**Title:** Efficacy of Mepolizumab Treatment on Oral Corticosteroid-Dependent Severe Eosinophilic Asthma Patients with Chronic Rhinosinusitis with Nasal Polyps: Single Center Real Life Study

**Running Title:** OCS dependant severe eosinophilic asthma with CRSwNP

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ABSTRACT

Background: Oral corticosteroid (OCS) dependent severe eosinophilic asthma with chronic rhinosinusitis with nasal polyps (SEA-CRSwNP) would be a suitable phenotype for mepolizumab treatment.

Objective: To evaluate the short-term efficacy of mepolizumab treatment on the OCS dependant SEA-CRSwNP

Methods: Baseline and 24th-week results [daily OCS doses, asthma exacerbation frequency, asthma control test (ACT) scores, blood eosinophil levels, FEV1 values and numerical analog scale (NAS) of CRSwNP symptoms] of the patients that were treated at least 24 week with mepolizumab were retrospectively evaluated and compared.

Results: A total of 16 patients were enrolled in the study. Mepolizumab was discontinued in one patient due to side effects. The daily OCS dosage was reduced from baseline in all patients and at week 24, OCS was discontinued in 40% of the patients (baseline mean steroid dose: 9.2 ± 5.2mg, 24th week: 1.3 ± 1.4mg; p<0.001). The number of asthma exacerbations within 24 weeks significantly decreased after starting of the mepolizumab treatment (2.1 ± 2.7 vs. 0.07 ± 0.26; p=0.012) and a significant increase in the ACT scores (baseline mean ACT: 18 ± 5.7; 24th week mean ACT: 23.3 ± 3; p=0.006) was observed despite the decrease the daily OCS dosages. There was no significant difference in FEV1 values between baseline and at week 24. Evaluation of the general symptoms of CRSwNP as per the NAS revealed that the baseline mean NAS was 5.6 ± 4.4 and the 24th week mean NAS was 3.2 ± 3.2 (p=0.021).

Conclusion: This is the first real-life study evaluating the short-term efficacy of mepolizumab treatment on the OCS dependant SEA-CRSwNP. This study demonstrates that mepolizumab is an effective and safe biologic for the treatment of this severe asthma subphenotype.
Keywords: Severe asthma, eosinophilic asthma, chronic rhinosinusitis, nasal polyps, mepolizumab, anti-IL5

1. INTRODUCTION

Anti-IL5 antibody mepolizumab was approved in 2015 and since then, has become an established therapy for patients with severe uncontrolled eosinophilic asthma (1). In the earliest studies, mepolizumab was administered to a non-specific population of patients with moderate, persistent asthma and variable levels of eosinophilia. Although no significant clinical results have been reported for asthma control in the earliest studies, its effectiveness in eosinophilic asthma is now well ascertained (2, 3). Clinical trials have shown that mepolizumab displays high clinical efficacy by means of reducing exacerbation rates, daily oral corticosteroid (OCS) intake, and enhancing the quality of life. It is apparent that a careful selection of patients is required in order to achieve the best results (4–6).

Among the several different phenotypes in asthma, eosinophilic inflammation occurs in more than 50% of the patients with either atopic or non-atopic asthma. High eosinophil counts in both peripheral blood and airways are associated with recurrent disease exacerbations and severe airflow limitation (7). Adult-onset eosinophilic asthma is increasingly recognized as one of the most severe asthma phenotype (8–11). Another characteristic feature of adult-onset eosinophilic asthma is comorbid chronic rhinosinusitis with nasal polyps (CRSwNP), a feature known for many years and in some cases linked with aspirin and other non-steroidal anti-inflammatory drug hypersensitivities (12–14). Concern regarding non-allergic, severe eosinophilic asthma, and its associated comorbidities has increased with the awareness that this subtype is characterized by high levels of the pro-eosinophilic cytokine IL-5 which is mainly produced by a unique population of type 2 innate lymphoid cells (15). We endorse an
“in-house” classification of asthma phenotypes and decision-making protocol which involves the first choice monoclonal antibody (mAb) and potential alternative mAbs in severe asthma phenotypes (12). We prefer anti-IL5 treatment especially for OCS-dependent severe eosinophilic asthma with CRSwNP (SEA-CRSwNP) phenotype.

