NEW DRUGS

Istodax for Cutaneous T-Cell Lymphoma

The FDA has approved romidepsin (Istodax, Gloucester Pharmaceuticals) for patients with cutaneous T-cell lymphoma (CTCL), a rare, slow-growing cancer. Most cases of CTCL start with dry skin, a red rash, and itching. The skin may develop tumors that can become ulcerated, causing infection. CTCL can spread to the blood, lymph nodes, or internal organs. Approximately 1,500 new cases are diagnosed each year in the U.S.

Patients with localized CTCL on the skin are treated with topical agents or phototherapy, but chemotherapy may be used if the cancer advances. Romidepsin, an injectable medication, interferes with cell replication and is indicated when CTCL worsens or recurs after at least one other type of chemotherapy has been used.

In two studies involving 167 patients, about 35% of patients in both trials experienced tumor responses and 6% had complete responses. Other drugs previously approved for CTCL include vorinostat (Zolmitil, Genentech/Merck) and Lenas’ denileukin difitox (Ontak) and bexarotene (Targretin).

Source: FDA, November 9, 2009

Pennsaid for Knee Osteoarthritis

A New Drug Application (NDA) has been approved for diclofenac sodium topical solution 1.5% (Pennsaid, Covidien/Nuvo Research) for treating signs and symptoms of osteoarthritis of the knee. Pennsaid, a nonsteroidal anti-inflammatory drug (NSAID), is expected to be available in the first half of calendar 2010. A medication guide will be provided for prescribers, pharmacists, and patients.

Sources: FDA, November 4, 2009; Nuvo, www.nuvoresearch.com

Another H1N1 Flu Vaccine

A supplemental Biologics License Application (sBLA) has been approved for GlaxoSmithKline’s unadjuvanted influenza A (H1N1) pandemic vaccine. The approval was filed as a “strain change supplement” to the company’s FluLaval seasonal flu vaccine. Adjuvants have not been used in approved flu vaccines in the U.S., although they are used in Europe.

As with the four earlier H1N1 influenza vaccines licensed by the FDA on September 15, 2009, ID Biomedical, a subsidiary of GlaxoSmithKline, will employ the established, licensed egg-based manufacturing process used for producing seasonal flu vaccine. This monovalent vaccine will be produced in multidose vials in Quebec, Canada, and will contain the preservative thimerosal.

Potential side effects are expected to be similar to those of the existing seasonal and H1N1 flu vaccines, such as soreness at the injection site, mild fever, body aches, and fatigue for a few days after the inoculation. The FDA is collaborating with other government agencies to enhance safety monitoring during and after the H1N1 2009 vaccination program.

The company expects to fulfill the federal government’s order of 7.6 million doses by the end of the year.

Sources: FDA, November 16, 2009; National Public Radio, November 11, 2009; World Pharma News, November 12, 2009

Qutenza for Postherpetic Pain

The FDA has approved a skin patch made of capsaicin 8% (Qutenza, Lohmann Therapie-Systems AD/NeurogesX) for relieving the pain of postherpetic neuralgia (PHN), a complication that can occur after a bout with shingles. PHN affects nerve fibers and skin, and it can cause excruciating pain for weeks, months, or even years. About 10% to 15% of patients who have shingles experience PHN. The complication is even more common in elderly patients.

Qutenza contains capsaicin, a compound found in chili peppers. Although some over-the-counter products have lower concentrations of capsaicin that are indicated for PHN, this is the first pure, concentrated, synthetic capsaicin-containing prescription drug to undergo FDA review.

Qutenza must be applied to the skin by a health care professional because placement of the patch can be painful. A local topical anesthetic is used in addition to ice or opioids. The patient must also be monitored for at least one hour because of the risk of elevated blood pressure following placement of the patch.

Adverse drug reactions have included pain, swelling, itching, and redness at the application site.

Source: FDA, November 17, 2009

NEW INDICATIONS

Colcrys for Prevention Of Gout Flares

Colchicine (Colcrys, URL Pharma, Inc.) has been approved for the prevention of gout flares. It was first approved in July 2009 to treat acute gout flares. Colcrys is also indicated for patients with familial Mediterranean fever.

A painful form of arthritis, gout often affects the joint of the big toe but can also involve the ankles, heels, knees, wrists, fingers, and elbows.

Colchicine has been used to treat gout for centuries. It is well tolerated when taken with uric acid–lowering agents such as allopurinol. This oral form of colchicine avoids most of the toxicity associated with unapproved products on the market. The recommended dosage for gout flare prophylaxis is one tablet (0.6 mg) once or twice a day. The maximum daily dose for prophylaxis is two tablets (1.2 mg).

