NEW DRUGS

Emtricitabine: Once-Daily HIV Therapy

Emtricitabine (Emtriva™, Gilead) is a newly approved 200-mg, one-capsule, once-daily nucleoside reverse transcriptase inhibitor (NRTI) for the treatment of human immunodeficiency virus (HIV) infection in adults in combination with other antiretroviral medications. This drug has been evaluated in clinical trials of both newly and previously treated HIV patients.

The Centers for Disease Control and Prevention (CDC) has estimated that 950,000 Americans are infected with HIV, which can progress to acquired immunodeficiency syndrome (AIDS). Approximately 360,000 infected individuals are receiving antiretroviral treatment for HIV infection in the U.S. today.

Emtricitabine helps to lower the viral load in patients and to increase the number of immune system cells (T cells or CD4 cells). These changes generally lead to improved health and decrease the likelihood of AIDS-related illnesses.

For more background on the treatment of HIV, see the article on antiretroviral therapy in this issue of P&T.

(Source: www.fda.gov; Gilead Sciences, news release, July 2, 2003.)

Omalizumab Approved for Allergy-Related Asthma

In June 2003, the Food and Drug Administration (FDA) approved the first genetically engineered protein to treat patients with allergy-related asthma.

Omalizumab (Xolair™, Genentech and Novartis) is a monoclonal antibody that has been safe and effective for people 12 years of age and older with moderate-to-severe allergy-related asthma that has been inadequately controlled with inhaled steroids. Omalizumab, injected under the skin, helps to decrease the number of asthma exacerbations.

Although asthma affects approximately 17 million Americans, only a small percentage of patients would be appropriate candidates for this new drug. It is a second-line treatment to be used only after first-line treatments have failed.

In two studies, 80% to 85% of patients receiving the drug had no exacerbations of their asthma symptoms, compared with 70% to 75% of patients receiving placebo.

For a complete discussion of omalizumab, see the June 2003 issue of P&T.

(Source: www.fda.gov; www.gene.com.)

DRUG NEWS

Inhaled Corticosteroids and Chronic Lung Disease

The jury is still out on whether inhaled corticosteroids slow the decline in lung function for patients with chronic obstructive pulmonary disease (COPD). COPD, which is characterized by limited airflow, is the fourth leading cause of death in the U.S.

Researchers from the Medical University of South Carolina say that the tradeoff of long-term improvement might not be worth the persistent effects of the drugs, and they support inhaled corticosteroids for symptomatic patients who have a spirometric response to them or who have frequent COPD exacerbations that require the use of oral corticosteroids or antibiotics.

(Source: Ann Intern Med 2003;138: 969–973.)

Pain with Tetracaine

Buffering tetracaine for anesthetic eye drops may actually increase pain instead of lessening it, according to researchers from the Department of Emergency Medicine at Indiana University.

One cause of the increased pain might be the presence of precipitate formed by the buffering process. The researchers also suggest that factors besides the pH change might be causing the reduced pain in other studies of ophthalmic anesthetic agents.

Contact lens usage was not a significant factor.

(Source: Ann Emerg Med 2003;41: 827–831.)

Vitamin K and Venous Thromboembolism

How long should a patient with venous thromboembolism take vitamin K antagonist therapy? Researchers from Academic Medical Center in Amsterdam and from Academic Hospital in Maastricht, The Netherlands, note that although treatment is usually continued for three to six months, the appropriate duration is still debatable. Their own review of 18 studies involving 3,186 patients suggests that treatment beyond three months should be approached cautiously.

Independent of the length of treatment, the monthly incidence of recurrent venous thromboembolism after therapy with vitamin K antagonists decreased over time, whereas the incidence of recurrent events seemed to stabilize nine months after the index event. Because the risk of bleeding associated with vitamin K antagonists does not decrease over time but, in fact, increases with age, the benefit of prolonged treatment offers diminishing returns, the researchers note.

The deciding factor might well be the effect on quality of life for these patients. Is reducing the risk of a possible recurrent thromboembolic event a sufficient tradeoff for patients in terms of the greater risk of bleeding and the burdens of treatment?

