National Committee for Clinical Research: Bulletin 1 & 2 - 2009

In this first online issue of the NCCR bulletin, we cover the recently launched Malaysian GLP Compliance Programme (CP). The National Pharmaceutical Control Bureau and the Department of Standards Malaysia are designated as the Malaysian Compliance Monitoring Authorities for this programme. In other clinical research developments, Collaborative Clinical Research Groups in specific clinical areas will be introduced to facilitate multi-centre studies. This would involve participation from all eligible institutions and investigators in Malaysia (or otherwise a nationally representative sample), from all sectors including the Ministry of Health, universities, as well as private and NGO healthcare organisations. We also discuss issues in bioequivalence studies, pharmacogenomics and traditional and complementary medicine as well as the IT progress for the National Medical Research Register and the Nasopharyngeal carcinoma treatment outcome database.

About NCCR

Established in 1997 to coordinate and encourage clinical trials in Malaysia, the National Committee for Clinical Research (NCCR) supports the enhancement and regulation of the quality of biomedical research as well as clinical research practice in Malaysia.

The NCCR is headed by Tan Sri Dato' Seri Dr Hj Mohd Ismail Merican, Director-General of Health and it is managed by the Clinical Research and Compliance Section of the National Pharmaceutical Control Bureau, Ministry of Health Malaysia who acts as secretariat.

The members of this committee consist of experts from Ministry of Health (MOH), various national Universities, the Malaysian Pharmaceutical Society (MPS), the Pharmaceutical Association of Malaysia (PhAMA), the Malaysian Organisation of Pharmaceutical Industries (MOPI), and other Non-Governmental Organizations.

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As we challenge ourselves to improve diagnostic and treatment methods, we need to be mindful that every finding, no matter how minor or how unexpected, will contribute to the business of saving lives, improving the quality of life or reducing disease burdens. Therefore, I urge us to utilise the resources we already have and seek out new opportunities.
Yg Bhg Tan Sri Dato' Seri Dr Hj Mohd Ismail Merican's (Director-General of Health) keynote address during the National Conference for Clinical Research 2009.

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Contact Us

Secretariat
National Committee for Clinical Research (NCCR)
National Pharmaceutical Control Bureau
Jalan Universiti
P.O.Box 319, 46730 Petaling Jaya, Malaysia

For the Attention of:
Dr Kamaruzaman Saleh
Tel: 03-7883 5581(Direct Line)
Fax: 03-7955 1030
Email: kzsmann@bpfk.gov.my

Malaysia as a non-member becomes provisional adherent to the OECD system for mutual acceptance of chemical safety data

Good Laboratory Practice
Dr Kamaruzaman Saleh
National Pharmaceutical Control Bureau

Malaysia is now the 8th non-member economy to join the Organisation for Economic Co-operation and Development (OECD) Council Decision on Mutual Acceptance Data (MAD) in assessing chemicals. The period of provisional adherence, during which time Malaysia will accept data from OECD member countries and other adhering economies while it establishes its GLP compliance monitoring programme, began in October 2008.

The MAD system begins with participation as a provisional adherence, during which time, non-members work with OECD countries to make their GLP compliance monitoring programme acceptable to all members. Provisional adherence to the OECD system means that the non-member must accept data from OECD countries generated under MAD conditions. Then a team of experts from three OECD governments will evaluate the non-member GLP compliance monitoring programme on site. Based on the outcome of this evaluation, the OECD Council can invite the provisional adherent to fully adhere to the Council Acts, with the same rights and obligations as OECD countries.

As full adherence to the OECD system, non-members will accept data from OECD countries generated under MAD conditions. Similarly, member countries will accept their data since they can ensure that their test facilities produce safety data work of comparable rigor and quality as test facilities throughout OECD. This removes potential non-tariff trade barrier between non-members and OECD countries for marketing chemicals that would have been caused by different standards and verification procedures. Furthermore, it will also open up the possibility for producers in OECD countries to have safety tests for their chemicals undertaken in adhering non-member economies.

Good Laboratory Practice (GLP) is a quality system concerned with the organisational process and the conditions under which non-clinical health and environment safety studies are planned, performed, monitored, recorded, archived and reported. The Principles of GLP are important to promote the development of quality data and should be applied to the non-clinical safety testing of test items contained in pharmaceutical products, pesticide products, cosmetics products, veterinary drugs as well as food additives, feed additives, and industrial chemicals. These test items are mainly synthetic chemicals, but they may be of natural or biological origin and, in some circumstances, may be living organisms. The purpose of testing these items is to obtain data on their properties and/or their safety with respect to human health and/or the environment. Non-clinical health and environmental safety studies covered by the Principles of GLP include work conducted in laboratory, greenhouses, and in the field.

OECD member countries will accept data from non-members if their data is generated under MAD conditions.

The National Pharmaceutical Control Bureau (NPCB), Ministry of Health Malaysia and Department of Standards Malaysia (STANDARDS MALAYSIA), Ministry of Science, Technology and Innovation, Malaysia had been designated as the Malaysian Compliance Monitoring Authorities (CMA) by the Malaysian Government. The National Pharmaceutical Control Bureau is the CMA for the non-clinical safety testing of test items contained in pharmaceutical products, cosmetics products, veterinary drugs and food additives while the STANDARDS MALAYSIA is the CMA for the non-clinical safety testing of test items contained in industrial chemicals, pesticides, feed additives, and biotechnology (non-pharmaceuticals). Ministry of Health Malaysia is also appointed as the coordinator for Good Laboratory Practice (GLP) Compliance Monitoring Programme (CMP) in Malaysia.

The Malaysian GLP Compliance Programme (CP) is intended to ascertain whether Test Facilities have implemented requirements as described in documents of Organisation for Economic Cooperation and Development (OECD) Series on Principles of Good Laboratory Practice and Compliance Monitoring. Test Facilities requesting for verification and certification of compliance to Principles of GLP, and subsequent inclusion into the CMAs GLP Compliance Programme need to make the relevant application to CMAs.

Director-General of Health launched the GLP Compliance Programme during the National Conference for Clinical Research 2009.

NPCB and STANDARDS MALAYSIA are designated as the Malaysian Compliance Monitoring Authorities.

Malaysia's National Medical Research Register (NMRR) complies with the WHO Trial Registration Data Set

National Medical Research Register
Datuk Dr Teoh Siang Chin & Revathy U.Thandapani
Clinical Research Centre

In light of recent calls for registration and reporting of clinical trials, it was inevitable that Malaysia take a more serious look at procedures for research application. There was the need to have web-based systems to replace traditional paper-based processes. Undoubtedly, the National Medical Research Register (NMRR) is just one of a number of initiatives designed to make Malaysia a more favourable destination for clinical research outsourcing as Asia becomes increasingly attractive. In a 2007 study of global clinical trials registered with US-based Clinicaltrials.gov, Malaysia was listed among the top 50 countries with an average annual growth rate of more than 30 percent in the global share for biopharmaceutical clinical trial sites. With an estimated USD2 billion of the contract research outsourcing market heading towards Asia (Frost & Sullivan report Oct 2007), Malaysia needs investigators that views clinical research as an opportunity to evaluate cutting-edge disease-prevention strategies and not be daunted by the obstacles.

