FDA Approves Type 2 Diabetes Drug

The US Food and Drug Administration (FDA) approved dapaglifozin (Fraxiga, Bristol-Myers Squibb and AstraZeneca) for treatment of type 2 diabetes in adults, according to a January 8 press announcement.

Dapaglifozin inhibits sodium-glucose co-transporter 2, blocking the reabsorption of glucose by the kidneys. The daily tablet lowers blood glucose levels and increases glucose excretion by allowing glucose to exit the body via urine.

Prior to approval, the drug was evaluated in 16 clinical trials involving more than 9400 patients with type 2 diabetes. An increased number of bladder cancer diagnoses were seen in participants taking the drug in clinical trials, so it is not recommended for use in patients with active bladder cancer.

As a condition of approval, the FDA has required 6 postmarketing studies. These trials aim to gather more information on cardiovascular risk, bladder cancer rates in patients with cardiovascular risk, liver abnormalities and pregnancy outcomes associated with the drug, and its use in pediatric patients. An animal study will assess urinary flow/rate and bladder tumor promotion in rodents.

Genital mycotic infection and urinary tract infection were the most common side effects in clinical trials. Dapaglifozin should not be used by patients with bladder cancer, impaired renal function, or type 1 diabetes.

Former Smokers at Reduced Risk for Cataract, but Higher Risk Than Nonsmokers

People who quit smoking begin to decrease their risk for developing cataracts, a Swedish-based study showed, but the risk persists for decades.[1] Additionally, the risk declined at a slower rate for former smokers with more intense smoking habits compared with those with a less intense smoking habit, according to study authors Birgitta Ejdervik Lindblad, MD, PhD, of Örebro University Hospital, in Örebro, Sweden, and colleagues.

The study followed 44 371 Swedish men aged 45 to 79 years who identified as smokers (25%), former smokers (39%), or never-smokers (36%). During a 12-year follow-up period, 12% of the study participants had cataract extractions.

Participants who smoked more than 15 cigarettes a day were 42% more likely to develop cataracts compared with those who had never smoked. After 20 years of not smoking, former smokers reduced their risk by half, making them only 21% more likely than never-smokers to develop cataract.

The study authors noted that former smokers who smoked less than 15 cigarettes per day showed the effects of cessation much earlier than former smokers who smoked more than 15 cigarettes per day. Still, former smokers with a less intense smoking habit never saw their risk for cataracts fall to the level of never-smokers, even after 20 years of not smoking.

"These findings emphasize the importance of early smoking cessation and preferably the avoidance of smoking," the study authors concluded.

1. Lindblad BE, Håkansson N, Wolk A. Smoking cessation and the risk of cataract: a prospective cohort study of cataract extraction among men [published online ahead of print January 2, 2014]. *JAMA Ophthalmol*. doi: 10.1001/jamaophthalmol.2013.6669.

Positive Results in Study of Personalized Cellular Therapy for Leukemia

Adults and children with leukemia who were treated with an investigational, personalized cellular therapy known as CTL019 experienced positive results, researchers at the Hospital of the University of Pennsylvania and the Children's Hospital of Philadelphia recently reported. The results in these 59 patients were presented at the American Society of Hematology Annual Meeting in New Orleans and described in a news release.[1]

Two of the first 3 patients with chronic lymphocytic leukemia (CLL) who participated in the study, which started in 2010, remain in remission, the news release said. Additionally, an 89% complete response rate among adult and pediatric patients with acute lymphoblastic leukemia (ALL) was observed.

The investigational treatment begins by removing a patient's T cells via an apheresis process and reprogramming them with a gene transfer technique using a lentivirus vector. The engineered T cells target tumor cells using chimeric antigen receptor, an antibody-like protein that is expressed on the surface of the T cells and designed to bind to the CD19 protein, found on the surface of the cancerous B cells associated with CLL and ALL. The modified cells are infused back into the patient's body following lymphodepleting chemotherapy. A signaling domain built into the chimeric antigen receptor promotes rapid growth of these cells, building an army of tumor-killing cells that tests reveal can grow to more than 10 000 new cells for each single engineered cell patients receive. Cells in the patient that do not express CD19 are left untouched by the modified T cells.

