UW–Madison SDAC

Sample Closed Session DMC Report

November 6, 2012

Statistical Data Analysis Center

Department of Biostatistics and Medical Informatics
University of Wisconsin–Madison

Contents

List of Figures and Tables

Part I

Introduction

1 Introduction

The University of Wisconsin Statistical Data Analysis Center (SDAC), part of the Department of Biostatistics and Medical Informatics, works to promote statistical practice, applications, and research in the design and analysis of clinical trials. SDAC serves as an independent biostatistics group providing interim analyses of accumulating data from ongoing clinical trials for review by independent data monitoring committees (DMCs).

We have prepared this sample DMC report based on simulated trial data in order to provide an example of a DMC report that can be shared externally.

2 Overview of Trial Protocol and Procedures

The *Introduction* to a typical DMC report begins with a brief overview of the trial design, including the treatment arms, planned sample size, and randomization scheme. Primary and secondary endpoints of the trial are listed. Summaries of eligibility criteria, study procedures, dosing regimen, and visit schedule are provided.

In this sample report, simulated datasets are used to represent a multi-center randomized clinical trial with 775 subjects in two treatment arms. Data are presented at baseline and from follow-up visits occurring every three months.

3 Overview of Report

This report has been prepared as a representative sample of the style of report prepared by SDAC for the Data Monitoring Committee of an ongoing clinical trial. The report illustrates the typical structure of a DMC report and provides specific examples of common data displays and page layouts.

There are two versions of this report. This version, the *Closed Session Report*, includes comparisons by assigned treatment and, for a real trial, would be viewed only by the DMC, SDAC, or others determined by the DMC. The other version, the *Open Session Report*, summarizes the data for all subjects, aggregated across treatment groups, and is intended for use by the Sponsor and other parties involved in the conduct of the study at the discretion of the Sponsor or the DMC.

Purpose of Report

The purpose of a DMC report is to summarize enrollment, selected baseline characteristics, adverse events, laboratory assessments, other safety measures and study endpoints as of the date of data transfer to SDAC. Modifications in study design and conduct may be recommended by the DMC if there are problems in these areas.

Report Production

SAS[1] and R[2] were used to perform the analyses and create the graphics and tables for the report. The document was typeset with LaTeX 2_ε.[3]

List of Abbreviations

ACE	Angiotensin-Converting Enzyme
AE	Adverse Event
BMI	Body Mass Index
CABG	Coronary Artery Bypass (Graft) Surgery
CHD	Coronary Heart Disease
CRF	Case Report Form
DMC	Data Monitoring Committee
ECG	Electrocardiogram
HDL	High-density Lipoprotein
HF	Heart Failure
IP	Investigational Product
IVRS	Interactive Voice Response System
LDL	Low-density Lipoprotein
LFT	Liver Function Test
LLN	Lower Limit of Normal
LVEF	Left Ventricular Ejection Fraction
MedDRA	Medical Dictionary for Regulatory Activities
MI	Myocardial Infarction
NYHA	New York Heart Association
SAE	Serious Adverse Event
SDAC	Statistical Data Analysis Center
ULN	Upper Limit of Normal

Abbreviated Report Outline

This sample report contains the following sections and chapters:

- Introduction
- Main Material
  - Accrual and Study Status
  - Baseline Characteristics
  - Adverse Events

[1] SAS Institute Inc.

[2] R Development Core Team (2005). *R: A language and environment for statistical computing*. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0. URL `http://www.R-project.org`.

[3] LaTeX3 Project Team (2001). *LaTeX 2_ε for Authors*. URL `http://www.latex-project.org`.

  - Central Laboratory Measures
  - Other Follow-up and Safety Measures
  - Study Endpoints
- Supporting Material

Sources of Data Included in Report

All data presented in this sample report have been randomly generated and do not reflect the results of actual research studies past or present.

In an actual DMC report, this section would describe the data files received from one or more sources (e.g., CRF datasets from the clinical study database, SAE listings from a safety database, enrollment files from an IVRS, etc.). The type of file(s) obtained from each source, and the method and date of transfer, would be noted.

4 Report Structure

Treatment Labels

In the *Closed Session Report*, treatment groups are identified by the codes “A” and “B”. The assignment of codes to treatment arms would be provided verbally to DMC members upon request. Codes are consistent across reports throughout a trial.

P-values

P-values for treatment comparisons in this report appear as “p.A.B”. These *p*-values should be viewed as screening tools *only* because no adjustment has been made for multiple tests performed. Given the large number of tests to be considered, it would be expected that a number of *p*-values will appear statistically significant (< 0.05) simply by chance.

P-values for continuous or ordered categorical data are computed using the nonparametric Kruskal-Wallis test. This test is appropriate for data with nonnormal distributions and has power near that of the Student’s *t*-test when the data are normal. Pearson’s chi-square test is used for dichotomous (e.g., gender) and unordered (e.g., race) categorical data. The log-rank test is used to obtain *p*-values for time-to-event endpoints.

Graphical Conventions

The primary mode of presentation in this report is graphical. The visual presentation allows the reviewer to easily examine the distribution of the data items and characterize the study population(s) at a glance. Treatment comparisons, both at baseline and over time, are easily examined, as are

time-related trends in the data. The majority of figures present categorical data as bar charts, continuous data represented as boxplots, or time-to-event data presented as Kaplan-Meier estimates of survival curves.

Bar charts. Bar charts indicate for categorical data the number or percent of subjects by category. A simple bar chart such as the one for gender in Figure DEMO–1 on page 22, is used to display a single categorical variable with mutually exclusive categories. Bar charts of related dichotomous variables are sometimes grouped together to form a multiple bar chart, as in the display of baseline medical conditions in Figure MDHX–1 on page 23. A more detailed bar chart is used to display categorical data which has additional ordered subdivisions, as in the display of liver function test elevations in Figure LFTABN–1 on page 36.

Boxplots. Boxplots indicate the distribution of continuous data based on percentiles (for example, the display for age in Figure DEMO–1 on page 22). The top and bottom edges of the box represent the 25th and 75th percentiles of the data. The 5th and 95th percentiles are represented by the "whiskers" extending from the top and bottom of the box. The plotting symbol inside the box represents the median of the data.

Kaplan-Meier plot. Dichotomous response variables such as death for subjects with variable lengths of follow-up are often displayed as Kaplan-Meier (product-limit) "survival" curves across time. These curves indicate the cumulative probability of experiencing an event, or of remaining event-free, as a function of time since randomization (for example, see Figure SAE–1 on page 27). The total number of events appear on the plot, as do the numbers of subjects at risk (event-free and uncensored) at various points of follow-up.

Relative risk graphic. A relative risk graphic, for example, Figure ENDPT–2 on page 55, is used to efficiently summarize subgroup analyses of a treatment group difference of a time-to-event response variable. This graphic displays point estimates (black box) and nominal 95% confidence intervals (solid line) for the relative risk (hazard ratio) of an event in one treatment group compared to another treatment group. Estimates are obtained using the Cox proportional hazards model.

Change from baseline. For variables which are measured at several fixed time points, change from baseline is usually provided below the figure for the observed data. For continuous variables, change can be given either in the original units or as percent change (see Figure VIT–3 on page 48). For dichotomous variables, change from baseline can be indicated by displaying follow-up data separately for each baseline group.

Annotations. Figures indicate the number of subjects used for the analysis, either directly under the corresponding portion of the plot, or labeled as "nA" or "nB" at the bottom of the panel. In the *Closed Session Report*, *p*-values corresponding to the comparisons of the treatment groups are included, where applicable. Figures are also annotated with the data source.

Figure identifier. In the top right corner of each page of figures will be a mnemonic figure identifier. These identifiers, which are listed alphabetically in the index at the back of the report, normally would not change over the course of the study and hence can be useful for locating corresponding figures in future or past reports.

5 Notes on Chapter Contents

This section of a report *Introduction* contains additional details about analysis conventions and the contents of specific chapters.

General Conventions

This sample report is based on simulated data. An actual DMC report includes data from all randomized subjects. This section would include a brief description of data-handling and analysis conventions used in the report: e.g., how the sample sizes or demoninators were determined for various chapters (all randomized subjects, or all subjects with a particular data element available), how a “Baseline” record was identified for display if multiple records were present, and censoring conventions for time-to-event analysis.

Interim analyses are frequently based on incomplete and inconsistent data. The assumptions, computations and conventions designed to handle the data problems encountered during preparation of the report would be described in this section, or in the more detailed chapter notes below.

Accrual and Study Status

This chapter begins with Figure ACCR–1 on page 12, a display of subject accrual over time, based on a simulated enrollment dataset. Displays of the number of clinical centers enrolling subjects over time (based on date of first subject enrollment) are often included in this chapter. For multinational studies, accrual by country, continent, or other geographic region could be displayed.

Information on data availability or follow-up status of enrolled subjects, as in Figures STAT–1 on page 17 through STAT–4 on page 20, is also typically presented. These graphics can be help assess the disposition of study subjects as well as the timeliness of data collection and entry.

Baseline Characteristics

A typical report displays treatment group comparisons for a large number of baseline variables including demographics, medical history, vital signs, and other trial- or disease-specific factors. In this sample report, selected variables are presented based on simulated data, beginning with Figure DEMO–1 on page 22.

Adverse Events

This chapter contains some typical displays of adverse event (AE) data, based on simulated datasets. It begins with a summary of serious adverse events (SAEs) in Figure SAE–1 on page 27. An SAE is an event which is fatal, is life-threatening, requires or prolongs a hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or is considered by the investigator to be a significant medical hazard.

In many clinical trials there is a separate mechanism for expedited reporting and data management of SAEs for regulatory purposes, with a subsequent reporting of the event on a study case report form. Because of the difficulty of merging data from different sources, information obtained from the SAE database is usually be displayed in a separate section. Information on the occurrence of SAEs is generally an important component of interim monitoring reports because of its greater timeliness and clinical significance.

Figures in this chapter provide summaries of SAEs, and of all AEs, overall and according to coded MedDRA system organ class terms and preferred terms. An actual DMC report might also include displays of specific event terms of interest in a trial, AEs considered to be related to investigational product (IP), or other analyses as appropriate.

Central Laboratory Measures

This chapter summarizes selected laboratory results recorded during screening and follow-up for randomized subjects. Typically in a clinical trial, blood samples are collected for hematology and chemistry assessments by a central laboratory at baseline and at specified times during follow-up. Results from any unscheduled or repeated lab tests are also recorded. Upper (ULN) and lower (LLN) limits of normal for each test, in some cases based on sex and/or age of the subject, are generally included in the laboratory data transferred to SDAC.

Figures LFTABN–1 on page 36, CHEMABN–1 on page 41 and HEMABN–1 on page 43 display the percentage of subjects with any post-randomization abnormal result for each measure. The denominators for percentages for each measure indicate the numbers of subjects with any post-randomization test results available for that measure.

The remaining figures in this chapter show measurements of selected tests by scheduled visit. Displays include absolute change from baseline and the percent of subjects with measurements above the ULN and/or below the LLN, as applicable, at each visit.

Other Follow-up and Safety Measures

Subject follow-up data may be collected by logging specified types of events (e.g., adverse events, hospitalizations, changes in dosing or concomitant medication), or by assessing subject status at designated visits or time points over the course of the follow-up period. The simulated datasets used to produce this sample report contain records for follow-up visits at 3, 6, 9 and 12 months after randomization.

Follow-up information can be displayed with bars representing the percent of subjects under observation who meet certain criteria at specified timepoints or with a boxplot to illustrate the distribution of continuous measures. Change from baseline is often presented on the same page, as displayed in Figure VIT–1 on page 46. For other types of data, such as concomitant medication in Figure CONMEDS–1 on page 52, the report summarizes information collected over the entire period of observation.

Study Endpoints

The Kaplan-Meier plot in Figure ENDPT–1 on page 54 displays all-cause mortality based on a simulated endpoint dataset. A relative risk graphic is also displayed, showing the treatment effect (hazard ratio) overall and for various baseline subgroups. Estimates of the hazard ratios and 95% confidence intervals were obtained using the Cox proportional hazards model.

A more extensive report would include analyses of secondary and other endpoints of interest. It might also contain Kaplan-Meier plots for subgroups of particular interest, displays of event classification resulting from an adjudication process, interim monitoring boundaries, and other items as appropriate for the trial.

Supporting Material

Part III, *Supporting Material*, contains back-up tables of univariate statistics and detailed frequency counts for the graphical displays of the previous chapters. These tables are cross-referenced to and from the corresponding graphical pages.

Ancillary Material

Additional information relevant to the interpretation of a report can be included as *Ancillary Material*. Early in a trial, copies of key study forms may be included to illustrate the source of certain data items or the data collection process in general. Detailed listings of subject accrual at each clinical center, reported serious adverse events, or other trial data may also be provided.

6 List of Key Participants

In an actual report, this final section of the *Introduction* would contain contact information for key study participants, including members of the Data Monitoring Committee, Sponsor personnel, SDAC, and others as appropriate. In this sample report, we provide contact information for SDAC.

Statistical Data Analysis Center (SDAC)

Department of Biostatistics and Medical Informatics
University of Wisconsin–Madison
WARF Office Building
610 Walnut Street
Madison, WI 53726–2397
Fax: (608) 263-0415
www.biostat.wisc.edu

Marian Fisher, PhD	(608) 263-7390
Director	fisher@biostat.wisc.edu
Gretchen Poulsen	(608) 265-6702
Program Manager	poulsen@biostat.wisc.edu

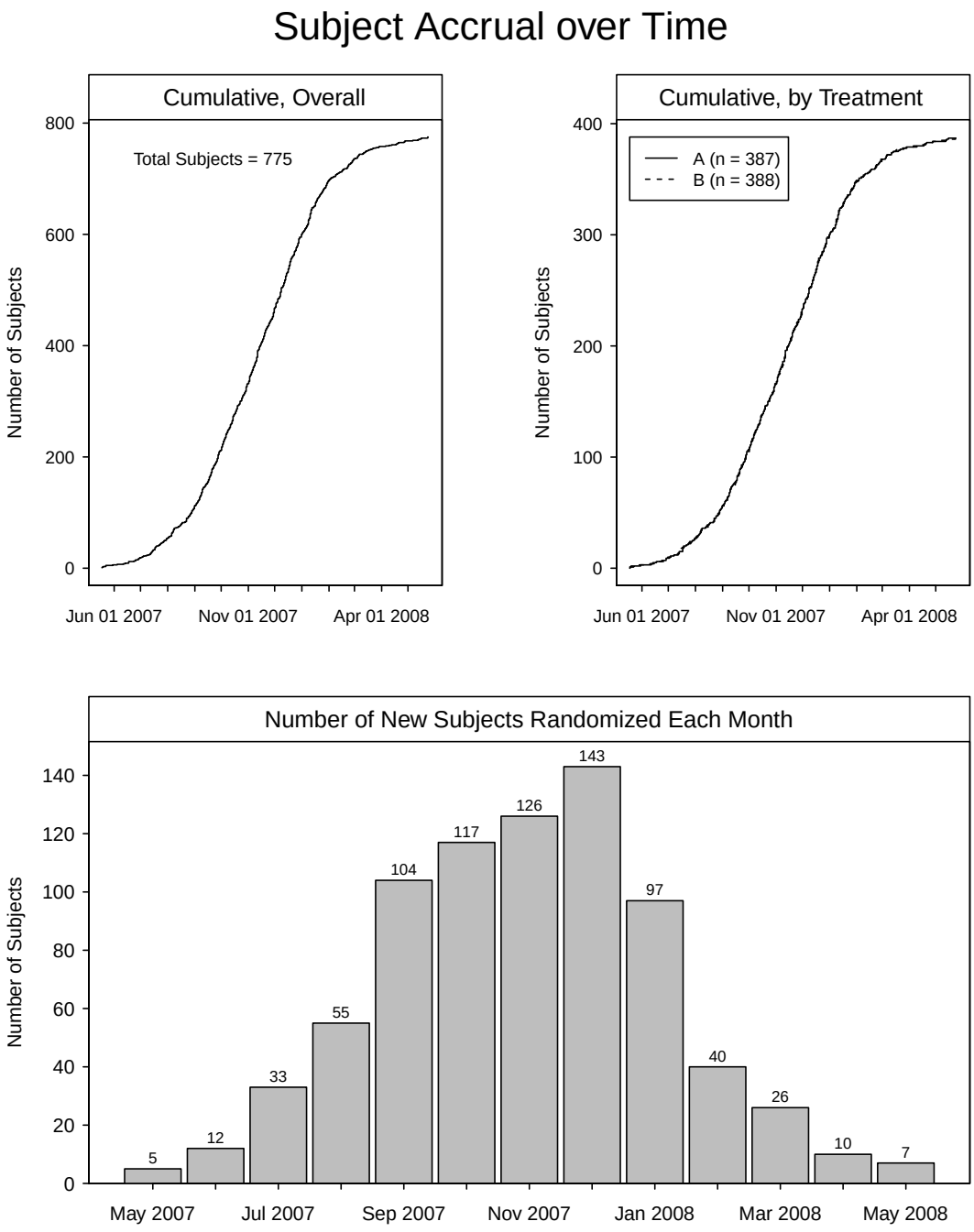
Part II

Main Material

Chapter 1

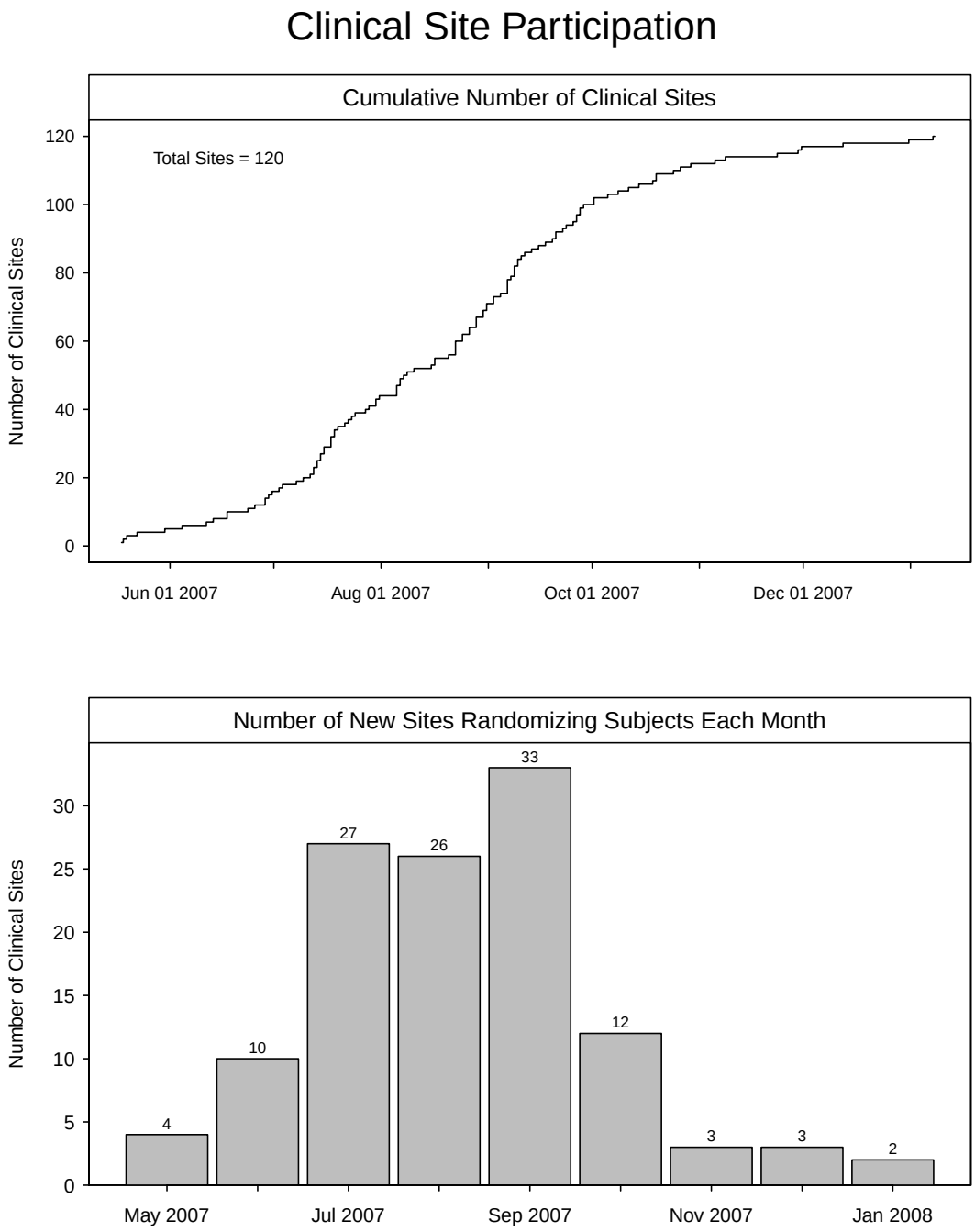
Accrual and Study Status

Figure ACCR–1



Information from a simulated enrollment dataset. The first subject was randomized on May 18, 2007.

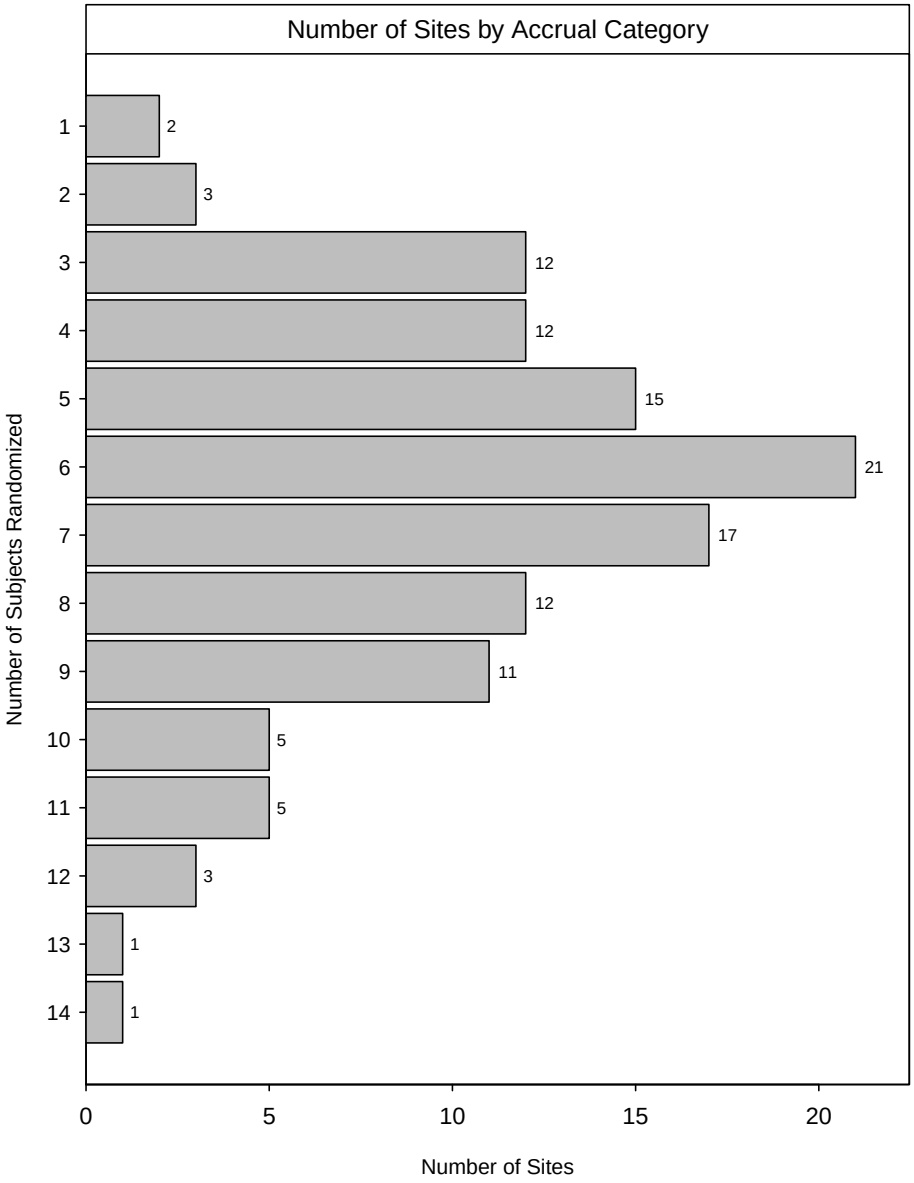
Figure ACCR–2



Information from a simulated enrollment dataset. Clinical sites are included if they have randomized at least one subject.

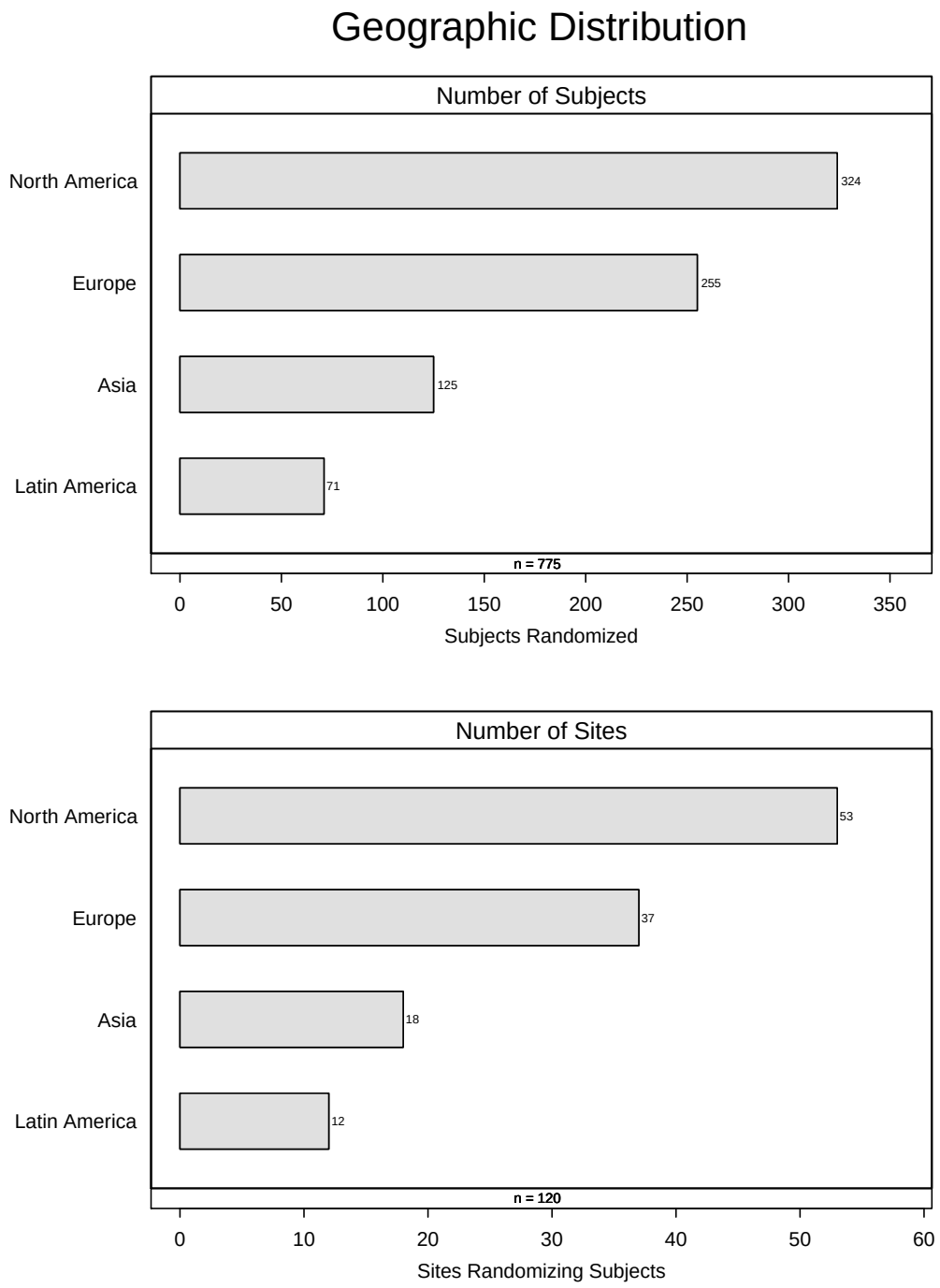
Figure ACCR–3

Distribution of Subjects Across Clinical Sites



Information from a simulated enrollment dataset.

Figure ACCR–4



Information from a simulated enrollment dataset.

See Table Set ACCR–4 on page 57.

