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Title:	Reporting and Analysis Plan for AMB112529: A randomized, open label study comparing safety and efficacy parameters for a high and a low dose of ambrisentan (adjusted for body weight) for the treatment of pulmonary arterial hypertension in paediatric patients aged 8 years up to 18 years.

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Description: This document outlines the safety and efficacy reporting planned for protocol AMB112529 by GlaxoSmithKline (GSK).

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ABBREVIATIONS

AE	adverse event
ALT	alanine aminotransferase
AST	aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical
DBF	Database Freeze
eCRF	Electronic case report form
ECG	electrocardiogram
GSK	GlaxoSmithKline
IDMC	Independent Data Monitoring Committee
IP	Investigational product
ITT	Intent-to-Treat
MedDRA	Medical Dictionary for Regulatory Activities
6MWD	6 minute walking distance
NT-Pro BNP	N-terminal pro-B-type natriuretic peptide
PAH	pulmonary arterial hypertension
PD	pharmacodynamic
PK	pharmacokinetic
PT	Preferred Term
RA	Right Atrial
RAP	Reporting and Analysis Plan
RUCAM	Roussel Uclaf Causality Assessment Method
RV	Right Ventricular
SAE	Serious Adverse Event
SAS	Statistical Analysis System
SD	Standard deviation
SOC	System Organ Class
TAPSE	Tricuspid Annular Plane Systolic Excursion
TFLs	Tables, Figures, Listings
TRJ	Tricuspid Regurgitant Jet
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 AMB112529 for provision to GSK.

In this RAP, reference is made to the protocol AMB112529 dated 2nd February 2011, and subsequent amendments.

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

2.1. Study Objective(s)

2.1.1. Primary Objective

The primary objective is the safety and tolerability of ambrisentan in the paediatric pulmonary arterial hypertension (PAH) population.

2.1.2. Secondary Objectives

The secondary objectives are the pharmacokinetics and efficacy of ambrisentan in the paediatric pulmonary arterial hypertension (PAH) population.

2.2. Study Endpoint(s)

2.2.1. Primary Endpoints

- Adverse Events.
- Serious Adverse Events.
- Clinical laboratory parameters.
- Physical examination
- Vital Signs.
- Pubertal development (change from baseline in endocrinology assessments at Weeks12 and 24).

2.2.2. Secondary Endpoints

2.2.2.1. Pharmacokinetics

- Population pharmacokinetic assessment based on one plasma sample per subject at Weeks 4 (trough), 8 (0.5 to 4 hours post-dose), 12 (trough), 16 (0.5 to 4 hours postdose), 20 (4 to 22 hours post-dose), and 24 (trough).
- Pharmacokinetic/pharmacodynamic modelling.

2.2.2.2. Efficacy

- The change from baseline in the 6 minute walking distance (6MWD) test evaluated after 24 weeks of therapy.
- Mean changes from baseline in the 6MWD test at Weeks 4, 8, 12, 16, and 20.
- The time to clinical worsening of PAH.

- The change from baseline in Subject Global Assessment to Week 24 using the SF-10 health survey for children.
- The change from baseline in World Health Organization (WHO) functional class to Week 24.
- Change from baseline in plasma N-Terminal pro-B-type Natriuretic Peptide (NT-Pro BNP) concentration at Week 24.
- School days missed due to PAH. (Note that this is not defined as an efficacy endpoint in the protocol but has been added to the RAP.)

2.2.2.3. Exploratory

- The change from 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 to Week 24.

2.2.2.4. Other

- Change from baseline in cardiopulmonary hemodynamics at Week 24 (a sub-study in subjects enrolled at centres where the collection of 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

Any statistical hypothesis relating to the pharmacokinetic endpoints will be described in a separate RAP. The analysis will be the responsibility of the Department of Clinical Pharmacology Modeling and Simulation (CPMS), Quantitative Sciences, GSK.

3. STUDY DESIGN

This study is a 6-month (24-week), randomized, open label evaluation of the safety, tolerability and efficacy of a high and low dose ambrisentan (adjusted for body weight) in 66 subjects (33 per treatment group) aged 8 years up to 18 years with PAH. The study will include a screening/baseline period and a treatment period. The treatment period will be 24 weeks or until the subject's clinical condition deteriorates to the point that alternative/additional treatment is necessary. Subjects who participate in the study will be eligible to enrol into study AMB 114588.

For further details regarding the study design, please refer to the protocol.

3.1. Randomisation

All subjects who meet the inclusion and exclusion criteria will be randomized to one of two dose groups (Low dose or High dose, based on body weight) of ambrisentan according to a computer-generated randomisation schedule.

Body Weight	Low Dose	High Dose
>=50kg	5 mg	10 mg
>=35 and <50 kg	5 mg	7.5 mg
>=20 and <35 kg	2.5 mg	5 mg

To ensure balance with respect to the number of patients assigned to each treatment group, the allocation schedule will be generated in blocks. Each subject will be assigned to a pack number according to the predefined randomisation list. A central Interactive Voice Response System (IVRS) will be used for treatment assignment.

Randomization will be stratified by the age groups 8 years up to 11 years and 12 years up to 18 years and by aetiology of PAH as follows:-

- idiopathic;
- heritable [familial];
- secondary to connective tissue disease; and
- persistent despite surgical repair of atrial septal defects, ventricular septal defects, atrio-ventricular septal defects, and persistent patent ductus.

Subjects will be assigned to study treatment in accordance with the randomization schedule.

4. PLANNED ANALYSES

4.1. Interim Analyses

The interim analyses conducted by the Independent Data Monitoring Committee (IDMC) are planned for this study. These analyses are described in a dedicated IDMC RAP.

To facilitate the communication between GSK and regulatory agency, an interim analysis was added post the finalization of the study protocol. For data collected up until January 2018, all safety, tolerability, pharmacokinetics and efficacy data will be reviewed, analysed and summarised.

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.

4.2.1. Changes in the conduct of the study or planned analyses

The final analyses were as planned in the protocol except for the following:-

- Protocol, Section 8.3.5.4 states summary analysis of the differences between Low and High groups will be performed. However, due to low subject numbers, this is not presented in this RAP.

- School days missed due to PAH has been added to the RAP.

5. SAMPLE SIZE CONSIDERATIONS

Due to the low prevalence of the disease in children, sample size was based on feasibility rather than formal power calculations. Recruitment of approximately 66 subjects (33 per treatment group with no prespecified number in each age group/aetiology stratum) is felt to be achievable within a reasonable period of time (~ 2 years) minimizing any impact of changing practice on the conduct and interpretation of the study.

6. ANALYSIS POPULATIONS

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

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

7. TREATMENT COMPARISONS

Treatment comparisons will be between low dose and high dose ambrisentan, by way of summary tables, figures and listings.

7.1. Data Display Treatment and Other Sub-group Descriptors

In the study report data displays, the treatment group descriptors will be the following:

- Ambrisentan Low Dose
- Ambrisentan High Dose

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, centre identification and subject identification number.

9.1. Premature Withdrawal and Missing Data

Subjects who withdraw from the study prior to Week 24 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. 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			
		I	**II**	**III**	**IV**
Baseline WHO FC	**II**	-1	0	+1	+2
	III	-2	-1	0	+1

9.2.4. WHO FC class change from baseline categorisation 2

Improved = -1 or -2 in Change from Baseline Categorisation
No change = 0 in Change from Baseline Categorisation
Deteriorated = +1 or +2 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.

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 to study drug will be calculated in days as (Treatment stop date – Treatment start date) + 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 = $100 \times \sqrt{[\exp(\sigma^2) - 1]}$

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
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					

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**
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.

10.3. 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.

10.4. 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.

10.5. Prior and Concomitant Medications

The GSK drug 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.

Concomitant 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 preferred term, by treatment group and overall.

The number and percentage of subjects with ongoing (at baseline) and concomitant PAH therapy at Week 24 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

10.6. Treatment Compliance

At each visit, 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.

10.7. Long-Term Study (AMB 114588)

The number and percentage of subjects continuing in study AMB 114588 will be summarised 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: <2 weeks, <4 weeks, <8 weeks, <12 weeks, <16 weeks, <20 weeks and <24 weeks.

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.

11.4. Deaths and Serious Adverse Events

Summary tables detailed in Section 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 Section 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. Clinical 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

11.8. 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.

11.9. 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.

11.10. Physical Examination

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

11.11. 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.

11.12. 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.

11.13. 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.

- The absolute value, change from 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.
- WHO Functional Class and change from baseline in WHO Functional Class.
- The absolute value and percent change from 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 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 "-2, -1, 0, +1, +2" and in terms of "Improved, No Change, Deteriorated" (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 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 summarised for each visit, by treatment group and overall.

- The absolute value and change from 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. CLINICAL PHARMACOLOGY DATA ANALYSES

13.1. Pharmacokinetic Analyses

Not applicable.

13.2. Pharmacodynamic Analyses

Not applicable.

13.3. Pharmacokinetic/Pharmacodynamic Analyses

Not applicable.

14. BIOMARKER DATA ANALYSIS

Not applicable.

15. PHARMACOGENETIC DATA ANALYSES

Not applicable.

16. VIRAL GENOTYPING/PHENOTYPING

Not applicable.

17. REFERENCES

Not Applicable.

18. ATTACHMENTS

18.1. Table of Contents for Data Display Specifications

18.1.1. 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.

Population Tables

Table Number	Title	Population	Template Table	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
1.1	Summary of Subject Disposition	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			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 Baseline By Drug Class and Preferred Term	Intent-to-Treat	1.9		X	Interim, SAC
1.10	Summary of Ongoing Background PAH Therapy at Week 24 By Drug Class and Preferred Term	Intent-to-Treat	1.9		X	Interim, SAC
1.11	Summary of Subjects who continue in the long term study (AMB 114588)	Intent-to-Treat	1.11			Interim, SAC

Table Number	Title	Population	Template Table	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
1.12	Summary of Compliance to Investigational Product since last visit	Intent-to-Treat	1.12			Interim, SAC
1.13	Summary of Investigational Product Compliance Overall	Intent-to-Treat	1.13			Interim, SAC
1.14	Summary of Important Protocol Deviation	Intent-to-Treat	1.14			Interim, SAC

Efficacy Tables

Table Number	Title	Population	Template Table	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
2.1	Summary of 6 Minute Walking Distance (meters)	Intent-to-Treat	2.1	X	X	Interim, SAC
2.2	Summary of Change from Baseline in 6 Minute Walking Distance (meters)	Intent-to-Treat	2.1	X	X	Interim, SAC
2.3	Summary of Percent Change from Baseline in 6 Minute Walking Distance (meters)	Intent-to-Treat	2.1	X	X	Interim, SAC
2.4	Summary of Walking Duration (minutes) for subjects who walked less than six minutes	Intent-to-Treat	2.4	X	X	Interim, SAC
2.5	Summary of use of Oxygen during 6 Minute Walking exercise (L/min)	Intent-to-Treat	2.5	X	X	Interim, SAC
2.6	Summary of Time to Clinical Worsening of PAH (days)	Intent-to-Treat	2.6	X		Interim, SAC
2.7	Summary of Clinical Worsening of PAH	Intent-to-Treat	2.7			Interim, SAC
2.8	Summary of WHO Functional Class	Intent-to-Treat	2.8	X	X	Interim, SAC
2.9	Summary of Change from Baseline in WHO Functional Class	Intent-to-Treat	2.8	X	X	Interim, SAC

