

DISCLOSURE

REDACTED STATISTICAL ANALYSIS PLAN

GED-0301-CD-004

PHASE 3, LONG-TERM ACTIVE TREATMENT EXTENSION STUDY OF MONGERSEN (GED-0301) IN SUBJECTS WITH CROHN'S DISEASE

The information contained in the attached report is the property of Celgene and should not be shared or used for any purpose other than that for which it was provided.

Celgene is committed to providing information about its clinical trials to researchers and patients with the goal of furthering science and enhancing healthcare worldwide. Laws and regulations require, however, that Celgene protects patient privacy. The company may further have legal or contractual obligations not to disclose commercial or technical information provided by or related to certain partner companies or vendors.

The attached report is presented in its original format, but certain information has been redacted in order to comply with the aforementioned obligations or to protect Celgene's confidential commercial information. The redactions are based on the following principles:

- Redacted information has been replaced by grey space, maintaining original spacing and pagination.
- Any information that might allow the identification of individuals has been redacted for anonymization.
- Attachments to this report that contain confidential information are not made available. Such attachments include those that contain identifiable patient information, such as subject listings, narratives, and profiles. They also may contain confidential commercial information such as methodologies, and hypothesis generating and exploratory analyses.
- Cross-references to these attachments (such as links to subject listings in Section 16.2) are not redacted from the body of the report. However, the hyperlinks in the electronic document are no longer functional.
- Information about Celgene vendors and their services are redacted because many contracts prohibit disclosure of that information. Further, laws and regulations prevent us from disclosing certain information about our vendors or their services because it is protected by copyright.

Information about Celgene's redaction policies and the availability of additional data from this report may be found at <http://www.celgene.com/research-development/clinical-trials/clinical-trials-data-sharing/>.

STATISTICAL ANALYSIS PLAN

A PHASE 3, LONG-TERM ACTIVE TREATMENT EXTENSION STUDY OF MONGERSEN
(GED-0301) IN SUBJECTS WITH CROHN'S DISEASE

STUDY DRUG: GED-0301
PROTOCOL NUMBER: GED-0301-CD-004
DATE FINAL: 12APR2018

Prepared by:



on behalf of

Celgene Corporation
86 Morris Avenue
Summit, NJ 07901

CONFIDENTIAL

The information contained in this document is regarded as confidential and, except to the extent necessary to obtain informed consent, may not be disclosed to another party unless such disclosure is required by law or regulations. Persons to whom the information is disclosed must be informed that the information is confidential and may not be further disclosed by them.

TABLE OF CONTENTS

SIGNATURE PAGE.....	5
1. LIST OF ABBREVIATIONS	7
2. INTRODUCTION.....	9
3. STUDY OBJECTIVES.....	10
4. INVESTIGATIONAL PLAN	11
4.1. Overall Study Design and Plan	11
4.2. Study Endpoints	14
4.3. Stratification, Randomization, and Blinding.....	15
4.4. Sample Size Determination and Power Considerations	15
5. GENERAL STATISTICAL CONSIDERATIONS	16
5.1. Treatment Grouping Approaches	16
5.2. Reporting Conventions	16
5.3. Time Points	17
5.3.2. Baseline Definitions	17
5.4. Analysis Population.....	17
6. SUBJECT DISPOSITION	19
7. PROTOCOL DEVIATIONS/VIOLATIONS	20
8. DEMOGRAPHICS AND BASELINE CHARACTERISTICS.....	21
8.1. Demographics and Baseline Characteristics	21
8.2. Baseline Disease Characteristics	21
9. EXTENT OF EXPOSURE TO INVESTIGATIONAL PRODUCT.....	23
9.1. Treatment Duration.....	23
9.2. Treatment Compliance.....	23
9.3. Overdose	23
10. CONCOMITANT MEDICATIONS AND PROCEDURES.....	24
10.1. Concomitant Medications	24
10.2. Concomitant Procedures	24
11. EFFICACY ANALYSIS	25
11.1. Missing Data Handling	25
11.2. Analyses of Efficacy Endpoints	25

