Presentation #:

MAM01 and L9LS Demonstrate Equipotent Protection Against *Plasmodium falciparum (Pf)* Malaria Infection in Mice

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Introduction

- Human monoclonal antibodies against distinct regions of the repeat domain of the circumsporozoite (CSP) protein of *Plasmodium falciparum* sporozoites are a promising approach for preventing malaria infection.
- The specificity of the most potent human anti-CSP antibodies bind the junction, minor repeat region or the central (NANP) repeats.
- MAM01 is human monoclonal antibody in development for single-encounter seasonal prophylaxis of malaria for children living in malaria endemic areas that recognizes the (NANP) repeats and the NVDPNANP-containing minor repeat region.
- The efficacy of MAM01 was compared to two human antibodies L9LS and CIS43LS.
- To understand the pharmacokinetic-pharmacodynamic relationship of MAM01, CIS43LS and L9LS their efficacy was determined in the mouse bite parasitemia and liver burden models, using transgenic *P. berghei* parasite expressing the *P. falciparum* CSP.
- Serum IgG concentrations at the time of challenge were evaluated. Time-course PK is pending.

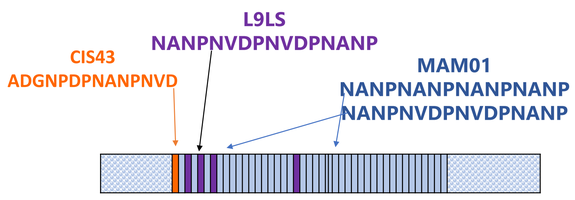

Figure 1. Epitope recognition of each monoclonal Ab of CSP protein.

Methods

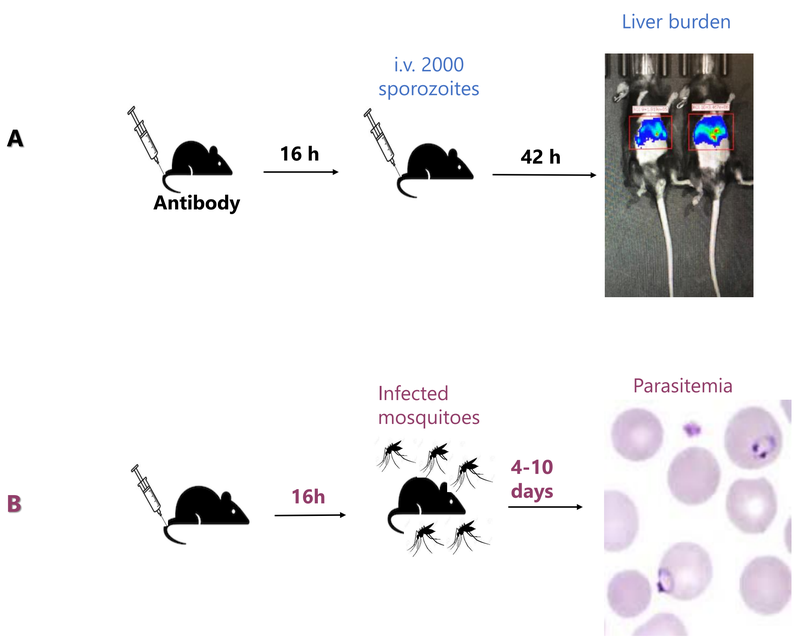

Figure 2. Evaluating liver burden and sterile immunity. (A) Mice received an i.v. injection of mAb in different amount. 16 hours later, mice are challenged with 2,000 SPZ. 42 hours after the challenge, mice are treated with D-Luciferin and then placed in an IVIS sporozoites (spz) imager to evaluate the parasite load in the liver by measuring the bioluminescence. The liver burden model measured the ability of circulating antibody to prevent hepatocyte invasion of bloodstream sporozoites following IV parasite challenge. **(B)** 16 hours after passive immunization, mice are exposed to the bites of mosquitoes from a population that has 80% infection. Four days after the mosquito bite infection, Giemsa-stained blood smears are examined by light microscopy to assess blood-stage infection.

Results

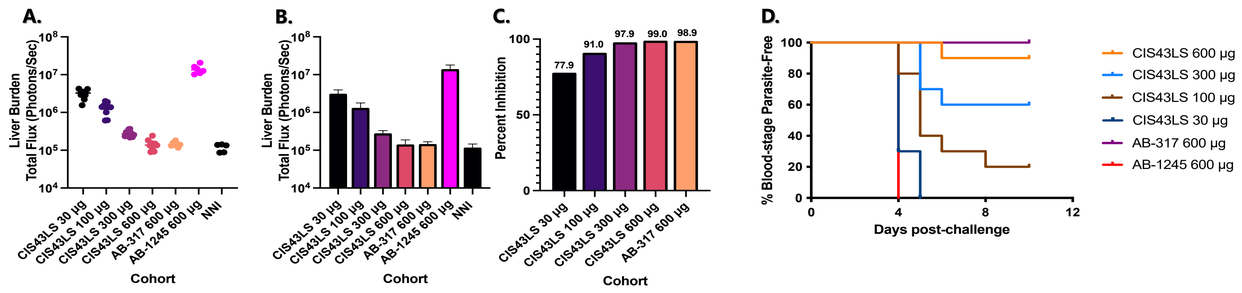

Figure 4. CIS43LS inhibits liver burden infection in a dose response manner and conferred partial sterile protection in mice challenged with the PbPf full CSP Tg parasite. C57BL/6 mice (n=10) were passively immunized with mAb CIS43LS and challenged 16 h later with 2000 transgenic spz for the liver burden model (**A**,**B**,**C**). For the sterile protection, mice were immunized and challenged with the bites of 5 infected mosquitos. The appearance of parasitemia was evaluated in blood smears (**D**).