To the best of our knowledge, no study evaluating the real-life efficacy of mepolizumab treatment in patients with OCS-dependent SEA-CRSwNP phenotype has been carried out till date. According to the literature, the data with regard to post-marketing studies are scarce that have evaluated the effects of mepolizumab in a real-world setting (16, 17). Thus, this short-term single-center study was carried out in a more specific group of asthmatic patients treated with add-on biologic therapy with mepolizumab.

2. METHODS

The adult patients (>18 years) with OCS dependent SEA-CRSwNP phenotype who were treated with mepolizumab between 2018 and 2019 were retrospectively evaluated. All patients were treated with high-dose, extra-fine inhaled glucocorticoids (ICS), and a long-acting β2-agonist, along with a second controller montelukast in addition to regular OCS therapy at least six months before the mepolizumab treatment. The indications to be treated with mepolizumab were approved on the basis of the Turkey Social Security Institution Health Application Communique, according to which, mepolizumab can be administered to patients with severe eosinophilic asthma having: a) blood eosinophil count ≥300 cells/µL (∼150 cells/µL: If the patient is under long-term regular OCS therapy); b) controlled or uncontrolled asthma treated with regular systemic steroids for at least six months and/or uncontrolled asthma (relatively two attacks per year requiring systemic corticosteroids for at least three days) despite use of a high combination dosage of ICS (> 800 mcg/day budesonide
or equivalent) and inhaler long-acting β2 agonist for at least one year (18). However, the authors have confined the criterion and mepolizumab was employed only in patients with GINA step 5 OCS-dependent SEA-CRSwNP (uncontrolled, partially controlled or if the patient developed OCS side effects even if asthma being under control). Mepolizumab was administered subcutaneously at a dose of 100 mg every four weeks, for at least 12 weeks. Mepolizumab was continued if there was a clinical response at week 12. Those patients who completed the treatment for at least 24 week were included in the study.

Throughout the study period, parameters including ACT score, blood eosinophil count and FEV\textsubscript{1} were measured at baseline, at week 12 and week 24 after the first injection of mepolizumab. In addition, the number of asthma exacerbations (exacerbations occurring within the previous 24 weeks) and daily intake of OCS (presented as methyl-prednisone equivalent in milligrams) were also recorded, respectively at baseline and week 24 with mepolizumab.

The scores for severity of nasal polyposis on numerical analog scale (NAS) were assessed by asking patients to indicate the severity of their CRSwNP on a scale of 0–10 by considering the irritability of the following symptoms in general: rhinorrhea, mucus in the throat, nasal blockage, and loss of smell. The score for the loss of smell on NAS was evaluated separately. Changes in the severity of nasal polyposis on NAS score from baseline to 24\textsuperscript{th} week were also recorded. In addition, the side effects of mepolizumab were assessed for all patients.

\textbf{2.1. Differentiation of severe asthma from difficult asthma}
Drug adherence, inhaler technique, comorbidities including allergic rhinitis, chronic rhinosinusitis/nasal polyp, gastroesophageal reflux, obstructive sleep apnea syndrome and trigger factors like allergens, smoking, occupational allergen and/or irritant, ACE inhibitors, non-specific beta-blockers which interfered with disease control were investigated for all patients. The measures taken for these comorbidities and triggers, drug compliance and techniques were analyzed. All patients under GINA step 5 treatment with controlled or uncontrolled asthma were considered to be severe asthmatic and OCS-dependent SEA-CRSwNP was identified as the appropriate asthma phenotype for mepolizumab treatment in these patients.

Since this asthma phenotype is associated with high eosinophilia, other diseases associated with higher peripheral eosinophilia and accompanied by asthma or asthma-like symptoms such as eosinophilic granulomatosis with polyangiitis, allergic bronchopulmonary aspergillosis, chronic eosinophilic pneumonia, hypereosinophilic syndrome, Loffler’s syndrome and pulmonary involvement of connective tissue diseases were ruled out.

2.2. Definitions:

Asthma exacerbations: An exacerbation was defined as worsening of asthma symptoms, requiring OCS at least three days a week or an increase in the OCS dose.

