

Minimizing the clinical burden of chronic rhinosinusitis with nasal polyposis

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A conversation between:



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How can early diagnosis reduce the burden of CRSwNP?

Dr Sietze Reitsma



Prevalence, symptoms and burden of CRSwNP

Prevalence



- CRSwNP affects 2–4% of people worldwide^{1–3}
- Average incidence of CRSwNP vs CRSsNP reported as 83 (\pm 13) vs 1048 (\pm 78) cases/100,000 person-years³
- Among patients with asthma, 20–57% have CRS^{3,5}

Symptoms



- Smell reduction, nasal obstruction, rhinorrhoea/postnasal drip³
- Facial pain/pressure³
- Bad breath*⁶
- Hearing impairment*⁶

Burden



- 75% report poor sleep quality; fatigue reported in 54%^{1,3}
- Profound effects on cognitive function, functional wellbeing and HRQoL^{1–3}
- Depression in 11–40% of patients^{1,3}

*Symptoms assessed in 15 participants from a patient advisory board of the EUFOREA.

CRS, chronic rhinosinusitis; CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; EUFOREA, European Forum for Research and Education in Allergy and Airways Diseases; HRQoL, health-related quality of life.

1. Orlandi RR, et al. *Int Forum Allergy Rhinol.* 2021;11:213–739; 2. Morse JC, et al. *J Asthma Allergy.* 2021;14:873–82; 3. Fokkens WJ, et al. *Rhinology.* 2020;58(Suppl. S29):1–464; 4. Bachart C, et al. *J Asthma Allergy.* 2021;14:127–34; 5. Maspero JM, et al. *J Allergy Clin Immunol Pract.* 2020;8:527–39.e9; 6. Claeys N, et al. *Front Allergy.* 2021;2:1–9.

How can the pathophysiology of CRSwNP guide treatment decisions?

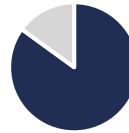
Dr Sietze Reitsma



Endotypes associated with CRSwNP

	Cytokines ^{1,2}	Source cells ¹	Effector cells ¹
Type 1	IFN- γ IL-12	Th1 CTL ILC1	M1 macrophages NK cells
Type 2	IL-4 IL-5 IL-13	Th2 MC ILC2	M2 macrophages Eosinophils Basophils
Type 3	IL-17 IL-22	Th17 ILC3	Neutrophils

- Type 2 is the predominant endotype, however there is a marked geographic variation in its prevalence among patients with CRSwNP²



~85% in the US and Europe²



<50% in Eastern Asia, but increasing^{1,3}

- Patients with CRSwNP with type 2 inflammation have a higher disease burden than those with other endotypes¹

