Predictors of Response to Biologics in Patients with Moderate-to-Severe Psoriasis: A Danish Nationwide Cohort Study

Christopher Willy SCHWARZ1,2, Nikolai LOFT1,2, Mads Kirchheiner RASMUSSEN1, Christoffer V. NISSEN4, Tomas Norman DAM4, Kawa Khaled AJGEIY1, Alexander EGBERG1,2 and Lone SKOV1,2

1Department of Dermatology and Allergy, Herlev and Gentofte Hospital, University of Copenhagen, Hellerup, 2Copenhagen Research Group for Inflammatory Skin, Herlev and Gentofte Hospital, Hellerup, 3Department of Dermatology, Aarhus University Hospital, Aarhus, 4Department of Dermatology, Bispebjerg Hospital, Copenhagen, 5Dermatology Clinic, Nykøbing Falster and 6Department of Dermatology, Odense University Hospital, Odense, Denmark

Identifying patient characteristics associated with achieving treatment response to biologics in patients with psoriasis could prevent expensive switching between biologics. The aim of this study was to identify patient characteristics that predict the efficacy of treatment for biologics that inhibit tumour necrosis factor-α, interleukin-12/-23, and -17A. The study investigated biologic-naïve patients from the DERMBIO registry treated with adalimumab, etanercept, infliximab, secukinumab, or ustekinumab. Multivariable logistic models were conducted to assess associations between patient characteristics and treatment response. A total of 2,384 patients were included (adalimumab n = 911; etanercept n = 327; infliximab n = 152; secukinumab n = 323; ustekinumab n = 671). Smoking (odds ratio 0.74; 95% confidence interval (CI) 0.56–0.97; p = 0.03) and higher bodyweight (odds ratio 0.989; 95% CI 0.984–0.994; p < 0.001) reduced the odds of achieving response defined as Psoriasis Area and Severity Index ≤2.0 after 6 months of treatment. In conclusion, higher bodyweight and smoking were associated with a reduced probability of treatment response for tumour necrosis factor-α inhibitors, ustekinumab, and secukinumab.

Key words: psoriasis; biologics; lifestyle; smoking; bodyweight.

Accepted Aug 19, 2021; Epub ahead of print Oct 13, 2021
Acta Derm Venereol 2021; 101: adv00579.

Corr: Christopher Willy Schwarz, Department of Dermatology and Allergy, Gentofte Hospitalsvej 15, 1. floor, DK-2900 Hellerup, Denmark. E-mail: christopher.willy.schwarz.01@regionh.dk

Treatment of psoriasis with biologics is often reserved for patients with moderate-to-severe psoriasis, and for those with lack of effect or with side-effects to classic systemic treatment. Biologics are typically effective (1) and disease clearance leads to an increase in quality of life (2). However, a considerable proportion of patients do not respond to the given biologic and a treatment switch to another biologic is often required. This trial-and-error approach is expensive and frustrating for patients (3). The 12-month retention rate for tumour necrosis factor (TNF)-α inhibitors, ustekinumab, and secukinumab, has been reported to be 55–70%, 80–90%, and 70–90%, respectively (4–10). Identifying ways to optimize the retention rate and finding the most suitable treatment for each patient is important, to avoid disappointment in patients and avoid unnecessary and expensive switching between biologics. Biological markers (11) and patient characteristics (12) could be ways to identify patients with a higher chance of responding to a given biologic. Indeed, patient characteristics, such as smoking, higher bodyweight, and female sex, have been associated with reduced treatment response (12). In addition, treatment of patients with psoriasis and concomitant psoriatic arthritis (PsA) has been associated with a higher risk of discontinuation due to ineffectiveness when the patients are treated with ustekinumab, and increased drug survival when patients are treated with adalimumab, leading to the possibility of individual choice of biological therapy (10). In general, studies investigating patient characteristics associated with treatment response to biologics are mostly limited to older drugs, such as TNF-α inhibitors and ustekinumab.

