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Oncology Clinical Trials in APAC

Martin Lachs, PhD, VP, Project Management, Oncology and Hematology, Clinical Research Services, ICON plc

Mary Pan, VP, General Management and Business Development, Head of Asia Pacific, ICON plc

INTRODUCTION

Although Asia Pacific (APAC) is sometimes referred to as a homogenous unit, it is a heterogeneous region, with divergent countries, languages, populations and cultures. The main pharmaceutical markets, Japan, China, South Korea, Taiwan and Australia, have different business, labor and regulatory environments, so the characteristics of clinical development also differ. Clinical research in APAC is very well established, with high-quality research infrastructure, and some Centers of Excellence have leapfrogged the West, especially in IT and equipment. Many multinational pharmaceutical companies and CROs have been in the region for more than 20 years, so there is a great depth of experience to draw on. In terms of the value of the pharmaceutical market, China and Japan are second and third in the world, respectively, after the US, which reflects their importance in the overall global market. In this article, we review some of the characteristics of clinical research in APAC and some of the factors affecting it, particularly in oncology.

RESOURCING AND OPERATIONS

With a large domestic pharmaceutical market and many local companies as well as a substantial international presence, China has a large population of clinical-trial professionals, many of whom are graduates with good English language skills and a high level of expertise. From a resource perspective, its labor market is fairly fluid due to high demand for experienced professionals and people tend to move freely between companies. In contrast, in Japan, the labor market is much more constrained as there is a shrinking population and the worst labor shortage in 25 years, especially in health care, making it difficult to attract new staff. These challenges have seen CROs and pharmaceutical companies investing in graduate recruitment programs to train and increase the talent pool for the industry.

From a quality perspective, it is important not only to have rigorous good clinical practice (GCP)-compliant systems and processes in place but also to ensure that staff turnover is low. Some of the challenges in resourcing and operations for multinational pharmaceutical companies are being driven by the tremendous growth in the market, which has increased by around 20% per year in the last three years, with the majority of the growth in oncology. A graduate recruitment program can help companies to keep up with the increased demand for staff, and oncology-specific training is a key part of any program. This is particularly important because, in operational terms, oncology trials tend to be more complex than those in other therapeutic areas. In Japan for example, one clinical research associate (CRA) could be assigned to six study sites on average but for an oncology trial it may be only three sites due to the additional complexity involved.

SITE ACCESS AND DATA QUALITY

Compared with Europe and the US, there is a much greater spectrum in APAC in the ease of site access, particularly for oncology trials. For site access across APAC, potential bottlenecks are not due to patient access but rather the time investigators and study coordinators have available to conduct clinical studies, and oncology study sites are especially busy. In response to this, China sites have tended to lean on support from site management organizations (SMOs), and regulatory changes implemented in 2017 have increased the number of potential study sites from a few hundred to more than a thousand. The regulatory environment in China is continually evolving and improving because of efforts by the government and there are early signs of improvement in regulatory processes and study start-up timelines. In Japan the site time restriction has translated to a heavier burden on CRAs.

The percentage of European Medicines Agency (EMA) critical findings and US Food and Drug Administration (FDA) official actions taken during inspections in Asia is lower than in North America, reflecting the high standard of international compliance. China is a key country for clinical trials, which is a reflection of the skills base that has been built up and the clinical experience that has been developed, particularly in immune-oncology and leading-edge adoptive cellular therapies (ACTs). Japan has a well-developed and long-established pharmaceutical market that aids the provision of high-quality data.

Australia also has a long-established clinical research industry and a wealth of experience in oncology, with very experienced research teams. Standards of care are much more closely aligned with those of Europe than other APAC countries. The lack of significant regulatory

barriers is an advantage particularly for Phase I studies. Site access is very good, but with a population of only about 25 million, resources are more limited, particularly from an oncology perspective.

PHASE I ONCOLOGY TRIALS

Throughout the region, it is important that pharmaceutical companies generate Phase I data in Asian populations. In all countries, the infrastructure is good and there are academic sites with expertise in running Phase I trials. Global pharmaceutical companies wanting to market a drug in APAC need to demonstrate key pharmacokinetic (PK) and pharmacodynamic parameters in an Asian population, particularly Chinese or Japanese populations. In recent years, there has been an increasing willingness for regulatory authorities to accept Phase I data generated in another country with appropriate bridging data (PK and pharmacogenomics).

In oncology, the pharmacogenomic profile of the Asian population is an important factor that further necessitates the requirement for Phase I data in local populations. One example is the genetic polymorphism for P450 enzymes that can lead to substantial variation in drug PK in different populations.

IMMUNO-ONCOLOGY

Immuno-oncology is the big growth area both globally and in APAC. In adoptive cell transfer (ACT), of which chimeric antigen receptor T-cell therapy (CAR-T) is a major component, the number of studies ongoing in China, over 140, exceeds that in the US, although to date, the majority of these have been investigator-initiated studies. This is now changing with an upturn in studies sponsored by Chinese companies. The development of immune checkpoint inhibitors is well established in all APAC countries. Until fairly recently, most of the target indications for ACT have been hematological cancers but this is now expanding to sarcomas and solid tumors, a development that is also likely to be seen in China. ACT clinical trials are highly complex logistically, and so require an appropriate base of experienced staff to facilitate high-quality studies and minimize risks to patients associated with these therapies. Antibody drug conjugates (ADCs) are also a significant area of research, but currently there is less of a focus in this therapeutic area in APAC than in the US.

SUMMARY

Clinical research has been well established in APAC for more than 20 years and the region will continue to be a major focus for multinational pharmaceutical companies in the future. Oncology and immuno-oncology are important areas of research in the region, with China in particular being a key country for ACT studies, and this trend is likely to continue.

The size and significance of the APAC market and the needs of its populations make clinical trials, on the cutting edge of oncology development, an attractive investment. ACT is just one noteworthy example. Although heterogeneous, in general the region has a robust evolving regulatory framework and the ability to track changes and regulatory developments, particularly with regard to gene and cellular therapies, will be important. APAC has a strong medical oncology community but it requires a level of attention to navigate it successfully. Access to resources to operationalize clinical trials also varies significantly between countries and therefore bespoke strategies are often required in the different constituent nations.