Achieving PASI 50 at 2 Weeks Was Associated With Better Long-term Clinical Outcomes and Low Discontinuation: A Subgroup Analysis of a Phase 3 Trial of Ixekizumab in Moderate-to-Severe Psoriasis

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BACKGROUND

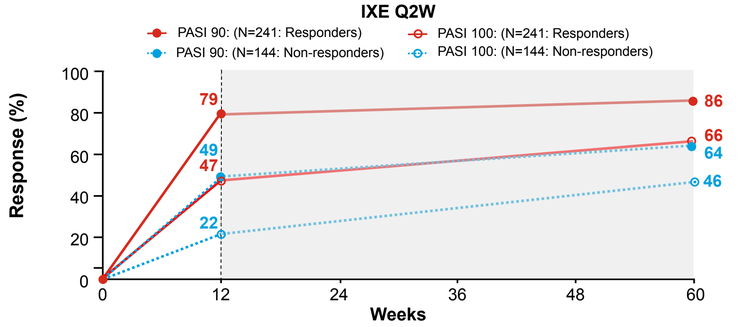
- Although many patients with psoriasis prioritize rapid improvements (eg, Psoriasis Area and Severity Index [PASI] 50) in their treatment goals,[1-3] it is not clear if rapid improvements are associated with better long-term outcomes
- UNCOVER-3 (NCT01646177) is a Phase 3 study of ixekizumab, a high-affinity monoclonal antibody that selectively targets interleukin-17A,[4] in patients with moderate-to-severe psoriasis
  - Ixekizumab is approved for the treatment of moderate-to-severe plaque psoriasis, active psoriatic arthritis, and active ankylosing spondylitis[5,6]
- Onset of efficacy can be seen as early as Week 2 in patients with moderate-to-severe psoriasis[7]

OBJECTIVE

- To evaluate the association between rapid onset of efficacy (PASI 50 at Week 2) and long-term clinical outcomes in UNCOVER-3

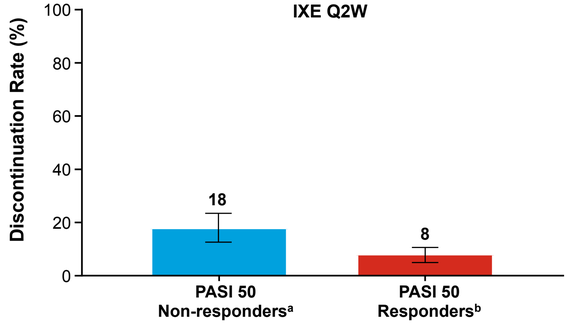
KEY RESULTS

PASI 90/100 Responses in Week 2 PASI 50 Responders and Non-responders Treated With Ixekizumab



Dashed lines represent the end of the double-blind induction period; the gray-shaded area represents extension period treated with IXE Q4W

Patient Discontinuation From Study Treatment at the End of Year 1: Early PASI Responders and Non-responders Treated With Ixekizumab



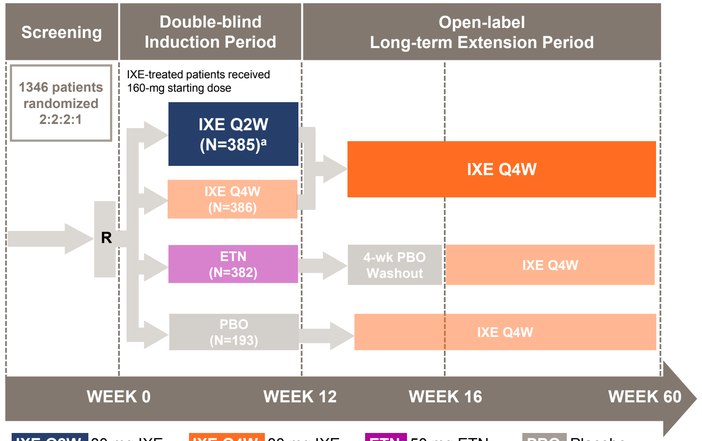
[a] Not achieved even once by Week 2 (N=139)
[b] Achieved at least once by Week 2 (N=246)

CONCLUSIONS

- Patients achieving a rapid response at Week 2 demonstrated higher responses over the long term compared with patients not achieving a rapid response at Week 2
  - Rapid responders treated with ixekizumab had higher PASI 90/100 response rates at Weeks 12 and 60 and lower rates of discontinuation
  - Many slower responders to ixekizumab still achieved PASI 90/100 at Week 60
- Early response can be a predictor of longer-term response and better drug survival

METHODS

Study Design
UNCOVER-3



IXE Q2W: 80 mg IXE every 2 weeks
IXE Q4W: 80 mg IXE every 4 weeks
ETN: 50 mg ETN twice weekly
PBO: Placebo

[a] Approved dose

- This post hoc analysis included patients receiving the label-approved dosing regimen of ixekizumab from the UNCOVER-3 trial