11.2.1.	Primary Efficacy Endpoint.....	25
11.2.2.	Analyses of Secondary Efficacy Endpoints.....	25
12.	SAFETY ANALYSIS	26
12.2.	Adverse Events.....	26
12.2.1.	Overall Summary of TEAEs	27
12.2.2.	All TEAEs.....	27
12.2.3.	Drug-related TEAEs	27
12.2.4.	TEAEs by Maximum Severity	27
12.2.5.	Serious TEAEs	27
12.2.6.	TEAEs Leading to Drug Withdrawal	27
12.2.7.	Deaths	28
12.3.	Clinical Laboratory Evaluations.....	28
12.4.	Vital Signs and Body Weight.....	29
12.5.	Electrocardiogram	29
15.	INTERIM ANALYSIS	32
16.	CHANGES TO THE STATISTICAL CONSIDERATIONS SECTION OF THE PROTOCOL	33
17.	REFERENCES	34

LIST OF TABLES

Table 1:	Abbreviations and Specialist Terms	7
Table 2:	Study Objectives – Adult Subjects (≥ 18 years of age at screening of core study) from GED-0301-CD-002	10
Table 3:	Protocol-specified Endpoints – Adult Subjects from GED-0301-CD-002.....	14
	[REDACTED]	
	[REDACTED]	
Table 6:	Laboratory Marked Abnormalities Criteria	35

LIST OF FIGURES

Figure 1	Overall Study Design.....	13
----------	---------------------------	----

SIGNATURE PAGE

STATISTICAL ANALYSIS PLAN (SAP) AND SAP AMENDMENT APPROVAL SIGNATURE PAGE	
SAP TITLE	GED-0301-CD-004 Statistical Analysis Plan
SAP VERSION, DATE	Version 1.0, 12 APR 2018
SAP AUTHOR	<div style="background-color: #cccccc; width: 100%; height: 15px;"></div>
	Printed Name and Title Signature and Date
PROTOCOL TITLE	A PHASE 3, LONG-TERM ACTIVE TREATMENT EXTENSION STUDY OF MONGERSEN (GED-0301) IN SUBJECTS WITH ACTIVE CROHN'S DISEASE
INVESTIGATIONAL PRODUCT	GED-0301
PROTOCOL NUMBER	GED-0301-CD-004
PROTOCOL VERSION, DATE	Protocol Amendment 1, 06 Jan 2017
SIGNATURE STATEMENT	By my signature, I indicate I have reviewed this SAP and find its contents to be acceptable.
Celgene Lead Statistician	
Signature	<div style="background-color: #cccccc; width: 100%; height: 20px;"></div>
Printed Name	<div style="background-color: #cccccc; width: 100%; height: 20px;"></div>
Celgene Statistical Therapeutic Area Head	
Signature	<div style="background-color: #cccccc; width: 100%; height: 20px;"></div>
Printed Name	<div style="background-color: #cccccc; width: 100%; height: 20px;"></div>
Celgene Lead Clinical Research Phy	
Signature	<div style="background-color: #cccccc; width: 100%; height: 20px;"></div>
Printed Name	<div style="background-color: #cccccc; width: 100%; height: 20px;"></div>

Celgene Lead Product Safety Physician

Signature

Printed Name

CELGENE PROPRIETARY INFORMATION

1. LIST OF ABBREVIATIONS

Table 1: Abbreviations and Specialist Terms

Abbreviation	Meaning
AE	Adverse event
ALT	Alternating
APTT	Activated partial thromboplastin time
ATC	Anatomical Therapeutic Chemical
ATC2	Anatomical Therapeutic Chemical: Therapeutic (Level 2)
BMI	Body mass index
BUN	Blood urea nitrogen
CBC	Complete blood count
CD	Crohn's Disease
CDAI	Crohn's Disease Activity Index
CIC	Clinical Improvement Criteria
DAO	Data as observed
EAIR	Exposure-adjusted incidence rate
ECG	Electrocardiograms
ET	Early Termination
IP	Investigational product
IRTS	Interactive response technology system

