WORLD CANCER DAY:

Reflecting on recent advances in cancer therapy

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Each year on 4 February, the world unites for World Cancer Day. The aim: to raise awareness of cancer and to encourage its prevention, detection and treatment. This year marks the launch of the new 'I Am and I Will' three-year campaign, which is a call to action urging for personal commitment, representing the power of individual action to impact the future. With an estimated 18.1 million new cases and 9.6 million deaths from cancer in 2018,[1] continued clinical research into its prevention, detection and treatment is critical. Despite these sobering statistics, there is much to be excited about in terms of recent progress in these areas and the potential benefits for patients. In particular, advances in the understanding of immunology and genetics have led to the development of new immunotherapeutic agents and improvements in personalised medicine, with promising results.

Immunotherapy

One of the functions of the immune system is to target and remove cancer cells; however, some cancer cells can evade these immune responses, enhancing metastasis and growth of tumours. Researchers are now beginning to understand the molecular mechanisms behind these evasion strategies, with much research interest focusing on immune checkpoint molecules such as PDL1/PD1.

> *"The World Health Organization estimated that the global cancer burden rose to 18.1 million new cases and 9.6 million deaths in 2018."*[1]

It is now understood that some cancer cells overexpress PDL1, which binds to PD1 receptors on activated T cells, inhibiting their cytotoxic action against cancer cells. By blocking PDL1 or PD1 with monoclonal antibodies, this process is inhibited,

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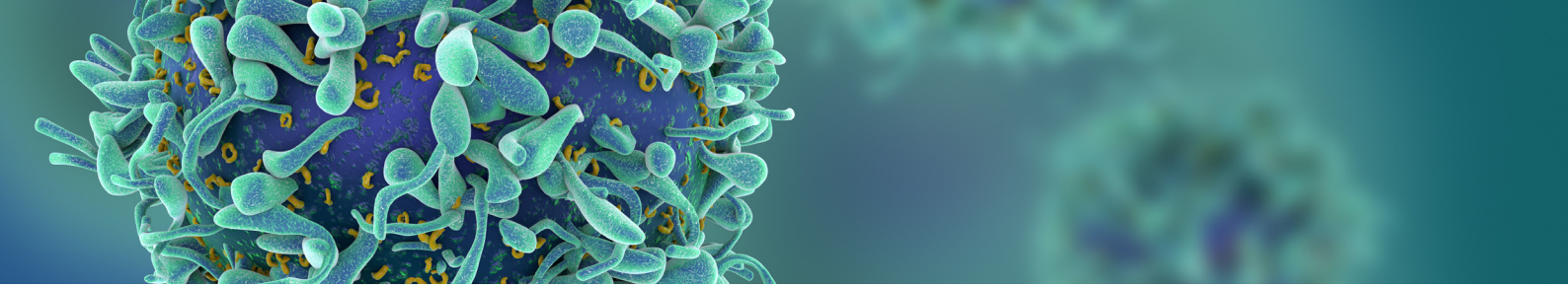

thus promoting the elimination cancer cells. There is particular excitement about anti-PDL1/PD1 therapies due to the good treatment-response rates across a number of cancer subtypes. Indeed, since the first anti-PD1 therapy was approved in 2014 to treat melanoma, anti-PD1/PDL1 therapies have been approved in a variety of cancer subsets at an unprecedented rate.

Research is currently ongoing to understand other immune checkpoint mechanisms and to translate these findings into new immunotherapeutic targets. Another growing area of interest in the field of immunotherapy is the possibility of engineering a patient's own T cells to target cancer cells (CAR T cell therapy). This has become a reality in acute lymphoblastic leukaemia and advanced lymphoma, with two CAR T cell therapies approved in 2017.[2] Research is currently ongoing to see whether CAR T cell therapy will be effective in non-haematological solid cancers.

Personalised medicine

Cancer is a complex and extremely heterogeneous group of diseases; even cancers in the same subset can be caused by different driver mutations that vary from person to person. Furthermore, it is now known that not all cancer cells within a patient are the same, with rare cancer-initiating cells largely responsible for propagating the cancer, relapse and drug resistance. While the concept of personalised medicine is not new, recent advancements in genomics, DNA-sequencing strategies and bioinformatic analyses have enhanced the analysis and identification of mutations and how they may influence the cancer cells. This may lead to the identification of novel therapies and improve personalised therapy for patients in the future.

Despite these recent advances in cancer therapeutics, there is still so much to do. The issues of relapse and drug resistance in both immunotherapy and personalised medicine are major challenges. The recent development of single-cell sequencing technologies may offer new hope that scientists will be able to uncover ways to eliminate the rare cancer-initiating cells and address the problem of drug resistance in the future.

Indeed, a number of mutation-specific targeted therapies were approved in 2018; these included osimertinib in non-small cell lung cancer with EGFR mutations,[3] encorafenib and binimetinib combination therapy in melanoma with BRAF mutations,[4] and gilteritinib in relapsed or refractory acute myeloid leukaemia with FLT3 mutations.[5]

1. World Health Organization. Latest global cancer data: cancer burden rises to 18.1 million new cases and 9.6 million cancer deaths in 2018 [press release]. 12 September 2018. https://www.iarc.fr/wp-content/uploads/2018/09/pr263_E.pdf. Accessed 8 January 2019; **2.** Milone MC, Bhoj VG. The Pharmacology of T Cell Therapies. *Mol Ther Methods Clin Dev* 2018;8:210–221; **3.** AstraZeneca. US FDA approves Tagrisso as 1st-line treatment for EGFR-mutated non-small cell lung cancer [press release]. 18 April 2018. https://www.astrazeneca.com/media-centre/press-releases/2018/us-fda-approves-tagrisso-as-1st-line-treatment-for-EGFR-mutated-non-small-cell-lung-cancer.html. Accessed 14 January 2020; **4.** US Food & Drug Administration. FDA approves encorafenib and binimetinib in combination for unresectable or metastatic melanoma with BRAF mutations [press release]. 27 June 2018. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-encorafenib-and-binimetinib-combination-unresectable-or-metastatic-melanoma-braf. Accessed 14 January 2020; **5.** US Food & Drug Administration. FDA approves gilteritinib for relapsed or refractory acute myeloid leukemia (AML) with a FLT3 mutatation [press release]. 14 December 2018. https://www.fda.gov/drugs/fda-approves-gilteritinib-relapsed-or-refractory-acute-myeloid-leukemia-aml-flt3-mutatation. Accessed 14 January 2020

Alpharmaxim has long-standing experience in cancer-related healthcare communications, and has worked on a wide variety of projects in lung, prostate, breast, pancreatic, bone and blood cancer.

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