(Source: Arch Intern Med 2003;163: 1285–1293.)
Donepezil and Activities of Daily Living

Even at the more advanced stages of Alzheimer’s disease (AD), donepezil (Aricept®; Eisai) can enhance quality of life for both patients and caregivers, according to a study of patients with moderate-to-severe AD.

Treatment with donepezil (5 mg/day for four weeks and 10 mg/day, subject to the clinician’s judgment, thereafter) significantly slowed a decline in performing instrumental activities of daily living (e.g., housekeeping), and in completing basic activities (e.g., dressing and bathing). By week 24, caregivers of the donepezil patients were spending nearly an hour less each day helping patients than were caregivers of patients in the placebo group.

(From: J Am Geriatr Soc 2003;51:737–744.)

Doxepin Relieves Chronic Itching from Burns

Many patients whose burns have healed find that they must still contend with sometimes disabling itching, which can last for months. Because the main mechanism is thought to include increased histamine release from the wound, leading to chronic inflammation, current treatment focuses on oral antihistamines, moisturizers, and sedatives. Researchers from Brigham and Women’s Hospital in Boston, however, believe that doxepin (Sinequan®, Pfizer), a tricyclic compound with potent antihistamine properties, is a better choice.

In a three-month study of 31 outpatients four to 12 months after they had received burns, the patients were randomly assigned to receive standard care (an oral antihistamine with dose adjustments to improve efficacy) or doxepin cream. All patients continued to use moisturizers because doxepin cream is not a good moisturizer, the researchers say. The patients applied the doxepin cream four times a day, followed 20 minutes later by a moisturizer.

The doxepin cream was effective in controlling post-burn itching, and erythema was significantly diminished. Itching disappeared in 75% of those taking doxepin but in only 20% of those taking oral antihistamines. The researchers suggest that doxepin might somehow alter the wound, perhaps by reducing the number of mast cells.


Methadone and Arrhythmias

Methadone may contribute to arrhythmias, according to preliminary findings from the Denver Health Medical Center. Of 17 patients hospitalized with torsades de pointes, which is characterized by an atypical rapid heartbeat, nine were receiving methadone as a treatment for opioid dependency; the other eight were receiving it for chronic pain.

The findings suggest that high doses of methadone affect cardiac repolarization and subsequent development of arrhythmia.

(From: Pharmacotherapy 2003;23:802–805.)

Does Finasteride Limit Risk of Prostate Cancer?

A drug that has been used to fight baldness and enlarged prostate glands might also protect men against prostate cancer. Sold as Propecia® for baldness and as Prosca® for benign prostatic hyperplasia (a noncancerous condition), finasteride (Merck) lowers levels of testosterone, a form of the male hormone that promotes the growth of prostate cells. In a massive study sponsored by the National Cancer Institute, the drug reduced the risk of prostate cancer by nearly 25%. The trial was stopped a year early because the results were so striking.

Although the trial suggests that prostate cancer might be partly preventable, experts urged caution, because although the drug appeared to reduce the overall number of cancers, patients might be at greater risk for more aggressive tumors.


Therapy for Low Testosterone

The FDA has approved a new form of testosterone hormone replacement therapy for men (Striant™, Columbia) that is delivered through the gum surface.

In clinical trials, most patients achieved a steady, consistent level of testosterone within 10 to 12 hours after beginning treatment. This novel delivery mechanism provides controlled therapeutic levels of testosterone.

Until now, patients were treated with transdermal patches, topical gels, or injectable formulations. The sustained-release buccal testosterone product, which resembles a small tablet, rapidly adheres to the buccal mucosa, the small, natural depression in the mouth where the gum meets the upper lip above the incisor teeth. As the product is exposed to saliva, it softens into a gel-like form and remains in place over each 12-hour dosing period. Columbia’s Bioadhesive Delivery System transports testosterone through the buccal mucosa, where it is absorbed into the bloodstream and carried directly into the superior vena cava, bypassing the gastrointestinal system and liver.

The most frequently reported adverse events have been gum or oral irritation, a bitter taste, gum pain and tenderness, headache, gum edema, and taste distortion.

