UW–Madison SDAC

Sample Closed Session DMC Report

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Statistical Data Analysis Center

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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. This report is intended to be representative of the style of presentation in DMC reports prepared by SDAC. It presents a hypothetical report for a single, generic and fictitious clinical trial. A final section of *Ancillary Material* includes additional displays illustrative of other types of reports or study designs.

> *Please note that analyses in this report are based entirely on simulated data, and the results should not be considered to be descriptive of any actual research studies.*

An electronic version of this report that may be freely shared is available on the SDAC web site:

https://www.biostat.wisc.edu/content/sdac-sample-dmc-reports

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 assigned randomly in a 1:1 ratio to one of 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.

Actual DMC reports are produced in two versions. The first 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. (This sample report takes the form of such a Closed Session Report.) The second version, the *Open Session Report*, summarizes selected data for all subjects, aggregated across treatment groups, and would be 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 primary 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. The DMC report will typically be based on randomized subjects only, and will include screeing and baseline information on such subjects. 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
CHD	Coronary Heart Disease
CRF	Case Report Form
CV	Cardiovascular
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
MACE	Major Adverse Cardiovascular Event
MedDRA	Medical Dictionary for Regulatory Activities
MI	Myocardial Infarction
NYHA	New York Heart Association
SAE	Serious Adverse Event
SDAC	Statistical Data Analysis Center
SOC	System Organ Class
ULN	Upper Limit of Normal

[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`.

Abbreviated Report Outline

This sample report contains the following sections and chapters:

- Introduction
- Main Material
  - Accrual and Study Status
  - Baseline Characteristics
  - Adverse Events
  - Central Laboratory Measures
  - Other Follow-up and Safety Measures
  - Study Endpoints
- Supporting Material
- Ancillary Material
  - Blinded Displays for an Open Session Report
  - Multi-Protocol Displays
  - Multi-Contrast Displays
  - Color Displays

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 a 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 28, 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 29. 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 49.

Boxplots. Boxplots indicate the distribution of continuous data based on percentiles (for example, the display for age in Figure DEMO–1 on page 28). 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 33). 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, such as Figure ENDPT–2 on page 70, is used to efficiently summarize subgroup analyses of a treatment group difference for a single time-to-event response variable, or to summarize multiple time-to-event variables in one display. 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 62). 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. For an actual DMC report, this section would include a brief description of data-handling and analysis conventions used in the report: e.g., how the sample sizes or denominators 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 18, 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 through STAT–4 on pages 23–26, is also typically presented. These graphics can be helpful in assessing 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 28.

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 33. 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 and reconciling 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. A 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. System organ classes (SOCs) are ordered according to the MedDRA internationally agreed order, which is based upon the relative importance of each SOC and is irrespective of language or alphabet.

Table AE–4 on page 42 is a summary of AEs for which there is a nominally significant difference between treatment groups ($p < 0.10$ in this example, but another level such as $p < 0.05$ may be used) *and* the event, according to MedDRA high level term or preferred term, was experienced by at least 0.5 percent of subjects in either treatment group (the minimum frequency for inclusion can be changed as appropriate for the stage of the trial and the amount of data). This display would only appear in a *Closed Session Report*.

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 49, CHEMABN–1 on page 55 and HEMABN–1 on page 57 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.

Other 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.

Figure BYPTLFT–1 on page 54 is an example of patient profile plots that can be created for a variety of situations. This example presents liver enzyme measurements over time for individual subjects who experienced elevated values during study follow-up. The panel for each subject is annotated with demographic and treatment status information, and an indicator of liver-related events that were reported as AEs.

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 in Figure VIT–1 on page 60. For other types of data, such as concomitant medication use displayed in Figure CONMEDS–1 on page 67, the report summarizes information collected over the entire period of observation.

Study Endpoints

This section of a DMC report would include analyses of primary and key secondary endpoints for the trial, and other endpoints of interest. It might also contain Kaplan-Meier plots for subgroups of particular interest, displays of event classifications resulting from an adjudication process (e.g., subcategories of myocardial infarction and stroke), interim monitoring boundaries, and other items as appropriate for the trial.

In this sample report, Figure ENDPT–1 on page 69 is a bar graph displaying the frequency of various endpoint events, including the primary composite endpoint, from a simulated endpoint dataset. Following this is a relative risk graphic showing hazard ratios and 95% confidence intervals, based on the Cox proportional hazards model, for the same set of endpoints.

The Kaplan-Meier plot in Figure ENDPT–3 on page 71 displays all-cause mortality over time by randomized treatment group. 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.

Figure DTH–1 on page 73 displays information about cause of death, as determined by an adjudication process. The upper panel summarizes deaths according to the adjudicated cause or as

unadjudicated. The lower panels include only adjudicated deaths, and display subcategories for cardiovascular deaths and for non-cardiovascular deaths.

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.

In this Sample Report, the *Ancillary Material* contains other examples of displays that may be presented for different types of reports or study designs, such as a multi-protocol program or a larger number of treatment arms.

Blinded Displays for an Open Session Report. Figure DEMOBL–1 on page 122 is an example of a parallel, blinded display created using aggregate data, which would be part of an *Open Session Report*. The page layout and the data presented are identical to Figure DEMO–1 on page 28 but with no information on treatment assignment. Another example, Figure SAEBL–1 on page 123, is a blinded version of Figure SAE–1 on page 33.

Multi-Protocol Displays. Figure MORT–1 on page 125 is an example of a possible page layout for summarizing a single dichotomous endpoint variable across the individual and pooled studies in a multi-protocol program. Figure LDL–1 on page 126 represents a way to summarize a particular lab measurement (in this case, LDL cholesterol) at a single time point, with change from baseline, across individual and pooled studies in a single display.

Multi-Contrast Displays. Figure ALTDEMO–1 on page 128 is an example of a page layout summarizing three treatment groups instead of two as in the rest of this sample report. This page shows the same information as Figure DEMO–1 on page 28 except that, for illustrative purposes, subjects have been randomly reassigned to one of three treatment groups.

Figures ALTABN–1 on page 129 and ALTLFT–1 on page 130 show similar examples for lab pages. Additionally, these pages include p-values for some of the possible contrasts that are available with more than two treatment groups. The contrast labeled “pAB.C” compares the combination of treatment groups A and B versus the single treatment group C, while the contrast labeled “pA.C” compares the single treatment groups A versus C.

Color Displays. Figure DEMOCOL–1 on page 132 is an example of a graphical display created using color instead of greyscale shading to distinguish between groups. The page layout and the data presented are identical to Figure DEMO–1 on page 28.

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.

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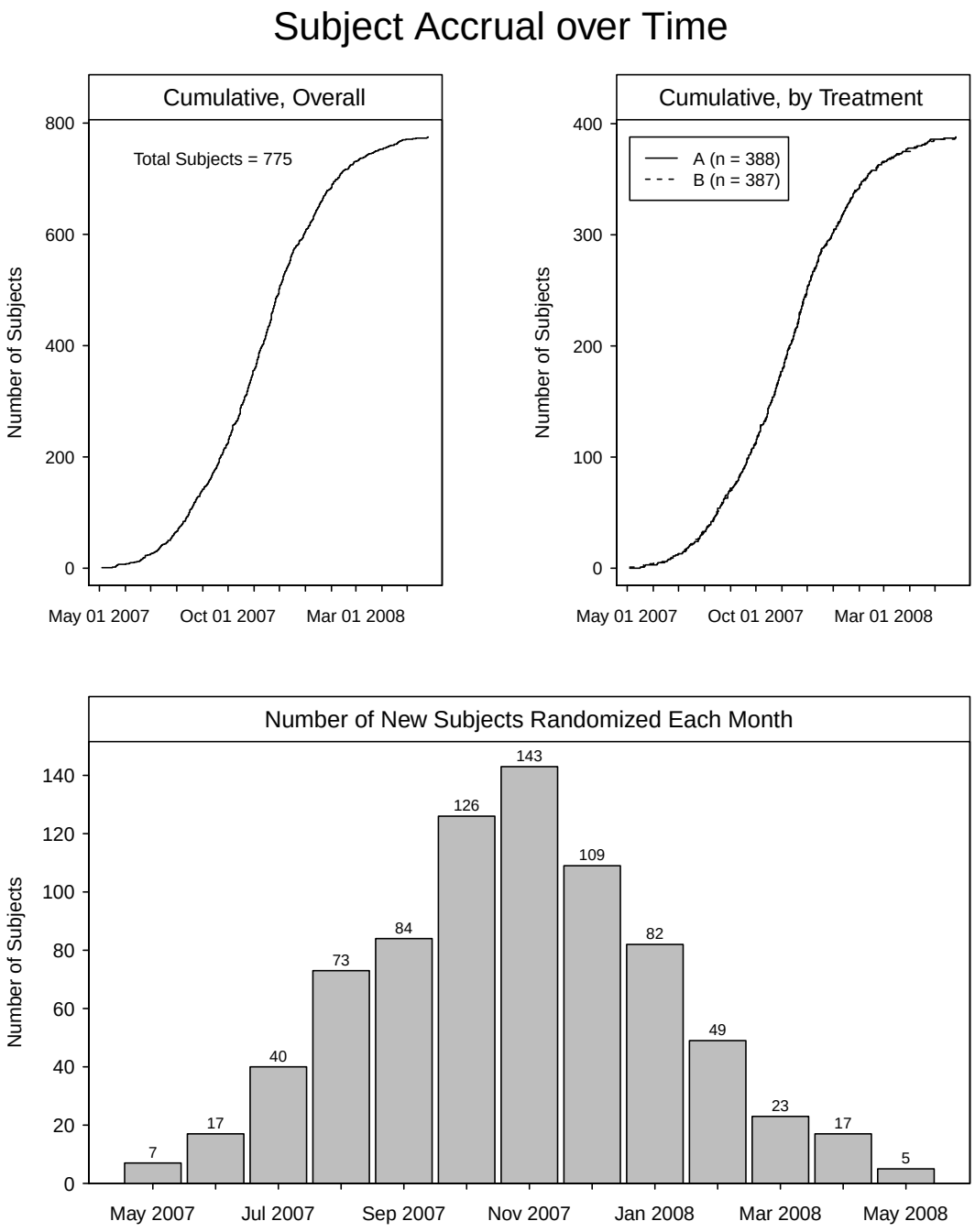
Part II

Main Material

Chapter 1

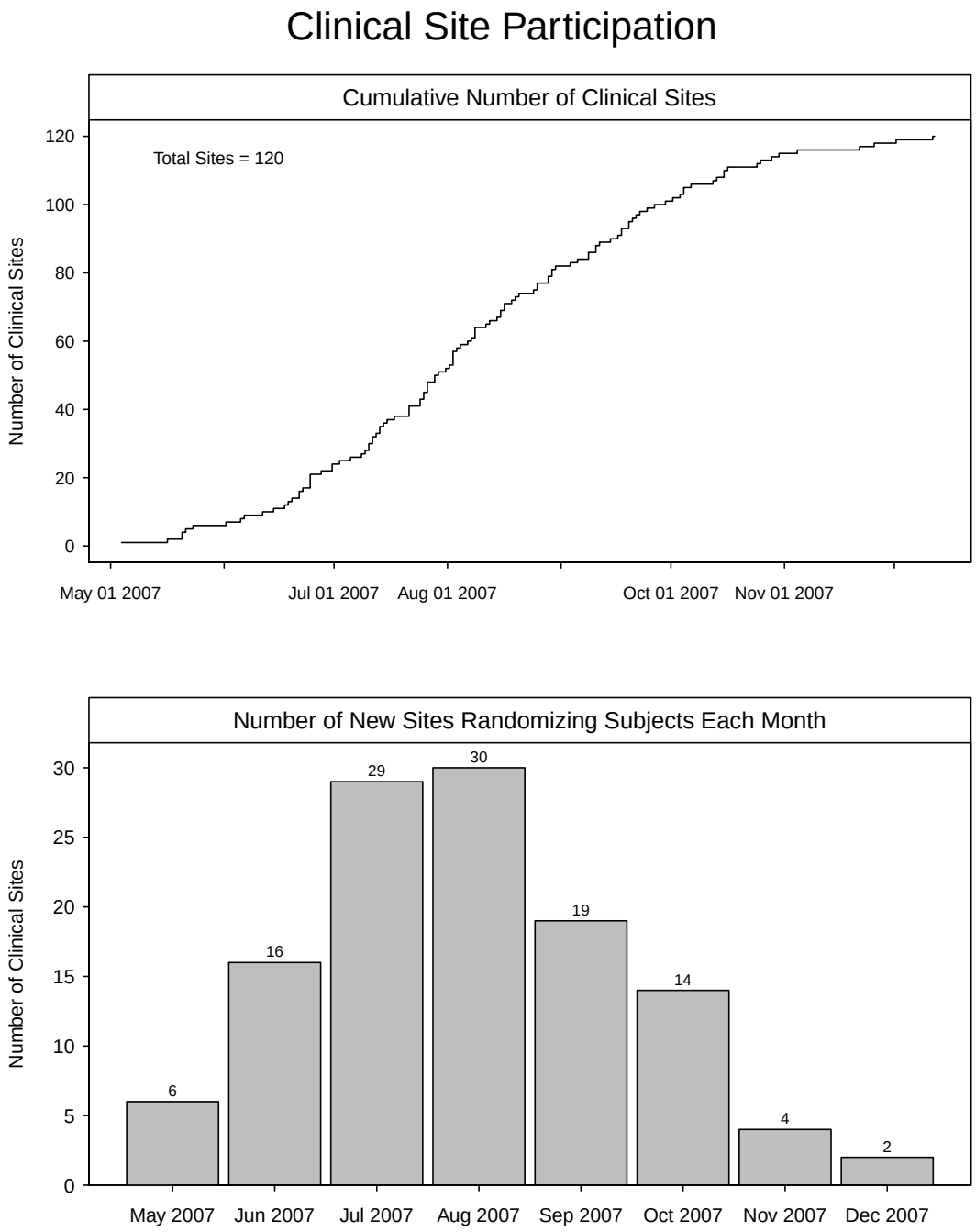
Accrual and Study Status

Figure ACCR–1



Information from a simulated enrollment dataset. The first subject was randomized on May 4, 2007.

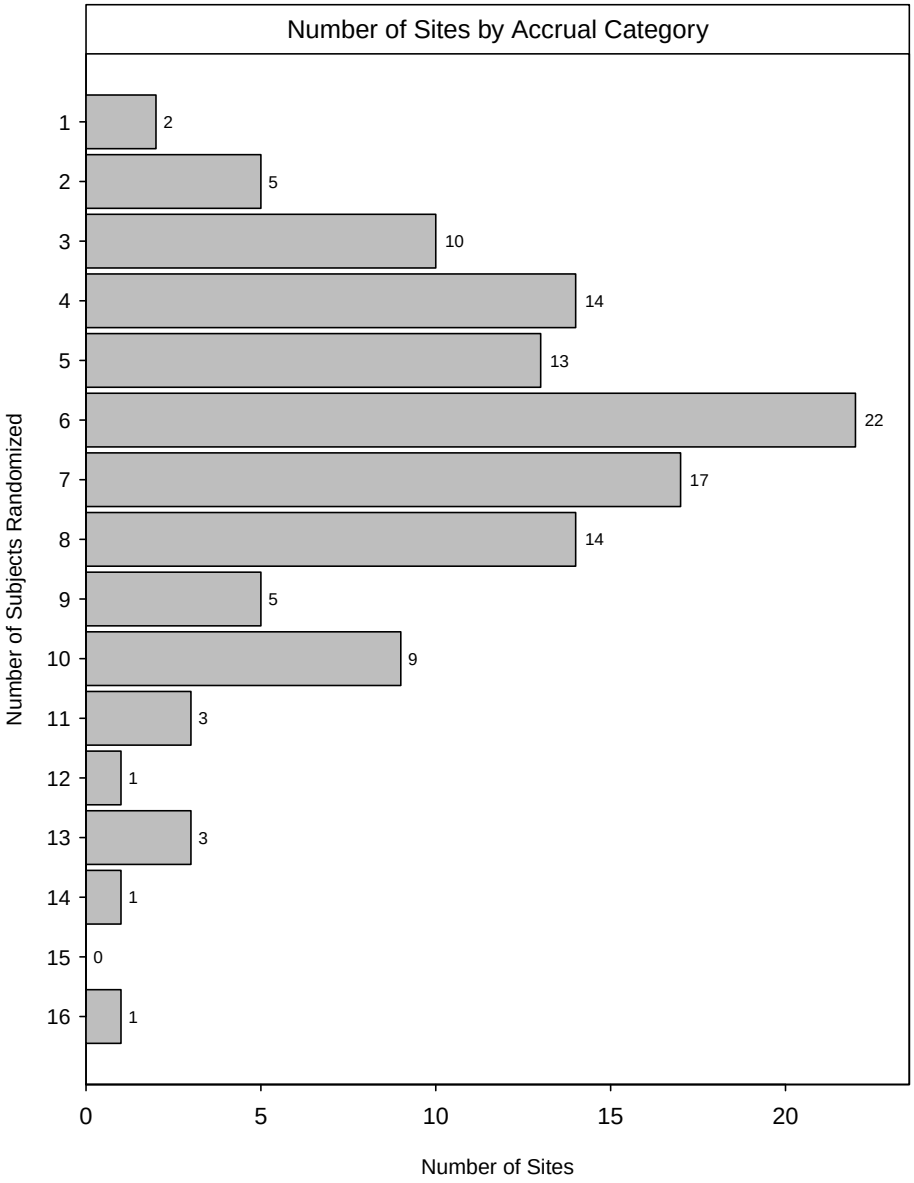
Figure ACCR–2



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

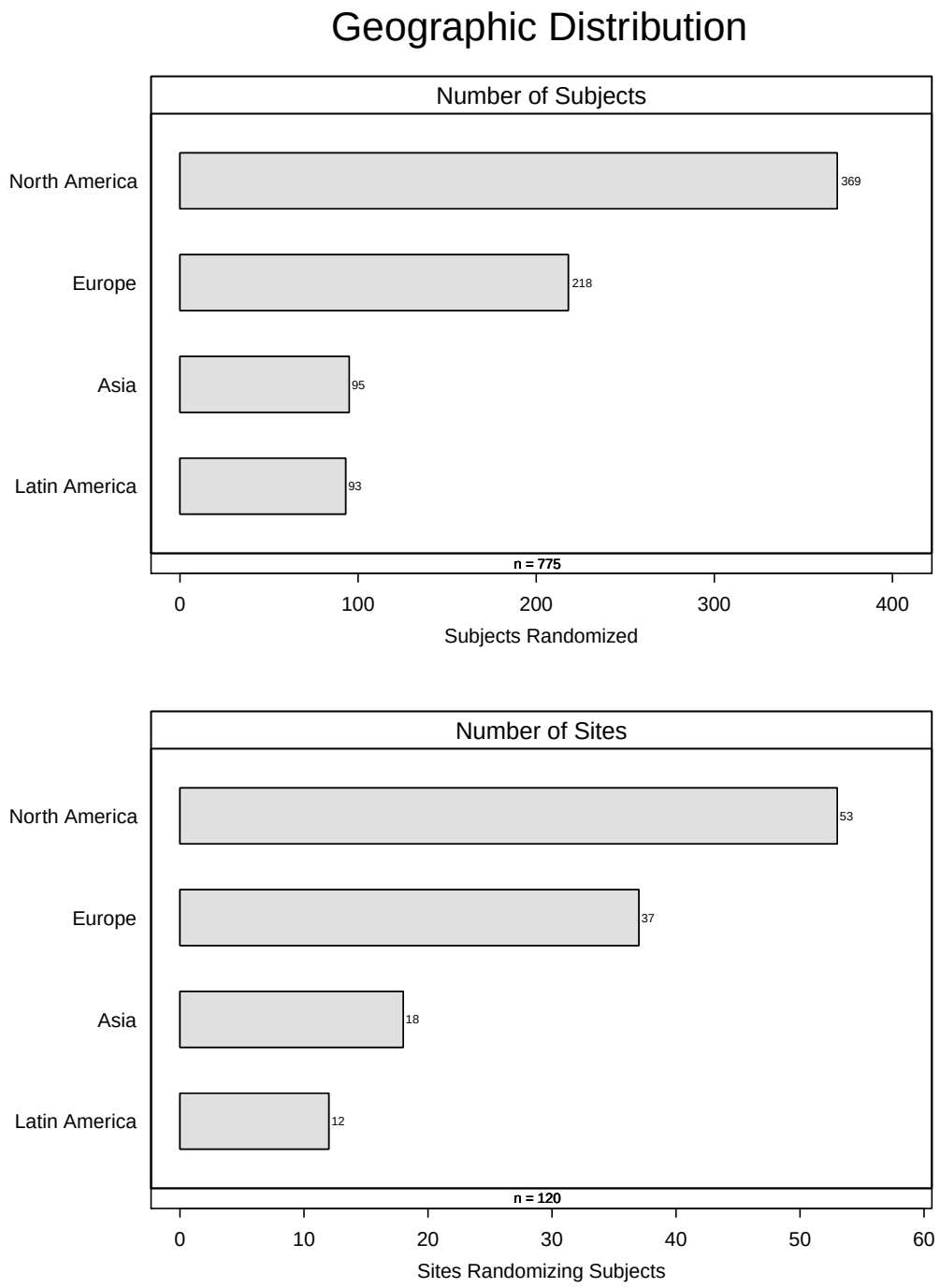
Figure ACCR–3

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 75.

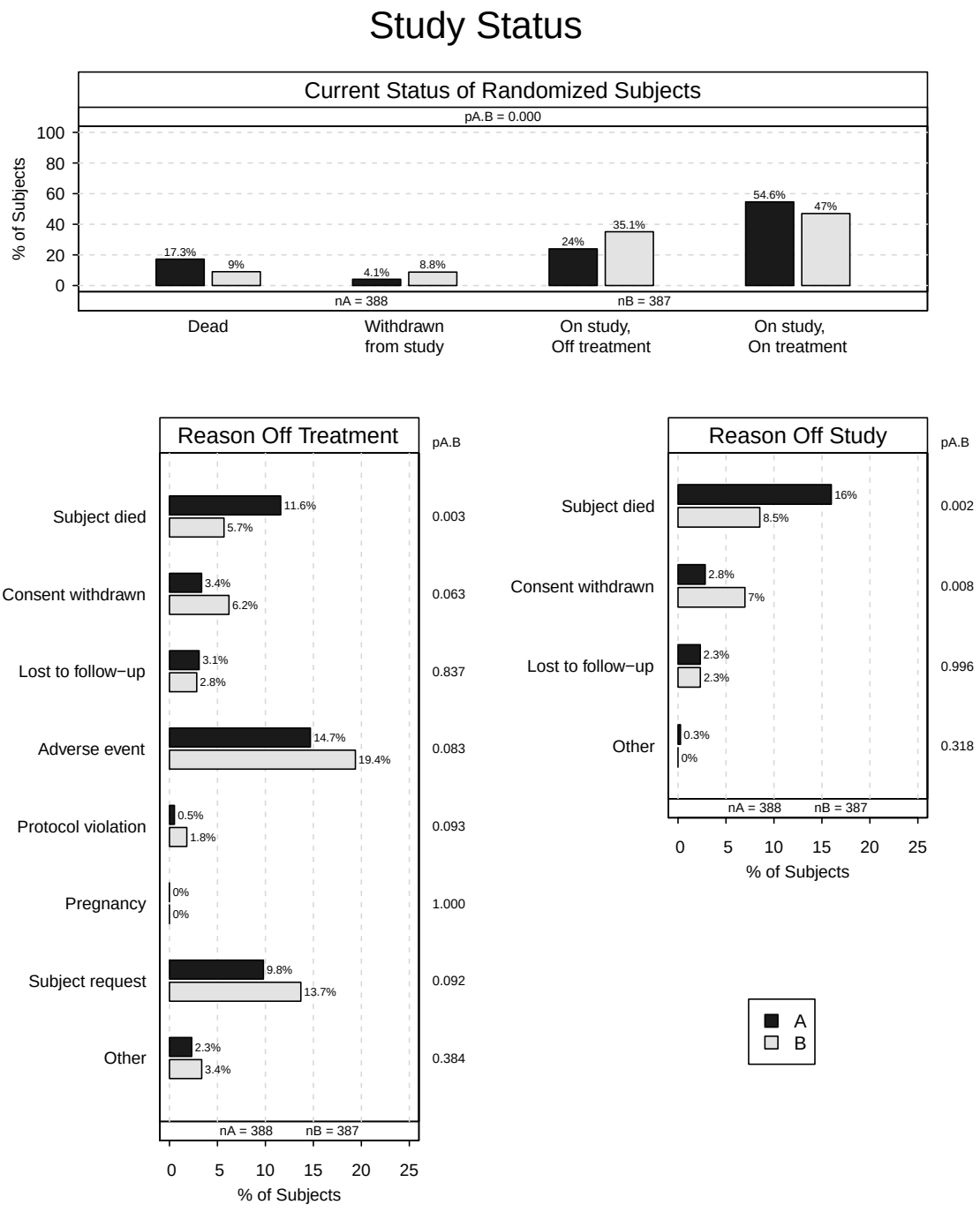
Table ACCR–5

Region and Country Participation

Enrollment by Region and Country	Date of First Subject Entry	Most Recent Subject Entry	Number of Sites	Number of Subjects Entered	Subjects Per Site (Mean)
OVERALL	*May 4, 2007*	*May 27, 2008*	*120*	*775*	*6.5*
North America	**May 22, 2007**	**May 27, 2008**	**53**	**369**	**7.0**
United States	May 22, 2007	May 27, 2008	38	273	7.2
Canada	Jun 21, 2007	Apr 27, 2008	15	96	6.4
Europe	**Jun 16, 2007**	**May 13, 2008**	**37**	**218**	**5.9**
United Kingdom	Jun 16, 2007	Apr 26, 2008	10	57	5.7
Spain	Jun 19, 2007	May 9, 2008	4	21	5.3
Germany	Jun 26, 2007	Apr 17, 2008	5	23	4.6
Portugal	Aug 30, 2007	Feb 12, 2008	3	16	5.3
Norway	Aug 21, 2007	Feb 18, 2008	3	16	5.3
France	Jul 10, 2007	Mar 24, 2008	3	28	9.3
Italy	Aug 10, 2007	Jan 31, 2008	3	12	4.0
Sweden	Aug 27, 2007	Apr 24, 2008	3	19	6.3
Finland	Jul 16, 2007	May 13, 2008	3	26	8.7
Asia	**Jun 7, 2007**	**May 1, 2008**	**18**	**95**	**5.3**
Japan	Jul 26, 2007	May 1, 2008	5	26	5.2
Hong Kong	Aug 14, 2007	Jan 19, 2008	3	16	5.3
Korea	Jul 2, 2007	Mar 8, 2008	4	18	4.5
Taiwan	Aug 6, 2007	Mar 18, 2008	3	16	5.3
Philippines	Jun 7, 2007	Mar 3, 2008	3	19	6.3
Latin America	**May 4, 2007**	**May 26, 2008**	**12**	**93**	**7.8**
Mexico	May 4, 2007	Feb 16, 2008	3	23	7.7
Brazil	May 22, 2007	May 26, 2008	3	28	9.3
Chile	May 18, 2007	Mar 14, 2008	3	24	8.0
Peru	Jul 4, 2007	Apr 23, 2008	3	18	6.0

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

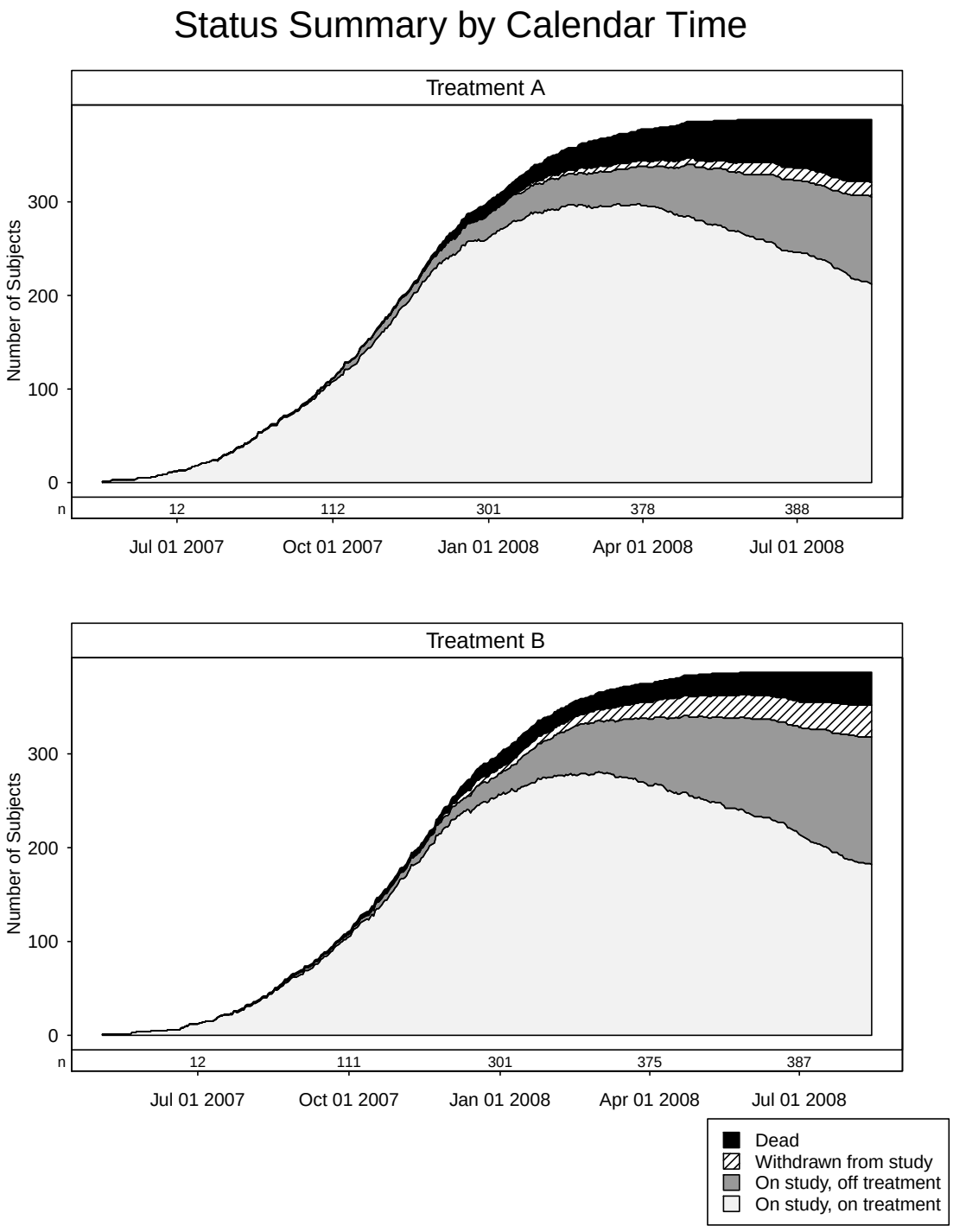
Figure STAT–1



Information from a simulated enrollment dataset. In the upper panel, subjects are assigned to the first applicable category (left to right). 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 75.

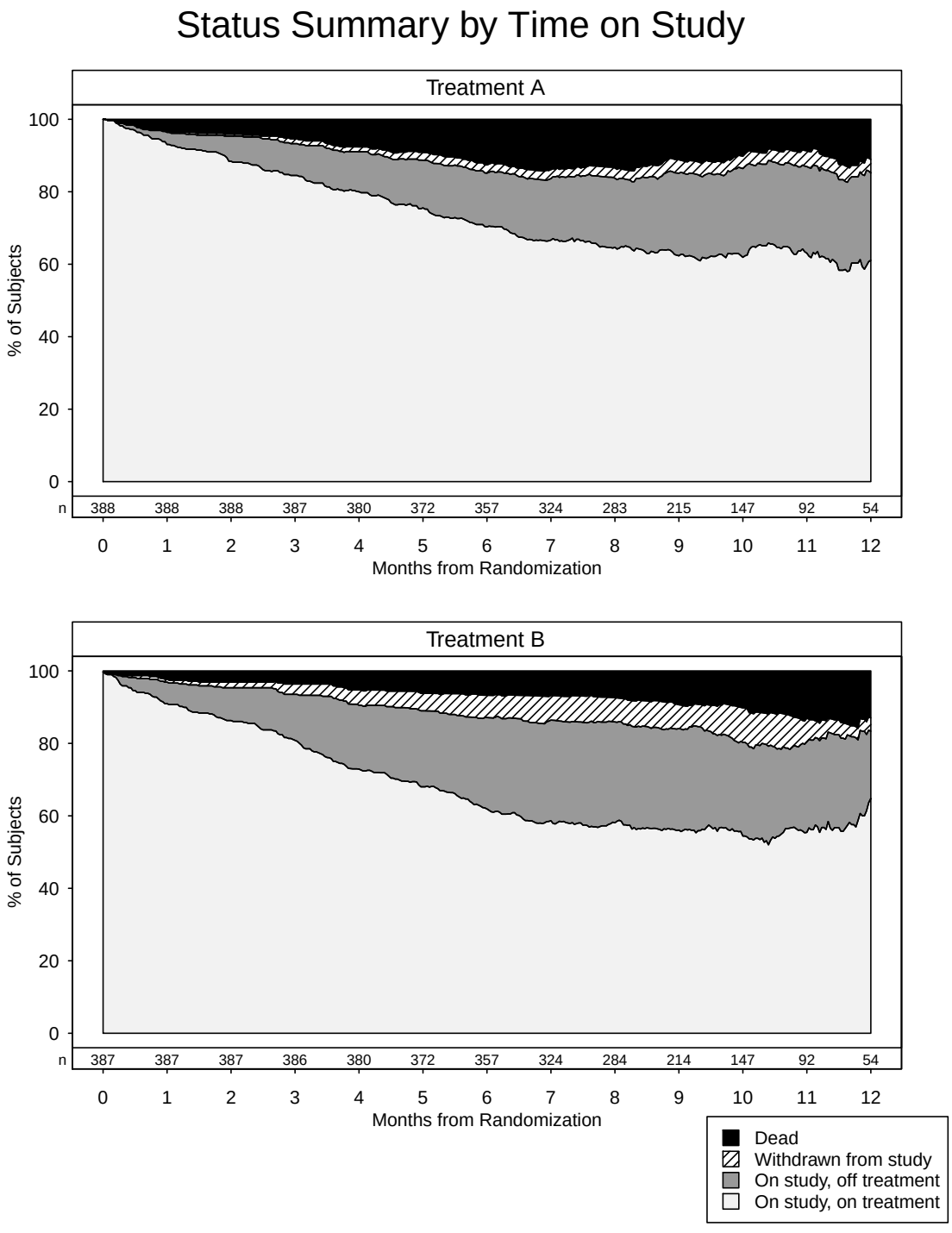
Figure STAT–2



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 77.

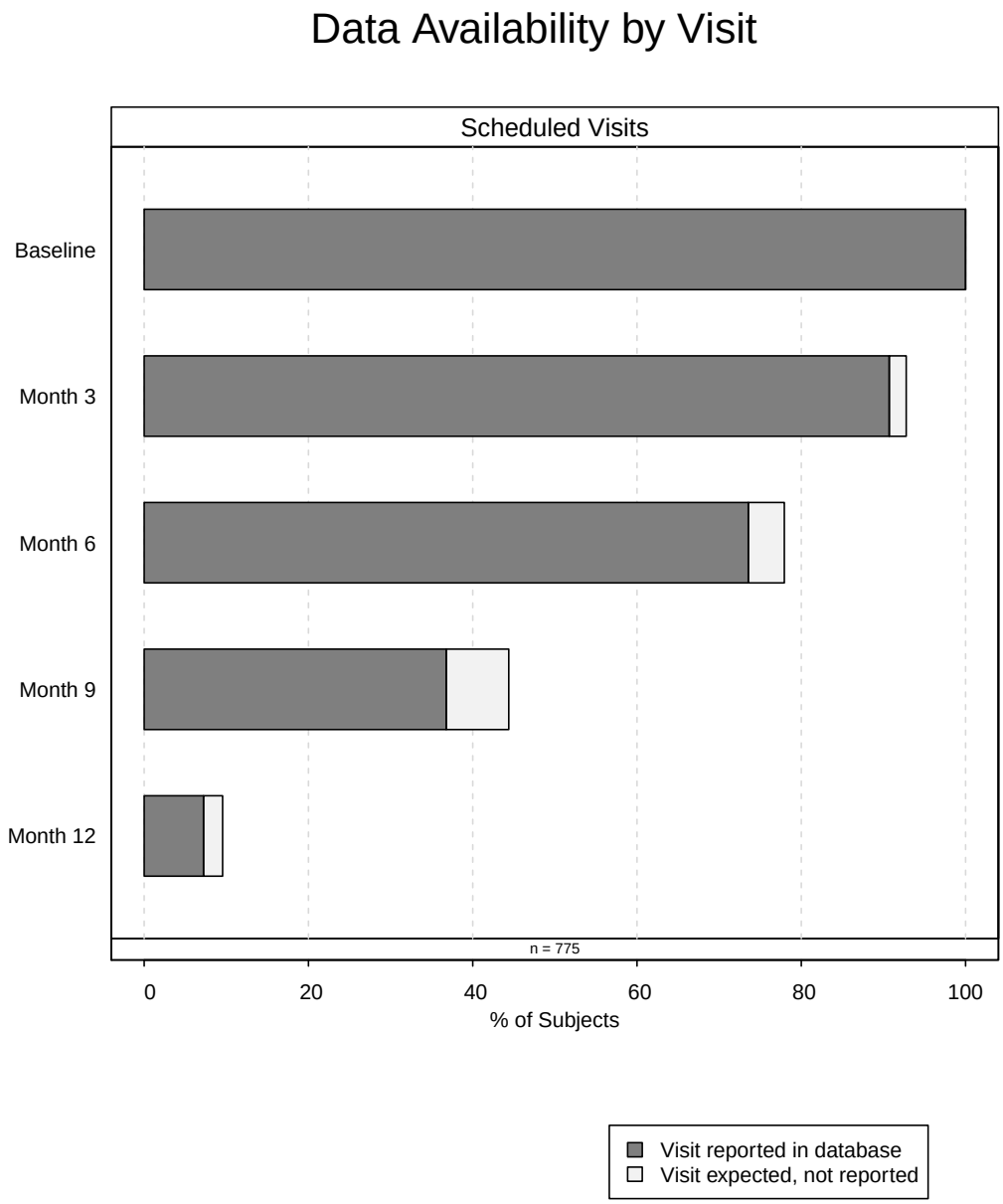
Figure STAT–3



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 77.

Figure STAT–4



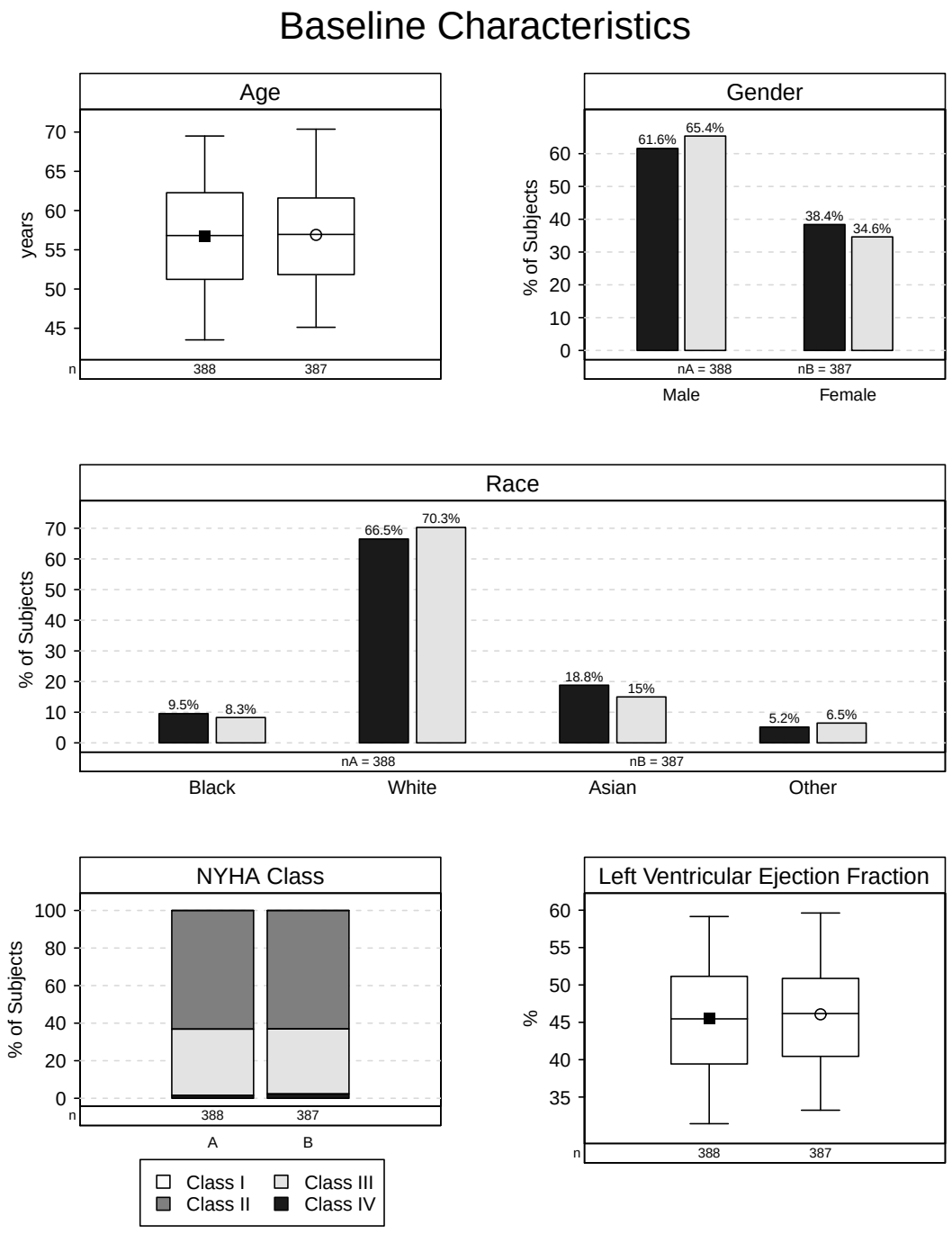
Information from simulated enrollment, laboratory and vital signs datasets. A scheduled visit is “reported” if a record of it exists in the laboratory or vital signs datasets for a given subject. A visit is “expected, not reported” if the anticipated visit date (randomization date plus an appropriate 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 78.