In Malaysia, medical research is seen as an effort of the Ministry of Health's (MOH) to define the extent of national health problems and to find measures to control or eradicate them to meet the changing health needs of the country. Various policies and committees were put in place to ensure compliance with regulations and procedures with applications to conduct research submitted in hardcopy forms. In addition, research involving human subjects required prior review and approval by the MOH Research and Ethics Committee (MREC) with final approval of all research publications by the Director-General of MOH.

In line with international best practices, the National Medical Research Register (NMRR) was initiated as an online registration process requiring clinical trials to be registered in publicly accessible research registers. As a web-based

It is a scientific, ethical and moral responsibility for all clinical trials to be publicly registered; World Health Organization (WHO)

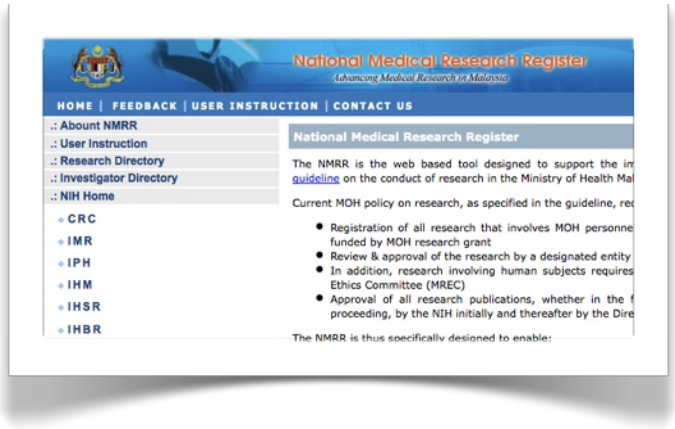
WHO regards trial registration as the publication of an internationally-agreed set of information about the design, conduct and administration of clinical trials. These details are published on a publicly-accessible website managed by a registry conforming to WHO standards.

The mission of the WHO International Clinical Trials Registry Platform is to ensure that a complete view of research is accessible to all those involved in health care decision making. This will improve research transparency and will ultimately strengthen the validity and value of the scientific evidence base. ***Excerpt from the WHO site of the International Clinical Trials Registry Platform (ICTRP) (http://www.who.int/ictrp/en/).***

tool, the NMRR supports the National Institutes of Health's (NIH) guidelines on research involving personnel, facilities or funds from MOH research grants. Registration in the NMRR ensures transparency and increases public trust in medical research. It also informs physicians and prospective volunteers about ongoing research they may wish to partcipate in, helps reduce processing time, enable easy access, captures data on research undertaken in the MOH, and allows management to track progress. In addition, passive information is compiled in a database as a Research Directory and an Investigator Directory.

Officially endorsed by the Director General of Health on 5 Sept 2007, an invitation has been extended to researchers from universities and private hospitals to register their studies online via the NMRR. With clearer procedures and shorter timelines for both institutional and ethics to review and approve, when fully implemented the NMRR should encourage more medical research in Malaysia. In line with national aspiration to reach developed nation status 2020, the NMRR will propel the MOH to be at the forefront of all R&D efforts that will contribute towards advancing the heath care sector.

Pilot tested since early 2007, the NMRR is being rolled-out to most of the 17 public hospitals nationwide under the Network of Clinical Research Centres as well as all six institutes under the NIH. Using the accessibility provided by the worldwide web, users are able to login anywhere and at anytime for online submission and have their study reviewed and approved by the appropriate authorities such NIH and MREC. The NMRR is also now linked to the National Pharmaceutical Control Bureau(NPCB). NPCB will make it mandatory for all CTIL/CTX application to be registered in NMRR.



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NPCB will make it mandatory for all CTIL/CTX application to be registered in NMRR.

Registration in the NMRR ensures transparency and increases public trust in medical research.

Issues in bioequivalence studies: Basic factors affecting bioavailability

Bio-Equivalence Studies
Dr Azizi Ayob & Pn Zarina Noordin
Malaysian Organisation of
Pharmaceutical Industries (MOPI)

Introduction

Generic substitution for drugs has become a widespread practice as the drug authorities of respective countries have approved bioequivalent drugs for hospitals, and clinics in both the private and government sectors. This is one of the significant approaches to trim healthcare costs. Generic substitution or relatively new product after patent expiry of the innovator can include proprietary to generic, one generic to another or generic to proprietary. In many cases, these generics pose no problem to the health of the patient provided they have been manufactured accordingly. Concerns have been raised, however, that uncontrolled use of such substitution may indeed be harmful in certain cases. For the medical practitioners, the greatest concern relates to the quality, safety and efficacy of such generic or substitutions to that of the innovator. For the pharmaceutical scientists and the industry players, high quality of the active ingredients and formulation stability would be the main focus in the development stage to achieve therapeutic equivalent.

For oral drug products, bioequivalence (BE) study is performed to confirm that a test product has the same quality as a reference product in terms of oral drug absorption. Bioequivalence products must show the same bioavailability of active drugs in both amount and rate after oral administration. Of major concern in bioequivalence study, the understanding on pharmacokinetics is the main component of bioavailability. Each drug can vary as a function of the formulation.

It is important that medical practitioners have a better understanding of generic drugs, how they are tested and the true comparative value of drug substitution to better treat patients and avoid any possible adverse consequences. This was made very clear when a 1997 questionnaire to assess attitudes, beliefs, knowledge and experiences with generic drugs and generic substitution was sent to 3,639 physicians nationwide. Cluster analysis was used to identify attitudinal groups that were then analysed with respect to differences in beliefs, knowledge, and experience with generic drugs. Perceptions of the therapeutic index for 15 branded drugs and comfort in substituting those products with generic alternatives were assessed. Only 17 percent of physicians could correctly identify the FDA standards for bioequivalency[1].

BE studies is conducted to confirm that a test product has similar oral drug absorption as a reference product.

In this article, several important factors which are sensitive to drug formulation and bioavailability were discussed. Bioavailability parameter is one of the measures used to assess bioequivalence between two drug products tested clinically in human subjects. The published guidance for waiver of *in vivo* bioavailability and bioequivalence studies based on the Biopharmaceutic Classification System (BCS)[2] in the U.S. Food and Drug Administration (FDA) has lead to both advantages and disadvantages in drug development for the industry players. Although the BCS concept has not yet been employed in Malaysian Guideline for the conduct of bioavailability and bioequivalence studies[3], the brief application of BCS is worth discussing here.

Factors affecting Bioavailability

Drug is absorbed from the gastrointestinal (GI) tract after being dissolved according to its intrinsic absorbability. If the test product shows the same pattern of drug dissolution in the GI tract *in vivo* as the reference one, that product must be equivalent unless other ingredients do not modulate the absorption of active drug. In other words, physicochemical properties of drugs such as water solubility and membrane permeability do not affect the bioequivalency of oral product.

