

Improving Care for Patients with Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)

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Disclosures

- **Dr. Lee** is a consultant for AstraZeneca, GlaxoSmithKline, Genentech, Lyra Therapeutics, OptiNose and Sanofi/Regeneron.

During the program, the faculty may mention the use of medications for FDA-approved and non-approved indications

All relevant financial relationships have been mitigated.

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Learning Objectives

- Identify strategies to manage CRSwNP that are aligned with evidence-based guidelines
- Discuss the clinical evidence for novel, emerging therapeutic agents for the treatment of CRSwNP
- Describe strategies to effectively select treatment based on patient-specific factors and expert guidance

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Pre-read Material

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CRSwNP Biomarkers

- No accurate biomarkers for CRSwNP currently available
- Type 2 inflammation often predominates in CRSwNP
 - Associated with elevated levels of eosinophils and type 2 cytokines, including IL-4, IL-5, and IL-13, IgE
- Modalities utilized to obtain potential biomarkers
 - Sinus-tissue biopsy or mucus may be most accurate in assessing local processes underlying inflammation
 - Peripheral blood does not always reflect local nasal inflammatory processes
 - With nasal lavage, inconsistent correlation between cytokines in nasal secretions compared with tissue

NS = nasal secretions; PB = peripheral blood; TSLP = thymic stromal lymphoprotein.
Workman AD, et al. *Immunol Allergy Clin North Am*. 2018;38:679-692.

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Diagnosis of Uncontrolled/Severe CRSwNP: EUFOREA

Uncontrolled CRSwNP

Persistent or recurring CRSwNP despite:

Long-term INCS
+
Receiving 21 course of systemic CS
(≥0.5–1 mg/Kg/day for ≥5 days)* in the last 2 years†
±
Previous sinonasal surgery (eg, resection of polyps,
conventional ESS, or extended approaches)*

Severe CRSwNP

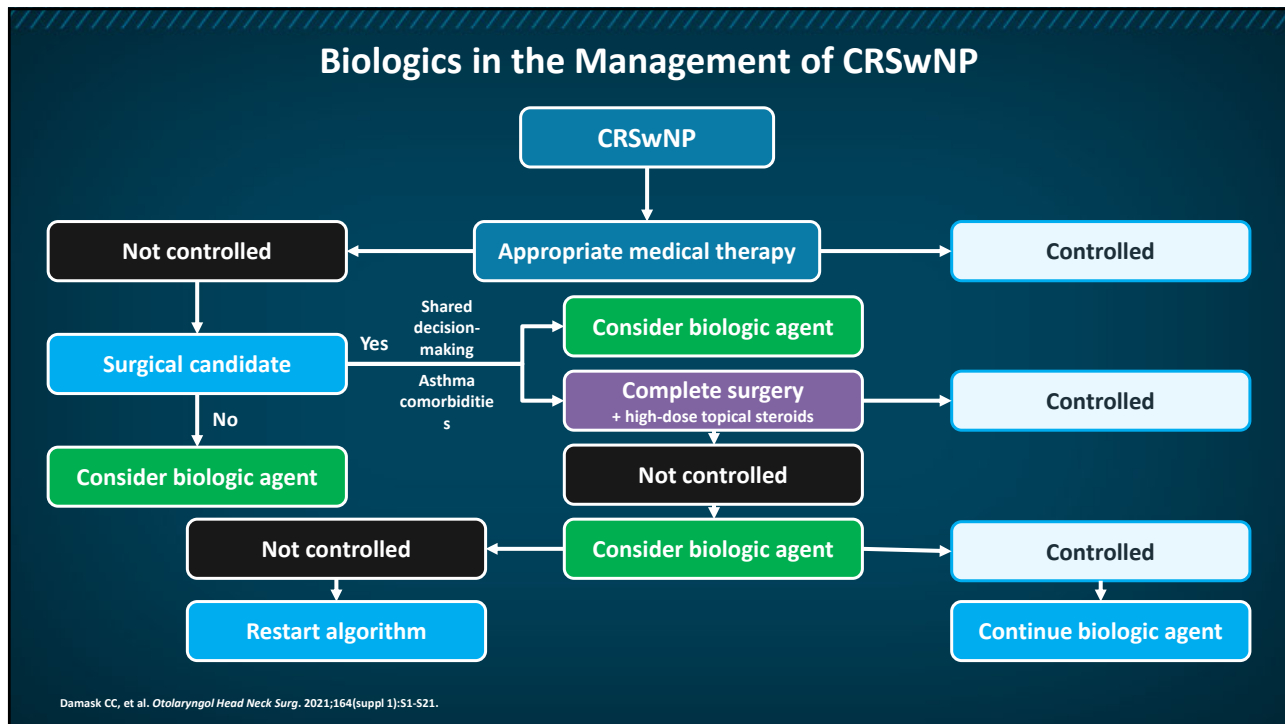
Defined as:

