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Part I

Introduction

1 Protocol and Procedures

Protocol ACTG 051 was a randomized, double-blind, placebo-controlled trial designed to evaluate intravenous gamma globulin (IVIG) in children with symptomatic HIV infection receiving zidovudine (ZIDO). It was a multicenter trial of the AIDS Clinical Trials group sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) in conjunction with pharmaceutical sponsors Cutter Biological and Burroughs-Wellcome Company.

The trial results were initially published in the 1994 paper:

“A Controlled Trial of Intravenous Immune Globulin for the Prevention of Serious Bacterial Infections in Children Receiving Zidovudine for Advanced Human Immunodeficiency Virus Infection” *New England Journal of Medicine (N Engl J Med)* 331:1181-1187, 1994.

Treatment Arms

A total of 255 subjects were enrolled and randomized to one of the following groups:

- oral zidovudine (180 mg/m² q6h) plus intravenous immunoglobulin (ZIDO/IVIG)
- oral zidovudine (180 mg/m² q6h) plus placebo (ZIDO/placebo)

Intravenous treatment was administered every 28 days during the duration of the study at a dose of 400 mg/kg of body weight. Subjects were stratified based on history of one or more serious bacterial infections within two years of entry into study, prior zidovudine therapy, and current prophylaxis with trimethoprim/Sulfamethoxazole.

Minimum treatment duration was 100 weeks. The median follow-up was 30.6 months.

Primary Outcome

The primary outcome of the study was the reduction in frequency of “serious bacterial infections”, defined as: meningitis, bacteremia, pneumonia, osteomyelitis, septic arthritis, acute sinusitis, acute mastoiditis, and abscess of an internal organ.

Secondary Outcomes

Secondary outcomes of the study included:

- reduction in frequency of other bacterial, opportunistic, and viral infections
- prolongation of survival
- comparative tolerance of the 2 regimens

- safety and tolerance of oral zidovudine
- safety and tolerance of IVIG
- slowing of the progression of HIV disease

Enrollment Criteria

Children between 3 months and 12 years of age identified as having AIDS (as defined by the CDC) or AIDS-related complex (as defined in the following) and laboratory-confirmed HIV infection were eligible for the study. Children were considered to have AIDS-related complex if they met either two of three major criteria (failure to thrive, persistent or recurrent oral candidiasis, and a CD4+lymphocyte count below 500 per cubic millimeter) within three weeks before entry into the study or one major and one minor criterion (persistent diarrhea, lymphadenopathy, organomegaly, cardiomyopathy, nephropathy, recurrent herpes simplex or herpes zoster, and thrombocytopenia) within two months before entry.

Children were excluded if they had known hypersensitivity to intravenous immune globulin, had an acute bacterial infection requiring treatment at entry, or had received within four weeks of entry antiretroviral therapy other than zidovudine or immunomodulating agents (including immune globulin), experimental drugs, or drugs known to cause prolonged neutropenia or nephrotoxic effects.

Study Procedures

Subjects were randomized to the study from October 1988 through August 1990. Subjects were recruited by 30 clinical centers sponsored by the NIAID Pediatric AIDS Clinical Trials Group and NICHD. Consent was obtained from a parent or legal guardian for each child. Visits were scheduled for every 28 days for the administration of the IV treatment and evaluation of intercurrent infections, medications and hospitalizations. Comprehensive physical examinations were conducted at randomization and every 8 weeks thereafter.

Interim Analysis

The study had a Data Monitoring Committee (DMC). The DMC was responsible for reviewing the study results by treatment group and evaluating the study treatment for beneficial and adverse effects. Interim analyses of efficacy were planned at approximately every six months as according to the protocol. The DMC met five times to review the accumulating trial data. To account for repeated testing, the logrank statistic for the primary endpoint analysis was compared to critical values corresponding to an O'Brien-Fleming interim monitoring boundary with an overall two-sided significance level of 5%, based on equivalent numbers of events between each of the analyses. The trial was completed as planned.

2 Overview of Report

The purpose of this report is to demonstrate the structure and content of a typical interim monitoring report prepared by Beta Biostatistics, Inc. with an illustrative subset of graphics and analyses. It is not intended to be a comprehensive presentation of the full final study data. Due to the limited nature of the datasets available, several of the graphics are based on data simulated from the original data for demonstration purposes only and are labeled as such on the graphic.

Report Production

Analyses for the report were performed using SAS (SAS Institute Inc.). Results were processed with R to create the figures and with \LaTeX (Leslie Lamport, *\LaTeX : A Document Preparation System*, Addison-Wesley, 1986) to compile the report.

Report Versions

There are typically two versions of an interim monitoring report. The *Open Session* Report summarizes the data without regard to assigned treatment and is intended for use in an open session or by anyone involved in the conduct of the study at the discretion of the sponsors or the Data Monitoring Committee. The *Closed Session* Report includes comparisons by assigned treatment and should only be viewed in closed session by the DMC, the statistical analysis center, or others determined by the DMC.

This sample report includes analyses by assigned treatment and is representative of a Closed Session Report. An example of a graphical display that would appear in an *Open Session* Report is displayed for a baseline characteristics page (OPEN–1 on page 22) following the corresponding *Closed Session* graphic (BASE–2 on page 21).

Abbreviated Report Outline

- Introduction
- Enrollment and Study Status
- Baseline Characteristics
- Efficacy Endpoints
- Safety Measures
- Adverse Events (not included in this report)
- Additional Follow-Up Measures (not included in this report)
- Supporting Material
- Ancillary Material (not included in this report)

List of Abbreviations

AIDS	acquired immunodeficiency syndrome
AE	adverse event
BBI	Beta Biostatistics, Inc.
CDC	Center for Disease Control and Prevention
CRF	Case Report Form
DMC	Data Monitoring Committee
IVIG	intravenous immunoglobulin
HIV	human immunodeficiency virus
NIAID	National Institute of Allergy and Infectious Diseases
NEJM	New England Journal of Medicine
NICHHD	National Institute of Child Health and Human Development
NTIS	National Technical Information Service
PATH	pathogens
SAE	Serious Adverse Event
SBI	Serious Bacterial Infection
STAPH EPI	staphylococcus infections
ZIDO	zidovudine
ZDV	zidovudine

Sources of Data Included in Report

This report is based on the final study datasets obtained from the National Technical Information Service (NTIS) under the Freedom of Information Act.

During an ongoing clinical trial, the study database is comprised of many individual datasets, which are frozen and transferred to Beta Biostatistics, Inc. at a point in time for the preparation of an interim monitoring report. The date and source of the data transfer, the names of datasets included in the transfer, and the specific CRFs associated with each of the datasets would be described in this section of the *Introduction*. Any other sources of data utilized in the report (such as endpoint information received independently as a form of verification) would also be described here.

3 Report Structure

Treatment Labels

In a typical *Closed Session* Report, treatment groups are indicated by code, such as the letters "A" and "B". The assignment of code to study drug is not usually provided in the report, but is consistent throughout the trial.

In this sample report, the treatment group designations are as follows:

- Group A – ZIDO/Placebo ($n = 126$)
- Group B – ZIDO/IVIG ($n = 129$).

P-values

P-values for treatment comparisons are given as “pA.B”. These p-values should be interpreted cautiously, since no adjustment has been made for multiple comparisons. Given the large number of comparisons considered, we would expect that a number of p-values would appear statistically significant (< 0.05) simply by chance. In studies with more than two treatment arms, p-values for multiple contrasts can be displayed.

P-values for continuous data are computed using the non-parametric Wilcoxon Rank Sum test with no stratification by site. This test is appropriate for data with non-normal distributions and has power near that of the Student t-test when the data are normal. Wilcoxon tests are also used for data which are ordered categorical (e.g., maximum severity of adverse events). For dichotomous and unordered categorical data (e.g., sex), the Pearson chi-square test is used. A logrank test is used to compare the distributions of survival times when Kaplan-Meier survival curves are displayed. The p-values associated with the estimates of hazard ratios are obtained from the Wald chi-square statistic.

Graphical Conventions

The primary mode of presentation in this report is graphical. The visual presentation is intended to allow the reviewer to examine easily the distribution of the variables and characterize the study population 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 representing the percent of subjects falling into a particular category, continuous data represented as boxplots, or time-to-event data represented as Kaplan-Meier estimates of survival curves. Supporting tables containing univariate statistics and detailed frequency counts for the graphical displays are cross-referenced to and from the corresponding graphical pages.

Bar chart: Bar charts indicate for categorical data the number or percent of subjects by category. Several types of bar charts are used. Simple bar charts display categorical variables with mutually exclusive categories, as in the plot for gender in Figure BASE–1 on page 20.

Multiple bar chart: Bar charts of related dichotomous variables are sometimes grouped together to form a multiple bar chart. This is the display format frequently used for medical history data. It can also be used to display categorical data with non-mutually exclusive categories, such as variables with “check-all-that-apply” types of responses.

Stacked bar chart: A more detailed bar chart is used to display categorical data which have additional ordered subdivisions. The percent of subjects within the ordered subdivisions are indicated by shading in a stacked bar chart, as in the display of number of hospitalizations in Figure HOSP–1 on page 35.

Boxplot: Boxplots indicate the distribution of continuous data by means of percentiles. 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. An example is the boxplot for age in Figure BASE–1 on page 20.

Kaplan-Meier plot: Dichotomous response variables such as death 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 remaining event-free as a function of time since randomization, as in Figure TTEVNT–1 on page 28. The total numbers of events appear on the plot, as do the numbers of subjects at risk (event-free and uncensored) at various points of follow-up.

Relative risk graphic: A relative risk graphic, for example for the first occurrence of a serious bacterial infection in Figure HAZ–1 on page 32, is used to summarize subgroup analyses of a treatment group difference. This type of graphic displays point estimates and nominal 95% confidence intervals for the relative risk of an event in one treatment group compared to another treatment group. Estimates are obtained using the Cox proportional hazards model. Consistency of a treatment effect across subgroups defined by baseline characteristics is easily assessed with this graphic.

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 CD4–1, page 37). For dichotomous variables, change from baseline can be indicated by displaying follow-up data separately for each baseline group.

Annotations: All 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. P-values corresponding to the comparisons of the two treatment groups are included, where applicable. In a typical interim report, figures are also annotated with the data source (names of datasets used and date of data transfer).

Figure identifier: In the top right corner of each page of figures is a mnemonic figure identifier. These identifiers are listed alphabetically in the index at the back of the report.

4 Notes on Chapter Contents

General Conventions

This report is based on data available from NTIS. In a typical interim monitoring report, this section would document the date of database transfer to Beta Biostatistics, Inc. and other issues related to the data in general.

The graphics and analyses in this report include all randomized subjects ($N = 255$). For displays in Chapter 2, *Baseline Characteristics*, the denominators for each graphic are the number of subjects with non-missing data for the variable(s) being displayed. For analyses in Chapter 3, *Efficacy*

Endpoints and Chapter 4, *Safety Measures*, the denominator (or risk set) is the set of all randomized subjects.

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.

Enrollment and Study Status

Enrollment began in October, 1988, and ended in August, 1990. A total of 255 subjects were enrolled at 30 clinical centers in the United States. Subject accrual over time is displayed in Figure ACCR–1 on page 14. Figure ACCR–2 on page 15 displays subject accrual at each clinical center, by assigned treatment group. As center was not included in the datasets, subjects were randomly assigned to a clinical site for display purposes by center only. No interpretations of the data by center should be undertaken.

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 could also be presented. These graphics can be designed to help assess the timeliness of data collection and entry.

Baseline Characteristics

A typical report would display treatment group comparisons for all baseline variables (except those items which appear in the database only as verbatim listings). Typically more information is collected at baseline than was available in the public dataset and would be presented in addition to what is in the sample report.

In this chapter, a sample of an *Open Session* report graphic (OPEN–1, page 22) is included following the corresponding *Closed Session* report graphic (BASE–2, page 21).

Efficacy Endpoints

Primary and secondary endpoint analyses would be displayed in this chapter. In this study, the primary endpoints of the study were (1) the time to death and (2) the time to first serious bacterial infection with confirmed pathogens. The protocol defined five types of documented serious bacterial events to be looked at:

- Type I: Documented Serious Bacterial Infection (not including staph epi.)
- Type II: Events are staph epi and other events possibly related to central lines i.e. bacillus species
- Type III: Events are pneumoniae documented by x-rays

- Type IV: All sinusitis events
- Type V: Are all documented SBIs and pneumoniaes without x-rays

Six time to bacterial event analyses were included in the dataset. They were:

- Primary Endpoint: Serious Bacterial Infection with known pathogen (including staph epi and bacillus)
- Serious Bacterial Infection with known pathogen (does not include staph epi and bacillus)
- All Types of SBI Events (types I, II, III, IV, and V above)
- Only SBI Events of Type I, II, and III
- Only SBI Events of Type I, II, III, and IV
- Only SBI Events of Type I and III

All other bacterial infections were categorized as non-serious and collected separately.

With the exception of a single graphic of interim analysis results (Figure BOUND–1 on page 33), the graphical displays in this chapter are based on data available from NHLBI after the final closing of the database.

In time-to-event analyses, subjects with no event are censored using the censoring time provided in the database, last seen date, which included death date if applicable.

The Kaplan-Meier plot in Figure TTEVNT–1 on page 28 displays time to first serious bacterial infection. Based on the final dataset, there were 22 first events (17.05%) in the IVIG group, and 32 first events (25.4%) in the ZIVO/placebo group. The Z -score from this final analysis is 1.837.

A more extensive report would include separate Kaplan-Meier plots for the primary endpoint analysis in subject subgroups of particular interest, as in Figure TTEVNT–1 on page 28. Figure HAZ–1 on page 32 is an example of a relative risk graphic assessing the treatment effect for various subgroups. Estimates of the hazard ratios and 95% confidence intervals were obtained using the Cox proportional hazards model.

More extensive analyses of secondary endpoints would usually be included in this chapter of a report.

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 (e.g. vital signs, laboratory values). This sample report displays a sampling of graphics looking at hospitalization data and CD4 counts.

Follow-up information (for CD4-type data) can be displayed with bars representing the percent of subjects under observation who meet certain criteria at specified timepoints (e.g., Figure CD–1 on page 37) or with a boxplot to illustrate the distribution of continuous measures. Change from

baseline for given cohorts is often presented on the same page as displayed in Figure CD–1 on page 37. For other types of data, the report summarizes information collected over the entire period of observation.

Adverse Events (AE) (not included in this report)

In a typical clinical trial, subjects are asked about adverse events they may have experienced since the previous visit. While this data was not included in the datasets received, a typical interim report chapter could include a summary of the adverse events. Depending on the data collected, a sample of AE summary displays could include the percentage of patients ever experiencing:

- any adverse event
- any moderate or severe adverse event
- any severe adverse event
- multiple adverse events
- any adverse event possibly or probably related to the treatment
- any adverse event that lead to the discontinuation of the treatment

AEs are also typically displayed at both at the body system level and at the level of preferred term, with stacked bars indicating severity (if available).

In many clinical trials there is a separate mechanism for expedited reporting and data management of serious adverse events (SAEs) for regulatory purposes, with a later reporting of the event on a study form. Because of the difficulty of merging data from different sources, information obtained from a separate SAE database would usually be displayed in a separate chapter. Information on the occurrence of SAEs was not included in the database, but is generally an important component of interim monitoring reports because of its greater timeliness and clinical significance.

Additional Analytic Considerations (not included in this report)

In a typical interim report, this chapter could include analyses of issues not addressed elsewhere that are relevant to the DMC deliberations concerning study conduct. The following analyses could be addressed in this section: comparisons of observed with expected accrual, and of observed with expected event rates; implications for study power and design if observed rates are lower (or higher) than expected; evaluation of changes in characteristics of enrolled subjects over time; and conditional power calculations.

Supporting Material

Part III, *Supporting Material*, includes backup 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 (not included in this report)

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 data may also be provided.

5 Contact Information

In an actual report, this section would include names and contact information for the members of the DMC, the Executive and/or Steering Committee, Beta Biostatistics, Inc. staff associated with the study, and sponsor-affiliated study personnel.

