Division: World Wide Development
Retention Category: GRS019
Information Type: Reporting and Analysis Plan

Title:	Reporting and Analysis Plan for AMB114588: An open-label, long term extension study for treatment of pulmonary arterial hypertension in paediatric patients aged 8 years up to 18 years who have participated in AMB112529 and in whom continued treatment with ambrisentan is desired.

Compound Number: GSK1325760

Effective Date: 03 Jun 2022

Description: This document outlines the safety and efficacy reporting planned for protocol AMB114588 by GlaxoSmithKline (GSK).
Identifier/Version Number: Version 2.0
Subject: GSK1325760, Pulmonary Arterial Hypertension, Long Term Extension, Paediatrics; Reporting; Tables, Figures, Listings (TFLs)
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ABBREVIATIONS

6MWD	6 minute walking distance test
AE	Adverse Event
ALT	alanine aminotransferase
AST	aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical
BMI	Body mass index
BSA	Body surface area
DBF	Database Freeze
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
FC	Functional Class
GGT	gamma glutamyl transferase
GSK	GlaxoSmithKline
IDSL	Integrated Data Standards Library
IP	Investigational Product
ITT	Intent-to-Treat
kg	Kilogram
m	Meter
MedDRA	Medical Dictionary for Regulatory Activities
mg	milligram
NT-Pro BNP	N-Terminal pro-B-type Natriuretic Peptide
PAH	Pulmonary Arterial Hypertension
PD	Pharmacodynamic
PDE-5	Phosphodiesterase type 5
PHS	Physical Summary
PK	Pharmacokinetic
PSS	Psychosocial Summary
PT	Preferred Term
RA	Right atrial
RV	Right ventricle
SAE	Serious Adverse Event
SAS	Statistical Analysis Ststem
SD	Standard Deviation
SF	Short Form
SOC	System Organ Class
TAPSE	Tricuspid annular plane systolic excursion
TEAE	Treatment-emergent adverse events
TRJ	Tricuspid regurgitant jet
ULN	Upper limit of normal
WHO	World Health Organization

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1. INTRODUCTION

This Reporting and Analysis Plan (RAP) outlines the safety and efficacy reporting planned for protocol AMB114588 for provision to GSK.
In this RAP, reference is made to the protocol AMB114588 dated 8th February 2011, and subsequent amendments.

2. STUDY OBJECTIVE(S) AND ENDPOINT(S)

2.1. Study Objective(s)

This final RAP was updated following Protocol Amendment 4, in which the study was brought to early closure prior to the remaining active subjects either completing 18 years of treatment (1 subject) and/or having a pubertal assessment at 20 years of age.

2.1.1. Primary Objective

The primary objective of this study is to evaluate the long term safety and tolerability of ambrisentan in the paediatric (aged 8 years up to 18 years) PAH population.

2.1.2. Secondary Objectives

The secondary objective is to obtain supportive efficacy data (change from baseline in efficacy parameters) on the paediatric use of ambrisentan in PAH.

2.2. Study Endpoint(s)

2.2.1. Primary Endpoints

- Adverse Events;
- Serious Adverse Events;
- Clinical laboratory parameters;
- Physical examination (including height, weight, body mass index / body surface area, oxygen saturation, jugular venous pressure, liver size, and presence of peripheral oedema and/or ascites);
- Vital Signs;
- Pubertal development (change from Study AMB112529 baseline in endocrinology assessments every six months and at 20 years of age unless pubertal maturity has been reached in previous visits)
- The time to change in dose of ambrisentan or other targeted PAH therapeutic agents (prostanoids, PDE-5 inhibitors) due to tolerability issues (e.g. adverse events).

2.2.2. Secondary Endpoints

2.2.2.1. Pharmacokinetics

Not applicable.

2.2.2.2. Efficacy

- All cause mortality;
- The change from Study AMB112529 baseline in the 6 minute walking distance (6MWD) test evaluated every six months;
- The time to clinical worsening of PAH;
- The time to addition of another targeted PAH therapeutic agents (prostanoids, PDE-5 inhibitors) due to the following reasons:
  - Deterioration of clinical condition;
  - Lack of beneficial effect with previous therapy (not reaching set treatment goals);
- The time to change in dose of ambrisentan or other targeted PAH therapeutic agents (prostanoids, PDE-5 inhibitors) due to deterioration of clinical condition;
- The change from Study AMB112529 baseline in Subject Global Assessment every three months using the SF-10 health survey for children;
- The change from Study AMB112529 baseline in WHO functional class every six months;
- Change from Study AMB112529 baseline in N-terminal pro-B-type natriuretic peptide (NT-Pro BNP) concentration every six months.
- School days missed due to PAH.

2.2.2.3. Exploratory

- The change from Study AMB112529 baseline in major prognostic factors based on echocardiogram: pericardial effusion, right atrial (RA) pressure, tricuspid annular plane systolic excursion (TAPSE), eccentricity index (systolic and diastolic), and right ventricular (RV) pressure by tricuspid regurgitant jet (TRJ) velocity at every 6 months.

2.2.2.4. Other

- The change from Study AMB112529 baseline in cardiopulmonary hemodynamic assessments data in subjects in whom hemodynamic data is considered part of the standard of care.

2.3. Statistical Hypotheses

No formal hypothesis is planned.

2.4. Pharmacokinetic (PK) and PK/Pharmacodynamic (PD) hypotheses

Not applicable.

3. STUDY DESIGN

This is an open label, long term extension to Study AMB112529. All subjects may remain in the extension study for a minimum of six months. Beyond the six month period, subjects may continue in the extension study until one of the following conditions is met:

- The subject turns 18 years of age (when the subject can receive marketed product). or the subject has reached pubertal maturity before 18 years of age and ambrisentan can be supplied through a named patient or expanded access program until the subject reaches 18 years of age;
- The product is approved and available for use in the subject's age group;
- Development for use in the paediatric population is discontinued;
- The subject decides he/she no longer wants to participate in the study;
- The investigator considers it is in the best interest of the subject to discontinue ambrisentan (e.g. for safety reasons).

Protocol waivers or exemptions are not allowed. Therefore, adherence to the study design requirements, including those specified in the Time and Events Table, are essential.
For further details regarding the study design, please refer to the protocol.

4. PLANNED ANALYSES

4.1. Interim Analyses

An interim analysis was added post the finalization of the study protocol, in order to provide analyses in support of regulatory interactions. All data collected by a pre-determined clinical cut-off date will be analyzed as per this RAP for the interim analysis report.

4.2. Final Analysis

This analysis plan outlines the final analysis that will be performed on the safety and efficacy endpoints of this study, once Database Freeze (DBF) has taken place.

5. SAMPLE SIZE CONSIDERATIONS

Sample size is based on feasibility. Due to low prevalence of the disease, no more than 66 subjects will be enrolled in the study. No sample size sensitivity calculations were performed. No sample size re-estimation is planned.

6. ANALYSIS POPULATIONS

The Intention-to-Treat (ITT) Population will consist of all subjects who received at least 1 dose of study drug. For the ITT population, subjects were considered as belonging to their treatment group at the start of study AMB114588. The ITT population will be used in all efficacy summaries.

The Safety Population is defined as all subjects who received at least 1 dose of study drug. Subjects were considered as belonging to the treatment group according to the highest dose received. The Safety Population will be used in all safety summaries.

The Idiopathic Group Population is defined as subjects having an Idiopathic Aetiology of PAH (IPAH) at start of study treatment in AMB112529.

7. TREATMENT COMPARISONS

There are no formal comparisons planned for this study. Doses of ambrisentan will be summarized descriptively based on available data.

7.1. Data Display Treatment and Other Sub-group Descriptors

Refer to the data display specification in Section 19 for examples showing how treatment groups will be displayed in the study report data displays.

8. GENERAL CONSIDERATIONS FOR DATA ANALYSES

All programming of tables, figures and listings will be performed using Statistical Analysis System (SAS®) version 8.2 or higher.

8.1. Examination of Subgroups

Selected safety and efficacy outputs will be produced by age strata (8-11, 12-18 years).

Selected outputs will also be produced for patients enrolled at centres in Japan to support registration activities.

9. DATA HANDLING CONVENTIONS

All data displays will be presented according to the GSK's Integrated Data Standards Library (IDSL) statistical display principles. The file extension used for landscape tables and listings will be L10, with point size of 10, line size of 108 and 43 lines per page. Where data are sparse, empty tables may be produced with the "Data too sparse for table to be produced" or "No Data to Report" or similar.

All data collected on the electronic case report form (eCRF) will be listed. Data collected outside of the eCRFs (eg. labs, SF10) will also be listed. All listings will be presented by treatment group and subject identification number.

9.1. Premature Withdrawal and Missing Data

Subjects who withdraw from the study will not be replaced and all information obtained from them will be included in the summaries.

9.1.1. Missing Efficacy Outcomes Data

No imputation will be made for any missing numerical data, unless otherwise specified.

Missing data will generally not be considered in the calculation of percentages (i.e., the denominator will not include subjects who have missing data at a given time point).

9.1.2. Missing AE data

Where a start date for an adverse event (AE) is partial or missing, the following imputation rules will be applied:

- If day portion is missing, set day to 1.
- If month portion is missing, set month to January.
- If the date is completely missing, or if the date imputed using the above rules is prior to the first dose date, set the date to first dose date.

Where an end date for an AE is partial or missing, the following imputation rules will be applied. These will only be applied to AEs that are resolved; if they are not resolved then nothing will be imputed.

- If day portion is missing, set day to the last day of the month.
- If month portion is missing, set month to December.
- If the date is completely missing, or if the date imputed using the above rules is after the treatment end date, set the date to the treatment end date or if the treatment end date is missing then set to date of discontinuation.

No further imputation will be performed for missing data.

9.1.3. Missing Dates (other than for AEs)

For any data type that collects partial dates, impute missing day as 01 and missing month as January. If date is completely missing then date should remain missing.
Where the start date of study medication is missing, the date of randomisation will be used. Where end date of study medication is partial or missing, the last complete non-missing date of dosing will be used as the last date for determining duration of exposure.

9.1.4. Missing Items on SF-10

The SF-10 will be scored in accordance with the developer's guidelines. Out-of-range values are converted to missing values and no algorithm is used to estimate missing values. The Physical and Psychosocial summary scores are not calculated if any component scores are missing.

9.2. Derived and Transformed Data

All listings will include all subjects that have the relevant data for each listing.
The number of subjects (N) in each treatment group and overall for the population being summarised, will be displayed in each table unless specified otherwise.
For continuous data, the following summary statistics will be presented: n, mean, standard deviation (SD), median, upper and lower quartiles, minimum and maximum. Mean and median values will be reported to one decimal place greater than the original data they were collected from while the SD will be reported to two decimal places greater than the original data however, if this results in a value of 0.00 being presented then a zero (0) will be presented. Minimum and maximum values will be reported with the same precision as they were collected.

All text fields must be left justified. Numeric or numeric with some text specification (e.g., not done, unknown, <4.5, …) must be right justified.

The format for dates will be DDMMMYYYY.
All tables and listings will have the protocol number and population in the top left-hand corner and the page number in the form of page x of n will be presented in the top right-hand corner. In the bottom left-hand corner of tables and listings the name of the person who created the output followed by a colon, the output filepath and the date and time of the production of the output, in the form DDMMMYYYY HH:MM, will be displayed.
If a count in a table summary is zero (0) then a percentage will not be presented.
To determine whether an adverse event is on-treatment and a medication is prior or concomitant, imputation of missing or partial start and stop dates is required (see RAP Section 9.1.2 and Section 9.1.3). Imputed dates will not be listed and adverse event duration will not be calculated if the start date or stop date had to be imputed.

9.2.1. Baseline

Baseline values are those collected prior to the first dose (from Study AMB112529). Therefore, if a subject has no data for a parameter on Day 1 (prior to first dose) then the data from their last pre-treatment assessment will be used.

9.2.2. Change from baseline and percentage change from baseline

For untransformed data change from baseline at Week X will be calculated as Week X value minus baseline value. The percentage change from baseline at Week X will be calculated as: 100 × (Week X value – baseline value) / baseline value.

For log-transformed data (see Section 9.2.8), ratio to baseline expressed as percentage change will be calculated by taking the mean change on the log scale, exponentiating, subtracting 1 and multiplying by 100.

(Exp(mean of (Log x - Log baseline)) -1)*100

9.2.3. WHO FC change from baseline categorisation 1

Note that based on the study inclusion criteria subjects must have a WHO FC of II or III at baseline. Change from baseline at Week X will be calculated as Week X value minus baseline value, thus categories may be -2, -1, 0, +1, +2.

	Post Baseline WHO FC
Baseline WHO FC	CCI [redacted]

9.2.4. WHO FC class change from baseline categorisation 2

CCI [redacted] in Change from Baseline Categorisation
CCI [redacted] in Change from Baseline Categorisation
CCI [redacted] in Change from Baseline Categorisation

9.2.5. Study Day

Study Day 1 is defined as the day of the first dose of study drug in AMB112529.
Relative Day to start of study medication for an Event is defined as:
Date of event - Date of first study medication + 1, if the event is on or after the first dose date.
Date of event - Date of first study medication, if the event is prior to the first dose date.
Relative Day to end of medication for an Event is defined as:
Date of event - Date of last study medication + 1, if the event is on or after the last dose date.
Date of event - Date of last study medication, if the event is prior to the last dose date.

9.2.6. Age Calculation

Age in years at baseline will be derived as a whole number according to the IDSL standard algorithm (see Appendix 1).

9.2.7. Duration of Exposure

Duration of exposure will be calculated in days as (Treatment stop date – Treatment start date in AMB112529) + 1.

9.2.8. Transformations for Efficacy Outcomes

A log transformation will be applied to NT-proBNP data.

Summaries of the relative changes from baseline based on analysis of log-transformed data will include the geometric mean and coefficient of variation (calculated as below based on the logged values) and the geometric mean of the ratio of the value of the endpoint at the time point of interest to the baseline value (see Section 9.2.2) .

Geometric mean = $\exp(\mu)$

Coefficient of variation =s $100 \times \sqrt{[\exp(\sigma^2) - 1]}$

9.2.9. Treatment Compliance Rates

Compliance to study medication is recorded at each visit in one of the following categorical groups:

- 0% compliant (subject did not take any doses)
- >0% and < 80% compliant (subject missed a number of doses)
- >=80% and <=120%, (number of doses taken was within compliance range)
- >120% compliant (number of doses taken exceeds compliance limits)

At the subject level compliance rate is calculated as
100*(the number of visits at which the subject was compliant (i.e. ≥80% and ≤120%) / (the sum of all study visits for the subject).

At a treatment group level compliance rate is calculated as
100*(the total number of visits at which all subjects in that group were compliant (i.e. ≥ 80% and ≤ 120%)) / (the sum of all study visits for all subjects in that group).

9.3. Assessment Windows

All data will be reported for the whole study period.
Unscheduled assessments will not be slotted to a particular time point, but will remain as unscheduled unless otherwise specified.
Time points relating to nominal visits will be used in tables, figures and listings.
Time to clinical worsening of PAH and time to liver event will be calculated using the date of assessment.

9.4. Values of Clinical Concern

9.4.1. Laboratory Parameters

The following values of potential clinical concern will be considered:

Values of potential clinical concern values will be defined for laboratory parameters as follows: **Parameter**	**Code**	**Units**	**Low Concern Value (SI units)**	**High Concern Value (SI units)**	**Worse case direction**
Hematology					
Hemoglobin	HGB	G/L	Males: < 98 Females: < 91	Males: > 180.0 Females: > 161.0	Low

Values of potential clinical concern values will be defined for laboratory parameters as follows: **Parameter**	**Code**	**Units**	**Low Concern Value (SI units)**	**High Concern Value (SI units)**	**Worse case direction**
Hematocrit	HCT	% (1)	Males: < 32.0 (<0.32) Females: <29.0 (<0.29)	Males: > 54.0 (>0.54) Females: > 50.6 (>0.506)	Low
Platelets	PLATE	10^9/L (same as GI/L)	< 100	> 500	Low
Chemistry					
Total bilirubin	BILTOT	UMOL/L	None	>= 34.2	High
AST	ASAT	IU/L	None	>= 3 x ULN	High
ALT	ALAT	IU/L	None	>= 3 x ULN	High
GGT	GGT	IU/L	None	>= 3 x ULN	High
Creatinine	CREAT	UMOL/L	None	>= 176.8	High

9.4.2. Vital Signs

The following criteria will be used to determine whether a subject's vital signs (blood pressure and heart rate) lie outside a pre-determined range of clinical concern:

Parameter	Code	Units	Low Concern Value	High Concern Value
Heart Rate	PUL	Bpm	< 50	> 120
Systolic	SYS	mm Hg	< 80	> 160 mm Hg > 30 mm Hg change from Baseline
Diastolic	DIA	mm Hg	< 40	> 110 mm Hg > 20 mm Hg change from Baseline
Body weight	WT	Kg	< 20	

10. STUDY POPULATION

Study population data will be presented for the Intent-to-Treat Population unless otherwise specified.

10.1. Disposition of Subjects

The number of subjects eligible for each of the analysis populations will be summarised by treatment group and overall, and by country and centre.
The number of subjects completing/withdrawing from the study along with the reasons for withdrawal will be summarised by treatment group and overall.

10.2. Protocol Deviations

The number of subjects with important protocol deviations will be summarised by treatment group and overall.

A summary of subjects who did not satisfy all inclusion and exclusion criteria will be provided by treatment group.

The protocol deviations will be reviewed by the clinical team after the database release and prior to the database freeze, to determine which ones are considered to be important Demographic and Baseline Characteristics.

The number and percentage of subjects in each category for categorical variables or summary statistics for continuous variables will be summarised by treatment group and overall. These include age, age strata, sex, child-bearing potential, ethnicity and geographic ancestry, aetiology of PAH strata, duration of PAH, PAH therapy use, WHO FC score and 6 minute walk distance.

10.3. Medical Conditions

The number and percentage of subjects with past or current medical conditions will be summarised by treatment group and overall, for any condition and by condition classification.

10.4. Prior and Concomitant Medications

The GSKdrug dictionary will be used to code drug names.
Prior medications are those that started and stopped prior to the date of first study treatment. Ongoing medications at baseline are those started before first dose date of study drug, which were continued during the treatment phase.
Lab medications are defined as:

- Medications that start prior to or on the date of first study treatment and that stopped prior to the date of last study treatment,
- Medications that start prior to or on the date of first study treatment and continued after the date of last study treatment,
- Medications that start after the date of first study treatment and that stopped prior to the date of the last study treatment,
- Medications that start after the date of first study treatment and continued after the date of last study treatment.

Any medications that started after the last study treatment are classed as post-treatment medications.
Note that it will be assumed that the medication has been taken by the medication start and stop dates recorded in the eCRF.
The number and percentage of subjects with concomitant medications will be summarised by Anatomical Therapeutic Chemical (ATC) Classification System code and drug name Preferred term by treatment group and overall.
The number and percentage of subjects with ongoing (at entry to AMB114588) and concomitant PAH therapy (at 6 months after entry into AMB114588 and then annually as well as the final visit) will be summarised by preferred term, by treatment group and overall. The ATC codes from the GSKDrug dictionary for the groupings of PAH therapy will be agreed with the Clinical Safety Group and provided in a separate file. This includes:

- PDE5i
- Prostanoid

10.5. Treatment Compliance

Every three months, treatment compliance will be recorded as 0%, >0% - <80%, =>80% - <=120% and >120%.
The number and percentage of subjects in each compliance category will be summarised at each visit by treatment group and overall.

11. SAFETY ANALYSES

Safety data will be presented for the Safety Population unless otherwise specified.

11.1. Extent of Exposure

The number of days of exposure to study drug will be summarised by treatment group and overall.
This number of days of exposure will be categorised in 30 day intervals as follows: <=30 days, 31-60 days, 61-90 days etc.
The number and percentage of subjects in each of these categories will be summarised by treatment group and overall.

11.2. Adverse Events

All AEs will be categorised into Preferred Term (PT) and associated System Organ Class (SOC) using the Medical Dictionary for Regulatory Activities (MedDRA) coding dictionary.
Only treatment-emergent adverse events (TEAEs) will be included in summary tables.
TEAEs are defined as those events that start on or after first dose date of study treatment.
Any subject with at least one reported TEAE will be classified as a subject with:

- A TEAE,
- A TEAE leading to study treatment discontinuation (definitive or temporary),
- A TEAE leading to study withdrawal,
- At least one serious TEAE.

The numbers and percentages of subjects with at least one reported TEAE will be summarised by treatment group and overall according to:

- PT,
- SOC and PT,
- SOC and PT by intensity,
- SOC and PT by relationship to study treatment,
- PT by action taken with investigational product (IP).

Recurring TEAEs (i.e. successive TEAEs classified with the same PT) for a given subject will only be counted once and only their most severe intensity will be tabulated.
The cumulative incidence of each TEAE will also be summarised by SOC and PT and the following categories: <=3 months, >3 to <=6months, etc.

TEAEs will be listed by SOC and PT, by treatment with the number of subjects who experienced the event and their subject numbers presented. A more detailed listing will also be produced for all subjects who experienced an AE.

11.3. Adverse Events Leading to Discontinuation of Investigational Product and/or Withdrawal from the Study and Other Significant Adverse Events

The numbers and percentages of subjects with at least one reported TEAE leading to discontinuation of the investigational product or withdrawal from the study will be summarised by SOC and PT for each treatment group and overall. Covid-19 adverse event data will be shown here if any exist.

11.4. Deaths and Serious Adverse Events

Summary tables detailed in sections 11.2 and Section 11.3 (with the exception of cumulative incidence) will be repeated for serious TEAEs.

Summary tables will also be presented for serious TEAEs by PT and outcome for each treatment group and overall.

A summary of serious TEAEs displaying the number of subjects and occurrences will also be presented.

In addition, the number of subjects with fatal TEAEs and fatal TEAEs related to IP will be summarised by SOC and PT for each treatment group and overall.

11.5. Adverse Events of Special Interest

Summary tables detailed in sections 11.2 and Section 11.3 (with the exception of tables by maximum intensity/grade, action taken and relation to IP) will be repeated for AEs of special interest. MedDRA preferred terms and codes for AEs of special interest will be agreed with Clinical Safety Group and provided in a separate file.

