2nd International Conference on
Clinical Trials and Therapeutic Drug Monitoring
August 22-24, 2016   Philadelphia, USA

Posters
Magnitude and characteristics of clinical trials in Saudi Arabia: A cross-sectional analysis

Sheraz Ali, Mesfer A Alghamdi, Jasser Ali S Alzhrani and Edward B Devol
King Saud Medical City, KSA

The clinical trial is an important type of research design in the spectrum of translational research. The extent to which clinical trials are conducted is a reflection of the level of advancement that exists within a healthcare system – a single provider, an organization (e.g. a hospital), or a national healthcare system. This study aims at describing the clinical trial activity within the Kingdom of Saudi Arabia since 2000 through reviewing those trials that have been registered with ClinicalTrials.gov in that time period. Since February 2000, 405 trials have been registered with ClinicalTrials.gov. These trials fall into one of 22 different ICD-10 codes, and with the top four being neoplasms (92), diseases of the circulatory system (57), endocrine, nutritional and metabolic diseases (46), and diseases of the respiratory system (25). Among the 405 trials, about half (200) were classified as trials with both safety and efficacy endpoints. Fifty-two percent were phase IV trials and 28% were phase III. About 64% were randomized, and with about equal numbers of those trials coming from industry (86) and university sponsors (85), and smaller numbers coming from hospitals (51) and other sponsors. Among the 185 university- or hospital-sponsored trials, the most common was a phase IV neoplasm trial (11) and next being a phase IV trial of diseases of the circulatory system (9). A total of 24 phase III university- or hospital-sponsored trials have been registered during the 15-year time period. With a population approaching 30 million and very large annual healthcare expenses, it would appear that the level of clinical trial activity within the Kingdom during the past 15 years has been rather paltry. The emphasis has been on post-marketing phase IV trials. The academic setting (i.e. universities and hospitals) has seen a new trial registered every 11 months on average. This study is solely based upon the information as registered in ClinicalTrials.gov. There is the possibility that other trials not registered could exist. However, it is thought that the resource would include those trials of a higher quality and more rigorous.

Biography

Sheraz Ali has completed his MPH degree on scholarship from University of Eastern Finland and PharmD from Baqai Medical University. He is currently working as a Researcher at Pharmaceutical Care Services, King Saud Medical City, Ministry of Health, Saudi Arabia, and involved in several clinical research projects. He also worked as a Clinical Research Associate in CRO and Pharmaceutical industry and is a part of local and international clinical trials. He is a registered researcher in Saudi Arabia and also a member of International Society for Disease Surveillance (ISDS).

sheraz@ksmc.med.sa
Assessment of awareness about ethics committee amongst the research scholars/teachers in government medical colleges of Punjab, India

Ramandeep Kaur Brar, Vikas Gupta, Ajay F Christopher and Parveen Bansal
Baba Farid University of Health Sciences, India

Ethics committee is supposed to play a great role in safe human research. It is mandatory that all research projects related to health sciences with involvement of patients/subjects should be approved by IEC before commencement. The data available reflects the low percentage of awareness amongst the routine project investigator. Being inclined towards medical education only, awareness amongst faculty members of medical colleges towards ethics committee is also expected not up to the mark. Indian Council of Medical Research has launched and funded development of Multidisciplinary Research Unit (MRU), a scheme for igniting research component in various medical colleges of India. Keeping in view the above situation, a study was designed to check the awareness about the composition, review procedure and functioning of IEC amongst the research scholars/teachers in government medical colleges of Punjab. The information was sought in form of a questionnaire from a total of 50 participants. From the study it was observed that only 10% had undergone ICH-GCP training. A few participants (6%) served as member of IEC and demonstrated a very poor knowledge index about IEC. Only 68.5% participants were aware about its composition and majority of respondents (86%) felt that there was a need of training before becoming a member of IEC. From the data it is very clear that there is strong need of training to faculty of medical colleges towards institutional ethical committee. There is a need to inculcate the IEC-ICH guideline in curriculum of post-graduates medical students and medical teachers.

Biography
Ramandeep Kaur Brar has completed her B.Pharm and currently pursuing MSc in Clinical Research at University Center of Excellence in Research, Baba Farid University of Health Sciences, India. She has published one chapter in book and one Paper “Scope and Bottlenecks in Clinical Trials of Herbal Drugs” in the Journal of Pharmaceutical Research.

raman7856@gmail.com
Clinical research is making toiling efforts for promotion and wellbeing of the health status of the people. There is a rapid increase in number and severity of diseases like cancer, hepatitis, HIV etc., resulting in high morbidity and mortality. Clinical research involves drug discovery and development whereas clinical trials are performed to establish safety and efficacy of drugs. Drug discovery is a long process starting with the target identification, validation and lead optimization. This is followed by the preclinical trials, intensive clinical trials and eventually post marketing vigilance for drug safety. Softwares and the bioinformatics tools play a great role not only in the drug discovery but also in drug development. It involves the use of informatics in the development of new knowledge pertaining to health and disease, data management during clinical trials and to use clinical data for secondary research.

