



Ocular adverse events during Dupilumab and Tralokinumab therapy: Data from the TREATgermany Registry

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Background

Ocular adverse events (oAEs) are a frequent and clinically relevant complication of IL-4/IL-13-targeted biologic therapy in atopic dermatitis (AD)¹. Real-world data are essential to characterize oAEs, identify patients at increased risk and support targeted monitoring strategies in clinical practice.

Results

Under dupilumab therapy, 305 of 1176 patients (25.9%) developed therapy-associated oAEs, leading to treatment discontinuation in 41 cases (13.4%). Under tralokinumab, oAEs occurred in 14 of 151 patients (9.3%), resulting in treatment discontinuation in five patients (35.7%) (Fig. 1). Conjunctivitis (including synonymous terms) was the most frequently reported event, followed by ocular dryness, pruritus, and blepharitis. Median time to oAE onset was 101 days for dupilumab and 90 days for tralokinumab, with most events occurring early after treatment initiation, although late-onset events were observed (Fig. 2). Symptom duration ranged from spontaneous resolution within weeks to persistence beyond one year. Seasonal distribution of oAEs under dupilumab showed slightly higher numbers of onsets in June, November and February, whereas the lowest numbers were observed in January and August (Fig. 3). Overall distribution was balanced across the year (mean 25.4 events/month). Multivariable analyses identified facial AD involvement at baseline (OR 1.45; $p=0.011$), comorbid bronchial asthma (OR 1.51; $p=0.0053$), prior systemic corticosteroid therapy (OR 1.95; $p<0.001$), and recent use of potent topical corticosteroids (class III; OR 1.52; $p=0.0039$) as independent risk factors (Fig. 4). Compared with dupilumab, tralokinumab was associated with a significantly lower overall oAE risk (OR 0.33; $p=0.0007$), although risk factor analyses were limited by sample size. Due to the small number of tralokinumab-treated patients with oAE, further analyses of seasonal distribution and time to first oAE were not statistically reliable and are therefore not presented.

Fig. 1: Distribution of oAEs under dupilumab and tralokinumab (n=1176/151)

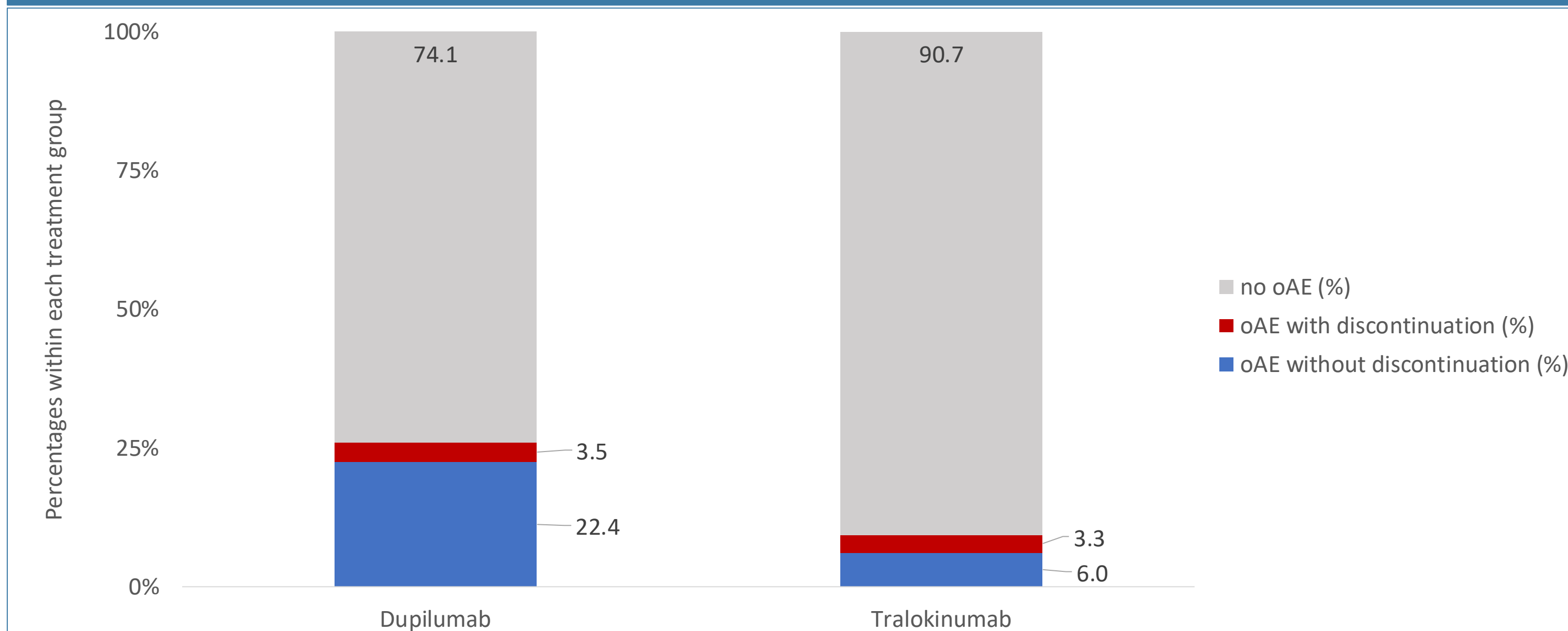
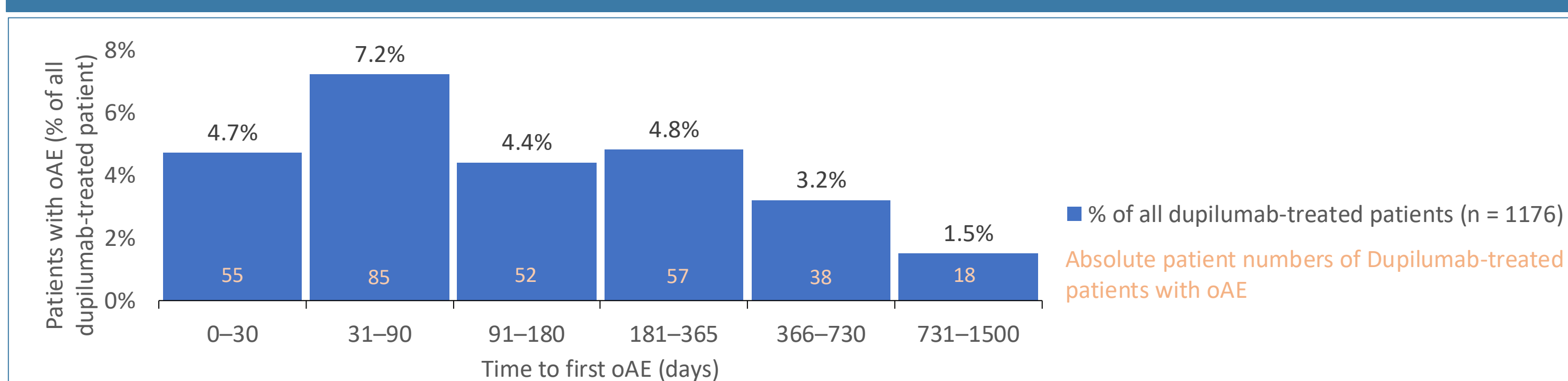


