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POSTER ABSTRACTS

311.DISORDERS OF PLATELET NUMBER OR FUNCTION: CLINICAL AND EPIDEMIOLOGICAL

Identifying Pregnancies at Higher Risk for HPA-1a Alloimmunization and Fetal/Neonatal Alloimmune Thrombocytopenia (FNAIT): An International, Prospective, Natural History Study

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Background and significance

Fetal and neonatal alloimmune thrombocytopenia (FNAIT) results from parental incompatibility of human platelet antigen (HPA) and subsequent maternal sensitization. When this occurs, fetal platelet production is impaired and platelet destruction accelerated. FNAIT is the platelet counterpart of Rhesus disease (RhD); however, FNAIT is rarer, more often occurs in first pregnancies, and alloimmunization may be detected as early as the 2nd trimester. Clinical presentation of FNAIT ranges from no/mild symptoms to severe thrombocytopenia and intracranial hemorrhage, which can take place in the second trimester and cause death or lifelong neurological impairment. Severe FNAIT outcomes impose substantial emotional and financial burden on affected families and healthcare systems. Among pregnant HPA-1a-negative women bearing an HPA-1a-positive fetus at risk of alloimmunization, ~27% carry the HLA-DRB3*01:01 gene variant, increasing sensitization risk ~25 fold and thus leading to much higher FNAIT risk.

Screening for FNAIT in pregnancy is not routinely performed, unlike in RhD, resulting in failure to identify at-risk pregnancies prior to birth. To prevent severe FNAIT outcomes, we believe at-risk pregnancies must be identified very early in the second trimester, and prophylactic interventions started immediately. Current management of women with existing alloimmunization due to a prior FNAIT-affected pregnancy involves months of weekly antenatal intravenous immunoglobulin with or without steroid administration. Although fetal platelet counts often improve, this therapy is very burdensome to patients.

Most data on FNAIT prevalence and risk are from Caucasian populations; studies in non-Caucasian populations have been too small to be informative. This is the first epidemiological study that seeks to identify HPA-1a-based FNAIT in a racially and ethnically diverse international population of pregnant women. Data to be tracked are: frequency of DRB3*0101 in HPA-1bb women; anti-HPA-1a alloimmunization; pregnancy outcomes; and neonatal thrombocytopenia. These data will provide a contemporary control population preceding future single-arm studies of a novel human anti-HPA-1a monoclonal antibody, RLYB212, in prophylaxis of maternal HPA-1a alloimmunization and FNAIT. The virtual elimination of RhD by screening of all pregnancies and administration of prophylaxis in at-risk cases remains one of the most significant medical advances ever achieved and provides a roadmap for FNAIT.

