CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN
for
DMID Protocol: 16-0119
Study Title:
A Phase I, Randomized, Placebo Controlled, Double-blind, Dose Escalation trial to Evaluate the Safety and Immunogenicity of an Andes Virus DNA Vaccine for the Prevention of Hantavirus Pulmonary Syndrome Using the PharmaJet Stratis® Needle-Free Injection System in Normal Healthy Adults

NCT03682107

Version 2.0

DATE: 17NOV2020

STUDY TITLE

Protocol Number Code:	**DMID Protocol: 16-0119**
Development Phase:	Phase I
Products:	ANDV DNA vaccine administered by the PharmaJet Stratis® Needle-Free Injection System in a 3 or 4 dose regimen at two doses, 2 or 4 mg
Form/Route:	Intramuscular
Indication Studied:	Hantavirus Pulmonary Syndrome (HPS)
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	February 14, 2019
Clinical Trial Completion Date:	September 23, 2020
Date of the Analysis Plan:	November 17, 2020
Version Number:	2.0

This study was performed in compliance with Good Clinical Practice.

TABLE OF CONTENTS

Table of Contents *(continued)*

Table of Contents *(continued)*

LIST OF ABBREVIATIONS

AE	Adverse Event
ALT	Alanine Aminotransferase
ANC	Absolute Neutrophil Count
ANDV	Andes Virus
BP	Blood Pressure
BPM	Beats Per Minute
BUN	Blood Urea Nitrogen
C	Celsius
CI	Confidence Interval
CMS	Clinical Materials Services
CRF	Case Report Form
CSR	Clinical Study Report
DMID	Division of Microbiology and Infectious Diseases
DNA	Deoxyribonucleic Acid
DSJI	Disposable Syringe Jet Injection
DSMB	Data and Safety Monitoring Board
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
F	Fahrenheit
FDA	Food and Drug Administration
GMT	Geometric Mean Titer
GMFR	Geometric Mean Fold Rise
HBsAg	Hepatitis B Surface Antigen
HCPS	Hantavirus Cardio/Pulmonary Syndrome
HCV	Hepatitis C Virus
HFRS	Hemorrhagic Fever with Renal Syndrome
Hgb	Hemoglobin
HgbA1C	Hemoglobin A1C
HIV	Human Immunodeficiency Virus
HPS	Hantavirus Cardio/Pulmonary Syndrome
HTNV	Hantaan Virus

LIST OF ABBREVIATIONS *(continued)*

ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ICS	Intracellular Staining
IP	Investigational Product
IRB	Institutional Review Board
ISM	Independent Safety Monitor
ITT	Intention to Treat
L	Liter
LPA	Lymphoproliferation Assay
LLN	Lower Limit of Normal
mcg	Microgram
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
mL	Milliliter
MOP	Manual of Procedures
N	Number (typically refers to subjects)
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
PBMC	Peripheral Blood Mononuclear Cell
PI	Principal Investigator
PP	Per Protocol
PRNT	Plaque Reduction Neutralization Assay
PsVNA	Pseudovirion Neutralization Assay
PT	Preferred Term
PUUV	Puumala Virus
RBC	Red Blood Cell
RCD	Reverse Cumulative Distribution
SAE	Serious Adverse Event
SD	Standard Deviation
SAP	Statistical Analysis Plan
SDCC	Statistical and Data Coordinating Center
SMC	Safety Monitoring Committee
SNV	Sin Nombre Virus

LIST OF ABBREVIATIONS *(continued)*

SOC	System Organ Class
SOP	Standard Operating Procedures
U	Units
ULN	Upper Limit of Normal
USAMRIID	Unites States Army Medical Research Institute of Infectious Diseases
VTEU	Vaccine Testing and Evaluation Unit
WBC	White Blood Cell
WHO	World Health Organization

1. PREFACE

The Statistical Analysis Plan (SAP) for "A Phase I, Randomized, Placebo Controlled, Double-blind, Dose Escalation trial to Evaluate the Safety and Immunogenicity of an Andes Virus DNA Vaccine for the Prevention of Hantavirus Pulmonary Syndrome Using the PharmaJet Stratis® Needle-Free Injection System in Normal Healthy Adults" (DMID Protocol 16-0119) describes and expands upon the statistical information presented in the protocol.

This document describes all planned analyses and provides reasons and justifications for these analyses. It also includes sample tables, listings, and figures planned for the final analyses. Regarding the final analyses and Clinical Study Report (CSR), this SAP follows the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines, as indicated in Topic E3 (Structure and Content of Clinical Study Reports), and more generally is consistent with Topic E8 (General Considerations for Clinical Trials) and Topic E9 (Statistical Principles for Clinical Trials). The structure and content of the SAP provides sufficient detail to meet the requirements identified by the FDA and ICH, while all work planned and reported for this SAP will follow internationally accepted guidelines published by the American Statistical Association and the Royal Statistical Society for statistical practice.

This document contains: a review of the study design, general statistical considerations, comprehensive statistical analysis methods for efficacy and safety outcomes, and a list of proposed tables and figures. Within the table, figure, and listing mock-ups (Appendices 1, 2, and 3), references to CSR sections are included. Any deviation from this SAP will be described and justified in protocol amendments and/or in the CSR, as appropriate. The reader of this SAP is encouraged to also review the study protocol for details on conduct of the study and the operational aspects of clinical assessments.

2. INTRODUCTION

Andes virus (ANDV) is one of over 50 species of hantaviruses found and identified worldwide. The two primary disease presentations in humans infected with hantaviruses are due to vascular leakage; hemorrhagic fever with renal syndrome (HFRS) and hantavirus cardio/pulmonary syndrome (HCPS or HPS).

HPS was first described in 1993 in the southwestern United States, with identification of Sin Nombre virus (SNV) as the causative agent. HPS typically presents as a non-specific viral illness with cough, fever, chills, nausea/vomiting, diarrhea, myalgia and/or headache for 3-6 days, followed by abrupt onset of pulmonary edema and shock. [1]. HPS is relatively uncommon (approximately 600 US cases & 4,000 South American from 1993-2012/13). In South America, ANDV is the predominant cause of HPS, with mortality rates of 35-40%, despite modern critical care support. [1, 2, and 3] There is no vaccine or effective therapy for HPS and treatment remains supportive and symptomatic. Unlike the other known hantaviruses, ANDV remains the only one with persuasive evidence of person-to-person transmission. [4 and 5] ANDV is classified as a Category A bioterrorism agent.

Vaccines developed against two viruses causing HFRS are being used in clinical trials with some success. A phase 1 clinical trial of Hantaan Virus (HTNV) and Puumala Virus (PUUV) DNA vaccines reported neutralizing antibodies of 30% and 40% to HTNV and PUUV, respectively. [6] When the same vaccine was administered using a different delivery system and administering 2 doses of vaccine, seroconversion was increased to 64% and 75% to HTNV and PUUV, respectively. [7] There is also an ongoing phase 1 trial evaluating HTNV and PUUV DNA vaccines delivered by the PharmaJet Stratis® Needle-Free Injection System (clinicaltrials.gov, NCT02776761), the same delivery system used in this trial.

In order to develop a pan-hantavirus DNA vaccine, an ANDV vaccine has been developed using the same strategy and plasmid backbone as the HTNV and PUUV DNA vaccines. The similarity in structure of this vaccine to the HTNV and PUUV vaccines, combined with the immunogenicity results of the previous hantavirus DNA vaccines, provides the rationale for evaluating the ANDV DNA vaccine administered by the PharmaJet Stratis® Needle-Free Injection System in humans.

Several pre-clinical studies using variations of the ANDV vaccine and different delivery systems have been published. Studies of the same plasmid product as the current proposal demonstrated that a combined ANDV DNA and SNV DNA vaccine elicited neutralizing antibodies in rabbits and nonhuman primates [8]. In this study, significantly higher neutralizing titers were seen using a disposable syringe jet injection (DSJI) system as compared to needle/syringe delivery. No safety issues or adverse events were reported. Subsequent studies in geese and transchromosomal bovine have also demonstrated that the ANDV DNA vaccines administered with a DSJI system elicit neutralizing antibodies. Administration of these purified antibodies protected hamsters from lethal ANDV infection. [9 and 10] As in the nonhuman primate study above, there were no safety concerns or adverse events reported with respect to the vaccine product or delivery method.

2.1. Purpose of the Analyses

These analyses will assess the immunogenicity and safety of ANDV DNA vaccine given in 3 doses at 2mg or 4mg, 4 doses given at 2mg or 4mg, or placebo and will be included in the clinical study report.

The protocol for DMID 16-0119 calls for a planned interim analysis of safety, reactogenicity, and immunologic response data once all subjects have completed the Day 197 visit and the data are entered in the database, validated, and monitored according to the clinical monitoring plan. The study statistician will provide the analysis of aggregate data unblinded at the group level to the investigators and sponsor staff for the purpose of manuscript, abstract preparation, or presentation. The information from the primary immunogenicity and safety review may be published or otherwise presented, pursuant upon executed

agreements between NIAID and VTEU investigators. The results will not be used to make any decisions concerning the conduct of this trial, but they may be used to make decisions on activities external to this trial such as the design of future trials of this vaccine.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

3.1.1. Primary Study Objective

- Assess the safety and reactogenicity of the ANDV DNA vaccine by dosage cohort and treatment arm when administered using the PharmaJet Stratis® Needle-Free Injection system in normal, healthy adults.

3.1.2. Secondary Study Objectives

- Assess the immunogenicity of the ANDV DNA vaccine by dosage cohort and treatment arm.

3.1.3. Exploratory Study Objectives

- Assess cellular immune response to ANDV DNA vaccine by dosage cohort and treatment arm.
- Assess immunogenicity of the ANDV DNA vaccine by dosage cohort and treatment arm at additional time points.

3.2. Endpoints

3.2.1. Primary Outcome Measures

- Occurrence of vaccine-related Serious Adverse Events (SAEs) through approximately 6 months post last vaccination.
- Occurrence of vaccine-related unsolicited Adverse Events (AEs) through 28 days post last vaccination.
- Occurrence of Serious Adverse Events (SAEs) through approximately 6 months post last vaccination.
- Occurrence of unsolicited Adverse Events (AEs) through 28 days post last vaccination.
- Occurrence of solicited local and systemic AEs through 7 days after each study vaccination.
- Occurrence of clinical safety laboratory AEs through 7 days after each study vaccination.

3.2.2. Secondary Outcome Measures

- Incidence of an ANDV-specific titer of ≥ 20 on Day 57 (3 dose regimen), Day 85 (4 dose regimen) and Day 197 (3 and 4 dose regimen) as measured by:
  - Plaque reduction neutralization titers
  - Pseudovirion neutralization titers
- Incidence of seroconversion (defined as a post-vaccination ANDV-specific titer ≥40 if baseline titer <20 or a minimum four-fold rise compared to baseline if baseline titer ≥ 20) on Day 57 (3 dose regimen), Day 85 (4 dose regimen) and Day 197 (3 and 4 dose regimen) as measured by:
  - Plaque reduction neutralization titers
  - Pseudovirion neutralization titers

3.2.3. Exploratory Outcomes

- Incidence of a >3 standard deviation increase in ANDV-specific, cytokine-secreting CD4+ and CD8+ cells on Day 29 (3 and 4 dose regimen), Day 57 (3 dose regimen), Day 85 (4 dose regimen), Day 169 (3 and 4 dose regimen) and Day 197 (3 and 4 dose regimen) compared to baseline (Day 1) as measured by flow-based intracellular staining (ICS).
- Incidence of a >3 standard deviation increase in ANDV-specific CD4+ and CD8+ cells on Day 29 (3 and 4 dose regimen), Day 57 (3 dose regimen), Day 85 (4 dose regimen), Day 169 (3 and 4 dose regimen) and Day 197 (3 and 4 dose regimen) compared to baseline (Day 1) as measured by a lymphoproliferation assay (LPA).Incidence of an ANDV-specific titer of ≥20 at additional time points as measured by:Pseudovirion neutralization titersPlaque reduction neutralization titers

3.3. Study Definitions and Derived Variables

The term "vaccination group" refers to dose of study product and number of doses that subjects are randomized to receive. Therefore, there are five vaccination groups: ANDV DNA 2mg 3 doses, ANDV DNA 2mg 4 doses, ANDV DNA 4mg 3 doses, ANDV DNA 4mg 4 doses, and placebo. The placebo group will include all subjects who received placebo from all cohorts. Results will also be displayed for all subjects where indicated.

Seroconversion is defined as a post-vaccination ANDV-specific titer ≥40 if baseline titer <20 or a minimum four-fold rise compared to baseline if baseline titer ≥20.

Geometric mean fold rise (GMFR) represents the geometric mean fold rise in antibody compared to baseline, calculated as the arithmetic mean of the difference in log antibodies back-transformed to the original scale.

Baseline is considered to be the last measurement taken prior to the first vaccination.

The lower limit of quantitation (LLOQ) for both PRT and PsVNA assay results is 20. Any values less than the LLOQ will be assigned a value of 14.1 by the lab. This imputed value will be used for the purpose of calculating summary statistics such as mean and GMT. All corresponding descriptive statistics that are <LLOQ will be reported as "<20" in summary tables.

4. INVESTIGATIONAL PLAN

Overall Study Design and Plan

This is a Phase 1, randomized, placebo controlled, double-blind, dose escalation trial of 48 males and non-pregnant females, 18-49 years old, inclusive, who are in good health and meet all eligibility criteria. This trial is designed to assess the safety, reactogenicity and immunogenicity of an ANDV DNA vaccine for the prevention of Hantavirus Pulmonary Syndrome (HPS). ANDV DNA vaccine or placebo will be administered using the PharmaJet Stratis® Needle-Free Injection System. This study is investigating administration of 2mg and 4mg doses delivered in 3 and 4 dose regimens.

The first 24 participants in Cohorts 1 and 2 include two sentinel subjects since this is a first-in-human Phase 1 study. Sentinel subjects receive 2 mg of study vaccine in an open label manner in a 3 or 4 dose regimen. One sentinel subject is vaccinated, followed for one day for safety and reactogenicity, and when no halting rules are met, the second sentinel subject receives study vaccine in an open-label manner. The two sentinels are followed for safety through Day 8 (laboratory and solicited/unsolicited AEs) and when no pre-defined halting rules are met and no safety concerns identified, enrollment of the 22 remaining subjects in Cohorts 1 and 2 proceeds. While safety data are evaluated for the sentinel subjects, no new subjects are enrolled, but screening continues.

The 22 non-sentinel subjects in Cohorts 1 and 2 are randomized in a 9:2:9:2 ratio (See Table 1 for study design) to receive either placebo or study vaccine (at a dose of 2 mg) in a 3 or 4 dose regimen, in double-blind fashion. The SMC reviews all available safety data through 7 days post second vaccination for all 24 subjects in Cohorts 1 and 2 and provides recommendations to proceed to Cohorts 3 and 4. While safety data are being evaluated by the SMC, no new subjects are enrolled, but screening for Cohorts 3 and 4 and vaccination of the remaining doses in Cohorts 1 and 2 continues.

The 24 participants in Cohorts 3 and 4 follows the same schedule as outlined for Cohorts 1 and 2 above. Sentinel subjects receive 4 mg of study vaccine open label in a 3 or 4 dose regimen and are followed for safety through Day 8. The remaining 22 non-sentinel subjects in Cohorts 3 and 4 are randomized in a 9:2:9:2 ratio (Treatment Arms 3b:3c:4b:4c) to receive placebo or study vaccine at a dose of 4 mg in a 3 or 4 dose regimen, in double-blind fashion.

Doses 2-4 for all vaccination groups are administered per the schedule outlined in Table 2, assuming no halting rules are met. As the vaccine was expected to be well-tolerated based on previously published studies in humans demonstrating the safety of Hantavirus DNA vaccines that use the same plasmid backbone [7], more than one dose was planned to better investigate safety and immunogenicity.

Reactogenicity is measured by the occurrence of solicited injection site symptoms and through 7 days post each vaccination. Unsolicited non-serious AEs are collected from the time of first study vaccination through approximately 28 days after last vaccination. SAEs occurring from the time of study vaccination through approximately 6 months after the last study vaccination are collected. Clinical safety labs are collected on Day 1 and 169, and 7 days after each vaccination; if labs are abnormal, they are repeated at the next scheduled visit (sooner if medically indicated) and followed to normal or stabilization.

Immunogenicity testing includes evaluation of the cellular immune response to ANDV peptide pools and assessment of humoral immune response as measured by ANDV Pseudovirion Neutralization Assay (PsVNA) and by ANDV Plaque Reduction Neutralization Test (PRNT). PBMCs are collected to be used in the cellular assays, flow-based ICS, and LPA for secondary and exploratory immunogenicity endpoints. The duration of this trial for each subject is approximately 12 months.

See Table 1 and Figure 1 for study design.

4.1. Discussion of Study Design, Including the Choice of Control Groups

This study is intended to examine the safety and immunogenicity of two doses of ANDV vaccine administered in two dose regimens as compared to placebo. The control group receives a placebo saline solution because there is currently no FDA-licensed vaccine for HPS or ANDV.

4.2. Selection of Study Population

4.2.1. Study Inclusion Criteria

Prospective subjects must meet all of the following inclusion criteria to be considered eligible for enrollment:

1. Provide written informed consent before initiation of any study procedures.
2. Are able to understand and comply with planned study procedures and be available for all study visits/phone calls.
3. Males or non-pregnant females ages 18-49, inclusive.
4. Are in good health*

   **As determined by medical history and physical examination to evaluate acute or currently ongoing chronic medical diagnoses or conditions, defined as those that have been present for at least 90 days which would affect the assessment of the safety of subjects or the immunogenicity of study vaccinations. Chronic medical diagnoses or conditions should be stable for the last 60 days (no hospitalizations, ER or urgent care for condition and no adverse symptoms that need medical intervention such as medication change/supplemental oxygen). This includes no change in chronic prescription medication, dose, or frequency as a result of deterioration of the chronic medical diagnosis or condition in the 60 days prior to enrollment. Any prescription change that is due to change of health care provider, insurance company, etc., or that is done for financial reasons, as long as in the same class of medication, will not be considered a deviation of this inclusion criterion. Any change in prescription medication due to improvement of a disease outcome, as determined by the site principal investigator or appropriate sub-investigator, will not be considered a deviation of this inclusion criterion. Subjects may be on chronic or as needed (prn) medications if, in the opinion of the site principal investigator or appropriate sub-investigator, they pose no additional risk to subject safety or assessment of reactogenicity and immunogenicity and do not indicate a worsening of medical diagnosis or condition. Similarly, medication changes subsequent to enrollment and study vaccination are acceptable provided there was no deterioration in the subject's chronic medical condition that necessitated a medication change, and there is no additional risk to the subject or interference with the evaluation of responses to study vaccination. Note: Topical, nasal, and inhaled medications (apart from steroids as outlined in the Subject Exclusion Criteria), herbals, vitamins, and supplements are permitted.*
5. Oral temperature is less than 100.0 °F (37.8ºC).
6. Pulse is 47 to 105 beats per minute (bpm), inclusive.
7. Systolic blood pressure (BP) is 85 to 150mm Hg, inclusive.
8. Diastolic blood pressure (BP) is 55 to 95 mm Hg, inclusive.
9. Have acceptable screening laboratories*,** within 28 days prior to enrollment.

   **Refer to Appendix B of the protocol for range of acceptable laboratory values.*

   Screening laboratory values that are outside acceptable range but are thought to be due to an acute condition or due to laboratory error may be repeated once. [see Manual of Procedures (MOP)]

10. Urine protein screen is negative or trace.
11. Drug screen for opiates is negative.
12. HgbA1C <6.3% at screening.
13. HIV – 1/2 antibody negative.
14. HCV antibody negative.
15. HBsAg negative.
16. Women of childbearing potential[*], must be using an effective method of contraception[**] from 30 days prior to the first study vaccination until 90 days after the last study vaccination.

    [*]*Women of childbearing potential are defined as those who have not been sterilized via tubal ligation, bilateral oophorectomy, hysterectomy, or successful Essure® placement (permanent, non-surgical, non-hormonal sterilization) with history of documented radiological confirmation test at least 90 days after the procedure (or with use of another birth control method if history of confirmation test not confirmed), AND are still menstruating or < 1 year since the last menses if perimenopausal.*

    [**]*For this study, we define an effective contraceptive method as one that results in a failure rate of less than 1% per year when it is used consistently and correctly. This includes, but is not limited to, non-male sexual relationships, abstinence from sexual intercourse with a male partner, monogamous relationship with a vasectomized partner, male condoms with the use of applied spermicide, intrauterine devices, NuvaRing®, and licensed hormonal methods such as implants, injectables or oral contraceptives ("the pill").*
17. Women of childbearing potential[*] must have a negative serum pregnancy test at screening and a negative urine pregnancy test within 24 hours prior to each study vaccination.

    [*]*See definition of women of childbearing potential above.*
18. Sexually active male participants whose partner is a woman of childbearing potential[*] and has not had a vasectomy[**] must agree not to father a child until 90 days after the last vaccination[***].

    [*]*See definition of women of childbearing potential above.*

    [**]*Performed > 1 year prior to screening*

    [***]*Must agree to use a barrier method of birth control e.g., either condom with spermicidal foam/gel/film/cream or partner reports usage of occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/suppository.*
19. Women agree to not donate eggs (ova, oocytes) and male subject agrees not to donate sperm from the start of screening onwards until at least 90 days after the last vaccination.
20. Agree not to participate in another clinical trial during the study period.
21. Agree not to donate blood to a blood bank for 3 months after receiving the last study vaccine.

4.2.2. Study Exclusion Criteria

Prospective subjects must not meet any of the following exclusion criteria to be considered eligible for enrollment:

1. Women who are pregnant, planning to become pregnant or lactating[*].

    [*]*Includes breastfeeding or planning to breastfeed at any given time from the receipt of study vaccination through the 12-month trial period.*

2. Known allergy or history of anaphylaxis, severe local or other serious adverse reactions to vaccines or vaccine products*, or history of severe allergic reactions.

   **This includes a known allergy to an aminoglycoside (e.g., gentamicin, tobramycin, neomycin, streptomycin).*

3. Received an experimental agent* within 3 months prior to study vaccination, or expects to receive an experimental agent** during the 12-month trial-reporting period.

   **Including vaccine, drug, biologic, device, blood product, or medication.*

   ***Other than from participation in this study.*

4. Received any licensed live vaccine within 28 days prior to or after each study vaccination.

5. Received a licensed inactivated vaccine within 14 days prior to or after each study vaccination.*

   **Allowable exception for inactivated seasonal influenza vaccine received more than 7 days prior to or after a study vaccination.*

6. Individuals in whom the ability to observe possible local reactions at the eligible injection sites (deltoid region) is, unacceptably obscured due to a physical condition or permanent body art.

7. Have an acute illness*, as determined by the site PI or appropriate sub-investigator, within 72 hours prior to study vaccination.

   **An acute illness which is nearly resolved with only minor residual symptoms remaining is allowable if, in the opinion of the site PI or appropriate sub-investigator, the residual symptoms will not interfere with the ability to assess safety parameters as required by the protocol. Subjects may re-screen after an acute illness is resolved*

8. Any confirmed or suspected immunosuppressive or immunodeficient condition* or use of anticancer chemotherapy or radiation therapy (cytotoxic) within 3 years prior to study vaccination.

   **Including HIV infection*

9. Administration of chronic (defined as more than 14 days) immunosuppressants or other immune modifying drugs within 6 months of receipt of study vaccine*

   **For corticosteroids, this means prednisone, or equivalent, greater than or equal to 0.5 mg/kg/day. Intranasal and topical steroids ARE allowed; daily inhaled steroids for treatment of asthma are NOT allowed.*

10. History of receipt of a Hantavirus vaccine, including vaccines for Hantaan virus, Puumala virus, or combination of both.

11. Exposed to ANDV* or plans to travel to an endemic area^^ from enrollment through 6 months post last vaccination.

    **Residence in an ANDV endemic area in the last 3 years or >2 consecutive weeks of travel to an ANDV endemic area^^ in the last 3 years.*

    ^^ANDV endemic areas include Chile, Brazil and Argentina [4 and 11]

12. Any chronic or active neurologic disorder, including seizures and epilepsy, excluding febrile seizures as a child.

13. History of receiving immunoglobulin or other blood product within the 3 months before enrollment in this study.

14. Current or past history of alcohol or drug abuse in the last 5 years.

15. Subjects with autoimmune disorders, chronic inflammatory disorders or neurological disorders with a potential autoimmune correlation.
16. Have any diagnosis, current or past, of schizophrenia, bipolar disease, or other psychiatric diagnosis that may interfere with subject compliance or safety evaluations.
17. Have been hospitalized for psychiatric illness, history of suicide attempt, or confinement for danger to self or others within 10 years prior to study vaccination.
18. Have received any antiviral within 3 days of study vaccination.
19. A diagnosis of Type I or II diabetes.
20. Current employee or staff paid entirely or partially by the contract for this trial, or staff who are supervised by the PI or Sub-Investigators.
21. Any condition that would, in the opinion of the Site Investigator or appropriate sub-investigator, is a contraindication to study participation.*

    Including acute or chronic (persisting for at least 90 days) clinically significant medical disease or condition, that would place the subject at an unacceptable risk of injury, render the subject unable to meet the requirements of the protocol, or may interfere with the evaluation of responses or the subject's successful completion of the study.

4.2.3. Reasons for Withdrawal and Discontinuation of Study Product Administration

Subjects may voluntarily withdraw their consent for trial participation at any time and for any reason, without penalty. The site principal investigator or appropriate sub-investigator may also choose to remove a subject from the study. A subject may withdraw or be withdrawn from this trial for any of the following reasons:

- Medical disease or condition, or any new clinical finding for which continued participation, in the opinion of the site principal investigator or appropriate sub-investigator, would compromise the safety of the subject, or would interfere with the subject's successful completion of this trial, or would interfere with the evaluation of adverse events or immunologic response.
- As deemed necessary by the site principal investigator or appropriate sub-investigator for noncompliance or other reasons.
- Subject withdrawal of consent.
- Subject lost to follow-up.
- Subject dies.
- Termination of this trial.
- New information becomes available that makes further participation unsafe.

Follow-up study vaccinations (2nd, 3rd and/or 4th dose) will not be administered to a subject if any of the following criteria are met:

- Pregnancy
- Receipt of disallowed licensed vaccine, experimental product or medication (see Section 4.3.2)
- New onset of illness or condition that meets the Exclusion Criteria (see Section 4.3.2)

- Medical condition or medication change for which continued participation, in the opinion of the site principal investigator or appropriate sub-investigator, would pose a risk to the subject or would likely confound interpretation of the results. Note: Medication changes subsequent to the first study vaccination are not exclusionary for receipt of the follow-up study vaccination provided there was no deterioration in the subject's chronic medical condition that necessitated a medication change, and there is no additional risk to the subject or interference with the evaluation of responses to study vaccination.
- Presence of signs or symptoms that could confound or confuse assessment of study vaccine reactogenicity.
- Any laryngospasm, bronchospasm, or anaphylaxis within 1 day after administration of study product that is considered related to study product.
- Any generalized urticaria after administration of study product that is considered related to study product.
- Serious adverse event related to the study vaccination.
- Grade 3 solicited or unsolicited (clinical sign or symptom) adverse event that occurs in the 7 days following study vaccination, lasts for 24 hours or more without decreasing to a Grade 1 or Grade 2, and does not have an alternative etiology. If the subject has a Grade 3 adverse event in the seven days following study vaccination and it lasts < 24 hours before decreasing to a Grade 2 or Grade 1 adverse event, see discontinuation criteria for Grade 2 below.
- Grade 3 solicited or unsolicited (clinical sign or symptom) adverse event that occurs >7 days following study vaccination and is ongoing at the time of the subsequent study vaccination (i.e., Day 29, Day 57 or Day 169). Conversely, if this Grade 3 adverse event was reduced to a Grade 1 or Grade 2 adverse event at the time of the subsequent study vaccination, investigational product (IP) may only be given, following the documented determination by the site principal investigator or appropriate sub-investigator, that it would not render study vaccination unsafe or interfere with the evaluation of adverse events or immunologic response.
- Grade 3 clinical safety laboratory value (according to the toxicity tables, Table 10 and Table 11) that does not decrease to Grade 1 or less prior to the follow-up study vaccination (i.e., Day 29, Day 57 or Day 169). Any clinical safety laboratory parameter may be re-evaluated only once at the local clinical laboratory to assess eligibility prior to the follow-up study vaccination. If the clinical safety laboratory value decreases to Grade 1 or less, the subject may receive the follow-up study vaccination. The study vaccination should be scheduled to occur within the acceptable protocol-specified window for that visit.
- Subjects who experienced any Grade 2 adverse event that is an unresolved Grade 2 or a Grade 1 at the time of the next vaccination, IP may only be given following the documented determination by the site principal investigator or appropriate sub-investigator, that it would not render study vaccination unsafe or interfere with the evaluation of adverse events or immunologic response.

4.3. Study Products

4.3.1. Vaccinations Administered

The ANDV DNA 2mg dosage cohorts (1 and 2) receive 1mg/0.5mL administered intramuscularly into each arm, and the ANDV DNA 4mg dosage cohorts (3 and 4) receive 2mg/0.5mL administered intramuscularly into each arm via the PharmaJet Stratis® Needle-Free Injection System. Subjects receive either 3 or 4 doses

according to their randomization assignment. Control subjects receive 0.5mL of 0.9% Sodium Chloride Injection, USP also administered via PharmaJet Stratis® Needle-Free Injection System.

4.3.2. Identity of Investigational Product(s)

ANDV DNA vaccine is a deoxyribonucleic acid (DNA) vaccine. The ANDV DNA vaccine plasmid is constructed on a well-characterized plasmid backbone, pWRG7077, and elements of the ANDV genome. The plasmid used for the ANDV DNA vaccine, pWRG/AND-M (opt2), is optimized for homo sapien codon usage and mRNA stability by Genewiz. The vaccine was developed by the Department of Molecular Virology, US Army Medical Research Institute of Infectious Diseases (USAMRIID; Fort Detrick, Maryland).

The ANDV DNA vaccine drug substance (Lot # 87763, date of manufacture 01 Dec 2017) was diluted to a concentration of 4.0 +/- 0.2 mg/mL in phosphate-buffered saline (PBS) at a pH of 7.2. It is clear, colorless and free of visible particulate. Study product must be stored at ≤ - 65º C. The ANDV DNA vaccine will be provided by Aldevron (Fargo, ND). The study product will be labeled according to manufacturer specifications and include the statement "Caution: New Drug – Limited by Federal Law to Investigational Use".

