Recent Pharma News

All FDA Drug Approvals Not Created Equal

Friday, 24 January 2014, -- Many patients and physicians assume that the safety and effectiveness of newly approved drugs is well understood by the federal Food and Drug Administration (FDA) - but a new study by researchers at Yale School of Medicine shows that the clinical trials used by the FDA to approve new drugs between 2005 and 2012 vary widely in their thoroughness. Published in the Jan. 22/29 issue of JAMA, the study is the first systematic analysis of the standard used by the FDA in making drug approval decisions.

"We found that during the study period, more than one-third of the drugs were approved on the basis of a single trial, without replication, and many other trials were small, short, and focused on lab values, or some other surrogate metric of effect, rather than clinical endpoints like death," said first author and Yale School of Medicine student Nicholas S. Downing, who conducted the study with senior author Joseph Ross, M.D., and colleagues at the Yale Center for Outcomes Research & Evaluation (CORE).

Downing and the team evaluated the strength of clinical trial evidence supporting FDA approval decisions for new drugs by characterizing key features of efficacy trials, such as trial size, design duration, and end points. They used publicly available FDA documents to identify 188 novel therapeutic agents for seven years. These medical review documents summarized in great detail the rationale behind FDA approvals.

"Based on our analysis, some drugs are approved on the basis of large, high-quality clinical trials, while others are approved based on results of smaller trials," said Ross, assistant professor of internal medicine at Yale School of Medicine. "There was a lack of uniformity in the level of evidence the FDA used."

He added: "We also found that only 40% of drug approvals involved a clinical trial that compared a new drug to existing treatment offerings. This is an important step for determining whether the new drug is a better option than existing, older drugs."

Downing said survey data shows that patients expect drugs approved by the FDA to be both safe and effective. "Based on our study of the data, we can't be certain that this expectation is necessarily justified, given the quantity and quality of the variability we saw in the drug approval process," he said.

Antipsychotic Drug Exhibits Cancer-Fighting Properties

Friday, January 10, 2014,-- In a prime example of finding new uses for older drugs, studies in zebrafish show that a 50-year-old antipsychotic medication called perphenazine can actively combat the cells of a difficult-to-treat form of acute lymphoblastic leukemia (ALL). The drug works by turning on a cancer-suppressing enzyme called PP2A and causing malignant tumor cells to self-destruct.

The findings suggest that developing medications that activate PP2A, while avoiding perphenazine's psychotropic effects, could help clinicians make much-needed headway against T-cell ALL, and perhaps other tumors as well. A study team led by Alejandro Gutierrez, MD, and A. Thomas Look, MD, of Dana-Farber/Boston Children's Cancer and Blood Disorders Center, and Jon Aster, MD, PhD, of Dana-Farber Cancer Institute and Brigham and Women's Hospital, reported the results Jan. 9 in the Journal of Clinical Investigation.

T-ALL is rarer and more aggressive than the B-cell form of ALL, and it has a relatively poor prognosis. Despite improvements in the treatments available, 20 percent of children and more than 50 percent of adults diagnosed with T-ALL succumb to it. To identify possible new treatment options, Gutierrez, Look and their collaborators screened a library of 4,880 compounds - including FDA-approved drugs whose patents had expired, small molecules and natural products - in a model of T-ALL engineered using zebrafish.

Strategies that identify new uses for existing drugs have grown in popularity in recent years as a way of quickly developing new disease therapies. Zebrafish models are cost-effective platforms for rapidly conducting drug screens, as well as basic stem cell, genetic, cancer and developmental research. "We wanted to see if there were drugs or known bioactive molecules that are active

against T-ALL that hadn't been tested yet," Look explained. "There may be drugs available for other indications that could be readily repurposed if we can show activity."

One of the strongest hits in the zebrafish screen was the drug perphenazine. It is a member of the phenothiazines, a family of antipsychotic medications used for 50 years, because they can block dopamine receptors. The team verified perphenazine's anti-leukemic potential in vitro in several mouse and human T-ALL cell lines. Biochemical studies indicated that perphenazine's anti-tumor activity is independent of its psychotropic activity, and that it attacks T-ALL cells by turning on PP2A.

