TALTZ® (ixekizumab): Maintenance of Response in Plaque Psoriasis

All 3 pivotal UNCOVER psoriasis clinical trials evaluated long-term efficacy of ixekizumab for up to a total of 5 years in patients who participated through the entire studies.[1,2]

UNCOVER-1 AND -2: EFFICACY THROUGH WEEK 60

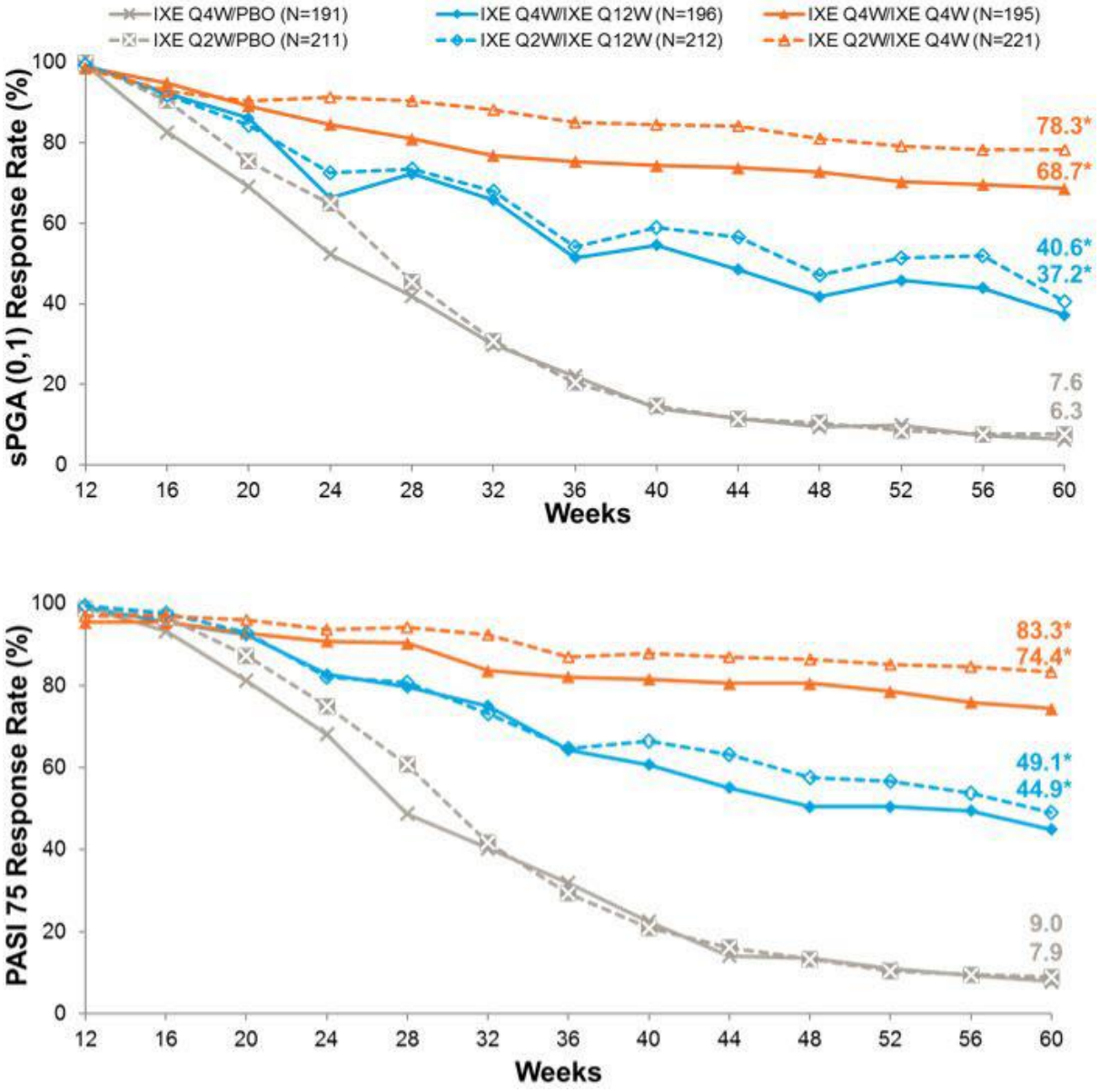
In UNCOVER-1 and -2, responders (ixekizumab-treated patients who achieved sPGA 0 or 1) at week 12 were rerandomized to ixekizumab 80 mg Q4W, ixekizumab 80 mg Q12W, or placebo (randomized withdrawal) through week 60.[1] Appendix: UNCOVER Study Designs provides brief descriptions of the UNCOVER clinical trials.