Abbreviation	Meaning
LDH	Lactic dehydrogenase
LOCF	Last observation carried forward
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
MCV	Mean corpuscular volume
MedDRA	Medical Dictionary for Regulatory Activities
NRI	Nonresponder imputation
PBO	Placebo
PT	Preferred term
Q1	25 th percentile
Q3	75 th percentile
QD	Once Daily
RBC	Red blood cell
SAP	Statistical analysis plan
SD	Standard deviation
SES-CD	Simple Endoscopic Score for Crohn's Disease
SGOT	Serum glutamic-oxaloacetic transaminase
SGPT	Serum glutamic-pyruvic transaminase
SOC	System organ class
TEAE	Treatment-emergent adverse event
ULN	Upper limit of normal
VAS	Visual analog scale
WBC	White blood cell
WHODD	World Health Organization Drug Dictionary

2. INTRODUCTION

This statistical analysis plan (SAP) describes the analyses and data presentations for Celgene's protocol GED-0301-CD-004 "A Phase 3, Long-term Active Treatment Extension Study of Mongersen (GED-0301) in Subjects with Crohn's Disease" as amended on 06 Jan 2017. It contains definitions of analysis populations, derived variables and statistical methods for the analysis of efficacy and safety.

The study was terminated early by Celgene following an October 2017 recommendation of the Data Monitoring Committee. As such, changes are made to some protocol-specified analyses; these changes are described in relevant sections and summarized in Section 16.

In this SAP, GED-0301 160 mg once daily (QD), GED-0301 40 mg QD, and placebo QD are referred to as GED 160, GED 40, and PBO, respectively. Subjects will be assigned to receive one of 5 GED-0301 treatment regimens during the study, based on the treatment received during the core GED-0301 Phase 3 study (GED-0301-CD-002), and whether the subject met the clinical improvement criteria. For the first 12 weeks of the study, subjects will receive blinded, active GED-0301 treatment as one of the following numbered treatment groups:

- 1) continuous GED 160 for 12 weeks;
- 2) GED 160 for 4 weeks, PBO for 4 weeks, GED 160 for 4 weeks;
- 3) PBO for 4 weeks, GED 160 for 4 weeks, PBO for 4 weeks;
- 4) continuous GED 40 for 12 weeks;
- 5) PBO for 4 weeks, GED 40 for 4 weeks, PBO for 4 weeks.

Beginning at Week 12 through Week 208, subjects from the above-numbered treatment groups will continue to receive blinded, active GED-0301 treatment for 196 weeks as the following:

- 1) alternating PBO for 4 weeks and GED 160 for 4 weeks, through Week 208;
- 2) alternating PBO for 4 weeks and GED 160 for 4 weeks, through Week 208;
- 3) alternating GED 160 for 4 weeks and PBO for 4 weeks, through Week 208;
- 4) continuous GED 40, through Week 208;
- 5) alternating GED 40 for 4 weeks and PBO for 4 weeks, through Week 208.

The treatment regimens of alternating GED 160 for 4 weeks and PBO for 4 weeks (irrespective of whether GED 160 or PBO is administered first in this extension study), continuous GED 40, alternating GED 40 for 4 weeks and PBO for 4 weeks, are referred to as GED 160 ALT, GED 40, and GED 40 ALT, respectively. Investigational product (IP) refers to GED 160, GED 40, or PBO.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

To streamline this SAP, the Study Design section of the protocol is copied below, with the understanding that the references to Study GED-0301-CD-003 are no longer applicable since the study was not initiated before the study termination.

This is a Phase 3, double-blind, long-term active treatment extension study to evaluate the long-term safety [REDACTED] of GED-0301 for 208 weeks in adult and adolescent subjects with CD who previously participated in either of the following two Phase 3 GED-0301 studies:

- Study GED-0301-CD-002 (Adult Subjects)
- Study GED-0301-CD-003 (Adult and Adolescent Subjects)

The purpose of this study is to assess long-term safety data of GED-0301 for a period of up to 208 weeks in adult subjects (ie, ≥ 18 years of age) who participated in the core Phase 3 GED-0301-CD-002 and GED-0301-CD-003 studies and adolescent subjects (ie, 12 to 17 years of age) who participated in the core Phase 3 GED-0301-CD-003 study.

Although all subjects will receive active treatment, this study is double-blinded for the entire 208 weeks for the purpose of preserving the blind of the subject's treatment allocation in the initial, core Phase 3 GED-0301 study.