The fact that perphenazine works by reactivating a protein shut down in cancer cells is itself novel in the drug development field. "We rarely find potential drug molecules that activate an enzyme," Gutierrez explained. "Most new drugs deactivate some protein or signal that the cancer cell requires to survive. But, here, perphenazine is restoring the activity of PP2A in the T-ALL cell."

Gutierrez and Look, along with their collaborators, are now working to better understand the interactions between PP2A and perphenazine. They also want to search for or develop molecules that bind to and activate the enzyme more tightly and specifically to avoid perphenazine's psychiatric effects. "The challenge is to use medicinal chemistry to develop new PP2A inhibitors similar to perphenazine and the other phenothiazines, but to dial down dopamine interactions and accentuate those with PP2A," Look said.

The researchers see future PP2A inhibitors not as magic bullets but as potentially important additions to the oncologist's arsenal when treating patients with T-ALL. "T-ALL patients are often on the borderline between a long remission and a cure," Look said. "If we can push the leukemia cells a little harder, we may get more patients who are actually cured. In this way, PP2A inhibitors may, in combination with other drugs, make a real difference for patients."

It may be that the benefits of PP2A-activating drugs could extend beyond T-ALL. "The proteins that PP2A suppresses, such as Myc and Akt, are involved in many tumors," Look noted. "We are optimistic that PP2A activators will have quite broad activity against different kinds of cancer, and we're anxious to study the pathway in other malignancies as well."

Take Aspirin at Bedtime to Better Protect Your Heart, Study Suggests

Tuesday, November 19, 2013, -- A daily dose of aspirin has become a common treatment for people at high risk for heart attacks or strokes, because it thins the blood and prevents clots from forming. A new Dutch study suggests that people who take aspirin at bedtime might get more protection against heart attacks or strokes.

The research involved nearly 300 heart attack survivors who were taking aspirin to ward off a second heart attack. During two separate three-month periods, half the patients took 100 milligrams of aspirin after they woke up in the morning while the other half took the same dose at bedtime. The researchers wanted to see if taking aspirin at night could better thin a person's blood and potentially lower their heart attack risk. Since the 1980s, it's been known that cardiovascular events happen more often in the morning. Morning hours are a peak period of activity for platelets, blood cells that aid in clotting. Doctors suspect that might have a hand in the increased risk of heart attacks and strokes in the morning. Aspirin reduces the activity of platelets, and thus reduces the chance that those platelets will clot in the bloodstream and cause a heart attack or stroke, according to the findings.

The results of research presented at meetings should be viewed as preliminary until published in a peer-reviewed medical journal.

Could Vaccines Someday Improve Heart Health?

Monday, November 18, 2013, -- People routinely get vaccinations to ward off the flu or prevent infectious diseases such as measles and whooping cough. Could there be a vaccine in the future that would prevent a heart attack?

Two animal studies suggest that vaccines might someday be used to reduce high cholesterol levels and lower blood pressure. In both cases, the vaccines interrupt processes in the body that, if left alone, can lead to high cholesterol and elevated blood pressure.

The first study, out of Vienna, found that mice and rats had lower cholesterol levels for a year following

treatment with a vaccine that protects a cell's ability to remove "bad" LDL cholesterol from the bloodstream. The vaccine targets an enzyme called PCSK9. This enzyme causes cells to become less able to yank LDL cholesterol from the bloodstream and convert it into hormones or other useful products. By reducing the amount of active PCSK9 in a body, the vaccine also reduces the cholesterol levels as cells become more efficient in using cholesterol.

The second study, this one from Japan, used a different vaccine to lower high blood pressure in laboratory rats for up to six months. This vaccine interferes with a hormone called angiotensin II, which increases blood pressure by causing blood vessels to constrict. Medications already are widely used to block angiotensin II and control blood pressure, but they have to be taken daily to be effective. In this study, the vaccine reduced the rats' blood pressure for months and reduced damage to the heart and blood vessels associated with high blood pressure. It also did not cause any damage to the kidneys, heart or liver.

