Lambda Research Newsletter

February 2018

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Volume 2 / February 2018

Clinical Research NEWSletter

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Contents

LAMBDA
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Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

Contents

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

GLOBAL NEWS

1. Brexit could lead to inaccessibility of medicines in Britain

The doctors, National Health Service (NHS) and pharmaceutical firms warn that after Brexit, patients could face delay in obtaining new drugs for a certain time interval. The NHS may also find difficulty to access newly developed medications for next one year as compared to other 27 European Union (EU) nations after the separation of Britain in March 2019.

According to a report presented by Brexit Health Alliance (BHS), the patients can suffer due to this unavailability of drugs until the government re-establishes the supply of drugs between UK and EU. The BHA includes 250,000 doctors from leading health care charities.

Now, the UK needs to form a new system for the introduction of 978 drugs in to the UK market, which was approved by the EU since 1995. Due to Brexit, patients can face the delay in the accessibility of potential lifesaving drugs in UK and EU. Several countries have agreements with EU and can start receiving new drugs in specified time after entry into EU like Switzerland in about 157 days.

EMA represents 25% of the world's overall pharmaceutical sales whereas the UK accounts for only 3% of it, and the pharmaceutical companies always target larger markets for introduction of their drugs.

Source: theguardian.com

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Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

GLOBAL NEWS

2. Pharma industry needs to work hard on antibiotic resistance

At World Economic Forum (WEF), the health care sectors presented their efforts to tackle antimicrobial resistance (AMR). American Medical Foundation for Peer Review and Education (AMF) presented the results of a survey. The reports presented were better than the expectations but pharma industries need to do further work on the field of antibiotic resistance.

According to experts we need more pharma companies for the development of new antibiotics. According to them, companies need to bring new drugs for multidrug resistant (MDR) pathogens or superbugs. At present, 28 novel drugs are on high priority for MDR, which are in phases 2 and 3 testing.

GlaxoSmithKline (GSK) and Johnson & Johnson (J&J) are the leading companies focusing on the development of new antibiotics against MDR. GSK is having 55 new projects under its pipeline for MDR followed by J&J, Pfizer, Novartis and Sanofi.

It was also discussed during the meeting that the generic companies are not doing enough to ensure rational use of antibiotics. AMF will conduct the survey again after 2 years.

Source: pmlive.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

GLOBAL NEWS

3. Canadian Government to reduce prices of generic drugs

As per the latest agreement between pan-Canadian Pharmaceutical Alliance and Canadian Generic Pharmaceutical Association, the prices of nearly 70 most prescribed generic drugs are going to fall between 25% and 40%. Canadian Pharmaceutical Alliance represents the provinces, territories and federal government.

The agreement between both the agencies is a part of a five-year plan to build off a 2014 framework. The main key point of this initiative is that, tendering will not be pursued over five years by the participating drug companies.

The list of generic drugs included in this initiative is manufactured by a number of generic companies, which ensures the supply of medicines to the Canadian patients. The predictability and stability of prices will also help pharmaceutical manufacturers to invest in bringing new cost saving generic drugs to the market in future.

According to the statement by Health Minister, Mr. Ontarion, this initiative will save an amount of around $3 billion for public drug plans. These generic drugs are used by the millions of Canadian patients for the treatment of high blood pressure, high cholesterol and depression. The reduction in prices will help the agencies to save more money.

Source: nationalpost.com, raps.org

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

GLOBAL NEWS

4. Smart pills toward rapid growth by 2025

The market of smart pills is estimated to grow to $3bn by the year 2025. In a report published by Grand View Research, the market of smart pills was valued at $779.9m in 2016 but the market is expected to grow with the annual growth rate of 15.5%.

The simple use of sensors, trackers and cameras in smart pills for the different aspects to monitor patient's health could become more common. The smart pills are expected to replace various invasive diagnostic techniques.

The various market leaders like Medtronic, Olympus Corporation, Proteus Digital Health, MediSafe and CapsoVision are expected to expend the market of latest smart pills.

These smart pills are capable to monitor gastrointestinal conditions so this could be a better alternative for endoscopy in future. Pills can monitor various other body functions such as respiratory rate and heart rate from inside the gastrointestinal tract (GIT).

Source: pharmaceutical-technology.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

PHARMA INDIA

1. Government of India's plan to reduce price faces pharma industry pushback

Theproposal of Indian government to introduce generic medicines by stripping innovators drugs faces a push back from domestic pharma companies. The draft guidelines prepared by the government are intended to improve the manufacturing standards and enforcement of medicinal products in India. The new draft pharmaceutical policy has made no progress since its circulation by the Department of Pharmaceuticals, Govt. of India. These new draft policies were opposed by the pharma industry as well as by some government agencies.

After this pushback, the department has been ordered to redraft the policy and a new draft is expected by 2019.

