AN AUDIENCE WITH...

Jonathan K. C. Knowles discusses the impact of pharmacogenomics on market segmentation

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Jonathan K. C. Knowles is President of Global Research at Roche, a member of the company's Executive Committee, board member of Genentech and board member of Chugai Pharmaceuticals. Before joining Roche in 1997, Knowles headed the research division of Glaxo Wellcome Europe. He also served as director of the Glaxo Institute for Molecular Biology in Geneva, Switzerland, which explored the use of new technologies for drug discovery. During his tenure at Glaxo, Knowles was instrumental in developing and implementing the company's global strategy in genomics. Knowles has previously held research and teaching positions at various universities in the United Kingdom, France, Finland, Japan and the United States. In 1979, he set up the molecular biology group at the Biotechnical Laboratory of the Technical Research Center of Finland (VTT), a government organization dedicated to research. He is a member of a number of science boards and organizations, including the European Molecular Biology Organization (EMBO), Heidelberg, Germany, and also holds an Honorary Professorship at the University of Basel, Switzerland.

Why is Roche investing so much in diagnostics and pharmacogenomics when this is likely to substantially segment its market?

Today we understand that the concept of the 'magic bullet' that will cure all patients is an illusion. We know that particular medicines can be extraordinarily effective for some patients, but might be completely ineffective for others. The present concept of 'market' is based on an average efficacy for patients defined as best we can in controlled clinical trials. New technologies and knowledge derived from genetics, genomics and proteomics will permit a deeper understanding of the molecular causes of disease. New diagnostic tests are expected to enable us to identify the differences between individual patients and the impact of these differences on prognosis with different therapeutic regimes. Medicine in the future will therefore become more personalized, and modern diagnostic tools will allow us to identify with a greater degree of accuracy which patients are really likely to benefit from a given treatment regime. Science will therefore segment the market, but each therapeutic treatment will have more value, because a successful outcome will be much more probable.

All parties in healthcare benefit from this approach: the patient benefits because these new drugs are expected to be more effective, and have less side effects, thanks to their targeted activity, which will increase patient acceptance and compliance; the doctor benefits because each consultation is more effective; the healthcare payers benefit because patients are more likely to respond, therefore making treatment more cost effective (although the impact on overall medical expenditures may be offset by continually increasing demands and expectations); and pharmaceutical and diagnostic companies benefit because targeted medicines and better diagnostics will provide a more effective way to treat patients compared with the alternatives. Most importantly, practicing state-of-the-art medicine is the only ethical approach in light of the scientific progress mankind is now making.

Will this personalization of medicine result in more segmented indications, each of which is so small that the development of specific pharmaceuticals is no longer economically viable?

This should not pose major issues. First, if, in the course of a clinical trial, a sub-population of more likely responders can be recognized, this group will probably be large enough to create an economically viable treatment group. Given the limitations in statistical power of trials, we would probably never find very small sub-populations in the first place. So there is an inherent scientific safeguard.

Second, if we were to recognize a very small new disease sub-entity formerly thought to be part of a larger indication, and were able to conceive of a superior way of treating individuals with this 'new' disease, then society has already devised, by way of orphan-drug regulations, the mechanisms to address such situations: incentives for industry and the pay structure for society (reduced taxes and longer exclusivity).

The same is true for diagnostic products. For example, Roche has created a gene chip that analyses variations in two genes that play a major role in the metabolism of many widely prescribed drugs, and thereby better define efficacy and dose. When many of today's drugs are generic, revenue might increasingly come from the development of high-value patented diagnostics. Such diagnostic tests will usher in a new era of medicine, and those healthcare companies that are able to identify likely responders to a drug will enjoy an important advantage as first movers. Use of these tests enables healthcare companies such as Roche to build a more effective business model, based on the ability to target likely responder populations more specifically, and with safer drugs that have fewer side effects. This approach should also reduce the attrition rate of the drug discovery and development process, so that more drugs in the pipeline will make it to the market.

When do you think we will see pharmacogenomics and advanced diagnostics reduce the attrition rate in drug development?

We are already seeing the first examples in cancer treatment. Trastuzumab (Herceptin; Roche) would, in all likelihood, never have received regulatory approval had we not matched it with a test that helps to single out the one in three breast cancer patients for whom it is likely to provide benefits. Recently, several other mechanism-based medicines for cancer have received attention due to data showing similar correlations with molecular variants of the target. And the leukaemia diagnostic chip that we have announced will be available next year promises not only to significantly shorten the time to diagnosis, but to also provide superior accuracy compared with currently used methods, thereby allowing more specific treatments early on.

I also believe that the treatment of inflammatory diseases such as rheumatoid arthritis will benefit from new diagnostics in the next few years. In ten years time, the treatment of many common diseases will become more personalized through modern diagnostic technologies.