Update on the management of Chronic Rhinosinusitis with nasal polyps

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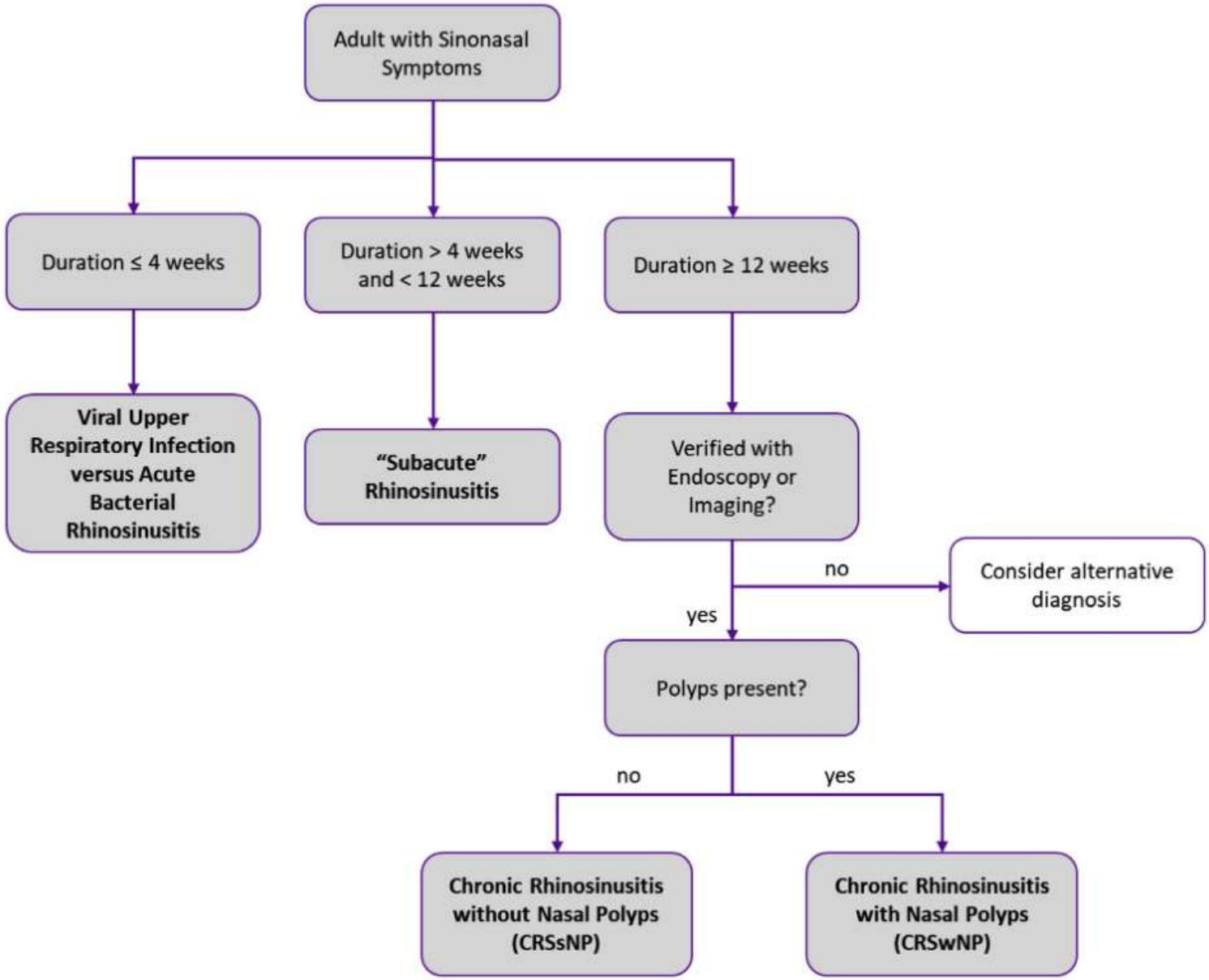


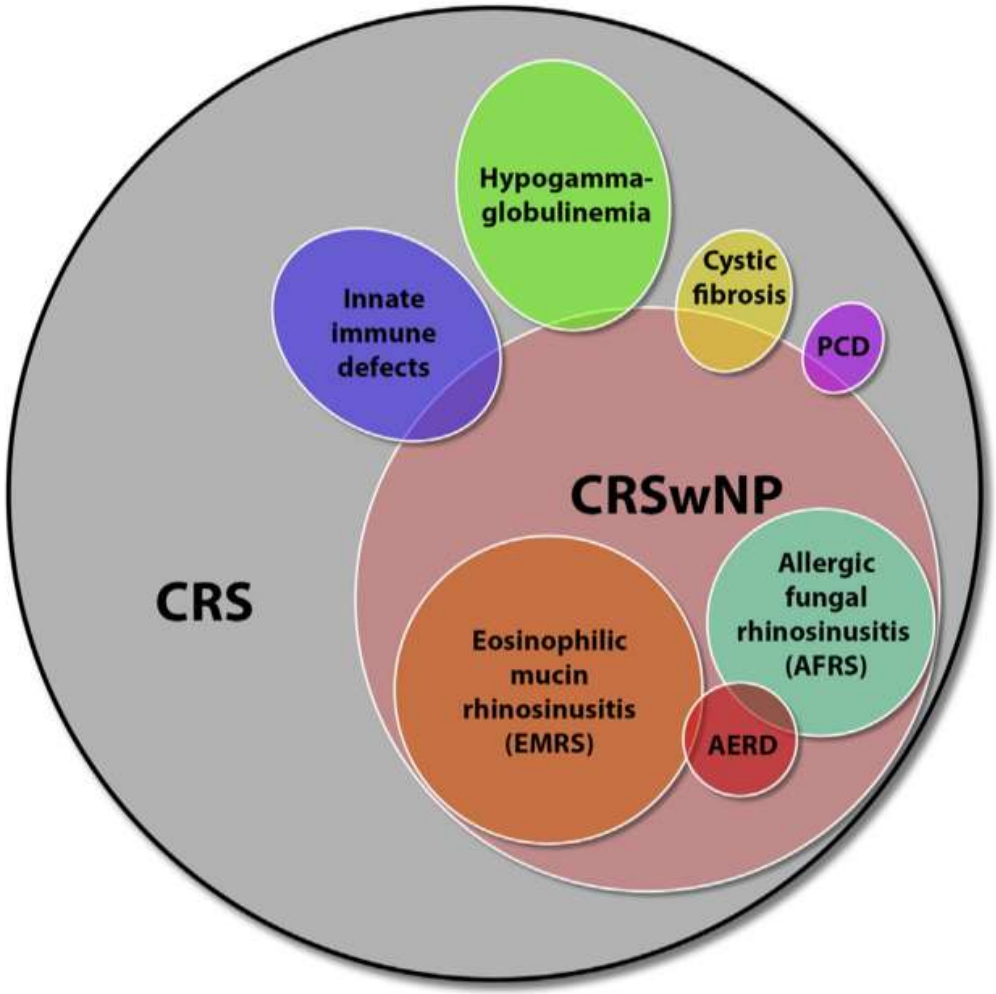
FIGURE I-1 Diagnostic algorithm for RS

International Forum of Allergy & Rhinology Volume 11, Issue 3 Mar 2021, Pages 211-739

TABLE I-2 Diagnostic criteria for diagnosis of CRS

Greater than or equal to 12 weeks of:
Two or more of the following symptoms:
Nasal discharge (rhinorrhea or post-nasal drip)
Nasal obstruction or congestion
Hyposmia
Facial pressure or pain
Cough (in Pediatric CRS)
AND
One or more of the following objective findings:
Evidence of inflammation on nasal endoscopy or computed tomography
Evidence of purulence coming from paranasal sinuses or ostiomeatal complex
AND
CRS is divided in to CRSsNP or CRSwNP based on the presence or absence of nasal polyps

Phenotypes of CRS



J Allergy Clin Immunol Pract. 2020 May ; 8(5): 1505–1511

Inflammatory endotypes in CRS

Table 1. Characteristics of inflammatory endotype in CRS.

Endotype	T1	T2	T3
Origin cell	Th1 cell ILC1	Th2 cell ILC2	Th17 cell ILC3
Inflammatory cytokines	TNF-α, IL-1β, IFN-γ, IL-12	IL-4, IL-5, IL-13	IL-17
Effector cells	NK cell M1 Macrophage	Basophil Eosinophil M2 Macrophage	Neutrophil
Target pathogens	Microbes, protozoa, viruses	Parasite	Bacteria, fungi
Clinical characteristics	Mucopurulent discharge Nasal polyp (limited)	Anosmia, Nasal polyposis, Asthma	Mucopurulent discharge Nasal polyp (limited)

Th, T helper cell; ILC, innate lymphoid cell; TNF-α, tumor necrosis factor; IFN-γ, interferon gamma; IL, interleukin; NK, natural killer.

