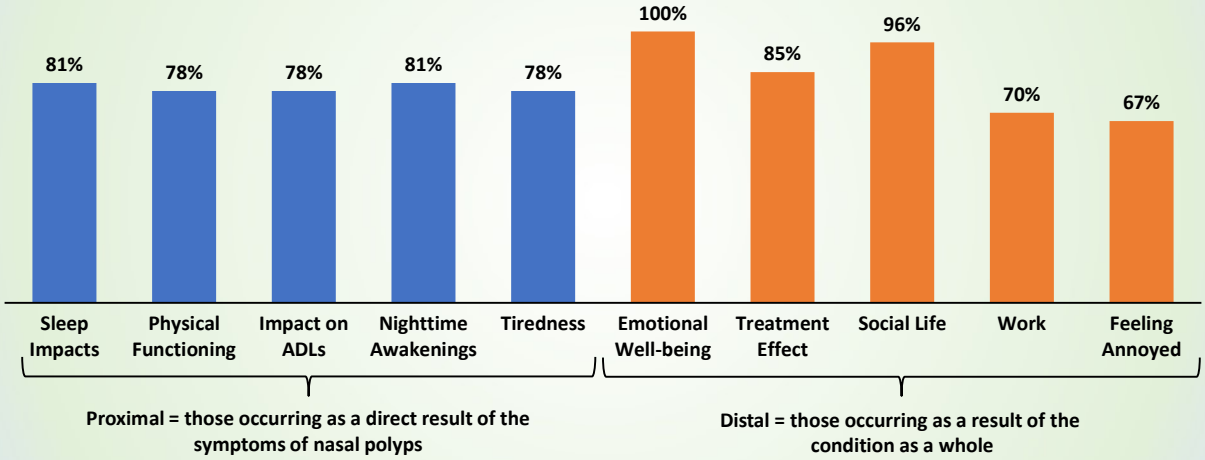
Patient Experience With Severe NP: A Qualitative Interview Study

Proximal and Distal Impacts of CRSwNP Reported in Patient Interviews (N=27)



ADL, activities of daily living.

Hall R, et al. *Value Health*. 2020 May;23(5):632-641.

Patient-Reported Outcome Measure: CRS-PRO

- 12-item patient-completed questionnaire assessing impact of CRS in previous 7 days
- Concise, valid, and reliable measure of CRS patient impact
- Developed with extensive input from patients with CRS
- Correlated highly with SNOT-22 in validation study

CRS-PRO – Please answer each of the following questions about how your chronic rhinosinusitis affects you. In the past 7 days …					
Physical Symptoms	**Not at All**	**A Little Bit**	**Somewhat**	**Quite a Bit**	**Very Much**
1. I had difficulty breathing through my nose	0	1	2	3	4
2. I felt pressure in my face	0	1	2	3	4
3. My face hurt	0	1	2	3	4
4. I had to blow my nose	0	1	2	3	4
5. I have been coughing	0	1	2	3	4
6. I had mucus in my throat	0	1	2	3	4
7. I had mucus in my nose	0	1	2	3	4
Sensory Impairment	**Not at All**	**A Little Bit**	**Somewhat**	**Quite a Bit**	**Very Much**
8. I had problems with my sense of smell	0	1	2	3	4
Psychosocial Effects	**Not at All**	**A Little Bit**	**Somewhat**	**Quite a Bit**	**Very Much**
9. My symptoms kept me awake at night	0	1	2	3	4
10. I felt fatigued	0	1	2	3	4
11. I worried that my condition will get worse	0	1	2	3	4
12. I was frustrated by my condition	0	1	2	3	4

CRS-PRO, Chronic Rhinosinusitis Patient-Reported Outcome; SNOT-22, Sino-nasal Outcome Test.

Ghadersohi S, et al. *J Allergy Clin Immunol Pract*. 2020;8(7):2341-2350.

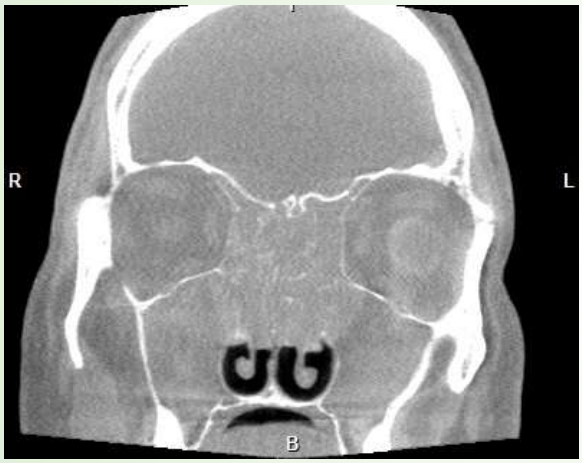
Josh, 36-year-old Male: Presentation

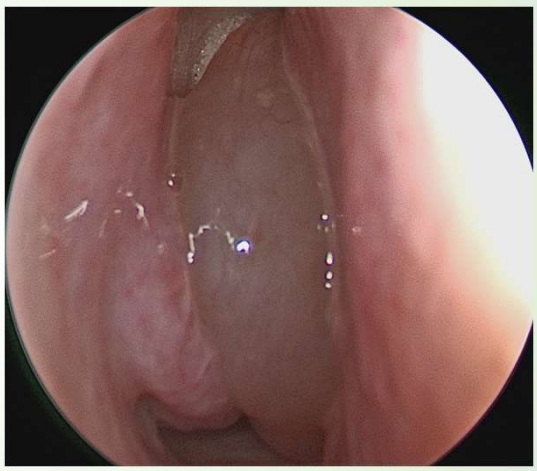
- Josh is a former Flyers hockey player who presents with severe nasal drainage, congestion, and loss of smell
- History:
  - Diagnosed 3 years ago with CRSwNP; no prior surgery
  - Mild atopic dermatitis with seasonal flares
  - Asthma since childhood
    - 2 exacerbations in past year requiring OCS
    - 1 exacerbation precipitated by use of NSAIDs following hockey injury
- Current medications:
  - Albuterol as needed for asthma
  - Intranasal steroid
  - Topical corticosteroids for atopic dermatitis flares
- FEV_1 = 69% predicted

INTEGRITY CONTINUING EDUCATION

OCS, oral corticosteroids; NSAID, nonsteroidal anti-inflammatory drug.

