OBSERVE-5: Observational postmarketing safety surveillance registry of etanercept for the treatment of psoriasis final 5-year results

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Background: OBSERVE-5 was a 5-year Food and Drug Administration—mandated surveillance registry of patients with psoriasis.

Objective: We sought to assess long-term etanercept safety and effectiveness.

Methods: Patients with moderate to severe psoriasis enrolled; a single baseline dose of etanercept was required. Key outcome measures included serious adverse events, serious infectious events, events of medical interest, psoriasis-affected body surface area, physician global assessment score, and Dermatology Life Quality Index score. Safety outcomes were assessed relative to data from the MarketScan database.

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Disclosures: Dr Kimball is a consultant for AbbVie Inc, Amgen Inc, Merck & Co Inc, Janssen-Ortho Inc, and Pfizer Inc; is an investigator for Janssen-Ortho Inc; and serves on an advisory board for Vascular Biogenics. Dr Rothman is an employee of RTI International, an independent nonprofit research organization that does work for government agencies and pharmaceutical companies. Drs Kricorian, Aras, Accortt, and Hooper, and Ms Rice are employees and shareholders of Amgen Inc. Dr Pariser is a consultant for Abbott Laboratories, Amgen Inc, Astellas Pharma US Inc, Bickel Biotechnology, Celgene Corp, Dermira, DUSA Pharmaceuticals Inc, LEO Pharma Inc, MelaSciences, Novartis Pharmaceuticals Corp, Procter & Gamble Co, and Valeant Pharmaceuticals International; is an investigator for Abbott Laboratories, Amgen Inc, Astellas Pharma US Inc, Asubio Pharmaceuticals Inc, Basliea, Celgene Corp, Eli Lilly and Co, Galderma Laboratories LP, Graceway Pharmaceuticals LLC, Intendis Inc, Johnson & Johnson Consumer Products Co, LEO Pharma Inc, Novartis Pharmaceuticals Corp, Novo Nordisk A/S, Ortho Dermatologics, Peplin Inc, Pfizer Inc, Photocure ASA, Stiefel a GSK Company, and Valeant Pharmaceuticals International; and serves on advisory boards for Galderma Laboratories LP, Genentech Inc, Janssen-Ortho Inc, Medicis Pharmaceutical Corp, Ortho Dermatologics, Pfizer Inc, and Stiefel a GSK Company. Dr Yamauchi is a consultant for AbbVie Inc, Amgen Inc, Baxter Healthcare Corp, Janssen-Ortho Inc, Novartis Pharmaceuticals Corp, and Pfizer Inc; is an investigator for Amgen Inc, Celgene Corp, Galderma USA, Janssen-Ortho Inc, LEO Pharma Inc, Lilly ICOS LLC, and Pfizer Inc; serves on speakers bureaus for AbbVie Inc, Amgen Inc, Galderma USA, Janssen-Ortho Inc, LEO Pharma Inc, and Novartis Pharmaceuticals Corp; and serves on an advisory board for Lilly ICOS LLC. Dr Menter serves on advisory boards for AbbVie Inc, Allergan Inc, Amgen Inc, Boehringer Ingelheim GmbH, Genentech Inc, Janssen Pharmaceuticals Inc, LEO Pharma Inc, and Pfizer Inc; is a consultant for AbbVie Inc, Allergan Inc, Amgen Inc, Convoy Therapeutics Inc, Eli Lilly and Co, Janssen Pharmaceuticals Inc, LEO Pharma Inc, Novartis AG, Pfizer Inc, Syntrix Biosystems Inc, Wyeth, and XenoPort Inc; is an investigator for AbbVie Inc, Allergan Inc, Amgen Inc, ApoPharma Inc, Boehringer Ingelheim GmbH, Celgene Corp, Convoy Therapeutics Inc, Eli Lilly and Co, Genentech Inc, Janssen Pharmaceuticals Inc, LEO Pharma Inc, Merck & Co Inc, Novartis AG, Pfizer Inc, SymBio Pharmaceuticals/Maruho Co Ltd, Syntrix Biosystems Inc, and Wyeth; and serves on speakers bureaus for AbbVie Inc, Amgen Inc, Janssen Pharmaceuticals Inc, LEO Pharma Inc, and Wyeth. Dr Teller is a consultant for Amgen Inc, AbbVie Inc, Janssen Pharmaceuticals Inc, and Celgene, and is an investigator for Amgen Inc. Dr Gelfand is a consultant for Pfizer Inc, Janssen Pharmaceuticals Inc, and Merck & Co Inc, and a consultant and investigator for Amgen Inc, Eli Lilly and Co, and AbbVie Inc.

