Division	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan

Title	:	Reporting and Analysis Plan for Study 201881: A Randomized, Double-blind, Sponsor un-Blinded, Placebo-controlled, Phase 2a Crossover Study to Evaluate the Effect of the TRPV4 Channel Blocker, GSK2798745, on Pulmonary Gas Transfer and Respiration in Patients with Congestive Heart Failure
Compound Number	:	GSK2798745
Effective Date	:	18-OCT-2017

Description:

- The purpose of this reporting and analysis plan (RAP) is to describe the final planned analyses and output to be included in the Clinical Study Report for Study 201881.
- This RAP is intended to describe the planned efficacy, safety & tolerability, pharmacokinetics analysis required for the study.
- This document will be provided to the study team members to convey the content of the final Statistical Analysis Complete (SAC) Deliverable.

Author's Name and Functional Area:

PPD Principal Statistician (Clinical Statistics)	18-OCT-2017
PPD Statistician (Clinical Statistics)	18-OCT-2017
PPD Director, (CPMS)	18-OCT-2017

Approved by:

PPD TA Director (Clinical Statistics)	18-OCT-2017

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1. REPORTING & ANALYSIS PLAN SYNOPSIS

Overview	Key Elements of the RAP
Purpose	• This RAP details all planned analyses and outputs required for the final Clinical Study Report (CSR) of Study 201881.
Protocol	• This RAP is based on the protocol amendment 02 (Dated: 19-APR-2016) for Study 201881 [GlaxoSmithKline Document Number: **Error! Reference source not found.**].
Primary Objective	• To assess the effect of GSK2798745 on pulmonary gas transfer
Primary Endpoint	• Change in the diffusing capacity for carbon monoxide (DLco)
Study Design	• This is a randomized, double-blind, sponsor-unblinded, placebo-controlled, 2X2 crossover study in adults with heart failure. • 12 subjects are planned to complete both treatment periods. Additional subjects up to 24 in total maybe needed based on interim decision
Planned Analyses	• Interim analyses are detailed within Section 4.1 where applicable. • All decisions regarding final analysis, as defined in this RAP document, will be made prior to Database Freeze (unblinding) of the study data.
Primary Analysis Population	• The 'All Subjects' Population is defined as all randomized subjects who receive at least one dose of study medication. • The 'Analysis Population' is defined as subjects in the 'All Subjects' population having baseline and post-baseline assessments of the endpoint of interest for both periods. • The 'Per Protocol' Population will consist of any 'Analysis Population' subjects who are compliant with protocol-specific criteria. Subjects with specified protocol deviations will be excluded. • The 'Pharmacokinetic (PK)' Population is defined as subjects for whom a pharmacokinetic sample was obtained and analysed.
Hypothesis	• An estimation approach will be used for the comparison between GSK2798745 treatment and placebo for the change from baseline in DLco at Day 4 and Day 7. Point estimates and associated 95% confidence intervals for the differences in means will be constructed to provide a plausible range of values for the true comparisons of interest.
Primary Analyses	• Profiles for DLco will be summarized and presented graphically by treatment group and visits as appropriate for the data. The change from baseline in DLco at Day 4, Day 6 and Day 7 will be calculated and summarized in tabular format and/or graphically by treatment. For the change from baseline in DLco, a statistical analysis will be performed using a mixed effect model with repeated measures with a fixed effect term for treatment, period and day, with a random effect for subject, and baseline as a covariate, if data permit. Point estimates and associated 95% confidence intervals will be constructed for the differences between the active treatment and placebo.

2. RAP AMENDMENTS

18- Oct-2017: Given the decision to not continue the TRPV4 HF work on this asset, the exploratory Bayesian analysis was removed. Addition of some FDAAA required tables, listing, and figures.

3. SUMMARY OF KEY PROTOCOL INFORMATION

3.1. Changes to the Protocol Defined Statistical Analysis Plan

There were no changes or deviations to the originally planned statistical analysis specified in the protocol amendment 02 (Dated: 19-APR-2016).

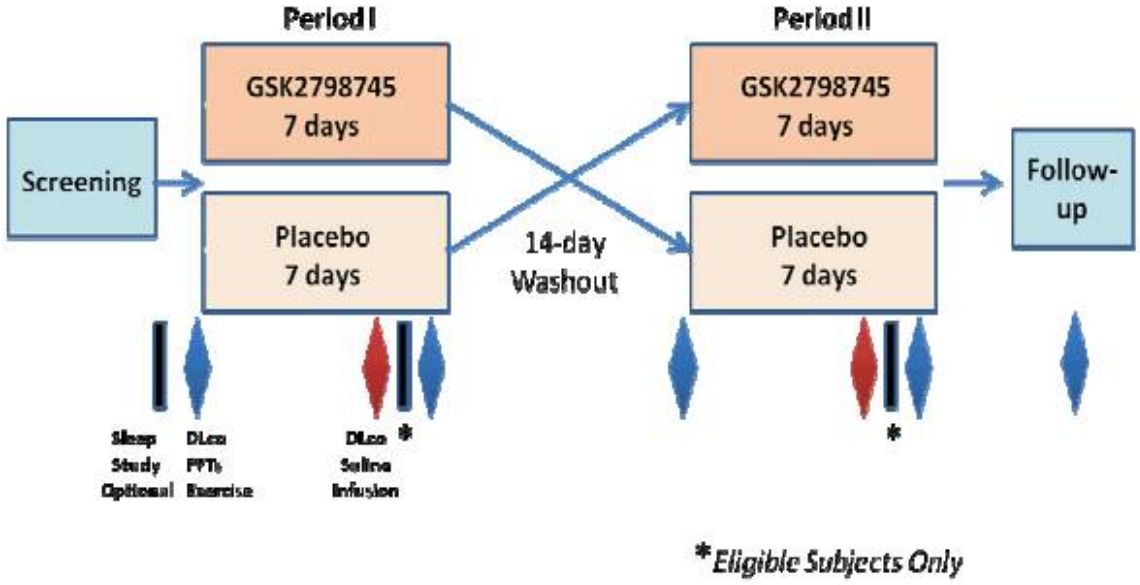
3.2. Study Objective(s) and Endpoint(s)

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
• To assess the effect of GSK2798745 on pulmonary gas transfer	• Change in the diffusing capacity for carbon monoxide (DLco)
Secondary Objectives	**Secondary Endpoints**
• To assess the effect of GSK2798745 on alveolar-capillary conductance (DM)	• Change in the diffusing capacity for nitric oxide (DLno), membrane conductance (DM), and capillary blood volume (Vc)
• To assess the effect of GSK2798745 on pulmonary gas transfer following exercise and following an intravenous saline infusion	• Change in diffusing capacity for carbon monoxide (DLco)
• To evaluate the effect of GSK2798745 on ventilatory efficiency	• Change in the VE/VCO2 slope determined during a standardized 3-minute step test
• To evaluate the effect of GSK2798745 on pulmonary function	• Changes in spirometry measures including forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1) as well as forced expiratory flows, FEF25-75 FEF50, and FEF75 • Change in functional residual capacity (FRC) and end-expiratory lung volume (EELV) measured by body plethysmograph
• To assess the effect of GSK2798745 on dyspnea	• Change in dyspnea score
• To assess the effect of GSK2798745 on respiratory rate	• Change in respiratory rate continuously measured by body sensor (Preventice Body Guardian)
• To evaluate the safety and tolerability of repeat administration of GSK2798745	• Clinical monitoring of vital signs, ECGs, and clinical laboratory safety data, including LFTs and troponin as well as reporting of adverse events (AEs)
• To assess the effect of GSK2798745 on quality of life	• Change in SF-36 acute score
• To characterize the pharmacokinetic profile of GSK2798745 in subjects with heart failure	• Area under the concentration time curve (AUC), maximum drug concentration (Cmax), time to maximum observed plasma concentration (tmax), and elimination halflife (T½)

Objectives	Endpoints
Exploratory Objectives	**Exploratory Endpoints**
• To determine the effect of GSK2798745 on oxygen saturation	• Change in minimum O2 saturation measured during polysomnography
• To assess effect of GSK2798745 on sleep disordered breathing patterns	• Change in apnea-hypopnea index (AHI) determined by polysomnography • Change in the central, obstructive and mixed apnea indexes as determined by polysomnography • Change in respiratory temporal dynamics during in-house sleep apnea evaluation
• To determine whether GSK2798745 affects sleep-disordered breathing leading to an improvement in sympathoadrenal activity	• Change in plasma and urinary catecholamine concentrations in subjects with sleep-disordered breathing
• To determine whether GSK2798745 affects electrocardiographic parameters	• Changes in time and frequency domain analyses of ECG: HR variability to define sympathetic activity
• To explore the impact of GSK2798745 on the exposure of HMG-CoA reductase inhibitors	• AUC of HMG-CoA reductase inhibitors and their key metabolites

3.3. Study Design

Overview of Study Design and Key Features



Design Features	• This is a randomized, double-blind, sponsor-unblinded, placebo-controlled, 2 X 2 crossover study in adults with heart failure. The

Overview of Study Design and Key Features	
	study will be conducted at multiple centers. • Subjects have an at least 3 month history of HF, be a NYHA Class II-IV,a NT-proBNP of greater than 400 pg/ml within the last 6 months and a % predicted DLco of < 80% at screening.
Dosing	• Subjects are dosed once daily for 7 days. Then there is a wash out period of at least 14 days, followed by another 7 days of once daily dosing.
Treatment Assignment	• Eligible subjects will be randomized to one of two treatment sequences. • A sufficient number of subjects with heart failure will be enrolled so that 12 subjects complete the two study periods and critical assessments. • Subjects will receive either GSK2798745 or placebo once daily for a period of 7 days. • After at least a 14-day washout period (preferably not greater than 30 days from last dose in Period I), subjects will participate in a second, identical 7-day study period and receive the alternate study medication.
Interim Analysis	• After approximately 5-6 subjects complete both study periods, a sponsor unblinded interim analysis will be performed. • After approximately 9 subjects complete both study periods, a sponsor unblinded interim analysis will be performed. • After 12 subjects complete both study periods, prior to SAC, an interim analysis will be performed to determine if additional subjects will be enrolled in the study (up to 24 subjects). Full details are in Section 3.1

3.4. Statistical Hypotheses

An estimation approach will be used for the comparison between GSK2798745 treatment and placebo for the change from baseline in DLCo at day 4 and day 7. Point estimates and associated 95% confidence intervals for the differences in means will be constructed to provide a plausible range of values for the true comparisons of interest.

4. PLANNED ANALYSES

4.1. Interim Analyses

- There will be ongoing data reviews by the study team of the un-blinded safety and pharmacokinetics data throughout the trial progression.

- After approximately 6 Subjects complete both study periods, a sponsor un-blinded interim analysis will be performed on DLco and other variables of potential clinical relevance. The programming code for this interim analysis will be provided by the study statistician.

- After approximately 9 subject complete both study periods, a sponsor un-blinded interim analysis will be performed.
- After 12 subjects complete both study periods, prior to DBF, a sponsor un-blinded interim analysis will be performed on DLco.

A Bayesian predictive probability of change in DLco with 18 patients will be calculated, and the intra-subject variability will be estimated. These analyses will inform a decision to enrol up to 12 additional subjects.
Given the decision to not continue the TRPV4 HF work on this asset, the Bayesian prediction was performed on 10 subjects and a decision was made to only enrol one more patient. Therefore, an interim analysis will not be performed on 12 subjects.

4.2. Final Analyses

The final planned analyses will be performed after the completion of the following sequential steps:

1. All subjects have completed the study as defined in the protocol.
2. All required database cleaning activities have completed the final database release and database freeze has been declared by Data Management.
3. All criteria for unblinding the randomisation codes have been met.
4. Randomisation codes have been distributed accordingly to RandAll NG procedures.

5. ANALYSIS POPULATIONS

Population	Definition / Criteria	Analyses Evaluated
All Subjects	• The 'All Subjects' Population is defined as all randomized subjects who receive at least one dose of study medication.	• Study Population • Safety/tolerability •
Enrolled	All participants who sign informed consent and for whom a record exists on the study database. This population will be used for the tables/listings of reasons for withdrawal before randomization and listings of AEs and SAEs for non-randomized participants.	• Subject Disposition • Reasons for withdrawal before randomization. • Inclusion, exclusion, and randomization criteria deviations
Analysis Population	• Subjects in the 'All Subjects' population having baseline and post-baseline assessments of the endpoint of interest for both periods	• Efficacy • PD/Biomarker
Screening Population	• The "Screening Population" is defined as all subjects who were screened as potential patients for the trial	• Screen Failure
Per Protocol	• Any 'Analysis Population' subjects who are compliant with protocol-specific criteria. Subjects with specified protocol deviations will be excluded.	• Efficacy
PK Population	• This population will include all subjects in the Safety Population for whom a pharmacokinetic blood sample was obtained and assayed.	• Concentration data summaries,

Population	Definition / Criteria	Analyses Evaluated
		listings, and graphs (including concentration-time profiles as appropriate)
PK Parameter Population	• This population will include all subjects in the PK Concentration Population for whom valid and evaluable pharmacokinetic parameters were derived.	• Listings, summary and analyses of PK parameters

NOTE :

- Please refer to Section 11.13 Appendix 11: List of Data Displays which details the population to be used for each display being generated.

5.1. Protocol Deviations

- Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management or patient assessment) will be summarised and listed.
- Important deviations which result in exclusion from the analysis population will also be summarised and listed. (Please refer to Appendix 1: Protocol Deviation Definitions for Per Protocol Population).
- Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan.
    - Data will be reviewed prior to unblinding and freezing the database to ensure all important deviations and deviations which may lead to exclusion from the analysis are captured and categorised on the protocol deviations dataset.
    - This dataset will be the basis for the summaries and listings of protocol deviations.

6. GENERAL CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

- There are no planned examinations of covariates. The only subgroups analysis planned is by site.
- There are no planned adjustments for multiple comparisons or multiplicity.

Table 1 provides an overview of appendices within the RAP for outlining general considerations for data analyses and data handling conventions.

Table 1 Overview of Appendices

Section	Component
11.1	Appendix 1: Protocol Deviation Definitions for Per Protocol Population
11.2	Appendix 2: Time and Events

Section	Component
11.3	Appendix 3: Treatment States and Phases
11.4	Appendix 4: Data Display Standards & Handling Conventions
11.5	Appendix 5: Derived and Transformed Data
11.6	Appendix 6: Premature Withdrawals & Handling of Missing Data
11.7	Appendix 7: Values of Potential Clinical Importance
11.8	Appendix 8: Laboratory A&R (QUEST: LAB) Dataset Details
11.9	Appendix 9: Biomarker A&R Dataset Details

7. STUDY POPULATION ANALYSES

7.1. Planned Analyses Overview

The study population analyses will be based on the "All Subjects" population, unless otherwise specified.

Table 2 provides an overview of the planned study population analyses with full details of data displays being presented in Appendix 11: List of Data Displays.

Table 2 Overview of Planned Study Population Analyses

Display Type	Data Display's Generated		
	Figure	Table	Listing
Randomisation			
Randomisation			Y
Subject Disposition			
Subject Disposition		Y	
Reasons for Screening Failures			Y
Reasons for Withdrawals		Y	Y
Important Protocol Deviations		Y	Y
Deviations Leading to Exclusions from PP Population		Y	Y
Inclusion and Exclusion Criteria Deviations			Y
Demography			
Demographics Characteristics		Y	Y
Race & Racial Combinations		Y	Y
Study Populations		Y	
Medical Condition & Concomitant Medications			
Medical Conditions (Current/Past)		Y	Y
Concomitant Medication		Y	Y

8. PRIMARY STATISTICAL ANALYSES

8.1. Efficacy Analyses

8.1.1. Overview of Planned Efficacy Analyses

The efficacy analyses will be based on the "Analysis Population", unless otherwise specified.

Table 3 provides an overview of the planned efficacy analyses with full details of data displays being presented in Appendix 11: List of Data Displays.

Table 3 Overview of Planned Efficacy Analyses

ENDPOINT	Absolute							Change from Baseline						
	Stats Analysis			Summary		Individual		Stats Analysis			Summary		Individual	
	T	F	L	T	F	F	L	T	F	L	T	F	F	L
DLco														
Diffusing capacity for carbon monoxide (DLco)	Y			Y	Y		Y	Y			Y	Y		Y

NOTES :

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

8.1.2. Statistical Model

Analysis of variance (ANOVA) with repeated measure will be performed on DLco. The primary interested outcome is to compare the treatment effects of the two treatments, where the treatment effect is defined as the change of DLco at the end of each treatment period from the corresponding baseline. Methodological differences in how DLco is collected at the two site causes variance differences by site so it will not be possible to pool DLco values across sites.

The model assumes no cross-over effect. This assumption will be tested by the following code:

```
data results;
      set results;
      contrast = 0.5*(baseline_period1 - baseline_period2);
run;

proc ttest alpha=0.10;
 class seq;
 var contrast;
run;
```

Due to the small sample size, this test has a low power to detect cross-over effects, so the assumption will also be tested graphically by looking at a plot of measures overtime. If there are any departures from the distributional assumptions, alternative models will be explored using appropriately transformed data.

9. SECONDARY STATISTICAL ANALYSES

9.1. Efficacy Analyses

9.1.1. Overview of Planned Efficacy Analyses

The secondary efficacy analyses will be based on the "Analysis Population", unless otherwise specified.

The study is being conducted at two sites. One of these two sites does not have the ability to collect DLno, DM, and Vc. Summaries of DLno, DM, and Vc will only be performed for subjects at the site which this data is collected.

When calculating summary statistics for efficacy data, pooled summaries and summaries for each site individually will be generated. Patient ID's in the PPD are from the Mayo Clinic and patients ID's in the PPD are from Hennepin.

Table 4 provides an overview of the planned efficacy analyses with further details of data displays being presented in Appendix 11: List of Data Displays.

All change from baseline table, listing, and figures, use the baseline measured just prior to the period, (i.e. period 1 measurements use the baseline measured just prior to period 1 and period 2 measures use the baseline measured just prior to period 2), unless otherwise specified.

Statistical analysis (adjusted means and/or posterior means) will be performed on secondary endpoints as shown in Table 4

Table 4 Overview of Planned Efficacy Analyses

Endpoint	Absolute						Change from Baseline					
	Stats Analysis		Summary		Individual		Stats Analysis		Summary		Individual	
	T	F	T	F	F	L	T	F	T	F	F	L
Diffusing capacity for nitric oxide (DLno)	Y		Y	Y	Y	Y			Y	Y	Y	Y
Membrane conductance (DM)	Y		Y	Y	Y	Y			Y	Y	Y	Y
Capillary blood volume (Vc)	Y		Y	Y	Y	Y			Y	Y	Y	Y
Dm/Vc	Y		Y		Y				Y			
Diffusing capacity for carbon monoxide (DLco) following exercise			Y	Y	Y	Y			Y	Y	Y	Y
Diffusing capacity for carbon monoxide (DLco) following saline infusion			Y	Y	Y	Y			Y	Y	Y*	Y
VE/VCO_2 ratio			Y	Y	Y	Y			Y	Y	Y	Y
Forced vital capacity (FVC)			Y	Y	Y	Y			Y	Y		Y
Forced expiratory volume in 1 second (FEV1)			Y	Y	Y	Y			Y	Y		Y
Forced expiratory flow, FEF25-75			Y	Y	Y	Y			Y	Y		Y
Forced expiratory flow, FEF50			Y	Y	Y	Y			Y	Y		Y
Forced expiratory flow, FEF75			Y	Y	Y	Y			Y	Y		Y
Respiratory rate (Preventice Body Guardian)			Y	Y	Y							
Troponin			Y			Y			Y			Y
SF-36 acute score			Y			Y			Y	Y		
Dyspnea score			Y			Y			Y	Y		Y

*Change from value is calculated by taking the post-saline measure to the prior saline measure

9.2. Safety Analyses

9.2.1. Overview of Planned Analyses

The safety analyses will be based on the "All Subjects" population, unless otherwise specified.

Table 5 provides an overview of the planned analyses with further details of data displays being presented in Appendix 11: List of Data Displays.

Table 5 Overview of Planned Safety Analyses

Endpoint	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L
Exposure								
Extent of Exposure	Y			Y				
Adverse Events								
All AE's [1]	Y			Y				
Common AE's	Y							
All Drug-Related AE's	Y			Y				
Serious AE's	Y			Y				
Withdrawal AE's	Y			Y				
C-SSR				Y				
SNAQ				Y				
Audiometry				Y				
Laboratory Values								
Clinical Chemistry [2] [3]	Y			Y	Y			Y
LFT's	Y			Y				
Hematology /Coagulation [2] [3]				Y	Y			Y
ECG's								
ECG Findings	Y			Y				
ECG Values					Y			
Vital Signs								
Vitals Values	Y			Y	Y			Y

Endpoint	Absolute				Change from Baseline			
	Summary		Individual		Summary		Individual	
	T	F	F	L	T	F	F	L

NOTES :

- T = Table, F = Figure, L = Listing, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (i.e. descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

1. Listings will include subject's numbers for individual AE's & AE system organ classes, preferred terms and verbatim text.
2. Chemistry & haematology summaries will include both changes from baseline & results by PCI criteria.
3. Listings of chemistry and haematology data for subjects with abnormalities of PCI will be listed.
4. Urinalysis summaries will include changes from baseline results by dipstick categories.

9.3. Pharmacokinetic Analyses

9.3.1. Overview of Planned Pharmacokinetic Analyses

The pharmacokinetic (PK) analyses will be based on the "Pharmacokinetic Parameter" population, unless otherwise specified.

Table 6 provides an overview of the planned analyses with full details being presented in Appendix 11: List of Data Displays.

Table 6 Overview of Planned Pharmacokinetic Analyses

Endpoints	Untransformed				Log-Transformed			
	Summary		Individual		Summary		Individual	
	F	T	F	L	F	T	F	L
Plasma Drug Concentrations	Y[2][3]	Y [3]	Y[1]	Y	Y[2][3]			
Derived PK Parameters		Y [3]		Y		Y [3]		

NOTES :

- T = Table, F = Figures, L = Listings, Y = Yes display generated.
- Stats Analysis = Represents TFL related to any formal statistical analyses (i.e. modelling) conducted.
- Summary = Represents TFL related to any summaries (descriptive statistics) of the observed raw data.
- Individual = Represents FL related to any displays of individual subject observed raw data.

