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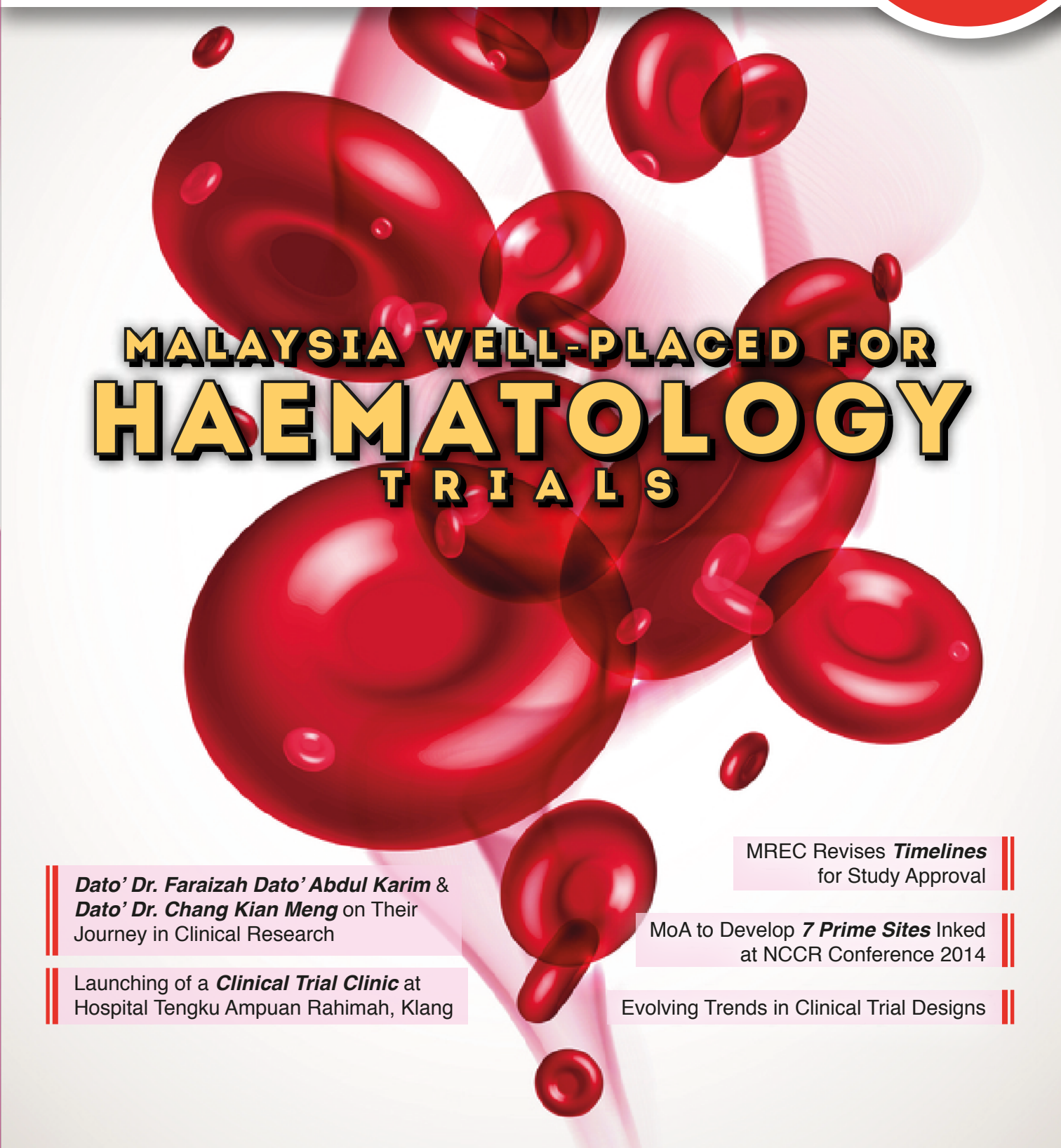

MALAYSIA WELL-PLACED FOR HAEMATOLOGY TRIALS

Dato' Dr. Faraizah Dato' Abdul Karim & ***Dato' Dr. Chang Kian Meng*** on Their Journey in Clinical Research

Launching of a ***Clinical Trial Clinic*** at Hospital Tengku Ampuan Rahimah, Klang

MREC Revises ***Timelines*** for Study Approval

MoA to Develop ***7 Prime Sites*** Inked at NCCR Conference 2014

Evolving Trends in Clinical Trial Designs

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From the **editor's** desk

CRM
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August 2014 marked the 2-year anniversary of CRM being operational, certainly a significant milestone in our evolution towards becoming an effective "one-stop" facilitator for sponsors and CROs, investigators, clinical trial sites, and other stakeholders. Our 2nd birthday also presented a suitable occasion to review the effectiveness of CRM's strategies and plans, and to adjust these where necessary to enable CRM to adapt and be responsive to the current and future needs of its "customers".

RAJESHPAL SINGH
Head of Communications & Relations
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The end of the 3rd quarter this year also marked a change of guard at CRM, with Chief Executive Officer Dr Mohamad Ali Abu Bakar deciding to leave CRM to pursue other interests upon the expiry of his contract. Pending the appointment of a new CEO, the Ministry of Health Malaysia has temporary assigned the responsibility to Dr Shahnaz Murad, the Deputy Director-General (Research & Technical Support) in the MOH.

Looking back over the past two years, with other stakeholders being consulted, sheds light on the direction that CRM needs to take for at least the next two years.

Among the review's key conclusions is that CRM has to strengthen cooperation and coordination with other MOH entities connected to clinical research, such as the Clinical Research Centre (CRC) network, Medical Research Ethics Committee (MREC), National Pharmaceutical Control Bureau (NPCB) and the Medical Device Authority (MDA). CRM also has to strengthen the scope and range of support it provides to investigators and sites, and to keep working on developing and growing the necessary human and physical capital to support the conduct of clinical trials.

Very encouragingly, the review adds credence to the proposition that Malaysia does offer a very good deal to sponsors, CROs and the clinical research industry in general. The multi-ethnic composition of our society, the presence of a large pool of patients, the modern healthcare system and facilities with well-trained and English literate doctors and allied health personnel, and not to forget the competitive pricing for conducting clinical trials in Malaysia, are factors that are of real genuine interest to the global ISR industry.

The path forward having been lighted, CRM will certainly have its hands full over the foreseeable future in seeking to balance the needs and requirements of investigators and trial sites, to the requirements and opportunities presented by the global ISR industry.

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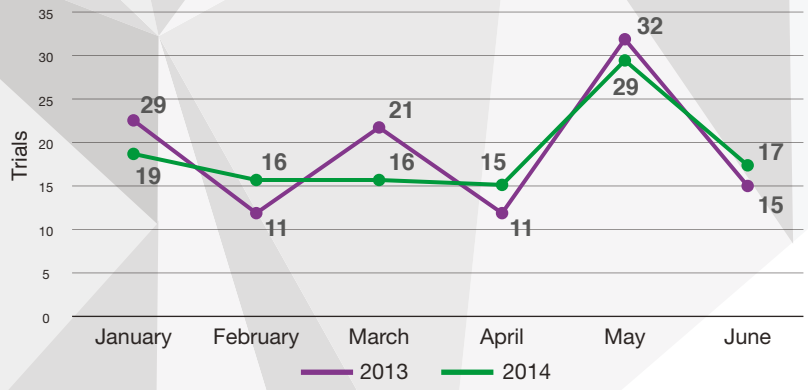
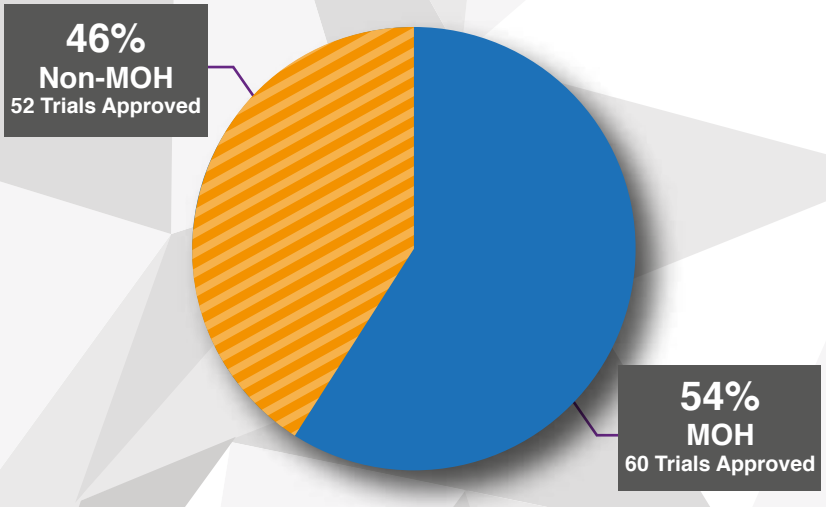
ISR STATISTICS



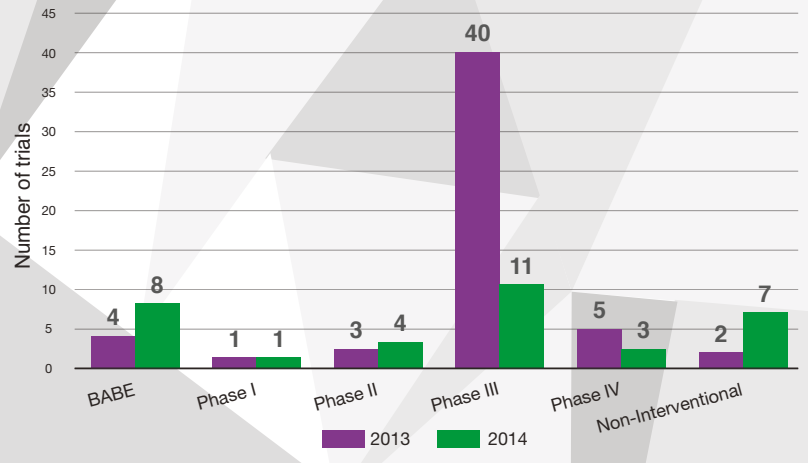
Trials approved by Institutional Review Boards (i.e. Ethics Committees) Jan-June 2014 vs. Jan-June 2013

112 new trials were approved in the first half of 2014 by the Medical Research and Ethics Committee i.e. MREC (for trials to be conducted in government hospitals) and by the other 12 IRBs (for private hospitals and universities), as compared to 119 trials in the first half of 2013.



