Scopus

Documents

Lek-Uthai, U.[a] , Suwanarusk, R.[b c] , Ruengweerayut, R.[d] , Skinner-Adams, T.S.[e] , Nosten, F.[f g h] , Gardiner, D.L.[e] , Boonma, P.[a] , Piera, K.A.[b] , Andrews, K.T.[e] , MacHunter, B.[b] , McCarthy, J.S.[e] , Anstey, N.M.[b] , Price, R.N.[b g] , Russell, B.[b c i]

Stronger activity of human immunodeficiency virus type 1 protease inhibitors against clinical isolates of Plasmodium vivax than against those of P. falciparum

(2008) *Antimicrobial Agents and Chemotherapy*, 52 (7), pp. 2435-2441. Cited 19 times.

[a] Department of Parasitology, Faculty of Public Health, Mahidol University, Bangkok, Thailand
[b] Infectious Diseases Division, Menzies School of Health Research, Charles Darwin University, Darwin, NT, Australia
[c] Laboratory for Malaria Immunobiology, Singapore Immunology Network, Agency for Science Technology and Research (ASTAR), Singapore, Singapore
[d] Mae Sod Hospital, Tak, Thailand
[e] Queensland Institute, Medical Research and Australian Centre, International and Tropical Health and Nutrition, Brisbane, QLD, Australia
[f] Shoklo Malaria Research Unit, Mae Sod, Thailand
[g] Centre for Clinical Vaccinology and Tropical Medicine, Churchill Hospital, Oxford OX3 7LJ, United Kingdom
[h] Faculty of Tropical Medicine, Mahidol University, Rajvithi Road, Bangkok, Thailand
[i] Laboratory for Malaria Immunobiology, Singapore Immunology Network, 8A Biomedical Grove, #03-06 Immunos, Singapore 138648, Singapore

Abstract
Recent studies using laboratory clones have demonstrated that several antiretroviral protease inhibitors (PIs) inhibit the growth of Plasmodium falciparum at concentrations that may be of clinical significance, especially during human immunodeficiency virus type 1 (HIV-1) and malaria coinfection. Using clinical isolates, we now demonstrate the in vitro effectiveness of two HIV-1 aspartic PIs, saquinavir (SQV) and ritonavir (RTV), against P. vivax (n = 30) and P. falciparum (n = 20) from populations subjected to high levels of mefloquine and artesunate pressure on the Thailand-Myanmar border. The median 50% inhibitory concentration values of P. vivax to RTV and SQV were 2,233 nM (range, 732 to 7,738 nM) and 4,230 nM (range, 1,326 to 8,452 nM), respectively, both within the therapeutic concentration range commonly found for patients treated with these PIs. RTV was fourfold more effective at inhibiting P. vivax than it was at inhibiting P. falciparum, compared to a twofold difference in SQV sensitivity. An increased P. falciparum mdr1 copy number was present in 33% (3/9) of isolates and that of P. vivax mdr1 was present in 9% of isolates (2/22), but neither was associated with PI sensitivity. The inter-Plasmodium sp. variations in PI sensitivity indicate key differences between P. vivax and P. falciparum. PI-containing antiretroviral regimens may demonstrate prophylactic activity against both vivax and falciparum malaria in HIV-infected patients who reside in areas where multidrug-resistant P. vivax or P. falciparum is found.

References

- Alker, A.P., Lim, P., Sem, R., Shah, N.K., Yi, P., Bouth, D.M., Tsuyuoka, R., Meshnick, S.R.
  Pfmdr1 and in vivo resistance to artesunate- mefloquine in falciparum malaria on the Cambodian-Thai border
  (2007) *Am. J. Trop. Med. Hyg*, 76, pp. 641-647.

- Andrews, K.T., Gatton, M.L., Skinner-Adams, T.S., McCarthy, J.S., Gardiner, D.L.
  HIV-malaria interactions: Don't forget the drugs
  (2007) *Science*, 315, p. 1791.

- Baird, J.K.
  Chloroquine resistance in Plasmodium vivax
  (2004) *Antimicrob. Agents Chemother*, 48, pp. 4075-4083.

- Banerjee, R., Liu, J., Beatty, W., Pelosof, L., Klemba, M., Goldberg, D.E.
  Four plasmepsins are active in the Plasmodium falciparum food vacuole, including a protease with an active-site histidine
  (2002) *Proc. Natl. Acad. Sci. USA*, 99, pp. 990-995.

- Bonilla, J.A., Bonilla, T.D., Yowell, C.A., Fujioka, H., Dame, J.B.
  Critical roles for the digestive vacuole plasmepsins of Plasmodium falciparum in vacuolar function
  (2007) *Mol. Microbiol*, 65, pp. 64-75.

- Brockman, A., Price, R.N., van Vugt, M., Heppner, D.G., Walsh, D., Sookto, P., Wimonwattrawatee, T., Nosten, F.
  Plasmodium falciparum antimalarial drug susceptibility on the north-western border of Thailand during five years of extensive use of artesunate-mefloquine
  (2000) *Trans. R. Soc. Trop. Med. Hyg*, 94, pp. 537-544.

