SHORT COMMUNICATION

Check for updates

Factors Associated with Receiving Biologics or Classic Systemic Therapy for Moderate-to-Severe Psoriasis: Evidence from the PSONET Registries

Paula DAVILA-SEIJO[1,2], Ignacio GARCIA-DOVAL[1–3], Luigi NALDI[4], Simone CAZZANIGA[4], Matthias AUGUSTIN[5], Stephan J. RUSTENBACH[5], Esteban DAUDÉN[6], Tomas NORMAN DAM[7], Chris BAKER[8], Phyllis I. SPULS[9], Robert S. STERN[10] and Arnon D. COHEN[11] on behalf of the PSONET Network

[1]Research Unit, Fundación Academia Española de Dermatología y Venereología, Ferraz 100, 1º izda. Madrid, Spain, [2]Dermatology and Venereology Department, Umeå University Hospital, Umeå, Sweden, [3]Department of Dermatology, Complexo Hospitalario Universitario de Vigo (CHUVI), Vigo, Spain, [4]Centro Studi GISED, Fondazione per la Ricerca, Ospedale Maggiore, Bergamo, Italy, [5]German Center for Health Services Research in Dermatology, University Clinics of Hamburg, Hamburg, Germany, [6]Department of Dermatology, Hospital Universitario La Princesa, Madrid, Spain, Departments of Dermatology, [7]Roskilde Hospital, Roskilde, Denmark, [8]Skin and Cancer Foundation, St Vincent's Hospital Melbourne, University of Melbourne, Australia, [9]Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands and [10]Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, USA, and [11]Department of Quality Measures and Research, Clalit Health Services. Tel Aviv, Siaal Research Center for Family Medicine and Primary Care, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel. E-mail: pauladavilaseijo@gmail.com

PSONET is an international network of independent partners that aims to document "real-life" use of systemic drugs for psoriasis in different countries (1–3). Differences in how the registries' populations are treated have implications for the analysis of data (as these factors could act as confounders for risk estimates), for the generalizability of results from individual registries, and for understanding dermatologist behaviour in different healthcare systems and countries.

The objective of this study is to describe and compare the characteristics of patients treated with classic and biological agents for psoriasis in participating registries.

METHODS

The study population are patients with moderate-to-severe psoriasis, over 18 years of age, who have received systemic treatment for psoriasis. Except for Clalit Health Services, which utilizes administrative data, participating registries are cohort studies that enrol patients when they first receive, or are currently receiving, a study drug.

Baseline data from 7 countries' registries included the Netherlands (Academic Medical Centre (AMC) psoriasis registry) (4, 5), Australia (Australasian Psoriasis Registry), Spain (BIOBADADERM) (6, 7), Israel (The Clalit Health Services), Denmark (DERMBIO) (8, 9), Germany (PSOBEST) (10) and Italy (PSOCARE) (11, 12).

Participating registries provided aggregated summary data concerning baseline, demographic and disease characteristics of their cohort. Table SI[1] gives information about the organization of each registry. Inclusion criteria for the different registers are earlier described in (3). In general, they include all biological treatments consecutively and a convenience sampling of classic drugs. All registries received approval from their local ethics committee, and comply with the principles of the Declaration of Helsinki.

