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Neisseria gonorrhoeae outer membrane vesicles-based vaccine for immunization against gonorrhea: pathway to first-time-in-human trial

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Background
GSK developed a vaccine against Neisseria gonorrhoeae (Ng), based on genetically detoxified outer membrane vesicles adsorbed on aluminum hydroxide, named Ng GMMA. The vaccine is currently tested in a Phase 1/2 clinical study [NCT05630859]. A pre-investigational new drug application meeting was requested to Center for Biologics Evaluation and Research (CBER), asking concurrence on the proposed clinical development and reactogenicity control strategy (RCS) plans.

Aim/Methods
The clinical development plan consists of a Phase 1/2 study aiming for early demonstration of vaccine safety and efficacy. The Phase 1 part is a first-time-in-human (FTiH) dose-escalation study in healthy adults; the Phase 2 part is a Proof of Concept study assessing vaccine efficacy in healthy adults at risk for gonorrhea. Reactogenicity control strategy (RCS) represents a fundamental part of Ng GMMA vaccine development. It is composed of a series of tests, aiming to predict compound-related side effects. Monocyte activating test (MAT), as part of RCS, was selected as preferred assay for pyrogenicity testing of genetically modified lipopolysaccharide and included as the release assay for the Phase 1/2 clinical lot. Additionally, at CBER request, we conducted two modified rabbit pyrogenicity tests (mRPT), on the toxicology and Phase 1/2 clinical lots respectively, as characterization assay.

Results
The MAT results of Ng GMMA vaccine confirmed the vaccine safety profile. A transient body temperature profile comparable to control (saline) was observed for both Ng GMMA vaccine lots tested in mRPT, supporting the clinical lot utilization in the Phase 1/2 study. Upon acceptance by CBER, the Phase 1/2 study was started in November 2022. Twenty-four healthy participants were enrolled in the Phase 1 part; no safety concerns have been identified so far.

Conclusions
The in vitro MAT data complemented with the in vivo mRPT data, and the repeat-dose toxicology study, support the prediction and assessment of an acceptable in vivo reactogenicity profile of the Ng GMMA vaccine. The in vivo reactogenicity is further assessed through a carefully executed FTiH dose escalation clinical study. Based on this experience, the use of MAT will be considered as reference standard in future stages of vaccine development.