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Personalised pharmacotherapy – who is it good for?

Candesic's **Dr Joe Taylor** considers the implications of personalised pharmacotherapy for life sciences and healthcare

Despite the hype, personalised pharmacotherapy will benefit some, but not all of us. It represents an evolution of clinical care, not a revolutionary step change. It will impact the market, and especially in a number of key therapeutic areas.

Personalised medicine is the tailoring of medical treatment to individual patients and their ailments. This is not in itself new – doctors have long sought the best combination of approaches for their patients. We are gradually moving away from trial-and-error prescribing. However, the falling costs of diagnostics and increasing understanding of disease is leading to a new generation of highly specific pharmacotherapies.

The fundamentals of the market remain the same: new drugs are difficult to discover, expensive to bring to market and challenging to get doctors to use. Consequently, personalised pharmaceuticals are likely to be viable for two principal indications: oncology and a small number of rare diseases.

Pharmacogenetics makes sense

People with the same clinically diagnosed pathology can have very different responses to drugs prescribed for their treatment. The genes we're born with change the way our bodies respond, both positively to treatment and also in terms of side effects. Therefore, it makes sense that the same condition will respond best to different drugs.

We recognise that particular drugs are ineffective in a significant part of the population for whom they are prescribed (*figure 1*), and much of this difference in response is down to differences in our genes. With the rapidly falling price of genome sequencing (*figure 2*), we have the potential to better predict drug responses and design new pharmaceuticals that will be both effective and well tolerated for certain sub-groups of the population.

Digital informatics is vital

The key elements of a personalised approach to pharmacotherapy include genomic profiling, clinical context, a broad range of diagnostics, existing medical therapy and each patient's lifestyle and life experiences. To use all these data points, drug developers and prescribers need integrated informatics.

The organisation of healthcare in the United Kingdom provides a unique health advantage; state provision of health and social care for the large majority enables the opportunity for integrated care records tied to personal and familial genomic profiles.

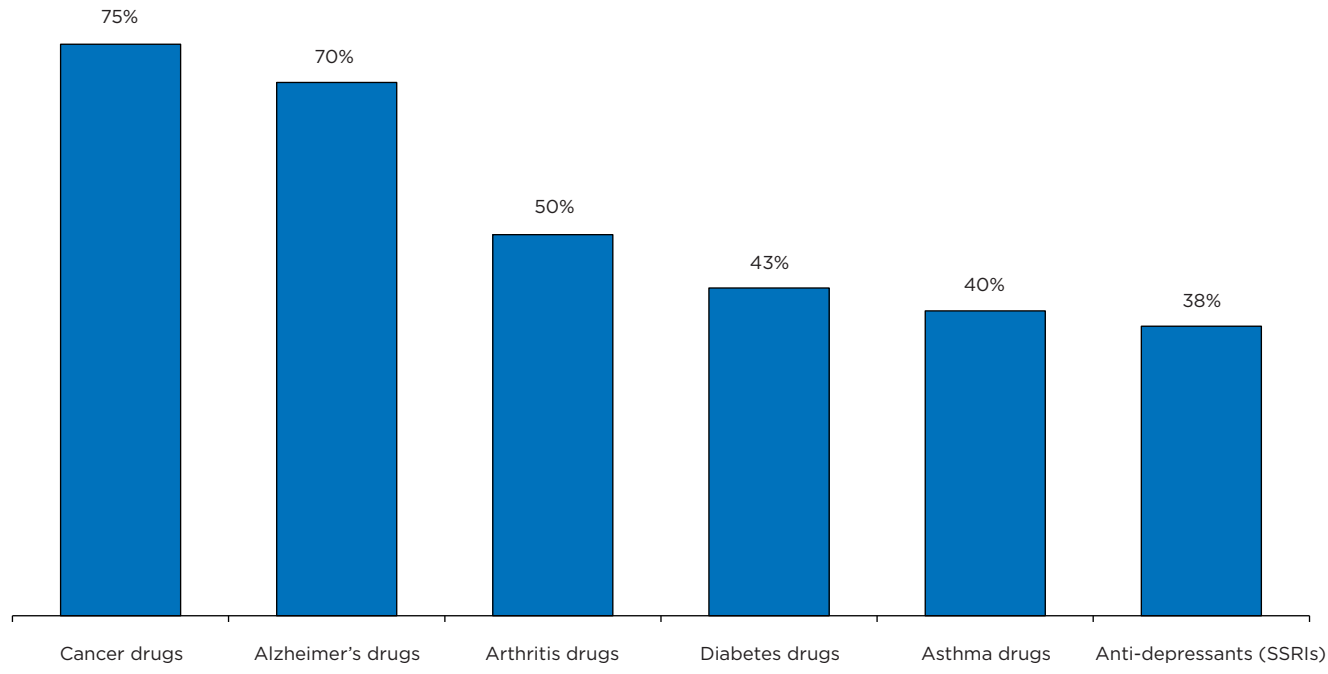
The NHS' '100,000 Genome' project is collecting data from people with cancer and whole families with rare diseases to support pharmaceutical personalisation. The wealth of integrated data, and world leading research and funding commitments mean that the UK will remain an important market for new personalised pharmaceuticals for years to come.

