Research letter

Real-world data on the effectiveness, safety and drug survival of dupilumab: an analysis from the TREATgermany registry

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Dear Editor, Multiple randomized clinical trials (RCTs) have demonstrated robust efficacy and favourable safety of the monoclonal anti-interleukin-4Rα antibody dupilumab in moderate-to-severe atopic dermatitis (AD).[1–4] However, in RCTs selected patient populations are studied in a mostly shorter timeframe, and the results do not always reflect outcomes under real-life conditions. Real-world studies offer insights into the ways in which a drug is actually used, and outcomes regarding toxicity and effectiveness in daily medical practice. Real-world evidence both supplements and complements information gleaned from the prevailing standard of RCTs. The TREATgermany registry is one of the largest AD registries worldwide with currently more than 1400 patients with moderate-to-severe AD followed up prospectively.[5,6]

In this interim analysis we aimed to analyse the real-world long-term effectiveness and safety and the drug survival of dupilumab compared with ciclosporin. All of the ethics committees of the participating recruitment centres have approved TREATgermany.

For the current analysis, data from 1211 patients with active moderate-to-severe AD (mean age 40·7 years, 42·2% female) were available (data release July 2021). The mean (SD) objective baseline scores were objective Scoring Atopic Dermatitis [oSCORAD, 40·5 (16·3)], Eczema Area and Severity Index [EASI, 16·1 (12·9)], Investigator' Global Assessment [3·2 (1·1)], Physician's Global Assessment [3·1 (1·2)], average itch numerical rating scale over the last 3 days [5·7 (2·8)], Patient-Oriented Eczema Measure [16·8 (7·6)] and Dermatology Life Quality Index [DLQI, 11·8 (7·8)]. Among the patients, 924 (76·3%) had received at least one systemic treatment for AD during observation in the registry. With a proportion of 81·9% (n = 757) dupilumab was the most widely used systemic drug. In contrast, before 1 December 2017, when dupilumab was launched in Germany, only 36·8% (n = 91) of the patients enrolled had received at least one systemic therapy during observation in the registry, with ciclosporin being the most commonly used drug (48%, n = 44; Figure 1a).

For safety and effectiveness, we analysed 369 and 41 patients who received dupilumab and ciclosporin, respectively, and had complete data from at least one scheduled follow-up visit. The baseline characteristics between the two groups did not differ significantly. The respective mean ages at initiation of dupilumab and ciclosporin were 41·3 and 39·2 years, and the proportions of male patients were comparable (58·1% and 56% for dupilumab and ciclosporin, respectively). The respective mean baseline EASI, oSCORAD and DLQI of patients treated with dupilumab were 21·5, 46·5 and 14·0; the respective mean scores for the ciclosporin group were 18·2, 45·0 and 14·7. Likewise, effectiveness outcomes were comparable for the two drugs (Figure 1b; and further data at https://doi.org/10.6084/m9.figshare.20342475.v2). However, discontinuation rates of ciclosporin were considerably higher. While dupilumab treatment was discontinued in only 5·0% and 11·4% of the patients until month 12 and 24, ciclosporin was discontinued in 78% and 100%, respectively (Figure 1d). The most frequent reasons for discontinuation of ciclosporin were side-effects (31%) and insufficient efficacy (27%); in 56% no reasons were reported. Nineteen (46%) of those who discontinued therapy with ciclosporin received dupilumab afterwards. The proportions of patients with ≥ 50%, ≥ 75% and ≥ 90% improvement in EASI were 80%, 50% and 20% respectively after 3 months of dupilumab treatment.

Adverse events (AEs) were reported in 42·5% of all dupilumab-treated patients. The most frequent dupilumab-associated AEs were ocular complaints, which were reported in 29·8% of the patients (mostly conjunctivitis, in 20·7% of dupilumab patients) (Figure 1c), 5·5% of whom discontinued therapy. In 48·2% of the cases the ocular AEs were reported in the first 3 months of treatment.

The results from this interim analysis demonstrate that in Germany dupilumab has rapidly emerged as the most commonly used systemic treatment and shows robust long-term effectiveness and favourable safety under real-life conditions. Ocular side-effects were more common than in trials, but rarely led to treatment discontinuation. Drug survival was high and compares favourably with a previous report from the BioDay registry.[7] Potential explanations are a continued treatment benefit, but potentially also a lack of discontinuation due to persistently controlled disease, and the lack of availability of alternative new systemic treatment options, such as tralokinumab and Janus kinase inhibitors, which have only recently become available. Thus, a re-evaluation needs to be done in due course. When interpreting ciclosporin survival, it has to be considered that most guidelines do not recommend continuous therapy for > 1–2 years.

