BRAC UNIVERSITY
Inspiring Excellence

PHARMA HIGHLIGHTS

ISSUE 16|February 2016

NSF introduces The New Excipient GMP Standard

The New Excipient GMP Standard has 363 requirements and was introduced by Executive Director of National Science Foundation International. It is the first national standard relating to GMP of excipients in America that has been made with significant input from FDA and is very crucial for drug manufacturers as well as manufacturers of excipients. James Morris, Executive Director of NSF International and QA/QC expert gave drug manufacturers an introduction to the new standard by highlighting the similarities and differences between the IPEC-PQC guide of 2006 and this new standard. He also emphasized the critical features like the 9 major requirements for certifying a new batch of excipient, the documents the sponsors must check or want the suppliers to provide when they change sub-suppliers and 6 important areas to examine while carrying out audit in supplier's place to ensure them that they are abiding by the standards. The 363 standard also describes the three most important considerations for drug makers: to determine whether excipient maker has completed an assessment against the standard, to determine if there were any faults or errors and to ascertain whether the management team of excipient maker complied with the required standards. Similarly, there are three most important considerations for excipient makers to evaluate the risk of cross contamination, understanding the process and its control points and to define the steps of process to which GMPs apply. To ensure regulatory compliance and to maintain high standards drug & excipient manufacturers should make it a priority to follow the new guidelines for the treatment of severe asthma.

–Nausheen Syeara

http://www.magnetmail.net/actions/email_web_version.cfm?recipient_id=2323357997&message_id=12011024&user_id=FDANEWS&group_id=1373975&jobid=32137773

For the Treatment of Severe Asthma of 12 Years and Older, FDA Approves NUCALA® (mepolizumab)

The United States Food and Drug Administration (FDA) has approved NUCALA (mepolizumab) subcutaneous (SC) injection as an add-on maintenance treatment for patients, age 12 years or older with severe asthma, and with an eosinophilic phenotype. The approved recommended dosage is 100 mg once every 4 weeks. It was suggested not to discontinue systemic or inhaled corticosteroids abruptly upon initiation of therapy with NUCALA. If appropriate the corticosteroids should be decreased gradually. Exhibited approximate dose-proportional of this drug increases in systemic exposure over the subcutaneous dose ranging from 12.5 to 250 mg (i.e., 0.125 to 2.5 times the approved recommended dosage) of which approximately 80% is absorbed following SC administration in the arm. Terminal half-life (mean) of this drug is about 16 to 22 days. The safety and effectiveness of NUCALA were evaluated in patients with severe asthma uncontrolled on standard of care therapy who also had blood eosinophils of greater than or equal to 150 cells/mcL at screening (within 6 weeks of dosing) or blood eosinophils of greater than or equal to 300 cells/mcL within 12 months of enrollment. A 52-week dose-ranging study and a 32-week confirmatory study demonstrated that 100 mg SC or 75 mg IV mepolizumab treatment significantly reduced the asthma exacerbation rate by about half compared with placebo treatment. Another 24-week confirmatory study demonstrated that 54% of subjects treated with 100 mg SC mepolizumab

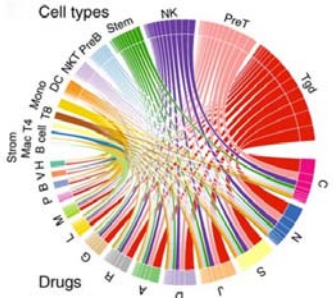
achieved at least a 50% reduction in the daily prednisone dose compared with 33% of subjects treated with placebo. The most common adverse reactions include headache, injection site reaction, back pain, and fatigue. Hypersensitivity reactions (e.g., angioedema, bronchospasm, hypotension, urticaria, rash) and Herpes zoster infections have occurred in patients receiving NUCALA.

-Fabiha Tasnim

http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/125526Orig1s000Lbl.pdf

This Computer Model Can Predict How a Drug Will Affect Your Immune System

Recently, a group from Icahn School of Medicine at Mount Sinai in New York City developed a sophisticated computer model to predict the effect of a drug on the immune system. The strategy behind this model was to create a profile of targets that a drug engages with (chemogenomic profile) and a profile of the various gene expression states an immune cell could be in (immunogenic profile). As a result of data generated from mice, the researchers categorized 304 state changes in 221 immune cell types that were matrixed with different drugs to create a list of possible drug-immune cell interactions. Using the 69,995 significant interactions from this list, immune cell pharmacology (IP) map was designed. Since the immune cell state change data and the drug data were generated from mice and humans respectively, it was unclear if integration of these two datasets from two different species could provide any useful results. In order to prove that the IP map predictions are actually