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Program Manager

Part II

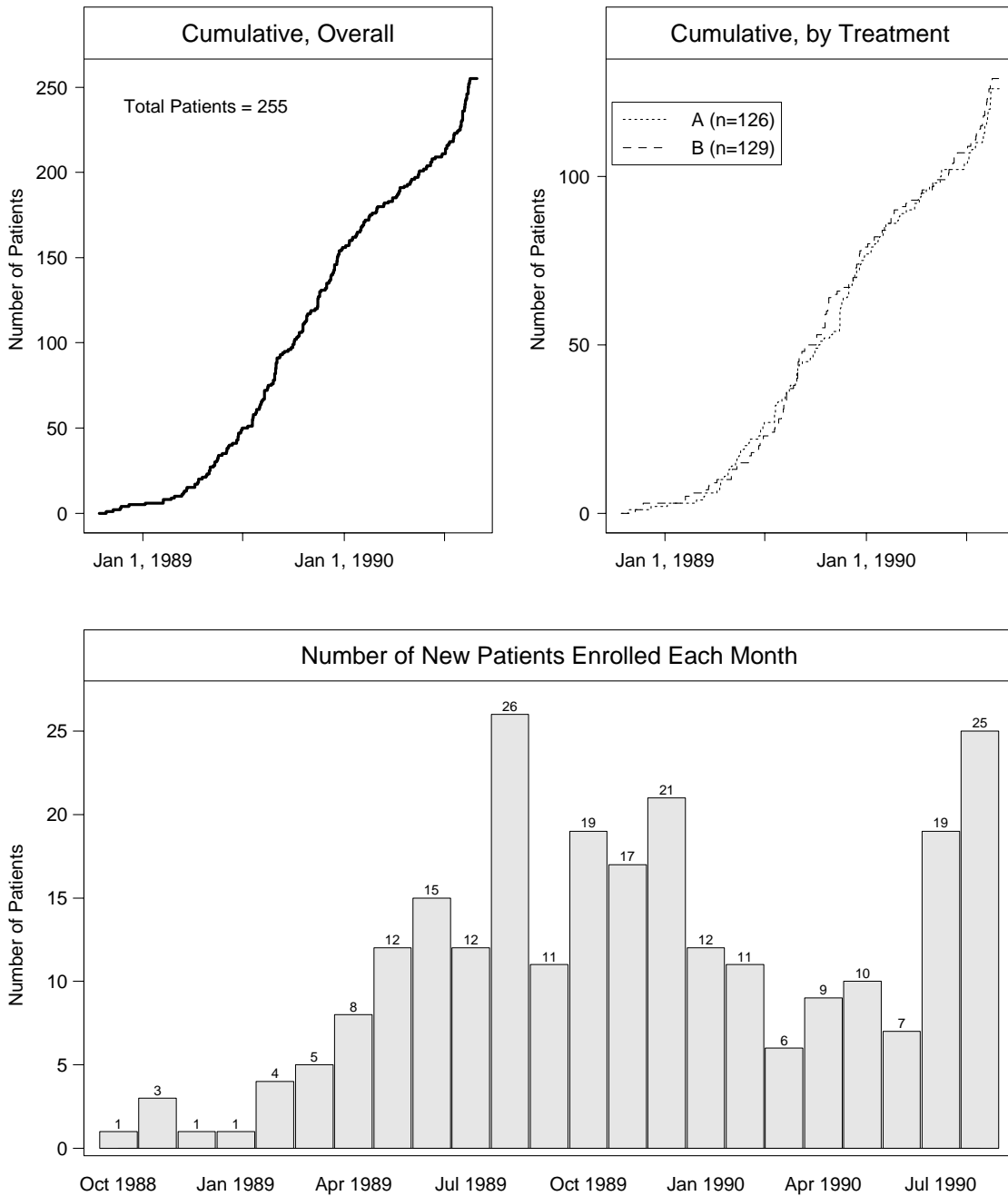
Main Material

Chapter 1

Enrollment and Study Status

Figure ACCR-1

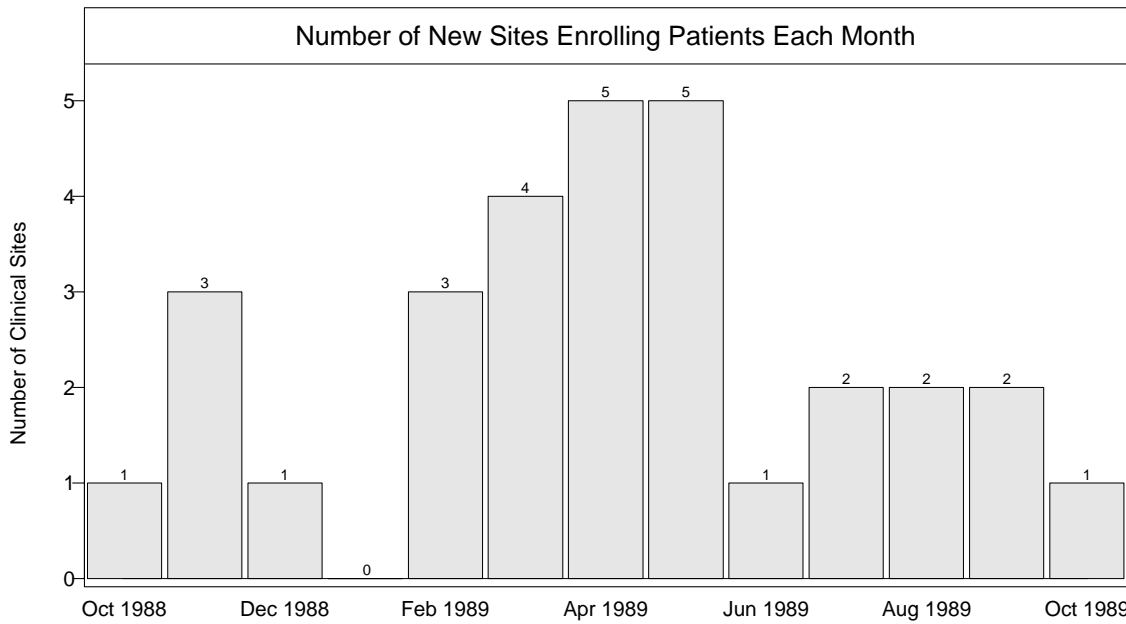
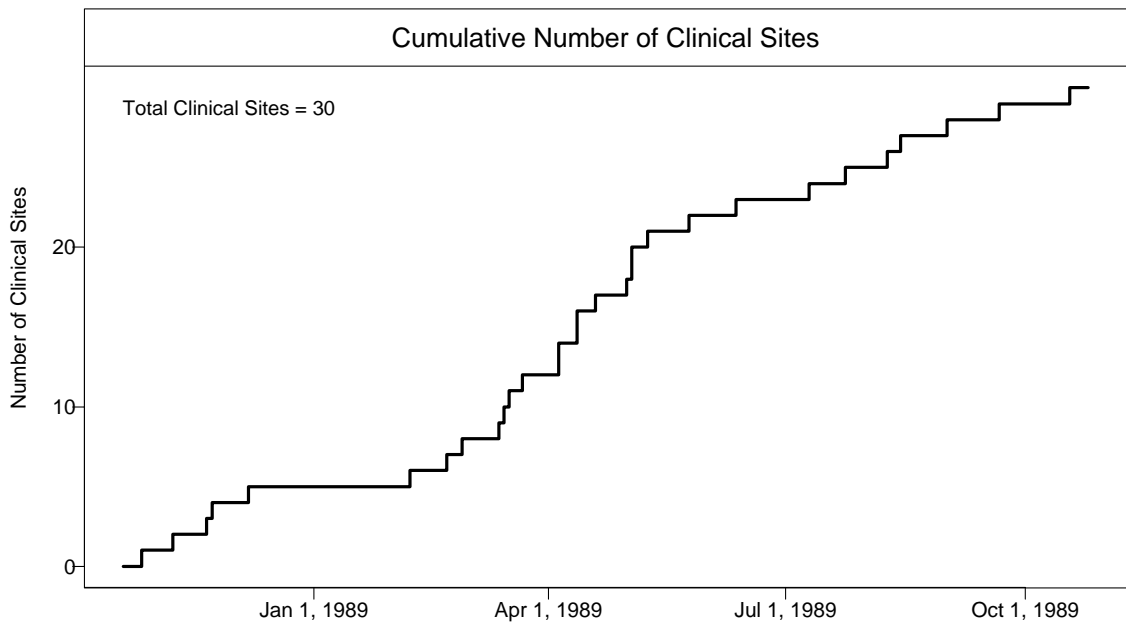
Patient Accrual over Time



Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994. The first patient was randomized on October 27, 1988; the last patient was randomized on August 16, 1990.

Figure ACCR-2

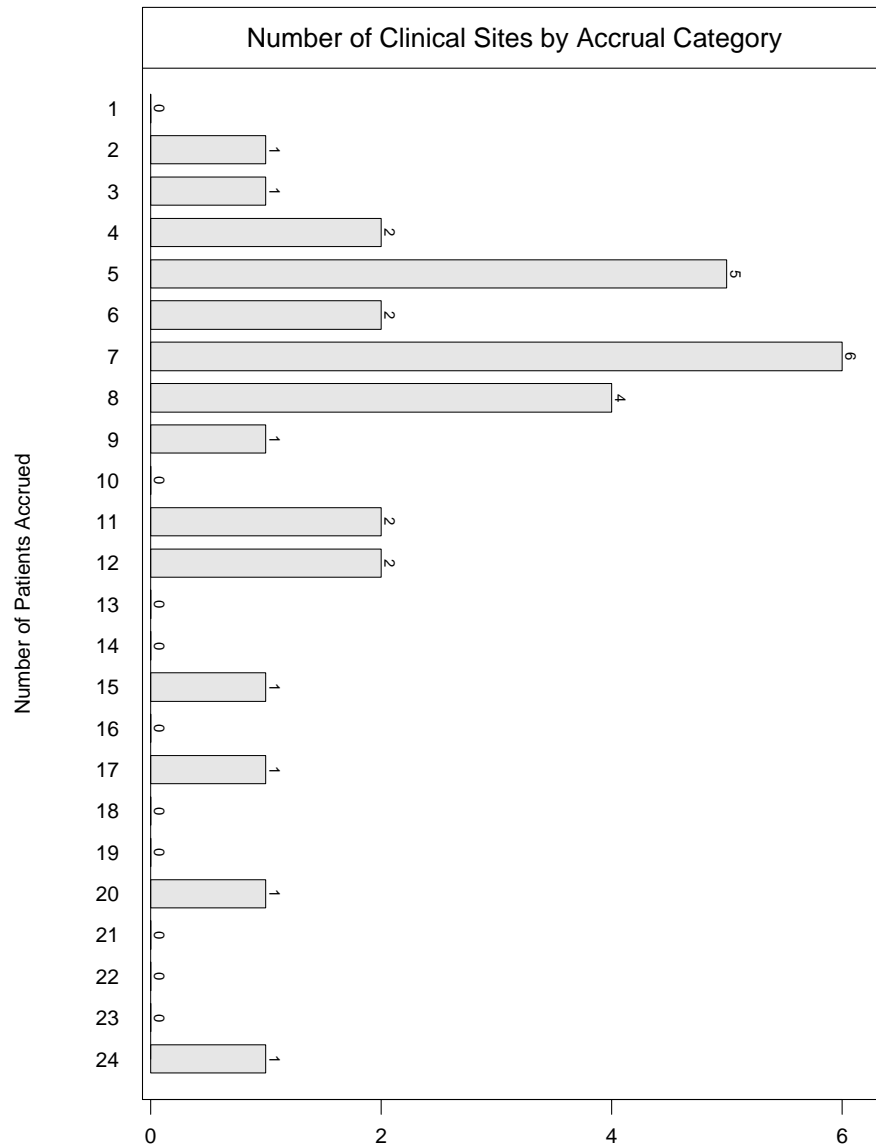
Clinical Site Participation



Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994. Information on accrual by center was not included in the dataset; this was randomly generated by BBI to demonstrate a more 'typical' accrual chapter.

Figure ACCR-3

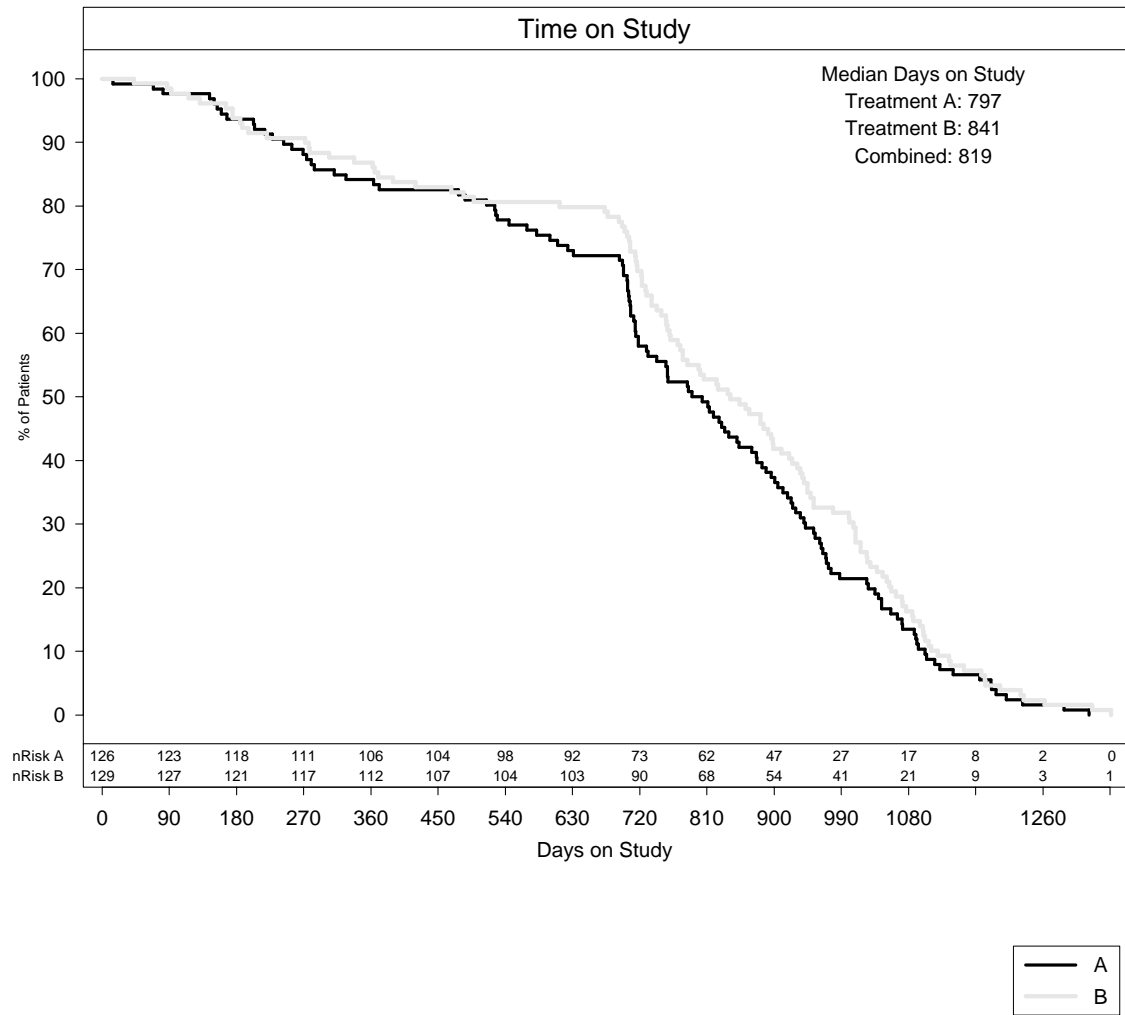
Distribution of Patients Across Clinical Sites



Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994. Information on accrual by center was not included in the dataset; this was randomly generated by BBI to demonstrate a more 'typical' accrual chapter.

Figure FU-1

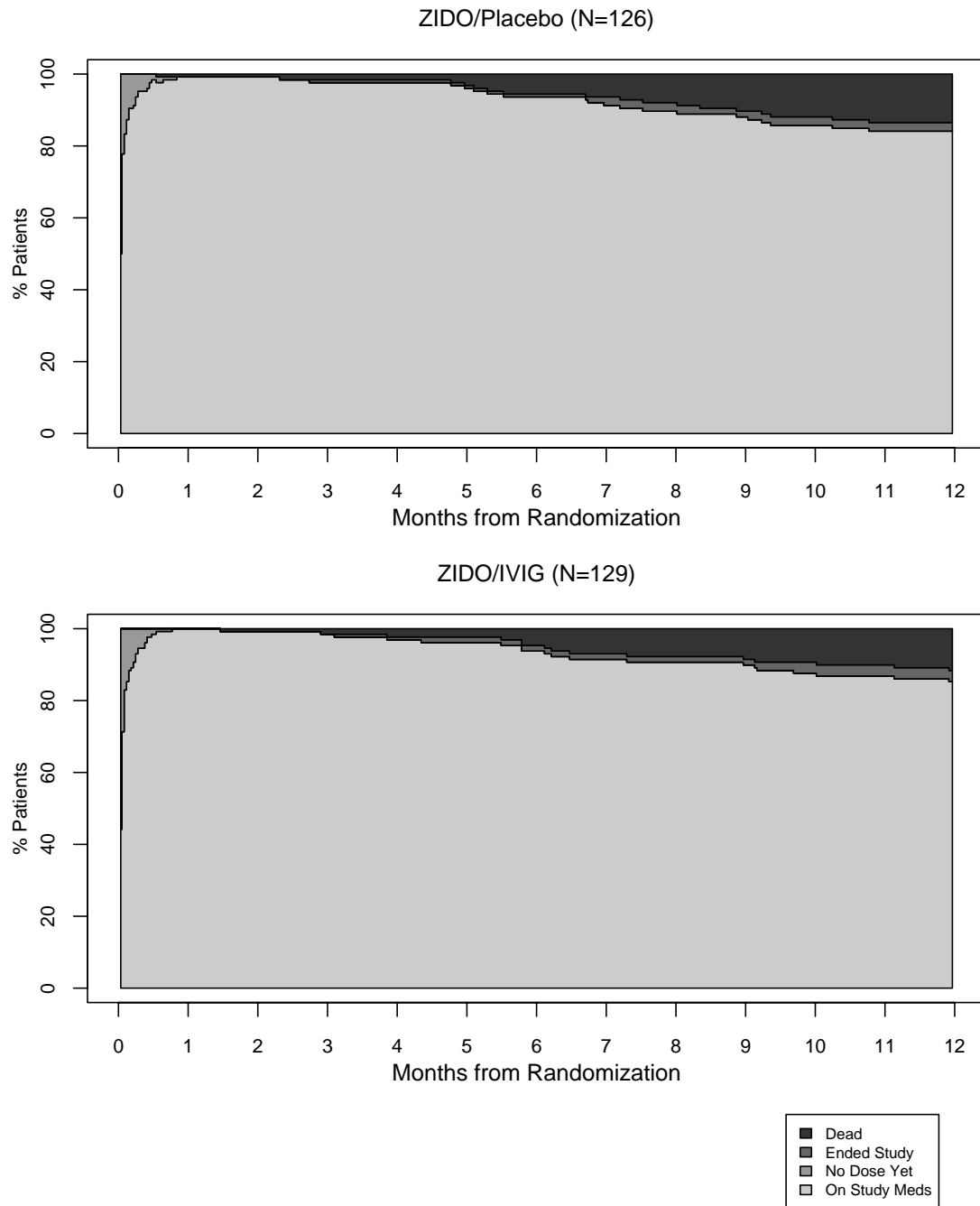
Cumulative Follow-Up Time



Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994.

