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Key Inforbits

- Selzentry™ and Isentress™, approval
- New combination products
- AIDS vaccine development halted
- AIDS in Alabama
- Pharmacist's role in Health Care
- Volunteer opportunities for the holidays

National AIDS Awareness Month

NEW DRUGS and other related stuff …

New Drug Approval … **Selzentry** ™ (maraviroc by Pfizer) was approved by the FDA in August 2007. Selzentry™ comes in 150 and 300 mg tablets with recommended dosing ranging from 150-600 mg twice daily. Its efficacy has been shown in the ongoing MOTIVATE -1 and -2 trails, in patients with chemokine receptor 5 (CCR5)-tropic HIV-1 disease. It is used in patients with active viral replication and HIV-1 disease in combination to other anti-viral medications. Maraviroc exerts its unique mechanism of action by binding to CCR5 coreceptors on CD4 cells where it prevents entry of the HIV virus into the cell. When combined with other active agents, maraviroc substantially increases the proportion of individuals achieving an optimal virological response and leads to increases in CD4+ cell counts. Maraviroc is only effective in patients with CCR5 predominant HIV disease. Adverse events include hepatotoxicity, myocardial ischemia, postural hypotension, and infection. Efficacy and safety have not been established in treatment naïve patients or in children <16 years of age.

Mayer H, van der Ryst E, Saag M, et al. Safety and efficacy of MARAVIROC, a novel CCR5 antagonist, when used in combination with optimized background therapy for the treatment of antiretroviral-experienced subjects infected with dual/mixed-tropic HIV-1: 24-week results of a phase 2b exploratory trial. In: Program and abstracts of the XVI International AIDS Conference; August 13-18, 2006; Toronto, Canada. Abstract THLB0215.

Lalezari J, Goodrich J, DeJesus E, et al. Efficacy and safety of maraviroc plus optimized background therapy in viremic ART-experienced patients infected with CCR5-tropic HIV-1: 24-week results of a phase 2b/3 study in the US and Canada. In: Program and abstracts of the 14th Conference on Retroviruses and Opportunistic Infections; February 25-28, 2007; Los Angeles, Calif. Oral 104bLB.

New Drug Approval… **Isentress™** (raltegravir by Merck & Co, Inc) was granted accelerated approval by the FDA on Oct 12, 2007 for the treatment of HIV-1 infection in combination with other antivirals. Raltegravir, dosed 400 mg twice daily, is the first agent of a new pharmacological class known as HIV integrase strand transfer inhibitors or integrase inhibitors. The mechanism of action includes blocking the HIV integrase enzyme that the virus needs in order to multiply ; thereby, slowing the advancement of the disease. Two studies, BENCHMRCK-1 and -2, indicated that raltegravir may effectively reduce viral load by inhibiting the incorporation of HIV genetic material into host cells; thereby, achieving viral suppression and may increase CD4 cells. The most common ADRs were gastrointestinal effects and, headache. Efficacy and safety have not been established in pregnant women and long term treatment effects are not known.

D Cooper, J Gatell, J Rockstroh, and others. Results from BENCHMRK-1, a phase III study evaluating the efficacy and safety of MK-0518, a novel HIV-1 integrase inhibitor, in patients with triple-class resistant virus. 14th Conference on Retroviruses and Opportunistic Infections (CROI). Los Angeles, February 25-28, 2007. Abstract 105aLB.

R Steigbigel, P Kumar, J Eron, and others. Results from BENCHMRK-2, a phase III study evaluating the efficacy and safety of MK-0518, a novel HIV-1 integrase inhibitor, in patients with triple-class resistant virus. 14th CROI. Los Angeles, February 25-28, 2007. Abstract 105bLB.

FDA approved changes in dosing regimens… On Oct 12, 2007, the FDA approved a new drug application for Lexiva™ (fosamprenavir calcium by GlaxoSmithKline). A 1400 mg once daily dose of fosamprenavir with 100mg ritonavir may be used in the treatment of therapy-naïve HIV infected patients. The approval was based on a bioavailability trial, which looked at the new regimen compare to fosamprenavir 1400 mg once-daily plus ritonavir 200 mg once daily regimen and the fosamprenavir 1400 mg twice daily dosing regimen. The study indicated the new dosing regimen produced drug levels comparable with the two previously existing regimens.

Lexiva™ is indicated in combination with other antiretroviral agents in the treatment of HIV-1 patients.

http://www.fda.gov/oashi/aids/listserve/listserve2007.html#d10242007

Ruane PJ, Luber AD, Wire MB, Lou Y, Shelton MJ, Lancaster CT. Plasma amprenavir pharmacokinetics and tolerability following administration of 1,400 milligrams of fosamprenavir once daily in combination with either 100 or 200 milligrams of ritonavir in healthy volunteers. Antimicrob Agents Chemother. 2007 Feb; 51(2):560-5.

