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Benralizumab reduces eosinophils and inflammatory markers in patients with severe eosinophilic asthma and chronic rhinosinusitis with nasal polyps: A pilot real-life study.

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ABSTRACT

Chronic rhinosinusitis with nasal polyps (CRSwNP) and Severe Eosinophilic Asthma (SEA) are both frequently sustained by eosinophilic inflammation and are probably the manifestation of a unique disease of upper and lower respiratory tract.

We retrospectively observed 11 patients with severe CRSwNP and concomitant SEA under add-on therapy with benralizumab evaluating symptoms using Sino Nasal Outcome Test-22 (SNOT-22), Visual Analogue Scale (VAS), and Asthma Control Test (ACT) and Nasal polyp size by endoscopic and radiological score by Nasal Polyp Score (NPS) and Lund-Mackay Score (LMS). At 6 and 12 months, the expression of cationic eosinophil protein (ECP), Interleukin 17 (IL-17), Interferon gamma (INF-γ), and vascular endothelial growth factor (VEGF) was measured by nasal scraping to assess mucosal inflammation.

After 12 months of benralizumab treatment, SNOT-22 decreased from 45 (23–97) to 14 (5–53) ($p < 0.05$), total VAS of rhinologic symptoms decreased from 30 (17–44) to 9 (5–37) ($p \leq 0.01$) and ACT score increased from 10 (5–15) to 24 (20–25) ($p \leq 0.01$).

NPS decreased from 5 (3–6) to 3 (2–4) after 6 months ($p < 0.05$) and to 2 (2–3) after one year respectively ($p < 0.05$) and LMS total score from 21 (15–24) to 17 (8–21) ($p \leq 0.01$) after 12 months from starting treatment.

Nasal mucosa scraping found differences in INF-γ and VEGF expression in patients compared to 10 healthy subjects, with a normalization of these markers during eosinophils depletion induced by benralizumab.

This is the first pilot real-life study conducted with an anti-IL5R monoclonal antibody in severe eosinophilic asthma and severe CRSwNP patients showing that this treatment can induce benefit both diseases not only from the clinical, but also from the inflammatory point of view. Moreover, our research pointed out that INF-γ and VEGF may represent potential response biomarker.

1. Introduction

Chronic rhinosinusitis (CRS) with nasal polyps (CRSwNP) is an inflammatory disorder of the nose and paranasal sinus known as a specific phenotype of chronic rhinosinusitis difficult-to-manage [1,2]. Of note, among patients with CRS, approximately 20–30% have CRSwNP [2]. CRSwNP medical treatment is limited to nasal rinses with saline solutions, topical corticosteroids (INCS), systemic corticosteroids (OCS) and/or functional endoscopic sinus surgery for severe cases, based on disease severity and characteristics [3]. Despite appropriate treatment many patients complain about relapsing symptoms and repeated surgeries, with a significant impact on quality of life [4]. A subgroup of these patients is characterized by the presence of asthma [2]. For instance, among patients with CRSwNP, from 30% to 70% are also affected by asthma, as well as from 70% to 90% of severe asthmatic

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Abbreviations

ACT	Asthma Control Test
ADCC	Antibody Dependent Cellular Cytotoxicity
BEC	Blood Eosinophil Count
CRS	Chronic Rhinosinusitis
CRSwNP	Chronic Rhinosinusitis with Nasal Polyps
ECP	Eosinophil Cationic Protein
GINA	Global Initiative for Asthma
ICS	Inhaled Corticosteroids
ILC2	Type 2 Innate Lymphoid Cells
INCS	Intranasal Corticosteroids
IFNγ	Interferon-gamma
IgE	Immunoglobulin E
IL-17	Interleukin-17
IQR	Interquartile Range
LABA	Long Acting Beta Agonist
LAMA	Long Acting Muscarinic Antagonist
LMS	Lund-Mackay Score
LTRA	Leukotriene Receptor Antagonist
MCID	Minimal Clinically Important Difference
NPS	Endoscopic Nasal Polyp Score
OCS	Oral Corticosteroids
SANI	Severe Asthma Network in Italy
SEA	Severe Eosinophilic Asthma
SNOT-22	Sino-Nasal Outcome Test on 22 items
Th2	T helper 2 Lymphocytes
VAS	Visual Analogue Scale for nasal symptoms
VEGF	Vascular Endothelial Growth Factor

patients have been reported to have CRSwNP [5]. In Italy, according to data collected by Severe Asthma Network in Italy (SANI), CRSwNP is reported in 42% of the severe asthmatic population [6]. The presence of both manifestations relates with higher disease burden and worse quality of life. Notably, comorbid CRSwNP has a negative impact on asthma control, exacerbation frequency, lung function, and use of OCS [7], as well as asthma severity correlates with the degree of nasal obstruction, hyposmia, and sinus CT scan alterations [8].