Chapter 2

Baseline Characteristics

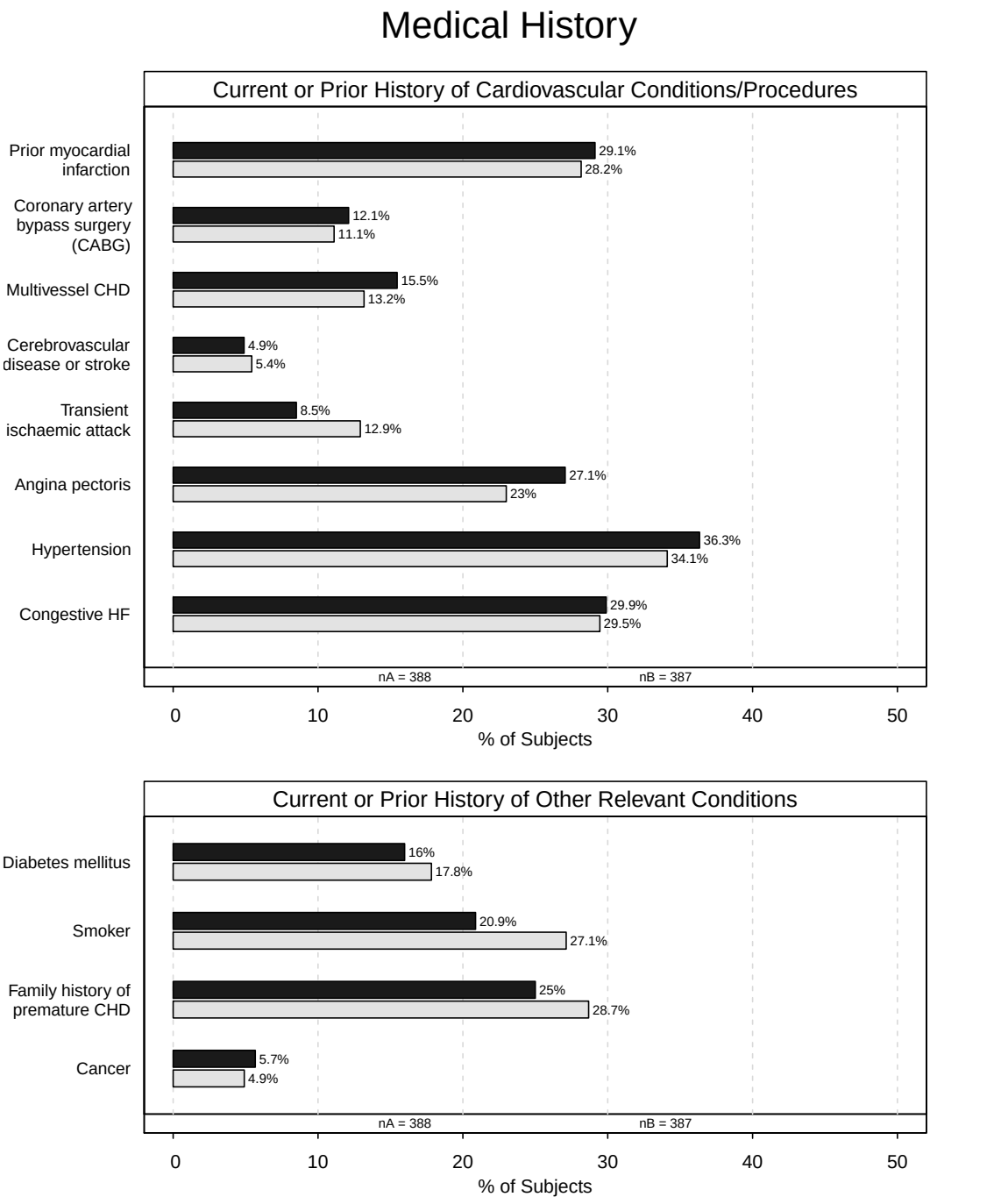
Figure DEMO–1



Information from a simulated baseline dataset. For data on race, presented in the middle panel, subjects were asked to specify a single race category. For an example of a parallel display using aggregate data, which would be part of an *Open Session Report*, see Figure DEMOBL–1 on page 122. For a color version, see Figure DEMOCOL–1 on page 132.

See Table Set DEMO–1 on page 79.

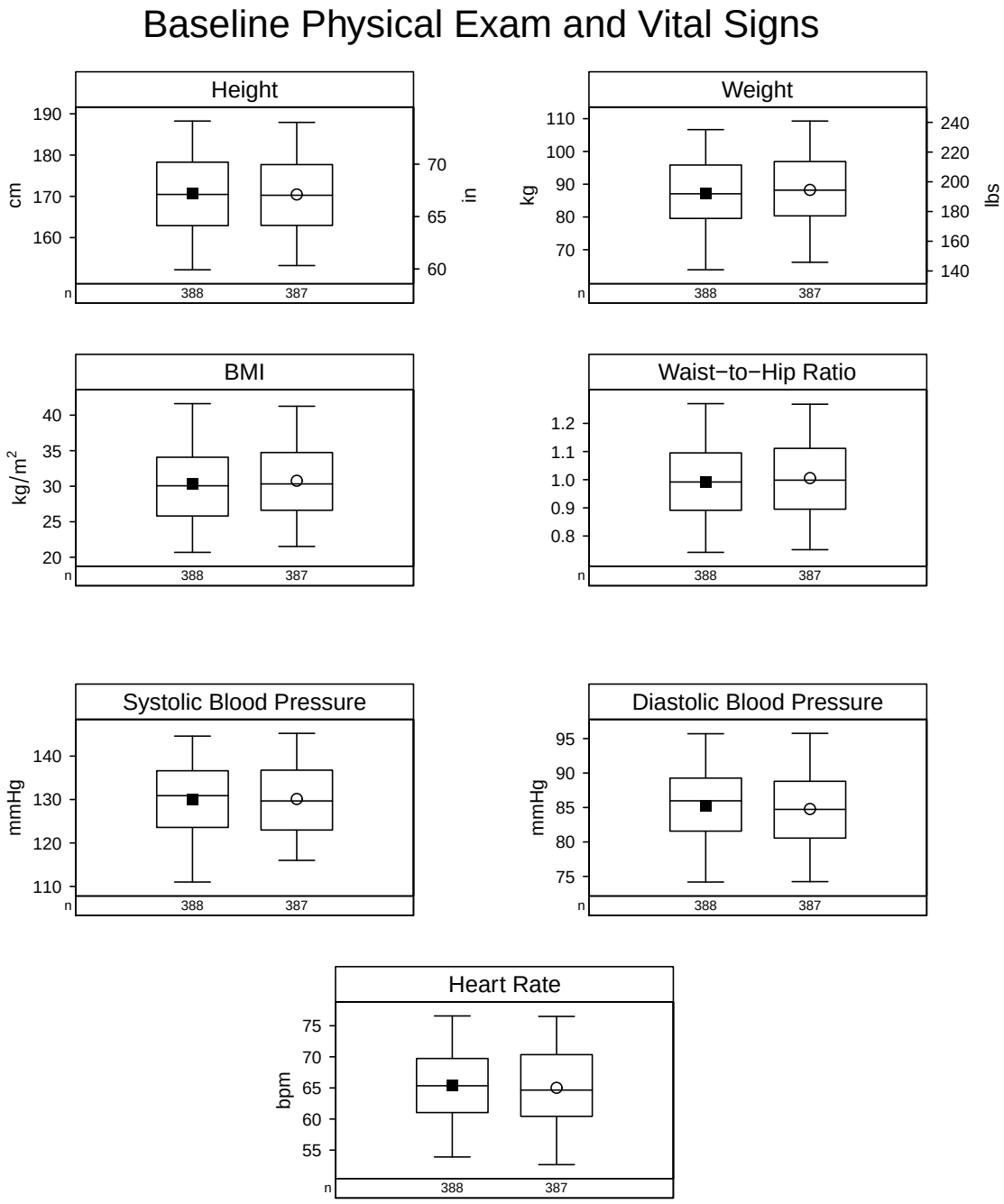
Figure MDHX–1



Information from a simulated baseline dataset.

See Table Set MDHX–1 on page 80.

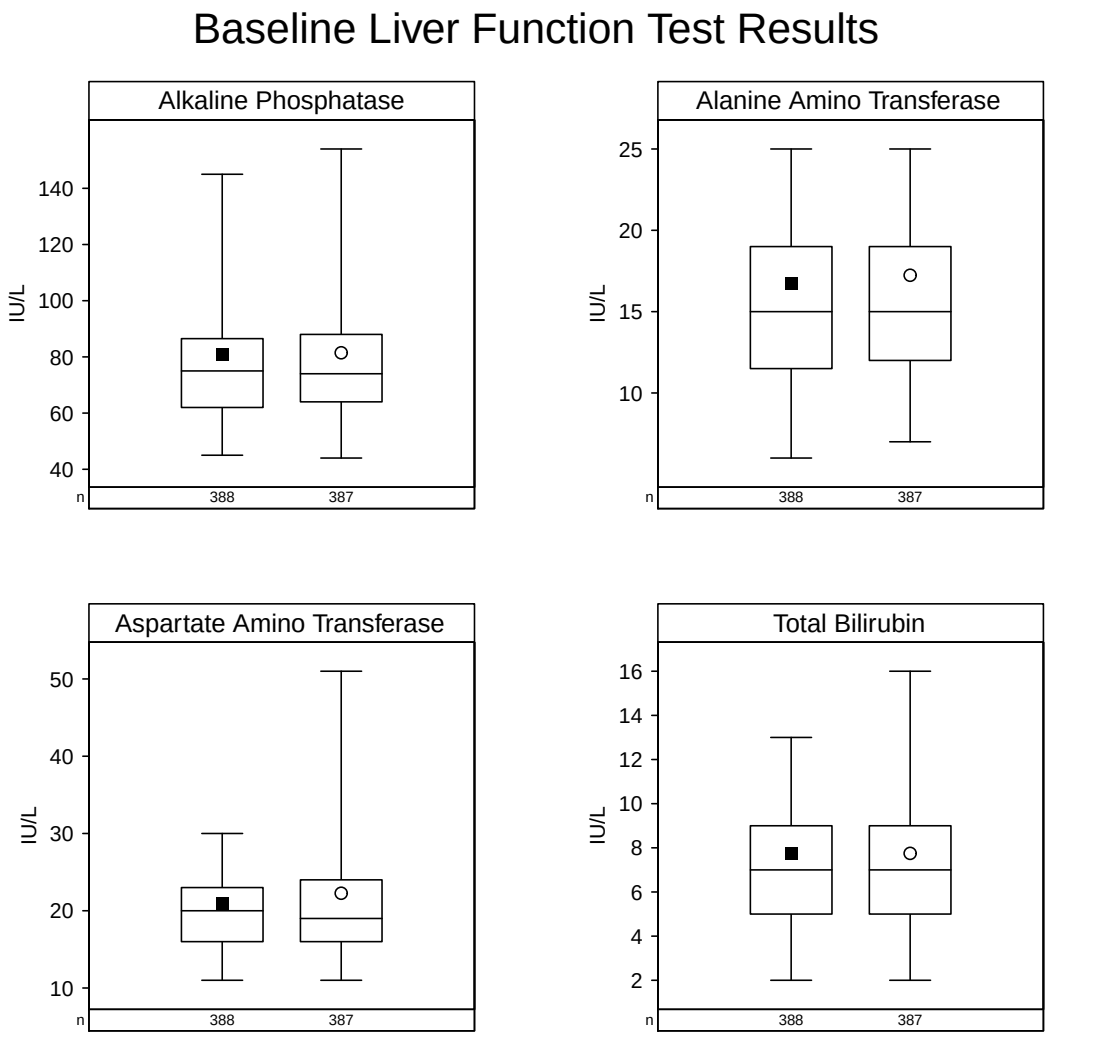
Figure VITB–1



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 81.

Figure LABB–1



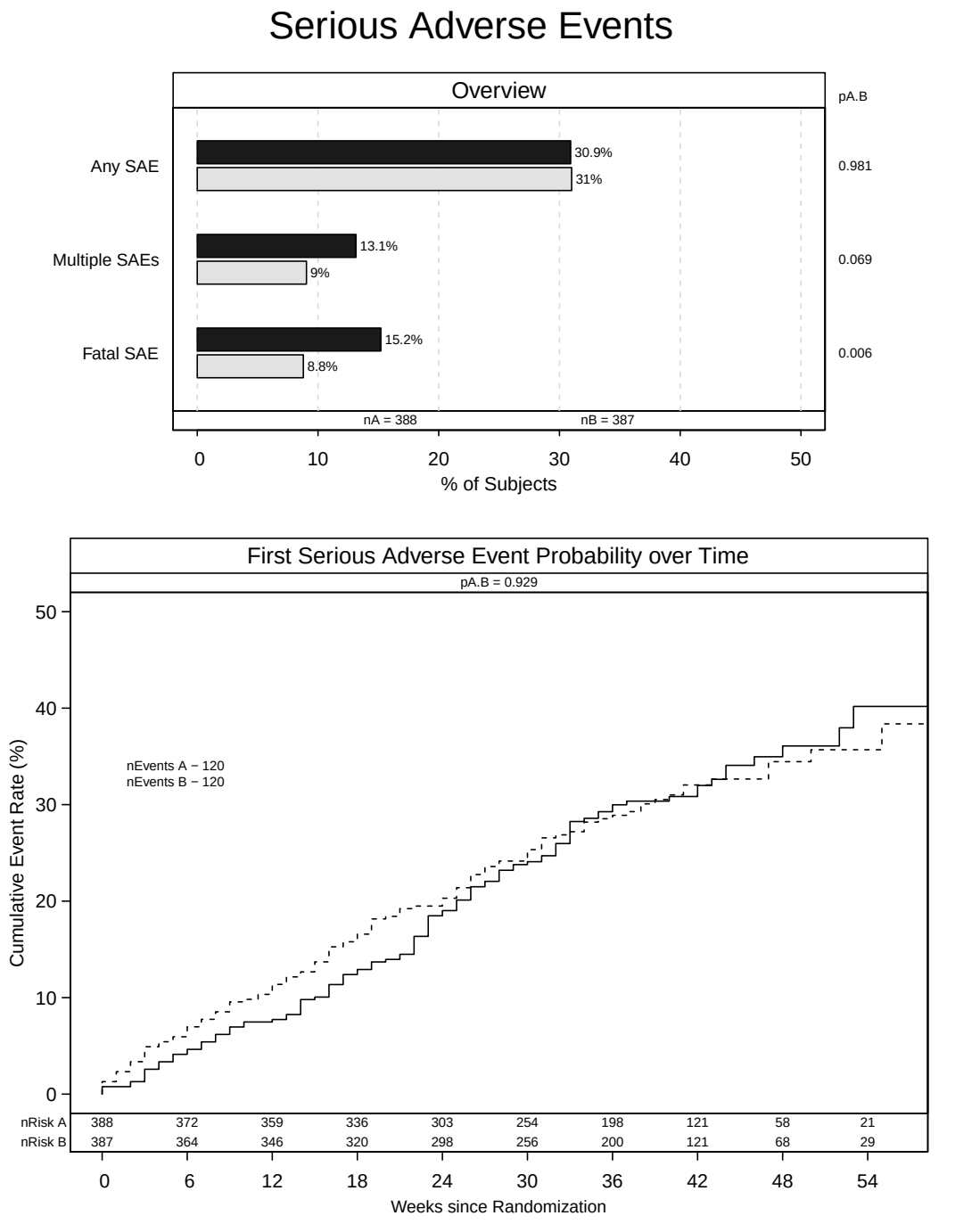
Information from a simulated laboratory dataset. The baseline value for each test is defined as the last measurement on or before the date of randomization, if more than one baseline assessment is recorded. This is a subset of laboratory measures that would typically be included in an actual DMC report.

See Table Set LABB–1 on page 82.

Chapter 3

Adverse Events

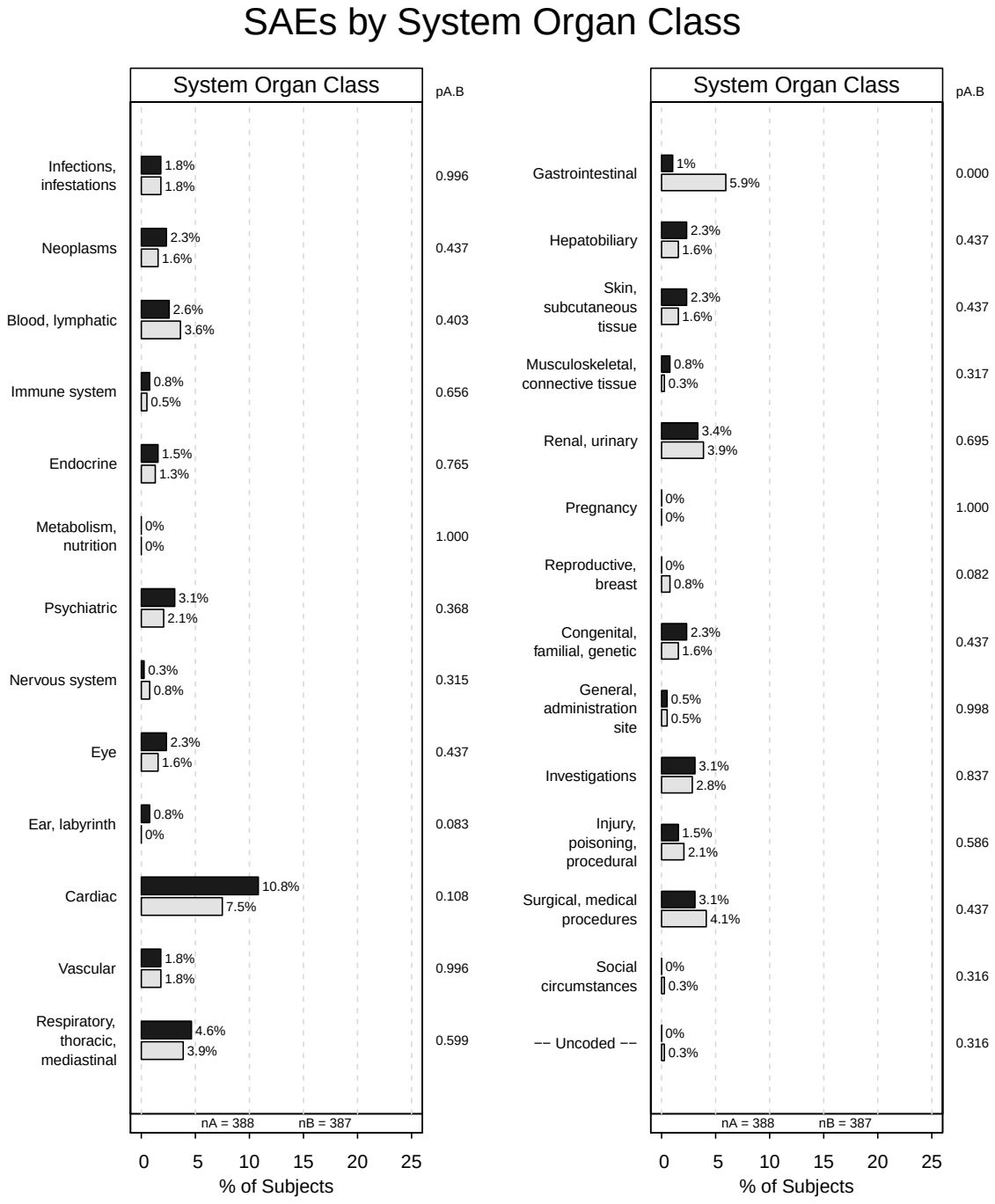
Figure SAE–1



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. For an example of a parallel display using aggregate data, which would be part of an *Open Session Report*, see Figure SAEBL–1 on page 123.

See Table Set SAE–1 on page 84.

Figure SAE–2



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. A tabulation of all SAEs by system organ class, high level term and preferred term is provided in Table SAETAB beginning on page 35. SOCs are ordered according to the MedDRA internationally agreed order.

See Table Set SAE–2 on page 86.

Table SAETAB

SAEs by SOC, High Level Term and Preferred Term

Cardiac disorders

MedDRA High Level Term ► Preferred Term	N Subjects (Events) A	B	ALL	Percent of Subjects A	B	ALL	P-Values pA.B
OVERALL	**42 (71)**	**29 (47)**	**71 (118)**	**10.8**	**7.5**	**9.2**	**0.108**
Accelerated and malignant hypertension	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Malignant hypertensive heart disease	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Breathing abnormalities	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Cardiac asthma	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Cardiac and vascular procedural complications	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Myocardial oedema	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Cardiac conduction disorders	1 (1)	1 (1)	2 (2)	0.3	0.3	0.3	0.999
Bundle branch block	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Long QT syndrome	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Cardiac disorders NEC	1 (2)	1 (1)	2 (3)	0.3	0.3	0.3	0.999
Cardiac disorder	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Cardiotoxicity	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Cardiac valve disorders NEC	0 (0)	2 (2)	2 (2)	0.0	0.5	0.3	0.156
Cardiac valve disease	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Heart valve incompetence	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Cardiomyopathies	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Hypertensive cardiomyopathy	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Cardiovascular injuries	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Atrial rupture	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Endocardial bacterial infections	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Endocarditis rheumatic	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Endocardial disorders NEC	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Endocardial fibrosis	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Haemorrhages NEC	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Pericardial haemorrhage	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Heart failures NEC	4 (5)	2 (2)	6 (7)	1.0	0.5	0.8	0.414
Cardiac failure	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Cardiac failure congestive	4 (5)	1 (1)	5 (6)	1.0	0.3	0.6	0.179
Ischaemic coronary artery disorders	20 (26)	12 (15)	32 (41)	5.2	3.1	4.1	0.151
Angina pectoris	9 (12)	4 (4)	13 (16)	2.3	1.0	1.7	0.163
Angina unstable	7 (9)	5 (8)	12 (17)	1.8	1.3	1.5	0.564
Myocardial infarction	3 (4)	2 (2)	5 (6)	0.8	0.5	0.6	0.656
Myocardial ischaemia	1 (1)	1 (1)	2 (2)	0.3	0.3	0.3	0.999
Mitral valvular disorders	2 (3)	0 (0)	2 (3)	0.5	0.0	0.3	0.157
Mitral valve calcification	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Mitral valve disease mixed	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Myocardial disorders NEC	3 (4)	1 (1)	4 (5)	0.8	0.3	0.5	0.317
Left atrial hypertrophy	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Papillary muscle rupture	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Right ventricular dysfunction	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Ventricular hypokinesia	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Noninfectious myocarditis	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Eosinophilic myocarditis	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Noninfectious pericarditis	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318

(Continued on next page.)

Information from a simulated adverse events dataset, with two system organ classes displayed as a sample. The denominators for percentages include all randomized subjects. Events known to have begun prior to randomization are not included.

In a DMC report, SAE tables with high level term and preferred term are often presented in *Ancillary Material*, while shorter tables containing only SOC and high level term are displayed in this section of *Main Material*.

SAEs by SOC, High Level Term and Preferred Term

Table SAETAB (*cont.*)

(Continued from previous page.)

Cardiac disorders

MedDRA High Level Term ► Preferred Term	N Subjects (Events) A	B	ALL	Percent of Subjects A	B	ALL	P-Values pA.B
Pericarditis adhesive	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Pericardial disorders NEC	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Pericardial rub	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Rate and rhythm disorders NEC	3 (3)	2 (2)	5 (5)	0.8	0.5	0.6	0.656
Bradycardia	2 (2)	1 (1)	3 (3)	0.5	0.3	0.4	0.564
Tachycardia	1 (1)	1 (1)	2 (2)	0.3	0.3	0.3	0.999
Right ventricular failures	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Kyphoscoliotic heart disease	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Supraventricular arrhythmias	5 (8)	8 (13)	13 (21)	1.3	2.1	1.7	0.399
Atrial fibrillation	3 (5)	6 (10)	9 (15)	0.8	1.6	1.2	0.313
Sinus bradycardia	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Supraventricular extrasystoles	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Supraventricular tachycardia	1 (1)	1 (1)	2 (2)	0.3	0.3	0.3	0.999
Ventricular arrhythmias and cardiac arrest	6 (9)	1 (2)	7 (11)	1.5	0.3	0.9	0.058
Parasystole	2 (2)	0 (0)	2 (2)	0.5	0.0	0.3	0.157
Ventricular extrasystoles	3 (5)	0 (0)	3 (5)	0.8	0.0	0.4	0.083
Ventricular tachyarrhythmia	1 (2)	1 (2)	2 (4)	0.3	0.3	0.3	0.999

Vascular disorders

MedDRA High Level Term ► Preferred Term	N Subjects (Events) A	B	ALL	Percent of Subjects A	B	ALL	P-Values pA.B
OVERALL	**7 (13)**	**7 (19)**	**14 (32)**	**1.8**	**1.8**	**1.8**	**0.996**
Aortic aneurysms and dissections	0 (0)	2 (4)	2 (4)	0.0	0.5	0.3	0.156
Aortic aneurysm	0 (0)	2 (4)	2 (4)	0.0	0.5	0.3	0.156
Aortic necrosis and vascular insufficiency	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Aortic necrosis	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Blood pressure disorders NEC	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Non-dipping	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Haemorrhages NEC	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Venous haemorrhage	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Non-site specific embolism and thrombosis	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Post thrombotic syndrome	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Non-site specific necrosis and vascular insufficiency NEC	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Arteriosclerosis	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Non-site specific vascular disorders NEC	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Microangiopathy	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Peripheral embolism and thrombosis	2 (2)	0 (0)	2 (2)	0.5	0.0	0.3	0.157
Subclavian artery embolism	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Subclavian vein thrombosis	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Peripheral vasoconstriction, necrosis and vascular insufficiency	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Peripheral arterial occlusive disease	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Phlebitis NEC	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Periphlebitis	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Site specific vascular disorders NEC	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318

(Continued on next page.)

Information from a simulated adverse events dataset, with two system organ classes displayed as a sample. The denominators for percentages include all randomized subjects. Events known to have begun prior to randomization are not included.

In a DMC report, SAE tables with high level term and preferred term are often presented in *Ancillary Material*, while shorter tables containing only SOC and high level term are displayed in this section of *Main Material*.

SAEs by SOC, High Level Term and Preferred Term

Table SAETAB (*cont.*)

(Continued from previous page.)

Vascular disorders

MedDRA High Level Term ► Preferred Term	N Subjects (Events) A	B	ALL	Percent of Subjects A	B	ALL	P-Values pA.B
Aortic disorder	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Varicose veins non-site specific	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Thrombosed varicose vein	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Vascular hypertensive disorders NEC	2 (2)	1 (1)	3 (3)	0.5	0.3	0.4	0.564
Hypertension	1 (1)	1 (1)	2 (2)	0.3	0.3	0.3	0.999
Systolic hypertension	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Vascular hypotensive disorders	1 (1)	2 (2)	3 (3)	0.3	0.5	0.4	0.561
Hypotension	1 (1)	2 (2)	3 (3)	0.3	0.5	0.4	0.561
Vasculitides	2 (2)	1 (1)	3 (3)	0.5	0.3	0.4	0.564
Diffuse vasculitis	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Pseudovasculitis	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Vasculitis necrotising	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Vena caval embolism and thrombosis	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Vena cava thrombosis	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316

Information from a simulated adverse events dataset, with two system organ classes displayed as a sample. The denominators for percentages include all randomized subjects. Events known to have begun prior to randomization are not included.

In a DMC report, SAE tables with high level term and preferred term are often presented in *Ancillary Material*, while shorter tables containing only SOC and high level term are displayed in this section of *Main Material*.

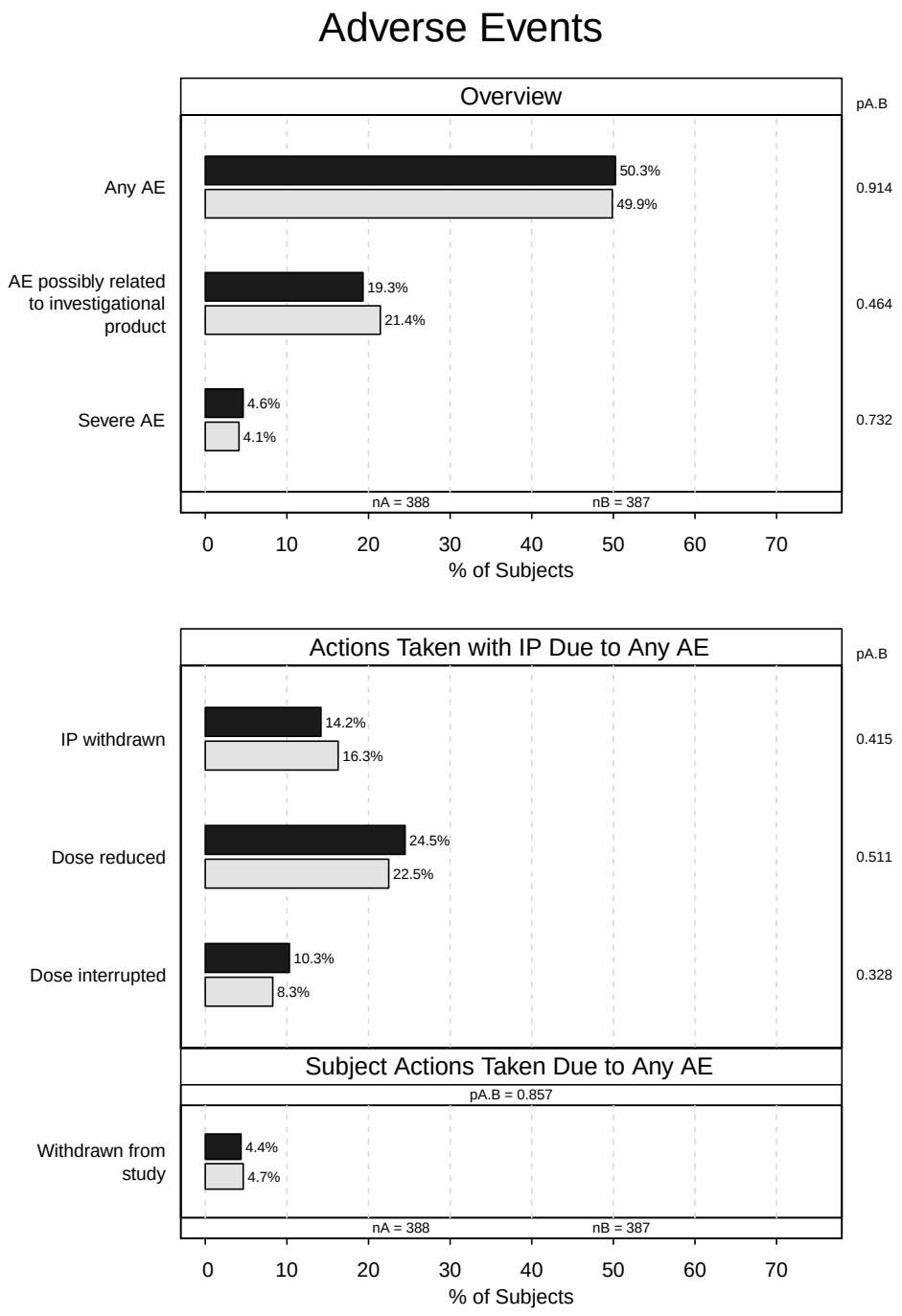
Figure AELISTING–1

Listing of Serious Adverse Events Reported on the Case Report Form

Trt Grp	Subject ID	Age	Sex	Race	Country	Rand Date	Study Day	MedDRA Preferred Term	Died	Action Taken w/ IP	W/D from Study	Outcome
A	1265	70	F	White	MEX	12SEP2007	12	Angina pectoris	No	Temp Stop	No	Resolved
							38	Left atrial hypertrophy	No	Temp Stop	No	Resolved
							50	Angina pectoris	No	Temp Stop	No	Resolved
							54	Aortic necrosis	No	Temp Stop	No	Resolved
							58	Ventricular extrasystoles	No	Temp Stop	No	Resolved
							101	Angina pectoris	No	Temp Stop	No	Resolved
	4533	60	M	Asian	CAN	05NOV2007	55	Angina unstable	No	None	No	Resolved
	4788	57	M	White	CAN	21APR2008	66	Diffuse vasculitis	No	None	No	Unresolved
	7763	57	F	Asian	PHL	07NOV2007	90	Bradycardia	No	None	No	Resolved
	7994	51	M	White	CAN	30JUL2007	49	Cardiac failure congestive	No	None	No	Resolved
							59	Cardiac failure congestive	No	None	No	Resolved
	8818	41	M	White	USA	26AUG2007	38	Tachycardia	No	None	No	Resolved
							59	Supraventricular tachycardia	No	None	No	Resolved
B	1265	70	F	White	MEX	12SEP2007	58	Aortic aneurysm	No	Temp Stop	No	Resolved
							61	Aortic aneurysm	No	Temp Stop	No	Resolved
	4675	48	F	White	USA	21AUG2007	99	Angina unstable	No	None	No	Unresolved
	6720	59	M	Black	USA	23NOV2007	83	Atrial fibrillation	No	Perm D/C	Yes	Resolved
	7763	57	F	Asian	PHL	07NOV2007	81	Cardiac failure	No	None	No	Resolved
	8482	71	F	White	MEX	28NOV2007	42	Pericardial haemorrhage	Yes	None	Yes	Fatal
	8818	41	M	White	USA	26AUG2007	1	Vasculitis necrotising	No	None	No	Resolved

Information from a simulated serious adverse event dataset.

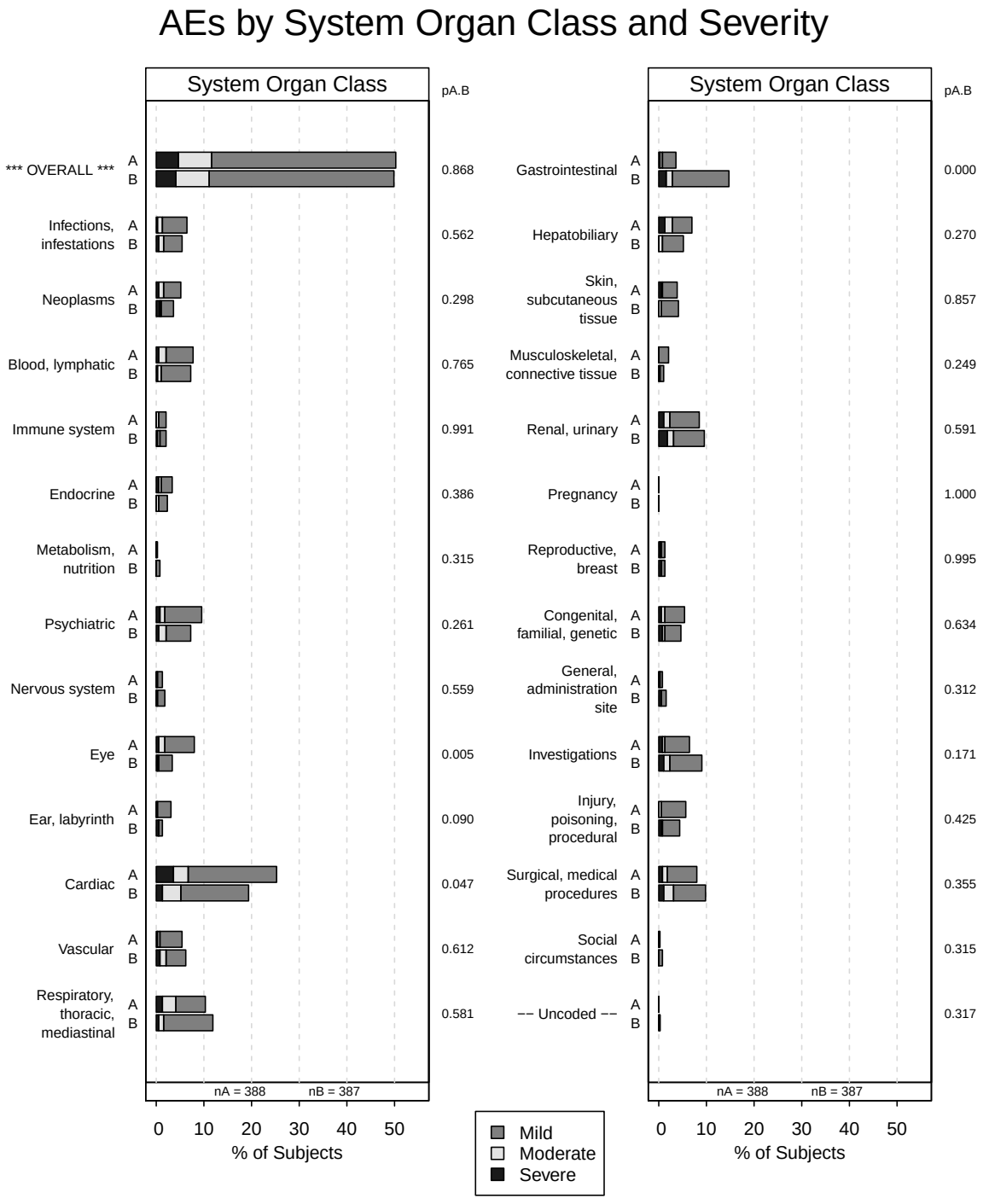
Figure AE–1



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 88.

Figure AE–2

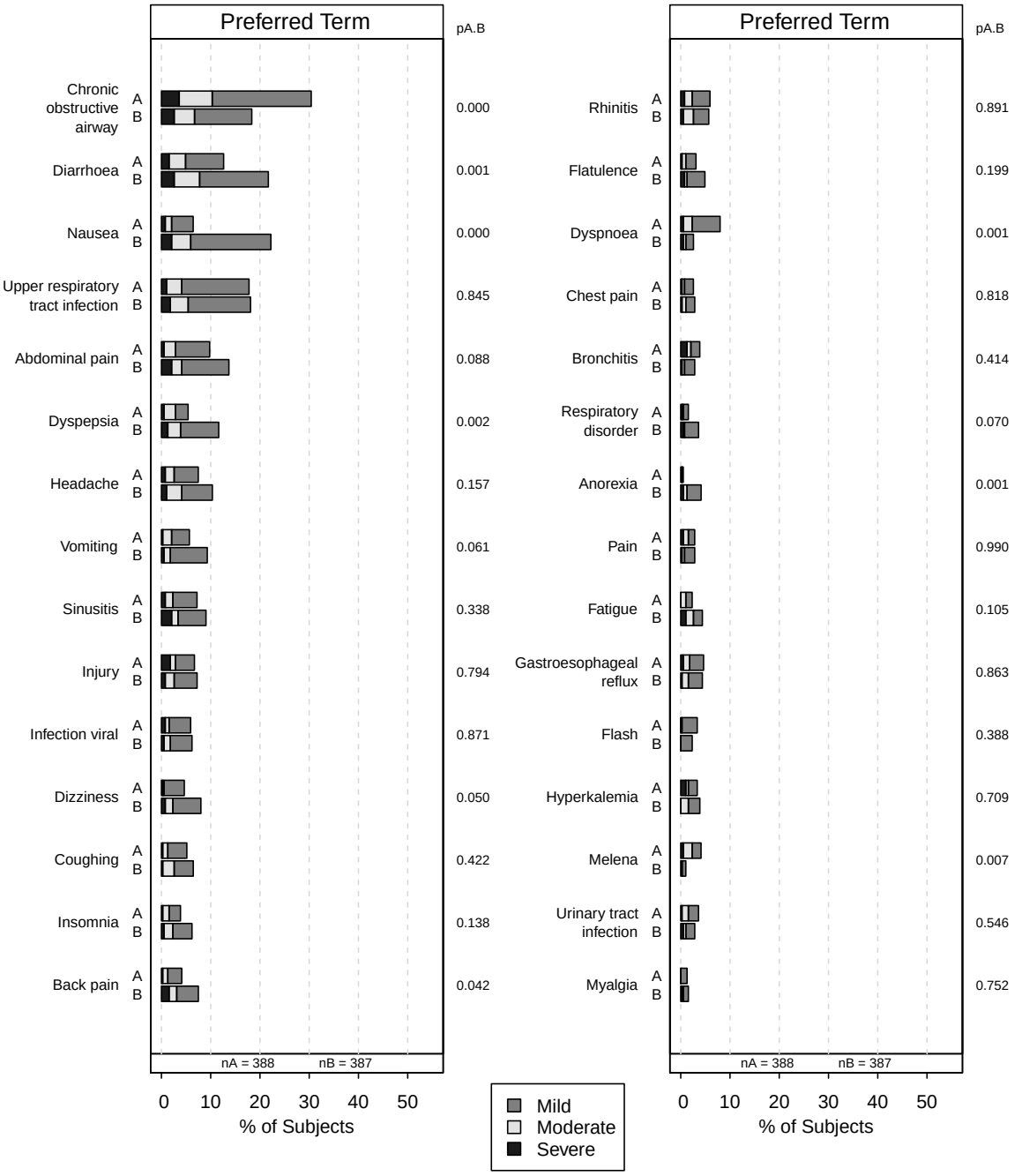


Information from a simulated adverse events dataset. Panels display the percent of subjects experiencing any AE within each coded system organ class. The denominators for percentages include all randomized subjects. Events known to have begun prior to randomization are not included. Within each system organ class, a subject was assigned to a single category based on the AE with the maximum severity. A tabulation of all AEs by system organ class, high level term and preferred term is provided in Table AETAB beginning on page 43. SOCs are ordered according to the MedDRA internationally agreed order.

See Table Set AE–2 on page 89.

Figure AE–3

Most Common AEs by Preferred Term and Severity



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 91.

Figure AE–4

Adverse Events, by MedDRA Term
Occurring in > 0.5% of Subjects in Either Treatment Group
with a Nominally Significant (p < 0.1) Difference between Treatments

(NB: Since preferred terms are coded within high level terms, the same event may be counted under both categories.)			*Treatment Group*				ChiSq P−val
			A		B		
			N	%	N	%	
Relative Frequency	***System Organ Class***	***High Level Term (HLT) or Preferred Term (PRT)***					
More in A	**Cardiac disorders**	**HLT: Myocardial disorders NEC**	8	2.1%	2	0.5%	0.057
		HLT: Ventricular arrhythmias and cardiac arrest	14	3.6%	4	1.0%	0.017
		PRT: Angina pectoris	27	7.0%	14	3.6%	0.038
		PRT: Ventricular extrasystoles	6	1.5%	1	0.3%	0.058
More in B	**Vascular disorders**	**HLT: Aortic aneurysms and dissections**	0	0.0%	3	0.8%	0.082
		HLT: Haemorrhages NEC	0	0.0%	3	0.8%	0.082
		HLT: Non−site specific vascular disorders NEC	0	0.0%	6	1.6%	0.014
		PRT: Aortic aneurysm	0	0.0%	3	0.8%	0.082

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.