1. Linear and Semi-Log plots will be created on the same display.
2. Mean (Linear and Semi-Log on same display) and Median (Linear and Semi-Log on same display) plots will be created.
3. Displays generated using the 'PK parameter populations.

9.3.2. Drug Concentration Measures

Refer to Appendix 4: Data Display Standards & Handling Conventions (Section 11.4.3 Reporting Process & Standards).

9.3.3. Pharmacokinetic Parameters

9.3.3.1. Deriving Pharmacokinetic Parameters

- Refer to Appendix 4: Data Display Standards & Handling Conventions (Section 11.4.3 Reporting Process & Standards).
- The pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using Win Nonlin.
- All calculations of non-compartmental parameters will be based on actual sampling times.

Table 7 Derived Pharmacokinetic Parameters

Parameter	Parameter Description
First and Second last Dose in each treatment period as data permit	
AUC(0-tau)	Area under the concentration-time curve over the dosing interval after first and last dose
Cmax	Maximum observed concentration, determined directly from the concentration-time data on Day 1 and Day 7.
tmax	Time to reach Cmax, determined directly from the concentration-time data.
If Assessable	
Lamda_z	Terminal phase rate constant
t½	Apparent terminal half-life will be calculated as: **t½ = ln2 / Lambda_z**

NOTES:

- Additional parameters may be included as required.

10. REFERENCES

GlaxoSmithKline Document Number 2014N221874_02 : A Randomized, Double-blind, Sponsor un0blinded, Placebo-controlled, Phase 2a Crossover Study to Evaluate the Effect of the TRPV4 Channel Blocker, GSK2798745, on Pulmonary Gas Transfer and Respiration in Patients with Congestive Heart Failure. Effective date: 19-APR-2016

11. APPENDICES

Section	Appendix
RAP Section 5 : Analysis Populations	
Section 11.1	Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population
RAP Section 6 : General Considerations for Data Analyses & Data Handling Conventions	
Section 11.2	Appendix 2: Time and Events
Section 11.3	Appendix 3: Treatment States & Phases
Section 11.4	Appendix 4: Data Display Standards & Handling Conventions • Study Treatment & Sub-group Display Descriptors • Baseline Definitions & Derivations • Reporting Process & Standards
Section 11.5	Appendix 5: Derived and Transformed Data • General, Study Population & Safety • Efficacy • Pharmacokinetic • Pharmacodynamic / Biomarkers
Section 11.6	Appendix 6: Premature Withdrawals & Handling of Missing Data • Handling of Missing Dates • Handling of Partial Dates
Section 11.7	Appendix 7: Values of Potential Clinical Importance • Laboratory Values • ECG's • Vital Signs
Section 11.8	Appendix 8 : Laboratory A&R Datasets
Section 11.9	Appendix 9 : Biomarker A&R Datasets
Other RAP Appendices	
Section 11.10	Appendix 10: Abbreviations & Trade Marks
Section 11.13	Appendix 11: List of Data Displays
Section 0	Appendix 12: Example Mock Shells for Data Displays

11.1. Appendix 1: Protocol Deviation Definitions for Per Protocol Population

11.1.1. Exclusions from Per Protocol Population

A subject meeting any of the following criteria will be excluded from the Per Protocol population:

Number	Exclusion Description
01	Subject takes prohibited Concomitant Medications
02	Others as defined in the PDMP

11.2. Appendix 2: Time and Events

Appendix 2: Time and Events

Procedure	Screening Period	Treatment Periods I and II (Day)										Follow-up
	Day -25 to Day -1 prior to Period I	-1	1	2	3	4	5	6	7	**8**	**9**	14 ± 4 days after last dose of study medication
Informed consent	X											
Inclusion and exclusion criteria	X											
Demography	X											
Full physical examination including height & weight	X											
Brief physical exam including weight		X				X			X			X
Medical history/Medication history	X											
Hepatitis B & C screen	X											
Echocardiogram	X											
Urine drug and alcohol breath test	X	X										
Clinical lab assessments[14]	X	X				X			X			X
NT-proBNP	X	X							X			
Serum CTX[11]		**X**							**X**			
Fecal Occult Blood Test[12]	**X**								**X**			
Pharmacokinetic sample[1]		X	X	X	X	X	X	X	X	**X**	**X**	
Digoxin sample[2]		X	X	X	X	X	X	X	X			X
Troponin	X	X		X		X			X			X
DLco/DLno[10]	X	X				X	**X**	**X**	X			X
12-lead ECG/ time & frequency domains[3]	X[9]	X[9]				X			X			X

Procedure	**Screening Period**	**Treatment Periods I and II (Day)**										**Follow-up**
	Day -25 to Day -1 prior to Period I	-1	1	2	3	4	5	6	7	**8**	**9**	14 ± 4 days after last dose of study medication
Vital signs	X	X	X	X	X	X	X	X	X			X
Weight			X	X	X		X	X				
Genetic sample		For subjects who provide consent, sample collected after start of treatment										
Study treatment[4]			X	X	X	X	X	X	X			
AE/SAE review		X	←==========→									X
Concomitant med review		X	←==========→									X
Pulmonary function tests		X				X			X			X
Step exercise test/breath-by-breath gas exchange		X							X			X
Dyspnea assessment		X					X		X			X
Orthopnea							X					
SF-36 Acute		X							X			X
Polysomnography including oximetry (Sleep Apnea Clinic)[5,13]		←==========→						←==========→				
Plasma and 8-hour urine catecholamines[6]		X						X				
Saline infusion							**X**	X				
Admission to CRU[7]			X									
Discharge from CRU[7]					X							
Meals[8]		X	X	X	X	X	X	X	X			
Appetite Assessment (SNAQ)		X				X			X			X
CSSRS (Suicidality)		X							X			X
Audiometry		X[13]							X			X
BodyGuardian Monitor (Preventice)		←==========Continuous==========→										

1. Pharmacokinetic samples to determine GSK2798745 and any metabolite(s) concentrations will be obtained at the following times on Day 1 of each treatment period: Predose, 0.5, 1, 1.5, 2, 3, 5, 8 and 12 hours and at the following times on Day 7 of each treatment period: Predose, 0.5, 1, 1.5, 2, 3, ~~and~~ 5 **and 10** hours. On Day 2 of each treatment period, samples will be collected predose and at 12 hours post dose. On Days 3 through 6, PK samples will be collected predose. **On Days 8 and 9, samples will be collected at 24 and 48 hours, respectively, after the last dose of study medication administered on Day 7.** The time points may be modified based on emerging data. Some of these timepoints may also be utilized to collect samples to determine concentrations of other medications (e.g., atorvastatin and/or simvastatin). See the SRM for detailed information.
2. Digoxin concentrations will be monitored only in those subjects who are taking digoxin
3. Time and frequency domains assessed by ECG obtained on Day -1 and Day 7
4. Subjects will remain in the CRU for a minimum of 4 hours after each administration of study medication. [Note: The first 6 subjects enrolled will remain in the CRU for 52 hours after the first dose of study medication in each period]
5. Only for subjects participating in the sub-study: At Day -1 of the first study period only, subjects will undergo an overnight sleep study. Only those subjects who are participating in the sub-study with sleep disordered breathing will undergo additional sleep studies on Day 6 of both study Periods I and II.
6. Only for subjects participating in the sub-study: Urinary norepinephrine (NE) and epinephrine (E) concentrations will be determined from 8-hour collections obtained during the overnight sleep study; urinary creatinine will also be measured to normalize the NE and E concentrations. A blood sample to determine plasma concentrations of NE and E will be obtained the morning after the sleep study between the hours of 9:00 am and 10:00 am after the subject has been supine for 20 minutes in a quiet room.
7. The first 6 subjects enrolled will remain in the CRU for two days (Day 1 and Day 2) after the first dose of study medication in each period.
8. Three meals per day will be provided by the dietary department either in the CRU or as a boxed meal(s) to take home.
9. ECGs to be performed in triplicate
10. On the days where exercise or the saline infusion is performed, DLco/DLno will be completed just prior to and after both exercise and the saline infusion.
11. **Blood sample for analysis of Serum CTX must be collected when the subject is fasting.**
12. **Fecal Occult Blood Test (FOBT) cards will be provided to subjects at the end of the screening visit and must be completed and sent back to the laboratory prior to the baseline visit according to the laboratory's standard collection procedures. Similarly, subjects will be given FOBT cards at the end of the Day 7 visit of each study period with completion instructions.**
13. **Day -1 audiometry and sleep study assessments may be completed 7 days prior to Day -1.**
14. **Clinical laboratory assessments will be collected as a fasting sample.**

11.3. Appendix 3: Treatment States and Phases

11.3.1. Treatment Phases

Assessments and events will be classified according to the time of occurrence relative to study treatment, unless otherwise specified.

Treatment Phase	Definition
Pre-Treatment 1	Date < Study Treatment Start Date for Period 1
On-Treatment 1	Study Treatment Start Date for Period 1≤ Date ≤ Study Treatment Stop Date for Period 1
Post-Treatment 1	Date > Study Treatment Stop Date for Period 1
Pre-Treatment 2	Date < Study Treatment Start Date for Period 2
On-Treatment 2	Study Treatment Start Date for Period 2 ≤ Date ≤ Study Treatment Stop Date for Period 2
Post-Treatment 2	Date > Study Treatment Stop Date for Period 2

11.3.2. Treatment States

Assessments and events will be classified according to time of occurrence relative to the start and/or stop date of the study treatment.

11.3.3. Treatment States for AE Data

Treatment State	Definition
AE = Pre-Treatment	AE Start Date < Study Treatment Start Date
AE = On-Treatment	If AE onset date is on or after the treatment start date and on or before the treatment stop date. Study Treatment Start Date ≤ AE Start Date ≤ Study Treatment Stop Date [+ 1]
AE = Post-Treatment	If AE onset date is after the treatment stop date. AE Start Date > Study Treatment Stop Date + 1
AE Onset Time Since 1st Dose (Days)	If Treatment Start Date > AE Onset Date : **= AE Onset Date - Treatment Start Date** If Treatment Start Date ≤ AE Onset Date : **= AE Onset Date – Treatment Start Date + 1** Missing otherwise
AE Duration (Days)	**AE Resolution Date – AE Onset Date + 1**
AE = Drug-related	If relationship is marked 'YES' on [Inform/CRF OR value is missing.

NOTES:

- If the study treatment stop date is missing then the AE will be considered to be On-Treatment

11.4. Appendix 4: Data Display Standards & Handling Conventions

11.4.1. Study Treatment & Sub-group Display Descriptors

Study Treatment Descriptions			
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order
A	GSK2798745 2.4 mg	GSK 2.4 mg	2
P	Placebo	Placebo	1

11.4.2. Baseline Definition & Derivations

11.4.2.1. Baseline Definitions

For all endpoints baseline value will be taken on Day -1 for each treatment period, unless otherwise specified.

11.4.2.2. Derivations and Handling of Missing Baseline Data

Definition	Reporting Details
Change from Baseline	= Post-Dose Visit Value – The corresponding Baseline
[% Change from Baseline]	= [(Post-Dose Visit Value – Baseline) / Baseline] x 100]

NOTE :

- Unless otherwise specified, the baseline definitions specified in 11.4.2.1Baseline Definitions will be used for derivations for endpoints / parameters and indicated on summaries and listings.
- Unless otherwise stated, if baseline data is missing no derivation will be performed and will be set to missing.
- The baseline definition will be footnoted on all change from baseline displays.

11.4.3. Reporting Process & Standards

Reporting Process	
Software	
• The currently supported versions of Spotfire, SAS and R software will be used to perform all data analyses, generate tables, figures, and listings.	
Reporting Area	
HARP Server	: US1SALX00259
HARP Area	: \arprod\gsk2798745\mid201881\final_01
QC Spreadsheet	: \arprod\gsk2798745\mid201881\final_01\documents
Analysis Datasets	
• Analysis datasets will be created according to Integrated Data Standards Library standards.	

Reporting Standards	
General	

• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated:
  • 4.03 to 4.23: General Principles
  • 5.01 to 5.08: Principles Related to Data Listings
  • 6.01 to 6.11: Principles Related to Summary Tables
  • 7.01 to 7.13: Principles Related to Graphics	

Formats	
• All data will be reported according to the actual treatment the subject received unless otherwise stated. • GSK IDSL Statistical Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the IDSL statistical principles but may be adjusted to a clinically interpretable number of DP's.	
Planned and Actual Time	

• Reporting for tables, figures and formal statistical analyses :
  • Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated.
  • The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate.
• Reporting for Data Listings:
  • Planned and actual time relative to study drug dosing will be shown in listings (Refer to IDSL Statistical Principle 5.05.1).
  • Unscheduled or unplanned readings will be presented within the subject's listings.
• Visits outside the protocol defined time-windows (i.e. recorded as protocol deviations) will be included in listings but omitted from figures, summaries and statistical analyses.	

Unscheduled Visits	
• Unscheduled visits will not be included in summary tables or figures, unless otherwise stated. • All unscheduled visits will be listed.	
Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %

Reporting of Pharmacokinetic Concentration	
Descriptive Summary Statistics	Refer to IDSL Statistical Principle 6.06.1 Assign zero NQ values (Refer to GUI_51487 for further details)
Reporting of Pharmacokinetic Parameters	
Descriptive Summary Statistics (Log Transformed Data)	N, n, geometric mean, 95% CI of geometric mean, standard deviation (SD) of logged data and between geometric coefficient of variation ($CV_{b/w}$ (%)): CV_b (%) = $\sqrt{}$ (exp(SD^2) - 1) * 100 (NOTE: SD is the SD of log transformed data)
Parameters Not Being Log Transformed	tmax, first point, last point and number of points used in the determination of Lambda_λz.
Parameters Not Being Summarised	tmax, first point, last point and number of points used in the determination of Lambda_λz.
Listings	Include the first point, last point and number of points used in the determination of Lambda_λz.
Graphical Displays	
• Refer to IDSL Statistical Principles 7.01 to 7.13.	

11.5. Appendix 5: Derived and Transformed Data

11.5.1. General

Multiple Measurements at One Time Point
• Mean of the measurements will be calculated and used in any derivation of summary statistics but if listed, all data will be presented. • For DLco standard practice is to attempt three measures. A pulmonologist will indicate which of the three measures are valid, and then a mean will be taken of all valid measures to be used as the measurement for that time point. If there is only one valid measure, that measure will be used.
Study Day
• Calculated as the number of days from randomisation date: [1] Ref Date = Missing → Study Day = Missing [2] Ref Date < Randomisation Date → Study Day = Ref Date – Randomisation Date [3] Ref Data ≥ Randomisation Date → Study Day = Ref Date – (Randomisation Date) + 1

11.5.2. Study Population

Demographics
Age
• GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as follows: [1] Any subject with a missing day will have this imputed as day '15'. [2] Any subject with a missing date and month will have this imputed as '30th June'. • Birth date will be presented in listings as 'YYYY'.
Body Mass Index (BMI)
• Calculated as **Weight (kg) / [Height (m)]^2**

Extent of Exposure
• Number of days of exposure to study drug will be calculated using dates from the trial medication form. The duration of exposure in days will be based on the formula: **Duration of Exposure in Days = Treatment Stop Date – (Start Date + 1)** • Subjects who were randomized but did not report a treatment start date will be categorized as having zero days of exposure. The cumulative dose will be based on the formula: **Cumulative Dose = Sum of (Number of Days x Total Daily Dose)** • If there are any treatment breaks during the study, then the exposure data will be adjusted accordingly.

11.5.3. Safety

+++ ECG Parameters +++

RR Interval

- IF RR interval (msec) is not provided directly, then RR can be derived as :
  - If QTcB is machine read & QTcF is not provided, then :

$$RR = \left[\left(\frac{QT}{QTcB}\right)^2\right] * 1000$$

  - If QTcF is machine read and QTcB is not provided, then:

$$RR = \left[\left(\frac{QT}{QTcB}\right)^3\right] * 1000$$

- If ECGs are manually read, the RR value preceding the measurement QT interval should be a collected value THEN do not derive.

Corrected QT Intervals

- When not entered directly in the eCRF, corrected QT intervals by Bazett's (QTcB) and Fredericia's (QTcF) formulas will be calculated, in msec, depending on the availability of other measurements.
- IF RR interval (msec) is provided then missing QTcB and/or QTCF will be derived as :

$$QTcB = \frac{QT}{\sqrt{\frac{RR}{1000}}} \qquad QTcF = \frac{QT}{\sqrt[3]{\frac{RR}{1000}}}$$

+++ Laboratory Parameters +++

- If a laboratory value which is expected to have a numeric value for summary purposes, has a non-detectable level reported in the database, where the numeric value is missing, but typically a character value starting with '<x' or '>x' (or indicated as less than x or greater than x in the comment field) is present, the number of significant digits in the observed values will be used to determine how much to add or subtract in order to impute the corresponding numeric value.
  - Example 1: 2 Significant Digits = '< x ' becomes x - 0.01
  - Example 2: 1 Significant Digit = '> x' becomes x + 0.1
  - Example 3: 0 Significant Digits = '< x' becomes x - 1.
- If there is more than one value of a particular parameter for a subject for a visit, the scheduled value will be used in summary; all values will be listed.

11.6. Appendix 6: Premature Withdrawals & Handling of Missing Data

11.6.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion was defined as Safety who either prematurely withdrawn or completed FU visits and assessments. • Withdrawn subjects were not replaced in the study. • All available data from subjects who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.

11.6.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument: [1] These data will be indicated by the use of a "blank" in subject listing displays. [2] Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as such.
Outliers	• Any subjects excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

11.6.2.1. Handling of Missing Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in subject listing displays.

Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event:
	  • For a missing start day, the 1st of the month will be used unless this is before the start date of investigational product; in this case the study treatment start date will be used (and hence the event is considered On-treatment as per Section 11.3 Appendix 1: Treatment States and Phases.
	  • For a missing stop day, the last day of the month will be used, unless this is after the stop date of study treatment; in this case the study treatment stop date will be used.
	• Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.
	• Start or end dates which are completely missing (i.e. no year specified) will

Element	Reporting Detail
	remain missing, with no imputation applied.

11.6.2.2. Handling of Partial Dates

Element	Reporting Detail

Concomitant Medications	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention:
	  • If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month
	  • If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month.
	• The recorded partial date will be displayed in listings.

Adverse Events	• Any partial dates for adverse events will be raised to data management. If the full date cannot be ascertained, the following assumptions will be made:
	  • If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month.
	  • However, if these results in a date prior to Week 1 Day 1 and the event could possibly have occurred during treatment from the partial information, then the Week 1 Day 1 date will be assumed to be the start date.
	  • The AE will then be considered to start on-treatment (worst case).
	  • If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month.
	• The recorded partial date will be displayed in listings.

11.7. Appendix 7: Values of Potential Clinical Importance

11.7.1. Laboratory Values

Haematology				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Hematocrit	Ratio of 1	Male		0.54
		Female		0.54
		Δ from BL	↓0.075	
Hemoglobin	g/L	Male		180
		Female		180
		Δ from BL	↓25	
Lymphocytes	$x10^9$/ L		0.8	
Neutrophil Count	$x10^9$/ L		1.5	
Platelet Count	$x10^9$/ L		100	550
While Blood Cell Count (WBC)	$x10^9$/ L		3	20

Clinical Chemistry				
Laboratory Parameter	**Units**	**Category**	**Clinical Concern Range**	
			Low Flag (< x)	**High Flag (>x)**
Albumin	mmol/L		30	
Calcium	mmol/L		2	2.75
Creatinine	mmol/L	Δ from BL		↑ 44.2
Glucose	mmol/L		3	9
Magnesium	mmol/L		0.5	1.23
Phosphorus	mmol/L		0.8	1.6
Potassium	mmol/L		3	5.5
Sodium	mmol/L		130	150
Total CO2	mmol/L		18	32

Liver Function			
Test Analyte	**Units**	**Category**	**Clinical Concern Range**
ALT/SGPT	U/L	High	≥ 2x ULN
AST/SGOT	U/L	High	≥ 2x ULN
AlkPhos	U/L	High	≥ 2x ULN
T Bilirubin	µmol/L	High	≥ 1.5xULN
T. Bilirubin + ALT	µmol/L U/L	High	1.5xULN T. Bilirubin + ≥ 2x ULN ALT

11.7.2. ECG

ECG Parameter	Units	Clinical Concern Range	
		Lower	**Upper**
Absolute			
Absolute QTc Interval	msec	> 450	
Absolute PR Interval	msec	< 110	> 220
Absolute QRS Interval	msec	< 75	> 110
Change from Baseline			
Increase from Baseline QTc	msec	> 60	

11.7.3. Vital Signs

Vital Sign Parameter (Absolute)	Units	Clinical Concern Range	
		Lower	**Upper**
Systolic Blood Pressure	mmHg	< 85	> 160
Diastolic Blood Pressure	mmHg	< 45	> 100
Heart Rate	bpm	< 40	> 110

11.8. Appendix 8: Laboratory A&R Dataset Details

Panel [1]	Parameter	Unit	Normal Range		Anticipated Direction of Change with Treatment
			Low	High	
Fasted Chemistry	Serum Albumin	G/L	32	50	Safety laboratory parameters not expected to change
	Alkaline Phosphatase	IU/L	20	125	
	ALT	IU/L	0	48	
	AST	IU/L	0	42	
	BUN (UREA)	MMOL/L	2.5	10.5	
	Calcium	MMOL/L	2.12	2.56	
	Chloride	MMOL/L	95	108	
	Creatinine	UMOL/L	67.2	129.1	
	Creatinine Clearance	N/A	N/A	N/A	
	Direct Bilirubin	UMOL/L	0	6	
	GGT	IU/L	0	75	
	Glucose, fasting	MMOL/L	3.9	5.5	
	Potassium	MMOL/L	3.5	5.3	
	Sodium	MMOL/L	135	146	
	Total Bilirubin	UMOL/L	0	22	
	Total Protein	G/L	60	85	
	Uric Acid	UMOL/L	240	510	
Lipid	HDL	MMOL/L	0.9	99.99	Safety laboratory parameters not expected to change
	LDL (Calculated)	MMOL/L	0	3.35	
	Total Cholesterol	MMOL/L	0	5.15	
	Triglycerides	MMOL/L	0	2.24	
Urinalysis	Blood	Dipstick	N/AP	N/AP	Not able to specify specifically.
	Bacteria	Microy	N/AP	N/AP	
	Hyaline Casts (N/A)	N/A	N/AP	N/AP	
	Nitrite	Dipstick	N/AP	N/AP	
	Protein	Dipstick	N/AP	N/AP	
	RBC	Microscopy	N/AP	N/AP	
	Specific Gravity	N/A	N/AP	N/AP	
	WBC	GI/L	3.8	10.8	
Haematology	Basophils	GI/L	0	0.2	Safety laboratory parameters not expected to change
	Eosinophils	GI/L	0.05	0.55	
	Hemoglobin	G/L	118	168	
	Hematocrit	1	0.41	0.5	
	Lymphocytes	GI/L	0.85	4.1	
	MCV	FL	82	103	
	MCH	PG	27	33	
	MCHC	G/L	320	360	
	Monocytes	GI/L	0.2	1.1	
	Neutrophils	GI/L	130	400	
	Platelet Count	GI/L	130	400	
	RBC Count	TI/L	3.7	5.5	
	WBC Count (Absolute)	GI/L	3.8	10.8	

NOTE :

- N/A = Not available on DM dataset during RAP completion.
- N/AP = No ranges are normally provided for parameters.