Chronic rhinosinusitis (CRS): All CRS subjects met the criteria for CRS as defined by the American Academy of Otolaryngology-Head and Neck Surgery Chronic Rhinosinusitis Task Force. The diagnosis of CRS was based on the presence of clinical symptoms (i.e., nasal congestion, rhinorrhea, facial pressure, hyposmia) for more than 12 weeks in addition to the objective evidence of chronic inflammatory disease on sinus CT imaging or nasal endoscopy.
Sinonasal involvement was assessed by paranasal sinus computerized tomography (PNCT) and nasal endoscopy (19).

**CRSwNP:** CRSwNP is characterized by the occurrence for more than 12 weeks of symptoms as nasal discharge, stuffiness, facial pressure or pain, dysfunction or loss of the sense of smell, and cough from post-nasal drip. The polypoid inflammation filling the nasal airway in the PNCT (20).

**NAS:** In NAS, the response to “How troublesome are your symptoms of CRSwNP?” is rated from 0—10 where 0=not troublesome, 10=worst possible.

**Treatment response to mepolizumab:** Based on placebo-controlled phase III-studies, recommendations published by National Institute for Health and Care Excellence (NICE) define the reduction of exacerbation rate by at least 50% or a clinically significant reduced dose of continuous OCS, as adequate response criteria (5, 6, 21).

### 2.3. Laboratory, functional, and imaging tests

The tests included; blood eosinophilia (reference range: <200 cells/mm³), C-reactive protein (CRP; reference range: 0–6 mg/L), erythrocyte sedimentation rate (ESR; reference range: 3–20 mm/hour), total immunoglobulin E (IgE; reference range: 0–100 IU/mL), *Aspergillus* specific IgE, antinuclear antibody, urinalysis, liver and renal function tests, parasite stool examination, creatine kinase, pulmonary function tests [including FEV₁, forced vital capacity (FVC), and FEV₁/FVC], thorax computed tomography, PNCT, and electromyography if the patients exhibited symptoms of peripheral neuropathy. The authors also necessitated advanced laboratory tests for Eosinophilic granulomatosis with polyangiitis (EGPA), Hypereosinophilic syndrome (HES) and lymphoreticular malignancy among patients who had >10% blood eosinophils (such as vitamin B12, antineutrophil cytoplasmic antibody, troponin, FIP1-like-
platelet-derived growth factor receptor alpha, JAK-2 mutation, Philadelphia chromosome, abdominal ultrasonography if suggested by hematologic consultation).

2.4. Glucocorticoid Reduction Phase Scheme

The dose of methylprednisone was reduced every four weeks according to a predefined Schedule (Table 1), if the patient had not had an exacerbation with a decrease in ACT score. In patients who were receiving a daily dose of 8 mg or more of methylprednisone at baseline, the dose of the drug was not reduced to zero without consulting endocrinology because of concern regarding withdrawal effects.

All patients under follow-up at our asthma outpatient clinic provided written informed consent. Ethics approval was obtained from Erciyes University, Ethics Committee (Approval date and number: 12 August 2019-20019/472).

2.5. Statistical analysis

Data were entered into Statistical Package for Social Sciences software version 17.0 (SPSS Inc; Chicago, IL, USA), and analyses were made using the same software program. All continuous variables were presented as mean ± standard deviation (SD) due to small sample size. For all non-parametric variables, between and within group comparisons were made by using Mann-Whitney U test and Wilcoxon test, respectively. p value of < 0.05 was considered to be significant in all analyses.

3. RESULTS
Data from 16 patients with OCS-dependent SEA-CRSwNP, who underwent treatment with mepolizumab were analyzed. All patients were classified as step 5 according to Global Initiative for Asthma (GINA) (1) and had uncontrolled asthma despite maximal therapy. The mean age of the patients was 48.6±11.9 years. The mean duration of the disease and the duration of regular OCS use prior to the initiation of mepolizumab treatment were 12.9±6.6 years and 5.1±2.6 years, respectively. Females accounted for 81% of all the study subjects. Of the 16 patients, 14 (88%) were non-smokers. Patient characteristics were shown in table 2.

Disease control was evaluated using ACT at baseline with a mean value of 18.2±5.5. Also, the lung function test prior to mepolizumab treatment evidenced a mean FEV$_1$ of 81%±30. All patients were receiving daily OCS therapy before mepolizumab, with a mean dose of 8.9±5.2 mg of methyl-prednisolone. The mean eosinophil count at baseline was 561±591 cells/µL. The mean eosinophil percent was 5.3%±5.7%.

