



Letter

Sex differences in the efficacy, safety, and tolerability of omalizumab after 1 year in Maltese patients with asthma

Omalizumab has been proven to be a safe and effective drug¹ in patients with severe, persistent, allergic IgE-mediated asthma. Sex differences in asthma prevalence and severity, including IgE-mediated allergic asthma, have been recognized, with women said to be more severely affected.^{2,3} Studies have identified that men and women respond differently to their asthma when comparing hospital admissions, quality of life, and use of inhalers.⁴ It is also postulated that responses to antiasthmatic drugs differ.⁵ Literature on the response to omalizumab between sex groups is scarce.

We sought to identify any differences between male and female patients receiving omalizumab, in terms of clinical efficacy, safety, and tolerability, after 1 year of treatment. Outcomes compared included Asthma Control Test (ACT) score, forced expiratory volume in 1 second (FEV₁), and number of exacerbations, hospitalizations, unscheduled health care visits, and systemic oral corticosteroids (OCSs) required.

Adult patients identified by their primary care physician to receive omalizumab treatment according to the Global Initiative for Asthma recommendations⁶ at Mater Dei Hospital in Malta, the only tertiary referral center in Malta, and who consented to participate in this ongoing prospective observational study were included. Patients were interviewed at baseline and then every 4 weeks until week 16 and every 8 weeks thereafter until 52 weeks of treatment. During every interview, the patients were questioned regarding any adverse effects possibly attributed to the drug, asthma exacerbations, asthma-related unscheduled health care visits, asthma-related hospitalizations, and OCS courses received. ACT scores⁷ and prebronchodilator FEV₁ values were measured at each visit. Treatment effectiveness was evaluated at 16 and 52 weeks based on the ACT score, FEV₁, and number of exacerbations, unscheduled health care visits, hospitalizations, and OCS courses. An asthma exacerbation was defined as an acute or subacute worsening in symptoms and lung function from the patient's usual status.⁶ Ethical approval was obtained from the University Research Ethics Committee. Statistical analysis was performed using SPSS statistical software, version 20 (SPSS Inc, Chicago, Illinois). $P < .05$ was taken to be statistically significant.

Our cohort included 34 patients, 20 men (mean [SD] age, 53.9 [9] years; mean [SD] baseline IgE, 436 [353] IU/mL) and 14 women (mean [SD] age, 50 ± [14] years; mean [SD] baseline IgE, 366 [449] IU/mL). The mean (SD) baseline ACT score was 13.6 (4.6) in men vs 15.7 (6.9) in women ($P = .30$). The mean (SD) baseline FEV₁ was 61.3 (20) vs 65 (22.6) ($P = .60$). There were a mean (SD) of 5.6 (8) vs 32 (66) unscheduled health care visits 1 year before treatment ($P = .15$), 0.95 (1.9) vs 0.5 (0.6) hospitalizations ($P = .33$), 4.6 (3.4) vs

4.6 (3.9) ($P = .97$) exacerbations, and 3.2 (3.1) vs 4.2 (3.9) ($P = .42$) OCS courses. During the 1-year study period, omalizumab treatment was discontinued in 1 man and 2 women because of treatment inefficacy at 16 weeks. Intolerable adverse effects, including arthralgias and myalgias, developed in 3 patients in whom treatment was also discontinued. Thus, the population included in the analysis consists of 28 patients, 17 men and 11 women. When comparing adverse effects in men vs women, headaches occurred in 15% vs 36%, injection site reactions in 10% vs 14%, nausea in 21% of women, myalgias in 5% vs 7%, and arthralgias in 5% of men. Table 1 compares the outcomes studied between the sex groups.

When comparing the ACT score after 1 year of treatment, there was no significant difference between men and women ($P = .46$) and likewise for the percentage predicted FEV₁ ($P = .92$) and mean numbers of unscheduled health care visits ($P = .25$), hospitalizations ($P = .97$), exacerbations ($P = .97$), and OCS courses required ($P = .34$).