A wide range of factors can influence the bioavailability of a drug. Basically, the availability of the drug or its metabolite to the target organ or receptor is controlled by three principal factors:

1.The rate and extent of drug release from its formulation, and its subsequent absorption.

2.The first-pass effect while passing through the liver after absorption.

3.The conjoint effect of plasma protein binding, drug distribution to various body fluids, metabolism and excretion.

For assessing bioavailability or clinical availability of a drug, its rate and extent of absorption and its first-pass metabolism must be evaluated. The clinical response of the patient or the amount of active drug at the target site of action at different time periods should also be assessed. In order to achieve targeted minimum level for therapeutic or clinical effect, the medical practitioner must understand various contributing factors that could affect the bioavailability. For the scientists, they must also be aware of some essential intrinsic factors that influence the formulation.

Bioavailability of a drug is assessed by evaluating the rate and extent its absorption and first-pass metabolism as well as the patient's clinical response.

In general, the following factors were discussed.

Physiological Factors

High variability in oral drug absorption is caused by several factors. Deviations in physiological conditions in the GI tract of volunteers would affect dissolution and permeation of drugs even in the same individual. For example, bile acid secretion into the small intestine promotes the dissolution of poorly soluble drugs to enhance the bioavailability[4]. On the other hand, it was reported that food intake often reduced the oral absorption of BCS class 3 drugs[5]. These facts indicate that low solubility and low permeability of drugs may cause not only the incomplete oral absorption but also the high variability in it.

Metabolism in the intestine and liver affects the oral bioavailability as the first-pass effects after absorption and deviations of the metabolic activity in pharmacokinetic parameters due to the change in total body clearance of drugs. High clearance of drugs therefore, might be one of the risk factors for high variability in a human BE study[6].

In short, the following physiological factors are known to affect bioavailability:

1.Effect of gastrointestinal fluids such as pH, mucus, bile salts, complexing components.

2.Gastric motility such as gastric emptying, presence of food, rest and exercise.

3.Gastrointestinal transit time which can be affected by a large number of drugs.

4.Absorption surface which the physiological integrity, area and blood flow.

5.Metabolism of drugs by the gut wall, liver, skin and bronchial mucosa.

6.The pharmacogenetic factors determining the rate of hepatic metabolism.

7.Various disease states such as malabsorption, achlorhydria, thryrotoxicosis and celiac disease.

8.Other factors include the gut flora, age, sex, weight and physical status of the patients.

Physicochemical Factors

There are various physicochemical factors that may influence absorption of drugs into the bloodstream. Dissolution testing is essential to establish a profile of each generic product with specific physicochemical characteristic of the solid dosage form. This testing will ensure the permeability and solubility of drugs. At the drug development stage, these factors are essential

In a human BE study, high clearance of drugs may cause high variability.

to be evaluated and should not be the direct causes of failure in a bio-equivalence study. The physicochemical factors which point to the need for dissolution testing include[7]:

1.Low drug solubility - to establish the evidence that the drug has a low aqueous solubility.

2.Poor product dissolution – to establish from the literature that the dissolution of one or more marketed or product to develop is poor when tested by official compendial test procedure.

3.Drug particle size – to establish the evidence that the particle size may affect bioavailability.

4.The physical form of drug – to establish that certain polymorphs, solvates or complexes have poor dissolution characteristics and hence bioavailability may be affected.

5.Presence of specific excipients – to establish evidence that specific excipients may alter dissolution or absorption, hence bioavailability may also be affected.

6.The nature of tablet or capsule coating – to establish evidence that coating may interfere with the disintegration or dissolution of the formulation.

Pharmacological Factors

The bioavailability of a drug given chronically may differ from that given in a single dose. This can be due to the metabolism of drug at the first-pass can be saturated by the gut and hepatic enzymes. Various pharmacological factors are known to affect bioavailability as outlined in the table [8]:

Various pharmacological factors known to affect bioavailability

Factors	Possible Cause/Effect
Variation in drug content	Inadequate quality control
Storage (drug and excipient stability)	Loss of effect (i.e. nitroglycerine)
State of drug:	
- Particle size	Variable effect (i.e. anticoagulants)
- Polymorphism	Different crystalline forms differ in dissolution rate (i.e. steroids, barbiturates)
- Solvate/hydrate	Variable bioavailability (i.e. ampicillin)
- Salts	Dissolution rate with sodium salts better (i.e. sodium tolbutamide)
- Esters	Antibiotic esters have increased bioavailability
- pH Excipients	For example: Dilantin mixed with calcium sulphate increases toxicity

Biopharmaceutic Classification System (BCS)

The biopharmaceutic classification system was developed primarily in the context of immediate release (IR) solid oral dosage forms. It is the scientific framework for classifying drug substances based on their aqueous solubility and intestinal permeability[9]. It is a drug development tool that allows estimation of the contributions of three major factors namely dissolution, solubility and intestinal permeability that affect oral drug absorption from immediate release solid oral dosage forms. The interest in this classification system is largely because of its application in early drug development and then in the management of product change through its life cycle. It was first introduced into regulatory decision-making process in the guidance document on Immediate Release Solid Oral Dosage Forms, Scale Up And Post Approval Changes[2,10].

Goals of the BCS Guidance:

1.To improve the efficiency of drug development and the review process by recommending a strategy for identifying expendable clinical bioequivalence tests.

2.To recommend a class of immediate-release (IR) solid oral dosage forms for which bioequivalence may be assessed based on *in vitro* dissolution tests.

3.To recommend methods for classification according to dosage form dissolution, along with the solubility and permeability characteristics of the drug substance.

Classification:

According to BCS, drug substances are classified as:

Class I: High Solubility – High Permeability

Class II: Low Solubility – High Permeability

Class III: High Solubility – Low Permeability

Class IV: Low Solubility – Low Permeability

Combined with the dissolution, the BCS takes into account the three major factors governing bioavailability parameters namely dissolution, solubility and permeability. This classification is associated with drug dissolution and absorption model, which identifies the key parameters controlling drug absorption as a set of dimensionless numbers. Absorption number is defined as the ratio of the mean residence time to mean absorption time. Dissolution number is defined as the ratio of mean residence time to mean dissolution time.

Conclusion:

An understanding of the basic bioavailability factors that influence BE is a prerequisite for predicting the therapeutic effect of generic product. In order to allow the prediction of the therapeutic effect, the performance of generic or substitution form must be of comparable to the originator

Knowledge in basic bioavailability factors that influence BE is important to predict the therapeutic effect of a generic product.

drugs. Thus bioavailability factors that have been discussed should thoroughly be reviewed at the preclinical and clinical levels.

In general, the pharmaceutical industry and their scientists have spent valuable development time to focus on this issue in order to minimise the failure or bioinequivalence consequences from BE study. Thus, it is becoming more than routine to apply the standard operating procedure to review all those factors before a generic product is developed and tested clinically. The proper monitoring especially at the preclinical or laboratory stage would then be resulted in significant drug development savings.

