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BVDU-**PCP**

Pharmawiz Newsletter

I am delighted to welcome you back to the 3rd Volume, Issue 1 of our newsletter, BVDU-PCP Pharmawiz. I want to thank the guest authors who have contributed to the BVDU-PCP Pharmawiz.

We are committed to the achievement and maintenance of excellence in education, research and healthcare for the benefit of humanity. We welcome the feedback of all the readers and their constructive suggestion.

Dr. Atmaram Pawar
Vice-Principal & HOD

INSIDE THIS ISSUE:

Patented heart-saving drug in India

Ticagrelor:

Trade name **Brilinta** in the US, **Brilique** and **Possia** in the EU) is a platelet aggregation inhibitor produced by AstraZeneca. The drug was approved for use in the European Union by the European Commission on December 3, 2010.[1][2] The drug was approved by the US Food and Drug Administration on July 20, 2011.[3]

It is a prescription medicine for people who have had a recent heart attack or severe chest pain that happened because their heart wasn't getting enough oxygen and who are being treated with medicines or procedures to open blocked arteries in the heart. Used with aspirin to lower your chance of having another serious problem with your heart or blood vessels such as heart attack, stroke, or blood clots in your stent if you received one. These can be fatal.

The **PLATO** clinical trial found that ticagrelor had better mortality rates than clopidogrel (9.8% vs. 11.7%, p<0.001) in treating patients with acute coronary syndrome.

Patients given ticagrelor were less likely to die from vascular causes, heart attack, or stroke but had greater chances of non-lethal bleeding (16.1% vs. 14.6%, p=0.0084), higher rate of major bleeding not related to coronary-artery bypass grafting (4.5% vs. 3.8%, P=0.03), including more instances of fatal intracranial bleeding. Rates of major bleeding were not different. Discontinuation of the study drug due to adverse events occurred more frequently with ticagrelor than with clopidogrel (in 7.4% of patients vs. 6.0%, P<0.001)[4]The PLATO trial showed a statistically insignificant trend toward worse outcomes with ticagrelor versus clopidogrel among US patients in the study

References:

1. European Medicines Agency. January 2011.

2. European Public Assessment Report Possia

3.FDA approves blood-thinning drug Brilinta to treat acute coronary syndromes". FDA. 20 July 2011.

4. Wallentin, Lars; Becker, RC; Budaj, A; Cannon, CP; Emanuelsson, H; Held, C; Horrow, J; Husted, S et al. (August 30, 2009). "Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes". NEJM 361 (11).

Diagnosis is not the end, but the beginning of practice. *-Martin H Fischer*

Designing of Study Protocol for Bioavailability and Bioequivalence Studies

The design, conduction and assessment of bioavailability and bioequivalence (BABE) studies have received more attention from academia and the pharmaceutical industry.

The situation in which bio equivalence studies required are- New drug application, Abbreviated new drug application, change in the manufacturing site, change in the manufacturing process, change in product formulation or dosage strength, change in the labeling to provide for a new indication, change in the labeling to provide for a new dosage regimen and information to permit waive the submission.In this article we would like to provide an overview and the steps involved in the study protocol development for typical BABE studies.

A protocol synopsis would be advisable prior to full length study protocol. During protocol development, the protocol writer works with the Clinical, Bioanalytical, Quality assurance team and the sponsor to develop a protocol that will be easily executed during the clinical phase. The following flowchart is describing the key elements to develop study protocol.

Conclusion:

Clinical research organizations and pharmaceutical industry are continuously confronted to identify process improvements from the appropriate regulatory agency. Experienced protocol writers will understand the expectations and necessities of the regulatory agencies as well as sponsor

"I don't think that's what the pharmacist meant when he said 'Take for two days and skip a day.'"