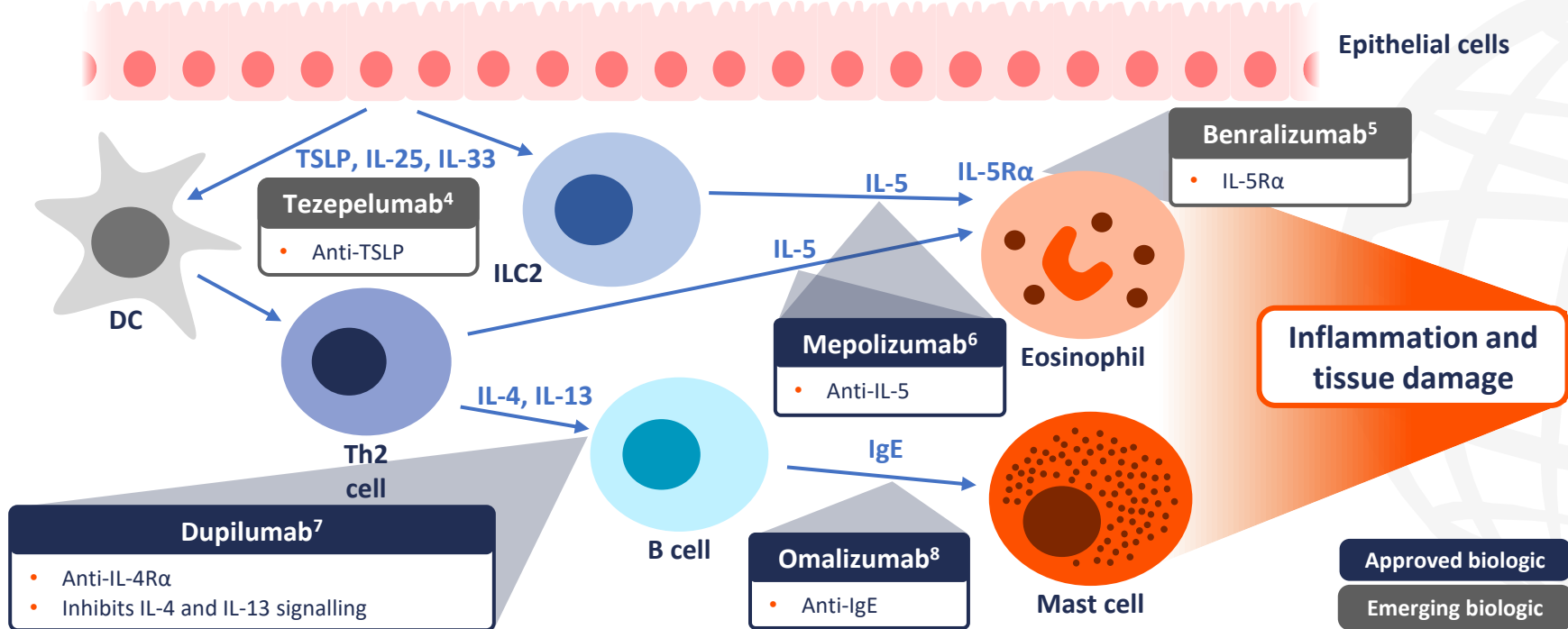
CRSwNP, chronic rhinosinusitis with nasal polyps; CTL, cytotoxic T lymphocyte; IFN, interferon; IL, interleukin; ILC, innate lymphoid cell; MC, mast cell; NK, natural killer; Th, T helper.

1. Kato A, et al. *Allergy*. 2021;77:812–26; 2. Staudacher AG, et al. *Ann Allergy Asthma Immunol*. 2020;124:318–25;

3. Cho SW, et al. *Asia Pac Allergy*. 2017;7:121–30.

Type 2 inflammation in CRSwNP and associated biologics¹⁻³

Allergens or pathogens



CRSwNP, chronic rhinosinusitis with nasal polyps; DC, dendritic cell; IgE, immunoglobulin E; IL, interleukin; ILC2, type 2 innate lymphoid cell; Rα, receptor alpha; Th2, T helper 2; TSLP, thymic stromal lymphopoietin.

1. Morse C, et al. *J Asthma Allergy*. 2021;14:873-82; 2. Hulse KE, et al. *Clin Exp Allergy*. 2015;45:328-46; 3. Ahern S, Cervin A. *Medicina (Kaunas)*. 2019;55:95;

4. Emson C, et al. *J Asthma Allergy*. 2021;14:91-9; 5. Bachert C, et al. *J Allergy Clin Immunol*. 2021. doi:10.1016/j.jaci.2021.08.030;

6. Han C, et al. *Lancet Resp Med*. 2021;9:1141-5; 7. Bachert C, et al. *Lancet*. 2019;394:1638-50; 8. Gevaert P, et al. *J Allergy Clin Immunol*. 2020;146:595-605.

What are the current and emerging treatment options for patients with CRSwNP?