Furthermore, there is strong scientific rationale to allow BCS-based waivers for even more compounds to realise even more savings. Yet, just as clear as the benefits, are the barriers that limit application. There are other issues related to BCS such as lack of international regulatory harmonisation, uncertainty in regulatory approval, and organisational barriers within the pharmaceutical industry. Once these barriers are overcome and additional applications are fully allowed, the full benefits of BCS applications will be realised.

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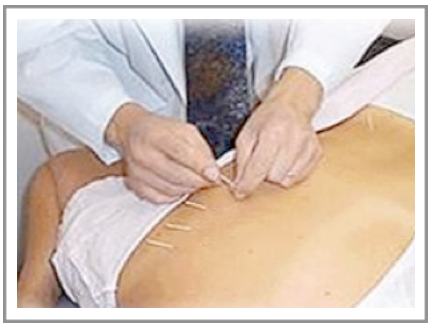
Research in traditional & complementary medicine

Complementary Medicine
Dr Ramli Abdul Ghani
Traditional & Complementary Medicine Division, Ministry of Health Malaysia

Malaysia is increasing its acceptance and use of Traditional & Complementary Medicine (T&CM). In response to the challenges of changing healthcare needs, the T&CM Division in the Ministry of Health has established a research unit to coordinate and facilitate research in T&CM in Malaysia, as stipulated in the National T&CM Policy 2001(revised 2007).

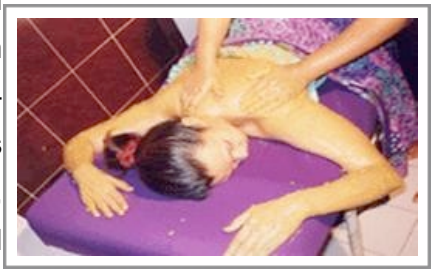
The focus is for scientific research to promote an evidence-based approach for the use of T&CM in healthcare. Current research is centred on activities in integrative medicine

such as acupuncture, Malay massage and use of selected herbs in oncology. Patient satisfaction, quality of life and individual case studies are ongoing at three integrated hospitals. These studies will promote new knowledge and options based on local environment for enhancing health and wellbeing that can be utilised in our modern healthcare environment.



Other priority areas of research include basic clinical research such as utilisation of herbs in selected disease conditions, T&CM policy research and behavioral research. All research in T&CM Division is conducted in collaboration with institutions under National Institutes of Health, MOH.

A strategy to further promote T&CM research in Malaysia is through networking and collaboration with established centres of research in T&CM/CAM in selected neighbouring countries such as China, India, Korea and Australia.



Currently, a database of local basic T&CM research conducted from year 2000 with emphasis on complementary medicines was established and linked to T&CM website (http://tcm.moh.gov.my)

T&CM Division in MOH collaborates with local NIH institutes and calls for similar partnerships with neighbouring countries.

Mistletoe Extract

Complementary Medicine
Dr Ramli Abdul Ghani
Traditional & Complementary Medicine Division, Ministry of Health Malaysia

Mistletoe or *Viscum album* Loranthaceae (*Viscum album* L. or European mistletoe) is a semiparasitic plant. It grows on several types of trees, and the chemical composition of extracts derived from it depends on the species of the host tree (e.g., apple, elm, oak, pine, poplar, and spruce). Mistletoe has been used for centuries for its medicinal properties. Modern interest in mistletoe as an anticancer treatment began in the 1920s. Reports of more than 30 clinical studies of mistletoe as a treatment for cancer have been published since the early 1960s.

In the United States (U.S.) *Viscum album* L. is listed in homeopathic pharmacopeia. Although the U.S. Food and Drug Administration (FDA) has regulatory authority over homeopathic drugs, this authority is usually not exercised unless the drugs are formulated for injection or there is evidence of severe toxicity. At present, the FDA does not allow the importation or distribution of injectable preparations of mistletoe, including homeopathic formulations, except for the purpose of clinical research. The extracts are not available commercially in the U.S. and are not approved as a cancer treatment. Although mistletoe is not permitted in the U.S., in Europe it is categorised as a prescription drug.

Mistletoe is a potential anticancer agent because its extracts have been shown to kill cancer cells in vitro and to stimulate immune system cells both *in vitro* and *in vivo*. Two components of mistletoe, namely viscotoxins and lectins, may be responsible for these effects.

The Cochrane-Review 'Mistletoe therapy in oncology' concludes that the available evidence is not sufficient to support mandatory administration of mistletoe therapy. German agency for HTA in their systematic review also summarise that the available evidence on whether the addition of mistletoe to chemotherapeutical regimes can reduce the toxicity of the latter is not conclusive. A case report by Wode et al, however, indicated it had beneficial effect against breast cancer-related fatigue and its therapeutic effect seemed quite remarkable. Currently, the best evidence reported for the addition of standardised mistletoe extract in the treatment with breast cancer can lead to improvement in HRQOL. Therefore further randomised controlled trials are needed with more patients with other cancer types and primary outcome studied should be treatment toxicity.

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Nasopharyngeal carcinoma treatment outcome database

Khoo ASB for the Malaysian Nasopharyngeal Carcinoma Study
Institute for Medical Research

Nasopharyngeal carcinoma (NPC) is a common cancer in Malaysia. According to the National Cancer Registry, there were 1,125 incident cases of NPC in Peninsular Malaysia in the year 2003, where it also was the second most common cancer among males.[1] The age-standardised incidence was 10.2 (for males) and 3.6 (for females) per 100,000 of the population in Peninsular Malaysia.[1] The incidence is particularly high in some native groups in Sarawak[2].

Improvement in the clinical outcome of cancer patients is a major goal of health care service. However, there is a paucity of data on the clinical outcome of NPC patients. In particular, no multi-centre prospective studies on the outcome of patients treated for this disease have been reported in the country probably because of logistic problems.

The identification of new markers for prognosis of the cancer would be useful for stratification of therapy and the rapid advances in genomics and proteomics has made such studies possible. To develop new markers for prognosis, reliable data on clinical outcome of patients from whom specimens are collected is critical. However, in most instances, specimens are collected at the time of diagnosis and there is limited clinical information of patients from whom the specimens are collected. It has been logistically very difficult to link high quality follow-up data of patients with specimens collected at the time of diagnosis.

Developments in information technology and the internet could be useful to facilitate collection of clinical data. However, to ensure patient confidentiality, various measures need to be taken to ensure the security of the data.

In order to collect and analyse the pattern of presentation and clinical outcome of NPC patients in Malaysia and to collect samples for research, we have established a multi-institutional study of NPC in Malaysia. The pilot study involves six major tertiary referral centres representing parts of Peninsular Malaysia (one centre each in Penang and Kelantan and two centres in Kuala Lumpur) and two in East Malaysia (one centre each in Sabah and Sarawak). The project is a multi-centre, prospective study recruiting all patients with confirmed NPC regardless of the stage, histopathology and duration of disease. These patients are seen at the following participating sites: Hospital Pulau Pinang, Hospital Kuala Lumpur / Universiti Putra Malaysia (UPM), Sarawak General Hospital (Hospital Umum Sarawak) / Universiti Malaysia Sarawak, Queen Elizabeth Hospital, Sabah,

Developments in IT; facilitates collection of clinical data.