CT and Endoscopic Exam Reveal





INTEGRITY CONTINUING EDUCATION

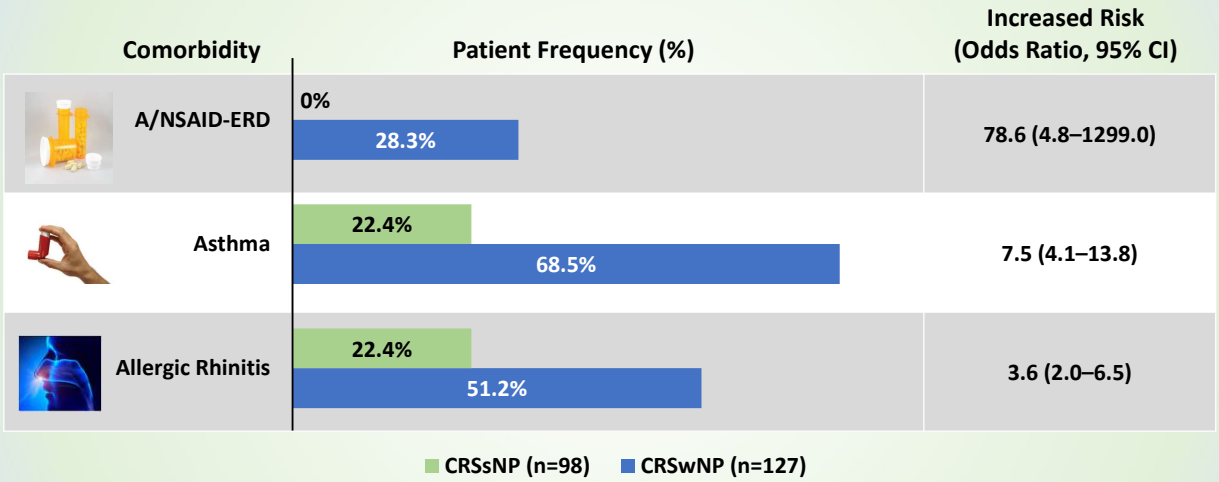
Josh, 36-year-old Male: Care Plan and Follow-up

- Josh was prescribed:
  - Short course OCS
  - Low-dose ICS for asthma
  - EDS-FLU
- Advised to avoid NSAIDS or ASA
- On follow-up 2 months later:
  - Josh reports compliance with therapies and described temporary relief following previous visit
  - After OCS, symptoms returned and he is experiencing a loss of smell and inability to sleep
  - Had asthma exacerbation 10 days ago requiring acute treatment with repeated bursts of albuterol and reports he had increase in daily asthma symptoms in week preceding exacerbation
  - Hospital pulmonologist prescribed a medium dose ICS + LABA for maintenance therapy and to be used as a reliever

INTEGRITY CONTINUING EDUCATION

CS, corticosteroids; EDS-FLU, Exhalation Delivery System With Fluticasone; ASA, aspirin; ICS + LABA, inhaled corticosteroids + long-acting beta agonist.

CRSwNP and Frequently Associated Comorbidities



A/NSAID-ERD, aspirin/nonsteroidal anti-inflammatory drug-exacerbated respiratory disease.

Batra PS, et al. *Laryngoscope*. 2013;123(Suppl 7):S1-S11.

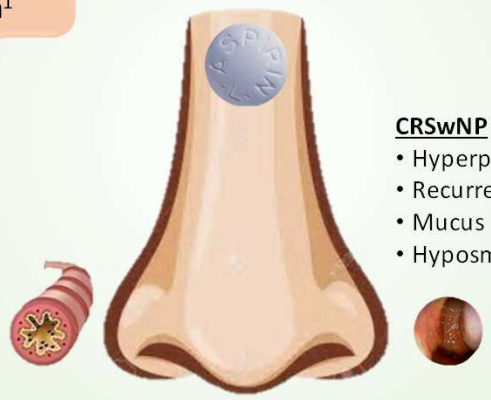
INTEGRITY CONTINUING EDUCATION

CRSwNP and Aspirin/NSAID-ERD

A/NSAID-ERD occurs in ~30% of patients with CRSwNP and asthma[1]

Hypersensitivity to aspirin & NSAIDs[2]
- Also reactive to COX-1 inhibitors
- Generally tolerate COX-2 inhibitors

Asthma
- More severe than average
- More difficult to control
- Increased risk of death
- Mucus production
- Smooth muscle contractility
- Bronchoconstriction
- Airway hyper-responsiveness
- Wheezing



CRSwNP
- Hyperplastic pansinusitis
- Recurrent eosinophil-rich nasal polyps
- Mucus production
- Hyposmia/anosmia

COX-1(-2), cyclo-oxygenase-1(-2).

1. Bachert C, et al. *Nat Rev Dis Primers*. 2020;6:86; **2**. Laidlaw TM, et al. *J Allergy Clin Immunol Pract*. 2021;9:1133-1141.

