

Reports on Scientific Meetings

Janssen Dinner Symposium

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The role of IL-23: from disease control to disease remission

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Interleukin-23 (IL-23) is a naturally occurring cytokine involved in the inflammatory and immune response. Interaction between IL-23 and its receptor drives the differentiation, proliferation, and survival of Th17 cells, which produce inflammatory cytokines. By blocking IL-23, the release of important pro-inflammatory cytokines in the pathogenesis of psoriasis is inhibited.

Guselkumab (Tremfya) is a human monoclonal IgG1 λ antibody that selectively binds to the p19 subunit of IL-23 and inhibits its interaction with the IL-23 receptor. It is used for treatment of moderate to severe plaque psoriasis.

The VOYAGE 1 study was a phase III, double-blinded, placebo- and active comparator-controlled trial that compared the efficacy of guselkumab with placebo and adalimumab in patients with psoriasis over a one-year treatment period. Results showed that guselkumab was superior to placebo at week 16 in PASI 90 (73.3% vs 2.9%; $p < 0.001$). Guselkumab was also superior to adalimumab in PASI 90 at week 16 (73.3% vs 49.7%), week 24 (80.2% vs 53.0%), and week 48 (76.3% vs 47.9%).

Guselkumab produced significant responses as early as week 2 compared with placebo. Guselkumab demonstrated sustained efficacy over two years of treatment. More than 80% of patients achieved PASI 90 at week 100. Moreover, efficacy among adalimumab-treated patients who crossed over to guselkumab improved from week 52 through week 100.

Unlike other biologics which require loading, guselkumab only requires standard interval dosing with subcutaneous injections at week 0, 4, and every 8 weeks thereafter, thus avoiding the extra cost. Guselkumab produces an IL-23 inhibitory response that outlasts the presence of the drug in the serum and tissue. This may be related to different pharmacokinetics and pharmacodynamics and possibly higher affinity of anti-p19. After stopping guselkumab, half of the patients maintain PASI 90 during the drug-free period.

Guselkumab may increase the risk of infection. Treatment should therefore not be initiated in patients with a clinically active infection.

Learning points:

Guselkumab (Tremfya) is the first selective IL-23 inhibitor with a novel mechanism of actions for the treatment of moderate to severe plaque psoriasis in this era.