TREATMENT OPTIONS FOR CHRONIC RHINOSINUSITIS WITH NASAL POLYPS

Dana V. Wallace, MD

FINANCIAL DISCLOSURES

- Optinose
- ALK
- Kaleo
- Bryan

LEARNING OBJECTIVES

At the conclusion of this lecture, the participant should be able to:

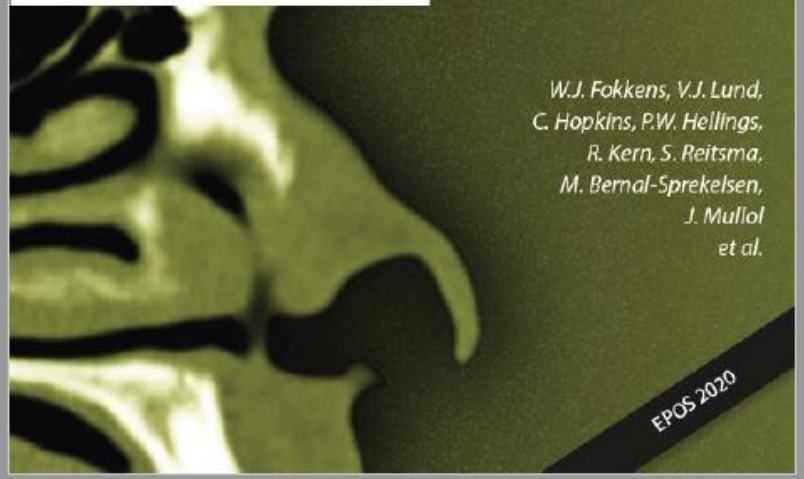
1) **Design a medical treatment plan for a patient with CRSwNP**
2) **Discuss the optimal timing of medical and surgical treatment options for CRSwNP**

VOLUME 58 | SUPPLEMENT 29 | FEBRUARY 2020

European Position Paper on Rhinosinusitis and Nasal Polyps

EPOS2020

European Position Paper on Rhinosinusitis and Nasal Polyps 2020



W.J. Fokkens, V.J. Lund,
C. Hopkins, P.W. Hellings,
R. Kern, S. Reitsma,
M. Bernal-Sprekelsen,
J. Mullol
et al.

EPOS 2020

RHINOLOGY
Official Journal of the European and International Rhinologic Societies and of the Confederation of European OTO-HNS

ERS

GRADING OF EVIDENCE FOR EPOS

CATEGORY OF EVIDENCE

Therapy/Prevention/Etiology/Harm:

1a:	Systematic reviews (with homogeneity) of randomized controlled trials
1b:	Individual randomized controlled trials (with narrow confidence interval)
1c:	All or none randomized controlled trials
2a:	Systematic reviews (with homogeneity) of cohort studies
2b:	Individual cohort study or low quality randomized controlled trials (e.g. <80% follow-up)
2c:	"Outcomes" Research; ecological studies
3a:	Systematic review (with homogeneity) of case-control studies
3b:	Individual case-control study
4:	Case-series (and poor quality cohort and case-control studies)
5:	Expert opinion without explicit critical appraisal, or based on physiology, bench research or "first principles"

Note: A minus sign "-" may be added to denote evidence that fails to provide a conclusive answer because it is *either* (a) a single result with a wide Confidence Interval; *OR* (b) a Systematic Review with troublesome heterogeneity. Such evidence is inconclusive, and therefore can only generate Grade D recommendations.

QUALITY OF EVIDENCE

- High
- Moderate
- Low
- Very Low
- Not stated (DW)

