



for advanced cSCC. Other agents of ICB also showed promising clinical results with objective and durable responses. However, most of the publications were case reports, which were rated as having poor quality of evidence and being at high risk of publication bias. Our analysis will help in clinical decision making and provide a comprehensive basis for future guideline development. Future efforts should be undertaken to conduct high-quality RCTs in order to provide results with the highest possible evidence.

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

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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 $\geq 50\%$ 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.

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 \pm SD	23.6 \pm 14.3	6.1 \pm 6.1, $P < 0.001$	5 \pm 5
EASI 50 response		77.1%	85%
EASI 75 response		57.1%	52%
EASI 90 response		25.7%	32%
Objective SCORAD (oSCORAD)			
Mean \pm SD	49.2 \pm 15.1	22.3 \pm 11.4, $P < 0.001$	22.0 \pm 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 \pm 0.7	2.0 \pm 1.0	1.9 \pm 0.9
Patient's Global Assessment	3.4 \pm 1.0	1.8 \pm 0.9	1.8 \pm 0.9
POEM	19.3 \pm 6.4	8.8 \pm 5.9, $P < 0.001$	7.9 \pm 5.9
NRS pruritus	6.4 \pm 2.2	2.7 \pm 2.1, $P < 0.001$	2.8 \pm 2.0
NRS sleeping problems	5.4 \pm 3.0	1.5 \pm 2.1, $P < 0.001$	1.5 \pm 2.1
DLQI	12.4 \pm 6.7	4.4 \pm 5.2, $P < 0.001$	4.2 \pm 4.5
Level of disease control within past 12 weeks			
Well-controlled weeks	3.3 \pm 3.1	8.5 \pm 3.7, $P < 0.001$	9.5 \pm 3.2
Completely controlled weeks	0.6 \pm 1.3	5.7 \pm 4.5, $P < 0.001$	6.3 \pm 4.5
Dryness of skin			
oSCORAD (intensity)	2.0 \pm 0.9	1.1 \pm 0.8, $P < 0.001$	1.2 \pm 0.8
POEM, question 7	3.4 \pm 1.1	2.0 \pm 1.5, $P < 0.001$	2.0 \pm 1.4

^aP-values by paired t-test for baseline vs. first follow-up visit. ^bIn paired t-tests for the first vs. second follow-up visits no significant differences were seen.

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 \pm 6.7 at baseline to 4.4 \pm 5.2 and 4.2 \pm 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.

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

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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.

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Indoor tanning use is associated with psoriasis in the Nurses' Health Study II

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DEAR EDITOR, Psoriasis is a chronic immune-mediated disease of the skin that affects approximately 2% of the US and Europe population.¹ The disease presents a significant burden for affected individuals and negatively affects their quality of life. Environmental and lifestyle factors play important roles in this disease, and several complex disorders have also been linked to psoriasis.^{1,2} Phototherapy, performed under medical supervision, is an effective treatment for psoriasis.¹ Indoor tanning produces artificial ultraviolet (UV) radiation and has been

Table 1 Odds ratios and 95% confidence intervals for the association between average indoor tanning frequency over the lifetime and psoriasis in the Nurses' Health Study II

Indoor tanning frequency ^a	Cases	Odds ratio (95% confidence interval)	
		Age adjusted	Multivariable adjusted ^b
None	1165	1.00	1.00
1–2 times per year	335	1.16 (1.02–1.31)	1.16 (1.02–1.32)
3–11 times per year	277	1.25 (1.10–1.43)	1.23 (1.08–1.41)
≥ 12 times per year	46	1.70 (1.25–2.30)	1.63 (1.20–2.21)
P-value for trend		< 0.001	< 0.001

^aFrequency of indoor tanning during high school or college, between ages 25 and 35 years, and over the past 2 years were determined by choosing from the following categories: none, 1–2, 3–5, 6–11, 12–23 or ≥ 24 times per year. These categories were represented as 0, 1.5, 4, 8.5, 17.5 and 24, respectively, at each of the three periods. The cumulative average frequency over a lifetime was calculated by averaging the frequency of indoor tanning during those three periods. This was then grouped into the four categories shown. ^bMultivariable-adjusted models were adjusted for covariate status at baseline (1989), including age (continuous), race (non-Hispanic white, Hispanic, African American, Asian), body mass index (< 25, 25–29.9, 30–34.9 or ≥ 35 kg m⁻²), smoking (never, past, currently smokes 1–14, 15–24, ≥ 25 or unknown cigarettes per day), alcohol intake (0, 0.1–4.9, 5–14.9 or ≥ 15 g per day), physical activity (metabolic equivalent hours per week, in quintiles) and annual ambient ultraviolet flux (in tertiles).