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Research Article / Araştırma Makalesi

Real-Life Data on the Use of Omalizumab in Patients with Severe Asthma and Chronic Urticaria and Mepolizumab in Patients with Severe Asthma: A Retrospective Study

Astım ve Kronik Ürtikerli Hastalarda Omalizumab'ın ve Şiddetli Astım Hastalarında Mepolizumab'ın Kullanımına İlişkin Gerçek Yaşam Verileri: Geriye Dönük Bir Çalışma

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Abstract: This study aimed to assess the real-life effectiveness of omalizumab and mepolizumab in patients with severe asthma and chronic spontaneous urticaria (CSU), explicitly examining changes in IgE levels and eosinophil counts during treatment. This retrospective study involved patients with severe asthma or CSU treated with biologic agents, including omalizumab and mepolizumab. The primary outcome measures were serum IgE levels, eosinophil counts, urticaria activity scores (UAS), and asthma control test scores (ACT). We studied 61 patients with severe asthma or chronic urticaria treated with biological agents. Patients with asthma exhibited a significant reduction in the median annual attack rate from 4 to 0 with omalizumab ($p<0.001$) and from 6 to 1 with mepolizumab ($p<0.001$). Eosinophil counts, and ACT scores significantly decreased with mepolizumab ($p<0.001$). Six patients who transitioned from omalizumab to mepolizumab did not experience severe asthma attacks in the first six months following the treatment switch. Patients with CSU showed a significant response to omalizumab ($p<0.001$). We observed significant improvements in various markers, including total IgE levels, eosinophil counts, UAS, and ACT scores, indicating that these treatments can effectively manage the symptoms of both conditions. These findings underscore the potential benefits of using these treatments as effective therapeutic options.
Keywords: Asthma, Mepolizumab, Omalizumab, Total IgE, Urticaria

Özet: Bu çalışmanın amacı, şiddetli astım ve kronik spontan ürtiker (CSU) hastalarında omalizumab ve mepolizumab'ın gerçek yaşam etkinliğini değerlendirmek, özellikle tedavi sırasında IgE seviyelerindeki ve eozinofil sayılarındaki değişiklikleri incelemekti. Bu geriye dönük çalışma, biyolojik ajanlarla, omalizumab ve mepolizumab dahil olmak üzere tedavi edilen şiddetli astım veya CSU hastalarını içermektedir. Birincil sonuç ölçümleri serum IgE seviyeleri, eozinofil sayıları, ürtiker aktivite puanları (UAS) ve astım kontrol testi puanları (ACT) idi. Veriler istatistiksel yazılım kullanılarak analiz edildi ve Wilcoxon işaretli sıra testi kullanılarak karşılaştırıldı. Biyolojik ajanlarla tedavi edilen şiddetli astım veya kronik ürtikerli 61 hastayı inceledik. Astımlı hastalar, omalizumab ile yıllık ortalama atak oranında 4'ten 0'a ($p<0.001$) ve mepolizumab ile 6'dan 1'e ($p<0.001$) önemli bir azalma gösterdi. Eozinofil sayıları ve ACT puanları mepolizumab ile önemli ölçüde azaldı ($p<0.001$). Omalizumab'dan mepolizumab'a geçiş yapan altı hasta, tedavi değişikliğinin ilk altı ayında şiddetli astım atakları yaşamadı. CSU'lu hastalar omalizumab'a önemli bir yanıt gösterdi ($p<0.001$). Toplam IgE seviyeleri, eozinofil sayıları, UAS ve ACT puanları da dahil olmak üzere çeşitli belirteçlerde önemli iyileşmeler gözlemledik, bu da bu tedavilerin her iki durumun semptomlarını etkili bir şekilde yönetebileceğini göstermektedir. Bu bulgular, bu tedavilerin etkili terapötik seçenekler olarak kullanılmasının potansiyel faydalarını vurgulamaktadır.
Anahtar Kelimeler: Astım, Kronik Ürtiker, Mepolizumab, Omalizumab, Immünglobulin E