Statistical analysis

Pooled analyses were performed using Stata 12.1 software (StataCorp College Station, TX, USA). To measure the association between exposure to biologics or classic systemic therapies and *a priori* defined variables, differences in means between groups were used for continuous variables, and odds ratios (OR) for categorical variables. To pool data from registries, forest plots were used and a random-effects meta-analysis was conducted to describe differences among groups exposed to biologics or conventional therapies. Pooled estimates of effects were produced if results were not too heterogeneous ($I^2 < 60\%$). Some registries were not able to provide data on all of the defined variables. Due to the lack of enrolment of patients receiving classic systemic therapy, AMC psoriasis registry data were not included in the forest plots and in comparisons of exposure cohorts. In all the other registries, if a patient began in the non-biological therapy group and subsequently received a biologic drug, his or her characteristics contributed to both groups in the analysis.
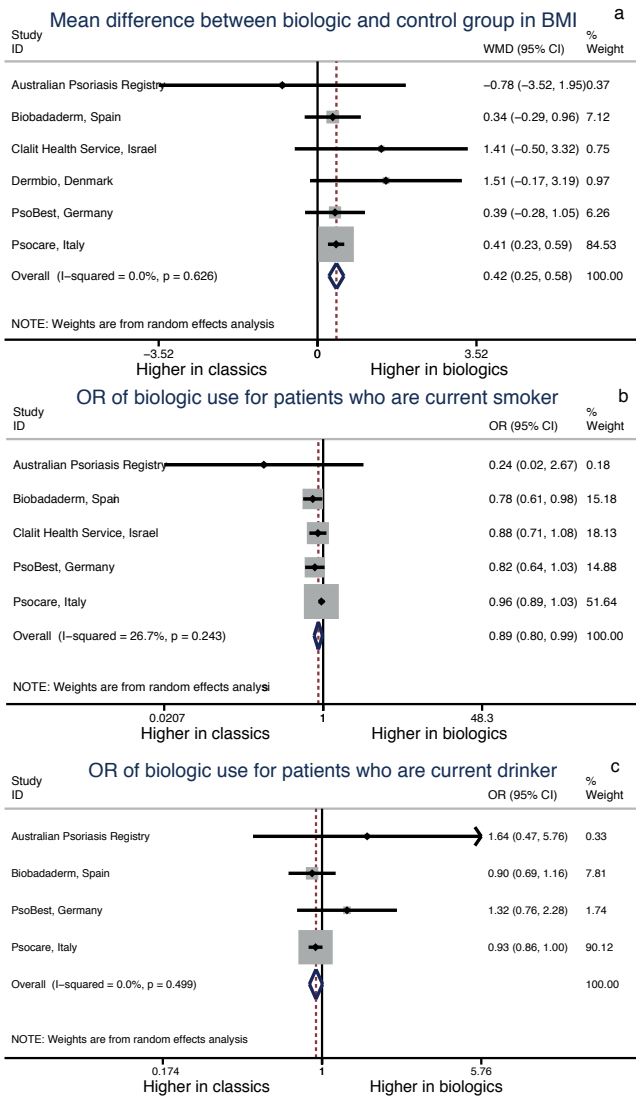
RESULTS

From the start of each registry to August 2012, a total of 20,232 patients had been enrolled in the registries and provided baseline information. This included 9,668 (47.8%) initially treated with biologics and 10,564 (52.2%) starting classic systemic therapies.

Demographic and disease characteristics are summarized in Tables SII and SIII[1].

Some differences between patients receiving biologics and those receiving classic drugs were homogeneous between registries ($I^2 \leq 60\%$). These are presented in forest plots in **Fig. 1,** which includes I^2 values, and pooled estimates. Overall, patients on biologics were 0.42 units of body mass index (BMI) heavier than those on classic systemic drugs (95% CI: 0.25–0.58). The OR of males vs. females receiving biologics was 1.08 (95% CI: 0.94–1.24). Use of biologics was slightly less likely in current smokers (OR 0.89, 95% CI: 0.80–0.99).

Fig. S1[1] shows the results in each registry, but not pooled estimates, because heterogeneity was too high ($I^2 > 60\%$). Age at entry, age at diagnosis and Psoriasis Area and Severity Index (PASI) at entry were too heterogeneous among registries to be combined in the meta-analysis. Italian and Spanish patients on biologics had a PASI significantly higher at entry and were significantly younger at diagnosis than those receiving classic systemic therapies. Few registries reported measurements of body surface area (BSA) and Dermatology Life Quality

Fig. 1. Forest plot showing the overall result in psoriasis characteristics of patients without substantial heterogeneity ($I^2 < 60\%$) in both biologic and control group among different registries: (a) differences in body mass index (BMI) between biologic and conventional treatment groups. (b) Odds ratio (OR) of biologic use compared with conventional treatment among current smokers. (c) OR of biologic use compared with conventional treatment among current drinkers.

Index (DLQI) or SKINDEX, making comparisons between registries difficult.

Patients with psoriatic arthritis or nail disease were more likely to receive biologics than classic therapies in almost all registries, but the results were heterogeneous despite the significant OR favouring the usage of biologics in most of them. In registries from Italy and Spain, patients with psoriasis different from plaque psoriasis were significantly more likely to receive conventional drugs.

DISCUSSION

In agreement with the findings of a previous PSO-NET analysis (1), the current study revealed that wide between-country heterogeneity exists in the distribution of covariates potentially influencing treatment selection (e.g. age, PASI and proportion with non-chronic plaque psoriasis). Beyond between registry variability, the current study found that some covariates are related *per se* with the odds of receiving a biologic or a classic treatment in most registries, e.g. BMI, psoriatic arthritis, nail disease or proportion of current smokers.

The strengths of this study are the increased power obtained from multiple registries compared with using each separately, the ability to describe and quantify between-country differences, and the use of a meta-analytical approach, in which each registry acts as its own control, which limits the risk of biases related to differences between registries. In addition, meta-analysis is a good way to define and quantify heterogeneity and to balance out differences in sizes among the registries.