Key Eligibility Criteria

- Inclusion criteria
  - Male or female, ≥18 years old
  - Chronic plaque psoriasis for ≥6 months prior to baseline
  - ≥10% body surface area involvement
  - Static Physician Global Assessment ≥3 and PASI ≥12
  - Candidates for phototherapy, systemic therapy, or both
  - Failure, contraindication, or intolerance to ≥1 systemic therapy[a]
- Exclusion criteria
  - Other forms of psoriasis
  - History of drug-induced psoriasis
  - Concurrent or recent use[b] of any biologic agent prior to baseline agent
  - Prior use of etanercept
  - Serious infection within the last 3 months

[a] Including cyclosporine, methotrexate, or phototherapy
[b] Within the following washout periods: etanercept <28 days; infliximab, adalimumab, or alefacept <60 days; golimumab <90 days; rituximab <12 months; or any other biologic agent <5 half-lives prior to baseline

Subgroups, Assessments, and Statistical Analysis

Subgroups
- Week 2 PASI 50 responders
- Week 2 PASI 50 non-responders

Assessments
- PASI 90/100 at Weeks 12 and 60
- Discontinuation rates at 1 year

Statistical Analysis
- Subgroup analysis was conducted using the Intention-to-Treat population randomized to ixekizumab every 2 weeks
- Missing data were imputed using non-responder imputation
- Discontinuation from treatment was summarized for each subgroup regardless of treatment

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RESULTS

Demographics and Characteristics

	IXE Q2W: All (N=385)	IXE Q2W: Week 2 PASI 50 Responders (N=241)	IXE Q2W: Week 2 PASI 50 Non-responders (N=144)
Age, years	45.6 (13.1)	44.8 (13.7)	46.9 (12.0)
Male, n (%)	254 (66.0)	155 (64.3)	99 (68.8)
BMI, kg/m²	30.2 (7.1)	29.6 (6.9)	31.3 (7.4)
BSA, %	28.0 (17.3)	28.4 (17.3)	27.2 (17.3)
Duration of psoriasis, years	17.8 (12.2)	18.4 (11.8)	16.8 (12.8)
Baseline sPGA	3.5 (0.6)	3.5 (0.6)	3.6 (0.6)
Baseline PASI	20.7 (8.2)	20.7 (8.0)	20.8 (8.5)

Data are mean (standard deviation) unless stated otherwise

- Following 2 weeks of treatment, 63% of patients treated with ixekizumab had achieved PASI 50

ABBREVIATIONS

BMI=body mass index; BSA=body surface area; ETN=etanercept; IXE=ixekizumab; IXE Q2W= 80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; PASI=Psoriasis Area and Severity Index; PASI 50/790/100=Psoriasis Area and Severity Index ≥50%/≥90%/100% response; PBO=placebo; R=randomization; sPGA=static Physicians Global Assessment

DISCLOSURES

- **D. Rosmarin** has received honoraria as a consultant for: AbbVie, Celgene, Dermavant, Incyte, Janssen, Lilly, Novartis, Pfizer, Regeneron, Sanofi, and Sun Pharmaceuticals; has received research support from: AbbVie, Bristol-Meyers Squibb, Celgene, Dermira, Incyte, Janssen, Lilly, Merck, Novartis, Pfizer, and Regeneron Pharmaceuticals Inc; and has served as a paid speaker for: AbbVie, Celgene, Janssen, Lilly, Novartis, Pfizer, Regeneron Pharmaceuticals Inc., and Sanofi; **J. Gorelick** has had a financial agreement or affiliation during the past year with the following commercial interests in the form of consultant: AbbVie, Dermira, Eli Lilly and Company, LEO Pharma, Novartis, Ortho Dermatologics, Pfizer, PruGen, Regeneron Pharmaceuticals, Sanofi Genzyme, Sun Pharma, and UCB; and has been on the speakers bureau of or on advisory board for: AbbVie, Dermira, Eli Lilly and Company, LEO Pharma, Novartis, Orth Dermatologics, Pfizer, PruGen, Regeneron Pharmaceytucaks, Sun Pharma, and UCB; **S. Smith** has performed clinical research studies for: Abbvie, Allergan, Boehringer Ingelheim, Brickell Biotech, Croma Pharma, Dermira, Eli Lilly and Company, Endo Pharmaceuticals, Evolus, Galderma, Glenmark Pharmaceuticals, Leo Pharma, Nielsen Biosciences, Novartis, Pfizer, Prollenium Medical Technologies, Revance Therapeutics, and Sun Pharmaceutical Industries; and has received fees and honoraria as a consultant from: Brickell Biotech, Galderma, Nielsen Biosciences, Prollenium Medical Technologies, Scarless Laboratories, and Teoxane; **M. McKean-Matthews** is an employee of Syneos Health; **D. Shrom**, **R. Burge**, **K. See**, **T. Ridenour**, and **C-Y Lin** are employees and shareholders of Eli Lilly and Company
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