Facts About Risperidone and Ropinirole

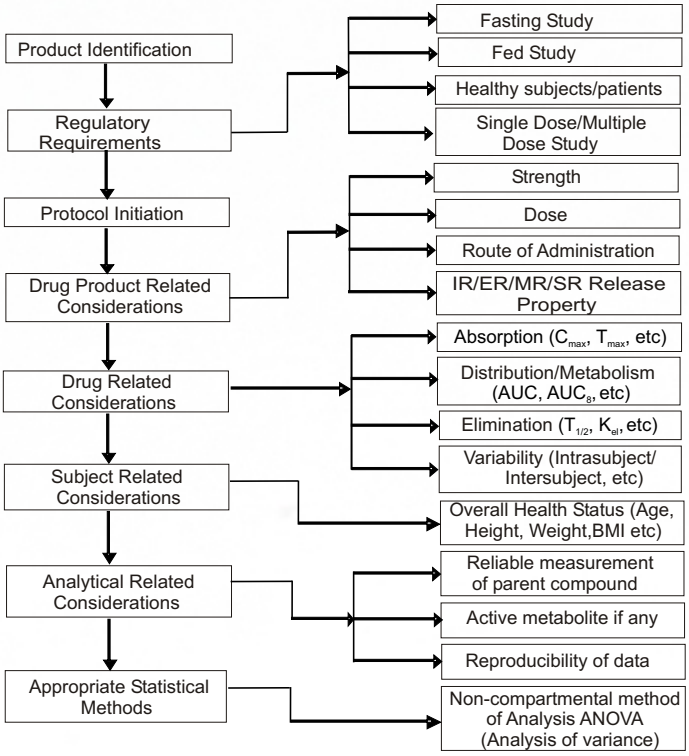
Risperidone (Risperdal) is an antipsychotic medication used to treat mental illnesses including schizophrenia, bipolar disorder, and irritability associated with autistic disorder.

Ropinirole (Requip) is a dopamine agonist used in the treatment of Parkinson's disease and Restless Legs Syndrome.

FDA Issues Update on Use of Pradaxa (Dabigatran Etexilate Mesylate)

Pradaxa is a blood-thinning medication used to reduce the risk of stroke and blood clots in patients with a specific condition called non-valvular atrial fibrillation (AF), a common heart rhythm abnormality that causes the upper chambers of the heart, or atria, to beat rapidly and irregularly.

Pradaxa is not indicated for patients with atrial fibrillation caused by heart valve problems.



Our Guest Column

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Protocol writers are exposing to a variety of tasks and they can propose insight in protocol design so that the data generated from the BABE will reflect the intended information needed for the study conduct, data interpretations, summaries of statistical data, highly complex data and offer suggestions for development improvements to sponsors.

Evidence Based Drug Review [Student Corner]

What is the evidence based support that Ondansetron results in Prolongation of QT interval in patients with postoperative nausea and vomiting?

Recently FDA has made a safety announcement regarding the use of *iv*. Ondansetron (32 mg) as a prophylactic agent that, it may affect the electrical activity of the heart (QT interval prolongation), which could pre-dispose patients to develop an abnormal and potentially fatal heart rhythm known as Torsades de Pointes.

Evidence: After doing an extensive literature review from Pub med, two studies were dedicated to identify adverse effects of *iv.ondansetron* in patients. In a randomized placebo-controlled study conducted by S.Dutta et al on different doses of *iv.* ondansetron as a prophylactic agent in post-operative surgical patients showed that a maximal QTc prolongation was recorded in 8 mg recipient participants at 3 min post administration period. In another study conducted by Hafermann M et al to assess the effect of *iv*.ondansetron on QT interval prolongation in patients with cardiovascular disease identified that ondansetron may significantly increase the QTc interval for up to 120 minutes after administration with one or more risk factors for torsades de pointes.

All the case reports published on *iv.* ondansetron show similar results. In a case report *iv.* ondansetron when given to a patient in left breast lumpectomy showed a reaction of atrial fibrillation and hypertension within 15 minutes after giving second dose (Kasinath, 2003).Two other case reports published reported severe cardiac effects like ST-depression, T- wave inversion, sustained ventricular tachycardia etc., at different intervals of time after giving *iv*. ondansetron as a prophylactic agent in post operative patients to control nausea and vomiting (Bosek 2000, Guigui 2008).

Conclusion: As the QT prolongation due to ondansetron occurs in a dose dependent manner, the use of a single 32 mg *i.v* dose of ondansetron should be avoided. The lower dose of 0.15 mg/kg every 4 hours for three doses intravenously may be used to avoid postoperative nausea and vomiting. However to avoid the risk of QT prolongation single IV dose should not exceed 16 mg and single oral dose of more than 24 mg.

