

Development of safe and effective Vaccine against Lassa Fever in Africa

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Concept and Ideas

- Partnership between public and life science private sectors provides the advantage of bringing high value innovation to the market and to the patients.
- Through the creation of a partnership between Merck (Life Science business), and Innovative Biotech LTD a privately held company registered and operating in Nigeria, **the goal of this project is to create an integrated vaccine development and production platform in Nigeria** to address the needs of priority diseases: **Lassa, Ebola, HIV, Cancers etc.**
- The project is based on a stepwise approach: first Innovative Biotech will build-up a vaccine fill/finish facility in Nigeria to respond quickly to epidemics needs.
- As a second step, the development and scale up of LASSA, EBOLA, HIV, Cancers etc candidate vaccines will be conducted between the partners to reach the point of scaling up the process and transferring it to the local manufacturing in Nigeria.
- Innovative technologies such as the recombinant Virus-like –particle (VLP) will allow for easy combination of the required antigens on the surface of a VLP structure thereby making it a flexible platform technology for the development of current and emerging infectious diseases threats locally and globally.

Introduction

- Lassa virus (LASV) causes Lassa fever (LF) including severe hemorrhagic disease and long-term complications.
- LF has a considerable disease burden in Nigeria and throughout West Africa including thousands of deaths and hospitalizations every year.
- Safe and effective vaccine is urgently needed to prevent outbreaks and epidemics in Nigeria and West African nations.
- However, despite 50-year history of LASV research, there are no licensed LF vaccine in the world.

Approach

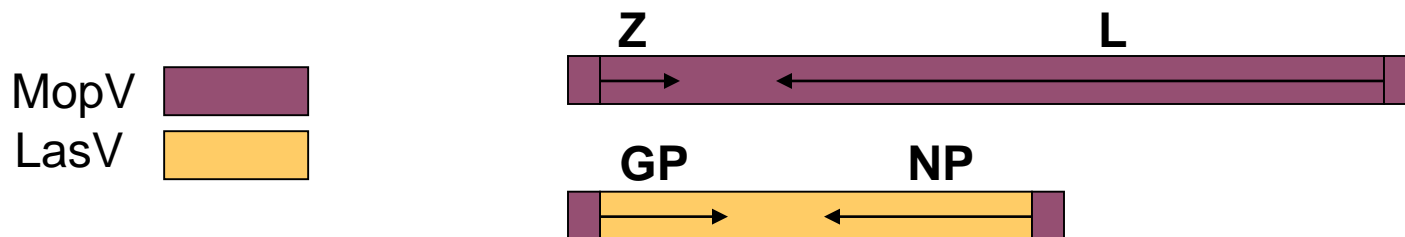
- In collaboration with Medigen, Inc. (USA) and the University of Maryland we are developing safe and effective live ML29 vaccine expressing LASV glycoprotein (GPC) and nucleoprotein (NP) antigens.
- Vaccine seed prepared using classic virus reassortment similar to FluMist reassortant influenza vaccine.
- Live replicating vaccine has a unique advantage for preventing and containing LF epidemics because only a single vaccination is required.
- The vaccine so far has been successfully tested in the multiple animal models of LF including non-human primates.

LASV Vaccine:

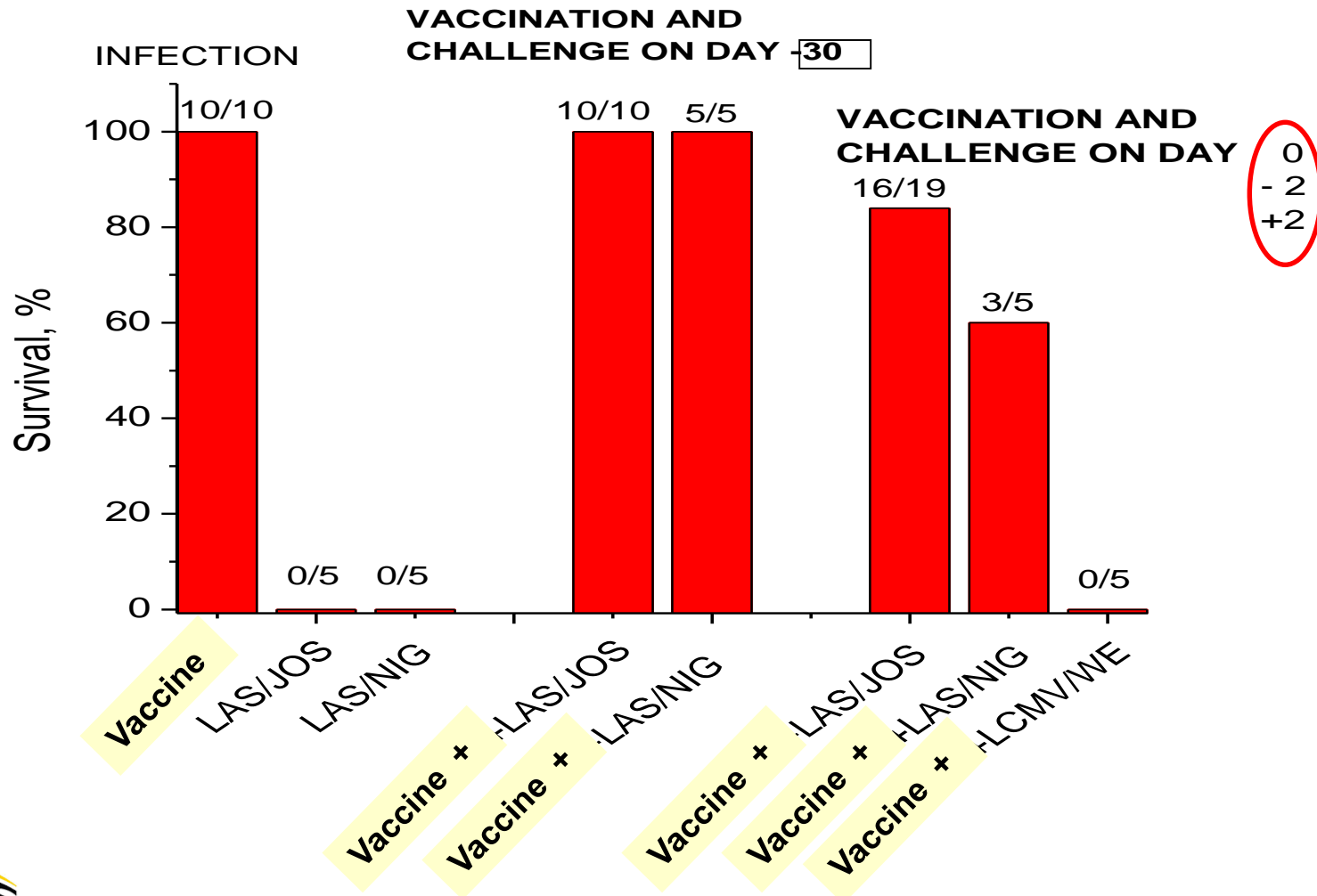
Live Reassortant Mopeia Virus (MopV) Expressing Lassa Fever Virus Structural Proteins

- LasV ML29 Vaccine: 68% MopV genome + 32% LASV Genes
- Reassortant vaccine against Lassa fever
- Vaccine is safe in rodent and NHP models

Genetic Structure of Reassortant Vaccine against LASV



Vaccination-Challenge Experiments in Guinea Pigs: Preventive and Therapeutic Applications of LASVV Vaccine



Vaccination with reassortant vaccine protects marmosets against fatal disease

Vaccination
1,000 PFU, s.c.

0

Challenge
1,000 LD50, s.c.

