Ixekizumab Demonstrates Sustained High Efficacy and Consistent Safety in Patients with Moderate-to-Severe Psoriasis: 5 Years of Follow-up from UNCOVER-3

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BACKGROUND

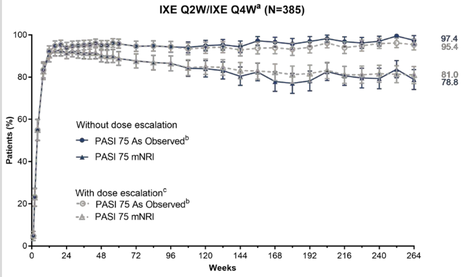
- Ixekizumab, a high-affinity monoclonal antibody that selectively targets interleukin-17A, is approved for treating moderate-to-severe plaque psoriasis
- In the Phase 3 UNCOVER-3 trial (NCT01646177), ixekizumab has previously demonstrated high efficacy with a consistent safety profile in patients with moderate-to-severe psoriasis[1]

OBJECTIVE

- To evaluate the efficacy and safety findings through 5 years of treatment with the approved ixekizumab dosing regimen (starting dose of 160 mg, then 80 mg every 2 weeks up to and including Week 12, followed by 80 mg every 4 weeks thereafter) in UNCOVER-3

KEY RESULTS

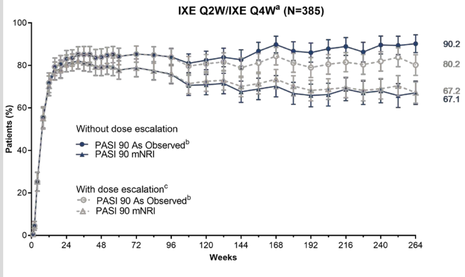
Figure 1. Ixekizumab PASI 75 Response Rates Through 5 Years of Treatment, As Observed and mNRI



[a] Approved ixekizumab dosing regimen: starting dose of 160 mg, then IXE Q2W up to and including Week 12, followed by IXE Q4W thereafter; [b] For observed data, response is calculated by n/N*100%; [c] From Week 60-264, patients and investigators could elect to escalate to IXE Q2W*IXE Q2W=80 mg ixekizumab every 2 weeks*
IXE Q4W=80 mg ixekizumab every 4 weeks; mNRI=modified non-responder imputation; Nx=number of patients with non-missing data; PASI 75/90/100=Psoriasis Area and Severity Index ≥75%/≥90%/100% response

KEY RESULTS

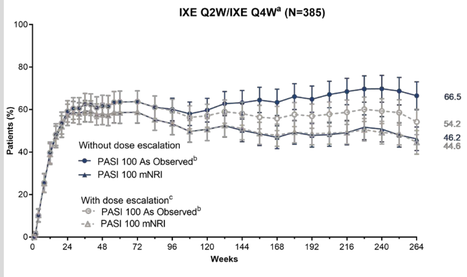
Figure 2. Ixekizumab PASI 90 Response Rates Through 5 Years of Treatment, As Observed and mNRI



[a] Approved ixekizumab dosing regimen: starting dose of 160 mg, then IXE Q2W up to and including Week 12, followed by IXE Q4W thereafter; [b] For observed data, response is calculated by n/N*100%; [c] From Week 60-264, patients and investigators could elect to escalate to IXE Q2W
IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; mNRI=modified non-responder imputation; Nx=number of patients with non-missing data; PASI 75/90/100=Psoriasis Area and Severity Index ≥75%/≥90%/100% response

KEY RESULTS

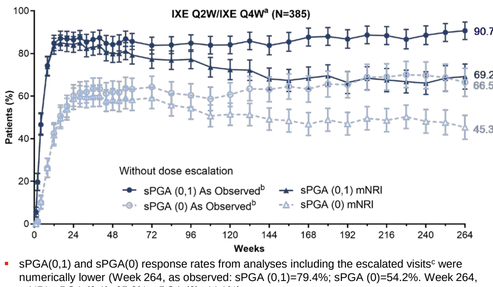
Figure 3. Ixekizumab PASI 100 Response Rates Through 5 Years of Treatment, As Observed and mNRI



[a] Approved ixekizumab dosing regimen: starting dose of 160 mg, then IXE Q2W up to and including Week 12, followed by IXE Q4W thereafter; [b] For as observed data, response is calculated by n/N*100%; [c] From Week 60-264, patients and investigators could elect to escalate to IXE Q2W
IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; mNRI=modified non-responder imputation; Nx=number of patients with non-missing data; PASI 75/90/100=Psoriasis Area and Severity Index ≥75%/≥90%/100% response

KEY RESULTS

Figure 4. Ixekizumab sPGA (0,1) and sPGA (0) Response Rates Through 5 Years of Treatment, As Observed and mNRI