Table Number	Title	Population	Template Table	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
2.10	Summary of WHO Functional Class Shifts from Baseline by Visit	Intent-to-Treat	2.10	X	X	Interim, SAC
2.11	Summary of WHO Functional Class Change from Baseline Categorisation	Intent-to-Treat	2.11	X	X	Interim, SAC
2.12	Summary of Plasma NT-Pro BNP concentration (ng/L)	Intent-to-Treat	2.12	X	X	Interim, SAC
2.13	Summary of Ratio to Baseline in Plasma NT-Pro BNP concentration (%)	Intent-to-Treat	2.12	X	X	Interim, SAC
2.14	Summary of Exploratory Echocardiogram	Intent-to-Treat	2.14	X	X	Interim, SAC
2.15	Summary of Change from Baseline in Exploratory Echocardiogram	Intent-to-Treat	2.15	X	X	Interim, SAC
2.16	Summary of Cardiopulmonary Hemodynamics	Intent-to-Treat	2.16	X		Interim, SAC
2.17	Summary of Change from Baseline in Cardiopulmonary Hemodynamics	Intent-to-Treat	2.16	X		Interim, SAC
2.18	Summary of Number of Subjects with School Days within the Past Month	Intent-to-Treat	2.18	X	X	Interim, SAC
2.19	Summary Statistics of School Days within the past month	Intent-to-Treat	2.19	X	X	Interim, SAC
2.20	Summary Statistics of Change from Baseline in School Days within the Past month	Intent-to-Treat	2.19	X	X	Interim, SAC
2.21	Summary of Subject Global Assessment (SF10 Health Survey for Children)	Intent-to-Treat	2.21	X	X	Interim, SAC
2.22	Summary of Change from Baseline in Subject Global Assessment (SF10 Health Survey for Children)	Intent-to-Treat	2.21	X	X	Interim, SAC
2.23	Summary of SF10 Health Survey – Number and Percentage of Subjects with Particular Item Responses	Intent-to-Treat	2.23	X	X	Interim, SAC

Safety Tables

Table Number	Title	Population	Template Table	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
3.1	Summary of Exposure to Investigational Product	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
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			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			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			Interim, SAC

Table Number	Title	Population	Template Table	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
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			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
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

Table Number	Title	Population	Template Table	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
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		Interim, SAC
3.37	Summary of Endocrinology assessments by Visit – Male	Safety	3.37	X		Interim, SAC
3.38	Summary of Pubertal Development Shifts from Baseline - Female	Safety	3.38	X		Interim, SAC
3.39	Summary of Pubertal Development Shifts from Baseline - Male	Safety	3.39	X		Interim, SAC
3.40	Summary of Testicular Volume Change from Baseline – Male	Safety	3.40	X		Interim, SAC
3.41	Summary of Change from Baseline in Plasma Endocrine Parameters – Female	Safety	3.41	X		Interim, SAC
3.42	Summary of Change from Baseline in Plasma Endocrine Parameters – Male	Safety	3.42	X		Interim, SAC

18.1.2. Listings

Population Listings

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

Efficacy Listings

Listing Number	Title	Population	Template Listing	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
2.1	Listing of 6 Minute Walk Distance Data	Intent-to-Treat	2.1			Interim, SAC
2.2	Listing of Clinical Worsening of PAH	Intent-to-Treat	2.2			Interim, SAC
2.3	Listing of WHO Functional Class Data	Intent-to-Treat	2.3			Interim, SAC
2.4	Listing of Plasma NT-Pro BNP Concentration (ng/L)	Intent-to-Treat	2.4			Interim, SAC
2.5	Listing of Exploratory Echocardiogram	Intent-to-Treat	2.5			Interim, SAC
2.6	Listing of Cardiopulmonary Hemodynamics	Intent-to-Treat	2.6			Interim, SAC
2.7	Listing of School Days	Intent-to-Treat	2.7			Interim, SAC
2.8	Listing of Subject Global Assessment (SF10 Health Survey for Children)	Intent-to-Treat	2.8			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

Listing Number	Title	Population	Template Listing	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
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
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			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			Interim, SAC

Listing Number	Title	Population	Template Listing	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
3.23	Listing of Pregnancy Results	Safety	3.23			Interim, SAC

18.1.3. Figures

Population Figures

Figure Number	Title	Population	Template Figure	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
1.1	Summary of Subject Accrual	Intent-to-Treat	1.1			Interim, SAC

Efficacy Figures

Figure Number	Title	Population	Template Figure	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
2.1	Box plots of 6 Minute Walking Distance (meters) by Week	Intent-to-Treat	3.4			Interim, SAC
2.2	Box plots of Change from Baseline in 6 Minute Walking Distance (meters) by Week	Intent-to-Treat	3.4			Interim, SAC
2.3	Kaplan-Meier Survival Curves with 95% Confidence Bands of Time to First Clinical Worsening of PAH	Intent-to-Treat	3.1			Interim, SAC
2.6	Box plots of Plasma NT-Pro BNP concentration by Week	Intent-to-Treat	3.4			Interim, SAC
2.7	Box plots of Change from Baseline in Plasma NT-Pro BNP concentration by Week	Intent-to-Treat	3.4			Interim, SAC
2.8	Box plots of Exploratory Echocardiogram Data by Week	Intent-to-Treat	3.4	X (Line plots of Exploratory Echocardiogram Data by Subject) see		Interim, SAC

Figure Number	Title	Population	Template Figure	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
				template 3.11)		
2.9	Box plots of Change from Baseline in Exploratory Echocardiogram Data by Week	Intent-to-Treat	3.5			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 Week (Selected Parameters)	Safety	3.4			Interim, SAC
3.5	Box plots of Change from Baseline in Haematology Data by Week (Selected Parameters)	Safety	3.4			Interim, SAC
3.6	Box plots of Chemistry Data by Week (Selected Parameters)	Safety	3.4			Interim, SAC
3.7	Box plots of Change from Baseline in Chemistry Data by Week (Selected Parameters)	Safety	3.4			Interim, SAC
3.8	Patient Profiles of Liver Function Tests	Safety	3.8			Interim, SAC

Figure Number	Title	Population	Template Figure	Japanese subgroup analysis	Age strata subgroup analysis	Deliverable
3.9	Box plots of Vital Signs Data by Week	Safety	3.4			Interim, SAC
3.10	Box plots of Change from Baseline in Vital Signs Data by Week	Safety	3.4			Interim, SAC
3.11	Line plots of Endocrinology Assessments by subject	Safety	3.11			Interim, SAC

18.2. Data Display Specifications

Protocol: AMB112529
Population: Intent-to-Treat

Table 1.1: Summary of Subject Disposition

	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Subject status			
Completed	XX (%)	XX (%)	XX (%)
Withdrawn	XX (%)	XX (%)	XX (%)
Died			
Primary reason for study withdrawal *			
Adverse event	XX (%)	XX (%)	XX (%)
Lack of Efficacy	XX (%)	XX (%)	XX (%)
Protocol Deviation	XX (%)	XX (%)	XX (%)
Subject reached protocol defined stopping criteria	XX (%)	XX (%)	XX (%)
Study closed/terminated	XX (%)	XX (%)	XX (%)
Lost to Follow-up	XX (%)	XX (%)	XX (%)
Investigator discretion	XX (%)	XX (%)	XX (%)
Withdrew consent	XX (%)	XX (%)	XX (%)

Note: * Percentages are based on the number of subjects in the treatment group.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Denominator for each primary reason for withdrawal is number of subjects in the Intent-to-Treat population per treatment group.

Protocol: AMB112529
Population: Randomised

Table 1.2: Summary of Study Populations

	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Randomised	XXX	XXX	XXX
Safety Population	XXX (%)	XXX (%)	XXX (%)
Intention-to-Treat population	XXX (%)	XXX (%)	XXX (%)

Note: The Safety Population is defined as all randomized subjects who received at least 1 dose of study drug. Subjects are considered as belonging to the treatment group according to highest dose received.
The Intention-to-Treat (ITT) Population is defined as all randomized subjects who received at least 1 dose of study drug. Subjects are considered as belonging to their randomized treatment group, regardless of the actual dose of ambrisentan received.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Intent-to-treat

Table 1.3: Summary of Subjects by Country and Centre

Country	Centre ID	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
XXXXXXXXX	All	XX (%)	XX (%)	XX (%)
	XXXXXX	XX (%)	XX (%)	XX (%)
XXXXXXXXX	All	XX (%)	XX (%)	XX (%)
	XXXXXX	XX (%)	XX (%)	XX (%)
XXXXXXXXX	All	XX (%)	XX (%)	XX (%)
	XXXXXX	XX (%)	XX (%)	XX (%)

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Protocol: AMB112529
Population: Intent-to-Treat

Table 1.4: Summary of Inclusion/Exclusion Criteria Deviations

	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Any criteria deviations	XX (%)	XX (%)	XX (%)
Inclusion			
I1	XX (%)	XX (%)	XX (%)
I2	XX (%)	XX (%)	XX (%)
Etc..			
Exclusion			
E1	XX (%)	XX (%)	XX (%)
E2	XX (%)	XX (%)	XX (%)
Etc..			

Note: Please refer to numbering of inclusion and exclusion criteria in protocol.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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: AMB112529
Population: Intent-to-Treat

Table 1.5: Summary of Demographic and Baseline Characteristics

	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Age (yrs)			
n	XXX	XXX	XXX
Mean	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X
Min.	XX	XX	XX
Max.	XX	XX	XX
Age (yrs)			
n	XXX	XXX	XX (%)
<8 years	XX (%)	XX (%)	XX (%)
8 – 11 years	XX (%)	XX (%)	XX (%)
12 - <18 years	XX (%)	XX (%)	XX (%)
>=18 years	XX (%)	XX (%)	XX (%)
Sex			
n	XXX	XXX	XX (%)
Female	XX (%)	XX (%)	XX (%)
Male	XX (%)	XX (%)	XX (%)

Note: * A subject may be represented in more than one geographic ancestry group.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Protocol: AMB112529
Population: Intent-to-Treat

Table 1.5: Summary of Demographic and Baseline Characteristics

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

Note: * A subject may be represented in more than one geographic ancestry group.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Protocol: AMB112529
Population: Intent-to-Treat

Table 1.5: Summary of Demographic and Baseline Characteristics

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

Note: * A subject may be represented in more than one geographic ancestry group.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Protocol: AMB112529
Population: Intent-to-Treat

Table 1.5: Summary of Demographic and Baseline Characteristics

	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Duration of PAH (days)			
n	XXX	XXX	XXX
Mean	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X
Min.	XX	XX	XX
Max.	XX	XX	XX
PAH Therapy Use			
n	XXX	XXX	XX (%)
Ongoing PAH therapy at baseline	XX (%)	XX (%)	XX (%)
Prior PAH therapy, not ongoing at baseline	XX (%)	XX (%)	XX (%)
No PAH therapy recorded	XX (%)	XX (%)	XX (%)

Note: * A subject may be represented in more than one geographic ancestry group.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Protocol: AMB112529
Population: Intent-to-Treat

Table 1.5: Summary of Demographic and Baseline Characteristics

	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
WHO Functional Class			
N	XXX	XXX	XX (%)
Class II	XX (%)	XX (%)	XX (%)
Class III	XX (%)	XX (%)	XX (%)
6 minute walk data (m)			
N	XXX	XXX	XXX
Mean	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X
Min.	XX	XX	XX
Max.	XX	XX	XX

Note: * A subject may be represented in more than one geographic ancestry group.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Protocol: AMB112529
Population: Intent-to-Treat

Table 1.6: Summary of Past Medical Conditions

Classification	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Any condition	XX (%)	XX (%)	XX (%)
Classification 1			
Any condition	XX (%)	XX (%)	XX (%)
Preferred Term 1	XX (%)	XX (%)	XX (%)
Preferred Term 2	XX (%)	XX (%)	XX (%)
etc			
Classification 2			
Any condition	XX (%)	XX (%)	XX (%)
Preferred Term 1	XX (%)	XX (%)	XX (%)
Preferred Term 2	XX (%)	XX (%)	XX (%)
etc			
Etc..			