In a nationwide cohort of patients with psoriasis, this study aimed to identify patient characteristics that predict the efficacy of treatment for biologics that inhibit TNF-α, interleukin (IL)-12/-23, and IL-17A. Furthermore, this study aimed to investigate whether the association between patient characteristics and treatment response differed between the individual biologics.

MATERIALS AND METHODS

Study design

The study was approved by the Danish Data Protection Agency (ref. HGH-2016-048, I-Suite: 04520 and VD-2018-286). Approval by an ethics committee is not required for register-based studies.
in Denmark. The study followed the recommendations of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (13).

A cohort study was conducted with data from the Danish National Patient Registry, the Danish National Prescription Registry, and the DERMBIO registry. The DERMBIO registry contains data on patients treated with biologics for psoriasis in Denmark (4).

Patients were included in the study if they were biologic naïve and if they initiated treatment with either adalimumab, etanercept, infliximab, secukinumab, or ustekinumab from January 2007 through October 2019. Patients treated with ixekizumab, brodalumab, and IL-23 inhibitors were excluded due to a lack of data. Patients were excluded from the study if no data on Psoriasis Area and Severity Index (PASI) were available after either 3, 6, or 12 months of treatment. The visits were defined with time-frames of ± 9 weeks. If a patient had multiple measures of PASI at baseline or at the 3-, 6-, or 12-month visit, the PASI recorded closest to the scheduled time was used.

Data sources

The following patient characteristics were included: biological therapy, sex, age at the start of biological treatment, bodyweight, smoking, alcohol abuse, baseline PASI (± 2 weeks), disease duration, PsA, diabetes, hypertension, severe cardiovascular disease (myocardial infarction (MI) and ischaemic stroke), Charlson Comorbidity Index, concomitant use of methotrexate, concomitant use of local treatment, and socioeconomic status in the cohort.

Subanalyses also included dose of biologic at 6 months, Charlson Comorbidity Index without diabetes, smoking (data from the DERMBIO registry, n = 355), and socioeconomic status in the Danish population.

The Charlson Comorbidity Index and severe cardiovascular disease were based on previously validated International Classification of Diseases, 10th Revision (ICD-10) codes from the Danish National Patient Registry (14–17). Smoking and alcohol abuse were defined by ICD-10 codes, pharmacological treatment, and treatment interventions. Dose of biologic at 6 months was defined as a categorical variable indicating whether the dose of the drug differed from the approved European Medicines Agency (EMA) label. Socioeconomic status was defined as 5 groups (group 1 with the lowest income) based on the mean gross annual income (standardized by age) during a 5-year period before patient inclusion to the DERMBIO registry. Hypertension and diabetes were defined by ICD-10 codes and pharmacological treatment. The approaches have been described in detail previously (18, 19).

The remaining patient characteristics were based on data from the DERMBIO registry.

The primary endpoint was a treatment response, defined as PASI ≤ 2.0 at the 6-month visit. The secondary endpoints were treatment responses defined as PASI ≤ 2.0 at the 3- and 12-month visits. Sensitivity analyses were conducted with treatment responses defined as 90% and 75% reduction in PASI (PASI 90 and PASI 75) at the 3-, 6-, and 12-month visits.

Subanalyses with PASI ≤ 2.0 at 6 months were conducted with the variables smoking (data from the DERMBIO registry), Charlson Comorbidity Index without diabetes, and socioeconomic status in the Danish population replacing the variables smoking, Charlson Comorbidity Index, and socioeconomic status in the cohort. Another subanalysis was conducted including the variable dose of biologic at 6 months.

Statistical methods

Preparation of the dataset was generated using SAS software, Version 9.4 of the SAS System for Windows. Copyright, SAS Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA. The data analyses were performed with RStudio, Version 1.2.1578. RStudio: Integrated Development for R. RStudio, PBC, Boston, MA, USA.

The patient characteristics were tested for potential outliers. Next, the association between the patient characteristics and the endpoints was tested with univariate analyses (t-tests for normally distributed continuous variables, Mann–Whitney U tests for non-normally distributed continuous variables, and χ²-tests for categorical and binary variables).

