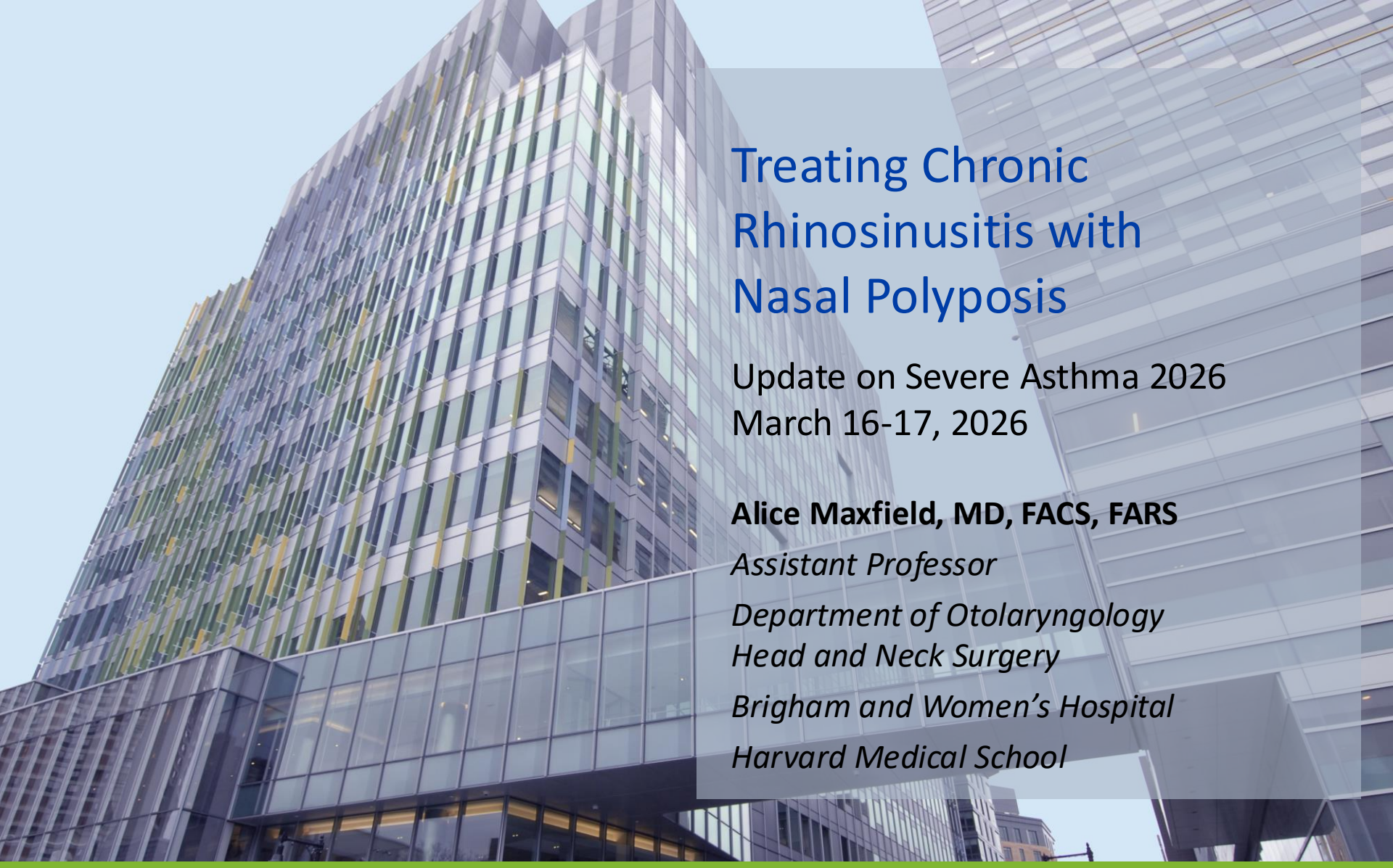

Treating Chronic Rhinosinusitis with Nasal Polyposis

Update on Severe Asthma 2026
March 16-17, 2026

Alice Maxfield, MD, FACS, FARS

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BRIGHAM HEALTH
BWH BRIGHAM AND WOMEN'S HOSPITAL

HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

Mass General Brigham

Disclosures

None

Discuss

- Case example
- Diagnosis of CRS
- Differentiate subtypes of CRS
- Treatment of CRS with nasal polyps

What is Chronic Rhinosinusitis?

Table I-2: Diagnostic criteria for diagnosis of CRS

Greater than or equal to 12 weeks of:
Two or more of the following symptoms:
Nasal discharge (rhinorrhea or post-nasal drip)
Nasal obstruction or congestion
Hyposmia
Facial pressure or pain
Cough (in Pediatric CRS)
AND
One or more of the following objective findings:
Evidence of inflammation on nasal endoscopy or computed tomography
Evidence of purulence coming from paranasal sinuses or ostiomeatal complex
AND
CRS is divided in to CRSsNP or CRSwNP based on the presence or absence of nasal polyps

ICAR 2020

Case Example

Patient A

- 41yof with sinus issues for the last 2 years
- Started with a cold that never went away
- FESS one year ago
- Persistent facial pressure, thick secretions, PND
- PMH: MS on Rituxan, MGUS, low IgM, prolactinoma

Patient Z

- 27yom with sinus issues for the last few years, worse in the last 6 months
- Feels it may be related to allergies
- Nasal obstruction, congestion, loss of smell
- PMH: seasonal allergies-dust

Patient A	Patient Z
• Cultures: Negative (after abx)	• Cultures: none
• Allergy testing: skin testing negative	• Allergy testing: skin testing positive for aspergillus, ragweed, grass, dog, cat, penicillium, birch, oak, dust mites
• Asthma: none	• Asthma: none
• ASA/NSAID: no sensitivity	• ASA/NSAID: no sensitivity
• SNOT22: 65	• SNOT22: 30

Patient A

- OC/OP: Significant yellow-green purulence along posterior pharyngeal wall, extending from nasopharynx
- Endoscopy exam:
  - Middle meatus w/ significant mucoid drainage
  - Scattered mucoid drainage throughout

Patient Z

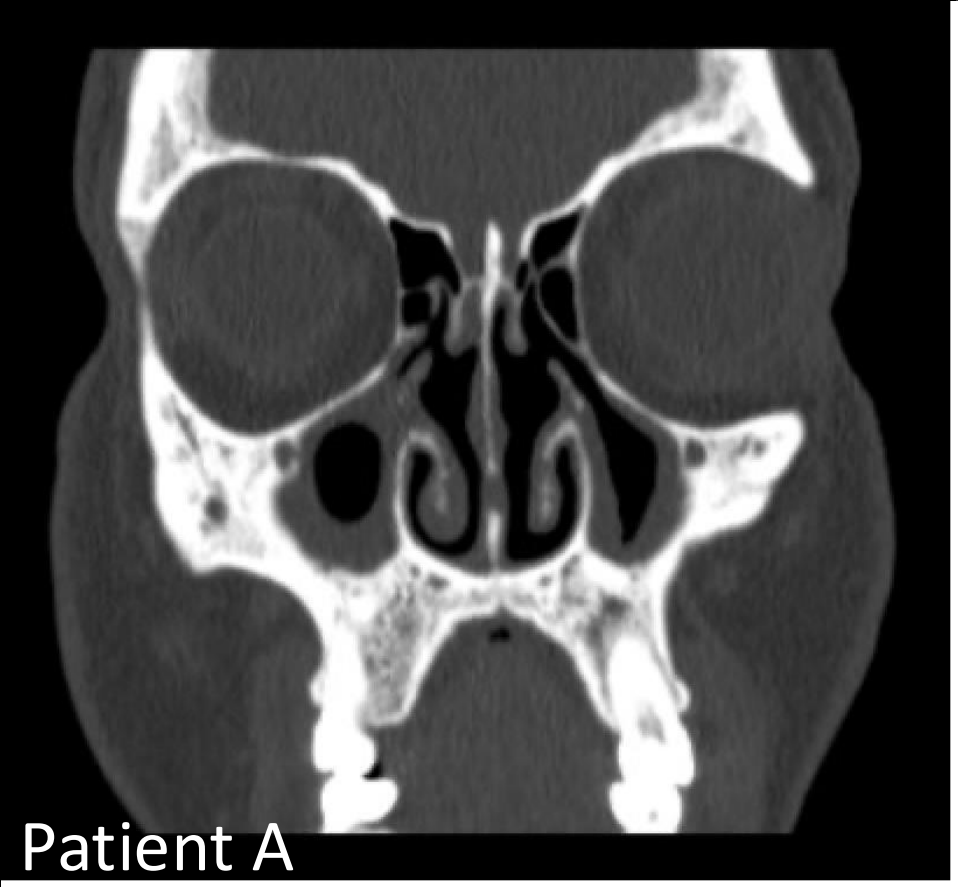
- Voice: hyponasal
- OC/OP: cobblestoning posterior pharynx
- Endoscopy exam:
  - Deviated septum
  - NP extending to floor medial to MT
  - NP full on left, but able to pass the scope