References:

1. *Sampa Dutta Gupta, Ranabir Pal et al. Evaluation of Ondansetron-induced QT interval prolongation in the prophylaxis of postoperative emesis. J Nat Sci Biol Med. 2011; 2(1): 119124.*

2. Matthew J Hafermann, Rocsanna Namdar,Gretchen E Seibold,Robert Lee.Effect of intravenous ondansetron on QT interval prolongation in patients with cardiovascular disease and additional risk factors for torsades:a prospective, observational study.Drug, Healthcare and Patient Safety.2011:3 53–58

-By Goutham Reddy Intern PharmD

Drug Information "Helpline" service

Drug Queries	Patients Counseled	Category of Drug Queries					
		Indication	ADR	Admn	Efficacy/ Safety	Poison	Others
46	12	10	4	8	4	1	19

We can help you with any questions you might have on the use of drugs or any information regarding the drugs . We assist you with any drug related problems you face in your daily practice.
Phone (020) 40555555 Ext. 308 **E-mail: bvpcp.dic@gmail.com**

1) WE DO NOT PRESCRIBE OR ADVISE TO TREAT ANY DISEASES. IT IS THE ROLE OF PHYSICIANS.
2) WE PURELY PROVIDE INFORMATION ON HOW A PRESCRIBED DRUG WORKS, DRUGS ADMINISTRATION TECHNIQUES, SIDE-EFFECTS, INTERACTION WITH OTHER DRUGS AND FOOD, COUNSEL ON DRUG PROBLEMS AND HEALTH PROBLEMS.
3) GUIDE PUBLIC REGARDING FALSE CLAIM MADE IN AN ADVERTISEMENT A DRUG OR DISEASE CURE METHOD BY DRUGS.
4) DO NOT PROVIDE ANY INFORMATION RELATED TO SURGERIES, ALLIED MEDICAL TREATMENTS. ALWAYS CONSULT THE RESPECTIVE HEALTH CARE PROVIDER.

ADR Reporting

Drug Induced Hyperkalemia & Diarrhea

A 53 year old female admitted to medicine ward with complaints of multiple joint pain, weight gain and bed sores. She has a history of long term rheumatoid arthritis (RA), hypothyroidism since 2 months and hypertension (HTN) since 2 years. Previous medication history reveals T.Lasilactone 50mg (Spironolactone+Frusemide), T.Nimsun 100mg (Nimusulide),T.Prednisolone 5mg, T.Alprax 0.5mg (Alprazolam), T.Thyrox 50mg (L-Thyroxine sodium).

Patient complained of significant weight gain in last one year, which may be attributed to the condition of hypothyroidism and long term steroid therapy for RA. Laboratory investigations Revelaed hyperkalemia since first day of hospitalization, which is a suspected adverse reaction associated with spironolactone.Similar event is documented in various case reports.[1,2] All the drugs were discontinued except frusemide and thyroxin sodium during hospitalization and patient was put on leflunomide and colchicine, following which, the patient complained of frequent loose motion of about 4-5 episodes from 5th day of therapy. Leflunomide drug review shows delayed GI disturbances (diarrhea, 17- 27%)[3] and colchicine induced diarrhea upto 23%.[3,4]Patient showed improved GI functions on withdrawal of both these suspected drugs.

Causal assessment of these ADRs i.e hyperkalemia and diarrhea on Naranjo's scale shows ***'possible'*** relation with suspected drugs and severity assessment was found to be **mild & moderate** respectively.

References:
1.Kamala P. Tamirisa, Keith D. Aaronson, and Todd M. Koelling. Spironolactone-induced renal insufficiency and hyperkalemia in patients with heart failure. Am Heart J 2004;148:9718.
2.Morten Svensson, Finn Gustafsson, Soren Galatus et. al. How Prevalent Is Hyperkalemia and Renal Dysfunction During Treatment With Spironolactone in Patients With Congestive Heart Failure? Journal of Cardiac Failure Vol. 10 No. 4 2004.
3.Micromedex Healthcare Series 2.0
4.Edmund K, Lai-Shan Tam, Brian Tomlinson. Leflunomide in the Treatment of Rheumatoid Arthritis.Clinical therapeutics Vol. 26, No. 4, 2004.