For each endpoint, patient characteristics with a p < 0.20 in the univariate analyses were included in the multivariable logistic model. The models were fitted with the patient characteristics as the independent variables and the binary-coded endpoint as the dependent variable. Independent variables with a p > 0.20 in the univariate analyses were included in the multivariable logistic model if they had a p < 0.05 when the other independent variables were adjusted for. The specific biologic was included as an independent variable in all the models. The independent variables with a p < 0.05 in the primary model (absolute PASI ≤ 2.0 within 6 months) were also included in the other models.

Missing data were accounted for by using R multivariate imputation by chained equation (mice-package) (20). Continuous variables were converted to categorical variables in subsequent models for easier interpretation of the odds ratio (OR) and to avoid false inferences, as any unit change should have the same impact on the response.

In addition to ORs, the average marginal effect was also calculated. The average marginal effect is the average change in probability of response, when 1 variable changes, and the others are held constant. It is important to note that the marginal effect for each variable differs between patients (21). Again, the numerical variables were converted to categorical variables for ease of interpretation.

To evaluate the performance of the models, this study assessed goodness of fit (calibration) with the Hosmer–Lemeshow test and the overall accuracy of the models (discrimination) with receiver operator characteristic (ROC) graphs. ROC graphs illustrate the relationship between the true-positive rate (sensitivity) and the false-positive rate (1-specificity) to summarize confusion matrices.

In a subsequent model with PASI ≤ 2.0 at 6 months as the endpoint, interaction terms were included to investigate if the biologics depended differently on the patient characteristics with a p < 0.20 in the primary model.

RESULTS

Characteristics of the cohort

In total, 3,109 patients were identified in the DERMBIO registry. Of these, 2,384 patients were biologic naïve and treated with adalimumab (n = 911), etanercept (n = 327), infliximab (n = 152), secukinumab (n = 323), or ustekinumab (n = 671) and had at least 1 PASI available at the 3-, 6-, or 12-month visit (Fig. 1).

Most of the patients were male (63.7%) and the mean age was 43.2 years (Table SII). More patients achieved PASI ≤ 2.0 at 6 months when treated with secukinumab (87.0%) compared with adalimumab, infliximab, and ustekinumab (65.1–67.9%), while only 42.4% achieved PASI ≤ 2.0 at 6 months when treated with etanercept (Table SII).
Predictors of response to biologics in psoriasis

Primary endpoint (PASI ≤ 2.0 at 6 months)

Treatment response, defined as PASI ≤ 2.0 at the 6-month visit, was the primary endpoint. Ten patient characteristics (excluding biological therapy and the variables used for subanalyses) had a p < 0.20 in the univariate analyses, resulting in 11 independent variables in the primary model (Table SIII). With adalimumab as reference, patients treated with etanercept had lower odds (OR 0.38; 95% confidence interval (95% CI), 0.27–0.52) of responding to treatment, and patients treated with secukinumab had higher odds (OR 3.57; 95% CI, 2.29–5.55) of responding to treatment. In addition, smoking, higher bodyweight, and higher baseline PASI reduced the odds of achieving treatment response (Table SIV).

Converting continuous variables to categorical variables revealed that an age of 45–60 years at the start of the treatment compared with age <30 years, and a bodyweight between 90 and 110 kg and 110+ kg compared with a bodyweight below 70 kg were associated with reduced odds of achieving response to treatment (Fig. 2).

For easier interpretation of the risk related to the individual variable, the average marginal effect was assessed (Table SV). The median probability of achieving treatment response, defined as PASI ≤ 2.0, at 6 months, was 67.5% in our cohort. Smokers were 6.2% less likely to achieve response on biologic treatment compared with non-smokers. Patients weighing 90–110 kg or 110+ kg compared with a bodyweight below 70 kg were associated with reduced odds of achieving response to treatment (Fig. 3).

Treatment stratification. In the subsequent model with PASI ≤ 2.0 at 6 months as the endpoint and interaction

---

**Fig. 1. Flowchart of the identification process.** ADA: adalimumab; ETA: etanercept; INF: infliximab; PASI: Psoriasis Area and Severity Index; SEC: secukinumab; UST: ustekinumab.

