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*Letter to the Editor*

# A 48-week update of a multicentre real-life experience of dupilumab in adult patients with moderate-to-severe atopic dermatitis

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***Conflicts of interest:***

P. Amerio received honoraria as a speaker and advisory board member from Sanofi-Genzyme. P. Betto has been principal investigator in clinical trials sponsored by and/or received honoraria from Sanofi-Genzyme and Sandoz. L. Bianchi has been principal investigator in clinical trials sponsored by and/or received personal fees from Sanofi Genzyme, Eli-Lilly, Abbvie. S.P. Cannavò has been principal investigator in clinical trials sponsored by and/or received personal fees from AbbVie, Celgene, Eli-Lilly, Janssen-Cilag, Leo Pharma, Novartis, Sanofi. C. Caruso declared no conflicts of interest. A. Costanzo has been principal investigator in clinical trials sponsored by and/or received personal fees from

AbbVie, Abiogen, Almirall, Amgen, Biogen, Celgene, Eli-Lilly, Genzyme, Leo Pharma, Novartis, Pfizer, Regeneron, Samsung, Sandoz and Sanofi. A. Cristaudo has been principal investigator in clinical trials sponsored by Abbvie, Leo Pharma and Pfizer. F. Cusano received honoraria as speaker and advisory board member from Sanofi Genzyme. M. Esposito has served as a speaker for Sanofi-Genzyme. M.C. Fargnoli has served on advisory board, received honoraria for lectures and research grants from Sanofi-Genzyme. S. Ferrucci has been principal investigator in clinical trials sponsored by and/or received personal fees from AbbVie, Eli-Lilly, Novartis, and Sanofi. G. Girolomoni has been principal investigator in clinical trials sponsored by and/or received personal fees from AbbVie, Abiogen, Almirall, Amgen, Biogen, Celgene, Eli-Lilly, Genzyme, Leo Pharma, Menlo therapeutics, Novartis, Pfizer, Regeneron, Samsung, Sandoz and Sanofi. S. Lembo has received honoraria as a consultant and for attending an academic international meeting. G. Malara has been principal investigator in clinical trials sponsored by and/or received personal fees from AbbVie, Eli-Lilly, Janssen, Celgene, Sanofi and Almirall. A. Offidani has been principal investigator in clinical trials and has been paid as consultant by AbbVie, Almirall, Amgen, Celgene, Eli-Lilly, Leo Pharma, Novartis, Pfizer, Regeneroni and Sanofi. A Patrizi has served as a speaker and received honoraria from Sanofi-Genzyme for lectures, research grants and as an advisory board member. C. Patruno has been reimbursed by Sanofi for Advisory Boards and for international conference attendance. C. Peccianti declared no conflicts of interest. G. Pellacani has been principal investigator in clinical trials sponsored by and/or received personal fees from AbbVie, Almirall, Eli-Lilly, Leo Pharma, Novartis, and Sanofi. K. Peris has received honoraria as speaker and advisory board member from Sanofi-Genzyme. F. Rongioletti has served on advisory board, received honoraria for lectures and research grants from Novartis, AbbVie, Janssen-Cilag, Eli-Lilly, Leo Pharma, Sanofi-Genzyme. G. Stinco has been principal investigator in clinical trials, received honoraria for lectures and research grants from Novartis, AbbVie, Janssen-Cilag, Eli-Lilly, Leo Pharma, Sandoz, UCB. L. Stingeni has been principal investigator in clinical trials sponsored by and/or received personal fees from AbbVie, Almirall, Celgene, Eli-Lilly, Janssen, Novartis, and Sanofi-

Genzyme. R. Tiberio has been principal investigator in clinical trials and received honoraria by Sanofi-Genzyme, Abbvie, Eli-Lilly.

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Abstract

The long-term efficacy and safety of dupilumab has been demonstrated in clinical trials and only in few real-world studies. We conducted an extension analysis from a previous 16-week study on 109 adult patients affected by moderate-to-severe atopic dermatitis treated with dupilumab. Eczema-Area-and-Severity-Index (EASI), itch numerical-rating-score (itch-NRS), Dermatology-Life-Quality-Index (DLQI) scores, drug survival rate and occurrence of adverse events after 24 and 48 weeks of dupilumab treatment were retrospectively collected. Dupilumab demonstrated sustained improvement of disease severity, pruritus, and quality of life in our series with an increasing percentage of patients gaining EASI75 and EASI90 response during the study period. Few patients interrupted treatment resulting in a very high drug survival rate. We also confirmed the favorable safety profile of the drug with absence of serious adverse events and serious infections throughout the 48-week period. The prevalence of conjunctivitis was low and mainly occurred in the mid-term with resolution of the majority of cases at 48 weeks.

