Statistical Analysis Plan	
EU Trial No.	2024-515124-36-00
Investigational medicinal product	IRL757 [redacted]
Trial code	IRL757C002
Protocol version and date	Final v2.1; 02OCT2024
SAP version and date	Final v1.0; 01NOV2024

A single-centre, open-label, phase I trial evaluating the pharmacokinetics of single ascending oral doses of IRL757 in healthy elderly volunteers.

Sponsor signatory

Joakim Tedroff, MD, PhD

Integrative Research Laboratories Sweden AB (IRLAB)
Arvid Wallgrens Backe 20
SE-413 46 Göteborg, Sweden

[redacted]

[redacted]

1 SIGNATURES

Author of this statistical analysis plan (SAP)

[redacted]

Sponsor signatory

Joakim Tedroff, MD, PhD, Sponsor's Medical representative
Integrative Research Laboratories Sweden AB (IRLAB)

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3 LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation	Explanation
ADaM	Analysis Data Model
AE	Adverse event
A_e	Amount excreted in urine
ATC	Anatomical therapeutic chemical
AUC	Area under the plasma concentration *vs.* time curve
$AUC_{0\text{-inf}}$	AUC from 0 to infinity
$AUC_{0\text{-last}}$	AUC from 0 to time of last measurable plasma concentration
BLQ	Below lower limit of quantification
BMI	Body mass index
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence interval
CL/F	Apparent total body clearance following extravascular administration
CL_R	Renal clearance
C_{max}	Maximum observed concentration
C-SSRS	Columbia-Suicide Severity Rating Scale
[redacted]	[redacted]
CTP	Clinical trial protocol
CV	Coefficient of variation
DDP	Data display plan
ECG	Electrocardiogram
eCRF	Electronic case report form
FAS	Full analysis set
FDA	United States Food and Drug Administration
F_e	Fraction of the dose excreted in urine
FIH	First-In-Human
Geo	Geometric
IG	Implementation guideline
IMP	Investigational medicinal product
$lambda_z$	Terminal elimination rate constant
lin	Linear
LLOQ	Lower limit of quantification

Abbreviation	Explanation
log	Logarithmic
Max	Maximum
MedDRA	Medical dictionary for regulatory activities
Min	Minimum
NA	Not applicable/not available
NC	Not calculated
NCA	Non-compartmental analysis
PK	Pharmacokinetic(s)
PKAS	PK analysis set
PT	Preferred term
SAE	Serious adverse event
SAP	Statistical analysis plan
SAS	Statistical analysis system
SD	Standard deviation
SDTM	Trial data tabulation model
SOC	System organ class
T_{last}	Time of occurrence of last observed plasma concentration
T_{max}	Time of occurrence of C_{max}
$T_{1/2}$	Terminal elimination half-life
ULOQ	Upper limit of quantification
V_z/F	Volume of distribution (associated with terminal phase) following extravascular administration
WHO	World Health Organization

4 INTRODUCTION

This Statistical analysis plan (SAP) gives a detailed description of the planned statistical analysis for trial IRL757C002.

4.1 Trial design

This is a single-centre, open-label, phase I trial evaluating the pharmacokinetics (PK) of single ascending oral doses of IRL757 in healthy elderly volunteers.

The trial will be a parallel group design with one (1) pre-defined starting dose [redacted] and one ascending dose level of IRL757 [redacted]

Please see the clinical trial protocol (CTP) for additional details.

4.2 Trial objectives and endpoints

Table 1 Trial objectives and endpoints

Objectives	Endpoints	Assessments	Analyses	Data display plan (DDP)
Primary objective	**Primary endpoints**			
To determine the single dose PK characteristics of IRL757 and its 3 main metabolites in elderly healthy volunteers.	*IRL757 and 3 main metabolites*: Area under the plasma concentration-time curve AUC_{0-t}, AUC_{0-24}, $AUC_{0->\infty}$, maximum concentration (C_{max}), time to maximum concentration (T_{max}), terminal elimination rate constant ($lambda_z$), terminal half-life ($T_{1/2}$), amount excreted in urine (A_e) *IRL757 only*: total apparent clearance of drug from plasma (CL/F), volume of distribution (V_z/F), fraction of the dose excreted in urine (Fe), renal clearance CL_R.	PK plasma and urine sampling	Descriptive statistics, Section 9.1.1	Sections 10.2.2.1, 10.3.1.1
	IRL757 and metabolites M5, M7: Dose proportionality after single oral doses based on AUC_{0-t}, $AUC_{0->\infty}$ and C_{max}		Dose proportionality analysis, Section 9.1.1.1	Section 10.3.1.2
Secondary objective	**Secondary endpoints**			
To evaluate the safety and tolerability of IRL757 after single oral dosing in healthy elderly volunteers.	Frequency, seriousness and intensity of adverse events (AEs).	AE reporting and questioning	Descriptive statistics, Section 9.2.1	Section 10.2.3.1
	Physical examination	Physical examinations	Descriptive statistics, Section 9.2.2	Section 10.2.3.2
	Electrocardiogram (ECG) recordings	12-lead safety ECG	Descriptive statistics, Section 9.2.3	Section 10.2.3.3
	Vital signs	Blood pressure, heart rate, respiratory rate, body temperature	Descriptive statistics, Section 9.2.4	Section 10.2.3.4
	Safety laboratory measurements	Blood sampling for haematology, clinical chemistry and coagulation	Descriptive statistics, Section 9.2.5	Section 10.2.3.5
	Columbia-Suicide Severity Rating Scale (C-SSRS)	C-SSRS questionnaire	Listings, Section 9.2.6	Section 10.4
Exploratory objective	**Exploratory endpoints**			

Objectives	Endpoints	Assessments	Analyses Data display plan (DDP)
To characterize the metabolite profile in plasma and urine in healthy elderly volunteers and compare with the profiles observed in healthy volunteers of the First-In-Human (FIH) study.	Metabolite pattern analysis in plasma in comparison with the metabolite profile in plasma from the FIH study	Plasma sampling	The analyses and results pertaining to the exploratory endpoints, plasma and urine metabolite profiles, will be detailed in a separate report and hence are not covered in this SAP.
	Profile of excreted metabolites in the urine	Urine sampling	

4.3 Randomisation and number of subjects

Twelve (12) eligible and consenting subjects will be included in one (1) of two (2) dose groups, six (6) subjects in each dose group.

This is a non-randomised trial. Trial will include one pre-defined starting dose [redacted] and one ascending dose level [redacted].

4.4 Subject replacement

The trial subjects withdrawn for medical/safety reasons will not be replaced.

Withdrawals due to non-medical/safety reasons including voluntary withdrawals can be replaced if subjects are not evaluable. See CTP for additional details.

4.5 Blinding

This is an open-label trial, and the allocation of treatments will not be blinded.

5 STATISTICAL AND ANALYTICAL PLANS

5.1 Statistical hypotheses

One of the trials endpoints is to investigate if the pharmacokinetic AUC and C_{max} are proportional to the dose administered. Please refer to section 9.1.1.1 below for more details about the dose proportionality analyses.

5.2 Sample size calculation

No formal sample size calculation has been performed for this trial. The size of the dose groups is considered sufficient to provide adequate information on the safety and PK parameters for the purpose of this trial.

5.3 Definition of analysis sets

The analysis sets defined for the trial are outlined in Table 2.

Table 2 Analysis sets

Analysis set	Definition	Use of analysis set
Full analysis set (FAS)	All subjects who have received treatment with investigational medicinal product (IMP)	The FAS will be used for safety and tolerability assessments and description of trial population.
Pharmacokinetic analysis set (PKAS)	All subjects who received IMP, who provided an evaluable plasma concentration profile and who have no AEs or protocol deviations judged to affect the PK analysis. Individual PK values may be excluded from the analysis.	PK endpoints.

5.4 Definition of baseline

Baseline is defined as the latest measurement prior to IMP exposure.

5.5 Rounding principles

Generally, no rounding of data will be done prior to calculating statistics. However, if reported data contains more than 8 significant digits it will be rounded to 8 significant digits in the database.

