By Clinical Research Malaysia

CRM bulletin

of Clinical Research and Therapy

ISSUE 12

KNOWING CLINICAL TRIALS 101

Esketamine Trial – A Success Story in Patient Recruitment

UP CLOSE & PERSONAL

Canvassing: Recruitment of Patients with Rare Condition in Clinical Trials

RESEARCH PERSONALITY

Dr. Ong Tiong Kiam

Clinical Trials Day 2017 : A Day to Remember

FEATURED SITE

Hospital Raja Permaisuri Bainun

TAPPING INTO THE NATION'S STRENGTH

ABOUT CLINICAL RESEARCH MALAYSIA

Clinical Research Malaysia (CRM) exists to advance global health solutions for a brighter, more hopeful future for the people by providing speedy and reliable end-to-end clinical research support for quality studies. As these studies unfold, we work together with our partners to create an impetus in delivering better treatment to our end consumers, while at the same time creating high-skilled job opportunities.

The strength of our operation lies in our innate understanding of the local clinical research landscape and implementation of international standards. This, when considered in parallel to the fundamental backing of the government ministries, provides us with an incomparable advantage, as we work hand-in-hand with our partners from the nascent stages of development to materialisation of the end product.

In the journey towards a brighter and better future, we facilitate the entry of industry-sponsored research into Malaysia, working closely with the government and relevant authorities to ensure that all regulations and best practices are met.

In CRM, we credit the outstanding performance to the team we have anchored from within our organisation. Their endless pursuit of innovation and continuous improvement have propelled CRM forward to optimise the opportunities that come our way. In tandem with our passion for the clinical research landscape, we ensure core values of transparency, honesty, accountability and trustworthiness resonate throughout CRM. These qualities are also cascaded to our principal investigators and Study Coordinators, who act as the catalysts of the clinical research process.

As CRM vouches for an aspiring future in the clinical research industry, we have implemented mechanisms to expand hospital capacity for clinical trials and tests. This is possible by tapping into our vast talent pool consisting of principal investigators and medical assistants.

MINISTRY OF HEALTH MALAYSIA

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FROM THE CEO's DESK

As we move into the third quarter of the year, several of our investigators have received recognition from sponsors/CROs for being the highest recruiter in their respective trials. In doing so, they have placed Malaysia in the global clinical research map by being one of the top recruiters among countries like South Korea, Japan and Taiwan. It gives me great pride knowing that we have become a force to be reckon with in this clinical research industry.

I am proud to introduce a revamp section highlighting Malaysian doctors' clinical paper publications.

One of CRM's streategy is to create awareness of clinical trials. The Clinical Trials Day and the I Am Aware campaign which is a patient engagement program has moved the nation a step ahead in creating clinical trial awareness. This effort would not be possible without the support from the Clinical Research Centers across the nation.

As part of completing the clinical research ecosystem in phase 1 clinical trials, CRM is sponsoring the National Pharmaceutical Regulatory Agency (NPRA) officers to develop their knowledge and capability in phase 1 studies at a globally recognized institution for one year. The Guideline for Phase 1 Clinical Trials has also went through its final review and we plan to launch it very soon. I must stress that collaboration with all stakeholders and industry players is imperative in creating a comprehensive landscape for clinical research.

Read more about the rest of our initiatives, research projects and personalities in this issue of the bulletin.

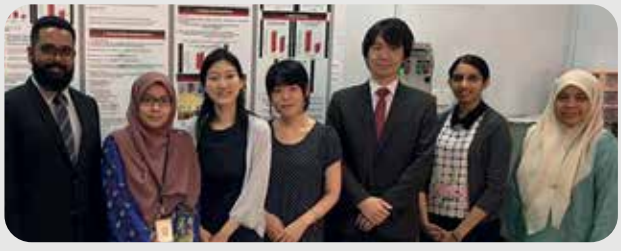
Placing Clinical Trials in the Limelight

PETALING JAYA, 18 July 2017 – Clinical Research Malaysia held a briefing session with the various press and media agencies to share about clinical research in Malaysia. Puan Nor Hizan Abd Rahman, a clinical trial patient, was also present to share her experience participating in a clinical trial.

The aim of this media briefing is to offer journalists and others from the media an opportunity to understand better the existence of a highly regulated clinical trial process to ensure patient safety in Malaysia, and how it can improve healthcare outcomes. This will enable better and factual reporting of clinical trials to the public in the near future.

'BRILLIANT' Performance by MoH Investigators

12 July 2017 – In the second quarter of this year, two of our MOH investigators had shown good subject enrollment at their respective sites. Dr. Nor'Izam Md. Alias of Hospital Tuanku Ja'afar was awarded the Top Recruiter Award for the BRILLIANTStudy for successfully enrolling 8 subjects. The BRILLIANT Study is on Blonanserin, an innovative transdermal formulation in antipsychotics.



Dr. Ruzita Jamaluddin (pic), the Head of Psychiatry Department of Hospital Tuanku Fauziah was awarded the STAR Recruiter Award for enrolling 5 subjects. Her achievement has been made after only 3 months since site activation. So far, her site has managed to screen 11 and randomized 8 subjects. This is an impressive accomplishment to the research team at Hospital Tuanku Fauziah as the site has been very new to clinical trials. This serves as an encouragement for other specialists to take up trials at that site. More industry sponsored research (ISR) trials are expected to be conducted at this site and the team is already seeing a growing interest among specialists in participating in ISR.

CRM Industry Sponsored Research Award 2017

PUTRAJAYA, 16 May 2017 – The CRM Industry Sponsored Research (ISR) Award is given out each year to outstanding Principle Investigators and clinical trial sites for their contribution in ISR, as well as to spur and encourage more of such efforts in the future. This year, CRM recognized several clinical trial sites and investigator for their contribution in last year's industry sponsored research.

CRM ISR Award Recipients:

- Dr. Rosaida bt Hj. Md Said (Hospital Ampang) – Highest number of positive responses in feasibilities studies in 2016.
- Sarawak General Hospital – Highest number of newly approved oncology clinical trials in 2016.
- Sarawak General Hospital, Heart Centre – Highest number of newly approved cardiology clinical trials.
- Hospital Putrajaya and Hospital Raja Perempuan Zainab II – Highest number of newly approved endocrinology clinical trials in 2016.
- Klinik Kesihatan Greentown – Highest number of newly approved trials among primary health clinics in Malaysia in 2016.

Clinical Trials Day 2017

A Day to Remember

PUTRAJAYA, 16 May 2017 – National Cancer Institute, the country's referral centre for cancer patients, witnessed the country's first Clinical Trials Day which saw the convergence of medical professionals involved in clinical research, patients, industry players, academia as well as patient support groups under one roof. This event, organised by Clinical Research Malaysia (CRM) in collaboration with the National Cancer Institute (NCI) and the Clinical Research Centre (CRC), is aimed at elevating the awareness level of clinical trials among the medical fraternity and general public.

As a run up to the Clinical Trials Day, a series of 'I AM AWARE' roadshows were held across the nation, driving awareness on the importance as well as benefits of participating in clinical trials among the general public. The roadshows were held at nine Ministry of Health (MOH) hospitals and two universities, and from there successfully registered close to 2,000 patients and volunteers. The roadshows are part of CRM's ongoing efforts in enhancing the current clinical research ecosystem in Malaysia by ensuring a robust pool of patients and volunteers for trials, while at the same time continuously investing in the infrastructure of qualified personnel, state-of-the-art clinical trial sites and stringent regulatory reviews.

"We aim to replicate the success we have achieved today and continuously grow the public's knowledge around the importance and benefits of clinical trials. This initiative is one of CRM's fundamental mandates to further strengthen Malaysia's clinical research landscape and offerings on the global stage" said Dr. Akhmal Yusof, CEO of CRM. The launching of Clinical Trials Day was officiated by the Minister of Health, Datuk Seri Dr. S. Subramaniam, and witnessed by the Secretary General, Ministry of Health, Datuk Dr. Chen Chew Min, Deputy Director-General of Health (Research & Technical Support), Datuk Dr. Shahnaz Murad, National Director of CRC, Dr. Goh Pik Pin, Director of NCI, Dr. Asmayani Khalib and CEO of CRM, Dr. Akhmal Yusof. Among the sessions that were held during that day include a forum on cancer patient support, career pathways in clinical research, and a case study of a clinical trial patient

Patient with nasogastric (NG) tube.
Copyright : Mr Mohd Hasif Jaafar

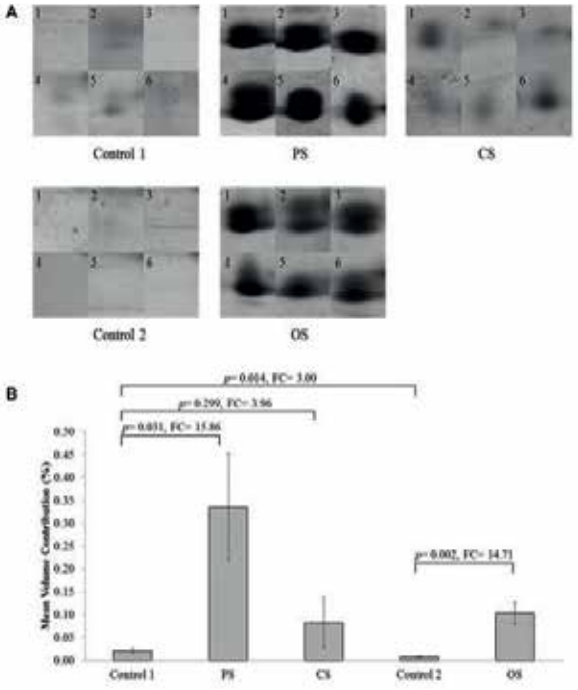
Artificial Tube Feeding in Older Adults: A Complex and Challenging Issue in Asia

Researchers from University of Malaya uncover significant obstacles to appropriate feeding for older Asians with swallowing difficulty. These obstacles involved cultural attitudes, healthcare professional perceptions and knowledge and limitations of healthcare funding, resulting in a poorer outcome for older Asians with swallowing problems.

To understand the decisions and choices made by healthcare professionals in Malaysia further, the researchers then conducted a qualitative study in a single institution, among various healthcare professionals at University Malaya Medical Centre. They revealed that major factors that influenced decision making included lack of financial support, poor knowledge among healthcare professionals, inadequate competency and skills, and insufficient information given to patients and caregivers regarding PEG tube feeding.

Further directed education of healthcare professionals is required and this needs to be done by the relevant professional organizations. It is anticipated that locally conducted clinical studies highlighting the benefits of PEG over NG feeding in Asian older patients, will help to change the attitudes of healthcare professionals in Malaysia.

Source: Asia Research News (June 16, 2017)



Cropped images of SAA spots and densitometry analysis of 2DE gels. (A) Six representative biological replicates of SAA spots from different 2DE gels for healthy adults (Control 1), PS patients, CS patients, healthy adolescents (Control 2), and patients with OS. (B) Mean percentage of volume contribution of SAA as analyzed by densitometry from 2DE gels (mean ± SEM). Copyright : Electrophoresis (2016) 37 (17-18): 2328-2337

Levels of Serum Amyloid A in Bone Sarcomas Patients: Indicator of Tumor Malignancy?

In a recent study published in Electrophoresis, University of Malaya's researchers found significant correlation between increased levels of serum amyloid A (SAA) in patients with three different bone sarcomas: pleomorphic sarcoma (PS), osteosarcoma (OS) and chondrosarcoma (CS) and the different degrees of tumor malignancy in PS, OS and CS.