Trails approved by MOH and Non-MOH IRBs between January and June 2014

From the total of 112 new trials approved between January - June 2014, some 54% were approved by MREC and 46% were approved by the 12 Non-MOH IRBs.



Trials managed by CRM, Jan-June 2014 vs. Jan-June 2013

An increase in the number of BABE studies, Phase II and non-interventional trials were observed between January and June 2014 compared to the same period in 2013. The decrease in Phase III studies over the time period being compared has to be interpreted cautiously, as a number of Phase III trials were awaiting initiation and will be captured in the statistics for the 2nd half of 2014.

Table 1. ISR Trial Sites in Malaysia

Public Hospitals	
Hospital Sultanah Aminah	Klinik Pergigian Gunung Rapat
Hospital Permai	Hospital Tuanku Fauziah
Hospital Sultan Ismail	Hospital Pulau Pinang
Hospital Sultanah Bahiyah	Hospital Seberang Jaya
Hospital Sultan Abdul Halim	Klinik Kesihatan Bandar Baru Air Itam
KK Simpang Kuala	Hospital Queen Elizabeth I
Hospital Raja Perempuan Zainab II	Hospital Mesra
Hospital Melaka	Hospital Wanita dan Kanak Kanak Likas
KK Tampin	Hospital Queen Elizabeth II
Hospital Tuanku Jaafar	Hospital Likas
KK Seremban 2	Hospital Umum Sarawak
Hospital Tuanku Ampuan Najihah	Hospital Sentosa
KK Ampangan	Hospital Miri
Hospital Tengku Ampuan Afzan	Hospital Sibu
Hospital Taiping	Hospital Serdang
Hospital Ampang	Hospital Selayang
Hospital Raja Permaisuri Bainun	Hospital Tunku Ampuan Rahimah
KK Greentown	KK Shah Alam Seksyen 7
Hospital Bahagia	Hospital Sultanah Nur Zahirah
Hospital Seri Manjung	Hospital Kuala Lumpur
KK Buntong	Pusat Darah Negara
KK Lenggong	Institut Perubatan Respiratori
Hospital Putrajaya	KK Cahaya Suria
KK Putrajaya	Hospital Pakar Sultanah Fatimah
Klinik Pergigian Putrajaya	Hospital Sungai Petani
Hospital Duchess of Kent	

Private Hospitals
Sime Darby Medical Centre
Prince Court Medical Centre
National Heart Centre
Loh Guan Lye Hospital
Gleneagles Hospital
Mount Miriam Hospital
Penang Adventist Hospital
Lam Wah Ee Hospital
Nilai Medical Centre
Pantai Hospital Penang
Mahkota Medical Centre
Pantai Hospital Ayer Keroh

MOHE Hospitals
University Malaya Medical Centre
Hospital University Kebangsaan Malaysia
Hospital University Sains Malaysia

KK = Klinik Kesihatan

Table 2. Phase I/BABE sites, Pre-clinical and GLP-certified laboratories in Malaysia

Phase I /BABE Sites
Hospital Ampang
Hospital Kuala Lumpur
Pusat Darah Negara
National Cancer Institute
Hospital Pulau Pinang
CRC Ampang Hospital
Hospital Raja Permaisuri Bainun
Hospital Sungai Buloh
Hospital Umum Sarawak
Hospital Sibu
Hospital Tuanku Jaafar
Hospital Putrajaya
Hospital Seberang Jaya
Hospital University Sains Malaysia
Questra Clinical Research Sdn Bhd

Pre-clinical Labs
Cerca Insights Sdn Bhd
IPharm Animal Research Facility (IPARF)
Environmental Technology Research Centre (ETRC), Sirim Berhad
Melaka Biotechnology Corporation
Info Kinetics Sdn Bhd
Institute for Medical Research

GLP Certified Labs
Environmental Technology Research Centre
Melaka Biotechnology Corporation
Info Kinetics Sdn Bhd
Non-clinical Research, Laboratory Animal Resource Unit, Medical Research Centre, Institute for Medical Research

HAEMATOLOGY STATISTICS IN MALAYSIA

HAEMOPHILIA

According to the World Federation of Haemophilia, about 1926 cases of bleeding disorders were reported in Malaysia in 2012, of which 53.8% and 9.4% were cases of haemophilia A and B respectively (Figure 1).[1] The proportion of other bleeding disorders in the Malaysian population is shown in Figure 2.

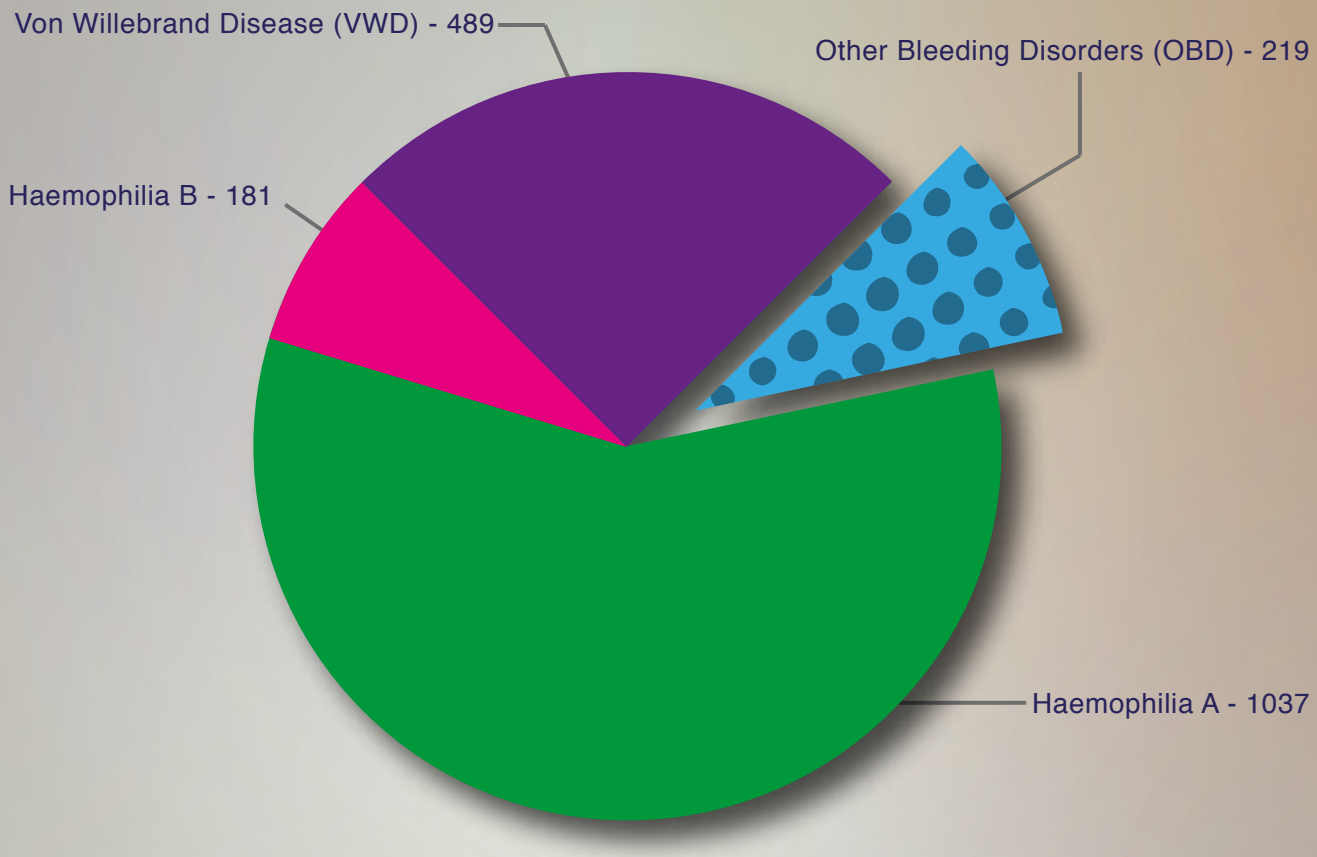


Figure 1. Proportional distribution of all bleeding disorders in Malaysia in 2012[1]
Source: World Federation of Haemophilia: Annual Global Survey 2012

Haemophilia is a panethnic disorder without racial predilection. In the United States, most people with haemophilia are diagnosed at a very young age. The median age at diagnosis is 36 months for people with mild haemophilia, 8 months for those with moderate haemophilia and 1 month for those with severe haemophilia.[2]

In Malaysia, a large proportion of haemophilia patients are below the age of 4 years. In about two thirds of cases, there is a family history of haemophilia. There are currently about 23 industry-sponsored haemophilia trials being conducted at various Ministry of Health (MOH) hospitals nationwide (Table 1), the majority being Phase III trials.

