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RESEARCH LETTER

Real-World Clinical Outcomes in Asthmatic Patients Switched from Omalizumab to Anti-Interleukin-5 Therapy

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Ireland has the fourth highest prevalence of asthma globally, with over 470,000 people with an asthma diagnosis.[1] In general, asthma symptoms can be controlled with inhaled corticosteroids, with the addition of a long-acting β_2-agonist as indicated, alongside other agents including long-acting anti-muscarinic agents and anti-leukotrienes.[2]

The GINA 2021 Guidelines state that many cases of difficult-to-treat-asthma are partly secondary to modifiable factors such as incorrect inhaler technique. An important distinction is that in severe refractory asthma, a subset of difficult-to-treat-asthma, despite adherence to maximized optimal therapies and the treatment of contributory factors, asthma remains uncontrolled.[3] In this subset of patients, symptoms remain inadequately controlled despite maximum conventional therapy and adherence, with 3–10% considered to have severe refractory disease.[4]

A number of biological agents targeting the components of type 2 inflammation have been transformative in the management of severe refractory asthma.[5] Omalizumab, the first such agent to be approved for use in severe allergic asthma, is a humanized anti-immunoglobulin E (IgE) antibody.[2] In Ireland, omalizumab is not reimbursed by national bodies but paid for directly by individual hospital budgets, potentially limiting access for patients.

Anti-interleukin-5 (IL-5) therapies were first approved for use in Ireland in 2018 and there are currently three agents available for treating adults with severe eosinophilic asthma that is inadequately controlled despite maximum conventional therapy. Mepolizumab and reslizumab target IL-5,[4] whereas benralizumab is an anti-eosinophil monoclonal antibody that binds to the alpha subunit of the IL-5 receptor.[6]

Irish guidelines state that patients may be eligible for anti-IL-5 therapy if they have a confirmed diagnosis of severe refractory eosinophilic asthma by a respiratory physician, they have been fully adherent to maintenance therapy, the blood eosinophil count is elevated, and they have had two or more exacerbations in the previous 12 months requiring systemic corticosteroids.[7,8]

We performed a retrospective, observational, single-centre review of clinical outcomes in patients switched from omalizumab to an anti-IL-5 therapy in a regional specialist asthma centre in Cork University Hospital, Ireland. This study was approved by the Clinical Research Ethics Committee, University College Cork. Informed consent was obtained from each of the included patients. The study complied with the Declaration of Helsinki. Clinical outcomes in severe eosinophilic asthmatics who remained suboptimally controlled despite omalizumab and were therefore switched to an anti-IL-5 therapy were assessed. Suboptimal control was defined as inadequate control of a patient's asthma and/or multiple exacerbations despite omalizumab.

All patients ≥18 years old who switched therapy in our centre from 2018 to 2020 were included. The parameters assessed included the Asthma Control Questionnaire (ACQ) score, annual community and hospital exacerbation rates, eosinophil count, maintenance oral corticosteroid (OCS) dose, and FEV_1. Outcomes were analysed at four time-points: baseline

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pre-commencement of omalizumab, one year established on omalizumab, baseline at commencement of anti-IL-5 therapy, and one year post-commencement of anti-IL-5 therapy.

Anonymized data were analysed using SPSS 28.0.1. Continuous variables were expressed as medians and interquartile ranges (IQRs). Categorical variables are expressed as number of events and frequency. Differences between pre-omalizumab and one-year post-commencement of omalizumab outcomes were examined. Differences between pre-switch to anti-IL-5 therapy (established on omalizumab) and one year post-anti-IL-5 therapy were examined. These groups were compared using the Wilcoxon signed rank test. A p-value <0.05 was considered significant.

Ten patients met the inclusion criteria, and all patients switched therapy between September 2018 and September 2020. All switches occurred following regular review at the asthma clinic. Patients were well established on omalizumab prior to switching biologic therapy. Six patients switched to benralizumab and four to mepolizumab.

There were significant reductions in hospital exacerbation rate and community exacerbation rate when comparing pre-omalizumab to one year post-commencement of omalizumab (median 1.5 vs 0, p=0.056, and 10 vs 5, p=0.043, respectively). There was a non-significant reduction in ACQ score (median 3.4 vs 3.0, p=0.465).

There were significant reductions in community exacerbation rate (median 6 vs 0, p=0.005) and serum eosinophil count (median 0.7×10^9/L vs 0×10^9/L, p=0.007), and a significant improvement in FEV_1 (median 62% vs 76%, p=0.046) from baseline to one year post-commencement of anti-IL-5 therapy. There were non-significant reductions in median OCS dose and median ACQ score (7.5 mg vs 2.5 mg, p=0.276, and 3.0 vs 1.9, p=0.352, respectively) from baseline at commencement of anti-IL-5 therapy to one year post-commencement of anti-IL-5 therapy (Table 1). Comparing all four time-points, significant reductions in community exacerbation rate and serum eosinophil count were seen (p=0.004 and p=0.003, respectively).

We observed that an alternative biologic agent can be beneficial in patients who are not fully controlled with omalizumab. Despite a small sample size, our findings are consistent with existing literature[4–6,9] in which clinically meaningful reductions were noted in exacerbation rate and other pertinent parameters. Our data represent real-world experience in a specialist centre in a country with a high asthma prevalence. We believe that a multicentre study with a larger sample size would be likely to support our findings.

This study did not directly assess the economic impacts of switching from omalizumab to an anti-IL-5 therapy in this cohort. Both agents are similarly priced in Ireland. Furthermore, an increment of drug price has previously been seen to be often offset by savings in costs related to multiple exacerbations.[10]

In conclusion, a number of agents are available for the management of type 2 inflammation in severe refractory asthma. Despite the small number of patients included in this study, the results are in keeping with existing literature.[2]

Table 1 Comparison of Outcomes Pre-Omalizumab and One Year Post-Commencement of Omalizumab, and Established on Omalizumab Pre-Switching to Anti-IL-5 Therapy and One Year Post-Commencement of Anti-IL-5 Therapy

Variable	Pre-Omalizumab	1 Year Post-Omalizumab	*p*-Value	Pre-Anti-IL-5	1 Year Post-Anti-IL-5	*p*-Value
Asthma Control Questionnaire	3.4 (2.4–5.0)	3.0 (1.6–3.8)	0.465	3.0 (1.7–3.3)	1.9 (0–4.0)	0.352
Hospital exacerbations/year	1.5 (0–4)	0 (0–2)	0.056	0 (0–3)	0 (0–2)	0.564
Community exacerbations/year	10 (4–12)	5 (0–9)	0.043	6 (4–24)	0 (0–6)	0.005
Serum eosinophil count ($\times10^9$/L)	0.50 (0.19–1.5)	0.60 (0.12–1.0)	1.00	0.70 (0.09–1.10)	0 (0–0.66)	0.007
Maintenance OCS (mg)	9.0 (0–20.0)	10.0 (0–15.0)	0.892	7.5 (0–15.0)	2.5 (0–15.0)	0.276
FEV_1 (% predicted)	56 (30–79)	57 (40–82)	1.00	62 (36–103)	76 (31–116)	0.046

Note: Data are expressed as median (range).

Our results suggest that further improvements in clinical outcomes can be achieved by switching to an anti-IL-5 agent in severe eosinophilic asthmatics who, although improved from baseline, remain suboptimally controlled with omalizumab.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

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