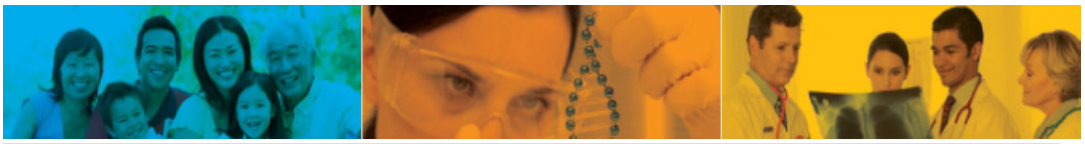

Clinical Research Newsletter Volume - 4, April 2016

LAMBDA

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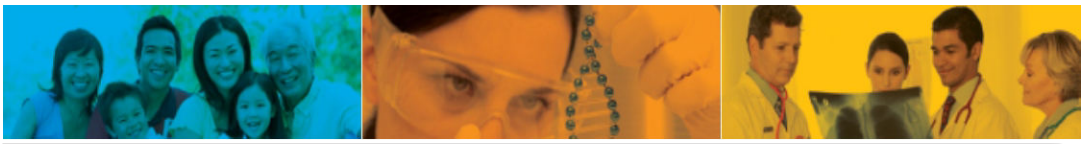


GLOBAL NEWS

1.1. Osteoporosis drugs linked to unusual fractures of the femur — March 02, 2016

- Osteoporosis drugs have significantly reduced the risk of bone fractures for millions of people, but also have been linked to unusual fractures of the femur (thigh bone). In the journal Current Geriatrics Reports, orthopaedic surgeons report the latest findings for treating these injuries, called atypical femur fractures.
- Drug bisphosphonates which is used in osteoporosis to decrease fractures and increase BMD cause a small risk of atypical femur fractures. These fractures typically occur with little or no force or trauma, and often are preceded by pain.

1.2. New Drug Holds Promise Against Zika — March 03, 2016

- TGV-Laboratories announced a potential major breakthrough in the fight against a host of life-threatening viruses, including Zika, Ebola, HIV, and Bird Flu.
- The New York-based pharmaceutical company said lab tests showed that its MV-4 drug candidate can break down the protective barriers of both enveloped and non-enveloped viruses, and can be developed into targeted synthetic antiviral drugs to treat the diseases.

1.3. EMA Proposes Major Changes to Pharmacovigilance Risk Management System Guidelines — March 03, 2016

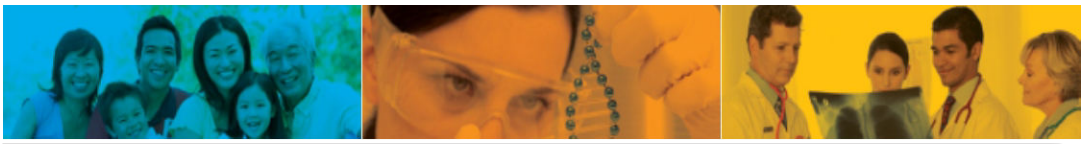
- The European Medicines Agency (EMA) has proposed major changes to its good pharmacovigilance practices (GVP) module on risk management systems.
- EMA wants to implement the modifications to bring the guidelines in line with its current thinking, which has evolved over the past three years as it has gained experience with the key areas of focus in risk management plans (RMPs).

1.4. Researchers find key brain receptor linked to depression, drug addiction and Alzheimer's disease — March 03, 2016

- Researchers at the University of Colorado Anschutz Medical Campus have found that a key receptor in the brain, once thought to only strengthen synapses, can also weaken them, offering new insights into the mechanisms driving depression, drug addiction and even Alzheimer's disease.
- For years, scientists believed that a special calcium permeable subtype of AMPA-type glutamate receptor only strengthened synapses, which send signals between brain cells. But Professor Mark Dell'Acqua, vice-chair of the Dept. of Pharmacology at the University of Colorado School of Medicine, and his team of researchers found that it also weakened synapses.

1.5. Study reveals direct regulatory role of serotonin in rheumatoid arthritis — March 10, 2016

- For the first time, serotonin (5-hydroxytryptamine, 5-HT) has been directly implicated in the pathophysiology of rheumatoid arthritis (RA).
- Although 5-HT is predominantly known as a neurotransmitter within the central nervous system, new evidence points to additional important functions for serotonin in the periphery. These findings may lay the groundwork for new treatment approaches for RA



LAMBDA

DOMESTIC NEWS

2.1. Indian Govt brings 200 more drug formulations under price control March 14, 2016

- At least 800 drug formulations derived from essential medicines including those used in the treatment of cancer, HIV/AIDS and cardiovascular diseases, are currently under price control by the government, the Press Trust of India reported.
- This is a direct result of the amendment of Schedule 1 of the Drugs Price control Order (DPCO), 2013, for substituting the National List of Essential Medicines (NLEM) 2011 by NLEM 2015, which has caused more than 200 drugs to be added to the list.

