Start of Phase II trial of intravenous artesunate for children with severe malaria

28 August 2007, The Hague - A multicentre Phase II trial of intravenous artesunate will begin recruitment of patients in September. The €5.3 M trial, funded by the European and Developing Countries Clinical Trials Partnership (EDCTP), and sponsored by Medicines for Malaria Venture (MMV) will be conducted in Gabon and Malawi. It will evaluate the efficacy of two intravenous artesunate dosing regimens in clearing Plasmodium falciparum parasites in children with severe malaria. The trial protocol has been approved by the ethics committees and national regulatory authorities in Malawi and Gabon.

Severe malaria kills more than one million African children each year. Antimalarial chemotherapy is the mainstay of treatment. In Africa, intravenous quinine is currently used to treat children with severe malaria but it is poorly tolerated and has several side effects. In some south-east Asian countries, artemisinin-based treatments are already used in preference to quinine. Intravenous artesunate is now recommended by the World Health Organization for the treatment of severe malaria in adults in low transmission areas, but there is little information on its efficacy in children in high transmission regions, such as Africa.

This phase II randomised, double-blind, dose-finding study of the efficacy, safety, tolerability and pharmacokinetics of intravenous artesunate in African children with severe malaria has two main objectives:

1. To increase the body of evidence for the use of this drug in children in high transmission areas and show that the use of the potentially more toxic intravenous quinine can be avoided
2. To simplify the dosing regimen of intravenous Artesunate from 5 to 3 injections.

On occasion of the start of the trial, Prof. Charles Mgone, EDCTP Executive Director said: "The most rational and effective way to combat a serious problem such as malaria in Africa is to combine all available resources. Working in collaboration with MMV, EDCTP is supporting this partnership of European and African scientists to find a safe, affordable and accessible treatment for malaria in children"

"If we can show superior efficacy and/or safety and tolerability of the new artesunate regimen in African children, we are likely to see a major policy change in the treatment of severe malaria in African children,” said Dr. J Carl Craft, Chief Scientific officer of MMV. "I.V. artesunate has the potential to save countless young lives.”

Note to the editor:

For more information, please contact:
EDCTP - Ilona van den Brink, +31 (6) 206 899 48 (Mobile), brink@edctp.org
MMV - Anna Wang, +41 (79) 204 2875 (Mobile), wanga@mmv.org
Background information

Previous large studies in Asia and Africa have compared quinine with artemether to treat severe malaria. Artemether is safer and easier to use than quinine, but may not be the best artemisinin derivative because of erratic and slow absorption from intramuscular injection sites.

In contrast, artesunate, a water-soluble artemisinin-derivative, has proved to be less neurotoxic than the lipid-soluble artemether in preclinical studies. Furthermore, artesunate can be given intravenously, unlike artemether, making it one of the most rapidly acting antiparasitic agents, and an excellent candidate to challenge quinine’s position as the current therapy of choice for severe malaria. This has been further corroborated by a recent study in Asia, where artesunate was shown to be superior to quinine for adults with severe malaria.

Several partners have joined forces to launch this trial of GMP-formulated intravenous artesunate:

- Severe Malaria in African Children network (SMAC) – trial investigators
- Walter Reed Army Institute of Research in the USA (WRAIR) - donor of the drug
- Eberhard Karls Universität Tübingen – supervisory role
- Medicines for Malaria Venture (MMV) - sponsor responsible for the trial, will finance the monitoring, data management and analysis of the study
- European and Developing Countries Clinical Trials Partnership (EDCTP) – the funder of the trial.

The Phase II trial will be performed at the Albert Schweitzer Hospital in Lambaréné, Gabon, the Université de Médecine et Science de la Santé, Gabon and the Queen Elizabeth Central Hospital in Blantyre, Malawi. Capacity strengthening and training will be done in Lambaréné under the supervision of and in cooperation with the Vienna School of Clinical Research (VSCR), Vienna, and EDCTP.

Project team:

- Principal investigator Professor Dr. Peter G. Kremsner, Eberhard Karls Universität Tübingen
- Project coordinator Dr. Carsten Köhler, Eberhard Karls Universität Tübingen
- Sponsor’s Representative Dr. Jörg Möhrle, Director Clinical Development, MMV
- Sponsor’s Medical Expert Dr. Stephan Duparc, Medical Director, MMV.

About EDCTP

The European and Developing Countries Clinical Trials Partnership (EDCTP) is a unique partnership between European and sub-Saharan countries, aiming to reduce poverty by developing new clinical interventions to fight HIV/AIDS, malaria and tuberculosis. It unites 14 European Union (EU) Member States, plus Norway and Switzerland, with 47 sub-Saharan African countries. The focus of projects eligible for EDCTP funding is on phase II and III clinical trials in sub-Saharan Africa. EDCTP supports multicentre projects which combine clinical trials, capacity building and networking. EDCTP is currently part of the European Commission’s Sixth Framework Programme (FP6) for research and technological development, the European Union’s main instrument for the funding research in Europe. Currently, 9 EDCTP calls for proposals are open for application. For more information please consult the EDCTP website; www.edctp.org.

About MMV

Medicines for Malaria Venture (MMV) is a non-profit organisation dedicated to reducing the burden of malaria in disease-endemic countries by discovering, developing and delivering safe, effective, and affordable antimalarial drugs through effective public-private partnerships. After seven years of operation, MMV is managing the largest-ever portfolio of malaria drug research with over 25 projects in different stages of drug research and development of which three new artemisinin combination therapies (ACTs)
have completed phase III clinical trials and are ready for registration by a stringent regulatory authority. MMV’s goal is to register at least one new antimalarial before 2010 and maintain a sustainable pipeline of antimalarials to meet the needs of the 2.4 billion people at risk from this deadly disease. For further information please consult http://www.mmv.org