In statistical output and descriptive summaries, the following principles will be used:

- Data will be presented as reported in input data in listings.
- Two (2) significant digits will be used for percentages (for example relative change from baseline).
- p-values and similar statistical output will be presented using 4 decimal places.
- Three (3) significant digits will be used for PK parameters when presenting min and max values in tables.
- Descriptive summaries (e.g., mean, SD, median etc.) of PK parameters will be presented with 4 significant digits.
- Descriptive summaries (e.g., mean, SD, median etc.) of all other numerical data will be presented with one extra decimal compared to reported input data.

5.6 Significance level

All statistical hypotheses in this trial will be answered using two-sided 90% confidence intervals.

5.7 Handling of dropouts, missing data and outliers

Outliers will be included in summary tables and listings and will not be handled separately in any analyses. All collected data, even if not tabulated, will be listed. Generally, no imputation of data will be performed. However, when calculating statistics for PK plasma concentrations, concentrations under LLOQ will be replaced with LLOQ/2 if more than 50% of the values for a given time point are above LLOQ. For figures presenting individual PK concentrations, no imputation is performed for values under LLOQ. For imputation of PK plasma concentration below LLOQ with the purpose of calculating PK parameters, see Section 9.1.1.

Safety laboratory concentrations under LLOQ will be replaced with LLOQ/2 and concentrations over ULOQ will be replaced with ULOQ for the purpose of calculating descriptive statistics.

In case of missing start and stop times of AEs that cannot be investigated further, missing data will be imputed according to a worst-case scenario, i.e., start time will be imputed as the closest time point post first intake of IMP and end time as 23:59, resulting in the longest possible treatment emergent duration of the AE.

6 CHANGES FROM THE CLINICAL TRIAL PROTOCOL

Changes to the planned analyses and the timing of these are summarised in Table 3.

Table 3 Changes in the planned statistical analyses

Change category	Timing of change	Description of change	Reason for change
Change in the SAP compared to the protocol	Prior to DBL	Added frequency tables for safety laboratory interpretations	To provide a better overview of the safety laboratory data.
Change in the SAP compared to the protocol	Prior to DBL	Removed dose proportionality for metabolite M1	Not relevant with dose proportionality for M1 due to [redacted] polymorphism

7 CLINICAL DATABASE PROCESSING

7.1 General information

The clinical database is processed and generated according to The Clinical Data Interchange Standards Consortium (CDISC). CDISC is a Standard Developing Organization which develops and publishes standards to normalise the structure of clinical trial data and thereby simplify submissions to and reviews by authorities such as the Food and Drug Administration (FDA).

The CDISC standards for clinical studies are the Trial Data Tabulation Model (SDTM) and the Analysis Data Model (ADaM). The trial data will be structured into a database model reflecting the SDTM and will be compliant to SDTM Implementation Guide (SDTM-IG) version 3.3. The data used for statistical analysis will be structured to reflect the ADaM and be compliant to ADaM Implementation Guide (ADaM-IG) version 1.3.

Data values are collected according to, or mapped into, controlled terminology codelists defined by CDISC, whenever possible. The codelists are updated quarterly at CTC and the latest version available at trial start will be used. As per default, controlled terminology codelists will be used in all tables, listings, and figures. Custom codelists for test or parameter names will be used if applicable upon Sponsor's request, to align with protocol texts, or to adhere to other standard naming conventions (e.g., PK parameter name "Tmax" will be used instead of the CDISC term "Time of CMAX"). These custom codelists will be mapped in the "Parameter Name" field in the ADaM structure, while the CT will be kept in the SDTM predecessor fields to provide traceability back to CDISC codelists.

7.1.1 CDISC Compliance

The trial database will be CDISC compliant which means that the clinical database will be processed and generated according to CDISC standard. The database will be validated against SDTM and ADaM Validation rules using Pinnacle 21.

The following CDISC documentation will be generated:

- SDTM Data Definition Specification (also referred to as a Define -XML)
  - Define-XML transmits metadata that describes any tabular dataset structure and supports the interchange of dataset metadata for clinical research applications in a machine-readable format.
- ADaM Data Definition Specification (also referred to as a Define -XML)
  - Define-XML transmits metadata that describes any tabular dataset structure and supports the interchange of dataset metadata for clinical research applications in a machine-readable format.
- Annotated Electronic Case Report Form (eCRF)
  - Links the data collection fields used to capture trial data to the corresponding variables in the trial database. It enables the user to understand how the trial data were collected and to trace back from trial analysis results to the origin where it was collected.
- SDTM Reviewers' Guide
  - Intended to provide additional context and act as a single point of orientation for the SDTM datasets.
- ADaM Reviewers' Guide
  - Provides regulatory agency reviewers an orientation to the submitted analysis data in a consistent way and usable format.

7.2 Database modeling of trial design

The trial design is mapped to a SDTM trial design model containing the following structural components:

EPOCH: An interval of time in the planned conduct of a trial. An epoch is associated with a purpose (e.g., screening, randomisation, treatment, follow-up), and applies across all arms of the trial. Trial epochs follow a controlled terminology to represent the different trial parts (e.g., SCREENING, TREATMENT [X], FOLLOW-UP)

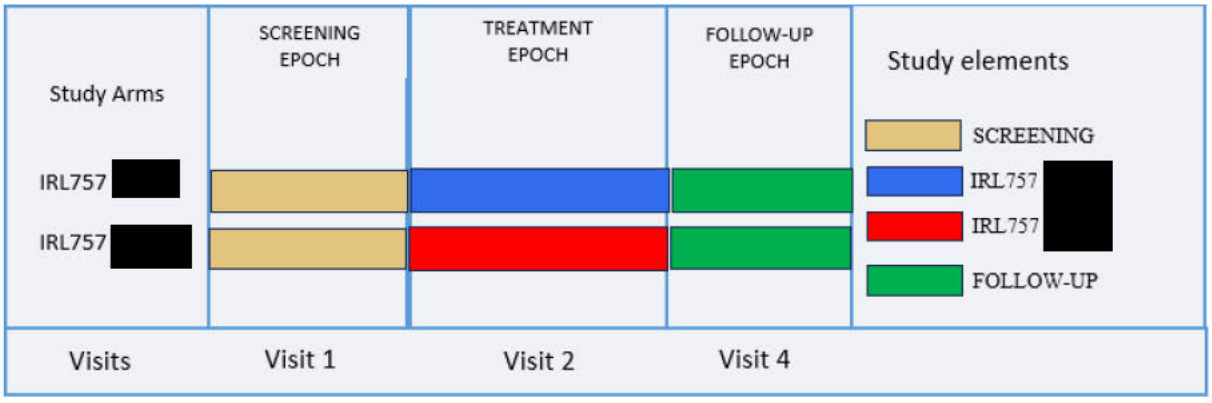
ELEMENT: Building blocks used to build up the entire trial length for all subjects. Information on ELEMENTs is extracted from the trial design and schedule of events in the protocol. ELEMENTs are defined to span the entire trial without gaps. One EPOCH may contain one or several ELEMENTs. All ELEMENTs must have transition rules in accordance with the protocol to determine start and end.

ARM: Subjects are allocated to trial arms depending on the trial design, either by randomisation or other allocation processes defined in the trial protocol. ARMs are defined as the total number of planned ways a subject can go through the trial (unique combination of trial ELEMENTs). All ARMs must contain a unique sequence of ELEMENTs.

VISIT: Trial visits are defined as planned timepoints during the trial where trial data is collected. A visit can be performed in clinic, by off-site contact with trial personnel (phone call, video conference or similar), or by subject initiated recordings of data. The visit schedule is extracted from protocol and eCRF design.

A schematic representation of the SDTM trial design is presented in Figure 1.

