

# Ixekizumab provides persistent improvements in health-related quality of life and the sexual impact associated with moderate-to-severe genital psoriasis in adult patients during a 52-week, randomised, placebo-controlled, phase 3 clinical trial

## Editor

Genital psoriasis (GenPs) has been reported in up to 63% of patients with psoriasis. It is often associated with significant impairment of health-related quality of life (HRQoL),<sup>1,2</sup> including a significantly greater impact on sexual health than psoriasis with no genital involvement.<sup>1,3</sup> Despite its prevalence and burden, GenPs is often underdiagnosed and undertreated.<sup>4,5</sup>

Ixekizumab (IXE), a high-affinity monoclonal antibody selectively targeting interleukin-17A (IL-17A), is the only United States Food and Drug Administration-approved treatment for patients with moderate-to-severe plaque psoriasis that includes labelling information about successful treatment of patients with genital involvement.<sup>6</sup> In the IXORA-Q trial, IXE provided significant improvements in HRQoL and in the sexual impact of GenPs following 12 weeks of treatment.<sup>7,8</sup> Here, we report the persistence of these improvements through 52 weeks.

Patient eligibility criteria have been previously published<sup>6–8</sup>; 149 patients were enrolled in the induction period (Weeks 0–12); patients randomised to either placebo (PBO) or Ixekizumab (IXEQ2W); most had GPSIS-Impact scores of  $\geq 3$  (moderate-to-very high), nearly one-third of patients had GPSIS-Avoidance score of 5 (always avoid sexual activity due to GenPs). At Week 12, 93% of patients (PBO:  $n = 65$ ; IXE Q2W:  $n = 74$ ) entered the open-label treatment period wherein all patients received IXE 80 mg every 4 weeks (Q4W) until Week 52, with initial PBO randomised patients receiving a 160 mg IXE starting dose. Dosing could be increased if necessary to achieve or maintain satisfactory disease control.<sup>6</sup>

Patients treated with IXE achieved persistent improvements in HRQoL, as measured by DLQI (0,1) and multiple domains of SF-36, and in the sexual impact of GenPs, at Week 12; these improvements persisted through Week 52. In the group that received IXE in both periods (IXE/IXE), the proportion of patients with GPSIS-Avoidance (1,2) response persisted through Week 52, with 80% ( $n = 24/30$ ) achieving GPSIS-Avoidance (1,2). Upon switching from PBO to IXE, GPSIS-Avoidance (1,2) responses rapidly increased from 26% ( $n = 9/35$ ) (Week 12) to 72% ( $n = 21/29$ ) (Week 16) and 79% ( $n = 23/29$ ) (Week 52)

(Fig. 1a). Upon switching from PBO to IXE, GPSIS-Impact (1,2) response rapidly increased from 53% ( $n = 9/17$ )<sup>1</sup> (Week 12) to 94% (15/16) (Week 16) and persisted through Week 52 (93%,  $n = 13/14$ ). GPSIS-Impact (1,2) responses were numerically higher in the PBO/IXE group during the open-label treatment period (Fig. 1b).

In the IXE/IXE population, 47% of patients achieved a DLQI (0,1) at Week 12 that persisted through Week 52 (Fig. 1c). DLQI item 9 (0,1) was achieved by 85% of IXE/IXE patients at Week 52 (Fig. 1d). 51% of patients in the PBO/IXE group achieved DLQI (0,1) at Week 52, and 94% of patients achieved DLQI item 9 (0,1) at Week 52 (Fig. 1c and 1d).

At Week 12, IXE treatment resulted in significantly greater mean change from baseline in six SF-36 domains,<sup>9</sup> and the physical component summary (PCS; Table 1). Upon switching to IXEQ4W, the mean change from baseline for all SF-36 domains and both component summary scores increased from Week 12 to Week 52 in the PBO/IXE group. In the IXE/IXE group, improvements observed at Week 12 generally persisted through Week 52 but were numerically lower.

The rapid onset of efficacy and significant improvement of signs and symptoms of GenPs with IXE, were reported previously.<sup>7,8</sup> Our results suggest IXE-treated patients achieved significant clinical improvements in GenPs symptoms, HRQoL, and the sexual impact of GenPs that persisted for up to 1 year, supporting the previous results of the IXORA-Q study and IXE as an efficacious treatment option for moderate-to-severe GenPs.