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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.

Protocol: AMB112529
Population: Intent-to-Treat

Table 1.8: Summary of Concomitant Medications

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

Note: A medication may be included in more than one ATC level category and appear more than once.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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.

Protocol: AMB112529
Population: Intent-to-Treat

Table 1.9: Summary of Ongoing Background PAH Therapy at Baseline
By Drug Class and Preferred Term

PAH Therapy	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Any medication	XX (%)	XX (%)	XX (%)
PDE5i (monotherapy)			
Any medication	XX (%)	XX (%)	XX (%)
Preferred Term 1	XX (%)	XX (%)	XX (%)
Preferred Term 1	XX (%)	XX (%)	XX (%)
Etc..			
Prostanoid (monotherapy)			
Any medication	XX (%)	XX (%)	XX (%)
Preferred Term 1	XX (%)	XX (%)	XX (%)
Preferred Term 1	XX (%)	XX (%)	XX (%)
Etc..			
PDE5i and prostanoid in combination			
Any medication	XX (%)	XX (%)	XX (%)
Preferred Term 1 + Preferred Term 2	XX (%)	XX (%)	XX (%)
Preferred Term 3 + Preferred Term 4	XX (%)	XX (%)	XX (%)
Etc..			

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Protocol: AMB112529
Population: Intent-to-Treat

Table 1.11: Summary of Subjects who continue in the long term study (AMB114588)

AMB 114588	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Yes	XX (%)	XX (%)	XX (%)
No	XX (%)	XX (%)	XX (%)

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Protocol: AMB112529
Population: Intent-to-Treat

Table 1.12: Summary of Compliance to Investigational Product since last visit

Planned Relative Time	Compliance assessment	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Week 2	n	XXX	XXX	XXX
	0% compliant	XX (%)	XX (%)	XX (%)
	>0% and < 80%	XX (%)	XX (%)	XX (%)
	>= 80% and <= 120%	XX (%)	XX (%)	XX (%)
	>120% compliant	XX (%)	XX (%)	XX (%)
Week 4	n	XXX	XXX	XXX
	0% compliant	XX (%)	XX (%)	XX (%)
	>0% and < 80%	XX (%)	XX (%)	XX (%)
	>= 80% and <= 120%	XX (%)	XX (%)	XX (%)
	>120% compliant	XX (%)	XX (%)	XX (%)
Etc..	Etc..			

Note: EW = Early Withdrawal.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Present for Weeks 2, 4, 8, 12, 16, 20, 24 and EW.

Protocol: AMB112529
Population: Intent-to-treat

Table 1.13: Summary of Investigational Product Compliance Overall

	Ambrisentan Lose Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Overall % of visits at which subject is compliant	XX	XX	XX
n	XX	XX	XX
Mean	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X
Min.	XX	XX	XX
Max.	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).
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Protocol: AMB112529
Population: Intent-to-Treat

Table 1.14: Summary of Important Protocol Deviation

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

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

Table 2.1: Summary of 6 Minute Walking Distance (meters)

Treatment	Planned Relative Time	n	Mean	SD	Q1	Median	Q3	Min.	Max.
Ambrisentan Low Dose	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)	Week 4								
	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
	Etc..								
	Week 24								
	EW								
Ambrisentan High Dose (N=XXX)	Etc..								
Total (N=XXX)	Etc..								

Note: * Baseline is the last value recorded prior to start of study treatment.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal.
EW = Early Withdrawal.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

Protocol: AMB112529
Population: Intent-to-Treat

Table 2.4: 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 Low Dose (N=XXX)		Baseline*	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 4	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 8	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 12	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 16	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 20	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 24	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		EW	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
Ambrisentan High Dose (N=XXX)		Baseline*	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 4	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 8	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 12	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 16	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 20	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 24	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		EW	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
Total (N=XXX)		Etc..								

Note: * Baseline is the last value recorded prior to start of study treatment.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
% out of the number of subjects who attempted the 6 minute walk.
EW = Early Withdrawal.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

Population: Intent-to-Treat

Table 2.5: 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 Low Dose (N=XXX)		Baseline*	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 4	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 8	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 12	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 16	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 20	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 24	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		EW	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
Ambrisentan High Dose (N=XXX)		Baseline*	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 4	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 8	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 12	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 16	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 20	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 24	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		EW	XX (%)	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Total (N=XXX)	Etc..								

Note: * Baseline is the last value recorded prior to start of study treatment.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
% out of the number of subjects who attempted the 6 minute walk.
EW = Early Withdrawal.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Protocol: AMB112529
Population: Intent-to-Treat

Table 2.6: Summary of Time to the first Clinical Worsening of PAH (days)

	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
N	XXX	XXX	XXX
Mean	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X
Min.	XX	XX	XX
Max.	XX	XX	XX

Note: Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Table 2.7: Summary of Clinical Worsening of PAH

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

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Protocol: AMB112529
Population: Intent-to-Treat

Table 2.8: Summary of WHO Functional Class

Treatment	Planned Relative Time	n	Mean	SD	Q1	Median	Q3	Min.	Max.
Ambrisentan Low Dose (N=XXX)	Baseline*	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 4	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 8	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 12	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 16	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 20	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 24	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	EW	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
Ambrisentan High Dose (N=XXX)	Baseline*	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 4	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 8	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 12	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 16	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 20	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 24	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	EW	XX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
Total (N=XXX)	Etc..								

Note: * Baseline is the last value recorded prior to start of study treatment.
There are 4 grades of WHO FC based on symptom severity (Class I=none, Class IV=most severe).
Grades mapped to numeric scale 1-4 (i.e. Class IV=4).
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Present Baseline and Weeks 4, 8, 12, 16, 20, 24 and EW.

Protocol: AMB112529
Population: Intent-to-Treat

Table 2.10: Summary of WHO Functional Class Shifts from Baseline by Visit

Treatment	Planned Relative Time	WHO Functional Class	Baseline WHO Functional Class	
			II	III
Ambrisentan Low Dose (N=XXX)	Week 4	I	XX (%)	XX (%)
		II	XX (%)	XX (%)
		III	XX (%)	XX (%)
		IV	XX (%)	XX (%)
		Unknown/ Not Recorded	XX	XX
	Week 8	I	XX (%)	XX (%)
		II	XX (%)	XX (%)
		III	XX (%)	XX (%)
		IV	XX (%)	XX (%)
		Unknown/ Not Recorded	XX	XX
Etc..				

Note: Baseline is the last value recorded prior to start of study treatment.
There are 4 grades of WHO FC based on symptom severity (Class I=none, Class IV=most severe).
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Present Weeks 4, 8, 12, 16, 20, 24 and EW, for each treatment group and overall.

Protocol: AMB112529
Population: Intent-to-Treat

Table 2.11: Summary of WHO Functional Class Change from Baseline Categorisation

Planned Relative Time	WHO Category	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Week 4	n	XXX	XXX	XXX
	Improved	XX (%)	XX (%)	XX (%)
	No Change	XX (%)	XX (%)	XX (%)
	Deteriorated	XX (%)	XX (%)	XX (%)
	-2	XX (%)	XX (%)	XX (%)
	-1	XX (%)	XX (%)	XX (%)
	0	XX (%)	XX (%)	XX (%)
	+1	XX (%)	XX (%)	XX (%)
	+2	XX (%)	XX (%)	XX (%)
Etc..				

Note: Baseline is the last value recorded prior to start of study treatment
There are 4 grades of WHO FC based on symptom severity (Class I=none, Class IV=most severe).
Grades mapped to numeric scale 1-4 (i.e. Class IV=4).
Change categorisation (based on -2, -1, 0, +1, +2); No Change (0), Improved (-1,-2), Deterioration (+1,+2).
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Present Weeks 4, 8, 12, 16, 20, 24 and EW, for each treatment group and overall.

Protocol: AMB112529
Population: Intent-to-Treat

Table 2.12: Summary of plasma NT-Pro BNP concentration (ng/L)

Treatment	Planned Relative Time	n	Geometric Mean	SD [logs]	Q1	Median	Q3	Min.	Max.
Ambrisentan Low Dose (N=XXX)	Baseline*	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 12	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 24	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	EW	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
Ambrisentan High Dose (N=XXX)	Baseline*	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 12	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 24	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	EW	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
Total (N=XXX)	Baseline*	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 12	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 24	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	EW	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX

Note: * Baseline is the last value recorded prior to start of study treatment.
EW = Early Withdrawal.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Protocol: AMB112529
Population: Intent-to-Treat

Table 2.14: Summary of Exploratory Echocardiogram

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

Note: * Baseline is the last value recorded prior to start of study treatment.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal. Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Present Baseline, Week 12, Week 24 and EW.

Table 2.14: Summary of Exploratory Echocardiogram

Planned Relative Time Baseline*		Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Eccentricity Index Systolic	N	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX
Eccentricity Index Diastolic	N	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX

Note: * Baseline is the last value recorded prior to start of study treatment.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Present Baseline, Week 12, Week 24 and EW.

Table 2.14: Summary of Exploratory Echocardiogram

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

Note: * Baseline is the last value recorded prior to start of study treatment.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Present Baseline, Week 12, Week 24 and EW.

Protocol: AMB112529
Population: Intent-to-Treat

Table 2.15: Summary of Change from Baseline in Exploratory Echocardiogram

Planned Relative Time Week 12		Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Pericardial Effusion	n	XXX	XXX	XXX
	No Change	XX (%)	XX (%)	XX (%)
	Absent	XX (%)	XX (%)	XX (%)
	Improved	XX (%)	XX (%)	XX (%)
	Worsened	XX (%)	XX (%)	XX (%)
Mean right Atrial Pressure (mmHg)	n	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX
Tricuspid Annular Plane Systolic Excursion (cm)	n	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX

Note: Baseline is the last value recorded prior to start of study treatment.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal. Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Present Week 12, Week 24 and EW.

Protocol: AMB112529
Population: Intent-to-Treat

Table 2.15: Summary of Change from Baseline in Exploratory Echocardiogram

Planned Relative Time Week 12		Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Eccentricity Index Systolic	n	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX
Eccentricity Index Diastolic	N	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX

Note: Baseline is the last value recorded prior to start of study treatment.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Present Week 12, Week 24 and EW.