Figure 1 Schematic representation of the SDTM trial design



8 STATISTICAL DELIVERABLES

The following items will be delivered:

- Statistical analyses, summary tables, listings and figures as described under Section 10
- Clinical trial database delivered as a SAS-export file (SDTM and ADaM) and Excel files (ADaM)
- Define -XML for SDTM
- Define -XML for ADaM
- Annotated eCRF
- SDTM Reviewer's Guide
- ADaM Reviewer's Guide

9 STATISTICAL METHODOLOGY

In general, data will be presented in tables with the number of observations, arithmetic mean, standard deviation (SD), median, minimum and maximum value for continuous data. In addition, 95% confidence intervals (CIs) will be added for ECG, vital signs and safety laboratory data. Categorical data will be presented with counts and percentages. All collected data will be listed by subject and dose group, except for data pertaining to the exploratory endpoints which will be reported elsewhere. Data is generally presented by dose group.

Details on statistical analyses and descriptive summaries are specified below.

All statistical analyses and descriptive summaries will be performed using SAS version 9.4 (SAS institute, Cary, NC).

PK parameters will be calculated by Non-Compartmental Analysis (NCA) using the software Phoenix WinNonlin® version 8.3 (Certara, U.S.A).

9.1 Analysis of the primary endpoints

9.1.1 Pharmacokinetic analysis

The following non-compartmental plasma PK parameters will be determined/calculated during the trial conduct:

Plasma IRL757:

- T_{max} – Time to reach C_{max}
- C_{max} – The maximum observed plasma concentration
- $AUC_{0\text{-}last}$ – Area under the plasma concentration versus time curve (AUC) from timepoint 0 to t, where t represents the timepoint of the last detectable plasma concentration
- $AUC_{0\text{-}24h}$ – AUC from timepoint 0 to 24 h
- $AUC_{0\text{-}inf}$ – AUC from timepoint 0 extrapolated to infinity
- CL/F – Apparent clearance
- V_z/F – Apparent volume of distribution associated with terminal phase
- $Lambda_z$ – Eliminate rate constant associated with the terminal phase
- $T_{1/2}$ – Terminal plasma elimination half-life

For the 3 main metabolites following PK parameters will be determined/calculated (if possible):

- T_{max}
- C_{max}
- $AUC_{0\text{-}last}$
- $AUC_{0\text{-}24h}$
- $AUC_{0\text{-}inf}$
- $Lambda_z$
- $T_{1/2}$

Parameters that are only presented in listings

- $Lambda_z$ lower – Lower limit on time for values to be included in the calculation of $Lambda_z$
- $Lambda_z$ upper – Upper limit on time for values to be included in the calculation of $Lambda_z$
- No points $lambda_z$ – Number of points used in computing $lambda_z$
- Span – The ratio between the interval used for determination of $lambda_z$ and the terminal $T_{1/2}$
- Rsq adj – Goodness of fit statistic for the terminal phase, adjusted for the number of points used in the estimation of $lambda_Z$.
- T_{last} – Time of last observed plasma concentration
- $AUC_{extr\%}$ – Percentage of $AUC_{0\text{-}inf}$ due to extrapolation from T_{last} to infinity
- $AUC_{0\text{-}48h}$ – (AUC) from timepoint 0 to 48 h

The following non-compartmental urine PK parameters will be calculated during the trial conduct:

- A_e – Amount IRL757 excreted unchanged (IRL757 and major metabolites)
- F_e – Fraction of dose excreted in urine (only IRL757)
- CL_{renal} – Renal clearance (only IRL757)

Following units will be used:

- Time: h
- Concentration: umol/L
- AUCs: h*umol/L
- Extrapolated AUC and F_e: %
- $Lambda_z$: /h
- Apparent Clearance: L/h
- Apparent Volume of distribution: L
- A_e: umol and/or mg

Non-compartmental analysis will be based on the actual sampling times recorded during the trial. For the purpose of calculating PK parameters, concentrations below lower limit of quantification (LLOQ) occurring before C_{max} will be treated as zero. Concentrations below LLOQ occurring after C_{max} will be omitted from the analysis.

T_{max}, T_{last}, and C_{max} will be based on the observed plasma concentration data.

All AUC will be assessed by integration of the plasma concentration vs time curve using linear interpolation for increasing plasma levels and logarithmic interpolation for decreasing plasma levels (Linear Up-Log Down method).

$AUC_{0\text{-}last}$ will be calculated from time 0 to the time t of the last detectable plasma concentration.

For $AUC_{0\text{-}inf}$ the area will be calculated to the last timepoint showing a measurable plasma concentration and then extrapolated to infinity using the concentration in the last quantifiable sample and $lambda_z$.

$$AUC_{0-inf} = AUC_{0-last} + \frac{C_{last}}{lambda_z}$$

Partial AUC will be derived according to specified time windows/dosing interval, if the end time of the interval does not occur at an actual timepoint either linear interpolation or extrapolation will be used for derivation of the partial AUC. Extrapolation, using $lambda_z$, will only be used if the end time of specified interval occur after last detectable plasma concentration.

Formulas for calculation of AUC

- Linear trapezoidal rule:

$$AUC|_{t1}^{t2} = \delta t \times \frac{C_1 + C_2}{2}$$

- Logarithmic trapezoidal rule:

$$AUC|_{t1}^{t2} = \delta t \times \frac{C_2 - C_1}{ln\left(\frac{C_2}{C_1}\right)}$$

where t = time, c = concentration, $\delta t = t_2 - t_1$.

Formulas for interpolation (to find C* at time t* for t1 < t* < t2)

- Linear interpolation rule:

$$C^* = C_1 + \left|\frac{t^* - t_1}{t_2 - t_1}\right| (C_2 - C_1)$$

- Logarithmic interpolation rule:

$$C^* = exp\,(ln(C_1) + \left|\frac{t^* - t_1}{t_2 - t_1}\right| * (ln(C_2) - ln(C_1)))$$

where t = time, c = concentration

$Lambda_z$, the first order rate constant associated with the terminal portion of the curve will be determined by lin-logarithmic regression of the terminal elimination phase of individual plasma concentration vs time curves. Determination of $lambda_z$ requires identification of a sufficiently linear terminal phase (as determined by visual inspection of the lin-log plasma concentration vs time plot with the regression line) consisting of at least 3 terminal concentration values (not including C_{max}). If this is not achieved, $lambda_z$ and its dependent PK parameters will not be reported for that profile.

In the following cases, lambda$_z$ dependent PK parameters will be flagged in listings as potentially unreliable:

- Lambda$_z$ estimation is based on a period of less than 1.5 times the resulting $T_{1/2}$.
- The Rsq adjusted value of the regression line is < 0.85.
- The estimated % extrapolated AUC is > 20% (($AUC_{0\text{-inf}}$ -$AUC_{0\text{-last}}$ / $AUC_{0\text{-inf}}$)*100).

$T_{1/2}$ will be calculated accordingly:

$$T_{1/2} = \frac{\ln(2)}{lambda_z}$$

Span will be calculated accordingly:

$$Span = \frac{lambda_z\ upper - \ lambda_z\ lower}{T_{1/2}}$$

CL will be calculated accordingly:

$$\frac{CL}{F} = \frac{Dose}{AUC_{0-inf}}$$

V_z will be calculated accordingly:

$$\frac{V_z}{F} = \frac{Dose}{lambda_z * AUC_{0-inf}}$$

A_e will be calculated accordingly:

$$A_e = \sum_{i=1}^{n} v_i * c_i$$

Let v be the volume of urine and c the concentration of drug in urine, the product of v and c for one interval (i) represent Ae. The A_e over 0-48 hours is the sum of all intervals. The weight of the collected urine fractions will be calculated assuming a urine density of 1.00 g/mL.

CL_{renal} will be calculated accordingly:

$$CL_{renal} = \frac{A_e}{AUC_{0-48h}}$$

If there is a confirmed dosing error during the trial, the pharmacokinetic data for that period will only be included in the listings but excluded from descriptive and statistical analyses. In case of missed blood samples, potential impact on PK parameters will be assessed for each individual case. PK parameters with a high degree of uncertainty due to missing samples (e.g., multiple samples missing around C_{max}) will be flagged as unreliable in the report and may in rare cases be excluded from summary tables, descriptive statistics, and statistical analysis.

Descriptive statistics for the PK parameters will be presented by dose group using summary statistics with the number of measurements (n), arithmetic mean, SD, as well as median, minimum and maximum values. For all applicable PK parameters, the geometric mean and geometric coefficient of variation (CV%) will be presented. For the parameter T_{max}, the number of observations, and median, minimum and maximum values will be presented only.