Dr Sietze Reitsma



Management of CRSwNP and disease recurrence

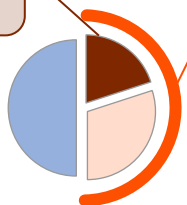
Stepwise treatment for CRSwNP



Failure to achieve disease control

20% of patients undergo revision surgery within 5 years¹

50% of patients show recurrence within 5 years¹



Disease recurrence

Considerations for biological treatment²

- Evidence of type 2 inflammation
- Confirmed diagnosis of severe uncontrolled CRSwNP*
- Comorbid asthma or N-ERD

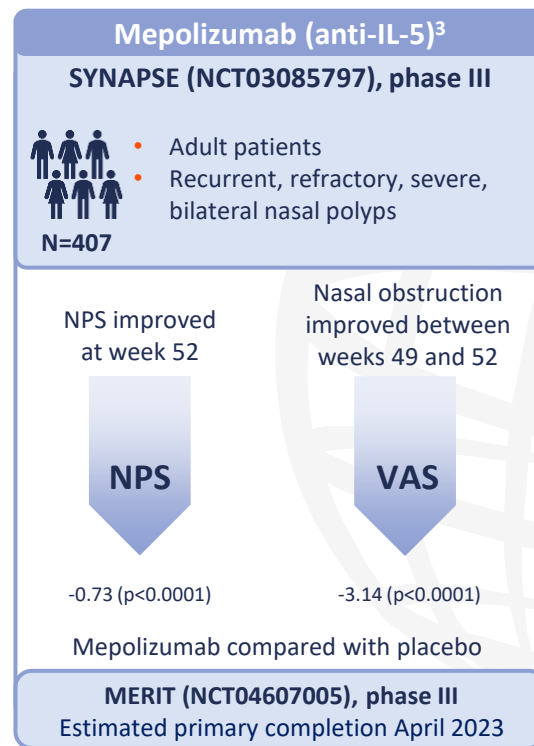
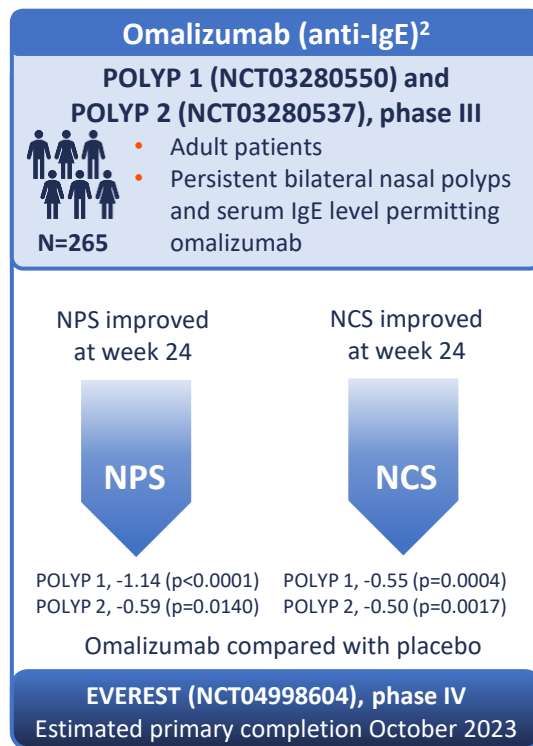
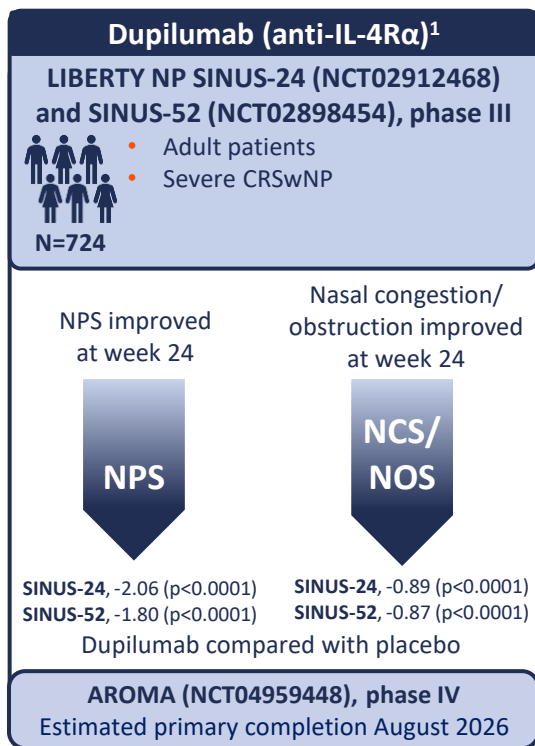
Dupilumab, mepolizumab or omalizumab