11.9. Appendix 9: Biomarker A&R Dataset Details

Parameters (BICATCD Code)	Sample	Unit	LLQ	ULQ
Dataset : Biomark (QUEST)				
Adiponectin **(ADPN)**	Serum	MG/L	2	61
Albumin **(ALB)**	Urine	MG/L	3	9999
Creatinine **(CREAT)**	Urine	MMOL/L	0.2	999999.9
C-peptide (MMT) **(CPEP)**	Serum	NMOL/L	0.1	9999.99
C-Reactive Protein, Highly Sensitive **(CRPHS)**	Serum	MG/L	0.3.	800
CXCL10 / IP-10 **(IP10)**	Serum	NG/L	54.5	56000
Fructosamine **(FRUC)**	Serum	UMOL/L	20	1000
Glucose (MMT) **(GLUC)**	Plasma	MMOL/L	1.1	277.5
Glucagon (MMT) **(No data for IA)**	Plasma	N/A	N/A	N/A
Glycohemoglobin A1c **(HbA1c)**	Whole Blood	MMOL/L	3	18.9
Highly Sensitive Interleukin-6 **(IL-6)**	Serum	NG/L	0.156	640
Insulin (MMT) **(INS)**	Serum	PMOL/L	12	99999
Intercellular Adhesion Molecule, Soluble **(sICAM)**	Serum	NG/L	312	3200000
Matrix Metalloproteinase-9 **(MMP-9)**	Serum	NG/L	975	40000000
Non-Esterified Fatty Acids **(NEFA)**	Serum	MMOL/L	0.03	9
Monocyte Chemotactic protein-1 **(MCP1)**	Urine	NG/L	3.12	800
Plasminogen Activator Inhibitor-1 **(PAI-1)**	Plasma	NG/L	153	20000000
Resistin **(RESIST)**	Serum	MCG/L	0.8	800
Dataset : IMGEN (GSK Clinical Immunology)				
Interleukin 18 – Complex **(IL18C)**	Serum	pg/mL	19.5	N/AP
Interleukin 18 – Free **(IL8F)**	Serum	pg/mL	4	N/AP

NOTE : .

- Urine biomarkers will be reported as ratios to creatinine i.e. Albumin/creatinine (ACR) and MCP-1/creatinine.
- N/A - Not available on DM dataset during RAP completion.
- N/AP = No ranges are normally provided for parameters.

11.10. Appendix 10 – Abbreviations & Trade Marks

11.10.1. Abbreviations

Abbreviation	Description
AE	Adverse Event
GSK	GlaxoSmithKline
AE	Adverse Event
ALT	Alanine aminotransferase (SGPT)
AST	Aspartate aminotransferase (SGOT)
AUC	Area under concentration-time curve
AUC(0-∞)	Area under the concentration-time curve from time zero (pre-dose) extrapolated to infinite time
BMI	Body mass index
BPM	Beat Per Minute
BQL	Below the quantification limit
CL	Systemic clearance of parent drug
Cmax	Maximum observed concentration
CI	Confidence Interval
CPMS	Clinical Pharmacology Modelling & Simulation
CPSR	Clinical Pharmacology Study Report
CS	Clinical Statistics
CPSSO	Clinical Pharmacology Science and Study Operations
CV	Coefficient of variance
DM	Data Management
FPG	Fasting Plasma Glucose
GSK	GlaxoSmithKline
HOMA-%B	Homeostasis Model Assessment (β-cell function)
HOMA-%S	Homeostasis Model Assessment (Insulin sensitivity)
HR	Heart rate
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
IDSL	Integrated Data Standards Library
IL	Interleukin
Kg	Kilogram
λz	Terminal phase rate constant
LLQ	Lower limit of quantification
MMRM	Mixed models repeated measures
MMT	Mixed Meal Test
msec	Milliseconds
NQ	Non-quantifiable concentration measured as below LLQ
OB	Obese
PK	Pharmacokinetic
QC	Quality control
QTc	QT duration corrected

Abbreviation	Description
QTcB	QT duration corrected for heart rate by Bazett's formula
QTcF	QT duration corrected for heart rate by Fridericia's formula
RAP	Reporting and Analysis Plan
RNA	Ribonucleic acid
SAS	Statistical Analysis Software
SI	System Independent
STAT	Signal tranducer and activator of transcription
SD	Standard deviation
SOP	Standard Operating Procedure
T	Infusion duration
t OR tlast	Time of last observed quantifiable concentration
t½	Terminal phase half-life
τ	Dosing interval
tlag	Lag time before observation of drug concentrations in sampled matrix
tmax	Time of occurrence of Cmax
TNF-α	Tumour necrosis factor – alpha
ULQ	Upper limit of quantification
ULN	Upper limit of normal
UK	United Kingdom
VAS	Visual analogue score
Vss	Volume of distribution at steady state
WBA	Whole blood assay
WBC	White blood cells

11.10.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

Trademarks not owned by the GlaxoSmithKline Group of Companies
NONMEM
SAS
WinNonlin

11.13. Appendix 11: List of Data Displays

11.13.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.01 to 1.11	N/A
Efficacy	2.01 to 2.32	2.01 to 2.72
Safety	3.01 to 3.21	N/A
Pharmacokinetic	4.01 to 4.05	4.01 to 4.02
Section	**Listings**	
ICH Listings	1 to 23	
Other Listings	24 to 41	

The numbering of the TLF's below is a suggestion and can be altered by the programmers if needed. If the programmers need to change the numbering, please add new numbers to the end of the sequence.

11.13.2. Deliverable [Priority]

Delivery Priority [1]	Description
IA	"Interim" Analysis Part A (after completion of approximately 6 patients)
SAC 2	Part A Final Statistical Analysis Complete

11.13.3. Mock Example Numbering

Non IDSL specifications will be referred as detailed below and where appropriate an example mock-up table is provided in Appendix 12:

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Efficacy	EFF_Fn	EFF_Tn	EFF_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln

NOTE:

- Non-Standard displays are indicated in the IDSL / TST ID / Example Shell' or Programming Notes' column as '[Non-Standard] + Reference.'

11.13.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.01	All Subjects	ES1	Summary of Subject Disposition		SAC [2]
1.02	Screening Population	ES6	Summary of Reasons for Screening Failure		SAC [2]
1.03	All Subjects	ES5	Summary of Reasons for Withdrawals		SAC [2]
1.04	All Subjects	DV1a	Summary of Important Protocol Deviations		SAC [2]
1.05	All Subjects	SA2	Summary of Deviations Leading to Exclusion from Per Protocol Population		SAC [2]
Demographics					
1.06	All Subjects	DM1	Summary of Demographic Characteristics	Make twice, pooled and by site	IA, SAC [2]
1.07	All Subjects	DM5	Summary of Race and Racial Combinations	Make twice, pooled and by site	SAC [2]
1.08	Enrolled	DM11	Summary of Age Ranges		SAC [2]
1.12	Enrolled	NS1	Summary of Number of Subjected by Country and Site ID		SAC[2]
1.09	All Subjects	SA1	Summary of Study Populations		SAC [2]
Medical Condition & Con Meds					
1.10	All Subjects	MH1	Summary of [Current/Past] Medical Conditions	Make twice, pooled and by site	SAC [2]

Study Population Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.11	All Subjects	CM1	Summary of Most Frequently used Concomitant Medications by Generic Term	Footnote: Most Frequently means the overall concomitant medication used is >= 10%	SAC [2]

11.13.5. Efficacy Tables

Efficacy Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
DLco					
2.01	Analysis	Non-Standard EFF_T1	Summary Statistics of DLco	DLco has measures on Baseline, Day 4, 5, and 7 for each treatment period and follow-up. Create this table twice, one table with only Mayo patients and another table with only Hennepin patients	IA, SAC [2]
2.02	Analysis	Non-Standard EFF_T2	Summary Statistics of DLco Change from Baseline	Create this table twice, one table with only Mayo patients and another table with only Hennepin patients	IA, SAC [2]
2.03	Analysis	Non-Standard EFF_T12	Summary Statistics of DLco Change from Intervention	Create this table twice, one table with only Mayo patients and another table with only Hennepin patients. This should be the Mean and SD of the Post-Pre difference.	IA, SAC [2]
2.04	Analysis	Non-Standard EFF_T6	Summary of Statistical Analysis Results of DLco	Models should be run with only Mayo patients. Hennepin patients are excluded because of methodological differences.	IA, SAC [2]
Alveolar-capillary Conductance (D_M)					
2.05	Analysis	Non-Standard EFF_T3	Summary Statistics of Gas Transfer Tests	DLno, Dm, Vc, and Dm/Vc have measures on Baseline, Day 4, 5, and 7 for each treatment period and follow-up	SAC [2]
2.06	Analysis	Non-Standard EFF_T2	Summary Statistics of Gas Transfer Tests Change from Baseline	DLno, Dm, Vc, and Dm/Vc have measures on Baseline, Day 4, 5, and 7 for each treatment period and follow-up. Baseline is day -1 for exercise and chronic values, but should be calculated as post minus pre for Saline.	SAC [2]

Efficacy Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.07	Analysis	Non-Standard EFF_T12	Summary Statistics of Gas Transfer Tests Change from Intervention	DLno, Dm, Vc, and Dm/Vc have measures on Baseline and Day 5 and 7 for each treatment period. This should be the Mean and SD of the Post-Pre difference.	IA, SAC [2]
Ventilatory Efficiency					
2.08	Analysis	Non-Standard EFF_T7	Summary Statistics of VE/VCO_2 Ratio	VE/VCO_2 ratio has measures on Baseline and Day 7 before and after 3-minutes step test. Create this table twice, one table with all patients and another table with Hennepin patients excluded from the statistics.	SAC [2]
2.09	Analysis	Non-Standard EFF_T8	Summary Statistics of VE/VCO_2 Ratio Change from Baseline	VE/VCO_2 ratio has measures on Baseline and Day 7 before and after 3-minutes step test. Create this table twice, one table with all patients and another table with Hennepin patients excluded from the statistics.	SAC [2]
Pulmonary Function					
2.10	Analysis	Non-Standard EFF_T4	Summary Statistics of Pulmonary Function Tests	Pulmonary function (FVC, FEV_1, FEF_{25-75}, FEF_{50}, FEF_{75}) has measures on Baseline, Day 4 and Day 7 for each treatment period. Pool all patients.	SAC [2]
2.11	Analysis	Non-Standard EFF_T5	Summary Statistics of Pulmonary Function Tests Change from Baseline	Pulmonary function (FVC, FEV_1, FEF_{25-75}, FEF_{50}, FEF_{75}) has measures on Baseline, Day 4, and Day 7 for each treatment period. Pool all patients.	SAC [2]
2.12	Analysis	Non-Standard EFF_T4	Summary Statistics of Pulmonary Function Tests by Site	Pulmonary function (FVC, FEV_1, FEF_{25-75}, FEF_{50}, FEF_{75}) has measures on Baseline, Day 4 and Day 7 for each treatment period. Create this table twice, one table with Mayo patients and another table with Hennepin patients.	SAC [2]

Efficacy Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.13	Analysis	Non-Standard EFF_T5	Summary Statistics of Pulmonary Function Tests Change from Baseline by Site	Pulmonary function (FVC, FEV_1, FEF_{25-75}, FEF_{50}, FEF_{75}) has measures on Baseline, Day 4, and Day 7 for each treatment period. Create this table twice, one table with Mayo patients and another table with Hennepin patients.	SAC [2]
Dyspnea					
2.14	Analysis	Non-Standard EFF_T9	Summary Statistics Dyspnea Score	Dyspnea Score has measures at Baseline pre and post exercise, Day 5 pre-saline sitting and supine, Day 7 pre and post exercise for each treatment period and at follow-up pre and post exercise	SAC [2]
2.15	Analysis	Non-Standard EFF_T5	Summary Statistics Change from Baseline Dyspnea Score	Dyspnea Score change from baseline has measures at Baseline post exercise, Day 5 pre-saline sitting and supine, Day 7 pre and post exercise for each treatment period and at follow-up pre and post exercise	SAC [2]
SF-36 score					
2.16	Analysis	SF2	Summary Statistics SF-36 Score	SF-36 Score has measures at Baseline and Day 7 for each treatment period and follow-up. Add additional rows for questions 3a to 3j to be looked at along with the domain scores	SAC [2]
2.17	Analysis	SF4	Summary Statistics of Change from Baseline SF-36 Score	SF-36 Score change from Baseline has a measure at Day 7 for each treatment period and follow-up. Add additional rows for questions 3a to 3j to be looked at along with the domain scores	SAC [2]

Efficacy Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Troponin					
2.18	All Subject	LB1	Summary Statistics of Troponin		SAC [2]
2.19	All Subject	LB3	Summary Statistics of Troponin Change from Baseline		SAC [2]
Respiratory Rate					
2.20	All Subject	EFF_T11	Summary Statistics of Respiratory Rate		SAC [2]

11.13.6. Efficacy Figures

Efficacy Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Gas transfer measure					
2.01	Analysis	Non-Standard EFF_F1	Spaghetti Plot of DLco	DLco has measures at Baseline, Day 4, Day 5, and Day 7 for each period as well as screening and follow-up. Includes pre/post exercise and saline challenge.	SAC [2]
2.02	Analysis	Non-Standard EFF_F22	Spaghetti Plot of DLco by Site	DLco has measures at Baseline, Day 4, Day 5, and Day 7 for each period. Excludes post exercise and post saline challenge.	SAC [2]
2.03	Analysis	Non-Standard EFF_F2	Mean (95% CI) Plot of DLco	Create this graph twice, one graph with Mayo patients and another graph with Hennepin patients	SAC [2]
2.04	Analysis	Non-Standard EFF_F3	Mean (95% CI) Plot of Chronic DLco	Create this graph twice, one graph with Mayo patients and another graph with Hennepin patients	SAC [2]
2.05	Analysis	Non-Standard EFF_F4	Plot of DLco by Individual and Treatment	DLco has measures at Baseline, Day 4, Day 5, and Day 7 for each treatment as well as screening and follow-up. Includes pre/post exercise and saline challenge. Horizontal line represents baseline values	SAC [2]
2.06	Analysis	Non-Standard EFF_F5	Plot of Change from Baseline for Chronic DLco by Individual and Treatment	Only pre-challenge DLco values	SAC [2]

Efficacy Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.07	Analysis	Non-Standard EFF_F6	Mean (95% CI) Plot of DLco Change from Baseline	DLco has means at Baseline, Day 4, Day 5, and Day 7 for each treatment and includes pre/post exercise and saline challenge. Baseline is minus day -1 for exercise and no challenge, but should be calculated as post minus pre for Saline. Create this graph twice, one graph with Mayo patients and another graph with Hennepin patients	SAC [2]
2.08	Analysis	Non-Standard EFF_F7	Mean (95% CI) Plot of Exercise DLco	DLco has measures at Baseline and Day 7 for each treatment and a follow-up. Graph should include pre/post exercise values. Create this graph twice, one graph with Mayo patients and another graph with Hennepin patients	SAC [2]
2.09	Analysis	Non-Standard EFF_F8	Mean (95% CI) Plot of Change from Exercise for DLco	DLco has means at Baseline and Day 7 for each treatment and a follow-up. The bars represent the mean change from just prior to exercise to post exercise. mean(Post-Pre) Create this graph twice, one graph with Mayo patients and another graph with Hennepin patients	SAC [2]
2.10	Analysis	Non-Standard EFF_F9	Mean (95% CI) Plot of Percent Change from Exercise for DLco	DLco has means at Baseline and Day 7 for each treatment and a follow-up. The bars represent the mean percent change from just prior to exercise to post exercise. Create this graph twice, one graph with Mayo patients and another graph with Hennepin patients	SAC [2]

Efficacy Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.11	Analysis	Non-Standard EFF_F10	Mean (95% CI) Plot of Percent Change from Saline for DLco	DLco has means at Day 5 for each treatment and a follow-up. The bars represent the mean percent change from just prior to exercise to post saline infusion. Create this graph twice, one graph with Mayo patients and another graph with Hennepin patients	SAC [2]
2.12	Analysis	Non-Standard EFF_F24	Bar Plot of Saline Challenge for DLco by Subject	Bars should be able to distinguish pre- and post-saline values. On the bars for each patient should be text. The text is the difference between before and after and the percent change, as seen in the mock up Create this graph twice, one graph with Mayo patients and another graph with Hennepin patients	SAC [2]
2.13	Analysis	Non-Standard EFF_F1	Spaghetti Plot of DLno	DLno has measures at Baseline, Day 4, Day 5, and Day 7 for each period as well as screening and follow-up. Includes pre/post exercise and saline challenge.	SAC [2]
2.14	Analysis	Non-Standard EFF_F2	Mean (95% CI) Plot of DLno		SAC [2]
2.15	Analysis	Non-Standard EFF_F3	Mean (95% CI) Plot of Chronic DLno		SAC [2]
2.16	Analysis	Non-Standard EFF_F4	Plot of DLno by Individual and Treatment	DLno has measures at Baseline, Day 4, Day 5, and Day 7 for each treatment as well as screening and follow-up. Includes pre/post exercise and saline challenge. Horizontal line represents baseline values	SAC [2]
2.17	Analysis	Non-Standard EFF_F5	Plot of Change from Baseline for Chronic DLno by Individual and Treatment	Only pre-challenge DLno values	SAC [2]

Efficacy Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.18	Analysis	Non-Standard EFF_F6	Mean (95% CI) Plot of DLno Change from Baseline	DLno has means at Baseline, Day 4, Day 5, and Day 7 for each treatment and includes pre/post exercise and saline challenge. Baseline is minus day -1 for exercise and no challenge, but should be calculated as post minus pre for Saline.	SAC [2]
2.19	Analysis	Non-Standard EFF_F7	Mean (95% CI) Plot of Exercise DLno	DLno has measures at Baseline and Day 7 for each treatment and a follow-up. Graph should include pre/post exercise values.	SAC [2]
2.20	Analysis	Non-Standard EFF_F8	Mean (95% CI) Plot of Change from Exercise for DLno	DLno has means at Baseline and Day 7 for each treatment and a follow-up. The bars represent the mean change from just prior to exercise to post exercise. mean(Post-Pre)	SAC [2]
2.21	Analysis	Non-Standard EFF_F9	Mean (95% CI) Plot of Percent Change from Exercise for DLno	DLno has means at Baseline and Day 7 for each treatment and a follow-up. The bars represent the mean percent change from just prior to exercise to post exercise.	SAC [2]
2.22	Analysis	Non-Standard EFF_F10	Mean (95% CI) Plot of Percent Change from Saline for DLno	DLno has means at Day 5 for each treatment and a follow-up. The bars represent the mean percent change from just prior to exercise to post saline infusion.	SAC [2]
2.23	Analysis	Non-Standard EFF_F24	Bar Plot of Saline Challenge for DLno by Subject	Bars should be able to distinguish pre- and post-saline values. On the bars for each patient should be text. The text is the difference between before and after and the percent change, as seen in the mock up Create this graph twice, one graph with Mayo patients and another graph with Hennepin patients	SAC [2]
2.24	Analysis	Non-Standard EFF_F1	Spaghetti Plot of D_M	D_M has measures at Baseline, Day 4, Day 5, and Day 7 for each period as well as screening and follow-up. Includes pre/post exercise and saline challenge.	SAC [2]

Efficacy Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.25	Analysis	Non-Standard EFF_F2	Mean (95% CI) Plot of D_M		SAC [2]
2.26	Analysis	Non-Standard EFF_F3	Mean (95% CI) Plot of Chronic D_M		SAC [2]
2.27	Analysis	Non-Standard EFF_F4	Plot of D_M by Individual and Treatment	D_M has measures at Baseline, Day 4, Day 5, and Day 7 for each treatment as well as screening and follow-up. Includes pre/post exercise and saline challenge. Horizontal line represents baseline values	SAC [2]
2.28	Analysis	Non-Standard EFF_F5	Plot of Change from Baseline for Chronic D_M by Individual and Treatment	Only pre-challenge D_M values	SAC [2]
2.29	Analysis	Non-Standard EFF_F6	Mean (95% CI) Plot of D_M Change from Baseline	D_M has means at Baseline, Day 4, Day 5, and Day 7 for each treatment and includes pre/post exercise and saline challenge. Baseline is minus day -1 for exercise and no challenge, but should be calculated as post minus pre for Saline.	SAC [2]
2.30	Analysis	Non-Standard EFF_F7	Mean (95% CI) Plot of Exercise D_M	D_M has measures at Baseline and Day 7 for each treatment and a follow-up. Graph should include pre/post exercise values.	SAC [2]
2.31	Analysis	Non-Standard EFF_F8	Mean (95% CI) Plot of Change from Exercise for D_M	D_M has means at Baseline and Day 7 for each treatment and a follow-up. The bars represent the mean change from just prior to exercise to post exercise. mean(Post-Pre)	SAC [2]
2.32	Analysis	Non-Standard EFF_F9	Mean (95% CI) Plot of Percent Change from Exercise for D_M	D_M has means at Baseline and Day 7 for each treatment and a follow-up. The bars represent the mean percent change from just prior to exercise to post exercise.	SAC [2]

