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A study of nipocalimab or intravenous immunoglobulin in pregnancies at risk of fetal and neonatal alloimmune thrombocytopaenia

Submission date
20/06/2024

Recruitment status
Recruiting

Registration date
13/09/2024

Overall study status
Ongoing

Last Edited
02/07/2025

Condition category
Haematological Disorders

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aim
Fetal Neonatal Alloimmune Thrombocytopenia (FNAIT) is a condition where a baby (in the womb or just after birth) has low platelets. This occurs because the mother's immune system develops antibodies (proteins) that attack the baby's platelets, which may lead to bleeding in the baby. There is no approved treatment available for FNAIT. The study drug, nipocalimab, is a monoclonal antibody* that binds to a protein called neonatal fragment crystallisable receptor and blocks the binding of immunoglobulin G (IgG) antibodies. This leads to a decrease in levels of antibodies that attack the baby's platelets. Intravenous immunoglobulin (IVIG), while not approved by health authorities for use in FNAIT, is
considered the standard of care treatment for FNAIT patients in many countries. In this study, researchers want to learn how well the study treatment works in reducing the risk of FNAIT that can lead to death, bleeding or low platelet count in babies.
*Protein designed to bind to a specific target.

Who can participate?
Pregnant individuals aged 18 to 45 years with a prior pregnancy affected by FNAIT.

What does the study involve?
The study consists of four periods:
1. Screening period (Up to 11 weeks): Participants will be screened from pregnancy Week 8 to 18.
2. Open-label treatment period (29 weeks): Participants will be randomly (by chance) assigned to one of the two arms on a weekly basis for every 7 days ± 1 day until delivery:
Arm 1: Nipocalimab infusion weekly until delivery.
Arm 2: Intravenous immunoglobulin infusion weekly until delivery
3. Follow-up period for maternal participants (delivery until Week 24 after delivery): Mothers will be followed up to monitor their health.
4. Follow-up period for newborns (birth until Week 104): Newborns will be followed up to monitor their health.

Participants will undergo study assessments including blood tests, vital signs, physical examination and fetal and cranial ultrasound imaging. Side effects will be recorded until the study ends for a participant and their baby (2 years and 7 months).

What are the possible benefits and risks of participating?
There is no established benefit to participants of this study. Based on scientific theory, taking nipocalimab may reduce the risk of FNAIT. However, this cannot be guaranteed because nipocalimab is still under investigation as a treatment and it is not known whether nipocalimab will work. If participants are assigned to treatment group 2, they will receive intravenous immunoglobulin (IVIG) with or without prednisone during this study. Participants may experience some benefit from participation in the study such as frequent visits and assessments, as well as monitoring of overall health. Participation may help other people with FNAIT in the future. Participants may have side effects from the drugs used in this study that may be mild to severe and even life-threatening, and they can vary from person to person.
Potential risks of nipocalimab treatment in maternal/fetal participants are: infection due to decreased serum Immunoglobulin G (IgG) concentrations, reduced vaccine effectiveness, latent virus activation due to decreased IgG, low albumin level, infusion reaction (including serious exaggerated response from the immune system (hypersensitivity reactions), increased lipids, localized area of dead tissue in the placenta due to lack of blood supply. Potential risks to neonates/infants due to pregnant individuals receiving nipocalimab treatment could include low IgG in neonates/infants. The potential risks of IVIG with prednisone treatment are unusually high levels of certain liver enzymes, formation of blood clots in the veins located deep inside the body, and inflammation in veins. The participant information sheet and informed consent form, which will be signed by every participant agreeing to participate in the study, includes a detailed section outlining the known risks of participating in the study. Not all possible side effects and risks related to nipocalimab are known at this moment. During the study, the sponsor may learn new information about nipocalimab. The study doctor will tell participants as soon as possible about any new information that might make them change their mind about being in the study, such as new risks.
To minimise the risk associated with taking part in the study, participants are frequently reviewed for any side effects and other medical events. Participants are educated to report any such events to their study doctor who will provide appropriate medical care. Any serious side effects that are reported to the sponsor are thoroughly reviewed by a specialist drug safety team. There are no costs to participants to be in the study. The sponsor will pay for nipocalimab, IVIG and prednisone, and tests that are part of the study. The participant will receive reasonable reimbursement for study-related costs (e.g., travel/parking costs).

