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Influence of biologic treatment on body mass index among severe asthmatics

Rita Guerreiro Soares Pinto

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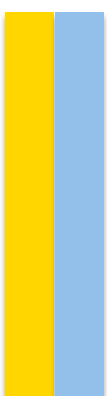

Influence of biologic treatment on body mass index among severe asthmatics

Dissertação de candidatura ao grau de Mestre em Medicina, submetida ao Instituto de Ciências Biomédicas Abel Salazar

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DEDICATÓRIA

Aos meus pais, que foram sempre o meu maior apoio ao longo de cada etapa da minha vida, que nunca me largaram a mão e nunca me deixaram cair, mas sempre me incutiram o pensamento de que o céu é o meu limite. São os meus maiores exemplos de vida e o meu maior motivo de orgulho. Se sou o que sou hoje, é graças a vocês e a tudo o que me proporcionaram. Amo-vos.

À minha irmã, que tentou sempre arranjar uma solução para cada problema meu ou que tentou desvalorizar os meus problemas para eu não *stressar* com eles. É um privilégio ser tua irmã.

Nota especial para a minha mãe e para a minha irmã, as principais motivações deste tema e deste trabalho. Obrigada por terem o diagnóstico de asma.

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Aos meus avós, que onde quer que estejam, espero que estejam orgulhosos de mim, do meu percurso até aqui, da pessoa que sou hoje e da médica que serei. Sei que estiveram comigo em cada passo do percurso.

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RESUMO

Introdução e objetivos: Doentes com asma grave podem estar predispostos ao aumento de peso e a obesidade modifica a gravidade da asma e a resposta ao tratamento. No entanto, o impacto da terapêutica biológica no índice de massa corporal (IMC) permanece pouco esclarecido na literatura. Neste estudo, avaliamos as alterações do IMC após o início de terapêutica biológica.

Materiais e métodos: Tratou-se de um estudo retrospetivo que incluiu adultos com asma grave sob terapêutica biológica durante ≥ 12 meses seguidos na Unidade Local de Saúde de Santo António (ULSSA). O IMC foi avaliado no início do estudo, aos 6 e 12 meses. Análises secundárias avaliaram a variação do IMC considerando a classe do biológico em curso e a categoria do IMC no início do estudo. Foram também avaliados parâmetros clínicos, funcionais e inflamatórios.

Resultados: Foram incluídos 30 doentes (54.5 ± 9.4 anos; 36.7% sexo feminino). O IMC basal foi de 27.7 ± 5.0 kg/m² (36.7% eram obesos). O IMC permaneceu estável (27.7 ± 5.0 to 28.0 ± 4.8 kg/m²; p = 0.349), sem diferenças significativas de acordo com a classe do biológico (p = 0.142) ou com a categoria de IMC basal (<25 vs ≥25 kg/m²; p = 0.490). O ACT score melhorou de 13.2 ± 5.9 para 21.0 ± 5.6, as exacerbações graves diminuíram de 2.1 ± 1.7 para 0.1 ± 0.4, e o uso de corticoterapia sistémica reduziu de 26 doentes para 13 (p < 0.001).

Discussão e Conclusões: A terapêutica biológica melhorou os parâmetros relativos à asma e reduziu o uso de corticoterapia mas não alterou o IMC ao longo de 12 meses, reforçando a importância de estratégias de controlo de peso na asma grave.

PALAVRAS-CHAVE: Asma, Terapêutica biológica, Índice de Massa Corporal; Desfecho do tratamento

ABSTRACT:

Introduction and objectives: Patients with severe asthma may be prone to weight gain, while obesity modifies asthma severity and treatment response. However, biologic therapy's impact on body mass index (BMI) remains unclear. We assessed BMI changes after biologic initiation.

Material and methods: This retrospective study included adults with severe asthma under biologic therapy for ≥12 months at Unidade Local de Santo António (ULSSA). BMI was assessed at baseline, 6 and 12 months. Secondary analyses evaluated BMI trajectories by biologic class and baseline BMI category. Clinical, functional, and inflammatory outcomes were assessed.

Results: Thirty patients were included (54.5 ± 9.4 years; 36.7% female). Baseline BMI was 27.7 ± 5.0 kg/m² (36.7% had obesity). BMI remained stable (27.7 ± 5.0 to 28.0 ± 4.8 kg/m²; p = 0.349), with no significant differences by biologic class (p = 0.142) or baseline BMI category (<25 vs ≥25 kg/m²; p = 0.490). ACT scores improved from 13.2 ± 5.9 to 21.0 ± 5.6, severe exacerbations decreased from 2.1 ± 1.7 to 0.1 ± 0.4, and systemic corticosteroid use decreased from 26 to 13 patients, all p < 0.001.

