A prospective, natural history study to assess the occurrence of HPA-1a alloimmunization in women identified at higher risk for Fetal and Neonatal Alloimmune Thrombocytopenia (FNAIT)

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IPA2002

A prospective, natural history study to assess the occurrence of HPA-1a alloimmunization in women identified at higher risk for Fetal and Neonatal Alloimmune Thrombocytopenia (FNAIT)

Statistical Analysis Plan

Version: V6.0

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SPONSOR SIGNATURE PAGE

Approved by: [redacted]_____ _[redacted]_____
Date

VP, Head of Clinical Operations
Rallybio IPA, LLC

PAREXEL SIGNATURE PAGE

Signatures below confirm that the Statistical Analysis Plan was developed in accordance with SOP-GDO-WW-019 and that it is approved for release.

This document has been approved and signed electronically on the final page by the following:

	Signatory
Author	[redacted] Project Role: Biostatistics Lead

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REVISION HISTORY

Version No.	Effective Date	Summary of Change(s)
1.0	[09 Sep 2024]	Finalized version.
2.0	[06 Jan 2025]	Added additional analyses about the proportion of participants by region, by pregnancy history, or by race and ethnicity and then further broken down by pre-natal FNAIT laboratory testing results in the Baseline Screened Population
3.0	[27 Jan 2025]	Added additional analysis about proportion of participants by region, by self-characterized race and ethnicity, or by OMB classification of race and ethnicity in the Baseline Screened Population
4.0	[19 Jun 2025]	Added additional outputs by race (White vs. Others), an additional table about summary of prior pregnancies (with prior pregnancy vs no pregnancy) by region, race and ethnicity, and a comparison table about OMB classification of Race and Ethnicity between Baseline Screened Population and Alloimmunization Follow-up Population for publication purposes
5.0	[23 Jul 2025]	Added a summary table about the median number of prior pregnancies in Baseline Screened Population broken down by Region, OMB Race and Ethnicity, and added an additional analysis about proportion of participants by region by OMB race and ethnicity.
6.0	[08 Sep 2025]	Added zero-count categories and related CI in two analyses: 1) Comparison of OMB classification of race and ethnicity between Baseline Screened Population and Alloimmunization Follow-up Population; 2) Summary of race and ethnicity by OMB classification in Alloimmunization Follow-up Population.

LIST OF ABBREVIATIONS

Abbreviation / Acronym	Definition / Expansion
CI	Confidence Interval
CRF	Case Report Form
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
FNAIT	Fetal and Neonatal Alloimmune Thrombocytopenia
GPP	Good Pharmacoepidemiology Practice
HLA	Huma Leukocyte Antigens
HPA	Human Platelet Antigen
ICF	Informed Consent Form
ICH	International Council on Harmonisation
IEC	Independent Ethics Committee
IQR	Interquartile Range
IRB	Institutional Review Board
OMB	Office of Management and Budget
SD	Standard Deviation

1 INTRODUCTION

FNAIT is a rare and potentially life-threatening disorder that can cause uncontrolled bleeding in the fetus and neonate due to maternal alloantibody-mediated destruction of fetal/neonatal platelets. It is estimated to occur in approximately 1 in 1,000 pregnancies and can result in potentially severe consequences, including fetal and neonatal intracranial hemorrhage (ICH) that can cause death of the fetus or newborn or irreversible brain damage that results in lifelong neurologic disability [1-4]. ICH due to HPA-1a alloimmunization is estimated to occur in approximately 1 in 10,000 pregnancies, which translates to approximately 1,000 annual cases of ICH in Europe and North America [1].