Table AETAB

AEs by SOC, High Level Term and Preferred Term

Cardiac disorders

MedDRA High Level Term ► Preferred Term	N Subjects (Events) A	N Subjects (Events) B	N Subjects (Events) ALL	Percent of Subjects A	Percent of Subjects B	Percent of Subjects ALL	P-Values pA.B
OVERALL	**98 (181)**	**75 (136)**	**173 (317)**	**25.3**	**19.4**	**22.3**	**0.049**
Accelerated and malignant hypertension	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Malignant hypertensive heart disease	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Breathing abnormalities	1 (1)	1 (1)	2 (2)	0.3	0.3	0.3	0.999
Cardiac asthma	1 (1)	1 (1)	2 (2)	0.3	0.3	0.3	0.999
Cardiac and vascular procedural complications	1 (1)	2 (4)	3 (5)	0.3	0.5	0.4	0.561
Coronary artery perforation	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Myocardial oedema	1 (1)	1 (2)	2 (3)	0.3	0.3	0.3	0.999
Cardiac conduction disorders	1 (1)	3 (4)	4 (5)	0.3	0.8	0.5	0.315
Bundle branch block	1 (1)	1 (1)	2 (2)	0.3	0.3	0.3	0.999
Long QT syndrome	0 (0)	2 (3)	2 (3)	0.0	0.5	0.3	0.156
Cardiac disorders NEC	1 (1)	3 (4)	4 (5)	0.3	0.8	0.5	0.315
Cardiac disorder	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Cardiotoxicity	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Intracardiac mass	0 (0)	2 (3)	2 (3)	0.0	0.5	0.3	0.156
Cardiac hypertensive complications	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Hypertensive heart disease	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Cardiac signs and symptoms NEC	1 (1)	1 (2)	2 (3)	0.3	0.3	0.3	0.999
Positive cardiac inotropic effect	1 (1)	1 (2)	2 (3)	0.3	0.3	0.3	0.999
Cardiac valve disorders NEC	2 (3)	2 (2)	4 (5)	0.5	0.5	0.5	0.998
Cardiac valve disease	1 (1)	1 (1)	2 (2)	0.3	0.3	0.3	0.999
Heart valve calcification	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Heart valve incompetence	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Cardiomyopathies	2 (3)	1 (2)	3 (5)	0.5	0.3	0.4	0.564
Hypertensive cardiomyopathy	1 (2)	1 (2)	2 (4)	0.3	0.3	0.3	0.999
Hypertrophic cardiomyopathy	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Cardiovascular injuries	0 (0)	2 (2)	2 (2)	0.0	0.5	0.3	0.156
Atrial rupture	0 (0)	2 (2)	2 (2)	0.0	0.5	0.3	0.156
Coronary artery disorders NEC	2 (2)	2 (2)	4 (4)	0.5	0.5	0.5	0.998
Coronary artery disease	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Coronary artery stenosis	1 (1)	1 (1)	2 (2)	0.3	0.3	0.3	0.999
Coronary ostial stenosis	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Endocardial bacterial infections	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Endocarditis rheumatic	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Endocardial disorders NEC	0 (0)	2 (4)	2 (4)	0.0	0.5	0.3	0.156
Endocardial fibrosis	0 (0)	2 (4)	2 (4)	0.0	0.5	0.3	0.156
Endocarditis NEC	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Lupus endocarditis	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Haemorrhages NEC	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Pericardial haemorrhage	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Heart failures NEC	12 (18)	7 (11)	19 (29)	3.1	1.8	2.5	0.248
Cardiac failure	6 (9)	3 (5)	9 (14)	1.5	0.8	1.2	0.316
Cardiac failure congestive	6 (9)	4 (6)	10 (15)	1.5	1.0	1.3	0.527
Ischaemic coronary artery disorders	48 (69)	34 (50)	82 (119)	12.4	8.8	10.6	0.105
Angina pectoris	27 (39)	14 (20)	41 (59)	7.0	3.6	5.3	0.038

(Continued on next page.)

Information from a simulated adverse events dataset, with two system organ classes displayed as a sample. The denominators for percentages include all randomized subjects. Events known to have begun prior to randomization are not included.

In a DMC report, AE tables with high level term and preferred term are often presented in *Ancillary Material*, while shorter tables containing only SOC and high level term are displayed in this section of *Main Material*.

AEs by SOC, High Level Term and Preferred Term

Table AETAB (*cont.*)

(Continued from previous page.)

Cardiac disorders

MedDRA High Level Term ► Preferred Term	N Subjects (Events) A		B		ALL		Percent of Subjects A	B	ALL	P-Values pA.B
Angina unstable	14	(18)	12	(19)	26	(37)	3.6	3.1	3.4	0.695
Myocardial infarction	6	(11)	7	(9)	13	(20)	1.5	1.8	1.7	0.776
Myocardial ischaemia	1	(1)	1	(2)	2	(3)	0.3	0.3	0.3	0.999
Left ventricular failures	0	(0)	1	(1)	1	(1)	0.0	0.3	0.1	0.316
Left ventricular failure	0	(0)	1	(1)	1	(1)	0.0	0.3	0.1	0.316
Lipid metabolism and deposit disorders NEC	1	(1)	0	(0)	1	(1)	0.3	0.0	0.1	0.318
Lipomatous hypertrophy of the interatrial septum	1	(1)	0	(0)	1	(1)	0.3	0.0	0.1	0.318
Mitral valvular disorders	3	(4)	2	(3)	5	(7)	0.8	0.5	0.6	0.656
Mitral valve calcification	1	(2)	0	(0)	1	(2)	0.3	0.0	0.1	0.318
Mitral valve disease mixed	1	(1)	1	(2)	2	(3)	0.3	0.3	0.3	0.999
Mitral valve sclerosis	1	(1)	1	(1)	2	(2)	0.3	0.3	0.3	0.999
Myocardial disorders NEC	8	(13)	2	(3)	10	(16)	2.1	0.5	1.3	0.057
Cardiomegaly	2	(4)	0	(0)	2	(4)	0.5	0.0	0.3	0.157
Chordae tendinae rupture	0	(0)	1	(1)	1	(1)	0.0	0.3	0.1	0.316
Left atrial hypertrophy	1	(1)	0	(0)	1	(1)	0.3	0.0	0.1	0.318
Left ventricular dysfunction	1	(1)	0	(0)	1	(1)	0.3	0.0	0.1	0.318
Papillary muscle rupture	1	(2)	1	(2)	2	(4)	0.3	0.3	0.3	0.999
Right ventricular dysfunction	1	(1)	0	(0)	1	(1)	0.3	0.0	0.1	0.318
Ventricular hypokinesia	1	(2)	0	(0)	1	(2)	0.3	0.0	0.1	0.318
Ventricular septal defect acquired	1	(2)	0	(0)	1	(2)	0.3	0.0	0.1	0.318
Noninfectious myocarditis	1	(2)	0	(0)	1	(2)	0.3	0.0	0.1	0.318
Eosinophilic myocarditis	1	(2)	0	(0)	1	(2)	0.3	0.0	0.1	0.318
Noninfectious pericarditis	1	(2)	0	(0)	1	(2)	0.3	0.0	0.1	0.318
Pericarditis adhesive	1	(2)	0	(0)	1	(2)	0.3	0.0	0.1	0.318
Pericardial disorders NEC	2	(4)	0	(0)	2	(4)	0.5	0.0	0.3	0.157
Pericardial disease	1	(2)	0	(0)	1	(2)	0.3	0.0	0.1	0.318
Pericardial rub	1	(2)	0	(0)	1	(2)	0.3	0.0	0.1	0.318
Pulmonary valvular disorders	2	(3)	2	(2)	4	(5)	0.5	0.5	0.5	0.998
Pulmonary valve calcification	1	(1)	1	(1)	2	(2)	0.3	0.3	0.3	0.999
Pulmonary valve disease	1	(2)	0	(0)	1	(2)	0.3	0.0	0.1	0.318
Pulmonary valve incompetence	0	(0)	1	(1)	1	(1)	0.0	0.3	0.1	0.316
Rate and rhythm disorders NEC	6	(9)	4	(6)	10	(15)	1.5	1.0	1.3	0.527
Bradycardia	3	(5)	3	(4)	6	(9)	0.8	0.8	0.8	0.997
Postural orthostatic tachycardia syndrome	1	(1)	0	(0)	1	(1)	0.3	0.0	0.1	0.318
Reperfusion arrhythmia	1	(1)	0	(0)	1	(1)	0.3	0.0	0.1	0.318
Tachycardia	1	(2)	1	(2)	2	(4)	0.3	0.3	0.3	0.999
Right ventricular failures	1	(1)	3	(3)	4	(4)	0.3	0.8	0.5	0.315
Acute right ventricular failure	0	(0)	2	(2)	2	(2)	0.0	0.5	0.3	0.156
Kyphoscoliotic heart disease	1	(1)	1	(1)	2	(2)	0.3	0.3	0.3	0.999
Supraventricular arrhythmias	13	(17)	13	(19)	26	(36)	3.4	3.4	3.4	0.995
Atrial fibrillation	9	(12)	9	(12)	18	(24)	2.3	2.3	2.3	0.996
Sinus arrest	1	(1)	1	(2)	2	(3)	0.3	0.3	0.3	0.999
Sinus bradycardia	1	(1)	1	(2)	2	(3)	0.3	0.3	0.3	0.999
Supraventricular extrasystoles	1	(1)	1	(2)	2	(3)	0.3	0.3	0.3	0.999
Supraventricular tachycardia	1	(2)	1	(1)	2	(3)	0.3	0.3	0.3	0.999
Ventricular arrhythmias and cardiac arrest	14	(20)	4	(7)	18	(27)	3.6	1.0	2.3	0.017

(Continued on next page.)

Information from a simulated adverse events dataset, with two system organ classes displayed as a sample. The denominators for percentages include all randomized subjects. Events known to have begun prior to randomization are not included.

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AEs by SOC, High Level Term and Preferred Term

Table AETAB (*cont.*)

(Continued from previous page.)

Cardiac disorders

MedDRA High Level Term ► Preferred Term	N Subjects (Events) A	B	ALL	Percent of Subjects A	B	ALL	P-Values pA.B
Cardiac arrest	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Parasystole	2 (3)	0 (0)	2 (3)	0.5	0.0	0.3	0.157
Torsade de pointes	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Ventricular extrasystoles	6 (7)	1 (2)	7 (9)	1.5	0.3	0.9	0.058
Ventricular fibrillation	1 (2)	1 (2)	2 (4)	0.3	0.3	0.3	0.999
Ventricular pre-excitation	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Ventricular tachyarrhythmia	1 (2)	1 (1)	2 (3)	0.3	0.3	0.3	0.999
Ventricular tachycardia	1 (2)	1 (2)	2 (4)	0.3	0.3	0.3	0.999

Vascular disorders

MedDRA High Level Term ► Preferred Term	N Subjects (Events) A	B	ALL	Percent of Subjects A	B	ALL	P-Values pA.B
OVERALL	**21 (50)**	**24 (64)**	**45 (114)**	**5.4**	**6.2**	**5.8**	**0.639**
Accelerated and malignant hypertension	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Tyramine reaction	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Aneurysms and dissections non-site specific	1 (2)	1 (2)	2 (4)	0.3	0.3	0.3	0.999
Aneurysm arteriovenous	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Artery dissection	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Aortic aneurysms and dissections	0 (0)	3 (5)	3 (5)	0.0	0.8	0.4	0.082
Aortic aneurysm	0 (0)	3 (5)	3 (5)	0.0	0.8	0.4	0.082
Aortic necrosis and vascular insufficiency	2 (2)	2 (4)	4 (6)	0.5	0.5	0.5	0.998
Aortic necrosis	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Aortic stenosis	1 (1)	2 (4)	3 (5)	0.3	0.5	0.4	0.561
Blood pressure disorders NEC	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Non-dipping	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Cardiac and vascular procedural complications	1 (1)	1 (1)	2 (2)	0.3	0.3	0.3	0.999
Phlebitis	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Vessel perforation	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Circulatory collapse and shock	1 (1)	1 (1)	2 (2)	0.3	0.3	0.3	0.999
Hypoperfusion	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Shock	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Duodenal and small intestinal stenosis and obstruction	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Superior mesenteric artery syndrome	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Haemorrhages NEC	0 (0)	3 (4)	3 (4)	0.0	0.8	0.4	0.082
Haematocoele	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Subgaleal haematoma	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Venous haemorrhage	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Lymphatic system disorders NEC	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Lymphangiectasia	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Non-site specific embolism and thrombosis	1 (2)	1 (1)	2 (3)	0.3	0.3	0.3	0.999
Arterial thrombosis	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Post thrombotic syndrome	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Non-site specific necrosis and vascular insufficiency NEC	1 (2)	4 (7)	5 (9)	0.3	1.0	0.6	0.177
Arterial insufficiency	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316

(Continued on next page.)

Information from a simulated adverse events dataset, with two system organ classes displayed as a sample. The denominators for percentages include all randomized subjects. Events known to have begun prior to randomization are not included.

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AEs by SOC, High Level Term and Preferred Term

Table AETAB (*cont.*)

(Continued from previous page.)

Vascular disorders

MedDRA High Level Term ► Preferred Term	N Subjects (Events) A	B	ALL	Percent of Subjects A	B	ALL	P-Values pA.B
Arteriosclerosis	1 (1)	2 (3)	3 (4)	0.3	0.5	0.4	0.561
Necrosis of artery	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Venous insufficiency	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Non-site specific vascular disorders NEC	0 (0)	6 (10)	6 (10)	0.0	1.6	0.8	0.014
Haemodynamic rebound	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Microangiopathy	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Phlebolith	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Vasodilatation	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Vein discolouration	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Venous lake	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Oncologic complications and emergencies	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Superior vena caval occlusion	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Peripheral aneurysms and dissections	2 (3)	1 (2)	3 (5)	0.5	0.3	0.4	0.564
Femoral artery dissection	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Peripheral artery aneurysm	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Subclavian artery aneurysm	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Peripheral embolism and thrombosis	3 (4)	1 (1)	4 (5)	0.8	0.3	0.5	0.317
Iliac artery embolism	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Subclavian artery embolism	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Subclavian vein thrombosis	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Venous thrombosis limb	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Peripheral vascular disorders NEC	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Peripheral vascular disorder	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Peripheral vasoconstriction, necrosis and vascular insufficiency	4 (5)	4 (5)	8 (10)	1.0	1.0	1.0	0.997
Arteriosclerosis obliterans	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Dependent rubor	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Iliac artery occlusion	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Iliac vein occlusion	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Peripheral arterial occlusive disease	2 (2)	1 (1)	3 (3)	0.5	0.3	0.4	0.564
Raynaud's phenomenon	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Phlebitis NEC	1 (1)	1 (1)	2 (2)	0.3	0.3	0.3	0.999
Periphlebitis	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Phlebitis deep	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Renal hypertensions	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Renovascular hypertension	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Site specific vascular disorders NEC	1 (1)	2 (3)	3 (4)	0.3	0.5	0.4	0.561
Aortic dilatation	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Aortic disorder	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Aortic elongation	0 (0)	1 (2)	1 (2)	0.0	0.3	0.1	0.316
Transient cerebrovascular events	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Subclavian steal syndrome	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Varicose veins non-site specific	2 (3)	0 (0)	2 (3)	0.5	0.0	0.3	0.157
Bleeding varicose vein	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Thrombosed varicose vein	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Vascular hypertensive disorders NEC	5 (7)	3 (4)	8 (11)	1.3	0.8	1.0	0.479
Diastolic hypertension	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318

(Continued on next page.)

Information from a simulated adverse events dataset, with two system organ classes displayed as a sample. The denominators for percentages include all randomized subjects. Events known to have begun prior to randomization are not included.

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AEs by SOC, High Level Term and Preferred Term

Table AETAB (*cont.*)

(Continued from previous page.)

Vascular disorders

MedDRA High Level Term ► Preferred Term	N Subjects (Events) A	B	ALL	Percent of Subjects A	B	ALL	P-Values pA.B
Hypertension	3 (4)	3 (4)	6 (8)	0.8	0.8	0.8	0.997
Systolic hypertension	1 (2)	0 (0)	1 (2)	0.3	0.0	0.1	0.318
Vascular hypotensive disorders	5 (8)	3 (5)	8 (13)	1.3	0.8	1.0	0.479
Diastolic hypotension	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Hypotension	4 (7)	3 (5)	7 (12)	1.0	0.8	0.9	0.707
Vasculitides	3 (3)	1 (1)	4 (4)	0.8	0.3	0.5	0.317
Diffuse vasculitis	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Pseudovasculitis	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Vasculitis	1 (1)	0 (0)	1 (1)	0.3	0.0	0.1	0.318
Vasculitis necrotising	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Vena caval embolism and thrombosis	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316
Vena cava thrombosis	0 (0)	1 (1)	1 (1)	0.0	0.3	0.1	0.316

Information from a simulated adverse events dataset, with two system organ classes displayed as a sample. The denominators for percentages include all randomized subjects. Events known to have begun prior to randomization are not included.

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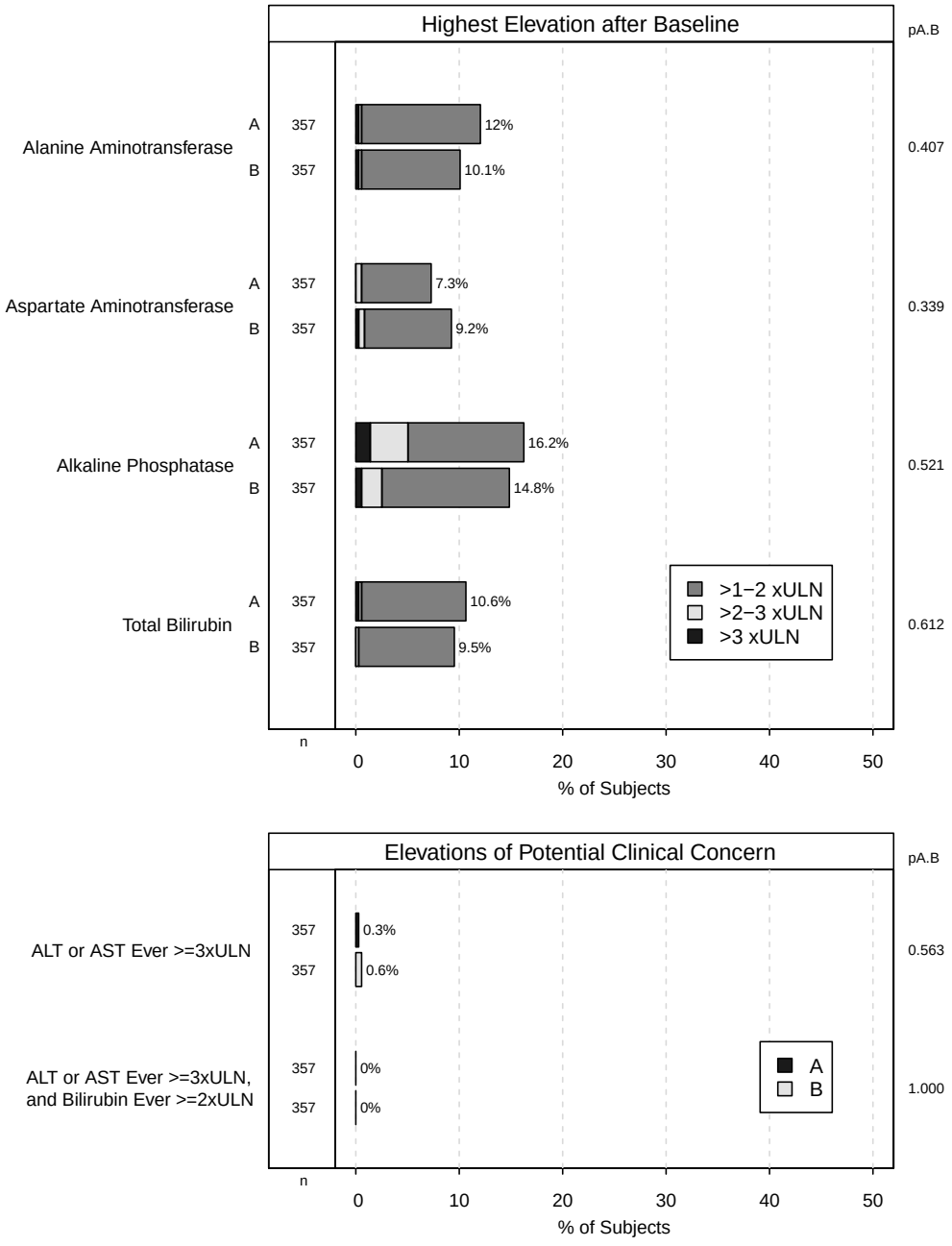
Chapter 4

Central Laboratory Measures

Figure LFTABN–1

Summary of Liver Function Test Elevations

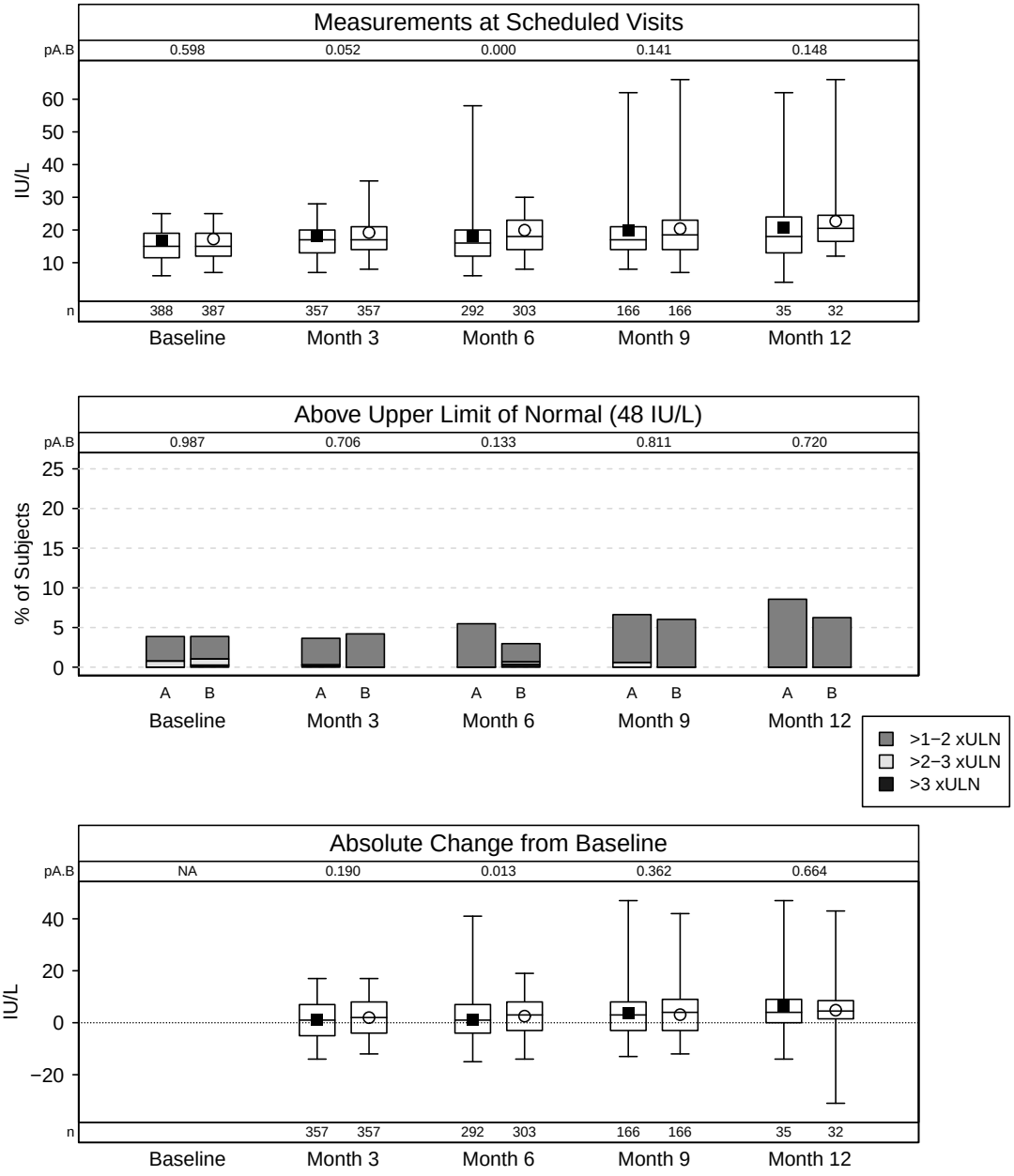


Information from a simulated laboratory dataset. This display summarizes the maximum post-baseline elevation for each subject, including repeated measurements and measurements recorded at unscheduled visits. The lower panel indicates whether a subject ever had alanine aminotransferase (ALT) or aspartate aminotransferase (AST) $\geq$3xULN, *and* total bilirubin $\geq$2xULN, at any time post-baseline (not necessarily at the same visit).

See Table Set LFTABN–1 on page 93.

Figure LFT–1

Alanine Amino Transferase

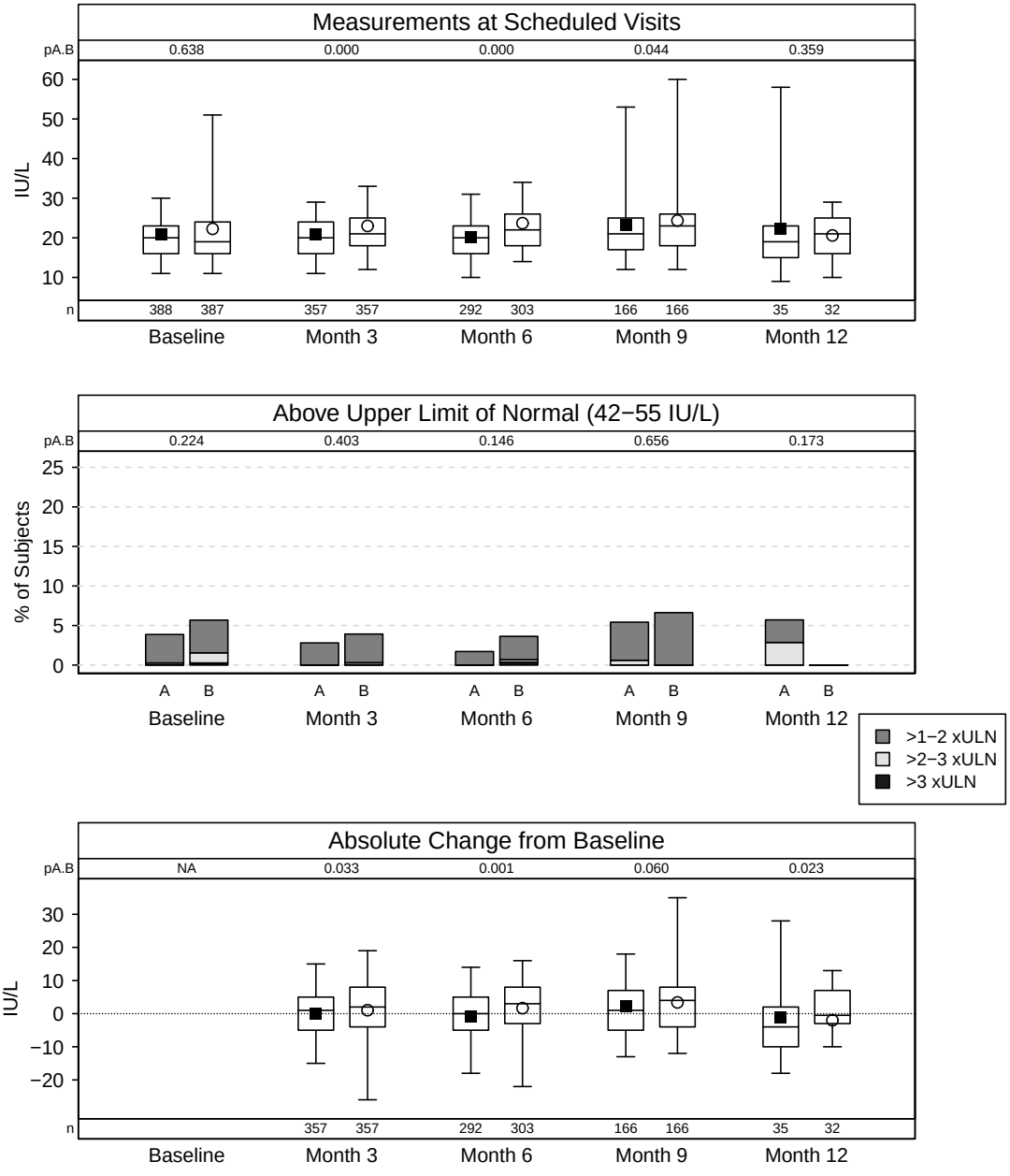


Information from a simulated laboratory dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed.

See Table Set LFT–1 on page 94.

Figure LFT–2

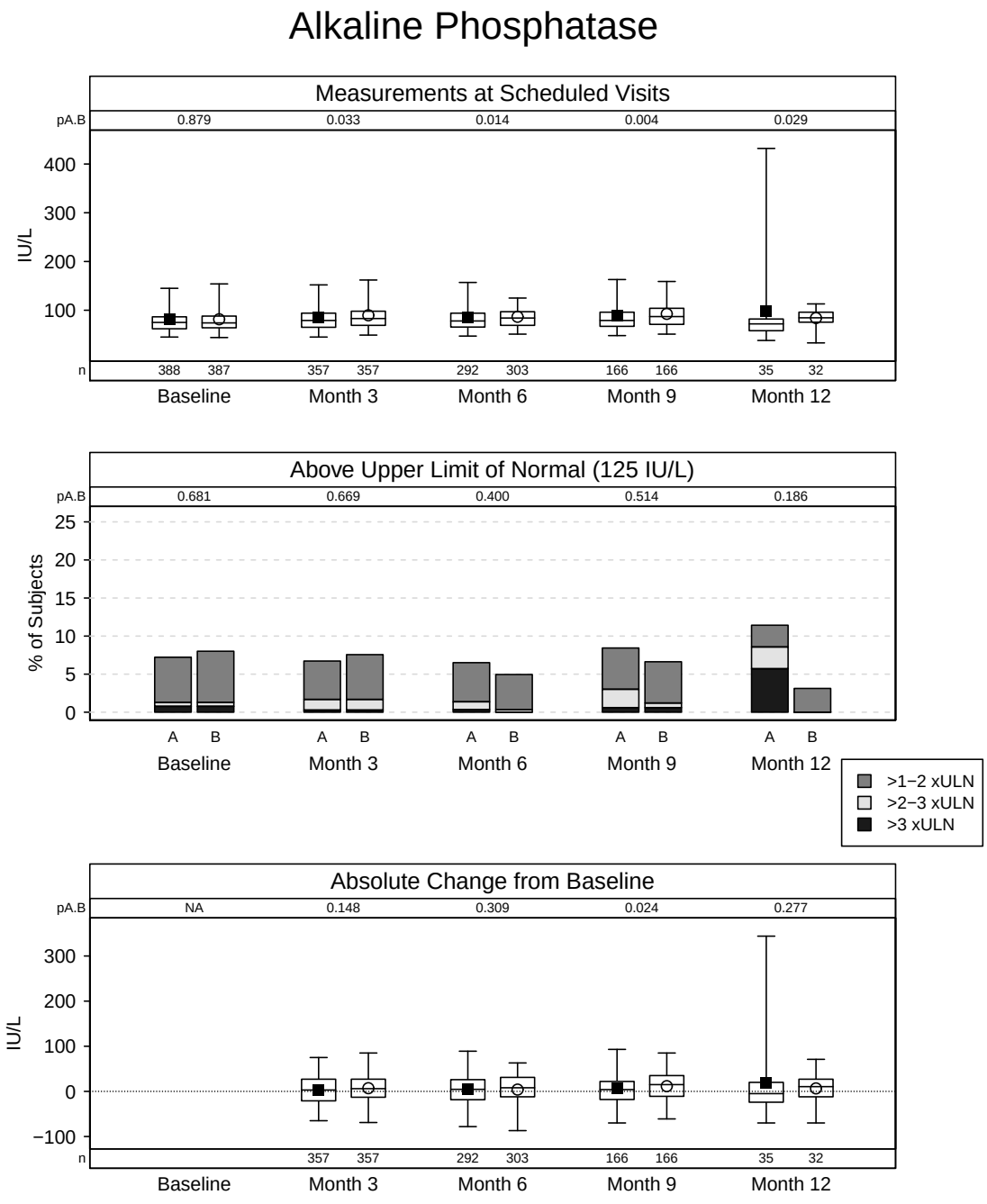
Aspartate Amino Transferase



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–2 on page 95.

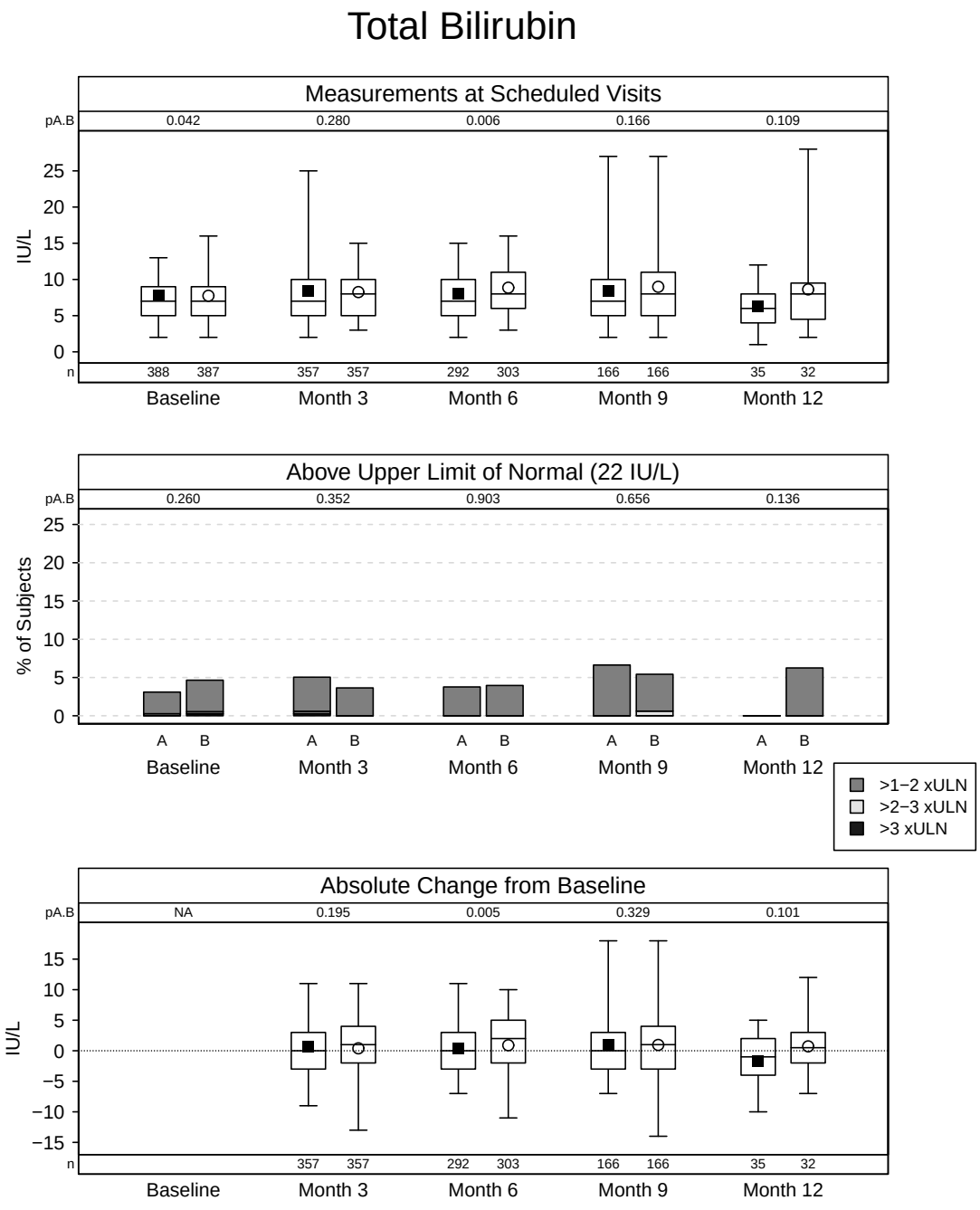
Figure LFT–3



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 96.

Figure LFT–4

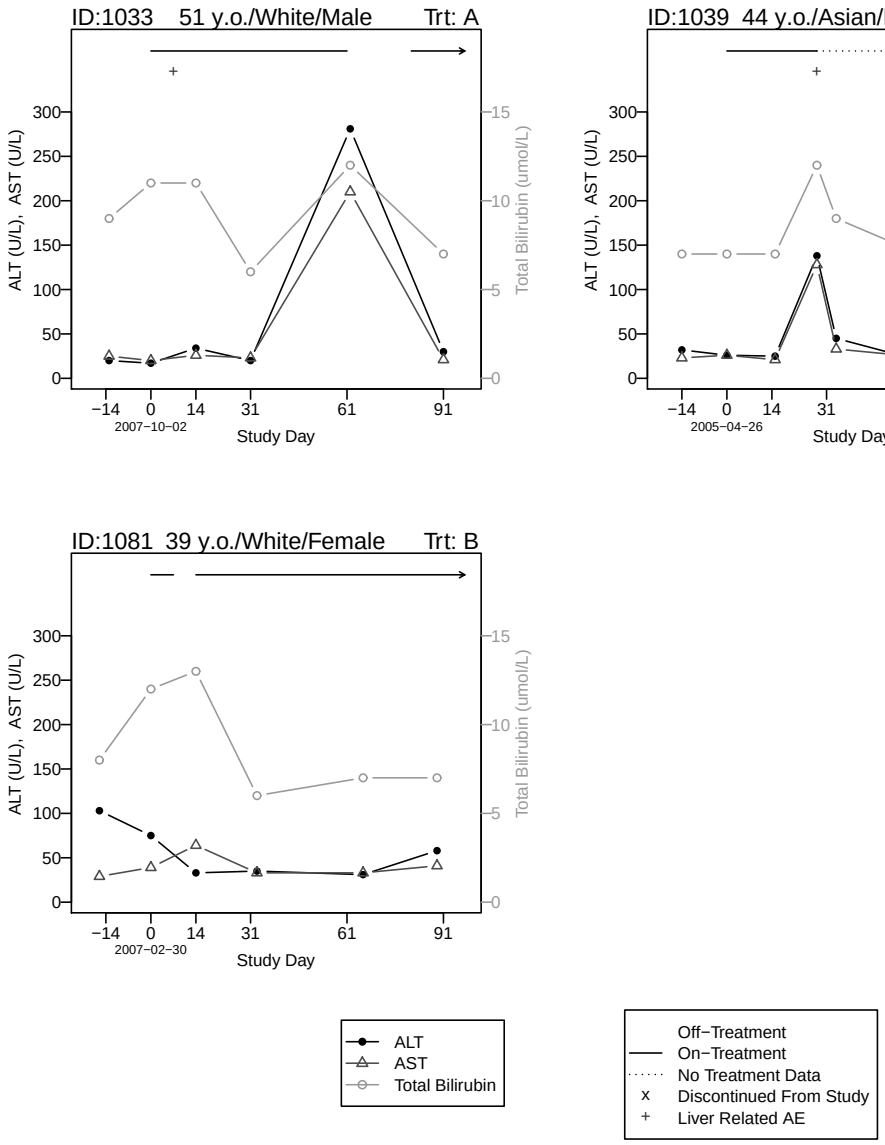


Information from a simulated laboratory dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed.

See Table Set LFT–4 on page 97.

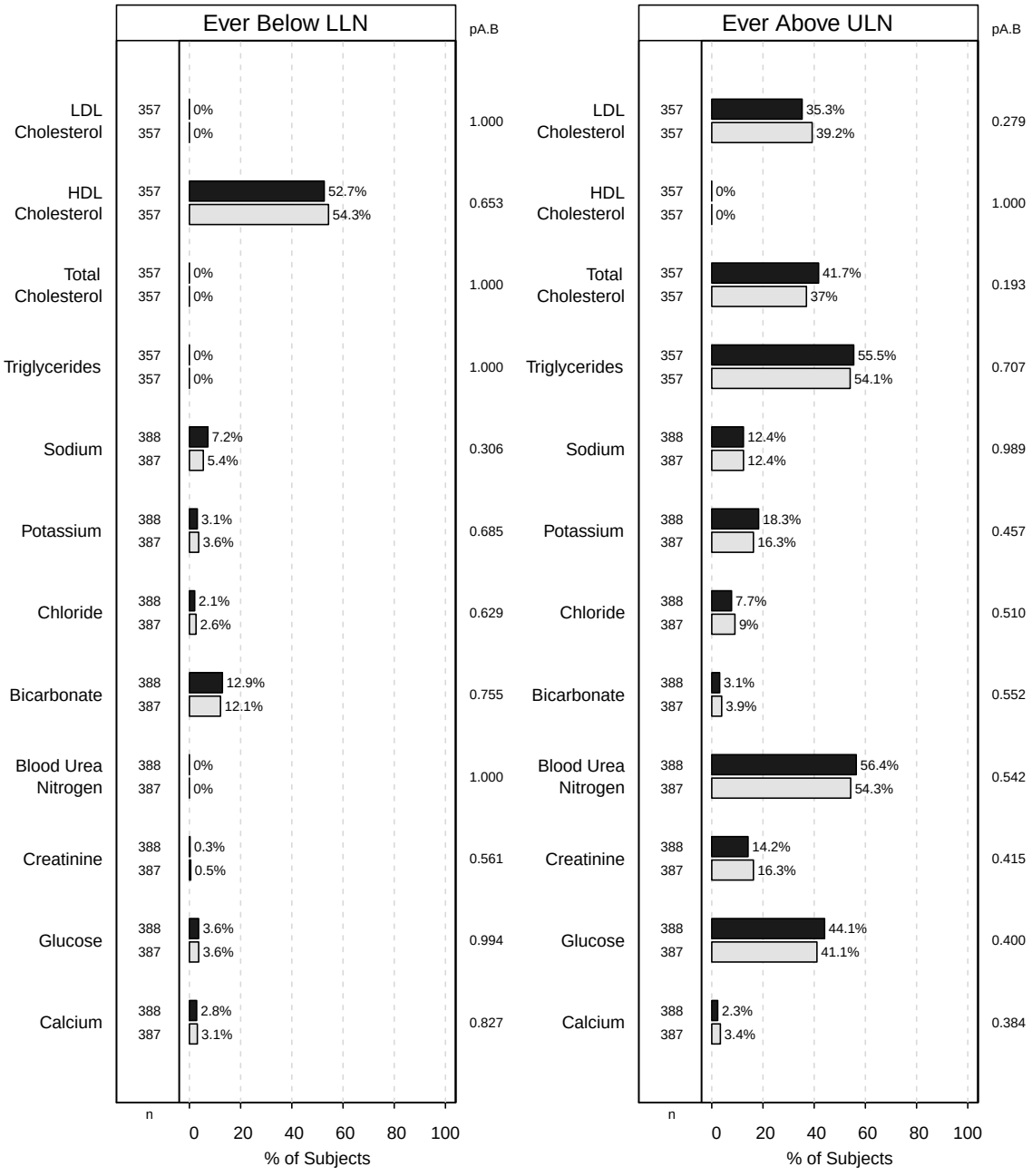
Figure BYPTLFT–1

Liver Enzymes over Time for Selected Subjects



Information from a simulated laboratory dataset. Panels display ALT, AST and total bilirubin measurements over time for selected subjects. Also shown are subject dosing status and liver-related adverse events. Subjects can be included according to specified laboratory thesholds or other criteria.