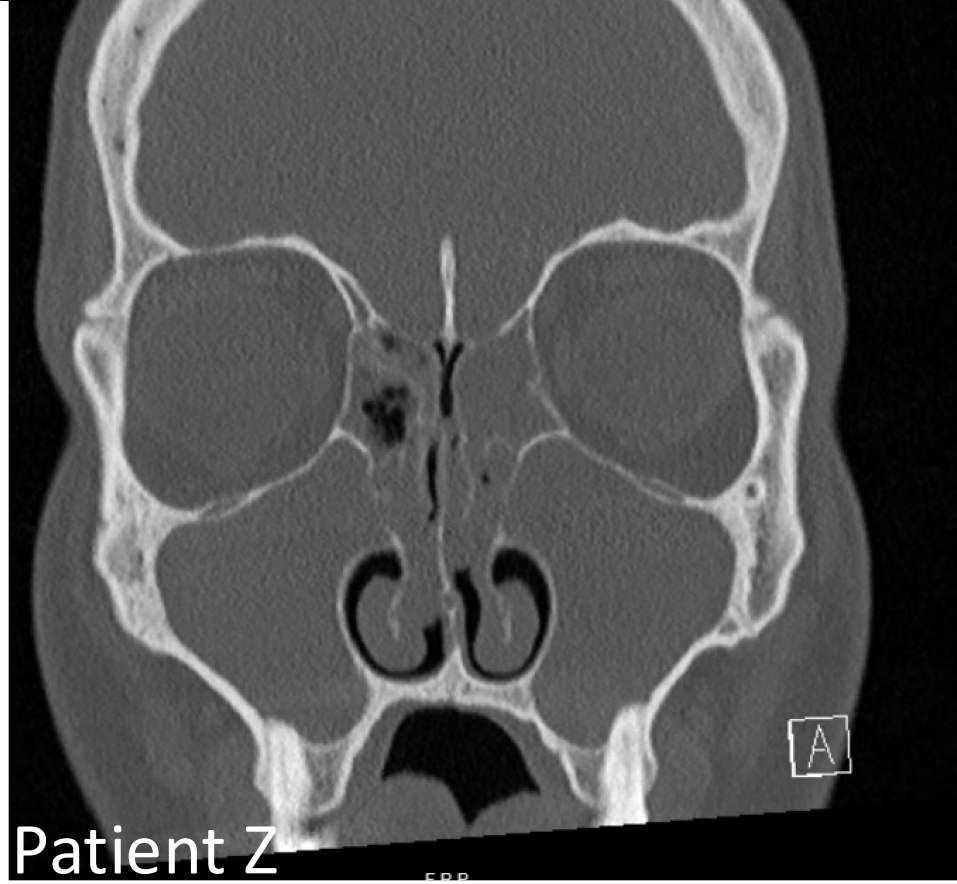
Patient A

- Cultures: Haemophilus influenzae +Beta lactamase

Patient Z

- Cultures: None





CT Imaging

Nasal Polyps on Endoscopy

Patient A

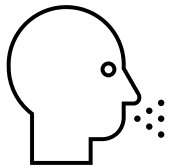
TABLE VII-11. The diagnostic criteria for CRSsNP

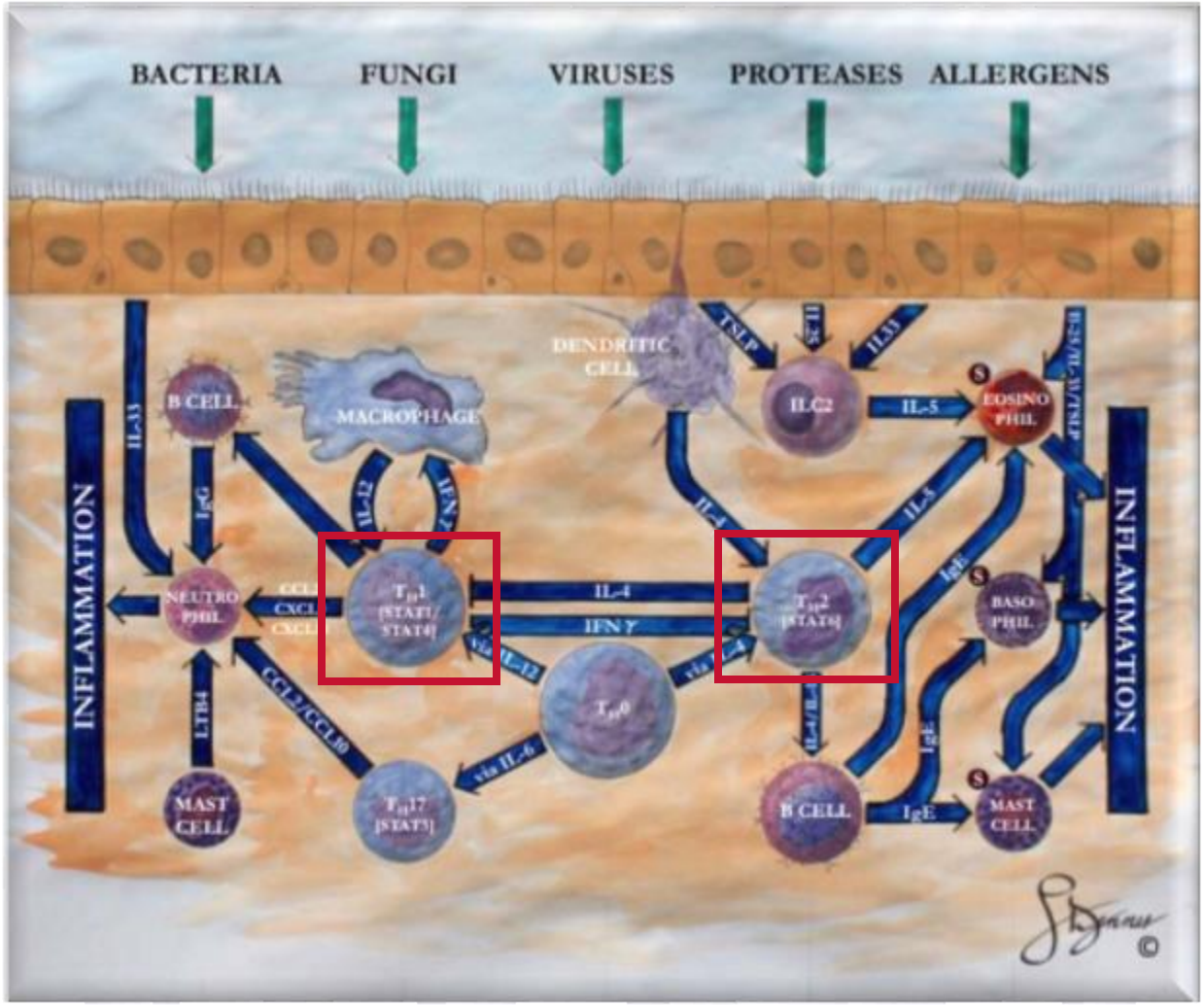
Greater than or equal to 12 weeks of:
2 or more of the following symptoms:
Mucopurulent discharge (rhinorrhea or PND)
Nasal obstruction and congestion
Decreased or absent sense of smell
Facial pressure or pain
AND
1 or more of the following findings:
Evidence of inflammation on paranasal sinus examination or CT
Evidence of purulence coming from paranasal sinuses or OMC
AND
Lack of polyps

