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REVIEW

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Early phase oncology clinical trials in Malaysia: current status and future perspectives

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Abstract

Historically, the majority of oncology clinical trials are conducted in Western Europe and North America. Globalization of drug development has resulted in sponsors shifting their focus to the Asia-Pacific region. In Malaysia, implementation of various government policies to promote clinical trials has been initiated over a decade ago and includes the establishment of Clinical Research Malaysia, which functions as a facilitator and enabler of industry-sponsored clinical trials on a nationwide basis. Although oncology clinical trials in Malaysia have seen promising growth, there are still only a limited number of early phase oncology studies being conducted. Hence, the Phase 1 Realization Project was initiated to develop Malaysia's early phase clinical trial capabilities. In addition, the adaptation of good practices from other countries contribute to the effective implementation of existing initiatives to drive progress in the development of early phase drug development set up in Malaysia. Furthermore, holistic approaches with emphasis in training and education, infrastructure capacities, strategic alliances, reinforcement of upstream activities in the value chain of drug development, enhanced patient advocacy, coupled with continued commitment from policy makers are imperative in nurturing a resilient clinical research ecosystem in Malaysia.

KEYWORDS
clinical trials, early phase oncology trials, Malaysia, oncology

1 | EARLY PHASE ONCOLOGY CLINICAL TRIALS IN ASIA

Cancer ranks as a leading cause of death and an important barrier to increasing life expectancy globally, accounting for nearly 10 million deaths in 2020.[1] The overall burden of cancer incidence and mortality is growing rapidly, and this reflects both aging and growth of the population as well as changes in the prevalence and distribution of the main risk factors for cancer, several of which are associated with socioeconomic status.

Oncology clinical trials are intended to evaluate the safety, toxicity, and efficacy of new anticancer agents and represent an essential component to drive advances in this field.[2,3] Historically, the majority of oncology clinical trials were conducted in high income countries, especially in Western Europe and North America. The reasons for this are multifactorial, including the availability of an established trial infrastructure incorporating both physical and manpower requirements, along with the geographical location of major pharmaceutical companies in these countries.[4] However, in recent years, globalization has resulted in a shift of this practice, with more clinical trials being conducted outside of Western Europe and North America, such as in Asia. One of the main reasons for this shift is attributed to the fact that clinical trial data are often collected from varied populations and ethnic groups to support a license application for a novel drug

or new drug combination. Geographically different trial sites are often needed to ensure the product is safe, possesses comparable pharmacokinetic profiles, and exerts the same or similar antitumor activity in varying ethnic groups.[5] Furthermore, clinical trials are also being conducted across more diverse countries for economic reasons.[6] This phenomenon has been witnessed by a sturdy growth of phase I oncology studies within the Asia Pacific region during the past decade. Several key oncology research centers in Korea, Japan, Taiwan, China, and Singapore have now been actively driving the early phase development of novel oncology therapeutic compounds in Asia Pacific by playing a leadership role.[5,7,8] There are numerous reasons for the positive growth and expansion of early phase clinical trials within this region, including the emergence of a generation consisting of committed and knowledgeable investigators, and also the availability of internationally accredited clinical trial facilities and their supporting infrastructure.[5]

In addition, with nearly 60% of the world population residing in Asia, countries within this region will be able to offer large and genetically diverse patient pools. This would complement the patient pools in occidental countries.[9] A recent review has examined the open-access clinical trial registry clinicaltrials.gov for registered interventional recruiting early phase trials (Phase I/II) in the BRIC (Brazil, Russia, India, and China) countries and found that China accounted for 95% (842/888) of the trials; with gastrointestinal (17%, 148/888), lung (11%, 94/888), and breast (17%, 53/888) cancers being the most studied. This review has also highlighted that early phase trial testing in hematology and oncology has increased significantly throughout Asia, especially in China, which now has 18.5% of the global population.[10] Moreover, countries in Asia also offer access to patient whose tumors harbor a wide diversity of genomic variants including certain molecular subsets, which occur at particularly high prevalence levels within the region.[5] An example is the existence of epidermal growth factor receptor *(EGFR)*-mutated nonsmall cell lung cancer (NSCLC) at higher prevalence in the Asian population.[11] The discovery of *EGFR* mutations in NSCLC launched the era of precision medicine with the use of EGFR tyrosine kinase inhibitors (TKIs). Early phase drug development for the treatment of this disease was robustly conducted by Asian clinical trial sites.[12–14] These studies have supplemented many successful landmark studies with leadership and participation from many Asian sites that have transformed the treatment landscape of advanced *EGFR*-mutated NSCLC globally.[11,15–17]

