Effect of biological treatment in uncontrolled severe chronic rhinosinusitis with nasal polyps in Belgium: a multicentre real-world data study

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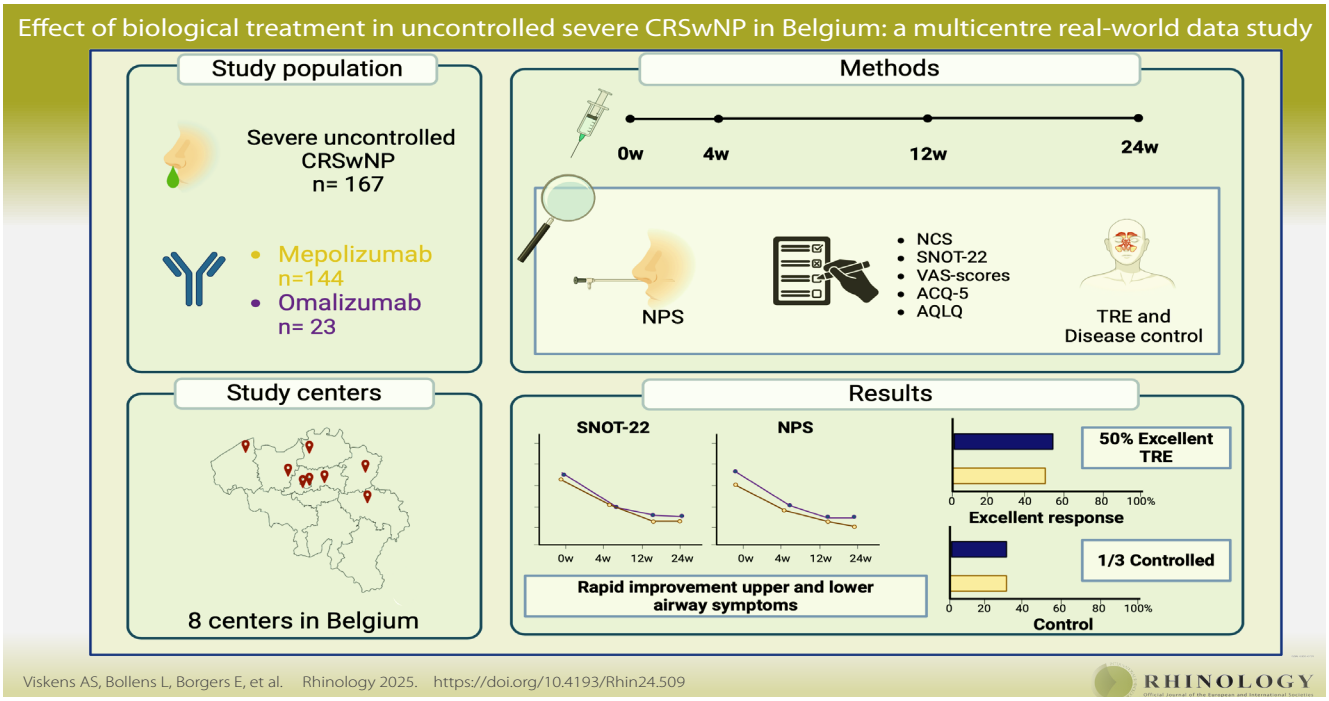

Abstract

Background: Double-blinded placebo-controlled trials have revealed the efficacy of mepolizumab and omalizumab in the treatment of chronic rhinosinusitis with nasal polyps (CRSwNP). However, real-world efficacy (RWE) data, data on therapeutic response and level of disease control for both biologicals are lacking. **Methodology**: 167 patients with uncontrolled severe CRSwNP, meeting national reimbursement criteria, were included with follow-up over 24 weeks. Primary outcomes included changes in nasal congestion (NCS), nasal polyp score (NPS), VAS-scores, SNOT-22, ACQ-5, and AQLQ scores. Secondary outcomes were therapeutic response and disease control according to EUFOREA/EPOS criteria. **Results**: Of the 167 CRSwNP patients, 144 received mepolizumab and 23 omalizumab. After 24 weeks, Patient reported outcomes and NPS significantly improved for both biologicals, with significant effects seen at 12 weeks, with further reduction in NPS by 24 weeks in mepolizumab patients. 74% of patients on omalizumab and 81% of patients on mepolizumab continued their therapy beyond 24 weeks, with 47% and 45% of patients on omalizumab and mepolizumab respectively showing an excellent therapeutic response, with only one out of seven having no/poor response. Disease control was reached in one third of the patients at 24 weeks. **Conclusions**: Both mepolizumab and omalizumab significantly improved patient-reported outcomes after 24-weeks, with major effects already observed at 12 weeks. Follow-up beyond 24-weeks might reveal additional effects on both control and remission.