The complexity of contextualised data combined with full genome sequences will inevitably challenge healthcare software platforms. The quest is on to develop electronic health records that can incorporate the information required for a further generation of genomic information and support clinical decision making.

Biotechs winning out

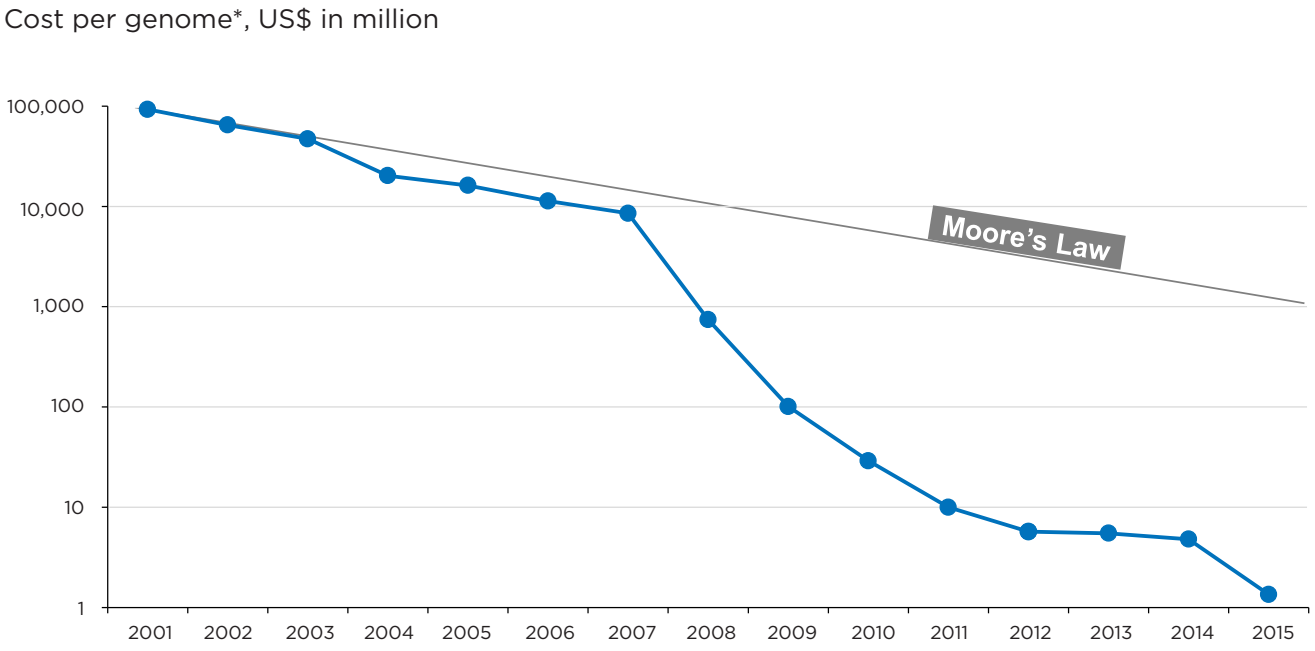
New opportunities for academia and industry to work together in the advancement of therapies are emerging. Whilst once academic institutions generated new molecular targets that were subsequently pursued by big pharma for commercial gain, the game has changed. ▶

