Treatment outcomes with ixekizumab in patients with moderate-to-severe psoriasis who have or have not received prior biological therapies: an integrated analysis of two Phase III randomized studies

A.B. Gottlieb, J.-P. Lacour, N. Korman, S. Wilhelm, Y. Dutronc, A. Schacht, J. Erickson, L. Zhang, L. Mallbris, S. Gerdes

1Department of Dermatology, New York Medical College, Valhalla, NY, USA
2Department of Dermatology, University Hospital of Nice, Nice, France
3Murdough Family Center for Psoriasis, University Hospitals Case Medical Center, Cleveland, OH, USA
4Global Medical Affairs, Lilly Deutschland GmbH, Bad Homburg, Germany
5Regional Medical Affairs, Lilly France, Neullly-sur-Seine, France
6Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN, USA
7Department of Dermatology, Psoriasis-Center, University Medical Center Schleswig-Holstein, Kiel, Germany

*Correspondence: A.B. Gottlieb. E-mail: alice.gottlieb@gmail.com

Abstract

Background  Biologics are effective for the treatment of psoriasis. However, treatment outcomes may differ among biologic-naive patients and those switched from previous biological therapies.

Objectives  The study’s objective was to investigate efficacy and safety of ixekizumab, a high-affinity anti-interleukin-17A antibody, in patients with psoriasis with and without previous exposure to biologics.

Methods  Data were integrated from the 12-week induction phase of two etanercept-controlled Phase III trials. Patients received 80 mg ixekizumab every 2 weeks (IXE Q2W; N = 736) or every 4 weeks (IXE Q4W; N = 733) following a 160-mg starting dose, or placebo (N = 361). Etanercept (50 mg twice weekly; N = 740) was administered as active control. Psoriasis Area and Severity Index (PASI) 75, PASI 90 and PASI 100 response rates at week 12 were evaluated in patients with or without previous exposure to biologics. Treatment effects were analysed with the Cochran–Mantel–Haenszel test stratified by study; missing values were imputed as non-response.

Results  Overall, 497 (19.3%) patients had prior exposure to biologics and 2073 (80.7%) were naive to biologic therapy. PASI 75 was achieved by 91.5% of biologic-experienced patients and 87.7% of biologic-naive patients for IXE Q2W, 76.2% and 82.2% for IXE Q4W, respectively, and 34.6% and 50.7%, respectively, for etanercept. Higher response rates favouring each ixekizumab dose over etanercept within subgroups were also seen regarding PASI 90 and PASI 100.

Conclusions  Contrary to etanercept, the efficacy of ixekizumab was similarly high in patients with and without previous exposure to biologics when administered 80 mg every 2 weeks.

Received: 10 June 2016; Accepted: 16 September 2016

Conflicts of Interest

Drs. Wilhelm, Dutronc, Schacht, Erickson, Mallbris and Ms. Zhang are all full-time employees of, and shareholders in, Eli Lilly and Company. Dr. Gottlieb has current consulting/advisory board agreements with Amgen Inc., Astellas, Akros, Centocor (Janssen), Inc., Celgene Corp., Bristol Myers Squibb Co., Beiersdorf, Inc., Abbott Labs. (Abbvie), TEVA, Actelion, UCB, Novo Nordisk, Novartis, Dermispor Ltd., Incyte, Pfizer, Canfile, Lilly, Coronado, Vertex, Karyopharm, CSL Behring Biotherapies for Life, Glaxo Smith Kline, Xenoprot, Catabasis, Meiiji Seika Pharma Co., Ltd, Takeda, Mitsubishi Tanabe Pharma Development America, Inc, Genentech, Baxalta, and Kineta One. Dr. Gottlieb has also received research/educational grants (paid to Tufts Medical Center) from Centocor (Janssen), Amgen, Abbott (Abbvie), Novartis, Celgene, Pfizer, Lilly, Coronado, Levi, Merck, Xenoprot, Dermis, and Baxalta. Dr. Lacour has been an advisor and/or received speaking fees and/or grants and/or participated in clinical trials of the following companies: Abbott/AbbVie, Amgen, Boehringer, Celgene, Eli Lilly, Galderma, Leo Pharma, MSD, Novartis, Pfizer, UCB Pharma and Regeneron. Dr. Gerdes has been an advisor and/or received speaking fees and/or grants and/or participated in clinical trials of the following companies: Abbott/AbbVie, Almirall-Hermal, Amgen, Biogen Idec, Celgene, DERMIRA INC., Eli Lilly, Forward Pharma,
Introduction

