Five-year analysis from the ESPRIT 10-year postmarketing surveillance registry of adalimumab treatment for moderate to severe psoriasis

Alan Menter, MD,[a] Diamant Thaçi, MD,[b] Kim A. Papp, MD,[c] Jashin J. Wu, MD,[d] Mareike Bereswill, MS,[e] Henrique D. Teixeira, PhD,[f] Simone Rubant, PhD,[e] and David A. Williams, MD[f]
Dallas, Texas; Lübeck and Ludwigshafen, Germany; Waterloo, Ontario, Canada; Los Angeles, California; and North Chicago, Illinois

Background: ESPRIT is an ongoing, 10-year, observational registry, evaluating long-term safety and effectiveness of adalimumab treatment in routine clinical practice for patients with moderate to severe, chronic plaque psoriasis.

Objectives: Initial 5-year results are reported.

Methods: Two populations were analyzed: the "all-treated" population received 1 or more adalimumab doses in registry, continuing adalimumab treatment from a current prescription or previous study participation, and included the "new-prescription" population initiating adalimumab 4 weeks or earlier preregistry entry.

Results: Data were collected from September 26, 2008, through November 30, 2013, for all-treated (n = 6059), which included new-prescription (n = 2580, 42.6%); median registry exposure was 765 and 677 days, respectively. In all-treated, rate (events per 100 patient-years of total adalimumab exposure [E/100PY]) of serious treatment-emergent adverse events (inside or outside of the registry) was 4.3 E/100PY, serious infection 1.0 E/100PY, malignancies 0.9 E/100PY (nonmelanoma skin cancers 0.6 E/100PY; melanomas <0.1 E/100PY). Standardized mortality ratio was 0.30 (95% confidence interval 0.19-0.44). Physician Global Assessment clear or minimal (effectiveness parameter) was achieved by 57.0% at 12 months and 64.7% at 60 months of treatment.

From Baylor University Medical Center, Dallas[a]; Comprehensive Center for Inflammation Medicine, University Medical School Schleswig Holstein, Campus Lübeck[b]; Probity Medical Research, Waterloo[c]; Kaiser Permanente Los Angeles Medical Center[d]; AbbVie Deutschland GmbH and Co KG, Ludwigshafen[e]; and AbbVie Inc, North Chicago.[f]

AbbVie funded this registry and participated in the design and conduct of the study; collection, management, analysis, and interpretation of data; preparation, review, and approval of the manuscript; and decision to submit the manuscript for publication. All authors were also involved in the decision to submit the manuscript for publication, and had the right to accept or reject comments or suggestions. A medical writer employed by AbbVie participated in the writing of this manuscript, and is acknowledged.

Disclosure: Dr Menter received grants and honoraria from AbbVie, Amgen, Janssen, and Wyeth for participation on advisory boards and as a consultant, investigator, and speaker, and from Stiefel as a consultant and investigator; received grants from Allergan, Celgene, Novartis, Novo Nordisk, Pfizer, and Syntrix Biosystems for participation as an investigator, and from Eli Lilly as an investigator and consultant; and received honoraria from Galderma for participation on advisory boards and as a consultant and investigator, and from Leo Pharma as a consultant and speaker. Prof Dr Thaçi received honoraria for serving on advisory boards for AbbVie, Amgen, Biogen-Idec, Celgene, Eli Lilly, Janssen, Leo Pharma, MSD, Novartis, Pfizer, and Regeneron, and for serving as a consultant for AbbVie, Dignity, Leo Pharma, L'Oreal, Mitsubishi, Regeneron, Sanofi, Sandoz, and Xenoport; received speaker's fees from AbbVie, Amgen, Biogen-Idec, Celgene, Janssen, Leo Pharma, Medac, Novartis, Pfizer, Roche-Possay, and Stiefel and research grants from AbbVie and Pfizer. Dr Wu received research funding from AbbVie, Amgen, Coherus Biosciences, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Regeneron, and Sandoz; and received honoraria for serving as a consultant for AbbVie, Amgen, Celgene, Dermira, DUSA Pharmaceuticals, Eli Lilly, and Pfizer. Dr Papp received honoraria or grants from AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, Kyowa, Leo Pharma, Merck, Novartis, and Pfizer for participation on advisory boards, and for participation as a consultant and investigator. Drs Williams, Rubant, and Teixeira, and Ms Bereswill each receive a salary as employees of AbbVie and receive stock and/or stock options.