Int. J. Mol. Sci. 2023, 24, 5015

Antibiotics

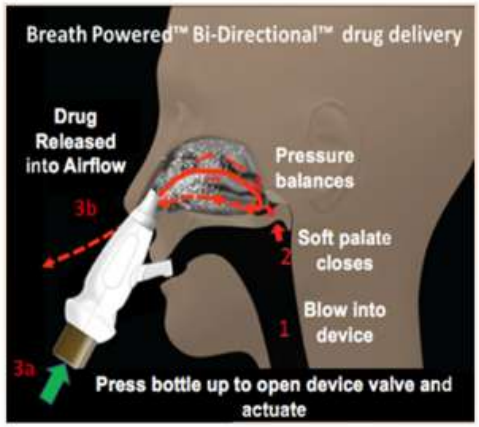
만성 비부비동염의 약물 치료 – 항생제

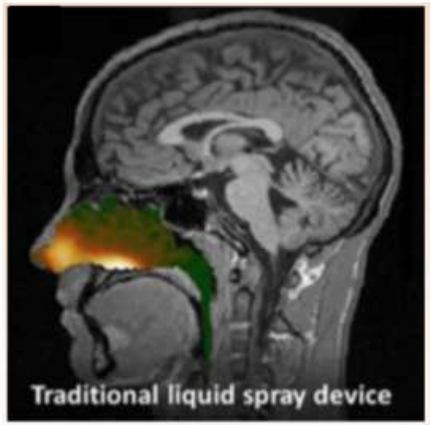
Short-term oral antibiotics	No recommendation
Long-term oral antibiotics (macrolide)	Option
Topical antibiotics	Recommendation against
Intravenous antibiotics	Recommendation against

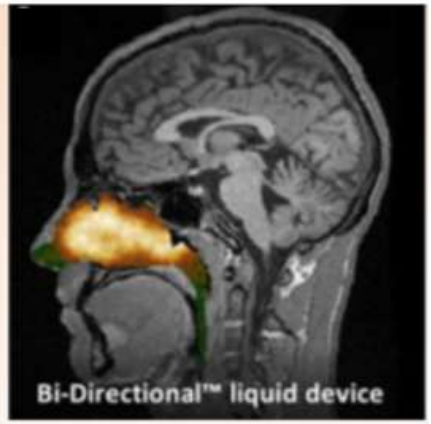
Antibiotics: not recommended except acute exacerbation of CRS

INCS

- Spray
- Drop
- Irrigation
- Exhalation delivery system-fluticasone





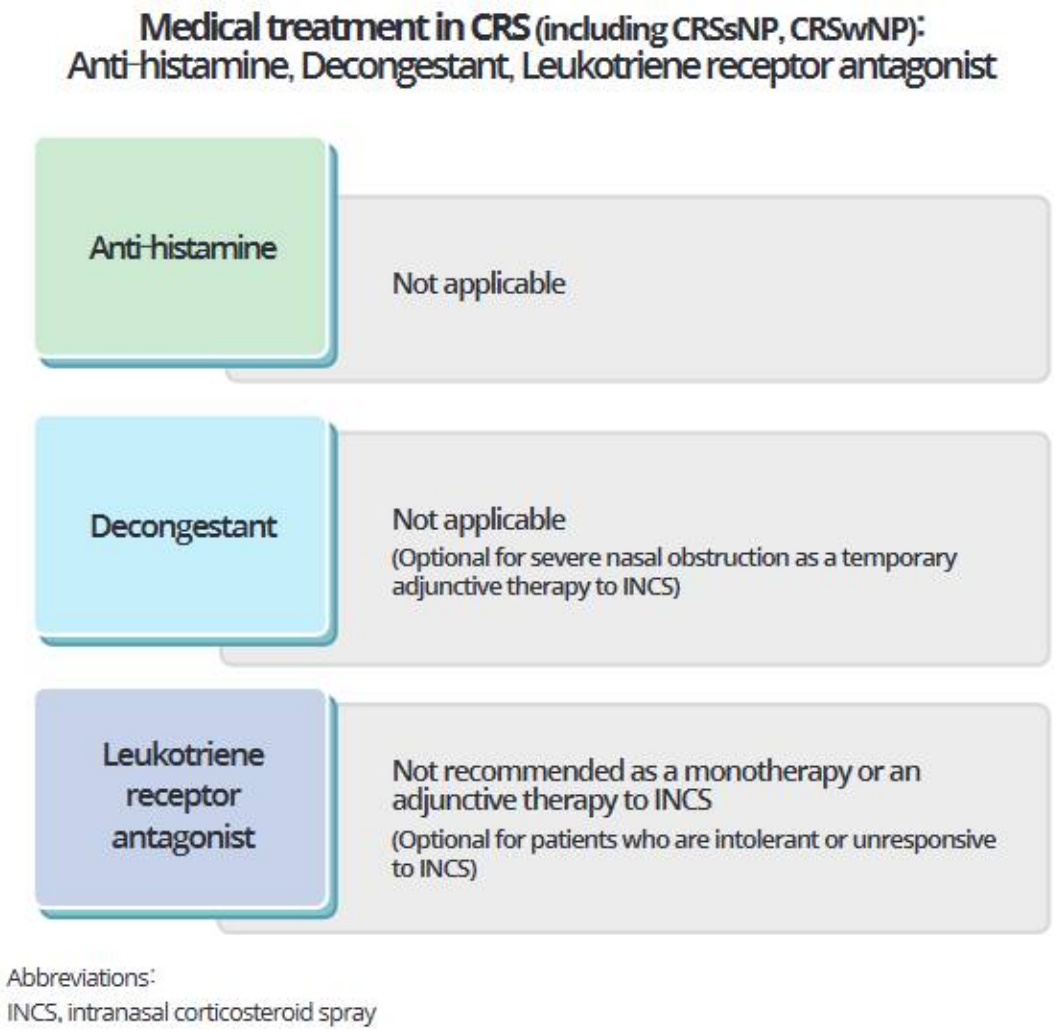


Oral corticosteroid

- CRSsNP: 단기간
- CRSwNP: effective, 단기간
- AFS: 장기간
- Increased risk: adjusted HR
  - Osteoporosis and fracture (3.11), pneumonia (2.68), CVA (1.53) Cataract (1.50), sleep apnea (1.40)
- Cummulative exposure
  - 1.0-2.5g: adverse outcome began
  - 0.5-1.0g: for some adverse outcome

Journal of Asthma and Allergy 2018:11 193–204

Anti-histamine, Decongestant, LTRA

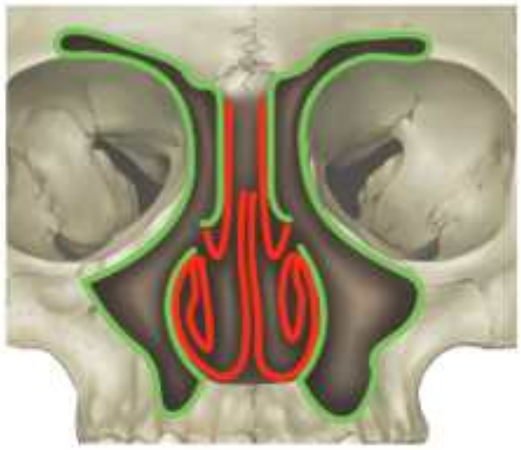


Extensive surgery for CRSwNP

- EMLP (Draf III)
- Mega-antrostomy, modified EMM
- Sphenoid drill-out
- Middle turbinate resection
- Reboot surgery

Reboot surgery

- Remove the mucosa of all the sinuses including maxillary sand frontal sinus as much as possible



The periosteum is intended to remain intact as far as possible, using mostly grasping surgical instruments, not drilling or shaving the sinus areas, so that the mucosa can regrow from the nasal cavity within a short time, taking an average of 2 weeks to cover all bony surfaces

› Eur Arch Otorhinolaryngol. 2022 Dec;279(12):5691-5699. doi: 10.1007/s00405-022-07470-z. Epub 2022 Jun 6.

Reboot surgery for chronic rhinosinusitis with nasal polyposis: recurrence and smell kinetics

Sara Costa Gomes [1], Carlo Cavaliere [2], Simonetta Masieri [3], Thibaut Van Zele [4], Philippe Gevaert [4], Gabriele Holtappels [4], Nan Zhang [4], Pathmanaban Ramasamy [5], Richard Louis Voegels [1], Claus Bachert [6 7 8]

Affiliations + expand

PMID: 35666318 DOI: 10.1007/s00405-022-07470-z

Abstract

Objective: To evaluate the time for recovery of the sense of smell in patients with CRSwNP who underwent Reboot surgery compared to patients undergoing ESS in a long-term follow-up study.