Placebo and Diluent, 0.9% Sodium Chloride Injection, USP will be provided by the DMID Clinical Materials Services (CMS), Fisher BioServices, and is shipped to the investigational site upon request and approval by DMID. Placebo and diluent must be stored at 20ºC to 25ºC (68°F to 77ºF).

The study product and placebo are administered using the PharmaJet Stratis® Needle-Free Injection System. This device delivers a 0.5 mL jet of liquid at high pressure that penetrates through the skin into the muscle. The device is FDA 510K cleared for use with approved medicines. [8]

4.3.3. Method of Assigning Subjects to Vaccination Groups (Randomization)

Enrollment and randomization of subjects is done online using the enrollment module of Advantage eClinical[SM].

The first 24 participants in Cohorts 1 and 2 included two sentinel subjects. Sentinel subjects were randomized 1:1 to dose regimen and received 2 mg of study vaccine open label and were followed for safety through Day 8. Because there were no safety concerns, the 22 non-sentinel subjects in Cohorts 1 and 2 were randomized in a 9:2:9:2 ratio to receive either study vaccine or placebo at a dose of 2 mg in a 3 or 4 dose regimen, in double-blind fashion.

After successful SMC review, the 24 participants in Cohorts 3 and 4 followed the same schedule as outlined for Cohorts 1 and 2 above. Sentinel subjects received 4 mg of study vaccine open label and were followed for safety through Day 8. The remaining 22 non-sentinel subjects in Cohort 3 and 4 were randomized in a 9:2:9:2 ratio to receive study vaccine or placebo at a dose of 4 mg in a 3 or 4 dose regimen, in double blind fashion.

Subjects who withdraw, or are withdrawn or terminated from this trial, or are lost to follow-up after signing the ICF, randomization, and receipt of study vaccine will not be replaced.

4.3.4. Selection of Doses in the Study

The ANDV DNA vaccine has never been administered to humans; however, related hantavirus DNA vaccines have been administered by gene gun, intramuscular electroporation, and PharmaJet Stratis® device (ongoing). These hantavirus DNA vaccines appear to be safe, well-tolerated, and immunogenic as measured by neutralizing antibody responses. The highest dose used in those clinical studies has been 2 mg of plasmid DNA per vaccination. A preclinical toxicity study testing the ANDV DNA vaccine in rabbits included doses

as high as 8 mg of DNA per vaccination using the PharmaJet Stratis® device. Even at that high dose in a relatively small animal the ANDV DNA vaccine was deemed safe. [8]

4.3.5. Selection and Timing of Dose for Each Subject

Each subject is randomly assigned to a vaccination group as described in Section 4.4.3. Study vaccines are administered on Day 1, Day 29 (+2 days), Day 57 (+2 days), and Day 169 (+5 days). The timing of the vaccine administration on study days is not specified.

4.3.6. Blinding

Except for the sentinel subjects who receive study vaccine open label, this is a double-blind trial. Sentinel subjects are blinded to dose schedule, but not dose level. Vaccine is prepared by an unblinded pharmacist who refers to the Treatment Key provided for the trial by the SDCC to determine the treatment for the subjects. The study products are administered by an unblinded study product administrator. The unblinded vaccine administrator is not involved in study-related assessments and does not have subject contact for data collection following study vaccine administration. Investigators, study personnel performing any study-related assessments following study vaccine administration, and laboratory personnel performing antibody assays are blinded to treatment arm assignment (i.e., placebo vs. study vaccine, and dose regimen).

A designated individual at the VTEU site was provided with a code list for emergency unblinding purposes, which is kept in a secure place. Additionally, in the case of a medical emergency, the PI or ISM may deem it medically necessary to unblind the subject's treatment assignment. If the PI or ISM believes that unblinding would benefit the medical care of the subject and time permits, DMID is consulted prior to unblinding, and concurrence is obtained. After DMID has approved the unblinding, an independent medical doctor or appropriate designee at the site, who is NOT the principal investigator or blinded staff, is to contact the SDCC. If the independent medical doctor or designee cannot make contact with SDCC staff, and/or time does not permit, the unblinding process can occur on-site by contacting the unblinded pharmacist or study staff.

4.3.7. Prior and Concomitant Therapy

Administration of any medications, therapies, or non-study vaccines is recorded on the appropriate data collection form. Concomitant medications include all current medications and medications taken within 60 days prior to signing the ICF through approximately 28 days after the last study vaccination or early termination (if prior to 28 days after the last study vaccination), whichever occurs first. Medications include prescription and over-the-counter drugs as well as herbals, vitamins, and supplements. Medications and non-study vaccines reported in the electronic case report form (eCRF) are limited to those received within 30 days prior to the first study vaccination through approximately 28 days after the last study vaccination.

Medications that might interfere with the evaluation of the investigational product(s) are not to be used from time of study vaccination through 28 days post the last vaccination unless clinically indicated as part of the subject’s health care. Medications in this category include the prohibited medications per the Subject Exclusion Criteria (see Section 4.3.2). In addition, the site principal investigator or appropriate sub-investigator may identify other medications that should not be used due to a risk to subject safety or assessment of reactogenicity and immunogenicity. Use of medications (anti-inflammatories or analgesics) as prophylaxis prior to study vaccination is prohibited. There are no known drug-vaccine interactions with the study vaccine and subjects are not being asked to discontinue current medications not listed in the exclusion criteria.

In the event medical conditions dictate use of medications, subjects are encouraged to obtain adequate care, comply with the course of therapy as prescribed by their physician and inform the site as soon as practicable.

Details of all medications taken during the medication reporting period for this study (date, indication, brand or generic name) will be recorded. Use of new medication should prompt evaluation for the occurrence of an AE or worsening of a pre-existing medical condition.

4.3.8. Treatment Compliance

All subjects are to receive four vaccines administered in the clinic. Subjects randomized to placebo receive four injections of normal saline. Subjects randomized to the 3-dose regimen receive ANDV DNA vaccine on Days 1, 29 and 169, and placebo on Day 57. Subjects assigned to the 4-dose regimen receive ANDV DNA on Days 1, 29, 57 and 169. Any deviations from this are recorded in protocol deviations and/or treatment administration forms.

4.4. Immunogenicity and Safety Variables

For additional details on study procedures and evaluations by study visits/days, see Table 2.

4.4.1. Safety Variables

The occurrence of an AE may come to the attention of study personnel during study visits and interviews of a study recipient presenting for medical care, or upon review by a study monitor. All AEs and SAEs are collected and recorded on the appropriate data collection form at each clinic visit. Subjects are instructed to notify the study center if they develop any severe reactions after study vaccination.

Subjects are observed for 30 minutes after the last injection of each dose is given. Subjects are provided with a memory aid and other study-related materials to record daily oral temperature, solicited site and systemic AEs, unsolicited AEs, and concomitant medications for 7 days post-vaccination. Subjects are encouraged to take their oral temperature around the same time each day. Subjects must not eat or drink anything hot or cold, or smoke within 10 minutes prior to taking oral temperature. Subjects are instructed on how to use their memory aid and how to measure and record AEs prior to discharge from the clinic.

Safety is assessed by the occurrence of:

1. Serious adverse events occurring from the time of study vaccination through approximately 6 months after the last study vaccination.
2. Solicited Adverse Events – reactogenicity events occurring from the time of study vaccination through 7 days after each study vaccination:
    a. Local AEs including pain, tenderness, erythema (redness), induration (hardness/swelling), bruising and skin discoloration. Refer to Table 5 and Table 6 for the applicable Toxicity Grading Scales.
    b. Systemic AEs including fever, feverishness (chills, shivering, sweating), fatigue (tiredness), malaise (general unwell feeling), myalgia (body aches/muscular pain), nausea, dizziness and headache. Refer to Table 7 and Table 8 for the applicable Toxicity Grading Scales.
3. Clinical safety laboratory adverse events occurring from the time of study vaccination through approximately 7 days after each study vaccination. Parameters to be evaluated include WBC, Hgb, platelet count, ANC, absolute lymphocyte count, creatinine, total bilirubin, AST, ALT and BUN. Refer to Table 10 and Table 11 for the applicable Toxicity Grading Scales.
4. Unsolicited Adverse Events –non-serious adverse events occurring from the time of study vaccination through approximately 28 days after the last study vaccination.

4.4.2. Immunogenicity Variables

Immunogenicity is measured using the following outcomes:

- Incidence of an ANDV-specific titer of ≥ 20 on Day 57 (3 dose regimen), Day 85 (4 dose regimen) and Day 197 (3 and 4 dose regimen) as measured by:
  - Plaque reduction neutralization titers
  - Pseudovirion neutralization titers
- Incidence of seroconversion (defined as a post-vaccination ANDV-specific titer ≥40 if baseline titer <20 or a minimum four-fold rise compared to baseline if baseline titer ≥20) on Day 57 (3 dose regimen), Day 85 (4 dose regimen) and Day 197 (3 and 4 dose regimen) as measured by:
  - Plaque reduction neutralization titers
  - Pseudovirion neutralization titers
- Geometric mean titer (GMT) at each visit and Geometric Mean Fold Rise (GMFR) of neutralizing antibodies to ANDV on Day 57 (3 dose regimen), Day 85 (4 dose regimen) and Day 197 (3 and 4 dose regimen) as compared to baseline (Day 1) titer and measured by:
  - Plaque reduction neutralization titers
  - Pseudovirion neutralization titers
- Incidence of a >3 standard deviation increase in the percent of ANDV-specific, cytokine-secreting CD4+ and CD8+ cells on Day 29 (3 and 4 dose regimen), Day 57 (3 dose regimen), Day 85 (4 dose regimen), Day 169 (3 and 4 dose regimen) and Day 197 (3 and 4 dose regimen) compared to baseline (Day 1) as measured by flow-based ICS.
- Incidence of a >3 standard deviation increase in the percent of ANDV-specific CD4+ and CD8+ cells on Day 29 (3 and 4 dose regimen), Day 57 (3 dose regimen), Day 85 (4 dose regimen), Day 169 (3 and 4 dose regimen) and Day 197 (3 and 4 dose regimen) compared to baseline (Day 1) as measured by a LPA.
- Incidence of an ANDV-specific titer of ≥20 at additional time points as measured by:
  - Pseudovirion neutralization titers
  - Plaque reduction neutralization titers

5. SAMPLE SIZE CONSIDERATIONS

The probability of rare adverse events cannot be accurately or precisely estimated in a clinical study of this size; however, the probabilities of observing one or more AEs given various true event rates are presented in Table 3.

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

Unless otherwise noted, continuous variables will be summarized using the following descriptive statistics: n (non-missing sample size), mean, standard deviation, median, maximum and minimum. The frequency and percentages (based on the non-missing sample size) of observed levels will be reported for all categorical measures. In general, all data will be listed, sorted by vaccination group and subject, and when appropriate by visit number within subject. Summary tables will be structured depending on the reporting period. For results based on data collected prior to dose 3, the two ANDV DNA 2mg groups will be combined and the two ANDV DNA 4mg groups will be combined. Post-dose 3 results will have a separate column for each vaccination group in the order (ANDV DNA 2mg 3 doses, ANDV DNA 2mg 4 doses, ANDV DNA 4mg 3 doses, ANDV DNA 4mg 4 doses, placebo). All columns will be annotated with the total population size relevant to that table/treatment and period where appropriate, including any missing observations.

6.2. Timing of Analyses

- After the completion of enrolling 24 subjects in Cohorts 1 and 2 (2 mg dose group), the SMC would review the data for Cohorts 1 and 2 through 7 days post the second vaccination.
- An interim analysis of safety, reactogenicity, and immunologic response data (excluding exploratory outcomes) was planned once all subjects (Cohort 1-4) have completed the Day 197 visit.
- The final analysis will be performed and a clinical study report completed when all primary safety endpoint data and all secondary immunogenicity endpoint data are available.
    - The CSR will be completed after the final data lock (through approximately Day 337 follow-up).
    - Any available data from the exploratory immunogenicity endpoints may also be included or if agreed upon, in an addendum to the CSR.

6.3. Analysis Populations

Summaries and analysis of safety data will be presented for the Safety Analysis Population. Summaries and analyses of immunogenicity data will be presented for the intent to treat (ITT) population. If there are major protocol deviations (as defined in Section 6.3.2) that result in the exclusion of data from at least 5% of all available visits across all groups, then a per-protocol (PP) analysis will also be performed for each immunogenicity end point.

6.3.1. Intention-to-Treat Analysis (ITT) Population

The intent-to-treat (ITT) population includes all subjects who received at least one dose of study vaccine and contributed both pre- and at least one post-study vaccination venous blood samples for immunogenicity testing for which valid results were reported. Subjects will be grouped as randomized.

6.3.2. Per Protocol Population

The per protocol (PP) population includes all subjects in the ITT subset with the following exclusions:

- Data from all available visits for subjects found to be ineligible at baseline.
- Data from all visits subsequent to major protocol deviations, such as:
    - Receipt of non-study licensed live vaccine within 28 days before or after study vaccination,

- Receipt of non-study licensed inactivated vaccine within 14 days before or after study vaccination,
- Receipt of immunosuppressive therapy (e.g., corticosteroids) within 30 days before or after study vaccination.
- Receipt of wrong study product.

- Data from any visit that occurs substantially out of window. See Table 2 for visit windows.

6.3.3. Safety Population

The Safety Analysis population includes all subjects who received at least one dose of study vaccine.

6.3.4. Immunogenicity Population

The immunogenicity analyses will be performed for the ITT population. If there are major protocol deviations, as defined in Section 6.3.2, then a PP analysis may be performed.

6.4. Covariates and Subgroups

The protocol does not define any formal subgroup analyses, and the study is not adequately powered to perform subgroup analyses.

6.5. Missing Data

All attempts will be made to collect all data per protocol. As missing data are expected to be minimal, no imputation will be performed for missing values. Any data point that appears to be erroneous or inexplicable based on clinical judgment will be investigated as a possible outlier. If data points are identified as outliers, sensitivity analyses will be performed to examine the impact of including or excluding the outliers. Any substantive differences in these analyses will be reported.

6.6. Interim Analyses and Data Monitoring

After the completion of enrolling 24 subjects in Cohorts 1 and 2 (2 mg dose group), the SMC reviewed the data for Cohorts 1 and 2 through 7 days after the second vaccination. These reviews did not involve any hypothesis testing and will not be considered in estimating the precision of any estimates made at the conclusion of the study.

An interim analysis of safety, reactogenicity, and immunologic response data (excluding exploratory outcomes) is planned once all subjects (Cohort 1-4) have completed the Day 197 visit and the data are entered in the database, validated and monitored according to the clinical monitoring plan. The study statistician will provide the analysis of aggregate data unblinded at the group level to the investigators and sponsor staff for the purpose of manuscript, abstract preparation or presentation. The information from the primary immunogenicity and safety review may be published or otherwise presented, pursuant upon executed agreements between NIAID and VTEU investigators. The laboratory staff that run the assays for the Day 253 and 337 visits will remain blinded, and the assessment of relationship to study product of any SAEs that may be reported at the Day 253 and 337 visits will be delegated to blinded sub-investigators at the clinical site. While the results will not be used to make any decisions concerning the conduct of this trial, they may be used to make decisions on activities external to this trial such as the design of future trials of this vaccine. Since this early analysis of the data is not intended to impact the conduct of the trial, it has no impact on Type I error and adjustments are not planned.

All Tables and Figures to be included in the interim report are highlighted in Appendix 4 Interim Tables and Figures.

6.7. Multicenter Studies

Not applicable. This study will take place at a single VTEU site (Cincinnati Children's Hospital).

6.8. Multiple Comparisons/Multiplicity

This study was not designed to test any specific null hypothesis and, as such, no adjustments for multiple testing are planned.

7. STUDY SUBJECTS

7.1. Disposition of Subjects

Table 15 will present a summary of the reasons that subjects were screened but not enrolled.

The composition of analysis populations, including reasons for subject exclusion, by vaccination group, will be presented in Table 13. A listing of subjects excluded from each analysis population will be presented in Listing 4.

The disposition of subjects in the study will be tabulated by vaccination group (Table 12). The table shows the total number of subjects that were screened, enrolled/randomized, received at least one treatment, received all scheduled treatments, completed all blood draws, completed Study Day 197 visit, completed follow-up (Study Day 337) and completed per protocol.

A flowchart showing the disposition of study subjects, adapted from the Consort Statement [12] will be included (Figure 2). This figure will present the number of subjects screened, enrolled, lost to follow-up, and analyzed, by vaccination group.

A listing of subjects who discontinued dosing or terminated from study follow-up and the reason will be included in Listing 1.

Dates of first treatment administration by vaccination group will be presented in Table 14.

7.2. Protocol Deviations

A summary of subject-specific protocol deviations will be presented by the reason for the deviation, the deviation category, and vaccination group for all subjects (Table 4). Deviations that are considered major deviations that will be reviewed for possible subject exclusion from the per protocol population include: receipt of non-study licensed live vaccine within 28 days before or after study vaccination, receipt of non-study licensed inactivated vaccine within 14 days before or after study vaccination (allowable exception for inactivated seasonal influenza vaccine received more than 7 days prior to or after a study vaccination), and receipt of immunosuppressive therapy (e.g., corticosteroids) within 30 days before or after study vaccination. All subject-specific protocol deviations and non-subject specific protocol deviations will be included in Appendix 3 as data listings (Listing 2 and Listing 3, respectively).

8. IMMUNOGENICITY EVALUATION

This study was not designed to test a specific null hypothesis; rather, the primary objectives include assessing the safety and tolerability of two dosages and two dose regimens of an ANDV DNA vaccine as compared to a placebo administration.

Immunogenicity and cellular assay data summaries and analyses will be presented by vaccination group for the ITT population, and for the PP population in the event of major protocol deviations (as defined in Section 6.3.2) or if any subjects are found to be ineligible at baseline. Summary statistics for continuous data will include mean, standard deviation (SD), median, minimum and maximum. For titer data, geometric mean and 95% CI will be calculated in place of arithmetic mean and standard deviation. Number of subjects, percentage (with denominator defined as the number of subjects with non-missing data), and exact (Clopper-Pearson) 95% confidence intervals will be presented for proportional endpoints.

8.1. Primary Immunogenicity Analysis

Not applicable.

8.2. Secondary Immunogenicity Analyses

Summaries and analysis of immunogenicity data will be presented for the ITT population. If there are major protocol deviations (as defined in Section 6.3.2) or if any subjects are found to be ineligible at baseline, a per-protocol (PP) analysis will also be performed.

Immune responses in terms of a titer ≥ 20 in antibody post vaccination, measured by PsVNA and PRNT will be summarized. These results are presented in Table 19, Table 20, Table 21, and Table 22, and graphically in Figure 11, Figure 12, Figure 13, and Figure 14.

Geometric mean fold rise, incidence of seroconversion, and geometric mean titers (GMT) will be calculated and compared between groups at various time points for PsVNA and PRNT. GMFR and seroconversion results are presented in Table 23, Table 24, Table 25, and Table 26. GMT results along with 95% confidence intervals are presented in Table 27, Table 28, Table 29, and Table 30.

Reverse cumulative distributions (RCD) curves will be presented for PsVNA and PRNT antibody titers. Plots for each assay will be generated with three panels (for each measurement), and separate curves within each panel for each vaccination group, as shown in Figure 3, Figure 4, Figure 5, and Figure 6.

Box-and Whisker graphs of PsVNA and PRNT antibody titers will be plotted on a log scale over time, by vaccination group at each time point (Figure 7, Figure 8, Figure 9, and Figure 10).

The Spearman correlation between PsVNA and PRNT titers will be evaluated and presented in Table 31 and Table 32. The correlation will be depicted in scatter plots as Figure 15 and Figure 16.

Data listings of PsVNA and PRNT assay results as reported by the laboratory will be provided in Listing 7. Listings will be sorted by vaccination group, subject identifier (ID), and visit.

No formal hypothesis testing is planned.

8.3. Exploratory Efficacy Analyses

Summaries and analysis of immunogenicity and cellular assay data will be presented for the ITT population. If there are major protocol deviations (as defined in Section 6.3.2) or if any subjects are found to be ineligible at baseline, a per-protocol (PP) analysis may also be performed.

Cellular assay data represent the percent of CD4+ and CD8+ T-Cells expressing each cytokine or combination of cytokines. For each endpoint, the standard deviation (SD) of the percent of cells at baseline will be calculated on a log scale across all groups combined. An individual positive response is then defined as the log percent of cells at a follow-up visit more than 3 SD greater than the baseline log percent.

Positive responses to each ANDV peptide pool (PP1, PP2) or to either pool, will be summarized. Intracellular cytokine (ICS) data will be presented by CD4+ and CD8+ T-Cell responses secreting each cytokine and cytokine combination. T-Cell lymphoproliferation (LPA) responses will be presented separately for CD4+ and CD8+ T-Cells. Measurements will be taken on Day 29 (3 and 4 dose regimen), Day 57 (3 dose regimen), Day 85 (4 dose regimen), Day 169 (3 and 4 dose regimen), and Day 197 (3 and 4 dose regimen). ICS results are presented in Table 33 through Table 44 and graphically for each cytokine combination in Figure 17, Figure 18 (IFNɣ), Figure 19, Figure 20 (TNFα), Figure 21, Figure 22 (IL-2), Figure 23, Figure 24 (IFNɣ and TNFα), Figure 25, Figure 26 (IFNɣ and IL-2), Figure 27, Figure 28 (TNFα and IL-2), Figure 29, and Figure 30 (IFNɣ, TNFα and IL-2). LPA results are presented in Table 45 and Table 46 and graphically in Figure 31 and Figure 32.

Immune responses in terms of a titer ≥20 in antibody post vaccination, measured by PsVNA and PRNT will be summarized for additional time points. The additional time points for PsVNA are Day 29, Day 85, and Day 169. The additional time point for PRNT is Day 169. These results are presented in Table 19, Table 20, Table 21, and Table 22 and graphically in Figure 11, Figure 12, Figure 13, and Figure 14.

Reverse cumulative distributions (RCD) curves will be presented for PRNT and PsVNA antibody titers. The plots are shown in Figure 3, Figure 4, Figure 5, and Figure 6.

Box-and Whisker graphs of PsVNA and PRNT antibody titers will be plotted on a log scale over time, by vaccination group at each time point (Figure 7, Figure 8, Figure 9, and Figure 10).

The Spearman correlation between PsVNA and PRNT titers will be evaluated and presented in Table 31 and Table 32. The correlation will be depicted in scatter plots as Figure 15 and Figure 16.

Data listings of ICS and LPA assay results as reported by the laboratory will be provided in Listing 7. Listings will be sorted by vaccination group, subject ID, and visit.

No formal hypothesis testing is planned.

9. SAFETY EVALUATION

9.1. Demographic and Other Baseline Characteristics

Summaries of age, sex, ethnicity, and race will be presented by vaccination group and overall (Table 16 and Table 17). Ethnicity is categorized as Hispanic or Latino, or not Hispanic and not Latino. In accordance with NIH reporting policy, subjects may self-designate as belonging to more than one race or may refuse to identify a race, the latter reflected in the CRF as "No" to each racial option.

Individual subject listings will be presented for all demographics (Listing 5).

9.1.1. Prior and Concurrent Medical Conditions

Complete medical history is obtained by interview of subjects at the screening visit and is reviewed and/or updated on Day 1 prior to study vaccination. At follow-up visits after study vaccination, an interim medical history is obtained by interview of subjects noting any changes since the previous clinic visit or contact. The interim medical history should include an assessment for new medical conditions. Subjects are queried regarding a history of significant medical disorders of the head, eyes, ears, nose, throat, mouth, cardiovascular system, lungs, gastrointestinal tract, liver, pancreas, kidney, urologic system, nervous system, blood, lymph nodes, endocrine system, musculoskeletal system, skin, and genital/reproductive tract. A history of any allergies, cancer, immunodeficiency, psychiatric illness, substance abuse, and autoimmune disease is solicited.

All current illnesses and past pre-existing medical conditions will be MedDRA® coded using MedDRA dictionary version 22.0 or higher. Summaries of subjects' pre-existing medical conditions will be presented by vaccination group (Table 18).

Individual subject listings will be presented for all medical conditions (Listing 6).

9.1.2. Prior and Concomitant Medications

Medication history (concomitant medications) includes a review of all current medications and medications taken within 60 days prior to signing the ICF through approximately 28 days after the last study vaccination or early termination (if prior to 28 days after the last study vaccination), whichever occurs first. Medications reported in the eCRF are limited to those taken within 30 days prior to the first study vaccination through approximately 28 days after the last study vaccination. Prescription and over-the-counter drugs are included as well as herbals, vitamins, and supplements. Use of new medication should prompt evaluation for the occurrence of any AE.

Summaries of medications that were started prior to dosing or continuing at the time of dosing will be presented by WHO Drug Terms 2 and 3 and vaccination group (Table 147).

Individual subject listings will be presented for all concomitant medications (Listing 16).

9.2. Measurements of Treatment Compliance

The subject disposition table (Table 12) will summarize the number of subjects that were screened, randomized, received at least one treatment, received all scheduled treatments, completed all blood draws, completed Study Day 197, and completed follow-up (Study Day 337).

Individual subject listings will be presented for all subjects who discontinued dosing (Listing 1).

9.3. Adverse Events

When calculating the incidence of adverse events (i.e., on a per subject basis), each subject will only be counted once and any repetitions of adverse events within a subject will be ignored; the denominator will be the number of subjects in the Safety population. All adverse events reported will be included in the summaries and analyses.

An overall summary of adverse events is presented in Table 47.

Adverse events occurring in 5% of subjects in any vaccination group will be presented in Table 48.

9.3.1. Solicited Events and Symptoms

Systemic solicited adverse events are collected pre-vaccination, and systemic and local solicited adverse events are collected 30 minutes post-vaccination and then daily for 7 days after each vaccination and graded on a scale of 0 (absent), 1 (mild), 2 (moderate) and 3 (severe). See Table 5, Table 6, Table 7, Table 8, and Table 9 for additional grading details. Systemic events include fever, feverishness, fatigue, malaise, myalgia, nausea, dizziness and headache. Local events include pain, tenderness, erythema, induration, ecchymosis, and skin discoloration. If a subject experiences the same local adverse event in both arms for a given vaccination, then the greatest severity between arms will be reported.

The proportion of subjects reporting at least one solicited adverse event will be summarized for each solicited adverse event, any systemic symptom, any local symptom, and any symptoms. The 95% CI calculated using Clopper-Pearson methodology from a binomial distribution (SAS Proc Freq with a binomial option) will be presented. These results are presented in Table 49, Table 50, Table 51, Table 52, and Table 53.

For each systemic and local event, any systemic event, any local event, and any solicited event, the maximum severity over 7 days after each vaccination will be summarized for the Safety population. The number and percentage of subjects reporting each event, as well as the 95% CI calculated using Clopper-Pearson methodology, will be summarized by the maximum severity and vaccination group, separately for each vaccination and over all vaccinations. For each event, the denominator is the number of subjects with non-missing data for the specific event (Table 54, Table 55, Table 56, Table 57, and Table 58).

The number of subjects reporting each solicited adverse event will be summarized for each day post vaccination for each vaccination and for all vaccinations, both in summary tables starting with Table 59 and ending with Table 80 and graphically starting with Figure 33 and ending with Figure 42.

Solicited adverse events by subject will be presented in Listing 9 and Listing 10.

9.3.2. Unsolicited Adverse Events

The proportion of subjects reporting at least one unsolicited adverse event will be summarized by MedDRA system organ class and preferred term for each vaccination and over all vaccinations. Denominators for percentages are the number of subjects in the Safety population who received the vaccination being summarized.

Unsolicited adverse events by subject will be presented in Listing 11.

The following summaries for unsolicited adverse events will be presented by MedDRA system organ class, preferred term, dose and vaccination group:

- Incidence and 95% CI of unsolicited adverse events after each dose and any time during the study will be summarized in Table 81, Table 82, Table 83, Table 84, and Table 85;

- The total frequency of unsolicited adverse events after each dose and any time during the study will be summarized in Table 86 and Table 87;
- Summary of severity and relationship to study product after dose 1 and dose 2 (Table 88, Table 89, and Table 90;
- Summary of severity and relationship to study product after dose 3 and dose 4 and at any time (Table 91, Table 92, Table 93, Table 94, Table 95, and Table 96;
- Incidence and 95% CI of unsolicited adverse events related to IP, after each dose and any time during the study will be summarized in Table 97, Table 98, Table 99, Table 100, and Table 101;
- The total frequency of unsolicited adverse events related to IP, after each dose and any time during the study will be summarized in Table 102 and Table 103;
- Subject listing of SAEs (Table 104);
- Bar chart of the total frequency of non-serious related unsolicited adverse events by severity and MedDRA system organ class (Figure 43, Figure 44, Figure 45, Figure 46, and Figure 47);
- Bar chart of the incidence of non-serious related unsolicited adverse events by maximum severity and MedDRA system organ class (Figure 48, Figure 49, Figure 50, Figure 51, and Figure 52);

9.4. Deaths, Serious Adverse Events and other Significant Adverse Events

A listing of deaths and other serious adverse events will be presented in Table 104, and all moderate or severe, non-serious unsolicited AEs will be listed in Table 105.

9.5. Pregnancies

For any subjects in the Safety population who become pregnant during the study, every attempt is made to follow these subjects to completion of pregnancy to document the outcome, including information regarding any complications with pregnancy and/or delivery. A table summarizing the total pregnancies, number of live births, and number of spontaneous abortions, elective abortions or still births by treatment will be presented. In addition, a listing of pregnancies and outcomes will be presented (Listing 17, Listing 18, Listing 19, Listing 20, and Listing 21).

9.6. Clinical Laboratory Evaluations

Clinical safety laboratory adverse events are collected at the time of study vaccination through approximately 7 days after each study vaccination. Parameters evaluated include white blood cell count, platelet count, hemoglobin concentration, ANC, sodium, potassium, total bilirubin, alanine aminotransferase (ALT), and creatinine. If creatine is above the normal range, blood urea nitrogen (BUN) is also assessed. Grading scales for safety laboratory parameters are presented in Table 10 and Table 11.

A listing of subject visits with any abnormal chemistry laboratory results (Grade 1 severity or higher) will be presented in Table 106. Subject visits with abnormal hematology laboratory results will be presented in Table 107.

