RESEARCH LETTER

Dupilumab Achieves Early Disease Control in Bullous Pemphigoid: A Case Series with TARC-based Biomarker Evaluation

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To the Editor,

Bullous pemphigoid (BP) is the most common autoimmune blistering disease in the elderly (1). Dupilumab, an interleukin (IL)-4/IL-13 receptor antagonist (2), has emerged as a promising option for patients who are refractory to conventional therapies or who require steroid-sparing approaches (3–5). However, real-world data on biomarker responses, particularly in Asian populations, remain limited.

We retrospectively analysed 18 patients with BP (median age 78 years; 9 males, 9 females) treated with dupilumab at our institution. Patients were categorized into 3 groups: steroid-refractory ($n=3$), relapse during corticosteroid tapering ($n=5$), and minocycline/topical corticosteroid-resistant ($n=10$). Baseline characteristics and prior treatments, including comorbidities such as hypertension (61.1%) and diabetes mellitus (44.4%), are summarized in Table SI. Median Bullous Pemphigoid Disease Area Index (BPDAI) scores at baseline were 46.0 (range: 24–78), and most patients (83.3%) exhibited elevated serum immunoglobulin E (IgE) levels.

Serum thymus and activation-regulated chemokine (TARC) levels, measured routinely in Japan for atopic dermatitis but not commonly used in Europe, were elevated in all cases (median 2,104 pg/mL). Disease control – defined as cessation of new blister formation and pruritus with healing of existing lesions – was achieved in 88.9% (16/18) of patients within 4 weeks (median: 14 days; **Fig. 1**). Subgroup response rates were as follows: 66.7% in the steroid-refractory group, 100% in the relapse group, and 90.0% in the minocycline/topical steroid-resistant group. Complete remission, defined as BPDAI=0 with no new lesions or pruritus, was also observed in 88.9% (16/18) of patients over 52 weeks, with remission rates of 22.2%, 33.3%, 72.2%, 88.9%, and 90.9% at weeks 2, 4, 12, 28, and 52, respectively (Fig. S1). Relapse occurred in 2 patients (11.1%) after dupilumab discontinuation (median: 23.3 weeks); both responded successfully to re-treatment.

Longitudinal changes in BPDAI, itch numerical rating scale (NRS), eosinophil count, serum IgE, TARC, and anti-BP180 antibody levels were visualized in individual spaghetti plots (Fig. S2). BPDAI, eosinophil counts, and serum TARC levels significantly decreased from week 4 onwards and remained suppressed through to week 52 ($p<0.05$ for all). NRS also improved significantly by week 4 and remained low throughout ($p<0.01$). One patient experienced transient worsening of pruritus at week 28 without flare of skin lesions. Serum IgE and anti-BP180 autoantibody titres showed a gradual decline, though changes were not statistically significant. Only 6 of 18 patients achieved normalization of anti-BP180

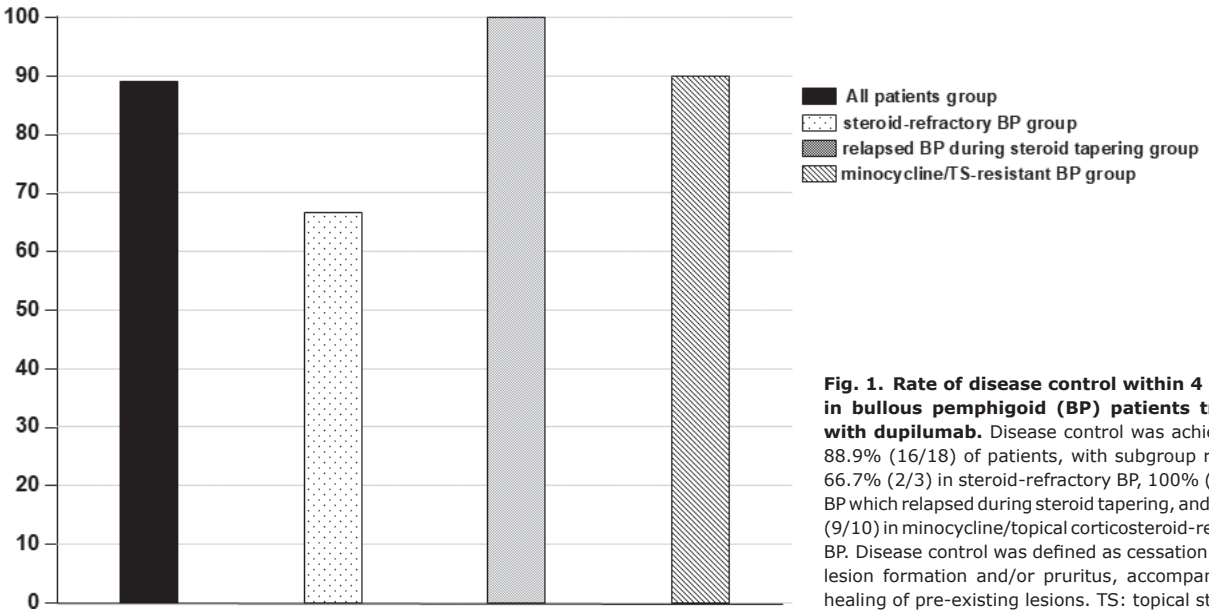

Fig. 1. Rate of disease control within 4 weeks in bullous pemphigoid (BP) patients treated with dupilumab. Disease control was achieved in 88.9% (16/18) of patients, with subgroup rates of 66.7% (2/3) in steroid-refractory BP, 100% (5/5) in BP which relapsed during steroid tapering, and 90.0% (9/10) in minocycline/topical corticosteroid-resistant BP. Disease control was defined as cessation of new lesion formation and/or pruritus, accompanied by healing of pre-existing lesions. TS: topical steroids.