9.1.1.1 Dose proportionality analysis

Dose-proportionality (an increase in dose corresponds to a proportional increase in PK outcome) after a single dose, will be assessed using the power model, i.e., linear regression modelling of $AUC_{0\text{-}t}$, $AUC_{0\text{-}inf}$, and C_{max} respectively on log-scale according to the formula:

$$\ln(PK) = \beta_0 + \beta_1 \times \ln(dose)$$

Let h be the highest dose and l be the lowest dose. Then the predicted PK geometric mean (back-transformed to normal scale) of the high dose is $e^{\beta_0} h^{\beta_1}$, and that of the low dose is $e^{\beta_0} l^{\beta_1}$. Let r be the maximal dose ratio, i.e., h/l. Dose proportionality corresponds to:

$$e^{\beta_0} h^{\beta_1} / e^{\beta_0} l^{\beta_1} = h/l \;\rightarrow\; (h/l)^{\beta_1 - 1} = r^{\beta_1 - 1} = 1$$

Let Θ_L=0.8 and Θ_H=1.25 be the lower and upper acceptance limits respectively, (0.8 and 1.25 being the industry standard limits). Dose-proportionality occurs when

$$\Theta_L < r^{\beta_1 - 1} < \Theta_H,$$

which on natural log scale equates to

$$\ln(\Theta_L) < (\beta_1 - 1)\ln(r) < \ln(\Theta_H) \rightarrow 1 + \frac{\ln(\Theta_L)}{\ln(r)} < \beta_1 < 1 + \frac{ln(\Theta_H)}{\ln(r)}$$

Specifically, dose-proportionality is declared when the 90% CI for β_1 from the linear regression model on log scale lies entirely within the acceptance region:

$$\left[1 + \frac{\ln(0.8)}{\ln(r)}, 1 + \frac{\ln(1.25)}{\ln(r)}\right]$$

9.2 Analysis of secondary endpoints

9.2.1 Adverse Events (AEs)

AEs and serious AEs (SAEs) will be recorded from the time when informed consent is obtained until the Follow-up Visit. AEs that occur before first treatment with IMP (baseline symptoms) will be listed separately.

All AEs will be described in terms of the dose at which they occurred. AEs will be summarised by System Organ Class (SOC) and Preferred Term (PT) using the Medical Dictionary for Regulatory Activities (MedDRA) vocabulary. The number of subjects reporting AEs, and the number of AEs reported will be presented. The events will be tabulated by SOC, PT and by severity and relationship to IMP. SAEs will be presented in the same tabulations.

9.2.2 Physical examinations

Normal and abnormal findings will be specified and summarised by dose group.

9.2.3 Electrocardiogram (ECG)

All continuous ECG data will be listed for each subject and summarised by dose group. In addition, ECGs will be categorised as ”normal”, ”abnormal, not clinically significant”, or ”abnormal, clinically significant” (as judged by the Investigator) and summarised by dose group.

9.2.4 Vital signs

Vital signs (blood pressure, heart rate, respiratory rate and body temperature) will be summarised by dose group.

9.2.5 Safety laboratory analyses

Safety laboratory data will be summarised by dose group. Safety laboratory interpretations will be summarised by dose groups using frequency tables.

9.2.6 Columbia-Suicide Severity Rating Scale (C-SSRS)

This rating scale will be administered for screening of suicidal ideation and behaviour throughout the trial. No formal statistical analysis of the outcome will be performed, i.e., the data will be listed only. Any abnormal findings will be listed and treated as AEs or SAEs.

9.3 Analysis of exploratory endpoints

The analysis and results pertaining to the exploratory endpoints, plasma and urine metabolite profiles, will be detailed in a separate report, and hence are not covered in this SAP.

9.4 Description of trial population

9.4.1 Disposition

A subject disposition will be presented showing the number of screened subjects; the number of withdrawn subjects prior to dose, including the reason for withdrawal; the number of included subjects in each dose group; the number of withdrawn subjects, including the reason for withdrawal; the number of completed subjects; the number of subjects included in the analysis sets, and the number of subjects at each visit.

9.4.2 Demographics and baseline characteristics

Descriptive statistics of demographics and other baseline characteristics will be presented by dose group.

9.4.3 Medical history and concomitant medication

Medical/surgical history and prior/concomitant medications will be presented by dose group.

Medications are classified as prior if the stop date and time was before or on the day of the dose administration (pre-dose) and as concomitant if ongoing on the day of the dose administration, stopped after the dose administration or started after the dose administration. To distinguish between prior and concomitant medications on the dosing day, the start time of any newly introduced medication or the stop time of any previously ongoing medication will be considered.

Medical/surgical history will be summarised by SOC and PT using the MedDRA vocabulary.

Prior and concomitant medications will be summarised by anatomical therapeutic chemical (ATC) classification and active ingredients using the World Health Organisation (WHO) WHODrug Global drug reference dictionary.

9.4.4 Treatment compliance

The subjects treated in each dose group and their individual doses will be listed.

9.5 Interim analysis

No formal interim analysis will be performed.

10 DATA DISPLAY PLAN

Tables and figures will only be generated if sufficient data, with sufficient variability exist to justify specific output being produced. Unscheduled/extra visits will generally not be presented in tables and summary figures but will be included in listings.

10.1 Table of contents DDP

10.2 Trial tables

10.2.1 Demographic data

Table DM 1 Baseline characteristics and demographics (Full analysis set)

Assessment (unit)		IRL757 [redacted] (N=6)	IRL757 [redacted] (N=6)	Total (N=12)
Age (years)	n	x	x	x
	Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
	Median (Min, Max)	xx.x (xx, xx)	xx.x (xx, xx)	xx.x (xx, xx)
Height (cm)	n	x	x	x
	Mean (SD)	xxx.x (xx.x)	xxx.x (xx.x)	xxx.x (xx.x)
	Median (Min, Max)	xxx.x (xxx, xxx)	xxx.x (xxx, xxx)	xxx.x (xxx, xxx)
Weight (kg)	n	x	x	x
	Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
	Median (Min, Max)	xx.xx (xx.x, xx.x)	xx.xx (xx.x, xx.x)	xx.xx (xx.x, xx.x)
Body Mass Index (kg/m2)	n	x	x	X
	Mean (SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
	Median (Min, Max)	xx.xx (xx.x, xx.x)	xx.xx (xx.x, xx.x)	xx.xx (xx.x, xx.x)
Sex	Female	xx (xx%)	xx (xx%)	xx (xx%)
	Male	xx (xx%)	xx (xx%)	xx (xx%)
Ethnicity	Hispanic or latino	xx (xx%)	xx (xx%)	xx (xx%)
	Not hispanic or latino	xx (xx%)	xx (xx%)	xx (xx%)
	Not reported	xx (xx%)	xx (xx%)	xx (xx%)
	Unknown	xx (xx%)	xx (xx%)	xx (xx%)
Race	American Indian or Alaska Native	xx (xx%)	xx (xx%)	xx (xx%)
	Asian	xx (xx%)	xx (xx%)	xx (xx%)
	Black or African American	xx (xx%)	xx (xx%)	xx (xx%)

Assessment (unit)		IRL757 [redacted] (N=6)	IRL757 [redacted] (N=6)	Total (N=12)
	Native Hawaiian or Other Pacific Islander	xx (xx%)	xx (xx%)	xx (xx%)
	White	xx (xx%)	xx (xx%)	xx (xx%)

Data based on [ANALYSIS SET]. N: number of subjects in treatment group. Mean values and percentages are based on n. n: Number of observations.
SD: Standard deviation. SAS program: [PROGRAM NAME].sas.
Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

Table DS 1 Subject disposition (All subjects)