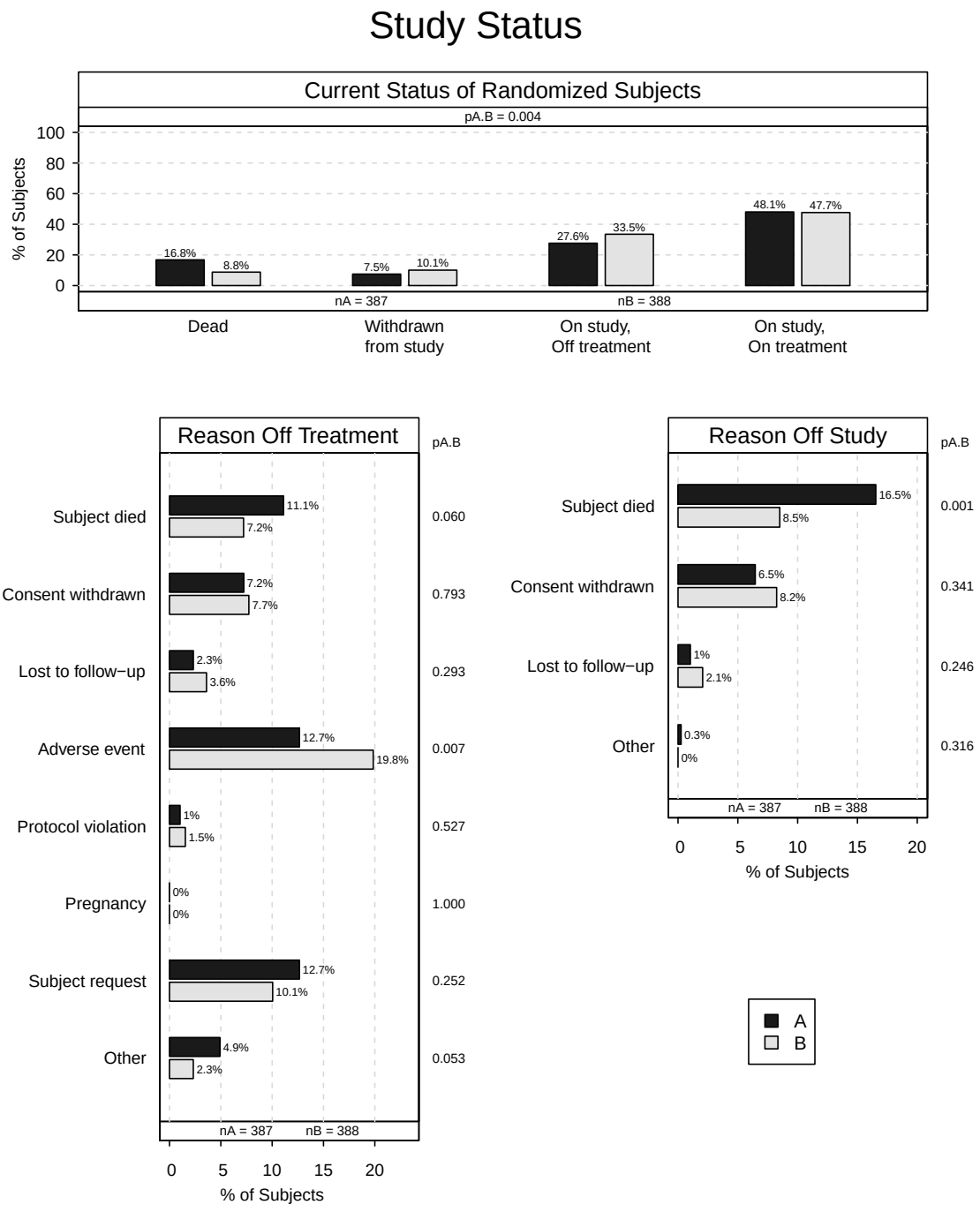
Figure ACCR–5

Country Participation

Randomization by Region and Country		Date First Subject Randomized	Most Recent Subject Randomized	Number of Sites Randomizing Subjects	Number of Subjects Randomized	Subjects Per Site (mean)
North America	**United States**	May 18, 2007	May 25, 2008	38	245	6.4
	Canada	May 20, 2007	Apr 14, 2008	15	79	5.3
	*** REGION TOTAL ***	May 18, 2007	May 25, 2008	53	324	6.2
Asia						
	Taiwan	May 21, 2007	Feb 17, 2008	3	19	6.3
	Japan	Jun 1, 2007	Mar 2, 2008	5	36	7.2
	Hong Kong	Jun 6, 2007	Feb 27, 2008	3	21	7.0
	Korea	Jun 30, 2007	May 25, 2008	4	29	7.3
	Philippines	Sep 10, 2007	Feb 24, 2008	3	20	6.7
	*** REGION TOTAL ***	May 21, 2007	May 25, 2008	18	125	7.0
Europe						
	Sweden	Jun 27, 2007	Mar 6, 2008	3	17	5.7
	United Kingdom	Jul 1, 2007	Apr 7, 2008	10	68	6.8
	Spain	Jul 2, 2007	Mar 18, 2008	4	25	6.3
	Portugal	Jul 16, 2007	Feb 4, 2008	3	28	9.3
	Italy	Jul 17, 2007	Mar 24, 2008	3	25	8.3
	France	Jul 19, 2007	Mar 23, 2008	3	15	5.0
	Finland	Jul 21, 2007	Mar 15, 2008	3	22	7.3
	Norway	Aug 1, 2007	Apr 20, 2008	3	16	5.3
	Germany	Aug 7, 2007	May 15, 2008	5	39	7.8
	*** REGION TOTAL ***	Jun 27, 2007	May 15, 2008	37	255	7.1
Latin America						
	Peru	Jul 4, 2007	May 18, 2008	3	13	4.3
	Brazil	Aug 1, 2007	Mar 8, 2008	3	17	5.7
	Mexico	Aug 2, 2007	Feb 24, 2008	3	25	8.3
	Chile	Aug 9, 2007	Apr 22, 2008	3	16	5.3
	*** REGION TOTAL ***	Jul 4, 2007	May 18, 2008	12	71	6.3
**** OVERALL ****		May 18, 2007	May 25, 2008	120	775	6.6

Information from a simulated enrollment dataset. The order of regions and countries in the table is determined by the date of first subject entry.

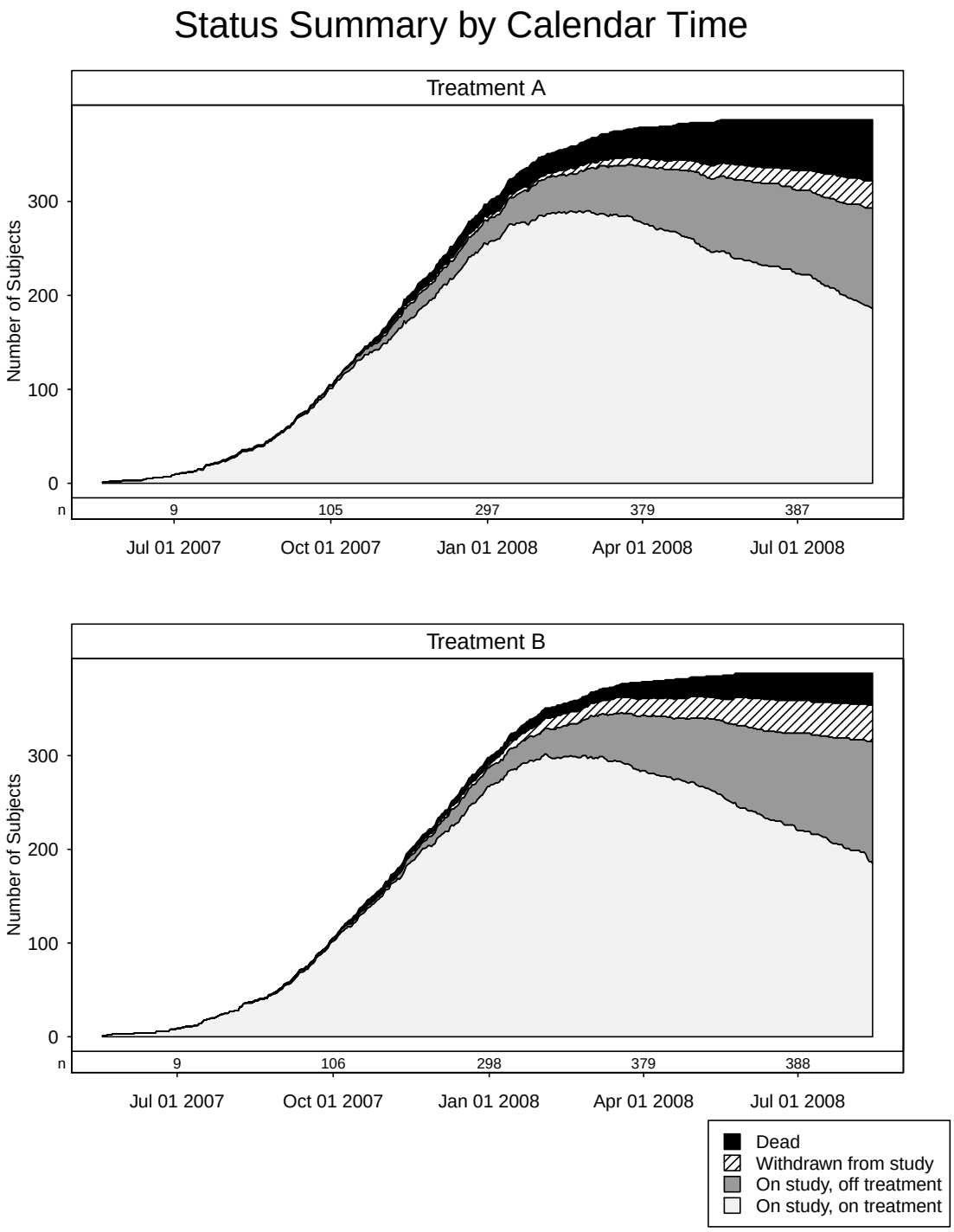
Figure STAT–1



Information from a simulated enrollment dataset. In the upper panel, subjects are assigned to the first applicable category. For data presented in the lower panels, investigators are asked to choose a single reason for each of withdrawal from treatment and withdrawal from study. Death information is taken from all available sources.

See Table Set STAT–1 on page 57.

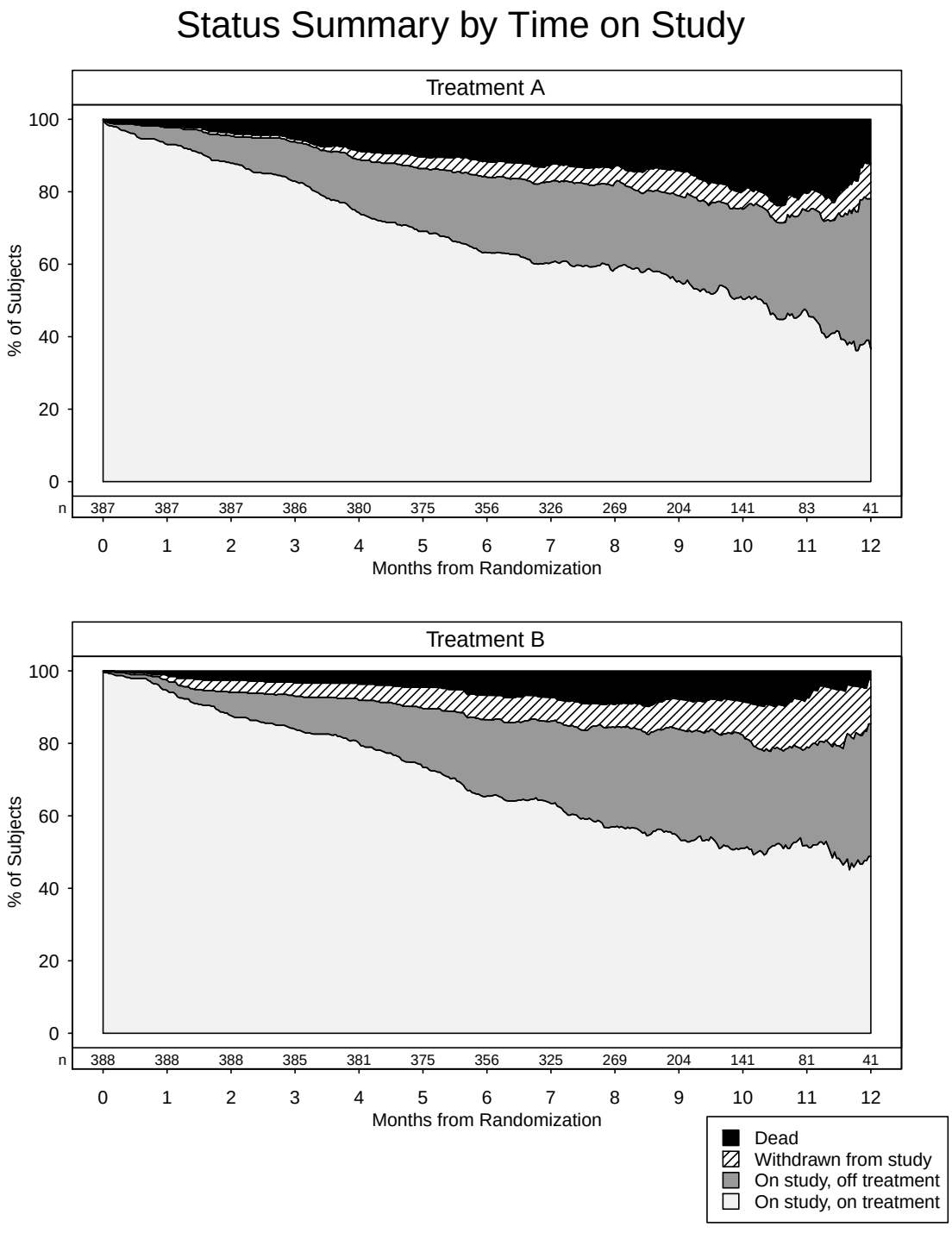
Figure STAT–2



Information from a simulated enrollment dataset. These plots summarize the study status of randomized subjects by calendar time. The sample sizes displayed are the number of subjects randomized as of a given date.

See Table Set STAT–2 on page 58.

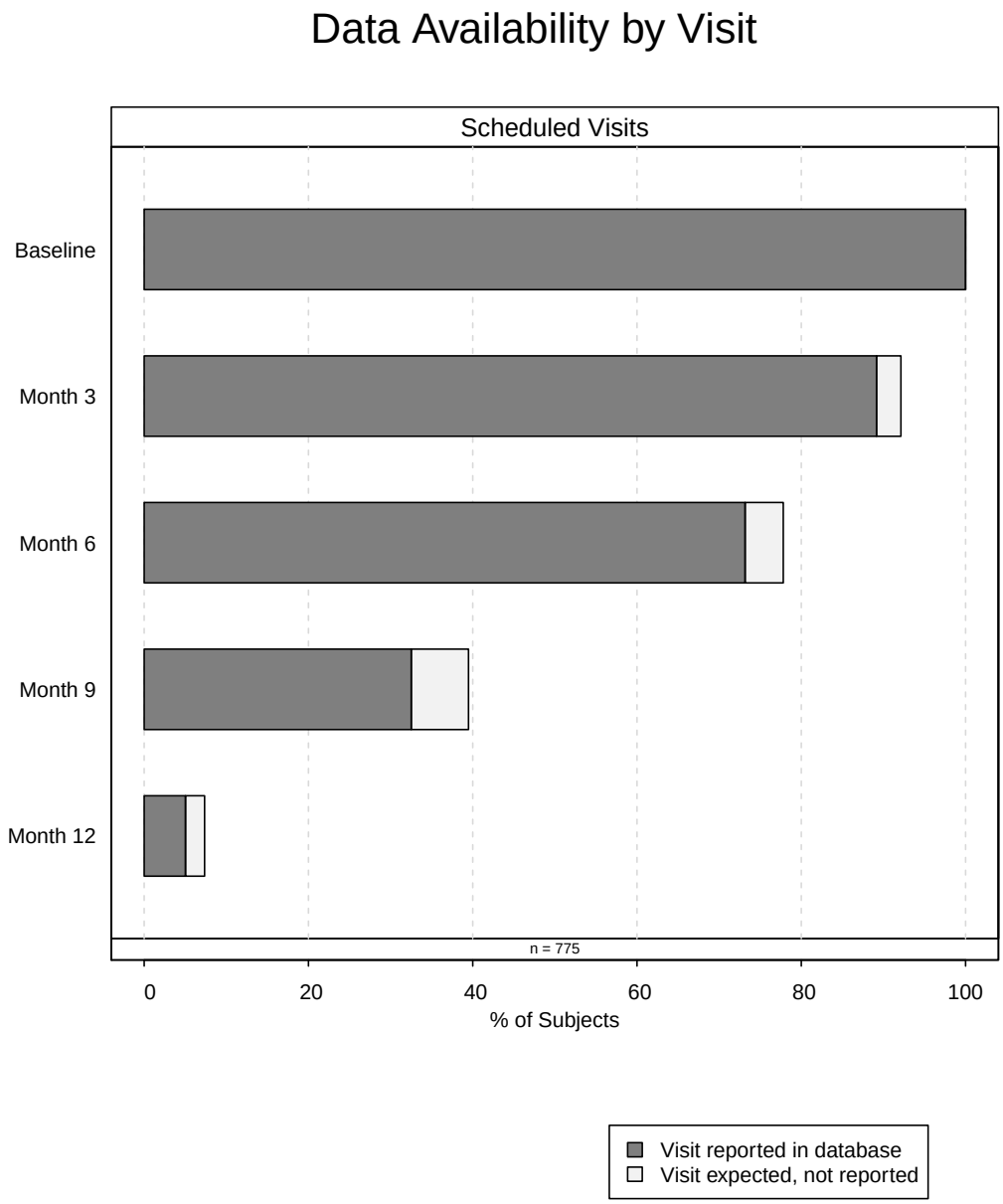
Figure STAT–3



Information from a simulated enrollment dataset. These plots summarize the study status of randomized subjects by day relative to randomization. In this display, a “month” is considered to be 30 days. The denominators for percentages are the number of subjects being followed at a given time.

See Table Set STAT–3 on page 59.

Figure STAT–4



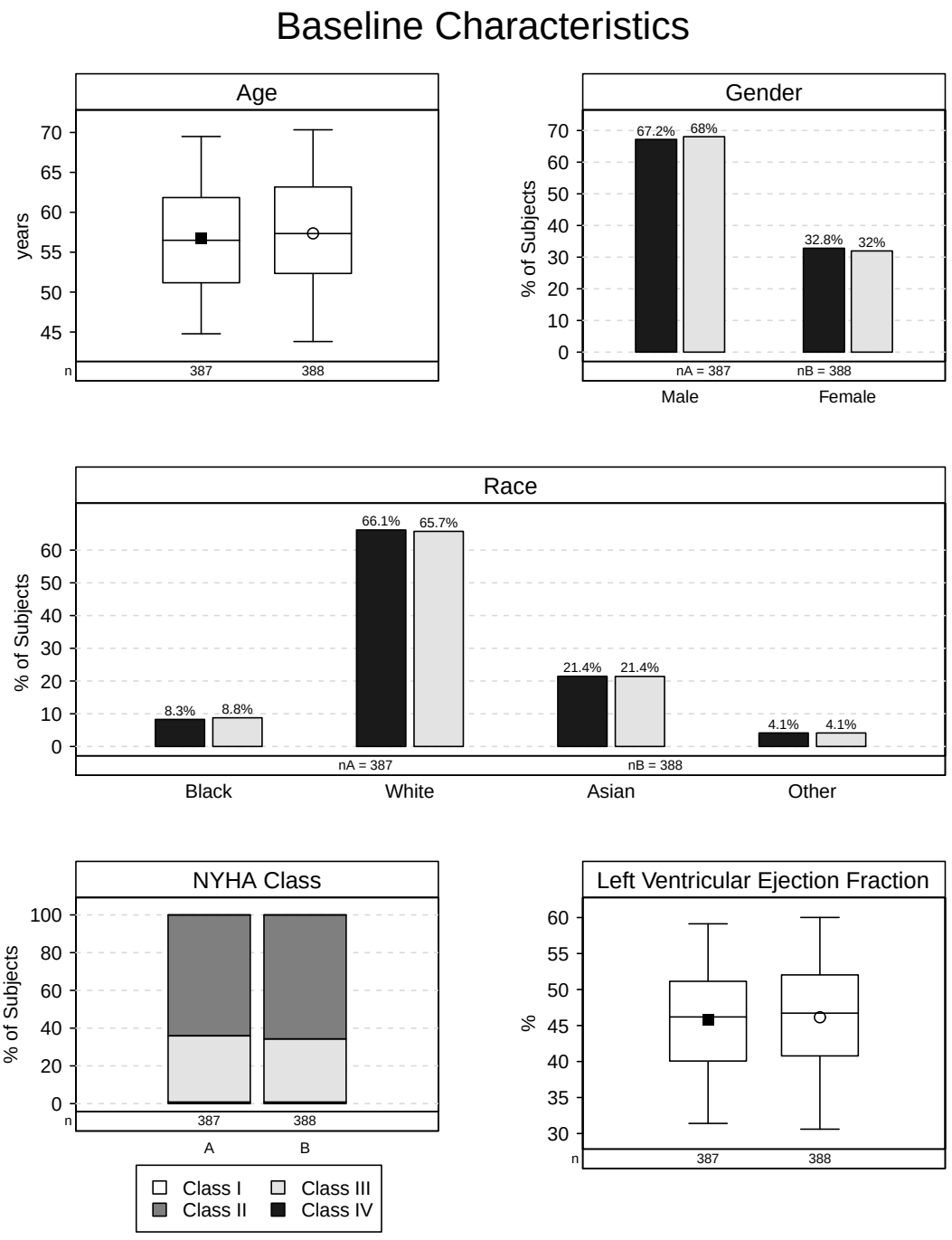
Information from simulated enrollment, laboratory and vital signs datasets. A scheduled visit is “reported” if a record of it exists in the laboratory or vital signs datasets for a given subject. A visit is “expected, not reported” if the anticipated visit date (randomization date plus an appropriate time interval, e.g., 30 days) is at least 14 days earlier than the data cut-off date, but there is not a record in the laboratory or vital signs datasets.

See Table Set STAT–4 on page 60.

Chapter 2

Baseline Characteristics

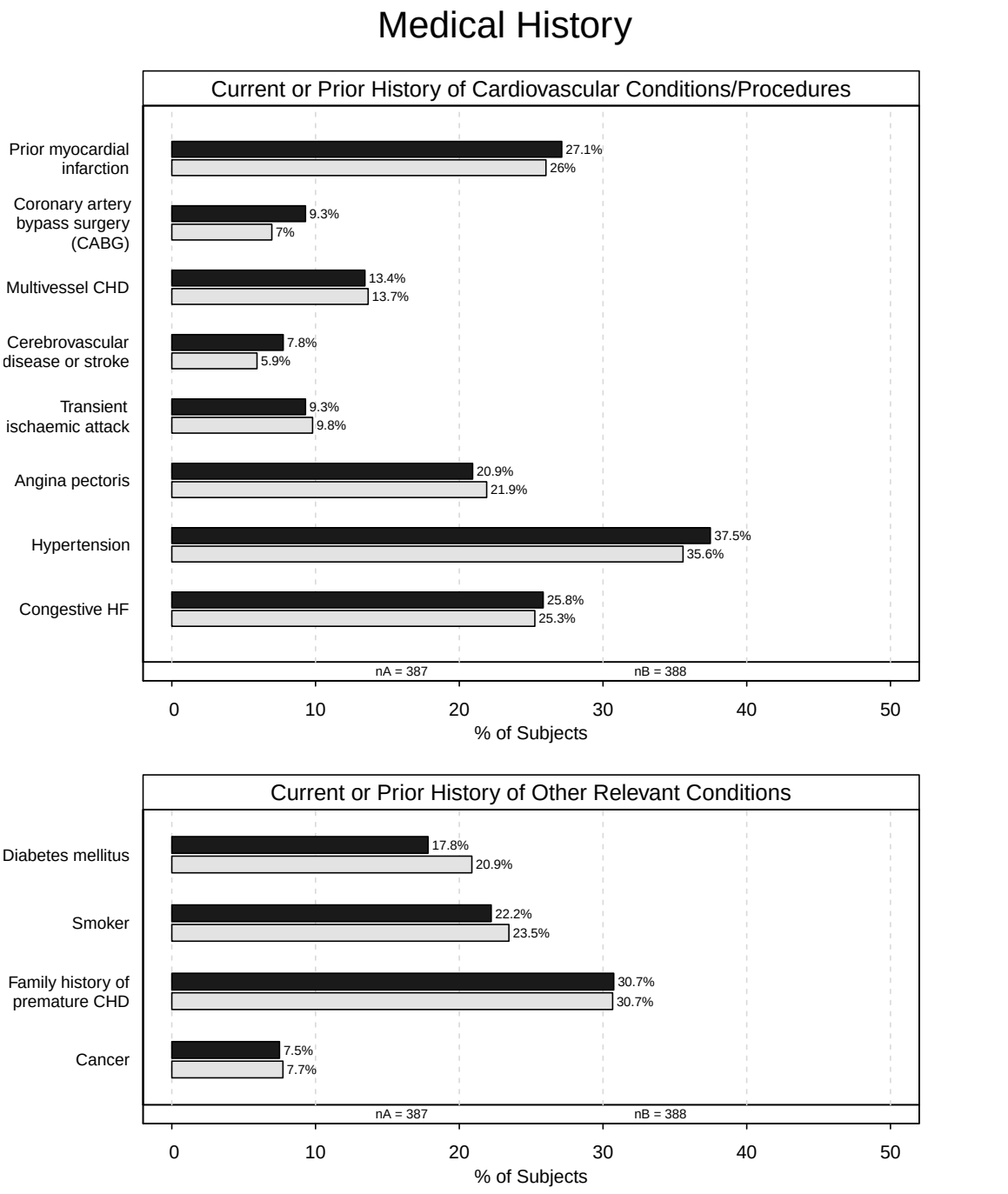
Figure DEMO–1



Information from a simulated baseline dataset. For data on race, presented in the middle panel, subjects were asked to specify a single race category.

See Table Set DEMO–1 on page 61.

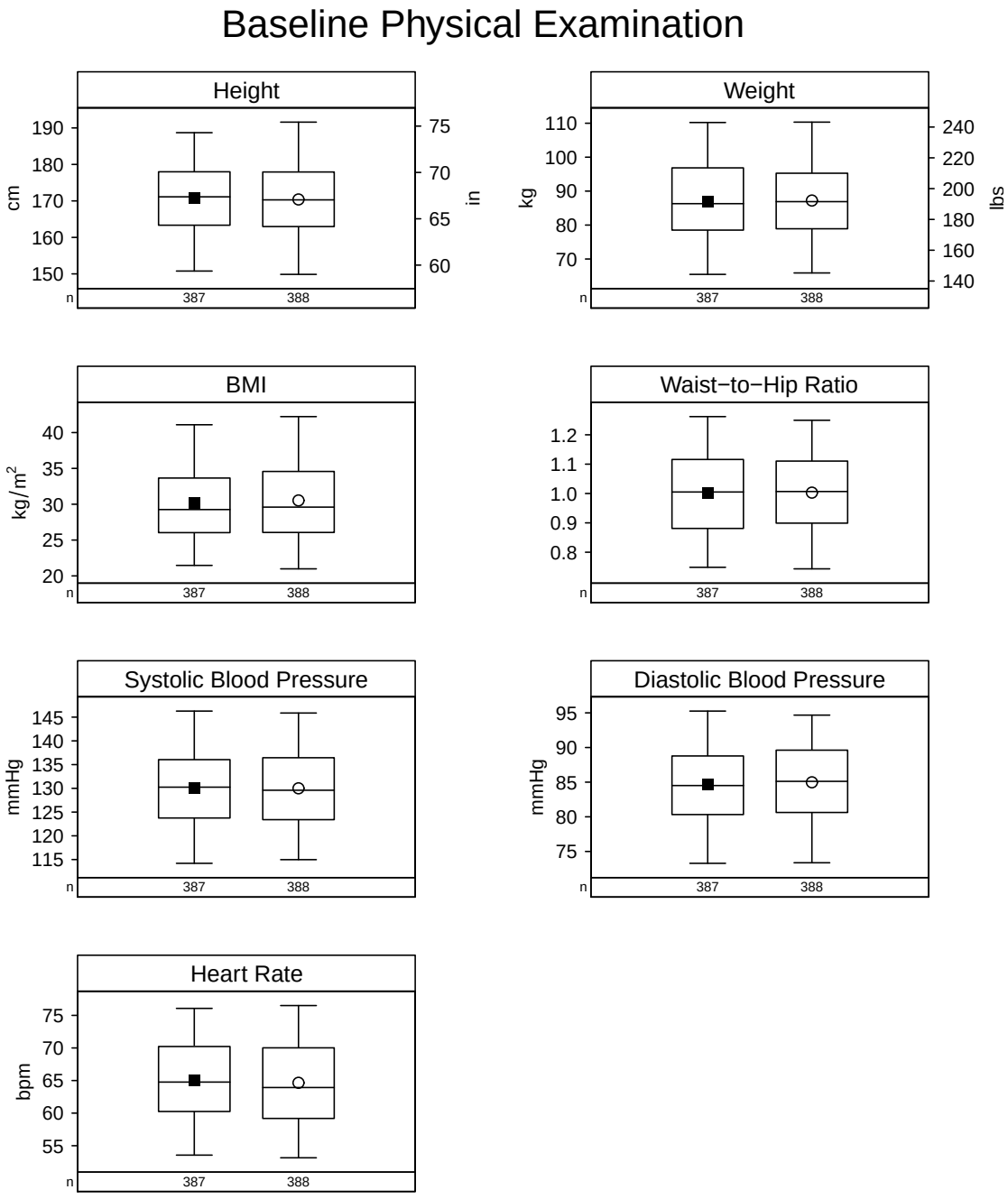
Figure MDHX–1



Information from a simulated baseline dataset.

See Table Set MDHX–1 on page 62.

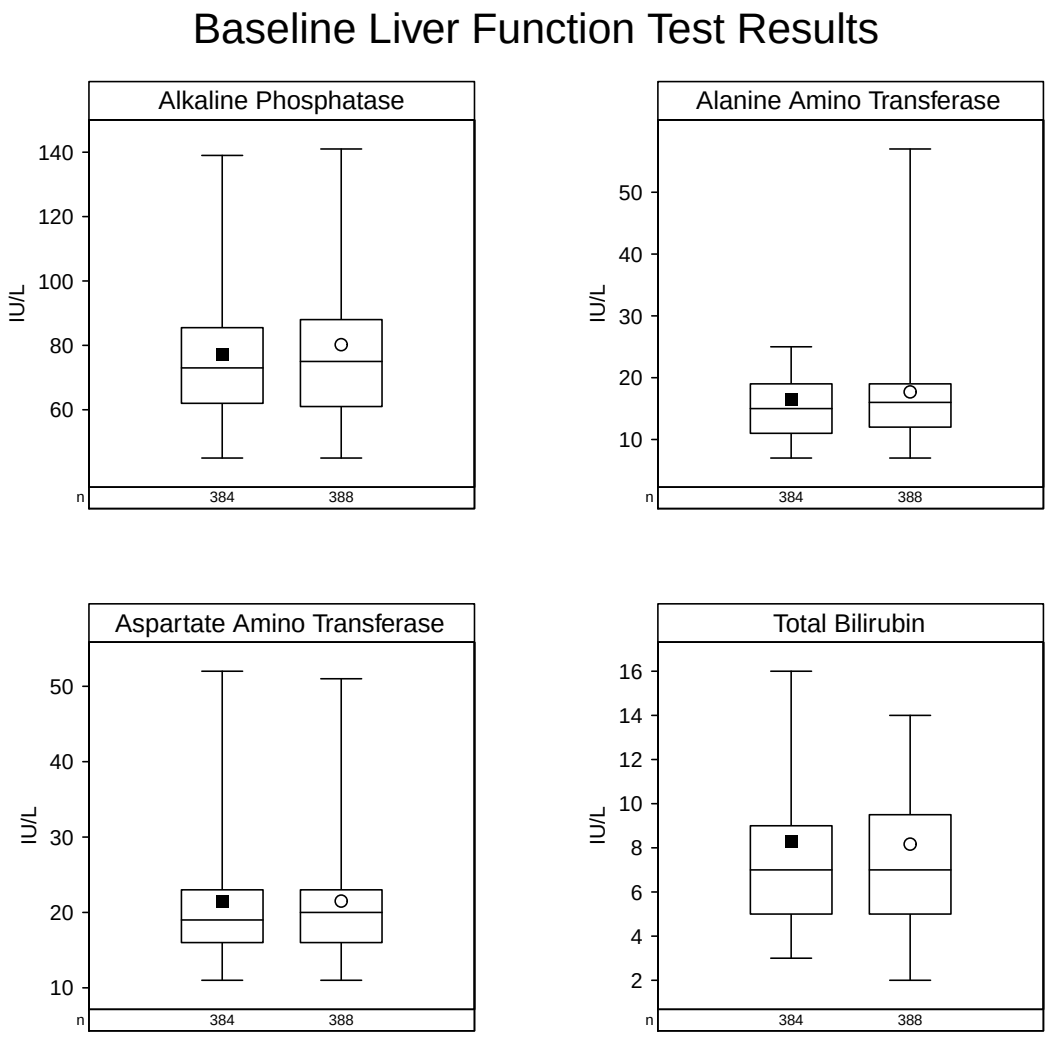
Figure VITB–1



Information from a simulated vital signs dataset. A physical examination is performed at the screening visit and vital signs are recorded at both the screening and randomization visits. For vital sign measurements, the baseline value for each item is defined as the value recorded at the randomization visit if available, otherwise the screening value is used.

