SOP Newsletter

Drug Information News From the School of Pharmacy Faculty Members

October 2014; Vol 2, issue 3

October 2014;
Volume 2, issue 3

In this edition:

Edited by:
Jihan Safwan, PharmD.
jihan.safwan@liu.edu.lb

Word of welcome from the dean

Dear Students,

Welcome to the Lebanese International University School of Pharmacy. I am honored to welcome you to the pharmacy community. Together, students, faculty, staff, alumni, and friends, we share a powerful connection. That connection lies in the education of future pharmacy professionals, in research that benefits humankind, in service to the profession, and answering the needs of our greater community. Further, I am proud to highlight the amazing work of our faculty members in the articles you'll find herein.

Our mission is to be a distinguished institution, where leaders in pharmacy practice, research and education are developed. We are eminent in our curriculum, students, and staff.

Our curriculum helps students develop their personality and expand their knowledge through extensive courses in pharmaceutical sciences, pharmacotherapy, management and marketing, disease management, pharmaceutical care, communication skills and, professional ethics. Since patients are placed at the center of the healthcare equation, and the pharmacist is a major component of this equation, we designed our curriculum to prepare our graduates to fulfill their commitment to patients' care. Also, pharmacy practice comprises a major component of this curriculum where students practice patient care in community and clinical settings under the supervision of highly qualified and dedicated faculty members.

Our students are the center of our education process. Classes are based on problem solving and case discussions where lecture notes are distributed to the students ahead of time. This gives the students the opportunity to be well prepared before attending their classes. Our laboratories are equipped with recent and essential equipment to facilitate the learning outcomes of didactic courses. Furthermore, academic advisors are assigned to every student to guide him/her throughout the years of study. We give our students the opportunity to participate in extracurricular activities in order to build their personalities and develop their skills in order to benefit the community and the profession.

What makes our school distinguished is the real family spirit, integrity and coordination among the faculty members to bring the best atmosphere needed for learning.

Finally, on the behalf of the faculty and staff of the school of pharmacy at LIU, I would like to welcome all new students who joined us this year and the continuing students, wishing them a fruitful year full of accomplishments and success.

Best regards,

Mohamad Rahal, PhD,
Dean of the School of Pharmacy

UPDATES IN

TOPIC IN THE NEWS

Fouad Sakr, PharmD.

EBOLA VACCINE IN TRIAL

Key point: Latest data from the World Health Organization (WHO) show about 2,500 people have died of Ebola in an outbreak that started in March and has infected almost 5,000 people in Guinea, Sierra Leone, Liberia and Nigeria.

Finer points: An Ebola vaccine, which GSK co-developed with the United States National Institutes of Health, has been given to 10 volunteers in a trial in the United States, and so far there were no signs of any serious adverse reactions.

The vaccine is designed to specifically target the Zaire strain of Ebola, the one circulating in the West Africa epidemic, the worst Ebola outbreak recorded.

"2,500 people have died of Ebola in an outbreak"

Since the vaccine contains no infectious Ebola virus material, only one of its genes, experts say there are no concerns that any of the subjects will contract the deadly disease.

GSK says it plans to begin making up to about 10,000 doses of the vaccine at the same time as the initial clinical trials, so that if they are successful, the vaccine could be made available immediately for an emergency immunization program.

Study data from an animal trial of an Ebola vaccine similar to this GSK one showed that it was effective for at least five weeks in lab monkeys but required boosting with an additional vaccine to extend its protection to 10 months.

However, the trials are seeking to determine not only whether the vaccine is safe, or causes adverse side effects, but also whether it triggers the production of antibodies against the Ebola virus. The aim is to complete the tests by the end of 2014, after which vaccines could be deployed on an emergency basis.

What you need to know: In short, there is clearly a need for this vaccine, but what is not clear is whether it will work well enough to protect someone from Ebola.

Source: Reuters Health Information

NEW DRUG OF THE MONTH

Dalal Hammoudi, RPh, MSc

FDA APPROVES ORBACTIV FOR TREATMENT OF SKIN INFECTIONS

Key point: On August 7th, 2014, the U.S. Food and Drug Administration approved Orbactiv® (oritavancin), a new antibacterial drug to treat adults with skin infections.

Finer points: Oritavancin is indicated for patients with acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible bacteria, including Staphylococcus aureus (both methicillin-susceptible and methicillin-resistant strains), various Streptococcus species and Enterococcus faecalis. With this approval, Oritavancin becomes the third new antibacterial drug approved by the FDA during the year 2014 to treat ABSSSI, after Dalvance® (dalbavancin) in May and Sivextro (tedizolid) in June. Marketed by The Medicines Company, New Jersey, Oritavancin was also designated as a Qualified Infectious Disease Product (QIDP), being an antibacterial or antifungal human drug intended to treat a serious or life-threatening infection.

Oritavancin is a semisynthetic lipoglycopeptide with bactericidal activity against gram-positive bacteria. Its concentration-dependent activity and prolonged half-life allow for single-dose (1200 mg) treatment. It is administered by intravenous infusion. Oritavancin's safety and efficacy were evaluated in two clinical trials with a total of 1,987 adults with ABSSSI. Participants were randomly assigned to receive Oritavancin or vancomycin. Results showed Oritavancin was as effective as vancomycin for the treatment of ABSSSI. Oritavancin has three mechanisms of action: (i) inhibition of cell wall biosynthesis by binding to peptidoglycan precursors; (ii) inhibition of the crosslinking step of cell wall biosynthesis; and (iii) disruption of bacterial cell membrane integrity,

"Oritavancin appears to be a promising antimicrobial alternative to vancomycin"

leading to depolarization, permeabilization, and cell death. These multiple mechanisms contribute to the concentration-dependent bactericidal activity of oritavancin. To date, resistance has not been observed in clinical studies.

The most common side effects identified were headache, nausea, vomiting, the formation of skin and soft tissue abscesses on arms and legs and diarrhea. Oritavancin's label also includes a warning regarding interference with coagulation tests and increased risk of bleeding upon co-administration with warfarin.

What you need to know: Oritavancin appears to be a promising antimicrobial alternative to vancomycin, with additional activity against Staphylococcus and Enterococcus resistant to vancomycin, for treatment of skin and skin structure infections.

