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Impact of dupilumab on health-related quality of life in patients with atopic dermatitis

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Linked Article: Tsianakas et al. *Br J Dermatol* 2018; **178**:406–414.

Dupilumab is the first biological drug approved for treating atopic dermatitis (AD).¹ It was granted a market authorization in March 2017 in the U.S.A., and in September 2017 in the European Union. It is a human monoclonal antibody against the interleukin (IL)-4 receptor alpha subunit, inhibiting the signalling of inflammatory cytokines IL-4 and IL-13, which are involved in the pathogenesis of atopic and allergic diseases such as AD, asthma, chronic sinusitis with nasal polyposis and eosinophil oesophagitis.²

Dupilumab is indicated for the treatment of moderate-to-severe AD in adult patients whose disease cannot be adequately controlled with topical therapies or when those therapies are not advisable. A very recent meta-analysis of dupilumab randomized controlled trials (RCTs) confirmed its efficacy and safety profile in AD.³ Combination of dupilumab with topical corticosteroids seems to improve the effects.⁴ In addition to efficacy, the impact on health-related quality of life (HRQoL) is crucial for patients with AD, particularly because of the often intolerable itching, sleep disturbances and emotional distress.⁵ Findings from phase III RCTs suggest that dupilumab therapy is associated with a significant improvement in HRQoL, measured by either generic (EuroQoL-5D) or dermatology-specific instruments (Dermatology Life Quality Index, DLQI).^{2,6,7}

In this issue of the *BJD*, Tsianakas et al. report data on the efficacy, safety and HRQoL effect of dupilumab from a 12-week phase II clinical trial.⁸ This is the first dupilumab RCT to employ a disease-specific HRQoL tool, namely the Quality of Life Index for Atopic Dermatitis (QoLIAD). The QoLIAD is a validated, 25-item needs-based questionnaire, covering the following needs frequently affected by AD: mental and emotional stimulation,

physical and emotional stability, security, sharing and belonging, self-esteem and personal development and fulfilment.⁹ Importantly, the QoLIAD has only a few items (e.g. feeling of embarrassment, clothing and leisure time) in common with the other HRQoL instruments widely used in patients with AD, such as the DLQI.^{5,10} Thus, the positive change in QoLIAD scores detected by Tsianakas et al. provides evidence on the favourable HRQoL effects of dupilumab from an entirely new perspective. To put it into numbers, dupilumab improved mean percentage change from baseline by almost 50% within 4 weeks, and 64% within 12 weeks assessed by QoLIAD.

Notwithstanding the rapid and sharp improvement in QoLIAD scores achieved with dupilumab, the small sample size (32 patients in the dupilumab arm), the lack of more frequent follow-up visits and the relatively short overall follow-up period are major limitations to the study. The real-world effectiveness and HRQoL impact of dupilumab need to be confirmed in future studies. Nevertheless, the approval of dupilumab is likely changing the HRQoL expectations of patients with moderate-to-severe AD, and should be a forerunner of the era of biologics in the treatment of AD.

Conflicts of interest

None declared.

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Safety gains don't translate into reduced costs or increased QALYs for doxycycline compared with prednisolone for patients with bullous pemphigoid

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Linked Article: Mason et al. *Br J Dermatol* 2018; **178**:415–423.

The article by Mason and colleagues¹ in this issue of the *BJD* is a concisely written paper reporting the economic results of the noninferiority BLISTER trial.² The clinical study found that doxycycline (D) was not clinically inferior to prednisolone (P)-initiated treatment in patients with bullous pemphigoid (BP) in terms of short-term blister control (given the *a priori* noninferiority margin of 37%) but was significantly safer (in terms of number of patients having a treatment-related severe, life-threatening or fatal adverse event) than P in the long term (defined as 52 weeks).

The economic evaluation is a within-trial (12 month) participant-level cost-effectiveness analysis comparing D vs. P-initiated treatment in patients with BP from a National Health Service perspective and meets the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist.³ It is an important article to publish given the limited economic research and difficulties of undertaking trials in this clinical area.

D was estimated to be £959 [95% confidence interval (CI) –24 to 1941] more expensive on average per participant than P, while Quality-Adjusted Life Years (QALYs) were 0.024 (95% CI –0.088 to 0.044) lower in the base case (UK 2013). In subgroup analyses these costs and QALYs changed to £269 (–662 to 1199) and 0.001 (–0.074 to 0.076) in mild-to-moderate disease and £2558 (–82 to 5198) and –0.090 (–0.222 to 0.042) in severe disease, respectively.

It is interesting to note that the significant safety effects found in the clinical paper do not seem to have translated into lower costs or higher QALYs for D compared with P, suggesting that the safety effects were not enough to offset the extra costs of D. There may also be some uncertainty as to whether the choice of outcome measure in the economic evaluation was able to detect important differences for this condition.

The study authors conclude that neither strategy is preferred in the treatment of BP in the case of mild or moderate blistering but that there is a 'clear preference' for P-initiated therapy for those with severe disease.¹ However, other interpretations are possible, for instance, if one accepts that resource allocation decisions ought to be based on mean net benefits.⁴ The mean estimates show that D is dominated by P, and that in the subgroup analysis the incremental cost-effectiveness ratio (ICER) for mild or moderate disease was significantly over the £30 000 NICE threshold (ICER £298 586), suggesting P should still also be preferred, although clearly there is much uncertainty around these results as stated by the authors. For those interested, a number of papers discuss different approaches that economic evaluations can take and the implication of approach on the interpretation of clinical and economic results.^{5–7}

The value of information analysis conducted within the study suggested there is likely to be little value of undertaking further research on this issue, given the small patient population likely to benefit.

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Conflicts of interest

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