2 | CLINICAL TRIALS AND EARLY PHASE ONCOLOGY CLINICAL TRIALS IN MALAYSIA

2.1 | Overview

Malaysia is a multiracial country and has a population of approximately 32.6 million in 2020 comprising 69.6% Bumiputera (consisting mainly of Malays), 22.6% Chinese, 6.8% Indian, and 1% other races.[18] This demographic profile has provided Malaysia an inherent advantage to conduct clinical trials with its large multiethnic population that offers genetic diversity. In 2010, the Malaysian government's Economic Transformation Program, comprising 12 National Key Economic Areas (NKEAs), was initiated with clinical trial development designated as a priority under the Healthcare NKEA.[19] Within this program, the Malaysian government intended to promote clinical trial activities with aims of conducting at least 1000 clinical trials and creation of at least 1000 skilled jobs by 2020.[19]

One of the pivotal steps of this initiative is the establishment of Clinical Research Malaysia (CRM). As a nonprofit entity established by the Ministry of Health Malaysia (MOH) in June 2012, CRM was created to position Malaysia as a preferred global destination for clinical trials. CRM plays an essential role to improve the local clinical research ecosystem to support growth in clinical trials, facilitate the needs and requirements of industry sponsors, and grow the pool of capable investigators, clinical study staff, and trial sites.[20] Prior to CRM's inception, there were several challenges encountered in the expansion of clinical trial activities in the country, and these had hampered clinical trial development in Malaysia in terms of speed, reliability, and the delivery of high quality study conduct and data to the relevant stakeholders. These challenges include the time-consuming hiring process and development of infrastructure that involved government bureaucracy, poor transparency of fund management and lack of activities to increase the number of investigators and well-equipped trial sites for the conduct of clinical trials.

In Malaysia, clinical trials are generally conducted in university and government hospitals across the country as the bulk of cancer patients is referred to these sites. The National Pharmaceutical Regulatory Agency is an agency under MOH that is empowered to review matters related to investigational product registration and approval for clinical trial import license (CTIL) or clinical trial exemption (CTX).[21] The institutional review board (IRB)/independent ethics committee (IEC) structure in Malaysia varies depending on the location or type of facility conducting the research. Generally, most university hospitals have their own IRB/IEC, while trials conducted at MOH facilities fall under the purview of the central IEC, which is the Medical Research and Ethics Committee (MREC).[22] At present, regulatory and ethical submissions are done in parallel, enabling Malaysia's approval timelines for clinical trials to be competitive with other countries in the region (CTIL/CTX application is processed within 30 working days, while the MREC approval takes 50 working days).[20]

Malaysia has the potential to attract clinical trials in oncology due to the high incidence of certain tumor types in the country that will provide a large pool of patients for conducting trials in these diseases.[23,24] For example, nasopharyngeal cancer (NPC) is generally a rare malignancy in the West, but the Bidayuh tribe in the state of Sarawak in Malaysia has one of the highest incidence of NPC in the world.[25] This will facilitate recruitment for therapeutic trials of this tumor type and concurrently providing new treatment options for this disease in high incidence area. Besides the parallel regulatory and approval pathway as well as the availability of patient pool for oncology studies, sponsors and clinical research organizations (CROs) are also drawn to Malaysia because of its competitive trial costs.[20]

