

Omalizumab for the treatment of chronic inducible urticaria in 80 patients

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DEAR EDITOR, An observational retrospective multicentre study was conducted by the Catalan and Balearic Urticaria Network (XURCB). We recruited 80 participants with conditions as follows: solar urticaria ($n = 27$), cold urticaria ($n = 22$), symptomatic dermographism ($n = 11$), cholinergic urticaria ($n = 10$), delayed pressure urticaria ($n = 7$), aquagenic urticaria ($n = 2$) and heat urticaria ($n = 1$). To compare the therapeutic benefits for different subtypes of chronic inducible urticaria (CIndU), we evaluated response to omalizumab 300 mg per 4 weeks using the urticaria control test (UCT),¹ grouping patients according to response [complete response (UCT = 16), satisfactory response (UCT ≥ 12 –15) and non-response (UCT < 12)]. We also analysed time to a satisfactory/complete response (fast ≤ 3 months and slow > 4 months). We used omalizumab according to the EAACI/GA²LEN/EDF/WAO guideline recommendations.² We used multivariate statistical analysis to evaluate the factors that could predict response: sex, age, body mass index, years with CIndU, personal atopy history, previous CIndU episodes, personal angio-oedema history, baseline total IgE (normal value ≤ 104 kU L⁻¹), baseline D-dimer (normal value ≤ 500 ng mL⁻¹) and baseline UCT. The study was approved by our Clinical Research Ethics Committee (2016/6606/IEUDRAC).

Patient demographic and clinical features are summarized in Table 1. Complete, satisfactory and no response to omalizumab 300 mg per 4 weeks was achieved in 32 (40%), 26 (33%) and 22 (28%) patients. Patients with solar urticaria

were observed to show a more complete response than patients with either symptomatic dermographism {63% [95% confidence interval (CI) 44.79–81.21] vs. 27.3% [95% CI 0.97–53.63], $P = 0.046$ } or cold urticaria [63% (95% CI 44.79–81.21) vs. 22.7% (95% CI 5.20–40.20), $P = 0.005$]. Complete or satisfactory response was achieved in almost three-quarters ($n = 58$) of patients. The response of patients with symptomatic dermographism was significantly poorer than that of patients with either solar urticaria [45.5% (95% CI 16.07–74.93) vs. 81.5% (95% CI 66.85–96.15), $P = 0.026$] or cholinergic urticaria [45.5% (95% CI 16.07–74.93) vs. 90% (95% CI 71.41–100.00), $P = 0.031$]. Updosing findings were as follows: when the dose was increased to 450 mg per 4 weeks in 14 of the 22 nonresponders, seven achieved complete or satisfactory disease control; and when the dose was increased to 600 mg per 4 weeks in four of the remaining seven nonresponders, one patient each achieved satisfactory and complete disease control. We ultimately considered omalizumab treatment to have definitively failed in only two patients with cold urticaria. No serious adverse effects were reported at any dose. While a good response in 12 patients led to omalizumab withdrawal, due to relapse, treatment was reinitiated in half of those patients, again achieving a good response. Response time at 300 mg per 4 weeks was fast in 57% of complete/satisfactory responders, with the fastest responses achieved for the cold and solar urticaria subtypes. A history of atopy and higher baseline total serum IgE were associated with a more efficacious response to omalizumab, but only to a statistically significant degree in the cold urticaria subtype [odds ratio (OR) 7 (95% CI 0.67–72.86), $P = 0.015$] and [OR 12 (95% CI 1.12–128.4), $P = 0.01$], respectively, with no statistical interaction. No significant differences existed for any other variables analysed.

Only four clinical trials, all with small samples, have been conducted on omalizumab to treat CIndU,^{3–6} while one clinical analysis of cases compared omalizumab efficacy for different subtypes.⁷ We observed that omalizumab is an effective treatment for patients with CIndU refractory to fourfold H₁-antihistamines, as reported elsewhere.⁸ We also observed that the best response to omalizumab was achieved for solar urticaria, while the poorest response – slightly worse than reported elsewhere⁵ – was achieved for symptomatic dermographism. We observed a slow response to omalizumab in patients with cholinergic urticaria corroborating clinical trial results reported by Gastaminza *et al.*³ In contradiction to a previous clinical analysis, we observed a slower response for patients with delayed pressure urticaria.⁷

Although further research is required to identify biomarkers that predict treatment response for CIndU, we observed that patients with high total serum IgE and a history of atopy responded well to omalizumab, while Metz *et al.*⁴ reported that patients with cold urticaria and a history of atopy responded well to omalizumab.

