Halofantrine Information Paper

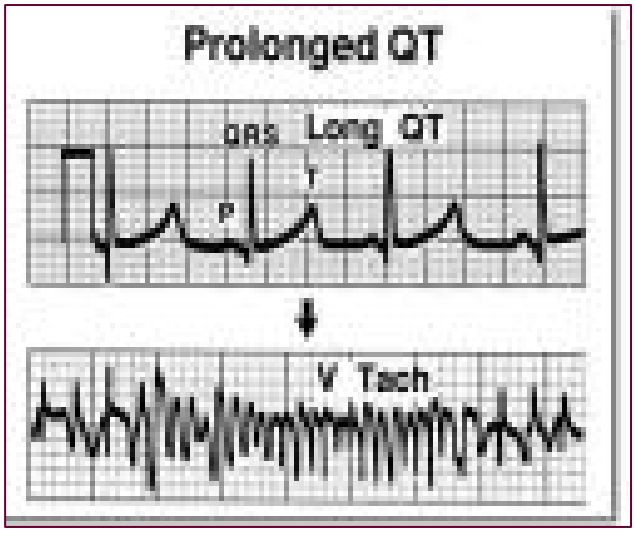
A licensed antimalarial drug developed by DoD and its partners

UNITED STATES ARMY MEDICAL RESEARCH AND MATERIEL COMMAND

Product Name: Halofantrine
Commercial name: Halfan
Application: Antimalarial drug for treatment only
Date of U.S. licensure: July 1992
Type of product: an aminoalcohol, member of the 9-phenanthrenemethanol class (not related to quinine)
Company of manufacture: SmithKline Beecham

Reasons for development: Halofantrine was developed as a back-up drug to mefloquine to treat chloroquine-resistant *P. falciparum* malaria.

Role of DoD: Halofantrine (WR 171669) was developed at WRAIR in collaboration with SmithKline and the World Bank/World Health Organization Special Programme for Training and Research in Tropical Diseases (WHO/TDR) beginning in the late 1960's and early 1970's. Halofantrine was created by replacing the quinoline moiety of the quinoline methanols (quinine-type compounds) by other aromatic groups to form the aryl(amino)carbinols. Of this class of compounds, halofantrine, a 9-phenanthrenemethanol, is the most potent. Commercial development began in the 1980's. The drug is used for treatment of falciparum malaria outside the U.S., but development as a prophylactic drug was stopped over concerns over the short half-life (1-2 days) and adverse effects.



Prolonged QT interval on an EKG strip.

Current status:
The usefulness of halofantrine is limited by possible cross-resistance with mefloquine, cardiac toxicity, and poor absorption. The drug is no longer licensed in the U.S. because of potential fatal cardiotoxicity related to prolonged QT intervals on electrocardiogram. It is not recommended for use in pregnant or breastfeeding women (the drug is embryotoxic and excreted in breast milk). Absorption is slow but enhanced by fatty foods, but serum levels are unpredictable. The drug is poorly soluble in water, and there is no injectable form of the drug. A micronized formulation was tested and proved promising but was not further developed.

The main metabolite of halofantrine appears to be less toxic and equally effacious as an antimalarial, but was not developed as a marketable product.

Halofantrine references:

Bryson HM, Goa KL. Halofantrine. A review of its antimalarial activity, pharmacokinetic properties and therapeutic potential. Drugs 1992; 43:236-258.