ABOUT THE AUTHORS

Alim R. Devani, MD, FRCPC

Dr. Devani completed his dermatology residency at the University of Alberta, earning certification in both Canada and the United States. Dr. Devani has received 5 major awards; authored 1 textbook chapter; published 10 peer-reviewed manuscripts in print or electronic format; and presented at numerous scientific meetings regionally and nationally. He currently practices at the Skin Health and Wellness Centre and the Dermatology Research Institute. Dr. Devani also conducts clinical trials for both adults and children and is the co-creator of The Dermatology Philosophy, as well as the co-founder and co-director of the Dermatology Learning Institute, Dermatology Research Institute, and Dermphi Therapeutics. He is an expert in acne, atopic dermatitis, psoriasis, skin cancer, and anti-aging.

Vimal H. Prajapati, MD, FRCPC

Dr. Prajapati is a Clinical Assistant Professor at the University of Calgary, co-creator of The Dermatology Philosophy, as well as co-founder and co-director of the Skin Health & Wellness Centre, Dermphi Centre, Dermatology Learning Institute, Dermatology Research Institute, Dermphi Therapeutics, and D&P Commercial Group. Additionally, he has started several subspecialty initiatives, including multidisciplinary clinics for pediatric morphea, pediatric scleroderma, and pediatric psoriasis in Calgary, rapid access clinics for psoriasis and eczema in Calgary, as well as rural outreach clinics for psoriasis and eczema in Medicine Hat.

TILDRAKIZUMAB FOR MODERATE-TO-SEVERE PLAQUE PSORIASIS: AN EVIDENCE-BASED REVIEW

Introduction

Tildrakizumab is a fully human monoclonal antibody that selectively targets the p19 subunit of interleukin-23 (IL-23). It has been approved for the treatment of adults with moderate-to-severe plaque psoriasis in several

countries. The standard dose is 100 mg by subcutaneous injection at weeks 0 and 4, then every 12 weeks thereafter, although a 200 mg dosage at the same interval does have approval in some jurisdictions.[1,2]

The aim of this article is to review the available evidence for tildrakizumab in treating moderate-to-severe chronic plaque psoriasis. In-depth discussion will be limited to pivotal studies and post hoc analyses.

Pivotal Studies

In the pivotal phase 2b study, tildrakizumab was compared to placebo.[3] This was a three-part, double-blind, randomized controlled trial. The primary endpoint was PASI 75 at week 16, while key secondary endpoints included PASI 75 at weeks 12 and 52, PASI 90 at week 16, PGA response at weeks 16 and 52, time to PASI 75, and mean change in DLQI at week 16. Safety was assessed in the all-participants-as-treated population.

A total of 355 subjects were randomized (1:2:2:2:1) to tildrakizumab 5 mg (n=42), tildrakizumab 25 mg (n=92), tildrakizumab 100 mg (n=89), tildrakizumab 200 mg (n=86), and placebo (n=46).[3] At week 16, tildrakizumab 5 mg, tildrakizumab 25 mg, tildrakizumab 100 mg, and tildrakizumab 200 mg were superior to placebo for PASI 75 (33%, 64%, 66%, and 74%, respectively, versus 4%; p≤0.001) and PGA 0/1 (33%, 58%, 62%, and 74%, respectively, versus 2%; p<0.001). At week 16, tildrakizumab 25 mg, tildrakizumab 100 mg, and tildrakizumab 200 mg were also superior to placebo for PASI 90 (25%, 39%, and 52%, respectively, versus 2%; p<0.001). In addition, the proportion of subjects achieving PASI 75 at week 12 was significantly greater (p≤0.001) for tildrakizumab 5 mg (24%), tildrakizumab 25 mg (59%), tildrakizumab 100 mg (61%), and tildrakizumab 200 mg (72%) compared with placebo (4%). The median time to PASI 75 in subjects receiving tildrakizumab was 85 days (25 mg), 84 days (100 mg), and 57 days (200 mg). Improvements in DLQI were noted for all tildrakizumab treatment groups compared with placebo. For PASI 75 responders at week 16, over 90% of these subjects continuing to receive doses of either 100 mg or 200 mg of tildrakizumab maintained PASI 75 through week 52. Furthermore, 96% and 93% of subjects receiving doses of 100 mg and 200 mg of tildrakizumab, respectively, maintained PASI 75 at week 72 following treatment discontinuation at week 52, with only 4% (8/222) of the PASI 75 responders at week 52 experiencing relapse.