Biologic agents have revolutionized the treatment of moderate-to-severe psoriasis over the past decade. Currently available agents target proinflammatory cytokines, such as tumour necrosis factor alpha, interleukin (IL)-12/23 and more recently IL-17A.1–6 Biologic drugs seem to provide higher levels of efficacy than conventional systemic drugs, and they have good safety profiles with no evidence for cumulative toxicity.7 However, data from registries report limited drug survival, with the main reason for patient discontinuation of biologic agents being loss of drug efficacy.8–12 Hence, most patients will receive multiple agents throughout their lives. Existing data, in particular from clinical trials, suggest that efficacy of biologics is lower in patients with previous exposure to other biologics,13,14 although the reasons for this remain uncertain. Hence, for therapies under development, it is clinically important to provide evidence of efficacy in patients who have been exposed to prior therapy, and especially in those exposed to prior biologics.

Ixekizumab is a high-affinity monoclonal antibody that selectively targets IL-17A. It has been shown to have significantly superior efficacy compared to placebo and etanercept in patients with psoriasis in UNCOVER Phase III studies.15,16 The objective of this analysis was to investigate the efficacy and safety of ixekizumab in patients with or without prior use of biologic therapy by utilizing integrated data from two Phase III clinical trials.

Materials and methods

Study population

As reported previously, eligible patients were ≥18 years of age with a diagnosis of chronic plaque psoriasis ≥6 months prior to baseline, candidates for phototherapy and/or systemic therapy, had ≥10% body surface area involvement, had a static Physician’s Global Assessment score of ≥3 and a Psoriasis Area and Severity Index (PASI) score of ≥12 at both screening and baseline visits.

Key exclusion criteria included diagnosis of non-plaque psoriasis; a clinically significant flare of psoriasis within 12 weeks prior to baseline visit; prior participation in any study involving ixekizumab or other IL-17 antagonists; any prior use of etanercept; use of conventional systemic non-biologic psoriasis therapy or phototherapy within 4 weeks prior to baseline visit or topical psoriasis treatment within 2 weeks prior to baseline; use of potent class 1–5 topical steroids within 2 weeks prior to baseline; having a serious infection, active or latent tuberculosis, human immunodeficiency virus, or hepatitis C or hepatitis B infections; or meeting specific laboratory criteria. Prior use of biologic therapies was allowed but required specific washout periods prior to baseline.

Study protocols and informed consent forms were approved by an investigational review board at each site. The study was conducted in accordance with ethical principles of Good Clinical Practice and the Declaration of Helsinki and its guidelines. Written informed consent was obtained from each patient at study entry before any study procedures.

Study designs

Integrated data from two Phase III multicenter, randomized, double-blind, placebo-controlled, parallel-group trials (UNCOVER-2 and UNCOVER-3) were used in this analysis. For the first 12 weeks of the trials, UNCOVER-2 and UNCOVER-3 compared the efficacy and safety of ixekizumab vs. etanercept, and vs. placebo.

We evaluated the efficacy and safety of ixekizumab in patients with or without prior exposure to biologic drugs relative to etanercept using these integrated data in which patients received placebo (N = 361), or ixekizumab every 2 weeks (IXE Q2W; N = 736) or 4 every weeks (IXE Q4W; N = 733) following a 160-mg initial ixekizumab dose. Etanercept (50 mg mg twice weekly; N = 740) was administered as active control. Efficacy and safety data in the overall population have already been reported.10

Further details regarding the individual study designs are presented in the Supplementary Material section (Supplementary Fig. S1a,b) and have already been reported.16

Efficacy and safety endpoints

Key efficacy endpoints for this analysis included the proportions of patients achieving PASI 75 (at least a 75% improvement in
PASI from baseline), PASI 90 (at least a 90% improvement in PASI from baseline), complete resolution of psoriasis plaques as defined by PASI 100 (100% improvement in PASI from baseline) and ≥4-point improvement in Itch Numeric Rating Scale (NRS).