Where is the study run from?
Janssen-Cilag International N.V. (Netherlands)

When is the study starting and how long is it expected to run for?
June 2024 to December 2029

Who is funding the study?
Janssen-Cilag International N.V. (Netherlands)

Who is the main contact?
medinfo@its.jnj.com

Contact information

Type(s)
Scientific

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Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
2023-509434-19-00

Integrated Research Application System (IRAS)
1010250

ClinicalTrials.gov (NCT)
NCT06533098

Protocol serial number
80202135FNAIT3003, CPMS 62590

Study information

Scientific Title
Multicentre, open-label, randomised study of nipocalimab or IVIG in pregnancies at risk of fetal and neonatal alloimmune thrombocytopaenia (FREESIA-3)

Acronym
FREESIA-3

Study objectives
Primary objectives:
To assess how well the study treatments work (efficacy) in reducing the risk of fetal and neonatal alloimmune thrombocytopaenia (FNAIT).

Secondary objectives:
1. To assess how well the study treatments work (efficacy) in reducing the risk of low platelet count (thrombocytopaenia) related to FNAIT at birth. Platelets are blood cells that help blood to clot and prevent bleeding.
2. To assess how well the study treatments work (efficacy) in reducing the risk of additional FNAIT-related outcomes (bruising, bleeding, intracranial haemorrhage [any bleeding in the brain and surrounding tissues], death).
3. To assess the safety of study treatments in pregnant individuals and babies.

Added 06/06/2025:
4. To assess the immune responses against the drug (immunogenicity) in pregnant individuals who receive nipocalimab treatment.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 23/08/2024, West of Scotland REC 1 West of Scotland Research Ethics Service (Ground Floor, Ward 11, Dykebar Hospital, Grahamston Road , Paisley , PA2 7DE, United Kingdom; +44 (0) 141 314 0212; WoSREC1@ggc.scot.nhs.uk), ref: 24/WS/0087

Study design
Open randomized controlled parallel-group trial

Primary study design
Interventional

Study type(s)
Treatment, Safety, Efficacy

Health condition(s) or problem(s) studied
Fetal and Neonatal Alloimmune Thrombocytopenia (FNAIT)

Interventions
Current interventions as of 02/07/2025:
1. Screening period (Up to 11 weeks): Participants will be screened from pregnancy Week 8 to 18.
2. Open-label treatment period (29 weeks): Participants will be randomly (by chance) assigned via IWRS to one of two treatment arms on a weekly basis for every 7 days ± 1 day until delivery:
Arm 1: Nipocalimab infusion weekly until delivery.
Arm 2: Intravenous immunoglobulin infusion weekly until delivery
3. Follow-up period for maternal participants (delivery until Week 24 after delivery): Mothers will be followed up to monitor their health.
4. Follow-up period for newborns (birth until Week 104): Newborns will be followed up to monitor their health.

Previous interventions:
The study consists of four periods:
1. Screening period (8 or fewer weeks): Participants will be screened from pregnancy Week 8 to 15.
2. Open-label treatment period (about 29 weeks): Participants will be randomly (by chance) assigned via IWRS to one of the two treatment arms:
Arm 1: Nipocalimab infusion weekly until delivery.
Arm 2: Intravenous immunoglobulin infusion weekly until delivery
3. Follow-up period for maternal participants (delivery until Week 24 after delivery): Mothers will be followed up to monitor their health.
4. Follow-up period for newborns (birth until Week 104): Newborns will be followed up to monitor their health.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Nipocalimab, intravenous immunoglobulin (Privigen), prednisone (prednison acis)

Primary outcome(s)
Fetus/neonate with the outcome of death or adjudicated severe bleeding or platelet count less than 30 x 10(9) per litre up to 1 week post-birth

