Full-length MSP-1 "SumayaVac1" vaccine candidate triggers long-lasting and multiple FC-mediated effector functional IgG and IgM antibodies in a phase 1a clinical trial.

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An increase in the estimated cases and deaths due to malaria have recently been reported by the WHO. New vaccine approaches are thus needed to fight against *P. falciparum* infections. Ongoing efforts are focused on refining pre-erythrocytic approaches, while less attention has been placed on blood stage vaccines. The merozoite surface antigen 1 (MSP1) is a promising blood stage and liver stage vaccine candidate, proven to be effective in animal models, but failed in humans. Past MSP1 clinical trials in humans only included the C terminal fragments of either p42 or p19, while ignoring the remaining ~80% of the protein containing numerous T-cell and B-cell epitopes. To test the safety and immunogenicity of the full-length MSP1 protein, in combination with GLA-SE adjuvant as a vaccine (*SumayaVac1*; produced by Sumaya-Biotech) we conducted a first in human single-center, randomized, double-blind, placebo and adjuvant-controlled, dose escalation phase 1a clinical trial. All vaccinees sero-converted and produced high MSP1-specific antibody titers. We now report that both IgG and IgM of vaccinees are capable of deploying a wide spectrum of long-lasting FC-mediated effector functions including complement fixation and formation of membrane attack complex, opsonic phagocytosis by neutrophils and monocytes as well as respiratory burst by neutrophils. The multifunctional potential of *SumayaVac1* is comparable to that of the natural immunity achieved by endemic exposed population malaria from Kenya. The different anti-parasitic effector functions are maintained above the pre-vaccination baseline even months after the last dose. Interestingly, high titters and functional antibodies against the highly conserved N-terminal p83 fragment, never included in previous MSP1 trials and found to be highly reactive to IgG from vaccinees using epitope mapping, are clearly observed, highlighting the strain-transcending potential of *SumayaVac1*. Preliminary immunophenotyping data suggests that *SumayaVac1* promotes an activation phenotype of $CD4^+$ and $CD8^+$ T cells as well as Tfh cells after 3 doses of the vaccine. A phase Ib trial is under development together with the Swiss TPH in Bagamoyo, Tanzania.