Figure 1 shows maintenance of response during the randomized withdrawal period (weeks 12-60) for week 12 responders (sPGA 0 or 1). These analyses were conducted using the NRI method.

For ixekizumab Q2W-treated week 12 responders (sPGA 0 or 1), 78.3% of those rerandomized to Q4W maintained that response [sPGA (0,1)] at week 60 with no occurrences of sPGA ≥3 at any visit between weeks 12 and 60. Additionally, at week 60, the percentage of patients treated with the recommended dosing of ixekizumab (ixekizumab 80 mg Q2W for the first 12 weeks, followed by ixekizumab 80 mg Q4W thereafter), attained or maintained

- PASI 75 was 83.3%
- PASI 90 was 76.5%, and
- PASI 100 was 57.5%.[1]

Figure 1. UNCOVER-1 and -2 Week 12 Responders: sPGA (0,1) and PASI 75 Response by Treatment Week During Randomized Withdrawal Period, Primary Maintenance Population, NRI[1]



Abbreviations: IXE Q2W = ixekizumab every 2 weeks; IXE Q4W = ixekizumab every 4 weeks; NRI = nonresponder imputation; PASI 75 = 75% improvement from baseline in Psoriasis Area and Severity Index; PBO = placebo; sPGA = static Physician Global Assessment.

* p<.001 vs PBO.

UNCOVER-1 AND -2: EFFICACY THROUGH WEEK 264

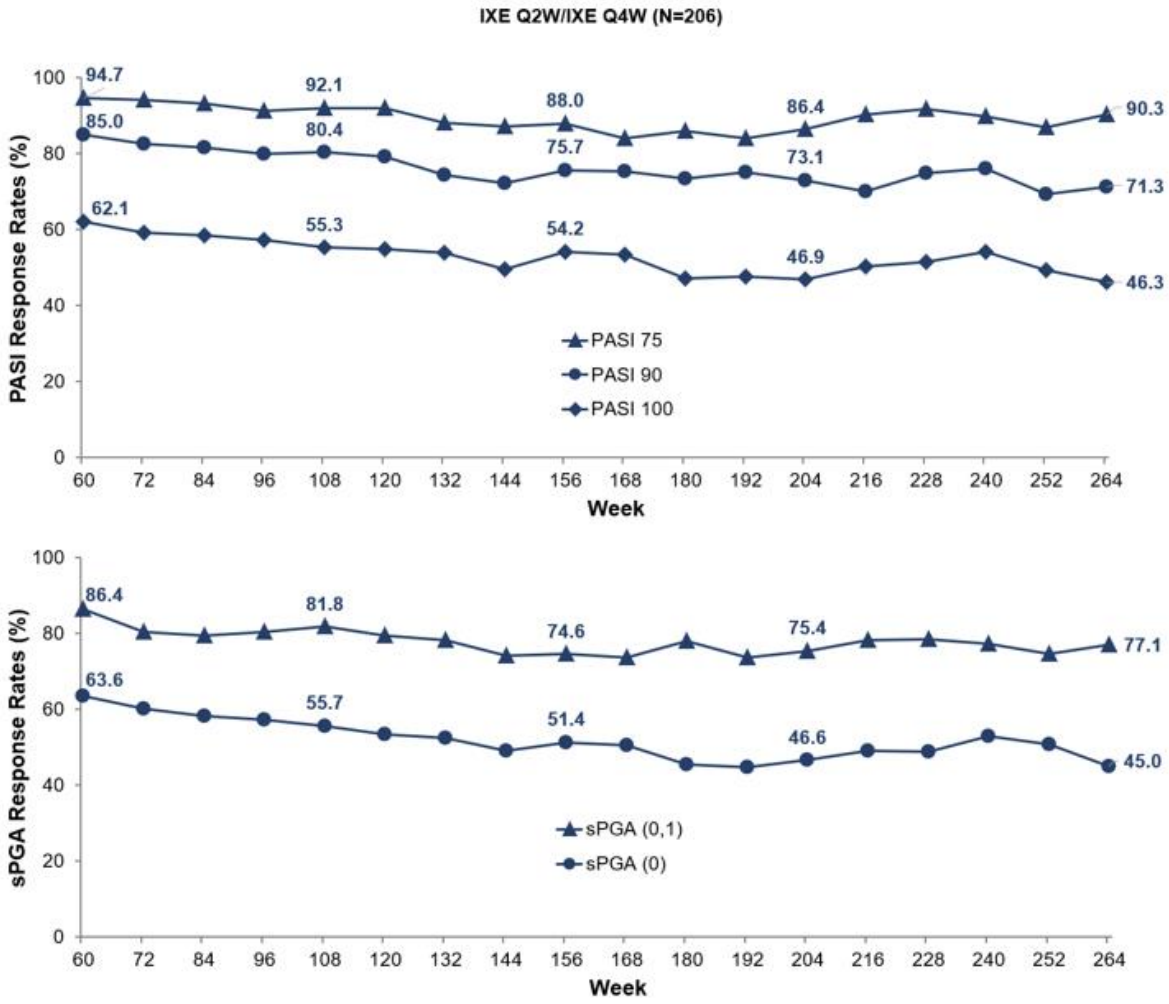
Figure 2 illustrates PASI and sPGA response rates in UNCOVER-1 and -2 through 264 weeks of treatment for patients receiving the recommended ixekizumab dosing regimen for moderate-to-severe plaque psoriasis. For the modified NRI method, missing data were considered

