Tidsskriftet Tidsskrift for Den norske legeforening

New treatment for alloimmunisation in pregnancy

FROM THE SPECIALTIES

CATHRINE EBBING

cathrine.ebbing@helse-bergen.no
Cathrine Ebbing, specialist in obstetrics and gynaecology, senior consultant at the Section for Fetal Medicine and Ultrasound, Department of Obstetrics and Gynaecology, Haukeland University Hospital, and professor at the Department of Clinical Science, University of Bergen.
The author has completed the ICMJE form and declares the following conflicts of interest: She is a research assistant and principal investigator at a fetal medicine centre involved in the nipocalimab clinical trial. She has also attended a training meeting for researchers in the FREESIA-1 study discussed in the article. Travel and accommodation expenses were covered by the commissioning party, Janssen.

KJELL ÅSMUND BLIX SALVESEN

Kjell Åsmund Blix Salvesen, specialist in obstetrics and gynaecology, department head at the National Centre for Fetal Medicine in the Centre for Women, Family and Children's Health, St Olav's Hospital, Trondheim University Hospital, and professor at the Department of Clinical and Molecular Medicine, Norwegian University of Science and Technology (NTNU).
The author has completed the ICMJE form and declares the following conflict of interest: He is a research assistant and principal investigator at a fetal medicine centre involved in the nipocalimab clinical trial.

VASILIS SITRAS

Vasilis Sitras, specialist in obstetrics and gynaecology, and head of the Department for Fetal Medicine at the Department of Obstetrics and Gynaecology, Oslo University Hospital.
The author has completed the ICMJE form and declares the following conflicts of interest: He is a research assistant and principal investigator at a fetal medicine centre involved in the nipocalimab clinical trial, and principal

investigator in the prophylaxis trial discussed in the article. He has also received travel expenses to attend a meeting in Rome about the FREESIA-1 study.

HEIDI TILLER

Heidi Tiller, specialist in obstetrics and gynaecology, senior consultant and fetal medicine specialist at the Department of Obstetrics and Gynaecology, University Hospital of North Norway, and professor at the Department of Clinical Medicine, UiT The Arctic University of Norway.
The author has completed the ICMJE form and declares the following conflicts of interest: She is principal investigator at a fetal medicine centre involved in the nipocalimab clinical trial, and principal investigator in the prophylaxis trial discussed in the article. She is also on the steering committee for Janssen Pharmaceuticals (FREESIA-1) and has previously received payment from Prophylix AS related to a patent on a monoclonal anti-HPA-1a antibody.

The introduction of blood type screening followed by anti-D prophylaxis is a success story in perinatology. New treatment principles are now being developed for alloimmunisation in pregnancy.

Haemolytic disease of the fetus and newborn was once a major contributor to perinatal morbidity and mortality. The treatment for fetal anaemia is intrauterine transfusion. Since the introduction of RHD genotyping of the fetus (using non-invasive prenatal testing) and antenatal prophylaxis for RhD-negative women in Norway in 2016, the number of intrauterine transfusions due to RhD alloimmunisation has decreased. In the period 2012–2016, there were 24 intrauterine transfusions in Norway each year, compared to 15 per year for this indication from 2022 to 2024 (Kjell Salvesen, personal communication). The total number of annual intrauterine transfusions is slightly higher as there are also other causes of fetal anaemia, such as parvovirus infections and Kell alloimmunisation (1).

New treatment principles offer new hope

A recent phase 2 study showed that a new drug, nipocalimab, can prevent severe haemolytic disease of the fetus (2). Nipocalimab is an anti-neonatal Fc receptor blocker that both shortens the half-life of IgG in maternal circulation and inhibits transplacental IgG transfer. In combination, this reduces IgG alloantibody transfer to the fetus. The study offers hope for the effective treatment of alloimmunisation.

Another immunisation disorder in the fetus and newborn is fetal/neonatal alloimmune thrombocytopenia (FNAIT). The mother forms alloantibodies against the fetal platelets, resulting in thrombocytopenia in the fetus and newborn. In approximately 10 % of cases, this can cause severe brain haemorrhages in the fetus and newborn, which may lead to perinatal death or serious neurological sequelae. Unlike Rhesus alloimmunisation, there is no screening to identify the approximately 2 % of pregnant

women with the platelet type that carries a risk of FNAIT, nor is there any prophylaxis. Current treatment involves weekly administration of intravenous immunoglobulin to the expectant mother. The benefit of treating pregnant women who have a known risk of FNAIT is controversial.

Four fetal medicine centres in Norway are currently participating in a randomised controlled trial in which women at risk of FNAIT are receiving either a placebo or nipocalimab (3). Two of the centres are also involved in a phase 2 study to evaluate an antibody-mediated prophylaxis to treat FNAIT (similar to the anti-D immunoglobulin prophylaxis for Rhesus alloimmunisation) (4).

If these new treatments prove to be safe and effective, they could mark a significant advancement in the prevention and treatment of several prenatal alloimmune disorders. Norway's participation in and contribution to these studies play a crucial role in this groundbreaking work.

REFERENCES

1. Prefumo F, Fichera A, Fratelli N et al. Fetal anemia: Diagnosis and management. Best Pract Res Clin Obstet Gynaecol 2019; 58: 2–14. [PubMed][CrossRef]

2. UNITY Study Group. Nipocalimab in Early-Onset Severe Hemolytic Disease of the Fetus and Newborn. N Engl J Med 2024; 391: 526–37. [PubMed][CrossRef]

3. NIH. A Study of Nipocalimab in Reducing the Risk of Fetal and Neonatal Alloimmune Thrombocytopenia (FNAIT) (FREESIA-1). https://clinicaltrials.gov/study/NCT06449651?intr=Nipocalimab&rank=4 Accessed 2.12.2024.

4. Phase NIH. 2 Study on the Pharmacokinetics and Safety of RLYB212 in Pregnant Women at Higher Risk for HPA-1a Alloimmunization. https://clinicaltrials.gov/study/NCT06435845?intr=Nipocalimab&limit=10&term=NCT06435845&rank=1 Accessed 2.12.2024.

Publisert: 16 January 2025. Tidsskr Nor Legeforen. DOI: 10.4045/tidsskr.24.0611
Received 19.11.2024, first revision submitted 3.12.2024, accepted 10.12.2024.