Maternal alloimmunization to fetal platelet antigens is the necessary, prerequisite event leading to FNAIT. A fetal-maternal mismatch in HPA-1 is the most common cause of maternal alloimmunization, accounting for approximately 75% to 80% of FNAIT cases [5-7]. The HPA-1 alleles arise from a single nucleotide polymorphism that results in either a leucine (HPA-1a) or a proline (HPA-1b) at residue 33 of integrin β3 [8]. If a woman is negative for the HPA-1a antigen (HPA-1b/b homozygous), fetal platelets or cell fragments positive for the HPA-1a antigen and which enter the maternal circulation, can induce production of maternal HPA-1a alloantibodies. The maternal HPA-1a alloantibodies can then traverse the placenta and destroy the fetal platelets, resulting in FNAIT [9]. Furthermore, in women who are positive for the Human Leukocyte Antigen (HLA)-DRB3*01:01 allele, the risk to become HPA-1a alloimmunized is approximately 25 times higher than in women who do not carry this allele [10]. There are currently no available treatments for the prevention of HPA-1a alloimmunization in pregnant women at risk for the occurrence of FNAIT.

Substantial data inform a ~2% frequency of the HPA-1b/b (i.e., HPA-1a negative) genotype in pregnant women with a predominant northern European heritage [11]. In contrast, data reporting on the frequency of the HPA-1b/b genotype in non-Caucasian populations is limited, with reports showing a lower frequency in African populations and in Asians [12]. Data reporting on the frequency of a population reporting Hispanic ethnicity are sparse.

Key objectives of Study IPA2002 are to inform on the frequency of higher risk for maternal HPA-1a alloimmunization among pregnant women of different racial and ethnic characteristics presenting for pre-natal care and to assess for the new occurrence of HPA-1a alloimmunization in these women. It is planned that data from this study will provide a contemporary external control for a future single arm registration study of an anti-HPA-1a antibody therapeutic being developed for the prevention of FNAIT caused by maternal alloimmunization to HPA-1a.

Pregnant women at risk for HPA-1a alloimmunization will be those who are confirmed at Gestational Week 10-14 to be HPA1b/b (HPA-1a negative). This cohort of HPA-1b/b women will be enriched for higher risk of alloimmunization by establishing those who are also HLA-DRB3*01:01 positive. A baseline negative anti-HPA-1a antibody test in women who are HPA-1b/b and HLA-DRB3*0101 positive will establish the absence of existing HPA-1a alloantibodies and allow assessment of the occurrence of new alloimmunization at Week 10 postpartum (or 10 weeks from the date of the pregnancy-terminating event [ie, abortion (spontaneous/elective) or

stillbirth] for pregnancies that do not result in a live birth). For the women with a baseline negative anti-HPA-1a antibody, assessment of fetal HPA-1 status will inform on the presence of the HPA-1a positive antigenic stimulus for maternal alloimmunization (cell-free fetal DNA [cffDNA]).

This Statistical Analysis Plan (SAP) has been prepared to accompany the clinical protocol for Study IPA2002 version 3.0 (20 May 2022) and the Annotated eCRF version 3 (26 January 2024).

2 RESEARCH OBJECTIVES AND OUTCOME VARIABLES

Table 1 Research Objectives and Outcome Variables

Research Objectives	Outcome Variables
Primary	
To inform the frequency of women at higher risk for HPA-1a alloimmunization among pregnant women of different racial and ethnic characteristics who present for pre-natal care.	The number of participants that are determined to be at higher risk for HPA-1a alloimmunization compared to the total number of pregnant women assessed for higher risk for HPA-1a alloimmunization, with attention to self-characterized race and ethnicity.
Secondary	
To inform the frequency of HPA-1a alloimmunization postpartum among pregnant women identified to be at higher risk for HPA-1a alloimmunization.	Occurrence of anti-HPA-1a maternal alloimmunization at Week 10 postpartum. *
To inform the frequency of specific pregnancy outcomes among pregnant women identified to be at higher risk for HPA-1a alloimmunization.	• Rate of spontaneous abortion, defined as non-deliberate fetal death which occurs prior to 19 weeks of gestation. • Rate of elective abortion, defined as deliberate termination of pregnancy at any time in gestation. • Rate of stillbirth, defined as non-deliberate fetal death anytime in gestation on or after 19 weeks of gestation. • Rate of premature birth, defined as live birth prior to 37 completed weeks of gestation. • Rate of live births (>=37 completed weeks of gestation).