Upregulated levels of SAA, particularly isoform SAA1, were found to be more apparent in patients with PS and OS as opposed to those with CS. This suggested that the contrasting increased levels of SAA in patients with PS, OS, and CS may be related to the different degrees of tumor malignancy. Thus, SAA has a potential to be developed into prognostic biomarker although this requires further validation in clinically representative populations. The levels of SAA should also be clinically investigated for use as a discriminative indicator of treatment efficiency and/or a signal for relapse.

Source: Asia Research News (June 19, 2017)

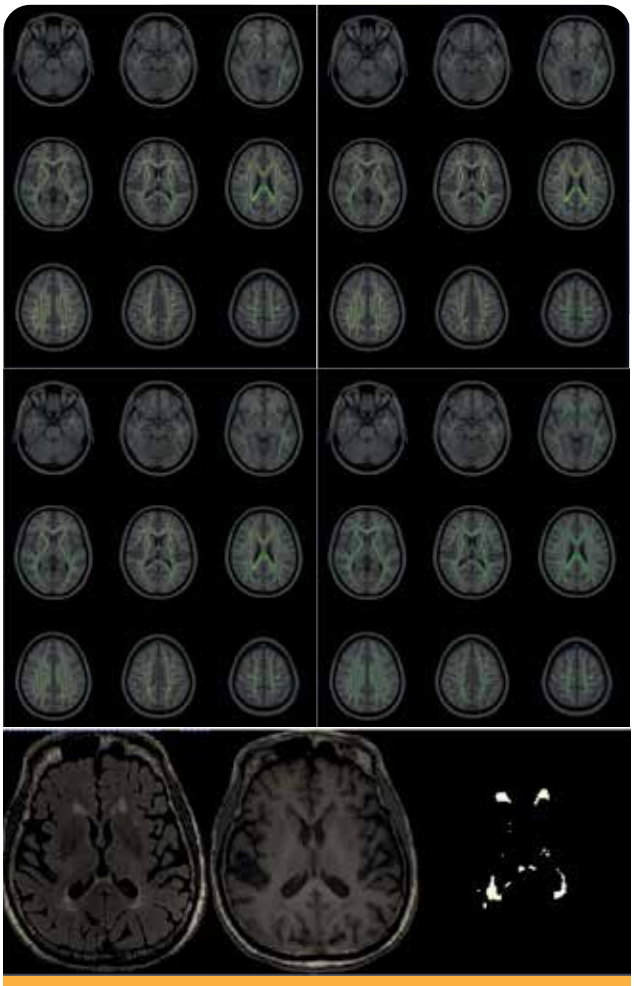
Improving the Survival Rates of Childhood Brain Tumours: Translating Discoveries

The future of children with brain tumours is very promising. To do nothing is to ignore the very real possibility of a treatment and cure. It is the time now to accelerate clinical and laboratory research in childhood brain tumours.

At the University of Malaya Medical Centre (UMMC), the care and long-term multidisciplinary follow-up for children with brain tumours are co-ordinated by the Paediatric Hematology-Oncology Unit. The UMMC team follows more than 150 brain tumour patients, from infancy through adulthood in outpatient oncology clinics and approximately 10-15 children and adolescents with brain tumours are diagnosed every year. A multidisciplinary neuro-oncology team was formed in 2013 comprising paediatric oncologists, neurosurgeons, radiotherapists, clinical oncologists, neuropathologists and radiologists.

Paediatric neuro-oncology has advanced significantly especially in the past 5 years. Whole genomic analysis of the entire spectrum of paediatric brain tumours has afforded an opportunity to the paediatric neuro-oncology community to reconsider current treatment strategies and design better therapeutic solutions for children with brain tumours. Realistically, however the incorporation of tumour genomic information into "standard" treatment protocols is a major challenge in low and middle income countries due to its high cost. Nevertheless, the paediatric oncology team in University of Malaya will implement several collaborative strategies with international partners over the next 5-10 years to allow children from this region to benefit from personalized therapy for a wide spectrum of brain cancers.

Source: Asia Research News (July 12, 2017)



Is Microstructural Integrity of White Matter Tracts Affected in Older Fallers? A DTI Study.

Researchers from Malaysia assessed the whole brain microstructural integrity of major nerve tracts among older fallers and non-fallers. They proposed the potential synergistic relationship between blood pressure fluctuations with standing, balance disorders and structural brain abnormalities observed among fallers.

This Diffusion Tensor Imaging (DTI) aspect of this study helps to understand further the neurobiology underpinning movement and coordination disturbances in older population with falls. It may also serve as potential biomarkers in future falls intervention trials.

Source: Asia Research News (July 13, 2017)

Dr. Ong Tiong Kiam

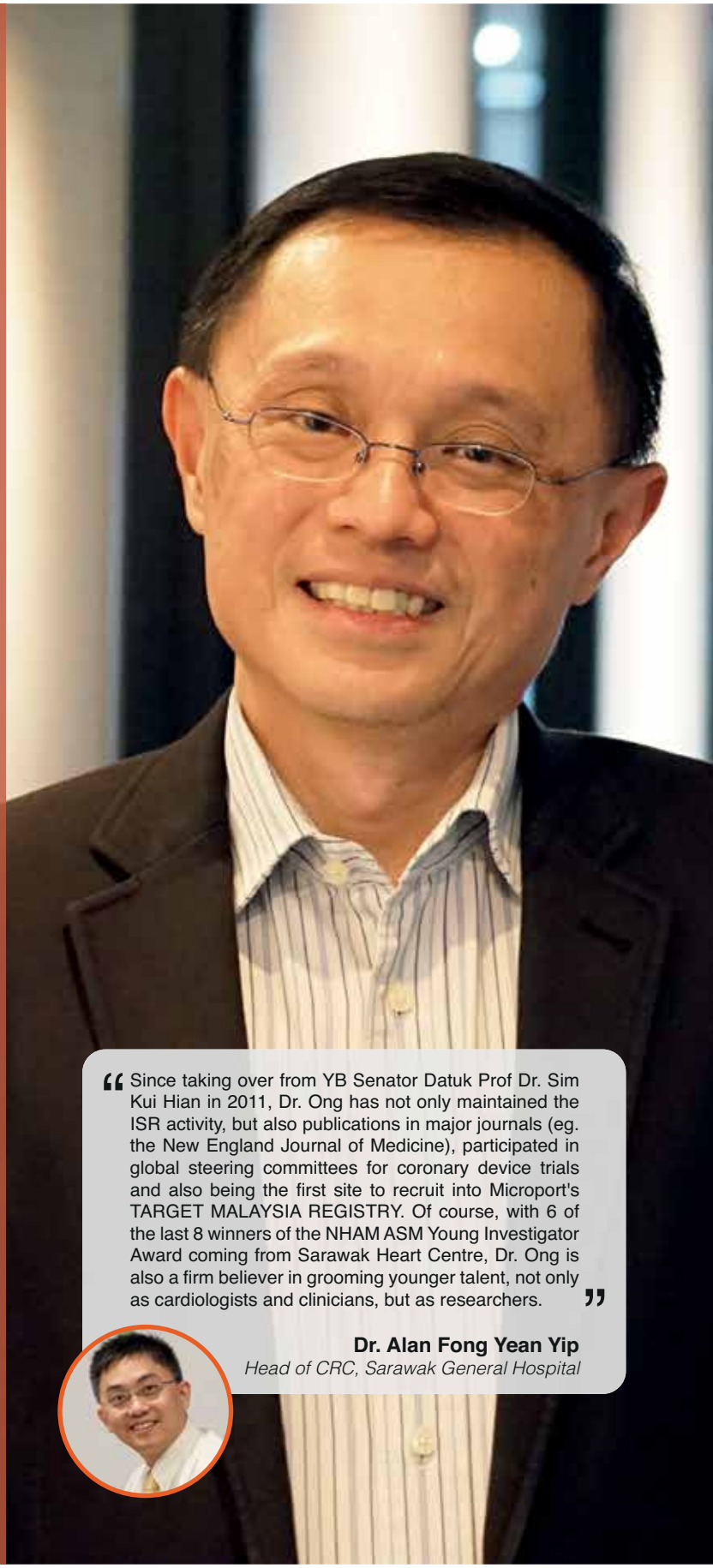
MBBS, MRCP, FAPSIC, FRCP, FNHAM, FACC, FESC, FAsCC

Senior Consultant Cardiologist & Head of Department of Cardiology, Sarawak General Hospital Heart Centre, Malaysia

Dr. Ong Tiong Kiam is currently a Senior Consultant Cardiologist and Head of Department of Cardiology at the Sarawak General Hospital Heart Centre, Malaysia. He earned his medical degree from the University of New South Wales, Australia and went on further to obtain several other professional qualifications. Besides his current responsibility as a Course Director for Siemens Clinical Training Workshop on Cardiac CT, he is Adjunct Lecturer at the Faculty of Medicine & Health Sciences, UNIMAS, Visiting Consultant Cardiologist at Kuching Specialist Hospital and a Member of the Credentialing Committee for the National Specialist Register Subcommittee for Cardiology.

Dr. Ong is an active member of various professional bodies such as the National Heart Association of Malaysia, Society of Pacing and Cardiac Electrophysiology of Malaysia, Society of Cardiovascular Computed Tomography and the Asia Pacific Society of Interventional Cardiology.

He has an impressive track record in conducting investigator initiated and industry-sponsored research (ISR). Since 2002, he was Principal Investigator and Co-Investigator for almost 90 trials. He has also authored numerous papers reporting clinical findings in international peer-reviewed journals. His latest publication was accepted and published in the International Journal of Cardiology and BMJ Open. Despite his busy schedule, Dr. Ong has presented at various international meetings on his areas of expertise.



> “Since taking over from YB Senator Datuk Prof Dr. Sim Kui Hian in 2011, Dr. Ong has not only maintained the ISR activity, but also publications in major journals (eg. the New England Journal of Medicine), participated in global steering committees for coronary device trials and also being the first site to recruit into Microport's TARGET MALAYSIA REGISTRY. Of course, with 6 of the last 8 winners of the NHAM ASM Young Investigator Award coming from Sarawak Heart Centre, Dr. Ong is also a firm believer in grooming younger talent, not only as cardiologists and clinicians, but as researchers.”

Dr. Alan Fong Yean Yip
Head of CRC, Sarawak General Hospital

Can you tell us how did you first got involved in research and where does this interest stem from?

My research career started in 2002 when I joined the Department of Cardiology. It was my former boss, Dr. Sim Kui Hian, who introduced research to me. He was instrumental in bringing many industry sponsored research to our department. I think for an institution to become a great research centre, it needs a champion. Someone who is passionate about research and can disseminate that enthusiasm to the rest of the team.

You have authored many clinical research papers and have successfully published them in internationally renowned medical journals like the New England Journal of Medicine. How do you find time writing research papers despite your busy schedules in clinical work and conducting research?

Doing research and writing papers for publication are not easy, especially when one works in a public institution where the demands of the service can be quite exhausting. It requires a lot of discipline and sacrifice because most of the work is done outside office hours. Collaboration with other investigators and co-authors is important. Writing a paper becomes a lot easier when different people are allocated separate roles, e.g., one person responsible for coming up with the draft and another person or persons helping with the corrections and revisions. In other words, team work is crucial.

The Sarawak General Hospital Heart Centre has recently been conferred the ISR Award for the Highest Number of Cardiology Clinical Trials for 2016. How do you motivate your study team to achieve and be where they are today?

To ensure that everyone doing research remains motivated and enthusiastic, it is important to share not just the work load but also the reward. A research project should not be allocated to only a few individuals. Everyone should get involved. For instance, all our cardiologists are sub-investigators for every trial conducted at our centre. Appreciation is shown to those directly or indirectly involved in various forms, such as financial support to attend conferences or provision of facilities such as internet access, computers and photocopiers. The opportunity to have one's name listed in a journal publication is also a strong motivating factor.

