Research letter

Implementation of dupilumab in routine care of atopic eczema: results from the German national registry TREATgermany

DOI: 10.1111/bjd.18958

Dear Editor, The German atopic eczema registry TREATgermany is a noninterventional multicentre patient cohort study for adult patients with current moderate-to-severe disease activity or current or previous anti-inflammatory systemic treatment.[1,2] Dupilumab was demonstrated to be an effective treatment for patients with moderate-to-severe atopic eczema in clinical trials.[3–5] Real-world evidence is now needed to evaluate its effectiveness and safety in routine care. Here we describe the first results of an interim analysis of the TREATgermany registry regarding the implementation of dupilumab as a new treatment option in routine care.

Between June 2016 and January 2019, 612 patients (mean age 42·6 years, 38·2% female) were enrolled by 32 recruitment sites centres (16 hospital outpatient departments and 16 registered dermatological offices).[2] Since December 2017, when dupilumab was launched in Germany, 200 registry patients have received a new systemic therapy within routine care. In total, 174 of these patients received dupilumab, of whom 137 were not switched from another systemic agent, so a systemic-treatment-free baseline value was available. In 35 of 137 patients (25·5%) dupilumab was the first systemic therapy used, while 102 of 137 patients had been exposed to at least one systemic therapy prior to enrolment in the registry. Overall, 32·8% (45 of 137) had previous therapy with oral corticosteroids only and 35·8% (49 of 137) had been exposed to ciclosporin prior to treatment with dupilumab.

Patients who received dupilumab during registry observation (n = 137) had a high disease activity at baseline, with mean Eczema Area and Severity Index (EASI) and objective Scoring Atopic Dermatitis (oSCORAD) scores of 22·9 ± 13·6 and 48·0 ± 15·7, respectively. In total, 40·9% and 63·8% of the patients treated with dupilumab had '(very) severe' disease based on EASI (≥ 23·0) and Investigator's Global Assessment (IGA; severe: 4 or 5), respectively.

As TREATgermany is an ongoing registry, information from 3-month and 6-month follow-up visits was available for 105 and 53 patients, respectively, at the time of database lock (Table 1). Response rates for ≥ 50% improvement in EASI (EASI 50), EASI 75 and EASI 90 were respectively 77·1%, 57·1%, and 25·7% after 3 months. At month 6, the respective EASI 50, EASI 75 and EASI 90 response rates were 85%, 52% and 32%. oSCORAD response rates were slightly lower (54·7% mean percentage change after 3 months) than EASI response rates (74·2% mean percentage change after 3 months). This was most likely due to the different weighting of disease extent and severity items, with crusting/oozing not scored by EASI. IGA 0 or 1 (clear/almost clear) was seen in 29·5% and 33% of the patients at months 3 and 6, respectively.

The mean Patient-Oriented Eczema Measure (POEM) reduction was 54·5% at month 3, while the average numerical rating scales for itch intensity and sleeping problems over the past 3 days had improved by 57·8% and 72·2%, respectively. The mean Dermatology Life Quality Index (DLQI) score showed a decrease from 12·4 ± 6·7 at baseline to 4·4 ± 5·2 and 4·2 ± 4·5 after 3 and 6 months, respectively, of treatment ($P < 0·001$ for both comparisons). The proportion of well- and completely controlled weeks (assessed by patients) improved from 27·5% and 5·0% at baseline to 70·8% and 47·5% after 3 months and 79% and 53% after 6 months. Furthermore, the degree of skin dryness as assessed by SCORAD and POEM showed significant improvements.

The use of topical anti-inflammatory treatment also decreased during dupilumab therapy. At initiation of treatment 92·4%, 34·3% and 41·9% of patients were using topical corticosteroids (TCS), pimecrolimus and tacrolimus, respectively. After 3 months, these proportions were reduced to 46·7%, 10·5% and 16·2%. In addition, in 48·8% of patients the application of TCS in a reactive application regimen could be stopped, and the proportion of proactively treated patients was doubled (26·7% after 3 months).

Only 12·4% of patients treated with dupilumab did not show a clinically meaningful response in any of the major outcome domains (EASI 75, ≥ 4-point reduction in numerical rating scale for weekly average itch, or ≥ 4-point reduction in DLQI score), which is comparable with the recently published results of nonresponders in a Dutch registry (11%).[6] Response was not significantly associated with any clinical characteristic, but there was a trend for higher response rates in patients with higher disease activity at baseline.

Three months after the initiation of treatment with dupilumab, conjunctivitis was reported in 13·3% of patients (14 of 105). This rate increased to 23% (12 of 53) after 6 months of dupilumab exposure. The proportion of patients developing new onset or worsening of conjunctivitis was comparable with data from previous phase III clinical trials (9–28%)[3–5] and was lower than in reported cohorts of patients in routine care (34–62%).[6–8]

In conclusion, the observations from this real-world patient population indicate no major efficacy–effectiveness gap for dupilumab, but largely confirm trial data. As the registry continues, more comparative real-world evidence on immunomodulatory therapies will become available.