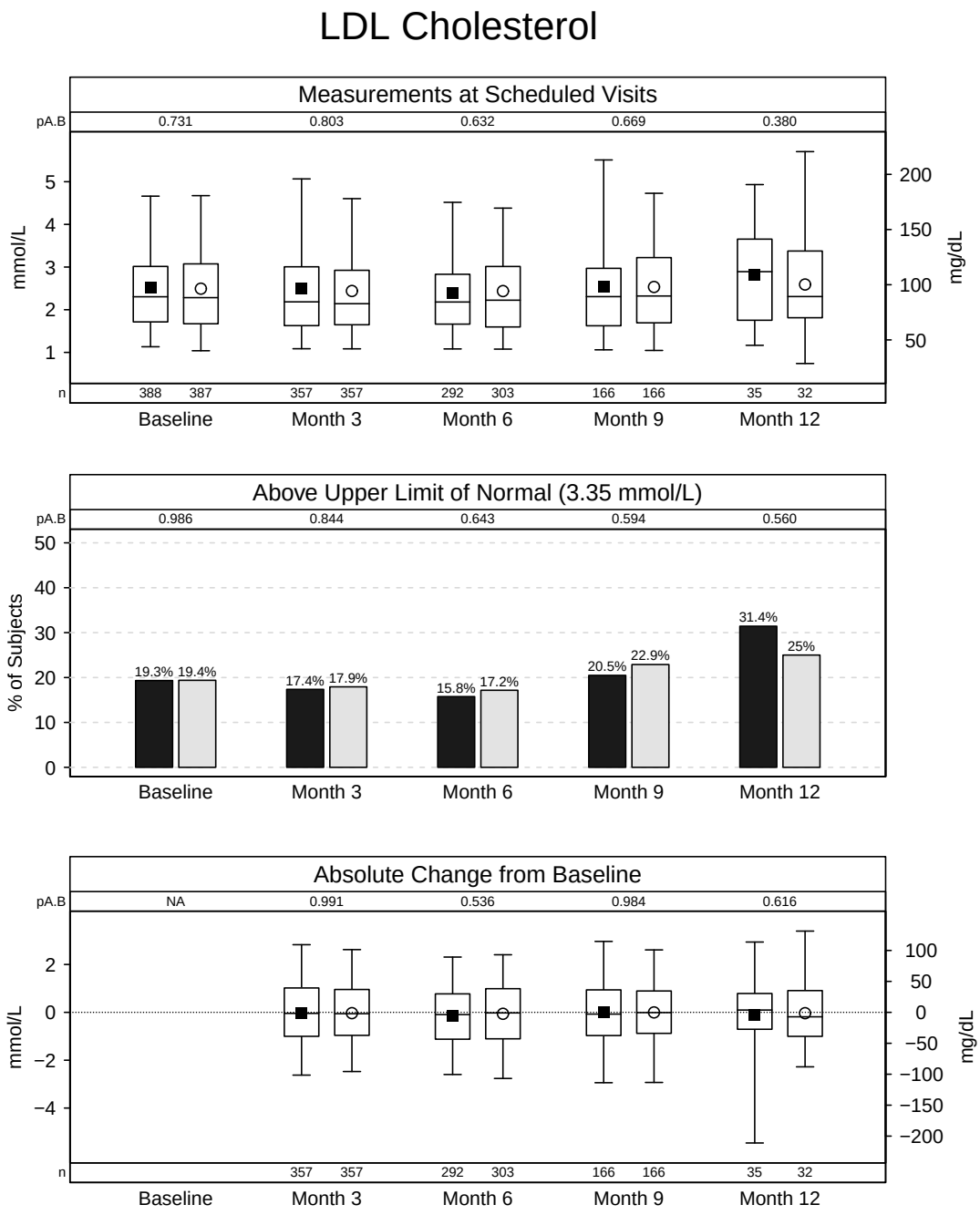
Figure CHEMABN–1



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. In a DMC report, this display could be revised to summarize values below or above other specified thresholds of clinical concern.

See Table Set CHEMABN–1 on page 99.

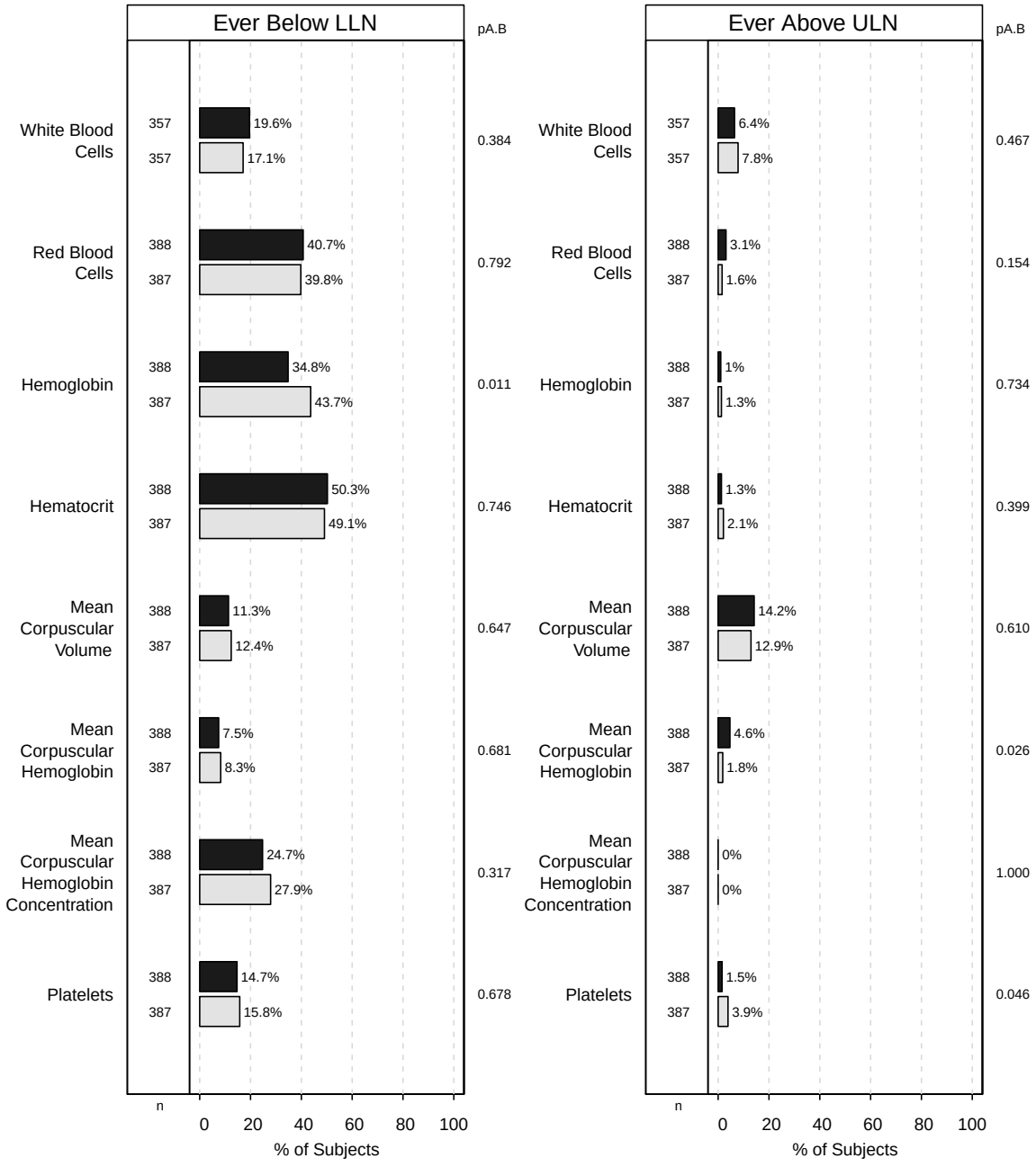
Figure CHEM–1



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 100.

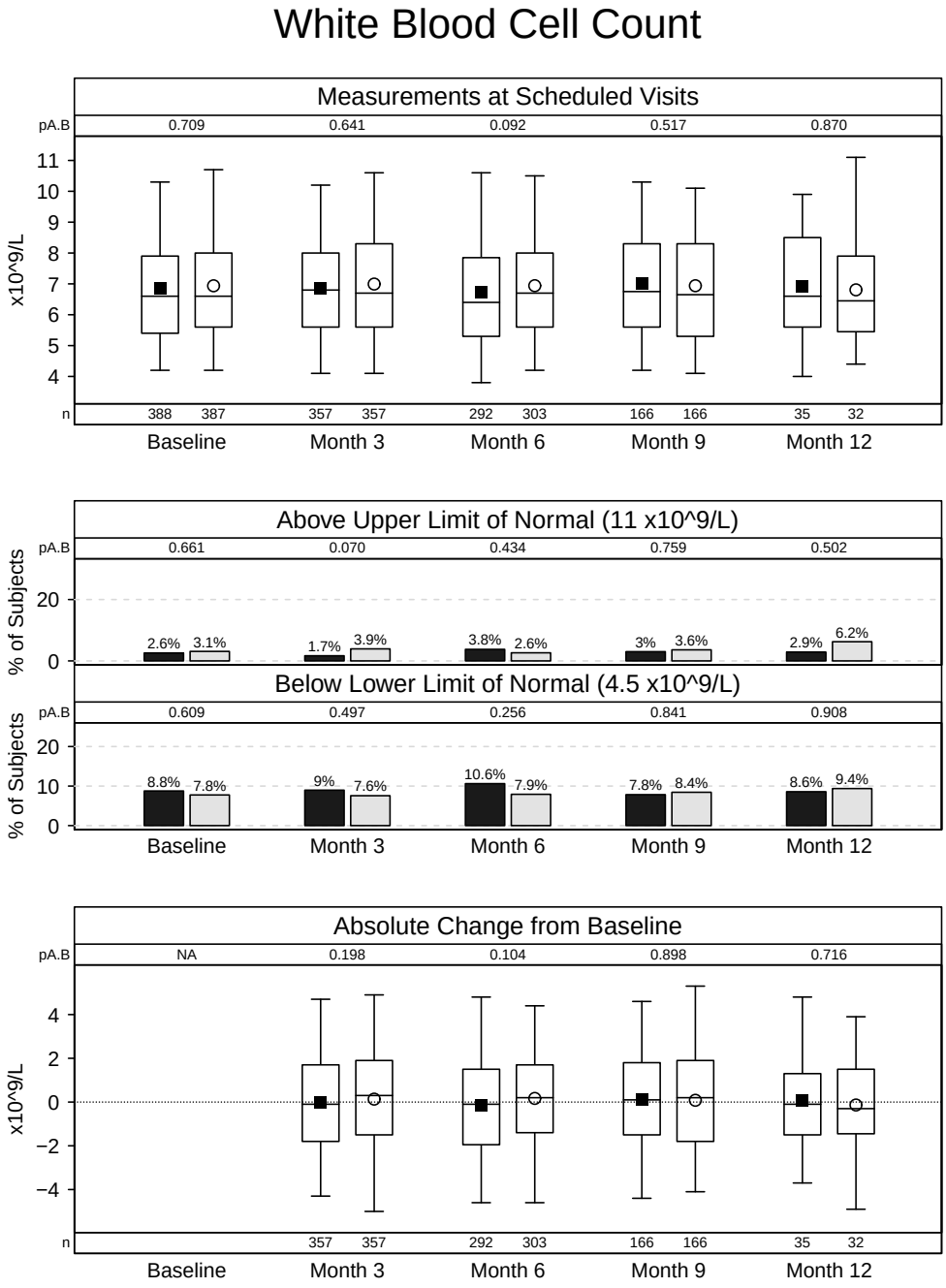
Figure HEMABN–1



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. In a DMC report, this display could be revised to summarize values below or above other specified thresholds of clinical concern.

See Table Set HEMABN–1 on page 102.

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.

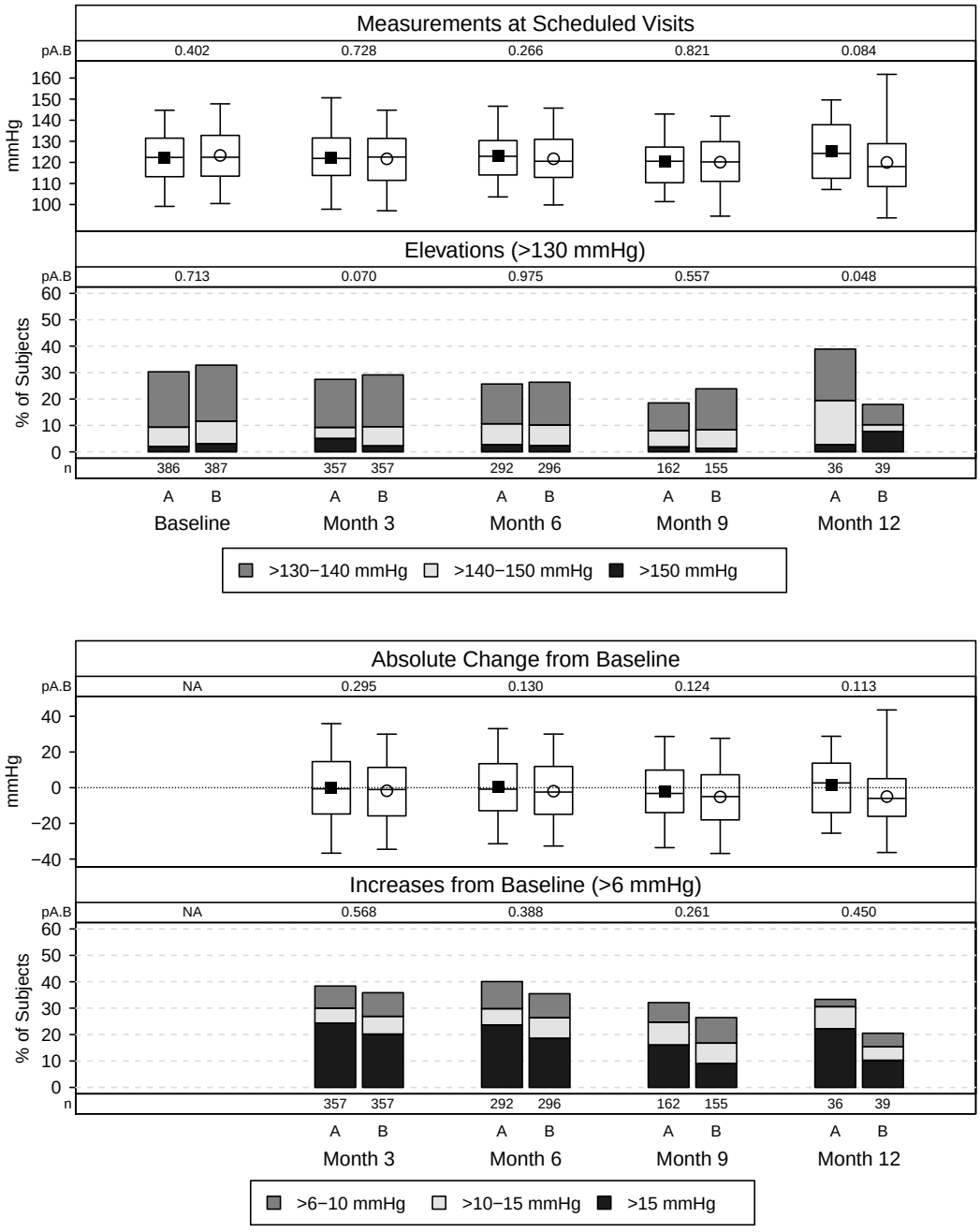
See Table Set HEM–1 on page 103.

Chapter 5

Other Follow-up and Safety Measures

Figure VIT–1

Systolic Blood Pressure

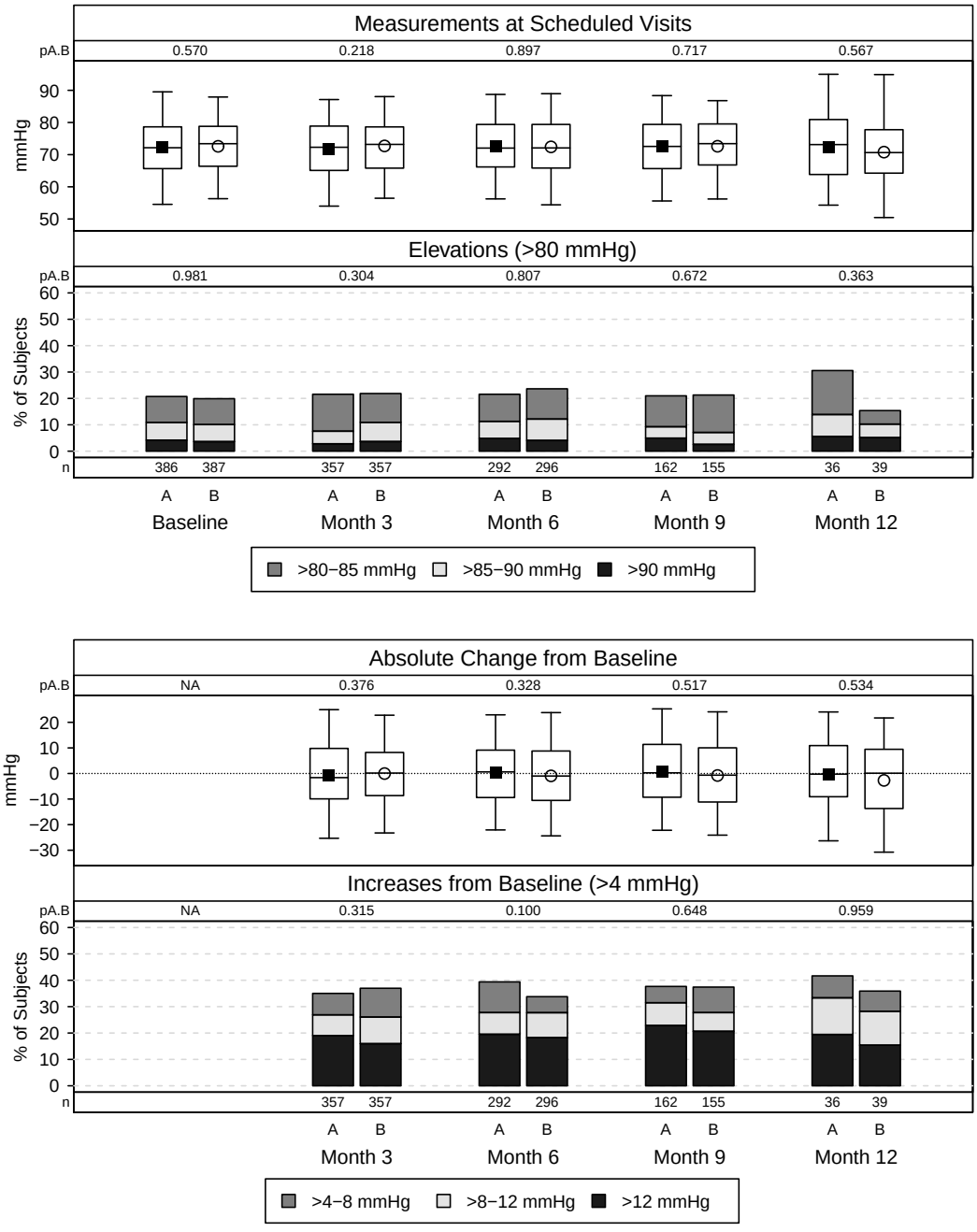


Information from a simulated vital signs dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed.

See Table Set VIT–1 on page 106.

Figure VIT–2

Diastolic Blood Pressure



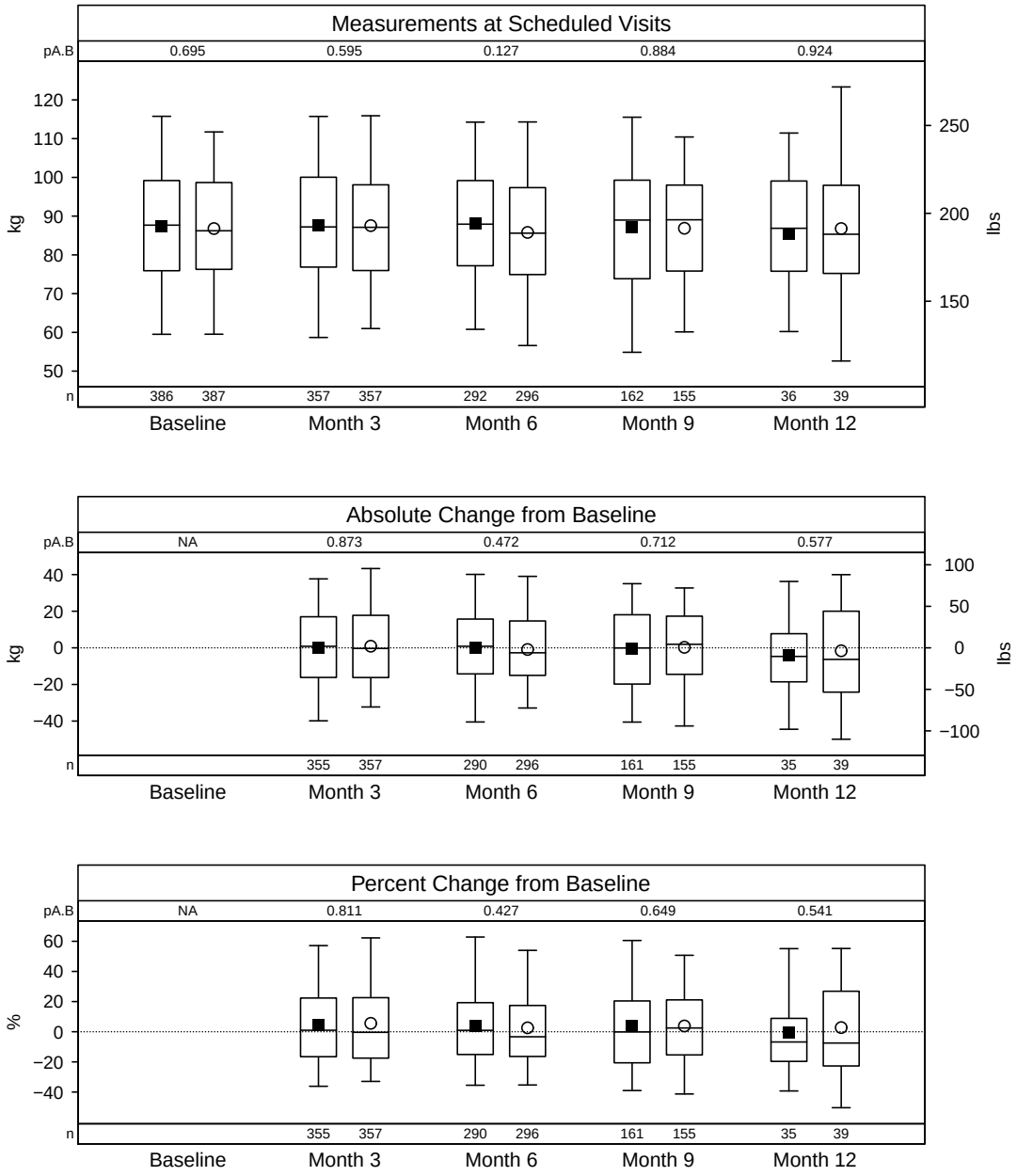
Information from a simulated vital signs dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed.

■ A
○ B

See Table Set VIT–2 on page 108.

Figure VIT–3

Weight

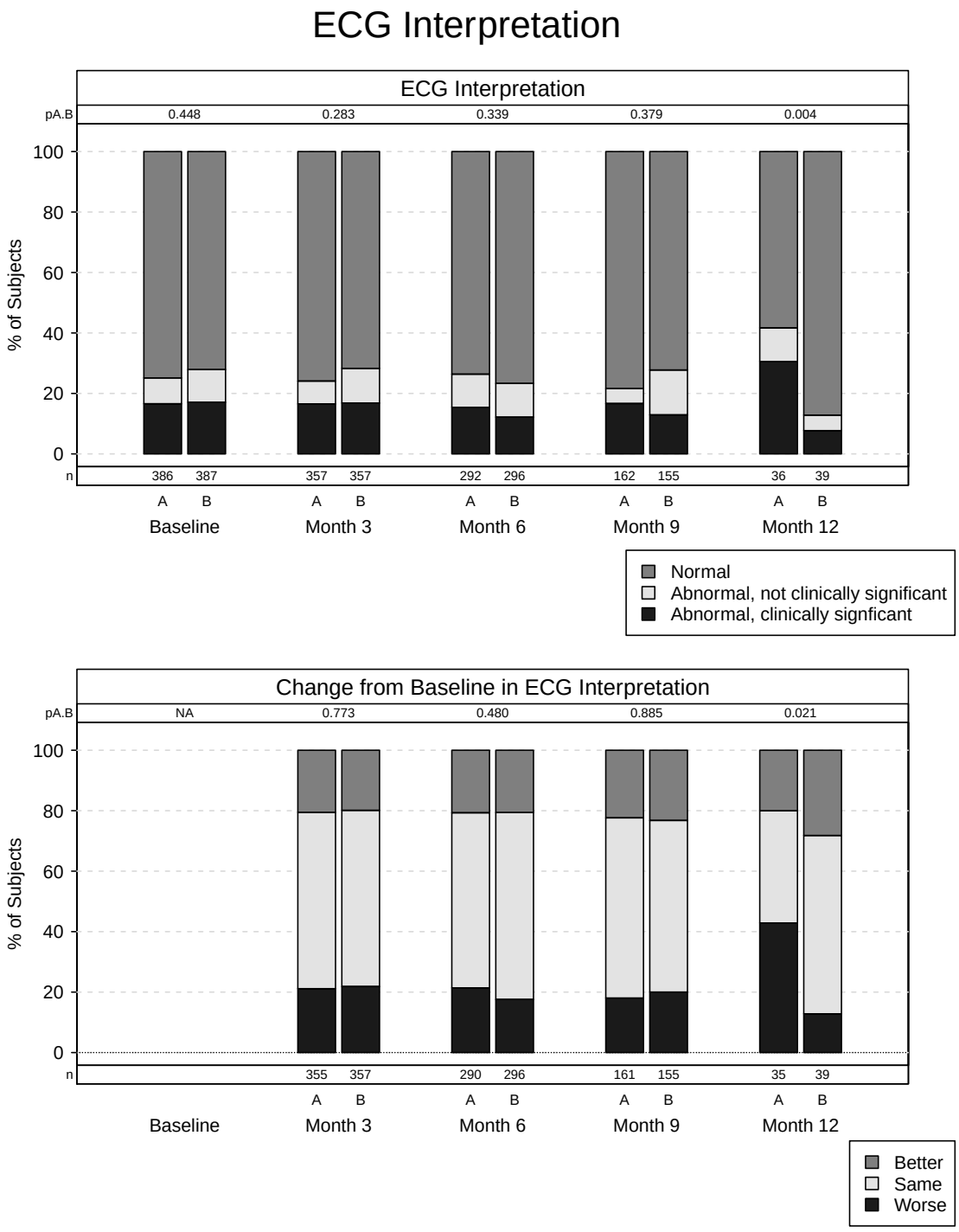


Information from a simulated vital signs dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed.

■ A
○ B

See Table Set VIT–3 on page 110.

Figure ECG–1

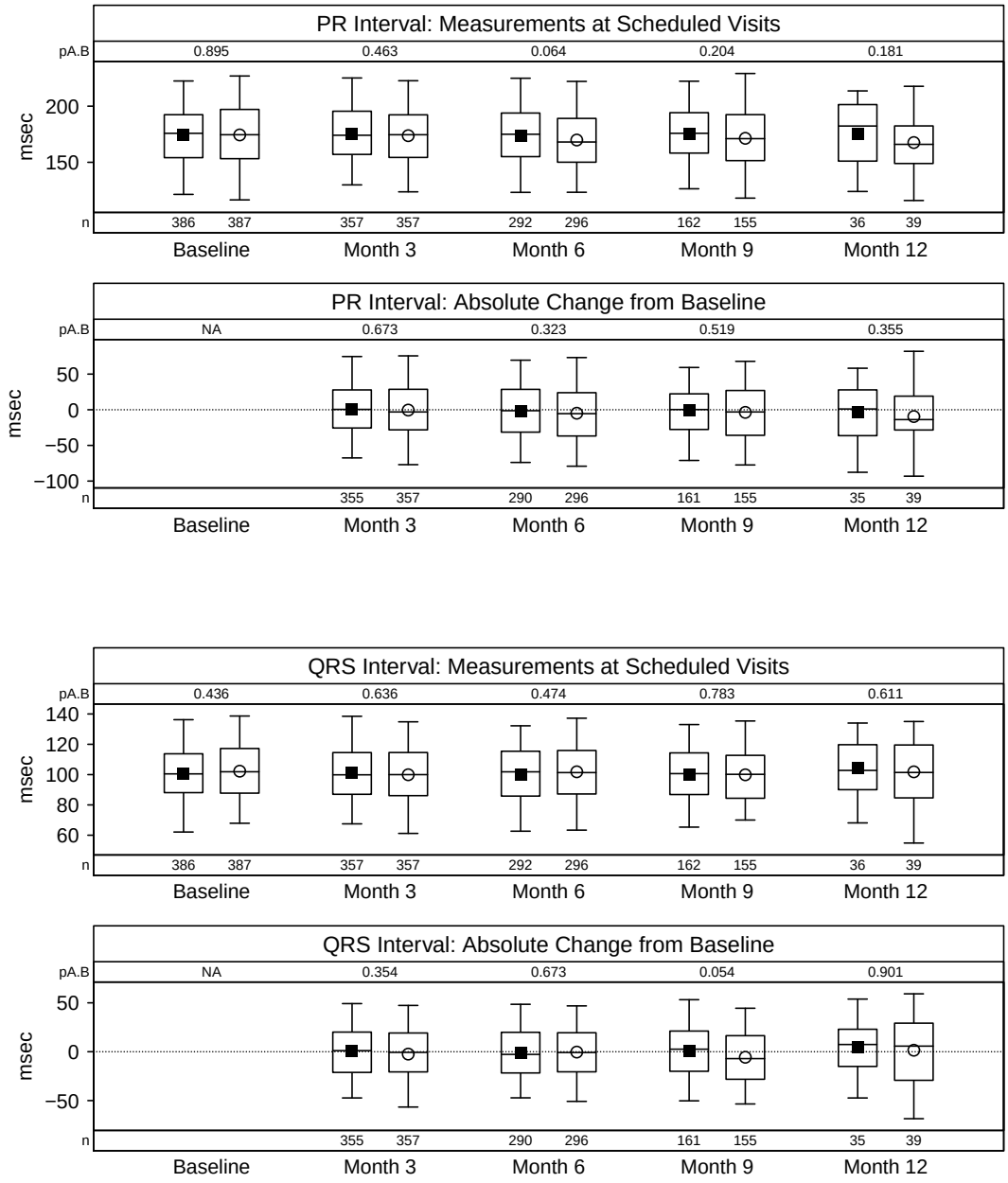


Information from a simulated ECG dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed.

See Table Set ECG–1 on page 111.

Figure ECG–2

ECG: PR Interval and QRS Interval



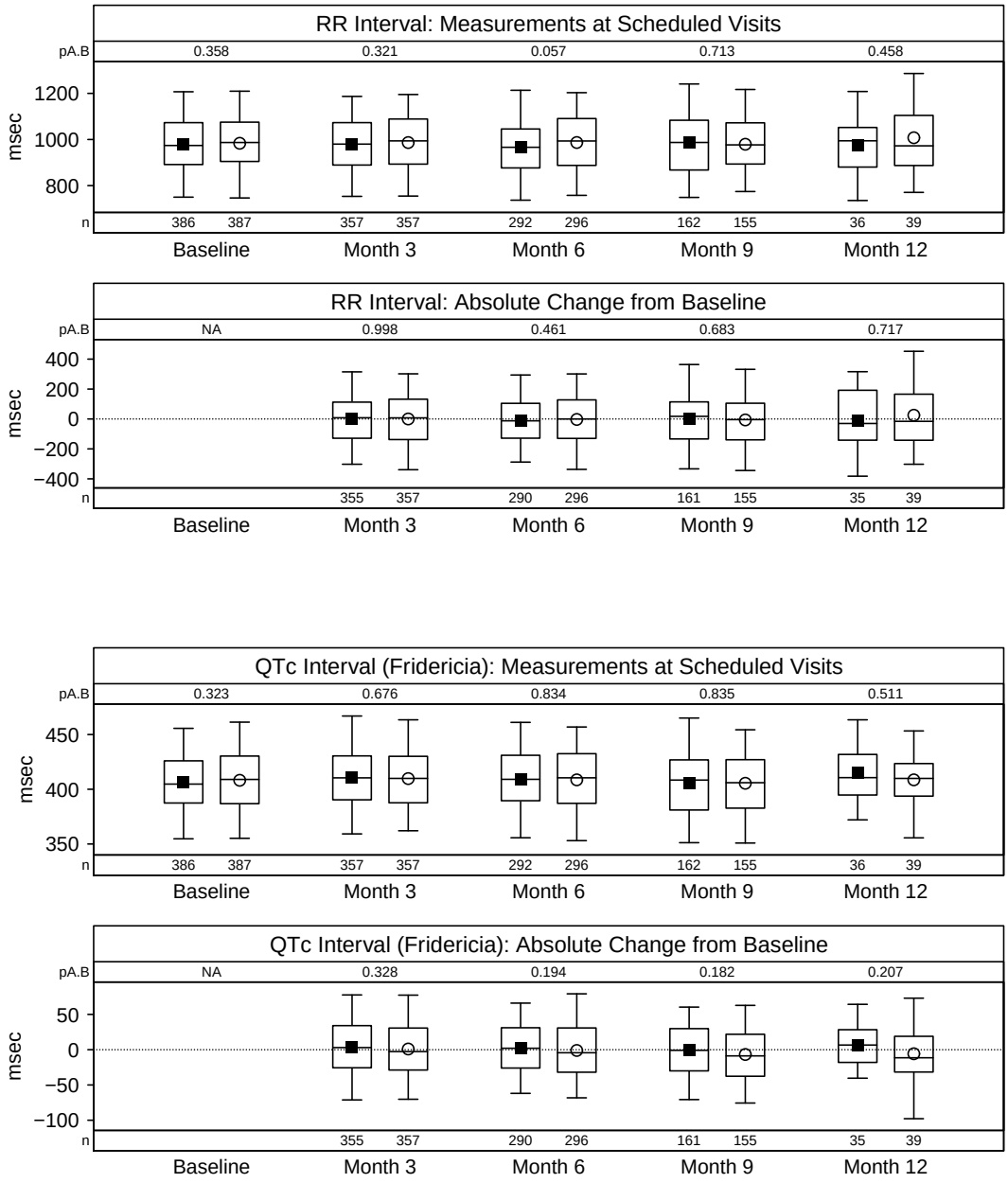
Information from a simulated ECG dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed.

■ A
○ B

See Table Set ECG–2 on page 112.

Figure ECG–3

ECG: RR Interval and QTc Interval (Fridericia)



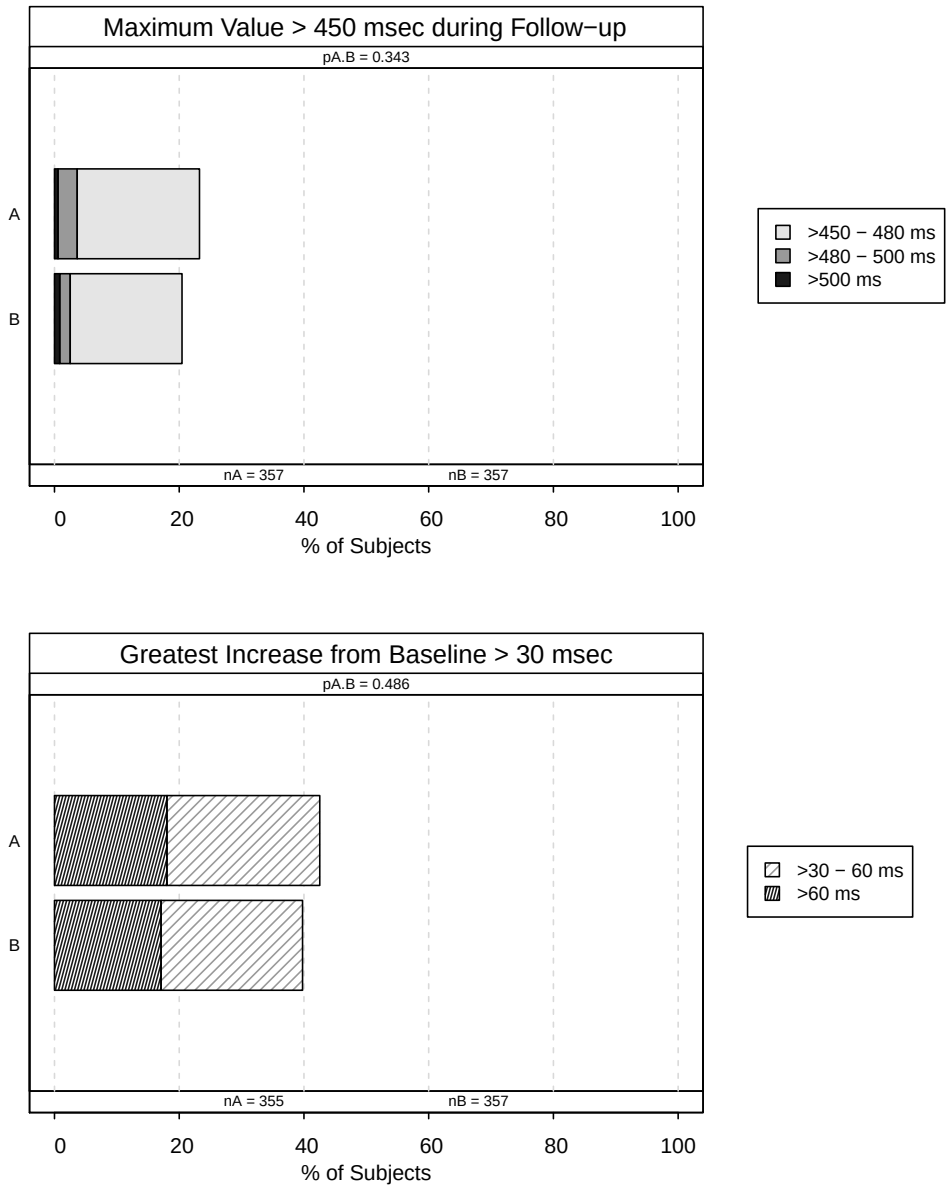
Information from a simulated ECG dataset. Baseline is defined as the last measurement on or before the date of randomization. For follow-up data in an actual report, multiple measurements may be available with the same visit label, in which case the first value would be displayed.

■ A
○ B

See Table Set ECG–3 on page 114.

Figure ECG–4

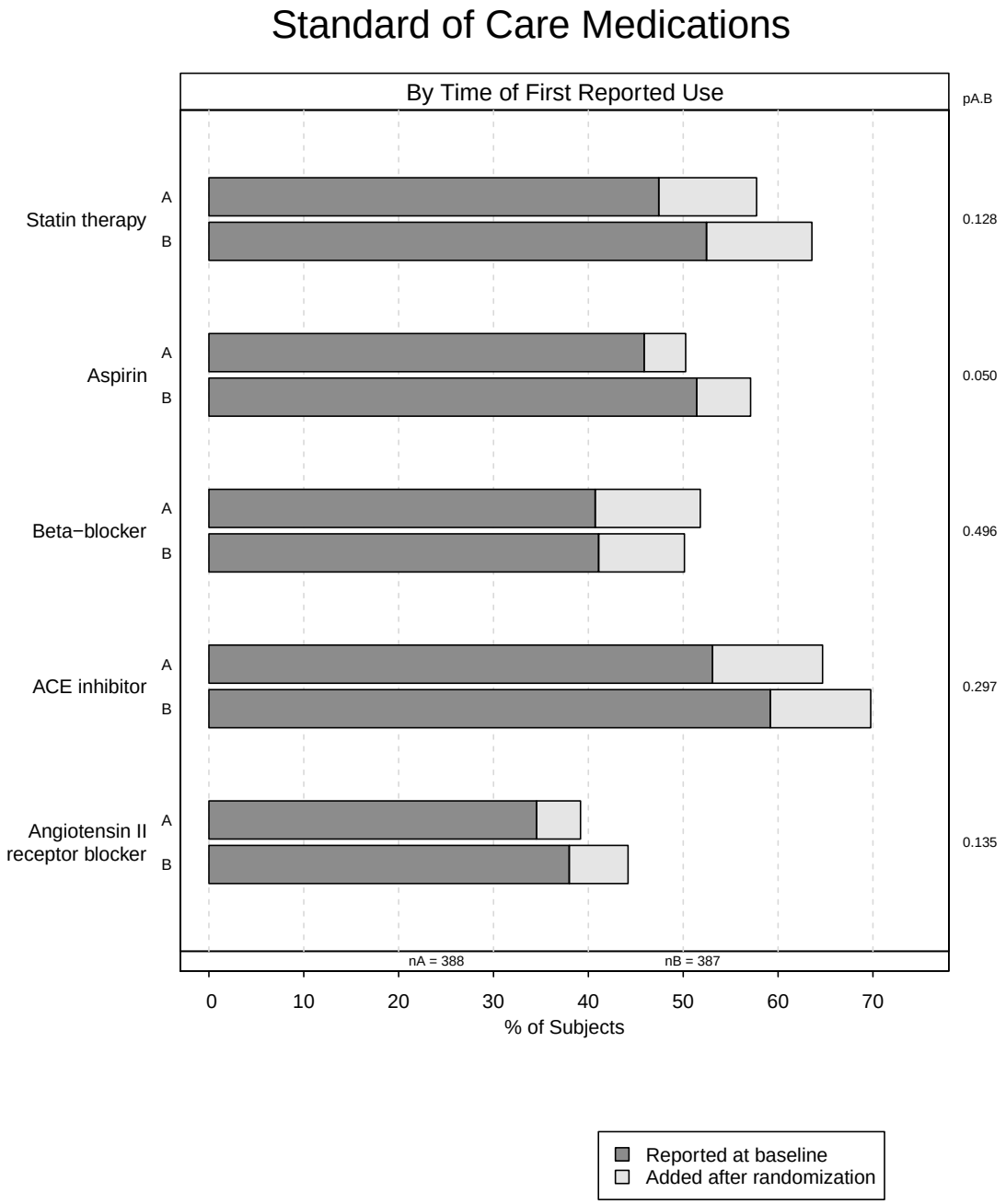
Maximum QTc (Fridericia) Intervals, Categorized



Information from a simulated ECG dataset. Categories represent increased levels of QTc (Fridericia) measurements that may be of interest in a cardiovascular trial. The denominator for the top panel is the number of subjects with any QTc measurement after baseline. The denominator for the bottom panel is subjects with measurements at both baseline and post-baseline.

