STATISTICAL ANALYSIS PLAN

STUDY TITLE:	A Phase 2 Open Label Study Investigating the Efficacy and Safety of Roxadustat (FG-4592) for Treatment of Anemia in Patients Receiving Chemotherapy Treatment for Non-Myeloid Malignancies
PROTOCOL NUMBER:	FGCL-4592-092
SPONSOR:	FibroGen, Inc. 409 Illinois Street San Francisco, California 94158 USA
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CONFIDENTIALITY STATEMENT

STATISTICAL ANALYSIS PLAN SIGNATURE PAGE

Approvals

I have reviewed and accepted the information in this document to be a true and accurate representation of the Statistical Analysis Plan, for Study FGCL-4592-092, Amendment 3.

Initiator:

Signature: *See appended final page for 21CFR Part 11 compliant **Date:**

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Signature Significance

The following significance is lent to the signatures on the Approvals page of this document.

Signatory	Significance
Initiator	By signing, the author is attesting that the content of the document is complete and accurate.

Reviewer	By signing, the reviewer is attesting that the document's approach and contents are compliant with the study protocol, all appropriate, regulatory requirements, and other significant guidelines. This individual(s) has reviewed the document for accuracy and completeness.

CHANGE HISTORY

Version	Date	Description

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ABBREVIATIONS

Abbreviation	Definition
~	Approximately
AE	Adverse Event
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
ANC	Absolute Neutrophil Count
AST	Aspartate Aminotransferase
BP	Blood Pressure
BSC	Best Supportive Care
BUN	Blood Urea Nitrogen
CBC	Complete Blood Count
CFR	Code of Federal Regulations
CHr	Reticulocyte Hemoglobin Content
CI	Confidence Interval
CIA	Chemotherapy Induced Anemia
CKD	Chronic Kidney Disease
Cmax	Maximum Concentration
CRF	Case Report Form
DD	Dialysis-dependent
DVT	Deep Vein Thrombosis
EC	Ethics Committee
ECOG	Eastern Cooperative Oncology Group
ECG/EKG	Electrocardiogram
EE	Efficacy Evaluable
EOS	End of Study
EOT	End of Treatment
EPO	Erythropoietin
ESA	Erythropoiesis-stimulating Agent
ESRD	End-stage Renal Disease
FACT-An	Functional Assessment of Cancer Therapy-Anemia
FACIT-F	Functional Assessment of Chronic Illness Therapy-Fatigue

FAS	Full analysis Set
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
GGT	Gamma-glutamyl Transferase
Hb	Hemoglobin
HBsAg	Hepatitis B Surface Antigen
hCG	Human Chorionic Gonadotropin
HCT	Hematocrit
HCV	Hepatitis C Virus
HDL	High-density lipoprotein (cholesterol)
HIF	Hypoxia-inducible Factor
HIF-PH	Hypoxia-inducible Factor Prolyl Hydroxylase
HIF-PHI	hypoxia-inducible factor prolyl hydroxylase inhibitor
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
HR	Heart Rate or Hazard Ratio
HRQoL	Health-Related Quality of Life
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee
IND	Investigational New Drug
INR	International Normalized Ratio
IRB	Institutional Review Board
ITT	Intention-to-treat
IU	International Unit
IV	Intravenous
LDH	Lactate Dehydrogenase
LDL	Low-density lipoprotein (cholesterol)
LLN	Lower Limit of Normal
LFT	Liver Function Test
LOCF	Last Observation Carried Forward

MCH	Mean Corpuscular Hemoglobin
MCHC	Mean Corpuscular Hemoglobin Concentration
MCV	Mean Corpuscular Volume
MDRD	Modification of Diet in Renal Disease
MDS	Myelodysplastic Syndromes
MedDRA	Medical Dictionary for Regulatory Activities
N	Sample Size
PD	Pharmacodynamics
PI	Principal Investigator
PK	Pharmacokinetics
PRO	Patient Reported Outcome
PTT/PT	Prothrombin Time/Partial Thromboplastin Time
QOL	Quality of Life
RBC	Red Blood Cell
RR	Respiratory Rate
SAE	Serious Adverse Event
SAF	Safety Population
SAP	Statistical Analysis Plan
SOA	Schedule of Assessments
Tbili	Total Bilirubin
TEAE	Treatment-emergent Adverse Event
TESAE	Treatment-emergent Serious Adverse Event
TIA	Transient ischemic Attack
TIBC	Total Iron Binding Capacity
TIW	Three Times Weekly
TSAT	Transferrin Saturation
UIBC	Unsaturated Iron-binding Capacity
ULN	Upper Limit of Normal
VEGF	Vascular Endothelial Growth Factor
VLDL	Very low-density lipoprotein (cholesterol)
WBC	White Blood Cell

1 INTRODUCTION

This Statistical Analysis Plan (SAP) documents planned analyses for Study FGCL-4592-092 (Amendment 3): A Phase 2 Open Label Study Investigating the Efficacy and Safety of Roxadustat (FG-4592) for Treatment of Anemia in Patients Receiving Chemotherapy Treatment for Non-Myeloid Malignancies.

This SAP includes detailed elaboration of statistical analysis methods, models, definitions, and data handling rules. It supersedes the statistical sections in the protocol in case of differences.

2 STUDY OBJECTIVES

Primary Objective:

- To evaluate the efficacy of roxadustat for the treatment of anemia in patients receiving multi-cycle treatments of myelosuppressive chemotherapy.

Secondary Objectives:

- Evaluate the safety of roxadustat
- Evaluate the impact of roxadustat on RBC transfusion requirements
- Evaluate effect of roxadustat on biological indicators: hemoglobin, hematocrit, reticulocytes, hepcidin, serum iron, ferritin, transferrin saturation and total iron binding capacity

3 STUDY DESIGN

3.1 Overview

This is a Phase 2, open label single-arm study. The study will evaluate the efficacy of roxadustat for the treatment of anemia in patients receiving multi-cycle treatments of myelosuppressive chemotherapy. A total of up to 100 patients will be enrolled in this trial.

This trial has three study periods:

Screening (up to 28 days)

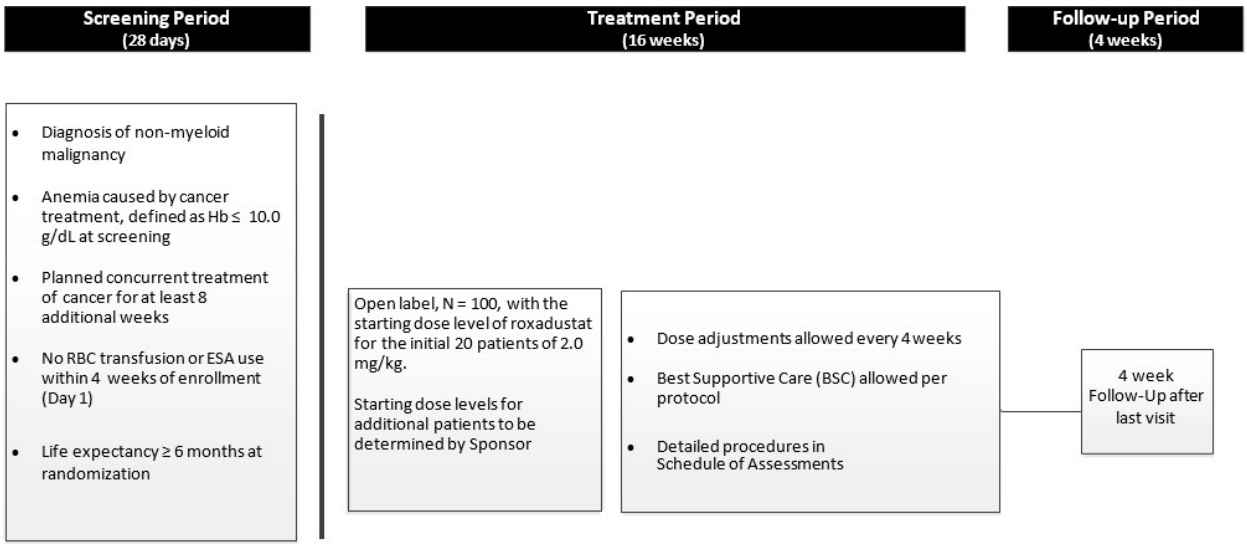
16-week Treatment with roxadustat

4-week Follow-Up

Patients undergo 16 weeks of study treatment with roxadustat. Study visits are scheduled every 2 weeks up to Week 12 and then after 4 weeks at Week 16. Patients' clinical status and safety will be regularly evaluated. Patient reported outcome on Health related Quality of Life (HRQOL) assessments via FACIT-F (fatigue) and FACT-An (anemia) at baseline (Day 1), and at various times as described in the SOA. If, per investigator, unexpected disease progression (malignancy) occurs during the treatment period, patients will be discontinued from study treatment and continue in the follow-up period.

A schematic overview of the study is provided in Figure 1.

Figure 1. Study Schema



3.2 Study Population

Patients with anemia caused by myelosuppressive chemotherapy.

3.3 Sample Size Determination

Up to approximately 100 patients will be enrolled into this study. The sample size is determined by clinical judgment, not by statistical power analysis.

3.4 Randomization and Treatment Blinding

This is an open-label single arm study. There is no randomization and study drug is not blinded.

3.5 Study Treatment

Study drug Roxadustat is administered 3 times a week (TIW) for up to 16 weeks. Starting dose is 2.0 mg/kg before protocol Amendment 3 and 2.5 mg/kg in protocol Amendment 3. Dose titration rules are described in the protocol Appendix 2.

3.6 Study Assessments

The schedule of assessments is presented in Appendix 1 of the protocol.