The company is establishing an assis-
tance program for patients with limited means.

Sources: Medical News Today, October 20, 2009; URL Pharma

**Lysteda for Menorrhagia**
The FDA has approved tranexamic acid tablets (Lysteda, Xanodyne) for women with heavy menstrual bleeding. Lysteda, a nonhormonal product, stabilizes a protein that helps blood to clot.

Tranexamic acid was first approved in 1986 as an injection with the brand name of Cyklokapron (Pfizer) to reduce or prevent bleeding during and following tooth extraction in patients with hemophilia.

In clinical trials, menstrual blood loss was significantly reduced in women who received Lysteda compared with those taking placebo. Common adverse reactions included headache, sinus and nasal symptoms, back pain, abdominal pain, muscle pain, joint pain, muscle cramps, anemia, and fatigue. Women who use Lysteda while taking hormonal contraceptives may have an increased risk of blood clots, stroke, or heart attack.

Source: FDA, November 13, 2009

**NEW FORMULATION**
**Renvela Powder for Patients With Kidney Disease**
Genzyme has introduced an oral suspension of sevelamer carbonate (Renvela), a powder to manage serum phosphorus levels in dialysis patients with chronic kidney disease. This is the only phosphate binder available in both tablet and powder dosing options.

Controlling phosphorus levels is important in dialysis patients, because elevated levels are associated with an increased risk of cardiovascular disease and mortality. Sevelamer also helps to reduce levels of low-density lipoprotein-cholesterol (LDL-C).

The powder will be available in a 2.4-g packet (equivalent to three sevelamer 800-mg tablets) and should be given three times daily with meals. Each 2.4-g packet is mixed with at least 2 ounces of water. The average prescribed daily dose is approximately 7.2 g/day.

As the next-generation version of sevelamer HCl (Renagel), sevelamer carbonate was originally approved in 2007 in the form of 800-mg tablets.


**DRUG NEWS**

**Orphan Drug Designations**
**TNFerade for Pancreatic Cancer**
The FDA has granted an orphan drug designation to TNFerade (GenVec) for patients with pancreatic cancer. This agent has already been granted a fast-track designation and is currently being investigated in a pivotal study of locally advanced pancreatic cancer.

TNFerade, which has not yet been approved, is an adenovector (a DNA carrier). It contains the gene for tumor necrosis factor-α (TNF-α), an immune system protein with potent anticancer effects. The medication is injected directly into tumors. After administration, TNFerade stimulates the production of TNF-α in the tumor.

Source: BioMed Reports, November 4, 2009

**Voreloxin for Leukemia**
Voreloxin (Sunesis Pharmaceuticals) is indicated for the treatment of acute myeloid leukemia (AML). The company is currently conducting two phase 2 clinical trials of voreloxin: a single-agent study (REVEAL-1) in newly diagnosed elderly patients with AML who are unlikely to benefit from standard induction chemotherapy, and a study evaluating the product plus cytarabine (DepoCyt, Enzon) in relapsed/refractory AML.

Source: TMClnt.com, November 5, 2009

**Abraxane for Treating Pancreatic Cancer and Melanoma**
Paclitaxel (Abraxane, Abraxis BioScience) has been granted orphan drug status for two indications. In September 2009, it was approved for treating pancreatic cancer, and in October 2009, it was approved to treat patients with stage IIb to IV melanoma.

A phase 3 study is being conducted to compare the product plus gemcitabine (Gemzar, eli Lilly) with gemcitabine alone as a first-line therapy for advanced metastatic pancreatic cancer. A phase 3 registration study comparing paclitaxel with dacarbazine (DTIC-Dome, Bayer) for treating stage IV melanoma is currently recruiting patients.

Abraxane was initially approved in 2005 to treat patients with breast cancer.


**Recalls**
**Propofol and Liposyn Products**
Hospira and the FDA have recalled 73 lots of Propofol Injectable Emulsion 1% and 85 lots of Liposyn II 10%, Liposyn II 20%, Liposyn III 10%, Liposyn III 20%, and Liposyn III 30% because some containers may have been contaminated with particulate matter. The involved products began with lot numbers 79 and 80 and were distributed between July 2009 and October 2009.