In addition, new technology likes molecular docking, molecular dynamics simulation, proteomics and quantitative structure activity relationship in clinical research results in faster and easier drug discovery process. During the preclinical trials, the software is used for randomization to remove bias and to plan study design. In clinical trials software like electronic data capture, Remote data capture and electronic case report form (eCRF) is used to store the data. The eClinical, Oracle clinical are softwares used for clinical data management and for statistical analysis of the data. After the drug is marketed the safety of a drug could be monitored by drug safety software like Oracle Argus or ARISg. Therefore, softwares are used from the very early stages of drug designing to drug development, clinical trials and during pharmacovigilance. This review describes different aspects related to application of computers and bioinformatics in drug designing, discovery and development, formulation designing and clinical research.

Biography
Supreet Kaur Gill has completed her Bachelor of Dental Surgery from Adesh Institute of Dental Sciences and Research, Baba Farid University of Health Sciences, India. Currently she is pursuing her Post-graduation (MSc) in Clinical Research from University Centre of Excellence in Research, Baba Farid University of Health Sciences, India. She has published one paper in Asian Journal of Pharmaceutics and Clinical Research.
Response adaptive design for clinical trials: A Markov decision process model for sequential chemotherapy treatment planning

Nazila Bazrafshan and M M Lotfi
Yazd University, Iran

Clinical trials play an increasingly important role in determining how treatment regimens are effective and safe. Treatment trials are the most common type of trials aimed at finding the best treatments causing the minimal side effects. They serve as a standard technique for evaluating chemotherapy treatment plans used to improve cancer treatment and care. Adaptive trials, on the other hand, test sequential treatments to select the appropriate treatment regimen in accordance with the patient’s condition. In fact, the intensity of advising the treatment regimen varies in response to the patient’s needs. We propose such a design using a Markov decision process (MDP) model for selecting the optimal policy of cancer chemotherapy treatment regimen according to the patient’s condition. The developed MDP model employs novel optimal cancer chemotherapy treatment regimens resulted from an optimization model which relies on previously published clinical trials. In this way, the MDP model benefits from the results of optimization model which propose the most-promising and cost-effective new chemotherapy combinations. Hence, the proposed approach takes the impact of the patient’s response to the treatment regimen into account and proposes the most-promising dynamic treatment regimens also costing reasonable. Results show that the proposed approach yields the optimal sequence of chemotherapy treatment regimens for a period of chemotherapy treatment which makes possible designing clinical trials for sequential treatments. Comparing to the existing implemented clinical trials, we show that our proposed design significantly improves both health outcomes and treatment costs of patients.

Biography

Nazila Bazrafshan has completed her M.Sc. in industrial engineering at Yazd University, Iran, in 2015. Her research interests are cancer treatment planning and medical decision-making.

bazrafshan.n@stu.yazd.ac.ir
The modification of UGT1A10 isoenzyme activity by C-1305 and C-1311 antitumor agents in non-cellular system and in HCT-116 colon cell line

Anna Bejrowska
Gdansk University of Technology, Poland

Modern cancer treatment provides promising outcomes, thanks to the combined therapies. However, aiming to decrease resistance against individual drugs, treatment can intensify their adverse and toxic effects. Therefore, it is important to examine the influence that potential therapeutics have on cellular metabolism. Our group previously revealed that antitumor acridinone derivatives, C-1305 and C-1311, are metabolized to a great extent by UGT1A10. Thus, the aim of the present study is to test the ability of these compounds to modulate the activity of UGT1A10 isoenzyme both in non-cellular and cellular systems. The experiments were performed using human recombinant isoenzyme UGT1A10 and colon cancer line HCT-116 over expressing UGT1A10. Enzyme activity in both models were measured using UGT-specific reaction, 7-hydroxy-4-(trifluoromethyl)-coumarin glucuronidation in the presence of selected acridinone derivatives, as well as without the drug (control experiments) by RP-HPLC analysis. The results showed that, C-1305 and C-1311 act differently towards UGT1A10 activity in dependence on the applied model. Enzymatic activity of UGT1A10 was reduced by both acridinone derivatives in non-cellular system. By contrast, higher level of UGT1A10 activity was observed in HCT-116 cells treated with both studied compounds. It is supposed that C-1305 and C-1311 potentially applied in multidrug therapy might modulate the effectiveness of UGT1A10 on the protein and the transcriptional level. This finding provides new insights into potential pharmacokinetic drug-drug interactions between C-1305 and C-1311 and the substrates of UGT1A10.

