Sample Data Monitoring Committee Report

Cancer Research And Biostatistics

Prepared by: Adam Rosenthal
Date: February 14, 2024

(Sample DMC Report)

Contents

I Introduction

Overview

Cancer Research And Biostatistics (CRAB) is an independent company providing services such as final and interim reporting on ongoing clinical trial data for use of data monitoring committees (DMCs). The following sample DMC report is based on simulated data and demonstrates examples of tables and figures that can be produced and formatted for the purposes of a final report. The document was created using R Markdown, and created by importing SAS datasets featuring simulated clinical trial data.

All results in the included sample report are based on simulated data and should not be considered as reflective of findings from any genuine research studies. The simulated data in this report reflects a multi-center, two-arm randomized clinical trial in which 500 subjects are assigned randomly to a 1:1 study comparing a control arm treating patients with Drug X to an experimental arm treating patients with a combination of Drug X and Drug Y. Stratification factors for randomization include age (<65 vs. ≥65), histology (squamous vs. adenocarcinoma), and genetic risk level (low vs. high). Both arms have a treatment duration of 1.5 years, with up to 3.5 years of additional follow-up. This report exemplifies an interim analysis taking place approximately 2 years following the most recent enrollment to trial.

A full typical DMC report will include a list of all primary and secondary endpoints, a summary of inclusion and exclusion criteria, and a summary of schedules for patient visits and dosing regimens.

Protocol Synopsis

Protocol Title	A Randomized Phase III Study of Drug X With or Without Drug Y in Patients with NSCLC
Study Phase	Phase III
Study Design	Multicenter, randomized, open-label study
Principal Investigator	Florence Cox, MD
Planned Accrual	500 subjects
Randomization	1:1 (Experimental vs Control)
Treatment Arms	Control Arm, Experimental Arm
Stratification Factors	Age (<65 vs. ≥65), Histology (Squamous vs. Adenocarcinoma), Genetic Risk (Low vs. High)
Planned Treatment Duration	1.5 years
Planned Follow-up Duration	Up to 3.5 years from end of treatment
Primary Endpoint	Overall Survival
Key Secondary Endpoints	Safety
Key Inclusion Criteria	Must be ≥18 years old with histologically confirmed NSCLC, measurable disease, EcOG PS 0-1
Key Exclusion Criteria	No prior exposure to Drug X or Drug Y, no metastatic disease, no significant cardiovascular disease

Protocol Schema

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                    │                         │
                    │      Randomization      │
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                     ╱                       ╲
        ┌──────────────────────┐    ┌──────────────────────┐
        │                      │    │                      │
        │    Control Arm:      │    │   Experimental Arm:  │
        │  Drug X (18 Cycles)  │    │ Drug X + Drug Y (18  │
        │                      │    │       Cycles)        │
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        ┌──────────────────────┐    ┌──────────────────────┐
        │                      │    │                      │
        │ Follow for up to 5   │    │ Follow for up to 5   │
        │ years from           │    │ years from           │
        │ randomization        │    │ randomization        │
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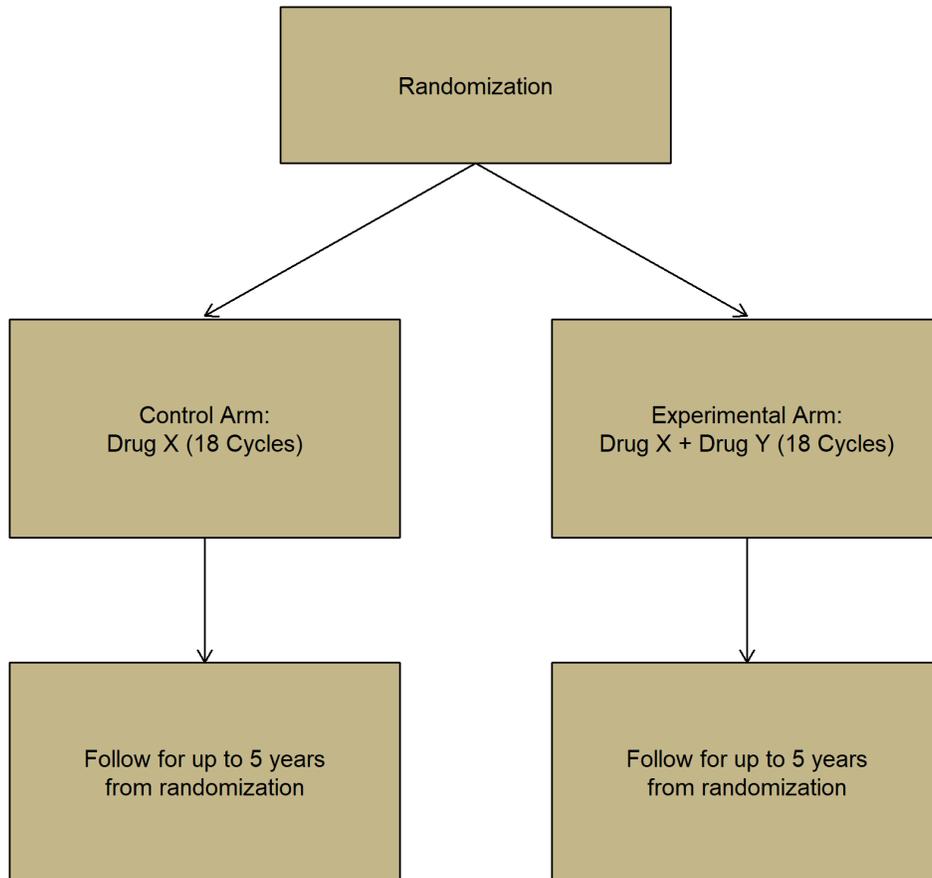
Data Handling

All data is based on a cut-off date of December 31, 2023. Additional follow-up of the study population would be planned prior to an anticipated final analysis date of July 01, 2027.

Chapter Contents

Accrual and Study Status

Figure ACC-01 displays enrollment to the trial over time. Figure ACC-02 displays the cumulative accrual patterns observed from the combined study arms in comparison to the expected patterns of accrual over time; this figure can alternatively be displayed separately by arm if requested. Figure ACC-03 displays accrual by treatment center, with separate enrollment totals by arm per center. Table ACC-04 displays the dates of first and most recent enrollment at each treatment center, with overall enrollment totals per center. The simulated data assumes all centers are within the same nation; for international studies, additional summarizations of accrual by country or other geographic region can be displayed, and accrual displays can be designed to summarize accrual by geographic region, or by sites sorted within geographic regions.

Figure ACC-05 displays the current status of patients as of the date of data cutoff. Similar displays can be created to show groupings by factors such as cause of death or specific off-study reason for all off-study patients, depending on the granularity of the data.

Demographics and Patient Characteristics

Table CHA-01 and Table CHA-02 are tables summarizing the demographics and baseline disease characteristics, respectively, of the study population. Figure CHA-03 and Figure CHA-04 are figures showing, respectively, the distributions by arm of several baseline hepatic laboratory results, and the distrubution of a hepatic laboratory measurement over time (taken at 6-month assessments). Figure CHA-05 shows the distribution of baseline vital signs by arm.

Adverse Events

Table AE-01 displays the maximal grade per patient of all serious adverse events observed on study, sorted by system organ class, and summarized separately by arm. Table AE-02 displays the maximal grade per patient of all adverse events observed on study, sorted by system organ class, and summarized separately by arm. Table AE-03 displays the maximal grade per patient of all adverse events observed on study with at least one incident of Grade 3 or higher, sorted by system organ class and summarized separately by arm, showing only those adverse events of grade 3 or higher. Additional tabular summaries of adverse events, or listings of key subsets of adverse events such as serious adverse events with dates of observation and resolution of adverse events, can also be provided as requested.

