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Preclinical Evidence for protective potential of a GMMA-based vaccine against gonococcus

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Author(s)

Erika Bartolini, n/a

Associate Director

GSK

Marco Spinsanti, n/a

Scientist

GSK

Monica Fabbrini, n/a

Associate Director

GSK

Giacomo Romagnoli, n/a

Senior Scientist

GSK

Elisabetta Monaci, n/a

Scientist

GSK

Andrea Guido Oreste Manetti, n/a

Senior Scientist

GSK

Federico Fontani, n/a

Principal Statistician

GSK

Giovanna Tuscano, n/a

Scientist

GSK

Claudia Gianfaldoni, n/a

Scientist

GSK

Alessandro Muzzi, n/a
Associate Director, Head of Bacterial Computational Genomics Team
GSK Vaccines

Silvana Savino, n/a
Associate Director
GSK

Michela Brazzoli, n/a
Associate Director
GSK

Christian Matano, n/a
Associate Director
GSK

Ugo D'Oro, n/a
Dir. Sr. Clinical Science Lead
GSK

Immaculada Margarit, n/a
Senior Director
GSK

Oretta Finco, n/a
Senior Director
GSK

Isabel Delany, n/a
Senior Director
GSK

Giulia Giordano, n/a
Vaccine Development Leader
GSK

Background
Gonorrhea is a sexually transmitted infection caused by Neisseria gonorrhoeae (Ng) with 87 million new cases of gonococcal infections occurring globally. The growing concern about the rapid evolution of antimicrobial resistance highlighted the limit of current antibiotic therapy and suggests vaccines as a sustainable and effective solution.

Aim/Methods
GSK has developed an investigational vaccine based on Generalized Modules for Membrane Antigens (GMMA) against gonococcus currently in a Phase I/II study, named Ng GMMA. The GSK vaccine is based on genetically detoxified outer membrane vesicles produced from the FA1090 strain engineered to reduce the lipid A endotoxin activity and to avoid any potential immune interference effect from the Reduction Modifiable Protein (Rmp). The Ng GMMA investigational vaccine was produced in fermentation scale and extensively characterized. The ability of the Ng GMMA vaccine to induce serum and mucosal immune responses in mice was assessed. The functionality of the vaccine-induced antibodies was explored through serum bactericidal activity and bacterial adhesion inhibition assays. The 4CMenB meningococcus B licensed vaccine has recently shown a moderate effectiveness in preventing Ng infection and was used as comparator vaccine

Results
Genetic detoxification was efficient in reducing the endotoxin activity of the Ng GMMA vaccine, measured through in vitro surrogates of reactogenicity, to a profile comparable to vaccines well tolerated in humans. The Ng GMMA vaccine was able to induce a robust immune response in mice, of higher and broader magnitude to that induced by the 4CMenB comparator vaccine. In particular, Ng GMMA was able to induce statistically superior bactericidal titers than 4CMenB against 9 of 11 tested strains in a panel of Ng representing the global variability of gonococcal outer membrane antigens. Moreover, high anti-GMMA IgG/A titers were measured in mice vaginal washes. Finally, Ng GMMA-elicited antibodies inhibited bacterial adhesion of two different Ng strains to primary ureteral cell lines representative of the urinary epithelial tract.

Conclusions
Overall, the obtained preclinical evidence shows that Ng GMMA outperforms 4CMenB in all serological and functional assays tested and suggests that Ng GMMA induces immune responses with a potential to block Ng infection through different mechanisms.