With respect to safety, the most common adverse events (AEs) were nasopharyngitis and headache.[3] The frequency of serious AEs was low. One patient receiving tildrakizumab 100 mg died. This individual had a history of alcohol abuse. Adjudication was unable to determine the cause of death. AEs of special interest, such as severe infections, malignancies, and major adverse cardiac events (MACE), were rare.

In the two pivotal phase 3 studies (reSURFACE 1 and reSURFACE 2), tildrakizumab was compared to placebo and etanercept.[4] These were parallel group, double-blind, randomized controlled trials. Each had three parts. For both reSURFACE 1 and reSURFACE 2, the co-primary endpoints were PASI 75 and PGA response (score of 0 or 1 with ≥2 grade score reduction from baseline) at week 12, while key secondary endpoints included PASI 90, PASI 100, and DLQI 0/1 at week 12. For reSURFACE 2, PASI 75, PGA response, and DLQI 0/1 at week 28 were also key secondary endpoints. Safety was assessed in the all-participants-as-treated population.

In reSURFACE 1 (n=772), subjects were randomized (2:2:1) to tildrakizumab 200 mg (n=308), tildrakizumab 100 mg (n=309), or placebo (n=155).[4] At week 12, tildrakizumab 200 mg and tildrakizumab 100 mg were superior to placebo (p<0.0001) for PASI 75 (62% and 64%, respectively, versus 6%), PASI 90 (35% and 35%, respectively, versus 3%), PASI 100 (14% and 14%, respectively, versus 1%), PGA response (59% and 58%, respectively, versus 7%), and DLQI 0/1 (44% and 42%, respectively, versus 5%). In reSURFACE 2 (n=1090), subjects were randomized (2:2:1:2) to tildrakizumab 200 mg (n=314), tildrakizumab 100 mg (n=307), placebo (n=156), or etanercept 50 mg twice weekly (n=313). At week 12, tildrakizumab 200 mg and tildrakizumab 100 mg were superior to placebo and etanercept for PASI 75 (66% and 61%, respectively, versus 6% and 48%, respectively; p<0.0001 for both tildrakizumab groups versus placebo; p<0.0001 for tildrakizumab 200 mg versus etanercept; p=0.0010 for tildrakizumab 100 mg versus etanercept). In addition, tildrakizumab 200 mg was superior to placebo and etanercept for PGA response (59% versus 4% and 48%, respectively; p<0.0001 for tildrakizumab 200 mg versus placebo; p=0.0031 for tildrakizumab 200 mg versus etanercept), while tildrakizumab 100 mg was superior to placebo,

but not significantly different than etanercept, for PGA response (55% versus 4% and 48%, respectively; p<0.0001 for tildrakizumab 100 mg versus placebo; p=0.0663 for tildrakizumab 100 mg versus etanercept). In both studies, a higher proportion of subjects achieved PASI 75, PASI 90, PASI 100, PGA response, and DLQI 0/1 with both doses of tildrakizumab at week 28 compared to week 12. Additionally, subjects initially assigned to placebo but subsequently re-randomized to receive either dose of tildrakizumab improved from week 12 to week 28 and had similar levels of response to those receiving either dose of tildrakizumab continuously from baseline **(Figure 1 and 2).**

With respect to safety, the most common AE in both reSURFACE 1 and reSURFACE 2 was nasopharyngitis.[4] The frequency of serious AEs was low and similar across treatment groups. One patient receiving tildrakizumab 100 mg died in reSURFACE 2. This individual had alcoholic cardiomyopathy and steatohepatitis. Adjudication was unable to determine the cause of death. For AEs of special interest, such as severe infections, malignancies, and MACE, no significant differences were noted between the treatment groups.