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1. Introduction

Biological therapy agents, such as omalizumab and mepolizumab, have become cornerstone treatments in recent years, offering significant improvements in the quality of life for patients with severe asthma and chronic spontaneous urticaria (CSU) (1, 2). These agents present an alternative to systemic corticosteroids, effectively controlling symptoms and enhancing patients' well-being. Omalizumab, a humanized monoclonal antibody, is approved for treating moderate to severe allergic asthma and CSU. It functions by binding to circulating free immunoglobulin E (IgE) antibodies, thereby reducing IgE-mediated immune responses pivotal to CSU pathogenesis (3, 4). A study evaluating response rates, baseline IgE levels, and total IgE levels after omalizumab treatment in patients with CSU found that alterations in IgE levels can predict the outcome of omalizumab treatment (5). In another study, Tamer et al. demonstrated that omalizumab reduced serum total eosinophil levels in a significant proportion of CSU patients, indicating that serum eosinophil count might be a valuable marker for guiding treatment decisions (6).

A study investigating changes in serum total IgE in severe asthmatics over one year with measurements repeated every two months reported that most of the variability was due to differences between patients, while the within-patient variability in total IgE levels was quite limited (7). Another study reported that the response to omalizumab is better predicted by the ratio of total IgE levels at week four to baseline levels, especially in patients with a ratio exceeding 2 (8). Furthermore, omalizumab has been linked to improved lung function and reduced eosinophil counts in patients with uncontrolled asthma (9). However, not all patients achieve symptom control and reduced exacerbations with omalizumab. The OSMO study indicated that patients with uncontrolled severe eosinophilic asthma (SEA) who switch from omalizumab to mepolizumab might experience notable improvements in asthma control and reduced exacerbations (10). An exploratory post hoc analysis of the OSMO study showed that patients with high baseline eosinophil levels might benefit from switching to mepolizumab from omalizumab, resulting in improved asthma control, quality of life, and fewer exacerbations (11).

Mepolizumab, another biological agent, inhibits interleukin-5 (IL-5) and is approved for treating SEA in adults and children aged six and above. It reduces blood eosinophil levels, a key contributor to asthma pathogenesis (12). This approach has been shown to improve asthma control and reduce the frequency of exacerbations (13, 14). Both post hoc analyses and prospective clinical studies indicate that baseline blood eosinophil counts can predict disease morbidity and identify patients likely to benefit most from mepolizumab (15, 16).

Given the profound impact of these biological agents on patient outcomes, there is a growing interest in understanding their clinical efficacy and safety. This study aims to gather real-life data on omalizumab in patients with severe allergic asthma and CSU, and mepolizumab in patients with SEA. Additionally, it seeks to assess changes in IgE levels and eosinophil counts during these treatments.

2. Materials and Methods

2.1 Study design and participants

This multicenter, retrospective study encompassed 36 adults with severe persistent asthma treated with omalizumab or mepolizumab and 25 patients with CSU treated with omalizumab. Six patients with severe persistent allergic asthma unresponsive to omalizumab underwent a wash-out period of three months before transitioning to mepolizumab. The primary objective was to assess changes in IgE concentrations and peripheral eosinophil counts. The secondary objective aimed to gather real-life data on the efficacy of these biological agents.

Atopy was assessed using skin prick tests and specific IgE measurements, with the puncture method employed. A mean wheal diameter ≥ 3mm compared to the negative control was considered positive. Specific IgE levels were determined using ImmunoCAP (Thermo Fisher Scientific, Uppsala, Sweden) for

prevalent allergens, with levels ≥ 0.35 kU/L indicating positivity.

CSU and asthma were diagnosed based on the EAACI/GA²LEN/EDF/WAO and Global Initiative for Asthma (GINA) guidelines, respectively (17, 18). CSU was identified by the recurrence of wheals, angioedema, or both for over six weeks, while asthma was determined through a combination of clinical history, physical examination, and spirometry findings, with severe asthma characterized as uncontrolled despite maximum medication adherence or exacerbation upon dose reduction.

Patients with CSU had been previously treated with high-dose oral antihistamines for at least 24 weeks but remained symptomatic despite treatment. Total IgE levels, eosinophil counts, eosinophil percentages, and urticaria activity scores were evaluated before and during omalizumab therapy. Clinical response and disease severity were evaluated using the UAS7, calculated from the weekly urticaria activity score (17). Medical records of the patients were reviewed retrospectively.