INTEGRITY CONTINUING EDUCATION

Standard-of-Care Medical Management

- Saline irrigation
  - Some benefit (compared with placebo) from daily, large-volume (150 mL) irrigation with hypertonic solution
  - No benefit from low-volume (5 mL) nebulized saline spray
- Intranasal corticosteroids
  - Nasal sprays, nasal installations/drops, EDS-FLU
- Oral corticosteroids
  - Acute relief for severe blockage and loss of smell
- Antibiotics
  - Prior RCT demonstrating small but significant benefit using doxycycline, possibly due to contribution of *S. aureus* to CRSwNP pathogenesis

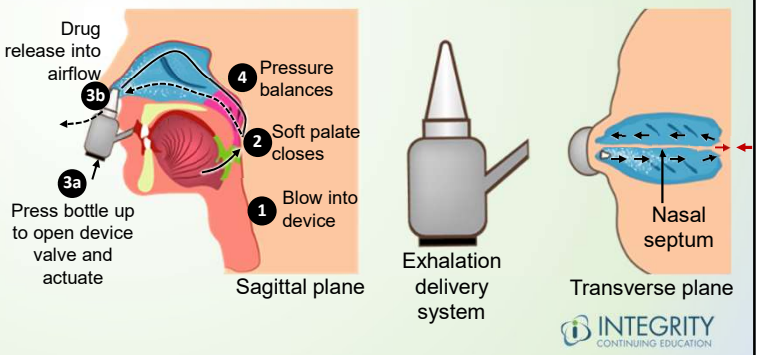
RCT, randomized controlled trial.

Blaiss MS. *Allergy Asthma Proc*. 2020;41:413-419; Chong LY, et al. *Cochrane Database Syst Rev*. 2016;4:CD011995; Naclerio R, et al. *J Allergy Clin Immunol Pract*. 2020;8:1532-1549; Kern RC, et al. *Int Forum Allergy Rhino*. 2018;8:471-481.

INTEGRITY CONTINUING EDUCATION

Exhalation Delivery System With Fluticasone

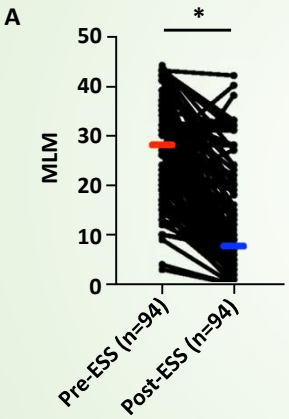
- EDS-FLU, intranasal spray delivers fluticasone to posterior sinus cavity
- FDA approved in 2017 based on results from phase 3 NAVIGATE II trial
  - 323 patients with moderate to severe CRSwNP for 16-week duration
  - Polyps reduced in size: ~-1.3 in EDS-FLU vs -0.6 in placebo
  - Polyps eliminated in 25% on at least 1 side by week 24 vs 8.7% with placebo
  - SNOT-22 score improved significantly, up to –21.4
  - Need for surgery decreased by 62%–67%



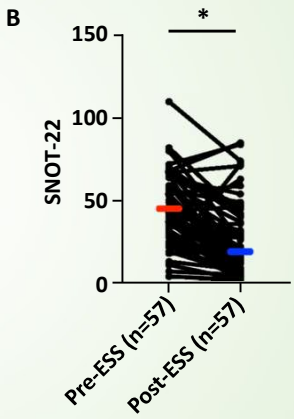
Leopold DA, et al. *J Allergy Clin Immunol*. 2019;143:126-134.

Evaluation of Disease Severity at Pre- and Post-ESS Time Points

Pre- and Post-ESS Radiographic Severity Measured by MLM (Matched Pairs)



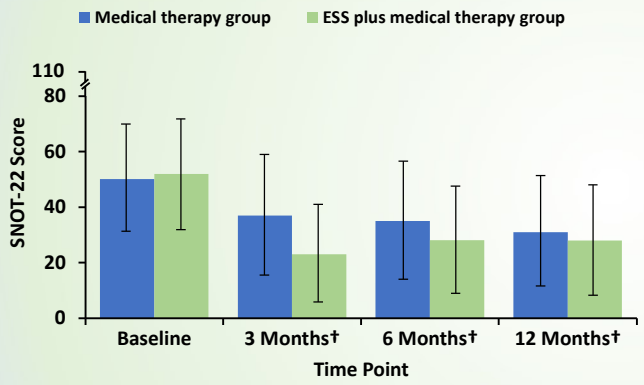
Pre- vs Post-ESS Levels of SNOT-22 (Matched Pairs)



Red and blue lines indication median for pre- and post-ESS, respectively. Wilcoxon matched-pairs signed-rank test used for comparison.
*P <.0001.
ESS, endoscopic sinus surgery; MLM, Modified Lund-Mackay Score.
Bai J, et al. *J Allergy Clin Immunol*. 2022. doi:10.1016/j.jaci.2022.02.029

ESS + Medical Therapy Improved CRSwNP Symptoms vs Medical Therapy Alone Over 12 Months – A Randomized Controlled Trial

Mean SNOT-22 Score at Each Time Point*



Baseline Severity in Both Treatment Arms

	ESS Plus Medical Therapy Group (n=118)	Medical Therapy Only Group (n=116)
Lund-Mackay score, points		
Mean	18.4 (4.3)	18.5 (4.9)
0–4	1/112 (1%)	0/111 (0%)
5–9	1/112 (1%)	4/111(4%)
10–14	20/112 (18%)	27/111 (24%)
15–24	90/112 (80%)	80/111 (72%)
Aeroallergen sensitization	64 (54%)	62 (53%)
SNOT-22 score		
Mean	51.9 (20.4)	50.5 (19.7)
0 to <20	10 (8%)	4 (3%)
20 to <40	24 (20%)	33 (28%)
40 to <60	39 (33%)	42 (36%)
60 to <80	34 (29%)	28 (24%)
≥80	11 (9%)	9 (8%)
EQ-5D-5L utility score	0.8 (0.2)	0.8 (0.2)
EQ-5D-5L VAS, mm	70.9 (17.02)	70.0 (17.2)

