23	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	24	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	24	xx.xx	0.xxx	0.xxx	0.xxx				
HORIZANT	25	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx
Placebo	25	xx.xx	0.xxx	0.xxx	0.xxx				

[1]Prevalence estimates are obtained from the weekly logistic regression models.

Table 233: Percentage of Subjects WHO 2-Level Decrease in Alcohol Consumption Weeks 18-25 with Imputation[a] (last 8 weeks) (mITT)

Table 234: Subjects with WHO 2-Level Decrease in Alcohol Consumption (mITT) – Logistic Regression, Weeks 18-25 (last 8 weeks), with Imputation[a]

Table 235: WHO Shift Baseline to Weeks 18-25 (last 8 weeks), No Imputation[a] (mITT)

Table 236: Percentage of Subjects WHO 1-Level Decrease in Alcohol Consumption Weeks 18-25 No Imputation (last 8 weeks) (mITT)

Table 237: Subjects with WHO 1-Level Decrease in Alcohol Consumption (mITT) – Logistic Regression, Weeks 18-25 (last 8 weeks), No Imputation

Table 238: Percentage of Subjects WHO 2-Level Decrease in Alcohol Consumption Weeks 18-25 No Imputation (last 8 weeks) (mITT)

Table 239: Subjects with WHO 2-Level Decrease in Alcohol Consumption (mITT) – Logistic Regression, Weeks 18-25 (last 8 weeks), No Imputation

Table 240: WHO Shift Baseline to Weeks 14-25 (last 12 weeks), with Imputation[a] (mITT)

Table 241: Percentage of Subjects WHO 1-Level Decrease in Alcohol Consumption Weeks 14-25 with Imputation[a] (last 12 weeks) (mITT)

Table 242: Subjects with WHO 1-Level Decrease in Alcohol Consumption (mITT) – Logistic Regression, Weeks 14-25 (last 12 weeks), with Imputation[a]

Table 243: Percentage of Subjects WHO 2-Level Decrease in Alcohol Consumption Weeks 14-25 with Imputation[a] (last 12 weeks) (mITT)

Table 244: Subjects with WHO 2-Level Decrease in Alcohol Consumption (mITT) – Logistic Regression, Weeks 14-25 (last 12 weeks), with Imputation[a]

Table 245: WHO Shift Baseline to Weeks 14-25 (last 12 weeks), No Imputation[a] (mITT)

Table 246: Percentage of Subjects WHO 1-Level Decrease in Alcohol Consumption Weeks 14-25 No Imputation (last 12 weeks) (mITT)

Table 247: Subjects with WHO 1-Level Decrease in Alcohol Consumption (mITT) – Logistic Regression, Weeks 14-25 (last 12 weeks), No Imputation

Table 278: Percentage of Subjects WHO 2-Level Decrease in Alcohol Consumption Weeks 2-25 (complete maintenance period) No Imputation (mITT)

Table 279: Subjects with WHO 2-Level Decrease in Alcohol Consumption (mITT) – Logistic Regression, Weeks 2-25 (complete maintenance period), No Imputation

12.1.6.4. Abstinent from Cigarette Smoking

Table 280: Percentage of Subjects Abstinent from Cigarettes among Smokers Weeks 24 + 26 – No Imputation (mITT)

	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)
Completely Abstinent			
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Table 281: Subjects Abstinent from Cigarettes among Smokers (mITT) – Logistic Regression, Weeks 24 + 26, No Imputation

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's h	OR	95% CI	
									Upper CI	Lower CI
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	Overall	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Site	1	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Site	2..10	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				

Parameter	DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's h	OR	95% CI	
								Upper CI	Lower CI
Cov	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx

Table 282: Percentage of Subjects Abstinent from Cigarettes among Smokers Weeks 24 + 26 – with Imputation[a] (mITT)

Table 283: Subjects Abstinent from Cigarettes among Smokers (mITT) – Logistic Regression, Weeks 24 + 26, No Imputation[a]

Table 284: Percentage of Subjects Abstinent from Cigarettes among Smokers Entire Maintenance Period – No Imputation (mITT)

Table 285: Subjects Abstinent from Cigarettes among Smokers (mITT) – Logistic Regression, Entire Maintenance Period, No Imputation

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's h	OR	95% CI	
									Upper CI	Lower CI
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	Overall	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Site	1	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Site	2..10	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Cov		x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx

Table 286: Percentage of Subjects Abstinent from Cigarettes among Smokers Entire Maintenance Period – with Imputation (mITT)

Table 287: Subjects Abstinent from Cigarettes among Smokers (mITT) – Logistic Regression, Entire Maintenance Period, with Imputation[a]

12.1.6.5. Blood PEth Levels

Table 288: Blood PEth Levels (ng/mL) (mITT) – Analysis of Covariance, Transformed, Week 26, No Imputation

Type III Wald Tests

Parameter	Num DF	Den DF	F Value	p-value
ARM	1	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
Baseline PEth	1	xxx	xxx.xx	0.xxx

Least Squares Means

			95% CI				Untransformed		Transformed	
Arm	Estimate	SE	Lower CI	Upper CI	Difference	SE	p-value	Cohen's d	p-value	Cohen's d
HORIZANT	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	xx.xx	0.xxx	0.xxx	0.xxx						

Table 289: Percentages of Negative Blood PEth Samples at Week 26 – No Imputation (mITT)

	Placebo (N=xx)	HORIZANT (N=xx)	Total (N=xxx)
Blood PEth Test			
Negative[1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Positive[2]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[1]Not detectable with lower limit of quantitation (LLOQ) of 8 ng/mL.
[2] PEth level > LLOQ.

Table 290: Samples with No Detectable Blood PEth Levels (mITT) – Logistic Regression, Week 26, No Imputation

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's d	OR	95% CI	
									Upper CI	Lower CI
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	Overall	x	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx
Site	1	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Site	2..10	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Cov		X	xx.xxx	xx.xxx	xx.xxx	0.xxx		xx.xxx	xx.xxx	xx.xxx

12.1.6.6. MINI AUD Symptoms

Table 291: MINI AUD Number of Symptoms (mITT) – Analysis of Covariance, Week 26, No Imputation

Type III Wald Tests

Parameter	Num DF	Den DF	F Value	p-value
ARM	1	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
MINI AUD	1	xxx	xxx.xx	0.xxx

Least Squares Means

			95% CI				Untransformed		Transformed	
Arm	Estimate	SE	Lower CI	Upper CI	Difference	SE	p-value	Cohen's d	p-value	Cohen's d
HORIZANT	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	xx.xx	0.xxx	0.xxx	0.xxx						

12.1.6.7 Continuous Secondary Endpoints With and Without Imputation for Last 4 Weeks and Entire Maintenance Period

Table 292: Percentage of Heavy Drinking Days per Week (mITT) – Mixed Effects, Transformed, Weeks 22-25, with Imputation[a]

Type III Wald Tests

Parameter	Num DF	Den DF	F Value	p-value
ARM	1	xxx	xxx.xx	0.xxx
Week	3	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
Cov	x	xxx	xxx.xx	0.xxx
ARM*Week	3	xxx	xxx.xx	0.xxx

Least Squares Means

				95% CI				Untransformed		Transformed	
Arm	Week	Estimate	SE	Lower CI	Upper CI	Difference	SE	p-value	Cohen's d	p-value	Cohen's d
HORIZANT	22	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	22	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	23	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	23	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	24	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	24	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	25	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	25	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx						

[a]Missing weeks are imputed using a multiple imputation model.