Many authors report a strong immunological link between CRS and asthma, with local inflammation of nasal mucosa and paranasal sinus correlating with lung inflammation. In this context, a central role of T2-high inflammation is described with eosinophils become active players in disease pathogenesis [9,10,11]. Indeed, within the Western population, the majority of CRSwNP cases are eosinophil-dominant and, in turn, the eosinophilic phenotype has been related to a more severe and debilitating disease when compared with non-eosinophilic CRSwNP [12, 13]. Moreover, endotypes of CRSwNP and severe asthma are often analogous, with a great percentage of both diseases frequently sustained by an inflammatory response consisting in eosinophilic infiltration induced by a cytokine released from both T helper 2 lymphocytes (Th2) and Type 2 innate lymphoid cells (ILC2) [14]. Eosinophils, under different stimuli, are able to accumulate both in bronchi and sinonasal mucosae and to sustain flogistic processes by releasing inflammatory mediators responsible for features and clinical consequences of the chronic persistent inflammation. Once enrolled and activated, eosinophils are active effectors and promoters of innate and adaptive immune responses able to induce tissue remodeling and fibrosis, to increase mucus viscosity and stability and to enroll and activate other immune cell like T cell and B cell inducing damage [15]. Given their crucial role, these granulocytes could represent an effective target to treat pathophysiological manifestation of both SEA and CRSwNP. In this inflammatory setting, it has been described that vascular endothelial growth factor (VEGF) is upregulated in the mucosa of patients with CRSwNP, promoting edema and epithelial growth in nasal polyps [16]. Furthermore, IL-5 seems to be able to stimulate VEGF production, thus creating a vicious circle [17]. Given the availability of benralizumab as add on treatment option for severe eosinophilic asthma, this pilot study evaluated its role as suitable treatment option for patients with concomitant SEA and CRSwNP. In particular, this study retrospectively describes the effect of benralizumab on clinical, hematological, cytological and inflammatory parameters in this subgroup of patients.

2. Methods

We evaluated retrospectively 11 patients with severe bronchial eosinophilic asthma and CRSwNP (five males and six females) recruited between march 2019 and january 2019 from the Rhino-allergology clinic of the Otolaryngology department of “Sapienza” University located in Rome, Italy.

Diagnosis of asthma and assessment of its severity was conducted following GINA 2019 guidelines [18]. Patients with a positive self-reported history of CRSwNP underwent nasal endoscopy, nasal scraping and CT imaging of the paranasal sinuses in axial, sagittal and coronal views, as per clinical practice. All patients had previously undergone at least one surgery for the treatment of nasal polyposis by endoscopic sinus surgery.

Patient population was compared at baseline with 10 healthy control free from sinus and bronchial disease.

2.1. Patient population

We included adult patients with severe persistent and eosinophilic asthma characterized by poor symptom control despite high dosages of ICS-LABA combinations and long-acting muscarinic antagonists (LAMA) which present a blood eosinophil count of at least 300 cells/μL at baseline together with two of the known CRSwNP symptoms (nasal obstruction, rhinorrhea, sense of pressure or facial pain, decreased sense of taste or smell) and had a total endoscopic score for nasal polyposis ⩾3.

Following GINA recommendation, Benralizumab 30 mg subcutaneous injections was administered as per clinical practice, every 4 weeks for the first 3 doses and every 8 weeks for following doses as add on treatment to maintenance therapy for up to a year.

2.2. Endpoints and assessment

Endpoints of this study were the variation from baseline (T0) of clinical features and inflammatory biomarkers and 6 months (T1) and 12 months (T2) after benralizumab introduction into therapy.

The following clinical features were captured in this retrospective study:

1) Asthma Control Test (ACT): a validated questionnaire that assesses asthma control [19];
2) Visual analogue scale for nasal symptoms (VAS): a psychometric instrument that subjectively quantifies patients’ symptoms severity in terms of obstruction, rhinorrhea, sneezing, anosmia and headache [20];
3) Sino-nasal outcome test on 22 items (SNOT-22): a validated questionnaire evaluating quality of life in patients suffering from chronic rhinosinusitis with and without nasal polyps [21];
4) Endoscopic Nasal Polyp Score (NPS): a score based on direct observation of nasal polyps by endoscopy which assigns a value from 0 to 3 to each nostril according to polyp size [22];

5) Lund-Mackay Score (LMS): evaluation of the opacification of paranasal sinuses (frontal sinus, anterior ethmoidal cells, posterior ethmoidal cells, maxillary sinus and sphenoid sinus) and the obstruction of the ostio-meatali complex with a score from 0 (absence) to 2 (complete opacification) for each site [23].