Safety was assessed based on reported adverse events and laboratory values obtained at study visits through week 12. Treatment-emergent adverse events (TEAEs) were defined as those that appeared or worsened any time after first injection and on or prior to the date of the last visit within the evaluation period.

Further details regarding the clinical outcome assessments have already been reported.16

**Statistical analysis**

Unless otherwise specified, the efficacy analyses were conducted on an intent-to-treat basis. For Itch NRS, the analysis was based on the intent-to-treat patients who had baseline Itch NRS ≥4. Characteristics were compared between biologic-naïve and biologic-experienced patients based on the Cochran–Mantel–Haenszel test stratified by study for categorical data and analysis of variance for continuous data with previous biologic status and study as independent factors. Treatment effects were analysed using the Cochran–Mantel–Haenszel test stratified by study; confidence intervals for risk differences were based on the normal approximation of the binomial distribution. Missing data were imputed using a non-responder imputation method, in which a patient was defined as a non-responder if he/she did not meet clinical response criteria or had missing clinical response data for any reason at analysis time point.

Safety analyses were conducted on patients who received at least one dose of study treatment. Treatment comparisons were conducted using the Cochran–Mantel–Haenszel (CMH) test stratified by study.

**Results**

**Baseline demographics and disposition**

In the overall population, patient baseline characteristics were well balanced among the different treatment groups across the individual studies included in the analysis (Supplementary Table S1). Table 1 provides details on previous psoriasis therapy for UNCOVER-2 and UNCOVER-3.

Table 2 displays patient demographics and other baseline characteristics examined by previous biologic status (biologic-naïve vs. biologic-experienced) for the integrated dataset. Key characteristics, including weight and disease severity at baseline, were similar between patients with and without prior biologic exposure. As expected, some baseline variables and clinical characteristics were significantly different between the two groups, including age (∼ < 0.001), geographical region (∼ < 0.001), previous non-biologic systemic therapy (∼ < 0.001), duration of psoriasis symptoms (∼ < 0.001), baseline Dermatology Life Quality Index (DLQI) score (∼ < 0.006) and baseline Itch NRS (∼ < 0.001). Biologic-experienced patients were older, were more frequently from North America, and had more non-biologic treatment exposure, a longer duration of disease and worse DLQI and Itch NRS scores at baseline.

**Efficacy – signs**

Psoriasis Area and Severity Index 75 was achieved by 91.5% (biologic-experienced) and 87.7% (biologic-naïve) of patients treated with IXE Q2W, 76.2% and 82.2% of patients treated with IXE Q4W compared to 34.6% and 50.7% of patients treated with etanercept respectively (Fig. 1). PASI 90 was achieved by 76.1% (biologic-experienced) and 67.7% (biologic-naïve) of patients treated with IXE Q2W, 55.2% and 64.4% of patients treated with IXE Q4W and 13.2% and 24.3% of patients treated with etanercept. PASI 100 was achieved by 47.2% (biologic-experienced) and 37.0% (biologic-naïve) of patients treated with IXE Q2W, 25.2% and 34.9% of patients treated with IXE Q4W and 3.7% and 7.0% of patients treated with etanercept.