Table 1. Ministry of Health Hospitals conducting Haemophilia trials

Pusat Darah Negara
Hospital Ampang
Hospital Pulau Pinang
Hospital Sibu
Hospital Tengku Ampuan Rahimah
Hospital Umum Sarawak

WFH Annual Global Survey Data: Proportional Distribution of Other Bleeding Disorders in Malaysia in 2012

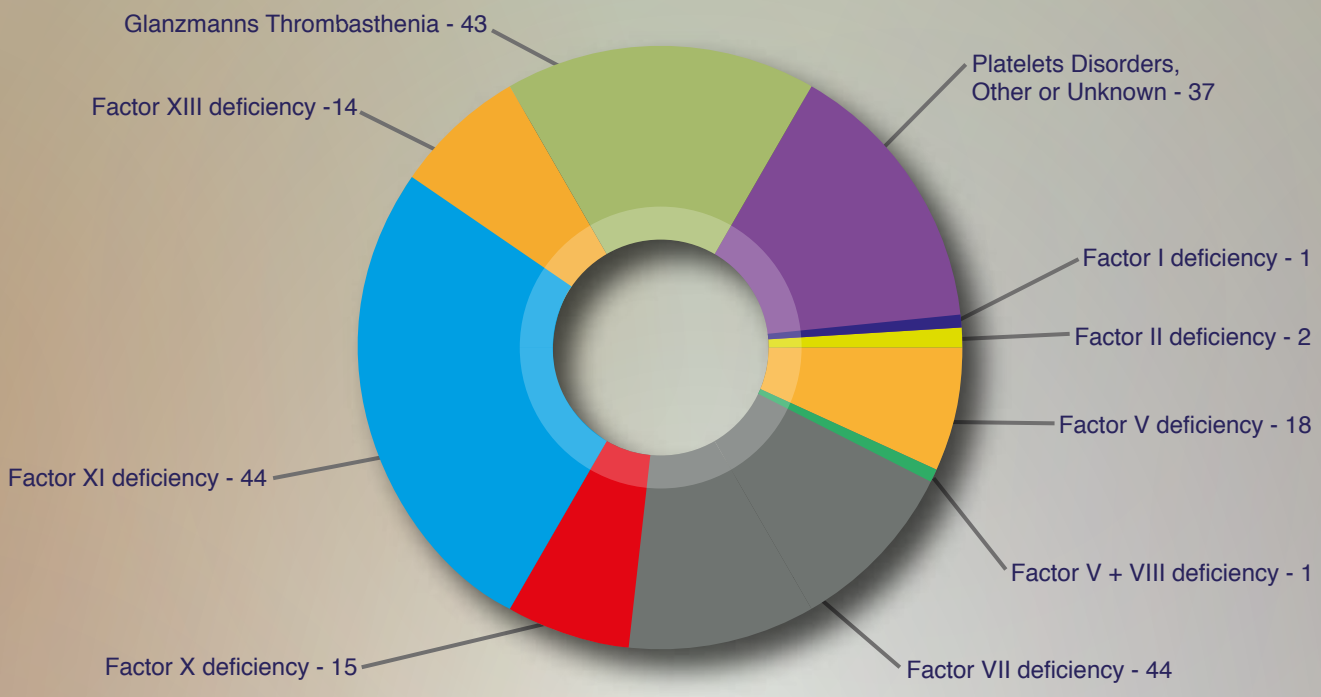


Figure 2. Proportional distribution of other bleeding disorders in Malaysia in 2012[1]

LYMPHOMA AND LEUKAEMIA

In 2007, there were 776 cases of lymphoma diagnosed and registered at the National Cancer Registry, compared to 741 cases of leukaemia.[3] Lymphoma is the sixth and eighth most common cancer among Malaysian men and women respectively. Among the various ethnic groups in Malaysia, Chinese were found to have a higher incidence rate compared to Malays and Indians (Table 2).

In contrast, leukaemia is the seventh most common cancer in both men and women and the most common cancer in children below 14 years of age. The incidence of lymphoma and leukaemia was slightly higher in men compared to women, and more than one third of both cases are diagnosed at stage 2.

There are currently about 9 industry sponsored clinical trials on multiple myeloma, lymphoma, anaemia and leukaemia being conducted in around 8 MOH hospitals in Malaysia (Table 3).

Table 2. The number of new lymphoma and leukaemia cases among the major ethnic groups in Malaysia.

	Men		Women	
	Number of new cases	Crude rate	Number of new cases	Crude rate
Lymphoma				
Malay	*221*	*3.2*	*172*	*2.5*
Chinese	*136*	*4.2*	*101*	*3.3*
Indian	*25*	*2.7*	*13*	*1.4*
Leukaemia				
Malay	*241*	*3.4*	*184*	*2.7*
Chinese	*103*	*3.2*	*63*	*2.0*
Indian	*29*	*3.1*	*28*	*2.9*

Source: National Cancer Registry Report, Malaysia Cancer Statistics 2007

Table 3. Ministry of Health Hospitals conducting clinical trials on haematologic diseases (apart from haemophilia)

Hospital Ampang
Hospital Kuala Lumpur
Hospital Ipoh
Hospital Melaka
Hospital Pulau Pinang
Hospital Sultanah Aminah
Hospital Tengku Ampuan Rahimah
Hospital Umum Sarawak

References: 1. Report on the Annual Global Survey 2012. World Federation of Hemophilia, 2013. **2.** Haemophilia: Data and Statistics. Center for Disease Control and Prevention, 2014. **3.** National Cancer Registry Report, Malaysia Cancer Statistics, 2007

Medical Research Ethics Committee (MREC) Revises Timelines for Study Approval

By Communications & Relations Department, Clinical Research Malaysia

The Medical Research Ethics Committee (MREC), which handles ethics approval for clinical research to be conducted in Ministry of Health Malaysia hospitals and institutions, has revised its approval process timelines to reflect a more reasonable and achievable timeframe for processing, evaluating and approving ethics approvals.

The new timelines are available on the websites of the National Medical Research Register (NMRR) and MREC; additionally sponsors and CROs have also been notified via e-mail.

Based on feedback submitted by industry players and CRM, MREC earlier this year took concrete action to improve its work processes, which included revising the initial approval timeframe from seven working days to ten working days and the study resubmission timeframe from 14 working days to 20 working days (Table 1).

Although some industry players would have instead preferred MREC to shorten its timelines, this would only have looked good on paper, but would have been non-realistic and extremely difficult for MREC with its limited resources to deliver consistently. The revised timelines were decided upon after an in-depth evaluation of the workload burden and resources available to MREC, and very importantly, to ensure that MREC will be able to consistently deliver as indicated.

In view that the industry appreciates consistency and reliability on the part of regulators and authorities, CRM supports MREC's concrete efforts to improve its processes and deliverables, as this only augurs well for attracting more higher-value and pivotal clinical research to Malaysia.

A recently conducted analysis by CRM of the number of ISR studies approved by MREC shows that, even with the new revised timelines, the number of ISR studies approved in 2014 (per month) was comparably higher than the number of ISR studies approved in 2012 and 2013 (per month). This shows that insofar as ISR is concerned, MREC's revised timelines did not lead to a reduction in the number of ISR studies submitted for ethics approval nor lower the rate of approval.

According to MREC, the most common reasons for delays in the approval process are: incomplete study submission; missing documents (e.g. informed consent form); or because the study involves stem cells or a traditional herbal medicine, whereby the ethics approval process may involve an additional review procedure.

Besides revising its timelines, MREC has also decided to only use email as the sole mode of communication between its secretariat officers and the industry. While this in some ways may sound "not so business friendly", MREC's experience is that its officers tend to get bogged down by

No.	Description	Previous Timeline	Revised Timeline
1.	**MREC INITIAL APPROVAL:** ***Timeline begins from date of NMRR ID issued (provided completed study submission has been made to MREC via NMRR)***		
a.	Study is forwarded to MREC - MREC Review	7 working days	At least 10 working days*
b.	MREC Review - MREC Decision Letter (Approval / Disapproval / Revision required)	7 working days	10 working days
c.	If revision required (Revision of study documents by PI/CP)	30 working days	30 working days
d.	Study resubmission by PI/CP - MREC decision (Provided all queries by MREC have been answered)	14 working days	20 working days
2.	**SUBMISSION POST MREC INITIAL APPROVAL:** ***Submission must be uploaded in NMRR. Timeline begins from the last date of submission by corresponding person***		
a.	Amendments that are non-substantial/less than minimal risk, submission of final study report, submission of study termination memorandum.	20 working days	20 working days
b.	Substantial amendments, submission for MREC ethical renewal.	30 working days	30 working days
3.	**ACKNOWLEDGEMENT OF DOCUMENTS:** ***Documents that are forwarded via courier/fax to MREC office will be acknowledged. Timeline begins from date of receipt.***		
a.	SUSARs (both Malaysian and global sites), SAEs (all Malaysian sites), protocol deviations (all MREC approved sites), other study related documents.	–	5 working days

*Please take note that the timelines stated is for guideline purposes only. These processing timelines may vary on a case to case basis depending on the availability of the MREC Secretariat, MREC reviewers or any other unforeseen circumstances.
CP = corresponding person; PI = principal investigator; SAE = severe adverse effect; SUSAR = suspected unexpected serious adverse reaction.

Note: In the event where a study is revised following its initial submission, the last submission date of the revised study will be taken and not the date of the first initial submission.

telephone enquiries plus there will also be no written record of what was discussed or requested via telephone, leading to the possibility of future disagreements, problems or delays between MREC and industry players. By limiting all communication to email, MREC hopes to overcome these issues.

MREC ensures that research conducted in MOH hospitals and institutions conform to international scientific and ethical standards, in order to safeguard the rights, safety and well-being of clinical trial participants. Submissions for ethics approval will be reviewed by a committee of at least five members whereby this quorum shall consist of at least one member whose primary area of expertise is in a non-scientific/non-medical area, one member whose primary area of interest is in medical science and at least one member who is independent of the applicant or trial site. The MREC members meet twice a month and will recommend either approval, modification to or rejection of the research study submission.