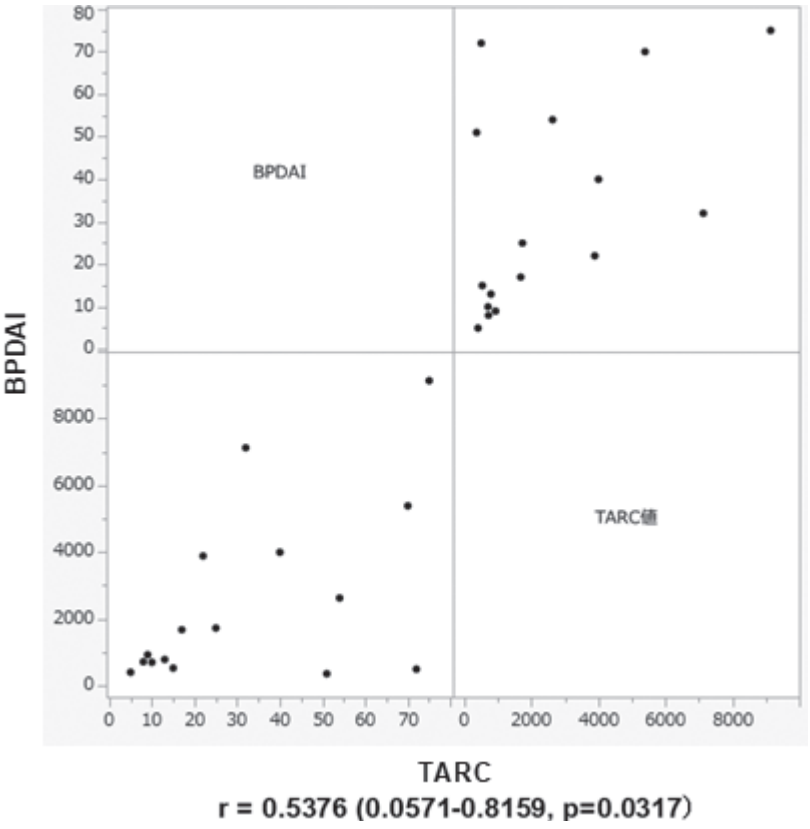

Fig. 2. Correlation between serum TARC levels and BPDAI scores in patients with bullous pemphigoid. This figure illustrates the correlation between serum thymus and activation-regulated chemokine (TARC) levels and Bullous Pemphigoid Disease Area Index (BPDAI) scores in patients with bullous pemphigoid treated with dupilumab. A statistically significant positive correlation was observed ($r=0.5376$, $p<0.05$), indicating that higher TARC levels are associated with greater disease severity.

titres, suggesting individual variability in immunological remission and a possible need for prolonged treatment in select cases.

Importantly, we evaluated serum TARC, a biomarker widely used in Japan to assess disease activity in atopic dermatitis (6). Although not routinely measured in Europe, recent studies have shown that TARC levels are also elevated in both serum and blister fluid of patients with BP and correlate with disease severity (7, 8). In our cohort, serum TARC levels declined in parallel with clinical improvement following dupilumab treatment. Furthermore, a moderate positive correlation was observed between baseline TARC levels and disease severity, measured by BPDAI scores ($r=0.5376$, $p=0.0317$; **Fig. 2**). These findings support the potential utility of TARC as a dynamic biomarker for disease monitoring in BP, particularly in Asian clinical settings where its use is more established. Further validation in broader populations, including Western cohorts, is warranted to determine its generalizability and clinical applicability in routine dermatological practice. Dupilumab was well tolerated; transient eosinophilia occurred in 11.1% but was not associated with worsening symptoms. No serious adverse events or discontinuations occurred.

This case series supports dupilumab as a rapid, effective, and safe option for BP, including steroid-refractory cases. However, this study has several limitations, including its retrospective single-centre design and small sample size, which may affect the generalizability of the findings. Additionally, the 52-week follow-up may not fully capture long-term outcomes. Despite these limitations, our results suggest that TARC – widely used in Japan for atopic dermatitis and elevated in both serum and blister fluid of BP patients – may serve as a candidate biomarker for BP disease activity. These findings warrant validation in larger, prospective, and international cohorts to establish dupilumab's long-term efficacy and the utility of TARC in clinical practice.

ACKNOWLEDGEMENTS

IRB approval status: This study was reviewed and approved by the institutional review board at Saitama Medical Center (Approval Number: 2023135). Due to the retrospective nature of the study using anonymized data, written informed consent was not required. An opt-out procedure was implemented in accordance with institutional and national ethical guidelines.

The author have no conflicts of interest to declare.

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