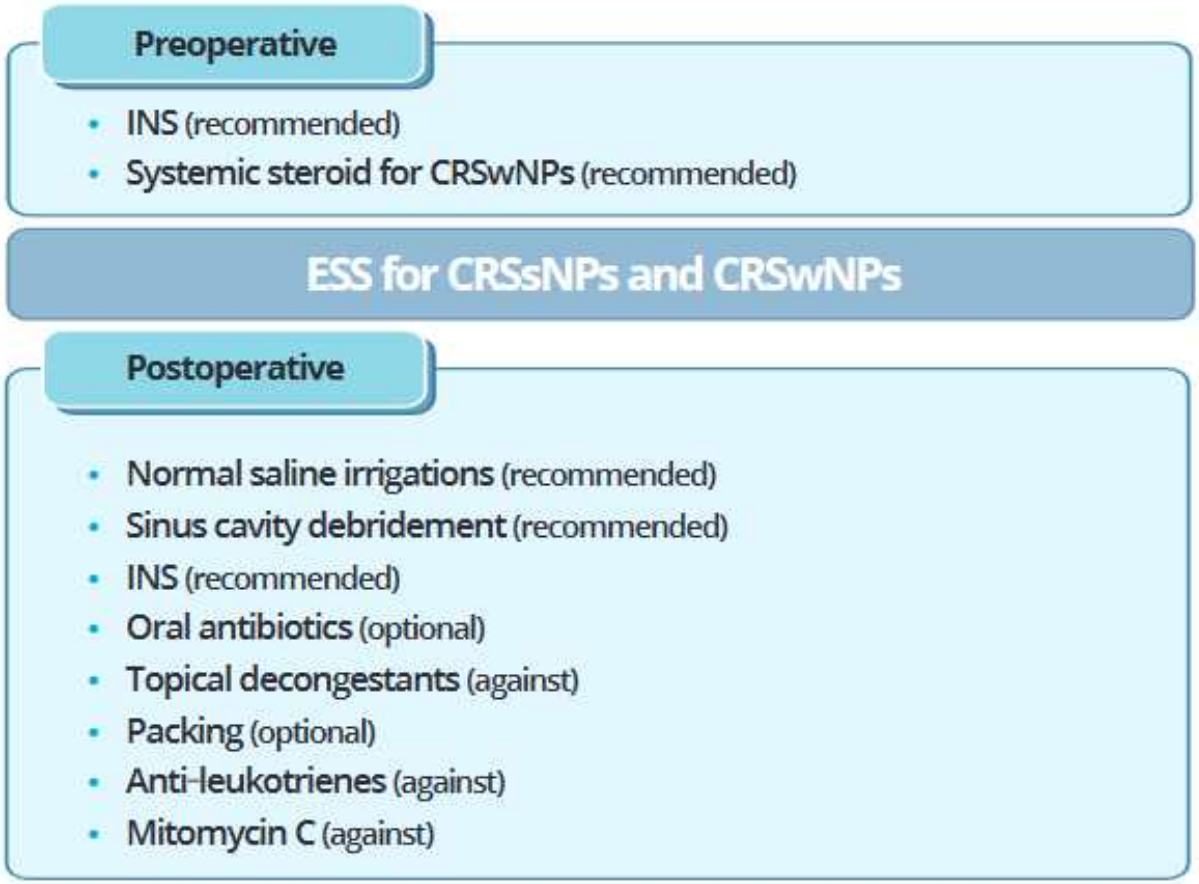
Methods: Data were collected retrospectively from 168 patients with severe uncontrolled CRSwNP, who underwent revision surgery, either as Extended Endoscopic Sinus Surgery (Reboot, 140 patients) or as regular Endoscopic Sinus Surgery (ESS, 28 patients) between January 1, 2014, and December 31, 2015, aiming to compare the outcome of surgeries after 2 years of follow-up. Sense of smell was scored as judged by the patient using scores 0 to 3 reflecting a percentage estimate of remaining smell.

Results: Smell improved similarly in the Reboot and ESS groups over the first 9 months, which was maintained over 24 months in the Reboot, but not the ESS group ($p = 0.007$ after 18 months, $p = 0.001$ after 24 months). Furthermore, polyp recurrence rates were significantly lower in the Reboot group.

Conclusion: Reboot surgery significantly improved olfactory function and significantly reduced nasal polyp recurrence rates over 2 years post-operatively. Therefore, Reboot should be considered for patients with uncontrolled severe CRSwNP, specifically when ESS failed, to offer long-term smell and a polyp-free status.

Level of evidence: 3b.

수술 전후 관리와 약물치료



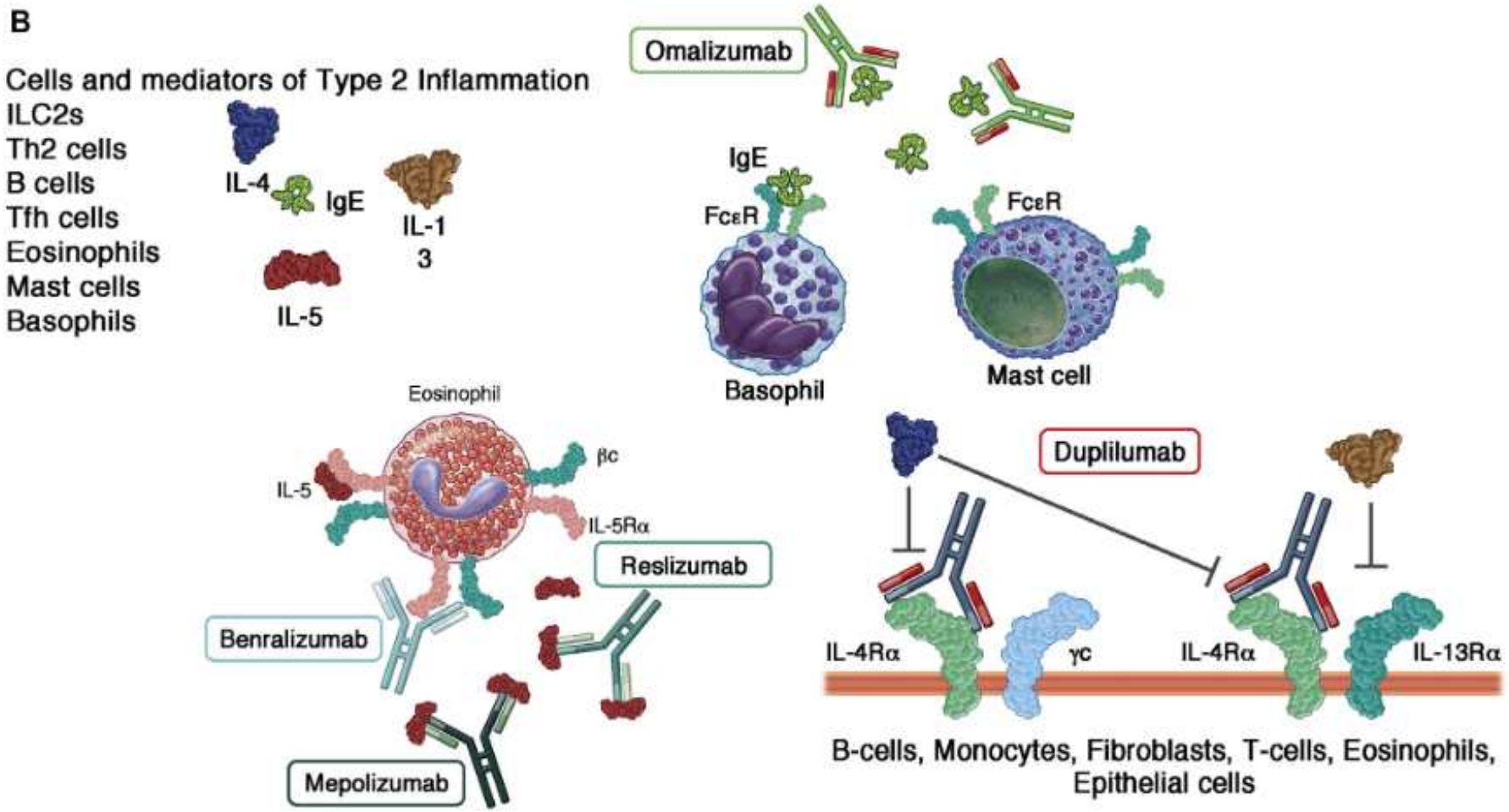
Abbreviations:

INS, intranasal steroid; CRSsNP, chronic rhinosinusitis without nasal polyp; CRSwNP, chronic rhinosinusitis with nasal polyp

Biologics for CRSwNP

Biologics	Trade Name	Target	Approval State
Omalizumab	Xolair®	Anti-IgE	FDA & Korea
Mepolizumab	Nucala®	Anti-IL-5	FDA & Korea
Dupilumab	Dupixent®	Anti-IL-4Ra	FDA & Korea
Benralizumab	Fasenra®	Anti IL-5La	Phase 3 tirals
Reslizumab	CINQAIR®	Anti IL-5	Phase 3 trials

To date, there are no studies that directly compare any of the biologic agents available for CRSwNP.



