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conference report

Drug discovery in the lion city

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IBC Drug Discovery and Development (Asia Pacific) conference
Singapore
1–3 June 2005

The IBC Drug Discovery and Development (Asia Pacific) conference was held in Singapore on June 1–3. The meeting brought together over 200 delegates from 13 countries representing diverse interests, ranging from large pharma, small biotech, support institutions (legal/intellectual property/venture capital), government regulatory agencies and academia. Among the many presentations at the conference, several talks were particularly noteworthy for their specific focus on key issues, challenges and opportunities faced by the drug-discovery industry in the Asia-Pacific region.

A general lack of NMEs

Delivering the keynote address, Kurt Stoeckli (Sanofi–Aventis) presented a broad summary of current difficulties facing the pharmaceutical industry, the most significant being the general lack of novel medical entities (NMEs) entering the market despite considerable investments in R&D. To reduce the numbers of compounds being abandoned late in the discovery pipeline, he suggested that drug companies should strive to enhance efficiency and cost-effectiveness early on in the discovery process. One way this could be achieved might be through implementing screening assays that deliver high data quality and consistency. As an example, he showed how utilizing bioassays of high reproducibility and robustness allowed his team to identify, in initial screening assays, lead compounds associated with only modest inhibitory activities (~20%). He also stressed the importance of establishing rigorous quality-control systems for compound management, as it is now clear that technical artifacts (e.g. aggregation, solubility, evaporation) can frequently lead to compounds being associated with incorrect IC_{50} values, which might affect their subsequent prioritization for further development. Specifically noting the valuable role of natural products (NPs) in drug discovery, Stoeckli predicted that companies in the Asia-Pacific would play a valuable role in this area, due to their access to a natural diversity of compounds within the region. The topic of NPs was an active subject of discussion later in the meeting (see below).

Future oncology therapy

A major topic at the conference was cancer and oncology. Lee Allen (Wyeth Research) stated that there are >400 oncology-related compounds in clinical development, and that the market for targeted therapies, exemplified by drugs such as Herceptin and Gleevec, is set to grow. However, he acknowledged that ultimately many of these targeted compounds are likely to produce only incremental survival benefits in the majority of cancer patients, because they lack broad-spectrum activity and are only active in specific individuals. He proposed that in the future, oncology treatment would be revolutionized by the use of molecular profiling platforms to taxonomize a patients' cancer in terms of specific aberrant pathways, to which a personalized cocktail of pathway inhibitory compounds could then be applied.

Supporting this premise, he presented a study showing that patient response to an experimental mTOR inihbitor (CCI-779) could be predicted by the presence of a characteristic 'responder' gene expression signature in peripheral blood. Continuing the concept of personalized medicine, Karol Sikora (Hammersmith Hospital, London) emphasized that a central challenge to the development of individualized therapies would be the identification of easily measurable biomarkers that could be used as robust surrogate clinical endpoints. Unfortunately, such biomarker identification activities have traditionally not been supported by large pharma, and have been difficult to conduct due to the lack of large ethically consented tissue banks and organized national research structures supporting translational research. In response, Patrick Tan (National Cancer Centre and Genome Institute of Singapore) described the efforts of the Singapore government to establish a national framework for such translational cancer research activities. The Singapore Cancer Syndicate aims to develop key areas essential for translational cancer research, such as biomarker discovery, clinical trials, and pharmacodynamics and pharmacokinetics, and will provide broad scientific and strategic coordination of these various groups to channel their combined efforts towards specific cancer questions. Using gastric cancer as an example, he also

1359-6446/05/$ – see front matter PII: S1359-6446(05)03568-3

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described how genomic technologies could be used in biomarker discovery to rapidly identify putative pathway genes for patient stratification.

