Efficacy of Ixekizumab in Patients Previously Treated with IL-17 Inhibitors

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BACKGROUND

- Previous use of biologics may detrimentally impact the efficacy of subsequent biologic therapies[1,2]
- Ixekizumab is a high-affinity monoclonal antibody that selectively targets IL-17A3
  - Is approved for treating moderate-to-severe plaque psoriasis

IL-17=interleukin-17; IL-17RA=interleukin-17 receptor A

OBJECTIVE

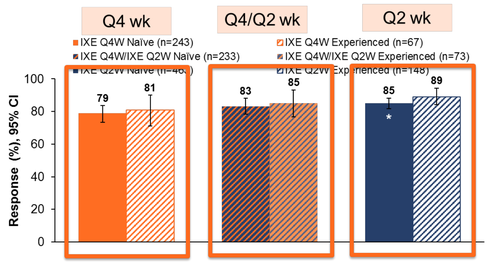
- To evaluate the impact of previous use of biologics, particularly those targeting the IL-17 pathway (brodalumab [IL-17RA antagonist] or secukinumab [IL-17A antagonist]), on the 52-week efficacy of ixekizumab (IL-17A antagonist) in patients with moderate-to-severe psoriasis

References

1. Ruiz Salas V, et al. *J Eur Acad Dermatol Venereol.* 2012;26:508-513.
2. Mazzotta A, et al. *Am J Clin Dermatol.* 2009; 10:319-324.
3. Liu L, et al. *J Inflamm Res.* 2016;9:39-50.

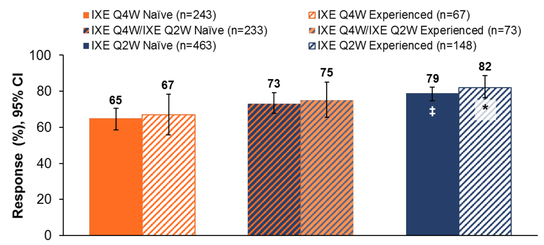
KEY RESULTS

PASI 75 Response at Week 52 by Previous IL-17 Inhibitor Exposure
NRI, Blinded Treatment Dosing Period, ITT Population



* p<.05 vs. IXE Q4W (Fisher's exact test)
CI=confidence interval; IL-17=interleukin-17; ITT=Intent-to-Treat; IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; NRI=non-responder imputation; PASI=Psoriasis Area and Severity Index

PASI 90 Response at Week 52 by Previous IL-17 Inhibitor Exposure
NRI, Blinded Treatment Dosing Period, ITT Population



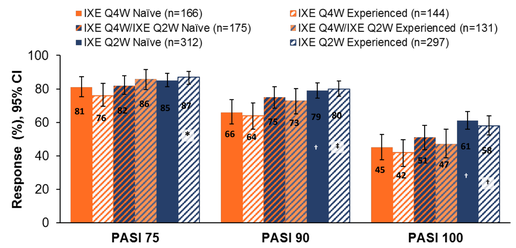
* p<.05 vs. IXE Q4W; ‡ p<.001 vs. IXE Q4W (Fisher's exact test)
CI=confidence interval; IL-17=interleukin-17; ITT=Intent-to-Treat; IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; NRI=non-responder imputation; PASI=Psoriasis Area and Severity Index

PASI 100 Response at Week 52 by Previous IL-17 Inhibitor Exposure
NRI, Blinded Treatment Dosing Period, ITT Population

** p<.05 vs. IXE Q4W; ‡ p<.001 vs. IXE Q4W (Fisher's exact test)*
CI=confidence interval; IL-17=interleukin-17; ITT=Intent-to-Treat; IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; NRI=non-responder imputation; PASI=Psoriasis Area and Severity Index

- Ixekizumab showed efficacy in patients regardless of previous exposure to an IL-17 inhibitor biologic

PASI Responses at Week 52 by Previous Biologic Exposure
NRI, Blinded Treatment Dosing Period, ITT Population



* p<.05 vs. IXE Q4W; † p<.01 vs. IXE Q4W; ‡ p<.001 vs. IXE Q4W (Fisher's exact test)
CI=confidence interval; IL-17=interleukin-17; ITT=Intent-to-Treat; IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; NRI=non-responder imputation; PASI=Psoriasis Area and Severity Index