Biography
Anna Bejrowska has graduated from Gdansk University of Technology (Poland) in the year 2013. She is a co-author of a paper about environmental tests based on nuclear receptors’ activity changes. Her curiosity and desire for intellectual development is what led her to pursue her PhD in the field of Drug Development. Currently, she is a PhD candidate in the Department of Pharmaceutical Technology and Biochemistry at Gdansk University of Technology. She is consistently developing her experience of working with active compounds, enzyme fractions and cell cultures. Her interest is focused on modulations and differentiation of drugs’ metabolism, including the role of nuclear receptors in those processes.

Notes:
Inhibition of UGT1A9 activity demonstrated for acridine antitumor agent C-1748 may implicate drug-drug interactions

Anna Mróz
Gdańsk University of Technology, Poland

UDP-glucuronosyltransferases (UGTs) are phase II conjugating enzymes catalyzing glucuronidation reaction of many exogenous and endogenous substances. Glucuronides are more polar than the native compounds which facilitates their excretion. UGT isoenzymes are in the spotlight in respect to antitumor therapy as glucuronidation is the major route of elimination for many anticancer drugs. Moreover, some drug-drug interactions can be explained on the basis of UGTs inhibition. The objective of the present study was to explore the inhibitory effect of C-1748, an acridine antitumor agent, toward isoenzyme UGT1A9 in order to predict the potential for drug-drug interactions. C-1748 showed strong cytotoxic activity against colon cancer cells and high antitumor activity against prostate carcinoma xenografts which allowed its selection for preclinical studies. Previous results indicated that C-1748 undergoes glucuronidation with human liver and intestinal microsomes. Our studies showed that C-1748 is not a substrate for UGT1A9, however it exerted dose-dependent inhibition toward this isoenzyme. The glucuronidation reactions of standard substrate 7-hydroxy-4-(trifluoromethyl)coumarin were conducted in the absence or presence of C-1748 and monitored by HPLC/UV-Vis method. The concentration of 0.25 mM of C-1748 inhibited more than 70% activity of UGT1A9. The inhibition kinetic type was determined to be noncompetitive on the basis of Lineweaver-Burk and Dixon plots and the inhibition kinetic parameter (Ki) was calculated to be 0.17 mM. Taking together, the presented UGT1A9 significant inhibition indicates the high possibility for drug-drug interactions in combined therapies using C-1748 anticancer agent. Therefore, clinical monitoring should be applied when co-administrating C-1748 with drugs mainly undergoing UGT1A9-mediated metabolism.

Biography
Anna Mróz has studied Biotechnology from Gdańsk University of Technology (Poland) and received her Master’s degree in the year 2013. She is now a PhD student at the Department of Pharmaceutical Technology and Biochemistry, Gdańsk University of Technology. Her scientific interests are related to the investigation of metabolism of new active compounds against cancer. She is a co-author of two papers in the field of UDP-glucuronosyltransferases-mediated metabolism.

anna.mroz89@gmail.com
Apoptotic and necrotic basal forebrain cholinergic neuronal loss after acute and long-term chlorpyrifos exposure

Javier del Pino1, Paula Moyano1, María Teresa Frejo1, María Jesús Díaz1, Gloria Gomez1, María José Anadón1, Margarita Lobo1, Jimena Garcia2, Miguel Andrés Capo1 and José Manuel Garcia1
1Complutense University of Madrid, Spain
2Alfonso X University, Spain

Chlorpyrifos (CPF) is an organophosphate insecticide reported to induce both after acute and repeated exposure learning and memory dysfunctions, although the mechanism is not completely known. CPF produces basal forebrain cholinergic neuronal loss, involved on learning and memory regulation, which could be the cause of such cognitive disorders. This effect was reported to be mediated through apoptotic process, although neuronal necrosis was also described after CPF exposure. Accordingly, we hypothesized that CPF induces basal forebrain cholinergic necrotic and apoptotic cell death. We evaluated in septal SN56 basal forebrain cholinergic neurons, the CPF effect after 24 h and 14 days exposure on the necrosis induction and the apoptotic and necrotic gene expression pathways. This study shows that CPF induces after acute and long-term exposure necrotic cell death at higher concentrations than which induces apoptotic cell death. Evaluation of cell death pathways revealed that some of them are altered at lower concentrations than which produces the effects observed and below the no observed adverse effect level (NOAEL). The present finding suggests that the use of gene expression profile could be a more sensitive and accurate way to determine the NOAEL.