Patient Z

TABLE VIII-6. The diagnostic criteria for CRSwNP

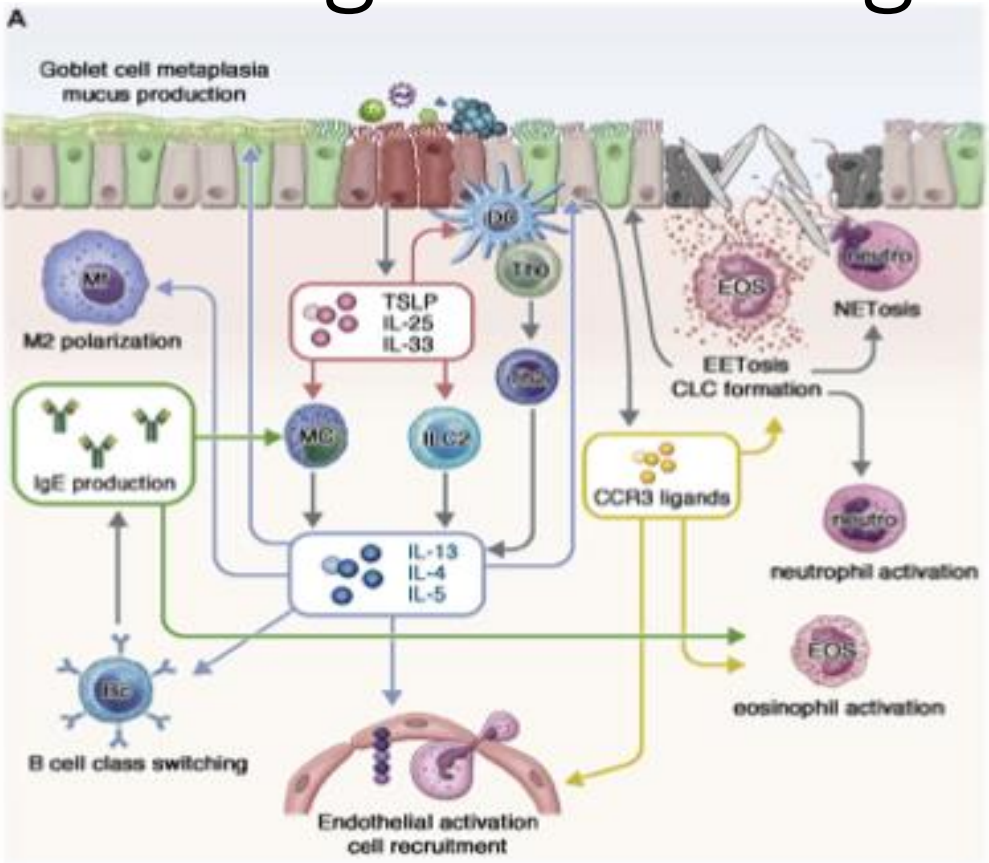
Greater than or equal to 12 weeks of:
2 or more of the following symptoms:
Mucopurulent discharge (rhinorrhea or PND)
Nasal obstruction and congestion
Decreased or absent sense of smell
Facial pressure or pain
AND
1 or more of the following findings:
Evidence of inflammation on paranasal sinus examination or CT
Evidence of purulence coming from paranasal sinuses or ostiomeatal complex
AND
Presence of polyps





Dennis et al. 2016.

Biologics and targets in CRSwNP



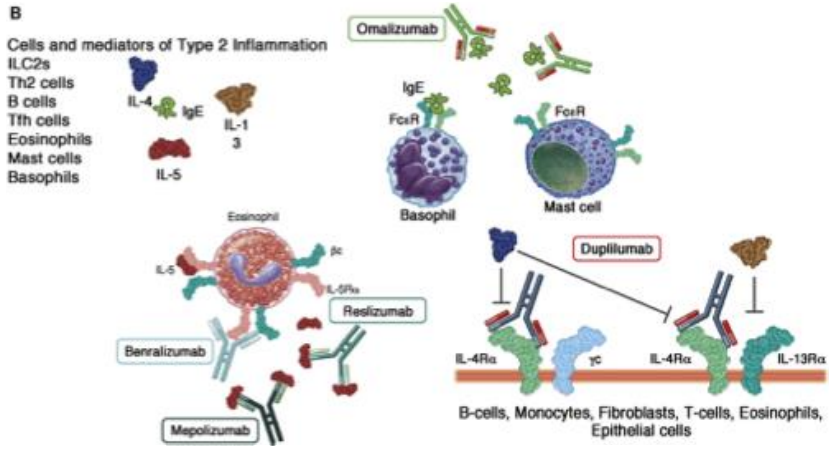
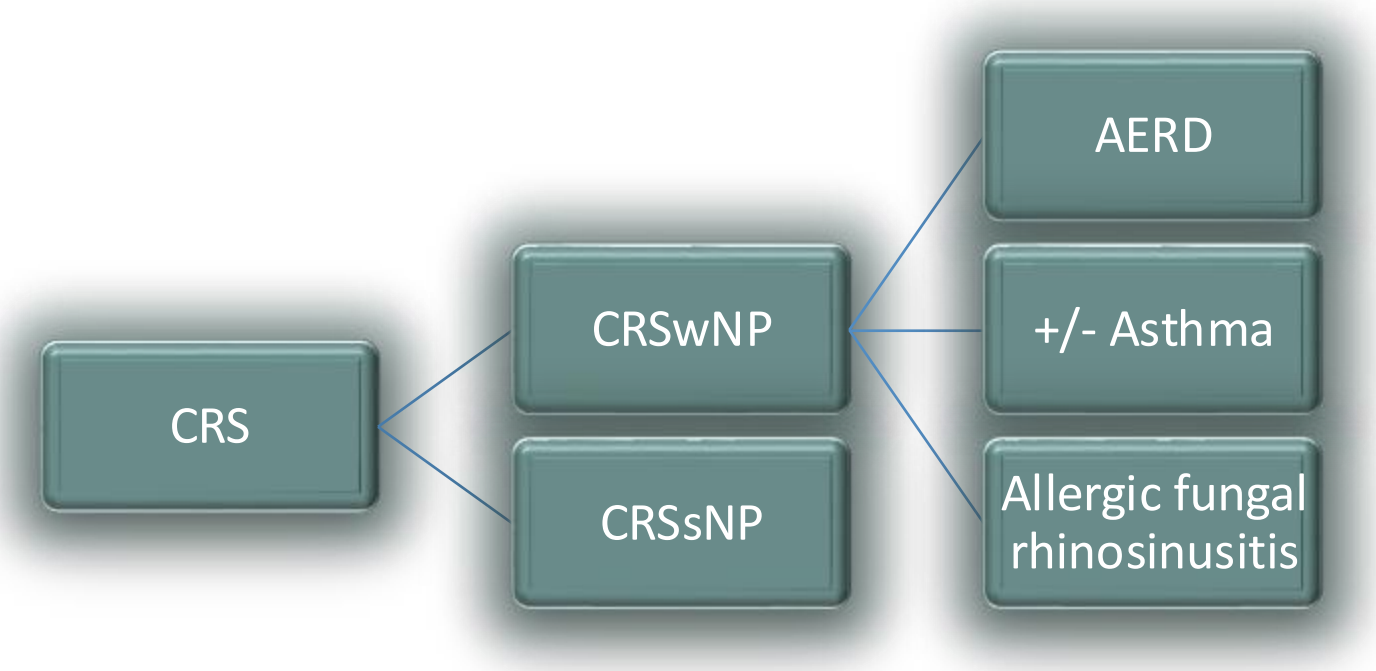


FIG 2. Continued.

FIG 2. Biologics and their targets in type 2 inflammation in CRSwNP. **A**, Target cytokines in type 2 immune reactions. **B**, Cells and mediators of type 2 inflammation and corresponding biologics. *CCR-3*, C-C motif chemokine receptor 3; *CLC*, Charcot-Leyden-Crystal; *DC*, dendritic cell; *EOS*, eosinophils; *IL-4Rα*, IL-4 receptor alpha; *IL-13Rα*, IL-13 receptor alpha; *neutro*, neutrophils.

Bachert et al. 2020.

What is the difference between the phenotypes of CRS?