Figure AE-04 displays a pie chart detailing the system organ classes of the serious adverse events that occurred on study, collapsing over arms. Figure AE-05 displays the frequency of the most commonly occurring adverse events, separated out by study arm.

Study Endpoints

Figure END-01 displays a preliminary Kaplan-Meier curve of overall survival by study arm. Figure END-02 displays a forest plot encompassing a preliminary summary of a univariate Cox regression for overall survival by treatment arm, both overall and within each level of the three stratification factors for enrollment.

II Main Results

Consort Diagram

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┌─────────────────────────────┐
│    Assessed for eligibility  │
│         (n = 500)            │
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              ▼
┌─────────────────────────────────────┐
│         Excluded (n = 0)             │
│ • Not meeting inclusion criteria (n = 0) │
│   • Declined to participate (n = 0)  │
│      • Other reasons (n = 0)         │
└─────────────────────────────────────┘
              │
              ▼
┌─────────────────────────────┐
│         Randomized           │
│         (n = 500)            │
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        │               │
        ▼               ▼
┌──────────────────────────┐   ┌────────────────────────────────┐
│ Randomized to Control    │   │ Randomized to Experimental     │
│ Arm (n = 253)            │   │ Arm (n = 247)                  │
│ Received treatment on    │   │ Received treatment on study    │
│ study (n = 253)          │   │ (n = 247)                      │
└──────────────────────────┘   └────────────────────────────────┘
        │                               │
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┌──────────────────────────┐   ┌────────────────────────────────┐
│ Analyzed for Primary     │   │ Analyzed for Primary Endpoint  │
│ Endpoint (n = 253)       │   │ (n = 247)                      │
│ Lost to follow-up (n = 0)│   │ Lost to follow-up (n = 0)      │
│ Withdrawn from study     │   │ Withdrawn from study (n = 22)  │
│ (n = 23)                 │   │                                │
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Executive Summary

Accrual

Figure ACC-01

- As of the data cutoff date of December 31, 2023, 500 patients have been enrolled.
  - 253 (50.6%) were enrolled to the Control Arm, and
  - 247 (49.4%) were enrolled to the Experimental Arm.

Figure ACC-05

- Within the Control Arm (n = 253),
  - 169 patients (66.8%) remain on study.
    - 134 patients (53%) of the Contol Arm patients are continuing to receive treatment as of the cut-off date of December 31, 2023, while
    - 35 patients (13.8%) of the Contol Arm patients have completed all treatments and remain in follow-up.
  - 84 patients (33.2%) are off study.
    - 61 patients (24.1%) of the Contol Arm patients have died, while
    - 23 patients (9.1%) of the Contol Arm patients have withdrawn from study.

- Within the Experimental Arm (n = 247),
  - 174 patients (70.4%) remain on study.
    - 136 patients (55.1%) of the Contol Arm patients are continuing to receive treatment as of the cut-off date of December 31, 2023, while
    - 38 patients (15.4%) of the Contol Arm patients have completed all treatments and remain in follow-up.
  - 73 patients (29.6%) are off study.
    - 51 patients (20.6%) of the Contol Arm patients have died, while
    - 22 patients (8.9%) of the Contol Arm patients have withdrawn from study.

Serious Adverse Events

Table AE-01

- 9 patients (1.8%) experienced at least one serious adverse event.
  - Control arm: 1/253 patients (0.4%)
  - Experimental arm: 8/247 patients (3.2%)

Adverse Events

Table AE-02

- 339 patients (67.8%) experienced at least one adverse event.
  - Control arm: 164/253 patients (64.8%)
  - Experimental arm: 175/247 patients (70.9%)

Efficacy

Figure END-01

- 112 patients (22.4%) have died.
  - Within the Control Arm, 61 patients (24.1%) have died.
  - Within the Experimental Arm, 51 patients (20.6%) have died.
- The log-rank p-value between study arms for overall survival is 0.427.
- The maximum amount of time for which any patient has been followed is 24.0 months.

Chapter 1: Accrual and Study Status

Figure ACC-01. Accrual by Time and Treatment

Accrual by 6-Month Period

Control Arm (n = 253)   Experimental Arm (n = 247)
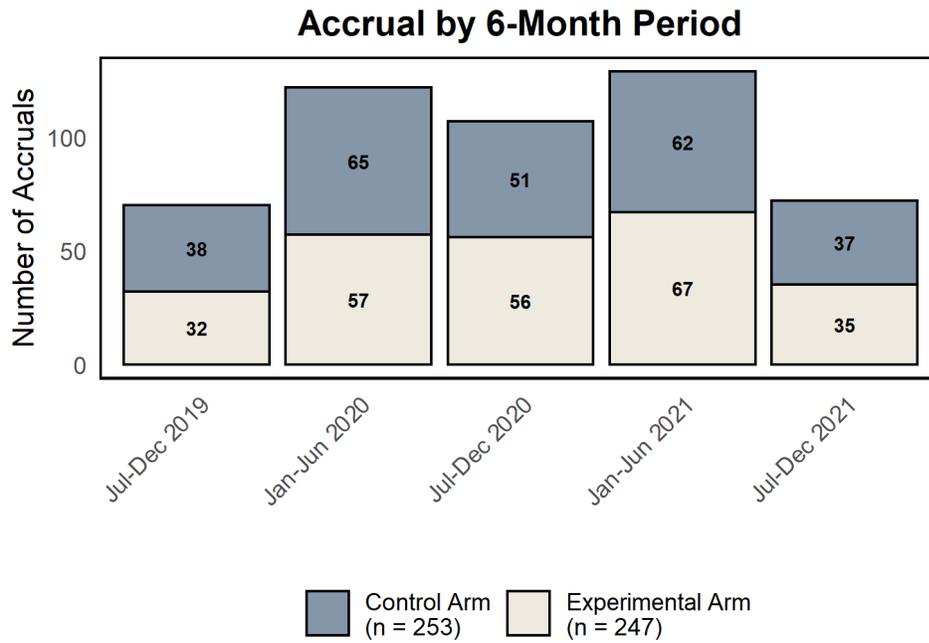
Figure ACC-02. Expected Accrual vs. Actual Accrual

Expected vs. Actual Accrual Over Time

Actual   Expected
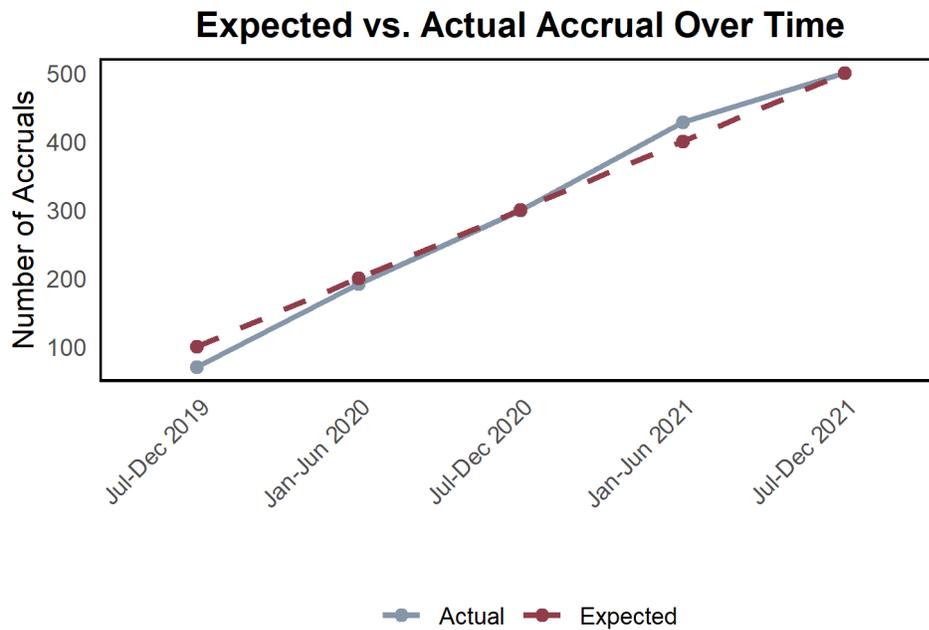
Figure ACC-03. Accrual by Center and Treatment