University of Malaya Medical Centre (UMMC) and Hospital Universiti Sains Malaysia (USM), Kubang Kerian, Kelantan. The study is monitored and data managed by the Department of Otorhinolaryngology and the Clinical Research Centre, Hospital Pulau Pinang in compliance with patient data protection. This study was approved by the Medical Research and Ethics Committee of the Ministry of Health and the institutional ethics committees of relevant university hospitals.

Data collection is web-based at www.acrm.org.my which is a secure clinical database (NPC-TOD / NCPR-NPC) to enable real-time collection of data. The database collects patient demography, medical history, clinical findings, histopathology, and treatment modalities and follow-up information. Data is entered through a web-based interface (https://app.acrm.org.my/NPC) into a secure database.

Due to the sensitivity and confidentiality of patient data, great emphasis is placed on data security in terms of hardware as well as software. The security standards conform to various local and international regulatory guidelines and laws (ISO/IEC17799:2002, HIPAA-45 CFR Parts 160-164, 21 CFR Part 11, European Network of Cancer Registries, Guidelines on Confidentiality in population-based Cancer Registration in the EU. Feb 2002). From the hardware point of view, the data centre offers state-of-the-art security features, namely, firewalls, VPN quarantine, instruction detection system (IDS), host-based intrusion detection system (HIDS), operating system (OS) hardening, patch management, anti-virus protection, etc. From the software point of view, the data from the web-application is transmitted via Secured Socket Layer (SSL), which provide for secure communication on the Internet. Sensitive information such as user authentication information and patient identifiable fields is highly encrypted (128-bit) to protect data confidentiality. Furthermore, the user authentication module has included CAPTCHA (Completely Automated Public Turing test to tell Computers and Humans Apart) based authentication code alongside username and password to deter hackers from gaining access to the data. All authorised users are briefed and are required to sign the Data Security and Confidentiality agreement before they are given any access rights to the web application.

The design of the NPC database allows for inclusion of new data source providers. NPC service providers in Malaysia who wish to participate as source data providers may contact the Database Manager through the website for further information and registration or e-mail npc@acrm.org.my .

Data is entered through a web-based interface into a secure database.

The current project is part of the Nasopharyngeal Carcinoma Research Program which is being coordinated by the Institute for Medical Research, Kuala Lumpur. Laboratory-based research projects within the program are being carried out at the Institute for Medical Research, University of Malaya, Cancer Research Initiatives Foundation (CARIF), Universiti Malaysia Sarawak (UNIMAS), and the International Medical University.

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For further enquiries regarding the NPC-TOD, please contact:

Manager

Nasopharyngeal Carcinoma Treatment Outcome Database

Clinical Research Centre

Penang General Hospital

Residensi Road,10450 Penang

Malaysia

Tel: +604-228 9246 / 2274982

Fax: +604-226 1579

E-mail: npc@acrm.org.my

Website: https://app.acrm.org.my/NPC

https://app.acrm.org.my/NPC/

www.acrm.org.my

Collaborative clinical research groups

Clinical Research Centre

What is CCRG?

Collaborative Clinical Research Group (CCRG) refers to a consortium of institutions and investigators from a particular clinical discipline, organised for the purpose of supporting the conduct and dissemination of research to broaden access to proven treatment as well as to make progress toward developing new diagnostics and therapeutics, for the ultimate goal to improve our patients' health.

The Collaborative Clinical Research Group strives to obtain participation from all eligible institutions and investigators in Malaysia (or otherwise a nationally representative sample), from all sectors including the Ministry of Health, universities, as well as private and NGO healthcare organisations. The CCRG is organised according to specific disease area (e.g. cancer), therapeutic focus (e.g. dialysis) or practice setting (e.g. General practices). The common thread, however, is the development and conduct of large-scale clinical research in multi-centre setting, which enables rapid accrual of patients and data, while reducing the possible bias of studies carried out at a single or a few institutions.

Why CCRG?

The network of clinical practices that constitute a CCRG represents a valuable national resource and infrastructure for medical research that otherwise would be impossible. Such network, by virtue of its scale and real world practice setting, makes numerous research projects

that could not be undertaken by one or a few institutions possible. A CCRG is akin to a natural laboratory which studies populations with a disease of interest under the care of clinical investigators.

CCRGs will have enduring positive effect on the progress of clinical research in Malaysia; as it will address questions that will impact the way we practice medicine and questions that matter to our patients.

CCRG is organised according to specific disease areas.

To illustrate the power of the CCRG concept, we describe below the typical range of research and statistical activities that CCRGs are expected to contribute:

1.Disease epidemiology and health outcomes

- Having timely and reliable estimates of disease incidence and prevalence, and the survival and quality of life outcomes of patients with the disease of interest, are fundamental to describing the burden of disease in Malaysia, and hence to commensurate therapeutic and research efforts required to better assist our patients.
- CCRG members provide a crucial source of data to enable such estimates.

2.Access to treatment

- It is widely perceived that there remain significant barriers of access to therapy for most common and serious diseases in Malaysia, and these have significantly and adversely impact the health outcomes of our patients.
- CCRG members have a responsibility to contribute data to document these limitations, and thereby enable an evidence-based approach to drive greater resource allocation to improve access to the newer medicines and devices.

3.Therapeutic research/ Clinical trial

- Therapeutic research aimed at improving our patients' survival and quality of life is clearly of the highest priority to clinicians participating in a CCRG.
- There are two types of such research that clinicians are encouraged to participate in:

a. Investigator-initiated study

This is grant-funded research, although often it comes with industry support in the form of trial medications or devices.

Apart from contributing to the evidence base for a therapy, and providing opportunities to publish original research and present results at medical conferences, such trials often provide an avenue for our patients to access therapy that are either unavailable in Malaysia or unaffordable to our patients.

Recent successful research collaborations in Malaysia include:

- Mycophenolate Mofetil (MMF) for severe lupus nephritis
- Tacrolimus for renal transplant
- Gemcitabine for nasopharyngeal carcinoma (NPC)
- Epoetin for renal anaemia

b. Industry- sponsored trial

Malaysia desires to be a regional hub for clinical trial; as the preferred location for the pharma and biotech companies to undertake clinical trial on their products. Our government

Investigator-initiated studies enable patients to access therapy that are unavailable in Malaysia.

is committed in developing this clinical research outsourcing (CRO) industry.

CCRGs have the ability to quickly recruit experienced investigators and enrol large number of patients, which are clearly important factors in attracting this industry to Malaysia and placing Malaysia on the clinical research map.

4.Patient registries and clinical databases (data banking)

Individual practice-based patient registries and clinical databases are critical information resources to support a CCRG's research efforts. The database:

- Facilitate and enable automated notification of cases to the relevant national disease registers.
- When linked to patients' prescription records, it provides a ready source of data to document any shortfall in access to treatment.
- When linked to national mortality and disease registers, it provides a ready source of data to evaluate patients' mortality and morbidity outcomes.
- When linked to biorepository (see next), it provides a powerful tool to support basic medical research on genomics and proteomics.
- Lastly, patient registry provides a sampling frame to obtain representative sample. Except for case notification to disease register, clinical research requires each investigator to enrol only a few patients from their practice.