FDA approved combination products… On Nov 2, 2007, The FDA granted tentative approval for a fixed dose combination of lamivudine/stavudine (Matrix Laboratories Limited) both the 150 mg/40 mg and the 150 mg/30 mg combination tablets. Combination products help to improve patient compliance by reducing the patient's daily pill burden. The approval was granted under the PEPFAR, President's Emergency Plan for AIDS Relief program, whose purpose is prevent the spread of HIV, and improve and provide treatments to patients world wide, provide palliative care for those suffering with AIDS, and to provide for children orphaned by AIDS.

http://www.fda.gov/oashi/aids/listserve/listserve2007.html#d10242007

New therapies under research… The Pharmaceutical Research and the Manufacturers Association of America (PhRMA) maintains a database of new drugs in development. New categories of drugs include:

- Entry inhibitors that interfere with HIV's ability to enter cells
- Integrase inhibitors, interfere with HIV's ability to insert genes into cell's normal DNA
- Assembly and budding inhibitors that interfere with the final stage of the HIV life cycle, when new virus particles are released into the bloodstream
- Cellular metabolism modulators that interfere with the cellular processes needed for HIV replication
- Gene therapy that uses modified genes inserted directly into cells to suppress HIV replication. These cells are designed to produce T cells that are genetically resistant to HIV infection

Also, there is current exploration in whether immune modulators may help improve the body's immune system response to the virus and improve responses to current antiretroviral therapies.
http://www.niaid.nih.gov/factsheets/treat-hiv.htm

FROM THE MEDICAL LITERATURE …

HIV Vaccine Development Halted…Two trials, the STEP and Phambili trials, evaluating Merck's new potential HIV vaccine have been stopped due to ineffectiveness in preventing HIV contraction or viral load reduction in patients who contracted HIV. Preliminary results indicate that patients may actually be more susceptible to contracting HIV if they have received the vaccine than if they were given placebo. Further research is being done to examine any potential causes for the vaccine's ineffectiveness or any increased susceptibility in the active treatment population; no immediate answers are apparent.

Merck [homepage on internet]. New Jersey: c1995-2007 [updated 2007 Oct 23; cited 2007 Nov 14]. Update regarding clinical trials of Merck's HIV vaccine candidate; Available from: http://www.merck.com/newsroom/press_releases/research_and_development/2007_1023.html

National Institutes of Health [homepage on internet]. Bethesda, Maryland: [updated 2007 Nov 7; cited 2007 Nov 14]. Statement of Anthony S. Fauci on the release of data from the HVTN 502 (STEP) HIV vaccine study; Available from: http://www.nih.gov/news/pr/nov2007/niaid-07.htm

Reviews of Note…

- Jayasuriya A, Robertson C, Allan PS. Twenty-five years of HIV management. *J R Soc Med*. 2007 Aug;100(8):363-6.
- Manzardo C, Zaccarelli M, Aguero F, Antinori A, Miro JM. Optimal timing and best antiretroviral regimen in treatment-naive HIV-infected individuals with advanced disease. *JAIDS*. 2007 Sep;46 Suppl 1:S9-18.
- Murphy RL. Antiretroviral therapy for advanced naive HIV-infected patients: current status and comparison of two different management strategies. *JAIDS*. 2007 Sep;46 Suppl 1:S1-2.
- Onyebujoh PC, Ribeiro I, Whalen CC. Treatment Options for HIV-Associated Tuberculosis. *J Infect Dis*. 2007 Aug 15;196 Suppl 1:S35-45.
- Carter NJ, Keating GM. Maraviroc. *Drugs*. 2007;67(15):2277-2288.
- Koziel MJ, Peters MG. Viral hepatitis in HIV infection. *N Engl J Med*. 2007 Apr 5;356(14):1445-1454.

FROM THE LAY LITERATURE about medicine …

AIDS in Alabama … Did you know?

- More than 14,000 people in Alabama have been infected with HIV disease (known cases; doesn't include those never tested or were tested in another state)
- 30% of these people live in the Birmingham area
- It is estimated that another 711 people will become infected in the state in the next year
- One-half of the new infections will be in people under the age of 25
- Almost one-third of the new infections will be among women of child-bearing age
- 4,286 reported cases of HIV/AIDS in Jefferson County (as of 4/26/07)

Alabama Dept of Public Health [homepage on the Internet]. Montgomery: Alabama Dept of Public Health. [cited 2007 Nov 16]. Available from: http://www.adph.org/aids/Default.asp?id=984

Pharmacist's role in Health Care for the HIV-Infected Patients:

- Maintain patient confidentiality at all times
- Educate yourself on the most current treatment regimens and HIV management
- Evaluate the patient's drug regimen for appropriateness of therapies, ADRs, and potential drug interactions.
- Increase the patient's understanding of the role of antiretroviral therapy to ensure successful treatment with highly active antiretroviral treatment (HAART).
- Provide ongoing education to patients. Counsel patients on adherence to medication regimen to prevent viral resistance, assess potential barriers to adherence.
- Enroll patients with financial difficulties in Patient Assistance Programs in order to obtain needed medications.

Volunteer opportunities in Alabama…

- http://www.aidsalabama.org
- http://www.maoi.org

The last "dose" …

"It is difficult to say what is impossible, for the dream of yesterday is the hope of today and the reality of tomorrow."
--Robert H. Goddard (1882 - 1945)

An electronic bulletin of drug and health-related news highlights, a service of …
Auburn University, Harrison School of Pharmacy, Drug Information Center
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