Our findings suggest that omalizumab is an effective treatment for CIndU and, furthermore, that updosing may prove

Table 1 Patient demographic and clinical variables ($n = 80$)

Demographic and clinical variables	n (%) or mean $\pm$ SD
Sex	
Female	49 (61)
Male	31 (39)
Mean age (years)	45.63 $\pm$ 16.3
Body mass index	24.1 $\pm$ 5
Angio-oedema history	12/80 (15)
High baseline IgE levels	37/77 (48)
High baseline D-dimer levels	5/50 (10)
Baseline UCT	5.14 $\pm$ 3.3
CIndU evolution before starting omalizumab (years)	9.65 $\pm$ 7.3
Atopy history	26/80 (33)
Previous episodes (long interval without active disease)	24/80 (30)
CIndU, chronic inducible urticaria; UCT, urticaria control test.	

beneficial for nonresponders. The main limitations of our study are its retrospective nature, the small number of patients for some CIndU subtypes and the lack of a disease activity scale common to all subtypes. Larger studies are needed to confirm our results.

V. Exposito-Serrano ¹, L. Curto-Barredo ², P. Aguilera Peiro,³ S. Gómez Armayones,³ E. Serra-Baldrich,⁴ J. Spertino,⁴ M. Bonfill Ortí,⁵ I. Figueras Nart,⁵ G. Melé-Ninot ⁶, C. Baliu-Piqué,⁷ A. Sala Cunill,⁸ M. Labrador-Horrillo,⁸ A. Guilabert Vidal,⁹ N. Fernández Chico¹ and A.M. Giménez-Arnau²

Departments of Dermatology at: ¹Hospital Universitari Parc Taulí, Sabadell, ²Hospital del Mar, ³Hospital Clínic de Barcelona, ⁴Hospital de la Santa Creu i Sant Pau, ⁵Hospital de Bellvitge, ⁶Hospital Universitari Sagrat Cor, ⁷Hospital d'Igualada-Consorci Sanitari de l'Anoia, ⁸Allergology Department, Hospital Universitari Vall d'Hebron; and ⁹Hospital General de Granollers, Spain
Email: expositovicente@gmail.com

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Evaluation of 'not relevant' responses on the Dermatology Life Quality Index (DLQI) and the DLQI-R scoring modification among Indian patients with vitiligo

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DEAR EDITOR, It has been suggested that the 'not relevant' responses (NRRs) in the Dermatology Life Quality Index (DLQI) may lead to an underestimation of disease burden.^{1–3} Recently, a modified DLQI scoring method, the DLQI-R, has been proposed to address this limitation by removing such items from the denominator for scoring.⁴ DLQI-R has shown better validity, responsiveness and discriminatory power than the DLQI in patients with psoriasis, morphea and pemphigus.^{4,5} We conducted this study to assess the impact of NRRs on vitiligo burden, and compare the performance of the DLQI-R with the DLQI in Indian patients with vitiligo.

This cross-sectional study re-analysed the data from an earlier study on minimal important change of the Vitiligo Impact Scale (VIS)-22, a validated vitiligo-specific quality-of-life instrument and DLQI in Indian patients with vitiligo.⁶ Measures of vitiligo burden [VIS-22, DLQI, affected body surface area (BSA)] were compared between patients with NRRs and those who responded 'not at all' for DLQI items 3–10 using the unpaired t-test. Logistic regression analysis was performed to identify the predictors of NRRs. Performance of DLQI-R was compared with DLQI by estimating the correlation (Spearman's rho) of their mean scores and agreement (percentage agreement, weighted κ) of their bands with Global Question (GQ) and VIS-22. Steiger's Z-test and two-proportion Z-test were used to compare the difference between correlation coefficients and percentage agreements of DLQI and DLQI-R. A P-value < 0.05 was considered statistically significant.

The data of 316 patients with vitiligo (178 acrofacial, 91 generalized, 24 segmental, 23 focal vitiligo) were analysed, of which 146 (46.2%) patients had one, 85 (26.9%) had two and 11 (3.5%) had three NRRs. An NRR was chosen most commonly for items 6, sports (n = 135, 42.7%) and 9, sexual difficulties (n = 129, 40.8%), followed by item 7, working/studying (n = 45, 14.2%). Vitiligo burden as measured by VIS-22 and DLQI scores, and physician-evaluated BSA involvement did not differ statistically significantly between patients with NRR and those who responded 'not at all' for most of the DLQI items. Patients with no, mild or moderate effect on life as estimated by GQ [odds ratio (OR) 2.62, 95% confidence interval (CI) 1.54–4.47, P < 0.001] and VIS-22 (OR 3.17, 95% CI 1.79–5.62, P < 0.001) were more likely to provide an NRR compared with those with large or very large effects. Sex, marital status, employment status and affected BSA had no statistically significant association with NRRs (data available on request).