The adverse events of special interest are:

- Anaemia
- Hepatoxicity
- Hypersensitivity
- Hypotension
- Male infertility
- Oedema
- Fluid retention

11.6. Non-serious Adverse Events

A summary of the most common (>=5%) non-serious TEAEs displaying the number of subjects and occurrences will also be presented.

11.7. Laboratory Evaluations

Absolute values and changes from baseline of laboratory data will be summarised for each visit, by treatment group and overall.

Separate tables will be presented for haematology data, clinical chemistry data and endocrine data (females only).
The number and percentages of subjects with laboratory values above and below reference ranges for potential clinical concern described in Section 9.4.1 will be summarised for each visit, by treatment group and overall.

11.7.1. Liver Events

The number and percentage of subjects reporting a liver event will be summarised: overall, during and post study treatment.

The following will be listed by treatment group, for subjects with liver events:

- liver chemistry result involved in the event.
- Time from first and last dose to start of event
- Patient specific information for liver events
- Medical conditions.
- Liver biopsy details.
- Liver imaging details.

11.7.2. Vital Signs

Absolute values and changes from baseline of vital signs data will be summarised for each visit, by treatment group and overall.
The number and percentages of subjects with vital signs values or change from baseline values above and below reference ranges for potential clinical concern described in Section 9.4.2 will be summarised for each visit, by treatment group and overall.

11.7.3. Physical Examination

Physical examination at each visit will be summarised by treatment group and overall.

11.8. 12-Lead ECG

The number and percentages of subjects with electrocardiogram (ECG) abnormalities (clinically significant and not clinically significant) will be summarised for each visit, by treatment group and overall.

11.9. Endocrinology

The following will be summarised for each visit (as appropriate) by treatment group and overall.

- Female breast development and pubic hair development.
- Male testicular volume, genital development and pubic hair development.
- Change from baseline in male testicular volume.
- Change from baseline in plasma endocrine parameters (Follicle Stimulating Hormone, Luteinizing Hormone, Sex Hormone Binding Globulin, Total Testosterone and Inhibin B) by gender.

The above tables will also be summarised by pubertal status at baseline defined as follows:

Male: Pre-pubertal: testicular volume < 4 ml, Post-pubertal: testicular volume ≥ 4 ml.
Female: Pre-pubertal: Stage 1 breast development, Post-pubertal: Stage ≥ 2 breast development.

11.10. Change in dose due to tolerability issues

The time to change in dose of ambrisentan or other targeted PAH therapeutic agents (prostanoids, PDE-5 inhibitors) due to tolerability issues (e.g. adverse events) will be summarised by treatment group and overall.

11.11. Pregnancies (as applicable)

A listing of pregnancy events will be provided, as necessary.

12. EFFICACY ANALYSES

Efficacy data will be presented for the Intent-to-Treat Population unless otherwise specified.
The following will be summarised for observed case data for each visit (as appropriate) by treatment group and overall.

- All cause mortality.
- The absolute value, change from Study AMB112529 baseline and % change from baseline in the 6 minute walking distance (6MWD) test, overall and by oxygen use.
- The walking duration for subjects who walked less than six minutes.
- The use of oxygen during the 6MWD test.
- The time to clinical worsening of PAH.
- The criteria for clinical worsening of PAH.
- The time to addition of another targeted PAH therapeutic agent (prostanoids, PDE-5 inhibitors) due to the following reasons:
    - Deterioration of clinical condition;
    - Lack of beneficial effect with previous therapy (not reaching set treatment goals);
- The time to change in dose of ambrisentan or other targeted PAH therapeutic agents (prostanoids, PDE-5 inhibitors) due to deterioration of clinical condition.
- WHO Functional Class and change from Study AMB112529 baseline in WHO Functional Class.
- The absolute value and percent change from Study AMB112529 baseline, using log-transformed data, in N-terminal pro-B-type natriuretic peptide (NT-Pro BNP) concentration.
- The absolute value and change from baseline in the number of school days, missed school days and missed school days due to PAH.
- The absolute value and change from Study AMB112529 baseline in Subject Global Assessment as measured by the SF-10 health survey for children and summarised for the physical summary score (PHS-10) and the psychosocial summary score (PSS-10).

Further table will be produced summarizing change in WHO FC scores categorized in terms of [redacted] and in terms of [redacted] (see Section 9.2.3 and Section 9.2.4).

12.1. Exploratory analyses

The following will be summarised for each visit, by treatment group and overall.

- The absolute value and change from Study AMB112529 baseline in exploratory echocardiogram: pericardial effusion, right atrial pressure, tricuspid annular plane systolic excursion, eccentricity index (systolic and diastolic), tricuspid regurgitant jet velocity and right ventricular pressure.

12.2. Other analyses

The following will be listed for each visit, by treatment group.

- The absolute value and change from Study AMB112529 baseline in cardiopulmonary hemodynamics (at centres where the collection of hemodynamic data is considered part of the standard of care):- heart rate, mean arterial blood pressure, mean pulmonary arterial pressure, mean right atrial pressure, left ventricular end diastolic pressure or pulmonary capillary wedge pressure, pulmonary vascular resistance, cardiac output, cardiac index (calculated value), arterial oxygen saturation and mixed venous oxygen saturation.

13. ADDITIONAL ANALYSES DUE TO THE COVID-19 PANDEMIC

13.1 Study Population

No changes required as enrollment was completed at time of COVID-19 restrictions.

13.2 Subject Disposition and Protocol Deviations

A country level listing of the dates of the COVID-19 Pandemic measures will be produced, as well as a listing of visits impacted by the COVID-19 Pandemic.

Phases of COVID-19 Pandemic Measures

Pandemic measures began in different countries at different times. A dataset containing the date when pandemic measures began, as determined by the GSK country Issue Management Teams (IMT), will be used to determine the start date of pandemic measures within each country. A copy of this dataset will be taken at the time of database freeze (DBF).

The 'Summary of Subject Status and Subject Disposition for the Study Conclusion Record' and the 'Summary of Treatment Status and Reasons for Discontinuation of Study Treatment' will be repeated, with the reason for withdrawal/discontinuation categorised as due to the COVID-19 pandemic, or non-due to the COVID-19 pandemic based on information collected on the COVID-19 Pandemic Study Impact form.

13.3 Protocol Deviations

In addition to the overall summary of important protocol deviations, a separate summary will be produced of important protocol deviations related to COVID-19.

13.4 Additional Displays for Participants with a COVID-19 Infection

A participant is defined as having a suspected, probable or confirmed COVID-19 infection during the study if the answer is "Confirmed", "Probable" or "Suspected" to the case diagnosis question from the COVID-19 coronavirus infection assessment eCRF. Summaries and/or listings of the numbers of participants with a suspected, probable or confirmed COVID-19 infection, and of COVID-19 test results will be presented.

13.5 Additional Analyses Due to the COVID-19 Pandemic

Visits and assessments missed due to the COVID-19 pandemic, together with visits conducted remotely, will be summarised in a table and listed by subject. The summaries will be based on GSK Core Data Standards, and details are provided in Section 4: List of Data Displays.

13.6 Assessment of COVID-19 AEs

A terms of interest list, list code 319259, created by the GSK dictionaries group, will be used to identify all COVID-19 AEs.

The incidence of AEs and SAEs (Fatal and Non-Fatal) of COVID-19, COVID-19 AEs leading to study drug discontinuation, and COVID-19 AEs leading to study withdrawal, and COVID-19 AEs by severity, will be obtained from standard AE and SAE summaries if data exist to meet the criteria. A listing of relevant data will be created.

14. CLINICAL PHARMACOLOGY DATA ANALYSES

14.1. Pharmacokinetic Analyses

Not applicable.

14.2. Pharmacodynamic Analyses

Not applicable.

14.3. Pharmacokinetic/Pharmacodynamic Analyses

Not applicable.

15. BIOMARKER DATA ANALYSIS

Not applicable.

16. PHARMACOGENETIC DATA ANALYSES

Not applicable.

17. VIRAL GENOTYPING/PHENOTYPING

Not applicable.

18. REFERENCES

19. ATTACHMENTS

19.1. Table of Contents for Data Display Specifications

19.1.1. Tables

Table numbering for the Japanese subgroup will be add 001 at the end of the table number. Thus, Table 1.1 will become 1.1001.
Table numbering for the Age Strata subgroup will be add 002 at the end of the table number. Thus, Table 1.5 will become 1.5002.

Japanese and Age subgroup analysis will not be needed for final SAC.

Population Tables

Table Number	Title	Population	Template Table	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
1.1	Summary of Subject Disposition **(See 2 additional rows added to existing table: 1) additional row 20 year count, and 1 covid death related row)** **Prog Note:** The deaths should be mutually exclusive (ie only in 1 category)	Intent-to-Treat	1.1	X		Interim, SAC
1.2	Summary of Study Populations	Randomised	1.2			Interim, SAC
1.3	Summary of Subjects by Country and Centre	Intent-to-Treat	1.3		Disclosure	Interim, SAC
1.4	Summary of Inclusion/Exclusion Criteria Deviations	Intent-to-Treat	1.4			Interim, SAC
1.5	Summary of Demographic and Baseline Characteristics	Intent-to-Treat	1.5	X	X	Interim, SAC
1.6	Summary of Past Medical Conditions	Intent-to-Treat	1.6		X	Interim, SAC
1.7	Summary of Current Medical Conditions	Intent-to-Treat	1.6		X	Interim, SAC
1.8	Summary of Concomitant Medications	Intent-to-Treat	1.8	X		Interim, SAC
1.9	Summary of Ongoing Background PAH Therapy at Entry Visit to AMB114588 By Drug Class and Preferred Term	Intent-to-Treat	1.9		X	Interim, SAC
1.10	Summary of Ongoing Background PAH Therapy by Drug Class and Preferred Term	Intent-to-Treat	1.9		X	Interim, SAC
1.11	Summary of Compliance to Investigational Product since last visit	Intent-to-Treat	1.11			Interim, SAC
1.12	Summary of Investigational Product Compliance Overall	Intent-to-Treat	1.12			Interim, SAC
1.13	Summary of initial dose of ambrisentan at entry to AMB114588 and highest dose received during study	Intent-to-Treat	1.13			Interim, SAC
1.14	Summary of initial dose of ambrisentan at entry to AMB114588 and final dose at end of study or termination	Intent-to-Treat	1.14			Interim, SAC
1.15	Summary of Important Protocol Deviation	Intent-to-Treat	1.15			Interim, SAC
1.16	Summary of Concomitant Medications starting in AMB114588	Intent-to-treat	1.8			Added at Interim

Covid-19 Tables

Table Number	Title	Population	Template Table	Deliverable	Programming Notes
1.17	Summary of Important COVID-19 Related Protocol Deviations	Intent-to-Treat	Same as protocol DV table except subset for COVID-19 related	SAC [1]	
1.18	Summary of COVID-19 Assessments for Subjects with Suspected, Probable or Confirmed COVID-19 Case Diagnosis	Intent-to-Treat	1.19	SAC [1]	
1.19	Summary of Visits impacted by COVID-19 Pandemic	Intent-to-Treat	1.20	SAC [1]	

Efficacy Tables

Table Number	Title	Population	Template Table	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
2.1	Summary of Time to Death (All cause) (days)	Intent-to-Treat	2.1	X	X	Interim, SAC
2.2	Summary of 6 Minute Walking Distance (meters)	Intent-to-Treat	2.2	X	X	Interim, SAC
2.3	Summary of Change from Baseline in 6 Minute Walking Distance (meters)	Intent-to-Treat	2.2	X	X	Interim, SAC
2.4	Summary of Percent Change from Baseline in 6 Minute Walking Distance (meters)	Intent-to-Treat	2.2	X	X	Interim, SAC
2.5	Summary of Walking Duration (minutes) for subjects who walked less than six minutes	Intent-to-Treat	2.5	X	X	Interim, SAC
2.6	Summary of use of Oxygen during 6 Minute Walking exercise (L/min)	Intent-to-Treat	2.6	X	X	Interim, SAC
2.7	Summary of Time to Clinical Worsening of PAH (days)	Intent-to-Treat	2.7	X		Interim, SAC
2.8	Summary of Clinical Worsening of PAH	Intent-to-Treat	2.8			Interim, SAC
2.9	Summary of Time to the addition of another targeted PAH therapeutic agent (prostanoids, PDE-5 inhibitors) (days)	Intent-to-Treat	2.9	X		Interim, SAC
2.10	Summary of Time to change in dose of ambrisentan or other targeted PAH therapeutic agents (prostanoids, PDE-5 inhibitors) due to deterioration of clinical condition (days)	Intent-to-Treat	2.10	X		Interim, SAC
2.11	Summary of WHO Functional Class	Intent-to-Treat	2.11	X	X	Interim, SAC
2.12	Summary of Change from Baseline in WHO Functional Class	Intent-to-Treat	2.11	X	X	Interim, SAC
2.13	Summary of WHO Functional Class Shifts from Baseline by Visit	Intent-to-Treat	2.13	X	X	Interim, SAC
2.14	Summary of WHO Functional Class Change from Baseline Categorisation	Intent-to-Treat	2.14	X	X	Interim, SAC
2.15	Summary of Plasma NT-Pro BNP concentration (ng/L)	Intent-to-Treat	2.15	X	X	Interim, SAC
2.16	Summary of Ratio to Baseline in Plasma NT-Pro BNP concentration (%)	Intent-to-Treat	2.15	X	X	Interim, SAC

Table Number	Title	Population	Template Table	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
2.17	Summary of Exploratory Echocardiogram	Intent-to-Treat	2.17	X	X	Interim, SAC
2.18	Summary of Change from Baseline in Exploratory Echocardiogram	Intent-to-Treat	2.18	X	X	Interim, SAC
2.19	Summary of Number of Subjects with School Days	Intent-to-Treat	2.19	X	X	Interim, SAC
2.20	Summary Statistics of School Days	Intent-to-Treat	2.20	X	X	Interim, SAC
2.21	Summary Statistics of Change from Baseline in School Days	Intent-to-Treat	2.20	X	X	Interim, SAC
2.22	Summary of Subject Global Assessment (SF10 Health Survey for Children)	Intent-to-Treat	2.22	X	X	Interim, SAC
2.23	Summary of Change from Baseline in Subject Global Assessment (SF10 Health Survey for Children)	Intent-to-Treat	2.22	X	X	Interim, SAC
2.24	Summary of SF10 Health Survey – Number and Percentage of Subjects with Particular Item Responses	Intent-to-Treat	2.24	X	X	Interim, SAC
2.25	Number of subjects who achieved a clinically significant improvement (20 Meters) in 6 min walk	Intent-to-Treat	2.25			GSK SAC, Internal
2.26	Number of subjects who achieved a clinically significant improvement (20 Meters) in 6 min walk	Idiopathic Group	2.26			GSK SAC, Internal
2.27	Number of subjects who achieved an NT-proBNP levels of less than 1200 ng/L	Intent-to-Treat	2.27			GSK SAC, Internal
2.28	Number of subjects who achieved an NT-proBNP levels of less than 1200 ng/L	Idiopathic Group	2.28			GSK SAC, Internal
2.29	Distribution of NT-proBNP levels at baseline and extent of change during treatment	Intent-to-Treat	2.29			GSK SAC, Internal
2.30	Distribution of NT-proBNP levels at baseline and extent of change during treatment	Idiopathic Group	2.30			GSK SAC, Internal
2.31	The Event Rate of the Clinical Worsening Endpoint per 100 Patient-Years	Intent-to-Treat	2.31			GSK SAC, Internal

Safety Tables

Table Number	Title	Population	Template Table	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
3.1	Summary of Exposure to Investigational Product **New Footnote:** For subjects missing their last exposure date at the time of study end, their last visit date in the study was used.	Safety	3.1	X	X	Interim, SAC
3.2	Summary of Treatment-Emergent Adverse Events	Safety	3.2	X	X	Interim, SAC
3.3	Summary of Treatment-Emergent Adverse Events by Preferred Term	Safety	3.3		X	Interim, SAC
3.4	Summary of Treatment-Emergent Adverse Events by Maximum Intensity	Safety	3.4	X		Interim, SAC
3.5	Summary of Treatment-Emergent Adverse Events by Action Taken with IP	Safety	3.5			Interim, SAC

Table Number	Title	Population	Template Table	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
3.6	Summary of Treatment-Emergent Adverse Events leading to Permanent Discontinuation of IP or Withdrawal from the Study	Safety	3.2		X	Interim, SAC
3.7	Summary of Treatment-Emergent Adverse Events related to IP	Safety	3.2	X	X	Interim, SAC
3.8	Summary of Cumulative Incidence of Treatment-Emergent Adverse Events by Time to First Occurrence	Safety	3.8			Interim, SAC
3.9	Summary of Serious Treatment-Emergent Adverse Events	Safety	3.2		X	Interim, SAC
3.10	Summary of Serious Treatment-Emergent Adverse Events – Number of Subjects and Occurrences	Safety	3.10		Disclosure	Interim, SAC
3.11	Summary of Serious Treatment-Emergent Adverse Events by Outcome	Safety	3.11			Interim, SAC
3.12	Summary of Serious Treatment-Emergent Adverse Events by Action Taken with IP	Safety	3.5			Interim, SAC
3.13	Summary of Serious Treatment-Emergent Adverse Events leading to Permanent Discontinuation of IP or Withdrawal from the Study	Safety	3.2			Interim, SAC
3.14	Summary of Serious Treatment-Emergent Adverse Events related to IP	Safety	3.2		Disclosure	Interim, SAC
3.15	Summary of Fatal Serious Treatment-Emergent Adverse Events	Safety	3.2			Interim, SAC
3.16	Summary of Fatal Serious Treatment-Emergent Adverse Events related to IP	Safety	3.2		Disclosure	Interim, SAC
3.17	Summary of Treatment-Emergent Adverse Events of Special Interest	Safety	3.2	X		Interim, SAC
3.18	Summary of Treatment-Emergent Adverse Events of Special Interest leading to Permanent Discontinuation of IP or Withdrawal from the Study	Safety	3.2			Interim, SAC
3.19	Summary of Cumulative Incidence of Treatment-Emergent Adverse Events of Special Interest by Time to First Occurrence	Safety	3.8			Interim, SAC
3.20	Summary of Most Common (>5%) Non-Serious Treatment-Emergent Adverse Events – Number of Subjects and Occurrences	Safety	3.10		Disclosure	Interim, SAC
3.21	Summary of Haematology Data	Safety	3.21	X		Interim, SAC
3.22	Summary of Change from Baseline in Haematology Data	Safety	3.21	X		Interim, SAC
3.23	Summary of Haematology Data of Potential Clinical Concern	Safety	3.23	X		Interim, SAC
3.24	Summary of Clinical Chemistry Data	Safety	3.21	X		Interim, SAC
3.25	Summary of Change from Baseline in Clinical Chemistry Data	Safety	3.21	X		Interim, SAC
3.26	Summary of Clinical Chemistry Data of Potential Clinical Concern	Safety	3.23	X		Interim, SAC
3.27	Summary of Endocrinology Laboratory Data (females only)	Safety	3.21	X		Interim, SAC
3.28	Summary of Change from Baseline in Endocrinology Laboratory Data (females only)	Safety	3.21	X		Interim, SAC
3.29	Summary of Liver Events Assessment	Safety	3.29			Interim, SAC

Table Number	Title	Population	Template Table	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
3.30	Summary of Vital Signs	Safety	3.30	X		Interim, SAC
3.31	Summary of Change from Baseline in Vital Signs	Safety	3.30	X		Interim, SAC
3.32	Summary of Vital Signs Data of Potential Clinical Concern	Safety	3.32	X		Interim, SAC
3.33	Summary of Change from Baseline in Vital Signs Data of Potential Clinical Concern	Safety	3.32	X		Interim, SAC
3.34	Summary of Physical Examination by Visit	Safety	3.34	X		Interim, SAC
3.35	Summary of 12-lead ECG	Safety	3.35	X		Interim, SAC
3.36	Summary of Endocrinology assessments by Visit – Female	Safety	3.36	X	ADDED: Footnote re 20 year assessments in all TLF's	Interim, SAC
3.37	Summary of Endocrinology assessments by Visit – Male	Safety	3.37	X	ADDED: Footnote	Interim, SAC
3.38	Summary of Pubertal Development Shifts from Baseline - Female	Safety	3.38	X	ADDED: Footnote	Interim, SAC
3.39	Summary of Pubertal Development Shifts from Baseline - Male	Safety	3.39	X	ADDED: Footnote	Interim, SAC
3.40	Summary of Testicular Volume Change from Baseline – Male	Safety	3.40	X	ADDED: Footnote	Interim, SAC
3.41	Summary of Change from Baseline in Plasma Endocrine Parameters – Female	Safety	3.41	X	ADDED: Footnote	Interim, SAC
3.42	Summary of Change from Baseline in Plasma Endocrine Parameters – Male	Safety	3.42	X	ADDED: Footnote	Interim, SAC
3.43	Summary of Time to change in dose of ambrisentan or other targeted PAH therapeutic agents (prostanoids, PDE-5 inhibitors) due to tolerability issues (days)	Safety	2.10	X		Interim, SAC
3.44	Summary of Treatment Emergent Adverse Events Starting in AMB114588	Safety	3.44			SAC
3.45	Summary of Treatment Emergent Adverse Events by PAH Therapy	Safety	3.44			GSK SAC, Internal S&P
3.46	Summary of Serious Treatment Emergent Adverse Events by PAH Therapy	Safety	3.44			GSK SAC, Internal S&P
3.47	Summary of Non-Serious Treatment Emergent Adverse Events by PAH Therapy	Safety	3.44			GSK SAC, Internal S&P
3.48	Summary of Common (>=5%) Treatment Emergent Adverse Events by PAH Therapy **Footnote:** Note: Common adverse events (>=5%) were those experienced by at least 5% of subjects in the total population (N=38) irrespective of dose group and/or PAH therapy.	Safety	3.44			GSK SAC, Internal S&P
3.49	Summary of Treatment Emergent Adverse Events by PAH Aetiology	Safety	3.48			GSK SAC, Internal S&P