Biography
Javier del Pino has received his PharmD degree from the University Complutense University of Madrid in the year 2004. He has done two Master’s in Sciences in the year 2009 and 2010. He did his Specialization in Neurotoxicology and Neurodevelopmental Toxicology and received his PhD in Toxicology in the year 2009. In 2010, he worked at Institute of Health Carlos III in the National Center of Environmental Health. From 2010 to 2012, he was an Associated Researcher at University of Massachusetts (UMASS), working at Sandra Petersen’s Lab in a National Institute of Health (NIH) project on developmental effects of TCDD endocrine disruptor on sexual differentiation. In 2016, he became an Associate Professor of Toxicology at the Complutense University of Madrid, Spain

jdelpino@pdi.ucm.es

Notes:
Cadmium induces cell death in SN56 cholinergic neurons from basal forebrain mediated by acetylcholinesterase variants altered expression

Javier del Pino1, Paula Moyano1, María Teresa Frejo1, María Jesús Díaz1, Gloria Gomez1, María José Anadón1, Margarita Lobo1, Jimena García2, Miguel Andrés Capo1 and José Manuel Garcia1

1Complutense University of Madrid, Spain  
2Alfonso X University, Spain

Cadmium is a neurotoxin compound which induces cognitive alterations similar to those produced by Alzheimer's disease (AD). However, the mechanism through which cadmium induces this effect remains unknown. In this regard, we described in a previous work that cadmium induces a more pronounced cell death on cholinergic neurons from basal forebrain. Degeneration of basal forebrain cholinergic neurons, as happens in AD, results in memory deficits attributable to the loss of cholinergic modulation of hippocampal synaptic circuits. Moreover, cadmium induces acetylcholinesterase (AChE) overexpression, which has been related to cell death induction. Moreover, AChE variants alteration has been reported to mediate apoptotic and necrotic cell loss induction of basal forebrain cholinergic neurons and development of AD. According to all above, we hypothesized that cadmium induces the more pronounced cell death on basal forebrain cholinergic neurons through alteration of AChE variants expression alteration. The present study is aimed at researching the mechanisms of cell death induced by cadmium on basal forebrain cholinergic neurons. For this purpose, we evaluated, in SN56 cholinergic murine septal cell line from basal forebrain region, the cadmium toxic effects on neuronal viability through AChE splice variants. This study proves that cadmium induces cell death on cholinergic neurons through overexpression of tetrameric AChE-S and down-regulation of monomeric AChE-R. Our present results provide new understanding of the mechanisms contributing to the harmful effects of cadmium on cholinergic neurons and suggest that cadmium could mediate this effect through AChE splices altered expression.

Biography
Javier del Pino has received his PharmD degree from the University Complutense University of Madrid in the year 2004. He has done two Master’s in Sciences in the year 2009 and 2010. He did his Specialization in Neurotoxicology and Neurodevelopmental Toxicology and received his PhD in Toxicology in the year 2009. In 2010, he worked at Institute of Health Carlos III in the National Center of Environmental Health. From 2010 to 2012, he was an Associated Researcher at University of Massachusetts (UMASS), working at Sandra Petersen’s Lab in a National Institute of Health (NIH) project on developmental effects of TCDD endocrine disruptor on sexual differentiation. In 2016, he became an Associate Professor of Toxicology at the Complutene University of Madrid, Spain

jdelpino@pdi.ucm.es

Notes:
KChIP1 regulation of Kv 4.3 potassium channels and GABAergic transmission in primary hippocampal cells

Javier del Pino1, Paula Moyano1, María Teresa Frejo1, María Jesús Díaz1, Gloria Gomez1, María José Anadón1, Margarita Lobo1, Jimena García2, Miguel Andrés Capo1 and José Manuel Garcia1

1Complutense University of Madrid, Spain
2Alfonso X University, Spain

4-Aminopyridine (4-AP) is a potassium channel blocker used for the treatment of neuromuscular disorders. Otherwise, it has been described to produce a large number of adverse effects, among them cell death mediated mainly by blockage of K+ channels. Specifically, 4-AP has been reported to produce cell death in central nervous system on hippocampal cells. On the other hand, Kv channel interacting protein 1 (KChIP1) is a neuronal calcium sensor protein that is predominantly expressed at GABAergic synapses and it has been related with modulation of K+ channels, GABAergic transmission and cell death. According to this, KChIP1 could modulate K+ channels and GABAergic transmission, which mediate the toxic effects induced by 4-AP. We evaluated, in wild type and KChIP1 silenced primary hippocampal neurons, the effect of 4-AP (0.25 mM to 2 mM) with or without semicarbazide (0.3 M) co-treatment after 24 h and after 14 days 4-AP alone exposure on KChIP1 and Kv 4.3 potassium channels gene expression and GABAergic transmission. We observed that 4-AP modulates KChIP1 which regulates Kv 4.3 channels expression and GABAergic transmission. Our study suggests that KChIP1 is a key gene that may have a protective effect up to certain concentration after short-term 4-AP treatment, but this protection would be erased after long term exposure, due to KChIP1 down-regulation predisposing cell to 4-AP induced damages. These data might help to explain protective and toxic effects observed after overdose and long term exposure.