Infectious diseases

Another important area of discussion was infectious disease. Akhter Molla (Abbot Laboratories) described the process of creating a new generation of protease inhibitor compounds for HIV. Using Kaletra, a novel formulation of two protease inhibitor compounds (lopinavir and ritonavir), he presented clinical data showing the combined formulation to be superior to nelfinavir, currently prescribed as the standard of care. Perhaps more importantly, even after periods of prolonged treatment (>4 years), viral resistance does not seem to occur with the combined formulation, a significant advantage from previous generations of compounds. Alex Matter (Novartis) of the Novartis Institute for Tropical Diseases (NITD) in Singapore then provided an overview of the many challenges facing the R&D of medicines for tropical diseases. He illustrated the tremendous disease burden facing the world community due to diseases such as HIV, malaria and TB, and acknowledged that many of these conditions (with the possible exception of HIV) have not been well investigated by the pharmaceutical industry, due to the real or perceived lack of commercial potential. Indeed, in the case of TB, there have been no new drugs for TB in the past 40 years, and the current diagnostic techniques for diagnosing TB are still based on 19th century techniques. Another important consideration in developing therapies for these conditions is the general state of healthcare in countries where these diseases are endemic. Matter argued that the ability of drugs to succeed in these countries rests on their being highly potent and stable, easily synthesized, available as oral formulations, and generally well-tolerated with minimal interactions with other anti-infective compounds (such as anti-TB drugs).

Given these challenges, the NITD would initially focus on the development of disease specific drug therapies for dengue fever and TB, and distribute these medicines to affected countries in a non-profit manner. To counter the traditional difficulty of generating funding to support this research, he emphasized the importance of collaborating with multiple partners at various points in the drug development pipeline, including charitable foundations (e.g. the Gates Foundation) in the discovery phase, to large scale NGOs (e.g. the WHO) to assist in subsequent downstream deployment and distribution.

Natural products

With respect to NPs, there was general agreement at the conference that the Asia-Pacific could play a substantial role in this particular industry space. Tony Buss (Merlion Pharmaceuticals) provided a succinct overview of the extraordinary structural diversity found in the NP arena, which has contributed to several 'first-in-kind' molecules in the anti-infective (vancomycin), immunosuppressive (tacrolimus), and oncology arenas (paclitaxel). However, traditional barriers facing NP development have been the high costs associated with acquiring and maintaining sample libraries, the poor compatibility of NPs to HTS approaches, and their complex chemical structures, which can prove highly challenging for synthetic optimization. As such, there has arisen a market need for companies that can provide efficient and rapid screening platforms for identifying novel NP lead compounds. As a proof-of-principle, he described the use of a high-throughput NP library to isolate a series of novel β-lactamase inhibitors.

Discussing the subject of NPs from a large pharma perspective, Frank Petersen (Novartis) used examples from Thailand and China to illustrate the importance of good corporate citizenship and establishing strong collaborative structures to ensure equitable benefit sharing between the pharmaceutical company and the originating country from which the compound was first derived. Such benefits might include developing joint ventures to co-develop and market the compound, and the transfer of technical know-how and scientific expertise back to the originating country through the financing of internships and visiting scientists.

Finally, the conference closed with a lively series of discussions on the challenges faced by US and European companies considering performing clinical trials in Asia. Rocco Zaninelli (Novartis) discussed the significant differences in cultural and social attitudes between patient populations from the different regions, and argued that it was imperative for local clinical coordinators to acquire 'cultural competency' and to be aware of these differences to minimize possible difficulties in patient recruitment and handling. Anthony Bishop (Quintiles) further discussed common but mistaken preconceptions held by western companies as they embarked on clinical trials in Asia, the most striking being the tendency to label a clinical site as inferior in quality if it lacked certain basic equipment pieces (e.g. faxes and fridges), or if the ground staff did not speak English. He noted that the necessity of obtaining approvals through site-specific Review Boards (IRBs) was now becoming more common throughout Asia, and that western companies will now need to factor in the extra time required to obtain these site-specific approvals being conducting their trials.

Conclusions

In summary, with the growing importance of the region's markets for the pharmaceutical industry, the conference attendees left the meeting with a strong conviction that Asia is likely to play an important role in shaping the future direction of the drug industry. In this regard, the conference was highly successful in establishing itself an important venue for business networking and the establishment of fruitful industrial collaborations. Although still a relatively young series (currently in its third year), the Asia-Pacific chapter of the IBC Drug Discovery and Development conference is undoubtedly emerging as one of the preeminent meeting places for industry players in the region.

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