relevant to humans, the researchers compared their map with data from two independent patient populations. For instance, the IP map predicts that the general anesthetic propofol will increase neutrophils and that spironolactone, an anti-hypertensive drug, will increase monocytes. Surprisingly, the shifts in the neutrophil and monocyte counts in patients who had received either of these drugs matched the shifts predicted by the IP map. The results were further confirmed by conducting the same procedure on electronic medical records from Columbia University Medical Center. Moreover, some drugs were also subjected to in vivo experimental validation on mice, thereby, producing the same outcome as predicted by IP map. The IP map also broadens the scope to study immune cells in cancer and their response to various drug combinations. Considering all these facts, this new technology definitely holds the potential to contribute significantly in the field of medicine assuring safe use of drugs. **-Tanisha Khan**

http://www.labroots.com/trending/id/2320/this-computer-model-can-predict-how-a-drug-will-affect-your-immune-system/clinical-and-molecular-dx

Treatment for Liposarcoma is Now Approved in USA Market by FDA

Liposarcoma, a specific type of soft tissue sarcoma occurring in fat cell which either cannot be removed (unresectable) or is advanced (metastatic) requires advanced chemotherapeutic treatment. Soft tissue sarcoma is the disease contributing to the development of cancerous cells in soft tissues of the body, including muscles, tendons, fat, blood vessels, nerve and tissues around joint resulting in 12,000 cases in United States, according to the National Cancer Institute. Halaven (eribulin mesylate) is approved by U.S. Food and Drug Administration specifically for patients receiving prior chemotherapy containing an anthracycline drug. Evaluation of the drug in terms of safety and efficacy was conducted on 143 clinical trial participants with advanced liposarcoma unresectable or locally advanced or metastatic who had already been treated. In a comparative study with dacarbazine, it was found out that the median overall survival of patients for Halaven was 15.6 months almost double the median survival of patients for dacarbazine in the event of liposarcoma. No efficacy study was conducted for leiomyosarcoma. Safety of the drug eribulin has been evaluated in 223 patients with liposarcoma and leiomyosarcoma where the common side effects were fatigue, nauseas, alopecia, peripheral neuropathy, abdominal pain and pyrexia. The most serious adverse reactions include neutropenia (4.9%) and pyrexia (4.5%), fatigue (0.9%) and thrombocytopenia (0.9%). The dose recommended for eribulin is 1.4mg/m2 on Day 1 and 8 of a 21-day cycle. FDA has granted the drug a priority to facilitate and expedite its development and review in light of its potential to benefit patients with serious or life-threatening conditions.

–Samin Huq

http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm483714.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

Microarrays Combat Antibiotic Resistance

About three-fourths of the patients worldwide end up on antibiotics an infection despite the fact that the majority have viral infections. To reduce the risk of antibiotic overuse, recently a diagnostic test has been developed that could indicate clearly whether a patient has a bacterial or viral infection. Ephraim Tsalik of Duke University and his colleagues developed a simple blood test that could distinguish between viral and bacterial infections, or non-infectious ailments.

As described in the journal Science Translational Medicine, the new test looks for changes in a patient's gene expression profiles induced by the infection rather than for evidence of a particular pathogen. To develop their test, the researchers used microarray technology, which enables simultaneous detection of the expression levels of around 25,000 genes from a small blood sample. However, simply looking at the expression data is not enough to give a diagnostic answer since individual gene changes are largely meaningless within such a large dataset with so many patient-to-patient variables. Instead, the team looked for patterns of change in large groups of genes to find correlations with different types of infections. The researchers recruited 273 volunteers who came to physicians with respiratory complaints. Their gene expression patterns, obtained from whole blood samples, were then compared with those from 44 healthy volunteers. Using these data, the researchers were able to determine gene expression signatures that directly corresponded to bacterial, viral, or non-infectious causes of disease with 87% accuracy, an improvement over currently used tests. Tsalik added that the test right now takes too long to return results within the timeframe of a single office visit. Tsalik's team is now working towards a test that can run on common clinical laboratory equipment while they wait for other technological advances to speed the analysis.

–Noshin Mubtasim

http://www.biotechniques.com/news/Microarrays-Combat-Antibiotic-Resistance/biotechniques-362815.html#.VrLw_U8mHIU

Newsletter Editorial Committee: Editor: Dr. Eva Rahman Kabir; Sub-editors: Dr. Zulfiquer Hossain and Zara Sheikh.
Design: Fabiha Tasnim