By Clinical Research Malaysia

CRM bulletin

of Clinical Research and Therapy

ISSUE 18

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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.

CRM
CLINICAL RESEARCH MALAYSIA
Your Global Solutions in One Nation

FROM THE CEO's DESK

2019 was a great year never short of excitements and challenges. The year marks CRM being self-sufficient and not depending on Government funds. The year also marks a new headquater, an important life event for CRM and with this new office requires our new thoughts, mind and actions. This is the year where CRM is put to the test on our Quality Management System. It is also a year where we check our sanity on what we do best, delivering clinical research with speed, reliability and quality through external feedback including the National Audit Department.

CRM's socio-economic contribution is coupled with the recognition from international organization namely IQVIA, Novotech, PhAMA, DNDi, ISO9001:2015 and the latest being the audit report from the National Audit Department which recognized CRM as being efficient in managing clinical research. The report was submitted to the Parliamentary Public Accounts Committee and made available to the public.

The recognition CRM received were the fruits of success we worked for in the past 5 years through the 5 key strategies. Clinical research was delivered with speed, reliability and quality. Apart from the ISO accreditation, we successfully gained trust among our stakeholders; 84% of good and above rating for our Study Coordinators, 83% recruitment rate and improved study start-up time by 50% from over 300 days to 150 days.

Improvement in processes within our day to day work should lead us to improve our services to our stakeholders. Self-changes made to fix issues, feedback given by auditors and survey from our customers are good indicators meant for continuous improvement. These yardsticks are important to CRM to continually enhance our performance as we strive to focus on Operational Excellence in 2020.

Thank you to all who have worked hand-in-hand with us steering the clinical research industry forward in Malaysia and I hope 2020 will be another great year for everyone.

Dr. Akhmal Yusof
CEO, Clinical Research Malaysia

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CME at National Institute of Health

SELANGOR, 21 June 2019 – CRM invited Dr Masliza Mahmod to the National Institute of Health (NIH) to give an inspirational talk on "How to Excel in Research in a Competitive Environment". The talk was attended by researchers and medical officers from all six institutes at NIH.

Hospital Seberang Jaya is Top Recruiter in Malaysia for Neurology Study

PENANG, 13 August 2019 – Congratulations to Dr Irene Looi and Hospital Seberang Jaya for the achievement of being the top recruiter in Malaysia for a neurology study. Kudos to our study coordinator team in Hospital Seberang Jaya for contributing their effort in making it a success.

Clinical Trials Day 2019

KUALA LUMPUR, 29 August 2019 – CRM collaborated with the Clinical Research Centre (CRC) of Kuala Lumpur Hospital to organized Clinical Trials Day 2019 with the objectives to elevate the awareness level of clinical trials in the country, as well as to encourage participation of medical professionals in clinical research. The event was officiated by the Deputy Director-General of Health (Research & Technical Support), YBhg Datuk Dr. Christopher Lee Kwok Choong.

VOCAL study by InterVenn is a Success in Malaysia

KUALA LUMPUR, 18 September 2019 – CRM has established a strategic partnership with InterVenn Biosciences (InterVenn) to conduct the VOCAL (Venn Ovarian Cancer Liquid Biopsy) study in Malaysia. The VOCAL study is one of the largest global ovarian cancer clinical trials, spanning over three countries and two continents. Thank you to Hospital Wanita dan Kanak-Kanak Sabah and Hospital Seberang Jaya's team for the endless supports and hard work!

Industry Dialogue 2019/2

KUALA LUMPUR, 24 October 2019 – CRM's biannual Industry Dialogue was held to provide avenue for pharmaceutical companies and CROs to directly convey issues, suggestions or opinions that they may have related to clinical research in the country. In addition to strengthening networking between all parties, CRM takes this opportunity to update the clinical research industry on local laws, guidelines and regulations.

Speakers for the Industry Dialogue include Mr Normanshally Mohammad (Associate Director of Clinical Operations, Merck Sharp and Dohme), Mdm Aiza Adlina Abdullah (Senior Principal Assistant Director, NPRA), Dr Asyraf Syahmi Mohd Noor (MREC Secretariat) and Mdm Aidahwaty Ariffin @ M. Olaybal (Head of Technical Evaluation Division, MDA).

ASCOMOS-CRM Research Track 2019

IPOH, 2 November 2019 – CRM collaborated with the Malaysian Oncological Society (MOS) for the 31st Annual Scientific Congress of Malaysian Oncological Society (ASCOMOS 2019). With the theme of 'Meeting of Minds in Cancer Research', the event was successfully held on 2nd November at Ipoh Convention Centre. A pioneer collaborative effort with MOS, this program featured symposiums by renowned Malaysia researchers from Cancer Research Malaysia, UM, UKM, USM, Monash University and UTAR as well as six short oral communication by shortlisted abstract presenters. Another first was the networking session organized which saw the meeting of professionals from various fields in discussion to explore collaborations and partnerships in furthering their research ideas.

Sarawak GH is Ready for First in Human Studies

SARAWAK, 10 December 2019 – CRC Sarawak General Hospital received the provosional certificate from the National Pharmaceutical Regulatory Authority (NPRA) and is now listed under NPRA's Phase 1 Unit Accreditation Programme. CRC Sarawak General Hospital is the first site in Malaysia to be listed in this program.

National Audit Department Audits CRM

KUALA LUMPUR, 10 December 2019 – CRM was audited by the National Audit Department and the overall report indicates that CRM has achieved its establishment objective, met satisfactory corporate governance and has stable financial position. Key recommendations were also made in the report to further ensure the sustainability of the company. A copy of the report is made available online at the National Audit Department website (www.audit.gov.my)

- ***Deputy Director-General (Research & Technical Support), Ministry of Health***

- ***Head, Paediatric Department, Hospital Kuala Lumpur***
- ***Senior Consultant Paediatrician, Consultant Paediatric Haematologist & Oncologist***
- ***National Head of Paediatric Services, Ministry of Health***
- ***Chairman of the Malaysian Thalassaemia Registry***

Dr Hishamshah Mohd Ibrahim

Clinical research, a journey

Dr Hishamshah's first taste of clinical research began in Pahang, in the nineties. It was part of the requirement to qualify as a paediatrician. He performed a study examining the lung health of primary school children, comparing rural and urban populations. The study consisted of taking the peak flow of 200 students. He wanted to look at the Bateq Orang Asli, as they were an ideal rural representation.

He travelled to Kuala Tahan, where the Bateq resided. As it was very remote, he took a long boat upstream for 3 hours. The journey, which was in itself challenging, was not made easier with a bulky peak flow meter in tow. He recalled how lucky he was that it was not the monsoon season.

Research takes a back seat

Work at the hospital was getting busier, and research was no longer the highest priority. He was also working on his Masters at the time, and he had a young family to care for.

Dr Hishamshah's supervisor (Dr Raja Khuzaiah Raja Abdul Razak) at the time had plans to set up Ministry of Health (MOH) first paediatric transplant unit. So, he went to do a stint at his own expenses at the Sydney Children's Hospital in Australia, to learn how to set up a transplant centre.

He recalled his mentors in Sydney, Marcus Vowels, David Ford, Reg Lam-Po-Tang and Glenn Marshall. He felt fortunate to learn from these giants of the field.