AEs, concomitant medications, non-drug procedures, and vital signs are collected at all study visits. Dosing records are collected at weeks 5, 9, 13 and 16. ECG and physical examination are performed before and at the end of treatment, and at post treatment follow up. FACT-An questionnaire is administered on Day 1 and weeks 5, 9, 13, and 16 (EOT). Lab test schedule is shown below.

Table 1. Central lab tests and schedule

Lab Category	Test Name	Assessment Time Point
CBC	Hb and ANC, HCT, MCH, MCHC, MCV, RBC, WBC, Neutrophils, Basophils, Eosinophils, Lymphocytes, Monocytes, Abs. Neutrophils, Abs. Basophils, Abs. Eosinophils, Abs. Lymphocytes, Abs. Monocytes, Platelets	Screening 1 and 2, Day 1, weeks 3, 5, 7, 9, 11, 13, 16 (EOT), and EOS
Serum chemistry	Albumin, Bicarbonate, Calcium, Chloride, Creatinine Enzymatic, Glucose Serum, Magnesium, Phosphorus, Potassium, Sodium, UREA (BUN), eGFR by MRD, LDH	Screening, Day 1, weeks 5, 9, 13, 16 (EOT), and EOS
LFTs	ALT, AST, Alkaline Phosphatase, Total Bilirubin	Screening, Day 1, weeks 5, 9, 13, 16 (EOT), EOS
Iron Biomarkers	Iron, Ferritin, Transferrin, Transferrin Saturation, TIBC, UIBC	Screening, Day 1, weeks 9, 16 (EOT), and EOS
Reticulocyte count; CHr	Reticulocyte Count, CHr	Day 1, weeks 5, 9, 13, 16 (EOT), EOS
Hepcidin	Hepcidin	Day 1, weeks 5, 9, 13, 16 (EOT), EOS
Serum Lipid Panel	Cholesterol, HDL Cholesterol, LDL Cholesterol Calculated, Triglyceride, VLDL Cholesterol Calculated	Day 1, weeks 9, 16 (EOT), and EOS

PT, PTT, INR	PT, APTT, INR	Day 1, EOT, EOS
Serum hCG pregnancy test	HCG, Quant	Screening 1
C-reactive protein	CRP, high sensitivity	Day 1, EOT
Exploratory biomarkers	VEGF, Erythropoietin	Screening 1, week 9, 16 (EOT)
B12, Folate	Vitamin B12, Folate	Screening 1
HbsAg, anti-HCV AB, HIV	Hep B Surface Ag, Hep C Ab Screen, HIV-1/-2 Ag and Ab Screen	Screening 1

Roxadustat PK Sub-study:

There is an optional population PK sub-study for roxadustat in this protocol. Patients are not required to participate in the sub-study, and this decision will not make them ineligible for the overall study protocol. Patients who volunteer to participate sign an additional informed consent form. Samples are taken after 4 weeks of treatment at each dose level at 1 or 2 pre-dose sample times and at 1-4 hours post-dose (ideally on the same day as the pre-dose sample but not required). In addition, two samples may be taken at > 5 hours after dosing (may be at different clinic visits consequent with other assessments).

Paclitaxel PK Sub-study:

This optional PK sub-study investigates the potential effect of Roxadustat timing of administration on the pharmacokinetics of paclitaxel. Participation in this sub-study is voluntary. Roxadustat dosing for participants are as follows:

- Dosing of roxadustat is separated from paclitaxel administration by approximately 24 hours or 1 day for the initial paclitaxel dose.
- Dosing of roxadustat is separated from paclitaxel administration by approximately 48 hours or 2 days for the next paclitaxel dose.
- Roxadustat and paclitaxel are dosed on the same day.

3.7 Protocol Amendments

Version	Date	Main Changes
Original	02Apr2019	
Amendment 1	16Jul2019	1. Added exclusion criteria #2 “Patients who are only receiving hormonal products, biological products, novel immunosuppressive products (such as PD-1

		and PD-L1 checkpoint inhibitors) or targeted biological or radiation therapy to treat/manage their cancer. (Patients receiving concomitant myelosuppressive therapy if not intended for cure may be allowed to participate)" 2. Added exclusion criteria #3 "Patients who prefer a Red Blood Cell (RBC) transfusion as treatment of anemia at time of study entry, over receiving the investigational drug Roxadustat" 3. Updated exclusion #13 to "Current condition requiring anticoagulants. Anticoagulant use for non-cardiovascular conditions are allowed. CV prophylaxis with low-dose aspirin, Plavix may be allowed" 4. Updated exclusion #21 to "History of leukemia (current or historical Chronic Lymphocytic Leukemia may be allowed)"
Amendment 2	30Jan2020	1. Added Inclusion # 9 " Estimated life expectancy ≥ 6 months at enrollment (Day 1)" 2. Updated exclusion #4 to "Received an RBC transfusion or ESA within 4 weeks of enrollment (Day 1)" 3. Removed exclusion #13 4. Added clarifications in analysis methods
Amendment 3	22May2020	1. Increased starting dose for newly enrolled patients from 2.0 mg/kg to 2.5 mg/kg 2. Reduced interval between roxadustat and paclitaxel dosing from 48 hours to 24 hours 3. Added Paclitaxel PK sub-study to evaluate the effect of roxadustat timing of administration on the pharmacokinetics of paclitaxel.

3.8 Changes from the Protocol

1. Definition of ITT population

   Original definition in the protocol:

   Defined as all patients enrolled in the roxadustat treatment period, regardless of whether patients received any study drug.

   New definition:

   The ITT population consists of all patients enrolled in the roxadustat treatment period and received at least one dose of study medication.

2. Analysis of Additional Exploratory Biomarkers

Descriptive summary of change from baseline to Week 9 in VEGF and erythropoietin is added.

3. An exploratory endpoint, number (%) of patients that require transfusion from Day 1 Week 16, is added.
4. An additional/exploratory endpoint, mean change in hemoglobin level from baseline up to 4 weeks after the last dose of chemotherapy during the treatment period (without RBC transfusion, is added.
5. An additional/exploratory endpoint, proportion of patients requiring chemotherapy dose reduction or dose hold primarily due to anemia (assessed by the investigator) during the treatment period, is added
6. Various Subgroup Analyses (Starting dose groups, baseline hs-CRP, and Age/gender/race) are added.

4 STUDY ENDPOINTS AND DEFINITIONS

4.1 Primary Efficacy Endpoint

The primary efficacy endpoint is maximum change in hemoglobin in 16 weeks from baseline without RBC transfusion.

Baseline Hb is defined as the mean of the assessments from central lab prior to first dose of the study treatment, which include up to two latest screening values prior to Day 1 and a value on Day 1. All central lab Hb assessments (scheduled and unscheduled) during the treatment period (from Day 1 to EOT or ET) are included in evaluation of this endpoint. Hb values within 4 weeks after an RBC transfusion will be excluded. If all post Day 1 Hb values are found to be under influence of transfusion (i.e. within 4 weeks of transfusion), Hb change from baseline for that subject will be considered "0". These rules are applied to all Hb-related endpoints.

4.2 Secondary Efficacy Endpoints

The secondary efficacy endpoints of this trial are:

- Mean change in hemoglobin level from baseline to week 16 (without RBC transfusion)
- Change in hemoglobin from baseline through week 8, 12, 16 (without RBC transfusion)
- Proportion of patients who achieved a ≥1 g/dL increase in hemoglobin from baseline through week 16
- Time to achieve a ≥1 g/dL increase in hemoglobin from baseline
- Proportion of patients who achieved a ≥1.5 g/dL increase in hemoglobin from baseline through week 16
- Proportion of patients who achieved a hematopoietic response at any time in the study (defined as an increase in Hb of 1.5 g/dL OR attaining a Hb of 11)
- Proportion of patients who achieved a ≥2 g/dL increase in hemoglobin from baseline through week 16
- Number (%) of patients who had a RBC transfusion from beginning of Week 5 (Day 29) to week 16

4.3 Additional Efficacy Endpoints

- Mean change in hemoglobin level from baseline up to 4 weeks after the last dose of chemotherapy during the treatment period (without RBC transfusion)
- Proportion of patients requiring chemotherapy dose reduction or dose hold primarily due to anemia (assessed by the investigator) during the treatment period
- Proportion of patients who achieved a ≥1 g/dL increase in hemoglobin from baseline through week 8 and 12
- Proportion of patients who achieved a ≥1.5 g/dL increase in hemoglobin from baseline through week 8 and 12
- Number (%) of patients that require transfusion from Day 1 Week 16
- Number (%) of patients that require transfusion as medical intervention and/or ESA (erythropoiesis stimulating agent) as a rescue agent. [Time Frame: 16 weeks]
- Percentage of Participants by Tumor Type with Improvement in FACIT-F (fatigue) and Increase in Hemoglobin ≥ 1 g/dL [Time Frame: baseline to week 16]
- Change from Baseline in Quality of life as measured by:

  Functional Assessment of Cancer Therapy-Anemia (FACT-An) test
  [Time Frame: baseline to week 8 and 16]

  Questionnaires of FACT-An (Functional Assessment of Cancer Therapy - Anemia, version 4) and FACIT - F (Functional Assessment of Chronic Illness Therapy Measurement System – Fatigue) are presented in Appendix D. Definitions of the domain scores and scoring algorithms are also included.