Bachert, et al. J Allergy Clin Immunol 2020;145:725-39

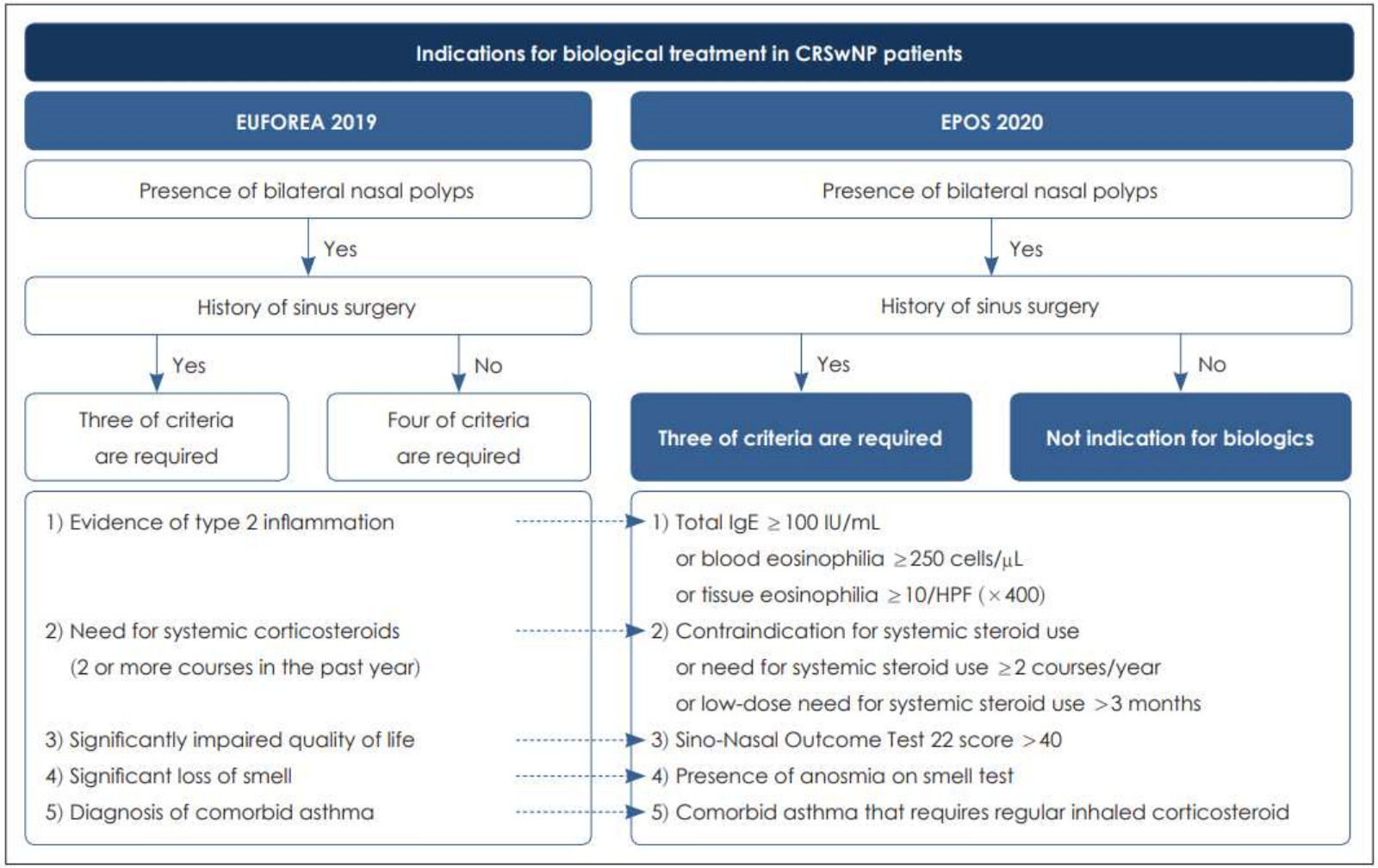


Fig. 2. Indications for biologics in the treatment of CRSwNP; guideline of the EUFOREA and EPOS 2020. CRSwNP, chronic rhinosinusitis with nasal polyp; EUFOREA, European Forum for Research and Education in Allergy and Airway Diseases; EPOS, European Position Paper on Rhinosinusitis and Nasal Polyps.

Korean J Otorhinolaryngol-Head Neck Surg 2021;64(10):693-702

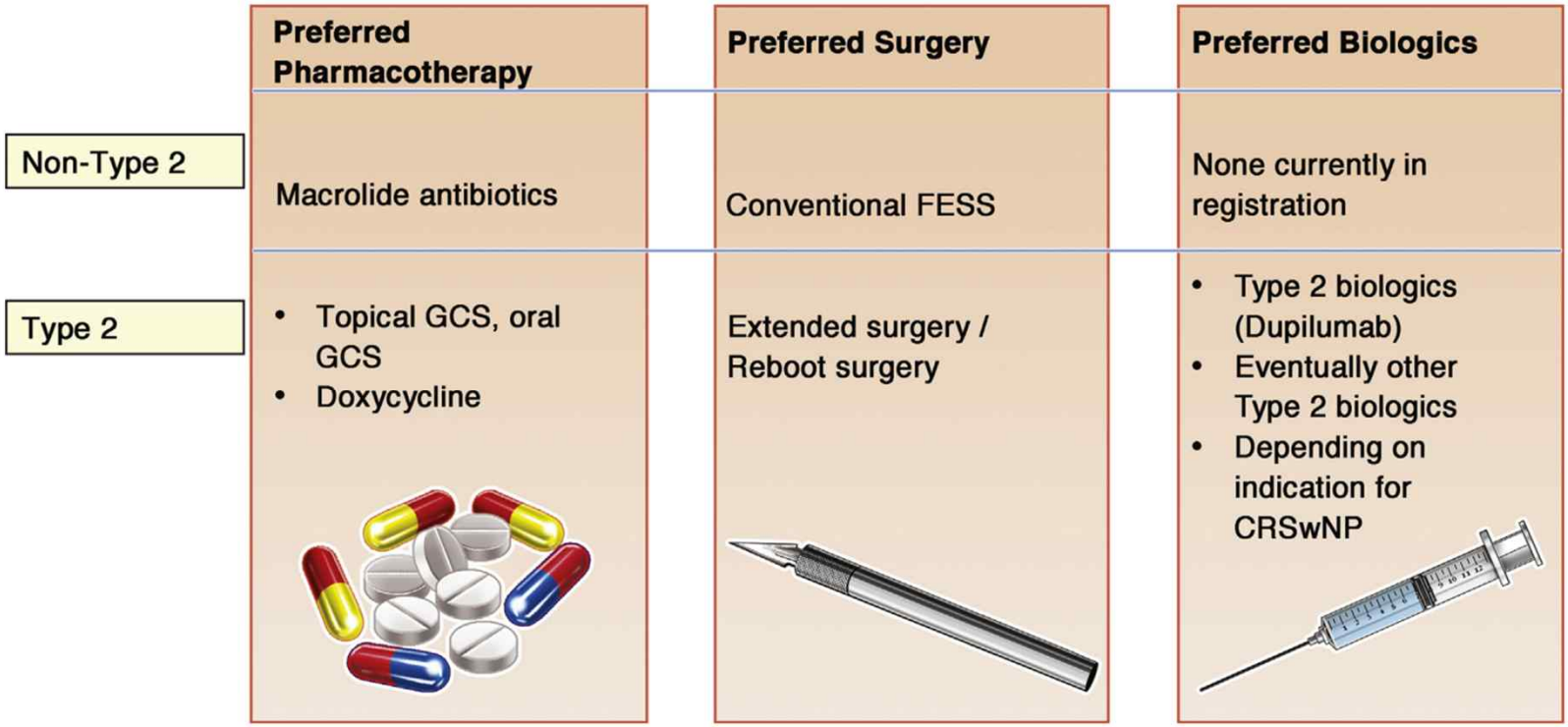


FIG 2. Impact of type 2 endotype on CRS treatment. *GCS*, Glucocorticosteroid; *FESS*, functional endoscopic sinus surgery.