What do you think are the barriers that prevents most doctors from participating in clinical research?

Most doctors have difficulty finding time to do research. The demands of the service can be quite overwhelming. In MOH institutions, unlike universities, doctors are usually not given protected time off to do research.

Why do you think it is important for doctors to take part in clinical research?

Doctors who do not take part in research will be blindly treating patients based on the recommendations of other doctors or pharmaceutical companies. Participating in research, however, will introduce them to the pitfalls of research such as a bad study design or wrong statistical analysis that could lead to a false conclusion. It allows them to be pioneers in the usage of new compounds or devices, even before these products become commercially available. Certain types of research also give their patients access to expensive treatment that would have been unaffordable or inaccessible to them.

RESEARCH PERSONALITY

What one word best describes your career as a clinical researcher/investigator? Why?

Rewarding. Doing research deepens my understanding of the disease for which the treatment is being tested. It can also be very gratifying when the study result eventually turns out to be positive and a new or more effective treatment becomes available to my patients. Knowing that I had contributed to the development of this new treatment is very satisfying.

In your years of experience as an investigator, is there any particular clinical trial which have left a mark in your career? Why?

I don't think there's any trial that stands up above all the rest. All clinical trials, big or small, positive or negative, are important and will contribute to scientific knowledge that can be used to improve patient care.

With the current services provided by CRM, how else do you think CRM can support investigators?

The biggest challenge faced by doctors is finding time to do research. Clearly, having a good research assistant or coordinator is a great bonus. If CRM can provide this service on a regular basis, more investigators might have less hesitation to take up clinical trials.

Do you think that Malaysia has what it takes to be on par with the rest of Asia when it comes to conducting high quality clinical trials? If no, what are we still lacking and what can we leverage on? If yes, what can we do more?

I have attended many investigators meetings, and sit on the global expert panels of several international trials. I would say that the quality of ISR in Malaysia in on par with the rest of Asia. In fact, we are probably better than many other countries in Asia.

In the field of clinical research, where do you wish to see Malaysia in the next 10 years?

Malaysia has enormous potential in clinical research. More and more doctors are realizing the importance and value of doing research in addition to routine clinical service. We have a diverse population with a wide range of diseases who are often quite willing to participate in clinical trials. I think in 10 years' time, the number of clinical investigators in Malaysia will have increased tremendously. The only concern is that as our patient population become more educated or informed, there might be increased reluctance to volunteer to participate in clinical trials, similar to the current situation in Singapore.

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The journey of a clinician researcher on NAFLD in Malaysia:

From epidemiology to non-invasive assessment to treatment

Non-alcoholic fatty liver disease (NAFLD) is characterized by the accumulation of fat in the liver, and is the result of over-nutrition. The prevalence of NAFLD has been increasing in recent years and parallels the increase in prevalence of obesity. Non-alcoholic steatohepatitis (NASH), the more severe form of NAFLD, is characterized by inflammation and ballooning of liver cells, and can lead to scarring of the liver. Scarring of the liver can progress to cirrhosis and eventually liver failure. NASH patients are also at increased risk of developing liver cancer, especially in the presence of excessive scarring in the liver. NAFLD is now recognized as one of the most common causes of chronic liver disease worldwide. The impact of the disease is big in countries such as Malaysia where the prevalence of obesity is high. NAFLD is also closely related to diabetes mellitus, hypertension and dyslipidemia, and patients with NAFLD are more susceptible to cardiovascular diseases as well as certain cancers.

A group of dedicated clinician researchers at the University of Malaya and the University of Malaya Medical Centre has been actively conducting research work on NAFLD for nearly a decade. Their effort has contributed to most of the published work on NAFLD in Malaysia found in the literature today, which includes the epidemiology of the disease, non-invasive methods for assessment of disease severity, and treatment. "My work on NAFLD started with a research project looking at the progression of the disease using paired liver biopsy.(1) As my interest in the subject grew, I started doing several other research projects, and the rest was history," said Dr. Chan Wah Kheong, who is Associate Professor at the Faculty of Medicine, University of Malaya, and an instrumental figure in NAFLD research there. "It is certainly not easy to juggle clinical work, research work and teaching, but when you know that your work has made a difference, you will find that the sacrifices were worth it," quipped Dr. Chan, who completed his PhD in NAFLD while teaching undergraduate and postgraduate students, and providing clinical service as a Consultant Physician and Gastroenterologist at the University of Malaya Medical Centre. "I hope the work that has been done will form the foundation for future work that will further enhance our understanding of NAFLD and eventually benefit all patients with the disease," he added.

Epidemiology of NAFLD

The prevalence of NAFLD in the general population was estimated to be 23% based on a study using ultrasonography on health check individuals in a private medical centre in Petaling Jaya about a decade ago.(2) "The work by Professor Dato Dr. Goh Khean Lee and his colleagues, provided primary data on the estimated prevalence of NAFLD in the general population in Malaysia," said Dr. Chan. Recently, the prevalence of NAFLD was found to be 57% based on a study using Fibroscan on health check individuals in a public medical facility in Kuala Lumpur. The study also found that 18% of the individuals had liver stiffness measurement consistent with excessive scarring in the liver.(3) "The figures from our latest work are indeed worrisome. More concerted efforts are needed to tackle obesity and obesity-related disease such as NAFLD," he said. The group also reported that

Dr. Chan is Associate Professor of Medicine at the University of Malaya and Consultant Physician and Gastroenterologist at the University of Malaya Medical Centre and the University of Malaya Specialist Centre. He graduated with distinction from the University of Malaya in 2005 and obtained the Membership of the Royal Colleges of Physicians of the United Kingdom in 2008. He served at the Kuala Lumpur General Hospital at the beginning of his career and subsequently returned to his alma mater in 2010 where he actively contributed to clinical, research and educational work. He completed his Ph.D. on non-alcoholic fatty liver disease (NAFLD) at the University of Malaya in 2015 and is a Member of the Academy of Medicine of Malaysia and a Committee Member for the Malaysian Society of Gastroenterology and Hepatology. He has published numerous papers in peer-reviewed journals and presented in both local and international conferences. He is also a reviewer for several international journals. His areas of special interest include diagnostic and therapeutic gastrointestinal endoscopy, viral hepatitis B and C, and non-alcoholic fatty liver disease.

half of the patients with diabetes mellitus seen at their hospital clinic had NAFLD,(4) and 8% of the students at their faculty had NAFLD.(5)

Non-invasive tests for NAFLD

Dr. Chan and his team was the first to report on the controlled attenuation parameter (CAP) for the detection and quantification of hepatic steatosis, specifically in NAFLD patients.(6) CAP is the decrease in the amplitude of ultrasound as it is propagated through liver tissue and can be estimated using the same radio-frequency data that is used for liver stiffness measurement using Fibroscan. "In our study on 101 biopsy-proven NAFLD patients, we found CAP to be excellent for the detection of significant hepatic steatosis. However, its accuracy was impaired by an increased body mass index, and it was less accurate to distinguish between the different grades of hepatic steatosis," explained Dr. Chan. Data from the work was subsequently combined in an international, multi-centre effort led by researchers from the University of Leipzig, Germany, that produced important reference cut-offs for CAP for the diagnosis of the different grades of hepatic steatosis.(7) Together with researchers from the Chinese University of Hong Kong, the group was also the first to report on CAP obtained using the XL probe for the detection and quantification of hepatic steatosis, specifically in NAFLD patients, using histology as reference standard.(8) "In the study on 57 biopsy-proven NAFLD patients with liver stiffness measurements using both the M and XL probes, we found both probes to have comparable accuracy for the diagnosis of the different grades of hepatic steatosis. Further work on whether similar cut-offs could be used for both the M and XL probes for the diagnosis of the different stages of hepatic steatosis is currently underway," he added excitedly.

The group also reported a 2-step approach for the assessment of the presence or absence of advanced fibrosis in NAFLD patients.(9) "The NAFLD fibrosis score has been used for identifying NAFLD patients with and without advanced fibrosis. However, 20-58% of patients would have an indeterminate score. Liver stiffness measurement using Fibroscan has been shown to have excellent accuracy for the exclusion of significant fibrosis and for the diagnosis of cirrhosis. However, it is less accurate for the diagnosis of advanced fibrosis. Moreover, it is not widely available. Patients with a low NAFLD fibrosis score are unlikely to have advanced fibrosis. Liver stiffness measurement by Fibroscan in patients with low NAFLD fibrosis score could lead to discordant results in over 30% of patients, and may lead to a liver biopsy being performed unnecessarily. Hence, we recommend using liver stiffness measurement by Fibroscan for diagnosis of advanced fibrosis only for those patients with indeterminate and high NAFLD fibrosis score. This can maintain the accuracy of identifying patients with advanced fibrosis and at the same time reduce the need for a liver biopsy. Moreover, only about one third of patients would require liver stiffness measurement by Fibroscan with this approach," he explained.

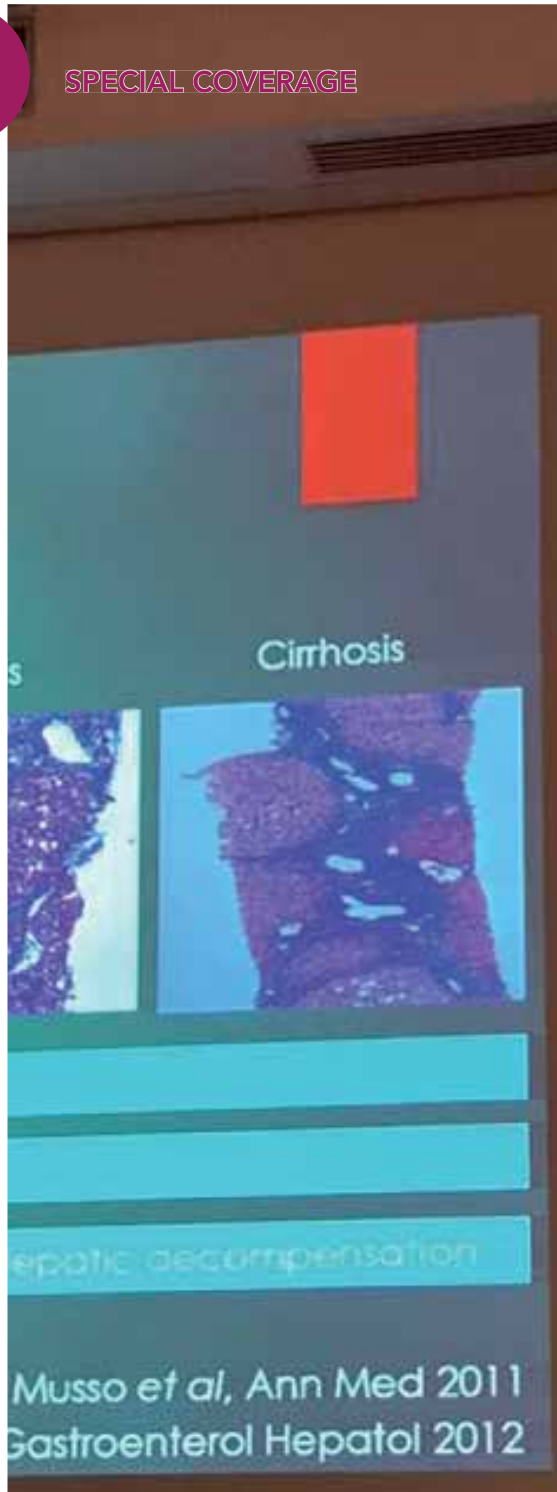
The group has also worked on several biomarkers for the assessment of disease severity in NAFLD, including the cytokeratin-18 fragment, M30,(10) and serum Wisteria floribunda agglutinin-positive Mac-2 binding protein.(11) "The availability of stored blood samples with corresponding histological data enables us to work on future biomarkers for NAFLD. We are also currently working with an overseas company on a novel magnetic resonance imaging technology for assessment of disease severity in NAFLD and are eagerly awaiting the results of this research project," said Dr. Chan.