Received: 2 November 2020 | Accepted: 9 November 2020

DOI: 10.1002/alr.22741

REVIEW ARTICLE

International consensus statement on allergy and rhinology: rhinosinusitis 2021

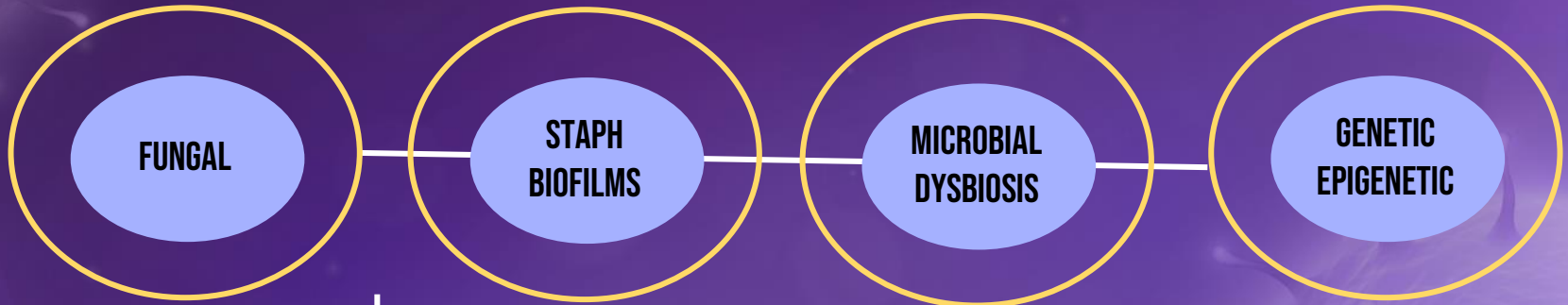
64 authors listed

Richard R. Orlandi MD[1] | Todd T. Kingdom MD[2] | Timothy L. Smith MD, MPH[3] | Benjamin Bleier MD[4] | Adam DeConde MD[5] | Amber U. Luong MD, PhD[6] |

TABLE IV-3 AAP defined strategy for recommendation development[141]

Evidence Quality	Preponderance of Benefit over Harm	Balance of Benefit and Harm	Preponderance of Harm over Benefit
A. Well-designed RCT's	*Strong Recommendation*	*Option*	*Strong Recommendation Against*
B. RCT's with minor limitations; Overwhelmingly consistent evidence from observational studies	*Recommendation*		
C. Observational studies (case control and cohort design)			*Recommendation Against*
D. Expert opinion, Case reports, Reasoning from first principles	*Option*	*No Recommendation*	

FAILURE OF ETIOLOGY-BASED TREATMENTS FOR CRS



#1

Anti-fungal Tx failure
Oral/topical

#2

Oral/topical
antibiotics failure

#3

Changing
microbiome failure

#4

Multiple genes
each gene small effect size

TREATMENT OF CRS: 1A SYSTEMATIC REVIEWS

[ICAR CRS 2021]

THERAPY	RECOMMENDATION	QUALITY OF EVIDENCE
NASAL STEROIDS [CRSwNP]	• Long-term use is both effective & safe • All pharmacological INS produce equal efficacy • Reduce poly size , > effect size if used after surgery • Reduce reoccurrences following endoscopic surgery • No effect on IOP or lens opacity • Higher doses (>2x AR dose) & alternate delivery methods may have larger effect size (mainly indirect comparisons and low quality evidence)	High [Strong Rec: A]
[CRSwNP]	• Use steroid irrigation if not controlled with INCS	[Strong Rec: B]
[CRSwNP]	• Use exhalation delivery if not controlled with INCS	[Option: B]

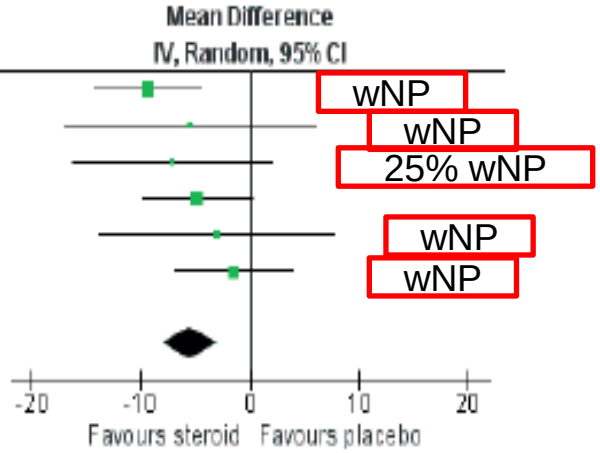
INS IMPROVE SNOT-22 (QOL)

Figure 6.1.5.1. Forest plot of the effect of nasal corticosteroids versus placebo on disease specific quality of life (SNOT-22) in patients with CRS.