Cardell, et al. J Allergy Clin Immunol 2020

Systematic review & **network meta-analysis**

(**indirect comparison of monoclonal antibodies & ATAD)**

	Patient-important outcomes						Surrogate outcomes	
	HRQoL SNOT-22 (0-110)‡	Symptoms VAS (0-10 cm)	Smell UPSIT (0-40)†	Rescue OCS	Rescue polyp surgery	Adverse events	Nasal polyp size (0-8)	CT score LMK (0-24)
Standard care*	50.11	6.84	14.04	31.96%	21.05%	73.78%	5.94	18.35
Dupilumab	**-19.91** (-22.50, -17.32)	**-3.25** (-4.31, -2.18)	**10.96** (9.75, 12.17)	**-21.73** (-24.61, -18.22) RR 0.32 (0.23, 0.43)	**-16.35** (-18.13, -13.48) RR 0.22 (0.14, 0.36)	**0.13** (-8.12, 9.88) RR 1.00 (0.88, 1.13)	**-2.04** (-2.73, -1.35)	**-7.51** (-10.13, -4.89)
Omalizumab	**-16.09** (-19.88, -12.30)	**-2.09** (-3.15, -1.03)	**3.75** (2.14, 5.35)	**-12.46** (-23.65, 12.78) RR 0.61 (0.26, 1.40)	**-7.40** (-11.04, -2.43) RR 0.65 (0.48, 0.88)	**-2.60** (-15.58, 13.28) RR 0.96 (0.79, 1.18)	**-1.09** (-1.70, -0.49)	**-2.66** (-5.70, 0.37)
Mepolizumab	**-12.89** (-16.58, -9.19)	**-1.82** (-3.13, -0.50)	**6.13** (4.07, 8.19)	**-10.23** (-15.98, -2.88) RR 0.68 (0.50, 0.91)	**-12.33** (-15.56, -7.22) RR 0.41 (0.26, 0.66)	**-3.07** (-13.44, 9.07) RR 0.96 (0.82, 1.12)	**-1.06** (-1.79, -0.34)	
Benralizumab	**-7.68** (-12.09, -3.27)	**-1.15** (-2.47, 0.17)	**2.95** (1.02, 4.88)	**-9.91** (-16.30, -0.96) RR 0.69 (0.49, 0.97)	**-2.53** (-9.05, 7.16) RR 0.88 (0.57, 1.34)	**-1.48** (-13.28, 12.54) RR 0.98 (0.82, 1.17)	**-0.64** (-1.39, 0.12)	**-1.00** (-3.83, 1.83)
Reslizumab					**-18.82** (-20.93, 20.56) RR 0.11 (0.01, 1.98)	**-2.55** (-19.49, 19.18) RR 0.97 (0.74, 1.26)		
AK001						**2.54** (-27.11, 51.03) RR 1.03 (0.63, 1.69)	**-0.20** (-1.61, 1.21)	
Etokimab	**-1.30** (-8.99 to 6.40)					**188.14** (-59.76, 4879.1) RR 3.55 (0.19, 67.13)	**-0.33** (-1.58, 0.92)	
ASA Desensitization	**-10.61** (-14.51, -6.71)	**-2.74** (-3.92, -1.57)	**2.72** (-1.17, 6.61)		**-16.00** (-19.79, 0.21) RR 0.24 (0.06, 1.01)	**209.21** (8.30, 901.87) RR 3.84 (1.11, 13.22)	**-0.95** (-2.44, 0.55)	**-0.31** (-3.50, 2.88)

Classification of intervention (colour)[24]				**Certainty (shading)[24, 29]**
Among most beneficial	Among intermediate beneficial	Among least beneficial/not clearly different from placebo	No data (blank)	High/moderate (solid)
Among most harmful	Among intermediate harmful			Low/very low (shaded)

J Allergy Clin Immunol 2022;149:1286-95

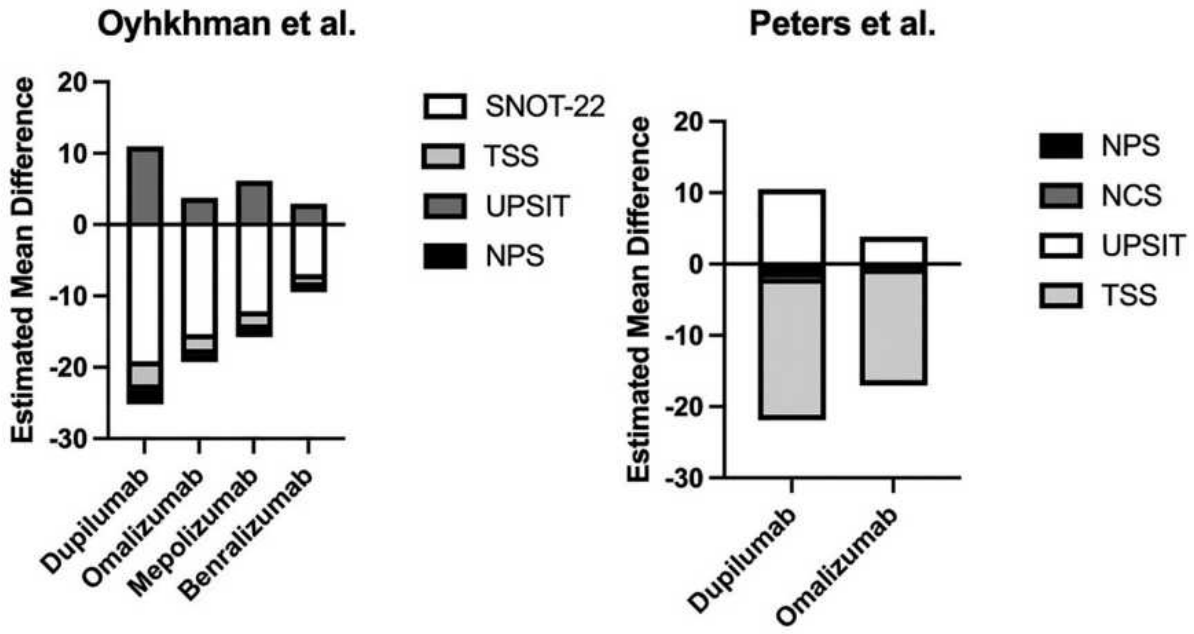


Figure 3. Indirect comparisons of biologic agents. Bars represent stacked reported estimated mean difference relative to reported values for the control treatment of the noted metric. Negative values for TSS, SNOT-22, NPS, and NCS denote an improvement relative to controls; positive value for UPSIT denotes improvement relative to controls.

Abbreviations: TSS, total symptom score; NCS, nasal congestion score; SNOT-22, sinonasal outcome-22; NPS, nasal polyp score; UPSIT, University of Pennsylvania Smell Identification Test.

Parameters	Sig-Total	D vs M	D vs O	D vs B	M vs O	M vs B	O vs B
ACT-Score: after-before	0.984	n.t.	n.t.	n.t.	n.t.	n.t.	n.t.
FEV1: after-before	0.658	n.t.	n.t.	n.t.	n.t.	n.t.	n.t.
GINA-Score: after-before	0.614	n.t.	n.t.	n.t.	n.t.	n.t.	n.t.
VAS: Blocked nose: after-before	0.000	n.s.	*	***	n.s.	*	n.s.
VAS: Loss of smell: after-before	0.000	*	*	***	n.s.	n.s.	n.s.
VAS: Runny nose: after-before	0.000	**	*	***	n.s.	n.s.	n.s.
VAS: Postnasal drip: after-before	0.000	***	**	***	n.s.	n.s.	n.s.
RSOM-31 Nasal Subscore: after-before	0.000	**	***	***	n.s.	n.s.	n.s.
RSOM-31 Eyes Subscore: after-before	0.038	n.s.	*	n.s.	n.s.	n.s.	n.s.
RSOM-31 Sleep Subscore: after-before	0.142	n.t.	n.t.	n.t.	n.t.	n.t.	n.t.
RSOM-31 Ears Subscore: after-before	0.207	n.t.	n.t.	n.t.	n.t.	n.t.	n.t.
RSOM-31 General: after-before	0.115	n.t.	n.t.	n.t.	n.t.	n.t.	n.t.
RSOM-31 Practical Problems: after-before	0.001	***	**	*	n.s.	n.s.	n.s.
RSOM-31 Emotions: after-before	0.000	**	n.s.	n.s.	n.s.	***	***
RSOM-31 Total: after-before	0.003	n.s.	**	**	n.s.	n.s.	n.s.