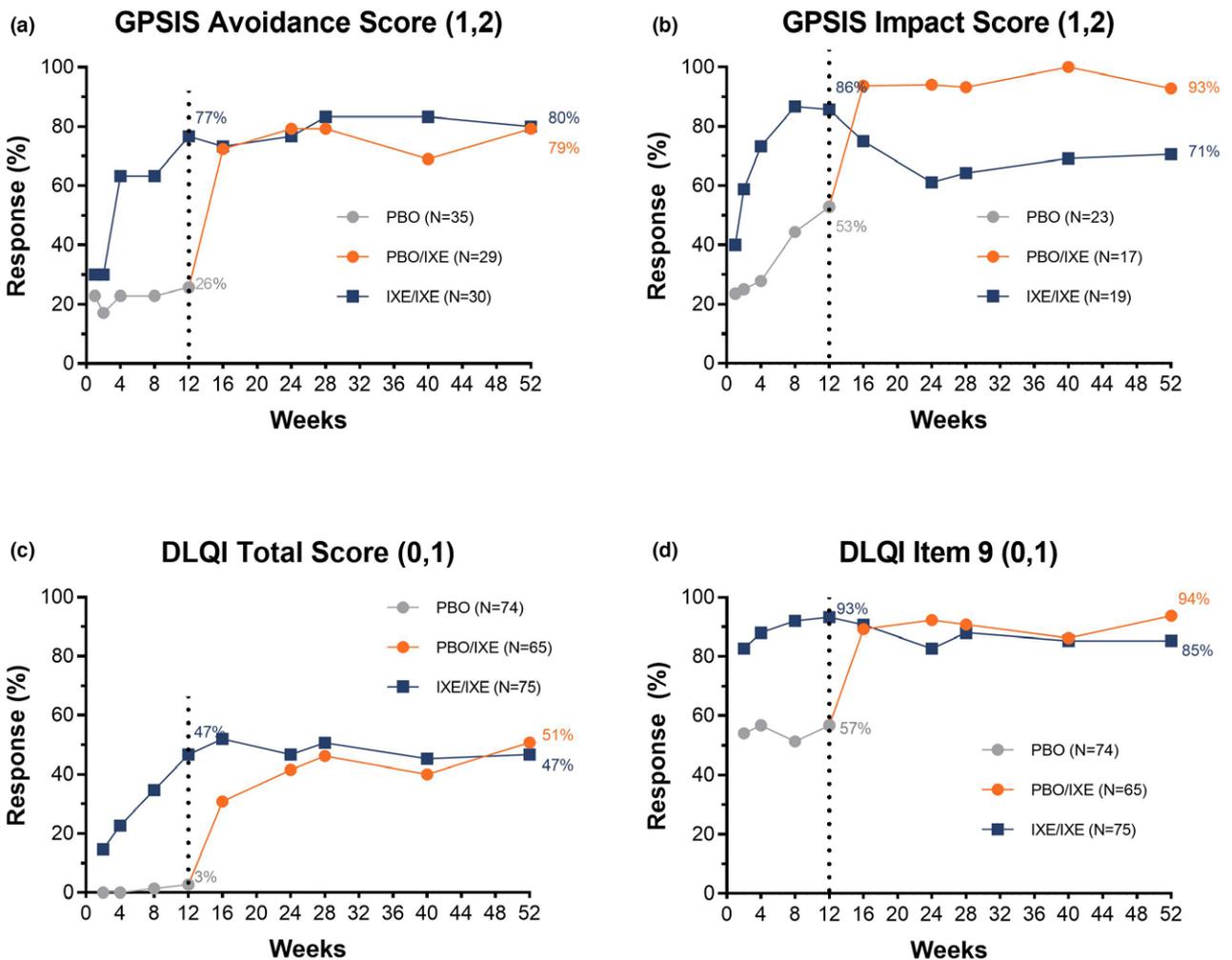
## Acknowledgements

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## Data availability statement

Lilly provides access to all individual participant data collected during the trial, after anonymization, except for pharmacokinetic or genetic data. Data are available to request 6 months after the indication studied has been approved in the US and EU and after primary publication acceptance, whichever is later. No expiration date of data requests is currently set once data are made available. Access is provided after a proposal has been approved by an independent review committee identified for this purpose and after receipt of a signed data sharing agreement. Data and documents, including the study protocol, statistical analysis plan, clinical study report, blank or annotated case report forms, will be provided in a secure data sharing

<sup>1</sup>Response for GPSIS-impact analysis based on the Mx+Px; abbreviations: Mx=number of patients who report being sexually active on the GPSIS Item 1; Px=number of patients who do not report on GPSIS Item 1.



**Figure 1** GPSIS-Avoidance (1,2), and GPSIS-Impact (1,2) outcomes, along with DLQI (0,1) and DLQI item 9 (0,1) responses rates, through Week 52 of IXORA-Q (non-responder imputation [based on patients with Mx + Px<sup>1</sup> for GPSIS-impact]) including blinded T2T and open-label T2T periods. (a) Proportion of patients who reported that they never (1) or rarely (2) avoided sexual activity due to GenPs (GPSIS-Avoidance [1,2]) [based on patients with GPSIS-avoidance score  $\geq 3$  at baseline]; (b) Proportion of patients who reported a very low or not at all (1) or low (2) level of worsening of GenPs symptoms following sexual activity (GPSIS-Impact [1,2]) [based on patients with GPSIS-avoidance score  $\geq 3$  at baseline]; (c) Proportion of patients achieving a response of (0,1) in DLQI total score indicating no effect on HRQoL; (d) Proportion of patients achieving a response of (0,1) on DLQI item 9, indicating 'no' (0) or 'a little' (1) sexual difficulties due to skin. The dotted line separates the double-blind treatment period (Weeks 0–12) and the open-label treatment period (Weeks 12–52).

environment. For details on submitting a request, see the instructions provided at [www.vivli.org](http://www.vivli.org).

