Tomorrow's Treatments

Big Pharma's support of the personalised approach to cancer care and the use of biomarkers and personalised medicine in oncology is transforming cancer treatment

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Ever since the time of Hippocrates who wrote about the individuality of disease and the necessity of giving different drugs to different patients – "for the sweet ones do not benefit everyone, nor do the astringent ones, nor are all the patients able to drink the same things" – a personalised approach to medicine has been recognised steadily, but it is only in recent decades that a fuller scientific understanding of the approach has become better appreciated.

However, the decoding of the human genome in 2003 saw a step-change in the acceleration of that understanding, and the medical community has long predicted that an era of personalised medicine will soon be ubiquitous. This article examines how that reality is now upon us and that the use of biomarkers and personalised medicine in oncology is transforming current cancer treatments.

New Ideas

While established cancer treatments such as surgery, radiation, and chemotherapy are still improving, excitement in the cancer arena today lies in the development of targeted therapies, otherwise known as 'personalised medicine'. This individualised approach includes not only the early stage diagnosis of every specific cancer, tailor-made therapeutic intervention, and the careful monitoring of patients' progress, but also heralds the prospect of personalised treatments that stimulate the body's immune system to fight cancer.

With the development of target-based agents, primed to attack only identified cancer cells, higher response rates for treatments, as well as less toxic and more effective outcomes, now appear possible. New drugs that are being developed today, and coming from this group, promise to greatly improve outcomes for cancer patients.

Despite cancer still being the second leading cause of death after heart disease worldwide, scientists believe that, with the advent of new technologies and tools, our understanding of cancer has been revolutionised, which, in turn, has allowed more targeted approaches to the disease to be developed. From a technical viewpoint, medicine is reasonably expected to one day be able to turn most cancers into either curable diseases or chronic ones that progress slowly. Indeed, if these cancers are caught early – and with the appropriate therapeutic approach – it is conceivable that many cancers will be treatable.

Personalised Medicine

Personalised medicine, in its broad interpretation, is the tailoring of a medical treatment to the characteristics of an individual patient. As the National Human Genome Research Institute defines, a personalised approach to medicine is one that includes "an individual's genetic profile to guide decisions made in regard to the prevention, diagnosis, and treatment of disease".

Personalised medicine has long been used across the medical profession. Even Hippocrates' writings refer to the individuality of disease and the necessity of giving a choice of drugs to different patients. His personalised approach to medicine is underlined by his advice: "It is more important to know what sort of person has a disease than to know what sort of disease a person has." A personalised approach to medicine has been present, but it has only recently begun to materialise in the sphere of drug development.

As science has developed over the past few decades, the way scientists approach medicine has steadily changed. The traditional route of drug development had been based on identifying treatments or therapies that target entire populations. However, as the understanding has improved of how patients carry and bear distinctive traits that can cause differences in their response to treatment, science has tailored its development of drugs via a more targeted approach so that patients' unique responses to a therapy can be addressed. This has led to a 'personalised' approach to medicine evolving and, seemingly, manifesting itself prominently in the field of oncology.

Ever since 2003 when the genome project was declared complete, there has been a step-change in its approach. The tailoring of treatments to the specific molecular or genetic profile of an individual patient became possible. What is taking place now is the increasing use of an individual patient's molecular and genetic information to inform and optimise their diagnosis, prognosis, and treatment in the prevention of cancer.

At the core of this change is the realisation that the molecular features of a tumour, such as its genetic traits, are key to its treatment and a deeper understanding of a patient's genetic profile is more important for the tumour's treatment than knowledge of where the tumour started growing, whether

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it be in the lung, prostate, brain, or breast. This personalised approach has also manifested itself in the way patients are diagnosed and in the way their bodies are interrogated – this is down to biomarkers.

Biomarkers

In the cancer space, a biomarker refers to a substance or process that is indicative of the presence of cancer in the body, and it may be a molecule secreted by a tumour or a specific response of the body to the presence of cancer. However, the use of these biomarkers alongside the latest cancer therapies is one of the fastest-growing areas of cancer research. Not only can biomarkers identify patients who are more likely to respond to a particular drug therapy, but they can also give a signpost as to whether a tumour is progressing, regressing, or mutating.