FIGURE 1: INFECTIVENESS OF SPECIFIC DRUGS WITHIN KEY THERAPEUTIC AREAS



Sources: Sources: Spear, BB, Heath-Chiozzi, M, Huff, J. Clinical application of pharmacogenetics. Trends in Molecular Medicine. 2001;7(5): 201-204; Candesic analysis

FIGURE 2: RAPIDLY DECREASING COST OF HUMAN GENOME SEQUENCING



* Human sized genome

Sources: National Human Genome Research Institute; Candesic analysis

▶ Whilst big pharmaceutical companies grew fat on the back of blockbuster drugs prescribed to millions, small biotechs have always been far more nimble. It's likely that they will be the engine house of personalised pharmaceutics.

Big pharma is increasingly outsourcing drug discovery and development to university spin-outs and smaller firms with a small portfolio of molecules. It's these smaller entities that represent the most exciting part of the market for potential investors. However, it's a high stakes game when many biotechs have just one agent or target in development and the risks of failure are high.

Consumers will drive personalisation

23andMe was a pioneer in developing low cost personal genomic services. Direct-to-customer genetic testing will be as challenging to healthcare professionals as "Doctor Google". With the massive reduction in the cost of full genomic sequencing,people will have ever more access to data about their own genetic code.

We're already a nation of 'cyberchondriacs'; it remains to be seen how widespread knowledge of our genetic profiles will influence our healthcare decisions and demand for clinical services.

Genomic information is most powerful in context, and this will go hand-in-hand with the increasing use of point of care diagnostics and consumer purchased healthcare monitors. Sorting the significant correlations from the accidental findings is an ongoing headache for clinicians, researchers (and now patients) but will be still more difficult with this wealth of personal information.

The powerful insight a genomic profile promises can only be realised with expert guidance, and today such expertise is not widespread in the medical profession. Can the online medical consultants of tomorrow capture this market of the 'worried well'?

Complexity of clinical trials

Data mining is a bit dodgy sometimes – if your drug wasn't any better than a placebo on average then you can usually find someone who got better by coincidence: a spurious correlate. The temptation is to declare "the drug effective for females of 27 years of age called Sandra who eat a banana every morning" if she was the one who improved on that trial. That is obviously not the route to effective personalised medicine. However, genomic correlations are preferable as they can provide a scientific rationale as to why a subset of the patient cohort improved.

Increasingly trials, by necessity, will have very few patients in them. CROs with wide networks of patients are best placed to recruit enough patients to adequately power studies in development of drugs that will be relevant for a tiny fraction of the population.