See Table Set VITB–1 on page 63.

Figure LABB–1



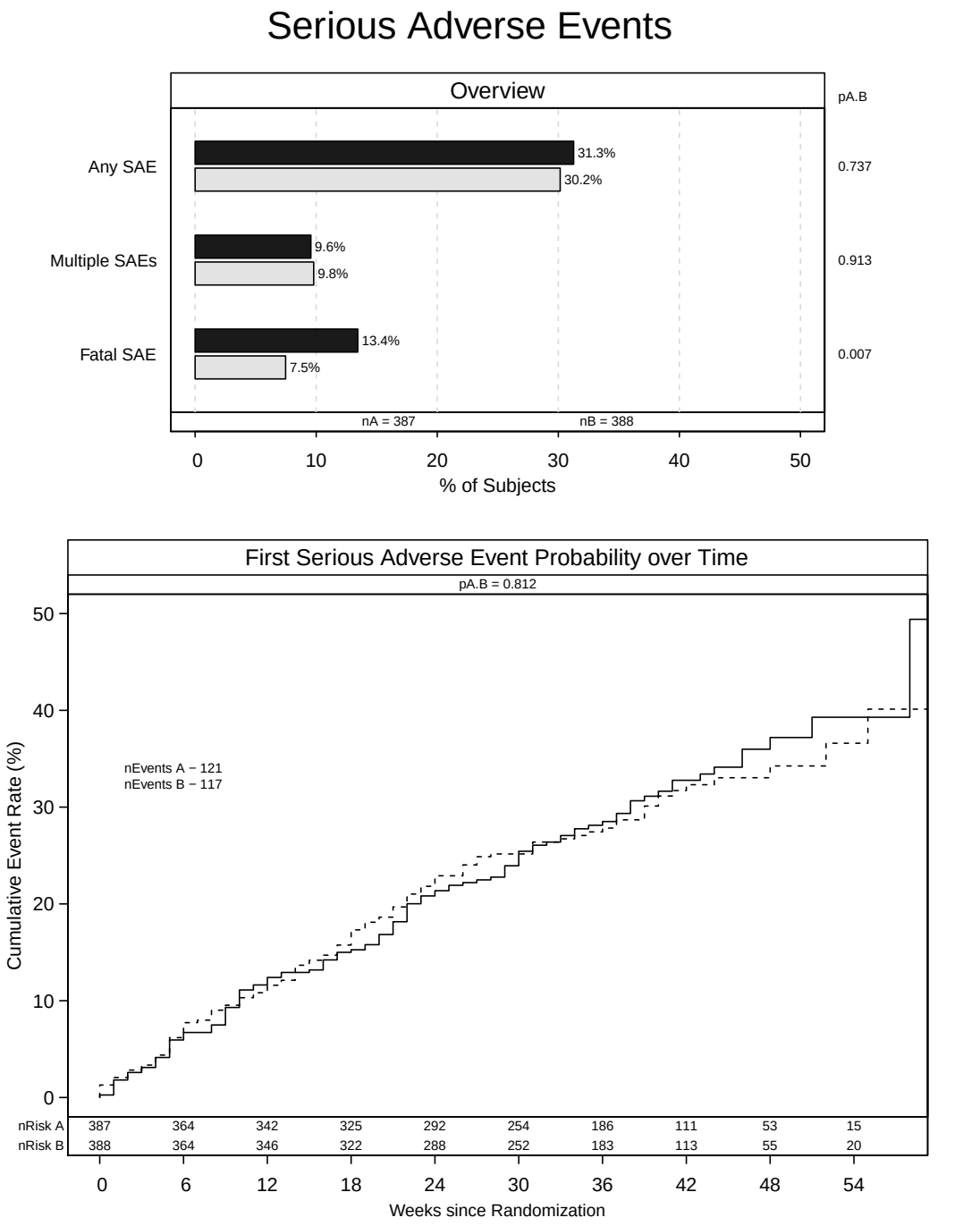
Information from a simulated laboratory dataset. The baseline value for each test is defined as the last measurement on or before the date of randomization, if more than one baseline assessment is recorded. This is a subset of laboratory measures that would typically be included in an actual DMC report.

See Table Set LABB–1 on page 64.

Chapter 3

Adverse Events

Figure SAE–1

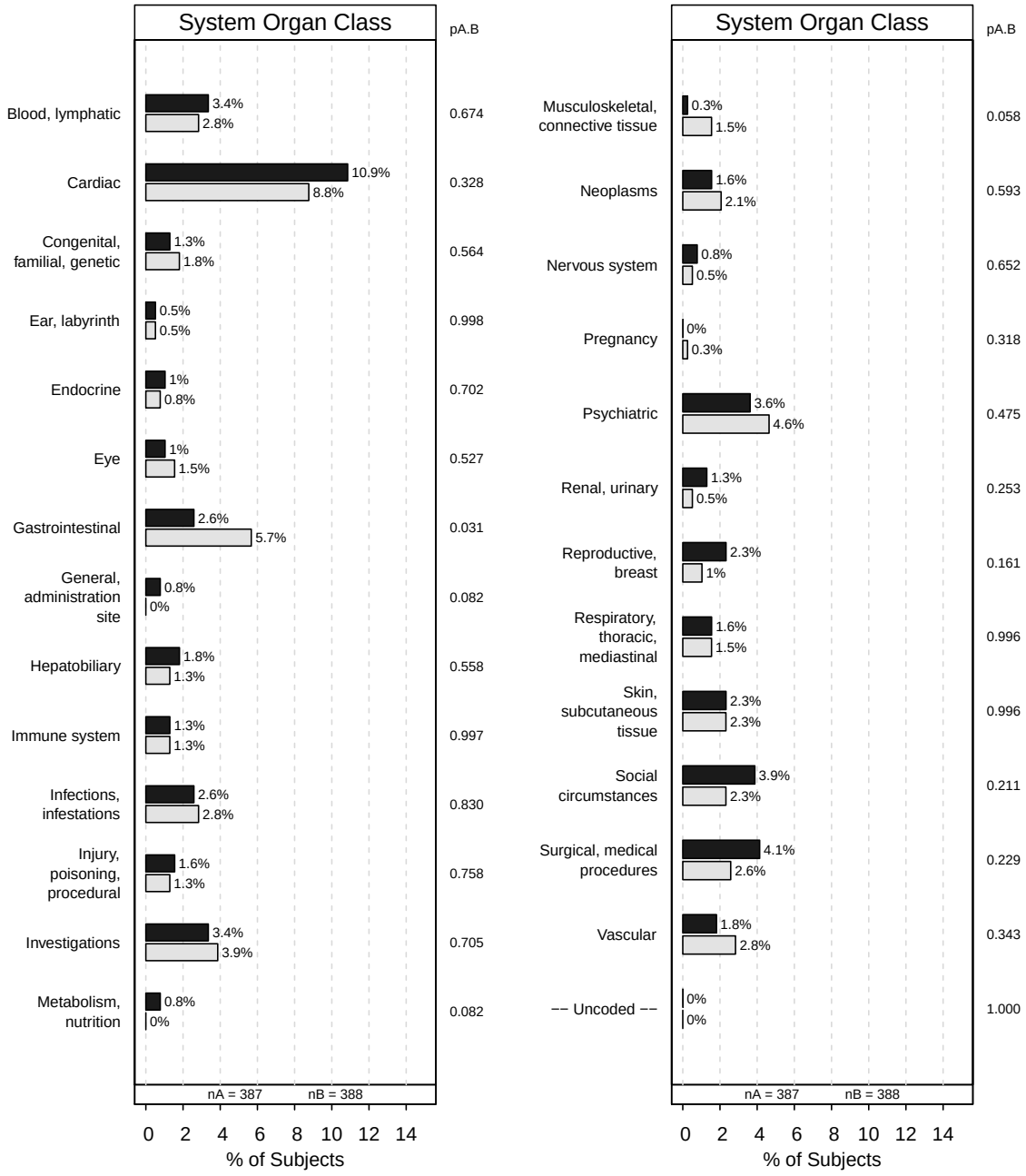


Information from a simulated serious adverse events dataset. In the lower panel, follow-up time for subjects with no SAE is censored at the date of data cut-off or at the date of withdrawal from study, if applicable. The denominators for percentages include all randomized subjects. Events known to have begun prior to randomization are not included.

See Table Set SAE–1 on page 65.

Figure SAE–2

SAEs by System Organ Class



Information from a simulated serious adverse events dataset. The denominators for percentages include all randomized subjects. Events known to have begun prior to randomization are not included.

See Table Set SAE–2 on page 66.

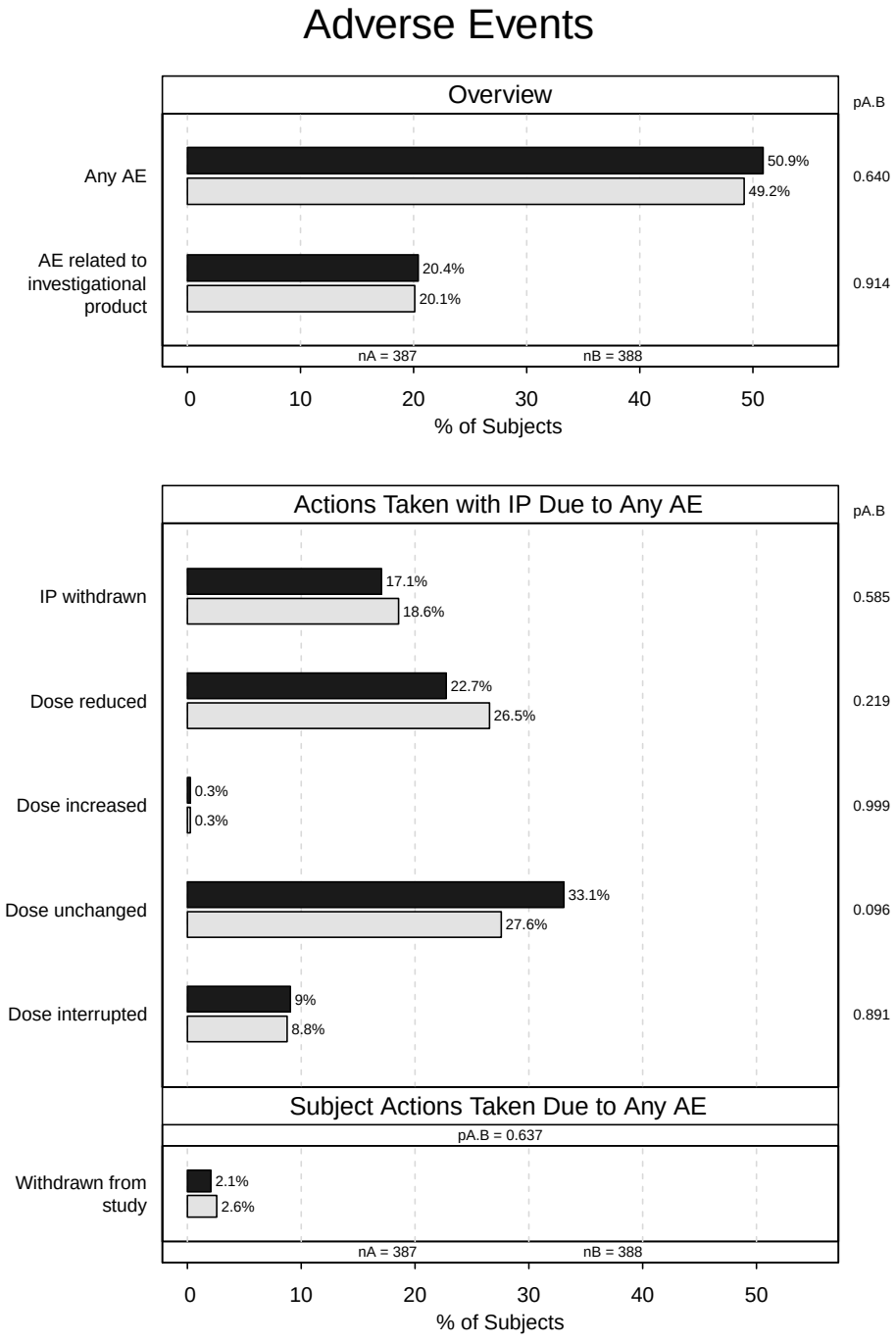
Table SAETAB

SAEs by System Organ Class and Preferred Term

Serious Adverse Event	N Subjects (Events)			Percent of Subjects			P-Values
MedDRA System Organ Class ► Preferred Term	A	B	ALL	A	B	ALL	pA.B
Cardiac disorders	**42 (64)**	**34 (44)**	**76 (108)**	**10.9**	**8.8**	**9.8**	**0.328**
Acquired cardiac septal defect	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.316
Angina pectoris	7 (12)	12 (14)	19 (26)	1.8	3.1	2.5	0.248
Angina unstable	8 (13)	2 (3)	10 (16)	2.1	0.5	1.3	0.056
Atrial fibrillation	5 (6)	1 (1)	6 (7)	1.3	0.3	0.8	0.100
Bradycardia	2 (3)	1 (1)	3 (4)	0.5	0.3	0.4	0.561
Bradycardia foetal	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.318
Bundle branch block	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.316
Bundle branch block right	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.318
Cardiac asthma	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.318
Cardiac failure	2 (4)	3 (4)	5 (8)	0.5	0.8	0.6	0.656
Cardiac failure congestive	3 (5)	0 (0)	3 (5)	0.8	0.0	0.4	0.082
Cardiac fibrillation	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.318
Cardiac pseudoaneurysm	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.316
Coronary artery perforation	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.316
Coronary artery stenosis	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.316
Cyanosis	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.318
Eosinophilic myocarditis	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.318
Foetal heart rate disorder	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.318
Intracardiac mass	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.318
Mitral valve sclerosis	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.316
Myocardial infarction	3 (3)	2 (2)	5 (5)	0.8	0.5	0.6	0.652
Myocardial ischaemia	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.316
Pericarditis lupus	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.318
Postural orthostatic tachycardia syndrome	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.316
Pulmonary valve calcification	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.316
Pulmonary valve sclerosis	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.318
Right ventricular failure	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.316
Supraventricular extrasystoles	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.316
Supraventricular tachycardia	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.316
Tachycardia	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.318
Ventricular extrasystoles	0 (0)	2 (2)	2 (2)	0.0	0.5	0.3	0.157
Ventricular fibrillation	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.318
Ventricular tachyarrhythmia	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.316

Information from a simulated adverse events dataset. The denominators for percentages include all randomized subjects. Events known to have begun prior to randomization are not included.

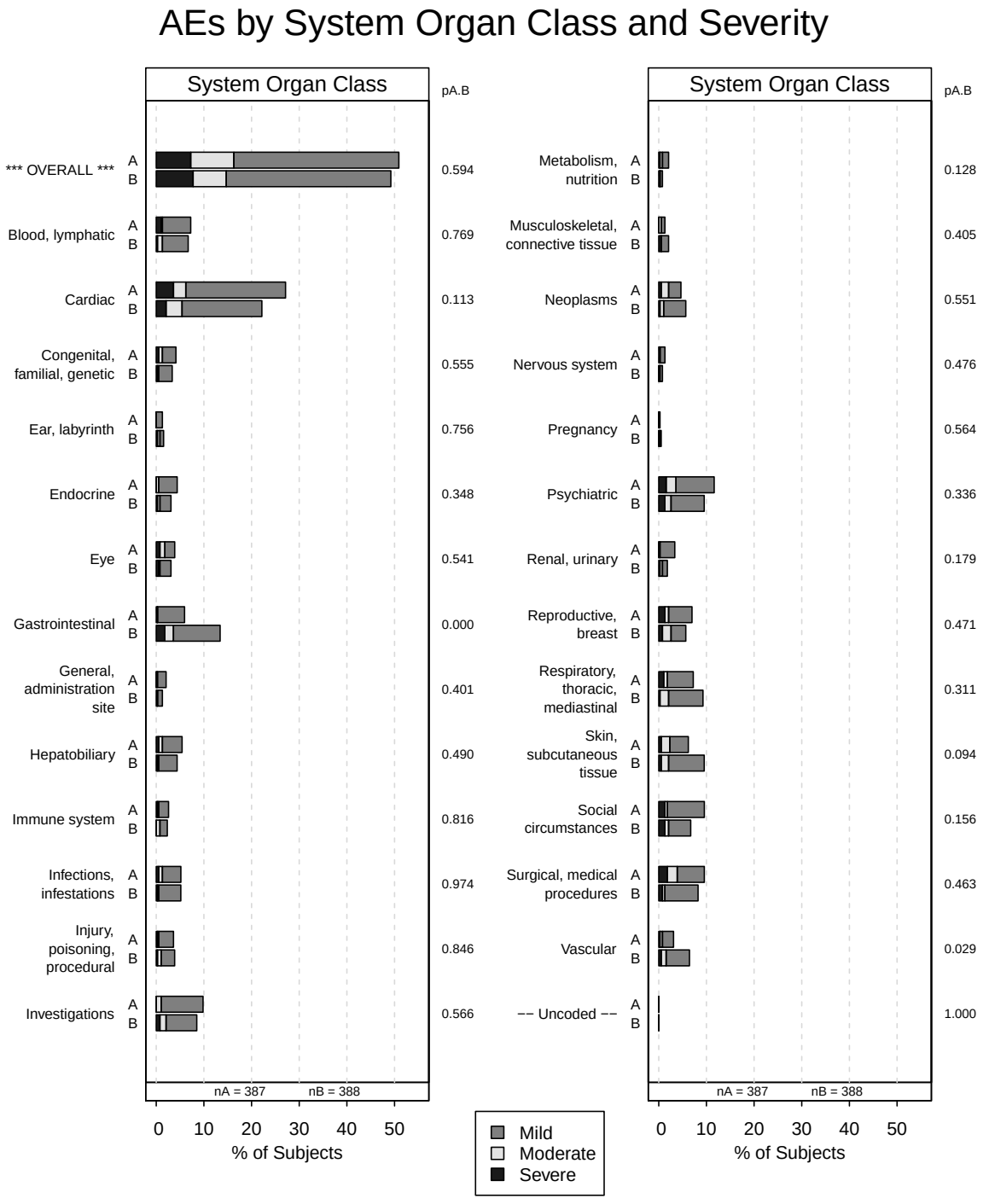
Figure AE–1



Information from a simulated adverse events dataset. Events known to have begun prior to randomization are not included.

See Table Set AE–1 on page 68.

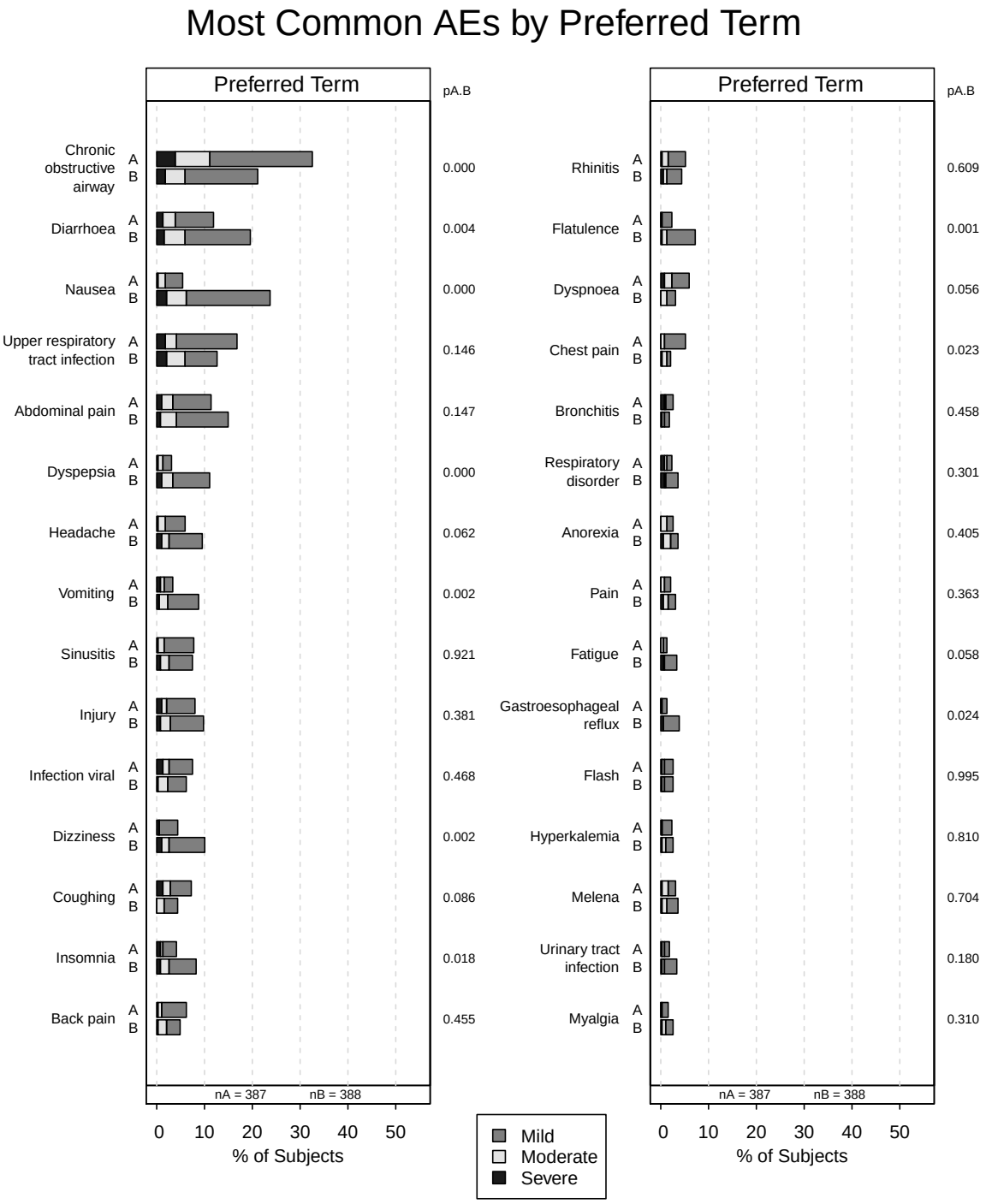
Figure AE–2



Information from a simulated adverse events dataset. Panels display the percent of subjects experiencing any AE within each coded system organ class. The denominators for percentages include all randomized subjects. Events known to have begun prior to randomization are not included. Within each system organ class, a subject was assigned to a single category based on the AE with the maximum severity.

See Table Set AE–2 on page 69.

Figure AE–3



Information from a simulated adverse events dataset. Display includes the 30 most common coded preferred terms, determined by the number of subjects with each term reported. The denominators for percentages include all randomized subjects. Events known to have begun prior to randomization are not included. Preferred terms are sorted by overall frequency. Within each preferred term, a subject was assigned to a single category based on the AE with the maximum severity.

See Table Set AE–3 on page 71.

Table AETAB

AEs by System Organ Class and Preferred Term

Adverse Event	N Subjects (Events)			Percent of Subjects			P-Values
MedDRA System Organ Class ► Preferred Term	A	B	ALL	A	B	ALL	pA.B
Cardiac disorders	**105 (165)**	**86 (132)**	**191 (297)**	**27.1**	**22.2**	**24.6**	**0.109**
Acquired cardiac septal defect	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.316
Agonal rhythm	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.318
Angina pectoris	22 (34)	29 (43)	51 (77)	5.7	7.5	6.6	0.315
Angina unstable	18 (27)	9 (15)	27 (42)	4.7	2.3	3.5	0.077
Atrial fibrillation	14 (21)	6 (8)	20 (29)	3.6	1.5	2.6	0.069
Atrial flutter	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.316
Atrial tachycardia	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.318
Atrioventricular block	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.316
Bradycardia	4 (6)	2 (4)	6 (10)	1.0	0.5	0.8	0.411
Bradycardia foetal	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.318
Bundle branch block	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.316
Bundle branch block bilateral	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.318
Bundle branch block left	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.316
Bundle branch block right	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.318
Cardiac arrest	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.318
Cardiac asthma	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.318
Cardiac discomfort	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.318
Cardiac disorder	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.316
Cardiac failure	4 (7)	7 (10)	11 (17)	1.0	1.8	1.4	0.365
Cardiac failure congestive	7 (14)	2 (3)	9 (17)	1.8	0.5	1.2	0.093
Cardiac fibrillation	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.318
Cardiac pseudoaneurysm	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.316
Cardiac valve vegetation	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.318
Coronary artery perforation	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.316
Coronary artery stenosis	1 (2)	1 (1)	2 (3)	0.3	0.3	0.3	0.999
Cyanosis	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.318
Diabetic cardiomyopathy	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.316
Eosinophilic myocarditis	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.318
Foetal arrhythmia	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.318
Foetal heart rate disorder	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.318
Hyperkinetic heart syndrome	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.316
Hypertensive heart disease	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.316
Intracardiac mass	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.318
Malignant hypertensive heart disease	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.316
Mitral valve sclerosis	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.316
Myocardial calcification	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.316
Myocardial infarction	6 (8)	3 (5)	9 (13)	1.6	0.8	1.2	0.313
Myocardial ischaemia	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.316
Neonatal tachycardia	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.316
Papillary muscle haemorrhage	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.318
Pericardial cyst	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.316
Pericardial haemorrhage	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.318
Pericarditis lupus	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.318
Postural orthostatic tachycardia syndrome	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.316

(Continued on next page.)

Information from a simulated adverse events dataset. The denominators for percentages include all randomized subjects. Events known to have begun prior to randomization are not included.

AEs by System Organ Class and Preferred Term

Table AETAB (*cont.*)

(Continued from previous page.)

Adverse Event	N Subjects (Events)			Percent of Subjects			P-Values
MedDRA System Organ Class ► Preferred Term	A	B	ALL	A	B	ALL	pA.B
Pulmonary valve calcification	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.316
Pulmonary valve incompetence	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.318
Pulmonary valve sclerosis	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.318
Reperfusion arrhythmia	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.316
Right ventricular failure	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.316
Right ventricular hypertrophy	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.316
Sick sinus syndrome	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.316
Sinus bradycardia	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.318
Supraventricular extrasystoles	2 (3)	0 (0)	2 (3)	0.5	0.0	0.3	0.156
Supraventricular tachycardia	2 (2)	0 (0)	2 (2)	0.5	0.0	0.3	0.156
Tachycardia	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.318
Tachycardia paroxysmal	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.316
Ventricular extrasystoles	1 (2)	4 (5)	5 (7)	0.3	1.0	0.6	0.179
Ventricular fibrillation	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.318
Ventricular hypertrophy	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.318
Ventricular tachyarrhythmia	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.316

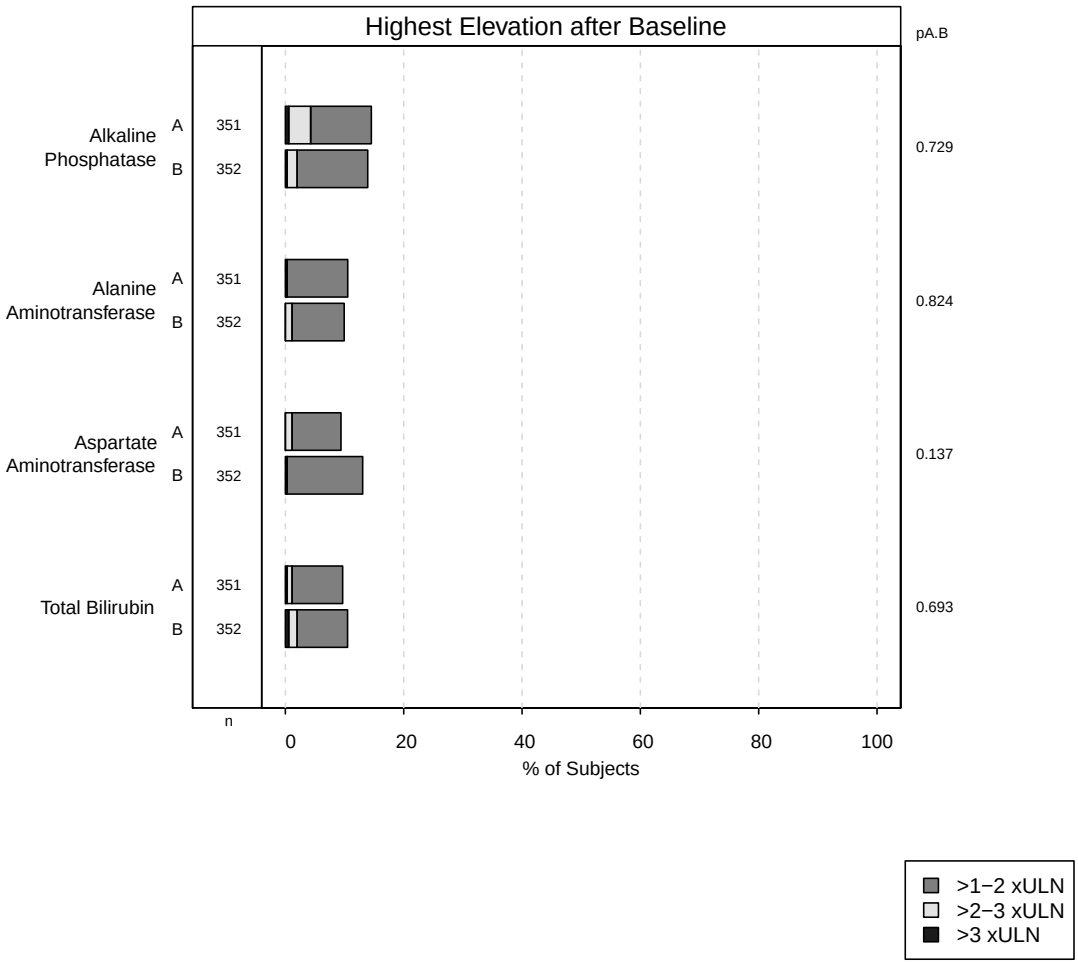
Information from a simulated adverse events dataset. The denominators for percentages include all randomized subjects. Events known to have begun prior to randomization are not included.

