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Ourania S. Kotsiou, Konstantinos I. Gourgoulidis & Zoe Daniil

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LETTER TO THE EDITOR



Clinical profile of severe asthmatics receiving biological treatment: see behind the scenes

Ourania S. Kotsiou, MD, PhD, Konstantinos I. Gourgoulisanis, MD, and Zoe Daniil, MD

Department of Respiratory Medicine, Faculty of Medicine, University of Thessaly, Larissa, Greece

ABSTRACT

The clinical phenotyping of severe asthma could improve treatment outcomes, quality of life, morbidity, and mortality of asthma patients. The growing availability of rich clinical data could provide opportunities to address a broad range of real-world questions regarding clinical phenotyping and effective therapeutic approaches of severe asthma. Accordingly, in this Letter to the Editor, we provide data relevant to constructing the clinical profile of a Greek severe asthma patient cohort who receive biological treatment.

Abbreviations: GINA: Global Initiative for Asthma; ISAR: International Severe Asthma Registry

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Asthma; Greece;
mepolizumab; omalizumab; phenotype

Dear Editor,

We read with great interest the well-presented article entitled “Clinical characteristics and burden of illness among adolescent and adult patients with severe asthma by asthma control: the IDEAL Study” by Müllerová et al. (1). The results of this study highlighted the importance of clinical phenotyping strategy for severe asthma patients to provide an effective therapeutic approach (1).

To emphasize the necessity of improving the therapeutic perspective, we provide some real-world data relevant to constructing the clinical profile of a Greek severe asthma patient cohort who receive omalizumab or mepolizumab. As the region's only tertiary care referral Center for severe asthmatics for entire Central Greece, our department serves a population of about 732,000 people who represent 6.8% of the total population of Greece. Approximately 1000 asthmatics are monitored annually. We retrospectively collected data in patients with severe asthma (≥ 18 years old), receiving biologics from December 2017 to December 2019. Signed informed consent was obtained from each patient.

Among all asthmatics, 3.2% (32 patients) received GINA Step 5 treatment, including a biological agent. Anti-IgE and anti-interleukin-5 were used by 41% and 59% of patients, respectively. The baseline demographical characteristics, clinical and laboratory data of the study population are summarized in Table 1. 68% were women (mean age 59 ± 14 years), nonsmokers, with a long-standing asthma history of 12 ± 10 years. The duration of asthma was significantly longer in the omalizumab group compared to the mepolizumab group (Table 1). Obesity,

allergic rhinitis, bronchiectasis, and gastroesophageal reflux disease were the most prevalent comorbidities observed in 100%, 50%, 23%, and 20% of the study population, respectively. No significant difference was found between omalizumab and mepolizumab groups regarding the number of comorbidities.

All severe asthmatic patients in our cohort were overweight/obese. It has been recently documented that most patients from an international severe asthma registry (ISAR) were overweight/obese (2). Obesity is a defining characteristic of severe asthma phenotypes across most ethnic and all sex and age groups (3). The increased prevalence of obesity may reflect the obesogenic effects of the systemic corticosteroids that are widely used in the severe asthma population (4). Besides, evidence suggests that the microbiome and/or the airway smooth muscle cells hyperresponsiveness might play a role in the pathogenesis of asthma in obese patients (5,6).

In this study, we found a non-significant reduction in mean peripheral blood absolute eosinophil counts in patients receiving omalizumab after a year in therapy (165 ± 93 vs. 150 ± 50 cells/mm³, $p > 0.05$) (Table 1). However, a significant decrease in peripheral eosinophilia in patients treated with mepolizumab was recorded after one year (731 ± 490 vs. 350 ± 53 cells/mm³, $p = 0.002$).

Notably, Campo et al. reported refractory eosinophilic inflammation in obese women with severe asthma after treatment with omalizumab for one year (7). In contrast to the Campo et al. study, we also found that half of severe asthmatics had fixed airflow obstruction with $FEV_1/FVC < 0.70$ and only an 8% improvement in post-

Table 1. Baseline demographical characteristics, clinical and laboratory data of the severe asthmatic population ($N=32$) and comparisons between treatment subgroups.