Study limitations are: missing data from some registries, missing data on some predefined variables and that only univariate analysis was performed and we could not rule out that the factors we found as being associated with treatment choices were, in fact, intercorrelated and not independently associated with the treatment selection. A further limitation is that we could only analyse commonly measured and coded variables. Finally, the data were not updated. This delay is due to the extreme difficulty in combining data from different national registries. But because of the already high number of participants, we consider that this should not affect the results and overall conclusions.

Methodological differences might explain some of the differences found. This is probably the case for the heterogeneity of the percentage of patients with psoriatic arthritis or in PASI values. PASI values are also influenced by the lack of wash-out periods before starting a new therapy (leading to variability and PASI decrease) in real-world registries and by the fact that a minimum PASI is mandatory to prescribe biologics in some countries (possibly leading to a factitious increase). Single outlying results may also hide otherwise homogenous effects, e.g. only in the Danish registry is there no greatly increased use of biologics for psoriasis arthritis; thus, the otherwise highly significant prediction by psoriasis arthritis disappears.

Conclusion

Knowledge of the factors related to drug selection is important in order to plan statistical analysis of observational data (13). Each registry could use this information to develop strategies for dealing with prescription bias, using methods such as propensity scores (14). Identification of differences in the international usage of drugs can be useful for interpretation of observational studies (e.g. generalization of results) (15), adds knowledge and understanding of different healthcare systems and might indicate areas for improvement in patient management.

ACKNOWLEDGEMENTS AND CONFLICT OF INTEREST (see Appendix SI[1])

REFERENCES

1. Garcia-Doval I, Rustenbach SJ, Stern R, Dam TN, Cohen AD, Baker C, et al. Systemic psoriasis therapy shows high between-country variation: a sign of unwarranted variation? Cross-sectional analysis of baseline data from the PSONET registries. Br J Dermatol 2013; 169: 710–714.
2. Lecluse LL, Naldi L, Stern RS, Spuls PI. National registries of systemic treatment for psoriasis and the European 'Psonet' initiative. Dermatology 2009; 218: 347–356.
3. Ormerod AD, Augustin M, Baker C, Chosidow O, Cohen AD, Dam TN, et al. Challenges for synthesising data in a network of registries for systemic psoriasis therapies. Dermatology 2012; 224: 236–243.
4. Lecluse LL, de Groot M, Bos JD, Spuls PI. Experience with biologics for psoriasis in daily practice: switching is worth a try. Br J Dermatol 2009; 161: 948–951.
5. Menting SP, Sitaram AS, Bonnerjee-van der Stok HM, de Rie MA, Hooft L, Spuls PI. Drug survival is not significantly different between biologics in patients with psoriasis vulgaris: a single-centre database analysis. Br J Dermatol 2014; 171: 875–883.
6. Carretero G, Ferrandiz C, Dauden E, Vanaclocha Sebastian F, Gomez-Garcia FJ, Herrera-Ceballos E, et al. Risk of adverse events in psoriasis patients receiving classic systemic drugs and biologics in a 5-year observational study of clinical practice: 2008–2013 results of the Biobadaderm registry. J Eur Acad Derm Venereol 2015; 29: 156–163.
7. Rivera R, Garcia-Doval I, Carretero G, Dauden E, Sanchez-Carazo J, Ferrandiz C, et al. [BIOBADADERM, the Spanish Registry of adverse events associated with biologic drugs in dermatology: first report]. Actas Dermosifiliogr 2011; 102: 132–141 (in Spanish).
8. Gniadecki R, Bang B, Bryld 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.
9. 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.
10. Augustin M, Spehr C, Radtke MA, Boehncke WH, Luger T, Mrowietz U, et al. German psoriasis registry PsoBest: objectives, methodology and baseline data. J Dtsch Dermatol Ges 2014; 12: 48–57.
11. Naldi L, Cazzaniga S. [Dermatology: experience with the disease registry for the treatment of psoriasis]. Recenti Progressi in Medicina 2013; 104: 236–240 (in Italian).
12. Nijsten T, Wakkee M. Psocare: Italy shows the way in post-marketing studies. Dermatology 2008; 217: 362–364.
13. Salah LA, Gillstedt M, Osmancevic A. A retrospective study of patients with psoriasis treated with biologics: relation to body mass index and gender. Acta Derm Venereol 2016; 96: 974–975.
14. Zink A, Askling J, Dixon WG, Klareskog L, Silman AJ, Symmons DP. European biologicals registers: methodology, selected results and perspectives. Ann Rheum Dis 2009; 68: 1240–1246.
15. Inzinger M, Wippel-Slupetzky K, Weger W, Richter L, Mlynek A, Fleischander B, et al. Survival and effectiveness of tumour necrosis factor-alpha inhibitors in the treatment of plaque psoriasis under daily life conditions: report from the Psoriasis Registry Austria. Acta Derm Venereol 2016; 96: 207–212.