Biomarkers fall into two camps: prognostic biomarkers are ones that highlight a patient's response to cancer therapy, and predictive biomarkers are used to identify subpopulations of patients that are most likely to respond to a given treatment. Both categories are having a profound impact on cancer medicine, with a growing number of cancer drugs in development being twinned with a biomarker.

Where Are We Now?

The increasing understanding of the genetic complexity of cancer is having a positive impact upon how cancer is treated. While two patients may have the same prostate cancer under the microscope, doctors today are able to identify significant differences between their respective prostate cancers, but at a genetic level.

Through the identification of these differences, the industry can better understand why one of those patients is cured and the other is not, despite both patients being in receipt of the same treatment.

Before this targeted approach and, historically, in the treatment of cancer, chemotherapy and radiotherapy were more indiscriminate and scattergun in their approach. However, biomarker-assisted diagnosis, prognosis, and targeted therapies are transforming the future of cancer care with scientists discovering new molecular targets and drug agents and seeing improvements in the pre-selection of patients for clinical trials.

Cancer patients are routinely offered a molecular diagnosis in clinical centres to allow oncologists to choose tailored treatments, thereby enhancing patients' chances of survival. Molecular Biologist Dr Satu Vainikka believes that we are not far from the time when most cancer cases will be given a targeted course of treatment.

Several personalised adjunct therapies and tests are on the market already that are starting to transform patients' lives. As far as breast cancer is concerned, about 30% of cases are characterised by the over-expression of the HER2 protein. For women with this form of the disease, an antibody drug called Herceptin can reduce the recurrence of a tumour by 52% when used in combination with chemotherapy, in comparison to chemotherapy alone. This personalised approach goes further as molecular diagnostic tests for HER2 are conducted to identify those women who would benefit from receiving the antibody drug. For lung cancer, Novartis' Zykadia is indicated for the treatment of non-small cell lung cancer. However, the drug is only effective on patients who express the abnormal (ALK) gene. In 2017, the FDA approved Zykadia for the expanded treatment of patients with ALK+ metastatic non-small cell lung cancer who have progressed on or are intolerant to crizotinib, another anti-cancer drug.

Following on behind, a growing number of small biotech companies undergoing clinical trials are striving to develop further novel anti-cancer compounds that target the disease from a variety of personalised angles. Loxo Oncology is developing a pipeline of purpose-built, targeted medicines against known genetic drivers of cancer. Its orphan drug, larotrectinib – which targets a rare genetic defect that is found across almost all types of tumour – is expected to launch in early 2018. In a similar vein, AIM listed, ValiRx, is developing novel treatments for cancer and associated biomarkers.

Its VAL201 drug against prostate cancer is a peptide compound with a unique mechanism of action that is increasingly showing in its Phase 1/2 clinical trials that it can provide a potent therapeutic benefit and has fewer side effects compared to standard hormone therapies. Indeed, taking the personalised medicine approach to the extreme, Novartis' chimeric antigen receptor therapy (Car-T) is a bespoke drug manufactured specifically for an individual patient, which re-engineers a patient's cells in a laboratory so they will attack cancer cells.

A New Era

Cancer care appears to be entering, or has just entered, a new era in which a focus on the principle of biomarker-

guided and personalised drug development is being increasingly embraced. Over the past two decades, and as a result of the Genome Project, scientists now better understand how cancer cells evolve and metastasise or spread. Advances in molecular biology and genetics have led to treatments that specifically block those erroneous pathways that give rise to cancers and other conditions or encourage their growth. Similarly, biomarkers have substantially transformed the ability to identify patients who are most likely to benefit from a specific treatment, so as to achieve the best possible medical outcome for them.

With Big Pharma appearing willing and supportive of the personalised approach to cancer care, the future seems bright for cancer patients and the oncology profession alike.

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