The following inflammatory biomarkers were evaluated:

1) Blood eosinophil count (BEC);
2) Eosinophil cationic protein (ECP);
3) Interferon-gamma (IFNγ);
4) VEGF;
5) Interleukin-17 (Il-17).

2.3. Nasal sampling and inflammatory biomarker evaluation

Nasal mucosa scraping was performed using a probe (Nasal scraping®, EP Medica, Fusignano (RA), Italy) at T0, T1 and T2, after patients were advised to discontinue topical corticosteroid/antihistamine therapy 14 days prior to collection. The technique led to draw superficial states of the mucous membrane of the middle turbinate in anterior rhinoscopy or under endoscopic guidance to perform nasal cytology useful to define the cellularity expressed in the nasal mucosa [24]. In our study, part of the scraped material was frozen at −80 °C to titrate ECP, IFN-γ, IL-17 and VEGF levels.

Biological samples collected were subjected to freeze-thaw in liquid nitrogen, sonicated and subsequently centrifuged at 10,000 g for 10 min to remove tissue residues. Protein concentration was evaluated by Lowry's method [25]. All lysates were boiled for 3 min in presence of glycerol, bromophenol blue and beta-mercapto-ethanol before subsequent Western blot analysis. All samples were normalized for protein load using actin, which served as protein loading control. The values were obtained from the ratio of arbitrary units derived from the protein band and the respective actin band. Samples were used to analyze expression of ECP, IFN-γ, IL-17 and vascular endothelial growth factor (VEGF). The baseline values of these markers were compared to healthy individuals at baseline.

All patients gave their informed consent to study participation and data processing. All study procedures were performed in accordance with the ethical standards of institutional and/or national research committees and with the 1964 Helsinki Declaration and its subsequent amendments.

2.4. Statistical analysis

Data are reported as median (range). Statistical analysis was performed using the Friedman test for the repeated variables of the group affected by nasal polyposis and severe asthma. Post-hoc comparisons were performed with Bonferroni correction by comparing the values at times T0, T1 and T2. Comparison of baseline values for ECP, IFN-γ, IL-17 and VEGF between patients receiving benralizumab and the control group was performed with the Mann-Whitney U test. Statistical analysis was performed with Statsoft. $P < 0.05$ was considered statistically significant.

3. Results

Patient population consisted in 11 subjects (6 females and 5 males) aged from 32 to 75 years (mean age 60.9 years) with SEA and concomitant CRSwNP and 10 healthy control (5 females, 5 males) aged between 35 and 73 years (mean age = 59.7 years) free from rhinosinusal and respiratory diseases. Of the 11 treated patients, 6 had one or more SPT positivity for perennial allergens (4 for Dermatophagoides Pteronyssinus and 4 for Alternaria) and/or seasonal allergens (2 Graminaceae mix). All patients had sinonasal disease in their clinical history with at least one endoscopic sinus surgery procedure for nasal polyp removal and they were under INCS treatment. We ascertained diagnosis by nasal endoscopy and CT imaging of the paranasal sinuses finding all patients with a NPS⩾3 at baseline.

Patients were receiving high dose ICS/LABA combination and/or other controller medication as LTRA, LAMA and/or systemic corticosteroids and, as per clinical practice, we confirmed diagnosis of severe eosinophilic asthma reassessing respiratory functions and following GINA 2019 criteria [18]. At time of clinical evaluation, all treated subjects had blood eosinophils values greater than 0.3×10^3 cells/μL as requested for benralizumab prescribing plan according to Italian Drug Agency indications.

Patients baseline characteristics are showed in Table 1 and are reported in median (IQR).

Table 2a and 2b resume the clinical and inflammatory outcomes, respectively before (T0) and after (T1 and T2) benralizumab introduction.

A statistically significant improvement of ACT was found, from a baseline median of 10 (5–15) to 23 (19–25) at T1, further maintained at T2. Concomitantly, total VAS showed an improvement at T1, confirmed at T2 when compared to T0, diminishing by a median of 15 points from baseline. Obstruction, sneezing and rhinorrhea were the most improved features of the VAS score.

Treatment with benralizumab was associated with improvement of quality of life, as highlighted by SNOT-22 value which decreased from 45 (23–97) to 17 (7–56) ($p < 0.05$) after 6 months and to 14 (5–53) after 12 months, exceeding the 8.9 point MCID threshold [21].