Efficacy Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.33	Analysis	Non-Standard EFF_F10	Mean (95% CI) Plot of Percent Change from Saline for D_M	D_M has means at Day 5 for each treatment and a follow-up. The bars represent the mean percent change from just prior to exercise to post saline infusion.	SAC [2]
2.34	Analysis	Non-Standard EFF_F1	Spaghetti Plot of Vc	Vc has measures at Baseline, Day 4, Day 5, and Day 7 for each period as well as screening and follow-up. Includes pre/post exercise and saline challenge.	SAC [2]
2.35	Analysis	Non-Standard EFF_F2	Mean (95% CI) Plot of Vc		SAC [2]
2.36	Analysis	Non-Standard EFF_F3	Mean (95% CI) Plot of Chronic Vc		SAC [2]
2.37	Analysis	Non-Standard EFF_F4	Plot of Vc by Individual and Treatment	Vc has measures at Baseline, Day 4, Day 5, and Day 7 for each treatment as well as screening and follow-up. Includes pre/post exercise and saline challenge. Horizontal line represents baseline values	SAC [2]
2.38	Analysis	Non-Standard EFF_F5	Plot of Change from Baseline for Chronic Vc by Individual and Treatment	Only pre-challenge Vc values	SAC [2]
2.39	Analysis	Non-Standard EFF_F6	Mean (95% CI) Plot of Vc Change from Baseline	Vc has means at Baseline, Day 4, Day 5, and Day 7 for each treatment and includes pre/post exercise and saline challenge. Baseline is minus day -1 for exercise and no challenge, but should be calculated as post minus pre for Saline.	SAC [2]
2.40	Analysis	Non-Standard EFF_F7	Mean (95% CI) Plot of Exercise Vc	Vc has measures at Baseline and Day 7 for each treatment and a follow-up. Graph should include pre/post exercise values.	SAC [2]

Efficacy Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.41	Analysis	Non-Standard EFF_F8	Mean (95% CI) Plot of Change from Exercise for Vc	Vc has means at Baseline and Day 7 for each treatment and a follow-up. The bars represent the mean change from just prior to exercise to post exercise. mean(Post-Pre)	SAC [2]
2.42	Analysis	Non-Standard EFF_F23	Forest Plot of DL End Points Change	Forest plot of Dlco, Dlno, Vc, and Dm change from baseline to day 7, change from pre and post saline for Dlco and change from pre/post exercise on day 7 for Dlco. Include the mean absolute change next to the box plot as seen in the mock-up	SAC[2]
2.43	Analysis	Non-Standard EFF_F9	Mean (95% CI) Plot of Percent Change from Exercise for Vc	Vc has means at Baseline and Day 7 for each treatment and a follow-up. The bars represent the mean percent change from just prior to exercise to post exercise.	SAC [2]
2.44	Analysis	Non-Standard EFF_F10	Mean (95% CI) Plot of Percent Change from Saline for Vc	Vc has means at Day 5 for each treatment and a follow-up. The bars represent the mean percent change from just prior to exercise to post saline infusion.	SAC [2]
Ventilatory Efficiency					
2.45-	Analysis	Non-Standard EFF_F11	Plot of VE/VCO_2	Has 5 measures at Baseline, Day 7, and Follow-Up	SAC[2]
2.46	Analysis	Non-Standard EFF_F12	Mean (95% CI) Plot of VE/VCO_2	Has means for each of the 5 measures at baseline, Day 7 and Follow-Up	SAC[2]
2.47	Analysis	Non-Standard EFF_F13	Plot of VE/VCO_2 Change from Day -1	Is the difference between day -1 and day 7 for each time point in the exercise test (e.g. at rest day 7 – at rest day -1, post 1 min day 7 - post 1 min day -1)	SAC[2]

Efficacy Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.48	Analysis	Non-Standard EFF_F14	Mean (95% CI) Change from Baseline Plot of VE/VCO_2	Mean values of the points calculated for previous plot	SAC[2]
2.49	Analysis	Non-Standard EFF_F15	Plot of VE/VCO_2 Change from Rest	Has 5 measures at baseline and Day 7 for each treatment along a with follow-up. Bars represent the difference the time measure and rest within a day and treatment. The number is the difference between the active and placebo bars.	SAC[2]
2.50	Analysis	Non-Standard EFF_F16	Mean (95% CI) Plot of VE/VCO_2 Change from Rest	Has means at Day 7	SAC[2]
Pulmonary Function					
2.51	Analysis	Non-Standard EFF_F17	Spaghetti Plot of FVC	FVC has means at Baseline, Day 4 and Day 7 for each treatment and a follow-up measure	SAC[2]
2.52	Analysis	Non-Standard EFF_F18	Mean (95% CI) Plot of FVC	FVC has means at Baseline, Day 4 and Day 7 for each treatment and a follow-up measure	SAC[2]
2.53	Analysis	Non-Standard EFF_F19	Mean (95% CI) Plot of FVC Change from Baseline	FVC has means at Day 4 and Day 7	SAC[2]
2.54	Analysis	Non-Standard EFF_F17	Spaghetti Plot of FEV_1	FEV_1 has means at Baseline, Day 4 and Day 7 for each treatment and a follow-up measure	SAC[2]
2.55	Analysis	Non-Standard EFF_F18	Mean (95% CI) Plot of FEV_1	FEV_1 has means at Baseline, Day 4 and Day 7 for each treatment and a follow-up measure	SAC[2]

Efficacy Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.56	Analysis	Non-Standard EFF_F19	Mean (95% CI) Plot of FEV_1 Change from Baseline	FEV_1 has means at Day 4 and Day 7.	SAC[2]
2.57	Analysis	Non-Standard EFF_F17	Spaghetti Plot of FEF_{25-75}	FEF_{25-75} has means at Baseline, Day 4 and Day 7 for each treatment and a follow-up measure	SAC[2]
2.58	Analysis	Non-Standard EFF_F18	Mean (95% CI) Plot of FEF_{25-75}	FEV_{25-75} has means at Baseline, Day 4 and Day 7 for each treatment and a follow-up measure	SAC[2]
2.59	Analysis	Non-Standard EFF_F19	Mean (95% CI) Plot of FEF_{25-75} Change from Baseline	FEF_{25-75} has means at Day 4 and Day 7	SAC[2]
2.60	Analysis	Non-Standard EFF_F17	Spaghetti Plot of FEF_{50}	FEF_{25-75} has means at Baseline, Day 4 and Day 7 for each treatment and a follow-up measure	SAC[2]
2.61	Analysis	Non-Standard EFF_F18	Mean (95% CI) Plot of FEF_{50}	FEF_{50} has means at Baseline, Day 4 and Day 7 for each treatment and a follow-up measure	SAC[2]
2.62	Analysis	Non-Standard EFF_F19	Mean (95% CI) Plot of FEF_{50} Change from Baseline	FEF_{50} has means at Day 4 and Day 7.	SAC[2]
2.63	Analysis	Non-Standard EFF_F17	Spaghetti Plot of FEF_{75}	FEF_{75} has means at Baseline, Day 4 and Day 7 for each treatment and a follow-up measure	SAC[2]
2.64	Analysis	Non-Standard EFF_F18	Mean (95% CI) Plot of FEF_{75}	FEF_{75} has means at Baseline, Day 4 and Day 7 for each treatment and a follow-up measure	SAC[2]

Efficacy Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.65	Analysis	Non-Standard EFF_F19	Mean (95% CI) Plot of FEF_{75} Change from Baseline	FEF_{75} has means at Day 4 and Day 7.	SAC[2]
2.66	Analysis	Non-Standard EFF_F23	Forest Plot of Pulmonary Function Test	Forest plot of FVC, FEV_1, FEF_{25-75}, FEF_{50}, FEF_{75}. Include the mean absolute change next to the box plot as seen in the mock-up	SAC[2]
Dyspnea					
2.67	Analysis	Non-Standard EFF_F17	Spaghetti Plot of Dyspnea	Dyspnea has measures at Baseline pre and post exercise, Day 5 pre-saline sitting and supine, and Day 7 pre and post exercise	SAC[2]
2.68	Analysis	Non-Standard EFF_F18	Mean (95% CI) Plot of Dyspnea	Dyspnea has means at Baseline pre and post exercise, Day 5 pre-saline sitting and supine, and Day 7 pre and post exercise.	SAC[2]
2.69	Analysis	Non-Standard EFF_F19	Mean (95% CI) Plot of Dyspnea Change from Baseline	Dyspnea has means at Baseline post exercise, Day 5 pre-saline sitting and supine, and Day 7 pre and post exercise	SAC[2]
SF-36 Score					
2.70	Analysis	Non-Standard EFF_F19	Mean (95% CI) Plot of SF-36 Acute Score Change from Baseline	SF-36 Acute Score has means at Day -1 and Day 7	SAC[2]
Respiratory Rate					
2.71	All Subject	Non-Standard EFF_F20	Individual Plot of 24-Hour Respiratory Monitoring	There will be a graph for each patient individually	SAC[2]
2.72	All Subject	Non-Standard EFF_F21	Mean (95% CI) Plot of 24 Hour Respiratory Rate Monitoring		SAC[2]

11.13.7. Safety Tables

Safety Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Exposure					
3.01	All Subjects	EX1	Summary of Extent of Exposure		SAC [2]
Adverse Events					
3.02	All Subjects	AE5	Summary of All Adverse Events by System Organ Class	Include total column. Exclude pre-treatment AEs and washout period AEs	SAC [2]
3.03	All Subjects	AE3	Summary of Common Adverse Events by Overall Frequency	AE is considered common if more than one subject experiences it regardless of treatment. Exclude pre-treatment AEs and washout period AEs	SAC [2]
3.04	All Subjects	AE5	Summary of Drug-Related Adverse Events by System Organ Class	Include total column. Exclude pre-treatment and washout period AEs	SAC [2]
3.05	All Subjects	AE1	Summary of Serious Adverse Events by System Organ Class		SAC [2]
3.06	All Subjects	AE1	Summary of Adverse Events Leading to Withdrawals from Study / Permanent Discontinuation of Study Treatment		SAC [2]
3.07	All Subjects	AE15	Summary of Common (>=20%) Non-serious Adverse Events by System Organ Class and Preferred Term		SAC [2]
3.08	All Subjects	AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term		SAC [2]

Safety Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Labs					
3.09	All Subjects	LB1	Summary of Clinical Chemistry Laboratory Values by Visit		SAC [2]
3.10	All Subjects	LB1	Summary of Chemistry Changes from Baseline by Visit		SAC [2]
3.11	All Subjects	LB3	Summary of Chemistry Results by Potential Clinical Importance Criteria		SAC [2]
3.12	All Subjects	LB2	Summary of LFTs of Potential Clinical Importance by Visit	Include ALT and total Bilirubin	SAC [2]
3.13	All Subjects	LB1	Summary of Percent Change from Baseline of LFTs by Visit		SAC [2]
3.14	All Subjects	LB1	Summary of Haematology/Coagulation Changes from Baseline by Visit		SAC [2]
3.15	All Subjects	LB17	Summary of Haematology Results by Potential Clinical Importance Criteria		SAC [2]
Vital Signs					
3.16	All Subjects	VS1	Summary of Vital Signs by Visit	Include the Respiration Rate and Temperature	SAC [2]
3.17	All Subjects	VS3	Summary of Change from Baseline in Vital Signs by Visit	Include the Respiration Rate and Temperature	SAC [2]
3.18	All Subjects	VS2	Summary of Vital Signs Results by Potential Clinical Importance Criteria		SAC [2]

Safety Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
ECGs					
3.19	All Subjects	EG1	Summary of ECG Findings by Visit		SAC [2]
3.20	All Subjects	EG2	Summary of Maximum QTc Values by Category.		SAC [2]
3.21	All Subjects	EG2	Summary of Change from Baseline in ECG Values by Visit.		SAC [2]

11.13.8. Pharmacokinetic Tables

Pharmacokinetic Tables					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
PK Concentration Data					
4.01	PK	PK01	Summary of Plasma GSK2798745 Pharmacokinetic Concentration-Time Data (ng/mL)		SAC [2]
4.02	Per Protocol	PK01	Summary of Plasma GSK2798745 Pharmacokinetic Concentration-Time Data (ng/mL)	Add Footnote	SAC [2]
PK Derived Parameters					
4.03	PK Parameter	PKPT1	Summary Statistics of Derived Plasma GSK2798745 Pharmacokinetic Parameters	Parameters with units	SAC [2]
4.05	PK Parameter	PKPT3	Summary Statistics of Log-Transformed Derived Plasma GSK2798745 Pharmacokinetic Parameters	Parameters with units	SAC [2]

11.13.9. Pharmacokinetic Figures

Pharmacokinetic Figures					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Individual Plots					
4.01	PK	PKCF1P	Individual GSK2798745 Plasma Concentration-Time Plot by Treatment (Linear and Semi-Log)	Paginate by Treatment	SAC [2]
Mean / Median Plots					
4.02	PK	PKCF2	Mean Plasma GSK2798745 Concentration-Time Plots by Treatment (Linear and Semi-log)	Paginate by Treatment	SAC [2]

11.13.10. ICH Listings

ICH Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Randomisation					
01	All Subjects	TA2	Listing of Randomised and Actual Treatments		SAC [2]
Subject Disposition					
02	All Subjects	ES3	Listing of Reasons for Study Withdrawal		SAC [2]
03	All Subjects	ES7	Listing of Reasons for Screening Failure		SAC [2]
04	All Subjects	SA3b	Listing of Subjects Excluded from Per Protocol Population	Only list subject that deviate from per protocol	SAC [2]
05	All Subjects	DV2	Listing of Important Protocol Deviations		SAC [2]
06	All Subjects	IE4	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		SAC [2]
Demographics					
07	All Subjects	DM4	Listing of Demographic Characteristics		SAC [2]
08	All Subjects	DM10	Listing of Race		SAC [2]
Medical Conditions & Concomitant Medication					
09	All Subjects	MH3	Listing of Medical Conditions (Current/Past)		SAC [2]
10	All Subjects	CM5	Listing of Concomitant Medication		SAC [2]

ICH Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Exposure					
11	All Subjects	EX4	Listing of Exposure		SAC [2]
Adverse Events					
12	All Subjects	AE9	Listing of All Adverse Events		SAC [2]
13	All Subjects	AE9	Listing of Serious Adverse Events	Only include AE's classified as serious	SAC [2]
14	All Subjects	AE9	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment.		SAC [2]
15	All Subjects	ECSSRS4	Listing of C-SSRS		SAC [2]
16	All Subjects	EFF_L1	Listing of SNAQ		SAC [2]
17	All Subjects	EFF_L1	Listing of Audiometry		SAC [2]
18	All Subjects	EFF_L1	Listing of Faecal Occult		SAC [2]
Labs					
19	All Subjects	LB6	Listing of Haematology Laboratory Data for Subjects with Abnormalities of Potential Clinical Importance		SAC [2]
20	All Subjects	LB6	Listing of Clinical Chemistry Laboratory Data for Subjects Abnormalities of Potential Clinical Importance		SAC [2]

ICH Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
21	All Subjects	LB6	Listing of LFT's for Subjects Abnormalities of Potential Clinical Importance		SAC [2]
22	All Subjects	LB6	Listing of Clinical Chemistry Laboratory Data for Subjects Abnormalities of Potential Clinical Importance As a Change from Baseline	Rather than have the value and normal range column just include a change from baseline column	SAC [2]
23	All Subjects	LB6	Listing of Haematology Laboratory Data for Subjects with Abnormalities of Potential Clinical Importance As a Change from Baseline	Rather than have the value and normal range column just include a change from baseline column	SAC [2]
ECGs					
24	All Subjects	EG4	Listing of ECG Values for Subjects with Abnormalities of Potential Clinical Importance.		SAC [2]
Vital Signs					
25	All Subjects	VS5	Listing of Vital Signs for Subjects with Abnormalities of Potential Clinical Importance		SAC [2]
26	All Subjects	VS5	Listing of Vital Signs for Subjects		SAC [2]

11.13.11. Non-ICH Listings

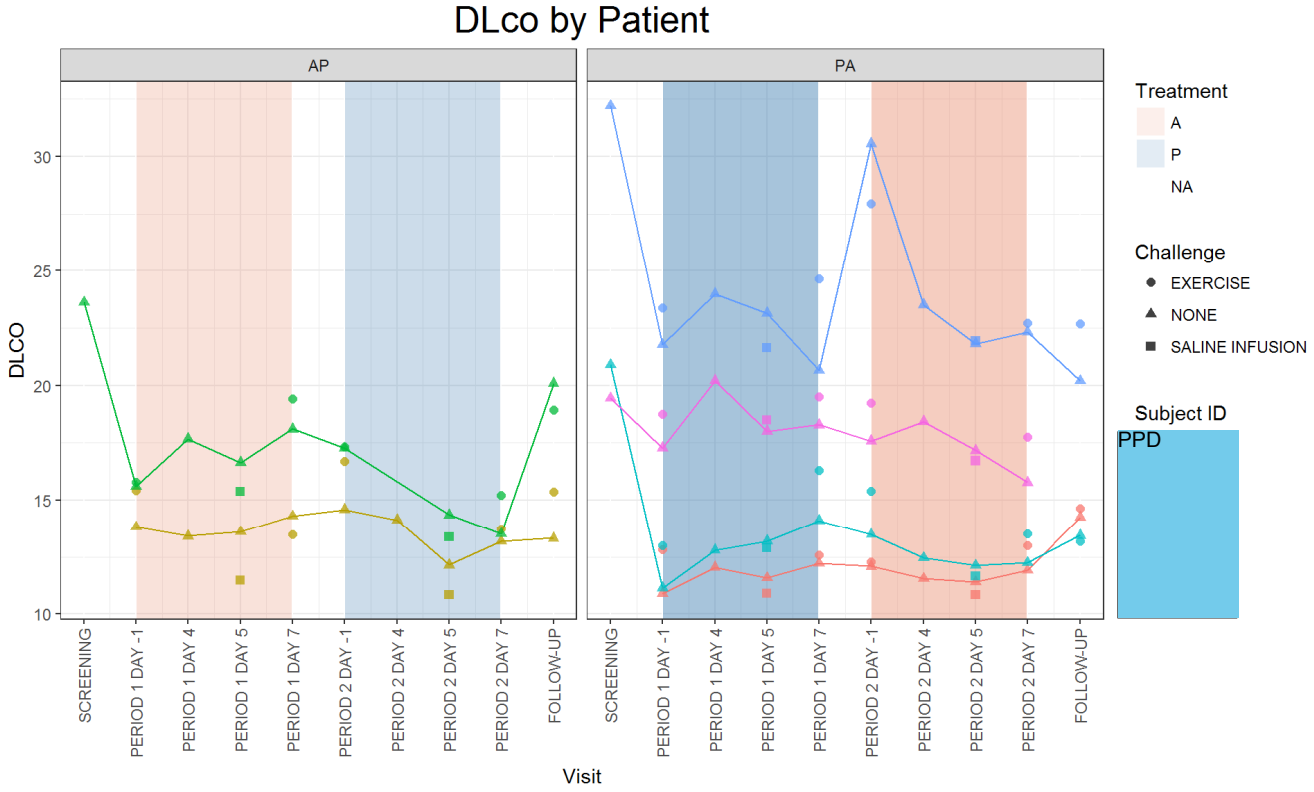
Non-ICH Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Efficacy					
28	All Subjects	Non-Standard EFF_L1	Listing of Gas Diffusion Outcomes (DLco, DLno, Dm, Vc)		SAC [2]
29	All Subjects	Non-Standard EFF_L2	Listing of Gas Diffusion Outcomes Change from Baseline (DLco, DLno, Dm, Vc)		SAC [2]
30	All Subjects	Non-Standard EFF_L1	Listing of VE/VCO_2	Rows for day -1 and day 7 only	SAC [2]
31	All Subjects	Non-Standard EFF_L2	Listing of VE/VCO_2 Change from Baseline	Rows for day -1 and day 7 only	SAC [2]
32	All Subjects	PFT9	Listing of Pulmonary Function Test (FVC, FEV1, FEF-25-75, FEF50, FEF75)	Rows for day -1, day 4, and day 7 only	SAC [2]
33	All Subjects	Non-Standard EFF_L2	Listing of Pulmonary Function Test Change from Baseline (FVC, FEV1, FEF-25-75, FEF50, FEF75)	Rows for day -1, day 4, and day 7 only	SAC [2]
34	All Subjects	LB6	Listing of Troponin	(Include change from baseline)	SAC [2]
35	All Subjects	SF6	Listing of SF-36 Acute Score		SAC [2]
36	All Subjects	MOS_S7	Listing of Sleep Study Variables	Include Minimum Oxygen Saturation during sleep, total sleep time, central apnea index, obstructive apnea index, mixed apnea index, hypopnea index, apnea hypopnea index	SAC[2]

Non-ICH Listings					
No.	**Population**	**IDSL / TST ID / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
40	All Subjects	EFF_L2	Listing of Change in Minimum Oxygen Saturation during Polysomnography		SAC[2]
41	All Subjects	EFF_L1	Listing of AUC of HMG-CoA reductase inhibitors and their key metabolites		SAC[2]
37	All Subjects	SF6	Listing of Dyspnea Score	(Include change from baseline)	SAC[2]
PK					
38	PK	PKCL1P	Listing of Plasma GSK2798745 Pharmacokinetic Concentration-Time Data		SAC [2]
39	PK	PKPL1P	Listing of Derived Plasma GSK2798745 Pharmacokinetic Parameters	Include dose and dose number	SAC [2]