A long-term extension of the pivotal phase 3 studies (reSURFACE 1 and reSURFACE 2) evaluated efficacy and safety of both tildrakizumab doses at week 148.[5] Efficacy was assessed for responders (PASI ≥75) and partial responders (PASI =50 to <75) to tildrakizumab 200 mg and tildrakizumab 100 mg at week 28. Responders were subsequently maintained on the same dose of tildrakizumab (every 12 weeks) while partial responders either stayed on the same dose of 200 mg tildrakizumab or were titrated to 200 mg tildrakizumab if they had been initiated on the 100 mg dose. Efficacy was also assessed for partial responders and non-responders (PASI <50) to etanercept 50 mg at week 28 who were subsequently (after 4-week washout) switched to tildrakizumab 200 mg (at weeks 32 and 36, then every 12 weeks). Safety was assessed in the all- patients-as-treated population.

	Tildrakizumab 200 mg (n=308)	Tildrakizumab 100 mg (n=309)	Placebo (n=154)
PASI 75	**62%**	**64%**	**6%**
% difference from placebo (95% CI; p value)	56.6% (49.6-62.8; p<0.0001)	58.0% (51.0-64.1; p<0.0001)	N/A
Clear or minimal PGA	**59%**	**58%**	**7%**
% difference from placebo (95% CI; p value)	52.1% (44.8-58.5; p<0.0001)	50.9% (43.6-57.4; p<0.0001)	N/A
PASI 90	**35%**	**35%**	**3%**
% difference from placebo (95% CI; p value)	32.9% (26.8-38.8; p<0.0001)	32.1% (25.9-38.0; p<0.0001)	N/A
PASI 100	**14%**	**14%**	**1%**
% difference from placebo (95% CI; p value)	12.7% (8.3-17.2; p<0.0001)	12.7% (8.0-17.3; p<0.0001)	N/A
DLQI score 0 or 1	**44%**	**42%**	**5%**
% difference from placebo (95% CI; p value)	38.9% (31.9-45.4; p<0.0001)	36.1% (26.3-42.5; p<0.0001)	N/A

The full analysis set population included all randomly assigned patients who received at least one dose of study medication. % differences and 95% CIs were calculated with the Miettinen-Nurminen method and stratified by bodyweight (≤90 kg vs >90 kg) and previous exposure to biologic therapy for psoriasis (yes or no) with sample size weights. p values were calculated with the Cochran-Mantel-Haenszel and stratified by bodyweight and exposure to biologic therapies; p values were not adjusted for multiplicity. Non-responder imputation was pre-specified and is shown for all data, except for DLQI, which were observed data. PASI=Psoriasis Area and Severity Index. N/A=not applicable. PGA=Physician's Global Assessment. DLQI=Dermatology Life Quality Index.

Figure 1. Primary and secondary efficacy endpoints at 12 weeks in reSURFACE 1 part 1 (full analysis set); adapted from Reich et al, 2020

Using the non-responder imputation (NRI) method to account for missing efficacy data, PASI 75, PASI 90, and PASI 100 responses at week 148 were: 80%, 60%, and 33%, respectively, for responders to tildrakizumab 200 mg; 73%, 54%, and 29%, respectively, for responders to tildrakizumab 100 mg; 47%, 28%, and 13%, respectively, for partial responders to tildrakizumab 200 mg; 33%, 25%, and 10%, respectively, for partial responders to tildrakizumab 100 mg; and 67%, 44%, and 15%, respectively, for partial responders or non-responders to etanercept 50 mg.[5] With respect to safety, rates of discontinuation due to AEs and exposure-adjusted serious AEs, such as severe infections, malignancies, and MACE, were low and comparable across all treatment groups, although severe infection rates tended to be higher