Accrual by Center
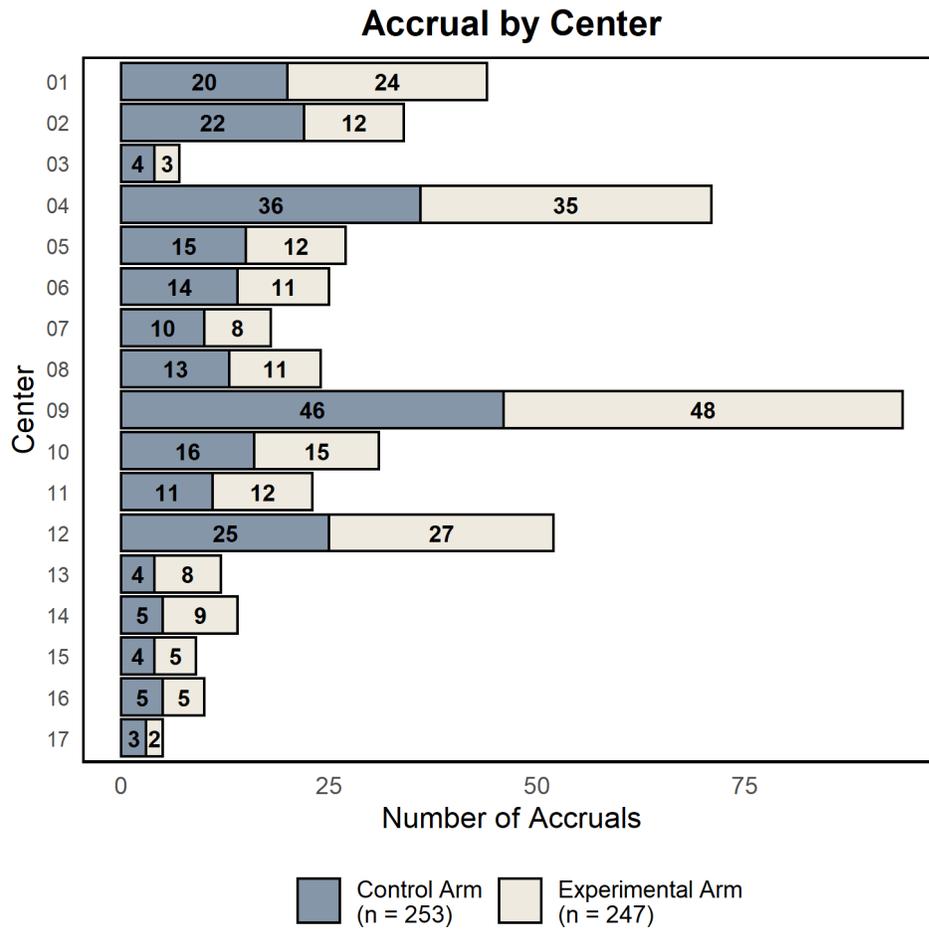
Table ACC-04. Participation by Accrual Center

Center	First Date of Registration	Most Recent Date of Registration	Total Patients
01	04-Oct-2019	19-Sep-2021	44
02	17-Nov-2019	23-Sep-2021	34
03	11-Mar-2020	22-Jul-2021	7
04	05-Oct-2019	29-Sep-2021	71
05	07-Oct-2019	06-Sep-2021	27
06	04-Oct-2019	09-Sep-2021	25
07	14-Dec-2019	04-Sep-2021	18
08	06-Dec-2019	31-Aug-2021	24
09	01-Oct-2019	29-Sep-2021	94
10	21-Oct-2019	30-Sep-2021	31
11	16-Oct-2019	28-Sep-2021	23
12	02-Oct-2019	13-Sep-2021	52
13	24-Jan-2020	27-Sep-2021	12
14	12-Dec-2019	30-Sep-2021	14
15	13-Jan-2020	27-Sep-2021	9
16	30-Nov-2019	24-May-2021	10
17	21-Oct-2019	23-Feb-2021	5

Figure ACC-05. Current Status of Randomized Patients

Current Status by Treatment Arm
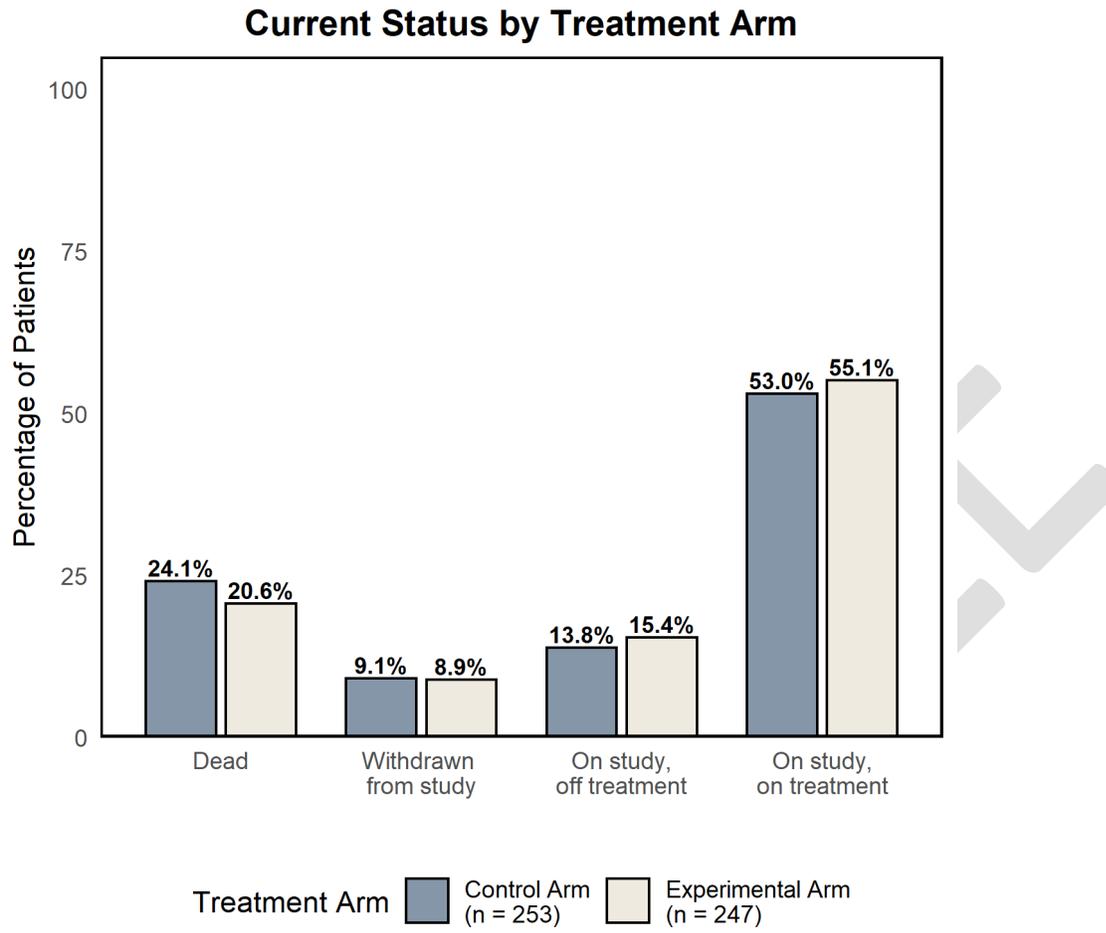
Chapter 2: Demographics and Patient Characteristics