Key words: chronic rhinosinusitis, nasal polyps, biological treatment, type 2 inflammation

Introduction

The availability of biologicals for severe uncontrolled chronic rhinosinusitis with nasal polyps (CRSwNP) has revolutionised the therapeutic landscape of nasal polyp patients, with biologicals being included in the latest international guidelines for patients with CRSwNP [1-4]. Omalizumab, mepolizumab and dupilumab are registered and reimbursed for the indication of severe uncontrolled CRSwNP in several countries worldwide [5,6]. The efficacy and safety of these biologicals have been demonstrated in large phase III double blinded placebo controlled randomized trials (DBRCT) and several indirect comparison studies have tried to compare the efficacy of those different biologicals [7-13]. However, due to the heterogenicity of the inclusion criteria and treatment outcomes in the different trials, a true comparison is impossible, highlighting the need for head-to-head comparison trials and real-world efficacy (RWE) registries. To date, RWE registries have mainly studied dupilumab in Italy [14], the Netherlands [15], Canada [16] and Germany [17]. Only limited, mostly retrospective, data are available on mepolizumab and omalizumab [18,19]. As these two biologicals were the first to be approved and reimbursed in Belgium [20], a multicentre RWE study was initiated across eight rhinology centres in Belgium. The study focused on the RWE of both biologicals in the first wave of patients with uncontrolled CRSwNP, treated for six months with biological therapy for uncontrolled CRSwNP, that met the national reimbursement criteria. In addition to studying the RWE of these biologicals, this study also addresses the impact of biological therapies on the recently updated definition of control in CRSwNP by EUFOREA/EPOS, defined as an absence of clinically relevant sinonasal symptoms of active disease [21]. As biologicals are thought to possibly have a disease-modifying potential [22], understanding their effect on long-term disease control without sings of active disease, also defined as remission [21], is of strategic importance for both patients as well as physicians.

Materials and methods

Patient population

This RWE study was coordinated by A.S.V. and P.H. at UZ Leuven, Belgium, and was performed in 8 national centres, 5 University hospitals (Leuven, Antwerp, Brussels, Liège and Saint-Luc) and 3 non-academic rhinology centres (Aalst, Genk and Bruges). The study was evaluated and approved by the medical ethical committee of the University Hospital of Leuven (S66646). Patients that fulfilled both clinical- and reimbursement criteria (Figure 1) for mepolizumab or omalizumab were included in the trial and followed up prospectively. Patients were excluded if they received another biological treatment for CRSwNP within the 3 months before the start of the study.

Baseline characteristics

General patient characteristics including age, gender, year of diagnosis of CRSwNP, comorbidities and general health were collected. Patients were asked about their comorbidities, which were verified using the patients' medical history in their medical record.

Evaluation of patient reported outcomes (PRO's)

Questionnaires were filled out at the start of treatment and at 4, 12 and 24 weeks of treatment. The questionnaires included questions about the upper airways (Nasal congestion score (NCS), Visual analogue scale (VAS)-score, Sinonasal Outcome test (SNOT) 22-score) and lower airways (asthma control questionnaire (ACQ- 5) and asthma quality of life questionnaire (AQLQ)).

Evaluation of nasal polyp score (NPS)

The nasal polyp size was scored via the NPS, ranging from 0 (no polyp) to 4 (nasal polyps reaching the bottom of the nasal cavity) on each side using nasal endoscopy, as reported before [23].

Evaluation of therapeutic response (TRE) and disease state

The therapeutic response to a biological was measured using the following 5 criteria in accordance with the EUFOREA/EPOS criteria [21]: 1) reduction in NPS, 2) reduced need for OCS/salvage surgery, 3) improved sense of smell, 4) improved quality of life and 5) reduction of the impact of comorbidities. A good-excellent response was defined as meeting 4 to 5 criteria, a moderate response 2 to 3 criteria and no/poor response 0 to 1 criteria. The level of control was measured according to the EUFOREA/EPOS criteria for assessment of control in CRSwNP patients at baseline and 3, 12 and 24 weeks after the start of biological therapy. Patients with a VAS-score of ≤ 5 cm for overall sinonasal symptom severity were defined as controlled. The overall symptom severity was based on the individual VAS-scores for nasal blockage, rhinorrea, anosmia, post-nasal drip, facial pain and headache [21].

Evaluation of adverse events and treatment adherence

At each outpatient visit, patients were asked whether they experienced any adverse events (AE), whether they were prescribed antibiotics and/or oral corticosteroids or whether they underwent a revision ESS. In addition, patients were checked for adherence to the treatment scheme with biologicals, with nasal corticosteroid and nasal irrigations as standard of care.

Data analysis

Statistical analyses were performed with GraphPad Prism VI for Macintosh Version 8.4.3 (GraphPad Software Inc., San Diego, CA, USA). Differences in baseline characteristics between the two biologicals were calculated using Fisher's exact test for categorical variables and unpaired t-test for continuous variables. Differences between nasal polyp score and the different PRO's at different timepoints were calculated using mixed effect analysis