nonresponders if patients discontinued treatment because of lack of efficacy, inadequate response, or AEs and imputed using multiple imputation in all other cases.[3]

Through 5 years of treatment in UNCOVER-1 and -2, the authors concluded that

- high-efficacy responses with the ixekizumab-approved dosing regimen were maintained with long-term treatment in patients with moderate-to-severe plaque psoriasis, and
- the safety profile of ixekizumab remained consistent with previous data.[3]

Figure 2. UNCOVER-1 and -2: Ixekizumab PASI and sPGA Response Rates Through 5 Years of Treatment, Approved Dosing Regimen Population, mNRI[3]



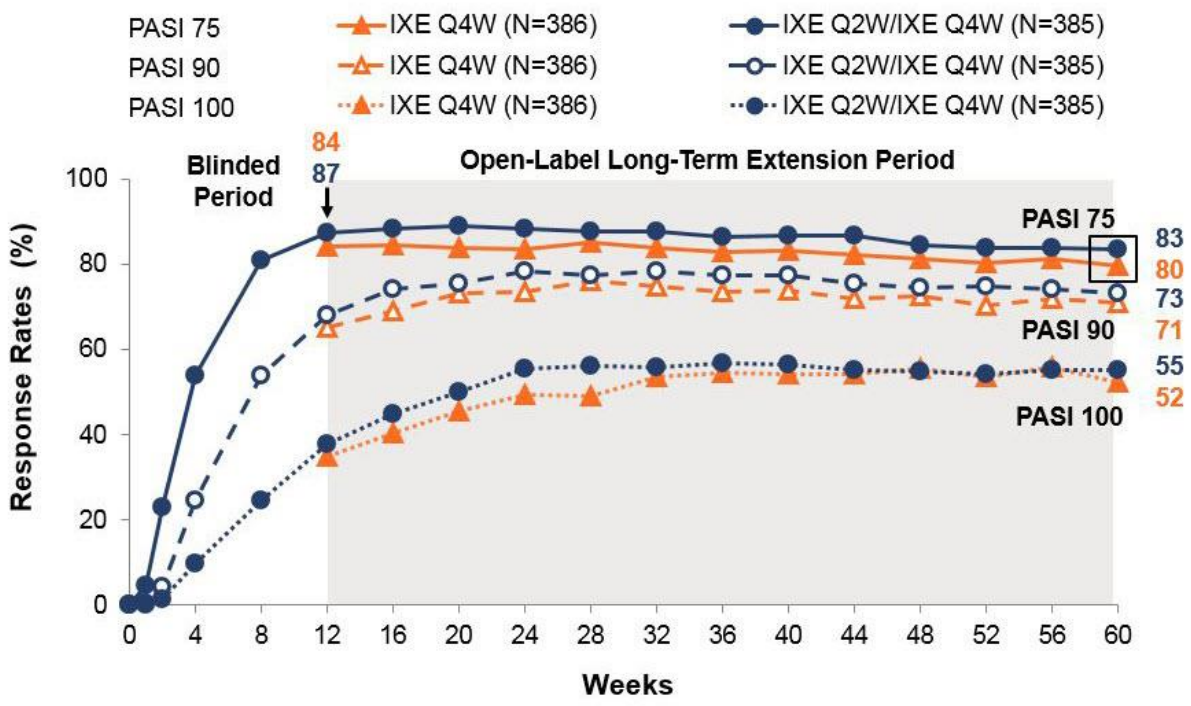
Abbreviations: IXE Q2W = ixekizumab every 2 weeks; IXE Q4W = ixekizumab every 4 weeks; mNRI = modified nonresponder imputation; PASI = Psoriasis Area and Severity Index; PASI 75 = 75% improvement from baseline in Psoriasis Area and Severity Index; PASI 90 = 90% improvement from baseline in Psoriasis Area and Severity Index; PASI 100 = 100% improvement from baseline in Psoriasis Area and Severity Index; sPGA = static Physician Global Assessment.