Pioneering the Transplant Unit

Fresh from Australia, he returned with a mission to pioneer Malaysia's first blood transplant unit. The Malaysian transplant protocol at the time was developed from his experience in Sydney. The first paediatric blood transplant was performed in August 1994 at Hospital Kuala Lumpur (HKL).

He recalled the difficulties of starting the transplant programme for the MOH, the hassle of paperwork and certification. He recounted the difficulties of procuring equipment crucial to blood transplants. Malaysia did not have a blood irradiator at the time, and one had to jump through regulatory hoops to acquire one.

A model culture of research

Fresh from his success, he was hungry for new challenges. He took a fellowship at the Fred Hutchinson Cancer Research Center in Seattle, USA. Locally known as the Hutch, it was an amazing place for research.

His experience there was fulfilling but it was hard work. People at the Hutch worked very hard. "I was quite fortunate, E. Donnall

Thomas, who won the Noble Prize (for his work on development of bone marrow transplantation) was still practising." He is also fortunate to directly worked with other doyen of stem cell transplant including Jean Sanders and Fred Appelbaum.

The Hutch's X-factor was the culture of research. One patient could have close to 10 ongoing studies, with every parameter under the sun observed. He was most impressed that this culture was so ingrained in everyone there, not just the doctors, but in nurses and technicians. It was one seamless entity and the culture permeated by example.

Hope for Malaysia

Upon his return to Malaysia, he felt changes especially some superiors were not so interested in research - as they were not setting a good example to their juniors. Dr Hishamshah said that elder statesmen like E. Donnall Thomas, were still doing their rounds even though they were frail.

Despite his scepticism, he expressed optimism in the abilities of Malaysian experts. There was no doubt in the technical abilities of Malaysians. "Look at our diaspora, they are all over the world. But once they come back you don't give them the support they require to excel." He expressed concern in the amount of obstacles put on budding talents and, the toxic environment they have to work in.

> ***"Never do research for the sake of money. It may motivate in the short-term but eventually it will kill your soul"***

Changelles in conducting clinical research

Lack of research culture or research mindset within the organization is the main challenges.

This ecosystem encouraged a restrictive and silo-minded mentality. In addition, there was no common vision of how things should work within the organization.

That was why Clinical Research Malaysia (CRM) was brought in. He expressed gratitude to CRM for its efforts to improve clinical research.

Holistically he believes that "Research must be for the greater good of humanity. So when you leave this world you can say 'God, I did my best and it is time for others to take over."

How to excel in clinical research

The passion for clinical research must come from within, "You must have focus, perseverance, and be stubborn." This tenacity and the motivation to do something for the right reasons will drive you forward. "Never do research for the sake of money. It may motivate in the short-term but eventually it will kill your soul. Clinical research is not about short-term thinking, it is generational thinking."

He said that Nobel Laureates worked hard and got their hands dirty. They experimented, failed and did it over and over again. They persevered and developed talents in others. These new talents were allowed to grow and eventually excel. People like E. Donnall Thomas may have passed away but their legacy lives on.

Advice to young researchers

He expressed hope that Malaysian clinical researchers will achieve success in everything if they put their minds to. "We must do the right research on things that matter and, put patients and the nation at the centre. Put aside personal glory and stay focused on research. The rest is up to God." He said there should be an emphasis on cooperation to pool resources and talents, and avoid unhealthy competition.

His parting words were, "Do the right thing and help will come your way from unexpected avenues. Sometimes inspiration comes from something staring you in the face. When you do good everything else will fall into place."

HOSPITAL TUNKU AZIZAH

Completed in 2018, Hospital Tunku Azizah or formerly known as Hospital Wanita dan Kanak - Kanak Kuala Lumpur (HWKKKL) provides Paediatrics service (medical and surgical-based), Obstetrics and Gynaecology. Two major hospitals (Paediatric Institute Hospital Kuala Lumpur & Maternity Hospital Kuala Lumpur) are the main departments established starting from early 2019 to September 2019.

SPECIALITY

- Obstetrics and Gynaecology
- General Paediatrics
- Paediatric Ambulatory Care Center
- Paediatric Cardiology
- Neonatology
- Paediatric Dermatology
- Adolescent Medicine
- Paediatric Haematology and Oncology
- Paediatric Neurology
- Paediatric Anaesthesiology
- Paediatric Infectious Disease
- Paediatric Nephrology
- Paediatric Respiratory
- Paediatric Endocrinology
- Paediatric Emergency
- Paediatric Palliative Care
- Paediatric Rehabilitation
- Developmental Paediatrics
- Diagnostic Imaging
- Dietetics
- Pharmacy
- Clinical Research Center
- Pathology and Laboratory Diagnostics
- Genetics
- Paediatric Surgery
- Paediatric Orthopaedics
- Paediatric Neurosurgery
- Paediatric Dentistry
- Child and Adolescent Psychiatry
- Paediatric Otorhinolaryngology
- Paediatric Ophthalmology
- Physiotherapy
- Occupational Therapy

Main lobby

CRC Hospital Tunku Azizah

The research centre started as Unit Penyelidikan in March 2019 and it was later endorsed by the Director General of Ministry of Health Malaysia - the establishment of Clinical Research Centre (CRC) in HWKKKL on 23 October 2019.

Facilities

The hospital has Pusat Pentadbiran Pasca Siswazah (PGMS) which designated for meetings and other activities.

1. Main auditorium
2. Six seminar rooms
3. Two teleconference rooms
4. Two meeting rooms

Accomplishments by Department of Paediatrics in research

1. CRC HKL Research Award for Best Performance in Investigator Initiated Research Hospital Kuala Lumpur (2018).

2. Top-3 Bilangan Penerbitan Dikumpulkan di Pusat Penyelidikan Klinikal Hospital Kuala Lumpur dari Januari ke Ogos 2018.

3. Bilangan Penyelidikan Terbanyak Didaftarkan di Pusat Penyelidikan Klinikal Hospital Kuala Lumpur tahun 2016.
(Kategori Investigator Initiated Research).

Site Overall Involvement in Clinical Trials Studies (All Sponsors)

LAUNCHING & EXHIBITION OF I AM AWARE PHOTOGRAPHY SERIES PANELS

"This programme aims to elevate the awareness level of clinical trials among patients and the general public.

Clinical trials offers innovative treatments and expand healthcare options to patients in the country."

Dato' Seri
Dr Chen Chaw Min

The event was launched by Secretary General of the Ministry of Health, Dato' Seri Dr Chen Chaw Min on 19 December 2019 at Ministry of Health Putrajaya.
The exhibition is continued from 19-24 December 2019 at the main lobby, Ministry of Health.

Media Coverage

Rising Stars in Oncology

In case there was any doubt, the future of oncology clinical trials in Malaysia is in good hands. In this section, CRM presents "Rising Stars in Oncology Clinical Research" that profiles exemplars of today's young and budding Principal/Sub Investigators. In this issue, we focus on four Malaysian oncologists who have contributed immensely in providing access to innovative medicines for cancer patients in the country through involvement in clinical trials.

Cancer treatment paradigm continues to evolve. What I learn during my Masters have changed gradually over the years. I need to keep myself updated from time to time to keep pace with the latest standard of cancer care. The nature of cancer is very unique. Until present, no definite cures have been found in most advanced cancer diseases. However, newfound drugs targeting specific oncogene drivers which are the core of cancer cell gene mutations have at least dampened the progress of disease progression, providing some glimpse of hope and lay the foundation for further research and breakthroughs yet to be discovered.