11.14. Appendix 12: Example Mock Shells for Data Displays

Example : EFF_F1
Protocol : 201881
Population : All Subjects

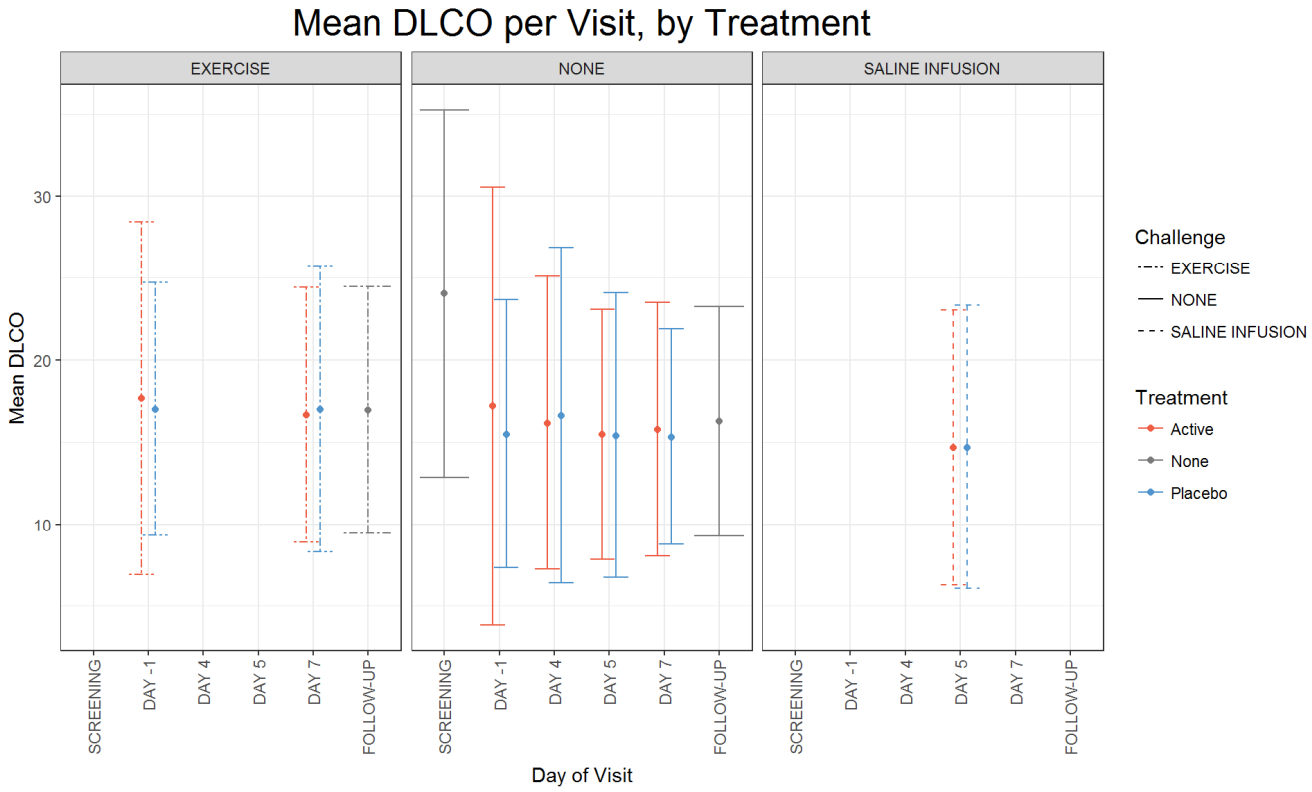
Figure 1.1
Spaghetti Plot of DLco Data



NOTE: Plot adjusted accordingly to study data

Example : EFF_F2
Protocol : 201881
Population : All Subjects

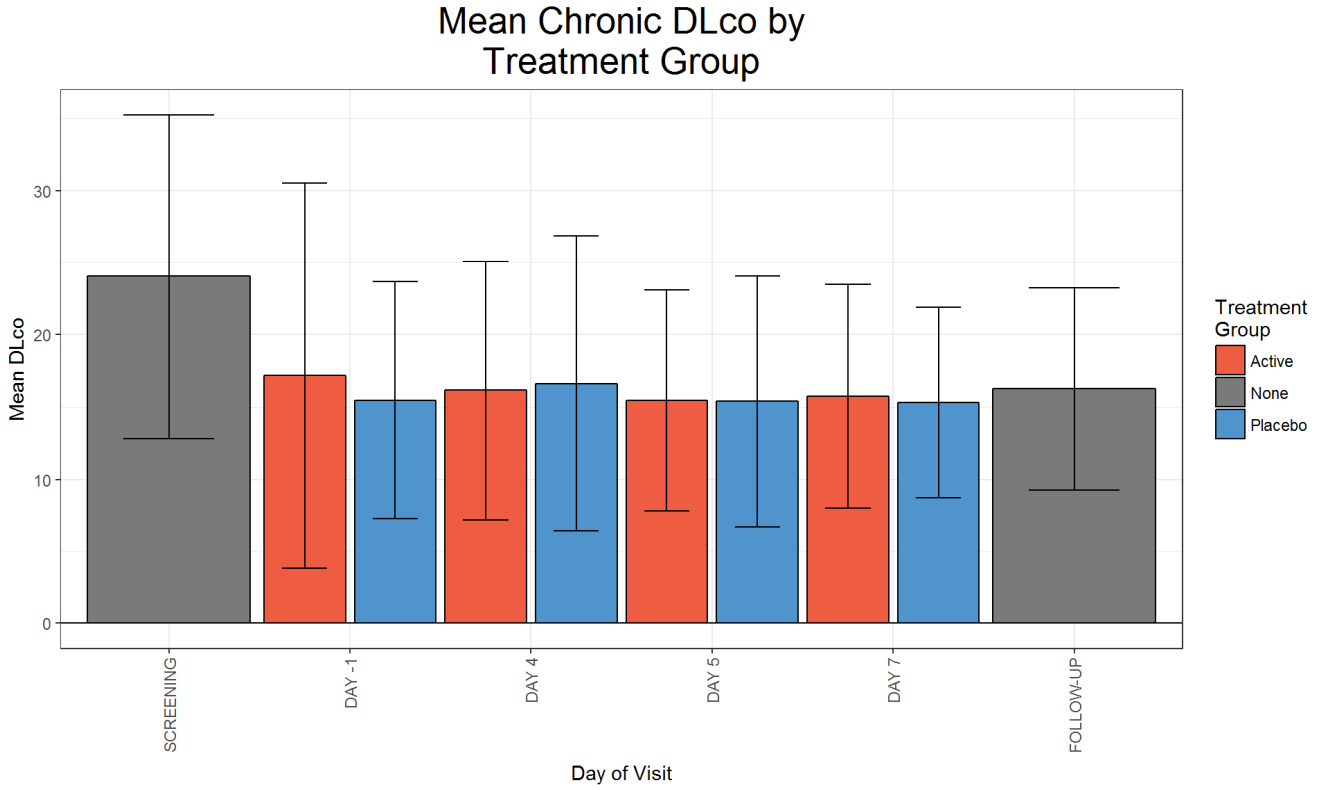
Figure 1.02
Mean (95% CI) Plot of DLco



NOTE: Plot adjusted accordingly to study data.

Example : EFF_F3
Protocol : 201881
Population : All Subjects

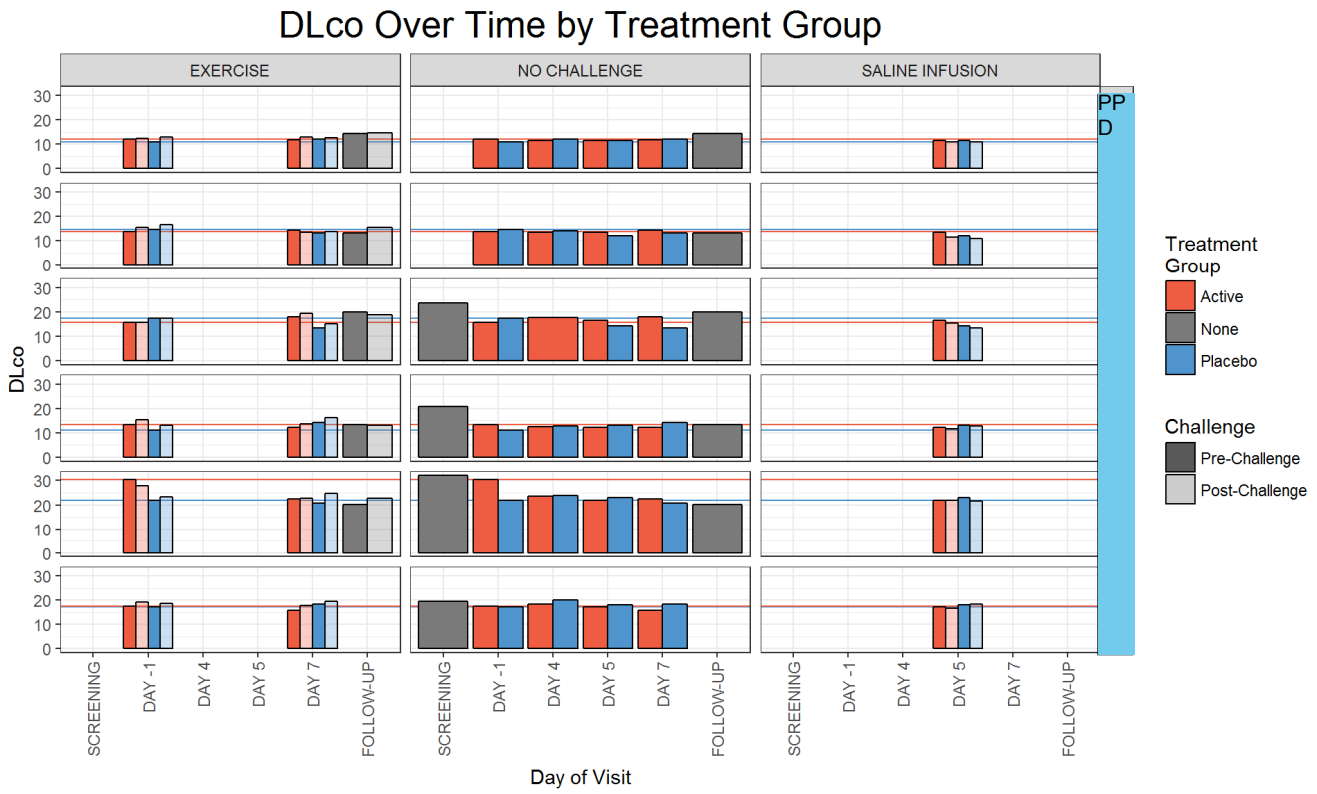
Figure 1.03
Mean (95% CI) Plot of DLco



NOTE: Plot adjusted accordingly to study data.

Example : EFF_F4
Protocol : 201881
Population : All Subjects

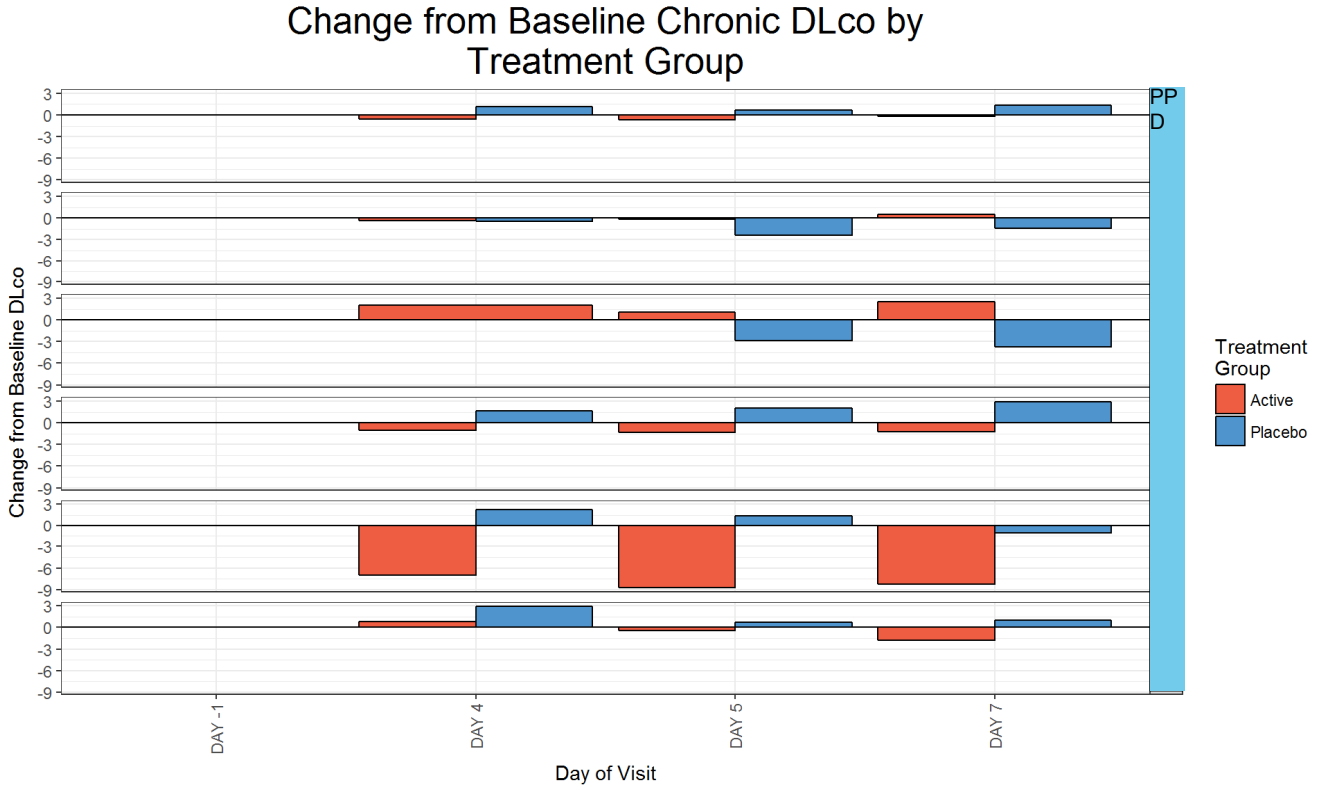
Figure 1.04
Plot of DLco by Individual and Treatment



NOTE: Plot adjusted accordingly to study data.

Example : EFF_F5
Protocol : 201881
Population : All Subjects

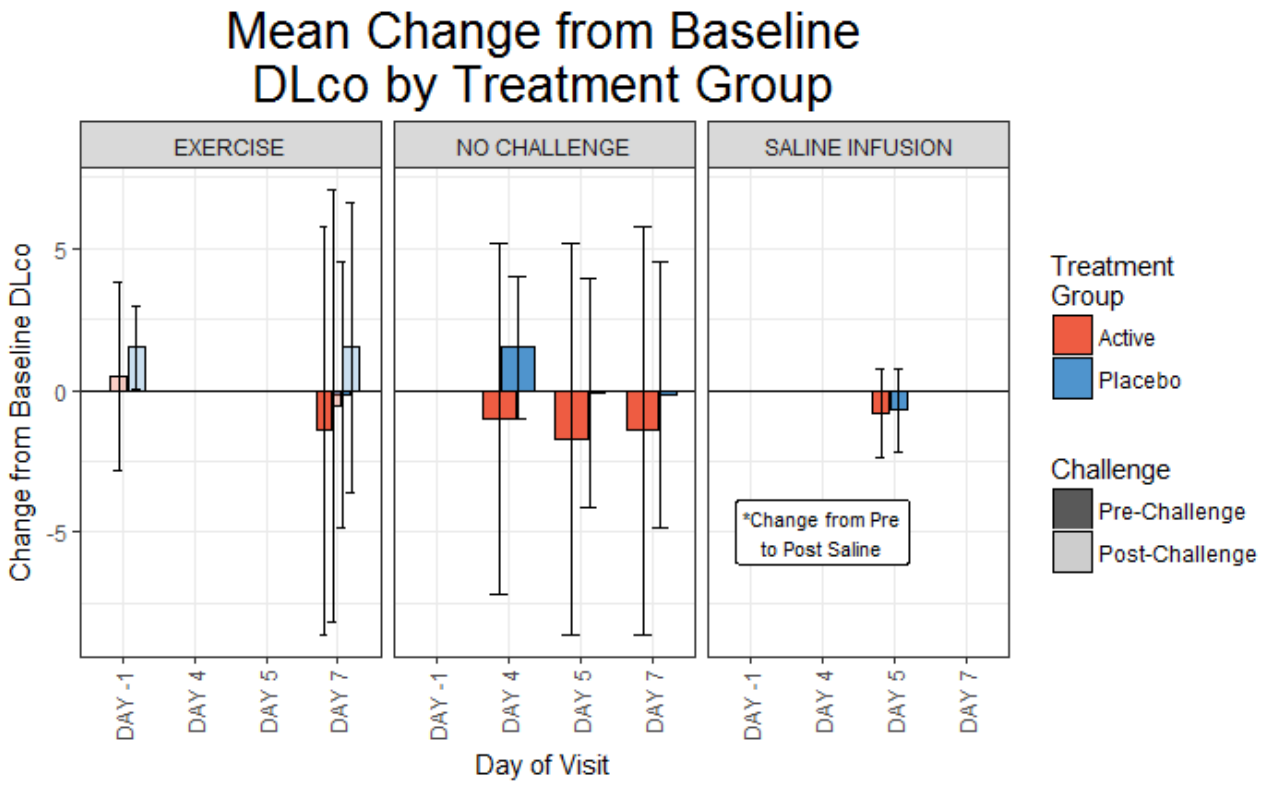
Figure 1.05
Change from Baseline DLco by Individual and Treatment



NOTE: Plot adjusted accordingly to study data.

Example : EFF_F6
Protocol : 201881
Population : All Subjects

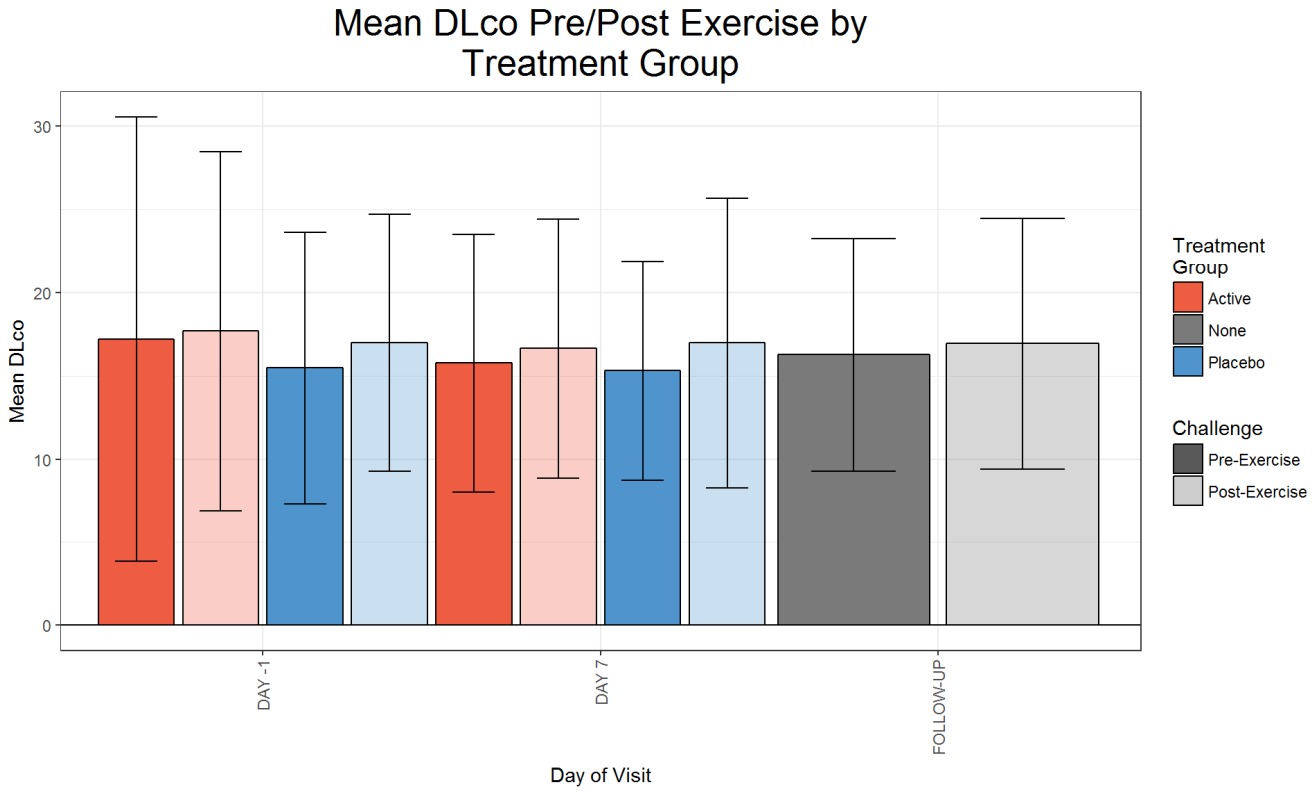
Figure 1.06
Mean Plot of DLco Change from Baseline



NOTE: Plot adjusted accordingly to study data.

Example : EFF_F7
Protocol : 201881
Population : All Subjects

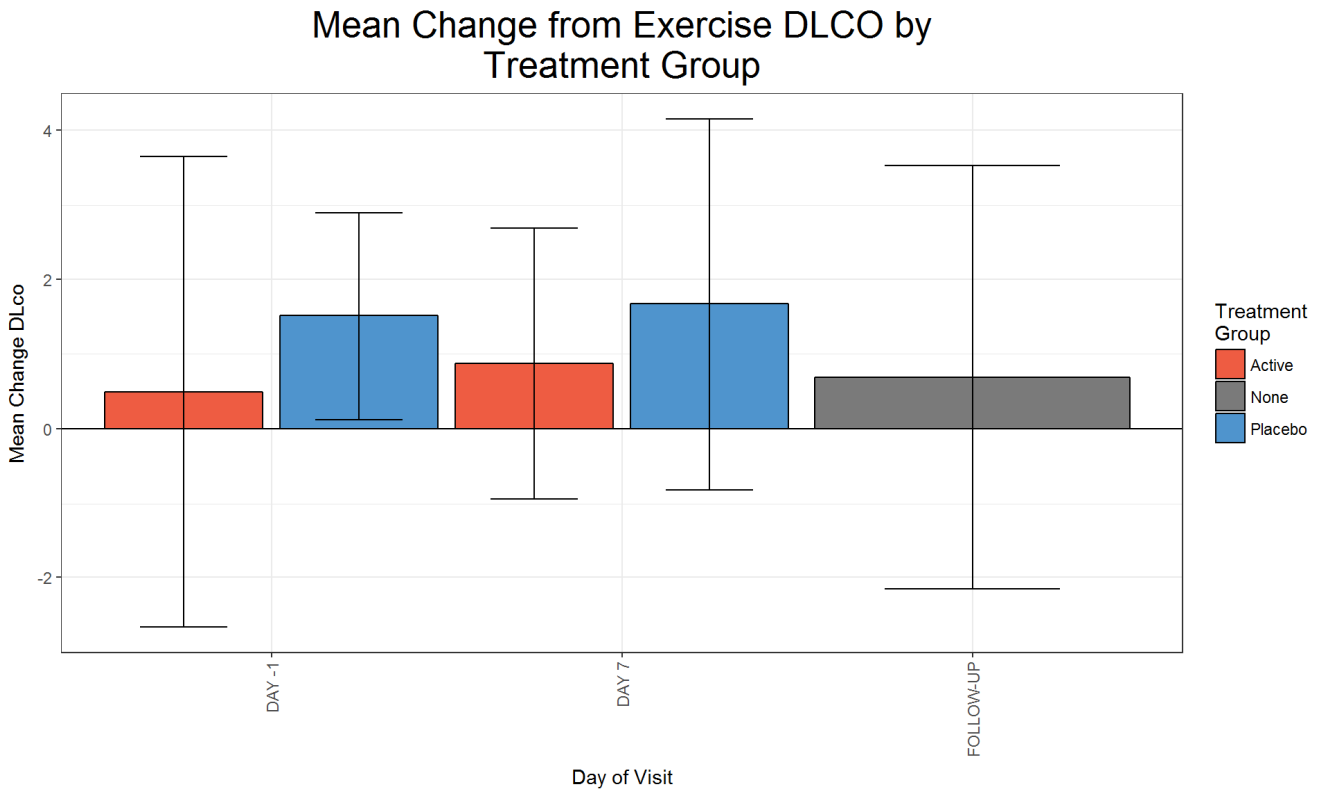
Figure 1.07
Mean Plot of DLco Pre/Post Exercise



NOTE: Plot adjusted accordingly to study data.