Discussion and conclusion: Biologic therapy improved asthma outcomes and reduced corticosteroid use but did not change BMI over 12 months, supporting weight-management strategies in severe asthma.

KEY-WORDS: Asthma; Biological Products; Body Mass Index; Treatment Outcome

ABREAVIATIONS LIST

ACT: Asthma Control Test

Anti-IgE: Anti- Immunoglobulin E

Anti- (IL)-5/IL-5Rα: Anti- Interleukin 5/Interleukin 5 receptor alpha

Anti- IL-4Rα: Anti- Interleukin 4 receptor alpha

Anti-TSLP: Anti- Thymic Stromal Lymphopoietin

BMI: Body Mass Index

COPD: Chronic Obstructive Pulmonary Disease

CRP: C-reactive protein

CS: Systemic corticosteroid

FeNO: Fractional exhaled Nitric Oxide

FEV1: Forced Expiratory Volume in 1 second

FEV1/FVC: Forced Expiratory Volume in 1 second/ Forced Vital Capacity

FVC: Forced Vital Capacity

GERD: Gastro-Esophageal Reflux Disease

GINA: Global Initiative for Asthma

ICS: Inhaled corticosteroid

ICS-LABA: Inhaled Corticosteroid and Long-Acting Beta 2 Agonist

OCS: Oral corticosteroid

IgE: Immunoglobulin E

IL- 4: Interleukin 4

IL - 4Rα: Interleukin 4 receptor alpha

IL- 5: Interleukin 5

IL- 5Rα: Interleukin 5 receptor alpha

IL-6: Interleukin 6

IL-8: Interleukin 8

LABA: Long-acting beta 2 agonist

LAMA: Long-acting muscarinic antagonist

PY: Pack-Years

SD: Standard deviation

TNF-α: Tumor necrosis factor alpha

TSLP: Thymic Stromal Lymphopoietin

ULSSA: Unidade Local de Saúde de Santo António

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INTRODUCTION

Asthma is considered a global health problem and affects more than 300 million people worldwide. [1-3] This is a various heterogenous disease, characterized by airway inflammation, bronchial hyperresponsiveness and variable airflow obstruction. [2–4] The classical symptoms associated to this condition are wheezing, cough, shortness of breath and chest tightness. [1,2,5] However, symptoms can vary according to the comorbidities present in each patient. [5] Even though the majority of patients achieve asthma control with the standard therapies available, there are still around 5-10% of patients whose asthma is uncontrolled. [2,3,6–8] These patients currently could meet the criteria for severe asthma. This type of asthma is defined by the Global Initiative for Asthma (GINA), as asthma that remains uncontrolled despite adherence with maximal optimized high-dose of inhaled corticosteroid and long-acting beta 2 agonist (ICS-LABA) treatment and management of contributory factors or asthma that worsens when high-dose treatment is decreased. [9] Patients with severe asthma often experience persistent respiratory symptoms and recurrent exacerbations as well as increased hospitalizations, side effects to treatment and above all, loss of quality of life. [1,2,4,6,7]

According to GINA, biologic therapy may be considered in patients with severe asthma who continue to experience exacerbations and/or poor symptom control despite taking at least high-dose ICS–LABA, who have evidence of Type 2 inflammation or require maintenance oral corticosteroids. [9] GINA describes evidence of type 2 inflammation as the presence of one or more of the following findings while the patient is taking high-dose ICS or daily OCS: blood eosinophils ≥150/μL, fractional exhaled nitric oxide (FeNO) ≥20 ppb, sputum eosinophils ≥2%, or asthma that is clinically allergen-driven. [9] GINA notes that these biomarkers may fluctuate and may be suppressed by oral corticosteroids. [9]

Biologic therapy should only be considered after treatment has been fully optimized, including correction of inhaler technique, assessment of adherence, management of comorbidities, and reduction of modifiable risk factors and should be selected according to the patient's phenotype and inflammatory status. [3,9] Currently there are, four biologic therapies available targeting immunoglobulin E (IgE), interleukin (IL)-5/IL-5Rα, interleukin (IL)-4Rα or thymic stromal lymphopoietin (TSLP). [2,4,8] Each of these therapies presents with specific criteria for their use: anti-IgE is recommended for patients with allergic asthma, with allergen sensibilization or levels of IgE within established values; anti (IL)-5/IL-5Rα are typically used in patients with eosinophilic phenotype, usually defined by blood eosinophilia ≥ 150 at the beginning of treatment or ≥ 300 cells/μL in the last 12 months; anti- IL-4Rα is recommended in type 2 inflammation, assessed by ≥