Outsourced provider growth

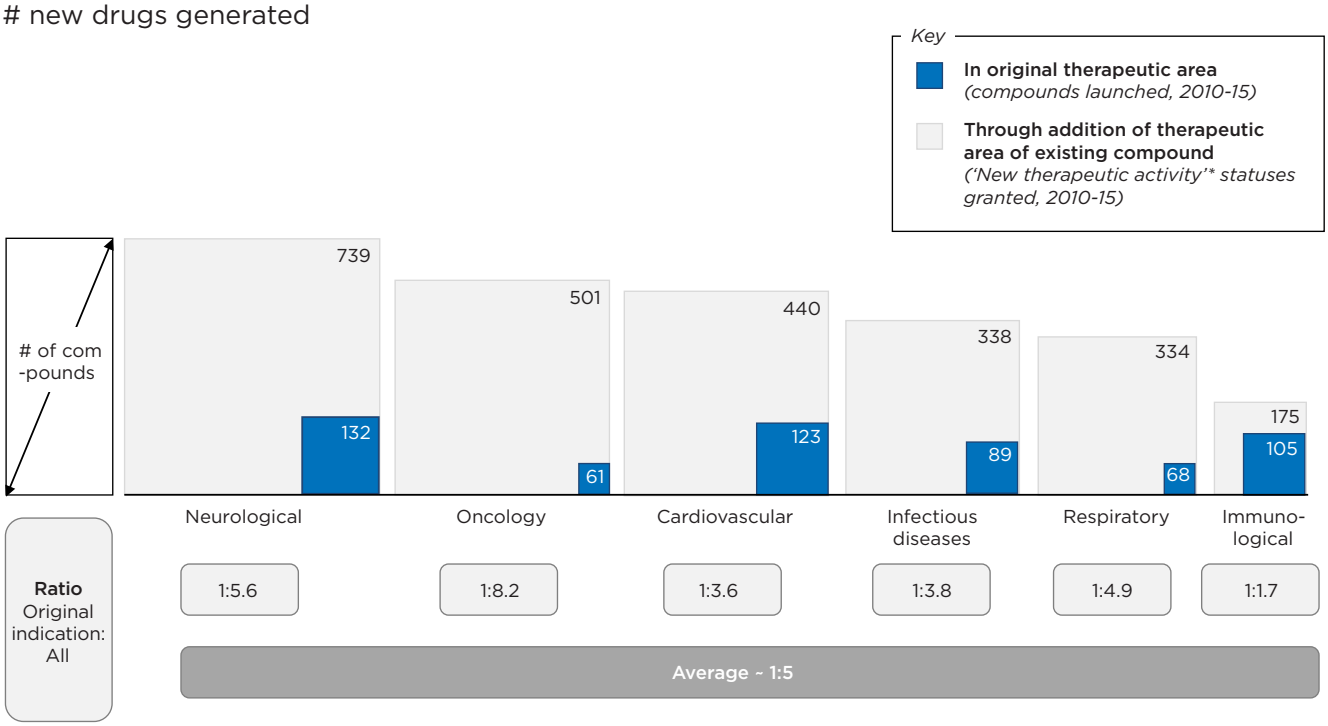
It's difficult to understand what big pharmaceutical companies' functions will be in the future as outsourcing trends appear unabated. It may be that they become effective selectors of new drugs from biotech, experienced commissioners of outsourced services and curators of drug portfolios until they reach maturity.

The move towards personalised medicine seems inexorable. The practicalities of developing an array of new agents and delivering them to patients have not yet been fully addressed. There are opportunities across the healthcare market to take advantage of the change in medical practice.

As the specificity, and therefore the complexity, of pharmaceuticals increases then so too will the demands for translating good drug candidates ▶