The administration of mepolizumab and omalizumab was sanctioned based on the criteria delineated in the Turkey Social Security Institution Health Application Communique. Criteria for omalizumab administration included severe persistent allergic asthma, body weight between 20-150 kg, sensitization to at least one perennial allergen, and serum IgE levels between 30-1500 IU/ml, and to have shown an inadequate response to high-dose corticosteroid, long-acting beta 2 agonist and/or leukotriene receptor antagonist therapy. The dose was determined by pre-treatment total IgE level and body weight. For mepolizumab, criteria included uncontrolled asthma requiring regular systemic steroid use for at least six months despite high-dose inhaled corticosteroids and long-acting beta-agonist inhalers for at least one year and an eosinophil count of ≥300 cells/µl (≥150 cells/µl for patients on regular systemic steroids). Patients with a history of omalizumab failure and an eosinophilic phenotype were switched to mepolizumab treatment. Clinical parameters, such as the Asthma Control Test (ACT) score, blood eosinophil count, and the frequency of asthma exacerbations, were obtained through a retrospective review of patient records. An exacerbation was characterized as a deterioration of asthma symptoms that necessitated oral corticosteroids (OCS) for at least three days per week and led to a significant decline in the asthma control test (ACT) score.

Routine screenings conducted during patient visits to various outpatient clinics in our hospital were used to assess total IgE levels and eosinophil counts. Total IgE levels and eosinophil counts were assessed when patients did not receive systemic steroids. Throughout the omalizumab and mepolizumab treatment period, changes in patients' regular controller medications, such as inhaled therapies, antihistamines, and leukotriene receptor antagonists, were adjusted based on individual patient needs and clinical responses. The time points are approximate, labeled as '6-month', '12-month', and '24-month'.

The Non-Interventional Clinical Research Ethics Committee of Eskişehir Osmangazi University, Turkey, approved this study (Approval Date: 13.07.2021, Approval Number: 2021 – 279/13).

2.2 Statistical Analysis

The data were inputted into the Statistical Package for Social Sciences software version 22.0 (SPSS Inc; Chicago, IL, USA) and analyzed using the same program. The Kolmogorov-Smirnov test was employed to determine the normality of the data distribution. For non-normally distributed data, median values were used. The mean and standard deviation (SD) of continuous variables were used to express data at baseline and after treatment with biological medications. The Wilcoxon two-sample test was used to compare results before and after treatment for comparative analyses of continuous variables. Comparisons among more than two groups were analyzed by Repeated Measures ANOVA. Categorical data were evaluated using the appropriate chi-square or Fisher's exact test. A P value of <.05

was considered to indicate statistical significance. Friedman's test was used for comparing time-varying effects. The standard deviations were reported as mean +- SD, and p-values below 0.001 were reported as p<0.001.

3. Results

We included 61 patients (57.4% female, median age 46 years). Among the participants, 59% (n=36) were administered a biological agent to treat severe asthma, and the remaining 41% (n=25) were treated with omalizumab for CSU. Of the patients receiving biologics for severe asthma, 19 were treated with omalizumab and 11 with mepolizumab. Six patients, initially treated with omalizumab, transitioned to mepolizumab due to an inadequate response to the initial treatment. The median treatment duration was 24 months for patients treated with omalizumab and 12 months for those treated with mepolizumab. Among the 36 patients who received a biological agent for asthma, 74.2% had allergic rhinitis, and 44.4% had chronic rhinosinusitis with nasal polyps (CRSwNP). Out of these, 28 patients were allergen-sensitive, while eight were non-atopic. These data are presented in Figure 1 and Table 1.

Table 1. Baseline Characteristics of Study Participants with Severe Asthma

	Treatment (n=36)		
	OMA	**Mepo**	**All Asthma Patients**
Number (n.)	25	11	36
Age, mean (SD) years	48.4 ± 15.0	51.8 ±10.6	49.5 ± 13.8
Female, n. (%)	13 (52.0%)	7 (63.6%)	20 (55.6%)
Sensitization to respiratory allergens (%)	25 (100%)	3 (27.3%)	28 (77.7%)
Allergic rhinitis, n. (%)	22 (88.0%)	3 (27.3%)	25 (69.4%)
CRSwNP, n. (%)	9 (36.0%)	7 (63.6%)	16 (44.4%)
Duration of asthma, mean (SD) years	8.4 ± 4.3	5.9 ± 3.2	7.6 ± 3.8
ACT score (Initial), mean (SD)	14.0 ± 3.1	13.2 ±3.7	13.8 ± 3.5
Exacerbation in the previous year, median (min.-max.)	4.0 (2-16)	6.0 (1-14)	5.0 (1-16)
Eosinophils (cell/µL) (Initial), mean (SD)	417.1 ± 347.8	2004.2 ± 1962.9	902.0 ± 450.4
Total IgE (kU/L) (Initial), median (min.-max.)	428.0 (42.4-2500.0)	504.0 (17.1-3095.0)	504.0 (17.1-3095.0)
Treatment duration, mean (SD) months	47.0 ± 36.8	15.0 ± 8.6	8.5 ± 6.1