As a Clinical Oncologist, I believed that in order to bring hope to my patients, I should not just provide treatment according to what that is existing in front of me, but to take one step further by actively involved in cancer research so that new found drugs would benefit future patients and humanity as a whole. This thought urged me to pursue further in cancer research and not just a sitting duck! As a physician, it is my responsibility to continue further learning for the future benefit of mankind.

DR. JENSON SOW WEN JEN
Clinical Oncologist
Sabah Women and Children's Hospital

Throughout my career as a medical practitioner, my exposure to research was minimal. It is a career changing experience for me during my service in Hospital Umum Sarawak. I was given plenty of opportunities and exposure to clinical trials by a good friend and mentor, Dr Voon Pei Jye. As you already know, he is awarded the Top Recruiter and Investigator of The Year by CRM for the past two years, and his passion for clinical trial is second to none. I am impressed by his passion and contribution to research. This is how my interest and passion on research started.

The opportunity to provide access and expand treatment options for patients are my main motivation. Through clinical trial, we are able to offer hope for patients who have exhausted their options. As a clinician, we always strive to do our best for better patient's outcome, and clinical trials have been proven to improve patient survival. I would encourage more quality clinical trials in our centres and put our country onto the world map for clinical research. Teamwork among all stakeholders, collaboration between centres and pooling of resources are the key in achieving this goal. In the long run, I hope Malaysia will have an ecosystem that looks into early phases of clinical trials such as preclinical and first-in-human trials.

DR. TAN CHIH KIANG
Clinical Oncologist
National Cancer Institute

Born in Singapore, I was brought up in various places and Penang is always the place I call home. Since graduation in year 2001, I have worked as a resident in one of the leading hospitals in China, Peking Union Medical College Hospital where I was trained in internal medicine. In 2005 I relocated back to Malaysia to accompany my aging grandparent. For the next few years I entered into the field that always intrigued me... oncology. From 2012-2014 I received the scholarship from the Federal Government of Malaysia to continue fellowship training in The Christie NHS, Manchester which housed one of the biggest clinical trial centers in Europe.

It is a fact that treatments under the current public health service could be limited by higher cost and when the treatment price has reduced, it would be at least 10 years later and novel agent has emerged by then. This causes frustration not just in patients but also clinicians alike. It is the main reason that drove me into clinical trials. It was after being a principal investigator that I realised clinical trials not only able to bring new treatments to patients, they also help to cut the medical cost of the department and in turn the saved fund could be utilised to pursue more expensive treatment for patients in public health care facilities, creating an exciting healthy cycle.

When I was in Manchester, there was a patient who was diagnosed with non-small cell lung cancer and has been surviving for 14 years, thanks to the availability of clinical trials which gave her all the new treatment, at the right time. In the long run, I hope that with more structured clinical trials available in the public health facilities, more of our younger generation of clinicians would stay back and enrich the specialty besides closing the gap in medical research.

DR. SOO HOO HWOEI FEN
Clinical Oncologist
Penang General Hospital

It is well known fact that Oncology among all the medical disciplines is one with the most incomplete science or with still a vast research potential in other words. Though the cancer treatment today has improved by leaps, for many cancer patients the prognosis is still dismal. As far as the scientific and clinical understanding of cancer and its treatment is concerned, we are probably making baby steps with a long journey ahead. As a clinical researcher, I wish to contribute effectively in testing new drugs and systemic agents that may change the way we treat cancer currently and give hope to those without hope.

Having to meet the demands of both clinical practice and research can be very taxing on medical doctors. This is more so when there are limited resources. Many clinicians are demotivated by this and chose to just concentrate on clinical services with little research activities either in private practice or government service. I always believe that we have one lifetime given by the Almighty and we should seek the most from it while contributing to humanity.

I hope in future we can initiate and run our own clinical trials with the support from CRM and other relevant organizations in the country and thorough global collaborations. To achieve this, a strong working relationship among colleagues and referring physicians needs to be developed. I would surely envy to be a leader in fostering this clinical research partnership and eventually ensuring it's success.

DR. SYADWA ABDUL SHUKOR
Clinical Oncologist
Sarawak General Hospital

KUALA LUMPUR, 29 August 2019 – Clinical Trials Day 2019 was celebrated for its third consecutive year at the newly opened Women and Children's Hospital Kuala Lumpur.

This event was organized by Clinical Research Malaysia (CRM) in collaboration with Clinical Research Centre (CRC) of Kuala Lumpur Hospital, aims to elevate the awareness level of clinical trials in the country, as well as to encourage participation of medical professionals in clinical research.

Clinical Trials Day is part of CRM's ongoing efforts in enhancing the current clinical research ecosystem in the country by ensuring a robust pool of patients and volunteers for trials, while at the same time continuously investing in the infrastructure of qualified personnel, addressing the industry needs and promoting Malaysia as a hub for clinical research.

The event was officiated by the **Deputy Director-General of Health (Research & Technical Support), YBhg Datuk Dr. Christopher Lee Kwok Choong.** Datuk Dr. Christopher touched on the importance of attracting sponsored research to the country as it provides access to ground-breaking as well as costly treatments that may not be available to patients outside of a clinical trial setting. He also commended the efforts and achievements of the doctors at Hospital Kuala Lumpur who have gone above and beyond their usual clinical practice to deliver clinical trials of good quality.

Sponsored Research Award 2019

CRM Sponsored Research Award is given out each year to outstanding Principal Investigators, clinical trials sites and the industry for their contribution in sponsored research to the nation. It is given to spur and encourage more of such efforts in the future. CRM would like to honour and acknowledge their dedication in participating in sponsored research and hope that they will keep up the good work. Congratulations to all recipients.

INVESTIGATOR & TOP RECRUITER OF THE YEAR - DR. VOON PEI JYE

Dr Voon Pei Jye received the Investigator of the Year & Top Recruiter of the Year Award. For Investigator of the Year Award, he conducted the most studies that were initiated in 2018 and has the highest number of oncology trials in that year. He was also PI for 7 studies that was approved in 2018, one of which is a Phase 1, dose escalation study. He also co-authored in 3 publications in 2018 and 8 of his research findings were presented in ESMO Munich, ESMO Asia, World Conference on Lung Cancer, EndoBarcelona and Malaysia-Singapore Congress of Medicine.

For the Recruiter of the Year Award, Dr Voon has achieved first-patient-in within 100 days from site activation in 5 of his studies initiated in 2018. Four out of these 5 studies to date, have successfully reached its recruitment target.

MSD

SPONSOR OF THE YEAR

Merck Sharp & Dohme (Malaysia) received the Sponsor of the Year Award for bringing in the highest number of studies that got initiated in 2018 and contributing to the highest value of sponsored research brought to the country.

CLINICAL TRIAL SITE OF THE YEAR

HOSPITAL PULAU PINANG

Hospital Pulau Pinang received the Clinical Trial Site of the Year Award for having conducted the highest number of sponsored research among all MOH sites. 27 sponsored research trials were conducted at this site in 2018, spanning 13 different therapeutic areas including areas of hematology, infectious disease, nephrology, gastroenterology, oncology and bioequivalence studies.