See Table Set ECG–4 on page 115.

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.

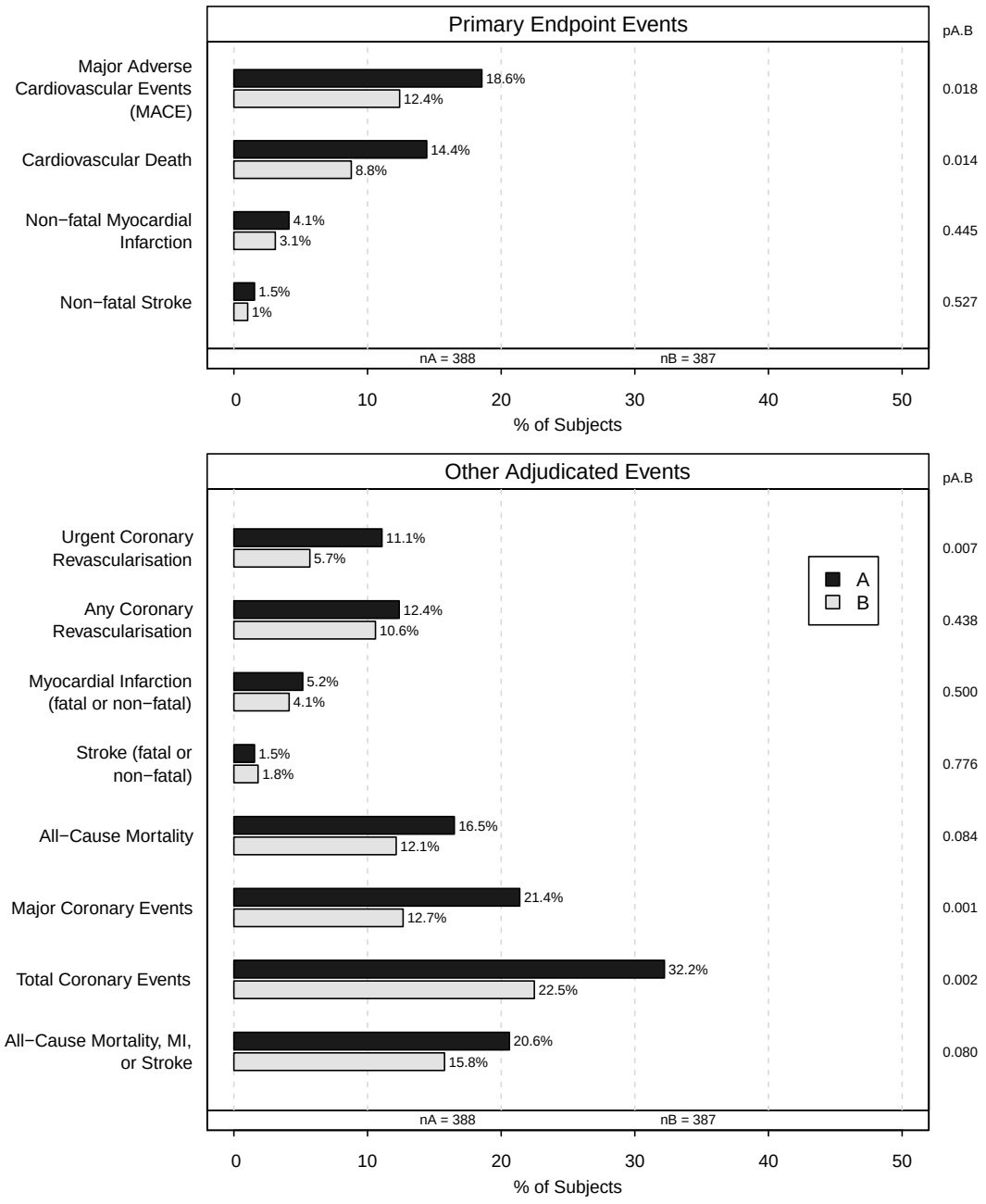
See Table Set CONMEDS–1 on page 116.

Chapter 6

Study Endpoints

Figure ENDPT–1

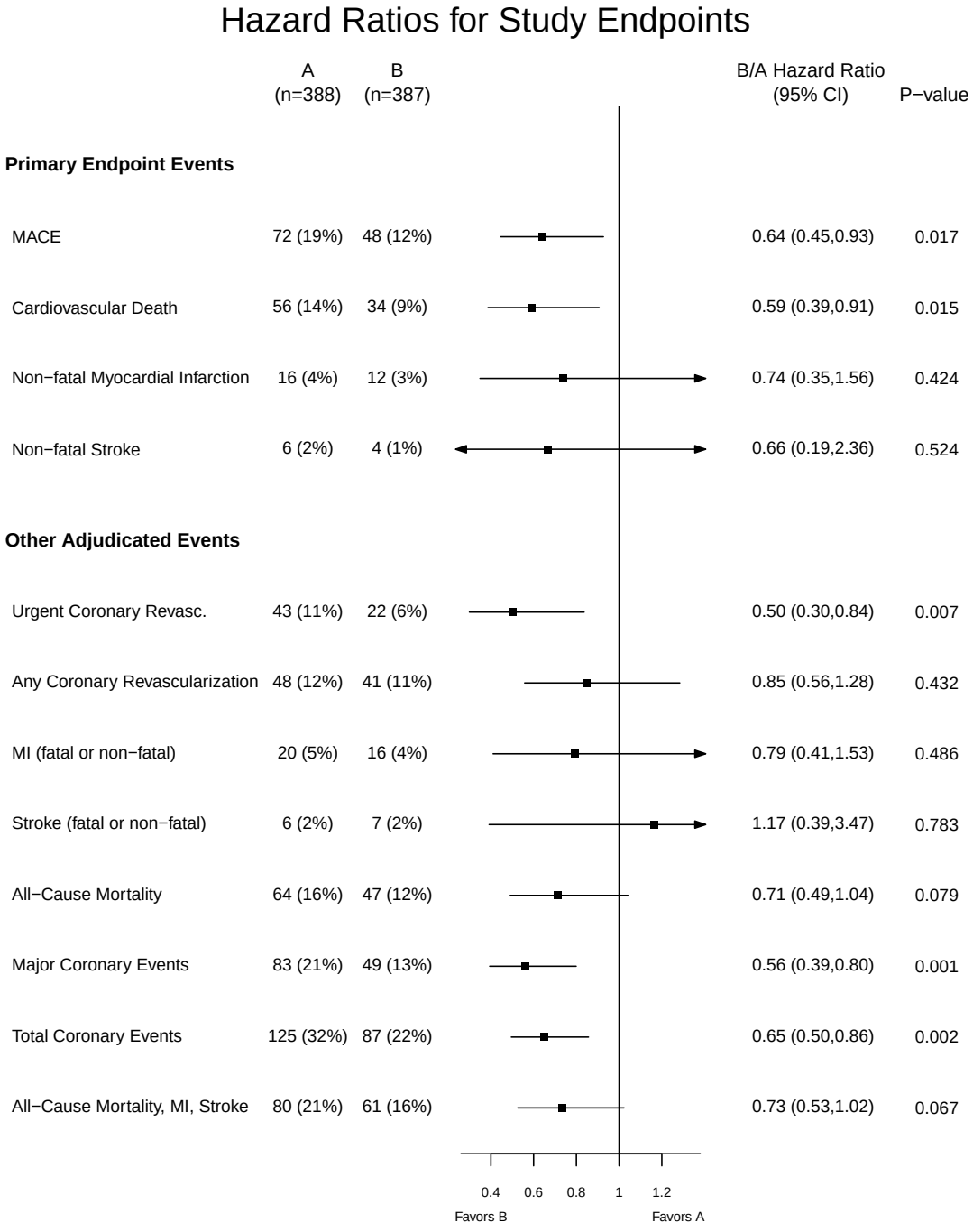
Primary and Other Study Endpoints



Information from a simulated endpoint dataset. In this example, the primary endpoint of MACE represents a composite of cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke.

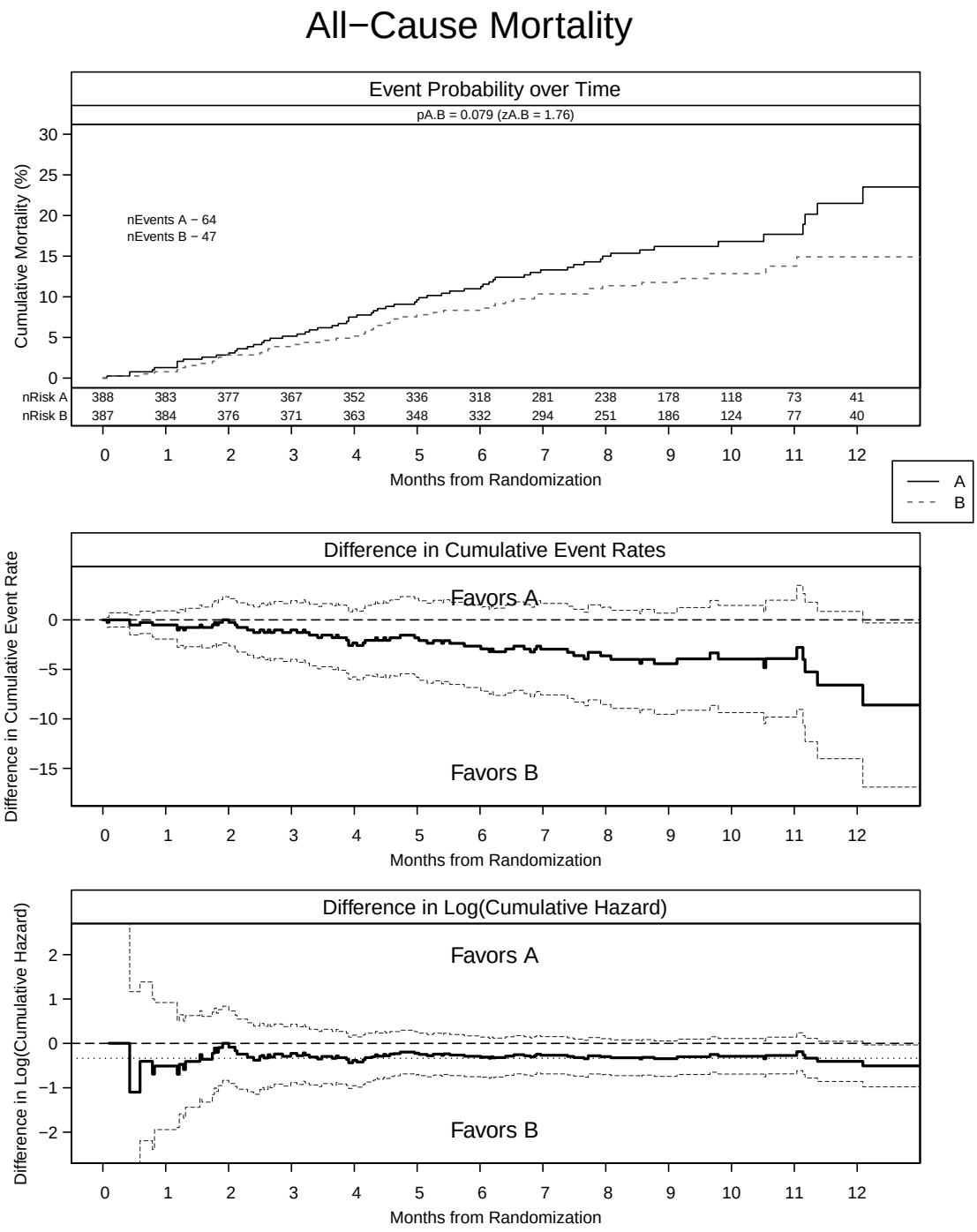
See Table Set ENDPT–1 on page 117.

Figure ENDPT–2



Information from a simulated endpoint dataset. The risk set includes all randomized subjects. Follow-up time for subjects not reporting an event was censored on the day of data transfer, or the date of withdrawal from study, if applicable. In this example, the primary endpoint of MACE represents a composite of cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke. Hazard ratios for treatment B versus treatment A are based on univariate analysis using an unstratified Cox proportional hazards model. Boxes to the left of the vertical line at 1 indicate lower risk of an event in treatment B. *P*-values are from a score test.

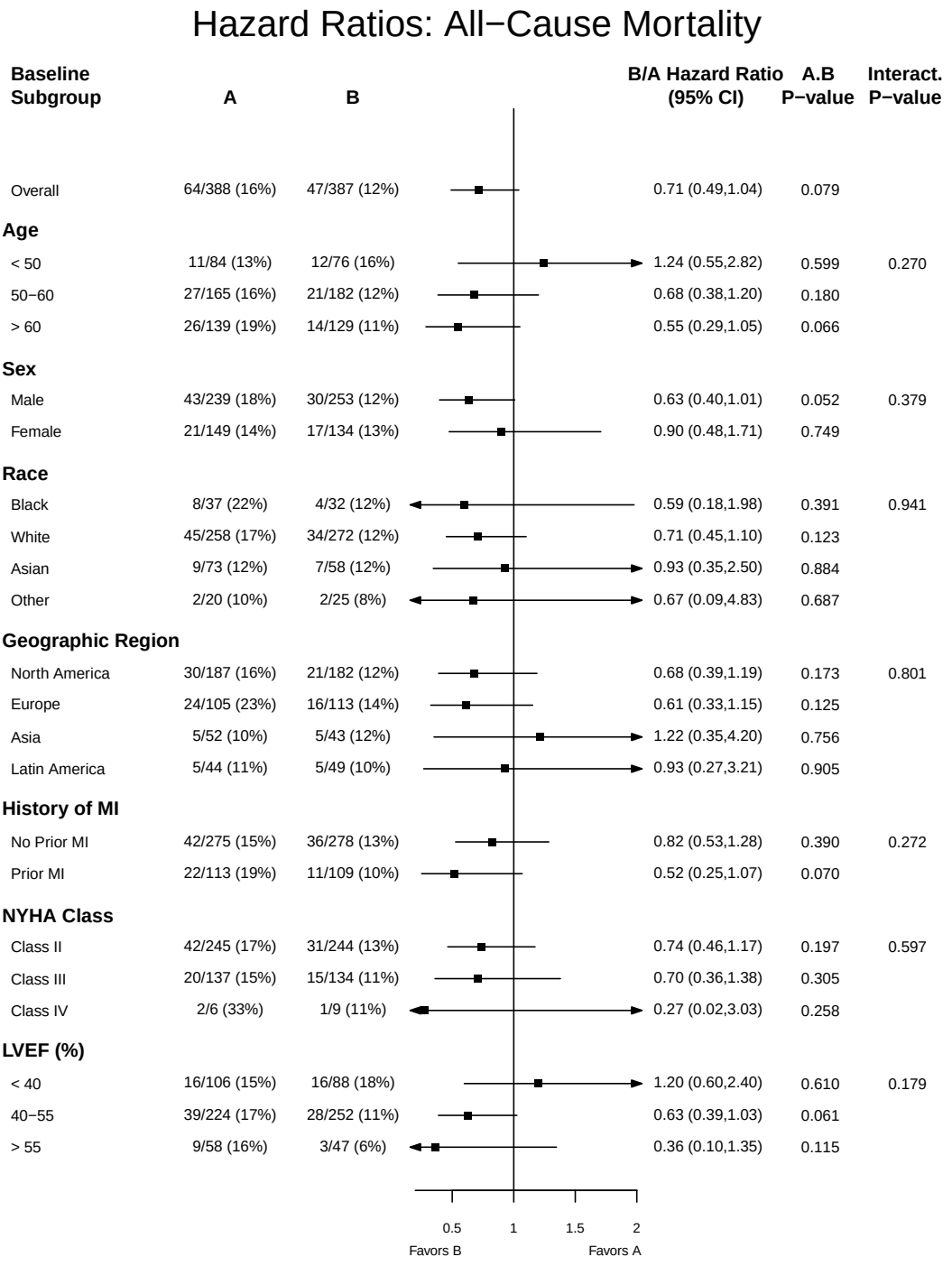
Figure ENDPT–3



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.

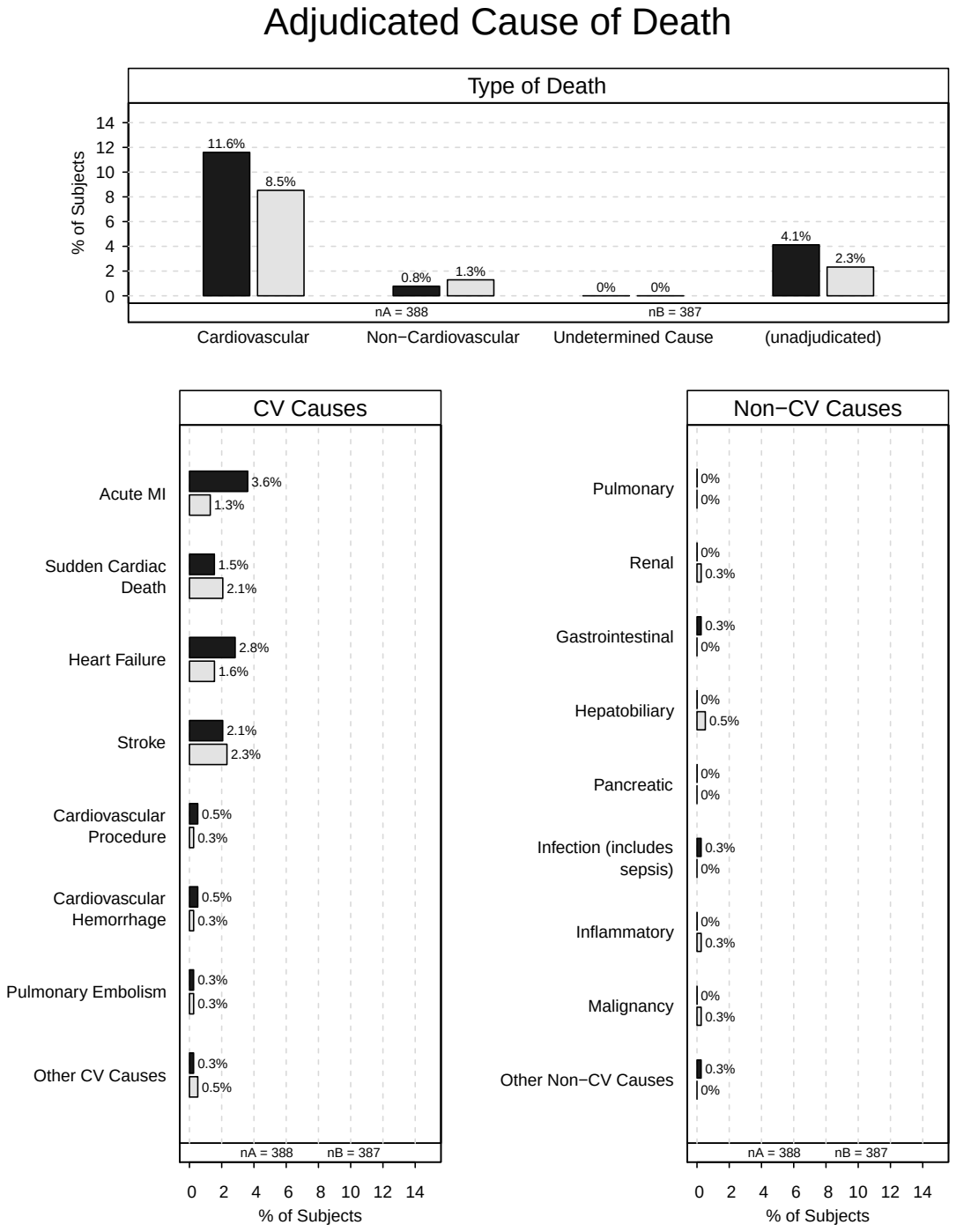
See Table Set ENDPT–3 on page 118.

Figure ENDPT–4



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. Boxes to the left of the vertical line at 1 indicate lower risk of an event in treatment B. All *p*-values are from a score test.

Figure DTH–1



Information from a simulated endpoint dataset. The upper panel summarizes deaths according to the adjudicated cause or as unadjudicated. The lower panels include only adjudicated deaths, and display subcategories for cardiovascular and for non-cardiovascular deaths.

See Table Set DTH–1 on page 119.

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 21.

		Value							
	Total	North America		Europe		Asia		Latin America	
Trt	Subjs	N	%	N	%	N	%	N	%
TOTAL	775	369	47.61	218	28.13	95	12.26	93	12.00

Geographic Distribution: Number of Sites

See Figure ACCR–4 on page 21.

		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 23.

		Value									
	Total	Dead		Withdrawn from study		On study, Off treatment		On study, On treatment			P-
Trt	Subjs	N	%	N	%	N	%	N	%	Contrast	Value
A	388	67	17.27	16	4.12	93	23.97	212	54.64	A.B	0.000
B	387	35	9.04	34	8.79	136	35.14	182	47.03		
TOTAL	775	102	13.16	50	6.45	229	29.55	394	50.84		

Study Status: Reason Off Treatment

See Figure STAT–1 on page 23.

			Value					
			Yes		No			P-
	Trt	Total Subjs	N	%	N	%	Contrast	Value
Subject died	A	388	45	11.60	343	88.40	A.B	0.003
	B	387	22	5.68	365	94.32		
	TOTAL	775	67	8.65	708	91.35		
Consent withdrawn	A	388	13	3.35	375	96.65	A.B	0.063
	B	387	24	6.20	363	93.80		
	TOTAL	775	37	4.77	738	95.23		
Lost to follow-up	A	388	12	3.09	376	96.91	A.B	0.837
	B	387	11	2.84	376	97.16		
	TOTAL	775	23	2.97	752	97.03		
Adverse event	A	388	57	14.69	331	85.31	A.B	0.083
	B	387	75	19.38	312	80.62		
	TOTAL	775	132	17.03	643	82.97		
Protocol violation	A	388	2	0.52	386	99.48	A.B	0.093
	B	387	7	1.81	380	98.19		
	TOTAL	775	9	1.16	766	98.84		
Pregnancy	A	388	0	0.00	388	100.00	A.B	1.000
	B	387	0	0.00	387	100.00		
	TOTAL	775	0	0.00	775	100.00		
Subject request	A	388	38	9.79	350	90.21	A.B	0.092
	B	387	53	13.70	334	86.30		
	TOTAL	775	91	11.74	684	88.26		
Other	A	388	9	2.32	379	97.68	A.B	0.384
	B	387	13	3.36	374	96.64		
	TOTAL	775	22	2.84	753	97.16		

Study Status: Reason Off Study

See Figure STAT–1 on page 23.

			Value					
			Yes		No			P-
	Trt	Total Subjs	N	%	N	%	Contrast	Value
Subject died	A	388	62	15.98	326	84.02	A.B	0.002
	B	387	33	8.53	354	91.47		
	TOTAL	775	95	12.26	680	87.74		
Consent withdrawn	A	388	11	2.84	377	97.16	A.B	0.008
	B	387	27	6.98	360	93.02		
	TOTAL	775	38	4.90	737	95.10		
Lost to follow-up	A	388	9	2.32	379	97.68	A.B	0.996
	B	387	9	2.33	378	97.67		
	TOTAL	775	18	2.32	757	97.68		
Other	A	388	1	0.26	387	99.74	A.B	0.318
	B	387	0	0.00	387	100.00		
	TOTAL	775	1	0.13	774	99.87		

Table Set STAT–2

Status Summary by Calendar Time: Treatment A

See Figure STAT–2 on page 24.

		Value							
	Total	On study, on treatment		On study, off treatment		Withdrawn from study		Dead	
Date	Subjs	N	%	N	%	N	%	N	%
Jul 01 2007	12	12	100.0	0	0.0	0	0.0	0	0.0
Oct 01 2007	112	108	96.4	3	2.7	0	0.0	1	0.9
Jan 01 2008	301	262	87.0	25	8.3	1	0.3	13	4.3
Apr 01 2008	378	296	78.3	42	11.1	6	1.6	34	9.0
Jul 01 2008	388	246	63.4	77	19.8	13	3.4	52	13.4

Status Summary by Calendar Time: Treatment B

See Figure STAT–2 on page 24.

		Value							
	Total	On study, on treatment		On study, off treatment		Withdrawn from study		Dead	
Date	Subjs	N	%	N	%	N	%	N	%
Jul 01 2007	12	12	100.0	0	0.0	0	0.0	0	0.0
Oct 01 2007	111	105	94.6	3	2.7	0	0.0	3	2.7
Jan 01 2008	301	256	85.0	23	7.6	6	2.0	16	5.3
Apr 01 2008	375	266	70.9	71	18.9	18	4.8	20	5.3
Jul 01 2008	387	214	55.3	114	29.5	27	7.0	32	8.3

Table Set STAT–3

Status Summary by Time on Study: Treatment A

See Figure STAT–3 on page 25.

		Value							
	Total	On study, on treatment		On study, off treatment		Withdrawn from study		Dead	
Months	Subjs	N	%	N	%	N	%	N	%
0	388	388	100.0	0	0.0	0	0.0	0	0.0
1	388	361	93.0	13	3.4	1	0.3	13	3.4
2	388	343	88.4	27	7.0	2	0.5	16	4.1
3	387	327	84.5	34	8.8	5	1.3	21	5.4
4	380	304	80.0	42	11.1	5	1.3	29	7.6
5	372	281	75.5	49	13.2	8	2.2	34	9.1
6	357	251	70.3	53	14.8	8	2.2	45	12.6
7	324	216	66.7	55	17.0	8	2.5	45	13.9
8	283	183	64.7	54	19.1	8	2.8	38	13.4
9	215	134	62.3	49	22.8	8	3.7	24	11.2
10	147	91	61.9	36	24.5	5	3.4	15	10.2
11	92	58	63.0	22	23.9	4	4.3	8	8.7
12	54	33	61.1	13	24.1	2	3.7	6	11.1

Status Summary by Time on Study: Treatment B

See Figure STAT–3 on page 25.

		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	0	0.0	0	0.0	1	0.3
1	387	352	91.0	23	5.9	3	0.8	9	2.3
2	387	334	86.3	35	9.0	6	1.6	12	3.1
3	386	312	80.8	49	12.7	11	2.8	14	3.6
4	380	277	72.9	67	17.6	16	4.2	20	5.3
5	372	253	68.0	78	21.0	18	4.8	23	6.2
6	357	221	61.9	90	25.2	22	6.2	24	6.7
7	324	190	58.6	90	27.8	22	6.8	22	6.8
8	284	165	58.1	79	27.8	19	6.7	21	7.4
9	214	120	56.1	60	28.0	14	6.5	20	9.3
10	147	80	54.4	38	25.9	14	9.5	15	10.2
11	92	51	55.4	23	25.0	6	6.5	12	13.0
12	54	35	64.8	10	18.5	2	3.7	7	13.0

Table Set STAT–4

Data Availability by Visit: Scheduled Visits

See Figure STAT–4 on page 26.

			Value			
		Total	Visit reported in database		Visit expected, not reported	
	Trt	Subjs	N	%	N	%
Baseline	TOTAL	775	775	100.00	0	0.00
Month 3	TOTAL	775	703	90.71	16	2.06
Month 6	TOTAL	775	570	73.55	34	4.39
Month 9	TOTAL	775	285	36.77	59	7.61
Month 12	TOTAL	775	56	7.23	18	2.32

Chapter 2

Baseline Characteristics

2.1 Demographics

Table Set DEMO–1

Baseline Characteristics: Age (years)

See Figure DEMO–1 on page 28.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	388	56.7	7.9	56.8	51.2	62.3	43.5	69.5
B	387	56.9	7.7	57.0	51.8	61.6	45.1	70.4
TOTAL	775	56.8	7.8	56.9	51.6	61.9	44.1	69.9

Baseline Characteristics: Gender

See Figure DEMO–1 on page 28.

		Value			
	Total	Male		Female	
Trt	Subjs	N	%	N	%
A	388	239	61.60	149	38.40
B	387	253	65.37	134	34.63
TOTAL	775	492	63.48	283	36.52

Baseline Characteristics: Race

See Figure DEMO–1 on page 28.

		Value							
	Total	Black		White		Asian		Other	
Trt	Subjs	N	%	N	%	N	%	N	%
A	388	37	9.54	258	66.49	73	18.81	20	5.15
B	387	32	8.27	272	70.28	58	14.99	25	6.46
TOTAL	775	69	8.90	530	68.39	131	16.90	45	5.81

Baseline Characteristics: NYHA Class

See Figure DEMO–1 on page 28.

		Value							
	Total	Class IV		Class III		Class II		Class I	
Trt	Subjs	N	%	N	%	N	%	N	%
A	388	6	1.55	137	35.31	245	63.14	0	0.00
B	387	9	2.33	134	34.63	244	63.05	0	0.00
TOTAL	775	15	1.94	271	34.97	489	63.10	0	0.00

Baseline Characteristics: Left Ventricular Ejection Fraction (%)

See Figure DEMO–1 on page 28.

	Total		Std					
Trt	Subjs	Mean	Dev	Median	Q1	Q3	P5	P95
A	388	45.5	8.5	45.5	39.4	51.2	31.4	59.2
B	387	46.1	7.9	46.2	40.4	50.9	33.2	59.6
TOTAL	775	45.8	8.2	45.7	39.9	51.1	32.3	59.6

2.2 Medical History

Table Set MDHX–1

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

See Figure MDHX–1 on page 29.

			Value			
		Total	Yes		No	
	Trt	Subjs	N	%	N	%
Prior myocardial infarction	A	388	113	29.12	275	70.88
	B	387	109	28.17	278	71.83
	TOTAL	775	222	28.65	553	71.35
Coronary artery bypass surgery (CABG)	A	388	47	12.11	341	87.89
	B	387	43	11.11	344	88.89
	TOTAL	775	90	11.61	685	88.39
Multivessel CHD	A	388	60	15.46	328	84.54
	B	387	51	13.18	336	86.82
	TOTAL	775	111	14.32	664	85.68
Cerebrovascular disease or stroke	A	388	19	4.90	369	95.10
	B	387	21	5.43	366	94.57
	TOTAL	775	40	5.16	735	94.84
Transient ischaemic attack	A	388	33	8.51	355	91.49
	B	387	50	12.92	337	87.08
	TOTAL	775	83	10.71	692	89.29
Angina pectoris	A	388	105	27.06	283	72.94
	B	387	89	23.00	298	77.00
	TOTAL	775	194	25.03	581	74.97
Hypertension	A	388	141	36.34	247	63.66
	B	387	132	34.11	255	65.89
	TOTAL	775	273	35.23	502	64.77
Congestive HF	A	388	116	29.90	272	70.10
	B	387	114	29.46	273	70.54
	TOTAL	775	230	29.68	545	70.32

Medical History: Current or Prior History of Other Relevant Conditions

See Figure MDHX–1 on page 29.

			Value			
			Yes		No	
	Trt	Total Subjs	N	%	N	%
Diabetes mellitus	A	388	62	15.98	326	84.02
	B	387	69	17.83	318	82.17
	TOTAL	775	131	16.90	644	83.10
Smoker	A	388	81	20.88	307	79.12
	B	387	105	27.13	282	72.87
	TOTAL	775	186	24.00	589	76.00
Family history of premature CHD	A	388	97	25.00	291	75.00
	B	387	111	28.68	276	71.32
	TOTAL	775	208	26.84	567	73.16
Cancer	A	388	22	5.67	366	94.33
	B	387	19	4.91	368	95.09
	TOTAL	775	41	5.29	734	94.71

2.3 Physical Examination

Table Set VITB–1

Baseline Physical Exam and Vital Signs: Height (cm)

See Figure VITB–1 on page 30.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	388	170.6	11.0	170.5	162.9	178.3	152.2	188.3
B	387	170.5	11.1	170.3	162.9	177.7	153.2	187.9
TOTAL	775	170.5	11.1	170.3	162.9	178.0	153.1	188.3

Baseline Physical Exam and Vital Signs: Weight (kg)

See Figure VITB–1 on page 30.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	388	87.1	13.0	87.1	79.6	95.9	63.9	106.7
B	387	88.3	12.9	88.2	80.3	96.9	66.2	109.3
TOTAL	775	87.7	13.0	87.7	79.9	96.6	65.3	108.4

Baseline Physical Exam and Vital Signs: BMI (kg/mˆ2)

See Figure VITB–1 on page 30.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	388	30.3	6.3	30.1	25.8	34.1	20.7	41.6
B	387	30.8	6.1	30.3	26.6	34.7	21.5	41.3
TOTAL	775	30.6	6.2	30.2	26.1	34.3	20.8	41.6

Baseline Physical Exam and Vital Signs: Waist-to-Hip Ratio

See Figure VITB–1 on page 30.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	388	0.99	0.16	0.99	0.89	1.10	0.74	1.27
B	387	1.01	0.16	1.00	0.90	1.11	0.75	1.27
TOTAL	775	1.00	0.16	0.99	0.89	1.10	0.74	1.27

Baseline Physical Exam and Vital Signs: Systolic Blood Pressure (mmHg)

See Figure VITB–1 on page 30.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	388	130.1	9.7	130.9	123.6	136.6	111.0	144.6
B	387	130.1	9.6	129.7	123.0	136.8	116.0	145.2
TOTAL	775	130.1	9.6	130.5	123.2	136.7	113.6	144.9

Baseline Physical Exam and Vital Signs: Diastolic Blood Pressure (mmHg)

See Figure VITB–1 on page 30.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	388	85.3	6.3	86.0	81.6	89.3	74.2	95.7
B	387	84.8	6.6	84.7	80.6	88.8	74.2	95.8
TOTAL	775	85.0	6.4	85.4	80.9	89.1	74.2	95.7

Baseline Physical Exam and Vital Signs: Heart Rate (bpm)

See Figure VITB–1 on page 30.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	388	65.5	6.9	65.3	61.0	69.7	53.9	76.6
B	387	65.0	7.3	64.7	60.4	70.4	52.7	76.5
TOTAL	775	65.2	7.1	65.0	60.7	70.0	53.0	76.6

2.4 Laboratory Data

Table Set LABB–1

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

See Figure LABB–1 on page 31.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	388	81.0	39.5	75.0	62.0	86.5	45.0	145.0
B	387	81.5	40.8	74.0	64.0	88.0	44.0	154.0
TOTAL	775	81.2	40.1	75.0	63.0	87.0	44.0	150.0

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

See Figure LABB–1 on page 31.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	388	16.7	12.0	15.0	11.5	19.0	6.0	25.0
B	387	17.2	13.5	15.0	12.0	19.0	7.0	25.0
TOTAL	775	17.0	12.7	15.0	12.0	19.0	7.0	25.0

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

See Figure LABB–1 on page 31.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	388	20.9	9.9	20.0	16.0	23.0	11.0	30.0
B	387	22.3	14.1	19.0	16.0	24.0	11.0	51.0
TOTAL	775	21.6	12.2	20.0	16.0	23.0	11.0	33.0

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

See Figure LABB–1 on page 31.

Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95
A	388	7.7	4.9	7.0	5.0	9.0	2.0	13.0
B	387	7.7	6.2	7.0	5.0	9.0	2.0	16.0
TOTAL	775	7.7	5.6	7.0	5.0	9.0	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 33.

			Value					
			Yes		No			P-
	Trt	Total Subjs	N	%	N	%	Contrast	Value
Any SAE	A	388	120	30.93	268	69.07	A.B	0.981
	B	387	120	31.01	267	68.99		
	TOTAL	775	240	30.97	535	69.03		
Multiple SAEs	A	388	51	13.14	337	86.86	A.B	0.069
	B	387	35	9.04	352	90.96		
	TOTAL	775	86	11.10	689	88.90		
Fatal SAE	A	388	59	15.21	329	84.79	A.B	0.006
	B	387	34	8.79	353	91.21		
	TOTAL	775	93	12.00	682	88.00		

Serious Adverse Events: First Serious Adverse Event Probability over Time

See Figure SAE–1 on page 33.

Weeks	Trt	nRisk	nEvents	% w/ Event	95% CI
0	A	388	3	0.8	(0.0, 1.6)
	B	387	5	1.3	(0.2, 2.4)
3	A	383	10	2.6	(1.0, 4.1)
	B	374	19	4.9	(2.7, 7.0)
6	A	372	18	4.6	(2.5, 6.7)
	B	364	27	7.0	(4.4, 9.5)
9	A	364	27	7.0	(4.4, 9.5)
	B	354	37	9.6	(6.6, 12.4)
12	A	359	30	7.7	(5.0, 10.4)
	B	346	44	11.4	(8.2, 14.5)
15	A	349	39	10.1	(7.0, 13.0)
	B	337	53	13.7	(10.2, 17.1)

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Serious Adverse Events: First Serious Adverse Event Probability over Time

See Figure SAE–1 on page 33.

Weeks	Trt	nRisk	nEvents	% w/ Event	95% CI
18	A	336	50	12.9	(9.5, 16.2)
	B	320	64	16.6	(12.8, 20.2)
21	A	326	56	14.5	(10.9, 17.9)
	B	306	74	19.2	(15.2, 23.1)
24	A	303	73	19.0	(15.0, 22.9)
	B	298	78	20.3	(16.2, 24.2)
27	A	280	84	22.1	(17.8, 26.1)
	B	279	90	23.6	(19.2, 27.7)
30	A	254	91	24.1	(19.6, 28.3)
	B	256	96	25.3	(20.8, 29.6)
33	A	227	104	28.3	(23.5, 32.7)
	B	226	102	27.2	(22.5, 31.6)
36	A	198	109	30.0	(25.0, 34.6)
	B	200	107	28.9	(24.1, 33.4)
39	A	156	110	30.4	(25.4, 35.0)
	B	157	111	30.5	(25.5, 35.2)
42	A	121	113	32.0	(26.8, 36.8)
	B	121	114	32.0	(26.8, 36.9)
45	A	82	116	34.1	(28.4, 39.3)
	B	92	115	32.7	(27.3, 37.6)
48	A	58	118	36.1	(29.9, 41.7)
	B	68	117	34.5	(28.7, 39.8)
51	A	40	118	36.1	(29.9, 41.7)
	B	49	118	35.7	(29.5, 41.4)
54	A	21	120	40.2	(31.8, 47.5)
	B	29	118	35.7	(29.5, 41.4)
57	A	9	120	40.2	(31.8, 47.5)
	B	16	119	38.4	(30.2, 45.6)
60	A	4	120	40.2	(31.8, 47.5)
	B	6	119	38.4	(30.2, 45.6)
63	A	0	120	40.2	(31.8, 47.5)
	B	3	120	50.7	(22.2, 68.7)
66	A	0	120	40.2	(31.8, 47.5)
	B	0	120	50.7	(22.2, 68.7)

Table Set SAE–2

SAEs by System Organ Class: System Organ Class

See Figure SAE–2 on page 34.

			Value					
			Yes		No			
	Trt	Total Subjs	N	%	N	%	Contrast	P-Value
Infections, infestations	A	388	7	1.80	381	98.20	A.B	0.996
	B	387	7	1.81	380	98.19		
	TOTAL	775	14	1.81	761	98.19		
Neoplasms	A	388	9	2.32	379	97.68	A.B	0.437
	B	387	6	1.55	381	98.45		
	TOTAL	775	15	1.94	760	98.06		
Blood, lymphatic	A	388	10	2.58	378	97.42	A.B	0.403
	B	387	14	3.62	373	96.38		
	TOTAL	775	24	3.10	751	96.90		
Immune system	A	388	3	0.77	385	99.23	A.B	0.656
	B	387	2	0.52	385	99.48		
	TOTAL	775	5	0.65	770	99.35		
Endocrine	A	388	6	1.55	382	98.45	A.B	0.765
	B	387	5	1.29	382	98.71		
	TOTAL	775	11	1.42	764	98.58		
Metabolism, nutrition	A	388	0	0.00	388	100.00	A.B	1.000
	B	387	0	0.00	387	100.00		
	TOTAL	775	0	0.00	775	100.00		
Psychiatric	A	388	12	3.09	376	96.91	A.B	0.368
	B	387	8	2.07	379	97.93		
	TOTAL	775	20	2.58	755	97.42		
Nervous system	A	388	1	0.26	387	99.74	A.B	0.315
	B	387	3	0.78	384	99.22		
	TOTAL	775	4	0.52	771	99.48		
Eye	A	388	9	2.32	379	97.68	A.B	0.437
	B	387	6	1.55	381	98.45		
	TOTAL	775	15	1.94	760	98.06		
Ear, labyrinth	A	388	3	0.77	385	99.23	A.B	0.083
	B	387	0	0.00	387	100.00		
	TOTAL	775	3	0.39	772	99.61		
Cardiac	A	388	42	10.82	346	89.18	A.B	0.108
	B	387	29	7.49	358	92.51		
	TOTAL	775	71	9.16	704	90.84		
Vascular	A	388	7	1.80	381	98.20	A.B	0.996
	B	387	7	1.81	380	98.19		
	TOTAL	775	14	1.81	761	98.19		
Respiratory, thoracic, mediastinal	A	388	18	4.64	370	95.36	A.B	0.599
	B	387	15	3.88	372	96.12		
	TOTAL	775	33	4.26	742	95.74		

SAEs by System Organ Class: System Organ Class

See Figure SAE–2 on page 34.