A pooled study performed Patella et al⁸ concluded that the efficacy of omalizumab was unaffected by sex. Our female patients had a higher nonsignificant baseline ACT score. Women with asthma were found to have a more positive attitude to their medication and had higher reported adherence,⁹ possibly explaining the overall higher levels of asthma control. After 1 year of treatment, both groups had a nonsignificant improvement in their percentage predicted FEV₁, as opposed to international studies, which found that omalizumab improves FEV₁,^{1,4} suggesting that spirometry is not a reliable indicator to predict response to omalizumab in either group. Our female cohort had more baseline asthma-related unscheduled health care visits to their general practitioner or to the local health centers, a finding reflected in other studies.⁴ After 1 year of treatment, there was a significant decrease in such visits in the male group, unlike the female group. Despite an improvement in asthma control after 1 year, as reflected in the ACT score in both groups, women still presented more frequently to their general practitioner or local health center for asthma-related symptoms. Women may need more reassurance when it comes to chronic conditions, such as asthma, or this finding could be attributable to the increased reported anxiety in women with asthma.⁹ Alternatively, the increased perception of dyspnea in the female cohort could explain this finding.¹⁰ Another explanation could be that there was 1 particular patient who had a large number of unscheduled health care visits, hence explaining the large variation, although the results were mirrored when this patient was excluded from the statistical analysis. Women have been noted to have increased hospital admissions for asthma in a number of countries.^{2,4} The men in our cohort had an increased hospitalization rate at baseline with minimal nonsignificant reductions after 1 year of treatment in both groups. However,

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Table 1
Sex Differences in the Outcomes of Omalizumab in Patients Who Completed 1 Year of Treatment in Malta

Outcome	Men (n = 17)	P value	Women (n = 11)	P value
ACT score				
Baseline				
Mean	13.7		17.1	
Median	14		18	
IQR	4		10.5	
1 Year		<.001		.003
Mean	20.1		21.6	
Median	22		22	
IQR	7		3.5	
FEV ₁				
Baseline				
Mean	62.9		65.9	
Median	58		64	
IQR	30		30	
1 Year		.29		.93
Mean	67.1		66.2	
Median	64		69	
IQR	23		24	
No. of exacerbations				
1 Year before				
Mean	4.2		3.5	
Median	3		2	
IQR	4		4	
1 Year after		.06		.09
Mean	2.4		2.4	
Median	2		1	
IQR	4		2.5	
No. of hospitalizations, mean				
1 Year before	0.52		0.36	
1 Year after	0.17	.32	0.18	.34
No. of OCS course, mean				
1 Year before	2.8		3.5	
1 Year after	1	.008	1.5	.01
No. of unscheduled health care visits				
1 Year before				
Mean	2.8		32.4	
Median	3		3	
IQR	6		11.5	
1 Year after		.008		.16
Mean	1.4		6.8	
Median	1		1	
IQR	2		2	

Abbreviations: ACT, Asthma Control Test; FEV₁, forced expiratory volume in 1 second; IQR, interquartile range; OCSs, oral corticosteroids.

hospitalization rates in both groups were low, even 1 year before omalizumab treatment, hence limiting the strength of our statistical analysis. The decrease in exacerbation rates after 1 year of

treatment did not reach statistical significance in both groups. The number of OCS courses prescribed decreased significantly in both groups. In the outcomes studied, the effect of omalizumab was mirrored in both sex groups, suggesting a similar effect in men and women. Our study was limited because it was a single-center study of a small population, although representative of the Maltese population.

In conclusion, our study found no difference between men and women in terms of the efficacy, tolerability, and response rates of omalizumab in our local cohort of patients. The need for increased health care visits, which persisted despite an improvement in asthma control in the women, could possibly reflect the need for more reassurance in this cohort. The effect of omalizumab on sex merits further investigation on a larger scale.

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