IQVIA™

CRO OF THE YEAR

IQVIA received the CRO of the Year Award with the highest number of studies and sites initiated in 2018 (9 studies and 22 sites), and having achieved over 71% of the total recruitment from the 22 sites activated.

NURTURING NEW TALENTS IN SPONSORED RESEARCH

NNT seminar is part of CRM's initiative to instill interest and promote clinical trials among clinicians by having prominent industry and renowned principal investigators in Malaysia to share their experience and expectation in conducting sponsored research. CRM hopes that this may translate into a healthy growth of principal investigators in the country.

6 Seminars Conducted in 2019

Experienced Investigators & Industry Speakers

Grow New Investigators in Malaysia

Conducted since 2017

NNT seminar is targeted for specialist, consultants and medical officers and the topics covered include:

1. Approaching Feasibility Studies
2. Quality Study Coordinators to Boost Your Clinical Research Experience
3. CRM Legal Review Process
4. Finance - Budget Negotiation & Management.
5. Industry's Expectations in Sponsored Research

NNTs in 2019 :

1. **Hospital Selayang**
2. **UKM Medical Centre**
3. **Hospital Tengku Ampuan Afzan**
4. **Hospital Miri**
5. **Hospital Wanita & Kanak-Kanak Likas Sabah**
6. **Jabatan Kesihatan Negeri, Negeri Sembilan**

TIPS 2019
Regional Training

Central Region | Southern Region | Northern Region | East Coast Region | Sabah | Sarawak

We have completed our 1st TIPS Training! "TIPS" stands for "Training to Improve Performance of Study coordinators".

The main objectives of this training are as a refresher training and a platform to share experience and practices amongst our study coordinators.

For 2019, we emphasized on "Effective Reconstruction of Events", touching on topics such as good documentation practices, site file management, study handovers, and protocol deviations reporting. We also shared on ICH GCP E6 R2 summary of changes, budget negotiation and basic Excel.

For this training, we adopted a different training model with a new delivery approach; one that empowers our internal team (i.e Associate Regional Managers (ARMs) / Designates) to deliver the training program together with the trainer.

Sabah

Sarawak

East Coast Region

Southern Region

Northern Region

Central Region

Clinical Trial Perspective

This article is contributed by Soon Wen Xian, a medical graduate from Volgograd State Medical University, who is now working as a Clinical Research Associate at an international pharmaceutical organization based in Singapore.

"Hi doctor, we are having a clinical trial that is in the area of your expertise. Are you interested in this trial?"

"I am busy as a bee with my daily work and I have no spare time to conduct clinical trials."

"Don't worry doctor, it will not give you much burden as there will be Study Coordinators that will assist and support you in many aspects, and all you need to do is focus on the patients' treatment."

"But what is the benefit of getting involved in clinical trials?"

This conversation sounds familiar when I was a Feasibility Specialist with Clinical Research Malaysia (CRM). Being one of the Feasibility Specialist in CRM, I was mandated to facilitate either sponsors or Contract Research Organization (CROs) to bring in industry-sponsored research to Malaysia and to be the mediator for our Principal Investigators (PI) for any particular clinical research. Unfortunately five years ago, most of our doctors in Malaysia are not active in clinical research. The main reasons for this are simply because they are not familiar with conducting clinical research as well as being fully occupied with their clinical work. With all the restrictions and limitations, it was a challenge for me to convince the doctors and to instill their interest in taking up clinical research.

Whenever confronted with similar questions, I will always explain to the doctor that clinical research will enhance their clinical acumen skills and most importantly provide them with the experience in using the new drug in the future.I strongly believe that it is a priceless experience and not every doctor will have the same

opportunity as the clinical research is only available when there is a new drug, treatment or medical device being developed by the sponsor.

I agree with the doctor when they state that they will have information about the drug when the drug is registered with the Ministry of Health and representative from the pharmaceutical company will invite them to a seminar to introduce the drug. However, there is a difference between a doctor who has experience using the drug in a clinical trial compared to one who obtains information on the drug from articles or from pharmaceutical / medical device companies.

Of recent, I joined a conference where the pharmaceutical company introduced a newly registered drug. The sharing was done by a Principal Investigator from Malaysia who is involved in the clinical trial. Introduction to the newly registered drug was made and it was highlighted that the drug gave very good effect on the patient with a specific disease compared to the existing drug available in the market.

Of course, most people are amazed by the data shared and the investigator is keen to use the drug on the other patients.

Unfortunately, when I thoroughly analysed the data, I found out that the drug is only effective for a specific group of patient only, ie.it gives most positive effect to Asia patients, - the effectiveness drops tremendously up to 50% in non-Asian populations. If a doctor is not involved in the clinical study, he/she might not be able to notice this. Hence, the drug may look great, but does the drug help all patients?

In my years of experience in the clinical research industry, I have also known of investigators in my country who displayed professional integrity and responsibility towards patients' safety. One such example is when an investigator has stopped recruiting patients for a particular study when he is concern with the effectiveness of the investigational product. At the end of the day, investigators must be aware and responsible for any treatment provided to their patients, whether in a clinical trial or otherwise.

Getting involved in clinical research for doctors is a huge responsibility and commitment in view of their hectic schedule. Most doctors will be overwhelmed by clinical work and may worry about the recruitment rate, documentation during patient's visit and missed out symptoms which may cause a serious side-effect. I believe CRM understands our doctors' dilemma and has thus offered the needed support to conduct clinical research by placing Good Clinical Practice-certified Study Coordinators at clinical research sites in Malaysia to assist the investigators. Clinical trials are important for the progress of medical treatment and should be viewed by doctors as an opportunity to participate and contribute to medical innovation, besides having first-hand experience in using the drugs/medical device before it becomes available in the market.

The International Conference on Harmonization - Good Clinical Practice (ICH-GCP) is an international ethical and scientific quality standard that ensures the rights, safety and well-being of clinical trial subjects are protected and that the clinical trial data generated are credible.[1]

Malaysia GCP Guideline was developed by National Pharmaceutical Regulatory Agency (NPRA) in 1999. This guideline adopts the basic principles outlined by ICH-GCP with some modifications to adapt to local conditions.2 The object of the Malaysia GCP Guideline is to ensure that drug-related trials in Malaysia are conducted in accordance with international ethical and scientific standards.[2] Although there is currently no legislative requirement for GCP training, mechanisms were in place to ensure that investigators are trained on GCP. For example, it is mandatory to submit a copy of Principal Investigator's GCP certificate when obtaining regulatory approval from NPRA to conduct a clinical trial.[3] In addition, all investigators must submit their GCP certificates for ethics committee's approval in Malaysia.[4] Since the first edition of Malaysian GCP to the current 4th edition, approximately 12,000 clinicians have been GCP certified.[5]

It is recommended for GCP certified personnel to be retrained on GCP guidelines every three years in order to stay up to date with updated regulations, standards, and guidelines.[6] With this, Clinical Research Malaysia (CRM), a research organization founded by Malaysia Ministry of Health (MOH), has taken the initiative to conduct GCP Refresher Workshop for clinicians, nurses, allied health professionals and study coordinators who have been certified with Malaysian GCP. The objective of the workshop was to provide a review on the principles of GCP, to improve participants' skills and knowledge on managing the conduct of a clinical trial, as well as to share recommendations on how to conduct a GCP-compliant clinical trial.