Key Tables

Table CHA-01. Demographics

	Control Arm	Experimental Arm	Total
Age			
<65	54/253 (21.3%)	50/247 (20.2%)	104/500 (20.8%)
≥65	199/253 (78.7%)	197/247 (79.8%)	396/500 (79.2%)
Sex			
Male	154/253 (60.9%)	151/247 (61.1%)	305/500 (61.0%)
Female	99/253 (39.1%)	96/247 (38.9%)	195/500 (39.0%)
Race			
White	156/253 (61.7%)	146/247 (59.1%)	302/500 (60.4%)
Black	33/253 (13.0%)	35/247 (14.2%)	68/500 (13.6%)
Asian	13/253 (5.1%)	13/247 (5.3%)	26/500 (5.2%)
Other	51/253 (20.2%)	53/247 (21.5%)	104/500 (20.8%)

Table CHA-02. Patient Characteristics

	Control Arm	Experimental Arm	Total
Histology			
Adenocarcinoma	225/253 (88.9%)	228/247 (92.3%)	453/500 (90.6%)
Squamous Cell Carcinoma	28/253 (11.1%)	19/247 (7.7%)	47/500 (9.4%)
Genetic Risk			
Low Risk	185/253 (73.1%)	181/247 (73.3%)	366/500 (73.2%)
High Risk	68/253 (26.9%)	66/247 (26.7%)	134/500 (26.8%)
EGFR Mutation			
No	72/192 (37.5%)	64/179 (35.8%)	136/371 (36.7%)
Yes	120/192 (62.5%)	115/179 (64.2%)	235/371 (63.3%)

Key Boxplots

Figure CHA-03. Baseline Hepatic Laboratory Results by Study Arm
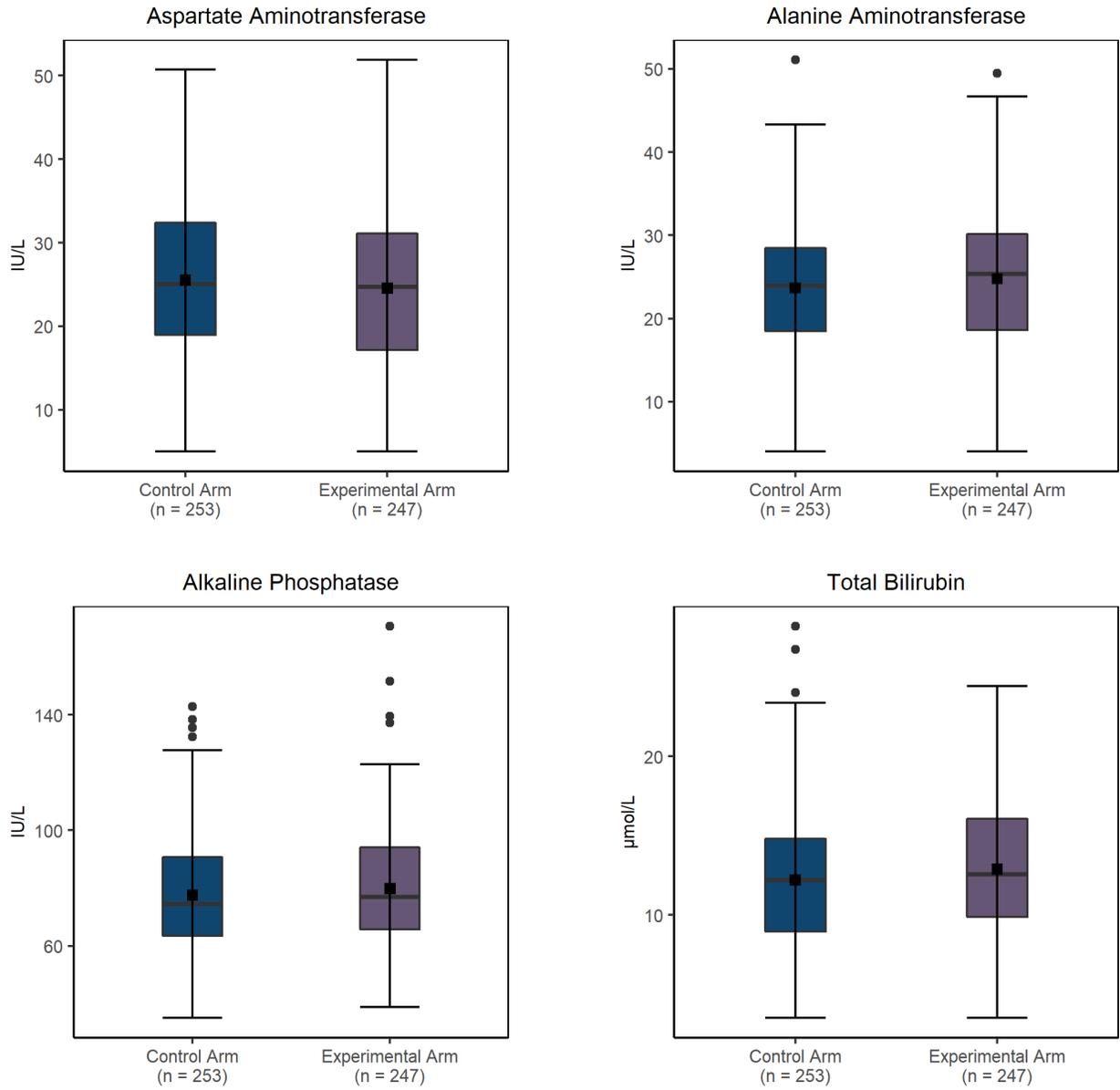
Figure CHA-04. Hepatic Laboratory Results over Study Visits by Study Arm