Table 293: Percentage of Heavy Drinking Days per Week (mITT) -- Mixed Effects, Transformed, Weeks 2-25 No Imputation

Type III Wald Tests

Parameter	Num DF	Den DF	F Value	p-value
ARM	1	xxx	xxx.xx	0.xxx
Week	23	xxx	xxx.xx	0.xxx
Site	9	xxx	xxx.xx	0.xxx
Cov	x	xxx	xxx.xx	0.xxx
ARM*Week	23	xxx	xxx.xx	0.xxx

Least Squares Means

				95% CI				Untransformed		Transformed	
Arm	Week	Estimate	SE	Lower CI	Upper CI	Difference	SE	p-value	Cohen's d	p-value	Cohen's d
HORIZANT	2	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	2	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	3	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	3	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	4	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	4	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	5	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	5	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	6	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	6	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	7	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx

				95% CI				Untransformed		Transformed	
Arm	**Week**	**Estimate**	**SE**	**Lower CI**	**Upper CI**	**Difference**	**SE**	**p-value**	**Cohen's d**	**p-value**	**Cohen's d**
Placebo	7	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	8	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	8	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	9	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	9	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	10	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	10	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	11	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	12	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	13	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	13	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	14	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	14	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	15	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	15	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	16	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	16	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	17	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	17	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	18	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	18	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	19	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	19	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	20	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	20	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	21	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx

				95% CI				Untransformed		Transformed	
Arm	Week	Estimate	SE	Lower CI	Upper CI	Difference	SE	p-value	Cohen's d	p-value	Cohen's d
Placebo	21	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	22	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	22	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	23	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	23	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	24	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	24	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	25	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	25	xx.xx	0.xxx	0.xxx	0.xxx						
HORIZANT	Overall	xx.xx	0.xxx	0.xxx	0.xxx	x.xxx	x.xxx	0.xxx	xx.xxx	0.xxx	xx.xxx
Placebo	Overall	xx.xx	0.xxx	0.xxx	0.xxx						

Table 294: Percentage of Heavy Drinking Days per Week (mITT) -- Mixed Effects, Transformed, Weeks 2-25, with Imputation

Table 295: Percentage of Days Abstinent per Week (mITT) – Mixed Effects, Transformed, Weeks 22-25, with Imputation

Table 296: Percentage of Days Abstinent per Week (mITT) – Mixed Effects, Transformed, Weeks 2-25, No Imputation

Table 297: Percentage of Days Abstinent per Week (mITT) – Mixed Effects, Transformed, Weeks 2-25, with Imputation

Table 298: Drinks per Week (mITT) – Mixed Effects, Transformed, Weeks 22-25, with Imputation

Table 299: Drinks per Week (mITT) – Mixed Effects, Transformed, Weeks 2-25, No Imputation

Table 300: Drinks per Week (mITT) – Mixed Effects, Transformed, Weeks 2-25, with Imputation

Table 301: Drinks per Drinking Day (mITT) – Mixed Effects, Transformed, Weeks 22-25, with Imputation

Table 302: Drinks per Drinking Day (mITT) – Mixed Effects, Transformed, Weeks 2-25, No Imputation

Table 303: Drinks per Drinking Day (mITT) – Mixed Effects, Transformed, Weeks 2-25, with Imputation

Table 304: ACQ-SR-R Score (mITT) – Mixed Effects, Transformed, Weeks 24 + 26, with Imputation

Table 305: ACQ-SR-R Score (mITT) – Mixed Effects, Transformed, Weeks 2-26, No Imputation

Table 306: ACQ-SR-R Score (mITT) – Mixed Effects, Transformed, Weeks 2-26, with Imputation

Table 307: ImBIBe Score (mITT) – Mixed Effects, Transformed, Weeks 24 + 26, with Imputation

Table 308: ImBIBe Score (mITT) – Mixed Effects, Transformed, Weeks 2-26, No Imputation

Table 309: ImBIBe Score (mITT) – Mixed Effects, Transformed, Weeks 2-26, with Imputation

Table 310: Mean Cigarettes Smoked per Week among Smokers (mITT) – Mixed Effects, Transformed, Weeks 24 + 26 with Imputation

Table 311: Mean Cigarettes Smoked per Week among Smokers (mITT) – Mixed Effects, Transformed, Weeks 2-26, No Imputation

Table 312: Mean Cigarettes Smoked per Week among Smokers (mITT) – Mixed Effects, Transformed, Weeks 2-26, with Imputation

Table 313: PSQI Score (mITT) – Mixed Effects, Transformed, Weeks 24 + 26, with Imputation

Table 314: PSQI Score (mITT) – Mixed Effects, Transformed, Weeks 2-26, No Imputation

Table 338: BDI-II Score (mITT) – Mixed Effects, Transformed, Weeks 2-26, No Imputation

Table 339: BDI-II Score (mITT) – Mixed Effects, Transformed, Weeks 2-26, with Imputation

12.1.6.8 Subjects with No Heavy Drinking Days by Moderators

Table 340: Subjects with No Heavy Drinking Days by MINI Withdrawal (mITT) – Logistic Regression, Weeks 22-25, with Imputation[a]

Parameter		DF	Estimate	Standard Error	Wald Chi-Square	Pr > Chi-Square	Cohen's d	OR	95% CI	
									Upper CI	Lower CI
Intercept		1	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Treatment	Horizant	x	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Site	1	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Site	2..10	x	xx.xxx	xx.xxx	xx.xxx	0.xxx				
Withdrawal		1	xx.xxx	xx.xxx	xx.xxx	0.xxx	0.xxx	xx.xxx	xx.xxx	xx.xxx
Withdrawal x Tx		x	xx.xxx	xx.xxx	xx.xxx	0.xxx				

[a]Missing day is imputed as a heavy drinking day

Adjusted Prevalence Estimates

Arm	Withdrawal	Estimate	SE	Cohen's h	95% CI		p-value
					Lower CI	Upper CI	
HORIZANT	No	xx.xx	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx
Placebo	No	xx.xx	0.xxx		0.xxx	0.xxx	
HORIZANT	Yes	xx.xx	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx
Placebo	Yes	xx.xx	0.xxx		0.xxx	0.xxx	

Additional models for moderators use the same shell with the moderator by treatment interaction and the adjusted prevalence table

Table 341: Subjects with No Heavy Drinking Days by BAI (mITT) – Logistic Regression, Weeks 22-25, with Imputation

Table 342: Subjects with No Heavy Drinking Days by BAI (mITT) – Logistic Regression, Weeks 22-25, with Imputation

Table 343: Subjects with No Heavy Drinking Days by PSQI Total Score (mITT) – Logistic Regression, Weeks 22-25, with Imputation

Table 344: Subjects with No Heavy Drinking Days by Smoking Status (mITT) – Logistic Regression, Weeks 22-25, with Imputation

Table 345: Subjects with No Heavy Drinking Days by POMS Total Mood Disturbance (mITT) – Logistic Regression, Weeks 22-25, with Imputation

Table 346: Subjects with No Heavy Drinking Days by POMS Tension-Anxiety (mITT) – Logistic Regression, Weeks 22-25, with Imputation