Around the world, generic copies of the innovator drugs are the cheaper way to keep health care costs low. India is the biggest exporter of generic medicines around the world. But in the home market, companies sell their branded drugs which are costly as compared to that of their generic medicines.

In favor of branded drugs, industry argues that in a country like India where the regulations are not that strong as compared to the developed countries, branded drugs can provide a safe and effective way to boost health in India.

Source: economictimes.indiatimes.com

LAMBDA
Research Accelerated

Clinical Research NEWS letter
www.lambda-cro.com

Volume 2 / February 2018

PHARMA INDIA

2. Domestic pharmaceutical companies to accelerate OTC drug market

Indian domestic pharmaceutical companies are now focusing to increase the market of over the counter (OTC) segment of medicines. Companies are working on the older prescription brands of the drugs and taking them through inorganic routes to beat the reduction in sales.

In 2017, the Indian pharma market dipped to 5.5%, which is the lowest growth rate in the past eight years. The OTC re-launch business of older prescription drugs will help the companies to promote the growth of sluggish products and will also extend the life of mature brands.

Under the new strategy, Lupin is re-launching its laxative Softovac in the OTC segment of drugs and targeting Rs 3 billion sales from the segment over the next five years. Other than OTC products, some companies are also focusing on other ways for growth, for example, Piramal Enterprises is growing its business through acquisitions; Sanofi has brought its American OTC topical analgesic brand Combiflam Icyhot to India. In the past 10 years, self-medication has grown from 23% to 41%.

Source: business-standard.com

LAMBDA
Research Accelerated

Clinical Research NEWS letter
www.lambda-cro.com

Volume 2 / February 2018

PHARMA INDIA

3. NPPA reduces marketing prices of medicines

The National Pharmaceutical Pricing Authority (NPPA) has revised and fixed the prices of 33 formulations including drugs use to treat diabetes, bacterial infections and high blood pressure. The list of drugs also includes 3 anticancer drugs - N-acetylcysteine, Gemcitabine and Amphotericin B - Lipid/ Liposomal.

The NPPA has mandated the fixation/revision of the retail price of the controlled bulk drugs in the country.

NPPA will also monitor the uncontrolled drugs in order to keep the prices reasonable. The agency will also try to recover the overcharged amounts by the manufacturers for the benefit of the consumers.

List of revised medicines includes:

Glimepiride + Metformin Tablet	Rosuvastatin + Aspirin Capsule	Voglibose + Glimeperide + Metformin Tablet
Cilnidipine + Metoprolol Tablet	Rosuvastatin + Aspirin + Clopidogrel Capsule	Cefixime + Ofloxacin Tablet
Escitalopram + Clonazepam Tablet	Voglibose + Glimeperide + Metformin Tablet	Trypsin + Bromelain + Rutoside + Diclofenac Tablet
Ceftriaxone sodium & Tazobactam Sodium Injection	Gliclazide + Metformin Tablet	Rosuvastatin + Clopidogrel Capsule
Olmesartan + Amlodipine Tablet		

Source: pharmabiz.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

PHARMA INDIA

4. Causality assessment committee to be set up by the adverse drug reaction monitoring centres for the detection of SAEs

The Union Health Ministry of India has instructed the adverse drug reaction monitoring centres (AMCs) to set up causality assessment committee at all the AMCs across the country for the safety of patients and clarity of Pharmacovigilance Programme of India (PvPI). According to the Health Ministry, this is one of the urgent requirements, as this will help in the establishment of clinical evidences between the drugs and the adverse drug reactions (ADR) or serious adverse events (SAE).

Causality assessment implies the determination of reasonable possibility for the occurrence of ADR and evaluation of temporal relationships, association with or lack of association with underlying disease, presence or absence of a more likely cause, and biologic plausibility.

Some companies perform causality assessment on regular basis and receive data from physicians regarding the suspected reactions due to the drug. The agency should emphasize that the company should not separate out the spontaneous reports they receive regarding the causality associated with the drug exposure and any other related possibilities.

The recent protocols for ADR monitoring will be implemented in an ongoing manner based on the learning of all the ongoing projects in different institutions in a timely manner.

Source: pharmabiz.com

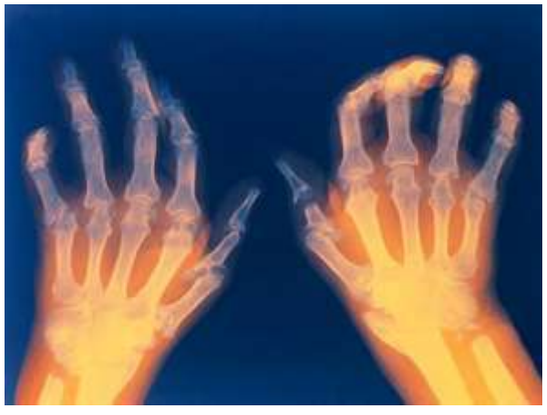
LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

REGULATORY ROUND-UP

1. New EMA guidelines for clinical evaluation of Rheumatoid arthritis treatments



The European Medicines Agency (EMA) has introduced new modified guidelines for the clinical evaluation of the rheumatoid arthritis (RA), an auto-immune disorder. These guidelines were initially drafted in 2011.