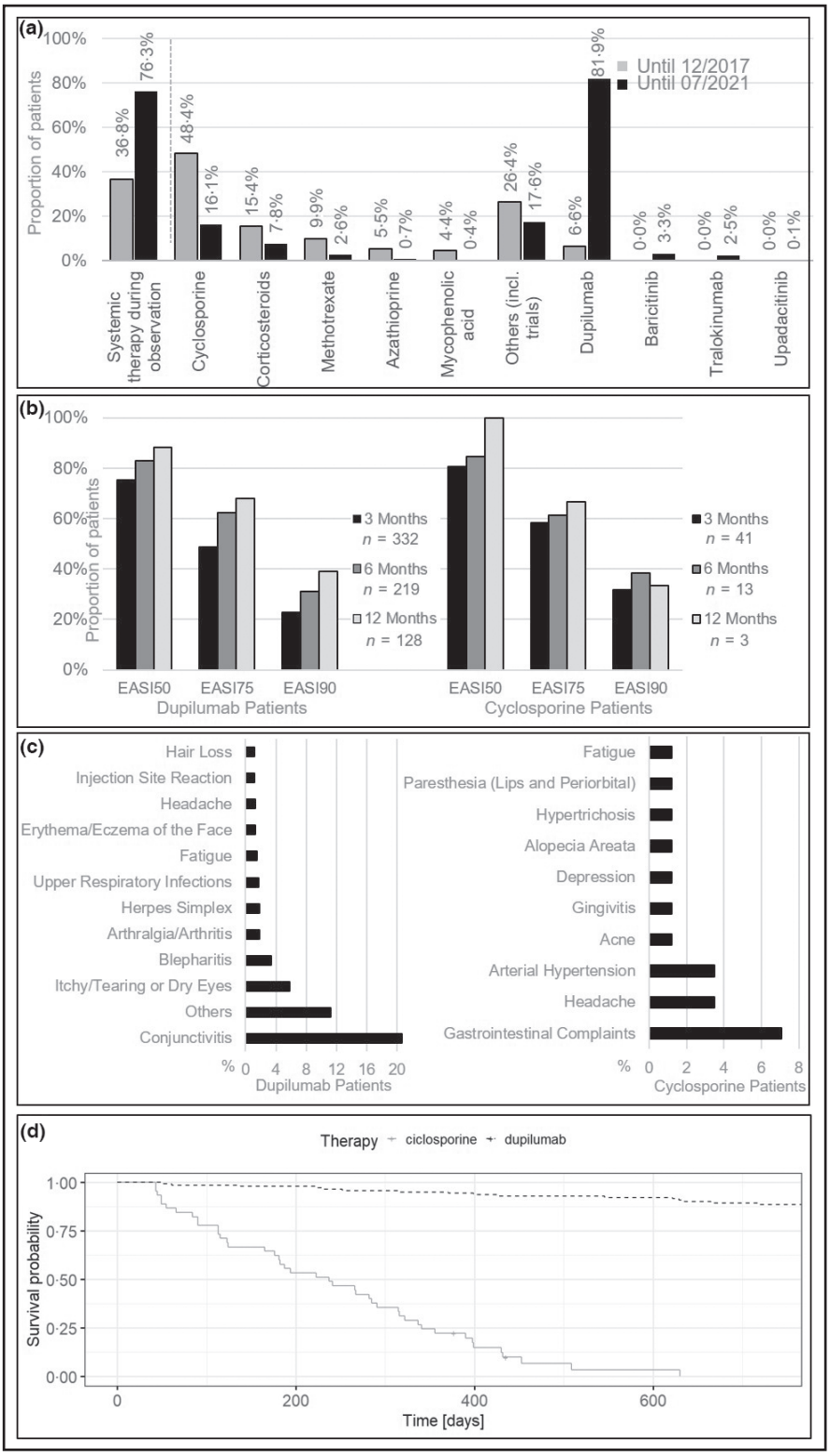

Figure 1 (a) Proportion of patients in the registry who had received systemic therapy for atopic dermatitis and the type of systemic therapy up to December 2017 and July 2021. (b) Effectiveness of dupilumab (n = 369 at baseline) and ciclosporin (n = 41): percentages with ≥ 50%, ≥ 75% and ≥ 90% improvement in Eczema Area and Severity Index (EASI). (c) Most frequently (> 1%) reported adverse events under therapy with dupilumab and ciclosporin. (d) Drug survival of dupilumab and ciclosporin over 24 months, Kaplan–Meier curve.

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Conflicts of interest: T.W. is co-principal investigator of the German Atopic Dermatitis Registry TREATgermany and has received honoraria for lectures or scientific advice on atopic dermatitis from AbbVie, Almirall, Galderma, Janssen/JNJ, LEO Pharma, Leti, Lilly, Novartis, Pfizer and Regeneron/Sanofi. S.W. is co-principal investigator of the German Atopic Dermatitis Registry TREATgermany; has received institutional research grants from LEO, Pfizer and Sanofi; and has performed consulting work and lectures for AbbVie, Almirall, Kymab, LEO Pharma, Lilly, Pfizer, Sanofi, Regeneron, LEO, Eli Lilly, AbbVie, Pfizer, GSK and Kymab. J.S. is leading principal investigator of the German Atopic Dermatitis Registry TREATgermany; has received institutional grants from Novartis and Pfizer for scientifically initiated research; and has received honoraria for consulting from Sanofi, Lilly, Novartis and ALK. S.A. has received lecture and/or consultancy fees from Novartis, LEO Pharma, Amgen, Lilly, Sanofi, Beiersdorf, Janssen, UCB and AbbVie. All of the other authors declare they have no conflicts of interest.

Data availability statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

Appendix S1 Full list of affiliations.

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