**Fig. 2. Odds ratios (ORs) for the primary endpoint (Psoriasis Area and Severity Index (PASI) ≤ 2.0 at 6 months).** *For every unit above 0. **An index above 0. ORs and 95% confidence interval (CI) for the primary multivariable logistic model investigating associations between PASI ≤ 2.0 at 6 months and patients’ characteristics.

**Fig. 3. Change in the probability of achieving Psoriasis Area and Severity Index (PASI) ≤ 2.0 at 6 months.** This diagram illustrates the average marginal effect of the variables with significant associations with the primary endpoint (PASI ≤ 2.0 at 6 months). The average marginal effect is the average change in probability, when 1 variable changes, and the others are held constant. For comparison purposes, the median probability of achieving PASI ≤2.0 at 6 months was 67.5%.
terms between the biological therapy and the independent variables, we wanted to investigate whether the biologics depended differently on the patient characteristics.

Analysis showed that the odds of treatment response were higher with increasing bodyweight when patients were treated with infliximab compared with adalimumab. There were no other significant interactions (Table SVIII).

**Secondary endpoints (PASI ≤ 2.0 at 3 and 12 months)**

The results of the models with the secondary endpoints also showed reduced odds of achieving treatment response among smokers (only at 3 months), patients with higher bodyweight, higher baseline PASI, and when treated with etanercept compared with adalimumab. The models also showed increased odds of achieving treatment response when treated with secukinumab compared with adalimumab. Age at the start of biological treatment, disease duration, diabetes, and concomitant local treatment were associated with only one of the secondary endpoints (Table SIV).

**Sensitivity analyses (endpoints: PASI 75 and 90 at 3, 6 and 12 months)**

As for the primary endpoint, similar results for higher bodyweight, etanercept, and secukinumab were observed with PASI 75 and PASI 90 as endpoints. Smoking also showed similar results, with PASI 90 as the endpoint, but no association for PASI 75 was observed. In contrast to the primary endpoint, higher baseline PASI was associated with increased odds of achieving PASI 75 and PASI 90.

Concomitant use of local treatment increased the odds, whereas higher age at the start of biological treatment reduced the odds, of treatment response in more than one of the sensitivity analyses (Tables SIV).

**Subanalyses**

Treatment with a higher dose than labelled of the given biologic at 6 months decreased the odds of PASI ≤ 2.0 at 6 months. There was still no association with PASI ≤ 2.0 at 6 months when Charlson Comorbidity Index without diabetes and socioeconomic status in the Danish population replaced Charlson Comorbidity Index and socioeconomic status in the cohort (Table SVII). Smoking (data from the DERM Bio registry) was not associated with PASI ≤ 2.0 at 6 months (Table SVIII).

**Goodness of fit**

The Hosmer–Lemeshow test of all 9 models had a high p-value (above 0.05) indicating a good fit to the data. The area under curve (AUC) of the ROC graphs of the 9 models was approximately 0.70, which is an acceptable accuracy of the models (22) (Table SIX).

**DISCUSSION**

This nationwide cohort of biologic-naive patients with psoriasis found that higher bodyweight and smoking reduced the odds of achieving PASI ≤ 2.0 after 6 months of treatment with either adalimumab, etanercept, infliximab, secukinumab, or ustekinumab. Treatment with etanercept or secukinumab compared with adalimumab reduced or increased the odds of achieving PASI ≤ 2.0 after 6 months of treatment, respectively.

Previous studies investigating patient characteristics associated with treatment response to biologics have found female sex, smoking, and high bodyweight to be associated with reduced efficacy in patients treated with adalimumab, etanercept, infliximab, and ustekinumab (12, 23). In another study, there were fewer smokers, and patients had lower bodyweight in groups with better response to treatment with secukinumab (24). In addition, in a network meta-analysis, secukinumab and etanercept had higher and lower efficacy, respectively, compared with adalimumab, infliximab, and ustekinumab (1).