Original Research—Sinonasal Disorders

Periostin as a Biomarker for Nasal Polyps in Chronic Rhinosinusitis

Alice Z. Maxfield, MD[1,2], Lukas D. Landegger, MD[2,3], Christopher D. Brook, MD[4], Ashton E. Lehmann, MD[2,3], Adam P. Campbell, MD[2,3], Regan W. Bergmark, MD[2,3], Konstantina M. Stankovic, MD, PhD[2,3]*, and Ralph Metson, MD[2,3]*

AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

Otolaryngology–Head and Neck Surgery 2018, Vol. 158(1) 181–186

DOI: 10.1177/0194599817737967
http://otojournal.org
SAGE

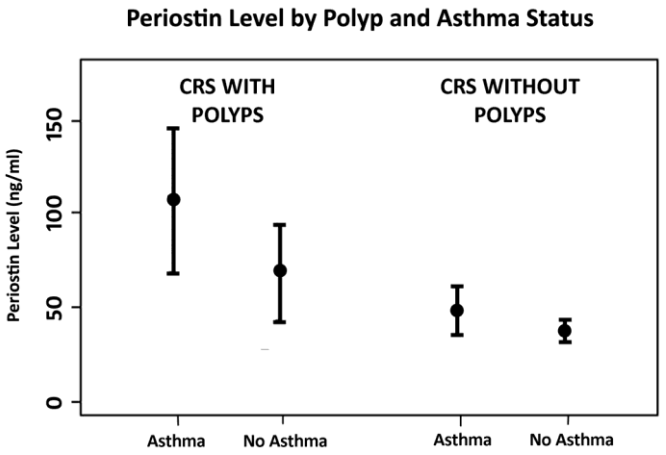


Figure 2. Periostin levels by nasal polyp and asthma status. Although mean serum periostin levels were higher for patients with asthma in both groups—chronic rhinosinusitis (CRS) with and without nasal polyps—this difference was not significant. Values are presented as means (95% CI).

Original Research—Sinonasal Disorders

AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

Otolaryngology–Head and Neck Surgery
2018, Vol. 158(1) 181–186
Ó American Academy of Otolaryngology—Head and Neck Surgery Foundation 2017
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DOI: 10.1177/0194599817737967
http://otojournal.org
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Periostin as a Biomarker for Nasal Polyps in Chronic Rhinosinusitis

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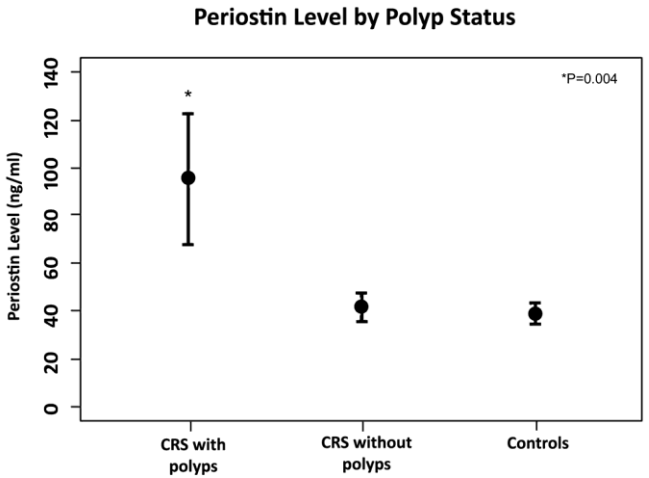


Figure 1. Periostin level by nasal polyp status. Serum periostin level was significantly higher in patients with chronic rhinosinusitis (CRS) and nasal polyps versus patients with CRS without nasal polyps and controls (P = .004). Values are presented as means (95% CI).

Goals

- Predict course of disease
- Predict response to treatment

Goals of treatment

- Increase quality of life
- Control disease progression

- Enhance mucociliary clearance
- Improving sinus drainage pathways
- Eradicate local infection/inflammation
- Improve access for delivery of topical medications

Challenges in Treatment of CRS

- Difficulty correlating patient symptoms with objective measures of inflammation
- Predicting long term response to medical therapy
- Relapses of symptoms and disease

ORIGINAL ARTICLE

International Consensus Statement on Allergy and Rhinology: Rhinosinusitis

CRSwNP Treatment

- Nasal saline irrigation
- Topical steroids
- Oral corticosteroids (A)
- Antibiotics
  - Oral
  - Irrigation (A) [CRSwNP and CRSsNP]
- ASA desensitization for AERD (A)
- Dupilumab (A)
- Endoscopic Sinus Surgery

CRSwNP Treatment

- Nasal saline irrigation (A)
- Topical steroids
  - Spray (A, strong recommendation)
  - Irrigation (ie budesonide) (A, strong recommendation)
- Oral corticosteroids (A)
- Antibiotics
  - Oral
    - Nonmacrolide <3 weeks (B)
    - Nonmacrolide >3 weeks (N/A)
    - Macrolide (B)
  - Irrigation (A) [CRSwNP and CRSsNP]
- ASA desensitization for AERD (A)
- Dupilumab (A)
- Endoscopic sinus surgery

Hopkins et al. 2015
Benninger et al 2016

Nasal Saline Irrigation

- Isotonic saline irrigation
- Low positive pressure
- Used in combination with intranasal corticosteroid spray
- RCT showed improved symptom severity, symptom frequency, QOL
- Benefits:
  - Mucociliary clearance
  - Clear eosinophilic mucin
  - Decreased viscosity
  - Decreased edema
  - Mechanical lavage of debris
  - Decreased medication usage, specifically antibiotics

Pynnonen et al. 2007

Topical Intranasal Corticosteroids (A, strong recommendation)

- Improvement:
  - sinonasal symptoms – nasal blockage, rhinorrhea, smell
    (not for facial pressure/pain)
  - polyp size and recurrence
  - QOL
  - olfaction
- Especially when used in combination with nasal saline irrigation.
- No difference in effectiveness between types of intranasal steroids.

Fokkens et al. 2012
Orlandi et al. 2016
Chong et al. 2016
Kalish et al. 2012

Oral Corticosteroids

(A, strong recommendation for short-term use)

- Short term improvement in sinonasal symptoms
- No long-term improvement
- Need to weigh risks and benefits/adverse effects

Oral Non-Macrolide Antibiotics
(B, recommendation against)

- Lack of good data regarding efficacy
- Some studies show benefit in patients with polyps
- Cochrane review – very little evidence that systemic antibiotics are effective in patients with CRS
- More studies needed in the subtypes of CRS
- Short course doxycycline appears to have some benefit in those with nasal polyp size reduction

- Long term macrolides have mixed results, no clear lasting benefit.

Barshak & Durand 2017

The Laryngoscope

General Antibiotic Exposure Is Associated With Increased Risk of Developing Chronic Rhinosinusitis

Alice Z. Maxfield, MD; Hakan Korkmaz, MD; Luciano L. Gregorio, MD; Nicolas Y. Busaba, MD; Stacey T. Gray, MD; Eric H. Holbrook, MD; Rong Guo, MS; Benjamin S. Bleier, MD

Oral Macrolide Antibiotics
(B, option)

- Macrolide antibiotics have anti-inflammatory and immunomodulatory properties.
- There is an effect on the neutrophilic components of the inflammatory response, thereby targeting Th1-mediated non eosinophilic CRS.
- Potentional adverse effects: Cardiovascular risk, prolonged QT interval, elevated LFTs, ototoxicity, GI side effects.

Barshak & Durand 2017

Topical Budesonide Irrigation

- ***Dilute irrigation:*** 240mL of saline
  - with 0.5mg/2mL respule of budesonide 1-2x daily
- ***Concentrated irrigation:*** 5mL of saline
  - 0.5mg/2mL respule of budesonide daily
- In AERD patients, significant improvement in SNOT22 and nasal polyp size
- Improved:
  - Symptoms
  - Radiographic scores
  - Endoscopy appearance
- No evidence of adrenal axis suppression

Talat et al. 2021

Topical Mometasone Irrigation

- Dilute irrigation: 240mL of saline
  - with 2mg of mometasone 1-2x daily
- Low concentration:
  - With 0.6 mg vs high concentration 2-4mg
- Superior pharmacokinetic profile, increased local efficacy, low systemic absorption
- Mometasone 2mg daily via nasal spray or large volume irrigation for 12 months
  - The irrigation group had larger improvement in nasal blockage, LM Score, and modified LK score.
  - Overall 12 month symptom VAS was better in the irrigation group.
- Corticosteroid irrigation is beneficial in long term maintenance in CRSwNP, and f/u longer than 3-6 months post ESS.
- In CRSwNP, no evidence of HPA axis suppression with mometasone irrigation (2mg twice daily).