- Brouwer, K.C., Mirel, L.B., Yang, C., Lal, R.B., Kolezak, M.S., Van Eijk, A.M., Ayisi, J., Lal, A.A.
  Subclinical Plasmodium falciparum infection and HIV-1 viral load
  (2007) *Emerg. Infect. Dis*, 13, pp. 351-353.

- Coombs, G.H., Goldberg, D.E., Klemba, M., Berry, C., Kay, J., Mottram, J.C.
  Aspartic proteases of Plasmodium falciparum and other parasitic protozoa as drug targets
  (2001) *Trends Parasitol*, 17, pp. 532-537.

- Dame, J.B., Yowell, C.A., Omara-Opyene, L., Carlton, J.M., Cooper, R.A., Li, T.
  Plasmepsin 4, the food vacuole aspartic proteinase found in all Plasmodium spp. infecting man
  (2003) *Mol. Biochem. Parasitol*, 130, pp. 1-12.

- Dupuis, M.L., Flego, M., Molinari, A., Cianfriglia, M.
  Saquinavir induces stable and functional expression of the multidrug transporter P-glycoprotein in human CD4 T-lymphoblastoid CEMrev cells
  (2003) *HIV Med*, 4, pp. 338-345.

- Dupuis, M.L., Tombesi, M., Sabatini, M., Cianfriglia, M.
  Differential effect of HIV-1 protease inhibitors on P-glycoprotein function in multidrug-resistant variants of the human CD4⁻ T lymphoblastid CEM cell line
  (2003) *Chemotherapy*, 49, pp. 8-16.

- Ersmark, K., Samuelsson, B., Hallberg, A.
  Plasmepsins as potential targets for new antimalarial therapy
  (2006) *Med. Res. Rev*, 26, pp. 626-666.

- Gusasira, A.F., Kamya, M.R., Achan, J., Mebrahtu, T., Kalyango, J.N.
  High risk of neutropenia in HIV-infected children following treatment with artesunate plus amodiaquine for uncomplicated malaria in Uganda
  (2008) *Clin. Infect. Dis*, 46, pp. 985-991.

- Li, T., Yowell, C.A., Beyer, B.B., Hung, S.H., Westling, J., Lam, M.T., Dunn, B.M., Dame, J.B.
  Recombinant expression and enzymatic subsite characterization of plasmepsin 4 from the four Plasmodium species infecting man
  (2004) *Mol. Biochem. Parasitol*, 135, pp. 101-109.

- Liu, J., Gluzman, I.Y., Drew, M.E., Goldberg, D.E.
  The role of Plasmodium falciparum food vacuole plasmepsins
  (2005) *J. Biol. Chem*, 280, pp. 1432-1437.

- Mendis, K., Sina, B.J., Marchesini, P., Carter, R.
  The neglected burden of Plasmodium vivax malaria
  (2001) *Am. J. Trop. Med. Hyg*, 64, pp. 97-106.

- Okereke, C.S.
  Management of HIV-infected pregnant patients in malaria-endemic areas: Therapeutic and safety considerations in concomitant use of antiretroviral and antimalarial agents
  (1999) *Clin. Ther*, 21, pp. 1456-1496,1427-1428.

- Omara-Opyene, A.L., Moura, P.A., Sulsona, C.R., Bonilla, J.A., Yowell, C.A., Fujioka, H., Fidock, D.A., Dame, J.B.
  Genetic disruption of the Plasmodium falciparum digestive vacuole plasmepsins demonstrates their functional redundancy
  (2004) *J. Biol. Chem*, 279, pp. 54088-54096.

- Owen, A., Janneh, O., Hartkoorn, R.C., Chandler, B., Bray, P.G., Martin, P., Ward, S.A., Back, D.J.
  In vitro synergy and enhanced murine brain penetration of saquinavir coadministered with mefloquine
  (2005) *J. Pharmacol. Exp. Ther*, 314, pp. 1202-1209.

- Parikh, S., Gut, J., Istvan, E., Goldberg, D.E., Havlir, D.V., Rosenthal, P.J.
  Antimalarial activity of human immunodeficiency virus type 1 protease inhibitors
  (2005) *Antimicrob. Agents Chemother*, 49, pp. 2983-2985.

- Parikh, S., Liu, J., Sijwali, P., Gut, J., Goldberg, D.E., Rosenthal, P.J.
  Antimalarial effects of human immunodeficiency virus type 1 protease inhibitors differ from those of the

aspartic protease inhibitor pepstatin
(2006) *Antimicrob. Agents Chemother*, 50, pp. 2207-2209.

- Price, R., Luxemburger, C., van Vugt, M., Nosten, F., Kham, A., Simpson, J., Looareesuwan, S., White, N.J.
Artesunate and mefloquine in the treatment of uncomplicated multidrug-resistant hyperparasitaemic falciparum malaria
(1998) *Trans. R. Soc. Trop. Med. Hyg*, 92, pp. 207-211.