150 cells/ µl, or FeNO ≥ 25ppb or dependence on oral corticosteroid therapy and anti-TSLP can be used despite the presence of specific biomarkers. [9] The use of biologics offers the possibility of changing the disease natural course while avoiding the side effects typically observed with systemic corticosteroid therapy which enables the thought of asthma remission as a possibility. [4]

Over the past years, researchers and clinicians have shown that some comorbidities, such as obesity, not only increases the risk of asthma but is also associated with poorer disease control, more frequent exacerbations, and reduced responsiveness to standard therapies. [10-14] This relationship is believed to be mediated, at least in part, by a chronic systemic inflammatory state related to excess adipose tissue. Adipocytes and associated immune cells release multiple pro-inflammatory mediators - including interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor-α (TNF-α), C-reactive protein (CRP), leptin, and adiponectin - which may influence airway inflammation and immune responses in asthma. [4,5,10,12,15,16]

Body Mass Index (BMI) is an indirect indicator of body fat obtained from the weight and height. It is calculated using weight in kilograms divided by height in meters squared (kg/m^2) and defines 4 weight categories: underweight (<18,5 kg/m^2), normal weight (18,5-24,9 kg/m^2), overweight (25-29.9 kg/m^2) and obesity (≥ 30 kg/m^2). [17]

Patients with severe asthma may be particularly susceptible to weight gain. Long-term exposure to systemic corticosteroids (CS) and persistent respiratory symptoms may contribute to reduced physical activity and impaired metabolic balance, further promoting weight increase. [1,18,19]

The introduction of biologic therapies in severe asthma has significantly improved clinical outcomes, including symptom control, exacerbation reduction, and decreased corticosteroid use [2,3,4,8,19,20]. Furthermore, studies have also shown that anti-IL-5 therapies are more effective in patients with a lower BMI. [13,21] However, while their clinical efficacy is well established, their potential impact on body weight and metabolic status remains unclear. [12,20,22]

Therefore, this study aimed to evaluate changes in body mass index (BMI) in patients with severe asthma following initiation of biologic therapy.

SUBJECTS AND METHODS

Study design

This was an observational retrospective study conducted on Pulmonology Department at Unidade Local de Saúde de Santo António (ULSSA), Porto, Portugal and based on the electronic clinical files. The study protocol was carried out in accordance with the Declaration of Helsinki and was approved by the local Ethics Committee. Due to its retrospective nature, the requirement for individual informed consent was waived by the committee.

The primary outcome was the change in BMI from baseline to 12 months. Secondary exploratory analyses evaluated BMI trajectories according to biologic drug class and baseline BMI category.

Patients

All patients included were 18 years old or older and were under biologic therapy for severe asthma for at least 12 months, with this period required to be completed by October 2025. Exclusion criteria included: cancer, pregnancy or patients that had no data regarding the biologic therapy, currently, at use or regarding BMI at the time of the study.

For the analysis of BMI variation according to drug class, patients with prior exposure to a different pharmacological class were excluded.

For the assessment of BMI variation according to baseline BMI category, patients were stratified into two groups based on baseline BMI: <25 kg/m² and ≥25 kg/m².

Collected data

For sample characterization, the following variables were analysed at the beginning of the therapy: age, gender, smoking history (smoker, ex-smoker, non-smoker and pack-years), comorbidities that worsen asthma (anxiety, depression, obesity, deconditioning, chronic rhinosinusitis, inducible laryngeal obstruction, gastro-esophageal reflux disease (GERD), chronic obstructive pulmonary disease (COPD), obstructive sleep apnea, bronchiectasis, cardiac disease and kyphosis due to osteoporosis), environmental exposures, previous biologic therapy, duration of prior biologic therapy, asthma duration and current biologic therapy.

BMI values were recorded at baseline, 6 months and 12 months. Additional clinical, functional, and inflammatory variables were assessed to characterize treatment response during follow-up, including: Asthma Control Test score (ACT score), blood eosinophil count, total immunoglobulin E (IgE), lung function variables (Forced Expiratory Volume in 1 second (FEV1);

Forced Vital Capacity (FVC); ratio FEV1/FVC, FeNO – expressed in absolute values and, when applicable, as a percentage of the predicted value) at 0 months, 6 months and 12 months after the beginning of biologic therapy, number of severe exacerbations (with severe exacerbation being defined as an exacerbation requiring oral corticosteroids or hospitalization or emergency department) visit at 0 months (defined as the period of 1 year before the beginning of biologic therapy), 6 months and 12 months after the beginning of biologic therapy, oral corticosteroids and inhalatory therapy at 0 months (defined as the period of 1 month before the beginning of biologic therapy), 6 months and 12 months after the beginning of biologic therapy.