The number of asthma exacerbations, as well as the mean eosinophil counts, were decreased while the results of ACT were improved under daily OCS treatment at the time before initiation of mepolizumab, in comparison to the time before regular OCS intake. There was also a non-significant increase in FEV$_1$ values after starting of regular daily OCS (Table 3).

Mepolizumab treatment was found to be very effective in all study subjects. With regard to the adverse events, only one patient showed side effects including arthralgia and malaise, which occurred on the following day after the administration of the first two doses. The patient also had a third reaction occurred on the following day after the administration and fever, nausea, and vomiting were reported. Mepolizumab was then discontinued and this
patient was excluded from the study. The patient was symptom-free during the follow-up period. Further comparisons between study subjects included only the remaining 15 patients.

When comparing the change in blood eosinophil counts, daily OCS doses and ACT scores between baseline and at week 12 under mepolizumab treatment, a marked decrease in peripheral eosinophil counts (5.5%±5.8 vs. 1.3%±0.7; p=0.013) and an increase in ACT scores (18±5.7 vs. 22.5±3.6; p=0.011) were observed. OCS dose was decreased in all of the patients; the daily OCS dosage was completely withdrawn in 3 (20%) patients and 15 out of 15 patients (100%) were classified as treatment responders in at week 12. No marked changes in FEV\(_1\) values were observed at this time point (80±30.7% vs. 84±26%) (Table 4).

After 24 week under mepolizumab treatment, the decrease in blood eosinophil counts (baseline eosinophil count: 5.5±5.8%; 24\(^{th}\) week eosinophil count: 1.9±1.4%; p=0.029) and improvement in ACT scores (baseline ACT: 18±5.7; 24\(^{th}\) week ACT: 23.3±3; p=0.006) was continued. OCS dose was additionally reduced in 9 (60%) patients when comparing to 12\(^{th}\) week results. OCS was completely withdrawn in 6/15 (40%) patients at week 24. A significant decrease in 24-week exacerbation rates of pre- and post-mepolizumab treatment was observed (2.1±2.7 vs. 0.07±0.26; p = 0.012) (Table 4). Despite the decrease in daily OCS dosages, improvement in all parameters was seen at week 24 under mepolizumab treatment.

Comparison of OCS dosage, number of asthma exacerbations, ACT, FEV\(_1\) and blood eosinophils at the beginning of mepolizumab and at 12\(^{th}\) and 24\(^{th}\) weeks after treatment was shown figure 1.
During the 6-month mepolizumab treatment, demographics, baseline blood eosinophil counts, exacerbation rates, FEV\textsubscript{1} values, and ACT scores were found to be similar irrespective of whether OCS was completely withdrawn in the patients.

On a 10 point NAS, the severity of CRSwNP symptoms decreased from 5.6±4.4 points to 3.2±3.2 points (p=0.021) and the severity of loss of smell decreased from 4±5.1 points to 2.4±4.2 points (p>0.05) after 24 weeks of mepolizumab treatment.

4. DISCUSSION

This is the first real-life study evaluating the short-term (24 weeks) efficacy of mepolizumab treatment on the specific subphenotype of asthma. Our study showed that in patients with OCS-dependent SEA-CRSwNP phenotype, after 24 week with mepolizumab treatment, OCS dose was decreased in all of the patients and 40% of them no longer required OCS. A decrease in the frequency of exacerbations and an increase in ACT scores were also observed, besides this decrease in daily OCS doses. However, there were no significant differences in FEV\textsubscript{1} values between week 24 and baseline.

Both, severe eosinophilic asthma and nasal polyposis are characterized by a marked local eosinophilic inflammation (22). IL-5 appears to play a key role in the pathogenesis of CRSwNP and eosinophilic asthma (22–26). In addition, according to the severe asthma guidelines of GINA, suggestions were made on which biologics should be preferred for the type-2 high asthma phenotype, and it was emphasized that factors determining the response to treatment should be taken into consideration (1). Therapy should be initiated with anti-IL5/anti-IL5R mAbs in patients with severe uncontrolled asthma having a blood eosinophil count of ≥300/µL. The factors that may predict a good response to anti-IL5/IL5R biologics
are defined as follows: (a) higher blood eosinophil count (strongly predictive); (b) more frequent severe exacerbations during the previous year (strongly predictive); (c) adult-onset asthma; (d) nasal polyposis; and e) maintenance with OCS at baseline. The efficacy of mepolizumab has individually been reported in OCS-dependent asthma, severe eosinophilic asthma, and CRSwNP (4–6, 27–29). Therefore, OCS-dependent SEA-CRSwNP phenotype appears to be the most appropriate phenotype for mepolizumab. In our study, all the study subjects presented with a history of frequent exacerbations, higher eosinophil levels, OCS-dependency, and CRSwNP. Owing to all these reasons, the authors decided to initiate mepolizumab therapy for this subphenotype of asthma.