The source of these contaminants is the stainless steel equipment used in the manufacturing process. Because these contaminants do not dissolve in blood, they have the potential to act as emboli and impede blood flow; they may also cause mechanical damage in the body. If the blood supply to tissues is restricted, stroke, respiratory failure, kidney failure, liver failure, heart attack, or death may result.

Customers should report any adverse events that may be related to the prod-
Vials of Enzyme-Replacement Agents May Be Contaminated

Genzyme Corporation is urging health care professionals to visually check for foreign particles in enzyme-replacement products. The involved drugs include imiglucerase for injection (Cerezyme) for Gaucher disease, agalsidase beta (Fabrazyme) for Fabry disease, alglucosidase alfa (Myozyme) for Pompe disease, laronidase (Aldurazyme) for mucopolysaccharidosis, and thyrotropin alfa for injection (Thyrogen) for thyroid cancer. The agents were purified at the company’s Allston Landing facility in Allston, Massachusetts.

A safety review has not confirmed that patients receiving these agents have been exposed to foreign particles, but a theoretical safety risk remains if a particle enters the bloodstream. Particles have been detected in these medications at a rate of approximately 1%.

Source: Genzyme, November 16, 2009

Warning: Don’t Use Clopidogrel With Certain PPIs

Patients should avoid using proton pump inhibitors that contain omeprazole (Prilosec, Prilosec OTC, AstraZeneca) with the anticoagulant agent clopidogrel (Plavix, Bristol-Myers Squibb/Sanofi-Synthelabo), the FDA warned on November 17.

When patients take both drugs together, the ability of clopidogrel to block platelet aggregation may be reduced by 50%. Patients at risk for heart attacks or strokes who use clopidogrel will not receive its full effect if they are also taking omeprazole. Clopidogrel does not have anticoagulant activity until it is converted or metabolized into its active form via the liver enzyme cytochrome P450 2C19. Omeprazole blocks this enzyme, thereby reducing the effectiveness of clopidogrel.

The label for clopidogrel has been updated with new warnings about the use of omeprazole and other drugs that inhibit the CYP 2C19 enzyme. It is unknown how other PPIs might interfere with clopidogrel.

Other drugs that should not be used with clopidogrel include esomeprazole (Nexium), cimetidine (Tagamet and Tagamet HB), fluconazole (Diflucan), ketoconazole (Nizoral), voriconazole (VFEND), etravirine (Intelenza), felbamate (Felbatol), fluoxetine (Prozac, Serafin, Symbyax), fluvoxamine (Luvox), and ticlopidine (Ticlid).

Drugs such as ranitidine (Zantac), famotidine (Pepcid), nizatidine (Axid), and antacids do not inhibit the CYP 2C19 enzyme and are not expected to interfere with the anticoagulant activity of clopidogrel.

Source: FDA, November 18, 2009

New Guidelines For Beta Blockers in Surgery

The American Heart Association and the American College of Cardiology have revised their guidelines for the use of beta blockers in patients undergoing surgery. The guidelines suggest that these drugs should not be started on the day of surgery if the patient has not already been using them.

All surgical procedures place some degree of stress on the heart, especially patients with underlying circulatory problems or other cardiovascular risk factors. In general, the higher the risk of surgery, from a cardiovascular standpoint, the more likely a patient is to benefit from beta blockers. However, data from the Perioperative Ischemic Evaluation trial (POISE) suggest that starting higher doses of beta blockers on the day of surgery might also be risky.

These drugs help protect against heart attacks by lowering the heart rate and by blocking the effects of stress hormones on the heart. The drugs will continue to
be given perioperatively to surgical patients who have already been taking them. Patients who are new to these drugs should begin taking them well before the procedure, and the dose should be titrated upward as blood pressure and the heart rate allow.

The revised guidelines are intended to reduce the risk of cardiac complications. Although perioperative myocardial infarction (MI) and cardiac events were reduced in POISE, beta blockers were associated with higher rates of stroke and overall mortality.


**Revised Exenatide (Byetta) Label and Kidney Problems**

The FDA has approved revisions to the prescribing information for exenatide (Byetta, Amylin/Lilly) because of post-marketing reports of altered kidney function. However, the label clarifies that exenatide is not nephrotoxic. An incretin-mimetic, exenatide is approved as an adjunct to diet and exercise to improve glycemic control in adults with type-2 diabetes.

From April 2005 through October 2008, the FDA received 78 reports of kidney malfunction in patients using exenatide. Some of these patients had pre-existing kidney disease or one or more risk factors for kidney problems. The 78 cases represent a small percentage of the total number of patients using the drug.