The distribution of abnormal chemistry laboratory results by maximum severity, time point, and vaccination group will be presented in Table 108, Table 109, Table 110, Table 111, Table 112, Table 113 and Table 114.

The distribution of chemistry laboratory results assessed as related to study IP, by maximum severity, time point, and vaccination group will be presented in Table 115, Table 116, Table 117, Table 118, Table 119, Table 120, and Table 121.

Descriptive statistics including mean, median, standard deviation, maximum and minimum values, by time point and vaccination group, for each chemistry laboratory parameter, including change from baseline, will be summarized in Table 122, Table 123, Table 124, Table 125, Table 126, and Table 127.

The distribution of abnormal hematology laboratory results by maximum severity, time point, and vaccination group will be presented in Table 128, Table 129, Table 130, Table 131, and Table 132.

The distribution of hematology laboratory results assessed as related to study IP, by maximum severity, time point, and vaccination group will be presented in Table 133, Table 134, Table 135, Table 136, and Table 137.

Descriptive statistics including mean, median, standard deviation, maximum and minimum values, by time point and vaccination group, for each hematology laboratory parameter, including change from baseline, will be summarized in Table 138, Table 139, Table 140, and Table 141.

The change from baseline in each chemistry laboratory value, showing the mean and SD at each time point, by gender and vaccination group, will be presented in Figure 53, Figure 54, Figure 55, Figure 56, and Figure 57. Similar results for hematology will be presented in Figure 58, Figure 59, Figure 60, and Figure 61.

Complete listings of individual chemistry and hematology laboratory results, including applicable reference ranges, will be presented in Listing 12 (chemistry) and Listing 13 (hematology).

9.7. Vital Signs and Physical Evaluations

Vital sign measurements, including pulse, systolic blood pressure, diastolic blood pressure and oral temperature, were assessed at Day 1, Day 29, Day 57, and Day 169. The distribution of severity will be tabulated overall and for each measurement, by visit and vaccination group (Table 142, Table 143, Table 144, Table 145, and Table 146). Vital sign findings per subject are detailed in Listing 14.

Physical examinations are performed at Day 1, Day 8, Day 29, Day 36, Day 57, Day 64, Day 85, Day 141, Day 169, Day 176, Day 197, Day 253, Day 337. At the screening visit, the physical examination includes the following organs and organ systems: general appearance, skin, head and neck, lungs, heart, liver, spleen, extremities, musculoskeletal, lymph nodes, and nervous system. At follow-up visits, targeted physical examination may be performed, if indicated based on review of complete medical history and any updates obtained by interview of subjects. Physical exam findings per subject are detailed in Listing 14.

9.8. Concomitant Medications

Concomitant medications will be coded to the Anatomical Therapeutic Classification using the WHO Drug Dictionary. The use of prior and concomitant medications taken during the study will be recorded on the CRFs. A by-subject listing of concomitant medication use will be presented (Listing 16). The use of concomitant medications during the study will be summarized by ATC1, ATC2 code and vaccination group for the Safety population (Table 147).

9.9. Other Safety Measures

Not applicable.

10. PHARMACOKINETICS

Not applicable.

11. OTHER ANALYSES

Not applicable.

12. REPORTING CONVENTIONS

Due to the small sample size, all p-values will be reported to 2 decimal places. The mean, standard deviation, and other statistics will be reported to 1 decimal place greater than the original data. The minimum and maximum will use the same number of decimal places as the original data. Proportions will be presented as 2 decimal places; proportions greater than zero but <0.01 will be presented as "<0.01". Percentages will be reported to the nearest whole number; values greater than zero but < 1% will be presented as "<1"; values greater than 99% but less than 100% will be reported as ">99". Estimated parameters, not on the same scale as raw observations (e.g. regression coefficients) will be reported to 3 significant figures.

13. TECHNICAL DETAILS

SAS version 9.4 or above, or R language and environment for statistical computing 3.5.2 or above, will be used to generate all tables, figures and listings.

14. SUMMARY OF CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSES

The changes made to the SAP from the analyses specified in the protocol are summarized below:

Geometric mean fold rise will also be reported in addition to seroconversion rates.

The interim analysis will be performed on locked data and will include safety data through study completion.

The changes made to the SAP from version 1.0 to version 2.0 are summarized below:

The total bilirubin reference range and Grade 1 values were updated in Table 11, per the changes in protocol version 4.0.

15. REFERENCES

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16. LISTING OF TABLES, FIGURES, AND LISTINGS

Table, figure, and listing shells are presented in Appendices 1, 2, and 3.

APPENDICES

APPENDIX 1. TABLE MOCK-UPS

Note: Tables for the primary immunogenicity and safety review will not include data from Day 253 and Day 337 visits.

LIST OF TABLES

9.1 Overall Study Design and Plan Description

Table 1: Study Design

Cohort	Subjects Enrolled	Randomization/ Treatment Arm*#	Day 1	Day 29	Day 57	Day 169
Cohort 1 2mg^	12	1a* n=1 Sentinel	ANDV DNA	ANDV DNA	Placebo	ANDV DNA
		1b# N=9 ANDV DNA	ANDV DNA	ANDV DNA	Placebo	ANDV DNA
		1c# n=2 Placebo	Placebo	Placebo	Placebo	Placebo
Cohort 2 2mg^	12	2a* n=1 Sentinel	ANDV DNA	ANDV DNA	ANDV DNA	ANDV DNA
		2b# N=9 ANDV DNA	ANDV DNA	ANDV DNA	ANDV DNA	ANDV DNA
		2c# n=2 Placebo	Placebo	Placebo	Placebo	Placebo
Cohort 3 4mg+	12	3a* n=1 Sentinel	ANDV DNA	ANDV DNA	Placebo	ANDV DNA
		3b# N=9 ANDV DNA	ANDV DNA	ANDV DNA	Placebo	ANDV DNA
		3c# n=2 Placebo	Placebo	Placebo	Placebo	Placebo
Cohort 4 4mg+	12	4a* n=1 Sentinel	ANDV DNA	ANDV DNA	ANDV DNA	ANDV DNA
		4b# N=9 ANDV DNA	ANDV DNA	ANDV DNA	ANDV DNA	ANDV DNA
		4c# n=2 Placebo	Placebo	Placebo	Placebo	Placebo
TOTAL		48 subjects				

* All sentinel subjects and study personnel will be unblinded to dose and blinded to treatment schedule.
# All non-sentinel subjects will be blinded to dose and treatment schedule.
^ 1mg ANDV DNA administered into the left and right deltoid
+ 2mg ANDV DNA administered into the right and left deltoid.

9.5.1 Efficacy/Immunogenicity and Safety Measurements Assessed and Flow Chart

Table 2: Schedule of Study Procedures

All Treatment Arms																
Study Visit (V)	**00**	**01**	**02**	**03**	**04**	**05**	**06**	**07**	**08**	**09**	**10**	**11**	**12**	**13**	**U/S[#]**	**ET[#]**
Study Day from Vaccine 1	**Day ≤ -28 Screen**	**Day 1 Vaccine 1**	**Day 8 +2**	**Day 29 +2**	**Day 36**	**Day 57**	**Day 64**	**Day 85**	**Day 141**	**Day 169**	**Day 176**	**Day 197**	**Day 253**	**Day 337**	**-**	**-**
Weeks from Vaccine 1		**0**	**1**	**4**	**5**	**8**	**9**	**12**	**20**	**24**	**25**	**28**	**36**	**48**	**-**	**-**
Study Day from Vaccine 2				**Day 1 Vaccine 2**	**Day 8 +2**	**Day 29 +2**	**Day 36**	**Day 57**	**Day 113**	**Day 141**	**Day 148**	**Day 169**	**Day 225**	**Day 309**	**-**	**-**
Study Day from Vaccine 3						**Day 1 Vaccine 3**	**Day 8 +2**	**Day 29 +2**	**Day 85 +/-5**	**Day 113+5**	**Day 120**	**Day 141**	**Day 197**	**Day 281**	**-**	**-**
Study Day from Vaccine 4										**Day 1 Vaccine 4**	**Day 8 +2**	**Day 29 +2**	**Day 85 +/-5**	**Day 169 +/-7**	**-**	**-**
Visit Type	**Screen**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**
Obtain Informed Consent[∞]	X															
Collect Demographic Information	X															
Height & Weight	X															
Physical Examination - Full	X															
Urine Dipstick, Opioid testing	X															
Screening Labs[~]	20[= & 2]															
Enrollment/Randomization		X														
Review Eligibility Criteria	X	X[†¬1]		X[†¬]		X[†¬]				X[†¬]						
Medical History[@]	X	X[†¬1]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant Medications [4]	X[√]	X[†¬]	X	X	X	X	X	X	X	X	X	X			X	X
Vital Signs (oral temp, pulse, BP)[%]	X	X[†$]		X[†]		X[†]				X[†]					X	X
Physical Examination – Targeted[0]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy Test[^]	X	X[†]		X[†]		X[†]				X[†]						
Clinical Safety Evaluations*		6.5	6.5		6.5		6.5			6.5	6.5				6.5	6.5
PBMCs (ICS, LPA)		40		40		40		40		40		40			40	40
Immunogenicity ANDV PRNT		10				10		10		10		10				
Immunogenicity ANDV PsVNA		10		10		10		10		10		10	10	10	10	10

All Treatment Arms																
Study Visit (V)	**00**	**01**	**02**	**03**	**04**	**05**	**06**	**07**	**08**	**09**	**10**	**11**	**12**	**13**	**U/S[#]**	**ET[#]**
Study Day from Vaccine 1	**Day ≤ -28 Screen**	**Day 1 Vaccine 1**	**Day 8 +2**	**Day 29 +2**	**Day 36**	**Day 57**	**Day 64**	**Day 85**	**Day 141**	**Day 169**	**Day 176**	**Day 197**	**Day 253**	**Day 337**	**-**	**-**
Weeks from Vaccine 1		**0**	**1**	**4**	**5**	**8**	**9**	**12**	**20**	**24**	**25**	**28**	**36**	**48**	**-**	**-**
Study Day from Vaccine 2				**Day 1 Vaccine 2**	**Day 8 +2**	**Day 29 +2**	**Day 36**	**Day 57**	**Day 113**	**Day 141**	**Day 148**	**Day 169**	**Day 225**	**Day 309**	**-**	**-**
Study Day from Vaccine 3						**Day 1 Vaccine 3**	**Day 8 +2**	**Day 29 +2**	**Day 85 +/-5**	**Day 113+5**	**Day 120**	**Day 141**	**Day 197**	**Day 281**	**-**	**-**
Study Day from Vaccine 4										**Day 1 Vaccine 4**	**Day 8 +2**	**Day 29 +2**	**Day 85 +/-5**	**Day 169 +/-7**	**-**	**-**
Visit Type	**Screen**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**
Future Exploratory Assays								40				40		40		
Pre-administration reactogenicity assessment		X		X		X				X						
Study Vaccination[3]		X		X		X				X						
30-minute evaluation post vax[>]		X		X		X				X						
Distribute Memory Aid/Materials		X		X		X				X						
Review Memory Aid/Site assessment			X		X		X				X				X	X
Assessment of Adverse Events		X	X	X	X	X	X	X	X	X	X	X			X	X
Assessment of SAEs		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

∞Prior to study procedures.
†Prior to study vaccination.
¬Review/confirm information or activity in subjects previously consented and screened.
[1]Review results of clinical screening laboratory evaluations.
[@]Complete medical history will be obtained by interview of subjects at the screening visit and will be updated on Day 1 prior to the first study vaccination and interim medical history will be obtained by interview of subjects at follow-up visits after the first study vaccination.
[%]Subjects must not eat or drink anything hot or cold, or smoke within 10 minutes prior to taking oral temperature.
[$]Vital signs assessed on Day 1 prior to the first study vaccination will be considered as baseline.
[√]All current medications and medications taken within 60 days prior to signing the ICF. Concomitant medications taken within 30 days of enrollment through Day 28 post last vaccination are collected in Advantage eClinical[SM].
[>]Observation period will begin after the study vaccination has been given.
^Serum pregnancy test will be performed on all females of childbearing potential at screening. A urine pregnancy test will be performed within 24 hours prior to study vaccination and results must be negative and known prior to each study vaccination.

9.7.1 Sample Size

Table 3: Sample Size/Probability Estimates

N	Hypothetical "True" Event Rate	Probability (%) of Observing at Least One Event	N	Hypothetical "True" Event Rate	Probability (%) of Observing at Least One Event
10	0.1%	1.0	20	0.1%	2.0
	0.5%	4.9		0.5%	9.5
	1.0%	9.6		1.0%	18.2
	2.0%	18.3		2.0%	33.2
	3.0%	26.3		3.0%	45.6
	4.0%	33.5		4.0%	55.8
	5.0%	40.1		5.0%	64.2
	10.0%	65.1		10.0%	87.8
	20.0%	89.3		20.0%	98.8

10.2 Protocol Deviations

Table 4: Distribution of Protocol Deviations by Category, Type, and Vaccination Group

Category	Deviation Type	ANDV DNA 2mg 3 Doses (N=X)		ANDV DNA 2mg 4 Doses (N=X)		ANDV DNA 4mg 3 Doses (N=X)		ANDV DNA 4mg 4 Doses (N=X)		Placebo (N=X)		All Subjects (N=X)	
		No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
Eligibility/enrollment	Any type												
	Did not meet inclusion criterion	x	x	x	x	x	x	x	x	x	x	x	x
	Met exclusion criterion												
	ICF not signed prior to study procedures												
	Other												
Treatment administration schedule	Any type												
	Out of window visit												
	Missed visit/visit not conducted												
	Missed treatment administration												
	Delayed treatment administration												
	Other												
Follow-up visit schedule	Any type												
	Out of window visit												
	Missed visit/visit not conducted												
	Other												
Protocol procedure/assessment	Any type												
	Incorrect version of ICF signed												
	Blood not collected												
	Urine not collected												
	Other specimen not collected												

Table 4: Distribution of Protocol Deviations by Category, Type, and Vaccination Group (Continued)

Category	Deviation Type	ANDV DNA 2mg 3 Doses (N=X)		ANDV DNA 2mg 4 Doses (N=X)		ANDV DNA 4mg 3 Doses (N=X)		ANDV DNA 4mg 4 Doses (N=X)		Placebo (N=X)		All Subjects (N=X)	
		No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
	Too few aliquots obtained												
	Specimen result not obtained												
	Required procedure not conducted												
	Required procedure done incorrectly												
	Study product temperature excursion												
	Specimen temperature excursion												
	Other												
Treatment administration	Any type												
	Required procedure done incorrectly												
	Study product temperature excursion												
	Other												
Blinding policy/procedure	Any type												
	Treatment unblinded												
	Other												

Note: N=Number of subjects in the Safety Population

12.2.2 Displays of Adverse Events

Table 5: Local (Injection Site) Reactogenicity Grading

Local (Injection Site) Reaction	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Pain – experienced without touching the injection site (spontaneous discomfort)	Subject is aware of pain, but it does not interfere with daily activity, **and** no pain medication is taken	Subject is aware of pain; there is interference with daily activity **or** it requires repeated use of a non-narcotic pain reliever for >24 hours	Subject is aware of pain, **and** it prevents daily activity or requires any use of a prescription medication
Tenderness – hurts only when injection site is touched or the arm is moved	The area immediately surrounding the injection site hurts only when touched or with arm motion, **and** it does **not** interfere with daily activity	The area immediately surrounding the injection site hurts when touched or with arm motion, **and** it interferes with daily activity	The area immediately surrounding the injection site hurts when touched or with arm motion, **and** it prevents daily activity
Erythema (Redness)*	Does not interfere with daily activity	Interferes with daily activity	Prevents daily activity
Induration (Hardness/Swelling)*	Does not interfere with daily activity	Interferes with daily activity	Prevents daily activity
Skin Discoloration	Barely perceptible difference compared to surrounding skin	Clearly discernable difference compared to surrounding skin	Unsightly difference when compared to surrounding skin
Ecchymosis (Bruising)*	Does not interfere with daily activity	Interferes with daily activity	Prevents daily activity

*In addition to grading the measured local reaction at the greatest single diameter, they should be evaluated and graded using the functional scale as well as the actual measurement. Size will not be used as halting criteria by itself.

Table 6: Local (Injection Site) Reactogenicity Measurements

Local (Injection Site) Reaction	Small	Medium	Large
Ecchymosis (Bruising)*	<20 mm	20 mm – 50 mm	>50 mm
Erythema (Redness)*	<20 mm	20 mm – 50 mm	>50 mm
Induration (Hardness)/Swelling*	<20 mm	20 mm – 50 mm	>50 mm

*In addition to grading the measured local reaction at the greatest single diameter, they should be evaluated and graded using the functional scale as well as the actual measurement. Size will not be used as halting criteria by itself.

Table 7: Subjective Systemic Reactogenicity Grading

Systemic (Subjective)	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Feverishness (chills/shivering/sweating)	noticeable but does not interfere with daily activity	interferes with daily activity	Significant interference in that it prevents daily activity
Malaise (General Unwell Feeling)	noticeable but does not interfere with daily activity	interferes with daily activity	Significant interference, prevents daily activity
Fatigue (Tiredness)	noticeable but does not interfere with daily activity	interferes with daily activity	Significant interference, prevents daily activity
Myalgia (Body Aches/Muscular Pain)*	noticeable but does not interfere with daily activity	interferes with daily activity	Significant interference, prevents daily activity
Headache	noticeable but does not interfere with daily activity	Any use of pain reliever or interferes with daily activity	Prevents daily activity or requires use of a prescription medication
Nausea	noticeable but does not interfere with daily activity	interferes with daily activity	Significant interference, prevents daily activity
Dizziness	noticeable but does not interfere with daily activity	interferes with daily activity	Significant interference, prevents daily activity

*Not at injection site

Table 8: Quantitative Systemic Reactogenicity Grading

Systemic (Quantitative)	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Fever* - oral†	37.8°C – 38.4°C 100.00°F – 101.1°F	38.5°C – 38.9°C 101.2°F – 102.0°F	>38.9°C >102.0°F

Oral temperature assessed on Day 1 prior to study vaccination will be considered as baseline.
*A fever can be considered not related to the study product if an alternative etiology can be documented.
†Subjects must not eat or drink anything hot or cold, or smoke within 10 minutes prior to taking oral temperature.

Table 9: Blood Pressure and Pulse Grading

Physiologic Parameter	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Bradycardia - beats per minute	45-46	40 – 44	<40
Tachycardia - beats per minute	106 – 130	131 – 155	>155
Hypotension (systolic) mmHg	80 – 84	75 – 79	<75
Hypotension (diastolic) mmHg	50 – 54	45 – 49	<45
Hypertension (systolic) mmHg	151 – 155	156 – 160	>160
Hypertension (diastolic) mmHg	96 – 100	101 – 105	>105

Pulse and blood pressure assessed on Day 1 prior to study vaccination will be considered as baseline.

12.4.1 Individual Laboratory Measurements and Abnormal Laboratory Values

Table 10: Laboratory Adverse Event Grading Scale - Hematology

Hematology	Clinical Laboratory Reference Range	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
WBC K/mcL (Decrease, 18 to < 21 years)	4.5 – 13.0	2.5 – 4.4	1.5 – 2.4	<1.5
WBC K/mcL (Decrease, ≥ 21 years)	4.5 – 11.0	2.5 – 4.4	1.5 – 2.4	<1.5
WBC K/mcL (Increase 18 to < 21 years)	4.5 – 13.0	13.1 – 15.0	15.1 – 20.0	>20.0
WBC K/mcL (Increase ≥ 21 years)	4.5 – 11.0	11.1 – 15.0	15.1 – 20.0	>20.0
Hgb g/dL (Decrease) (Female)	11.7 – 15.7	10.1 – 11.6	8.5 – 10	<8.5
Hgb g/dL (Decrease) (Male)	13.3 – 17.7	11.0 – 13.2	9.5 – 10.9	<9.5
Platelet count K/mcL (Decrease)	135 - 466	125 – 134	100 – 124	<100
Platelet count K/mcL (Increase)	135 - 466	467 - 517	518 – 750	>750
Absolute Neutrophil Count, K/mcL* (18 to < 21 years)	1.80 – 8.00	1.5-<1.8	1.0-<1.5	<1.0
Absolute Neutrophil Count, K/mcL* (≥ 21 years)	1.80 – 7.70	1.5-<1.8	1.0-<1.5	<1.0
Absolute Neutrophil Count, K/mcL - Benign Ethnic Neutropenia*	≥ 0.8	0.6 – 0.7	0.4 – 0.5	< 0.4

Clinical laboratory evaluations assessed at the Day 1 visit will be considered as baseline.
*ANC for subjects that are of African American and Middle Eastern descent may have values as low as 0.8 K/mcL. Subjects of this descent must have an ANC ≥ 0.8 K/mcL to be eligible to participate in the study if all other study criteria are met.

Table 11: Laboratory Adverse Event Grading Scale - Chemistry

Chemistry	Clinical Laboratory Reference Range	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
ALT unit/L (Increase)	≤49	50-123	124-245	> 245
Total Bilirubin mg/dL (Increase) – when accompanied by any increase in ALT	0.10 – 1.2	1.3 – 1.5	1.6 – 1.8	>1.8
Total Bilirubin mg/dL (Increase) – when ALT is normal	0.10 – 1.2	1.3 – 1.8	1.9 – 2.4	>2.4
Creatinine mg/dL (Increase) (Female)	0.50 – 0.80	0.81 – 1.70	1.71 – 2.00	>2.00
Creatinine mg/dL (Increase) (Male)	0.60 – 1.10	1.11 – 1.70	1.71 – 2.00	>2.00
Sodium, low, mmol/L	136 – 145	130 - 135	123-129	<123
Sodium, high, mmol/L	136 - 145	146 - 150	151-157	>157
Potassium, high, mmol/L	3.5 – 5.1	5.2 - 6.0	6.1-6.5	>6.5
Potassium, low, mmol/L	3.5 – 5.1	3.0 - 3.4	2.5-2.9	<2.5
Blood Urea Nitrogen (BUN) mg/dL	9.00 – 23.00	24 – 26	27 - 31	>31

Clinical laboratory evaluations assessed at the Day 1 visit will be considered as baseline.

14.1 Description of Study Subjects

14.1.1 Disposition of Subjects

Table 12: Subject Disposition by Vaccination Group

Subject Disposition	ANDV DNA 2mg 3 Doses (N=X)		ANDV DNA 2mg 4 Doses (N=X)		ANDV DNA 4mg 3 Doses (N=X)		ANDV DNA 4mg 4 Doses (N=X)		Placebo (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%	n	%	n	%	n	%
Screened	--	--	--	--	--	--	--	--	--	--	x	--
Enrolled/Randomized	x	100	x	100	x	100	x	100	x	100	x	100
Received at least one Treatment	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Received All Scheduled Treatments[a]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed All Blood Draws	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Study Day 197 Visit	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Follow-up (Study Day 337)[a]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Per Protocol[b]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

Note: N=Number of subjects in the Safety Population
[a] Refer to Listing 16.2.1 for reasons subjects discontinued or terminated early.
[b] Refer to Listing 16.2.3 for reasons subjects are excluded from the analysis populations.

Table 13: Analysis Populations by Vaccination Group

Analysis Populations	Reason Subjects Excluded	ANDV DNA 2mg 3 Doses (N=X)		ANDV DNA 2mg 4 Doses (N=X)		ANDV DNA 4mg 3 Doses (N=X)		ANDV DNA 4mg 4 Doses (N=X)		Placebo (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%
Safety	Did not receive study product	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Intent to Treat	Any Reason												
	Missed pre-study vaccination venous blood draw												
	No post-study vaccination venous blood draw												
	Invalid results from venous blood draw tests												
Per Protocol	Any Reason												
	Ineligible at baseline												
	Major protocol deviation												
	Study visit occurred substantially out of window												

Note: N=Number of randomized subjects

Table 14: Dates of First Treatment by Vaccination Group

Dates of Dosing	ANDV DNA 2mg 3 Doses (N=X)	ANDV DNA 2mg 4 Doses (N=X)	ANDV DNA 4mg 3 Doses (N=X)	ANDV DNA 4mg 4 Doses (N=X)	Placebo (N=X)	All Subjects (N=X)
Total (Entire period of enrollment)						
DDMMMYYYY-DDMMMYYYY	x	x	x	x	x	x

Note: N=Number of subjects in the Safety Population

Table 15: Ineligibility Summary of Screen Failures

[Implementation Note: Only inclusion criteria not met or exclusion criteria met will be presented in the table.]

Inclusion/Exclusion Category	Inclusion/Exclusion Criterion	n[a]	%[b]
Any reason	Total number of subjects screened but not randomized	x	100
Eligible	Number of subjects who were eligible but not randomized	x	xx
Inclusion and Exclusion	Number of subjects failing any eligibility criterion	x	xx
Inclusion	Any inclusion criterion	x	xx
	Provide written informed consent before initiation of any study procedures.	x	xx
	Are able to understand and comply with planned study procedures and be available for all study visits/phone calls.	x	xx
	Males or non-pregnant females ages 18-49, inclusive.	x	xx
	Are in good health.		
	Oral temperature is less than 100.0 °F (37.8° C).		
	Pulse is 47 to 105 beats per minute (bpm), inclusive.		
	Systolic blood pressure (BP) is 85 to 150mm Hg, inclusive.		
	Diastolic blood pressure (BP) is 55 to 95 mm Hg, inclusive.		
	Have acceptable screening laboratories, within 28 days prior to enrollment.		
	Urine protein screen is negative or trace.		
	Drug screen for opiates is negative.		
	HgbA1C <6.3% at screening.		
	HIV – 1/2 antibody negative.		
	HCV antibody negative.		
	HBsAg negative.		
	Women of childbearing potential must be using an effective method of contraception from 30 days prior to the first study vaccination until 90 days after the last study vaccination.		
	Women of childbearing potential must have a negative serum pregnancy test at screening and a negative urine pregnancy test within 24 hours prior to each study vaccination.		
	Sexually active male participants whose partner is a woman of childbearing potential and has not had a vasectomy must agree not to father a child until 90 days after the last vaccination.		
	Women agree to not donate eggs (ova, oocytes) and male subject agrees not to donate sperm from the start of screening onwards until at least 90 days after the last vaccination.		

Table 15: Ineligibility Summary of Screen Failures (Continued)

Inclusion/Exclusion Category	Inclusion/Exclusion Criterion	n[a]	%[b]
	Agree not to participate in another clinical trial during the study period.		
	Agree not to donate blood to a blood bank for 3 months after receiving the last study vaccine.		
Exclusion	Any exclusion criterion	x	xx
	Women who are pregnant, planning to become pregnant or lactating.	x	xx
	Known allergy or history of anaphylaxis, severe local or other serious adverse reactions to vaccines or vaccine products, or history of severe allergic reactions.	x	xx
	Received an experimental agent within 3 months prior to study vaccination or expects to receive an experimental agent during the 12-month trial-reporting period.	x	xx
	Received any licensed live vaccine within 28 days prior to or after each study vaccination.		
	Received a licensed inactivated vaccine within 14 days prior to or after each study vaccination.		
	Individuals in whom the ability to observe possible local reactions at the eligible injection sites (deltoid region) is, unacceptably obscured due to a physical condition or permanent body art.		
	Have an acute illness, as determined by the site PI or appropriate sub-investigator, within 72 hours prior to study vaccination.		
	Any confirmed or suspected immunosuppressive or immunodeficient condition or use of anticancer chemotherapy or radiation therapy (cytotoxic) within 3 years prior to study vaccination.		
	Administration of chronic (defined as more than 14 days) immunosuppressants or other immune modifying drugs within 6 months of receipt of study vaccine.		
	History of receipt of a Hantavirus vaccine, including vaccines for Hantaan virus, Puumala virus, or combination of both.		
	Exposed to ANDV or plans to travel to an endemic area from enrollment through 6 months post last vaccination.		
	Any chronic or active neurologic disorder, including seizures and epilepsy, excluding febrile seizures as a child.		
	History of receiving immunoglobulin or other blood product within the 3 months before enrollment in this study.		
	Current or past history of alcohol or drug abuse in the last 5 years.		
	Subjects with autoimmune disorders, chronic inflammatory disorders or neurological disorders with a potential autoimmune correlation.		
	Have any diagnosis, current or past, of schizophrenia, bipolar disease, or other psychiatric diagnosis that may interfere with subject compliance or safety evaluations.		
	Have been hospitalized for psychiatric illness, history of suicide attempt, or confinement for danger to self or others within 10 years prior to study vaccination.		
	Have received any antiviral within 3 days of study vaccination.		

Table 15: Ineligibility Summary of Screen Failures (Continued)

Inclusion/Exclusion Category	Inclusion/Exclusion Criterion	n[a]	%[b]
	A diagnosis of Type I or II diabetes.		
	Current employee or staff paid entirely or partially by the contract for this trial, or staff who are supervised by the PI or Sub-Investigators.		
	Any condition that would, in the opinion of the Site Investigator or appropriate sub-investigator, is a contraindication to study participation.		
Eligible but not enrolled	Any reason		

[a] More than one criterion may be marked per subject.
[b] Denominator for percentages is the total number of screen failures.

14.1.2 Demographic Data by Study Group

Table 16: Summary of Categorical Demographic and Baseline Characteristics by Vaccination Group

Variable	Characteristic	ANDV DNA 2mg 3 Doses (N=X)		ANDV DNA 2mg 4 Doses (N=X)		ANDV DNA 4mg 3 Doses (N=X)		ANDV DNA 4mg 4 Doses (N=X)		Placebo (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%
Sex	Male	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Female												
Ethnicity	Not Hispanic or Latino	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Hispanic or Latino												
	Not Reported												
	Unknown												
Race	American Indian or Alaska Native	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Asian												
	Native Hawaiian or Other Pacific Islander												
	Black or African American												
	White												
	Multi-Racial												
	Unknown												

Note: N=Number of subjects in the Safety Population

Table 17: Summary of Continuous Demographic and Baseline Characteristics by Vaccination Group

Variable	Statistic	ANDV DNA 2mg 3 Doses (N=X)	ANDV DNA 2mg 4 Doses (N=X)	ANDV DNA 4mg 3 Doses (N=X)	ANDV DNA 4mg 4 Doses (N=X)	Placebo (N=X)	All Subjects (N=X)
Age	Mean						xx
	Standard Deviation						xx
	Median						xx
	Minimum						x
	Maximum						x

Note: N=Number of subjects in the Safety Population

14.1.3 Prior and Concurrent Medical Conditions

Table 18: Summary of Subjects with Pre-Existing Medical Conditions by MedDRA System Organ Class and Vaccination Group

MedDRA System Organ Class	ANDV DNA 2mg 3 Doses (N=X)		ANDV DNA 2mg 4 Doses (N=X)		ANDV DNA 4mg 3 Doses (N=X)		ANDV DNA 4mg 4 Doses (N=X)		Placebo (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%	n	%	n	%	n	%
Any SOC	x	xx										
[SOC 1]												
[SOC 2]												

Note: N=Number of subjects in the Safety Population; n = Number of subjects reporting medical history within the specified SOC. A subject is only counted once per SOC.

