Personalised Medicine – Pharma and Dx firms share wider horizons[1]

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Personalised medicine might be a popular catch-phrase at the moment, but the term often causes confusion, as there is still no uniform definition for it. The expression can include areas as diverse as the measurement of individual risk, early detection using biomarker testing, stratification of patients suffering from a disease and predictions about its course.

The term 'companion diagnostics' (CDx) is a much clearer expression. It refers to diagnostics linked to medications that enable predictions to be made about the effects (responder/non-responder) or dosage of a medication. Diagnostics therefore accompany any decisions made about therapy, and the two together are often described metaphorically as a tandem bicycle – with diagnostics steering in the front seat and therapy in the back pumping hard on the pedals. Companion diagnostics are used, for example, to stratify patients so that each subgroup receives the best therapy. Tests are often developed at the same time as the medication ('companion') with the diagnostics forming part of the approval (label), although they can also be designed for existing therapies that are already test) or to verify success in clinical trials.

Personalised medicinal products benefit everyone involved: doctors can prescribe more effective and safer therapies for the patient, while the patient is spared unnecessary and stressful attempts to find the right therapy. For a pharmaceutical industry searching for the next blockbuster, stratification of patients may seem at first glance to act as a deterrent, as it decreases the size of the patient population under consideration. It has also grown increasingly difficult to verify a significant evidence-based additional benefit for new medicinal products. Nevertheless, the field of CDx offers many advantages to pharmaceuticals companies. For example, if there is a parallel diagnostic concept available that identifies responders/non-responders or that excludes groups who would suffer unjustifiable side effects, companion diagnostics increase market opportunities for a medication.

Additionally, regulatory authorities have made it clear that in future, companies are expected to have a concept that enables the identification of responders and the exclusion of people with an unacceptable risk of side effects. And greater efficacy with lower risk for patients not only increases therapy compliance. It also creates a barrier for alternative therapy options not based on biomarkers. Diagnostic tests can increase the effectiveness of clinical studies and improve chances of receiving approval by providing evidence that the group of patients in question have benefited significantly. Efficiency also increases with faster recruitment of suitable volunteers. Ideally, a diagnostic tool should be established as early as the development phase of a medicinal product.

However, even after a product is available on the market, the combination of medicinal product and diagnostic tool expands the range of applications for the medication, and thus extends product life-cycle. By excluding non-responders, study results are also improved, meaning that even substances that have previously failed and are sitting in a pharmaceutical company's basement ('fallen angels') can be dusted off and given a second chance.

CDx for biologicals

For some companion diagnostics that are now established in the area of biologicals, approval for the medicinal product indicates a specific patient subgroup that must be confirmed diagnostically (e.g. Erbitux and Vectibix are only for K-RAS wildtype patients). Current examples of parallel medication and companion diagnostic approvals include Zelboraf® (vemurafenib) from Roche – a treatment for an aggressive form of skin cancer – and Xalkori® (crizotinib) from Pfizer to treat non- small-cell lung cancer. In the US, Zelboraf may only be used if the Cobas 4800 BRAF V600 test, which was developed by Roche and also approved by the FDA, is positive. The test detects a BRAF mutation that is present in about 50% of melanoma patients. Roche began developing the test kits in Phase I of the trials. Xalkori® is only effective in the 3–5% of patients in whom the anaplastic lymphoma kinase gene (ALK gene) is active, which inhibits the corresponding kinase. The test (Vysis ALK Break Apart FISH Probe Kit), which was developed by Abbott and submitted for approval at the same time, enabled Pfizer to obtain FDA approval within about three months, in part because the test precisely identified those patients who would probably benefit from the medication, and that in turn helped the company achieve good study results. With a 'one drug fits all' approach, Pfizer would have had no chance of succeeding in clinical trials with Xalkori for this numerically small group of patients with lung cancer.

Like the entire field of pharmaceutical development, personalised medicine is of course a high-risk area. Pharmaceutical companies are therefore not yet considering it as an alternative strategy, but rather as one that can complement the blockbuster strategy. Some businesses, however, have already started moving towards personalised medicine in order to capture at least a small market for particular active ingredients.

Opportunity for diagnostics firms

This cooperation also opens up attractive future opportunities for mediumsized niche providers. They can position themselves successfully with innovations that lead to the further development of known active ingredients, by for example improving efficacy and reducing side effects. In this case, CDx provides an opportunity – even with a relatively low R&D budget – to stabilise and secure products in development or even those already on the market in the area of the particular indication. Another impediment is that in many cases, doctors prefer conservative forms of treatment. Experts assume, however, that more efficient and safer therapeutic agents are more quickly and widely used in clinical practice (increased adoption rate) while also boosting compliance, and thus the connection between the patient and the particular treatment strategy. Both regulatory requirements and the ability to reimburse diagnostics are the subject of current discussions in the area of personalized medicine.

The development of companion diagnostics for personalised medicine is a strategically important focus of the diagnostics network (Netzwerk Diagnostik Berlin-Brandenburg e.V.). The network combines the expertise and resources of its 33 members. These companies include highly innovative medium-sized diagnostics companies, device manufacturers, suppliers, renowned research facilities and users from hospitals and medical laboratories in the Berlin-Brandenburg region, and they develop and produce in vitro diagnostic products along the entire value-added chain.

A Companion Diagnostics Working Group has been established within the network to initiate projects with pharmaceutical companies, because the CD concept requires close collaboration between experts who until now have worked separately in either the pharmaceutical or diagnostic business. The foundations for the practical implementation of personalised medicine are suitable technology platforms, such as testing and analytical procedures that enable biomarkers to be reliably identified, but which can also be used routinely in clinical practice. The network provides diagnostic solutions for all phases of medicinal product development and the accompanying application. The expertise available includes validation and evaluation of biomarkers (e.g. epigenetic and genetic markers, proteins, cell-based markers), clinical trials as well as the development, manufacture and marketing of test systems, devices, software and bioinformatics solutions.

For customers, the advantage of the BB diagnostics network is that joint development projects can be advanced quickly, and are driven by results for the benefit of the requesting pharmaceutical companies. A network cooperative also minimises the risk of project failure, which can kill small diagnostics companies during the development and approval period or cause them to become financially dependent during the development process. Interested customers are more than welcome to contact the network management regarding any query or concern.

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