A portion of the data in this manuscript was presented in at the Fall European Academy of Dermatology and Venereology 23rd Congress in Amsterdam on October 8, 2014.

Supplemental information and tables are available at http://www.jaad.org.

Accepted for publication June 14, 2015.

Reprint requests: Alan Menter, MD, Baylor University Medical Center, 3900 Junius St, Suite 145, Dallas, TX 75246. E-mail: amderm@gmail.com.

Published online July 16, 2015.

0190-9622

http://dx.doi.org/10.1016/j.jaad.2015.06.038

Limitations: Observational data are subject to outcome-reporting bias.

Conclusion: No new safety signals were observed with adalimumab treatment during this initial 5-year registry review. Observed number of deaths was below expected. As-observed effectiveness remained stable through 60 months. (J Am Acad Dermatol 2015;73:410-9.)

Key words: adalimumab; adverse events; long-term safety; malignancy; registry; serious infections.

Psoriasis is a chronic, systemic, immune-mediated disease, associated with multiple comorbidities,[1,2] including risk factors for cardiovascular disease and metabolic syndrome (hypertension, diabetes, hyperlipidemia, and obesity) especially in patients with severe psoriasis,[3-6] with an increased risk for myocardial infarction (MI)[7] and psoriatic arthritis.[1,2] Long-term efficacy and/or safety of anti–tumor necrosis factor-alfa agents, including adalimumab, has been demonstrated in moderate to severe psoriasis for up to 5 years in clinical trials and observational registries,[8-13] and in a database analysis across multiple indications of adalimumab (including psoriasis) in patients with up to 12 years of adalimumab exposure.[14] ESPRIT is an ongoing, multicenter, postmarketing, 10-year, international, observational registry (NCT00799877) with the objective of prospectively evaluating long-term safety and effectiveness of adalimumab in patients treated for chronic psoriasis per local product label in routine clinical practice, who are candidates for systemic therapy or phototherapy. Enrollment completed November 8, 2012. The objective of this prespecified analysis was to determine the cumulative, long-term safety and effectiveness of adalimumab over the first 5-year period.

CAPSULE SUMMARY

- Adalimumab has an established safety profile in psoriasis and across different indications.
- Findings from the first 5 years of ESPRIT, a prospective registry of patients with psoriasis treated with adalimumab per local label in daily practice, support the safety of long-term treatment.
- Results afford opportunities for clinician/patient interactions on treatment safety.

METHODS

Eligible patients were adults (≥18 years of age) with chronic plaque psoriasis who had been prescribed adalimumab according to local product labeling, signed an informed consent before collection of registry-related data, and met 1 of the following entry criteria: (1) initiated adalimumab within 4 weeks before entry into the registry; or (2) previously initiated adalimumab and were not off drug more than 70 consecutive days, or previously participated in an adalimumab clinical trial ("feeder trial") sponsored by AbbVie Inc, North Chicago, IL, and were not off drug more than 70 consecutive days after study completion. An independent or central ethics committee, or central or local institutional review board, approved the study. Two registry populations are identified: the all-treated population received at least 1 dose of adalimumab during the registry; the new-prescription population, a subgroup of the all-treated population, received the initial (first-ever) dose within 4 weeks before registry enrollment. The registry design and maximum follow-up schedule are illustrated in Fig 1. Patients are encouraged to remain in the registry but can discontinue at any time. Those who discontinue adalimumab are encouraged to continue in the registry to allow complete collection of safety information.

Adalimumab is dosed according to the local product label. Patients are allowed concomitant therapy for psoriasis in accordance with their physician's usual and customary medical practice; however, concurrent use of anakinra, abatacept, or other biologic agents is prohibited. Patients are allowed to continue in the registry if they were being treated with a systemic psoriasis therapy other than adalimumab. For patients who initiated adalimumab therapy before entering the registry or who continued therapy after completing a feeder trial, the full period between initial dose or the end of the previous study and the start of the registry is considered as exposure time since patients received continuous therapy per protocol inclusion criteria (ie, no more than 70 days off drug).

In this analysis, safety was evaluated throughout the registry for both populations by analysis of adverse events (AEs) that were serious, of special interest, spontaneously reported, or led to registry or registry drug discontinuation. Special-interest AEs were defined as those of most concern during adalimumab treatment or those with higher rates compared with placebo in clinical psoriasis trials, and were analyzed in the first 5 years of the