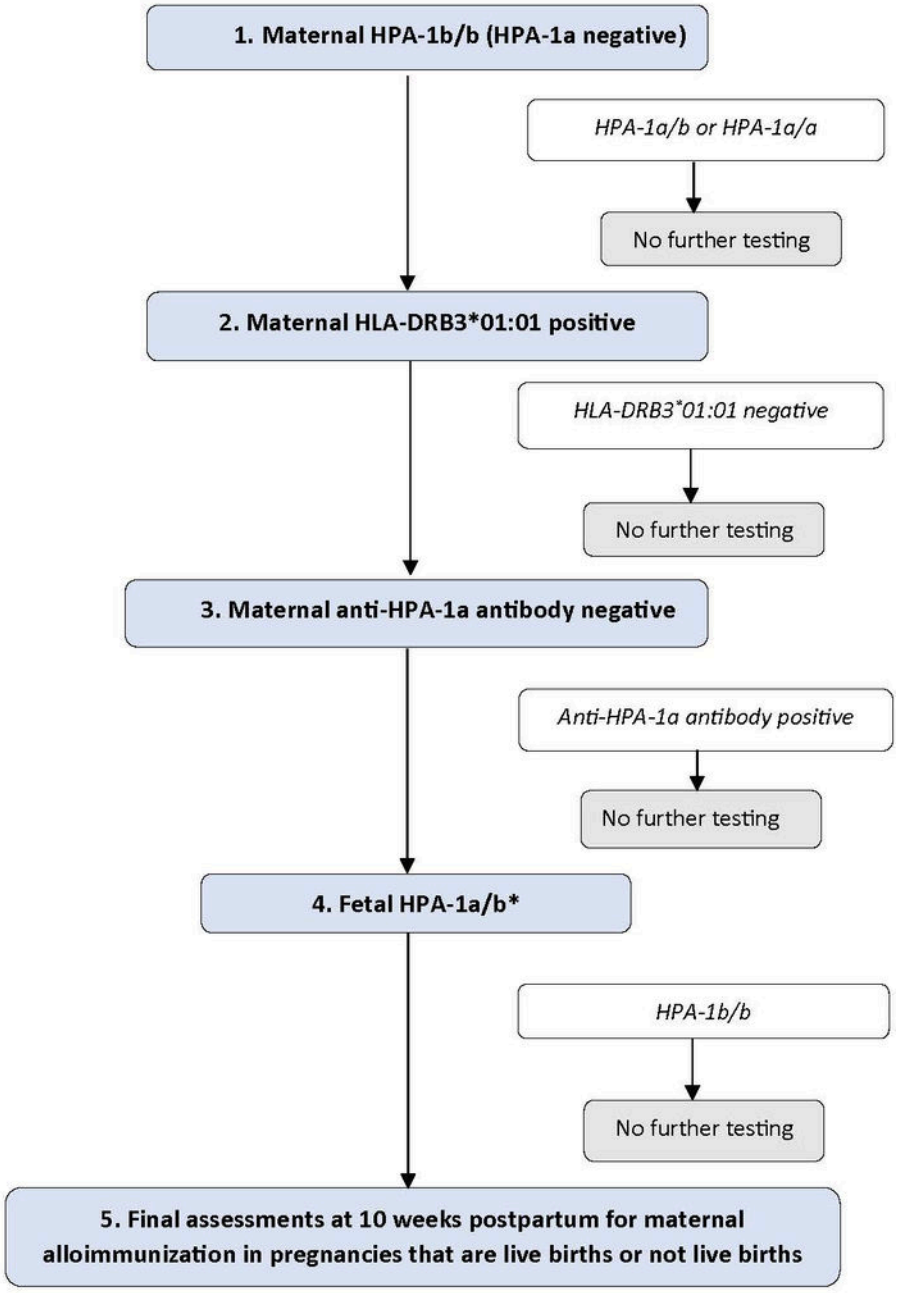
Study design and methods
Prospective, non-interventional, natural-history study assessing HPA-1a alloimmunization in pregnant women, conducted across multiple European centers in Norway, Netherlands, UK, and Germany, and in the USA. It will provide insights into anti-HPA-1a-mediated FNAIT risk and frequency among Caucasian and non-Caucasian pregnant women. Up to 30,000 women will be screened at gestational weeks 10-14 to enable early identification and follow-up of those women at higher alloimmunization risk, so that in the future, prophylaxis of the higher-risk women could be initiated. Informed consent will be requested for blood-sample collection at the 10-14 week visit for evaluation of FNAIT risk.
Inclusion criteria
Pregnant women aged ≥18 years
Exclusion criteria
Prior history of FNAIT or known HPA-1a alloimmunization
Statistical methods
Demographic, baseline characteristics and discrete variables will be summarized
Primary objective
To inform frequency of higher FNAIT risk among pregnant women of diverse racial and ethnic characteristics (all comers). **(Figure)**
Secondary objectives
Frequency of HPA-1a maternal alloimmunization at Weeks 10-14 postpartum in pregnant women at higher FNAIT risk and outcomes such as:
- Spontaneous abortion: non-deliberate fetal death prior to 19 weeks of gestation
- Elective abortion: deliberate termination of pregnancy at any time in gestation
- Stillbirth: non-deliberate fetal death after 19 weeks of gestation
- Premature birth: live birth prior to 37 completed weeks of gestation
- Live births: ≥37 completed weeks of gestation

Neonatal and severe neonatal thrombocytopenia: platelet count $<150 \times 10^9$/L and $<50 \times 10^9$/L, respectively, within 72 hours of birth
Current status
Enrolment for clinical-trial NCT05345561 is ongoing and expected to continue for ~3 years.

Disclosures Armstrong: *Rallybio Inc:* Current Employment. **Bombara:** *Rallbio Inc.:* Current Employment. **Lawrence:** *Rallybio Inc.:* Current Employment. **Patki:** *Rallybio Inc.:* Current Employment. **Skupski:** *Organon & Co:* Consultancy. **Bussel:** *Novartis:* Consultancy; *argenx:* Consultancy; *Sobi:* Consultancy; *UCB:* Consultancy, Other: Data and safety monitoring board; *Janssen:* Consultancy; *Amgen:* Consultancy; *AstraZeneca:* Consultancy; *Rigel:* Consultancy.

OffLabel Disclosure: RLYB212 is a human monoclonal antibody against Antigen-1A Immunoglobulin (HPA-1A). It is currently being developed by Rallybio for the prevention of fetal and neonatal alloimmune thrombocytopenia.

Figure. Prenatal FNAIT laboratory testing at gestation



*Cell-free fetal DNA test to inform on the presence of the antigenic stimulus for maternal alloimmunization

Figure 1

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