WITS RHI

Project Brief: MVX0004

Full Title of Study/Programme	A multicentre, multinational, parallel group, observer-blind, randomised, placebo- controlled study on the Group B Streptococcus vaccine (GBS-NN/NN2), investigating the immunogenicity and safety of four vaccination regimens in pregnant women, assessing IgG specific to AlpN proteins in cord blood, and the safety profile in mother and infant up to six months post-delivery.
Technical Focus Area	Research (Paediatrics and Maternal)
Rationale	MVX0004 is a phase II placebo-controlled study. The 50 µg GBS-NN/NN2 vaccine will be administered to healthy pregnant women. The study will be conducted in compliance with ICH GCP E6 (R2) and applicable regulatory requirements. The overall purpose of the study is to determine how four investigated vaccination regimens affect the concentrations of IgG antibodies, against the four AlpN proteins, in cord blood, namely, the vaccination regimens of; two doses at 22- and 26-weeks GA, 22- and 30-weeks GA, 26- and 30-weeks GA, and a single dose at 26 weeks GA, all doses administered by intramuscular injection.
Primary Objectives	• To compare the concentrations of IgG specific to the AlpN proteins (RibN, Alp1N, Alp2N and AlpCN) in cord blood from babies, born to women who received the GBS-NN/NN2 vaccine or placebo, according to four vaccination regimens during pregnancy, between the GBS-NN/NN2 and placebo groups. • Group 1: 2 doses GBS-NN/NN2 at 26-& 30-weeks GA (1st dose given 3rd trimester; 4 weeks interval). • Group 2: 2 doses GBS-NN/NN2 at 22 & 26-weeks GA (1st dose given 2nd trimester; 4 weeks interval). • Group 3: 2 doses GBS-NN/NN2 at 22& 30-weeks GA (1st dose given 2nd trimester; 8 weeks interval). • Group 4: 1 dose GBS-NN/NN2 at 26 weeks GA (one dose given 3rd trimester). • Group 5: Placebo at 22, 26 and 30-weeks GA (1st placebo dose given 2nd trimester, 4 weeks interval)
Secondary Objectives	To compare the concentrations of IgG, specific to the AlpN proteins (RibN, Alp1N, Alp2N and AlpCN) in maternal blood at delivery, from women who received the GBS-NN/NN2 vaccine or placebo, according to four vaccination regimens during pregnancy, between the GBS-NN/NN2 and placebo groups (same groups as specified under primary objective). <u>Other secondary immunogenicity objectives are:</u> • To compare the concentrations of IgG specific to the AlpN proteins, in maternal blood

	at 4 weeks after each dose of vaccine/placebo for the different vaccination regimens. • To evaluate the ratios of antibody concentrations between maternal and cord blood at delivery. • To evaluate the concentrations of IgG specific to the AlpN proteins, up to 3 months post-delivery, in infant blood.
Primary Endpoint/Outcome	The following primary endpoint(s) will be evaluated, by group: • Concentrations of IgG antibodies specific to the AlpN proteins in µg/mL in cord blood from each baby: The geometric mean antibody concentrations at birth will be calculated. The proportions of babies who achieve a concentration of IgG specific to the AlpN proteins above 0.1, 0.2, 0.5, 1, 2, 4 and 8 µg/mL at birth will be calculated.
Secondary Endpoint/Outcome	Secondary immunogenicity endpoints will be evaluated, by group and time-point, to support the secondary immunogenicity objectives: • Concentrations of IgG antibodies specific to the AlpN proteins in µg/mL in maternal blood. • The geometric mean antibody concentrations at delivery, and geometric mean concentration ratios relative to baseline will be calculated. • The proportions of mothers who achieve a concentration of IgG specific to the AlpN proteins above 0.1, 0.2, 0.5, 1, 2, 4 and 8 µg/mL at delivery will be calculated. • The geometric mean antibody concentrations at 4 weeks after each dose of vaccine/placebo and geometric mean concentration ratios relative to baseline will be calculated. • The ratios of antibody concentrations between maternal and cord blood at delivery will be calculated. <u>The following immunogenicity endpoints will be evaluated in the baby:</u> • Concentrations of IgG antibodies specific to the AlpN proteins in µg/mL in blood from each baby at 1 month and 3 months of age. • The geometric mean antibody concentrations at 1 month and 3 months after birth will be calculated. • The proportions of babies who achieve a concentration of IgG specific to the AlpN proteins above 0.1, 0.2, 0.5, 1, 2, 4 and 8 µg/mL at 1 month and 3 months after birth will be calculated

Study Design	The present study is a phase II, multicentre, multinational, parallel group, observer-blind, randomised and placebo-controlled study on the Group B Streptococcus vaccine (GBS-NN/NN2), investigating the immunogenicity and safety of four vaccination regimens in healthy, pregnant. women, assessing IgG specific to AlpN proteins in cord blood and maternal blood, and the safety profile in mother and baby up to 6 months post-delivery. There will be five treatment groups; three groups of 60 subjects to receive two doses of GBSNN/NN2 and one of placebo (saline), one group of 60 subjects to receive one dose of GBSNN/NN2 and two of placebo, and one group of 30 subjects to receive three doses of placebo(saline). The study is observer blind. There will be an unblinded vaccine administering team, separate from the team assessing the participants for safety tolerability and collecting the blood samples for assessment of the immune response. The analysis of the immune responses will be undertaken. across all groups,
Study Population and size	A total of 270 pregnant women are planned to be randomised.
Follow-up/Duration	6 Months post-delivery
Study/Programme Sites	Wits RHI Shandukani Research Centre (SRC)
Study/Programme Duration	24 Months
Investigators	**Dr Elizea Horne: Principal Investigator** **Dr Faeezah Patel: Sub-Investigator** **Mrinmayee Dhar: Sub-Investigator** **Muneerah Khan: Sub-Investigator** **Muneerah Khan: Sub-Investigator** **Jeanne Coetzee: Sub-Investigator** **Tiffany Seef: Clinical Associate** **Othusitse Segalo: Clinical Associate**
Other Partners & Collaborators	None
Sponsors/Donors	Minervax
Publications/Key Presentations to Date	N/A
Progress Update as of Mar 2024	Screened: 34 Screen failed: 12 Enrolled: 22 Withdrew consents: 2 Deliveries: 20 Maternal completed: 20 Infants completed: 19

Frequency of Donor Narrative Report	6 Monthly
Overall Study/Project Contact	Dr Elizea Horne (EHorne@wrhi.ac.za).
Briefing Owner and Date	Nothando Faith Mtshali (fmtshali@wrhi.ac.za) Mar 2024