*Dear Editor*,

The long-term efficacy and safety of dupilumab has been demonstrated in clinical trials [1,2] and only in few real-world studies [3-5]. We recently published a retrospective real-life Italian multicentre short-term experience with dupilumab in 109 adult patients with moderate-to-severe AD patients [6]. We herein report an extension analysis of our study beyond 16 weeks, retrospectively collecting from medical records Eczema-Area-and-Severity-Index (EASI), itch numerical-rating-score (itch-NRS) and Dermatology-Life-Quality-Index (DLQI) scores, analyzing drug survival rate and recording adverse events after 24 and 48 weeks of dupilumab treatment.

Baseline demographic and clinical characteristics of the 109 (71M/38F) adult moderate-to-severe AD patients enrolled as well as study design were previously reported [6]. Briefly, dupilumab was prescribed according to the approved indication and dosage [7]. Concomitant topical medications were permitted as needed while patients receiving other systemic treatments were excluded from the analysis. A last observation carried forward analysis was conducted for missing data imputation. Patients signed an informed consent allowing data publication for scientific purposes (IRB approval no. 27/2019, University of L'Aquila).

A significant reduction of mean EASI score was observed from baseline to week 4, 16, 24 and 48 ($p<0.0001$ for all assessment) (Figure 1a). Mean EASI percentage improvement from baseline was 75.8% after 24 weeks and 81.7% after 48 weeks. Mean itch-NRS and mean DLQI scores also demonstrated a significant reduction from baseline at all timepoints ($p<0.0001$ for all) (Figures 1b and c). EASI50, EASI75 and EASI90 were achieved by 85.3%, 68.8%, 36.7 % of patients at 24 weeks and by 89.9%, 81.9%, 50.5% at week 48, respectively (Figure 1d).

Concerning adverse events (AE), conjunctivitis was diagnosed in 20.5% (21/102) of patients at week 24 and in 8.1% (8/98) at week 48, suggesting remission in most cases. Additional AE were experienced by 7.8% (8/102) and 7.1% (7/98) of patients at 24 and 48

weeks, respectively, and included facial dermatitis, urticaria/angioedema, alopecia, molluscum contagiosum, guttate psoriasis, keratoconus, increase of eosinophils, miscarriage and thyroiditis. Treatment was discontinued by 4 patients at week 24, due to inefficacy (3) and diagnostic redefinition (1) and by additional 4 patients at week 48, due to patient decision (2), logistic difficulties (1) and AE (thyroiditis in 1 patient). Notably, drug survival showed a persistence rate of 97.2% (106/109) at weeks 4 and 16, 93.5% (102/109) at week 24 and 89.9% (98/109) at week 48 (Figure 2).

Few real-life studies described the long-term effectiveness and safety of dupilumab [3-5]. A reduction of 79.3% in EASI, 69.9% in VAS pruritus and 62.8% in DLQI was observed in a Spanish cohort of 70 AD patients at week 24 [3]. Long-term maintenance of response with no emerging AE was described in an independent sample of 30 Spanish patients after 52 weeks of dupilumab treatment [4]. A higher proportion of IGA responders than in randomized trials was recently reported in a 52-week Canadian study, likely explained by the concomitant use of adjunctive medications [5].

In line with the literature, dupilumab demonstrated sustained improvement of disease severity, pruritus, and quality of life in our series with an increasing percentage of patients gaining EASI75 and EASI90 response during the study period. Few patients interrupted treatment resulting in a high drug survival rate. We also confirm the favorable safety profile of the drug with absence of serious AE and serious infections throughout the 48-week period. The prevalence of conjunctivitis was low and mainly occurred in the mid-term with resolution of the majority of cases at 48 weeks. Limitations of this study include the small sample size, the retrospective design, a non-systematic AE reporting and the absence of a control group.

In conclusion, dupilumab demonstrated effectiveness in reducing disease severity and improving quality of life and maintained a favorable safety profile in the long-term in adult patients affected by moderate-to-severe, difficult-to-treat AD in the real-life setting.