The researchers reported the following findings from 3 patient groups: 15 of 32 adults with CLL responded to the therapy, and 7 experienced complete remission; all 5 adult patients with ALL treated to date experienced complete remission, the longest of which continued 6 months after treatment; and 19 of 22 pediatric patients with ALL experienced complete remissions.

The first pediatric patient treated, now 8 years old, remains in remission 20 months after treatment. Five patients have relapsed, including 1 whose tests revealed new tumor cells that do not express the protein targeted by the reprogrammed cells.

1. Penn Med team reports on study of first 59 leukemia patients who received personalized cellular therapy [news release]. Philadelphia, PA: Penn; December 7, 2013. http://www.upenn.edu/pennnews/news/penn-med-team-reports-study-first-59-leukemia-patients-who-received-personalized-cellular-thera. Accessed December 20, 2013.

FDA Announces Plans to Reduce Partially Hydrogenated Oils and Trans Fat

Partially hydrogenated oils (PHOs), the source of artificial trans fat in processed foods, are "not generally recognized as safe," the FDA announced in November. In December, the FDA extended an initially scheduled 60-day public comment period on the new designation of these substances to March 8. The FDA said it will also use that period to gauge how long it would take food manufacturers to adjust their products that contain trans fat in response to the change.

Public awareness of the dangers posed by trans fat have led to the food manufacturing industry voluntarily reducing PHO levels in their products, particularly in products that can be produced without PHOs, according to the FDA. As a result, American consumers' consumption of trans fat dropped from 4.6 grams per day in 2003 to about 1 gram per day in 2012. Nonetheless, FDA Commissioner Margaret A. Hamburg, MD, said, the presence of trans fat in foods is still problematic. "Current intake remains a significant public health concern," Dr. Hamburg said in the news release. She praised the FDA's action, specifically referencing the decision's impact on heart health.

"The FDA's action today is an important step toward protecting more Americans from the potential dangers of trans fat," she said. "Further reduction in the amount of trans fat in the American diet could prevent an additional 20 000 heart attacks and 7000 deaths from heart disease each year—a critical step in the protection of Americans' health."

Following the 60-day comment period, the FDA will determine whether PHOs should be labeled as "food additives," meaning they could be used in food only if authorized by regulation. In its news release, the FDA stated that if it were to label PHOs as food additives, the agency would provide food manufacturers with adequate time to reconfigure their products.

Anastrozole Reduced Breast Cancer Rate in High-Risk Postmenopausal Women

Anastrozole reduced the incidence of breast cancer in postmenopausal women at high risk for the disease compared with placebo, according to a study published online in *The Lancet*.[1]

Jack Cuzick, PhD, of the Wolfson Institute of Preventive Medicine, Queen Mary University of London, London, UK, and colleagues recruited approximately 3900 postmenopausal women aged 40 to 70 years from 18 countries for the double-masked, randomized, placebo-controlled trial. Participants were randomly assigned to receive 1 mg oral anastrozole every day for 5 years or placebo. After 5 years, the group receiving anastrozole reported 40 incidents of breast cancer (2.0%), while the group receiving placebo reported 85 incidents of breast cancer (4.3%) (95% CI, 0.32—0.68, $P < .0001$).

"Anastrozole effectively reduces incidence of breast cancer in high-risk postmenopausal women," the study authors wrote. They concluded that this finding "provides support for the use of anastrozole in postmenopausal women at high risk of breast cancer."

1. Cuzick, J, Sestak, I, Forbes, JF, et al. Anastrozole for prevention of breast cancer in high-risk postmenopausal women (IBIS-II): an international, double-blind, randomised placebo-controlled trial. *Lancet* [published online ahead of print]. December 12, 2013. doi: 10.1016/S0140-6736(13)62292-8.