Table Number	Title	Population	Template Table	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
3.50	Summary of Serious Treatment Emergent Adverse Events by PAH Aetiology	Safety	3.48			GSK SAC, Internal S&P
3.51	Summary of non-Serious Treatment Emergent Adverse Events by PAH Aetiology	Safety	3.48			GSK SAC, Internal S&P
3.52	Summary of Common (>=5%)Treatment Emergent Adverse Events by PAH Aetiology **Footnote:** Note: Common adverse events (>=5%) were those experienced by at least 5% of subjects in the total population (N=38) irrespective of dose group and/or PAH Aetiology.	Safety	3.48			GSK SAC, Internal S&P
3.53	Summary of Cardiopulmonary Hemodynamics	Safety	3.52			SAC-New

19.1.2. Listings

Population Listings

Listing Number	Title	Population	Template Listing	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
1.1	Listing of Reasons for Study Withdrawal	Intent-to-Treat	1.1			Interim, SAC
1.2	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	Intent-to-Treat	1.2			Interim, SAC
1.3	Listing of Demographic Characteristics	Intent-to-Treat	1.3			Interim, SAC
1.4	Listing of Race	Intent-to-Treat	1.4			Interim, SAC
1.5	Listing of Disease History	Intent-to-Treat	1.5			Interim, SAC
1.6	Listing of Medical Conditions	Intent-to-Treat	1.6			Interim, SAC
1.7	Listing of Medications	Intent-to-Treat	1.7			Interim, SAC
1.8	Listing of PAH Therapy	Intent-to-Treat	1.8			Interim, SAC
1.9	Relationship between ATC Level 1, Ingredient and Verbatim Text	Intent-to-Treat	1.9			Interim, SAC
1.10	Listing of Compliance Data	Intent-to-Treat	1.10			Interim, SAC
1.11	Listing of initial, highest and final dose of ambrisentan	Intent-to-Treat	1.11			
1.12	Listing of Protocol Deviation	Intent-to-Treat	1.12			Interim, SAC

Efficacy Listings

Listing Number	Title	Population	Template Listing	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
2.1	Listing of Time to Death (All cause)	Intent-to-Treat	2.1			Interim, SAC
2.2	Listing of 6 Minute Walking Distance Data	Intent-to-Treat	2.2			Interim, SAC
2.3	Listing of Clinical Worsening of PAH	Intent-to-Treat	2.3			Interim, SAC
2.4	Listing of Time to the addition of another targeted PAH therapeutic agent (prostanoids, PDE-5 inhibitors)	Intent-to-Treat	2.1			Interim, SAC
2.5	Listing of Time to change in dose of ambrisentan or other targeted PAH therapeutic agents (prostanoids, PDE-5 inhibitors) due to deterioration of clinical condition	Intent-to-Treat	2.1			Interim, SAC
2.6	Listing of WHO Functional Class Data	Intent-to-Treat	2.6			Interim, SAC
2.7	Listing of Plasma NT-Pro BNP Concentration (ng/L)	Intent-to-Treat	2.7			Interim, SAC
2.8	Listing of Exploratory Echocardiogram	Intent-to-Treat	2.8			Interim, SAC
2.9	Listing of Cardiopulmonary Hemodynamics	Intent-to-Treat	2.9			Interim, SAC
2.10	Listing of School Days	Intent-to-Treat	2.10			Interim, SAC
2.11	Listing of Subject Global Assessment (SF10 Health Survey for Children)	Intent-to-Treat	2.11			Interim, SAC

Safety Listings

Listing Number	Title	Population	Template Listing	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
3.1	Listing of Exposure and Compliance to Investigational Product	Safety	3.1			Interim, SAC
3.2	Listing of All Adverse Events	Safety	3.2			Interim, SAC
3.3	Listing of Relationship between Adverse Event System Organ Class, Preferred Term and Verbatim Text	Safety	3.3			Interim, SAC
3.4	Listing of Subject Numbers for Specified Adverse Events	Safety	3.4			Interim, SAC
3.5	Listing of Serious Adverse Events	Safety	3.2			Interim, SAC
3.6	Listing of Fatal Serious Adverse Events	Safety	3.2			Interim, SAC
3.7	Listing of Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study	Safety	3.2			Interim, SAC
3.8	Listing of Haematology	Safety	3.8			Interim, SAC
3.9	Listing of Haematology Data for Subjects with Abnormalities of Potential Clinical Concern	Safety	3.9			Interim, SAC

Listing Number	Title	Population	Template Listing	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
3.10	Listing of Clinical Chemistry	Safety	3.8			Interim, SAC
3.11	Listing of Clinical Chemistry Data for Subjects with Abnormalities of Potential Clinical Concern	Safety	3.9			Interim, SAC
3.12	Listing of Endocrinology Laboratory Data - Females only	Safety	3.8		ADDED: Footnote (See listing 3.22)	Interim, SAC
3.13	Listing of Liver Event Results and Time of Event Relative to Treatment	Safety	3.13			Interim, SAC
3.14	Listing of patient specific information for liver events	Safety	3.14			Interim, SAC
3.15	Listing of Medical Conditions for Subjects with Liver Events on Treatment	Safety	3.15			Interim, SAC
3.16	Listing of Liver Biopsy Details	Safety	3.16			Interim, SAC
3.17	Listing of Liver Imaging Details	Safety	3.17			Interim, SAC
3.18	Listing of Vital Signs	Safety	3.18			Interim, SAC
3.19	Listing of Vital Signs Data for Subjects with Abnormalities of Potential Clinical Concern	Safety	3.9			Interim, SAC
3.20	Listing of Physical Examination	Safety	3.20			Interim, SAC
3.21	Listing of 12-Lead ECG Findings	Safety	3.21			Interim, SAC
3.22	Listing of Endocrinology Assessments	Safety	3.22		ADDED: Footnote	Interim, SAC
3.23	Listing of Time to change in dose of ambrisentan or other targeted PAH therapeutic agents (prostanoids, PDE-5 inhibitors) due to tolerability issues	Safety	2.1			Interim, SAC
3.24	Listing of Pregnancy Results	Safety	3.24			Interim, SAC
3.25	Listing of Endocrinology Parameters - 20 Year Visit	Safety	3.25		ADDED: Footnote	New Listing for SAC
Covid-19 Listings						
3.26	Listing of Country Level Start Dates of COVID-19 Pandemic Measures	Intent-to-Treat	3.26			SAC
3.27	Listing of Visits and Assessments Impacted by COVID-19 Pandemic	Intent-to-Treat	3.27			SAC
3.28	Listing of COVID-19 Assessments for Subjects with COVID-19 Adverse Events	Safety				SAC

19.1.3. Figures

Efficacy Figures

Figure Number	Title	Population	Template Figure	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
2.1	Kaplan-Meier Survival Curves with 95% Confidence Bands of Time to Death (All Cause)	Intent-to-Treat	3.1			Interim, SAC
2.2	Box plots of 6 Minute Walking Distance (meters) by Visit	Intent-to-Treat	3.4			Interim, SAC
2.3	Box plots of Change from Baseline in 6 Minute Walking Distance (meters) by Visit	Intent-to-Treat	3.4			Interim, SAC
2.4	Kaplan-Meier Survival Curves with 95% Confidence Bands of Time to First Clinical Worsening of PAH	Intent-to-Treat	3.1			Interim, SAC
2.5	Kaplan-Meier Survival Curves with 95% Confidence Bands of Time to the addition of another targeted PAH therapeutic agent (prostanoids, PDE-5 inhibitors)	Intent-to-Treat	3.1			Interim, SAC
2.6	Kaplan-Meier Survival Curves with 95% Confidence Bands of Time to change in dose of ambrisentan or other targeted PAH therapeutic agents (prostanoids, PDE-5 inhibitors) due to deterioration of clinical condition	Intent-to-Treat	3.1			Interim, SAC
2.7	Box plots of Plasma NT-Pro BNP concentration by Visit	Intent-to-Treat	3.4			Interim, SAC
2.8	Box plots of Change from Baseline in Plasma NT-Pro BNP concentration by Visit	Intent-to-Treat	3.4			Interim, SAC
2.9	Box plots of Exploratory Echocardiogram Data by Visit	Intent-to-Treat	3.4	X (Line plots of Exploratory Echocardiogram Data by Subject) see template 3.11)		Interim, SAC
2.10	Box plots of Change from Baseline in Exploratory Echocardiogram Data by Visit	Intent-to-Treat	3.4			Interim, SAC

Safety Figures

Figure Number	Title	Population	Template Figure	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
3.1	Kaplan-Meier Survival Curves with 95% Confidence Bands of Time to First Treatment-Emergent Adverse Event	Safety	3.1			Interim, SAC
3.2	Kaplan-Meier Survival Curves with 95% Confidence Bands of Time to First Serious Adverse Event	Safety	3.1			Interim, SAC
3.3	Bar Chart of Treatment-Emergent Adverse Events Occurring in Two or More Subjects in any Treatment Group	Safety	3.3			Interim, SAC
3.4	Box plots of Haematology Data by Visit (Selected Parameters)	Safety	3.4			Interim, SAC

Figure Number	Title	Population	Template Figure	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
3.5	Box plots of Change from Baseline in Haematology Data by Visit (Selected Parameters)	Safety	3.4			Interim, SAC
3.6	Box plots of Chemistry Data by Visit (Selected Parameters)	Safety	3.4			Interim, SAC
3.7	Box plots of Change from Baseline in Chemistry Data by Visit (Selected Parameters)	Safety	3.4			Interim, SAC
3.8	Patient Profiles of Liver Function Tests	Safety	3.8			Interim, SAC
3.9	Box plots of Vital Signs Data by Visit	Safety	3.4			Interim, SAC
3.10	Box plots of Change from Baseline in Vital Signs Data by Visit	Safety	3.4			Interim, SAC
3.11	Line plots of Endocrinology Assessments by subject	Safety	3.11		ADDED: Footnote	Interim, SAC
3.12	Kaplan-Meier Survival Curves with 95% Confidence Bands of Time to change in dose of ambrisentan or other targeted PAH therapeutic agents (prostanoids, PDE-5 inhibitors) due to tolerability issues	Safety	3.1			Interim, SAC

19.2. Data Display Specifications

Protocol: AMB114588
Population: Intent-to-Treat

Table 1.1: Summary of Subject Disposition

	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Subject status					
Completed	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Withdrawn	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Died					
Died due to Covid-19 Complications					
Primary reason for study withdrawal *					
Adverse event	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Lack of Efficacy	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Protocol Deviation	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Subject reached protocol defined stopping criteria	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Study closed/terminated	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Lost to Follow-up	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Investigator discretion	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Withdrew consent	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Number of subjects who returned for a pubertal assessment at 20-years of age	xx (%)	xx (%)	xx (%)	xx (%)	xx (%)

Note: * Percentages are based on the number of subjects in the treatment group.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time
Programming notes: Denominator for each primary reason for withdrawal is number of subjects in the Intent-to-Treat population per treatment group.

Protocol: AMB114588
Population: Randomised

Table 1.2: Summary of Study Populations

	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Randomised	XXX	XXX	XXX	XXX	XXX
Safety Population	XXX (%)	XXX (%)	XXX (%)	XXX (%)	XXX (%)
Intention-to-Treat population	XXX (%)	XXX (%)	XXX (%)	XXX (%)	XXX (%)

Note: The Safety Population is defined as all subjects who received at least 1 dose of study drug.
Subjects are considered as belonging to the treatment group according to the highest dose received.

The Intention-to-Treat (ITT) Population will consist of all subjects who received at least 1 dose of study drug. Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: See notes above relating to denominators for percentages.

Protocol: AMB114588
Population: Intent-to-treat

Table 1.3: Summary of Subjects by Country and Centre

Country	Centre ID	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
XXXXXXXXX	All	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	XXXXXX	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
XXXXXXXXX	All	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	XXXXXX	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
XXXXXXXXX	All	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	XXXXXX	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)

Note: Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Protocol: AMB114588
Population: Intent-to-Treat

Table 1.4: Summary of Inclusion/Exclusion Criteria Deviations

	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Any criteria deviations	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Inclusion					
I1	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
I2	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..					
Exclusion					
E1	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
E2	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..					

Note: Please refer to numbering of inclusion and exclusion criteria in protocol.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Only present criteria where there is at least one (total) deviation. “Any criteria deviations” is the number of subjects who had at least one deviation.

Protocol: AMB114588
Population: Intent-to-Treat

Table 1.5: Summary of Demographic and Baseline Characteristics

	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Age (yrs)**					
N	XXX	XXX	XXX	XXX	XXX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X	XX.X	XX.X
Min.	XX	XX	XX	XX	XX
Max.	XX	XX	XX	XX	XX
Age (yrs)**					
N	XXX	XXX	XXX	XXX	XX (%)
<8 years	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
8 - 11 years	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
12 - <18 years	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
>=18 years	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Sex					
N	XXX	XXX	XXX	XXX	XX (%)
Female	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Male	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)

Note: ** At start of study treatment in AMB112529
* At entry to AMB114588
$ A subject may be represented in more than one geographic ancestry group.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Table 1.5: Summary of Demographic and Baseline Characteristics

	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Child Bearing Potential (Females only) *					
N	XXX	XXX	XXX	XXX	XXX
Pre-menarcheal	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Sterile (of child bearing age)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Potentially able to bear children	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Ethnicity **					
N	XXX	XXX	XXX	XXX	XXX
Hispanic/Latino	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Not Hispanic/Latino	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Geographic Ancestry **$					
n	XXX	XXX	XXX	XXX	XXX
African American/African Heritage	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
American Indian or Alaskan Native	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Asian - Central/South Asian Heritage	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Asian - East Asian Heritage	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Asian - Japanese Heritage	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Asian - South East Asian Heritage	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Native Hawaiian or Other Pacific Islander	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
White - Arabic/North African Heritage	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
White - White/Caucasian/European Heritage	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)

Note: ** At start of study treatment in AMB112529
* At entry to AMB114588
$ A subject may be represented in more than one geographic ancestry group.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Protocol: AMB114588
Population: Intent-to-Treat

Table 1.5: Summary of Demographic and Baseline Characteristics

	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Weight (kg)*					
N	XXX	XXX	XXX	XXX	XXX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X	XX.X	XX.X
Min.	XX	XX	XX	XX	XX
Max.	XX	XX	XX	XX	XX
Weight (kg)*					
N	XXX	XXX	XXX	XXX	XX (%)
<20 kg	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
20 - <35 kg	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
35 - <50 kg	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
>=50 kg	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Aetiology of PAH Randomised Strata **					
n	XXX	XXX	XXX	XXX	XX (%)
Idiopathic (IPAH)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Familial (FPAH)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Persistent PAH despite surgical repair	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Secondary to connective tissue disease	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)

Note: ** At start of study treatment in AMB112529
* At entry to AMB114588
$ A subject may be represented in more than one geographic ancestry group.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Table 1.5: Summary of Demographic and Baseline Characteristics

	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Duration of PAH (days)**					
N	XXX	XXX	XXX	XXX	XXX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X	XX.X	XX.X
Min.	XX	XX	XX	XX	XX
Max.	XX	XX	XX	XX	XX
PAH Therapy Use **					
n	XXX	XXX	XXX	XXX	XX (%)
Ongoing PAH therapy at baseline	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Prior PAH therapy, not ongoing at baseline	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
No PAH therapy recorded	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)

Note: ** At start of study treatment in AMB112529
* At entry to AMB114588
$ A subject may be represented in more than one geographic ancestry group.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Table 1.5: Summary of Demographic and Baseline Characteristics

	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
WHO Functional Class **					
N	XXX	XXX	XXX	XXX	XX (%)
Class II	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Class III	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
WHO Functional Class *					
N	XXX	XXX	XXX	XXX	XX (%)
Class II	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Class III	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
6 minute walk data (m)**					
N	XXX	XXX	XXX	XXX	XXX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X	XX.X	XX.X
Min.	XX	XX	XX	XX	XX
Max.	XX	XX	XX	XX	XX
6 minute walk data (m)*					
N	XXX	XXX	XXX	XXX	XXX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X	XX.X	XX.X
Min.	XX	XX	XX	XX	XX
Max.	XX	XX	XX	XX	XX

Note: ** At start of study treatment in AMB112529
* At entry to AMB114588
$ A subject may be represented in more than one geographic ancestry group.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.
USER ID: Directory/Program.sas Date Time

Protocol: AMB114588
Population: Intent-to-Treat

Table 1.6: Summary of Past Medical Conditions

Classification	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Any condition	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Classification 1					
Any condition	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Preferred Term 1	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Preferred Term 2	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
etc					
Classification 2					
Any condition	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Preferred Term 1	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Preferred Term 2	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
etc					
Etc..					

Note: Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: "Any condition" relates to the number and percentage of subjects who had at least one condition. Subjects may be counted more than once across classifications.
Produce table for data collected in AMB112529 for the subset of subjects who entered AMB114588.

Protocol: AMB114588
Population: Intent-to-Treat

Table 1.8: Summary of Concomitant Medications

ATC Level 1 Preferred Term	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Any medication	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Endocrine & Metabolic					
Any medication	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Fluticasone propionate	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Beclomethasone dipropionate	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Anti-infectives & immunologicals					
Any medication	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Amoxycillin	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Amoxycillin trihydrate	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Clamoxyl	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Cefaclor	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Cefproxil	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..					

Note: A medication may be included in more than one ATC level category and appear more than once.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

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Programming notes: Medications will be sorted in descending order of total incidence across treatment groups for the ATC level 1 and in descending order of total incidence for the preferred term within each ATC level. If the total incidence for any two or more preferred terms is equal, they will be presented in alphabetical order.

Table 1.9: Summary of Ongoing Background PAH Therapy at Entry Visit to AMB114588
By Drug Class and Preferred Term

PAH Therapy	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Any medication	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
PDE5i (monotherapy)					
Any medication	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Preferred Term 1	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Preferred Term 1	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..					
Prostanoid (monotherapy)					
Any medication	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Preferred Term 1	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Preferred Term 1	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..					
PDE5i and prostanoid in combination					
Any medication	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Preferred Term 1 + Preferred Term 2	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Preferred Term 3 + Preferred Term 4	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..					

Note: Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: For Table 1.10, data will be presented at 6 months after entry into AMB114588 and then annually as well as the final visit.

Protocol: AMB114588
Population: Intent-to-Treat

Table 1.11: Summary of Compliance to Investigational Product since last visit

Planned Relative Time	Compliance assessment	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Month 3	n	XXX	XXX	XXX	XXX	XXX
	0% compliant	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	>0% and < 80%	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	>= 80% and <= 120%	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	>120% compliant	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Month 6	n	XXX	XXX	XXX	XXX	XXX
	0% compliant	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	>0% and < 80%	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	>= 80% and <= 120%	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	>120% compliant	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..	Etc..					

Note: Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits and End of Study.

Table 1.12: Summary of Investigational Product Compliance Overall

	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Overall % of visits at which subject is compliant	XX	XX	XX	XX	XX
N	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X	XX.X	XX.X
Min.	XX	XX	XX	XX	XX
Max.	XX	XX	XX	XX	XX

Note: Q1 = 1st quartile, Q3 = 3rd quartile.
Compliant visits are those at which subjects are ≥80% and ≤120% compliant. Compliance is determined by the site.
At a subject level compliance = 100*(the number of visits at which the subject was compliant)/(the sum of all study visits for the subject). At a treatment group level the overall compliance = 100*(the total number of visits at which all subjects in that group were compliant)/(the sum of all study visits for all subjects in that group).
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

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Table 1.13: Summary of initial dose of ambrisentan at entry to AMB114588 and highest dose received during study

	Highest Dose				
Initial Dose	2.5mg	5mg	7.5mg	10mg	Total
2.5 mg	XX	XX	XX	XX	XX
5 mg	XX	XX	XX	XX	XX
7.5 mg	XX	XX	XX	XX	XX
10 mg	XX	XX	XX	XX	XX
Total	XX	XX	XX	XX	XX

Protocol: AMB114588
Population: Intent-to-treat

Table 1.14: Summary of initial dose of ambrisentan at entry to AMB114588 and final dose at end of study or termination

	Final Dose				
Initial Dose	2.5mg	5mg	7.5mg	10mg	Total
2.5 mg	XX	XX	XX	XX	XX
5 mg	XX	XX	XX	XX	XX
7.5 mg	XX	XX	XX	XX	XX
10 mg	XX	XX	XX	XX	XX
Total	XX	XX	XX	XX	XX

Protocol: AMB114588
Population: Intent-to-Treat

Table 1.15: Summary of Important Protocol Deviation

Protocol Deviation Category	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Any Deviation	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Eligibility criteria not met	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Not withdrawn after developing withdrawal criteria	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Prohibited medication or device	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Visit window	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Informed consent procedure	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Administer/dispense study medication	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Failure to report SAE, Pregnancy, or liver function abnormalities per protocol	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Study blind/ unblind procedures	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Study treatment supply procedures	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Biological specimen sample procedures	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Assessment procedures	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Diary Card procedures	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Equipment procedures	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Randomization procedures	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
IP taken inappropriately	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Procedures/Assessments not performed per protocol	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Other	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)

Note: Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Protocol: AMB114588
Population: Intent-to-Treat

Table 1.19
Summary of COVID-19 Assessments for Subjects with Suspected, Probable or Confirmed COVID-19 Case Diagnosis

Assessments	Treatment A (N=300)	Treatment B (N=300)
COVID-19 Case Diagnosis [1]	100 (33%)	100 (33%)
Confirmed	29 (10%)	29 (10%)
Probable	50 (17%)	50 (17%)
Suspected	21 (7%)	21 (7%)
COVID-19 Test Performed [2]		
n	100	100
No	50 (50%)	50 (50%)
Yes	50 (50%)	50 (50%)
Result of the COVID-19 Test		
n	50	50
Negative	10 (20%)	10 (20%)
Positive	30 (60%)	30 (60%)
Indeterminate	10 (20%)	10 (20%)

[1] COVID-19 Case Diagnosis is based on WHO Definition as of dd-mmm-yyyy.

[2] COVID-19 Test Performed is only captured for subjects with a COVID-19 Case Diagnosis.

Programmer Notes: For COVID-19 Test Performed, the small n is based on the number of subjects with a COVID-19 Case Diagnosis.
For Result of the COVID-19 Test, the small n is based on the COVID-19 Test Performed=Yes.
There are multiple collection forms, select the appropriate display format, PAN1 or PAN1A, depending on the form used in the study. Use PAN1 when the COVID-19 assessments can only be captured once during the study and use PAN1A if the COVID-19 assessments are captured using repeating form design.