4.4 Exploratory Evaluations

- Effect on hepcidin and iron metabolism

  Change from baseline to assessment time points in hepcidin and iron parameters (iron, ferritin, transferrin, TSAT, TIBC, UIBC)

- Effect on cholesterol parameters and lipid metabolism

  Change from baseline to assessment time points in cholesterol, HDL, LDL, VLDL, and triglyceride

- Analysis of change from baseline to Week 9 in VEGF and erythropoietin is added

4.5 Subgroup Analyses

- Starting dose groups
- Tumor Type (breast, lung, ovary, pancreas, stomach-GI tract)
- Chemotherapy regimen (platinum, paclitaxel, gemcitabine)
- Baseline hs-C-reactive protein (CRP) <=ULN vs. >ULN
- Age/Gender/Race

4.6 PK Parameters and Biomarkers

- Roxadustat PopPK
- Paclitaxel DDI

4.7 Safety Parameters

Safety parameters include the following:

- AEs and SAEs
- Laboratory tests
- Vital signs
- 12-lead electrocardiograms (ECGs)
- Physical examinations

5 GENERAL STATISTICAL CONSIDERATIONS

5.1 Statistical Hypothesis Testing

This is an open-label single arm study. No formal hypothesis testing will be performed. Efficacy and safety data will be summarized descriptively with 95% confidence interval (CI) for the key statistics.

5.2 Analysis Populations

5.2.1 All Enrolled or Intent-to-Treat (ITT) Population

The ITT population consists of all patients enrolled in the roxadustat treatment period and received at least one dose of study medication.

5.2.2 Full Analysis Set (FAS)

Full analysis set (FAS) consists of all enrolled patients who receive at least one dose of roxadustat, have a baseline Hb and at least one central lab Hb assessment during the treatment period.

FAS population will be used for all efficacy analysis.

5.2.3 Efficacy Evaluable (EE)

Efficacy Evaluable (EE) population consists of all enrolled patients who have at least one Hb value after 4 weeks of treatment.

5.2.4 Safety (SAF) Population

Safety (SAF) population consists of all patients who took at least one dose of study medication. The primary analysis of safety will be based on the Safety population.

5.2.5 PK Analysis Set (PKS)

The PK Analysis Set consists of subjects who participated in the PK substudy.

5.3 Handling of Dropouts or Missing Data

All data collected in the study database will be included in the analysis. Missing efficacy and safety values will not imputed, with the exception of the cases described below.

5.3.1 Handling Missing Hb Assessment

For subjects in the FAS population, if all post Day 1 Hb values are found to be under influence of transfusion (i.e. within 4 weeks of post-transfusion), Hb change from baseline for these subjects will be considered “0”. No other imputation will be performed.

5.3.2 Handling Missing/Incomplete AE Onset Date

If the AE onset date is incomplete or missing, the following rules will be applied to obtain imputed AE onset date:

- If year and month are present, only day is missing,
  a) If AE onset Year/month = Day 1 Year/month, assign onset date = date of Day 1;
  b) If AE onset Year/month ≠ Day 1 Year/month, assign onset Day = 1;

- If year is present, month and day are missing,
  a) If onset year = year of Day 1, assign onset date = date of Day 1;
  b) If onset year ≠ year of Day 1, assign January 1st to onset month and day.
- If onset date is completely missing, assign onset date = date of Day 1.

If the AE stop date is complete and the imputed AE onset date is after the stop date, then the AE onset date will be re-assigned to be the same as the stop date.

5.3.3 Handling Missing/Incomplete CM Start/Stop Dates

The following rules will be used to impute incomplete CM start and end date:

- Incomplete CM start date: assign 1 to missing Day, January to missing Month.
- Incomplete CM end date: assign 30 to missing Day, December to missing Month. Impute CM end date only if 'ONGOING' is not checked.

If the imputed end date is before the start date (imputed or non-imputed start date), then the imputed end date will be replaced with the start date.

No imputation will be performed for the following cases:

- CM end date will not be imputed if 'ONGOING' is checked.
- Year of CM start or end is missing. If CM end year is missing, then the CM will be assumed to have been used during the study treatment period.

5.4 Adjustment for Covariates

Comparison between starting doses may be performed with adjustment of tumor type, chemo type, and other baseline characteristics.

5.5 Definition of Baseline

Baseline Hb is defined in Section 4.1.

Baseline for the iron parameters (iron, ferritin, transferrin, transferring saturation, TIBC, UIBC) is defined as mean of the last screening value and Day 1 value.

Baseline for other lab tests and vital sign parameters is defined as Day 1 value, or the latest screening value if Day 1 value is missing.

5.6 Analysis Visit Window

Scheduled visits are on the following days: -28 days to Day 1 for screening/baseline visits, days 15, 29, 43, 57, 71, 85, 113 (EOT) for treatment visits, and 141 (EOS) for follow up visit.

Study assessments are scheduled on the first day of Weeks 3, 5, 7, … to evaluate treatment effect up to the week before, such as change from baseline to Weeks 2, 4, 6, … In other words, 'change from baseline to week 3' based on the timing of data collection and 'change from baseline to week 2' based on the actual treatment duration are equivalent.

5.6.1 Hb Analysis Visit Window

Scheduled Hb assessments are on the following days: -42 to -1 (Screenings 1 and 2), 1 (pre-dose), 15, 29, 43, 57, 71, 85, 113 (EOT), and 141 (EOS).

Table 3. Hb analysis window

Analysis Visit	Window
Baseline	Prior to first dose on Day 1
Week 3 - 11	X = 3, 5, 7, 9, 11 Target day = 7 * (X – 1) + 1 Window = [Target day – 7, Target day + 6]
Week 13	[78, 98]
Week 16	[99, day of EOT/ET record
EOS	After EOT/ET record

5.6.2 CHr, Hepcidin, and PRO Analysis Visit Window

Scheduled assessments for CHr, hepcidin, and PRO are on the following days: Day 1 (pre-dose), 29, 57, 85, 113 (EOT), and 141 (EOS).

Table 4. CHr, Hepcidin, and PRO analysis window

Analysis Visit	Window
Baseline	Prior to first dose on Day 1
Week 5 - 13	X = 5, 9, 13 Target day = 7 * (X – 1) + 1 Window = [Target day – 14, Target day + 13]
Week 16	[99, EOT/ET]
EOS	After EOT/ET record

5.6.3 Iron Marker and Lipid Analysis Visit Window

Scheduled iron marker assessments are on the following days: Screening 1 (iron markers), Day 1 (pre-dose), 57, 113 (EOT), and 141 (EOS)

Table 5. Iron marker and lipid analysis window

Analysis Visit	Window
Baseline	Prior to first dose on Day 1
Week 9	X = 9 Target day = 7 * (X – 1) + 1 Window = [Target day – 28, Target day + 27]
Week 16	[85, EOT/ET]

EOS	After EOT/ET record

5.6.4 Safety Assessment Analysis Visit Window

Safety data (lab tests, vital signs, ECG, ECOG, physical exams) are summarized by nominal clinic visit. Data collected during the unscheduled visits are not included in the by-visit summary tables, but are included in data listings and in evaluations for clinically significant abnormal changes.

5.7 Pooling Data of Study Sites

All study sites are pooled in all analyses due to the small number of subjects enrolled at each site.

5.8 General Layout

All study parameters, including baseline characteristics, efficacy, safety, PK and biomarker, will be summarized descriptively. Descriptive statistics including the number of subjects (n), mean, 95% CI of the mean, standard deviation (SD), median, minimum and maximum will be presented for continuous variables. For continuous PK parameters, coefficient (CV) and geometric mean may also be presented. Number (n) and percentage (%) of subjects in each category will be summarized for categorical variables. 95% CI will be presented for response rate. Median and other quartiles will be presented for time to response.

5.9 Data Errata and Hard-Coding

Data errors identified after database lock are documented in an errata log. Under special circumstances, hard-coding in SAS programs is necessary to correct data errors in order to avoid obscure study results. Only limited cases deemed necessary and are approved by study team will be hard-coded. The changed values as well as approval from the study team will be documented.

6 STATISTICAL ANALYSES

6.1 Subject Enrollment and Disposition

The number of subjects enrolled in each study site will be summarized.

The number of subjects in each study population (Enrolled/Safety, FAS, EE, and PK) will be summarized. The number of subjects who completed or discontinued the study as well as the reasons for early discontinuation will be summarized.

Subject who discontinued the study prematurely and the reasons will be listed.

6.2 Protocol Deviations

Protocol deviations will be categorized as follows:

- Entry Deviation: Subject entered study, but did not satisfy eligibility criteria.
- Withdrawal Deviation: Subject met withdrawal criteria during the study but was not withdrawn.
- Dosing Deviation: Subject received the wrong treatment or more than the maximum dose allowed (>3.5 mg/kg) or failed to hold dose when Hb >13.0 g/dL
- Prohibited Medication Deviation: Subject received an excluded concomitant treatment.
- Operational Deviation: All other deviations; including, but not limited to: informed consent form-related deviations other than consent not obtained, IRB/IEC approval expired, study drug not stored under protocol-specified conditions, missing laboratory report, out-of window visit, etc.; includes missed visits, and subject refusal of a study procedure or procedures.

Important deviations are defined as those that are likely to affect a) the safety or physical or mental integrity of the subject, b) the scientific value of the trial. Medical Monitor will identify important deviations, following the guidelines, before the database lock.

Deviations are summarized by subject count and by event count, by study site. All recorded protocol deviations are listed. Reported items that are not considered as protocol deviations are not included in summary tables and data listings, but remain in the database for reference.

6.3 Demographic and Baseline Characteristics

6.3.1 Demographic and Other Baseline Variables

Demographic variables will include age in years, gender, race, ethnicity, and country. Age is defined as the age on the day of signing informed consent.

6.3.2 Baseline Parameters

The following demographics and other baseline variables will be summarized descriptively.