Since the first workshop in October 4, 2016, CRM has conducted 31 GCP refresher workshops throughout Malaysia to approximately 450 participants at no cost. The majority of the participants are clinicians, nurses, allied health professionals from government hospitals who are involved in clinical trials. Over the course of the conduct of the workshop, modifications have been made based on participants' feedback to improve the quality and the learning outcome of the workshop. A summary of the changes in the workshop agenda is listed in Table 1.

Date	04Oct2016	19Nov2016	16Mar2017	3May2017
Agenda	½ day course	One day course	One day course	One day course
Introduction & revision to ICH GCP	✓	✓	✓	✓
Investigator's Responsibilities	✓	✓	✓	✓
Sponsor's Responsibilities	✓	✓	✓	✓
Informed Consent	✓	✓	✓	✓
Patient Recruitment & Retention	✓	-	-	-
Role of Institutional Review Board/ Ethics Committee	-	✓	✓	✓
Adverse Events Reporting	-	-	-	✓
Pre- and Post-Workshop Assessment Test	-	-	✓	✓
Protocol Deviations	-	-	-	✓

Table 1: Changes in presented topics from 2016 to present

As shown in Table 1, pre- and post- workshop assessment test was introduced in March 16, 2017 in order to evaluate the effectiveness of the workshop on participants' knowledge on GCP.

In this paper, we analyzed the pre- and post-workshop assessment score for workshops conducted since March 16, 2017.

Methodology

Before the start of the workshop, participants were required to complete 20 multiple-choice GCP-related questions (pre-workshop assessment). The questionnaires were then collected before the start of the workshop. After the workshop, participants are then required to complete the same set of questions (post-workshop assessment). Participants were

given 30 minutes to complete the questionnaire.

The average score of the pre- and post-assessment results from participants of the same workshop will then be calculated. This will constitute one set of data point.

The average score of pre- and post- workshop assessment from each workshop conducted since the introduction of the assessment in March 16, 2017 were compiled. Of the 28 workshops conducted since then, five workshops' data could not be retrieved, hence only 23 sets of data point were analyzed.

The compiled average score of pre- and post-workshop were then compared using Microsoft Excel's t-test assuming unequal variance to evaluate if there is any significant improvement in the average assessment score after the workshop.

Results

Table 2 shows the compiled data from 23 workshops. 420 participants completed the pre-workshop assessment, and 434 participants completed the post-workshop assessment. There is on average, 20% improvement in the assessment score before and after the workshop.

Workshop Session	Number of participants (n= 420)	Average Pre-Workshop Assessment Results (%)	Number of participants (n= 434)	Average Post-Workshop Assessment Results (%)	Difference in pre- and post-workshop assessment (%)
1	20	70	20	84	14
2	15	62	15	75	13
3	25	63	25	81	18
4	29	63	29	86	23
5	24	61	27	87	26
6	10	71	12	80	9
7	15	55	15	75	20
8	25	55	26	79	24
9	14	66	14	89	23
10	17	56	17	74	18
11	14	55	14	80	25
12	15	75	15	95	20
13	17	58	21	71	13
14	18	66	18	89	23
15	30	43	31	60	17
16	19	42	20	57	15
17	17	45	16	55	10
18	23	46	25	64	18
19	6	38	7	60	22
20	19	46	18	70	24
21	16	52	16	70	18
22	18	47	19	72	25
23	14	41	14	73	32
				Average score difference:	20%

Table 2: Compilation of the average pre- and post- workshop assessment score.

	Variable 1	*Variable 2*
Mean	55.47826087	75.04347826
Variance	112.4426877	118.8616601
Observations	23	23
Hypothesized Mean Difference	0	
Df	44	
t Stat	-6.169595592	
P(T<=t) one-tail	0.0000000950	
t Critical one-tail	1.680229977	
P(T<=t) two-tail	0.0000001900	
t Critical two-tail	2.015367574	

Table 3: Result of T-test assuming unequal variances comparing the pre- and post- workshop average scores.

As shown in table 3, the p-value is less than 0.05, suggesting that there the improvement in the score is significant after participants attended the GCP Refresher Workshop.

Discussion

Training of investigators and allied health professions involved in clinical trials on the regulations and standards that govern clinical trials is important to improve the quality of studies and ensure maximum safety for the study subjects. A survey amongst clinical researchers in Saudi Arabia on their ICH-GCP knowledge found that its poor understanding of investigator's responsibilities on informed consent, and prompt reporting to the ethics committee.[7] Hence, refreshing investigators' awareness of their responsibilities could help to improves the performance of investigators in conducting clinical trials particularly in these important ethical aspects.

The GCP refresher workshop conducted by CRM fulfills its objective to provide revision of the principles of GCP to participants, with more an average of 20% improvement in assessment score after the workshop.

The factors that potentially contribute to the success of the CRM GCP Refresher workshop in improving participant's score was discussed below:

Case studies discussion

Case studies were included for "Informed Consent", "Adverse Event Reporting" and "Protocol Deviations" for discussion. Participants were given real-life scenario case studies and they were required to answer guided questions in groups. Study have shown that case studies are more effective than textbook reading at promoting learning of key concepts and comprehension of the relevance of concepts to real life scenario.[8]

Interactive workshop

Several methods were used to make the workshop interactive such as games, quizzes, videos, group activities and group discussion. Active engagement of participants helps in the retain of information.[9]

Trainers would also actively engage participants by asking questions and encouraging participants to share their experience and practices. Regulations of clinical research can be understood more easily when participants can reflect the principles upon their own experience.[10]

Feedback from participants

Participants were given evaluation forms at the end of the workshop to provide their feedback and opinion of the workshop. Based on their feedback, modifications were made to improve the conduct of the workshop:

1. Duration of workshop

The first GCP Refresher Workshop is a half-day (4 hours) workshop. Participants reflected that the workshop felt rushed and suggested to make it a full-day course. Subsequent workshops were then conducted one full day (8 hours) to ensure participants can learn at a better pace, contributing a better learning outcome.

2. Content of workshop

One of the earlier feed-back received is to include more activities especially for safety reporting and protocol deviations. Modifications based on this feedback is the shift from a lecture-style workshop to activity-based workshop. Presentation slides were also revised to be more concise to retain attention.

3. Provision of GCP booklet

Following a feedback from participants, the current edition of the Malaysian GCP Guideline booklets were provided for participants to refer to during the workshop.

Conclusion

It is important for investigators and allied health professions who are involved in clinical studies to be trained on the latest GCP guideline.

The GCP Refresher Workshop conducted by CRM is effective in refreshing participants' knowledge on the GCP guideline. The success of the workshop could be attributed to providing case studies for discussion, interactive activities as well as taking participants' feedbacks into consideration. We would recommend other governing bodies to support the conduct of similar interactive workshops in their jurisdiction; and to take participants' feedback for continuous improvement.

