

How Will Personalised Medicine Have an Impact on Clinical Trials?

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HOW CAN GENOMICS have an impact on the management of your clinical trials? With the growing understanding of genetic code within personalised medicine, could this signal a change in the size and scope of clinical trials? What does this mean for the pharmaceutical industry and the patient?

“Personalised medicine refers to the tailoring of medical treatment to the individual characteristics of each patient.”



□ “PERSONALISED MEDICINE” IS a current buzzword, but what does it actually mean? Some say it has the potential to affect the entire landscape of our healthcare system over the next ten to 20 years.

A useful definition is given in ‘Priorities for Personalised Medicine’ September 2008:1 ‘Personalised medicine refers to the tailoring of medical treatment to the individual characteristics of each patient. It does not literally mean the creation of drugs or medical devices that are unique to a patient but rather the ability to classify individuals into subpopulations that differ in their susceptibility to a particular disease or their response to a specific treatment. Preventive or therapeutic interventions can then be concentrated on those who will benefit, sparing expense and side effect for those who will not.’

Since the publication of the first draft of the human genome in 2001, the use of genetic techniques in personalised medicine has increased. At first glance, it may be considered an extension of traditional approaches in understanding and treating disease but with much greater accuracy.

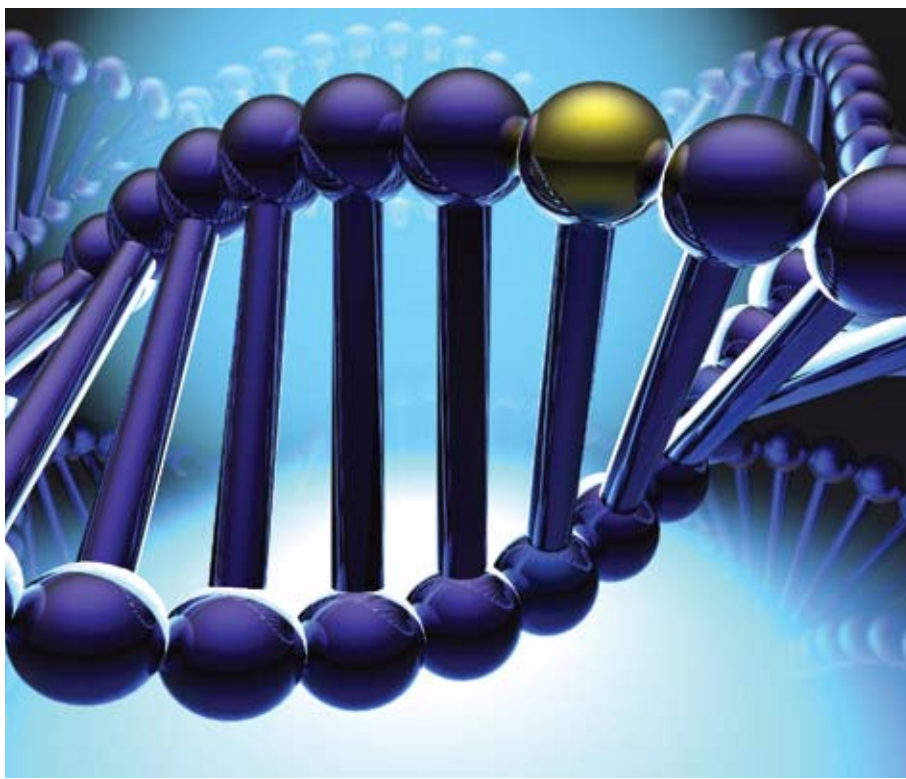
In personalised medicine, the profile of a patient’s genetic variation can be used to guide the drugs or treatments chosen to produce a more successful result or to minimize unpleasant or harmful side effects. It can also affect the dosage of a drug being prescribed, as genetics can determine the rate of absorption. Knowing the genetic make-up can also show susceptibility to certain conditions before they appear, giving the doctor and patient the opportunity to devise a plan for monitoring and prevention. In short, it could mean enabling the right drug for the right person, first time.

Precise tools

□ WHILST SOME BELIEVE personalised medicine is just an extension to conventional clinical approaches to understanding and treating disease, it actually goes a great deal further. It is not just using observable evidence to make a diagnosis or prescribe a treatment; with personalised medicine the tools are more precise and take into account the molecular make-up of each patient.