- Age (<=64, 65 – 74, >=75)
- Sex
- Race (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, Other)

- Ethnicity (Hispanic or Latino, Not Hispanic or Latino)
- BMI (<25, 25 -<30, 30 -<35, >=35)
- Weight (<50, 50 -<70, 70 – <100, >=100 kg)

Lab parameters at baseline

- Baseline Hb level (<8, 8 -<9, >=9 g/dL)
- Baseline CRP (<= ULN, >ULN)
- Baseline ferritin (<100, 100 – 400, >400 ug/L)
- Baseline TSAT (<20%, 20 – 40%, >40%)
- Baseline iron repletion status [(TSAT>=20% and Ferritin>=100ug/L) versus (TSAT<20% or Ferritin<100ug/L)]
- Baseline hepcidin (<=ULN, >ULN)

Weight collected at Day 1 is considered as bassline and used for starting dose calculation and dose adjustments. Height collected at Screening, BMI calculated based on height and weight collected at Screening are defined as baseline.

6.3.3 Medical History

Medical conditions captured in the Medical History CRF, including allergies and surgeries, will be coded in system organ class (SOC) and preferred term (PT) using MedDRA (version 24.0). The coded terms will be tabulated by SOC and PT. Detail data will be presented in data listing.

6.3.4 Tumor Type and Disease Burden

Cancer diagnosis (tumor type) is captured in Medical History CRF and is identified using SOC = Neoplasms benign, malignant and unspecified (incl cysts and polyps), or SOC code = 10029104.

The stage (TNM) of the primary cancer is captured in Disease Burden CRF.

6.3.5 Prior and Concomitant Medications

The World Health Organization Drug Dictionary Enhanced version (March 01, 2021) will be used to classify concomitant medications by therapeutic class and generic name.

Prior medications are defined as medications that ended prior to the first dose of the study drug. Concomitant medications are defined as medications that are taken on or after the date of first dose of the study drug regardless of the start date of the medications.

Prior and concomitant medications will be summarized and listed.

Chemotherapies

Chemo-therapies are captured on the Concomitant CRF. To identify paclitaxel, platinum, and gemcitabine the following ATC codes will be used.

Chemotherapy Type	ATC Code	Drug Name
Paclitaxel	L01CD01	paclitaxel
	L01CD02	docetaxel

	L01CD03	paclitaxel poliglumex
	L01CD04	cabazitaxel
Platinum	L01XA01	cisplatin
	L01XA02	carboplatin
	L01XA03	oxaliplatin
	L01XA04	satraplatin
	L01XA05	polyplatillen
gemcitabine	L01BC05	

If Paclitaxel (e.g. Taxol® or Abraxane®) is given as part of a chemotherapy regimen, roxadustat dosing should be held for 24 hours before and after treatment (time 0 = start of infusion) with this drug. Roxadustat dosing frequency may be adjusted, as needed.

Other Potential Drug Interactions

Dose adjustments of strong modulators of CYP2C8 (e.g. gemfibrozil, clopidogrel) and UGT enzymes per physician judgment are allowed.

Phosphate Binders

Concomitant use of phosphate binders (ATC4 code = A02AB for aluminum compounds and ATC4 code = V03AE for treatment of hyperkalemia and hyperphosphatemia) will be summarized.

Statins

Concomitant use of statins (ATC4 code = C10AA for HMG CoA reductase inhibitors, ATC4 code = C10BA for HMG CoA reductase inhibitors in combination with other lipid modifying agents, and ATC4 code = C10AX for other lipid modifying agents) will be summarized. Proportion of patients who used the higher than recommended dose will be tabulated.

Table x. Recommended Maximum Daily Dose of Statins

Statins	Recommended Maximum Dose (mg/day)
Atorvastatin	40
Simvastatin	5
Rosuvastatin	5
Pravastatin	40
Fluvastatin	20
Pitavastatin	2
Lovastatin	20

ESA Use

ESA (ATC4 code = B03XA) use will be summarized by study period: screening up to Day 1, treatment period (defined as from first dose of study drug to Hb assessment at EOT), and post-treatment period.

Supplemental Iron Use

Oral iron supplementation (ATC4 code = B03AA) is allowed. IV iron (ATC4 code = B03AC) use is prohibited, but may be considered if patient is iron-deficient and unresponsive to oral iron supplementation and lacking erythroid response to study medication. Use of oral and IV iron will be summarized by study period.

6.4 Study Treatment and Other Intervention

6.4.1 Study Drug Exposure

Duration of study drug exposure is defined as:

Days on treatment = Date of EOT/ET Hb assessment - first dose date + 1.

Total weekly study drug exposure is defined as the total dose (in mg or mg/kg) of study drug administered within the week as recorded in the dosing record.

Duration of exposure, average weekly dose during treatment and weekly dose by week, as well as total study drug exposure will be summarized. In addition, cases of roxadustat dose exceeding 400 mg or 3.5 mg/kg/dose, whichever is lower, will be listed separately.

Starting dose for initial 20 patients is approximately 2.0 mg/kg (for first 4 weeks), as shown below the dose level at different weight ranges:

Body Weight	**45 to < 70 kg**	**70 - 100 kg**	**> 100 kg**
Dose Level	100 mg	150 mg	200 mg

Patients enrolled after protocol Amendment 3 receive approximately 2.5 mg/kg (for first 4 weeks) as starting dose, as shown below the dose level at different weight ranges.

Body Weight	**45 to < 70 kg**	**70 - 100 kg**	**> 100 kg**
Dose Level	150 mg	200 mg	250 mg

Dose adjustment evaluation will be made every 4 weeks, and dose will be titrated to Hb level and rate of Hb change according to the titration algorithm in **Error! Reference source not found.** of the protocol.

6.4.2 Treatment Compliance

Treatment compliance is defined as the total number of correct doses actually taken by a patient divided by the prescribed doses expected to be taken multiplied by 100.

6.4.3 RBC Transfusions

RBC transfusion from Week 5 (Day 29) to Week 16/EOT is a secondary efficacy endpoint. Planned analysis is described in Section 6.5.3.

6.5 Efficacy Analyses

The efficacy analyses will be primarily based on the FAS population. Sensitivity analyses will be performed based on the EE population for selected key endpoints, including but not limited to primary and secondary efficacy endpoints.

6.5.1 Primary Efficacy Analysis: Maximum Hb Change from Baseline

The primary efficacy endpoint, maximum change from baseline in Hb without RBC transfusion during the treatment period, is defined in Section 4.1. This endpoint will be summarized descriptively including mean (SD), median, range, and 95% CI of the mean.

6.5.2 Secondary Analyses of Hb Change from Baseline

Mean Hb change from baseline over the treatment period, without RBC transfusion, will be computed using the mean area-under-the-curve trapezoid method, from Day 1 to last Hb assessment during treatment. Hb change from baseline (without RBC transfusion) by visit is defined by the analysis visit window in Section 5.6. These endpoints will be summarized descriptively, similar to the primary endpoint.

Hb treatment response during the treatment period without RBC transfusion is defined by the following different criteria:

- ≥1 g/dL increase
- ≥1.5 g/dL increase
- ≥1.5 g/dL increase or attaining a Hb ≥ 11 g/dL
- ≥2 g/dL increase

Proportion of responders will be tabulated, along with the 95% CI estimated using the Clopper-Pearson method. Proportion of responders will also be tabulated by visit based on observed data only.

Median as well as 25th and 75th percentiles of time to Hb response, will be estimated via Kaplan-Meier product limit method. If there is no Hb response during the treatment period, then time to response is censored on the date of last Hb assessment that is not under influence of RBC transfusion.

6.5.3 Analysis of Other Secondary Endpoints

Proportion of subjects who used RBC transfusion (1) from Day 29 (week 5) to date of EOT/ET Hb assessment and (2) from Day 1 to date of EOT/ET Hb assessment will be tabulated, along with the 95% CI estimated using the Clopper-Pearson method. Total number of RBC transfusions and time-adjusted incidence rate will also be summarized.

Change from baseline in FACT-An domain scores will be summarized descriptively by visit and by Hb response. Detailed definitions of domain scores are described in Appendix D.

6.5.4 Exploratory Analyses

6.5.4.1 Effect on Hepcidin

Hepcidin levels are measured on Day 1, week 5, week 9, week 13, week 16 (or EOT/ET) and follow-up. Measured value and change from baseline will be summarized descriptively by visit.

6.5.4.2 Effect on Iron Biomarkers

Iron biomarkers (Transferrin, TIBC, UIBC, TSAT and Ferritin, serum iron) are at screening, Day 1, week 9, week 16 (or EOT/ET) and follow-up. Measured value and change from baseline in iron parameters will be summarized descriptively by visit.

6.5.4.3 Effect on Cholesterol and Lipid Metabolism

Lipids panel (non-fasting) parameters include total cholesterol, LDL, HDL, LDL/HDL ratio and triglycerides. Serum samples are collected on Day 1, weeks 9, 16 (EOT), and EOS. Measured value and change from baseline in iron parameters will be summarized descriptively by visit.

6.5.4.4 Analysis of Change from Baseline to Week 9 in VEGF and Erythropoietin

Samples for VEGF and Erythropoietin are collected at screening, week 9, week 16 (or EOT) and follow-up. Measured value and change from baseline in iron parameters will be summarized descriptively by visit.

6.5.5 Subgroup Analyses

The key efficacy endpoints will summarized by the following subgroups:

- Starting dose groups
- Tumor type
- Chemotherapy regimen
- Baseline hs-C-reactive protein (CRP) <=ULN vs. >ULN
- Age/Gender/Race

6.6 PK Analysis

6.6.1 Roxadustat Plasma Concentrations

Optional population PK sub-study to measure roxadustat plasma concentration at various time points, before and after roxadustat dosing.

