

# 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<sup>1–3</sup>
- Average incidence of CRSwNP vs CRSsNP reported as 83 ( $\pm$  13) vs 1048 ( $\pm$  78) cases/100,000 person-years<sup>3</sup>
- Among patients with asthma, 20–57% have CRS<sup>3,5</sup>

## Symptoms



- Smell reduction, nasal obstruction, rhinorrhoea/postnasal drip<sup>3</sup>
- Facial pain/pressure<sup>3</sup>
- Bad breath<sup>\*6</sup>
- Hearing impairment<sup>\*6</sup>

## Burden



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

\*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?*

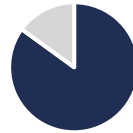
Dr Sietze Reitsma



# Endotypes associated with CRSwNP

	Cytokines <sup>1,2</sup>	Source cells <sup>1</sup>	Effector cells <sup>1</sup>
Type 1	IFN- $\gamma$ 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 CRSwNP<sup>2</sup>



~85% in the US and Europe<sup>2</sup>



<50% in Eastern Asia, but increasing<sup>1,3</sup>

- Patients with CRSwNP with type 2 inflammation have a higher disease burden than those with other endotypes<sup>1</sup>

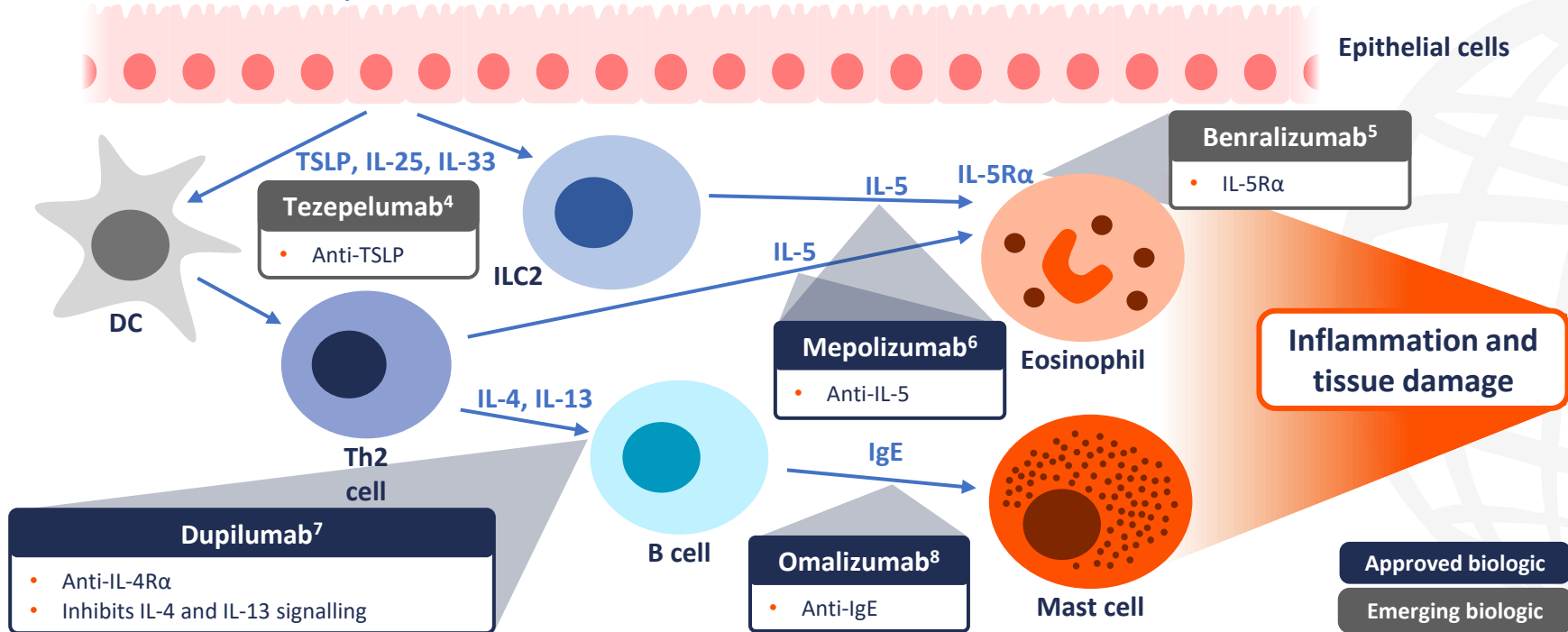
CRSwNP, chronic rhinosinusitis with nasal polyps; CTL, cytotoxic T lymphocyte; IFN, interferon; IL, interleukin; ILC, innate lymphoid cell; MC, mast cell; NK, natural killer; Th, T helper.