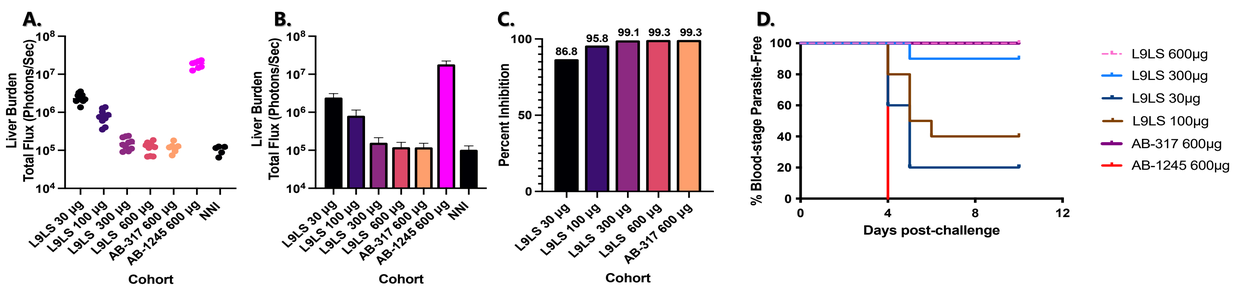

Figure 5. L9LS inhibits liver burden infection and confers sterile protection in a dose response manner in mice challenged with the PbPf full CSP Tg parasite. C57BL/6 mice (n=10) were passively immunized with mAb L9LS and challenged 16 h later with 2000 transgenic spz for the liver burden model (**A**,**B**,**C**). For sterile protection, mice were immunized and challenged with the bites of 5 infected mosquitos. The appearance of parasitemia was evaluated in blood smears (**D**).

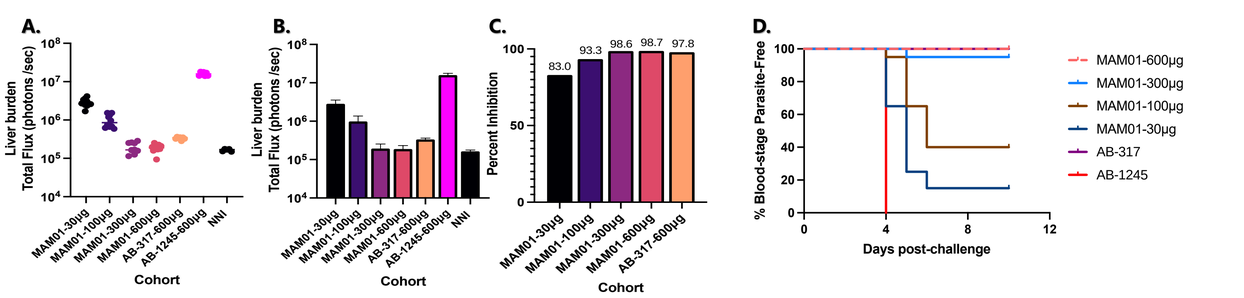

Figure 6. MAM01 inhibits liver burden infection and confers sterile protection in a dose response manner in mice challenged with the PbPf full CSP Tg parasite. C57BL/6 mice (n=10) were passively immunized with MAM01 and challenged 16 h later with 2000 transgenic spz for the liver burden model (**A**,**B**,**C**). For sterile protection, mice were immunized and challenged with the bites of 5 infected mosquitos. The appearance of parasitemia was evaluated in blood smears (**D**) .

Conclusions

- All three antibodies displayed dose-dependent parasite reduction, however only MAM01 and L9LS were equipotent in both mouse models, liver burden and bite parasitemia. CIS43 showed less potency in protection in both models.
- In the parasitemia model, MAM01 600 µg and L9LS 600 µg provided 100% protection through Day 10 post challenge; 300 µg was 95% protective for MAM01 and 90% protective for L9LS. Breakthrough infections occurred at lower doses (100 µg and 30 µg), which were 40% and 15% protective, respectively for MAM01 and 40% and 20% as protective for L9LS.
- For MAM01, in the liver burden assay, approximately 40 µg/mL of this antibody was shown to provided 95% protection from infection; similar levels of protection in the parasitemia assay, required a higher concentration (approximately 140 µg/mL).
- The equipotency of MAM01 with L9LS, which recently demonstrated protection in a human challenge model supports further development of MAM01.