Some variables weren't available in all patients as a result of new techniques that were recently introduced at the respiratory function laboratory of ULSSA, due to tests conducted outside ULSSA without full transcription of the results or the fact they weren´t mandatory for the beginning of biologic therapy. These situations were considered missing data, without the exclusion of the respective patients. Consequently, the number of patients included in certain subanalysis was lower than in the primary analysis.

Statistical analysis

Categorical variables were described with frequency and percentages. Continuous variables were described as means and standard deviations.

To respond to the main objective of the study, the Friedman test was used, comparing the body mass index during the follow up period at 0,6 and 12 months. We also compared the variation of the BMI at 0,6 and 12 months in each drug class currently approved for severe asthma treatment (anti-IgE; anti (IL)-5/IL-5Rα; anti- IL-4Rα and anti-TSLP) using ANOVA for repeated measures. For the analysis stratified by baseline BMI category the Greenhouse-Greisser corrected interaction was used. The Paired Samples Proportions Test was used to compare corticosteroids use at 0 and 6 months. The other continuous variables were compared across baseline, 6 and 12 months using the Friedman Test.

A p-value of <0.05 was considered statistically significant. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 29.0.0.0. All graphical representations were created using GraphPad.

RESULTS

A total of 45 patients were initially identified. After excluding 15 patients who did not meet the inclusion criteria, 30 patients were included in the final analysis. All the baseline demographic and clinical characteristics of the population are listed in Table I. The mean age at the time of the study was 54,5 years and 11 patients (36,5%) were female. At baseline the BMI mean was 27,7 ± 5,0 and 0 patients were underweight (<18,5 kg/m^2), 11 (36,7%) patients were normal weight (18,5-24,9 kg/m^2), 8 (26,7%) patients were overweight (25-29.9 kg/m^2) and 11 (36,7%) patients were obese (≥ 30 kg/m^2). The majority of patients are currently treated with an anti-(IL)-5/ IL-5Rα (n=21), followed by an anti-IL4Rα (n=6), anti-IgE (n=2) and anti-TSLP (n=1).

Changes in BMI at start of biologic therapy and after 6 and 12 months are presented in Figure 1. Following 12 months of treatment with biologic therapy there was no significant change in the BMI (p=0,349). Although there was a decrease between 6 and 12 months, the values never dropped below baseline levels.

In the exploratory analysis by biologic drug class (Table II), after excluding patients previously exposed to a different biologic class, no statistically differences in BMI trajectories were observed across biologic classes (p>0.05), however, this analysis was limited by small and imbalanced subgroup sizes. Similarly, in the exploratory analysis stratified by baseline BMI category, no significant difference in BMI trajectories was observed between patients with baseline BMI <25 kg/m² and those with BMI ≥25 kg/m² (p = 0.490; Figure 2).

As shown in Figure 3 there was a significant increase in the ACT score (p<0.001). Following 6 months of treatment, the mean ACT score had increased from 13,2 ± 5,9 to 19,8 ± 5,3; following 12 months it had increased to 21,0 ± 5, 6. Figure 4 shows that during the 12 months preceding the study, patients were having a mean 2,1 ± 1,7 severe exacerbations and following 6 months of treatment, the mean number of severe exacerbations had decreased to 0,4 ± 0,6 and to 0,1 ± 0,4 after 12 months (p<0.001). We also analysed the number of exacerbations by sex, smoking status and age of onset and no significant differences were observed (p>0.05).

Table III summarizes the changes in medication related variables. Of the 30 patients initially included, 26 were using systemic corticosteroids at baseline. Therefore, the analysis regarding systemic corticosteroids was restricted to the patients using this therapy (n=26). The comparison was made between baseline and 6 months, as the number of patients receiving systemic corticosteroids remained unchanged between 6 and 12 months. A significant difference was observed between baseline and 6 months (p<0.001). Regarding inhaled therapy, at the beginning of the study 25 patients (83,3%) were using triple inhaled therapy (ICS/LABA/LAMA) and 5 patients

(16,7%) were using double inhaled therapy (ICS/LABA), all with high-dose of inhaled corticosteroids. No changes in inhaled therapy were recorded during the follow-up period.