One of the main endpoints of all biologics is the withdrawal of the use of OCS in severe asthma (30). In this real-life study, all patients were prescribed with daily OCS (9.2±5.2 mg of methyl-prednisone or equivalent). OCS dose was successfully reduced in all patients and 40% patients completely discontinued OCS after 24 weeks of mepolizumab therapy. Comparing to baseline, at week 24, a significant decrease in the frequency of exacerbations and an increase in ACT scores were observed, besides this decrease in daily OCS doses. In the large, placebo-controlled trials, treatment with mepolizumab significantly reduced the exacerbation rates and daily OCS doses (4–6). The Steroid Reduction with Mepolizumab Study (SIRIUS) demonstrated that mepolizumab, in addition to decreasing asthma exacerbations and improving the quality of life, was also capable of significantly diminishing daily OCS intake (reduction: 50%, complete discontinuation: 14%) (4). However, OCS reduction (100%) or complete discontinuation (40%) rates in our study were much higher at week 24. This positive outcome could be due to the fact that the add-on therapy with mepolizumab was initiated in a specific eosinophilic asthma subphenotype that may have a higher potential to be benefitted from mepolizumab therapy. In another real-life study supporting the results of the present
study, Pelaia et al. established that OCS could be reduced in all patients with significant
reduction in exacerbations after 24 weeks of initiation of the mepolizumab therapy in patients
with OCS-dependent severe eosinophilic asthma (31). The common feature of these studies is
that all of the patients in both studies were OCS dependent and the initial eosinophil counts
during OCS therapy were higher (580±607 cells/μl, 647.1±274.7 cells/μl, respectively).
However, nasal polyp ratios were not reported in this study. These two real-life studies shown
that the early results of mepolizumab are quite good, especially in patients having high blood
eosinophilia and OCS dependency. Considering these patients with priority will be more
meaningful in terms of treatment success in patients indicated for mepolizumab therapy.

In the present study, the clinically relevant improvement in asthma control, elicited by
mepolizumab, was paralleled by a prominent and sustained decrease in blood eosinophil
counts. This finding confirms the results of previous, several large cohort and real-life studies
(5, 31). Undeniably, blood eosinophils are now considered as a reliable biomarker for
predicting and assessing the therapeutic efficacy of mepolizumab in severe eosinophilic
asthma (1, 32, 33). The initial high eosinophil levels in patients in the present study were
associated with a good response to mepolizumab. Increased blood eosinophil count (300 or
400 cells/μl) in asthmatic patients is associated with an increased risk of exacerbations (34,
35). Therefore, one of the goals of mepolizumab treatment that should be emphasized is to
keep the blood eosinophils below these cut-off values in severe eosinophilic asthma (36). In
the present study, the remarkable decrease in blood eosinophil levels evoked by mepolizumab
was paralleled by a reduction in the rate of asthma exacerbation and improvement in asthma
control.
Contradictory reports on the effects of mepolizumab on FEV$_1$ have been published. Some studies have indicated a modest increase in FEV$_1$ with mepolizumab therapy (6, 27, 37), while others claim that FEV$_1$ did not improve with the administration of mepolizumab (2, 5, 38, 39). In the present study, no significant change in FEV$_1$ values was noted after 12 or 24 weeks of mepolizumab treatment compared to baseline. Yet, the important point here is that there is no deterioration in pre-treatment FEV$_1$ values, despite dosage reduction or discontinuation of OCS.