In line with previous findings, the current study found a higher bodyweight to be negatively associated with treatment response. We provide further evidence that this association also exists within the first 12 months of treatment with secukinumab (anti-IL-17A) (15). The association can be linked to increased clearance of the drugs and higher volume of distribution with higher bodyweight, together with the fact that increased serum drug levels for adalimumab leads to an increased treatment response (25, 26). Thus, patients with higher bodyweight might need higher doses of biologics. In agreement with this hypothesis, the current study found that patients treated with infliximab, the only fully weight-adjusted biologic, had a better treatment response with increasing bodyweight compared with patients treated with adalimumab. There is a potential prescription bias, as patients treated with infliximab were heavier than patients treated with the other biologics. However, this bias only reduces the negative association between higher bodyweight and treatment response.

Patients weighing 90–110 kg or 110+ kg had 8.2 or 17.0 percentage points decreased probability of achieving treatment response, respectively. Investigating ways to optimize treatment in patients weighing over 90 kg are important, as 41.7% of the patients in this study weighed more than 90 kg. Interestingly, a recent study found no effect of bodyweight on the efficacy of risankizumab (anti-IL-23), although it is unclear if this also applies to real-life use of this drug (27). A 1-year real-life study on guselkumab (anti-IL-23) found no association between obesity (defined as body mass index > 30) and poorer response. The study included only 52 patients (28).

A subanalysis found that treatment with higher doses of biologics than labelled reduced the odds of achieving PASI ≤ 2.0 after 6 months. However, treatment with higher doses than labelled is most likely a consequence of the patient not initially responding fully to the labelled dose.
The negative association between smoking and treatment response to biologics is consistent with most studies on psoriasis (23, 24, 29) and other disease areas, such as PsA, rheumatoid arthritis, and ankylosing spondylitis (30–32). The results of the current study regarding the difference in probability of achieving treatment response for smokers compared with non-smokers is similar to that found in the study by Warren et al. (12), which investigated patients with psoriasis enrolled in the UK and Republic of Ireland-based registry BADBIR. Another study comprising 1,264 patients found a tendency, but no significant difference, in treatment response between current smokers and non-smokers after 12 months of treatment (33). However, this study was limited by patients being excluded due to discontinuation of treatment in the study period and lower baseline PASI in the non-smoking group. Taken together, smoking appears to result in a worse treatment outcome, and smoking cessation might be a way to increase treatment response. In the current study, when smoking data from the DERM BIO registry was used, we no longer observed an association between smoking and PASI ≤ 2.0 at 6 months. However, this sub-analysis was limited to include only 10% of the original cohort, as routine registration of smoking has only been introduced recently to the DERM BIO registry.

Not surprisingly, baseline PASI was associated with all endpoints. For relative reductions in PASI there was a positive association with higher baseline PASI, and for absolute reductions in PASI there was a negative association with higher baseline PASI. In clinical trials, PASI 75 and PASI 90 are often used as efficacy responses, whereas response criteria based on absolute PASI are more suitable for real-world studies due to the lack of a wash-out period. The current consensus is that an absolute PASI ≤ 2.0 is a preferable treatment outcome (34, 35).

Finally, higher age at the start of biological treatment was negatively associated with the endpoints defined as PASI ≤ 2.0, PASI 75, and PASI 90 at 3 months. There are potential confounding factors regarding this variable that our analyses did not consider, such as previous classic systemic treatments. One hypothesis supporting our result is that early intervention with effective systemic therapy can alter the course of the disease before the chronicity of the disease sets in, and early treatment intervention might be a way to optimize response (36). To our knowledge, this is the first study to find an association between higher age and worse treatment response and it should be replicated in independent cohorts.

This study has some limitations. The variables smoking and alcohol abuse were only identified if the patients had had interactions with the healthcare system regarding smoking or alcohol abuse (18, 19). Thus, only patients with high exposure to smoking and alcohol were categorized as smokers or alcohol abusers, leading to some misclassification. However, such misclassification would lead to a reduction in the effect estimate towards no association.

The low number of treatment series with some of the biologics and missing data, most prominent for disease duration, could lead to loss of statistical power. However, we believe that these data are missing completely at random and hence do not influence the interpretation of the results. Strengths of the current study include the nationwide coverage and the validated endpoints and patient characteristics investigated.