Subjects from Study GED-0301-CD-002 who completed the study at Week 52, or who met the early escape criteria (Appendix H of the protocol) and were discontinued during the time period beginning at Week 12 through Week 52, may be eligible to enter this study.

Subjects from Study GED-0301-CD-003 who completed the study at Week 12 may also be eligible to enter this long-term active treatment study.

Subjects who discontinued Studies GED-0301-CD-002 or GED-0301-CD-003 prior to the Week 12 Visit are not eligible for this study.

This long-term active treatment study will consist of 3 periods:

- Screening Period – up to 4 weeks (ie, 1 day to 28 days depending on when long-term active treatment is available for the subject at the study center)
- Long-term Active Treatment Period – 208 Weeks (Week 0 to Week 208)
- Follow-up Period – 4 weeks (ie, no IP taken)

At Week 12, subjects will be evaluated to determine if they should be discontinued from the study based on clinical criteria. Subjects, who meet the following criteria, will be discontinued from the study at Week 12:

Subjects who complete this study through Week 208 will have a 4-week Follow-up Visit. Subjects who prematurely discontinue treatment from the study at any time prior to Week 208 will have an ET Visit and a 4-week Follow-up Visit. The ET Visit should be scheduled as soon as possible after the last dose of IP. If the ET Visit occurs 28 days after the last dose of IP, then the Follow-up Visit is not required.

At the Screening Visit in this study, all subjects who meet the inclusion criteria and do not meet the exclusion criteria will be eligible and assigned a subject identification number using a centralized interactive response technology system (IRTS).

Once the subject is eligible and registered in the IRTS, the assigned treatment is based on the clinical improvement criteria from the core GED-0301 study to determine the subject's course of treatment for the entire 208 weeks in this study.

Please note that all 160 mg once daily treatments are taken as four 40 mg tablets once daily in this study. That is, GED-0301-treated subjects who received one 160 mg tablet QD in GED-0301-CD-003 will receive four 40 mg tablets QD in this study.

Subjects will receive the following treatments:

Previously-treated GED-0301 subjects in Study GED-0301-CD-002 who met the clinical improvement criteria at Week 52:

- Will continue to receive their same blinded treatment, which will be:
 - Alternating PBO QD for 4 weeks and GED-0301 40 mg QD for 4 weeks, or
 - Continuous GED-0301 40 mg QD, or
 - Alternating PBO QD for 4 weeks and GED-0301 160 mg QD for 4 weeks.

Previously-treated GED-0301 subjects in Study GED-0301-CD-003 who met the clinical improvement criteria at Week 12:

- Will receive blinded treatment with:
 - Alternating PBO QD for 4 weeks and GED-0301 160 mg QD for 4 weeks.

Previously-treated PBO subjects who met the clinical improvement criteria:

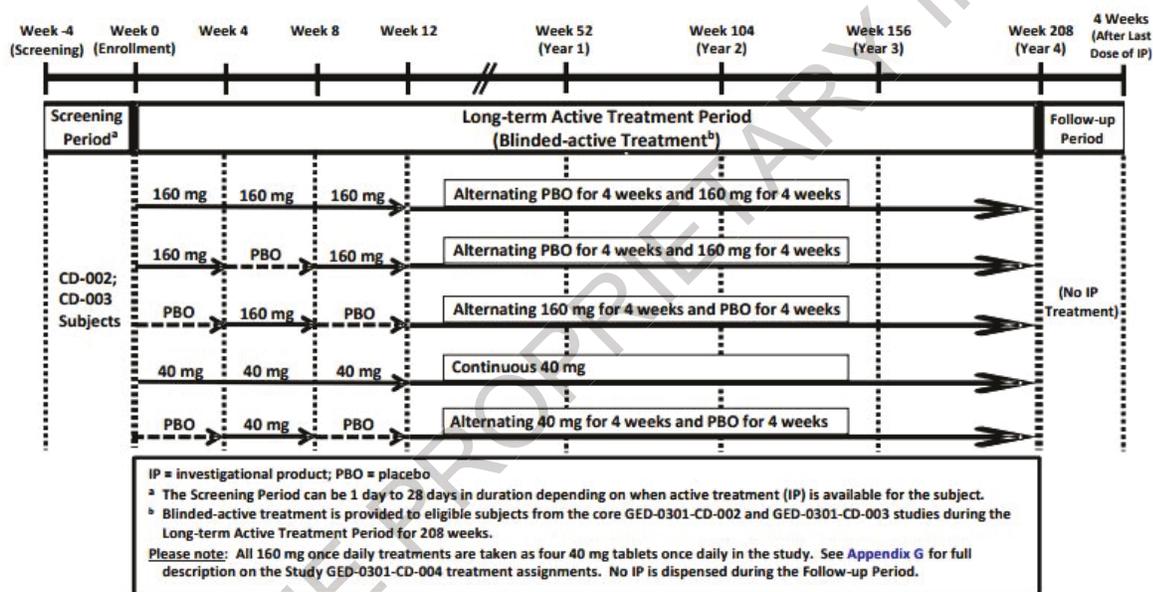
- At Week 52 in Study GED-0301-CD-002; or
- At Week 12 in Study GED-0301-CD-003
- Will receive blinded treatment with:
 - Alternating GED-0301 160 mg QD for 4 weeks and PBO QD for 4 weeks.