Bilirubin at Scheduled Visits by Study Arm

Patients Above Bilirubin ULN (21 µmol/L) Over Time by Study Arm
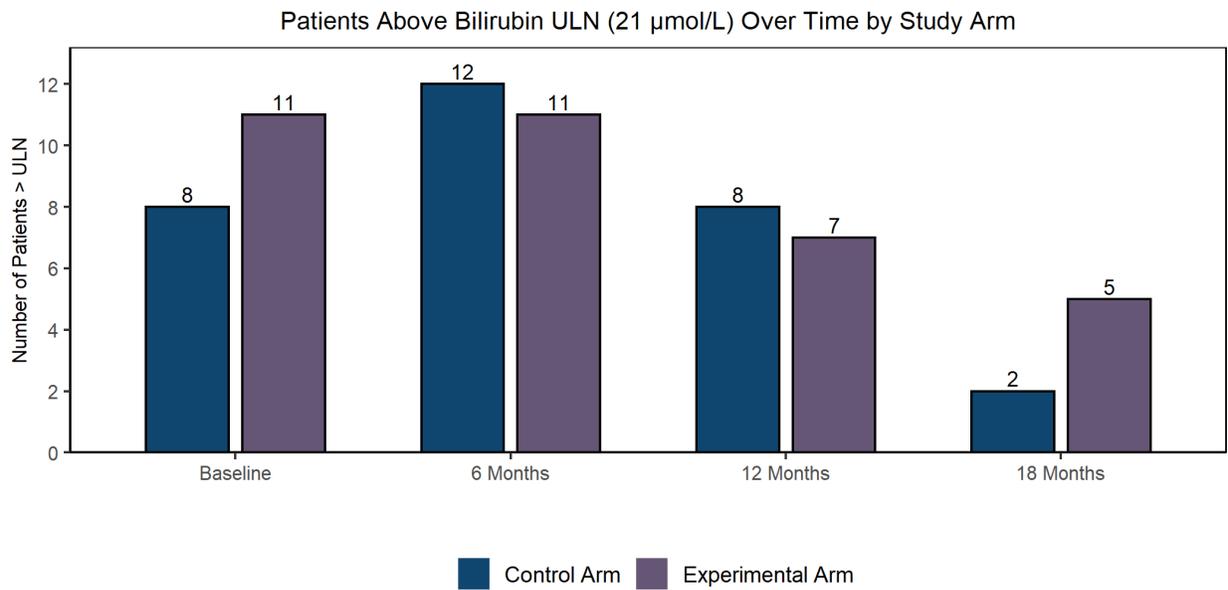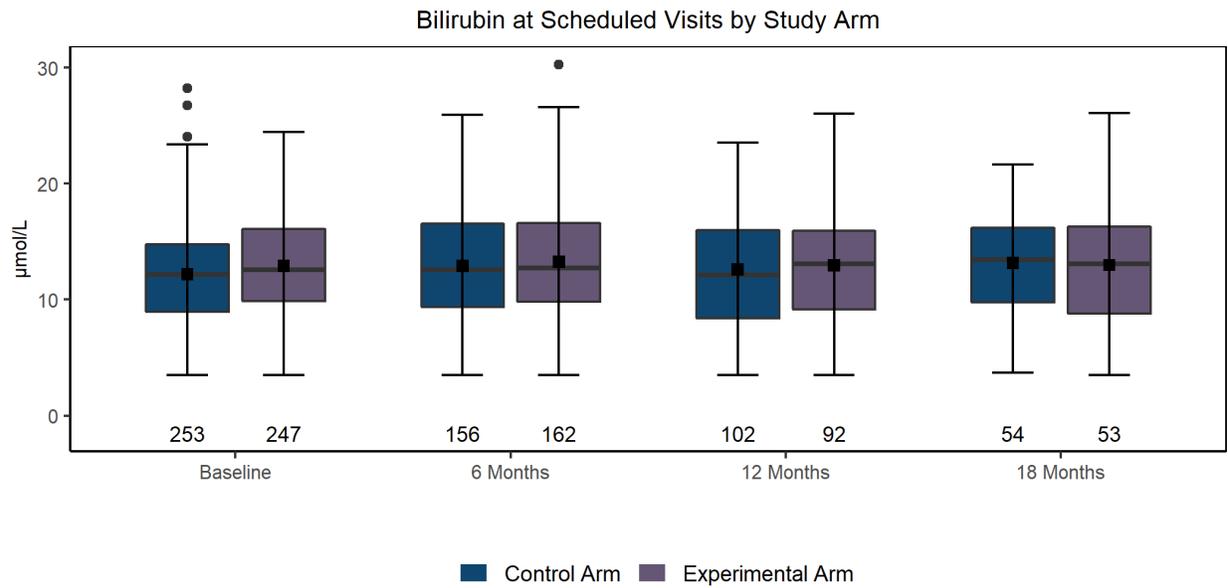
Figure CHA-05. Baseline Physical Exam
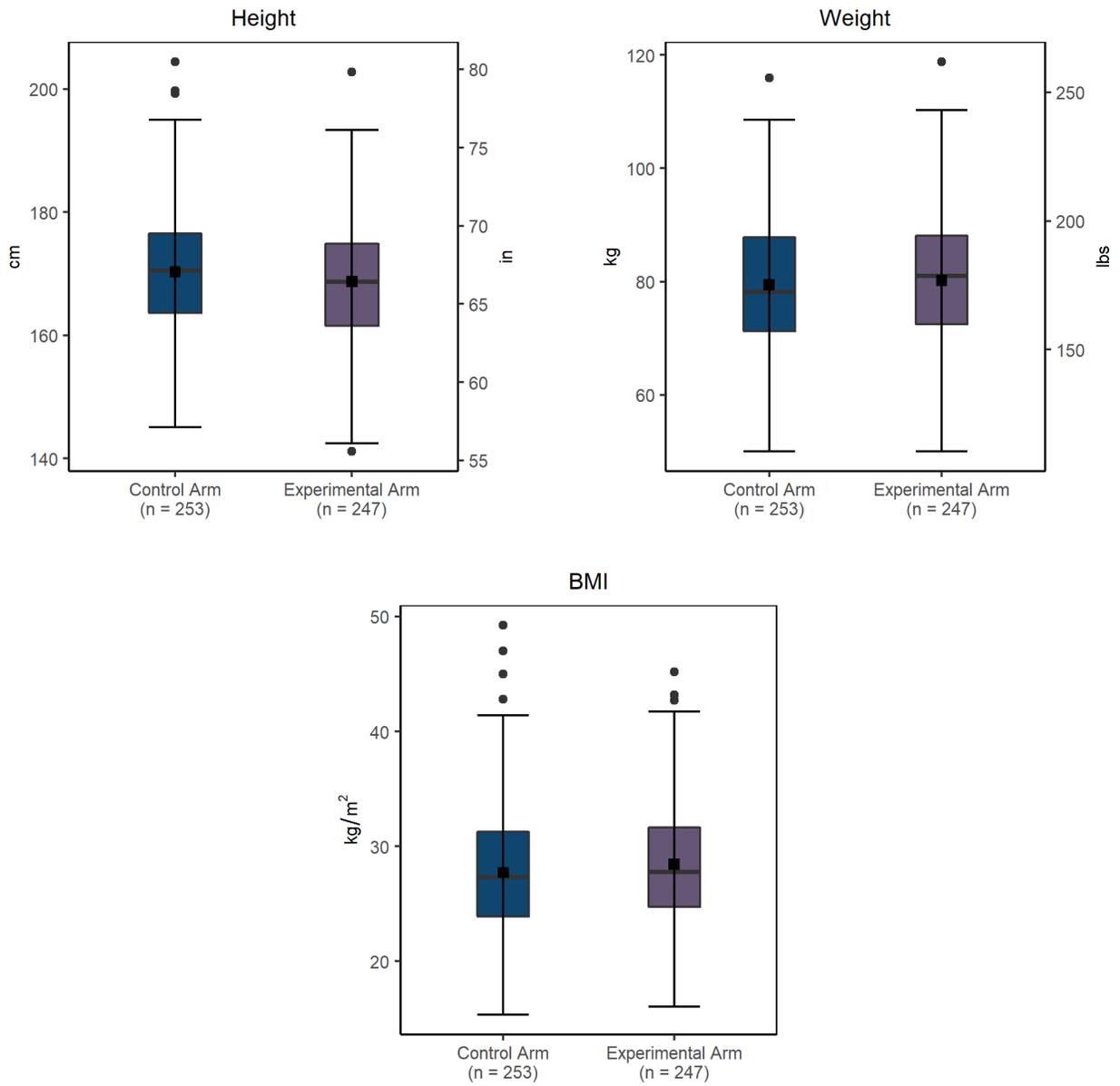
Chapter 3: Adverse Events

Table AE-01. Severe Adverse Events by Specified Term

	Control Arm (n=253)						Experimental Arm (n=247)					
	1	2	3	4	5	Total	1	2	3	4	5	Total
Catheter related infection	0	0	0	0	0	0	0	0	3	0	0	3
COVID-19	0	0	0	0	0	0	0	0	2	0	0	2
Myocardial infarction	0	0	0	0	0	0	0	0	0	1	0	1
Persistent vomiting	0	0	1	0	0	1	0	0	1	0	0	1
Seizure	0	0	0	0	0	0	0	0	1	0	0	1