FDA Proposes New Labeling for Antibacterial Soaps

The FDA proposed new rules regarding the labeling and formulation of antibacterial hand soaps and body washes. Under the proposed rule, manufacturers will have to reformulate or relabel their products if they cannot prove that those products are safe for long-term use and that they are more effective in preventing the spread of illness than regular soap and water. The proposed rule would not affect hand sanitizers, wipes, and alcohol-based antibacterial products.

In a statement, the FDA cited data tying long-term exposure to the active ingredients in antibacterial soap (triclosan in liquid soap and triclocarban in bar soap) to possible health risks, such as bacterial resistance and hormonal effects. Further, the FDA expressed concern that consumer perception may not align with scientific

evidence. "Although consumers generally view these products as effective tools to help prevent the spread of germs," the FDA said in a press release, "there is currently no evidence that they are any more effective at preventing illness than washing with plain soap and water."

"Due to consumers' extensive exposure to the ingredients in antibacterial soaps, we believe there should be a clearly demonstrated benefit from using antibacterial soap to balance any potential risk," said Janet Woodcock, MD, director of the FDA's Center for Drug Evaluation and Research, in the statement.

The proposed rule is available for public comment for 180 days, and a 1-year period for companies to submit new data and information was started concurrently. If the FDA finalizes the proposed rule, manufacturers that cannot support their products' antibacterial claims must either remove the antibacterial ingredients or remove antibacterial claims in labeling.

Vitamin E May Slow Functional Decline in Alzheimer Disease

Vitamin E may benefit patients with mild to moderate Alzheimer disease (AD), slowing the rate of functional decline by about 6 months, a study suggests.[1] The double-masked, placebo-controlled, parallel-group, randomized clinical trial included 613 AD patients seen in Veterans Affairs medical centers between August 2007 and September 2012. Nearly all of the participants were men, and mean age was 79 years.

Participants were randomly assigned to 1 of 4 groups, each receiving a daily dosage of either 2000 IU vitamin E, 200 mg memantine, both vitamin E and memantine, or placebo. With a mean follow-up of 2.27 years (standard deviation [SD], 1.22 years), the group consuming vitamin E alone had a 6.2-month delay in functional decline. With this delay, caregiver time per patient also decreased.

The study's results showed no evidence that high-dosage vitamin E had any impact on memory. High-dosage consumption of vitamin E has not been shown to prevent AD in previous studies. In fact, earlier studies have shown that consumption of vitamin E may confer other risks. In the HOPE-TOO study, participants who consumed 400 IU vitamin E per day had an increased risk of heart failure (13%) and hospitalization for heart conditions (21%) vs placebo.[2] The SELECT trial found that healthy men older than 50 years taking 400 IU vitamin E daily had a 17% increased risk of prostate cancer compared with those taking placebo.[3] A 2004 meta-analysis of 19 studies' data concluded that a high consumption of vitamin E supplement was associated with a higher overall risk of mortality.[4]

1. Dysken MW, Sano M, Asthana S, et al. Effect of vitamin E and memantine on functional decline in Alzheimer disease: The TEAM-AD VA Cooperative Randomized Trial. *JAMA*. 2014;311(1):33-44.
2. Lonn E, Brosch J, Yusuf S, et al. Effects of long-term vitamin E supplementation on cardiovascular events and cancer: a randomized controlled trial. *JAMA*. 2005;293(11):1338-1347.
3. Klein EA, Thompson Jr. IM, Tangen CM, et al; Vitamin E and the risk of prostate cancer: the Selenium and Vitamin E Cancer Prevention Trial (SELECT). *JAMA*. 2011;306:1549-1556.
4. Miller III ER, Pastor-Barriuso R, Dalal D, Riemersma, R, Appel, L, Guallar, Eliseo. Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. *Ann Intern Med*. 2005;142(1):37-46.

Google Unveils Prototype Contact Lens for Diabetes Monitoring

Google researchers have developed a smart contact lens that monitors glucose levels in tears. Brian Otis and Babak Parviz, the cofounders of the project at GoogleX, a research lab within Google, announced the project on Google's official blog.

