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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To inform the frequency of women at higher FNAIT risk among pregnant women of different racial and ethnic characteristics who present for pre-natal care and to assess the occurrence of HPA-1a alloimmunization in these women. It is planned that data...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Platelet disorders
Study type	Observational invasive

Summary

ID

NL-OMON54467

Source
ToetsingOnline

Brief title
FNAIT Natural History Study

Condition

- Platelet disorders
- Neonatal and perinatal conditions

Synonym
Blood platelet shortage, NAIT

Research involving
Human

Sponsors and support

Primary sponsor: Rallybio
Source(s) of monetary or material Support: door Rallybio

Intervention

Keyword: fetal and neonatal alloimmune thrombocytopenia, fHPA-1a alloimmunization, FNAIT, Phase 0 natural history study

Outcome measures

Primary outcome

Primary objective:

To inform the frequency of women at higher FNAIT risk among pregnant women of different racial and ethnic characteristics who present for pre-natal care.

Primary outcome:

The number of participants that are determined to be at higher FNAIT risk compared to the total number of pregnant women assessed for higher FNAIT risk, with attention to self-characterized race and ethnicity.

Secondary outcome

Secondary objectives:

* To inform the frequency of human platelet antigen (HPA)-1a alloimmunization

among pregnant women identified at higher FNAIT risk.

* To inform the frequency of pregnancy outcomes among pregnant women identified at higher FNAIT risk

* To inform the frequency, where data are available, of neonatal thrombocytopenia in infants born to women who have alloimmunized, as determined by detectable anti-HPA-1a antibody at Week 10 postpartum

Secondary outcomes:

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

* 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 still birth, defined as non-deliberate fetal death anytime in gestation on or after 19 weeks of gestation

• Rate of premature delivery, defined as live birth prior to 37 completed weeks of gestation

• Rate of live births (>= 37 completed weeks of gestation)

* Neonatal thrombocytopenia, as determined by a platelet count < 50 × 109/L within 72 hours of birth, where data are available

Study description

Background summary

Of the approximately 2% of Caucasian pregnant women who are HPA-1a negative (ie, HPA-1b/b), approximately 85% will be carrying an HPA-1a positive fetus. Overall, approximately 10% of these pregnant women will become alloimmunized and among the fetuses or neonates of lloimmunized women, about 10% will have severe thrombocytopenia (50 x 109/L; < 50,000 platelets/mL)), many with bleeding sequelae; about 1% of the incompatible fetuses or neonates will suffer intracranial hemorrhage. Among the women who become alloimmunized, 90%-98% will come from among the approximately 27% who are HLA-DRB3*01:01 positive, meaning that those women with this HLA allele face an alloimmunization risk of approximately 25%-30%, vs 1% to 2% for those without the allele. Human platelet antigen genotype frequencies vary by race, and an alloimmune response to HPA-1a, the immunodominant platelet antigen in Caucasians (~75% to 80% of cases), is implicated in the majority of FNAIT cases (ie, in HPA-1bb homozygous pregnant women exposed to fetal platelets expressing HPA-1a derived from a HPA-1a positive father). 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. Data reporting on the frequency of a population reporting Hispanic ethnicity are sparse. Data from this study will inform the frequency of women at higher FNAIT risk among pregnant women of different racial and ethnic characteristics obtaining pre-natal care at the involved institutions and consenting for the study and will assess the occurrence of HPA-1a alloimmunization in these women. It is planned that data from this study be used as an external control for a future single arm registration study of an anti-HPA-1a antibody therapeutic for the prevention of FNAIT.

Study objective

To inform the frequency of women at higher FNAIT risk among pregnant women of different racial and ethnic characteristics who present for pre-natal care and to assess the occurrence of HPA-1a alloimmunization in these women. It is planned that data from this study be used as an external control for a future single arm registration study of an anti-HPA-1a antibody therapeutic for the prevention of FNAIT.

Study design

This is a prospective, non-interventional, natural history study into FNAIT.

Study burden and risks

This is a low-risk study: in the vast majority of cases, an extra tube of blood will be taken from women during a regular venipuncture. In a (very) small number of cases, there will be an increased risk of FNAIT and an extra tube of

blood will be taken as part of a study. Being aware of an increased risk of FNAIT can be a psychological burden.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Inclusion criteria

Pregnant women (>= 18 years of age) who have provided informed consent for the study.

Exclusion criteria

Prior history of FNAIT

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-09-2022
Enrollment:	2000
Type:	Actual

Ethics review

Approved WMO

Date:	25-03-2022
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	17-11-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	05-06-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	19-02-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL78636.058.21