Differences compared to the etanercept group in PASI 75 response rates ranged from 31.5% (IXEQ4W-naïve) to 57.0% (IXEQ2W-experienced) (Table 3). Differences in PASI 90 response rates compared to the etanercept group ranged from

![Table 1](https://example.com/table1.png)

| Characteristics | UNCOVER-2 (N = 1224) | UNCOVER-3 (N = 1346) |
|-----------------|----------------------|----------------------|
| **Patients with ≥1 previous psoriasis therapy, N (%)** | | |
| **Previous psoriasis therapy type, N (%)** | | |
| Topical prescription | 1007 (82.3) | 1063 (79.0) |
| Topical non-prescription | 172 (14.1) | 244 (18.1) |
| Biologic agent, N (%) | | |
| Efalizumab | 14 (1.1) | 13 (1.0) |
| Ustekinumab | 102 (8.3) | 74 (5.5) |
| Infliximab | 55 (4.5) | 28 (2.1) |
| Etanercept | 0 (0.0) | 1 (0.1) |
| Alefacept | 16 (1.3) | 5 (0.4) |
| Adalimumab | 101 (8.3) | 77 (5.7) |
| Golimumab | 5 (0.4) | 1 (0.1) |
| Other* | 95 (7.8) | 68 (5.1) |
| Non-biological systemic agent, N (%) | | |
| Cyclosporine | 122 (10.0) | 63 (4.7) |
| Methotrexate | 377 (30.8) | 332 (24.7) |
| Acitretin | 164 (13.4) | 105 (7.8) |
| Other† | 228 (18.6) | 311 (23.1) |
| Phototherapy, N (%) | | |
| PUVA | 243 (19.9) | 218 (16.2) |
| UBV | 392 (32.0) | 342 (25.4) |
| Unknown | 28 (2.3) | 42 (3.1) |

*Names of biologic agents were not documented.
†Names of non-biological systemic agents were not documented.
PUVA, psoralen and ultraviolet light A; UVB, ultraviolet light B.
40.1% (IXEQ4W-naive) to 62.8% (IXEQ2W-experienced) (Table 3). PASI 100 response rate differences, compared to the etanercept group, ranged from 21.5% (IXEQ4W-experienced) to 43.5% (IXEQ2W-experienced) (Table 3). Greater differences compared to etanercept were observed for the IXEQ2W treatment arm for all outcomes and biologic-experienced patients in the IXEQ2W arm had higher differences relative to etanercept for all outcomes.

Efficacy – symptoms

At least four points reduction in Itch NRS was achieved by 82.4% (biologic-experienced) and 84.1% (biologic-naive) of patients from the IXE Q2W arm, 80.3% and 77.9% of the patients from the IXE Q4W arm compared to 55.0% and 62.4% of patients treated from the etanercept arm (Fig. 1). Itch NRS ≥4 response rate differences, compared to the etanercept arm ranged from 11.7% (IXEQ4W-naive) to 24.0% (IXEQ2W-experienced) (Table 3).

Safety

A total of 687 (58.3%) biologic-naive and 156 (54.7%) biologic-experienced, ixekizumab-treated patients in the induction dosing period, who received at least one dose of study medication, experienced at least one TEAE. In comparison, 324 (53.6%) and 75 (55.6%) etanercept-treated patients and 126 (44.4%) and 34 (44.7%) placebo-treated patients experienced at least one TEAE respectively. Serious adverse events (SAEs) were reported by 2.1% or fewer of patients in each treatment group, with SAE incidence slightly higher in naive vs. experienced patients across all treatment groups. There were no deaths in the induction period.
dosing period. Overall, a similar safety profile was observed between biologic-naive and biologic-experienced patients.

Table 4 shows adverse events of special interest during the induction period by previous biologic status (biologic-naive vs. biologic-experienced). There was no difference in overall infections among biologic-experienced patients across treatment groups. For IXE Q4W- and IXE Q2W-treated patients, rates of infection between biologic-naive (26.1% and 26.0% respectively) and biologic-experienced (26.6% and 25.4% respectively) patients were comparable, while rates were slightly lower for biologic-naive patients in the placebo (19.4%) and etanercept (20.9%) groups. The rate of infections was 24.4% in biologic-experienced and 20.9% in biologic-naive etanercept-treated patients which overall was similar in comparison to ixekizumab-treated patients. Three major adverse cerebro-cardiovascular events were reported; non-fatal myocardial infarction (n = 2) by a placebo-treated and an etanercept-treated patient and non-fatal stroke (n = 1) by an IXE Q4W-treated patient. Lastly, few cases of candidiasis were reported across treatment groups.