UNCOVER-3: Efficacy Through Week 60

In UNCOVER-3, patients who completed the 12-week randomized induction period were able to continue to the open-label, long-term extension and received ixekizumab Q4W from weeks 12 to 60.[1] The long-term extension period lasted up to week 264. Appendix: UNCOVER Study Designs provides brief descriptions of the UNCOVER clinical trials.

High rates of response observed at week 12 were generally maintained over the long-term extension period to week 60 (Figure 3). At week 60, among patients treated with the recommended dosing of ixekizumab Q2W for the first 12 weeks, followed by Q4W thereafter, 75% attained or maintained sPGA (0,1).[1]

Figure 3. UNCOVER-3: PASI Responses by Treatment Week, ITT Population, NRI[1]



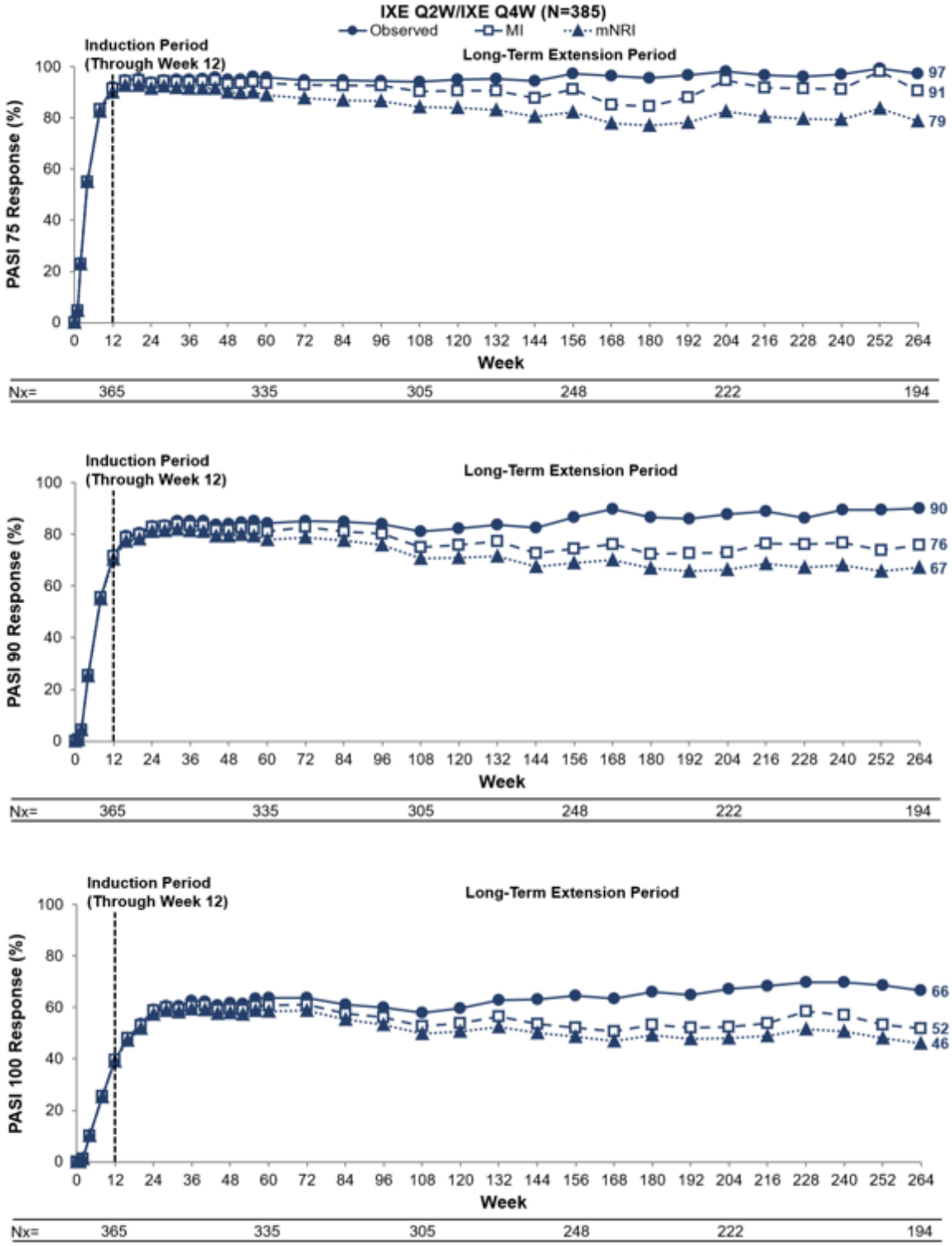
Abbreviations: ITT = intent to treat; IXE Q2W = ixekizumab every 2 weeks; IXE Q4W = ixekizumab every 4 weeks; NRI = nonresponder imputation; PASI = Psoriasis Area and Severity Index; PASI 75 = 75% improvement from baseline in Psoriasis Area and Severity Index; PASI 90 = 90% improvement from baseline in Psoriasis Area and Severity Index; PASI 100 = 100% improvement from baseline in Psoriasis Area and Severity Index.