Table AE-02. Adverse Events by System Organ Class and Specified Term

	Control Arm (n=253)						Experimental Arm (n=247)					
	1	2	3	4	5	Total	1	2	3	4	5	Total
Blood and lymphatic system disorders	2	3	1	0	0	6	8	7	3	0	0	18
Anemia	0	2	1	0	0	3	4	5	2	0	0	11
Neutropenia	1	1	0	0	0	2	2	1	1	0	0	4
Thrombopenia	1	0	0	0	0	1	2	0	0	0	0	2
Leukopenia	0	0	0	0	0	0	0	1	0	0	0	1
Cardiac disorders	0	0	0	0	0	0	0	1	0	1	0	2
Angina pectoris	0	0	0	0	0	0	0	1	0	0	0	1
Myocardial infarction	0	0	0	0	0	0	0	0	0	1	0	1
Congenital, familial and genetic disorders	0	0	1	0	0	1	0	0	0	0	0	0
Aplasia	0	0	1	0	0	1	0	0	0	0	0	0
Ear and labyrinth disorders	1	5	0	0	0	6	2	1	0	0	0	3
Unspecified hearing loss	0	4	0	0	0	4	0	1	0	0	0	1
Vertigo	1	1	0	0	0	2	1	0	0	0	0	1
Tinnitus	0	0	0	0	0	0	1	0	0	0	0	1
Endocrine disorders	0	2	0	0	0	2	0	2	0	0	0	2
Hypothyroidism	0	2	0	0	0	2	0	2	0	0	0	2
Eye disorders	5	1	0	0	0	6	7	1	0	0	0	8
Eyes tearing	2	0	0	0	0	2	2	0	0	0	0	2
Visual disturbances	2	0	0	0	0	2	1	0	0	0	0	1
Blurred vision	1	0	0	0	0	1	1	0	0	0	0	1
Epiphora	0	1	0	0	0	1	0	1	0	0	0	1
Watering eyes	0	0	0	0	0	0	2	0	0	0	0	2
Dry eyes	0	0	0	0	0	0	1	0	0	0	0	1
Gastrointestinal disorders	29	17	1	0	0	47	29	13	2	0	0	44
Nausea	4	7	0	0	0	11	4	6	1	0	0	11
Constipation	6	4	0	0	0	10	7	1	0	0	0	8
Diarrhea	2	3	0	0	0	5	6	3	0	0	0	9

	Control Arm (n=253)						Experimental Arm (n=247)					
	1	2	3	4	5	Total	1	2	3	4	5	Total
Abdominal pain	4	0	0	0	0	4	3	1	0	0	0	4
Mucositis oral	3	0	0	0	0	3	3	0	0	0	0	3
Vomiting	2	1	0	0	0	3	0	1	0	0	0	1
Obstipation	0	0	0	0	0	0	3	0	0	0	0	3
Belching	1	0	0	0	0	1	1	0	0	0	0	1
Colic	1	0	0	0	0	1	1	0	0	0	0	1
Oral ulceration	0	1	0	0	0	1	0	1	0	0	0	1
Persistent vomiting	0	0	1	0	0	1	0	0	1	0	0	1
Pyrosis	2	0	0	0	0	2	0	0	0	0	0	0
Abdominal distension	0	0	0	0	0	0	1	0	0	0	0	1
Aphtha	1	0	0	0	0	1	0	0	0	0	0	0
Epigastralgia	1	0	0	0	0	1	0	0	0	0	0	0
Gastroesophageal reflux	0	1	0	0	0	1	0	0	0	0	0	0
Gum disorder	1	0	0	0	0	1	0	0	0	0	0	0
Hemorrhoids	1	0	0	0	0	1	0	0	0	0	0	0
General disorders and administration site conditions	15	8	0	0	0	23	20	10	0	0	0	30
Fatigue	5	4	0	0	0	9	4	6	0	0	0	10
Asthenia	1	3	0	0	0	4	5	4	0	0	0	9
Infusion site phlebitis	3	0	0	0	0	3	2	0	0	0	0	2
Mucositis	2	0	0	0	0	2	2	0	0	0	0	2
Edema face	2	0	0	0	0	2	1	0	0	0	0	1
Weakness	1	0	0	0	0	1	2	0	0	0	0	2
Pain	0	0	0	0	0	0	2	0	0	0	0	2
Chest pain	0	0	0	0	0	0	1	0	0	0	0	1
Chest pain (non-cardiac)	1	0	0	0	0	1	0	0	0	0	0	0
Diffuse pain	0	1	0	0	0	1	0	0	0	0	0	0
Hypothermia	0	0	0	0	0	0	1	0	0	0	0	1
Hepatobiliary disorders	0	2	0	0	0	2	0	2	0	0	0	2

	Control Arm (n=253)						Experimental Arm (n=247)					
	1	2	3	4	5	Total	1	2	3	4	5	Total
Cholestasis	0	2	0	0	0	2	0	2	0	0	0	2
Infections and infestations	13	6	0	0	0	19	10	8	5	0	0	23
Acute bronchitis	5	0	0	0	0	5	1	0	0	0	0	1
COVID-19	0	2	0	0	0	2	0	1	2	0	0	3
Eye infection NOS	1	0	0	0	0	1	3	0	0	0	0	3
Bronchiolitis	0	0	0	0	0	0	0	3	0	0	0	3
Catheter related infection	0	0	0	0	0	0	0	0	3	0	0	3
Conjunctivitis	1	1	0	0	0	2	1	0	0	0	0	1
Rhinitis	1	0	0	0	0	1	2	0	0	0	0	2
Tooth infection	0	0	0	0	0	0	0	3	0	0	0	3
Infective rhinitis	0	1	0	0	0	1	0	1	0	0	0	1
Skin infection	1	0	0	0	0	1	1	0	0	0	0	1
Urinary tract infection	0	2	0	0	0	2	0	0	0	0	0	0
Bronchial infection	0	0	0	0	0	0	1	0	0	0	0	1
Bronchitis	1	0	0	0	0	1	0	0	0	0	0	0
Erysipelas	1	0	0	0	0	1	0	0	0	0	0	0
Laryngitis	0	0	0	0	0	0	1	0	0	0	0	1
Lung infection	1	0	0	0	0	1	0	0	0	0	0	0
Rhinopharyngitis	1	0	0	0	0	1	0	0	0	0	0	0
Injury, poisoning and procedural complications	2	0	0	0	0	2	2	0	0	0	0	2
Incision site pain	0	0	0	0	0	0	2	0	0	0	0	2
Tendon rupture	2	0	0	0	0	2	0	0	0	0	0	0
Investigations	18	8	1	0	0	27	13	3	2	0	0	18
Lymphocyte count decreased	3	3	0	0	0	6	6	0	0	0	0	6
Creatinine increased	5	1	0	0	0	6	2	1	0	0	0	3
Neutrophil count decreased	0	4	0	0	0	4	0	1	1	0	0	2
Platelet count decreased	5	0	0	0	0	5	0	0	0	0	0	0
Alkaline phosphatase increased	2	0	0	0	0	2	1	0	0	0	0	1