To inform the frequency, where data are available, of neonatal thrombocytopenia in infants born to women who have alloimmunized to HPA-1a*.	Occurrence of neonatal thrombocytopenia and severe neonatal thrombocytopenia

*For pregnancies that do not result in a live birth, the assessment of alloimmunization will be at 10 weeks from the date of the pregnancy-terminating event (ie, abortion [spontaneous/elective] or stillbirth).

3 STUDY DESIGN

3.1 Study Overview

This is a prospective, non-interventional, natural history study open to all pregnant women presenting at a Gestation Week 10 to 14 prenatal visit at the involved institutions. At this pre-natal visit, the participant will be invited to provide informed consent and blood samples will be collected for determining whether the woman is at higher risk for the occurrence of HPA-1a alloimmunization, as described in Table 2.

Table 2 Pre-Natal FNAIT Laboratory Testing at Gestation Week 10 to 14

Test No.	Test	Description		Result	Protocol Specific Action
1	Maternal HPA-1 genotype	Test will identify women who are HPA-1b/b, indicating risk for HPA-1a sensitization and occurrence of FNAIT	1a	HPA-1b/b (HPA-1a negative)	Perform Test 2
			1b	HPA-1a/b HPA-1a/a	None – no further testing
2	Maternal HLA-DRB3*01:01 genotype	Test will identify women who are HLA-DRB3*01:01 positive, indicating higher FNAIT risk	2a	HLA-DRB3*01:01 positive	Perform Test 3
			2b	HLA-DRB3*01:01 negative	None – no further testing
3	Maternal anti-HPA-1a antibody	Test will establish women who have no detectable anti-HPA-1a antibody	3a	Anti-HPA-1a antibody negative	Perform Test 4
			3b	Anti-HPA-1a antibody positive	None – no further testing
4	Fetal HPA-1 genotype	A cell-free fetal DNA (cffDNA) test to inform on the presence of the antigenic stimulus for maternal alloimmunization	4a	HPA-1a/b	Will be followed for final assessments
			4b	HPA-1b/b	None – no further testing

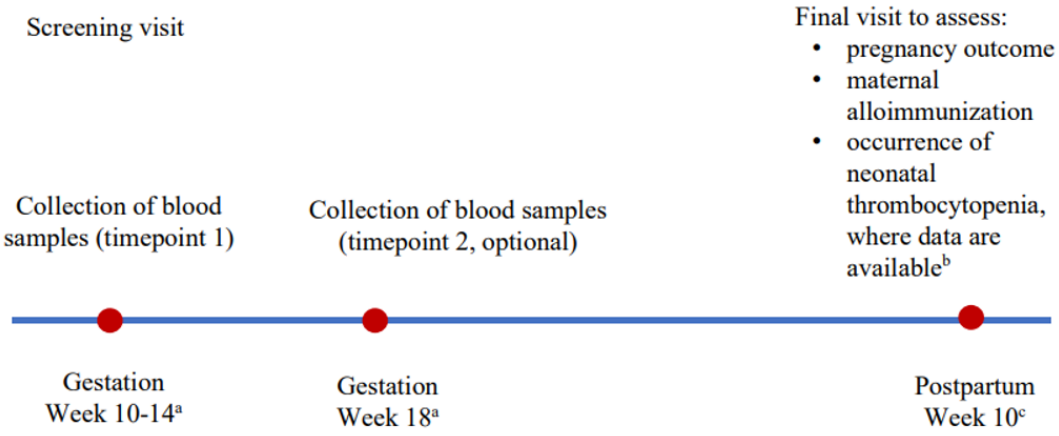
DNA = deoxynucleic acid; FNAIT = fetal and neonatal alloimmune thrombocytopenia; HLA = human leukocyte antigen; HPA = human platelet antigen

If the participant meets the study-specific blood test results, ie, genotype HPA-1b/b, genotype HLA-DRB3*01:01 positive, anti-HPA-1a antibody negative, and carries an HPA-1a positive fetus (Table 2, Test Results 1a, 2a, 3a, and 4a), a follow-up determination will be made at Week 10 postpartum on the occurrence of HPA-1a alloimmunization, pregnancy outcome and, for participants who have alloimmunized, the occurrence of neonatal thrombocytopenia (where data are available).