Previously-treated GED-0301 or PBO subjects who did not meet the clinical improvement criteria:

- At Week 12 through Week 52 in Study GED-0301-CD-002; or
- At Week 12 in Study GED-0301-CD-003
- Will receive blinded treatment with:
 - Alternating GED-0301 160 mg QD for 4 weeks and PBO QD for 4 weeks, if the subject previously received GED-0301 treatment, or
 - GED-0301 160 mg QD for 12 weeks, if the subject previously received PBO, and after Week 12, subjects will receive alternating PBO QD for 4 weeks and GED-0301 160 mg QD for 4 weeks.

See the overall study design (Figure 1) for an overview of the study blinded-active treatments. All subjects will receive a blinded-active GED-0301 treatment regimen for 208 weeks, and the full descriptions of the treatment assignments are detailed in Appendix G of the protocol.

Figure 1 Overall Study Design



[REDACTED]

[REDACTED]

[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
		[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]
		[REDACTED]	[REDACTED]
[REDACTED]	[REDACTED]	[REDACTED]	[REDACTED]

[REDACTED]

4.3. Stratification, Randomization, and Blinding

There is no randomization or stratification in this study. Eligible subjects will be assigned via an IRTS to receive one of 5 double-blind GED-0301 treatment regimens (Section 2) during the study, based on the treatment received during the initial, core GED-0301 Phase 3 study, and whether the subject met the clinical improvement criteria.

4.4. Sample Size Determination and Power Considerations

No sample size and power calculations are performed for this long-term active treatment study.

5. GENERAL STATISTICAL CONSIDERATIONS

5.1. Treatment Grouping Approaches

In listings, treatment will be displayed in 5 treatment regimens (corresponding to the 5 numbered treatment groups in Section 2), as follows:

- GED 160 12WK/PBO/GED 160 ALT
- GED 160/PBO ALT
- PBO/GED 160 ALT
- GED 40
- PBO/GED 40 ALT

The following treatment grouping will be used in tables.

- GED 40 ALT
- GED 40
- GED 160 ALT (combining all variants of this regimen)
- GED Total

5.2. Reporting Conventions

The following reporting conventions apply generally to tables, listings, and figures:

- P-values will not be reported.
- Confidence intervals (CIs) will be presented as 2-sided 95% CIs.
- Summary statistics will consist of the number and percentage of subjects in each category for discrete variables, and the sample size, mean, standard deviation (SD), median, minimum, 25th percentile (Q1), 75th percentile (Q3), and maximum for continuous variables.
- [REDACTED]
- [REDACTED]
- Change from baseline is calculated as the post-baseline value minus the baseline value. Percent change from baseline is calculated as $100 \times (\text{change from baseline} / \text{baseline})$. To assess change from baseline, a baseline value and at least 1 post-baseline value are required.



CEL GENE PROPRIETARY INFORMATION

6. SUBJECT DISPOSITION

The number of subjects screened, the numbers and percentages of subjects enrolled and not enrolled, and the numbers and percentages of the eligibility criteria failed will be summarized based on all subjects screened.