The new guidelines will be effective from 1st July 2018, and includs criteria and standards for patient selection, possible indications or treatment goals, how to assess efficacy, strategy and design of clinical trials, and clinical safety evaluations along with studies in special populations (i.e., elderly and children).

The new EMA guidelines explain that currently a number of biomarkers are under development to predict disease progression and response, which can lead to a more individually targeted treatment approach in future.

The optimum treatment goal is remission of the disorder or at least low disease activity in the patients who are non-responders to previous treatments. New criteria for classification of RA have been developed by the American College of Rheumatology's European League against Rheumatism that allows for earlier disease-modifying anti-rheumatic drug (DMARD) use.

Source: raps.org

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

REGULATORY ROUND-UP

2. FDA to release portion of clinical trial data after drug approvals

The US Food and Drug Administration (FDA) plans to release a small portion of clinical trial data and summaries of pivotal trials after the approval of drugs. This new pivotal trial will select up to 9 recently approved new drug applications (NDAs) whose sponsors want to participate in the release of pivotal clinical study reports (CSRs).

These reports will include summary on the methods used and results of the clinical studies. This new way facilitates sponsors for decision making and will also enhance the access of data to researchers for further studies.

Under this new program, FDA will post the parts of studies, which were most important to FDA's assessment regarding the safety and efficacy of the drug product. The agency will mainly include the protocol and amendments along with the statical analysis plan.

This USFDA move will push the European Medicines Agency to release more clinical data for approved products. In addition to data release, the agency will also add the ClinicalTrials.gov identifier number for better tracking.

Source: raps.org

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

REGULATORY ROUND-UP

3. FDA updates guidance for payment and reimbursement of research subjects

The US Food and Drug Administration (FDA) has updated the guidelines for institutional review boards (IRBs) as well as for clinical investigators regarding payments and reimbursement to research subjects.

This new update clarifies about the reimbursements that are acceptable towards travel expenses to and from the clinical trial site as well as the associated costs such as airfare, parking and lodging. This new update by the agency is provided in response to inquiries form the stakeholders about appropriate reimbursement practices.

The new sheet information title is revised again to reflect the changes and entitled as payment and reimbursement to research subjects. According to the FDA, the payment for participation should be just and fair. The amount and schedule should be presented to the IRB for their initial review, and IRB should review the method and timing of disbursement.

Source: raps.org

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

REGULATORY ROUND-UP

4. FDA introduces revised guidances for generic drug makers

The US Food and Drug Administration (FDA) has introduced new and revised product specific draft guidances for generic makers. These guidances include the design of bioequivalence (BE) studies for the support of abbreviated new drug applications (ANDAs). The 35 new and 22 revised guidance documents include 19 guidance documents for complex generics.

To date, FDA has published about 1,600 of these product-specific guidances, laying out the path for developing generics to specific products, including more than 350 guidances for developing generics of complex drugs.

The draft guidances are different according to the complexity of the generic's formulation, ability to accurately measure its bioavailability and scientific method to demonstrate bioequivalence. The latest draft issued is based on the specific guidances for the developers of generics for bringing competition to the market for:

- Eucrisa (crisaborole) by Pfizer for the treatment of eczema, approved in 2016PARP inhibitor Zejula (niraparib), by Tesaro for various cancers, approved in 2017
- PARP therapy Rubraca (rucaparib), by Clovis Oncology approved in 2016 for advanced ovarian cancer
- Ninlaro (ixazomib) for Multiple myeloma treatment, by Takeda in 2015

Among the revised product-specific drafts are one each for oxycodone and lansoprazole.

Source: raps.org

LAMBDA
Research Accelerated

Clinical Research NEWS letter
www.lambda-cro.com

Volume 2 / February 2018

MERGERS /ACQUISITIONS /COLLABORATIONS

1. Beacon and Janssen collaborate for the treatment of metabolic disorders

For the discovery and development of small molecular compounds to treat various metabolic diseases, Beacon Discovery has entered into a collaboration with Janssen Pharmaceuticals. This multi-year collaboration will work on the discovery and development of small molecules targeting G-protein couple receptors (GPCRs).

Under this collaboration, the companies will work to identify drug candidates for the treatment of obesity and some unmet medical conditions. Janssen will try to acquire worldwide rights for the development, manufacturing as well as commercialization of products resulting from this collaboration.

Janssen will pay an upfront amount to Beacon along with some milestone based payments as well as royalties on the basis of further sales of the products.

The GPCR belongs to the family of cell surface receptors which were reported to respond to external signals. Beacon is mainly focused on the utilization of internally enabled GPCR targets along with small molecular modulators for the discovery of newdrugs.