*Error bars indicate SDs. In the medical therapy group, 116 patients were assessable at baseline, 113 at 3 months, 107 at 6 months, and 103 at 12 months. In the ESS plus medical therapy group, 118 at baseline, 106 at 3 months, 107 at 6 months, and 103 at 12 months.
†The minimal clinically important difference of SNOT-22 is 9 points. Adjusted mean differences at 3, 6, and 12 months, were -15.2, -8.3, and -4.9, respectively.
EQ-5D-5L, EuroQuol Five Dimension, Five Level scale; SD, standard deviation; VAS, visual analogue scale.
Lourijsen E, et al. *The Lancet*. 2022;10(4):337-346.

INTEGRITY CONTINUING EDUCATION

Martha, 41-year-old Female: Presentation

- Martha is a 41-year-old female with asthma and allergic rhinitis (AR). She presents to your clinic with nasal congestion and a decrease in the sense of smell. On exam you notice bilateral nasal polyps. Her asthma is not bothering her.

PMHx:

- Asthma
- AR (skin test + dust mites, molds)

Clinical Values:

- FEV_1: 69% predicted

INTEGRITY CONTINUING EDUCATION

FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; PMHx, prior medical history.

OCS Was Prescribed But Did Not Offer Relief. What Is Your Next Step?

OCS is prescribed to Martha; however, her symptoms came back as soon as she finished her course. OCS course really bothered Martha as well because it kept her up at night which made her unproductive for work.

OCS, oral corticosteroids.

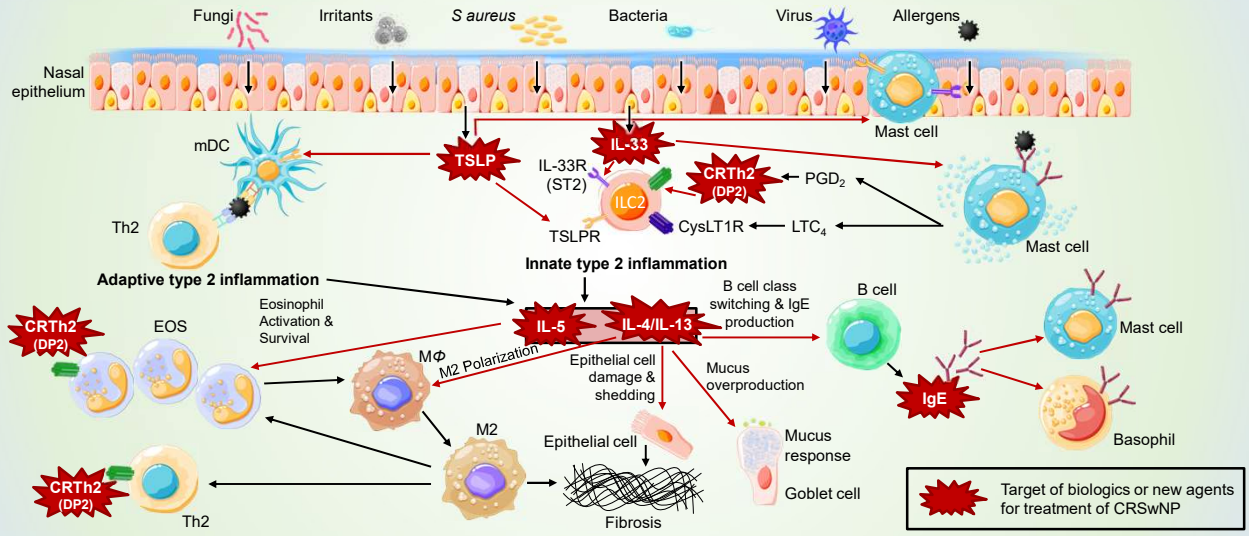
INTEGRITY CONTINUING EDUCATION

Treatment Options

ENT evaluation for surgery and/or biologic

INTEGRITY CONTINUING EDUCATION

Immunopathology of CRSwNP and Current Therapeutic Targets



CRTh2, chemoattractant receptor-homologous molecule expressed on Th2 cells; CysLT1r, cysteinyl leukotriene type 1 receptor; IgE, immunoglobulin E; IL, interleukin; LTC4, leukotriene C4; mDC, myeloid dendritic cell; PGD2, prostaglandin D2; Th, T-helper cell; TSLP, thymic stromal lymphopoietin.
Laidlaw TM, et al. *Ann Allergy Asthma Immunol*. 2020;124:326-332.