Chapter 4

Central Laboratory Measures

Figure LFTABN–1

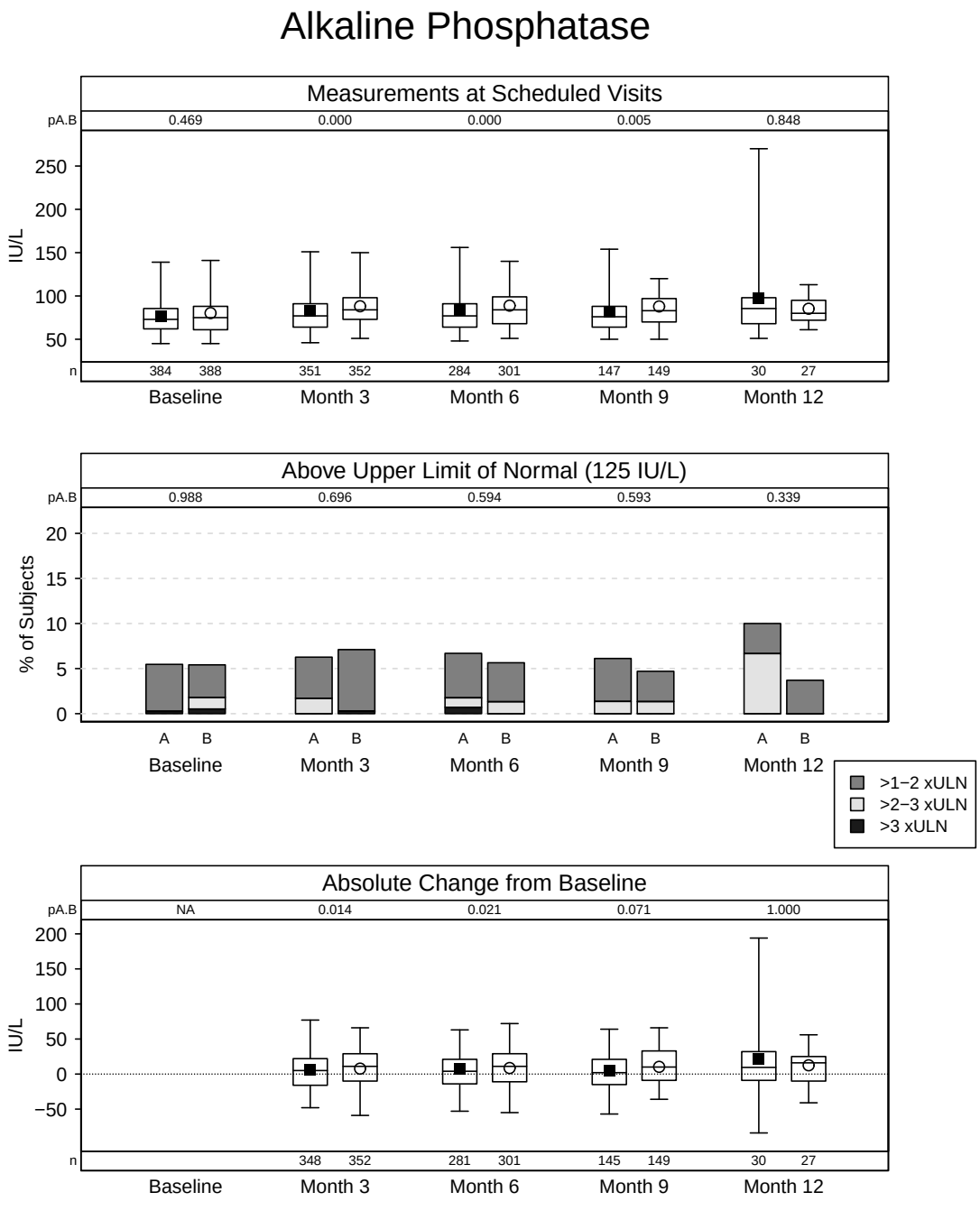
Summary of Liver Function Test Elevations



Information from a simulated laboratory dataset. This display summarizes the maximum post-baseline elevation for each subject, including repeated measurements and measurements recorded at unscheduled visits.

See Table Set LFTABN–1 on page 73.

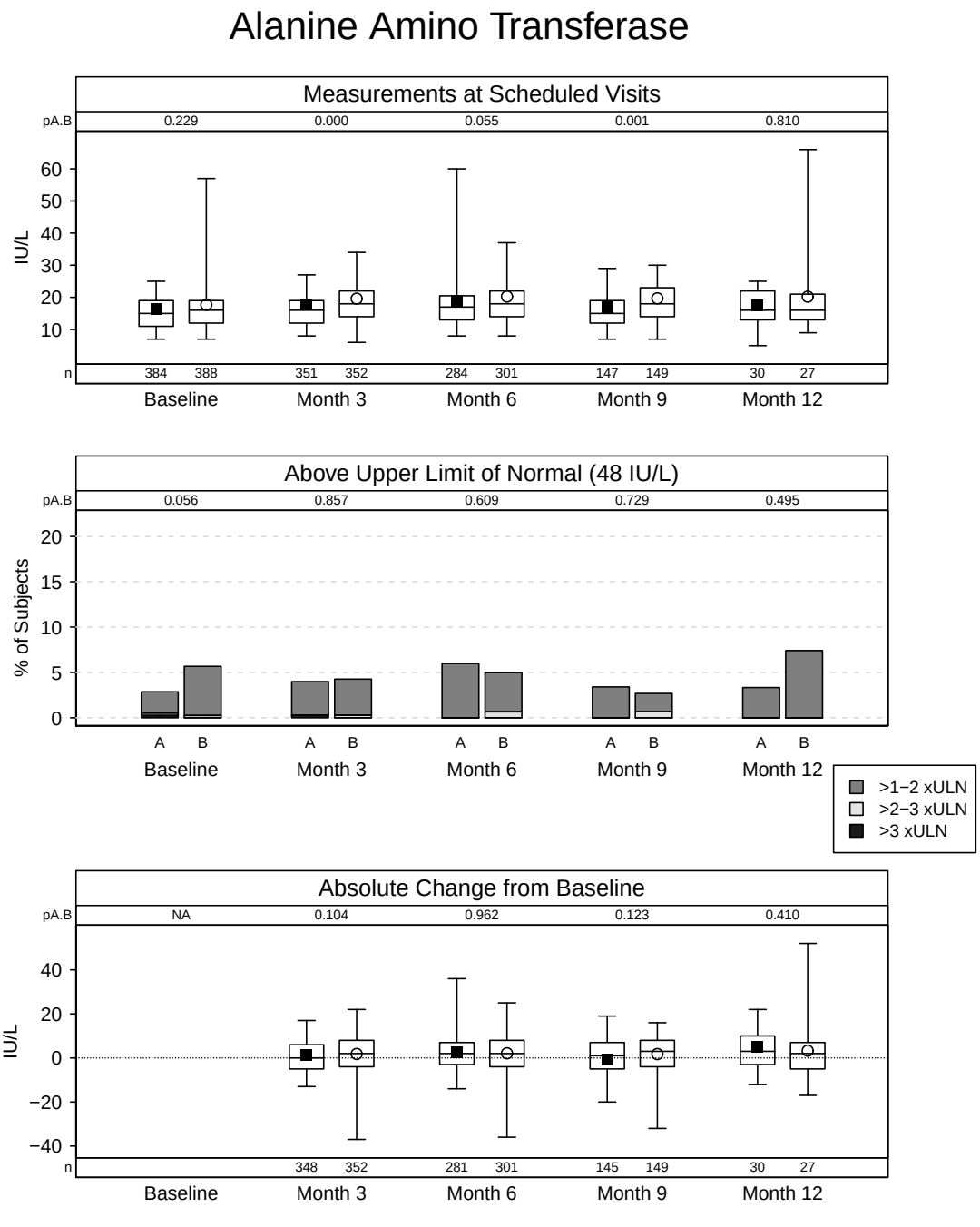
Figure LFT–1



Information from a simulated laboratory dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed.

See Table Set LFT–1 on page 74.

Figure LFT–2

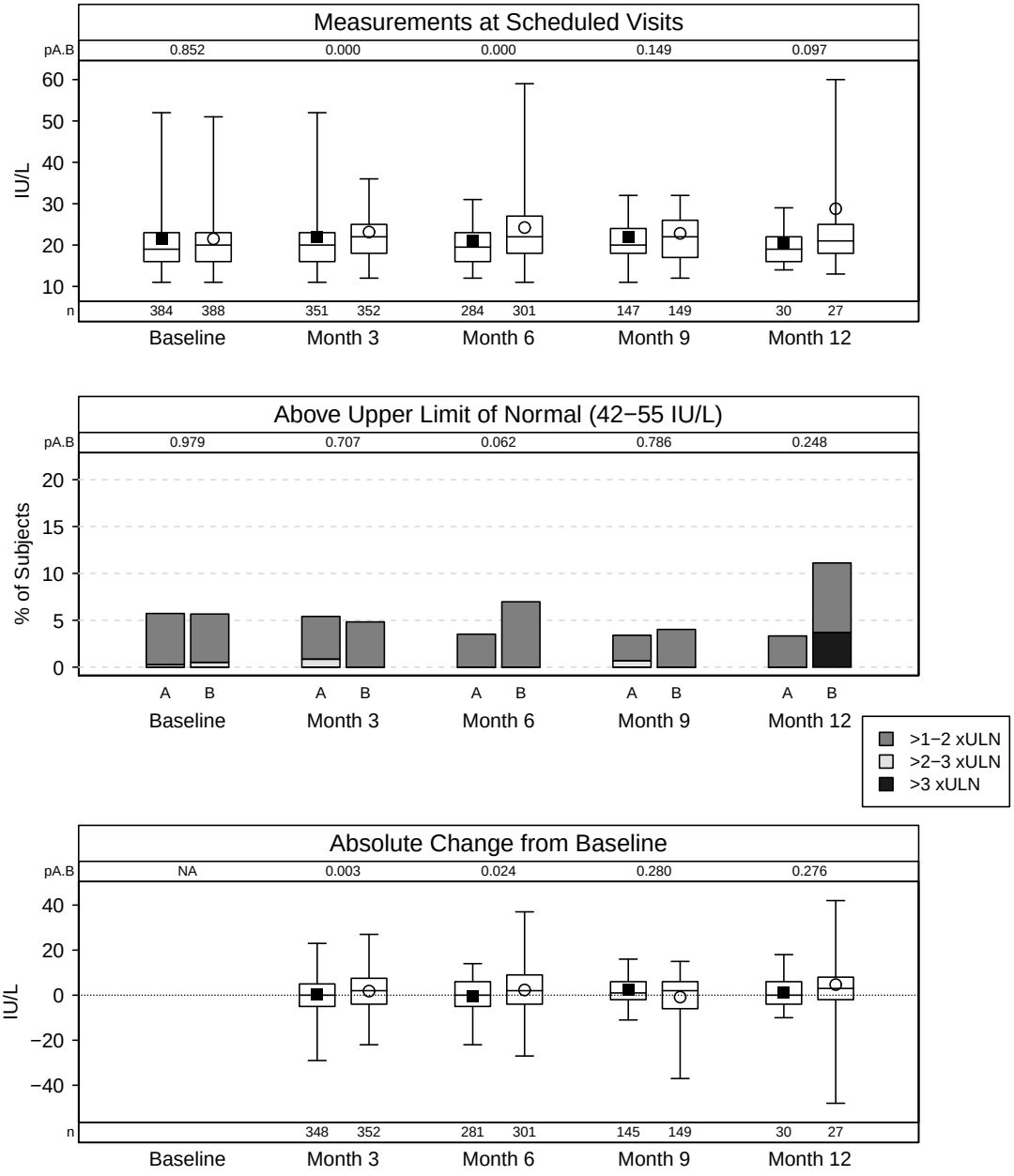


Information from a simulated laboratory dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed.

See Table Set LFT–2 on page 75.

Figure LFT–3

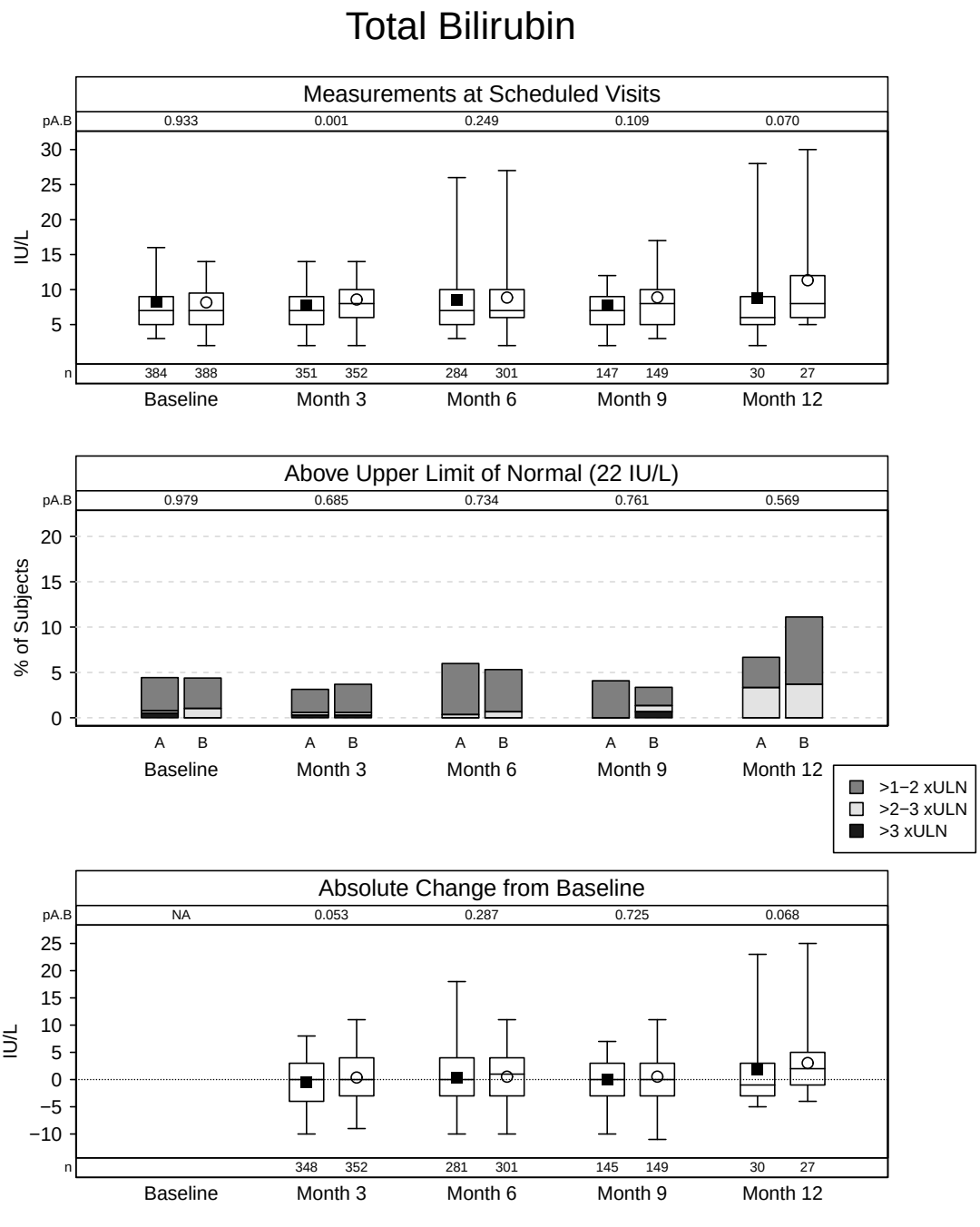
Aspartate Amino Transferase



Information from a simulated laboratory dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed.

See Table Set LFT–3 on page 76.

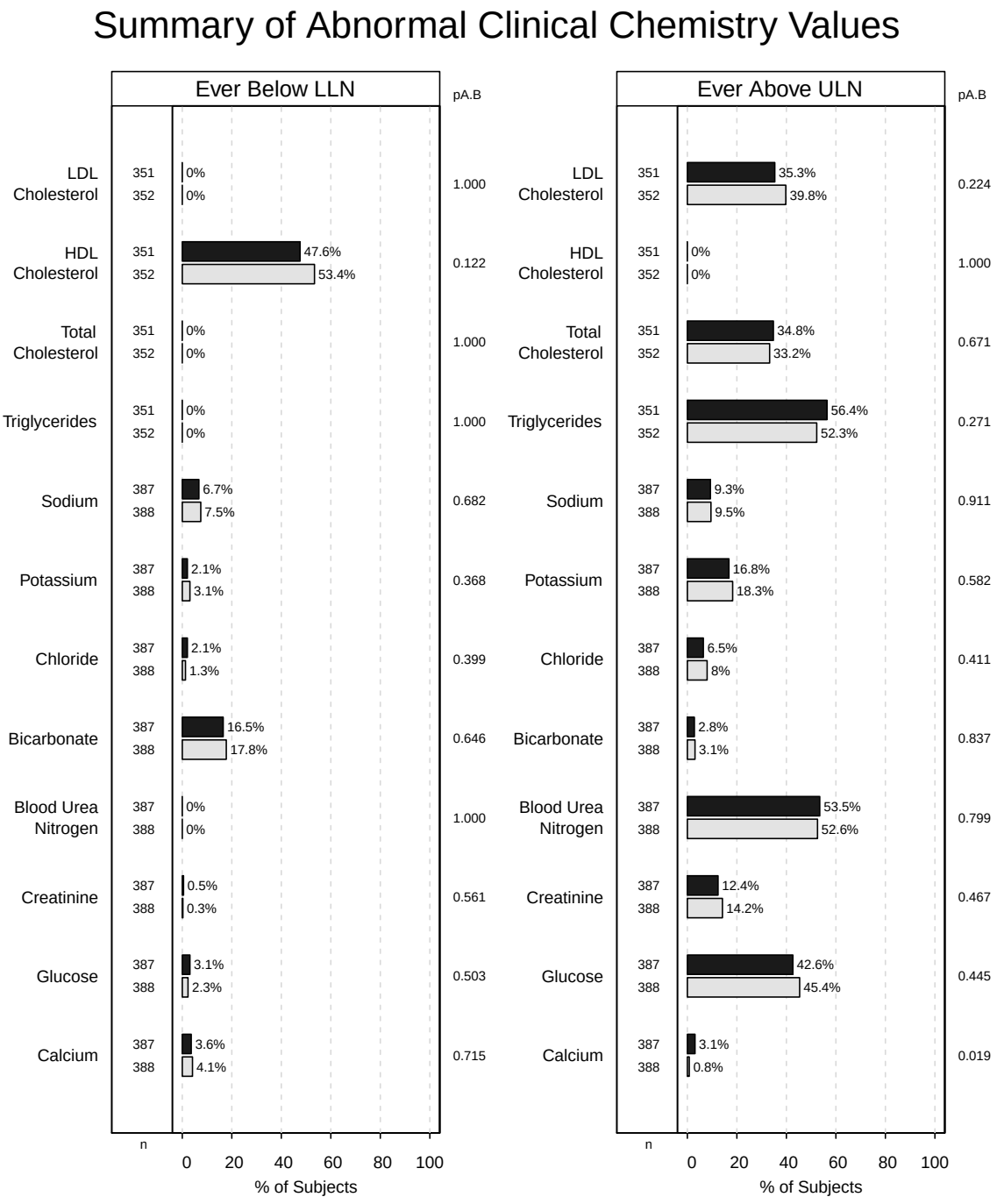
Figure LFT–4



Information from a simulated laboratory dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed.

See Table Set LFT–4 on page 77.

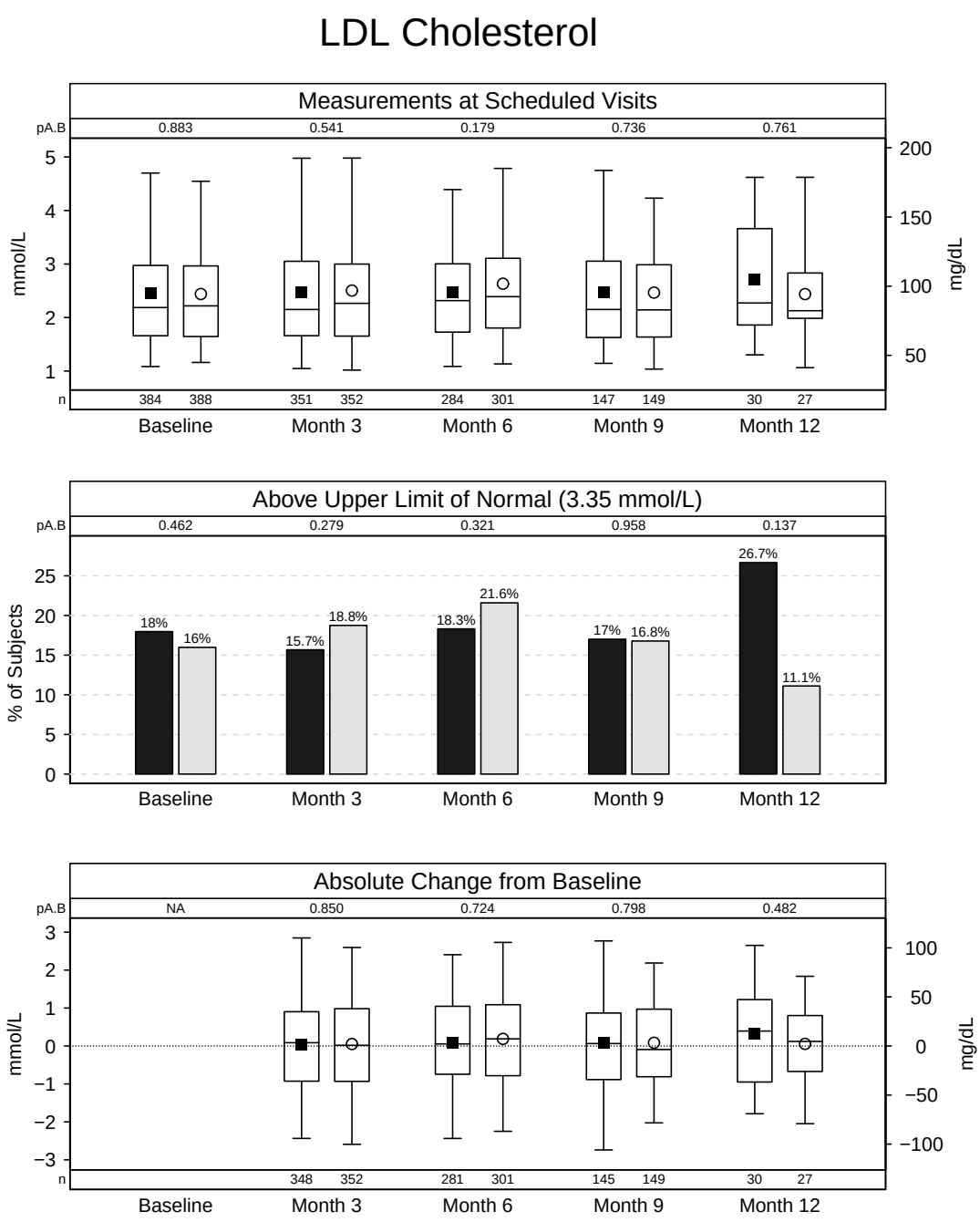
Figure CHEMABN–1



Information from a simulated laboratory dataset. Panels display the percent of subjects with any post-randomization value reported below the lower limit of normal (LLN) or above the upper limit of normal (ULN), as applicable, for each test, including repeated measurements and measurements recorded at unscheduled visits.

See Table Set CHEMABN–1 on page 78.

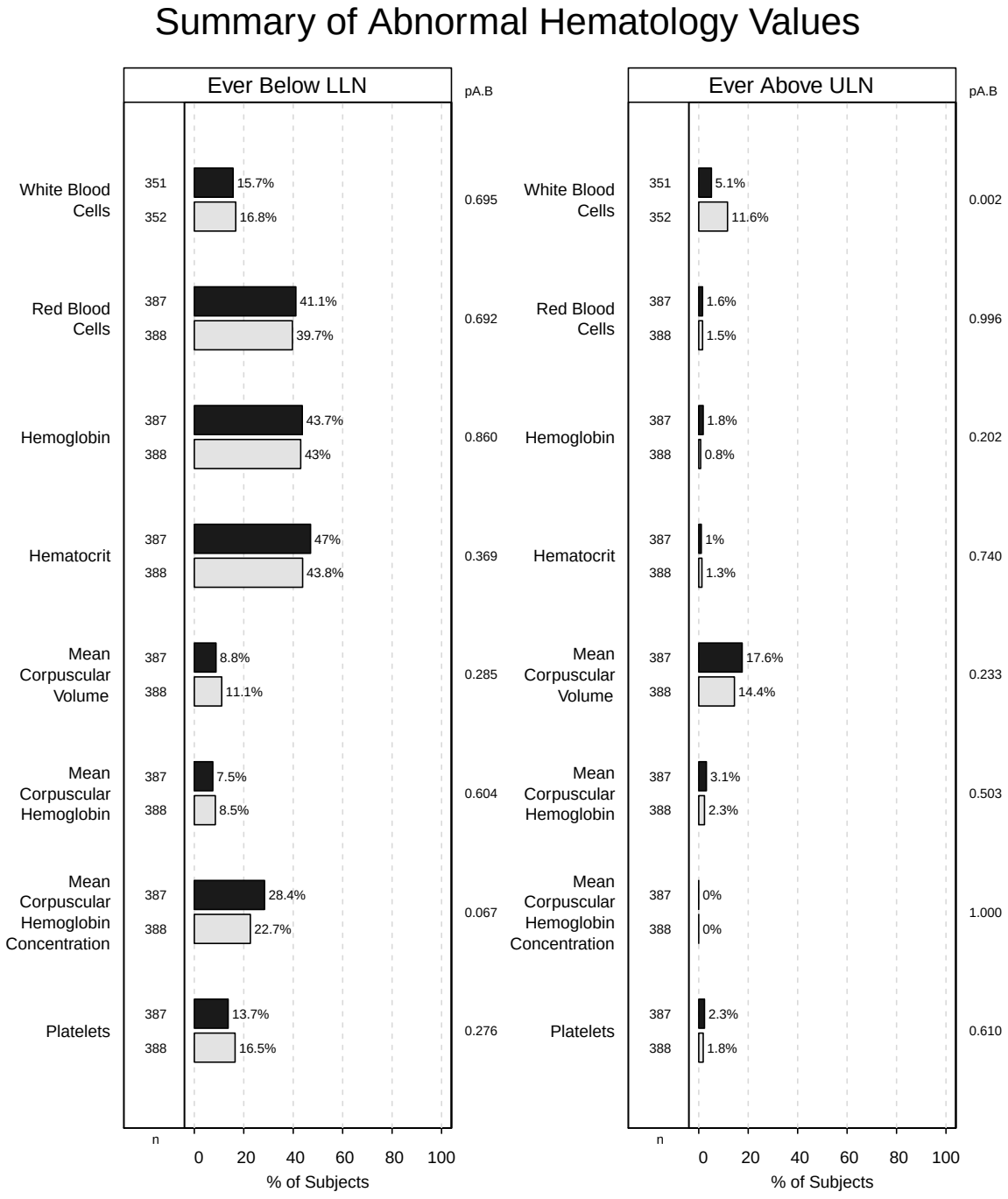
Figure CHEM–1



Information from a simulated laboratory dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed. In an actual DMC report, a similar page would be included for each laboratory measure.

See Table Set CHEM–1 on page 79.

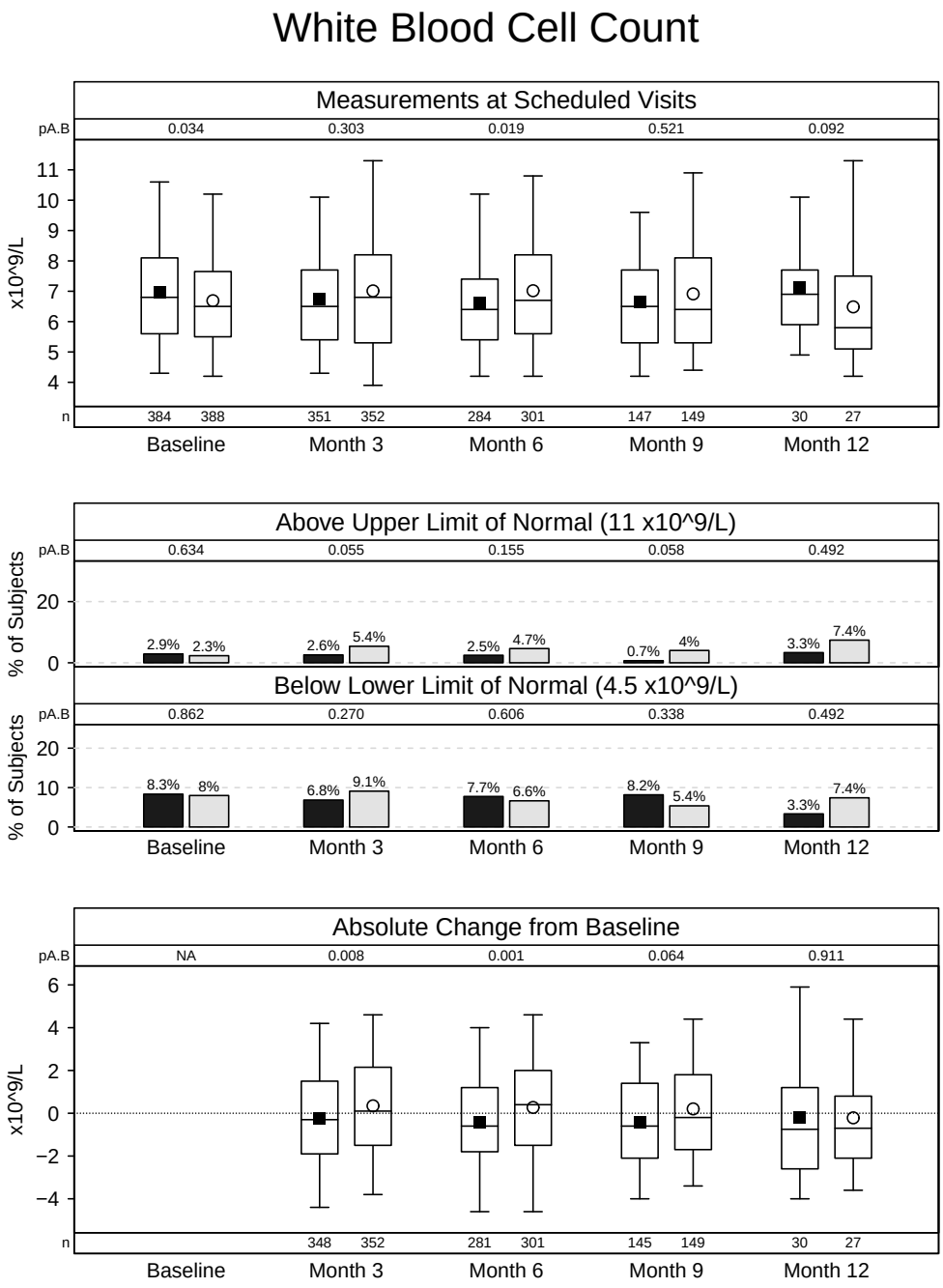
Figure HEMABN–1



Information from a simulated laboratory dataset. Panels display the percent of subjects with any post-randomization value reported below the lower limit of normal (LLN) or above the upper limit of normal (ULN), as applicable, for each test, including repeated measurements and measurements recorded at unscheduled visits.