Side effects include nausea, vomiting, and diarrhea. These events might have contributed to kidney malfunction, which can cause a buildup of waste products in the blood, leading to serious illness or life-threatening conditions.

Kidney disorders can lead to changes in urine color, an increased frequency of urination, an increased amount of urine, swelling of the hands or feet, fatigue, changes in appetite or digestion, or a dull ache in the mid to lower back. Patients who experience any of these symptoms should see a health care professional.

Source: FDA, November 3, 2009

**Support Program For Adults with ADHD**

Shire has re-launched FOCUS, an online patient-support program for adults taking once-daily lisdexamfetamine dimesylate (Vyvanse) capsules CII to treat attention-deficit/hyperactivity disorder (ADHD). The free program offers tips to help patients manage their daily activities. Patients receive reminders about appointments and prescriptions, a timer to help allocate blocks of time to finish projects, and a white-noise player to help drown out distractions.

Sources: PharmaLive, Shire, November 11, 2009, www.vyvanse.com

**Bivalirudin (Angiomax) Alone Beats Heparin Combo**

Using monotherapy with bivalirudin (Angiomax, The Medicines Company) instead of using unfractionated heparin plus tirofiban (Aggrastat, Merck) appears to be successful in patients who are undergoing elective percutaneous coronary intervention. In the Novel Approaches for Preventing Limiting Events (NAPLES) study of 335 diabetic patients, this antithrombotic agent was found to be safe, effective, and associated with decreased bleeding in the hospital.

At the 30-day point, the composite incidence of death, urgent repeated revascularization, MI, and bleeding was lower in the bivalirudin patients (18%) than the heparin/tirofiban group (32%). In fact, no patients in either group died, had MIs, or needed urgent revascularization.

The difference in bleeding between the two groups was striking: 8.4% of the bivalirudin patients experienced bleeding, compared with 20.8% of patients receiving heparin plus tirofiban.

The researchers attributed the difference mainly to the lower rate of minor bleeding (7.8% for bivalirudin, 18.5% for the combination). The rate of major bleeding was comparable: 0.6% for bivalirudin and 2.4% for the combination. Most bleeding events occurred at a femoral vascular access site.

Source: Am J Cardiol 2009;104:1222–1228

**Tiotropium (Spiriva) for COPD**

Tiotropium (Spiriva, Pfizer/Boehringer Ingelheim) may slow the rate of decline of postbronchodilator FEV₁, and reduce the risk of exacerbations in patients with stage 2 chronic obstructive pulmonary disease (COPD). (FEV represents the volume of air that can be forced out in one second after a deep breath.) In the Understanding Potential Long-Term Impacts on Function with Tiotropium (UPLIFT) trial, patients taking tiotropium also had better lung function and health-related quality of life throughout the study.

UPLIFT was a randomized, double-blind, placebo-controlled trial of 5,993 patients in 487 centers in 37 countries. The patients, 40 years of age and older, received four years of therapy with either once-daily tiotropium or matching placebo, delivered by an inhalation device.

At the baseline, 2,739 patients had GOLD stage 2 disease (Global Initiative for Chronic Obstructive Lung Disease) with a mean postbronchodilator FEV₁ of 1.63 L. The rate of this decline was lower in the tiotropium patients (43 mL/year) than in the placebo patients (49 mL/year), and the time to the first exacerbation and the time to exacerbation leading to hospital admission were longer with tiotropium.

continued on page 665
Although the effect on postbronchodilator FEV₁ was small and might not be clinically significant, long-acting anticholinergic drugs may have substantial benefits in patients with moderate COPD and may therefore provide a rational basis for starting therapy for patients with stage 2 disease. The reduction in the rate of decline in postbronchodilator FEV₁ is of interest because it has the potential to alter the course of the disease at an early stage.

Source: Lancet 2009;374:1171–1178

Interleukin-2 Boosts CD4+ Counts

Adding interleukin-2 (IL-2) to antiretroviral therapy substantially boosts CD4+ cell counts and can keep counts high. However, compared with antiretroviral therapy alone, those increases don’t specifically reduce the risk of opportunistic disease or death. Investigators for the International Network for Strategic Initiatives in Global HIV Trials (INSIGHT) concluded that not all CD4+ cells are equal when it comes to host defense.

