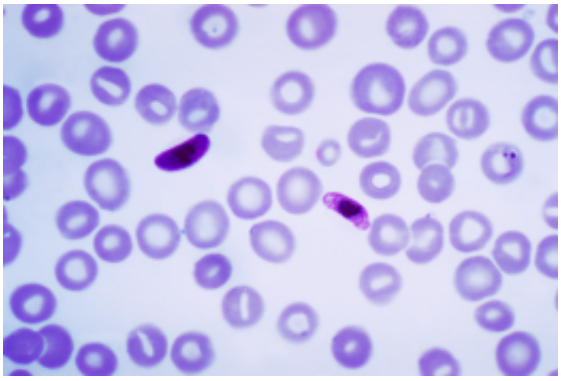
Successful preclinical tests for new agent against severe malaria

February 6 2017



This photomicrograph of a blood smear contains a macro- and microgametocyte of the Plasmodium falciparum parasite. Credit: Wikipedia.

Scientists from the Heidelberg University Hospital and the German Center for Infection Research (DZIF) have developed a new substance that has cured severe malaria in humanised mice.

Severe malaria, caused by the *Plasmodium falciparum* parasite, causes dangerous circulatory disorders and neurological complications. If the affected person is not treated immediately, the disease will inevitably lead to death. On the one hand, the currently used drugs artesunate and quinine have unwanted side effects and, on the other, more and more plasmodia are becoming resistant to them. Developing new drugs with other mechanisms of action is therefore essential.

"New drugs for treating severe malaria are indeed urgently needed," emphasizes Prof Michael Lanzer, DZIF scientist at the Heidelberg University Hospital. In a DZIF project, he developed the first promising candidate together with his research team: SC83288, the promising substance with a somewhat prosaic name has the required properties, and has already been successfully used to treat severe malaria in humanised mice.

Animal tests successful

The starting point of the drug development was benzamidine derivatives, which had been effective against different parasites in veterinary medicine but were not used as they have severe side effects. The scientists have now tried to modify these substances so that they become suitable to treat severe malaria. The substance was chemically modified to make it more tolerable without forfeiting its effect against parasites. "The new chemical structure is very well tolerated, is metabolised rapidly in the body and the crucial factor: in animal models, it can kill the severe malaria parasites in a short period of time," explains Lanzer.

For their tests, the scientists used mice with human blood cells and that had been infected with severe malaria. In this model system, SC83288 was effective in the late stages of malaria, during which the parasites are in the blood cells where they cause severe damage. Detailed preclinical studies on pharmacokinetics and toxicology showed consistent positive results for the substance which is to be administered intravenously. "We are now in the process of conducting the regulatory preclinical procedures and hope to initiate the clinical trials in 2018," says Lanzer.

More information: Stefano Pegoraro et al, SC83288 is a clinical development candidate for the treatment of severe malaria, *Nature Communications* (2017). DOI: 10.1038/NCOMMS14193

Provided by German Center for Infection Research