UNCOVER-3: Efficacy Through Week 264

UNCOVER-3 efficacy and safety data through 108 weeks, 156 weeks, and 204 weeks have been previously reported.[4-6] Figure 4 presents the UNCOVER-3 PASI response rates through 264 weeks for patients receiving the approved ixekizumab dosing regimen. Missing data were imputed using multiple imputation, where the missing data were handled by estimating what the observations would have been if the patient continued with the hypothetical treatment, and the modified NRI method, where missing data were considered nonresponders if patients discontinued treatment because of AEs, lack of efficacy, or relapse and imputed using multiple imputation in all other cases.[7]

Through 5 years of treatment in UNCOVER-3, the authors concluded that ixekizumab demonstrated sustained efficacy and a consistent safety profile in patients receiving the approved dosing regimen.[7]

Figure 4. UNCOVER-3: PASI 75, PASI 90, and PASI 100 Response Rates Through Week 264, Approved Dosing Regimen Population, Observed Data, MI, and mNRI[7,8]



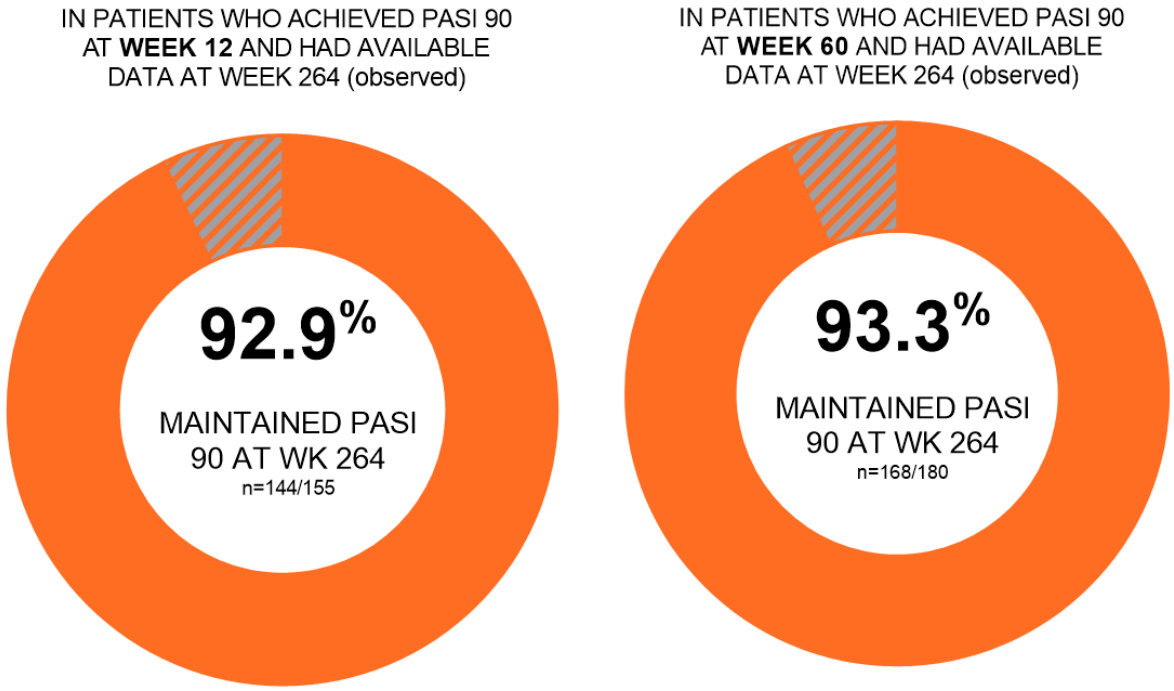
Abbreviations: IXE = ixekizumab; MI = multiple imputation; mNRI = modified nonresponder imputation; PASI 75 = 75% improvement from baseline in Psoriasis Area and Severity Index; PASI 90 = 90% improvement from baseline in Psoriasis Area and Severity Index; PASI 100 = 100% improvement from baseline in Psoriasis Area and Severity Index; Q2W = every 2 weeks; Q4W = every 4 weeks.

UNCOVER-3: Week 264 Efficacy in Patients With PASI 90 Response at Week 12 and Week 60

An analysis was conducted to assess if achievement of PASI 90 at an early timepoint (week 12) and a mid-term timepoint (week 60) correlated with a long-term PASI 90 response (week 264) in patients who received the approved ixekizumab dosing regimen for moderate-to-severe psoriasis in the UNCOVER-3 trial .[9]