2.2. Health ministry amends D&C Rules to exempt clinical trials for academic research from DCGI nod March 28, 2016

- The Union health ministry has amended the Drugs and Cosmetics Rules, 1945 for providing exemption in the case of clinical trials undertaken in the medical institutions or hospitals for academic research.
- Once the amendment is done, these institutions and hospitals do not have to take the now mandatory prior permission from the Drugs Controller General of India (DCGI).

2.3. CDSCO plans to increase audits of mfg units to ensure quality of drugs in global markets March 29, 2016

- Against the backdrop of growing global scrutiny from international regulators in the past five years on drug quality, Central Drugs Standard Control Organisation (CDSCO) plans to increase audits in the manufacturing units across the country towards compliance to Good Manufacturing Practices (GMP) as per the requirements of the respective markets globally.
- Says a senior CDSCO official, "Any product which does not comply with good manufacturing practices of overseas markets is being considered as adulterated and hence faces the chance of losing the market. The surprise audits will help streamline the objective of meeting the GMP requirements of respective countries where the drug is exported."

REGULATORY NEWS

3.1. Rodent Carcinogenicity Testing: Changes to ICH Guidance Proposed March 02, 2016

- The European Medicines Agency (EMA) is considering changes to International Council for Harmonisation (ICH) guidance on rodent carcinogenicity testing to improve the evaluations, reduce use of animals and drug development resources and reduce timelines to market authorization in some cases without compromising patient safety.
- The goal of the potential changes to the S1 guidance, according to EMA, is to introduce a better way to address the risk of human carcinogenicity of small molecule pharmaceuticals and to define the conditions under which two-year rat carcinogenicity studies add value to that assessment. The changes, if implemented, will not be applicable to biologics.

3.2. New Guidance Spells Out How to Comply With EMA's Clinical Data Publication Policy

March 03, 2016

- The European Medicines Agency (EMA) has published new guidance for pharmaceutical companies on how to comply with its new policy on the publication of clinical data.
- The policy, which entered into force on 1 January 2015, applies to clinical reports contained in all marketing authorization applications (MAAs) submitted on or after this date and the reports will be made publicly available in September 2016.

3.3. EMA sets clear rules for drug firms seeking clinical data redactions

March 07, 2016

- Drug makers seeking to stop "commercially confidential information" being made public in trial reports will need to demonstrate the likely economic harm publishing it would cause.
- The European Medicines Agency made the comments in guidelines designed to help marketing authorization holders comply with its policy on trial data dissemination.

3.4. Indian Health Ministry bans nearly 350 combo drugs

March 14, 2016

- The Indian Health Ministry has banned nearly 350 fixed-dose combination (FDCs) drugs because of the likely risk of harm to humans, the Times of India reports.
- Abbot Laboratories' Aimnic AZ brand, a combination of the antibiotics cefixime and azithromycin, was one of the banned FDCs, as was Pfizer's Corex cough syrup

3.5. India releases new biosimilar guidance

March 28, 2016

- India's Central Drugs Standard Control Organization on Saturday released new guidance for biosimilar developers as new biosimilars come to market there before other regions, and as India's regulators look to develop more specific guidance on postmarketing studies.
- among the major changes, CDCSCO now says that if the reference biologic (for which the biosimilar is being developed) is not marketed in India, the reference biologic can be licensed in any ICH country (i.e. EU, Japan, US, Canada and switzerland).

DRUG APPROVALS AND LAUNCHES

4.1. U.S. FDA Approves Gilead's Second TAF-Based Single Tablet Regimen Odefsey®

March 01, 2016

- U.S. FDA Approves Gilead's Second TAF-Based Single Tablet Regimen Odefsey® (Emtricitabine, Rilpivirine, Tenofovir Alafenamide) for the Treatment of HIV-1 Infection.
- Odefsey is indicated as a complete regimen for the treatment of HIV-1 infection in patients 12 years of age and older who have no antiretroviral treatment history and HIV-1 RNA levels less than or equal to 100,000 copies per mL.

4.2. IMBRUVICA® (ibrutinib) Approved by U.S. FDA for the First-line Treatment of Chronic Lymphocytic Leukemia March 04, 2016

- AbbVie, a global biopharmaceutical company, announced that the U.S. FDA approved IMBRUVICA® (ibrutinib) as a first-line treatment for patients with chronic lymphocytic leukemia (CLL).
- The approval is based on data from the randomized, multi-center, open-label Phase 3 RESONATE™-2 trial showing an 84% reduction in the risk of progression or death with IMBRUVICA.
- IMBRUVICA is the first FDA-approved chemotherapy-free treatment option for first-line CLL patients and CLL is 5th treatment indication for it.