As presented in Table IV, significant ($p<0.05$) improvements were also observed on the variables regarding lung function. FEV1 (%) from 55,9 ± 18,4 to 79,8 ± 23,5 after 6 months and to 83,7 ± 22,3 after 12 months. FEV1 (real) from 1,7 ± 0,8 to 2,3 ± 0,9 after 6 months and to 2,5 ± 0,9 after 12 months. FVC (%) from 76,8 ± 19,1 to 94,5 ± 23,8 after 6 months and to 94,7 ± 20,8 after 12 months. FVC (real) from 2,9 ± 1,3 to 3,4 ± 1,4 after 6 months and to 3,5 ± 1,3 after 12 months. FEV1/FVC from 58,3 ± 11,8 to 70.0 ± 9,5 after 6 months and to 72,1 ± 9,0 after 12 months.

Changes in inflammatory markers related variables are shown in Table V. An improvement was observed in blood eosinophils count ($p<0.001$). After 6 months of treatment, it had decreased from 491, 7 ± 632, 5 to 155,7 ± 257,7 and to 184,4 ± 292,8, after 12 months. There were no significant changes on IgE ($p=0.819$) and FeNO ($p=0.368$), after the 12 months follow-up.

DISCUSSION

BMI remained largely stable over the 12-month follow-up period in this cohort of patients with severe asthma receiving biologic therapy. Although a slight decrease was observed between 6 and 12 months, values remained close to baseline, suggesting weight stabilization rather than clinically meaningful weight loss. However, it can be hypothesized that although the reduction observed between 6 and 12 months did not surpass the initial baseline value, a longer follow-up period could potentially demonstrate a further decline. Furthermore, reliance on BMI alone for weight assessment may be insufficient, therefore, additional anthropometric measures, could have been considered.

Several studies have examined weight trajectories in patients with severe asthma with inconsistent findings. Our results are consistent with those reported by Cusack et al. [23], who similarly found no significant change in BMI. In contrast, other studies reported modest but significant reductions in BMI [22,24,25], although important methodological differences warrant caution when making direct comparisons. In one of these studies, the follow-up period was considerably longer, which may have facilitated the detection of more gradual changes. [24] In another study, the overall change in BMI was not described, with a significant effect observed only in women. [25] Also, all these studies were in patients under anti-IL-5 therapy.

From a mechanistic standpoint, anti-IL-5 therapies have attracted growing interest because of the emerging role of eosinophils in adipose tissue homeostasis, although data on weight changes remain controversial. [22-25] Preclinical studies on the role of IL-4/IL-4Rα signalling in adipogenesis, lipolysis, and diet-related weight gain are also emerging. [26,27] However, these findings cannot be

directly extrapolated to clinical outcomes in patients treated with these therapies, and confirmation in prospective studies is warranted.

To limit bias introduced by prior treatment history, the secondary analysis was restricted to biologic-naïve patients, allowing a clearer assessment of weight evolution following biologic initiation. No clear differences in BMI trajectories were observed across each drug class currently approved for severe asthma treatment. However, this analysis was exploratory and should be interpreted with caution given the small and imbalanced subgroup sizes, with a predominance of anti-IL-5/IL-5Rα in our cohort and only a single patient under anti-TSLP class.

Similarly, when patients were stratified according to baseline BMI category, no significant differences in BMI trajectories were observed between those with BMI <25 kg/m² and those with BMI ≥25 kg/m². This suggests that baseline BMI status did not substantially modify BMI evolution during the first 12 months of biologic therapy, as seen in other previous studies. [25] However, given the limited sample size, BMI categories were dichotomized to avoid excessively small subgroups, precluding a more detailed assessment across standard BMI categories such as normal weight, overweight, and obesity. Therefore, these findings should be interpreted as exploratory. It should also be highlighted that our sample is mainly composed of normal weight and over-weight patients with only 11 individuals classified as obese. Metabolic and inflammatory alterations associated with adipose tissue are generally more pronounced in established obesity. [15,18,20] Consequently, nearly two thirds of the cohort may not present the same degree of weight-associated inflammatory status as would be expected in a predominantly obese population, which may partly explain the absence of substantial BMI changes. It could also be suggested that patients with severe asthma, but normal weight may maintain a relatively higher, though still limited, level of physical activity compared to obese patients, which may attenuate the weight reduction after the initiation of biologic therapy, potentially affecting BMI variation.

The clinical outcomes observed in our cohort reinforce the efficacy of biologic therapies in severe asthma, including improvements in symptom control, lung function, inflammatory markers and reductions in severe exacerbations and systemic corticosteroid exposure. [2,3,6,8,28]

Given that ACT score reflects asthma control, a significant increase in ACT values suggests better disease control following the initiation of biologic therapy, reinforcing evidence of its efficacy. [16,20] Within this framework, the observed improvement in ACT score suggesting better disease control, could be associated with reduced sedentary behaviour and increased physical activity, thereby potentially influencing BMI over time.