For participants, who meet the study specific tests results (ie, Test Results 1a, 2a, 3a, and 4a in Table 2) but the pregnancy does not result in a live birth, the assessment of alloimmunization will be at 10 weeks from the date of the pregnancy-terminating event (ie, abortion [spontaneous/elective] or stillbirth).

The study will be conducted across multiple sites in the United States and Europe.

Figure 1 Study schematic



[a] It is preferred that all samples be collected at the Gestation Week 10 to 14-visit. If all blood samples cannot be collected during one visit, the collection can be split into 2 timepoints. The first timepoint should include blood samples for maternal human platelet antigen (HPA)-1 genotype, maternal HLA-DRB3*01:01 genotype and the maternal anti-HPA-1a antibodies and must be collected at the Gestation Week 10 to 14-visit. The second timepoint should include blood samples for the fetal HPA-1 genotype and should be collected by 18 weeks of gestation.
For pregnant women who are HPA-1b/b genotype (ie, HPA-1a negative), HLA-DRB3*01:01 positive, and anti-HPA-1a antibody negative, a second blood sample at the next pre-natal visit will be requested to determine the fetal HPA-1 genotype.

[b] Neonatal thrombocytopenia to be sourced from the neonate's medical records.

[c] For pregnancies that do not result in a live birth, the assessment of alloimmunization will be at 10 weeks from the date of the pregnancy-terminating event (ie, abortion [spontaneous/elective] or stillbirth).

3.2 Populations for Analysis

Based on the results of the study specific screening tests to determine a participant's risk for HPA-1a alloimmunization and to meet the primary and secondary objectives of this protocol, two populations are defined for analysis:

- Baseline Screened Population
- Alloimmunization Follow-up Population

3.2.1 Baseline Screened Population

The Baseline Screened Population consists of all enrolled participants who meet Inclusion/Exclusion criteria (Inclusion Criteria: Pregnant women (≥ 18 years of age) who have provided informed consent for the study; Exclusion Criteria: Prior history of FNAIT), and who have complete final FNAIT screening tests results.

3.2.2 Alloimmunization Follow-up Population

The Alloimmunization Follow-up Population consists of all participants identified at screening to be at higher risk for HPA-1a alloimmunization (i.e., HPA-1b/b, HLA-DRB3*01:01 positive, anti-HPA-1a antibody negative, carrying an HPA-1a positive fetus), and who have a Week 10 postpartum HPA-1a alloimmunization test result.

4 DATA SOURCE

The primary data source for this study will be the raw data which is collected by Cisiv and FNAIT laboratory data from GCL Electronic Data Capture (EDC). Source documents provide evidence for the existence of the participants and substantiate the integrity of the data collected. Source documents are filed at the investigator's site.

Data reported on the case report form (CRF) or entered in the electronic CRF (eCRF) that are transcribed from source documents must be consistent with the source documents or any discrepancies must be explained. The investigator may need to request previous medical records or transfer records, depending on the study. Also, current medical records must be available. Definition of what constitutes source data can be found in the Source Data Agreement (eg, Site Trial Binder, other site communications).

5 STATISTICAL METHODS

5.1 Data Quality Assurance

All tables, figures, and listings to be included in the report will be independently checked for consistency, integrity and in accordance with standard Parexel procedures for analysis and reporting.

The data for the planned analysis will be quality controlled as per applicable Parexel standard operating procedures. The data extraction will be set to an appropriate date so that all data cleaning activities which include any corrections will have been already completed.

Where required, a process has been carefully implemented to onboard any useful SOPs originally designed to govern the delivery of primary/secondary data studies for regulatory submission to be used for natural history studies.

5.2 General Presentation Considerations

As this study is intended to be descriptive in nature, no hypotheses will be tested.

Continuous variables will be summarized using means and SD or medians and IQRs, as appropriate. Continuous data that is expected to be skewed will be presented in terms of the maximum, median, minimum and number of observations.

The SD will be reported to two more decimal places than the raw data recorded in the database. In general, the maximum number of decimal places reported shall be four for any summary statistic.