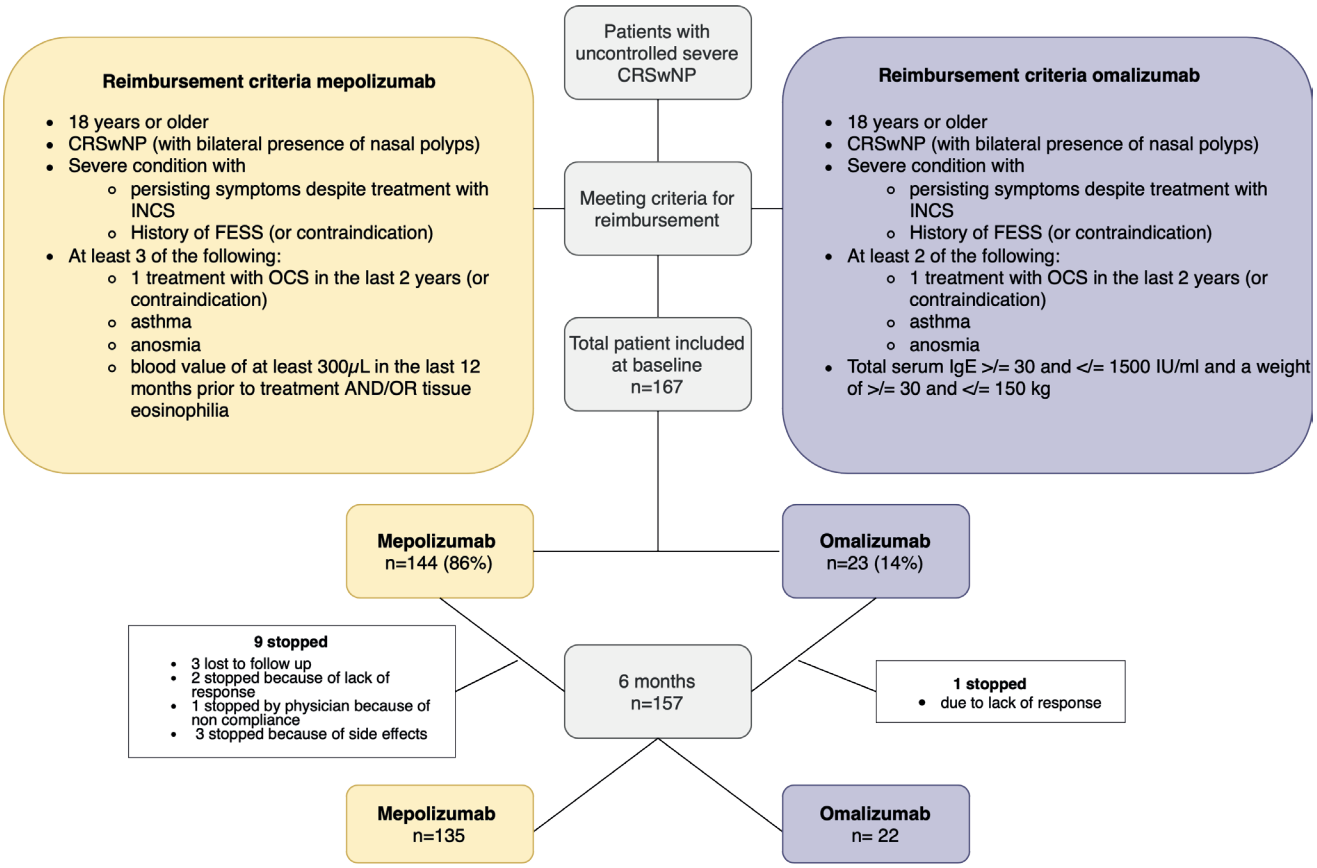

Figure 1. Flowchart of patients included in RELIBIO-trial.

with Tukey's multiple comparisons test. Differences between the VAS-scores at 24 weeks and baseline were calculated using paired T-test or Wilcoxon signed rank test depending on normality. Values will be considered statistically significant if $p < 0.05$.

Results

Baseline characteristics

167 CRSwNP patients were included at baseline of which, 144 (86 %) were treated with mepolizumab and 23 (14 %) with omalizumab, on top of nasal rinses and nasal corticosteroid therapy (Figure 1). The mean age was 53 years in both groups. There were almost 10% more males than females in our cohort, an average disease duration of more than 10 years, and the majority of patients had undergone one or two ESS in the past. All of the patients on omalizumab had comorbid asthma compared to 75 % of patients on mepolizumab. This difference can be attributed to the reimbursement criteria for omalizumab in Belgium in 2022 and 2023 with comorbid asthma being a criterium, which changed in November 2023. Patients in the mepolizumab group had a significant higher blood eosinophil count compared to the omalizumab group. Other parameters are listed in Table1.

Evaluation of main clinical parameters

A significant difference was seen between baseline and 24 weeks of treatment for both biologicals on all main clinical parameters: NPS, SNOT-22, loss of smell and NCS.

The mean NPS at baseline was 4.1 (CI 4.4-3.8) for mepolizumab and 4.5 (CI 5.4-3.8) for omalizumab and dropped with a mean difference of 1.3 (CI -1.7 to -0.97) and 2.2 (CI -3.6 to -1.0) points, respectively (Figure 2A). The mean SNOT-22 score at baseline was 44.8 (CI 48.0-41.5) and 51.0 (CI 61.4-40.7) and dropped with a mean of -17.2 (CI -21.1 to -13.3) and -18.9 (CI -28.6 to -9.2) for mepolizumab and omalizumab, respectively (Figure 2B). The nasal congestion score dropped from 2 (IQR 3-1) at baseline to 1 (IQR 2-0) at 4 weeks, and remain stable around this level throughout the trial, representing only mild symptoms (Figure 2C). Moreover, there was a significant reduction in VAS-scores for anosmia between baseline and 24 weeks with a mean reduction of -27 (CI -36 to -18) mm for mepolizumab and -32 (CI -57 to -7) mm for omalizumab. Although, the mean VAS-score for anosmia at 24 weeks remained high at 55 (CI 62-47) for mepolizumab and 51 (CI 71-31) for omalizumab (Figure 2D). Between 12 and 24 weeks, the NPS decreased significantly further in the mepolizumab but not in the omalizumab group. This reduction was not seen for SNOT-22, NCS and smell impairment scores (Figure 2A-D).

