ORIGINAL ARTICLE

ORBIT (Outcome and Retention Rate of Biologic Treatments for Psoriasis): A retrospective observational study on biologic drug survival in daily practice

Eva Vilarrasa, MD,[a] Jaume Notario, MD,[c] Xavier Bordas, PhD,[c] Anna López-Ferrer, PhD,[a] Ignasi J. Gich, PhD,[b] and Lluís Puig, PhD[a]
Barcelona, Spain

Background: Biologic drug survival in psoriasis reflects long-term performance in real-life settings. Previous studies have yielded inconsistent results.

Objectives: We sought to analyze long-term biologic survival and its associated variables in a large, real-life cohort of patients with moderate to severe chronic plaque psoriasis.

Methods: This was an observational retrospective study. Data were extracted from clinical records of 427 patients treated with biologic agents over a 4-year period. Drug survival was analyzed using the Kaplan-Meier method and the influence of several covariates was assessed using Cox regression.

Results: We analyzed 703 treatment courses. Overall median drug survival was 31.0 months. Cumulative probability of drug survival was lower in obese patients (23.0 months, 95% confidence interval 17.4-28.6) than in patients with body mass index less than 30 (37.3 months, 95% confidence interval 29.4-45.1, $P = .001$), and it was significantly higher for ustekinumab than for any other biologic agent (log rank test $P < .001$). Multivariate analysis showed that obesity, etanercept treatment, and strict adherence to approved doses were associated with an increased probability of drug withdrawal, whereas ustekinumab treatment, and PASI75 and PASI90 responses at week 16 prolonged drug survival.

Limitations: Data were collected retrospectively.

Conclusions: These findings can facilitate the daily treatment of psoriatic patients and promote long-term effectiveness of biologic therapies. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2016.01.037.)

Key words: adalimumab; biologics: cohort; efficacy; etanercept; infliximab; psoriasis; real-life; survival; treatment; ustekinumab.

Adalimumab (ADA), etanercept (ETN), infliximab (IFX), and ustekinumab (UST) have been approved by the European Medicines Agency (EMA) for treatment of moderate to severe chronic plaque psoriasis in adults who fail to respond to, have a contraindication to, or are intolerant to systemic therapies such as cyclosporine, methotrexate, or psoralen plus ultraviolet A. Randomized clinical trials do not provide adequate information on the long-term effectiveness of these treatments or

From the Departments of Dermatology[a] and Clinical Epidemiology and Public Health,[b] Hospital de la Santa Creu i Sant Pau, Universitat Autònoma de Barcelona; and Department of Dermatology, Hospital Universitari de Bellvitge, Universitat de Barcelona.[c]

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Reprint requests: Lluís Puig, PhD, Department of Dermatology, Hospital de la Santa Creu i Sant Pau, Universitat Autònoma de Barcelona, Barcelona, Catalonia, Spain. E-mail: llpuig@santpau.cat.

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their adverse events, and open-label extension studies are biased by selection of responding patients. Furthermore, patients eligible for inclusion in clinical trials do not resemble those in daily clinical practice, where dose individualization, combination treatment, and switching are commonplace. Reports on registries and cohorts of patients can thus add useful information regarding the relative effectiveness, safety, and drug survival of currently available biologics.[1] Because the main reason for drug discontinuation is loss of efficacy, drug survival can be considered a simple and clinically relevant measure of the probability of success with any given treatment.

CAPSULE SUMMARY

- Biological drug survival reflects long-term performance in real life.
- Ustekinumab treatment, and PASI75 and PASI90 responses at week 16, are independently associated with increased drug survival.
- These findings can promote adherence to biologic treatment.

The aim of this observational retrospective study was to analyze drug survival and its associated variables in a cohort of patients with moderate to severe chronic plaque psoriasis treated with biologics according to the EMA-approved Summary of Product Characteristics (SmPC) indications at 2 university-affiliated departments of dermatology in the metropolitan area of Barcelona, Spain.

METHODS

Study design

This was an observational, retrospective 2-center study. Clinical data were extracted from the clinical records at the Departments of Dermatology of Hospital de la Santa Creu i Sant Pau and Hospital Universitari de Bellvitge in Barcelona. These data included patient demographics and baseline characteristics, concomitant diseases, previous and concomitant therapies for psoriasis, Psoriasis Area and Severity Index (PASI) assessments at every follow-up visit, adverse events occurring throughout the observational period, and detailed information concerning treatment duration and reasons for withdrawal. Reasons for withdrawal were classified as primary or secondary ineffectiveness, adverse events or other reasons (including patients' decision, change of residence, pregnancy planning, and elective surgical procedures). Data were retrieved from digital databases and/or medical records and recorded using a study-specific electronic case report form.

Variables included for statistical analysis were center; sex; age; obesity; presence of psoriatic arthritis and other comorbidities; PASI at the start of each treatment course; PASI50, PASI75, and PASI90 responses after 16 weeks of treatment; drug; and ordinal number of the biologic for each patient (patients were considered to be naïve only in the first course of treatment with any biologic). Dose was also recorded and coded as: (1) prescribed according to the SmPC, (2) increased (usually by shortening the administration intervals), or (3) decreased (usually by lengthening the administration intervals). Other variables collected included combination treatment (with methotrexate, acitretin, cyclosporine, or phototherapy/psoralen plus ultraviolet A), status of treatment (ongoing or discontinued) at the last visit before data collection, and reason for discontinuation.

The ethical committees at both institutions approved the use of the clinical records for scientific research in this noninterventional retrospective study, which was conducted in accordance with the principles of the Declaration of Helsinki.

Study setting

All patients included in this study were adults with moderate to severe chronic plaque psoriasis treated for at least 3 months between January 2007 and June 2013 with 1 or more courses of ADA, ETN, IFX, or UST, outside clinical trials, according to the EMA-approved SmPC and the Spanish Guidelines.[2,3]

Assessment of effectiveness and drug survival

Effectiveness was analyzed in terms of PASI reduction with respect to baseline at week 16 of treatment by intention-to-treat analysis. According to the Spanish Guidelines, primary failure is defined as the inability to achieve a PASI50 response with the biologic drug in monotherapy, at a standard dose, by the time specified for assessment of failure in the corresponding SmPC, or according to the joint decision of clinician and patient. Secondary failure was defined as the loss of adequate response (PASI50 response or absolute PASI score >5, regardless of Dermatology Life Quality Index score). The therapeutic goal of psoriasis treatment for dermatologists at both centers, in accordance with the Spanish Guidelines, was to achieve at least a PASI75 response by week 16, and thereafter maintain such a response and an absolute PASI value below 2 and 3, or a Physician Global Assessment score of 0 (clear) or 1 (almost clear), in agreement with the patient.