6.6.2 Paclitaxel PK Analysis

Optional Paclitaxel PK sub-study to investigate the potential effect of roxadustat timing of administration on the pharmacokinetics of paclitaxel.

6.7 Safety Data Analysis

Safety analyses will include summary of adverse events (including treatment emergent AEs, treatment emergent serious AEs, AEs leading to treatment discontinuation, and deaths), lab test

results, vital signs, ECGs, and physical exams. In general, safety data will only be summarized descriptively based on the Safety population and no rigorous inferential statistical procedures will be applied.

6.7.1 Adverse Events

AEs and SAEs are collected on the AE CRFs. SAEs are special cases of AEs. The definitions of AEs, SAEs, severity, and relationship to study medication are described in Section 9 of the protocol. Adverse events are coded using the Medical Dictionary for Regulatory Activities (MedDRA: version 24.0) for system organ class (SOC) and preferred term (PT).

Due to various reasons, some patients were unable to return the dosing diary. So the date of last dose was not captured in some patients. In this study, all AEs occurred on or after the date of the first study drug (Day 1) are considered treatment emergent adverse events (TEAEs).

All reported AEs are presented in listings. The number and percent of subjects experiencing TEAEs will be tabulated by SOC and PT and will be sorted alphabetically by SOC and by decreasing order of frequency of PT within each SOC. The decreasing order of frequency of preferred terms will be based on the overall population. A subject with multiple adverse events within a SOC is only counted once in this SOC. Similarly, a subject with multiple adverse events within a PT is only counted once in this PT.

TEAE will also be tabulated by severity grade. In the case of multiple events within the same preferred term, the event with the highest severity grade is included. Missing data in the severity grade will not be imputed and is ranked the lowest severity grade in the case of multiple events.

The following summaries will be presented:

- Overview of the AE Profile
- Summary of AEs by SOC and PT
- Summary of most common AEs (≥5% incidence rate) by PT
- Summary of SAEs by SOC and PT
- Summary AEs that led to treatment discontinuation by SOC and PT
- Summary Fatal AEs by SOC and PT
- Summary AEs with severity Grade >=3 by SOC and PT
- Summary Related (including possibly and probably) AEs by SOC and PT
- Summary Related (including possibly and probably) SAEs by SOC and PT
- Summary AEs of special interest (eg, deep vein thrombosis, pulmonary embolism, seizures, infection, sepsis requiring hospitalization, MI, and stroke)

The following events are presented in data listings.

- All reported AEs
- SAEs
- Fatal AEs
- AEs leading to treatment or study discontinuation

- AEs of special interest

All reported adverse events (regardless of treatment emergent or not) will be presented in data listings.

6.7.2 Deaths

Deaths and cause of death captured on the Death CRF will be listed.

6.7.3 Clinical Laboratory Assessments

Change from baseline in laboratory tests listed in Section 3.6 will be summarized descriptively by visit. Incidence of treatment emergent potentially clinically significant (PCS) changes from baseline during the study will also be summarized. Patients whose baseline value is in the PCS range will be excluded from the corresponding summary of treatment emergent PCS change. PCS cutoff values are presented in Appendix A. Only scheduled assessments are included in the by-visit summaries; however, all scheduled and unscheduled assessments are included in evaluation of PCS change.

The following scatter plots for evaluation of drug induce severe hepatotoxicity (eDISH plots) will be presented

- Scatter plot of peak total bilirubin vs. peak ALT
- Scatter plot of peak total bilirubin vs. peak AST

The peak values in the above eDISH plots may not be from the same sample. Listing of patients who met the criteria of moderate or severe liver abnormality (3x ULN in AST and 2x ULN in total bilirubin, or 3x ULN in ALT and 2xULN in total bilirubin) from the same sample will be presented.

6.7.4 Vital Signs

Change from baseline in vital sign parameters [systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR)] will be summarized descriptively by visit. Incidence of treatment emergent potentially clinically significant (PCS) changes from baseline during the study will also be summarized. PCS cutoff values are presented in Appendix A.

6.7.5 ECG

Change from baseline in vital sign parameters [heart rate, QRS interval, QT interval, QT interval – Bazett correction (QTC_B), QT interval – Fridericia correction (QTC_F), RR interval and PR interval] will be summarized descriptively by visit. Incidence of treatment emergent potentially clinically significant (PCS) changes from baseline during the study will also be summarized. PCS cutoff values are presented in Appendix A.

6.7.6 Physical Examination

Physical examination findings will be listed by subject, visit, and body system.

6.7.7 Additional Data Presentations

Data listings, using all available data collected, will be provided.

6.8 Interim Analysis

Informal interim analyses will be conducted to evaluate the initial dose and response as well as safety and tolerability.

APPENDIX A POTENTIALLY CLINICALLY SIGNIFICANT VALUES

1 Lab PCS Cutoff Values

Parameter	SI Unit	Lower Limit	Higher Limit
CHEMISTRY			
Alanine Aminotransferase (ALT)	U/L		≥3 * ULN
Alkaline Phosphatase (ALP)	U/L		≥3 * ULN
Aspartate Aminotransferase (AST)	U/L		≥3 * ULN
Gamma-Glutamyl Transferase (GGT)	U/L		≥3 * ULN
Calcium	mmol/L	<0.8*LLN	>1.2 * ULN
Creatine Phosphokinase(CPK)	U/L		>10 * ULN
Creatinine	µmol/L		> 1.5 x Baseline Value
Potassium	µmol/L	<0.75*LLN	>1.2 * ULN
Sodium	mmol/L	<0.9*LLN	>1.1 * ULN
Total Bilirubin	µmol/L		>2 * ULN
Total Protein	µmol/L	<0.9 * LLN	>1.1 * ULN
Urea (BUN)	mmol/L		>1.5x Baseline Value
HEMATOLOGY			
Neutrophils	10^9/L	≤1	
Platelet Count	10^9/L	≤ 100	≥700
White Blood Cell Count	10^9/L	≤2.5	≥15
LLN: Lower limit of normal, value provided by the laboratory ULN: Upper limit of normal, value provided by the laboratory			

CTCAE TOXICITY GRADING FOR LABORATORY TESTS

The following table is extracted from NCI Common Terminology Criteria for Adverse Events (CTCAE) Version 4.03 (June 14, 2010)

Chemistry

		Grade 1	Grade 2	Grade 3	Grade 4
Albumin	Decreased	3 g/dL – LLN	2 - <3 g/dL	<2 g/dL	
Alkaline phosphatase (ALP)		ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	> 20.0 x ULN
ALT		ULN – 3.0 x ULN	>3.0 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN
AST		ULN – 3.0 x ULN	>3.0 – 5.0 x ULN	>5.0 – 20.0 x ULN	>20.0 x ULN
Total bilirubin		ULN – 1.5 x ULN	>1.5 – 3.0 x ULN	>3.0 – 10.0 x ULN	>10.0 x ULN
Calcium (Corrected)	Decreased	8.0 mg/dL – LLN	7.0 - <8.0 mg/dL	6.0 - <7.0 mg/dL	<6.0 mg/dL
		ULN – 11.5 mg/dL	>11.5 – 12.5 mg/dL	>12.5 – 13.5 mg/dL	>13.5 mg/dL
GGT		ULN – 2.5 x ULN	>2.5 – 5.0 x ULN	>5.0 – 20.0 x ULN	> 20.0 x ULN
Glucose (Random)	Decreased	55 mg/dL – LLN	40 - <55 mg/dL	30 - <40 mg/dL	<30 mg/dL
Glucose (Fasting)		ULN – 160 mg/dL	>160 – 250 mg/dL	>250 – 500 mg/dL	> 500 mg/dL
Phosphorous	Decreased	2.5 -<LLN mg/dL	2.0 -<2.5 mg/dL	1.0 - <2.0 mg/dL	<1.0 mg/dL
Potassium	Decreased	3.0 mmol/L – LLN	3.0 mmol/L – LLN[1]	2.5 - <3.0 mmol/L	<2.5 mmol/L
		ULN – 5.5 mmol/L	>5.5 – 6.0 mmol/L	>6.0 – 7.0 mmol/L	>7.0 mmol/L
Sodium	Decreased	130 mmol/L – LLN	None	120 - <130 mmol/L	<120 mmol/L
		ULN – 150 mmol/L	>150 – 155 mmol/L	>155 – 160 mmol/L	>160 mmol/L
Magnesium	Decreased	1.2 mg/dL – LLN	0.9 - <1.2 mg/dL	0.7 - <0.9 mg/dL	<0.7 mg/dL
		ULN – 3.0 mg/dL	None	>3.0 – 8.0 mg/dL	>8.0 mg/dL

Serum Hematology

		Grade 1	Grade 2	Grade 3	Grade 4
Uric acid		ULN – 10 mg/dL[2]	None	ULN – 10 mg/dL[3]	>10 mg/dL
Creatinine Enzymatic		>1 – 1.5 x baseline[4] ULN – 1.5 x ULN	>1.5 – 3.0 x baseline[4] >1.5 – 3.0 x ULN	>3.0 x baseline[4] >3.0 – 6.0 x ULN	>6.0 x ULN
Triglycerides		150 – 300 mg/dL	>300 – 500 mg/dL	>500 – 1,000 mg/dL	>1,000 mg/dL
Hgb	Decreased	10.0 g/dL – LLN	8.0 - <10.0 g/dL	<8.0 g/dL	
		>0 – 2 g/dL (+ ULN/Baseline)[5]	>2 – 4 g/dL (+ ULN/Baseline)[5]	>4 g/dL (+ ULN/Baseline)[5]	
Platelet	Decreased	75,000 /mm^3 – LLN	50,000 – <75,000 /mm^3	25,000 - <50,000 /mm^3	<25,000 /mm^3
WBC	Decreased	3,000 /mm^3 – LLN	2,000 - <3,000 /mm^3	1,000 - <2,000 /mm^3	<1,000 /mm^3
		None	None	>100,000 /mm^3	
aPTT		ULN – 1.5 x ULN	>1.5 – 2.5 x ULN	>2.5 x ULN	
Lymphocytes	Decreased	800 /mm3 – LLN	500 - <800 /mm^3	200 - <500 /mm^3	<200 /mm^3
		None	>4,000 – 20,000 /mm^3	>20,000 /mm^3	
Neutrophils	Decreased	1,500 /mm3 – LLN	1,000 - <1,500 /mm^3	500 - <1,000 /mm^3	<500 /mm^3

Decreased: below LLN; Otherwise, above ULN;

[1] Symptomatic, Intervention indicated

[2] without physiologic consequences

[3] with physiologic consequences

[4] Baseline is used if it is above ULN

[5] Increase from ULN/baseline: if baseline is above ULN, the increase should be above the baseline; otherwise, the increase should be above ULN.