INTEGRITY CONTINUING EDUCATION

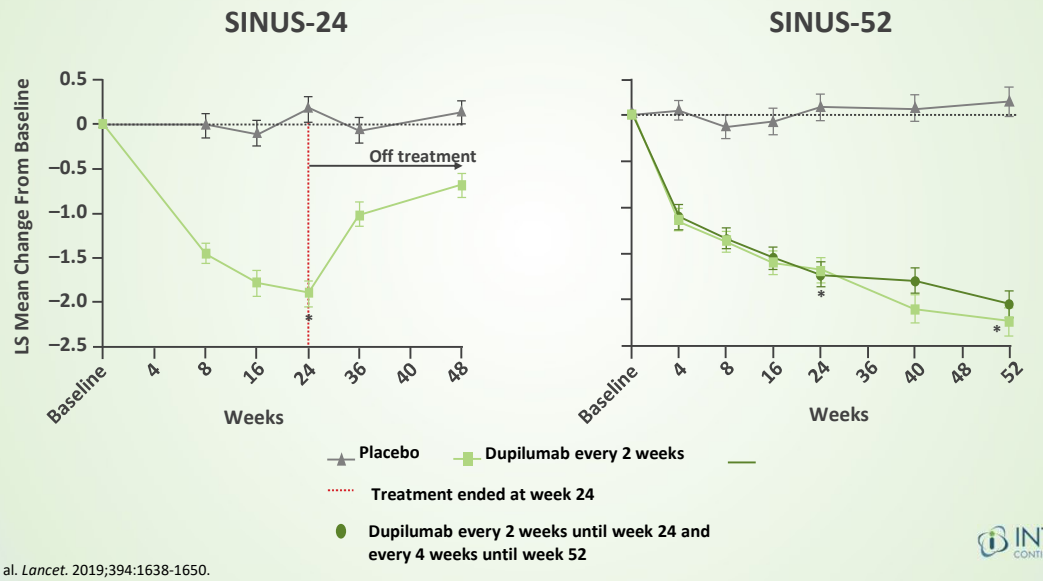
FDA-Approved Biologics for CRSwNP

Biologic	Target	FDA Indication	Phase 3 Trials	Number of Patients
Dupilumab	IL-4 IL-13	Add-on maintenance treatment in adult patients with inadequately controlled CRSwNP.	SINUS-24[1] SINUS-52[1]	276 448
Omalizumab	IgE	Nasal polyps in adult patients 18 years of age and older with inadequate response to nasal corticosteroids, as add-on maintenance treatment.	POLYP-1[2] POLYP-2[2]	138 127
Mepolizumab	IL-5	Add-on maintenance treatment of adult patients 18 years and older with CRSwNP.	SYNAPSE[3,4]	407

1. Bachert C, et al. *Lancet*. 2019;394:1638-1650. **2**. Geveart P, et al. *J Allergy Clin Immunol*. 2020;146:595-605. **3**. Han JK, et al. *Lancet Respir Med*. 2021;9:1141-1153.
4. Hopkins C, et al. *Eur Respir J*. 2020;56:4616.
Dupixent (dupilumab) [package insert]. Revised 2022. Accessed 2022. https://www.regeneron.com/downloads/dupixent_fpi.pdf
Xolair (omalizumab) [package insert]. Revised 2021. Accessed 2022. https://www.gene.com/download/pdf/xolair_prescribing.pdf
Nucala (mepolizumab) [package insert]. Revised 2021. Accessed 2022.
https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Nucala/pdf/NUCALA-PI-PIL-IFU-COMBINED.PDF.

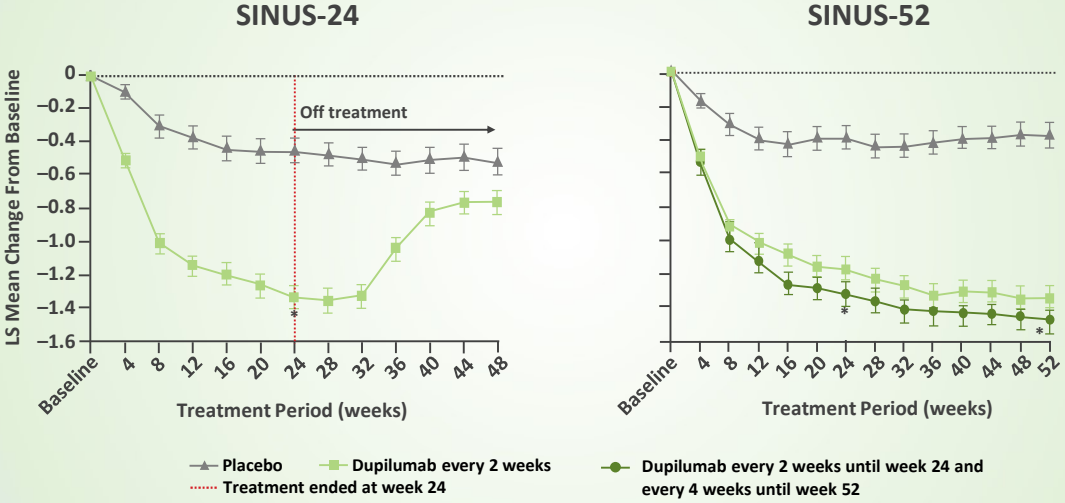
INTEGRITY CONTINUING EDUCATION

Decrease in Polyp Size With Dupilumab



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

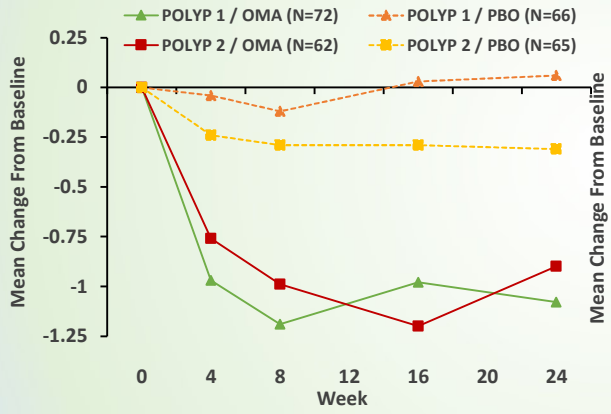
Decrease in Nasal Congestion With Dupilumab



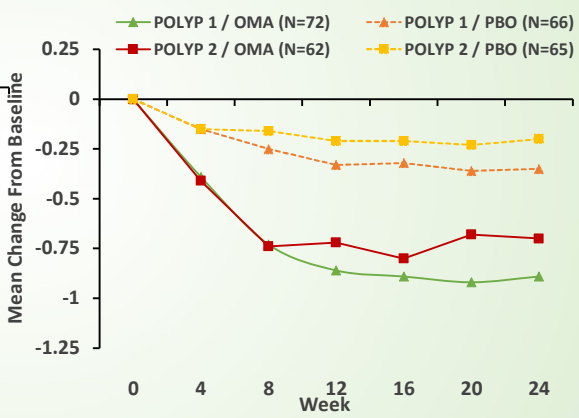
Bachert C, et al. *Lancet*. 2019;394:1638-1650.