Brown et al. 2021
Harvey et al. 2018
Talat et al. 2021

ASA Desensitization in AERD
(A, recommendation)

- Improvement in
  - HRQoL
  - Sinusitis symptoms
  - Smell
  - Rescue nasal polyp surgery
  - Nasal polyp size
- Lasting endoscopic and symptomatic improvement

Oykhman et al. 2021

Updated Treatment of Non-Steroidal Anti-Inflammatory Drug-Exacerbated Respiratory Disease: How to Decide on Aspirin Therapy After Desensitization or Biologics? When? How? An EAACI Task Force Report

Gülfem E. Çelik[1] | Joanna S. Makowska[2] | Maria Jose Torres[3,4] | Cristobalina Mayorga[5,6] | Tanya M. Laidlaw[7] | Alessandra Vultaggio[8] | Sanna Toppila-Salmi[9,10,11] | Ludger Klimek[12] | Aslı Gelincik[13] | Annick Barbaud[14,15] | Lene H. Garvey[16,17] | Ömür Aydın[18] | Thomas Eiwegger[19,20,21,22] | Katharine M. Woessner[23]

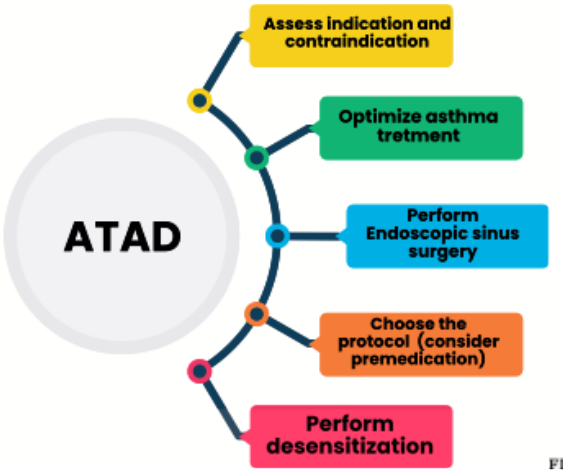


FIGURE 2 | Steps to be taken on ATAD.

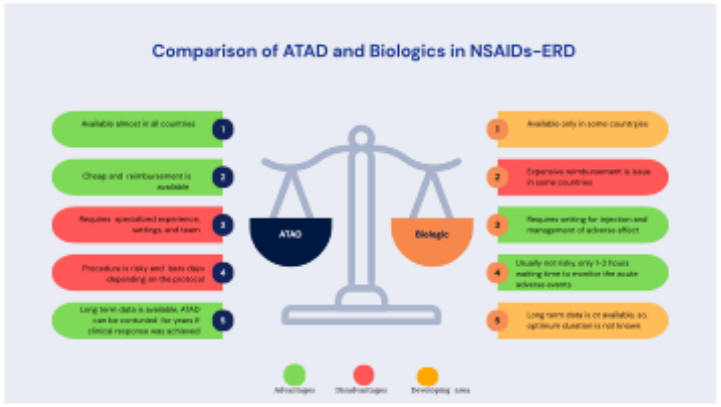


FIGURE 6 | Comparison of ATAD and Biological treatments in the management of NSAID-ERD.

Endoscopic Sinus Surgery

Mucosal preserving

Widen sinus drainage pathways

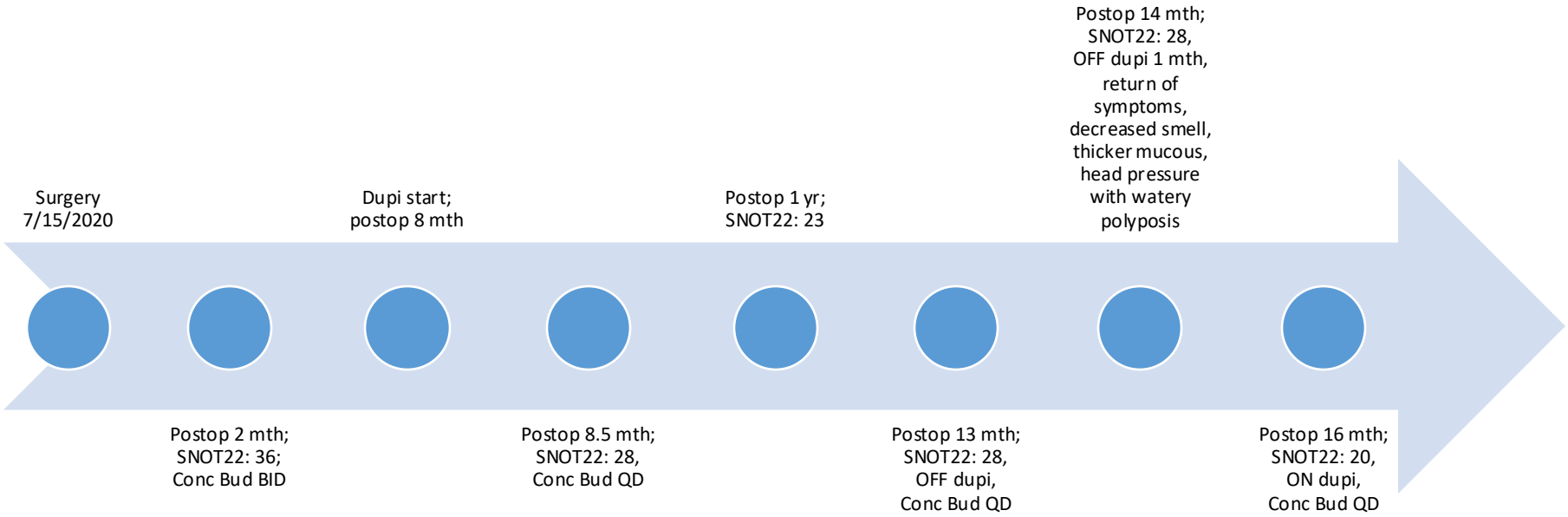
Allow better delivery of medication

Establish nasal airway and sinus outflow

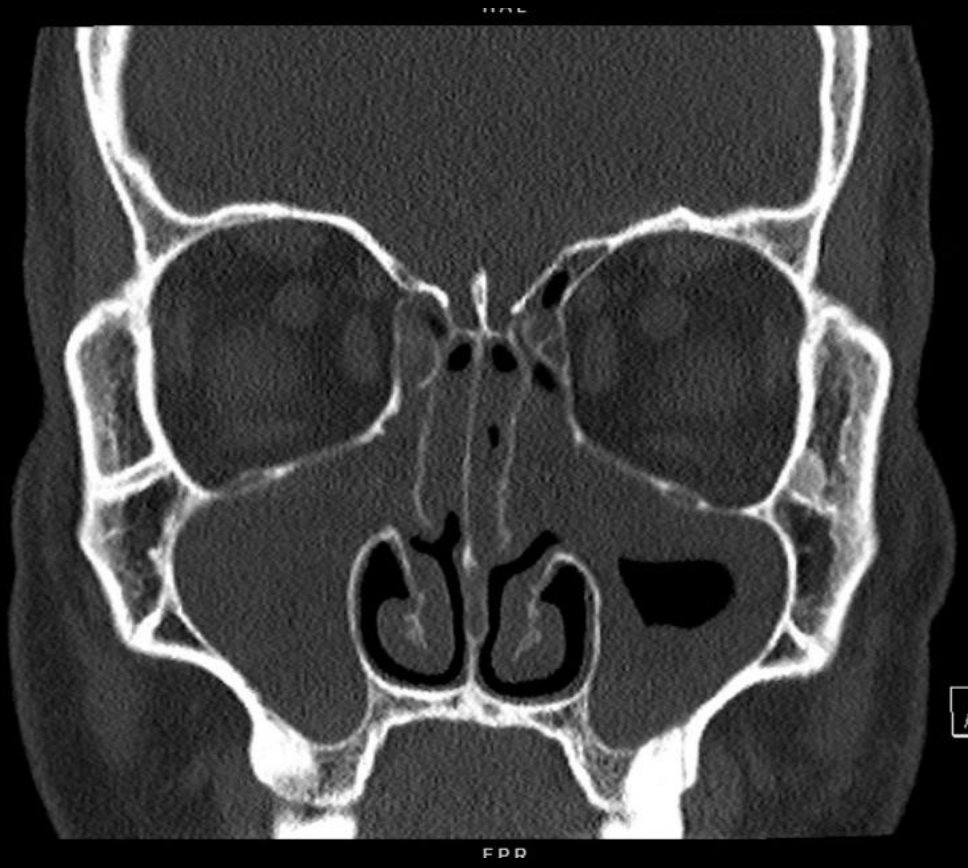
Decrease overall inflammatory disease burden