	Tildrakizumab 200 mg (n=314)	Tildrakizumab 100 mg (n=307)	Placebo (n=156)	Etanercept (n=313)
PASI 75	**66%**	**61%**	**6%**	**48%**
% difference from placebo (95% CI; p value)	59.8% (52.9 to 65.9; p<0.0001)	55.5% (48.3 to 61.8; p<0.0001)	N/A	N/A
% difference from etanercept (95% CI; p value)	17.4% (9.7 to 24.9; p<0.0001)	13.1 (5.3 to 20.7; p=0.001)	N/A	N/A
Clear or minimal PGA	**59%**	**55%**	**4%**	**48%**
% difference from placebo (95% CI; p value)	54.7 (47.9 to 60.8; p<0.0001)	50.2 (43.2 to 56.5; p<0.0001)	N/A	N/A
% difference from etanercept (95% CI; p value)	11.7 (4.0 to 19.3; p=0.0031)	7.3 (-0.5 to 15.0; p=0.0663)	N/A	N/A
PASI 90	**37%**	**39%**	**1%**	**21%**
% difference from placebo (95% CI; p value)	35.3% (29.2 to 41.1; p<0.0001)	37.5% (31.1 to 43.4; p<0.0001)	N/A	N/A
% difference from etanercept (95% CI; p value)	15.2% (8.3 to 22.1; p<0.0001)	17.4% (10.3 to 24.4; p<0.0001)	N/A	N/A
PASI 100	**12%**	**12%**	**0**	**5%**
% difference from placebo (95% CI; p value)	11.7% (7.8 to 16.0; p<0.0001)	12.4% (8.5 to 16.6; p<0.0001)	N/A	N/A
% difference from etanercept (95% CI; p value)	7.0% (2.8 to 11.6; p=0.0014)	7.6% (3.3 to 12.3; p=0.0006)	N/A	N/A
DLQI	**47%**	**40%**	**8%**	**36%**
% difference from placebo (95% CI; p value)	39.3% (31.8 to 46.1; p<0.0001)	32.1% (24.5 to 39.1; p<0.0001)	N/A	N/A
% difference from etanercept (95% CI; p value)	11.9% (4.1 to 19.5; p=0.0029)	4.8% (-2.9 to 12.5; p=0.2206)	N/A	N/A

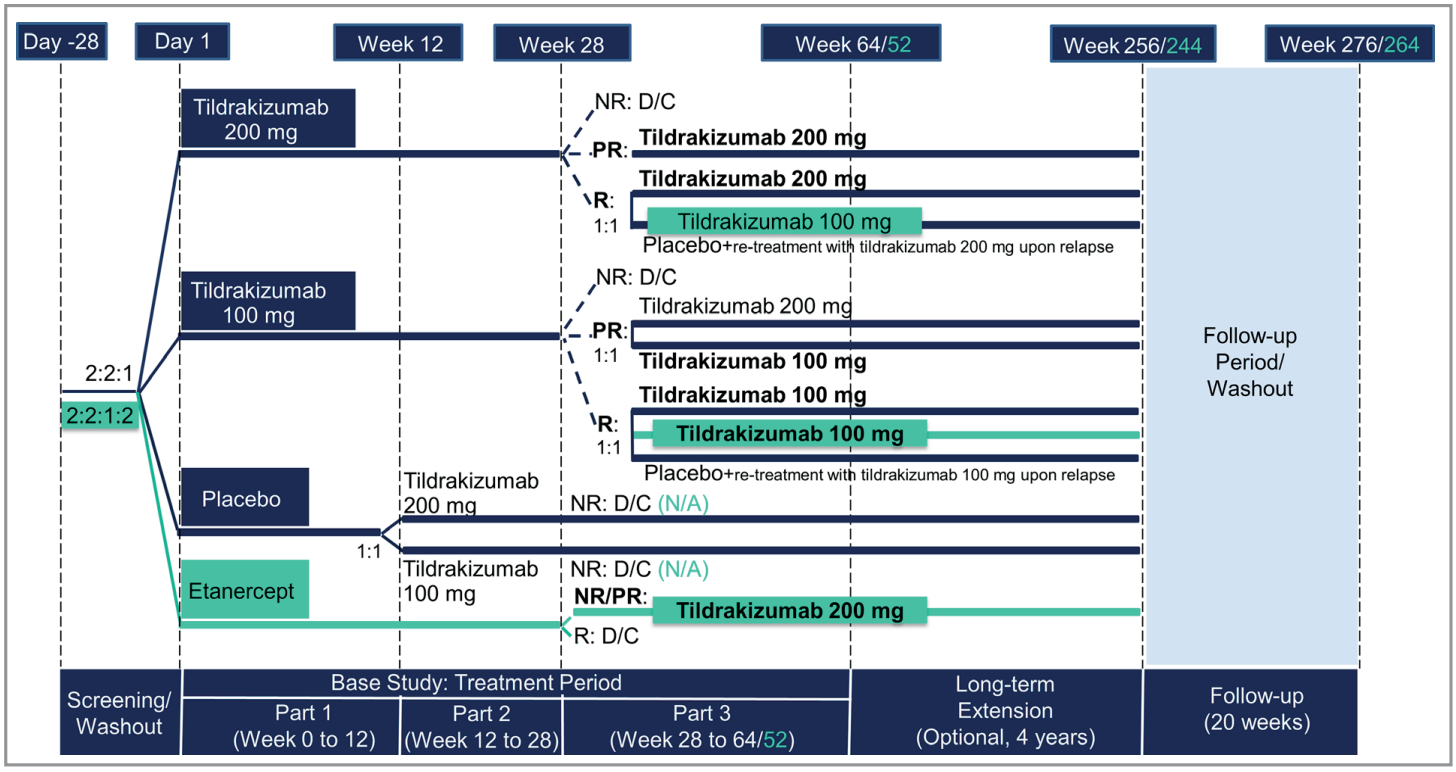
The full analysis set population included all randomly assigned patients who received at least one dose of study medication. % differences and 95% CIs were calculated with the Miettinen-Nurminen method and stratified by bodyweight (≤90 kg vs >90 kg) and previous exposure to biologic therapy for psoriasis (yes or no) with sample size weights. p values were calculated with the Cochran-Mantel-Haenszel (CMH) and stratified by bodyweight and exposure to biologic therapies; p values were not adjusted for multiplicity. Non-responder imputation was pre-specified and is shown for all data, except for DLQI, for which were observed data are shown. PASI=Psoriasis Area and Severity Index. N/A=not applicable. PGA=Physician's Global Assessment. DLQI=Dermatology Life Quality Index.