Abbreviations: OMA, Omalizumab; Mepo, Mepolizumab; SD, Standard Deviation; µL, Microliter; kU/L, kilounits per liter; IgE, Immunoglobulin E.

Among the 25 patients receiving omalizumab for chronic idiopathic urticaria, 20% had allergic rhinitis, and 16% had asthma. Out of these, seven patients were allergen-sensitive, while 18 were categorized as non-atopic based on skin prick and specific IgE tests. These data are presented in Table 2.

Table 2. Baseline Characteristics of Study Participants with Chronic Spontaneous Urticaria

Treatment (n=25)	**Omalizumab**
Age, mean (SD) years	37.8 ± 13.6
Female, n. (%)	15 (60.0%)
Sensitization to any respiratory allergen (%)	7 (28.0%)
Duration of CSU, mean (SD) months	20.9 ± 8.5
UAS7 score (Initial), mean (SD)	33.5 ± 6.7
Eosinophils (cell/µL) (Initial), mean (SD)	164.3 ± 138.0
Total IgE (kU/L) (Initial), median (min.-max.)	166 (24.2-2109.0)
Treatment duration, mean (SD) months	20.9 ± 8.5

Abbreviations: n, Number; CSU, Chronic Spontaneous Urticaria; SD, Standard Deviation; µL: Microliter; kU/L, kilounits per liter; IgE, Immunoglobulin E; UAS7, Urticaria activity score-7.

The median annual attack rate for patients with asthma receiving omalizumab was 4 (minimum-maximum: 2-16). Post-treatment, this rate decreased to a median of 0 (minimum-maximum: 0-11) ($p<0.001$). Before treatment, patients with asthma receiving mepolizumab had a median annual attack rate of 6 (minimum-maximum: 1-14). This decreased to a median of 1 (minimum-maximum: 0-4) after treatment ($p<0.001$).

Patients with CSU showed a significant response to omalizumab treatment, especially at the 12 and 24-month marks, as evidenced by comparing the UAS-7 before and after treatment (Figure 2). Among these patients, 11 continued with omalizumab treatment as their symptoms consistently recurred upon treatment interruption but were manageable with continued therapy. In contrast, nine patients discontinued treatment after a median duration of 12 months (6-36) and did not experience urticaria attacks in the following period. We could not obtain current status information for three patients due to their absence from follow-up visits over the past six months. For two patients unresponsive to the standard 300mg dose of omalizumab given every 28 days, the dosage was adjusted to 450mg. Upon analysis without differentiating by diagnosis, we observed that the median IgE levels of all patients undergoing omalizumab treatment increased over the treatment duration (Figure 3).

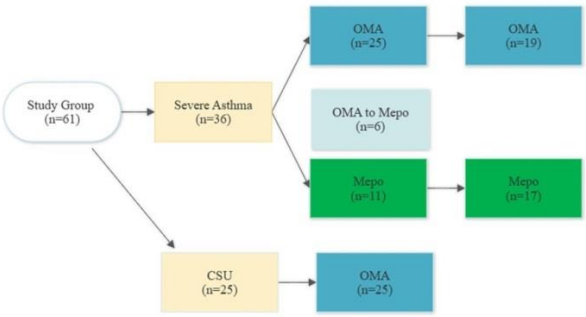

Figure 1. Flowchart of Patient Allocation and Treatment (OMA: Omalizumab, Mepo: Mepolizumab) Of the 61 patients in the study, 36 received a biological agent for severe asthma, with 19 treated with omalizumab and 11 with mepolizumab. Six patients initially received omalizumab but switched to mepolizumab due to an inadequate response. The remaining 25 patients were treated with omalizumab as a biological agent for chronic urticaria.