2 Vital Signs PCS Cutoff Values

Vital Sign Parameter	Flag	Criteria	
		Observed Value	Change from Baseline
Systolic Blood Pressure (mmHg)	High	≥ 170	Increase of ≥ 20
	Low	≤ 90	Decrease of ≥ 20
Diastolic Blood Pressure (mmHg)	High	≥ 110	Increase of ≥ 15
	Low	≤ 50	Decrease of ≥ 15
Pulse Rate (bpm)	High	≥ 120	Increase of ≥ 20
	Low	≤ 50	Decrease of ≥ 20

3 ECG PCS Cutoff Values

ECG	Unit	Higher Limit
QRS interval	msec	≥ 150
PR interval	msec	≥ 250
QTc interval	msec	> 500; Change from baseline > 30 and > 60

APPENDIX B GENERAL SPECIFICATIONS FOR TABLES, LISTINGS, FIGURES

1 Software Used

All programming of tables, listings and figures (TLFs) will be performed using the statistical software package SAS® version 9.4 or greater.

2 General

All TLFs are based on SDTM and/or ADaM datasets. By default, data listings reflect the actual values captured in SDTM and ADaM datasets, including date/time variables and missing values. Except for concatenation of some variables for compact display purpose, data are presented directly with minimum manipulation. In general, the character standard result variables, such as –STRESC, are presented in data listings. Date are presented in listings in format yyyy-mm-dd. For incomplete date, CDISC presentation convension is followed.

For continuous variables that are recorded as "<X" or ">X", the value of "X" will be used in the calculation of summary statistics. The value "X" is also captured in the numeric variable in the SDTM datasets as well as in the ADaM datasets for consistency, although SDTMIG recommends capturing missing values in the numeric variables.

In general, reported verbatim, such as terms of AE, medical history, medication names, specifications to the 'Other' fields, findings, etc., are presented in upper case. However, when reported fields are long, such as comments and protocol deviation descriptions, listing in lower case enhances readability.

3 Table/Listing/Figure Output File Type and Organization

In general, the final set of TLFs will include both PDF and RTF files. Outputs are combined in several large PDF files, eg, all tables, all listings, and all figures, in the order as in the planned TLF in Section 12. A table of content should be included with hyperlinking to individual outputs. True RTF files (in-text format) will be created for tables and listings. SAS outputs for statistical procedures used in analysis of primary, secondary, and exploratory efficacy endpoints will also be included.

4 Page Layout

All column headers (consisting of one or several words) will start with uppercase and thereafter only lowercase characters, except for acronyms and abbreviations. In case values from the database will be displayed in column headers, they may be displayed as in the database. Pages will be numbered as 'Page x of y', where 'y' is the total number of pages of the corresponding table or listing. The page specifications are presented in Table A.

Table A. Specifications for Page Layout

Paper Size	Letter
Orientation	Landscape
Alignment	Center
Font size	9
Font type	Courier New (default)
Margins	
Top	0.75”
Bottom	0.38”
Left	0.75”
Right	0.38”

The margin sizes and font size for listings may be flexible to provide sufficient information on a single page to facilitate review and comparison.

When created using SAS, tables and listings will be created using ODS, and output files will be produced in RTF. When RTF files are produced, titles and footnotes will appear as document headers/footers.

5 Titles and Footnotes

All tables and listings will have a header showing “FibroGen, Inc.”, the protocol number, database cutoff date or ‘Final Database’, and Page x of y. A footer will show the program file path/name, output file path/name, run date and time.

All titles are written in title format, with uppercase at the beginning of each word; articles, prepositions, and conjunctions, which are of three characters length or less will start with lowercase letters (Mixed Case). Footnotes are in regular text format.

Titles

In total there are up to 10 titles available, defined as following:

first title	“FibroGen, Inc.” (left aligned) and “Database extraction date: ddMMMyyy” or “Final Locked Database” (right aligned)
second title	protocol number + “Clinical Study Report” (left aligned) and “Page x of y” (right aligned)
third title	blank
fourth title:	table/listing/figure number
fifth title:	table/listing/figure title

sixth title:	population names if provided in SAP, or brief definition of specific analysis set

Footnotes

Up to 10 footnote lines are available for tables, listings and figures. Footnotes 1, 9 and 10 are standard. Footnotes 2 to 8 (left aligned) might be used as needed. They are to be specified in the Shell.

first footnote	is a separating horizontal line.
second – eighth	are free text which can be used for explanations. Footnotes will be referenced using numbers in square brackets, starting with [1], followed by [2] etc.
ninth footnote	left blank; in case needed may also be used as for explanations.
tenth footnote	the program name (left aligned); the date and time in the format ddMMMyyyy hh:mm when the output was created; the version (e.g. draft or final); and the word "Confidential".

Footnotes are denoted by [1], [2], and so on.

If footnotes take more than 30% of the space of a long listing, they may be presented only on a standalone first page.

TLF numbers and titles should be inputted from an external file that can be directly copy-and-pasted from the SAP planned TLFs, rather than including in the body of the program. This is to ensure consistency between the SAP and the actual outputs.

Footnotes may be inputted from an external file as well for ease of managing changes.

For summary tables, the corresponding listings with the parameters being summarized should be footnoted as reference. For figures, the corresponding summary table should be footnoted as reference.

7 Significant Digits of Summary Statistics

- All percentages will be rounded to one decimal place and aligned by the decimal place.
- If the count is zero, the percentage will be suppressed and only '0' will be presented.
- Any p-values will be rounded to four decimal places and will be presented as '<.0001' if they are less than 0.0001 after rounding.
- For variables of direct measurements, summary statistics are displayed with the following specifications of decimal places in Table B.

Table B. Significant Digits of Summary Statistics

Description	Characteristic	Number of decimal places
Count	N	0
Mean	Mean	As in source + 1
Standard deviation	Std	As in source + 1
Standard error of the mean	SEM	As in source + 2
Confidence Interval	CI	As in source + 1
Minimum	Min	As in source
Median	Median	As in source
Maximum	Max	As in source
Q1 / Q3	Q1/Q3	As in source
10% / 90%	10%/90%	As in source
Percentage	%	All percentages will be rounded to one decimal place and lined up by the decimal place. The percentage will be suppressed when the count is zero
Coefficient of variation	CV (%)	1
p-value	p-value	p-values will be rounded to four decimal places and will be presented as '<.0001' if they are less than 0.0001 after rounding

N=number; Std=Standard deviation; CI=Confidence Interval; Min=minimum; Max=maximum; CV=Coefficient of variation

As a general guideline for derived parameters, 3 significant digits may be displayed for a parameter with an overall mean less than 100; otherwise, 1 decimal place may be used. If a derived parameter is in the same scale as some related measured parameters, such as MAP, QTc, the same display format may be used as the measured parameters.

Summary Statistics are to be displayed in the following order: Count, Mean, Standard Deviation, <Coefficient of Variation, Standard Error of the Mean, Confidence Interval>, Minimum, <10%>, <Q1>, Median, <Q3>, <90%>, Maximum.

For categorical variables the categories will be displayed in the TLFs in the same order they appear in the CRF.

8 Figure Specifications

- In general, figures should include annotation of key summary statistics: n, mean, SD or SE, median for continuous variables; n and percent for categorical variables; number of subjects at risk and cumulative number of events as well as median and 95% CI for time-to-event data. Other statistics such as quartiles, ranges may be included depending on need and space.

- P-values should be presented if comparisons are of interest.

- For scatter plots, linear or non-linear trend lines should be included if the association of the two variables is of interest. Correlation coefficient or regression coefficients as well as corresponding p-values should be presented.

- For box plots, 'BOXSTYLE=SCHEMATIC' should be used. The whiskers are drawn to the most extreme points in the group that lie within the fences. The upper fence is defined as the third quartile (represented by the upper edge of the box) plus 1.5 times the interquartile range. The lower fence is defined as the first quartile (represented by the lower edge of the box) minus 1.5 times the interquartile range. Observations outside the fences are identified with a special symbol.