### Discussion

Currently, little data are available regarding the difference in therapeutic response of biologic therapy when used in biologic-naive patients or after exposure to other biologics. Several phenomena can be responsible for the loss of efficacy of a biologic agent but they are rarely identified in clinical practice. It is generally thought to be beneficial to switch to a different mechanism of action after loss of efficacy or failure of the initial biologic. In the UNCOVER Phase III studies, ixekizumab, an anti-IL-17A monoclonal antibody, was shown to be highly effective in treating moderate-to-severe plaque psoriasis, with superiority to etanercept, with respect to PASSI and Itch NRS measures. Here, we show that ixekizumab has similarly high efficacy in patients with and without prior biologic experience and results of this integrated analysis also demonstrate that ixekizumab was significantly more effective compared to etanercept, regardless of previous biologic treatment.

Both IXE Q2W and IXE Q4W 80-mg dose regimens provided statistically significantly higher response rates across all efficacy endpoints vs. etanercept in both biologic-naive and biologic-experienced. However, the IXE Q2W dosing regimen, which had the highest response rates, led to more predictable treatment outcomes with the lowest differences in response between the biologic-naive and biologic-experienced subgroups. In these trials, etanercept showed lower efficacy in patients with previous exposure to biologic therapy compared to patients who were
biologic-naive, which is consistent with data reported from an observational study.\textsuperscript{14} Weight and disease severity have been hypothesized to influence the clinical response of biologics.\textsuperscript{17} These characteristics were similar between patients with and without previous exposure to biologic therapy. Interestingly, patients with previous exposure to biologic therapy tended to be older (47.2 vs. 44.9 years) and had a longer duration of psoriasis symptoms (21.4 vs. 17.7 years). Additionally, more patients were from North America (65.4\% vs. 47.6\%) and more patients had received previous non-biologic systemic therapy (60.0\% vs. 50.9\%). Lastly, patients with previous exposure to biologic therapy scored 1 point higher on the DLQI at baseline (13.0 vs. 12.0), and 0.6 point more itch on the Itch NRS at baseline (6.9 vs. 6.3), reflecting a higher burden of diseases. It is probable that these differences might be due to different access to medication among different countries and that patients with prior exposure represent more difficult-to-treat patients with worse quality of life and more severe pruritus.

For safety, patients who had previous exposure to biologic therapy experienced fewer TEAEs or SAEs when treated with either dose of ixekizumab. Patients who had previous exposure to biologic therapy did not experience more infections when treated with IXE Q2W, whereas there was a numerical increase from 20.9\% to 24.4\% in patients treated with etanercept.