The SIRIUS study, which included OCS-dependent eosinophilic asthma patients, reported the rate of nasal polyps to be 23%. In another study which included OCS-dependent eosinophilic asthma patients, this rate was 30% (4, 27). However, the effect of mepolizumab on nasal polyp was not evaluated in these studies. In a randomized, double-blind, placebo-controlled study recruiting adult patients with recurrent nasal polyposis requiring surgery, the patients received 750 mg intravenous mepolizumab. A significant improvement in the all individual VAS symptom scores in the mepolizumab group was observed in comparison to placebo (28). In the present study, a significant improvement in NAS scores assessed CRSwNP general symptoms (at 24 weeks for rhinorrhea, nasal blockage, postnasal drip, and loss of smell) was observed. However, there was no significant improvement when NAS was evaluated only for smell loss. We speculate that other pathways may be more dominant in the development of eosinophilic inflammation in the nasal polyposis in these subgroups (IL4/IL13 dominant Type 2 inflammation) or the dose of mepolizumab may be insufficient to reduce eosinophilic inflammation at the tissue level (dose of mepolizumab used in the two studies on CRSwNP mentioned above was 750 mg, while that used in the present study was 100 mg).
The major limitations of the present study were the inclusion of a small number of patients and its retrospective design. We could not recruit a high number of patients as the study was conducted in a very specific patient cohort. Although we obtained good clinical results with mepolizumab therapy for specific asthma subphenotype, a large-scale series is still necessary for robust results. Another limitation was that we compared asthma exacerbation rates only before and after six months of mepolizumab initiation. As exacerbations mainly occur during winter, assessment for at least twelve months is necessary to properly reflect the exacerbation rates (40). However, patients who received mepolizumab for at least six months underwent through the autumn of 2018 and winter and spring of 2019. In other words, the patients were treated with mepolizumab during the period in which the risk of asthma exacerbation is high and the results were compared six months before the mepolizumab initiation. Yet, it can be speculated that the decrease in exacerbations during 12 months may be even better.

In conclusion, the authors document that subcutaneous mepolizumab administration significantly decreased blood eosinophil levels, asthma exacerbations, and daily OCS doses. These excellent therapeutic effects were associated with a marked improvement in symptoms as well as a very good short term safety profile of drug and tolerability in this single centered study. Therefore, the availability of mepolizumab in daily medical practice may undoubtedly represent a valuable advancement in the management of patients with OCS-dependent SEA-CRSwNP. The ideal scenario for a therapeutic intervention would be specific selection criteria with a clear prediction of clinical benefits. This small study was clinically directed and highlighted the importance of patient selection for investigating the use of mepolizumab in severe asthma. Nevertheless, further extended real-life investigations are required to confirm the results obtained in our study.
5. REFERENCES

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https://ginasthma.org/severeasthma/


18- Turkey Social Security Institution Health Application Communique. Available at:


21- National Institute for Health and Care Excellence (NICE). Mepolizumab for treating severe refractory eosinophilic asthma.


6. TABLES

Table 1. Glucocorticoid Reduction Phase Scheme

<table>
<thead>
<tr>
<th>Methylprednisolone Dose (mg/day)</th>
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<th></th>
<th></th>
<th></th>
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<td>20.0</td>
<td>16.0</td>
<td>12.0</td>
<td>10.0</td>
<td>8.0</td>
<td>6.0</td>
<td>4.0</td>
</tr>
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<td>16.0</td>
<td>12.0</td>
<td>10.0</td>
<td>8.0</td>
<td>6.0</td>
<td>4.0</td>
<td>2.0</td>
</tr>
<tr>
<td>12.0</td>
<td>10.0</td>
<td>8.0</td>
<td>6.0</td>
<td>4.0</td>
<td>2.0</td>
<td>2.0*</td>
</tr>
<tr>
<td>10.0</td>
<td>8.0</td>
<td>6.0</td>
<td>4.0</td>
<td>2.0</td>
<td>2.0*</td>
<td>0.0</td>
</tr>
<tr>
<td>8.0</td>
<td>6.0</td>
<td>4.0</td>
<td>2.0</td>
<td>2.0*</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>6.0</td>
<td>4.0</td>
<td>2.0</td>
<td>2.0*</td>
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<tr>
<td>4.0</td>
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</tr>
<tr>
<td>2.0</td>
<td>2.0*</td>
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<td>0.0</td>
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<tr>
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<td>0.0</td>
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</tr>
</tbody>
</table>