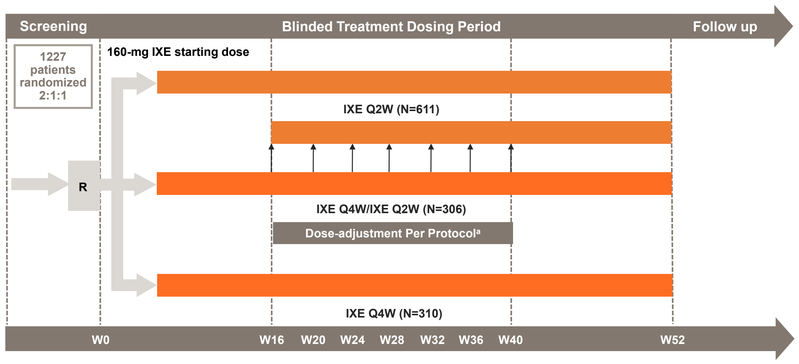
- Ixekizumab showed efficacy in patients regardless of previous exposure to a biologic

CONCLUSIONS

- Previous exposure to biologics, including those targeting the IL-17 pathway (brodalumab or secukinumab), did not impact the 52-week efficacy of ixekizumab

METHODS

Study Design - IXORA-P



[a] Dose-adjustment (IXE Q4W to IXE Q2W) based on whether a patient achieved sPGA ≥2 at 2 consecutive visits during Week 12 through Week 40; investigators were blinded to the predefined criteria and timing

IXE=ixekizumab; IXE Q4W=80 mg IXE every 4 weeks; IXE Q2W=80 mg IXE every 2 weeks; IXE Q4W/IXE Q2W dose adjustment=80 mg IXE every 4 weeks/every 2 weeks; R=randomization; sPGA=static Physician's Global Assessment; W=Week

Baseline Demographics and Disease Characteristics by Previous IL-17 Inhibitor Exposure

	IL-17 Inhibitor Naïve (N=939)	IL-17 Inhibitor Experienced (N=288)
Age, years	48.1 (13.6)	46.6 (13.1)
Male, n (%)	609 (64.9)	201 (59.8)
Weight, kg	91.1 (23.7)	89.9 (22.5)
Psoriasis duration, years	18.5 (12.5)	22.2 (12.9)
Percentage of BSA involved	26.1 (17.4)	27.5 (18.0)
Previous biologic therapy, n (%)	284 (30.2)	288 (100.0)
Used 1	186 (19.8)	197 (68.4)
Used 2	58 (6.2)	62 (21.5)
Used ≥3	40 (4.3)	29 (10.1)
Previous secukinumab therapy, n (%)	0	13 (4.5)
Previous brodalumab therapy, n (%)	0	277 (96.2)
PASI	20.1 (8.0)	21.2 (9.0)

Data are mean (standard deviation) unless otherwise stated
BSA=body surface area; IL-17=interleukin-17; PASI=Psoriasis Area and Severity Index

Safety Overview by Previous IL-17 Inhibitor Exposure - Blinded Treatment Dosing Period, Safety Population

n (%)	IXE Q4W		IXE Q4W/ IXE Q2W		IXE Q2W	
	Naïve (n=243)	Experienced (n=67)	Naïve (n=233)	Experienced (n=73)	Naïve (n=461)	Experienced (n=148)
≥1 TEAE	202 (83.1)	45 (67.2)	180 (77.3)	50 (68.5)	346 (75.1)	201 (69.8)
Death	1 (0.4)	0	0	0	2 (0.4)	0
≥1 SAE	13 (5.3)	3 (4.5)	12 (5.2)	4 (5.5)	25 (5.4)	7 (4.7)
Discontinuation due to AE	5 (2.1)	1 (1.5)	10 (4.3)	3 (4.1)	13 (3.0)	5 (3.4)
Infections	135 (55.6)	31 (46.3)	120 (51.5)	30 (41.1)	211 (45.8)	67 (45.3)
Injection-site reactions	27 (11.1)	4 (6.0)	15 (6.4)	3 (4.1)	66 (14.3)	12 (8.1)
Allergic reactions/hypersensitivities	24 (9.9)	4 (6.0)	22 (9.4)	3 (4.1)	53 (11.5)	6 (4.1)
Depressions	4 (1.6)	1 (1.5)	3 (1.3)	1 (1.4)	8 (1.7)	4 (2.7)
Cerebrocardiovascular events	2 (0.8)	1 (1.5)	2 (0.9)	0	9 (0.2)	0
Inflammatory bowel disease	1 (0.4)	0	1 (0.4)	0	3 (0.7)	1 (0.7)
Malignancies	2 (0.8)	0	5 (2.1)	1 (1.4)	0	2 (1.4)

AE=adverse event; IL-17=interleukin-17; IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; SAE=serious adverse event; TEAE=treatment-emergent adverse event

Disclosures

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