FIGURE 3: THE IMPORTANCE OF SECONDARY INDICATION DRUGS

new drugs generated

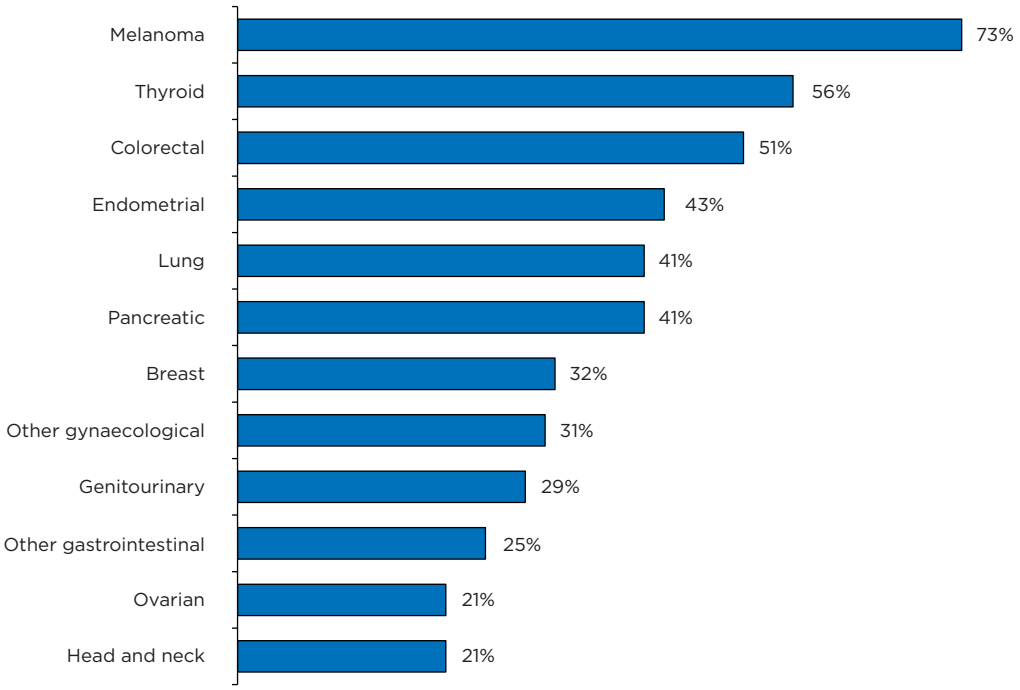


*Notes: *A new therapeutic area of activity is identified for or applied to a particular compound*

Sources: PharmaProjects; Candesic analysis

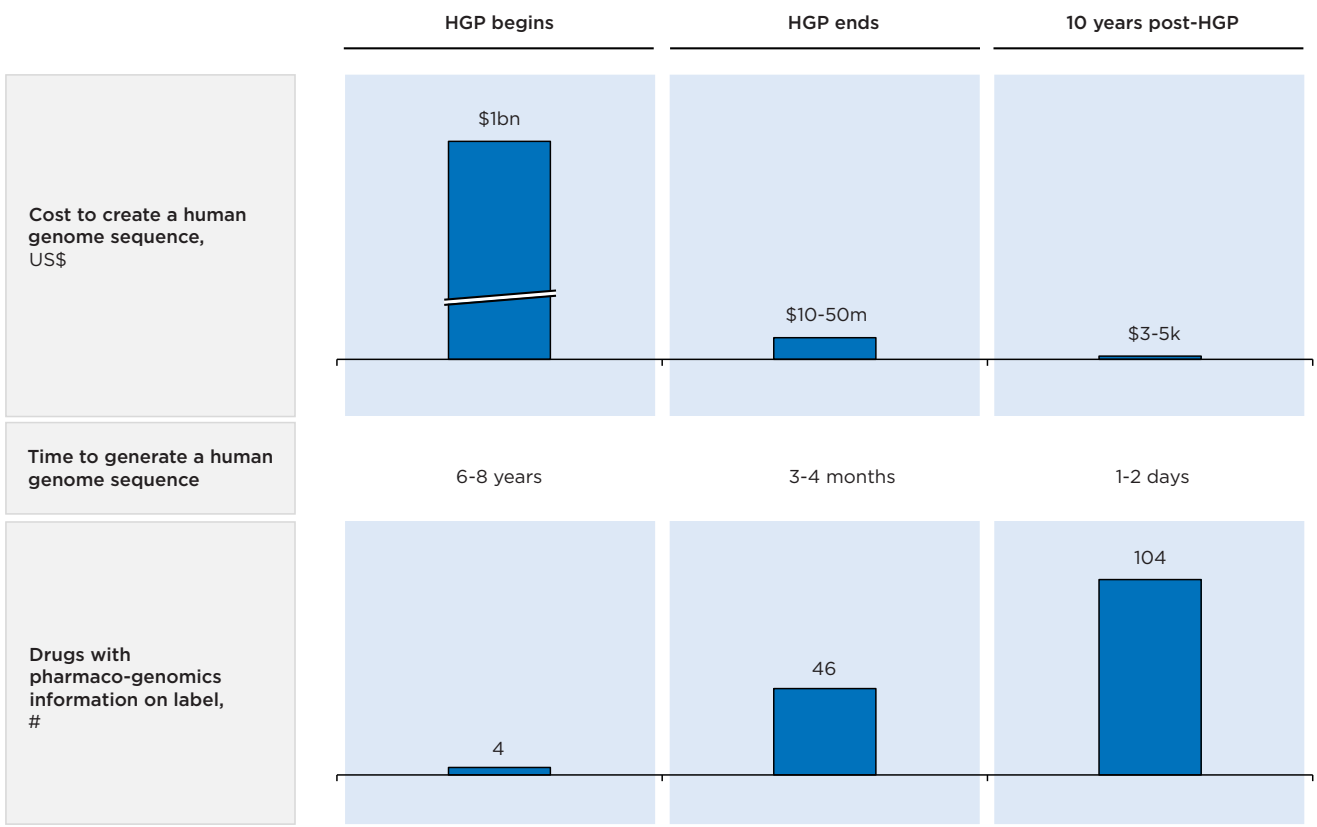
FIGURE 4: NEED FOR A TARGETED APPROACH IN ONCOLOGY