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Results: For 2510 patients, 5-year cumulative incidence was 22.2% (95% confidence interval [CI] 20.3%-24.2%) for serious adverse events; 6.5% (95% CI 5.4%-7.7%) for serious infectious events; 3.2% (95% CI 2.3%-4.1%) for malignancies excluding nonmelanoma skin cancer; 3.6% (95% CI 2.7%-4.5%) for nonmelanoma skin cancer; 2.8% (95% CI 2.0%-3.6%) for coronary artery disease; 0.7% (95% CI 0.3%-1.2%) for psoriasis worsening; 0.2% (95% CI 0.0%-0.4%) for central nervous system demyelinating disorder; 0.1% (95% CI 0.0%-0.3%) for lymphoma and for tuberculosis; and 0.1% (95% CI 0.0%-0.2%) for opportunistic infection and for lupus; 55 fatal events were reported. Rates of malignancies, lymphomas, nonmelanoma skin cancer, and hospitalization-associated infections were not higher than expected relative to administrative claims data. The percentage of patients rated as clear/almost clear was 12% at baseline, which increased to 51% at month 6 and remained relatively stable throughout 5 years.

Limitations: No internal comparator group was included; rare events may not have been detected.

Conclusion: No new safety signals were observed with long-term, real-world etanercept use. (J Am Acad Dermatol 2015;72:115-22.)

Key words: adverse events; etanercept; infections; malignancy; plaque psoriasis; registry; safety; surveillance.

Etanercept is a tumor necrosis factor (TNF) blocker indicated for the treatment of adults with chronic moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy, and for treatment of rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, psoriatic arthritis, and ankylosing spondylitis.[1] An analysis of long-term safety in 506 patients with psoriasis who initiated etanercept in 2 phase-III clinical trials showed a favorable safety profile, with no cumulative toxicity noted for up to 4 years of treatment.[2]

CAPSULE SUMMARY

- OBSERVE-5 evaluated long-term safety of etanercept in 2510 patients.
- Rates of malignancies, lymphomas, nonmelanoma skin cancer, and hospitalization-associated infections were not higher than expected relative to claims data (standardized incidence ratios < 1.0).
- No new/unexpected safety signals were noted for up to 5 years of real-world use of etanercept.

Although short-term clinical trials provide important information on the efficacy and safety of a drug, long-term registry studies are also needed to detect rare adverse events in a broader patient population. OBSERVE-5 was a 5-year observational registry that enrolled 2510 patients with plaque psoriasis who received etanercept.[3] We now report the final analysis of OBSERVE-5 data representing long-term, real-world experience with etanercept therapy.

METHODS

Study design

OBSERVE-5 was a phase-IV, prospective, multicenter, observational, surveillance registry and has been previously described.[4] Briefly, etanercept was self-administered at the dose and regimen determined by the investigator and patients were evaluated at 6-month intervals for up to 5 years. Patients could have discontinued etanercept, switched to another antipsoriatic therapy, used etanercept in combination with other antipsoriatic therapies, or discontinued any or all antipsoriatic treatments during the study. The study was approved by institutional review boards at all study sites. Written informed consent was provided by all patients before initiation of any study-related procedures. This study was registered under ClinicalTrials.gov identifier NCT00322439.

Patients

As previously described,[4] patients with plaque psoriasis for whom etanercept therapy was indicated per prescribing information and for whom the treating physician decided to initiate, reinitiate, or continue etanercept therapy according to usual care were eligible. Initially, patients were etanercept-naïve but a protocol amendment allowed patients with prior etanercept exposure to enroll (capped at 50%). Patients were ineligible if they were contraindicated for etanercept treatment according to the prescribing information,[1] had been treated with other TNF blockers or with commercial etanercept before April 2004 in the United States or December 2005 in Canada (when etanercept was approved for