9 Unit Conversion

Units Presented in TLFs	Units Reported or Derived from CRF	Conversion Formula
Kilogram (kg)	Pound (lb)	kg = lb/2.2
Centimeter (cm)	Inch (in)	cm = 2.54 * in
Celsius C°	Fahrenheit (F°)	C° = (5/9) * (F° – 32)
Year	Day	1 year = 365.25 days
Months	Day	1 month = 30.4375 days

10 Definitions and Formulas

(1) Age is calculated as of date that the informed consent form was signed.

age = INTCK('YEAR', Birth Date, Date of Informed Consent, 'C')

(2) Duration of treatment (days) is calculated as: date of EOT/ET Hb assessment – first dose date +1

(3) BMI = Weight (kg) / (Height (m))^2

(4) eGFR will be calculated using the following Modification of Diet in Renal Disease (MDRD) equation:

eGFR (in mL/min per 1.73m2) = 186 x (SCr in mg/dL)-1.154 x (Age in years)-0.203 x (0.742 if female) x (1.210 if African American)

where SCr = serum creatinine concentration

(5) Mean Arterial Pressure (MAP) will be derived using the following equation:

MAP = (2/3) * DBP + (1/3) SBP

APPENDIX C GENERAL SPECIFICATIONS FOR SUBMISSION DATA

1 Study Data Tabulation Model (SDTM)

Raw datasets will be mapped to SDTM datasets following variable names and attributes specified in the SDTM Implementation Guide (version 3.3 and subsequent update). Data coding is also mapped to the SDTM controlled terminology. Pinnacle 21 will be used to check compliance to the SDTM guidelines. Deviations from the guidelines will be documented. Detailed mapping specifications are documented in Define.xml and annotation CRFs.

Table A contains a list of SDTM datasets to be created for the study. The corresponding supplemental datasets are not included. This set of SDTM datasets includes only data for the Randomized Treatment Period as described in Section 1.

Table A. Study Data Tabulation Model Datasets (SDTM)

SDTM Domain	SDTM Domain Description	SDTM Domain Structure	General Observation Class	Source Data Used	Key Variables
AE	Adverse Events	One record per adverse event per subject	Events	AE	STUDYID, USUBJID, AESTDTC, AEDECOD, AESPID
CM	Concomitant Medications	One record per recorded medication occurrence per subject	Interventions	CM, CMIPF	STUDYID, USUBJID, CMCAT, CMSPID, CMTRT, CMSTDTC
DD	Death Details	One record per subject	Findings	DTH	STUDYID, USUBJID, DDTESTCD
DM	Demographics	One record per subject	Special Purpose Domains	DM, EX, ICF, DTH, SITE_INV	STUDYID, USUBJID
DS	Disposition	One record per disposition status or protocol milestone per subject	Events	DS, ICF, DTH, EX	STUDYID, USUBJID, DSSTDTC, DSDECOD, DSSPID, EPOCH
DV	Protocol Deviations	One record per protocol deviations per subject	Events	DV	STUDYID, USUBJID, DVTERM
EC	Exposure as Collected	One record per protocol-specified study treatment per collected-dosing interval per subject	Interventions	EX	STUDYID, USUBJID, ECTRT, ECSTDTC, ECGRPID
EG	ECG Test Results	One record per ECG observation per visit per subject	Findings	EG	STUDYID, USUBJID, EGTESTCD, VISITNUM

EX	Exposure	One record per constant dosing interval per subject	Interventions	EX	STUDYID, USUBJID, EXTRT, EXSTDTC
IE	Inclusion/Exclusion Criteria Not Met	One record per inclusion/exclusion criterion not met per subject	Findings	IE	STUDYID, USUBJID, IETESTCD
LB	Laboratory Test Results	One record per lab test per specimen per method per LOINC code per reason not done per visit per subject	Findings	eDT LB, RAND, LBC, LBPREG	STUDYID, USUBJID, LBCAT, LBTESTCD, VISITNUM, LBMETHOD, LBREASND, LBLOINC
MH	Medical History	One record per medical history event per time interval per subject	Events	MH	STUDYID, USUBJID, MHSPID, MHDECOD, MHSTDTC, MHENDTC
PC	Pharmacokinetic Concentrations	One record per time-point concentration or sample characteristic per analyte per subject	Findings	Source documents, PKC	STUDYID, USUBJID, PCTESTCD, VISITNUM, PCTPTNUM
PE	Physical Examination	One record per body system or abnormality per visit per subject	Findings	PE	STUDYID, USUBJID, PETESTCD, VISITNUM
PP	Pharmacokinetic Parameters	One record per PK parameter per time-concentration profile per modeling method per subject	Findings	Source documents	STUDYID, USUBJID, PPTESTCD, PPCAT, VISITNUM, PPTPTREF
PR	Procedures	One record per recorded procedure per occurrence per subject	Interventions	NDT, OU	STUDYID, USUBJID, PRCAT, PRTRT, PRSPID
QS	Questionnaires	One record per question per questionnaire per visit per subject	Findings	SGRQ, UCSD	STUDYID, USUBJID, QSTESTCD, VISITNUM
SC	Subject Characteristics	One record per characteristic per subject	Findings	DM	STUDYID, USUBJID, SCTESTCD
SE	Subject Elements	One record per actual Element per subject	Special Purpose Domains	SDTM.DM, SDTM.EX, SDTM.DS, SDTM.SV	STUDYID, USUBJID, TAETORD, SESTDTC
SU	Substance Use	One record per substance type per subject	Intervention	SUTOB	STUDYID, USUBJID, SUTRT

SV	Subject Visits	One record per actual visit per subject	Special Purpose Domains	All datasets including visits	STUDYID, USUBJID, VISITNUM
TA	Trial Arms	One record per planned Element per Arm	Trial Design	N/A	STUDYID, ARMCD, TAETORD
TE	Trial Elements	One record per planned Element	Trial Design	N/A	STUDYID, ETCD
TI	Trial Inclusion/Exclusion Criteria	One record per I/E criterion per protocol criteria version	Trial Design	N/A	STUDYID, TIVERS, IETESTCD
TS	Trial Summary	One record per Trial Summary parameter per occurrence	Trial Design	N/A	STUDYID, TSPARMCD, TSSEQ
TV	Trial Visits	One record per planned Visit per Arm	Trial Design	N/A	STUDYID, VISITNUM, ARMCD
VS	Vital Signs	One record per vital sign measurement per time point per visit per subject	Findings	VS, SC	STUDYID, USUBJID, VSTESTCD, VISITNUM, VSDTC

2 Analysis Data Model (ADaM)

The ADaM datasets are created based on the SDTM datasets following the ADaM Implementation Guide (version 1.0 and subsequent update). They include derived parameters and flags that are needed to generate tables/listings/figures. ADSL and ADAE are created using the specifications provided in the ADaMIG. Study endpoints are included in analysis files in ADaM Basic Data Structure (BDS). Horizontal analysis files are created for analyses on relationship of multiple endpoints. Variable names and labels of the horizontal files are from PARAMCD and PARAM of the corresponding BDS files. Detail derivations of each variable in the ADaM datasets are documented in the Metadata.

Table B. Analysis Data Model (ADaM)

Dataset	Description	Structure	Keys
ADSL	Subject-Level Analysis Dataset	One record per subject	STUDYID SUBJID
ADAE	Analysis Dataset Adverse Events	One record per subject per adverse event	STUDYID SUBJID AESTDTC AETERM
ADCM	Analysis Dataset Concomitant Medications	One record per subject per recorded medication	STUDYID SUBJID CMCAT APERIOD

		occurrence per start date of medication occurrence	CMTRT CMSTDTC CMENDTC
ADDD	Analysis Dataset Death	One record per subject per paramter	STUDYID SUBJID PARAMCD
ADEG	Analysis Dataset for ECG Test Results	One record per subject per visit	STUDYID SUBJID AVISITN ADT
ADEX	Analysis Dataset Exposure	One record per subject per parameter per visit	STUDYID SUBJID PARAMCD AVISITN ASTDTM
ADLB	Analysis Dataset Laboratory Test Results	One record per subject per parameter per visit	STUDYID SUBJID PARAMCD AVISITN
ADMH	Analysis Dataset Medical History	One record per subject per medical history per start date of medical history	STUDYID SUBJID MHTERM MHSTDTC MHENDTC
ADPC	Analysis Dataset PK Concentrations	One record per subject per visit per time point per parameter	STUDYID SUBJID AVISITN ATPTN PARAMCD
ADPE	Analysis Dataset Physical Examination	One record per subject per category per parameter per visit	STUDYID SUBJID PARCAT1 PARAMN AVISITN
ADPP	Analysis Dataset Pharmacokinetic Parameters	One record per subject per parameter	STUDYID SUBJID AVISITN PARAMCD
ADQS	Analysis Dataset for Questionnaire	One record per subject per category per parameter per visit	STUDYID SUBJID PARCAT1N PARAMCD AVISITN ADT
ADTTE	Analysis Dataset Time-to-Event	One record per subject per period per parameter	STUDYID SUBJID APERIOD AVAL PARAMCD
ADVS	Analysis Dataset Vital Signs	One record per subject per parameter per visit per timepoint	STUDYID SUBJID PARAMCD DTYPE VSSEQ AVISITN ATPTN

APPENDIX D FACT-AN (VERSION 4)

The Functional Assessment of Cancer Therapy – General (FACT-G; version 4) contains 27 items that cover four dimensions of well-being: physical (PWB) – 7 items, functional (FWB) – 7 items, social/family (SWB) – 7 items, and emotional (EWB) – 6 items.

The 'additional concerns' section contains 20 items: 13 fatigue specific items plus 7 additional items related to anemia were developed for use in conjunction with the FACT-G (Cella 1997). The 13 fatigue items plus the seven additional items related to anemia comprise the Anemia Subscale (AnS). Administration of the FACT-G plus the Anemia Subscale (AnS) is referred to as the FACT-An. The FACT-An has a recall period of the 'past seven days'. Respondents are asked to provide responses, (i.e., 'Not at all', 'A little bit', 'Somewhat', 'Quite a bit' and 'Very much'), to a list of statements which are either positively or negatively phrased. A final higher score indicates better QoL.

