Sustained response following withdrawal of guselkumab treatment with reduced TH17 and TH22 effector cytokine levels

ABSTRACT | Clinical Outcomes

Sustained response following withdrawal of guselkumab treatment with reduced TH17 and TH22 effector cytokine levels

P Brainard, K Scott, Z Yao S1, Y Wang, M Song, K Campbell and E Muñoz-Elías
J Am Acad Dermatol, 2017, Volume 77, Issue 6, Suppl 1, Pages S1-S2

Guselkumab (GUS) is a human therapeutic antibody targeting IL-23, a key driver of pathogenic TH17 and TH22 response in psoriasis (PSO). VOKA (NCT01648682) is a Phase 3 study that investigated the efficacy of GUS in moderate-to-severe PSO and included a randomized withdrawal experiment. We explored the potential association of serum biomarkers and clinical parameters with response following treatment withdrawal. Subjects initially randomized to GUS who achieved ≥75% improvement from baseline in PASI score were randomized to either continue GUS (n = 193) or withdraw from GUS (n = 182). Serum biomarkers were evaluated at baseline, last dose and 4 weeks after treatment withdrawal. Disease activity was assessed using clinical, laboratory and self-reported measures. A total of 185 patients (111 continued GUS and 74 stopped GUS) were included in the final analysis, of whom 182 had serum samples at the above time points and were included in the biomarker analysis. The greatest changes from baseline in biomarkers were observed in patients who stopped GUS, with significant differences in certain cytokines, especially IL-22 (WK 4 - 205.5 pg/mL, p < 0.001), IL-17A (WK 4 - 22.9 pg/mL, p < 0.001) and IL-23 (WK 4 - 3.8 pg/mL, p < 0.001) levels following GUS withdrawal. Importantly, IL-22 levels in patients who stopped GUS were significantly higher (p = 0.0014) than those who continued GUS. These data support the hypothesis that IL-23 contributes to IL-22 production in PSO and that IL-22 may have a role in maintaining TH17 polarization. In conclusion, short-term treatment withdrawal provides a unique opportunity to explore the kinetics of cytokines in PSO, and may provide insights into the disease mechanisms of TH17, TH22 and TH17/TH22 effector cytokines. These findings may inform the development of biomarkers to monitor response to IL-23 antagonists.