			Value					
		Total	Yes		No			P-
	Trt	Subjs	N	%	N	%	Contrast	Value
Gastrointestinal	A	388	4	1.03	384	98.97	A.B	0.000
	B	387	23	5.94	364	94.06		
	TOTAL	775	27	3.48	748	96.52		
Hepatobiliary	A	388	9	2.32	379	97.68	A.B	0.437
	B	387	6	1.55	381	98.45		
	TOTAL	775	15	1.94	760	98.06		
Skin, subcutaneous tissue	A	388	9	2.32	379	97.68	A.B	0.437
	B	387	6	1.55	381	98.45		
	TOTAL	775	15	1.94	760	98.06		
Musculoskeletal, connective tissue	A	388	3	0.77	385	99.23	A.B	0.317
	B	387	1	0.26	386	99.74		
	TOTAL	775	4	0.52	771	99.48		
Renal, urinary	A	388	13	3.35	375	96.65	A.B	0.695
	B	387	15	3.88	372	96.12		
	TOTAL	775	28	3.61	747	96.39		
Pregnancy	A	388	0	0.00	388	100.00	A.B	1.000
	B	387	0	0.00	387	100.00		
	TOTAL	775	0	0.00	775	100.00		
Reproductive, breast	A	388	0	0.00	388	100.00	A.B	0.082
	B	387	3	0.78	384	99.22		
	TOTAL	775	3	0.39	772	99.61		
Congenital, familial, genetic	A	388	9	2.32	379	97.68	A.B	0.437
	B	387	6	1.55	381	98.45		
	TOTAL	775	15	1.94	760	98.06		
General, administration site	A	388	2	0.52	386	99.48	A.B	0.998
	B	387	2	0.52	385	99.48		
	TOTAL	775	4	0.52	771	99.48		
Investigations	A	388	12	3.09	376	96.91	A.B	0.837
	B	387	11	2.84	376	97.16		
	TOTAL	775	23	2.97	752	97.03		
Injury, poisoning, procedural	A	388	6	1.55	382	98.45	A.B	0.586
	B	387	8	2.07	379	97.93		
	TOTAL	775	14	1.81	761	98.19		
Surgical, medical procedures	A	388	12	3.09	376	96.91	A.B	0.437
	B	387	16	4.13	371	95.87		
	TOTAL	775	28	3.61	747	96.39		
Social circumstances	A	388	0	0.00	388	100.00	A.B	0.316
	B	387	1	0.26	386	99.74		
	TOTAL	775	1	0.13	774	99.87		
– Uncoded –	A	388	0	0.00	388	100.00	A.B	0.316
	B	387	1	0.26	386	99.74		
	TOTAL	775	1	0.13	774	99.87		

3.2 Adverse Events

Table Set AE–1

Adverse Events: Overview

See Figure AE–1 on page 39.

			Value					
		Total	Yes		No			P-
	Trt	Subjs	N	%	N	%	Contrast	Value
Any AE	A	388	195	50.26	193	49.74	A.B	0.914
	B	387	193	49.87	194	50.13		
	TOTAL	775	388	50.06	387	49.94		
AE possibly related to investigational product	A	388	75	19.33	313	80.67	A.B	0.464
	B	387	83	21.45	304	78.55		
	TOTAL	775	158	20.39	617	79.61		
Severe AE	A	388	18	4.64	370	95.36	A.B	0.732
	B	387	16	4.13	371	95.87		
	TOTAL	775	34	4.39	741	95.61		

Adverse Events: Actions Taken with IP Due to Any AE

See Figure AE–1 on page 39.

			Value					
		Total	Yes		No			P-
	Trt	Subjs	N	%	N	%	Contrast	Value
IP withdrawn	A	388	55	14.18	333	85.82	A.B	0.415
	B	387	63	16.28	324	83.72		
	TOTAL	775	118	15.23	657	84.77		
Dose reduced	A	388	95	24.48	293	75.52	A.B	0.511
	B	387	87	22.48	300	77.52		
	TOTAL	775	182	23.48	593	76.52		
Dose interrupted	A	388	40	10.31	348	89.69	A.B	0.328
	B	387	32	8.27	355	91.73		
	TOTAL	775	72	9.29	703	90.71		

Adverse Events: Subject Actions Taken Due to Any AE

See Figure AE–1 on page 39.

		Value					
	Total	Withdrawn from study		Not withdrawn from study			P-
Trt	Subjs	N	%	N	%	Contrast	Value
A	388	17	4.38	371	95.62	A.B	0.857
B	387	18	4.65	369	95.35		
TOTAL	775	35	4.52	740	95.48		

Table Set AE–2

AEs by System Organ Class and Severity: System Organ Class

See Figure AE–2 on page 40.

			Value									
		Total	Severe		Moderate		Mild		None			P-
	Trt	Subjs	N	%	N	%	N	%	N	%	Contrast	Value
*** OVERALL ***	A	388	18	4.64	27	6.96	150	38.66	193	49.74	A.B	0.868
	B	387	16	4.13	27	6.98	150	38.76	194	50.13		
	TOTAL	775	34	4.39	54	6.97	300	38.71	387	49.94		
Infections, infestations	A	388	1	0.26	4	1.03	20	5.15	363	93.56	A.B	0.562
	B	387	2	0.52	4	1.03	15	3.88	366	94.57		
	TOTAL	775	3	0.39	8	1.03	35	4.52	729	94.06		
Neoplasms	A	388	2	0.52	4	1.03	14	3.61	368	94.85	A.B	0.298
	B	387	3	0.78	1	0.26	10	2.58	373	96.38		
	TOTAL	775	5	0.65	5	0.65	24	3.10	741	95.61		
Blood, lymphatic	A	388	2	0.52	6	1.55	22	5.67	358	92.27	A.B	0.765
	B	387	1	0.26	3	0.78	24	6.20	359	92.76		
	TOTAL	775	3	0.39	9	1.16	46	5.94	717	92.52		
Immune system	A	388	0	0.00	2	0.52	6	1.55	380	97.94	A.B	0.991
	B	387	1	0.26	2	0.52	5	1.29	379	97.93		
	TOTAL	775	1	0.13	4	0.52	11	1.42	759	97.94		
Endocrine	A	388	2	0.52	2	0.52	9	2.32	375	96.65	A.B	0.386
	B	387	0	0.00	2	0.52	7	1.81	378	97.67		
	TOTAL	775	2	0.26	4	0.52	16	2.06	753	97.16		
Metabolism, nutrition	A	388	0	0.00	0	0.00	1	0.26	387	99.74	A.B	0.315
	B	387	0	0.00	0	0.00	3	0.78	384	99.22		
	TOTAL	775	0	0.00	0	0.00	4	0.52	771	99.48		
Psychiatric	A	388	3	0.77	4	1.03	30	7.73	351	90.46	A.B	0.261
	B	387	2	0.52	6	1.55	20	5.17	359	92.76		
	TOTAL	775	5	0.65	10	1.29	50	6.45	710	91.61		
Nervous system	A	388	0	0.00	1	0.26	4	1.03	383	98.71	A.B	0.559
	B	387	0	0.00	1	0.26	6	1.55	380	98.19		
	TOTAL	775	0	0.00	2	0.26	10	1.29	763	98.45		
Eye	A	388	2	0.52	5	1.29	24	6.19	357	92.01	A.B	0.005
	B	387	1	0.26	1	0.26	11	2.84	374	96.64		
	TOTAL	775	3	0.39	6	0.77	35	4.52	731	94.32		
Ear, labyrinth	A	388	0	0.00	1	0.26	11	2.84	376	96.91	A.B	0.090
	B	387	2	0.52	0	0.00	3	0.78	382	98.71		
	TOTAL	775	2	0.26	1	0.13	14	1.81	758	97.81		
Cardiac	A	388	14	3.61	12	3.09	72	18.56	290	74.74	A.B	0.047
	B	387	5	1.29	15	3.88	55	14.21	312	80.62		
	TOTAL	775	19	2.45	27	3.48	127	16.39	602	77.68		
Vascular	A	388	1	0.26	2	0.52	18	4.64	367	94.59	A.B	0.612
	B	387	3	0.78	5	1.29	16	4.13	363	93.80		
	TOTAL	775	4	0.52	7	0.90	34	4.39	730	94.19		
Respiratory, thoracic, mediastinal	A	388	5	1.29	11	2.84	24	6.19	348	89.69	A.B	0.581
	B	387	2	0.52	4	1.03	40	10.34	341	88.11		
	TOTAL	775	7	0.90	15	1.94	64	8.26	689	88.90		

AEs by System Organ Class and Severity: System Organ Class

See Figure AE–2 on page 40.

			Value									
		Total	Severe		Moderate		Mild		None			P-
	Trt	Subjs	N	%	N	%	N	%	N	%	Contrast	Value
Gastrointestinal	A	388	1	0.26	2	0.52	11	2.84	374	96.39	A.B	0.000
	B	387	6	1.55	5	1.29	46	11.89	330	85.27		
	TOTAL	775	7	0.90	7	0.90	57	7.35	704	90.84		
Hepatobiliary	A	388	5	1.29	6	1.55	16	4.12	361	93.04	A.B	0.270
	B	387	0	0.00	3	0.78	17	4.39	367	94.83		
	TOTAL	775	5	0.65	9	1.16	33	4.26	728	93.94		
Skin, subcutaneous tissue	A	388	2	0.52	1	0.26	12	3.09	373	96.13	A.B	0.857
	B	387	0	0.00	2	0.52	14	3.62	371	95.87		
	TOTAL	775	2	0.26	3	0.39	26	3.35	744	96.00		
Musculoskeletal, connective tissue	A	388	0	0.00	0	0.00	8	2.06	380	97.94	A.B	0.249
	B	387	0	0.00	1	0.26	3	0.78	383	98.97		
	TOTAL	775	0	0.00	1	0.13	11	1.42	763	98.45		
Renal, urinary	A	388	4	1.03	5	1.29	24	6.19	355	91.49	A.B	0.591
	B	387	7	1.81	5	1.29	25	6.46	350	90.44		
	TOTAL	775	11	1.42	10	1.29	49	6.32	705	90.97		
Pregnancy	A	388	0	0.00	0	0.00	0	0.00	388	100.00	A.B	1.000
	B	387	0	0.00	0	0.00	0	0.00	387	100.00		
	TOTAL	775	0	0.00	0	0.00	0	0.00	775	100.00		
Reproductive, breast	A	388	1	0.26	1	0.26	3	0.77	383	98.71	A.B	0.995
	B	387	2	0.52	0	0.00	3	0.78	382	98.71		
	TOTAL	775	3	0.39	1	0.13	6	0.77	765	98.71		
Congenital, familial, genetic	A	388	2	0.52	3	0.77	16	4.12	367	94.59	A.B	0.634
	B	387	3	0.78	2	0.52	13	3.36	369	95.35		
	TOTAL	775	5	0.65	5	0.65	29	3.74	736	94.97		
General, administration site	A	388	0	0.00	1	0.26	2	0.52	385	99.23	A.B	0.312
	B	387	2	0.52	0	0.00	4	1.03	381	98.45		
	TOTAL	775	2	0.26	1	0.13	6	0.77	766	98.84		
Investigations	A	388	3	0.77	2	0.52	20	5.15	363	93.56	A.B	0.171
	B	387	4	1.03	5	1.29	26	6.72	352	90.96		
	TOTAL	775	7	0.90	7	0.90	46	5.94	715	92.26		
Injury, poisoning, procedural	A	388	0	0.00	2	0.52	20	5.15	366	94.33	A.B	0.425
	B	387	2	0.52	1	0.26	14	3.62	370	95.61		
	TOTAL	775	2	0.26	3	0.39	34	4.39	736	94.97		
Surgical, medical procedures	A	388	3	0.77	4	1.03	24	6.19	357	92.01	A.B	0.355
	B	387	4	1.03	8	2.07	26	6.72	349	90.18		
	TOTAL	775	7	0.90	12	1.55	50	6.45	706	91.10		
Social circumstances	A	388	0	0.00	0	0.00	1	0.26	387	99.74	A.B	0.315
	B	387	0	0.00	0	0.00	3	0.78	384	99.22		
	TOTAL	775	0	0.00	0	0.00	4	0.52	771	99.48		
– Uncoded –	A	388	0	0.00	0	0.00	0	0.00	388	100.00	A.B	0.317
	B	387	0	0.00	1	0.26	0	0.00	386	99.74		
	TOTAL	775	0	0.00	1	0.13	0	0.00	774	99.87		

Table Set AE–3

Most Common AEs by Preferred Term and Severity: Preferred Term

See Figure AE–3 on page 41.

			Value									
		Total	Severe		Moderate		Mild		None			P-
	Trt	Subjs	N	%	N	%	N	%	N	%	Contrast	Value
Chronic obstructive airway	A	388	14	3.61	26	6.70	78	20.10	270	69.59	A.B	0.000
	B	387	10	2.58	16	4.13	45	11.63	316	81.65		
	TOTAL	775	24	3.10	42	5.42	123	15.87	586	75.61		
Diarrhoea	A	388	6	1.55	13	3.35	30	7.73	339	87.37	A.B	0.001
	B	387	10	2.58	20	5.17	54	13.95	303	78.29		
	TOTAL	775	16	2.06	33	4.26	84	10.84	642	82.84		
Nausea	A	388	3	0.77	5	1.29	17	4.38	363	93.56	A.B	0.000
	B	387	8	2.07	15	3.88	63	16.28	301	77.78		
	TOTAL	775	11	1.42	20	2.58	80	10.32	664	85.68		
Upper respiratory tract infection	A	388	4	1.03	12	3.09	53	13.66	319	82.22	A.B	0.845
	B	387	7	1.81	14	3.62	49	12.66	317	81.91		
	TOTAL	775	11	1.42	26	3.35	102	13.16	636	82.06		
Abdominal pain	A	388	2	0.52	9	2.32	27	6.96	350	90.21	A.B	0.088
	B	387	8	2.07	8	2.07	37	9.56	334	86.30		
	TOTAL	775	10	1.29	17	2.19	64	8.26	684	88.26		
Dyspepsia	A	388	2	0.52	9	2.32	10	2.58	367	94.59	A.B	0.002
	B	387	5	1.29	10	2.58	30	7.75	342	88.37		
	TOTAL	775	7	0.90	19	2.45	40	5.16	709	91.48		
Headache	A	388	3	0.77	7	1.80	19	4.90	359	92.53	A.B	0.157
	B	387	4	1.03	12	3.10	24	6.20	347	89.66		
	TOTAL	775	7	0.90	19	2.45	43	5.55	706	91.10		
Vomiting	A	388	1	0.26	7	1.80	14	3.61	366	94.33	A.B	0.061
	B	387	2	0.52	5	1.29	29	7.49	351	90.70		
	TOTAL	775	3	0.39	12	1.55	43	5.55	717	92.52		
Sinusitis	A	388	3	0.77	6	1.55	19	4.90	360	92.78	A.B	0.338
	B	387	8	2.07	5	1.29	22	5.68	352	90.96		
	TOTAL	775	11	1.42	11	1.42	41	5.29	712	91.87		
Injury	A	388	7	1.80	4	1.03	15	3.87	362	93.30	A.B	0.794
	B	387	3	0.78	7	1.81	18	4.65	359	92.76		
	TOTAL	775	10	1.29	11	1.42	33	4.26	721	93.03		
Infection viral	A	388	3	0.77	3	0.77	17	4.38	365	94.07	A.B	0.871
	B	387	2	0.52	5	1.29	17	4.39	363	93.80		
	TOTAL	775	5	0.65	8	1.03	34	4.39	728	93.94		
Dizziness	A	388	1	0.26	1	0.26	16	4.12	370	95.36	A.B	0.050
	B	387	3	0.78	6	1.55	22	5.68	356	91.99		
	TOTAL	775	4	0.52	7	0.90	38	4.90	726	93.68		
Coughing	A	388	1	0.26	4	1.03	15	3.87	368	94.85	A.B	0.422
	B	387	1	0.26	9	2.33	15	3.88	362	93.54		
	TOTAL	775	2	0.26	13	1.68	30	3.87	730	94.19		
Insomnia	A	388	1	0.26	5	1.29	9	2.32	373	96.13	A.B	0.138
	B	387	2	0.52	7	1.81	15	3.88	363	93.80		
	TOTAL	775	3	0.39	12	1.55	24	3.10	736	94.97		
Back pain	A	388	1	0.26	4	1.03	11	2.84	372	95.88	A.B	0.042
	B	387	6	1.55	6	1.55	17	4.39	358	92.51		
	TOTAL	775	7	0.90	10	1.29	28	3.61	730	94.19		

Most Common AEs by Preferred Term and Severity: Preferred Term

See Figure AE–3 on page 41.

			Value									
		Total	Severe		Moderate		Mild		None			P-
	Trt	Subjs	N	%	N	%	N	%	N	%	Contrast	Value
Rhinitis	A	388	3	0.77	6	1.55	14	3.61	365	94.07	A.B	0.891
	B	387	2	0.52	8	2.07	12	3.10	365	94.32		
	TOTAL	775	5	0.65	14	1.81	26	3.35	730	94.19		
Flatulence	A	388	1	0.26	3	0.77	8	2.06	376	96.91	A.B	0.199
	B	387	3	0.78	2	0.52	14	3.62	368	95.09		
	TOTAL	775	4	0.52	5	0.65	22	2.84	744	96.00		
Dyspnoea	A	388	2	0.52	7	1.80	22	5.67	357	92.01	A.B	0.001
	B	387	2	0.52	2	0.52	6	1.55	377	97.42		
	TOTAL	775	4	0.52	9	1.16	28	3.61	734	94.71		
Chest pain	A	388	1	0.26	2	0.52	7	1.80	378	97.42	A.B	0.818
	B	387	1	0.26	3	0.78	7	1.81	376	97.16		
	TOTAL	775	2	0.26	5	0.65	14	1.81	754	97.29		
Bronchitis	A	388	5	1.29	3	0.77	7	1.80	373	96.13	A.B	0.414
	B	387	1	0.26	2	0.52	8	2.07	376	97.16		
	TOTAL	775	6	0.77	5	0.65	15	1.94	749	96.65		
Respiratory disorder	A	388	1	0.26	1	0.26	4	1.03	382	98.45	A.B	0.070
	B	387	2	0.52	1	0.26	11	2.84	373	96.38		
	TOTAL	775	3	0.39	2	0.26	15	1.94	755	97.42		
Anorexia	A	388	1	0.26	0	0.00	1	0.26	386	99.48	A.B	0.001
	B	387	2	0.52	3	0.78	11	2.84	371	95.87		
	TOTAL	775	3	0.39	3	0.39	12	1.55	757	97.68		
Pain	A	388	2	0.52	4	1.03	5	1.29	377	97.16	A.B	0.990
	B	387	1	0.26	2	0.52	8	2.07	376	97.16		
	TOTAL	775	3	0.39	6	0.77	13	1.68	753	97.16		
Fatigue	A	388	0	0.00	4	1.03	5	1.29	379	97.68	A.B	0.105
	B	387	4	1.03	6	1.55	7	1.81	370	95.61		
	TOTAL	775	4	0.52	10	1.29	12	1.55	749	96.65		
Gastroesophageal reflux	A	388	2	0.52	5	1.29	11	2.84	370	95.36	A.B	0.863
	B	387	1	0.26	5	1.29	11	2.84	370	95.61		
	TOTAL	775	3	0.39	10	1.29	22	2.84	740	95.48		
Flash	A	388	0	0.00	1	0.26	12	3.09	375	96.65	A.B	0.388
	B	387	0	0.00	0	0.00	9	2.33	378	97.67		
	TOTAL	775	0	0.00	1	0.13	21	2.71	753	97.16		
Hyperkalemia	A	388	4	1.03	2	0.52	7	1.80	375	96.65	A.B	0.709
	B	387	0	0.00	6	1.55	9	2.33	372	96.12		
	TOTAL	775	4	0.52	8	1.03	16	2.06	747	96.39		
Melena	A	388	2	0.52	7	1.80	7	1.80	372	95.88	A.B	0.007
	B	387	1	0.26	0	0.00	3	0.78	383	98.97		
	TOTAL	775	3	0.39	7	0.90	10	1.29	755	97.42		
Urinary tract infection	A	388	1	0.26	5	1.29	8	2.06	374	96.39	A.B	0.546
	B	387	2	0.52	2	0.52	7	1.81	376	97.16		
	TOTAL	775	3	0.39	7	0.90	15	1.94	750	96.77		
Myalgia	A	388	0	0.00	0	0.00	5	1.29	383	98.71	A.B	0.752
	B	387	1	0.26	1	0.26	4	1.03	381	98.45		
	TOTAL	775	1	0.13	1	0.13	9	1.16	764	98.58		

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 49.

		Treatment Group							
		A		B		TOTAL			P-
	Value	N	%	N	%	N	%	Contrast	Value
Alanine Aminotransferase	Total Subjs	357		357		714		A.B	0.407
	>3 xULN	1	0.28	1	0.28	2	0.28		
	>2-3 xULN	1	0.28	1	0.28	2	0.28		
	>1-2 xULN	41	11.48	34	9.52	75	10.50		
	≤ ULN	314	87.96	321	89.92	635	88.94		
Aspartate Aminotransferase	Total Subjs	357		357		714		A.B	0.339
	>3 xULN	0	0.00	1	0.28	1	0.14		
	>2-3 xULN	2	0.56	2	0.56	4	0.56		
	>1-2 xULN	24	6.72	30	8.40	54	7.56		
	≤ ULN	331	92.72	324	90.76	655	91.74		
Alkaline Phosphatase	Total Subjs	357		357		714		A.B	0.521
	>3 xULN	5	1.40	2	0.56	7	0.98		
	>2-3 xULN	13	3.64	7	1.96	20	2.80		
	>1-2 xULN	40	11.20	44	12.32	84	11.76		
	≤ ULN	299	83.75	304	85.15	603	84.45		
Total Bilirubin	Total Subjs	357		357		714		A.B	0.612
	>3 xULN	1	0.28	0	0.00	1	0.14		
	>2-3 xULN	1	0.28	1	0.28	2	0.28		
	>1-2 xULN	36	10.08	33	9.24	69	9.66		
	≤ ULN	319	89.36	323	90.48	642	89.92		

Summary of Liver Function Test Elevations: Elevations of Potential Clinical Concern

See Figure LFTABN–1 on page 49.

		Treatment Group							
		A		B		TOTAL			P-
	Value	N	%	N	%	N	%	Contrast	Value
ALT or AST Ever ≥3xULN	Total Subjs	357		357		714		A.B	0.563
	Yes	1	0.28	2	0.56	3	0.42		
ALT or AST Ever ≥3xULN, and Bilirubin Ever ≥2xULN	Total Subjs	357		357		714		A.B	1.000
	Yes	0	0.00	0	0.00	0	0.00		

Table Set LFT–1

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

See Figure LFT–1 on page 50.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	388	16.7	12.0	15.0	11.5	19.0	6.0	25.0	A.B	0.598
	B	387	17.2	13.5	15.0	12.0	19.0	7.0	25.0		
	TOTAL	775	17.0	12.7	15.0	12.0	19.0	7.0	25.0		
Month 3	A	357	18.1	12.5	17.0	13.0	20.0	7.0	28.0	A.B	0.052
	B	357	19.2	11.4	17.0	14.0	21.0	8.0	35.0		
	TOTAL	714	18.7	12.0	17.0	13.0	21.0	7.0	29.0		
Month 6	A	292	18.1	11.8	16.0	12.0	20.0	6.0	58.0	A.B	0.000
	B	303	19.9	14.8	18.0	14.0	23.0	8.0	30.0		
	TOTAL	595	19.1	13.4	17.0	13.0	21.0	7.0	32.0		
Month 9	A	166	20.0	14.1	17.0	14.0	21.0	8.0	62.0	A.B	0.141
	B	166	20.4	13.4	18.5	14.0	23.0	7.0	66.0		
	TOTAL	332	20.2	13.7	17.0	14.0	22.0	8.0	63.0		
Month 12	A	35	20.7	14.1	18.0	13.0	24.0	4.0	62.0	A.B	0.148
	B	32	22.7	12.8	20.5	16.5	24.5	12.0	66.0		
	TOTAL	67	21.6	13.5	19.0	15.0	24.0	9.0	62.0		

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

See Figure LFT–1 on page 50.

			Value									
		Total	>3 xULN		>2-3 xULN		>1-2 xULN		≤ ULN			P-
	Trt	Subjs	N	%	N	%	N	%	N	%	Contrast	Value
Baseline	A	388	0	0.00	3	0.77	12	3.09	373	96.13	A.B	0.987
	B	387	1	0.26	3	0.78	11	2.84	372	96.12		
	TOTAL	775	1	0.13	6	0.77	23	2.97	745	96.13		
Month 3	A	357	1	0.28	0	0.00	12	3.36	344	96.36	A.B	0.706
	B	357	0	0.00	0	0.00	15	4.20	342	95.80		
	TOTAL	714	1	0.14	0	0.00	27	3.78	686	96.08		
Month 6	A	292	0	0.00	0	0.00	16	5.48	276	94.52	A.B	0.133
	B	303	1	0.33	1	0.33	7	2.31	294	97.03		
	TOTAL	595	1	0.17	1	0.17	23	3.87	570	95.80		
Month 9	A	166	0	0.00	1	0.60	10	6.02	155	93.37	A.B	0.811
	B	166	0	0.00	0	0.00	10	6.02	156	93.98		
	TOTAL	332	0	0.00	1	0.30	20	6.02	311	93.67		
Month 12	A	35	0	0.00	0	0.00	3	8.57	32	91.43	A.B	0.720
	B	32	0	0.00	0	0.00	2	6.25	30	93.75		
	TOTAL	67	0	0.00	0	0.00	5	7.46	62	92.54		

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

See Figure LFT–1 on page 50.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	357	1.2	17.1	1.0	-5.0	7.0	-14.0	17.0	A.B	0.190
	B	357	2.0	17.8	2.0	-4.0	8.0	-12.0	17.0		
	TOTAL	714	1.6	17.4	2.0	-4.0	8.0	-14.0	17.0		
Month 6	A	292	1.2	17.8	1.0	-4.0	7.0	-15.0	41.0	A.B	0.013
	B	303	2.5	20.6	3.0	-3.0	8.0	-14.0	19.0		
	TOTAL	595	1.9	19.3	2.0	-4.0	8.0	-15.0	20.0		
Month 9	A	166	3.6	20.1	3.0	-3.0	8.0	-13.0	47.0	A.B	0.362
	B	166	3.1	20.7	4.0	-3.0	9.0	-12.0	42.0		
	TOTAL	332	3.3	20.4	3.0	-3.0	9.0	-12.0	47.0		
Month 12	A	35	6.5	15.0	4.0	0.0	9.0	-14.0	47.0	A.B	0.664
	B	32	4.8	15.4	4.5	1.5	8.5	-31.0	43.0		
	TOTAL	67	5.7	15.1	4.0	0.0	9.0	-14.0	46.0		

Table Set LFT–2

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

See Figure LFT–2 on page 51.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	388	20.9	9.9	20.0	16.0	23.0	11.0	30.0	A.B	0.638
	B	387	22.3	14.1	19.0	16.0	24.0	11.0	51.0		
	TOTAL	775	21.6	12.2	20.0	16.0	23.0	11.0	33.0		
Month 3	A	357	20.9	8.4	20.0	16.0	24.0	11.0	29.0	A.B	0.000
	B	357	23.0	10.7	21.0	18.0	25.0	12.0	33.0		
	TOTAL	714	22.0	9.6	21.0	17.0	25.0	12.0	31.0		
Month 6	A	292	20.1	7.1	20.0	16.0	23.0	10.0	31.0	A.B	0.000
	B	303	23.7	13.2	22.0	18.0	26.0	14.0	34.0		
	TOTAL	595	21.9	10.8	21.0	17.0	25.0	12.0	32.0		
Month 9	A	166	23.2	13.1	21.0	17.0	25.0	12.0	53.0	A.B	0.044
	B	166	24.3	11.8	23.0	18.0	26.0	12.0	60.0		
	TOTAL	332	23.8	12.5	22.0	18.0	26.0	12.0	60.0		
Month 12	A	35	22.3	16.8	19.0	15.0	23.0	9.0	58.0	A.B	0.359
	B	32	20.6	5.4	21.0	16.0	25.0	10.0	29.0		
	TOTAL	67	21.5	12.6	20.0	16.0	24.0	10.0	29.0		

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

See Figure LFT–2 on page 51.

			Value									
		Total	>3 xULN		>2-3 xULN		>1-2 xULN		≤ ULN			P-
	Trt	Subjs	N	%	N	%	N	%	N	%	Contrast	Value
Baseline	A	388	0	0.00	1	0.26	14	3.61	373	96.13	A.B	0.224
	B	387	1	0.26	5	1.29	16	4.13	365	94.32		
	TOTAL	775	1	0.13	6	0.77	30	3.87	738	95.23		
Month 3	A	357	0	0.00	0	0.00	10	2.80	347	97.20	A.B	0.403
	B	357	0	0.00	1	0.28	13	3.64	343	96.08		
	TOTAL	714	0	0.00	1	0.14	23	3.22	690	96.64		
Month 6	A	292	0	0.00	0	0.00	5	1.71	287	98.29	A.B	0.146
	B	303	1	0.33	1	0.33	9	2.97	292	96.37		
	TOTAL	595	1	0.17	1	0.17	14	2.35	579	97.31		

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

See Figure LFT–2 on page 51.

			Value									
		Total	>3 xULN		>2-3 xULN		>1-2 xULN		≤ ULN			P-
	Trt	Subjs	N	%	N	%	N	%	N	%	Contrast	Value
Month 9	A	166	0	0.00	1	0.60	8	4.82	157	94.58	A.B	0.656
	B	166	0	0.00	0	0.00	11	6.63	155	93.37		
	TOTAL	332	0	0.00	1	0.30	19	5.72	312	93.98		
Month 12	A	35	0	0.00	1	2.86	1	2.86	33	94.29	A.B	0.173
	B	32	0	0.00	0	0.00	0	0.00	32	100.00		
	TOTAL	67	0	0.00	1	1.49	1	1.49	65	97.01		

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

See Figure LFT–2 on page 51.

		Total		Std							P-
	Trt	Subjs	Mean	Dev	Median	Q1	Q3	P5	P95	Contrast	Value
Month 3	A	357	-0.1	13.0	1.0	-5.0	5.0	-15.0	15.0	A.B	0.033
	B	357	1.0	16.3	2.0	-4.0	8.0	-26.0	19.0		
	TOTAL	714	0.5	14.8	1.0	-5.0	6.0	-16.0	16.0		
Month 6	A	292	-1.0	12.6	0.0	-5.0	5.0	-18.0	14.0	A.B	0.001
	B	303	1.7	19.1	3.0	-3.0	8.0	-22.0	16.0		
	TOTAL	595	0.4	16.2	1.0	-4.0	7.0	-20.0	15.0		
Month 9	A	166	2.1	16.2	1.0	-5.0	7.0	-13.0	18.0	A.B	0.060
	B	166	3.4	17.1	4.0	-4.0	8.0	-12.0	35.0		
	TOTAL	332	2.8	16.7	2.0	-5.0	8.0	-13.0	35.0		
Month 12	A	35	-1.3	17.6	-4.0	-10.0	2.0	-18.0	28.0	A.B	0.023
	B	32	-2.0	23.2	-0.5	-3.0	7.0	-10.0	13.0		
	TOTAL	67	-1.6	20.3	-1.0	-7.0	5.0	-15.0	14.0		

Table Set LFT–3

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

See Figure LFT–3 on page 52.

		Total		Std						P-
	Trt	Subjs	Mean	Dev	Median	Q1	Q3	P5	P95	Contrast	Value
Baseline	A	388	81.0	39.5	75.0	62.0	86.5	45.0	145.0	A.B	0.879
	B	387	81.5	40.8	74.0	64.0	88.0	44.0	154.0		
	TOTAL	775	81.2	40.1	75.0	63.0	87.0	44.0	150.0		
Month 3	A	357	84.9	39.5	79.0	65.0	94.0	45.0	152.0	A.B	0.033
	B	357	89.6	42.4	83.0	69.0	98.0	49.0	162.0		
	TOTAL	714	87.3	41.0	81.0	67.0	95.0	46.0	156.0		
Month 6	A	292	84.7	37.5	78.0	65.5	94.0	47.0	157.0	A.B	0.014
	B	303	86.6	28.7	84.0	69.0	97.0	51.0	125.0		
	TOTAL	595	85.7	33.3	82.0	68.0	96.0	48.0	152.0		
Month 9	A	166	88.8	47.3	79.0	67.0	96.0	48.0	163.0	A.B	0.004
	B	166	92.6	43.2	87.0	71.0	104.0	51.0	159.0		
	TOTAL	332	90.7	45.3	82.0	69.0	100.5	48.0	163.0		
Month 12	A	35	97.9	92.9	72.0	58.0	82.0	38.0	432.0	A.B	0.029
	B	32	84.0	22.5	84.5	75.5	96.0	33.0	113.0		
	TOTAL	67	91.3	68.8	80.0	65.0	94.0	38.0	171.0		

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

See Figure LFT–3 on page 52.

			Value									
		Total	>3 xULN		>2-3 xULN		>1-2 xULN		≤ ULN			P-
	Trt	Subjs	N	%	N	%	N	%	N	%	Contrast	Value
Baseline	A	388	3	0.77	2	0.52	23	5.93	360	92.78	A.B	0.681
	B	387	3	0.78	2	0.52	26	6.72	356	91.99		
	TOTAL	775	6	0.77	4	0.52	49	6.32	716	92.39		
Month 3	A	357	1	0.28	5	1.40	18	5.04	333	93.28	A.B	0.669
	B	357	1	0.28	5	1.40	21	5.88	330	92.44		
	TOTAL	714	2	0.28	10	1.40	39	5.46	663	92.86		
Month 6	A	292	1	0.34	3	1.03	15	5.14	273	93.49	A.B	0.400
	B	303	0	0.00	1	0.33	14	4.62	288	95.05		
	TOTAL	595	1	0.17	4	0.67	29	4.87	561	94.29		
Month 9	A	166	1	0.60	4	2.41	9	5.42	152	91.57	A.B	0.514
	B	166	1	0.60	1	0.60	9	5.42	155	93.37		
	TOTAL	332	2	0.60	5	1.51	18	5.42	307	92.47		
Month 12	A	35	2	5.71	1	2.86	1	2.86	31	88.57	A.B	0.186
	B	32	0	0.00	0	0.00	1	3.12	31	96.88		
	TOTAL	67	2	2.99	1	1.49	2	2.99	62	92.54		

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

See Figure LFT–3 on page 52.

		Total		Std							P-
	Trt	Subjs	Mean	Dev	Median	Q1	Q3	P5	P95	Contrast	Value
Month 3	A	357	3.2	57.3	3.0	-21.0	27.0	-65.0	75.0	A.B	0.148
	B	357	7.1	59.8	6.0	-13.0	27.0	-69.0	85.0		
	TOTAL	714	5.1	58.5	5.0	-15.0	27.0	-68.0	81.0		
Month 6	A	292	4.5	55.7	4.5	-18.5	26.0	-78.0	89.0	A.B	0.309
	B	303	4.0	54.9	8.0	-12.0	31.0	-87.0	63.0		
	TOTAL	595	4.2	55.3	6.0	-17.0	28.0	-81.0	71.0		
Month 9	A	166	7.1	63.2	4.0	-18.0	22.0	-70.0	93.0	A.B	0.024
	B	166	11.6	57.6	15.0	-11.0	35.0	-61.0	85.0		
	TOTAL	332	9.3	60.4	8.0	-14.0	29.0	-65.0	90.0		
Month 12	A	35	19.2	97.0	-5.0	-24.0	20.0	-70.0	344.0	A.B	0.277
	B	32	6.6	39.9	10.5	-12.0	27.0	-70.0	71.0		
	TOTAL	67	13.2	75.1	-1.0	-16.0	26.0	-70.0	125.0		

Table Set LFT–4

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

See Figure LFT–4 on page 53.

		Total		Std						P-
	Trt	Subjs	Mean	Dev	Median	Q1	Q3	P5	P95	Contrast	Value
Baseline	A	388	7.7	4.9	7.0	5.0	9.0	2.0	13.0	A.B	0.042
	B	387	7.7	6.2	7.0	5.0	9.0	2.0	16.0		
	TOTAL	775	7.7	5.6	7.0	5.0	9.0	2.0	14.0		
Month 3	A	357	8.4	6.4	7.0	5.0	10.0	2.0	25.0	A.B	0.280
	B	357	8.3	5.0	8.0	5.0	10.0	3.0	15.0		
	TOTAL	714	8.3	5.7	7.0	5.0	10.0	3.0	15.0		
Month 6	A	292	8.0	5.0	7.0	5.0	10.0	2.0	15.0	A.B	0.006
	B	303	8.9	5.2	8.0	6.0	11.0	3.0	16.0		
	TOTAL	595	8.4	5.1	8.0	5.0	10.0	2.0	15.0		

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

See Figure LFT–4 on page 53.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 9	A	166	8.4	5.9	7.0	5.0	10.0	2.0	27.0	A.B	0.166
	B	166	9.0	6.6	8.0	5.0	11.0	2.0	27.0		
	TOTAL	332	8.7	6.2	8.0	5.0	11.0	2.0	27.0		
Month 12	A	35	6.3	3.0	6.0	4.0	8.0	1.0	12.0	A.B	0.109
	B	32	8.6	6.1	8.0	4.5	9.5	2.0	28.0		
	TOTAL	67	7.4	4.9	7.0	4.0	9.0	2.0	13.0		

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

See Figure LFT–4 on page 53.

			Value									
			>3 xULN		>2-3 xULN		>1-2 xULN		≤ ULN			
	Trt	Total Subjs	N	%	N	%	N	%	N	%	Contrast	P-Value
Baseline	A	388	0	0.00	1	0.26	11	2.84	376	96.91	A.B	0.260
	B	387	1	0.26	1	0.26	16	4.13	369	95.35		
	TOTAL	775	1	0.13	2	0.26	27	3.48	745	96.13		
Month 3	A	357	1	0.28	1	0.28	16	4.48	339	94.96	A.B	0.352
	B	357	0	0.00	0	0.00	13	3.64	344	96.36		
	TOTAL	714	1	0.14	1	0.14	29	4.06	683	95.66		
Month 6	A	292	0	0.00	0	0.00	11	3.77	281	96.23	A.B	0.903
	B	303	0	0.00	0	0.00	12	3.96	291	96.04		
	TOTAL	595	0	0.00	0	0.00	23	3.87	572	96.13		
Month 9	A	166	0	0.00	0	0.00	11	6.63	155	93.37	A.B	0.656
	B	166	0	0.00	1	0.60	8	4.82	157	94.58		
	TOTAL	332	0	0.00	1	0.30	19	5.72	312	93.98		
Month 12	A	35	0	0.00	0	0.00	0	0.00	35	100.00	A.B	0.136
	B	32	0	0.00	0	0.00	2	6.25	30	93.75		
	TOTAL	67	0	0.00	0	0.00	2	2.99	65	97.01		

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

See Figure LFT–4 on page 53.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	357	0.6	8.1	0.0	-3.0	3.0	-9.0	11.0	A.B	0.195
	B	357	0.4	8.2	1.0	-2.0	4.0	-13.0	11.0		
	TOTAL	714	0.5	8.2	0.0	-2.0	4.0	-10.0	11.0		
Month 6	A	292	0.4	6.3	0.0	-3.0	3.0	-7.0	11.0	A.B	0.005
	B	303	0.9	8.3	2.0	-2.0	5.0	-11.0	10.0		
	TOTAL	595	0.7	7.4	1.0	-3.0	4.0	-8.0	10.0		
Month 9	A	166	0.9	7.0	0.0	-3.0	3.0	-7.0	18.0	A.B	0.329
	B	166	1.0	8.2	1.0	-3.0	4.0	-14.0	18.0		
	TOTAL	332	0.9	7.6	0.0	-3.0	4.0	-9.0	18.0		
Month 12	A	35	-1.6	5.2	-1.0	-4.0	2.0	-10.0	5.0	A.B	0.101
	B	32	0.7	6.5	0.5	-2.0	3.0	-7.0	12.0		
	TOTAL	67	-0.5	5.9	0.0	-3.0	2.0	-9.0	8.0		

4.2 Clinical Chemistry

Table Set CHEMABN–1

Summary of Abnormal Clinical Chemistry Values: Ever Below LLN

See Figure CHEMABN–1 on page 55.

			Value					
		Total	Yes		No			P-
	Trt	Subjs	N	%	N	%	Contrast	Value
LDL Cholesterol	A	357	0	0.00	357	100.00	A.B	1.000
	B	357	0	0.00	357	100.00		
	TOTAL	714	0	0.00	714	100.00		
HDL Cholesterol	A	357	188	52.66	169	47.34	A.B	0.653
	B	357	194	54.34	163	45.66		
	TOTAL	714	382	53.50	332	46.50		
Total Cholesterol	A	357	0	0.00	357	100.00	A.B	1.000
	B	357	0	0.00	357	100.00		
	TOTAL	714	0	0.00	714	100.00		
Triglycerides	A	357	0	0.00	357	100.00	A.B	1.000
	B	357	0	0.00	357	100.00		
	TOTAL	714	0	0.00	714	100.00		
Sodium	A	388	28	7.22	360	92.78	A.B	0.306
	B	387	21	5.43	366	94.57		
	TOTAL	775	49	6.32	726	93.68		
Potassium	A	388	12	3.09	376	96.91	A.B	0.685
	B	387	14	3.62	373	96.38		
	TOTAL	775	26	3.35	749	96.65		
Chloride	A	388	8	2.06	380	97.94	A.B	0.629
	B	387	10	2.58	377	97.42		
	TOTAL	775	18	2.32	757	97.68		
Bicarbonate	A	388	50	12.89	338	87.11	A.B	0.755
	B	387	47	12.14	340	87.86		
	TOTAL	775	97	12.52	678	87.48		
Blood Urea Nitrogen	A	388	0	0.00	388	100.00	A.B	1.000
	B	387	0	0.00	387	100.00		
	TOTAL	775	0	0.00	775	100.00		
Creatinine	A	388	1	0.26	387	99.74	A.B	0.561
	B	387	2	0.52	385	99.48		
	TOTAL	775	3	0.39	772	99.61		
Glucose	A	388	14	3.61	374	96.39	A.B	0.994
	B	387	14	3.62	373	96.38		
	TOTAL	775	28	3.61	747	96.39		
Calcium	A	388	11	2.84	377	97.16	A.B	0.827
	B	387	12	3.10	375	96.90		
	TOTAL	775	23	2.97	752	97.03		

Summary of Abnormal Clinical Chemistry Values: Ever Above ULN

See Figure CHEMABN–1 on page 55.