Example : EFF_F8
Protocol : 201881
Population : All Subjects

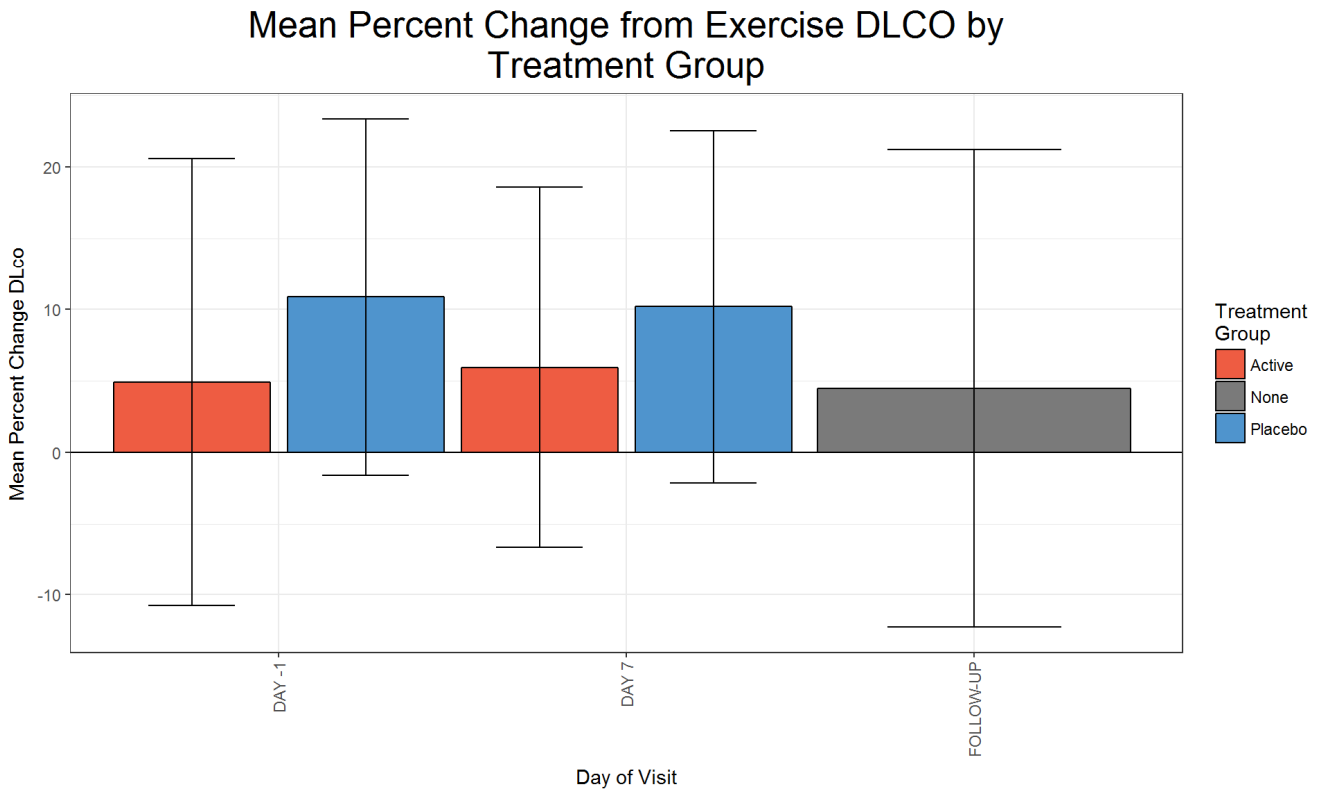
Figure 1.08
Mean Plot of DLco Change from Exercise



NOTE: Plot adjusted accordingly to study data.

Example : EFF_F9
Protocol : 201881
Population : All Subjects

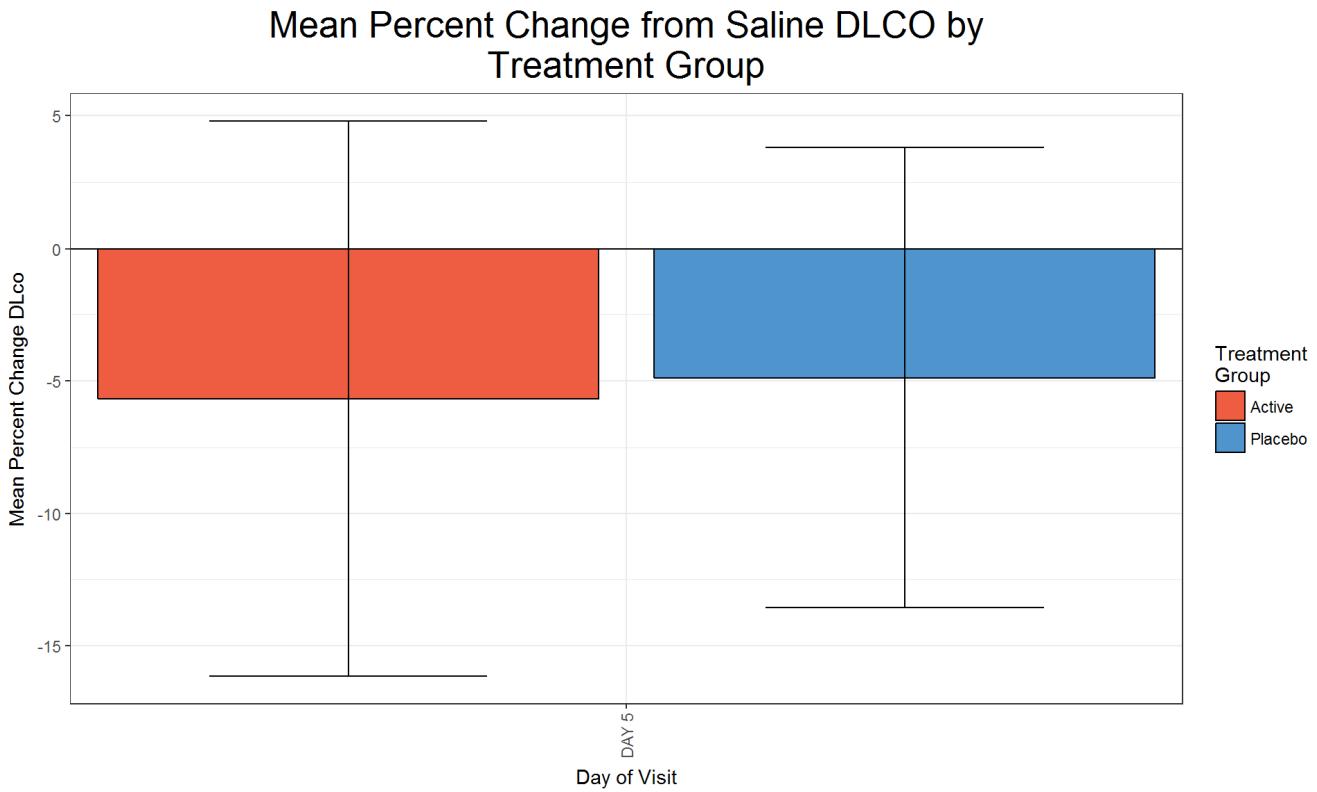
Figure 1.09
Mean Plot of Percent Change DLco from Exercise



NOTE: Plot adjusted accordingly to study data.

Example : EFF_F10
Protocol : 201881
Population : All Subjects

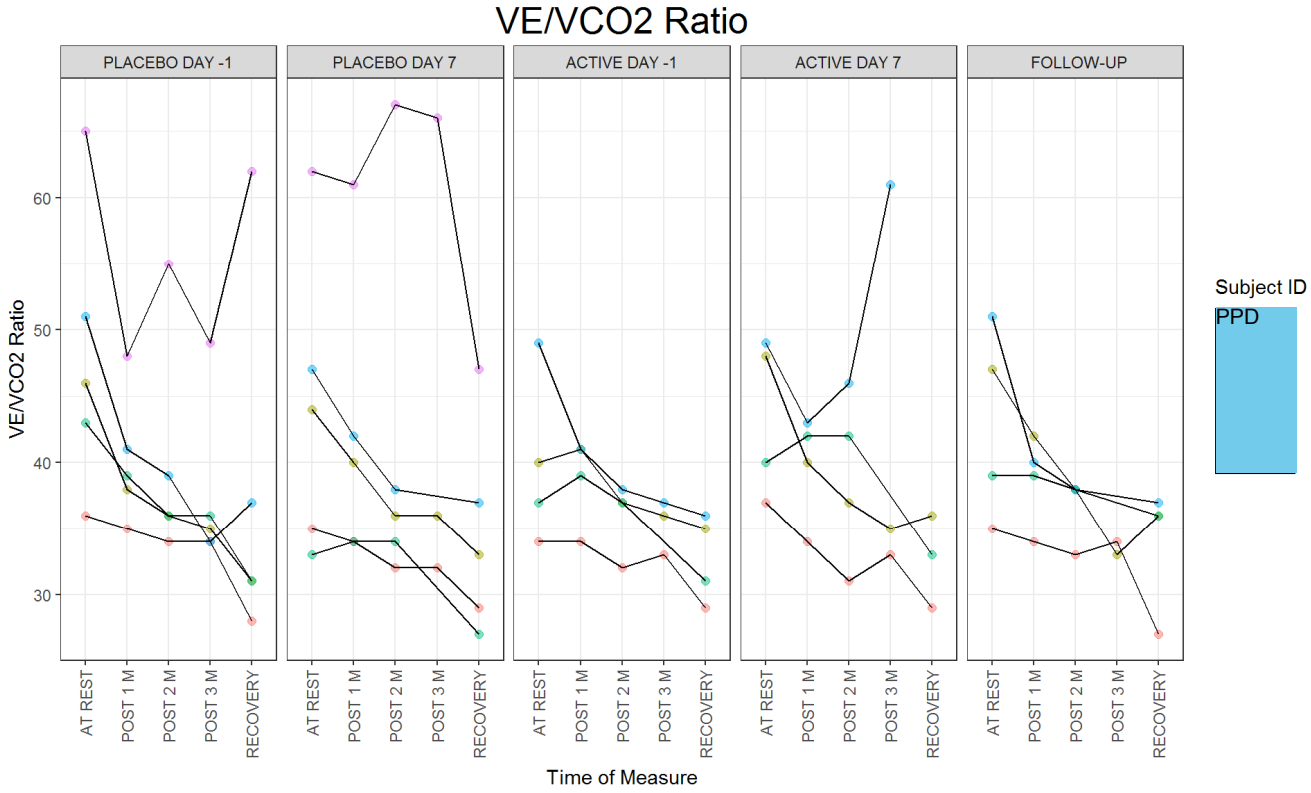
Figure 1.10
Mean Plot of Percent Change DLco from Saline



NOTE: Plot adjusted accordingly to study data.

Example : EFF_F11
Protocol : 201881
Population : All Subjects

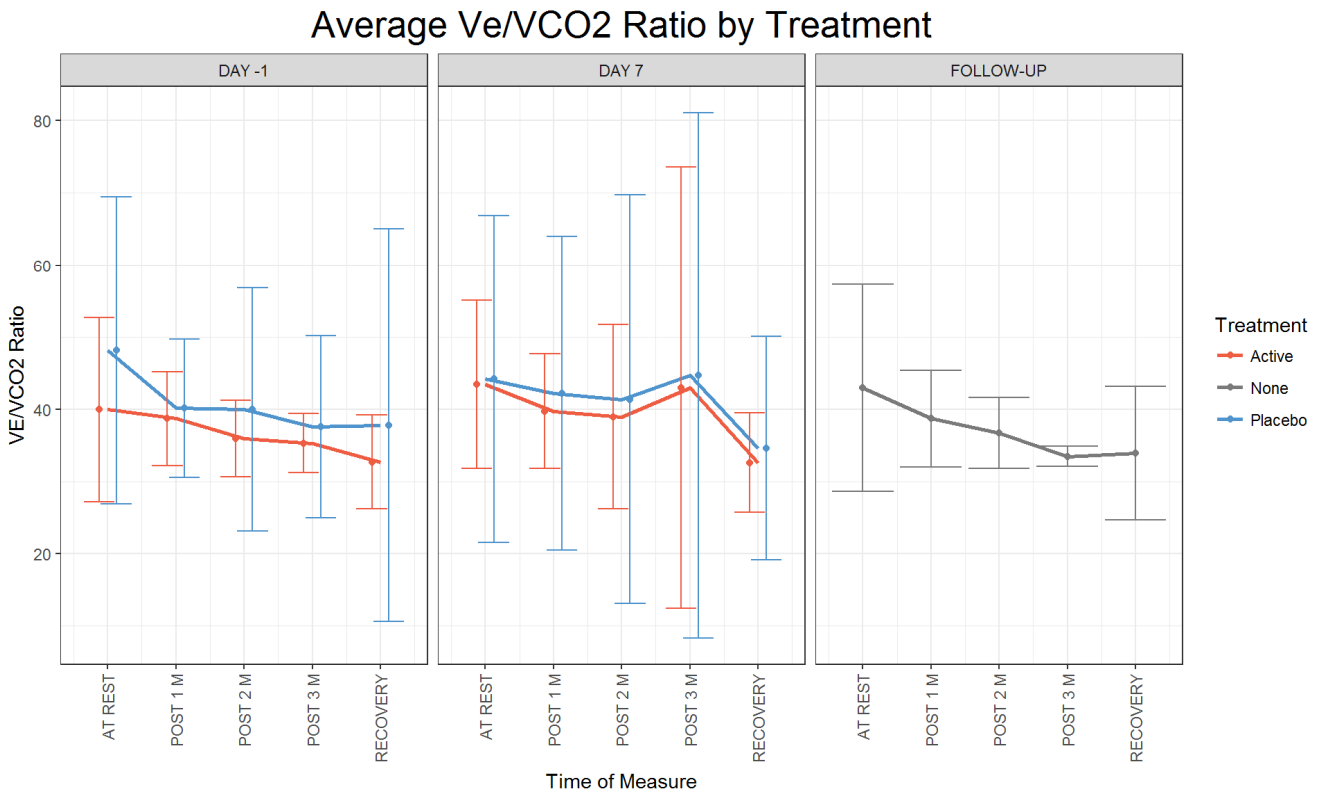
Figure 1.11
Plot of VE/VCO_2



NOTE: Plot adjusted accordingly to study data.

Example : EFF_F12
Protocol : 201881
Population : All Subjects

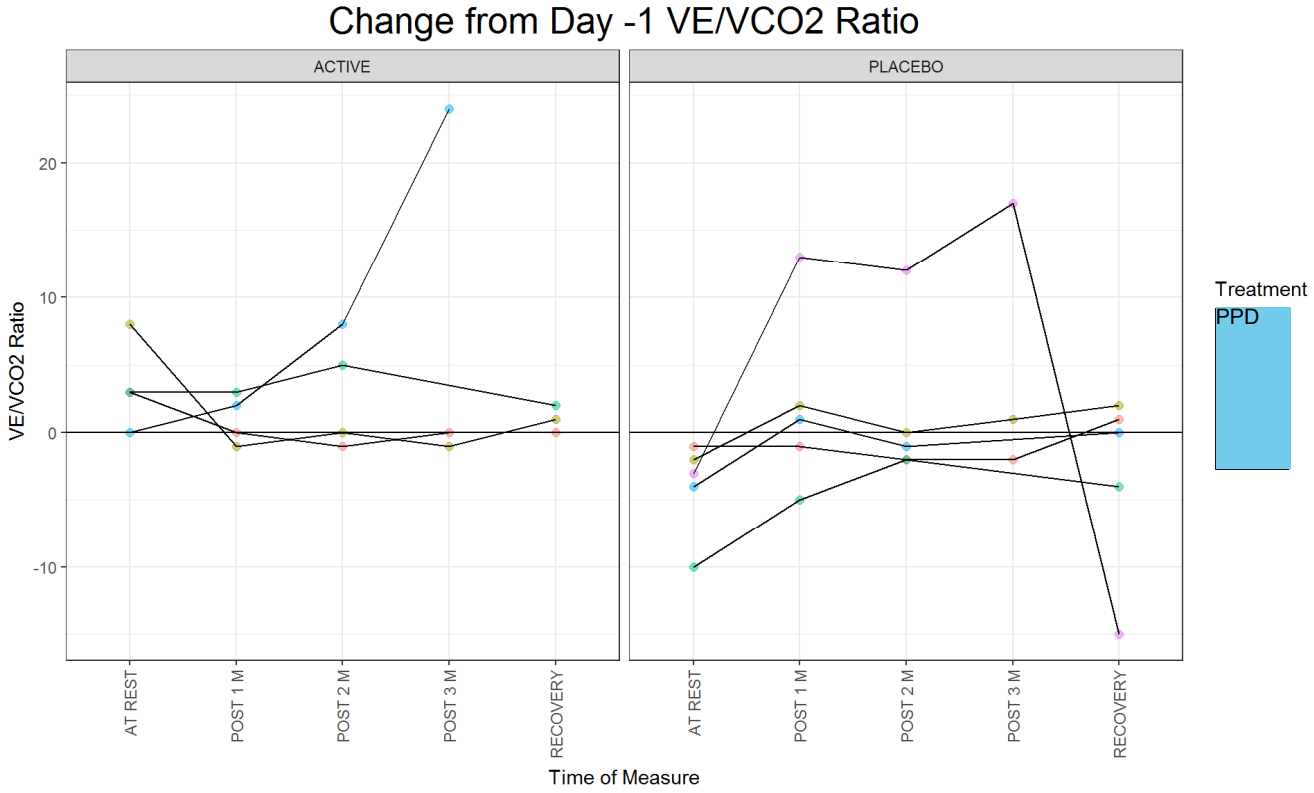
Figure 1.12
Mean (95% CI) Plot of VE/VCO_2



NOTE: Plot adjusted accordingly to study data.

Example : EFF_F13
Protocol : 201881
Population : All Subjects

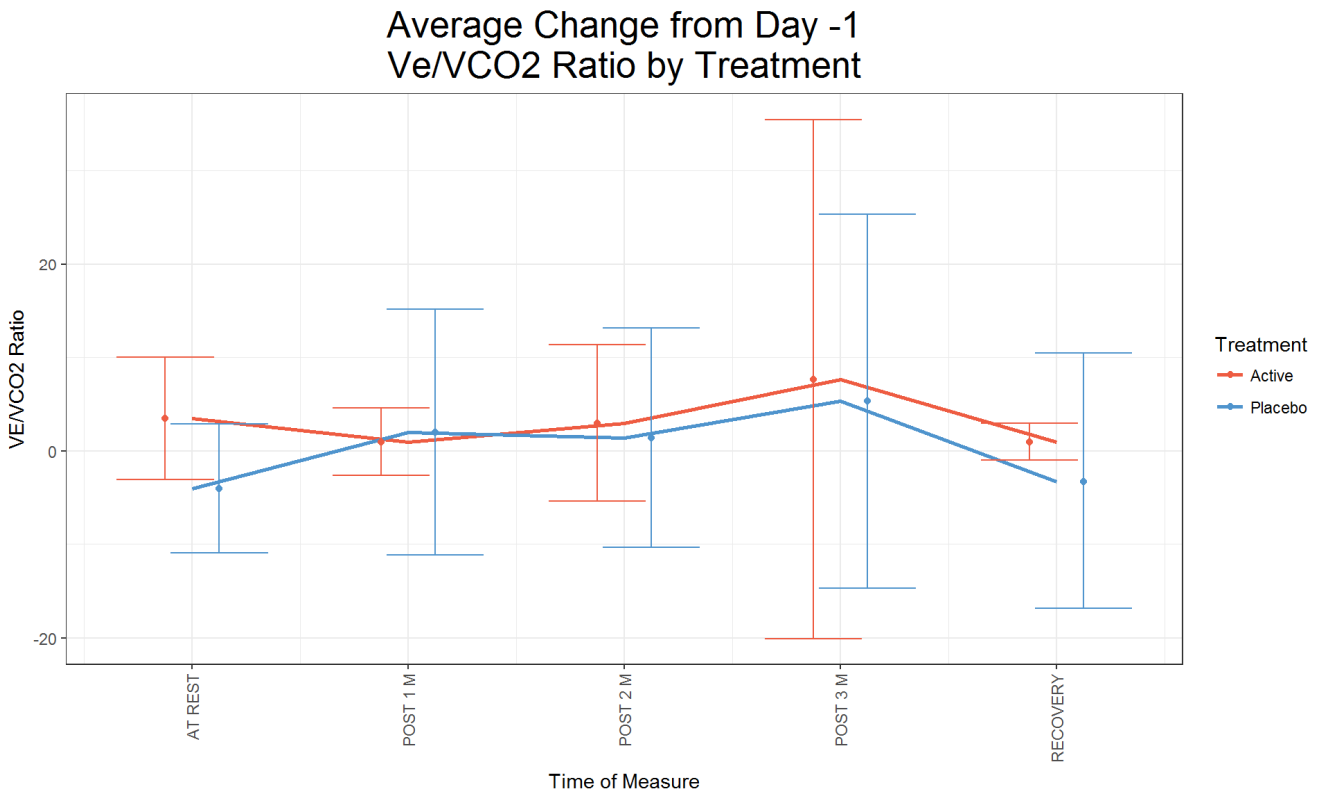
Figure 1.13
Plot of VE/VCO_2 Change from Day -1



NOTE: Plot adjusted accordingly to study data.