**Table 4** Adverse events of special interest (UNCOVER-2 and -3) according to biologic status

| Event                                      | PBO (\(N = 360\)) | ETN (\(N = 739\)) | IXE Q4W 80 mg (\(N = 729\)) | IXE Q2W 80 mg (\(N = 734\)) |
|--------------------------------------------|--------------------|-------------------|-----------------------------|-----------------------------|
| **≥1 TEAE**                                |                    |                   |                             |                             |
| Naive                                      | 126 (44.4)         | 324 (53.6)        | 341 (58.2)                  | 346 (58.4)                  |
| Experienced                                | 34 (44.7)          | 75 (53.6)         | 78 (54.5)                   | 78 (54.9)                   |
| **≥1 SAE**                                 |                    |                   |                             |                             |
| Naive                                      | 6 (2.1)            | 12 (2.0)          | 12 (2.0)                    | 12 (2.0)                    |
| Experienced                                | 1 (1.3)            | 2 (1.5)           | 2 (1.4)                     | 2 (1.4)                     |
| **Death**                                  |                    |                   |                             |                             |
| Naive                                      | 0 (0.0)            | 0 (0.0)           | 0 (0.0)                     | 0 (0.0)                     |
| Experienced                                | 0 (0.0)            | 0 (0.0)           | 0 (0.0)                     | 0 (0.0)                     |
| **Infections**                             |                    |                   |                             |                             |
| Naive                                      | 55 (19.4)          | 126 (20.9)        | 153 (26.1)                  | 154 (26.0)                  |
| Experienced                                | 19 (25.0)          | 33 (24.4)         | 38 (26.6)                   | 36 (25.4)                   |
| **Major adverse cerebro-cardiovascular events** |                    |                   |                             |                             |
| Cardiovascular death                       |                    |                   |                             |                             |
| Naive                                      | 0 (0.0)            | 0 (0.0)           | 0 (0.0)                     | 0 (0.0)                     |
| Experienced                                | 0 (0.0)            | 0 (0.0)           | 0 (0.0)                     | 0 (0.0)                     |
| Non-fatal myocardial infarction            |                    |                   |                             |                             |
| Naive                                      | 1 (0.4)            | 0 (0.0)           | 0 (0.0)                     | 0 (0.0)                     |
| Experienced                                | 0 (0.0)            | 1 (0.7)           | 0 (0.0)                     | 0 (0.0)                     |
| Non-fatal stroke                           |                    |                   |                             |                             |
| Naive                                      | 0 (0.0)            | 0 (0.0)           | 1 (0.2)                     | 0 (0.0)                     |
| Experienced                                | 0 (0.0)            | 0 (0.0)           | 0 (0.0)                     | 0 (0.0)                     |
| Oral candidiasial                          |                    |                   |                             |                             |
| Naive                                      | 0 (0.0)            | 1 (0.2)           | 0 (0.0)                     | 3 (0.5)                     |
| Experienced                                | 0 (0.0)            | 0 (0.0)           | 1 (0.7)                     | 2 (1.4)                     |
| Vulvovaginal candidiasis                   |                    |                   |                             |                             |
| Naive                                      | 0 (0.0)            | 0 (0.0)           | 2 (1.1)                     | 0 (0.0)                     |
| Experienced                                | 0 (0.0)            | 1 (1.9)           | 0 (0.0)                     | 0 (0.0)                     |
| Skin candidia                              |                    |                   |                             |                             |
| Naive                                      | 0 (0.0)            | 0 (0.0)           | 0 (0.0)                     | 2 (0.3)                     |
| Experienced                                | 0 (0.0)            | 0 (0.0)           | 0 (0.0)                     | 0 (0.0)                     |
| Crohn’s disease                            |                    |                   |                             |                             |
| Naive                                      | 0 (0.0)            | 0 (0.0)           | 0 (0.0)                     | 1 (0.2)                     |
| Experienced                                | 0 (0.0)            | 0 (0.0)           | 0 (0.0)                     | 0 (0.0)                     |
| Ulcerative colitis                         |                    |                   |                             |                             |
| Naive                                      | 0 (0.0)            | 0 (0.0)           | 0 (0.0)                     | 1 (0.2)                     |
| Experienced                                | 0 (0.0)            | 0 (0.0)           | 0 (0.0)                     | 0 (0.0)                     |

ETN, etanercept; IXE, ixekizumab; MedDRA, Medical Dictionary for Regulatory Activities; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks; SAE, serious adverse event; TEAE, treatment-emergent adverse event.
Some limitations to this analysis should be considered. A major limitation was that the included studies were not stratified by prior treatment. Another limitation was that the information regarding biologic treatment is retrospective. Although patients from many geographic regions were included, the study populations were mainly Whites. Evaluation in a larger population of non-white participants who are biologic-naive or biologic-experienced would help to understand the efficacy and safety of ixekizumab in a more genetically diverse population. Lastly, the analysis only included data from the first 12 weeks of the studies. Further investigations could possibly target later time points to see if different profiles of the biologic-naive and biologic-experienced populations are observed.

Both doses of ixekizumab were significantly superior to etanercept for biologic-naive and biologic-experienced patients. Treatment differences in IXE Q2W vs. etanercept increased for patients with previous exposure to biologics compared to patients who were naive, with comparable safety findings. The IXE Q2W dosing regimen consistently provided greater benefit with more predictable treatment outcomes across subgroups relative to the IXE Q4W dosing regimen.