Bilateral CRSwNP (polyps by nasal endoscopy)
+
NPS ≥4 (out of 8)
±
Persistent symptoms despite long-term INCS with
the need for add-on treatment, assessed by

- Loss of smell score (0–3) ≥2 points
- NCS (0–3) ≥2 points
- SNOT-22 ≥35 points
- Total symptom VAS ≥5 out of 10 cm

*Unless having a medical contraindication or rejection by the patient. †Long-term low dose systemic corticosteroids is not recommended in CRSwNP.
CS = corticosteroid; ESS = endoscopic sinus surgery; INCS = intranasal corticosteroids; NCS = nasal congestion score; NPS = nasal polyp score; SNOT-22 = 22-item sinonasal outcome test; VAS = visual analog scale
Bachert C, et al. *J Allergy Clin Immunol*. 2021;147(1):29-36.

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Outcomes of Dupilumab vs Endoscopic Sinus Surgery

Inclusion criteria

- Adults (>18 years)
- Dupilumab treatment (with 23 months follow-up) or bilateral total FESS (with concomitant use of topical steroids)

Matching criteria

- NPS
- SNOT-22
- Age
- Sex
- Ethnicity

2015

2021

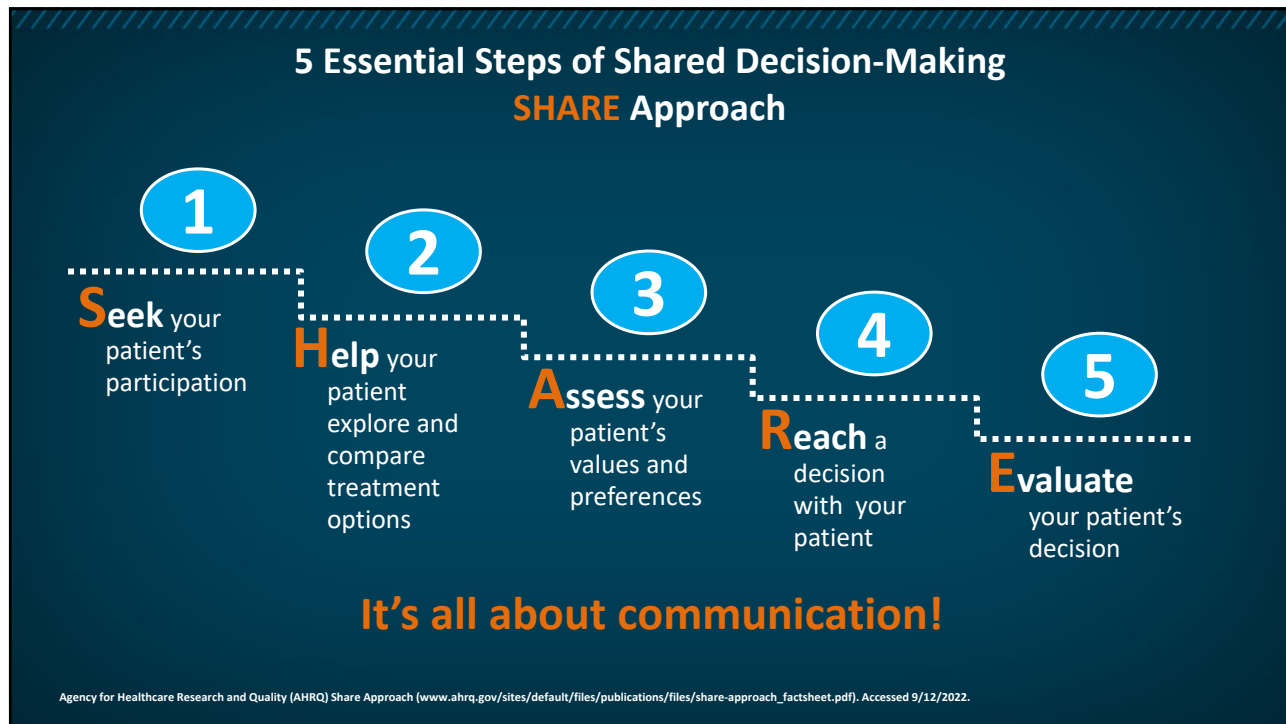
N = 108

| Baseline characteristics | | | | | |
|-----------------------------|-----------|----------|----------|----------|----------|
| | Dupilumab | NPS | SNOT-22 | FESS | NPS |
| N | 54 | 54 | 54 | 54 | 54 |
| Age (mean) | 52 years | 52 years | 52 years | 53 years | 53 years |
| NPS (mean) | 5.9 | 5.9 | 5.9 | 6.3 | 6.3 |
| SNOT-22 (mean score) | 38.2 | 38.2 | 38.2 | 43.1 | 43.1 |
| prior FESS (mean number of) | 2 | 2 | 2 | 1 | 1 |

CRSwNP = chronic rhinosinusitis with nasal polyps; FESS = functional endoscopic sinus surgery; NPS = nasal polyp score; q2w = every 2 weeks; SC = subcutaneous; SNOT-22 = Sino-Nasal Outcome Test-22.

Dharmarajan H, et al. *Int Forum Allergy Rhinol.* 2022;1-10.

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Corticosteroids: Evidence and Use for CRSwNP

Topical: Standard Delivery

Intranasal corticosteroids (standard delivery) for CRSwNP

Evidence: A (Level 1: 2 studies, Level 2: 5 studies)

Benefit: Improved symptoms, endoscopic appearances, polyp size, and QoL, objective tests of olfaction, airway analysis (NPIF) and polyp recurrence but the magnitude of the clinical effect is small