Reported By- *Chetan Sonar, Tanmay Pore*

FDA LABEL CHANGE (Ref: FDA medwatch issued ***December 2011***)

Levocetirizine dihydrochloride (oral solution and tablets)
WARNINGS AND PRECAUTIONS
Urinary Retention: Urinary retention has been reported post-marketing....
ADVERSE REACTIONS: added ..... urinary retention

Health ministry to withdraw licences issued to more than 200 irrational FDCs....

Most of the **atrovastatin combinations, rabeprazole combinations, paracetamol combinations and multivitamin combinations will be withdrawn from the market**

Pharmabiz.com/***Ramesh Shankar, Mumbai***
Thursday, November 01, 2012

The Union health ministry issued a directive to the health departments of all states and Union Territories instructing them to grant or renew licenses for manufacture or sale of drugs only in generic names. Effective implementation of the new order may enable patients to purchase low priced drugs in one therapeutic category with the advice of the pharmacists.

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Departmental News And Activities

AROGYA SAMVAD

Community Awareness Programme

Dr. Atmaram Pawar has been involved in community pharmacy care from past 10 yrs. Recently he was invited for an open talk for public on the Generic Medicines on 27th October 2012 jointly organized by PM Shah Foundation and Vardhman Pratisthan, Pune. The focous of discussion was on the understanding of a generics compared to the branded medicines available at retail outlets. Most of the participants had an idea that generics means cheap, but hardly few were concerned about its effectiveness in treating a condition. The participants were made aware that they should not only consider generic drugs as they are cheap, but they should monitor its effectiveness in regular use. In India bioequivalent generics are not readily available in community pharmacy though India is a market of generics for western countries.

Articles in Newspapers:

Dr. Atmaram Pawar, Vice-Pricipal and HOD of Dept. of clinical Pharmacy has been involved in raising social issues pertaining to the medicines, continuously in many leading local marathi and english newspapers like Sakal Times and Maharashtra Times. In his writings the issues like concept of generic and branded drugs, availability of cost-effective generic drugs in India, dispensing and distribution of medicines by prescribers and many more. By highlighting these issues FDA took regulatory steps for control of drug distribution and dispensing. General public were made aware about the right use of drugs and availability and concept of generics.

Drug Dose Division:

It is a professional dispensing activity extended to Dept. of Pediatrics, Bharati Hospital. The drugs which are very costly and out of reach of poor patients are dose divided without affecting the efficacy of drug and dispensed by proper labelling. Dose division is performed meticulously depending upon the requirement of the dose of pediatric patients. The patient attendees are counseled regarding the administration and storage of dispensed doses.

Guest Lecture:

Dr. Madhura Joshi; Associate Scientist from Lupin Bioresearch Centre delivered a Presentation on '**Clinical Trial Monitoring**' on 8th Dec, 2012. She focused on types of monitoring visits, pre-visit preparation and site visit assessment, clinical study initiation, stages of monitoring visit, CRF review, errors in CRF and CRF corrections, Monitoring report and Site close out visit activities. Useful for the students who aspire to be a clinical trial monitor.

Paper Presentations at International Conference:

1. Ms. Asawari Raut, Asst. Professor, presented a paper titled Antibiotics adverse drug reactions: severity & cost, at International conference on"pharmacoeconomics and good pharmacy practice" oraganized by ISPRO, IPA, RIPER , Andhra Pradesh (13th-14th October 2012).
2. Papers presented by PharmD Interns at 7th Asian conference on "Medication Safety and Effectiveness: Building evidence through good pharmacoepidemiological Practice"- organized by ISPE, ISCR, JSS University,Bengaluru(26th- 28th October-2012).The research papers focused on compliance in antitubercular therapy, drug Utilization evaluation in pregnancy induced hypertension and Comparative efficacy study of diclofenac and its combinations.

PharmD Interns with ISPE President Mrs. Stella Blackburn