Table 1 Effectiveness of dupilumab in patients with first exposure to dupilumab within the registry observation period and with ≥ 3 months of follow-up after the first dupilumab prescription (n = 105; mean age 44·6 years, 32·4% female)

	Before dupilumab exposure (n = 105)	At 3 month follow-up (n = 105)[a]	At 6 month follow-up (n = 53)[b]
EASI			
Mean ± SD	23·6 ± 14·3	6·1 ± 6·1, P < 0·001	5 ± 5
EASI 50 response		77·1%	85%
EASI 75 response		57·1%	52%
EASI 90 response		25·7%	32%
Objective SCORAD (oSCORAD)			
Mean ± SD	49·2 ± 15·1	22·3 ± 11·4, P < 0·001	22·0 ± 11·4
oSCORAD 50 response		57·4%	48%
oSCORAD 75 response		20·0%	17%
oSCORAD 90 response		4·8%	7%
Investigator's Global Assessment	3·8 ± 0·7	2·0 ± 1·0	1·9 ± 0·9
Patient's Global Assessment	3·4 ± 1·0	1·8 ± 0·9	1·8 ± 0·9
POEM	19·3 ± 6·4	8·8 ± 5·9, P < 0·001	7·9 ± 5·9
NRS pruritus	6·4 ± 2·2	2·7 ± 2·1, P < 0·001	2·8 ± 2·0
NRS sleeping problems	5·4 ± 3·0	1·5 ± 2·1, P < 0·001	1·5 ± 2·1
DLQI	12·4 ± 6·7	4·4 ± 5·2, P < 0·001	4·2 ± 4·5
Level of disease control within past 12 weeks			
Well-controlled weeks	3·3 ± 3·1	8·5 ± 3·7, P < 0·001	9·5 ± 3·2
Completely controlled weeks	0·6 ± 13	5·7 ± 4·5, P < 0·001	6·3 ± 4·5
Dryness of skin			
oSCORAD (intensity)	2·0 ± 0·9	1·1 ± 0·8, P < 0·001	1·2 ± 0·8
POEM, question 7	3·4 ± 1·1	2·0 ± 1·5, P < 0·001	2·0 ± 1·4

[a]P-values by paired t-test for baseline vs. first follow-up visit. [b]In paired t-tests for the first vs. second follow-up visits no significant differences were seen.

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A full list of affiliations as well as acknowlegements are provided in Appendix S1 (see Supporting Information).

References

1 Schmitt J, Abraham S, Trautmann F *et al.* Usage and effectiveness of systemic treatments in adults with severe atopic eczema: first results of the German Atopic Eczema Registry TREATgermany. *J Dtsch Dermatol Ges* 2017; **15**:49–60.

2 Heratizadeh A, Haufe E, Stölzl D *et al.* Baseline characteristics, disease severity and treatment history of patients with atopic dermatitis included in the German AD registry TREATgermany. *J Eur Acad Dermatol Venereol* 2020; DOI: 10.1111/jdv.16078

3 Blauvelt A, de Bruin-Weller M, Gooderham M *et al.* Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): a 1-year, randomized, double-blinded, placebo-controlled, phase 3 trial. *Lancet* 2017; **389**:2287–303.

4 Simpson EL, Bieber T, Guttman-Yassky E *et al.* Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. *N Engl J Med* 2016; **375**:2335–48.

5 De Bruin-Weller M, Thaçi D, Smith CH *et al.* Dupilumab with concomitant topical corticosteroid treatment in adults with atopic dermatitis with an inadequate response or intolerance to ciclosporin A or when this treatment is medically inadvisable: a placebo-controlled, randomized phase III clinical trial (LIBERTY AD CAFÉ). *Br J Dermatol* 2018; **178**:1083–101.

6 Ariëns LFM, van der Schaft J, Bakker DS *et al.* Dupilumab is very effective in a large cohort of difficult-to-treat adult atopic dermatitis patients: first clinical and biomarker results from the BioDay registry. *Allergy* 2020; **75**:116–26.

7 Faiz S, Giovannelli J, Podevin C *et al.* Effectiveness and safety of dupilumab for the treatment of atopic dermatitis in a real-life French multicenter adult cohort. *J Am Acad Dermatol* 2019; **81**:143–51.
8 De Wijs LEM, Bosma AL, Erler NS *et al.* Effectiveness of dupilumab treatment in 95 patients with atopic dermatitis: daily practice data. *Br J Dermatol* 2020; **182**:418–26.

Funding sources: TREATgermany is financially supported by Sanofi-Aventis Deutschland GmbH.

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 authors and affiliations.
Appendix S2 Conflicts of interest statements.

Acknowledgments: we would like to thank all of the participating patients, study physicians and study staff in the participating clinics and practices, as well as the documentation team of the data and analysis centre in Dresden for their support of the German Atopic Eczema Registry TREATgermany.