Effective Management of Chronic Rhinosinusitis with Nasal Polyps (CRSwNP): Tips for the Practicing Community-based Clinician

Stella E. Lee, MD

Section Chief, Rhinology
Division of Otolaryngology—Head and Neck Surgery
Department of Surgery
Brigham and Women's Hospital
Harvard Medical School
Boston, MA

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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 scaleE
Bachert C, et al. *J Allergy Clin Immunol.* 2021;147(1):29-36.

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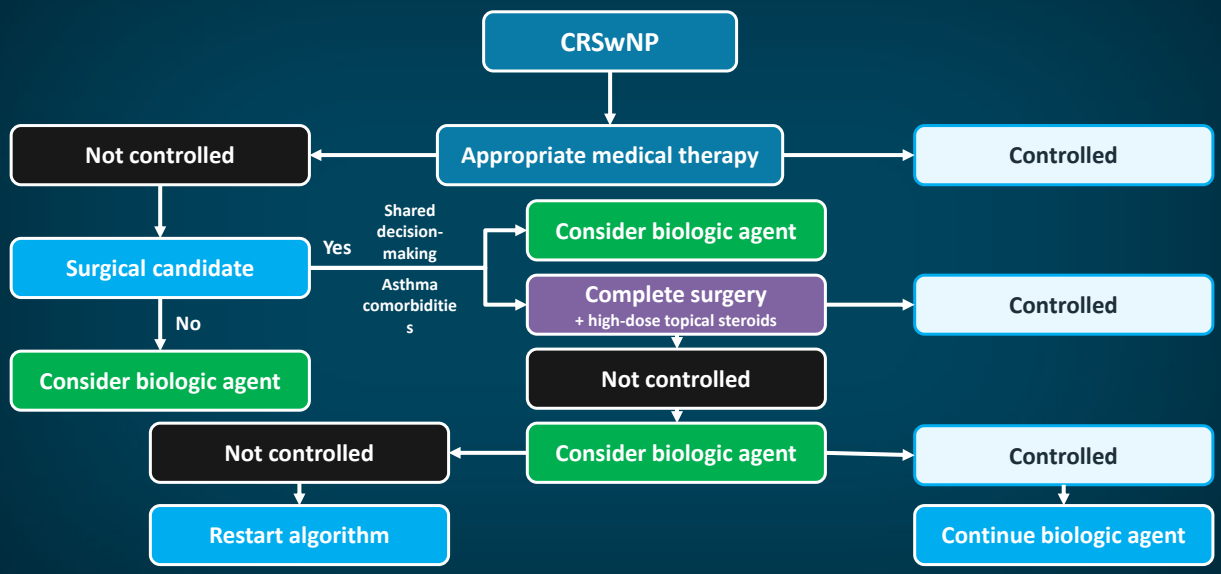
Biologics in the Management of CRSwNP



Damask CC, et al. *Otolaryngol Head Neck Surg*. 2021;164(suppl 1):S1-S21.

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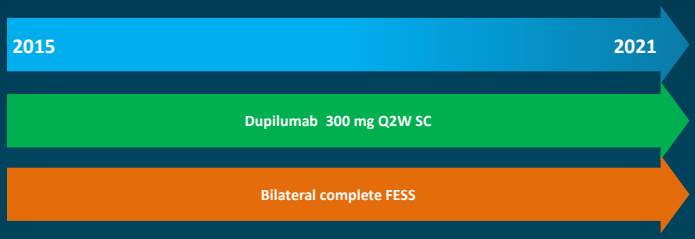
Outcomes of Dupilumab vs Endoscopic Sinus Surgery

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



N = 108

Baseline characteristics

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.