14.2 Immunogenicity Data

14.2.1 Secondary Immunogenicity Data

Table 19: Plaque Reduction Neutralization Seroconversion by Time Point and Vaccination Group - Intent to Treat Population

	ANDV DNA 2mg						ANDV DNA 4mg						Placebo	
Time Point	Cohort 1 3 Doses (N=X)		Cohort 2 4 Doses (N=X)		All (N=X)		Cohort 3 3 Doses (N=X)		Cohort 4 4 Doses (N=X)		All (N=X)		All (N=X)	
	N	%	N	%	N	%	N	%	n	%	n	%	n	%
Baseline (Day 1) †	x	x												
29 Days Post Dose 2 (Day 57) †														
29 Days Post Dose 3 (Day 85)														
Pre-Dose 4 (Day 169)†														
29 Days Post Dose 4 (Day 197)														

Note: N=Number of subjects in the Intent to Treat Population
†Day of study vaccination. Sample collected prior to vaccination.
Secondary outcomes are specific to days 57, 85 and 197.

Table with similar format:

Table 20: Plaque Reduction Neutralization Seroconversion by Time Point and Treatment Group - Per Protocol Population

Table 21: Pseudovirion Neutralization Seroconversion by Time Point and Vaccination Group - Intent to Treat Population

	ANDV DNA 2mg						ANDV DNA 4mg						Placebo	
	Cohort 1 3 Doses (N=X)		Cohort 2 4 Doses (N=X)		All (N=X)		Cohort 3 3 Doses (N=X)		Cohort 4 4 Doses (N=X)		All (N=X)		All (N=X)	
Time Point	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Baseline (Day 1) †	x	x												
29 Days Post Dose 1 (Day 29) †														
29 Days Post Dose 2 (Day 57) †														
29 Days Post Dose 3 (Day 85)														
Pre-Dose 4 (Day 169) †														
29 Days Post Dose 4 (Day 197)														
Day 85 Post Dose 4 (Day 253)														
Day 169 Post Dose 4 (Day 337)														

Note: N=Number of subjects in the Intent to Treat Population; n=number of subjects with PsVNA ≥20.
†Day of study vaccination. Sample collected prior to vaccination.
Secondary outcomes are specific to days 57, 85 and 197.

Table with similar format:

Table 22: Pseudovirion Neutralization Seroconversion by Time Point and Vaccination Group - Per Protocol Population

Table 23: Plaque Reduction Neutralization GMFR and Seroconversion Results by Time Point and Vaccination Group - Intent to Treat Population

		ANDV DNA 2mg			ANDV DNA 4mg			Placebo
Time Point	Statistic	Cohort 1 3 Doses (N=X)	Cohort 2 4 Doses (N=X)	All (N=X)	Cohort 3 3 Doses (N=X)	Cohort 4 4 Doses (N=X)	All (N=X)	All (N=X)
29 Days Post Dose 2 (Day 57) †*	n	x	x	x	x	x	x	x
	GMFR	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	95% CI for GMFR	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
	Seroconversion[a]	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	95% CI	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
Repeat for:								
29 Days Post Dose 3 (Day 85)*								
Pre-Dose 4 (Day 169)†								
29 Days Post Dose 4 (Day 197)*								
Any Time Point	n							
	Seroconversion[a]							
	95% CI							

Note: N=Number of subjects in the Intent to Treat Population; n=Number of subjects with data available at that time point. GMFR = Geometric mean fold-rise from baseline.
[a] Seroconversion is defined as a subject having a post-dose antibody ≥40 if baseline titer < 20 or at least a 4-Fold Rise in antibody compared to pre-dose 1 if baseline titer ≥ 20.
†Day of study vaccination. Sample collected prior to vaccination.
*Secondary Immunogenicity outcome measure.

Table with similar format:

Table 24: Plaque Reduction Neutralization GMFR and Seroconversion Results by Time Point and Vaccination Group - Per Protocol Population

Table 25: Pseudovirion Neutralization GMFR and Seroconversion Results by Time Point and Vaccination Group - Intent to Treat Population

		ANDV DNA 2mg			ANDV DNA 4mg			Placebo
Time Point	**Statistic**	**Cohort 1 3 Doses (N=X)**	**Cohort 2 4 Doses (N=X)**	**All (N=X)**	**Cohort 3 3 Doses (N=X)**	**Cohort 4 4 Doses (N=X)**	**All (N=X)**	**All (N=X)**
29 Days Post-Dose 1 (Day 29)†	n	x	x	x	x	x	x	x
	GMFR	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	95% CI	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
	Seroconversion[a]	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	95% CI	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
Repeat for:								
29 Days Post-Dose 2 (Day 57)†*								
29 Days Post Dose 3 (Day 85)*								
Pre-Dose 4 (Day 169)†								
29 Days Post Dose 4 (Day 197)*								
85 Days Post Dose 4 (Day 253)								
169 Days Post Dose 4 (Day 337)								
Any Time Point	n							
	Seroconversion[a]							
	95% CI							

Note: N=Number of subjects in the Intent to Treat Population; n=Number of subjects with data available at that time point.
[a] Seroconversion is defined as a subject having a post-dose antibody ≥40 if baseline titer < 20 or at least a 4-Fold Rise in antibody compared to pre-dose 1 if baseline titer ≥ 20.
†Day of study vaccination. Sample collected prior to vaccination.
*Secondary Immunogenicity outcome measure.

Table with similar format:

Table 26: Pseudovirion Neutralization GMFR and Seroconversion Results by Time Point and Vaccination Group - Per Protocol Population

Table 27: Plaque Reduction Neutralization Geometric Mean Titer (GMT) Results with 95% Confidence Intervals by Time Point and Vaccination Group - Intent to Treat Population

		ANDV DNA 2mg			ANDV DNA 4mg			Placebo
Time Point	Statistic	Cohort 1 3 Doses (N=X)	Cohort 2 4 Doses (N=X)	All (N=X)	Cohort 3 3 Doses (N=X)	Cohort 4 4 Doses (N=X)	All (N=X)	All (N=X)
Baseline (Day 1)†*	n	x	x	x	x	x	x	x
	GMT	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	95% CI	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
29 Days Post Dose 2 (Day 57) †*	n							
	GMT							
	95% CI							
29 Days Post Dose 3 (Day 85)*	n							
	GMT							
	95% CI							
Pre-Dose 4 (Day 169)†	n							
	GMT							
	95% CI							
29 Days Post Dose 4 (Day 197)*	n							
	GMT							
	95% CI							

Note: N=Number of subjects in the Intent to Treat Population; n=Number of subjects with data available at that time point.
†Day of study vaccination. Sample collected prior to vaccination.
*Secondary Immunogenicity outcome measure.

Table with similar format:

Table 28: Plaque Reduction Neutralization Geometric Mean Titer (GMT) Results with 95% Confidence Intervals by Time Point and Vaccination Group - Per Protocol Population

Table 29: Pseudovirion Neutralization Geometric Mean Titer (GMT) Results with 95% Confidence Intervals by Time Point and Vaccination Group - Intent to Treat Population

		ANDV DNA 2mg			ANDV DNA 4mg			Placebo
Time Point	Statistic	Cohort 1 3 Doses (N=X)	Cohort 2 4 Doses (N=X)	All (N=X)	Cohort 3 3 Doses (N=X)	Cohort 4 4 Doses (N=X)	All (N=X)	All (N=X)
Baseline (Day 1)†*	n	x	x	x	x	x	x	x
	GMT	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	95% CI	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
29 Days Post-Dose 1 (Day 29)†	n							
	GMT							
	95% CI							
29 Days Post-Dose 2 (Day 57)†*	n							
	GMT							
	95% CI							
29 Days Post Dose 3 (Day 85)*	n							
	GMT							
	95% CI							
Pre-Dose 4 (Day 169)†	n							
	GMT							
	95% CI							
29 Days Post Dose 4 (Day 197)*	n							
	GMT							
	95% CI							
85 Days Post Dose 4 (Day 253)	n							
	GMT							
	95% CI							
169 Days Post Dose 4 (Day 337)	n							
	GMT							
	95% CI							

Note: N=Number of subjects in the Intent to Treat Population; n=Number of subjects with data available at that time point.
†Day of study vaccination. Sample collected prior to vaccination.
*Secondary Immunogenicity outcome measure.

Table with similar format:

Table 30: Pseudovirion Neutralization Geometric Mean Titer (GMT) Results with 95% Confidence Intervals by Time Point and Vaccination Group - Per Protocol Population

Table 31: Correlation Between Plaque Reduction Neutralization and Pseudovirion Neutralization Antibody Titers - Intent to Treat Population

Time Point	Correlation[a]						
	ANDV DNA 2mg			ANDV DNA 4mg			Placebo
	Cohort 1 3 Doses (N=X)	Cohort 2 4 Doses (N=X)	All (N=X)	Cohort 3 3 Doses (N=X)	Cohort 4 4 Doses (N=X)	All (N=X)	All (N=X)
Baseline (Day 1)†	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx
29 Days Post-Dose 2 (Day 57)†	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx
29 Days Post Dose 3 (Day 85)	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx
Pre-Dose 4 (Day 169)†	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx
29 Days Post Dose 4 (Day 197)	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx
All the above time points	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx	0.xxx

[a]Spearman rank-order correlation coefficient between PsVNA and PRNT results.
Note: N=Number of subjects in the Intent to Treat Population

Table with similar format:

Table 32: Correlation Between Plaque Reduction Neutralization and Pseudovirion Neutralization Antibody Titers - Per Protocol Population

14.2.2 Exploratory Immunogenicity Data

Table 33: Intracellular Cytokine Staining (ICS), Incidence of >3 Standard Deviation Increase in CD4+ T-Cells Compared to Baseline by Time Point and Vaccination Group - ANDVGP-PP1 - Intent to Treat Population

	ANDV DNA 2mg			ANDV DNA 4mg			Placebo
	Cohort 1 3 Doses (N=X)	Cohort 2 4 Doses (N=X)	All (N=X)	Cohort 3 3 Doses (N=X)	Cohort 4 4 Doses (N=X)	All (N=X)	All (N=X)
Time Point	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Percent Activated CD4+ T-Cells Secreting IFNɣ							
29 Days Post Dose 1 (Day 29)†							
29 Days Post Dose 2 (Day 57)†							
29 Days Post Dose 3 (Day 85)							
Pre-Dose 4 (Day 169)†							
29 Days Post Dose 4 (Day 197)							
Repeat for:							
Percent Activated CD4+ T-Cells TNFα							
Percent Activated CD4+ T-Cells Secreting IL-2							
Percent Activated CD4+ T-Cells Secreting IFNɣ + TNFα							
Percent Activated CD4+ T-Cells Secreting IFNɣ + IL-2							
Percent Activated CD4+ T-Cells Secreting TNFα + IL-2							
Percent Activated CD4+ T-Cells Secreting IFNɣ + TNFα + IL-2							

Note: N=Number of subjects in the Intent to Treat Population; n = Number of subjects with an increase from baseline of >3 standard deviations (see Section 8.3).
†Day of study vaccination. Sample collected prior to vaccination.

Tables with similar format:

Table 34: Intracellular Cytokine Staining (ICS), Incidence of >3 Standard Deviation Increase in CD4+ Cells Compared to Baseline by Time Point and Vaccination Group - ANDVGP-PP1- Per Protocol Population

Table 35: Intracellular Cytokine Staining (ICS), Incidence of >3 Standard Deviation Increase in CD4+ T-Cells Compared to Baseline by Time Point and Vaccination Group - ANDVGP-PP2 - Intent to Treat Population

Table 36: Intracellular Cytokine Staining (ICS), Incidence of >3 Standard Deviation Increase in CD4+ T-Cells Compared to Baseline by Time Point and Vaccination Group - ANDVGP-PP2 - Per Protocol Population

[Tables 37 and 38 will summarize the proportion of subjects with responses to either PP1 or PP2]

Table 37: Intracellular Cytokine Staining (ICS), Incidence of >3 Standard Deviation Increase in CD4+ T-Cells Compared to Baseline by Time Point and Vaccination Group - ANDVGP - Intent to Treat Population

Table 38: Intracellular Cytokine Staining (ICS), Incidence of >3 Standard Deviation Increase in CD4+ T-Cells Compared to Baseline by Time Point and Vaccination Group - ANDVGP - Per Protocol Population

CD8+ Cells

Table 39: Intracellular Cytokine Staining (ICS), Incidence of >3 Standard Deviation Increase in CD8+ Cells Compared to Baseline by Time Point and Vaccination Group - ANDVGP-PP1- Intent to Treat Population

Table 40: Intracellular Cytokine Staining (ICS), Incidence of >3 Standard Deviation Increase in CD8+ Cells Compared to Baseline by Time Point and Vaccination Group - ANDVGP-PP1- Per Protocol Population

Table 41: Intracellular Cytokine Staining (ICS), Incidence of >3 Standard Deviation Increase in CD8+ Cells Compared to Baseline by Time Point and Vaccination Group - ANDVGP-PP2- Intent to Treat Population

Table 42: Intracellular Cytokine Staining (ICS), Incidence of >3 Standard Deviation Increase in CD8+ Cells Compared to Baseline by Time Point and Vaccination Group - ANDVGP-PP2- Per Protocol Population

[Tables 43 and 44 will summarize the proportion of subjects with responses to either PP1 or PP2]

Table 43: Intracellular Cytokine Staining (ICS), Incidence of >3 Standard Deviation Increase in CD8+ Cells Compared to Baseline by Time Point and Vaccination Group - ANDVGP - Intent to Treat Population

Table 44: Intracellular Cytokine Staining (ICS), Incidence of >3 Standard Deviation Increase in CD8+ Cells Compared to Baseline by Time Point and Vaccination Group - ANDVGP - Per Protocol Population

Table 45: Lymphoproliferation Assay (LPA) Incidence of >3 Standard Deviation Increase in Percent of Proliferating CD4+ and CD8+ T-Cells Compared to Baseline by ANDVGP Pool, Time Point, and Vaccination Group - Intent to Treat Population

	ANDV DNA 2mg			ANDV DNA 4mg			Placebo
	Cohort 1 3 Doses (N=X)	Cohort 2 4 Doses (N=X)	All (N=X)	Cohort 3 3 Doses (N=X)	Cohort 4 4 Doses (N=X)	All (N=X)	All (N=X)
Time Point	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Percent of Proliferating CD4+ T-Cells, ANDVGP-PP1							
29 Days Post Dose 1 (Day 29)†							
29 Days Post Dose 2 (Day 57)†							
29 Days Post Dose 3 (Day 85)							
Pre-Dose 4 (Day 169)†							
29 Days Post Dose 4 (Day 197)							
Repeat for:							
Percent of Proliferating CD4+ T-Cells, ANDVGP-PP2							
Percent of Proliferating CD4+ T-Cells, ANDVGP††							
Percent of Proliferating CD8+ T-Cells, ANDVGP-PP1							
Percent of Proliferating CD8+ T-Cells, ANDVGP-PP2							
Percent of Proliferating CD8+ T-Cells, ANDVGP††							

Note: N=Number of subjects in the Intent to Treat Population; n = Number of subjects with an increase from baseline of >3 standard deviations (see Section 8.3).
†Day of study vaccination. Sample collected prior to vaccination.
†† Proportion of subjects with responses to either PP1 or PP2.

Table with similar format:

Table 46: Lymphoproliferation Assay (LPA) Incidence of >3 Standard Deviation Increase in Percent of Proliferating CD4+ and CD8+ T-Cells by ANDVGP Pool, Time Point, and Vaccination Group - Per Protocol Population

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 47: Overall Summary of Adverse Events

	ANDV DNA 2mg						ANDV DNA 4mg						Placebo			
	Cohort 1 3 Doses (N=X)		Cohort 2 4 Doses (N=X)		All (N=X)		Cohort 3 3 Doses (N=X)		Cohort 4 4 Doses (N=X)		All (N=X)		All (N=X)		All Subjects (N=X)	
Subjects[a] with:	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
At least one local solicited adverse event	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one systemic solicited adverse event	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one unsolicited adverse event	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one related unsolicited adverse event	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Mild (Grade 1)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Moderate (Grade 2)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Severe (Grade 3)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Not yet assessed																
At least one severe (Grade 3) unsolicited adverse event	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Related	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Unrelated	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one serious adverse event[b]	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one related, serious adverse event	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one adverse event leading to early termination[c]	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

N=Number of subjects in the Safety Population
[a] Subjects are counted once for each category regardless of the number of events.
[b] A listing of Serious Adverse Events is included in Table 91.
[c] As reported on the Adverse Event eCRF.

Table 48: Adverse Events Occurring in 5% of Subjects in Any Vaccination Group by MedDRA System Organ Class and Preferred Term, and Vaccination Group - Safety Population

[Note: include all solicited and unsolicited AEs]

MedDRA Classification	ANDV DNA 2mg						ANDV DNA 4mg						Placebo			
System Organ Class Preferred Term	Cohort 1 3 Doses (N=X)		Cohort 2 4 Doses (N=X)		All (N=X)		Cohort 3 3 Doses (N=X)		Cohort 4 4 Doses (N=X)		All (N=X)		All (N=X)		All Subjects (N=X)	
	n (%)	Events	n (%)	Events	n (%)	Events	n (%)	Events	n (%)	Events	n (%)	Events	n (%)	Events	n (%)	Events
Serious Adverse Events																
Any SOC																
Any PT	x (x)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	X
[PT 1]																
Etc.																
[SOC 1]																
Any PT	x (x)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	X
[PT 1]																
Etc.																
Other (Non-serious) Adverse Events																
Any SOC																
Any PT	x (x)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	X
[PT 1]																
Etc.																
[SOC 1]																
Any PT	x (x)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	X
[PT 1]																
Etc.																

N=Number of subjects in the Safety Population (number of subjects at risk).
n=Number of subjects reporting any solicited or unsolicited adverse event.
Events=total frequency of events reported.

14.3.1.1 Solicited Adverse Events

Table 49: Number and Percentage of Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom, Dose, and Vaccination Group - Post Dose 1

	Cohorts 1 + 2 ANDV DNA 2 mg (N=X)		Cohorts 3 + 4 ANDV DNA 4 mg (N=X)		All Placebo (N=X)		All Subjects (N=X)	
Symptom	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**
Any Symptom								
Any Systemic Symptom								
Feverishness								
Malaise								
Fatigue								
Myalgia								
Headache								
Nausea								
Dizziness								
Fever								
Any Local Symptom								
Pain								
Tenderness								
Erythema								
Erythema (Measurement)								
Induration								
Induration (Measurement)								
Skin Discoloration								
Ecchymosis								
Ecchymosis (Measurement)								

Note: N=Number of subjects in the Safety Population; n=Number of subjects experiencing the symptom.

Table with similar format:

Table 50: Number and Percentage of Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom, Dose, and Vaccination Group - Post Dose 2

Table 51: Number and Percentage of Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom, Dose, and Vaccination Group - Post Dose 3

	ANDV DNA 2mg				ANDV DNA 4mg				Placebo			
	Cohort 1 3 Doses (N=X)		Cohort 2 4 Doses (N=X)		Cohort 3 3 Doses (N=X)		Cohort 4 4 Doses (N=X)		All Placebo (N=X)		All Subjects (N=X)	
Symptom	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**
Any Symptom												
Any Systemic Symptom												
Feverishness												
Malaise												
Fatigue												
Myalgia												
Headache												
Nausea												
Dizziness												
Fever												
Any Local Symptom												
Pain												
Tenderness												
Erythema												
Erythema (Measurement)												
Induration												
Induration (Measurement)												
Skin Discoloration												
Ecchymosis												
Ecchymosis (Measurement)												

Table with similar format:

Table 52: Number and Percentage of Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom, Dose, and Vaccination Group - Post Dose 4

Table 53: Number and Percentage of Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom, Dose, and Vaccination Group - Post Any Dose

	ANDV DNA 2mg				ANDV DNA 4mg				Placebo			
	Cohort 1 3 Doses (N=X)		Cohort 2 4 Doses (N=X)		Cohort 3 3 Doses (N=X)		Cohort 4 4 Doses (N=X)		All Placebo (N=X)		All Subjects (N=X)	
Symptom	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**
Any Symptom												
Any Systemic Symptom												
Feverishness												
Malaise												
Fatigue												
Myalgia												
Headache												
Nausea												
Dizziness												
Fever												
Any Local Symptom												
Pain												
Tenderness												
Erythema												
Erythema (Measurement)												
Induration												
Induration (Measurement)												
Skin Discoloration												
Ecchymosis												
Ecchymosis (Measurement)												

Table 54: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Vaccination Group - Post Dose 1

Symptom	Severity	Cohorts 1 + 2 ANDV DNA 2 mg (N=X)		Cohorts 3 + 4 ANDV DNA 4 mg (N=X)		All Placebo (N=X)		All Subjects (N=X)	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
Any Symptom	None	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x
	Mild								
	Moderate								
	Severe								
Repeat for:									
Any Systemic Symptom									
Feverishness									
Malaise									
Fatigue									
Myalgia									
Headache									
Nausea									
Dizziness									
Fever									
Any Local Symptom									
Pain									
Tenderness									
Erythema (Severity)									
Erythema (Measurement)									
Induration (Severity)									
Induration (Measurement)									
Skin Discoloration									
Ecchymosis (Severity)									
Ecchymosis (Measurement)									

Note: N=Number of subjects in the Safety Population who received the specified dose; n=Number of subjects experiencing the symptom. Severity is the maximum severity reported over all solicited symptoms post dosing for each subject.
*Does not include measurements.

Table with similar format:

Table 55: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Vaccination Group - Post Dose 2

Table 56: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Vaccination Group - Post Dose 3

		ANDV DNA 2mg				ANDV DNA 4mg				Placebo			
		Cohort 1 3 Doses (N=X)		Cohort 2 4 Doses (N=X)		Cohort 3 3 Doses (N=X)		Cohort 4 4 Doses (N=X)		All Placebo (N=X)		All Subjects (N=X)	
Symptom	**Severity**	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**
Any Symptom	None	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x
	Mild												
	Moderate												
	Severe												
Repeat for:													
Any Systemic Symptom													
Feverishness													
Malaise													
Fatigue													
Myalgia													
Headache													
Nausea													
Dizziness													
Fever													
Any Local Symptom													
Pain													
Tenderness													
Erythema (Severity)													
Erythema (Measurement)													
Induration (Severity)													

Table 56: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Vaccination Group - Post Dose 3 (Continued)

		ANDV DNA 2mg				ANDV DNA 4mg				Placebo			
		Cohort 1 3 Doses (N=X)		Cohort 2 4 Doses (N=X)		Cohort 3 3 Doses (N=X)		Cohort 4 4 Doses (N=X)		All Placebo (N=X)		All Subjects (N=X)	
Symptom	Severity	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
Induration (Measurement)													
Skin Discoloration													
Ecchymosis (Severity)													
Ecchymosis (Measurement)													

Table with similar format:

Table 57: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Vaccination Group - Post Dose 4

Table 58: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Vaccination Group - Post Any Dose

		ANDV DNA 2mg				ANDV DNA 4mg				Placebo			
		Cohort 1 3 Doses (N=X)		Cohort 2 4 Doses (N=X)		Cohort 3 3 Doses (N=X)		Cohort 4 4 Doses (N=X)		All Placebo (N=X)		All Subjects (N=X)	
Symptom	**Severity**	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**
Any Symptom	None	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x
	Mild												
	Moderate												
	Severe												
Repeat for:													
Any Systemic Symptom													
Feverishness													
Malaise													
Fatigue													
Myalgia													
Headache													
Nausea													
Dizziness													
Fever													
Any Local Symptom													
Pain													
Tenderness													
Erythema													
Erythema (Measurement)													
Induration													
Induration (Measurement)													
Skin Discoloration													
Ecchymosis													
Ecchymosis (Measurement)													

Table 59: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – Cohorts 1 and 2 ANDV DNA 2mg - Post Dose 1

Cohorts 1+2 ANDV DNA 2mg, Post Dose 1 (N=X)																			
		Pre-Dose		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7+	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any Symptom	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
Repeat for:																			
Any Systemic Symptom																			
Feverishness																			
Malaise																			
Fatigue																			
Myalgia																			
Headache																			
Nausea																			
Dizziness																			
Any Local Symptom*																			
Pain																			
Tenderness																			
Erythema (Severity)																			
Erythema (Measurement)																			
Induration (Severity)																			
Induration (Measurement)																			

Table 59: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – Cohorts 1 and 2 ANDV DNA 2mg - Post Dose 1 (Continued)

Cohorts 1+2 ANDV DNA 2mg, Post Dose 1 (N=X)																			
		Pre-Dose		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7+	
Symptom	Severity	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Skin Discoloration																			
Ecchymosis (Severity)																			
Ecchymosis (Measurement)																			

Note: N=Number of subjects in the Safety Population who received the specified dose; n=Number of subjects experiencing the symptom. Severity is the maximum severity reported post dosing for each subject for each day.
*Does not include measurements

Tables with similar format:

Table 60: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – Cohorts 3 and 4 ANDV DNA 4mg - Post Dose 1

Table 61: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – All Placebo - Post Dose 1

Table 62: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – All Subjects - Post Dose 1

Post-Dose 2

Table 63: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – Cohorts 1 and 2 ANDV DNA 2mg - Post Dose 2

Table 64: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – Cohorts 3 and 4 ANDV DNA 4mg - Post Dose 2

Table 65: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – All Placebo - Post Dose 2

Table 66: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – All Subjects - Post Dose 2

Post-Dose 3

Table 67: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – Cohort 2 ANDV DNA 2mg - Post Dose 3

Table 68: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – Cohort 4 ANDV DNA 4mg - Post Dose 3

Table 69: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – All Placebo Including Cohorts 1 and 3 - Post Dose 3

Table 70: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – All Subjects - Post Dose 3

Post-Dose 4

Table 71: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – Cohorts 1 and 2 ANDV DNA 2mg - Post Dose 4

Table 72: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – Cohorts 3 and 4 ANDV DNA 4mg - Post Dose 4

Table 73: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – All Placebo - Post Dose 4

Table 74: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – All Subjects - Post Dose 4

Post-Any Dose

14.3.1.2 Unsolicited Adverse Events

Table 81: Frequency and Proportion of Subjects with Unsolicited Adverse Events by MedDRA System Organ Class, Preferred Term, and Vaccination Group – Post-Dose 1

	Cohorts 1 + 2 ANDV DNA 2 mg (N=X)		Cohorts 3 + 4 ANDV DNA 4 mg (N=X)		All Placebo (N=X)		All Subjects (N=X)	
	n (%)	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**	**n (%)**	**95% CI**
Any SOC								
Any PT	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x
[SOC 1]								
Any PT								
[PT 1]								
[PT 2]								
Etc..								
[Etc.]								

Note: N=Number of subjects in the Safety Population who received the specified dose; n=Number of subjects experiencing an AE within the SOC and PT combination.
95% CI = Exact Clopper-Pearson confidence interval.
Includes any mild or greater AEs reported post-dose 1 and prior to dose 2, or through 28 days post dose 1 if dose 2 not received.

Table with similar format:

Table 82: Frequency and Proportion of Subjects with Unsolicited Adverse Events by MedDRA System Organ Class, Preferred Term, and Vaccination Group – Post-Dose 2

Table 83: Frequency and Proportion of Subjects with Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term and Vaccination Group – Post-Dose 3

	Cohort 1 ANDV DNA 2 mg (N=X)		Cohort 2 ANDV DNA 2 mg (N=X)		Cohort 3 ANDV DNA 4 mg (N=X)		Cohort 4 ANDV DNA 4 mg (N=X)		All Placebo (N=X)		All Subjects (N=X)	
	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
Any SOC												
Any PT	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x	x (x.x)	x.x, x.x
[SOC 1]												
Any PT												
[PT 1]												
[PT 2]												
Etc..												
[Etc.]												

Note: N=Number of subjects in the Safety Population who received the specified dose; n=Number of subjects experiencing an AE within the SOC and PT combination.
95% CI = Exact Clopper-Pearson confidence interval.
Includes any mild or greater AEs reported post-dose 3 and prior to dose 4, or through 28 days post dose 3 if dose 4 not received.

Tables with similar format:

Table 84: Frequency and Proportion of Subjects with Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term and Vaccination Group – Post-Dose 4

Table 85: Frequency and Proportion of Subjects with Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term and Vaccination Group – Through 28 Days Post-Final Dose Received

Table 86: Frequency of Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term and Vaccination Group – Post Dose 1 and Post-Dose 2

	Cohorts 1 + 2 ANDV DNA 2 mg (N=X)			Cohorts 3 + 4 ANDV DNA 4 mg (N=X)			All Placebo (N=X)			All Subjects (N=X)		
	Dose 1 n	Dose 2 n	Total n	Dose 1 n	Dose 2 n	Total n	Dose 1 n	Dose 2 n	Total n	Dose 1 n	Dose 2 n	Total n
Any SOC												
Any PT	x	x	x	x	x	x	x	x	x	x	x	x
[SOC 1]												
Any PT												
[PT 1]												
[PT 2]												
Etc..												
[Etc.]												

Note: N=Number of subjects in the Safety Population who received the specified dose; n=Total number of AEs within the SOC and PT combination.
Total = AEs reported post dose 1 or post-dose 2.
Includes all mild or greater AEs reported at any time post-each dose, or through 28 days post dose if subsequent dose not received.

