Use of tildrakizumab in the treatment of moderate-severe plaque psoriasis

Plaque Psoriasis

Psoriasis is a chronic, inflammatory autoimmune condition that affects the skin, nails and joints. There are a number of different types of psoriasis such as pustular, flexural and guttate psoriasis. The most common of these is known as plaque psoriasis. Plaque psoriasis most commonly presents in patients as red or silver, scaly, itchy patches on any area of the skin although it affects mostly the knees and elbows (Better Health Channel, 2018). These scales are known as plaques and are a result the body creating excessive skin cells.

This inflammation is likely to be a response of the immune system; however, it is believed that other factors contribute to the disease. This condition is not life threatening and can be well managed with pharmacological treatments, particularly with recent drug developments. One of these drugs is tildrakizumab, a biological agent which is used to reduce the immune response and thus induce remission of the condition. Despite having these advances in pharmacological treatments, there is no cure for plaque psoriasis and in many cases the condition will involve periods of exacerbation and remission.

Pathophysiology of Plaque Psoriasis

The pathophysiology of plaque psoriasis is mostly unknown; however, it is believed to be related to a number of factors; including, genetics, immune system and environment. In recent years, research has been able to give a better understanding of the immunological pathophysiology which has allowed for the development of targeted drug therapies (Beck et al., 2018).

In many cases, there appears to be a strong genetic link between family history and the development of the disease. If one parent is affected, the risk of their offspring developing plaque psoriasis increases by 16%. If both are affected, the risk increases by 50% (Handa and Mahajan, 2013). There are also a number of different environmental factors that may contribute to the development of plaque psoriasis including stress, infections and the use of medications such as beta-blockers, tetracyclines and alcohol. The best-known cause for plaque psoriasis is an unnecessary activation of the immune system which causes the body to produce markers such as insulin like growth factor (IGF) and epidermal growth factor (EGF). The increase in EGF causes an increase in the production of epidermal cells and contributes to the formation of plaques (Badri and Oakley, 2018).

Current Therapies for Plaque Psoriasis

Current therapies include a range of pharmacological and non-pharmacological methods which are used to control the symptoms. Non-pharmacological therapies include phototherapies and the use of emollients. The light therapies use short wavelengths of UVA and UVB light to prevent the over proliferation of skin cells by dampening the immune system (Nakamura, Farahnik and Bhutani, 2016).

Pharmacological therapies are classified into topical, systemic and biological therapies. Topical therapies include the use of lotions, creams, ointments and gels containing the drug. Corticosteroids such as betamethasone, vitamin D analogues such as calcipotriol, retinoids such as tretinoin as well as coal tar, dithranol and salicylic acid or urea products (Todd et al., 2010).

Corticosteroids have an anti-inflammatory and immunosuppressive action as

well as reducing cell proliferation by binding to the nuclear glucocorticoid receptor, which changes the production of proteins in the cell (Kwatra and Mukhopadhyay, 2017). Vitamin D analogues reduce the proliferation of keratinocytes in the skin and display anti-inflammatory properties (Barrea et al., 2017).

Systemic therapy for plaque psoriasis include those that are administered orally or parenterally. These are usually reserved for cases of plaque psoriasis which are resistant to topical treatment or those that are very complex or severe. Such treatments include prednisolone, methotrexate, cyclosporine, mycophenolate, leflunomide and other immunosuppressive agents (Kelly, Foley and Strober, 2015). Most of these immunosuppressive agents work by reducing the activity of T-cells in the immune system, either by suppressing proliferation or by preventing the activation of these cells (Pillans, 2006).

In recent years, the emergence of biological agents known as monoclonal antibodies have vastly improved the way plaque psoriasis is treated. Monoclonal antibodies are drugs that have been engineered to target a specific mediator in the immune system and has proven useful in the treatment of autoimmune diseases, including plaque psoriasis. The earliest biological therapies targeted the production of T cells, preventing their proliferation and include alefacept and efalizumab (Maverakis et al., 2010). Although these agents were seen to be very effective, newer agents targeting Tumour Necrosis Factor (TNF-✔) which is involved in the immune system’s inflammatory response and include adalimumab and etanercept.

Tildrakizumab

A newer monoclonal antibody, called tildrakizumab, has recently been approved by the US Food and Drug Administration (FDA). Tildrakizumab is a humanised IgG1κ antibody which targets interleukin 23, one of the cytokines believed to be responsible for the immune system's inflammatory response in severe plaque psoriasis (Markham, 2018). This antibody was originally produced in mice and has been bioengineered to create a very similar, humanised version. Tildrakizumab works to selectively inhibit the p19 subunit that is found on interleukin 23 in the body and neutralise it, preventing the inflammation of the skin (Beck et al., 2018). This antibody has been engineered to have a high affinity for the p19 subunit and as such is effective in exerting its effects.

One of the risks associated with the use of monoclonal antibodies is an increased risk of infection, such as tuberculosis. Phase III studies of tildrakizumab suggest that the drug has a relatively low risk of infection compared to other monoclonal antibodies that are currently being marketed and as such could be safer than the earlier therapies (Crowley et al, 2018).

Further phase III studies suggest that that doses of 200mg and 100mg were efficacious in the treatment of moderate to severe plaque psoriasis, when compared to a placebo and etanercept. The same study also found that the use of this drug was well tolerated in patients treated with this medicine (Reich et al., 2017). A similar trial stated that there was a similar efficacy, with patients who relapsed during treatment able to reach a similar level of effectiveness (Papp et al., 2017). According to late phase II trials, the main

adverse effects of tildakizumab appear to be related to infection in the bones and skin (Papp et al., 2015).

Conclusion

In conclusion, the development of tildakizumab has shown very promising results in the treatment of moderate to severe plaque psoriasis. Tildakizumab is a high affinity monoclonal antibody which targets the p19 subunit of interleukin 23 to dampen the inflammatory response of the immune system. Several studies have shown that this agent has less adverse effects in comparison to its predecessors, adalimumab and etanercept, although it demonstrates a similar efficacy.

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