5.Biorepository (tissue banking)

- CCRG offers the possibilities for large-scale collection of biological samples. This provides the CCRG with unique opportunities to address scientific questions about molecular genetics, proteomics and other pre-clinical studies. Such investigations will add considerable strength and credibility to CCRG's scientific program.
- Presently, huge amount of surplus surgical tissues not required for diagnosis are routinely discarded in Malaysia.
- A CCRG provides the necessary scale and cooperative arrangement to make the development of biorepository feasible, in order to maximise the use of the discarded surgery by-products for research purposes.

6.Research methodology

A CCRG provides a unique framework for research in clinical research methodology. Clinicians, epidemiologists and biostatisticians associated with a CCRG are encouraged to develop and experiment with new study designs and statistical methods.

CCRGs have the ability to quickly recruit investigators and patients for clinical research.

Development and organisation of a CCRG

Suitably experienced key opinion leaders in a clinical discipline should come forward to lead the CCRG; to enlist colleagues to sign up as CCRG members and galvanise their commitment to accomplish the CCRG's mission.

A Steering Committee, comprising representatives from a CCRG membership, is established to:

1.Determine the purposes of the CCRG.

2.Establish a CCRG membership and operating procedures.

3.Oversee the overall management of the CCRG.

4.Oversee the recruitment and monitoring of participating practices.

5.Establish criteria and standards for practice participation in CCRG studies.

6.Select questions for studies.

7.Report results obtained from CCRG studies.

8.Appoint and define function of the Advisory Group, various Expert panels and staff.

9.Accept and respond to concerns and suggestions from CCRG membership.

10.Seek funding for the CCRG.

11.Report policy and progress to sponsor or funding bodies.

Role of the Clinical Research Centre

The Clinical Research Centre (CRC), Ministry of Health plays a strictly supportive role in nurturing the development of CCRG, which is seen as a key strategy to advance clinical research in Malaysia.

The CRC shall:

- Provide secretariat function and recruit all the necessary supporting staff to operate the CCRGs.
- Secure funding for CCRG, either directly from CRC funds or from other sources. In this regards, it is CRC's policy that at all times, research proposal from CCRGs be accorded higher priority for funding than application from others. The existence of an active CCRG in an area of interest is sufficient evidence of the commitment of investigators working in the area.
- Establish the Information and Communication Technology (ICT) infrastructure to facilitate communication and collaboration, and to manage studies and capture study data.
- Provide methodological and technical inputs and support, such as for study design, epidemiological and economics method, biostatistics and management of complex medical databases.
- Facilitate access to key laboratory facility and biorepository for purpose of research
- CRC, being a neutral third party, provide the necessary ethical oversight for CCRG's

CCRGs have the ability to quickly recruit investigators and patients for clinical research.

research to ensure its compliance with international ethics guidelines and regulations governing the design and conduct of human research.

- Provide Clinical Trial and Professional Indemnity Insurance to indemnify both CCRG-initiated trials and participating investigators as well as their staff and institutions, in the event of injury to study subjects arising from the subjects' participation in the research.

For More Information and CCRG Registration

For institutions and investigators or doctors interested in forming a CCRG or wishing to advertise the existence of their CCRG or increase their membership, kindly contact

Research Management Unit

Clinical Research Centre

Level 3, Dermatology Block

Kuala Lumpur Hospital

Jalan Pahang

50586 Kuala Lumpur

Malaysia

Tel : 603 26980310 Fax: 603 26911682

Website: www.crc.gov.my

CCRGs have the ability to quickly recruit investigators and patients for clinical research.

Pharmacogenomics: Leading the way to personalised medicine

Prof Zahurin Mohamed
Professor & Head, Pharmacogenomics Laboratory, Department of Pharmacology, Faculty of Medicine, University of Malaya

The field of pharmacogenetics was introduced more than 40 years ago to emphasise the role of heredity in person-to-person differences in drug response.[1,2] The focus of pharmacogenetic investigations such as extreme drug responses resulting from a single gene effect has traditionally been unusual. Pharmacogenomic studies, on the other hand, encompass the sum of all genes, that is, the genome. Numerous genes may play a role in drug response and toxicity, introducing a daunting level of complexity into the search for candidate genes. The high speed and specificity associated with newly emerging genomic technologies enable the search for relevant genes and their variants to include the entire genome. These new technologies have essentially spawned a new discipline, termed pharmacogenomics, which seeks to identify the variant genes affecting the response to drugs in individual patients. Moreover, pharmacogenomic analysis can identify disease susceptibility genes representing potential new drug targets. All of this will lead to novel approaches to drug discovery, an individualised application of drug therapy, and new insights into disease prevention.

The twentieth century has brought us a broad arsenal of therapies against all major disease: infections, cardiovascular disease, neoplastic disease and mental disorders. However, drug therapy often fails to be curative and may in fact cause substantial adverse effects. Moreover, worldwide use of these drugs has revealed substantial inter-individual differences in therapeutic response. Any given drug can be therapeutic in some individuals but ineffective in others, and some individuals experience adverse drug effects whereas others are unaffected. Often, distinct molecular mechanisms underlie therapeutic and adverse effects.

Recognition of inter-individual differences in drug response is an essential step towards optimising therapy. Over the past decades, much evidence has emerged indicating that a substantial portion of variability in drug response is genetically determined, with age, nutrition, health status, environmental exposure, and concurrent therapy playing important contributory roles.

Pharmacogenomics has the potential to lead to personalised medicine, which is the use of information and data from the patient's genotype, or level of gene expression to select a medication, provide a therapy, or initiate a preventative measure that is particularly suited to that patient at the time of administration. This concept has been highlighted as "therapy with the right drug at the right dose in the right

Substantial portion of variability in drug response is genetically determined.

patient."[3] Its urgency emerged in a survey of studies on adverse drug effects in hospitalised patients: adverse drug reactions may rank as the fifth leading cause of death in the United States.[4] Thus it is anticipated that pharmacogenomics will play an integral role in disease assessment, drug discovery and development, and selection of type of drug. Moreover, it may provide information useful to the selection of dosage regimen for an individual patient. Pharmacogenomics may be one of the most immediate clinical application of the human genome project.

Generally, at present, medicine still targets therapy to the broadest patient population that might possibly benefit from it, and relies on statistical analysis of this population's response for predicting therapeutic outcome in individual patients. Therapists then make decisions about the choice of drug and appropriate dosage based on the information derived from population averages. This "one drug fits all" approach could, with pharmacogenomics, evolve into an individualised approach to therapy where optimally effective drugs are matched to a patient's unique genetic profile. This involves classifying patients with the same phenotypic disease profile into smaller subpopulations, defined by genetic variations associated with disease, drug response, or both. The assumption here is that drug therapy in genetically defined subpopulations can be more efficacious and less toxic than in a broad population. To achieve individual drug therapy with a reasonably predictive outcome, one must further account for different patterns of drug response among geographically and ethnically-distinct populations.