The substantial reduction in the number of exacerbations observed may lead to a lower use of systemic corticosteroids consistent with our results and prior studies. [5,20] Interestingly, the substantial reduction in systemic corticosteroid exposure did not translate into weight loss. This

highlights the complex and multifactorial nature of obesity in severe asthma, in which metabolic, behavioural, and inflammatory mechanisms interact. [10-12] While corticosteroids are known contributors to weight gain, the reduction in their use may primarily prevent further weight increase rather than induce weight loss, particularly over relatively short follow-up periods.

Regarding respiratory function parameters the significant improvements observed in our cohort support the efficacy of biologic therapy, as previously described in the literature. [6,7,15]

Concerning inflammatory markers, the improvement in peripheral eosinophil count supports the efficacy of biologic therapy. [20] The lack of significant changes in IgE and FeNO does not refute this finding, given the limited sample size in these sub-analyses.

In line with real-world clinical practice, inhaled maintenance therapy was kept constant during the study. Currently, there is insufficient evidence to support the step down of inhaled therapy following the initiation of most biologic therapies, even more in shorter follow-up periods. [29]

Several limitations should be considered, such as the small sample size and the retrospective design. Data were collected from electronic health records, where lung function parameters and other clinical variables were not always consistently recorded, resulting in smaller sample sizes in certain subanalyses, which may have limited statistical power. Additionally, BMI alone does not capture changes in body composition or metabolic health. Also, the predominance of anti-IL-5/IL-5Rα therapy in our cohort also limited class-specific conclusions, and the 12-month observation period may be insufficient to capture longer-term effects of sustained corticosteroid reduction on body weight, as suggested by studies with longer follow-up periods. [22]

CONCLUSIONS

Overall, our findings support the concept that biologic therapy improves respiratory outcomes but does not significantly modify body weight, highlighting the need for integrated metabolic management in patients with severe asthma. Future studies, with a prospective design, should incorporate more assessments, including bioimpedance, physical activity monitoring and adipokine profiling to better characterize metabolic responses to biologic therapy.

APPENDIX

Table I – Baseline demographic and clinical characteristics of the population, at the beginning of the study (n=30)

Demografic variables	
Age (years), mean ± SD	54,5 ± 9,4
Female, N (%)	11 (36,7)
BMI (kg/m^2) (0 months), mean ± SD	27,7 ± 5,0
Duration of disease, mean ± SD	18,9 ± 15,6
Onset during childhood (≤18 years), N (%)	14 (46,7)
Late onset (> 18 years), N (%)	16 (53,3)
BMI categories	
Underweight (<18,5 kg/m^2), N (%)	0 (0)
Normal weight (18,5-24,9 kg/m^2), N (%)	11 (36,7)
Overweight (25-29,9 kg/m^2), N (%)	8 (26,7)
Obese (> 29.9 kg/m^2), N (%)	11 (36,7)
Smoking status	
Never smoked, N (%)	19 (63.3)
Previously smoked, N (%)	11 (36.7)
Currently smokes, N (%)	0 (0)
Pack years in previously smoked and currently smokes (PY), mean ± SD	15,9 ± 12,2
Environmental Exposure	
Yes, N (%)	3 (10)
Comorbidities	
Atopy, N (%)	4 (13.3)
Obesity, N (%)	11 (36,7)
Chronic rhinosinusitis, N (%)	8 (26.7)
Rhinitis, N (%)	8 (26.7)
Nasal polyposis, N (%)	9 (30)
Depression, N (%)	1 (3.3)
Symptom control	
ACT Score (0 months) mean ± SD	14.0 ± 7.4
Exacerbations on the past 12 months (0 months), mean ± SD	2.1 ± 1.7

Medication Use	
ICS/ LABA/ LAMA, N (%)	25 (83.3)
ICS/ LABA, N (%)	5 (16,7)
Systemic corticosteroid, N (%)	26 (86,7)
Lung Function	
FEV1 (L), mean ± SD	1,8 ± 1.0
FEV1 (%), mean ± SD	60,4 ± 26,6
FVC (L), mean ± SD	2,9 ± 1,1
FVC (%), mean ± SD	78,9 ± 20.0
FEV1/FVC, mean ± SD	60,6 ± 14,6
Inflammatory Markers	
Blood eosinophils (uL), mean ± SD	400.0 ± 235.8
IgE (KU/L), mean ± SD	264.0 ± 266,5
FeNO (ppb), mean ± SD	45.0 ± 46.2
Previous Biologic Therapy	
None	24 (80.0)
Anti-IgE	2 (6.7)
Anti-(IL)-5/ IL-5Rα	4 (13.3)
Duration of prior biologic therapy (months), mean ± SD	14,2 ± 13,8
Current Biologic Therapy	
Anti IgE, N (%)	2 (6.7)
Anti-(IL)-5/ IL-5Rα, N (%)	21 (70.0)
Anti-IL4Rα, N (%)	6 (20.0)
Anti- thymic stromal lymphopoietin (Anti-TSLP), N (%)	1 (3.3)
Duration of current biologic therapy (months), mean ± SD	42,6 ± 25,7