As shown in Figure 5, patients treated with the approved ixekizumab dosing regimen who achieved PASI 90 at early (week 12) and mid (week 60) time points showed a sustained high level of response for PASI 90 at week 264.[9]

Figure 5. UNCOVER-3: PASI 90 Response Rate at Week 264 in Patients Who Achieved PASI 90 at Week 12 or Week 60, Approved Ixekizumab Dosing Regimen, Observed Data[9]



Abbreviations: PASI 90 = 90% improvement from baseline in Psoriasis Area and Severity Index; WK = week.

Last Reviewed: 16-June-2021

Enclosed Prescribing Information

TALTZ® (ixekizumab) injection, for subcutaneous administration, Lilly

REFERENCES

The published references below are available by contacting 1-800-LillyRx (1-800-545-5979).

1. Gordon KB, Blauvelt A, Papp KA, et al; UNCOVER-1, UNCOVER-2, and UNCOVER-3 Study Groups. Phase 3 trials of ixekizumab in moderate-to-severe plaque psoriasis. *N Engl J Med.* 2016;375(4):345-356. http://dx.doi.org/10.1056/NEJMoa1512711

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3. Leonardi C, Reich K, Foley P, et al. Efficacy and safety of ixekizumab through 5 years in moderate-to-severe psoriasis: long-term results from the UNCOVER-1 and UNCOVER-2 phase-3 randomized controlled trials. *Dermatol Ther (Heidelb).* 2020;10(3):431-447. http://dx.doi.org/10.1007/s13555-020-00367-x

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8. Data on file, Eli Lilly and Company and/or one of its subsidiaries.

9. Rosmarin D, Guenther L, Gallo G, et al. Long-term response for ixekizumab is demonstrated through five years for early- and mid-term responders for patients with moderate-to-severe psoriasis. Poster presented at: International Federation of Psoriasis Associations Virtual Congress; June 30-July 3, 2021.