Table 87: Frequency of Unsolicited Adverse Events, by MedDRA System Organ Class and Preferred Term and Vaccination Group – Post Dose 3, Post-Dose 4, and Post-Any Dose

	Cohort 1 ANDV DNA 2 mg (N=X)			Cohort 2 ANDV DNA 2 mg (N=X)			Cohort 3 ANDV DNA 4 mg (N=X)			Cohort 4 ANDV DNA 4 mg (N=X)			All Placebo (N=X)			All Subjects (N=X)		
	Dose 3	Dose 4	Any Time	Dose 3	Dose 4	Any Time	Dose 3	Dose 4	Any Time	Dose 3	Dose 4	Any Time	Dose 3	Dose 4	Any Time	Dose 3	Dose 4	Any Time
Any SOC																		
Any PT																		
[SOC 1]																		
Any PT																		
[PT 1]																		
[PT 2]																		
Etc..																		
[Etc.]																		

Note: N=Number of subjects in the Safety Population who received the specified dose; n=Total number of AEs within the SOC and PT combination.
Includes all mild or greater AEs reported at any time post-each dose, or through 28 days post dose if subsequent dose not received.
Any Time = number of AEs reported at any time post-dose 1.

Table 88: Frequency and Percent of Subjects with Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Relationship – ANDV DNA 2 mg - Post-Doses 1 and 2

MedDRA System Organ Class	Preferred Term	Severity	Events Related to IP		Events Not Related to IP		Any Event	
			n	%	n	%	n	%
Post Dose 1 (N = X)								
Any SOC	Any PT	Any Severity	x	xx	x	xx	x	xx
		Mild						
		Moderate						
		Severe						
SOC 1	PT 1	Any Severity						
		Mild						
		Moderate						
		Severe						
	PT 2	Any Severity						
		Mild						
		Moderate						
		Severe						
Repeat for								
Post Dose 2 (N = X)								
Post Dose 1 or 2 (N = X)								

Note: N=Number of subjects in the Safety Population; n=Number of subjects experiencing an AE within the SOC and PT combination. Severity is the maximum severity reported post dosing for each subject for each day.

Tables with similar format:

Table 89: Frequency and Percent of Subjects with Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Relationship – ANDV DNA 4 mg - Post-Doses 1 and 2

Table 90: Frequency and Percent of Subjects with Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Relationship – Placebo - Post-Doses 1 and 2

Table 91: Frequency and Percent of Subjects with Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Relationship – ANDV DNA 2 mg (3 Doses) - Post-Dose 3 and 4, and At Any Time

MedDRA System Organ Class	Preferred Term	Severity	Events Related to IP		Events Not Related to IP		Any Event	
			n	%	n	%	n	%
Post Dose 3 (N = X)								
Any SOC	Any PT	Any Severity	x	xx	x	xx	x	xx
		Mild						
		Moderate						
		Severe						
SOC 1	PT 1	Any Severity						
		Mild						
		Moderate						
		Severe						
	PT 2	Any Severity						
		Mild						
		Moderate						
		Severe						
Repeat for								
Post Dose 4 (N = X)								
Any Time[1] (N = X)								

Note: N=Number of subjects in the Safety Population; n=Number of subjects experiencing an AE within the SOC and PT combination. Severity is the maximum severity reported post dosing for each subject for each day.
[1] Any AE reported post-dose 1.

Tables with similar format:

Table 92: Frequency and Percent of Subjects with Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Relationship – ANDV DNA 2 mg (4 Doses) - Post-Dose 3 and 4, and At Any Time

Table 93: Frequency and Percent of Subjects with Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Relationship – ANDV DNA 4 mg (3 Doses) - Post-Dose 3 and 4, and At Any Time

Table 94: Frequency and Percent of Subjects with Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Relationship – ANDV DNA 4 mg (4 Doses) - Post-Dose 3 and 4, and At Any Time

Table 95: Frequency and Percent of Subjects with Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Relationship – Placebo - Post-Dose 3 and 4, and At Any Time

Table 96: Frequency and Percent of Subjects with Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Relationship – All Subjects

MedDRA System Organ Class	Preferred Term	Severity	Events Related to IP		Events Not Related to IP		Any Event	
			n	%	n	%	n	%
Post Dose 1 (N = X)								
Any SOC	Any PT	Any Severity	x	xx	x	xx	x	xx
		Mild						
		Moderate						
		Severe						
SOC 1	PT 1	Any Severity						
		Mild						
		Moderate						
		Severe						
	PT 2	Any Severity						
		Mild						
		Moderate						
		Severe						
Repeat for								
Post Dose 2 (N = X)								
Post Dose 3 (N = X)								
Post Dose 4 (N = X)								
Any Time[1] (N = X)								

Note: N=Number of subjects in the Safety Population; n=Number of subjects experiencing an AE within the SOC and PT combination. Severity is the maximum severity reported post dosing for each subject for each day.
[1] Any AE reported post-dose 1.

AEs related to IP

Same format as Table 81:

Table 97: Frequency and Percent of Subjects with Unsolicited Adverse Events Related to IP by MedDRA System Organ Class, Preferred Term, and Vaccination Group – Post-Dose 1

Table 98: Frequency and Percent of Subjects with Unsolicited Adverse Events Related to IP by MedDRA System Organ Class, Preferred Term, and Vaccination Group – Post-Dose 2

Same format as Table 83:

Table 99: Frequency and Percent of Subjects with Unsolicited Adverse Events Related to IP by MedDRA System Organ Class, Preferred Term, and Vaccination Group – Post-Dose 3

Table 100: Frequency and Percent of Subjects with Unsolicited Adverse Events Related to IP by MedDRA System Organ Class, Preferred Term, and Vaccination Group – Post-Dose 4

Table 101: Frequency and Percent of Subjects with Unsolicited Adverse Events Related to IP by MedDRA System Organ Class, Preferred Term, and Vaccination Group – Any Time

Same format as Table 86:

Table 102: Frequency of Unsolicited Adverse Events Related to IP by MedDRA System Organ Class and Preferred Term and Vaccination Group – Post Dose 1 and Post-Dose 2

Same format as Table 87:

Table 103: Frequency of Unsolicited Adverse Events Related to IP by MedDRA System Organ Class and Preferred Term and Vaccination Group – Post Dose 3, Post-Dose 4 and Any Time

14.3.2 Listing of Deaths, Other Serious and Significant Adverse Events

Table 104: Listing of Serious Adverse Events

Adverse Event	Associated with Dose No.	No. of Days Post Associated Dose (Duration)	No. of Days Post Dose the Event Became Serious	Reason Reported as an SAE	Severity	Relationship to Study Product	If Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Vaccination Group: , Subject ID: , AE Number:												
Comments:												
Vaccination Group: , Subject ID: , AE Number:												
Comments:												

Table 105: Listing of Non-Serious, Unsolicited, Moderate or Severe Adverse Events

Adverse Event	Associated with Dose No.	No. of Days Post Associated Dose (Duration)	Severity	Relationship to Study Product	If Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Vaccination Group: , Subject ID: , AE Number:										
Comments:										
Vaccination Group: , Subject ID: , AE Number:										
Comments:										

14.3.3 Narratives of Deaths, Other Serious and Significant Adverse Events

(not included in SAP, but this is a placeholder for the CSR)

14.3.4 Abnormal Laboratory Value Listings (by Subject)

Table 106: Listing of Abnormal Laboratory Results - Chemistry

Vaccination Group	Subject ID	Sex	Age (years)	Planned Time Point	Actual Study Day	Number of Doses Received	Laboratory Parameter (Units)	Result (Severity)	Relationship to Treatment	If Not Related, Alternate Etiology	Action Taken with Study Treatment	Subject Discontinued Due to Result?

Table 107: Listing of Abnormal Laboratory Results - Hematology

Vaccination Group	Subject ID	Sex	Age (years)	Planned Time Point	Actual Study Day	Number of Doses Received	Laboratory Parameter (Units)	Result (Severity)	Relationship to Treatment	If Not Related, Alternate Etiology	Action Taken with Study Treatment	Subject Discontinued Due to Result?

14.3.5 Displays of Laboratory Results

14.3.5.1 Chemistry Results

Table 108: Abnormal Laboratory Results by Maximum Severity, Time Point, and Vaccination Group – Any Chemistry Parameter

Time Point	Vaccination Group	ANDV DNA Schedule # Doses	N	None		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
				n	%	n	%	n	%	n	%	n	%
Baseline (Day 1)	ANDV DNA 2mg	3 or 4	x	x	xx	x	xx	x	xx	x	xx	x	xx
	ANDV DNA 4mg	3 or 4											
	Placebo	-											
	All Subjects	-											
Day 8 (Day 8 Post Dose 1)	ANDV DNA 2mg	3 or 4											
	ANDV DNA 4mg	3 or 4											
	Placebo	-											
	All Subjects	-											
Day 36 (Day 8 Post Dose 2)	ANDV DNA 2mg	3 or 4											
	ANDV DNA 4mg	3 or 4											
	Placebo	-											
	All Subjects	-											
Day 64 (Day 8 Post Dose 3)	ANDV DNA 2mg	3											
		4											
	ANDV DNA 4mg	3											
		4											
	Placebo	-											
	All Subjects	-											
Repeat for:													
Day 169 (Pre-Dose 4)													
Day 176 (Day 8 Post Dose 4)													
Max Severity Post Baseline													

Note: The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.
N=Number of subjects in the Safety Population; n=Number of subjects with laboratory values in the respective category.

Tables with similar format:

Table 109: Abnormal Laboratory Results by Maximum Severity, Time Point, and Vaccination Group – Alanine Aminotransferase

Table 110: Abnormal Laboratory Results by Maximum Severity, Time Point, and Vaccination Group – Total Bilirubin

Table 111: Abnormal Laboratory Results by Maximum Severity, Time Point, and Vaccination Group – Creatinine

Table 112: Abnormal Laboratory Results by Maximum Severity, Time Point, and Vaccination Group – Sodium

Time Point	Vaccination Group	ANDV DNA Schedule # Doses	N	None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Missing	
				n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Baseline (Day 1)	ANDV DNA 2mg	3 or 4	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	ANDV DNA 4mg	3 or 4																	
	Placebo	4																	
	All Subjects	3 or 4																	
Day 8 (Day 8 Post Dose 1)	ANDV DNA 2mg	3 or 4																	
	ANDV DNA 4mg	3 or 4																	
	Placebo	4																	
	All Subjects	3 or 4																	
Day 36 (Day 8 Post Dose 2)	ANDV DNA 2mg	3 or 4																	
	ANDV DNA 4mg	3 or 4																	
	Placebo	4																	
	All Subjects	3 or 4																	
Day 64 (Day 8 Post Dose 3)	ANDV DNA 2mg	3																	
		4																	
	ANDV DNA 4mg	3																	
		4																	
	Placebo	4																	
	All Subjects	3 or 4																	
Repeat for:																			
Day 169 (Pre-Dose 4)																			
Day 176 (Day 8 Post Dose 4)																			
Max Severity Post Baseline																			

Note: The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.
N=Number of subjects in the Safety Population; n=Number of subjects with laboratory values in the respective category.

Table with similar format:

Table 113: Abnormal Laboratory Results by Maximum Severity, Time Point, and Vaccination Group – Potassium

Table with similar format to Table 108:

Table 114: Abnormal Laboratory Results by Maximum Severity, Time Point, and Vaccination Group – Blood Urea Nitrogen

Table 115: Abnormal Laboratory Results Related to Study Treatment by Maximum Severity, Time Point, and Vaccination Group – Any Chemistry Parameter

Time Point	Vaccination Group	ANDV DNA Schedule # Doses	N	Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
				n	%	n	%	n	%
Baseline (Day 1)	ANDV DNA 2mg	3 or 4	x	x	xx	x	xx	x	xx
	ANDV DNA 4mg	3 or 4							
	Placebo	4							
	All Subjects	3 or 4							
Day 8 (Day 8 Post Dose 1)	ANDV DNA 2mg	3 or 4							
	ANDV DNA 4mg	3 or 4							
	Placebo	4							
	All Subjects	3 or 4							
Day 36 (Day 8 Post Dose 2)	ANDV DNA 2mg	3 or 4							
	ANDV DNA 4mg	3 or 4							
	Placebo	4							
	All Subjects	3 or 4							
Day 64 (Day 8 Post Dose 3)	ANDV DNA 2mg	3							
		4							
	ANDV DNA 4mg	3							
		4							
	Placebo	4							
	All Subjects	3 or 4							
Repeat for:									
Day 169 (Pre-Dose 4)									
Day 176 (Day 8 Post Dose 4)									
Max Severity Post Baseline									

Note: The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.
N=Number of subjects in the Safety Population; n=Number of subjects with laboratory values in the respective category.

Tables with similar format:

Table 116: Abnormal Laboratory Results Related to Study Treatment by Maximum Severity, Time Point, and Vaccination Group – Alanine Aminotransferase

Table 117: Abnormal Laboratory Results Related to Study Treatment by Maximum Severity, Time Point, and Vaccination Group – Total Bilirubin

Table 118: Abnormal Laboratory Results Related to Study Treatment by Maximum Severity, Time Point, and Vaccination Group – Creatinine

Table 119: Abnormal Laboratory Results Related to Study Treatment by Maximum Severity, Time Point, and Vaccination Group – Sodium

Time Point	Vaccination Group	ANDV DNA Schedule # Doses	N	Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)	
				n	%	n	%	n	%	n	%	n	%	n	%
Baseline (Day 1)	ANDV DNA 2mg	3 or 4	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	ANDV DNA 4mg	3 or 4													
	Placebo	4													
	All Subjects	3 or 4													
Day 8 (Day 8 Post Dose 1)	ANDV DNA 2mg	3 or 4													
	ANDV DNA 4mg	3 or 4													
	Placebo	4													
	All Subjects	3 or 4													
Day 36 (Day 8 Post Dose 2)	ANDV DNA 2mg	3 or 4													
	ANDV DNA 4mg	3 or 4													
	Placebo	4													
	All Subjects	3 or 4													
Day 64 (Day 8 Post Dose 3)	ANDV DNA 2mg	3													
		4													
	ANDV DNA 4mg	3													
		4													
	Placebo	4													
	All Subjects	3 or 4													
Repeat for:															
Day 169 (Pre-Dose 4)															
Day 176 (Day 8 Post Dose 4)															
Max Severity Post Baseline															

Note: The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.
N=Number of subjects in the Safety Population; n=Number of subjects with laboratory values in the respective category.

Table with similar format to Table 119:

Table 120: Abnormal Laboratory Results Related to Study Treatment by Maximum Severity, Time Point, and Vaccination Group – Potassium

Table with similar format to Table 115:

Table 121: Abnormal Laboratory Results Related to Study Treatment by Maximum Severity, Time Point, and Vaccination Group – Blood Urea Nitrogen

Table 122: Laboratory Summary Statistics by Time Point and Vaccination Group – Alanine Aminotransferase (ALT, IU/L)

Time Point		Vaccination Group	ANDV DNA Schedule # Doses	n	Mean	Standard Deviation	Median	Min, Max
Baseline (Day 1)	Results	ANDV DNA 2mg	3 or 4	x	xx.x	xx.x	xx.x	xx.x, xx.x
		ANDV DNA 4mg	3 or 4					
		Placebo	4					
		All Subjects	3 or 4					
Day 8 Post Dose 1	Results	ANDV DNA 2mg	3 or 4					
		ANDV DNA 4mg	3 or 4					
		Placebo	4					
		All Subjects	3 or 4					
	Change from Baseline	ANDV DNA 2mg	3 or 4					
		ANDV DNA 4mg	3 or 4					
		Placebo	4					
		All Subjects	3 or 4					
Day 36 (Day 8 Post Dose 2)	Results	ANDV DNA 2mg	3 or 4					
		ANDV DNA 4mg	3 or 4					
		Placebo	4					
		All Subjects	3 or 4					
	Change from Baseline	ANDV DNA 2mg	3 or 4					
		ANDV DNA 4mg	3 or 4					
		Placebo	4					
		All Subjects	3 or 4					
Day 64 (Day 8 Post Dose 3)	Results	ANDV DNA 2mg	3					
			4					
		ANDV DNA 4mg	3					
			4					
		Placebo	4					
		All Subjects	3 or 4					
	Change from Baseline	ANDV DNA 2mg	3					
			4					
		ANDV DNA 4mg	3					
			4					
		Placebo	4					
		All Subjects	3 or 4					
Repeat for:								
Day 169 (Pre-Dose 4)								
Day 176 (Day 8 Post Dose 4)								

n=Number of subjects with laboratory values.

Tables with similar format:

Table 123: Laboratory Summary Statistics by Time Point and Vaccination Group – Total Bilirubin (mg/dL)

Table 124: Laboratory Summary Statistics by Time Point and Vaccination Group – Creatinine (mg/dL)

Table 125: Laboratory Summary Statistics by Time Point and Vaccination Group – Sodium (mEq/L)

Table 126: Laboratory Summary Statistics by Time Point and Vaccination Group – Potassium (mEq/L)

Table 127: Laboratory Summary Statistics by Time Point and Vaccination Group – Blood Urea Nitrogen (mg/dL

14.3.5.2 Hematology Results

Table with similar format to Table 108:

Table 128: Abnormal Laboratory Results by Maximum Severity, Time Point, and Vaccination Group – Any Hematology Parameter

Table with similar format to Table 112 (abnormal low/high):

Table 129: Abnormal Laboratory Results by Maximum Severity, Time Point, and Vaccination Group – White Blood Cells (10^3/µL)

Table with similar format to Table 108 (abnormal low):

Table 130: Abnormal Laboratory Results by Maximum Severity, Time Point, and Vaccination Group – Hemoglobin (g/dL)

Table with similar format to Table 112 (abnormal low/high):

Table 131: Abnormal Laboratory Results by Maximum Severity, Time Point, and Vaccination Group – Platelet Count (10^3/µL)

Table with similar format to Table 108 (abnormal low):

Table 132: Abnormal Laboratory Results by Maximum Severity, Time Point, and Vaccination Group – ANC (10^3/µL)

Abnormal labs related to IP

Table with similar format to Table 108:

Table 133: Abnormal Laboratory Results Related to Study Treatment by Maximum Severity, Time Point, and Vaccination Group – Any Hematology Parameter

Table with similar format to Table 112 (abnormal low/high):

Table 134: Abnormal Laboratory Results Related to Study Treatment by Maximum Severity, Time Point, and Vaccination Group – White Blood Cells

Table with similar format to Table 108 (abnormal low):

Table 135: Abnormal Laboratory Results Related to Study Treatment by Maximum Severity, Time Point, and Vaccination Group – Hemoglobin

Table with similar format to Table 112 (abnormal low/high):

Table 136: Abnormal Laboratory Results Related to Study Treatment by Maximum Severity, Time Point, and Vaccination Group – Platelet Count

Table with similar format to Table 108 (abnormal low):

Table 137: Abnormal Laboratory Results Related to Study Treatment by Maximum Severity, Time Point, and Vaccination Group – ANC

Summary stats

Tables with similar format to Table 122:

Table 138: Laboratory Summary Statistics by Parameter, Time Point, and Vaccination Group – White Blood Cells (10^3/µL)

Table 139: Laboratory Summary Statistics by Parameter, Time Point, and Vaccination Group – Hemoglobin (g/dL)

Table 140: Laboratory Summary Statistics by Parameter, Time Point, and Vaccination Group – Platelet Count (10^3/µL)

Table 141: Laboratory Summary Statistics by Parameter, Time Point, and Vaccination Group – Absolute Neutrophil Count (10^3/µL)

14.3.6 Displays of Vital Signs

Table 142: Vital Signs by Maximum Severity, Time Point, and Vaccination Group – Any Assessment

Time Point	Vaccination Group	ANDV DNA Schedule # Doses	N	None		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
				n	%	n	%	n	%	n	%	n	%
Baseline (Day 1)	ANDV DNA 2mg	3 or 4	x	x	xx	x	xx	x	xx	x	xx	x	xx
	ANDV DNA 4mg	3 or 4											
	Placebo	4											
	All Subjects	3 or 4											
Day 29 Post-Dose 1 (Pre-Dose 2)	ANDV DNA 2mg	3 or 4											
	ANDV DNA 4mg	3 or 4											
	Placebo	4											
	All Subjects	3 or 4											
Day 57 (29 Days Post-Dose 2) (Pre-Dose 3)	ANDV DNA 2mg	3 or 4											
	ANDV DNA 4mg	3 or 4											
	Placebo	4											
	All Subjects	3 or 4											
Day 169 (Pre-Dose 4)	ANDV DNA 2mg	3											
		4											
	ANDV DNA 4mg	3											
		4											
	Placebo	4											
	All Subjects	3 or 4											
Max. Severity Post-Baseline	ANDV DNA 2mg	3											
		4											
	ANDV DNA 4mg	3											
		4											
	Placebo	4											
	All Subjects	3 or 4											

Note: The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.
N=Number of subjects in the Safety Population; n=Number of subjects with laboratory values in the respective category.

Table with similar format:

Table 143: Vital Signs by Maximum Severity, Time Point, and Vaccination Group – Oral Temperature

Table 144: Vital Signs by Assessment, Maximum Severity, Time Point, and Vaccination Group – Pulse

Time Point	Vaccination Group	ANDV DNA Schedule # Doses	N	None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Missing	
				n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Baseline (Day 1)	ANDV DNA 2mg	3 or 4	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	ANDV DNA 4mg	3 or 4																	
	Placebo	4																	
	All Subjects	3 or 4																	
Day 29 Post-Dose 1 (Pre-Dose 2)	ANDV DNA 2mg	3 or 4																	
	ANDV DNA 4mg	3 or 4																	
	Placebo	4																	
	All Subjects	3 or 4																	
Day 57 (29 Days Post-Dose 2) (Pre-Dose 3)	ANDV DNA 2mg	3 or 4																	
	ANDV DNA 4mg	3 or 4																	
	Placebo	4																	
	All Subjects	3 or 4																	
Day 169 (Pre-Dose 4)	ANDV DNA 2mg	3																	
		4																	
	ANDV DNA 4mg	3																	
		4																	
	Placebo	4																	
	All Subjects	3 or 4																	
Max. Severity Post-Baseline	ANDV DNA 2mg	3																	
		4																	
	ANDV DNA 4mg	3																	
		4																	
	Placebo	4																	
	All Subjects	3 or 4																	

Note: The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.
N=Number of subjects in the Safety Population; n=Number of subjects with laboratory values in the respective category.

Tables with similar format:

Table 145: Vital Signs by Assessment, Maximum Severity, Time Point, and Vaccination group – Systolic Blood Pressure

Table 146: Vital Signs by Assessment, Maximum Severity, Time Point, and Vaccination group – Diastolic Blood Pressure

14.4 Summary of Concomitant Medications

Table 147: Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification and Vaccination Group

WHO Drug Code Level 1 Anatomic Group	WHO Drug Code Level 2 Therapeutic Subgroup	ANDV DNA 2mg 3 Doses (N=X)		ANDV DNA 2mg 4 Doses (N=X)		ANDV DNA 4mg 3 Doses (N=X)		ANDV DNA 4mg 4 Doses (N=X)		Placebo (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%
Any Level 1 Codes	Any Level 2 Codes	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
[ATC Level 1 - 1]	Any [ATC 1 – 1]												
	[ATC 2 - 1]												
	[ATC 2 - 2]												
	[ATC 2 - 3]												
[ATC Level 1 – 2]	[ATC 2 - 1]												
	[ATC 2 - 2]												
	[ATC 2 - 3]												

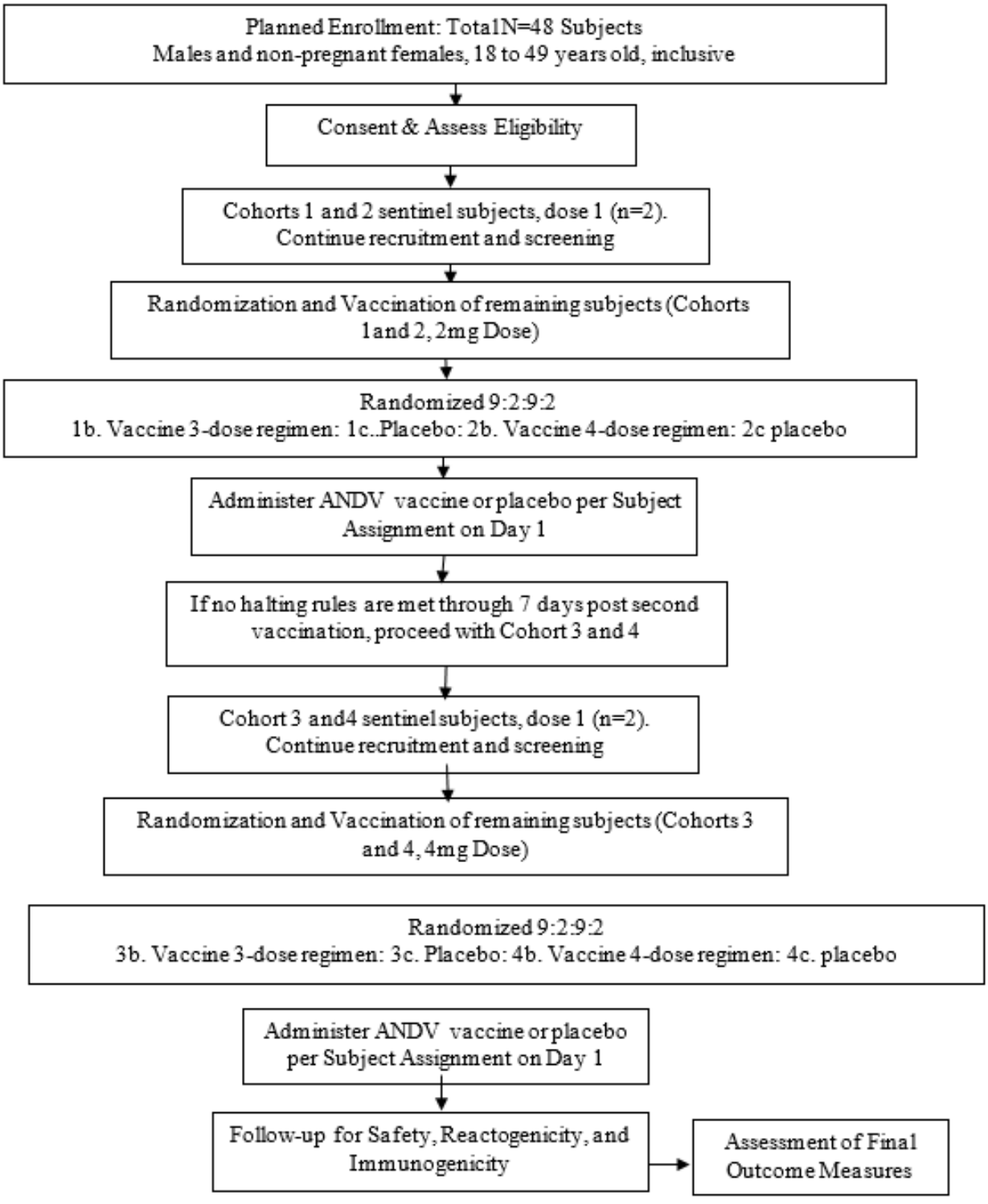
N=Number of subjects in the Safety Population. n=Number of subjects reporting taking at least one medication in the specific WHO Drug Class.
Includes medications taken prior to or at enrollment (day 1).

APPENDIX 2. FIGURE MOCK-UPS

Note: Figures for the primary immunogenicity and safety review will not include data from Day 253 and Day 337 visits.

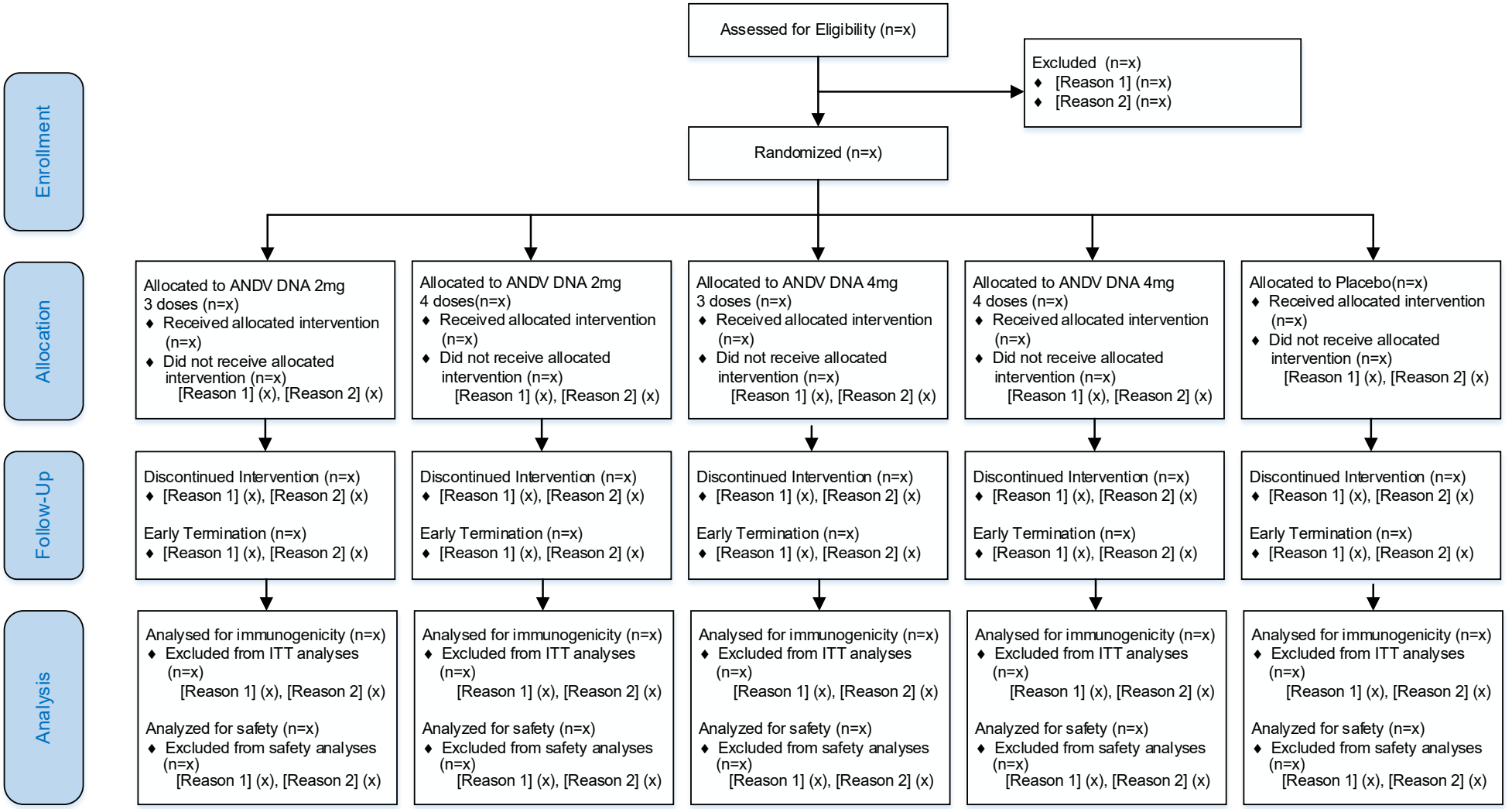
LIST OF FIGURES

Figure 1: Study Schema



10.1 Disposition of Subjects

Figure 2: CONSORT Flow Diagram



14.2.2 Immunogenicity

Figure 3: Reverse Cumulative Distribution of Plaque Reduction Neutralization by Time Point and Vaccination Group - Intent to Treat Population

[Implementation Note: A sample figure based on mock data is shown below.]