Discrete variables will be summarized using numbers and percentages. Categorical data will be summarized in terms of the number of participants providing data at the relevant time point (N), frequency counts and percentages.

Percentages will be presented to one decimal place. Percentages will not be presented for zero counts except two situations: 1) Comparison of OMB classification of race and ethnicity between Baseline Screened Population and Alloimmunization Follow-up Population; 2) Summary of race and ethnicity by OMB classification in Alloimmunization Follow-up Population. Percentages will be calculated using N as the denominator.

Confidence intervals will be presented to one more decimal place than the raw data. Confidence intervals for proportions will be calculated using the exact (Clopper-Pearson) method, unless stated otherwise.

All report outputs will be produced using SAS® version 9.4 or a later version in a secure and validated environment. All report outputs will be provided to the Sponsor in a single Microsoft Word document.

5.3 Statistical Methods and Analyses to be Performed

The proportion of FNAIT laboratory test subgroups among Baseline Screened Population or Alloimmunization Follow-up Population will be presented with their respective 80%, 90% and 95% confidence intervals.

5.3.1 Discussion of Analytical Approaches

The statistical analyses will be performed in accordance with Good Pharmacoepidemiology Practice (GPP) guideline / International Conference on Harmonisation (ICH) E9 guideline and will be based on the pooled data from the individual study sites, unless otherwise stated. The Statistical analysis will be performed by Parexel and reviewed by Rallybio.

5.3.2 Analysis of the Baseline Screened Population

The proportion of participants at higher risk for HPA-1a alloimmunization will be determined from the Baseline Screened Population and summarized descriptively.

The proportion will be calculated as (the number of participants determined at baseline to be at higher risk for HPA-1a alloimmunization) / (all enrolled participants who meet Inclusion/Exclusion criteria and who have complete final FNAIT screening tests results, as defined in Section 3.2.1). Listing for participants who are HPA-1b/b, HLA-DRB3*01:01 positive and HPA-1a alloantibody negative at baseline (Baseline Screened Population) and listing for Participants who are HPA-1b/b, HLA-DRB3*01:01 positive and HPA-1a alloantibody positive at baseline (Baseline Screened Population) are provided for publication purposes.

In addition to the above, maternal demographics, obstetric history and other baseline characteristics will be analyzed, including:

- Age at screening and BMI
- Obstetric History will be summarized by 1 or more prior pregnancies, 2 or more prior pregnancies, 3 or more prior pregnancies, and 4 or more prior pregnancies (including history of prior pregnancies with mode of delivery, pregnancy outcomes)
- Proportion of participants by region, by self-characterized classification of race and ethnicity or by race (White vs. Others), and by OMB classification of race and ethnicity
    - With attention to region (Europe vs. North America), first vs. second or later pregnancy, self-characterized classification of race and ethnicity or by race (White vs. Others), and OMB classification of race and ethnicity
    - With attention to region (Europe vs. North America) and then further broken down by OMB classification of race and ethnicity
- Proportion of participants who are HPA-1b/b
    - With attention to region (Europe vs. North America), first vs. second or later pregnancy, self-characterized classification of race and ethnicity or by race (White vs. Others), and OMB classification of race and ethnicity
- Proportion of participants who are HPA-1b/b and HLA-DRB3*0101 positive
    - With attention to region (Europe vs. North America), first vs. second or later pregnancy, self-characterized classification of race and ethnicity or by race (White vs. Others), and OMB classification of race and ethnicity
- Proportion of participants who are HPA-1b/b, HLA-DRB3*0101 positive and HPA-1a alloantibody negative

