Improved Pain and Fatigue With Ixekizumab Treatment in Patients With Active Psoriatic Arthritis and Previous Inadequate Response to TNF Inhibitors: 3-Year Follow-up From a Phase 3 Study (SPIRIT-P2)

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BACKGROUND

- Psoriatic arthritis (PsA) is a chronic inflammatory disease with articular and extra-articular symptoms[1]
- Pain and fatigue are 2 of the most common patient-reported symptoms of PsA[2]
- Ixekizumab is a high-affinity monoclonal antibody that selectively targets interleukin-17A[3]
  - Improvements in pain and fatigue have been demonstrated with up to 2 years of treatment with ixekizumab in patients who had an inadequate response or intolerance to tumor necrosis factor inhibitors (TNFi)[4,5]

OBJECTIVE

- To report improvements in pain and fatigue in TNFi-experienced patients with PsA who were treated with ixekizumab for up to 3 years (156 weeks)

REFERENCES

1. Gladman DD, et al. *Ann Rheum Dis*. 2005;(Suppl 2):ii14-17.
2. Nowell WB, et al. *Arthritis Rheumatol*. 2016;71(Suppl 10):[abstract 436].
3. Liu L, et al. *J Inflamm Res*. 2018;9:39-50.
4. Kavanaugh A, et al. *Clin Exp Rheumatol*. 2019;37:566-576.
5. Nash P, et al. *Arthritis Rheumatol*. 2019;71(Suppl 10):[abstract 2077].
6. Beaton DE, et al. *J Rheumatol*. 2010;42:1960-1979.
7. Ludwig DP. *Pharmacoeconomics*. 2004;22(Suppl 1):27-36.
8. Gladman D, et al. *RMD Open*. 2020;6:e000939. doi: 10.1136/rmdopen-2019-000939.

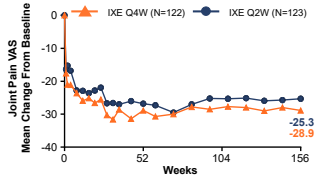
ABBREVIATIONS

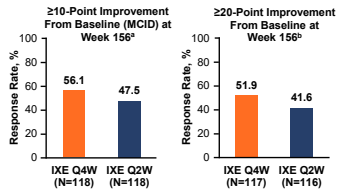
CASPAR=Classification Criteria for Psoriatic Arthritis; *cDMARD*=conventional disease-modifying antirheumatic drug; *CRP*=C-reactive protein; *IL*=interleukin; *IR*=inadequate responder; *IXE Q4W*=80 mg ixekizumab every 4 weeks; *IXE Q2W*=80 mg ixekizumab every 2 weeks; *IXE Q4W/Q2W*=80 mg ixekizumab every 4 weeks, then every 2 weeks; *MCID*=minimal clinically important difference; *MTX*=methotrexate; *NRS*=numeric rating scale; *PBO*=placebo; *PsA*=psoriatic arthritis; *R*=randomization; *RT*=concurrent therapy; *SF-36*=Medical Outcomes Study 36-Item Short Form Health Survey; *TNFi*=tumor necrosis factor inhibitor; *VAS*=visual analog scale

KEY RESULTS

Joint Pain VAS

- Improvements from baseline in joint pain were sustained in both treatment groups through 156 weeks
- Overall, 52% of patients reported clinically meaningful improvement (MCID ≥10) of joint pain at Week 156

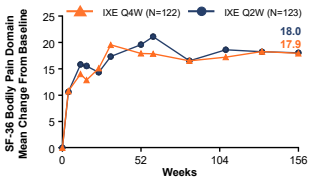


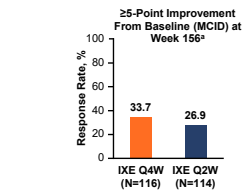


[a] In patients with baseline Joint Pain VAS ≥10; [b] In patients with baseline Joint Pain VAS ≥20

SF-36 Bodily Pain Domain

- Improvements from baseline in bodily pain were sustained in both treatment groups through 156 weeks
- Overall, 30% of patients reported clinically meaningful improvement of bodily pain at Week 156

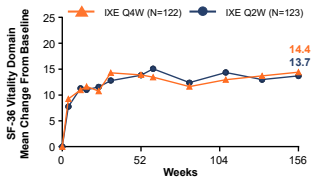


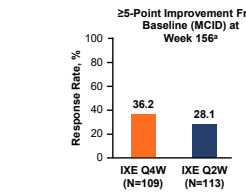


[a] In patients with baseline Bodily Pain domain score ≥5

SF-36 Vitality Domain

- Improvements from baseline in vitality were sustained in both treatment groups through 156 weeks
- Overall, 32% of patients reported clinically meaningful improvement of vitality at Week 156

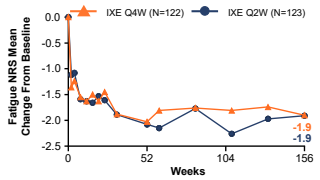


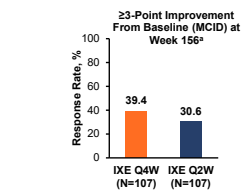


[a] In patients with baseline Vitality domain score ≥5

Fatigue Numeric Rating Scale

- Improvements from baseline in fatigue were sustained in both treatment groups through 156 weeks
- Overall, 35% of patients reported clinically meaningful improvement of fatigue at Week 156





