Why Japan lags in global clinical studies?

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Q: What is the current clinical research landscape in Japan?

Despite its high quality, output of clinical research in Japan has been regrettably low, with a significant gap between basic and clinical research productivity (Rahman & Fukui: New E J Med; 347:1211, 2002). To improve this situation, various measures have been proposed, some already embarked, by the Japanese government, academia and industry. Next couple of years will see to what extent these attempts lead to tangible changes. Having said that, I am deeply concerned whether the expected improvement in clinical research may be nullified by ever worsening conditions (some even call it deterioration) of medicine in Japan, due mainly to the severely capped national healthcare budget and research grants. This has brought about declining morale, and occasional exodus, of overstretched physicians who are supposed to contribute to clinical research.

Q: What opportunities can Japan offer for CROs to do clinical trials?

There seem to be an increasing demand for the CROs in Japan. On the one hand, in spite of many difficulties, most big pharmas make efforts to conduct clinical trials in Japan for increasing novel compounds in their pipelines from stages much earlier than before. For a long time, only the medicines already approved or about to be approved overseas were developed in Japan, but now the trend is to develop candidate compounds as early and feasible as possible in Japan in accordance with global development, in an effort to shorten the so-called drug lag. Many companies have preferred conducting trials in-house, but in order to deal quickly with ever increasing projects, they have to outsource more to CROs.

On the other hand, although not in the least on par with the demand from industry, potential opportunities for CROs also exist in Japanese academia. This is because Japanese academicians are, due to the aforementioned grave conditions, inundated with clinical workload with little time and resources left to carry out their own research plans; hence very few large-scale, investigator-initiated clinical research comes from Japan. I believe CROs may be able to take this opportunity and share

Interview

Prof Yuji Sato, a founding professor of the Center for Clinical Research at Keio University School of Medicine, Tokyo is Vice President of Japan Association of Pharmaceutical Medicine, and holds membership of various other academic and professional organizations, including Japanese Center of Pharmaceutical Medicine, Japanese Society of Psychiatry and Neurology, and the Cambridge and Oxford Society. His areas of interest include psychiatry, psychopharmacology, pharmaceutical medicine and psychodynamic psychotherapy.

Before taking over the role of founding professor at the Center for Clinical Research, Mr Yuji Sato was working with Banyu Pharmaceuticals (a subsidiary of Merck & Co.) as director leading CNS drug development and as assistant professor in neurpsychiatry at Nihon University. Prof Yuji Sato shared his views with *BioSpectrum* about the market scenario of clinical research organizations in Japan. Excerpts of the interview

In April 2007, the Japan CRO Association has introduced a guideline to train CRAs in accordance with global standard, so that high-quality monitoring service can be provided

with Japanese investigators first-class experience in managing trials. At Keio University Hospital, some CROs are providing investigators with operational and technical assistance. Such collaboration turns out to be beneficial to CROs in accessing state-of-the-art research directions and seeds rich in academia.

Q: What challenges the CROs in Japan are currently facing?

First, Japanese investigational sites are not yet very used to working closely with CROs; one can even witness some sites that are reluctant to accept CRO-field monitors and demand sponsor's in-house clinical research associates instead. Second, some Japanese sponsors are not too familiar with the business practice of effectively outsourcing and delegating important research functions. I know some cases where miscommunication between sponsors and CROs has led to some issues at the sites, only to exacerbate investigators' reluctance to collaborate with CROs. Third, CROs seem to suffer from dearth of experienced CRAs, whilst it always takes time to develop and train newcomers; high-performing CRAs are constantly coveted.

Q: What initiatives were taken to support the growth of CROs in Japan?

In April 2007, the Japan CRO Association has introduced a guideline to train CRAs in accordance with global standard, so that high-quality monitoring service can be provided, and that they can duly deal with global trials that are expected to increase in Japan.

Q: In spite of having good infrastructure, why is Japan lagging behind in participating in the global clinical trial studies?

In a nutshell, this is because conducting global trials in Japan is, at least at the moment, costly, time-consuming and difficult.

The said 'good' infrastructure is merely in a narrow sense of the word; e.g., endoscopes, MRIs and intensive care units. In terms of resources to efficiently support clinical trials, there are very few Japanese sites that meet the global standard, although there have been governmental initiatives to rectify this situation. As for study cost, clinical trials in Japan are still very expensive, even in comparison with the US. However, the most fundamental issue in trial competitiveness in Japan seems to be, in my view, related to enrollment.

There exists a dilemma: clinics run by Site Management Organizations are beginning to achieve high enrollment efficiency, but often have difficulty in enrolling severe and/or rare diseases and in accepting English documents. On the other hand, teaching hospitals do deal with these patients, and often have investigators trained overseas, with no difficulty in English. But most of these hospitals have enormous managerial issues, including physicians with horrendous clinical overload, hence efficient conduct of trials is extremely difficult, enrollment can hardly be maximized.

In addition to these rate-limiting issues at the sites, some regulatory hurdles also exist, such as time-consuming obligation to translate protocols and brochures into Japanese to be submitted to the agency before study initiation.

Q: What is the current size of the clinical research/trial market in Japan and who are the major players (both local and global)?

According to the Japan CRO Association, the total sales of its 41-member CROs in 2007 are $9.6 billion, a 15 percent increase from that in 2006. Major players include Quintiles Transnational Japan, CMIC and EPS.

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