See Table Set HEMABN–1 on page 80.

Figure HEM–1



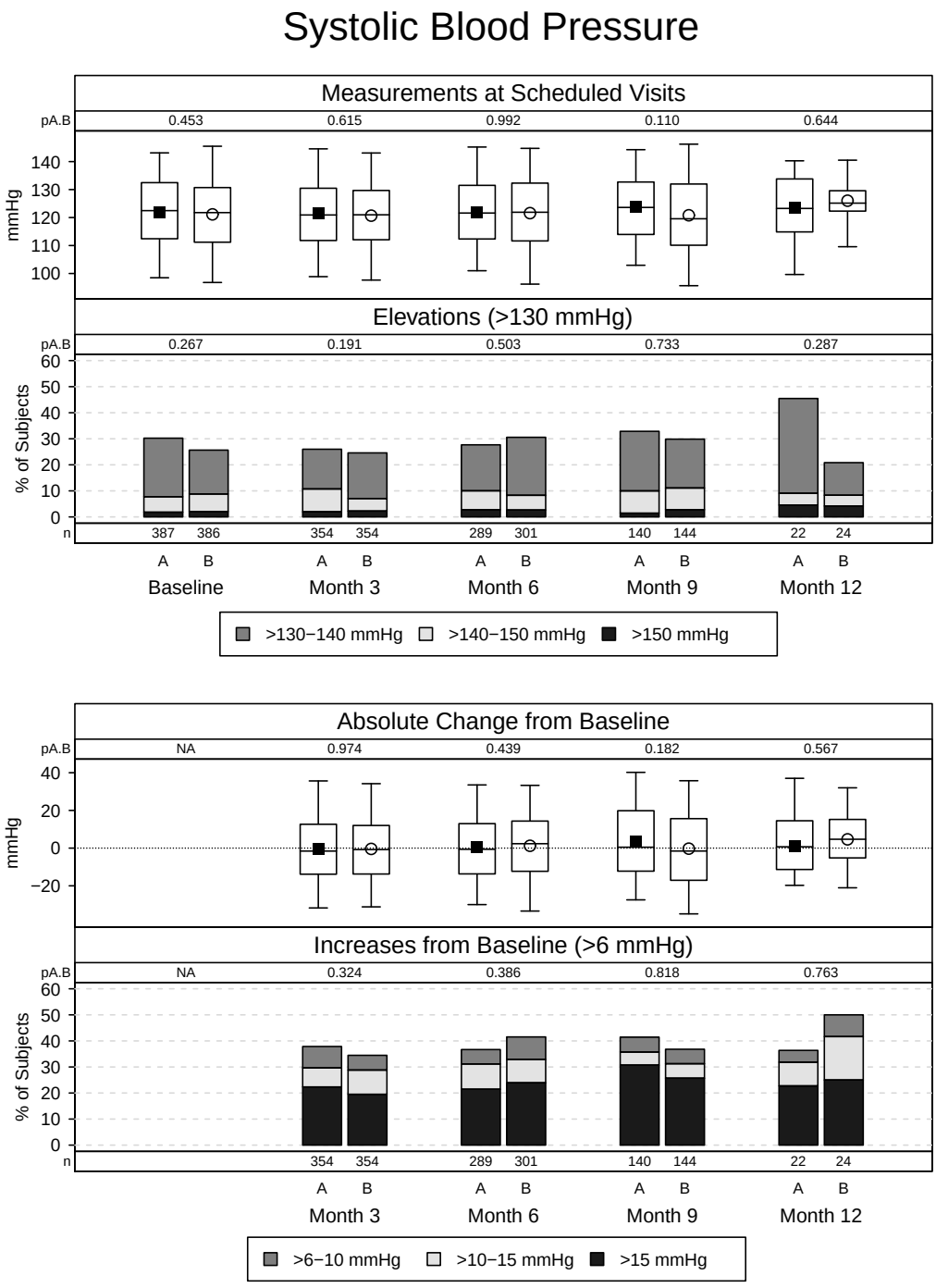
Information from a simulated laboratory dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed. In an actual DMC report, a similar page would be included for each laboratory measure.

See Table Set HEM–1 on page 81.

Chapter 5

Other Follow-up and Safety Measures

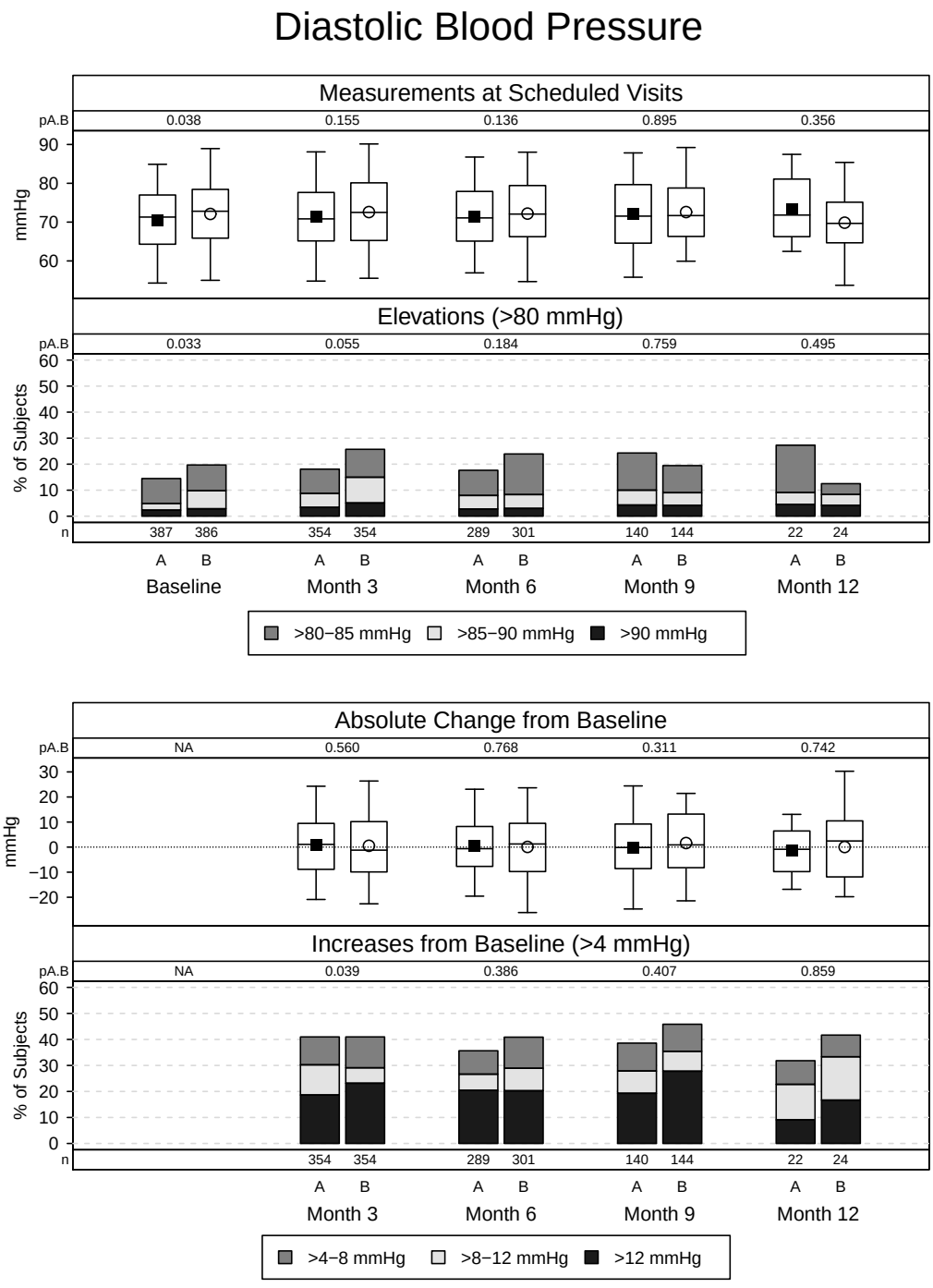
Figure VIT–1



Information from a simulated vital signs dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed.

See Table Set VIT–1 on page 84.

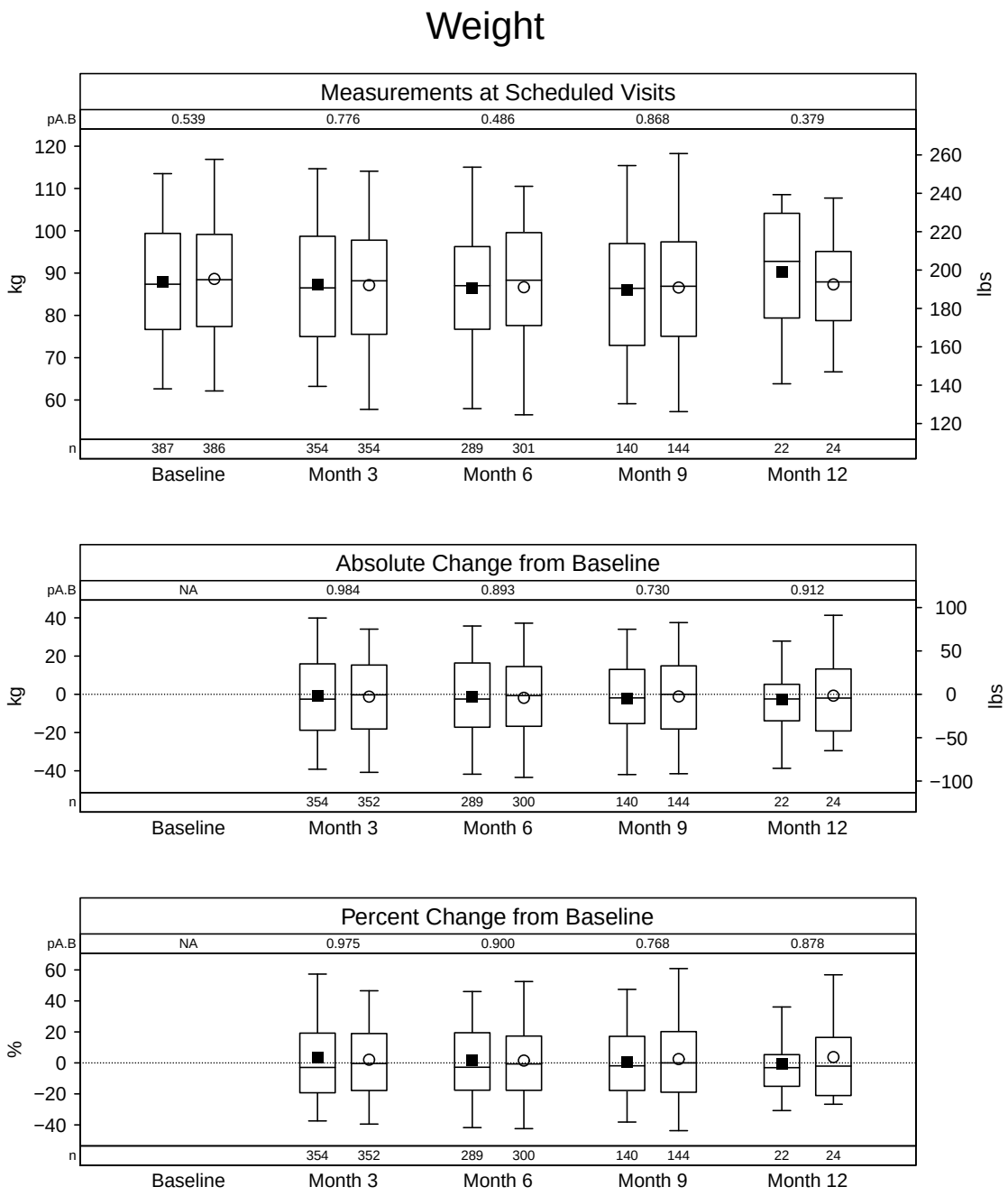
Figure VIT–2



Information from a simulated vital signs dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed.

See Table Set VIT–2 on page 86.

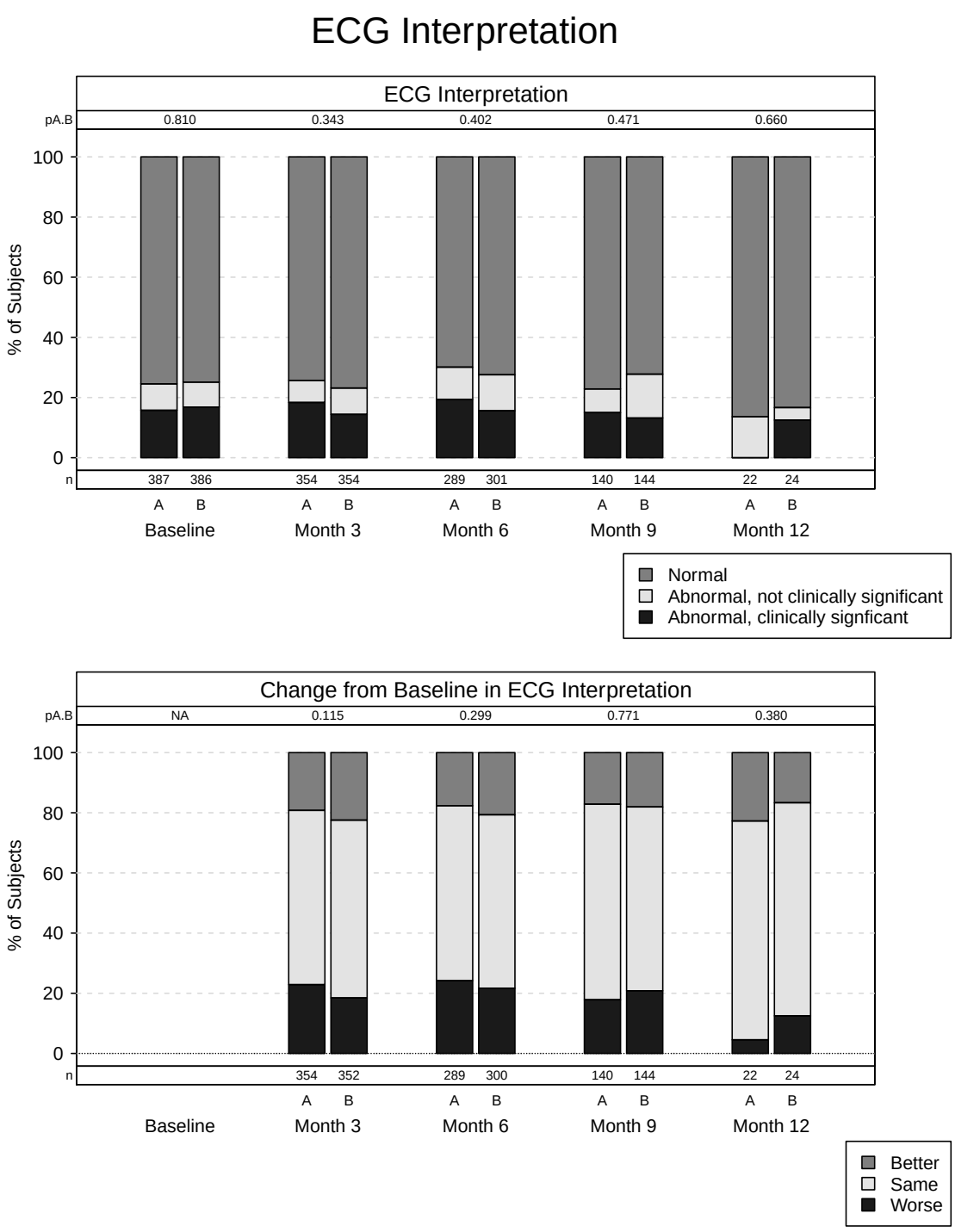
Figure VIT–3



Information from a simulated vital signs dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed.

See Table Set VIT–3 on page 87.

Figure ECG–1

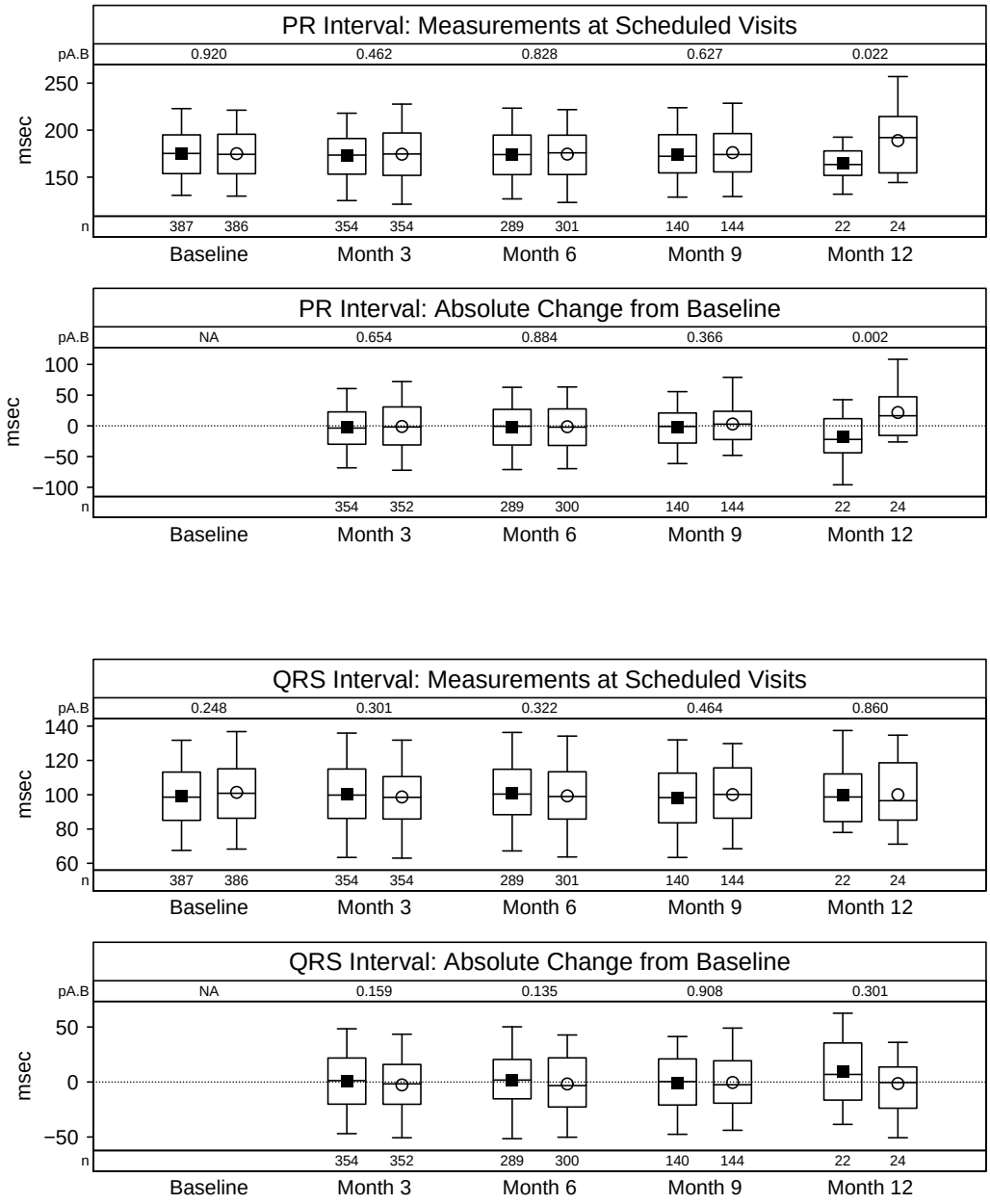


Information from a simulated ECG dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed.

See Table Set ECG–1 on page 88.

Figure ECG–2

ECG: PR Interval and QRS Interval



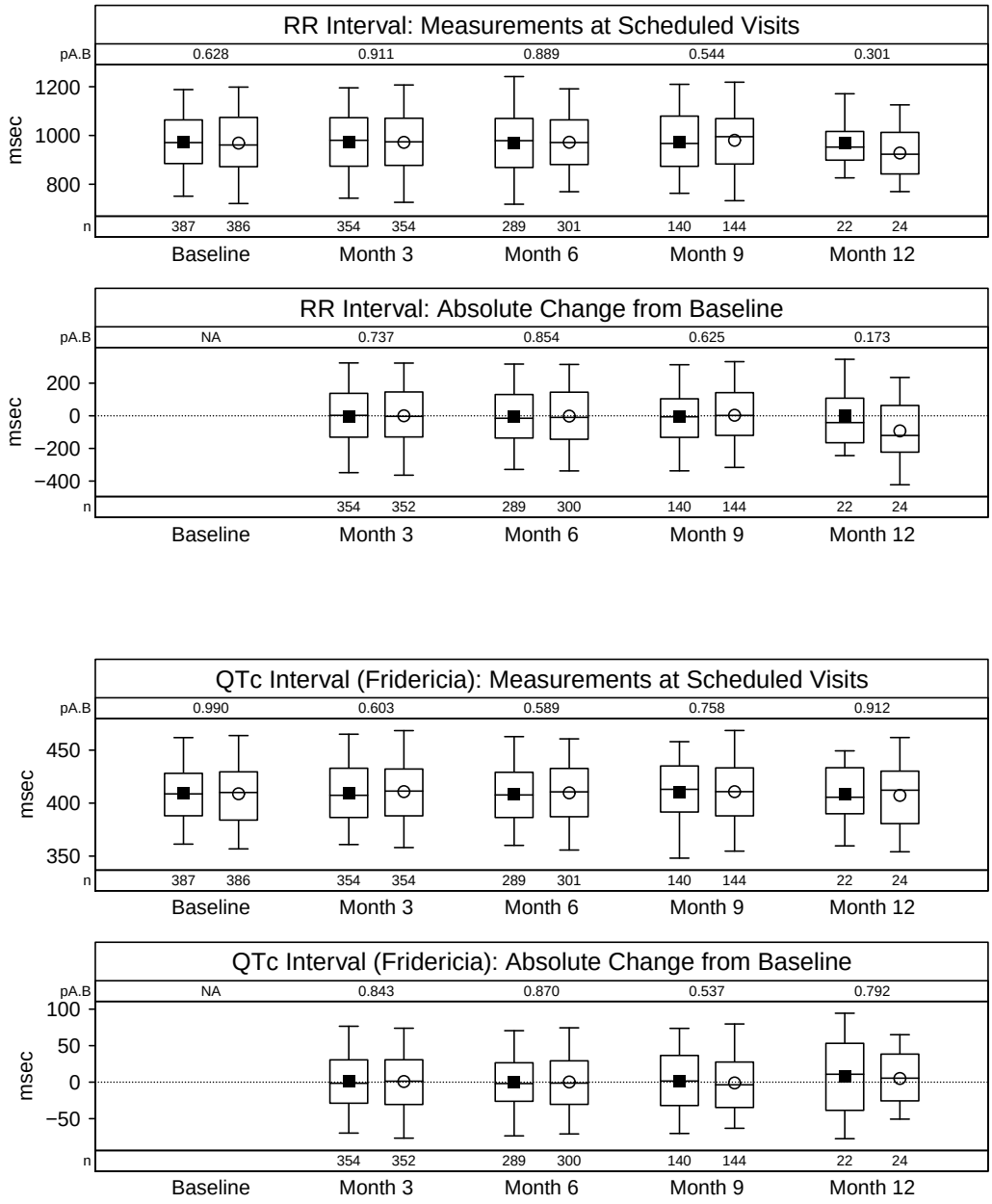
Information from a simulated ECG dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed.

■ A
○ B

See Table Set ECG–2 on page 89.

Figure ECG–3

ECG: RR Interval and QTc Interval (Fridericia)

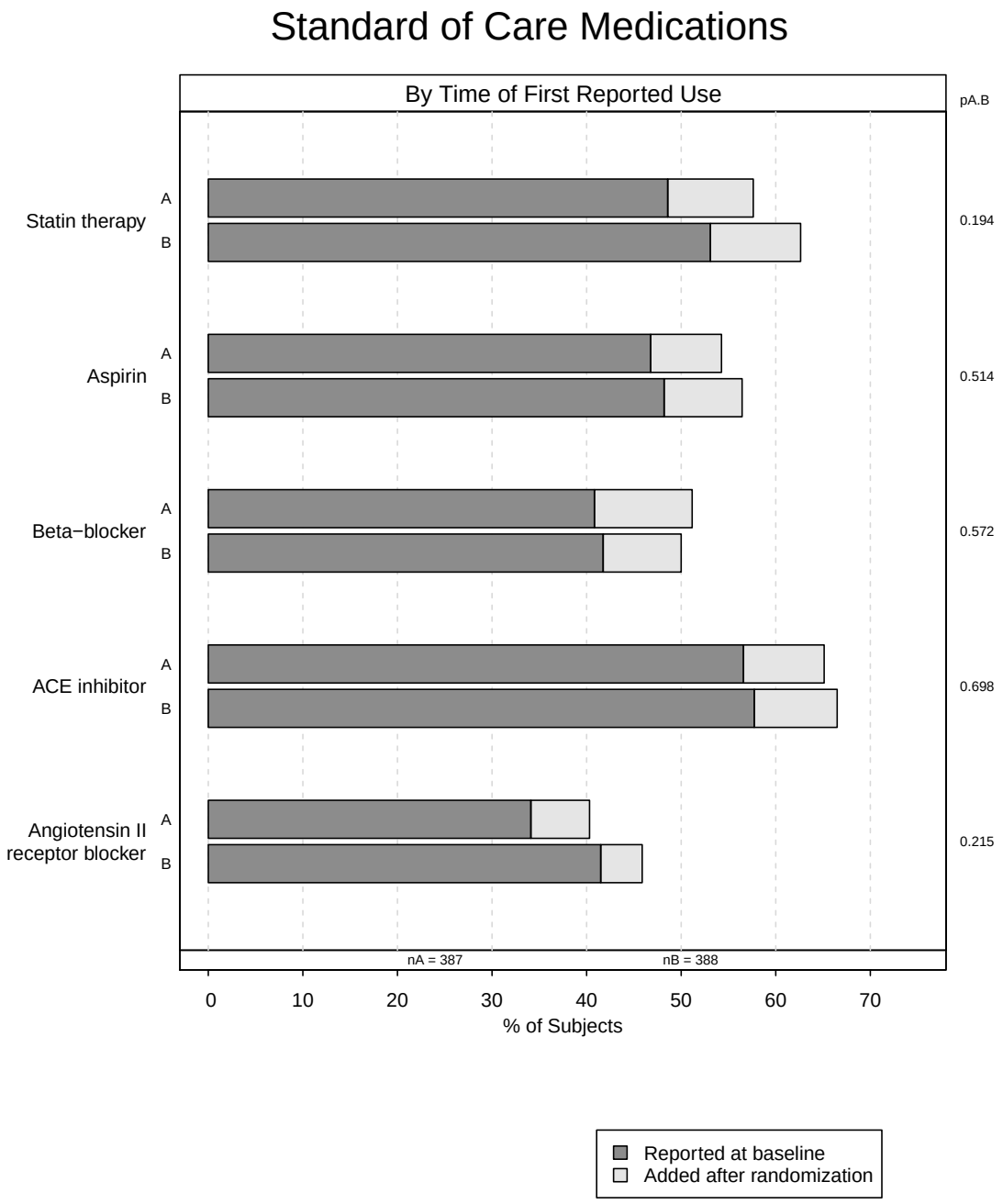


Information from a simulated ECG dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed.

■ A
○ B

See Table Set ECG–3 on page 91.

Figure CONMEDS–1



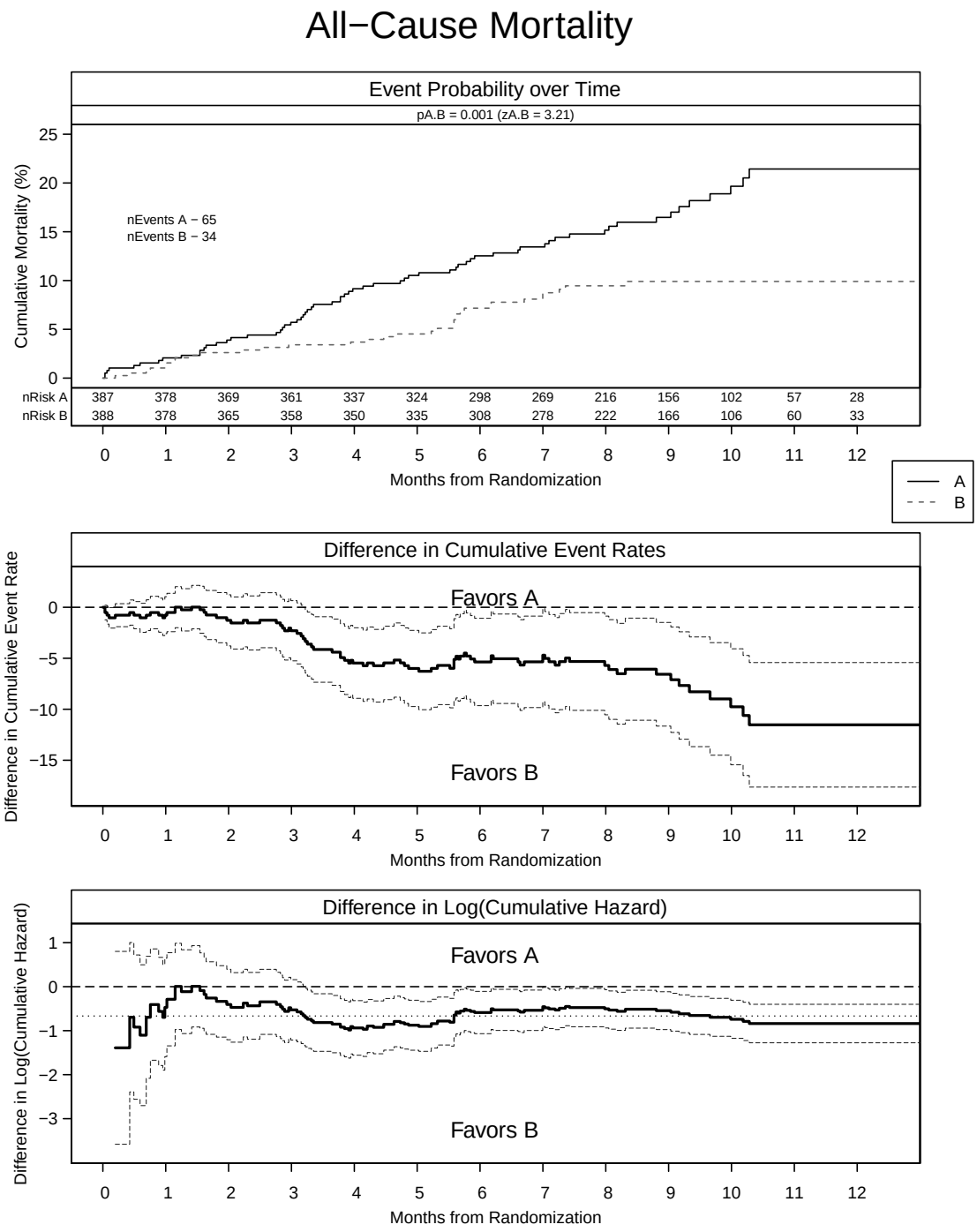
Information from a simulated concomitant medications dataset. The denominator for percentages includes all subjects with any CRF data submitted. Medications which were terminated prior to randomization have been excluded.