2.2 | Progress

Based on data obtained from CRM, since its inception until 2021, a total of 1806 industry-sponsored clinical trials were conducted in MOH facilities, alongside the creation of 2291 skilled jobs in clinical research.[26] In line with the growth trend of cancer research globally, oncology has been one of the top therapeutic areas of sponsored-clinical trials in Malaysia for the past few years. In 2021, a total of 215 clinical trials were initiated in MOH facilities, with oncology trials making up about 15.3% (n = 33) of the total. Majority of these oncology trials were late phase trials (n = 15) with only four phase II and one phase I trials initiated in the same year (Table 1).[26] In order to map out current activity and identify any gaps that could be filled, we conducted a landscape assessment, collecting and analyzing all Malaysian oncology clinical trial literature that had been published. Searches were conducted in PUBMED, MEDLINE, EMBASE, and CINAHL databases, together with American Society of Clinical Oncology and European Society for Medical Oncology proceedings from 2011 to 2021. The search yielded 165 citations after elimination of duplicates in accordande to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Figure 1). An initial screening process of these 165 titles and abstracts has resulted in a first classification whereby 38 papers were included for abstract and/or full-text review. However, only 36 abstracts or full text articles were included based on the eligibility of this scoping review. Of these abstracts or full text articles 82% (n = 30) were phase II and III with only four involved phase I or Ib/II clinical trials. The two most studied tumor types were lung and breast cancers (Table 2). Most of the evaluated abstracts or full text articles involved the investigation of targeted/immunotherapeutic agents such as bortezomib, cetuximab, ceritinib, crizotinib, docetaxel, erlotinib, gefitinib, letrozole, neratinib, osimertinib, panobinostat, pazopanib, pembrolizumab, ribociclib, sunitinib, and tepotinib.

The lack of early phase oncology trials in the country has led to the launching of the Phase 1 Realization Project (P1RP), an initiative to develop Malaysia's early drug development capabilities. This initiative, which commenced in May 2016, utilizes a multipronged strategy that aims to establish national guidelines for conducting phase I trials, setting up of a scientific panel to review first-in-human trials (FIH), postgraduate training for regulatory officers and investigators in early phase drug development, preparation and upgrading of a phase 1 unit, as well as risk management training (Table 3 and Figure 2).[27]

TABLE 1 Sponsored clinical trials conducted in Ministry of Health Malaysia (MOH) facilities 2021

All therapeutic areas	Number (n = 215)	Percentage (%)
Oncology	33	15.3
Phase I	1	
Phase II	4	
Phase III	15	
Not applicable (observational)	13	
Infections and infectious diseases	40	18.6
Hematology	15	7.0
Others	13	6.0
Pediatrics/Neonatology	13	6.0
Cardiology/Vascular diseases	11	5.1
Endocrinology	10	4.7
Healthy volunteers	10	4.7
Nephrology	9	4.2
Psychiatry/Psychology	7	3.3
Hepatology (liver, pancreatic, gall bladder)	6	2.8
Dermatology	5	2.3
Ophthalmology	5	2.3
Pulmonary/Respiratory diseases	5	2.3
Gastroenterology	4	1.9
Obstetrics/Gynecology (women's health)	4	1.9
Neurology	3	1.4
Orthopedics/Orthopedic surgery	3	1.4
Rheumatology	3	1.4
Urology	3	1.4
Dental and oral health	2	.9
Family medicine	2	.9
Genetic disease	2	.9
Nutrition and weight loss	2	.9
Otolaryngology (ear, nose, throat)	2	.9
Trauma (Emergency, Injury, Surgery)	2	.9
Immunology	1	.6

[†] Data obtained from Clinical Research Malaysia.

2.3 | Future perspectives

There has been a significant rise in the number of newly diagnosed cancer cases in Malaysia, which were predominantly made up by breast, colorectal, and lung cancers between 2012 and 2016. The reported cancer incidence rate for the period of 2012–2016 was 86 cases for every 100,000 males and 102 cases for every 100,000 females, which represents 11% increments compared to the 2007–2011 report; this may be secondary to low cancer awareness and screening, delays in seeking medical attention, delays in detection and diagnosis, and insufficient access to high-quality cancer care.[28,29] Despite the rise in cancer incidence, there are slightly over 150 oncologists in Malaysia, which is about 50% of the required 300 to fulfill the oncology service requirement of the country.[29,30] Every year, there is a move of oncologists streaming out from the public service into private practice; with the low number of oncologists in public service, it is increasingly difficult to expand the number of new cancer studies at public hospitals, which are the main sites where trials are conducted. These challenges are further compounded by the perception of many that