- sPGA(0,1) and sPGA(0) response rates from analyses including the escalated visits[c] were numerically lower (Week 264, as observed: sPGA (0,1)=79.4%; sPGA (0)=54.2%. Week 264, mNRI: sPGA (0,1)=65.8%; sPGA (0)=44.1%)

[a] Approved ixekizumab dosing regimen: starting dose of 160 mg, then IXE Q2W up to and including Week 12, followed by IXE Q4W thereafter; [b] For as observed data, response is calculated by n/N*100%; [c] From Week 60-264, patients and investigators could elect to escalate to IXE Q2W
IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; mNRI=modified non-responder imputation; Nx=number of patients with non-missing data; sPGA (0,1) or (0)=static Physician's Global Assessment response of clear/minimal or clear plaque psoriasis

KEY ELIGIBILITY CRITERIA

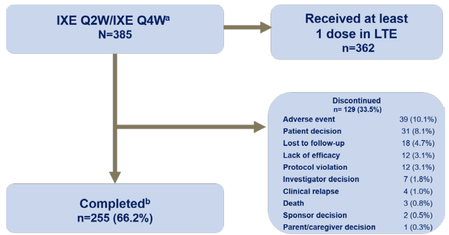
Inclusion criteria

- ≥18-years of age with moderate-to-severe plaque psoriasis
- Psoriasis Area and Severity Index (PASI) ≥12 at both screening and baseline visits
- ≥10% body surface area affected at both screening and baseline visits
- Static Physician's Global Assessment (sPGA) score ≥3 at both screening and baseline visits

Exclusion criteria

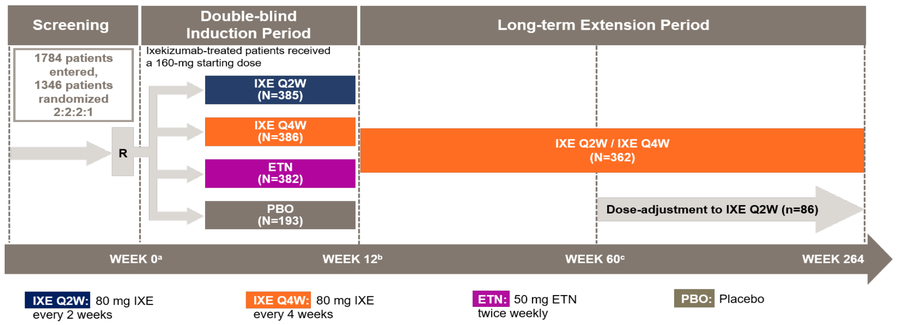
- Prior exposure to etanercept

PATIENT DISPOSITION



[a] Approved ixekizumab dosing regimen: starting dose of 160 mg, then IXE Q2W up to and including Week 12, followed by IXE Q4W thereafter; [b] Due to site early closure, one patient did not complete the study disposition form and the status for this subject was unknown; *IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks*

STUDY DESIGN



[a] Week 0: patients randomized to IXE Q2W, IXE Q4W, ETN, or PBO; [b] Week 12: all patients entered long term extension period with IXE Q4W; [c] From Week 60-264, patients and investigators could elect to escalate to IXE Q2W; *IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; ETN=etanercept; PBO=placebo*

ASSESSMENTS

Efficacy
- PASI 75/90/100
- sPGA (0,1) or (0)

Safety
- TEAEs

PASI 75/90/100=Psoriasis Area and Severity Index ≥75%/ ≥ 90%/100% response; sPGA (0,1) or (0)=static Physician's Global Assessment response of clear/minimal or clear plaque psoriasis; TEAEs=treatment-emergent adverse events

STATISTICAL ANALYSIS

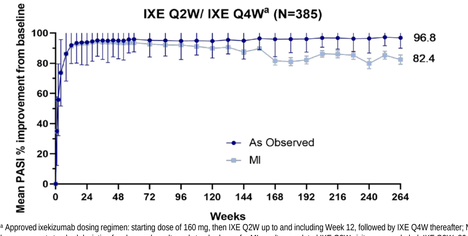
- Analysis population: Intent-to-treat (ITT) population defined as all randomized patients
- Efficacy was reported using as observed and modified non-responder imputation (mNRI) for categorical variables, and using multiple imputation (MI) for continuous variables
- Safety was summarized by incidence rate per 100 patient-years for patients randomized to IXE Q2W during the first 12 weeks and then received IXE Q4W in the Long-term Extension Period
  - Data from visits with escalated IXE Q2W were included in the analyses
  - IRs were calculated based on total patient-years in the time period

Table 1. Treatment-emergent Adverse Events Through Week 264 of Ixekizumab Treatment[a]

n (IR)	IXE Q2W/IXE Q4W (N=362) PY=1493.8
Patients with ≥1 treatment-emergent AE	323 (21.6)
Mild	80 (5.4)
Moderate	186 (12.5)
Severe	57 (3.8)
Serious AEs	55 (3.7)
Discontinuation due to AEs	33 (2.2)
Death	3 (0.2)