While these findings are promising, there needs to be more study before it is ready as a vaccine for humans. At this point, the vaccine is at least five to six years away from human trials, according to study author because the studies were presented at a medical meeting, the data and conclusions should be viewed as preliminary until published in a peer-reviewed journal.

First Effective Malaria Vaccine May Be Near, Experts Say

Tuesday, October 8, 2013 -- Promising results from a large-scale clinical trial mean that the world's first malaria vaccine may be on the market by 2015 and could potentially save hundreds of thousands of lives a year.

The phase III clinical trial of more than 15,000 infants and young children in Africa found that the vaccine -- called RTS,S -- continued to protect the youngsters from malaria for up to 18 months after vaccination. The ongoing trial of the RTS,S vaccine is being conducted by 11 research centers in seven African countries, together with the PATH Malaria Vaccine Initiative and drug maker GlaxoSmithKline.

During the 18-month follow-up period, there was a 46 percent reduction in the number of malaria cases in children aged 5 months to 17 months at first vaccination, working out to 941 fewer cases of malaria for every 1,000 children (a child can contract more than one case of malaria, the experts noted). Cases of severe malaria were reduced by 36 percent and malaria hospitalizations were reduced by 42 percent.

Among infants who were 6 to 12 weeks old at first vaccination, there was a 27 percent reduction in the number of malaria cases during the 18-month follow-up, which works out to 444 fewer cases of malaria for every 1,000 infants. There was also a 15 percent reduction in cases of severe malaria and 17 percent fewer hospitalizations for malaria, the investigators found.

The latest findings from the trial were presented at the Multilateral Initiative on Malaria Pan African Conference in South Africa. Based on the data, vaccine maker GlaxoSmithKline plans to apply next year to have the vaccine approved by the European Medicines Agency. If the agency approves the vaccine, the World Health Organization said it could issue a recommendation for the vaccine as early as 2015.

Common Antidiabetic Drugs May Carry Risk, Study Suggests

Thursday, September 26, 2013 -- Diabetes patients who take drugs called sulfonylureas as an initial therapy have a higher risk of death than those who take the diabetes drug metformin, a new study says. The British researchers said the findings suggest that it may no longer be appropriate to offer sulfonylureas as a first-line treatment. Diabetes experts in the United States agreed that the study could have an impact on care.

Both metformin and sulfonylureas are commonly prescribed as first-line therapies for patients and have been available since the 1950s. Researchers analyzed data from thousands of people in the United Kingdom who were diagnosed with type 2 diabetes and began first-line blood sugar-lowering treatments between 2000 and 2012 and were followed for an average of three years.

Patients who took sulfonylureas only were 58 percent more likely to die from any cause than those who took metformin only, according to the study, which was presented at the annual meeting of the European Association for the Study of Diabetes in Barcelona, Spain. Findings presented at medical meetings are typically

considered preliminary until published in a peer-reviewed journal.

Common Anrtihypertensive Drugs May Help Slow Dementia

Friday, July 26, 2013 -- Older adults with dementia who use certain blood pressure medications may have a slower rate of mental decline, new research suggests. The study, reported July 25 in *BMJ Open*, found that dementia patients on particular ACE inhibitors showed a somewhat slower decline in memory and other mental skills than patients not on the drugs.

The drugs linked to the benefit are known as centrally acting ACE inhibitors, which means they cross from the blood into the brain. They include commonly used medications such as captopril, fosinopril, lisinopril, perindopril, ramipril and trandolapril. However, the findings do not mean that people with dementia should be started on those ACE inhibitors, according to a neurologist who was not involved with the research.

The study was not a clinical trial set up to test the effects of ACE inhibitors rather it was an "observational" study, where researchers followed more than 350 older adults with Alzheimer's or other forms of dementia - about one-quarter of whom happened to be on ACE inhibitors. Those types of studies cannot prove that a drug is the reason for a particular benefit. On the other hand, the findings support the "larger message" that better cardiovascular health - including controlling blood pressure and cholesterol levels - can benefit the brain as well.