The number and percentage of subjects included in the analysis population will be summarized based on all subjects enrolled.

Subject disposition (entered, completed, discontinued, along with the primary reason for discontinuation) will be summarized for

- Week 12 (based on all subjects enrolled)
- Long-term Active Treatment Period (based on all subjects enrolled)
- Follow-up Period (based on all subjects who enter the Follow-up Period).

A listing of discontinued subjects with reason for discontinuation will be provided.

The number and percentage of subjects by region, country, and site will be provided based on all subjects enrolled.

7. **PROTOCOL DEVIATIONS/VIOLATIONS**

Protocol violations and deviations will be summarized using the long-term active treatment population.

A listing of all protocol violations and deviations in the study will be provided.

CELGENE PROPRIETARY INFORMATION

8. DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Demographics and baseline characteristics, as collected or calculated in the core GED-0301 Phase 3 study, will be summarized based on the long-term active treatment population. Subject data listings will be provided.

8.1. Demographics and Baseline Characteristics

The following characteristics will be summarized as continuous variables:

- Age (years)
- Baseline body weight (kg)
- Baseline body mass index ($BMI = \text{weight (kg)} / [\text{height(m)}]^2$; kg/m^2)

The following characteristics will be summarized as categorical variables:

- Age (< 65, ≥ 65 years; < 40, 40 – < 65, 65 – < 75, ≥ 75 years)
- Sex (Male, Female)
- Race (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, Not Collected or Reported, Other)
- Ethnicity (Hispanic or Latino, not Hispanic or Latino, Unknown, Not Reported)
- Region (North America, Western Europe, Eastern Europe, Asia Pacific)
- Baseline body weight (< 55, 55 – < 70, 70 – < 85, 85 – < 100, ≥ 100 kg)
- Baseline BMI (< 18.5, 18.5 – < 25, 25 – < 30, 30 – < 35, 35 – < 40, and ≥ 40 kg/m^2)
- Alcoholic beverages (yes [< 1 drink per week, 1 – 14 drinks per week, > 14 drinks per week], no)
- Tobacco history (never smoked, past smoker, current smoker, passive smoker, smokeless tobacco user)

8.2. Baseline Disease Characteristics

The following baseline disease characteristics will be summarized as continuous variables:

- Baseline CDAI score
- Baseline SES-CD score (central read)



- Baseline CDAI score (≤ 300 , > 300 ; < 220 , $220 - < 270$, $270 - < 330$, $330 - < 390$, $390 - \leq 450$, > 450)
- Baseline SES-CD (central read; < 6 , $6 - 12$, > 12)

9. EXTENT OF EXPOSURE TO INVESTIGATIONAL PRODUCT

9.1. Treatment Duration

Treatment duration will be summarized for Weeks 0-208 using the long-term active treatment population.

Treatment duration will be summarized as a continuous variable, and as a categorical variable with the following exposure intervals:

- Weeks 0-208: ≤ 13 , $> 13 - \leq 26$, $> 26 - \leq 39$, $> 39 - \leq 52$, $> 52 - \leq 65$, $> 65 - \leq 78$, $> 78 - \leq 91$, $> 91 - \leq 104$, $> 104 - \leq 117$, $> 117 - \leq 130$, $> 130 - \leq 143$, $> 143 - \leq 156$, $> 156 - \leq 169$, $> 169 - \leq 182$, $> 182 - \leq 195$, > 195 weeks.

A subject data listing of study drug records will be provided.

9.2. Treatment Compliance

As part of the routine recording of the amount of IP taken by each subject, the numbers of tablets dispensed and returned will be recorded at each visit (except the screening and follow-up visits). These records will be used to calculate treatment compliance. Treatment compliance will be summarized for Weeks 0-208 using the long-term active treatment population.

Treatment compliance rate will be summarized as a continuous variable, and as a categorical variable with the following categories: $< 75\%$, $\geq 75\% - \leq 120\%$, and $> 120\%$.

A subject data listing of drug accountability records will be provided.

9.3. Overdose

A subject data listing of overdose records will be provided.