4.3. Xalkori® (crizotinib) approved by u.s. fda for additional indication March 11, 2016

- Pfizer Inc. announced that the U.S. FDA has approved a supplemental New Drug Application (sNDA) for XALKORI® (crizotinib) to treat patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are ROS1-positive.
- In 2015, the FDA granted Breakthrough Therapy and Priority Review designations for this indication. XALKORI also is indicated for patients with metastatic NSCLC whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

4.4. US Food, Drug Administration Gives 'Emergency' Approval for Zika Virus Test March 18, 2016

- US Drug regulators issued an emergency use authorization that allows a newly available test for the Zika virus to be distributed in the United States and several other nations, the Centers for Disease Control (CDC) announced in a statement.
- Previously, three separate tests were required to positively diagnose Zika infections because of the virus' similarity with pathogens responsible for two other tropical diseases chikungunya and dengue fever.

4.5. Eli Lilly's ixekizumab gets green light from FDA March 22, 2016

- The FDA approved Taltz (ixekizumab, Eli Lilly and Company) injection 80 mg/mL March 22 for treatment of moderate-to-severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.
- Ixekizumab clinical trial investigator Paul Yamauchi, M.D., Ph.D., tells Dermatology Times that Taltz is the only biologic agent for psoriasis to have data for PASI 100 and sPGA 0 scores at week 12.

DRUGS IN DEVELOPMENT AND CLINICAL TRIALS

5.1. Phase 3 Monotherapy Study Demonstrating Superiority of Sarilumab vs. Adalimumab March 02, 2016

- Regeneron Pharmaceuticals, Inc. and Sanofi announced that a Phase 3 monotherapy study met its primary endpoint demonstrating that sarilumab was superior to adalimumab (marketed by AbbVie as HUMIRA®) in improving signs and symptoms in patients with active rheumatoid arthritis (RA) at Week 24.

5.2. Celator Announces Phase 3 Trial for VYXEOS™ (CPX-351) March 14, 2016

- Celator Pharmaceuticals, Inc. announced positive results from the Phase 3 trial of VYXEOS™ (cytarabine: daunorubicin) Liposome for Injection (also known as CPX-351) in patients with high-risk (secondary) acute myeloid leukemia (AML) compared to the standard of care regimen of cytarabine and daunorubicin known as 7+3.
- The trial met its primary endpoint demonstrating a statistically significant improvement in overall survival.

5.3. Pfizer's Xeljanz rheumatoid arthritis drug meets endpoints in ulcerative colitis March 21, 2016

- Pfizer's rheumatoid arthritis drug Xeljanz (tofacitinib) has met primary and key secondary endpoints in two phase trials to treat ulcerative colitis (UC).
- In the Octave Induction 1 and Octave Induction 2 studies, tofacitinib reduced symptoms of moderate to severe UC and induced remission of the disease.

5.4. Amgen And UCB Announce Positive Top-Line Results From The Phase 3 Study Of Romosozumab March 21, 2016

- Amgen and UCB announced top-line results from the Phase 3 placebo-controlled FRActure study in postmenopausal woMen with ostEoporosis (FRAME).
- These data showed FRAME met the co-primary endpoints by reducing the incidence of new vertebral fracture through months 12 and 24 in postmenopausal women with osteoporosis treated with romosozumab. The study also met the secondary endpoint of reducing the incidence of clinical fractures.

MERGER/ACQUISITIONS/COLLABORATION

6.1. Horizon Discovery and Centauri launch joint venture March 02, 2016

- Horizon Discovery Group plc, the leading international gene editing company, announces that it has formed an immuno-oncology joint venture, Avvinity Therapeutics, with Centauri Therapeutics Limited, a UK-based biotechnology company focused on the discovery and development of novel molecules targeting life-threatening infectious diseases.
- Avvinity will combine Horizon's gene editing, immunology, oncology and drug discovery capabilities with Centauri's Alphamer technology to provide a powerful and proprietary platform to discover and develop novel immuno-oncology therapeutics, for both solid tumours and leukaemias.

6.2. Merck, Pfizer and Verastem join forces on testing avelumab combo March 03 , 2016

- German drug major Merck along with Pfizer has joined forces with Verastem to develop the trial drug candidate avelumab to treat advanced ovarian cancer. The study will be done combining avelumab with Verastem's trial focal adhesion kinase (FAK) inhibitor. Avelumab is currently under clinical investigation across a broad range of tumor types.

6.3. AbbVie, Boehringer in Immunology Alliance — March 07, 2016

- AbbVie and Boehringer Ingelheim have entered a global collaboration to develop and commercialize BI 655066, an anti-IL-23 monoclonal antibody in Phase III development for psoriasis.
- The companies are also evaluating the drug's potential in Crohn's disease, psoriatic arthritis and asthma. In addition to the anti-IL-23 antibody, AbbVie gains rights to an anti-CD-40.