Previous studies have linked better blood pressure control - and various classes of blood pressure drugs - to both a lower risk of developing dementia and a slower progression of the disease. The study included 361 dementia patients, average age 77, who completed standard tests of memory, planning and other mental abilities. Of those, 85 were already on a centrally acting ACE inhibitor, and 30 more started on one during the study period.

Aspirin Every Other Day May Lower Women's Colon Cancer Risk

Monday, July 15, 2013 -- Taking a low-dose aspirin every other day may reduce the risk of colorectal cancer, according to a study that focused on nearly 40,000 women aged 45 and older. The protection does seem to take some time to surface, said the correspondent researchers at Brigham and Women's Hospital and Harvard Medical School. After 10 years, they started to see an effect. After 18 years of follow-up, they saw a 20 percent reduction in colon cancer over the whole time period. When they looked at the 10-to-18 year mark, the reduction was 42 percent. However, risks linked with aspirin, such as gastrointestinal bleeding, must also be considered.

The study, funded by the U.S. National Cancer Institute and U.S. National Heart, Lung, and Blood Institute, is published July 16 in the *Annals of Internal Medicine*.

Fish Oil Pills Might Cut Diabetes Risk, Researchers Say

Wednesday, May 22, 2013 -- Fish oil supplements could help reduce the risk for type 2 diabetes, new research suggests. The supplements, also known as omega-3 fatty acids, increase levels of a hormone called adiponectin that's linked to insulin sensitivity, Harvard researchers found. Higher levels of this hormone in the bloodstream have also been linked to a lower risk for heart disease.

For their study, the researchers conducted a "meta-analysis" of 14 clinical trials. A meta-analysis reviews existing research and attempts to find a consistent pattern. In this case, the studies that were reviewed were all randomized, placebo-controlled trials, which is considered the gold standard in research.

Overall, the new study looked at 682 people who took fish oil supplements, and 641 who were given placebos such as sunflower or olive oil. Among the people treated with fish oil, adiponectin levels increased by 0.37 micrograms per milliliter of blood. This hormone plays a beneficial role in processes that affect metabolism, such as blood sugar regulation and inflammation. Because the effects of fish oil varied significantly in the studies analyzed, the researchers suggested that omega-3 fatty acids could have a stronger effect in certain groups of people. The investigators concluded that more research is needed to determine which people would benefit most from fish oil supplements.

The study is scheduled for publication in the *Journal of Clinical Endocrinology & Metabolism*. It was supported by grants from the National Institutes of Health's National Heart, Lung, and Blood Institute.

How to Quickly Spot Signs of Stroke: Experts

Monday, May 13, 2013 -- Sudden numbness or weakness in the face, arms or legs on one side of the body, confusion and trouble speaking are among the signs that someone is having a stroke. The sooner a stroke is recognized and treated, the greater the chances of recovery, experts say. "The most effective way to prevent the permanent damage associated with stroke is to recognize the signs of an attack and to seek medical attention immediately."

Dizziness and trouble walking, loss of vision in one or both eyes and a severe headache that comes on suddenly for no apparent reason are other signs that someone is having a stroke. Early treatment, however, can prevent or possibly reverse the damage caused by strokes. The experts advised remembering the acronym "FAST" to help people recognize a stroke sooner and reduce any long-term damage.

- **F for Face:** Does someone's face look uneven?
- **A for Arm:** Do you notice one arm hanging down?
- **S for Speech:** Check for slurred speech or other signs of trouble speaking.
- **T for Time:** Visit doctors and seek immediate medical attention.

Source: www.drugs.com; www.worldpharmanews.com
Information collected and compiled by-

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One of the most common treatments for stroke is tissue plasminogen activator, the "clot-busting" treatment also known as TPA. The drug is injected into an artery or vein to dissolve a clot and restore blood flow to the brain.