Harm: Epistaxis, nasal irritation, headache

Cost: Moderate depending on preparation

Intervention: Topical nasal CS (sprays or drops) are recommended for CRSwNP before or after sinus surgery; consideration for twice daily dosing or additional short-term corticosteroid drop if initial treatment effect is small

NPIF = nasal peak inspiratory flow.
Orlandi R, et al. *Int Forum Allergy Rhinol.* 2021;11(3):213-739.

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Corticosteroids: Evidence and Use for CRSwNP

Topical: Nonstandard Delivery

Intranasal corticosteroids (nonstandard delivery) for CRSwNP

Evidence (vs standard delivery):

Corticosteroid irrigation: A (Level 1: 5 studies, level 3: 1 study)

Exhalation delivery: A (Level 1: 4 studies)

Atomization/nebulization: A (Level 1: 4 studies)

Direct injection: N/A (Level 1: 1 study)

Benefit:

Corticosteroid irrigation: Benefit over INCS

Exhalation delivery: Benefit only over placebo

Atomization/nebulization: Benefit over INCS

Direct injection: Potential avoidance of oral corticosteroid

Harm: Some evidence of systemic absorption with first generation CS especially with multiple modalities of therapy

Cost: Moderate; exhalation system costs are significantly higher than standard therapy

Intervention: Following sinus surgery, those patients with CRSwNP that have moderate to severe disease or are not controlled with simple INCS should be offered CS irrigation and/or atomized delivery

Orlandi R, et al. *Int Forum Allergy Rhinol.* 2021;11(3):213-739.

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Recurrence of Polyps Following ESS

- In a cohort study comparing continued medical management vs ESS, subjects undergoing ESS were significantly more likely to experience
 - Improvement in thick nasal discharge (OR = 4.36)
 - Decreased facial pain/pressure (OR = 3.56)
 - Reduced blockage/congestion (OR = 2.76)
 - Return of smell and taste
- However, in a study of 560 patients 3 to 5 years post-ESS, 36.8% had partly controlled symptoms and 43.7% were uncontrolled

OR = odds ratio.

DeConde AS, et al. *Int Forum Allergy Rhinol.* 2015;5:36-45. van der Veen J, et al. *Allergy.* 2017;72:282-290.