See Table Set CONMEDS–1 on page 92.

Chapter 6

Study Endpoints

Figure ENDPT–1



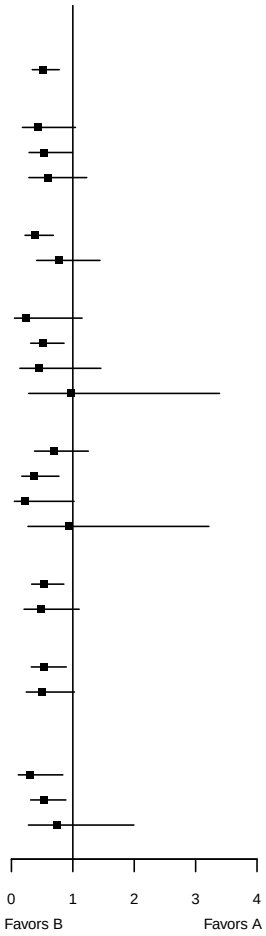
Information from a simulated endpoint dataset. The risk set includes all randomized subjects. Follow-up time for subjects who did not die is censored at the date of data transfer, or the date of withdrawal from study, if applicable. The *p*-value in the upper panel is from a log-rank test. In the lower two panels, the dashed lines are pointwise 95% confidence intervals for the difference displayed. In the bottom panel, the dotted horizontal line indicates the fitted value of the log hazard ratio.

See Table Set ENDPT–1 on page 93.

Figure ENDPT–2

Hazard Ratios: All−Cause Mortality

Baseline Subgroup	A	B	B/A Hazard Ratio (95% CI)	Score pA.B	Score Int. P
Overall	65/387 (17%)	34/388 (9%)	0.51 (0.34,0.78)	0.001	
Age					
< 50	17/76 (22%)	7/68 (10%)	0.43 (0.18,1.04)	0.055	0.838
50−60	30/179 (17%)	15/172 (9%)	0.53 (0.29,0.99)	0.044	
> 60	18/132 (14%)	12/148 (8%)	0.59 (0.28,1.23)	0.153	
Sex					
Male	42/260 (16%)	17/264 (6%)	0.39 (0.22,0.68)	<0.001	0.114
Female	23/127 (18%)	17/124 (14%)	0.77 (0.41,1.44)	0.414	
Race					
Black	7/32 (22%)	2/34 (6%)	0.24 (0.05,1.15)	0.052	0.524
White	44/256 (17%)	23/255 (9%)	0.52 (0.31,0.86)	0.009	
Asian	9/83 (11%)	4/83 (5%)	0.45 (0.14,1.46)	0.170	
Other	5/16 (31%)	5/16 (31%)	0.98 (0.28,3.39)	0.972	
Geographic Region					
North America	26/165 (16%)	18/159 (11%)	0.69 (0.38,1.25)	0.216	0.276
Europe	25/125 (20%)	9/130 (7%)	0.36 (0.17,0.77)	0.006	
Asia	9/63 (14%)	2/62 (3%)	0.22 (0.05,1.02)	0.034	
Latin America	5/34 (15%)	5/37 (14%)	0.93 (0.27,3.22)	0.909	
History of MI					
No Prior MI	48/282 (17%)	26/287 (9%)	0.53 (0.33,0.85)	0.008	0.798
Prior MI	17/105 (16%)	8/101 (8%)	0.48 (0.21,1.10)	0.076	
NYHA Class					
Class II	42/248 (17%)	23/255 (9%)	0.54 (0.32,0.89)	0.015	0.670
Class III	22/136 (16%)	11/130 (8%)	0.50 (0.24,1.03)	0.054	
Class IV	1/3 (33%)	0/3 (0%)	NA (NA,NA)	NA	
LVEF (%)					
< 40	16/96 (17%)	5/86 (6%)	0.31 (0.11,0.84)	0.015	0.513
40−55	40/241 (17%)	22/248 (9%)	0.53 (0.31,0.89)	0.014	
> 55	9/50 (18%)	7/54 (13%)	0.74 (0.28,1.99)	0.554	



Information from simulated endpoint and baseline datasets. Hazard ratios for treatment B versus treatment A are based on univariate analysis using the Cox proportional hazards model. All *p*-values are from a score test.

Part III

Supporting Material

Chapter 1

Accrual and Study Status

1.1 Accrual

Table Set ACCR–4

Geographic Distribution: Number of Subjects

See Figure ACCR–4 on page 15.

		Value							
	Total	North America		Europe		Asia		Latin America	
Trt	Subjs	N	%	N	%	N	%	N	%
TOTAL	775	324	41.81	255	32.90	125	16.13	71	9.16

Geographic Distribution: Number of Sites

See Figure ACCR–4 on page 15.

		Value							
	Total	North America		Europe		Asia		Latin America	
Trt	Subjs	N	%	N	%	N	%	N	%
TOTAL	120	53	44.17	37	30.83	18	15.00	12	10.00

1.2 Study Status

Table Set STAT–1

Study Status: Current Status of Randomized Subjects

See Figure STAT–1 on page 17.

		Value									
	Total	Dead		Withdrawn from study		On study, Off treatment		On study, On treatment			P-
Trt	Subjs	N	%	N	%	N	%	N	%	Contrast	Value
A	387	65	16.80	29	7.49	107	27.65	186	48.06	A.B	0.004
B	388	34	8.76	39	10.05	130	33.51	185	47.68		

Study Status: Reason Off Treatment

See Figure STAT–1 on page 17.

			Value					
			Yes		No			P-
	Trt	Total Subjs	N	%	N	%	Contrast	Value
Subject died	A	387	43	11.11	344	88.89	A.B	0.060
	B	388	28	7.22	360	92.78		
Consent withdrawn	A	387	28	7.24	359	92.76	A.B	0.793
	B	388	30	7.73	358	92.27		
Lost to follow-up	A	387	9	2.33	378	97.67	A.B	0.293
	B	388	14	3.61	374	96.39		
Adverse event	A	387	49	12.66	338	87.34	A.B	0.007
	B	388	77	19.85	311	80.15		
Protocol violation	A	387	4	1.03	383	98.97	A.B	0.527
	B	388	6	1.55	382	98.45		
Pregnancy	A	387	0	0.00	387	100.00	A.B	1.000
	B	388	0	0.00	388	100.00		
Subject request	A	387	49	12.66	338	87.34	A.B	0.252
	B	388	39	10.05	349	89.95		
Other	A	387	19	4.91	368	95.09	A.B	0.053
	B	388	9	2.32	379	97.68		

Study Status: Reason Off Study

See Figure STAT–1 on page 17.

			Value					
			Yes		No			P-
	Trt	Total Subjs	N	%	N	%	Contrast	Value
Subject died	A	387	64	16.54	323	83.46	A.B	0.001
	B	388	33	8.51	355	91.49		
Consent withdrawn	A	387	25	6.46	362	93.54	A.B	0.341
	B	388	32	8.25	356	91.75		
Lost to follow-up	A	387	4	1.03	383	98.97	A.B	0.246
	B	388	8	2.06	380	97.94		
Other	A	387	1	0.26	386	99.74	A.B	0.316
	B	388	0	0.00	388	100.00		

Table Set STAT–2

Status Summary by Calendar Time: Treatment A

See Figure STAT–2 on page 18.

		Value							
	Total	On study, on treatment		On study, off treatment		Withdrawn from study		Dead	
Date	Subjs	N	%	N	%	N	%	N	%
Jul 01 2007	9	9	100.0	0	0.0	0	0.0	0	0.0
Oct 01 2007	105	101	96.2	3	2.9	0	0.0	1	1.0
Jan 01 2008	297	254	85.5	25	8.4	4	1.3	14	4.7
Apr 01 2008	379	277	73.1	60	15.8	9	2.4	33	8.7
Jul 01 2008	387	223	57.6	89	23.0	21	5.4	54	14.0

Status Summary by Calendar Time: Treatment B

See Figure STAT–2 on page 18.

		Value							
	Total	On study, on treatment		On study, off treatment		Withdrawn from study		Dead	
Date	Subjs	N	%	N	%	N	%	N	%
Jul 01 2007	9	9	100.0	0	0.0	0	0.0	0	0.0
Oct 01 2007	106	102	96.2	2	1.9	1	0.9	1	0.9
Jan 01 2008	298	267	89.6	20	6.7	4	1.3	7	2.3
Apr 01 2008	379	284	74.9	59	15.6	18	4.7	18	4.7
Jul 01 2008	388	220	56.7	104	26.8	35	9.0	29	7.5

Table Set STAT–3

Status Summary by Time on Study: Treatment A

See Figure STAT–3 on page 19.

		Value							
	Total	On study, on treatment		On study, off treatment		Withdrawn from study		Dead	
Months	Subjs	N	%	N	%	N	%	N	%
0	387	386	99.7	1	0.3	0	0.0	0	0.0
1	387	360	93.0	18	4.7	1	0.3	8	2.1
2	387	340	87.9	29	7.5	3	0.8	15	3.9
3	386	320	82.9	42	10.9	3	0.8	21	5.4
4	380	282	74.2	56	14.7	9	2.4	33	8.7
5	375	259	69.1	65	17.3	12	3.2	39	10.4
6	356	225	63.2	74	20.8	15	4.2	42	11.8
7	326	197	60.4	73	22.4	15	4.6	41	12.6
8	269	158	58.7	64	23.8	12	4.5	35	13.0
9	204	113	55.4	48	23.5	14	6.9	29	14.2
10	141	71	50.4	35	24.8	7	5.0	28	19.9
11	83	39	47.0	23	27.7	4	4.8	17	20.5
12	41	15	36.6	17	41.5	4	9.8	5	12.2

Status Summary by Time on Study: Treatment B

See Figure STAT–3 on page 19.

		Value							
	Total	On study, on treatment		On study, off treatment		Withdrawn from study		Dead	
Months	Subjs	N	%	N	%	N	%	N	%
0	388	387	99.7	1	0.3	0	0.0	0	0.0
1	388	367	94.6	11	2.8	5	1.3	5	1.3
2	388	340	87.6	25	6.4	13	3.4	10	2.6
3	385	323	83.9	35	9.1	14	3.6	13	3.4
4	381	305	80.1	45	11.8	17	4.5	14	3.7
5	375	275	73.3	61	16.3	22	5.9	17	4.5
6	356	233	65.4	75	21.1	24	6.7	24	6.7
7	325	206	63.4	74	22.8	21	6.5	24	7.4
8	269	153	56.9	74	27.5	17	6.3	25	9.3
9	204	110	53.9	61	29.9	17	8.3	16	7.8
10	141	72	51.1	44	31.2	13	9.2	12	8.5
11	81	42	51.9	22	27.2	11	13.6	6	7.4
12	41	20	48.8	15	36.6	5	12.2	1	2.4

Table Set STAT–4

Data Availability by Visit: Scheduled Visits

See Figure STAT–4 on page 20.

			Value			
			Visit reported in database		Visit expected, not reported	
	Trt	Total Subjs	N	%	N	%
Baseline	TOTAL	775	775	100.00	0	0.00
Month 3	TOTAL	775	691	89.16	23	2.97
Month 6	TOTAL	775	567	73.16	36	4.65
Month 9	TOTAL	775	252	32.52	54	6.97
Month 12	TOTAL	775	39	5.03	18	2.32

Chapter 2

Baseline Characteristics

2.1 Demographics

Table Set DEMO–1

Baseline Characteristics: Age (years)

See Figure DEMO–1 on page 22.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	387	56.7	7.5	56.5	51.2	61.8	44.8	69.5
B	388	57.4	7.8	57.3	52.3	63.2	43.8	70.3

Baseline Characteristics: Gender

See Figure DEMO–1 on page 22.

		Value			
	Total	Male		Female	
Trt	Subjs	N	%	N	%
A	387	260	67.18	127	32.82
B	388	264	68.04	124	31.96

Baseline Characteristics: Race

See Figure DEMO–1 on page 22.

		Value							
	Total	Black		White		Asian		Other	
Trt	Subjs	N	%	N	%	N	%	N	%
A	387	32	8.27	256	66.15	83	21.45	16	4.13
B	388	34	8.76	255	65.72	83	21.39	16	4.12

Baseline Characteristics: NYHA Class

See Figure DEMO–1 on page 22.

		Value							
	Total	Class IV		Class III		Class II		Class I	
Trt	Subjs	N	%	N	%	N	%	N	%
A	387	3	0.78	136	35.14	248	64.08	0	0.00
B	388	3	0.77	130	33.51	255	65.72	0	0.00

Baseline Characteristics: Left Ventricular Ejection Fraction (%)

See Figure DEMO–1 on page 22.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	387	45.8	8.2	46.2	40.1	51.1	31.4	59.1
B	388	46.1	8.6	46.7	40.8	52.0	30.6	60.0

2.2 Medical History

Table Set MDHX–1

Medical History: Current or Prior History of Cardiovascular Conditions/Procedures

See Figure MDHX–1 on page 23.

	Trt	Total Subjs	Value: Yes N	Yes %	No N	No %
Prior myocardial infarction	A	387	105	27.13	282	72.87
	B	388	101	26.03	287	73.97
Coronary artery bypass surgery (CABG)	A	387	36	9.30	351	90.70
	B	388	27	6.96	361	93.04
Multivessel CHD	A	387	52	13.44	335	86.56
	B	388	53	13.66	335	86.34
Cerebrovascular disease or stroke	A	387	30	7.75	357	92.25
	B	388	23	5.93	365	94.07
Transient ischaemic attack	A	387	36	9.30	351	90.70
	B	388	38	9.79	350	90.21
Angina pectoris	A	387	81	20.93	306	79.07
	B	388	85	21.91	303	78.09
Hypertension	A	387	145	37.47	242	62.53
	B	388	138	35.57	250	64.43
Congestive HF	A	387	100	25.84	287	74.16
	B	388	98	25.26	290	74.74

Medical History: Current or Prior History of Other Relevant Conditions

See Figure MDHX–1 on page 23.

	Trt	Total Subjs	Value: Yes N	Yes %	No N	No %
Diabetes mellitus	A	387	69	17.83	318	82.17
	B	388	81	20.88	307	79.12
Smoker	A	387	86	22.22	301	77.78
	B	388	91	23.45	297	76.55
Family history of premature CHD	A	387	119	30.75	268	69.25
	B	388	119	30.67	269	69.33
Cancer	A	387	29	7.49	358	92.51
	B	388	30	7.73	358	92.27

2.3 Physical Examination

Table Set VITB–1

Baseline Physical Examination: Height (cm)

See Figure VITB–1 on page 24.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	387	170.7	11.6	171.1	163.3	178.0	150.8	188.7
B	388	170.4	11.9	170.3	163.0	177.9	149.9	191.6

Baseline Physical Examination: Weight (kg)

See Figure VITB–1 on page 24.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	387	86.8	13.4	86.3	78.5	96.9	65.5	110.2
B	388	87.2	12.6	86.9	78.9	95.3	65.9	110.3

Baseline Physical Examination: BMI (kg/mˆ2)

See Figure VITB–1 on page 24.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	387	30.2	6.2	29.3	26.0	33.7	21.5	41.1
B	388	30.5	6.4	29.6	26.1	34.6	21.0	42.2

Baseline Physical Examination: Waist-to-Hip Ratio

See Figure VITB–1 on page 24.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	387	1.00	0.16	1.01	0.88	1.12	0.75	1.26
B	388	1.00	0.15	1.01	0.90	1.11	0.74	1.25

Baseline Physical Examination: Systolic Blood Pressure (mmHg)

See Figure VITB–1 on page 24.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	387	130.1	9.5	130.2	123.8	136.0	114.2	146.3
B	388	130.0	9.8	129.6	123.4	136.4	115.0	145.9

Baseline Physical Examination: Diastolic Blood Pressure (mmHg)

See Figure VITB–1 on page 24.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	387	84.6	6.4	84.5	80.3	88.8	73.3	95.3
B	388	85.0	6.5	85.1	80.6	89.6	73.4	94.7

Baseline Physical Examination: Heart Rate (bpm)

See Figure VITB–1 on page 24.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	387	65.0	7.1	64.8	60.3	70.2	53.6	76.1
B	388	64.7	7.3	63.9	59.2	70.0	53.1	76.5

2.4 Laboratory Data

Table Set LABB–1

Baseline Liver Function Test Results: Alkaline Phosphatase (IU/L)

See Figure LABB–1 on page 25.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	384	77.0	28.8	73.0	62.0	85.5	45.0	139.0
B	388	80.2	39.3	75.0	61.0	88.0	45.0	141.0

Baseline Liver Function Test Results: Alanine Amino Transferase (IU/L)

See Figure LABB–1 on page 25.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	384	16.5	11.7	15.0	11.0	19.0	7.0	25.0
B	388	17.7	11.8	16.0	12.0	19.0	7.0	57.0

Baseline Liver Function Test Results: Aspartate Amino Transferase (IU/L)

See Figure LABB–1 on page 25.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	384	21.4	10.7	19.0	16.0	23.0	11.0	52.0
B	388	21.5	11.3	20.0	16.0	23.0	11.0	51.0

Baseline Liver Function Test Results: Total Bilirubin (IU/L)

See Figure LABB–1 on page 25.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	384	8.3	6.8	7.0	5.0	9.0	3.0	16.0
B	388	8.2	6.1	7.0	5.0	9.5	2.0	14.0

Chapter 3

Adverse Events

3.1 Serious Adverse Events

Table Set SAE–1

Serious Adverse Events: Overview

See Figure SAE–1 on page 27.

			Value					
			Yes		No			
	Trt	Total Subjs	N	%	N	%	Contrast	P-Value
Any SAE	A	387	121	31.27	266	68.73	A.B	0.737
	B	388	117	30.15	271	69.85		
Multiple SAEs	A	387	37	9.56	350	90.44	A.B	0.913
	B	388	38	9.79	350	90.21		
Fatal SAE	A	387	52	13.44	335	86.56	A.B	0.007
	B	388	29	7.47	359	92.53		

Serious Adverse Events: First Serious Adverse Event Probability over Time

See Figure SAE–1 on page 27.

Weeks	Trt	nRisk	nEvents	% w/ Event	95% CI
0	A	387	1	0.3	(0.0, 0.8)
	B	388	5	1.3	(0.2, 2.4)
3	A	377	12	3.1	(1.4, 4.8)
	B	377	13	3.4	(1.5, 5.1)
6	A	364	26	6.7	(4.2, 9.2)
	B	364	30	7.7	(5.0, 10.4)
9	A	358	36	9.3	(6.4, 12.2)
	B	353	37	9.5	(6.6, 12.4)
12	A	342	48	12.4	(9.1, 15.6)
	B	346	45	11.6	(8.4, 14.7)
15	A	337	51	13.2	(9.7, 16.5)
	B	333	55	14.2	(10.6, 17.6)
18	A	325	59	15.3	(11.6, 18.8)
	B	322	67	17.3	(13.5, 21.0)

(Continued on next page.)

(Continued from previous page.)

Serious Adverse Events: First Serious Adverse Event Probability over Time

See Figure SAE–1 on page 27.

Weeks	Trt	nRisk	nEvents	% w/ Event	95% CI
21	A	315	70	18.2	(14.2, 21.9)
	B	308	76	19.7	(15.6, 23.6)
24	A	292	82	21.4	(17.2, 25.4)
	B	288	88	22.9	(18.6, 27.0)
27	A	276	86	22.5	(18.2, 26.6)
	B	269	95	24.9	(20.4, 29.1)
30	A	254	96	25.4	(20.9, 29.7)
	B	252	96	25.2	(20.7, 29.4)
33	A	219	101	27.1	(22.4, 31.5)
	B	221	101	26.7	(22.1, 31.1)
36	A	186	105	28.5	(23.7, 33.0)
	B	183	104	27.8	(23.1, 32.3)
39	A	147	111	31.1	(26.0, 35.9)
	B	150	109	30.1	(25.1, 34.8)
42	A	111	114	32.8	(27.4, 37.7)
	B	113	113	32.3	(26.9, 37.3)
45	A	83	116	34.1	(28.5, 39.3)
	B	85	114	33.0	(27.5, 38.1)
48	A	53	119	37.2	(30.7, 43.1)
	B	55	115	34.3	(28.3, 39.7)
51	A	30	120	39.3	(31.6, 46.1)
	B	34	115	34.3	(28.3, 39.7)
54	A	15	120	39.3	(31.6, 46.1)
	B	20	116	36.6	(29.1, 43.3)
57	A	7	120	39.3	(31.6, 46.1)
	B	6	117	40.1	(29.8, 48.9)
60	A	4	121	49.4	(26.2, 65.3)
	B	3	117	40.1	(29.8, 48.9)
63	A	3	121	49.4	(26.2, 65.3)
	B	1	117	40.1	(29.8, 48.9)
66	A	0	121	49.4	(26.2, 65.3)
	B	0	117	40.1	(29.8, 48.9)

Table Set SAE–2

SAEs by System Organ Class: System Organ Class

See Figure SAE–2 on page 28.

			Value					
		Total	Yes		No			P-
	Trt	Subjs	N	%	N	%	Contrast	Value
Blood, lymphatic	A	387	13	3.36	374	96.64	A.B	0.674
	B	388	11	2.84	377	97.16		

(Continued on next page.)

(Continued from previous page.)

SAEs by System Organ Class: System Organ Class

See Figure SAE–2 on page 28.

			Value					
			Yes		No			
	Trt	Total Subjs	N	%	N	%	Contrast	P-Value
Cardiac	A	387	42	10.85	345	89.15	A.B	0.328
	B	388	34	8.76	354	91.24		
Congenital, familial, genetic	A	387	5	1.29	382	98.71	A.B	0.564
	B	388	7	1.80	381	98.20		
Ear, labyrinth	A	387	2	0.52	385	99.48	A.B	0.998
	B	388	2	0.52	386	99.48		
Endocrine	A	387	4	1.03	383	98.97	A.B	0.702
	B	388	3	0.77	385	99.23		
Eye	A	387	4	1.03	383	98.97	A.B	0.527
	B	388	6	1.55	382	98.45		
Gastrointestinal	A	387	10	2.58	377	97.42	A.B	0.031
	B	388	22	5.67	366	94.33		
General, administration site	A	387	3	0.78	384	99.22	A.B	0.082
	B	388	0	0.00	388	100.00		
Hepatobiliary	A	387	7	1.81	380	98.19	A.B	0.558
	B	388	5	1.29	383	98.71		
Immune system	A	387	5	1.29	382	98.71	A.B	0.997
	B	388	5	1.29	383	98.71		
Infections, infestations	A	387	10	2.58	377	97.42	A.B	0.830
	B	388	11	2.84	377	97.16		
Injury, poisoning, procedural	A	387	6	1.55	381	98.45	A.B	0.758
	B	388	5	1.29	383	98.71		
Investigations	A	387	13	3.36	374	96.64	A.B	0.705
	B	388	15	3.87	373	96.13		
Metabolism, nutrition	A	387	3	0.78	384	99.22	A.B	0.082
	B	388	0	0.00	388	100.00		

SAEs by System Organ Class: System Organ Class

See Figure SAE–2 on page 28.

			Value					
			Yes		No			
	Trt	Total Subjs	N	%	N	%	Contrast	P-Value
Musculoskeletal, connective tissue	A	387	1	0.26	386	99.74	A.B	0.058
	B	388	6	1.55	382	98.45		
Neoplasms	A	387	6	1.55	381	98.45	A.B	0.593
	B	388	8	2.06	380	97.94		
Nervous system	A	387	3	0.78	384	99.22	A.B	0.652
	B	388	2	0.52	386	99.48		
Pregnancy	A	387	0	0.00	387	100.00	A.B	0.318
	B	388	1	0.26	387	99.74		
Psychiatric	A	387	14	3.62	373	96.38	A.B	0.475
	B	388	18	4.64	370	95.36		

(Continued on next page.)

(Continued from previous page.)

SAEs by System Organ Class: System Organ Class

See Figure SAE–2 on page 28.

			Value					
			Yes		No			
	Trt	Total Subjs	N	%	N	%	Contrast	P-Value
Renal, urinary	A	387	5	1.29	382	98.71	A.B	0.253
	B	388	2	0.52	386	99.48		
Reproductive, breast	A	387	9	2.33	378	97.67	A.B	0.161
	B	388	4	1.03	384	98.97		
Respiratory, thoracic, mediastinal	A	387	6	1.55	381	98.45	A.B	0.996
	B	388	6	1.55	382	98.45		
Skin, subcutaneous tissue	A	387	9	2.33	378	97.67	A.B	0.996
	B	388	9	2.32	379	97.68		
Social circumstances	A	387	15	3.88	372	96.12	A.B	0.211
	B	388	9	2.32	379	97.68		
Surgical, medical procedures	A	387	16	4.13	371	95.87	A.B	0.229
	B	388	10	2.58	378	97.42		
Vascular	A	387	7	1.81	380	98.19	A.B	0.343
	B	388	11	2.84	377	97.16		
– Uncoded –	A	387	0	0.00	387	100.00	A.B	1.000
	B	388	0	0.00	388	100.00		

3.2 Adverse Events

Table Set AE–1

Adverse Events: Overview

See Figure AE–1 on page 30.

			Value					
			Yes		No			
	Trt	Total Subjs	N	%	N	%	Contrast	P-Value
Any AE	A	387	197	50.90	190	49.10	A.B	0.640
	B	388	191	49.23	197	50.77		
AE related to investigational product	A	387	79	20.41	308	79.59	A.B	0.914
	B	388	78	20.10	310	79.90		

Adverse Events: Actions Taken with IP Due to Any AE

See Figure AE–1 on page 30.

			Value					
			Yes		No			
	Trt	Total Subjs	N	%	N	%	Contrast	P-Value
IP withdrawn	A	387	66	17.05	321	82.95	A.B	0.585
	B	388	72	18.56	316	81.44		
Dose reduced	A	387	88	22.74	299	77.26	A.B	0.219
	B	388	103	26.55	285	73.45		
Dose increased	A	387	1	0.26	386	99.74	A.B	0.999
	B	388	1	0.26	387	99.74		

(Continued on next page.)

(Continued from previous page.)

Adverse Events: Actions Taken with IP Due to Any AE

See Figure AE–1 on page 30.

			Value					
		Total	Yes		No			P-
	Trt	Subjs	N	%	N	%	Contrast	Value
Dose unchanged	A	387	128	33.07	259	66.93	A.B	0.096
	B	388	107	27.58	281	72.42		
Dose interrupted	A	387	35	9.04	352	90.96	A.B	0.891
	B	388	34	8.76	354	91.24		

Adverse Events: Subject Actions Taken Due to Any AE

See Figure AE–1 on page 30.

		Value					
	Total	Withdrawn from study		Not withdrawn from study			P-
Trt	Subjs	N	%	N	%	Contrast	Value
A	387	8	2.07	379	97.93	A.B	0.637
B	388	10	2.58	378	97.42		

Table Set AE–2

AEs by System Organ Class and Severity: System Organ Class

See Figure AE–2 on page 31.

			Value									
		Total	Severe		Moderate		Mild		None			P-
	Trt	Subjs	N	%	N	%	N	%	N	%	Contrast	Value
*** OVERALL ***	A	387	28	7.24	35	9.04	134	34.63	190	49.10	A.B	0.594
	B	388	30	7.73	27	6.96	134	34.54	197	50.77		
Blood, lymphatic	A	387	4	1.03	1	0.26	23	5.94	359	92.76	A.B	0.769
	B	388	1	0.26	4	1.03	21	5.41	362	93.30		
Cardiac	A	387	14	3.62	10	2.58	81	20.93	282	72.87	A.B	0.113
	B	388	8	2.06	13	3.35	65	16.75	302	77.84		
Congenital, familial, genetic	A	387	2	0.52	3	0.78	11	2.84	371	95.87	A.B	0.555
	B	388	1	0.26	1	0.26	11	2.84	375	96.65		
Ear, labyrinth	A	387	0	0.00	0	0.00	5	1.29	382	98.71	A.B	0.756
	B	388	1	0.26	2	0.52	3	0.77	382	98.45		
Endocrine	A	387	0	0.00	2	0.52	15	3.88	370	95.61	A.B	0.348
	B	388	1	0.26	2	0.52	9	2.32	376	96.91		
Eye	A	387	3	0.78	4	1.03	8	2.07	372	96.12	A.B	0.541
	B	388	2	0.52	1	0.26	9	2.32	376	96.91		
Gastrointestinal	A	387	1	0.26	0	0.00	22	5.68	364	94.06	A.B	0.000
	B	388	7	1.80	7	1.80	38	9.79	336	86.60		
General, administration site	A	387	0	0.00	1	0.26	7	1.81	379	97.93	A.B	0.401
	B	388	1	0.26	0	0.00	4	1.03	383	98.71		
Hepatobiliary	A	387	2	0.52	3	0.78	16	4.13	366	94.57	A.B	0.490
	B	388	1	0.26	1	0.26	15	3.87	371	95.62		
Immune system	A	387	1	0.26	1	0.26	8	2.07	377	97.42	A.B	0.816
	B	388	0	0.00	3	0.77	6	1.55	379	97.68		

(Continued on next page.)

(Continued from previous page.)

AEs by System Organ Class and Severity: System Organ Class

See Figure AE–2 on page 31.

			Value									
		Total	Severe		Moderate		Mild		None			P-
	Trt	Subjs	N	%	N	%	N	%	N	%	Contrast	Value
Infections, infestations	A	387	2	0.52	3	0.78	15	3.88	367	94.83	A.B	0.974
	B	388	1	0.26	1	0.26	18	4.64	368	94.85		
Injury, poisoning, procedural	A	387	1	0.26	1	0.26	12	3.10	373	96.38	A.B	0.846
	B	388	1	0.26	3	0.77	11	2.84	373	96.13		
Investigations	A	387	0	0.00	4	1.03	34	8.79	349	90.18	A.B	0.566
	B	388	3	0.77	5	1.29	25	6.44	355	91.49		

AEs by System Organ Class and Severity: System Organ Class

See Figure AE–2 on page 31.