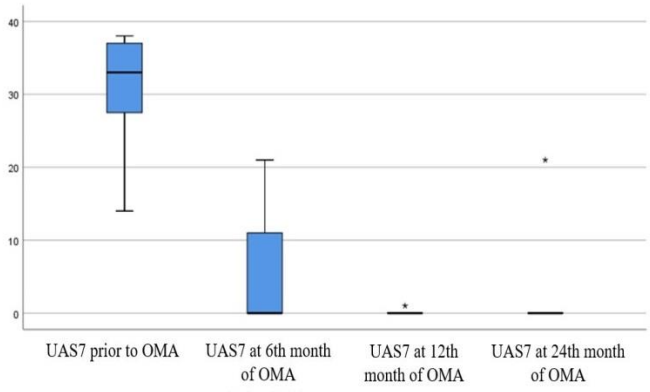

Figure 2. Change in Urticaria Activity Score Following Omalizumab Treatment. The graph shows the change in urticaria activity score (UAS) at different time points before and after treatment with omalizumab in patients with chronic idiopathic urticaria. The UAS ranges from 0 to 42, with higher scores indicating greater disease activity. The data are presented as mean ± standard deviation (SD) for each time point. The scores at 12 and 24 months after treatment were significantly lower than those at baseline, indicating a significant improvement in disease activity following omalizumab treatment.

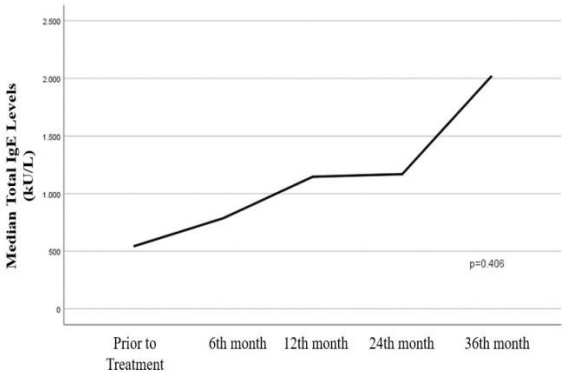

Figure 3. Median IgE Levels in Patients Treated with Omalizumab Over Time. Median IgE levels were measured at baseline and 6-month intervals during treatment with omalizumab. The line shows the median IgE levels (in kU/L) over time for all patients receiving omalizumab, regardless of diagnosis. A non-significant increase in median IgE levels over time was observed (p=0.406).

Table 3 showcases the variations in total IgE levels, eosinophil counts, percentages, and asthma control scores for the 17 patients with severe asthma treated with mepolizumab. While the patient's serum total IgE levels did not show a statistically significant alteration, there was a notable reduction in eosinophil counts and an enhancement in ACT scores ($p<0.001$). Six of the patients who transitioned from omalizumab to mepolizumab did not encounter severe asthma flare-ups in the initial six months post-switch. However, two patients began experiencing exacerbations after the sixth month of treatment. The attack frequency diminished for the other four patients. For those transitioning from omalizumab to mepolizumab, the median interim was three months (minimum-maximum: 2-6). For these five patients, the annual exacerbation rates averaged 12.5 ± 5.1 prior to initiating omalizumab, 7.3 ± 3.7 while on omalizumab, and 1.6 ± 1.5 during mepolizumab therapy.

Table 3. Changes in Total IgE, Eosinophil Levels, and Asthma Control Test Scores in Patients Treated with Mepolizumab

	Prior to Treatment		**3. month**		**6. month**		**12. month**		**24. month**		
	N	Median (Min-Max)	N	Median (Min-Max)	N	Median (Min-Max)	N	Median (Min-Max)	N	Median (Min-Max)	P*
Total IgE	17	504 (17-3095)	8	373 (30-1941)	14	150 (35-1404)	9	80 (18-1527)	4	239 (23-493)	0,706
Eos. x10^3	17	1080 (290-7414)	11	120 (70-786)	12	220 (50-410)	9	90 (50-400)	4	90 (70-160)	**<0.001**
ACT Score	16	13 (9-22)	15	22 (18-25)	12	24 (17-25)	9	25 (20-25)	4	24 (24-25)	**<0.001**

**p: Friedman's test (The analysis did not include the 24th month due to the low number of patients)*
Abbreviations: ACT, Asthma Control Test; Eos, Eosinophil; IgE, Immunoglobulin E.