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Omalizumab: Phase 3 POLYP 1 and POLYP 2 Trials

2 identical phase 3 trials investigating omalizumab in patients with inadequately controlled CRSwNP despite daily INCS therapy

Inclusion criteria

- 18 to 75 years of age
- Persistent bilateral NPs
- Nasal congestion
- Impaired HRQoL
- Weight and serum IgE levels permitting omalizumab dosing
- ≤4 weeks of INCS therapy before screening
- Total NPS of ≥5 (≥2 for each nostril)
- NCS of ≥2 at Day -35
- SNOT-22 score of ≥20 at Day -35 and randomization

| Week | -5 | -1 | 0 | 4 | 8 | 12 | 16 | 20 | 24 | 28 |
|----------------------|-----|----|---|----|----|----|-----|-----|-----|-----|
| Day | -35 | -7 | 1 | 28 | 56 | 84 | 112 | 140 | 168 | 196 |
| Screening visit | | | | | | | | | | |
| Randomization (1:1) | | | | | | | | | | |
| Background treatment | | | | | | | | | | |
| Assessment schedule | | | | | | | | | | |
| NPS | | • | | • | • | | | | • | • |
| SNOT-22 | • | | • | • | • | | | | • | • |
| UPSIT | | | • | • | • | | | | • | • |
| AQLQ | | | • | | | | | | • | • |

HRQoL = health-related QoL; PBO = placebo; Q2W = every 2 weeks; Q4W = every 4 weeks; SFU = safety follow-up; UPSIT = University of Pennsylvania Smell Identification Test.
Gevaert P, et al. *J Allergy Clin Immunol.* 2020;146:595-605.

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POLYP 1 and POLYP 2: More Results

| Improvement | Placebo (n = 131) | Omalizumab (n = 134) | P-value |
|--------------------------|-------------------|----------------------|----------------|
| NPS ≥2-point improvement | ~12% | ~32% | $P = .0003$ |
| NPS ≥1-point improvement | ~29% | ~56% | $P < .0001$ |
| NCS ≥1-point improvement | ~22% | ~45% | $P \leq .0001$ |

■ Placebo (n = 131)
■ Omalizumab (n = 134)

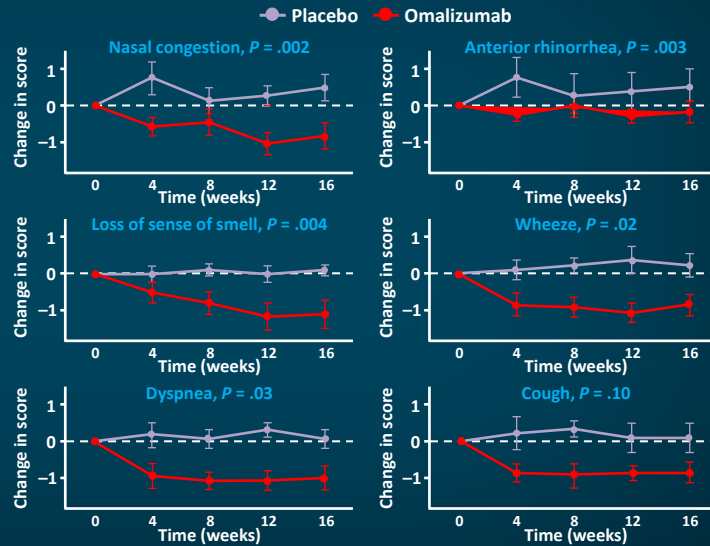
50.4% of omalizumab-treated patients and 58.5% of placebo-treated patients experienced at least 1 treatment-emergent adverse event (AE).

Gevaert P, et al. *J Allergy Clin Immunol.* 2020;146:595-605.

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Omalizumab in Allergic and Nonallergic Patients With Nasal Polyps and Asthma

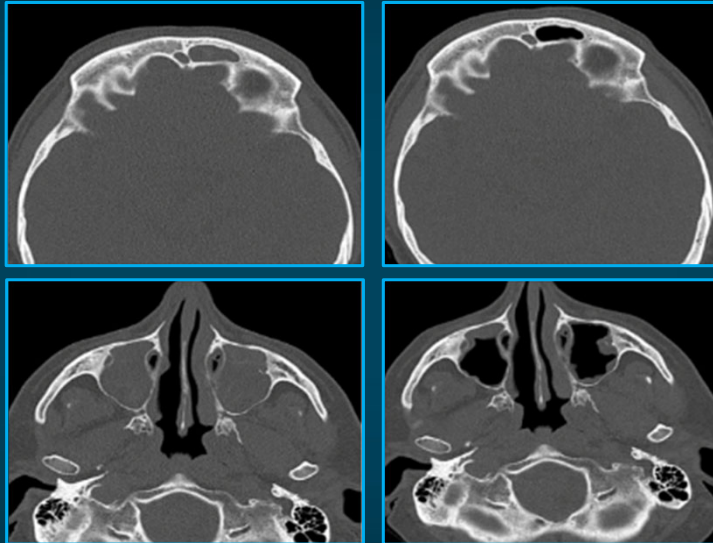
- RDBPC study of 24 patients with NPs and comorbid asthma
- Dosing based on IgE levels and body weight (max dose of 375 mg)
- Decrease in NPS after 16-week treatment (-2.67 , $P = .001$)
- Improvement in nasal and asthma symptom scores