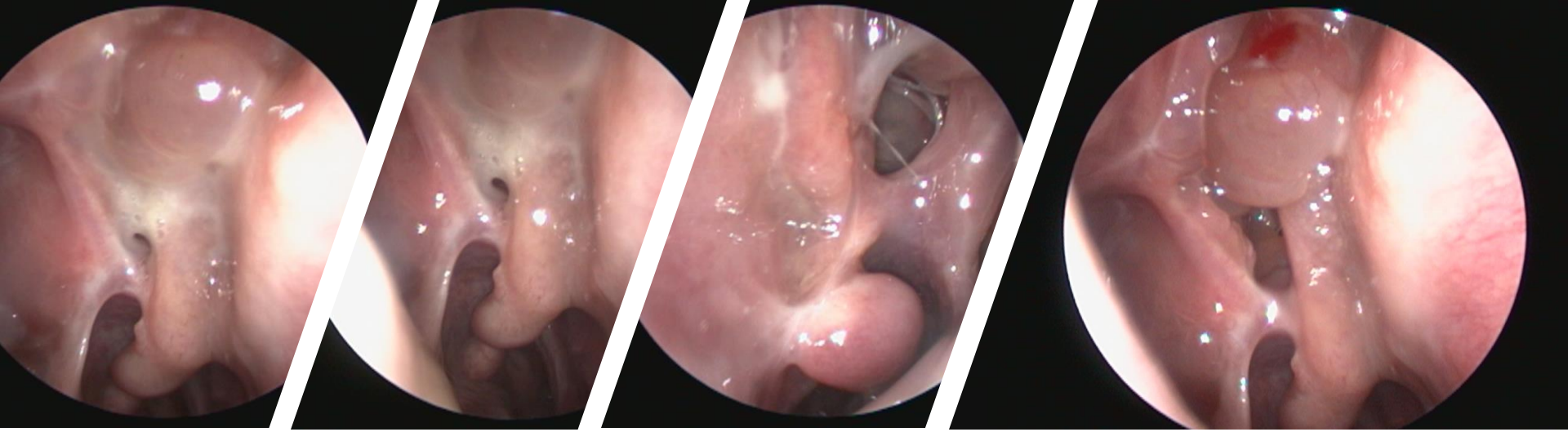
CRSwNP s/p surgery, budesonide dilute

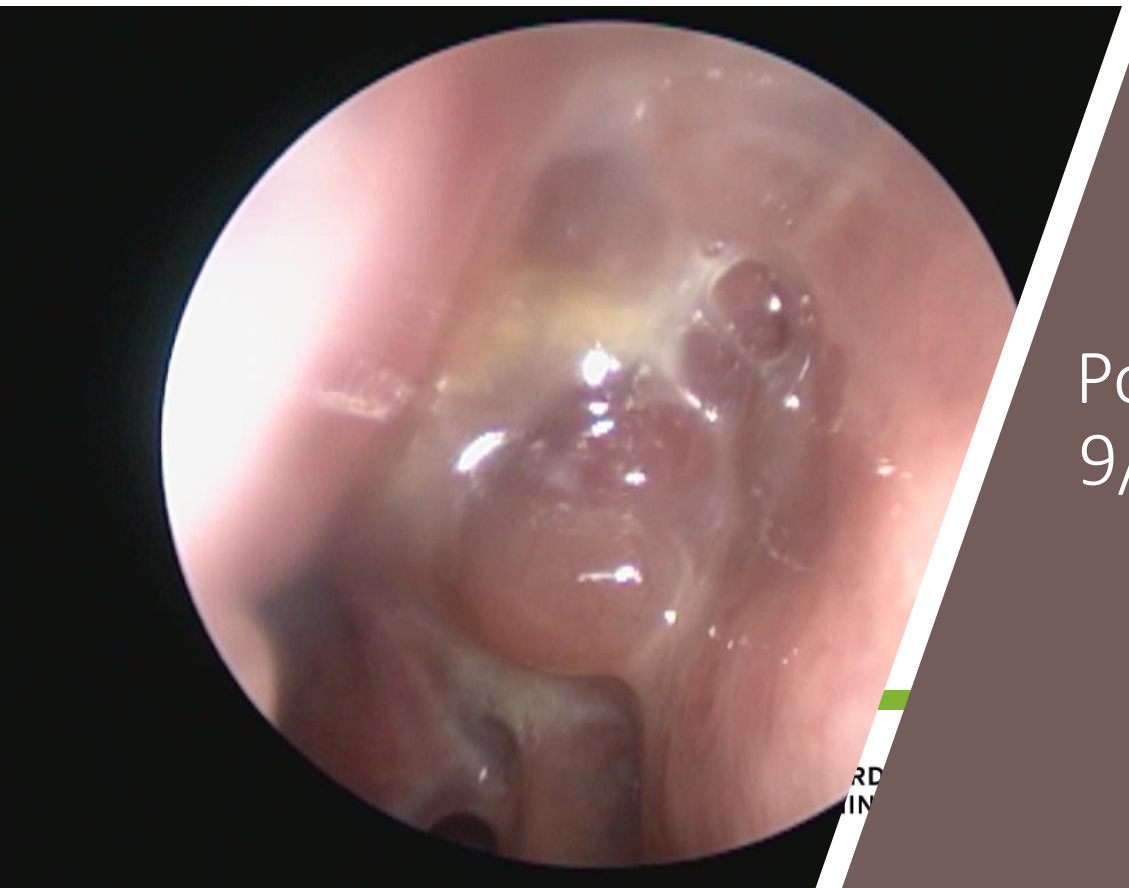
Patient RR


Surgery
7/15/2020
Postop 2 mth;
SNOT22: 36;
Conc Bud BID
Dupi start;
postop 8 mth
Postop 8.5 mth;
SNOT22: 28,
Conc Bud QD
Postop 1 yr;
SNOT22: 23
Postop 13 mth;
SNOT22: 28,
OFF dupi,
Conc Bud QD
Postop 14 mth;
SNOT22: 28,
OFF dupi 1 mth,
return of
symptoms,
decreased smell,
thicker mucous,
head pressure
with watery
polyposis
Postop 16 mth;
SNOT22: 20,
ON dupi,
Conc Bud QD