Example : EFF_F14
Protocol : 201881
Population : All Subjects

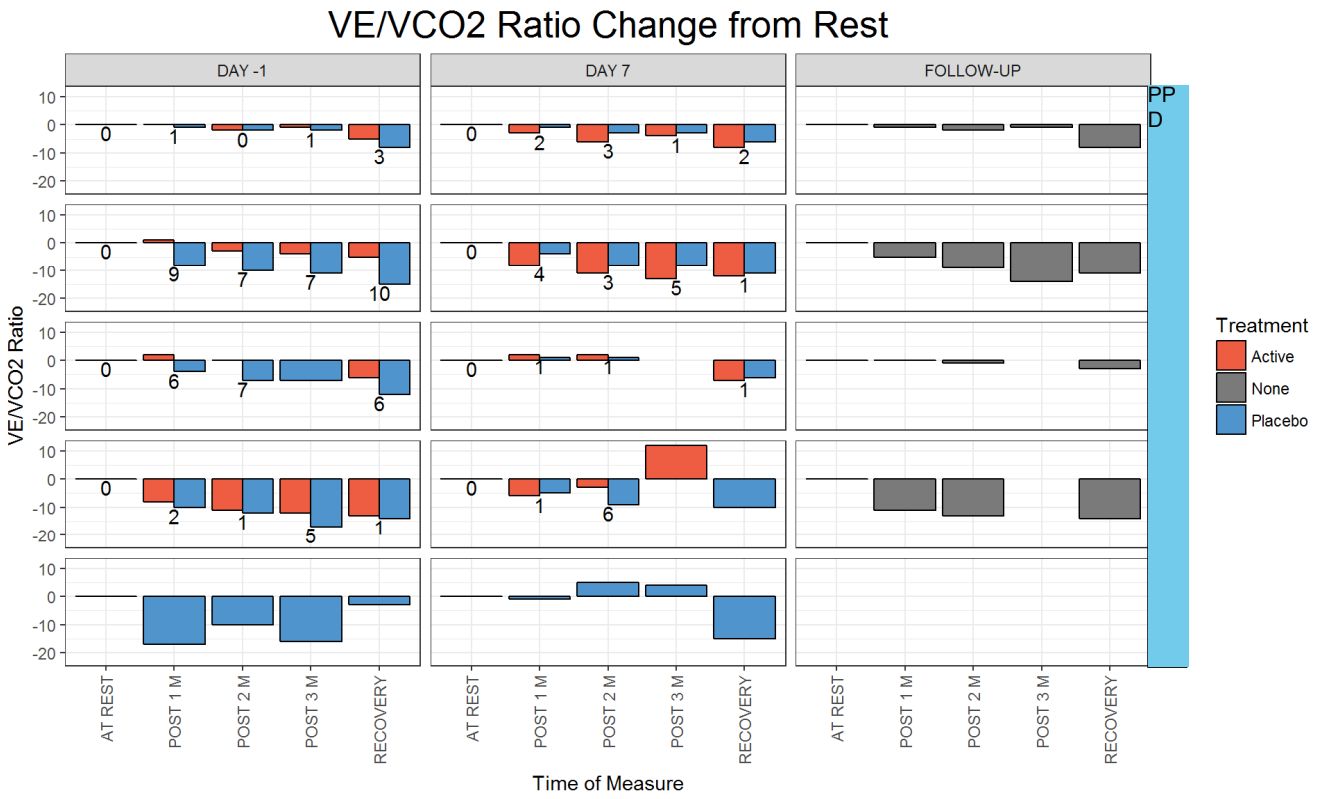
Figure 1.14
Plot of Mean VE/VCO_2 Change from Day -1



NOTE: Plot adjusted accordingly to study data.

Example : EFF_F15
Protocol : 201881
Population : All Subjects

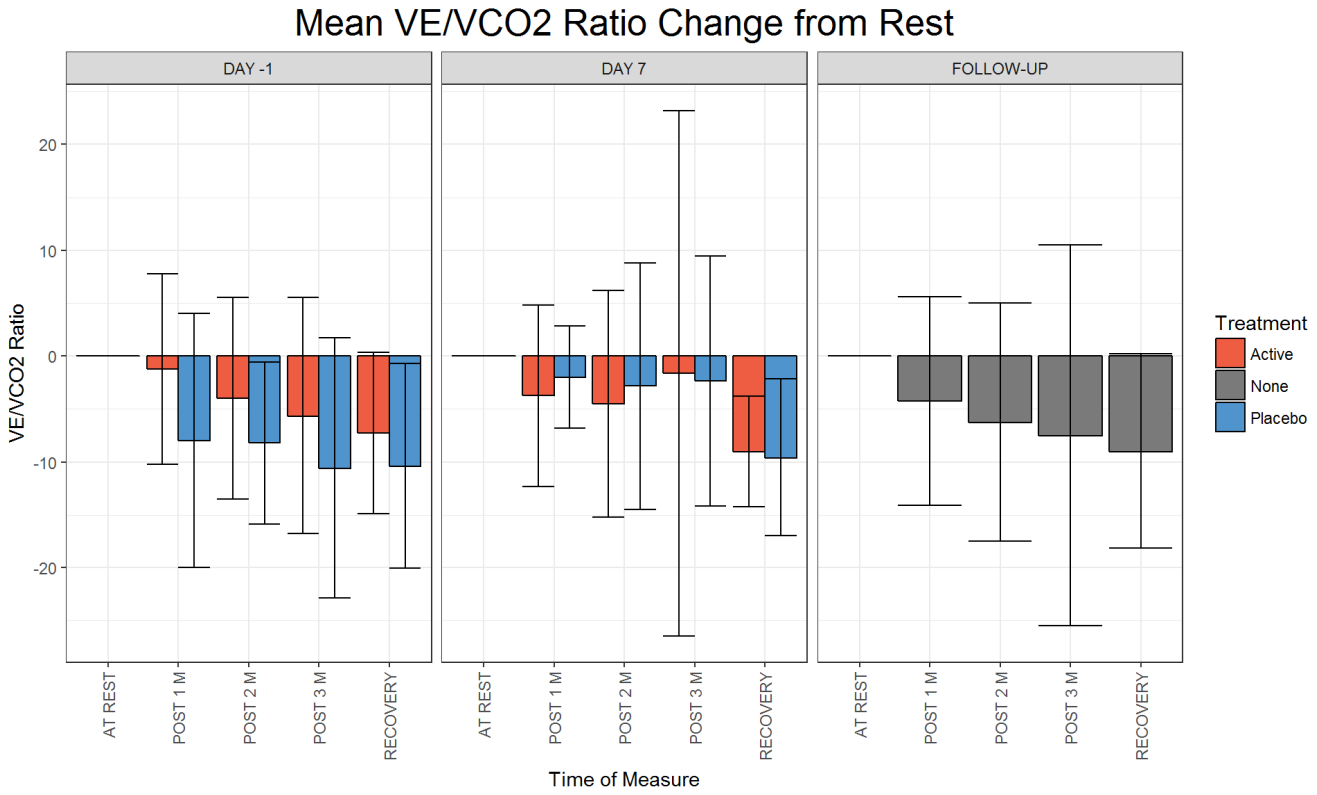
Figure 1.15
Plot of VE/VCO_2 Change from Rest



NOTE: Plot adjusted accordingly to study data.

Example : EFF_F16
Protocol : 201881
Population : All Subjects

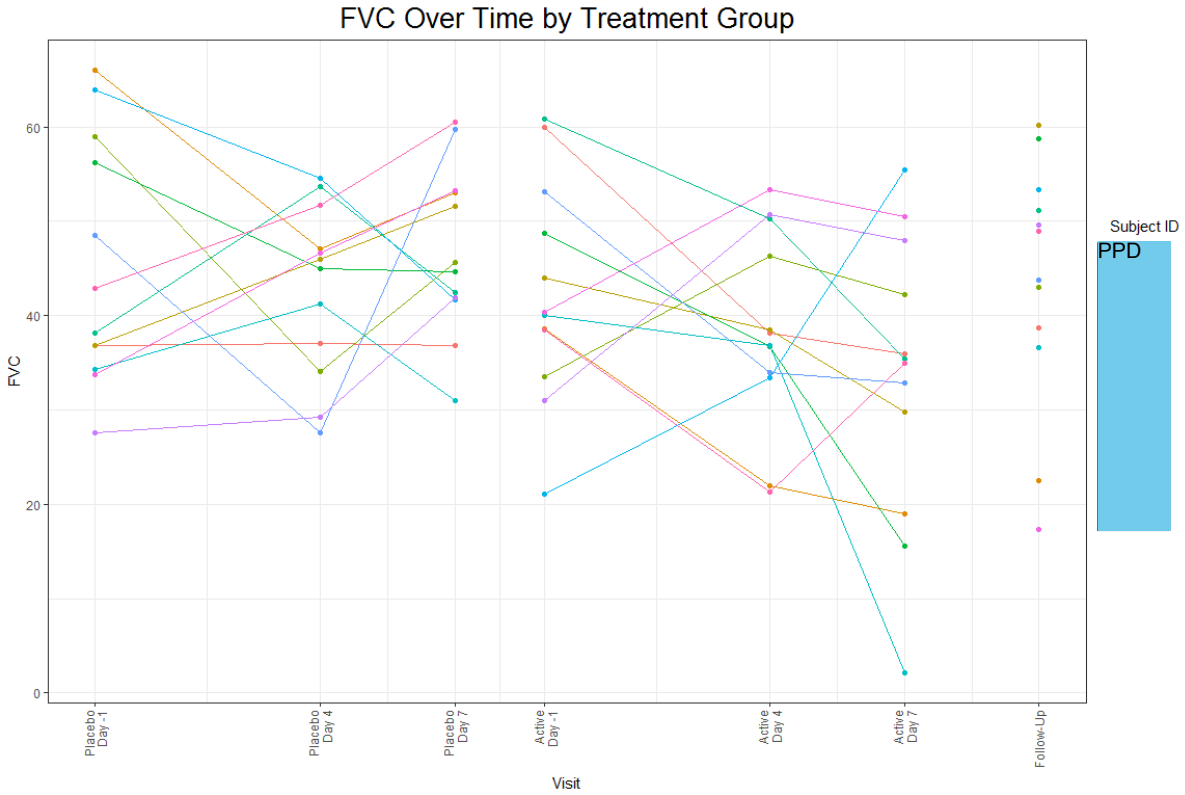
Figure 1.16
Plot of Mean VE/VCO_2 Change from Rest



NOTE: Plot adjusted accordingly to study data.

Example : EFF_F17
Protocol : 201881
Population : All Subjects

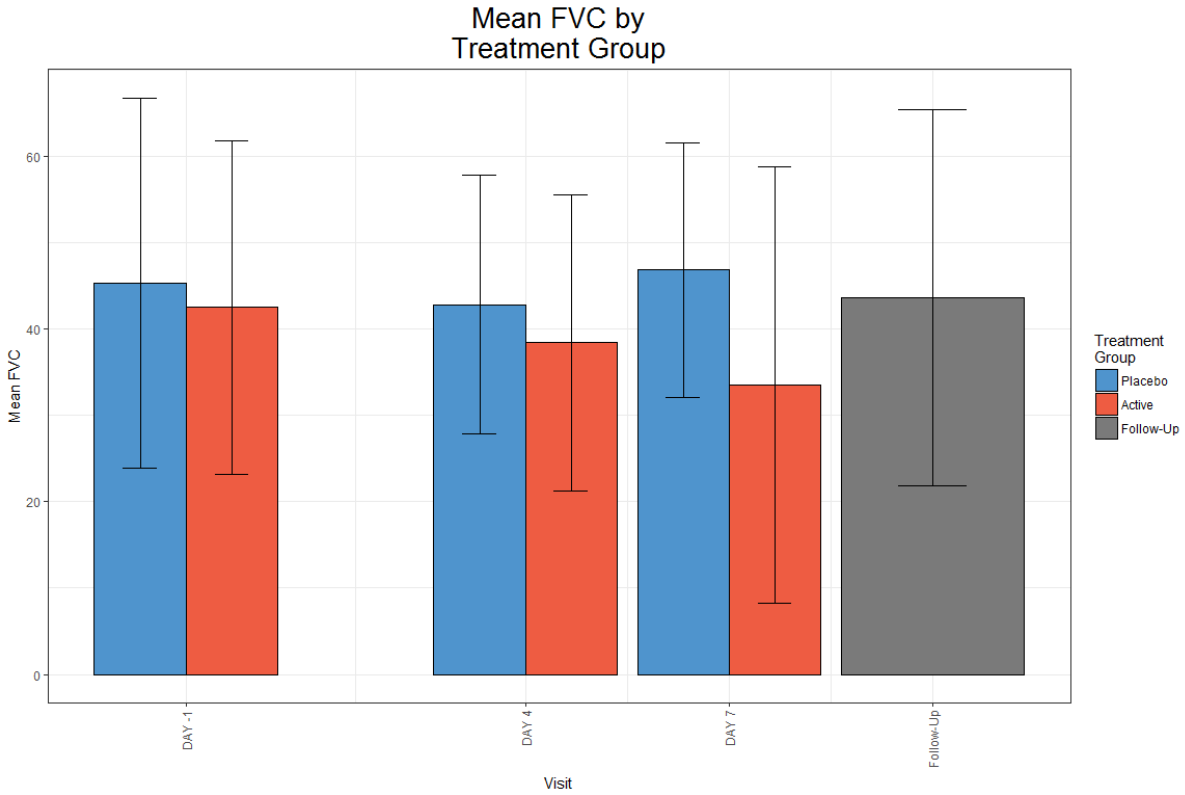
Figure 1.17
Spaghetti Plot of FVC



NOTE: Plot adjusted accordingly to study data.

Example : EFF_F18
Protocol : 201881
Population : All Subjects

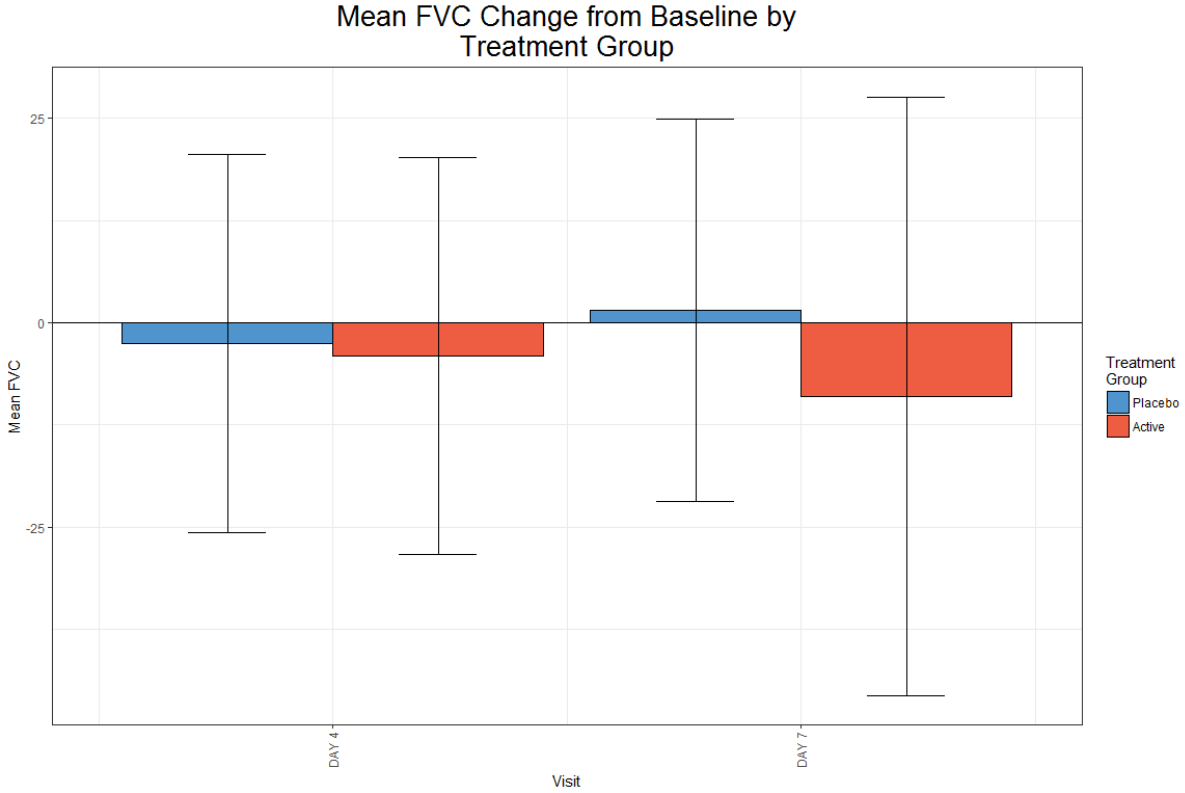
Figure 1.18
Mean (95% CI) Plot of FVC



NOTE: Plot adjusted accordingly to study data.

Example : EFF_F19
Protocol : 201881
Population : All Subjects

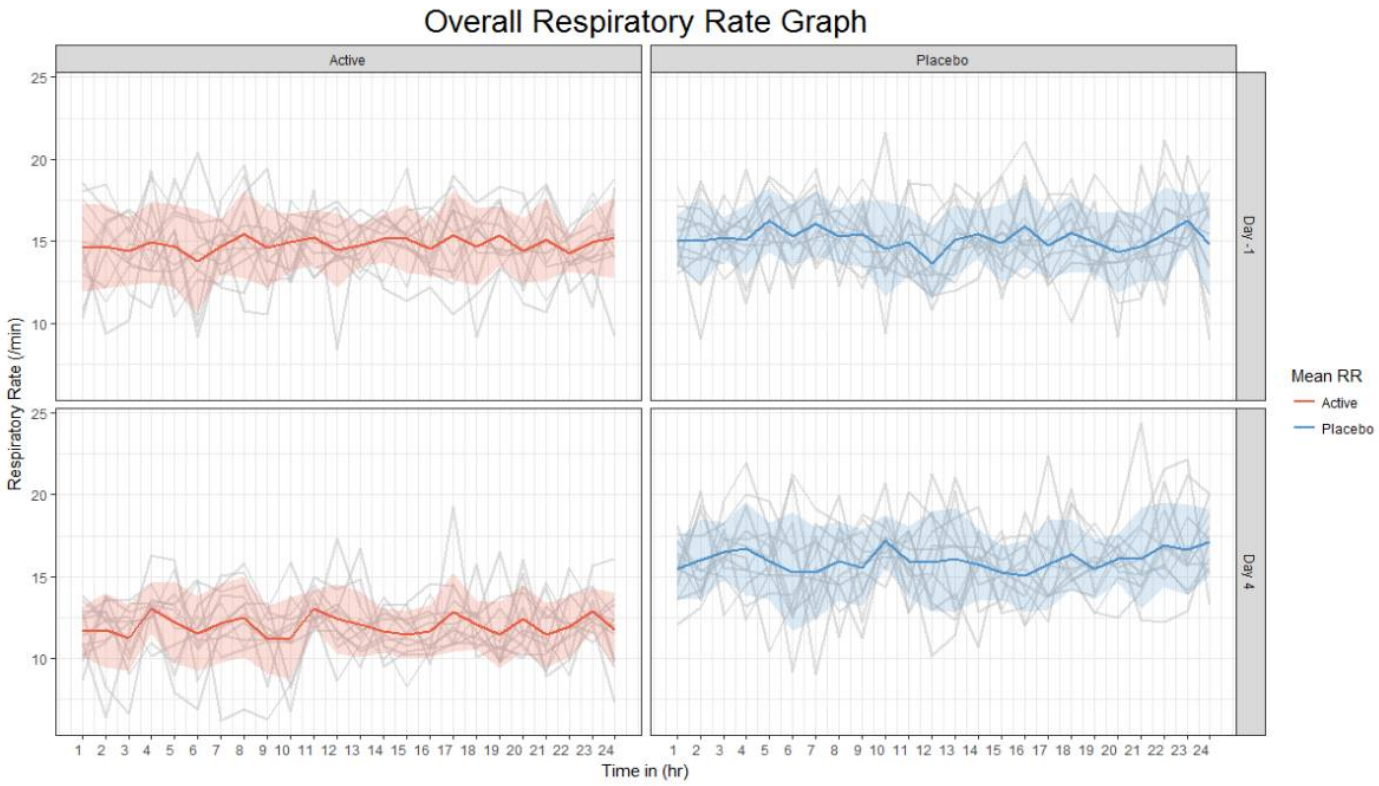
Figure 1.19
Mean (95% CI) Plot of FVC Change from Baseline



NOTE: Plot adjusted accordingly to study data.