Biography

Javier del Pino has received his PharmD degree from the University Complutense University of Madrid in the year 2004. He has done two Master’s in Sciences in the year 2009 and 2010. He did his Specialization in Neurotoxicology and Neurodevelopmental Toxicology and received his PhD in Toxicology in the year 2009. In 2010, he worked at Institute of Health Carlos III in the National Center of Environmental Health. From 2010 to 2012, he was an Associated Researcher at University of Massachusetts (UMASS), working at Sandra Petersen’s Lab in a National Institute of Health (NIH) project on developmental effects of TCDD endocrine disruptor on sexual differentiation. In 2016, he became an Associate Professor of Toxicology at the Complutense University of Madrid, Spain

jdelpino@pdi.ucm.es
Assessment of gestational diabetes, urinary tract infections, and folic acid intake in Lebanese pregnant females

Sara Al Zein
Lebanese International University, Lebanon

Pregnancy is associated with multiple health problems, which can be controlled by raising awareness about the complications that occur. Many Lebanese females in their childbearing age are not knowledgeable about the importance of folic acid intake and the risk of developing gestational diabetes mellitus (GDM) or urinary tract infections (UTI) during pregnancy. The aim of this study was to check whether females have been screened for GDM, counseled for UTI and the intake of periconceptional and postconceptional folic acid. The study was conducted in females that experienced at least 1 pregnancy in a community setting by filling a 10 minutes survey. Concerning GDM, 42.3% stated their knowledge of its screening importance, whereby 59.1% were screened with an OGTT and 32.8% with an FBG. This resulted in having 3.5% positive tests for this type of diabetes (3.1% had gained <18 kilos; p-value>0.05) for which 69% implemented dietary changes and 46% took metformin. As for folic acid intake, 85.6% took 5 mg dose: 33.1% for 1 month before gestation, 46.7% in the first trimester, 27.3% up to the second, and 11.5% throughout the pregnancy. It was noted that a big percentage of the females don’t know the role of GDM screening and its impact on pregnancy. Moreover, the role of periconceptional intake of folic acids is not sufficiently disseminated to young women, whereas the postconceptional was appropriate, but not based on risk factors. Furthermore, therapeutic management of UTIs in pregnancy requires thorough understanding of antimicrobial agents to optimize maternal and fetal outcomes.

Biography
Sara Alzein has completed her PharmD and Bachelor's degree of Pharmacy from Lebanese International University (LIU). She participated in the 7th Pharmacy Day “Facts and Myths in Pharmacy Practice” in May 2012 with a poster presentation, in LIU. The abstract of her PharmD thesis entitled, “Pregnancy complications in the Lebanese population” which was accepted by the American Journal of Health-System Pharmacy (ASHP).

sara.alzein@hotmail.com
Drug Utilization Evaluation (DUE) on Enoxaparin in Venous Thromboembolism (VTE) prophylaxis for hip and knee replacement surgery

Chung Yue Ling1, Ng Kai Xin1 and Lai Kah Weng1
1 National University Hospital, Singapore

This study aims to assess the adequacy and appropriateness of the use of chemical prophylaxis/enoxaparin in total knee and/or hip replacement (TKR and/or THR) surgery patients at National University Hospital (NUH). A retrospective drug utilization evaluation was performed for NUH patients aged ≥18 years old who have undergone TKR and/or THR surgery from 1st January to 31st March 2013 and excluded foreigners not residing in Singapore. The study indicators included compliance/non-compliance of chemoprophylaxis/enoxaparin prescribing patterns to NUH Venous-Thromboembolism (VTE) Prophylaxis guidelines. Efficacy and safety related clinical outcomes in terms of VTE and hemorrhagic events respectively in a 3-months follow-up period post surgery were also measured. Data for a total of 82 patients were collected and analyzed. Chemoprophylaxis prescribing patterns for only 46 (56.1%) patients were compliant to NUH guidelines in terms of indication. The need for chemoprophylaxis exceeded bleeding risks for 55 (67.1%) patients but only 30 (36.6%) patients were given chemoprophylaxis (enoxaparin). When enoxaparin was prescribed, none of the dosing regimens were compliant to NUH guidelines in all three aspects of dose and frequency, prophylaxis duration and time of first dose initiation. During the 3-months follow-up, no bleeding events due to enoxaparin occurred. 9 (11.0%) patients developed thrombosis. Among which, one patient developed pulmonary embolism while another developed thrombosis in the femoral vein. The study revealed the baseline chemoprophylaxis and enoxaparin usage patterns in NUH TKR and THR patients. The adverse clinical outcomes that occurred identified potential safety gaps within the prescribing practices, for which recommendations were made to improve the safe and effective use of VTE chemoprophylaxis in NUH post-surgical orthopedic patients.