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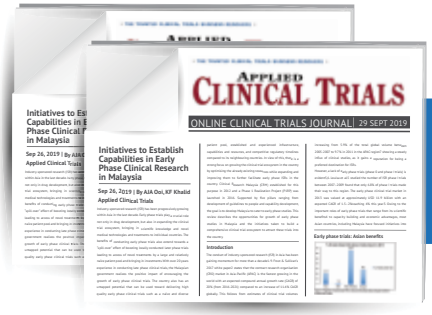

Initiatives to Establish Capabilities in Early Phase Clinical Research in Malaysia – Applied Clinical Trials

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Industry-sponsored research (ISR) has been progressively growing within Asia in the last decade. Early phase trials play a crucial role not only in drug development, but also in expanding the clinical trial ecosystem, bringing in scientific knowledge and novel medical technologies and treatments to individual countries. The benefits of conducting early phase trials also extend towards a "spill-over" effect of boosting locally conducted later phase trials leading to access of novel treatments by a large and relatively naïve patient pool and bringing in investments. With over 20 years experience in conducting late phase clinical trials, the Malaysian government realizes the positive impact of encouraging the growth of early phase clinical trials. The country also has an untapped potential that can be used toward delivering high quality early phase clinical trials such as a naïve and diverse patient pool, established and experienced infrastructure, capabilities and resources, and competitive regulatory timelines compared to its neighbouring countries. In view of this, there is a strong focus on growing the clinical trial ecosystem in the country by optimising the already existing resources while expanding and improving them to further facilitate early phase ISRs in the country. Clinical Research Malaysia (CRM) established for this purpose in 2012 and a Phase 1 Realization Project (P1RP) was launched in 2016. Supported by five pillars ranging from development of guidelines to people and capability development, the goal is to develop Malaysia to cater to early phase studies. This review describes the opportunities for growth of early phase studies in Malaysia and the initiatives taken to build a comprehensive clinical trial ecosystem to attract these trials into the country.

Introduction

The conduct of industry-sponsored research (ISR) in Asia has been gaining momentum for more than a decade[1-9]. Frost & Sullivan's 2017 white paper[2] states that the contract research organisation (CRO) market in Asia-Pacific (APAC) is the fastest growing in the world with an expected compound annual growth rate (CAGR) of 20% (from 2016-2021) compared to an increase of 11.4% CAGR globally. This follows from estimates of clinical trial volumes increasing from 5.9% of the total global volume between 2005-2007 to 9.7% in 2011 in the APAC region[7] showing a steady influx of clinical studies, as it gains a reputation for being a preferred destination for ISRs. However, a lack of early phase trials (phase 0 and phase I trials) is evident[5,6]. Louisa et al.[5] studied the number of ISR phasenly 6.8% of phase I trials made their way to this region. The early phase clinical trial market in 2013 was valued at approximately USD 11.9 billion with an expected CAGR of 1.5–2%reaching 4% this year[3]. Owing to the important roles of early phase trials that range from its scientific benefits[4] to capacity building and economic advantages, most Asian countries, including Malaysia have focused initiatives into building adequate infrastructure to attract them.

Early phase trials: Asian benefits

To date (as of 12 July 2018), there are 16,248 interventional ISRs covering all phases globally, 27.2% (4,424) are early phase (phase 0 and phase I) trials[10]. Figures 1 and 2 show the proportion of early phase trials in Asia and Southeast Asia which are significantly smaller compared to North America and Europe.

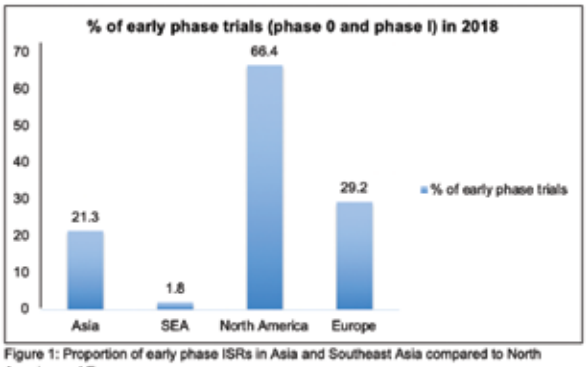

Figure 1: Proportion of early phase ISRs in Asia and Southeast Asia compared to North America and Europe.

Figure 1: Proportion of early phase ISRs in Asia, Southeast Asia, North America and Europe for the year 2018. Search criteria for these and all other values were recruiting, not yet recruiting, active–not recruiting, enrolling by invitation, interventional studies, phase 0, phase I and industry funded. Asia: North Asia, South Asia, East Asia and Southeast Asia; total number of trials in the region will defer from number of trials in an individual country due to inclusion of multicentre trials.

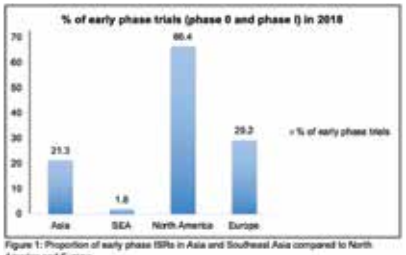

Figure 1: Proportion of early phase ISRs in Asia and Southeast Asia compared to North America and Europe.

Figure 2: Number of early phase ISRs in Southeast Asia. Total number of ISRs registered in Clinicaltrial.gov as of July 2018 in Asia is 5,126 (of 16,248) and total number of early phase ISRs is 943 (of 4,424). Search criteria for these and all other values were recruiting, not yet recruiting, active –not recruiting, enrolling by invitation, interventional studies, phase 0, phase I and industry funded. Asia: North Asia, South Asia, East Asia and Southeast Asia; total number of trials in the region will defer from number of trials in an individual country due to inclusion of multicentre trials.

There are several benefits in conducting early phase trials in Asia. These are for example, certain diseases which are more prevalent compared to the west wherein epidemiology, health services, social determinants, co-morbidities and genetic components of the population can have an effect on how a treatment may be used, and, differences in genetics and gastrointestinal microbiome effect on the pharmacokinetics and pharmacodynamics of drug molecules[4,5]. There have also been concerns that racial and ethnic minorities, women and the elderly are often underrepresented in early drug development programmes making Asia an attractive destination for clinical trials[1].

Therefore, the conduct of more early phase trials in regions within Asia, like Southeast Asia, plays a pivotal role to ensure that the populations proportional to the potential uses of the product after its registration and approval are conducted from the earliest stages[5].

Early phase trials: opportunities for growth in Malaysia

Diverse and accessible subject pool

Malaysia, located in Southeast Asia, is a multi-racial country consisting of Malays, Chinese, Indians and numerous indigenous people who are mostly treatment naïve. This provides the genetic diversity that is important in every clinical trial. The epidemiology of diseases in an individual country is also a crucial consideration when determining the the success of a clinical trial as it signifies the availability of study subjects and mitigates the risks of poor accrual rates that can cause trials to fail at huge costs[11]. Though a strong presence of the disease provides for a rich source of ready patients for later phase clinical trials, it also serves as an important incentive for governments to encourage testing of novel treatments in FIH trials within the country.

Patient pool with cardiovascular risks — diabetes, hypertension and hypercholesterolemia

At a global level, the top 20 indications of industry-sponsored clinical trials, regardless of phase of study include cardiovascular disease, diabetes mellitus, hypertension and hypercholesterolemia[7]. Conducting early phase trials targeting these conditions would be doubly beneficial to countries like Malaysia that face major public health concerns with them. Early phase trials would allow access to novel treatments and changing standards of care and with a ready pool of relatively naïve patients, sponsors and CROs would have an easy access to subjects for later phase trials. Being part of the drug development process from its early stages allows investigators and clinical trial staff to become familiar with the treatment, thereby allowing continued progress of clinical study phases to occur more smoothly.