	Steroid			Placebo				Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year
Leopold 2019	-21.05	15.213	82	-11.7	16.0876	79	28.3%	-9.35 [-14.19, -4.51]	2019
Kobayashi 2018	-9.796	8.21559	10	-4.30733	18.1977039	12	5.2%	-5.49 [-16.98, 6.00]	2018
Tait 2018	-20.7	17.9	29	-13.6	18.8	32	8.1%	-7.10 [-16.31, 2.11]	2018
Dixon 2015	-11.2	25.5708	189	-6.37	24.6868	199	27.4%	-4.83 [-9.64, 0.16]	2015
Rawal2015	16	14.81	24	19	19.26	19	6.0%	-3.00 [-13.69, 7.69]	2015
Rotenberg2011	28.2	9.1	20	29.7	8.3	21	24.1%	-1.50 [-6.84, 3.84]	2011
Total (95% CI)			**354**			**361**	**100.0%**	**-5.46 [-8.08, -2.84]**	

Heterogeneity: Tau² = 0.00; Chi² = 4.98, df = 5 (P = 0.42); I² = 0%

Test for overall effect: Z = 4.09 (P < 0.0001)



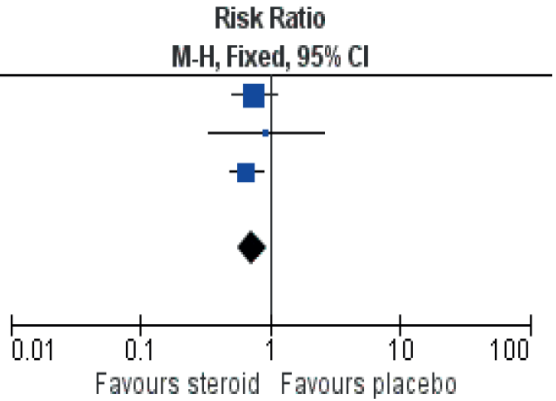
INS PREVENT NASAL POLYP RECURRENCE AFTER FESS

Figure 6.1.5.14. Forest plot of the effect of nasal corticosteroid versus placebo on the prevention of nasal polyp recurrence after sinus surgery in CRSwNP patients

	steroid		placebo			Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year
Stjarne 2009	26	79	35	80	52.2%	0.75 [0.50, 1.12]	2009
Dijkstra 2004	4	13	7	21	8.0%	0.92 [0.33, 2.55]	2004
Gulati 2001	22	38	22	25	39.8%	0.66 [0.48, 0.89]	2001
Total (95% CI)		**130**		**126**	**100.0%**	**0.73 [0.56, 0.94]**	
Total events	52		64				

Heterogeneity: Chi² = 0.66, df = 2 (P = 0.72); I² = 0%

Test for overall effect: Z = 2.40 (P = 0.02)