	Total (N=12)
Screened subjects	xxx
Withdrawn prior to dose	xxx
Reason for withdrawal prior to dose	
--- Reason 1	xxx
--- Reason 2	xxx
--- …	xxx
Subjects included in trial	xxx
Allocated to arm	
--- IRL757[redacted]	xxx
--- IRL757[redacted]	xxx
Withdrawn subjects	
--- Reason 1	xxx
--- Reason 2	xxx
--- …	xxx
Completed subjects	xxx
Included in Full analysis set	xxx
Included in Pharmacokinetic analysis set	xxx
Subjects at each visit	
--- Visit 1 - Screening	xxx
--- Visit 2 - In-clinic	xxx
--- Follow-up visit - Ambulatory	xxx

Data based on All subjects. SAS program: [PROGRAM NAME].sas.
Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

Table MH 1 Medical history events by system organ class and preferred term (Full analysis set)

	IRL757 [redacted] (N=6)		IRL757 [redacted] (N=6)		Total (N=12)	
System organ class Preferred term	n (%)	m	n (%)	m	n (%)	m
Total	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[SOC 1]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[SOC 1 PT 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 1 PT 2]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 1 PT …]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 2]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[SOC 2 PT 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 2 PT 2]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 2 PT …]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC …]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[SOC … PT 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC … PT 2]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC … PT …]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx

Data based on [ANALYSIS SET]. N: number of subjects in treatment group. Percentages are based on N. n: number of subjects. m: number of events.
The following events are coded with multiple terms and are represented as separate events in tables and listings: '[MH TERM 1], [MH TERM 2]'. See listings for detailed information. SAS program: [PROGRAM NAME].sas.
Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

Table CM 1 Prior medications by ATC classification and active ingredients (Full analysis set)

	IRL757 [redacted] (N=6)		IRL757 [redacted] (N=6)		Total (N=12)	
ATC classification Active Ingredients	n (%)	m	n (%)	m	n (%)	m
Total	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[ATC classification 1]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[ATC classification 1 Active Ingredients 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[ATC classification 1 Active Ingredients 2]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[ATC classification 1 Active Ingredients …]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[ATC classification 2]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[ATC classification 2 Active Ingredients 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[ATC classification 2 Active Ingredients 2]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[ATC classification 2 Active Ingredients …]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[ATC classification …]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[ATC classification … Active Ingredients 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[ATC classification … Active Ingredients 2]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[ATC classification … Active Ingredients …]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx

Data based on [ANALYSIS SET]. N: number of subjects in treatment group. Percentages are based on N. n: number of subjects. m: number of events.
The following records are coded with multiple terms and are represented as separate events in tables and listings: '[CM TERM 1], [CM TERM 2]'.
See listings for detailed information. SAS program: [PROGRAM NAME].sas.
Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

Table CM 2 Concomitant medications by ATC classification and active ingredients (Full analysis set)

Same layout as Table CM 1

10.2.2 Primary endpoints

10.2.2.1 Pharmacokinetic analysis

Table PC 1 Plasma concentrations of IRL757 (Pharmacokinetic analysis set)

Assessment (unit)	Assessment timepoint		IRL757 [redacted] (N=6)	IRL757 [redacted] (N=6)
[PARAMETER 1] (unit)	[Assessment timepoint 1]	n/BLQ	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)
	[Assessment timepoint 2]	n/BLQ	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)

Data based on [population]. LLOQ is xx (unit). See listing 16.2.5-1 for a per subject LLOQ summary. n: Number of observations. BLQ: Below lower limit of quantification. SD: Standard deviation. CV%: Coefficient of variation described as percentage. Geo CV%: Geometric coefficient of variation described as percentage calculated using log-transformed standard deviation. NC: Not calculated - number of evaluable observations less than 3 or more than half of the observations are BLQ. NA: Not available - no evaluable observations. SAS program: [PROGRAM NAME].sas.
Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

Table PC 2 Plasma concentrations of 3 main metabolites of IRL757 (Pharmacokinetic analysis set)

Same layout as Table PC 1

Table PP 1 Plasma PK parameters of IRL757 (Pharmacokinetic analysis set)

Assessment (unit)		IRL757 [redacted] (N=6)	IRL757 [redacted] (N=6)
Tmax (unit)	n	xx	xx
	Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
Cmax (unit)	n	xx	xx
	Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
	Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)
AUC0-last (unit)	n	xx	xx
	Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
	Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)
AUC0-24h (unit)	n	xx	xx
	Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
	Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)
AUC0-inf (unit)	n	xx	xx
	Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
	Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)
CL/F (unit)	n	xx	xx
	Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
	Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)
Vz/F (unit)	n	xx	xx
	Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
	Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)

Assessment (unit)		IRL757 [redacted] (N=6)	IRL757 [redacted] (N=6)
Lambdaz (unit)	n	xx	xx
	Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
	Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)
T1/2 (unit)	n	xx	xx
	Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
	Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)

Data based on [population]. n: Number of observations. SD: Standard deviation. CV%: Coefficient of variation described as percentage. Geo CV%: Geometric coefficient of variation described as percentage calculated using log-transformed standard deviation. NC: Not calculated - number of evaluable observations less than 3 or more than half of the observations are BLQ. NA: Not available - no evaluable observations. SAS program: [PROGRAM NAME].sas.
Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

Table PP 2 Urinary excretion of IRL757 (Pharmacokinetic analysis set)

			Parameter (unit)		
Cohort	Assessment time interval		IRL757 concentration (unit)	Urine volume (unit)	Ae per time interval (unit)
IRL757 [redacted], XX umol (N=6)	0-6 h	n/BLQ	xx/xx	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)
	6-12 h	n/BLQ	xx/xx	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)
	12-24 h	n/BLQ	xx/xx	xx/xx	xx/xx

			Parameter (unit)		
Cohort	Assessment time interval		IRL757 concentration (unit)	Urine volume (unit)	Ae per time interval (unit)
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)
	24-36 h	n/BLQ	xx/xx	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)
	36-48 h	n/BLQ	xx/xx	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)
IRL757 [redacted] XX umol (N=6)	0-6 h	n/BLQ	xx/xx	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)
	6-12 h	n/BLQ	xx/xx	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)
	12-24 h	n/BLQ	xx/xx	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)
	24-36 h	n/BLQ	xx/xx	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)

			Parameter (unit)		
Cohort	Assessment time interval		IRL757 concentration (unit)	Urine volume (unit)	Ae per time interval (unit)
	36-48h	n/BLQ	xx/xx	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)

Data based on [population]. Volume is calculated assuming density of 1.00 g/mL. n: Number of observations. LLOQ is xx (unit). See listing 16.2.5-1 for a per subject LLOQ summary. n: Number of observations. BLQ: Below lower limit of quantification. SD: Standard deviation. CV%: Coefficient of variation described as percentage. Geo CV%: Geometric coefficient of variation described as percentage calculated using log-transformed standard deviation. NC: Not calculated - number of evaluable observations less than 3 or more than half of the observations are BLQ. NA: Not available - no evaluable observations. SAS program: [PROGRAM NAME].sas.
Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

Table PP 3 Renal PK parameters of IRL757 (Pharmacokinetic analysis set)

Assessment (unit)		IRL757 [redacted] (N=6)	IRL757 [redacted] (N=6)
Ae (unit)	n	xx	xx
	Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
	Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)
Fe (unit)	n	xx	xx
	Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
	Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)
CLrenal (unit)	n	xx	xx
	Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
	Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)

Data based on [population]. n: Number of observations. n: Number of observations. BLQ: Below lower limit of quantification. SD: Standard deviation. CV%: Coefficient of variation described as percentage. Geo CV%: Geometric coefficient of variation described as percentage calculated using log-transformed standard deviation. NC: Not calculated - number of evaluable observations less than 3 or more than half of the observations

are BLQ. NA: Not available - no evaluable observations. SAS program: [PROGRAM NAME].sas.
Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

Table PP 4 Plasma PK parameters of 3 main metabolites of IRL757 (Pharmacokinetic analysis set)

Metabolite	Assessment (unit)		IRL757 [redacted] (N=6)	IRL757 [redacted] (N=6)
[Metabolite name]	Tmax (unit)	n	xx	xx
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
	Cmax (unit)	n	xx	xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)
	AUC0-last (unit)	n	xx	xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)
	AUC0-24h (unit)	n	xx	xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)
	AUC0-inf (unit)	n	xx	xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)
	Lambdaz (unit)	n	xx	xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)
	T1/2 (unit)	n	xx	xx