Source: 1. Corey GR, Kabler H, Mehra P, Gupta S, Overcash JS, Porwal A, et al. Single-dose oritavancin in the treatment of acute bacterial skin infections. N Engl J Med. 2014 Jun 5;370(23):2180–90. 2. Mendes RE, Sader HS, Flamm RK, Farrell DJ, Jones RN. Oritavancin activity against Staphylococcus aureus causing invasive infections in U.S. and European hospitals: a 5-year international surveillance program. Antimicrob Agents Chemother. 2014 May;58(5):2921–4. 3. The US Food and Drug Administration News and Events; News Release, August 7th, 2014.

DRUG APPROVAL

Nisreen Mourad, PharmD.

THE LONG-ACTING BETA-AGONISTS WELCOMES A NEW MEMBER "OLODATEROL"

Key point: Chronic obstructive pulmonary disease (COPD) is a common disease of the airways characterized by the gradual and progressive loss of lung function that is not fully reversible. COPD symptoms often worsen over time thus limiting people's ability to perform routine activities. According to the latest World Health Organization (WHO) estimates, currently 64 million people suffer from COPD while 3 million people died of it. In fact, WHO predicts that by the year 2030 COPD will become the third leading cause of death worldwide, and thus the search for new treatment options remains a major concern in the pharmaceutical world. On July 31st, 2014 the US Food and Drug Administration (FDA) approved olodaterol (Striverdi® Respimat® 5 µg, Boehringer Ingelheim) a long-acting beta-agonist (LABA) as a once-daily, long-term maintenance bronchodilator treatment for airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema.

Finer points: The approval of olodaterol was based on the data from the Phase III olodaterol clinical trial program. These trails demonstrated improvements in lung function provided by the once-daily dosing of olodaterol 5 µg in 4,900 patients with moderate to very severe COPD compared to placebo. However, it should be kept in mind that olodaterol is not indicated for patients with acutely deteriorating COPD or asthma. Furthermore, it shouldn't be used as a rescue therapy for acute episodes of bronchospasm.

Currently, olodaterol is delivered via a propellant-free inhalation spray that generates a soft, slow-moving mist where the most commonly reported adverse effects associated with its use are nasopharyngitis, upper respiratory tract infection, bronchitis, cough, urinary tract infection, dizziness, rash, diarrhea, back pain, and arthralgia. Other more serious side effects include paradoxical bronchospasm and cardiovascular effects. In addition, as other LABAs olodaterol carries a boxed warning about the increased risk for asthma-related death and should be used with caution in patients with convulsive disorders, thyrotoxicosis, diabetes mellitus, ketoacidosis, in patients with known or suspected prolongation of the QT interval, and in patients who are unusually responsive to sympathomimetic amines.

"Olodaterol carries a boxed warning about the increased risk for asthma-related death"

What you need to know: Olodaterol seems to be a promising drug for COPD, where in August 19th, 2014 the FDA accepted for review the New Drug Application (NDA) for the fixed-dose combination of tiotropium and olodaterol delivered via the Respimat® inhaler for similar indication as olodaterol.

Source:1.http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm407465.htm.2.http://us.boehringer-ingelheim.com/news_events/press_releases/press_release_archive/2014/08-19-14-boehringer-ingelheim-us-filing-fixed-dose-combination-tiotropium-plus-olodaterol-patients-copd.html. 3. http://www.who.int/respiratory/copd/en/

ENDOCRINOLOGIC DISORDERS

Rima Abdul Khalek, PharmD.

FDA APPROVAL OF LIRAGLUTIDE FOR OBESITY TREATMENT FURTHER EXPANDS TREATMENT OPTIONS

Key point: The glucagonlike peptide-1 (GLP-1) analogue liraglutide has received approval by the FDA panel as a prescription drug for long-term treatment of obesity. It is to be used as an adjunct to a reduced calorie diet and increased physical activity at a dose of 3 mg injected once-daily. It will be marketed under the proposed brand name of Saxenda.

Finer points: It was until 2012, that orlistat (Xenical®) was the only treatment left for the long-term management of obesity, after which several drugs have been approved for this indication, expanding the available choices. In 2012, lorcaserin (Belviq®) and the combination of phentermine/topiramate (Qsymia®) received approval (Table 1). During the month of September 2014, the FDA follows the approval of bupropion/naltrexone (Contrave®) by the 14 to 1 vote for the approval of liraglutide (Saxenda®) for the management of obesity; however, at a higher dose than that used for treatment of diabetes. Taking into consideration the nature and the better understanding of obesity, the FDA approves these drugs as an adjunct to diet and exercise in adults who are obese (BMI $\geq$ 30kg/m2) or who are overweight (BMI $\geq$ 27kg/m2) and have at least one weight-related condition such as hypertension, type 2 diabetes or others.

The efficacy of liraglutide was derived from 3 phase 4 trials, in which more than 3000 patients had received liraglutide. The drug should be discontinued if there is no clinically meaningful weight loss after 12 weeks, where clinically meaningful is specified by the FDA to be a loss of 5% of baseline body weight. As with previous drugs that have left the market, safety issues are a concern, not with the milder side effects such as nausea, vomiting, diarrhea and hypoglycemia, but with the more serious acute pancreatitis, acute gallstone disease, thyroid neoplasm and increase in heart rate of 2 to 3 bpm. The panel has required that these issues be addressed in post-marketing trials, including the ongoing Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results (LEADER) study that will elucidate the cardiovascular risks.

What you need to know: Although liraglutide has received approval for the long-term treatment of obesity, the serious adverse events have required its monitoring through post-marketing trials, which will show if it will eventually remain in the market or be removed as other obesity treatments.

Source: 1.Tucker M. FDA Panel Endorses Liraglutide as Obesity Treatment September 12, 2014.(Available at: http://www.medscape.com/viewarticle/831609.) 2. Endocrinologic and Metabolic Drugs Advisory Committee Meeting Hyattsville, MD September 11,2014 (http://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/drugs/endocrinologicandmetabolicdrugsadvisorycommittee/ucm416154.pdf). 3. Colman E, Golden J, Roberts M. The FDA's assessment of two drugs for chronic weight management. N Engl J Med. 2012;367:1577-1579.