RDBPC = randomized, double-blind, placebo-controlled.
Gevaert P, et al. *J Allergy Clin Immunol*. 2013;131:110-116.e1.

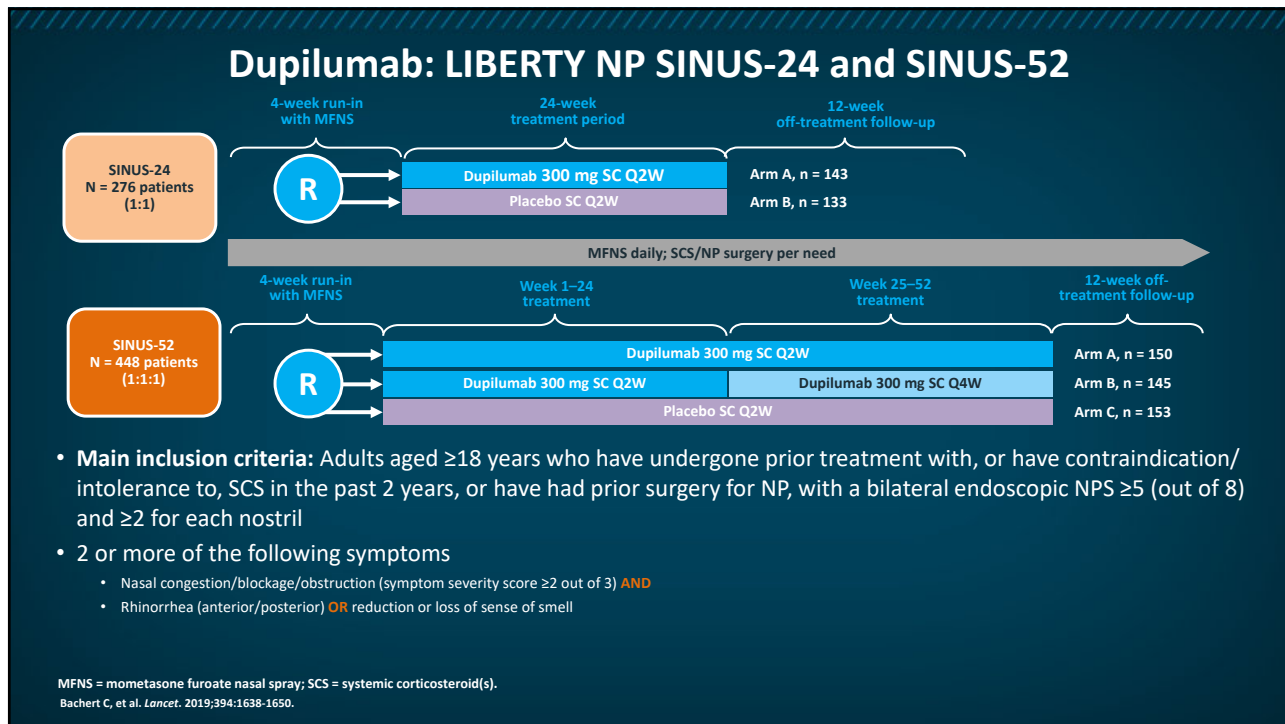
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CT Scans of Sinuses Before and 3 Months After Omalizumab