Research Personality

Dato' Dr. Faraizah Dato' Abdul Karim

Deputy Director and Senior Consultant Pathologist, National Blood Centre, Kuala Lumpur

Dato' Dr. Faraizah Bt Dato' Abdul Karim is an internationally recognised expert in haemophilia care and has a longstanding interest in blood transfusion services. She is currently the Deputy Director and a Senior Consultant Pathologist, specialising in haematology and blood transfusion, at the National Blood Centre, Kuala Lumpur.

Dato' Dr. Faraizah earned her medical degree from Universiti Sains Malaysia and a Diploma in Clinical Pathology from the University of London. She then went on to obtain a Master of Science in Haematology at the Imperial College School of Medicine before embarking on sub-specialty training in transfusion medicine at the North London Blood Transfusion Service and Hammersmith Hospital, London.

Before assuming her current position, she served as Deputy Director and Consultant Pathologist at the Blood Services Centre in Hospital Kuala Lumpur from 1998 to 2000. She is further engaged in various committees and drafting of policies and guidelines at the Ministry of Health Malaysia, and has been invited as a speaker at conferences in Hong Kong, Sweden, Taiwan and the Philippines, among others.

Dato' Dr. Faraizah has been the Principal Investigator in more than 20 multi-national clinical trials and has co-authored papers reporting clinical trial findings in several international peer-reviewed journals. She is a member of various international societies including the International Society of Blood Transfusion and the World Federation of Haemophilia. Currently she is the President of the Haemophilia Society of Malaysia and Vice President of the Malaysia Blood Transfusion Society.

Dato' Dr. Faraizah, can you briefly describe how you first got involved in clinical research?

My first trial was in 1997 when I was at Hospital Kuala Lumpur (HKL) managing haemophilia patients. During that period, most of the haemophilia patients were not responding to the treatments that were available and my colleagues and I had nothing else to offer. We jumped at the opportunity when a sponsor wanted to bring in a haemophilia trial to HKL. It was at this time that I first got involved in clinical trials and became a sub-investigator. The trial drug showed positive results and the patients responded well. The success of this first trial set the precedence for subsequent trials to be conducted at HKL and Pusat Darah Negara (National Blood Centre).

What are the type of trials that you mostly conduct?

Only haemophilia trials and these are all industry-sponsored research. My first was a Phase III trial followed by a post-marketing trial and Phase II trial. When my superior, who was the then hospital director and principal investigator retired, I took on the role of principal investigator. Here at PDN, Phase I trials are conducted in collaboration with HKL whereby we have been provided access to the critical care unit (CCU) beds, necessary for any first-in-man studies.

What are the aspects that you look for before agreeing to undertake a trial?

Apart from reviewing the protocol, I try to ensure that the trial drug would bring potential benefits to my patients by studying published journal articles of that particular drug or treatment. Only when I am convinced of the possible advantages of the drug will I undertake the study. This may be one of the reasons why patients have placed their trust in me. As with any clinical trial, the safety of patients is our utmost priority and it is our responsibility to safeguard their interest.

As the Deputy Director of PDN (National Blood Centre), what do you see are the strengths of PDN with regards to conducting clinical trials?

Over the years, PDN has secured itself as an established site with a track record of numerous successful multi-national haemophilia trials being carried out here. While at the moment I am the only principal investigator at PDN, we have a number of young sub-investigators who are well-trained and dedicated to the trials that are conducted here.

You have been invited by some sponsors to contribute or author research papers arising out of multi-national clinical trials. Why do you think this is so, and how many journal papers have you co-authored so far?

Every sponsor has their own selection criteria. In my case, I understand that it was based on the number of patients which I have recruited and the inputs that I provided to the trial. Thus far, two papers out of five which I co-authored have been published while the rest are still under review.

If an investigator and the sponsor have a difference in opinion, say over the trial results, how do they resolve this and move on to writing journal papers?

A meeting would usually be held between the author and co-authors, and during this time, all contributors will discuss and come to an agreement on the data that we want to be presented in the manuscript.

How do you influence or encourage your sub-investigators to conduct clinical trials?

I wouldn't say that I personally influenced them. Their involvement in trials stem from their interest in managing haemophilia patients and maybe to a certain extent looking

up to me as their role model. In fact, I have a few medical officers who are keen to conduct trials and have expressed their interest to do so once they complete their master's programme.

What would be the hardest part in conducting a trial?

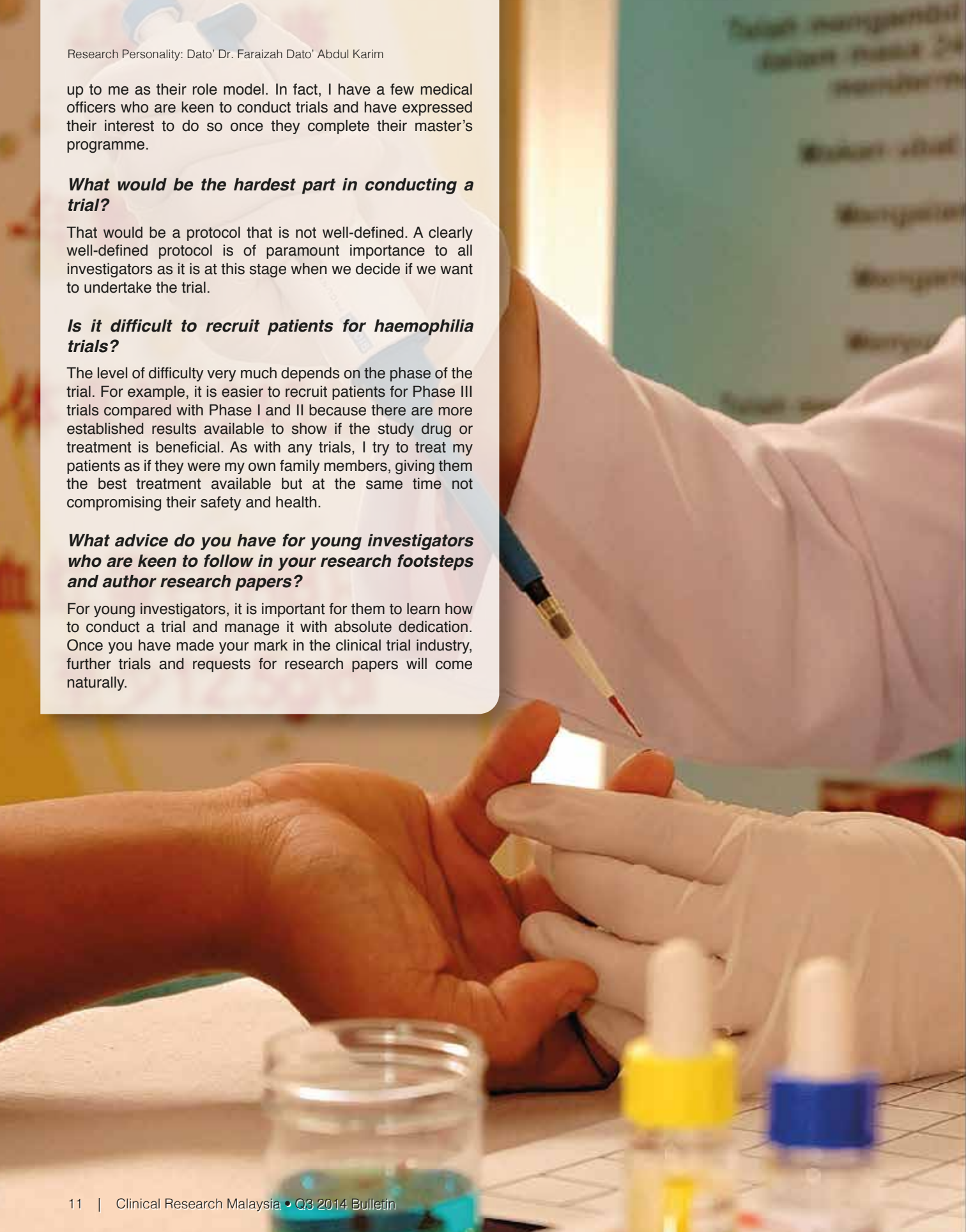
That would be a protocol that is not well-defined. A clearly well-defined protocol is of paramount importance to all investigators as it is at this stage when we decide if we want to undertake the trial.

Is it difficult to recruit patients for haemophilia trials?

The level of difficulty very much depends on the phase of the trial. For example, it is easier to recruit patients for Phase III trials compared with Phase I and II because there are more established results available to show if the study drug or treatment is beneficial. As with any trials, I try to treat my patients as if they were my own family members, giving them the best treatment available but at the same time not compromising their safety and health.

What advice do you have for young investigators who are keen to follow in your research footsteps and author research papers?

For young investigators, it is important for them to learn how to conduct a trial and manage it with absolute dedication. Once you have made your mark in the clinical trial industry, further trials and requests for research papers will come naturally.



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The print run is complemented by an online subscriber base of 2000 readers currently, who receive an online copy of the CRM Bulletin.

The bulletin's objectives are to spread awareness about Malaysia's capabilities in industry sponsored clinical research (ISR), inform and attract industry players to Malaysia, motivate and educate potential investigators and support staff, build public awareness about the importance of clinical research, and finally serve as a forum to share news and development relevant to all stakeholders.

If you are seeking a means to reach out to the clinical research "eco-system" in Malaysia, then talk to us about advertising your message in the CRM Bulletin.