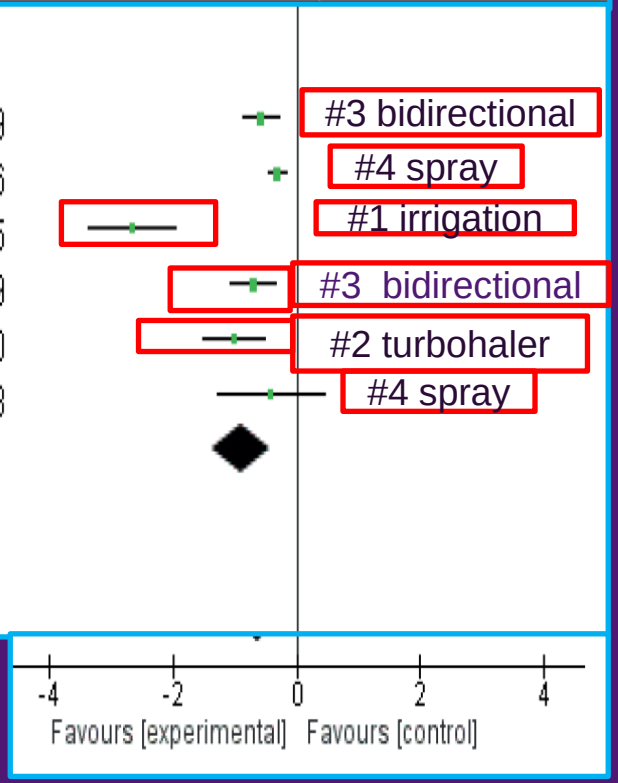


EFFECT OF INS DELIVERY METHOD IN CRS WITH NASAL POLYPS ON SYMPTOM SCORE

Study or Subgroup	Favors steroid Mean	SD	Total	Favors placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year	Std. Mean Difference IV, Random, 95% CI
1.2.2 CRSwNP										
Leopold 2019	-0.62	0.63	82	-0.24	0.62	79	10.4%	-0.61 [-0.92, -0.29]	2019	#3 bidirectional
Zhou 2016	-1.08	0.75	350	-0.84	0.73	336	11.8%	-0.32 [-0.47, -0.17]	2016	#4 spray