  - With attention to region (Europe vs. North America), first vs. second or later pregnancy, self-characterized classification of race and ethnicity or by race (White vs. Others), and OMB classification of race and ethnicity
- Proportions of participants who are HPA-1b/b, HLA-DRB3*0101 positive, HPA-1a alloantibody negative, and are bearing an HPA-1a antigen positive fetus
  - With attention to region (Europe vs. North America), first vs. second or later pregnancy, self-characterized classification of race and ethnicity or by race (White vs. Others), and OMB classification of race and ethnicity
- Proportion of participants who are HPA-1b/b, HLA-DRB3*0101 and HPA-1a alloantibody positive at baseline
  - With attention to region (Europe vs. North America), first vs. second or later pregnancy, self-characterized classification race and ethnicity or by race (White vs. Others), and OMB classification of race and ethnicity
- Proportion of participants by region by pre-natal FNAIT laboratory testing results
- Proportion of participants by pregnancy history by pre-natal FNAIT laboratory testing results
- Proportion of participants by self-characterized classification of race and ethnicity by pre-natal FNAIT laboratory testing results
- Proportion of participants by race (White vs. Others) by pre-natal FNAIT laboratory testing results
- Proportion of participants by OMB classification of race and ethnicity by pre-natal FNAIT laboratory testing results
- Summary of pregnancy history (with prior pregnancy vs no pregnancy) by region, race and ethnicity: a column about total number of participants in specific region, race, or ethnicity category in Baseline Screened Population needs to be included, and the proportion of those with prior pregnancy or no pregnancy is the number of specific region, race, or ethnicity participants with prior pregnancy or no pregnancy divided by the total number of specific region, race, or ethnicity participants
- Summary of prior pregnancies for participants who are HPA-1b/b and HLA-DRB3*01:01 positive and participants who are HPA-1b/b, HLA-DRB3*01:01 positive and HPA-1a alloantibody negative by region (Total included)
- Summary of the median number of prior pregnancies in Baseline Screened Population broken down by Region, OMB race and ethnicity

5.3.3 Analysis of the Alloimmunization Follow-up Population

5.3.3.1 Baseline characteristics

Baseline characteristics include age at screening, BMI, self-characterized classification of race and ethnicity or by race (White vs. Others), OMB classification of race and ethnicity, estimated gestational age, and obstetric history (including history of prior pregnancies with mode of delivery, gestational age of delivery, pregnancy outcome).

5.3.3.2 Occurrence of anti-HPA-1a maternal alloimmunization at Week 10 postpartum

The proportion of participants who HPA-1a alloimmunize among the Alloimmunization Follow-up Population will be summarized descriptively.

The proportion will be calculated as (the number of participants with HPA-1a alloimmunization postpartum) / (the total number of pregnant women identified to be at higher risk for HPA-1a alloimmunization, and who have a Week 10 postpartum HPA-1a alloimmunization test result) and with attention to region (Europe vs. North America), first vs. second or later pregnancy, -self-characterized classification of race and ethnicity or by race (White vs. Others), and OMB classification of race and ethnicity.

A comparison table for the summary of OMB classification of Race and Ethnicity between Baseline Screened Population and Alloimmunization Follow-up Population is needed for publication purposes.

A listing of all participants in the Alloimmunization follow up population will be provided, sorted by those with a positive alloimmunization and those with a negative alloimmunization at week 10 postpartum. In addition, a listing with the same data elements will be provided for those participants at higher risk for HPA-1a alloimmunization for whom a 10 week follow up alloimmunization determination is missing.

Data elements for both listings will include Participant ID, Country, maternal age at screening, race (self-characterized), ethnicity, BMI, pregnancy outcome (live births, premature births, stillbirths, spontaneous abortions, elective abortions), reason for termination for pregnancy, gestational age at birth, obstetric history, any interventions for FNAIT during the pregnancy (e.g. IVIG, or interventions other than IVIG), 10-week postpartum HPA-1a alloimmunization status, neonatal platelet count (where available), and additional neonate outcome.

For the separate listing of those who did not have 10 weeks alloimmunization determination, data elements will be the same with the addition of the reason for no determination will be listed as well (e.g. lost to follow-up, withdrew consent) and “unknown” or column deleted for week 10 postpartum HPA-1a alloimmunization status.