Figure DOSE-1

Dosing level Summary for First 365 Days



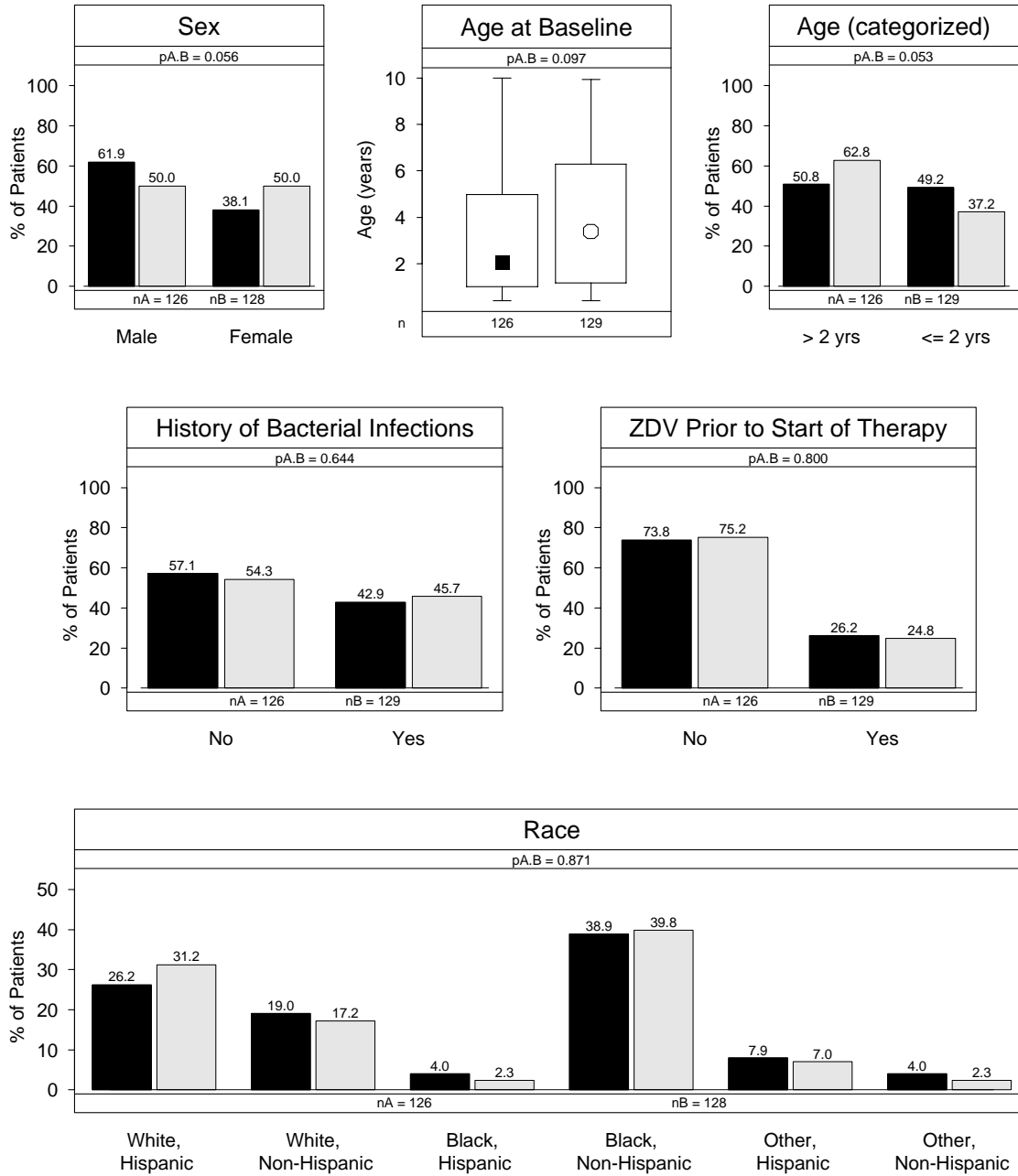
Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994.

Chapter 2

Baseline Characteristics

Figure BASE-1

Baseline Characteristics



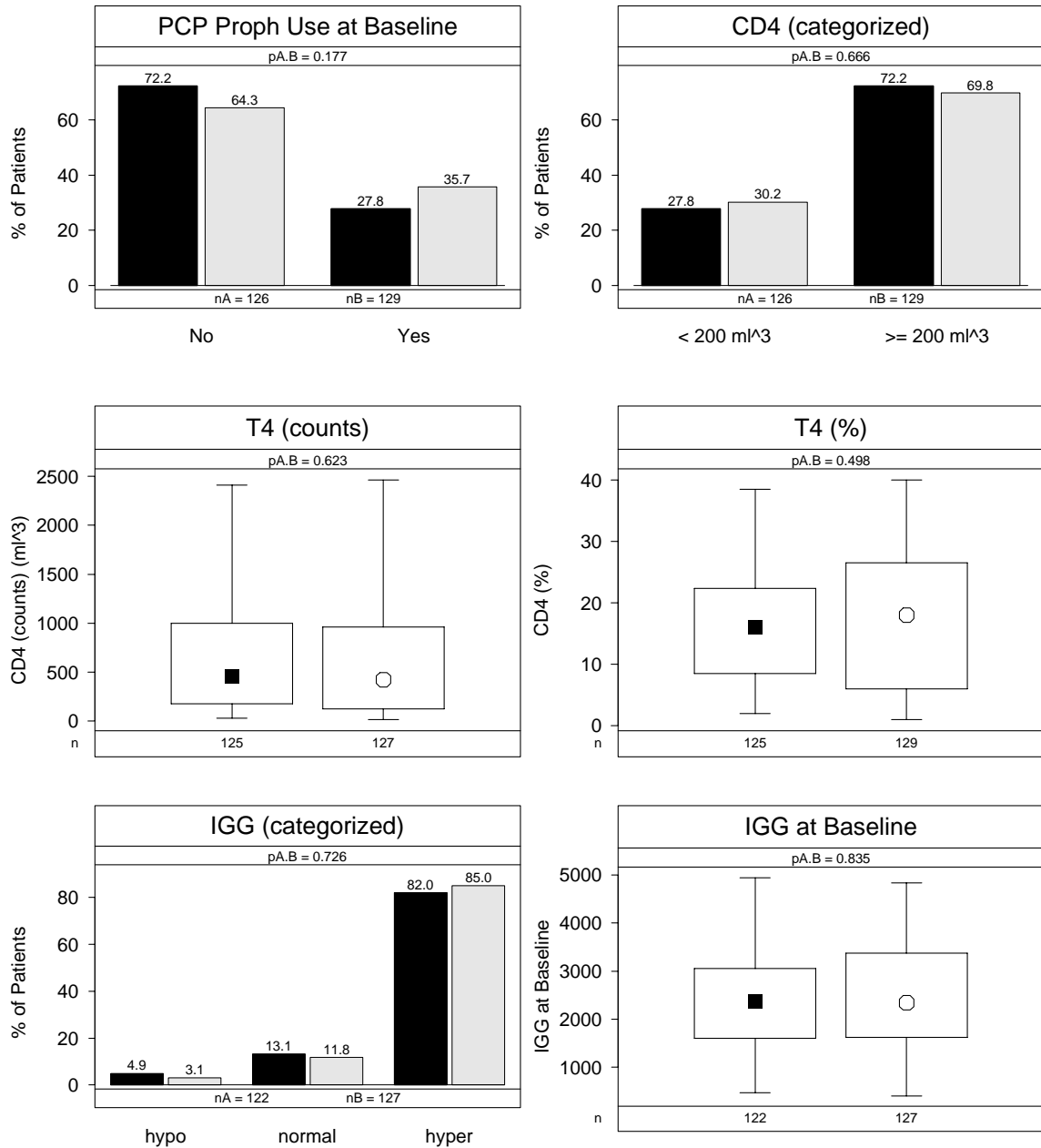
Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994. Age was computed from the birthdate and date of randomization. The sample sizes for each graphic are the number of patients with non-missing data for the variable being displayed.



See Table Set BASE-1 on page 40.

Figure BASE-2

Baseline CD4 Counts and IGG (Closed Session Version)



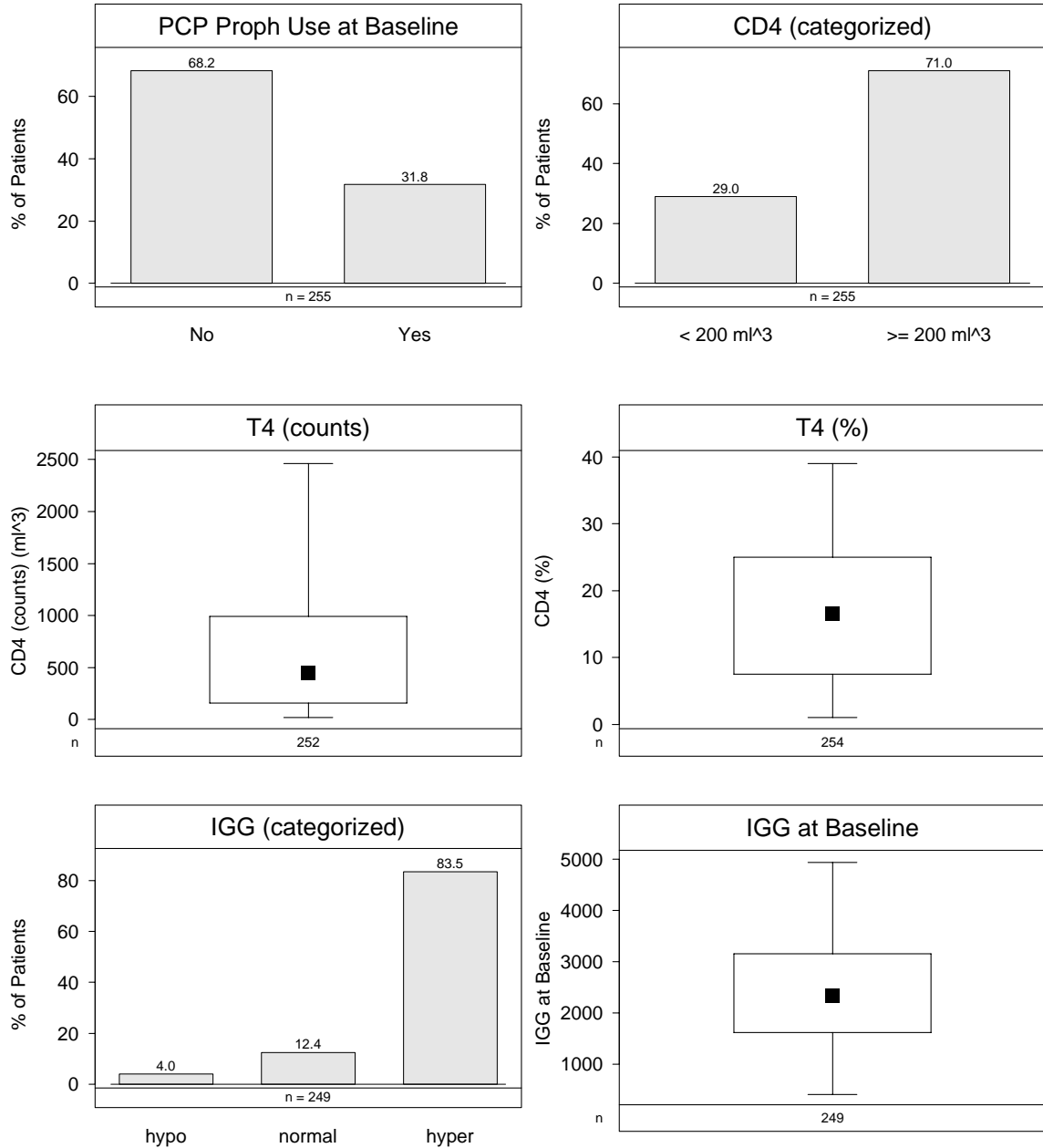
Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994. The sample sizes for each graphic are the number of patients with non-missing data for the variable being displayed.



See Table Set BASE-2 on page 41.

Figure OPEN-1

Baseline CD4 Counts and IGG Open Session Version

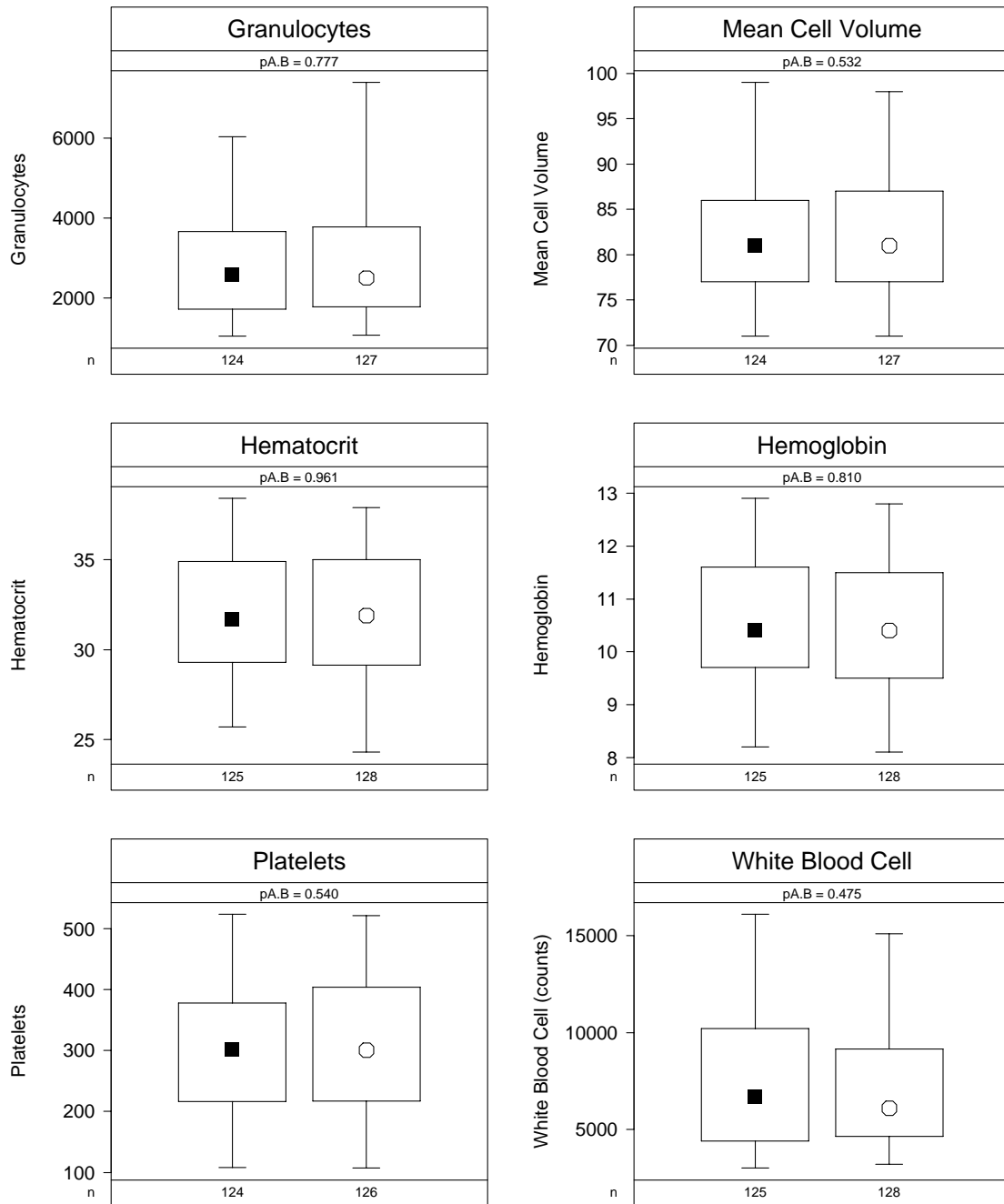


Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994. The sample sizes for each graphic are the number of patients with non-missing data for the variable being displayed. This is an example of an *Open Session* Report version of the previous page's *Closed Session* graphic (BASE-2).

See Table Set OPEN-1 on page 42.

Figure BASE-3

Baseline Laboratory Measures



Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994.