Omalizumab: Co-Primary Endpoints: Change from Baseline to Week 24 in Nasal Congestion Score and Nasal Polyp Score

Nasal Polyp Score



Nasal Congestion Score



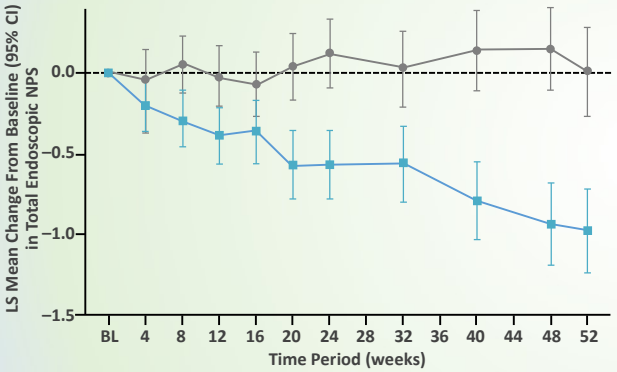
INTEGRITY CONTINUING EDUCATION

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

Mepolizumab: SYNAPSE Results

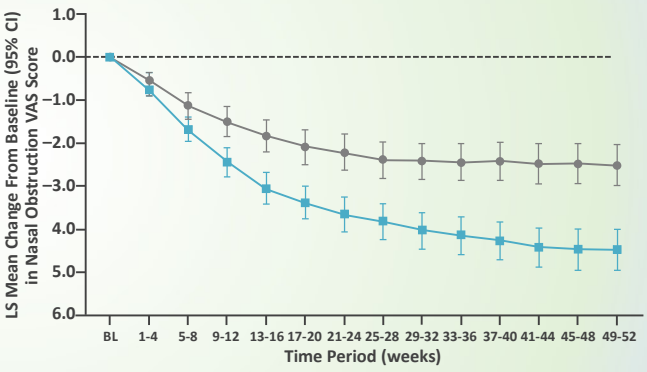
Total Endoscopic NPS (Week 52)

Median difference (95% CI): -0.73 (-1.11, -0.34); *P* <.001



Nasal Obstruction VAS Score (Weeks 49-52)

Median difference (95% CI): -3.14 (-4.09, -2.18); *P* <.001



Mepolizumab ● Placebo

StudY in NAsal Polyps patients to assess the Safety and Efficacy of mepolizumab

NPS, Nasal Poylp Score.

INTEGRITY CONTINUING EDUCATION

Han JK, et al. *Lancet Respir Med.* 2021;9:1141-1153.

Quality of Life Comparison Based On Number Of Revisions Performed

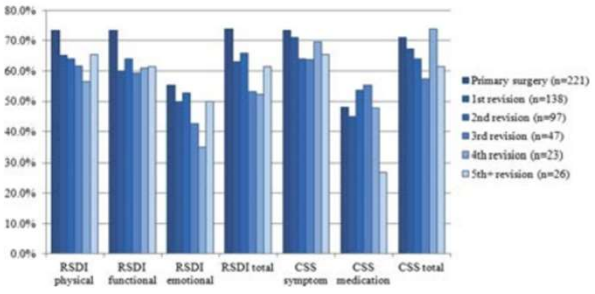


FIGURE 1. Comparison of the frequency of improvement in QOL across all patients with follow-up. QOL = quality of life.

RSDI, Rhinosinusitis Disability Index; CSS, Chronic Sinusitis Survey.

Clinger JD, et al. *Int Forum Allergy Rhinol*. 2012;2(6):444-452

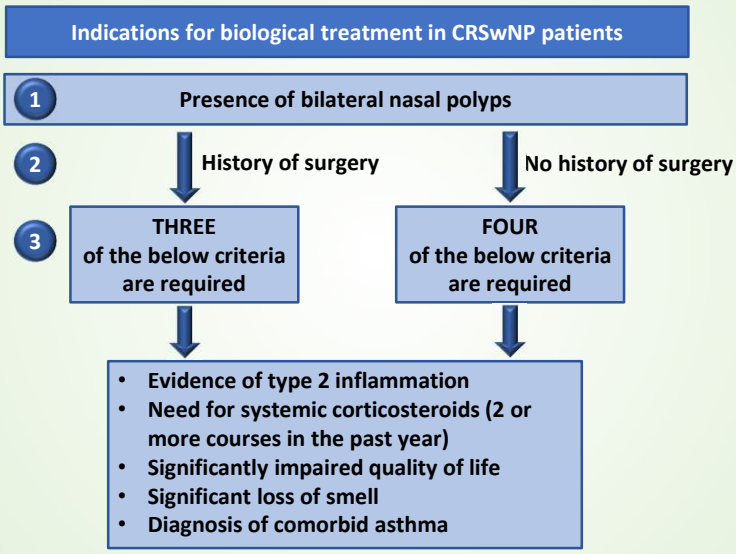
Meta-Analysis Comparing Safety and Efficacy of Monoclonal Antibodies and ASA Desensitization

	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 (0.83, 1.33)	**-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, 0.68)	**-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, 8.91)	**-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, 1.11)	**-0.64** (-1.39, 0.12)	**-1.00** (-3.83, 1.83)
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 color				Certainty (shading)
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)

Oykhman P, et al. *Rhinitis, sinusitis, and ocular allergy* 2021;149(4):1286-1295

EUFOREA Criteria for Considering Biological Treatment



Fokkens WJ, et al. *Allergy*. 2019;74:2312–2319.

