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“Immutep has started exploring the potential of the first ever triple combination therapy with Eftilagimod”

15 March 2023 | News

Australian firm Immutep is a global pioneer and leader in the development of LAG-3 therapeutics. Its lead product candidate is eftilagimod alpha (LAG-3Ig or IMP321), a first-in-class antigen presenting cell (APC) activator currently being investigated in clinical trials as a treatment (in combination with chemotherapy or immunotherapy) for various cancer indications. To study, eftilagimod, in combination with avelumab (BAVENCIO), the firm has partnered with Merck and Pfizer for a new Phase I clinical study in patients with urothelial cancer. In an email interaction with BioSpectrum Asia, Immutep, CEO, Marc Voigt highlights the pioneering work that the company is undertaking in the immuno-oncology field and the trends and developments in the sector.

Can you describe your immunotherapy research and how Immutep’s approach compares to other immunotherapies?

Immutep is the global pioneer and leader in the development of LAG-3 therapeutics. LAG-3 was discovered by Immutep’s Chief Medical Officer and Chief Scientific Officer, Prof. Frederic Triebel. It is a naturally occurring protein that activates the antigen presenting cells (APCs) of the immune system by binding to the Major Histocompatibility Complex (MHC II). The interaction between the LAG-3 protein and the MHC II can be influenced or changed to help the body fight cancer by activating or inhibiting the immune system.

Today, LAG-3 is considered the most promising new immune checkpoint in immuno-oncology since the success of PD-1 related treatments. LAG-3 drugs have the potential to overcome many of the limitations of other oncology drugs, such as chemotherapy and even established immuno-oncology treatments such as anti-PD-1 monotherapy, a common immune checkpoint therapy where unfortunately 70-80 per cent of patients fail to respond.

Immutep is developing four drug candidates based on LAG-3, including our lead product candidate, efti which is advancing in late-stage clinical trials. It is an “immune booster” with a broad immune activation and the versatility to be paired with existing standard of care treatments such as PD-1 (or PD-L1) antagonists in combination therapies.

Efti also has a strong safety profile and a unique mode of action, differentiated from anti-LAG-3 products. Acting as an APC activator, efti complements the effect of immune checkpoint inhibitor (ICI) drugs, such as the blockbuster drug Keytruda, also known as pembrolizumab.

Efti is the only MHC II agonist (APC activator) product candidate currently in clinical development and has shown encouraging clinical results in multiple cancer settings, including non-small cell lung cancer, head and neck squamous cell carcinoma, metastatic breast cancer and melanoma.

How do you see the cancer immunotherapy field evolving over the next five years, and what breakthroughs might we see?

In general, we believe cancer immunotherapy will continue to play a key role in treating many different carcinomas. Interest and investment in LAG-3 therapeutics has accelerated significantly over the last year since LAG-3 was validated via the approval of BMS’s Relatlimab by the US FDA, and is expected to rise even more. There is still work to do to fully realise the significance of the LAG-3 / MHCII interaction in cancer; however, many therapies are advancing rapidly through late-stage trials towards approval, including Efti.

Overall, we will continue to see a high number of clinical trials testing different combinations of therapies in order to get the best outcome for as many patients as possible. This may imply we will see a more fragmented treatment landscape and that the role of biomarkers will continue to increase.

Also, I’m excited by the opportunity ahead to explore LAG-3 related treatments in autoimmunity.

What are the latest trends and challenges in cancer immunotherapy?

Combination therapies, where we pair an immuno-oncology drug with, for example, a chemotherapy or radiotherapy, are a relatively new paradigm. The idea is to get the immune system functioning well enough to fight the cancer alongside another treatment. In some cases, there can be advantages beyond improved efficacy, such as the ability to give lower doses of chemo which are more tolerable for patients.

Immutep has already reported encouraging efficacy results from its combination trials and has now started exploring the potential of the first ever triple combination therapy with efti in conjunction with an existing approved standard of care therapy consisting of a chemotherapy agent and an anti-PD-1 therapy. We’re hopeful this approach will provide a new option to many cancer patients.

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