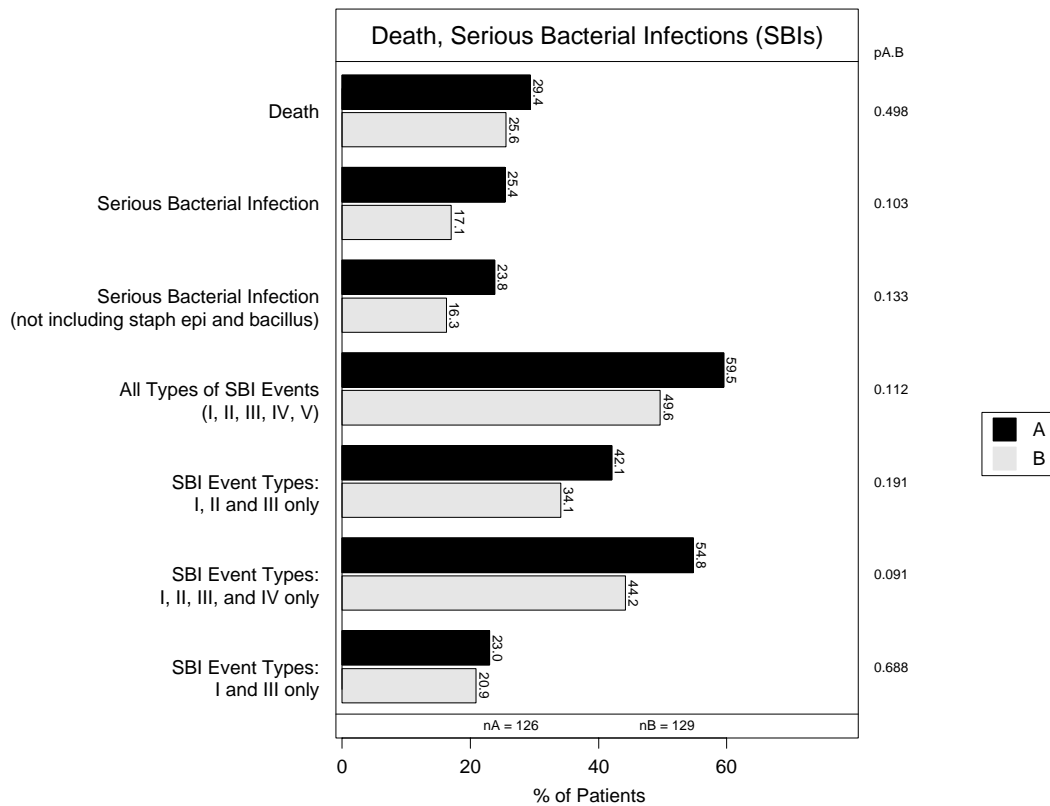
See Table Set BASE-3 on page 43.

Chapter 3

Efficacy Endpoints

Figure ENDPT-1

Summary of Endpoint Events

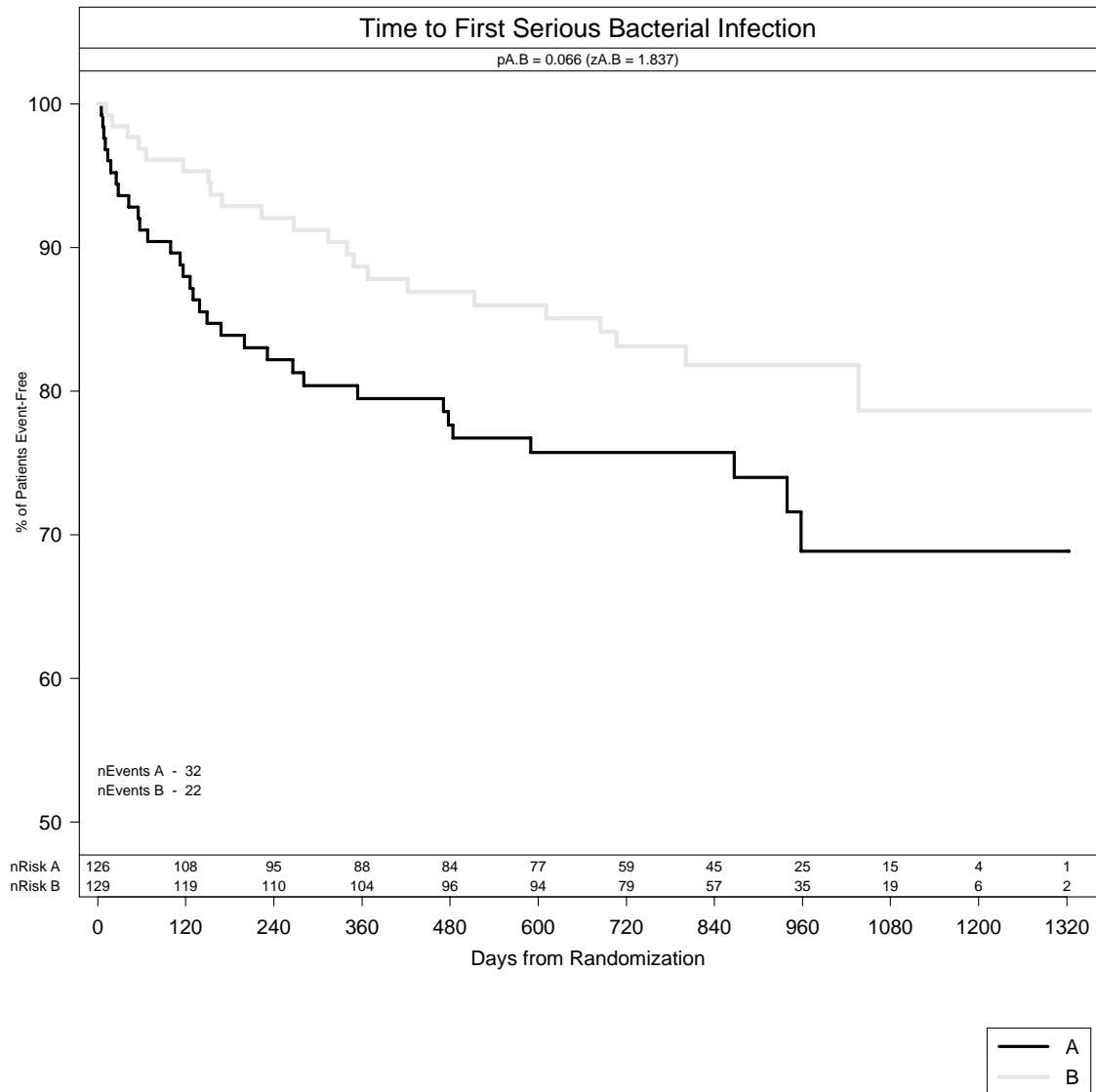


	Trt	Total Pats	Value		Contrast	P-Value
			Yes			
			N	%		
Death	A	126	37	29.37	A.B	0.498
	B	129	33	25.58		
Serious Bacterial Infection	A	126	32	25.40	A.B	0.103
	B	129	22	17.05		
Serious Bacterial Infection (not including staph epi and bacillus)	A	126	30	23.81	A.B	0.133
	B	129	21	16.28		
All Types of SBI Events (I, II, III, IV, V)	A	126	75	59.52	A.B	0.112
	B	129	64	49.61		
SBI Event Types: I, II and III only	A	126	53	42.06	A.B	0.191
	B	129	44	34.11		
SBI Event Types: I, II, III, and IV only	A	126	69	54.76	A.B	0.091
	B	129	57	44.19		
SBI Event Types: I and III only	A	126	29	23.02	A.B	0.688
	B	129	27	20.93		

Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994. The denominator for percentages is all randomized patients. See the *Introduction* for a more detailed description of the types of serious bacterial infections.

Figure PRIMARY-1

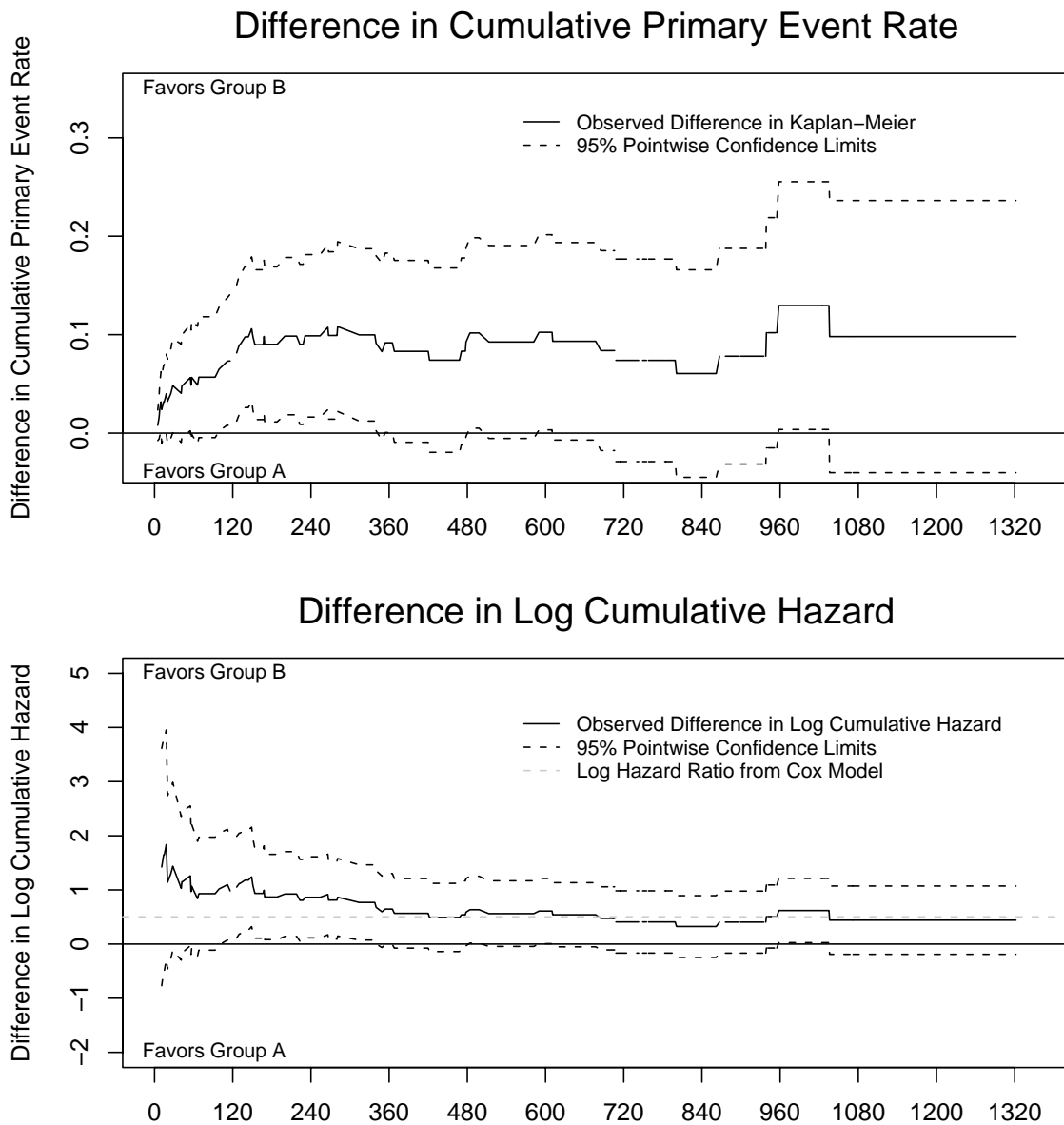
Serious Bacterial Infection



Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994. Patients with no event are censored at the date of last known contact.

See Table Set PRIMARY-1 on page 45.

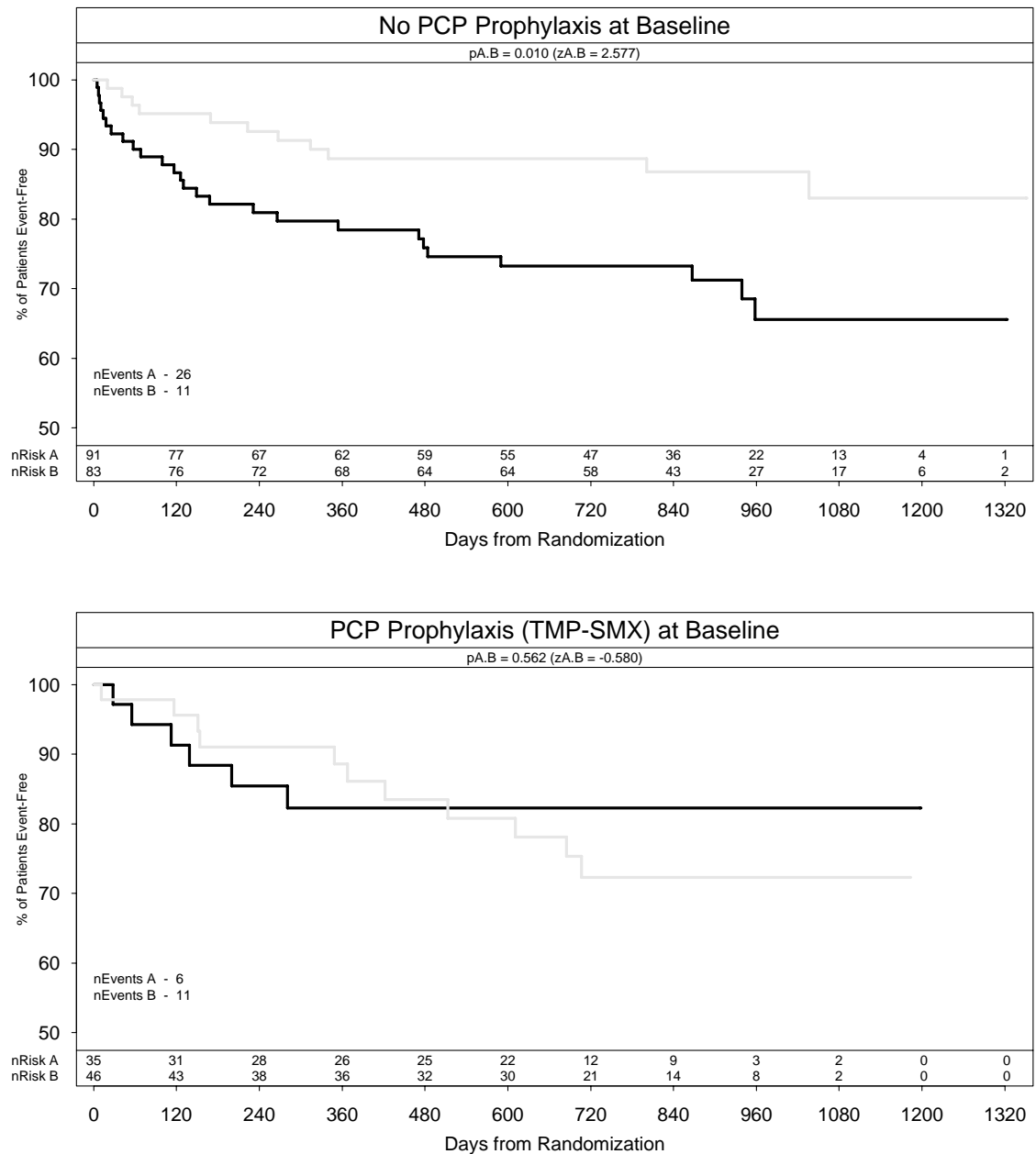
Figure PRIMARY-2



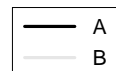
Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994.

Figure TTEVNT-1

Serious Bacterial Infection by Prophylaxis Use at Baseline



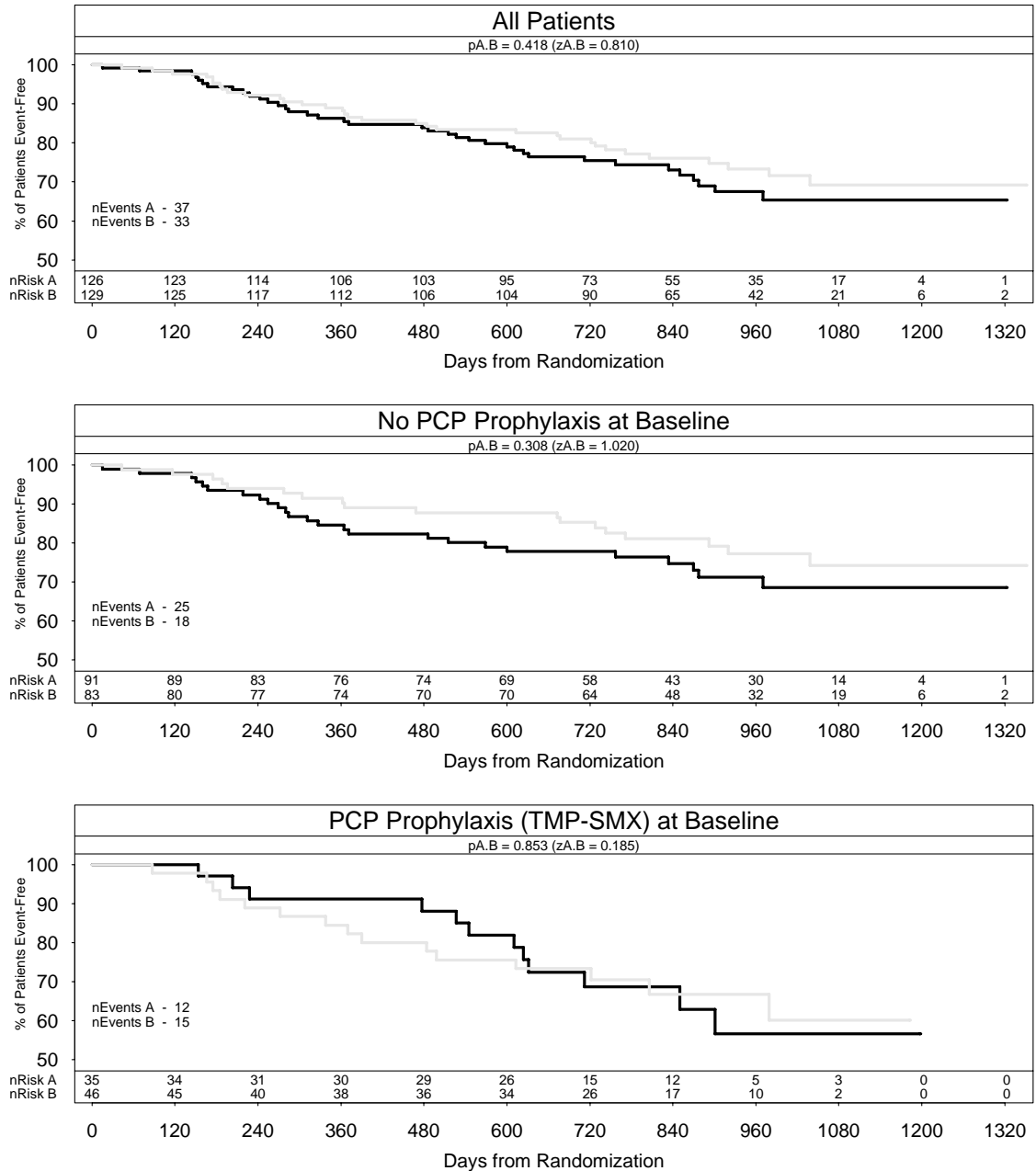
Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994. Patients with no event are censored at the date of last known contact.