EPOS2020 Steering Group: Indications for Biological Treatments in CRSwNP

Indications for biological treatment in CRSwNP

Presence of bilateral polyps in a patient who had ESS*

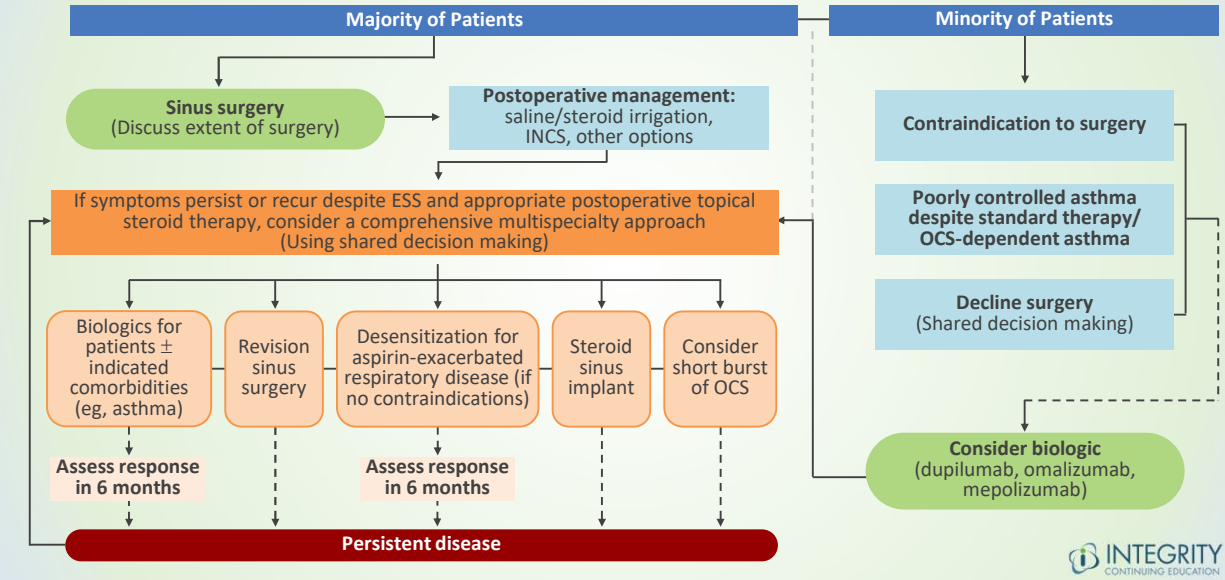
THREE criteria are required

Criteria	Cut-off Points
• Evidence of type 2 inflammation	• Tissue eos ≥10/hpf, OR blood eos ≥250 u/L, OR total IgE ≥100 IU/mL
• Need for systemic corticosteroids or contraindication to systemic steroids	• ≥2 courses per year, OR long term (>3 months) low dose steroids
• Significantly impaired quality of life	• SNOT-22 ≥40
• Significant loss of smell	• Anosmic on smell test (score depending on test)
• Diagnosis of comorbid asthma	• Asthma needing regular inhaled corticosteroids

*Exceptional circumstances excluded (eg, not fit for surgery).
eos, eosinophils; EPOS, European Position Paper on Rhinosinusitis and Nasal Polyps; hpf, high power field (×400).

Fokkens WJ, et al. *Rhinology*. 2020;58(29):1–464.

Multidisciplinary Management Algorithm for CRSwNP



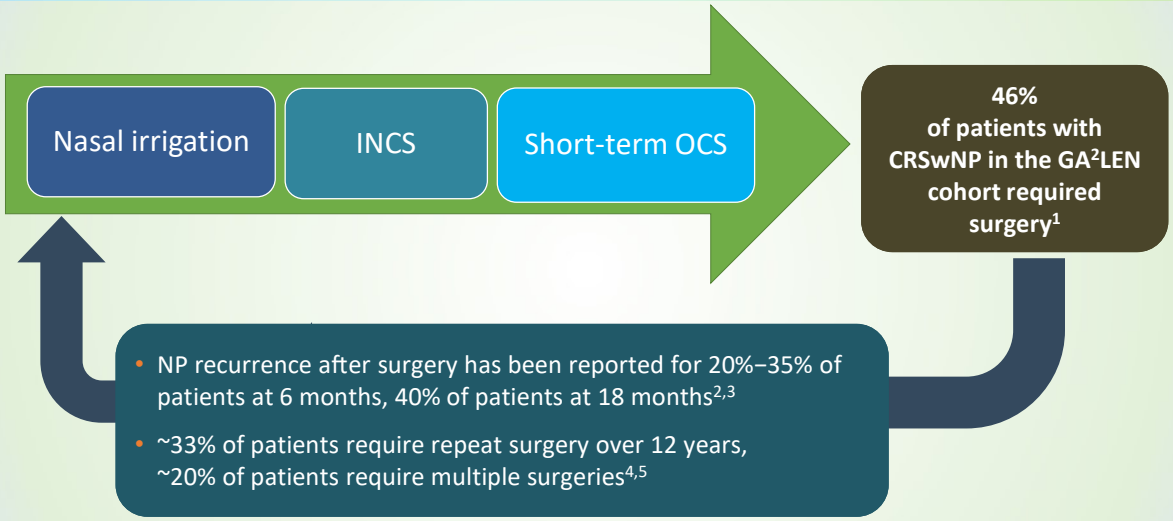
Han JK, et al. *Int Forum Allergy Rhinol.* 2021;11:1407-1416.