Therapeutics for NAFLD

Recently, his team also found that silymarin may be useful for the treatment of NASH.(12) Silymarin is an extract from the milk thistle plant Silybum marianum and has been used for centuries as a herbal remedy for chronic liver disease. It consists of 6 major flavonolignans, namely silybin A and B, isosilybins A and B, silychristin and silydianin, as well as other minor polyphenolic compounds. Its anti-oxidant, anti-inflammatory and anti-fibrotic activity has been demonstrated in numerous in vitro and animal studies. Several human clinical trials have also suggested that silymarin may be useful for the treatment of NAFLD. However, robust evidence was still lacking. "Our work provides primary histological data on the potential efficacy of silymarin in improving liver fibrosis in patients with NASH," said Dr. Chan, who is one of the main investigators of the research project. The study randomized biopsy-proven NASH patients to silymarin 700 mg

three times daily or placebo for 48 weeks, and a repeat liver biopsy was performed at the end of the study. All patients received lifestyle advice. The study found that a significantly higher proportion of patients who received silymarin had fibrosis improvement compared with those who received placebo. The improvement in fibrosis was further supported by improvement in liver stiffness measurement by Fibroscan. Silymarin was safe and well tolerated with an adverse event profile that appeared no different than placebo. "There are currently limited treatment options for NASH. Although weight loss through diet restriction and physical exercise has been shown to improve NASH, only a minority of patients are able to achieve the desired amount of weight loss to have a significant impact on the disease. The findings from our study should prompt further work to better define the role of silymarin in the treatment of NAFLD," he added.

The full report of the study has been published in Clinical Gastroenterology and Hepatology, the prestigious journal of the American Gastroenterological Association, and was immediately highlighted by NEJM Journal Watch. "We are happy that our research work has received the recognition from our peers and hope to continue to contribute in the field of NAFLD. We would like to take this opportunity to thank our collaborator, Dr. Nik Raihan Nik Mustapha, Consultant Pathologist from Hospital Sultanah Bahiyah, Alor Setar, and all others who have contributed to the success of this research project, especially the patients and their family members," said Professor Sanjiv Mahadeva, the other main investigator of the research project. The group is currently actively conducting further research in NAFLD, including a pilot study on the use of empaglifozin, a sodium-glucose co-transporter-2 inhibitor, for the treatment of NASH in patients with diabetes mellitus, and welcomes collaboration for further advancement in the field of NAFLD. "I would like to take this opportunity to thank my mentors in my work on NAFLD and my supervisors for my PhD, Professor Dato Dr. Goh Khean Lee and Professor Dr. Sanjiv Mahadeva for their guidance, without which all these work would not have been possible. I would also like to thank my wife, Lai Yong for her understanding and support in my work," said Dr. Chan.



CANVASSING:
RECRUITMENT OF PATIENTS WITH RARE CONDITION IN CLINICAL TRIALS – SHARING EXPERIENCE FROM OUR PERSPECTIVE

Ranita Kirubakaran[1], Vijaya Kumar L. Suppan[2]
[1]Clinical Pharmacist, Hospital Sultan Abdul Halim, Kedah
[2]Head of Orthopaedic Department & Clinical Research Centre, Hospital Sultan Abdul Halim, Kedah

Acute hematogenous osteomyelitis (AHO) is an inflammatory disorder of the musculoskeletal system and mainly, a disease of growing bones. It is a common invasive infection in paediatric and the incidence is 8 cases per 100,000 children/year [1, 2]. In children, osteomyelitis (OM) arises from bacteremic seeding of the bone metaphysic [3]. Primary bones affected are femur, tibia, humerus and less frequently, pelvis and vertebra [3]. Staphylococcus aureus is the most common pathogen, causing between 25 - 60% of cases with known etiologies [4, 5, 6]. Other causative bacteria include Streptococcus pyogenes (Group A streptococci), Kingella kingae and Haemophilus influenza type b [4, 5]. Children are treated empirically with intravenous (IV) therapy directed against the likely pathogen and then, guided by culture results with continued IV or oral therapy.

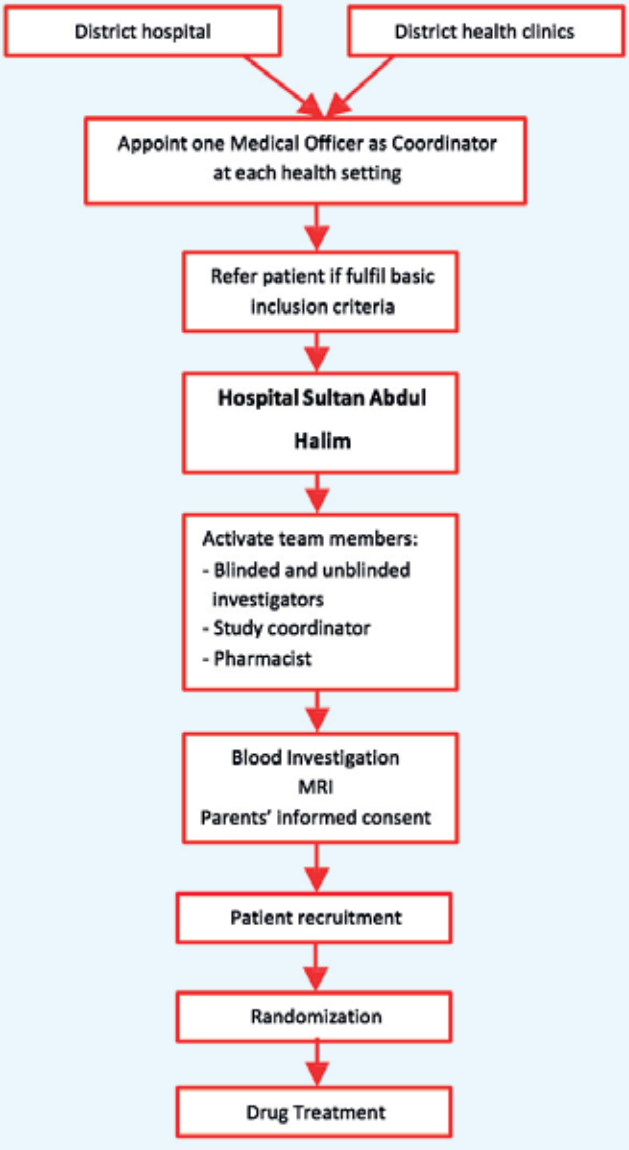
Recently, our institution was selected to conduct an orthopaedic based Industry Sponsored Research (ISR). The study is a multicenter, randomized double-blinded comparative study to evaluate the efficacy, safety, and pharmacokinetics of an investigational product versus an active comparator in paediatric subjects with AHO due to gram-positive organisms. The study was approval by Medical Research and Ethics Committee (MREC) and only four public hospitals in Malaysia were involved in this ISR. The target was to recruit at least 3 patients per centre. As the coordinating principle investigator in Malaysia, our institution aimed to recruit and enroll at least one patient for the study, despite the fact that we were given only 3 months for patient recruitment, bearing in mind that AHO is a rare case with poor patient pool at our institution. Also, the study protocol was quite challenging. The study required us to recruit children with acute onset of OM, fulfilling 3 clinical symptoms parameters (pain, inflammation and limb function) with radiologic confirmation of AHO. In addition, subject should not have prior exposure to any effective antibiotic therapy for AHO.

Being a novice in ISR, our team brainstormed on ways to recruit such rare subjects for the study. Our institution decided to opt for a special approach, namely canvassing where our team consisting of doctors and pharmacists would canvas the nearby public hospitals and district health clinics during lunch break. We provided a short power point presentation to the doctors on the patient pool that we were looking for and ways for them to refer potential patients to us. Slide presentation handouts were distributed to healthcare professionals together with our team investigators contact numbers to facilitate referral. Refreshments were provided for those who attended the talk thereafter. Sponsor approval and budget allocation were obtained prior to canvassing. We managed to cover 4 district hospitals and 3 district health clinics. Permission was obtained from the hospital directors and family medicine specialists at the district health clinics prior to our visit.

One Medical Officer (MO) was elected as a coordinator at each health setting to facilitate referral and patient recruitment irrespective of time with prior consent from the parents and patient to be transferred to our hospital for further management. We emphasized that their support for the study, in the form of patient referral, would be greatly appreciated as we assured them that the patients will be given high standard of care. Our involvement will be strictly study-related and referral doctor(s) will be notified if patient is enrolled. In addition, we decided to provide referral fees to doctors who referred potential patients to us, if the patient is successfully recruited in the study.

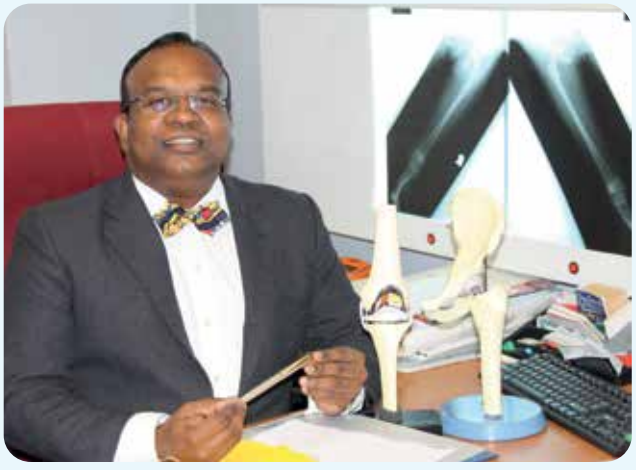
From our approach, we managed to recruit one patient into the study through referral from one of the public hospitals which we covered during canvassing. The 1 year 4 month old child was transported and admitted to the orthopaedic ward in our hospital at 5.00 pm. Patient's parents were explained regarding the intensive study protocol especially on the

Flow chart from canvassing till patient recruitment:



frequency of blood taking and were given adequate time to think and read the consent form. Once consented, we conducted steps as per protocol such as blood taking, magnetic resonance imaging (MRI) which was done externally and etc. Once inclusion criteria were fulfilled, randomization was made at 12.00 am. The first dose of drug was given to the patient at 1.00 am.

We were the sole institution in Malaysia which managed to recruit patient for the ISR. Thus, canvassing is a way to go for patient recruitment in rare conditions for any clinical trials. Our method of recruitment was audited by a Senior Consultant



from Falcon Consulting Group, Inc, America and we were awarded with a Good Clinical Practice Services Audit Certificate. Lastly, we would like to take this opportunity to thank all the team members who worked very hard to ensure the study was a successful one.

Acknowledgement to the team members:
1) Dr. Choo Chong Ming, Head of Paediatric Department & Infectious Disease Consultant
2) Dr. Kartina Binti Md Noor, Head of Pathology Department
3) Dr. Tan Chin Siong, Medical Officer (Orthopaedic)
4) Dr. Chew Yu Wei, Medical Officer (Orthopaedic)
5) Dr. Vijay Kumar A/L Nanta Kumar, Medical Officer (Orthopaedic)
6) Dr. Wong Bor Chern, Medical Officer (Orthopaedic)
7) Dr. Kelvin Anak Polycarp, Medical Officer (Paediatric)
8) Dr. Firdaus Bin Izhar, Medical Officer (Paediatric)
9) Madam Hasliza Binti Halim, Study Coordinator
10) Madam Law Yen Sin, Pharmacist
11) Miss Nor Suhada Binti Sooaid, Pharmacist
12) Mr. Amme Bin Ammeran, Microbiologist
13) Mr. Mohamad Raheimi Bin Md Saad, Microbiologist
14) Staff nurses from Kenanga 6

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CLINICAL RESEARCH CENTRE

HOSPITAL RAJA PERMAISURI BAINUN

Hospital Raja Permaisuri Bainun (HRPB) is currently the third largest Ministry of Health Hospital after Hospital Kuala Lumpur and Hospital Pulau Pinang. It is the main regional referral (tertiary) hospital for the state of Perak with major subspecialties servicing 14 other hospitals and 52 heath clinics. HRPB is also an active training centre for undergraduate, postgraduate, basic nursing and post basic nursing programs.