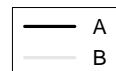
See Table Set TTEVNT-1 on page 46.

Figure TTEVNT-2

Death



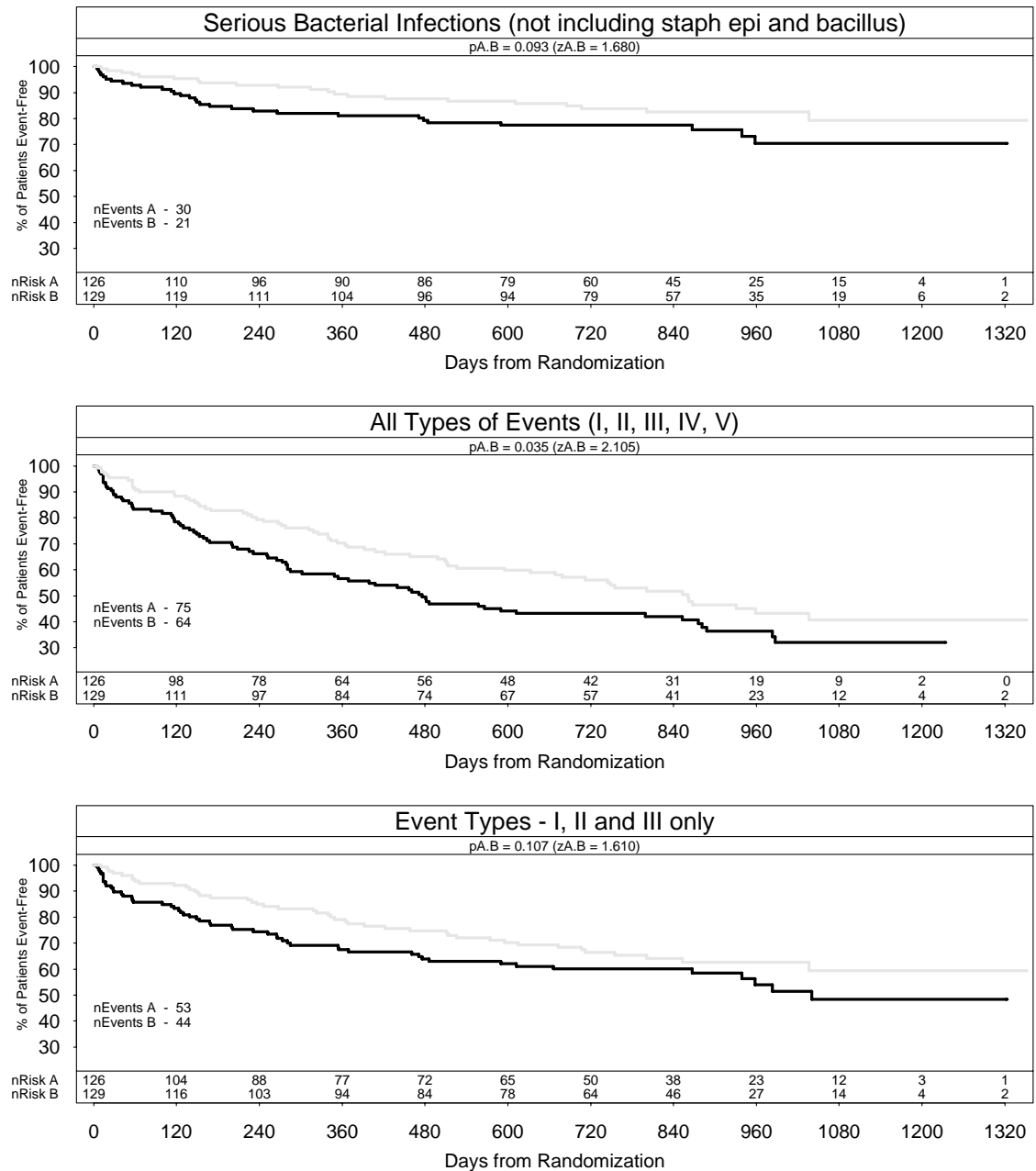
Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994. Patients with no event are censored at the date of last known contact.



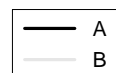
See Table Set TTEVNT-2 on page 47.

Figure TTEVNT-3

Other Serious Bacterial Infections



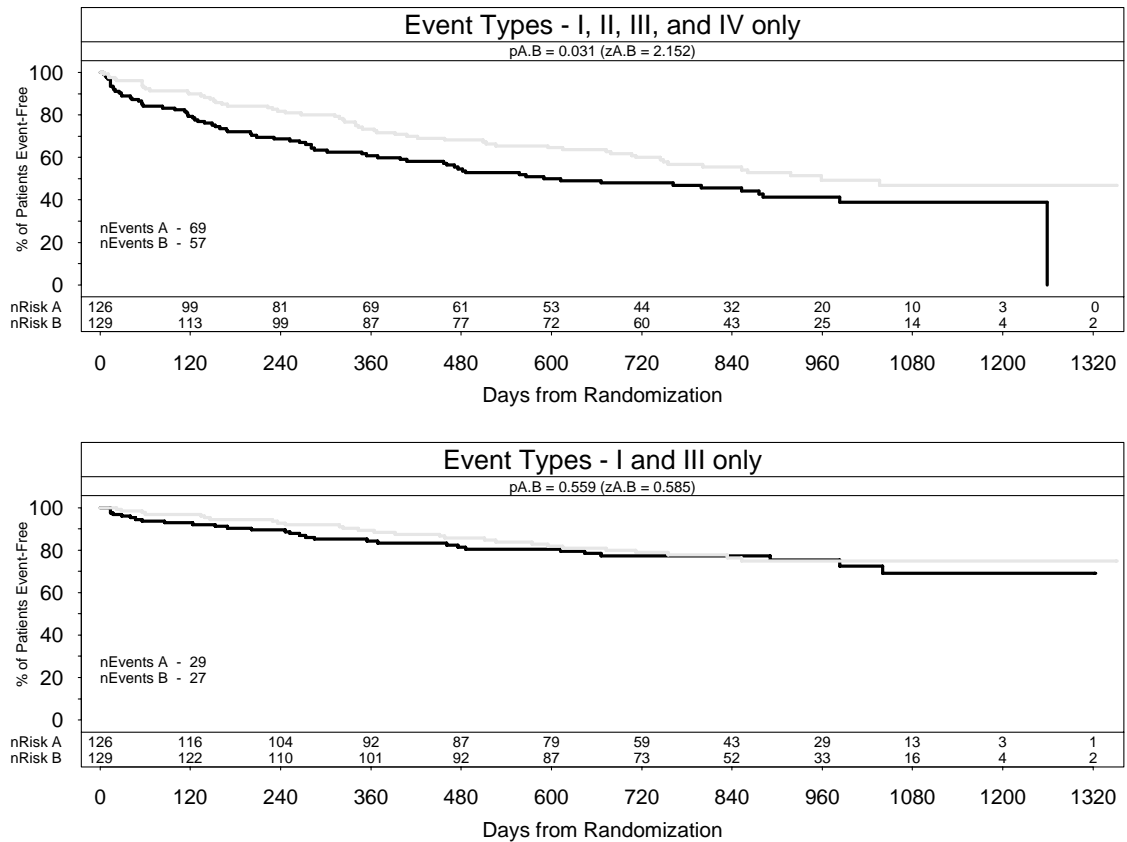
Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994. Patients with no event are censored at the date of last known contact. See the *Introduction* for a more detailed description of the types of serious bacterial infections.



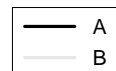
See Table Set TTEVNT-3 on page 49.

Figure TTEVNT-4

Other Serious Bacterial Infections



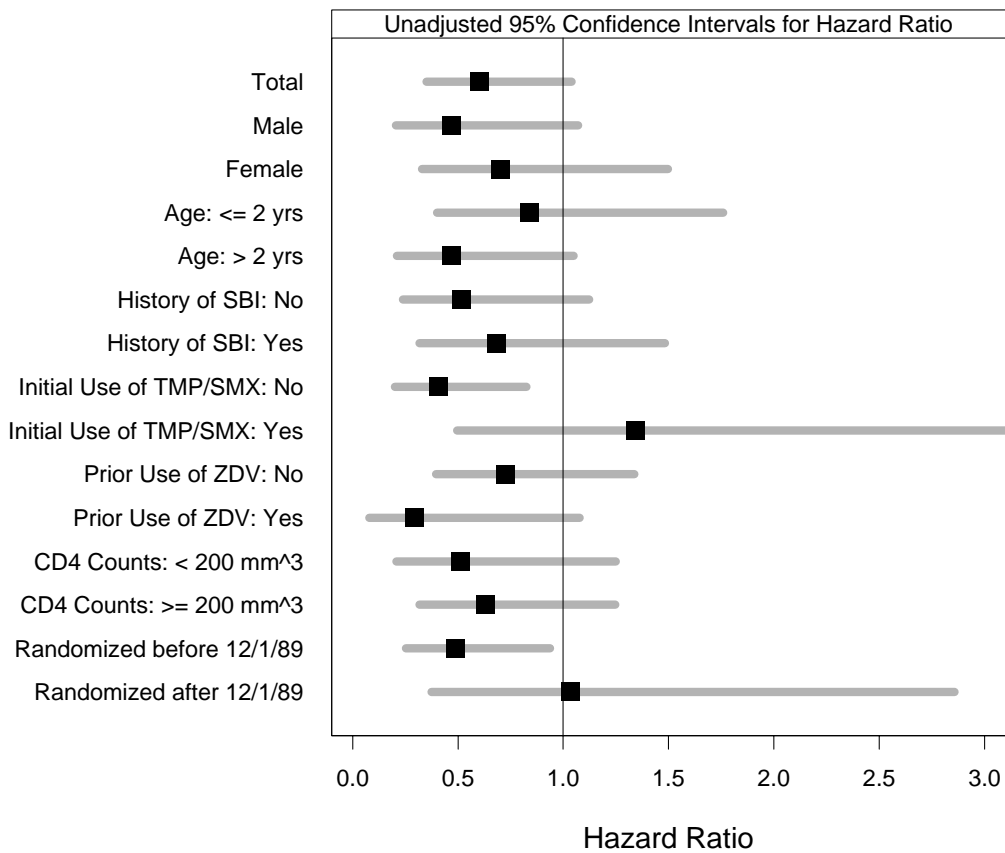
Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994. Patients with no event are censored at the date of last known contact. See the *Introduction* for a more detailed description of the types of serious bacterial infections.



See Table Set TTEVNT-4 on page 51.

Figure HAZ-1

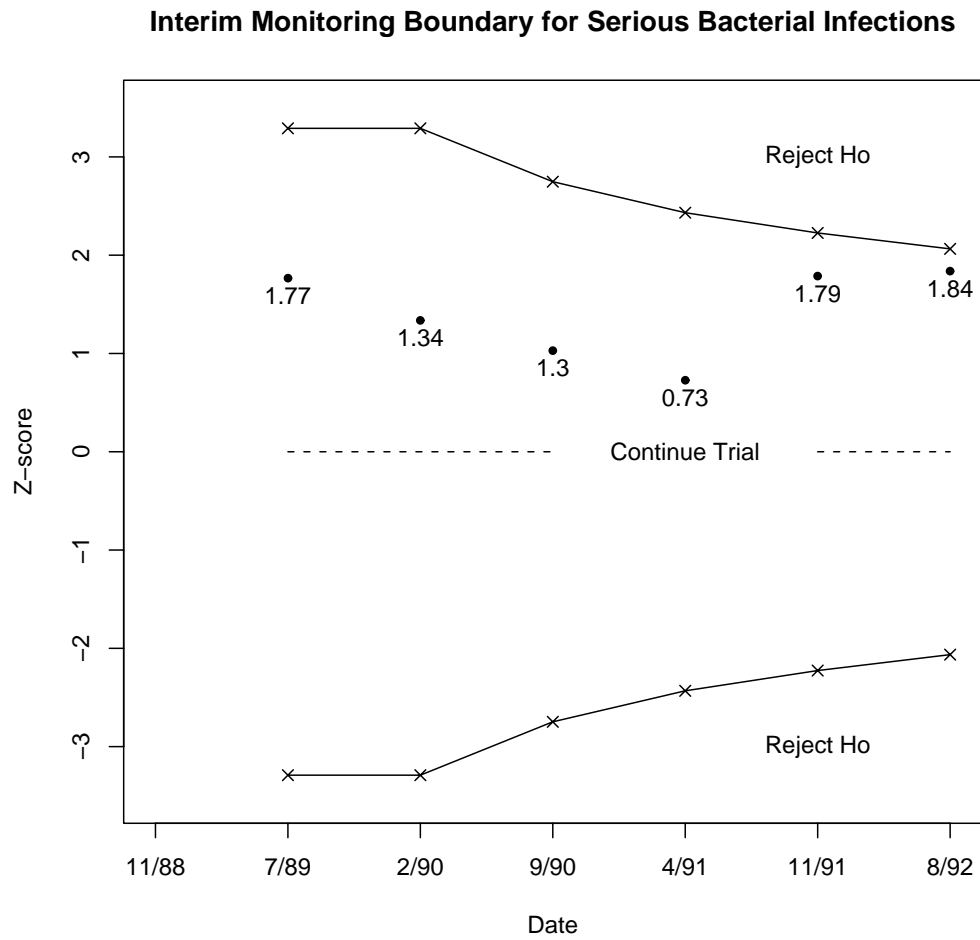
Hazard Ratios for Serious Bacterial Infections (B/A)



Subgroup	Tot		Events/N Pats (%)				Hazard Ratio	(95% CI)	P Value
			A		B				
Total	54/255	21.2%	32/126	25.4%	22/129	17.1%	0.60	(0.35,1.04)	0.069
Male	27/142	19.0%	19/78	24.4%	8/64	12.5%	0.47	(0.21,1.07)	0.072
Female	27/112	24.1%	13/48	27.1%	14/64	21.9%	0.70	(0.33,1.50)	0.361
Age: ≤ 2 yrs	29/110	26.4%	17/62	27.4%	12/48	25.0%	0.84	(0.40,1.76)	0.643
Age: > 2 yrs	25/145	17.2%	15/64	23.4%	10/81	12.3%	0.47	(0.21,1.05)	0.065
History of SBI: No	28/142	19.7%	18/72	25.0%	10/70	14.3%	0.52	(0.24,1.12)	0.095
History of SBI: Yes	26/113	23.0%	14/54	25.9%	12/59	20.3%	0.69	(0.32,1.48)	0.338
Initial Use of TMP/SMX: No	37/174	21.3%	26/91	28.6%	11/83	13.3%	0.41	(0.20,0.83)	0.013
Initial Use of TMP/SMX: Yes	17/81	21.0%	6/35	17.1%	11/46	23.9%	1.34	(0.50,3.63)	0.563
Prior Use of ZDV: No	42/190	22.1%	23/93	24.7%	19/97	19.6%	0.73	(0.40,1.34)	0.307
Prior Use of ZDV: Yes	12/65	18.5%	9/33	27.3%	3/32	9.4%	0.29	(0.08,1.08)	0.064
CD4 Counts: < 200 mm ³	20/74	27.0%	12/35	34.3%	8/39	20.5%	0.51	(0.21,1.25)	0.141
CD4 Counts: ≥ 200 mm ³	34/181	18.8%	20/91	22.0%	14/90	15.6%	0.63	(0.32,1.25)	0.184
Randomized before 12/1/89	39/135	28.9%	25/67	37.3%	14/68	20.6%	0.49	(0.25,0.94)	0.031
Randomized after 12/1/89	15/120	12.5%	7/59	11.9%	8/61	13.1%	1.04	(0.38,2.86)	0.946

Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994. Hazard ratios > 1 indicate benefit for group "A"; hazard ratios < 1 indicate benefit for group "B."