Figure 2. Primary and secondary efficacy endpoints at 12 weeks in reSURFACE 2 part 1 (full analysis set); adapted from Reich et al, 2020

for etanercept 50 mg. A total of nine deaths occurred during the 148-week study period—none were deemed related to the medication by the investigators.

Post Hoc Analyses

In a post hoc analysis of the efficacy data from the combined pivotal phase 2 and 3 studies (n=2081), it was found that tildrakizumab 200 mg (n=708) and tildrakizumab 100 mg (n=705) were superior to placebo (n=355) at week 12 (p<0.0001) for PASI 75 (65% and 62%, respectively, versus 6%), PASI 90 (37% and 36%, respectively, versus 2%), PASI 100 (13% and 13%, respectively, versus 1%), and PGA 0/1 (60% and 57%, respectively, versus 6%).[6] Responses to tildrakizumab 200 mg (n=581) and tildrakizumab 100 mg (n=575) increased from week 12 to week 28 for PASI 75 (78% and 77%, respectively), PASI 90 (58% and 54%, respectively), PASI 100 (29% and 23%, respectively), and PGA 0/1 (70% and 66%, respectively). In the same publication, results of additional subgroup analyses were also reported.[6] The efficacy of tildrakizumab was greater in subjects with lower baseline weight versus higher baseline weight at week 12. Additionally, responses to tildrakizumab were numerically higher with the 200 mg dose compared to the 100 mg dose in those with higher baseline weight at week 12. The difference in proportion of subjects achieving PASI 75, PASI 90, PASI 100, and PGA 0/1 at week 12 with either dose of tildrakizumab was significant compared with placebo across the weight cut-offs that were investigated. The efficacy of tildrakizumab was also typically numerically greater in biologic-naïve versus biologic-experienced subjects but the difference was not statistically significant. Although PASI 75 responses with either dose of tildrakizumab versus placebo were similar in both populations, compared to those with prior biologic exposure, the PASI 90, PASI 100, and PGA 0/1 responses were generally higher in subjects without prior biologic exposure—the exception being that PASI 100 responses were similar for the 200 mg dose in biologic-naïve and biologic-experienced subjects. Lastly, baseline PASI, PGA, and BMI were not found to be predictive of PASI 90 response to tildrakizumab at weeks 12 and 28, while achievement of PASI ≥50 by week 8 with tildrakizumab was predictive of PASI ≥90 at weeks 12 and 28.