Individualising drug therapy with the use of pharmacogenomics thus hold the potential to revolutionalise medical therapeutics, by challenging the "one drug fits all" approach, enabling prescribers to identify patients for whom they will be both effective and safe.

Pharmacogenomics has been applied in personalised medicine in the case of warfarin. It is estimated that between 300,000 and 500,000 new prescriptions for warfarin are written every year, while between 2 million and 5 million people are taking the drug every day.[5] The use of warfarin has, however, long been associated with risk of adverse bleeding events. A study showed that over 2,000 bleeding events were reported during a 30-month period, of which more than 80% resulted in hospitalisation, disability, life-threatening sequelae and/or death.[6,7]

Furthermore, warfarin was ranked in the top ten drugs with serious adverse events over a 5-year period (2000 to 2005) with more than 6,000 reported cases, and accounts for 3.6% of all drug-induced adverse events and 15.1%

Pharmacogenomics is vital for disease assessment and drug discovery.

of all severe drug-induced adverse events. In August 2008, FDA updated the labelling for the anticoagulant warfarin, to include genetic testing information, saying the information can help physicians determine the safest starting dose for their patients. A month later, the agency approved a genetic test that can reveal which patients have some variations in two genes, CYP2C9; the enzyme primarily responsible for warfarin metabolism, and VKORC1 gene, the site of action for warfarin.

Clinical studies have shown that patients with variations in those genes may need a lower dose of the anticoagulant. There are now genetic tests available for patients beginning drug therapy with warfarin. The goal of the warfarin test is to decrease the time it takes to titrate a patient to his or her effective dose and minimise the risk of bleeding events. This was not the first time that pharmacogenomic information has been cited in prescription drug labelling. It can be found in a handful of other labels, including the oncology drugs; irinotecan for colon cancer and 6-mercaptopurine for acute lymphatic leukaemia. However, that was the first time that pharmacogenomic information was included in a drug as widely used as warfarin. Larry Lesko, director of the Office of Clinical Pharmacology at FDA's Centre for Drug Evaluation and Research (CDER), said the agency's update of warfarin labelling was significant because "it means that personalised medicine is no longer an abstract concept, but it has moved into the mainstream where it is recognised as a factor in a product used by millions of Americans".

A first example of a genetically-specific drug was introduced in the form of Herceptin, used in the treatment of breast cancer which is usually an aggressive disease with high risk of relapse and even death. This drug is only effective in women with a genetic defect which results in the overproduction of the HER2neu receptor when present in excessive numbers on the surface of certain breast cells. These receptors promote cellular growth which leads to tumours. Herceptin is a monoclonal antibody directed against the HER2neu receptor and therefore only helps women who have an increased number of copies of the relevant HER2neu gene. In all other women, this highly specific drug is much less effective. Herceptin can therefore be used only in conjunction with a genetic test which measures HER2neu overexpression in which a positive result predicts response to the drug whereas a negative result redirects therapy elsewhere.

There are, however, obstacles to the personalised approach to therapeutics. The dy-

The first widely-used drug that included pharmacogenomic information was warfarin.

namic complexity of the human genome multigenic nature of disease origins could obscure prediction of disease susceptibility and drug response across patient populations. Furthermore, the realisation of an individualised approach to drug discovery and therapy will require decreases in operating costs, with enhanced accuracy and reduced complexity. In addition, ethical issues need to be resolved since information about an individual's genetic makeup raises privacy questions and ethical dilemmas about disease susceptibility, prognosis and treatment options. Such information must be safeguarded to ensure privacy.

Whether or not these new genomic technologies find their way into everyday clinical use, they will prove valuable tools in clinical research directed at optimising drug therapy. Ultimately, the vision of pharmacogenomics encompasses a genetic profile for each individual, containing sufficient information to select which drugs are most likely to be safe and effective in that person. However, obstacles to the implementation of this vision are formidable.

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Published Research

Anne John Michael
Clinical Research Centre

Diosmectite significantly decreases stool output and is recommended as adjunct therapy to oral rehydration solution for acute watery diarrhoea in children

In two parallel double-blind studies in Peru and Malaysia, children between the ages of 1 and 36 months with three or more watery stools per day were randomised to receive placebo or diosmectite. Both groups were also given oral rehydration solution. Each site recruited about 300 children, of which 22% (Peru study) and 12% (Malaysia study) were positive for rotavirus. Diosmectite effects on stool output were especially beneficial for the rotavirus-positive cases and researchers attributed this to either a pharmacological effect or diosmectite's ability to counteract with the secretory process induced by the virus at the enterocyte level. This finding is important as before this, only two other acute watery diarrhea treatments (bismuth and racecadotril), were found to reduce stool output. Importantly as children who were rotavirus-negative also benefited from the treatment, diosmectite can be used as an adjunct therapy to oral rehydration solution, especially in countries that are unable to afford systematic rotavirus testing.

Source

Oral Diosmectite Reduces Stool Output and Diarrhea Duration in Children with Acute Watery Diarrhea.

Christopher Dupon, Jimmy Lee Kok Foo, Philippe Garnier, Nicholas Moree, Helene Mathiex-Fortunet, and Eduardo Salazar-Lindo for the Peru and Malaysia Diosmectite Study Group. Clinical Gastroenterology And Hepatology 2009;7:456 - 462.

Integrated care approach with involvement of nephrologists enables higher than national penetration rates for peritoneal dialysis.

Peritoneal dialysis (PD) in Malaysia, which has been used in the country for over 20 years, still has low penetration rate (10%) compared with other renal replacement therapies (RRTs). According to researchers in the Department of Neurology in Serdang Hospital, PD is often used for patients with numerous comorbidities or patients not able to tolerate haemodialysis. In a survey of their own PD programme which incorporates catheter insertion by nephrologists, they found the penetration rate to be 4.5 times higher than the national average. The improvement is attributed to the interventions by the nephrologists which increased patient confidence in continuous ambulatory peritoneal dialysis (CAPD) and ensured timely placements of PD catheters.

Source

Does Peritoneal Dialysis Catheter Insertion by Interventional Nephrologists Enhance Peritoneal Dialysis Penetration?

Bak Leong Goh, Yudisthra M. Ganeshadeva, Siew Eng Chew, and Mohd Sulaiman Dalimi

Seminars in Dialysis 2008;21:561-566

CUSUM method may be applied as a quality control and standards set for Tenckhoff catheter insertion programs in Malaysia

The same Malaysian clinical researchers that found interventional nephrologist initiated peritoneal dialysis (PD) to improve PD penetration rates in their centre went on to evaluate the learning curve of these nephrologists when conducting Tenckhoff catheter insertion. Using the CUSUM (cumulative summation) method, they found that it took 23 procedures for a trainee nephrologist to familiarise himself with the peritoneoscope Tenckhoff catheter insertion technique. They also found that catheters directed to the right iliac fossae had better survival (94.6%) compared with those directed to the left (48.6%). This approach also detected unsatisfactory performances earlier. Therefore, the researchers recommended using continuous CUSUM monitoring as quality control and a set standard. Surgeons still skeptical about peritoneoscope Tenckhoff catheter implantation by interventional nephrologists may adopt this analysis to monitor primary catheter dysfunction, primary leak and primary peritonitis.