TABLE 1: FDA APPROVED AGENTS FOR CHRONIC WEIGHT MANAGEMENT IN OBESE ADULTS, AS AN ADJUNCT TO A REDUCED-CALORIE DIET AND INCREASED PHYSICAL EXERCISE.

Brand	Drug	Manufacturer	Approval date
Saxenda®	Liraglutide	Novo Nordisk	2014
Contrave®	Bupropion/naltrexone	Orexigen Pharmaceuticals	2014
Belviq®	Lorcaserin	Arena Pharmaceuticals	2012
Qsymia®	Phentermine/topiramate	Vivus	2012
Xenical®	Orlistat	Roche Laboratories	1999

RESPIRATORY DISEASES

Nermine Chouman, PharmD.

NEW DRUG MAY CHANGE TREATMENT OF ASTHMA

Key point: It is estimated that approximately 300 million people worldwide are known to have asthma, with 180,000 deaths annually. For the majority of asthma patients, standard treatments can control the disease. However, an estimated 10% to 20% of patients with moderate-to-severe, persistent allergic type asthma, are less than optimally controlled despite existing therapies placing them at risk for repeated exacerbations hospitalizations and negative outcomes.

Finer points: Recently, researchers have developed a new drug to treat the underlying pathology associated with asthma, reducing flare-ups by nearly 87%, according to results of a new trial. Dupilumab is a monoclonal antibody targeting the alpha subunit of the interleukin 4 receptor (IL-4R alpha), which regulates signaling of both IL-4 and IL-13, that have been linked to inflammation.

The small phase 2a study enrolled 104 patients with moderate-to-severe, chronic asthma that was not well controlled with inhaled glucocorticosteroids (ICS) and long-acting beta agonist (LABA) therapy, and who had elevated blood or sputum eosinophils.
The primary objective of the trial was to assess the effect of subcutaneous dupilumab, administered weekly at a dose of 300 mg for 12 weeks.
Patients were treated with dupilumab (N=52) or placebo (N=52) in addition to ICS and LABA therapy for the first 4 weeks of the study. The LABA was withdrawn at week 4 and the ICS was tapered to withdrawal between the sixth and ninth week. Patients were treated for 12 weeks or until they experienced a protocol-defined asthma exacerbation, the primary endpoint of the study. 23 patients (44.2%) receiving placebo experienced an asthma exacerbation compared to 3 patients (5.8%) receiving dupilumab, resulting in an 87% reduction

"Dupilumab, is a new promising class of drug that can treat the root of asthma"

in the incidence of asthma exacerbations for the dupilumab arm compared to placebo ($p<.001$). In terms of secondary endpoints, dupilumab helped to improve symptoms and standard measures of lung function as forced expiratory volume over one second (FEV1) and reduced the need for standard drugs such as LABA and steroids. Adverse effects were generally non-specific and of mild-to-moderate intensity including injection-site reaction, nasopharyngitis, upper respiratory tract infection, headache and nausea.

What you need to know: Within such a promising new therapeutic scenario, anti-IL-4 and anti-IL-13 treatments could be very important, given the key role exerted by these two cytokines in the pathophysiology of asthma, particularly for patients with moderate to severe persistent asthma that are not well controlled by standard drugs. However, larger trials of longer duration are required to widen and validate these early findings.

Source: Vatrella A, Fabozzi I, Calabrese C, Maselli R, Pelaia G. Dupilumab: a novel treatment for asthma. J Asthma Allergy. 2014; 7: 123–130.

NEUROLOGIC DISEASES

Samar Younes, PharmD.

MIGRAINES IN MIDDLE AGE, PARKINSON'S RISK LATER?

Key points: Migraine is the most common brain disorder in both men and women, affecting 6% to 7% of men and 17% to 18% of women in the general population. Studies have demonstrated that patients with migraine disease have an increased risk of cardiovascular and psychiatric disorders. While this relationship has been demonstrated in several studies, less is known about migraine and other comorbid conditions. Recently, results from a large, longitudinal study of patients in Reykjavik, Iceland suggest a link between midlife migraine and Parkinson's disease.

Finer points: Over the course of 25 years, a total of 5,620 people who were between the ages of 33 and 65 were followed in the Reykjavik Study (RS). The study was established in 1967, and included men and women who were born between 1907 and 1935. The 5,620 people were classified into 4 groups: 3924 with no headache, 1028 with nonmigraine headache, 238 with migraine without aura, and 430 with migraine with aura. Follow-up was conducted between 2002 and 2006 in the Age, Gene/Environment Susceptibility-Reykjavik Study (AGES-Reykjavik Study) on 5764 RS survivors. Study participants were assessed for symptoms of Parkinson's, diagnosis of Parkinson's, or symptoms of restless legs syndrome (RLS).

Results of the study showed that people with midlife migraine, especially those with migraine with aura, were more likely than others to have symptoms of Parkinson's later in life (odds ratio [OR] = 3.6 [95% Confidence interval (CI) 2.7-4.8]). Additionally, those with migraine with aura were also more likely to be diagnosed with Parkinson's disease (OR = 2.5 [95% CI 1.2-5.2]) later in life. Further, women with migraine with aura had an increased likelihood of having a parent (OR = 2.26 [95% CI 1.3-1.4]) or sibling (OR = 1.78 [95% CI 1.1-2.9]) with Parkinson's disease. Restless-leg syndrome later in life was associated with headache.

Study investigators concluded that there appears to be a link between migraine and multiple indicators of Parkinson's disease, but that link

"Link between migraine and multiple indicators of Parkinson's disease"

is not fully understood. Dr. Scher, lead author of the study publication, noted that there could be multiple factors driving the association between midlife migraine and Parkinson's disease later in life. One potential mechanism Scher noted is head injury. She also proposed the possibility that iron deposition may be a potential common factor, as some studies have shown that iron deposition in the basal ganglia occurs in people with Parkinson's disease, while other studies have demonstrated that people with migraine are more likely to have iron deposition.

What you need to know: It appears that there is an association between mid-life migraine and Parkinson's disease later in life; however, more research is required to elucidate the potential causes of this relationship.

Source: 1. Scher A, Ross W, Sigurdsson S, et al. Midlife migraine and latelife parkinsonism. Neurology. 2014;82: Supplement I9-2.001. 2. Anderson P. Midlife migraine linked to later parkinson's. Medscape.com. September 17, 2014.

