



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

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FAS
Fondo Aree
Sottoutilizzate
2007-2013



11th International Conference on
Typhoid & Other invasive
Salmonellosis
March 26-28, 2019 Hanoi, Vietnam



Fondazione Achille Sclavo

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**

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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 (\approx 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

(**) Ao TT, Feasey NA, Gordon MA, Keddy KH, Angulo FJ, Crump JA, Global Burden of Invasive Nontyphoidal *Salmonella* Disease, 2010. E.I.D. Vol21, No.6, June 2015



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€

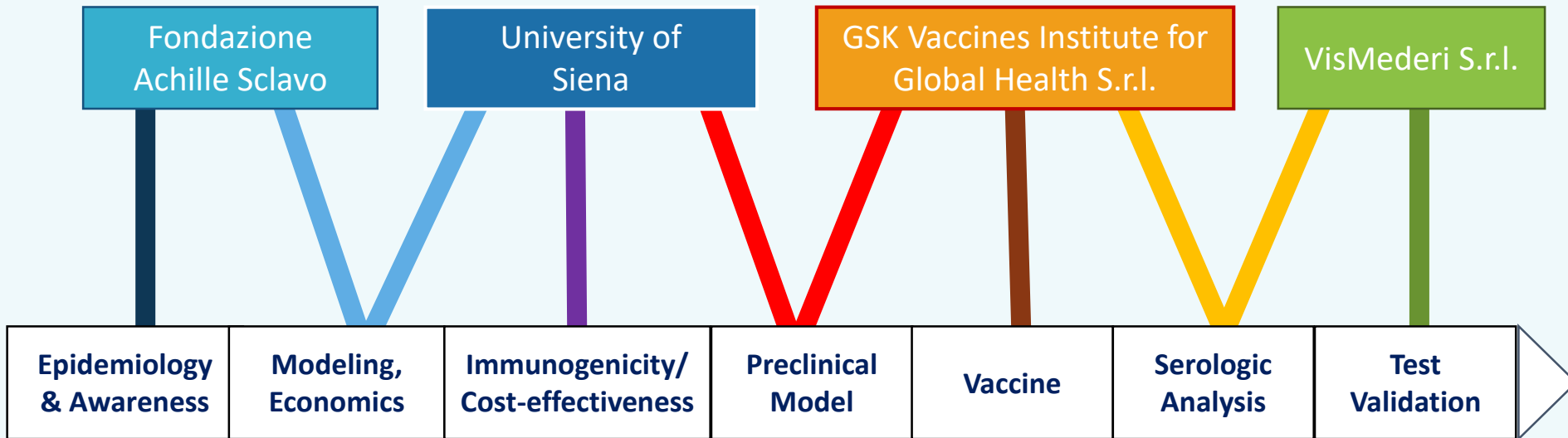
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S-AFRIVAC project:

A multidisciplinary approach against a neglected disease



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)



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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

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Bridging the valley of death for a vaccine against a neglected disease of poverty...

First Valley of Death (Fonte: PATH 2018)

Tuscany Region

Follow-up funding

S-AFRIVAC
Partnership

Research and
pre-clinical
development

Disease model
Sustainability plan
Technology Development
Tox. and immunological
Studies

GMP Lot
production
for clinical
studies

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

GVGH Co-financing



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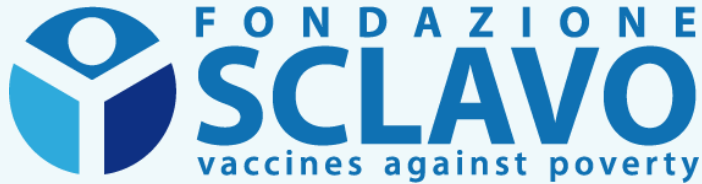
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Summary/Conclusions

- 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!



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