Table II – Changes in body mass index (BMI) at baseline, 6 and 12 months according to biologic therapy class in patients with severe asthma

Biologic Therapy	0 months	6 months	12 months	p value	n
Anti-IgE	22,5 ± 2,7	23,8 ± 0,9	22,5 ± 0,4	p > 0.05	2
Anti-(IL)-5/ IL-5Rα	28,9 ± 5,6	29,6 ± 5,1	29,7 ± 5,1		18
Anti-IL4Rα	28,1 ± 2,4	28,8 ± 2,1	26,8 ± 2,5		4
Anti-TSLP	25,3	25,6	29,4		1

Table III – ICS/LABA/LAMA, ICS/LABA and systemic corticosteroid use at baseline, 6 and 12 months

Medication use	0 months	6 months	12 months	P value	n
ICS/LABA/LAMA (n)	25 (83,3)	25 (83,3)	25 (83,3)	NA	30
ICS/LABA (n)	5 (16,7)	5 (16,7)	5 (16,7)	NA	30
Systemic corticosteroid (n)	26 (86,7)	13 (43,3)	13 (43,3)	<0.001	30

Table IV – FEV1, FVC and FEV1/FVC ratio at baseline, 6 and 12 months

Lung Function	0 months	6 months	12 months	P value	n
FEV1(L)	1,7 ± 0,8	2,3 ± 0,9	2,5 ± 0,9	0.006	10
FEV1 (% predicted)	58,7 ± 19,4	74,5 ± 24,2	81,8 ± 20,2	<0.001	13
FVC (L)	2,8 ± 1,3	3,4 ± 1,4	3,5 ± 1,3	0.009	10
FVC (% predicted)	76,5 ± 17,3	92,2 ± 22,1	93,1 ± 19,2	0.017	12
FEV1/FVC (%)	58,3 ± 11,8	70.0 ± 9,5	72,1 ± 9,0	0.001	12

Table V – Changes in peripheral blood eosinophils, total IgE and FeNO at baseline, 6 and 12 months

Inflammatory markers	0 months	6 months	12 months	P value	n
Blood eosinophils (uL)	491, 7 ± 632, 5	155,7 ± 257,7	184,4 ± 292,8	<0.001	23
IgE (Ul/ml)	451,2 ± 296,9	647,0 ± 535,3	611, 4 ± 446, 1	0.819	5
FeNO (ppb)	80,0 ± 57, 7	77,7 ± 50,4	45,7 ± 34,3	0.368	3