Table 347: Subjects with No Heavy Drinking Days by POMS Depression-Dejection (mITT) – Logistic Regression, Weeks 22-25, with Imputation

Table 348: Subjects with No Heavy Drinking Days by POMS Confusion-Bewilderment (mITT) – Logistic Regression, Weeks 22-25, with Imputation

Table 349: Subjects with No Heavy Drinking Days by POMS Vigor-Anxiety (mITT) – Logistic Regression, Weeks 22-25, with Imputation

Table 350: Subjects with No Heavy Drinking Days by POMS Anger-Hostility (mITT) – Logistic Regression, Weeks 22-25, with Imputation

Table 351: Subjects with No Heavy Drinking Days by POMS Fatigue-Inertia (mITT) – Logistic Regression, Weeks 22-25, with Imputation

Table 352: Subjects with No Heavy Drinking Days by ACQ-SR-R (mITT) – Logistic Regression, Weeks 22-25, with Imputation

Table 353: Subjects with No Heavy Drinking Days by Number of Days Abstinent from Alcohol (7 Days Prior to Randomization) (mITT) – Logistic Regression, Weeks 22-25, with Imputation

Table 354: Subjects with No Heavy Drinking Days by Years Drinking Regularly (mITT) – Logistic Regression, Weeks 22-25, with Imputation

12.2. Listings

Listing 1. Subject Disposition - All Subjects

Subject ID	Date of Consent	Treatment Group	mITT	Eval-uable	Study Completion	(Day) Date of Study Completion or Early Discontinuation	Reason for Early Discontinuation	Subject confined or incar-cerated	Start Date/ End Date of incar-ceration
xxx	mm/dd/yyyy	HORIZANT	Yes	Yes	Yes	(xx) mm/dd/yyyy	xxxxxx	Yes	mm/dd/yyyy / mm/dd/yyyy
		Placebo	No	No	No			No	
		None							

Note: Day is relative to Study Day 0.

Listing 2. Enrollment and Randomization – All Consented Subjects

Subject ID	Treatment Group	Date of Consent	Did the subject meet all eligibility criteria?	Randomized?	Date of Randomization	Kit Number
xxx	HORIZANT	mm/dd/yyyy	Yes	Yes	mm/dd/yyyy	xxx
	Placebo		No	No		

Listing 3. Reason not Eligible – Screen Failures

Subject ID	Criterion Type	Criterion
Xxx	Inclusion Criteria	
	Exclusion Criteria	

Listing 4. Protocol Deviations – mITT Subjects

Subject ID	Treatment Group	Deviation Date	Protocol Deviation	Details
xxx	HORIZANT Placebo	mm/dd/yyyy	Subject Failed to Meet the Inclusion/Exclusion Criteria Source Documentation was Not Available Pregnancy Test Not Performed Required study data was not obtained or obtained late due to site error Informed Consent Deviation AE/SAE Reporting Deviation Other Deviation:	 xxxxxxxxxxxxxx

Note: Only subjects with protocol deviation are listed.

Listing 5. Subjects Excluded from the Efficacy Analysis or Evaluable Set

Subject ID	Treatment Group	Reason for Exclusion from mITT	Reason for Exclusion from Evaluable Set
Xxx	HORIZANT Placebo	xxxxxx	

Note: Only subjects excluded from the efficacy analysis or evaluable set are listed.

Listing 6. Demographics Data – mITT Subjects

Subject ID	Treatment Group	Gender	Age (yrs)	Ethnicity	Race	Marital Status
xxx	HORIZANT Placebo	Male Female	xx	Hispanic or Latino Not Hispanic or Latino Unknown	American Indian or Alaska Native Asian Native Hawaiian or Other Pacific Islander Black or African American White Other Unknown	Married Divorced Living with Partner Widowed Separated Never Married Unknown Missing

Listing 6. Demographics Data - mITT(continued)

Subject ID	Treatment Group	Years of Education	Years of Formal Education (GED=12years)	Usual Employment Pattern in the last 30 days
xxx	HORIZANT Placebo	xx	xxx	Full-time, 35+ hrs/week Part-time, regular hours Part-time, irregular hours/daywork Student Military service Unemployed Retired/Disabled Homemaker In controlled environment Unknown

Listing 7. Baseline Drinking Characteristics – mITT Subjects

Subject ID	Treatment Group	Drinks/Day (Days -1 to -28)	Drinks/Day (Days -1 to -14 Pre-randomization)	Drinks/ Drinking Day (Days -1 to -28)	Drinks/Drinking Day (Days -1 to -14 Pre-randomization)	Weekly % Heavy Drinking Days (Days -1 to -28)	Weekly % Heavy Drinking Days (Days -1 to -14 Pre-randomization)
xxx	HORIZANT Placebo	xxx.x	xxx.x	xxxx	xxx.x		

Note: Exclude the three abstinent days during pre-randomization period.

Listing 7. Baseline Drinking Characteristics mITT (continued)

Subject ID	Treatment Group	Weekly %Very Heavy Drinking Days (Days -1 to -28)	Weekly % Very Heavy Drinking Days (Days -1 to -14 Pre-randomization)	Weekly % Days Abstinent (Days -1 to -28)	Weekly % Days Abstinent (Days -1 to -14 Pre-randomization)
xxx	HORIZANT Placebo	xxx.x	xxx.x	xxx.x	xxx.x

Note: Exclude the three abstinent days during pre-randomization period.

Listing 8. Baseline Smoking Characteristics – mITT Subjects

Subject ID	Treatment Group	How often do you smoke?	How soon after you wake up do you smoke your first cigarette?	Difficult to refrain from smoking?	Which cigarette do you hate to give up the most?	How many cigarettes per day?	Smoke more frequently during 1st hours of waking?	Do you smoke if you are ill and in bed?	Score
xxx	HORIZANT	Occasionally	Within 5 min	No	First morning	10 or less	No	No	xx
	Placebo	Daily	Within 6-30 min	Yes	All others	11-20	Yes	Yes	
		Not at all	Within 31-60 min			21-30			
			After 60 min			31 or more			

Listing 9. Family Members with History of Alcohol Problems

Subject ID	Treatment Group	Relative 1 with Problem	Relative 2 with Problem
xxx	HORIZANT	Father	Father
	Placebo	Mother	Mother
		Brother	Brother
		Sister	Sister
		Child	Child

Note: only list those family members with problems

Listing 10. MINI DSM5 Disorders – mITT Subjects

Subject ID	Treatment Group	Visit Date	Diagnosis	Timeframe
xxx	HORIZANT Placebo	mm/dd/yyyy	xxxxxx	Current (2 weeks) Past Recurrent

Note: Only subjects with a diagnosis of a disorder will be listed.

