

Experimental anti-malarial drug shows promise in first clinical trial

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Co-first author Aditya Gaur, MD, of St. Jude Infectious Diseases has discovered a fast-acting anti-malarial compound. Credit: St. Jude Children's Research Hospital

A fast-acting anti-malarial compound discovered at St. Jude Children's Research Hospital was well tolerated and showed promising anti-malarial



effects in the first study in humans. The findings appear online first this week in the journal *Lancet Infectious Diseases*.

"The results support further development of the compound SJ733 as a fast-acting component of combination anti-malarial therapy," said corresponding author Aditya Gaur, M.D., of the St. Jude Department of Infectious Diseases. "The drug was well tolerated and well absorbed with a rapid anti-parasitic effect." Gaur and James McCarthy, M.D., MBBS, of QIMR Berghofer Medical Research Institute, Australia, are the co-first authors.

Researchers are exploring ways to increase and/or extend blood levels of SJ733 to maximize its effectiveness in patients.

The challenge

Malaria is caused by a parasite that is transmitted by infected mosquitos and destroys <u>red blood cells</u>. The disease remains a leading cause of illness and death worldwide. Young children are among the most vulnerable. Artemisinin-based combination drug therapy is currently being used as first-line treatment for malaria. But its success is threatened by emerging <u>drug resistance</u>.

"Safe and effective anti-malarial drugs that work by new mechanisms are critically needed to combat drug-resistant disease," said senior author R. Kip Guy, Ph.D., dean of the University of Kentucky College of Pharmacy. Guy led the anti-malarial drug-discovery effort and preclinical development of SJ733 while chair of the St. Jude Department of Chemical Biology and Therapeutics. The preclinical trials showed that SJ733 worked against malaria parasites that are resistant to current frontline drugs.

The research effort reflects the global reach of this disease, Gaur said.



He noted that the work involved scientists working collaboratively and seamlessly exchanging information on three continents and across multiple time zones.

SJ733

SJ733 is one of the first in a new class of anti-malarial compounds to reach clinical trials. It works by disrupting the malaria parasite's ability to remove excess sodium from red blood cells. As sodium builds up, infected cells become less flexible. The cells are removed by the immune system or get caught in small blood vessels.

A total of 38 <u>healthy volunteers</u> were recruited as part of the Phase 1a study in Memphis and Phase 1b study in Brisbane, Australia. The 23 healthy volunteers in Memphis received increasing doses of SJ733 as part of the first-in-human study to understand SJ733 dosing, safety profile and metabolism, including absorption.

Based on those results the 15 Australian volunteers received SJ733 after being infected with malaria to understand the anti-malarial effectiveness of this new <u>drug</u>. The participants later received a curative dose of conventional anti-malarial combination therapy.

No significant SJ733 treatment-related side-effects were identified in any of the volunteers.

More information: Aditya H Gaur et al, Safety, tolerability, pharmacokinetics, and antimalarial efficacy of a novel Plasmodium falciparum ATP4 inhibitor SJ733: a first-in-human and induced blood-stage malaria phase 1a/b trial, *The Lancet Infectious Diseases* (2020). DOI: 10.1016/S1473-3099(19)30611-5



Provided by St. Jude Children's Research Hospital

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