P17

A Head-to-Head Comparison of Ixekizumab versus Guselkumab in Patients with Moderate-to-Severe Plaque Psoriasis: 12-Week Efficacy, Safety, and Speed of Response from a Randomized, Double-Blinded Trial

Andrew Blauvelt,[1] Kim Papp,[2] Abel Jarell,[3] Kristian Reich,[4] Alice Gottlieb,[5] Renata Gontijo Lima,[6] Hany Elmaraghy,[6] Gaia Gallo,[6] Lisa Renda,[6] So Young Park,[6] Jerry Bagel,[7] Eva Moelants (Non-author Presenter)[8]

[1]Oregon Medical Research Center, Portland, OR, USA; [2]Probity Medical Research, Inc., Waterloo, Ontario, Canada; [3]Northeast Dermatology Associates, Portsmouth, NH, USA; [4]Translational Research in Inflammatory Skin Diseases, Institute for Health Services Research in Dermatology and Nursing, University Medical Center Hamburg-Eppendorf, and Skinflammation® Center, Hamburg, Germany; [5]Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [6]Eli Lilly and Company, Indianapolis, IN, USA; [7]Psoriasis Treatment Center of Central New Jersey, East Windsor, NJ, USA; [8]Eli Lilly Benelux, Brussels, Belgium

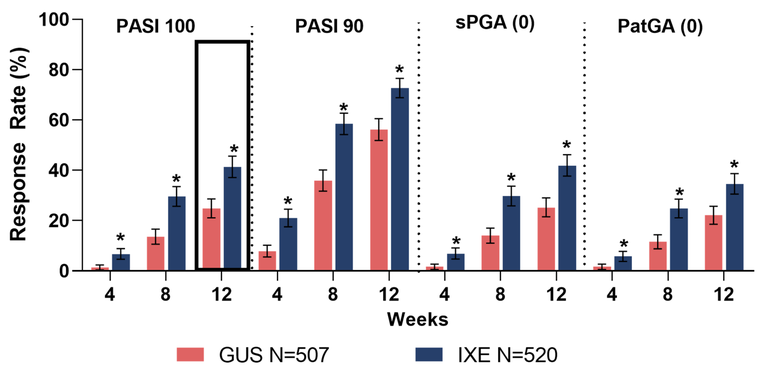
BACKGROUND

- Biologics targeting the interleukin (IL)-17/IL-23 pathway have demonstrated benefits to patients with high levels of skin improvement.
- As these drugs have come to market, there is an increasing need to directly compare efficacy and safety between new products to better inform dermatologists and patients regarding drug selection.
- Comparing speed of response is also important, as this has been identified as a key drug attribute by physicians and patients when choosing a therapeutic option.
- Ixekizumab (IXE), a high affinity monoclonal antibody that selectively targets IL-17A, has demonstrated greater skin clearance than etanercept[1] and ustekinumab[2] with consistent long-term efficacy and safety for up to 5 years of continuous treatment.[3,4]

OBJECTIVE

- To report 12-week results of IXORA-R (NCT03573323), which compared the efficacy, safety, and speed of response of IXE versus guselkumab (GUS), an IL-23p19 inhibitor, in patients with moderate-to-severe plaque psoriasis.

ACHIEVEMENT OF KEY EFFICACY ENDPOINTS



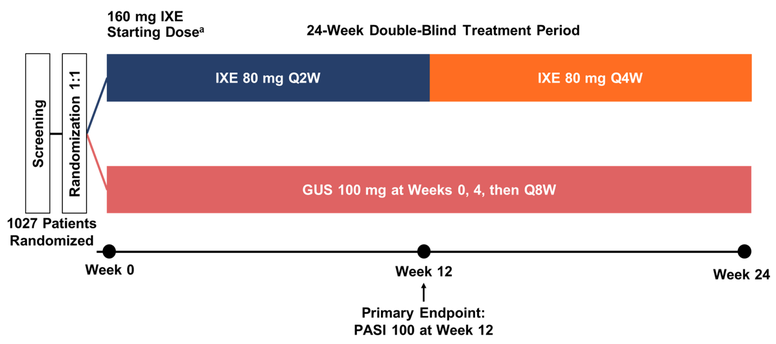
*p<0.001 versus GUS. Error bars represent 95% confidence intervals constructed using the asymptotic method without continuity correction. GUS, guselkumab; IXE, ixekizumab; PASI, Psoriasis Area and Severity Index; PatGA, Patient's Global Assessment; sPGA, static Physician's Global Assessment.