Listing 11. MINI DSM5 AUD – mITT Subjects

Subject ID	Treatment Group	Visit Date	# of Symptoms
xxx	HORIZANT Placebo	mm/dd/yyyy	xx

Listing 12. Medical History – mITT Subjects

Subject ID No.	Treatment Group	SOC	Specify	Start Date	Ongoing
xxx	HORIZANT Placebo	Blood and Lymphatic System Cardiovascular Endocrinologic/Metabolic Gastrointestinal HEENT Hepatobiliary Hematologic/Oncologic Immune System Infectious Disease Musculoskeletal Nervous system Psychiatric Renal/Urinary Reproductive System Respiratory Skin Other:xxxxxxxxx	xxxxxxxxxxx	mm/dd/yyyy	No Yes

Programming note: Only identify items that were scored "yes"

Listing 13. Drinking Treatment History mITT

Subject ID No.	Treatment Group	Age first started drinking alcohol regularly	Number of lifetime inpatient visits to get help with reducing or quitting drinking	Number of lifetime inpatient hospitalizations for illnesses, injuries, or accidents due to drinking	Number of times in lifetime underwent alcohol detoxification using medication	Number of lifetime outpatient visits with a health professional to get help with reducing or quitting drinking	Number of group meetings attended for alcohol problems or drinking in the past year
xxx	HORIZANT Placebo	xxx	xxx	xxx	xxx	xxx	xxx

Listing 14. Drinking Goal – mITT Subjects

Subject ID	Treatment Group	Visit Date	What GOAL have you chosen for yourself about drinking at this time?	How motivated are you to reach this goal	How confident you are that you will be able to reach this goal
xxx	HORIZANT Placebo	mm/dd/yyyy	Controlled use of alcohol Temporary abstinence from drinking Occasional drinking when urges strongly felt Total abstinence, but realize a slip is possible Total abstinence-never drink again No goal	1 = Not motivated 2, 3, 4, 5, 6, 7, 8, 9, 10= Extremely motivated	1 = Not confident 2, 3, 4, 5, 6, 7, 8, 9, 10= Extremely confident

Listing 15. Surgical History – mITT Subjects

Subject ID No.	Treatment Group	Has the subject had any past surgeries?	Date of Surgery	Type of Surgery
xxx	HORIZANT Placebo	Yes No	mm/dd/yyyy	xxxxxxxxxxxxx

Listing 16. Physical Exam – mITT Subjects

Subject ID No.	Treatment Group	Exam Date	Body System	Specify	Any abnormal finding during the physical exam?	Describe clinically significant findings
xxx	HORIZANT Placebo	mm/dd/yyyy	Oral Cavity HEENT Heart Lungs Abdomen Spleen Liver Extremities Skin Neurological Psychiatric General Appearance Other:xxxxxxxx	xxxxxxxxxxx	Yes No	xxxxxxxx

Programming Note: Only report the items that are abnormal

Listing 17. Daily and Weekly Standard Drink Units (TLFB) During Treatment

Subject ID	Treatment Group	Week	D1	D2	D3	D4	D5	D6	D7	Mean drinks/day	Mean drinks/ drinking day	Heavy drinking days	% days abstinent
xxx	HORIZANT Placebo	1 2 3, etc	xx	xx	xx	xx	xx	xx	xx				

Listing 18. Drinking Question – mITT Subjects

Subject ID	Treatment Group	Date of Assessment	Did the subject have any drinking days since the last visit?	Did the subject have any heavy drinking days since the last visit?	Date of last visit
xxx	HORIZANT Placebo	mm/dd/yyyy	Yes No	Yes No	mm/dd/yyyy

Listing 19. Drinking Consequences, Craving, Impulsiveness, Anxiety and Depression Scores

Subject ID	Treatment Group	Week	ImBIBe	ACQ-SR-R	BAI	BDI-II	BIS
xxx	HORIZANT Placebo		xxx	xxx	xxx	xxx	

Listing 20. Pittsburg Sleep Quality Index Scores

Subject ID	Treatment Group	Week	Subjective sleep quality	Sleep latency	Sleep duration	Habitual sleep disturbances	Use of sleep medication	Day time dysfunction	Total score
xxx	HORIZANT Placebo		xx	xx	xx	xx	xx	xx	xx

Listing 21. Smoking Data– mITT Subjects

Subject ID	Treatment Group	Week	Visit Date	Over the past week, how many days did you smoke cigarettes?	On the days you smoked, how many cigarettes did you smoke on average?	Used any other tobacco or nicotine products during the past week?
xxx	HORIZANT Placebo	2, 3, 5, 7, 9, 13	mm/dd/yyyy	x	xx	No Yes

Listing 22. PEth Levels – mITT Subjects

Subject ID	Treatment Group	Date collected	Week	PEth (ng/mL)	Last Date SDU[a] >0 reported prior to blood draw	Days since last report of SDU >0 prior to blood draw
xxxx	HORIZANT Placebo	mm/dd/yyyy				

[a]SDU is the standard drink unit obtained from the Timeline Follow Back

Listing 23. MINI AUD End of Study – mITT Subjects

Subject ID	Treatment Group	Item											# of Symptoms
		1	2	3	4	5	6	7	8	9	10	11	
xxx	HORIZANT	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
	Placebo	**N**	**N**	**N**	**N**	**N**	**N**	**N**	**N**	**N**	**N**	**N**	
		NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	

Item #	List of Items
1	a. During the times when you drank alcohol, did you end up drinking more than you planned when you started?
2	b. Did you repeatedly want to reduce or control your alcohol use? Did you try to cut down or control your alcohol use, but failed? IF YES TO EITHER, MARK YES.
3	c. On the days that you drank, did you spend substantial time obtaining alcohol, drinking, or recovering from the effects of alcohol?
4	d. Did you crave or have a strong desire or urge to use alcohol?
5	e. Did you spend less time meeting your responsibilities at work, at school, or at home, because of your repeated drinking?
6	f. If your drinking caused problems with your family or other people, did you still keep on drinking?
7	g. Were you intoxicated more than once in any situation where you or others were physically at risk, for example, driving a car, riding a motorbike, using machinery, boating, etc.?
8	h. Did you continue to use alcohol, even though it was clear that the alcohol had caused or worsened psychological or physical problems?
9	i. Did you reduce or give up important work, social or recreational activities because of your drinking?
10	j. Did you need to drink a lot more in order to get the same effect that you got when you first started drinking or did you get much less effect with continued use of the same amount?
11	K1. When you cut down on heavy or prolonged drinking did you have any of the following: [increased sweating or heart rate; hand tremor or "the shakes"; trouble sleeping; nausea or vomiting; hearing or seeing things other people could not see or hear or having sensations in your skin for no apparent reason; agitation; anxiety; seizures] (If yes to 2 or more of these, check yes for this question), OR K2. Did you drink alcohol to reduce or avoid withdrawal symptoms or to avoid being hung over? If K1 or K2 = yes, then score as yes.