10. CONCOMITANT MEDICATIONS AND PROCEDURES

Concomitant medications and procedures during the Long-term Active Treatment Period will be summarized for Weeks 0-208 using the long-term active treatment population.

10.1. Concomitant Medications

[REDACTED]

Concomitant medications will be coded according to the ATC coding scheme of the WHODD, and summarized by ATC2 level and standardized medication name, with ATC2 levels and standardized medication names within each ATC2 level sorted in descending order of frequency.

10.2. Concomitant Procedures

Concomitant procedures are defined similarly to concomitant medications. Concomitant procedures will be coded according to the MedDRA, and summarized by SOC and PT, with SOCs sorted in alphabetical order and PTs within each SOC in descending order of frequency.

11. EFFICACY ANALYSIS

The efficacy endpoints will be summarized descriptively.

11.1. Missing Data Handling

Continuous endpoints by time point will be summarized based on data as observed (DAO), where only subjects with sufficient data at the time point under consideration will be included in the summary of that time point.

11.2. Analyses of Efficacy Endpoints

11.2.1. Primary Efficacy Endpoint

There is no primary efficacy endpoint in this study.

11.2.2. Analyses of Secondary Efficacy Endpoints

As Study GED-0301-CD-003, where adolescent subjects were to be enrolled, was not initiated before the early termination of this study, there are no secondary efficacy endpoints.

[REDACTED]

[REDACTED]

12. SAFETY ANALYSIS

Safety will be evaluated via descriptive statistics and point estimates. No inferential testing for statistical significance will be performed.

[REDACTED]

12.2. Adverse Events

Adverse events (AE) will be coded according to the MedDRA. Unless otherwise specified, AEs will be summarized by SOC and PT, with SOCs sorted in alphabetical order and PTs within each SOC in descending order of subject incidence of the GED Total group combining all GED-0301 treatment regimens.

For the analysis of AEs, the following point estimates are provided, unless otherwise specified:

- Subject incidence: Subject incidence (ie, percentage [%] used in a frequency summary) is defined as the number of subjects with the specific event divided by the number of subjects included in the analysis. Subjects with multiple occurrences of the specific event in the specific analysis period will be counted only once in the numerator.

- [REDACTED]

A subject data listing of all AEs (including treatment-emergent AEs [TEAEs] and non-TEAEs) will be provided.

12.2.1. Overall Summary of TEAEs

An overall summary of the following TEAE categories will be provided for Weeks 0-208:

- Any TEAE
- Any drug-related TEAE
- Any severe TEAE
- Any serious TEAE
- Any serious drug-related TEAE
- Any TEAE leading to drug interruption
- Any TEAE leading to drug withdrawal
- Any TEAE leading to death

12.2.2. All TEAEs

All TEAEs will be summarized by SOC and PT as well as by PT only (in descending order of subject incidence of the GED Total group combining all GED-0301 treatment regimens) for Weeks 0-208.

12.2.3. Drug-related TEAEs

Drug-related TEAEs will be summarized for Weeks 0-208.

12.2.4. TEAEs by Maximum Severity

All TEAEs will be summarized by maximum severity (mild, moderate, and severe) for Weeks 0-208. If a subject reports multiple occurrences of a specific event within a specific analysis period, the subject will be counted only once by the maximum severity. If the severity is missing for one or more of the occurrences, the maximum severity of the remaining occurrences will be used.

12.2.5. Serious TEAEs

Serious TEAEs will be summarized for Weeks 0-208.

A subject data listing of all serious AEs (both TEAEs and non-TEAEs) will be provided.

12.2.6. TEAEs Leading to Drug Withdrawal

TEAEs leading to drug withdrawal will be summarized for Weeks 0-208.

A subject data listing of AEs leading to drug withdrawal will be provided.

12.2.7. Deaths

A subject data listing of all deaths will be provided.