Example : EFF_F20
Protocol : 201881
Population : All Subjects

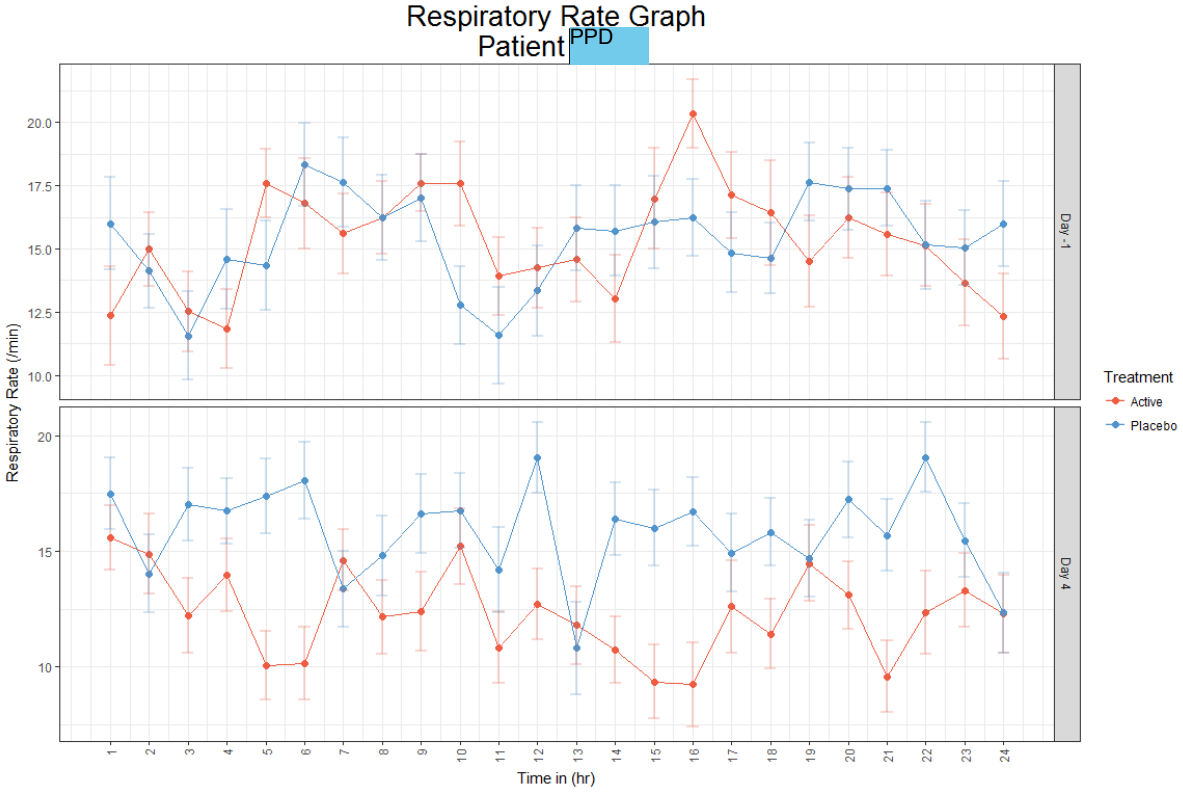
Figure 1.20
Individual Plot of 24-Hour Respiratory Monitoring



NOTE: Plot adjusted accordingly to study data.

Example : EFF_F21
Protocol : 201881
Population : All Subjects

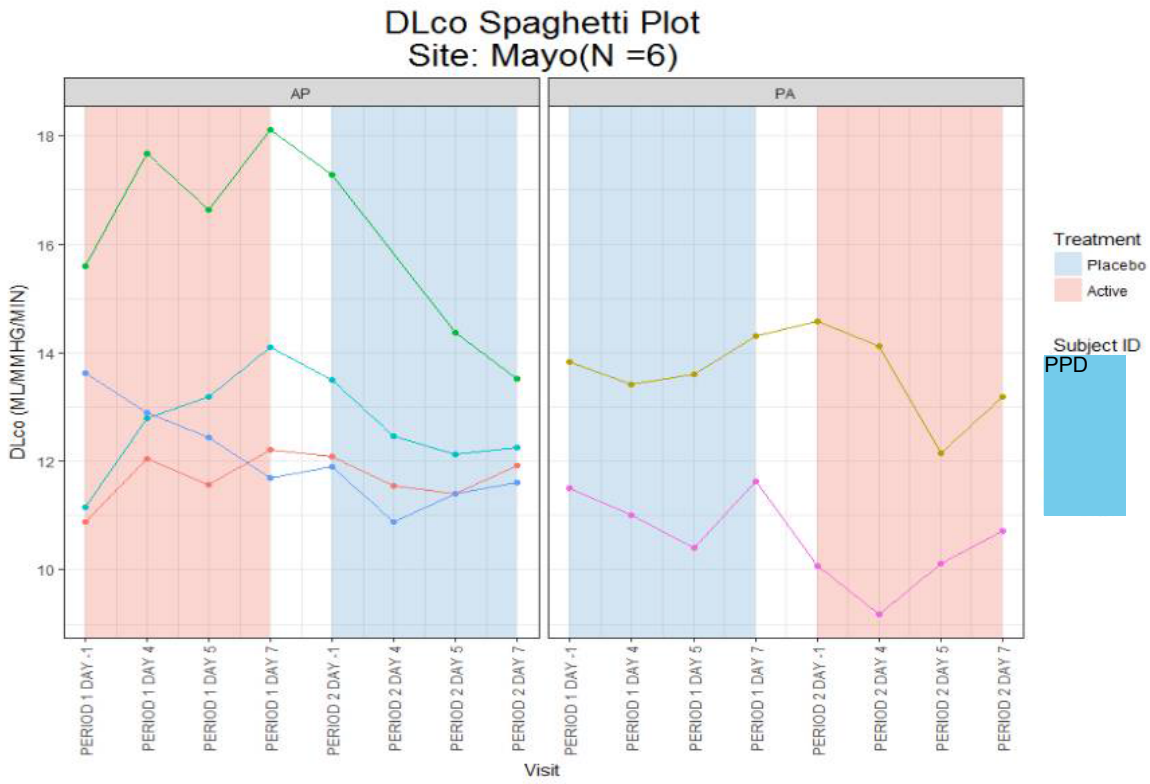
Figure 1.21
Mean (95% CI) Plot of 24 Hour Respiratory Rate Monitoring



NOTE: Plot adjusted accordingly to study data.

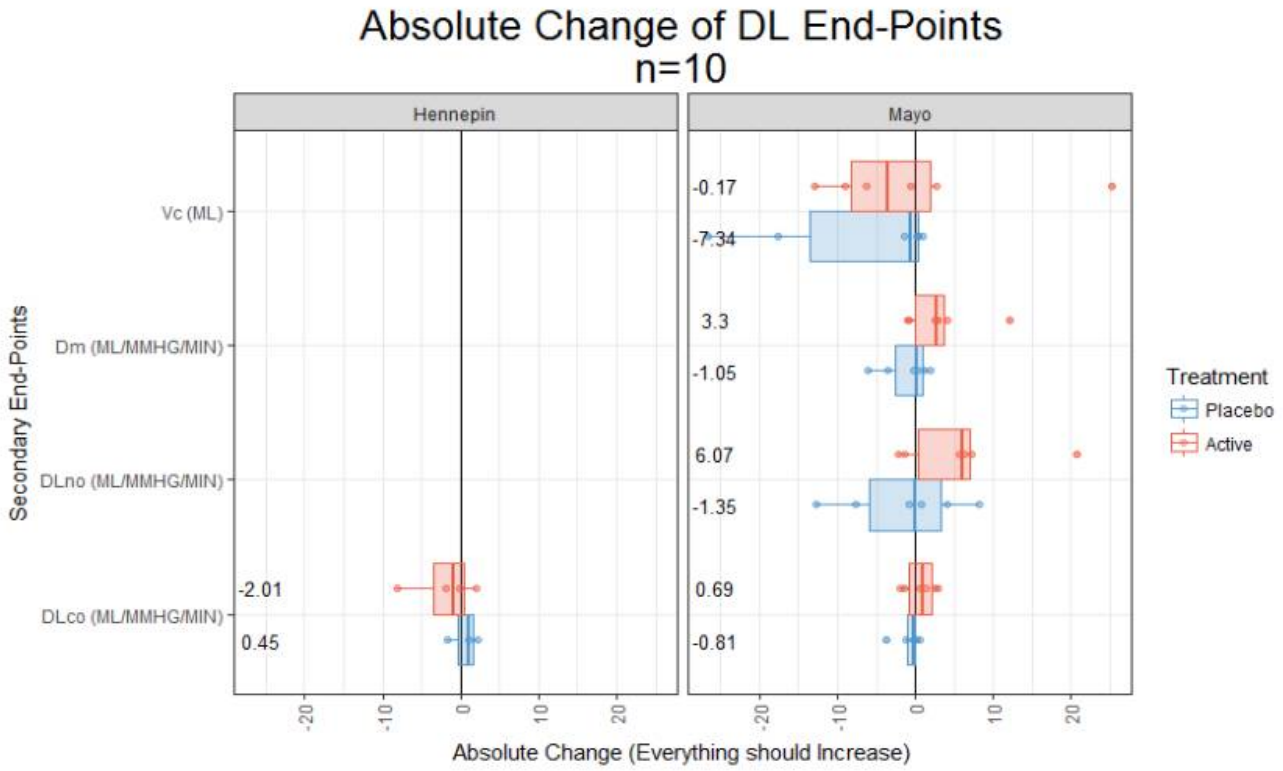
Example : EFF_F22
Protocol : 201881
Population : All Subjects

Figure 1.22
DLco Spaghetti Plot by Site



NOTE: Plot adjusted accordingly to study data.

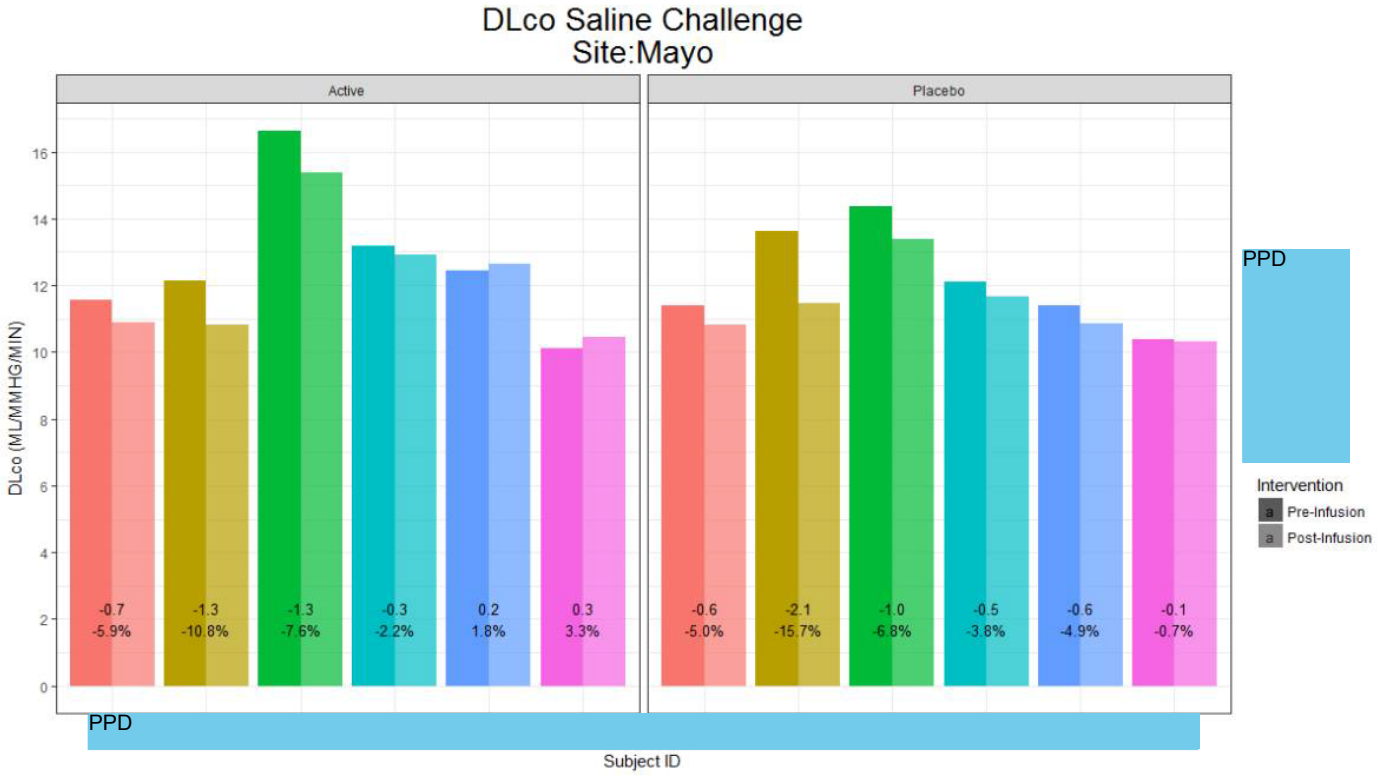
Figure 1.23
Forest Plot of End Points



NOTE: Plot adjusted accordingly to study data, text values are the mean change from baseline.

Example : EFF_F24
Protocol : 201881
Population : All Subjects

Figure 1.24
Dlco Saline Challenge Graph



NOTE: Plot adjusted accordingly to study data. The text is the difference between before and after and the percent change

Example : EFF_T1
Protocol : 201881
Population : Analysis

Table 1.01
Summary Statistics of DLco

Visit	Treatment	N	n	Mean	SD	Mean Percent Predicted	Percent Predicted SD
Screen		X	X	XX.X	XX.XX	XX.X	XX.XX
Baseline	A	X	X	XX.X	XX.XX		
Baseline after exercise	A	X	X	XX.X	XX.XX		
Day 4	A	X	X	XX.X	XX.XX		
Day 5	A	X	X	XX.X	XX.XX		
Day 5 after saline infusion	A	X	X	XX.X	XX.XX		
Day 7	A	X	X	XX.X	XX.XX		
Day 7 after exercise	A	X	X	XX.X	XX.XX		
Baseline	B	X	X	XX.X	XX.XX		
Baseline after exercise	B	X	X	XX.X	XX.XX		
Day 4	B	X	X	XX.X	XX.XX		
Day 5	B	X	X	XX.X	XX.XX		
Day 5 after saline infusion	B	X	X	XX.X	XX.XX		
Day 7	B	X	X	XX.X	XX.XX		
Day 7 after exercise	B	X	X	XX.X	XX.XX		
Follow-up	NA	X	X	XX.X	XX.XX		

Example : EFF_T2
Protocol : 201881
Population : Analysis

Table 1.02
Summary Statistics of DLco Change from Baseline

Visit	Treatment	N	n	Mean	SD
Baseline after exercise	A	X	X	XX.X	XX.XX
Day 4	A	X	X	XX.X	XX.XX
Day 5	A	X	X	XX.X	XX.XX
Day 5 after saline infusion	A	X	X	XX.X	XX.XX
Day 7	A	X	X	XX.X	XX.XX
Day 7 after exercise	A	X	X	XX.X	XX.XX
Baseline after exercise	B	X	X	XX.X	XX.XX
Day 4	B	X	X	XX.X	XX.XX
Day 5	B	X	X	XX.X	XX.XX
Day 5 after saline infusion	B	X	X	XX.X	XX.XX
Day 7	B	X	X	XX.X	XX.XX
Day 7 after exercise	B	X	X	XX.X	XX.XX

Example : EFF_T3
Protocol : 201881
Population : Analysis

Table 1.03
Summary Statistics of DLno

Visit	Treatment	N	n	Mean	SD
Screen		X	X	XX.X	XX.XX
Baseline	A	X	X	XX.X	XX.XX
Baseline after exercise	A	X	X	XX.X	XX.XX
Day 4	A	X	X	XX.X	XX.XX
Day 5	A	X	X	XX.X	XX.XX
Day 5 after saline infusion	A	X	X	XX.X	XX.XX
Day 7	A	X	X	XX.X	XX.XX
Day 7 after exercise	A	X	X	XX.X	XX.XX
Baseline	B	X	X	XX.X	XX.XX
Baseline after exercise	B	X	X	XX.X	XX.XX
Day 4	B	X	X	XX.X	XX.XX
Day 5	B	X	X	XX.X	XX.XX
Day 5 after saline infusion	B	X	X	XX.X	XX.XX
Day 7	B	X	X	XX.X	XX.XX
Day 7 after exercise	B	X	X	XX.X	XX.XX
Follow-up	NA	X	X	XX.X	XX.XX

Example : EFF_T4
Protocol : 201881
Population : Analysis

Table 1.04
Summary Statistics of FVC

Visit	Treatment	N	n	Mean	SD
Baseline	A	X	X	XX.X	XX.XX
Day 4	A	X	X	XX.X	XX.XX
Day 7	A	X	X	XX.X	XX.XX
Baseline	B	X	X	XX.X	XX.XX
Day 4	B	X	X	XX.X	XX.XX
Day 7	B	X	X	XX.X	XX.XX
Follow-up	NA	X	X	XX.X	XX.XX

Example : EFF_T5
Protocol : 201881
Population : Analysis

Table 1.05
Summary Statistics of FVC Change from Baseline

Visit	Treatment	N	n	Mean	SD
Day 4	A	X	X	XX.X	XX.XX
Day 7	A	X	X	XX.X	XX.XX
Day 4	B	X	X	XX.X	XX.XX
Day 7	B	X	X	XX.X	XX.XX

Example : EFF_T6
Protocol : 201881
Population : Analysis

Table 1.06
Summary of Statistical Analysis Results of DLco

		Adjusted Mean Difference Estimate	95% CI
Treatment	Placebo		
XX.XX	XX.XX	XX.XX	(XX.XX, XX.XX)

NOTE: Table adjusted accordingly to the study data, with model details added as footnotes.

Example : EFF_T7
Protocol : 201881
Population : Analysis

Table 1.07
Summary Statistics of Ve/VCO2 Ratio

Period	Sequence	Treatment	N	Visit	Mean At Rest	SD At Rest	Mean Post 1 Min	SD Post 1 Min	Mean Post 2 Min	SD Post 2 Min	Mean Post 3 Min	SD Post 3 Min	Mean Recovery	SD Recovery
1	AB	A	X	Baseline	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX
		A	X	Day 7	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX
2	AB	B	X	Baseline	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX
		B	X	Day 7	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX
Follow-up	AB	NA	X	Follow-up	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX
1	BA	B	X	Baseline	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX
		B	X	Day 7	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX
2	BA	A	X	Baseline	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX
		A	X	Day 7	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX
Follow-up	BA	NA	X	Follow-up	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX

Example : EFF_T8
Protocol : 201881
Population : Analysis

Table 1.08
Summary Statistics of Ve/VCO2 Ratio Change from Baseline

Period	Sequence	Treatment	N	Visit	Mean At Rest	SD At Rest	Mean Post 1 Min	SD Post 1 Min	Mean Post 2 Min	SD Post 2 Min	Mean Post 3 Min	SD Post 3 Min	Mean Recovery	SD Recovery
1	AB	A	X	Day 7	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX
2	AB	B	X	Day 7	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX
Follow-up	AB	NA	X	Follow-up	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX
1	BA	B	X	Day 7	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX
2	BA	A	X	Day 7	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX
Follow-up	BA	NA	X	Follow-up	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX	XX.X	XX.XX

Example : EFF_T9
Protocol : 201881
Population : Analysis

Table 1.09
Summary Statistics of Dyspnea

Visit	Treatment	N	n	Mean	SD	Median	Range	Percent of Patients with at Least 1-Point Improvement[1]	Frequency of Item Scores				
									1	2	3	4	5
Baseline Pre-Exercise	A	X	X	XX.X	XX.XX	XX.X	X - X		X	X	X	X	X
Baseline Post-Exercise	A	X	X	XX.X	XX.XX	XX.X	X - X	XX.XX	X	X	X	X	X
Day 5 Sitting	A	X	X	XX.X	XX.XX	XX.X	X - X	XX.XX	X	X	X	X	X
Day 5 Supine	A	X	X	XX.X	XX.XX	XX.X	X - X	XX.XX	X	X	X	X	X
Day 7 Pre-Exercise	A	X	X	XX.X	XX.XX	XX.X	X - X	XX.XX	X	X	X	X	X
Day 7 Post-Exercise	A	X	X	XX.X	XX.XX	XX.X	X - X	XX.XX	X	X	X	X	X
Baseline Pre-Exercise	B	X	X	XX.X	XX.XX	XX.X	X - X		X	X	X	X	X
Baseline Post-Exercise	B	X	X	XX.X	XX.XX	XX.X	X - X	XX.XX	X	X	X	X	X
Day 5 Sitting	B	X	X	XX.X	XX.XX	XX.X	X - X	XX.XX	X	X	X	X	X
Day 5 Supine	B	X	X	XX.X	XX.XX	XX.X	X - X	XX.XX	X	X	X	X	X
Day 7 Pre-Exercise	B	X	X	XX.X	XX.XX	XX.X	X - X	XX.XX	X	X	X	X	X
Day 7 Post-Exercise	B	X	X	XX.X	XX.XX	XX.X	X - X	XX.XX	X	X	X	X	X
Follow-up	NA	X	X	XX.X	XX.XX	XX.X	X - X		X	X	X	X	X

Example : EFF_T11
Protocol : 201881
Population : Analysis

Table 1.11
Summary Statistics of Respiratory Rate

	Day -1						Day 4						Day 7					
	Treatment			Placebo			Treatment			Placebo			Treatment			Placebo		
	Mean	SD	Number of Hours Included	Mean	SD	Number of Hours Included	Mean	SD	Number of Hours Included	Mean	SD	Number of Hours Included	Mean	SD	Number of Hours Included	Mean	SD	Number of Hours Included
Lying																		
Standing																		
Leaning																		

Example : EFF_T12
Protocol : 201881
Population : Analysis

Table 1.12
Summary Statistics of DLco Change from Intervention

Visit	Treatment	N	n	Mean	SD
Baseline change from exercise	A	X	X	XX.X	XX.XX
Day 5 change from saline infusion	A	X	X	XX.X	XX.XX
Day 7 change from exercise	A	X	X	XX.X	XX.XX
Baseline change from exercise	B	X	X	XX.X	XX.XX
Day 5 change from saline infusion	B	X	X	XX.X	XX.XX
Day 7 change from exercise	B	X	X	XX.X	XX.XX

Example : EFF_L1
Protocol : 201881
Population : All Subjects

Listing 1
Listing of Gas Diffusion

Sequence	Treatment	Subject	Visit	DLco	DLno	D_M	VE/VCO_2
AB		1	Screening				
			Period 1 Baseline				
	A		Period 1 Day -1 Post Exercise				
	A		Period 1 Day 4				
	A		Period 1 Day 5				
	B		Period 1 Day 5 Post-Saline				
			Period 2 Baseline				
	B		Period 2 Day -1 Post Exercise				
	B		Period 2 Day 4				
	B		Period 2 Day 5				
	B		Period 2 Day 5 Post-Saline				
			Follow-Up				

Example : EFF_L2
Protocol :
Population : Safety

Listing 2
Listing of Gas Diffusion Change from Baseline

Sequence	Treatment	Subject	Visit	Change in DLco	Change in DLno	Change in D_M	Change in VE/VCO_2
AB	A		Period 1 Day -1 Post Exercise				
	A		Period 1 Day 4				
	A		Period 1 Day 5				
	A		Period 1 Day 5 Post-Saline				
	B		Period 2 Day -1 Post Exercise				
	B		Period 2 Day 4				
	B		Period 2 Day 5				
	B		Period 2 Day 5 Post-Saline				