Nasal objective measurement highlighted significant reduction in total Nasal Polyp Score, intended both as individual score of nasal cavities and sum of the two nasal cavities, after 6 months ($p < 0.05$) and after 1 year of treatment ($p < 0.05$). Analogous results were recorded in total radiological score, one year after the initiation of benralizumab therapy: the significant improvement ($p < 0.01$) on CT imaging indicated reduction in polypoid formations and in the related inflammatory condition (Fig. 1 and Fig. 2). Better improvements have been recorded at osteo meatal complex ($p < 0.01$), in anterior ethmoid ($p < 0.01$) and in the maxillary sinus ($p = 0.01$) level. (Table 2a)

Such remarkable clinical amelioration occurred along with a statistically significant depletion in peripheral blood eosinophils ($p < 0.01$).

Table 1
Baseline characteristics of the patient population. Data are presented as median (range/IQR) or in number of patients.

Table 1. Baseline characteristics

History [median (range)]	Treatment group	Control group
Mean Age y	60,9 (32–75)	59,7 (35–73)
Gender (Female/Male)	6/5	5/5
BMI	24,7 (22–31)	23,5 (22–29)
Duration of asthma (years)	14 (10–30)	na
Duration of CRSwNP (years)	10 (6–15)	na
Polyp surgeries (number)	2 (1–4)	na
OCS courses during the last 12 months	3 (2–4)	na
Clinical assessments [median (IQR)]		
SNOT-22	45 (23–97)	na
ACT score	10 (5–15)	na
VAS score	30 (17–44)	na
NPS	5 (3–6)	na
CT Lund-Mackay	21 (15–24)	na
Anosmia (yes/no)	11/0	na
Atopy (yes/no)	6/5	na
Laboratory assessments [median (IQR)]		
Eosinophils (x10^3 cell/μL)	0.51 (0.45–1.5)	na
Neutrophils (x10^3 cell/μL)	3.21 (2.07–4.53)	na
Lymphocytes (x10^3 cell/μL)	1.61 (1.46–2.07)	na
IgE, Total serum [kU/L]	183 (24–1335)	na
Nasal scraping (a.u.) [median (IQR)]		
ECP	1.34 (0.52–3.84)	1.11 (0.56–1.29)
INF-γ	0.14 (0.04–0.7)	0.91 (0.52–1.86)
IL-17	1.09 (0.29–1.62)	1.01 (0.5–1.49)
VEGF	2.54 (0.68–6.43)	0.88 (0.42–1.69)

Table 2a
SNOT-22, total and per symptoms VAS, ACT, total and per cavity VAS, total and per area LMS. Value are expressed in median (range). *p<0,05; **$p \leq$ 0,01; °p>0,05.

Table 2a. Clinical and radiological scores at baseline and after 6 and 12 months

	Baseline	6 months	12 months
SNOT-22	45 (23–97)	17 (7–56) *	14 (5–53) *
VAS Total	30 (17–44)	15 (6–49) *	15 (6–49) *
Obstruction	7 (4–10)	3 (0–10)*	3 (0–10)*
Rhinorrea	8 (4–10)	3 (0–10)*	3 (0–10)*
Sneezing	4 (0–10)	2 (0–9)*	2 (0–9)*
Anosmia	8 (6–10)	7 (0–10)°	7 (0–10)°
Headache	1 (0–8)	1 (0–10)°	1 (0–10)°
ACT	10 (5–15)	23 (19–25)*	23 (19–25)*
NPS Total	5 (3–6)	3 (2–4)*	2 (2–3)*
Right nasal cavity	2 (1–3)	2 (1–2)	1 (1–2)
Left nasal cavity	2 (2–3)	1 (1–2)	1 (1–1)
Lund-Mackay Score Total	21 (15–24)	Nd	17 (8–21) **
Mascellar	3 (2–4)	Nd	2 (1–4)**
Sfenoid	3 (1–4)	Nd	3 (2–3)*
Antherior Ethmoid	4 (4–4)	Nd	3 (2–4)**
Posterior Ethmoid	4 (3–4)	Nd	3 (0–4)*
Frontal	3 (2–4)	Nd	3 (2–4)°
OsteoMeatal Complex	4 (2–4)	Nd	2 (0–2)**

Table 2b
Hematological and Scraping results. Value are expressed in median (range). *p < 0,05; **$p \leq$ 0,01; °p > 0,05.