Protocol: AMB114588

Population: Intent-to-Treat

Table 1.20
Summary of Visits impacted by COVID-19 Pandemic

	Treatment A (N=100)	Treatment B (N=100)	Total (N=200)
Any Visit Impacted			
Number of subjects with visits impacted	80 (80%)	80 (80%)	160 (80%)
Impact [4]			
MISSED VISIT	25 (25%)	25 (25%)	50 (25%)
Primary Reason for Impact [4]			
SUBJECT ACQUIRED COVID-19 INFECTION [1]	15 (15%)	15 (15%)	30 (15%)
SUBJECT RELATED IMPACT [2]	15 (15%)	15 (15%)	30 (15%)
SITE RELATED IMPACT [3]	15 (15%)	15 (15%)	30 (15%)
SITE VISIT WITH ONE OR MORE ASSESSMENTS MISSED	45 (45%)	45 (45%)	90 (45%)
Primary Reason for Impact [4]			
SUBJECT ACQUIRED COVID-19 INFECTION [1]	25 (25%)	25 (25%)	50 (25%)
SUBJECT RELATED IMPACT [2]	15 (15%)	15 (15%)	30 (15%)
SITE RELATED IMPACT [3]	15 (15%)	15 (15%)	30 (15%)
REMOTE VISIT WITH NO ASSESSMENTS MISSED	15 (15%)	15 (15%)	30 (15%)
Primary Reason for Impact [4]			
SUBJECT ACQUIRED COVID-19 INFECTION [1]	10 (10%)	10 (10%)	20 (10%)
SUBJECT RELATED IMPACT [2]	10 (10%)	10 (10%)	20 (10%)
SITE RELATED IMPACT [3]	10 (10%)	10 (10%)	20 (10%)
REMOTE VISIT WITH ONE OR MORE ASSESSMENTS MISSED	15 (15%)	15 (15%)	30 (15%)
Primary Reason for Impact [4]			
SUBJECT ACQUIRED COVID-19 INFECTION [1]	10 (10%)	10 (10%)	20 (10%)
SUBJECT RELATED IMPACT [2]	10 (10%)	10 (10%)	20 (10%)
SITE RELATED IMPACT [3]	10 (10%)	10 (10%)	20 (10%)
Visit #			
Number of impacted subjects at the visit (n)	60	60	120
Impact			
MISSED VISIT	6 (10%)	6 (10%)	12 (10%)
Primary Reason for Impact			
SUBJECT ACQUIRED COVID-19 INFECTION [1]	3 (5%)	3 (5%)	6 (5%)
SUBJECT RELATED IMPACT [2]	0	0	0
SITE RELATED IMPACT [3]	3 (5%)	3 (5%)	6 (5%)
SITE VISIT WITH ONE OR MORE ASSESSMENTS MISSED	36 (60%)	36 (60%)	72 (60%)
Primary Reason for Impact			
SUBJECT ACQUIRED COVID-19 INFECTION [1]	0	0	0

SUBJECT RELATED IMPACT [2]	6 (10%)	6 (10%)	12 (10%)
SITE RELATED IMPACT [3]	30 (50%)	30 (50%)	60 (50%)

Visit …

[1] Subject acquired COVID-19 includes suspected, probable and confirmed.

[2] Subject related impact include subject discretion and travel restrictions.

[3] Site related impacts include site temporarily closed, site staff unavailable, and study drug unavailable.

[4] Subjects may be counted in more than one category.

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Programmer notes: After the overall summary of any impacted visits, the summary is then produced by visit starting with the first impacted visit. This is represented in the mock-up as # for the first impacted visits and #+1 for each visit thereafter.

Protocol: AMB114588
Population: Intent-to-Treat

Table 2.1: Summary of Time to Death (All cause) (days)

	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
N	XXX (XX%)	XXX (XX%)	XXX (XX%)	XXX (XX%)	XXX (XX%)
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X	XX.X	XX.X
Min.	XX	XX	XX	XX	XX
Max.	XX	XX	XX	XX	XX

Note: Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Protocol: AMB114588
Population: Intent-to-Treat

Table 2.2: Summary of 6 Minute Walking Distance (meters)

Treatment	Planned Relative Time	n	Mean	SD	Q1	Median	Q3	Min.	Max.
Ambrisentan 2.5mg	Baseline**								
	Overall	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	With oxygen use	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Without oxygen use	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
(N=XXX)	Entry Visit*								
	Overall	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	With oxygen use	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Without oxygen use	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Month 6								
	Etc..								
Ambrisentan 5mg (N=XXX)	Etc..								
Ambrisentan 7.5mg (N=XXX)	Etc..								
Ambrisentan 10mg (N=XXX)	Etc..								
Total (N=XXX)	Etc..								

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits, End of Study and Follow-Up.

Protocol: AMB114588
Population: Intent-to-Treat

Table 2.5: Summary of Walking Duration (minutes) for subjects who walked less than six minutes

Treatment	Number of subjects who attempted the 6 minute walk	Planned Relative Time	n	Mean	SD	Q1	Median	Q3	Min.	Max.
Ambrisentan 2.5mg (N=XXX)	XX	Baseline**	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	XX	Entry Visit*	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	XX	Month 6	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	XX	Etc..	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
Ambrisentan 5mg (N=XXX)		Etc..								
Ambrisentan 7.5mg (N=XXX)		Etc..								
Ambrisentan 10mg (N=XXX)		Etc..								
Total (N=XXX)		Etc..								

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits, End of Study and Follow-Up.

Protocol: AMB114588
Population: Intent-to-Treat

Table 2.6: Summary of use of Oxygen during 6 Minute Walking exercise (L/min)

Treatment	Number of subjects who attempted the 6 minute walk	Planned Relative Time	n	Mean	SD	Q1	Median	Q3	Min.	Max.
Ambrisentan 2.5mg (N=XXX)	XX	Baseline**	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	XX	Entry Visit*	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	XX	Month 6	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	XX	Etc..	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
Ambrisentan 5mg (N=XXX)		Etc..								
Ambrisentan 7.5mg (N=XXX)		Etc..								
Ambrisentan 10mg (N=XXX)		Etc..								
Total (N=XXX)		Etc..								

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits, End of Study and Follow-Up.

Protocol: AMB114588
Population: Intent-to-Treat

Table 2.7: Summary of Time to the first Clinical Worsening of PAH (days)

	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
N	XXX (XX%)	XXX (XX%)	XXX (XX%)	XXX (XX%)	XXX (XX%)
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X	XX.X	XX.X
Min.	XX	XX	XX	XX	XX
Max.	XX	XX	XX	XX	XX

Note: Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Protocol: AMB114588
Population: Intent-to-Treat

Table 2.8: Summary of Clinical Worsening of PAH

	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Subjects with at least one criteria	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Death (all cause) or placed on active list for lung transplant	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Hospitalisation for worsening of PAH	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Addition/increased dose of other targeted PAH therapetic agents and/or atrial septostomy	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
PAH related deterioration	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
PAH related deterioration:-					
Increase from baseline in WHO functional class	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Deterioration in exercise testing	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Clinical signs or symptoms of right sided heart failure	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)

Note: Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Table 2.9: Summary of Time to the addition of another targeted PAH therapeutic agent (prostanoids, PDE-5 inhibitors) (days)

	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Due to Deterioration of Clinical Condition					
N	XXX (XX%)	XXX (XX%)	XXX (XX%)	XXX (XX%)	XXX (XX%)
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X	XX.X	XX.X
Min.	XX	XX	XX	XX	XX
Max.	XX	XX	XX	XX	XX
Due to Lack of beneficial effect with previous therapy					
N	XXX (XX%)	XXX (XX%)	XXX (XX%)	XXX (XX%)	XXX (XX%)
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X	XX.X	XX.X
Min.	XX	XX	XX	XX	XX
Max.	XX	XX	XX	XX	XX
Overall					
N					
Mean					
Etc..					

Note: Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.
USER ID: Directory/Program.sas Date Time
Programming notes: Use CONMEDS dataset where CMTYPCD is 84(PAH Therapy) and CMSTRSCD = 46 (Deterioration of clinical condition) or = 47 (Lack of beneficial effect with previous therapy).

Protocol: AMB114588
Population: Intent-to-Treat

Table 2.10: Summary of Time to change in dose of ambrisentan or other targeted PAH therapeutic agents (prostanoids, PDE-5 inhibitors) due to deterioration of clinical condition (days)

	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
N	XXX (XX%)	XXX (XX%)	XXX (XX%)	XXX (XX%)	XXX (XX%)
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X	XX.X	XX.X
Min.	XX	XX	XX	XX	XX
Max.	XX	XX	XX	XX	XX

Note: Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time
Programming notes: Use CONMEDS dataset where CMTYPCD is 84(PAH Therapy) and CMSTRSCD = 46 (Deterioration of clinical condition) or EXPOSURE dataset where EXCHRSCD =58 (Deterioration of clinical condition).

Protocol: AMB114588
Population: Intent-to-Treat

Table 2.11: Summary of WHO Functional Class

Treatment	Planned Relative Time	n	Mean	SD	Q1	Median	Q3	Min.	Max.
Ambrisentan 2.5mg (N=XXX)	Baseline**	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Entry Visit*	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Month 6	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Etc..	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
Ambrisentan 5mg (N=XXX)	Etc..								
Ambrisentan 7.5mg (N=XXX)	Etc..								
Ambrisentan 10mg (N=XXX)	Etc..								
Total (N=XXX)	Etc..								

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
There are 4 grades of WHO FC based on symptom severity ([redacted]).
Grades mapped to numeric scale 1-4 (i.e. Class IV=4).
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.
USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits, End of Study and Follow-Up.

Protocol: AMB114588
Population: Intent-to-Treat

Table 2.13: Summary of WHO Functional Class Shifts from Baseline by Visit

Treatment	Planned Relative Time	WHO Functional Class	Baseline** WHO Functional Class	
			II	III
Ambrisentan 2.5mg (N=XXX)	Entry Visit*	I	XX (%)	XX (%)
		II	XX (%)	XX (%)
		III	XX (%)	XX (%)
		IV	XX (%)	XX (%)
		Unknown/ Not Recorded	XX	XX
	Month 6	I	XX (%)	XX (%)
		II	XX (%)	XX (%)
		III	XX (%)	XX (%)
		IV	XX (%)	XX (%)
		Unknown/ Not Recorded	XX	XX
	Etc..			
Ambrisentan 5mg (N=XXX)	Etc..			
Ambrisentan 7.5mg (N=XXX)	Etc..			
Ambrisentan 10mg (N=XXX)	Etc..			
Total (N=XXX)	Etc..			

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
There are 4 grades of WHO FC based on symptom severity (CCI [redacted]).
Grades mapped to numeric scale 1-4 (i.e. Class IV=4).
Baseline WHO functional class not shown for III and IV because no subjects met the criteria for these categories at baseline.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.
USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits, End of Study and Follow-Up.

Table 2.14: Summary of WHO Functional Class Change from Baseline Categorisation

Planned Relative Time	WHO Category	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Entry Visit*	N	XXX	XXX	XXX	XXX	XXX
	Improved	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	No Change	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	Deteriorated	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	-2	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	-1	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	0	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	+1	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	+2	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)

Etc..

Note: * Entry Visit is at entry to AMB114588.
Baseline is the last value recorded prior to start of study treatment from AMB112529.
There are 4 grades of WHO FC based on symptom severity (CCI [redacted]).
Grades mapped to numeric scale 1-4 (i.e. Class IV=4).
Change categorisation (based on -2, -1, 0, +1, +2); CCI [redacted],
CCI [redacted].
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits, End of Study and Follow-Up.

Protocol: AMB114588
Population: Intent-to-Treat

Table 2.15: Summary of plasma NT-Pro BNP concentration (ng/L)

Treatment	Planned Relative Time	n	Geometric Mean	SD [logs]	Q1	Median	Q3	Min.	Max.
Ambrisentan 2.5mg (N=XXX)	Baseline**	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Entry Visit*	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Month 6	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Etc..	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
Ambrisentan 5mg (N=XXX)	Etc..								
Ambrisentan 7.5mg (N=XXX)	Etc..								
Ambrisentan 10mg (N=XXX)	Etc..								
Total (N=XXX)	Etc..								

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.
USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits, End of Study and Follow-Up.

Table 2.17: Summary of Exploratory Echocardiogram

Planned Relative Time Baseline**		Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Pericardial Effusion	N	XXX	XXX	XXX	XXX	XXX
	Absent	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	Trace: separation of pericardial layers in both systole and diastole	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	Small: diastolic separation equals 1cm	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	Moderate: diastolic separation of 1 to 2cm	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	Large: diastolic separation equals 2cm	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Mean right Atrial Pressure (mmHg)	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX
Tricuspid Annular Plane Systolic Excursion (cm)	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits (including Entry Visit), End of Study and Follow-Up.

Protocol: AMB114588
Population: Intent-to-Treat

Table 2.17: Summary of Exploratory Echocardiogram

Planned Relative Time Baseline**		Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Eccentricity Index Systolic	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX
Eccentricity Index Diastolic	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits (including Entry Visit), End of Study and Follow-Up.

Table 2.17: Summary of Exploratory Echocardiogram

Planned Relative Time Baseline**		Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Tricuspid Regurgitant Jet Velocity (m/s)	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX
Right Ventricular Pressure (mmHg)	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits (including Entry Visit), End of Study and Follow-Up.

Table 2.18: Summary of Change from Baseline in Exploratory Echocardiogram

Planned Relative Time Entry Visit*		Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Pericardial Effusion	n	XXX	XXX	XXX	XXX	XXX
	No Change	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	Absent	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	Improved	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	Worsened	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Mean right Atrial Pressure (mmHg)	n	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX
Tricuspid Annular Plane Systolic Excursion (cm)	n	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX

Note: * Entry Visit is at entry to AMB114588.
Baseline is the last value recorded prior to start of study treatment from AMB112529.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time
Programming notes: Present available visits, End of Study and Follow-Up.

Table 2.18: Summary of Change from Baseline in Exploratory Echocardiogram

Planned Relative Time Entry Visit*		Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Eccentricity Index Systolic	n	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX
Eccentricity Index Diastolic	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX

Note: * Entry Visit is at entry to AMB114588.
Baseline is the last value recorded prior to start of study treatment from AMB112529.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits, End of Study and Follow-Up.

Table 2.18: Summary of Change from Baseline in Exploratory Echocardiogram

Planned Relative Time Entry Visit*		Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Tricuspid Regurgitant Jet Velocity (m/s)	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX
Right Ventricular Pressure (mmHg)	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX

Note: * Entry Visit is at entry to AMB114588.
Baseline is the last value recorded prior to start of study treatment from AMB112529.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits, End of Study and Follow-Up.

Protocol: AMB114588
Population: Intent-to-treat

Table 2.19: Summary of Number of Subjects with School Days

Planned Relative Time	Ambrisentan 2.5mg (N=XX)	Ambrisentan 5mg (N=XX)	Ambrisentan 7.5mg (N=XX)	Ambrisentan 10mg (N=XX)	Total (N=XX)
Baseline**					
Subjects with scheduled days	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Subjects with at least one scheduled day missed	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Number of scheduled days missed / Number of scheduled days	xx/xxx (xx%)	xx/xxx (xx%)	xx/xxx (xx%)	xx/xxx (xx%)	xx/xxx (xx%)
Subjects with at least one scheduled day missed due to PAH	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Number of scheduled days missed due to PAH / Number of scheduled days	xx (xx%) xx/xxx (xx%)	xx (xx%) xx/xxx (xx%)	xx (xx%) xx/xxx (xx%)	xx (xx%) xx/xxx (xx%)	xx (xx%) xx/xxx (xx%)
Entry Visit*					
Subjects with scheduled days	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Subjects with at least one scheduled day missed	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Number of scheduled days missed / Number of scheduled days	xx/xxx (xx%)	xx/xxx (xx%)	xx/xxx (xx%)	xx/xxx (xx%)	xx/xxx (xx%)
Subjects with at least one scheduled day missed due to PAH	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Number of scheduled days missed due to PAH / Number of scheduled days	xx (xx%) xx/xxx (xx%)	xx (xx%) xx/xxx (xx%)	xx (xx%) xx/xxx (xx%)	xx (xx%) xx/xxx (xx%)	xx (xx%) xx/xxx (xx%)
Etc..					

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
This summary excludes subjects with 0 scheduled days of school for the given period.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits, End of Study and Follow-Up.

Protocol: AMB114588
Population: Intent-to-Treat

Table 2.20: Summary Statistics of School Days

Planned Relative Time Baseline**		Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Number of scheduled days	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX
Number of missed days	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX
Number of missed days due to PAH	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
This summary excludes subjects with 0 scheduled days of school for the given period.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits (including Entry Visit), End of Study and Follow-Up.

Table 2.20: Summary Statistics of School Days

Planned Relative Time Entry Visit		Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Proportion of days missed (%)	n	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX
Proportion of days missed due to PAH(%)	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
This summary excludes subjects with 0 scheduled days of school for the given period.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits (including Entry Visit), End of Study and Follow-Up.

Protocol: AMB114588
Population: Intent-to-Treat

Table 2.22: Summary of Subject Global Assessment (SF10 Health Survey for Children)

Planned Relative Time Baseline**		Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Physical Health Summary	n	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX
Psychosocial Summary	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits (including Entry Visit), End of Study and Follow-Up.

Protocol: AMB114588
Population: Intent-to-Treat

Table 2.24: Summary of SF10 Health Survey – Number and Percentage of Subjects with Particular Item Responses

Planned Relative Time Baseline**	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Completed SF-10 ^	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
In general, would you say your child's health is					
N	XX	XX	XX	XX	XX
Excellent	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Very Good	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Good	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Fair	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Poor	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
During the past 4 weeks, has your child been limited doing things that take some energy such as riding a bike or skating due to HEALTH problems?					
N	XX	XX	XX	XX	XX
Yes, limited a lot	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Yes, limited some	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Yes, limited a little	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
No, not limited	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
During the past 4 weeks, has your child been limited during bending, lifting or stooping due to HEALTH problems?					
N	XX	XX	XX	XX	XX
Yes, limited a lot	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Yes, limited some	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Yes, limited a little	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
No, not limited	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
etc...					

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
^ Completed at least one of the 10 items of SF-10
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits (including Entry Visit), End of Study and Follow-Up.

Protocol: AMB114588
Population: Intent-to-treat

Table 2.25
Number of subjects who achieved an increase in 6MWD >=20 metres

	N=xx
>/= 20 meters increase from baseline (LOCF) at 12 months	xx (xx%)
>/= 20 meters increase from baseline at last observation	xx (xx%)

Note: Baseline is the last value recorded prior to the start of study treatment from AMB112529.
USER ID: Directory/Program.sas Date Time

Protocol: AMB114588
Population: Intent-to-treat

Table 2.26
Number of subjects who achieved an increase in 6MWD >=20 metres by Idiopathic group

Idiopathic group		N=100
Idiopathic group		xx
	>/= 20 meters increase from baseline at 12 months (LOCF)	xx (xx%)
	>/= 20 meters increase from baseline at last observation	xx (xx%)
Non-idiopathic group		xx
	>/= 20 meters increase from baseline at 12 months (LOCF)	xx (xx%)
	>/= 20 meters increase from baseline at last observation	xx (xx%)

Note: Baseline is the last value recorded prior to the start of study treatment from AMB112529.
'Idiopathic group' refers to those with an idiopathic aetiology of PAH in 112529, and 'non-idiopathic' refers to those classified as having: an aetiology of familial, persistent PAH despite surgical repair, or secondary to connective tissue disease.
For subjects with missing data at 12 months, the post-baseline last observation was carried forward (LOCF) to the 12 month visit.

USER ID: Directory/Program.sas Date Time

Protocol: AMB114588
Population: Intent-to-treat

Table 2.27
Number of subjects who achieved an NT-proBNP level of less than 1200 ng/L

	N=xx
NT-proBNP level of less than 1200 ng/L at 12 months (LOCF)	xx (xx%)
NT-proBNP level of less than 1200 ng/L at last observation	xx (xx%)

Note: For subjects with missing data at 12 months, the post-baseline last observation was carried forward (LOCF) to the 12 month visit.

USER ID: Directory/Program.sas Date Time

Protocol: AMB114588
Population: Intent-to-treat

Table 2.28
Number of subjects who achieved an NT-proBNP level of less than 1200 ng/L by Idiopathic group

Idiopathic group		N=xx
Idiopathic group		xx
	NT-proBNP level of less than 1200 ng/L at 12 months (LOCF)	xx (xx%)
	NT-proBNP level of less than 1200 ng/L at last observation	xx (xx%)
Non-idiopathic group		xx
	NT-proBNP level of less than 1200 ng/L at 12 months (LOCF)	xx (xx%)
	NT-proBNP level of less than 1200 ng/L at last observation	xx (xx%)

Note: 'Idiopathic group' refers to those with an idiopathic aetiology of PAH in 112529, and ‘non-idiopathic’ refers to those classified as having: an aetiology of familial, persistent PAH despite surgical repair, or secondary to connective tissue disease.
For subjects with missing data at 12 months, the post-baseline last observation was carried forward (LOCF) to the 12 month visit.