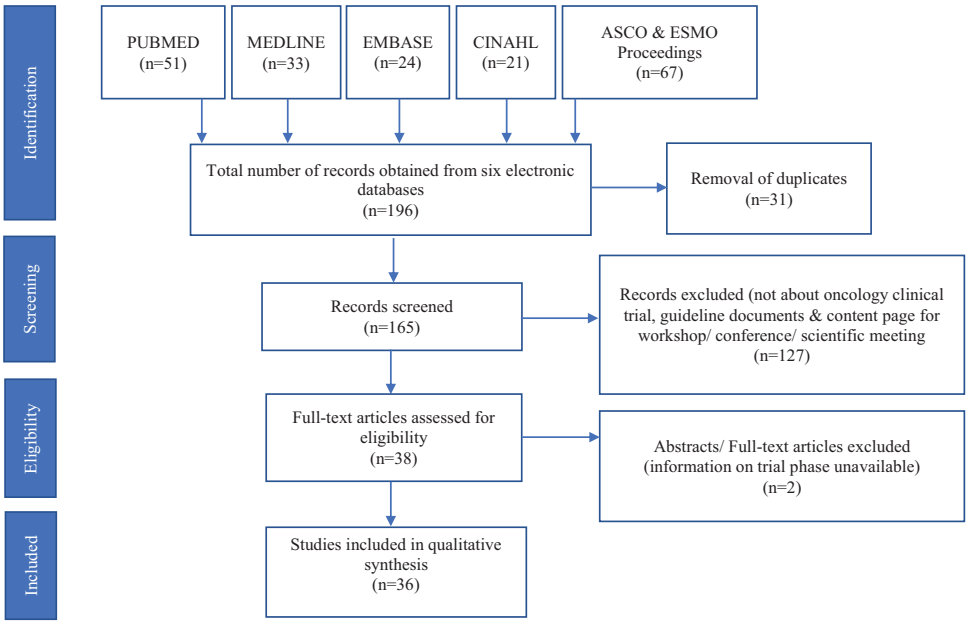

FIGURE 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram for scoping review on published literature on oncology clinical trial in Malaysia (2011–2021) [Colour figure can be viewed at wileyonlinelibrary.com]

clinical research in public hospitals is often not accorded the recognition and importance as it would be in teaching institutions, and only comes second or third after clinical service. Hence, to ensure the ecosystem of oncology clinical trial in the country is conducive to perform early phase studies; there exists the need to introduce novel solutions to retain oncologists in the public sector. This includes extending protected time for oncologists to take up more clinical research. In addition, creation of a special career pathway of clinician scientist for public hospital oncologists would also encourage their active participation in clinical oncology research. Moreover, there is also a need to increase the number of placements available for oncology specialist training. One of the recent positive developments is the implementation of parallel clinical oncology training programs with foreign universities whereby promising young clinical oncology trainees will be sent to these cancer centers of excellence abroad for 2 years of their total 4-year training program. Such exposure especially during their early career paths will provide them invaluable exposure and subsequently inculcate their interest and passion in oncological research.

In addition, enhancement of innovative national policies is essential in encouraging drug development programs in Malaysia. Drug development is often considered risky with low success rate, resource intensive, and time consuming.[31] To spur pharmaceutical industry to invest in research and development (R&D) activities, various tax incentives such as the pioneer status and investment tax allowance are available in Malaysia. Furthermore, BioNexus status company, an initiative introduced in 2005 in conjunction with the National Biotechnology Policy 2005–2020 (NBP 2005–2020) was eligible for 10 years tax exemption. Although NBP 2005–2020 has ended in 2020, the Malaysian government has proposed to extend the BioNexus tax incentives to

TABLE 2 Overview of published literature on oncology clinical trial in Malaysia (2011–2021)

Characteristic	Number ($n = 36$)	Percentage (%)
Clinical trial phase		
Phase I	2	6
Phase II	11	29
Phase III	19	53
Phase IV	2	6
Others (Phase Ib/II)	2	6
Type of cancer		
Breast	10	28
Lung	9	25
Colorectal	3	8
Head and neck squamous cell carcinoma (including NPC)	6	17
Renal cell carcinoma	3	8
Others (e.g., peripheral T-cell lymphoma, gastric cancer, ovarian cancer and NK/T-cell lymphoma, etc.)	5	14
Type of intervention		
Drug	31	85
Procedure	2	6
Herb	2	6
Combination of drug and procedure	1	3

Abbreviations: NK, natural killer; NPC, nasopharyngeal carcinoma.