- Patients should be monitored after 6 and 12 months of biologic treatment to inform therapy continuation, switching or surgery²

*Severe uncontrolled CRSwNP defined as: persistent or recurring CRSwNP despite long-term ICS; systemic corticosteroids (≥1 course in the past 2 years) and/or previous sinonasal surgery (unless patient has a contraindication to/rejected surgery); bilateral CRSwNP with NPS ≥4. CRSwNP, chronic rhinosinusitis with nasal polyps; ICS, inhaled corticosteroids; N-ERD, nonsteroidal anti-inflammatory drug-exacerbated respiratory disease; NPS, nasal polyp score; OCS, oral corticosteroids.

1. Fokkens WJ, et al. *Allergy*. 2019;74:2312–19; 2. Bachert C, et al. *J Allergy Clin Immunol*. 2021;147:29–36.

Approved biologics for CRSwNP: Summary of RCT data



CRSwNP, chronic rhinosinusitis with nasal polyps; IgE, immunoglobulin E; IL, interleukin; IL-4R α , IL-4 receptor alpha; NCS, nasal congestion score; NOS, nasal obstruction score; NPS, nasal polyps score; RCT, randomized controlled trial; VAS, visual analogue scale.

1. Bachert C, et al. *Lancet*. 2019;394:1638–50; 2. Gevaert P, et al. *J Allergy Clin Immunol*. 2020;146:595–605; 3. Han C, et al. *Lancet Respi Med*. 2021;9:1141–53.

Clinical trials listed by their identifiers at: ClinicalTrials.gov (accessed 28 January 2022).

Emerging biologics for CRSwNP: Summary of RCT data

Benralizumab (anti-IL-5R α)¹

OSTRO (NCT03401229), phase III



N=413

- Adult patients
- Severe CRSwNP
- Symptomatic despite standard of care

NPS improved
at Week 40



($p \leq 0.005$)

NBS improved
at Week 40



($p \leq 0.005$)

Benralizumab compared
with placebo

ORCHID (NCT04157335), phase III

- Adults with ECRS with nasal polyps
- Recruiting (estimated enrolment: 276)
- Estimated primary completion September 2023

Tezepelumab (anti-TSLP)²

Post hoc analysis of PATHWAY (NCT04851964), phase IIb



n=82

- N=550 adult patients with severe asthma
- 15.2% of the study population had nasal polyps

Comparable AAER reduction at 52 weeks

CRSwNP



-75%

CRSsNP



-73%

Tezepelumab compared
with placebo

WAYPOINT (NCT04851964), phase III

- Adults with CRSwNP
- Recruiting (estimated enrolment: 400)
- Estimated primary completion February 2024

AAER, annual asthma exacerbation rate; CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; ECRS, eosinophilic chronic rhinosinusitis; IL-5R α , IL-5 receptor alpha; NBS, nasal blockade score; NPS, nasal polyps score; RCT, randomized controlled trial; TSLP, thymic stromal lymphopoietin.

1. Bachert C, et al. *J Allergy Clin Immunol*. 2021. doi:10.1016/j.jaci.2021.08.030; 2. Emson C, et al. *J Asthma Allergy*. 2021;14:91–9.

Clinical trials listed by their identifiers at: ClinicalTrials.gov (accessed 28 January 2022).