Population Served in 2016

Patient Population: 72,413 (in-patients) , 579,694 (out-patients including A&E patients)

Specialities Area

Anaesthesiology (Pain Therapy Clinic and Accupuncture), Cardiology, Dental Oral Surgery, Dermatology, Dietetic, Emergency and Trauma, Endocrinology ,Haematology, Infectious Diseases, Nephrology, Neurology , Neurosurgery, Obstetrics & Gynaecology, Ophthalmology, Orthopaedics, Otorhinolaryngology, Pathology, Paediatrics, Paediatric Oncology, Plastic Surgery, Psychiatry and Mental Health, Radiology, Rheumatology, Respiratory Medicine, Sports Medicine, Surgery (Endoscopy, Laparoscopy and Bariatric Surgery Facilities), Women's Health and all major surgical disciplines.

Hospital Facility

8-level hospital complex with 990 bed capacity (includes 16 adult intensive care beds, 8 adult coronary care beds, 7 pediatric intensive care (PICU) beds and 12 neonatal intensive care (NICU) beds), 16 operating halls, specialist clinic complex and a 4-Level Ambulatory Care Center (ACC). Specialized equipment include CT Scan, Ultrasound, MRI, BMD, Advanced Cardiology Unit, Fluoroscopy, Mammography and Interventional Radiology.

Medical Workforce

148 Specialists, 298 Medical Officers, 119 Pharmacists, 5 Dieticians, 1619 Nurses, 165 Medical Assisstants, 97 Lab Technicians. CRC and CRM Clinical Trial Support staffs: Administrative Manager, 5 Medical Officers, 4 Pharmacist, 2 Biostaticisions, 3 Research Asssitants and 5 CRM Study Coordinators.

Clinical Research Centre (CRC) / Clinical Research Malaysia (CRM) - Perak

- The site has dynamic and proactive regional CRC and CRM with dedicated staff including healthcare professional associates and resources.
- They have actively encourage clinicians to cultivate interest towards clinical research that improves patient care. By building a close relationship with CRM, the hospital also aims to accelerate the growth of industrial sponsored clinical trials.
- On average more than 10 trainings are conducted yearly such as Post Basic (Nursing) proposal and data analysis workshop, Qualitative workshop, Literature Searching and Referencing Workshop, Questionnaire validation and Reliability Test workshop, SPSS Analysis Workshop, Study Coordinator Hands-On Workshop, GCP Refresher, Recruitment and Retention workshop, Protocol Deviation Awareness Workshop and FDA / Inspection Workshop
- The site also extend their support and assistance to other district hospital in Perak as Hospital Seri Manjung, Taiping and all the health clinics in Perak.

Dedicated Clinical Trial Facility

- Clinical Trial Hub equipped with Freezer -30°C , Freezer -80°C, Fridge 2 – 8°C , Temperature Monitoring System, Temperature-Controlled Centrifuge, Portable Centrifuge, Syringe Pump ,Infusion Pump, ECG Machine and emergency cart.
- Documents storage area, rooms for meeting/monitoring and internet.
- Dedicated area for patient examination and review.

START UP TIMELINES, METRICS, QUALITY AND ACHIEVEMENTS

AVERAGE DAYS

SIV to FPFV: Site Initiation Visit to First Patient First Visit:	<60 days*
Contract Executed timelines:	30 days

STANDARD OPERATING PROCEDURES (SOP)

- Availability of CRM SOPs at site enable site to use it as reference/guide for the conduct of clinical trial.
- Each CRM SCs are certified and they are able to train other hospital site staff on the proper conduct of clinical trial.

HRPB AS PRIME SITE AND INSPIRE SITE

Prime Site:

- In collaboration with CRC, CRM and Quintiles, HRPB along with another 11 hospitals were selected as Prime Site.This partnership enables to benchmark Malaysia with other global countries for these contributing factors; increase number of clinical trial, improve start up timeline, High quality and meet/ exceed patient recruitment targets.
- Pfizer recommended HRPB to be a potential site to participate in a Pfizer's INSPIRE Site Program, part of the Investigator Networks, Site Partnerships and Infrastructure for Research Excellence Program.

INSPIRE Site Program:

- Preferred site or Pfizer's clinical trials.
- Pfizer will provide investigator training and site development support.
- INSPIRE sites are a strategic set of sites that are highly productive and effective.
- Site will have the privileges of having early access to Pfizer portfolio and advanced information regarding clinical trials sponsored by Pfizer

KEY ACHIVEMENTS

- At any one time between 20-25 clinical trials are ongoing, particularly Phase II and III multicenter trials in Paediatrics, Rheumatology, Nephrology, Endocrine, Psychiatry, Hematology and other disciplines.
- Has keen investigators, conducting trials of diverse therapeutic areas, with some achieving highest recruitment target.
- To date most of the clinicians are GCP trained.
- Top recruiter for Malaysia site for Neuroscience, Nephrology and Dermatology studies.
- Dr Sree Kantan Nayar (Klinik Kesihatan Greentown) – Awarded for **"The Highest Number of Newly approved ISR among Primary Health Clinics in Malaysia in year 2016 "**.

Therapeutic Area	No. of Approved Trials in 2016	No. of Approved Trials in 2015	No. of Approved Trials in 2014
Hospital Raja Permaisuri Bainun (HRPB)			
Cardiology / Vascular diseases	4	0	1
Dermatology	0	0	1
Endocrinology	0	0	1
Epidemiology	1	1	0
Gastroenterology	0	2	0
Hematology	1	2	0
Infectious Disease	1	1	1
Nephrology	3	2	1
Neurology	1	2	2
O & G	0	0	1
Oncology	1	0	1
Orthopaedic	0	1	0
Psychiatry	0	0	3
Pulmonary/Respiratory Disease	0	1	0
Rheumatology	1	0	1
Total # Approved Trials at HRPB	**13**	**12**	**13**
Klinik Kesihatan Greentown			
Endocrinology	2	0	2
Neurology	1	0	0
Vaccine	1	0	0
Total # Approved Trials at KK Greentown	**4**	**0**	**2**
Klinik Kesihatan Kg Simee			
Endocrinology	1	0	0
Klinik Kesihatan Jelapang			
Endocrinology	0	1	0
Klinik Kesihatan Gunung Rapat			
Infectious Disease	1	0	0

Processing & Storage Room in HRPB's Clinical Trial Hub

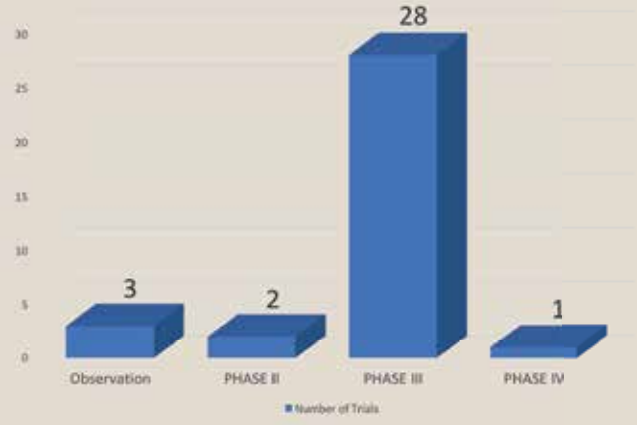
Entrance of CRC in HRPB

CRM Study Coordinators team in HRPB

Some of the clinical trial equipments in HRPB's CRC Clinical Trial Hub

SITE OVERALL INVOLVEMENT IN CLINICAL TRIALS (ALL SPONSORS)

2016 (Newly 2016 approved and On-going)



Number of Potential Investigators

Site Name	Potential Investigators
Hospital Raja Permaisuri Bainun Ipoh	34
KK Greentown	2
KK Kg Simee	1
KK Jelapang	1
KK Gunung Rapat	2
KK Buntong	1

NCCR 2017

11th National Conference for Clinical Research

In conjunction with

THE REACTA FORUM

REGIONAL ASIAN CLINICAL TRIAL ASSOCIATION ANNUAL FORUM

27th - 29th SEPTEMBER 2017

Putrajaya International Convention Centre (PICC), Putrajaya, Malaysia

PRECISION MEDICINE - THE FUTURE IS NOW

Save the date and be part of this exciting gathering of great minds in clinical research!

CPD POINTS AWARDED

Welcome!

The **National Conference for Clinical Research (NCCR)** is the most prestigious meeting on clinical research in Malaysia. For this year, we have a conjoint conference, partnering with the **REACTA** (Regional Asian Clinical Trial Association – www.reacta.asia) in hosting global experts from the USA, United Kingdom, Japan, Korea, Singapore and Malaysia on topics revolving around the theme **"Precision Medicine – The Future is Now"**

OVERVIEW

The NCCR 2017 together with the REACTA Forum 2017 aims to communicate the latest global developments in **precision medicine** and its implications on the future of healthcare in Malaysia and in Asia besides clinical trial developments and research collaborations.

By bringing together global experts and thought-leaders of industry, healthcare and academia from across various disciplines in research and technology, the conference will provide valuable insights in this exciting and incredible promise for superior healthcare and better patient outcome.

The conference examines how close we are in this new era of healthcare as well as developments in global clinical trials and research collaborations in Asia. Keynote address, plenaries and symposium sessions will run concurrently with an exhibition by clinical research industry partners as well as poster sessions. The conference will provide excellent networking opportunities between researchers in different countries and to form potential research collaborations.

DISCOVER: New findings, latest development in research and technology and are we close to realizing the arrival of precision medicine.

LEARN: Key challenges, opportunities and good practices that will advance healthcare delivery.

NETWORK: Enhance your personal and professional network, engage with influential key opinion leaders and connect with peers and industry experts from all career levels and organizations.

Showcase Your Company or Institution and to be Noticed!

Contact us if you would like to enhance your brand visibility and target the right audience either by becoming a sponsor, taking up a booth or an ad page.

LEARN FROM THE EXPERTS!

- Precision Medicine in Oncology |Hematology| Hepatic | Respiratory | Oral | Bladder| Diagnostics & Therapeutics | Genomics | Population Health
- Current Impact of for Individual & Community I Implications in Primary Care
- Evolution of Precision Medicine | Emerging Precision Medicine in Asia
- Collaborative Research in Asia
- Global Initiatives: Collaboration and Best Practices Forum

Precision Medicine in Cancer-Where are we now? Genetic Testing for Hereditary Cancer Syndrome

Assoc. Prof. Dr. Lee Soo Chin - Singapore

Associate Director (Research) and Senior Consultant, Dept. of Haematology-Oncology National University Cancer Institute
Associate Professor, Cancer Science Institute of Singapore, National University Singapore

Precision Medicine in the Management of Cancer Risk in the Population

Prof. Dr. Teo Soo-Hwang - Malaysia

CEO of Cancer Research Malaysia

Precision Medicine: How we Encourage Innovation in Oncology

Koichi Miyazaki - Japan

Senior Director, Clinical Group, Asia Development Dept., R&D Division, Daiichi Sankyo Co., Ltd., Japan

Building a Global Clinical Trial Centre: KCGI Present and Future

Prof. Dr. Park Min Soo - Korea

Chair of Korea Clinical Trials Global Initiative (KCGI), Ministry of Health and Welfare

Novel Biomarkers and Detection Platform for Early Diagnosis and Prognosis of Cancers

Prof. Dr. Chen Kuan-Chou - Taiwan

Director of Graduate Institute of Clinical Medicine & Chief of Dept. of Urology, Taipei Medical University, Shuang-Ho Hospital, Taiwan

RESEARCH POSTER COMPETITION DR WU LIEN-TEH RESEARCH AWARDS

An opportunity to display your research, present research findings and obtain recognition for your work. There will be 3 categories; Research, Clinical Audit and Case Report/Series. Visit conference's website for more information, guidelines and online submission. Cash and medals await the winners.

