

UC-781



Drug Description

UC-781 is a thiocarboxanilide nonnucleoside reverse transcriptase inhibitor (NNRTI). [1]

HIV/AIDS-Related Uses

UC-781 is a nonnucleoside reverse transcriptase inhibitor currently being developed as a vaginal microbicide. UC-781 has been studied in animal models and will soon enter a Phase I clinical trial in humans.[2]

Pharmacology

In vitro studies have shown UC-781 to be a rapid tight-binding inhibitor of HIV-1 reverse transcriptase.[3] It is effective against transmission of both cell-free and cell-associated HIV and has an intracellular antiviral protective effect with a half-life of 5.5 days.[4] [5]

In vitro exposure of human cervical tissue to 0.5 microM UC-781 for 30 minutes, followed by extensive wash of the residual drug, resulted in 95% reduction of subsequent viral infection as determined by immunohistochemistry and p24 determination. Furthermore, 1 microM UC-781 pretreatment for 20 minutes, or 10 microM UC-781 pretreatment for 2 minutes, resulted in total protection of the cervical tissue from both T- and M- tropic HIV-1 isolates, as well as from cell-associated HIV-1 infection. Twenty minute incubation with 10 microM UC-781 completely protected the cervical tissue even when it was challenged with HIV-1 48 hours after the drug pretreatment. UC-781 was not toxic to the cervical tissue, even when the tissue was exposed to 10 microM UC-781 for 24 hours.[6]

UC-781 has been studied with AZT in vitro. A 1:1 molar combination of AZT plus UC-781 showed high-level synergy in inhibiting replication of an AZT-resistant clinical isolate of HIV. The time to development of HIV resistance to a 1:1 molar combination of AZT plus UC-781 was significantly delayed compared to that for either drug alone.[7]

Clinical Trials

For information on clinical trials that involve UC-781, visit the ClinicalTrials.gov web site at <http://www.clinicaltrials.gov>. In the Search box, enter: UC-781 AND HIV Infections.

Dosing Information

Mode of Delivery: Intravaginal.[8]

Dosage Form: Gel.[9]

Other Names

UC781[10]

N-[4-chloro-3-(3-methyl-2-butenyloxy)phenyl]-2-methyl-3-furancbothiamide[11]

Further Reading

Zussman A, Lara L, Lara HH, Bentwich Z, Borkow G. Blocking of cell-free and cell-associated HIV-1 transmission through human cervix organ culture with UC781. *AIDS*. 2003 Mar 28;17(5):653-61.

Motakis D, Parniak MA. A tight-binding mode of inhibition is essential for anti-human immunodeficiency virus type 1 virucidal activity of nonnucleoside reverse transcriptase inhibitors. *Antimicrob Agents Chemother*. 2002 Jun;46(6):1851-6.

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Manufacturer Information

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For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

- Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET
- Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

References

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2. Biosyn, Inc - Available at <http://www.biosyn-inc.com>. Accessed 10/16/03.
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4. J Virol - 1997 Apr;71(4):3023-30.
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6. Conf Retroviruses Opportunistic Infect. - Ninth. February 2002. Abstract 780-W.
7. Antimicrob Agents Chemother - 1999 Feb;43(2):259-63.
8. Biosyn, Inc - Available at <http://www.biosyn-inc.com>. Accessed 10/16/03.
9. Biosyn, Inc - Available at <http://www.biosyn-inc.com>. Accessed 10/16/03.
10. Conf Retroviruses Opportunistic Infect. - Ninth. February 2002. Abstract 780-W.
11. J Pharm Pharmacol - 2001 Aug;53(8):1109-16.