GLOSSARY

AE = adverse event

NRI = nonresponder imputation

PASI = Psoriasis Area and Severity Index

PASI 75 = 75% improvement from baseline in Psoriasis Area and Severity Index

PASI 90 = 90% improvement from baseline in Psoriasis Area and Severity Index

PASI 100 = 100% improvement from baseline in Psoriasis Area and Severity Index

Q2W = every 2 weeks

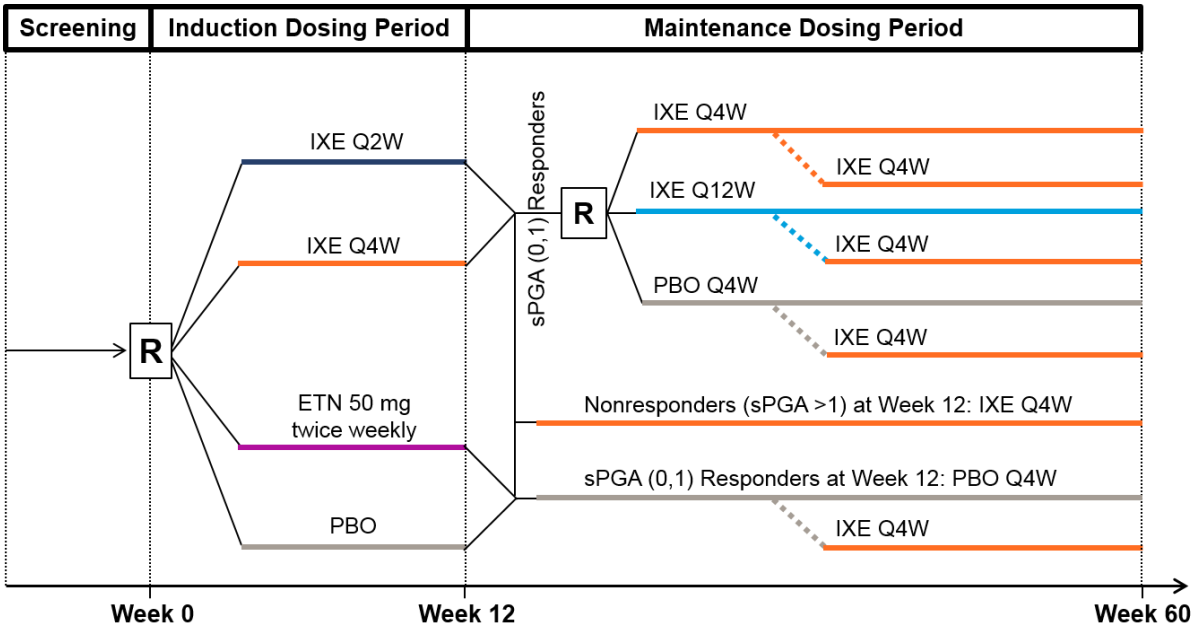
Q4W = every 4 weeks

Q12W = every 12 weeks

sPGA = static Physician Global Assessment

APPENDIX: UNCOVER STUDY DESIGNS

Figure 6. Study Design of Induction (UNCOVER-1, -2, and -3) and Maintenance (UNCOVER-1 and -2) Dosing Periods[1]



Abbreviations: ETN = etanercept; IXE Q2W = ixekizumab 80 mg every 2 weeks; IXE Q4W = ixekizumab 80 mg every 4 weeks; IXE Q12W = ixekizumab 80 mg every 12 weeks; PBO = placebo; R = randomization; sPGA = static Physician Global Assessment.

Notes:
Etanercept arm was not included in UNCOVER-1.
Responders (sPGA 0 or 1) to ixekizumab at week 12 were rerandomized to receive IXE Q4W, IXE Q12W, or PBO.
In UNCOVER-2 study, nonresponders to ETN at week 12 were switched to IXE Q4W (without a 160-mg starting dose) after a 4-week washout period.
Nonresponders to PBO at week 12 received a 160-mg starting dose of ixekizumab followed by IXE Q4W.
⋮ (dotted line) indicates relapse (sPGA ≥3).
UNCOVER-3 study is not represented in maintenance period design as the extension period consisted of open-label treatment with IXE Q4W.