In Malaysia, the National Health and Morbidity Survey published in 2015 showed that prevalence of diabetes mellitus among Malaysian adults of 18 years and above was 17.5% (8.3% known and 9.2% undiagnosed)[12]. The overall prevalence for hypertension and hypercholesterolemia were 30.3% (13.1% known and 17.2% undiagnosed) and 47.7% (9.1% known and 38.6% undiagnosed), respectively. In 2016, disease of the circulatory system was in the top five principal causes of hospital admissions (both private and public hospitals), at 7.44% of total admissions and within the top five principal causes of mortality[13]. With regards to Type 2 diabetes mellitus, it has more than doubled since 1996 and coupled with a prevalence of 27–31% in overweight and obesity in school children, this disease poses a major public health concern[14].

With the high prevalence of cardiovascular risk factors such as diabetes, hypertension and hypercholesterolemia, not only has Malaysia a ready, diverse and relatively naïve patient pool for later phase ISRs that fit into the top 20 clinical trial indications, but it also gives the Malaysian government a strong incentive to encourage early phase trials.

Oncology patient pool

Studies in the field of oncology treatment are currently the top indication for clinical trials. Using the following search criteria, start date 01/01/2013-31/12/2017, recruiting, not yet recruiting, active – not recruiting, enrolling by invitation, early phase I and phases I-III, indication for cancer takes up 54.5% of the total industry sponsored interventional studies [10]. Additionally, projected distributions of available new active substances in the global market by disease type from 1996–2020 show[15] a projected growth in oncology biopharmaceutical and pharmaceutical products making up 13% of the total new active substances.Thirty-three percent of novel drug approvals in 2015 by the United States Food and Drug Administration (USFDA) were for oncology related products whilst 27% were approved in 2017[16-18]. In the US alone, there were 836 drugs and vaccines for cancer in various stages of clinical development or awaiting USFDA approvals[19].

In Malaysia, cancer is within the top five causes of mortality and in 2016, the total hospital admissions for neoplasms were 4.2% (based on total admissions of > 3 million)[13]. Breast cancer is the most common of all cancers (17.7%) followed by colorectal (13.2%) and cancer of the

trachea, bronchus and lung (10.2%)[20].

FIH trials of oncology drugs differ from early phase trials in other therapeutic areas as they are evaluated in patients rather than healthy volunteers. The characteristics of oncology products, mainly its safety profile, do not allow for testing in healthy volunteers. In the absence of alternative effective treatments in oncology, participation in these trials using novel compounds are considered an opportunity to these patients[21].

Therefore, with the global pipeline of oncology drugs in clinical development having seen a robust growth over the past two decades[22], combined with the strong presence of cancer among Malaysians, not only are sponsors presented an opportunity to tap into the available pool of cancer patients, it is also a considerable push for the Malaysian government to spur the growth of early phase oncology clinical trials within the country.

Cost Effectiveness

The cost of developing a new molecular entity can be over USD 1 billion with an average estimate of USD 2.6 billion[8]. Added to that, the development of a new medicine from identification through approval for marketing can take up to or more than 12 years. In view of the extreme financial investments, Asian countries like Malaysia, which provide treatments and medical procedures at a lower cost than in developed countries[1,9], can be seen by sponsors and CROs as an ideal site for conducting clinical trials with lower investments.

The 2017 Frost & Sullivan white paper's[1] costing estimates of conducting clinical research per patient, per visit in all therapeutic areas in all phases shows Malaysia as having the second lowest cost coming before India (USD 350 vs. USD 330) while costs in Singapore was similar to that in the USA (USD 1,210 vs.USD 1,380) and that in South Korea was USD 890.

Regulatory Timelines

One of the complexities of performing clinical trials in Asia is the heterogeneous nature of the regulatory processes and timelines among the countries in the region[1-3,6].

However, countries in the region have attempted to harmonise these to ensure better data acceptability and reduce trial and drug approval timelines[1]. Malaysia is part of the ASEAN Free Trade Area (AFTA) that undertook the ASEAN Common Technical Documents (ACTD) and ASEAN Common Technical Requirements (ACTR) initiatives to standardise drug approval processes.

In Malaysia, ethics review and regulatory approvals together with import licensing and contract negotiations occur concurrently allowing for faster processing timelines and is comparable with timelines in South Korea and Singapore (approximately 2-3 months[1]). In a recent report, regulatory timelines have been improved to within 30 working days[23] while the centralized ethics committee under the Ministry of Health has shortened its timelines to 51 calendar days.

Established infrastructure, resources and capabilities

An established and functioning network of clinical trial centres with advanced equipment and technology; knowledgeable physicians and available key opinion leaders in different specialties also play an important role in attracting ISRs[1].

Malaysia has a well-developed and equipped healthcare system manned by medical doctors that practice and comply with international clinical practice standards[24]. ISRs in Malaysia are conducted at government hospitals, teaching institutions, private hospitals and government health clinics. Government hospitals receive and treat the largest number of patients thus presenting a unique opportunity for access to the primary care patient pool.

Developing an ecosystem for early phase clinical research in Malaysia

The Government of Malaysia realizing the potential positive impact of early phase trials for patients, scientific advancements and economic growth is stepping up its existing clinical trial capabilities by building new initiatives to drive early phase clinical research capacity in-country and develop an attractive early phase clinical trial ecosystem.

In lieu of this, the Malaysian government included the creation of a supportive ecosystem with the establishment of Clinical Research Malaysia (CRM) a non-profit company, wholly owned by the Ministry of Health[24], to equip the ecosystem of clinical research in the country[25]. Its goal is to reach at least 1,000 clinical trials by the year 2020. Part of the initiatives stated in this section is to set up more clinical research centres, develop more Good Clinical Practice (GCP) certified investigators and improve existing IRB and EC timelines. The Phase 1 Realization Project (P1RP) initiated by CRM in 2016 was aimed at realizing this aspiration of making sure Malaysia is capable in conducting early phase studies.

The benefits of conducting early phase trials in Malaysia as laid out by the P1RP are the increase of phase II and III trials as a result of a spillover effect from conducting more phase I trials, contribution to the transfer of knowledge and technologies to Malaysians, creation of new jobs in clinical research, spurring local innovation, prevention of investment outflow and moving the country as a whole higher up the clinical research value chain. For patients, it increases the opportunity to receive novel medications or treatment that is not yet available in the market as the

majority of ISRs are interventional in nature providing treatment at no cost to patients. It also provides a means for the government to expand its healthcare resources to include more patients and medications especially oncology treatment that are costly.

The P1RP Blueprint

The P1RP stands on 5 pillars, which are the establishment of guidelines for conducting phase I clinical trials in the country, people development, capability development, preparation of sites and risk management. To date, all of the P1RP pillars have been implemented and fulfilled. In the first quarter of 2019, the country's regulatory authority has indicated that it is ready to review FIH studies by June 2019.

The P1RP strategy is multi-pronged wherein regulatory agencies are equipped with the right knowledge to review phase I clinical trials and conforming to international standards, local experts are trained with the necessary skills to analyze early phase trials through engagement with international consultants, preparation of clinical trial unit at hospitals to conduct phase I studies, and the development of an action plan to manage and mitigate any given crisis that may occur during the clinical trial process.