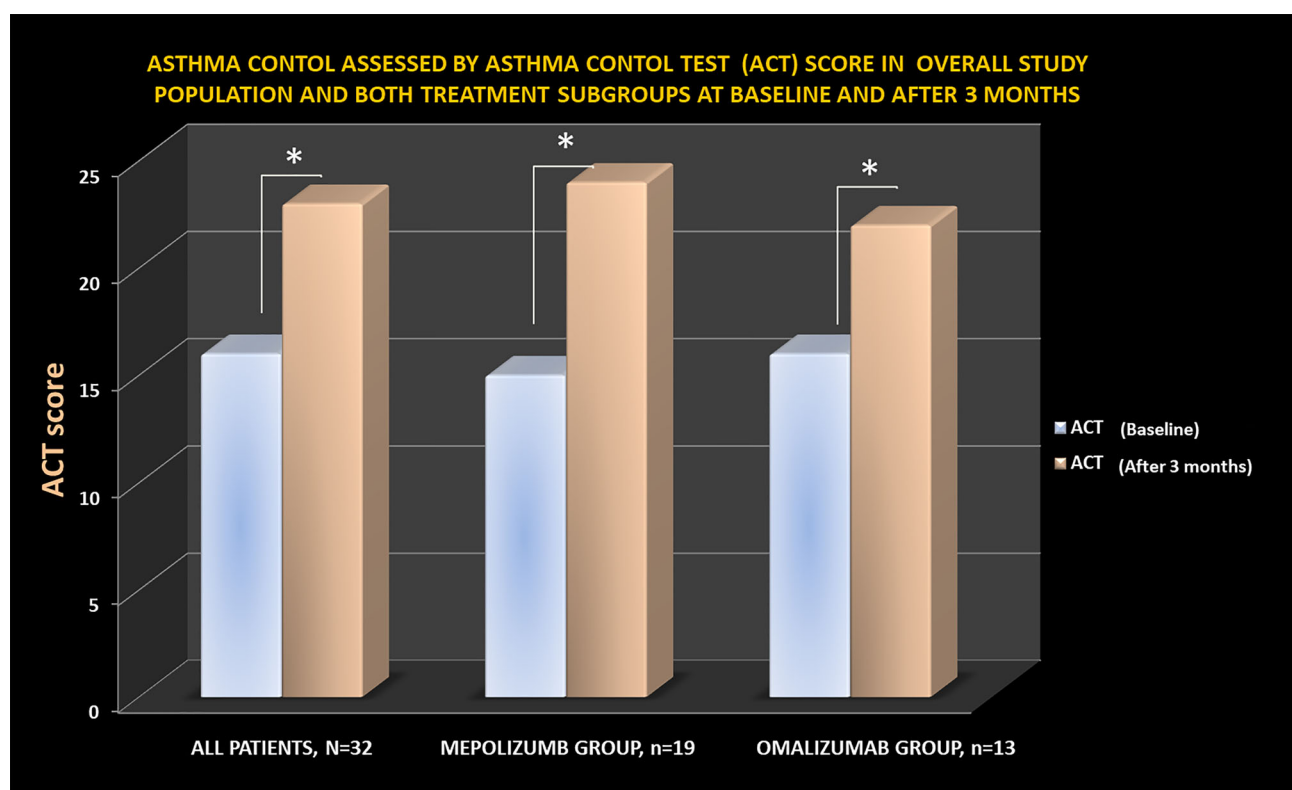
	Total ($N=32$)	Mepolizumab ($n=19$)	Omalizumab ($n=13$)	p -value
Gender				
Males (%)	10 (31.2)	7 (36.8)	3 (23.0)	0.372*
Females (%)	22 (68.8)	12 (63.2)	10 (77.0)	
Age (years)	59.0 $\pm$ 14.1	63.1 $\pm$ 7.8	54.9 $\pm$ 20.3	0.198 [‡]
BMI (kg/m^2)	30.5 $\pm$ 4.7	28.9 $\pm$ 3.7	32.1 $\pm$ 5.5	0.158 [‡]
Duration of asthma (years)	12 $\pm$ 10	6 $\pm$ 3	17 $\pm$ 7	0.050 [‡]
Work-related asthma, yes, n (%)	6 (18.8)	3 (15.8)	3 (23.1)	0.199*
Comorbidities, yes, n (%)	9 (28.1)	3 (15.4)	6 (44.4)	0.166 [‡]
Baseline eosinophils (cells/mm^3)	448 $\pm$ 420	731 $\pm$ 490	165 $\pm$ 93	0.001 [‡]
Eosinophils at 12 months (cells/mm^3)	250 $\pm$ 52	350 $\pm$ 53	150 $\pm$ 50	0.056 [‡]
IgE (mg/dL)	252 $\pm$ 175	125 $\pm$ 34	379 $\pm$ 346	0.004 [‡]
FeNO (ppb)	18 $\pm$ 2	16 $\pm$ 6	20 $\pm$ 4	0.253 [‡]
Nasal polyps, yes, n (%)	7 (21.8)	4 (21.1)	3 (23.1)	0.152*
Skin prick testing positive, n (%)	13 (41.0)	0 (0)	13 (100.0)	0.040*
FEV1/FVC < 0.70 yes (%)	16 (50.0)	8 (42.1)	8 (61.5)	0.408 [‡]
FEV1 (mL)	1.83 $\pm$ 0.8	2.09 $\pm$ 0.7	1.56 $\pm$ 0.9	0.275 [‡]
FEV1 (%)	77.4 $\pm$ 33.6	83.8 $\pm$ 32.5	71.1 $\pm$ 35.9	0.546 [‡]
Absolute change in FEV1 from baseline at 3 months (mL)	473 $\pm$ 451	518 $\pm$ 493	428 $\pm$ 410	0.120 [‡]

