Retrovirology

BioMed Central

Oral presentation



# Viciriviroc Is a Novel, Potent CCR5 Inhibitor With Outstanding Pharmaceutic, Pharmacokinetic and PharmaCodynamic (PK/PD) Properties

Lisa Dunkle*‡, Anther Keung, Angela Sansone and Julie Strizki

Address: Schering-Plough Research Institute, Kenilworth, NJ 07033 USA

Email: Lisa Dunkle* - lisa.dunkle@spcorp.com

* Corresponding author ‡Presenting author

*from* 2005 International Meeting of The Institute of Human Virology
Baltimore, USA, 29 August – 2 September 2005

Published: 8 December 2005

*Retrovirology* 2005, **2**(Suppl 1):S12 doi:10.1186/1742-4690-2-S1-S12

The CCR5 chemokine receptor is a promising target for antiretroviral therapy because of its role as a coreceptor for HIV entry and propagation of infection. Viciriviroc, a small molecule CCR5 inhibitor being studied in clinical trials, has shown potent *in vitro* activity against HIV ($IC_{90}$<13 nM). In addition, the pharmaceutic and PK/PD properties of viciriviroc appear to distinguish it from other compounds in clinical development.

Viciriviroc is highly water-soluble and demonstrates oral bioavailability of >89% in rats and monkeys. The compound is modestly human plasma protein-bound (≈ 84%) and widely distributed in the extra vascular space. Absorption and exposure in humans are linear and dose-proportional, with a terminal phase half-life >24 hours supportive of once daily dosing. Variability in absorption is modest (20–40%). Exposure to viciriviroc, a substrate for CYP3A4, is "boosted" by CYP3A4 inhibition with ritonavir (RTV), without being affected by other metabolizing enzymes or pGp. Because of the high oral bioavailability and highly predictable exposure, particularly when boosted with as little as 100 mg RTV, potent HIV suppression of 1.5 $\log_{10}$ is anticipated with as little as 10 mg viciriviroc daily with RTV. Dosage adjustments are not expected in combination regimens.

Viciriviroc shows particular promise as an HIV therapeutic due to pharmaceutic, PK/PD properties that support its potent activity and convenient once daily dosing.