12.3. Clinical Laboratory Evaluations

The following protocol-specified parameters from the central laboratory will be summarized:

- Hematology panel will include: complete blood count (CBC) with differential, including red blood cell (RBC) count, hemoglobin, hematocrit, mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular volume (MCV), white blood cell (WBC) count (with differential), and platelet count.
- Serum chemistry panel will include: total protein, albumin, calcium, phosphorous, glucose, total cholesterol, triglycerides, uric acid, total bilirubin, alkaline phosphatase, aspartate aminotransferase (AST)/serum glutamic oxaloacetic transaminase (SGOT), alanine aminotransferase (ALT)/serum glutamic pyruvic transaminase (SGPT), sodium, potassium, magnesium, chloride, carbon dioxide, blood urea nitrogen (BUN), creatinine, and lactic dehydrogenase (LDH), .
- Coagulation assessment will include: prothrombin time and activated partial thromboplastin time (APTT)
- Complement activation factor panel will include: compliment activation factors Bb, C3a and C5a.
- Urinalysis will include specific gravity and pH.

Summary statistics of observed values and changes from baseline will be provided by time point (time points include the scheduled visits for labs, the follow-up visit, and the end of Weeks 0-208).

Frequency summaries (shift tables) of shifts from baseline to post-baseline time points (time points include the scheduled visits for labs, the end of Weeks 0-208, and the worst value of Weeks 0-208) by category of low/normal/high/both low and high (the last category for the shift to the worst value only) will be provided for hematology and serum chemistry.

A summary of laboratory marked abnormalities as defined in Section 18.1 will be provided for Weeks 0-208.

A separate summary of laboratory marked abnormalities will also be presented by normal baseline and abnormal baseline.

A subject data listing of all laboratory data (including urinalysis) will be provided.

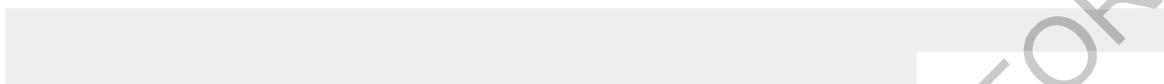
12.4. Vital Signs and Body Weight

For vital signs and body weight, summary statistics of observed values and changes from baseline (also percent change from baseline for body weight) will be provided by time point (time points include the scheduled visits for vital signs/body weight, the follow-up visit, and the end of Weeks 0-208).

A subject data listing of all vital signs and body weight will be provided.

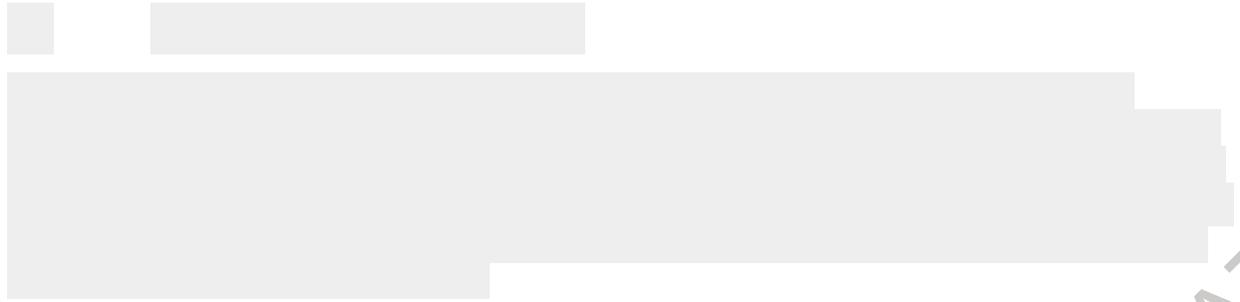
12.5. Electrocardiogram

A frequency summary (shift table) of the shift from baseline to the end of Weeks 0-208 in investigator clinical interpretation of ECG (normal; abnormal, not clinically significant; and abnormal, clinically significant) will be provided.





CEL GENE PROPRIETARY INFORMATION



CELGENE PROPRIETARY INFORMATION

15. INTERIM ANALYSIS

There will be no interim analysis.

CEL GENE PROPRIETARY INFORMATION

16. CHANGES TO THE STATISTICAL CONSIDERATIONS SECTION OF THE PROTOCOL

Due to the early termination of the study, the following changes to the Statistical Considerations section of the protocol have been made in this SAP.

- [REDACTED]
- [REDACTED]

- Protocol specifies interim analyses may be performed. This SAP excludes those analyses.

17. REFERENCES

There are no references.

CELGENE PROPRIETARY INFORMATION



CEL GENE PROPRIETARY INFORMATION