Integrated design of the reSURFACE 1 and reSURFACE 2 trials. Differences in design for reSURFACE 2 vs. reSURFACE 1 are shown in turquoise colour. Groups of interest for efficacy analyses are marked in bold. D/C, discontinued; N/A, not applicable; NR, nonresponders [< 50% improvement in Psoriasis Area and Severity Index PASI <50]; PR, partial responders PASI ≥ 50 to < 75); R, responders (PASI ≥ 75); adapted from Reich et al, 2020

Another post hoc analysis of the pivotal phase 3 studies evaluated the impact of body weight on the efficacy of tildrakizumab.[7] Data were stratified by weight deciles. At week 12, a slightly greater median percentage improvement in PASI was observed in the lower weight deciles: 87.4%, 86.6%, 83.6%, 88.9%, 81.5%, 84.3%, 83.1%, 78.0%, 76.7%, and 77.5% (lowest to highest decile). However, by week 28, these differences had narrowed: 91.6%, 91.9%, 92.6%, 90.4%, 91.1%, 90.6%, 91.2%, 87.7%, 87.0%, and 86.0% (lowest to highest decile). Treatment responses were subsequently maintained across all weight deciles: 100%, 96.9%, 96.9%, 96.6%, 96.6%, 97.2%, 95.3%, 93.4%, 93.5%, and 90.8% (lowest to highest decile).

In a post hoc analysis of the efficacy data from the pivotal phase 3 studies (n=1862), different treatment scenarios, such as continuous long-term dosing of tildrakizumab, interruption/reinitiation of tildrakizumab, dose adjustment of tildrakizumab, and switching from etanercept to tildrakizumab, were investigated.[8] For week 28 partial responders (PASI ≥50 to <75) receiving the same dosage of either 100 mg or 200 mg tildrakizumab from baseline to the end of study, continuous long-term dosing allowed a greater proportion of subjects to become responders (PASI ≥75) over time. In addition, among subjects experiencing a relapse following withdrawal of either 100 mg or 200 mg tildrakizumab (defined as a 50% reduction in the maximum PASI response), reinitiation resulted in 86% (tildrakizumab 100 mg) and 83% (tildrakizumab 200 mg) achieving PASI 75 by week 64, usually within 12 weeks of re-instituting therapy. Furthermore, PASI 75 responses to tildrakizumab increased for week 28 partial responders when the dose was subsequently adjusted from 100 mg to 200 mg, but remained consistent for week 28 responders when the dose was subsequently adjusted from 200 mg to 100 mg. Lastly, for subjects receiving 50 mg etanercept from baseline who were classified as partial responders or non-responders (PASI <50) at week 28, switching to tildrakizumab 200 mg allowed a greater proportion of subjects to become responders (PASI ≥75) over time. In all four of the above treatment scenarios, the PASI 90, PASI 100, and PGA 0/1 responses were generally consistent with the PASI 75 results.

In another post hoc analysis of the efficacy data from the pivotal phase 3 studies, patient-level PASI score distributions were used to investigate how disease activity varied across the study population before and after treatment with tildrakizumab 100 mg (n=616) and placebo (n=309).[9] Median baseline PASI was 17.9 for subjects receiving tildrakizumab 100 mg.

At week 12, median PASI was 2.9, with a dichotomous PASI 90 response rate of 37%, while 64%, 51%, and 23% achieved absolute PASI <5.0, <3.0, and <1.0, respectively. At week 28, median PASI was 1.7, with a dichotomous PASI 90 response rate of 52%, while 75%, 63%, and 38% achieved absolute PASI <5.0, <3.0, and <1.0, respectively. DLQI and PASI scores were correlated through week 28 (r=0.51, p≤0.0001). This study showed that post-treatment disease activity was more reliably estimated by absolute PASI scores compared to percentage PASI improvement, which may partially explain disparities between clinical trial efficacy and real-world effectiveness.

Several other post hoc analyses have been performed. These found that treatment with tildrakizumab resulted in rapid and progressive improvement of scalp, face, and neck involvement as evidenced by decreases in PASI scores[10]; pre-existing metabolic syndrome did not alter the efficacy, safety, and drug survival of tildrakizumab[11]; tildrakizumab was well-tolerated with low rates of serious AEs, discontinuations due to AEs, and AEs of special interest[12]; tildrakizumab did not have any additional risk of candidiasis[12], inflammatory bowel disease[12,13], MACE[12,14], malignancy[12], or suicide[12]; injection-site reactions with tildrakizumab were infrequent (tildrakizumab 200 mg: 4%; tildrakizumab 100 mg: 3%)[12]; exposure to tildrakizumab was not associated with new safety signals concerning increased rates of spontaneous abortions or birth defects/anomalies.[15]

Conclusion

Tildrakizumab has sustained efficacy, convenient dosing, and favorable safety profile. Improvements in quality of life have also been observed. Robust clinical trial data supports use of this IL-23 inhibitor for treating moderate-to-severe plaque psoriasis in adults.