Metabolite	Assessment (unit)		IRL757 [redacted] (N=6)	IRL757 [redacted] (N=6)
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)

Data based on [population]. Number of observations. SD: Standard deviation. CV%: Coefficient of variation described as percentage. Geo CV%: Geometric coefficient of variation described as percentage calculated using log-transformed standard deviation. NC: Not calculated - number of evaluable observations less than 3 or more than half of the observations are BLQ. NA: Not available - no evaluable observations. SAS program: [PROGRAM NAME].sas.
Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

Table PP 5 Urinary excretion of 3 main metabolites of IRL757 (Pharmacokinetic analysis set)

			Parameter (unit)						
Cohort	Assessment time interval		M1 concentration (unit)	M5 concentration (unit)	M7 concentration (unit)	Urine volume (unit)	M1 Ae per time interval (unit)	M5 Ae per time interval (unit)	M7 Ae per time interval (unit)
IRL757 [redacted] XX umol (N=6)	0-6 h	n/BLQ	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)
	6-12 h	n/BLQ	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)
	12-24 h	n/BLQ	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)

			Parameter (unit)						
Cohort	Assessment time interval		M1 concentration (unit)	M5 concentration (unit)	M7 concentration (unit)	Urine volume (unit)	M1 Ae per time interval (unit)	M5 Ae per time interval (unit)	M7 Ae per time interval (unit)
	24-36 h	n/BLQ	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)
	36-48 h	n/BLQ	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)
IRL757 [redacted] XX umol (N=6)	0-6 h	n/BLQ	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)
	6-12 h	n/BLQ	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)
	12-24 h	n/BLQ	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)
	24-36 h	n/BLQ	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)

			Parameter (unit)						
Cohort	Assessment time interval		M1 concentration (unit)	M5 concentration (unit)	M7 concentration (unit)	Urine volume (unit)	M1 Ae per time interval (unit)	M5 Ae per time interval (unit)	M7 Ae per time interval (unit)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)
	36-48 h	n/BLQ	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx	xx/xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)	x.xxx (x.x%)

Data based on [population]. Volume is calculated assuming density of 1.00 g/mL. n: Number of observations. LLOQ is xx (unit). See listing 16.2.5-1 for a per subject LLOQ summary. n: Number of observations. BLQ: Below lower limit of quantification. SD: Standard deviation. CV%: Coefficient of variation described as percentage. Geo CV%: Geometric coefficient of variation described as percentage calculated using log-transformed standard deviation. NC: Not calculated - number of evaluable observations less than 3 or more than half of the observations are BLQ. NA: Not available - no evaluable observations. SAS program: [PROGRAM NAME].sas.
Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

Table PP 6 Renal PK parameters of 3 main metabolites of IRL757 (Pharmacokinetic analysis set)

Assessment (unit)	Metabolite		IRL757 [redacted] (N=6)	IRL757 [redacted] (N=6)
Ae (unit)	M1	n	xx	xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)
	M5	n	xx	xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)
	M7	n	xx	xx
		Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
		Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
		Geometric Mean (geo CV%)	x.xxx (x.x%)	x.xxx (x.x%)

Data based on [population]. n: Number of observations. n: Number of observations. BLQ: Below lower limit of quantification. SD: Standard deviation. CV%: Coefficient of variation described as percentage. Geo CV%: Geometric coefficient of variation described as percentage calculated using log-transformed standard deviation. NC: Not calculated - number of evaluable observations less than 3 or more than half of the observations are BLQ. NA: Not available - no evaluable observations. SAS program: [PROGRAM NAME].sas.
Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

10.2.3 Secondary endpoints

10.2.3.1 Adverse events

Table AE 1 Overview of adverse events (Full analysis set)

	IRL757 [redacted] (N=6)		IRL757 [redacted] (N=6)		Total (N=12)	
	n (%)	m	n (%)	m	n (%)	m
Any AE	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Any SAE	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Any AE leading to withdrawal from trial	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Any AE leading to death	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Relationship to study treatment						
Not related	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Possible	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Probable	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Severity						
Mild	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Moderate	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Severe	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Life-Threatening	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
Death	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx

Data based on [ANALYSIS SET]. N: number of subjects in treatment group. Percentages are based on N. n: number of subjects. m: number of events.
The following AEs are coded with multiple MedDRA terms and are represented as separate AEs in tables and listings: '[AE TERM 1]', '[AE TERM 2]', '[AE TERM 3]. See listings for detailed information. SAS program: [PROGRAM NAME].sas.
Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

Table AE 2 Adverse events by system organ class and preferred term (Full analysis set)

	IRL757 [redacted] (N=6)		IRL757 [redacted] (N=6)		Total (N=12)	
System organ class Preferred term	n (%)	m	n (%)	m	n (%)	m
Total	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[SOC 1]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[SOC 1 PT 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 1 PT 2]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 1 PT …]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 2]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[SOC 2 PT 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 2 PT 2]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC 2 PT …]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC …]	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**	**xx (xx%)**	**xx**
[SOC … PT 1]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC … PT 2]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx
[SOC … PT …]	xx (xx%)	xx	xx (xx%)	xx	xx (xx%)	xx

Data based on [ANALYSIS SET]. N: number of subjects in treatment group. Percentages are based on N. n: number of subjects. m: number of events.
The following events are coded with multiple terms and are represented as separate events in tables and listings: '[AE TERM 1], [AE TERM 2]'. See listings for detailed information. SAS program: [PROGRAM NAME].sas.
Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

Table AE 3 Treatment related adverse events by system organ class and preferred term (Full analysis set)

Same layout as Table AE 2. The following footnote will be added: An AE is considered causally related to the use of the IMP when the causality assessment is probable or possible.

10.2.3.2 Physical examinations

Table PE 1 Physical examinations (Full analysis set)

Assessment	Assessment timepoint		IRL757 [redacted] (N=6)	IRL757 [redacted] (N=6)
[PARAMETER 1]	[Assessment timepoint 1]	[RESULT 1]	xx/XX (xx%)	xx/XX (xx%)
		[RESULT 2]	xx/XX (xx%)	xx/XX (xx%)
		[RESULT 3]	xx/XX (xx%)	xx/XX (xx%)
	[Assessment timepoint 2]	[RESULT 1]	xx/XX (xx%)	xx/XX (xx%)
		[RESULT 2]	xx/XX (xx%)	xx/XX (xx%)
		[RESULT 3]	xx/XX (xx%)	xx/XX (xx%)

Data based on [population]. SAS program: [PROGRAM NAME].sas.
Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

10.2.3.3 12-lead ECG

Table EG 1 ECG measurements (Full analysis set)

Assessment (unit)	Result category	Assessment timepoint		IRL757 [redacted]	IRL757 [redacted] (N=6)
[PARAMETER 1] (unit)	Measured value	[Assessment timepoint 1]	n	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
			95% CI (lower, upper)	(x.xxxx, x.xxxx)	(x.xxxx, x.xxxx)
		[Assessment timepoint 2]	n	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
			95% CI (lower, upper)	(x.xxxx, x.xxxx)	(x.xxxx, x.xxxx)
	Change from baseline	[Assessment timepoint 2]	n	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
			95% CI (lower, upper)	(x.xxxx, x.xxxx)	(x.xxxx, x.xxxx)
	Relative change from baseline (%)	[Assessment timepoint 2]	n	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
			95% CI (lower, upper)	(x.xxxx, x.xxxx)	(x.xxxx, x.xxxx)

Data based on [population]. CI: Confidence interval. n: Number of observations. SD: Standard deviation. NC: Not calculated - number of evaluable observations less than 3. NA: Not available - no evaluable observations. SAS program: [PROGRAM NAME].sas.
Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

Table EG 2 ECG interpretations (Full analysis set)