			Value					
		Total	Yes		No			P-
	Trt	Subjs	N	%	N	%	Contrast	Value
LDL Cholesterol	A	357	126	35.29	231	64.71	A.B	0.279
	B	357	140	39.22	217	60.78		
	TOTAL	714	266	37.25	448	62.75		
HDL Cholesterol	A	357	0	0.00	357	100.00	A.B	1.000
	B	357	0	0.00	357	100.00		
	TOTAL	714	0	0.00	714	100.00		
Total Cholesterol	A	357	149	41.74	208	58.26	A.B	0.193
	B	357	132	36.97	225	63.03		
	TOTAL	714	281	39.36	433	60.64		
Triglycerides	A	357	198	55.46	159	44.54	A.B	0.707
	B	357	193	54.06	164	45.94		
	TOTAL	714	391	54.76	323	45.24		
Sodium	A	388	48	12.37	340	87.63	A.B	0.989
	B	387	48	12.40	339	87.60		
	TOTAL	775	96	12.39	679	87.61		
Potassium	A	388	71	18.30	317	81.70	A.B	0.457
	B	387	63	16.28	324	83.72		
	TOTAL	775	134	17.29	641	82.71		
Chloride	A	388	30	7.73	358	92.27	A.B	0.510
	B	387	35	9.04	352	90.96		
	TOTAL	775	65	8.39	710	91.61		
Bicarbonate	A	388	12	3.09	376	96.91	A.B	0.552
	B	387	15	3.88	372	96.12		
	TOTAL	775	27	3.48	748	96.52		
Blood Urea Nitrogen	A	388	219	56.44	169	43.56	A.B	0.542
	B	387	210	54.26	177	45.74		
	TOTAL	775	429	55.35	346	44.65		
Creatinine	A	388	55	14.18	333	85.82	A.B	0.415
	B	387	63	16.28	324	83.72		
	TOTAL	775	118	15.23	657	84.77		
Glucose	A	388	171	44.07	217	55.93	A.B	0.400
	B	387	159	41.09	228	58.91		
	TOTAL	775	330	42.58	445	57.42		
Calcium	A	388	9	2.32	379	97.68	A.B	0.384
	B	387	13	3.36	374	96.64		
	TOTAL	775	22	2.84	753	97.16		

Table Set CHEM–1

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

See Figure CHEM–1 on page 56.

		Total	Std							P-
	Trt	Subjs	Mean	Dev	Median	Q1	Q3	P5	P95	Contrast	Value
Baseline	A	388	2.52	1.19	2.30	1.71	3.01	1.13	4.66	A.B	0.731
	B	387	2.49	1.15	2.28	1.67	3.07	1.04	4.67		
	TOTAL	775	2.51	1.17	2.29	1.69	3.02	1.08	4.67		

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

See Figure CHEM–1 on page 56.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	357	2.49	1.23	2.18	1.63	3.01	1.09	5.07	A.B	0.803
	B	357	2.44	1.16	2.14	1.65	2.92	1.08	4.60		
	TOTAL	714	2.46	1.20	2.17	1.63	2.95	1.09	4.92		
Month 6	A	292	2.39	1.08	2.18	1.66	2.83	1.08	4.52	A.B	0.632
	B	303	2.44	1.12	2.22	1.60	3.01	1.08	4.38		
	TOTAL	595	2.41	1.10	2.21	1.63	2.94	1.08	4.49		
Month 9	A	166	2.54	1.31	2.31	1.62	2.97	1.06	5.51	A.B	0.669
	B	166	2.53	1.20	2.32	1.69	3.22	1.05	4.73		
	TOTAL	332	2.54	1.25	2.32	1.65	3.18	1.05	5.07		
Month 12	A	35	2.81	1.25	2.89	1.75	3.65	1.17	4.93	A.B	0.380
	B	32	2.59	1.35	2.31	1.81	3.38	0.74	5.70		
	TOTAL	67	2.71	1.29	2.43	1.78	3.53	0.97	5.11		

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

See Figure CHEM–1 on page 56.

			Value					
		Total	Yes		No			P-
	Trt	Subjs	N	%	N	%	Contrast	Value
Baseline	A	388	75	19.33	313	80.67	A.B	0.986
	B	387	75	19.38	312	80.62		
	TOTAL	775	150	19.35	625	80.65		
Month 3	A	357	62	17.37	295	82.63	A.B	0.844
	B	357	64	17.93	293	82.07		
	TOTAL	714	126	17.65	588	82.35		
Month 6	A	292	46	15.75	246	84.25	A.B	0.643
	B	303	52	17.16	251	82.84		
	TOTAL	595	98	16.47	497	83.53		
Month 9	A	166	34	20.48	132	79.52	A.B	0.594
	B	166	38	22.89	128	77.11		
	TOTAL	332	72	21.69	260	78.31		
Month 12	A	35	11	31.43	24	68.57	A.B	0.560
	B	32	8	25.00	24	75.00		
	TOTAL	67	19	28.36	48	71.64		

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

See Figure CHEM–1 on page 56.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	357	-0.02	1.70	-0.04	-1.00	1.02	-2.62	2.83	A.B	0.991
	B	357	-0.03	1.57	-0.06	-0.96	0.96	-2.47	2.62		
	TOTAL	714	-0.03	1.64	-0.05	-0.99	0.98	-2.56	2.81		
Month 6	A	292	-0.16	1.63	-0.09	-1.12	0.77	-2.60	2.31	A.B	0.536
	B	303	-0.06	1.61	-0.02	-1.11	0.99	-2.76	2.41		
	TOTAL	595	-0.11	1.62	-0.04	-1.11	0.85	-2.74	2.41		
Month 9	A	166	0.02	1.84	-0.07	-0.97	0.94	-2.94	2.96	A.B	0.984
	B	166	-0.00	1.70	-0.01	-0.88	0.89	-2.93	2.61		
	TOTAL	332	0.01	1.77	-0.02	-0.96	0.91	-2.94	2.96		

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

See Figure CHEM–1 on page 56.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 12	A	35	-0.12	2.07	0.10	-0.71	0.79	-5.46	2.94	A.B	0.616
	B	32	-0.04	1.72	-0.19	-1.00	0.91	-2.28	3.40		
	TOTAL	67	-0.08	1.89	-0.10	-0.93	0.79	-2.35	3.36		

4.3 Hematology

Table Set HEMABN–1

Summary of Abnormal Hematology Values: Ever Below LLN

See Figure HEMABN–1 on page 57.

			Value					
			Yes		No			
	Trt	Total Subjs	N	%	N	%	Contrast	P-Value
White Blood Cells	A	357	70	19.61	287	80.39	A.B	0.384
	B	357	61	17.09	296	82.91		
	TOTAL	714	131	18.35	583	81.65		
Red Blood Cells	A	388	158	40.72	230	59.28	A.B	0.792
	B	387	154	39.79	233	60.21		
	TOTAL	775	312	40.26	463	59.74		
Hemoglobin	A	388	135	34.79	253	65.21	A.B	0.011
	B	387	169	43.67	218	56.33		
	TOTAL	775	304	39.23	471	60.77		
Hematocrit	A	388	195	50.26	193	49.74	A.B	0.746
	B	387	190	49.10	197	50.90		
	TOTAL	775	385	49.68	390	50.32		
Mean Corpuscular Volume	A	388	44	11.34	344	88.66	A.B	0.647
	B	387	48	12.40	339	87.60		
	TOTAL	775	92	11.87	683	88.13		
Mean Corpuscular Hemoglobin	A	388	29	7.47	359	92.53	A.B	0.681
	B	387	32	8.27	355	91.73		
	TOTAL	775	61	7.87	714	92.13		
Mean Corpuscular Hemoglobin Concentration	A	388	96	24.74	292	75.26	A.B	0.317
	B	387	108	27.91	279	72.09		
	TOTAL	775	204	26.32	571	73.68		
Platelets	A	388	57	14.69	331	85.31	A.B	0.678
	B	387	61	15.76	326	84.24		
	TOTAL	775	118	15.23	657	84.77		

Summary of Abnormal Hematology Values: Ever Above ULN

See Figure HEMABN–1 on page 57.

			Value					
		Total	Yes		No			P-
	Trt	Subjs	N	%	N	%	Contrast	Value
White Blood Cells	A	357	23	6.44	334	93.56	A.B	0.467
	B	357	28	7.84	329	92.16		
	TOTAL	714	51	7.14	663	92.86		
Red Blood Cells	A	388	12	3.09	376	96.91	A.B	0.154
	B	387	6	1.55	381	98.45		
	TOTAL	775	18	2.32	757	97.68		
Hemoglobin	A	388	4	1.03	384	98.97	A.B	0.734
	B	387	5	1.29	382	98.71		
	TOTAL	775	9	1.16	766	98.84		
Hematocrit	A	388	5	1.29	383	98.71	A.B	0.399
	B	387	8	2.07	379	97.93		
	TOTAL	775	13	1.68	762	98.32		
Mean Corpuscular Volume	A	388	55	14.18	333	85.82	A.B	0.610
	B	387	50	12.92	337	87.08		
	TOTAL	775	105	13.55	670	86.45		
Mean Corpuscular Hemoglobin	A	388	18	4.64	370	95.36	A.B	0.026
	B	387	7	1.81	380	98.19		
	TOTAL	775	25	3.23	750	96.77		
Mean Corpuscular Hemoglobin Concentration	A	388	0	0.00	388	100.00	A.B	1.000
	B	387	0	0.00	387	100.00		
	TOTAL	775	0	0.00	775	100.00		
Platelets	A	388	6	1.55	382	98.45	A.B	0.046
	B	387	15	3.88	372	96.12		
	TOTAL	775	21	2.71	754	97.29		

Table Set HEM–1

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

See Figure HEM–1 on page 58.

		Total		Std						Contrast	P-Value
	Trt	Subjs	Mean	Dev	Median	Q1	Q3	P5	P95		
Baseline	A	388	6.8	1.9	6.6	5.4	7.9	4.2	10.3	A.B	0.709
	B	387	6.9	2.0	6.6	5.6	8.0	4.2	10.7		
	TOTAL	775	6.9	2.0	6.6	5.5	7.9	4.2	10.5		
Month 3	A	357	6.9	1.8	6.8	5.6	8.0	4.1	10.2	A.B	0.641
	B	357	7.0	2.0	6.7	5.6	8.3	4.1	10.6		
	TOTAL	714	6.9	1.9	6.8	5.6	8.1	4.1	10.5		
Month 6	A	292	6.7	2.1	6.4	5.3	7.8	3.8	10.6	A.B	0.092
	B	303	6.9	1.9	6.7	5.6	8.0	4.2	10.5		
	TOTAL	595	6.8	2.0	6.6	5.4	7.9	4.0	10.5		
Month 9	A	166	7.0	1.9	6.8	5.6	8.3	4.2	10.3	A.B	0.517
	B	166	6.9	2.0	6.7	5.3	8.3	4.1	10.1		
	TOTAL	332	7.0	2.0	6.7	5.5	8.3	4.1	10.3		
Month 12	A	35	6.9	2.0	6.6	5.6	8.5	4.0	9.9	A.B	0.870
	B	32	6.8	2.0	6.5	5.5	7.9	4.4	11.1		
	TOTAL	67	6.9	2.0	6.5	5.6	8.0	4.4	10.0		

White Blood Cell Count: Above Upper Limit of Normal (11 x10ˆ9/L)

See Figure HEM–1 on page 58.

			Value					
		Total	Yes		No			P-
	Trt	Subjs	N	%	N	%	Contrast	Value
Baseline	A	388	10	2.58	378	97.42	A.B	0.661
	B	387	12	3.10	375	96.90		
	TOTAL	775	22	2.84	753	97.16		
Month 3	A	357	6	1.68	351	98.32	A.B	0.070
	B	357	14	3.92	343	96.08		
	TOTAL	714	20	2.80	694	97.20		
Month 6	A	292	11	3.77	281	96.23	A.B	0.434
	B	303	8	2.64	295	97.36		
	TOTAL	595	19	3.19	576	96.81		
Month 9	A	166	5	3.01	161	96.99	A.B	0.759
	B	166	6	3.61	160	96.39		
	TOTAL	332	11	3.31	321	96.69		
Month 12	A	35	1	2.86	34	97.14	A.B	0.502
	B	32	2	6.25	30	93.75		
	TOTAL	67	3	4.48	64	95.52		

White Blood Cell Count: Below Lower Limit of Normal (4.5 x10ˆ9/L)

See Figure HEM–1 on page 58.

			Value					
		Total	Yes		No			P-
	Trt	Subjs	N	%	N	%	Contrast	Value
Baseline	A	388	34	8.76	354	91.24	A.B	0.609
	B	387	30	7.75	357	92.25		
	TOTAL	775	64	8.26	711	91.74		
Month 3	A	357	32	8.96	325	91.04	A.B	0.497
	B	357	27	7.56	330	92.44		
	TOTAL	714	59	8.26	655	91.74		
Month 6	A	292	31	10.62	261	89.38	A.B	0.256
	B	303	24	7.92	279	92.08		
	TOTAL	595	55	9.24	540	90.76		
Month 9	A	166	13	7.83	153	92.17	A.B	0.841
	B	166	14	8.43	152	91.57		
	TOTAL	332	27	8.13	305	91.87		
Month 12	A	35	3	8.57	32	91.43	A.B	0.908
	B	32	3	9.38	29	90.62		
	TOTAL	67	6	8.96	61	91.04		

White Blood Cell Count: Absolute Change from Baseline (x10ˆ9/L)

See Figure HEM–1 on page 58.

		Total		Std						P-
	Trt	Subjs	Mean	Dev	Median	Q1	Q3	P5	P95	Contrast	Value
Month 3	A	357	-0.01	2.58	-0.10	-1.80	1.70	-4.30	4.70	A.B	0.198
	B	357	0.13	2.79	0.30	-1.50	1.90	-5.00	4.90		
	TOTAL	714	0.06	2.69	0.10	-1.70	1.80	-4.50	4.70		
Month 6	A	292	-0.13	2.81	-0.10	-1.95	1.50	-4.60	4.80	A.B	0.104
	B	303	0.17	2.68	0.20	-1.40	1.70	-4.60	4.40		
	TOTAL	595	0.02	2.75	0.10	-1.60	1.60	-4.60	4.60		

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

See Figure HEM–1 on page 58.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 9	A	166	0.13	2.76	0.10	-1.50	1.80	-4.40	4.60	A.B	0.898
	B	166	0.08	2.90	0.20	-1.80	1.90	-4.10	5.30		
	TOTAL	332	0.10	2.83	0.15	-1.60	1.90	-4.30	5.00		
Month 12	A	35	0.06	2.52	-0.10	-1.50	1.30	-3.70	4.80	A.B	0.716
	B	32	-0.13	2.91	-0.30	-1.45	1.50	-4.90	3.90		
	TOTAL	67	-0.03	2.70	-0.20	-1.50	1.40	-3.70	3.90		

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 60.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	386	122.1	14.0	122.4	113.2	131.5	99.1	144.7	A.B	0.402
	B	387	123.3	14.5	122.4	113.5	132.8	100.5	147.8		
	TOTAL	773	122.7	14.2	122.4	113.4	132.2	99.4	145.6		
Month 3	A	357	122.2	14.6	121.9	113.8	131.6	97.8	150.6	A.B	0.728
	B	357	121.7	14.3	122.5	111.5	131.4	97.1	144.8		
	TOTAL	714	122.0	14.5	122.3	112.4	131.5	97.4	146.3		
Month 6	A	292	123.0	13.2	122.9	114.0	130.4	103.6	146.6	A.B	0.266
	B	296	121.7	13.9	120.5	112.9	130.9	99.8	145.8		
	TOTAL	588	122.4	13.6	121.7	113.8	130.8	100.9	146.0		
Month 9	A	162	120.3	12.2	120.5	110.4	127.3	101.4	142.9	A.B	0.821
	B	155	120.1	14.0	120.2	111.0	129.8	94.5	141.9		
	TOTAL	317	120.2	13.1	120.3	110.7	128.7	98.8	142.9		
Month 12	A	36	125.5	14.0	124.2	112.5	137.9	107.1	149.6	A.B	0.084
	B	39	120.0	16.5	118.0	108.5	128.9	93.7	161.8		
	TOTAL	75	122.6	15.5	119.6	109.9	133.4	101.7	153.9		

Systolic Blood Pressure: Elevations (>130 mmHg)

See Figure VIT–1 on page 60.

		Treatment Group							
		A		B		TOTAL			P-
	Value	N	%	N	%	N	%	Contrast	Value
Baseline	Total Subjs	386		387		773		A.B	0.713
	>150 mmHg	8	2.07	12	3.10	20	2.59		
	>140-150 mmHg	28	7.25	33	8.53	61	7.89		
	>130-140 mmHg	81	20.98	82	21.19	163	21.09		
Month 3	Total Subjs	357		357		714		A.B	0.070
	>150 mmHg	18	5.04	8	2.24	26	3.64		
	>140-150 mmHg	15	4.20	26	7.28	41	5.74		
	>130-140 mmHg	65	18.21	70	19.61	135	18.91		
Month 6	Total Subjs	292		296		588		A.B	0.975
	>150 mmHg	8	2.74	7	2.36	15	2.55		
	>140-150 mmHg	23	7.88	23	7.77	46	7.82		
	>130-140 mmHg	44	15.07	48	16.22	92	15.65		
Month 9	Total Subjs	162		155		317		A.B	0.557
	>150 mmHg	3	1.85	2	1.29	5	1.58		
	>140-150 mmHg	10	6.17	11	7.10	21	6.62		
	>130-140 mmHg	17	10.49	24	15.48	41	12.93		
Month 12	Total Subjs	36		39		75		A.B	0.048
	>150 mmHg	1	2.78	3	7.69	4	5.33		
	>140-150 mmHg	6	16.67	1	2.56	7	9.33		
	>130-140 mmHg	7	19.44	3	7.69	10	13.33		

Systolic Blood Pressure: Absolute Change from Baseline (mmHg)

See Figure VIT–1 on page 60.

		Total		Std							P-
	Trt	Subjs	Mean	Dev	Median	Q1	Q3	P5	P95	Contrast	Value
Month 3	A	355	-0.0	20.9	-0.6	-14.7	14.6	-36.7	35.9	A.B	0.295
	B	357	-1.7	19.9	-1.0	-15.8	11.4	-34.5	30.0		
	TOTAL	712	-0.9	20.4	-0.7	-15.3	12.6	-34.9	32.9		
Month 6	A	290	0.4	19.6	-0.8	-12.9	13.4	-31.4	33.1	A.B	0.130
	B	296	-2.0	19.4	-2.4	-14.9	11.9	-32.7	30.0		
	TOTAL	586	-0.8	19.5	-1.4	-14.1	13.1	-32.1	31.5		
Month 9	A	161	-2.2	18.3	-3.2	-14.0	9.9	-33.6	28.7	A.B	0.124
	B	155	-5.2	18.5	-5.0	-18.1	7.2	-36.9	27.7		
	TOTAL	316	-3.7	18.4	-4.0	-16.7	8.3	-34.3	28.7		
Month 12	A	35	1.5	17.9	2.7	-13.9	13.7	-25.5	28.8	A.B	0.113
	B	39	-5.0	20.0	-6.0	-16.1	5.1	-36.3	43.6		
	TOTAL	74	-1.9	19.2	-1.8	-15.3	8.0	-33.8	28.8		

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

See Figure VIT–1 on page 60.

		Treatment Group							
		A		B		TOTAL			P-
	Value	N	%	N	%	N	%	Contrast	Value
Month 3	Total Subjs	357		357		714		A.B	0.568
	>15 mmHg	87	24.37	72	20.17	159	22.27		
	>10-15 mmHg	20	5.60	24	6.72	44	6.16		
	>6-10 mmHg	30	8.40	32	8.96	62	8.68		

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

See Figure VIT–1 on page 60.

		Treatment Group							
		A		B		TOTAL			P-
	Value	N	%	N	%	N	%	Contrast	Value
Month 6	Total Subjs	292		296		588		A.B	0.388
	>15 mmHg	69	23.63	55	18.58	124	21.09		
	>10-15 mmHg	18	6.16	23	7.77	41	6.97		
	>6-10 mmHg	30	10.27	27	9.12	57	9.69		
Month 9	Total Subjs	162		155		317		A.B	0.261
	>15 mmHg	26	16.05	14	9.03	40	12.62		
	>10-15 mmHg	14	8.64	12	7.74	26	8.20		
	>6-10 mmHg	12	7.41	15	9.68	27	8.52		
Month 12	Total Subjs	36		39		75		A.B	0.450
	>15 mmHg	8	22.22	4	10.26	12	16.00		
	>10-15 mmHg	3	8.33	2	5.13	5	6.67		
	>6-10 mmHg	1	2.78	2	5.13	3	4.00		

Table Set VIT–2

Diastolic Blood Pressure: Measurements at Scheduled Visits (mmHg)

See Figure VIT–2 on page 61.

		Total		Std							P-
	Trt	Subjs	Mean	Dev	Median	Q1	Q3	P5	P95	Contrast	Value
Baseline	A	386	72.2	10.2	72.1	65.7	78.6	54.5	89.5	A.B	0.570
	B	387	72.6	9.7	73.4	66.4	78.8	56.3	87.9		
	TOTAL	773	72.4	9.9	72.6	66.4	78.7	55.4	88.6		
Month 3	A	357	71.7	10.1	72.3	65.1	78.9	54.0	87.1	A.B	0.218
	B	357	72.7	9.7	73.2	65.8	78.6	56.4	88.0		
	TOTAL	714	72.2	9.9	72.7	65.4	78.7	55.1	87.9		
Month 6	A	292	72.5	9.7	72.0	66.2	79.4	56.2	88.7	A.B	0.897
	B	296	72.4	10.6	72.1	65.8	79.4	54.4	88.9		
	TOTAL	588	72.5	10.2	72.0	66.0	79.4	54.9	88.7		
Month 9	A	162	72.5	10.1	72.6	65.7	79.4	55.6	88.4	A.B	0.717
	B	155	72.6	9.3	73.4	66.8	79.5	56.2	86.8		
	TOTAL	317	72.5	9.7	73.0	66.4	79.4	55.6	87.9		
Month 12	A	36	72.4	11.5	73.1	63.8	80.9	54.3	95.0	A.B	0.567
	B	39	70.8	11.4	70.6	64.2	77.8	50.4	94.9		
	TOTAL	75	71.5	11.4	72.9	64.2	78.6	52.3	94.9		

Diastolic Blood Pressure: Elevations (>80 mmHg)

See Figure VIT–2 on page 61.

		Treatment Group							
		A		B		TOTAL			P-
	Value	N	%	N	%	N	%	Contrast	Value
Baseline	Total Subjs	386		387		773		A.B	0.981
	>90 mmHg	16	4.15	14	3.62	30	3.88		
	>85-90 mmHg	26	6.74	25	6.46	51	6.60		
	>80-85 mmHg	38	9.84	38	9.82	76	9.83		
Month 3	Total Subjs	357		357		714		A.B	0.304
	>90 mmHg	10	2.80	13	3.64	23	3.22		
	>85-90 mmHg	17	4.76	26	7.28	43	6.02		
	>80-85 mmHg	50	14.01	39	10.92	89	12.46		

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Diastolic Blood Pressure: Elevations (>80 mmHg)

See Figure VIT–2 on page 61.

		Treatment Group							
		A		B		TOTAL			P-
	Value	N	%	N	%	N	%	Contrast	Value
Month 6	Total Subjs	292		296		588		A.B	0.807
	>90 mmHg	14	4.79	12	4.05	26	4.42		
	>85-90 mmHg	19	6.51	24	8.11	43	7.31		
	>80-85 mmHg	30	10.27	34	11.49	64	10.88		
Month 9	Total Subjs	162		155		317		A.B	0.672
	>90 mmHg	8	4.94	4	2.58	12	3.79		
	>85-90 mmHg	7	4.32	7	4.52	14	4.42		
	>80-85 mmHg	19	11.73	22	14.19	41	12.93		
Month 12	Total Subjs	36		39		75		A.B	0.363
	>90 mmHg	2	5.56	2	5.13	4	5.33		
	>85-90 mmHg	3	8.33	2	5.13	5	6.67		
	>80-85 mmHg	6	16.67	2	5.13	8	10.67		

Diastolic Blood Pressure: Absolute Change from Baseline (mmHg)

See Figure VIT–2 on page 61.

		Total		Std							P-
	Trt	Subjs	Mean	Dev	Median	Q1	Q3	P5	P95	Contrast	Value
Month 3	A	355	-0.8	14.9	-1.6	-9.9	9.8	-25.3	25.0	A.B	0.376
	B	357	-0.0	13.4	0.2	-8.6	8.2	-23.3	22.8		
	TOTAL	712	-0.4	14.1	-0.7	-9.5	8.6	-24.2	24.0		
Month 6	A	290	0.2	13.5	0.6	-9.4	9.1	-22.1	22.9	A.B	0.328
	B	296	-0.9	14.3	-1.0	-10.5	8.8	-24.4	23.8		
	TOTAL	586	-0.4	13.9	-0.1	-10.0	9.0	-23.1	23.5		
Month 9	A	161	0.6	14.3	0.3	-9.3	11.4	-22.2	25.3	A.B	0.517
	B	155	-0.8	14.7	-0.7	-11.2	10.0	-24.1	24.1		
	TOTAL	316	-0.1	14.5	-0.2	-10.0	10.4	-23.1	25.1		
Month 12	A	35	-0.4	13.8	-0.3	-9.1	10.9	-26.3	24.1	A.B	0.534
	B	39	-2.7	15.4	0.1	-13.7	9.5	-30.8	21.7		
	TOTAL	74	-1.6	14.6	-0.1	-13.0	10.0	-26.3	21.7		

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

See Figure VIT–2 on page 61.

		Treatment Group							
		A		B		TOTAL			P-
	Value	N	%	N	%	N	%	Contrast	Value
Month 3	Total Subjs	357		357		714		A.B	0.315
	>12 mmHg	68	19.05	57	15.97	125	17.51		
	>8-12 mmHg	28	7.84	36	10.08	64	8.96		
	>4-8 mmHg	29	8.12	39	10.92	68	9.52		
Month 6	Total Subjs	292		296		588		A.B	0.100
	>12 mmHg	57	19.52	54	18.24	111	18.88		
	>8-12 mmHg	24	8.22	28	9.46	52	8.84		
	>4-8 mmHg	34	11.64	18	6.08	52	8.84		
Month 9	Total Subjs	162		155		317		A.B	0.648
	>12 mmHg	37	22.84	32	20.65	69	21.77		
	>8-12 mmHg	14	8.64	11	7.10	25	7.89		
	>4-8 mmHg	10	6.17	15	9.68	25	7.89		

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

See Figure VIT–2 on page 61.

		Treatment Group							
		A		B		TOTAL			P-
	Value	N	%	N	%	N	%	Contrast	Value
Month 12	Total Subjs	36		39		75		A.B	0.959
	>12 mmHg	7	19.44	6	15.38	13	17.33		
	>8-12 mmHg	5	13.89	5	12.82	10	13.33		
	>4-8 mmHg	3	8.33	3	7.69	6	8.00		

Table Set VIT–3

Weight: Measurements at Scheduled Visits (kg)

See Figure VIT–3 on page 62.

		Total		Std							P-
	Trt	Subjs	Mean	Dev	Median	Q1	Q3	P5	P95	Contrast	Value
Baseline	A	386	87.3	17.2	87.7	75.9	99.2	59.5	115.8	A.B	0.695
	B	387	86.8	16.3	86.2	76.3	98.7	59.5	111.7		
	TOTAL	773	87.1	16.8	86.8	76.0	98.9	59.5	115.0		
Month 3	A	357	87.7	17.1	87.2	76.8	100.0	58.7	115.7	A.B	0.595
	B	357	87.5	17.3	87.1	76.0	98.1	61.0	115.9		
	TOTAL	714	87.6	17.2	87.2	76.3	98.7	60.4	115.7		
Month 6	A	292	88.1	16.1	87.9	77.2	99.2	60.8	114.3	A.B	0.127
	B	296	85.8	17.2	85.6	74.9	97.4	56.6	114.3		
	TOTAL	588	86.9	16.7	86.7	76.3	98.2	59.5	114.3		
Month 9	A	162	87.0	18.4	89.0	73.8	99.3	54.9	115.5	A.B	0.884
	B	155	86.9	15.5	89.1	75.8	98.0	60.1	110.4		
	TOTAL	317	86.9	17.0	89.0	75.2	98.9	56.9	112.1		
Month 12	A	36	85.5	16.6	86.9	75.8	99.1	60.2	111.4	A.B	0.924
	B	39	86.8	18.3	85.3	75.2	97.9	52.6	123.3		
	TOTAL	75	86.2	17.4	85.3	75.7	99.0	57.5	118.0		

Weight: Absolute Change from Baseline (kg)

See Figure VIT–3 on page 62.

		Total		Std							P-
	Trt	Subjs	Mean	Dev	Median	Q1	Q3	P5	P95	Contrast	Value
Month 3	A	355	0.2	23.9	0.8	-16.2	17.0	-39.9	37.7	A.B	0.873
	B	357	0.9	24.0	-0.3	-16.2	17.7	-32.3	43.3		
	TOTAL	712	0.5	24.0	0.5	-16.2	17.3	-35.8	40.8		
Month 6	A	290	0.0	23.1	0.9	-14.2	15.7	-40.5	40.1	A.B	0.472
	B	296	-0.9	23.1	-2.7	-15.0	14.7	-32.9	39.0		
	TOTAL	586	-0.4	23.1	-1.6	-14.3	15.4	-38.6	39.1		
Month 9	A	161	-0.4	24.9	-0.1	-19.8	18.1	-40.5	35.0	A.B	0.712
	B	155	0.3	22.1	1.9	-14.5	17.3	-42.7	32.7		
	TOTAL	316	-0.1	23.5	1.5	-16.1	17.5	-41.5	34.4		
Month 12	A	35	-4.0	23.1	-4.7	-18.6	7.7	-44.5	36.3	A.B	0.577
	B	39	-1.6	28.2	-6.3	-24.2	20.0	-49.9	40.0		
	TOTAL	74	-2.8	25.8	-5.5	-18.6	13.6	-48.1	38.6		

Weight: Percent Change from Baseline (%)

See Figure VIT–3 on page 62.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	355	4.3	29.6	1.0	-16.6	22.4	-36.2	57.1	A.B	0.811
	B	357	5.6	34.9	-0.4	-17.5	22.6	-32.9	62.2		
	TOTAL	712	5.0	32.3	0.7	-17.1	22.5	-34.2	60.2		
Month 6	A	290	4.0	29.0	0.9	-15.1	19.3	-35.5	62.8	A.B	0.427
	B	296	2.6	29.9	-3.3	-16.4	17.4	-35.3	54.0		
	TOTAL	586	3.3	29.4	-1.8	-15.8	18.3	-35.3	58.6		
Month 9	A	161	3.8	32.4	-0.1	-20.6	20.4	-39.0	60.5	A.B	0.649
	B	155	3.8	27.1	2.5	-15.4	21.1	-41.3	50.7		
	TOTAL	316	3.8	29.9	1.6	-17.1	21.1	-39.2	56.2		
Month 12	A	35	-0.8	31.9	-6.8	-19.7	8.9	-39.3	55.1	A.B	0.541
	B	39	2.7	34.8	-7.5	-22.7	26.9	-50.4	55.2		
	TOTAL	74	1.1	33.3	-6.9	-19.7	16.7	-42.5	55.1		

5.2 ECG

Table Set ECG–1

ECG Interpretation: ECG Interpretation

See Figure ECG–1 on page 63.

		Treatment Group							
		A		B		TOTAL			P-
	Value	N	%	N	%	N	%	Contrast	Value
Baseline	Total Subjs	386		387		773		A.B	0.448
	Abnormal, clinically signficant	64	16.58	66	17.05	130	16.82		
	Abnormal, not clinically significant	33	8.55	42	10.85	75	9.70		
	Normal	289	74.87	279	72.09	568	73.48		
Month 3	Total Subjs	357		357		714		A.B	0.283
	Abnormal, clinically signficant	59	16.53	60	16.81	119	16.67		
	Abnormal, not clinically significant	27	7.56	41	11.48	68	9.52		
	Normal	271	75.91	256	71.71	527	73.81		
Month 6	Total Subjs	292		296		588		A.B	0.339
	Abnormal, clinically signficant	45	15.41	36	12.16	81	13.78		
	Abnormal, not clinically significant	32	10.96	33	11.15	65	11.05		
	Normal	215	73.63	227	76.69	442	75.17		
Month 9	Total Subjs	162		155		317		A.B	0.379
	Abnormal, clinically signficant	27	16.67	20	12.90	47	14.83		
	Abnormal, not clinically significant	8	4.94	23	14.84	31	9.78		
	Normal	127	78.40	112	72.26	239	75.39		
Month 12	Total Subjs	36		39		75		A.B	0.004
	Abnormal, clinically signficant	11	30.56	3	7.69	14	18.67		
	Abnormal, not clinically significant	4	11.11	2	5.13	6	8.00		
	Normal	21	58.33	34	87.18	55	73.33		

ECG Interpretation: Change from Baseline in ECG Interpretation

See Figure ECG–1 on page 63.

		Treatment Group							
		A		B		TOTAL			P-
	Value	N	%	N	%	N	%	Contrast	Value
Month 3	Total Subjs	355		357		712		A.B	0.773
	Worse	75	21.13	78	21.85	153	21.49		
	Same	207	58.31	208	58.26	415	58.29		
	Better	73	20.56	71	19.89	144	20.22		
Month 6	Total Subjs	290		296		586		A.B	0.480
	Worse	62	21.38	52	17.57	114	19.45		
	Same	168	57.93	183	61.82	351	59.90		
	Better	60	20.69	61	20.61	121	20.65		
Month 9	Total Subjs	161		155		316		A.B	0.885
	Worse	29	18.01	31	20.00	60	18.99		
	Same	96	59.63	88	56.77	184	58.23		
	Better	36	22.36	36	23.23	72	22.78		
Month 12	Total Subjs	35		39		74		A.B	0.021
	Worse	15	42.86	5	12.82	20	27.03		
	Same	13	37.14	23	58.97	36	48.65		
	Better	7	20.00	11	28.21	18	24.32		

Table Set ECG–2

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

See Figure ECG–2 on page 64.

		Total		Std							P-
	Trt	Subjs	Mean	Dev	Median	Q1	Q3	P5	P95	Contrast	Value
Baseline	A	386	174.3	29.8	175.8	154.1	192.4	121.4	222.4	A.B	0.895
	B	387	174.4	32.2	174.6	153.2	197.1	116.5	226.9		
	TOTAL	773	174.3	31.0	175.0	153.6	194.1	118.4	224.7		
Month 3	A	357	175.6	28.3	174.1	157.0	195.5	129.9	225.1	A.B	0.463
	B	357	173.7	29.4	174.6	154.3	192.3	123.7	222.7		
	TOTAL	714	174.6	28.9	174.3	156.0	193.5	126.8	223.1		
Month 6	A	292	173.9	31.3	175.0	155.0	193.9	123.2	224.9	A.B	0.064
	B	296	169.8	31.0	168.1	150.1	189.1	123.3	222.1		
	TOTAL	588	171.9	31.2	169.7	153.2	191.4	123.3	224.1		
Month 9	A	162	175.3	29.2	175.8	158.2	194.2	126.4	222.2	A.B	0.204
	B	155	171.4	32.0	171.1	151.5	192.4	118.1	229.1		
	TOTAL	317	173.4	30.6	173.7	155.9	193.5	120.2	224.7		
Month 12	A	36	175.4	29.8	182.3	151.1	201.4	124.0	213.6	A.B	0.181
	B	39	167.6	34.1	166.0	148.9	182.4	116.0	217.7		
	TOTAL	75	171.3	32.1	170.6	148.9	199.5	120.3	213.6		

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

See Figure ECG–2 on page 64.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	355	0.8	43.7	0.5	-25.6	27.8	-67.5	74.7	A.B	0.673
	B	357	-0.4	43.3	-3.1	-28.2	28.7	-77.0	75.6		
	TOTAL	712	0.2	43.5	-0.7	-27.4	28.2	-69.5	75.2		
Month 6	A	290	-1.6	42.1	-1.3	-31.4	28.6	-73.9	69.5	A.B	0.323
	B	296	-4.9	45.3	-5.5	-36.8	23.9	-79.1	73.2		
	TOTAL	586	-3.2	43.8	-3.3	-33.5	26.1	-75.6	70.0		
Month 9	A	161	-0.9	39.7	0.3	-27.6	22.3	-71.1	59.3	A.B	0.519
	B	155	-3.7	45.7	-3.1	-35.8	27.0	-77.4	67.9		
	TOTAL	316	-2.2	42.7	-1.0	-30.3	24.7	-76.4	65.8		
Month 12	A	35	-3.5	43.0	1.1	-36.3	27.9	-87.7	58.3	A.B	0.355
	B	39	-9.5	46.2	-13.8	-28.4	19.1	-93.1	82.0		
	TOTAL	74	-6.6	44.5	-6.7	-28.4	23.6	-87.7	76.1		

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

See Figure ECG–2 on page 64.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	386	100.4	21.6	100.5	88.1	113.7	62.1	136.2	A.B	0.436
	B	387	102.3	21.7	101.9	87.8	117.2	67.9	138.7		
	TOTAL	773	101.3	21.6	101.2	87.9	115.5	63.8	137.8		
Month 3	A	357	101.0	21.0	99.9	87.0	114.5	67.5	138.5	A.B	0.636
	B	357	99.9	21.9	100.0	86.1	114.6	61.2	134.8		
	TOTAL	714	100.4	21.5	100.0	86.7	114.6	64.4	136.5		
Month 6	A	292	100.0	21.3	101.8	85.8	115.4	62.6	132.2	A.B	0.474
	B	296	101.8	22.0	101.3	87.2	115.9	63.4	137.2		
	TOTAL	588	101.0	21.7	101.7	86.6	115.5	62.7	135.6		
Month 9	A	162	100.0	20.6	100.7	86.9	114.3	65.3	133.0	A.B	0.783
	B	155	99.9	19.6	100.2	84.4	112.7	70.0	135.4		
	TOTAL	317	99.9	20.1	100.2	85.7	113.1	68.0	133.5		
Month 12	A	36	104.4	19.3	102.8	90.0	119.7	68.1	134.0	A.B	0.611
	B	39	101.8	21.5	101.4	84.6	119.5	54.9	135.0		
	TOTAL	75	103.1	20.4	101.9	88.2	119.5	66.7	134.0		

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

See Figure ECG–2 on page 64.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	355	0.4	28.8	1.1	-21.2	20.1	-47.3	49.2	A.B	0.354
	B	357	-2.4	31.0	-0.7	-20.6	19.1	-56.6	47.3		
	TOTAL	712	-1.0	29.9	0.4	-20.7	19.4	-51.4	47.6		
Month 6	A	290	-0.8	29.6	-2.7	-21.7	19.8	-47.2	48.5	A.B	0.673
	B	296	-0.4	30.8	-0.8	-20.6	19.4	-50.8	46.9		
	TOTAL	586	-0.6	30.2	-1.3	-21.1	19.8	-49.3	48.2		
Month 9	A	161	0.7	32.4	2.6	-20.0	21.1	-50.3	53.2	A.B	0.054
	B	155	-5.7	29.8	-7.1	-28.2	16.4	-53.5	44.5		
	TOTAL	316	-2.4	31.3	-1.6	-24.6	18.0	-53.5	52.4		
Month 12	A	35	4.3	30.8	7.4	-15.1	22.9	-47.3	53.8	A.B	0.901
	B	39	1.5	37.7	5.7	-29.3	29.2	-68.5	59.2		
	TOTAL	74	2.8	34.4	6.7	-22.5	27.7	-51.3	56.7		

Table Set ECG–3

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

See Figure ECG–3 on page 65.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	386	977.5	135.9	974.0	891.4	1073.0	749.9	1207.1	A.B	0.358
	B	387	983.5	138.5	987.0	904.7	1075.2	746.4	1209.4		
	TOTAL	773	980.5	137.1	980.9	897.8	1073.0	746.7	1209.4		
Month 3	A	357	979.6	129.1	979.9	889.1	1073.1	753.3	1186.9	A.B	0.321
	B	357	986.7	135.2	993.9	893.1	1088.8	754.6	1195.1		
	TOTAL	714	983.1	132.1	985.5	891.0	1080.9	754.6	1186.9		
Month 6	A	292	968.4	135.1	966.2	876.7	1045.5	736.8	1213.5	A.B	0.057
	B	296	986.8	136.6	993.5	887.6	1090.7	757.7	1203.1		
	TOTAL	588	977.7	136.0	978.8	881.4	1069.8	746.9	1205.0		
Month 9	A	162	985.6	155.5	987.1	867.6	1083.5	748.8	1240.8	A.B	0.713
	B	155	979.4	140.9	976.6	893.5	1072.2	774.3	1217.0		
	TOTAL	317	982.6	148.3	981.7	876.4	1075.8	755.6	1232.2		
Month 12	A	36	974.9	131.9	994.3	880.4	1052.1	735.4	1208.2	A.B	0.458
	B	39	1007.6	146.3	972.5	887.1	1104.5	770.5	1286.3		
	TOTAL	75	991.9	139.6	990.0	882.5	1082.0	770.5	1208.2		

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

See Figure ECG–3 on page 65.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	355	4.2	185.2	8.2	-128.8	112.6	-302.5	314.9	A.B	0.998
	B	357	0.2	193.2	7.5	-137.5	132.2	-339.0	301.6		
	TOTAL	712	2.2	189.1	7.7	-132.1	123.6	-312.9	311.4		
Month 6	A	290	-8.4	186.1	-12.3	-128.2	104.6	-287.9	293.8	A.B	0.461
	B	296	-3.2	191.0	0.1	-129.8	127.5	-336.7	301.1		
	TOTAL	586	-5.7	188.4	-2.8	-128.8	111.6	-313.1	297.1		
Month 9	A	161	3.0	199.8	17.7	-133.4	114.3	-333.3	363.8	A.B	0.683
	B	155	-6.4	201.7	-4.2	-139.4	105.2	-344.3	331.7		
	TOTAL	316	-1.6	200.5	5.9	-135.6	113.8	-344.3	345.0		
Month 12	A	35	-11.7	204.8	-30.1	-141.7	191.8	-382.2	316.0	A.B	0.717
	B	39	25.1	236.1	-15.8	-142.2	165.6	-302.5	452.3		
	TOTAL	74	7.7	221.1	-18.4	-141.7	165.6	-347.3	380.2		

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

See Figure ECG–3 on page 65.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Baseline	A	386	406.4	29.6	404.7	387.4	426.0	354.7	455.7	A.B	0.323
	B	387	408.2	32.5	409.0	386.8	430.3	355.2	461.3		
	TOTAL	773	407.3	31.0	406.9	387.3	427.5	354.9	459.7		
Month 3	A	357	410.5	32.1	410.4	390.3	430.5	359.2	466.9	A.B	0.676
	B	357	409.7	31.2	409.9	387.6	430.1	362.1	463.4		
	TOTAL	714	410.1	31.7	410.1	389.1	430.3	360.1	466.4		

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

See Figure ECG–3 on page 65.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 6	A	292	409.4	31.0	409.1	389.5	431.0	355.7	461.1	A.B	0.834
	B	296	408.6	31.9	410.5	387.1	432.5	353.1	456.9		
	TOTAL	588	409.0	31.4	409.7	388.4	431.5	355.6	458.4		
Month 9	A	162	405.9	35.1	408.4	381.1	426.8	351.2	465.1	A.B	0.835
	B	155	405.5	32.4	406.0	382.7	427.0	350.9	454.3		
	TOTAL	317	405.7	33.8	407.3	381.9	426.8	350.9	463.5		
Month 12	A	36	414.9	29.1	410.6	394.7	431.8	372.0	463.4	A.B	0.511
	B	39	408.6	27.7	409.9	393.8	423.5	355.6	453.3		
	TOTAL	75	411.6	28.4	409.9	393.9	430.7	364.6	459.3		

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

See Figure ECG–3 on page 65.