there was a significantly better response to dupilumab in rhinological parameter

World Allergy Organization Journal (2023) 16:10074

Olfaction changes on biologics

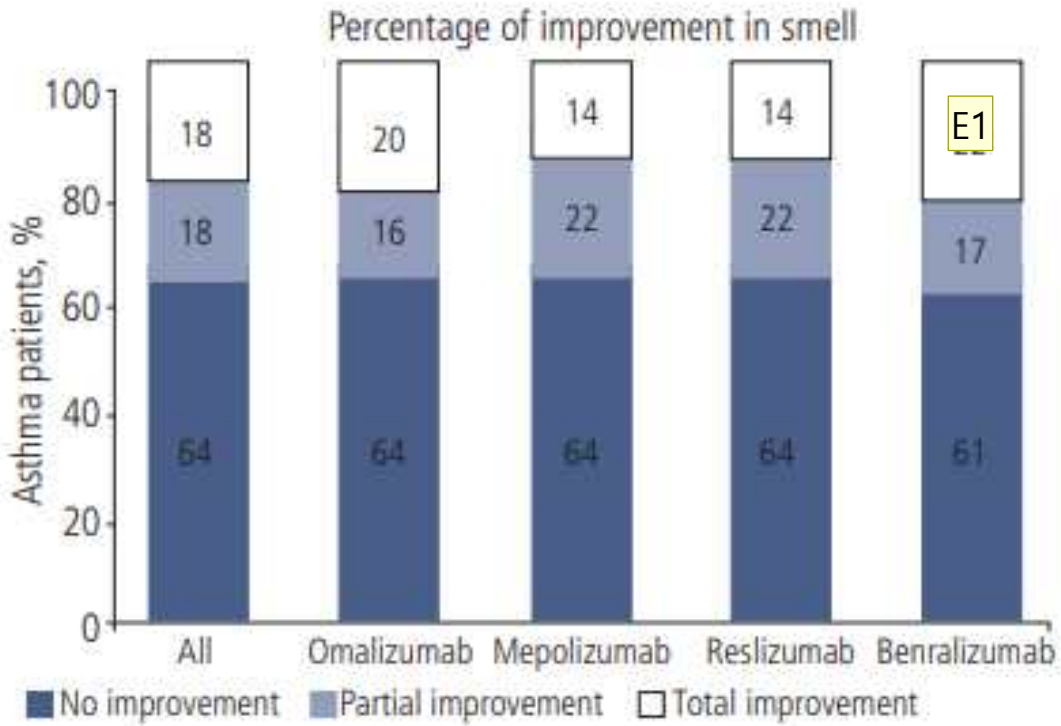


Figure. Changes in olfaction. No improvement, partial improvement (change from anosmia to hyposmia), and total improvement (from anosmia or hyposmia to normosmia). No statistically significant differences were found between the normosmia, hyposmia, and anosmia groups for any of the biologics.

Investig Allergol Clin Immunol 2023; Vol. 33(1): 37-44

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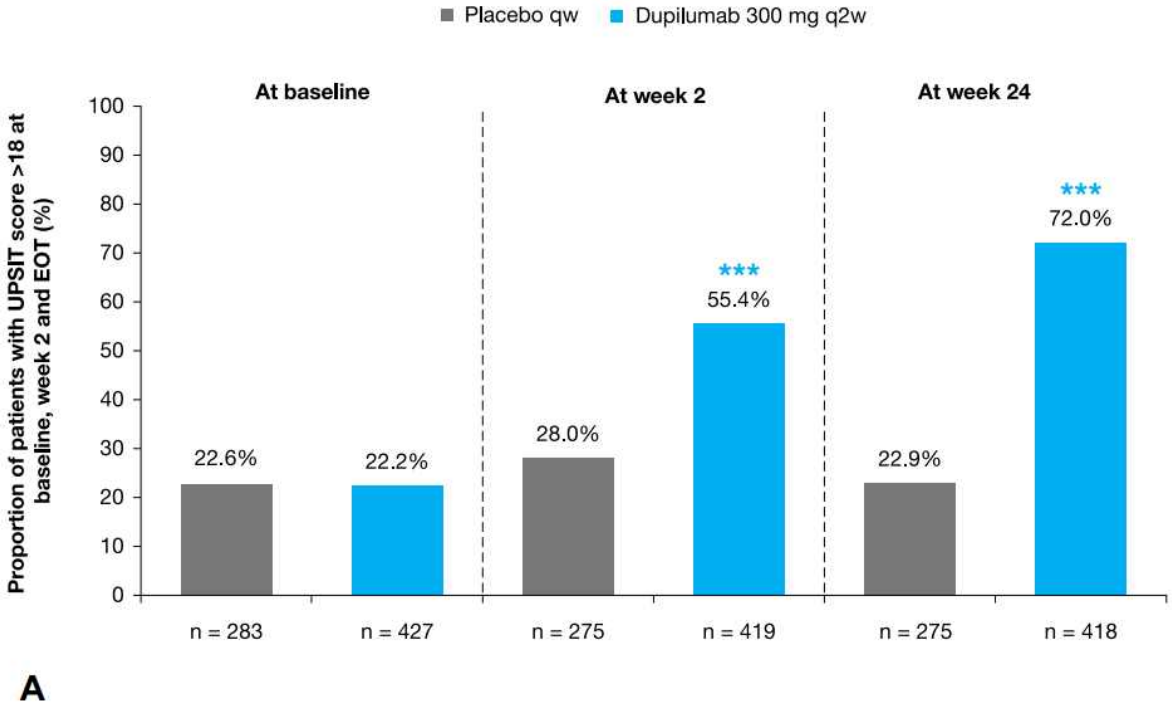
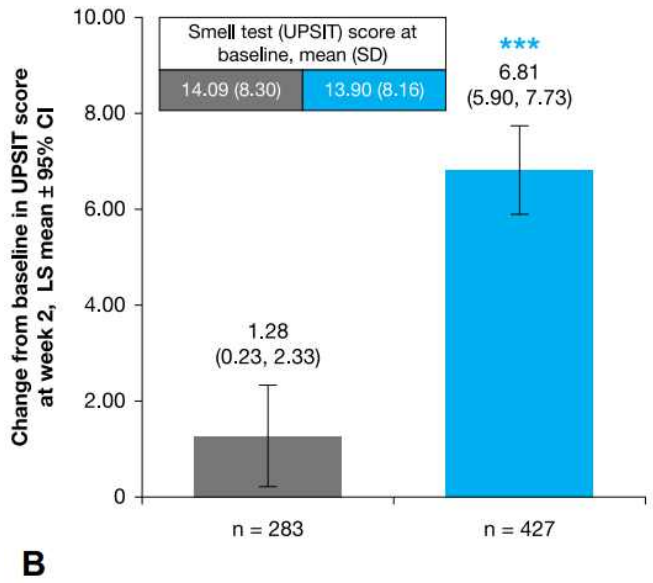
Rapid onset of dupilumab



UPSIT score greater than 18 at baseline and weeks 2 and 24.



Change from baseline in UPSIT score at week 2

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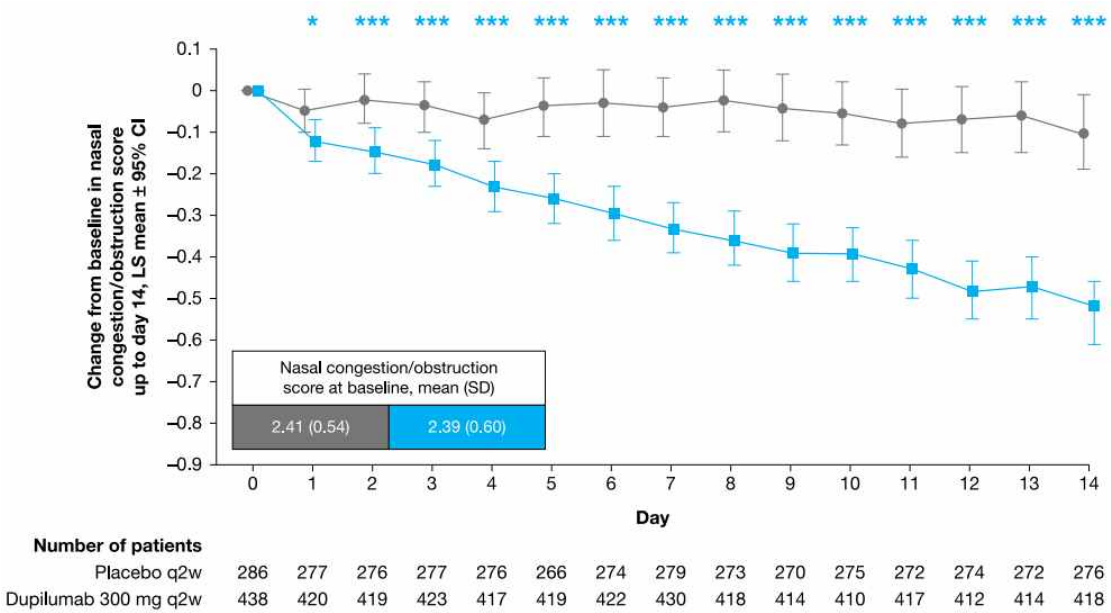
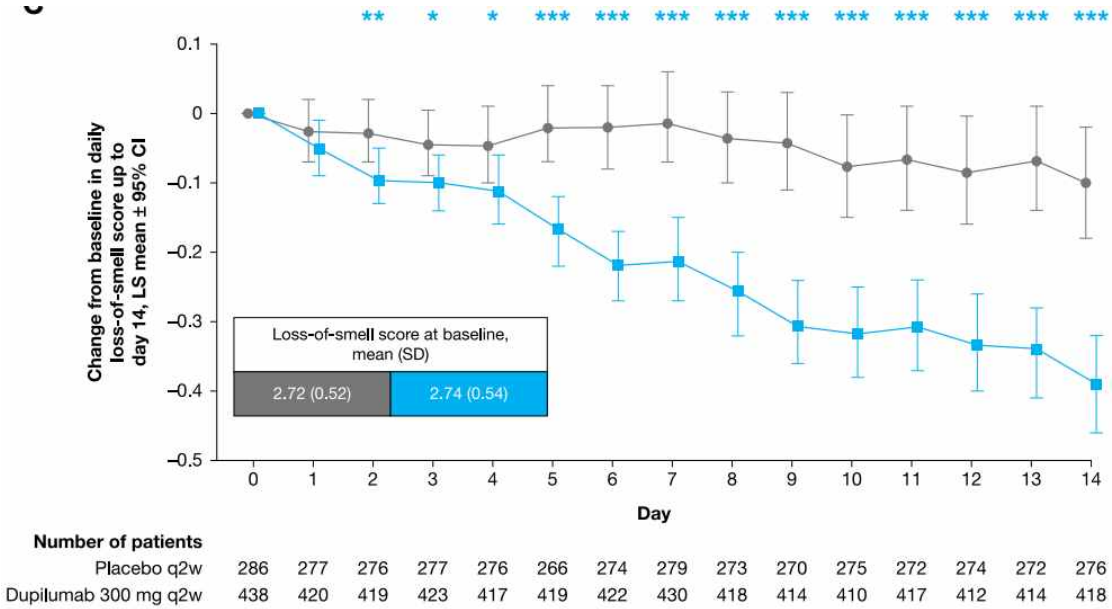