Two trials were conducted: Subcutaneous Recombinant, Human Interleukin-2 in HIV-Infected Patients with Low CD4+ Counts under Active Antiretroviral Therapy (SILCAAT) and Evaluation of Subcutaneous Proluekin in a Randomized International Trial (ESPRIT). In each trial, patients with HIV infection were randomly assigned to receive IL-2 plus antiretroviral therapy or antiretroviral therapy alone. SILCAAT enrolled 1,695 patients with median CD4+ cell counts of 202 cells/mm³. ESPRIT included 4,111 patients with median counts of 457 cells/mm³.

Over a median follow-up period of seven to eight years, the IL-2 patients experienced increased CD4+ cell counts, by 53 and 159 cells/mm³, on average, compared with patients receiving antiretroviral agents alone. However, the risks of acquiring an opportunistic disease or dying were similar regardless of treatment.

The researchers suggest at least two hypotheses to explain their results. First, the CD4+ T cells that were induced by IL-2 might have no role in host defense. Second, the cells are at least partially functional, or IL-2 may have a modestly beneficial effect that is not mediated through CD4+ cells, but the negative effects of IL-2 may neutralize any improvements in host defense brought about by the treatment. Whether these findings are relevant to other immunotherapies is uncertain.


Fibrates Improve Lipid Profiles for Patients Intolerant to Statins

Statins are the gold standard of cholesterol treatment, but some patients don’t respond to or can’t tolerate these agents for lowering cholesterol. Other patients might be receiving the maximal allowable statin dose but still can’t reach their goals. For these patients, fibrates might be the answer.

Researchers from four facilities in Quebec, Canada, reviewed 20 randomized, controlled studies on fibrates that involved 25,655 patients. Fibrates as a class substantially reduced triglyceride levels, modestly reduced low-density lipoprotein-cholesterol (LDL-C) and total cholesterol levels, and slightly raised high-density lipoprotein-cholesterol (HDL-C) concentrations. They were also associated with a decrease in nonfatal MI but did not affect all-cause mortality.

The researchers advise physicians to consider fibrates as an adjunct to statins, as monotherapy for patients who are intolerant of or resistant to statins, and as monotherapy for patients with hypertriglyceridemia.


Relieving Pain With Gabapentin (Neurontin) Plus Nortriptyline (Pamelor)

A study from the University of Manitoba in Winnipeg, Canada, suggests that combining gabapentin (Neurontin, Pfizer) and the antidepressant nortriptyline (e.g., Pamelor, Mallinckrodt) might be the most effective strategy for relieving neuropathic pain.

The double-blind, double-dummy, crossover trial involved 56 patients with diabetic polyneuropathy or postherpetic neuralgia. The patients had a daily pain score of at least 4 on a scale of 0 to 10. They received one of three sequences of daily oral gabapentin, nortriptyline, and a combination of these. Each group received different sequences in three six-week treatment periods.

For the 47 patients who completed at least two of the three treatment periods, their pain with the combination regimen was significantly lower than with either single drug alone. Mean daily pain scores at the maximum tolerated dose were 3.2 for gabapentin, 2.9 for nortriptyline, and 2.3 for the combination. No serious adverse drug events (ADEs) were recorded; the most common ADE was dry mouth. Patients receiving the combination also experienced significantly improved sleep (sleep interference can be a major complication of neuropathic pain).

The researchers designed their trial to use simultaneous combination treatment, instead of sequential treatment, which is more commonly used. Sequential treatment, they noted, restricts exposure of patients to more than one drug if they report incomplete relief with the first drug tried, but it might lead to suboptimal dose ratios for combination treat-
ment if both drugs have common overlapping side effects. Thus, if a balanced ratio of the two drugs is required for optimal analgesic interaction, simultaneous dose titration might be preferable. Indeed, maximum tolerated doses of gabapentin and nortriptyline were significantly lower as a combination treatment than as monotherapy. However, superior efficacy was achieved without an increased frequency of ADEs. The authors concluded that the overall therapeutic profile favored the combination.

Source: Lancet 2009;374:1752–1761

Inappropriate Antibiotic Therapy Linked to Longer Hospital Stays

Patients who acquire skin and soft-tissue infections (SSTIs) in hospitals or in other health care settings may be more likely to receive inappropriate antibiotic therapy at the beginning of their treatment. As a result, they also may have significantly longer hospital stays.

In a study conducted by the Henry Ford Health System based in Detroit, researchers evaluated records of patients who acquired SSTIs in hospitals and health care settings and patients who acquired similar infections in the community. Results from the study were presented at the 47th annual meeting of the Infectious Diseases Society of America in Philadelphia.