Key secondary outcome(s))
1. Platelet count in a neonate at birth
2. Fetus/neonate with outcome of death up to 1 week post-birth
3. Neonate with platelet count less than 10 x 10(9)/L at birth
4. Neonate with platelet count less than 30 x 10(9)/L at birth
5. Neonate with platelet count less than 50 x 10(9)/L at birth
6. Neonate with platelet count less than 150 x 10(9)/L at birth
7. Nadir platelet count of a neonate up to 1 week post-birth
8. Number of neonates requiring platelet transfusion up to 1 week post-birth
9. Number of platelet transfusions per neonate up to 1 week post-birth
10. Number of donor exposures for a neonate who received at least one platelet transfusion up to 1 week post-birth
11. Number of neonates/fetuses with adjudicated bleeding up to 1 week post-birth
12. Number of neonates requiring postnatal IVIG for the treatment of thrombocytopenia up to 1 week post-birth
13. Number of neonates/infants with the treatment-emergent adverse event of infection from the day of birth to Week 104
An adverse event is any untoward medical occurrence in a participant participating in a clinical study that does not necessarily have a causal relationship with the intervention under study. Treatment-emergent adverse events are defined as adverse events with onset or worsening on or after the date of the first dose of study treatment.

Added 06/06/2025:
14. Maternal participants with TEAE, SAE and AESI will be reported. An Adverse event (AE) is any

untoward medical occurrence in a participant participating in a clinical study that does not necessarily have a causal relationship with the
intervention under study up to Week 24
15. Maternal participants with TEAE leading to discontinuation of study intervention will be reported up to Week 24
16. Neonate/infants with TEAE, SAE and AESI will be reported. An AE is any untoward medical occurrence in a participant participating in a clinical study that does not necessarily have a causal relationship with the intervention under study from Day of Birth to week 104
17. Fetus/neonates with a TEAE of bleeding will be reported from Day of Birth to Week 104
18. Neonates with a TEAE of infection will be reported from Day of Birth to Week 104
19. The Bayley Scales of infant development are considered the standard assessment of early child development and includes cognition, language, motor skills, social emotional, and adaptive behavior will be reported. The Bayley Scales (3rd edition) are reference standards that measure infant and toddler development in five areas: cognition, language, motor skills, social-emotional and adaptive behavior. The cognition, language and motor skills scales are directly administered to the infant, while social-emotional, and adaptive behavior scales are caregiver questionnaires. The scores are standardized using norm reference samples with representative demographics and age adjusted for prematurity. Higher scores in the Bayley Scales indicate better outcomes. Measured At Week 52 and Week 104
20. Incidence of antibodies to nipocalimab including neutralizing antibodies in maternal serum during pregnancy and postpartum will be reported up to Week 4

Completion date
05/12/2029

Eligibility

Key inclusion criteria
Current inclusion criteria as of 02/07/2025:

1. Female 18 to 45 years of age.
2. Pregnant and at an estimated gestational age of 13 to 18 weeks at the point of randomisation.
3. Has a history of one or more prior pregnancy with FNAIT based on medical records including:
3.1. Neonatal platelet count less than 150 × 10(9) per litre with no fetal/neonatal intracranial haemorrhage (ICH) or severe fetal/neonatal haemorrhage (standard-risk) OR
3.2. Fetus/neonate with ICH or severe haemorrhage in a fetus/neonate based on medical records (high-risk)
4. Current pregnancy with presence of maternal anti-HPA-1a and/or anti-HPA-5b alloantibody and positive fetal HPA-1a and/or anti-HPA-5b genotype as confirmed by cell-free fetal DNA in maternal blood.
5. Health status considered stable by the investigator based on physical examination, medical history, vital signs, 12-lead electrocardiogram ECG, and clinical laboratory tests performed at screening.
6. For maternal participant and neonate/infant, willing to forego participation in another clinical study of an investigational therapy until the last follow-up visit

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Previous inclusion criteria as of 12/11/2024:

1. Female 18 years or older
2. Pregnant and at an estimated gestational age of 13 to 16 weeks at the point of randomisation
3. Has a history of one or more prior pregnancy with FNAIT based on medical records including:
3.1. Neonatal platelet count less than 150 × 10(9) per litre with no fetal/neonatal intracranial haemorrhage (ICH) or severe fetal/neonatal haemorrhage (standard-risk) OR
3.2. Fetus/neonate with ICH or severe haemorrhage in a fetus/neonate based on medical records (high-risk)
4. Current pregnancy with presence of maternal anti-HPA-1a and/or anti-HPA-5b alloantibody and positive fetal HPA-1a and/or anti-HPA-5b genotype as confirmed by cell-free fetal DNA in maternal blood.
5. Health status considered stable by the investigator based on physical examination, medical history, vital signs, 12-lead electrocardiogram ECG, and clinical laboratory tests performed at screening.
6. For maternal participant and neonate/infant, willing to forego participation in another clinical study of an investigational therapy until the last follow-up visit

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Previous inclusion criteria:

1. Female 18 years or older
2. Pregnant and at an estimated gestational age of 13 to 16 weeks at the point of randomisation
3. Has a history of one or more prior pregnancy with FNAIT based on medical records including:
3.1. Neonatal platelet count less than 150 × 10(9) per litre with no fetal/neonatal intracranial haemorrhage (ICH) (standard-risk) OR
3.2. Fetus/neonate with ICH or severe haemorrhage in a fetus/neonate based on medical records (high-risk)
4. Current pregnancy with presence of maternal anti-HPA-1a and/or anti-HPA-5b alloantibody and positive fetal HPA-1a and/or anti-HPA-5b genotype as confirmed by cell-free fetal DNA in maternal blood.
5. Health status considered stable by the investigator based on physical examination, medical history, vital signs, 12-lead electrocardiogram ECG, and clinical laboratory tests performed at screening.
6. For maternal participant and neonate/infant, willing to forego participation in another clinical study of an investigational therapy until the last follow-up visit

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
45 years

Sex
Female

Key exclusion criteria
1. Currently pregnant with multiple gestations (twins or more)
2. History of severe pre-eclampsia in a previous pregnancy
3. History of myocardial infarction, unstable ischemic heart disease or stroke
4. Known allergies, hypersensitivity or intolerance to nipocalimab or its excipients or to IVIG or its excipients
5. Has any confirmed or suspected clinical immunodeficiency syndrome or has a family history of congenital or hereditary immunodeficiency unless confirmed absent in the participant

Date of first enrolment
31/10/2024

Date of final enrolment
11/05/2027

Locations

Countries of recruitment
United Kingdom

England

Austria

Germany

Netherlands

Poland

United States of America

Study participating centre
Birmingham Women's Hospital
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Study participating centre
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Study participating centre
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W12 0HS

Study participating centre
John Radcliffe Hospital
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OX3 9DU

Sponsor information

Organisation
Janssen-Cilag International NV

Funder(s)

Funder type
Industry

Funder Name
Janssen Research and Development

Alternative Name(s)
Janssen R&D, Janssen Research & Development, Janssen Research & Development, LLC, Janssen Research & Development LLC, Janssen Pharmaceutical Companies of Johnson & Johnson, Research & Development at Janssen, JRD, J&J PRD

Funding Body Type
Private sector organisation

Funding Body Subtype

For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
Current IPD sharing plan as of 06/06/2025:
The data sharing policy of Johnson & Johnson Innovative Medicine is available at https://innovativemedicine.jnj.com/our-innovation/clinical-trials/transparency. As noted on this site, requests for access to the study data can be submitted through the Yale Open Data Access (YODA) Project site at yoda.yale.edu

Previous IPD sharing plan:
The data sharing policy of the Janssen Pharmaceutical Companies of Johnson & Johnson is available at https://www.janssen.com/clinicaltrials/ transparency. As noted on this site, requests for access to the study data can be submitted through the Yale Open Data Access (YODA) Project site at yoda.yale.edu

IPD sharing plan summary
Available on request