TABLE 3 Five pillars of phase 1 realization project (P1RP)

Pillar	Measures
Development of phase I clinical trial guidelines	• Malaysian Phase I Clinical Trial Guidelines was launched in November 2017 • Based on ABPI 2012 version of phase I clinical trial guidelines • Local regulatory bodies and agencies' existing procedures, and the local clinical trial environment were considered to facilitate the applicability of the ABPI guidelines in the country
Human capital development	• Regulatory officers and investigators were sent to pursue their postgraduate studies to leading centers in United Kingdom and Canada to gain experience and understanding in designing and delivering of phase I studies
Capability development	• SRP for FIH clinical trials was established to support the MREC, a centralized ethics committee, in performing scientific evaluations of FIH trials conducted in clinical trial sites in Malaysia • Members of SRP consist of local and international experts in early phase study as well as clinical pharmacologists who have experience in evaluating FIH studies
Preparation of sites	• Sarawak General Hospital is accredited by the NPRA as a Phase I Unit. This hospital is a major medical center with a ready access to large patient populations, and its clinical trial center is equipped with comprehensive clinical trial facilities encompassing intensive and high dependency research unit, dedicated research laboratory, and correlative studies facilities, and it is also operated by well-trained scientific and medical staffs
Risk management	• FIH crises management guidelines were created in April 2017. It contained SOP to prepare for and manage all types of crises requiring immediate attention during early phase trials to ensure all actions are coordinated, timely, accurate, consistent and effective in minimizing the potential for confusion and misinformation

Abbreviations: ABPI, The Association of the British Pharmaceutical Industry; FIH, first in human; MREC, Medical Research and Ethics Committee; NPRA, National Pharmaceutical Regulatory Agency; SOP, standard operation procedure; SRP, scientific review panel.