Biography

Chung Yue Ling graduated from National University of Singapore in 2013 with a Bachelor of Science (Pharmacy) degree, First Class Honours. She is now working as an inpatient hospital pharmacist at the National University Hospital of Singapore, taking charge of general medicine and oncology wards.

yue_ling_chung@nuhs.edu.sg

Notes:
Rethinking training and operational approaches with investigative sites

Adam Chasse
OnPoint CRO, USA

Clinical research is critically important to develop new treatments and substantial regulations help to protect patient safety and data integrity. However, poor patient recruitment continues to increase clinical study costs and timelines. In the United States, the pharma/CRO industry has reacted by developing tactics to engage patients directly and “match” them with “qualified” investigators (i.e., physicians with a successful track record in clinical research), yet macro-level data do not suggest this has had positive impact. To fix the problem, industry must acknowledge and address the shortage of physicians willing/able to become involved with clinical research (and the business-related reasons for this) and that the “matchmaking” approach incorrectly assumes patients will be enthusiastic about seeing doctors other than their own. Boosting patient participation in studies; means increasing the number of physicians willing to serve as investigators. The industry can no longer depend on a free market approach in which the best potential research sites voluntarily invest in the infrastructure necessary to be successful, because quite simply, the benefits of doing so are uncertain and not enough to offset the many other regulatory and resource demands in today’s healthcare environment. This session will explore barriers to physician and patient participation in clinical research, the strengths and weaknesses of today’s normative approaches to investigator training/selection and potential solutions that the pharma/CRO industry must consider.

adam.chasse@onpointcro.com

Efficacy and safety of iota-carrageenan nasal spray versus placebo in early treatment of the common cold in adults: The ICICC trial

Stephan Koelsch
Boehringer Ingelheim Pharma GmbH & Co. KG, Germany

Iota-carrageenan (I-C) is active against respiratory viruses in vitro and was effective as nasal spray in three clinical trials with common cold patients. To further investigate I-C, a fourth randomized, placebo-controlled, double-blind clinical trial was conducted in 200 adult patients with self-diagnosed colds that were confirmed by baseline symptom scores. Respiratory viruses were quantified at baseline and on treatment day 3 or 4. Primary endpoint was the mean total symptom score of 8 cold symptoms on Days 2 to 4. The primary endpoint did not demonstrate a statistically significant difference between I-C and placebo but showed a trend towards I-C benefit. Exploratory analyses indicated significant reduction of cold symptoms in the I-C group and also substantiated I-C’s activity against rhinovirus. To observe trends rather than statistically significant outcomes obviously was based on an unexpected low power of the trial. In particular, the proportion of virus-positive patients was smaller than anticipated. Only 23.6% had rhinovirus in contrast to 50-90% in other studies. This low frequency of rhinovirus-positive patients in the ICICC study demonstrates that there may often be a trade-off when the standard design for cold studies is used. When a controlled study tries to recruit patients at the earliest stages of a cold, patients may incorrectly believe they are coming down with a cold, prior to full blown cold symptoms. Hence, the peculiarities of the ICICC study may trigger a discussion among the scientific community about more suitable study designs to investigate common cold treatments.

stephan.koelsch@boehringer-ingelheim.com
Innovations in response-adaptive designs for clinical trials

Vishal Ahuja
Southern Methodist University, USA

Clinical trials have traditionally followed a fixed randomized design, where patients are typically allocated once, at random, and usually equally to various treatments. Such designs provide a clean way of separating out the effects of alternate treatments. Response-adaptive designs, where assignment to treatments evolves dynamically as patient outcomes are observed, are gaining in popularity due to potential for improvements in both cost and efficiency over traditional designs. An ideal adaptive design is one where patients are treated as effectively as possible without sacrificing the potential learning or compromising the integrity of the trial. We propose such a design, termed Jointly Adaptive, which uses forward-looking algorithms to fully exploit learning from multiple patients simultaneously. Compared to the best existing implementable adaptive design that employs a multi-armed bandit framework in a setting where multiple patients arrive sequentially, we show that our proposed design improves health outcomes of patients in the trial, in expectation, by 8.6% under a set of considered scenarios. We also demonstrate our design's effectiveness using data from a recently conducted stent trial, where we demonstrate an improvement of over 37%, in expectation. A consequence of using forward-looking algorithms in the above approach is that the problem size grows exponentially with the number of patients and time periods, making it computationally challenging to solve. To address this, we propose grid-based approximation methods that reduce problem dimensionality and allow for the implementation of adaptive designs to large clinical trials. We use numerical examples to demonstrate the effectiveness of our approach.

vahuja@mail.smu.edu

Synergistic effect of biogenic silver-nanoparticles with β-lactam Cefotaxime against resistant Staphylococcus arlettae AUMC b-163 isolated from T3A pharmaceutical cleanroom, Assiut, Egypt

Ahmed Abdelfattah Mohammed Shoreit, Mohammad Hassan A Hassan, Mady Ahmed Ismail and Ahmad Mohammad Moharram
Assiut University, Egypt