Figure BOUND-1



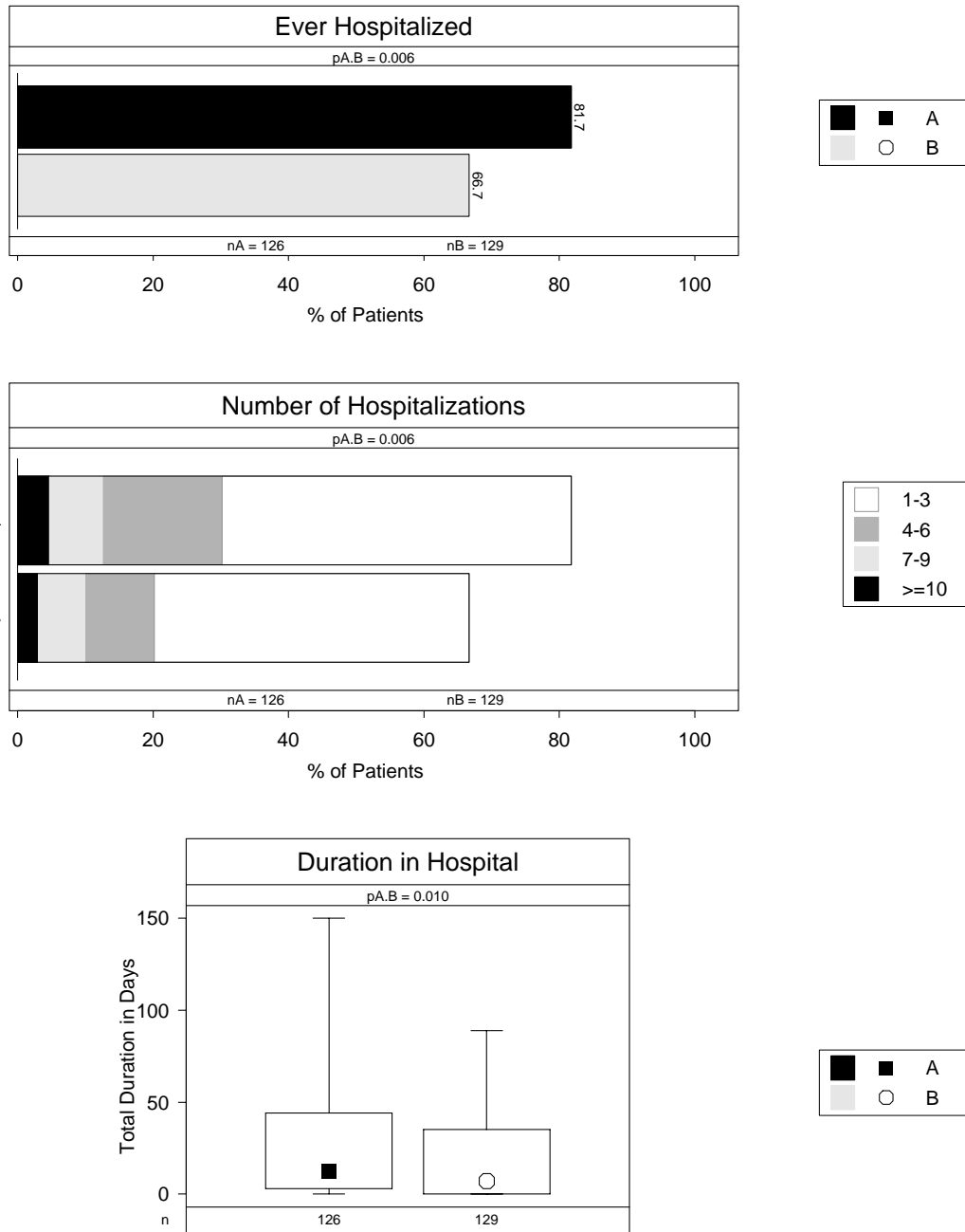
Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994. Z-values and dates were estimated by Beta Biostatistics, Inc. from the data for display purposes only.

Chapter 4

Safety Measures

Figure HOSP-1

Hospitalization Summary

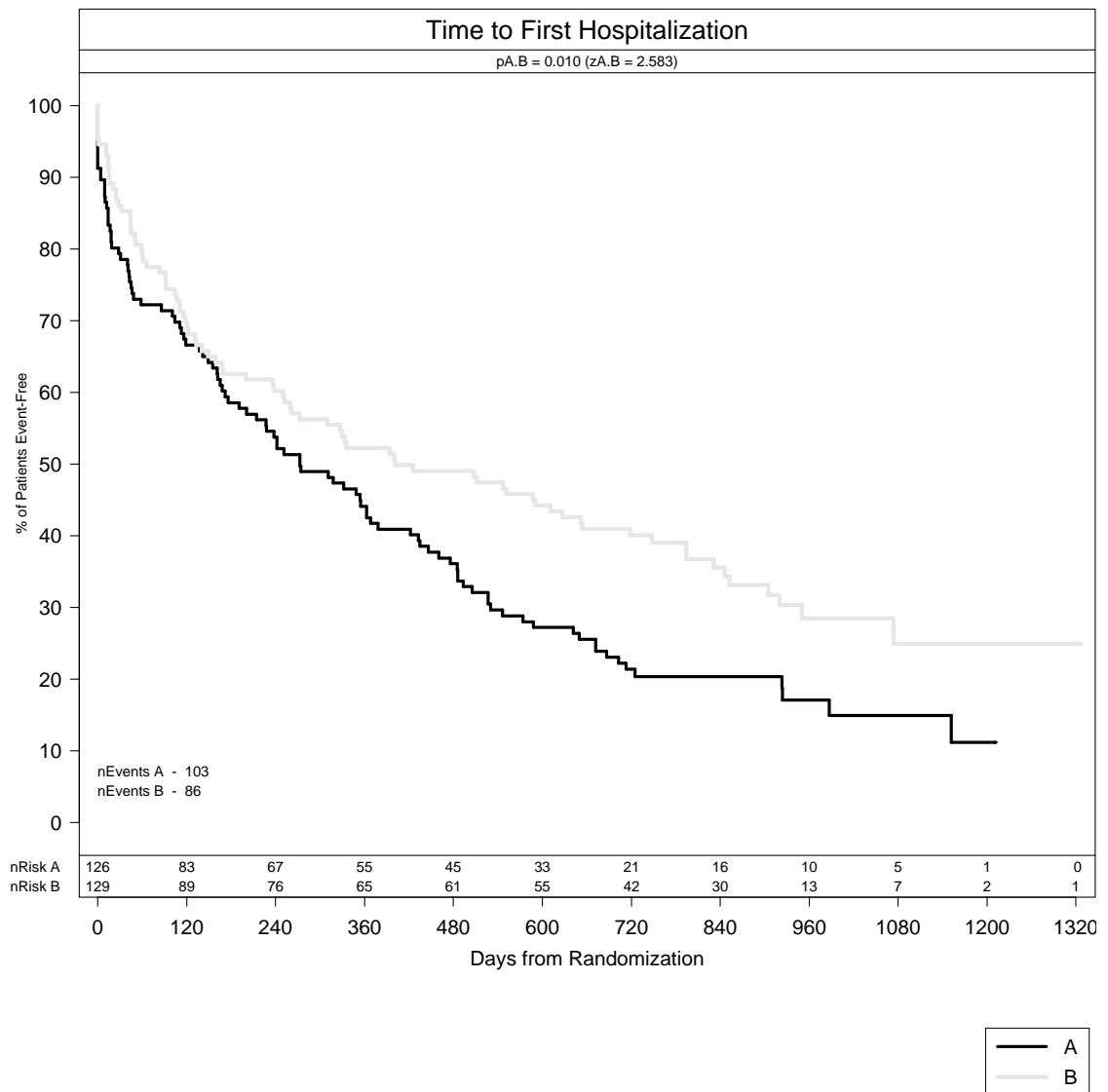


Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994. The denominator for percentages is all randomized patients.

See Table Set HOSP-1 on page 53.

Figure HOSP-2

Kaplan Meier Plot of Hospitalization

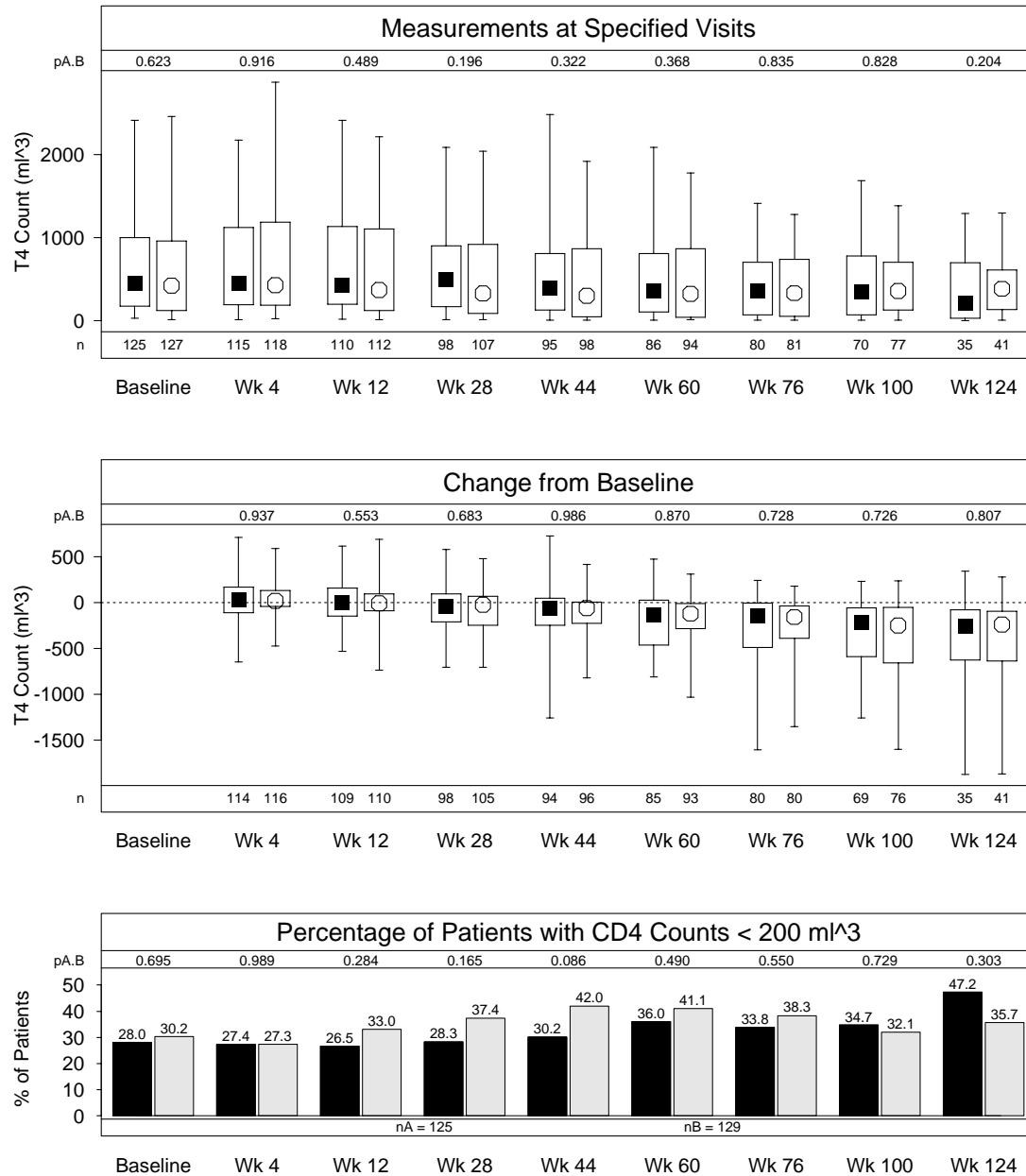


Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994. Patients with no event are censored at the last day of known contact.

See Table Set HOSP-2 on page 54.

Figure CD-1

CD4 Counts, by Visit



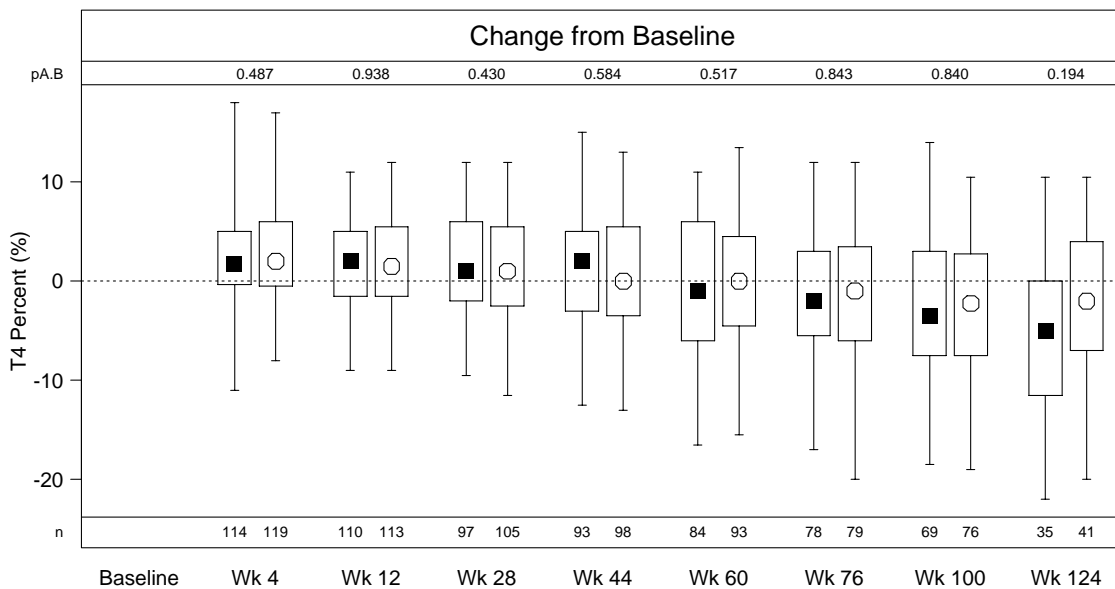
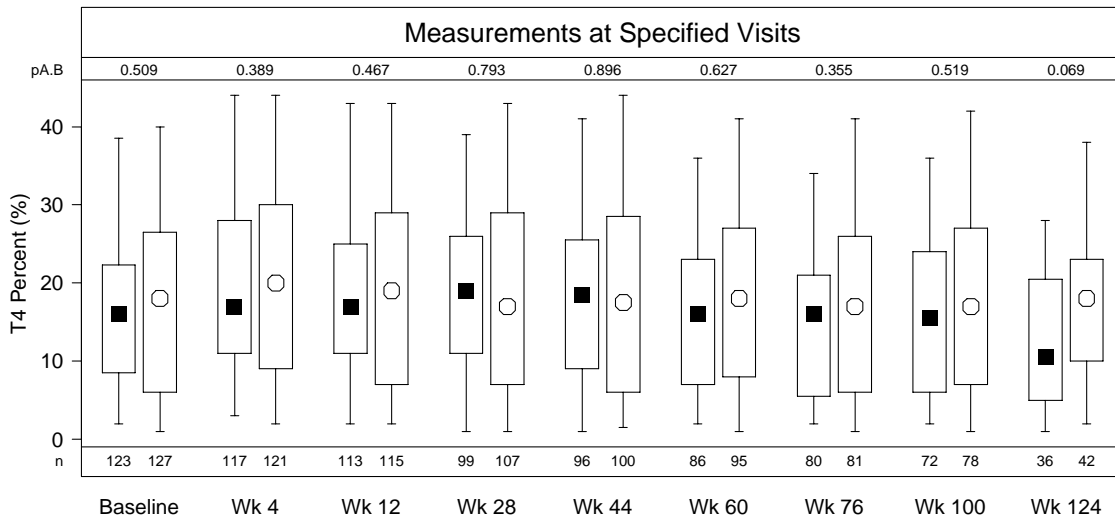
Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994. The sample sizes for each graphic are the number of patients with non-missing data for the variable being displayed.



See Table Set CD-1 on page 54.

Figure CD-2

CD4 Percentages, by Visit



Information from the *Intravenous Immune Globulin and Zidovudine use in Children with HIV* study sponsored by the National Institute of Child Health and Human Development and the Pediatric AIDS Clinical Trials group which was published in *NEJM* on November 3, 1994. The sample sizes for each graphic are the number of patients with non-missing data for the variable being displayed.



See Table Set CD-2 on page 56.

Part III

Supporting Material

Chapter 2

Baseline Characteristics

Table Set BASE-1

Baseline Characteristics: Sex

See Figure BASE-1 on page 20.

Trt	Total Pats	Value				Contrast	P- Value
		Male		Female			
		N	%	N	%		
A	126	78	61.90	48	38.10	A.B	0.056
B	128	64	50.00	64	50.00		

Baseline Characteristics: Age at Baseline

See Figure BASE-1 on page 20.

Trt	Total Pats	Std		Median	Q1	Q3	P5	P95	Contrast	P- Value
		Mean	Dev							
A	126	3.37	3.08	2.03	1.01	4.98	0.41	10.00	A.B	0.097
B	129	4.01	3.14	3.39	1.17	6.29	0.41	9.94		

Baseline Characteristics: Age (categorized)

See Figure BASE-1 on page 20.

Trt	Total Pats	Value				Contrast	P- Value
		> 2 yrs		≤ 2 yrs			
		N	%	N	%		
A	126	64	50.79	62	49.21	A.B	0.053
B	129	81	62.79	48	37.21		

Baseline Characteristics: History of Bacterial Infections

See Figure BASE-1 on page 20.

Trt	Total Pats	Value				Contrast	P- Value
		No		Yes			
		N	%	N	%		
A	126	72	57.14	54	42.86	A.B	0.64
B	129	70	54.26	59	45.74		

Baseline Characteristics: ZDV Prior to Start of Therapy

See Figure BASE-1 on page 20.

Trt	Total Pats	Value				Contrast	P-Value
		No		Yes			
		N	%	N	%		
A	126	93	73.81	33	26.19	A.B	0.80
B	129	97	75.19	32	24.81		

Baseline Characteristics: Race

See Figure BASE-1 on page 20.