Other publications by CRM

NCCR bulletin

Guide for Industry

Patient Brochure

Evolving Trends in Clinical Trial Designs

By Mihir Gandhi
Article reprinted with permission from BioSpectrum Asia

In the current competitive era of drug development, establishing the superiority of a new medical intervention compared to a relevant standard with a big effect size is difficult. If a moderate to small effect size is all that can be realistically expected, persuading regulatory bodies, clinical practitioners and patients to use the intervention will require demonstrating other advantages such as improved safety, better quality of life, cost-effectiveness and convenience of administration. From a commercial angle, it is also critically important to shorten the development timeline in order to enjoy longer patent protection time or market dominance before a competitor appears. Thus, pharmaceutical companies and academic researchers are in constant search for innovative clinical trial designs which can accelerate the drug development process, save resources, assess the advantages of the intervention in multiple ways and that are acceptable to regulatory bodies.

One of the recent initiatives for improving clinical trial efficiency is to use adaptive designs. These allow more flexibility in trial conduct such as re-estimating the sample size as the trial is ongoing, dropping a less efficacious intervention arm after an interim evaluation, combining phase II and phase III trial designs and re-randomization of patients to an alternative intervention after the primary intervention fails. Such designs help to shorten the clinical development timeline, allow testing of multiple intervention strategies in the same trial and reduce exposure of patients to less efficacious interventions.

Research methodologies for analyzing data from several types of adaptive designs are still evolving and under debate. The primary concerns are the chance of erroneous positive conclusions and the difficulty in interpreting the results from a complex trial design. Hence, adaptive designs are mainly employed in the exploratory phase, with as yet limited application in confirmatory clinical trials. A recent helpful development is that regulatory bodies such as the US Food and Drug Administration and the European Medical Agency have issued guidelines declaring which adaptive designs are "well-understood and have valid approaches to implementation" and which are "not well-understood".

In addition to analysis and interpretation, adaptive designs place additional challenges on trial execution; demanding strong project management and effective cross-function coordination. Activities such as patient recruitment, drug supply, remote data capture, site monitoring and data cleaning need to be highly integrated.

There are several instances where the infrastructure and processes developed for conventional clinical trials do not meet the requirements of an adaptive designed trial and adapting the conventional processes can be a challenge. For example, the requirement of short timelines for clean and verified data to support decision-making at the interim stage of the trial may not be feasible with conventional site monitoring and data cleaning frequency practices. The study team will need to be creative to find a solution for this, for example, by prioritizing data verification and cleaning only for the key endpoints required for decisionmaking at the interim stage. Thus adaptive designs may look attractive, but the challenges involved in planning and conducting the trial may outweigh the benefits. However, in the long run once enough experience is gained with such trial designs, it could be rewarding.

Another prominent trend in clinical trial design is to incorporate assessments of patient-reported outcomes (PRO) such as quality of life (QoL) into intervention effectiveness measurement. Because PROs by definition are important and relevant to patients, significant improvements can be advantageously incorporated in product labeling. In 2009, the US Food and Drug Administration released a guideline on the use of PRO measures to support labeling claims. Recently, in 2014, the European Medical Agency also published a draft guideline on the use of PRO specifically for oncology studies.

Many questionnaires measuring multiple dimensions of QoL (e.g., mobility, pain, depression etc.) have been developed. They are broadly classified into two groups: generic QoL questionnaires and disease specific QoL questionnaire. A disease-specific QoL questionnaire covers dimensions that can potentially be affected by the disease or its treatment. For example, the EORTC's QoL questionnaire, EORTC QLQC30, developed for cancer patients measures QoL using dimensions related to functional activities (physical, role, cognitive, emotional, social) as well as cancer-specific symptoms such as fatigue, pain, nausea/vomiting, appetite loss etc. In contrast, generic QoL questionnaires are not disease-specific and can be used for patients with any medical conditions.

A general belief is that a disease-specific QoL questionnaire can detect a change in the QoL more sensitively than a generic QoL questionnaire. However, in reality, this is not necessarily true. For example, a recent Singapore study of breast cancer patients found that a simple generic questionnaire, the EuroQol-5 dimension (EQ-5D) with only 5 questions, is discriminatively non-inferior to a more complex disease specific questionnaire, the Functional Assessment of Cancer Therapy-Breast (FACT-B) with 44 questions. On the other hand, generic QoL questionnaires can sometimes be insensitive to particular aspects of QoL in certain conditions. In such cases, it is useful to include a disease-specific QoL questionnaire. In practice, different QoL questionnaires are suitable for different types of research questions, depending on how a particular intervention impacts on QoL. Currently, the EQ-5D questionnaire is the most commonly used QoL questionnaire. It is available in many languages and validated in many medical conditions.

A generic QoL questionnaire, such as EQ-5D or Short Form-6 dimension (SF-6D), is preferred in late stage clinical trials because it provides utility values (preference for the health states). Currently, very few of disease-specific QoL questionnaires provide utility values. Utility values are required in order to calculate quality-adjusted life years (survival time discounted for QoL) - an important outcome for pharmacoeconomic evaluations. An intervention that requires less money per quality-adjusted life year is considered more cost-effective. Such studies also require collecting healthcare cost data under realistic conditions, which is not an easy task. Due to dramatically rising medical costs, economic evaluation of healthcare interventions has received increased emphasis among various stakeholders. It helps stakeholders judge if resources were well spent on the intervention. In countries where government is the major payer for healthcare such as Canada, UK, Australia and some European countries, medical reimbursement and coverage decisions are increasingly based on cost-effectiveness evaluations.

Investigators and policy makers in the Asia-Pacific region have also started evaluating healthcare interventions from the cost-effectiveness perspective. This has resulted in the increasing use of QoL questionnaires in clinical trials. Many researchers are also focusing on methodological research related to QoL and pharmacoeconomics. For example, initially in 2002, the EQ-5D utility valuation set derived from the Japanese general population was the only available utility valuation set for the EQ-5D health states in the Asia-Pacific region. But in recent years, locally derived EQ-5D utility valuation sets have become available for use in Singapore, Malaysia, Thailand, Taiwan and South Korea. Furthermore, researchers are increasingly publishing "mapping" algorithms to convert a QoL summary score from a disease-specific QoL questionnaire into a utility value of a generic QoL questionnaire whose utility valuation set is available. This would enable researchers to perform an economic evaluation in a clinical trial, which has collected QoL data using a disease-specific QoL questionnaire, but not a generic QoL questionnaire.

Although clinical trials are increasingly used as a vehicle for economic evaluations, there are several potential difficulties with this integration. The key focus of clinical trials is to assess the intervention effect under strictly controlled conditions defined by inclusion/exclusion criteria and adherence to the trial protocol. On the other hand, the economic evaluation expects to collect healthcare cost data under pragmatic conditions without the trial protocol-driven restrictions. There is no straightforward way to overcome these challenges, though some recommendations are available on how to conduct economic evaluation alongside clinical trials. If carefully addressed, conducting an economic evaluation alongside a clinical trial provides an invaluable early opportunity to produce estimates of cost-effectiveness of the medical intervention.

Patient Testimonial

I AM IN A CLINICAL TRIAL

Sharmila Valli Narayanan explains what it is like to be part of a clinical trial for a new drug designed to help Type 2 diabetic patients to better manage their disease.

• • •

Have you ever wondered how and why clinical trials are conducted? Even if one does not have a medical background, you may have guessed that it involves testing a promising new drug or medical device on human patients in order to prove that the new drug or device is safe and effective as claimed.

The clinical trial process will be closely monitored by medical professionals and health authorities, with patient safety being the highest priority. The findings from the clinical trial must prove the claims made for the new drug or medical device, and only upon satisfactory completion and findings will the new drug or device be accepted for registration by the health or pharmaceutical authorities of a country. Then and only then can the new drug or device be marketed for sale or be accepted as a better form of treatment.

In 2010, I found myself in a worldwide clinical trial conducted by a big pharmaceutical company for a new diabetic drug that is supposed to give a better blood glucose level control in Type 2 diabetic patients. It was the doctor treating me for diabetes, who also happened to be one of the investigators for the trial in Malaysia, who urged me to participate as he felt it could be medically beneficial for me. I presently go to the Government clinic near where I live for my diabetic care.

Before I was accepted as a participant in the trial, I had to undergo a series of tests (i.e. screening process) to determine whether I fit the patient profile sought by the trial (i.e. the inclusion/exclusion criteria). One of the requirements was of course to be a Type 2 diabetic patient who does not have good control of their blood glucose levels. Sadly for me, I passed all the criteria needed to fit into this group! It took about three months from the time I underwent the screening tests to when I was actually enrolled as a participant in the clinical trial.

The next stage was when I was given a drug and told to take it for a month, with strict instructions on the timing on when to take the medication. I also had to record the meals that I took and my blood sugar level before and after each meal for at least three times a week. The reason, I was later told why I had to do this, was to ensure that I was a participant who would follow instructions and do what I was told. Not surprisingly, a patient's value to the clinical trial will be severely diminished if the patient is unable or unwilling to follow the instructions given.

The next visit to the doctor involved careful checking of the records to determine that I had been a disciplined patient and could be trusted to do my part. The doctor then patiently explained to me what the trial was all about and what the potential risk factors and benefits were to me. I was given time to go through some forms carefully and then I had to sign a consent form to confirm that I was aware and accepted the factors related to the trial (i.e. the informed consent process). The consent form clearly explained everything and I did not have many questions for the doctor.

Subsequently, I was enrolled into the trial and given the new drug.

As I write this in late 2014, I am still part of the clinical trial which is supposed to last for six years. Besides Malaysia, there are other countries in Asia, South America, North America and Europe that are part of this trial. Being part of this has made me realise the huge scale of resources, time and effort that pharmaceutical companies and doctors pour into research.