Consistent with previous research, this study found that higher bodyweight and smoking were associated with a reduced probability of treatment response to older biologics that inhibit TNF-α and IL-12/-23. It was also found that these patient characteristics reduce the probability of treatment response with secukinumab (anti-IL-17A).

ACKNOWLEDGEMENTS

The DERM BIO registry has entered into agreements with Abbvie, Eli Lilly, Almirall, UCB, Novartis, Janssen, and LEO Pharma. They receive post-marketing data and had no influence on the data collection, statistical analyses, manuscript preparation or the decision to submit. Funding. CWS was supported by a grant provided by The Research Foundation, Herlev and Gentofte Hospital. Conflicts of interest. CWS reports no conflicts of interest. NL has been an honorary speaker for Eli Lilly and Janssen-Cilag, MKR has been a paid speaker for AbbVie, Almirall, and LEO Pharma, and has been a consultant or serving on expert/advisory boards with AbbVie, Almirall, Janssen-Cilag, and Eli Lilly. He has served as investigator for Janssen-Cilag and Novartis. CVSN has served on an advisory board for Almirall and received travel grants from AbbVie and Janssen. TND has been a paid speaker for Janssen-Cilag and has been a consultant or has served on Advisory Boards with AbbVie, Janssen-Cilag, Novartis, Eli Lilly, and LEO Pharma. KKA have no conflicts of interest to declare. AE has received research funding from Pfizer, Eli Lilly, Novartis, AbbVie, Janssen Pharmaceuticals, the Danish National Psoriasis Foundation, the Simon Spies Foundation, and the Kgl Hofbundmager Aage Bang Foundation, and honoraria as consultant and/or speaker from AbbVie, Almirall, LEO Pharma, Samsung Bioepis Co., Ltd, Pfizer, Eli Lilly and Company, Novartis, Galderma, Dermavant, UCB, Mylan, Bristol Myers Squibb, and Janssen Pharmaceuticals. LS has been a paid speaker for AbbVie, Eli Lilly, Novartis, and LEO Pharma, and has been a consultant or has served on advisory boards with AbbVie, Janssen-Cilag, Novartis, Eli Lilly, LEO Pharma, UCB, Almirall, and Sanofi. She has served as an investigator for AbbVie, Sanofi, Janssen-Cilag, Boehringer Ingelheim, AstraZeneca, Eli Lilly, Novartis, Regeneron, and LEO Pharma, and has received research and educational grants from Pfizer, Novartis, Sanofi, Janssen-Cilag, Bristol Myers Squibb, and LEO Pharma.

REFERENCES

1. Jabbar-Lopez ZK, Yiu ZZN, Ward V, Exton LS, Mohd Mustapa M, Samarasekera E, et al. Quantitative evaluation of biologic therapy options for psoriasis: a systematic review and network meta-analysis. J Invest Dermatol 2017; 137: 1646–1654.
2. Loft ND, Eggeberg A, Rasmussen MK, Bryld LD, Gniadecki R, Dam TN, et al. Patient-reported outcomes during treatment in patients with moderate-to-severe psoriasis: a Danish nationwide study. Acta Derm Venereol 2019; 99: 1224–1230.
3. Foster SA, Zhu B, Guo J, Nikai E, Ojei C, Malatestinic W, et al. Patient characteristics, health care resource utilization,
and costs associated with treatment-regimen failure with biologics in the treatment of psoriasis. J Manag Care Spec Pharm 2016; 22: 396–405.

4. Niadecki RB, Madsen LE, Iversen L, Lasthein S, Skov L. Comparison of long-term drug survival and safety of biologic agents in patients with psoriasis vulgaris. Br J Dermatol 2015; 172: 244–252.

5. Mahlich J, Alba A, Hadad L EI, Leisten M-K, Peitsch WK. Drug survival of biological therapies for psoriasis treatment in Germany and associated costs: a retrospective claims database analysis. Adv Ther 2019; 36: 1684–1699.

