To the Editor:

Pruritus burden in atopic dermatitis (AD) is underestimated\(^1\). Dupilumab significantly reduced pruritus in clinical trials\(^2-5\). We aimed to characterize pruritus burden in severe AD patients and to analyze dupilumab’s effect on skin pruritus.

Prospective study including AD patients with 52 weeks(w) of dupilumab of a Portuguese tertiary hospital. The study was approved by the hospital’s ethics committee and a written informed consent was obtained for every patient. Itch Severity Scale (ISS) and Pruritus Numerical Rating Scale (NRS-P) were applied at 0, 2, 4, 16, 24 and 52w of treatment to assess pruritus severity.
Correlations with SCORAD/EASI, DLQI and NRS for sleep disturbance (NRS-SD) at the same time-points, were investigated. Subgroup analyses of ISS and NRS-P in patients reaching <50% or ≥50% improvement in EASI at 4w, and patients reaching <75% or ≥75% improvement in EASI at 16w, were also performed. Statistical analyses were performed with IBM SPSS software (v25.0). P-values <0.05 were considered statistically significant.

Total of 16 patients, 69% female, mean age 36.5±12.2years [17-60], mean AD duration 31.5±10.2years [14-48], 94% had allergic rhinitis, 63% asthma, 31% allergic conjunctivitis and 25% food allergy. Median TIgE 7863U/mL [254-27365] and median Eos 570/mm³ [60-2020].

Considering baseline pruritus characterization, the majority of patients (n=15; 94%) reported worsening by night, describing their itch mostly as “annoying” (n=15; 94%), “unbearable” (n=14; 88%) and “worrisome” (n=13; 81%). All body surface areas were implicated. When evaluating pruritus in its average state, 10 (63%) patients considered it “strong”, while in its worst state 15 (94%) patients gave a classification of “very strong”. Disturbances of mood (n=15; 94%), particularly agitation and trouble in concentration (n=10; 63%), were reported. Sexual activity was also impacted, with 56% (n=9) complaining of lower sexual desire and 38% (n=6) impaired sexual function. All patients considered pruritus led to difficulty in sleeping, with 81% (n=13) also reporting awakenings and 69% (n=11) needing medication to sleep (considering sleep disturbance related to pruritus).

Analyses of both pruritus scales (ISS/NRS-P) evolution during dupilumab treatment revealed a significant reduction since 2w (figure 1A), with ISS improving from 15.3 points (median) at baseline, to 10.8 points at 2w and 3.4 points after 52w, and NRS-P changing from 7.5 points (median) at baseline, to 6 points at 2w and 2 points after 52w. Considering ISS, all items improved significantly (figure 1B), with all patients reporting no mood affection or sleep disturbance related to pruritus at 52w. Subgroup analyses of patients reaching <50% or ≥50% improvement in EASI at 4w, and patients reaching <75% or ≥75% improvement in EASI at 16w, revealed a significant reduction in ISS (figure 1C.1-2) and NRS-P (figure 1C.3-4) for both subgroups in each timepoint (4w and 16w), including those patients with lower severity indexes improvement. ISS showed
correlations with NRS-P (r 0.555, p 0.026) and DLQI (r 0.655, p 0.045). NRS-P also correlated with DLQI (r 0.550, p 0.042). Correlation of both pruritus scales with NRS-SD did not reach statistical significance, as well as with severity indexes.

AD has one of the highest pruritus prevalence and intensity⁶, although studies addressing its burden, particularly in severe AD patients, are scarce. Clinical trials²,³,⁵, as well as real-life studies⁷,⁸ reported pruritus improvement in severe AD patients treated with dupilumab using only NRS-P. We also applied ISS to assess pruritus severity as this seven-item questionnaire⁹ complements pruritus qualitative evaluation, covering other domains (body extension, effects on mood, sexual activity and sleep)¹⁰. Although further studies with larger samples are needed to allow extrapolations of results, both scales showed good correlation with each other and with QoL, highlighting pruritus rapid and significant improvement in severe AD patients treated with dupilumab. The authors emphasize the importance of pruritus burden assessment as it may contribute to identify early treatment responders, especially in patients with lower severity indexes’ improvement, as well as to improve patients’ motivation to therapeutic adherence.

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RB, AL: study design; RB, RL: data collection; RB, RL: data analysis; RB: writing – original draft; RL, EP, AL: writing – review & editing.

Declaration of interest:
The authors declare that they have no relevant conflicts of interest.
REFERENCES:


**Fig 1.** Pruritus improvement using ISS (Itch Severity Scale) and NRS-P (Pruritus Numerical Rating Scale). 1A: ISS items’ scores evolution – weeks 0, 2 and 52 of Dupilumab treatment. *p<0.05. 1B: ISS and NRS-P scores evolution during treatment with Dupilumab. All values were statistically significant (p<0.05). 1C: ISS (C.1-2) and NRS-P (C.3-4) improvement in patients reaching <50% or ≥50% improvement in EASI at 4w, and patients reaching <75% or ≥75% improvement in EASI at 16w, in these time courses.