Source: pharmaceutical-technology.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

MERGERS /ACQUISITIONS /COLLABORATIONS

2. Takeda collaborates with Denali therapeutics for development and commercialization of therapies for neurodegenerative diseases

Takeda Pharmaceutical Company has entered into a strategic collaboration with Denali Therapeutics for the development and commercialization of three new drug candidates specifically developed for the treatment of neurodegenerative disorders such as Alzheimer's disease and other indications. This new collaboration will also strengthen Takeda's portfolio of new validated therapies for neurodegenerative disorders.

Under this agreement, Takeda needs to give an initial upfront payment of $150 million to Denali Therapeutics through a combination of cash and the purchase of Denali equity. Denali is also eligible to receive an additional amount as development and commercial milestone payments, which include $90 million in preclinical milestones and opt-in payments.

Under this agreement, Denali will be responsible for early clinical developments and costs prior to IND filing for each of the three programs. Takeda will lead the late stage clinical trials and have the option to co-develop and co-commercialize each of the three programs.

Source: pharmpro.com

LAMBDA
Research Accelerated

Volume 2 / February 2018

Clinical Research NEWSletter
www.lambda-cro.com

MERGERS /ACQUISITIONS /COLLABORATIONS

3. Celgene buys Impact Biomedicines for $1.1bn upfront payments

Celgene Biotechnology has signed a definitive agreement to buy Impact Biomedicines with an upfront payment of about $1.1bn. Celgene will also pay $1.25bn in contingent payments depending on the regulatory approval milestones for myelofibrosis. The company will also pay additional payments for other indications.

The agreement also includes some other payments of around $4.5bn in the future, based on potential sales milestones, if global sale is more than $5bn annually.

Currently, Impact Biomedicines is working on the development of Fedratinib, a Janus kinase inhibitor 2 (JAK2 kinase inhibitor) for the treatment of myelofibrosis. Fedratinib is being studied on a total of 877 subjects across 18 clinical trials. It is reported to show a statistically significant improvement in the splenic responses and total symptom scores during the pivotal Phase 3 JAKARTA-1 trial conducted in treatment-naïve patients.

Similar to the Phase 3 trial, a multicentre, single-arm Phase 2 study conducted in the subjects who were ruxolitinib-resistant or intolerant, also demonstrated improvements.

Source: pharmaceutical-technology.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

MERGERS /ACQUISITIONS /COLLABORATIONS

4. Sandoz enters into a global collaboration with Biocon for next generation biosimilars

Sandoz and Biocon biopharmaceuticals have entered into a global collaboration for the development, manufacturing and commercialization of a number of biosimilars in immunology and oncology TAs.

Under this agreement, both the companies will share end-to end responsibilities for the development, manufacturing and global regulatory approvals for the various products. The companies will have a global cost and profit share arrangement. with responsibilities divided between both the companies for specific geographies.

Sandoz will lead commercialization in the regions of North America as well as in the Europian Union (EU), whereas Biocon will lead commercialization in the rest of the world.

Sandoz is mainly focusing on access for high-quality biosimilars. Sandoz, a division of Novartis, is a global leader in the biosimilars market with 5 biosimilars worldwide. Biocon is an innovation led biopharmaceutical company having a range of novel biologics, biosimilar antibodies, rh-insulin and insulin analogs in the basket.

Source: worldpharmanews.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

DRUGS: APPROVALS AND LAUNCHES

1. AstraZeneca receives USFDA approval for Lynparza to treat inherited breast cancer

AstraZeneca PLC has received the US Food and Drug Administration (FDA) extended approval for Lynparza (Olaparib). The drug is now approved for the treatment of patients with inherited breast cancer gene (BRCA) mutations who have undergone prior chemotherapy. The drug is already in the market for the treatment of ovarian cancer from 2014.

Olaparib is the 1st in a new class of medicines called poly ADP ribose polymerase (PARP) inhibitors to be approved for the management of breast cancer. PARP inhibitors prevent DNA repair in cancer cells resulting in DNA damage. This is a new class of drugs approaching the underlying genetic causes of cancer.

A companion blood test from Myriad Genetic Laboratories Inc is also approved by the USFDA for the detection of BRCA mutations. The drug Lynparza is marketed jointly by UK-based AstraZeneca and Merck & Co and will cost $13,886 per month without insurance. At present, there is no cure for metastatic breast cancer. Olaparib will offer a new targeted option to delay disease progression.

This approval for extended indication was given on the basis of a study conducted in 302 women with metastatic breast cancers who had BRCA gene mutations. The median progression-free survival was significantly longer in the olaparib group than in the standard-therapy group (7.0 months vs. 4.2 months; P<0.001). The response rate was 59.9% in the olaparib group whereas 28.8% in the standard-therapy group. The complete study was published in the *New England Journal of Medicine* in November 2017.