Since 2010, I have been dutifully going for my appointments with my doctor once every three months. The doctor is ably supported by a dedicated team. During my every visit, my weight is carefully recorded, my blood pressure taken not once but three times to get a uniform reading, and my blood and urine samples are taken for a variety of tests to be run. These samples are sent to Singapore for testing.

Sometimes my ECG is taken and this is examined by the doctor and a copy sent to the pharmaceutical company's headquarters in Europe for record keeping.

I have not stopped taking the drugs prescribed by the doctor in the Government clinic. One of the requirements of this clinical trial is that I continue seeing my regular doctor and keep taking my usual drugs. At the Government clinic, because of the sheer number of patients, the doctor is only able to see me for a maximum of five minutes. Despite this, I am grateful for the Government clinic because I get the medicines for my diabetes and other ailments for a very minimum amount. We are lucky in Malaysia to enjoy this luxury which is hard to come by in other countries.

The greatest benefit to me for being part of this clinical trial is the excellent care that I receive from my doctor who is a renowned specialist in the field of endocrinology. If I had to pay for this kind of care and monitoring from a private hospital, it would burn a major hole in my pocket. During each visit, not only am I given a thorough examination by the doctor, he also sits down with me and explains what the results of the blood and urine tests mean. He also examines me and talks to me about how I am feeling. Personally I feel this clinical trial is a blessing and I am very grateful to my doctor for urging me to be a part of it.

There are other perks of being in this clinical trial as well. I was given a brand new glucose meter (which cost nearly RM400) and glucose strips for free to monitor my blood glucose level. For each visit, I will receive reimbursement for transport costs incurred during my visit to the hospital.

If you are given the opportunity to participate in a clinical trial, I urge you to give it a try. Do your research – find out about the company doing the clinical trial and the doctor who is in charge of you. Read the consent form carefully and clear any doubts you have with your doctor. As for myself, if another clinical trial comes along, I will gladly be a part of it especially if it is headed by this same doctor.

Myth: Once I sign an Informed Consent form for a clinical study I won't be able to drop out (withdraw) without it jeopardising my treatment.

Fact: This is not true. You may withdraw (drop out) from a clinical study at any time. This will be explained to you at the consent process and it will be recorded on the Informed Consent form that you sign if you decide to take part in the study.

Research Personality

Dato' Dr. Chang Kian Meng

Head of Department and Consultant Haematologist at Ampang Hospital, Selangor D.E.
Chairman of the Medical Research Ethics Committee (MREC)
National Advisor of Clinical Haematology Services, Ministry of Health Malaysia

Dato' Dr. Chang Kian Meng is an acknowledged expert in Haematologic Malignancies and in Stem Cell and Bone Marrow transplants. He is currently the Head of the Haematology Department and a Consultant Haematologist at Ampang Hospital, Selangor. He graduated with an MBBS from the University of Malaya before obtaining MRCP (UK), FRCP (London) and FRCPA (Haem) between 1992 and 2011. He concurrently holds the posts of National Advisor of Clinical Haematology Services and Chairman of the Medical Research Ethics Committee (MREC), Ministry of Health Malaysia.

Dato' Dr. Chang was the past President of the Malaysian Society of Haematology from 2010 to 2013 and continues to be a member of the National Stem Cell Research and Therapy Committee and a member of the Malaysian Society of Transplantation. He has been the Principal Investigator and a Co-investigator in more than 30 multi-centre and multi-national clinical trials and has successfully published over 40 articles in international peer-reviewed journals.

Dato' Dr. Chang recently shared with CRM some of his experiences and insights as a clinician researcher.

Dato', you are currently undertaking several important and leading roles within the hospital and Ministry of Health. How do you still stay active in research and why do you feel it is important to do so?

In the past, I have served as a Principal Investigator for industry-sponsored research (ISR). However, because of my commitments to the MREC, I now mostly undertake the role of a Co-investigator and thus I am still able to stay very much active in clinical research, particularly in investigator initiated research (IIR) whereby I collaborate with teaching institutions to collate data. I believe that it is important for clinicians to design and conduct their own clinical trials to address the health concerns of our region.

Can you share with us some of your research which have been published in top tier journals?

One would be on Hepatitis B Virus Reactivation in B Cell Lymphoma Patients Treated with Rituximab which was published in the European Journal of Cancer. Another would be the Haematological Reference Intervals in a Multi-ethnic Population as well as Polymorphisms in Methylenetetrahydrofolate Reductase Gene and Risk of Non-Hodgkin's Lymphoma in Multi-ethnic Population, published in PLoS One and the Journal of Human Genetics respectively.

What do you see are the challenges that arise when you engage in clinical research?

Firstly, as clinicians, we work in an environment whereby healthcare service is the main thrust. However, when the focus was shifted to driving a research culture among clinicians, clinical research became an added responsibility. I am saying this because research requires its own infrastructure and support staff; but within a hospital setting the laboratory, wards, clinics and healthcare personnel are put in place primarily for clinical service. Thus, we have to take it upon ourselves and rely on our own motivation and commitment to drive an initiative to carry out research. Most often than not, promotion in the government hospitals are mostly based on clinical service output and seniority.

Do you think it will be a good move to have "protected time" to enable clinicians to conduct research?

If there are sufficient number of doctors in the service, it would be worth considering. But this has never happened over my career for the last 28 years. Perhaps the only way is to make clinical research as a private entity and making it happen in a more structured fashion. This means that clinicians can take an unpaid day off from their official duties to conduct clinical research. It definitely is an uphill battle to get clinicians to do trials in terms of finding time and resources.

Nurses station at Haematology ward at Hospital Ampang

Can you briefly describe when you first began conducting trials and how did it go?

I started conducting clinical trials in the late 90's. The first ISR trial was on patients with Chronic Myeloid Leukaemia using Nilotinib. During that time, it was a one-man show. In 2006, when I became the Head of Department, I placed a nurse to solely collect data for clinical trials. Although this was met with disapproval from the Nursing department, I was adamant with my decision as I believe that if you want to do something well, there must be a person carrying out that job full time.

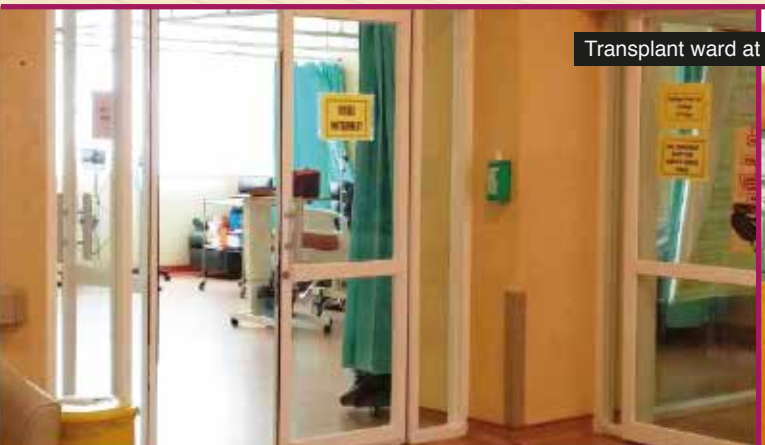
From your experience, what is a common problem that trials in Malaysia face?

Well, in most hospitals we don't have a patient registry. At the end of the day, the clinicians have to estimate the number of patients that they see. More often than not, when clinicians look at the inclusion and exclusion criteria of a trial, they tend to omit the fact that out of the total number of patients that they see, one third will refuse to join the trial, one third will have logistical issues and only one third will give their consent. In Ampang Hospital, we are fortunate to have our own haematology registry, enabling clinicians to give a more accurate projection of the number of patients with certain conditions that we can roughly provide for a trial. At the end of the day, we never promise you what we can't deliver. Thus, I cannot emphasise enough the importance of patient registries at hospitals to tackle patient recruitment issues.

If I may add, the scenario here in Malaysia is different from that in the United States. In Malaysia, our healthcare is paid for by the government. Whereas in the U.S., patients without insurance coverage would either have to fork out money from their own pocket or enter a trial in order to receive treatment. In Malaysia, regardless of a patient consenting to participate in a trial, he or she would just need to pay a minimal fee to receive treatment. This may be another reason why patients do not feel it necessary to participate in a trial. Changing the mind-set of patients to participate in a trial for the purpose of contributing to the betterment of healthcare requires time and continued public awareness.

There are patients who may feel that by participating in a clinical trial, they are being used as guinea pigs. So, how do you go about explaining and alleviating their fears?

It is the clinician's role to convince the patients that the trials are very well monitored and that they are being treated by a group of people who are experts in that field. It is important to educate them that the trial will at no time jeopardise their outcome or survival. This goes to say that at any point in time when a patient has adverse side effects, the treatment will be ceased or if patients want to withdraw from the study, they can do so at any time. The responsibility rests on the clinician to reassure their patients that trials are conducted in a regulated environment and that they won't be harmed. Equally crucial is for the patients themselves to have the mind-set that they are participating in a trial because they want to contribute to the research question.



Transplant ward at Hospital Ampang

As MREC Chairman, what do you see are the common issues that delay the approval process of a trial?

I feel that the website of the National Medical Research Register (NMRR) has too many procedures and steps, thus making it complicated especially for first-timers who are using it. As a matter of fact, these first timers, especially those conducting IIRs, spend 4 to 6 months just to complete an online submission. In the West, I know of private ethics committees that can give approval in a week. These ethics committees are privatised and have a quorum of 5 members. Reviewing and commenting on the proposed trial by these members are done online and submitted to an external private company who will then send it to the contract research organisation (CRO). However, if you were to rely on government agencies whereby its members have their full time clinical practice and are contributing to the ethics approval process on a voluntary basis, it invariably will take longer. For MREC, 6 to 8 weeks is the standard approval timeline.