Table 2.15: Summary of Change from Baseline in Exploratory Echocardiogram

Planned Relative Time Week 12		Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Tricuspid Regurgitant Jet Velocity (m/s)	N	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX
Right Ventricular Pressure (mmHg)	N	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX

Note: Baseline is the last value recorded prior to start of study treatment.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Present Week 12, Week 24 and EW.

Table 2.16: Summary of Cardiopulmonary Hemodynamics

Parameter	Treatment	Planned Relative Time	n	Mean	SD	Q1	Median	Q3	Min.	Max.
<Parameter (units)>	Ambrisentan Low Dose (N=XXX)	Baseline*	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 24	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		EW	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Ambrisentan High Dose (N=XXX)	Baseline*	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 24	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		EW	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Total (N=XXX)	Baseline*	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 24	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		EW	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX

Note: * Baseline is the last value recorded prior to start of study treatment.
EW = Early Withdrawal.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Include 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.

Protocol: AMB112529
Population: Intent-to-treat

Table 2.18: Summary of Number of Subjects with School Days within the Past Month

Planned Relative Time Baseline*	Low Dose (N=XX)		High Dose (N=XX)		Total (N=XX)	
Subjects with scheduled days	xx	(xx%)	xx	(xx%)	xx	(xx%)
Subjects with at least one scheduled day missed	xx	(xx%)	xx	(xx%)	xx	(xx%)
Number of scheduled days missed / Number of scheduled days	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%)
Number of scheduled days missed due to PAH / Number of scheduled days	xx	(xx%)	xx	(xx%)	xx	(xx%)
	xx/xxx	(xx%)	xx/xxx	(xx%)	xx/xxx	(xx%)

Note: * Baseline is the last value recorded prior to start of study treatment.
This summary excludes subjects with 0 scheduled days of school for the given period.
There were no subjects with follow up visits (of the 3 subjects who did not participate in study AMB11488, one died, one was lost to follow-up and the other withdrew consent).
EW = Early Withdrawal.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Present Baseline, Weeks 4, 8, 12, 16, 20, 24 and EW.

Protocol: AMB112529
Population: Intent-to-Treat

Table 2.19: Summary Statistics of School Days within the Past month

Planned Relative Time Baseline*		Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Number of scheduled days	n	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX
Number of missed days	N	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX
Number of missed days due to PAH	N	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX

Note: * Baseline is the last value recorded prior to start of study treatment.
This summary excludes subjects with 0 scheduled days of school for the given period.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal. Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Present Baseline, Weeks 4, 8, 12, 16, 20, 24 and EW.

Protocol: AMB112529
Population: Intent-to-Treat

Table 2.19: Summary Statistics of School Days within the Past month

Planned Relative Time Baseline*		Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Proportion of days missed (%)	n	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX
Proportion of days missed due to PAH(%)	N	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX

Note: * Baseline is the last value recorded prior to start of study treatment.
This summary excludes subjects with 0 scheduled days of school for the given period.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal. Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Present Baseline, Weeks 4, 8, 12, 16, 20, 24 and EW.

Protocol: AMB112529
Population: Intent-to-Treat

Table 2.21: Summary of Subject Global Assessment (SF10 Health Survey for Children)

Planned Relative Time Baseline*		Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Physical Health Summary	n	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX
Psychosocial Summary	N	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX

Note: * Baseline is the last value recorded prior to start of study treatment.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Present Baseline, Weeks 4, 8, 12, 16, 20, 24 and EW.

Population: Intent-to-Treat

Table 2.23: Summary of SF10 Health Survey – Number and Percentage of Subjects with Particular Item Responses

Planned Relative Time Baseline*	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Completed SF-10 ^	XX (%)	XX (%)	XX (%)
In general, would you say your child's health is			
n	XX	XX	XX
Excellent	XX (%)	XX (%)	XX (%)
Very Good	XX (%)	XX (%)	XX (%)
Good	XX (%)	XX (%)	XX (%)
Fair	XX (%)	XX (%)	XX (%)
Poor	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
Yes, limited a lot	XX (%)	XX (%)	XX (%)
Yes, limited some	XX (%)	XX (%)	XX (%)
Yes, limited a little	XX (%)	XX (%)	XX (%)
No, not limited	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
Yes, limited a lot	XX (%)	XX (%)	XX (%)
Yes, limited some	XX (%)	XX (%)	XX (%)
Yes, limited a little	XX (%)	XX (%)	XX (%)
No, not limited	XX (%)	XX (%)	XX (%)
etc...			

Note: * Baseline is the last value recorded prior to start of study treatment.
^ Completed at least one of the 10 items of SF-10
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Present Baseline, Weeks 4, 8, 12, 16, 20, 24 and EW.

Protocol: AMB112529
Population: Safety

Table 3.1: Summary of Exposure to Investigational Product

		Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Number of days of exposure	n	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX
Interval of days of exposure	n	XXX	XXX	XXX
	<=30 days	XX (%)	XX (%)	XX (%)
	31 to 60 days	XX (%)	XX (%)	XX (%)
	61 to 90 days	XX (%)	XX (%)	XX (%)
	Etc..	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.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Protocol: AMB112529
Population: Safety

Table 3.2: Summary of Treatment-Emergent Adverse Events

System Organ Class Preferred term	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Any event	XX (%)	XX (%)	XX (%)
Gastrointestinal disorders			
Any event	XX (%)	XX (%)	XX (%)
Dyspepsia	XX (%)	XX (%)	XX (%)
Nausea	XX (%)	XX (%)	XX (%)
Nervous system disorders			
Any event	XX (%)	XX (%)	XX (%)
Headache	XX (%)	XX (%)	XX (%)
Dizziness	XX (%)	XX (%)	XX (%)
Somnolence	XX (%)	XX (%)	XX (%)
Tremor	XX (%)	XX (%)	XX (%)
Sedation	XX (%)	XX (%)	XX (%)
Etc..			

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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: AMB112529
Population: Safety

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

Preferred term	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Any event	XX (%)	XX (%)	XX (%)
Dyspepsia	XX (%)	XX (%)	XX (%)
Nausea	XX (%)	XX (%)	XX (%)
Headache	XX (%)	XX (%)	XX (%)
Dizziness	XX (%)	XX (%)	XX (%)
Somnolence	XX (%)	XX (%)	XX (%)
Tremor	XX (%)	XX (%)	XX (%)
Sedation	XX (%)	XX (%)	XX (%)
Etc..			

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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: AMB112529
Population: Safety

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

	Ambrisentan Low Dose (N=XXX)			Ambrisentan High Dose (N=XXX)		
System Organ Class Preferred Term	Mild	Moderate	Severe	Mild	Moderate	Severe
Any Event	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Cardiovascular disorders	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Any Event	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Hypertension	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Syncope	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Aneurysms	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Hypotension	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)	XX (%)
Etc..						

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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: AMB112529
Population: Safety

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

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

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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: AMB112529
Population: Safety

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

Treatment: Ambrisentan Low Dose (N=XXX)

System Organ Class Preferred term	Time Since Start of Study Medication							Overall
	<2 Wks	<4 Wks	<8 Wks	<12 Wks	<16 Wks	<20 Wks	<24 Wks	
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: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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 Ambrisentan High Dose and Total groups.

Protocol: AMB112529
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 Low Dose	x	x	x	x	x	x
	Ambrisentan High Dose	x	x	x	x	x	x
	Total	x	x	x	x	x	x
Bradyarrhythmia	Ambrisentan Low Dose	x	x	x	x	x	x
	Ambrisentan High Dose	x	x	x	x	x	x
	Total	x	x	x	x	x	x
etc							

Note: * Drug-related as determined by the investigator.

PPD

Protocol: AMB112529
Population: Safety

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

System Organ Class Preferred term Outcome	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Any event	XX (%)	XX (%)	XX (%)
<System Organ Class 1>			
<Any event>	XX (%)	XX (%)	XX (%)
Recovered/Resolved	XX (%)	XX (%)	XX (%)
Recovering/Resolving	XX (%)	XX (%)	XX (%)
Recovered/Resolved with sequelae	XX (%)	XX (%)	XX (%)
Not Recovered/ Not Resolved	XX (%)	XX (%)	XX (%)
<Preferred Term 1>	XX (%)	XX (%)	XX (%)
Recovered/Resolved	XX (%)	XX (%)	XX (%)
Recovering/Resolving	XX (%)	XX (%)	XX (%)
Recovered/Resolved with sequelae	XX (%)	XX (%)	XX (%)
Not Recovered/ Not Resolved	XX (%)	XX (%)	XX (%)
Etc..			

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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: AMB112529
Population: Safety

Table 3.21: Summary of Haematology Data

Parameter: <Parameter (units)>

Treatment	Planned Relative Time	N	Mean	SD	Q1	Median	Q3	Min.	Max.
Ambrisentan Low Dose (N=XXX)	Baseline*	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 2	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 4	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 8	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 12	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 16	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 20	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 24	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	EW	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
Ambrisentan High Dose (N=XXX)	Baseline*	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 2	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 4	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 8	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 12	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 16	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 20	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Week 24	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	EW	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
Total (N=XXX)	Etc..								

Note: * Baseline is the last value recorded prior to start of study treatment.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal. Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Protocol: AMB112529
Population: Safety

Table 3.23: Summary of Haematology Data of Potential Clinical Concern

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

Planned Relative Time	Category	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Baseline*	N	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)
Week 2	N	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)
Week 4	N	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)
Week 8	N	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)
Week 12	N	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)

Note: * Baseline is the last value recorded prior to start of study treatment.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal.
For 'Any time post-baseline':-
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.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

Table 3.23: Summary of Haematology Data of Potential Clinical Concern

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

Planned Relative Time	Category	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Week 16	N	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)
Week 20	N	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)
Week 24	n	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)
EW	n	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)
Any time post-baseline	n	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)

Note: * Baseline is the last value recorded prior to start of study treatment.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal.
For 'Any time post-baseline':-
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.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

Table 3.29: Summary of Liver Events Assessment

	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Subjects reporting a significant liver chemistry result *	XX (XX%)	XX (XX%)	XX (XX%)
Subjects with event occurring while receiving study treatment	XX (XX%)	XX (XX%)	XX (XX%)
Subjects with event occurring after stopping study treatment	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.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Protocol: AMB112529
Population: Safety

Table 3.30 Summary of Vital Signs

Parameter	Treatment	Planned Relative Time	n	Mean	SD	Q1	Median	Q3	Min.	Max.
<Parameter (units)>	Ambrisentan Low Dose (N=XXX)	Baseline*	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 2	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 4	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 8	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 12	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 16	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 20	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 24	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		EW	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Ambrisentan High Dose (N=XXX)	Baseline*	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 2	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 4	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 8	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 12	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 16	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 20	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		Week 24	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
		EW	XXX	XX.X	XX.XX	XX.X	XX.X	XX.X	XX	XX
	Total (N=XXX)	Etc..								

Note: * Baseline is the last value recorded prior to start of study treatment.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal. Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Include Height, Weight, Systolic BP, Diastolic BP, Heart Rate, BSA and BMI.

