



## Trends in phase 1 oncology drug development in East-Asia and Australia

North America and Europe have been the traditional strongholds for conducting early phase clinical trials in oncology. However, the under-representation of Asians in cancer trials conducted especially in the United States (US) implies that the clinical data generated may not be generalizable to Asian patients from the rest of the world (1,2). This is because population-based differences in drug response has been well recognized (3,4), and drug approval by the regulatory authorities of some Asian countries mandate the inclusion of clinical data from local patient populations. Despite the fact that 57 cancer drugs had gained regulatory approval for 23 different cancer types between 2014 to 2018, only patients in the US, Germany and United Kingdom (UK) have access to more than 40 of these new drugs due to reasons such as drug companies failing to apply for or being granted drug approval outside these three countries (5). Another challenge is that in an attempt to hasten the drug approval process, the landscape of phase 1 oncology drug development has changed significantly over the last decade (6). There is an increasing adoption of seamless adaptive trial designs and biomarker-based selection of unique molecular subgroups that are found only in certain ethnic populations (6), as well as the landmark development of tissue-agnostic drug approvals based on the tumor's mismatch repair/microsatellite instability (MMR/MSI) status and expression of neurotrophic-tropomyosin receptor kinase (*NTRK*) gene alterations. According to a recent report, the number of trials that utilizes pharmaco-genomic criteria for selecting or stratifying patients has increased almost three times since 2010 and represents 39% of oncology trials in 2018 (5). Furthermore, the discovery of new drug pipelines and the new FDA designation of accelerated drug approval based on early phase single-arm efficacy data especially for immune-oncology (IO) agents have all contributed to a staggering rise of 46% in new phase I trials since 2015 (5,6). These phase 1 trials are becoming larger in terms of sample size and participating sites, more complex in design and the duration of enrollment a lot shorter—dropping to around nine months in phase I trials (5). All of these factors have all contributed to the recent trend in expanding phase 1 oncology studies beyond the boundaries of Western countries, in order to meet the stringent demands for patient enrollment and timeline for drug approval. In this regard, several key oncology centers in East Asia and Australia have played a leadership role in driving the early phase development of new oncology drugs over the last decade, especially for cancer types that are prevalent to this region such as lung cancer, certain gastrointestinal cancers and virus-associated cancers such as liver and nasopharyngeal cancers.

In the last 5 to 7 years, the Asia-Pacific (APAC) region has become a preferred hub for attracting both local and international pharmaceutical companies, for evaluating their new drug pipelines including first-in-human and/or first-in-class compounds – as supported by the views of two consultancy reports published by Frost and Sullivan in 2017 and 2018 (7). Some of the reasons for this trend are outlined in *Table 1*. One of the foremost reasons is the high quality of clinical and translational research that is emerging from the APAC region. Cancer researchers from some centers of excellence in the APAC region such as China, Japan, Australia, Taiwan and Hong Kong are ranked within the top 30 in the world in terms of h-index for oncology—one of the ranking criteria for the scientific literature from 1996 to 2018 (<https://www.scimagojr.com/countryrank.php?area=2700&category=2730>). The region is also the home of many highly experienced clinical trial teams and these premier phase 1 centers are often supported by advanced precision oncology programs, where patients may undergo molecular pre-screening of their tumors using advanced next generation sequencing (NGS)-based molecular profiling. The information derived from this program may facilitate the genomic matching of candidate patients to phase 1 drug trials of targeted therapies. Another advantage of conducting phase 1 clinical trials in the APAC region is that some expert centers are already accredited by local regulatory authorities and/or pharmaceutical sponsors, and are thus capable of producing high-quality clinical trial data. Moreover, these centers have well-established locally and regional internationally accredited collaborative networks. In terms of epidemiology, some of these APAC regions have diverse ethnicities which enable a much broader representation of population-based pharmacogenomics. Some of these APAC countries are supported by advanced healthcare infrastructure and governmental policies that facilitate the approval of new drug trials, new drug registration and filing of new scientific patents. All of these factors have created an attractive and competitive environment for biopharmaceutical companies to conduct phase 1 clinical trials and/or move their Research and Development (R&D) facilities to the APAC region.