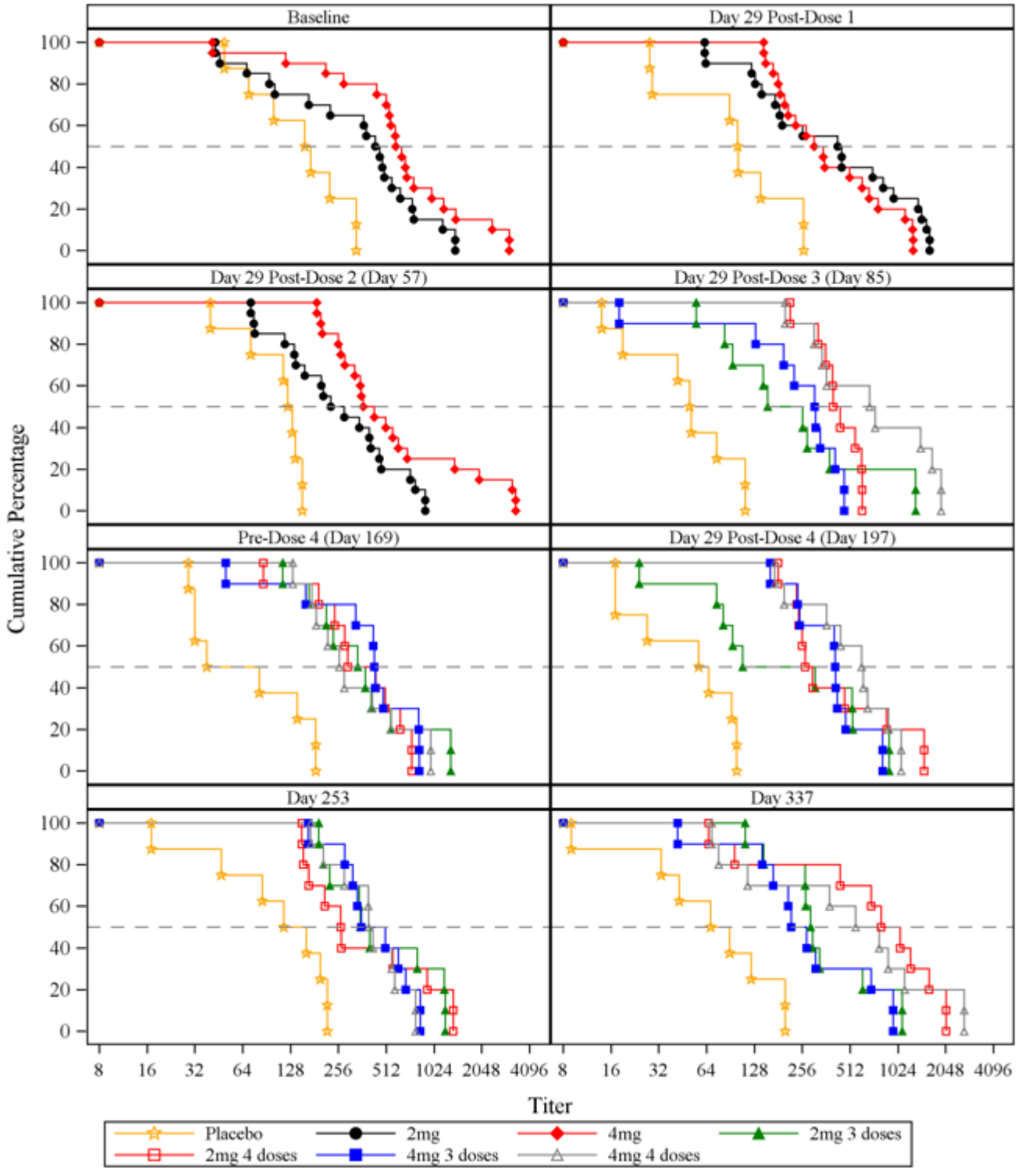


Figure with similar format:

Figure 4: Reverse Cumulative Distribution of Plaque Reduction Neutralization by Time Point and Vaccination Group - Per Protocol Population

Figure 5: Reverse Cumulative Distribution of Pseudovirion Reduction Neutralization by Time Point and Vaccination Group - Intent to Treat Population

[Implementation Note: A sample figure based on mock data is shown below]

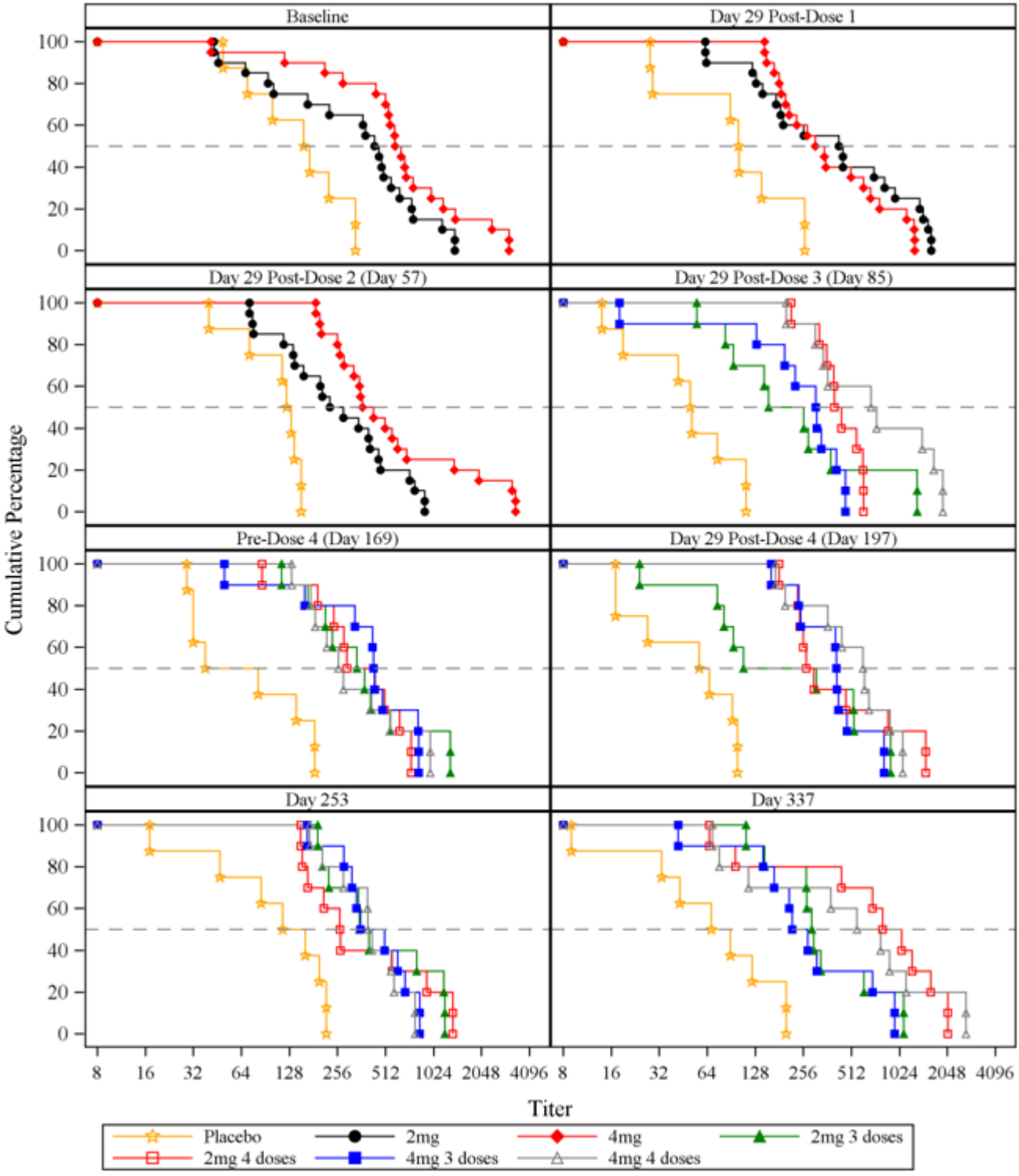


Figure with similar format:

Figure 6: Reverse Cumulative Distribution of Pseudovirion Reduction Neutralization by Time Point and Vaccination Group - Per Protocol Population

Figure 7: Plaque Reduction Neutralization Titers Over Time Point and Vaccination Group - Intent to Treat Population

[Implementation Note: A sample figure is shown below.]

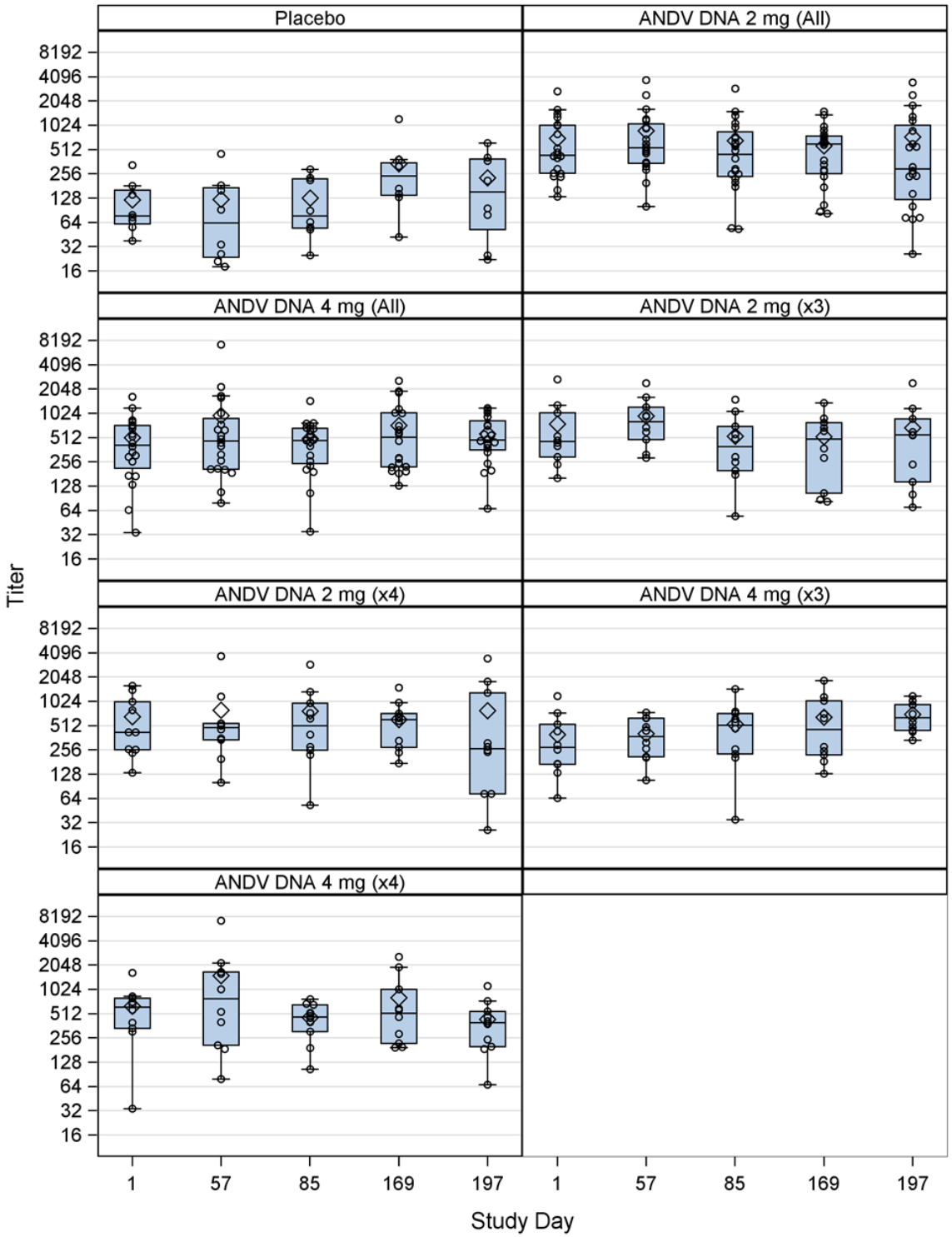


Figure with similar format:

Figure 8: Plaque Reduction Neutralization Titers Over Time Point and Vaccination Group - Per Protocol Population

Figure 9: Pseudovirion Neutralization Titers Over Time Point and Vaccination Group - Intent to Treat Population

[Implementation Note: A sample figure is shown below.]

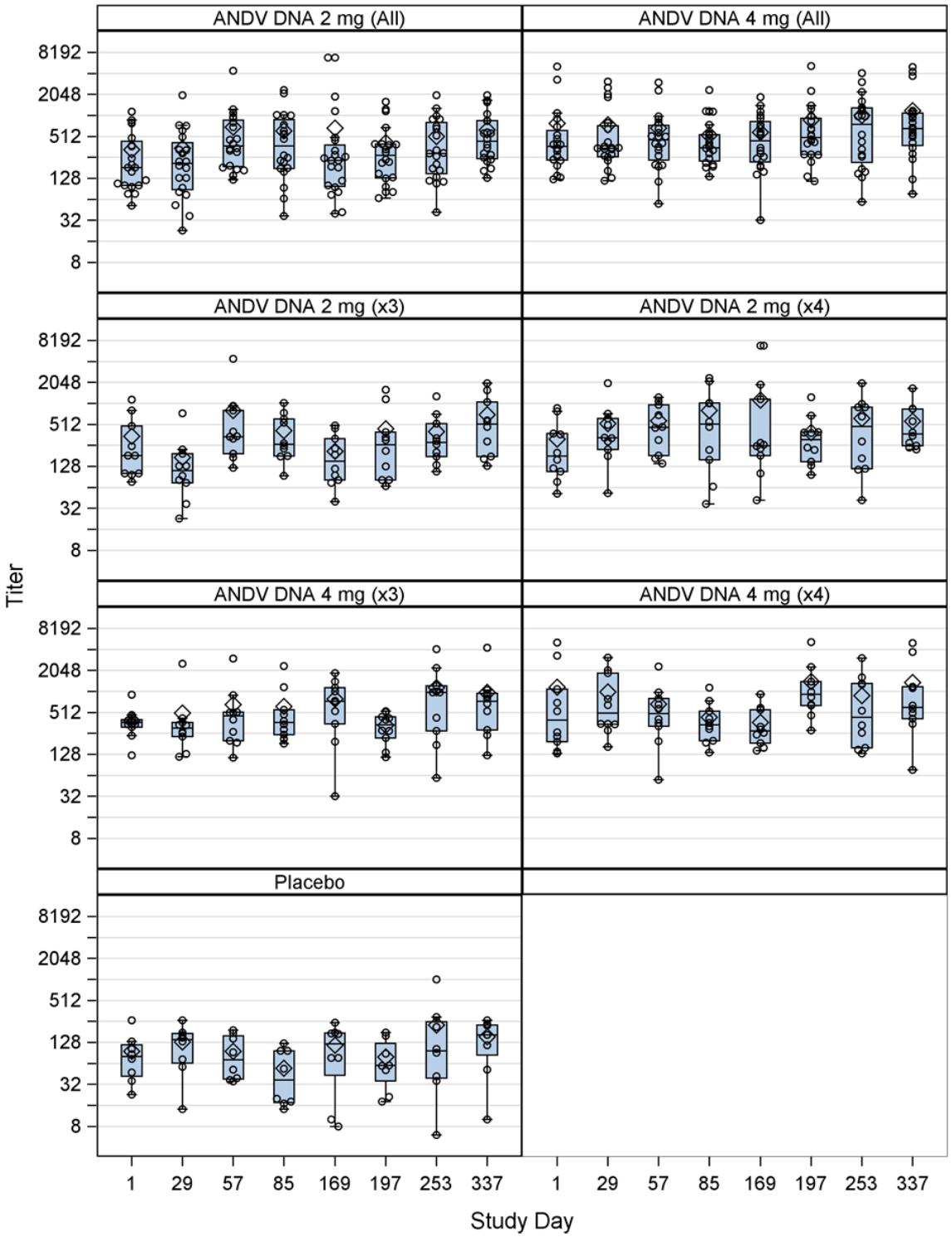
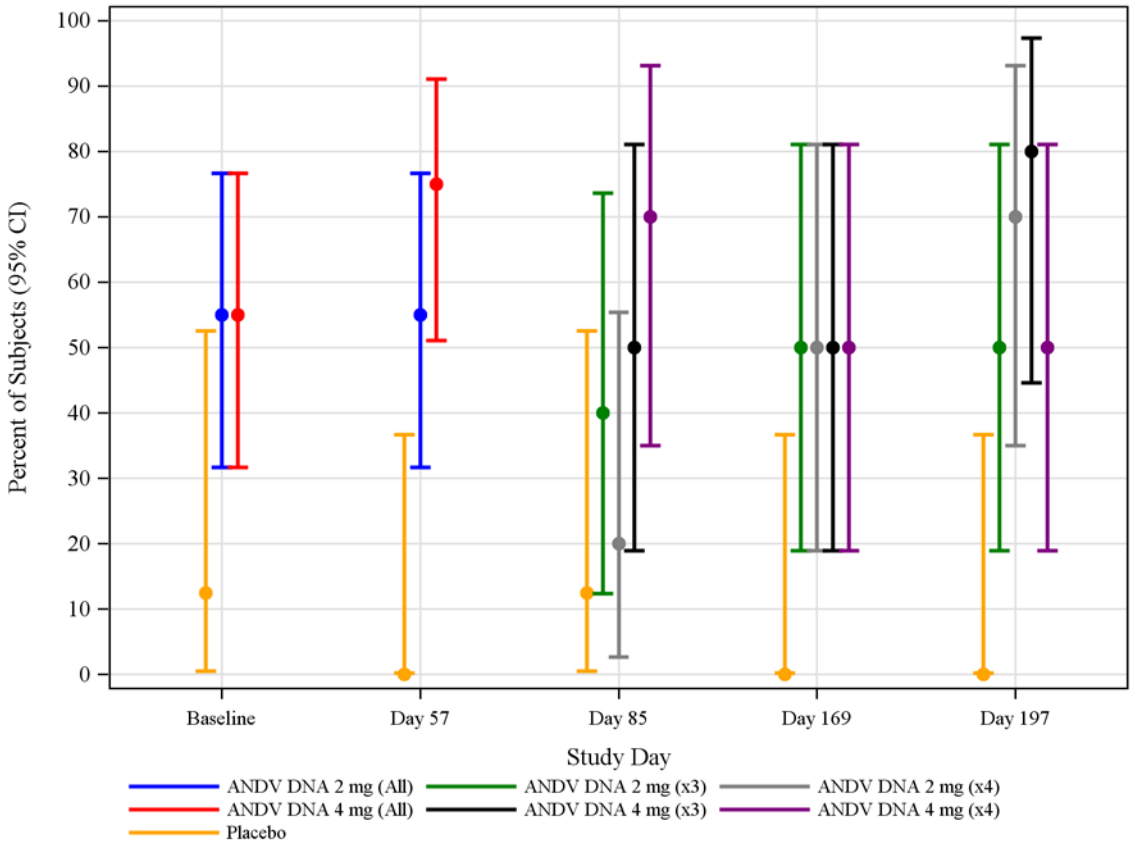


Figure with similar format:

Figure 10: Pseudovirion Neutralization Titers Over Time Point and Vaccination Group - Per Protocol Population

Figure 11: Incidence of Plaque Reduction Neutralization Titer ≥20 by Time Point and Vaccination Group - Intent to Treat Population

[Implementation Note: Below is an example figure.]



Each bar represents the proportion of subjects with a positive response and the exact, Clopper-Pearson 95% CI.

Figure with similar format:

Figure 12: Incidence of Plaque Reduction Neutralization Titer ≥20 by Time Point and Vaccination Group - Per Protocol Population

Figure 13: Incidence of Pseudovirion Neutralization Titer ≥20 by Time Point and Vaccination Group - Intent to Treat Population

[Implementation Note: Below is an example figure.]

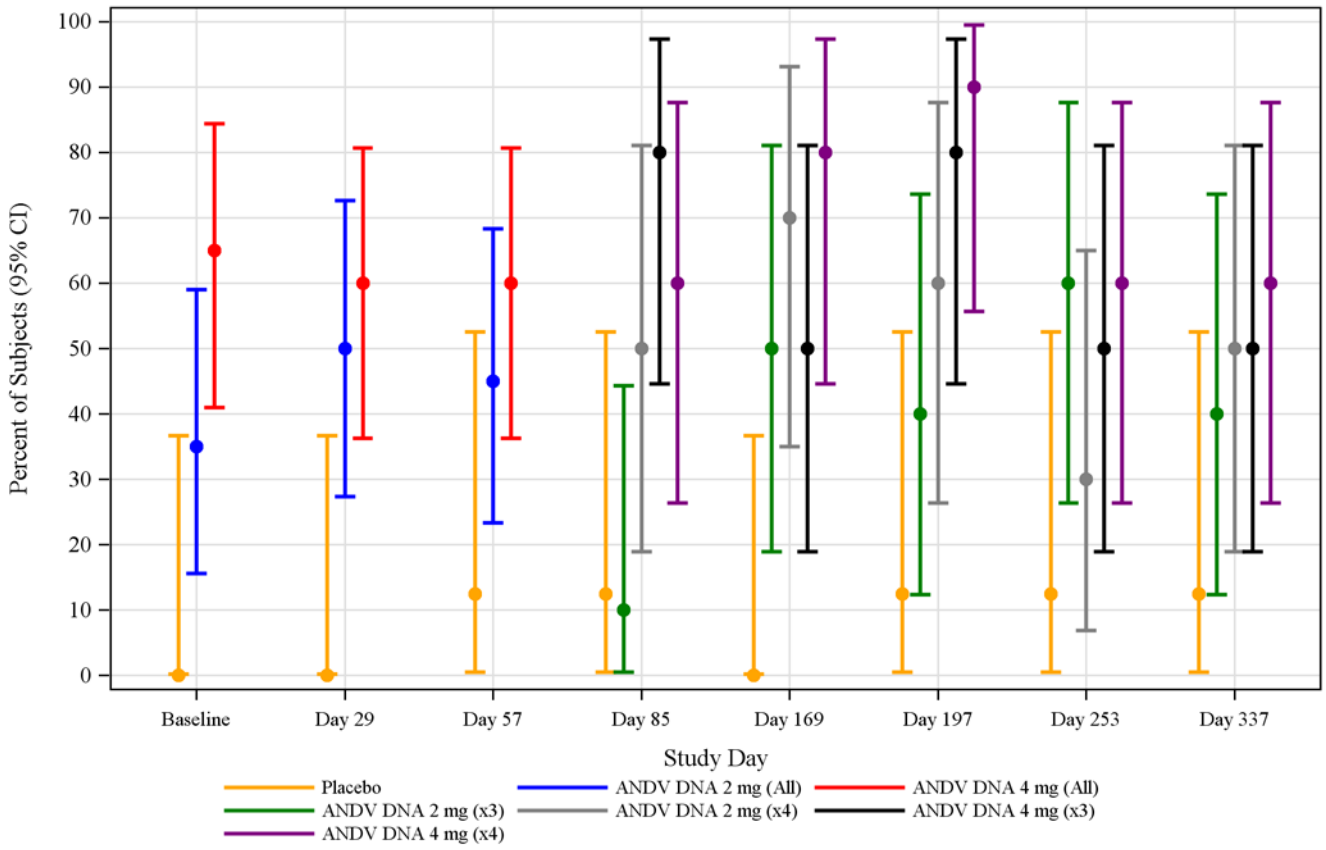
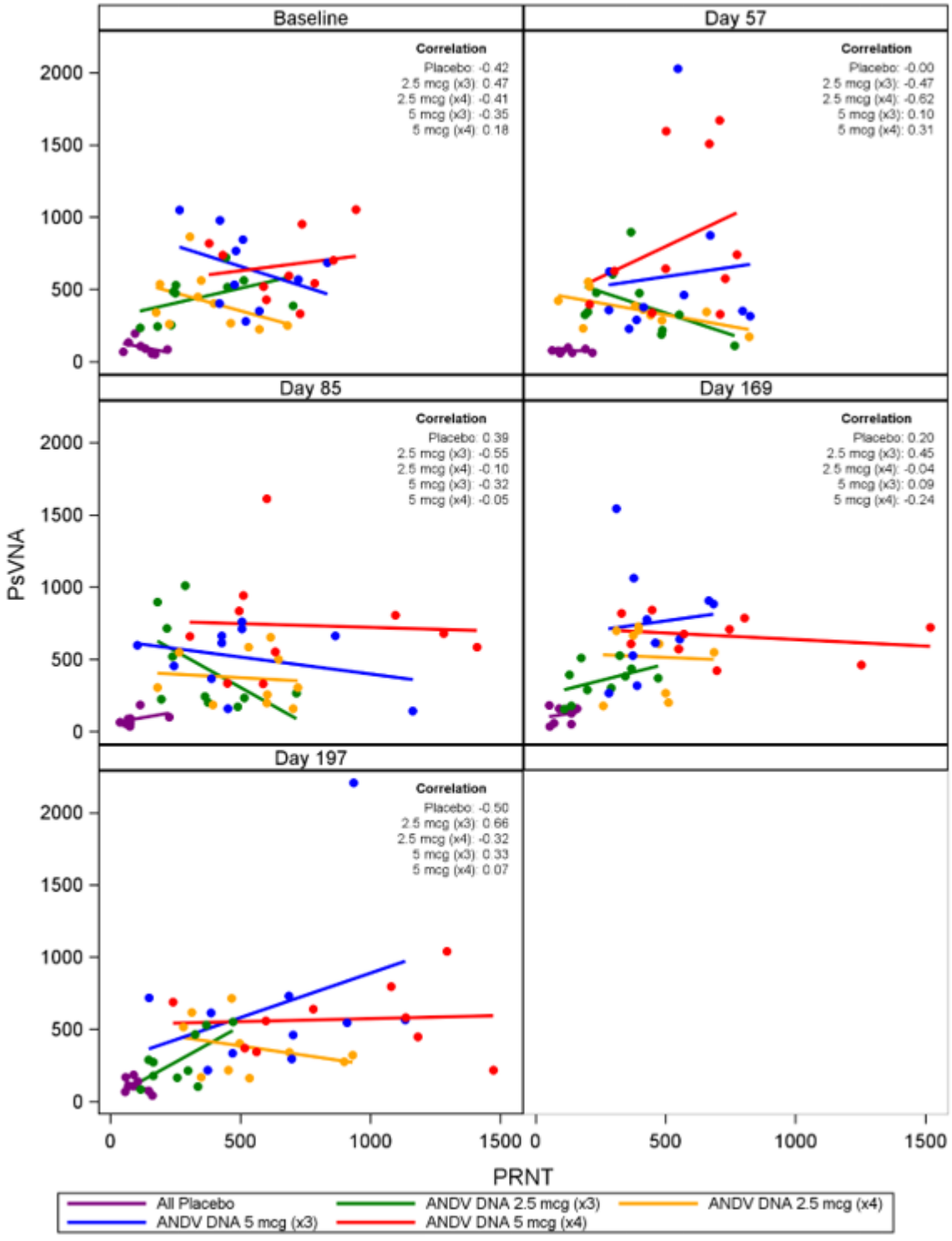


Figure with similar format:

Figure 14: Incidence of Pseudovirion Neutralization Titer ≥20 by Time Point and Vaccination Group - Per Protocol Population

Figure 15: Correlation Between Plaque Reduction Neutralization and Pseudovirion Neutralization by Time Point and Vaccination Group - Intent-to-Treat Population



Correlation = Spearman Correlation Coefficient

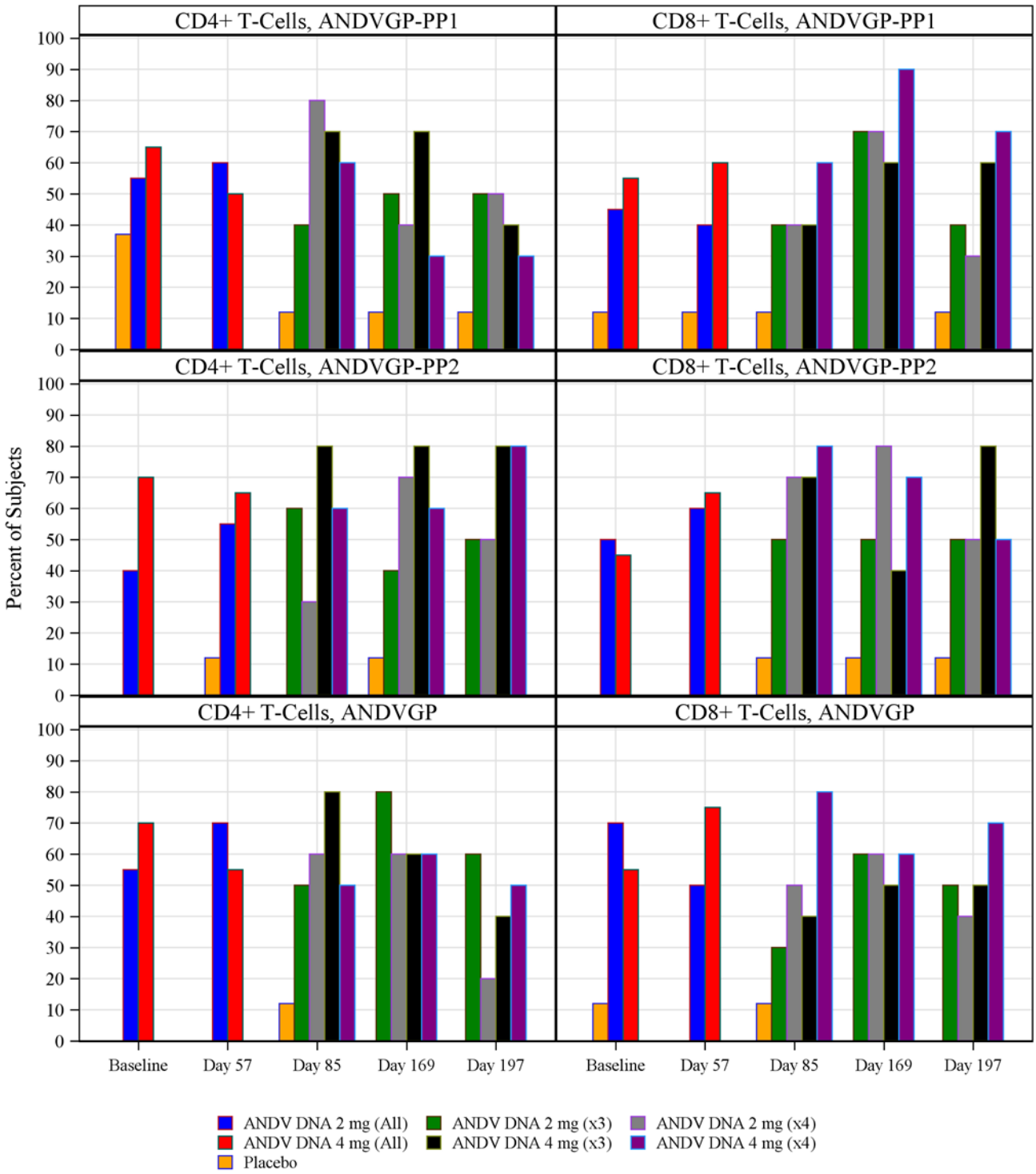
Figure with similar format:

Figure 16: Correlation Between Plaque Reduction Neutralization and Pseudovirion Neutralization by Time Point and Vaccination Group - Per Protocol Population

Correlation = Spearman Correlation Coefficient

Figure 17: Intracellular Staining (ICS) Incidence of >3 Standard Deviation Increase in Percent of CD4+ and CD8+ Cells by ANDVGP Pool, Time Point, and Vaccination Group – Cells Secreting IFNɣ - Intent to Treat Population

[Implementation Note: Below is an example figure. May be with different colors.]