USER ID: Directory/Program.sas Date Time

Protocol: AMB114588
Population: Intent-to-treat

Table 2.29
Distribution of NT-proBNP levels at baseline and extent of change during treatment

	N=xx
NT-proBNP value above 1200 ng/L at baseline	x (18%)
How many stayed over 1200	x (3%)
How many had at least 1 value < 1200	x (13%)
How many had value <1200 as last value	x (13%)
Other (a)	x (3%)
NT-proBNP value above 1200 ng/L at any time during the study	xx (29%)
NT-proBNP value between 500 ng/L and 1200 ng/L at baseline	x (8%)
How many had at least 1 value >1200?	x (3%)
and how many of these stayed over 1200?	x (3%)
How many stayed between 500 and 1200?	x (3%)
How many fell below 500	x (5%)
Of those how many were <500 as last value?	x (3%)
Other (b)	x (3%)
NT-proBNP value < 500 ng/L at baseline	xx (71%)
How many had at least 1 value > 1200	x (8%)
and of these how many stayed over 1200?	x (5%)
Other (c)	x (3%)
How many rose to between 500 and 1200?	x (13%)
how many stayed there?	x (5%)
Other (d)	x (8%)
How many stayed below 500?	xx (55%)

Note:
(a) Subject PPD did not have a baseline visit in AMB112529.
(b) Subject only had a baseline value.
(c) Subject went up to>1200, back down to 500-1200
(d) Subject fell below 500 then up above 1200
(e) Subject went up to 500-1200 but ended above 1200
(f) Subject fell below 500 then back up to 500-1200

USER ID: Directory/Program.sas Date Time

Protocol: AMB114588
Population: Intent-to-treat

Table 2.30
Distribution of NT-proBNP levels at baseline and extent of change during treatment - by Idiopathic group

Group: Idiopathic group

	N=xx
Idiopathic group	xx
NT-proBNP value above 1200 ng/L at baseline	xx (xx%)
How many stayed over 1200	x (x%)
How many had at least 1 value < 1200	xx (xx%)
How many had value <1200 as last value	xx (xx%)
Other (a)	xx (x%)
NT-proBNP value above 1200 ng/L at any time during the study	xx (xx%)
NT-proBNP value between 500 ng/L and 1200 ng/L at baseline	x (xx%)
How many had at least 1 value >1200?	0
and how many of these stayed over 1200?	X (x%)
How many stayed between 500 and 1200?	x (x%)
How many fell below 500	x (x%)
Of those how many were <500 as last value?	X (x%)
NT-proBNP value < 500 ng/L at baseline	xx (63%)
How many had at least 1 value > 1200	x (x%)
and of these how many stayed over 1200?	x (x%)
Other (b)	x (x%)
How many rose to between 500 and 1200?	x (x%)
how many stayed there?	x (x%)
Other (c)	x (x%)
How many stayed below 500?	xx (x%)

Group: Non-idiopathic group-all other categories

	N=xx
Number in non-idiopathic group	xx
NT-proBNP value above 1200 ng/L at baseline	0
How many stayed over 1200	0
How many had at least 1 value < 1200	0
How many had value <1200 as last value	0
NT-proBNP value above 1200 ng/L at any time during the study	x (xx%)
NT-proBNP value between 500 ng/L and 1200 ng/L at baseline	x (xx%)
How many had at least 1 value >1200?	x (xx%)
and how many of these stayed over 1200?	X (xx%)
How many stayed between 500 and 1200?	x
How many fell below 500	x (xx%)
Of those how many were <500 as last value?	x (xx%)
Other (d)	x (xx%)
NT-proBNP value < 500 ng/L at baseline	xx (xx%)
How many had at least 1 value > 1200	0

and of these how many stayed over 1200?	0
How many rose to between 500 and 1200?	x (xx%)
how many stayed there?	x (xx%)
Other (e)	x (xx%)
How many stayed below 500?	0 (xx%)

Note:
(a) Subject PPD did not have a baseline visit in AMB112529.
(b) Subject only had a baseline value.
(c) Subject went up to>1200, back down to 500-1200
(d) Subject fell below 500 then up above 1200
(e) Subject went up to 500-1200 but ended above 1200
(f) Subject fell below 500 then back up to 500-1200

USER ID: Directory/Program.sas Date Time

Protocol: AMB114588
Population: Intent-to-Treat

Table 2.31
The Event Rate of the Clinical Worsening Endpoint per 100 Patient-Years

Treatment	N	The number of subjects with at least one clinical worsening	Total exposure time (year)	Event rate per 100 patient-years
Total	xx	xx	xxxx.x	x.x

Note: Total Exposure time in years is calculated by the sum for all subjects of (last exposure date - first exposure date + 1) / 365.25. If the last exposure date is missing, the last study visit date is used.
For the subjects with at least one clinical worsening, the first event date should be used instead of the last exposure date.
Event rate per 100 patient-years: The number of subjects with at least one clinical worsening / Total exposure time (year) * 100;

Protocol: AMB114588
Population: Safety

Table 3.1: Summary of Exposure to Investigational Product

		Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Number of days of exposure	n	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX
Interval of days of exposure	n	XXX	XXX	XXX	XXX	XXX
	<=1 month	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	>1 month to <=2 months	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	>2 month to <=3 months	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	Etc..	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)

Note: For each patient, exposure (days) = date of last dose of study drug – first dose date + 1 day.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to the treatment group according to the highest dose received.
For subjects missing their last exposure date at the time of study end, their last visit date in the study was used.

Protocol: AMB114588
Population: Safety

Table 3.2: Summary of Treatment-Emergent Adverse Events

System Organ Class Preferred term	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Any event	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Gastrointestinal disorders					
Any event	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Dyspepsia	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Nausea	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Nervous system disorders					
Any event	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Headache	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Dizziness	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Somnolence	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Tremor	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Sedation	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..					

Note: Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Events will be sorted in descending order of total incidence across treatment groups for the System Organ Class and in descending order of total incidence for the preferred term within each System Organ Class. If the total incidence for any two or more preferred terms is equal, they will be presented in alphabetical order.

Protocol: AMB114588
Population: Safety

Table 3.3: Summary of Treatment-Emergent Adverse Events by Preferred Term

Preferred term	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Any event	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Dyspepsia	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Nausea	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Headache	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Dizziness	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Somnolence	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Tremor	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Sedation	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..					

Note: Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Events will be sorted in descending order of total incidence across treatment groups for the preferred term. If the total incidence for any two or more preferred terms is equal, they will be presented in alphabetical order.

Protocol: AMB114588
Population: Safety

Table 3.4: Summary of Treatment-Emergent Adverse Events by Maximum Intensity

	Ambrisentan 2.5mg (N=XXX)			Ambrisentan 5mg (N=XXX)			Ambrisentan 7.5mg (N=XXX)			Ambrisentan 10mg (N=XXX)		
	Mild	Moderate	Severe	Mild	Moderate	Severe	Mild	Moderate	Severe	Mild	Moderate	Severe
System Organ Class Preferred Term												
Any Event	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Cardiovascular disorders	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Any Event	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Hypertension	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Syncope	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Aneurysms	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Hypotension	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..												

Note: Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Repeat display for Total group on following page. Subjects who experience the same event several times, with different intensities/grades, will only be counted with the maximum intensity/grade. For example, a subject who had three headaches, two severe and one mild, is counted only once, under the preferred term "Headache" in the "Severe" column of the table. Likewise, each subject is counted only once, at the maximum severity/grade, within each SOC even though they may have several different PT events at different intensities/grades within that SOC. Events will be sorted in descending order of total incidence across treatment groups for the System Organ Class and in descending order of total incidence for the preferred term within each System Organ Class. If the total incidence for any two or more preferred terms is equal, they will be presented in alphabetical order.

Protocol: AMB114588
Population: Safety

Table 3.5: Summary of Treatment-Emergent Adverse Events by Action Taken with IP

System Organ Class Preferred term Action Taken	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Any event	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
<System Organ Class 1>					
<Any event>	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
IP withdrawn	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Dose interrupted	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Dose reduced	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Dose not changed	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Dose increased	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Not applicable	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
<Preferred Term 1>	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
IP withdrawn	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Dose interrupted	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Dose reduced	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Dose not changed	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Dose increased	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Not applicable	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..					

Note: Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Subjects who experience the same event several times, with different Action Taken, will only be counted once for the overall and Preferred Term category, but more than once in the Action Taken categories. Events will be sorted in descending order of total incidence across treatment groups for the preferred term. If the total incidence for any two or more preferred terms is equal, they will be presented in alphabetical order.

Protocol: AMB114588
Population: Safety

Table 3.8: Summary of Cumulative Incidence of Treatment-Emergent Adverse Events by Time to First Occurrence

Treatment: Ambrisentan 2.5mg (N=XXX)

System Organ Class Preferred term	Time Since Start of Study Medication in AMB114588							Overall
	<=3 months	>3 to <=6 months	>6 to <=9 months	Etc..	Etc..	Etc..	Etc..	
Any event	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Gastrointestinal disorders								
Any event	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Dyspepsia	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Nausea	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Nervous system disorders								
Any event	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Headache	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Dizziness	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Somnolence	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Tremor	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Sedation	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..								

Note: Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Events will be sorted in descending order of total incidence across treatment groups for the preferred term. If the total incidence for any two or more preferred terms is equal, they will be presented in alphabetical order. Repeat for all Ambrisentan and Total groups.

Protocol: AMB114588
Population: Safety

Table 3.10: Summary of Serious Treatment-Emergent Adverse Events – Number of Subjects and Occurrences

System Organ Class Preferred Term	Treatment Group	Subjects Affected, Number	Subjects Exposed, Number	Occurrences All, Number	Occurrences Causally Related to Treatment, Number*	Fatalities, Number	Fatalities Causally Related to Treatment, Number*
CARDIAC DISORDERS							
Atrial fibrillation	Ambrisentan 2.5mg	x	x	x	x	x	x
	Ambrisentan 5mg	x	x	x	x	x	x
	Ambrisentan 7.5mg	x	x	x	x	x	x
	Ambrisentan 10mg	x	x	x	x	x	x
	Total	x	x	x	x	x	x
Bradyarrhythmia							
etc							

Note: * Drug-related as determined by the investigator.
Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Protocol: AMB114588
Population: Safety

Table 3.11: Summary of Serious Treatment-Emergent Adverse Events by Outcome

System Organ Class Preferred term Outcome	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Any event	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
<System Organ Class 1>					
<Any event>	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Recovered/Resolved	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Recovering/Resolving	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Recovered/Resolved with sequelae	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Not Recovered/ Not Resolved	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
<Preferred Term 1>	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Recovered/Resolved	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Recovering/Resolving	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Recovered/Resolved with sequelae	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Not Recovered/ Not Resolved	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..					

Note: Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Subjects who experience the same event several times, with different Outcome, will only be counted once for the overall and Preferred Term category, but more than once in the Outcome categories. Events will be sorted in descending order of total incidence across treatment groups for the preferred term. If the total incidence for any two or more preferred terms is equal, they will be presented in alphabetical order.

Protocol: AMB114588
Population: Safety

Table 3.21: Summary of Haematology Data

Central/Local Laboratory
Parameter: <Parameter (units)>

Treatment	Planned Relative Time	N	Mean	SD	Q1	Median	Q3	Min.	Max.
Ambrisentan 2.5mg (N=XXX)	Baseline**	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Entry Visit*	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Month 1	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Month 2	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Month 3	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Month 4	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Month 5	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Month 6	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Etc..	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
Ambrisentan 5mg (N=XXX)	Etc..								
Ambrisentan 7.5mg (N=XXX)	Etc..								
Ambrisentan 10mg (N=XXX)	Etc..								
Total (N=XXX)	Etc..								

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to the treatment group according to the highest dose received.
USER ID: Directory/Program.sas Date Time
Programming notes: Present available visits, End of Study and Follow-Up. Absolute value tables done separately for central and local labs. Change from baseline required only for the subset of subjects who have QUEST Central labs throughout.

Protocol: AMB114588
Population: Safety

Table 3.23: Summary of Haematology Data of Potential Clinical Concern

Central/Local Laboratory
Parameter: <Parameter (units) [Reference range = xx.x to xx.x]>

Planned Relative Time	Category	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Baseline**	N	XXX	XXX	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Entry Visit*	N	XXX	XXX	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Month 1	N	XXX	XXX	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Month 2	N	XXX	XXX	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..						
Any time post-baseline	N	XXX	XXX	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
For 'Any time in AMB114588 (Entry to End of Study)':-
Subjects with both Normal and Low values are counted once under their worst case (Low).
Subjects with both Normal and High values are counted once under their worst case (High).
Subjects with both High and Low values are counted under both categories.
Subjects are considered as belonging to the treatment group according to the highest dose received.
USER ID: Directory/Program.sas Date Time
Programming notes: Present available visits, End of Study and Follow-Up.

Table 3.29: Summary of Liver Events Assessment

	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Subjects reporting a significant liver chemistry result *	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Subjects with event occurring while receiving study treatment	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Subjects with event occurring after stopping study treatment	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)

Note: * A significant liver chemistry result is any result which meets the stopping criteria defined in the protocol.
Detailed information on liver events assessment can be found in related listings.
Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Table 3.30 Summary of Vital Signs

Parameter	Treatment	Planned Relative Time	n	Mean	SD	Q1	Median	Q3	Min.	Max.
<Parameter (units)>	Ambrisentan 2.5mg (N=XXX)	Baseline**	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Entry Visit	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Month 3	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Month 6	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Month 9	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Month 12	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Etc..	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Ambrisentan 5mg (N=XXX)	Etc..								
	Ambrisentan 5mg (N=XXX)	Etc..								
	Ambrisentan 5mg (N=XXX)	Etc..								
	Total (N=XXX)	Etc..								

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits, End of Study and Follow-Up. Include Height, Weight, Systolic BP, Diastolic BP, Heart Rate, BSA and BMI.

Protocol: AMB114588
Population: Safety

Table 3.32: Summary of Vital Signs Data of Potential Clinical Concern

Parameter: <Parameter (units) [Reference range = xx.x to xx.x]>

Planned Relative Time	Category	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Baseline**	n	XXX	XXX	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Entry Visit*	n	XXX	XXX	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Month 3	n	XXX	XXX	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Month 6	n	XXX	XXX	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..						
Any time Post-baseline	n	XXX	XXX	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
For 'Any time in AMB114588 (Entry to End of Study)':-
Subjects with both Normal and Low values are counted once under their worst case (Low).
Subjects with both Normal and High values are counted once under their worst case (High).
Subjects with both High and Low values are counted under both categories.
Subjects are considered as belonging to the treatment group according to the highest dose received.
USER ID: Directory/Program.sas Date Time
Programming notes: Present available visits, End of Study and Follow-Up. Include Systolic BP, Diastolic BP and Heart Rate.

Protocol: AMB114588
Population: Safety

Table 3.34: Summary of Physical Examination by Visit

Planned Relative Time: Entry Visit*	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Liver Size					
Normal	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Abnormal	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Jugular Venous Pressure					
Normal	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Abnormal	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Ascites					
Absent	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Present	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Peripheral Oedema					
Absent	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Present	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Saturated Oxygen (units)					
n	XXX	XXX	XXX	XXX	XXX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X	XX.X	XX.X
Min.	XX	XX	XX	XX	XX
Max.	XX	XX	XX	XX	XX

Note: * Entry Visit is at entry to AMB114588.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Present for available visits, Follow-Up and End of Study.

Protocol: AMB114588
Population: Safety

Table 3.34: Summary of Physical Examination by Visit

Planned Relative Time: Month 6	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Liver Size					
N	XX	XX	XX	XX	XX
Normal	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Abnormal:Improved	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Abnormal:Unchanged	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Abnormal:Worsened	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Jugular Venous Pressure					
N	XX	XX	XX	XX	XX
Normal	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Abnormal:Improved	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Abnormal:Unchanged	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Abnormal:Worsened	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Ascites					
n	XX	XX	XX	XX	XX
Absent	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Present:Improved	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Present:Unchanged	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Present:Worsened	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Peripheral Oedema					
n	XX	XX	XX	XX	XX
Absent	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Present:Improved	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Abnormal:Worsened	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Abnormal:Unchanged	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)

Note: * Entry Visit is at entry to AMB114588.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Present for available visits, Follow-Up and End of Study.

Table 3.34: Summary of Physical Examination by Visit

Planned Relative Time: Month 6	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Saturated Oxygen (units)					
n	XXX	XXX	XXX	XXX	XXX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X	XX.X	XX.X
Min.	XX	XX	XX	XX	XX
Max.	XX	XX	XX	XX	XX

Note: * Entry Visit is at entry to AMB114588.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Present for available visits, Follow-Up and End of Study.

Protocol: AMB114588
Population: Safety

Table 3.35: Summary of 12-lead ECG

Planned Relative Time	Category	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Baseline**	n	XXX	XXX	XXX	XXX	XXX
	Normal	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	Abnormal, not clinically significant	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	Abnormal, clinically significant	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Entry Visit*	n	XXX	XXX	XXX	XXX	XXX
	Normal	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	Abnormal, not clinically significant	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	Abnormal, clinically significant	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Month 6	n	XXX	XXX	XXX	XXX	XXX
	Normal	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	Abnormal, not clinically significant	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	Abnormal, clinically significant	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Month 12	n	XXX	XXX	XXX	XXX	XXX
	Normal	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	Abnormal, not clinically significant	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	Abnormal, clinically significant	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..						
Any time post-study entry	n	XXX	XXX	XXX	XXX	XXX
	Normal	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	Abnormal, not clinically significant	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
	Abnormal, clinically significant	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
For 'Any time in AMB114588 (Entry to End of Study)' if a subject had more than one ECG result, the worst case will be chosen for a conservative approach.
Subjects are considered as belonging to the treatment group according to the highest dose received.
USER ID: Directory/Program.sas Date Time
Programming notes: Present for available visits, Follow-Up and End of Study.

Table 3.36: Summary of Endocrinology assessments – Female

Overall

Planned Relative Time Baseline**	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Female breast development					
N	XXX	XXX	XXX	XXX	XXX
Pre-adolescent	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Breast bud stage	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Female pubic hair development					
N	XXX	XXX	XXX	XXX	XXX
Pre-adolescent	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Sparse growth	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Subjects are considered as belonging to the treatment group according to the highest dose received.
Pre-pubertal at baseline: Stage 1 breast development, Post-pubertal at baseline: Stage ≥ 2 breast development.
For some patients, pubertal development assessments were not repeated at 20 years of age if pubertal maturity had been reached in a previous visit.

USER ID: Directory/Program.sas Date Time

Programming notes: Present for Baseline, Entry Visit, all available visits, End of Study and Follow Up. Present Overall and by Pubertal Status (Pre-pubertal, Post Pubertal).

Protocol: AMB114588
Population: Safety

Table 3.37: Summary of Endocrinology assessments – Male
Overall

Planned Relative Time Baseline**	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Right Testicular volume (units)					
N	XXX	XXX	XXX	XXX	XXX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X	XX.X	XX.X
Min.	XX	XX	XX	XX	XX
Max.	XX	XX	XX	XX	XX
Left Testicular volume (units)					
N	XXX	XXX	XXX	XXX	XXX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X	XX.X	XX.X
Min.	XX	XX	XX	XX	XX
Max.	XX	XX	XX	XX	XX

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to the treatment group according to the highest dose received.
Pre-pubertal at baseline: testicular volume < 4 ml, Post-pubertal at baseline: testicular volume ≥ 4 ml
For some patients, pubertal development assessments were not repeated at 20 years of age if pubertal maturity had been reached in a previous visit.

USER ID: Directory/Program.sas Date Time

Programming notes: Present for Baseline, Entry Visit, all available visits, End of Study and Follow Up. Present Overall and by Pubertal Status (Pre-pubertal, Post Pubertal).

Table 3.37: Summary of Endocrinology assessments – Male
Overall

Planned Relative Time Baseline**	Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Male genital development					
N	XXX	XXX	XXX	XXX	XXX
Pre-adolescent	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Male pubic hair development					
N	XXX	XXX	XXX	XXX	XXX
Pre-adolescent	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Sparse growth	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc.	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to the treatment group according to the highest dose received.
Pre-pubertal at baseline: testicular volume < 4 ml, Post-pubertal at baseline: testicular volume ≥ 4 ml
For some patients, pubertal development assessments were not repeated at 20 years of age if pubertal maturity had been reached in a previous visit.
USER ID: Directory/Program.sas Date Time

Programming notes: Present for Baseline, Entry Visit, all available visits, End of Study and Follow Up. Present Overall and by Pubertal Status (Pre-pubertal, Post Pubertal).

Protocol: AMB114588
Population: Safety

Table 3.38: Summary of Pubertal Development Shifts from Baseline – Female
Overall

Female Breast Development

Treatment	Planned Relative Time	Code	Baseline** Code 1	2	3	4	5
Ambrisentan 2.5mg (N=XXX)	Entry Visit*	1	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
		2	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
		3	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
		4	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
		5	XX (%)	XX (%)	XX (%)	XX (%)	XX
		Unknown/ Not Recorded	XX	XX	XX	XX	XX
	Etc..	1	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
		2	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
		3	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
		4	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
		5	XX (%)	XX (%)	XX (%)	XX (%)	XX
		Unknown/ Not Recorded	XX	XX	XX	XX	XX
Etc..							

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Subjects are considered as belonging to the treatment group according to the highest dose received.
Pre-pubertal at Baseline: Stage 1 breast development, Post-pubertal at Baseline: Stage ≥ 2 breast development.
For some patients, pubertal development assessments were not repeated at 20 years of age if pubertal maturity had been reached in a previous visit.
USER ID: Directory/Program.sas Date Time
Programming notes: Present for Female Breast Development and Female Pubic Hair Development, for each treatment group, overall and by Pubertal Status (Pre-pubertal, Post Pubertal), at all available visits. Put coding below on first page on listing:-
Female Breast Development:-
1=Pre-adolescent; elevation of papilla only, **2**=etc…
Female Pubic Hair Development:-
1=Pre-adolescent; vellus over pubes not developed over anterior abdominal wall, 2=etc…

Protocol: AMB114588
Population: Safety

Table 3.39: Summary of Pubertal Development Shifts from Baseline - Male
Overall

Male Genital Development

Treatment	Planned Relative Time	Code	Baseline** Code 1	2	3	4	5
Ambrisentan 2.5mg N=XXX)	Entry Visit*	1	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
		2	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
		3	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
		4	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
		5	XX (%)	XX (%)	XX (%)	XX (%)	XX
		Unknown/ Not Recorded	XX	XX	XX	XX	XX
	Etc..	1	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
		2	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
		3	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
		4	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
		5	XX (%)	XX (%)	XX (%)	XX (%)	XX
		Unknown/ Not Recorded	XX	XX	XX	XX	XX
Etc..							

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Subjects are considered as belonging to the treatment group according to the highest dose received.
Pre-pubertal at Baseline: testicular volume < 4 ml, Post-pubertal at Baseline: testicular volume ≥ 4 ml
For some patients, pubertal development assessments were not repeated at 20 years of age if pubertal maturity had been reached in a previous visit.
USER ID: Directory/Program.sas Date Time
Programming notes: Present for Male Genital Development and Male Pubic Hair Development, for each treatment group, overall and by Pubertal Status (Pre-pubertal, Post Pubertal), at all available visits. Put coding below on first page on listing:-
Male Genital Development:-
1=Pre-adolescent; testes, scrotum and penis same size and proportion, **2**=etc…
Male Pubic Hair Development:-
1=Pre-adolescent; velus over pubes no further developed than over abdominal wall, 2=etc…

Protocol: AMB114588
Population: Safety

Table 3.40: Summary of Testicular Volume Change from Baseline - Male Overall

Planned Relative Time		Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Entry Visit*	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX
Etc..	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX
Etc..						