Table 2b. Hematological and Scraping results at baseline and after 6 and 12 months

	Baseline	6 months	12 months
Eosinophils (x10^3 cell/μL)	0.51 (0.45–1.5)	0.01 (0.01–0.1)**	0**
Neutrophils (x10^3 cell/μL)	3.21 (2.07–4.53)	2.99 (2.2–4.23)°	3.23 (2.19–4.83)°
Lymphocites (x10^3 cell/μL)	1.61 (1.46–2.07)	1.64 (1.14–2.3)°	1.45 (1.07–2.19)°
ECP (a.u.)			
Treatment Group	1,34 (0,52–3,84)	0,57 (0,14–0,93)*	0,72 (0,32–1,12)*
Control Group	1,11 (0,56–1,29)°		
IFNγ (a.u.)			
Treatment Group	0,14 (0,04–0,7)	0,32 (0,14–1,47)*	0,29 (0,08–0,89)°
Control Group	0,91 (0,52–1,86)**		
IL-17 (a.u.)			
Treatment Group	1,09 (0,29–1,62)	0,54 (0,2–1,01)*	0,86 (0,29–1,09)°
Control Group	1,01 (0,5–1,49)°		
VEGF (a.u.)			
Treatment Group	2,54 (0,68–6,43)	0,54 (0,28–1,43)*	1,35 (0,26–2,02)*
Control Group	0,88 (0,42–1,69)*		

At nasal mucosal scraping, baseline values of ECP, INF-γ, IL-17 and VEGF were found significantly higher in severe asthma patients compared to healthy subjects (Table 1). Inflammatory biomarkers levels are shown in Table 2b and Fig. 3. In treated patients, ECP values significantly decreased after 6 months ($p < 0.05$) and lower values were maintained after 12 months of treatment. Non-significant variations of INF-γ and IL-17 were detected after 12 months of treatment. VEGF expression underwent significant reductions after 6 and 12 months of treatment ($p < 0.05$), reaching values similar to healthy control group (Table 2b). Benralizumab was well tolerated with no safety issues reported during the year of treatment.

4. Discussion

Our real-life study confirms the substantial effectiveness of benralizumab in patients with SEA and showed efficacy in comorbid severe CRSwNP. Indeed, the control of asthma was obtained within the first 6 months of therapy together with an amelioration of CRSwNP measured by endoscopy, CT-scan and patient reported outcomes (PROs).

Post-hoc analyses of pivotal studies demonstrated that the presence of nasal polyps represents the best predictor of enhanced response of asthma outcomes to benralizumab [26,27,28]. For this reason, further clinical trials (ANDHI-NP, 28) and real-life experiences [27,29,30] have been published into literature. The ANDHI trial confirmed the efficacy and safety of benralizumab in SEA patients, with a special focus on quality of life. A sub-study on 153 patients presenting a positive medical history of nasal polyposis, demonstrated a significant reduction of SNOT-22 and confirmed the enhanced efficacy of benralizumab in this subgroup of patients (28). In real-life, Bagnasco et al. [28] and Menzella et al. [30] were able to demonstrate the efficacy of benralizumab in reducing the exacerbations rates, OCS use while improving lung function, supporting the enhanced response of CRSwNP positive patients. Lombardo et al. [31] for the first time demonstrated in real-life that benralizumab is able to improve CRSwNP-related parameters in patients with comorbid SEA and CRSwNP. Indeed, in a small cohort of 10 patients they were able to demonstrate a significant reduction of NPS, LMS and SNOT-22 after six months of treatment. Our study confirms the magnitude of improvement reached by benralizumab in this subgroup of patients. In particular, SNOT-22 improved of 28 points, thus exceeding the 8.9 points determining the MCID for this score [21]. VAS improved as well, with a reduction of the 50% from baseline, and a well-distributed improvement of all the VAS-related items. ACT improvement clearly had an impact on the SNOT-22 scores confirming the theory of "united airways disease" according to which inflammation of the upper and lower airways cannot be understood as two different diseases separated from each other, but as a pathophysiological unicum that requires a complex and multidisciplinary evaluation involving pulmonologists, immunologists and otolaryngologists [32,33].

The subjective improvement of these scores was accompanied by the objective significant improvement of NPS and the Lund-Mackay score. Our study, differently from Lombardo et al., found a beneficial effect for a longer follow-up period confirming that benralizumab-induced eosinophil depletion resulted an effective strategy to restore several disease parameters of both SEA and CRSwNP. Regarding LMS, CT is the main diagnostic tool in planning surgery after endoscopy that allow to identify the anatomical landmarks and formulate the surgical approach according to the alterations caused by previous surgery [34]. In this study, the reduction in total radiological score was almost 20% in one year, showing the greater effect in the anterior compartments, particularly the osteo meatal complex and the anterior maxillary and ethmoid sinuses Fig. 4.