6. Sibidan E, Mezzarobba M, Weil A, Coste J, Rudant J. Persistence of treatment with biologics for patients with psoriasis: a real-world analysis of 16 545 biologic-naive patients from the French National Health Insurance database (SNIRAM). Br J Dermatol 2019; 180: 86–93.

7. Egeberg A, Bryld LE, Skov L. Drug survival of secukinumab and ixekizumab for moderate-to-severe plaque psoriasis. J Am Acad Dermatol 2019; 81: 173–181.

8. Egeberg A, Ottoson MB, Niadecki R, Bresby-Olsen S, Dam TN, Bryld LE, et al. Safety, efficacy and drug survival of biologics and biosimilars for moderate-to-severe plaque psoriasis. Br J Dermatol 2018; 178: 509–519.

9. van den Reek JMAP, van Vught LJ, van Doorn MBA, van der Kraaij GE, de Kot WJA, Lucker GPH, et al. Initial results of secukinumab drug survival in patients with psoriasis: a multicentre daily practice cohort study. Acta Derm Venereol 2018; 98: 648–654.

10. Yi ZZN, Mason KJ, Hampton PJ, Reynolds NJ, Smith CH, Lunt M, et al. Drug survival of adalimumab, ustekinumab and secukinumab in patients with psoriasis: a prospective cohort study from the British Association of Dermatologists Biologics and Immunomodulators Register (BADBIR). J Dermatol Treat 2020; 1: 294–302.

11. Loft ND, Skov L, Iversen L, Niadecki R, Dam TN, Brandslund I, et al. Associations between functional polymorphisms and response to biological treatment in Danish patients with psoriasis. Pharmacogenomics J 2018; 18: 494–500.

12. Warren RB, Marsden A, Tomenson B, Mason KJ, Soliman MM, Burden AD, et al. Identifying demographic, social and clinical predictors of biologic therapy effectiveness in psoriasis: a multicentre longitudinal cohort study. Br J Dermatol 2019; 180: 1069–1076.

13. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet 2007; 370: 1453–1457.

14. Thygensen SK, Christiansen CF, Christensen S, Lash TL, Sørensen HT. The predictive value of ICD-10 diagnostic coding used to assess Charlson comorbidity index conditions in the population-based Danish National Registry of Patients. BMC Med Res Methodol 2011; 11: 83.

15. Madsen M, Davidsen M, Rasmussen S, Abildstrom SZ, Osler M. The validity of the diagnosis of acute myocardial infarction in routine statistics: a comparison of mortality and hospital discharge data with the Danish MONICA registry. J Clin Epidemiol 2003; 56: 124–130.

16. Krarup LH, Boysen G, Janjua H, Prescott E, Truelsen T. Validity of stroke diagnoses in a national register of patients. Neuroepidemiology 2007; 28: 150–154.

17. Egeberg A, Gislason GH, Hansen PR. Risk of major adverse cardiovascular events and all-cause mortality in patients with hidradenitis suppurativa. JAMA Dermatol 2016; 152: 429–434.

18. Egeberg A, Malbrils L, Gislason GH, Skov L, Hansen PR. Risk of multiple sclerosis in patients with psoriasis: a Danish nationwide cohort study. J Invest Dermatol 2016; 136: 93–98.

19. Egeberg A, Hansen PR, Gislason GH, Skov L, Malbrils L. Risk of self-harm and nonfatal suicide attempts, and completed suicide in patients with psoriasis: a population-based cohort study. Br J Dermatol 2016; 175: 493–501.

20. van Buuren S, Groothuis-Oudshoor K. mice: multivariate imputation by chained equations in R. J Stat Softw 2011; 45: 1–67.

21. Norton EC, Dowd BE, Maciejewska ML. Marginal effects – quantifying the effect of changes in risk factors in logistic regression models. JAMA 2019; 321: 1304–1305.

22. Magnabosco B, Bryld LE, van Buuren S, Groothuis-Oudshoor K. mice: multivariate imputation by chained equations in diagnostic test assessment. J Thorac Oncol 2010; 5: 1315–1316.