Development of phase I clinical trial guidelines

The Malaysian Phase I Clinical Trial Guidelines[26] was launched in November 2017. Prior to this, the country did not have a specific guideline on phase I clinical trials. The effort saw the coming together of experts and investigators in the field of clinical trials from the Ministry of Health, Ministry of Higher Education, ethics and regulatory bodies as well as industry experts. International key opinion leaders on clinical trials were also invited as subject matter experts. The guidelines were based on The Association of the British Pharmaceutical Industry (ABPI) 2012 version of phase I clinical trial guidelines[27] as this document took into account and expanded its content to reflect the latest changes in conducting FIH trials. The Malaysian guidelines in turn considered local regulatory bodies and agencies' existing procedures, and the local clinical trial environment, adapting relevant areas to facilitate the applicability of the ABPI guidelines in Malaysia.

People Development

To gain knowledge and experience in phase I clinical trials so as to implement and impart these to relevant agency officers, three regulatory officers were sent to pursue their postgraduate studies at The Christie, Manchester, as well as King's College London, under a collaborative scholarship between CRM and the Public Service Department. This will allow them to work within a leading phase I clinical trial unit and gain experience and understanding in the designing and delivering of phase I studies. This attachment is important as these regulatory officers will be the ones responsible in reviewing the dossiers of phase I studies in Malaysia.

The Ministry of Health has also planned to send local investigators to be attached at reputable phase I centres, including the Princess Margaret Cancer Center, to be exposed to the experience in conducting FIH studies.

The government has also started initiatives to bring back Malaysians from overseas. Experts or specialists from higher-income countries coming back would have an edge due to a global mindset. Coupled with an in-depth knowledge of the country, people and the culture, it creates a world-class pool of specialists that can support early phase trials[2].

Initiatives to develop and perform centralized professional training for study coordinators to complement the work of investigators have also began. To attract more specialists to participate in clinical trials, the Ministry of Health now allows for 20% of a work-week (or one full day off) for investigators to focus solely on research.

Capability development

In a 2011 report presentation of the Health Committee at the 49th Parliament sitting in New Zealand[28], some of the recommendations put forward to increase New Zealand's presence in the clinical trial industry were, to establish a strong intra-governmental collaboration between different ministries, ensure a culture that values research within the public health system and requiring the Standing Committee on Therapeutic Trials to carry out all scientific reviews within 30 calendar days.

As part of the capability development pillar of P1RP, a Scientific Review Panel (SRP) for FIH clinical trials was established to support the Medical Research and Ethics Committee (MREC), a centralized ethics committee, in performing scientific evaluations of FIH trials undertaken by and/or conducted in clinical trial sites in Malaysia. The scope of review includes all FIH studies on new chemical, biological and biosimilar drugs not registered in Malaysia.

The intensity of early phase clinical trials is more time-consuming requiring more physical exams, vital signs monitoring, electrocardiogram (ECG) monitoring and pharmacokinetic laboratory tests compared to later phase trials[29]. The P1RP project and initiatives will harness the available resources and capabilities available within the country's health system as well as increase its knowledge with international collaborations to ensure that the country is ready to meet with the demands of early phase trials.

Capability development

Sarawak General Hospital located in a major city in East Malaysia is targeted to be fully equipped to

handle early phase clinical trials. It also serves as a template for future units to be developed in other hospitals. This hospital is already a major medical centre with a ready access to large patient populations and the clinical trial centre is well-equipped and operated by well-trained scientific and medical staff.

Risk management

In June 2007, the "Guideline on Strategies to Identify and Mitigate Risks for First-in-Human Clinical Trials with Investigational Medicinal Products" was finalised by the EMA[30]. The scope of the guidance encompasses both biologics and new chemical entities and, was recently updated in 2016 (EMA/CHMP/SWP/28367/07)[31] and places the focus on the pharmacological characteristics of a new drug.

The document was created to support the transition from non-clinical to the early phase of clinical development and identifies influencing risk factors of a product, includes consideration of quality aspects, testing strategies, designs for FIH studies and mitigation strategies such as initial dosing calculation and dose escalation[30].

Therefore, part of the P1RP initiative is the preparation and training of risk management guidelines and to manage any crisis in relation to early phase clinical trials. These include creation of a standard operation procedure (SOP) to prepare for and manage all types of crises requiring immediate attention during early phase trials (i.e. unexpected side effects from a clinical trial). The SOP is designed to also ensure that all actions are coordinated, timely, accurate, consistent and effective in minimising the potential for confusion, rumor and misinformation. The overall objective of this effort is to offer support to the organisation and processes of early phase trials in difficult situations and to the greatest possible extent, limit potential injury to patients, consumers or the reputation of the institutions.

The guidelines were based on The Association of the British.

ACCELERATE Project

CRM initiated the ACCELERATE project to move the nation's focus further upstream to early phase drug discovery and development, utilising readily available resources in the country. The project involves converging expertise and collaborations across agencies, clinical research industries and universities on pre-clinical projects. Through this initiative, CRM has intensified collaborations with various universities and research institutes in 'bench to bedside' projects. The conversion of pre-clinical studies into early and late phase trials may spur discovery, local innovation and eventually manufacturing of innovator drugs in Malaysia. Additionally, it can prevent outflow of investments and move the country higher up the clinical research value chain.

Conclusion

Malaysia's effort through the P1RP and ACCELERATE project underlines the government's commitment to bring the country into a new phase in the clinical trial industry. In the local context, early phase clinical trials play a key role in enhancing the capability of the country in the development of medical science and treatment of disease as well as placing Malaysia at the cutting edge of research. To this end, the Malaysian government's goal is to develop the country into becoming the preferred destination for industry-sponsored research.

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CRM in Photos

Meeting with My Dental International Clinics Sdn Bhd, 26 June

Meeting with Bayer, 25 July

Visit by Prof James from the University of Southampton, 25 July

Talk by Dr Albiruni Razak at the National Health Institute, 12 August

Meeting with Novo Nordisk, 16 August

Visit by Hematogenix, 11 September

Meeting with Parexel, 20 September

Meeting with Prof Yuji Kumagai (Kitasato University) & Mr Koichi Hagita (TryAngle), 20 September

ESMO Congress 2019, 27 September - 1 October

Meeting with Fresenius Medical Care, 17 October

Meeting with Legal Advisor & Secretary Division of Policy and International Relations of MOH, 23 October

Meeting with Henlius Biotech Inc., 25 October

REACTA Annual Forum 2019, 18 November

Meeting with Intervenn Biosciences, 27 November

Meeting with Syneos Health, 4 December

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in collaboration with

UNIVERSITY OF SURREY - UNIMAS

11 April 2020 (Saturday) | 8:00 am – 5:30 pm | KL Convention Centre

HIGHLIGHTS

Top Presenter Awards | Oral Communication | Poster Presentation | Networking lunch

KEYNOTE SPEAKERS

Prof. Philip Aston, University of Surrey
Mathematician expert with research interests in mathematical biology, including pharmacology, hepatitis C infection and DNA damage repair.

Dr Richard Hoglund, University of Oxford
Research expertise in application of pharmacokinetics, pharmacodynamics, and mathematical modelling in tropical medicine research.

Dr Olexsandra Prysyazhna, Queen Mary University of London
Research expert in cardiovascular research specifically in studying cardiovascular redox sensing and signalling.

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