% of patients whose tumours were driven by certain genetic mutations that could be targeted by specific drugs, by types of cancer



Sources: Wall Street Journal; Candesic analysis

FIGURE 5: THE HUMAN GENOME PROJECT'S IMPACT



Notes: Graphs not to scale; HGP: the Human Genome Project

Sources: National Human Genome Institute; Candesic analysis

▶ into clinically utilised agents. Drug discovery firms with outstanding clinical science capabilities will be key players in this developing market.

A new beginning

Drug repurposing is an important means of taking advantage of drugs reaching the end of their patent life or those that proved expensive failures in prior clinical trials. A great many drugs find other applications beyond their original indications (*figure 3*) and this trend is set to continue.

Genomic profiling is accelerating the path to repurposing, and allowing pharmaceutical companies to extend the life cycle of agents more efficiently.

Personalised cancer care

One of the promising clinical areas for the delivery of personalised drugs is oncology. Cancers, even of the same type, vary widely and their susceptibility to specific chemotherapies can be very different. Examining the cells from a tumour to identify which genes have been changed and how these affect the expression of proteins, is already a key tool in selecting a treatment (*figure 4*).

For example, molecular stratification now allows lung cancers to be identified as EGFR positive, in which case responsive to antibody therapy, or ALK positive, and therefore responsive to small molecule therapy. This enables patients to start the most effective treatment regime from the start.

Oncology will continue to be an earlier adopter of development in personalised pharmacotherapy as drug prices will remain high and consequences of suboptimal treatment perilous for patients.

Is it for you, me or us all?

Although there has been increasing growth in the number of drugs with pharmacogenomics indications on the label (*figure 5*), they still only number about 100.

Much has been talked about the rise of the polypill, where huge swathes of the population are indiscriminately prescribed regular medication to prevent common cardiovascular disease. This antithesis to personalised medicine is likely to prove reasonably effective. Common conditions addressed with generic medications will remain an important part of care.

Personalised pharmaceuticals will become a not uncommon tool in the clinical arsenal as science and technology advances. Certainly, the establishment of the Genomic Medicine Centres by the NHS will make it more accessible. For the time being though there are great hurdles to adoption of pharmacogenetics at scale.

Patients will benefit as we move away from the one-size-fits-all model of pharmaceutical prescribing. Whilst cancer and rare diseases will be leaders in the adoption of personalised pharmacotherapy, other common disorders will continue to be treated by the good care doctors and nurses have been practising for decades. ■

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