SAFETY OVERVIEW

	GUS N=506 n (%)	IXE N=519 n (%)
TEAE overall	277 (55)	293 (56)
TEAE by severity[a]		
Mild	167 (33)	175 (34)
Moderate	92 (18)	101 (20)
Severe	18 (3.6)	17 (3.3)
Death	0	0
Serious adverse event	13 (2.6)	16 (3.1)
Discontinuation due to adverse events	8 (1.6)	12 (2.3)

[a]Patients with multiple occurrences of the same event are counted under the highest severity. A single patient may present with several events. Safety analyses included all pts who received ≥1 dose of either drug. Safety frequencies represent all safety events reported as of 12-week database lock; exposure for many patients exceeded 12 weeks. IXORA-R is still blinded for investigators, sponsor's study team, and patients; thus, not all safety data are disclosed here to maintain study blinding and integrity. AE, adverse event; GUS, guselkumab; IXE, ixekizumab; TEAE, treatment-emergent adverse event.

STUDY DESIGN



[a]Administered as two 80-mg injections at Week 0. GUS, guselkumab; IXE, ixekizumab; PASI, Psoriasis Area and Severity Index; Q2W, every 2 weeks; Q4W, every 4 weeks; Q8W, every 8 weeks.

GATED PRIMARY AND MAJOR SECONDARY ENDPOINTS

Outcome measures	Response rate (%) GUS N=507	Response rate (%) IXE N=520	Significance p value
Primary efficacy endpoint			
PASI 100 at Week 12	24.9	41.3	<.001
Major secondary endpoints			
PASI 50 at Week 1	9.3	27.5	<.001
PASI 75 at Week 2	5.1	22.9	<.001
PASI 90 at Week 4	7.9	21.0	<.001
PASI 90 at Week 8	35.9	58.5	<.001
PASI 100 at Week 4	1.4	6.7	<.001
PASI 100 at Week 8	13.6	29.6	<.001
sPGA (0) at Week 12	25.2	41.9	<.001
PASI 100 at Week 24[a]	-	-	-

[a]Week 24 data were not available at this database lock. GUS, guselkumab; IXE, ixekizumab; PASI, Psoriasis Area and Severity Index; sPGA, static Physician's Global Assessment.

CONCLUSIONS

- Ixekizumab was superior to guselkumab in achieving complete skin clearance (PASI 100) at Week 12
- All major secondary endpoints up to Week 12 were achieved
- More patients on ixekizumab showed improvement over guselkumab as early as Week 1 for PASI 50, Week 2 for PASI 75, and Week 4 for sPGA [0], PASI 90, and PASI 100
- Both drugs demonstrated safety data consistent with their known safety profiles

Key Inclusion Criteria

- Chronic plaque psoriasis based on a diagnosis for ≥6 months before baseline, as determined by the investigator
- Candidate for phototherapy and/or systemic therapy
- sPGA ≥3 and PASI ≥12 both at screening and at baseline
- Have ≥10% BSA involvement at screening and at baseline

Key Exclusion Criteria

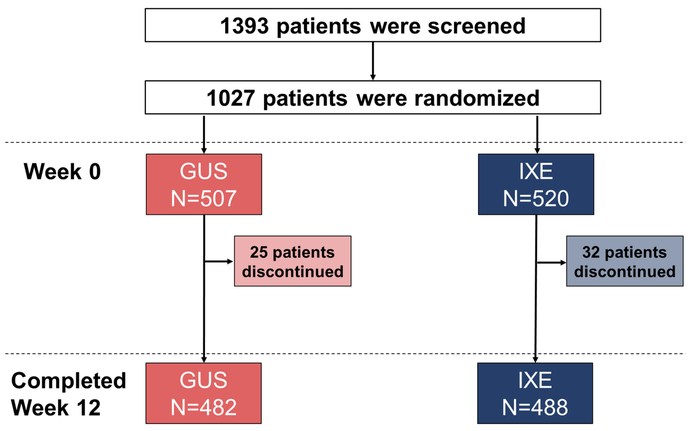
- Predominant pattern of pustular, erythrodermic, and/or guttate forms of psoriasis
- History of drug-induced psoriasis
- Clinically significant flare of psoriasis during the 12 weeks before baseline
- Use of tanning booths for at least 4 weeks before baseline and during the study, per investigator assessment
- Concurrent or recent use of any biologic agent within the specified periods prior to baseline[a]
- Prior use of IL-23p19 antagonists or any condition/contraindication as addressed in the local labeling for guselkumab that would preclude the patient from participating in this protocol
- Previous participation in any trial investigating ixekizumab or IL-23p19 antagonists, or have received treatment with ixekizumab
- Have previously failed to respond to an IL-17 antagonist, per investigator assessment

[a]Etanercept <28 days; infliximab, adalimumab, certolizumab pegol, or alefacept <60 days; golimumab <90 days; secukinumab <5 months; rituximab <12 months; or any other biologic agent (eg, ustekinumab) <5 half lives.