			Value									
		Total	Severe		Moderate		Mild		None			P-
	Trt	Subjs	N	%	N	%	N	%	N	%	Contrast	Value
Metabolism, nutrition	A	387	1	0.26	2	0.52	5	1.29	379	97.93	A.B	0.128
	B	388	1	0.26	0	0.00	2	0.52	385	99.23		
Musculoskeletal, connective tissue	A	387	0	0.00	2	0.52	3	0.78	382	98.71	A.B	0.405
	B	388	2	0.52	0	0.00	6	1.55	380	97.94		
Neoplasms	A	387	2	0.52	6	1.55	10	2.58	369	95.35	A.B	0.551
	B	388	1	0.26	3	0.77	18	4.64	366	94.33		
Nervous system	A	387	1	0.26	0	0.00	4	1.03	382	98.71	A.B	0.476
	B	388	0	0.00	1	0.26	2	0.52	385	99.23		
Pregnancy	A	387	0	0.00	0	0.00	1	0.26	386	99.74	A.B	0.564
	B	388	0	0.00	1	0.26	1	0.26	386	99.48		
Psychiatric	A	387	6	1.55	8	2.07	31	8.01	342	88.37	A.B	0.336
	B	388	5	1.29	5	1.29	27	6.96	351	90.46		
Renal, urinary	A	387	0	0.00	1	0.26	12	3.10	374	96.64	A.B	0.179
	B	388	1	0.26	2	0.52	4	1.03	381	98.20		
Reproductive, breast	A	387	5	1.29	3	0.78	19	4.91	360	93.02	A.B	0.471
	B	388	3	0.77	7	1.80	12	3.09	366	94.33		
Respiratory, thoracic, mediastinal	A	387	4	1.03	3	0.78	21	5.43	359	92.76	A.B	0.311
	B	388	1	0.26	7	1.80	28	7.22	352	90.72		
Skin, subcutaneous tissue	A	387	2	0.52	7	1.81	15	3.88	363	93.80	A.B	0.094
	B	388	2	0.52	6	1.55	29	7.47	351	90.46		
Social circumstances	A	387	5	1.29	2	0.52	30	7.75	350	90.44	A.B	0.156
	B	388	5	1.29	3	0.77	18	4.64	362	93.30		
Surgical, medical procedures	A	387	7	1.81	8	2.07	22	5.68	350	90.44	A.B	0.463
	B	388	3	0.77	2	0.52	27	6.96	356	91.75		
Vascular	A	387	1	0.26	2	0.52	9	2.33	375	96.90	A.B	0.029
	B	388	2	0.52	4	1.03	19	4.90	363	93.56		
– Uncoded –	A	387	0	0.00	0	0.00	0	0.00	387	100.00	A.B	1.000
	B	388	0	0.00	0	0.00	0	0.00	388	100.00		

Table Set AE–3

Most Common AEs by Preferred Term: Preferred Term

See Figure AE–3 on page 32.

			Value									
		Total	Severe		Moderate		Mild		None			P-
	Trt	Subjs	N	%	N	%	N	%	N	%	Contrast	Value
Chronic obstructive airway	A	387	15	3.88	28	7.24	83	21.45	261	67.44	A.B	0.000
	B	388	7	1.80	16	4.12	59	15.21	306	78.87		
Diarrhoea	A	387	5	1.29	10	2.58	31	8.01	341	88.11	A.B	0.004
	B	388	6	1.55	17	4.38	53	13.66	312	80.41		
Nausea	A	387	1	0.26	6	1.55	14	3.62	366	94.57	A.B	0.000
	B	388	8	2.06	16	4.12	68	17.53	296	76.29		
Upper respiratory tract infection	A	387	7	1.81	9	2.33	49	12.66	322	83.20	A.B	0.146
	B	388	8	2.06	15	3.87	26	6.70	339	87.37		
Abdominal pain	A	387	4	1.03	9	2.33	31	8.01	343	88.63	A.B	0.147
	B	388	3	0.77	13	3.35	42	10.82	330	85.05		
Dyspepsia	A	387	1	0.26	4	1.03	7	1.81	375	96.90	A.B	0.000
	B	388	4	1.03	9	2.32	30	7.73	345	88.92		
Headache	A	387	1	0.26	6	1.55	16	4.13	364	94.06	A.B	0.062
	B	388	4	1.03	6	1.55	27	6.96	351	90.46		
Vomiting	A	387	3	0.78	3	0.78	7	1.81	374	96.64	A.B	0.002
	B	388	2	0.52	7	1.80	25	6.44	354	91.24		
Sinusitis	A	387	1	0.26	5	1.29	24	6.20	357	92.25	A.B	0.921
	B	388	3	0.77	7	1.80	19	4.90	359	92.53		
Injury	A	387	4	1.03	4	1.03	23	5.94	356	91.99	A.B	0.381
	B	388	3	0.77	8	2.06	27	6.96	350	90.21		
Infection viral	A	387	5	1.29	5	1.29	19	4.91	358	92.51	A.B	0.468
	B	388	1	0.26	8	2.06	15	3.87	364	93.81		
Dizziness	A	387	2	0.52	0	0.00	15	3.88	370	95.61	A.B	0.002
	B	388	4	1.03	6	1.55	29	7.47	349	89.95		
Coughing	A	387	5	1.29	6	1.55	17	4.39	359	92.76	A.B	0.086
	B	388	0	0.00	6	1.55	11	2.84	371	95.62		
Insomnia	A	387	3	0.78	2	0.52	11	2.84	371	95.87	A.B	0.018
	B	388	3	0.77	7	1.80	22	5.67	356	91.75		
Back pain	A	387	1	0.26	3	0.78	20	5.17	363	93.80	A.B	0.455
	B	388	1	0.26	7	1.80	11	2.84	369	95.10		

Most Common AEs by Preferred Term: Preferred Term

See Figure AE–3 on page 32.

			Value									
		Total	Severe		Moderate		Mild		None			P-
	Trt	Subjs	N	%	N	%	N	%	N	%	Contrast	Value
Rhinitis	A	387	1	0.26	5	1.29	14	3.62	367	94.83	A.B	0.609
	B	388	2	0.52	3	0.77	12	3.09	371	95.62		
Flatulence	A	387	0	0.00	1	0.26	8	2.07	378	97.67	A.B	0.001
	B	388	1	0.26	4	1.03	23	5.93	360	92.78		
Dyspnoea	A	387	3	0.78	6	1.55	14	3.62	364	94.06	A.B	0.056
	B	388	0	0.00	5	1.29	7	1.80	376	96.91		
Chest pain	A	387	0	0.00	3	0.78	17	4.39	367	94.83	A.B	0.023
	B	388	1	0.26	4	1.03	3	0.77	380	97.94		
Bronchitis	A	387	3	0.78	1	0.26	6	1.55	377	97.42	A.B	0.458
	B	388	1	0.26	2	0.52	4	1.03	381	98.20		
Respiratory disorder	A	387	3	0.78	2	0.52	4	1.03	378	97.67	A.B	0.301
	B	388	3	0.77	1	0.26	10	2.58	374	96.39		
Anorexia	A	387	0	0.00	5	1.29	5	1.29	377	97.42	A.B	0.405
	B	388	2	0.52	6	1.55	6	1.55	374	96.39		
Pain	A	387	0	0.00	3	0.78	5	1.29	379	97.93	A.B	0.363
	B	388	2	0.52	4	1.03	6	1.55	376	96.91		
Fatigue	A	387	0	0.00	2	0.52	3	0.78	382	98.71	A.B	0.058
	B	388	2	0.52	1	0.26	10	2.58	375	96.65		
Gastroesophageal reflux	A	387	0	0.00	1	0.26	4	1.03	382	98.71	A.B	0.024
	B	388	2	0.52	0	0.00	13	3.35	373	96.13		
Flash	A	387	1	0.26	2	0.52	7	1.81	377	97.42	A.B	0.995
	B	388	1	0.26	2	0.52	7	1.80	378	97.42		
Hyperkalemia	A	387	1	0.26	0	0.00	8	2.07	378	97.67	A.B	0.810
	B	388	1	0.26	3	0.77	6	1.55	378	97.42		
Melena	A	387	1	0.26	5	1.29	6	1.55	375	96.90	A.B	0.704
	B	388	1	0.26	4	1.03	9	2.32	374	96.39		
Urinary tract infection	A	387	1	0.26	2	0.52	4	1.03	380	98.19	A.B	0.180
	B	388	1	0.26	2	0.52	10	2.58	375	96.65		
Myalgia	A	387	0	0.00	1	0.26	5	1.29	381	98.45	A.B	0.310
	B	388	1	0.26	3	0.77	6	1.55	378	97.42		

Chapter 4

Central Laboratory Measures

4.1 Liver Function Tests

Table Set LFTABN–1

Summary of Liver Function Test Elevations: Highest Elevation after Baseline

See Figure LFTABN–1 on page 36.

		Treatment Group					
		A		B			P-
	Value	N	%	N	%	Contrast	Value
Alkaline Phosphatase	Total Subjs	351		352		A.B	0.729
	>3 xULN	2	0.57	1	0.28		
	>2-3 xULN	13	3.70	6	1.70		
	>1-2 xULN	36	10.26	42	11.93		
	≤ ULN	300	85.47	303	86.08		
Alanine Aminotransferase	Total Subjs	351		352		A.B	0.824
	>3 xULN	1	0.28	0	0.00		
	>2-3 xULN	0	0.00	4	1.14		
	>1-2 xULN	36	10.26	31	8.81		
	≤ ULN	314	89.46	317	90.06		
Aspartate Aminotransferase	Total Subjs	351		352		A.B	0.137
	>3 xULN	0	0.00	1	0.28		
	>2-3 xULN	4	1.14	0	0.00		
	>1-2 xULN	29	8.26	45	12.78		
	≤ ULN	318	90.60	306	86.93		
Total Bilirubin	Total Subjs	351		352		A.B	0.693
	>3 xULN	1	0.28	2	0.57		
	>2-3 xULN	3	0.85	5	1.42		
	>1-2 xULN	30	8.55	30	8.52		
	≤ ULN	317	90.31	315	89.49		

Table Set LFT–1

Alkaline Phosphatase: Measurements at Scheduled Visits (IU/L)

See Figure LFT–1 on page 37.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	384	77.0	28.8	73.0	62.0	85.5	45.0	139.0	A.B	0.469
	B	388	80.2	39.3	75.0	61.0	88.0	45.0	141.0		
Month 3	A	351	82.7	36.9	77.0	64.0	91.0	46.0	151.0	A.B	0.000
	B	352	88.1	32.5	84.0	73.0	98.0	51.0	150.0		
Month 6	A	284	83.5	43.1	77.0	64.0	91.0	48.0	156.0	A.B	0.000
	B	301	88.8	36.9	84.0	68.0	99.0	51.0	140.0		
Month 9	A	147	82.1	34.8	76.0	64.0	88.0	50.0	154.0	A.B	0.005
	B	149	87.9	36.0	83.0	70.0	97.0	50.0	120.0		
Month 12	A	30	97.8	57.0	85.5	68.0	98.0	51.0	270.0	A.B	0.848
	B	27	85.3	20.8	80.0	72.0	95.0	61.0	113.0		

Alkaline Phosphatase: Above Upper Limit of Normal (125 IU/L)

See Figure LFT–1 on page 37.

			Value									
		Total	>3 xULN		>2-3 xULN		>1-2 xULN		≤ ULN			P-
	Trt	Subjs	N	%	N	%	N	%	N	%	Contrast	Value
Baseline	A	384	1	0.26	0	0.00	20	5.21	363	94.53	A.B	0.988
	B	388	2	0.52	5	1.29	14	3.61	367	94.59		
Month 3	A	351	0	0.00	6	1.71	16	4.56	329	93.73	A.B	0.696
	B	352	1	0.28	0	0.00	24	6.82	327	92.90		
Month 6	A	284	2	0.70	3	1.06	14	4.93	265	93.31	A.B	0.594
	B	301	0	0.00	4	1.33	13	4.32	284	94.35		
Month 9	A	147	0	0.00	2	1.36	7	4.76	138	93.88	A.B	0.593
	B	149	0	0.00	2	1.34	5	3.36	142	95.30		
Month 12	A	30	0	0.00	2	6.67	1	3.33	27	90.00	A.B	0.339
	B	27	0	0.00	0	0.00	1	3.70	26	96.30		

Alkaline Phosphatase: Absolute Change from Baseline (IU/L)

See Figure LFT–1 on page 37.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	348	6.3	46.4	5.0	-16.0	22.0	-48.0	77.0	A.B	0.014
	B	352	7.7	52.2	11.0	-10.0	29.0	-59.0	66.0		
Month 6	A	281	7.2	52.6	4.0	-14.0	21.0	-53.0	63.0	A.B	0.021
	B	301	8.6	51.7	11.0	-11.0	29.0	-55.0	72.0		
Month 9	A	145	4.3	50.8	2.0	-15.0	21.0	-57.0	64.0	A.B	0.071
	B	149	10.3	55.1	10.0	-9.0	33.0	-36.0	66.0		
Month 12	A	30	21.2	64.3	9.5	-9.0	32.0	-84.0	194.0	A.B	1.000
	B	27	12.5	31.1	16.0	-10.0	25.0	-41.0	56.0		

Table Set LFT–2

Alanine Amino Transferase: Measurements at Scheduled Visits (IU/L)

See Figure LFT–2 on page 38.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	384	16.5	11.7	15.0	11.0	19.0	7.0	25.0	A.B	0.229
	B	388	17.7	11.8	16.0	12.0	19.0	7.0	57.0		
Month 3	A	351	17.7	12.7	16.0	12.0	19.0	8.0	27.0	A.B	0.000
	B	352	19.6	12.7	18.0	14.0	22.0	6.0	34.0		
Month 6	A	284	19.0	11.9	17.0	13.0	20.5	8.0	60.0	A.B	0.055
	B	301	20.3	14.6	18.0	14.0	22.0	8.0	37.0		
Month 9	A	147	17.0	9.8	15.0	12.0	19.0	7.0	29.0	A.B	0.001
	B	149	19.7	12.9	18.0	14.0	23.0	7.0	30.0		
Month 12	A	30	17.4	9.8	16.0	13.0	22.0	5.0	25.0	A.B	0.810
	B	27	20.2	14.5	16.0	13.0	21.0	9.0	66.0		

Alanine Amino Transferase: Above Upper Limit of Normal (48 IU/L)

See Figure LFT–2 on page 38.

			Value									
		Total	>3 xULN		>2-3 xULN		>1-2 xULN		≤ ULN			P-
	Trt	Subjs	N	%	N	%	N	%	N	%	Contrast	Value
Baseline	A	384	1	0.26	1	0.26	9	2.34	373	97.14	A.B	0.056
	B	388	0	0.00	1	0.26	21	5.41	366	94.33		
Month 3	A	351	1	0.28	0	0.00	13	3.70	337	96.01	A.B	0.857
	B	352	0	0.00	1	0.28	14	3.98	337	95.74		
Month 6	A	284	0	0.00	0	0.00	17	5.99	267	94.01	A.B	0.609
	B	301	0	0.00	2	0.66	13	4.32	286	95.02		
Month 9	A	147	0	0.00	0	0.00	5	3.40	142	96.60	A.B	0.729
	B	149	0	0.00	1	0.67	3	2.01	145	97.32		
Month 12	A	30	0	0.00	0	0.00	1	3.33	29	96.67	A.B	0.495
	B	27	0	0.00	0	0.00	2	7.41	25	92.59		

Alanine Amino Transferase: Absolute Change from Baseline (IU/L)

See Figure LFT–2 on page 38.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	348	1.2	17.5	0.0	-5.0	6.0	-13.0	17.0	A.B	0.104
	B	352	1.8	18.2	2.0	-4.0	8.0	-37.0	22.0		
Month 6	A	281	2.6	17.7	2.0	-3.0	7.0	-14.0	36.0	A.B	0.962
	B	301	2.1	18.9	2.0	-4.0	8.0	-36.0	25.0		
Month 9	A	145	-0.7	19.6	1.0	-5.0	7.0	-20.0	19.0	A.B	0.123
	B	149	1.8	18.2	3.0	-4.0	8.0	-32.0	16.0		
Month 12	A	30	4.9	11.3	3.0	-3.0	10.0	-12.0	22.0	A.B	0.410
	B	27	3.3	17.9	2.0	-5.0	7.0	-17.0	52.0		

Table Set LFT–3

Aspartate Amino Transferase: Measurements at Scheduled Visits (IU/L)

See Figure LFT–3 on page 39.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	384	21.4	10.7	19.0	16.0	23.0	11.0	52.0	A.B	0.852
	B	388	21.5	11.3	20.0	16.0	23.0	11.0	51.0		
Month 3	A	351	22.0	12.8	20.0	16.0	23.0	11.0	52.0	A.B	0.000
	B	352	23.1	10.4	22.0	18.0	25.0	12.0	36.0		
Month 6	A	284	20.9	8.8	19.5	16.0	23.0	12.0	31.0	A.B	0.000
	B	301	24.2	12.7	22.0	18.0	27.0	11.0	59.0		
Month 9	A	147	21.9	10.5	20.0	18.0	24.0	11.0	32.0	A.B	0.149
	B	149	22.8	10.2	22.0	17.0	26.0	12.0	32.0		
Month 12	A	30	20.6	8.7	19.0	16.0	22.0	14.0	29.0	A.B	0.097
	B	27	28.8	29.0	21.0	18.0	25.0	13.0	60.0		

Aspartate Amino Transferase: Above Upper Limit of Normal (42-55 IU/L)

See Figure LFT–3 on page 39.

			Value									
		Total	>3 xULN		>2-3 xULN		>1-2 xULN		≤ ULN			P-
	Trt	Subjs	N	%	N	%	N	%	N	%	Contrast	Value
Baseline	A	384	0	0.00	1	0.26	21	5.47	362	94.27	A.B	0.979
	B	388	0	0.00	2	0.52	20	5.15	366	94.33		
Month 3	A	351	0	0.00	3	0.85	16	4.56	332	94.59	A.B	0.707
	B	352	0	0.00	0	0.00	17	4.83	335	95.17		
Month 6	A	284	0	0.00	0	0.00	10	3.52	274	96.48	A.B	0.062
	B	301	0	0.00	0	0.00	21	6.98	280	93.02		
Month 9	A	147	0	0.00	1	0.68	4	2.72	142	96.60	A.B	0.786
	B	149	0	0.00	0	0.00	6	4.03	143	95.97		
Month 12	A	30	0	0.00	0	0.00	1	3.33	29	96.67	A.B	0.248
	B	27	1	3.70	0	0.00	2	7.41	24	88.89		

Aspartate Amino Transferase: Absolute Change from Baseline (IU/L)

See Figure LFT–3 on page 39.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	348	0.4	16.5	0.0	-5.0	5.0	-29.0	23.0	A.B	0.003
	B	352	1.8	15.2	2.0	-4.0	7.5	-22.0	27.0		
Month 6	A	281	-0.5	13.5	0.0	-5.0	6.0	-22.0	14.0	A.B	0.024
	B	301	2.3	17.3	2.0	-4.0	9.0	-27.0	37.0		
Month 9	A	145	2.4	13.8	1.0	-2.0	6.0	-11.0	16.0	A.B	0.280
	B	149	-0.8	16.1	2.0	-6.0	6.0	-37.0	15.0		
Month 12	A	30	1.3	11.7	0.0	-4.0	6.0	-10.0	18.0	A.B	0.276
	B	27	4.7	36.3	3.0	-2.0	8.0	-48.0	42.0		

Table Set LFT–4

Total Bilirubin: Measurements at Scheduled Visits (IU/L)

See Figure LFT–4 on page 40.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	384	8.3	6.8	7.0	5.0	9.0	3.0	16.0	A.B	0.933
	B	388	8.2	6.1	7.0	5.0	9.5	2.0	14.0		
Month 3	A	351	7.8	6.1	7.0	5.0	9.0	2.0	14.0	A.B	0.001
	B	352	8.6	6.4	8.0	6.0	10.0	2.0	14.0		
Month 6	A	284	8.5	6.0	7.0	5.0	10.0	3.0	26.0	A.B	0.249
	B	301	8.9	6.6	7.0	6.0	10.0	2.0	27.0		
Month 9	A	147	7.7	4.9	7.0	5.0	9.0	2.0	12.0	A.B	0.109
	B	149	8.9	8.1	8.0	5.0	10.0	3.0	17.0		
Month 12	A	30	8.8	9.3	6.0	5.0	9.0	2.0	28.0	A.B	0.070
	B	27	11.3	10.4	8.0	6.0	12.0	5.0	30.0		

Total Bilirubin: Above Upper Limit of Normal (22 IU/L)

See Figure LFT–4 on page 40.

			Value									
		Total	>3 xULN		>2-3 xULN		>1-2 xULN		≤ ULN			P-
	Trt	Subjs	N	%	N	%	N	%	N	%	Contrast	Value
Baseline	A	384	2	0.52	1	0.26	14	3.65	367	95.57	A.B	0.979
	B	388	0	0.00	4	1.03	13	3.35	371	95.62		
Month 3	A	351	1	0.28	1	0.28	9	2.56	340	96.87	A.B	0.685
	B	352	1	0.28	1	0.28	11	3.12	339	96.31		
Month 6	A	284	0	0.00	1	0.35	16	5.63	267	94.01	A.B	0.734
	B	301	0	0.00	2	0.66	14	4.65	285	94.68		
Month 9	A	147	0	0.00	0	0.00	6	4.08	141	95.92	A.B	0.761
	B	149	1	0.67	1	0.67	3	2.01	144	96.64		
Month 12	A	30	0	0.00	1	3.33	1	3.33	28	93.33	A.B	0.569
	B	27	0	0.00	1	3.70	2	7.41	24	88.89		

Total Bilirubin: Absolute Change from Baseline (IU/L)

See Figure LFT–4 on page 40.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	348	-0.5	8.9	0.0	-4.0	3.0	-10.0	8.0	A.B	0.053
	B	352	0.4	9.0	0.0	-3.0	4.0	-9.0	11.0		
Month 6	A	281	0.4	8.9	0.0	-3.0	4.0	-10.0	18.0	A.B	0.287
	B	301	0.5	9.3	1.0	-3.0	4.0	-10.0	11.0		
Month 9	A	145	-0.0	7.6	0.0	-3.0	3.0	-10.0	7.0	A.B	0.725
	B	149	0.5	10.3	0.0	-3.0	3.0	-11.0	11.0		
Month 12	A	30	1.9	9.3	-1.0	-3.0	3.0	-5.0	23.0	A.B	0.068
	B	27	3.0	13.6	2.0	-1.0	5.0	-4.0	25.0		

4.2 Clinical Chemistry

Table Set CHEMABN–1

Summary of Abnormal Clinical Chemistry Values: Ever Below LLN

See Figure CHEMABN–1 on page 41.

			Value					
		Total	Yes		No			P-
	Trt	Subjs	N	%	N	%	Contrast	Value
LDL Cholesterol	A	351	0	0.00	351	100.00	A.B	1.000
	B	352	0	0.00	352	100.00		
HDL Cholesterol	A	351	167	47.58	184	52.42	A.B	0.122
	B	352	188	53.41	164	46.59		
Total Cholesterol	A	351	0	0.00	351	100.00	A.B	1.000
	B	352	0	0.00	352	100.00		
Triglycerides	A	351	0	0.00	351	100.00	A.B	1.000
	B	352	0	0.00	352	100.00		
Sodium	A	387	26	6.72	361	93.28	A.B	0.682
	B	388	29	7.47	359	92.53		
Potassium	A	387	8	2.07	379	97.93	A.B	0.368
	B	388	12	3.09	376	96.91		
Chloride	A	387	8	2.07	379	97.93	A.B	0.399
	B	388	5	1.29	383	98.71		
Bicarbonate	A	387	64	16.54	323	83.46	A.B	0.646
	B	388	69	17.78	319	82.22		
Blood Urea Nitrogen	A	387	0	0.00	387	100.00	A.B	1.000
	B	388	0	0.00	388	100.00		
Creatinine	A	387	2	0.52	385	99.48	A.B	0.561
	B	388	1	0.26	387	99.74		
Glucose	A	387	12	3.10	375	96.90	A.B	0.503
	B	388	9	2.32	379	97.68		
Calcium	A	387	14	3.62	373	96.38	A.B	0.715
	B	388	16	4.12	372	95.88		

Summary of Abnormal Clinical Chemistry Values: Ever Above ULN

See Figure CHEMABN–1 on page 41.

			Value					
		Total	Yes		No			P-
	Trt	Subjs	N	%	N	%	Contrast	Value
LDL Cholesterol	A	351	124	35.33	227	64.67	A.B	0.224
	B	352	140	39.77	212	60.23		
HDL Cholesterol	A	351	0	0.00	351	100.00	A.B	1.000
	B	352	0	0.00	352	100.00		
Total Cholesterol	A	351	122	34.76	229	65.24	A.B	0.671
	B	352	117	33.24	235	66.76		
Triglycerides	A	351	198	56.41	153	43.59	A.B	0.271
	B	352	184	52.27	168	47.73		

(Continued on next page.)

(Continued from previous page.)

Summary of Abnormal Clinical Chemistry Values: Ever Above ULN

See Figure CHEMABN–1 on page 41.

			Value					
			Yes		No			
	Trt	Total Subjs	N	%	N	%	Contrast	P-Value
Sodium	A	387	36	9.30	351	90.70	A.B	0.911
	B	388	37	9.54	351	90.46		
Potassium	A	387	65	16.80	322	83.20	A.B	0.582
	B	388	71	18.30	317	81.70		
Chloride	A	387	25	6.46	362	93.54	A.B	0.411
	B	388	31	7.99	357	92.01		
Bicarbonate	A	387	11	2.84	376	97.16	A.B	0.837
	B	388	12	3.09	376	96.91		
Blood Urea Nitrogen	A	387	207	53.49	180	46.51	A.B	0.799
	B	388	204	52.58	184	47.42		
Creatinine	A	387	48	12.40	339	87.60	A.B	0.467
	B	388	55	14.18	333	85.82		
Glucose	A	387	165	42.64	222	57.36	A.B	0.445
	B	388	176	45.36	212	54.64		
Calcium	A	387	12	3.10	375	96.90	A.B	0.019
	B	388	3	0.77	385	99.23		

Table Set CHEM–1

LDL Cholesterol: Measurements at Scheduled Visits (mmol/L)

See Figure CHEM–1 on page 42.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	384	2.46	1.18	2.19	1.66	2.97	1.08	4.70	A.B	0.883
	B	388	2.44	1.07	2.22	1.65	2.96	1.16	4.55		
Month 3	A	351	2.47	1.27	2.15	1.66	3.05	1.05	4.98	A.B	0.541
	B	352	2.50	1.20	2.27	1.65	3.00	1.02	4.98		
Month 6	A	284	2.48	1.13	2.32	1.73	3.00	1.09	4.39	A.B	0.179
	B	301	2.63	1.28	2.39	1.80	3.11	1.13	4.79		
Month 9	A	147	2.47	1.23	2.15	1.63	3.05	1.14	4.75	A.B	0.736
	B	149	2.47	1.48	2.14	1.64	2.99	1.04	4.23		
Month 12	A	30	2.72	1.25	2.27	1.86	3.66	1.30	4.62	A.B	0.761
	B	27	2.44	0.90	2.13	1.99	2.83	1.06	4.62		

LDL Cholesterol: Above Upper Limit of Normal (3.35 mmol/L)

See Figure CHEM–1 on page 42.

			Value					
			Yes		No			
	Trt	Total Subjs	N	%	N	%	Contrast	P-Value
Baseline	A	384	69	17.97	315	82.03	A.B	0.462
	B	388	62	15.98	326	84.02		
Month 3	A	351	55	15.67	296	84.33	A.B	0.279
	B	352	66	18.75	286	81.25		
Month 6	A	284	52	18.31	232	81.69	A.B	0.321
	B	301	65	21.59	236	78.41		
Month 9	A	147	25	17.01	122	82.99	A.B	0.958
	B	149	25	16.78	124	83.22		
Month 12	A	30	8	26.67	22	73.33	A.B	0.137
	B	27	3	11.11	24	88.89		

LDL Cholesterol: Absolute Change from Baseline (mmol/L)

See Figure CHEM–1 on page 42.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	348	0.03	1.70	0.09	-0.93	0.90	-2.44	2.85	A.B	0.850
	B	352	0.05	1.63	0.02	-0.93	0.98	-2.59	2.60		
Month 6	A	281	0.08	1.57	0.05	-0.75	1.05	-2.44	2.41	A.B	0.724
	B	301	0.19	1.64	0.19	-0.78	1.09	-2.25	2.73		
Month 9	A	145	0.08	1.70	0.06	-0.89	0.87	-2.74	2.77	A.B	0.798
	B	149	0.08	1.84	-0.09	-0.81	0.97	-2.03	2.19		
Month 12	A	30	0.34	1.40	0.39	-0.95	1.22	-1.79	2.65	A.B	0.482
	B	27	0.06	1.23	0.12	-0.67	0.80	-2.05	1.84		

4.3 Hematology

Table Set HEMABN–1

Summary of Abnormal Hematology Values: Ever Below LLN

See Figure HEMABN–1 on page 43.

			Value					
			Yes		No			
	Trt	Total Subjs	N	%	N	%	Contrast	P-Value
White Blood Cells	A	351	55	15.67	296	84.33	A.B	0.695
	B	352	59	16.76	293	83.24		
Red Blood Cells	A	387	159	41.09	228	58.91	A.B	0.692
	B	388	154	39.69	234	60.31		
Hemoglobin	A	387	169	43.67	218	56.33	A.B	0.860
	B	388	167	43.04	221	56.96		
Hematocrit	A	387	182	47.03	205	52.97	A.B	0.369
	B	388	170	43.81	218	56.19		
Mean Corpuscular Volume	A	387	34	8.79	353	91.21	A.B	0.285
	B	388	43	11.08	345	88.92		

(Continued on next page.)

(Continued from previous page.)

Summary of Abnormal Hematology Values: Ever Below LLN

See Figure HEMABN–1 on page 43.

			Value					
			Yes		No			
	Trt	Total Subjs	N	%	N	%	Contrast	P-Value
Mean Corpuscular Hemoglobin	A	387	29	7.49	358	92.51	A.B	0.604
	B	388	33	8.51	355	91.49		
Mean Corpuscular Hemoglobin Concentration	A	387	110	28.42	277	71.58	A.B	0.067
	B	388	88	22.68	300	77.32		
Platelets	A	387	53	13.70	334	86.30	A.B	0.276
	B	388	64	16.49	324	83.51		

Summary of Abnormal Hematology Values: Ever Above ULN

See Figure HEMABN–1 on page 43.