Looking at the VAS-scores for the different sinonasal symptoms, the largest reduction in VAS-scores was for smell impairment,

Table 1. Baseline characteristics.

Baseline characteristics			
Patient's included	Total n=167 (100%)	Mepolizumab n=144 (86%)	Omalizumab n=23 (14%)
Age (mean ±SD)	53y (± 13 y)	53y (± 13y)	53y (± 14y)
Gender n (%)			
Male	97 (58%)	84 (58%)	13 (57%)
Female	70 (42%)	60 (42%)	10 (43%)
Smoker n (%)			
No	102 (65%)	89 (66%)	13 (59%)
Yes	11 (7%)	10 (7%)	1 (5%)
Ex-smoker	45 (28%)	37 (27%)	8 (36%)
Years with disease n (%)			
<5 Years	35 (25%)	29 (24%)	6 (30%)
5-10 Years	33 (23%)	30 (25%)	3 (15%)
>10 Years	74 (52%)	63 (52%)	11 (55%)
Comorbidities n (%)			
Asthma*	131(78%)	108 (75%)	23 (100%)
Aspirin intolerance (based on history)	44 (28%)	38 (27%)	6 (30%)
Airborne allergies	98 (59%)	85(59%)	13 (57%)
Number of sinus surgeries n (%)			
0	1 (1%)	1 (1%)	0 (0%)
1	68 (43%)	63 (46%)	5 (23%)
2	51 (32%)	41 (30%)	10 (45%)
>2	40 (24%)	33 (23%)	7 (32%)
Structural nasal pathology n (%)			
Septal deviation, valve pathology, septal perforation	17 (10%)	17 (12%)	0 (0%)
Biomarkers (mean ±SD)			
Total IgE (KU/L)	256.3 ± 394.9	263.8 ± 422.3	216.3 ± 196.5
Eosinophils (*10^9/L)*	0.5± 0.3	0.5 ± 0.3	0.3 ± 0.2

Significant difference ($p<0.05$) indicated with *, significance was calculated using Fisher's exact test for categorical variables and unpaired t-test for continuous variables.

as reported above. Other important symptoms were nasal blockage and postnasal drip. The nasal blockage VAS-scores reduced with a mean of -23 (CI -30 to -16) mm for mepolizumab and -19 (CI -35 to -2) mm for omalizumab. For postnasal drip the VAS-scores reduced with a mean of -21 (CI -28 to -15) mm for mepolizumab and -19 (CI -35 to -3.0) mm for omalizumab. Other symptoms such as headache and facial pain were already scored quite low at baseline, with VAS-score for headaches only significantly improving in mepolizumab with -12(CI -17 to -6) mm and VAS-score for facial pain in omalizumab -20 (CI -35 to -5.5) mm (Table 2).

Evaluation of lower airway symptoms

This study also evaluated the effects of the biologicals on lower airway symptoms in CRSwNP, since 80% of our patient cohort had comorbid asthma. A significant effect was observed on patient reported control of asthma as measured with the ACQ-5 score (Figure 3A). Most of our patients suffered from an uncontrolled asthma at baseline with a mean ACQ-5 score of 1.8 (CI 2.0-1.5) in the mepolizumab group and 2.3 (CI 3.0-1.7) in the omalizumab group. Under biotherapy, the ACQ-5 score generally improved to partially controlled asthma at 24 weeks, with a mean improvement of -0.8 (CI -1.1 to -0.5) for mepolizumab and -1.1 (CI 2.0 to -0.3) for omalizumab. (Figure 3A) Looking at the quality of life, measured with the AQLQ score, a significant improvement for mepolizumab at 24 weeks with a mean improvement of 0.5 (CI 0,3 to 0,8) was seen (Figure 3B). A significant improvement for both biologicals was seen on the wheezing VAS-score, with a mean reduction of -11 (CI -17 to -6) mm for mepolizumab and -15 (CI -27 to-3) mm for omalizumab (Table 2).