Finally, how has conducting trials changed the way you manage patient care?

In clinical care, there is a certain degree of subjectivity to the way we diagnose and treat patients, banking on how much experience a clinician has. In contrast, clinical trials happen in a more regulated environment and is very much evidence-based. Clinical trials have been a good training ground for me and I now handle adverse reactions in a different approach. For example, when I administer a certain drug, I make sure that it is because of that particular drug rather than assessing it subjectively. As far as haematology trials are concerned, it provides an alternative option to patients who are refractory to the current medication or not going into remission. This was actually the first reason why I wanted to do clinical trials – to provide access of new or expensive drugs to patients.

New Clinical Trial Clinic at Hospital Tengku Ampuan Rahimah, Klang

Hospital Tengku Ampuan Rahimah (HTAR), on the 2nd of September 2014, launched its first Clinical Trial Clinic which was built with the purpose of creating a conducive and comfortable space for the conduct of clinical trials. Before the setting up of this clinic, clinical investigators and their study team carried out trials at their respective departments, without a particular space dedicated for clinical trials.

The decision to build this clinic started in June 2012 with Clinical Research Malaysia (CRM) agreeing to collaborate with the hospital authorities to help fund the project. By August this year, the renovation of the Clinical Trial Clinic was finally completed. This accomplishment was made possible with tremendous effort and support from the hospital's Clinical Research Centre (CRC) which was primarily sparked by the vision of Dr. Sukumar Mahesan, the Director of Hospital Tengku Ampuan Rahimah, and Dr. Tan Swee Looi, the former Head of CRC at HTAR.

Located at the ground floor of the hospital, the Clinical Trial Clinic is divided into three different sections; a waiting room, procedure room, and a specimen processing area. The clinic is well equipped with an ECG, a patient bed, a vital signs monitor, a fully equipped emergency trolley, centrifuge and a 4 °C and –80 °C refrigerator. There is also a computer for the trial team to record data in a timely manner.

The clinic was designed to provide a comfortable environment for patients enrolled in clinical trials and to provide a conducive venue for study teams to carry out their trials. CRC, CRM and the hospital authorities anticipate that with the establishment of the Clinical Trial Clinic, sponsors and CROs will be encouraged to channel more clinical trials to HTAR, and the clinic at the same time will enable more investigator-initiated studies to be conducted by HTAR's own clinicians.

CRM extends its heartiest congratulations to the CRC team and to the staff and management of HTAR for their significant achievement in developing and putting in place the infrastructure to support the conduct of clinical trials. This achievement can serve as a blueprint for improving other clinical trial sites in Malaysia, especially the public hospitals and medical institutions owned by the Ministry of Health.

Facilities at the new clinical trial clinic.

Guest at the launching

National Agenda To Promote Clinical Research Gets A Boost With Successful Conclusion of the 8th National Conference for Clinical Research

By Communications & Relations Department, Clinical Research Malaysia.

L-R: Dr. Alan Fong (Cardiologist, SGH, & Conference Director), Dr. Shahnaz Murad (Deputy DG, MOH), Dr. Goh Pik Pin (National CRC Head, MOH) & Dr. Jamilah Hashim (Deputy Director, Sarawak State Health Department, MOH)

The 8th National Conference for Clinical Research (NCCR) was successfully concluded from 30th September to 2nd October 2014 in Kuching, Sarawak, the first time the premier event has been held in East Malaysia. This year's edition of the NCCR Conference attracted over 530 delegates, the majority of whom are from the medical fraternity, and featured well-established medical and clinical research experts from Japan, New Zealand, Singapore, South Korea, Thailand and the US, as speakers and panelists.

"This is the biggest crowd we have seen so far which is very encouraging as it shows more and more of our doctors are getting interested in clinical research, while the presence of many foreign experts further indicates that Malaysia is increasingly on the radar screens of the international clinical research community," noted Dr. Goh Pik Pin, an Ophthalmologist and Head of the Ministry of Health Malaysia's Clinical Research Centre (CRC) network.

Held annually, the NCCR Conferences are organized by the CRC with the aim of providing a conducive forum for the sharing of research experiences and the latest scientific and medical breakthroughs, as well as to foster collaboration between Malaysian medical professionals and industry players from the pharmaceutical, medical device and biotech sectors. One of its core objectives is to grow the pool of investigators in Malaysia by attracting and facilitating younger doctors to embark on clinical research.

The three-day 8th NCCR Conference was packed with seven plenaries and six symposium sessions which included more than 30 talks and some 90 poster presentations. Carrying the theme of "Research That Matters", the event brought cutting-edge discoveries and research breakthroughs to the doorstep of local researchers, clinicians and scientists. The opening ceremony was officiated by the Deputy Director-General of Health (Research & Technical Support), Dr. Shahnaz Murad, who represented the Minister of Health, Datuk Seri Dr. S. Subramaniam.

Dr. Goh Pik Pin, Head of the CRC Network, welcoming the participants

MoA to Develop *7 Prime Sites* Inked

This year's conference was extra special in that it witnessed the inking of a tripartite Memorandum of Agreement (MoA) between the CRC (on behalf of the Malaysian Government), Clinical Research Malaysia (CRM) and major industry player Quintiles Malaysia Sdn Bhd. The MoA commits the parties to cooperate together to develop seven prime sites concurrently in Malaysia, a very ambitious undertaking that is already being implemented. According to Quintiles, the Prime Sites programme has the potential to help accelerate the development of new and more effective medicines and medical devices.

In her keynote address, Dr. Shahnaz highlighted that the Prime Site MoA will allow the three parties to improve innovation and industry best practices at the identified seven prime sites. This in turn will make Malaysia more attractive to sponsors and contract research organizations (CROs) and attract more pivotal and higher-value clinical research to Malaysia.

The seven MOH hospitals involved in the Prime Site Programme are Hospital Tengku Ampuan Rahimah (Klang), Hospital Raja Permaisuri Bainun (Ipoh), Hospital Sultanah Nur Bahiyah (Alor Setar), Hospital Raja Perempuan Zainab II (Kota Bharu), Hospital Umum Sarawak (Kuching), Hospital Sibu (Sibu) and Hospital Queen Elizabeth II (Kota Kinabalu).

Dr. Shahnaz Murad
Deputy DG (Research & Technical Support), MOH
Acting CEO of CRM

Lecture by Dr. Swee Tan from Gillies McIndoe Research Institute, NZ

Inking of the Memorandum of Agreement

The 7 Prime Sites

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HOSPITAL RAJA PEREMPUAN ZAINAB II
15586 Kota Bharu, Kelantan

HOSPITAL UMUM SARAWAK
Jalan Hospital, 93586 Kuching, Sarawak

HOSPITAL SIBU
Batu 5 ½ , Jalan Ulu Oya, 96000 Sibu, Sarawak

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Strategic site selection could help reduce study delays

By David Horsburgh
Article reprinted with permission from BioSpectrum Asia

With surveys indicating that 70 percent of clinical trials across Asia, Europe, Canada and Latin America experience delays and only 15 percent of Asian trials are completed on time[1,2] — contributing to higher development costs and delays in getting more efficacious treatments to patients, there are great incentives to isolate the root cause of delays. One key factor is clinical study site selection.

A comprehensive site identification and startup solution is of the essence, considering feasibility, regulatory, documentation, patient recruitment, and perhaps foremost, review of each site's previous trial experience for an indication of how sites are performing.

What about sites without trial experience, called naïve sites in industry parlance. Should a lack of experience be considered a red flag? Quite the contrary, recent analysis using data from 14 studies across Asia conducted by Quintiles suggests that naïve sites could provide a solution to struggling recruitment and reduce the burden of increasing study timelines.

The analysis covered five key therapeutic areas including oncology, diabetes, cardiology, psychiatry, and rheumatology. Based on records in Quintiles internal databases and Clinicaltrial.gov, sites that had conducted protocols were classified as experienced and those that had not conducted prior protocols were classified as naïve. Experienced sites were further grouped according to enrolment performance on their previous studies into high, middle, or low performers.

Results across the 14 studies indicated a vast disparity among experienced sites. While some sites have proven to be capable of high patient enrollment, there are sites that have consistently enrolled at a low level; enrolling 0.28 patients per month or at a rate only 34 percent of what is seen at top performing locations. Most interesting of all however, was naïve sites that were conducting a clinical trial for the first time also regularly enrolled patients at a faster rate than experienced sites with a history of low performance. The average enrollment rate from naïve sites was 0.47 patient per month, which is 68 percent higher than experienced low performers, with this pattern repeated in four out of the five therapeutic areas investigated including oncology, diabetes, cardiology and rheumatology.

The potential of naïve sites was also demonstrated through theoretical enrollment models showing the impact that including these sites could have on reducing overall recruitment timelines. By substituting enrollment data collected from low performing experienced sites with that of naïve sites, there was a significant reduction of timelines by an average of two months per study.

The results of this analysis defy conventional wisdom in site selection and suggest an alternative approach to the current focus on experienced sites. This new approach could involve a conscious effort to include a number of closely-monitored naïve sites in site selection strategies. An analysis of naïve sites may hold the key to a pool of untapped high-potential sites that could reduce study delays and act as a viable alternative to known underperforming sites.

With up to 50 percent of trial sites failing to meet enrollment targets[1], site selection was a hot topic at the recent 2014 Drug Information Association (DIA) conference; where the analysis of this data by Quintiles' Asian feasibility team was recognized as the best professional poster out of more than 90 participating posters.