(From: PRNewswire/First Call, June 20, 2003; www.columbialabs.com; www.quantiles.com.)
NEW DRUGS

**UTIs Difficult to Treat**

Despite the availability of modern antibiotics, many people experience repeated episodes of urinary tract infections (UTIs). A new study suggests that the cause is a bacterium that invades the bladder to build a fort-like colony that resists both drugs and the body’s own immune system.

Highly resistant UTIs are a major medical problem, especially in women. These infections cause frequent and painful urination and fever and can result in more dangerous kidney infections.

About eight million UTIs are diagnosed each year, resulting in approximately 100,000 hospital admissions annually, at a cost of $1.6 billion.

Researchers at Washington University School of Medicine in St. Louis, using an electron microscope, discovered that pods of bacteria routinely formed inside the cells lining the walls of the bladder in mice with *Escherichia coli* bacterial infections of the urinary tract. The bacteria form a *biofilm* inside the cells, and thousands of individual bacteria become unified into a colony that resists attack. The discovery of the biofilm, which resembles a slimy mesh, might explain why bladder infections persist.

If the formation of biofilm is confirmed in humans, as it was in mice, then it will become increasingly important to find alternate ways to treat stubborn UTIs.


**The “Polypill” for Heart Disease and Stroke**

A single pill might be able to reduce heart attacks and strokes by more than 80%, concludes a study from England. Heart attacks, stroke, and other preventable cardiovascular diseases kill or seriously affect 50% of people in Britain.

Professor Nicholas Wald and Malcolm Law propose a “polypill” that would contain six active components—aspirin, a cholesterol-lowering drug, three blood pressure-lowering drugs at half the standard dose, and folic acid. The pill would be taken daily by all people aged 55 and over and is expected to have a huge effect on preventing disease in the Western world.

Their radical strategy is based on evidence from more than 750 trials involving 400,000 participants.

These medications are well tolerated, and new problems are unlikely because they have been studied extensively and have often been used in combination.

(Source: *BMJ* 2003;326:1427–1431; www.nature.com.)

**Breast Cancer Risk and HRT**

Estrogen–progestin combination therapy (Prempro™, Wyeth), which was recommended for many years to treat the symptoms of menopause, also appears to make mammograms less reliable or more difficult to read and may delay the diagnosis of breast cancer.

Findings from the Women’s Health Initiative (WHI) in 2003 prompted millions of American women to discontinue hormone replacement therapy (HRT), which had once been viewed as a panacea for menopausal complaints.

Because of the apparent health risks, the estrogen–progestin part of the WHI study was stopped early in 2002. The new data found a 24% increase in breast cancer risk (an increase in the lifetime risk from one in eight to about one in seven).

Although earlier studies indicated that hormone users tended to have curable, slow-growing breast tumors, the WHI found that these tumors were likely to be as aggressive as those in nonusers. Hormone users also had a higher number of abnormal mammograms, with larger and more advanced tumors at diagnosis. This might be because HRT increases breast density, making mammograms less reliable, or because the hormones stimulate cancerous growth, or both.

(Source: *Philadelphia Inquirer*, June 25, 2003; *JAMA* 2003;289:3243–3253.)

**New Drug-Coated Stents and Thrombosis Risk**

Cordis Corporation has informed health care professionals of the rare but potential risk of thrombosis associated with its Cypher Sirolimus-Eluting Coronary Stent.

The drug-eluting stent was approved in April 2003 for patients undergoing angioplasty procedures to open clogged coronary arteries. Since its introduction, more than 50,000 patients have received the new stent. As of July, the FDA had received 47 reports of stent thrombosis occurring at the time of implantation or within a few days afterward.

The FDA is reviewing the reports and is working with the company to determine the cause of and to reduce the incidence of thrombosis. For now, the company recommends:

- selecting a stent of appropriate size
- choosing only patients with previously untreated vessels
- using adequate antiplatelet therapy
- ensuring that the stent is in contact with the vessel wall.

(Source: *FDA News*, July 8, 2003; *Philadelphia Inquirer*, July 9, 2003; www.fda.gov/bbs/topics/news/cordis_1tr.pdf.)