Protocol: AMB112529
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 Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Baseline*	n	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)
Week 2	n	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)
Week 4	n	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)
Week 8	n	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)
Week 12	n	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)

Note: * Baseline is the last value recorded prior to start of study treatment.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal.
For 'Any time post-baseline':-
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.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Include Systolic BP, Diastolic BP and Heart Rate

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 Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Week 16	n	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)
Week 20	n	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)
Week 24	n	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)
EW	n	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)
Any time Post-baseline	n	XXX	XXX	XXX
	> reference range high	XX (%)	XX (%)	XX (%)
	< reference range low	XX (%)	XX (%)	XX (%)

Note: * Baseline is the last value recorded prior to start of study treatment.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal.
For 'Any time post-baseline':-
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.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Include Systolic BP, Diastolic BP and Heart Rate

Population: Safety

Table 3.34: Summary of Physical Examination by Visit

Planned Relative Time: Baseline	Low Dose (N=XXX)	High Dose (N=XXX)	Total (N=XXX)
Ascites			
Absent	XX (%)	XX (%)	XX (%)
Present	XX (%)	XX (%)	XX (%)
Peripheral Oedema			
Absent	XX (%)	XX (%)	XX (%)
Present	XX (%)	XX (%)	XX (%)
Saturated Oxygen (units)			
N	XXX	XXX	XXX
Mean	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX
Median	XX.X	XX.X	XX.X
Min.	XX	XX	XX
Max.	XX	XX	XX

Note: * Baseline is the last value recorded prior to start of study treatment.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Table 3.34: Summary of Physical Examination by Visit

Planned Relative Time: Week 12	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Ascites			
n	XX	XX	XX
Absent	XX (%)	XX (%)	XX (%)
Present:Improved	XX (%)	XX (%)	XX (%)
Present:Unchanged	XX (%)	XX (%)	XX (%)
Present:Worsened	XX (%)	XX (%)	XX (%)
Peripheral Oedema			
n	XX	XX	XX
Absent	XX (%)	XX (%)	XX (%)
Present:Improved	XX (%)	XX (%)	XX (%)
Abnormal:Worsened	XX (%)	XX (%)	XX (%)
Abnormal:Unchanged	XX (%)	XX (%)	XX (%)
Saturated Oxygen (units)			
n	XXX	XXX	XXX
Mean	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X
Min.	XX	XX	XX
Max.	XX	XX	XX

Note: * Baseline is the last value recorded prior to start of study treatment.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Present for Week 12, Week 24 and EW.

Table 3.35: Summary of 12-lead ECG

Planned Relative Time	Category	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Baseline*	n	XXX	XXX	XXX
	Normal	XX (%)	XX (%)	XX (%)
	Abnormal, not clinically significant	XX (%)	XX (%)	XX (%)
	Abnormal, clinically significant	XX (%)	XX (%)	XX (%)
Week 12	n	XXX	XXX	XXX
	Normal	XX (%)	XX (%)	XX (%)
	Abnormal, not clinically significant	XX (%)	XX (%)	XX (%)
	Abnormal, clinically significant	XX (%)	XX (%)	XX (%)
Week 24	n	XXX	XXX	XXX
	Normal	XX (%)	XX (%)	XX (%)
	Abnormal, not clinically significant	XX (%)	XX (%)	XX (%)
	Abnormal, clinically significant	XX (%)	XX (%)	XX (%)
EW	n	XXX	XXX	XXX
	Normal	XX (%)	XX (%)	XX (%)
	Abnormal, not clinically significant	XX (%)	XX (%)	XX (%)
	Abnormal, clinically significant	XX (%)	XX (%)	XX (%)
Any time post-baseline	n	XXX	XXX	XXX
	Normal	XX (%)	XX (%)	XX (%)
	Abnormal, not clinically significant	XX (%)	XX (%)	XX (%)
	Abnormal, clinically significant	XX (%)	XX (%)	XX (%)

Note: * Baseline is the last value recorded prior to start of study treatment.
There were no subjects with post-last dose follow up visits. Of the 3 subjects who did not participate in study AMB115488, one died, one was lost to follow-up and the other was investigator discretion.
EW = Early Withdrawal.
For 'Any time post-baseline' if a subject had more than one ECG result, the worst case will be chosen for a conservative approach.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

Protocol: AMB112529
Population: Safety

Table 3.36: Summary of Endocrinology assessments – Female

Overall

Planned Relative Time Baseline*	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Female breast development			
n	XXX	XXX	XXX
Pre-adolescent	XX (%)	XX (%)	XX (%)
Breast bud stage	XX (%)	XX (%)	XX (%)
Etc..	XX (%)	XX (%)	XX (%)
Female pubic hair development			
n	XXX	XXX	XXX
Pre-adolescent	XX (%)	XX (%)	XX (%)
Sparse growth	XX (%)	XX (%)	XX (%)
Etc..	XX (%)	XX (%)	XX (%)

Note: * Baseline is the last value recorded prior to start of study treatment.
EW = Early Withdrawal.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).
Pre-pubertal: Stage 1 breast development, Post-pubertal: Stage ≥ 2 breast development.

PPD

Programming notes: Present for Baseline, Week 12, Week 24 and EW, Overall and by Pubertal Status (Pre-pubertal, Post Pubertal).

Protocol: AMB112529
Population: Safety

Table 3.37: Summary of Endocrinology assessments – Male
Overall

Planned Relative Time Baseline*	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Right Testicular volume (units)			
N	XXX	XXX	XXX
Mean	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X
Min.	XX	XX	XX
Max.	XX	XX	XX
Left Testicular volume (units)			
N	XXX	XXX	XXX
Mean	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX
Q1	XX.X	XX.X	XX.X
Median	XX.X	XX.X	XX.X
Q3	XX.X	XX.X	XX.X
Min.	XX	XX	XX
Max.	XX	XX	XX

Note: * Baseline is the last value recorded prior to start of study treatment.
EW = Early Withdrawal.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).
Pre-pubertal: testicular volume < 4 ml, Post-pubertal: testicular volume ≥ 4 ml

PPD

Programming notes: Present for Baseline, Week 12, Week 24 and EW, Overall and by Pubertal Status (Pre-pubertal, Post Pubertal).

Protocol: AMB112529
Population: Safety

Table 3.37: Summary of Endocrinology assessments – Male
Overall

Planned Relative Time Baseline*	Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Male genital development			
N	XXX	XXX	XXX
Pre-adolescent	XX (%)	XX (%)	XX (%)
Etc..	XX (%)	XX (%)	XX (%)
Male pubic hair development			
N	XXX	XXX	XXX
Pre-adolescent	XX (%)	XX (%)	XX (%)
Sparse growth	XX (%)	XX (%)	XX (%)
Etc.	XX (%)	XX (%)	XX (%)

Note: * Baseline is the last value recorded prior to start of study treatment.
EW = Early Withdrawal.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).
Pre-pubertal: testicular volume < 4 ml, Post-pubertal: testicular volume ≥ 4 ml

PPD

Programming notes: Present for Baseline, Week 12, Week 24 and EW, Overall and by Pubertal Status (Pre-pubertal, Post Pubertal).

Protocol: AMB112529
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 Low Dose (N=XXX)	Week 12	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
	Week 24	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.
EW = Early Withdrawal.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).
Pre-pubertal: Stage 1 breast development, Post-pubertal: Stage ≥ 2 breast development.

PPD

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 week 12, 24 and EW. 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: AMB112529
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 Low Dose (N=XXX)	Week 12	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
	Week 24	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.
EW = Early Withdrawal.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).
Pre-pubertal: testicular volume < 4 ml, Post-pubertal: testicular volume ≥ 4 ml

PPD

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 week 12, 24 and EW. 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: AMB112529
Population: Safety

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

Planned Relative Time		Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Week 12	N	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX
Week 24	N	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX
Etc..				

Note: Baseline is the last value recorded prior to start of study treatment.
EW = Early Withdrawal.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).
Pre-pubertal: testicular volume < 4 ml, Post-pubertal: testicular volume ≥ 4 ml

PPD

Programming notes: Present overall and by Pubertal Status (Pre-pubertal, Post Pubertal), at week 12, 24 and EW.

Protocol: AMB112529
Population: Safety

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

Parameter: <Parameter (units)>

Planned Relative Time		Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Week 12	N	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX
Week 24	N	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX
Etc..				

Note: Baseline is the last value recorded prior to start of study treatment.
EW = Early Withdrawal.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).
Pre-pubertal: Stage 1 breast development, Post-pubertal: Stage ≥ 2 breast development.

PPD

Programming notes: Present overall and by Pubertal Status (Pre-pubertal, Post Pubertal), at week 12, 24 and EW, for Follicle Stimulating Hormone, Luteinizing Hormone, Sex Hormone Binding Globulin, Total Testosterone and Inhibin B.

Protocol: AMB112529
Population: Safety

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

Parameter: <Parameter (units)>

Planned Relative Time		Ambrisentan Low Dose (N=XXX)	Ambrisentan High Dose (N=XXX)	Total (N=XXX)
Week 12	N	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX
Week 24	N	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X
	SD	XX.XX	XX.XX	XX.XX
	Q1	XX.X	XX.X	XX.X
	Median	XX.X	XX.X	XX.X
	Q3	XX.X	XX.X	XX.X
	Min.	XX	XX	XX
	Max.	XX	XX	XX
Etc..				

Note: Baseline is the last value recorded prior to start of study treatment.
EW = Early Withdrawal.
Q1 = 1st quartile, Q3 = 3rd quartile.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).
Pre-pubertal: testicular volume < 4 ml, Post-pubertal: testicular volume ≥ 4 ml

PPD

Programming notes: Present overall and by Pubertal Status (Pre-pubertal, Post Pubertal), at week 12, 24 and EW, for Follicle Stimulating Hormone, Luteinizing Hormone, Sex Hormone Binding Globulin, Total Testosterone and Inhibin B.

Protocol: AMB112529
Population: Intent-to-treat

Listing 1.1: Listing of Randomised and Actual Treatments

Country: Argentina
Centre ID: XXXXXX

Centre ID/ Subject ID	Randomisation Number / Date	Randomisation Strata	Actual Strata	Randomised / Actual Treatment	Treatment Start Date	Deviation [1]
XXXXXX	XXXXXX / DDMMMYYYY	Aetiology - IPAH / Age 12-18	IPAH / Age 12-18	Low dose / Low dose	DDMMMYYY	
XXXXXX	XXXXXX / DDMMMYYYY	Aetiology – HPAH / Age 12-18	HPAH / Age 12-18	Low dose / Low dose	DDMMMYYY	

Note: 1 = Indicates subjects who have a deviation between their randomised and actual strata or treatment.
IPAH, idiopathic PAH; HPAH, heritable [familial] PAH; PAH-CTD, secondary to connective tissue disease; PAH-CHD,persistent despite surgical repair of atrial/ventricular/atrio-ventricular septal defects, and persistent patent ductus.

Programming notes: Sort by Country, Centre ID, Subject ID.

