A multidisciplinary approach to increase awareness and strengthen the case for the introduction of a vaccine against invasive non-typhoidal *Salmonella*

Gianluca Breghi
FONDAZIONE ACHILLE SCLAVO
Siena, Italy

11th International Conference on Typhoid & Other invasive Salmonelloses
March 26-28, 2019 Hanoi, Vietnam
Mission: Reduce infant mortality and improve health and living conditions in low-income countries, by accelerating availability of new affordable life-saving vaccines to eliminate neglected infectious diseases and training local health workers, thereby reducing poverty.

- Established in 2011 by private founders, is based in Sienna, Italy
- Member of the UN Sustainable Solution Network, SDSM-MED, SDSN-IT

MAIN ACTIVITIES:
- Research on iNTS
- Coordination of the 5th Master in Vaccinology and Pharmaceutical Clinical Development, offered by UNISI to MDs from LMICs
iNTS Disease burden

• Included in the last two GBDs(*): **burden estimates are increasing**

• **Sub-Saharan Africa (SSA) has the highest number of deaths, about 50,000 [27566-53365], particularly in infants under 5 aged (≈29500) and is the most common cause of bacteremia**

• Major cause of <5 mortality, with 68% of cases in children under 5 of age and immuno-compromised patients (***)

• Closely associated with HIV, malaria, anaemia, malnutrition (***)

• Difficult to diagnose (only blood culture is reliable); CFR 20%

• **Increase in AMR evidence**

(*) A systematic analysis for the GBD study 2017, Lancet vol 392, 2018
iNTS disease: treatment & prevention

- Public health care interventions that can be implemented (sanitization, water purification & increased hygiene) cannot eradicate the disease and be effective long-term,

- Vaccination has been indicated as a high priority for prevention, also considering uncertainties about disease transmission,

- Development of vaccines for Africa is in progress:
  1. Glycoconjugate (Preclinical)
  2. Live attenuated (Phase I)
  3. Protein-based subunit & GMMA technology (Preclinical)

- No licensed vaccines are available or close to licensing: funding is a major issue

Is iNTS a neglected disease?
iNTS disease as a neglected tropical disease

iNTS meets all of WHO’s requirements to be a NTD!

a. Disproportionately affect population living in poverty and cause important morbidity and mortality;
b. Primarily affect populations living in tropical and sub-tropical areas;
c. Immediately amenable to broad control, elimination or eradication by applying one or more of the five public health strategies adopted by the Department of control of NTDs;
d. Relatively neglected by research, when it comes to developing new diagnostics, medicines and other control tools.

Process for review of list of NTDs
S-AFRIVAC Project: Goal

Accelerate development and availability of an effective GMMA-based vaccine against a deadly neglected disease endemic in Africa at risk for increasing AMR

Coordinator: Dr. Rino Rappuoli,

Funded by the Tuscany Region with 1MM€
Funded by Partners with 1MM€
S-AFRIVAC project: A multidisciplinary approach against a neglected disease

Epidemiology & Awareness | Modeling, Economics | Immunogenicity/Cost-effectiveness | Preclinical Model | Vaccine | Serologic Analysis | Test Validation

The Italian collaborative network against iNTS
**S-AFRIVAC project: deliverables**

**Area 1**
Epidemiology update; Epidemiological and mathematical disease models; (Sclavo/UNISI) + Pharmaco-economic study of alternative immunization scenarios in SSA (UNISI)

**Area 2**
Advance a new vaccine towards clinical trials, through preclinical studies and production of a GMP lot for early clinical development (GVGH/Sclavo)

**Area 3**
evaluate vaccine’s mucosal and cellular immunological response in preclinical animal infection models (UNISI)

**Area 4**
Qualification and validation of immuno-assays (VisMederi)

Fondazione Achille Sclavo own main deliverables

Koeberling *et al.* poster

Fiorino *et al.* poster
S-AFRIVAC project:  
Fondazione Achille Sclavo’s main activities

• Scientific and technical coordination:  
  Scientific Coordinator is Dr. Rino Rappuoli

• Project Management (by Dr. Diletta Magini)

• Dissemination of results and disease awareness

• Financial commitment for the co-funding

• Research activities:
  • Sponsorship and supervision of vaccine toxicology study  
    (in collaboration with GVGH)
  • Literature monitoring and publications (by Dr. Tiziana Spadafina)
  • Epidemiological model of iNTS disease and economic model of  
    vaccine sustainability  
    (in collaboration with UNISI)

Integrated Public Health Approach
S-AFRIVAC project results(*):
Comprehensive approach to the fight against iNTS disease

- Literature update of iNTS epidemiology in endemic SSA countries
- Delivery of a mathematical compartmental model capturing known iNTS disease features:
  - Spread of disease in SSA
  - iNTS-GMMA vaccine impact (different immunization strategies)
- Economic evaluation of iNTS disease/vaccine:
  - Vaccine introduction modeling (routine+/- catch-up)
  - Broad estimation of the iNTS economical burden
  - C/E Analysis also comparing different immunization strategies
- Vaccine development
- Assay validation

(*) results under publication
Bridging the valley of death for a vaccine against a neglected disease of poverty...

First Valley of Death (Fonte: PATH 2018)

Tuscany Region

S-AFRIVAC Partnership

Follow-up funding

- Phase I clinical studies
- Advanced modelling: disease and sustainability
- Epidemiology, B.o.D.
- Increase disease awareness, knowledge

GVGH Co-financing

- Research and pre-clinical development
- Disease model
- Sustainability plan
- Technology Development
- Tox. and immunological Studies
- GMP Lot production for clinical studies

Regione Toscana | FAS Fondo Aree Sottoutilizzate 2007-2013 | REPUBBLICA ITALIANA
Summary/Conclusions

• iNTS Disease:
  • Major cause of bloodstream infections in SSA. AMR increasing
  • Major burden for children and disadvantaged patients groups
  • Truly neglected tropical disease

• S-AFRIVAC completed:
  • iNTS–GMMA vaccine preclinical package
  • an epidemiology compartmental model of the disease
  • three alternative immunizations scenarios
  • a first-cut Cost/Effectiveness Analysis
  • publications are following up to increase awareness

• H2020 project will continue the work
• This is the time to instep up the fight against iNTS disease
Acknowledgments . . . Thank you!

Rino Rappuoli
Angelo Riccaboni
Stefano Malvolti

Diletta Magini
Tiziana Spadafina

Our Partners:

Oliver Koeberling
Allan James Saul
Laura Bartle Martin

Emanuele Montomoli

Donata Medaglini
Nicola Dimitri
Maria Pia Maraghini
Fabio Fiorino
Daniele Cassese
Patrice De Micco

Travel Award