5.3.3.3 Pregnancy outcomes

Pregnancy outcomes include the rate of spontaneous abortion, elective abortion, stillbirth, premature birth, and live births among pregnant women identified to be at higher risk for HPA-1a alloimmunization and who have a Week 10 postpartum HPA-1a alloimmunization test result (Alloimmunization Follow-up Population). Pregnancy outcomes will be further broken down by HPA-1a alloimmunization status at Week 10 postpartum (alloimmunized/not alloimmunized) and with attention to region (Europe vs. North America), first vs. second or later pregnancy, and self-characterized classification of race and ethnicity or by race (White vs. Others), and OMB classification of race and ethnicity. Additional listing about pregnancy outcomes for Alloimmunization Follow-up Population will be provided, and the data elements will include pregnancy outcome, HPA-1a alloimmunization status at Week 10 postpartum, race and ethnicity.

5.3.3.4 Occurrence of Neonatal thrombocytopenia and severe neonatal thrombocytopenia

Outcome of non-severe or severe neonatal thrombocytopenia will be calculated as (type of thrombocytopenia) / (number of neonates for whom a platelet count was available), with attention to Week 10 postpartum alloimmunization status (i.e., alloimmunized vs. not alloimmunized).

Based on the anticipated small numbers of neonates with thrombocytopenia in this study, there will be no further sub-analyses of the data beyond maternal Week 10 postpartum alloimmunization status.

For each neonate with non-severe or severe thrombocytopenia, there will be a listing with the following data elements: Participant ID, region, race, ethnicity, maternal obstetric history, gestational age at birth, and Week 10 postpartum HPA-1a alloimmunization status, and any FNAIT-related interventions during the pregnancy.