Protocol: AMB112529
Population: Intent-to-Treat

Listing 1.2: Listing of Reasons for Study Withdrawal

Treatment: Ambrisentan Low Dose

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: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Listing 1.3: Listing of Subjects with Inclusion/Exclusion Criteria Deviations

Treatment: Ambrisentan Low Dose

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

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Intent-to-Treat

Listing 1.4: Listing of Demographic Characteristics

Treatment: Ambrisentan Low Dose

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

Note: Age is based on full date of birth.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Intent-to-Treat

Listing 1.5: Listing of Race

Treatment: Ambrisentan Low Dose

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

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Intent-to-treat

Listing 1.6: Listing of Disease History

Treatment: Ambrisentan Low Dose

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: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Listing 1.7: Listing of Medical Conditions

Treatment: Ambrisentan Low Dose

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: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Intent-to-Treat

Listing 1.8: Listing of Medications

Treatment: Ambrisentan Low Dose

Centre ID/ Subject ID	ATC Level 1/ Ingredient/ Verbatim Text	Unit Dose/ Units/ Freq/ Route	Date Started/ Study Day	Date Stopped/ Study Day
XXXXXX/ XXXXXX	Endocrine & metabolic/ Fluticasone propionate/ FLIXOTIDE #	2/ MG/ 2XD/ IH	PPD 15	
	Endocrine & metabolic/ Fluticasone propionate/ FLIXOTIDE #	4/ MG/ 2XD/ IH	PPD 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
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Intent-to-Treat

Listing 1.9: Listing of PAH Therapy

Treatment: Ambrisentan Low Dose

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 discontinued or changed?
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
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Intent-to-Treat

Listing 1.10: Relationship between ATC Level 1, Ingredient and Verbatim Text

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

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Intent-to-Treat

Listing 1.11: Listing of Protocol Deviation

Treatment: Ambrisentan Low Dose

Centre ID/ Subject ID	Important Protocol Deviations	Protocol Deviation Category	Protocol Deviation Description	Protocol Deviation Date/ Study Day	Visit Phase	Action taken
XXXXXX/ XXXXXX	Y	Biological specimen sample procedures	XXXXXXXXXXXXXXXXXXXX XXX *	DDMMMYYYY/ XX	XXXXXXXX	XXXXXXXXXXX XXXXXXXXXXX X
XXXXXX/ XXXXXX	N	Other: XXXXXXXXXXXXXXXXXXXXXX	XXXXXXXXXXXXXXXXXXXX XXX	DDMMMYYYY/ XX	XXXXXXXX	XXXXXXXXXXX XXXXXXXXXXX X
		Etc..				
Etc..						

Note: * Important Deviation
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Intent-to-Treat

Listing 2.1: Listing of 6 Minute Walk Distance Data

Treatment: Ambrisentan Low Dose

Centre ID/ Subject ID	Visit	Visit Date/ 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	XXXXXXX	DDMMMYYYY/ XX	XXX			Y/ XXXXXXXXXXXX	XXX	Y	XXXX
	XXXXXXX	DDMMMYYYY/ XX	XXX	XXX	XXX	Y/ XXXXXXXXXXXX	XXX	Y	XXXX
	XXXXXXX	DDMMMYYYY/ XX	XXX	XXX	XXX	N		N	
	XXXXXXX	DDMMMYYYY/ XX	XXX	XXX	XXX	N		N	
	Etc..								
Etc..									

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Listing 2.2: Listing of Clinical Worsening of PAH

Treatment: Ambrisentan Low Dose

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: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Intent-to-Treat

Listing 2.3: Listing of WHO Functional Class Data

Treatment: Ambrisentan Low Dose

Centre ID/ Subject ID	Visit	Visit Date/ Study Day	WHO pulmonary hypertension functional classification	Actual *	Change from Baseline	Change Categorisation
XXXXXX/ XXXXXX	XXXXXXX	DDMMMYYYY/ XX	Class II	2		
	XXXXXXX	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: There are 4 grades for WHO FC based on severity of symptoms (Class I = none, Class IV = most severe).
* Grades mapped to numeric scale 1-4 (i.e. Class IV = 4).
Change categorisation (based on -2, -1, 0, +1, +2); NC=No Change (0), Imp=Improved (-1,-2), Det=Deterioration (+1,+2).
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Intent-to-Treat

Listing 2.4: Listing of Plasma NT-Pro BNP Concentration (ng/L)

Treatment: Ambrisentan Low Dose

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

Note: * Log (change from baseline) = Log (Visit) – Log (Baseline).
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Intent-to-Treat

Listing 2.5: Listing of Exploratory Echocardiogram

Treatment: Ambrisentan Low Dose

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	XXXXXXX	DDMMMYYYY/ XX	Absent	XXX	XXX	XXX	XXX	XXX	XXX
	XXXXXXX	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: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Intent-to-Treat

Listing 2.6: Listing of Cardiopulmonary Hemodynamics

Treatment: Ambrisentan Low Dose

Centre ID/ Subject ID	Visit	Right Heart Catheterization Date / 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	XXXXXXX	DDMMMYYYY/ XX	XXX	XXX	XXX	XXX
	XXXXXXX	DDMMMYYYY/ XX	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX
	XXXXXXX	DDMMMYYYY/ XX	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX
	XXXXXXX	DDMMMYYYY/ XX	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX
	Etc..					
Etc..						

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Intent-to-Treat

Listing 2.6: Listing of Cardiopulmonary Hemodynamics

Treatment: Ambrisentan Low Dose

Centre ID/ Subject ID	Visit	Right Heart Catheterization Date / 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	XXXXXXX	DDMMMYYYY/ HH:MM/ XX	XXXXXXXXXXX/ XXXXXXXXXX	XXX	XXX	XXX
	XXXXXXX	DDMMMYYYY/ HH:MM/ XX	XXXXXXXXXXX/ XXXXXXXXXX	XXX/ XXX	XXX/ XXX	XXX/ XXX
	XXXXXXX	DDMMMYYYY/ HH:MM/ XX	XXXXXXXXXXX/ XXXXXXXXXX	XXX/ XXX	XXX/ XXX	XXX/ XXX
	XXXXXXX	DDMMMYYYY/ HH:MM/ XX	XXXXXXXXXXX/ XXXXXXXXXX	XXX/ XXX	XXX/ XXX	XXX/ XXX
	Etc..					
Etc..						

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Intent-to-Treat

Listing 2.6: Listing of Cardiopulmonary Hemodynamics

Treatment: Ambrisentan Low Dose

Centre ID/ Subject ID	Visit	Right Heart Catheterization Date / 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	XXXXXXX	DDMMMYYYY/ HH:MM/ XX	XXX	XXX	XXX	XXX
	XXXXXXX	DDMMMYYYY/ HH:MM/ XX	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX
	XXXXXXX	DDMMMYYYY/ HH:MM/ XX	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX
	XXXXXXX	DDMMMYYYY/ HH:MM/ XX	XXX/ XXX	XXX/ XXX	XXX/ XXX	XXX/ XXX
	Etc..					
Etc..						

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Intent-to-Treat

Listing 2.7: Listing of School Days

Treatment: Ambrisentan Low Dose

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
		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
		XXXXXXX	DDMMMYYYY/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX
		Etc..						
Etc..								

Note: * In past month at Baseline; since baseline visit at Week 4; and since the patient's last clinic visit (all other assessments).
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Intent-to-Treat

Listing 2.8: Listing of Subject Global Assessment (SF10 Health Survey for Children)

Treatment: Ambrisentan Low Dose

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	XXXXXXX	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
	XXXXXXX	DDMMMYYYY/ XX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX
	Etc..							
Etc..								

Note: 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.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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 Subject Global Assessment (SF10 Health Survey for Children)

Treatment: Ambrisentan Low Dose

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	XXXXXXX	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
	XXXXXXX	DDMMMYYYY/ XX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XXXXXXXX	XX/ XX	XX/ XX
	Etc..							
Etc..								

Note: 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.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Safety

Listing 3.1: Listing of Exposure and Compliance to Investigational Product

Treatment: Ambrisentan Low Dose

Centre ID/ Subject ID	IP Start Date	IP Stop Date	Duration (Days)	% of compliant visits	Visit	Visit Date/ Study Day	Compliance since the last visit
XXXXXX/ XXXXXX	DDMMMYYYY	DDMMMYYYY	XX	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.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Listing 3.2: Listing of All Adverse Events

Treatment: Ambrisentan Low Dose

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
XXXXXX/ XXXXXX	XX/ XXXXXX/ XXXXXX/ XX	XXXXXXXXXXX/ XXXXXXXXXXX *	XXXXXXXXX/ DDMMMYYYY/ DDMMMYYYY/ XXXXXXXXX	XX/ XX/ XX	XXXX/ XXX/ XXX	XXXXXXXX/ XX
		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.
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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	Heart palpitation
	Tachycardia nos	Tachycardia
Etc..		

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Safety

Listing 3.4: Listing of Subject Numbers for Specified Adverse Events

Treatment: Ambrisentan Low Dose

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: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Safety

Listing 3.8: Listing of Haematology

Central Laboratory
Treatment: Ambrisentan Low Dose

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)>	Screening	DDMMMYYYY	XX	XXX	XXX - XXX			
	XXXXXX/		Baseline	DDMMMYYYY	XX	XXX	XXX - XXX			
	XXXXXX/		Week 2	DDMMMYYYY	XX	XXX	XXX - XXX	H	H	H
	XX		Week 4	DDMMMYYYY	XX	XXX	XXX - XXX	H		H
			Week 8	DDMMMYYYY	XX	XXX	XXX - XXX			
			Week 12	DDMMMYYYY	XX	XXX	XXX - XXX			
			Week 16	DDMMMYYYY	XX	XXX	XXX - XXX			
			Week 20	DDMMMYYYY	XX	XXX	XXX - XXX	L	L	L
			EW	DDMMMYYYY	XX	XXX	XXX - XXX			
			Follow-Up	DDMMMYYYY	XX	XXX	XXX - XXX	L		
		<Parameter (units)>	Etc..							
Etc..										

Note: * NR for Normal Range flag, CC for Clinical Concern flag; BL for Change from Baseline
H=Above range, L=Below range
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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: AMB112529
Population: Safety

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

Central Laboratory
Treatment: Ambrisentan Low Dose

Centre ID/ Subject ID	Age(y)/ Sex/ Race/ Baseline Weight(kg)	Lab test (units)	Planned Relative Time	Date	Study Day	Converted Data Value	Normal Range	Low Concern	High Concern	Flag * NR	CC	BL
XXXXXX/ XXXXXX	XX/	<Parameter (units)>	Screening	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX			
	XXXXXX/		Baseline	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX			
	XXXXXX/		Week 2	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX	H	H	H
	XX		Week 4	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX	H		H
			Week 8	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX			
			Week 12	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX			
			Week 16	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX			
			Week 20	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX	L	L	L
			EW	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX			
			Follow-Up	DDMMMYYYY	XX	XXX	XXX - XXX	XXX	XXX	L		
		<Parameter (units)>	Etc..									
Etc..												

Note: * NR for Normal Range flag, CC for Clinical Concern flag; BL for Change from Baseline
H=Above range, L=Below range
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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.

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

Treatment: Ambrisentan Low Dose

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/	DDMMMYYYY/	X	X	ALT (alanine aminotransferase)
	XXXXXX/ XXXXXX/ XX	XX			
Etc..					