The aim of this study was to biosynthesize silver nanoparticles (AgNPs) from Staphylococcus arlettae AUMC b-163 isolated from T3A pharmaceutical company clean room, its antimicrobial activity, and the synergistic effect of AgNPs in combination with commonly used antibiotic Cefotaxime sodium against resistant bacteria. The synthesized AgNPs from bacterial were characterized by using UV-VS spectrophotometer analysis, Fourier Transform Infrared Spectroscopy (FTIR), X-ray diffraction (XRD) and Transmission Electron Microscopy (TEM). UV-VS spectrophotometer analysis showed a peak at 420 nm corresponding to the Plasmon absorbance of silver nanoparticles and FTIR analysis showed the potential biomolecule responsible for the reduction of silver. The structural properties of silver nanoparticles were confirmed using XRD technique, while TEM micrographs revealed that the silver nanoparticles are dispersed and aggregated, and mostly having spherical shape within the size range between 8 and 35 nm. The synthesized silver nanoparticles exhibited a varied growth inhibition activity against the tested pathogenic bacteria. A significant increase in area of growth inhibition was observed when a combination of silver nanoparticles and Cefotaxime antibiotics was applied. The current results revealed that the synthesized silver nanoparticles produced by the bacterial strain Staphylococcus arlettae AUMC b-163 is promising to be used in medical therapy due to their broad spectrum against some pathogenic bacteria, fungi and resistant tested bacteria.

ahmedshoreit@yahoo.com
The new EU clinical trials regulation

David R Jones
MHRA Clinical Trials Unit, UK

The EU is introducing legislation aimed at harmonizing the way in which clinical trials conducted in the Europe are authorized and at improving the reliability of data generated in those trials. The Regulation replaces the EU Clinical Trials Directive (EUCTD), which was approved in 2001 and implemented in May 2004. The regulation will introduce and include a number of key provisions. There is an authorization procedure for clinical trials based on a single submission dossier via a single EU portal, an assessment procedure leading to a single decision on all aspects per member state, rules on the protection of subjects and informed consent, and transparency requirements. Other aspects include more detailed safety provisions, new indemnity provisions and a category for low interventional trials. The new regulation also intends to make it easier for Pharma companies to conduct multinational clinical trials. The talk will cover review the new Regulation, highlighting what will change from the Directive and advise companies how to gear up for its implementation.

david.jones@mhra.gsi.gov.uk

Culturally competent strategies for recruitment and retention of African-American populations into clinical trials

Jane A Otado, John Kwagyan, Diana Edwards, Alice Ukaegbu, Faun Rockcliffe and Nana Osafo
Howard University, USA

Purpose: To identify successful recruitment strategies, challenges and best practices for researchers to engage African American communities in clinical studies taken into consideration target participants' culture and context.

Methods: We reviewed 50 studies conducted from 2001-2012 at an inner-city research center to determine the type, duration, anticipated enrollments and actual enrollments. Survey was sent to study coordinators to obtain data on recruitment and retention strategies, challenges and dropout rates. We also interviewed 25 study coordinators on challenges and strategies.

Results: Of the 50 studies, 24 had completed recruitment at the time of this report. The completed studies achieved a median recruitment rate of 88% [range: 50-110]. Successful recruitment and retention strategies included field-based strategy and snowballing. Major barriers were distrust, compensation, education disadvantage, lack of interest and inability to have study partner. Strategies to reduce barriers included providing informational sessions, disseminating newsletters about study outcomes. Best practices include being culturally sensitive including demonstrating a caring attitude and being responsive to participants needs.

Conclusions: Cultural competence is critical in order to design and implement successful recruitment strategies in this population. Research teams should comprise of multi-ethnic staff, involve the community, demonstrate trust and deliver concise education of the research endeavor.

j_otado@Howard.edu
Innovation in clinical research technologies and software systems: Mir-208a/b can be a potential drug target in regulation of cell proliferation and apoptosis in oral squamous cell carcinoma-first report

Ajay Francis Christopher, Mridula Gupta and Parveen Bansal
Baba Farid University of Health Sciences, India

Introduction: Although substantial advancement has been achieved in the techniques and therapies related to oral squamous cell carcinoma (OSCC). Still, there is requisite for the novel approaches to reveal the various pathways and their regulators to treat the disease. We aim to find out key genes and miRNAs involved in positive regulation of cell proliferation and negative apoptosis.

Method: To analyze the genes, differentially expressed OSCC genes were obtained from various published papers and databases. Gene ontology (GO) was done using STRING v 10 to obtain genes involved in cell proliferation (CP) and apoptosis (AP) and their positive (+ve) and negative (-ve) regulations. Experimentally validated miRNA-target interactions (MTIs) were retrieved from miRTarBase. The target genes of miRNAs were predicted through utilizing tools TargetScan. Key miRNAs and genes were identified for cell proliferation, positive regulation cell proliferation and negative regulation of apoptosis using Cytoscape 3.3.0.