Young Investigator Awards (Oral Presentation)

1st Prize : RM 1000 + medal
2nd Prize : RM 750
3rd Prize : RM 500

Best Poster Awards

1st Prize : RM 500 + medal
2nd Prize : RM 300
3rd Prize : RM 200

All abstracts accepted/qualified will be given certificates of participation.

IMPORTANT DATES

Call for Abstract: 15th February 2017
Deadline: 15th July 2017 (11:59 PM. GMT+8)

For more information, please contact: Conference Secretariat NCCR 2017 | Tel: +603 - 7726 8000 | Fax: +603 - 7733 7007 | Email: confsec@crestevendz.com.my

www.nccrconference.com.my

Supported by: CRC Ministry of Health Malaysia – Research that matters to patients

Organised by: CRM Clinical Research Malaysia; ACRM Real Patient Real Data; REACTA

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Research Poster Competition Awards Sponsored by:

Esketamine Trial – A Success Story in Patient Recruitment

By Chan Wei Quan, Site Manager, Janssen

Of all the illnesses out there today, which one would you say is the leading cause of disability around the globe? The answer may surprise you.

It's depression, which affects more than 15 million adults in the U.S. and more than 300 million worldwide, according to the World Health Organization (WHO). It can cause the affected person to suffer greatly and function poorly at work, at school and in the family. At its worst, depression can lead to suicide. Close to 800 000 people die due to suicide every year.

All existing antidepressants work on the same premise by increasing the brain levels of serotonin and/or norepinephrine—neurotransmitters. However, only about half of the patients receive an adequate response from them, which typically takes four to eight weeks or longer for someone to start feeling better. When you are that depressed and possibly on the point of contemplating suicide, 4 to 8 weeks is a long time.

Janssen is studying a compound that works more quickly to alleviate the symptoms of depression. Just google "Esketamine". Janssen has received a breakthrough designation from the FDA for its potential use in people with treatment-resistant depression and in those who are suicidal.

In Malaysia, there are five centers participating in the Esketamine trial. Today's highlight would be the success story from one of the centers, Hospital Kuala Lumpur (HKL), which was led by Dr Hjh Salina Abd Aziz and her team. Janssen approached HKL in the year of 2015 as a potential site for the Esketamine trial. Considering the complexity of the trial and the site resource, Dr Salina was hesitating on the numbers of patients that HKL could enroll in the study. In the end, HKL decided to commit to 3 subjects within a 6 months' of recruitment timeline. HKL psychiatry department was new to multicentre clinical trials. However, with the combined effort from Clinical Research Malaysia (CRM), Janssen and Dr Tan Lee Khing, one of the main sub-investigatorstheir journey to becoming one of the best recruiting sites in Malaysia began as they took the lead to recruit the very first patient at site. Unfortunately, the response from the first patient was not favorable, which in turn shook the confidence of the team towards Esketamine.

In spite of the disappointing start of this trial, the spirit of the team to get more patients was not defeated as more evidence was needed on whether Esketamine will still be beneficial. With the help from the medical officers in the Psychiatry Department, another patient was referred to Dr Tan for the trial. This patient responded well to Esketamine, and the patient's condition showed significant improvement. This patient's testimonial was shared to other participating centers during a local investigator meeting.

Meanwhile, due to rapid recruitment of the trial globally, study recruitment timeline was shortened from 2 months to 1 week out of a sudden. This hurdle was not a barrier for with teamwork from. Dr Salina and her team who fully utilized the one week period to enroll 3 more patients. Kai Sin, the pharmacist, identified potential patients based on the prescription slips and, Ikram the study coordinator identified patients from the advertisement published on nationwide newspaper. Our investigators, Dr Razak, Dr Nurzurian and Dr Riana, spent their invaluable time to screen the patients on top of their copious routine work.

With proper management, coordination and cooperation between the study team members, HKL managed to recruit 3 more patients, making it a total of 6 patients in the trial, which doubled the digit of our initial commitment. In short, they exceeded their recruitment target in a short period.

How did they achieve this in such challenging timelines? The answer lies within their great teamwork and time management that is exemplary and commendable. It was challenging but we are inspired and impressed by the potential and teamwork that the HKL Psychiatry team has shown. Special thanks for HKL andencouragement as they are one of the newer clinical trial sites compared to other psychiatry departments/hospitals who have been running clinical trials for more than 10 years. Their efforts will help continue to put Malaysia on the map on being a country that has clinical trial talent and potential.

Country commitment would not be able to achieve with just one single site. Sincere thanks to University Malaya Medical Centre lead by Prof Dr Ahmad Hatim and his team, Hospital Permai lead by Dr Abdul Kadir and his team, Hospital Bahagia Ulu Kinta lead by Dato' Dr Suarn and his team and the Royal College of Medicine, Perak lead by Dr Esther and her team, for making the Esketamine program a success in Malaysia.

New drug development cannot be achieved without clinical trials and patient participation. The number of patients required in each trial is used to support statistical analysis and study sites which can recruit the number of subjects committed and help contribute towards the success of the drug development process. Every site that achieves or exceeds the patient target planned, helps put the country in a favorable light for more trials to Malaysia.

Lastly, Husseini Manji, M.D., Global Therapeutic Area Head for Neuroscience, Janssen Research & Development said: "At the same time, when people learn that depression can be treated effectively, I believe the attitude toward mental illness will change. My hope is that diseases of the mind will someday be viewed like any other illness—no stigma, no shame, just support and sympathy."

CRM'S QUALITY IMPROVEMENT PLAN

By Wong Sok Yee,
Clinical Operations Manager, CRM

At clinical research sites, Standard Operating Procedures (SOPs) help define the study team standard practices and daily processes to assure execution of study tasks are in accordance with the requirements. SOPs should contain enough detail to guide the study team through a particular procedure and thereby establish uniformity in the everyday functions of each site.

The quality of clinical trial depends on the integrity of the data and protection of subjects. Study Coordinators (SCs) play an important role in a Site Management Organization to ensure compliance and delivery of clinical trials.

At Clinical Research Malaysia (CRM), a Quality Improvement Project (QIP) has been initiated in January 2016. The QIP aims to improve the site management organization processes in CRM and to direct the organization to achieve its performance. The QIP is mainly divided into three stages i) QIP planning; ii) Project Implementation; iii) Process improvement. In QIP planning, the Project Management Planning is used to ensure the success of the QIP. In stage 2, process improvement was carried out where the Plan-Do-Check-Act model is used for drafting and reviewing the Standard Operating Procedure (SOP). A quality manager is assigned to monitor the progress of the QIP.

A bimonthly meeting was carried out to ensure the project progress is reviewed and supported by the top management team. A quality team was also assigned to assist in the QIP. In 2016, a total number of 110 SCs were deployed at 32 sites throughout Malaysia. These sites include public hospitals, health clinics, National Cancer institute and universities. The challenge of this project is to have one standard SOP for all sites and to meet the project deadline.

The QIP begins with identifying the needs of developing new processes and reviewing of the current processes at sites. Internal and external reviewers then reviewed the SOPs.

For implementation of SOP, two session of SOP trainings were conducted. All SCs must passed the validation assessment (80%) in order to be rewarded with a certificate.

The Clinical Operations team continues to strive for continuous improvement by performing the SOP compliance check followed by internal audit as part of the quality assurance procedures.

GCP REFRESHER WORKSHOP

Good Clinical Practice

Good Clinical Practice (GCP) is an international ethical and scientific quality standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials set by the International Conference of Harmonisation (ICH) GCP. Compliance with the GCP standard provides public assurance that the rights, safety and wellbeing of trial subjects are protected and that the clinical trial data are credible.

All study staff involved in clinical trials are recommended to update their knowledge of GCP at least once every two years. A GCP refresher course reinforces the importance of concepts covered in the basic level of GCP for clinical trials.

GCP Refresher Training in 2016

On July 2016, Clinical Research Malaysia (CRM) began conducting GCP Refresher Trainings at investigational sites throughout Malaysia. The trainings involved the transfer of theoretical and practical knowledge in line with the required core competencies related to clinical trials. The training sessions consisted of lectures, videos, demonstrations, group discussions and exercises.

This GCP Refresher Training will refresh a participant's knowledge on:

i) Basics of Good Clinical Practice
ii) Investigator's role and responsibilities
iii) Sponsor's role and responsibilities
iv) Institutional Review Board (IRB)/ Independent Ethic Committee's (IEC) roles and responsibilities
v) Protocol deviations
vi) Informed consent process
vii) Safety reporting

"When I took my GCP for the first time, I felt I was lost and unsure how a clinical trial is conducted. With this GCP Refresher, I'm able to grasp more information and I strongly encourage those with GCP certification to attend this refresher course"

–Dr. Rozita Zakaria, FMS, Klinik Kesihatan Sultan Ismail, Johor

"I took my GCP 9 years ago, and I stop doing research for while. Through this GCP refresher course, I found that it's important to look back at the guidelines and at the same time gain experience from fellow investigators."

–Dr. Mohd Fauzi Adbullah, FMS, Klinik Kesihatan Kuah, Kedah

Completed GCP Refresher training at investigational sites from July 2016 until May 2017

2016	2017
Hospital Sultan Bahiyah (HSB)	Hospital Tengku Fauziah (HTF)
Hospital Sultan Abdul Halim (HSAH)	International Islamic University Malaysia (IIUM)
Hospital Queen Elizabeth (HQE)	Hospital Sultan Ismail (HSI)
Info Trek Amcorp Mall	Hospital Raja Perempuan Bainun (HRPB)
	Vue Residence for Hospital Kuala Lumpur

International Islamic University Malaysia (IIUM)

Hospital Sultan Bahiyah (HSB)

Hospital Sultan Abdul Halim (HSAH)

Hospital Queen Elizabeth (HQE)

"The GCP certification itself is challenging for me, but for this refresher course I find it very interesting and I gain more understanding through the training videos. I'll encourage my fellow clinicians to attend this course."

–Dr. Rohayah Ismail, FMS, Klinik Kesihatan Sentul, Kuala Lumpur

"This is a good course to attend as it changes my views compared with my first time attending GCP course previously. The tips and encouragement given motivates me to persue more clinical trials."

–Dr. Teoh See Wee, FMS, Klinik Kesihatan Segamat, Johor

As a clinical study coordinator, what should I do before a Clinical Research Associate (my CRA) arrives for monitoring?

Planning Prior to Monitoring Visit (MV)

1. Schedule a mutually convenient date and time to conduct the MV with the CRA, assuring the availability of study team as required.
2. Collate the study subject files, screen fail subject notes, and also randomized patient records:
   - √ Ensure all Informed Consent Forms are filled.
   - √ Check for complete records documenting the investigational procedures required per protocol at each visit (i.e. ECG tracings, laboratory results, etc.).
   - √ Ensure that all data queries in the Case Report Forms (CRF) are resolved.
3. Check the last monitoring visit follow up letter to review and address pending items recorded from previous monitoring visit.
4. Prepare Electronic Medical Records (EMR) for CRA for their usage during monitoring visit.
5. Inform all required study team of the expectation to be present during the MV:
   - √ Remind all of the required study team 2 days prior to the Monitoring Visit.
   - √ Inform pharmacist in-charge regarding the planned monitoring visit as they need to be available to the CRA and provide the complete pharmacist binder, and access to Investigational Product (IP) & updated temperature/dispensing/accountability logs for review.
   - √ Inform Principal Investigator (PI) regarding the visit and check on their availability during the visit – this is important so that the CRA can solve any pending issues during the site monitor visit.