Assessment	Assessment timepoint		IRL757 [redacted] (N=6)	IRL757 [redacted] (N=6)
[PARAMETER 1]	[Assessment timepoint 1]	[RESULT 1]	xx/XX (xx%)	xx/XX (xx%)
		[RESULT 2]	xx/XX (xx%)	xx/XX (xx%)
		[RESULT 3]	xx/XX (xx%)	xx/XX (xx%)
	[Assessment timepoint 2]	[RESULT 1]	xx/XX (xx%)	xx/XX (xx%)
		[RESULT 2]	xx/XX (xx%)	xx/XX (xx%)
		[RESULT 3]	xx/XX (xx%)	xx/XX (xx%)

Data based on [population]. SAS program: [PROGRAM NAME].sas.
Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

10.2.3.4 Vital signs

Table VS 1 Vital signs measurements (Full analysis set)

Assessment (unit)	Result category	Assessment timepoint		IRL757 [redacted] (N=6)	IRL757 [redacted] (N=6)
[PARAMETER 1] (unit)	Measured value	[Assessment timepoint 1]	n	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
			95% CI (lower, upper)	(x.xxxx, x.xxxx)	(x.xxxx, x.xxxx)
		[Assessment timepoint 2]	n	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
			95% CI (lower, upper)	(x.xxxx, x.xxxx)	(x.xxxx, x.xxxx)
	Change from baseline	[Assessment timepoint 2]	n	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
			95% CI (lower, upper)	(x.xxxx, x.xxxx)	(x.xxxx, x.xxxx)
	Relative change from baseline (%)	[Assessment timepoint 2]	n	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
			95% CI (lower, upper)	(x.xxxx, x.xxxx)	(x.xxxx, x.xxxx)

Data based on [population]. CI: Confidence interval. n: Number of observations. SD: Standard deviation. NC: Not calculated - number of evaluable observations less than 3. NA: Not available - no evaluable observations. SAS program: [PROGRAM NAME].sas.
Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

10.2.3.5 Safety laboratory

Table LB 1 Safety laboratory measurements: Clinical chemistry (Full analysis set)

Assessment (unit)	Result category	Assessment timepoint		IRL757 [redacted] (N=6)	IRL757 [redacted] (N=6)
[PARAMETER 1] (unit)	Measured value	[Assessment timepoint 1]	n	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
			95% CI (lower, upper)	(x.xxxx, x.xxxx)	(x.xxxx, x.xxxx)
		[Assessment timepoint 2]	n	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
			95% CI (lower, upper)	(x.xxxx, x.xxxx)	(x.xxxx, x.xxxx)
	Change from baseline	[Assessment timepoint 2]	n	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
			95% CI (lower, upper)	(x.xxxx, x.xxxx)	(x.xxxx, x.xxxx)
	Relative change from baseline (%)	[Assessment timepoint 2]	n	xx	xx
			Mean (SD)	x.xx (x.xx)	x.xx (x.xx)
			Median (Min, Max)	x.xx (x.x, x.x)	x.xx (x.x, x.x)
			95% CI (lower, upper)	(x.xxxx, x.xxxx)	(x.xxxx, x.xxxx)

Data based on [population]. CI: Confidence interval. n: Number of observations. SD: Standard deviation. NC: Not calculated - number of evaluable observations less than 3. NA: Not available - no evaluable observations. SAS program: [PROGRAM NAME].sas.
Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

Table LB 2 Safety laboratory interpretations: Clinical chemistry (Full analysis set)

Assessment	Assessment timepoint		IRL757 [redacted] (N=6)	IRL757 [redacted] (N=6)
[PARAMETER 1]	[Assessment timepoint 1]	[RESULT 1]	xx/XX (xx%)	xx/XX (xx%)
		[RESULT 2]	xx/XX (xx%)	xx/XX (xx%)
		[RESULT 3]	xx/XX (xx%)	xx/XX (xx%)
	[Assessment timepoint 2]	[RESULT 1]	xx/XX (xx%)	xx/XX (xx%)
		[RESULT 2]	xx/XX (xx%)	xx/XX (xx%)
		[RESULT 3]	xx/XX (xx%)	xx/XX (xx%)

Data based on [population]. SAS program: [PROGRAM NAME].sas.
Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

Table LB 3 Safety laboratory measurements: Haematology (Full analysis set)

Same layout as Table LB 1

Table LB 4 Safety laboratory interpretations: Haematology (Full analysis set)

Same layout as Table LB 2

Table LB 5 Safety laboratory measurements: Coagulation (Full analysis set)

Same layout as Table LB 1

Table LB 6 Safety laboratory interpretations: Coagulation (Full analysis set)

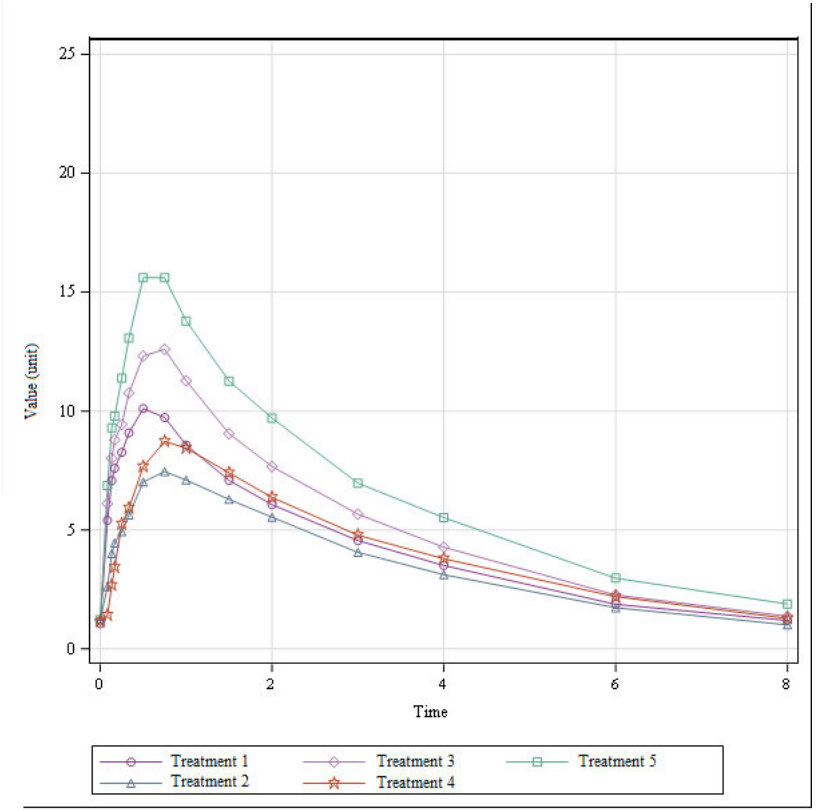
Same layout as Table LB 2

10.3 Trial figures

10.3.1 Primary endpoints

10.3.1.1 Pharmacokinetic analysis

Figure PC 1 Geometric mean plasma concentrations of IRL757 over time 0-48h (lin-log) (Pharmacokinetic analysis set)



Example figure. Note that the numbers do not reflect real data. This template figure will be adjusted as needed depending on the collected data.

Data based on [population]. LLOQ is xx (unit). See listing 16.2.5-1 for a per subject LLOQ summary. lin: Linear. SAS program: [PROGRAM NAME].sas. Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data extracted: YYYY-MM-DDTHH:MM:SS.