Methods

- Primary and major secondary endpoints were analyzed according to a pre-specified graphical multiplicity adjustment approach.
- Comparisons in the ITT population were made using Cochran-Mantel-Haenszel test adjusted by pooled site using non-responder imputation for missing data.
- Safety analyses included all patients who received ≥1 dose of either drug.
- IXORA-R is still blinded for investigators, sponsor's study team, and patients.
- Not all efficacy and safety data have been disclosed at this time to maintain study blinding and integrity.

Patient Completion and Disposition Through Week 12



Note: 485 patients in the IXE arm and 482 patients in the GUS arm continued study treatment after 12 weeks. GUS, guselkumab; IXE, ixekizumab

Baseline Demographics and Disease Activity

	GUS N=507	IXE N=520
Age (years), mean (SD)	49 (14.9)	49 (13.9)
Male, n (%)	314 (62)	338 (65)
White race, n (%)	431 (85)	439 (85)
Weight (kg), mean (SD)	95 (24.9)	97 (24.9)
<100 kg, n (%)	336 (66)	322 (62)
≥100 kg, n (%)	171 (34)	197 (38)
BMI (kg/m²), mean (SD)	33 (7.9)	33 (7.9)
Country		
Canada, n (%)	106 (21)	103 (20)
United States, n (%)	401 (79)	417 (80)
PASI total score, mean (SD)	19.3 (7.1)	19.5 (7.9)
sPGA category, n (%)		
=3	252 (50)	266 (51)
=4	232 (46)	224 (43)
=5	23 (4.5)	29 (5.6)
% BSA, mean (SD)	23.8 (15.4)	24.1 (16.1)
Duration of psoriasis (years), mean (SD)	16.3 (13.8)	17.5 (13.8)
DLQI total score, mean (SD)	13.2 (7.4)	12.8 (6.9)
Itch NRS, mean (SD)	7.1 (2.5)	6.9 (2.4)
Skin pain VAS, mean (SD)	47.2 (30.5)	47.0 (29.9)

BMI, body mass index; BSA, body surface area; DLQI, Dermatology Life Quality Index; GUS, guselkumab; IXE, ixekizumab; NRS, Numeric Rating Scale; PASI, Psoriasis Area and Severity Index; sPGA, static Physician's Global Assessment; SD, standard deviation; VAS, Visual Analog Scale.

Previous Treatments

	GUS N=507	IXE N=520
Prior nonbiologic treatment		
Nonbiologic systemic, n (%)[a]	140 (28)	170 (33)
Topical therapy, n (%)[b]	352 (69)	373 (72)
Phototherapy, n (%)[c]	63 (12)	77 (15)
Prior biologics use, n (%)[d]	133 (26)	137 (26)
Number of prior biologics		
1	96 (19)	95 (18)
2	27 (5.3)	28 (5.4)
≥3	10 (2.0)	14 (2.7)
Prior biologic class		
IL-12/IL-23 only	14 (2.8)	11 (2.1)
IL-17 only	16 (3.2)	11 (2.1)
TNF only	67 (13)	84 (16)
Other	10 (2.0)	2 (0.4)
Multiple	26 (5.1)	29 (5.6)
Prior biologic failures	36 (7.1)	41 (7.9)

[a]Previous nonbiologic systemic therapy includes cyclosporine, methotrexate, corticosteroids, acitretin, fumaric acid derivatives, apremilast and other systemic agent. [b]Previous topical therapy includes prescription and non-prescription agents. [c]Previous phototherapy includes PUVA and UVB. [d]Previous biologic therapy includes efalizumab, ustekinumab, infliximab, etanercept, alefacept, adalimumab, golimumab, certolizumab pegol, secukinumab, brodalumab and other biologic agent. GUS, guselkumab; IL, interleukin; IXE, ixekizumab; TNF, tumor necrosis factor.

REFERENCES

1. Griffiths CE, et al. Lancet. 2015;386(9993):541-51.
2. Reich K, et al. Br J Dermatol. 2017;177(4):1014-1023.
3. Blauvelt, et al. Poster presented at: EADV-26th Congress. 2017 September 13-17; Geneva, Switzerland.
4. Reich, et al. Poster presented at: World Congress of Dermatology; 2019 June 10-15; Milan, Italy.

DISCLOSURE

Previously presented at the Maui Derm NP+PA Fall 2019, Asheville, NC; 2-5 October 2019

6th Belgian Dermatology Days (BDD) 2020; Brussels, Belgium; March 12-13, 2020

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