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THE ERA OF IL-23: INTRODUCTION OF TILDRAKIZUMAB

Targeting the p19 subunit of interleukin (IL)-23 has been a major development in the management of plaque psoriasis because of the durable efficacy and safety of this mechanism of action. This supplement will review the pivotal data in the tildrakizumab development program: reSURFACE-1 and reSURFACE-2. Dr. Devani and Dr. Prajapati provide a comprehensive evidence-based review of the pivotal trials including the post-hoc analyses which review specific patient subpopulations, interruption/retreatment as well as a discussion of patient-level PASI score distributions across severities. Dr. Grewal also discusses the benefit of tildrakizumab treatment in patients with the comorbidity of metabolic syndrome using a case-based approach.

Since this supplement was prepared, there have been updates presented at the late-breaking session of the virtual EADV 2020 meeting. Specifically, the 5-year efficacy and safety data of the long-term extension trials of the reSURFACE clinical trial program were presented. The long-term durable relative PASI responses were reported with PASI75 rates of 89%, PASI90 rates of 66% and PASI100 rates of 33% in subjects receiving tildrakizumab 100 mg. The more clinically meaningful absolute achievements, including PASI <5 in 89%, PASI <3 in 79% and PASI <1 in 48% at 5 years of treatment with tildrakizumab 100 mg, based on multiple imputation analysis, were also presented.

Additional data encompassing over 5,400 patient years of exposure to tildrakizumab, included low rates of treatment emergent adverse events (TEAEs) at 27 events per 100 patient years (PY), and low rates of discontinuation due to TEAEs, at less than 2 per 100 PY was also presented. Severe infection rates were low at 1.2 per 100 PY and rates of major adverse cardiovascular events (MACE), malignancy and hypersensitivity were all less than 1 per 100 PY. Also new this year was the presentation of the Phase 2b psoriatic arthritis program at the virtual EULAR 2020 by Mease et al. showing promising efficacy that will need to be confirmed in future Phase 3 trials.

Although some patients may benefit from the high levels of response with IL-17 inhibitors for both skin and joint disease, and the broader treatment of TNF inhibitors (i.e. treating skin, joints and bowel disease) clinicians need to consider that IL-23 therapy is also simple, convenient and safe. Tildrakizumab requires 4 doses per year after the loading dose, has been proven to be both effective and safe over the long-term and data shows that targeting IL-23 is also effective in treating the joints and the bowel, with other programs investigating IL-23 inhibition in psoriatic arthritis and inflammatory bowel disease. Given the chronic nature of plaque psoriasis, these late-breaking 5-year durable efficacy and safety data are important additions to medical knowledge, thereby allowing clinicians to make informed decisions when choosing the right therapy for their patients.