Source

Establishing Learning Curve for Tenckhoff Catheter Insertion by Interventional Nephrologist Using CUSUM Analysis: How Many Procedures and in Which Situation?

Bak Leong Goh, M. Ganeshadeva Yudisthra, and Teck Onn Lim

Seminar in Dialysis 2009;22:199-203.

Other notable publications

Optimal cut-off levels to define obesity: body mass index and waist circumference, and their relationship to cardiovascular disease, dyslipidaemia, hypertension and diabetes in Malaysia.

Zaki Morad, Robayaah Zambari, Siew Pheng Chan, Vadivale Muruga, Bernard Ng, Geeta Appannah and Lim Teck Onn. Asia Pac J Clin Nutr 2009;18:209-216

A multicenter study to determine the efficacy and safety of a generic atorvastatin.

Punithavathi N, Loke Meng Ong LM, Lena Yap, Teck Onn Lim on behalf of the Storvas

Clinical Trial Study Group.Medical Journal Malaysia 2009;64:150-154.

Observational cohort study to determine the long-term safety and efficacy of Gerepo for the treatment of renal anemia in patients with chronic kidney disease.

Loke Meng Ong, Bak Leong Goh, Sarojini Sivanandam, Teck Onn Lim and Zaki Morad for the Biogeneric EPO Study Group. Nephrology 2009;14:264–265.

These CRC publications may be downloaded at www.crc.gov.my/publication/journal

Global Initiatives & Industry Updates

Dr Sharmila Ramachandran
Pharmaceutical Association of Malaysia (PhAMA)
Anne John Michael
Clinical Research Centre

Global initiatives

Europe may implement that a Single Clinical Trial Authorisation (CTA) in Multinational Clinical Trials to ensure patients have faster access to treatments and research in the continent remains competitive. In the current Clinical Trial Directive, protocols need to go through ethical committees of each country the trial is conducted in and researchers, pharmaceutical companies, clinical research organisations, ethics committees, European Commission and patient organisations during a meeting in Brussels reached a consensus to have a single CTA for multinational trials. Click for the source.

The UK's National Institute for Health and Clinical Excellence's move to implement an Innovation Pass scheme, a three-year fast-track access for selected drugs, is welcomed both by the country's life sciences trade organisations and the industry. This accelerated process not only means that patients have faster access to breakthrough medicines, but also expedites research into the next generation of treatment. Click for the source.

The U.S. Food and Drug Administration will widen access to experimental drugs for seriously ill patients in the country. This latest announcement is an expansion of FDA's existing 30-year policy in allowing investigational treatments to be used in critical patients. In addressing the pharmaceutical companies' concerns on its effects on clinical trial patient recruitments and regulatory approvals, FDA estimates that this move may only involve about 3000 additional patients annually. Click for the source.

It is important that new research findings are publicly accessible. One way is to publish results in a journal but this has its limitations as not all clinical studies are successfully published. Another way is to post result summaries in internet-based registers. GSK practices this and the company includes not only its clinical trials but also observational studies and meta-analyses. Indeed, this would ensure that information is readily accessible. The end goal, however, is still publication in peer-reviewed journals, but having the option to display findings in the public domain as soon as the study will ensure transparency and increase public trust in medical research. Public disclosure of clinical research. Lancet 2009;DOI:10.1016/S0140–6736(09)60613–9

Industry updates

Colorectal cancer is the world's third most common cancer and is the second most common cause of deaths from cancer. Xeloda (capecitabine), already approved as monotherapy for early colon cancer, was used in a Phase III trial to study its effects when used in combination with intravenous oxaliplatin. Patients on this combination were found to have better disease-free survival than those on intravenous chemotherapy combination 5-fluorouracil/leucovorin (5-FU/LV). Click for the source.

Chronic obstructive pulmonary disease (COPD) is currently treated with inhaled bronchodilators and inhaled corticosteroids. But recent findings from Phase III trials using Daxas (roflumilast) to treat symptomatic COPD revealed positive effects for exacerbation rates and pulmonary function (FEV1). The drug if approved by the U.S. Food and Drug Administration (FDA), is a first in its class as it targets cells and mediators in the body that may be part of the COPD disease process. Click for the source.

News of potential treatment for lupus will bring hope to the more than 5 million people affected with this complex chronic autoimmune disease. In a 52-week Phase III study, patients given BENLYSTA experienced significant improvement in overall disease activity compared to those on placebo. This largest ever Lupus study also found the patients on BENLYSTA to have less intake of steroid medications. Click for the source.

H1N1 news

Japan, Canada, Denmark, Hong Kong, China and Singapore have reported Tamiflu-resistant H1N1 viruses. But according to the World Health Organization, there were no signs of spread as these resistant viruses were isolated cases. Click for the source.

The United States of America started trials for a vaccine for the pandemic influenza in August. The initial study will involve 1,000 volunteer adults and children in ten centres throughout the country. Click for the source

Researchers in Southampton General Hospital and Jenner Institute at Oxford University are collaborating on clinical trials of a vaccine that has the potential to protect across different flu types. Unlike regular flu vaccines that targets the outer part of the flu virus, this advanced vaccine will target the interior section which is quite similar in different strains. If successful, annual vaccination will not be needed as the vaccine would be able to protect against different types of influenza viruses. Click for the source.

Almost 40% of residents who were contacted during a telephone survey in England, Scotland and Wales in early May this year revealed that almost 40% said that they will adhere to recommendations to change one or more of their routine behaviours to reduce the risk of H1N1 flu.But only 5% reported any avoidance behaviour such as avoiding public transportations or large crowds. This survey was conducted two weeks after the WHO raised the pandemic alert status for H1N1 outbreak to five. Despite huge media coverage and government campaigns, the public did not perceive it as a major problem. Nevertheless, continuous efforts to educate the public are still advisable.

Rubin GJ, Amlo R, Page L et al. Public perceptions, anxiety, and behaviour change in relation to the swine flu outbreak: cross sectional telephone survey. BMJ 2009;339. b2651doi: 10.1136/bmj.b2651.

GSK has completed patient enrolment for its first trial on a vaccine for pandemic (H1N1) 2009 influenza. The vaccine will consist of an adjuvanted formulation and contains antigen of H1N1 influenza strain. Preliminary data from this trial in Germany will be submitted to regulatory authorities by September. GSK will start similar trials elsewhere involving healthy adults, children and infants and the elderly. Click for the source.

In order to update pharmaceutical and contract research outsourcing companies with the MOH's progress and guidelines in clinical research, CRC regularly conducts industry dialogues. These dialogues are also where industry representatives meet regulators to get their queries addressed and issues highlighted.