Results: Twenty four genes were found to be regulating CP+ve and AP-ve. Micronome of CP, AP and its +ve and -ve regulator revealed 11 common miRNAs (miR-379-5p, miR-106b-3p, miR-208b-3p, miR-208a-3p, miR-504-5p, miR-33a-3p, miR-328-3p, miR-376c-3p, miR-197-3p, miR-496 and miR-758-3p). The direct target of these miRNAs were EDN1, HSPA5; HIF1A, NFE2L2; CDKN1A; CDKN1A, ETS1; MDM2; RARB, GSK3B; SFRP1; DAPK1, TGFA; IL18; MDM2 and MDM2 respectively. Gene Ontology based network of CP, CP+ve and AP-ve revealed CDKN1A as key regulator of these pathways. The Target Scan showed direct miRNA-mRNA interactions of mir-208a-3p and mir-208b-3p with CDKN1A.

Conclusion: miR208a/b-3p controls both positive regulation of cell proliferation and negative regulation of apoptosis via CDKN1A gene which are potential candidate for drug targets in OSCC.

ajbees@rediffmail.com

The influence of resilient liner and clip attachments for bar-implant retained mandibular over-dentures on opposing maxillary ridge: A 5-year randomized clinical trial

Moustafa Abdou Elsyad
Mansoura University, Egypt

This study aimed to compare the influence of resilient liner and clip attachments for bar-implant retained mandibular over-dentures on opposing maxillary ridge after 5 years of denture wearing. Thirty edentulous male patients received 2 implants in the anterior mandible after being allocated into 2 equal groups using balanced randomization. After 3 months, implants were connected with resilient bars. New maxillary complete dentures were then constructed and mandibular over-dentures were retained to the bars with either clips (group I, GI) or silicone resilient liners (group II, GII). The prosthetic and soft tissue complications of the maxillary dentures were recorded 6 months (T6m), 1 year (T1), 3 years (T3) and 5 years (T5) after over-denture insertion. Traced rotational tomograms were used for measurements of maxillary alveolar bone loss (R). Change in R immediately before (T0) and after 5 years (T5) of over-denture insertion was calculated. Maxillary denture relining times and frequency of flabby anterior maxillary ridge occurred significantly more often in GI compared to GII. The change of R in anterior part of maxilla was significantly higher than change of R in posterior part in both groups. GI showed significant resorption of anterior residual ridge compared to GII. Relining times and frequencies of flabby ridge were significantly correlated with change in R. Within the limitations of this study, resilient liner attachments for bar-implant retained mandibular over-dentures are associated with decreased resorption and flabbiness of maxillary anterior residual ridge and fewer maxillary denture relining times when compared to clip attachments.

m_syad@mans.edu.eg
Project management in medical writing

Hetal Shah
Medical Writing & Clinical Research Consultant, India

Medical writing has now evolved from being a sub-specialty service to a full-fledged line of business in the Healthcare Industry. A lucrative career option in itself, medical writing offers avenues not only as individual contributors, but also leadership and managerial positions. While, typically, medical writers develop documents individually or as a team, it would be worth extrapolating and comparing medical writing as an operation and treating each assignment as a project. With this, principles of project management usually applied to operational scenario can also be implemented to Medical writing profile and projects to further ease out and systematize the medical writing as a function. In medical writing, it is estimated that while 60% of a writer’s job is actually writing, 40% is project management. Hence, besides being technically equipped to execute the core activity i.e. draft the required document, project management skills are also desired in a medical writer. Project management is the application of knowledge, skills and techniques to execute projects effectively and efficiently. The concept of project management revolves around balancing The Triple constraints – Time, Scope, Cost; keeping Quality as the core. The discipline of project management is about providing the tools and techniques that enable the project team to organize their work to meet these constraints. Project management processes falls into five categories – Initiation, Planning & Design, Executing, Monitoring and Controlling, and Close-out. This presentation shall describe the extrapolation of project management concepts to Medical Writing as a function, and involve discussion on each aspect of project lifecycle in lines of a medical writing project, and a step-wise schedule of events/activities for handling a medical writing assignment from initiation to close.

Clinical Research in Arabian Peninsula from ClinicalTrials.gov

Jasser Ali S Alzhrani
King Saud Medical City, KSA

The ClinicalTrials.gov web site supply an appropriate link to look up any study results, however quantitative analyses’ format cannot be downloaded. Thus the purpose is to directly download study results from this web site and provides a link to retrieve all of the results in a sheet format in order to be analyzed properly and by analyzing them, and then we describe the clinical trial activity in the Arabian Peninsula. An expert validated the outcome classification algorithms that we used in this against classification. We created databases of the study results ready for analysis by identifying the studies by intervention, population, or outcome of interest. However, this study is simply based upon the information that is in ClinicalTrials.gov. Therefore, our conclusion is that expanding the usefulness of the ClinicalTrials.gov registry by having a database ready for analysis. The benefit from doing this is increases the speed of comparative research.