Atovaquone-Proguanil for Falciparum Malaria in the Philippines

To the Editor—Bustos et al. consider that atovaquone-proguanil (AP) constitutes an important therapeutic advance for the treatment of falciparum malaria in the Philippines and elsewhere [1]. This claim is made because the 100% cure rate of AP in their study was significantly higher than the cure rates of the 2 other regimens evaluated, chloroquine alone and chloroquine-sulfadoxine-pyrimethamine (CSP). However, CSP cured 88% of patients, which, as the authors themselves state in their discussion section, is a reasonably good cure rate. The data presented show that chloroquine resistance is clinically important in the study population but do not support the authors’ contention that Plasmodium falciparum in the Philippines is “resistant to standard antimalarial drugs.” No published data document that P. falciparum parasites highly resistant to sulfadoxine-pyrimethamine are prevalent in the Philippines. On the contrary, the high cure rate achieved by CSP, reported by Bustos et al., is encouraging because it suggests that affordable drugs, like this combination, could still be effective.

AP is potentially susceptible to the rapid development of resistance if deployed alone, since single-point mutations in the P. falciparum cytochrome B gene confer high-level resistance [2]. At current prices, the cost of AP treatment is almost 200 times that of CSP. It might be better to reserve AP as a second-line alternative for malaria therapy in the Philippines while less-expensive options are still available.

George Watt
HIV Interaction Section, Retrovirology Department,
US Army Medical Component±Armed Forces Research Institute of Medical Sciences, Bangkok, Thailand

References

Reply

To the Editor—Atovaquone/proguanil was developed as a fixed-dose combination tablet (Malarone) because atovaquone-resistant parasites can be selected rapidly in about one-third of patients after treatment with atovaquone alone [1]. Recrudescence after treatment with these 2 drugs in combination is rare, the combination is effective against proguanil-resistant malaria, and the few parasites isolated after treatment with the combination have not been resistant to atovaquone [2]. Although resistance has not been an issue in individual patients treated with atovaquone/proguanil, widespread use of any antimalarial drug will increase the risk that resistance may occur and spread. In addition, atovaquone is expensive to manufacture and atovaquone/proguanil therefore costs more than other antimalarial drugs.

Thus we agree with Dr. Watt that atovaquone/proguanil should be reserved, in endemic areas, for second- or third-line therapy of patients who have failed treatment with first- and second-line drugs. In fact, this is the policy of the Malarone Donation Program—a program created by Glaxo Wellcome in partnership with the Task Force for Child Survival and Development, to make this highly effective but expensive treatment available to those who need it most but are least able to afford it. The Program also stipulates various procedures to ensure appropriate use of donated product, thereby preserving its utility as a valuable antimalarial drug [3]. For patients who have failed therapy with other agents and for nonimmune persons who may be infected with multidrug-resistant Plasmodium falciparum, atovaquone/proguanil is an important therapeutic advance.

Dorina Bustos1 and David B. A. Hutchinson2
1Research Institute for Tropical Medicine, Manila, Philippines; 2Westerham, Kent, United Kingdom

References

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