This project has received funding from the European Union’s Horizon 2020 research and innovation programme under grant agreement No 815439

SEROEPIDEMIOLOGY IN AFRICA OF INTS (SAINTS)
MALAWI, KENYA, GHANA, BURKINA FASO

Helen Dale, University of Liverpool,
Malawi-Liverpool Wellcome Research Programme

Coalition Against Typhoid Conference
5th December 2023
Accelerating iNTS vaccines - VacciINTS consortium, EU H2020

GMP Vaccine Manufacture
- WP1 (GVGH): Technology transfer, GMP manufacture and release of vaccine and placebo lots
- WP2 (GVGH): Stability assessment of vaccine lots

Planning vaccine deployment and uptake in poor resource countries
- WP7 (UOL): Sero-epidemiology study
- WP8 (SVA): Increase knowledge and awareness of iNTS disease burden
- WP9 (UCAM): Cost-of-illness study and cost-effectiveness analyses of an iNTS vaccine for uptake in limited-resource settings (SSA)

Vaccine Profile
- Clinical trials
  - WP3 (UOXF): Phase I (stage 1) clinical study to demonstrate safety and immunogenicity of iNTS-GMMA in healthy European adults
  - WP4 (UOXF): Phase I (stage 2) clinical study to demonstrate safety and immunogenicity of iNTS-GMMA in healthy African adults

- Immunological analysis
  - WP5 (GVGH): Serological analysis of clinical trial samples
  - WP6 (UOXF): Exploratory immunological analysis

WP10 (UNISI): Training

WP15-18 (SVA): Dissemination, communication and impact assessment

WP11-14 (SVA): Project coordination and management
Study Aims

• To understand across different sub-Saharan African sites:
  • Age of acquisition of humoral immunity to non-typhoidal salmonella (NTS)
    • Children 0-5 years
    • Common iNTS serovars: Typhmurium & Enteritidis
    • O-Ag IgG
    • Serum bactericidal activity
Seroepidemiology in Africa of iNTS (SAiNTS)

VacciNTS consortium
4 African countries
• 1000 samples aged 0-5 years per site
• 200 per annual age-stratum
• Children randomly selected from mapped and censused study areas

• 2 commonest serovars causing invasive disease (Typhimurium, Enteritidis)
  • ELISA (OAg IgG)
  • Serum Bactericidal Activity
Recruitment by site

- **Burkina Faso:**
  - 21\textsuperscript{st} February – 28\textsuperscript{th} March 2022 (1 month)
    - 1008 serum samples

- **Ghana:**
  - 12\textsuperscript{th} August 2021 - 24\textsuperscript{th} May 2022 (8 months)
    - 1032 serum samples

- **Kenya:**
  - 26\textsuperscript{th} April – 29\textsuperscript{th} July 2021 (3 months)
    - Rainy season
    - 1346 serum samples

- **Malawi:**
  - 13\textsuperscript{th} January – 30\textsuperscript{th} March 2022 (14 months)
    - Across seasons and geographic regions
    - 2412 serum samples
Laboratory assays

**Assays developed by GSK Vaccines Institute for Global Health (GVGH)**

- **ELISA**: IgG to O antigen: S. Tm/ S. En
- High-throughput Serum Bactericidal Activity (SBA) assay: S. Tm/ S. En
  - New technology platform for African sites
  - Samples processed at Kamuzu University of Health Sciences (KUHES), Malawi and Kwame Nkrumha University of Science and Technology (KNUST), Ghana
- Serum standard for assays across VaccINTS sites
- Assays to reflect those used in assessment of immunogenicity from phase 1 trials

Salmonella Typhimurium O-Antigen IgG

Malawi: OAg IgG to S. Typhimurium

Kenya: OAg IgG to S. Typhimurium

Burkina Faso: OAg IgG to S. Typhimurium
Salmonella Enteritidis O-Antigen IgG

N = 999

Malawi: OAg IgG to S. Enteritidis

N = 999

Kenya: OAg IgG to S. Enteritidis

N = 999

Burkina Faso: OAg IgG to S. Enteritidis

N = 999
O-Antigen IgG vs Serum Bactericidal Activity

Malawi: OAg IgG to S. Typhimurium

Malawi: SBA to S. Typhimurium

N = 2240

N = 993
Salmonella Typhimurium: Serum Bactericidal Activity

N = 993

Malawi: SBA to S. Typhimurium

N = 845

Kenya: SBA to S. Typhimurium

N = 934

Burkina Faso: SBA to S. Typhimurium
Low early-life incidence may be caused by low stool exposure in first 6 months

H Dale, unpublished data
O-Antigen S. typhimurium IgG in Malawian Children 0-5 years

Sericatalytic Model
Conclusions

• Maternal antibodies offer less bactericidal function than naturally acquired immunity (IgG & IgM)

• Age-pattern of iNTS disease likely due to faeco-oral exposure patterns after weaning

• Variation in nadirs, peaks and plateaus indicate a variable force of e-NTS infection.

• Levels of natural protection likely to be different at different sites
Next steps

• Additional testing of samples for IgA and IgM
• Systems serology/ functional assays – **OptiVaNTS**
• Parameters estimates from these models to develop mechanistic and dynamic modelling to understand relationships in age-distribution of:
  • Invasive disease
  • Enteric NTS
  • Serological correlates of protection
• Cross-validate models across multiple epidemiological/ geographical settings; additional data collection from multiple high burden sites
• Possible tool to monitor WASH interventions
Participating organizations

1. University of Liverpool – lead participant (Prof. Gordon)
2. l’Institut Supérieur des Sciences de la Population (ISSP), Burkina Faso (Prof. Soura)
3. Kwame Nkrumha University of Science and Technology (KNUST), Ghana (Prof. Owusu-Dabo)
4. Centre for Microbiology Research Kenyan Medical Research Institute (KEMRI), Kenya (Prof. Kariuki)
5. GSK Vaccines Institute for Global Health, Italy
6. University of Cambridge (Prof. Marks)
7. International Vaccine Institute (IVI), South Korea