INFECTIOUS DISEASES

Fouad Sakr, PharmD.

EARLY AZITHROMYCIN IN INFANTS RISKS PYLORIC STENOSIS

Key points: Erythromycin is known to be associated with the development of pyloric stenosis. After this discovery was made in 1999, another macrolide antibiotic (azithromycin) replaced erythromycin as the prophylaxis of choice in infants exposed to pertussis.

Finer points: A new study suggests that newborns exposed to azithromycin in the first 6 weeks of life have a significantly increased risk of developing hypertrophic pyloric stenosis. Those results were presented at the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC).

"Weigh the risks and benefits when prescribing azithromycin"

A retrospective study included 4875 infants on a prescription of azithromycin. There was an 8-fold increased risk of developing the condition for those exposed in the first 14 days (P < .001) and a 3-fold increased risk for those exposed between days 15 and 42 (P = .15). The risk for infantile hypertrophic pyloric stenosis was much higher in infants exposed to erythromycin. The risk was 13-fold for infants exposed in the first 14 days of life (P < .001) and 4-fold for those exposed between days 15 and 90 (P = .002). As well, pyloromyotomy was performed after a median of 13 days following exposure to erythromycin, and a median of 29.5 days following exposure to azithromycin.

What you need to know: In fact, "pyloric stenosis" was added to the azithromycin package insert as a potential side effect a year or so ago. Practitioners must carefully weigh the risks and benefits when prescribing azithromycin, particularly to male infants, in the first few weeks of life. These infants should be monitored for signs and symptoms of pyloric stenosis for 6 weeks following treatment.

Source: 54th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC): Abstract G-993. Presented September 7, 2014.

CARDIOLOGIC DISEASES

Michelle Cherfan, PharmD.

WARFARIN OR NOVEL ORAL ANTICOAGULANTS FOR ATRIAL FIBRILLATION

Key Points: For decades, warfarin has been the only oral anticoagulant available to prevent stroke in patients with nonvalvular atrial fibrillation. Three new oral anticoagulants have been approved in recent years as alternatives: dabigatran (Pradaxa® - Boehringer Ingelheim), rivaroxaban (Xarelto® - Bayer/Johnson & Johnson), and apixaban (Eliquis® - Bristol-Myers Squibb/Pfizer). Although the clinical use of newer agents has expanded rapidly, individual controlled trials of these agents in atrial fibrillation were underpowered to detect differences in secondary outcomes and subgroups.

Finer Points: Investigators conducted a meta-analysis of four Phase III randomized controlled trials that compared efficacy and safety of newer oral anticoagulants to warfarin in subjects with nonvalvular atrial fibrillation (mean age 72 years). The analysis included 42,411 participants who received newer oral anticoagulants and 29,272 who received warfarin. One-third were women, and participants were followed for a median of 2.2 years.

Compared with warfarin, the newer oral anticoagulants significantly reduced stroke or systemic embolic events (3.79% versus 3.11%, relative risk [RR] 0.81, 95% CI 0.73–0.91; p<0·0001). The reduced risk with newer agents was driven primarily by reduced hemorrhagic stroke (0.44% versus 0.9%, RR 0.49, 95% CI 0.38–0.64; p<0·0001), with a significant decrease in total mortality (6.9% versus 7.68%, RR 0.9, 95% CI 0.85–0.95; p=0·0003). Newer anticoagulants were also linked to decreased intracranial hemorrhage but increased gastrointestinal bleeding. Decreased risk was consistent across various subgroups

defined by factors such as age, sex, diabetes status, history of stroke, and renal function. Low-dose new oral anticoagulant regimens showed similar overall reductions in stroke or systemic embolic events to warfarin (1·03, 0·84—1·27; p=0·74), and a more favorable bleeding profile (0.65, 0.43—1.00; p=0.05), but significantly more ischemic strokes (1.28, 1.02—1.60; p=0.045).

This is the first meta-analysis to include all four large randomized controlled trials of newer oral anticoagulants in patients with atrial fibrillation. Overall, the new oral anticoagulants show a favorable balance between efficacy and safety compared with warfarin, which is consistent across a wide range of patients with atrial fibrillation known to be at high risk for both ischemic and bleeding events, the authors concluded. However, authors of an accompanying editorial noted that the current analysis "does not really answer which novel oral anticoagulant is best, whether from an efficacy or safety perspective."

A separate meta-analysis of trial data with lower doses of newer agents revealed similar risk reduction compared with warfarin for stroke or systemic embolism events and superior results for reducing hemorrhagic stroke and mortality. However, lower doses were associated with increased risk of ischemic stroke and myocardial infarction compared with warfarin.

Pharmacists continue to play a vital role in patients' education to recognize signs and symptoms of an embolic or bleeding event. With newer anticoagulants, pharmacists can also provide guidance on dose adjustments for patients with decreased renal function and maintain vigilance for potential drug–drug interactions.

"Low-dose new oral anticoagulant regimens showed similar overall reductions"

What you need to know: According to a recent analysis, newer oral anticoagulants are superior to warfarin for preventing strokes, intracranial bleeds, and death in patients with atrial fibrillation. The risk of major bleeds is similar to that seen with warfarin, but gastrointestinal bleeding occurs more in patients on the newer agents.

Sources: 1. Ruff CT et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomized trials. Lancet. 2014;383:955–62. 2. Larsen TB, Lip, GYH. Warfarin or novel oral anticoagulants for atrial fibrillation. Lancet. 2014;383:931–3.

RHEUMATOLOGIC DISEASES

Diana Malaeb, PharmD.

RHEUMATOID ARTHRITIS

Key Points: Disease modifying antirheumatic drugs (DMARDs) is a drug class which is used in various arthritic conditions to arrest the progression of disease along with relief from pain.

Finer Points: Currently non-biological DMARDs like methotrexate, sulfasalazine, hydroxychloroquine and azathioprine serve the purpose of relieving pain and inhibiting the progression of disease. Biological DMARDs like toclizumab, adalimumab, infliximab, golimumab and abatacept have shown more efficacy and lesser side effects as compared to non-biological DMARDs but their access to patients is less because of their higher cost.