- Price, R.N.C., Cassar, Brockman, A., Duraisingh, M., van Vugt, M., White, N.J., Nosten, F., Krishna, S.
The pfmdr1 gene is associated with a multidrug-resistant phenotype in Plasmodium falciparum from the western border of Thailand
(1999) *Antimicrob. Agents Chemother*, 43, pp. 2943-2949.

- Price, R.N., Tjitra, E., Guerra, C.A., Yeung, S., White, N.J., Anstey, N.M.
Vivax malaria: Neglected and not benign
(2007) *Am. J. Trop. Med. Hyg*, 77, pp. 79-87.

- Price, R.N., Uhlemann, A.C., Brockman, A., McGready, R., Ashley, E., Phaipun, L., Patel, R., Krishna, S.
Mefloquine resistance in Plasmodium falciparum and increased pfmdr1 gene copy number
(2004) *Lancet*, 364, pp. 438-447.

- Pukrittayakamee, S., Chantra, A., Simpson, J.A., Vanijanonta, S., Clemens, R., Looareesuwan, S., White, N.J.
Therapeutic responses to different antimalarial drugs in vivax malaria
(2000) *Antimicrob. Agents Chemother*, 44, pp. 1680-1685.

- Redmond, A.M., Skinner-Adams, T., Andrews, K.T., Gardiner, D.L., Ray, J., Kelly, M., McCarthy, J.S.
Antimalarial activity of sera from subjects taking HIV protease inhibitors
(2007) *AIDS*, 21, pp. 763-765.

- Rojanawatsirivet, C., K. Congpuong, S. Vijaykadga, S. Thongphua, K. Thongsri, K. N. Bangchang, P. Wilairatana, and W. H. Wernsdorfer. 2004. Declining mefloquine sensitivity of Plasmodium falciparum along the Thai-Myanmar border. Southeast Asian J. Trop. Med. Public Health 35:560-565.

- Russell, B., Chalfein, F., Prasetyorini, B., Kenangalem, E., Piera, K., Suwanarusk, R., Brockman, A., Price, R.N.
Determinants of in vitro drug susceptibility testing of Plasmodium vivax
(2008) *Antimicrob. Agents Chemother*, 52, pp. 1040-1045.

- Russell, B.M., Udomsangpetch, R., Rieckmann, K.H., Kotecka, B.M., Coleman, R.E., Sattabongkot, J.
Simple in vitro assay for determining the sensitivity of Plasmodium vivax isolates from fresh human blood to antimalariais in areas where P. vivax is endemic
(2003) *Antimicrob. Agents Chemother*, 47, pp. 170-173.

- Skinner-Adams, T.S., Andrews, K.T., Melville, L., McCarthy, J., Gardiner, D.L.
Synergistic interactions of the antiretroviral protease inhibitors saquinavir and ritonavir with chloroquine and mefloquine against Plasmodium falciparum in vitro
(2007) *Antimicrob. Agents Chemother*, 51, pp. 759-762.

- Skinner-Adams, T. S., J. S. McCarthy, D. L. Gardiner, and K. T. Andrews. 2 May 2008, posting date. HIV and malaria co-infection: interactions and consequences of chemotherapy. Trends Parasitol. doi:10.1016/j.pt.2008.03.008.

- Skinner-Adams, T.S., McCarthy, J.S., Gardiner, D.L., Hilton, P.M., Andrews, K.T.
Antiretrovirals as antimalarial agents
(2004) *J. Infect. Dis*, 190, pp. 1998-2000.

- Slutsker, L., Marston, B.J.
HIV and malaria: Interactions and implications
(2007) *Curr. Opin. Infect. Dis*, 20, pp. 3-10.

- Suwanarusk, R., Russell, B., Chavchich, M., Chalfein, F., Kenangalem, E., Kosaisavee, V., Prasetyorini, B., Price, R.N.
Chloroquine resistant Plasmodium vivax: In vitro characterisation and association with molecular polymorphisms
(2007) *PLoS ONE*, 2, pp. e1089.

- Uhlemann, A.C., McGready, R., Ashley, E.A., Brockman, A., Singhasivanon, P., Krishna, S., White, N.J., Price, R.N.
Intrahost selection of Plasmodium falciparum pfmdr1 alleles after antimalarial treatment on the northwestern border of Thailand
(2007) *J. Infect. Dis*, 195, pp. 134-141.

- Verhoeff, F.H., Brabin, B.J., Hart, C.A., Chimsuku, L., Kazembe, P., Broadhead, R.L.
Increased prevalence of malaria in HIV-infected pregnant women and its implications for malaria control
(1999) *Trop. Med. Int. Health*, 4, pp. 5-12.

- Williams, G.C., Liu, A., Knipp, G., Sinko, P.J.
Direct evidence that saquinavir is transported by multidrug resistance-associated protein (MRP1) and canalicular multispecific organic anion transporter (MRP2)
(2002) *Antimicrob. Agents Chemother*, 46, pp. 3456-3462.

Document Type: Article
Source: Scopus