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

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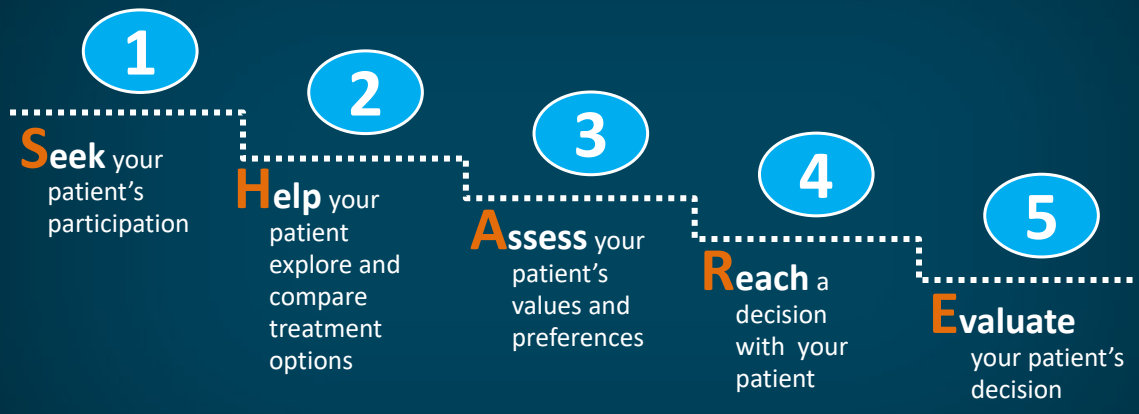
5 Essential Steps of Shared Decision-Making
SHARE Approach



It's all about communication!

Agency for Healthcare Research and Quality (AHRQ) Share Approach (www.ahrq.gov/sites/default/files/publications/files/share-approach_factsheet.pdf). Accessed 9/12/2022.

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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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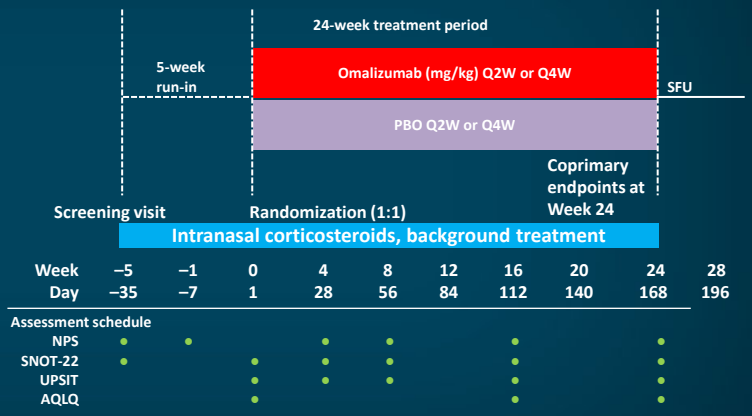
Omalizumab: Phase 3 POLYP 1 and POLYP 2 Trials

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



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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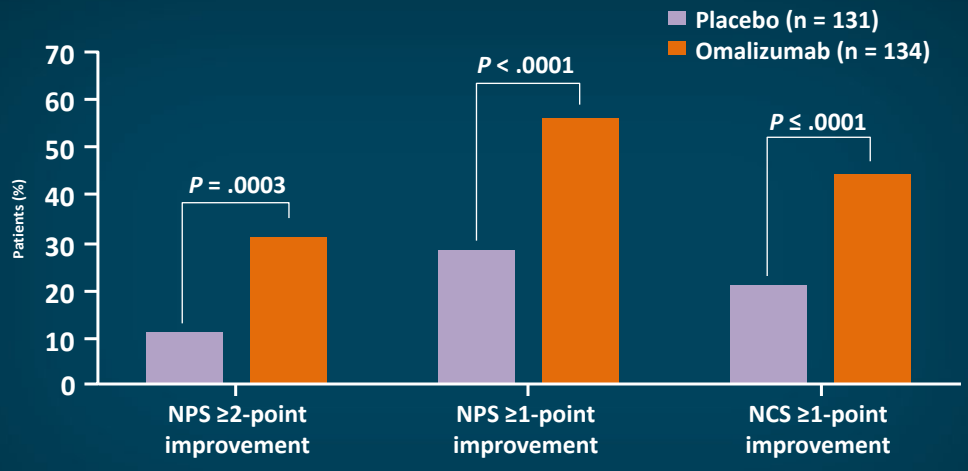
POLYP 1 and POLYP 2: More Results