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***Figure legends***

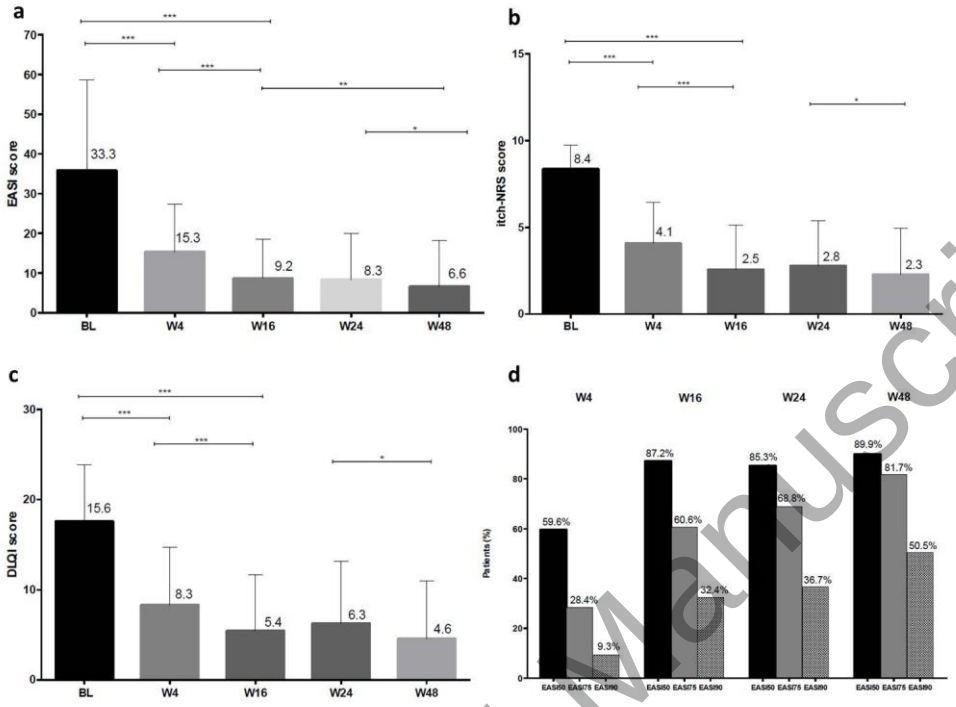


**Figure 1.** Mean value of EASI (a), itch-NRS (b) and DLQI (c) at baseline, week 4, 16, 24 and 48. Mean values are indicated on the bars; thin lines refer to Standard Deviation. (d) Percentage of patients achieving EASI50, EASI75 and EASI90 at week 4, 16, 24 and 48. Percentage values are indicated on the bars. ***p<0.0001; **p<0.001; *p<0.05.

BL, baseline; W4, week 4; W16, week 16; W24, week 24; W48, week 48.

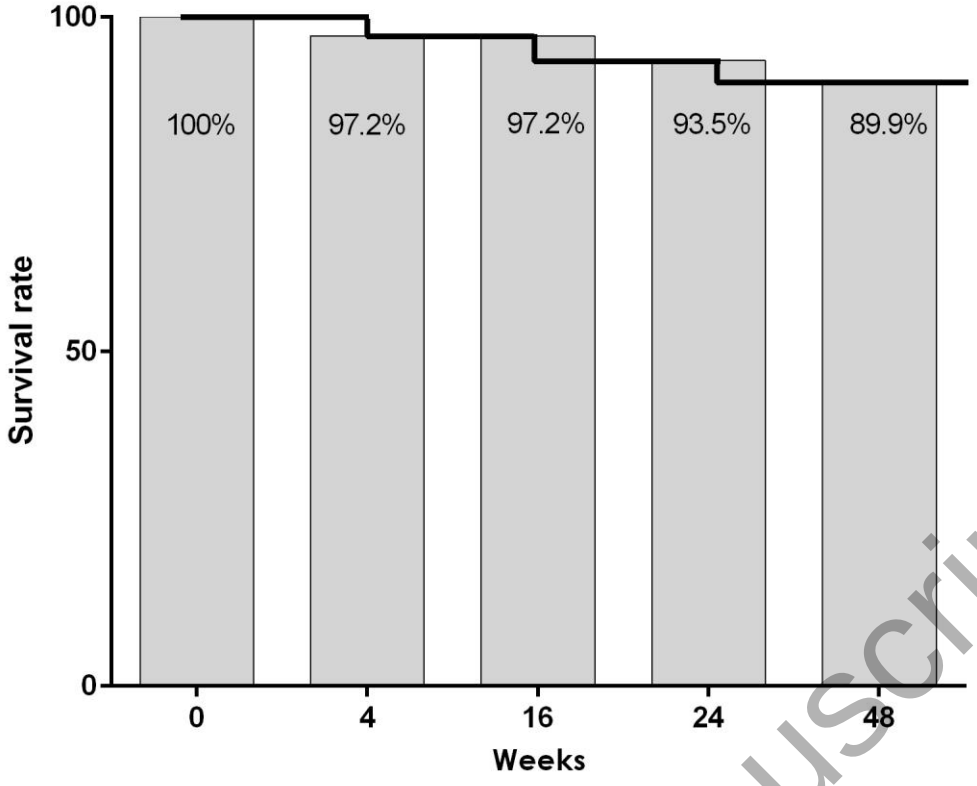


**Figure 2.** Drug survival rates of dupilumab during the 48-week observation period. Percentage values of patients treated with dupilumab across the study period are indicated on the bars.