Complicated SSTIs (cSSTIs) account for almost 10% of all hospital admissions in the U.S. According to the Centers for Disease Control and Prevention, approximately 25% to 30% of the American population has some form of *Staphylococcus aureus* on the skin, and an increasing number of those individuals are carrying the more resistant form, methicillin-resistant *S. aureus* (MRSA).

In the hospitalized patient population, three risk factors were identified as being associated with receiving inappropriate antibiotic treatment: recent exposure within a nursing home or clinic, presence of a gram-negative pathogen, and presence of a pathogen other than *Streptococcus* species.

Researchers analyzed the medical records of 368 patients hospitalized between late 2005 and 2008 with a diagnosis of a cSSTI upon admission. Patients were classified as having health care–associated infections if they were recently hospitalized, were immunocompromised, receiving hemodialysis, or admitted from a nursing home. All other patients were classified as having community-acquired infections. Initial empirical therapy was considered appropriate if antibiotics active against the pathogen were given within 24 hours of admission.

Among patients with SSTIs whose infection was confirmed by culture, those who acquired an infection in a hospital or other health care setting were more likely to be treated inappropriately than those who acquired an infection in a community setting (35% vs. 21%, respectively). When other risk factors were adjusted, patients who received inappropriate initial therapy remained in the hospital almost six days longer, on average, than patients who received appropriate initial therapy.

*S. aureus* was found to be the most common pathogen in patients with both health care–associated infection (56%) as well as community-associated infection (58%). Most of these organisms were MRSA. This infection has become an increasingly common cause of SSTIs, as evidenced by the prevalence of MRSA in this study.

Source: Infectious Diseases Society of America, October 30, 2009

**Niacin plus Statin Combo May Reduce Atherosclerosis Better Than Statins Alone**

Last year, a large study had found that Merck’s Vytorin, a combination tablet of ezetimibe (Zetia) and a statin (simvasatin), was no more effective than simvastatin (Zocor) alone for lowering cholesterol. More recently, patients at high cardiovascular risk were found to expe-
The use of postmenopausal hormone replacement therapy (HRT) has decreased over time in the U.S. and might have played a role in the declining rate of atypical ductal hyperplasia (ADH), a risk factor for breast cancer. In a study from Elmhurst Hospital Center in New York, HRT was associated with increased rates of benign breast biopsies and early and late stages of cancer in postmenopausal women.

ADH is characterized by the presence of abnormal cells in the milk ducts of the breast. Women with ADH have a three- to five-fold increased risk of developing breast cancer.

Between 1996 and 2005, the use of postmenopausal HRT decreased from 35% to 11% and ADH decreased from 5.5 per 10,000 mammograms in 1999 to 2.4 in 2005. Cases of ADH associated with cancer reached a peak of 4.3 per 10,000 mammograms in 2003 but decreased to 3.3 in 2005.

Breast cancer in association with ADH is usually not aggressive. ADH is generally associated with low-grade cancers or those at an early stage, providing evidence to suggest a separate pathway for the development of low-grade and high-grade breast cancers. The researchers suggest that future work address the influence of exogenous hormones on benign proliferative lesions of the breast.

Source: Cancer Epidemiol Biomarkers Prev, November 9, 2009

**Protein from Pregnancy Hormone May Prevent Breast Cancer**

With the finding that hormones produced during pregnancy induce a protein that inhibits the growth of breast cancer, researchers hope that alpha-fetoprotein (AFP) may serve as a well-tolerated agent for preventing this cancer in the future.

Hormones released during pregnancy, such as estrogen, progesterone, and human chorionic gonadotropin (hCG), have been found to reduce the risk of breast cancer. AFP is normally produced by the liver and yolk sac of a fetus. Researchers tried to determine whether giving these hormones to carcinogen-exposed rats led them to produce AFP, which produces the protective effect of pregnancy in the absence of pregnancy.

The results showed that estrogen plus progesterone, estrogen alone, or hCG reduced the incidence of mammary cancers in rats. Each treatment raised serum levels of AFP, which inhibited the growth of breast cancer cells growing in culture.

Even though these findings suggest a role of AFP in breast cancer prevention, they are not yet ready to be used in the clinic.

The researchers did not directly demonstrate cancer-preventive activity of AFP but did find an association in preventing mammary tumors. None of the treatments prevented mammary tumors in 100% of the rats; AFP appeared to delay mammary tumor formation in 30% to 50% of the rats. This work, although promising, suggests that additional animal studies need to be done before the results can be applied to humans.

