Synthetic antimalaria drug enters clinical trials

Researchers, supported by funding from the Medicines for Malaria Venture (MMV), have developed a synthetic antimalaria drug that works on the same principle as artemisinin (Nature 2004; 430: 900–04). The new drug, OZ277, has entered phase I safety trials in the UK and, according to MMV chief executive officer Chris Hentschel, “if OZ277 fulfils its early promise, it could be registered for use as early as 2008”.

Chloroquine, which costs US$0.10 per course, has been the mainstay of malaria treatment for more than 50 years. But chloroquine is increasingly impotent against Plasmodium falciparum, and the price tag of newer drugs such as artemisinin, a natural product isolated from sweet wormwood, and its semisynthetic derivatives is beyond the pockets of developing countries.

Consequently, researchers have been trying to design cheaper, totally synthetic compounds containing the active peroxide bond of artemisinin. But to date, says author Jonathan Vennerstrom (University of Nebraska Medical Center, Omaha, NE, USA), “all these attempts have failed”.

OZ277, says Vennerstrom, may provide a solution. “During its development process, we predetermined the characteristics we wanted of a synthetic endoperoxide-based drug. For example, it had to be inexpensive to make and it had to be curative within 3 days of treatment.”

MMV became involved in the development of OZ277 in 2000. At that time, MMV, a non-profit organisation dedicated to discovering, developing, and delivering affordable antimalarials through public-private partnership, was looking for early projects that merited being advanced to full pharmaceutical research and development status. MMV’s know-how and funding enabled Vennerstrom and his collaborators to execute a research plan with all the parts typically found in a pharmaceutical company. The result, OZ277, is now being further developed by MMV in collaboration with Ranbaxy Laboratories, Ltd (New Delhi, India).

“This synthetic peroxide is interesting and promising”, comments Nicholas White, professor of tropical medicine at Mahidol University (Bangkok, Thailand) and Oxford University (Oxford, UK), “but many drugs fail the clinical testing stage”.

Tuberculosis vaccine trial underway

South Africa is to start the first human trial of a new tuberculosis vaccine in the southern hemisphere; this was announced on August 16, 2004 during a paediatrics and allergy meeting in Cape Town.

The trial, coordinated by Greg Hussey (Paediatric Infectious Diseases Division, University of Cape Town), is a phase 1, randomised, double-blind study aimed at assessing the safety and immunogenicity of the rBCG30 vaccine administered intradermally. Approximately 50 healthy adults from the Boland-Overberg region of the Western Cape will be enrolled into the study, which is expected to continue for up to 5 years.

According to Hussey, in some developing countries where tuberculosis is endemic, extensive neonatal vaccination programmes using BCG have reduced the incidence of severe childhood tuberculosis. However, the efficacy of vaccination with BCG against the development of pulmonary tuberculosis in adults has been as poor as 0% in countries with the greatest burden of tuberculosis. Possible explanations for the lack of protection against adult pulmonary tuberculosis include prior sensitisation to environmental mycobacteria, and variation in BCG substrains used for production of the vaccine.

Given the rapidly worsening global malaria situation, White cautions against over reliance on new discoveries that “might in the fullness of time lead to something good. We need to get the already available artemisinin combinations up and deployed now”. This strategy, which is endorsed by MMV, will require governments and financial institutions to commit funds of US$300–500 million per year to subsidise drug costs, according to a recent US Institute of Medicine report (http://www.nap.edu/openbook/030909218/html/1.html).

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