### Conflicts of interest

CR has received compensation as a speaker, consultant, or advisor for AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Dermira, Dr Reddys, Janssen, LEO Pharma, Eli Lilly and Company, Novartis, Regeneron-Sanofi, and UCB. LG has been a consultant, investigator, and speaker for AbbVie, Amgen, Celgene, Eli Lilly and Company, Janssen, LEO Pharma, Merck, and Pfizer; has been a speaker and consultant for Valeant and Tribute; and has been an

investigator for UCB and Sun Pharmaceuticals. PF has served as an investigator, speaker, advisor, or received travel/grant/research support from 3M/iNova/Valeant, Abbott/AbbVie, Amgen, Arcutis, Ascent, Aslan, Aspen, Australian Ultraviolet Services, Biogen Idec, Boehringer Ingelheim, Botanix, Bristol-Myers Squibb, Celgene, Celtaxsys, Clinuvel, Cutanea, Dermira, CSL, Eli Lilly and Company, Galderma, Genentech, GlaxoSmithKline/Stiefel, Hexima, Janssen-Cilag, LEO Pharma/Peplin, Merck Serono, Novartis, Regeneron, Reistone, Roche, Sanofi, Schering-Plough/MSD, Sun Pharma, UCB Pharma, Valeant, and Wyeth/Pfizer. JW has been an investigator for AbbVie, Amgen, Biogen, Boehringer Ingelheim, Celgene, Eli

**Table 1** Mean change from baseline in SF-36 domains at Weeks 12 and 52

| Domain                                     | Week 12                       |                               |                  | Week 52                        |                                |
|--|-------------------------------|-------------------------------|------------------|--------------------------------|--------------------------------|
|  | PBO/IXE (N = 65)<br>LSM (±SE) | IXE/IXE (N = 74)<br>LSM (±SE) | P-value          | PBO/IXE (N = 65)<br>Mean (±SE) | IXE/IXE (N = 74)<br>Mean (±SE) |
| Physical functioning                       | 1.7 (1.8)                     | 9.7 (1.8)                     | <b>0.002</b>     | 10.6 (3.0)                     | 5.9 (2.1)                      |
| Role limitations due to physical health    | 1.3 (2.0)                     | 13.5 (2.0)                    | <b>&lt;0.001</b> | 10.10 (3.7)                    | 9.8 (2.8)                      |
| Bodily pain                                | 4.1 (2.5)                     | 20.9 (2.5)                    | <b>&lt;0.001</b> | 19.6 (3.7)                     | 13.9 (3.3)                     |
| General health perceptions                 | 2.6 (1.6)                     | 5.5 (1.6)                     | 0.215            | 5.2 (2.5)                      | 3.7 (1.7)                      |
| Vitality                                   | 2.9 (1.9)                     | 7.6 (1.9)                     | 0.081            | 9.4 (2.7)                      | 4.5 (2.2)                      |
| Social functioning                         | 2.9 (2.1)                     | 14.5 (2.1)                    | <b>&lt;0.001</b> | 16.2 (3.3)                     | 9.5 (3.3)                      |
| Role limitations due to emotional problems | 4.1 (1.6)                     | 9.4 (1.6)                     | <b>0.02</b>      | 10.1 (3.0)                     | 4.4 (2.6)                      |
| Mental health                              | 3.7 (1.3)                     | 7.5 (1.3)                     | <b>0.041</b>     | 6.5 (2.0)                      | 5.9 (1.8)                      |
| PCS  | 0.7 (0.8)                     | 5.2 (0.8)                     | <b>&lt;0.001</b> | 4.5 (1.2)                      | 2.5 (1.1)                      |
| Mental health component summary (MCS)      | 2.2 (0.7)                     | 4.0 (0.7)                     | 0.085            | 4.9 (1.3)                      | 3.6 (0.9)                      |

Data is change from baseline (mBOCF). The ANCOVA model includes treatment, baseline BSA category, and baseline value.

Abbreviations: BSA, body surface area; IXE, ixekizumab; LSM, least squares mean; mBOCF, modified baseline observation carried forward; MCS, mental health component summary; PBO, placebo; PCS, physical component summary; SE, standard error.

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## Atopic dermatitis and depressive symptoms. Results of the German national AD Registry TREATgermany

Dear Editor,

TREATgermany is a multicentre academic registry for the long-term observation of patients with moderate-to-severe atopic dermatitis (AD). Eligibility criteria, study procedures and baseline characteristics including previous treatments have already been