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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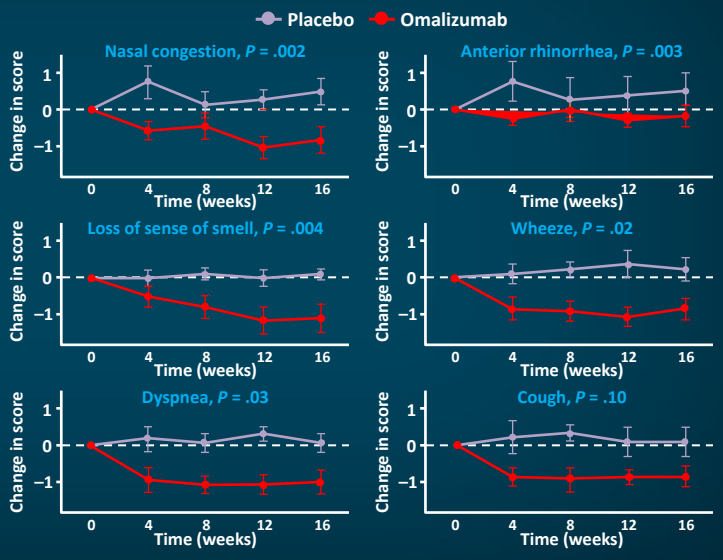
Omalizumab in Allergic and Nonallergic Patients With Nasal Polyps and Asthma

- 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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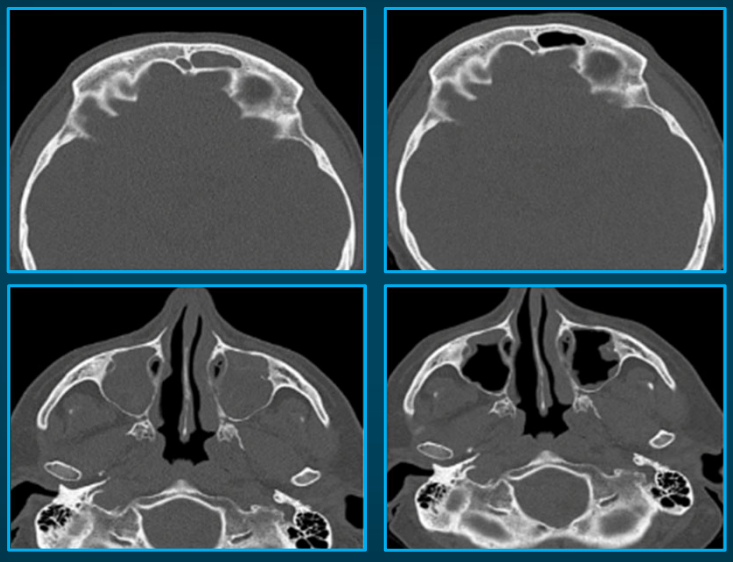
CT Scans of Sinuses Before and 3 Months After Omalizumab



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

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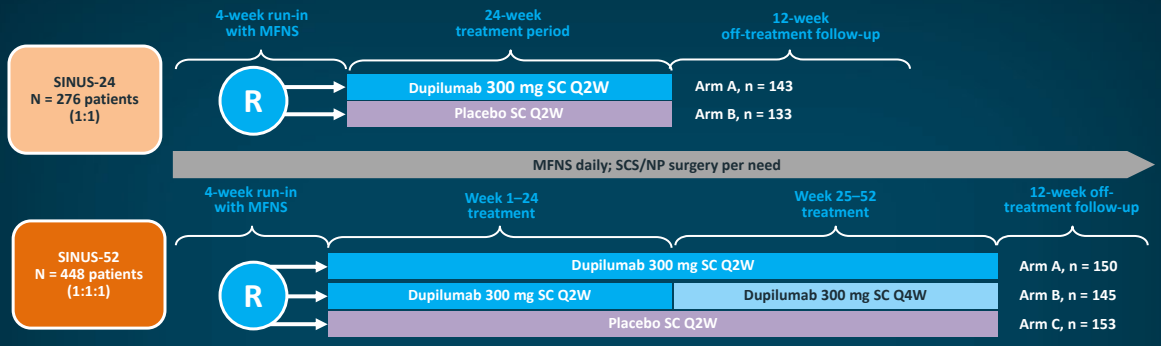
Dupilumab: LIBERTY NP SINUS-24 and SINUS-52



- **Main inclusion criteria:** Adults aged ≥18 years who have undergone prior treatment with, or have contraindication/ intolerance to, SCS in the past 2 years, or have had prior surgery for NP, with a bilateral endoscopic NPS ≥5 (out of 8) and ≥2 for each nostril
- 2 or more of the following symptoms
  - Nasal congestion/blockage/obstruction (symptom severity score ≥2 out of 3) **AND**
  - Rhinorrhea (anterior/posterior) **OR** reduction or loss of sense of smell

MFNS = mometasone furoate nasal spray; SCS = systemic corticosteroid(s).