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Safety

Listing 3.14: Listing of patient specific information for liver events

Treatment: Ambrisentan Low Dose

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: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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 Low Dose	XXXXXX/ XXXXXX	XX/ XXXXXXX/ XXXXXX	Hepatobiliary	HEPATITIS A	Current
			Psychiatric	PARANOIA COMBINED WITH MANIA.	Past
	XXXXXX/ XXXXXX	XX/ XXXXXXX/ XXXXXX	Eye	ASTIGMATISM	Current
Ambrisentan High Dose	XXXXXX/ XXXXXX	XX/ XXXXXXX/ XXXXXX	Metabolism and nutrition	RICKETS	Current

Listing 3.16: Listing of Liver Biopsy Details

Treatment: Ambrisentan Low Dose

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: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Listing 3.17: Listing of Liver Imaging Details

Treatment: Ambrisentan Low Dose

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: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Safety

Listing 3.18: Listing of Vital Signs

Treatment: Ambrisentan Low Dose

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	XXXXXXX	DDMMMYYYY/ 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
		XXXXXXX	DDMMMYYYY/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX	XX/ XX
		Etc..								
Etc..										

Note: H=Above clinical concern, L=Below clinical concern,
Change from Baseline HC=Above clinical concern, LC=Below clinical concern
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Population: Safety

Listing 3.20: Listing of Physical Examination

Treatment: Ambrisentan Low Dose

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	XXXXXXX	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: I=Improved, W=Worsened, U=Unchanged
Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Safety

Listing 3.21: Listing of 12-Lead ECG Findings

Treatment: Ambrisentan Low Dose

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

Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Safety

Listing 3.22: Listing of Endocrinology Assessments

Treatment: Ambrisentan Low Dose

Centre ID/ Subject ID	Age(y)/ Sex/ Race	Visit	Endocrinology Assessment Date/ Study Day	Assessment Type	Assessment Result
XXXXXX/ XXXXXX	XX/ Male/ XXXXXX	XXXXXXX	DDMMMYYYY/ XX	Testicular volume Right/Left (units)	XXX / XXX
				Male genital development	XXXXXXXXXX XXX
				Male pubic hair development	XXXXXXXXXX XXX
		XXXXXXX	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: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Listing 3.23: Listing of Pregnancy Results

Treatment: Ambrisentan Low Dose

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..					

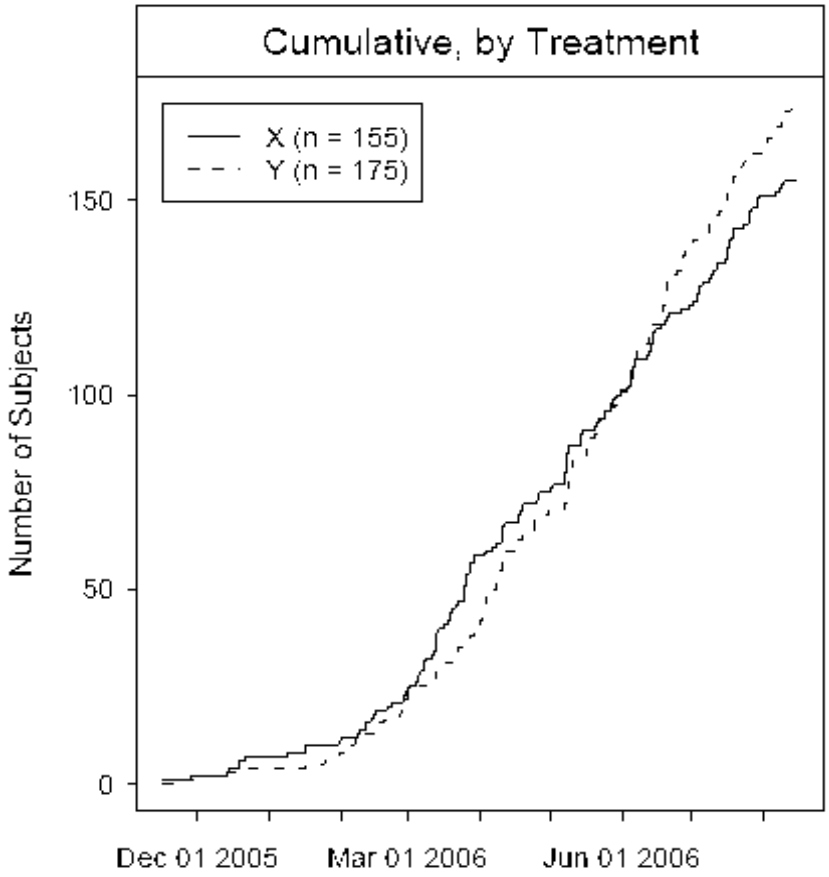
Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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

Protocol: AMB112529
Population: Intent-to-Treat

Figure 1.1: Summary of Subject Accrual

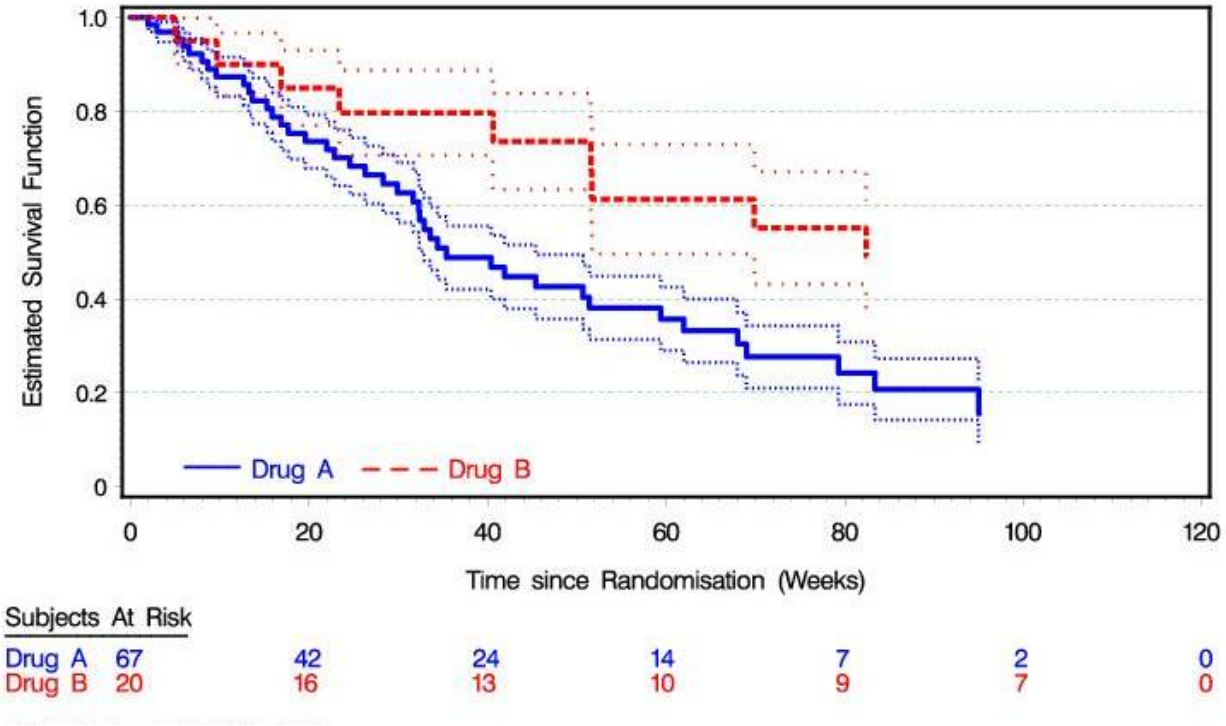


Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Change Labels: X -> Ambrisentan Low Dose, Y -> Ambrisentan High Dose.

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



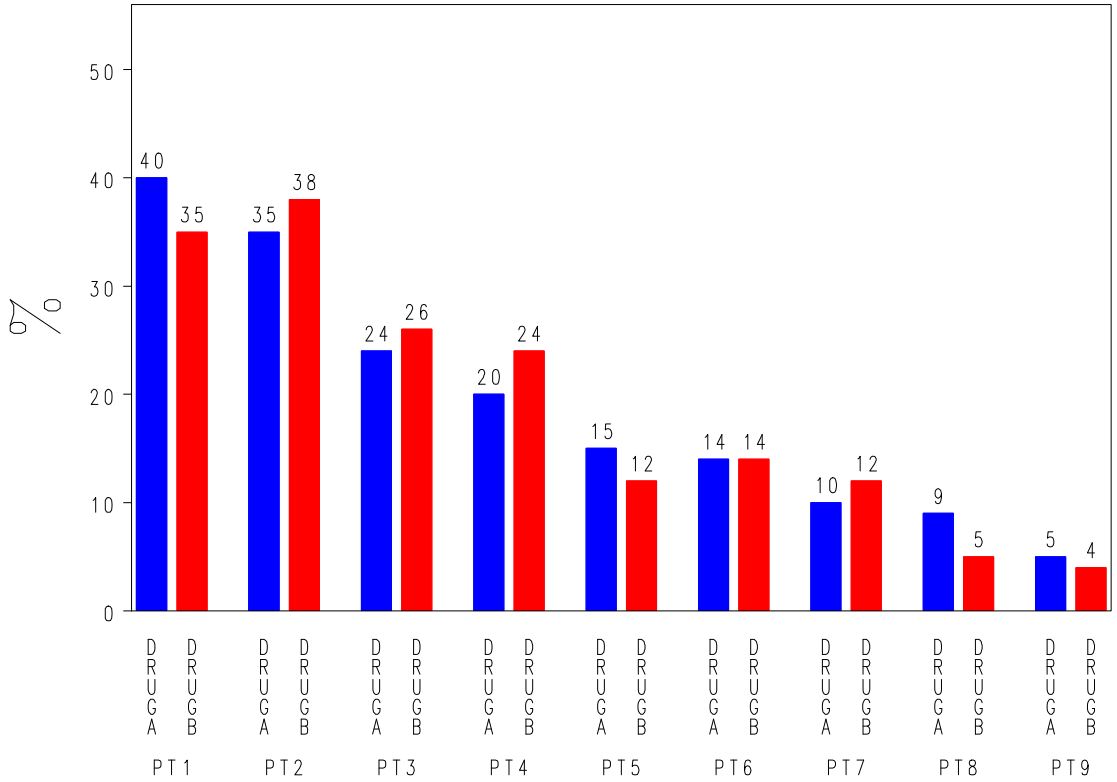
Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Change Labels: Drug A -> Ambrisentan Low Dose, Drug B -> Ambrisentan High Dose. Also present combined group. Annotate to display number of events in each group also.