Each individual item is scored from 0 (Not at all) to 4 (Very much), and then the total score is obtained by summation of the resulted scores.

If there are missing items, subscale scores can be standardized. This is done by multiplying the sum of the subscale by the number of items in the subscale, then dividing by the number of items actually answered. This can be done on the scoring guide or by using the formula below:

Prorated subscale score = [Sum of item scores] x [N of items in subscale] / [N of items answered]

When there are missing data, standardizing by subscale in this way is acceptable (Webster 2003) as long as more than 50% of the items were answered (e.g., a minimum of 4 of 7 items, 4 of 6 items, etc.). The total score is then calculated as the sum of the un-weighted subscale scores. The FACT scale is considered to be an acceptable indicator of a subject's quality of life as long as overall item response rate is greater than 80% (e.g., at least 22 of 27 FACT-G items completed). This is not to be confused with individual subscale item response rate, which allows a subscale score to be prorated for missing items if greater than 50% of items are answered. In addition, a total score should only be calculated if ALL of the component subscales have available scores.

Below is a list of statements that other people with your illness have said are important.
Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	PHYSICAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GP1	I have a lack of energy	0	1	2	3	4
GP2	I have nausea	0	1	2	3	4
GP3	Because of my physical condition, I have trouble meeting the needs of my family	0	1	2	3	4
GP4	I have pain	0	1	2	3	4
GP5	I am bothered by side effects of treatment	0	1	2	3	4
GP6	I feel ill	0	1	2	3	4
GP7	I am forced to spend time in bed	0	1	2	3	4

	SOCIAL/FAMILY WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GS1	I feel close to my friends	0	1	2	3	4
GS2	I get emotional support from my family	0	1	2	3	4
GS3	I get support from my friends	0	1	2	3	4
GS4	My family has accepted my illness	0	1	2	3	4
GS5	I am satisfied with family communication about my illness	0	1	2	3	4
GS6	I feel close to my partner (or the person who is my main support)	0	1	2	3	4
Q1	*Regardless of your current level of sexual activity, please answer the following question. If you prefer not to answer it, please mark this box ☐ and go to the next section.*					
GS7	I am satisfied with my sex life	0	1	2	3	4

FACT-An (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	EMOTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GE1	I feel sad	0	1	2	3	4
GE2	I am satisfied with how I am coping with my illness	0	1	2	3	4
GE3	I am losing hope in the fight against my illness	0	1	2	3	4
GE4	I feel nervous	0	1	2	3	4
GE5	I worry about dying	0	1	2	3	4
GE6	I worry that my condition will get worse	0	1	2	3	4

	FUNCTIONAL WELL-BEING	Not at all	A little bit	Some-what	Quite a bit	Very much
GF1	I am able to work (include work at home)	0	1	2	3	4
GF2	My work (include work at home) is fulfilling	0	1	2	3	4
GF3	I am able to enjoy life	0	1	2	3	4
GF4	I have accepted my illness	0	1	2	3	4
GF5	I am sleeping well	0	1	2	3	4
GF6	I am enjoying the things I usually do for fun	0	1	2	3	4
GF7	I am content with the quality of my life right now	0	1	2	3	4

FACT-An (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	ADDITIONAL CONCERNS	Not at all	A little bit	Some-what	Quite a bit	Very much
HI7	I feel fatigued	0	1	2	3	4
HI12	I feel weak all over	0	1	2	3	4
An1	I feel listless ("washed out")	0	1	2	3	4
An2	I feel tired	0	1	2	3	4
An3	I have trouble starting things because I am tired	0	1	2	3	4
An4	I have trouble finishing things because I am tired	0	1	2	3	4
An5	I have energy	0	1	2	3	4
An6	I have trouble walking	0	1	2	3	4
An7	I am able to do my usual activities	0	1	2	3	4
An8	I need to sleep during the day	0	1	2	3	4
An9	I feel lightheaded (dizzy)	0	1	2	3	4
An10	I get headaches	0	1	2	3	4
B1	I have been short of breath	0	1	2	3	4
An11	I have pain in my chest	0	1	2	3	4
An12	I am too tired to eat	0	1	2	3	4
BL4	I am interested in sex	0	1	2	3	4
An13	I am motivated to do my usual activities	0	1	2	3	4
An14	I need help doing my usual activities	0	1	2	3	4
An15	I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
An16	I have to limit my social activity because I am tired	0	1	2	3	4

FACT-An Scoring Guidelines

Instructions:* 1. Record answers in "item response" column. If missing, mark with an X
2. Perform reversals as indicated, and sum individual items to obtain a score.
3. Multiply the sum of the item scores by the number of items in the subscale, then divide by the number of items answered. This produces the subscale score.
4. Add subscale scores to derive total scores (TOI, FACT-G & FACT-An).
5. The higher the score, the better the QOL.

Subscale	Item Code	Reverse item?		Item response	Item Score
PHYSICAL WELL-BEING (PWB)	GP1	4	-	_____	=_____
	GP2	4	-	_____	=_____
	GP3	4	-	_____	=_____
	GP4	4	-	_____	=_____
	GP5	4	-	_____	=_____
Score range: 0-28	GP6	4	-	_____	=_____
	GP7	4	-	_____	=_____

Sum individual item scores: _____

Multiply by 7: _____

Divide by number of items answered: _____

=**PWB subscale score**

SOCIAL/FAMILY WELL-BEING (SWB)	GS1	0	+	_____	=_____
	GS2	0	+	_____	=_____
	GS3	0	+	_____	=_____
	GS4	0	+	_____	=_____
	GS5	0	+	_____	=_____
Score range: 0-28	GS6	0	+	_____	=_____
	GS7	0	+	_____	=_____

Sum individual item scores: _____

Multiply by 7: _____

Divide by number of items answered: _____

=**SWB subscale score**

EMOTIONAL WELL-BEING (EWB)	GE1	4	-	_____	=_____
	GE2	0	+	_____	=_____
	GE3	4	-	_____	=_____
	GE4	4	-	_____	=___
Score range: 0-24	GE5	4	-	_____	=_____
	GE6	4	-	_____	=_____

Sum individual item scores: _____

Multiply by 6: _____
Divide by number of items answered: _____

=EWB subscale score

FUNCTIONAL	GF1	0	+	_____	= _____
WELL-BEING	GF2	0	+	_____	= _____
(FWB)	GF3	0	+	_____	= _____
	GF4	0	+	_____	= _____
	GF5	0	+	_____	= _____
Score range: 0-28	GF6	0	+	_____	= _____
	GF7	0	+	_____	= _____

Sum individual item scores: _____

Multiply by 7: _____

Divide by number of items answered: _____

=**FWB subscale score**

Subscale	**Item Code**	**Reverse item?**		**Item response**	**Item Score**
ANEMIA	HI7	4	-	_____	= _____
SUBSCALE	HI12	4	-	_____	= _____
(AnS)	An1	4	-	_____	= _____
	An2	4	-	_____	= _____
	An3	4	-	_____	= _____
Score range: 0-80	An4	4	-	_____	= _____
	An5	0	+	_____	= _____
	An6	4	-	_____	= _____
	An7	0	+	_____	= _____
	An8	4	-	_____	= _____
	An9	4	-	_____	= _____
	An10	4	-	_____	= _____
	B1	4	-	_____	= _____
	An11	4	-	_____	= _____
	An12	4	-	_____	= _____
	BL4	0	+	_____	= _____
	An13	0	+	_____	= _____
	An14	4	-	_____	= _____
	An15	4	-	_____	= _____
	An16	4	-	_____	= _____

Sum individual item scores: _____

Multiply by 20: _____

Divide by number of items answered: _____

=**An Subscale score**

To derive a FACT-An Trial Outcome Index (TOI):

Score range: 0-136

_____+_____+_____=_____=**FACT-An TOI**
(**PWB** score) (**FWB** score) (**AnS** score)

To Derive a FACT-G total score:

Score range: 0-108

_____+_____+_____+_____=_____=**FACT-G Total score**
(**PWB** score) (**SWB** score) (**EWB** score) (**FWB** score)

To Derive a FACT-An total score:

Score range: 0-188

_____+_____+_____+_____+_____=_____=**FACT-An Total score**

(**PWB** score) (**SWB** score) (**EWB** score) (**FWB** score) (**AnS** score)

*For guidelines on handling missing data and scoring options, please refer to the Administration and Scoring Guidelines in the manual or on-line at www.facit.org.

FACIT-Fatigue Subscale Scoring Guidelines

Instructions:* 1. Record answers in "item response" column. If missing, mark with an X

2. Perform reversals as indicated, and sum individual items to obtain a score.
3. Multiply the sum of the item scores by the number of items in the subscale, then divide by the number of items answered. This produces the subscale score.
4. The higher the score, the better the QOL.

Subscale	**Item Code**	**Reverse item?**		**Item**	
response	**Item Score**				
FATIGUE	HI7	4	-	_____	=__
SUBSCALE	HI12	4	-	_____	=__
	An1	4	-	_____	=__
	An2	4	-	_____	=__
Score range: 0-52	An3	4	-	_____	=__
	An4	4	-	_____	=__
	An5	0	+	_____	=__
	An7	0	+	_____	=__
	An8	4	-	_____	=__
	An12	4	-	_____	=__
	An14	4	-	_____	=__
	An15	4	-	_____	=__
	An16	4	-	_____	=__

Sum individual item scores: _____

Multiply by 13: _____

Divide by number of items answered: _____

=Fatigue Subscale score

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