Listing 24. Exit Interview – mITT Subjects

Subject ID	Treatment Group	Visit Date	What study drug do you believe you were taking?	Why do you think you received that drug?	Do you feel the study drug helped you to reduced drinking?	How would you describe your experience taking the study drug?
xxx	HORIZANT	mm/dd/yyyy	Placebo	Had side effects	Very Much	Experienced no unwanted side effects and benefited from taking the medication
	Placebo		Active medication	Had no side effects	Much	Experienced some unwanted side effects but benefited from taking the medication
			Both placebo and active	Staff told me	Moderately	Experienced a lot unwanted side effects but benefited from taking the medication
			Don't know	Staff treatment me different	A Little	Experienced no unwanted side effects but did not benefit from taking the medication
			Other substance	No improvement in drinking	Not Little	Experienced some unwanted side effects and did not benefit from taking the medication
				Had improvement in drinking	Not at all	Experienced a lot of unwanted side effects and did not benefit from taking the medication
				Had a hunch		
				I just felt different		
				Other: xxxxx		

Listing 24. Exit Interview – mITT Subjects (Continued)

Subject ID	Treatment Group	Visit Date	If a friend were in need of help for a drinking problem, would you recommend taking the study drug to him/her?	If you were to need treatment in the future, would you choose to take the study drug again?	How much do you think of yourself as wanting to please other people (people pleaser)?
xxx	HORIZANT Placebo	mm/dd/yyyy	Yes, definitely Yes, generally Neither yes nor no No, not really No, definitely not	Definitely yes Probably yes Maybe Probably not Definitely not	More than average Average Less than average

Listing 25. Other Services Use – mITT Subjects

Subject ID	Group	Date	Week	Since your last visit did you attend any AA, 12-step, SOS, or similar group meeting?	How many?	Have you visited another health professional to get help reducing drinking?	What type of professional?
xxx	HORIZANT Placebo	mm/dd/yyyy	xx	Yes No	xxxx	Yes No	xxxxx

Listing 26. Blood for DNA and RNA Testing – mITT Subjects

Subject ID	Treatment Group	Was blood drawn for DNA testing?	Date of blood draw for DNA testing?	Was blood drawn for RNA testing?	Date of blood draw for RNA testing:	Did the subject agree to optional genetics testing for a broader range of research?
xxxx	HORIZANT	Yes	mm/dd/yyyy	Yes	mm/dd/yyyy	Yes
	Placebo	No		No		No

Listing 27. Drug Exposure – mITT Subjects

Subject ID No.	Treatment Group	Study Week	Date Start of Week	Date End of Week	# Capsules Prescribed	# Capsules Taken	Reason for Discontinuation
xxx	HORIZANT Placebo	1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23 24, 25, 26	mm/dd/yyyy	mm/dd/yyyy	xx	xx	

Listing 28. Adverse Events - mITT Subjects

Subject ID	Treatment Group	Adverse Event (Verbatim) S: SOC P: PT Term	Start Date/ Day	Stop Date/ Day	Duration in Days	Severity	Relation-ship	Actions Taken	Outcome	Serious
xxx	HORIZANT Placebo	Verbatim S: xxxx P: xxxx	mm/dd/yyyy xx	mm/dd/yyyy xx		1 2 3 4	1 2 3 4 5	1 2 3 4 5 6	1 2 3 4 5	Yes No

Notes: Day is relative to Study Day 0.
Severity: 1=Mild; 2=Moderate; 3=Severe; 4=Potentially Life-threatening.
Relationship: 1= Unrelated; 2=Unlikely; 3=Possibly; 4=Probably; 5=Definitely
Action Taken Due to AE: 1=None; 2=Treated with Drugs; 3=Non-drug treatment; 4=ER/Outpatient visit; 5=Hospitalization; 6=Referral for treatment
Outcome: 1=Resolved; 2=Recovered with sequelae; 3=Ongoing; 4=Required treatment; 5=Unknown

Programmer's Note: If "Were any AEs reported?" checkbox=No, then display "None Reported" in the Adverse Event column and SOC/PT column. If an AE started and stopped the same day, the duration is 1 day.

Listing 29. Serious Adverse Events - mITT Subjects

Subject ID	Treatment Group	SAE Verbatim S: SOC P: PT	Start Date/ Day	Stop Date/ Day	SAE Category	Severity	Relationship
xxx	HORIZANT Placebo	Verbatim S: XXX P: XX	mm/dd/yyyy Xx	mm/dd/yyyy Xx	Death Life-threatening Hospitalization Disability Congenital Anomaly/Birth Defect Required Intervention to Prevent Permanent Impairment / Damage Other	1 2 3 4 5	1 2 3 4 5

Listing 29. Serious Adverse Events - mITT Subjects (continued)

Subject ID No.	SAE	Continued Study Participation	Study Drug Start Date	Date of last administration of study drug prior to SAE	SAE Abated after study drug stopped?	Continued study drug Administration	SAE reappeared after rechallenge?	Outcome
xxx	Verbatim	Yes No	mm/dd/yyyy	mm/dd/yyyy	Yes No n/a	Yes No	Yes No n/a	1 2 3

Notes: Day is relative to Study Day 0.
Severity: 1=Mild; 2=Moderate; 3=Severe; 4=Potentially Life-threatening.
Relationship: 1= Unrelated; 2=Unlikely; 3=Possibly; 4=Probably; 5=Definitely
Outcome: 1=Recovered/Resolved; 2=Recovering/Resolving; 3=Not Recovered/Not Resolved; 4=Recovered/Resolved With Sequelae; 5=Fatal (Date of Death)

Listing 30. POMS Scores

Subject ID	Treatment Group	Week	Scores						
			Total Mood Disturbance	Tension	Depression	Anger	Fatigue	Confusion	Vigor
xxx	HORIZANT Placebo		xxx	xxx	xxx	xxx	xxx	xxx	xxx

Listing 31. Columbia-Suicide Severity Scale – mITT Subjects

Subject ID	Treatment Group	Visit Date	Study Week	Response to Question: Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13
xxx	HORIZANT	mm/dd/yyyy	-1, 2 , 4	Yes	Yes	Yes	Yes	Yes	Yes	Type 1	1	1	0	0	0	Yes
	Placebo		6, 8, 10,	No	No	No	No	No	No	Type 2	2	2	1	1	1	No
			12, 14, 16							Type 3	3	3	2	2	2	
			18, 20, 22							Type 4	4	4	3	3	3	
			24, 26							Type 5	5	5	4	4	4	
													5	5	5	

Suicide Ideation

1. Have you wished you were dead or wished you could go to sleep and not wake up?
2. Have you actually had any thoughts of killing yourself?
3. Have you been thinking about how you might do this?
4. Have you had these thoughts and had some intention of acting on them?
5. Have you started to work out or worked out the details of how to kill yourself?
6. Do you intend to carry out this plan?

Intensity of Ideation

7. The following features should be rated with respect to the most severe type of ideation (i.e. 1-5 with 1 being the least severe and 5 being the most severe)
8. How many times have you had these thoughts?1=Less than once a week; 2=Once a week; 3=2-5 times a week; 4=Daily or almost; 5=Many times each day
9. When you have the thoughts, how long do they last? 1=Fleeting-few seconds or minutes; 2=Less than 1 hr-some of the time; 3=1-4 hrs/a lot of time; 4=4-8 hrs/most of day; 5=More than 8 hours/persistent or continuous
10. Could/can you stop thining about killing yourself or wanting to die if you want to? 1=Easily; 2=Little Difficulty; 3=Some Difficulty; 4=Lot of Difficulty; 5=Unable to control; 0=Does not attempt to control
11. Are there things that stop you from wanting to die or acting on thoughts of committing suicide? 1=Definite deterrents; 2=Probably Deterrents; 3=Uncertain Deterrents; 4=Unlikely Deterrents; 5=No Deterrents; 0=Does not apply
12. What sort of reasons did you have for thinking about wanting to die or killing yourself? Was it to end pain or stop the way you were feeling or to get attention, revenge or reaction from others 1=Completely to get attention or revenge or reaction; 2=Mostly to get attention or revenge or reaction; 3=Equally to get attention or revenge or reaction and stop pain; 4=Mostly to stop pain; 5=Completely to stop pain; 0=Does not apply

