

Does immunotherapy work for prostate cancer

By Kalli Spencer

Immunotherapies as a single agent have not been shown to be effective for treating advanced prostate cancer till now. In this research blog we will try find out why they are not effective and what the potential alternatives are. Numerous blogs in the past have addressed the concept of immunotherapy and the types available. The premise of immunotherapy is that it harnesses the body's own immune system to target and kill off cancer cells. They can be administered intravenously or as a vaccine. Sipuleucel-T was one of the first FDA approved immunotherapies, a vaccine that showed only a 4-month overall survival benefit originally (IMPACT Trial) with subsequent trials showing no survival advantage (PROSTVAC Trial)¹. Other agents are the PARP inhibitors (olaparib) and pembrolizumab. Immunotherapy has shown good results for cancers of the bladder, kidneys, lung and skin, but why not for prostate cancer?

Prostate cancer is considered a “cold” tumour and with an immunosuppressive tumour microenvironment². The tumour microenvironment is what's responsible for tumour survival, growth and spread. Under a microscope there is a very low infiltration rate of immunological cells called “T Cells”. This is thought to be due to the fact that the inside of the tumour is hypoxic (has relatively low oxygen levels)³. There is a low supply of micronutrients to sustain the immune cells in this milieu. Therefore, scientists can't use the immune system to fight the cancer cells in the tumour. Another point to consider is that bone is the most common metastatic site, and it is often the case that bone metastases are far less responsive to immunotherapy than metastases situated in soft tissues. However, there are many other components to the immune system and other target areas that are being explored (immune-intensification and immune-modulation)⁴. There are cells of the immune system surrounding the tumour that result in growth of the tumour and these could be potential targets for new therapeutic agents as well².

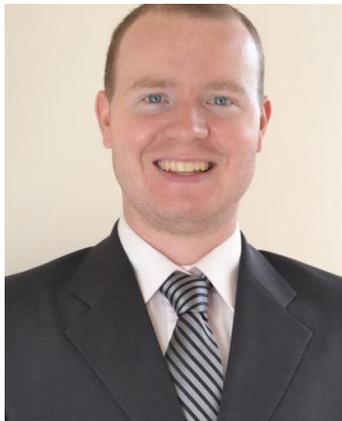
Immunotherapies are also being combined in trials to take advantage of tumour cell destruction through multiple pathways. Immunotherapy is also being combined with androgen deprivation therapy, conventional chemotherapy as well as radiation. These treatment modalities release neoantigens when tumour cells are killed making immunotherapy more effective⁴. It has also been combined with tumour vaccines.

The immune system's response to immunotherapy also varies between individuals and tumours themselves. Tumours that show a low mutational burden are less likely to respond to treatment. Individualised genomic studies may need to be carried out and then based on predictive factors of response/resistance - treatments can be tailored accordingly. This is already done for those who have microsatellite instability or mismatch repair gene defects and receive pembrolizumab after disease has progressed on conventional treatments – early data shows a response rate of 40% in this subgroup⁵. Going forward an immunogenic classification needs to be developed based on genomic profiling and a scoring system created to guide future treatment⁶. New tumour markers other than PSA are required (e.g. PD-1) to monitor the effects of these treatments as well as novel imaging approaches such as specialised PET Scans.

Currently research is focusing on immunotherapy for advanced disease but perhaps in the future these treatments may be used for earlier disease. Genomic testing of localised prostate cancer could be utilised to determine which tumours will recur or metastasize at a later stage and immunotherapy treatment regime initiated at that point.

References

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Kalli is an internationally renowned Urological Surgeon, specialising in oncology and robotic surgery. He trained and worked in South Africa, before relocating to Australia where he has worked at Macquarie University Hospital and Westmead Hospital. His passion for what he does extends beyond the operating room, through public health advocacy, education and community awareness of men's health, cancer and sexuality.

Kalli has been involved with the Prostate Cancer Foundation of Australia for many years, advocating for improved cancer care and facilitating community prostate cancer support groups.