Wang 2015	-11.5	3.82	29	-0.7	3.82	28	6.2%	-2.79 [-3.53, -2.05]	2015	#1 irrigation
Vickova 2009	-1.11	1.91	54	0.31	1.93	52	9.6%	-0.73 [-1.13, -0.34]	2009	#3 bidirectional
Filiaci 2000	-1.15	0.91	36	-0.15	0.95	31	8.3%	-1.06 [-1.58, -0.55]	2000	#2 turbohaler
Lund 1998	2	4.44	10	4	4.44	9	4.9%	-0.43 [-1.34, 0.48]	1998	#4 spray
Subtotal (95% CI)			**561**			**535**	**51.2%**	**-0.93 [-1.43, -0.44]**		

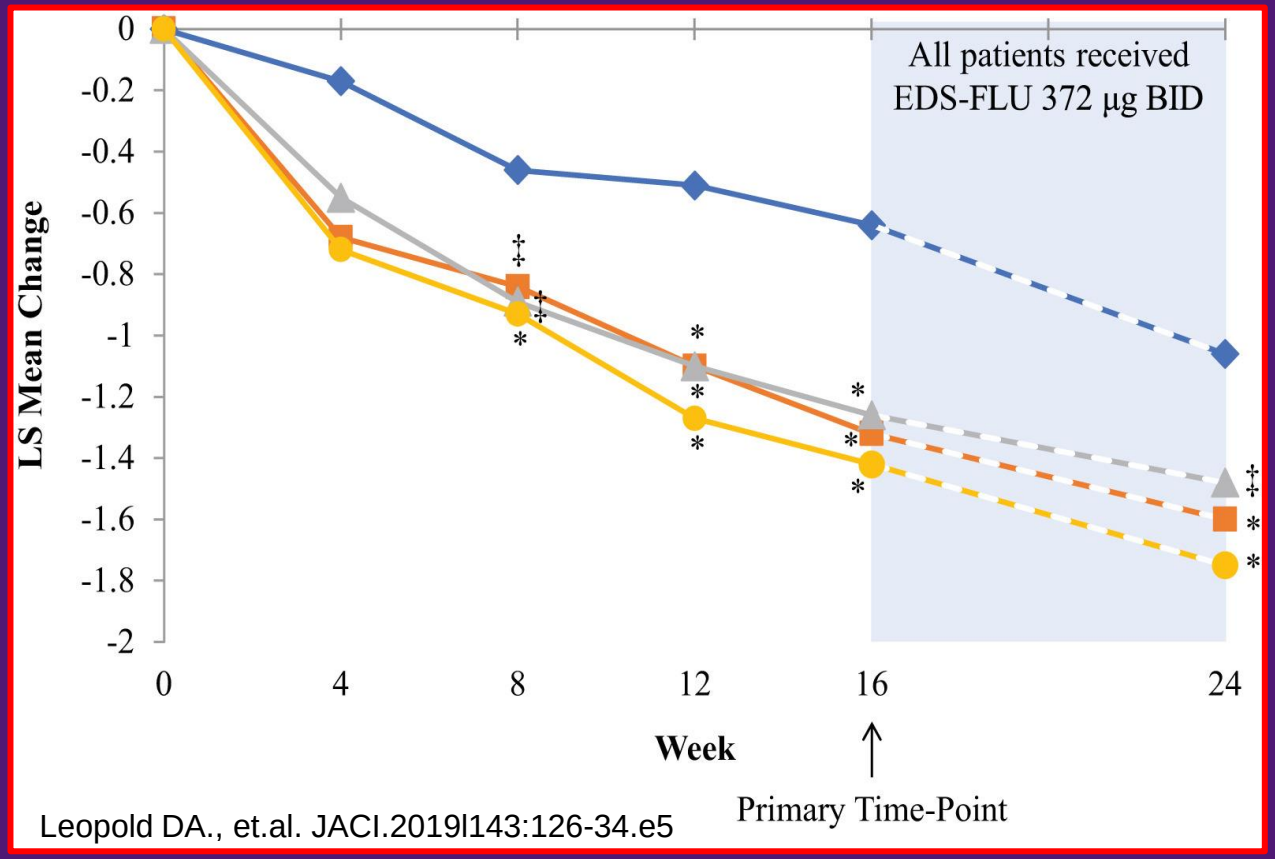
Heterogeneity: Tau² = 0.31; Chi² = 48.12, df = 5 (P < 0.00001); I² = 90%