Source: cbsnews.com

DRUGS: APPROVALS AND LAUNCHES

2. Zydus Pharmaceutical's Clomipramine receives USFDA approval for the treatment of OCD

The US Food and Drug Administration (USFDA) has approved the marketing authorization for Clomipramine Hydrochloride capsules of Zydus Pharmaceuticals (USA) Inc for the treatment of obsessive compulsive disorder (OCD).

The approval has been given to three different strengths of Clomipramine Hydrochloride capsules containing 25 mg, 50 mg and 75 mg of the drug. The drug will be produced at their formulations manufacturing facility at SEZ, Ahmedabad (Gujarat, India).

Clomipramine Hydrochloride is effective in the treatment of OCD, which is characterized by uncontrollable, re-occurring thoughts and behaviours.

Zydus Pharmaceuticals Inc is a wholly-owned subsidiary of Cadila Healthcare Ltd having more than 180 drug approvals and filed over 310 abbreviated new drug applications (ANDAs) since 2003-04.

Source: health.economictimes.indiatimes.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

DRUGS: APPROVALS AND LAUNCHES

3. EU approves Amgen and Allergan's Avastin biosimilar

The European regulatory agency has approved the first biosimilar of Roche's Avastin (bevacizumab). The biosimilar of Amgen and Allergan's Mvasi® (biosimilar bevacizumab) has received the marketing approval for a range of indications like non-squamous non-small cell lung cancer, spanning carcinoma of the colon or rectum, renal cell cancer, platinum-sensitive, or platinum-resistant recurrent epithelial ovarian cancer, breast cancer, fallopian tube, or primary peritoneal cancer and cervical cancer.

The biosimilar was approved after the data from the clinical trial showed a high degree of similarity between Mvasi and the reference drug used. The trial showed no clinically meaningful differences in terms of efficacy, safety and immunogenicity between the products.

The biosimilar was already approved by the US Food and drug Administration (FDA) in September 2017. Mvasi is the 1st product borne out of an alliance between Amgen and Allergan to bag marketing authorization from the European Commission (EC).

Source: pharmatimes.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

DRUGS: APPROVALS AND LAUNCHES

4. USFDA approves first and only OTC eye drop for eye redness

The US Food and Drug Administration (FDA) has approved LUMIFY by Bausch + Lomb as the first and only over-the-counter (OTC) eye drop developed for the treatment of ocular redness. LUMIFY is an eye drop containing low dose brimonidine tartrate ophthalmic solution of 0.025%.

Brimonidine was initially approved by FDA in 1996 for the reduction of intraocular pressure (IOP) in glaucoma patients. For the indication of IOP, the drug is available at higher dose strengths.

Ocular redness is a common condition due to inflammation of the eye. Low-dose brimonidine containing LUMIFY selectively constricts veins in the eye and increases the availability of oxygen to the surrounding tissues.

The approval was based on 6 clinical studies conducted on 600 patients to evaluate the safety and efficacy of low-dose brimonidine tartrate for relieving ocular redness. Studies were conducted on both pediatric and geriatric subjects. A Phase 3 double-blind, randomized, placebo-controlled study showed significant symptom improvement at 1 minute in 95% of subjects, whereas 79% of subjects maintained significant redness reduction at 8 hours.

Source: ir.valeant.com, 4-traders.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

DRUGS: DEVELOPMENT & CLINICAL TRIALS

1. Lundbeck's Idalopirdine shows no benefits in Alzheimer's disease

Once again a new treatment option faced setback for the treatment of Alzheimer's disease (AD). Idalopirdine from the Danish international pharmaceutical company Lundbeck faced this setback. Previous trials show that idalopirdine might improve cognition in AD when drug is taken along with the existing drugs.

The studies conducted previously showed that idalopirdine along with cholinesterase inhibitors improves the symptoms but not by stopping the disease from developing. But the latest trials have dashed such hopes.

To explore the effects of idalopirdine, researchers conducted three clinical trials on a total of 2,525 participants in 34 countries. The complete research was published in the ***Journal of the American Medical Association***. The patients involved in the trail were aged ≥50 years with mild to moderate AD.

All the three studies were 24 weeks, randomized, double-blind trials, and patients were assigned to either receive a particular dose of idalopirdine or a placebo in addition to their existing Alzheimer's medication.

The results from the studies were disappointing, revealing that idalopirdine did nothing to improve cognition and to limit the decline of AD, irrespective of dose introduced.

Source: theguardian.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

DRUGS: DEVELOPMENT & CLINICAL TRIALS

2. Esketamine shows positive results for the treatment of treatment-resistant depression

Esketamine by Janssen Research & Development showed positive results in a Phase 2 trial for treatment-resistant depression. Esketamine is an intranasal formulation of ketamine. The company was working on the development of Esketamine from several years. Results of Phase 2 trial for the intranasal formulation were released.

Ketamine is a notable animal tranquilizer and drug-of-abuse also known as Special K, for the treatment of severe depression. The results of Phase 2 study are promising as well as concerning. The results were significant in terms of clinically meaningful as well as fast-acting improvement in the symptoms of depression as compared to an intranasal placebo. The results were concerning in terms of perceptual changes/dissociative symptoms along with sedation.