DMARDs act by different mechanisms against inflammation like inhibition of tumor necrosis factor, suppression of IL-1, induction of apoptosis of inflammatory cells, by increasing chemotactic factors, inhibition of purine synthesis, pyrimidine metabolism or purine metabolism. DMARDs have important applications in diseases like rheumatoid arthritis, Crohn's disease, juvenile idiopathic arthritis, psoriatic arthritis and myasthenia gravis.

Golimumab is a novel anti-TNF-alpha monoclonal antibody that is in clinical development for the treatment of RA, psoriatic arthritis (PsA), and ankylosing spondylitis (AS), either as a first-line biologic therapy or an alternative after other TNF-alpha inhibitors have been discontinued. Golimumab has demonstrated significant efficacy in randomized, double-blind, placebo-controlled trials when administered subcutaneously once every four weeks. It has been generally well tolerated in clinical trials and demonstrates a safety profile comparable with currently available TNF-alpha inhibitors. However,

golimumab has the potential advantage of once monthly subcutaneous administration and the possibility of both subcutaneous and intravenous administration.

What you need to know: DMARDs are being used by about 83% of the population worldwide. The withdrawal of COX-2 inhibitors because of their cardiovascular side effects and the short-term action associated with glucocorticoids has motivated many drug companies to develop newer DMARDs, like golimumab.

Source: 1. Joshi P, and Dhaneshwar SS. An update on disease modifying anti-rheumatic drugs. Inflamm Allergy Drug Targets. 2014;13(4):249-61. 2. Kay J and Rahman MU. Golimumab: A novel human anti-TNF-alpha monoclonal antibody for the treatment of rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis. Core Evid. 2010 Jun 15;4:159-70.

CARDIOPULMONARY DISEASES

Mariam Dabbous, PharmD.

TWO DRUGS BETTER THAN ONE FOR COPD

Key Points: For older adults with chronic obstructive pulmonary disease (COPD), combination therapy with long-acting β-agonists (LABAs) and inhaled corticosteroids (ICSs) produces better outcomes than treatment with LABAs alone, a new study suggests.

Finer Points: In a retrospective, population-based analysis of 11,872 people aged 66 years or older, rates of mortality or hospitalization for COPD were lower among new users of LABAs plus ICSs than new users of LABAs alone. The differences were modest but statistically significant.

The salutary effect of LABAs and ICSs was even more pronounced in subgroups of patients who had asthma or who were not taking long-acting anticholinergic drugs (LAAs).

These findings could have a real effect on everyday clinical practice. The finding of an association between LABAs and ICSs and their outcomes helps clarify the management of patients with COPD and asthma, as many studies of COPD medications have excluded people with asthma and vice versa. In addition, practice guidelines for COPD recommend that LABAs be considered first-line treatment while asthma guidelines warn against the use of LABAs without ICSs. The new findings also offer insight into the optimal treatment of COPD patients without asthma, those who would not be considered especially corticosteroid responsive.

The primary outcome measure was a composite of all-cause mortality and COPD hospitalization. Secondary outcomes included hospitalization for pneumonia or fragility fractures of the spine, hip, pelvis, or forearm, all of which may be adverse effects of ICSs.

The primary outcome occurred in 5594 (64.2%) of patients receiving the LABA-ICS combination, including 5010 (57.5%) who died or were hospitalized for COPD within 5 years. Of the patients using LABA alone, the primary outcome occurred in 2129 (67.4%), including 1933 (61.2%) within 5 years. Use of the combination therapy was associated with a hazard ratio of 0.92 (95% confidence interval [CI], 0.88 - 0.96) for the primary outcome compared with people taking LABAs alone ($P < .001$). The hazard ratio for death associated with combination therapy was 0.92 (95% CI, 0.87 - 0.97; $P < .001$) compared with LABAs only, and for hospitalization for COPD, it was 0.91 (95% CI, 0.85 - 0.98; $P = .01$). There were no significant differences in secondary outcomes.

In the subset of patients with asthma, use of the LABA-ICS combination was associated with a hazard ratio of 0.84 (95% CI, 0.77 - 0.91) for primary outcomes compared with LABAs alone ($P < .001$). Similarly, combination therapy for patients with asthma who did not take LAAs was associated with a hazard ratio of 0.79 (95% CI, 0.73 - 0.86; $P < .001$) compared with LABAs alone. Receipt of LAAs was not associated with any significant differences between the groups.

What you need to know: The data presented in this study suggest that the overlap of asthma and COPD is a common clinical problem among older COPD patients and merits treatment with a LABA-ICS combination. Conversely, patients without an asthma history taking a long-acting antimuscarinic agent may not benefit from ICS use.

Source: Calverley PM. Treating COPD in the real world. JAMA 2014;312(11):1101-2.

CLINICAL PRACTICE

Hussein Sabry, MSc.

UPDATES IN ISMPS LIST OF HIGH ALERT MEDICATIONS

Key Points: High-alert medications are drugs that bear a heightened risk of causing significant patient harm when they are used in error. Although mistakes may or may not be more common with these drugs, the consequences of an error are clearly more devastating to patients. Based on error reports submitted to the ISMP (The Institute for Safe Medication Practices) National Medication Errors Reporting Program, reports of harmful errors in the literature, studies that identify the drugs most often involved in harmful errors, and input from practitioners and safety experts, ISMP created and periodically updates a list of potential High-Alert medications.

Finer Points: During May and June 2014, practitioners responded to an ISMP survey designed to identify which medications were most frequently considered High-Alert medications by individuals and organizations. Further, to assure relevance and completeness, the clinical staffs at ISMP, members of the ISMP advisory board, and safety experts throughout the US were asked to review the potential list. This list of drugs and drug categories reflects the collective thinking of all who provided input. (Table 2)

The 2014 update includes additions of subcutaneous epinephrine and insulin U-500.