If successful, the lens would replace subcutaneous glucose monitors, which are uncomfortable, and finger-prick glucose monitors, which discourage patients with diabetes from monitoring their glucose levels as often as they ought to, Mr. Otis and Mr. Parviz wrote.

"Over the years, many scientists have investigated various body fluids—such as tears—in the hopes of finding an easier way for people to track their glucose levels," Mr. Otis and Mr. Parviz wrote. "But as you can imagine, tears are hard to collect and study. At GoogleX, we wondered if miniaturized electronics…might be a way to crack the mystery of tear glucose and measure it with greater accuracy."

The prototype features a glucose sensor embedded between 2 layers of soft contact lens material, which transmits information to a wearer's smartphone. Some prototypes measure glucose levels once per second. The product's designers plan to place LED lights in the lens, which could alert the wearer when glucose levels have risen above or fallen below a certain threshold.

Mr. Otis and Mr. Parviz said that they are in discussions with the FDA, but noted that they must continue to conduct research before they can release the project to the public.

"We've always said that we'd seek out projects that seem a bit speculative or strange," the co-founders wrote. "We thought this project was worth a shot."

1 Otis B, Parviz B. Introducing our smart contact lens project. Google. http://googleblog.blogspot.com/2014/01/introducing-our-smart-contact-lens.html. Published January 16, 2014. Accessed January 20, 2014.

Vitamin D Level a Risk Factor for Progression of Multiple Sclerosis

A low level of vitamin D in patients who experienced an event indicative of multiple sclerosis (MS) was an indicator for long-term progression of the disease,

Alberto Ascherio, MD, DrPH, and colleagues reported in *JAMA Neurology*.[1] Conversely, patients with high levels of vitamin D showed lower levels of disease progression.

The study tracked 465 patients who had symptoms indicative of MS based on magnetic resonance imaging, brain volume, the number of new brain lesions, and the volume of T2 lesions.

Patients who received 20 ng/mL of the active metabolite in vitamin D, 25(OH)D, over 12 months showed a 0.41% lower yearly loss of brain volume ($P = .07$), a 57% lower rate of new active lesions ($P < .001$), and a 25% lower yearly increase in T2 lesion volume ($P < .001$).

The 20 ng/mL regimen over 12 months "predicted lower disability (Expanded Disability Status Scale score, −0.17; $P = .004$) during the subsequent 4 years," the study authors wrote, concluding that "low 25(OH)D levels early in the disease course are a strong risk factor for long-term MS activity and progression."

1. Ascherio A, Munger K, White R, et al. Vitamin D as an Early Predictor of Multiple Sclerosis Activity and Progression [published online ahead of print January 20, 2014]. *JAMA Neurol*. doi:10.1001/jamaneurol.2013.5993

High Omega-3 Levels in Postmenopausal Women Correlated with Larger Brain Volume

Higher omega-3 levels in postmenopausal women correlated with larger total brain volume and hippocampal volume, James V. Pottala, PhD, and colleagues found in a study published in *Neurology*.[1]

Omega-3 levels and brain volumes were measured in 1111 postmenopausal women at baseline and 8 years later. The study authors concluded that patients with higher omega-3 levels (1 SD greater) had a mean 2.1 cm^3 larger brain volume ($P = .048$). A 1 SD greater omega-3 index also correlated with greater mean hippocampal volume (50 mm^3, $P = .036$).

"While normal aging results in overall brain atrophy," the study authors wrote, "lower omega-3 index may signal increased risk of hippocampal atrophy." ■

1. Pottala JV, Yaffe K, Robinson JG, Espeland MA, Wallace R, Harris WS. Higher RBC EPA + DHA corresponds with larger total brain and hippocampal volumes: WHIMS-MRI Study [published online ahead of print January 22, 2014]. *Neurology*.

David S. Boyer, MD, is a Clinical Professor of Ophthalmology at the University of Southern California Keck School of Medicine, Department of Ophthalmology, in Los Angeles. Dr. Boyer is a Retina Today *Editorial Board member. He may be reached at +1 310 854 6201; or via email at vitdoc@aol.com.*