Change from baseline in daily nasal congestion or obstruction score up to day 14



Change from baseline in daily loss of smell score up to day 14

J Allergy Clin Immunol Pract 2022;10:1515-26

Real-world-effectiveness of biological treatment for severe chronic rhinosinusitis with nasal polyps

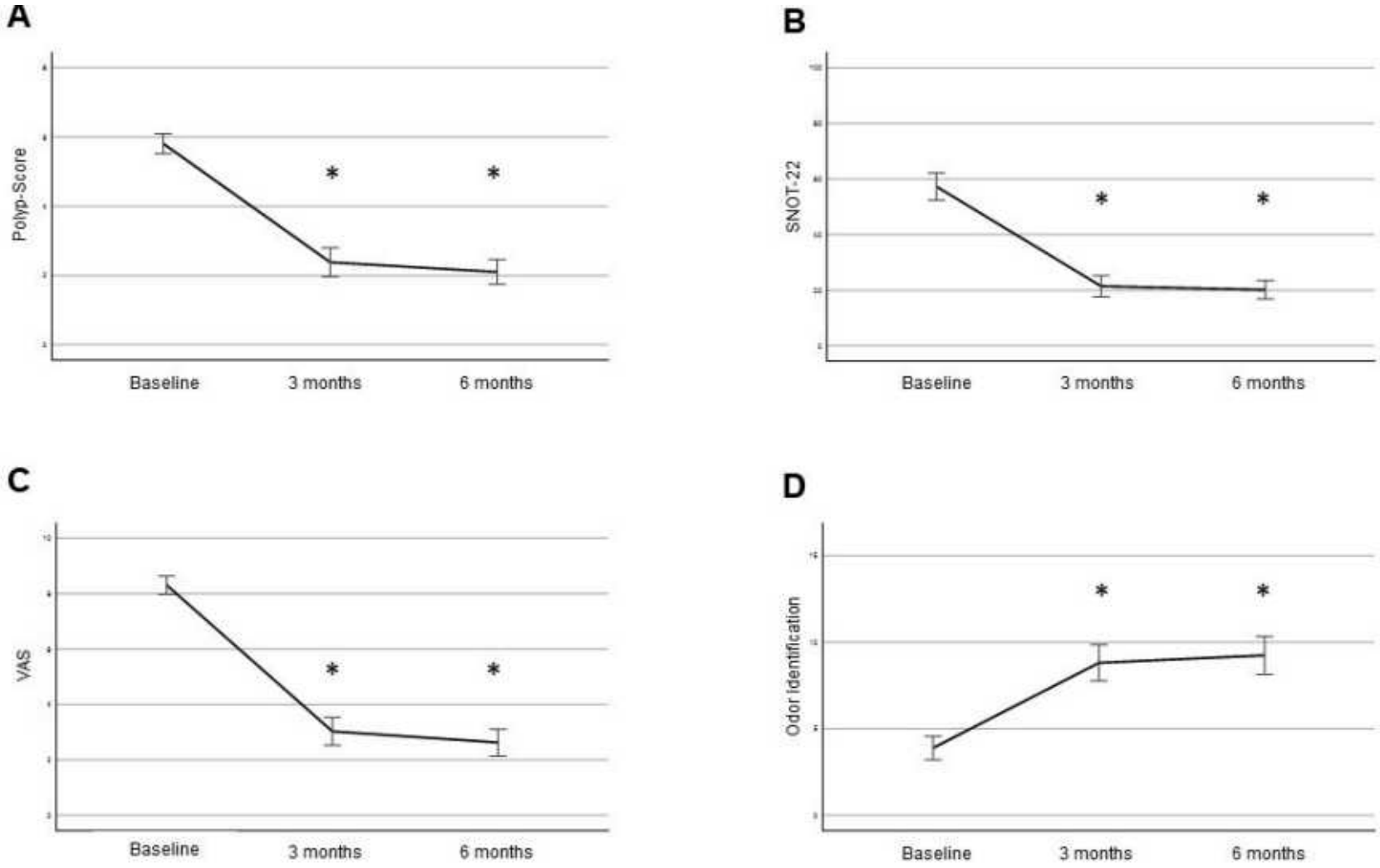


Figure 2. Mean values (including 95% confident interval) at baseline, 3 and 6 months after start of monoclonal antibody treatment for CRSwNP for a) endonasal polyp score (0-8), b) SNOT-22-score (0-110), c) VAS score of nasal health rating (0-10); d) Sniffin´ Sticks 16-Item Identification Score (0-16). Significant changes are marked by *.

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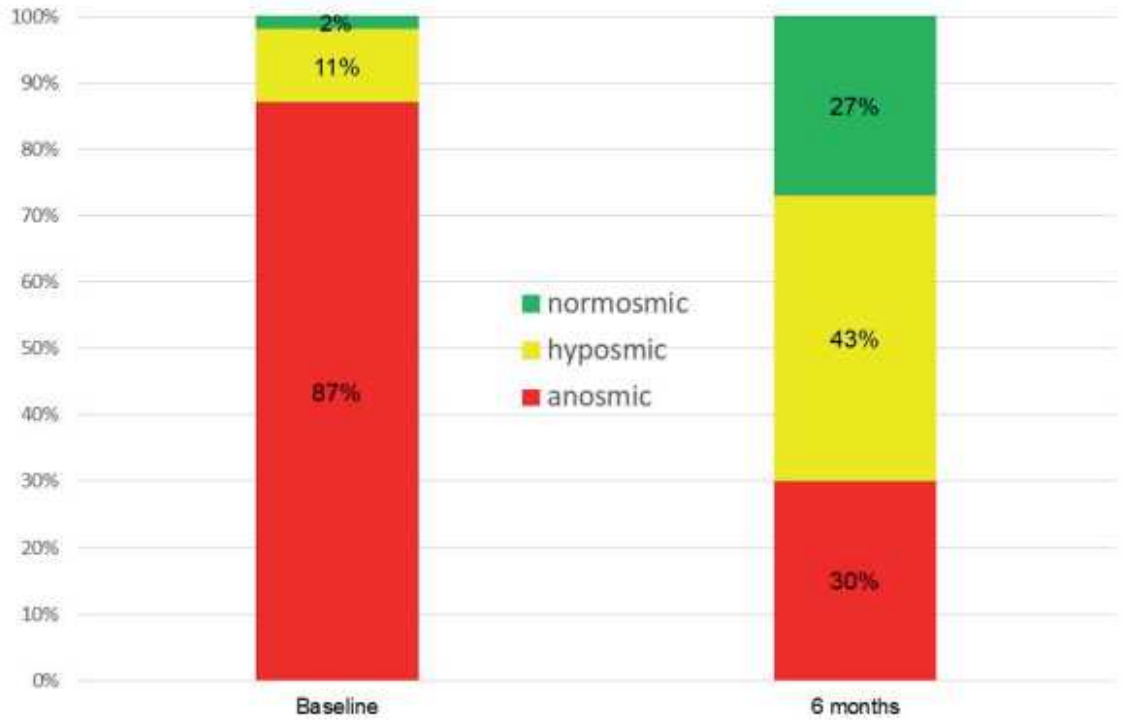

Figure 3. Percentual proportion of patients in the different classifications of olfaction (normosmic, hyposmic or anosmic) at baseline and 6 months after therapy with monoclonal antibodies for CRSwNP.