			Value					
			Yes		No			
	Trt	Total Subjs	N	%	N	%	Contrast	P-Value
White Blood Cells	A	351	18	5.13	333	94.87	A.B	0.002
	B	352	41	11.65	311	88.35		
Red Blood Cells	A	387	6	1.55	381	98.45	A.B	0.996
	B	388	6	1.55	382	98.45		
Hemoglobin	A	387	7	1.81	380	98.19	A.B	0.202
	B	388	3	0.77	385	99.23		
Hematocrit	A	387	4	1.03	383	98.97	A.B	0.740
	B	388	5	1.29	383	98.71		
Mean Corpuscular Volume	A	387	68	17.57	319	82.43	A.B	0.233
	B	388	56	14.43	332	85.57		
Mean Corpuscular Hemoglobin	A	387	12	3.10	375	96.90	A.B	0.503
	B	388	9	2.32	379	97.68		
Mean Corpuscular Hemoglobin Concentration	A	387	0	0.00	387	100.00	A.B	1.000
	B	388	0	0.00	388	100.00		
Platelets	A	387	9	2.33	378	97.67	A.B	0.610
	B	388	7	1.80	381	98.20		

Table Set HEM–1

White Blood Cell Count: Measurements at Scheduled Visits (x10^9/L)

See Figure HEM–1 on page 44.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	384	7.0	1.9	6.8	5.6	8.1	4.3	10.6	A.B	0.034
	B	388	6.7	1.7	6.5	5.5	7.7	4.2	10.2		
Month 3	A	351	6.8	1.8	6.5	5.4	7.7	4.3	10.1	A.B	0.303
	B	352	7.0	2.3	6.8	5.3	8.2	3.9	11.3		
Month 6	A	284	6.6	1.8	6.4	5.4	7.4	4.2	10.2	A.B	0.019
	B	301	7.0	2.0	6.7	5.6	8.2	4.2	10.8		
Month 9	A	147	6.6	1.7	6.5	5.3	7.7	4.2	9.6	A.B	0.521
	B	149	6.9	2.1	6.4	5.3	8.1	4.4	10.9		

(Continued on next page.)

(Continued from previous page.)

White Blood Cell Count: Measurements at Scheduled Visits (x10^9/L)

See Figure HEM–1 on page 44.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 12	A	30	7.1	1.9	6.9	5.9	7.7	4.9	10.1	A.B	0.092
	B	27	6.5	2.0	5.8	5.1	7.5	4.2	11.3		

White Blood Cell Count: Above Upper Limit of Normal (11 x10^9/L)

See Figure HEM–1 on page 44.

			Value					
			Yes		No			
	Trt	Total Subjs	N	%	N	%	Contrast	P-Value
Baseline	A	384	11	2.86	373	97.14	A.B	0.634
	B	388	9	2.32	379	97.68		
Month 3	A	351	9	2.56	342	97.44	A.B	0.055
	B	352	19	5.40	333	94.60		
Month 6	A	284	7	2.46	277	97.54	A.B	0.155
	B	301	14	4.65	287	95.35		
Month 9	A	147	1	0.68	146	99.32	A.B	0.058
	B	149	6	4.03	143	95.97		
Month 12	A	30	1	3.33	29	96.67	A.B	0.492
	B	27	2	7.41	25	92.59		

White Blood Cell Count: Below Lower Limit of Normal (4.5 x10^9/L)

See Figure HEM–1 on page 44.

			Value					
			Yes		No			
	Trt	Total Subjs	N	%	N	%	Contrast	P-Value
Baseline	A	384	32	8.33	352	91.67	A.B	0.862
	B	388	31	7.99	357	92.01		
Month 3	A	351	24	6.84	327	93.16	A.B	0.270
	B	352	32	9.09	320	90.91		
Month 6	A	284	22	7.75	262	92.25	A.B	0.606
	B	301	20	6.64	281	93.36		
Month 9	A	147	12	8.16	135	91.84	A.B	0.338
	B	149	8	5.37	141	94.63		
Month 12	A	30	1	3.33	29	96.67	A.B	0.492
	B	27	2	7.41	25	92.59		

White Blood Cell Count: Absolute Change from Baseline (x10^9/L)

See Figure HEM–1 on page 44.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	348	-0.24	2.61	-0.30	-1.90	1.50	-4.40	4.20	A.B	0.008
	B	352	0.35	2.83	0.10	-1.50	2.15	-3.80	4.60		
Month 6	A	281	-0.43	2.62	-0.60	-1.80	1.20	-4.60	4.00	A.B	0.001
	B	301	0.27	2.73	0.40	-1.50	2.00	-4.60	4.60		
Month 9	A	145	-0.41	2.34	-0.60	-2.10	1.40	-4.00	3.30	A.B	0.064
	B	149	0.20	2.51	-0.20	-1.70	1.80	-3.40	4.40		
Month 12	A	30	-0.22	3.00	-0.75	-2.60	1.20	-4.00	5.90	A.B	0.911
	B	27	-0.21	2.62	-0.70	-2.10	0.80	-3.60	4.40		

Chapter 5

Other Follow-up and Safety Measures

5.1 Vital Signs

Table Set VIT–1

Systolic Blood Pressure: Measurements at Scheduled Visits (mmHg)

See Figure VIT–1 on page 46.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	387	121.8	13.9	122.5	112.4	132.5	98.5	143.1	A.B	0.453
	B	386	121.1	14.3	121.8	111.2	130.7	96.8	145.5		
Month 3	A	354	121.4	14.4	120.9	111.8	130.5	98.9	144.6	A.B	0.615
	B	354	120.7	13.7	121.0	112.1	129.7	97.7	143.1		
Month 6	A	289	121.9	13.4	121.6	112.3	131.5	101.0	145.2	A.B	0.992
	B	301	121.6	14.9	121.9	111.6	132.3	96.2	144.7		
Month 9	A	140	123.7	13.4	123.6	114.0	132.7	102.9	144.3	A.B	0.110
	B	144	120.8	15.7	119.6	110.1	132.0	95.6	146.2		
Month 12	A	22	123.6	15.2	123.3	114.9	133.8	99.6	140.3	A.B	0.644
	B	24	126.0	10.5	125.2	122.3	129.6	109.6	140.5		

Systolic Blood Pressure: Elevations (>130 mmHg)

See Figure VIT–1 on page 46.

		Treatment Group					
		A		B			P-
	Value	N	%	N	%	Contrast	Value
Baseline	Total Subjs	387		386		A.B	0.267
	>150 mmHg	7	1.81	8	2.07		
	>140-150 mmHg	23	5.94	26	6.74		
	>130-140 mmHg	87	22.48	65	16.84		
Month 3	Total Subjs	354		354		A.B	0.191
	>150 mmHg	7	1.98	8	2.26		
	>140-150 mmHg	31	8.76	17	4.80		
	>130-140 mmHg	54	15.25	62	17.51		

(Continued on next page.)

(Continued from previous page.)

Systolic Blood Pressure: Elevations (>130 mmHg)

See Figure VIT–1 on page 46.

		Treatment Group					
		A		B			P-
	Value	N	%	N	%	Contrast	Value
Month 6	Total Subjs	289		301		A.B	0.503
	>150 mmHg	8	2.77	8	2.66		
	>140-150 mmHg	21	7.27	17	5.65		
	>130-140 mmHg	51	17.65	67	22.26		
Month 9	Total Subjs	140		144		A.B	0.733
	>150 mmHg	2	1.43	4	2.78		
	>140-150 mmHg	12	8.57	12	8.33		
	>130-140 mmHg	32	22.86	27	18.75		
Month 12	Total Subjs	22		24		A.B	0.287
	>150 mmHg	1	4.55	1	4.17		
	>140-150 mmHg	1	4.55	1	4.17		
	>130-140 mmHg	8	36.36	3	12.50		

Systolic Blood Pressure: Absolute Change from Baseline (mmHg)

See Figure VIT–1 on page 46.

		Total		Std							P-
	Trt	Subjs	Mean	Dev	Median	Q1	Q3	P5	P95	Contrast	Value
Month 3	A	354	-0.4	19.7	-1.6	-13.8	12.7	-31.7	35.6	A.B	0.974
	B	352	-0.4	19.3	-0.8	-13.7	12.0	-31.2	34.2		
Month 6	A	289	0.4	19.2	-0.6	-13.7	13.0	-30.0	33.5	A.B	0.439
	B	300	1.2	21.0	2.3	-12.3	14.3	-33.4	33.3		
Month 9	A	140	3.5	20.9	0.5	-12.2	19.8	-27.4	40.2	A.B	0.182
	B	144	-0.3	21.7	-1.5	-17.1	15.6	-34.9	35.8		
Month 12	A	22	1.0	22.3	0.7	-11.3	14.5	-19.7	37.0	A.B	0.567
	B	24	4.6	17.4	4.7	-5.2	15.2	-21.0	32.0		

Systolic Blood Pressure: Increases from Baseline (>6 mmHg)

See Figure VIT–1 on page 46.

		Treatment Group					
		A		B			P-
	Value	N	%	N	%	Contrast	Value
Month 3	Total Subjs	354		354		A.B	0.324
	>15 mmHg	79	22.32	69	19.49		
	>10-15 mmHg	26	7.34	33	9.32		
	>6-10 mmHg	29	8.19	20	5.65		
Month 6	Total Subjs	289		301		A.B	0.386
	>15 mmHg	62	21.45	72	23.92		
	>10-15 mmHg	28	9.69	27	8.97		
	>6-10 mmHg	16	5.54	26	8.64		
Month 9	Total Subjs	140		144		A.B	0.818
	>15 mmHg	43	30.71	37	25.69		
	>10-15 mmHg	7	5.00	8	5.56		
	>6-10 mmHg	8	5.71	8	5.56		
Month 12	Total Subjs	22		24		A.B	0.763
	>15 mmHg	5	22.73	6	25.00		
	>10-15 mmHg	2	9.09	4	16.67		
	>6-10 mmHg	1	4.55	2	8.33		

Table Set VIT–2

Diastolic Blood Pressure: Measurements at Scheduled Visits (mmHg)

See Figure VIT–2 on page 47.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	387	70.5	9.8	71.3	64.3	77.0	54.3	84.9	A.B	0.038
	B	386	72.1	9.9	72.8	65.9	78.4	55.0	88.9		
Month 3	A	354	71.3	10.2	70.8	65.2	77.6	54.8	88.1	A.B	0.155
	B	354	72.6	10.7	72.5	65.3	80.1	55.5	90.1		
Month 6	A	289	71.3	9.4	71.1	65.1	77.9	56.9	86.8	A.B	0.136
	B	301	72.2	10.3	72.1	66.2	79.4	54.7	88.0		
Month 9	A	140	72.1	10.4	71.5	64.6	79.7	55.8	87.8	A.B	0.895
	B	144	72.6	9.2	71.7	66.3	78.8	59.9	89.2		
Month 12	A	22	73.2	9.6	71.8	66.3	81.1	62.5	87.5	A.B	0.356
	B	24	69.8	9.3	69.7	64.7	75.1	53.7	85.4		

Diastolic Blood Pressure: Elevations (>80 mmHg)

See Figure VIT–2 on page 47.

		Treatment Group					
		A		B			P-
	Value	N	%	N	%	Contrast	Value
Baseline	Total Subjs	387		386		A.B	0.033
	>90 mmHg	9	2.33	11	2.85		
	>85-90 mmHg	10	2.58	27	6.99		
	>80-85 mmHg	37	9.56	38	9.84		
Month 3	Total Subjs	354		354		A.B	0.055
	>90 mmHg	12	3.39	18	5.08		
	>85-90 mmHg	19	5.37	35	9.89		
	>80-85 mmHg	33	9.32	38	10.73		
Month 6	Total Subjs	289		301		A.B	0.184
	>90 mmHg	8	2.77	9	2.99		
	>85-90 mmHg	15	5.19	16	5.32		
	>80-85 mmHg	28	9.69	47	15.61		
Month 9	Total Subjs	140		144		A.B	0.759
	>90 mmHg	6	4.29	6	4.17		
	>85-90 mmHg	8	5.71	7	4.86		
	>80-85 mmHg	20	14.29	15	10.42		
Month 12	Total Subjs	22		24		A.B	0.495
	>90 mmHg	1	4.55	1	4.17		
	>85-90 mmHg	1	4.55	1	4.17		
	>80-85 mmHg	4	18.18	1	4.17		

Diastolic Blood Pressure: Absolute Change from Baseline (mmHg)

See Figure VIT–2 on page 47.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	354	0.8	13.8	1.1	-8.9	9.5	-20.9	24.3	A.B	0.560
	B	352	0.5	14.8	-1.2	-9.9	10.2	-22.6	26.4		
Month 6	A	289	0.6	13.3	-0.6	-7.7	8.2	-19.6	23.1	A.B	0.768
	B	300	0.1	15.0	1.3	-9.7	9.5	-26.1	23.7		
Month 9	A	140	-0.1	14.9	-0.2	-8.6	9.2	-24.7	24.4	A.B	0.311
	B	144	1.6	14.1	0.9	-8.2	13.2	-21.4	21.4		
Month 12	A	22	-1.4	10.3	-0.9	-9.8	6.4	-16.8	13.1	A.B	0.742
	B	24	0.0	15.7	2.5	-11.9	10.5	-19.8	30.3		

Diastolic Blood Pressure: Increases from Baseline (>4 mmHg)

See Figure VIT–2 on page 47.

		Treatment Group					
		A		B			P-
	Value	N	%	N	%	Contrast	Value
Month 3	Total Subjs	354		354		A.B	0.039
	>12 mmHg	66	18.64	82	23.16		
	>8-12 mmHg	41	11.58	21	5.93		
	>4-8 mmHg	38	10.73	42	11.86		
Month 6	Total Subjs	289		301		A.B	0.386
	>12 mmHg	59	20.42	61	20.27		
	>8-12 mmHg	18	6.23	26	8.64		
	>4-8 mmHg	26	9.00	36	11.96		
Month 9	Total Subjs	140		144		A.B	0.407
	>12 mmHg	27	19.29	40	27.78		
	>8-12 mmHg	12	8.57	11	7.64		
	>4-8 mmHg	15	10.71	15	10.42		
Month 12	Total Subjs	22		24		A.B	0.859
	>12 mmHg	2	9.09	4	16.67		
	>8-12 mmHg	3	13.64	4	16.67		
	>4-8 mmHg	2	9.09	2	8.33		

Table Set VIT–3

Weight: Measurements at Scheduled Visits (kg)

See Figure VIT–3 on page 48.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	387	87.9	15.9	87.4	76.7	99.4	62.6	113.5	A.B	0.539
	B	386	88.6	16.2	88.4	77.4	99.1	62.1	116.9		
Month 3	A	354	87.2	16.5	86.5	75.0	98.7	63.2	114.7	A.B	0.776
	B	354	87.2	16.8	88.2	75.5	97.8	57.8	114.1		
Month 6	A	289	86.5	16.8	87.0	76.7	96.3	58.0	115.0	A.B	0.486
	B	301	86.7	17.1	88.3	77.6	99.6	56.5	110.5		
Month 9	A	140	86.1	17.6	86.4	72.9	97.0	59.1	115.4	A.B	0.868
	B	144	86.6	18.1	86.9	75.1	97.4	57.2	118.3		
Month 12	A	22	90.4	15.0	92.8	79.4	104.1	63.8	108.5	A.B	0.379
	B	24	87.3	12.7	87.9	78.8	95.1	66.7	107.7		

Weight: Absolute Change from Baseline (kg)

See Figure VIT–3 on page 48.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	354	-0.6	23.8	-2.5	-18.8	15.9	-39.2	39.9	A.B	0.984
	B	352	-1.2	22.9	-0.3	-18.1	15.3	-40.8	34.1		
Month 6	A	289	-1.5	23.5	-2.5	-17.2	16.4	-41.8	35.7	A.B	0.893
	B	300	-1.8	23.6	-0.7	-16.7	14.5	-43.4	37.2		
Month 9	A	140	-2.3	23.4	-1.9	-15.3	13.0	-42.0	34.0	A.B	0.730
	B	144	-1.1	24.9	0.0	-18.1	14.9	-41.5	37.5		
Month 12	A	22	-2.9	19.9	-2.4	-13.8	5.2	-38.7	27.8	A.B	0.912
	B	24	-0.7	22.5	-2.0	-19.2	13.3	-29.5	41.3		

Weight: Percent Change from Baseline (%)

See Figure VIT–3 on page 48.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	354	3.2	30.0	-2.9	-19.3	19.2	-37.4	57.3	A.B	0.975
	B	352	2.1	27.5	-0.4	-17.8	18.9	-39.5	46.5		
Month 6	A	289	1.9	29.1	-2.8	-17.6	19.5	-41.7	46.0	A.B	0.900
	B	300	1.5	28.9	-0.7	-17.7	17.3	-42.4	52.5		
Month 9	A	140	0.8	27.4	-1.9	-17.8	17.1	-38.2	47.4	A.B	0.768
	B	144	2.5	30.9	0.0	-18.9	20.2	-43.7	60.9		
Month 12	A	22	-0.9	22.1	-3.1	-15.1	5.3	-30.8	36.1	A.B	0.878
	B	24	3.8	30.9	-2.1	-21.1	16.4	-26.7	56.8		

Table Set ECG–1

ECG Interpretation: ECG Interpretation

See Figure ECG–1 on page 49.

		Treatment Group					
		A		B			P-
	Value	N	%	N	%	Contrast	Value
Baseline	Total Subjs	387		386		A.B	0.810
	Abnormal, clinically signficant	61	15.76	65	16.84		
	Abnormal, not clinically significant	34	8.79	32	8.29		
	Normal	292	75.45	289	74.87		
Month 3	Total Subjs	354		354		A.B	0.343
	Abnormal, clinically signficant	65	18.36	51	14.41		
	Abnormal, not clinically significant	26	7.34	31	8.76		
	Normal	263	74.29	272	76.84		
Month 6	Total Subjs	289		301		A.B	0.402
	Abnormal, clinically signficant	56	19.38	47	15.61		
	Abnormal, not clinically significant	31	10.73	36	11.96		
	Normal	202	69.90	218	72.43		
Month 9	Total Subjs	140		144		A.B	0.471
	Abnormal, clinically signficant	21	15.00	19	13.19		
	Abnormal, not clinically significant	11	7.86	21	14.58		
	Normal	108	77.14	104	72.22		

(Continued on next page.)

(Continued from previous page.)

ECG Interpretation: ECG Interpretation

See Figure ECG–1 on page 49.

		Treatment Group					
		A		B			P-
	Value	N	%	N	%	Contrast	Value
Month 12	Total Subjs	22		24		A.B	0.660
	Abnormal, clinically signficant	0	0.00	3	12.50		
	Abnormal, not clinically significant	3	13.64	1	4.17		
	Normal	19	86.36	20	83.33		

ECG Interpretation: Change from Baseline in ECG Interpretation

See Figure ECG–1 on page 49.

		Treatment Group					
		A		B			P-
	Value	N	%	N	%	Contrast	Value
Month 3	Total Subjs	354		352		A.B	0.115
	Worse	81	22.88	65	18.47		
	Same	205	57.91	208	59.09		
	Better	68	19.21	79	22.44		
Month 6	Total Subjs	289		300		A.B	0.299
	Worse	70	24.22	65	21.67		
	Same	168	58.13	173	57.67		
	Better	51	17.65	62	20.67		
Month 9	Total Subjs	140		144		A.B	0.771
	Worse	25	17.86	30	20.83		
	Same	91	65.00	88	61.11		
	Better	24	17.14	26	18.06		
Month 12	Total Subjs	22		24		A.B	0.380
	Worse	1	4.55	3	12.50		
	Same	16	72.73	17	70.83		
	Better	5	22.73	4	16.67		

Table Set ECG–2

ECG: PR Interval and QRS Interval: PR Interval: Measurements at Scheduled Visits (msec)

See Figure ECG–2 on page 50.

		Total		Std							P-
	Trt	Subjs	Mean	Dev	Median	Q1	Q3	P5	P95	Contrast	Value
Baseline	A	387	175.2	29.1	175.2	153.8	195.0	130.7	222.9	A.B	0.920
	B	386	175.0	29.2	174.3	153.6	195.6	129.9	221.2		
Month 3	A	354	172.5	28.3	173.5	153.2	191.1	125.1	218.0	A.B	0.462
	B	354	174.4	31.6	174.6	151.9	197.0	121.3	227.7		
Month 6	A	289	174.1	29.3	174.0	152.7	194.7	126.9	223.4	A.B	0.828
	B	301	174.5	30.2	175.9	152.8	194.6	123.1	221.8		
Month 9	A	140	174.0	29.5	172.2	154.6	195.2	128.8	223.8	A.B	0.627
	B	144	176.1	29.9	174.1	155.6	196.4	129.4	228.6		
Month 12	A	22	164.6	30.8	163.4	151.9	177.9	131.9	192.5	A.B	0.022
	B	24	188.9	36.8	192.1	154.6	214.5	144.3	257.0		

ECG: PR Interval and QRS Interval: PR Interval: Absolute Change from Baseline (msec)

See Figure ECG–2 on page 50.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	354	-2.7	39.4	-3.6	-30.0	22.7	-68.4	60.7	A.B	0.654
	B	352	-1.0	45.3	-1.8	-31.1	30.8	-72.3	72.0		
Month 6	A	289	-1.7	40.4	-0.7	-31.3	26.8	-71.2	62.7	A.B	0.884
	B	300	-1.4	42.1	-2.1	-32.0	27.5	-69.7	63.2		
Month 9	A	140	-2.4	36.9	-1.1	-28.0	20.9	-61.4	55.6	A.B	0.366
	B	144	3.0	39.0	2.7	-22.4	23.6	-48.1	78.9		
Month 12	A	22	-18.6	48.9	-22.1	-43.9	11.7	-95.9	42.5	A.B	0.002
	B	24	21.7	40.8	16.4	-15.7	47.3	-26.3	108.3		

ECG: PR Interval and QRS Interval: QRS Interval: Measurements at Scheduled Visits (msec)

See Figure ECG–2 on page 50.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	387	99.2	20.9	98.6	85.1	113.2	67.5	131.8	A.B	0.248
	B	386	101.4	21.2	100.8	86.3	115.1	68.3	136.8		
Month 3	A	354	100.1	21.3	99.8	86.2	115.0	63.4	136.0	A.B	0.301
	B	354	98.7	19.8	98.5	85.8	110.6	63.0	131.8		
Month 6	A	289	101.0	20.7	100.4	88.4	114.9	67.2	136.4	A.B	0.322
	B	301	99.4	21.1	99.0	85.8	113.4	63.7	134.2		
Month 9	A	140	98.0	20.9	98.3	83.6	112.6	63.4	132.0	A.B	0.464
	B	144	100.1	19.4	100.2	86.3	115.7	68.5	129.8		
Month 12	A	22	99.7	21.7	98.7	84.3	112.1	78.0	137.5	A.B	0.860
	B	24	100.1	24.9	96.5	85.2	118.6	71.2	134.8		

ECG: PR Interval and QRS Interval: QRS Interval: Absolute Change from Baseline (msec)

See Figure ECG–2 on page 50.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	354	0.6	29.0	1.3	-20.1	21.8	-46.9	48.4	A.B	0.159
	B	352	-2.6	28.4	-1.7	-20.2	16.0	-50.7	43.4		
Month 6	A	289	1.8	30.0	1.8	-15.3	20.5	-51.5	50.2	A.B	0.135
	B	300	-1.8	29.7	-3.2	-22.7	21.9	-50.2	42.8		
Month 9	A	140	-1.0	28.4	0.4	-20.9	21.0	-47.5	41.3	A.B	0.908
	B	144	-0.4	28.2	-2.5	-19.2	19.3	-43.9	49.0		
Month 12	A	22	9.4	32.3	6.9	-16.4	35.5	-38.5	62.5	A.B	0.301
	B	24	-1.4	28.6	-0.5	-23.8	13.6	-50.7	36.1		

Table Set ECG–3

ECG: RR Interval and QTc Interval (Fridericia): RR Interval: Measurements at Scheduled Visits (msec)

See Figure ECG–3 on page 51.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	387	973.7	133.0	970.8	884.9	1064.0	751.1	1188.1	A.B	0.628
	B	386	968.8	149.4	961.0	872.1	1074.0	721.0	1198.4		
Month 3	A	354	973.4	139.5	980.2	874.0	1072.9	743.0	1195.3	A.B	0.911
	B	354	971.9	146.9	973.9	877.4	1070.7	726.0	1207.0		
Month 6	A	289	970.7	151.9	978.7	868.6	1069.8	718.2	1241.6	A.B	0.889
	B	301	972.2	130.1	971.1	880.8	1064.0	769.4	1191.1		
Month 9	A	140	972.3	144.8	967.2	873.4	1079.4	763.0	1209.8	A.B	0.544
	B	144	980.2	142.4	995.1	883.0	1069.2	732.6	1218.5		
Month 12	A	22	968.0	120.9	952.4	898.9	1016.6	826.3	1171.1	A.B	0.301
	B	24	928.2	126.0	923.2	842.3	1012.8	769.9	1125.6		

ECG: RR Interval and QTc Interval (Fridericia): RR Interval: Absolute Change from Baseline (msec)

See Figure ECG–3 on page 51.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	354	-2.7	197.3	2.6	-130.9	137.6	-348.3	323.8	A.B	0.737
	B	352	0.2	210.8	-3.2	-129.7	145.8	-363.9	322.9		
Month 6	A	289	-2.4	200.7	-15.1	-136.1	130.4	-328.6	316.9	A.B	0.854
	B	300	-1.9	197.9	-9.7	-143.7	144.6	-337.6	314.5		
Month 9	A	140	-7.8	181.5	-6.0	-132.0	104.2	-337.3	312.7	A.B	0.625
	B	144	3.4	199.9	2.1	-120.1	141.7	-316.3	331.7		
Month 12	A	22	1.7	198.5	-41.6	-165.1	107.9	-243.8	346.1	A.B	0.173
	B	24	-92.5	210.7	-120.5	-222.8	63.4	-422.6	234.8		

ECG: RR Interval and QTc Interval (Fridericia): QTc Interval (Fridericia): Measurements at Scheduled Visits (msec)

See Figure ECG–3 on page 51.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	387	409.1	30.2	408.7	388.0	428.1	361.3	461.8	A.B	0.990
	B	386	408.8	33.4	410.1	384.0	429.5	356.8	463.8		
Month 3	A	354	409.6	32.0	407.4	386.4	432.9	360.9	465.1	A.B	0.603
	B	354	410.9	32.4	411.4	388.0	432.2	358.0	468.5		
Month 6	A	289	408.9	31.4	407.7	386.4	429.1	360.1	462.8	A.B	0.589
	B	301	409.7	32.1	410.6	387.2	432.7	355.7	460.6		
Month 9	A	140	410.5	33.5	413.0	391.6	435.1	348.1	458.0	A.B	0.758
	B	144	410.8	35.0	410.8	388.0	433.3	354.7	468.6		
Month 12	A	22	408.2	30.0	405.6	390.0	433.4	359.7	449.3	A.B	0.912
	B	24	407.3	34.8	412.2	380.7	430.2	354.1	461.9		

ECG: RR Interval and QTc Interval (Fridericia): QTc Interval (Fridericia): Absolute Change from Baseline (msec)

See Figure ECG–3 on page 51.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	354	1.1	45.8	-1.6	-28.8	30.6	-69.7	76.5	A.B	0.843
	B	352	0.9	45.5	1.3	-30.6	30.7	-76.7	73.9		
Month 6	A	289	0.1	42.9	-1.9	-26.2	26.5	-73.6	70.5	A.B	0.870
	B	300	0.2	43.7	-1.3	-30.4	29.2	-70.9	74.4		
Month 9	A	140	1.1	45.4	1.5	-32.0	36.6	-70.3	73.6	A.B	0.537
	B	144	-1.1	47.0	-3.6	-34.7	27.6	-63.2	79.7		
Month 12	A	22	8.5	54.4	10.8	-38.6	53.2	-77.4	94.4	A.B	0.792
	B	24	5.0	41.2	5.5	-25.6	38.4	-50.6	65.0		

5.2 Concomitant Medications

Table Set CONMEDS–1

Standard of Care Medications: By Time of First Reported Use

See Figure CONMEDS–1 on page 52.

		Treatment Group					
		A		B			P-
	Value	N	%	N	%	Contrast	Value
Statin therapy	Total Subjs	387		388		A.B	0.194
	Reported at baseline	188	48.58	206	53.09		
	Added after randomization	35	9.04	37	9.54		
	Not reported	164	42.38	145	37.37		
Aspirin	Total Subjs	387		388		A.B	0.514
	Reported at baseline	181	46.77	187	48.20		
	Added after randomization	29	7.49	32	8.25		
	Not reported	177	45.74	169	43.56		
Beta-blocker	Total Subjs	387		388		A.B	0.572
	Reported at baseline	158	40.83	162	41.75		
	Added after randomization	40	10.34	32	8.25		
	Not reported	189	48.84	194	50.00		
ACE inhibitor	Total Subjs	387		388		A.B	0.698
	Reported at baseline	219	56.59	224	57.73		
	Added after randomization	33	8.53	34	8.76		
	Not reported	135	34.88	130	33.51		
Angiotensin II receptor blocker	Total Subjs	387		388		A.B	0.215
	Reported at baseline	132	34.11	161	41.49		
	Added after randomization	24	6.20	17	4.38		
	Not reported	231	59.69	210	54.12		

Chapter 6

Study Endpoints

Table Set ENDPT–1

All-Cause Mortality: Event Probability over Time

See Figure ENDPT–1 on page 54.

Months	Trt	nRisk	nEvents	% w/ Event	95% CI
0	A	387	0	0.0	(0.0, 0.0)
	B	388	0	0.0	(0.0, 0.0)
1	A	378	8	2.1	(0.6, 3.5)
	B	378	5	1.3	(0.2, 2.4)
2	A	369	15	3.9	(1.9, 5.8)
	B	365	10	2.6	(1.0, 4.2)
3	A	361	22	5.7	(3.4, 8.0)
	B	358	13	3.4	(1.6, 5.2)
4	A	337	35	9.2	(6.2, 12.0)
	B	350	14	3.7	(1.8, 5.6)
5	A	324	40	10.5	(7.4, 13.6)
	B	335	17	4.5	(2.4, 6.6)
6	A	298	47	12.5	(9.1, 15.8)
	B	308	26	7.2	(4.5, 9.8)
7	A	269	50	13.4	(9.9, 16.9)
	B	278	31	8.8	(5.7, 11.7)
8	A	216	55	15.2	(11.4, 18.8)
	B	222	33	9.5	(6.3, 12.5)
9	A	156	58	16.5	(12.4, 20.3)
	B	166	34	9.9	(6.7, 13.0)
10	A	102	63	19.7	(14.8, 24.2)
	B	106	34	9.9	(6.7, 13.0)
11	A	57	65	21.4	(16.1, 26.5)
	B	60	34	9.9	(6.7, 13.0)
12	A	28	65	21.4	(16.1, 26.5)
	B	33	34	9.9	(6.7, 13.0)

Index of Figures and Tables

Page numbers for main material appear in normal (unslanted) type; page numbers for supporting material, if any, are given in italics.