The Phase 2 study was conducted on 126 patients, who were also taking oral antidepressants or the standard of care. The positive effects of the drug were noted on 3 different doses of esketamine administered twice weekly. The results were dose dependent.

Ketamine acts on N-methyl-D-aspartate receptor (NMDA receptors), and is designated as a Breakthrough Therapy by the U.S. Food and Drug Administration (FDA) in November 2013 for treatment-resistant depression. The drug is now being evaluated in Phase 3 trial for treatment-resistant depression and for patients with major depressive disorder.

Source: biospace.com

LAMBDA
Research Accelerated

Volume 2 / February 2018

Clinical Research NEWSletter
www.lambda-cro.com

DRUGS: DEVELOPMENT & CLINICAL TRIALS

3. New target identification could help in the treatment of cancer

Researchers of Sussex academics have identified a new target for the treatment of cancer. The researchers have shown that the enzyme EXD2 is involved in forming proteins in the mitochondria. Mitochondria are mainly responsible for the protein product of the cell and cell replication. The researchers are expecting that by targeting this protein, tumors can be treated.

According to the research published in the journal ***Nature Cell Biology***, this new discovery could be used to target cancer patients in a new way by understanding the role of mitochondria in protein synthesis and replication of cells.

The researchers explain that mitochondrial ribosomes responsible for protein production interact with EXD2. In normal process, ribosomes read RNA messages for the conversion of generic information encoded in the genes for the production of proteins. In cells, the mitochondria need to assemble first, and prematurely bind to the RNA molecules, resulting clogging. The role of EXD2 is to bind to these RNA molecules and cut them up to prevent clogging.

The study also showed that EXD2 play an important role in suppression of reactive oxygen species generation due to mitochondrial defects.

Source: health.economictimes.indiatimes.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

DRUGS: DEVELOPMENT & CLINICAL TRIALS

4. Nanobiotix receives USFDA approval for first immuno-oncology trial

The US Food and Drug Administration has approved Nanobiotix's Phase 1/2 clinical trials for NBTXR3, which is a first-in-class nanoparticle mainly designed for the direct injection into cancerous tumors in combination with an anti-programmed cell death protein 1 (anti-PD1) antibody (nivolumab or pembrolizumab).

This approval will enable Nanobiotix to initiate NBTXR3-1100, a Phase 1/2 prospective, multi-center, open-label, non-randomized clinical trial.

36 to 72 patients will be enrolled in Phase 1 and 40 patients in Phase 2, for evaluating the efficacy and safety of NBTXR3 as primary and secondary endpoints, activated by stereotactic ablative radiotherapy combined with checkpoint inhibitors (nivolumab or pembrolizumab).

The clinical trial includes three cohorts of patients with recurrent and/or metastatic head and neck squamous cell carcinoma, or with metastatic non-small cell lung cancer. The study will be conducted in two consecutive phases:

- The dose escalation phase to identify the appropriate dose (classical 3+3 Phase I study)
- Dose expansion phase

In these trials, the doses of NBTXR3 and radiotherapy will be increased whereas the dose of anti-PD1 antibody will remain constant.

Source: pharmpro.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

1. Sun Pharma settle Linzess patent litigation with Ironwood and Allergan

Sun Pharmaceuticals has signed an agreement with Ironwood Pharmaceuticals and Allergan to resolve the patent litigation by the companies against Sun Pharmaceutical. This litigation was associated with the new abbreviated new drug application (ANDA) submitted by Sun pharmaceutical for the generic version of Linzess (linaclotide) in the US.

Linaclotide is a drug for the treatment of constipation-predominant irritable bowel syndrome and chronic idiopathic constipation. It is a guanylate cyclase-C (GC-C) agonist, which locally binds to the GCIC receptors present in the intestinal epithelium. Currently, it is marketed by Ironwood and Allergan in the US and various other parts around the world.

Under this settlement, Ironwood and Allergan will grant marketing licence to Sun Pharma to introduce generic version in the market by 2031 or may be earlier depending on the circumstances. This settlement will dismiss the litigation against Sun Pharmaceutical but the litigations against other firms are yet to be resolved.

Source: pharmaceutical-technology.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

2. US court invalidates J&J patent on Zytiga

After a short and successful run, Johnson & Johnson's (J&J) Zytiga faces the prospect of generics this year. Zytiga is a leading drug of J&J for the treatment of prostate cancer. In a recent meeting, the US Patent Trial and Appeal Board invalidated the Zytiga's 2027 patent in the US. The patent was challenged by the generic maker company Argentum Pharmaceuticals.

The generic of Zytiga is expected to enter the market by October 2018. The big branded drug manufacturing companies protested against the inter partes review (IPR) process few years back as this tool can create prescription drug saving by ensuring that non-innovative patents do not block competition.