Suicidal Behavior

13. Have you made a suicide attempt?

Listing 31. Columbia-Suicide Severity Scale mITT (continued)

Subject ID No.	Treatment Group	Study Week	Response to Question: Q14	Q15	Q16	Q17	Q18	Q19	Q20	Q21	Q22	Q23	Q24
xxx	HORIZANT	-1, 2 , 4	xx	Yes	Yes	xx	Yes	xx	Yes	Yes	Yes	0	0
	Placebo	6, 8, 10		No	No		No		No	No	No	1	1
		12, 14, 16										2	2
		18, 20, 22										3	
		24, 26										4	
												5 (date mm/dd/yyyy)	

14. Number of attempts
15. Has the subject engaged in non-suicidal self-injurious behavior?
16. Has there been a time when you started to do something to end your life but someone or something stopped you before actually did anything?
17. Number interrupted
18. Has there been a time when you stared to do something to try to end your life but you stopped yourself before you actually did anything?
19. Number aborted
20. Have you taken any step towards making a suicide attempt or preparing to kill yourself?
21. Suicidal behavior was present during the assessment period
22. Completed suicide?
23. Actual Lethality/Medical Damage; 0=No physical damage; 1=Minor physical damage; 2=Moderate physical Damage; 3=Moderately severe physical damage; 4=Severe physical damage; 5=Death
24. Potential Lethality; 0=Behavior not likely to result in injury; 1=Behavior likely to result in injury, but not death; 2=Behavior likely to result in death

Listing 32. Blood Chemistries – mITT Subjects

Subject ID	Treatment Group	Visit Date	Test Name	Result	Units	Flag	Evaluation
xxxx	HORIZANT	mm/dd/yyyy	Creatinine	x.xx	mg/dL	H (high)	WNL
	Placebo		Total Bilirubin	xxx	mg/dL	L (low)	Abnormal, NCS
			ALT	xx.x	U/L		Abnormal, CS
			AST	x.xx	U/L		
			GGT	xx.x	U/L		

Listing 33. Pregnancy Test/Birth Control Data – mITT Subjects

Subject ID	Treatment Group	Pregnancy Test Performed?	Pregnancy Test Date	Pregnancy Result	Methods of birth control
xxx	HORIZANT	Not Done	mm/dd/yyyy	Negative	Oral Contraceptive
	Placebo			Positive	Contraceptive Sponge
					Contraceptive Skin Patch
					Double Barrier
					Intrauterine
					Etonogestrel implant
					Medroxyprogesterone
					Complete Abstinence
					Hormonal Viginal contraceptive Ring
					Surgically Sterile
					Postemopausal
					Partner surgically Sterile
					Other : xxxxxxxxxxxxxxx

Programming note: Only indicate birth control methods that were indicated as Yes

Listing 34. Blood Alcohol Concentration – mITT Subjects

Subject ID	Treatment Group	Visit Date	Study Week	BAC Performed	Time of BAC	BAC %
xxx	HORIZANT Placebo	mm/dd/yyyy	Screen 2 4 6 8 10, 12 16, 20 24, 26 27	Done Not Done	hh:mm	x.xxx

Listing 35. Urine Drug Screen

Subject ID	Treatment Group	Visit Date	Study Week	AMP	Benzos	Coc	Bup	Meth	Methadone	Opioids	THC
xxx	HORIZANT Placebo	mm/dd/yyyy	Screen 2, 4 6, 8 10, 12 16, 20 24, 26 27	Yes No	Yes No	Yes No	Yes No	Yes No	Yes No	Yes No	Yes No

Listing 36. Vital Signs and Body Weights– mITT Subjects

Subject ID	Treatment Group	Visit Date	Study Week	Weight (Kg)	Heart Rate (beats/min)	Systolic Pressure (mmHg)	Diastolic Pressure (mmHg)
xxx	HORIZANT Placebo	mm/dd/yyyy	Screening 4 8 12, 16, 20 24, 26, 27	xxx	xxx	xxx	xxx

Listing 37. ECG – mITT Subjects

Subject ID	Treatment Group	Visit Date	Study Week	Result	If abnormal, specify finding
xxx	HORIZANT Placebo	mm/dd/yyyy	Screen 1 27	Normal Abnormal, NCS Abnormal, CS	xxxxxxxxxxx

Listing 38. Prior and Concomitant Medications – mITT Subjects

Subject ID	Treatment Group	Prior Med?	Verbatin Med/ Coded Med	Indication	Route	Frequency	Dose	Start Date	Stop Date	Continuing?
xxx	HORIZANT	Yes	xxx/ xxxx/ xxxxxx	xxxxxx	xxxxxx	xxxxxx	xxxxxx	dd/mmm/yyyy	dd/mmm/yyyy	Yes
xxx	Placebo	No	xxx/ xxxx/ xxxxxx							No

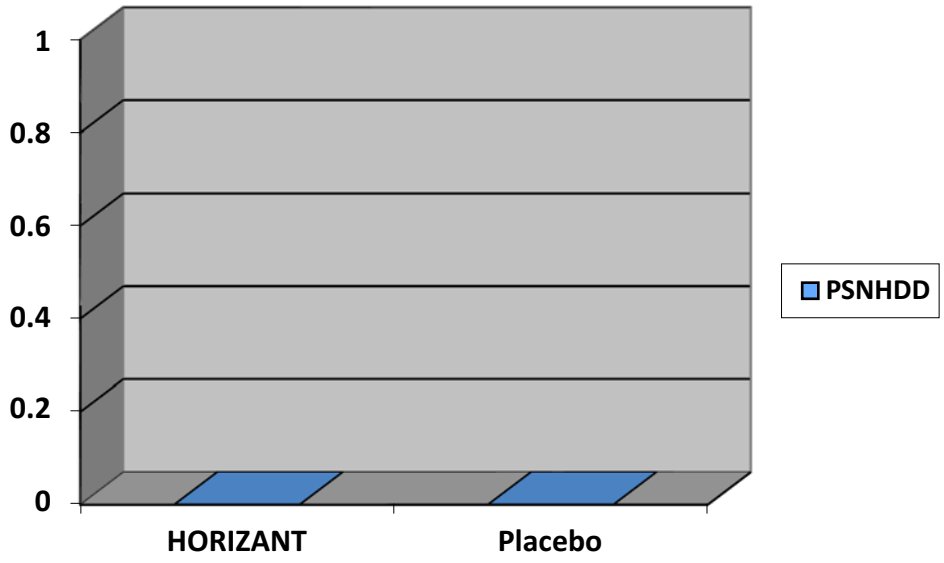
Concomitant medications will be coded to a drug term using the WHO Drug Dictionary (recent version).