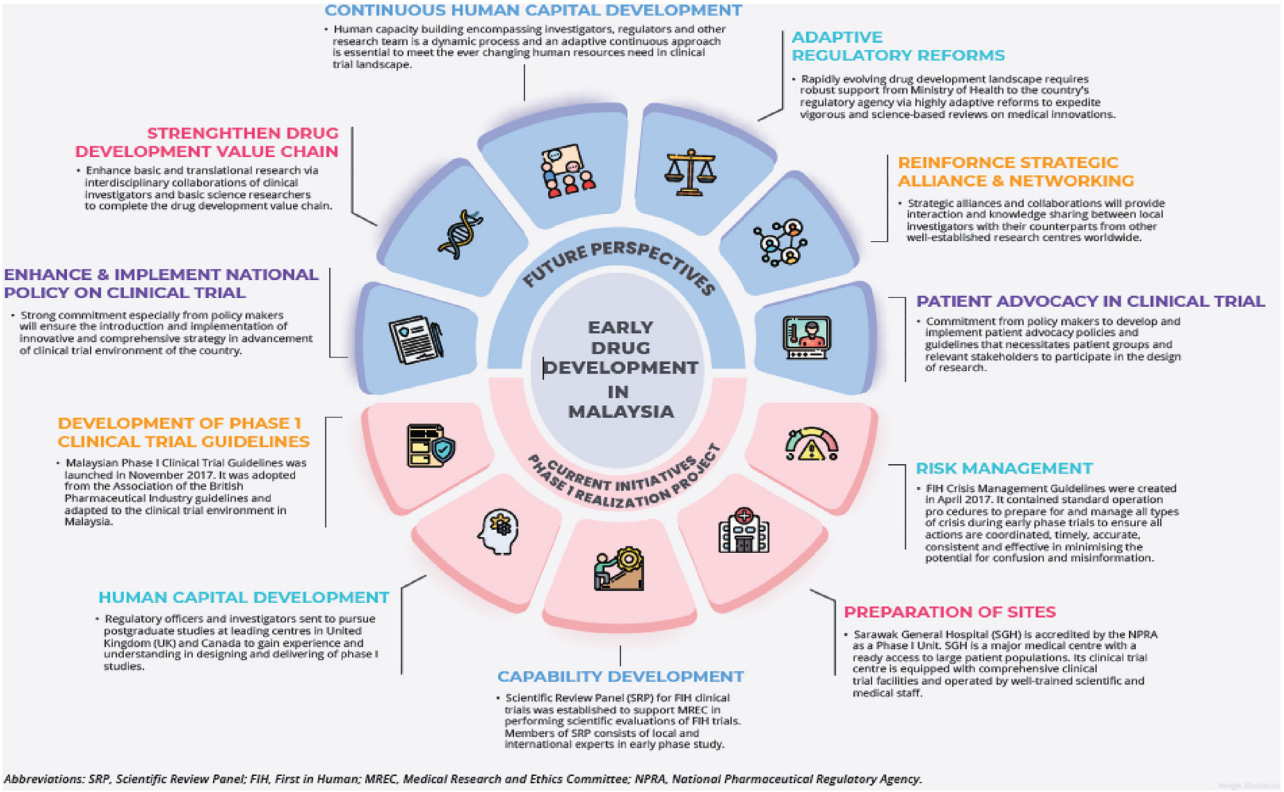

FIGURE 2 Early drug development in Malaysia: Current initiatives and future perspectives [Colour figure can be viewed at wileyonlinelibrary.com]

2022.[32] Hence, to catalyze sustainable growth, long term bioeconomy-based tax incentives should be reintroduced as this cash refund offers a vital source of cash-flow assistance to small and medium enterprises in which it can be reinvested back into the ongoing and future R&D activities.[33]

Likewise, adequate funding should be allocated in key priority areas of research identified by the government to produce impactful discoveries that will change the course of certain diseases and influence overall health care policy making. According to a Malaysian published report, the top five Organization for Economic Cooperation and

Development (OECD) countries with the highest R&D expenditure in 2018 were the USA, Japan, Germany, South Korea, and France; while Malaysia ranked 18th in R&D expenditure.[34] Malaysia's gross expenditure on R&D (GERD) per gross domestic product in 2018 was 1.04%; while Singapore, USA, Japan, and South Korea are 1.8%, 2.9%, 3.3%, and 4.5%, respectively.[34,35] Hence, it is pertinent to increase Malaysia's GERD in-line with other top performing OECD countries and intensify funding for clinical research.

Moreover, to strengthen existing P1RP initiative, support should also be provided to the country's regulatory agency to expedite vigorous and science-based reviews on medical innovations. Sufficient exposure via postgraduate training of regulatory officers in experimental cancer medicine in leading universities abroad, sharing of knowledge, and regulatory harmonization with other global regulatory authorities will ensure readiness of Malaysia's local regulators to review FIH studies. Such regulatory reforms are needed in this rapidly evolving landscape that mandates regulators to keep up with advances in science and making preparation for future challenges. In addition, it is essential for Malaysian regulators to be adaptive in providing supports to industry stakeholders and clients with different needs by enhancing existing capacity in the provision of adequate regulatory advice to them. Early and continuous regulatory support to drug development researchers and pharmaceutical/ biotechnology companies is crucial especially for those who are new to the industry with limited regulatory knowledge. Such regulatory support during the early phase of their drug development research is imperative to mitigate potential regulatory challenges that may arise at the later stage of their drug development project.