- Concerning insulin, all forms of insulin (subcutaneous and IV), are considered a class of high-alert medications. Insulin U-500 has been singled out for special emphasis to bring attention to the need for distinct strategies to prevent the types of errors that occur with this concentrated form of insulin. For example, a patient with diabetes receives a 5-fold overdose of U-500 insulin after a nurse draws the dose into a U-100 syringe, and a double-check by another nurse fails to detect the error.
- Concerning SQ epinephrine, ISMP listed it as High-Alert drug after recently receiving reports of 2 critical incidents of epinephrine miss-use. Those incidents involving an epinephrine dose intended for subcutaneous (SC) or intramuscular (IM) injection that was inadvertently administered as an intravenous (IV) bolus to patients requiring the drug for hypersensitivity reactions.

What you need to know: ISMP's List of High-Alert Medications which is updated every year or two years provides a guide for acute care setting facilities to determine which medications require special safeguards to reduce the risk of errors.

Source: 1. John E. Brunner, M. F. (2012, April). American Diabetes Association. Retrieved from http://clinical.diabetesjournals.org/content/30/2/70.full. 2. https://www.ismp.org/tools/institutionalhighAlert.asp. 3. http://ismp-canada.org/ISMPC-SafetyBulletins.htm

TABLE 2: ISMP LIST OF HIGH-ALERT MEDICATIONS IN ACUTE CARE SETTINGS

Classes/Categories of Medications	Specific Medications
Adrenergic agonists, IV	EPINEPHrine, subcutaneous
Adrenergic antagonists,	Epoprostenol, IV
Anesthetic agents, general, inhaled and IV	Insulin U-500
Antiarrhythmics, IV	Magnesium sulfate injection
Antithrombotic agents	Methotrexate, oral, nononcologic use
Cardioplegic solutions	Opium tincture
Chemotherapeutic agents, parenteral and oral	Oxytocin, IV
Dextrose, hypertonic, 20% or greater	Nitroprusside sodium for injection
Dialysis solutions, peritoneal and hemodialysis	Potassium chloride for injection concentrate
Epidural or intrathecal medications	Potassium phosphates injection
Hypoglycemics, oral	Promethazine, IV
Inotropic medications, IV	Vasopressin, IV or intraosseous

Classes/Categories of Medications
Insulin, subcutaneous and IV
Liposomal forms of drugs and conventional counterparts
Moderate sedation agents, IV
Moderate sedation agents, oral, for children
Narcotics/opioids: IV, Transdermal, Oral
Neuromuscular blocking agents
Parenteral nutrition preparations
Radiocontrast agents, IV
Sterile water for injection, inhalation, and irrigation (excluding pour bottles) in containers of 100 mL or more
Sodium chloride for injection, hypertonic, greater than 0.9% concentration

MEN'S HEALTH

Marwan Akel, PharmD.

MALE FERTILITY AND SEMEN ANALYSIS

Key Points: About 25% of all infertility is caused by a male problem. It is sometimes hard to know whether the male factor problem is the only cause, or just a contributing cause to the infertility.

Finer Points: Experience has demonstrated that:

- Men with very low sperm counts and low motility scores can sometimes have children.
- Some men with normal counts are infertile without using IVF "in vitro fertilization" and ICSI "intra-cytoplasmic sperm injection."

What matters is not really how many or how fast they swim, but whether they can fertilize the female partner's eggs. This is a biochemical issue at the molecular level.

Semen analysis is a very simple and important test and should be done early in the evaluation process. Sometimes the test should be done 2, or even 3 times to get an accurate reflection of the numbers and their variation over time.

The most important parameters in a semen analysis are:

1. Concentration (often called "count"): How many sperms are in each milliliter of semen?
2. Motility: What percent of them are swimming forward?
3. Morphology: What percent of them are normally shaped?

The World Health Organization's 5th edition of "normal semen analysis" values is shown below:

Liquefaction is another factor to be considered. When semen is ejaculated, it should be thick and gelatinous helping it to adhere to the cervix. The semen eventually liquefies to enable the sperm to swim better. Semen should normally liquefy within 20 to 30 minutes of ejaculation.

What you need to know: Although many people still think of infertility as a "woman's problem," one-third of infertility cases can be attributed to male problems, including low sperm count. So it's crucial that men get tested for fertility as well as women. Yes, it can be embarrassing, but discovering male fertility problems early can mean earlier treatment and a successful pregnancy. Male infertility testing can also spare women unnecessary discomfort and expense.

Source: 1. Cooper et al. World Health Organization reference values for human semen characteristics. Human Reproduction Update, Vol.16, No.3 pp. 231–245, 2010. 2. Mayo Clinic Family Health Book, 4th Edition

Table 3: Normal semen analysis

Semen Analysis Parameter	Normal Values
Volume	1.5 ml or more
pH	> or equal to 7.2
Sperm concentration	15,000,000/ml or more
Total motility	40% or more
Progressive motility	32% or more
Morphology	4% or more normal
Vitality	58% or more live
White blood cells	Less than 1,000,000/ml

PEDIATRIC POPULATION

Jihan Safwan, PharmD.

USE OF BROAD-SPECTRUM ANTIBIOTICS IN INFANTS TIED TO OBESITY

Key Point: Infants between the ages of 0 to 23 months who had repeated exposure to broad-spectrum antibiotics are more likely to be obese at age 5 years than children who did not receive antibiotics, according to a new study. The association was not seen in children who receive multiple courses of narrow-spectrum antibiotics, suggesting antibiotic selection may be a modifiable risk factor for childhood obesity.

Finer Points: Investigators at the Children's Hospital of Philadelphia in Pennsylvania published the results of their cohort study online September 29 in JAMA Pediatrics. They analyzed primary care visit data from the electronic health records of a large cohort (n = 64,580) of children who were seen in primary care practices affiliated with Children's Hospital of Philadelphia. They focused on the first 24 months of life because these months represent a period of major shifts in diet and growth, as well as the establishment of the gut microbiome. The team found that 69% of children were exposed to antibiotics during the first 24 months of life, leaving a significant percentage who did not receive antibiotics.

"Guidelines should emphasize limiting antibiotic use for common pediatric conditions"

Children exposed to 4 or more doses of any type of antibiotic had an 11% increased relative risk of obesity at the age of 5 (P = .02) compared with those who had no exposure. When the researchers stratified the cohort according to narrow- or broad-spectrum antibiotic exposure, they found a 16% increased relative risk of obesity among those exposed to 4 or

more courses of broad-spectrum antibiotics (95% confidence interval, 1.06 - 1.29), but none among those exposed to narrow-spectrum drugs. The investigators also found smaller, but still significant, associations among those exposed to 1 or 2 courses of broad-spectrum antibiotics; the risk was not significant for those who had been exposed to 3 courses.