Table 4 outlines the changes in total IgE levels, eosinophil counts, and asthma control test scores for patients with severe asthma undergoing omalizumab treatment. Significantly, there was a minor yet statistically relevant rise in the patient's serum total IgE levels ($p=0.029$), while eosinophil counts remained consistent with no marked variation ($p=0.887$). Clinically, the ACT scores displayed a pronounced enhancement, signaling improved asthma management, a statistically significant change ($p<0.001$).

Table 4. Changes in Total IgE, Eosinophil Levels, and Asthma Control Test Scores in Patients Treated with Omalizumab

	Prior to Treatment		3. month		6. month		12. month		24. month		
	N	Median (Min-Max)	N	Median (Min-Max)	N	Median (Min-Max)	N	Median (Min-Max)	N	Median (Min-Max)	P*
Total IgE	25	428.0 (42.0-2500.0)	18	530.5 (54.0-2900.0)	17	610.0 (76.0-3100.0)	16	681.5 (90.0-3500.0)	16	568.5 (67.0-4115.0)	**0.029**
Eos. x10^3	25	450.0 (70-1200.0)	18	400.0 (30.0-1100.0)	17	450.0 (100.0-1200.0)	16	410.0 (100.0-1400.0)	16	350.0 (50.0-1000.0)	0.887
ACT Score	25	14 (9-19)	18	17 (15-24)	17	20 (14-25)	16	21 (9-25)	16	23.5 (11-25)	**<0.001**

**p: Friedman's test*
Abbreviations: ACT, Asthma Control Test; Eos, Eosinophil; IgE, Immunoglobulin E.

Within our study cohort, we noted two instances of breast cancer and one case of chronic lymphocytic leukemia (CLL) among those treated with omalizumab. It is crucial to highlight that no definitive association existed between these malignancies and omalizumab treatment. For the two patients diagnosed with breast cancer, omalizumab treatment was not discontinued. Both patients were apprised of the situation, and after detailed discussions, they gave their informed consent to persist with the treatment. Conversely, the patient diagnosed with CLL had their treatment halted due to the necessity of chemotherapy.

4. Discussion and Conclusion

Our study emphasizes the efficacy of omalizumab for patients with severe allergic asthma and CSU, and mepolizumab for SEA management. These insights add to the expanding literature endorsing these biological agents.

We observed marked enhancements in clinical outcomes, especially among patients with elevated total IgE levels and eosinophilic inflammation. Ertas et al. proposed that serum total IgE levels might forecast the omalizumab response in CSU patients. Specifically, those with diminished serum IgE levels had a notably reduced likelihood of therapy responsiveness (5). Although our research did not identify a statistically significant uptick in IgE levels, we contend that an IgE increase does not inherently align with clinical decline. This perspective is congruent with Ertas et al.'s findings. Beyond its efficacy, our data highlighted a significant drop in eosinophil counts and diminished intrasubject variability in total IgE concentrations among omalizumab-treated patients. These findings align with previous research on the drug's mechanism of action (9, 19). Omalizumab is recognized for its selective targeting of Th2 inflammation, proficiently reducing eosinophil counts in both blood and sputum samples (20-22). Nevertheless, the precise mechanism underlying omalizumab's reduction of eosinophil counts remains debatable. It is hypothesized that the drug may have a direct effect or that reduced IgE levels and T-cell-derived cytokines may trigger eosinophil apoptosis (23). Omalizumab has been shown to improve asthma symptom control, enhance the quality of life, and reduce exacerbation rates in appropriately selected patients with persistent allergic asthma (24-26). In line with our observation of omalizumab's efficacy in diminishing the annual attack rate for severe allergic asthma patients, a recent real-world Turkish study showcased that integrating omalizumab into the standard care regimen led to marked reductions in oral corticosteroid usage, asthma medication inhalers, and short-acting rescue meds. This also correlated with fewer hospitalizations, emergency room visits, and unscheduled outpatient appointments (27). This study further highlighted the cost-effectiveness of omalizumab, underscoring its clinical, quality of life, and economic benefits in treating severe allergic asthma (27).

Our findings also advocate for mepolizumab as a potent treatment option for patients with severe asthma. By inhibiting IL-5, mepolizumab curtails eosinophil counts, mitigates airway inflammation, and augments lung functionality in severe asthma patients.

We observed a significant decrease in eosinophil counts in patients treated with mepolizumab, a finding consistent with previous studies that have demonstrated the drug's effectiveness in reducing eosinophilic inflammation in patients with severe asthma (14, 15, 24, 25).

