DOI: 10.1111/all.14035

LETTER TO THE EDITOR

Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY EAACI WILEY

Mepolizumab and reslizumab, two different options for severe asthma patients with prior failure to omalizumab

To the Editor,

Until recently, omalizumab was the only biologic approved by the regulatory agencies for treating asthma. Nowadays, more alternatives are available, and a significant proportion of severe asthma patients may qualify for both anti-IgE and anti-IL-5 therapies. To choose between the two options in an allergic patient with blood or sputum eosinophilia, a clinician should consider not only the number of exacerbations but also the symptoms, quality of life, pulmonary function, corticosteroid dependence and the patient's social status and working conditions. If omalizumab is chosen as the first choice, we must be very strict in the evaluation of clinical response, because two studies[1,2] have recently shown the effectiveness of mepolizumab and reslizumab in patients who were not well controlled with anti-IgE. Baseline demographic and clinical characteristics, and the main results of both studies are

TABLE 1 Design, baseline characteristics, and results in both studies

	Reslizumab	Mepolizumab
Design	Open label, single-arm, multicenter	Open label, single-arm, multicenter
Follow-up period, weeks	24	32
Patients included	29	145
Duration of omalizumab therapy prior to treatment, months, median (range)	11 (6, 23)	29.6 (4, 161)
Omalizumab washout	Yes (>5 mo)	No
Age years, mean (SD)	50.8 (13.2)	53.6 (13.83)
Female, n (%)	18 (62)	86 (59)
Baseline eosinophils, cells/μ, geometric mean	306	290
Baseline prebronchodilator FEV1 (L), mean (SD)	1.60 (0.7)	1.76 (0.68)
Baseline prebronchodilator FEV1 (% theor; SD)	54.4% (18.02)	59.5 (17.94)
Clinically significant exacerbations in the prior 12 mo, mean (SD)	3.7 (4.0)	3.3 (2.65)
Exacerbations requiring hospitalization in the prior 12 mo, n (%)	3 (10.3)	17 (12)
Baseline AQLQ, mean (SD)	4.1 (1.5)	NA
Baseline SGRQ, mean (SD)	NA	56.6 (17.36)
Maintenance OCS use at baseline, n (%)	21 (72%)	35 (24%)
Δ FEV1, mL, mean (SD)	198 (36.2)	159 (40.7)
ACT ≥ 20 at the end of follow-up (%)	60	NA
ACQ < 1.5 at the end of follow-up (%)	NA	45
Δ ACT ≥ 3 (%)	64	NA
Δ ACQ ≥ 0.5 (%)	NA	77
Δ AQLQ ≥ 0.5 (%)	83	NA
Δ SGRQ ≥ 0.5 (%)	NA	79
≥1 clinically significant exacerbation during follow-up, n (%)	5 (17.4)	60 (41)
≥1 hospitalization during follow-up, n (%)	1 (3.4)	9 (6.2)
% patients controlled at the end of follow-up	60%	NA
% patients who withdrew OCS at the end of follow-up (%)	20.4%	NA

Abbreviations: Δ, change between baseline and end of follow-up; ACQ, Asthma Control Questionnaire (ranges from 0 to 6; controlled asthma ≤ 0.75); ACT, Asthma Control Test (ranges from 5 to 25: controlled asthma ≥ 20); AQLQ, asthma quality of life questionnaire (ranges from 1 to 7, with higher scores indicating a better quality of life); FEV1, forced expiratory volume in one second; NA, not available; OCS, oral corticosteroids; SGRQ, Saint George Respiratory Questionnaire (total score ranges from 0 to 100, and higher scores indicate poorer quality of life).

summarized in Table 1. The principal difference in their design is the lack of an omalizumab washout period in the mepolizumab study (a minimum of 5 months was required in the reslizumab study). Chapman et al decided to reflect clinical practice—where mepolizumab would be started 2-4 weeks after the final dose of omalizumab—assuming a potential interaction between the two biologics. It has been shown that omalizumab average elimination half-life is around 26 days.[3] The maximum inhibition of basophil FcεRI expression occurs within 14 days of omalizumab treatment, and this reduction is maintained at least for 42 days.[4] Therefore, although Chapman et al found no evidence of greater efficacy during the first half of mepolizumab treatment period, some degree of overlap between both drugs is to be expected. Other relevant differences between the studies are the higher number of included patients and the longer follow-up period of the mepolizumab study, which could (at least in part) explain the discrepancy found in exacerbations and hospital admissions. In addition, the reslizumab study included six patients (20.7%) in whom omalizumab was discontinued because adverse events, whereas the mepolizumab study included only asthmatics with suboptimal control while on treatment with the monoclonal anti-IgE antibody, something that might bias the comparison in favor of reslizumab.

Despite that, results with reslizumab seem to be better in terms of clinical control and pulmonary function, as shown in Table 1. Although baseline characteristics were similar in the two studies (with worse pulmonary function and a higher rate of maintenance oral corticosteroid use in the reslizumab study) we must acknowledge the limitations of indirect comparisons between monoclonal antibodies in asthma. Keeping this in mind, the observed differences in response to both anti-IL-5 drugs are in accordance with those published by Mukherjee et al, who found that weight-adjusted IV reslizumab was superior to fixed-dose SC mepolizumab in attenuating airway eosinophilia in prednisone-dependent patients with asthma, resulting in a clinically meaningful improvement in asthma control and FEV1.[5] From a pharmaceutical point of view, it has been recently shown in head-to-head assays that reslizumab has higher binding affinity for (predominantly due to the more rapid antigen binding) and greater in vitro potency against human IL-5 (measured by cell proliferation assay) compared with mepolizumab.[6] Taken together, these data could partially explain the differences found in this study between the two monoclonal antibodies.

In absence of head-to-head clinical trials, real world data collected in international registries such as the International Severe Asthma Registry (ISAR), a sample more representative of clinical practice, may be able to inform clinicians on important factors for biologic therapy comparison (effectiveness, safety, affordability, etc). In the meantime, the possibility of switching between monoclonal antibodies should make us more demanding about the categorization of clinical response in individual severe asthma patients.

CONFLICTS OF INTEREST

L. A. Perez de Llano reports personal fees from Novartis, AstraZeneca, GlaxoSmithKline, Teva, Boehringer-Ingelheim, Chiesi, Sanofi, Mundipharma,and Esteve; nonfinancial support from Novartis, GlaxoSmithKline, Teva, Boehringer-Ingelheim, Menarini, Mundipharma, and Esteve; and grants from AstraZeneca, Teva, and Chiesi, outside the submitted work. B. G. Cosío reports personal fees from Novartis, AstraZeneca, Teva, Boehringer-Ingelheim, Chiesi, Sanofi, and Mundi-pharma; nonfinancial support from Novartis, Teva, Boehringer-Ingelheim, and Menarini; and grants from AstraZeneca, GlaxoSmithKline, Teva, Boehringer-Ingelheim, and Chiesi, outside the submitted work. David Dacal Rivas declares no conflicts of interest.

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