Additionally, it is essential to reinforce strategic alliance and global networking with relevant oncology research centers worldwide and pharmaceutical industry. This is critical in the competitive space of early phase drug development whereby only a limited number of sites are selected to participate in such trials. A firm engagement between these entities will not only facilitate the clinical aspect of drug development process but also the upfront involvement of preclinical and translational research with an earlier pipeline access. These alliances will also provide opportunities for new and upcoming sites to learn from other well-established centers through interaction and knowledge sharing between investigators. Currently, key cancer centers in the country are actively participating in various research projects, including genomic studies and clinical trials with other regional academic centers and drug development consortia such as the Asian Thoracic Oncology Research Group (ATORG) and Asia Pacific Oncology Drug Development Consortium. Essentially, as a newcomer in early phase clinical trials, Malaysia needs to learn from the experience of other countries in the Asia Pacific and neighboring regions. For the past decade, China had experienced significant growth in multiple aspects of drug development including phase I oncology trials. Various challenges have been identified, and measures had been taken to overcome these shortcomings.[15,36–39] These challenges and the measures that had been adopted in China and other countries of this region are invaluable lessons for Malaysia to learn from (Table 4). Their successful interventions have contributed to the Asia-Pacific CRO market to be valued at approximately USD$7.6 billion as of 2021 and is forecasted to reach USD$11.9 billion by 2025.[40] Such robust progression was also evidenced by the tremendous growth rate of 344 to 474 percent increased activity observed in several Asian countries between 2007 and 2012 based on an analysis from the International Clinical Trials Registry Platform.[41]

Introducing a new drug to market is a complex process, and the drug development value chain generally involves target discovery, target validation, lead compound identification and optimization, preclinical drug development, and eventually clinical trials. A majority of current oncology research activities conducted by MOH investigators are focusing on "downstream" activities in the value chain of drug development (i.e., clinical trial), with limited integration of discovery research, which focuses on targeting the fundamental biology of cancer. Lack of discovery research in the drug development value chain will blunt and discourage progress in the advancement of novel oncology therapeutic agents in the country. Hence, it is paramount to intensify oncology discovery research and encourage interdisciplinary cooperation by integrating various representatives of different scientific fields from the entire value chain. This could be achieved by encouraging more communications and collaborations between MOH investigator from both the clinical and basic research settings, initiating more collaborative research with local and international academic research organizations as well as international pharmaceutical partners. These strengthening of upstream activities in this value chain will indirectly encourage and strengthen subsequent development of early phase clinical trial in the country.

The development of novel therapeutic approaches in oncology clinical trials has been increasingly more complex. As a result, the need for patient and caregiver input into clinical trial design and conduct is crucial. Such holistic research development has been made feasible with robust participation from cancer patient advocacy group. Their roles have evolved over time from the initial involvement of fund raising for cancer research to the current involvement as essential study team members that bring unique and important patient perspectives to the table, such as ensuring the relevance and prioritization of research questions, the success and transparency of research activities, the identification of opportunities and barriers to enrolment, as well as the dissemination of findings into clinical practise.[42,43] In MOH, CRM is collaborating closely with the National Cancer Society of Malaysia, the National Cancer Council of Malaysia, and others to improve clinical trial awareness among patients via talks at some of these societies' events and has kept them up to date on the trials that are currently recruiting participants. An online platform known as Find A Clinical Trial (https://clinicalresearch.my/fact/) was developed and is freely accessible to those who wish to participate in potentially relevant ongoing clinical trials in the country.

Although there has been fledgling progress of patient advocacy in clinical research activities in Malaysia, there is still a lack of legislation and standards to govern this effort. In order to ensure the success of clinical trials, policymakers must commit to develop and implement appropriate patient advocacy policies and guidelines. For example, the Health Research Authority policy framework for health and social care research in the United Kingdom requires that

TABLE 4 Challenges and achievements of early phase oncology clinical trial in Asia