Regarding inflammatory biomarkers, this study evaluated the change of ECP, IFN-γ, IL-17 and VEGF levels over time. As previously demonstrated by early studies and pivotal clinical trials [35,36], benralizumab is able to reduce ECP levels, in keeping with its direct action on eosinophils through an Antibody Dependent Cellular Cytotoxicity (ADCC) mechanism [37].

IFN-γ is a well-recognized marker of type 1 inflammation [38], and it has been demonstrated to be reduced in the presence of type 2, eosinophilic inflammation [39]. Our cohort of patients presented lower IFN-γ levels at baseline when compared to the healthy control group. This result is also in line with the altered anti-viral response demonstrated in severe asthmatic patients [40,41,42]. Treatment with benralizumab

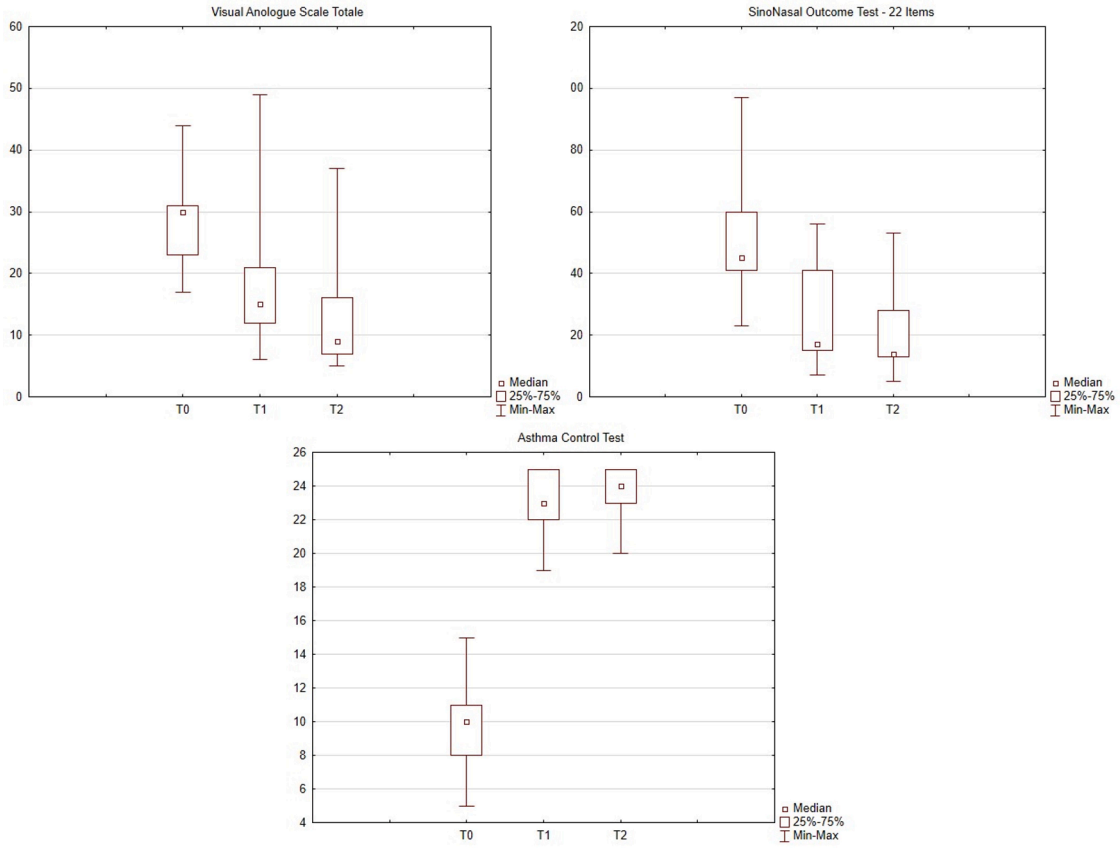

Fig. 1. ACT, SNOT-22, and total VAS at 0, 6 and 12 months.