Listing 39. Comments – mITT Subjects

Subject ID	Treatment Group	Comments
Xxx	HORIZANT Placebo	xxxxxxxxxxxxx

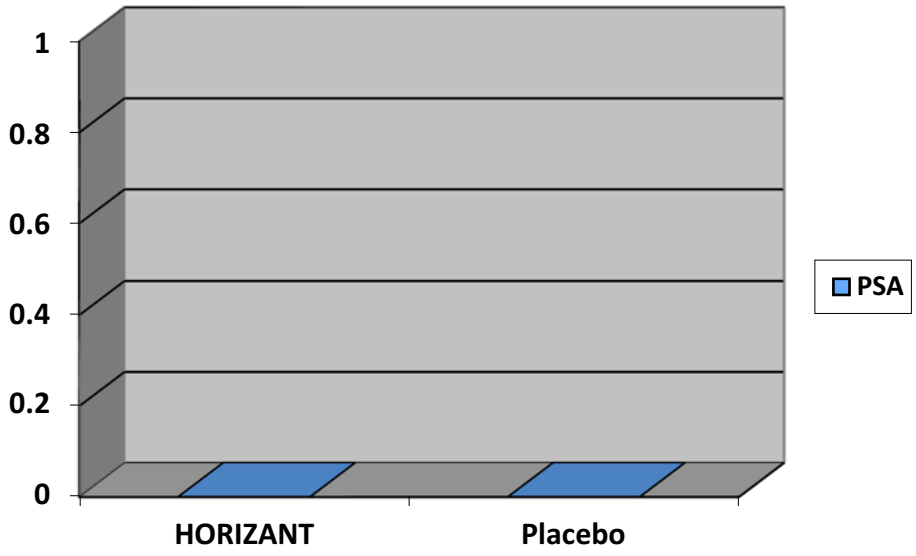
12.3. Figures

Figure 1: Percentage of Subjects No Heavy Drinking Days Weeks 22-25 with Imputation



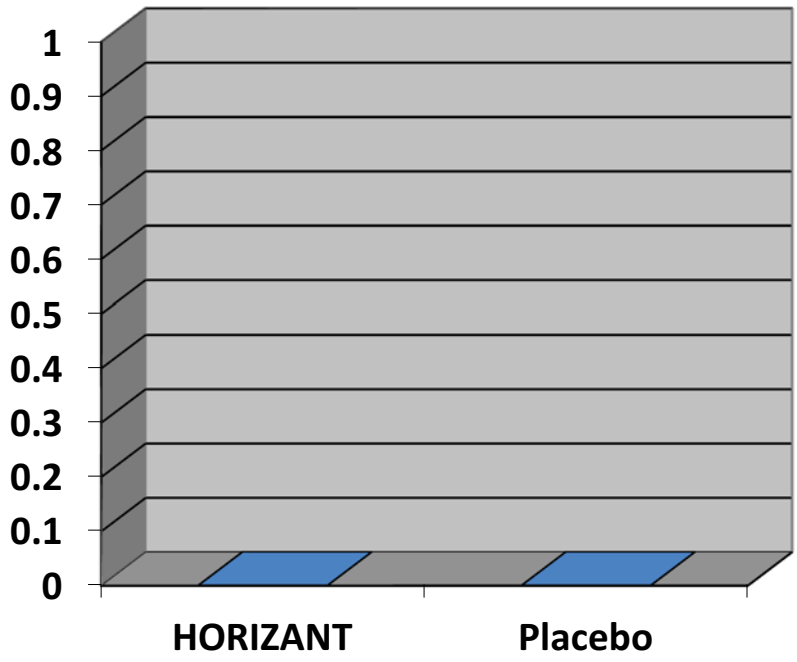
*Programmer note: Use percent on y-axis, bar graph of PSNHDD add Cohen's h, * a significant p-value, put values on graph*

Figure 2: Percentage of Subjects Abstinent Weeks 22-25 No Imputation



*Programmer note: bar graph of PSA add Cohen's h, * a significant p-value, put values on graph*

Figure 3: Percentage of Subjects with WHO 1-Level Decrease in Alcohol Consumption Weeks 22-25 No Imputation



*Programmer note: bar graph of WHO 1-level add Cohen's h, * a significant p-value, put values on graph*

Figure 4: Percentage of Subjects with WHO 2-Level Decrease in Alcohol Consumption Weeks 22-25 No Imputation

*Programmer note: bar graph of WHO 2-level add Cohen's h, * a significant p-value, put values on graph*

Figure 5: Weekly Percentage of Subjects No Heavy Drinking Days with Imputation (mITT)

*Programmer note: graph of estimates out to 25 weeks. Include 95% confidence intervals for each estimate and * on statistically significant differences between treatment groups.*

Figure 6: Monthly Percentage of Subjects No Heavy Drinking Days with Imputation (mITT)

Note: 4 week month periods start on Week 2 of maintenance period

Figure 7: Weekly Percentage of Subjects Abstinent with Imputation (mITT)

Figure 8: Monthly Percentage of Subjects Abstinent with Imputation (mITT)

Note: 4 week month periods start on Week 2 of maintenance period

Figure 9: Weekly Percentage WHO 1-Level Decrease in Alcohol Consumption No Imputation (mITT)

Figure 10: Monthly Percentage WHO 1-Level Decrease in Alcohol Consumption No Imputation (mITT)

Note: 4 week month periods start on Week 2 of maintenance period

Figure 11: Weekly Percentage WHO 2-Level Decrease in Alcohol Consumption No Imputation (mITT)

Figure 12: Monthly Percentage WHO 2-Level Decrease in Alcohol Consumption No Imputation (mITT)

Note: 4 week month periods start on Week 2 of maintenance period

Figure 13: Cumulative Grace Periods for Percentage of Subjects No Heavy Drinking Days with Imputation (mITT)

Programmer note put all of the grace periods (full maintenance period, last 20 weeks, 16 weeks, 12 weeks, 8 weeks, and 4 weeks) on the same graph

Figure 14: Cumulative Grace Periods for Percentage of Subjects Abstinent No Imputation (mITT)

Programmer note put all of the grace periods (full maintenance period, last 20 weeks, 16 weeks, 12 weeks, 8 weeks, and 4 weeks) on the same graph

Figure 15: Cumulative Grace Periods for Percentage WHO 1-Level Decrease in Alcohol Consumption no Imputation (mITT)

Programmer note put all of the grace periods (full maintenance period, last 20 weeks, 16 weeks, 12 weeks, 8 weeks, and 4 weeks) on the same graph

Figure 16: Cumulative Grace Periods for Percentage WHO 2-Level Decrease in Alcohol Consumption no Imputation (mITT)

Programmer note put all of the grace periods (full maintenance period, last 20 weeks, 16 weeks, 12 weeks, 8 weeks, and 4 weeks) on the same graph

Figure 17: Percentage Days Abstinent per Week Least Squares Means – (Untransformed) no Imputation (mITT)

Figure 18: Percent Heavy Drinking Days per Week Lease Squares Means – (Untransformed) no Imputation (mITT)

Figure 19: Mean Drinks per Week Lease Squares Means – (Untransformed) no Imputation (mITT)

Figure 20: Mean Drinks per Drinking Day by Week Least Squares Means – (Untransformed) no Imputation (mITT)

Figure 21: Weekly Number of Cigarettes Smoked in Smokers Over Entire Maintenance Period – Least Squares Means no Imputation (mITT)

*Programmer note: graph of estimates out to 25 weeks. Include 95% confidence intervals for each estimate and * on statistically significant differences between treatment groups.*

Figure 22: ACQ-SR-R Score by Visit Least Squares Means – (Untransformed) no Imputation (mITT)

Figure 23: ImBIBe Score by Visit Least Squares Means – (Untransformed) no Imputation (mITT)

Figure 24: PSQI Score by Visit Least Squares Means – (Untransformed) no Imputation (mITT)