Preoperative



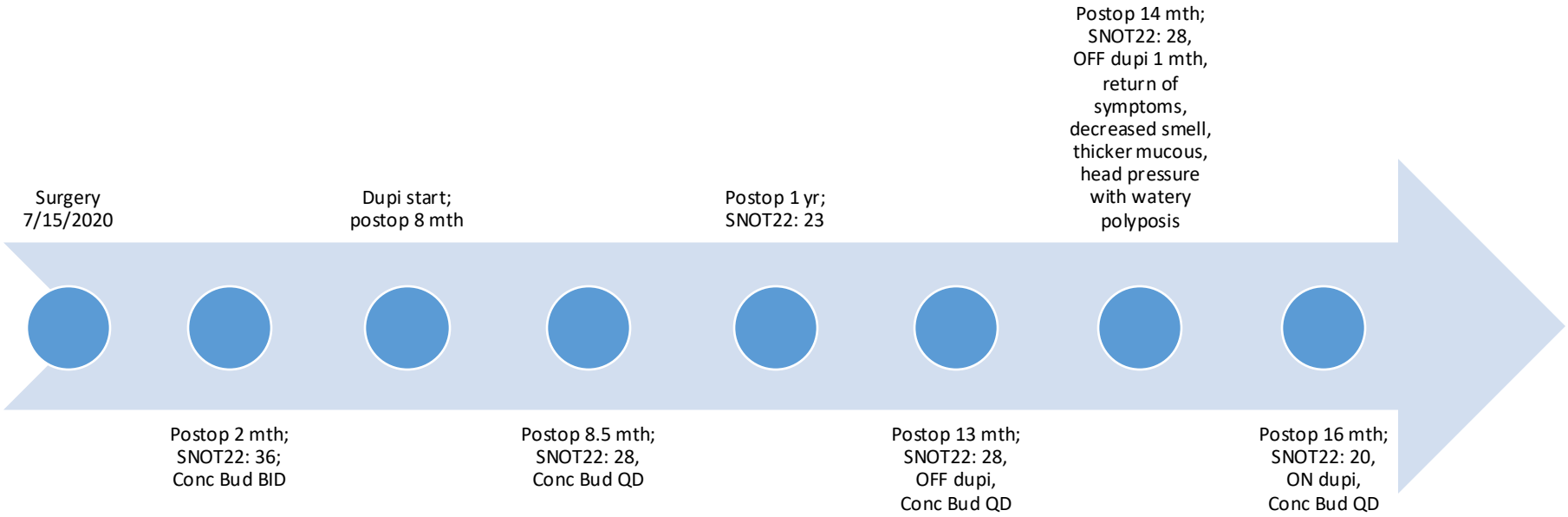




Postoperative 2 months 9/25/2020: SNOT22 39, conc budesonide BID

ON dupilumab for 5 mths, OFF for 1 mth

Patient RR


Surgery
7/15/2020
Postop 2 mth;
SNOT22: 36;
Conc Bud BID
Dupi start;
postop 8 mth
Postop 8.5 mth;
SNOT22: 28,
Conc Bud QD
Postop 1 yr;
SNOT22: 23
Postop 13 mth;
SNOT22: 28,
OFF dupi,
Conc Bud QD
Postop 14 mth;
SNOT22: 28,
OFF dupi 1 mth,
return of
symptoms,
decreased smell,
thicker mucous,
head pressure
with watery
polyposis
Postop 16 mth;
SNOT22: 20,
ON dupi,
Conc Bud QD

Biologics

REVIEW ARTICLE

The role of biologics in chronic rhinosinusitis: a systematic review

Isma Z. Iqbal, PgCertMEd, FRCS(ORL-HNS)[1], Stephen Shih-Teng Kao, MBBS, MClinSc[2] and Eng Hooi Ooi, PhD, FRACS[3]

Table 1 Table Describing Biologics Discussed Including: Name, Target, FDA Approvals, Mechanism, Dosing and Side Effects

Generic Name	Trade Name	Target	FDA Approvals	Dosing	Side Effects
Omalizumab	Xolair	Anti-IgE via Fc receptor blockade	CRSwNP; Allergic Asthma; Chronic Uticaria	Subcutaneous injection every 2–4 weeks	• Sinusitis • Headache • Pharyngitis • Injection site reaction • 0.2% risk of anaphylaxis
Mepolizumab	Nucala	Anti-IL5	Eosinophilic Asthma	Monthly subcutaneous injections	• Headache • Fatigue • Injection site reaction
Benralizumab	Fasenra	Anti-IL5 via IL5-R alpha receptor blockade		Monthly subcutaneous injections for 3 months then every other month	• Headache • Pharyngitis • Injection site reaction
Dupilumab	Dupixent	Anti-IL4 and IL-13 via IL-4Ra receptor blockade	CRSwNP; Atopic Dermatitis	Subcutaneous injection every other week	• Nasopharyngitis • Headache • Injection site reaction

Anti-IL33

Tezepelumab (Tezspire) - Anti-TSLP

Morse, Miller, Senior. 2021

Biologics for Nasal Polyposis

- Cost
  - Estimated cost per year >$30,000 on average
  - Cost utility analysis of dupilumab vs ESS
    - Surgery cost $50,346.99 with 9.80 QALYs vs. dupilumab cost $536,420.22 with 8.95QALYs
    - Authors concluded that ESS was less costly and more effective than dupilumab.

(Scangas et al)

International Archives of Allergy and Immunology

Clinical Allergy – Research Article

Int Arch Allergy Immunol 2022;183:279–288
DOI: 10.1159/000519228

Received: May 10, 2021
Accepted: June 4, 2021
Published online: October 4, 2021

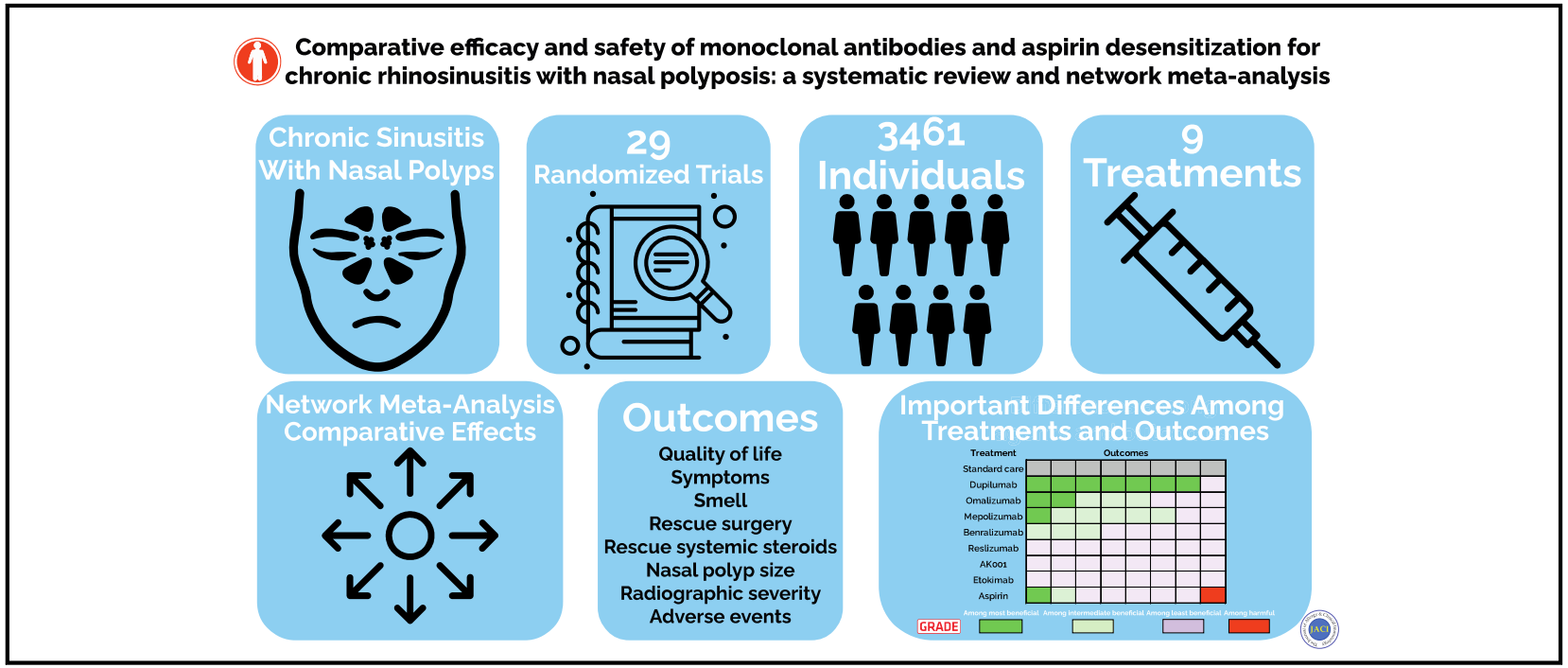
Which Is the Best Biologic for Nasal Polyps: Dupilumab, Omalizumab, or Mepolizumab? A Network Meta-Analysis

Qingwu Wu[a, b] Yana Zhang[a] Weifeng Kong[a] Xinyue Wang[a] Lianxiong Yuan[c] Rui Zheng[a] Huijun Qiu[a] Xuekun Huang[a, b] Qintai Yang[a, b]

[a]Department of Otorhinolaryngology-Head and Neck Surgery, The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China; [b]Department of Allergy, The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China; [c]Department of Science and Research, The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China

Paul Oykhman, MD, MSc,[a] Fernando Aleman Paramo, MD,[a] Jean Bousquet, MD,[d,e,f] David W. Kennedy, MD,[g] Romina Brignardello-Petersen, PhD,[b] and Derek K. Chu, MD, PhD[a,b,c] *Hamilton, Ontario, Canada; Berlin, Germany; Montpellier, France; and Philadelphia, Pa*