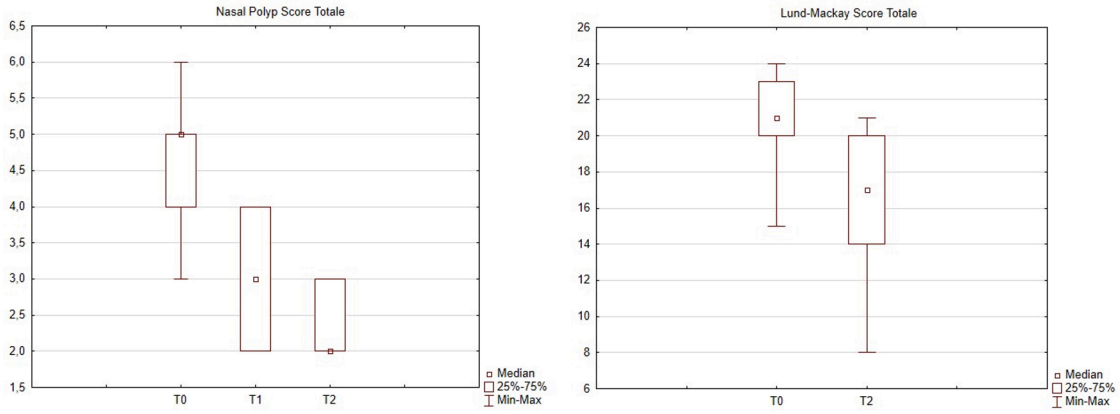

Fig. 2. Total NPS and total LMS at 0, 6 and 12 months.

more than doubled IFN-γ levels after 6 and 12 months of treatment, even if it was not able to restore its levels compared to healthy control. However, it is important to underline how no exacerbation was registered in the 12-month period of retrospective follow-up of these patients.

IL-17 levels, on the contrary, were not different at baseline when compared to healthy controls. This can be related to the fact that CRSwNP is usually eosinophilic in its nature, at least in the Western countries [12]. Moreover, the presence of concomitant SEA in this cohort, reinforces the role of eosinophils as key inflammatory players. Indeed, no measurable alterations of IL-17 were expected after the introduction of benralizumab in this study.

Our report confirms that VEGF is upregulated in the nasal mucosa of patients with SEA and CRSwNP compared to healthy controls, and that the administration of benralizumab is able to restore physiological VEGF levels as soon as after six months of treatment. Other reports demonstrated that VEGF levels are proportionally increased in the respiratory mucosa of asthmatic patients based on their severity [43] and that IL-5 stimulates eosinophils to release VEGF, which in turn acts as an eotaxin able to mediate the release of ECP [17]. Moreover, basophils are responsive to IL-5, and VEGF has been found in granules of basophils infiltrating the nasal mucosa [44]. As benralizumab is able to deplete at least the 70% of the circulating basophils [45], we can thus speculate the enhanced ability of benralizumab in reducing this inflammatory marker when compared to our previous report involving the use of mepolizumab in a similar cohort of SEA and CRSwNP patients [46].