Therapeutic response evaluation (TRE) and disease state at 24 weeks

At 24 weeks, the prolongation of the treatment is decided based on the TRE on the one hand and the national reimbursement criteria on the other hand. In 81% of patients on mepolizumab and 74% on omalizumab the treatment was continued beyond 24 weeks (Figure 4A). 45% of patients on mepolizumab and 47% of patient on omalizumab had an excellent TRE according to the

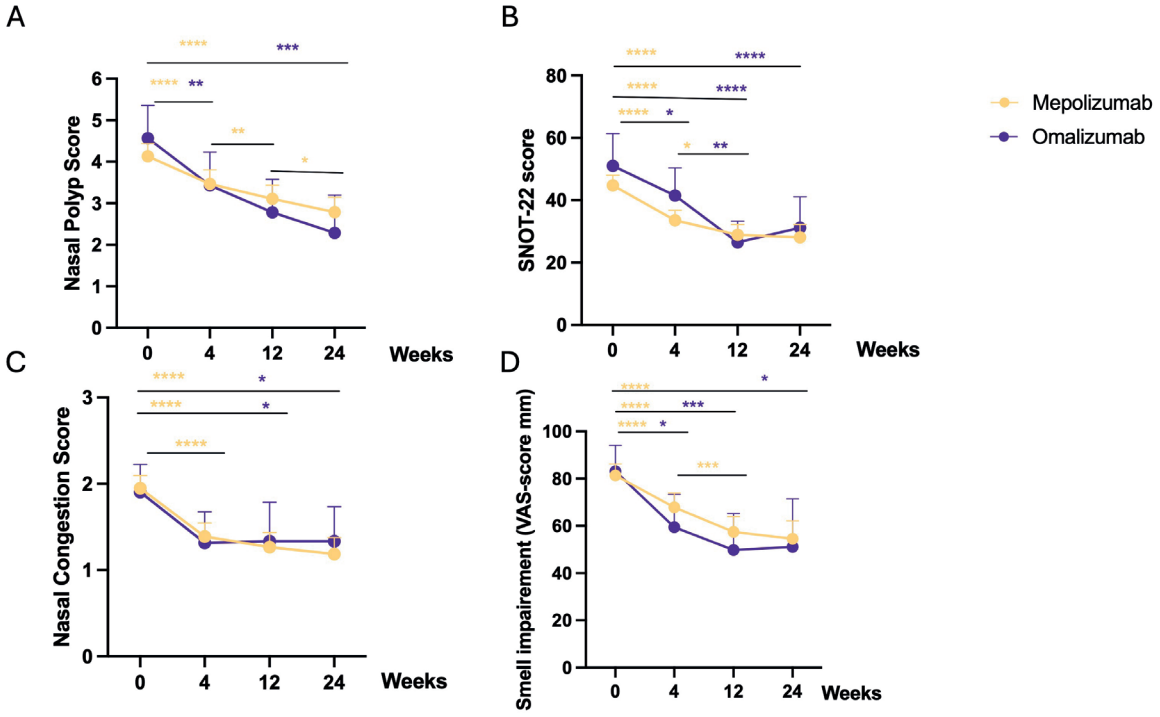

Figure 2. Changes in upper airway parameters with biological treatment over time. Data are shown as mean ± 95% CI, significance calculated using mixed effect analysis with Tukey's multiple comparisons test, ****: P<0.0001, ***:P <0.001, **P < 0.01, *: P < 0.05. (A) Change in Total NPS (range, 0-8). $n_{mepolizumab}$=142; $n_{omalizumab}$=23. (B) Change in SNOT-22 (range, 0-110). $n_{mepolizumab}$= 131; $n_{omalizumab}$ =21. (C) Change in NCS (range, 0-3). $n_{mepolizumab}$ =118; $n_{omalizumab}$=21. (D) Change in anosmia VAS-score (range, 0-100). $n_{mepolizumab}$=128 $n_{omalizumab}$=23.

EUFOREA/EPOS criteria with only 14% of mepolizumab and 12% of omalizumab patients having no/poor response to a biological (Figure 4B). Although almost 50% of patients had an excellent response to their biological at 24 weeks, control was only reached in 34% of mepolizumab and 35% of omalizumab patients (Figure 4D). Amongst those with an excellent TRE, 65% on mepolizumab and 75% on omalizumab met the criteria of being controlled (Figure 4C). In the patient cohort that continued their biological therapy, control was reached in 41% and 46% of patients on mepolizumab and omalizumab, respectively. Lastly, In the group that stopped their biological the main reason was lack of response, only three patients stopped because of side effects (shingles and/or musculoskeletal pain) and one patient was stopped by the physician because of a lack of compliance (Figure 1). 50 % of patients who stopped omalizumab and 36% of patients who mepolizumab were switched to another biological.

Treatment adherence and safety

No severe adverse events were reported during the initiation and course of the biological therapy. Most patients self-administered their injections at home after two or three injections in the clinic under medical supervision. Self-reported treatment adherence was good with only 5% of patients reporting to have missed an injection, primarily due to external factors such as limited availability of the biological at the pharmacy or expiration of reimbursement coverage before all syringes could be obtained. As mentioned before, only three patients stopped their treatment early because of side effects (Figure 1).

Discussion

This registry in eight rhinology centres in Belgium includes 167 patients with severe CRSwNP and reports on the RWE of omalizumab and mepolizumab in patients with CRSwNP meeting national reimbursement criteria. This RWE study confirms the efficacy of both biologicals, as reported in DBRCT, with a significant improvement on all primary outcome parameters at 12 and 24 weeks of therapy. Disease control was achieved in one third of patients in both groups at 24 weeks.