Obesity has many causes, many of which fall out of the domain of physicians. The authors point out that physicians must identify and manage risk factors they can modify. Prescription of broad-spectrum antibiotics may be a modifiable risk factor that is truly in the hands of the physician.

What you need to know: Narrow-spectrum antibiotics are currently recommended as first-line treatment for common childhood infections. The research suggests treatment guidelines should emphasize limiting antibiotic use for common pediatric conditions. In addition, antibiotics should only be used when there is a demonstrated efficacy, and whenever possible, narrow-spectrum antibiotics should be prescribed over broad-spectrum antibiotics.

Sources: Bailey, C. et al. Use of Broad-Spectrum Antibiotics in Infants Tied to Obesity. JAMA Pediatr. Published online September 29, 2014.

PUBLIC HEALTH

Nermine Chouman, PharmD.

RARE RESPIRATORY VIRUS SENDING CHILDREN TO HOSPITAL IN THE UNITED STATES OF AMERICA

Key Point: Since it was first identified in 1962 amongst 4 cases in California, there have been at least six reported outbreaks of respiratory illnesses associated with Enterovirus D68 (EV-D68), all occurring after 2008 in Asia, Europe and the United States (U.S).

Based on current available information in the U.S, from mid-August to September 23, 2014, a total of 213 people in 30 states were confirmed to have respiratory illness caused by EV-D68. The cases of EV-D68 infection were confirmed by Centers for Disease Control and Prevention (CDC) or state public health laboratories that notified CDC. So far, all the cases have been among children, except for one adult.

Finer Points: Enteroviruses, members of the Picornavirus family, are quite common, with more than 100 different types identified. It is estimated that up to 10-15 million enteroviral infections occur annually in the U.S, with the majority occurring during the summer or fall.

The enteroviruses can affect multiple organ systems in the body, leading to respiratory, gastrointestinal, myocardial and central nervous disease.

Unlike other enteroviruses, EV-D68 shares epidemiologic and biologic features with human rhinoviruses (HRV), causing primarily respiratory symptoms ranging from relatively mild illness that do not require hospitalization to severe illness requiring intensive care and mechanical ventilation. Symptoms of the virus can include cough, fever, sneezing, runny nose, nasal congestion, body and muscle aches, rash, mouth blisters and neurologic illness, such as aseptic meningitis and encephalitis. In general, infants, children, and teenagers are most likely to get infected with enteroviruses and become ill. However, the virus may be especially dangerous for those children with asthma, and could result in compromised breathing leading to a higher rate of complications such as pneumonia or need for mechanical ventilation. Neonates with weak immune systems, especially B-cell deficiencies, may be at great risk for respiratory complications and death.

Infection with EV-D68, just as other enteroviruses, is spread through close contact with infected people. Fecal–oral transmission has been well documented due to prolonged shedding of virus in the gastrointestinal tract, and is a major mode of transmission. The virus is also transmitted directly via secretions, as well as inhalation of airborne viruses in respiratory droplets. EV-D68 can only be diagnosed by doing specific lab tests on specimens from a person's nose and throat. CDC recommends that clinicians only consider EV-D68 testing for patients with severe respiratory illness and when the cause is unclear.

To reduce the risk of acquiring infection with EV-D68, washing hands with soap and water for 20 seconds is important, especially after changing diapers. It is also recommended that people avoid touching their eyes, nose and mouth with unwashed hands or after contact with anyone with active respiratory symptoms in general. It is also important to avoid sharing cups or utensils with those persons with active symptoms, as well as avoiding kissing and hugging. Disinfecting surfaces such as computer keyboards, doorknobs or toys may also help to reduce transmission of the virus. There is no specific treatment, such as antiviral medications available to treat patients with EV-D68 infection. The majority of infections are mild and self-limited (within 1 to 2 weeks), and require just supportive care such as medicine to treat fever, and fluids for hydration. Since patients with asthma are higher risk for respiratory illnesses, they should regularly take medicines, maintain control of their illness during this time and take advantage of influenza vaccine. Vaccines to prevent EV-D68 are not currently available.

What you need to know: Regardless of the magnitude of increased risk, clinicians should be aware of EV-D68 as one of many causes of hospitalized patients with respiratory infections and should report clusters of unexplained respiratory illness to the appropriate public health agency.

Sources: 1. Centers for Disease Control and Prevention. Non-Polio Enterovirus-Enterovirus D68. Available at: http://www.cdc.gov/non-polio-enterovirus/about/ev-d68.html; 2. National Collaborating Centre for Infectious Diseases. Disease Debrief: EV-D68. Available at: http://www.nccid.ca/disease-debrief-ev-d68

ELECTRONIC CIGARETTE

Etwal Bou Raad, PharmD.

E-CIGARETTES: A SCIENTIFIC REVIEW

Key Point: Electronic cigarettes (e-cigarettes) are products that deliver a nicotine-containing aerosol (commonly called vapor) to users by heating a solution typically made up of propylene glycol or glycerol (glycerin), nicotine, and flavoring agents invented in their current form by Chinese pharmacist Hon Lik in the early 2000s.

Finer Points: The US patent application describes the e-cigarette device as "an electronic atomization cigarette that functions as substitutes [sic] for quitting smoking and cigarette substitutes". By 2013, the major multinational tobacco companies had entered the e-cigarette market. E-cigarettes are marketed via television, the Internet, and print advertisements (that often feature celebrities) as healthier alternatives to tobacco smoking, as useful for quitting smoking and reducing cigarette consumption, and as a way to circumvent smoke-free laws by enabling users to "smoke anywhere. There has been rapid market penetration of e-cigarettes despite many unanswered questions about their safety, efficacy for harm reduction and cessation, and total impact on public health. The individual risks and benefits and the total impact of these products occur in the context of the widespread and continuing availability of conventional cigarettes and other tobacco products, with high levels of dual use of e-cigarettes and conventional cigarettes at the same time among adults and youth.