Figure 25: PSQI Sleep Quality Score by Visit Least Squares Means – (Untransformed) no Imputation (mITT)

Figure 26: PSQI Sleep Latency Score by Visit Least Squares Means – (Untransformed) no Imputation (mITT)

Figure 27: PSQI Sleep Duration Score by Visit Least Squares Means – (Untransformed) no Imputation (mITT)

Figure 28: PSQI Sleep Disturbanced Score by Visit Least Squares Means – (Untransformed) no Imputation (mITT)

Figure 29: PSQI Use of Sleep Medication Score by Visit Least Squares Means – (Untransformed) no Imputation (mITT)

Figure 30: PSQI Daytime Dysfuction Score by Visit Least Squares Means – (Untransformed) no Imputation (mITT)

Figure 31: BAI by Visit Least Squares Means – (Untransformed) no Imputation (mITT)

Figure 32: BDI-II by Visit Least Squares Means – (Untransformed) no Imputation (mITT)

Figure 33: ROC BAI by PSNHDD Weeks 22-25 (mITT)

Figure 34: ROC BDI-II by PSNHDD Weeks 22-25 (mITT)

Figure 35: ROC PSQI Total Score by PSNHDD Weeks 22-25 (mITT)

Appendix A. Scale and Scoring Instructions for Pittsburg Sleep Quality Index

Instructions:

The following questions relate to your usual sleep habits during the past month *only*. Your answers should indicate the most accurate reply for the *majority* of days and nights in the past month. Please answer all questions.

1. During the past month, when have you usually gone to bed at night?

   USUAL BED TIME _____

2. During the past month, how long (in minutes) has it usually take you to fall asleep each night?

   NUMBER OF MINUTES _____

3. During the past month, when have you usually gotten up in the morning?

   USUAL GETTING UP TIME _____

4. During the past month, how many hours of *actual sleep* did you get at night? (This may be different than the number of hours you spend in bed.)

   HOURS OF SLEEP PER NIGHT _____

For each of the remaining questions, check the one best response. Please answer *all* questions.

5. During the past month, how often have you had trouble sleeping because you...

   (a) Cannot get to sleep within 30 minutes

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____

   (b) Wake up in the middle of the night or early morning

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____

   (c) Have to get up to use the bathroom

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____

   (d) Cannot breathe comfortably

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____

   (e) Cough or snore loudly

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____

   (f) Feel too cold

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____

   (g) Feel too hot

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____

   (h) Had bad dreams

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____

   (i) Have pain

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____

(j) Other reason(s), please describe _____

_____

How often during the past month have you had trouble sleeping because of this?

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____

6. During the past month, how would you rate your sleep quality overall?

Very good	_____
Fairly good	_____
Fairly bad	_____
Very bad	_____

7. During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____

8. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____

9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

No problem at all	_____
Only a very slight problem	_____
Somewhat of a problem	_____
A very big problem	_____

10. Do you have a bed partner or roommate?

No bed partner or roommate	_____
Partner/roommate in other room	_____
Partner in same room, but not same bed	_____
Partner in same bed	_____

If you have a roommate or bed partner, ask him/her how often in the past month you have had...

(a) Loud snoring

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____

(b) Long pauses between breaths while asleep

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____

(c) Legs twitching or jerking while you sleep

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____

(d) Episodes of disorientation or confusion during sleep

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____

(e) Other restlessness while you sleep; please describe _____

_____

Not during the past month _____	Less than once a week _____	Once or twice a week _____	Three or more times a week _____

Scoring Instructions for the Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index (PSQI) contains 19 self-rated questions and 5 questions rated by the bed partner or roommate (if one is available). Only self-rated questions are included in the scoring. The 19 self-rated items are combined to form seven "component" scores, each of which has a range of 0-3 points. In all cases, a score of "0" indicates no difficulty, while a score of "3" indicates severe difficulty. The seven component scores are then added to yield one "global" score, with a range of 0-21 points, "0" indicating no difficulty and "21" indicating severe difficulties in all areas.

Scoring proceeds as follows:

Component 1: Subjective sleep quality

Examine question #6, and assign scores as follows:

Response	Component 1 score
"Very good"	0
"Fairly good"	1
"Fairly bad"	2
"Very bad"	3

Component 1 score: _____

Component 2: Sleep latency

1. Examine question #2, and assign scores as follows:

Response	Score
≤ 15 minutes	0
16-30 minutes	1
31-60 minutes	2
> 60 minutes	3

Question #2 score: _____

2. Examine question #5a, and assign scores as follows:

Response	Score
Not during the past month	0
Less than once a week	1
Once or twice a week	2
Three or more times a week	3

Question #5a score: _____

3. Add #2 score and #5a score

Sum of #2 and #5a: _____

4. Assign component 2 score as follows:

Sum of #2 and #5a	Component 2 score
0	0
1-2	1
3-4	2
5-6	3

Component 2 score: _____

Component 3: Sleep duration

Examine question #4, and assign scores as follows:

Response	Component 3 score
> 7 hours	0
6-7 hours	1
5-6 hours	2
< 5 hours	3

Component 3 score: _____

Component 4: Habitual sleep efficiency

(1) Write the number of hours slept (question # 4) here: _____

(2) Calculate the number of hours spent in bed:

Getting up time (question # 3): _____

– Bedtime (question # 1): _____

Number of hours spent in bed: _____

(3) Calculate habitual sleep efficiency as follows:

(Number of hours slept/Number of hours spent in bed) × 100 = Habitual sleep efficiency (%)

(_____/_____) × 100 = _____%

(4) Assign component 4 score as follows:

Habitual sleep efficiency %	Component 4 score
> 85%	0
75-84%	1
65-74%	2
< 65%	3

Component 4 score: _____

Component 5: Sleep disturbances

(1) Examine questions # 5b-5j, and assign scores for *each* question as follows:

Response	Score
Not during the past month	0
Less than once a week	1
Once or twice a week	2
Three or more times a week	3

#5b score _____

c score _____

d score _____

e score _____

f score _____

g score _____

h score _____

i score _____

j score _____

(2) Add the scores for questions # 5b-5j:

Sum of # 5b-5j: _____

(3) Assign component 5 score as follows:

Sum of # 5b-5j	Component 5 score
0	0
1-9	1
10-18	2
19-27	3

Component 5 score: _____

Component 6: Use of sleeping medication

Examine question # 7 and assign scores as follows:

Response	Component 6 score
Not during the past month	0
Less than once a week	1
Once or twice a week	2
Three or more times a week	3

Component 6 score: _____

Component 7: Daytime dysfunction

(1) Examine question # 8, and assign scores as follows:

Response	Score
Never	0
Once or twice	1
Once or twice each week	2
Three or more times each week	3

Question # 8 score: _____

(2) Examine question # 9, and assign scores as follows:

Response	Score
No problem at all	0
Only a very slight problem	1
Somewhat of a problem	2
A very big problem	3

Question # 9 score: _____

(3) Add the scores for question # 8 and # 9:

Sum of #8 and #9: _____

(4) Assign component 7 score as follows:

Sum of # 8 and #9	Component 7 score
0	0
1-2	1
3-4	2
5-6	3

Component 7 score: _____

Global PSQI Score

Add the seven component scores together:

Global PSQI Score: _____