Country/Region	Challenges	Measures	Achievements
China[15,36,37,38,39]	1. "Drug lag" due to longer regulatory approval compared other countries 2. Data quality, a rate-limiting factor in drug development 3. Majority are developing "me-too drugs" (best-in-class) 4. Repetitive study designs in phase 1 trials (only 16 (9%) were FIH studies of innovative treatments) 5. Paucity of experienced and fully equipped study sites and a severe inequality in the geographical distribution of studies 6. Less study on local high disease burden tumor types like gastric carcinoma, hepatocellular carcinoma, esophageal carcinoma, and nasopharyngeal carcinoma	1. Government's prioritization and regulatory reforms 2017 2. Collaboration with regulatory peers in the USA and Europe via educational events to provide a platform for the spread of regulatory ideas and practices 3. Educational efforts on equipping clinical trial investigators with GCP principles 4. Stricter definition of innovative drugs and a four colors light strategy to prioritize drug 5. Funding supports and applied technology innovation service platforms for drug discovery process 6. Site network for collaborative exchanges	1. 102% increase in the number of phase I trials and 85% increase in the number of phase I agents 2. Chinese Phase I Oncology Trial consortium to provide a platform for sharing experience and expertise 3. Shift of focus from generic drugs to innovative drug R&D. In 2017, 161 (89%) of phase I studies were sponsored by Chinese biopharmaceutical companies
Asia-Pacific[7,8]	1. Healthcare disparities with significant variation across the countries for total health expenditure in the region 2. Drug approval timelines with delay in approval and access of new anticancer therapies 3. Lack of clinical and translational research expertise 4. Inadequate standard-of-care healthcare provisions to ensure the optimal care for subjects who may have toxicities 5. Challenging regulatory environment for clinical trials drug registration 6. Competitive speed of study population enrolment 7. Difficult coordination of studies across multinational sites	1. Application of ICH E5 for harmonization and mutual recognition of clinical trial results between different health agencies to improve the efficiency of the drug development process in the region 2. Focus on Asian-prevalent cancers such as hepatocellular carcinoma, nasopharyngeal cancer and gastric cancer for capitalization of sizable patient population in the region 3. Improvement of infrastructure to conduct biomarker driven clinical trials 4. Harmonization of specific SOPs between different clinical trial sites, requirements for registration and filing of investigational new drugs and free-passage of clinical samples between participating clinical trial sites in different countries	1. Inception of AsiaOne as collaborative framework of early phase new drug development institutions in Asia for opportunities sharing and collective, coordinated effort of international collaborative clinical trials especially for Asian specific cancers 2. Formation of ATORG aiming to coordinate clinical trials and translational research in lung cancer across Asia 3. Establishment of large-scale international genomic screening infrastructure collaboration like LC-SCRUM for lung cancer in Asia

Abbreviations: AsiaOne, Asian Early Phase 1 Oncology Drug Development Consortium; ATORG, Asian Thoracic Oncology Research Group; FIH, first in human; GCP, good clinical practice; ICH, International Conference on Harmonization; LC-SCRUM, lung cancer genomic screening project for individualized medicine; R&D, research and development; SOPs, standard operating procedures.

patients, service users, and the general public to participate in the design, management, conduct, and dissemination of research unless an exception can be made. Such measures will expedite the absorption of evidence into clinical practice, and patients will be subsequently better equipped to participate in shared decision-making with their physicians.[44]

Overall, the pre-existing approaches based on the P1RP initiatives integrated with a pragmatic planning as discussed above are pivotal in ensuring a successful early drug development program in Malaysia. These initiatives are summarized in Figure 2.

3 | CONCLUSION

Malaysia is one of the emerging clinical trial sites, and this was achieved due to various government efforts such as the establishment of CRM

and the P1RP initiative. To date, although it has accomplished tremendous progress in the conduct of pivotal or late phase clinical trials, there is a need to sow and provide fertile ground for the growth of early phase trials. The successful conduct and delivery of early phase trials may raise the confidence of trial sponsors, which will result in a spillover effect of more phase II and III studies into the country. This is especially crucial in the current era whereby there is an emergence of different innovative trial designs in drug development; and one of the examples is "phase agnostic seamless drug development," which is deemed to be more efficient than the conventional clinical designs with better utilization of resources and reducing the time it takes to complete the process of drug development.[45] This has underscored the urgent need of Malaysia in building a robust clinical trial ecosystem encompassing early phase through to late phase drug development as the boundary of "phases" of oncology studies has increasingly blurred, and the country will certainly be left behind if it is still focusing on late phase drug development.

Vigorous partnerships between academic research center and cancer service providers, efficient networking with the regional peers and industries as well as strong commitment and continuous investment from the Malaysian government are imperative in building a sustainable and conducive ecosystem for oncology research in the country. Ultimately, building and nurturing a robust clinical research ecosystem is dependent on the understanding of cancer biology and applying experimental therapeutics with an eventual goal to provide high quality cancer care to patients.

AUTHOR CONTRIBUTIONS

Pei-Jye Voon, Lillian L. Siu, and Albiruni R. Abduk Razak conceived and designed this review. All authors were involved in preparing the manuscript and its final approval.

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CONFLICT OF INTEREST

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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