Test for overall effect: Z = 3.70 (P = 0.0002)

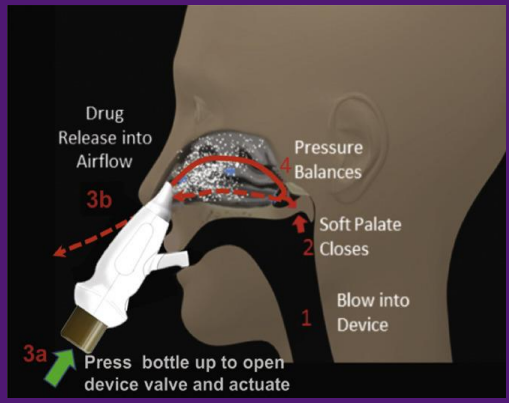


SMD: Spray: -0.30 (7 studies)
Bidirectional: -0.68 (3 studies)

EXHALATIONAL DELIVERY DEVICE– MEAN CHANGE BILATERAL POLYP SCORES



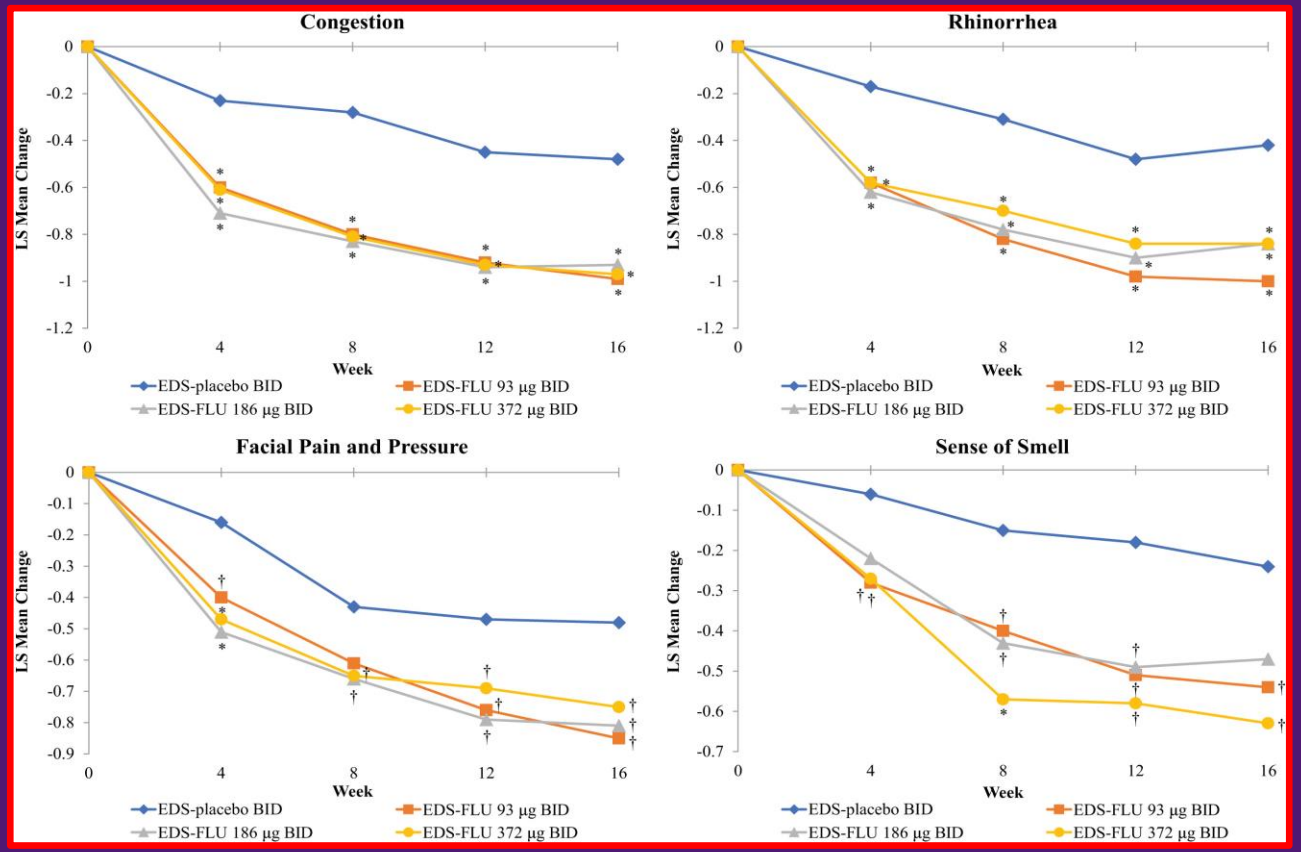
Leopold DA., et.al. JACI.2019l143:126-34.e5



- EDS-FLU 93 µg BID
- EDS-FLU 372 µg BID
- EDS-FLU 93 µg followed by 372 µg BID
- EDS-FLU 372 µg followed by 372 µg BID

- EDS-placebo BID
- EDS-FLU 186 µg BID
- EDS-placebo followed by EDS-FLU 372 µg BID
- EDS-FLU 186 µg followed by 372 µg BID

EXHALATIONAL DELIVERY DEVICE– AM INSTANTANEOUS SYMPTOMS



Leopold DA., et.al. JACI.2019l143:126-34.e5

INS FOR NASAL POLYPS
DIRECT COMPARISONS OF DELIVERY METHODS—3 STUDIES

- 3 studies with direct comparison but low to moderate certainty of evidence
- Nasal steroid drops more effective than nasal sprays for polyps but 4x higher dose used for drops in the one comparison trial [1]
- Nasal steroid irrigation is more effective than nasal sprays for CRS post-op.[2]
- Cadaver studies showed better sinus cavity distribution for irrigation vs. nasal sprays (using Netipot or squeeze bottle)[3]
- 2.5% fluid irrigation fluid retained in sinuses following irrigation (human study)[3]
- Endoscopic surgery greatly enhances fluid distribution [2,3]
- Most studies used 60 ml/nostril but total of 240 ml/day steroid irrigation solution , e.g., 2000 mcg mometasone/240 ml
- Long-term studies (6-12 mo.) comparing nasal steroid spray vs. nasal saline irrigation in meta-analysis have not shown a significant difference

1.Demirel T. Kulak Burun Bogaz Ihtis Derg. 2008;18(3):1-6. 2. Harvey RJ. Int Forum Allergy Rhinol. 2018;8(4):461-70. 3. Harvey RJ. Immunol Allergy Clin North Am. 2009;29(4):689-703.