When comparing these Belgian real-world data with the reported DBRCT trials [7,9,10,12] several observations can be made. Firstly, the baseline SNOT-22 score, and the mean improvement observed in our study (-17.2 to -18.9) were comparable to the average reduction reported in both DBRCT of omalizumab and mepolizumab (-9.40 to -16.2), indicating comparable efficacy in reducing disease burden [12].

NCS reduction in this trial at 24 weeks was similar to the one reported in the omalizumab phase III trials [7], as was the case with VAS-scores for loss of smell, with the reductions observed here

Table 2. Analysis of VAS-scores.

VAS scores (mm)	Mepolizumab (n=94)			Omalizumab (n=16)		
	Baseline (Mean ± SD)	6 months (Mean ± SD)	Treatment difference (95% CI of diff; p value)	Baseline (Mean ± SD)	6 months (Mean ± SD)	Treatment difference (95% CI of diff; p value)
Anosmia	83 (±28)	57 (±38)	-26(-34 to -18; p<0001)*	79(±28)	54(± 39)	-24(-44 to -5; p=0.01)*
Nasal blockage	52 (± 30)	29(±29)	-23(-30 to -16; p<0.0001)*	56(±29)	37(±31)	-19(-35 to -2; p <0.05)*
Postnasal drip	52(±30)	31(±30)	-21(-28 to -15; p<0.0001)*	57(±26)	38(±23)	-19(-35 to -3.0 p<0.05)*
Headache	33(±31)	21(±26)	-12 (-17 to -6; p<0.0001)*	41(±35)	29(±28)	-12 (-25 to 1; p= 0.07)
Facial pain	20(±26)	16(±23)	-4(-9 to 1; p=0.1)	28 (±32)	7.6 (±7.6)	-20 (-35 to -5.5; p <0.001)*
Runny nose	30(±28)	24(±26)	-6 (-13 to 0); p=0.08)	41(±31)	28(±22)	-13(-33 to 8; p=0.20)
Itchy eyes	19 (±24)	16(±21)	-4(-8 to 0; p=0.07)	26 (± 27)	20 (± 21)	-6.7 (-20 to 6; p=0.28)
Cough	32(±28)	15(±20)	-17(-22 to -11; p <0.0001)*	34(±30)	28 (±27)	-6 (-21 to 9.8; p= 0.4)
Shortness of breath	35(±28)	20(±25)	-14 (-20 to -9; p<0.0001)*	41(±33)	28(±24)	-12 (-30 to 5; p=0.15)
Wheezing	28(±29)	17(± 23)	-11 (-17 to -6; p<0.0001)*	38 (±34)	23 (±25)	-15 (-27 to -3.0; p<0.01) *
Pressure on the chest	16(±22)	11(±16)	-5 (-10 to -1; p= 0.03`)*	25(±33)	12(±16)	-13 (- 29 to 3.5; p= 0.07)

Significance was calculated using paired T-test or Wilcoxon signed rank test depending on normality. Significant results are indicated with a *.

being similar as in the mepolizumab phase III trials [9]. Interestingly, the baseline NPS in the current cohort was lower (4.1–4.5) than in DBRCTs, where a TNPS of 5 or more was an inclusion criterium for randomization. In spite of the lower baseline NPS in this registry, the standard mean difference at 24 weeks in NPS reported here was larger 1.3 (CI -1.7 to -0.97) and 2.2 (CI -3.6 to -1.0), compared to the DBRCTs -0.85 (CI -1.06 to -0.64). This observation might be explained by the inclusion of less severe patients in our RWE than in the RDBCT, or by the unblinded scoring of NPS in the RWE compared to RDBCT. Haxel et al. [17] also reported a similar trend of more pronounced clinical improvements in their RWE data compared to the mean changes in the phase III data. They suggested a better type II inflammatory disease selection in real-life settings, where type II-associated co-morbidities, such as asthma, are more prevalent than in RDBCTs. Indeed, in our cohort 80% has comorbid asthma, which in line with other RWE studies [15,17,24,25] but is notably higher than the 60-70% reported in phase III trials [7,9].

Interestingly, major effects of biological therapy were seen at 12 weeks of therapy without significant further improvement in PRO's such as NCS, SNOT-22 score, AQLQ or ACQ5 -score between 12 and 24 weeks. Of note, the NPS did further decrease between 12 and 24 weeks of therapy in the mepolizumab group only, without the associated impact on subjective parameters. This observation warrants some context. Firstly, NPS does not directly correlate with patient relevant outcome parameters like smell loss, congestion or SNOT scores [26]. Secondly, the lack of additional benefit of omalizumab after 12 weeks does not exclude an additional benefit beyond 24 weeks of therapy and might be a consequence of the limited sample size compared to the mepolizumab group. An indirect comparison study in the past [10], already hinted at a possible plateau effect after 14 weeks of therapy with limited differences seen between 16 and 24 weeks of treatment in the clinical trials with both omalizumab and mepolizumab. This phenomenon was further confirmed by several other RWE studies focusing on dupilumab and/or omalizumab [16,17]. We now confirm this finding in both omalizumab and mepolizumab patients. We can only speculate on a further decrease in both NPS and/or patient relevant parameters beyond 24 weeks of therapy. However, the study of Cavaliere et al. showed a significant improvement between 24 weeks and 52 weeks on NPS, SNOT-22 and loss of smell VAS-scores in patient treated with mepolizumab.