30

35

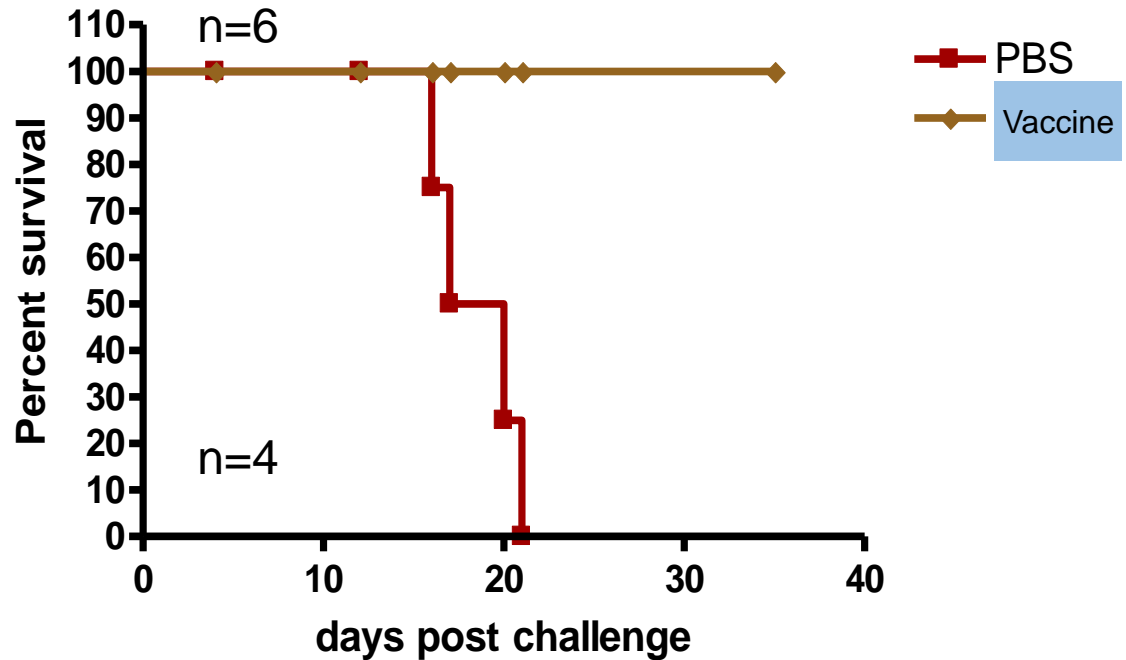
45

50

65 bleed. days



Efficacy in Marmosets



Summary of Results

- Vaccination of non-human primates (marmosets) and subsequent challenge with the wild-type pathogenic LASV resulted in complete protection.
- Remarkably, vaccination of SIV-infected rhesus macaques did not result in arenavirus infection symptoms and did not exacerbate SIV-induced disease.
- These results suggest the highest level of vaccine safety even in the immunocompromised vaccine recipients.
- Furthermore, DNA array analysis of human PBMC confirmed safety profile of the LASV vaccine.
- Finally, we have shown that our vaccine is the only known vaccine that provided protection against LASV variants currently circulating in Nigeria.

Conclusions

- We conclude that ML29 is safe and effective vaccine against LASV in Nigeria and has advantages for containing outbreaks and large-scale epidemics of LF.
- Currently, plans are underway to manufacture cGMP vaccine product and to launch a phase I clinical trial in Nigeria and in the U.S. in partnership with the U.S. and Nigerian institutions.
- Successful clinical development of this vaccine in Nigeria will result in the first vaccine against Lassa fever in the world.

Future Commercialization Plans

- Medigen HAS EXCLUSIVE LICENSE from the University of Maryland in Baltimore (UMB) for ML29 reassortant Lassa vaccine and partners with Innovative Biotech Nigeria for use in West Africa.
- Experimental vaccine manufacturing:
 - -Seed stock of Reassortant Lassa vaccine is available;
 - -GMP-manufactured Master Cell Bank and Working Cell Bank is available;
 - -Contract Manufacturing Organization (CMO) has been identified.
- Experimental vaccine needs to be tested in Phase I and in Phase II clinical trials or ring vaccination in Nigeria.

Partners

- Innovative Biotech, Nigeria.
- University of Louisville, KY, USA.
- University of Maryland, Baltimore, MD, USA.
- Medigen Inc., MD, USA.