[a] From Week 60-264, patients and investigators could elect to escalate to IXE Q2W; *AE=adverse event; IR=incidence rate per 100 PY; IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; PY=patient-years*

Figure 5. Mean PASI Percent Improvement, As Observed and MI



[a] Approved ixekizumab dosing regimen: starting dose of 160 mg, then IXE Q2W up to and including Week 12, followed by IXE Q4W thereafter; Note: Error bars represent standard deviation for observed results and standard error for MI results; escalated IXE Q2W visits were excluded; *IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; MI= multiple imputation*

Table 2. Adverse Events of Special Interest Through Week 264 of Ixekizumab Treatment[a]

AEs of special interest n (IR)	IXE Q2W/IXE Q4W (N=362) PY=1493.8
Infection	263 (17.6)
Injection-site reactions[b]	33 (2.2)
Allergic reactions/hypersensitivities	
Potential anaphylaxis	2 (0.1)
Non-anaphylaxis	56 (3.7)
Hepatic events	30 (2.0)
Cytopenias	14 (0.9)
Cerebro-cardiovascular events	13 (0.9)
Depression	11 (0.7)
Malignancy	9 (0.6)
Crohn's disease	2 (0.1)
Ulcerative colitis	1 (0.1)

[a] From Week 60-264, patients and investigators could elect to escalate to IXE Q2W; [b] Identified based on MedDRA High Level Terms; *AE=adverse event; IR=incidence rate per 100 PY; IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; MedDRA= Medical Dictionary for Regulatory Activities; PY=patient-years*

CONCLUSIONS

- This study demonstrated that high-efficacy response with ixekizumab was durable on a long-term horizon, with sustained response through 5 years of continuous treatment
- The safety profile remained consistent with prior findings, with no new or unexpected safety concerns

ACKNOWLEDGEMENT

The authors wish to thank the study participants, investigators, and trial staff for their participation in the UNCOVER-3 study

DISCLOSURES

- A. Blauvelt has served as a scientific adviser and/or clinical study investigator for AbbVie, Aclaris, Almirall, Arena, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Dermira, Eli Lilly and Company, Forte, Galderma, Janssen, Leo, Novartis, Ortho, Pfizer, Rapt, Regeneron, Sandoz, Sanofi Genzyme, Sun Pharma, and UCB Pharma, and as a paid speaker for AbbVie.
- T. Mabuchi has served as a paid speaker for Eli Lilly, Maruho, Kyowa Kirin, Celgene, and Janssen, and received research funds from Kyowa Kirin, Torii, Maruho, Taiho, and Leo Pharma.
- A. Leung is an employee of Syneos Health, on behalf of Eli Lilly.
- A. Garrelts, H. Crane, H. ElMaraghy, H. Patel, T. Ridenour, G. Gallo are employees of Eli Lilly and Company and own stock.
- M. Lebwohl is an employee of Mount Sinai and receives research funds from: AbbVie, Amgen, Arcutis, AstraZeneca, Boehringer Ingelheim, Celgene, Clinuvel, Eli Lilly, Incyte, Janssen Research & Development, LLC, Kadmon Corp., LLC, Leo Pharmaceuticals, Medimmune, Novartis, Ortho Dermatologics, Pfizer, Sciderm, UCB, Inc., and Vidac. Dr. Lebwohl is also a consultant for Allergan, Almirall, Arcutis, Inc., Avotres Therapeutics, BirchBioMed Inc., Boehringer-Ingelheim, Bristol-Myers Squibb, Cara Therapeutics, Castle Biosciences, Corrona, Dermavant Sciences, Evelo, Foundation for Research and Education in Dermatology, Inozyme Pharma, LEO Pharma, Meiji Seika Pharma, Menlo, Mitsubishi, Neurodem, Pfizer, Promius/Dr. Reddy's Laboratories, Theravance, and Verrica.
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- Previously presented at Maui Derm Virtual Congress; 24-27 June 2020

ABBREVIATIONS

AE=adverse event; ETN=etanercept; IR=incidence rate; ITT=intent-to-treat; IXE=ixekizumab; IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; MedDRA= Medical Dictionary for Regulatory Activities; MI= multiple imputation; mNRI= modified non-responder imputation; Nx=number of patients with non-missing data; PASI=Psoriasis Area and Severity Index; PASI 75/90/100=Psoriasis Area and Severity Index ≥75%/≥90%/100% response; PBO=placebo; PY= patient-years; sPGA (0,1) or (0)=static Physician's Global Assessment response of clear/minimal or clear plaque psoriasis; TEAEs=treatment-emergent adverse events

REFERENCE

1. Lebwohl MG, et al. *J Eur Acad Dermatol Venereol.* 2020;34:301-309.

Study was sponsored by Eli Lilly and Company