Note: * Entry Visit is at entry to AMB114588.
Baseline is the last value recorded prior to start of study treatment from AMB112529.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to the treatment group according to the highest dose received.
Pre-pubertal at Baseline: testicular volume < 4 ml, Post-pubertal at Baseline: testicular volume ≥ 4 ml
For some patients, pubertal development assessments were not repeated at 20 years of age if pubertal maturity had been reached in a previous visit.
USER ID: Directory/Program.sas Date Time
Programming notes: Present overall and by Pubertal Status (Pre-pubertal, Post Pubertal), at all available visits.

Protocol: AMB114588
Population: Safety

Table 3.41: Summary of Change from Baseline in Plasma Endocrine Parameters – Female
Overall

Central Laboratory
Parameter: <Parameter (units)>

Planned Relative Time		Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Entry Visit*	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX
Etc..	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX
Etc..						

Note: * Entry Visit is at entry to AMB114588.
Baseline is the last value recorded prior to start of study treatment from AMB112529.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to the treatment group according to the highest dose received.
Pre-pubertal at Baseline: Stage 1 breast development, Post-pubertal at Baseline: Stage ≥ 2 breast development.
For some patients, pubertal development assessments were not repeated at 20 years of age if pubertal maturity had been reached in a previous visit.
USER ID: Directory/Program.sas Date Time

Programming notes: Present overall and by Pubertal Status (Pre-pubertal, Post Pubertal), at available visits, for Follicle Stimulating Hormone, Luteinizing Hormone, Sex Hormone Binding Globulin, Total Testosterone and Inhibin B. Change from baseline presented only for the subset of subjects who have QUEST Central labs throughout.

Protocol: AMB114588

Population: Safety

Table 3.42: Summary of Change from Baseline in Plasma Endocrine Parameters – Male
Overall

Central Laboratory
Parameter: <Parameter (units)>

Planned Relative Time		Ambrisentan 2.5mg (N=XXX)	Ambrisentan 5mg (N=XXX)	Ambrisentan 7.5mg (N=XXX)	Ambrisentan 10mg (N=XXX)	Total (N=XXX)
Entry Visit*	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX
Etc..	N	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X	XX.X	XX.X
	Min.	XX	XX	XX	XX	XX
	Max.	XX	XX	XX	XX	XX
Etc..						

Note: * Entry Visit is at entry to AMB114588.
Baseline is the last value recorded prior to start of study treatment from AMB112529.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to the treatment group according to the highest dose received.
Pre-pubertal at Baseline: testicular volume < 4 ml, Post-pubertal at Baseline: testicular volume ≥ 4 ml
For some patients, pubertal development assessments were not repeated at 20 years of age if pubertal maturity had been reached in a previous visit.
USER ID: Directory/Program.sas Date Time

Programming notes: Present overall and by Pubertal Status (Pre-pubertal, Post Pubertal), at available visits, for Follicle Stimulating Hormone, Luteinizing Hormone, Sex Hormone Binding Globulin, Total Testosterone and Inhibin B. Change from baseline presented only for the subset of subjects who have QUEST Central labs throughout.

Protocol: AMB114588
Population: Intent-to-Treat

Table 3.43
Summary of Time to change in dose of ambrisentan or other targeted PAH therapeutic agents (prostanoids, PDE-5 inhibitors) due to tolerability issues (days)

	Ambrisentan Dose Group				
	2.5mg (N=x)	5mg (N=xx)	7.5mg (N=x)	10mg (N=xx)	Total (N=xx)
n	x	x	x	x	x
Mean	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x
SD		xx.xx		xxx.xx4	xxx.xx
Q1	xxx.x	xxx.x	xxx.x	xxx.x	xxx.x
Median	xxx.x	xxx.x	xxx.x	xxxx.x	xxx.x
Q3	xxx.x	xxx.x	xxx.x	xxxx.x	xxx.x
Min.	xxx	xxx	xxx	xxx	xxx
Max.	xxx	xxx	xxx	xxxx	xxxx

Table 3.44
Summary of Treatment-Emergent Adverse Events by PAH Therapy

System Organ Class Preferred Term	Treatment A (N=100) None N=x	Any N=x	PDE5i Only N=x	Prost. Only N=x	Both N=x	Treatment B (N=100) None N=x	Any N=x	PDE5i Only N=x	Prost. Only N=x	Both N=x
ANY EVENT	x (100%)	x (100%)	x (100%)	0	0	x (57%)	x (100%)	x (100%)	0	0
Infections and infestations										
Any event	x (100%)	x (67%)	x (67%)	0	0	x (29%)	x (67%)	x (67%)	0	0
Upper respiratory tract infection	x (100%)	x (33%)	x (33%)	0	0	x (14%)	x (22%)	x (22%)	0	0
Nasopharyngitis	0	0	0	0	0	x (14%)	x (44%)	x (44%)	0	0
Pharyngitis	0	x (33%)	x (33%)	0	0	0	x (33%)	x (33%)	0	0
Gastroenteritis	0	x (33%)	x (33%)	0	0	0	x (22%)	x (22%)	0	0
Influenza	0	0	0	0	0	0	x (33%)	x (33%)	0	0
Pneumonia	0	x (33%)	1 (33%)	0	0	0	x (11%)	x (11%)	0	0
Bronchitis	0	0	0	0	0	0	x (11%)	x (11%)	0	0
Gastroenteritis viral	0	0	0	0	0	0	x (22%)	x (22%)	0	0
Hordeolum	0	0	0	0	0	0	x (11%)	x (11%)	0	0
Otitis externa	0	0	0	0	0	0	x (22%)	x (22%)	0	0
Otitis media	0	1 (33%)	x (33%)	0	0	0	0	0	0	0
Otitis media chronic	0	1 (33%)	x (33%)	0	0	0	0	0	0	0
Pharyngotonsillitis	0	0	0	0	0	0	0	0	0	0
Respiratory tract infection	0	0	0	0	0	0	0	0	0	0
Rhinitis	0	0	0	0	0	0	x (11%)	x (11%)	0	0
Sinusitis	0	0	0	0	0	0	1 (11%)	x (11%)	0	0

Note: Prost.=Prostanoids.

USER ID: Directory/Program.sas Date Time

Programming Notes:
Repeat for

3.45	Summary of Serious Treatment Emergent Adverse Events by PAH Therapy
3.46	Summary of Non-Serious Treatment Emergent Adverse Events by PAH Therapy
3.47	Summary of Common (>=5%) Treatment Emergent Adverse Events by PAH Therapy **Footnote:** Note: Common adverse events (>=5%) were those experienced by at least 5% of subjects in the total population (N=38) irrespective of dose group and/or PAH therapy

Protocol: AMB114588
Population: Safety

Table 3.48
Summary of Treatment Emergent Adverse Events by PAH Aetiology

System Organ Class Preferred Term	Treatment A (N=100)		Treatment B (N=100)		Treatment C (N=6)	
	Idiopathic N=xx	Non-Idiopathic N=xx	Idiopathic N=xx	Non-Idiopathic N=xx	Idiopathic N=xx	Non-Idiopathic N=xx
ANY EVENT	0	x (xx%)	x (xx%)	x (xx%)	x (xx%)	x (xx%)
Infections and infestations						
Any event	0	x (xx%)	x (xx%)	x (xx%)	x (xx%)	x (xx%)
Upper respiratory tract infection	0	x (xx%)	x (xx%)	x (xx%)	x (xx%)	x (xx%)
Nasopharyngitis	0	0	x (xx%)	x (xx%)	x (xx%)	0
Pharyngitis	0	x (xx%)	x (x%)	x (xx%)	0	0
Gastroenteritis	0	x (xx%)	0	xx (xx%)	0	0
Influenza	0	0	x (xx%)	x (xx%)	0	0
Bronchitis	0	0	0	1 (xx%)	x (xx%)	0
Gastroenteritis viral	0	0	x (x%)	1 (xx%)	0	0
Hordeolum	0	0	0	1 (xx%)	1 (xx%)	0
Otitis externa	0	0	0	2 (xx%)	0	0
Otitis media	0	x (xx%)	0	0	0	0

Note: Idiopathic group refers to those with an idiopathic aetiology of PAH at baseline in study AMB112529 and non-idiopathic refers to those classified as having an aetiology of familial, persistent PAH despite surgical repair, or secondary to connective tissue disease.

USER ID: Directory/Program.sas Date Time

Programming Notes:
Repeat for

3.49	Summary of Serious Treatment Emergent Adverse Events by PAH Aetiology
3.50	Summary of non-Serious Treatment Emergent Adverse Events by PAH Aetiology
3.51	Summary of Common (>=5%)Treatment Emergent Adverse Events by PAH Aetiology **Footnote:** Note: Common adverse events (>=5%) were those experienced by at least 5% of subjects in the total population (N=38) irrespective of dose group and/or PAH Aetiology.

Protocol: AMB114588
Population: Safety

Table 3.52 Summary of Cardiopulmonary Hemodynamics

Parameter	Treatment	Planned Relative Time	n	Mean	SD	Q1	Median	Q3	Min.	Max.
<Parameter (units)>	Ambrisentan 2.5mg (N=XXX)	Baseline**	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Entry Visit	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Month 3	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Month 6	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Month 9	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Month 12	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Etc..	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Ambrisentan 5mg (N=XXX)	Etc..								
	Ambrisentan 5mg (N=XXX)	Etc..								
	Ambrisentan 5mg	Etc..								

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Q1 = 1st quartile, Q3 = 3rd quartile.
Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Present available visits, End of Study and Follow-Up. Include all the available parameters.

Protocol: AMB114588
Population: Intent-to-Treat

Listing 1.1: Listing of Reasons for Study Withdrawal

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Date of Withdrawal	Study Day	Reason for Withdrawal
XXXXXX/ XXXXXX	DDMMMYYYY	XX	XXXXXXXXXXXXX
XXXXXX/ XXXXXX	DDMMMYYYY	XX	XXXXXXXXXXXXX
XXXXXX/ XXXXXX	DDMMMYYYY	XX	XXXXXXXXXXXXX
Etc..			

Note: Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group and Centre/Subject ID. Sort by treatment group, Centre ID, Subject ID.

Protocol: AMB114588
Population: Intent-to-Treat

Listing 1.2: Listing of Subjects with Inclusion/Exclusion Criteria Deviations

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Type	Criterion
XXXXXX/ XXXXXX	Inclusion	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
	Exclusion	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX
Etc..		

Note: Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group and Centre/Subject ID. Sort by treatment group, Centre ID, Subject ID.

Protocol: AMB114588
Population: Intent-to-Treat

Listing 1.3: Listing of Demographic Characteristics

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Partial Date of Birth	Age (years)*	Sex	Child Bearing Potential	Has Child Bearing Potential Changed?	Date of Child Bearing Potential Change	Ethnicity
XXXXXX/ XXXXXX	YYYY	XX	Female	Pre-menarcheal	Yes	DDMMMYYYY ^	Hispanic/Latino
Etc..							

Note: * Age at start of study treatment in AMB112529
^ Date of first menses
# Date of final menses
~ Date became sterile
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group and Centre/Subject ID. Sort by treatment group, Centre ID, Subject ID.

Protocol: AMB114588
Population: Intent-to-Treat

Listing 1.4: Listing of Race

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Race
XXXXXX/ XXXXXX	Asian – East Asian Heritage
Etc..	

Note: Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group and Centre/Subject ID. Sort by treatment group, Centre ID, Subject ID.

Protocol: AMB114588
Population: Intent-to-treat

Listing 1.5: Listing of Disease History

Treatment: Ambrisentan 2.5mg

Centre ID / Subject ID	Diagnosis	Sub category	Date of Diagnosis	Duration of PAH (yrs)	Baseline WHO FC
XXXXXX / XXXXXX	Idiopathic PAH		DDMMMYYYY	X.X	I
XXXXXX / XXXXXX	Persistent PAH despite surgical repair	Atrio-ventricular septal defects	DDMMMYYYY	X.X	II
Etc..					

Note: Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group and Centre/Subject ID. Sort by treatment group, Centre ID, Subject ID.
Produce listing for data collected in AMB112529 for the subset of subjects who entered AMB114588.

Protocol: AMB114588
Population: Intent-to-Treat

Listing 1.6: Listing of Medical Conditions

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Age (y)/ Sex/	Classification	Preferred Term	Condition	Status
XXXXXX/ XXXXXX	XX/ XXXXXX	Hepatobiliary disorders	XXXXXXXXXXXXXXX	HEPATITIS A	Current
		Psychiatric disorders	XXXXXXXXXXXXXXXX	PARANOIA COMBINED WITH MANIA.	Past
XXXXXX/ XXXXXX	XX/ XXXXXX	Eye disorders	XXXXXXXXXXXXXXXX	ASTIGMATISM	Current
XXXXXX/ XXXXXX	XX/ XXXXXX	Metabolism and nutrition disorders	XXXXXXXXXXX	RICKETS	Current
Etc..					

Note: Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group and Centre/Subject ID. Sort by treatment group, Centre ID, Subject ID.
Produce listing for data collected in AMB112529 for the subset of subjects who entered AMB114588.

Protocol: AMB114588
Population: Intent-to-Treat

Listing 1.7: Listing of Medications

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	ATC Level 1/ Ingredient/ Verbatim Text	Total Daily Dose/ Units/ Freq/ Route	Date Started/ Study Day	Date Stopped/ Study Day	Reason For Medication
XXXXXX/ XXXXXX	Endocrine & metabolic/ Fluticasone propionate/ FLIXOTIDE #	2/ MG/ 2XD/ IH	27SEP1999/ 15	02OCT1999	xxxxxxxxxx
	Endocrine & metabolic/ Fluticasone propionate/ FLIXOTIDE #	4/ MG/ 2XD/ IH	03OCT1999/ 21	Ongoing	
	Etc..				
Etc..					

Note: * Prior, # Concomitant, $ Post-treatment.
PAH Therapies are not included within this listing, for PAH Therapy please see Listing 1.7
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group and Centre/Subject ID. Sort by treatment group, Centre ID, Subject ID.

Protocol: AMB114588
Population: Intent-to-Treat

Listing 1.8: Listing of PAH Therapy

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Drug Class/ ATC Level 1/ Ingredient/ Verbatim Text/	Total Daily Dose/ Units	Date Started/ Study Day	Date Stopped/ Study Day	Reason the medication started?
XXXXXX/ XXXXXX	XXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXX/ XXXXXXXXXXX #@	X/ XX	DDMMMYYYY/ XX	DDMMMYYYY	XXXXXXXXXXXXXXX
XXXXXX/ XXXXXX	XXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXX/ XXXXXXXXXXX #	X/ XX	DDMMMYYYY/ XX	Ongoing	XXXXXXXXXXXXXX
	Etc..				
Etc..					

Note: * Prior, # Concomitant, $ Post-treatment.
@ Ongoing background PAH therapy at baseline
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group and Centre/Subject ID. Sort by treatment group, Centre ID, Subject ID.

Protocol: AMB114588
Population: Intent-to-Treat

Listing 1.9: Relationship between ATC Level 1, Ingredient and Verbatim Text

ATC Level 1	Ingredient	Verbatim Text
Endocrine & metabolic	Fluticasone Propionate Prednisolone	FLIXOTIDE PREDNISOLONE
Drugs acting via the nervous system	Paracetamol	PANADOL CHILDREN'S PANADOL 1-5YERS
Etc..		

USER ID: Directory/Program.sas Date Time

Programming notes: Sort by ATC level 1treatment group, Ingredient.

Protocol: AMB114588
Population: Intent-to-Treat

Listing 1.10: Listing of Compliance Data

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	% of compliant visits	Visit	Visit Date/ Study Day	Compliance since the last visit
XXXXXX/ XXXXXX	100	XXXXXXXXX	DDMMMYYYY/ XX	
		XXXXXXXXX	DDMMMYYYY/ XX	>=80% and <=120%
		XXXXXXXXX	DDMMMYYYY/ XX	>=80% and <=120%
		XXXXXXXXX	DDMMMYYYY/ XX	>=80% and <=120%
		XXXXXXXXX	DDMMMYYYY/ XX	>=80% and <=120%
		XXXXXXXXX	DDMMMYYYY/ XX	>=80% and <=120%
		XXXXXXXXX	DDMMMYYYY/ XX	>=80% and <=120%

Etc..

Note: Compliant visits are those at which subjects are >=80% and <=120% compliant.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group, Centre/Subject ID and time-point. Sort by treatment group, Centre ID, Subject ID and time-point.

Protocol: AMB114588
Population: Intent-to-Treat

Listing 1.11: Listing of initial, highest and final dose of ambrisentan

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Initial dose mg/kg	Highest dose mg/kg	Final dose mg/kg
XXXXXX/ XXXXXX	X.X	X.X	X.X
XXXXXX/ XXXXXX	X.X	X.X	X.X
	Etc..		
Etc..			

Note: Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Protocol: AMB114588
Population: Intent-to-Treat

Listing 1.12: Listing of Protocol Deviation

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Important Protocol Deviations	Protocol Deviation Category	Protocol Deviation Description	Protocol Deviation Date/ Study Day	Visit Phase	Action taken	Escalated for Medical Oversight ?
XXXXXX/ XXXXXX	Y	Biological specimen sample procedures	XXXXXXXXXXXXXXXXXXXX XXX *	DDMMMYYYY/ XX	XXXXXXXX	XXXXXXXXX XXXXXXXXX XXXXX	
XXXXXX/ XXXXXX	N	Other: XXXXXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXX XXX	DDMMMYYYY/ XX	XXXXXXXX	XXXXXXXXX XXXXXXXXX XXXXX	
		Etc..					
Etc..							

Note: * Important Deviation
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group and Centre/Subject ID. Sort by treatment group, Centre ID, Subject ID.

Protocol: AMB114588
Population: Intent-to-Treat

Listing 2.1: Listing of Time to Death (All cause)

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Death Date/ Study Day	Details
XXXXXX/ XXXXXX	DDMMMYYYY/ XX	
	DDMMMYYYY/ XX	
Etc..		

Note: Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group and Centre/Subject ID. Sort by treatment group, Centre ID, Subject ID.

Protocol: AMB114588
Population: Intent-to-Treat

Listing 2.2: Listing of 6 Minute Walking Distance Data

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Visit	Visit Date/ Time/ Study Day	Distance Walked (m)			Did subject walk less than 6 minutes?/ Reason for stopping prematurely	Duration walked (seconds)	Did subject use supplemental oxygen	Oxygen flow rate (L/min)
			Actual	Change from Baseline	Percentage Change from Baseline				
XXXXXX/ XXXXXX	Baseline **	DDMMMYYYY/ HH:MM/ XX	XXX			Y/ XXXXXXXXXXXX	XXX	Y	XXXX
	Entry Visit *	DDMMMYYYY/ HH:MM/ XX	XXX	XXX	XXX	Y/ XXXXXXXXXXXX	XXX	Y	XXXX
	XXXXXXX	DDMMMYYYY/ HH:MM/ XX	XXX	XXX	XXX	N		N	
	XXXXXXX	DDMMMYYYY/ HH:MM/ XX	XXX	XXX	XXX	N		N	
	Etc..								
	Etc..								

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group, Centre/Subject ID and time-point. Sort by treatment group, Centre ID, Subject ID and time-point.

Protocol: AMB114588
Population: Intent-to-Treat

Listing 2.3: Listing of Clinical Worsening of PAH

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Event Date/ Study Day	Clinical worsening criteria
XXXXXX/ XXXXXX	DDMMMYYYY/ XX	Hospitalisation for worsening of PAH
	DDMMMYYYY/ XX	PAH related deterioration: Clinical signs or symptoms of right sided heart failure
Etc..		

Note: Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group and Centre/Subject ID. Sort by treatment group, Centre ID, Subject ID.

Protocol: AMB114588
Population: Intent-to-Treat

Listing 2.6: Listing of WHO Functional Class Data

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Visit	Visit Date/ Study Day	WHO pulmonary hypertension functional classification	Actual $	Change from Baseline	Change Categorisation
XXXXXX/ XXXXXX	Baseline **	DDMMMYYYY/ XX	Class II	2		
	Entry Visit *	DDMMMYYYY/ XX	Class II	2	0	NC
	XXXXXXX	DDMMMYYYY/ XX	Class IV	4	2	Det
	XXXXXXX	DDMMMYYYY/ XX	Class I	1	-1	Imp
	Etc..					
Etc..						

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
There are 4 grades for WHO FC based on severity of symptoms (CCI [redacted]).
$ Grades mapped to numeric scale 1-4 (i.e. Class IV = 4).
Change categorisation (based on -2, -1, 0, +1, +2); CCI [redacted],
CCI [redacted].
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group, Centre/Subject ID and time-point. Sort by treatment group, Centre ID, Subject ID and time-point.

Protocol: AMB114588
Population: Intent-to-Treat

Listing 2.7: Listing of Plasma NT-Pro BNP Concentration (ng/L)

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Visit	Visit Date/ Study Day	Visit Value		Change from Baseline	
			Raw	Log	Raw	Log$
XXXXXX/ XXXXXX	Baseline **	DDMMMYYYY/ XX	XXX.X	X.XX		
	Entry Visit *	DDMMMYYYY/ XX	XXX.X	X.XX	XXX.X	X.XX
	XXXXXXX	DDMMMYYYY/ XX	XXX.X	X.XX	XXX.X	X.XX
	XXXXXXX	DDMMMYYYY/ XX	XXX.X	X.XX	XXX.X	X.XX
	Etc..					
Etc..						

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
$ Log (change from baseline) = Log (Visit) – Log (Baseline).
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group, Centre/Subject ID and time-point. Sort by treatment group, Centre ID, Subject ID and time-point.

