The emergence of precision medicine for oncology

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Dr Priya Hays, PhD, considers how the rapid development of precision medicine for oncology has impacted diagnosis, treatment, and clinical outcomes in cancer care

Personalised medicine, also referred to as precision medicine, had its early conceptual foundations in the Human Genome Project, the multi-institutional effort to sequence the entire base pair sequences of the human genome, or DNA sequences in the cell.

The sequencing revealed variations between individuals in their DNA sequences. This variation, or what came to be known as genomic variation, could be mobilised to differentiate diagnosis and treatment between individual genomes.

Targeted therapies – small molecule inhibitors designed to attack cancer cells exclusively by affecting signalling pathways – were developed as viable treatment options defined by the personalised medicine pathway.

Precision oncology emerged as a new field encompassing small molecular inhibitors and biologics.

One such small molecular inhibitor that first appeared was imatinib for the targeted treatment of chronic myeloid leukaemia, a blood cell disorder involving myeloid cell precursors.

This design of destroying cancer cells while leaving normal cells intact rapidly expanded to other tumour types such as melanoma, breast cancer, lung cancer, colorectal cancer and prostate cancer, along with other carcinomas such as renal cell carcinoma and hepatocellular carcinoma, in addition to a whole host of other cancers in blood cell categories such as chronic lymphocytic leukaemia and acute lymphocytic leukaemia.

Precision medicine for oncology in lung cancer

Initial successes of precision medicine for oncology came in lung cancer, which targeted a specific histologic sub-type of lung cancer called non-small cell lung cancer.

Drugs such as lorlatinib for ALK-positive mutations, osimertinib
for EGFR mutants, and adagrasib for resistant KRAS mutants were developed for non-small cell lung cancer.

Targets for BRAF mutations emerged for melanoma, and this solid tumour became particularly amenable for immunotherapy approaches such as the immune checkpoint inhibitors nivolumab and ipilimumab, also known as PD-1 inhibitors since they remove the inhibition of cytotoxic T cells to destroy the foreign antigens on cancer cells.

Gene therapy, wherein a patient's T cells could be genetically re-engineered ex-vivo and re-administered back into the patient to kill abnormally expanding cells, also known as chimeric antigen T cells, was developed for paediatric lymphomas, a hematologic malignancy with poor prognosis.

While many of these small molecular inhibitors, biologics and cellular therapies were accompanied by adverse events, including hematologic disorders, cytokine release syndrome and neurotoxicities, ranging from mild to moderate to severe, many responders exhibited robust long-term positive clinical outcomes.

Improving prognostic and predictive indicators in cancer care

It was not only in the realm of treatment that personalised medicine had its impact.

Novel technologies such as liquid biopsy and companion diagnostics accompanied evolving trends in personalised medicine and prognostic and predictive markers such as minimal residual disease; PD-L1 status became relevant in helping cancer patients and their providers manage the disease's genotypic and phenotypic complexity. For breast cancer, the companion diagnostic for HER-2 antibodies was FDA (Food and Drug Administration) approved, along with Herceptin, to detect the presence of the mutation and improve outcomes.

In addition, diagnostic tools became widely adopted for the predictability of treatments for breast cancer, such as OncotypeDx and MammaPrint.

Traditionally, diagnosis and prognosis of cancers are usually done through tumour biopsy, an invasive way of determining tumour characteristics.

Liquid biopsy, derived from the blood and contains samples of the tumour DNA, is now being developed as a viable approach to characterise a tumour's spatial and temporal heterogeneity and thereby give measured prognostic and predictive indicators.

Liquid biopsy has the additional benefit of being non-invasive.

A whole new world of clinical data

With the advent of personalised medicine, new approaches to clinical trials that complemented randomised controlled trials and took advantage of molecular variation in patient populations entered the medical realm.

Precision medicine trials, such as adaptive trials, have the potential to accelerate the clinical trial and drug development process while reducing overall costs.

These trials involve dividing patient populations by biomarkers and administering targeted therapies accordingly.

Basket trials involve molecular profiling of tumours, while umbrella trials offer distinct treatments based on biomarker results.

Clinical trials in oncology are measured by what are known as endpoints, and these statistical measures give a good indication of the treatment potential of these drugs.

With the advent of personalised medicine, enormous streams of clinical data emerged for analysis and interpretation. KEYNOTE, IMpower, and CheckMate evaluated key targets, particularly immunotherapies, for determining the clinical meaningfulness of precision medicine therapies which for many tumour types has become the standard of care.

Precision medicine for oncology is the ‘best thing’ to happen in patient care

In this medicine paradigm, personalised medicine has become a mainstay. It is perhaps one of the ‘best things’ to happen to medicine in recent years in terms of innovation and patient care, with the potential for even greater developments in the future.

However, healthcare equity remains a factor to be considered in ensuring that the benefits of personalised medicine reach all populations.

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