

Clinical Development of NPC-BKSE36/CpG Malaria Vaccine

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Project Outline

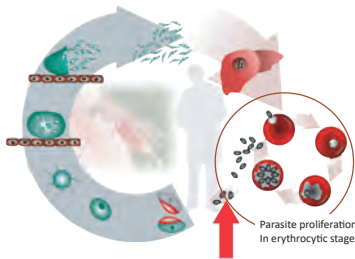
BK-SE36 malaria vaccine is a combination of recombinant SE36 protein and aluminum hydroxide gel (AHG). From a clinical study in Uganda, a **72% protective efficacy** could be obtained, with children from 6-10 years old responding more to the vaccine. A study in children 1-5 years old was also successfully carried out in Burkina Faso. In further clinical trials with Japanese adults, adding CpG-ODN(K3), a nucleic acid adjuvant, to BK-SE36 malaria vaccine resulted in 3-4 times increase in the antibody titer. We have completed a BK-SE36/CpG clinical trial in Burkina Faso from adults to 1 year-old child without vaccine related severe side effects and we are now under analysis of obtained data. We also plan to carry out a Phase I/IIa trial utilizing controlled human malaria infection to have supporting efficacy data. BK-SE36 was renamed as NPC-SE36, reflecting the development of the vaccine with Nobelpharma Co., Ltd. as sponsor.



Patients in Apac, Uganda.

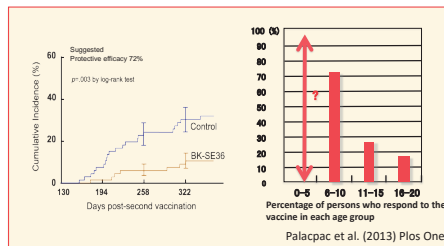
In 2018, there were roughly 400,000 deaths due to malaria.

Life cycle of the falciparum malaria parasite



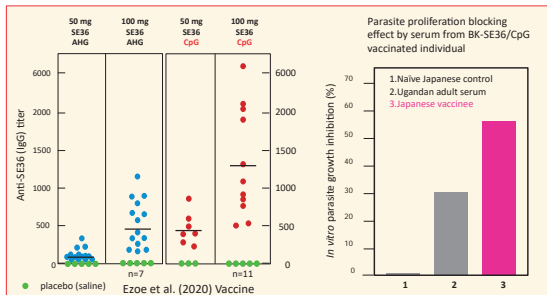
anti SE36 antibody targets the late stages of the blood-stage life cycle.

Results of BK-SE36/AHG Phase Ib trial in Uganda



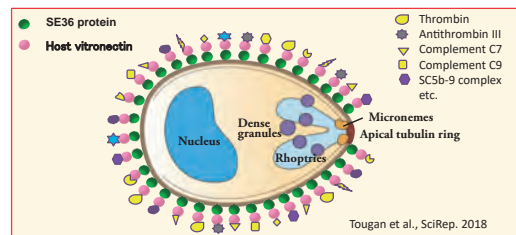
In Uganda a promising 72% protective efficacy against high parasitemia and fever was obtained. A larger number of vaccine responders were observed in the younger age group, suggesting **immune tolerance** occurs with repeated malaria infection. Children, 0-5 years old, the target age group under WHO, are expected to respond favorably to the vaccine.

Results of BK-SE36/CpG Phase Ia clinical trial



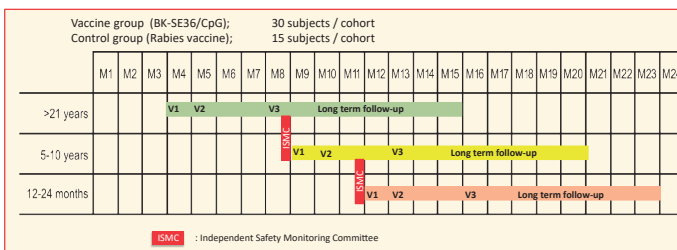
A comparison of vaccine induced antibody titers from Japanese male adults vaccinated with BK - SE 36 and BK-SE 36/CpG (left panel), highlights the increase in antibody titer 3 weeks after the second vaccine dose. Combination of CpG enhanced antibody titer resulted in more than 3 times higher antibody titer compared to BK-SE36 alone. Furthermore, using serum obtained from 1 volunteer vaccinated with BK-SE36/CpG, *in vitro* growth inhibition assay (GIA) showed inhibition of parasite proliferation.

Biological function of SE36 protein



SE36 protein tightly binds to host vitronectin that binds to other host proteins, components of complement. These complex camouflage the surface of merozoite to evade host immune attack. The complex of SE36 with host vitronectin causes **immune tolerance** against SE36. Thus resulted immune tolerance causes low antibody response in the endemic area, then the observed **low genetic polymorphism** of SE36 gene is thought to be by this low host immune pressure.

Outline of NPC-SE36/CpG Phase Ib clinical trial in Burkina Faso



As shown above, Phase Ib clinical trial of NPC-SE36 / CpG was conducted in infants by the age de-escalation of in endemic areas. Currently, the data is being analyzed. No vaccine related serious side effects have been reported. In the future, we will evaluate the efficacy in higher-level clinical trials targeting infants in endemic areas and travelers from non-endemic countries, and proceed to regulatory approval.

Target disease: Malaria; Patent information: (1) Patent No. 4145145 (June 27, 2008), (2) No. 4145348 (June 27, 2008), (3) Patent No. 5748658 (May 22, 2015); Technical features: New malaria vaccine of plasmodium antigen polypeptide SE36 and its variants combined with adjuvant CpGODN (K3); Marketability: Falciparum malaria is an infectious disease that infects 200-300 million people annually and kills more than 400,000 people, mainly infants under the age of 5 (WHO Report 2018). The development of a highly effective vaccine is expected as a drastic measure. Development challenges: Obtaining funding to conduct large-scale clinical trials in endemic areas. Information to clarify the division of roles between companies and academia: Joint research agreement with Nobelpharma (concluded on March 18, 2019)