During Site Monitor Visits

1. Arrive early to ensure all the required items are available for the CRA.
2. Upon arrival, inform the CRA on the plan for the day and scheduled appointment times to meet with the PI and pharmacist.
3. Accompany Monitor to visit specific areas : Subject's treatment area, IP storage area.
4. Accompany Monitor to resolve CRF discrepancies, entry errors, omissions, or illegibility concerns in site during the monitoring visit.
5. Raise all pending issues regarding the study, eg : payment, patient recruitment, IP.
6. Ensure the CRA signs the Site Monitor Visit log.

Best Practices Post-Monitoring Visit

- √ Return all source documents to respective department in a timely manner.
- √ Resolve all queries and pending items within 5 working days.

ABOUT THE AUTHOR

Mohana Priya Velesamy graduated with a Bachelor in Medical Science (Hons) in 2010 and started her career in clinical research when she joined Clinical Investigator Center(CIC), University Malaya Medical Center In 2011 as an Oncology study coordinator. She is an effectively articulate communicator with her clinical trial colleagues and shares her clinical research advice with you. Currently she is working with Clinical Research Malaysia as Senior Study Coordinator for the Oncology Department.

How a Centralized Feasibility Service Attracts Sponsors and Contract Research Organizations to Malaysia

Khalid KF, Ooi AJA, Tay WC

CRM CLINICAL RESEARCH MALAYSIA
Your Global Solutions in One Nation

Objective

A single point of contact for sponsors and contract research organizations (CROs) is vital in streamlining and accelerating feasibility studies in a particular country. This poster describes how a centralized feasibility service streamlines and accelerates feasibility studies in Malaysia.

Methods

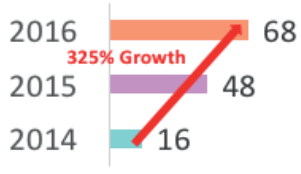
Records on the number of feasibility studies and companies who have utilized Clinical Research Malaysia's centralized feasibility service were obtained and an analysis was done to determine the growth of companies who have engaged this service and the number of feasibilities received from 2014 – 2016.

Results

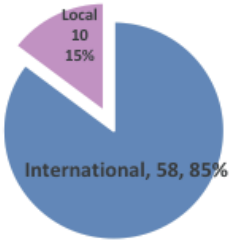
The centralized feasibility service resulted in :

- 325% growth in companies who have engaged CRM with feasibility assessments from 2014–2016
- 85% (n=58) are international organizations and the rest being local CROs and sponsors.
- Full feasibilities received in 2016 increased to 98 from 59 in 2014.

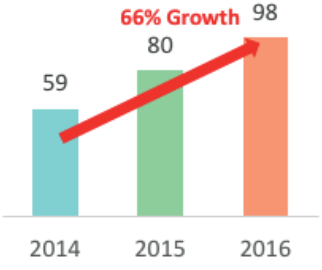
Growth of Sponsors and CROs



Types of CROs and Sponsors



Full Feasibility Received



Conclusion

Our data indicate that a centralized feasibility management has garnered increased number of sponsors and contract research organizations (CROs) in Malaysia.

Prior to having a centralized feasibility management service in Malaysia:

- Sponsors and CROs conducts feasibility assessments individually.
- Rely on their own internal databases to conduct feasibility assessments.
- Individual company databases are based on each company's experiences with previous feasibility approaches.

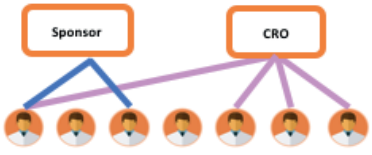
A centralized feasibility service by Clinical Research Malaysia (CRM):

- **Functions as a single point of contact.**
- **Is offered as a complimentary basis to sponsors and CROs.**
- **Capitalizes on a comprehensive updated internal database of investigators.**
- **Enables outreach to a wider range of investigators and sites.**
- **Results in a centralized knowledge of the research environment**
- **Leads to streamlined communications which reduces delay and confusion on the ground.**

The average timeline taken from the start of the feasibility to reverting back to the Sponsor/CRO is 13.1 days. In 2016, of the 466 positive responses received, 73% of investigators answered within the timeline given.

The positive growth of sponsors/CROs is made possible through a centralized feasibility team coordinating and overseeing communications with sites. Thus, on a nationwide perspective, a centrally managed feasibility structure is an attractive alternative to sponsors and CROs looking to enhance efficiency and width of a feasibility outreach, avoid redundant processes and promote a more accurate assessment of Malaysia's capabilities.

Before a Centralized Feasibility Point of Contact



After a Centralized Feasibility Point of Contact

Disclosure

The authors of this presentation have nothing to disclose.

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Poster presented at the International Conference on Non Communicable Diseases 2017

Trends in Industry-Sponsored Non-Communicable Disease Clinical Trials in Malaysia

Gurcharan Singh G.K., Ooi A.J.A., Mohd Murad I.M.

Background

Non-communicable diseases (NCDs) present a significant and growing global public health problem. Industry-sponsored clinical trials in cardiovascular diseases, cancer, chronic respiratory diseases and diabetes have broaden the treatment options available for patients, besides providing new and better treatment for them.

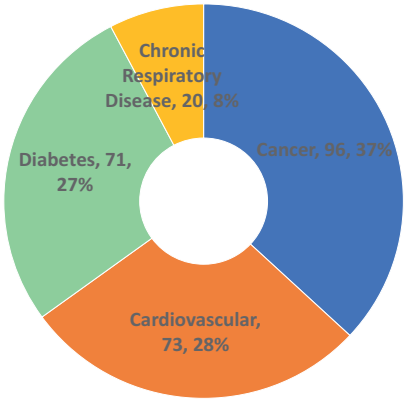
Method

The total number of approved industry-sponsored non-communicable disease clinical trials in Malaysia between 2012 and 2016 was compiled from all thirteen ethics committees (ECs) in Malaysia.

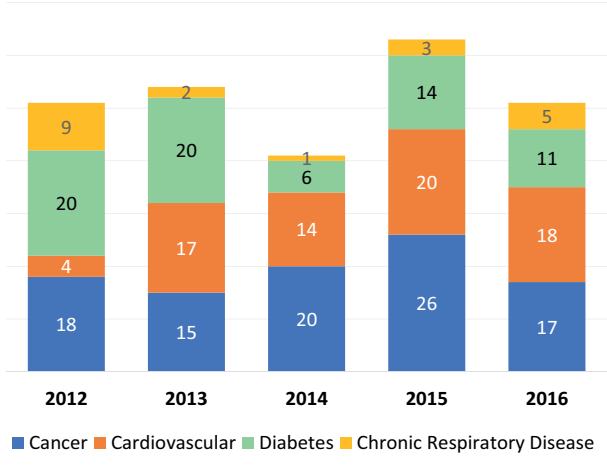
Results

- From 2012 to 2016, cancer accounts for the largest fraction of industry-sponsored NCD clinical trials in Malaysia (37%), followed by cardiovascular (28%), diabetes (27%) and chronic respiratory disease (8%).
- Asthma made up about two thirds of clinical trials in chronic respiratory diseases while ischemic heart disease made up 41% of cardiovascular trials.
- In the last five years, a total of 369 principal investigators participated in NCD clinical trials, with an average of 79 sites each year having conducted these trials.
- Within the 5-year period, diabetes and chronic respiratory disease trials have slightly reduced, while cardiovascular trials have increased.

Proportion of NCD clinical trials in Malaysia



Trends in Non-Communicable Clinical Trials in Malaysia (2012 – 2016)



Conclusion

In the last five years, diseases in cancer, cardiovascular and diabetes represented the highest number of clinical trials that were recorded in Malaysia. This is due to the rise of lifestyle diseases such as diabetes, obesity, hypertension and various cancers brought about by the rapid urbanization rate in the country. With the availability of a large and increasing number of Good Clinical Practice-certified investigators and support staff, there is still potential to attract more clinical trials in non-communicable diseases into Malaysia. Malaysia's attractiveness in industry-sponsored research also lies in an established and comprehensive ethical review process, short regulatory and ethical approval timelines, as well as the strong support and commitment from the Malaysian government, through Clinical Research Malaysia, to create a thriving clinical research ecosystem in the country.

Participation of Family Medicine Specialists in Industry-Sponsored Research in Malaysia

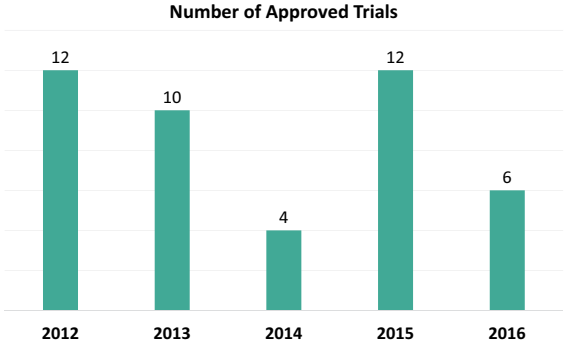
Mat Radi N., Ooi A.J.A., Mohd Murad I.M.

Background

Malaysia's public health system is based on the World Health Organization's district health system model. The district health clinics are managed by family medicine specialists (FMS) and are self-contained with their own basic laboratories and basic diagnostic facilities. These specialists attend to patients with stable chronic diseases, acute medical cases as well as provide maternal and child healthcare services. In the last five years, a number of family medicine specialists have undertaken industry sponsored research (ISR) at their respective health clinics. The objective of this report is to illustrate the involvement of family medicine specialists in industry sponsored research in Malaysia.

Method

The total number of approved industry sponsored research in Malaysia participated by family medicine specialists between 2012 and 2016 was compiled from all thirteen ethics committees (ECs) in Malaysia and were characterized according to the types of trials and the overall number sites where they are conducted.

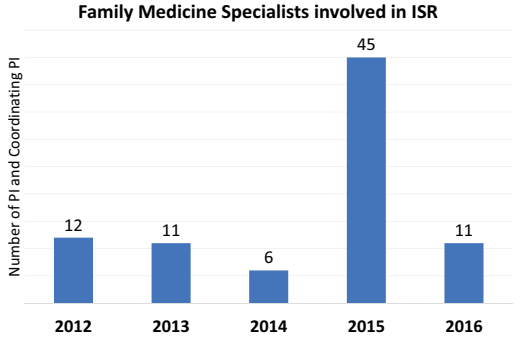


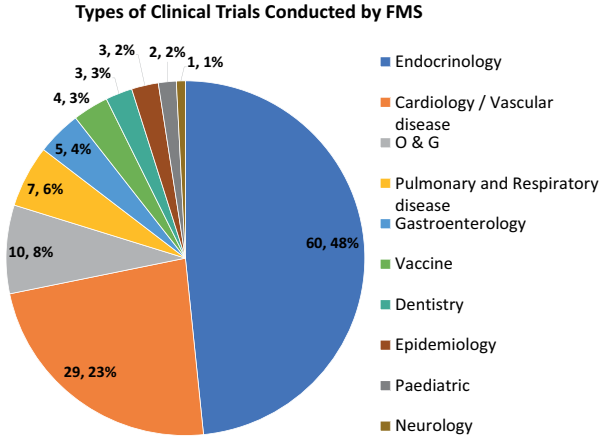
62 investigators involved in FMS trials (2012 – 2016)

68 Health Clinics where FMS trials were conducted (2012 – 2016)

Results

From 2012 to 2016, a total of 44 industry sponsored research (ISR) was conducted by family medicine specialists in Malaysia. The highest number of trials were recorded in 2012 and 2015 (12 trials) followed by 10 trials in 2013, 6 trials in 2016 and 4 trials in 2014. Within these five years, a total of 62 family medicine specialists have been involved in ISR, some of whom have conducted more than one trial in a single year. These specialists who are principal investigators or coordinating principal investigators in their respective clinical trials are from a total of 68 health clinics throughout the country. In 2015, there was a spike in the number of FMS involved in ISRs (45) compared to the year before and after it. The type of trials undertaken by them largely comprised of endocrinology (60) and cardiovascular (29) trials.