	Treatment Group				Contrast	P-Value
	A		B			
	N	%	N	%		
Total Patients	126		128		A.B	0.87
White, Hispanic	33	26.19	40	31.25		
White, Non-Hispanic	24	19.05	22	17.19		
Black, Hispanic	5	3.97	3	2.34		
Black, Non-Hispanic	49	38.89	51	39.84		
Other, Hispanic	10	7.94	9	7.03		
Other, Non-Hispanic	5	3.97	3	2.34		

Table Set BASE-2

Baseline CD4 Counts and IGG (Closed Session Version): PCP Proph Use at Baseline

See Figure BASE-2 on page 21.

Trt	Total Pats	Value				Contrast	P-Value
		No		Yes			
		N	%	N	%		
A	126	91	72.22	35	27.78	A.B	0.18
B	129	83	64.34	46	35.66		

Baseline CD4 Counts and IGG (Closed Session Version): CD4 (categorized)

See Figure BASE-2 on page 21.

Trt	Total Pats	Value				Contrast	P-Value
		< 200 ml ³		≥ 200 ml ³			
		N	%	N	%		
A	126	35	27.78	91	72.22	A.B	0.67
B	129	39	30.23	90	69.77		

Baseline CD4 Counts and IGG (Closed Session Version): T4 (counts)

See Figure BASE-2 on page 21.

Trt	Total Pats	Std							Contrast	P-Value
		Mean	Dev	Median	Q1	Q3	P5	P95		
A	125	730	756	455	175	1000	28	2412	A.B	0.62
B	127	717	788	423	124	963	14	2462		

Baseline CD4 Counts and IGG (Closed Session Version): T4 (%)

See Figure BASE-2 on page 21.

Trt	Total Pats	Std							Contrast	P-Value
		Mean	Dev	Median	Q1	Q3	P5	P95		
A	125	17.8	16.1	16.0	8.5	22.3	2.0	38.5	A.B	0.50
B	129	17.9	12.5	18.0	6.0	26.5	1.0	40.0		

Baseline CD4 Counts and IGG (Closed Session Version): IGG (categorized)

See Figure BASE-2 on page 21.

Trt	Total Pats	Value						Contrast	P-Value
		hypo		normal		hyper			
		N	%	N	%	N	%		
A	122	6	4.92	16	13.11	100	81.97	A.B	0.73
B	127	4	3.15	15	11.81	108	85.04		

Baseline CD4 Counts and IGG (Closed Session Version): IGG at Baseline

See Figure BASE-2 on page 21.

Trt	Total Pats	Std							Contrast	P-Value
		Mean	Dev	Median	Q1	Q3	P5	P95		
A	122	2430	1252	2365	1600	3050	471	4943	A.B	0.84
B	127	2573	1653	2340	1618	3375	406	4830		

Table Set OPEN-1

Baseline CD4 Counts and IGG Open Session Version: PCP Proph Use at Baseline

See Figure OPEN-1 on page 22.

Trt	Total Pats	Value			
		No		Yes	
		N	%	N	%
Total	255	174	68.24	81	31.76

Baseline CD4 Counts and IGG Open Session Version: CD4 (categorized)

See Figure OPEN-1 on page 22.

Trt	Total Pats	Value			
		< 200 ml ³		≥ 200 ml ³	
		N	%	N	%
Total	255	74	29.02	181	70.98

Baseline CD4 Counts and IGG Open Session Version: T4 (counts)

See Figure OPEN-1 on page 22.

Trt	Total Pats	Std						
		Mean	Dev	Median	Q1	Q3	P5	P95
Overall	252	723	771	444	156	991	18	2462

Baseline CD4 Counts and IGG Open Session Version: T4 (%)

See Figure OPEN-1 on page 22.

Trt	Total Pats	Std						
		Mean	Dev	Median	Q1	Q3	P5	P95
Overall	254	17.9	14.3	16.5	7.5	25.0	1.0	39.0

Baseline CD4 Counts and IGG Open Session Version: IGG (categorized)

See Figure OPEN-1 on page 22.

Trt	Total Pats	Value					
		hypo		normal		hyper	
		N	%	N	%	N	%
Total	249	10	4.02	31	12.45	208	83.53

Baseline CD4 Counts and IGG Open Session Version: IGG at Baseline

See Figure OPEN-1 on page 22.

Trt	Total Pats	Std						
		Mean	Dev	Median	Q1	Q3	P5	P95
Overall	249	2503	1469	2340	1618	3155	416	4943

Table Set BASE-3

Baseline Laboratory Measures: Granulocytes

See Figure BASE-3 on page 23.

Trt	Total Pats	Std							Contrast	P-Value
		Mean	Dev	Median	Q1	Q3	P5	P95		
A	124	2923	1765	2570	1718	3661	1036	6039	A.B	0.78
B	127	3076	2056	2496	1770	3774	1060	7392		

Baseline Laboratory Measures: Mean Cell Volume

See Figure BASE-3 on page 23.

Trt	Total Pats	Std							Contrast	P-Value
		Mean	Dev	Median	Q1	Q3	P5	P95		
A	124	88.0	62.3	81.0	77.0	86.0	71.0	99.0	A.B	0.53
B	127	82.0	8.5	81.0	77.0	87.0	71.0	98.0		

Baseline Laboratory Measures: Hematocrit

See Figure BASE-3 on page 23.

Trt	Total Pats	Std							Contrast	P-Value
		Mean	Dev	Median	Q1	Q3	P5	P95		
A	125	31.93	4.03	31.70	29.30	34.90	25.70	38.40	A.B	0.96
B	128	31.82	4.12	31.90	29.15	35.00	24.30	37.90		

Baseline Laboratory Measures: Hemoglobin

See Figure BASE-3 on page 23.

Trt	Total Pats	Std							Contrast	P- Value
		Mean	Dev	Median	Q1	Q3	P5	P95		
A	125	10.56	1.42	10.40	9.70	11.60	8.20	12.90	A.B	0.81
B	128	10.49	1.41	10.40	9.50	11.50	8.10	12.80		

Baseline Laboratory Measures: Platelets

See Figure BASE-3 on page 23.

Trt	Total Pats	Std							Contrast	P- Value
		Mean	Dev	Median	Q1	Q3	P5	P95		
A	124	315	219	302	216	378	108	523	A.B	0.54
B	126	308	123	300	217	404	107	521		

Baseline Laboratory Measures: White Blood Cell

See Figure BASE-3 on page 23.

Trt	Total Pats	Std							Contrast	P- Value
		Mean	Dev	Median	Q1	Q3	P5	P95		
A	125	7854	4697	6700	4400	10200	3000	16100	A.B	0.47
B	128	7394	4031	6100	4650	9150	3200	15100		

Chapter 3

Efficacy Endpoints

Table Set PRIMARY-1

Serious Bacterial Infection: Time to First Serious Bacterial Infection

See Figure PRIMARY-1 on page 26.

Treatment A						
Days	Number at Risk	Number of Events	Event-Free %	Std Error	95% Confidence Limits	
					Lower	Upper
0	126	0	100.0	0.0	100.0	100.0
120	108	15	88.0	2.9	82.5	93.9
240	95	7	82.2	3.4	75.7	89.2
360	88	3	79.5	3.7	72.6	87.0
480	84	2	77.7	3.8	70.5	85.5
600	77	2	75.7	3.9	68.4	83.9
720	59	0	75.7	3.9	68.4	83.9
840	45	0	75.7	3.9	68.4	83.9
960	25	3	68.8	5.3	59.2	80.0
1080	15	0	68.8	5.3	59.2	80.0
1200	4	0	68.8	5.3	59.2	80.0
1320	1	0	68.8	5.3	59.2	80.0

Serious Bacterial Infection: Time to First Serious Bacterial Infection

See Figure PRIMARY-1 on page 26.

Treatment B						
Days	Number at Risk	Number of Events	Event-Free %	Std Error	95% Confidence Limits	
					Lower	Upper
0	129	0	100.0	0.0	100.0	100.0
120	119	6	95.3	1.9	91.7	99.0
240	110	4	92.1	2.4	87.4	96.9
360	104	4	88.7	2.9	83.2	94.4
480	96	2	86.9	3.1	81.1	93.1
600	94	1	86.0	3.2	80.0	92.4
720	79	3	83.1	3.5	76.6	90.2
840	57	1	81.8	3.7	74.9	89.3
960	35	0	81.8	3.7	74.9	89.3
1080	19	1	78.7	4.7	70.0	88.4
1200	6	0	78.7	4.7	70.0	88.4
1320	2	0	78.7	4.7	70.0	88.4

Table Set TTEVNT-1

Serious Bacterial Infection by Prophylaxis Use at Baseline: No PCP Prophylaxis at Baseline

See Figure TTEVNT-1 on page 28.

Treatment A						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	91	0	100.0	0.0	100.0	100.0
120	77	12	86.7	3.6	80.0	94.0
240	67	5	80.9	4.2	73.1	89.5
360	62	2	78.4	4.4	70.3	87.5
480	59	2	75.9	4.6	67.3	85.5
600	55	2	73.2	4.8	64.4	83.3
720	47	0	73.2	4.8	64.4	83.3
840	36	0	73.2	4.8	64.4	83.3
960	22	3	65.6	6.1	54.7	78.6
1080	13	0	65.6	6.1	54.7	78.6
1200	4	0	65.6	6.1	54.7	78.6
1320	1	0	65.6	6.1	54.7	78.6

Serious Bacterial Infection by Prophylaxis Use at Baseline: No PCP Prophylaxis at Baseline

See Figure TTEVNT-1 on page 28.

Treatment B						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	83	0	100.0	0.0	100.0	100.0
120	76	4	95.2	2.4	90.6	99.9
240	72	2	92.6	2.9	87.1	98.5
360	68	3	88.7	3.5	82.0	96.0
480	64	0	88.7	3.5	82.0	96.0
600	64	0	88.7	3.5	82.0	96.0
720	58	0	88.7	3.5	82.0	96.0
840	43	1	86.8	4.0	79.4	94.9
960	27	0	86.8	4.0	79.4	94.9
1080	17	1	83.0	5.3	73.3	94.1
1200	6	0	83.0	5.3	73.3	94.1
1320	2	0	83.0	5.3	73.3	94.1

Serious Bacterial Infection by Prophylaxis Use at Baseline: PCP Prophylaxis (TMP-SMX) at Baseline

See Figure TTEVNT-1 on page 28.

Treatment A						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	35	0	100.0	0.0	100.0	100.0
120	31	3	91.3	4.8	82.4	100.0
240	28	2	85.4	6.0	74.4	98.1
360	26	1	82.3	6.6	70.4	96.2
480	25	0	82.3	6.6	70.4	96.2
600	22	0	82.3	6.6	70.4	96.2
720	12	0	82.3	6.6	70.4	96.2
840	9	0	82.3	6.6	70.4	96.2
960	3	0	82.3	6.6	70.4	96.2
1080	2	0	82.3	6.6	70.4	96.2

Serious Bacterial Infection by Prophylaxis Use at Baseline: PCP Prophylaxis (TMP-SMX) at Baseline

See Figure TTEVNT-1 on page 28.

Treatment B						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	46	0	100.0	0.0	100.0	100.0
120	43	2	95.6	3.0	89.8	100.0
240	38	2	91.1	4.3	83.0	99.8
360	36	1	88.6	4.8	79.6	98.5
480	32	2	83.5	5.7	73.0	95.5
600	30	1	80.8	6.1	69.6	93.8
720	21	3	72.3	7.2	59.5	87.9
840	14	0	72.3	7.2	59.5	87.9
960	8	0	72.3	7.2	59.5	87.9
1080	2	0	72.3	7.2	59.5	87.9

Table Set TTEVNT-2

Death: All Patients

See Figure TTEVNT-2 on page 29.

Treatment A						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	126	0	100.0	0.0	100.0	100.0
120	123	2	98.4	1.1	96.3	100.0
240	114	8	92.0	2.4	87.4	96.9
360	106	7	86.3	3.1	80.5	92.6
480	103	3	83.9	3.3	77.6	90.6
600	95	6	78.9	3.7	72.0	86.5
720	73	4	75.4	3.9	68.2	83.5
840	55	2	73.0	4.1	65.4	81.6
960	35	4	67.5	4.7	59.0	77.3
1080	17	1	65.3	5.0	56.2	75.9
1200	4	0	65.3	5.0	56.2	75.9
1320	1	0	65.3	5.0	56.2	75.9

Death: All Patients

See Figure TTEVNT-2 on page 29.

Treatment B						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	129	0	100.0	0.0	100.0	100.0
120	125	3	97.7	1.3	95.1	100.0
240	117	7	92.2	2.4	87.6	96.9
360	112	4	89.0	2.8	83.7	94.6
480	106	5	85.0	3.2	79.0	91.5
600	104	2	83.4	3.3	77.2	90.1
720	90	3	81.0	3.5	74.4	88.1
840	65	5	76.1	3.9	68.8	84.2
960	42	2	73.4	4.2	65.5	82.1
1080	21	2	69.2	4.9	60.2	79.6
1200	6	0	69.2	4.9	60.2	79.6
1320	2	0	69.2	4.9	60.2	79.6

Death: No PCP Prophylaxis at Baseline

See Figure TTEVNT-2 on page 29.

Treatment A						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	91	0	100.0	0.0	100.0	100.0
120	89	2	97.8	1.5	94.8	100.0
240	83	5	92.3	2.8	87.0	97.9
360	76	7	84.5	3.8	77.4	92.3
480	74	2	82.3	4.0	74.8	90.6
600	69	4	77.8	4.4	69.7	86.9
720	58	0	77.8	4.4	69.7	86.9
840	43	2	74.7	4.7	66.0	84.6
960	30	2	71.2	5.1	61.8	82.0
1080	14	1	68.6	5.6	58.5	80.4
1200	4	0	68.6	5.6	58.5	80.4
1320	1	0	68.6	5.6	58.5	80.4

Death: No PCP Prophylaxis at Baseline

See Figure TTEVNT-2 on page 29.

Treatment B						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	83	0	100.0	0.0	100.0	100.0
120	80	2	97.6	1.7	94.3	100.0
240	77	3	93.9	2.6	88.9	99.2
360	74	2	91.5	3.1	85.6	97.7
480	70	3	87.7	3.6	80.9	95.2
600	70	0	87.7	3.6	80.9	95.2
720	64	2	85.2	3.9	77.8	93.3
840	48	3	81.0	4.4	72.8	90.2
960	32	2	77.2	5.0	68.0	87.6
1080	19	1	74.2	5.6	64.0	86.1
1200	6	0	74.2	5.6	64.0	86.1
1320	2	0	74.2	5.6	64.0	86.1

Death: PCP Prophylaxis (TMP-SMX) at Baseline

See Figure TTEVNT-2 on page 29.

Treatment A						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	35	0	100.0	0.0	100.0	100.0
120	34	0	100.0	0.0	100.0	100.0
240	31	3	91.2	4.9	82.1	100.0
360	30	0	91.2	4.9	82.1	100.0
480	29	1	88.1	5.6	77.9	99.8
600	26	2	81.9	6.7	69.8	96.2
720	15	4	68.7	8.3	54.2	87.0
840	12	0	68.7	8.3	54.2	87.0
960	5	2	56.7	10.3	39.6	81.0
1080	3	0	56.7	10.3	39.6	81.0

Death: PCP Prophylaxis (TMP-SMX) at Baseline

See Figure TTEVNT-2 on page 29.

Treatment B						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	46	0	100.0	0.0	100.0	100.0
120	45	1	97.8	2.2	93.7	100.0
240	40	4	88.9	4.7	80.2	98.6
360	38	2	84.5	5.4	74.6	95.7
480	36	2	80.0	6.0	69.2	92.6
600	34	2	75.6	6.4	64.0	89.2
720	26	1	73.4	6.6	61.5	87.5
840	17	2	66.8	7.5	53.7	83.2
960	10	0	66.8	7.5	53.7	83.2
1080	2	1	60.2	9.2	44.5	81.3

Table Set TTEVNT-3

Other Serious Bacterial Infections: Serious Bacterial Infections (not including staph epi and bacillus)

See Figure TTEVNT-3 on page 30.

Treatment A						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	126	0	100.0	0.0	100.0	100.0
120	110	13	89.6	2.7	84.4	95.1
240	96	8	83.0	3.4	76.6	89.9
360	90	2	81.2	3.5	74.5	88.4
480	86	2	79.3	3.7	72.4	86.9
600	79	2	77.4	3.8	70.3	85.4
720	60	0	77.4	3.8	70.3	85.4
840	45	0	77.4	3.8	70.3	85.4
960	25	3	70.4	5.3	60.8	81.5
1080	15	0	70.4	5.3	60.8	81.5
1200	4	0	70.4	5.3	60.8	81.5
1320	1	0	70.4	5.3	60.8	81.5

Other Serious Bacterial Infections: Serious Bacterial Infections (not including staph epi and bacillus)

See Figure TTEVNT-3 on page 30.

Treatment B						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	129	0	100.0	0.0	100.0	100.0
120	119	6	95.3	1.9	91.7	99.0
240	111	3	92.9	2.3	88.5	97.5
360	104	4	89.5	2.8	84.2	95.1
480	96	2	87.7	3.0	82.0	93.7
600	94	1	86.8	3.1	80.9	93.0
720	79	3	83.9	3.4	77.5	90.8
840	57	1	82.5	3.6	75.7	89.9
960	35	0	82.5	3.6	75.7	89.9
1080	19	1	79.4	4.7	70.7	89.0
1200	6	0	79.4	4.7	70.7	89.0
1320	2	0	79.4	4.7	70.7	89.0

Other Serious Bacterial Infections: All Types of Events (I, II, III, IV, V)

See Figure TTEVNT-3 on page 30.