Figures with similar format:

Figure 18: Intracellular Staining (ICS) Incidence of >3 Standard Deviation Increase in Percent of CD4+ and CD8+ Cells by ANDVGP Pool, Time Point, and Vaccination Group – Cells Secreting IFNɣ - Per Protocol Population

Figure 19: Intracellular Staining (ICS) Incidence of >3 Standard Deviation Increase in Percent of CD4+ and CD8+ Cells by ANDVGP Pool, Time Point, and Vaccination Group – Cells Secreting TNFα - Intent to Treat Population

Figure 20: Intracellular Staining (ICS) Incidence of >3 Standard Deviation Increase in Percent of CD4+ and CD8+ Cells by ANDVGP Pool, Time Point, and Vaccination Group – Cells Secreting TNFα - Per Protocol Population

Figure 21: Intracellular Staining (ICS) Incidence of >3 Standard Deviation Increase in Percent of CD4+ and CD8+ Cells by ANDVGP Pool, Time Point, and Vaccination Group – Cells Secreting IL-2 - Intent to Treat Population

Figure 22: Intracellular Staining (ICS) Incidence of >3 Standard Deviation Increase in Percent of CD4+ and CD8+ Cells by ANDVGP Pool, Time Point, and Vaccination Group – Cells Secreting IL-2 - Per Protocol Population

Figure 23: Intracellular Staining (ICS) Incidence of >3 Standard Deviation Increase in Percent of CD4+ and CD8+ Cells by ANDVGP Pool, Time Point, and Vaccination Group – Cells Secreting IFNɣ and TNFα - Intent to Treat Population

Figure 24: Intracellular Staining (ICS) Incidence of >3 Standard Deviation Increase in Percent of CD4+ and CD8+ Cells by ANDVGP Pool, Time Point, and Vaccination Group – Cells Secreting IFNɣ and TNFα - Per Protocol Population

Figure 25: Intracellular Staining (ICS) Incidence of >3 Standard Deviation Increase in Percent of CD4+ and CD8+ Cells by ANDVGP Pool, Time Point, and Vaccination Group – Cells Secreting IFNɣ and IL-2 - Intent to Treat Population

Figure 26: Intracellular Staining (ICS) Incidence of >3 Standard Deviation Increase in Percent of CD4+ and CD8+ Cells by ANDVGP Pool, Time Point, and Vaccination Group – Cells Secreting IFNɣ and IL-2 - Per Protocol Population

Figure 27: Intracellular Staining (ICS) Incidence of >3 Standard Deviation Increase in Percent of CD4+ and CD8+ Cells by ANDVGP Pool, Time Point, and Vaccination Group – Cells Secreting TNFα and IL-2 - Intent to Treat Population

Figure 28: Intracellular Staining (ICS) Incidence of >3 Standard Deviation Increase in Percent of CD4+ and CD8+ Cells by ANDVGP Pool, Time Point, and Vaccination Group – Cells Secreting TNFα and IL-2 - Per Protocol Population

Figure 29: Intracellular Staining (ICS) Incidence of >3 Standard Deviation Increase in Percent of CD4+ and CD8+ Cells by ANDVGP Pool, Time Point, and Vaccination Group – Cells Secreting IFNɣ, TNFα and IL-2 - Intent to Treat Population

14.3.1.1 Solicited Adverse Events

Figure 33: Maximum Severity of Solicited Local Symptoms per Subject by Day Post Treatment and Product Received – Post-Dose 1

[Implementation Note: Below is an example figure. There will be five panels: one for each dose plus any dose. Y-axis will display Pre-Vac, Post-Vac and Day 1-8.]

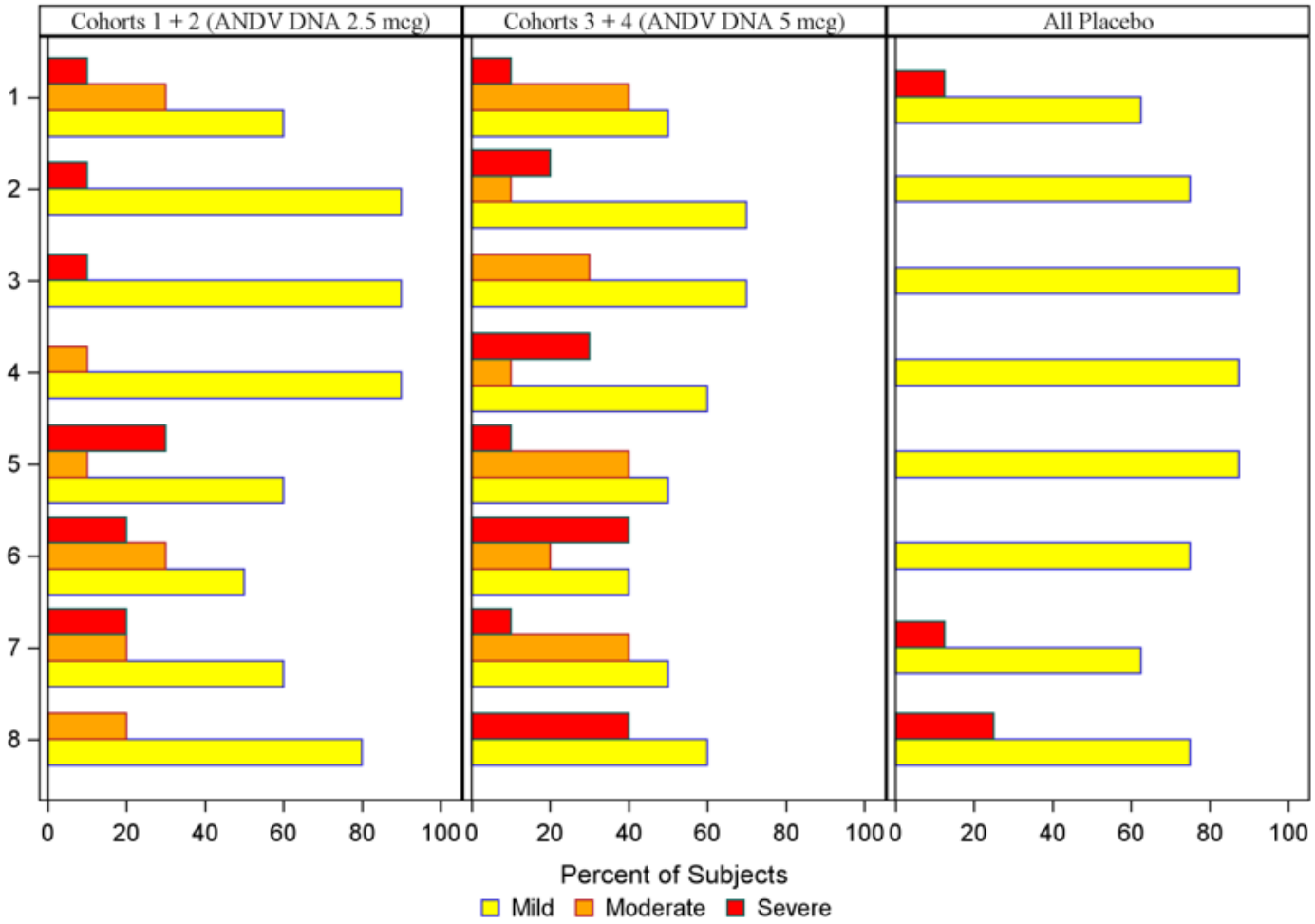


Figure with similar format:

Figure 34: Maximum Severity of Solicited Local Symptoms per Subject by Day Post Treatment and Product Received – Post-Dose 2

Figure 35: Maximum Severity of Solicited Local Symptoms per Subject by Day Post Treatment and Product Received – Post-Dose 3

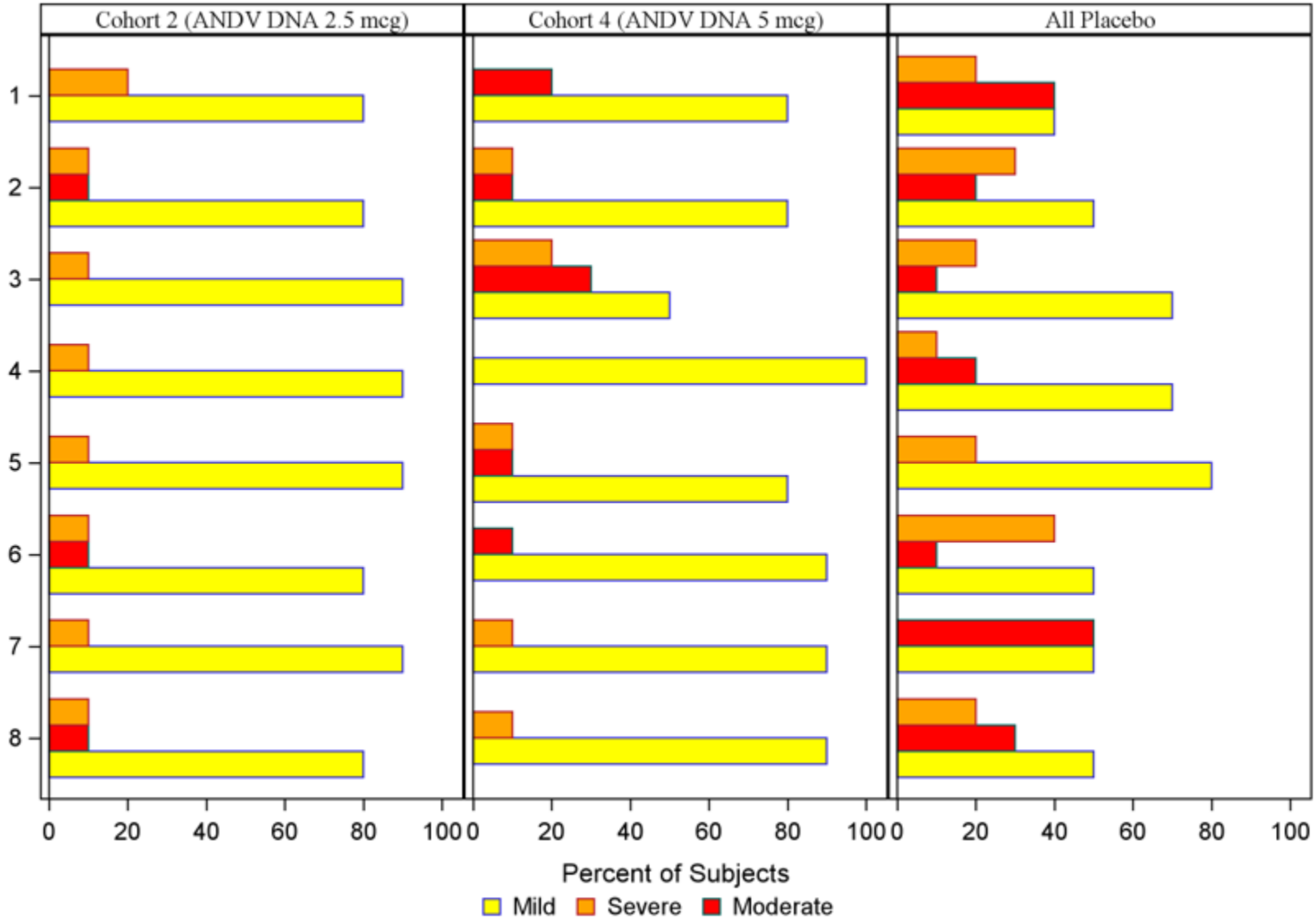
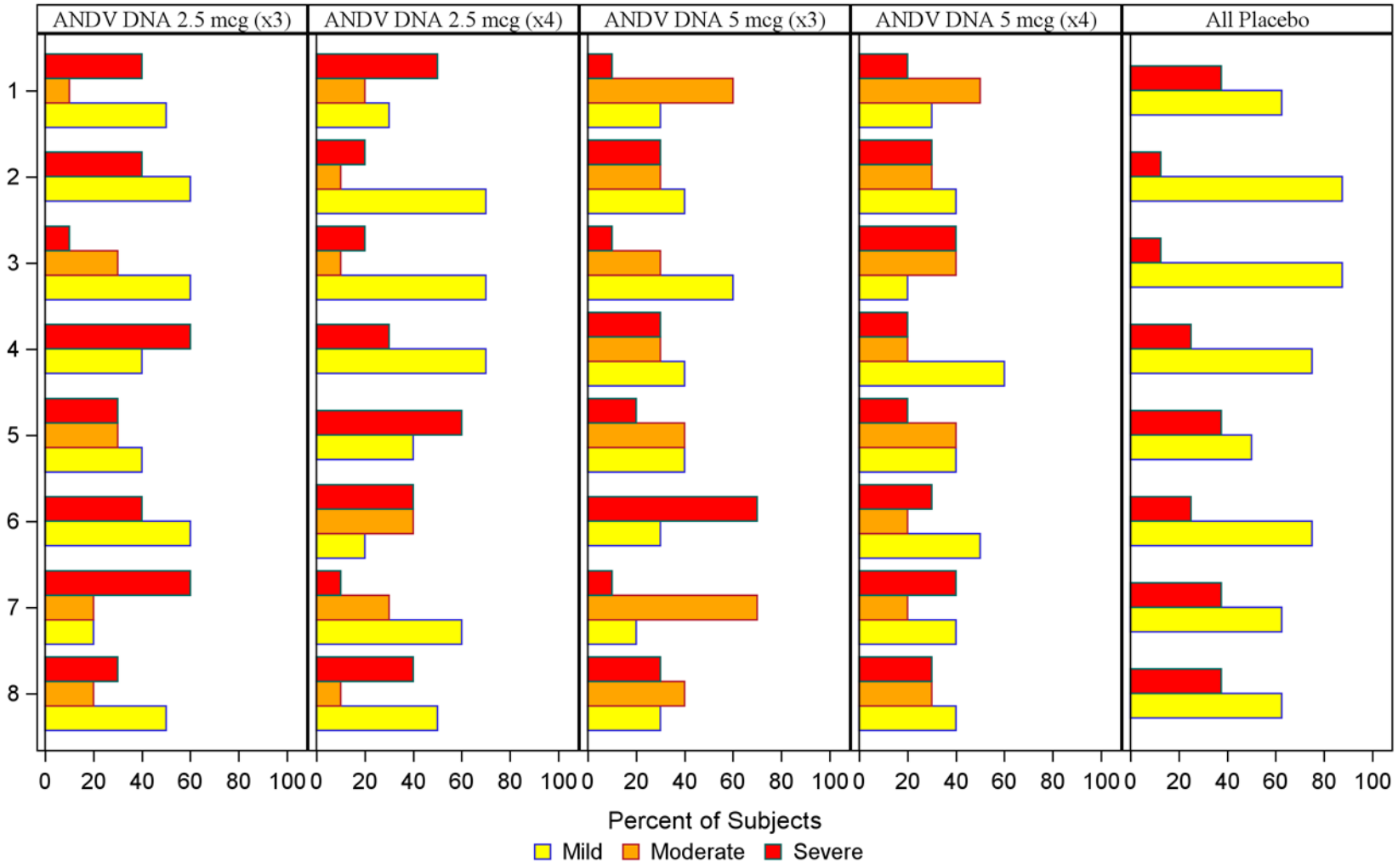


Figure 36: Maximum Severity of Solicited Local Symptoms per Subject by Day Post Treatment and Product Received – Post-Dose 4

[Figure 36 will be similar to Figure 33]

Figure 37: Maximum Severity of Solicited Local Symptoms per Subject by Day Post Treatment and Vaccination Group – Post-Any Dose



Figures with similar format to Figure 33:

Figure 38: Maximum Severity of Solicited Systemic Symptoms per Subject by Day Post Treatment and Product Received – Post-Dose 1

Figure 39: Maximum Severity of Solicited Systemic Symptoms per Subject by Day Post Treatment and Product Received – Post-Dose 2

Figure with similar format to Figure 35:

Figure 40: Maximum Severity of Solicited Systemic Symptoms per Subject by Day Post Treatment and Product Received – Post-Dose 3

Figure with similar format to Figure 33:

Figure 41: Maximum Severity of Solicited Systemic Symptoms per Subject by Day Post Treatment and Product Received – Post-Dose 4

Figure with similar format to Figure 37:

Figure 42: Maximum Severity of Solicited Systemic Symptoms per Subject by Day Post Treatment and Vaccination Group – Post-Any Dose

14.3.1.2 Unsolicited Adverse Events

Figure 43: Frequency of Related Adverse Events by MedDRA System Organ Class, Severity, and Product Received – Post-Dose 1

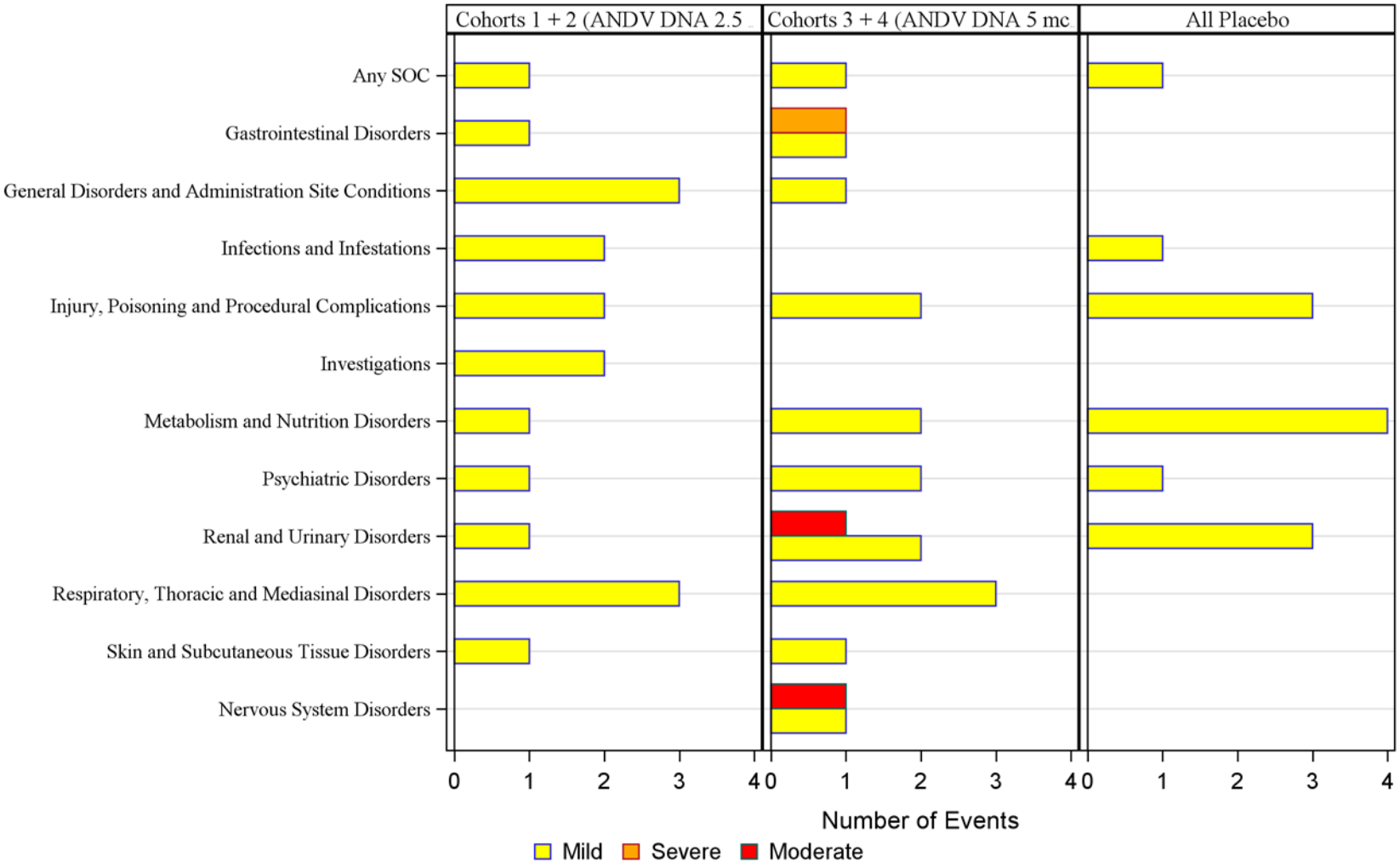


Figure with similar format:

Figure 44: Frequency of Related Adverse Events by MedDRA System Organ Class, Severity, and Product Received – Post-Dose 2

Figure 45: Frequency of Related Adverse Events by MedDRA System Organ Class, Severity, and Product Received – Post-Dose 3

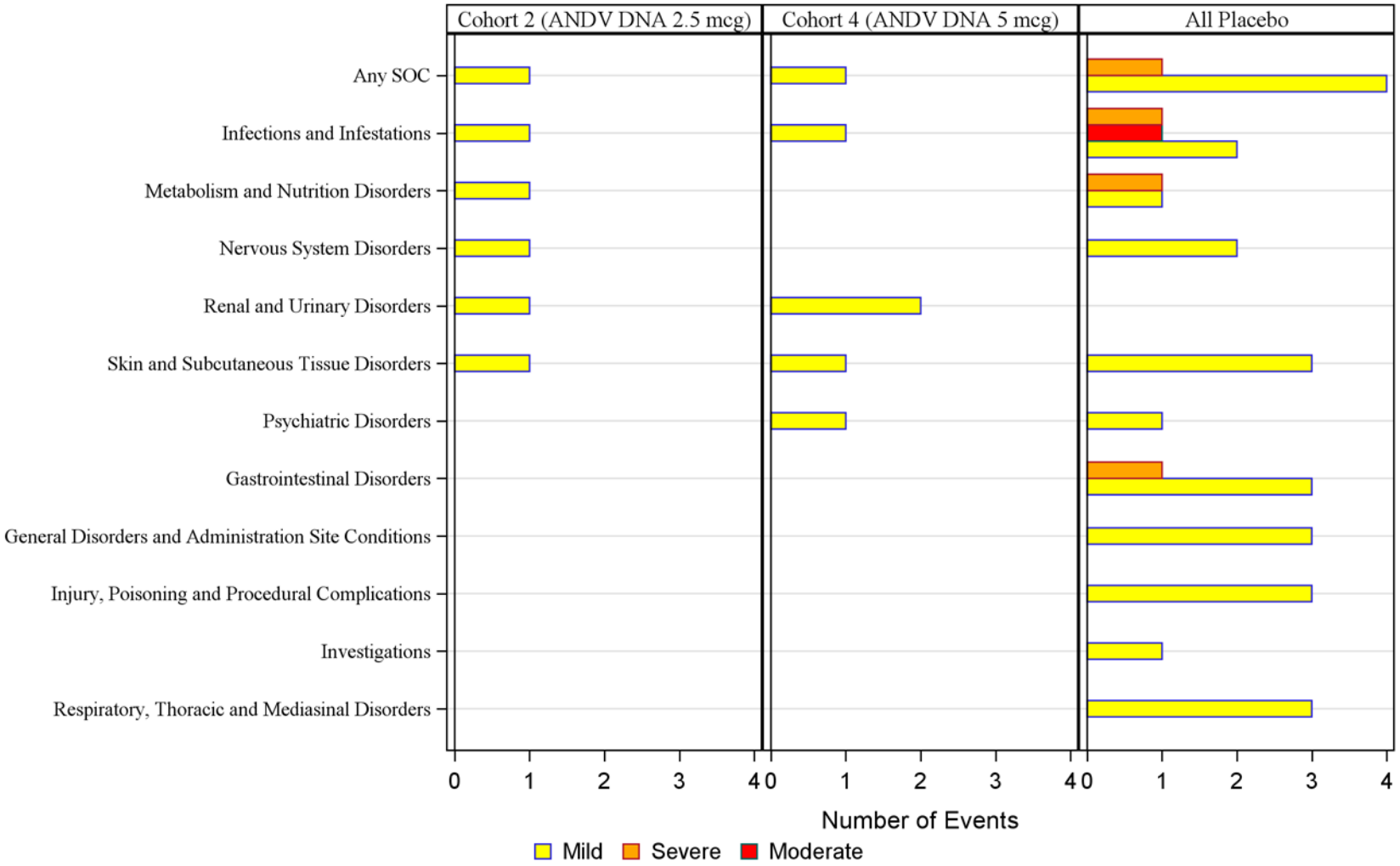
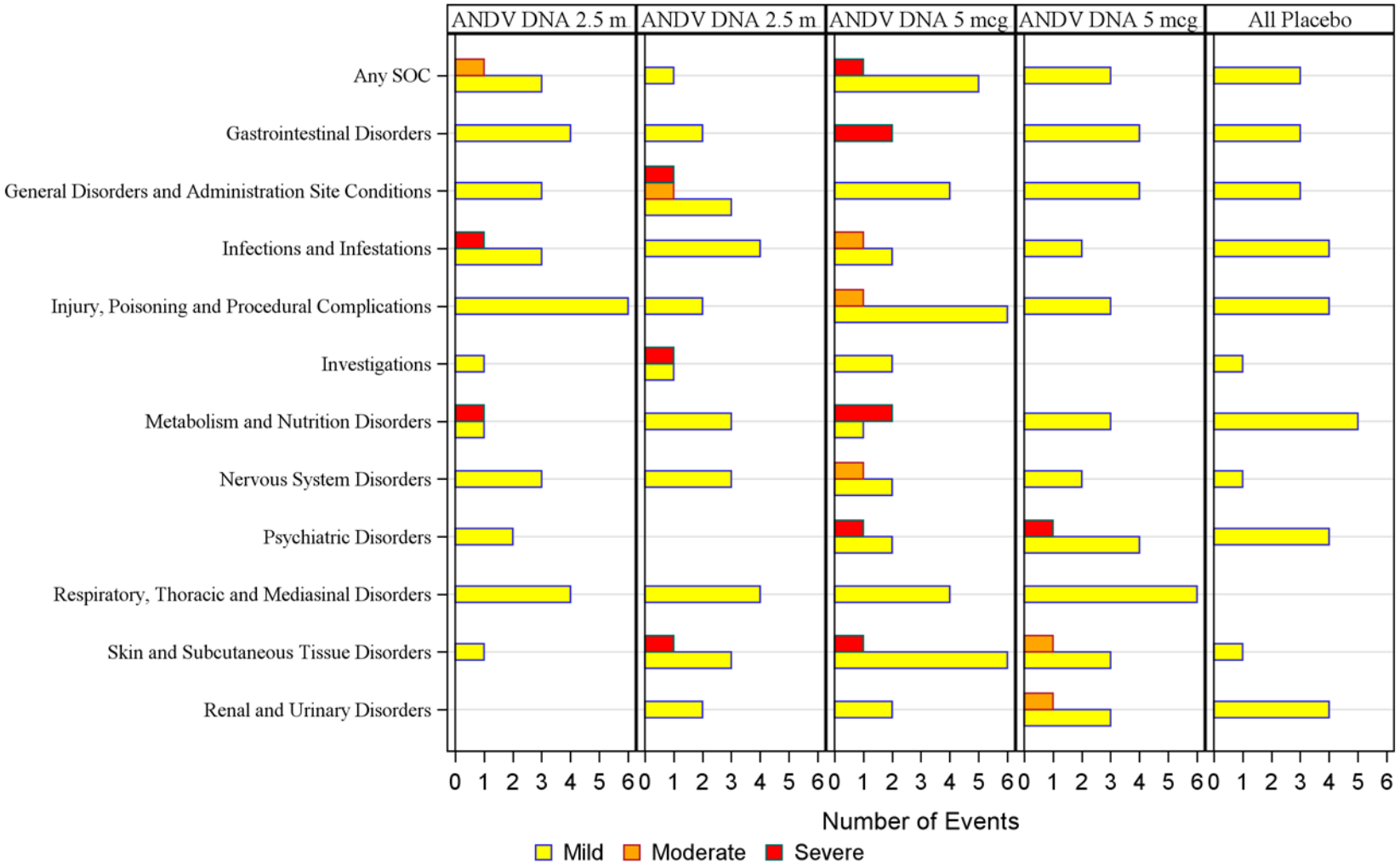


Figure with similar format to Figure 43

Figure 46: Frequency of Related Adverse Events by MedDRA System Organ Class, Severity, and Product Received – Post-Dose 4

Figure 47: Frequency of Related Adverse Events by MedDRA System Organ Class, Severity, and Vaccination Group – Post-Any Dose



Figures with similar format to Figure 43:

Figure 48: Incidence of Related Adverse Events by MedDRA System Organ Class, Maximum Severity, and Product Received – Post-Dose 1

Figure 49: Incidence of Related Adverse Events by MedDRA System Organ Class, Maximum Severity, and Product Received – Post-Dose 2

Figure with similar format to Figure 45:

Figure 50: Incidence of Related Adverse Events by MedDRA System Organ Class, Maximum Severity, and Product Received – Post-Dose 3

Figure with similar format to Figure 43:

Figure 51: Incidence of Related Adverse Events by MedDRA System Organ Class, Maximum Severity, and Product Received – Post-Dose 4

Figures with similar format to Figure 47:

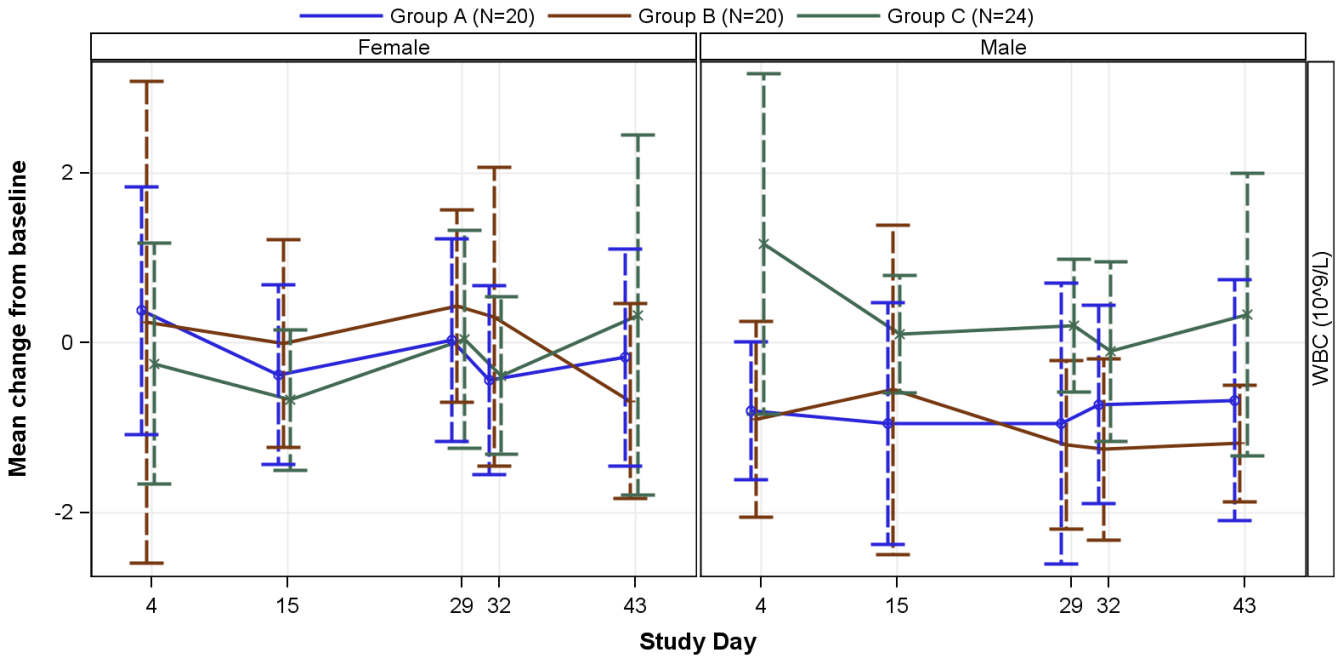
Figure 52: Incidence of Related Adverse Events by MedDRA System Organ Class, Maximum Severity, and Vaccine Group – Post-Any Dose

[Note: X-axis will be "Percent of Subjects"]

14.3.5 Displays of Laboratory Results

Figure 53: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter and Vaccination Group –ALT

[Implementation Note: Below is an example figure. The figure will have 5 curves (one for each vaccination group) and one panel. The x-axis will show Days 8, 36, 64, 169, and 176.]



