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Letter to the Editor |  Full Access

Dual biologic therapy with Omalizumab and Dupilumab for refractory atopic disease

Alexis Arasu , Niyati Sharma, Anousha Yazdabadi, Michael Sladden

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Dear Editor,

Eczema and asthma are common, chronic inflammatory atopic conditions, both of which have a subset of patients with treatment refractory disease. Asthma co-exists in 25% of patients with atopic dermatitis.¹ Treatment outcomes of these conditions and quality of life have significantly improved with the introduction of targeted biologic therapies, specifically omalizumab for asthma and dupilumab for eczema.^{2, 3} Biologic therapies have become popular given their favourable safety profile and high rates of efficacy. Use of dual or multiple biologics will likely become more common given the number of patients with co-existent inflammatory diseases. However, there are limited data regarding the efficacy and tolerability of combining different biologics in patients with multiple diagnoses. We present three patients who have benefitted from dual treatment of omalizumab and dupilumab for approved atopic conditions of asthma and eczema.

At time of presentation for management of their lifelong, severe, refractory eczema, all three patients had already been safely and successfully treated for several years with omalizumab for severe asthma. The omalizumab, although effective for asthma, did not benefit their skin disease and all had persistent, severe eczema.

Case 1, a 56-year-old male patient with severe eczema was poorly responsive to topical and oral corticosteroids, phototherapy, azathioprine and mycophenolate. Once available on the Australian PBS scheme in 2021, he commenced dupilumab. After three months, he showed significant clinical improvement of his eczema across parameters of itch, sleep and pruritus

and ceased all corticosteroid therapy. He reported mild side effects of dry eyes, managed with emollients. At six monthly review, dual therapy has been well tolerated. He continues with three monthly follow-up with both immunology and dermatology.

Case 2, a 50-year-old female patient with a complex history including vulval cancer precluded the use of many systemic treatments for her severe eczema. She required multiple hospital admissions for eczema management, intensive topical therapy and prednisolone courses. After commencing dupilumab in 2018, her skin markedly improved with a reported improvement from nine out of ten to one out of ten across all parameters of itch, sleep and quality of life (visual analogue scales). In addition, EASI (31.2 down to 3.2), DLQI (27 down to 2) and PGA (4 down to 1) all improved, and she has ceased corticosteroid treatment. She has continued both biologic agents for 3 and a half years with the only side effect reported as mild conjunctivitis from dupilumab. She undergoes three monthly respiratory and dermatology follow-up.

Case 3, a 54-year-old man had required multiple courses of oral, as well as topical, steroids for atopic disease control resulting in significant steroid induced adverse effects including cataracts, bilateral hip surgery for avascular necrosis of the femoral heads and chronic osteomyelitis. Given his co-morbidities, it was deemed that systemic therapies including methotrexate, cyclosporin, azathioprine and mycophenolate be avoided. He started dupilumab when it became available in Australia with rapid clinical improvement of his eczema. After six months, he showed significant reduction in EASI (45.4 down to 3.2), DLQI (20 down to 1) and PGA (4 down to 1), improved itch, sleep and pruritus and has ceased corticosteroid use. He reports no eye problems, no other side effects and undergoes regular 3-monthly follow-up.

There are limited robust data examining combination biologic therapy, but data are available from a few, small observational studies. Two studies evaluated dual combination therapy for ten patients using omalizumab for chronic spontaneous urticaria, with concurrent use of a tumour necrosis factor (TNF) inhibitors for either psoriasis, inflammatory bowel disease or rheumatoid arthritis.^{4,5} Neither study documented an increased rate of adverse effects over and above single biologic therapy and demonstrated strong clinical response for the respective conditions. Safety and efficacy of combination of multiple monoclonal agents including dupilumab, secukinumab and benralizumab has further been demonstrated in the treatment for concurrent asthma and psoriasis.⁶

Use of dual biologics for single indications has also been reported. Combination of a TNF inhibitor with ustekinumab has been used for the treatment of psoriasis.⁷ Of the four patients, the authors report therapy-related infectious complications in two patients: one patient with relapsing herpes zoster and another patient developing a retrotonsillar abscess. Clinicians and patients should remain cognisant of potential infection risk given the immunosuppressive profiles of these agents. Combination therapy with omalizumab and dupilumab has been used effectively for off-label treatment of recalcitrant bullous

pemphigoid leading to disease quiescence.⁸ As in our study, no new safety signals were reported with this combination.

There may be a subset of patients where dupilumab monotherapy may achieve disease control. Previous systematic reviews have shown improvement of asthma with dupilumab.⁹ Omalizumab is generally considered as first-line therapy for patients with allergic, non-eosinophilic asthma and agents such as dupilumab may not be as broadly effective.¹⁰ Thus, in our patients, given the severity of their asthma, their respiratory physicians were reluctant to cease omalizumab based on the level of response. However, over time, there may be flexibility to trial changing the regime of omalizumab or transitioning to a single agent.

To our knowledge, this is the first report to demonstrate treatment benefit and short-term safety of combining dupilumab and omalizumab for approved atopic conditions of eczema and asthma. Our experience, along with other observational data, suggests combination therapy to be safe and effective, but this is based on short-term follow-up of a small number of patients. Combination biologic therapy requires further evaluation in appropriately designed randomised trials to assess long-term safety and efficacy. Meanwhile, we advise close clinical monitoring to minimise adverse events from combination therapy.

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