Revascularization is another treatment for stroke in which micro-catheters are placed inside the artery to remove blockages. In all cases, immediate medical attention can help reduce the damage caused by a stroke, according to the news release. Learning how to prevent strokes with certain lifestyle changes can also save lives, the experts pointed out. Lifestyle changes that can significantly reduce the risk of having a stroke include the following:

- Cut back on salt,
- Eat a healthy diet,
- Quit smoking,
- Exercise

Even with these lifestyle changes, the experts pointed out that people aged 55 years or older are still at greater risk for stroke. Also at greater risk are black people, Hispanics and those with a family history of stroke or "mini-stroke" (also called a transient ischemic attack).

Although strokes are more common in men, women who have strokes are more likely to die from them, according to the news release.

New Drugs Approval

Hetlioz

Generic Name : Tasimelteon
Date of Approval : January 31, 2014
Company : Vanda Pharmaceuticals, Inc.

Treatment for : *Non-24-Hour Sleep Wake Disorder*

The U.S. Food and Drug Administration (FDA) has approved Hetlioz (tasimelteon) 20mg capsules for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24).

Non-24 is a chronic, circadian rhythm disorder resulting from the misalignment of the endogenous master body clock to the 24-hour day, disrupting the sleep-wake cycle. Non-24 affects the majority of totally blind individuals.

Farxiga

Generic Name : Dapagliflozin
Date of Approval : January 8, 2014
Company : Bristol-Myers Squibb Company and AstraZeneca

Treatment for : *Type 2 Diabetes*

The United States Food and Drug Administration (FDA) has approved Farxiga (dapagliflozin), a sodium-glucose cotransporter 2 (SGLT2) inhibitor indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Tretten

Generic Name : Coagulation Factor XIII A-Subunit (Recombinant)
Date of Approval : December 23, 2013
Company : Novo Nordisk A/S

Treatment for : *Factor XIII A-Subunit Deficiency*

The U.S. Food and Drug Administration (FDA) has approved Tretten (Coagulation Factor XIII A-Subunit [Recombinant]) for the routine prophylaxis of bleeding in people with congenital factor XIII (FXIII) A-subunit deficiency.

Orenitram

Generic Name : Treprostinil
Date of Approval : December 20, 2013
Company : United Therapeutics Corporation

Treatment for : *Pulmonary arterial hypertension (PAH)*

The United States Food and Drug Administration (FDA) has approved Orenitram (treprostinil) Extended-Release Tablets for the treatment of pulmonary arterial hypertension (PAH) in WHO Group I patients to improve exercise capacity.

Sovaldi

Generic Name : Sofosbuvir
Date of Approval : December 6, 2013
Company : Gilead Sciences, Inc.

Treatment for : *Chronic Hepatitis C*

The U.S. Food and Drug Administration (FDA) has approved Sovaldi (sofosbuvir) 400 mg tablets, a once-daily oral nucleotide analog polymerase inhibitor for the treatment of chronic hepatitis C (CHC) infection as a component of a combination antiviral treatment regimen.

Velphoro

Generic Name : Sucroferric oxyhydroxide
Date of Approval : November 27, 2013
Company : Fresenius Medical Care Renal Pharma

Treatment for : *Hyperphosphatemia of Renal Failure*

The United States Food and Drug Administration (FDA) has approved Velphoro (sucroferric oxyhydroxide), an iron-based, calcium-free, chewable phosphate binder for the control of serum phosphorus levels in patients with Chronic Kidney Disease (CKD) on dialysis.

Olysio

Generic Name : Simeprevir
Date of Approval : November 22, 2013
Company : Janssen Therapeutics

Treatment for : *Chronic Hepatitis C*

The U.S. Food and Drug Administration (FDA) has approved Olysio (simeprevir), an NS3/4A protease inhibitor, for the treatment of chronic hepatitis C infection as part of an antiviral treatment regimen. Efficacy was demonstrated in combination with pegylated interferon and ribavirin in genotype 1 infected adults with compensated liver disease, including cirrhosis.

Source: www.drugs.com

Information collected and compiled by: **Md. Akbar Hossain**, Assistant Professor, Department of Pharmacy, Dhaka International University.