Treatment A						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	126	0	100.0	0.0	100.0	100.0
120	98	27	78.5	3.7	71.7	86.0
240	78	15	66.3	4.2	58.4	75.1
360	64	11	56.7	4.5	48.5	66.2
480	56	8	49.6	4.6	41.3	59.4
600	48	6	44.2	4.6	36.0	54.1
720	42	1	43.2	4.6	35.1	53.2
840	31	1	42.1	4.6	33.9	52.1
960	19	4	36.3	4.8	28.1	47.1
1080	9	2	32.1	5.1	23.5	43.8
1200	2	0	32.1	5.1	23.5	43.8

Other Serious Bacterial Infections: All Types of Events (I, II, III, IV, V)

See Figure TTEVNT-3 on page 30.

Treatment B						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	129	0	100.0	0.0	100.0	100.0
120	111	15	88.3	2.8	83.0	94.1
240	97	11	79.4	3.6	72.7	86.8
360	84	11	70.3	4.1	62.7	78.9
480	74	6	65.1	4.3	57.2	74.1
600	67	6	59.8	4.5	51.6	69.2
720	57	4	56.1	4.6	47.9	65.8
840	41	4	51.7	4.7	43.2	61.8
960	23	6	43.2	5.1	34.3	54.4
1080	12	1	40.7	5.4	31.3	52.7
1200	4	0	40.7	5.4	31.3	52.7
1320	2	0	40.7	5.4	31.3	52.7

Other Serious Bacterial Infections: Event Types - I, II and III only

See Figure TTEVNT-3 on page 30.

Treatment A						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	126	0	100.0	0.0	100.0	100.0
120	104	21	83.3	3.3	77.0	90.1
240	88	11	74.3	3.9	67.0	82.4
360	77	8	67.4	4.2	59.6	76.3
480	72	4	63.9	4.4	55.9	73.1
600	65	2	62.0	4.4	53.9	71.4
720	50	2	60.1	4.5	51.8	69.6
840	38	0	60.1	4.5	51.8	69.6
960	23	3	53.9	5.3	44.5	65.4
1080	12	2	48.3	6.1	37.8	61.8
1200	3	0	48.3	6.1	37.8	61.8
1320	1	0	48.3	6.1	37.8	61.8

Other Serious Bacterial Infections: Event Types - I, II and III only

See Figure TTEVNT-3 on page 30.

Treatment B						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	129	0	100.0	0.0	100.0	100.0
120	116	10	92.2	2.4	87.7	97.0
240	103	9	84.9	3.2	78.9	91.4
360	94	7	79.1	3.7	72.3	86.6
480	84	5	74.8	3.9	67.4	82.9
600	78	5	70.3	4.2	62.5	79.0
720	64	4	66.5	4.4	58.5	75.6
840	46	2	64.0	4.5	55.7	73.6
960	27	1	62.6	4.7	54.1	72.4
1080	14	1	59.4	5.4	49.8	71.0
1200	4	0	59.4	5.4	49.8	71.0
1320	2	0	59.4	5.4	49.8	71.0

Table Set TTEVNT-4

Other Serious Bacterial Infections: Event Types - I, II, III, and IV only

See Figure TTEVNT-4 on page 31.

Treatment A						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	126	0	100.0	0.0	100.0	100.0
120	99	26	79.3	3.6	72.5	86.7
240	81	13	68.7	4.2	61.0	77.4
360	69	9	60.8	4.4	52.7	70.2
480	61	7	54.6	4.6	46.3	64.3
600	53	5	50.0	4.6	41.7	59.9
720	44	2	48.1	4.6	39.8	58.1
840	32	2	45.6	4.7	37.3	55.9
960	20	3	41.2	4.9	32.6	52.0
1080	10	1	38.9	5.1	30.0	50.4
1200	3	0	38.9	5.1	30.0	50.4

Other Serious Bacterial Infections: Event Types - I, II, III, and IV only

See Figure TTEVNT-4 on page 31.

Treatment B						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	129	1	100.0	0.0	100.0	100.0
120	113	13	89.9	2.7	84.8	95.3
240	99	10	81.8	3.4	75.3	88.8
360	87	10	73.4	4.0	66.0	81.6
480	77	6	68.2	4.2	60.4	77.0
600	72	4	64.6	4.4	56.6	73.7
720	60	5	60.0	4.5	51.7	69.5
840	43	4	55.5	4.7	47.0	65.5
960	25	4	49.4	5.1	40.3	60.5
1080	14	1	46.8	5.5	37.2	58.8
1200	4	0	46.8	5.5	37.2	58.8
1320	2	0	46.8	5.5	37.2	58.8

Other Serious Bacterial Infections: Event Types - I and III only

See Figure TTEVNT-4 on page 31.

Treatment A						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	126	0	100.0	0.0	100.0	100.0
120	116	9	92.9	2.3	88.5	97.5
240	104	4	89.6	2.7	84.3	95.1
360	92	6	84.2	3.3	78.0	91.0
480	87	3	81.4	3.6	74.7	88.8
600	79	1	80.5	3.7	73.6	88.0
720	59	3	77.3	4.0	70.0	85.5
840	43	0	77.3	4.0	70.0	85.5
960	29	1	75.4	4.3	67.4	84.3
1080	13	2	69.1	5.8	58.5	81.5
1200	3	0	69.1	5.8	58.5	81.5
1320	1	0	69.1	5.8	58.5	81.5

Other Serious Bacterial Infections: Event Types - I and III only

See Figure TTEVNT-4 on page 31.

Treatment B						
Days	Number at Risk	Number of Events	Survival %	Std Error	95% Confidence Limits	
					Lower	Upper
0	129	0	100.0	0.0	100.0	100.0
120	122	4	96.9	1.5	94.0	99.9
240	110	5	92.8	2.3	88.4	97.5
360	101	4	89.3	2.8	84.0	95.0
480	92	4	85.7	3.2	79.6	92.2
600	87	4	81.9	3.6	75.2	89.3
720	73	3	79.0	3.8	71.8	86.9
840	52	2	76.3	4.2	68.6	84.9
960	33	1	74.8	4.3	66.8	83.8
1080	16	0	74.8	4.3	66.8	83.8
1200	4	0	74.8	4.3	66.8	83.8
1320	2	0	74.8	4.3	66.8	83.8

Chapter 4

Safety Measures

Table Set HOSP-1

Hospitalization Summary: Ever Hospitalized

See Figure HOSP-1 on page 35.

Trt	Total Pats	Value		Contrast	P-Value
		Yes N	%		
A	126	103	81.75	A.B	0.0060
B	129	86	66.67		

Hospitalization Summary: Number of Hospitalizations

See Figure HOSP-1 on page 35.

Trt	Total Pats	Value								Contrast	P-Value
		10 or More		7-9		4-6		1-3			
		N	%	N	%	N	%	N	%		
A	126	6	4.76	10	7.94	22	17.46	65	51.59	A.B	0.0065
B	129	4	3.10	9	6.98	13	10.08	60	46.51		

Hospitalization Summary: Duration in Hospital

See Figure HOSP-1 on page 35.

Trt	Total Pats	Std							Contrast	P-Value
		Mean	Dev	Median	Q1	Q3	P5	P95		
A	126	35.2	49.2	12.5	3.0	44.0	0.0	150.0	A.B	0.0099
B	129	22.3	35.0	7.0	0.0	35.0	0.0	89.0		

Table Set HOSP-2

Kaplan Meier Plot of Hospitalization: Time to First Hospitalization

See Figure HOSP-2 on page 36.

Treatment A						
Days	Number at Risk	Number of Events	Event-Free %	Std Error	95% Confidence Limits	
					Lower	Upper
0	126	11	91.3	2.5	86.5	96.3
120	83	31	66.6	4.2	58.8	75.4
240	67	16	53.8	4.5	45.7	63.2
360	55	12	44.1	4.4	36.2	53.8
480	45	10	36.1	4.3	28.6	45.6
600	33	11	27.2	4.0	20.4	36.3
720	21	7	21.4	3.7	15.2	30.0
840	16	1	20.3	3.7	14.3	28.9
960	10	2	17.1	3.7	11.1	26.2
1080	5	1	14.9	3.8	9.0	24.7
1200	1	1	11.2	4.3	5.3	23.9

Kaplan Meier Plot of Hospitalization: Time to First Hospitalization

See Figure HOSP-2 on page 36.

Treatment B						
Days	Number at Risk	Number of Events	Event-Free %	Std Error	95% Confidence Limits	
					Lower	Upper
0	129	6	95.3	1.9	91.8	99.1
120	89	33	69.7	4.0	62.2	78.1
240	76	12	60.2	4.3	52.3	69.3
360	65	10	52.3	4.4	44.3	61.7
480	61	4	49.0	4.4	41.1	58.6
600	55	6	44.2	4.4	36.4	53.8
720	42	5	40.0	4.4	32.3	49.6
840	30	4	35.6	4.4	27.9	45.4
960	13	5	28.5	4.6	20.8	39.1
1080	7	1	24.9	5.2	16.5	37.6
1200	2	0	24.9	5.2	16.5	37.6
1320	1	0	24.9	5.2	16.5	37.6

Table Set CD-1

CD4 Counts, by Visit: Measurements at Specified Visits

See Figure CD-1 on page 37.

	Trt	Total Pats	Std							Contrast	P-Value
			Mean	Dev	Median	Q1	Q3	P5	P95		
Baseline	A	125	730	756	455	175	1000	28	2412	A.B	0.62
	B	127	717	788	423	124	963	14	2462		
Wk 4	A	115	708	679	452	193	1123	14	2178	A.B	0.92
	B	118	781	885	428	186	1190	25	2875		
Wk 12	A	110	739	809	431	200	1134	21	2414	A.B	0.49
	B	112	721	851	372	124	1105	11	2218		
Wk 28	A	98	676	715	499	170	901	14	2090	A.B	0.20
	B	107	621	748	328	88	921	11	2040		

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CD4 Counts, by Visit: Measurements at Specified Visits

See Figure CD-1 on page 37.

	Trt	Total Pats	Std							Contrast	P- Value
			Mean	Dev	Median	Q1	Q3	P5	P95		
Wk 44	A	95	653	785	389	131	807	10	2487	A.B	0.32
	B	98	591	831	302	46	868	10	1918		
Wk 60	A	86	618	685	365	107	807	9	2087	A.B	0.37
	B	94	526	604	326	44	868	11	1781		
Wk 76	A	80	489	519	357	70	703	8	1416	A.B	0.84
	B	81	461	441	333	55	743	6	1278		
Wk 100	A	70	504	526	344	70	778	7	1687	A.B	0.83
	B	77	501	487	361	130	706	7	1386		
Wk 124	A	35	384	446	211	33	702	3	1291	A.B	0.20
	B	41	461	413	386	133	614	9	1300		

CD4 Counts, by Visit: Change from Baseline

See Figure CD-1 on page 37.

	Trt	Total Pats	Std							Contrast	P- Value
			Mean	Dev	Median	Q1	Q3	P5	P95		
Wk 4	A	114	13	443	33	-114	168	-650	708	A.B	0.94
	B	116	53	443	20	-45	133	-475	590		
Wk 12	A	109	43	523	-4	-148	157	-530	614	A.B	0.55
	B	110	-13	428	-10	-91	93	-736	690		
Wk 28	A	98	-59	482	-43	-210	92	-704	580	A.B	0.68
	B	105	-89	390	-25	-249	68	-704	476		
Wk 44	A	94	-153	580	-63	-250	46	-1257	728	A.B	0.99
	B	96	-102	448	-59	-225	6	-819	416		
Wk 60	A	85	-220	543	-134	-464	24	-808	474	A.B	0.87
	B	93	-200	392	-121	-283	-9	-1030	308		
Wk 76	A	80	-324	608	-146	-488	-4	-1603	240	A.B	0.73
	B	80	-293	429	-158	-390	-40	-1351	180		
Wk 100	A	69	-366	555	-212	-592	-60	-1258	233	A.B	0.73
	B	76	-401	514	-250	-660	-50	-1600	238		
Wk 124	A	35	-468	637	-261	-626	-82	-1871	340	A.B	0.81
	B	41	-467	661	-241	-636	-94	-1870	280		

CD4 Counts, by Visit: Percentage of Patients with CD4 Counts < 200 ml³

See Figure CD-1 on page 37.

	Trt	Total Pats	Value		Contrast	P-Value
			N	%		
Baseline	A	125	35	28.00	A.B	0.70
	B	129	39	30.23		
Wk 4	A	117	32	27.35	A.B	0.99
	B	121	33	27.27		
Wk 12	A	113	30	26.55	A.B	0.28
	B	115	38	33.04		
Wk 28	A	99	28	28.28	A.B	0.17
	B	107	40	37.38		
Wk 44	A	96	29	30.21	A.B	0.09
	B	100	42	42.00		
Wk 60	A	86	31	36.05	A.B	0.49
	B	95	39	41.05		
Wk 76	A	80	27	33.75	A.B	0.55
	B	81	31	38.27		
Wk 100	A	72	25	34.72	A.B	0.73
	B	78	25	32.05		
Wk 124	A	36	17	47.22	A.B	0.30
	B	42	15	35.71		

Table Set CD-2

CD4 Percentages, by Visit: Measurements at Specified Visits

See Figure CD-2 on page 38.

	Trt	Total Pats	Std							Contrast	P-Value
			Mean	Dev	Median	Q1	Q3	P5	P95		
Baseline	A	123	17.7	16.2	16.0	8.5	22.3	2.0	38.5	A.B	0.51
	B	127	17.9	12.5	18.0	6.0	26.5	1.0	40.0		
Wk 4	A	117	19.7	12.5	17.0	11.0	28.0	3.0	44.0	A.B	0.39
	B	121	21.0	13.2	20.0	9.0	30.0	2.0	44.0		
Wk 12	A	113	18.4	11.3	17.0	11.0	25.0	2.0	43.0	A.B	0.47
	B	115	19.7	13.2	19.0	7.0	29.0	2.0	43.0		
Wk 28	A	99	19.1	11.2	19.0	11.0	26.0	1.0	39.0	A.B	0.79
	B	107	19.2	13.8	17.0	7.0	29.0	1.0	43.0		
Wk 44	A	96	18.4	11.6	18.5	9.0	25.5	1.0	41.0	A.B	0.90
	B	100	18.7	13.8	17.5	6.0	28.5	1.5	44.0		
Wk 60	A	86	16.7	11.2	16.0	7.0	23.0	2.0	36.0	A.B	0.63
	B	95	18.2	13.1	18.0	8.0	27.0	1.0	41.0		
Wk 76	A	80	15.7	11.1	16.0	5.5	21.0	2.0	34.0	A.B	0.35
	B	81	17.8	13.2	17.0	6.0	26.0	1.0	41.0		

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CD4 Percentages, by Visit: Measurements at Specified Visits

See Figure CD-2 on page 38.

	Trt	Total Pats	Std							Contrast	P- Value
			Mean	Dev	Median	Q1	Q3	P5	P95		
Wk 100	A	72	16.2	11.0	15.5	6.0	24.0	2.0	36.0	A.B	0.52
	B	78	17.8	12.1	17.0	7.0	27.0	1.0	42.0		
Wk 124	A	36	13.0	10.3	10.5	5.0	20.5	1.0	28.0	A.B	0.07
	B	42	17.7	11.1	18.0	10.0	23.0	2.0	38.0		

CD4 Percentages, by Visit: Change from Baseline

See Figure CD-2 on page 38.

	Trt	Total Pats	Std							Contrast	P- Value
			Mean	Dev	Median	Q1	Q3	P5	P95		
Wk 4	A	114	2.07	14.34	1.75	-0.33	5.00	-11.00	18.00	A.B	0.49
	B	119	2.87	6.70	2.00	-0.50	6.00	-8.00	17.00		
Wk 12	A	110	1.12	13.45	2.00	-1.50	5.00	-9.00	11.00	A.B	0.94
	B	113	1.81	6.60	1.50	-1.50	5.50	-9.00	12.00		
Wk 28	A	97	0.72	13.69	1.00	-2.00	6.00	-9.50	12.00	A.B	0.43
	B	105	0.78	7.57	1.00	-2.50	5.50	-11.50	12.00		
Wk 44	A	93	1.30	7.43	2.00	-3.00	5.00	-12.50	15.00	A.B	0.58
	B	98	0.70	6.98	0.00	-3.50	5.50	-13.00	13.00		
Wk 60	A	84	-2.16	15.24	-1.00	-6.00	6.00	-16.50	11.00	A.B	0.52
	B	93	-0.35	8.05	0.00	-4.50	4.50	-15.50	13.50		
Wk 76	A	78	-3.05	16.06	-2.00	-5.50	3.00	-17.00	12.00	A.B	0.84
	B	79	-2.12	9.19	-1.00	-6.00	3.50	-20.00	12.00		
Wk 100	A	69	-3.59	16.80	-3.50	-7.50	3.00	-18.50	14.00	A.B	0.84
	B	76	-2.59	8.89	-2.25	-7.50	2.75	-19.00	10.50		
Wk 124	A	35	-8.07	20.83	-5.00	-11.50	0.00	-22.00	10.50	A.B	0.19
	B	41	-2.79	9.26	-2.00	-7.00	4.00	-20.00	10.50		

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