Figures with similar format:

Figure 54: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter and Vaccination Group – Total Bilirubin

Figure 55: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter and Vaccination Group – Creatinine

Figure 56: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter and Vaccination Group – Sodium

Figure 57: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter and Vaccination Group – Potassium

Figure 58: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter and Vaccination Group – WBC

Figure 59: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter and Vaccination Group – Hemoglobin

Figure 60: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter and Vaccination Group – Platelets

Figure 61: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter and Vaccination Group – ANC

APPENDIX 3. LISTINGS MOCK-UPS

Note: Listings will not be included for the primary immunogenicity and safety review.

LISTINGS

16.1.6 Listing of Subjects Receiving Investigational Product

Not described in SAP, but this is a required listing for the CSR.

16.2 Database Listings by Subject

16.2.1 Discontinued Subjects

Listing 1: 16.2.1 Early Terminations or Discontinued Subjects

[Implementation Note: Category will be either "Early Termination" or "Treatment Discontinued." For subjects who terminated early and discontinued treatment, then both reasons should be displayed, separated by a comma ("Early Termination, Treatment Discontinued") so there is only one row per subject. In the "Reason" column, concatenate any "specify" fields, including AE number and DV number. Sort order: Vaccination Group, Subject ID, alphabetically by Category (in the case a subject both terminates early and discontinues treatment).]

Vaccination Group	Subject ID	Category	Reason for Early Termination or Treatment Discontinuation	Study Day

16.2.2 Protocol Deviations

Listing 2: 16.2.2.1: Subject-Specific Protocol Deviations

[Implementation Note: In the "Deviation" column, concatenate any and all "specify" fields (including visit number, etc.). If "Reason for Deviation" is "Other," concatenate "specify" field, separate by a colon, e.g., "Other: Subject refusal." Sort order: Vaccination Group, Subject ID, DV Number.]

Vaccination Group	Subject ID	DV Number	Deviation	Deviation Category	Study Day	Reason for Deviation	Deviation Resulted in AE?	Deviation Resulted in Subject Termination?	Deviation Affected Product Stability?	Deviation Resolution	Comments

Listing 3: 16.2.2.2: Non-Subject-Specific Protocol Deviations

[Implementation Note: In the "Deviation" column, concatenate any and all "specify" fields (including visit number, etc.). If "Reason for Deviation" is "Other," concatenate "specify" field, separate by a colon, e.g., "Other: Subject refusal." Sort order: Site, Start Date.]

Site	Start Date	Deviation	End Date	Reason for Deviation	Deviation Resulted in Subject Termination?	Deviation Affected Product Stability?	Deviation Category	Deviation Resolution	Comments

16.2.3 Subjects Excluded from the Efficacy Analysis

Listing 4: 16.2.3: Subjects Excluded from Analysis Populations

[Implementation Note: Sort order: Vaccination Group, Subject ID.]

Vaccination Group	Subject ID	Analyses in which Subject is Included	Analyses from which Subject is Excluded	Results Available?	Reason Subject Excluded
		[e.g., Safety, ITT, PP]	[e.g., Safety, ITT, PP, Day x]		

Note: "Yes" in the "Results available" column indicates that available data were removed from the analysis. "No" indicates that no data were available for inclusion in the analysis.

16.2.4 Demographic Data

Listing 5: 16.2.4.1: Demographic Data

[Implementation Note: If a subject is multi-racial, in "Race" column, note "Multiple: (list races, separated by a comma).] Sort order: Vaccination Group, Subject ID.]

Vaccination Group	Subject ID	Sex	Age at Enrollment (years)	Ethnicity	Race

Listing 6: 16.2.4.2: Pre-Existing and Concurrent Medical Conditions

[Implementation Note: "Condition Start Day" and "Condition End Day" are relative to enrollment (which is Day 1, day before enrollment is Day -1). Rather than use exact study days, categorize as follows: 5 years prior to enrollment, 1-5 years prior to enrollment, 1-12 months prior to enrollment, Within 1 month of enrollment, During study. If ongoing, display "Ongoing" in the "Condition End Day" column. Sort order: Vaccination Group, Subject ID, MH Number.]

Vaccination Group	Subject ID	MH Number	Medical History Term	Condition Start Day	Condition End Day	MedDRA System Organ Class	MedDRA Preferred Term

16.2.5 Compliance and/or Drug Concentration Data (if available)

Not Applicable.

16.2.6 Individual Efficacy/Immunogenicity Response Data

Listing 7: 16.2.6.1: Individual Efficacy/Immunogenicity Response Data, PRNT and PsVNA Assays

[Implementation Note: Sort order: Vaccination Group, Subject ID, Planned Time Point.]

Vaccination Group	Subject ID	Planned Time Point	Actual Study Day	PRNT Titer	PsVNA Titer

Listing 8: 16.2.6.2: Individual Efficacy/Immunogenicity Response Data, ICS and LPA Cellular Assays

[Implementation Note: Sort order: Vaccination Group, Subject ID, Planned Time Point.]

Vaccination Group	Subject ID	Planned Time Point	Actual Study Day	ANDVGP Pool	Cell Type	ICS Assay Percent Activated T-Cells Secreting:							Lympho-proliferation Assay
						IFNɣ	TNFα	IL-2	IFNɣ TNFα	IFNɣ IL-2	TNFα IL-2	IFNɣ TNFα IL-2	LPA
				PP1	CD4+								
					CD8+								
				PP2	CD4+								
					CD8+								

16.2.7 Adverse Events

Listing 9: 16.2.7.1: Solicited Events – Systemic Symptoms

[Implementation Note: Indicate severity for quantitative symptoms (e.g., temperature, measurements), by including the grade in parentheses after the number, e.g., 100.7 (Mild). Sort order: Vaccination Group, Subject ID, Dose Number, Post Dose Day, Symptom.]

Vaccination Group	Subject ID	Dose Number	Post Dose Day	Assessment[a]	Symptom	Severity	Attributed to Alternate Etiology?[b]	Alternate Etiology
				MA				
				Clinic				

[a] MA = Data reported by subject on the Memory Aid and reviewed by clinic staff and reported in Solicited Events eCRF.
Clinic = Data collected by clinic staff during physical exam or symptom assessment (treatment administration record, in-clinic assessment, etc.)
[b] Grade 3 events in all subjects, Grade 2 and 3 events in sentinel subjects.

Listing 10: 16.2.7.2: Solicited Events – Local Symptoms

[Implementation Note: Include local site measurements (ecchymosis, erythema, and induration measurements) and indicate grading by including the grade in parentheses after the number, e.g., 25 (Medium). Sort order: Vaccination Group, Subject ID, Dose Number, Post Dose Day, Arm, Symptom.]

Vaccination Group	Subject ID	Dose Number	Post Dose Day	Assessment[a]	Symptom	Severity (Left Arm)	Severity (Right Arm)
				MA			
				Clinic			

[a] MA = Data reported by subject on the Memory Aid and reviewed by clinic staff and reported in Solicited Events eCRF.
Clinic = Data collected by clinic staff during physical exam or symptom assessment (treatment administration record, in-clinic assessment, etc.)

Listing 11: 16.2.7.3: Unsolicited Adverse Events

[Implementation Note: If the event is ongoing (no stop date), indicate "ongoing" in the "Duration" column. In the "If Not Related, Alternate Etiology" column, merge the 2 data fields for collecting alternate etiology, separate by a colon. If there are no comments for an event, populate 'Comments' row with 'None'. Sort order: Vaccination Group, Subject ID, Associated with Dose No., No. of Days Post Associated Dose.]

Adverse Event	Associated with Dose No.	No. of Days Post Associated Dose (Duration)	Severity	SAE?	Relationship to Study Product	In Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Vaccination Group: , Subject ID: , AE Number:											
Comments:											
Vaccination Group: , Subject ID: , AE Number:											
Comments:											

Note: For additional details about SAEs, see Table: 91.

16.2.8 Individual Laboratory Measurements and Other Safety-Related Assessments

Listing 12: 16.2.8.1: Clinical Laboratory Results – Chemistry

[Implementation Note: Severity should be included in parentheses after the result for abnormal results, e.g., 16.2 (Mild).]

Vaccination Group	Subject ID	Planned Time Point	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Severity Grade)	Reference Range Low	Reference Range High

Listing 13: 16.2.8.2: Clinical Laboratory Results – Hematology

[Implementation Note: Severity should be included in parentheses after the result for abnormal results, e.g., 16.2 (Mild).]

Vaccination Group	Subject ID	Planned Time Point	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Severity Grade)	Reference Range Low	Reference Range High

Listing 14: 16.2.8.3: Vital Signs

[Implementation Note: Severity should be included in parentheses after the result for abnormal assessments, e.g., 100.7 (Mild).]

Vaccination Group	Subject ID	Planned Time Point	Actual Study Day	Temperature (°C)	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Heart Rate (beats/min)	Weight (kg)	Height (cm)

Listing 15: 16.2.8.4: Physical Exam Findings

[Implementation Note: This listing includes all physical exam findings, scheduled and unscheduled. If a subject does not have any findings upon examination, they will not be included in this listing. If reported as an AE, display "Yes" with the AE Number in parentheses, e.g., "Yes (7)"]

Vaccination Group	Subject ID	Planned Time Point	Actual Study Day	Body System	Abnormal Finding	Reported as an AE? (AE Description; Number)

Listing 16: 16.2.8.5: Concomitant Medications

[Implementation Note: "Medication Start Day" and "Medication End Day" are the number of days relative to enrollment (which is Day 1, day before enrollment is Day -1). Medications that stopped prior to enrollment will have negative numbers in these columns if study days is used. For medication start dates that are > 30 days prior to enrollment, rather than use exact study days, categorize as follows: 5 years prior to enrollment, 1-5 years prior to enrollment, 1-12 months prior to enrollment, If ongoing, display "Ongoing" in the "Medication End Day" column. If taken for an AE or MH, display "Yes" with the AE or MH Number in parentheses, e.g., "Yes (7)". Sort order: Vaccination Group, Subject ID, and CM Number.]

Vaccination Group	Subject ID	CM Number	Medication	Medication Start Day	Medication End Day	Indication	Taken for an AE? (AE Description; Number)	Taken for a condition on Medical History? (MH Description; Number)	ATC Level 1 (ATC Level 2)

Listing 17: 16.2.8.6: Pregnancy Reports – Maternal Information

[Implementation Note: Only include the "Pregnancy Number" column if a subject has more than 1 pregnancy. Date of Conception will be calculated based on estimated delivery date. BMI will be calculated based on pre-pregnancy height and weight. Mother's weight gain will be calculated based on pre-pregnancy weight and end of pregnancy weight. If a major congenital anomaly with previous pregnancy, display "Yes" and the text from the "specify" field, separated by a colon. If any substance use is reported, include a listing of substance use. If autopsy revealed an alternate etiology, display "Yes" and the text from the "specify" field, separated by a colon. If abnormality in product of conception, display "Yes" and the text from the "specify" field, separated by a colon. Sort order: Treatment Group, Subject ID, Pregnancy Number.]

Vaccination Group	Subject ID	Pregnancy Number	Study Day Corresponding to Estimated Date of Conception	Source of Maternal Information	Pregnancy Status	Mother's Pre-Pregnancy BMI	Mother's Weight Gain During Pregnancy	Tobacco, Alcohol, or Drug Use During Pregnancy?	Medications During Pregnancy?	Maternal Complications During Pregnancy?	Maternal Complications During Labor, Delivery, or Post-Partum?

Note: Maternal Complications are included in the Adverse Event listing. Medications taken during pregnancy are included in the Concomitant Medications Listing.

Listing 18: 16.2.8.7: Pregnancy Reports – Gravida and Para

			Live Births												
Subject ID	Pregnancy Number	Gravida	Extremely PB[a]	Very Early PB[a]	Early PB[a]	Late PB[a]	Early TB[b]	Full TB[b]	Late TB[b]	Post TB[b]	Still Births	Spontaneous Abortion/ Miscarriage	Elective Abortions	Therapeutic Abortions	Major Congenital Anomaly with Previous Pregnancy?

[a] Preterm Birth
[b] Term Birth
Note: Gravida includes the current pregnancy, para events do not.

Listing 19: 16.2.8.8: Pregnancy Reports – Live Birth Outcomes

Subject ID	Pregnancy Number	Fetus Number	Pregnancy Outcome (for this Fetus)	Fetal Distress During Labor and Delivery?	Delivery Method	Gestational Age at Live Birth	Size for Gestational Age	Apgar Score, 1 minute	Apgar Score, 5 minutes	Cord pH	Congenital Anomalies?	Illnesses/ Hospitalizations within 1 Month of Birth?

Note: Congenital Anomalies are included in the Adverse Event listing.

Listing 20: 16.2.8.9: Pregnancy Reports – Still Birth Outcomes

Subject ID	Date of Initial Report	Fetus Number	Pregnancy Outcome (for this Fetus)	Fetal Distress During Labor and Delivery?	Delivery Method	Gestational Age at Still Birth	Size for Gestational Age	Cord pH	Congenital Anomalies?	Autopsy Performed?	If Autopsy, Etiology for Still Birth Identified?

Listing 21: 16.2.8.10: Pregnancy Reports – Spontaneous, Elective, or Therapeutic Abortion Outcomes

Subject ID	Date of Initial Report	Fetus Number	Pregnancy Outcome (for this Fetus)	Gestational Age at Termination	Abnormality in Product of Conception?	Reason for Therapeutic Abortion

APPENDIX 4. INTERIM REPORT TABLES AND FIGURES

CSR Tables and Figures: Highlighted rows will be excluded from the Interim Report.

Tables	
Table 1	Study Design
Table 2	Schedule of Study Procedures
Table 3	Sample Size/Probability Estimates
Table 4	Distribution of Protocol Deviations by Category, Type, and Vaccination Group
Table 5	Local (Injection Site) Reactogenicity Grading
Table 6	Local (Injection Site) Reactogenicity Measurements
Table 7	Subjective Systemic Reactogenicity Grading
Table 8	Quantitative Systemic Reactogenicity Grading
Table 9	Blood Pressure and Pulse Grading
Table 10	Laboratory Adverse Event Grading Scale - Hematology
Table 11	Laboratory Adverse Event Grading Scale - Chemistry
Table 12	Subject Disposition by Vaccination Group
Table 13	Analysis Populations by Vaccination Group
Table 14	Dates of First Treatment by Vaccination Group
Table 15	Ineligibility Summary of Screen Failures
Table 16	Summary of Categorical Demographic and Baseline Characteristics by Vaccination Group
Table 17	Summary of Continuous Demographic and Baseline Characteristics by Vaccination Group
Table 18	Summary of Subjects with Pre-Existing Medical Conditions by MedDRA System Organ Class and Vaccination Group
Immunogenicity, ITT only (second table would be PPP)	
Table 19-20	Incidence of Plaque Reduction Neutralization Titer ≥20

APPENDIX 4: Interim Report Tables and Figures *(continued)*

Tables	
Table 21-22	Incidence of Pseudovirion Neutralization Titer ≥20
Table 23-24	Plaque Reduction Neutralization GMFR and Seroconversion
Table 25-26	Pseudovirion Neutralization GMFR and Seroconversion
Table 27-28	Plaque Reduction Neutralization Geometric Mean Titer (GMT)
Table 29-30	Pseudovirion Neutralization Geometric Mean Titer (GMT)
Table 31-32	Correlation Between Plaque Reduction Neutralization and Pseudovirion Neutralization Antibody Titers - Intent to Treat Population
Exploratory Immunogenicity, ITT only	
Table 33-34	ICS Incidence of >3 SD Increase in CD4+ T-Cells, ANDVGP PP1
Table 35-36	ICS Incidence of >3 SD Increase in CD4+ T-Cells, ANDVGP PP2
Table 37-38	ICS Incidence of >3 SD Increase in CD4+ T-Cells, ANDVGP
Table 39-40	ICS Incidence of >3 SD Increase in CD8+ T-Cells, ANDVGP PP1
Table 41-42	ICS Incidence of >3 SD Increase in CD8+ T-Cells, ANDVGP PP2
Table 43-44	ICS Incidence of >3 SD Increase in CD8+ T-Cells, ANDVGP
Table 45-46	LPA Incidence of >3 SD Increase in CD4+ and CD8+ T-Cells, ANDVGP PP1, PP2, Both

Tables - Safety			
Overall Summary of Adverse Events	Post-Any Dose	Table 47	By Group
Adverse Events Occurring in 5% of Subjects in Any Vaccination Group by MedDRA System Organ Class and Preferred Term, and Vaccination Group	Post-Any Dose	Table 48	By Group

APPENDIX 4: Interim Report Tables and Figures *(continued)*

Tables - Safety			
Number and Percentage of Subjects Experiencing **Solicited Events** with 95% Confidence Intervals by Symptom, Dose, and Vaccination Group	Post-Dose 1 Post-Dose 2 Post-Dose 3 Post-Dose 4 Post-Any Dose	Table 49 Table 50 Table 51 Table 52 Table 53	By Group
Number and Percentage of Subjects Experiencing **Solicited Events** by Symptom, **Maximum Severity**, Dose, and Vaccination Group	Post-Dose 1 Post-Dose 2 Post-Dose 3 Post-Dose 4 Post-Any Dose	Table 54 Table 55 Table 56 Table 57 Table 58	By Group
Number and Percentage of Subjects Experiencing **Solicited Events** by Symptom, **Maximum Severity**, Dose, and Vaccination Group	Post-Dose 1 Post-Dose 2 Post-Dose 3 Post-Dose 4 Post-Any Dose	Table 54 Table 55 Table 56 Table 57 Table 58	By Group
Number and Percentage of Subjects Experiencing **Solicited Events** by Symptom, Severity, and Day Post Dosing	Post-Dose 1	Table 59 Table 60 Table 61 Table 62	Cohorts 1 and 2 ANDV DNA 2mg Cohorts 3 and 4 ANDV DNA 4mg All Placebo All Subjects
	Post-Dose 2	Table 63 Table 64 Table 65 Table 66	Cohorts 1 and 2 ANDV DNA 2mg Cohorts 3 and 4 ANDV DNA 4mg All Placebo All Subjects
	Post-Dose 3	Table 67 Table 68 Table 69 Table 70	Cohort 2 ANDV DNA 2mg - Post Dose 3 Cohort 4 ANDV DNA 4mg - Post Dose 3 All Placebo All Subjects
	Post-Dose 4	Table 71 Table 72 Table 73 Table 74	Cohorts 1 and 2 ANDV DNA 2mg Cohorts 3 and 4 ANDV DNA 4mg All Placebo All Subjects

APPENDIX 4: Interim Report Tables and Figures *(continued)*

Tables - Safety			
	Post-Any Dose	Table 75 Table 76 Table 77 Table 78 Table 79 Table 80	Cohort 1 ANDV DNA 2mg (3 Doses) Cohort 2 ANDV DNA 2mg (4 Doses) Cohort 3 ANDV DNA 4mg (3 Doses) Cohort 4 ANDV DNA 4mg (4 Doses) All Placebo All Subjects
Frequency and Percent of Subjects with **Unsolicited** Adverse Events by MedDRA System Organ Class, Preferred Term, and Vaccination Group	Post-Dose 1 Post-Dose 2 Post-Dose 3 Post-Dose 4 Post-Any Dose	Table 81 Table 82 Table 83 Table 84 Table 85	By Group
Frequency of Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term and Vaccination Group	Post-Dose 1 + 2 Post-Dose 3 + 4	Table 86 Table 87	By Group
Frequency and Percent of Subjects with Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Relationship	Post-Dose 1 + 2	Table 88 Table 89 Table 90	Cohorts 1 and 2 (2 mg) Cohorts 3 and 4 (4 mg) All Placebo
	Post-Dose 3 + 4 and Any Time	Table 91 Table 92 Table 93 Table 94 Table 95	Cohort 1 2 mg (x3) Cohort 2 2 mg (x4) Cohort 3 4 mg (x3) Cohort 4 4 mg (x4) All Placebo
	By Dose and Overall	Table 96	All Subjects
Frequency and Percent of Subjects with Unsolicited Adverse Events Related to IP by MedDRA System Organ Class, Preferred Term, and Vaccination Group	Post-Dose 1 Post-Dose 2 Post-Dose 3 Post-Dose 4 Post-Any Dose	Table 97 Table 98 Table 99 Table 100 Table 101	By Group
Frequency of Unsolicited Adverse Events Related to IP by MedDRA System Organ Class and Preferred Term and Vaccination Group	Post-Dose 1 + 2 Post-Dose 3 + 4 and Any Time	Table 102 Table 103	By Group

APPENDIX 4: Interim Report Tables and Figures *(continued)*

Tables - Safety			
Listing of Serious Adverse Events	NA	Table 104	All events
Listing of Non-Serious, Unsolicited, Moderate or Severe Adverse Events	NA	Table 105	All events
Listing of Abnormal Laboratory Results - Chemistry	NA	Table 106	All events

Tables - Clinical Labs			
Chemistry			
Abnormal Laboratory Results by Maximum Severity, Time Point, and Vaccination Group	By visit	Table 108 Table 109 Table 110 Table 111 Table 112 Table 113 Table 114	Any Chemistry Parameter Alanine Aminotransferase Total Bilirubin Creatinine Sodium Potassium Blood Urea Nitrogen
Abnormal Laboratory Results Related to Study Treatment by Maximum Severity, Time Point, and Vaccination Group	By visit	Table 115 Table 116 Table 117 Table 118 Table 119 Table 120 Table 121	Any Chemistry Parameter Alanine Aminotransferase Total Bilirubin Creatinine Sodium Potassium Blood Urea Nitrogen
Laboratory Summary Statistics by Time Point and Vaccination Group	By visit	Table 122 Table 123 Table 124 Table 125 Table 126 Table 127	Alanine Aminotransferase Total Bilirubin Creatinine Sodium Potassium Blood Urea Nitrogen

APPENDIX 4: Interim Report Tables and Figures *(continued)*

Tables - Clinical Labs			
Hematology			
Abnormal Laboratory Results by Maximum Severity, Time Point, and Vaccination Group	By visit	Table 128 Table 129 Table 130 Table 131 Table 132	Any Hematology Parameter White Blood Cells Hemoglobin Platelet Count ANC
Abnormal Laboratory Results Related to Study Treatment by Maximum Severity, Time Point, and Vaccination Group	By visit	Table 133 Table 134 Table 135 Table 136 Table 137	Any Hematology Parameter White Blood Cells Hemoglobin Platelet Count ANC
Laboratory Summary Statistics by Time Point and Vaccination Group	By visit	Table 138 Table 139 Table 140 Table 141	White Blood Cells Hemoglobin Platelet Count ANC
Vital Signs			
Vital Signs by Maximum Severity, Time Point, and Vaccination Group	By Visit	Table 142 Table 143 Table 144 Table 145 Table 146	Maximum severity over all assessments Oral Temperature Pulse Systolic Blood Pressure Diastolic Blood Pressure
Concomitant Medications			
Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification and Vaccination Group	By ATC Level 1 and Level 2	Table 147	By Treatment Group

APPENDIX 4: Interim Report Tables and Figures *(continued)*

Figures		
Study Schema	Figure 1	
CONSORT Flow Diagram	Figure 2	
Immunology – ITT only		
Reverse Cumulative Distribution of **Plaque Reduction** Neutralization by Time Point and Vaccination Group	Figure 3-4	By Visit and Group
Reverse Cumulative Distribution of **Pseudovirion** Reduction Neutralization by Time Point and Vaccination Group	Figure 5-6	
Plaque Reduction Neutralization Titers Over Time Point and Vaccination Group	Figure 7-8	
Pseudovirion Neutralization Titers Over Time Point and Vaccination Group	Figure 9-10	
Incidence of **Plaque Reduction** Neutralization Titer ≥20 by Time Point and Vaccination Group	Figure 11-12	
Incidence of **Pseudovirion** Neutralization Titer ≥20 by Time Point and Vaccination Group	Figure 13-14	
Correlation Between Plaque Reduction Neutralization and Pseudovirion Neutralization by Time Point and Vaccination Group	Figure 15-16	

Exploratory Immunology Outcomes – ITT only:			
Intracellular Staining (ICS) Incidence of >3 Standard Deviation Increase in Percent of CD4+ and CD8+ Cells by ANDVGP Pool, Time Point, and Vaccination Group	Figure 17-18 Figure 19-20 Figure 21-22 Figure 23-24 Figure 25-26 Figure 27-28 Figure 29-30	Cells Secreting IFNɣ Cells Secreting TNFα Cells Secreting IL-2 Cells Secreting IFNɣ + TNFα Cells Secreting IFNɣ + IL-2 Cells Secreting TNFα + IL-2 Cells Secreting IFNɣ + TNFα + IL-2	By Visit and Group
Lymphoproliferation Assay (LPA) Incidence of >3 Standard Deviation Increase in Percent of CD4+ and CD8+ Cells by ANDVGP Pool, Time Point, and Vaccination Group	Figure 31-32	PP1, PP2 and Either Pool	

APPENDIX 4: Interim Report Tables and Figures *(continued)*

Safety Figures		
Maximum Severity of Solicited **Local Symptoms** per Subject by Day Post Treatment and Product Received	Figure 33 Figure 34 Figure 35 Figure 36 Figure 37	Post-Dose 1 Post-Dose 2 Post-Dose 3 Post-Dose 4 Post-Any Dose
Maximum Severity of Solicited **Systemic Symptoms** per Subject by Day Post Treatment and Product Received	Figure 38 Figure 39 Figure 40 Figure 41 Figure 42	Post-Dose 1 Post-Dose 2 Post-Dose 3 Post-Dose 4 Post-Any Dose
Frequency of **Related Adverse Events** by MedDRA System Organ Class, Severity, and Product Received	Figure 43 Figure 44 Figure 45 Figure 46 Figure 47	Post-Dose 1 Post-Dose 2 Post-Dose 3 Post-Dose 4 Post-Any Dose
Incidence of **Related Adverse Events** by MedDRA System Organ Class, Maximum Severity, and Product Received	Figure 48 Figure 49 Figure 50 Figure 51 Figure 52	Post-Dose 1 Post-Dose 2 Post-Dose 3 Post-Dose 4 Post-Any Dose
Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter and Vaccination Group	Figure 53 Figure 54 Figure 55 Figure 56 Figure 57 Figure 58 Figure 59 Figure 60 Figure 61	ALT Total Bilirubin Creatinine Sodium Potassium WBC Hemoglobin Platelets ANC