Listing 2.8: Listing of Exploratory Echocardiogram

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Visit	Visit Date/ Study Day	Pericardial effusion/ Change from Baseline	Mean right atrial pressure (mmHg)/ Change from Baseline	Tricuspid annular plane systolic excursion (cm)/ Change from Baseline	Systolic Eccentricity Index/ Change from Baseline	Diastolic Eccentricity Index/ Change from Baseline	Tricuspid regurgitant jet (m/s)/ Change from Baseline	Right Ventricular Pressure (mmHg)/ Change from Baseline
XXXXXX/ XXXXXX	Baseline **	DDMMMYYYY/ XX	Absent	XXX	XXX	XXX	XXX	XXX	XXX
	Entry Visit *	DDMMMYYYY/ XX	Trace/ Worsened	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX
	XXXXXXX	DDMMMYYYY/ XX	Small/ Worsened	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX
	XXXXXXX	DDMMMYYYY/ XX	Trace/ Worsened	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX
	Etc..								
Etc..									

Note: Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group, Centre/Subject ID and time-point. Sort by treatment group, Centre ID, Subject ID and time-point.

Protocol: AMB114588
Population: Intent-to-Treat

Listing 2.9: Listing of Cardiopulmonary Hemodynamics

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Right Heart Catheterization Date / Time/ Study Day	Heart Rate(bpm)/ Change from Baseline	Mean Pulmonary Arterial Pressure (mmHg)/ Change from Baseline	Mean Right Atrial Pressure (mmHg)/ Change from Baseline	Pulmonary Capillary Wedge Pressure (mmHg)/ Change from Baseline
XXXXXX/ XXXXXX	DDMMMYYYY/ HH:MM/ XX	XXX	XXX	XXX	XXX
	DDMMMYYYY/ HH:MM/ XX	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX
	DDMMMYYYY/ HH:MM/ XX	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX
	DDMMMYYYY/ HH:MM/ XX	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX
Etc..					

Note: Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group, Centre/Subject ID and time-point. Sort by treatment group, Centre ID, Subject ID and time-point.

Listing 2.9: Listing of Cardiopulmonary Hemodynamics

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Right Heart Catheterization Date / Time/ Study Day	Method used to Calculate Cardiac Output/ Oxygen Consumption	Cardiac Output (Litres/minute)/ Change from Baseline	Cardiac index (L/min/meters/ square)/ Change from Baseline	Pulmonary Vascular Resistance (mmHg/L/min)/ Change from Baseline
XXXXXX/ XXXXXX	DDMMMYYYY/ HH:MM/ XX	XXXXXXXXXXXX/ XXXXXXXXXXX	XXX	XXX	XXX
	DDMMMYYYY/ HH:MM/ XX	XXXXXXXXXXXX/ XXXXXXXXXXX	XXX/ XXX	XXX/ XXX	XXX/ XXX
	DDMMMYYYY/ HH:MM/ XX	XXXXXXXXXXXX/ XXXXXXXXXXX	XXX/ XXX	XXX/ XXX	XXX/ XXX
	DDMMMYYYY/ HH:MM/ XX	XXXXXXXXXXXX/ XXXXXXXXXXX	XXX/ XXX	XXX/ XXX	XXX/ XXX

Etc..

Note: Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group, Centre/Subject ID and time-point. Sort by treatment group, Centre ID, Subject ID and time-point.

Listing 2.9: Listing of Cardiopulmonary Hemodynamics

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Right Heart Catheterization Date / Time/ Study Day	Left Ventricle End Diastolic Pressure (mmHg)/ Change from Baseline	Arterial Oxygen Saturation Percentage/ Change from Baseline	Venous Oxygen Saturation/ Change from Baseline	Mean Arterial Pressure (mmHg)/ Change from Baseline
XXXXXX/ XXXXXX	DDMMMYYYY **/ HH:MM/ XX	XXX	XXX	XXX	XXX
	DDMMMYYYY/ HH:MM/ XX	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX
	DDMMMYYYY/ HH:MM/ XX	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX
	DDMMMYYYY/ HH:MM/ XX	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX

Etc..

Note: ** Baseline - the last value recorded prior to start of study treatment from AMB112529.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group, Centre/Subject ID and time-point. Sort by treatment group, Centre ID, Subject ID and time-point.

Protocol: AMB114588
Population: Intent-to-Treat

Listing 2.10: Listing of School Days

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Age(y)/ Sex/ Race	Visit	Visit Date / Study Day	School Days Scheduled/ Change from Baseline	School Days missed/ Change from Baseline	School Days missed due to PAH/ Change from Baseline	Proportion of days missed (%)/ Change from Baseline	Proportion of days missed due to PAH (%)/ Change from Baseline
XXXXXX/ XXXXXX	XX/ Male/ XXXXXX	Baseline **	DDMMMYYYY/ XX	XX	XX	XX	XX	XX
		Entry Visit *	DDMMMYYYY/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX
		XXXXXXX	DDMMMYYYY/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX
		XXXXXXX	DDMMMYYYY/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX
		Etc..						
Etc..								

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group, Centre/Subject ID and time-point. Sort by treatment group, Centre ID, Subject ID and time-point.

Protocol: AMB114588
Population: Intent-to-Treat

Listing 2.11: Listing of Subject Global Assessment (SF10 Health Survey for Children)

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Visit	Visit Date / Study Day	1.Childs General Health	2a.Limited Riding and Skating	2b.Limited Bending	3.Physical Problems Limit Schoolwork	4.Emotional Problems Limit Schoolwork	5.Bodily pain
XXXXXX/ XXXXXX	Baseline **	DDMMMYYYY/ XX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX
	Entry Visit *	DDMMMYYYY/ XX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX
	XXXXXXX	DDMMMYYYY/ XX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX
	XXXXXXX	DDMMMYYYY/ XX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX
	Etc..							
Etc..								

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
The Physical Summary Score (aggregate of item responses 1, 2a, 2b, 3 and 5) and Psychosocial Summary Score (aggregate of item responses 4, 6, 7, 8 and 9) were calculated by QualityMetrics Health Outcomes software.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group, Centre/Subject ID and time-point. Sort by treatment group, Centre ID, Subject ID and time-point.

Listing 2.11: Listing of Subject Global Assessment (SF10 Health Survey for Children)

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Visit	Visit Date / Study Day	6.Satisfied with friendships	7.Satisfied with life overall	8.Time bothered or upset	9.General behaviour	Physical Health Summary/ Change from Baseline	Psychosocial Summary/ Change from Baseline
XXXXXX/ XXXXXX	Baseline **	DDMMMYYYY/ XX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XX	XX
	Entry Visit *	DDMMMYYYY/ XX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XX/ XX	XX/ XX
	XXXXXXX	DDMMMYYYY/ XX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XX/ XX	XX/ XX
	XXXXXXX	DDMMMYYYY/ XX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XX/ XX	XX/ XX
	Etc..							
Etc..								

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
The Physical Summary Score (aggregate of item responses 1, 2a, 2b, 3 and 5) and Psychosocial Summary Score (aggregate of item responses 4, 6, 7, 8 and 9) were calculated by QualityMetrics Health Outcomes software.
Subjects are considered as belonging to their treatment group at the start of study AMB114588.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group, Centre/Subject ID and time-point. Sort by treatment group, Centre ID, Subject ID and time-point.

Protocol: AMB114588
Population: Safety

Listing 3.1: Listing of Exposure Investigational Product

Treatment: Ambrisentan 2.5mg

Subject ID	IP Start Date	IP Stop Date	Duration (Months)	Start Date of Dose/ Study Day	End Date of Dose / Study Day	Dose	Dose Unit	Primary reason for change
XXXXXX	DDMMMYYYY	DDMMMYYYY	XXX	DDMMMYYYY/ XX	DDMMMYYYY/ XX	X^	XX	
				DDMMMYYYY/ XX	DDMMMYYYY/ XX	X^	XX	XXXXXXXXXXXX
				DDMMMYYYY/ XX	DDMMMYYYY/ XX	Xv	XX	XXXXXXXXXXXX
Etc..								

Note: ^ Up titration, v Down titration, # Restart of investigational product.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group, subject and time-point.

Protocol: AMB114588
Population: Safety

Listing 3.2: Listing of All Adverse Events

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Age (y)/ Sex/ Race/ Weight (kg)	Preferred Term/ Verbatim Text	Outcome/ Onset Date/ Resolution Date/ Frequency	Time Since First Dose/ Last Dose/ Duration (days)	Maximum Intensity/ Serious/ Withdrawal	Action Taken/ Relation to Study Drug	Further Details if Serious Event
XXXXXX/ XXXXXX	XX/ XXXXXX/ XXXXXX/ XX	XXXXXXXXXXX/ XXXXXXXXXXX *	XXXXXXXXX/ DDMMMYYYY/ DDMMMYYYY/ XXXXXXXXX	XX/ XX/ XX	XXXX/ XXX/ XXX	XXXXXXXX/ XX	e.g. Results in death, Results in disability/ Incapacity, Congential anomaly/ birth defect, Possible drug induced liver injury, Life threatening, Requires prolonged hospitalisation, Caused by activity related to study, Etc..
		XXXXXXXXXXX/ XXXXXXXXXXX #	XXXXXXXXX/ DDMMMYYYY/ DDMMMYYYY/ XXXXXXXXX	XX/ XX/ XX	XXXX/ XXX/ XXX	XXXXXXXX/ XX	
XXXXXX/ XXXXXX	XX/ XXXXXX/ XXXXXX/ XX	XXXXXXXXXXX/ XXXXXXXXXXX $	XXXXXXXXX/ DDMMMYYYY/ DDMMMYYYY/ XXXXXXXXX	XX/ XX/ XX	XXXX/ XXX/ XXX	XXXXXXXX/ XX	
	Etc..						

Note: * Prior, # Treatment-emergent, $ Post-treatment, ~ AE started pre extension study.
Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time
Programming notes: Present each treatment group and Centre/Subject ID. Sort by treatment group, Centre ID, Subject ID and Onset date.

Listing 3.3: Listing of Relationship between Adverse Event System Organ Class, Preferred Term and Verbatim Text

System Order Class	Preferred Term	Verbatim Text
Blood and lymphatic system disorder	Lymphadenopathy	Enlarged lymph node
Cardiac disorder	Palpitations Tachycardia nos	Heart palpitation Tachycardia
Etc..		

USER ID: Directory/Program.sas Date Time

Programming notes: Continue for all combinations. Sort in order of SOC, PT, and verbatim text.

Listing 3.4: Listing of Subject Numbers for Specified Adverse Events

Treatment: Ambrisentan 2.5mg

System Organ Class Preferred term	No. with Event	Centre ID/Subject ID
Gastrointestinal disorders		
Dyspepsia	9	XXXXXX/XXXXXX, XXXXXX/XXXXXX, XXXXXX/XXXXXX, XXXXXX/XXXXXX, XXXXXX/XXXXXX, XXXXXX/XXXXXX, XXXXXX/XXXXXX, XXXXXX/XXXXXX, XXXXXX/XXXXXX,
Nausea	1	XXXXXX/XXXXXX
Etc..		

Note: Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group. Sort by treatment group, SOC, PT.

Protocol: AMB114588
Population: Safety

Listing 3.8: Listing of Haematology

Central / Local Laboratory
Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Age(y)/ Sex/ Race/ Baseline Weight(kg)	Lab test (units)	Planned Relative Time	Date	Study Day	Converted Data Value	Converted Data Normal Range	Flag $ NR	Flag $ CC	Flag $ BL
XXXXXX/ XXXXXX	XX/	<Parameter (units)>	Baseline **	DDMMMYYYY	XX	XXX	XXX - XXX			
	XXXXXX/		Entry Visit*	DDMMMYYYY	XX	XXX	XXX - XXX			
	XXXXXX/		XXXXXXXXX	DDMMMYYYY	XX	XXX	XXX - XXX	H	H	H
	XX		XXXXXXXXX	DDMMMYYYY	XX	XXX	XXX - XXX	H		H
			XXXXXXXXX	DDMMMYYYY	XX	XXX	XXX - XXX			
			XXXXXXXXX	DDMMMYYYY	XX	XXX	XXX - XXX			
			XXXXXXXXX	DDMMMYYYY	XX	XXX	XXX - XXX			
			XXXXXXXXX	DDMMMYYYY	XX	XXX	XXX - XXX	L	L	L
			XXXXXXXXX	DDMMMYYYY	XX	XXX	XXX - XXX			
			XXXXXXXXX	DDMMMYYYY	XX	XXX	XXX - XXX	L		
		<Parameter (units)>	Etc..							
Etc..										

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
$ NR for Normal Range flag, CC for Clinical Concern flag; BL for Change from Baseline
H=Above range, L=Below range
Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group, Centre/Subject ID and time-point. Sort by treatment group, Centre ID, Subject ID and time-point. Continue for all parameters.

Protocol: AMB114588
Population: Safety

Listing 3.9 Listing of Haematology Data for Subjects with Abnormalities of Potential Clinical Concern

Central /Local Laboratory
Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Age(y)/ Sex/ Race/ Baseline Weight(kg)	Lab test (units)	Planned Relative Time	Date	Study Day	Converted Data Value	Converted Data Normal Range	Converted Data Low Concern	Converted Data High Concern	Flag $ NR	Flag $ CC	Flag $ BL
XXXXXX/ XXXXXX	XX/	<Parameter (units)>	Baseline **	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX			
	XXXXXX/		Entry Visit*	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX			
	XXXXXX/		XXXXXXXXX	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX	H	H	H
	XX		XXXXXXXXX	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX	H		H
			XXXXXXXXX	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX			
			XXXXXXXXX	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX			
			XXXXXXXXX	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX			
			XXXXXXXXX	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX	L	L	L
			XXXXXXXXX	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX			
			XXXXXXXXX	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX	L		
		<Parameter (units)>	Etc..									
		Etc..										

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
$ NR for Normal Range flag, CC for Clinical Concern flag; BL for Change from Baseline
H=Above range, L=Below range
Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time
Programming notes: Present each treatment group, Centre/Subject ID and time-point. Sort by treatment group, Centre ID, Subject ID and time-point. Continue for all parameters.

Protocol: AMB114588
Population: Safety

Listing 3.13: Listing of Liver Event Results and Time of Event Relative to Treatment

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Age (y)/ Sex/ Race/	Event Date/ Study Day	Days from first dose to start of event	Days from last dose to start of event	Event that reached or exceeded protocol defined criteria
XXXXXX/ XXXXXX	XX/ XXXXXX/ XXXXXX/ XX	DDMMMYYYY/ XX	X	X	ALT (alanine aminotransferase)
Etc..					

Note: Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group and Centre/Subject ID. Sort by treatment group, Centre ID, Subject ID.

Protocol: AMB114588
Population: Safety

Listing 3.14: Listing of patient specific information for liver events

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Age (y)/ Sex/ Race/	Event that reached or exceeded protocol defined criteria	Event Date/ Study Day	Days from last dose to start of event	Assessment	Result
XXXXXX/ XXXXXX	XX/	XXXXXXXXXXXXX	DDMMMYYYY/	X	Subject become pregnant?	No
	XXXXXX/		XX		Was a biopsy taken?	Yes
	XXXXXX/				Any unconventional medications	No
	XX				Fasting or significant dietary change	No
					Is this event serious?	Yes
					Evaluation interval	During the treatment period
					Does the subject consume alcohol?	Yes
					Average number of units of alcohol consumed per week	XX
Etc..						

Note: Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group and Centre/Subject ID. Sort by treatment group, Centre ID, Subject ID.

Listing 3.15: Listing of Medical Conditions for Subjects with Liver Events on Treatment

Treatment	Centre ID/ Subject ID	Age (y)/ Sex/ Race/	Classification	Condition	Status
Ambrisentan 2.5mg	XXXXXX/ XXXXXX	XX/ XXXXXXX/ XXXXXX	Hepatobiliary	HEPATITIS A	Current
			Psychiatric	PARANOIA COMBINED WITH MANIA.	Past
	XXXXXX/ XXXXXX	XX/ XXXXXXX/ XXXXXX	Eye	ASTIGMATISM	Current
Ambrisentan 5mg	XXXXXX/ XXXXXX	XX/ XXXXXXX/ XXXXXX	Metabolism and nutrition	RICKETS	Current
Etc..					

Note: Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Protocol: AMB114588
Population: Safety

Listing 3.16: Listing of Liver Biopsy Details

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Age (y)/ Sex/ Race/	Event that reached or exceeded protocol defined criteria	Biopsy Date/ Study Day	Biopsy Size (mm)	Liver biopsy test	Liver biopsy result
XXXXXX/ XXXXXX	XX/	XXXXXXXXXXXXX	DDMMMYYYY/	X	Bile ducts	Other: Bile ducts blocked
	XXXXXX/		XX		Final diagnosis	Alcoholic hepatic cirrhosis
	XXXXXX/				Description of liver cells/hepatocytes	Normal
	XX				Liver cell/hepatocyte inclusion/vacuole	No inclusions
					Hepatocyte/liver cell nuclear abnorm	None
					Etc..	
Etc..						

Note: Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group and Centre/Subject ID. Sort by treatment group, Centre ID, Subject ID.

Protocol: AMB114588
Population: Safety

Listing 3.17: Listing of Liver Imaging Details

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Age (y)/ Sex/ Race/	Event that reached or exceeded protocol defined criteria	Imaging Date/ Study Day	Liver imaging method	Are images technically adequate?	Liver imaging test	Liver imaging result
XXXXXX/ XXXXXX	XX/	XXXXXXXXXXXXX	DDMMMYYYY/	X	XX	Liver Size	Hypertrophy (or enlarged)
	XXXXXX/		XX			Liver Texture	Normal
	XXXXXX/					Liver fatty infiltrate grade	Not applicable - No fatty infiltration
	XX					Ascites present	None present
						Focal hepatic lesions character	Not applicable - no hepatic lesions
						Gallstones or gallbladder lesions	None
						Biliary ductal lesions	None
						Portal/Hepatic vein abnormalities	None

Etc..

Note: Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group and Centre/Subject ID. Sort by treatment group, Centre ID, Subject ID.

Protocol: AMB114588
Population: Safety

Listing 3.18: Listing of Vital Signs

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Age(y)/ Sex/ Race	Visit	Visit Date/ Study Day	Systolic Blood Pressure (mmHg)/ Change from Baseline	Diastolic Blood Pressure (mmHg)/ Change from Baseline	Heart Rate (bpm)/ Change from Baseline	Height (units)/ Change from Baseline	Weight (units)/ Change from Baseline	BMI (units)/ Change from Baseline	BSA (units)/ Change from Baseline
XXXXXX/ XXXXXX	XX/ XXXXXX/ XXXXXX	Baseline **	DDMMMYYYY/ XX	XX	XX	XX	XX	XX	XX	XX
		Entry Visit *	DDMMMYYYY/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX
		XXXXXXX	DDMMMYYYY/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX
		Etc..								
Etc..										

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
H=Above clinical concern, L=Below clinical concern,
Change from Baseline HC=Above clinical concern, LC=Below clinical concern
Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group, Centre/Subject ID and time-point. Sort by treatment group, Centre ID, Subject ID and time-point.

Protocol: AMB114588
Population: Safety

Listing 3.20: Listing of Physical Examination

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Age(y)/ Sex/ Race	Visit	Visit Date/ Study Day	Liver Size	Jugular Venous Pressure	Ascites	Peripheral Oedema	Saturated Oxygen (units)
XXXXXX/ XXXXXX	XX/ XXXXXX/ XXXXXX	Entry Visit *	DDMMMYYYY/ XX	XXXXXX	XXXXXXXX	XXXXXXX	XXXXXXX	XX.XXX
		XXXXXXX	DDMMMYYYY/ XX	XXXXXX	XXXXXXXX (I)	XXXXXXX	XXXXXXX	XX.XXX
		XXXXXXX	DDMMMYYYY/ XX	XXXXXX	XXXXXXXX	XXXXXXX (W)	XXXXXXX	XX.XXX
		XXXXXXX	DDMMMYYYY/ XX	XXXXXX	XXXXXXXX (U)	XXXXXXX	XXXXXXX	XX.XXX

Etc..

Note: * Entry Visit is at entry to AMB114588.
I=Improved, W=Worsened, U=Unchanged
Subjects are considered as belonging to the treatment group according to the highest dose received.
USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group, Centre/Subject ID and time-point. Sort by treatment group, Centre ID, Subject ID and time-point.

Protocol: AMB114588
Population: Safety

Listing 3.21: Listing of 12-Lead ECG Findings

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Age(y)/ Sex/ Race	Visit	Visit Date/ Study Day	Result
XXXXXX/ XXXXXX	XX/ XXXXXX/ XXXXXX	Baseline **	DDMMMYYYY/ XX	XXXXXXXXXXXX
		Entry Visit *	DDMMMYYYY/ XX	XXXXXXXXXXXX
		XXXXXXX	DDMMMYYYY/ XX	XXXXXXXXXXXX
		Etc..		
Etc..				

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group, Centre/Subject ID and time-point. Sort by treatment group, Centre ID, Subject ID and time-point.

Protocol: AMB114588
Population: Safety

Listing 3.22: Listing of Endocrinology Assessments

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Age(y)/ Sex/ Race	Visit	Endocrinology Assessment Date/ Study Day	Assessment Type	Assessment Result
XXXXXX/ XXXXXX	XX/ Male/ XXXXXX	Baseline **	DDMMMYYYY/ XX	Testicular volume Right/Left (units)	XXX / XXX
				Male genital development	XXXXXXXXXX XXX
				Male pubic hair development	XXXXXXXXXX XXX
		Entry Visit *	DDMMMYYYY/ XX	Testicular volume Right/Left (units)	XXX / XXX
				Male genital development	XXXXXXXXXX XXX
				Male pubic hair development	XXXXXXXXXX XXX
		Etc..			
XXXXXX/ XXXXXX	XX/ Female/ XXXXXX	XXXXXXX	DDMMMYYYY/ XX	Female breast development	XXXXXXXXXX XXX
				Female pubic hair development	XXXXXXXXXX XXX
		Etc..			
Etc..					

Note: ** Baseline is the last value recorded prior to start of study treatment from AMB112529.
* Entry Visit is at entry to AMB114588.
Subjects are considered as belonging to the treatment group according to the highest dose received.
For some patients, pubertal development assessments were not repeated at 20 years of age if pubertal maturity had been reached in a previous visit.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group, Centre/Subject ID and time-point. Sort by treatment group, Centre ID, Subject ID and time-point.

Protocol: AMB114588
Population: Safety

Listing 3.24: Listing of Pregnancy Results

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Age(y)/ Race	Visit	Visit Date/ Study Day	Result	Subject became pregnant?
XXXXXX/ XXXXXX	XX/ XXXXXX/ XXXXXX	XXXXXXX	DDMMMYYYY/ XX	XXXXXXXXXXXXX	No
		XXXXXXX	DDMMMYYYY/ XX	XXXXXXXXXXXXX	
		XXXXXXX	DDMMMYYYY/ XX	XXXXXXXXXXXXX	
		Etc..			
Etc..					