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 biologics<sup>1-3</sup>

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

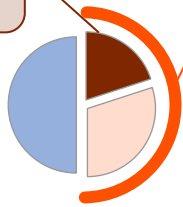
### Considerations for biological treatment<sup>2</sup>

- 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 surgery<sup>2</sup>

20% of patients undergo revision surgery within 5 years<sup>1</sup>

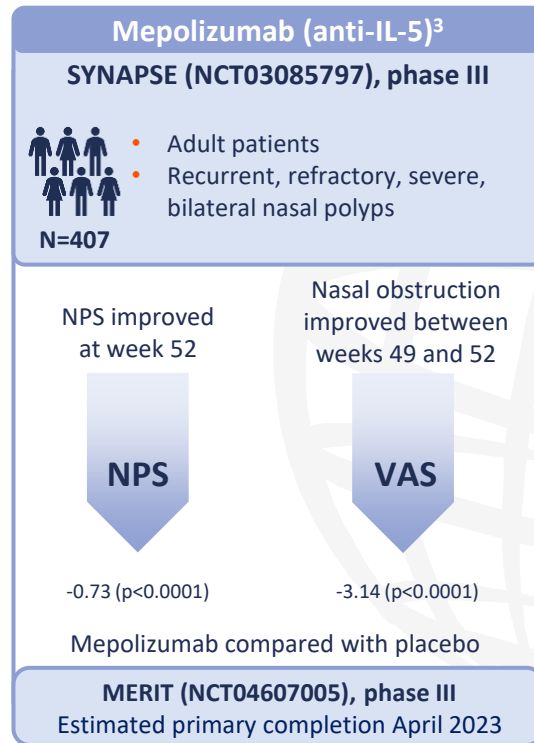
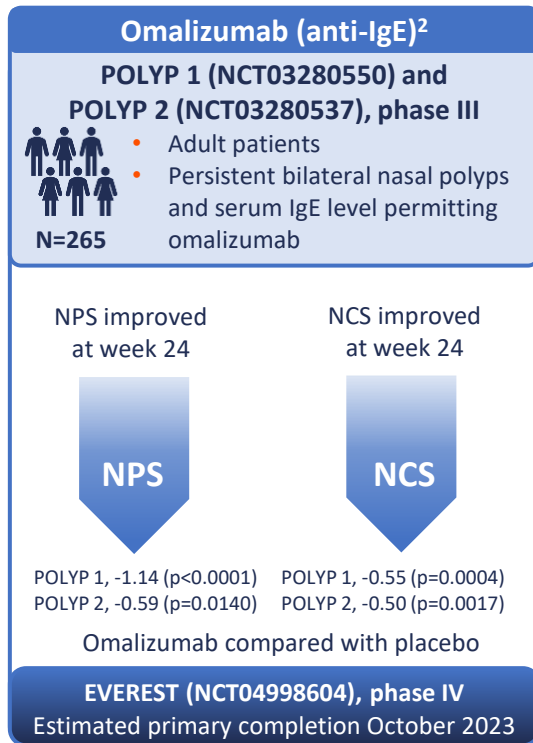
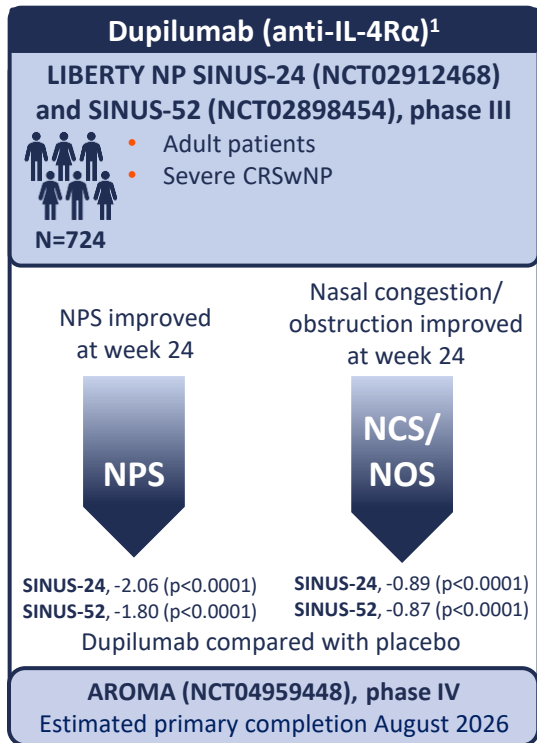


50% of patients show recurrence within 5 years<sup>1</sup>

\*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 $\alpha$ , 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](https://clinicaltrials.gov) (accessed 28 January 2022).

# Emerging biologics for CRSwNP: Summary of RCT data

## Benralizumab (anti-IL-5R $\alpha$ )<sup>1</sup>

### 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)<sup>2</sup>

### 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 $\alpha$ , 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](https://ClinicalTrials.gov) (accessed 28 January 2022).