Source: Cancer Prev Res 2009;2(12), www.aacrjournals.org

**Bevacizumab (Avastin) Holds Promise for Biliary Tract Cancer**

Bevacizumab (Avastin, Genentech/Roche), an angiogenesis inhibitor, was well tolerated and showed antitumor activity in patients with advanced cancers of the biliary tract when given in addition to gemcitabine (Gemzar, Eli Lilly) plus oxaliplatin (Eloxatin, Sanofi-Synthelabo).

In previous studies, gemcitabine/oxaliplatin (Gem/Ox) delayed disease progression and had acceptable toxicity in patients with biliary tract cancers. Bevacizumab has also shown promise in treating colorectal, breast, and lung cancers.

In a phase 2 study conducted at Massachusetts General Hospital Cancer Center in Boston, the authors gave all three drugs intravenously (Gemox-b) to 35 patients and examined whole-body positron-emission tomography (PET) scans to help identify those patients most likely to benefit from treatment. The Gemox-b patients had an overall response rate of 40% (14 patients with confirmed partial responses). Stable disease was observed in an additional 10 patients (29%). PET showed encouraging results for moni-
toring responses.

Source: Lancet Oncol, online, November 23, 2009

RESEARCH NEWS
NIH Grants $85 Million To Study Drugs for Children

The scarcity of pediatric studies makes it difficult for health care professionals to predict drug dosing, safety and efficacy in children. To address this gap, the National Institutes of Health (NIH) has announced 18 grants to help determine outcome measures and to increase the likelihood of success of future trials of therapies for children. The funds, provided by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, will support studies in three critical areas: pediatric cardiology, neonatology and pediatric neurology.

The Best Pharmaceuticals for Children Act of 2002 established a way to study on-patent and off-patent drugs for children. As an example, premature infants with bronchopulmonary dysplasia (BPD) require oxygen and are at a high risk for chronic respiratory obstruction later in life. However, the success of therapies for BPD in newborns has not necessarily correlated with the ability to prevent chronic conditions. To address this deficiency, two projects to be conducted at the University of North Carolina at Chapel Hill and at Tufts University will establish a registry to track the onset and extent of chronic lung problems in these at-risk infants as they grow older.

As another example, blood pressure cuffs were originally manufactured for adults. Researchers at Case Western Reserve University have now received funding to adapt the cuffs to children. In addition, investigators at the Albert Einstein College of Medicine plan to enroll children between 10 and 18 years of age into a six-month study to assess the effect of dietary and lifestyle changes on blood pressure.


DEVICES IN THE NEWS
New Design for Dey EpiPen

Dey Pharma, LP, has introduced a patient-friendly, next-generation EpiPen Auto-Injector. These devices are indicated for the emergency treatment of allergic reactions for people with a history of an anaphylactic reaction. The EpiPen releases 0.3 mg of epinephrine, and the EpiPen Jr. releases 0.15 mg.

Immediate access to epinephrine is critical during the first few minutes of an anaphylactic reaction. This is the only epinephrine auto-injector with no exposed needle before and after use. An easy-to-grasp oval barrel prevents the device from rolling out of reach. The device also comes with illustrated instructions. A flip-top carrying case allows for rapid, single-handed removal. The bright orange color has arrows that identify the end of the needle and reduce the risk of accidental thumb puncture.

Patients who currently use EpiPen or EpiPen Jr. should continue to carry it until the pen is used or reaches its expiration date. Patients will automatically receive the new EpiPen device when they renew their prescription.

Source: Dey/Mylan, October 27, 2009

Test for Platelet Contamination

The FDA has approved the Platelet PGD Test System, made by Verax. This is the first rapid test for detecting bacterial contamination in pooled platelets derived from whole blood.

Platelets are used to prevent or treat bleeding in patients with inadequate or dangerously low platelet counts and in those undergoing chemotherapy, following major trauma, and during or after surgery. Because platelets have the potential to be contaminated with bacteria, it is important to detect any contamination before transfusion. Contaminated platelets pose the risk of serious and potentially life-threatening infections.

A single-use test strip produces a signal that indicates the presence of bacteria in less than 60 minutes. The test is intended for use mainly by hospitals. In clinical studies, this device improved the sensitivity for detecting bacterial levels by 100-fold to 1,000-fold over current methods used.

Source: FDA, November 13, 2009

Predicting Resistance To Anticlotting Therapy

Three devices that test platelet function all identified heart patients whose blood cells will remain sticky, thereby increasing the risk of a heart attack even after pretreatment with two anticoagulating agents before coronary stenting. Results were reported at the American Heart Association’s 2009 Scientific Sessions.