Initial searches conducted via PubMed yielded 151 studies also including the technical reports prepared by health organizations, news articles, and relevant Web sites. The results of these searches were used to prepare a report commissioned by the World Health Organization Tobacco Free Initiative,

"E-cigarette emissions are not merely harmless water vapor"

which provides details of individual studies.

Although data are limited, it is clear that e-cigarette emissions are not merely "harmless water vapor," as is frequently claimed, and can be a source of indoor air pollution. Smoke-free policies protect nonsmokers from exposure to toxins and encourage smoking cessation. One hundred percent smoke-free policies have larger effects on consumption and smoking prevalence, as well as hospital admissions for myocardial infarction, stroke, and other cardiovascular and pulmonary emergencies, than weaker policies.

What you need to know: Introducing e-cigarettes into clean air environments may result in population harm if use of the product reinforces the act of smoking as socially acceptable or if use undermines the benefits of smoke-free policies.

Source: 1. Grana, R.A., Ling, P.M., 2014. "Smoking revolution": a content analysis of electroniccigarette retail websites. Am. J. Prev. Med. 46 (4), 395–403 (Apr). 2. Grana, R.A., Popova, L., Ling, P.M., 2014a. A longitudinal analysis of electronic cigarette useand smoking cessation. JAMA Intern. Med. 174 (5), 812–813 (May).

FLU VACCINE

Jihan Safwan, PharmD.

2014 - 2015 FLU SEASON: VACCINE RECOMMENDATIONS

Influenza vaccination recommendations for the 2014-2015 influenza season. CDC continues to recommend that everyone aged 6 months and older have a yearly flu vaccine with rare exceptions. The main change to this season's recommendations is a preferential recommendation for the intranasal vaccine for healthy children aged 2-8 years.

Recommendation for young children

This year, like every year, children aged 6 months to 8 years who have never been vaccinated against influenza, or in whom vaccination history is unknown, will require two doses of influenza vaccine, administered at least 4 weeks apart, for full protection. However, because the virus composition of the 2014-2015 seasonal influenza vaccine is the same as it was for the 2013-2014 season, children aged 6 months through 8 years need only one dose of vaccine in 2014-2015 if they received one or more doses of 2013-2014 seasonal influenza vaccine, regardless of previous vaccination history.

Vaccine options for people aged 65 or older

CDC recommends that everyone aged 6 months or older (with rare exceptions) receive a seasonal flu vaccine. Vaccination is especially important for people aged 65 years or older because they are at increased risk for complications from flu. For people aged 65 years or older, two flu injections are available to choose from: a regular-dose flu vaccine and a high-dose flu vaccine.

Common misconceptions that pregnant women might have about the influenza vaccine

Pregnant women do not always know that they are at higher risk of developing influenza-related complications. In fact, changes in the immune system, heart, and lungs during pregnancy make pregnant women more prone to severe illness, hospitalization, and even death from influenza. Infants born to women severely ill with influenza also have an increased risk for adverse birth outcomes, including preterm birth and small size for gestational age.

Pregnant women often are unaware of the benefits of influenza vaccination for their baby. Flu shots during pregnancy protect not only the pregnant woman, but also her unborn baby and even her infant during the first 6 months of life. Studies have also shown that vaccinating the mother during pregnancy may reduce the occurrence of adverse outcomes like small size for gestational age and preterm birth in infants.

Source: CDC Expert commentary, October 6th, 2014.
www.medscape.com/resource/influenza

ANNOUNCEMENTS

EVENTS

- The SOP organized the 9th pharmacy day in Bekaa campus on May 31st, 2014.
- The SOP graduates marched in the commencement ceremony on June 24th, 2014.
- The Extracurricular Activities Committee (EAC) organized an annual Iftar for the faculty members of the SOP during the Holy month of Ramadan. The iftar took place in Anjar restaurant on July, 16th, 2014.
- The SOP graduates achieved great results in the colloquium exam on August 4th, 2014 with 100% passing rate.
- The Continuing Education Committee organized and attended CE lectures as part of the Continuing Education Program (CEP) in collaboration with the Lebanese Order of Pharmacists. The lectures were attended by many pharmacists from all over Lebanon and 2 CE credits were granted to the attendees.
  - ◊ "Oral Contraceptives: Updates"; presented by Dr. Diana Malaeb
    - * On August 6th, 2014 - Beirut campus
  - ◊ " Oral Contraceptives: Update "; presented by Dr. Nisreen Mourad
    - * On August 13th, 2014 - Bekaa Campus
- The EAC has organized the E-library workshop for hospital pharmacists on September 30th, 2014, which was followed by a dinner at Leila restaurant.
- The dean Dr. Mohamad Rahal, accompanied by Dr. Diana Malaeb, Dr. Etwal Bou Raad, and Dr. Dalal Hammoudi attended and presented posters at the "17th Scientific Congress of the Association of Pharmacy Colleges in the Arab World" at Ain Shams University - Cairo, Egypt. (October 14th –16th, 2014)
- The faculty members at the SOP, Dr. Faraj Saade, Dr. Marwan Akel, and Dr. Jihan Safwan, will be presenting three lectures at the OPL 22nd Annual Congress. (October 24th – 26th, 2014).
- The EAC is organizing the 9th annual pharmacy dinner. It will take place at Le Commodore Hotel on October 31st, 2014.
- The SOP would like to congratulate Dr. Michelle Cherfan and Dr. Samar Younes for having their new baby borns.
- The SOP would like to congratulate Mrs. Jana Wattar, Dr. Razan Mehanna, and Dr. Lina Jadid for their marriage.

Useful Links

Pharmacy-related

- LIU e-library: www.liu-elibrary.com
- Order of Pharmacists of Lebanon: www.opl.org.lb
- Ministry of Health: www.moph.gov.lb
- Scientific Association of Colleges of Pharmacy in the Arab World: www.asscph-aw.net
- U.S Food and Drug Administration: www.fda.gov
- Center for Disease Control and Prevention: www.cdc.gov

LIU Social Media

- Facebook: www.facebook.com/liu.edu.lb
- Youtube: www.youtube.com/lebintuni
- Twitter: @lebintuni
- Instagram: @lebintuni
- BBM: 25b43b71

The Scope

- Facebook: www.facebook.com/thescopeliu
- Youtube: www.youtube.com/thescopeliu
- Twitter: @thescopeliu