Figure PC 2 Geometric mean plasma concentrations of IRL757 over time 0-48h (lin-lin) (Pharmacokinetic analysis set)

Same layout as Figure PC 1

Figure PC 3 Geometric mean plasma concentrations of 3 main metabolites of IRL757 over time 0-48h (lin-log) (Pharmacokinetic analysis set)

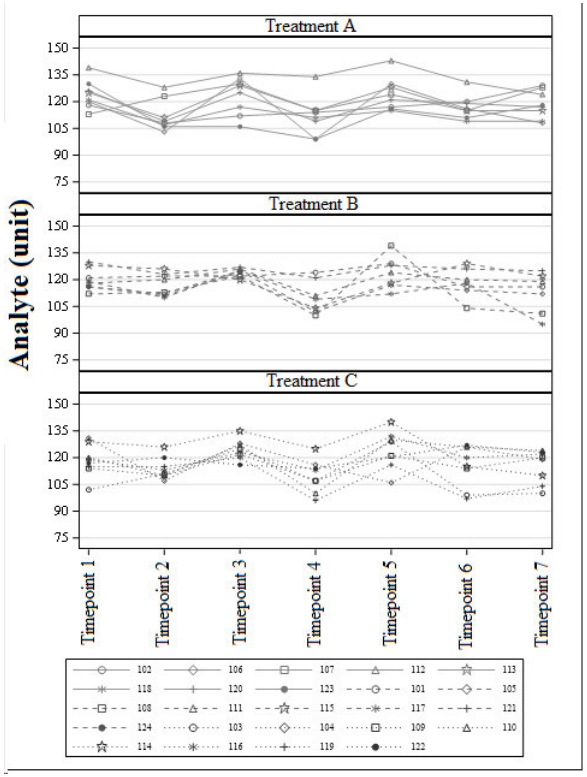
Same layout as Figure PC 1

Figure PC 4 Geometric mean plasma concentrations of 3 main metabolites of IRL757 over time 0-48h (lin-lin) (Pharmacokinetic analysis set)

Same layout as Figure PC 1

Figure PC 5 Individual plasma concentrations of IRL757 over time 0-48h by treatment (lin-log) (Full analysis set)

Individual values under LLOQ will be excluded from the figure. The full analysis set is used for individual graphs to ensure all data are plotted. However, ensure to clarify in a footnote if a subject is not in PKAS and why.



Example figure. Note that the numbers do not reflect real data. This template figure will be adjusted as needed depending on the collected data.

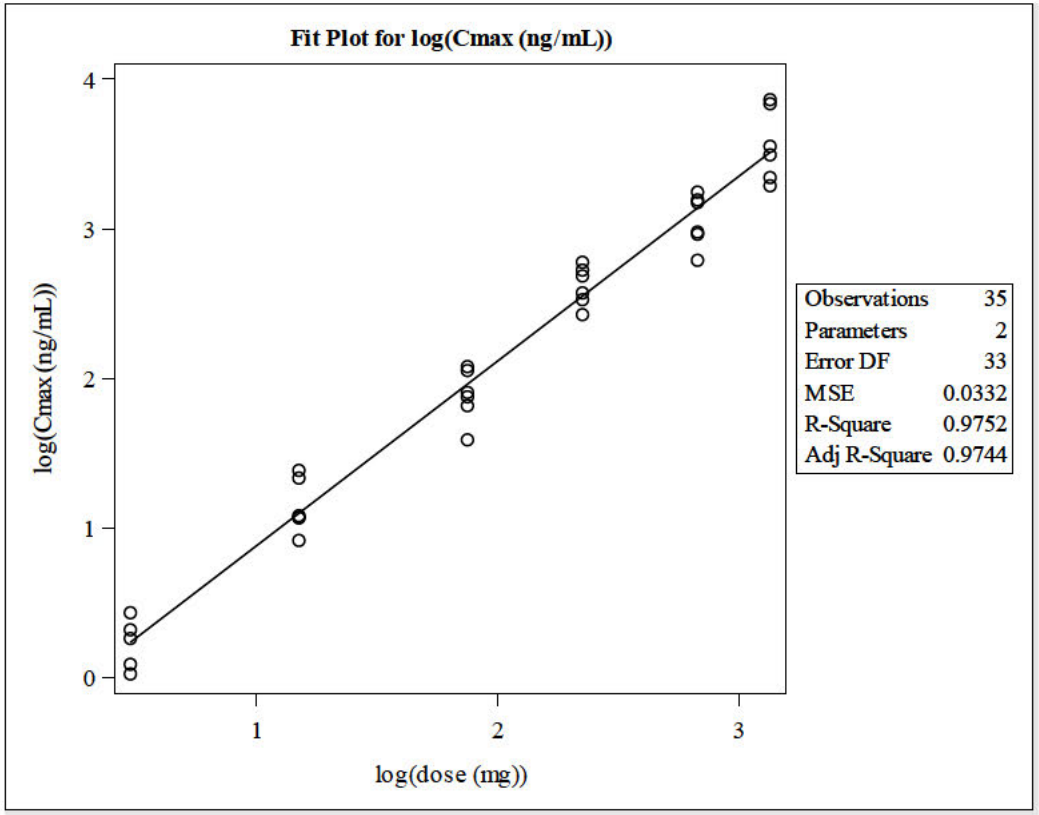
```
Data based on [population]. Individual values under LLOQ are excluded from the figure. LLOQ is xx (unit). See listing 16.2.5-1 for a per subject
LLOQ summary. SAS program: [PROGRAM NAME].sas. Dataset version: ADXX YYYY-MM-DDTHH:MM:SS. Run by: [USERNAME] YYYY-MM-DDTHH:MM:SS. EDC data
extracted: YYYY-MM-DDTHH:MM:SS.
```

Figure PC 6 Individual plasma concentrations of IRL757 over time 0-48h by treatment (lin-lin) (Full analysis set)

Same layout as Figure PC 5

10.3.1.2 Dose proportionality analysis

Figure PP 1 Dose proportionality for Cmax (Pharmacokinetic analysis set)



Example figure. Note that the numbers do not reflect real data.

Include a footnote with the regression equation. Include a footnote with the 90% CI for the slope parameter/coefficient in the model, the calculated acceptance region described in Section 9.1.1.1 and the conclusion of dose-proportionality/non-dose-proportionality. It will also be specified in the footnote which data are used.

Figure PP 2 Dose proportionality for AUC0-t (Pharmacokinetic analysis set)

Same layout as Figure PP 1

Figure PP 3 Dose proportionality for AUC0-inf (Pharmacokinetic analysis set)

Same layout as Figure PP 1

10.4 Trial listings

16.2.1 Discontinued subjects

- **Listing 16.2.1- 1 Discontinued subjects**
- **Listing 16.2.1- 2 Non-eligible subjects**
- **Listing 16.2.1- 3 Disposition (All subjects)**
- **Listing 16.2.1- 4 Subject visits (All subjects)**
- **Listing 16.2.1- 5 Subject elements (All subjects)**

16.2.2 Protocol deviations

- **Listing 16.2.2- 1 Protocol deviations (All subjects)**

16.2.3 Subjects excluded from the efficacy analysis

- **Listing 16.2.3- 1 Population definitions (All subjects)**

16.2.4 Demographic data

- **Listing 16.2.4- 1 Demography (All subjects)**
- **Listing 16.2.4- 2 Medical History (All subjects)**
- **Listing 16.2.4- 3 Prior and concomitant medications (All subjects)**
- **Listing 16.2.4- 4 Baseline events (All subjects)**

16.2.5 Compliance and/or Drug Concentration Data

- **Listing 16.2.5- 1 Plasma concentration data (All subjects)**
- **Listing 16.2.5- 2 Urine concentration data (All subjects)**
- **Listing 16.2.5- 3 Pharmacokinetic parameters (All subjects)**
- **Listing 16.2.5- 4 IMP administration (All subjects)**

16.2.6 Individual Efficacy Response Data

NA

16.2.7 Adverse event listings (each subject)

- **Listing 16.2.7- 1 Adverse events (All subjects)**
- **Listing 16.2.7- 2 Serious adverse events (All subjects)**

16.2.8 Listings of individual laboratory measurements subject

- **Listing 16.2.8- 1 Safety laboratory measurements: Clinical chemistry (All subjects)**
- **Listing 16.2.8- 2 Safety laboratory measurements: Haematology (All subjects)**
- **Listing 16.2.8- 3 Safety laboratory measurements: Coagulation (All subjects)**
- **Listing 16.2.8- 4 Other laboratory measurements (All subjects)**

Pregnancy test, Drug test, Alcohol screen

- **Listing 16.2.8- 5 Virology (All subjects)**

16.2.9 Listings of vital signs, ECG, physical examination data by subject

- **Listing 16.2.9- 1 Vital signs (All subjects)**
- **Listing 16.2.9- 2 ECG (All subjects)**
- **Listing 16.2.9- 3 Physical examinations (All subjects)**

16.2.10 Other data by subject

- **Listing 16.2.10- 1 Columbia-Suicide Severity Rating Scale (All subjects)**