	Control Arm (n=253)						Experimental Arm (n=247)					
	1	2	3	4	5	Total	1	2	3	4	5	Total
White blood cell decreased	0	0	1	0	0	1	1	0	1	0	0	2
Blood lactate dehydrogenase increased	0	0	0	0	0	0	2	0	0	0	0	2
Serum creatinine increased	1	0	0	0	0	1	1	0	0	0	0	1
Alanine aminotransferase increased	1	0	0	0	0	1	0	0	0	0	0	0
Blood sugar increased	1	0	0	0	0	1	0	0	0	0	0	0
GOT increased	0	0	0	0	0	0	0	1	0	0	0	1
Metabolism and nutrition disorders	10	6	1	0	0	17	1	1	3	0	0	5
Anorexia	7	3	1	0	0	11	1	0	2	0	0	3
Appetite decreased NOS	2	0	0	0	0	2	0	0	0	0	0	0
Dehydration	0	2	0	0	0	2	0	0	0	0	0	0
Hypokalemia	0	1	0	0	0	1	0	1	0	0	0	1
Gout attack	1	0	0	0	0	1	0	0	0	0	0	0
Hypercalcemia	0	0	0	0	0	0	0	0	1	0	0	1
Musculoskeletal and connective tissue disorders	2	0	1	0	0	3	8	0	0	0	0	8
Myalgia	1	0	0	0	0	1	2	0	0	0	0	2
Arthralgia	0	0	0	0	0	0	2	0	0	0	0	2
Tendinopathy	1	0	0	0	0	1	1	0	0	0	0	1
Back pain	0	0	1	0	0	1	0	0	0	0	0	0
Bone pain	0	0	0	0	0	0	1	0	0	0	0	1
Leg pain	0	0	0	0	0	0	1	0	0	0	0	1
Neck pain	0	0	0	0	0	0	1	0	0	0	0	1
Nervous system disorders	17	1	0	0	0	18	15	5	1	0	0	21
Headache	7	1	0	0	0	8	7	5	0	0	0	12
Paresthesia	5	0	0	0	0	5	3	0	0	0	0	3
Carpal tunnel syndrome	1	0	0	0	0	1	1	0	0	0	0	1
Dizziness	1	0	0	0	0	1	1	0	0	0	0	1
Neuropathy	1	0	0	0	0	1	1	0	0	0	0	1

| | Control Arm (n=253) | | | | | | Experimental Arm (n=247) | | | | | |
	1	2	3	4	5	Total	1	2	3	4	5	Total
Dysgeusia	1	0	0	0	0	1	0	0	0	0	0	0
Neuropathic pain	0	0	0	0	0	0	1	0	0	0	0	1
Peripheral sensory neuropathy	0	0	0	0	0	0	1	0	0	0	0	1
Seizure	0	0	0	0	0	0	0	0	1	0	0	1
Trembling	1	0	0	0	0	1	0	0	0	0	0	0
Psychiatric disorders	1	0	0	0	0	1	0	0	0	0	0	0
Restlessness	1	0	0	0	0	1	0	0	0	0	0	0
Renal and urinary disorders	1	1	0	0	0	2	0	1	0	0	0	1
Urinary incontinence	0	1	0	0	0	1	0	1	0	0	0	1
Renal failure	1	0	0	0	0	1	0	0	0	0	0	0
Respiratory, thoracic and mediastinal disorders	6	3	0	0	0	9	3	6	0	0	0	9
Cough	0	1	0	0	0	1	2	2	0	0	0	4
Dyspnea	2	0	0	0	0	2	0	2	0	0	0	2
COPD exacerbation	0	1	0	0	0	1	0	2	0	0	0	2
Epistaxis	1	0	0	0	0	1	1	0	0	0	0	1
Dry cough	1	0	0	0	0	1	0	0	0	0	0	0
Dyspnoea	1	0	0	0	0	1	0	0	0	0	0	0
Pulmonary embolism	1	0	0	0	0	1	0	0	0	0	0	0
Voice disturbance, unspecified	0	1	0	0	0	1	0	0	0	0	0	0
Skin and subcutaneous tissue disorders	9	3	0	0	0	12	10	6	0	0	0	16
Alopecia	2	1	0	0	0	3	1	2	0	0	0	3
Pruritus	2	1	0	0	0	3	1	2	0	0	0	3
Facial rash	4	0	0	0	0	4	1	0	0	0	0	1
Rash maculo-papular	1	0	0	0	0	1	2	0	0	0	0	2
Skin discoloration	0	0	0	0	0	0	3	0	0	0	0	3
Maculopapular rash	0	1	0	0	0	1	0	1	0	0	0	1
Dermatitis	0	0	0	0	0	0	0	1	0	0	0	1
Dry skin	0	0	0	0	0	0	1	0	0	0	0	1

	Control Arm (n=253)						Experimental Arm (n=247)					
	1	2	3	4	5	Total	1	2	3	4	5	Total
Rash acneiform	0	0	0	0	0	0	1	0	0	0	0	1
Vascular disorders	4	0	1	0	0	5	6	0	2	0	0	8
Hot flashes	4	0	0	0	0	4	3	0	0	0	0	3
Hypertension	0	0	1	0	0	1	2	0	2	0	0	4
Hypotension	0	0	0	0	0	0	1	0	0	0	0	1

Table AE-03. Adverse Events With At Least One Grade 3-5 Incident by System Organ Class and Specified Term

	Control Arm (n=253)				Experimental Arm (n=247)			
	3	4	5	Total	3	4	5	Total
Blood and lymphatic system disorders	1	0	0	1	3	0	0	3
Anemia	1	0	0	1	2	0	0	2
Neutropenia	0	0	0	0	1	0	0	1
Cardiac disorders	0	0	0	0	0	1	0	1
Myocardial infarction	0	0	0	0	0	1	0	1
Congenital, familial and genetic disorders	1	0	0	1	0	0	0	0
Aplasia	1	0	0	1	0	0	0	0
Gastrointestinal disorders	1	0	0	1	2	0	0	2
Persistent vomiting	1	0	0	1	1	0	0	1
Nausea	0	0	0	0	1	0	0	1
Infections and infestations	0	0	0	0	5	0	0	5
Catheter related infection	0	0	0	0	3	0	0	3
COVID-19	0	0	0	0	2	0	0	2
Investigations	1	0	0	1	2	0	0	2
White blood cell decreased	1	0	0	1	1	0	0	1
Neutrophil count decreased	0	0	0	0	1	0	0	1
Metabolism and nutrition disorders	1	0	0	1	3	0	0	3
Anorexia	1	0	0	1	2	0	0	2
Hypercalcemia	0	0	0	0	1	0	0	1
Musculoskeletal and connective tissue disorders	1	0	0	1	0	0	0	0
Back pain	1	0	0	1	0	0	0	0
Nervous system disorders	0	0	0	0	1	0	0	1
Seizure	0	0	0	0	1	0	0	1
Vascular disorders	1	0	0	1	2	0	0	2
Hypertension	1	0	0	1	2	0	0	2