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1. Tufts Center for the Study of Drug Development Report, Jan 2013, http://csdd.tufts.edu/files/uploads/02_-_jan_15,_2013_-_recruitment-retention.pdf
2. CenterWatch Surveys of Asian (2006, n=156), Latin American (2005, n=317), and European and Canadian (2006, n=356) investigative sites

INDUSTRY News

GSK update on current development status of the GSK/NIH Ebola vaccine candidate

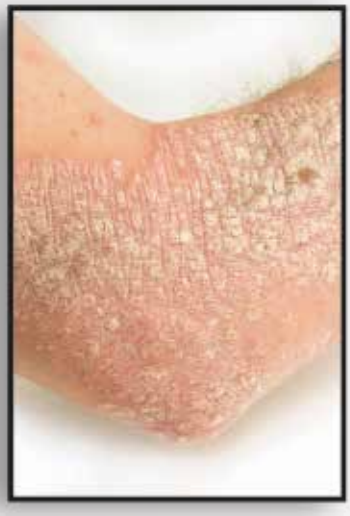
London London UK -- 18 October 2014 -- With the Ebola crisis in west Africa continuing, GSK is working closely with the World Health Organization (WHO), regulators and other partners to respond to the outbreak, to accelerate development of its investigational Ebola vaccine and to ramp up production as quickly as possible. Development of the vaccine candidate is progressing at an unprecedented rate, with first Phase 1 safety trials with the vaccine candidate underway in the USA, UK and Mali, and further trials due to start in the coming weeks.

Source: http://www.drugs.com/clinical_trials.html

FDA approves Lutonix 035 DCB – First drug-coated angioplasty balloon catheter to treat vascular disease

October 10, 2014 -- The U.S. Food and Drug Administration today approved the Lutonix 035 Drug Coated Balloon Percutaneous Transluminal Angioplasty Catheter (Lutonix DCB). This is the first drug-coated balloon used to re-open arteries in the thigh (superficial femoral arteries) and knee (popliteal arteries) when narrowed or blocked as a result of peripheral artery disease (PAD).

Source: http://www.drugs.com/clinical_trials.html



Amgen and AstraZeneca announce positive results from third and final pivotal Phase 3 study of Brodalumab

THOUSAND OAKS, Calif. and LONDON, Nov. 25, 2014 /PRNewswire/ -- Amgen (NASDAQ: AMGN) and AstraZeneca (NYSE: AZN) today announced that AMAGINE-2TM, a pivotal, multi-arm Phase 3 trial evaluating two doses of brodalumab in more than 1,800 patients with moderate-to-severe plaque psoriasis, met its primary endpoints when compared with both Stelara® (ustekinumab) and placebo at week 12. Brodalumab 210 mg given every two weeks and the brodalumab weight-based analysis group were each shown to be superior to Stelara on the primary endpoint of achieving total clearance of skin disease, as measured by the Psoriasis Area Severity Index (PASI 100). When compared with placebo, a significantly greater proportion of patients treated with brodalumab achieved at least a 75 percent improvement from baseline in disease severity at week 12, as measured by the Psoriasis Area Severity Index (PASI 75). A significantly greater proportion of patients treated with brodalumab also achieved clear or almost clear skin at week 12 compared with placebo, according to the static Physician Global Assessment (sPGA 0 or 1).

Source: http://www.drugs.com/clinical_trials.html

Malaysia is the Second Highest Recruiter for the REDUCE Study

Zwolle, The Netherlands – 6 December – Malaysia is the second highest recruiter after the Netherlands in the REDUCE study. This study, which is a randomized controlled trial, compares the 3-mo vs 12-mo of dual antiplatelets therapy after the implantation of a new generation of coronary stent, called COMBO, which combined two technology on the stents. The stents elute cytotoxic Sirolimus to reduce intimal hyperplasia, while the abluminal surface of stent is coated with bioengineered endothelial progenitor cell (EPC) capturing monoclonal antibody. Together, the combination reduces risk of in-stent restenosis, and enhanced re-endothelialization of the stent. The latter effect promote healing, and potentially reduced the risk of stent thrombosis. The prospective study will provide the much needed evidence of efficacy and safety of shorter duration of dual antiplatelets therapy.

Of the 114 patients recruited in Europe and Asia, Queen Elizabeth II Hospital (Sabah), University Malaya Medical Centre (Kuala Lumpur) and the National Heart Institute (Kuala Lumpur) contributed 11, 10 and 2 patients respectively. By comparison, the top recruiter Netherlands managed to enrol 80 patients. The patient recruitment target for the REDUCE clinical study is to enroll 1500 patients by the end of 2015.

Source: REDUCE Study Newsletter

News & Discoveries
Haematology

Newly donated blood reduces complications from heart surgery, study shows

Heart surgery patients who received newly donated blood have significantly fewer post-operative complications than those who received blood that had been donated more than two weeks before their surgery, a study presented at the Canadian Cardiovascular Congress has shown.

Source: Heart and Stroke Foundation of Canada (27 October 2014)
Photo by: Institute Jantung Negara (IJN), Malaysia

Blood test may help diagnose pancreatic cancer

Cancer researchers have found that a simple blood test might help diagnose pancreatic cancer, one of the most deadly forms of the disease. They report that they have found that several microRNAs – small RNA molecules – circulate at high levels in the blood of pancreatic cancer patients, which may be detectable through a simple blood test.

Source: Indiana University (28 October 2014)

Obese youth with leukaemia more likely to have persistent disease

Obese youths with acute lymphoblastic leukemia (ALL) are known to have worse outcomes than their lean counterparts. To find out why, investigators at Children's Hospital Los Angeles studied patients who were obese at the time of their diagnosis with ALL to determine if body mass index (BMI) impacted response to initial chemotherapy. This response to initial chemotherapy (or induction therapy) is measured by the absence of leukemia cells in the bone marrow. Called minimal residual disease (MRD), in which residual leukemia cells cannot be seen under microscope but can be detected by more sensitive methods, it is among the strongest predictors of long-term survival and disease recurrence. As reported in First Edition of the journal Blood on October 27, following induction chemotherapy, obese patients were more than twice as likely to have minimal residual disease, than non-obese patients.

Source: Children's Hospital Los Angeles Saban Research Institute (27 October 2014)

Many older people have mutations linked to leukemia, lymphoma in their blood cells

At least 2 percent of people over age 40 and 5 percent of people over 70 have mutations linked to leukemia and lymphoma in their blood cells, according to new research. Mutations in the body's cells randomly accumulate as part of the aging process, and most are harmless. For some people, genetic changes in blood cells can develop in genes that play roles in initiating leukemia and lymphoma even though such people don't have the blood cancers, scientists report.

Source: Washington University in St. Louis (19 October 2014)Source: Washington University in St. Louis (19 October 2014)

Third quarter 2014 in photos

NCSM: Relay for Life Malaysia
Dataran Petaling Jaya

NCCR Conference & Exhibition
Kuching, Sarawak

6th Sarawak State Health Research Day
Sarawak General Hospital, Kuching

Gorgaden Pharmaceuticals visit to CRM
CRM HQ, Petaling Jaya

CME- Opthalmology Department
Kuala Lumpur Hospital

Kelantan State Research Day
Raja Perempuan Zainab II Hospital, Kelantan

CRC Clinical Trial Clinic Launching
Tengku Ampuan Rahimah Hospital, Klang

About CLINICAL RESEARCH MALAYSIA

Clinical Research Malaysia (CRM) is a non-profit organization wholly owned by the Government of Malaysia. CRM was established in June 2012 to position Malaysia as a preferred global destination for industry-sponsored research (ISR), and to function as an enabler and facilitator to the industry and medical fraternity.

By working with other stakeholders, CRM strives to improve the local ecosystem to support growth in ISR, facilitate the needs and requirements of industry players, grow the pool of capable investigators, support staff and trial sites, and improve their capabilities and capacities to conduct ISR.

With the Ministry of Health's backing and clear knowledge of the local research environment, CRM is able to provide sponsors (primarily from the pharmaceutical, biotech and medical device industries) and contract research organizations (CRO) with an extensive range of services that includes feasibility studies, investigator selection, site research associates, management of trial budget, review of clinical trial agreements and updates on local laws, guidelines and regulations. CRM also undertakes marketing and promotional activities to build industry awareness about the opportunities for ISR in Malaysia, and create public and patient awareness of clinical trials.

Publish in the CRM bulletin

We welcome submissions of feature articles, write-ups and events related to industry sponsored clinical research for publishing in the CRM bulletin, which is issued quarterly. You can send your submission to contact@clinicalresearch.my or contact us at +60 3 7960 5153 should you have any queries. CRM has the right to edit any submission to suit the needs of the bulletin.

Collage of CRM Activities in the 3rd Quarter 2014

Life Beyond Breast Cancer

19-21 March 2015
Connexion@Nexus
Bangsar South City
Kuala Lumpur

Teaching Symposium for Survivors

Benefits of Attending :
Learn New Therapies in Breast Cancer
Understand Genetic Risks of Breast Cancer
Fertility & Pregnancy - Know Your Options
10 years Tamoxifen - Yes or No?

Who Should Attend:
Survivors, Care Givers, Doctors
Nurses : Breast Care / Oncology / General Nursing

Organised by :

PINK RIBBON™
Wellness (L) Foundation

Partners :

CRM
CLINICAL RESEARCH MALAYSIA
Your Global Solutions in One Nation

Rotary Club of Bangsar

CONNEXION @ NEXUS

Registration Fee :
RM600 per pax
(after 40% subsidy)

Registration fee will cover all conference sessions, conference kit, exhibition, coffee breaks, all lunches, welcome reception (19 March 2015), themed dinner party (20 March 2015) and 2 nights at 4-star apartment hotel on 19 & 20 March 2015

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