Conclusion

Clinical trials undertaken by family medicine specialists are based entirely in the primary care setting at district health clinics. The sharp rise in the number of family medicine specialists' involvement in ISR as observed in 2015 was due to an interventional cardiovascular study which had activated 23 different sites, thus requiring a higher number of family medicine specialists' participation. The prevalence of non-communicable diseases like diabetes and hypertension in Malaysia provides the large patient pool for endocrinology and cardiovascular trials. Patients with these illnesses are typically treated by family medicine specialists at health clinics, enabling them to be recruited easily for these types of trials, thus explaining the high number of endocrinology and cardiovascular trials undertaken by family medicine specialists in Malaysia in the last five years.

Several strategies were initiated by the Ministry of Health (MOH) to develop a supportive and thriving clinical research ecosystem in the country to attract more ISRs. This include allocating protected time for investigators to conduct trials, equipping the sites with the relevant facilities and raising awareness of clinical trials amongst the public and healthcare professionals. These initiatives were carried out by a concerted effort of Clinical Research Centre (CRC), the clinical research arm of the MOH, and Clinical Research Malaysia (CRM), a non-profit company established by the MOH that provides speedy and reliable end-to-end clinical research support to trial sites, investigators and the industry, with the main aim of making Malaysia a clinical research hub in the region.

Poster presented at the MyNeuro 2017

Industry-Sponsored Neurology Clinical Trials in Malaysia from 2012 to 2016

Tay W.C., Ooi A.J.A., Mohd Murad I.M.

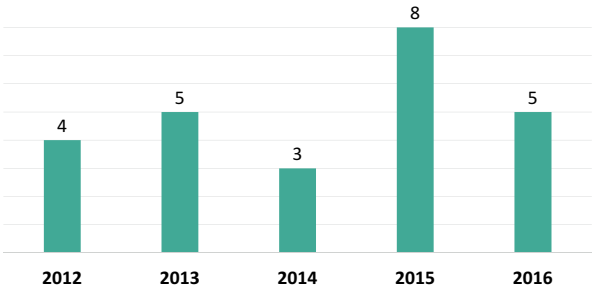
Background

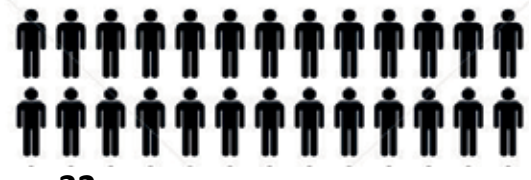
The pipeline of drugs for neurological disorders currently stands at more than 400 compounds, many of which have undergone testing in clinical trials to find new breakthroughs in treating these complex diseases.

Results

From 2012 to 2016, a total of 25 neurology clinical trials were conducted in Malaysia, with the highest number recorded in 2015 (n=8 trials). During this time period, 32 neurologists have taken up these trials, some of whom have conducted more than one trial in a single year. The majority of sites involved in these trials are the Ministry of Health (MOH) hospitals and health clinics (80%), and rest being public (10%) and private universities (10%). Clinical trials in epilepsy/seizure (20%) account for the largest type of trials being conducted in Malaysia, followed by neuropathy and Alzheimer's (16%), multiple sclerosis (12%), stroke (8%), neuromyelitis optica (8%), syncope (4%), dystonia (4%) meningitis/encephalitis (4%), amyotrophic lateral sclerosis (4%) and intracerebral haemorrhage (4%).

Number of Industry-Sponsored Neurology Clinical Trials in Malaysia (2012-2016)



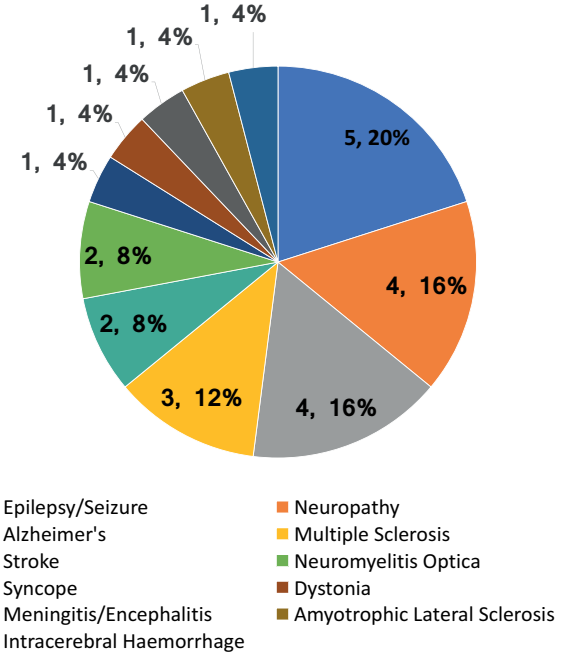


32 investigators involved in neurology clinical trials from 2012 to 2016

Method

The total number of approved industry-sponsored neurology clinical trials in Malaysia between 2012 and 2016 was compiled from all thirteen ethics committees in Malaysia and are characterized into the types of studies, number of principal investigators as well as sites that have conducted these trials.

Neurology Clinical Trials by Indication



Breakdown of Trial Sites

Trials according to Phases

Conclusion

The Ministry of Health has developed several strategies to create a supportive clinical research ecosystem in the country to attract more ISRs. This include allocating protected time for investigators to conduct clinical research, equipping the sites with the relevant facilities and raising awareness of clinical research amongst healthcare professionals. These initiatives were carried out by a concerted effort of Clinical Research Centre (CRC), the clinical research arm of the MOH, and Clinical Research Malaysia (CRM), a non-profit company established by the MOH that provides speedy and reliable end-to-end clinical research support to trial sites, investigators and the industry.

CRM in Photos

I AM AWARE Roadshow: Hospital Raja Permaisuri Bainun, 25th Apr


GCP Refresher Course: IIUM, 27th - 28th Apr

I AM AWARE Roadshow: Hospital Ampang, 28th Apr


I Am Aware Campus Roadshow: Taylor's University, 9th May


Clinical Trials Day 2017, 16th May

I AM AWARE Campus Roadshow: UTAR Sg. Long Campus, 25th - 27th May


Interview with Astro Awani's Smart Money, 25th May

CRM & CRC SGH visit to Siriraj Clinical Research Centre, 5th Jun


DIA 2017 Annual Meeting I Chicago, 19th - 21st Jun


Chief Scientific Officer of A.I. in Medical Epidemiol Visit CRM, 5th Jul


Interview with The Nation, Bernama News Channel, 14th Jul


CRM Media Briefing, 18th Jul


The 2017 Malaysian Thoracic Society Annual Congress, 21st - 23rd Jul


CRM visit to C&R Research in South Korea, 1st Aug


20th FMS Conference, 2nd - 5th Aug

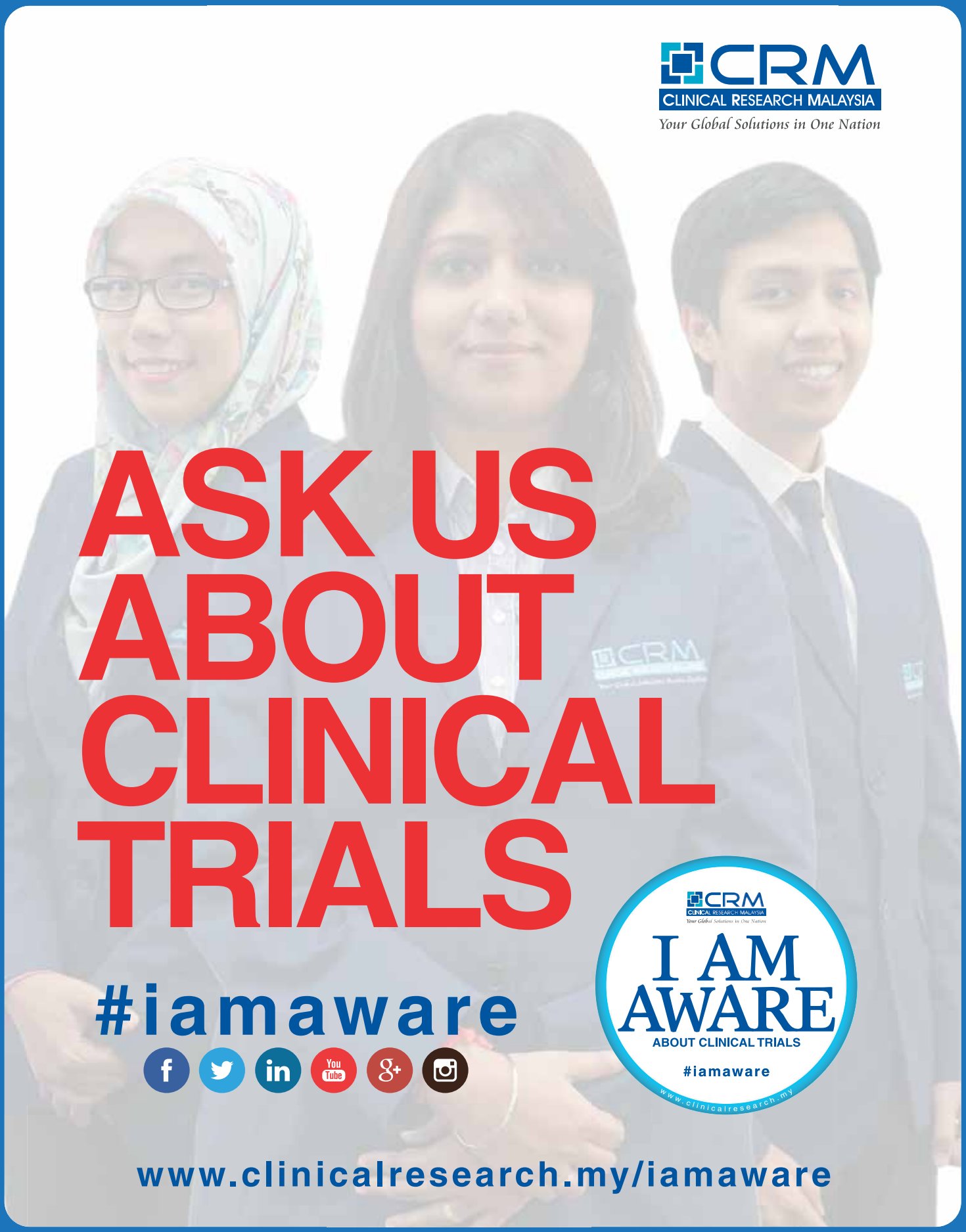

Janssen Pharmaceutical (Companies of J&J) visits CRM, 11th Aug


MyNeuro 2017, 11th - 13th Aug


National Dengue and Arboviruses Infection Conference 2017, 12th - 13th Aug

6th Selangor Research Week, 14th - 16th Aug


I AM AWARE Roadshow: Hospital Sultanah Aminah, 14th Aug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