6.4. PeptiDream Announces License of PDPS Technology to Lilly — March 08, 2016

- PeptiDream Inc., a public Tokyo-based biopharmaceutical company announced that it has entered into a Technology License Agreement with U.S.-based Eli Lilly and Company to nonexclusively license PeptiDream's proprietary Peptide Discovery Platform System (PDPS) technology.
- Under the terms of the Technology License Agreement, PeptiDream will receive upfront and annual technology access payments, and will be eligible to receive development milestones and royalties on future sales of products (both peptide and small molecule therapeutics) that arise from use of the PDPS technology.

6.5. Bristol-Myers Squibb to Acquire Padlock Therapeutics, Inc. — March 23, 2016

- Bristol-Myers Squibb Company and Padlock Therapeutics, Inc. announced that the companies have signed a definitive agreement under which Bristol-Myers Squibb will acquire all of the outstanding capital stock of Padlock, a private, Cambridge, Massachusetts-based biotechnology company.
- The acquisition will give Bristol-Myers Squibb full rights to Padlock's Protein/Peptidyl Arginine Deiminase (PAD) inhibitor discovery program focused on the development of potentially transformational treatment approaches for patients with rheumatoid arthritis (RA).

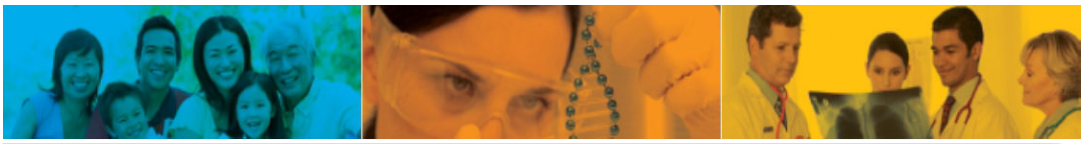
PATENT (NEW APPROVAL/ LITIGATION/SETTLEMENTS)

7.1. Amgen targets Sandoz's Enbrel biosim with patent infringement suit — March 02, 2016

- Amgen ($AMGN) wants to do everything that it can to protect its best-selling RA drug Enbrel from potential biosimilar competition, and now, the company is shoring up its defenses by suing Novartis' ($NVS) Sandoz unit in federal court.
- Thousand Oaks, CA-based Amgen in the U.S. District Court for the District of New Jersey filed a suit claiming that Sandoz infringed some of its patents for Enbrel by seeking FDA approval for its biosimilar of the med. Amgen also wants the court to grant an injunction that would prevent Sandoz from selling its biosimilar, if and when it is approved.

7.2. MSF Opposes Pfizer Pneumonia Vaccine India Patent Application — March 16, 2016

- Doctors Without Borders/Médecins Sans Frontières (MSF) is challenging Pfizer's attempt to patent its Prevenar 13 (PCV13) pneumococcal conjugate vaccine in India so that other manufacturers can produce more affordable versions of the pneumonia vaccine.
- The move marked the first time a vaccine patent has been challenged in India by a medical organization and, if successful, would allow the availability of more affordable versions in developing countries and to humanitarian organizations.



TECHNOLOGY/NDDS NEWS

8.1. New Tobacco-Based Vaccines: Alternative to Egg-Based Influenza Vaccine March 11, 2016

- A new tobacco-based seasonal influenza vaccine being developed by Mitsubishi Tanabe Pharma and currently in Phase III studies could potentially rival traditional chicken egg-based vaccines, as it aims to launch in the US for the 2018-19 flu season, according to an analyst with research and consulting firm GlobalData.
- The technology involved in the new vaccine, which can be produced in four weeks, six times faster than egg-based methods, involves implanting influenza genetic material into tobacco leaves, a manufacturing process originally developed by Medicago, a Canadian company acquired by Mitsubishi Tanabe in 2013.

8.2. Siemens Healthcare launches new MR applications to help hospitals reduce scan times in neurology March 17, 2016

- Siemens Healthcare has launched a range of new MR applications to help hospitals reduce the time needed for MR imaging within neurology.
- An application designed to help organisations increase patient throughput in order to maintain an efficient workflow is, Simultaneous Multi-Slice (SMS) EPI, employs an innovative technique to acquire imaging slices simultaneously rather than sequentially, reducing 2D acquisition times with acceleration factors up to eight.
- Simultaneous Multi-Slice (SMS) EPI can bring DTI and BOLD into clinical routine. This can particularly benefit surgical neurology cases through surgical mapping, potentially helping to reduce post-surgical deficits, and ultimately leading to improved efficiency in the utilisation of operating room resources.