Protocol: AMB112529
Population: Safety

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



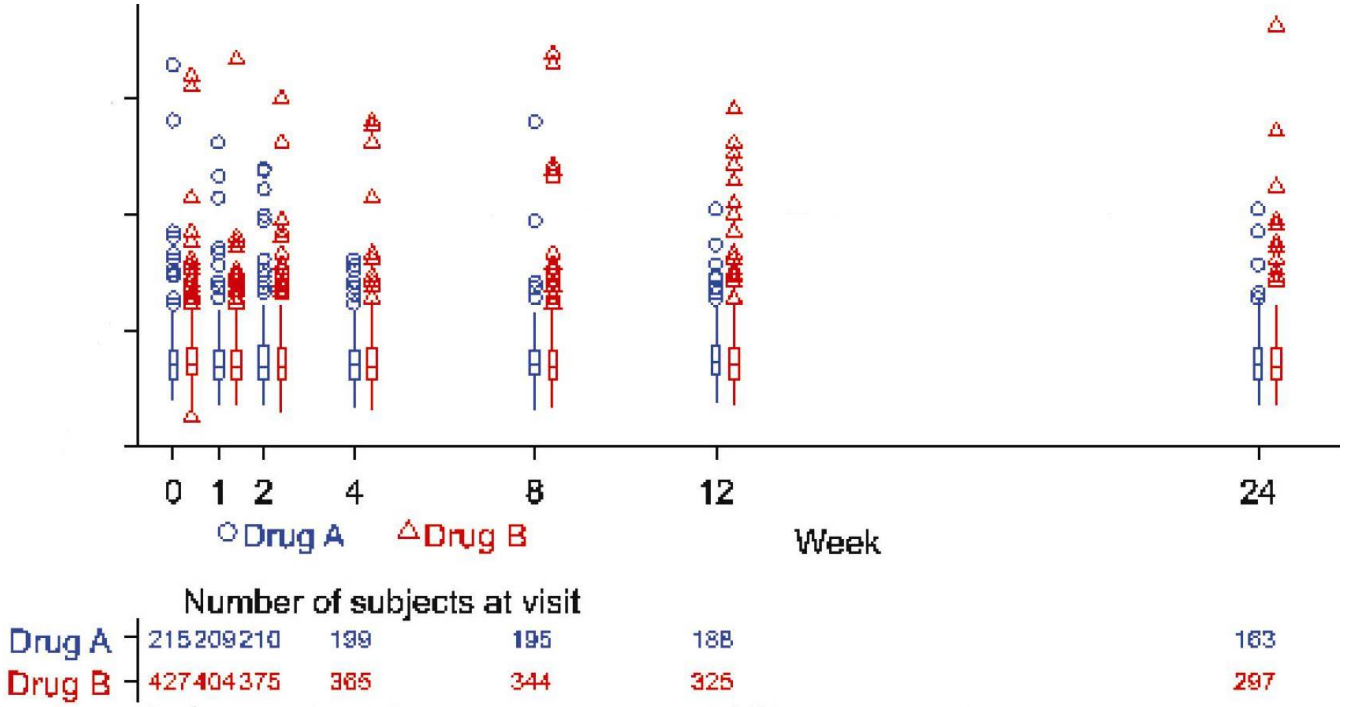
Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Change Labels: DrugA -> Ambrisentan Low Dose, DrugB -> Ambrisentan High Dose. Also present combined group. Continue for each preferred term.

Protocol: AMB112529
Population: Safety

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

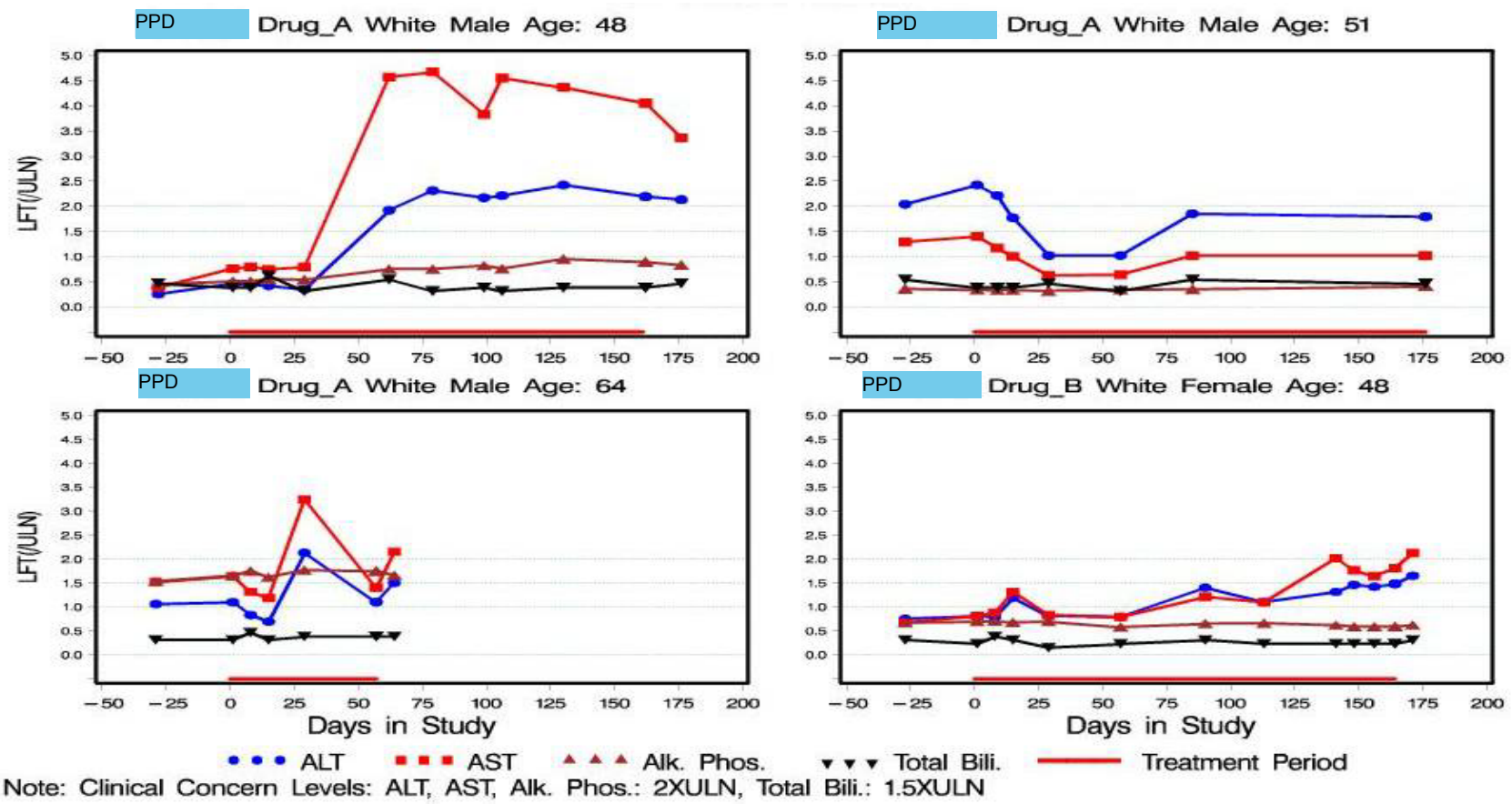


Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Change Labels: Drug A -> Ambrisentan Low Dose, Drug B -> Ambrisentan High Dose. Also present combined group. Label vertical axes with parameter name and units. Label horizontal axis with appropriate week 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 (Figure 2.6 and Figure 2.7).

Figure 3.8: Patient Profiles of Liver Function Tests



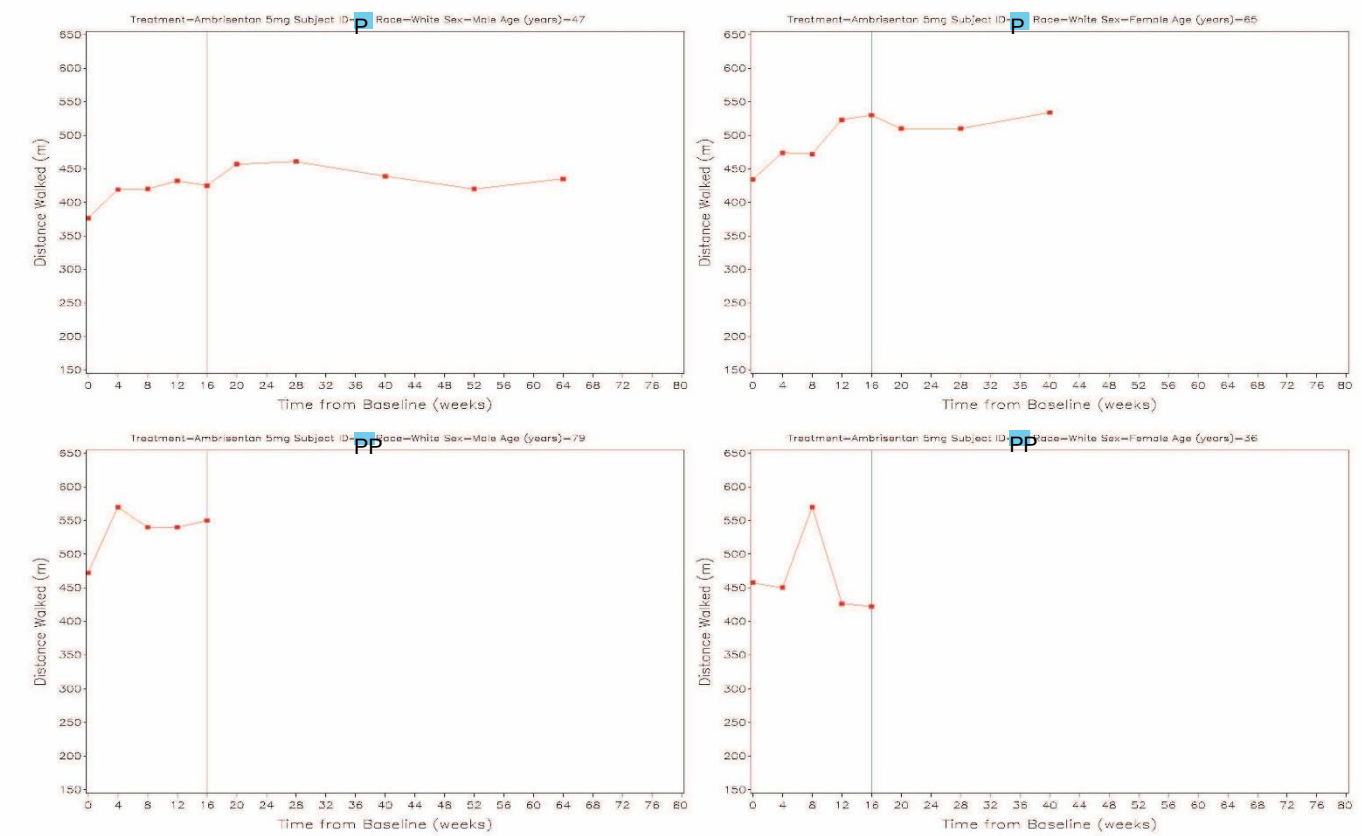
Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

Programming notes: Change Labels: Drug A -> Ambrisentan Low Dose, Drug B -> Ambrisentan High Dose. Also present combined group. Present parameters ALT, AST, Alk. Phos, Total Bilirubin. Present one patient per page only, not grid of 4 patients.

Protocol: AMB112529
Population: Safety

Figure 3.11: Line plots of Endocrinology Assessments by Subject



Note: Low dose, 2.5 mg (body weight >=20 kg and <35 kg); 5 mg (>= 35 kg).
High dose, 5 mg (body weight >=20 kg and <35 kg); 7.5 mg (>=35 kg and <50 kg); 10 mg (>= 50 kg).

PPD

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 2.8 (Japanese subset) plot echocardiogram parameters. For coded data, plot the numeric code and present codes on first page of the plot.

19. APPENDICES

19.1. 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) .