Fig. 2: Distribution of time to first oAE among dupilumab-treated patients. Percentages refer to all dupilumab-treated patients in the registry (n = 1176). Absolute patient numbers are displayed at the bottom of each bar.



Methods

TREATgermany is a nationwide, multicenter clinical research registry and one of the largest AD registries worldwide, comprising >2,500 adults and >500 children and adolescents with AD with >90 dermatology clinics and practices across Germany as recruiting centers². This analysis included 1,849 adults with moderate-to-severe AD until July 2023. Inclusion criteria were age ≥ 18 years and moderate-to-severe AD (oSCORAD >20 and/or ongoing or initiated systemic anti-inflammatory therapy within the past 24 months²). Patients receiving dupilumab or tralokinumab were identified using physician-reported treatment data. oAEs were identified via predefined adverse event fields and systematic screening of ocular-related free-text entries. Events were excluded if onset preceded biologic therapy or if causality was ruled out by the treating physician. Time to onset and duration of oAEs were assessed using visit-based intervals, accounting for incomplete documentation by predefined duration categories. For analysis of seasonal distribution, the date of first oAE occurrence was used. Patients with recurrent events were included according to each individual onset, so that every documented start of an oAE was counted separately. Baseline risk factors were analyzed using multivariable logistic regression with forward-backward stepwise selection. Principal component analysis was applied for dimensionality reduction prior to model fitting, and odds ratios (OR) were calculated to identify independent predictors of oAEs.

Fig. 3: Seasonal distribution of oAEs under dupilumab (absolute patient counts n=320, due to several patients with recurrent events)