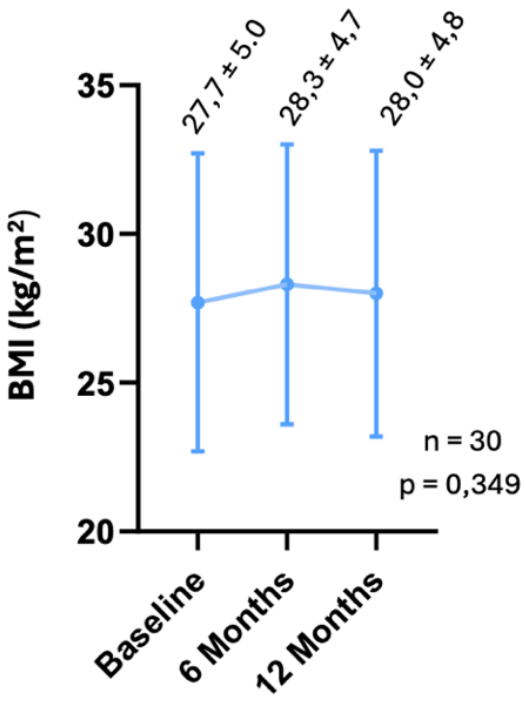

Figure 1 – Changes in body mass index (BMI) at baseline, 6 and 12 months

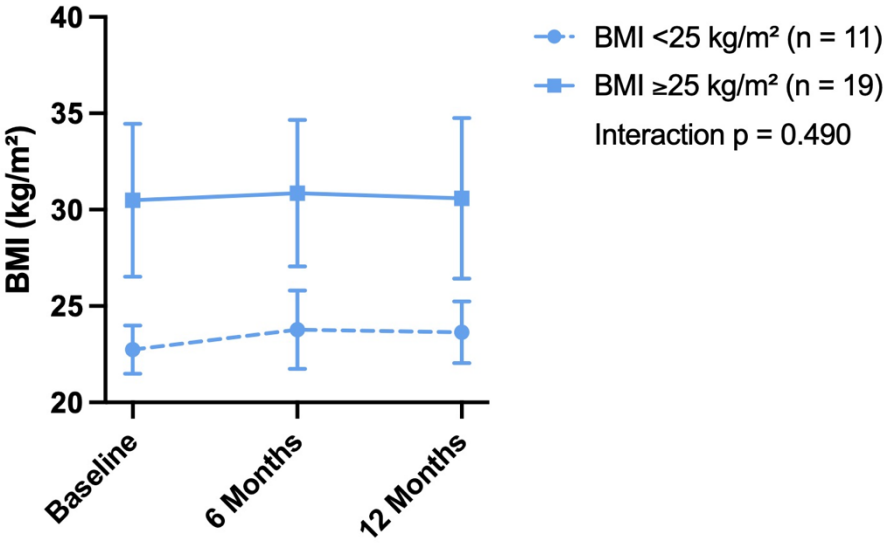

Figure 2 - Changes in body mass index (BMI) at baseline, 6 and 12 months according to baseline BMI category. BMI < 25kg/m^2: Baseline – 22,7 ± 1,3; 6 Months – 23,8 ± 2,0; 12 Months – 23,6 ± 1,6; BMI ≥ 25kg/m^2: Baseline – 30,5 ± 4,0; 6 Months – 30,9 ± 3,8; 12 Months – 30,6 ± 4,2

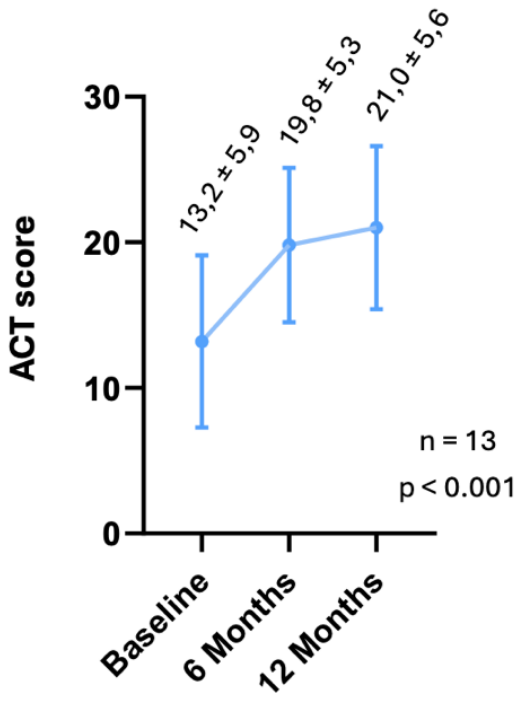

Figure 3 – Changes in Asthma Control Test (ACT) score at baseline, 6 and 12 months

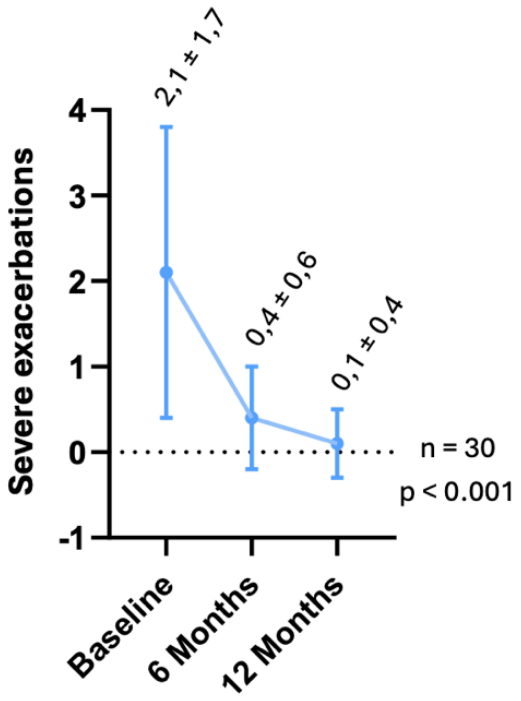

Figure 4 – Changes in severe exacerbations at baseline, 6 and 12 months

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