Acknowledgments
The authors thank all the investigators, their clinical staff members and the patients who participated in these studies. The authors also thank Shannon E. Gardell, PhD and Angela Lorio, ELS, of inVentiv Health Clinical, LLC, for their assistance with preparation of this manuscript.

References
1. Menter A. The status of biologic therapies in the treatment of moderate to severe psoriasis. Curr Opin Rheumatol 2009; 21(4 Suppl): 14–24.
2. Menter A, Korman NJ, Elmets CA et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: section 6. Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. J Am Acad Dermatol 2011; 65: 137–174.
3. Nast A, Boehncke WH, Mrowietz U et al. German S3-guidelines on the treatment of psoriasis vulgaris (short version). Arch Dermatol Res 2012; 304: 87–113.
4. Pathirana D, Ormerod AD, Saig P et al. European S3-guidelines on the systemic treatment of psoriasis vulgaris. J Eur Acad Dermatol Venereol 2009; 23(Suppl 2): 1–70.
5. Smith CH, Anstey AV, Barker JN et al. British Association of Dermatologists’ guidelines for biologic interventions for psoriasis 2009. Br J Dermatol 2009; 161: 987–1019.
6. Langley RG, Elewski BE, Lebwohl M et al. Secukinumab in plaque psoriasis—results of two phase 3 trials. N Engl J Med 2014; 371: 326–338.
7. Boehncke WH, Schön MP. Psoriasis. Lancet 2015; 386: 983–994.
8. Gniadecki R, Kragballe K, Dam TN, Skov L. Comparison of drug survival rates for adalimumab, etanercept and infliximab in patients with psoriasis vulgaris. Br J Dermatol 2011; 164: 1091–1096.
9. Esposito M, Gisondi P, Cassano N et al. Survival rate of anti-TNF alpha treatments for psoriasis in routine dermatological practice: a multicenter observational study. Br J Dermatol 2013; 169: 666–672.
10. Van den Reek JMPA, van LHumig PPM, Driessen RJ et al. Determinants of drug survival for etanercept in a long-term daily practice cohort of patients with psoriasis. Br J Dermatol 2014; 170: 415–424.
11. Menting SP, Sitaram AS, Bonnerjee-van der Stok HM et al. Drug survival not significantly different between biologics in patients with psoriasis vulgaris: a single-centre database analysis. Br J Dermatol 2014; 171: 875–883.
12. Van den Reek JM, Zweegers J, Kievit W et al. ‘Happy’ drug survival of adalimumab, etanercept and ustekinumab in psoriasis in daily practice care – results from the BioCAPTURE network. Br J Dermatol 2014; 171: 1189–1196.
13. Ruiz Salas V, Puig L, Alomar A. Ustekinumab in clinical practice: response depends on dose and previous treatment. J Eur Acad Dermatol Venereol 2012; 26: 508–513.
14. Mazzotta A, Esposito M, Costanzo A, Chimenti S. Efficacy and safety of etanercept in psoriasis after switching from other treatments: an observational study. J Am Acad Dermatol 2009; 60: 319–324.
15. Gordon K, Blauvelt A, Langley RG et al. Ixekizumab for treatment of moderate-to-severe plaque psoriasis: 12-week results from a phase 3 study (UNCOVER-1). Poster presented at: World Congress of Dermatology; June 8–13, 2015; Vancouver, Canada.
16. Griffiths CE, Reich K, Lebwohl M et al. Comparison of ixekizumab with etanercept or placebo in moderate-to-severe psoriasis (UNCOVER-2 and UNCOVER-3): results from two phase 3 randomised trials. Lancet 2015; 386: 541–551.
17. Edson-Heredia E, Sterling KL, Alatorre CI et al. Heterogeneity of response to biologic treatment: perspective for psoriasis. J Invest Dermatol 2014; 134: 18–23.

Supporting Information
Additional Supporting Information may be found in the online version of this article:

Figure S1. Study design for (A) UNCOVER-2 and (B) UNCOVER-3. Abbreviations: Pbo, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks; Q12W, every 12 weeks; LV, last visit; LY, LY2438921 (ixekizumab); V, visit; W, week.