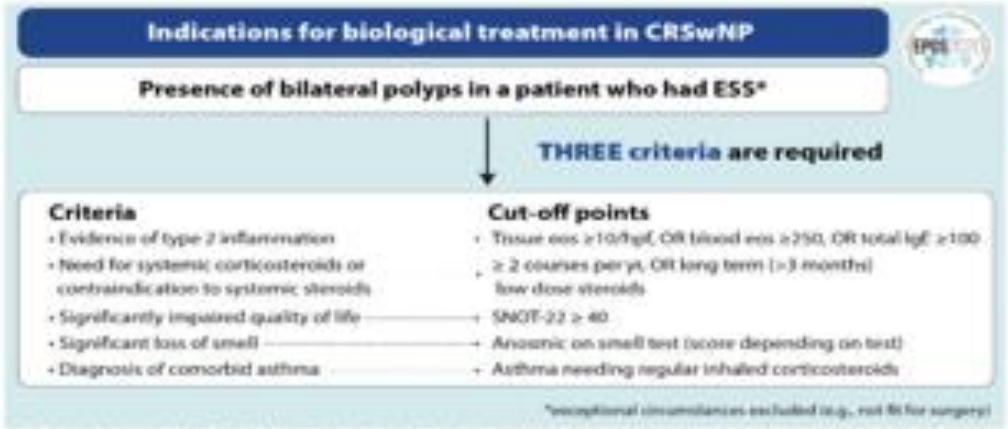
GRAPHICAL ABSTRACT



	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 (0.88, 1.13)	**-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, 0.88)	**-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, 8.19)	**-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, 1.17)	**-0.64** (-1.39, 0.12)	**-1.00** (-3.83, 1.83)
Reslizumab					**-18.82** (-20.93, 20.56) RR 0.11 (0.01, 1.98)	**-2.55** (-19.49, 19.18) RR 0.97 (0.74, 1.26)		
AK001						**2.54** (-27.11, 51.03) RR 1.03 (0.63, 1.69)	**-0.20** (-1.61, 1.21)	
Etokimab	**-1.30** (-8.99 to 6.40)					**188.14** (-59.76, 4879.1) RR 3.55 (0.19, 67.13)	**-0.33** (-1.58, 0.92)	
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 (colour)[24]				**Certainty (shading)[24, 29]**
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)

EPOS2020 criteria



EPOS/EUFOREA 2023 criteria

Figure 1. Adjustments in EPOS/EUFOREA criteria. The only change is the reduction of blood eosinophils to 150 cells/µl.

Unanswered questions

- Which type of patient?
  - Refractory disease
- Timing of biologic?
- Is there a clear advantage of biologic over surgery?
  - Durability of surgery is improved compared to dupilumab.
- Is there advantage between biologics?
  - Current FDA approval and trial data suggests dupilumab is most efficacious choice in Caucasian populations with CRSwNP.
- Long term results?
- Long term side effects?

Morse, Miller, Senior. 2021

Maximal Medical Therapy?

- There is no standardized medical therapy regimen for CRS.
- Lal et al. treated with minimum 4 weeks -
  oral antibiotics, oral steroids, topical nasal steroids, topical nasal decongestant rotation, saline irrigation
  - 51% successfully treated
  - 17% partial improvement
  - 31% underwent surgery

Lal et al. 2014.

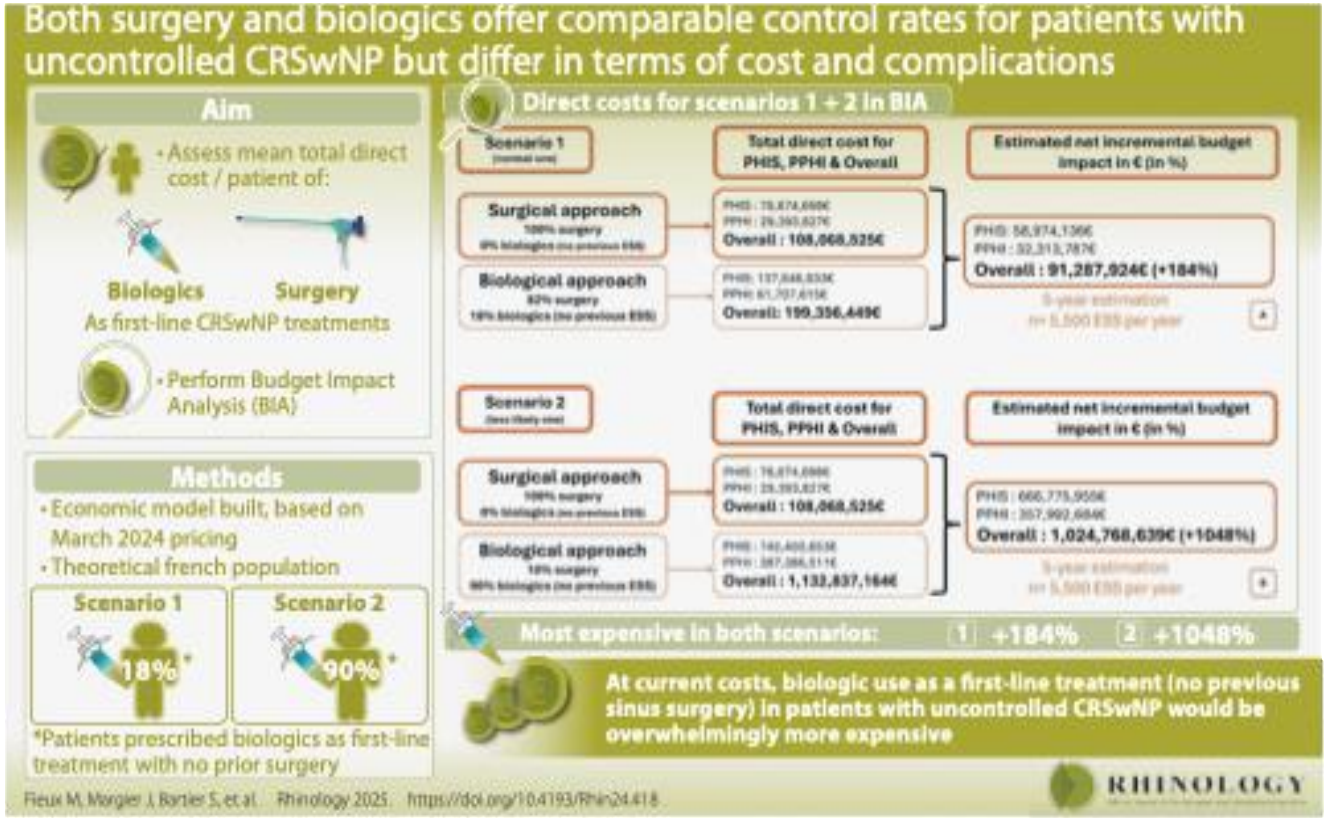
- Mucosal preserving
- Widen sinus drainage pathways
- Allow better delivery of medication
- Establish nasal airway and sinus outflow
- Decrease overall inflammatory disease burden

The extra cost of biologics as first-line treatment in uncontrolled chronic rhinosinusitis with nasal polyps with no previous sinus surgery is overwhelming: a budget impact analysis

OPEN

Maxime Fieux[1,2]*, Jennifer Margier[3]*, Sophie Bartier[4], Michael Chang[5], Florent Carsuzaa[6], Peter H. Hwang[5], Zara M. Patel[5], Stéphane Tringali[1,2], Valentin Favier[7], Thibault Savary[1]

Rhinology 63: 4, 495 - 504, 2025
https://doi.org/10.4193/Rhin24.418



Endotyping

- CRS currently classified by phenotype.
- 38-51% of CRS patients fail to respond to recommended medical therapies.
- This highlights the limitations of the current treatments of CRS.
- There is heterogeneity within cellular and molecular pathways that lead to these subtypes.
- Thus, defining molecular biomarkers to further endotype these subtypes is crucial in determining targeted therapies.

Lal et al. 2016.
Baguley et al. 2014

Summary

- CRSwNP is a type II mediated inflammatory process.
- Asthma and CRS are highly associated and consideration of both is necessary for optimizing treatment.
- Nasal saline irrigation with corticosteroid spray is the first line and has been found to be useful.
- Topical corticosteroids are recommended for CRSwNP, with consideration for twice daily dosing.

Summary

- It is important to delineate the subtypes of CRSwNP to determine best treatment.
- INCS/topical steroids, nasal saline irrigation, endoscopic sinus surgery, AERD management, and biologics can be used in combination to optimize treatment.
- Patient symptomatology, characteristics, adherence, healthcare access should all be considered when making treatment plans with a multidisciplinary team.

Thank you!