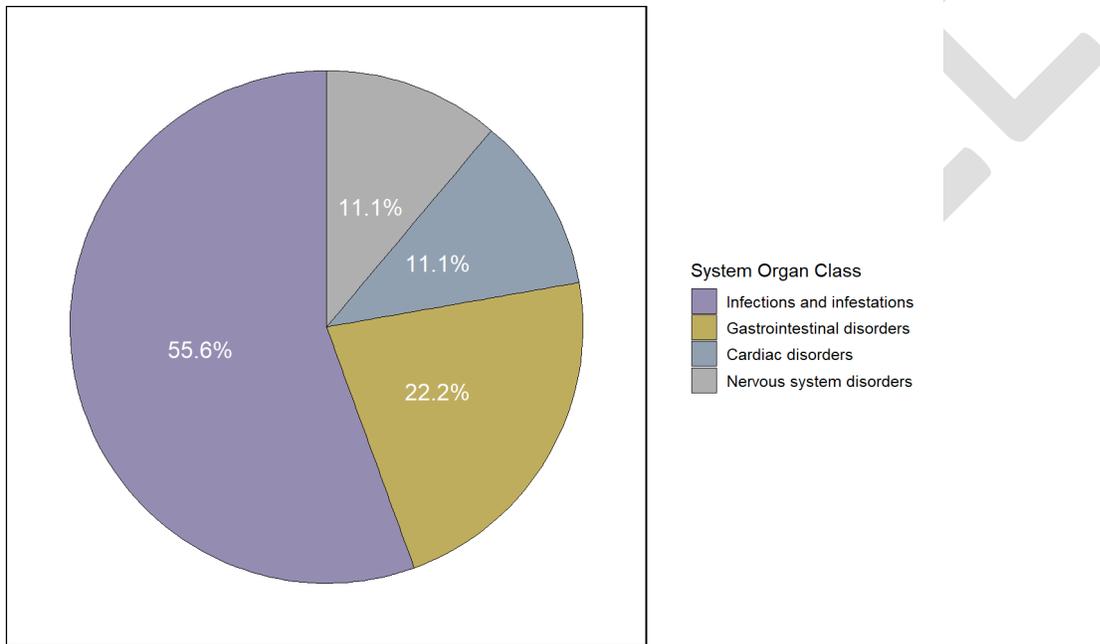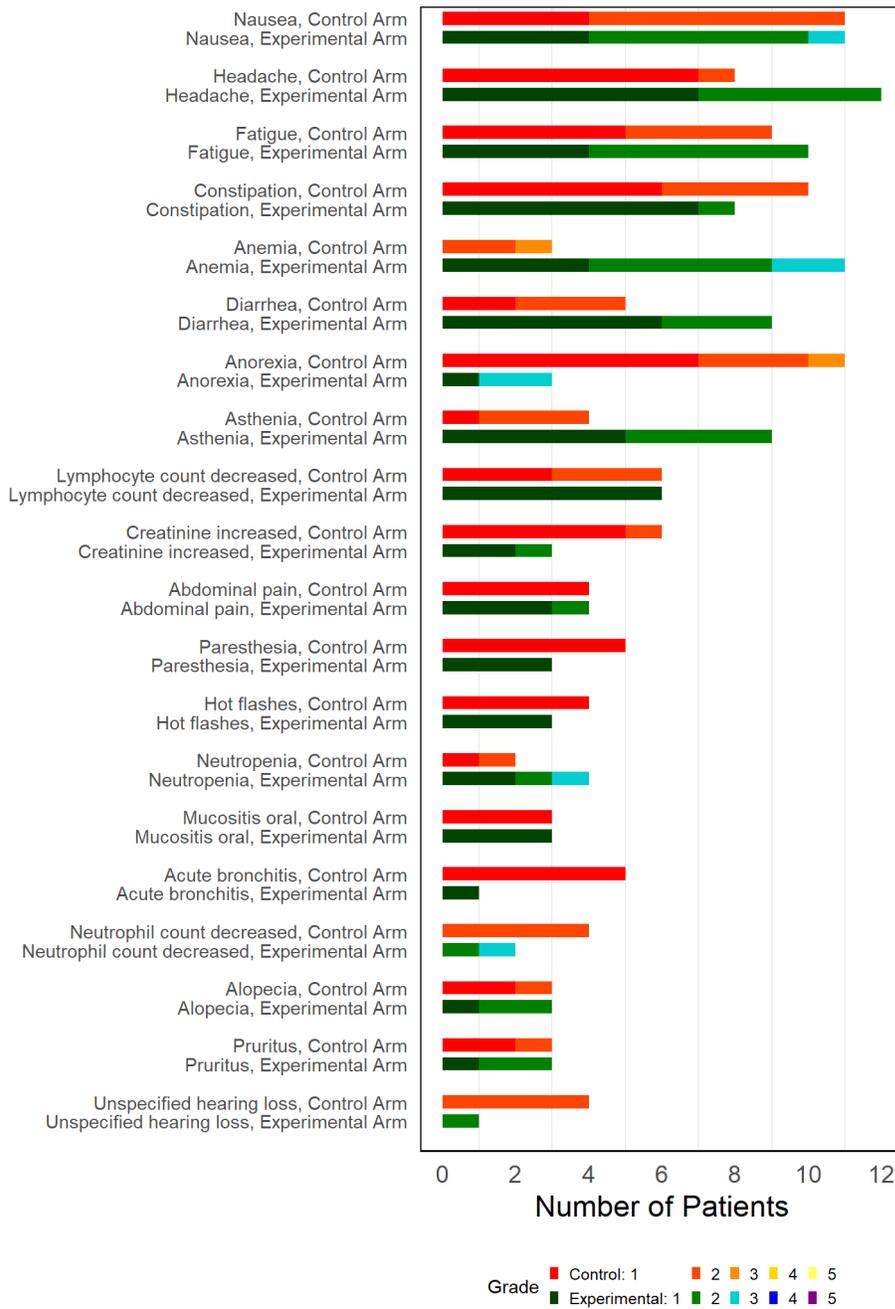## *Figure AE-04. Serious Adverse Events by System Organ Class*

Figure AE-05. Top 20 Most Commonly Occuring Adverse Events

Chapter 4: Study Endpoint - Overall Survival

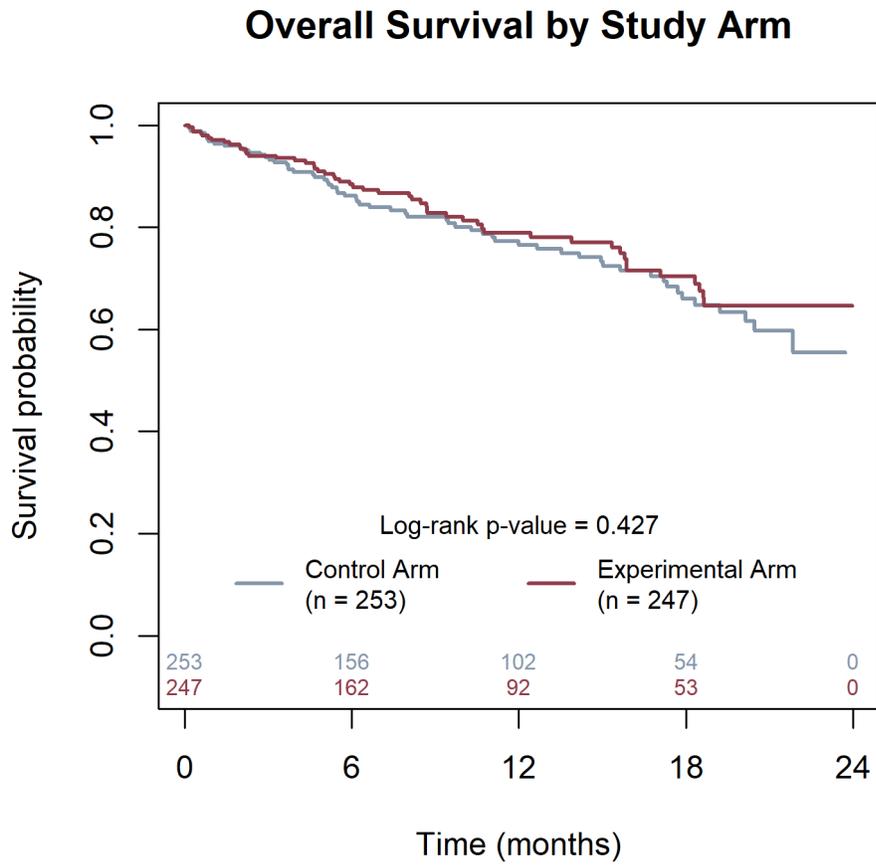## *Figure END-01. Overall Survival by Study Arm*

Overall Survival by Study Arm

Figure END-02. Overall Survival - Forest Plot

Univariate Hazard Ratios for Study Arm Within Strata Levels

	Events in Patients w Trait	Events in Patients w/o Trait		HR (95% CI)
Overall (Control vs. Experimental)	247/500	253/500		0.86 (0.59, 1.25)
Within: Age < 65	50/104	54/104		0.24 (0.07, 0.83)
Within: Age >= 65	197/396	199/396		1.04 (0.70, 1.56)
Within: Histology - Squamous	19/47	28/47		1.98 (0.63, 6.24)
Within: Histology - Adenocarcinoma	228/453	225/453		0.80 (0.54, 1.18)
Within: Genetic Risk - Low	181/366	185/366		0.80 (0.52, 1.25)
Within: Genetic Risk - High	66/134	68/134		1.04 (0.52, 2.09)

Favors Control Arm <-- --> Favors Experimental Arm

```