

Artesunate-Mefloquine Fixed-Dose Combination (ASMQ FDC) Proves Safe and Efficacious to Treat Children in Africa with Malaria

Clinical Trial Results Provide Evidence for Introducing This Artemisinin Derivative-based Combination Therapy (ACT) into Africa's Current Malaria Treatment Arsenal to Help Tackle the Number One Parasitic Killer

[New Orleans, USA, 4 November 2014] Presented today at the 63rd annual meeting of the American Society of Tropical Medicine and Hygiene (ASMTH), results of a multi-centre clinical trial in Africa, launched in 2008, to test the efficacy and tolerability of ASMQ fixed-dose combination (FDC) in children under 5 years of age with uncomplicated *falciparum* malaria showed that ASMQ FDC is as safe and efficacious as Artemether-Lumefantrine (AL) FDC – Africa's most widely adopted treatment.

The Phase IV, open-label, randomized, controlled, non-inferiority clinical trial included 945 children under 5 years of age, who were followed for 63 days. ASMQ FDC was administered once a day during three days. The study was conducted in three African countries: Burkina Faso, Kenya, and Tanzania.

Topline efficacy results, based on WHO efficacy analysis parameters (polymerase chain reaction (PCR) corrected):

- Efficacy of ASMQ is non inferior to AL
 - o Day 28: ASMQ = 97.5% / AM-LM = 94.6 %
 - o Day 42: ASMQ = 93.6% / AM-LM = 92.1%
 - o Day 63 : ASMQ = 90.9% / AM-LM = 89.7%

- No concerns of tolerability were demonstrated with ASMQ or with AL
 - o Very limited cases of vomiting, particularly early vomiting, led to treatment discontinuation in both treatments
 - o No unexpected adverse effects events were noted

Data in Africa on the combination (AS+MQ non fixed-dose) had previously demonstrated high efficacy, acceptable safety, and tolerability. Obtaining further clinical data on the combination of Artesunate with Mefloquine in children in Africa was recommended by the World Health Organization (WHO) and its Prequalification Programme. ASMQ FDC is one of several recommended ACTs that aim to delay the emergence of resistance to the individual drug components of the combination treatment. The treatment regimen is easier to administer by the fact that the two drugs are combined into one tablet that only requires once-a-day administration over three days (as compared to twice-a-day over three days for AL).

'The ASMQ fixed-dose combination has proven its importance among tools recommended by the WHO and can now be available to African children suffering from uncomplicated falciparum malaria', said Dr Bernard Pécoul, Executive Director of DNDi. 'Considering that a child dies every 30 seconds from malaria, we hope that governments in affected African countries will now take up this additional treatment option to ensure their populations have access to several ACTs.'

ASMQ FDC was originally developed by DNDi and the Brazilian government-owned pharmaceutical company Farmanguinhos/Fiocruz and was registered in Brazil in 2008. A South-South technology transfer between Farmanguinhos and Cipla, India, was achieved in 2010 to facilitate the implementation of ASMQ FDC worldwide and was pre-qualified by the WHO Prequalification Programme in 2012. ASMQ FDC is currently registered in Brazil, India, Myanmar, Malaysia, Vietnam, Tanzania, and Niger, and pending registration in 17 countries in Africa and Asia.

Study Funding & Partners

Funding for this study was provided to DNDi by the Swiss Agency for Development and Cooperation (SDC), Switzerland; European and Developing Countries Clinical Trials Partnerships (EDCTP); French Development Agency (AFD), France; Department for International Development (DFID), United Kingdom; Dutch Ministry of Foreign Affairs (DGIS), The Netherlands; Médecins Sans Frontières (Doctors Without Borders); and the Fondation ARPE, Switzerland. Partners in the study include: staff at study sites; study monitors; Data Safety Monitoring Committee (DSMC) ; Cardinal Systems, Paris, France; Epicentre, Mbarara, Uganda; CHUV, Lausanne, Switzerland; and Farmanguinhos, Brazil. Clinical investigators of the study were from the following partner institutions: Centre National de Recherche et de Formation sur le Paludisme, Ouagadougou, Burkina Faso; Kenya Medical Research Institute (KEMRI), Kisumu, Kenya; National Institute for Medical Research, Korogwe, United Republic of Tanzania; Ifakara Health Institute, Bagamoyo, United Republic of Tanzania; National Institute for Medical Research, Kilosa, United Republic of Tanzania; Centre for Clinical Research, Kenya Medical Research Institute (KEMRI), Nairobi, Kenya; and Drugs for Neglected Diseases *initiative*, Geneva, Switzerland.

About Malaria

Since the year 2000, remarkable progress has been made in the fight against malaria, with a 42% reduction in deaths globally. The WHO estimates that in 2012 there were 207 million of cases of malaria, and that 627,000 deaths were attributable to the disease, mostly in Africa (90%). Children continue to be the worst affected, accounting for 77% of all deaths, with an estimated 462,000 deaths in African children under the age of five in 2012. Most deaths were due to *Plasmodium falciparum*, however *P. vivax* is increasingly recognized as a cause of severe malaria and death.

About ASMQ FDC

- Simple prescription which is easy to use, based on once-daily administration
- Dosage selection of the tablets allows for a simple and adapted regimen for children and adults
- Adapted packaging
- High compliance
- WHO Prequalification in September 2012 (Cipla)
- Registered in Brazil in 2008, India in 2011, Malaysia and Myanmar in 2012, Tanzania in 2013, Vietnam and Niger in 2014
- Currently filed for registration in 17 additional countries in Africa and Asia

About DNDi

The Drugs for Neglected Diseases *initiative* (DNDi) is a not-for-profit research and development (R&D) organization working to deliver new treatments for the most neglected diseases, in particular sleeping sickness (human African trypanosomiasis), Chagas disease, leishmaniasis, filaria, and paediatric HIV/AIDS. Since its inception in 2003, DNDi has delivered six new treatments: two fixed-dose antimalarials (ASMQ and ASMQ); nifurtimox-eflornithine combination therapy (NECT) for late-stage sleeping sickness; sodium stibogluconate and paromomycin (SSG&PM) combination therapy for visceral leishmaniasis in Africa; a set of combination therapies for visceral leishmaniasis in Asia; and a paediatric dosage form of benznidazole for Chagas disease. DNDi was founded by Médecins Sans Frontières/Doctors without Borders (MSF), Indian Council of Medical Research, Kenya Medical Research Institute, Brazil's Oswaldo Cruz Foundation, Ministry of Health of Malaysia, and Institut Pasteur in France, with the UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR) as a permanent observer.

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