	Trt	Total Subjs	Mean	Std Dev	Median	Q1	Q3	P5	P95	Contrast	P-Value
Month 3	A	355	3.2	44.1	3.0	-25.7	34.1	-71.2	77.6	A.B	0.328
	B	357	1.0	43.4	-2.7	-28.8	30.6	-70.3	77.3		
	TOTAL	712	2.1	43.7	-0.0	-26.7	31.7	-71.0	77.3		
Month 6	A	290	2.4	40.4	2.0	-26.0	31.1	-61.9	66.0	A.B	0.194
	B	296	-1.1	45.3	-4.3	-31.9	30.8	-68.2	79.2		
	TOTAL	586	0.6	42.9	0.2	-29.8	31.1	-66.4	72.0		
Month 9	A	161	-0.6	43.5	-0.9	-30.0	29.8	-70.7	60.4	A.B	0.182
	B	155	-6.8	43.9	-8.8	-37.6	21.9	-75.6	62.8		
	TOTAL	316	-3.6	43.7	-4.6	-32.5	27.8	-73.7	62.8		
Month 12	A	35	6.0	34.2	6.6	-18.0	28.3	-40.4	64.3	A.B	0.207
	B	39	-5.8	41.2	-11.5	-31.7	18.9	-97.8	73.0		
	TOTAL	74	-0.2	38.3	-1.4	-22.4	25.1	-62.1	64.3		

Table Set ECG–4

Maximum QTc (Fridericia) Intervals, Categorized: Maximum Value > 450 msec during Follow-up

See Figure ECG–4 on page 66.

		Value							
	Total	>500 ms		>480 - 500 ms		>450 - 480 ms		Contrast	P-Value
Trt	Subjs	N	%	N	%	N	%		
A	357	2	0.56	11	3.08	70	19.61	A.B	0.343
B	357	3	0.84	6	1.68	64	17.93		
TOTAL	714	5	0.70	17	2.38	134	18.77		

Maximum QTc (Fridericia) Intervals, Categorized: Greatest Increase from Baseline > 30 msec

See Figure ECG–4 on page 66.

		Value					
	Total	>60 ms		>30 - 60 ms		Contrast	P-Value
Trt	Subjs	N	%	N	%		
A	355	64	18.03	87	24.51	A.B	0.486
B	357	61	17.09	81	22.69		
TOTAL	712	125	17.56	168	23.60		

5.3 Concomitant Medications

Table Set CONMEDS–1

Standard of Care Medications: By Time of First Reported Use

See Figure CONMEDS–1 on page 67.

		Treatment Group							
		A		B		TOTAL			P-
	Value	N	%	N	%	N	%	Contrast	Value
Statin therapy	Total Subjs	388		387		775		A.B	0.128
	Reported at baseline	184	47.42	203	52.45	387	49.94		
	Added after randomization	40	10.31	43	11.11	83	10.71		
	Not reported	164	42.27	141	36.43	305	39.35		
Aspirin	Total Subjs	388		387		775		A.B	0.050
	Reported at baseline	178	45.88	199	51.42	377	48.65		
	Added after randomization	17	4.38	22	5.68	39	5.03		
	Not reported	193	49.74	166	42.89	359	46.32		
Beta-blocker	Total Subjs	388		387		775		A.B	0.496
	Reported at baseline	158	40.72	159	41.09	317	40.90		
	Added after randomization	43	11.08	35	9.04	78	10.06		
	Not reported	187	48.20	193	49.87	380	49.03		
ACE inhibitor	Total Subjs	388		387		775		A.B	0.297
	Reported at baseline	206	53.09	229	59.17	435	56.13		
	Added after randomization	45	11.60	41	10.59	86	11.10		
	Not reported	137	35.31	117	30.23	254	32.77		
Angiotensin II receptor blocker	Total Subjs	388		387		775		A.B	0.135
	Reported at baseline	134	34.54	147	37.98	281	36.26		
	Added after randomization	18	4.64	24	6.20	42	5.42		
	Not reported	236	60.82	216	55.81	452	58.32		

Chapter 6

Study Endpoints

6.1 Study Endpoint Events

Table Set ENDPT–1

Primary and Other Study Endpoints: Primary Endpoint Events

See Figure ENDPT–1 on page 69.

			Value			
			Yes			
	Trt	Total Subjs	N	%	Contrast	P-Value
Major Adverse Cardiovascular Events (MACE)	A	388	72	18.56	A.B	0.018
	B	387	48	12.40		
	TOTAL	775	120	15.48		
Cardiovascular Death	A	388	56	14.43	A.B	0.014
	B	387	34	8.79		
	TOTAL	775	90	11.61		
Non-fatal Myocardial Infarction	A	388	16	4.12	A.B	0.445
	B	387	12	3.10		
	TOTAL	775	28	3.61		
Non-fatal Stroke	A	388	6	1.55	A.B	0.527
	B	387	4	1.03		
	TOTAL	775	10	1.29		

Primary and Other Study Endpoints: Other Adjudicated Events

See Figure ENDPT–1 on page 69.

			Value			
			Yes			
	Trt	Total Subjs	N	%	Contrast	P-Value
Urgent Coronary Revascularisation	A	388	43	11.08	A.B	0.007
	B	387	22	5.68		
	TOTAL	775	65	8.39		
Any Coronary Revascularisation	A	388	48	12.37	A.B	0.438
	B	387	41	10.59		
	TOTAL	775	89	11.48		
Myocardial Infarction (fatal or non-fatal)	A	388	20	5.15	A.B	0.500
	B	387	16	4.13		
	TOTAL	775	36	4.65		

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Primary and Other Study Endpoints: Other Adjudicated Events

See Figure ENDPT–1 on page 69.

	Trt	Total Subjs	Value Yes N	Value Yes %	Contrast	P-Value
Stroke (fatal or non-fatal)	A	388	6	1.55	A.B	0.776
	B	387	7	1.81		
	TOTAL	775	13	1.68		
All-Cause Mortality	A	388	64	16.49	A.B	0.084
	B	387	47	12.14		
	TOTAL	775	111	14.32		
Major Coronary Events	A	388	83	21.39	A.B	0.001
	B	387	49	12.66		
	TOTAL	775	132	17.03		
Total Coronary Events	A	388	125	32.22	A.B	0.002
	B	387	87	22.48		
	TOTAL	775	212	27.35		
All-Cause Mortality, MI, or Stroke	A	388	80	20.62	A.B	0.080
	B	387	61	15.76		
	TOTAL	775	141	18.19		

6.2 All-Cause Mortality

Table Set ENDPT–3

All-Cause Mortality: Event Probability over Time

See Figure ENDPT–3 on page 71.

Months	Trt	nRisk	nEvents	% w/ Event	95% CI
0	A	388	0	0.0	(0.0, 0.0)
	B	387	0	0.0	(0.0, 0.0)
1	A	383	5	1.3	(0.2, 2.4)
	B	384	3	0.8	(0.0, 1.6)
2	A	377	11	2.8	(1.2, 4.5)
	B	376	11	2.8	(1.2, 4.5)
3	A	367	20	5.2	(2.9, 7.3)
	B	371	16	4.1	(2.1, 6.1)
4	A	352	29	7.5	(4.8, 10.1)
	B	363	20	5.2	(2.9, 7.4)
5	A	336	37	9.6	(6.6, 12.5)
	B	348	30	7.8	(5.1, 10.4)
6	A	318	42	11.0	(7.8, 14.1)
	B	332	32	8.3	(5.5, 11.1)
7	A	281	50	13.3	(9.8, 16.7)
	B	294	39	10.3	(7.2, 13.4)
8	A	238	55	15.0	(11.2, 18.6)
	B	251	42	11.4	(8.0, 14.6)
9	A	178	58	16.2	(12.2, 20.0)
	B	186	43	11.8	(8.4, 15.0)

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All-Cause Mortality: Event Probability over Time

See Figure ENDPT–3 on page 71.

Months	Trt	nRisk	nEvents	% w/ Event	95% CI
10	A	118	59	16.8	(12.7, 20.7)
	B	124	45	12.9	(9.2, 16.4)
11	A	73	60	17.7	(13.2, 21.9)
	B	77	46	13.8	(9.7, 17.7)
12	A	41	63	21.5	(15.4, 27.2)
	B	40	47	14.9	(10.3, 19.3)

Table Set DTH–1

Adjudicated Cause of Death: Type of Death

See Figure DTH–1 on page 73.

	Treatment Group					
	A		B		TOTAL	
Value	N	%	N	%	N	%
Total Subjs	388		387		775	
Cardiovascular	45	11.60	33	8.53	78	10.06
Non-Cardiovascular	3	0.77	5	1.29	8	1.03
Undetermined Cause	0	0.00	0	0.00	0	0.00
(unadjudicated)	16	4.12	9	2.33	25	3.23

Adjudicated Cause of Death: CV Causes

See Figure DTH–1 on page 73.

	Treatment Group					
	A		B		TOTAL	
Value	N	%	N	%	N	%
Total Subjs	388		387		775	
Acute MI	14	3.61	5	1.29	19	2.45
Sudden Cardiac Death	6	1.55	8	2.07	14	1.81
Heart Failure	11	2.84	6	1.55	17	2.19
Stroke	8	2.06	9	2.33	17	2.19
Cardiovascular Procedure	2	0.52	1	0.26	3	0.39
Cardiovascular Hemorrhage	2	0.52	1	0.26	3	0.39
Pulmonary Embolism	1	0.26	1	0.26	2	0.26
Other CV Causes	1	0.26	2	0.52	3	0.39

Adjudicated Cause of Death: Non-CV Causes

See Figure DTH–1 on page 73.

	Treatment Group					
	A		B		TOTAL	
Value	N	%	N	%	N	%
Total Subjs	388		387		775	
Pulmonary	0	0.00	0	0.00	0	0.00
Renal	0	0.00	1	0.26	1	0.13
Gastrointestinal	1	0.26	0	0.00	1	0.13
Hepatobiliary	0	0.00	2	0.52	2	0.26
Pancreatic	0	0.00	0	0.00	0	0.00
Infection (includes sepsis)	1	0.26	0	0.00	1	0.13
Inflammatory	0	0.00	1	0.26	1	0.13
Malignancy	0	0.00	1	0.26	1	0.13
Other Non-CV Causes	1	0.26	0	0.00	1	0.13

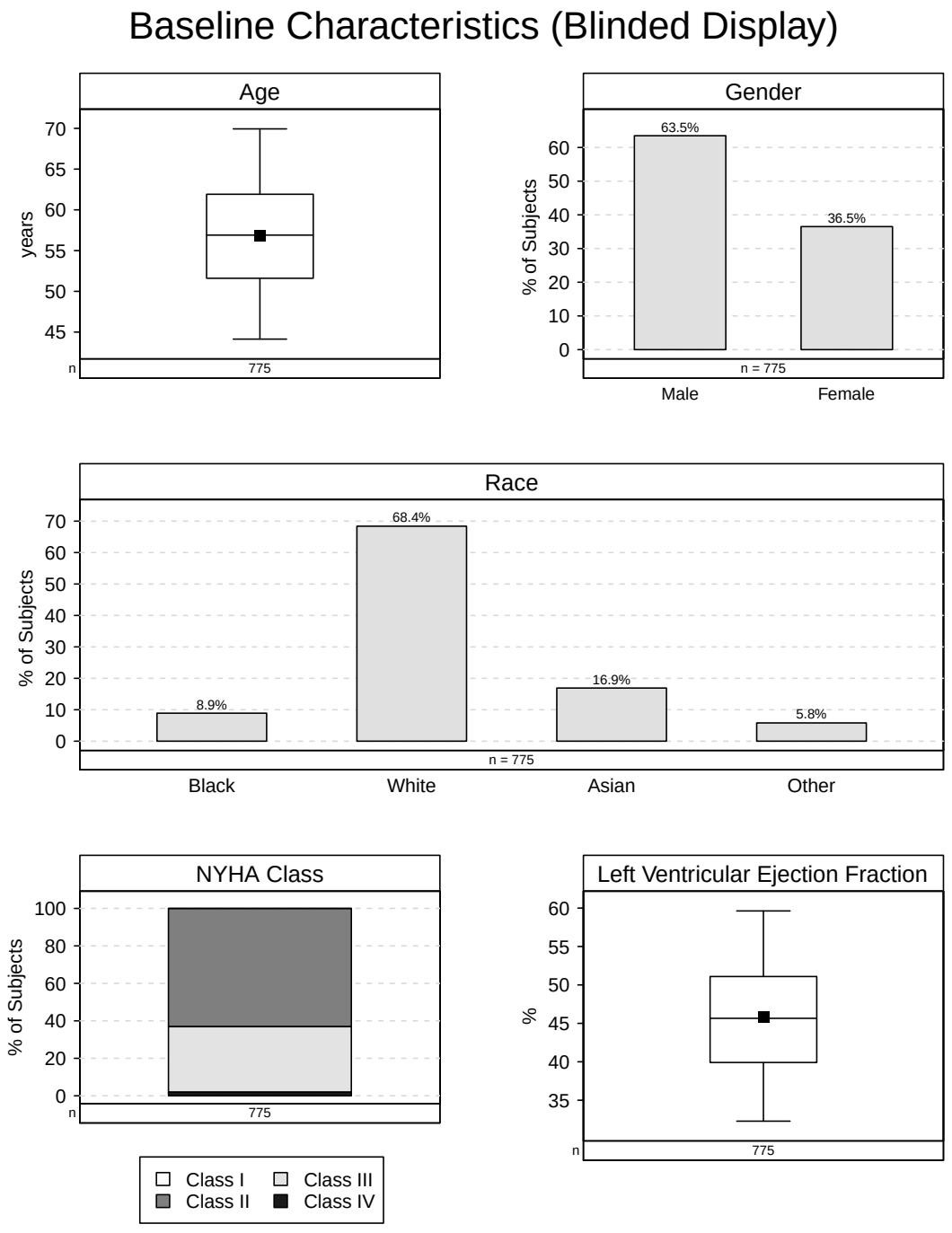
Part IV

Ancillary Material: Additional Sample Displays

Chapter A1

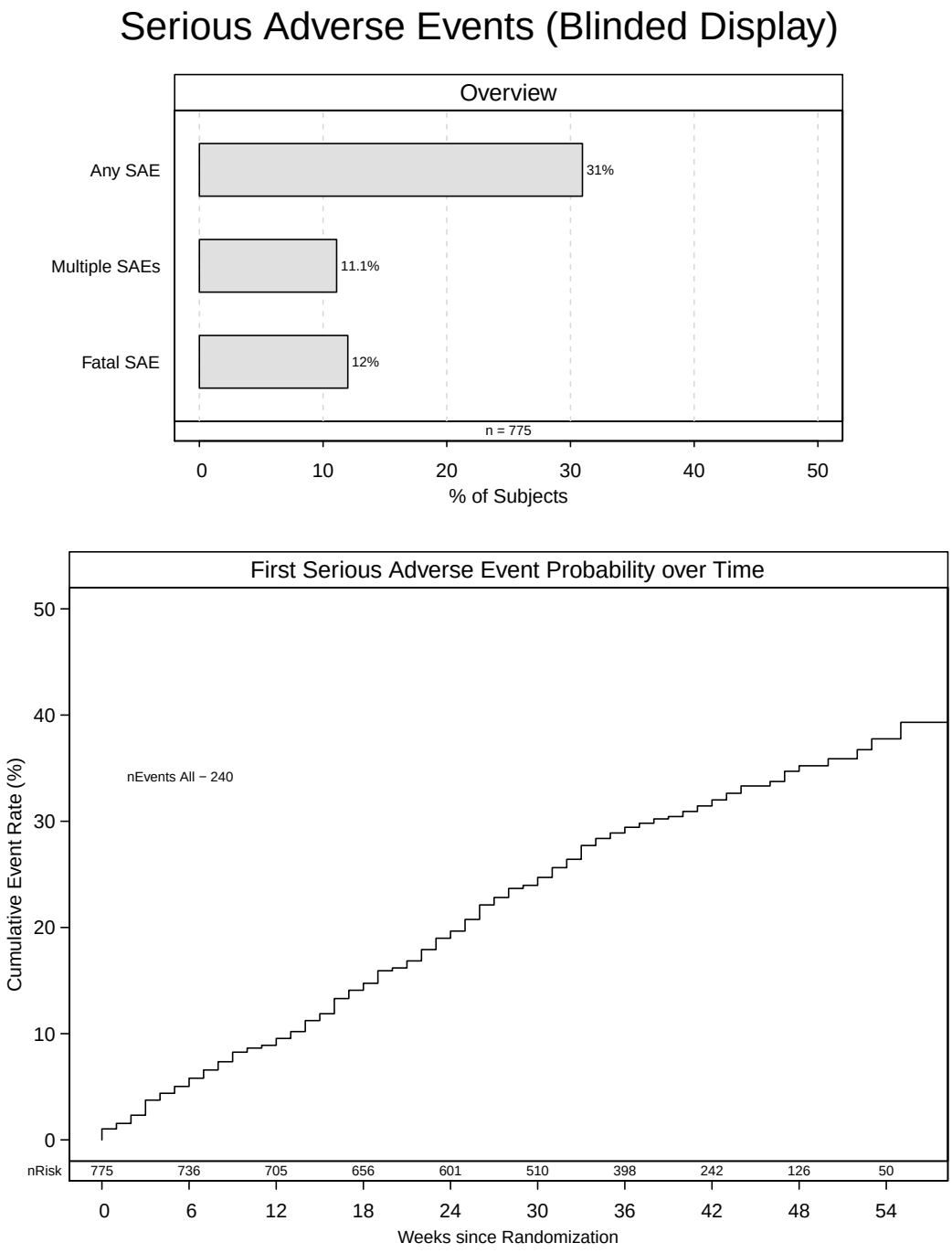
Blinded Displays for an Open Session Report

Figure DEMOBL–1



Information from a simulated baseline dataset. This is an example of a parallel display using aggregate data, which would be part of an *Open Session Report*; the contents are the same as in Figure DEMO–1 on page 28 but with no treatment information.

Figure SAEBL–1



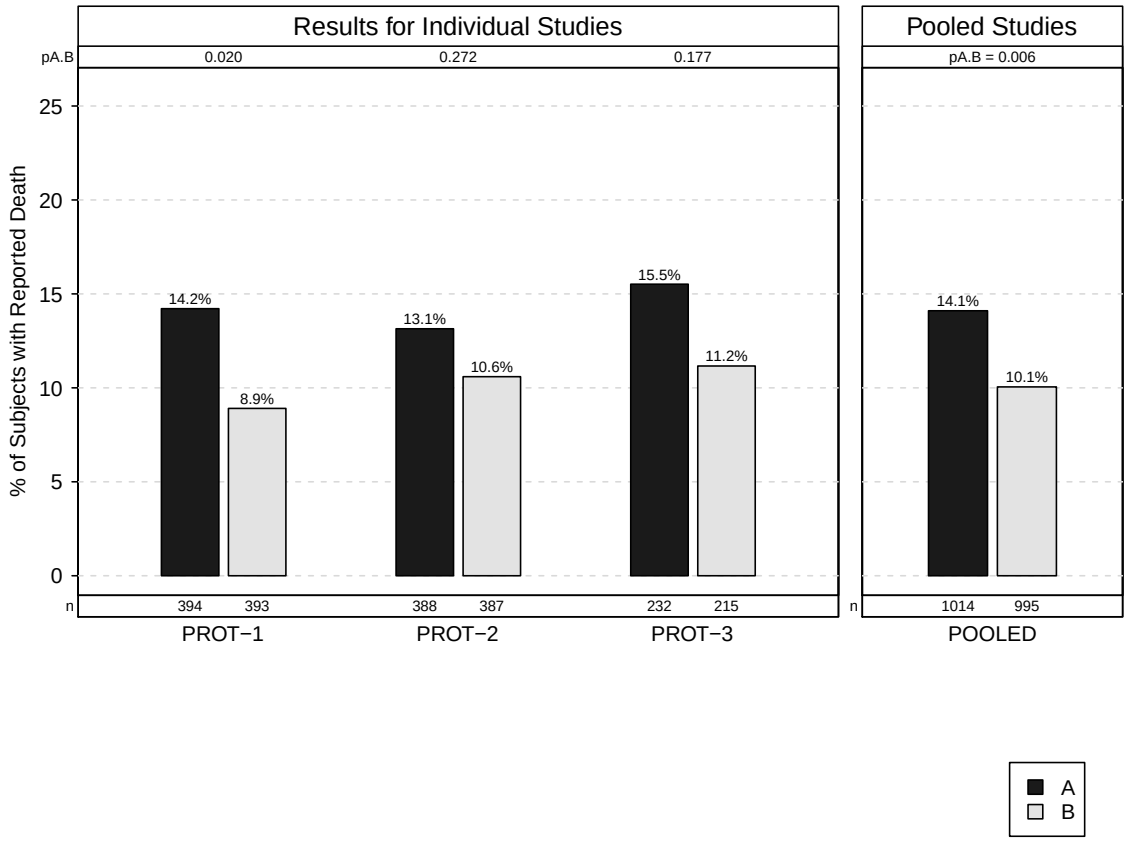
Information from a simulated serious adverse events dataset. This is an example of a parallel display using aggregate data, which would be part of an *Open Session Report*; the contents are the same as the displays in Figure SAE–1 on page 33 but with no treatment information.

Chapter A2

Multi-Protocol Displays

Figure MORT–1

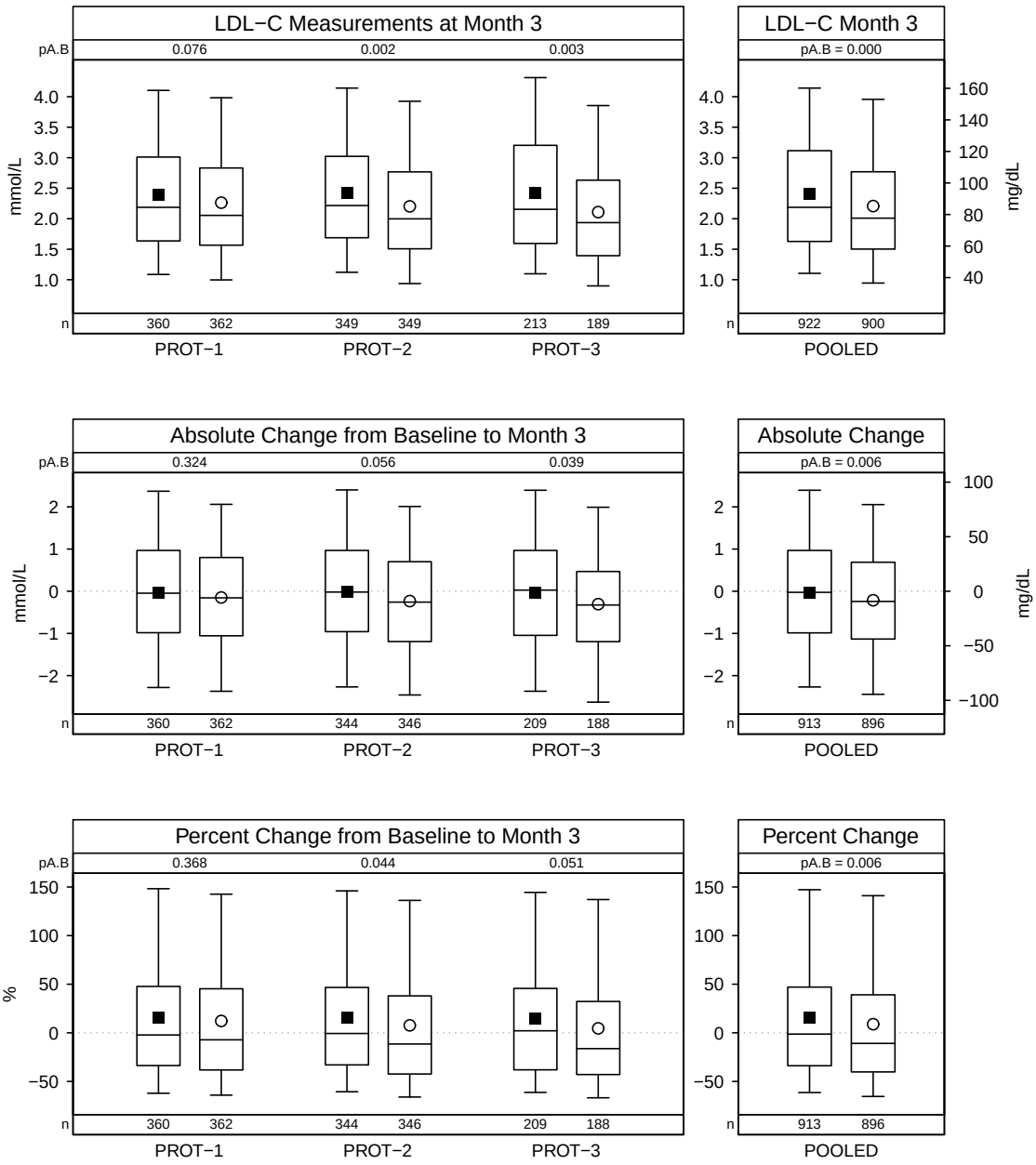
All−Cause Mortality, by Study and Pooled



Information from a simulated endpoint dataset. This display represents a possible page layout for summarizing a single dichotomous endpoint variable across individual and pooled studies in a multi-protocol program. The p-value displayed for the pooled studies is from a stratified analysis by study.

Figure LDL–1

LDL Cholesterol at Month 3, by Study and Pooled

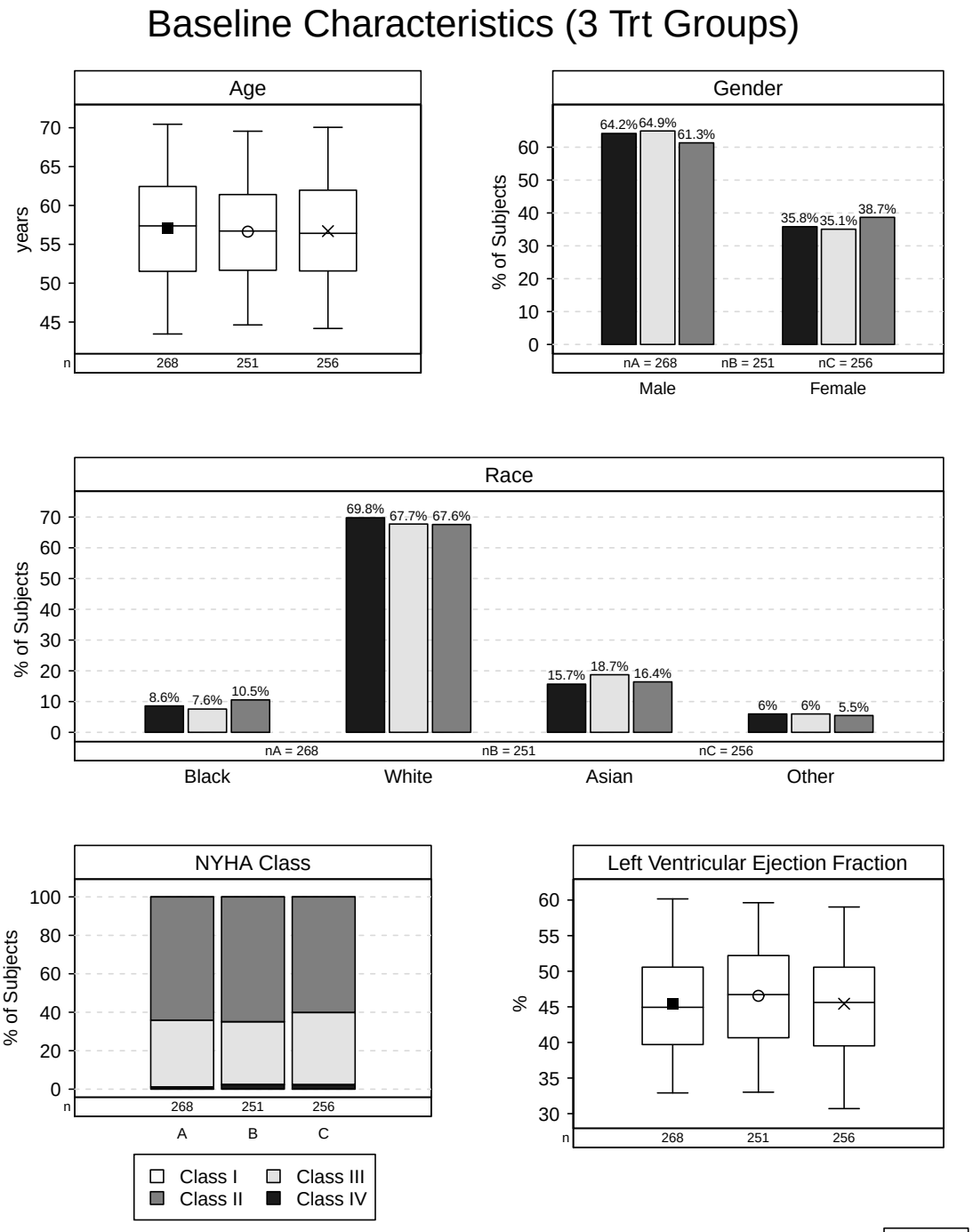


Information from a simulated laboratory dataset. This display represents a possible page layout for summarizing a lab measurement at a single time point, with change from baseline, across individual and pooled studies in a multi-protocol program. P-values displayed for the pooled studies are from a stratified analysis by study.

Chapter A3

Multi-Contrast Displays

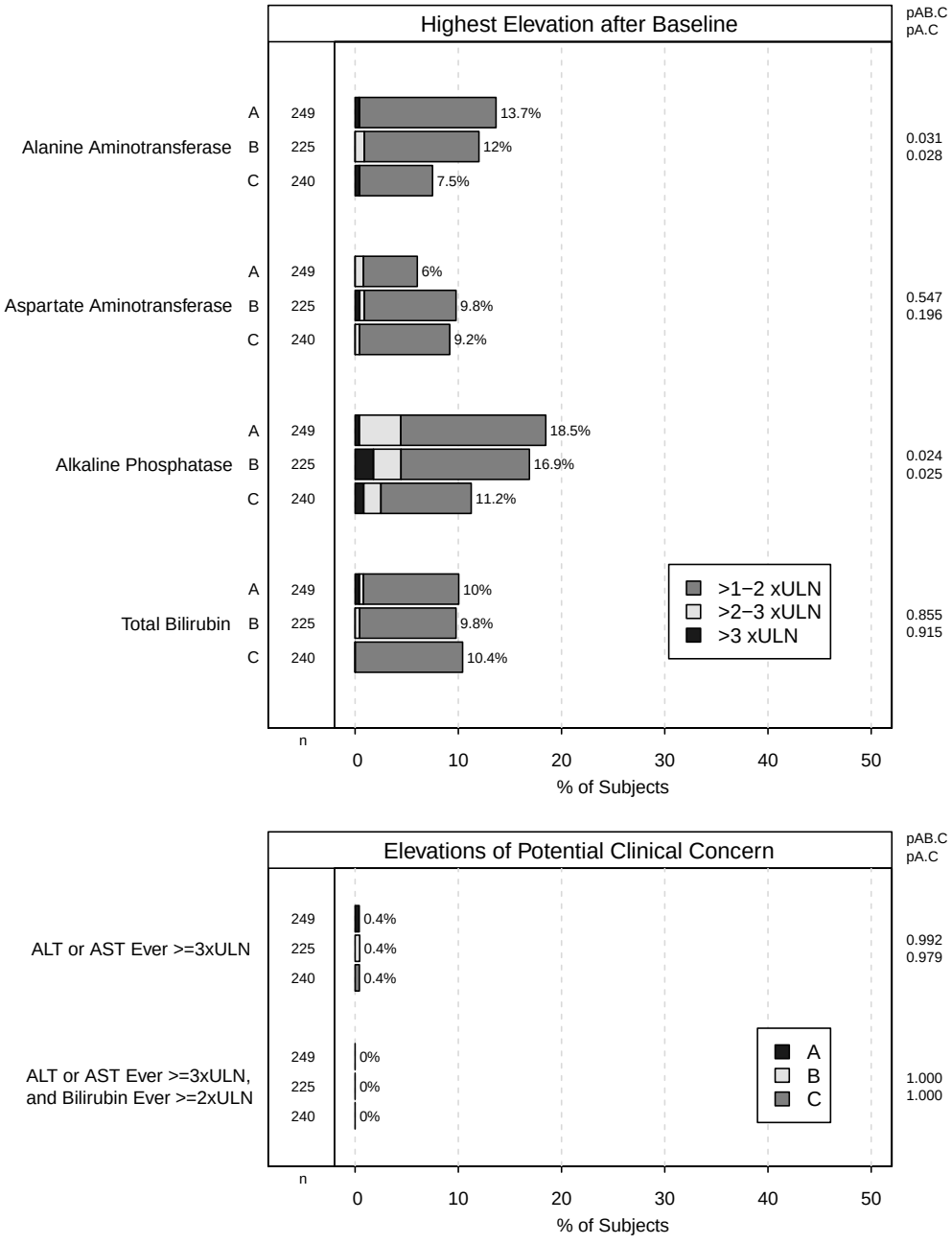
Figure ALTDEMO–1



Information from a simulated baseline dataset with three treatment groups. This page displays the same information as in Figure DEMO–1 on page 28 except that, for illustrative purposes, subjects have been randomly reassigned to one of three treatment groups instead of the previous two.

Figure ALTABN–1

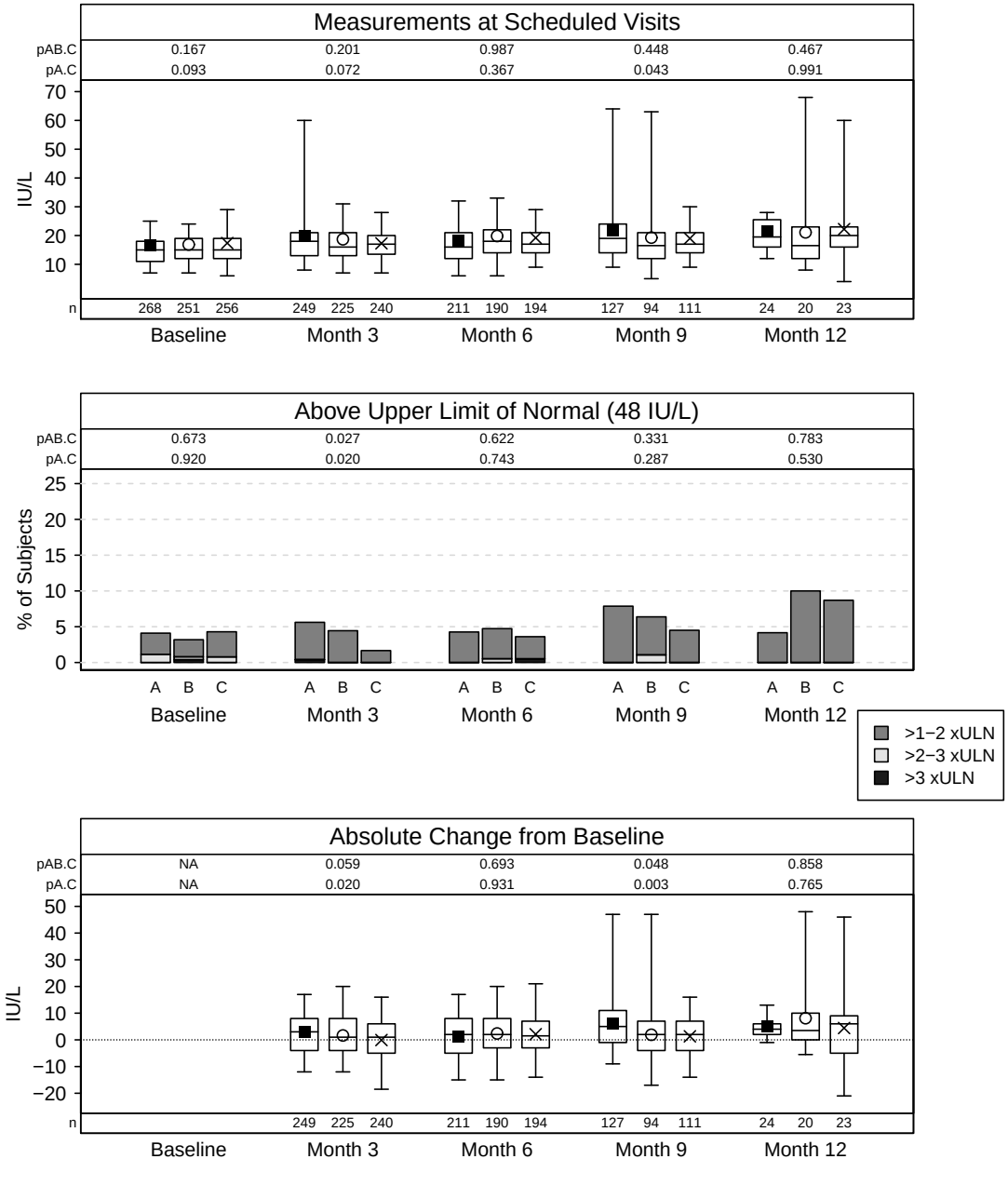
Summary of Liver Function Test Elevations (3 Trt Groups)



Information from a simulated laboratory dataset for three treatment groups with multiple contrasts. This display shows the same information as in Figure LFTABN–1 on page 49 except that, for illustrative purposes, subjects have been randomly reassigned to one of three treatment groups instead of the previous two. The p-values shown are “pAB.C” for comparing the combined treatment groups of A and B versus treatment group C, and “pA.C” for comparing treatment group A versus treatment group C. The displays are flexible and can easily handle reasonable numbers of treatment groups and contrasts.

Figure ALTLFT–1

Alanine Amino Transferase (3 Trt Groups)

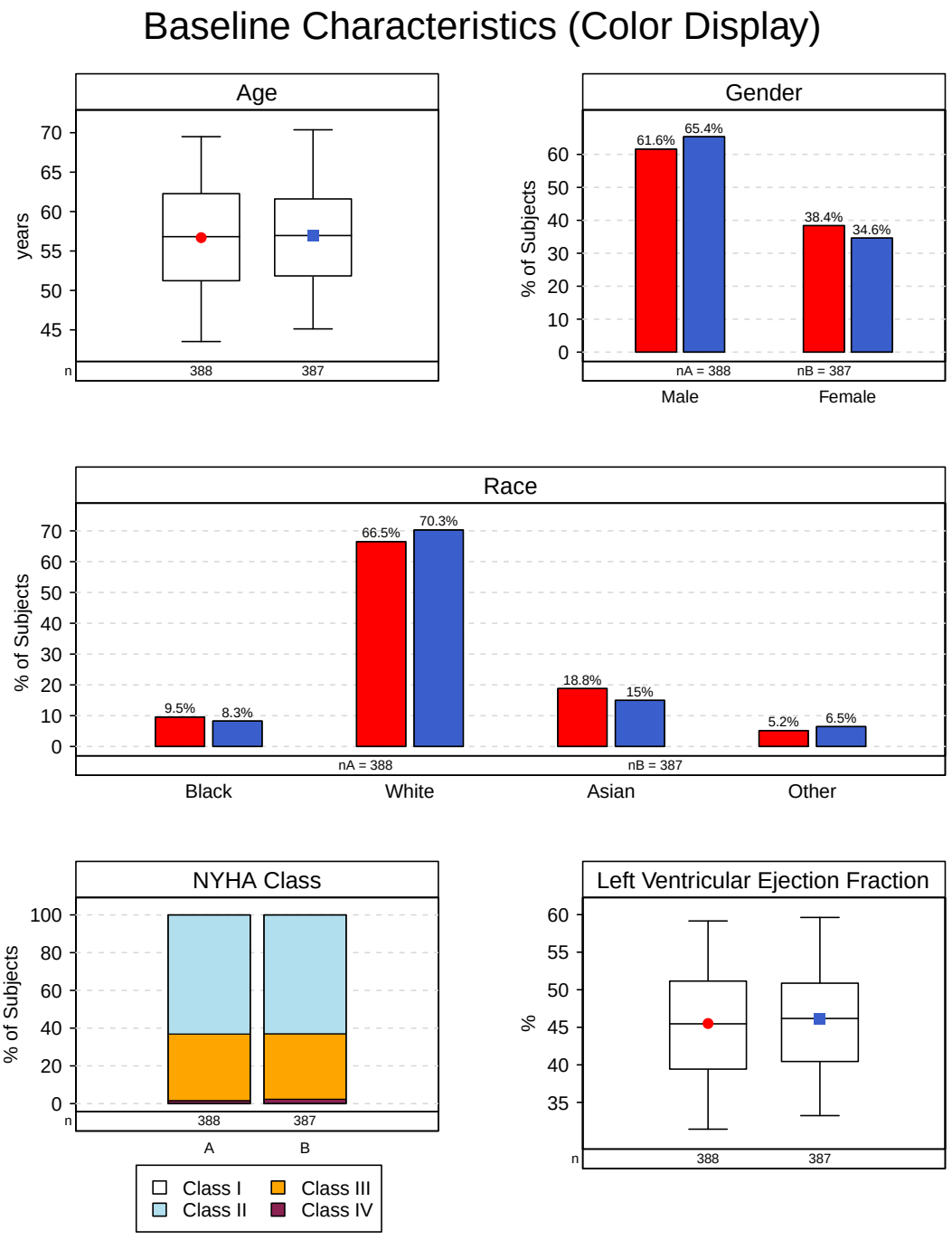


Information from a simulated laboratory dataset for three treatment groups with multiple contrasts. This page displays the same information as in Figure LFT–1 on page 50 except that, for illustrative purposes, subjects have been randomly reassigned to one of three treatment groups instead of the previous two. The p-values shown are “pAB.C” for comparing the combined treatment groups of A and B versus treatment group C, and “pA.C” for comparing treatment group A versus treatment group C. The displays are flexible and can easily handle reasonable numbers of treatment groups and contrasts.

Chapter A4

Color Displays

Figure DEMOCOL–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. The display contents are the same as in Figure DEMO–1 on page 28.

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.