For those with severe asthma, therapies involving omalizumab and mepolizumab notably curtailed asthma exacerbation rates, resonating with prior research (3, 4, 28). Our study also demonstrated that treatment with mepolizumab was associated with a significant reduction in eosinophil counts, which correlated with improved asthma control, as evidenced by higher ACT scores. These findings are consistent with previous studies demonstrating the efficacy of mepolizumab in reducing exacerbation rates and improving asthma control in patients with SEA (5, 6, 15, 29). However, in our research, mepolizumab-treated patients did not exhibit a marked shift in serum total IgE levels. This finding aligns with previous studies, which also reported that mepolizumab does not significantly influence IgE levels (24).

Multiple studies propose that patients with elevated baseline blood eosinophil counts or accompanying nasal polyps might reap enhanced clinical advantages by transitioning straight from omalizumab to mepolizumab (10, 11). Our study found that transitioning from omalizumab to mepolizumab for some patients with severe asthma resulted in observable clinical improvements. This finding aligns with previous studies suggesting the potential clinical benefits of switching to mepolizumab in patients who do not respond to omalizumab (11, 27).

Consistent with previous studies, omalizumab treatment has significantly reduced urticaria activity scores among CSU patients (25, 26). Our study also demonstrated that continued treatment with omalizumab was necessary to maintain symptom control in some patients, as discontinuation of treatment led to symptom recurrence in some cases. Furthermore, some patients required an increased dose of omalizumab to achieve symptom control, which aligns with previous studies reporting that higher doses may be necessary for some patients (7).

Our research identified two breast cancer cases and one chronic lymphocytic leukemia instance among omalizumab-administered patients. The relationship between omalizumab and malignancy has been a topic of interest in the medical community. A 5-year observational study involving 5007 omalizumab-treated and 2829 non-omalizumab-treated patients found similar incidence rates of primary malignancies between both groups (30). A disproportionality analysis within VigiBase identified 1380 reports of neoplasms associated with omalizumab, suggesting a potential association with a higher risk of malignancies (31). Contrarily, a Danish National Patient Registry study found no difference in cancer incidence rates between participants treated with omalizumab and those not treated (32). An analysis of pooled data from randomized, double-blind, placebo-controlled asthma trials further supported the lack of association between omalizumab use and malignancy (33). Given the mixed evidence, it is crucial to approach omalizumab cautiously, especially in patients with a history of cancer.

There are inherent limitations in our study that warrant consideration during interpretation. Its retrospective nature might infuse bias since data was not gathered prospectively, and treatment choices were not randomized. Given our study's retrospective design and the impediments from the COVID-19 pandemic, we could not undertake a quality-of-life evaluation. Such an assessment might have offered more profound insights into treatment impacts on daily living. Our limited sample size could curtail the extrapolation of our insights to a more expansive patient demographic with severe asthma and CSU. Additionally, the lack of a control group prevents us from making definitive conclusions about the efficacy of these treatments. Lastly, the unavailability of routine pulmonary function tests (PFTs), attributed to COVID-19 constraints, might constrain our lung function evaluation. However, some studies suggest that PFT parameters may not change significantly with

the treatments used in our study (14, 34). Therefore, although the lack of PFTs may limit our assessment of lung function, we believe our study still provides essential insights into the effectiveness of omalizumab and mepolizumab.

In conclusion, our findings support the effectiveness of omalizumab and mepolizumab in reducing asthma attacks and improving symptoms in patients with severe asthma and CSU. While baseline eosinophil and IgE levels may offer some insight into the clinical response, our data suggest that comprehensive clinical evaluation is necessary for monitoring treatment. Further research is needed to confirm these findings and better understand these treatments' long-term safety and efficacy.

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Ethics

Ethics Ethics Committee Approval: The study was approved by Eskisehir Osmangazi University Noninvasive Ethical Committee (Approval Date/ Number: 13.07.2021 /13)

Informed Consent: The authors declared that it was not considered necessary to get consent from the patients because the study was a retrospective data analysis.

Author Contributions: Idea/concept: P.C., T.E., Design: P.C., T.E., Data Collection: P.C., T.E., Data Processing: P.C., T.E., Analysis/Comment: P.C., T.E., Literature research/review: P.C., Writing: P.C., All authors discussed the results and contributed to the final manuscript.

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