**Table 1** Potential advantages of conducting phase 1 clinical trials in the Asia-Pacific region

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Unique cancer and molecular sub-types, especially infection-associated cancers
Unique population-based differences in pharmacokinetics
Research and healthcare infrastructure is well established in some expert centers
High-quality data and clinical trial management
Data acceptance by major international organizations and regulatory authorities such as the US Food Drug Administration (FDA) and the European Medicines Agency (EMA)
Network of internationally-accredited institutions
Experienced and highly-skilled research teams
Governmental support, strong patent laws, public policy laws, tax advantage
Competitive costs and trial start-up time

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This issue of the Journal focused on the achievements and recent development of phase 1 oncology research in East Asia and Australia. Drs Loong, Tan and Shimizu presented a comprehensive overview of the history and challenges of phase 1 drug development in Hong Kong, Singapore and Japan. Together with key stakeholders from South Korea and Taiwan, this group of dedicated phase 1 researchers has established unique research consortia in East Asia including the Asian Oncology Early Phase 1 Consortium (‘Asia One’) for promoting multicenter phase 1 studies in Asian populations, and the Asian Thoracic Oncology Research Group (ATORG) for promoting clinical trials and translational research in lung cancer across Asia. Dr. Im and colleagues focused on the great contribution of Korean researchers and collaborators in the development of new therapies for cancers that are prevalent in Korea. In a concise review, Dr Lin from Taiwan described the important contribution of biomarker-driven phase 1 trial designs for facilitating drug development in the different molecular subgroups in lung cancer. Dr Desai and colleagues gave a historical account of how the landscape of early drug development in oncology has evolved in Australia over the past decades. These phase 1 experts highlighted the process of how over the years, cancer research centers in their region have formed close strategic partnerships with key stakeholders such as healthcare policy-makers from the local government, regional hospitals in other parts of their country or area, and most of all the academia and bio-pharmaceutical sponsors. These relationships have helped to shape their region as one of the premier hubs for conducting phase 1 oncology research.

In Hong Kong, this year marks the 25<sup>th</sup> Anniversary of the opening of the Sir YK Pao Cancer Centre at the Prince of Wales Hospital—the first comprehensive cancer center of its kind in Hong Kong that is devoted to research of cancers that are prevalent in Asia. With over 20 years of experience in conducting cancer clinical trials, researchers from the Chinese University of Hong Kong (CUHK) have contributed significantly to the development of new drug therapies especially in the treatment of lung, nasopharyngeal cancer and certain gastrointestinal cancers. As we mark the 6<sup>th</sup> anniversary since the opening of the CUHK Phase 1 Clinical Trial Centre at the Prince of Wales Hospital—an accredited center for phase 1 clinical trial by China’s National Medical Products Administration, we endeavor to advance phase 1 oncology research by establishing a precision oncology program in the near future for individualizing patients into phase 1 cancer trials. We shall work towards strengthening our research network of international collaborators from the academia and pharmaceutical field, with the aim of increasing Hong Kong’s competitiveness as a preferred partner in phase 1 oncology research. Ultimately, we aspire to bring hope to our cancer patients by bringing more promising new targeted therapies and immunotherapies to Hong Kong.

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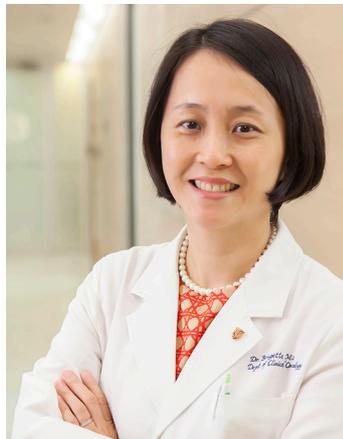
## Footnote

*Conflicts of Interest:* The author has no conflicts of interest to declare.

*Ethical Statement:* The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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