[a] In patients with baseline Fatigue NRS ≥3

CONCLUSIONS

- In patients with PsA who had an inadequate response or intolerance to TNFi, improvements in pain and fatigue were sustained through 3 years of ixekizumab treatment in the IXE Q2W and IXE Q4W treatment groups
- >50% of patients receiving IXE Q4W had clinically meaningful improvement in pain (Joint Pain VAS) at 3 years
  - Supported by improvement on the SF-36 Bodily Pain domain
- Almost 40% of patients receiving IXE Q4W had clinically meaningful improvement in fatigue (Fatigue NRS) at 3 years
  - Supported by improvement on the SF-36 Vitality domain

DISCLOSURES

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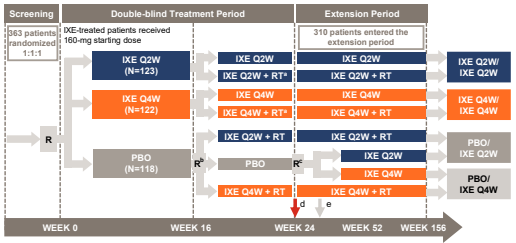
METHODS

Study Design, SPIRIT-P2



IXE Q2W: 80 mg IXE every 2 weeks; **IXE Q4W:** 80 mg IXE every 4 weeks; **PBO:** Placebo; **PBO/IXE Q2W:** PBO/80 mg IXE Q2W from Week 24 or Week 16 if IR; **PBO/IXE Q4W:** PBO/80 mg IXE Q4W from Week 24 or Week 16 if IR

[a] Inadequate responders (IRs) in IXE arms at Week 16 maintained their IXE dose but received rescue treatment (RT; modifications to the patient's background therapy); [b] IRs in the PBO arm at Week 16 were randomized to IXE Q2W + RT or IXE Q4W + RT after a 160-mg starting dose. Responders continued on PBO until Week 24; [c] Patients receiving PBO until Week 24 were randomized to IXE Q2W or IXE Q4W after a 160-mg starting dose; [d] Primary endpoint; [e] Patients failing to demonstrate at least 20% improvement from baseline in tender joint count and swollen joint count at Week 32 or any subsequent visit were discontinued

Key Eligibility Criteria

Inclusion Criteria

- ≥18 years of age
- Established active PsA ≥6 months and currently meet CASPAR:
  - ≥3 tender joints and ≥3 swollen joints
- Prior treatment with ≥1 cDMARD[a] and 1 to 2 TNFi (TNFi discontinued owing to IR or intolerance)
- Active psoriatic skin lesion or documented personal history of psoriasis

Exclusion Criteria

- Current or recent use[b] of ≥1 biologic agent for the treatment of PsA or psoriasis
- Current use of >1 cDMARD[a] at study entry
- Previous treatment with α4-integrin–, IL-17–, or IL-12/23–targeted monoclonal antibodies
- Diagnosis of active inflammatory arthritis syndromes or spondyloarthropathies other than PsA
- Serious infection ≤3 months

[a] Methotrexate, sulfasalazine, leflunomide, or hydroxychloroquine; [b] Etanercept <28 days; infliximab, adalimumab, certolizumab pegol, or alefacept <60 days; golimumab <90 days; rituximab <12 months; or any other biologic agent or small molecule <5 half-lives prior to baseline

Patient-Reported Outcomes

- Patients self-rated symptoms using:
  - Joint Pain visual analog scale
    - Score range: 0 (none) to 100 mm (worst imaginable)
    - Minimal clinically important difference (MCID): ≥10-point (mm) improvement from baseline[6]
    - 20-point (mm) improvement from baseline (appreciably important to patients)[6]
  - Medical Outcomes Study 36-Item Short Form Health Survey
    - Bodily Pain and Vitality domains (part of the physical component summary and mental component summary, respectively)
    - Domain range: 0 (worst) to 100 (best)
    - MCID: ≥5-point improvement from baseline[7]
  - Fatigue numeric rating scale
    - Score range: 0 (none) to 10 (worst imaginable)
    - MCID: ≥3-point improvement from baseline[8]

Statistical Analyses

- Data presented are for patients in the Intent-to-Treat population who were originally randomized to ixekizumab at baseline (Week 0)
  - Patients randomized to placebo were excluded from the analyses
- Missing values were imputed by modified baseline observation carried forward for continuous variables and modified non-responder imputation for categorical variables
- Observed data for Week 16 inadequate responders were treated as missing during the inadequate response period

RESULTS

Baseline Demographics and Clinical Characteristics

	IXE Q4W (N=122)	IXE Q2W (N=123)
Age, years	52.6 (13.6)	51.7 (11.9)
Male, n (%)	63 (51.6)	50 (40.7)
Time since PsA diagnosis, years	11.0 (9.6)	9.9 (7.4)
Tender joint count (68 joints)	22.0 (14.1)	25.0 (17.3)
Swollen joint count (66 joints)	13.1 (11.2)	13.5 (11.5)
Joint Pain VAS, mm	63.9 (21.4)	62.7 (20.9)
Fatigue NRS	5.9 (2.5)	6.0 (2.5)
CRP, mg/L	17.0 (27.5)	13.5 (26.1)
Background cDMARD therapy		
Current use, n (%)	60 (49.2)	73 (59.3)
MTX, n (%)	48 (39.3)	61 (49.6)
MTX mean weekly dose, mg	15.9 (4.8)	16.0 (4.6)
Previous TNFi therapy, n (%)		
Inadequate response to 1 TNFi	71 (58.2)	65 (52.8)
Inadequate response to 2 TNFi	41 (33.6)	46 (37.4)
Intolerant to a TNFi	10 (8.2)	12 (9.8)

Data are mean (standard deviation) unless stated otherwise

- The proportions of patients who completed Week 156 were 70/122 (57%) in the ixekizumab every 4 week (IXE Q4W) group and 55/123 (45%) in the ixekizumab every 2 week (IXE Q2W) group

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