The ability to profile the structure, sequence and expression level of genes, proteins and metabolites is redefining how we classify diseases and choose treatments. Today’s understanding of diseases is more complex. Diseases such as heart disease, cancer and Alzheimer’s are caused by combinations of genetic and environmental factors. They are often chronic, which can be a burden on the healthcare system. The

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promise of personalised medicine is to provide a set of tools to better manage chronic diseases with more effective treatments.

It is currently estimated that around 20% of clinical trials in the US involve genetic analysis to some degree.² So, how is personalised medicine affecting the way we conduct clinical trials?

Drug development is not only a lengthy, but also an expensive process. Using pharmacogenomic data, or information about how a patient’s genes can affect their drug responses, could, in theory, reduce the time and cost of drug development. Importantly, it could also lower the number of drug failures by enabling researchers to focus on sub-sets of patient populations where efficacy or safety is likely to be proved.

Closely targeted

Trials can therefore be more targeted. With personalised medicine, the people trialling the drug would be chosen according to their genetic make up. This would entail carrying out DNA sequencing on all potential participants in the trial; although this is still a costly test to implement today, prices are coming down fast with improvement in sequencing technologies. In the future,

this could theoretically be done at birth and the data stored for later use when administering drugs or treatment.

Researchers can preselect patients for studies. Perhaps misleadingly, this is called ‘enriching the clinical trial pool’, whereas increasingly, de-selected subsets of the population are not chosen for trialling.

More cost-effective?

There is evidence that using pharmacogenomics can cut the length of trials, with early success shortening the trial and so reducing cost. It can also lower the failure rate.

Over the years, many drugs in development have fallen by the wayside, with mixed population trials abandoned because of adverse reactions which have cost companies a great deal of money. With personalised medicine, you can in theory associate a drug with a genetic test at the clinical research stage, identifying what is likely to work for people with a certain genetic code.

This could also be helpful for companies with a back catalogue of drugs, some of which could be brought back for clinical trials with a more selective cohort. This revival could result in effective use of older products with a specific subset of patients.

“... personalised medicine could have the effect of attracting companies to have a broader product portfolio with smaller drug brands...”

Benefits

More targeted clinical trials leading to greater successes and fewer abandoned trials along the way, not only benefit companies in the pharma industry but also the patient who will have been screened to ensure the drug or treatment given is likely to be more effective and less likely to produce unpleasant side effects.

The rate of patient compliance is also likely to be increased; perhaps more people will be willing to take their medicines if they work and they don't suffer from side effects?

Challenges for the future

□ THE USE OF genomics in clinical trials is likely to increase markedly over the next decade. In applying genomics technologies in clinical trials, there are a number of complex technical, ethical, regulatory and economic challenges still to be addressed.

Conducting clinical trials requiring new and advanced technology could be more expensive per person. This, of course, must be weighed against the benefits of smaller patient cohorts, exposing fewer people or patients to the drug.

From a commercial point of view, personalised medicine could have the effect of attracting companies to have a broader product portfolio with smaller drug brands rather than the 'blockbuster' approach.

Technical challenges

If genetics data is used or required in clinical trials, the organisation handling the DNA samples will need to put a system in place to collect, store and track the samples. These will need to be 'attached' to a patient consent form; if consent is withdrawn at a later stage, the sample will need to be localised and destroyed.

If genetics data is to be generated from a large number of patients, an IT infrastructure to deal with this new kind of data will be required for easy storage and access and more importantly for meaningful analysis. These aspects have been worked on in many an academic research setting but not yet streamlined in a clinical trial setting.

Regulatory challenges

Regulators (including the FDA and EMEA) will need to adapt, provide and help to set up new rules for the incorporation of

pharmacogenetic data within the submission process leading to a Marketing Approval for new products. Otherwise, pharmaceutical and biotech companies will have little economic or commercial incentive to include pharmacogenetic data within their already-expensive clinical trial programmes.

Ethics

Issues around data privacy are still to be solved. There is a concern that, although genetic data can be used for the benefit of patients, this kind of data can also be used to discriminate against people on a genetics basis; for example, an insurer could refuse to offer life cover because it thinks the patient has too high a risk of stroke. Answers are needed to decide who can or cannot access this data, for what purpose and what the liabilities are surrounding this.

There is also a potential downside of 'cherry picking' of more 'valuable' subsets of the population for clinical trials: those where efficacy is likely to be proved or less likely to be susceptible to side effects. There may also be the question of particular subsets being more economically 'valuable' to pharma companies or governments. This approach could leave many other subsets of the population with no treatments...

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