Note: Data are expressed as mean $\pm$ SD or as frequencies (percentages).

Abbreviations: BMI, body mass index; FeNO, fractional exhaled nitric oxide; FEV1, forced expiratory volume in one second; FVC: forced vital capacity; IgE, immunoglobulin E.

*Chi-square test.

[‡]Student's t -test.

**Figure 1.** Asthma control assessed by the Asthma Control Test (ACT) score in the overall study population and both treatment subgroups at baseline and three months after the biologic treatment initiation.

bronchodilator FEV₁ for both omalizumab and mepolizumab groups regardless of whether the patients were nonsmokers or former smokers (7) (Table 1). Similarly, Eileen et al. reported that severe asthmatics had a longer history of asthma, fixed airway obstruction, and only slight improvement in FEV₁ post-bronchodilator therapy

irrespective of smoking history (2). The accelerated decline in lung function is the same for all asthma patients as most retain normal or near normal lung function throughout life. However, in some patients, there is a progressive long-lasting lung function decline with age and with duration and severity of asthma (8).

Both childhood onset and adulthood onset asthma patients demonstrated a deleterious decline in lung function.

Nevertheless, a significant increase in mean absolute FEV₁ value (473 ± 451 mL) was detected for both severe asthma groups at three months (Table 1). Furthermore, pre-and post-treatment levels of asthma control were assessed using the 5-point scoring system of the Asthma Control Test (ACT). We found better asthma control within the first three months after starting biologics for both groups compared to baseline ACT scores (Figure 1). These data emphasize the need for a timely transition to biologic therapies that appear to benefit more patients with unmet medical needs than ever before.

Thus, clinical phenotyping severe asthma patients could improve treatment outcomes, quality of life, morbidity, and mortality of asthma patients. Even though the evidence provided here is based on a small sample size, a specific clinical profile of severe asthmatics receiving biological therapy is reported. The growing availability of rich clinical data could provide opportunities to address a broad range of real-world questions regarding clinical phenotyping and effective management of severe asthma.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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