*Taken as 2.0mg administered every other day
**Table 2. Characteristics of the patients**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=16</th>
</tr>
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<tbody>
<tr>
<td>Female Gender (%)</td>
<td>13 (81)</td>
</tr>
<tr>
<td>Age, years, mean±SD</td>
<td>48.6 ±11.9</td>
</tr>
<tr>
<td>Smoking story (%)</td>
<td></td>
</tr>
<tr>
<td>Never smoked</td>
<td>14 (88)</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Active smoker</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Asthma duration, years, mean±SD</td>
<td>12.9 ±6.6</td>
</tr>
<tr>
<td>Mean clinical follow-up duration, years±SD</td>
<td>5.1 ±2.6</td>
</tr>
<tr>
<td>NERD (%)</td>
<td>10 (63)</td>
</tr>
<tr>
<td>Atopy (%)</td>
<td>3 (19)</td>
</tr>
<tr>
<td>Baseline total IgE levels, IU/ml, mean±SD</td>
<td>545 ±977</td>
</tr>
</tbody>
</table>

NERD: NSAID-exacerbated respiratory disease
Table 3. Comparison of the clinical, laboratory and functional parameters prior and after OCS

<table>
<thead>
<tr>
<th>N=16</th>
<th>Prior to OCS</th>
<th>Under OCS prior to Mepolizumab</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of asthma exacerbations in the last 24 week, mean±SD</td>
<td>9.6±8.7</td>
<td>2±2.6</td>
<td>0.001</td>
</tr>
<tr>
<td>ACT, mean±SD</td>
<td>11.9±3.7</td>
<td>18.2±5.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Blood eos %, mean±SD</td>
<td>13.3±8.9</td>
<td>5.3±5.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Blood eos count mean±SD</td>
<td>1371±1182</td>
<td>561±591</td>
<td>0.002</td>
</tr>
<tr>
<td>FEV₁ %, mean±SD</td>
<td>71.4±19</td>
<td>81±30</td>
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</tr>
<tr>
<td>FEV₁ L/s, mean±SD</td>
<td>1920±805</td>
<td>2091±962</td>
<td>0.425</td>
</tr>
</tbody>
</table>

ACT: asthma control test, eos: eosinophil, OCS: Oral corticosteroid
Table 4. Comparison of the clinical, laboratory and functional parameters at the baseline, 12th and 24th week

<table>
<thead>
<tr>
<th>N=15</th>
<th>Pre-Mepolizumab</th>
<th>Mepolizumab 12th Week</th>
<th>p*</th>
<th>Mepolizumab 24th Week</th>
<th>p**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylprednisolone equivalent systemic steroid dose, mg, mean±SD</td>
<td>9.2±5.2</td>
<td>2.8±2.2</td>
<td>&lt;0.001</td>
<td>1.3±1.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of asthma exacerbations in the last 24 week, mean±SD</td>
<td>2.1±2.7</td>
<td>0.07±0.26</td>
<td>-</td>
<td>0.07±0.26</td>
<td>0.012</td>
</tr>
<tr>
<td>ACT mean±SD</td>
<td>18±5.7</td>
<td>22.5±3.6</td>
<td>0.011</td>
<td>23.3±3</td>
<td>0.006</td>
</tr>
<tr>
<td>Eos %, mean±SD</td>
<td>5.5±5.8</td>
<td>1.3±0.7</td>
<td>0.013</td>
<td>1.9±1.4</td>
<td>0.029</td>
</tr>
<tr>
<td>Eos count mean±SD</td>
<td>580±607</td>
<td>106±73</td>
<td>0.01</td>
<td>177±137</td>
<td>0.019</td>
</tr>
<tr>
<td>FEV1 %, mean±SD</td>
<td>80±30.7</td>
<td>84±26</td>
<td>0.342</td>
<td>84.6±26</td>
<td>0.392</td>
</tr>
<tr>
<td>FEV1 L/s, mean±SD</td>
<td>2092±995</td>
<td>2156±922</td>
<td>0.434</td>
<td>2232±875</td>
<td>0.533</td>
</tr>
</tbody>
</table>

ACT: asthma control test, eos: eosinophil

*Comparison of pre-mepolizumab and mepolizumab 12th week

**Comparison of pre-mepolizumab and mepolizumab 24th week
7. FIGURE LEGEND

Figure 1. Comparison of OCS dosage (A), number of asthma exacerbations (B), ACT (C), FEV₁ (D) and blood eosinophils (E) at the beginning of mepolizumab and at 12th and 24th weeks after treatment.