In just 9 months of 2017, Zytiga showed a total sale of $826 million in the US; full year results were not reported by J&J. In 2016, the total market of the drug was $1.1 billion. The drug was expected to generate a huge revenue for the company but due to IPR attack, the sale of drug is expected to fall down after generic entry.

50% of overall sales of Zytiga come from outside the US, where drug is patented till 2022. The drug is still expected to remain a big earner for J&J. Zygtiga’s protection was very short-lived as the drug was approved by FDA in 2011 only.

Source: fiercepharma.com

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Clinical Research NEWSletter
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Volume 2 / February 2018

PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

3. Rexahn Pharmaceuticals receives US patent for RX-5902 (Supinoxin)

Rexahn Pharmaceuticals Inc. has received the patent for RX-5902 (Supinoxin) from the US Patent and Trademark Office. The patent is provided for the use of Supinoxin in the treatment of various types of cancers including triple negative breast cancer either as monotherapy or in combination with other anti-tumor agents such as cytotoxic agents or immune checkpoint inhibitors.

The patent is entitled as "Quinoxalinyl Piperazinamide Methods of Use" and patent is granted until 2036. This application will extend the period of patent protection of the drug as well as increase the value and future potential of the drug.

The drug is currently in a Phase 2a trial. The trial will be a monotherapy study in cancer patients, and company is expected to present preliminary data in the second quarter of this year.

RX-5902 (Supinoxin®) is administered orally and is a potential first drug in the class of small molecule; inhibitor of phosphorylated-p68 (P-p68). P-p68 is selectively expressed in cancer cells and is absent in normal tissues. In a Phase 1 dose escalation study, it was found to be safe and well tolerated in cancer patients.

Source: streetinsider.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

PATENTS: NEW APPROVALS /LITIGATIONS /SETTLEMENTS

4. Viiv files lawsuit against Gilead for Julucc patent infringement

Viiv healthcare has filed a lawsuit against Gilead Sciences, Inc. for the patent infringement of Viiv's HIV drug Tivicay. On 7th February 2018, Gilead received the US Food and Drug Administration (FDA) approval for their new HIV drug Biktarvy® as a once-daily, single-tablet regimen for the treatment of HIV-1 and on the same day, Viiv filed a lawsuit against the company.

Biktarvy® contains HIV integrase inhibitor bictegravir marketed by Viiv as Tivicay. According to Viiv, bictegravir's unique chemical scaffold by Viiv is patented.

ViiV Healthcare's Tivicay was approved by the USFDA in November 2017 and patented in 2012. Tivicay is one of the best selling drugs of ViiV with sales of £1.4 billion in 2017. The drug is expected to have market sales of about $1 billion in 2018.

The companies are working to develop a simple treatment to keep HIV under control. Before the approval of this single tablet regimen, HIV patients were required to take multiple pills daily.

Source: pharmaceutical-technology.com

LAMBDA
Research Accelerated

Volume 2 / February 2018

Clinical Research NEWSletter
www.lambda-cro.com

TECHNOLOGY /NDDS

1. New method can stabilize blood for longer duration to help CTC profiling

Researchers of Massachusetts General Hospital Center for Engineering in Medicine (MGH-CEM) have developed a new method for the stabilization of blood samples. This stabilization method will prolong the lifespan of blood samples for microfluidic sorting and transcriptome profiling and will also stabilize rare circulating tumor cells (CTCs) as well as living cancer cells carried in the bloodstream. The complete development process is published in the journal of ***Nature Communications***.

At present, chemical fixation is the one and only FDA approved method for blood stabilization but this method kills the cells and heavily degrades sensitive biomolecules, mainly RNA. Isolation of extremely fragile and rare cells from the fresh blood totally depends on the timing, else delay may lead to the breakdown of red cells, leukocyte activation or clot formation. Normally, various important factors such as CTCs in a sample and high-quality RNA decrease by about 50% within the first four to five hours after sample collection.

Researchers of MGH took a comprehensive approach to prevent breakdown of the cells and to slow down the biological clock as much as possible by using hypothermia. Initially, they analyzed an optimal storage condition as cooling causes profound activation of platelets.

To prevent formation of platelet aggregates, researchers added glycoprotein IIb/IIIa inhibitors, which are commonly used in cardiovascular medicine and are effective in countering cooling-induced platelet aggregation. The team noted that by using these strategies they were able to preserve whole blood for 3 days if it was freshly drawn, with very high purity and virtually no loss in the number of CTCs.