References:

1. Tildrakizumab (Ilumya) Product Monograph. US FDA.

2. Tildrakizumab (Ilumya) Product Monograph. EMA.

3. Papp K, Thaci D, Reich K, et al. Tildrakizumab (MK-3222), an anti-interleukin-23p19 monoclonal antibody, improves psoriasis in a phase IIb randomized placebo-controlled trial. Br J Dermatol. 2015;173(4):930-939.

4. Reich K, Papp KA, Blauvelt A, et al. Tildrakizumab versus placebo or etanercept for chronic plaque psoriasis (reSURFACE 1 and reSURFACE 2): results from two randomised controlled, phase 3 trials. Lancet. 2017;390(10091):276-288.

5. Reich K, Warren RB, Iversen L, et al. Long-term efficacy and safety of tildrakizumab for moderate-to-severe psoriasis: pooled analyses of two randomized phase III clinical trials (reSURFACE 1 and reSURFACE 2) through 148 weeks. Br J Dermatol. 2020;182(3):605-617.

6. Papp KA, Reich K, Blauvelt A, et al. Efficacy of tildrakizumab for moderate-to-severe plaque psoriasis: pooled analysis of three randomized controlled trials at weeks 12 and 28. J Eur Acad Dermatol Venereol. 2019;33(6):1098-1106.

7. Menter A, Draelos Z, Heim J, Parno J, Mendelsohn A, Rozzo S, Griffiths C. Impact of Body Weight on Efficacy of Tildrakizumab in Moderate-to-Severe Plaque Psoriasis [abstract]. Arthritis Rheumatol. 2019; 71 (suppl 10). https://acrabstracts.org/abstract/impact-of-body-weight-on-efficacy-of-tildrakizumab-in-moderate-to-severe-plaque-psoriasis/. Accessed September 12, 2020.

8. Kimball AB, Papp KA, Reich K, et al. Efficacy and safety of tildrakizumab for plaque psoriasis with continuous dosing, treatment interruption, dose adjustments and switching from etanercept: results from phase III studies. Br J Dermatol. 2020;182(6):1359-1368.

9. Gordon KB, Reich K, Crowley JJ, et al. Disease activity and treatment efficacy using patient-level Psoriasis Area and Severity Index scores from tildrakizumab phase 3 clinical trials. J Dermatol Treat. 2020; Online ahead of print.

10. Menter MA, Murakawa GJ, Glover H, et al. Clearance of head and neck involvement in plaque psoriasis with tildrakizumab treatment in the phase 3 reSURFACE 1 study. J Eur Acad Dermatol Venereol. 2020. Online ahead of print.

11. Lebwohl MG, Leonardi CL, Mehta NN, et al. Tildrakizumab efficacy and safety are not altered by metabolic syndrome status in patients with psoriasis: Post hoc analysis of 2 phase 3 randomized controlled studies (reSURFACE 1 and reSURFACE 2). J Am Acad Dermatol. 2020;82(2):519-522.

12. Blauvelt A, Reich K, Papp KA, et al. Safety of tildrakizumab for moderate-to-severe plaque psoriasis: pooled analysis of three randomised controlled trials. Br J Dermatol. 2018;179(3):615-622.

13. Gooderham M, Elewski BE, Pariser DM, et al. Incidence of serious gastrointestinal events among tildrakizumab-treated patients with psoriasis: letter to the editor. J Eur Acad Dermatol Venereol. 2019;33(10):e350-e352.

14. Bissonnette R, Fernandez-Penas P, Puig L, et al. Incidence of cardiovascular events among tildrakizumab-treated patients with moderate-to-severe plaque psoriasis: pooled data from three large randomised clinical trials. J Eur Acad Dermatol Venereol. 2020;34(1):e21-e24.

15. Haycraft K, DiRuggiero D, Rozzo SJ, Mendelsohn AM, Bhutani T. Outcomes of pregnancies from the tildrakizumab phase I-III clinical development programme. Br J Dermatol. 2020;183(1):184-186.