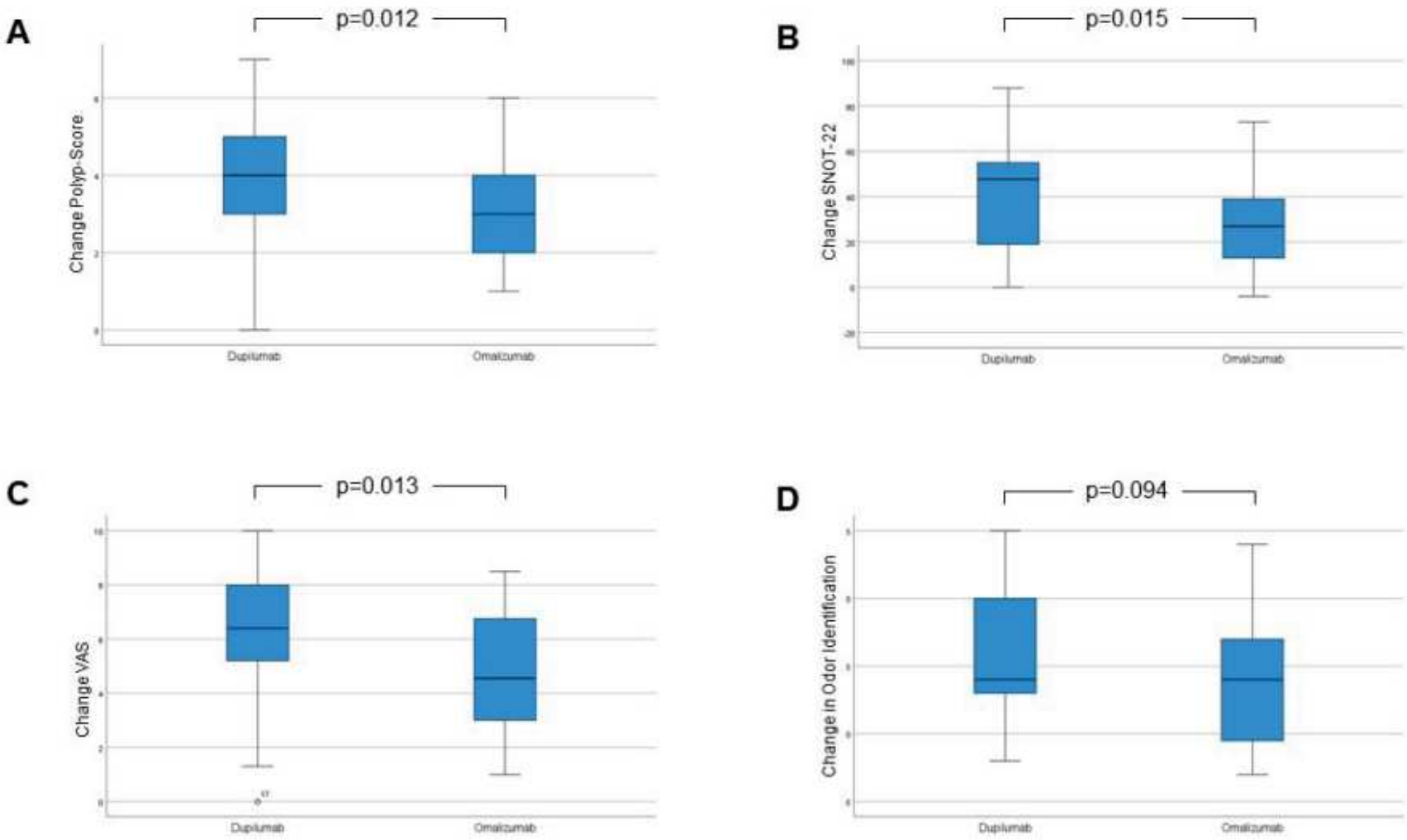

Figure 4. Boxplots of changes of a) nasal polyp score; b) SNOT-22 score; c) VAS-score; d) Sniffin´ Sticks 16-Item Identification score 6 month after start of therapy in the dupilumab (n=49) and omalizumab (n=21) treatment group. The lines represent the medians; the boxes include 75% of the results; the whiskers include 95% of the results. The circles demonstrate outliers. Significant differences are indicated.

Allergic fungal rhinosinusitis

- Type 2 inflammation with deficient type 3 immune response
- Very high total serum IgE (>1,000U/mL)
- Removal of eosinophilic mucin & corticosteroid (topical or systemic)
- Trial of biologic agents is ongoing
- Anti-IgE monoclonal antibody can be logical first-option

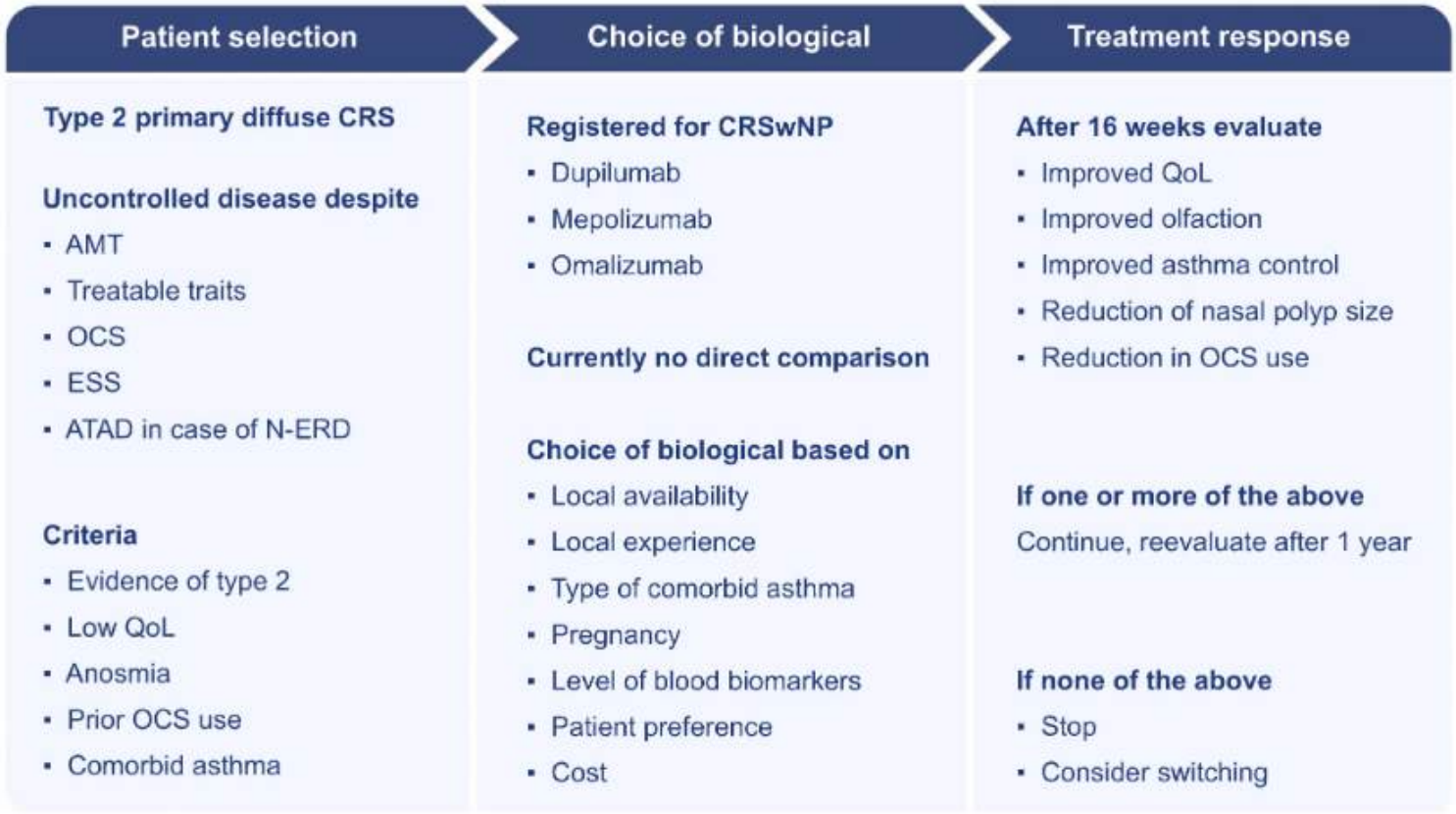

FIGURE 2 Principles in selection of biologicals and monitoring response. Legend: AMT, Appropriate medical therapy; ATAD, Aspirin therapy after desensitization CRS, Chronic rhinosinusitis; CRSwNP, Chronic rhinosinusitis with nasal polyps; ESS, Endoscopic sinus surgery; N-ERD, Non-steroidal anti-inflammatory drug-exacerbated respiratory disease; OCS, Oral corticosteroids; QoL, Quality of life

Allergy Volume 77, Issue 12 Dec 2022 3481-3705

Beyond 1 year

- Biologicals do not appear to have long-term disease modifying effect after cessation of treatment
- Optimal duration is needed to determine