Source: news-medical.net

LAMBDA
Research Accelerated

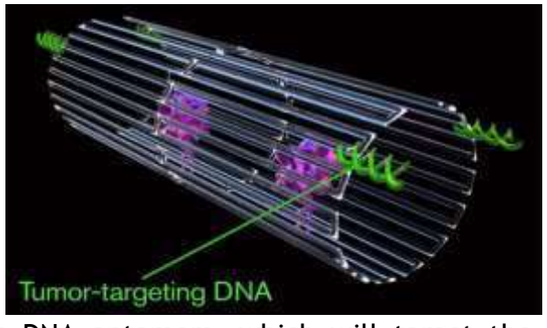
Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

TECHNOLOGY /NDDS

2. New nanomachine to kill tumors by clinging to tumor vessels

Researchers of the Arizona State University and National Center for Nanoscience and Technology have developed a new nano device which can kill the tumors by clinging the walls of tumor vessels. This nano device is a robot-like device, which will cling the walls of the blood vessels supplying blood to the tumor cells. This device will act by releasing a clotting agent, which will prevent the tumor cells to receive nutrients.



The nano device contains a sheet of strings of DNA, which contains DNA aptamers, which will target the protein produced only by certain tumor types. These sheets are rolled up into cylinders and thrombin, whereas the clotting enzyme is attached to the interior of the newly formed tubes.

When the nano device is injected, aptamers come out and attach to the tumors responsible for the production of target proteins, whereas thrombin promotes blood to coagulate.

So far, the study was conducted in mice with different types of tumors including breast, ovarian, melanoma, and lung cancer. This technique was found to be effective in all tumor types. The safety analysis showed that the injected nano robots seemed to be safe without any immune response. The research was conducted on healthy animals as well to check animal's clearance.

Source: medgadget.com

LAMBDA
Research Accelerated

Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

TECHNOLOGY /NDDS

3. New balloon test to detect Barrett's esophagus in the initial stages

Researchers of the Case Western Reserve University School of Medicine and University Hospitals Cleveland Medical Center have developed a new cheaper and easier way for the detection of Barrett's esophagus. Barrett's esophagus (BE) is a precursor lesion for esophageal adenocarcinoma (EAC), a highly lethal type of cancer. The EAC can be prevented by detecting BE in the earlier stages that presently can be detected by endoscopy only, an expensive and invasive test.

The common symptoms of BE such as heartburn is also present in the patients of acid reflux disease without BE. Heartburn symptoms can be treated by normal over the counter medications and patients are not tested for BE. As a result, when EAC develops, 95% of patients remain undiagnosed.

Researchers have developed a 5-minute outpatient method for the detection of BE. This test contains a vitamin pill sized balloon for the detection of BE. The device is a pill-sized capsule with a thin silicone catheter. After entering in the stomach, air is injected through the catheter to inflate the balloon. Then the inflated balloon is maneuvered to swab the lower esophagus near the stomach. Lower esophagus is the region where BE begins and a sample is collected from the lining cells and the balloon is deflated through the catheter and inverted back into the capsule. Capsule is retrieved back through the mouth and DNA is extracted from the balloon surface for DNA methylation test.

The complete development of the test and the clinical trial in patients was published in the journal of ***Science Translational Medicine***. In the clinical trial, 82% of patients tolerated the balloon test with little and no anxiety, pain or choking.

Source: medicalxpress.com

LAMBDA
Research Accelerated

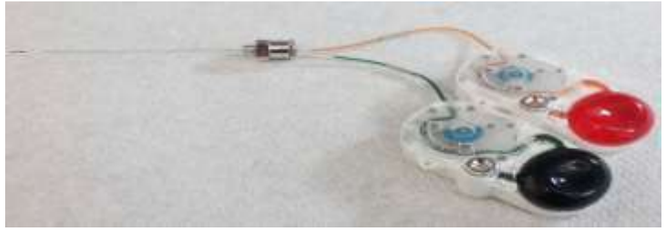
Clinical Research NEWSletter
www.lambda-cro.com

Volume 2 / February 2018

TECHNOLOGY /NDDS

4. New brain implant to deliver drug at the specific site of action

The Massachusetts Institute of Technology researchers have developed a new radical way for the treatment of various neurodegenerative disorders like Parkinson's disease. The researchers have developed a tiny pump to deliver the drug at the target site. The pump needs to be implanted in the specific targeted area of the brain.



The pump works on the concept of miniaturized neural drug delivery system (MiNDS). The pump can treat specific clusters of neurons without causing side effects as the drug will be delivered only at the target. So far, the pump is tested only on laboratory animals to treat Parkinson's like symptoms. The complete research was published in the journal *Science Translational Medicine*.

The most common treatment option for Parkinson's disease is carbidopa and levodopa, but these drugs can elevate the symptoms and can also create long-term side effects. The major advantage of the device is that it allows introducing the drug at a specific site of action of the brain, as small as one cubic millimeter. This device also allows measuring the area being treated and enables them to monitor side effects of the drugs.

The major complication associated with the device is that it is implanted deep into brain tissue that can cause bumping of the head. The additional complication is due to the introduction of a foreign object into brain tissue which can cause surrounding tissue to become inflamed and potentially die. To overcome this issue, researchers are using stainless steel and borosilicate (glass) as the main materials for the probe.

Source: yahoo.com

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