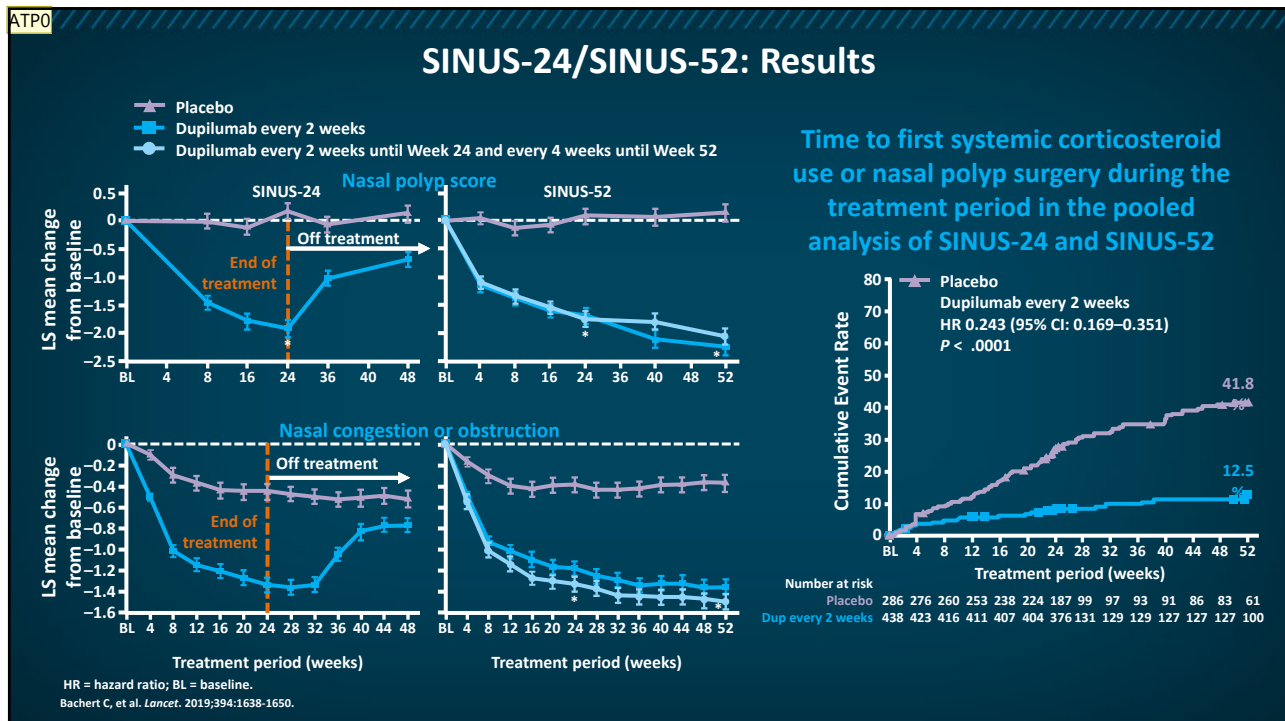


Bachert C, et al. *J Allergy Clin Immunol*. 2015;136:1431-1440.

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SINUS-24/SINUS-52: Conclusions

- In patients with severe uncontrolled CRSwNP, dupilumab as add-on to MFNS
 - Significantly improved NP size, sinus opacification, and CRS symptoms
 - Reduced anosmia and improved HRQoL
 - Improved all outcome measures, which were noted at first assessment timepoint and continued to improve across 52-week treatment period
- Dupilumab reduced SCS use and need for NP surgery
- Dupilumab improved lung function and asthma control in patients with CRSwNP with comorbid asthma, a difficult-to-treat patient population
- Compared with 300 mg Q2W to Q4W, the 300 mg Q2W regimen had
 - Better sustained improvements in objective measures of NPS and LMK-CT scan score
 - Fewer breakthrough TEAEs of worsening of nasal polyps, asthma, and sinusitis

Bachert C, et al. *Lancet*. 2019;394:1638-1650.

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2015

2021

Dupilumab 300 mg Q2W SC

Bilateral complete FESS

N = 108

Baseline characteristics

Matching criteria

- NPS
- SNOT-22
- Age
- Sex
- Ethnicity

| | Dupilumab | N = 54 | 52 years (mean age) | 5.9 NPS (mean) | 38.2 SNOT-22 (mean score) | 2 prior FESS (mean number of) |
|--|-----------|--------|------------------------|-------------------|------------------------------|----------------------------------|
| | FESS | N = 54 | 53 years (mean age) | 6.3 NPS (mean) | 43.1 SNOT-22 (mean score) | 1 prior FESS (mean number of) |

CRSwNP = chronic rhinosinusitis with nasal polyps; FESS = functional endoscopic sinus surgery; NPS = nasal polyp score; q2w = every 2 weeks; SC = subcutaneous; SNOT-22 = Sino-Nasal Outcome Test-22.

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