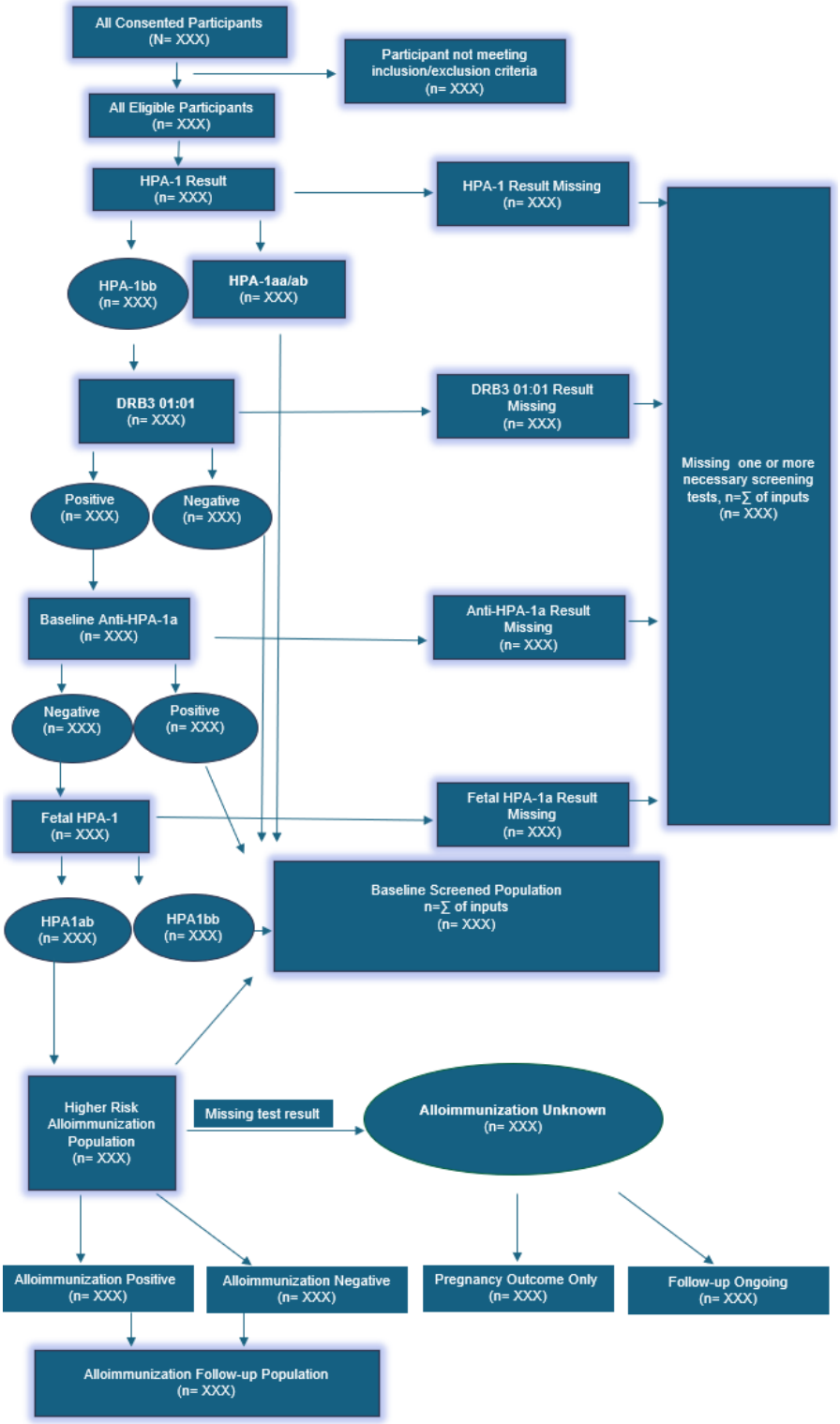
5.3.4 Sensitivity Analyses

No formal sensitivity analysis will be performed.

5.4 Study Participants

The alloimmunization study populations are characterized in the flowchart (Figure 2). Consented participants are those that have provided informed consent for the study. Eligible participants are those that meet protocol inclusion and exclusion criteria.

Figure 2 Flowchart of Participant Disposition



A clear accounting of the disposition of all participants who enter the study will be provided, from initial consent to study completion. This will include the numbers of the following groups:

- Number of participants consented
- Number of eligible participants
- Number of participants confirmed HPA-1b/b (vs. HPA-1aa or HPA-1a/b)
- Number of HPA-1b/b participants confirmed HLA-DRB3*01:01 positive (vs. negative)
- Number of HPA-1b/b and HLA-DRB3*01:01 positive participants who are HPA-1a alloantibody negative (vs. positive)
- Number of HPA-1b/b and HLA-DRB3*01:01 positive participants who are HPA-1a alloantibody negative and who have an HPA-1a positive fetus (vs. HPA-1b/b fetus)
- Number of HPA-1b/b and HLA-DRB3*01:01 positive participants who are HPA-1a alloantibody negative and have an HPA-1a positive fetus and who are assessed for presence of HPA-1a alloantibodies at 10 weeks postpartum
- Number of participants missing expected FNAIT Laboratory results as described by the testing sequence and their prior test result(s)

5.5 Obstetric History

Obstetric history will be presented in a descriptive manner including mode of delivery, gestational age of delivery, live birth, and abortion.

5.6 Handling of Missing and Uninterpretable Data

5.6.1 Analysis Visit Windows

No analysis visit window will be applied to the analysis. The participants whose blood sample is collected before gestation Week 10 or after gestation Week 18 will also be included in the analysis, but the participants whose blood sample is collected before 8 weeks postpartum need to be excluded from the analysis for postpartum anti-HPA-1a, in order to avoid false negatives.

5.6.2 Missing Data Imputation

Based on the nature of the study (prospective, non-interventional, natural history), missing data will not be replaced in the statistical analysis of primary and secondary endpoints.

If there is a significant number of missing values for a participant (or if there is confirmed data appearing spurious), a decision will be made following consultation with the sponsor regarding the handling of these data in summaries, prior to DB lock.

5.7 Ongoing Analyses

Analyses will be conducted quarterly during the ongoing conduct of the study and for each, the laboratory data with Cisiv data will be merged. Rerun of SDTM and ADaM datasets will also be included.

5.8 Determination of Sample Size

It is anticipated that approximately 20,000 to 30,000 participants will be enrolled with the goal of identifying approximately 30 to 50 pregnant women at higher risk for HPA-1a alloimmunization. Of the women identified to be at higher risk for HPA-1a alloimmunization, it is anticipated that approximately 10 to 20 may alloimmunize to HPA-1a.

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