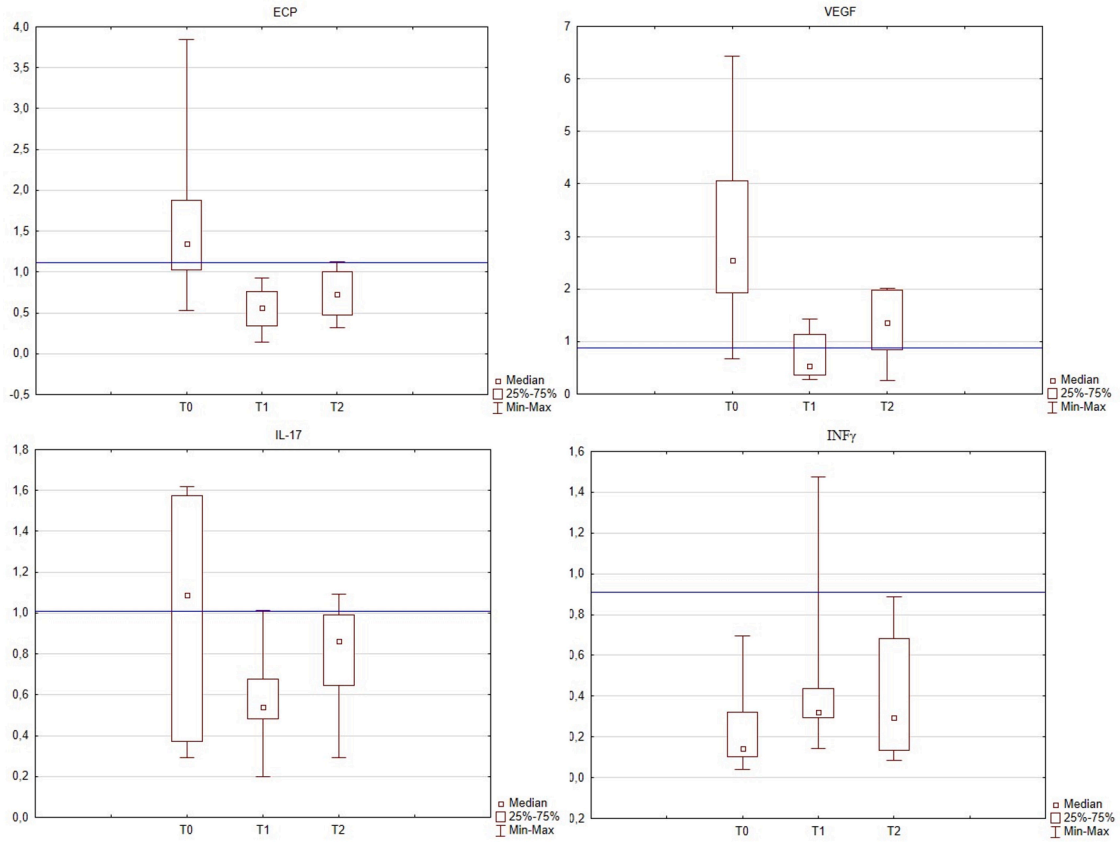

Fig. 3. ECP, VEGF, IL-17 and INF-γ at 0, 6 and 12 months. The horizontal line identifies the marker reference value of the control group.

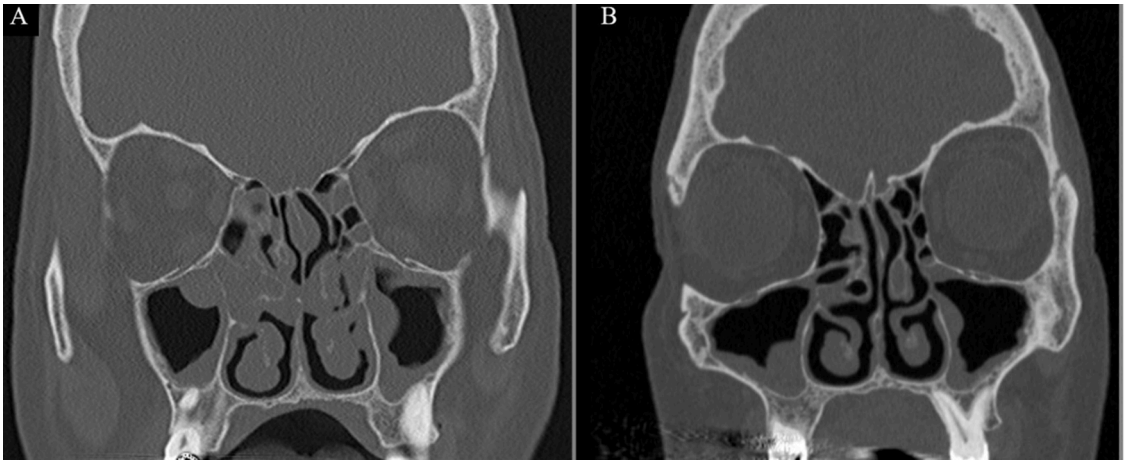

Fig. 4. Coronal CT scan of a patients at T0 (A) and T2 (B) showing a marked improvement in the maxillary sinuses, anterior ethmoid and nasal cavities at T2 compared to T0.

Markers taken through nasal scraping allowed to identify a well-defined population affected by eosinophilic CRSwNP with clinical-anamnestic hallmark of Type 2 inflammation. We can assume that ECP, IFN-γ, and VEGF could be considered potential markers for therapeutic efficacy because of their variation during treatment in patients who showed improvement in symptoms and in endoscopic and radiological outcomes. It is noteworthy to consider that all these positive results were observed along with a complete reduction in circulating eosinophils, reinforcing that granulocytes depletion led to pronounced clinical effects.

As previously mentioned, the major limitation of our study is the small sample of patients examined, even though this issue did not prevent to highlight clinically significant changes in all the measured parameters, supporting our initial hypothesis that benralizumab is an effective strategy for severe CRSwNP in SEA patients.

5. Conclusions

This is the first pilot real-life study with benralizumab in SEA and CRSwNP patients showing that patients suffering from nasal polyposis can benefit from the action of the anti-IL-5Rα monoclonal antibody non only from the clinical, but also from the inflammatory point of view.

Clinically relevant effects were obtained on disease control, symptomatology and quality of life together with reduction in polyp size and inflammation of the sinuses. Scraping from the nasal mucosa found differences in the expression of INF-γ and VEGF in patients compared to healthy subjects, with a normalization of these markers in treated patients after benralizumab therapy. Prospective studies evaluating the role of VEGF in CRSwNP pathophysiology and as a predictor of monoclonal antibodies efficacy in CRSwNP are warranted.

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Declaration of Competing Interest

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