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

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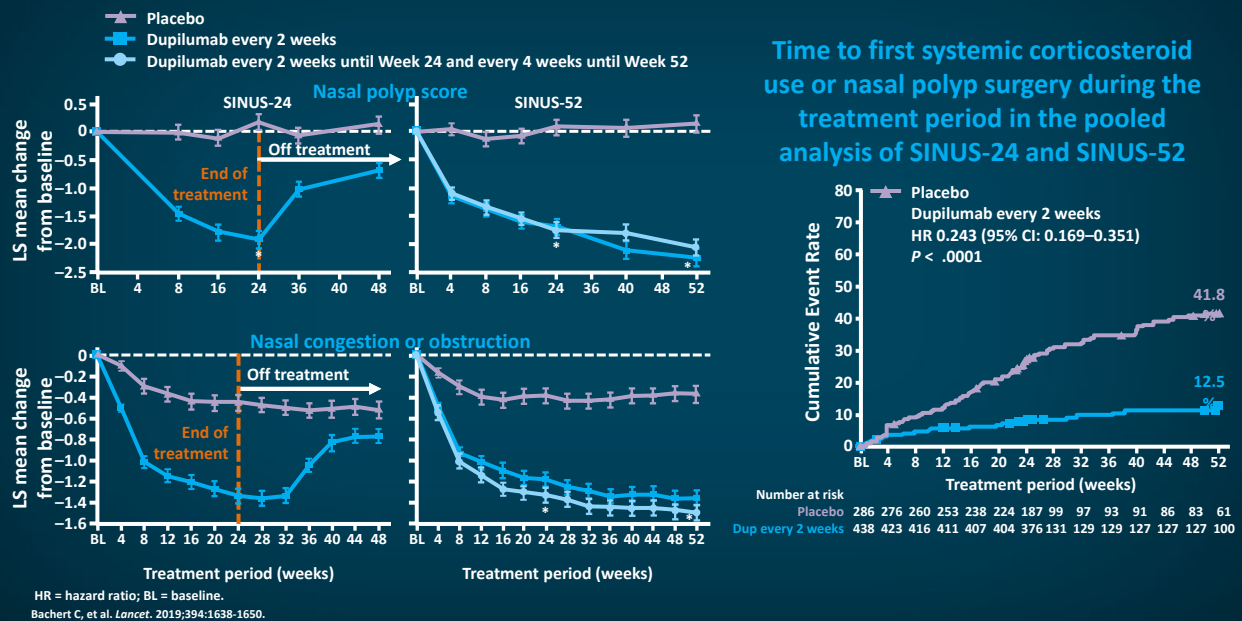
ATP0

SINUS-24/SINUS-52: Results



HR = hazard ratio; BL = baseline.

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

Time to first systemic corticosteroid use or nasal polyp surgery during the treatment period in the pooled analysis of SINUS-24 and SINUS-52

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Slide 18

ATP0 Too busy. There are figures available.
Anju Tripathi Peters, 2023-07-20T22:04:48.227

DG0 0 Added figures
Debra Gordon, 2023-07-27T15:00:46.917

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

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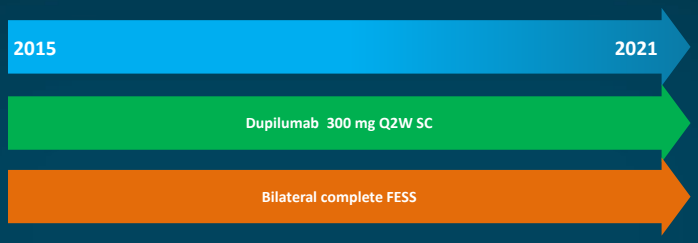

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