Note: Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Present each treatment group, Centre/Subject ID and time-point. Sort by treatment group, Centre ID, Subject ID and time-point.

Protocol: AMB114588
Population: Safety

Listing 3.25: Listing of Endocrinology Parameters - 20 Year Visit

Treatment: Ambrisentan 2.5mg

Centre ID/ Subject ID	Age(y)/ Sex/ Race	20 Year Visit Date/ 20 Year Visit	Endocrine Assessment Date/Day	Assessment Type	Assessment Result	Converted Data	
						Value	Normal Range
XXXXXX/ XXXXXX	XX/ XXXXXX/ XXXXXX	DDMMMYYYY/ 20 Years Old	DDMMMYYYY/ XX	Total Testosterone	XXXXXXXXXXXXX		
			DDMMMYYYY/ XX	Luteinizing Hormone	XXXXXXXXXXXXX	XXX	XXX - XXX
			DDMMMYYYY/ XX	etc.	XXXXXXXXXXXXX	XXX	XXX - XXX
						XXX	XXX - XXX
XXXXXX/ XXXXXX	XX/ XXXXXX/ XXXXXX	DDMMMYYYY/ 20 Years Old	DDMMMYYYY/ XX	Total Testosterone	XXXXXXXXXXXXX	XXX	XXX - XXX
			DDMMMYYYY/ XX	Luteinizing Hormone	XXXXXXXXXXXXX	XXX	XXX - XXX

Note: Endocrinology assessments are only displayed for subjects who completed their 20-year visit and for which endocrinology parameters are available.

USER ID: Directory/Program.sas Date Time

Programming notes: a listing that only include those subjects with a 20 Year Old Visit have the columns below i.e the ID/Sex/Last Visit Date/Last Visit/last Visit with Endo labs and the date, and then all the endo labs on that date.
Listing of and all Endo labs on that date - endocrine parameters (Follicle Stimulating Hormone, Luteinizing Hormone, Sex Hormone Binding Globulin, Total Testosterone and Inhibin B)

```
(where=(lbtestcd in ('FSH_PLC', 'LH_PLC','TT_PLC','FT_PLC','FT_PLQ','SHBG_PLC',
                     'INHB_PLC','OEST_PLC', 'ESTRO_PLC','ESTFR_PLC','ESTFR_PLQ',
                      'ESTRIO_PLC', 'EST_PLC')))
```

Population: Intent-to-Treat

Listing 3.26

Country Level Listing of Start Dates of COVID-19 Pandemic Measures

Country	Pandemic Measures Start Date
Overall [1]	2020-01-01
Italy	2020-01-01
Germany	2020-02-12
etc	2020-03-12

[1] The Overall row reflects the earliest pandemic measures start date.
/Directory/program.sas 01JAN2002 12:01

Programming Note: Please list participating countries only

Protocol: AMB114588
Population: Intent-to-Treat

Listing 3.27
Listing of Visits and Assessments Impacted by COVID-19 Pandemic

Site Id.: PPD
Country: Brazil

Treatment	Unique Subject Id./ Subject Id.	Impacted Visit	Impact	Primary Reason for Impact
Trt A	PPD	Visit 6	MISSED VISIT	SUBJECT RELATED IMPACT [2]
		Visit 7	REMOTE VISIT WITH NO ASSESSMENTS MISSED	SITE RELATED IMPACT [3]
Trt B		Visit 4	SITE VISIT WITH ONE OR MORE ASSESSMENTS MISSED	SITE RELATED IMPACT [3]
		Visit 5	MISSED VISIT	SUBJECT ACQUIRED COVID-19 INFECTION [1]

[1] Subject acquired COVID-19 includes suspected, probable and confirmed.
[2] Subject related impact include subject discretion and travel restrictions.
[3] Site related impacts include site temporarily closed, site staff unavailable, and study drug unavailable.

Protocol: AMB114588

Population: Safety

Listing 3.28

Listing of COVID-19 Assessments and Symptom Assessments for Subjects with COVID-19 Adverse Events

Treatment: xxxxx

Centre ID/ Subject ID	Adverse Event	AE Start Date	COVID-19 Case Diagnosis [1]	COVID-19 Test Performed/ Test Date/ Results	Assessments and Symptom Assessments	*Result*
xxxxxxx/ xxxx	Coronavirus infection	2020-04-16	Suspected	Yes/ 2020-04-17/ Indeterminate	*Travel to Location with Community Transmission [2]*	*No*
					Visited Health Care Facility [2]	*No*
					Contact with COVID-19 Confirmed/Probable Case [2]	*Unknown*
					Medication Taken to Treat COVID-19	*Yes*
					Fever	*Yes*
					Home Quarantined/Isolated	*Unknown*
	COVID-19 pneumonia	2020-05-20	Confirmed	Yes/ 2020-05-22 Positive	*Travel to Location with Community Transmission [2]*	*Yes*
					Visited Health Care Facility [2]	*No*
					Contact with COVID-19 Confirmed/Probable Case [2]	*Yes*
					Medication Taken to Treat COVID-19	*No*
					Sore Throat	*No*
					Loss of Smell	*Unknown*
					Loss of Taste	*No*
	Coronavirus infection	2020-04-16	Probable	Yes/ 2020-04-17/ Indeterminate	*Travel to Location with Community Transmission [2]*	*Yes*
					Visited Health Care Facility [2]	*No*
					Contact with COVID-19 Confirmed/Probable Case [2]	*Yes*
					Medication Taken to Treat COVID-19	*No*
					Fever	*Yes*
					Cough	*Yes*
					Asymptomatic	*No*
					Home Quarantined/Isolated	*Yes*

[1] COVID-19 Case Diagnosis is based on WHO Definition as of dd-mmm-yyyy

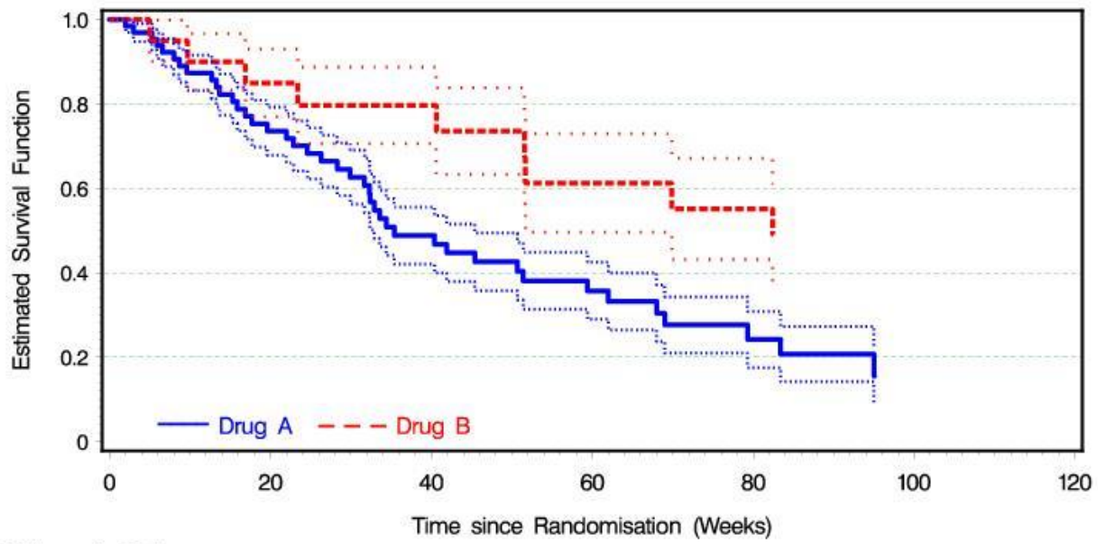
[2] Within 14 days prior to symptom onset.

/Directory/program.sas 01JAN2002 12:01

Programming Note: *The COVID-19 AE terms include: Asymptomatic COVID-19, Coronavirus infection, COVID-19, COVID-19 pneumonia, Suspected COVID-19. Note that the number of COVID-19 AE terms may change*

Protocol: AMB114588
Population: Safety

Figure 3.1: Kaplan-Meier Survival Curves with 95% Confidence Bands of Time to First Treatment-Emergent Adverse Event

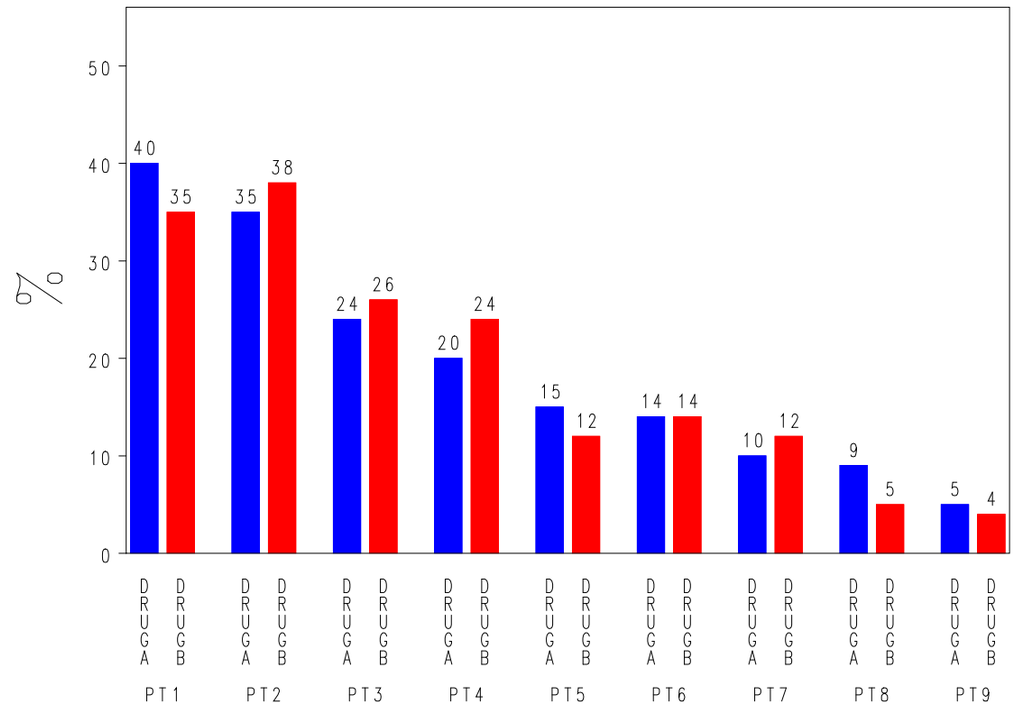


Note: Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Change Treatment Labels. Also present Total group. Annotate to display number of events in each group also.

Figure 3.3: Bar Chart of Treatment-Emergent Adverse Events Occurring in Two or More Subjects in any Treatment Group



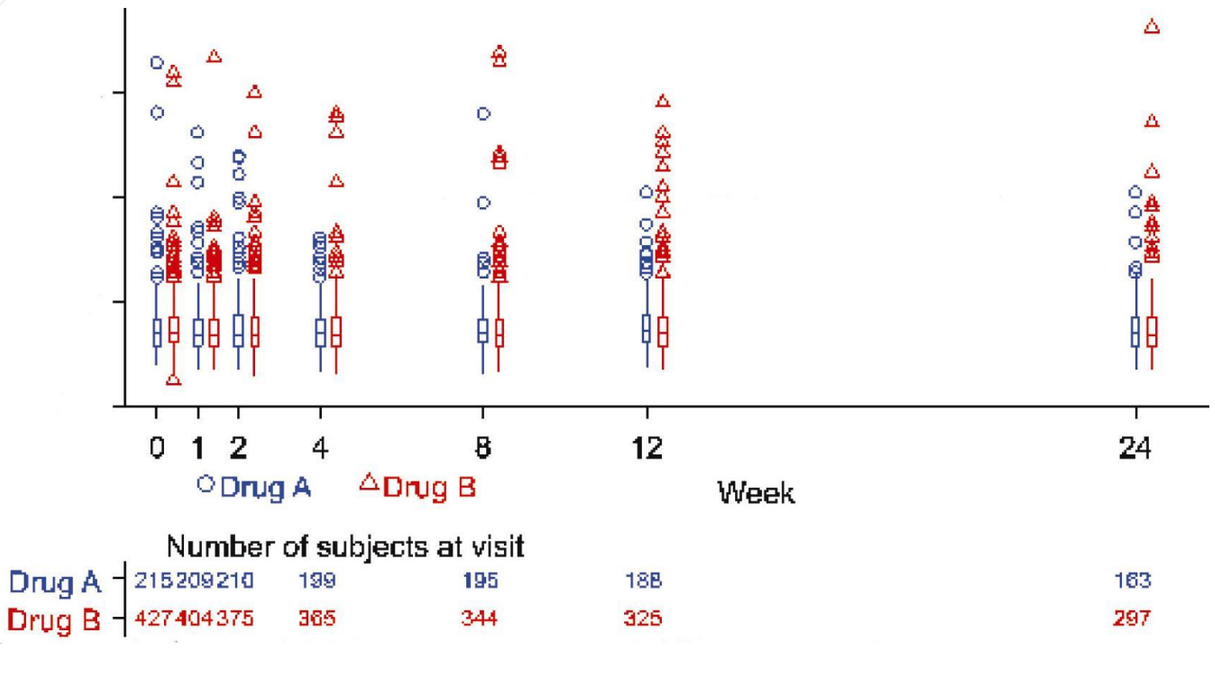
Note: Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Change Treatment Labels. Also present Total group. Continue for each preferred term.

Protocol: AMB114588
Population: Safety

Figure 3.4: Box plots of Haematology Data by Visit (Selected Parameters)
Parameter = <Parameter (units)>

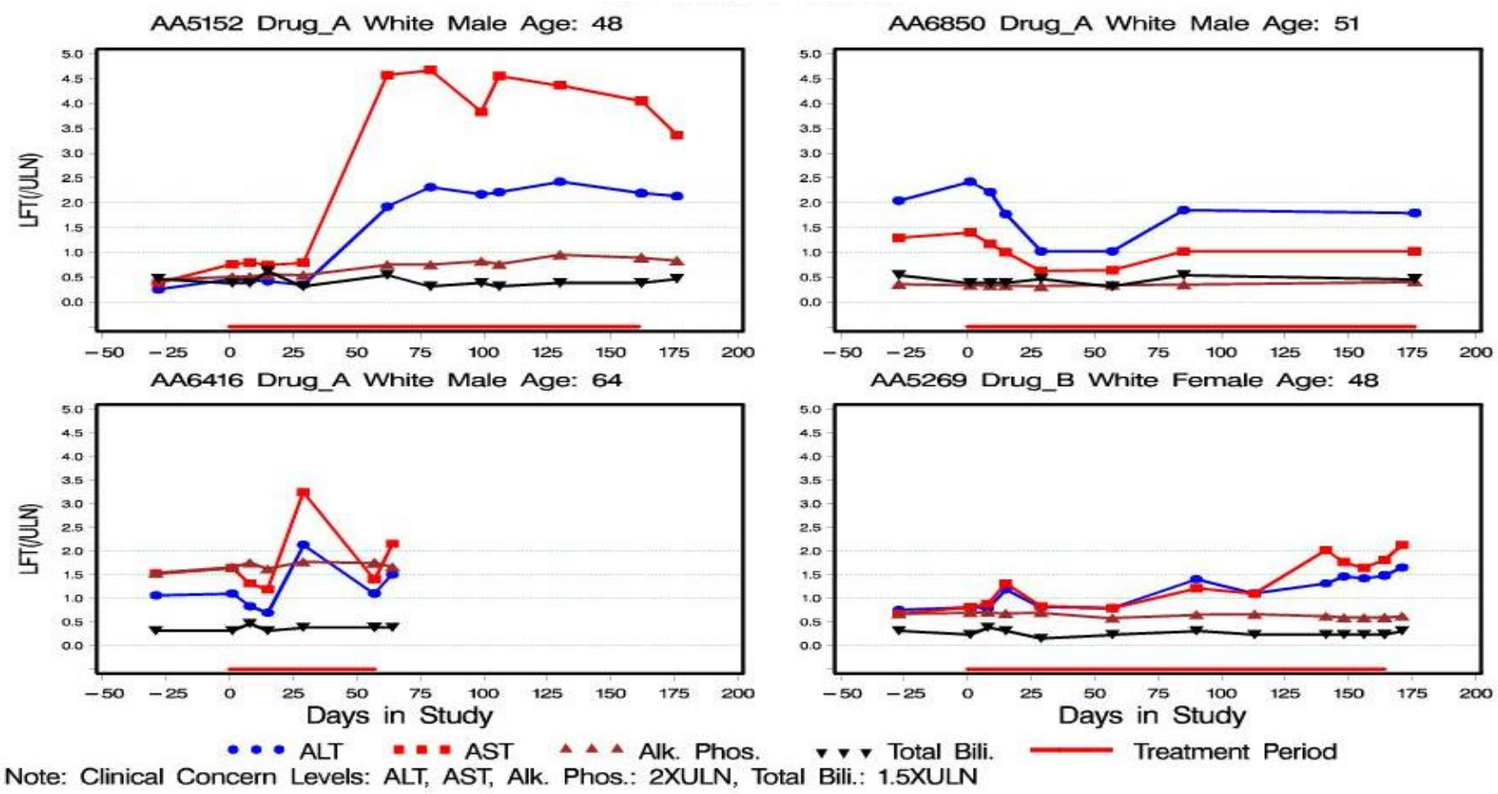


Note: Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Change Treatment Labels. Also present Total group. Label vertical axes with parameter name and units. Label horizontal axis with appropriate visit structure. Repeat for each parameter. Haematology parameters (haemoglobin, hematocrit, platelets), Chemistry parameters (Total bilirubin, AST, ALT, GGT, Creatinine). Use log scale for Plasma NT-Pro BNP (Figures 2.7 and 2.8).

Figure 3.8: Patient Profiles of Liver Function Tests

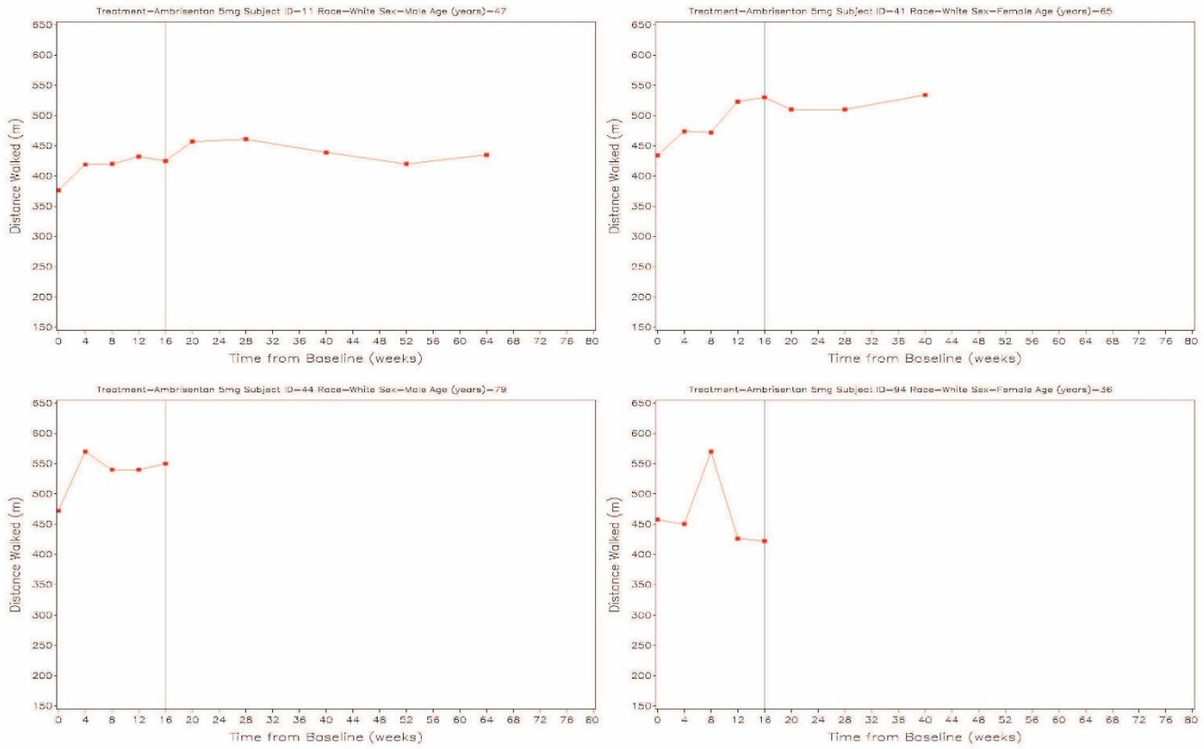


Note: Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Change Treatment Labels. Also present Total group. Present parameters ALT, AST, Alk. Phos, Total Bilirubin. Present one patient per page only, not grid of 4 patients.

Figure 3.11: Line plots of Endocrinology Assessments by Subject



Note: Subjects are considered as belonging to the treatment group according to the highest dose received.

USER ID: Directory/Program.sas Date Time

Programming notes: Only one patient on a page, with a grid of plots on each page for each parameter. For Figure 3.11, plot female breast development and pubic hair development; male testicular volume, genital development and pubic hair development and change from baseline in male testicular volume (left and right separately). For Figure 2.9 (Japanese subset) plot echocardiogram parameters. For coded data, plot the numeric code and present codes on first page of the plot.

20. APPENDICES

20.1. Appendix 1 – IDSL Age Calculation

IDSL standard/GSK standard of the derivation of AGE:

```
AGE = intck('year',DEMO.BIRTHDT, AGEREFDT) –
        (month(AGEREFDT) < month(DEMO.BIRTHDT) or
          (month(AGEREFDT)=month(DEMO.BIRTHDT) and
              day(AGEREFDT) <  day(DEMO.BIRTHDT)
          ));
```

For this study, it was decided that the AGE is calculated based on the date of the baseline visit ie.
AGEREFDT = Date of record with VISITNUM=20 in the VISIT dataset.
BIRTHDT = derived by DM in DEMO dataset which contains imputed date for
date of birth (ie. 30JUNYYYY) .