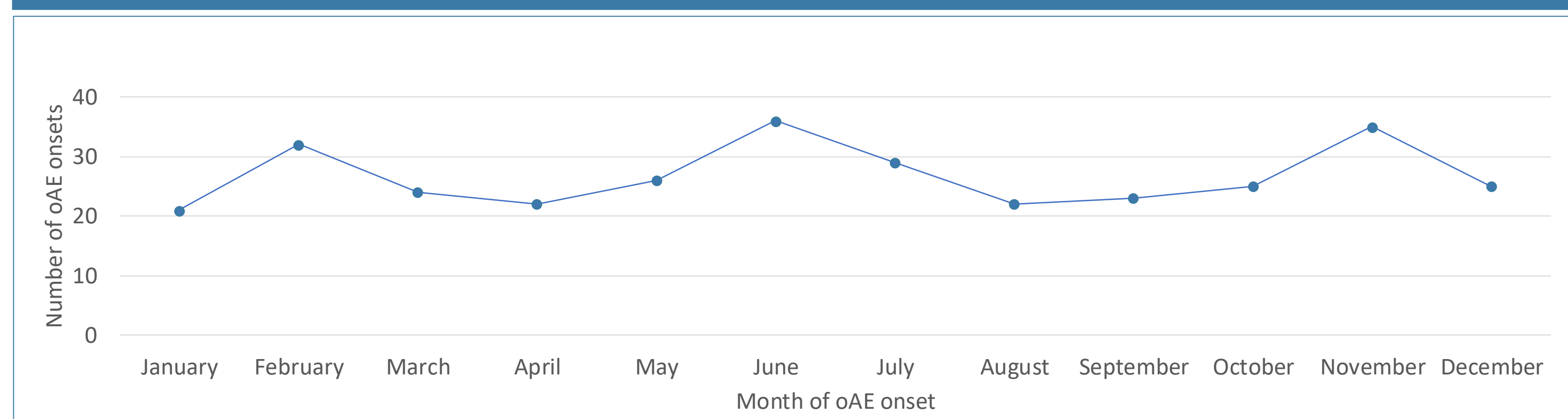
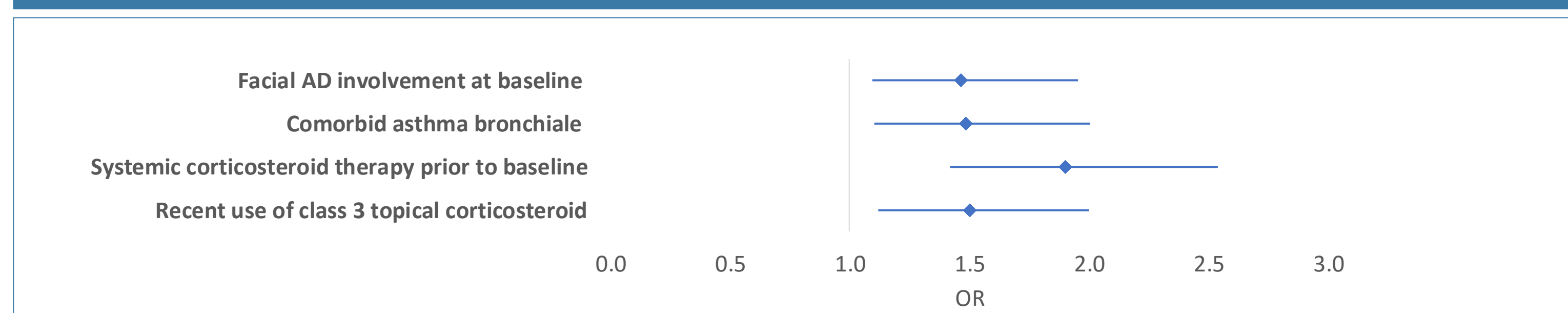


Fig. 4: Independent baseline risk factors for oAEs in dupilumab-treated patients (OR, 95% CI)



Limitations

Risk estimates and identification of independent predictors could only be calculated for dupilumab. Due to the limited number of patients treated with tralokinumab, no statistically reliable risk profile could be established for this subgroup. With increasing sample size, similar associations might emerge for tralokinumab; however, the current registry data are insufficient to draw definitive conclusions. A limitation of this analysis is the lack of a standardized baseline assessment of pre-existing ocular symptoms in TREATgermany, which may allow residual confounding. Although higher AD severity has been associated with oAEs, disease severity alone is unlikely to explain the observed differences. In clinical practice, patients with severe AD are not preferentially treated with dupilumab, and pre-existing conjunctivitis often discourages its use. Moreover, comparisons across different systemic therapies within the same registry reduce confounding by indication.

Conclusions

- oAEs are common under IL-4/IL-13-targeted therapy, occurring more frequently with dupilumab (26%) than with tralokinumab (9%) in real-world care
- oAEs typically arise within the first months of treatment, although prolonged courses may occur
- A higher-risk profile includes:
 - Facial AD involvement
 - Comorbid asthma
 - Prior systemic or potent topical corticosteroid use
- improved baseline documentation of ocular comorbidities, early risk stratification at treatment initiation, close ophthalmologic monitoring during the early treatment phase, and timely interdisciplinary management to prevent treatment discontinuation and optimize long-term patient outcomes
- Identifying high-risk patients at baseline may facilitate preventive eye care and support uninterrupted biologic therapy

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*The TREATgermany Study Group members are listed on the registry website www.treatgermany.org (short link: <https://t1p.de/tgstgr22>)



References

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