23. Warren RB, Smith CH, Yi ZZN, Ashcroft DM, Barker JNW, Burden AD, et al. Differential drug survival of biologic therapies for the treatment of psoriasis: a prospective observational cohort study from the British Association of Dermatologists Biologic Interventions Register (BADBIR). J Invest Dermatol 2015; 135: 2632–2640.

24. Pinter A, Gerdos S, Papavassili C, Reinhardt M. Characterization of responder groups to secukinumab treatment in moderate to severe plaque psoriasis. J Dermatolog Treat 2020; 31: 769–775.

25. Mostafa NM, Nader AM, Noertersheuser P, Okun M, Awini WM. Impact of immunogenicity on pharmacokinetics, efficacy and safety of adalimumab in adult patients with moderate to severe chronic plaque psoriasis. J Eur Acad Dermatol Venereol 2017; 31: 490–497.

26. Wilkinson N, Tsakok T, Dand N, Bloem K, Duckworth M, Baudry D, et al. Defining the therapeutic range for adalimumab and predicting response in psoriasis: a multicenter prospective observational cohort study. J Invest Dermatol 2019; 139: 115–123.

27. Strober B, Menter A, Leonard C, Gordon K, Lambert J, Puig L, et al. Efficacy of risankizumab in patients with moderate-to-severe plaque psoriasis by baseline demographics, disease characteristics and prior biologic therapy: an integrated analysis of the Phase III UltIMMa-1 and UltIMMa-2 Studies. J Eur Acad Dermatol Venereol 2020; 34: 2830–2838.

28. Galluzzo M, Tofani L, Lombardo P, PetruzzeLLIS, Alivaggio D, Egan CG, et al. Use of guselkumab for the treatment of moderate-to-severe plaque psoriasis: a 1 year real-life study. J Clin Med 2020; 9: 2170.

29. Umezawa Y, Saeki H, Nakagawa H. Some clinical factors affecting quality of the response to ustekinumab for psoriasis. J Dermatol 2014; 41: 690–696.

30. Højgaard P, Glinkborg B, Hetland ML, Hansen TH, Lange-Hansen PR, Petersen MH, et al. Association between tobacco smoking and response to tumour necrosis factor-alpha inhibitor treatment in psoriatic arthritis: results from the DANBIO registry. Ann Rheum Dis 2015; 74: 2130–2136.

31. Hyrich KL, Watson KD, Silman AJ, Symmons DPM. Predictors of response to anti-TNF-α therapy among patients with rheumatoid arthritis: results from the British Society for Rheumatology Biologics and Immunomodulators Register. J Rheumatology 2006; 45: 1558–1565.

32. Glinkborg B, Højgaard P, Lund Hetland M, Steen KrogH N, Kollerup G, Jensen J, et al. Impact of tobacco smoking on response to tumour necrosis factor-alpha inhibitor treatment in patients with ankylosing spondylitis: results from the Danish nationwide DANBIO registry. Rheumatol (UK) 2016; 55: 659–668.

33. Anzengruber F, Augustin M, Radtke MA, Thaci D, Yawalkar N, Streit M, et al. Smoking does not alter the therapy response to systemic anti-psoriatic therapies: a two-country, multicentre, prospective, non-interventional study. Acta Derm Venereol 2019; 99: 871–877.

34. Mahil SK, Wilson N, Dand N, Reynolds NJ, Griffiths CEM, Emsley R, et al. Psoriasis treat to target: defining outcomes in psoriasis using data from a real-world, population-based cohort study (British Association of Dermatologists Biologics and Immunomodulators Register, BADBIR). Br J Dermatol 2020; 182: 1158–1166.

35. Loft N, Egeberg A, Rasmussen MK, Bryld LE, Nissen CV, Dam TN, et al. Response to biologics during the first six months of therapy in biologic-naïve patients with psoriasis: a prospective observational cohort study from the British Association of Dermatologists Biologics and Immunomodulators Register (BADBIR). J Clin Med 2020; 9: 2170.

36. Iversen L, Eidsmo L, Austad J, de Rie M, Osmancevic A, Skov L, et al. Secukinumab treatment in new-onset psoriasis: a prospective, multicentre, non-interventional study. Acta Derm Venereol 2021; 101: adv00357.