



7th International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV

13–16 November 2005, Dublin, Ireland

A review of the discovery and exploratory development of Maraviroc (UK-427,857): a novel CCR5 antagonist for the treatment of HIV

CA Hitchcock

Pfizer Global Research and Development, Sandwich Laboratories, Sandwich, UK

***Antiviral Therapy* 2005; 10:L2 (abstract no. P3)**

The successful future management of patients infected with HIV requires the discovery and development of new agents that combine novel mechanisms of action with pharmacokinetic, safety and toleration profiles that are consistent with chronic, durable therapy. It is against this backdrop, that the inhibition of HIV fusion and entry into immune function cells is one of the most promising approaches to discovering new classes of antiretroviral agents that have the potential to meet the aforementioned target profile.

Maraviroc is a novel CCR5 antagonist and is the most advanced clinical candidate in Pfizer's CCR5 discovery and development programme. It is exquisitely selective for the CCR5 receptor and demonstrates potent activity in vitro against both lab-adapted and primary clinical HIV isolates spanning all of the clades, including viruses that are resistant to current classes of HIV agents. Maraviroc has been evaluated in >500 volunteers and in 95 patients infected with HIV, including 40 women. It was well tolerated and at doses up to and including 300mg twice daily the adverse event profile was similar to that of placebo. The most common treatment-related adverse events were headache, dizziness, nausea, asthenia, flatulence and rhinitis. There was no dose-related change in QTcF.

Maraviroc has demonstrated encouraging short-term (10 day), single-agent efficacy as measured by reductions in viral loads in asymptomatic HIV patients; doses of 300 mg once daily and 300 mg twice daily resulted in mean maximum HIV RNA reductions of 1.60 log₁₀ and 1.84 log₁₀, respectively.

The clinical pharmacology of Maraviroc has been studied extensively in volunteers. It is a substrate for cytochrome P-450 3A4 (CYP 3A4), but it does not significantly inhibit or induce CYP 3A4 or other cytochrome P-450 enzymes. Studies both with CYP 3A4 inhibitors and inducers have demonstrated that Maraviroc will have manageable drug interactions when used in the setting of HIV patients receiving highly active antiretroviral therapy.

In summary, Maraviroc has potency, pharmacokinetic and toleration profiles that merit its further evaluation as a new therapy for patients with HIV/AIDS.



[Download PDF of this abstract.](#)

051113
P3

Copyright © 2005 - [International Medical Press Ltd.](#) Reproduction of this abstract (other than one copy for personal reference) must be cleared through the International Medical Press Ltd. 2-4 Idol Lane, London EC3R 5DD UK.