Comparing our TRE data with other RWE studies of biologicals, we can primarily draw comparisons with dupilumab registries such as the Italian registry of De Corso et al. [14], the Dutch cohort of Van der Lans et al. [15] and the German study of Haxel et al. [17], which was the only one to analyse TRE on a population that comprised of both dupilumab as well as omalizumab patients [14,15,17].

Strikingly, more patients in the Italian cohort (57.7%) and the German cohort (56%) reached an excellent therapeutic response compared to our cohort (45-47%) and the study from Van der Lans et al. (40.7%). Moreover, a higher percentage of non-responders was seen in our patient cohort (12-14%) compared to the cohort from De Corso et al. (1.2-1.9%), Van der Lans et al. (3.7%) and Haxel et al. (1%) [14,15,17]. However, it may well be that longer treatment, or follow-up might reveal a higher percentage of patients with good to excellent therapeutic response than currently reported at 24 weeks. Caution is warranted when inter-

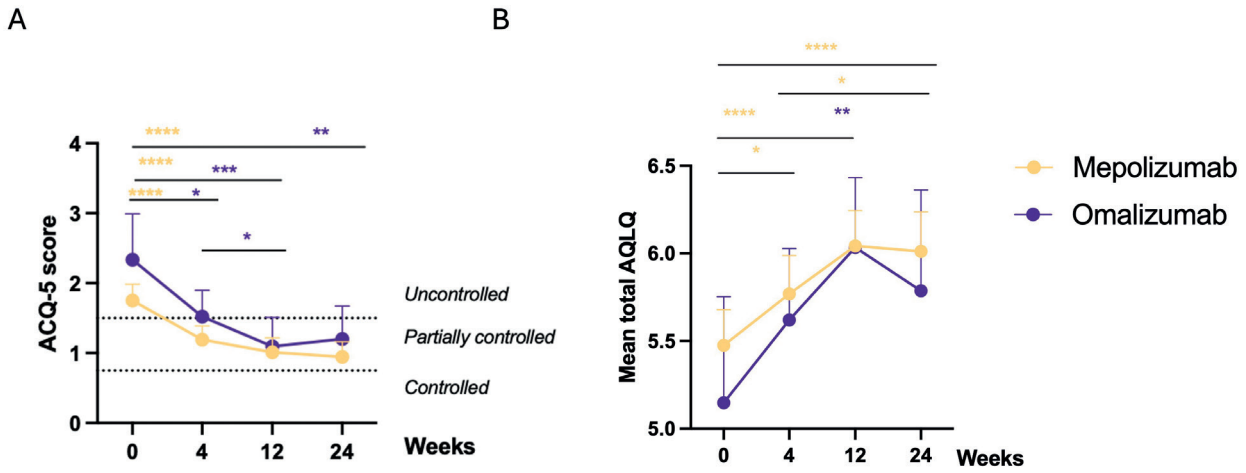

Figure 3. Effect of biological treatment on lower airways over time. Data are shown as mean ± 95% CI, significance was calculated by using mixed effect analysis with Tukey's multiple comparisons test , ****: P<0.0001,***:P <0.001, **P < 0.01, *: P < 0.05. (A) Change in mean ACQ-5 score (range 0-6); $n_{mepolizumab}$=102; $n_{omalizumab}$=23 (B) Change in mean total AQLQ score (range (1-7) $n_{mepolizumab}$=101; $n_{omalizumab}$=22.