In the POPULAR study (Do Point-of-Care Platelet Function Assays Predict Clinical Outcomes in Clopidogrel Pre-Treated Patients Undergoing Elective PCiP), researchers compared six different tests of platelet reactivity in 1,069 consecutive patients undergoing angioplasty with stent placement, including one year of follow-up. High platelet reactivity was recorded by three of the tests—Light Transmittance Aggregometry (LTA), the VerifyNow-P2Y12-cartridge, and the Plateletworks assay. Three other tests did not predict outcomes.

Of the three predictive tests, the LTA, the most labor-intensive, cannot be performed at the bedside. Plateletworks must be performed within 10 minutes of drawing blood. VerifyNow-P2Y12 does not have those limitations.

Source: American Heart Association, November 15, 2009
NEW MEDICAL DEVICES

Marvin M. Goldenberg, PhD, RPh, MS

**Name:** FlexStent Biliary Self-Expanding Stent System

**Manufacturer:** Flexible Stenting Solutions, Inc., Eatontown, N.J.

**Approval Date:** September 17, 2009

**Indication:** This stent system is indicated for the palliative treatment of patients with biliary strictures resulting from malignant neoplasms.

**Description:** The stent provides superior radial stiffness and low chronic outward force. Helically wound struts are integrated with helical flexible coils.

**Benefit:** The key to the delivery technology is simplicity, ease of use, and placement. The technology provides needed clinical solutions in the interventional radiology, gastroenterology, neurovascular, and cardiology device marketplace.

**Sources:** www.marketwatch.com; www.news-medical.net

**Name:** Mirena Intrauterine System

**Manufacturer:** Bayer Health Care Pharmaceuticals, Inc., Wayne, N.J.

**Approval Date:** October 1, 2009

**Indication:** Mirena, an intrauterine device (IUD) that releases levonorgestrel, is designed to treat heavy menstrual bleeding in women who are using intrauterine contraception. This IUD was first approved as a contraceptive in 2000. This is the first IUD approved by the FDA for this additional indication.

**Description:** The small, flexible device is inserted into the uterus by a trained health care professional. Mirena is made of a light, plastic, T-shaped frame. The stem of the T contains a tiny stored amount of levonorgestrel.

**Benefit:** The IUD is beneficial in women who experience heavy, prolonged menstrual periods that can interfere with daily activities. After three months of use, the patient’s average blood loss is reduced by 85%, and by 12 months the flow is reduced by 97% every cycle. About one-third of women using the device do not have any periods at all. Although women initially find it a bit unusual not to have a menstrual period, there is no accumulation of blood; the hormone in the IUD prevents the lining of the womb from building up at all. It is often the excessive thickening of this lining that is the cause of the problems in the first place.

**Precautions:** Serious side effects have included ectopic and intrauterine pregnancy (when the IUD is in place), group A streptococcal sepsis, pelvic inflammatory disease, embedment of the IUD in the uterine wall, and perforation of the uterine wall or cervix.

**Sources:** Reuters, October 1, 2009; FDA, October 7, 2009; http://womenshealth.about.com

**Devices in the News**

**Small coronary stent.** A smaller version of Cordis’ Cypher sirolimus-eluting coronary stent, measuring 2.25 mm in diameter, has been approved to treat coronary blockages in small vessels. Many patients, especially women, have small-vessel disease, which is often difficult to treat. Small coronary vessels have been associated with an increased risk of restenosis after stent implantation, and another procedure is required to reopen the vessel. The smaller the artery, the more the regrowth of cells within a stent.

**Sources:** Medical News Today, September 23, 2009; Pharma Live, http://pharmalive.com

**Excess radiation in brain perfusion scans.** The FDA has learned of radiation overexposure during brain perfusion computed tomography (CT) imaging, often used to aid in the diagnosis and treatment of stroke.

Over an 18-month period, 206 patients received radiation doses that were almost eight times the expected concentration. Instead of receiving a maximum of 0.5 gray (Gy) to the head, they received 3 to 4 Gy. In some cases, this excessive dose resulted in hair loss and erythema.

This situation may reflect more widespread problems with CT quality assurance programs and might not be isolated to the facility or the imaging procedure. If doses are higher than the expected level but not high enough to produce obvious signs of radiation injury, the problem may go undetected, putting patients at increased risk for long-term radiation effects. The FDA encourages all facilities to review their CT protocols. These indices include the volume CT dose index and the dose–length product.

**Source:** FDA, October 8, 2009