Dan, 53-year-old Male: Presentation

- Diagnosed with allergic rhinitis and CRSwNP 8 years ago
  - In the past, he has tried nasal steroid spray, EDS-FLU, and short burst of oral steroid. Recent post treatment CT of sinus shows pansinusitis.
  - About 9 months ago, Dan underwent complete ESS with postoperative topical steroid
    - Unfortunately, nasal polyps and symptoms of nasal congestion/loss of smell has returned. Oral steroid was given and his symptoms of congestion and loss of smell improved but gradually got worse
- Post treatment CT of sinus shows opacification of all the sinuses and thorough opening of all the sinuses

CT, computed tomography.

Surgery, Polyp Recurrence, and Revision Surgery

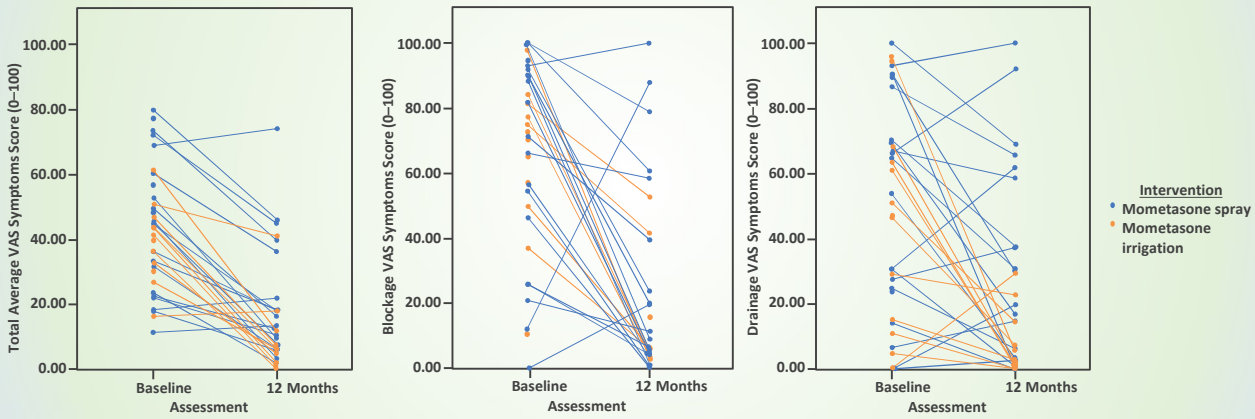


GA²LEN, Global Allergy and Asthma European Network.

1. Vandeplas G. *Clin Transl Allergy*. 2015;5(Suppl. 4):1. **2**. Bassiouni A, et al. *Laryngoscope*. 2013;123:36-41. **3**. DeConde AS, et al. *Laryngoscope*. 2017;127:550-555. **4**. Gevaert P, et al. *J Allergy Clin Immunol*. 2015;135:AB238. **5**. DeConde AS, et al. *Laryngoscope*. 2017;127:550-555.

Post-ESS Choice of CS Delivery May Effect Surgical Outcomes

CS Nasal Spray vs CS Irrigation at 12 months



The VAS values from total or average (A), nasal blockage (B), and mucus drainage (C) show significant differences at the 12-month assessment. Most striking is the deterioration seen in some patients in the nasal spray (blue) compared to the nasal irrigation (orange) groups.
CS, corticosteroids.

Harvey RJ, et al. *Int Forum Allergy Rhinol*. 2018;1-10.

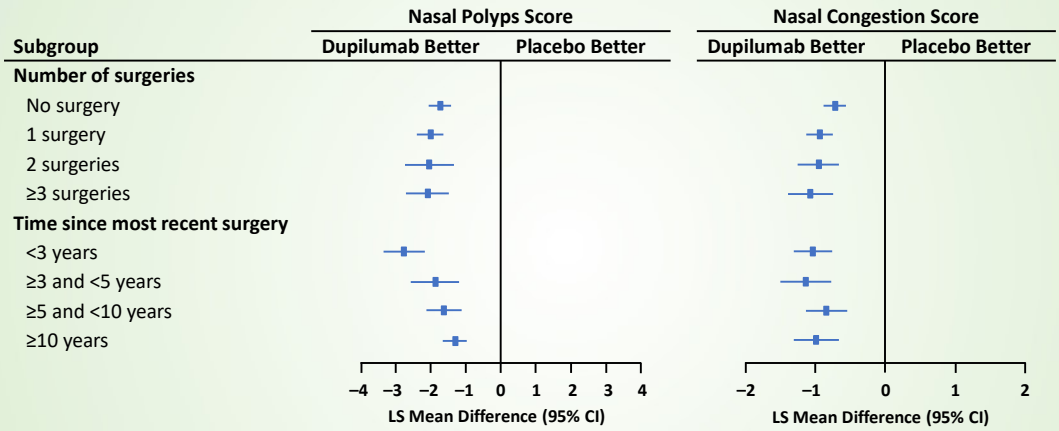
Median Time to Revision Surgery or Polyp Recurrence in Patients With CRSwNP Alone or With Comorbidities

Patient Category	Median Years to Revision Surgery	Median Years to Polyp Recurrence
CRSwNP alone	20	20
CRSwNP with asthma	11	4
CRSwNP with asthma and NSAID-ERD	7	0.66

INTEGRITY CONTINUING EDUCATION

Bachert C, et al. *J Asthma Allergy*. 2021;14:127-134; Leung RM, et al. *Int Forum Allergy Rhinology*. 2014;4(11):871-876.

Dupilumab Efficacy in Patients With Previous FESS



Dupilumab improved CRSwNP outcomes irrespective of surgery history, with greater improvements in endoscopic outcomes in patients with shorter duration since last surgery.

INTEGRITY CONTINUING EDUCATION

Hopkins C, et al. *Allergy & Rhinology*. 2021;11(7):1087-1101.