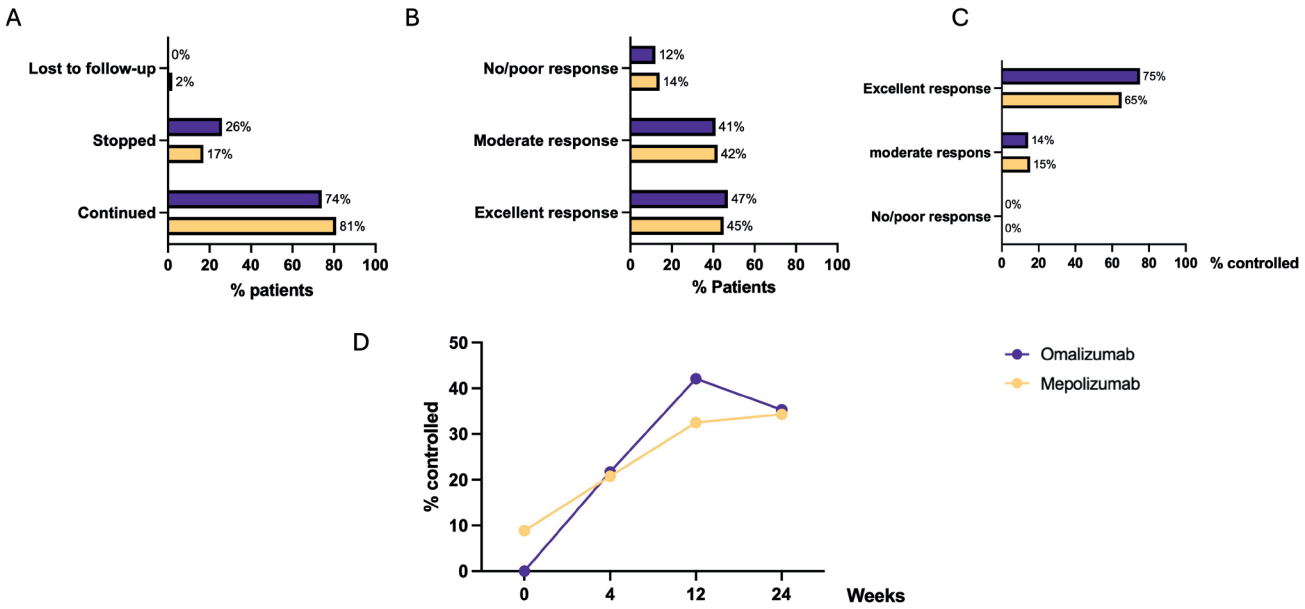

Figure 4. Responder and control analysis. (A) Percentage of patients that continued/stopped their biological or were lost to follow-up for mepolizumab n= 144; omalizumab n=23. (B) Response according to EUFOREA criteria of response to a biologics for mepolizumab n= 96; omalizumab n=17. (C) Level of control in patients with excellent (n=48)/moderate(n=46)/no-poor (n=15) response. (D) Percentage of patients controlled throughout the study according to the EPOS/EUFOREA criteria of control; $n_{mepolizumab}$=124; $n_{omalizumab}$=22.

preting results from different registries as the historic criteria to define a therapeutic response slightly differ between registries, and reimbursement criteria differ between countries [1,14,15,17].

As mentioned before, this report is made to include the newly consented definition of control in the real-world context of a Belgian registry [21]. It is striking that, although nearly 50% of patients treated with omalizumab or mepolizumab showed an excellent response to their biological according to the EUFOREA/EPOS criteria [21], only about one-third achieved disease control. This discrepancy can be largely attributed to the fact that the mean anosmia VAS-score at 24 weeks remained rather high around 54 out of 100, despite a significant reduction in loss of smell VAS-score. This prevented many patients from meeting a disease state of control, as defined by a lack of bothersome symptoms with VAS-scores of < 50 mm. Several factors should be considered when interpreting this data: most patients initially presented with a high VAS-score (i.e. 8/10). Despite anosmia

VAS-scores remaining high at 24 weeks, both treatment groups showed a significant average reduction of 2 points. Additionally, most of our patients had 1 or 2 sinus surgeries in the past, which may have contributed to the persistent loss of sense of smell. This factor could have potentially influenced the anosmia VAS scores. For this reason, the effectiveness of biologics is analysed not solely on the sense of smell but through several other clinical outcome parameters such as the effects on SNOT-22 and NPS. We acknowledge that semi-objective smell testing would have given additional information as to the extent of the anosmia. However, as this was not part of the standard of care in most hospitals, it was not incorporated into this observational trial.

As more long-term data will become available, it will be interesting to observe how the level of control will change in these patients and if some of them are on the path to remission.

In our registry, we do not seem to observe differences in efficacy nor control state between mepolizumab and omalizumab at 12 and 24 weeks. However, this might be influenced by the smaller cohort of patients on omalizumab (23 patients) compared to the mepolizumab cohort (144 patients), reflecting the stricter reimbursement criteria for omalizumab in the first year of reimbursement in Belgium, which seemed an important determinant in the choice of a biological in our Belgian cohort. Additionally, the lack of a need for dose calculations or multiple injection schemes with mepolizumab may have contributed to its perceived ease of prescription.

Lastly, patient adherence to their biological was notably high, with 95% of patients not missing a single injection, and dropout rates were as low as 2%. When missed injections occurred, they were primarily due to external factors such as limited availability of the biological at the pharmacy or expiration of reimbursement coverage before all syringes could be obtained. This high adherence rate is likely attributable to the relatively rapid and significant clinical improvements experienced by patients receiving biologicals, in contrast to other treatments such as nasal rinses and/or intranasal corticosteroids and may potentially also be contributed to the high cost of the therapy. Consistent with findings from other clinical trials and RWE studies, the safety profile was good with only minor side effects reported. Specifically, only three patients out of the 167 discontinued treatment due to potential biological-related adverse effects, such as shingles or musculoskeletal pain [13,27].

Conclusion

Six months of treatment with either mepolizumab or omalizumab significantly improved patient-reported outcomes, with major effects seen at 12 weeks and further reduction in NPS between 12 and 24 weeks in the mepolizumab treated group. Nearly half of the included patients showed an excellent therapeutic response to their biological with one third reaching control by week 24. Additional follow-up beyond six months is warranted for the evaluation of additional effects on the one hand and progress to remission on the other hand.

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Authorship contribution

PH: conceptualization, methodology, review and editing, supervision; ASV: Data Collection, formal analysis, writing, original draft preparation, review and editing; LB: data collection, formal analysis; EB: data collection, review and editing; SH, VH, MJ, WL, FR, KS, LVG, OV, BV, AV: data collection, review and editing; KM: review and editing; All authors have read and agreed to the published version of the manuscript.

Conflict of interest

All authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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