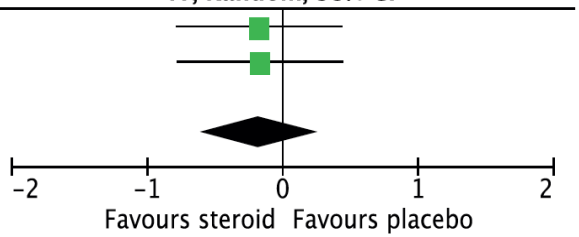
INS VS SALINE IRRIGATION IN CRSwNP– LONG TERM NO SIGNIFICANT DIFFERENCE

Figure 6.1.5.10. SNOT score at six months after steroid irrigation versus saline irrgation in CRS compared to placebo.CRS patients.

	steroid irrigation			placebo				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Rawal2015	16	14.81	24	19	19.26	18	50.1%	-0.17 [-0.79, 0.44]
Rotenberg2011	28.2	9.1	20	29.7	8.3	21	49.9%	-0.17 [-0.78, 0.44]
Total (95% CI)			**44**			**39**	**100.0%**	**-0.17 [-0.61, 0.26]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.00$, df = 1 (P = 0.99); $I^2 = 0\%$

Test for overall effect: Z = 0.78 (P = 0.44)



Both studies were with CRSwNP patients

TREATMENT OF CRS: 1A SYSTEMATIC REVIEWS

[ICAR CRS 2021]

THERAPY	RECOMMENDATION	QUALITY OF EVIDENCE
CS-ELUTING IMPLANTS (ETHMOIDS AT SURGERY) [CRSwNP]	• Reduces need for repeat surgery • Reduces NP score but minimal effect on nasal obstruction • Consider as Tx **option**	Moderate to high [Option: A]
SYSTEMIC STEROIDS (SHORT COURSE 7-17 DAYS) [CRSwNP]	• Improves symptom score • Reduces polyp score for 3 months • No effect on QOL & significant side effects • **Only use 1-2x/year for uncontrolled dz**	Not stated [Strong Rec: A]

TREATMENT OF CRS: 1A SYSTEMATIC REVIEWS

[ICAR CRS 2021]

THERAPY	RECOMMENDATION	QUALITY OF EVIDENCE
NASAL IRRIGATION SALINE	• 20 studies but mixed results • Overall saline irrigation with saline or Ringer's lactate shows some efficacy and it is conditionally recommended • Nasal douching with head on floor gives better distribution than irrigation or sprays BUT no data showing a difference in symptom reduction • Large volume, low pressure irrigation or squeeze bottle vs. high pressure low volume spray **may not make a difference** • Addition of xylitol, Na hyaluronate, & xyloglucan may be beneficial • Baby shampoo, honey, or dexpanthenol has **no added benefit** • Higher temp and/or increased salt content has **no added benefit**	Low **[Rec.]**

[ICAR CRS 2021]

TREATMENT OF CRS : 1A SYSTEMATIC REVIEWS

THERAPY	RECOMMENDATION	LEVEL OF EVIDENCE
ASA TX AFTER DESENSITIZATION WITH ORAL ASA IN N-ERD [CRSwNP]	• **Consider Tx option** in compliant pt • Reduced symptoms for 6 months following desensitization	Moderate to high [Rec: A]

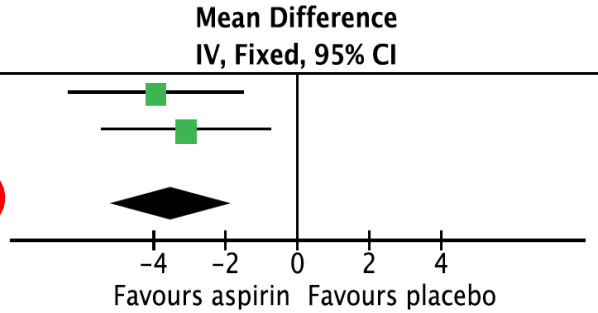
ASA DESENSITIZATION AND TX IN N-ERD
EFFECT ON CRS SYMPTOM SCORE- 6 MONTHS

Figure 6.1.12.2. Forest plot of the effect of ATAD versus standard treatment alone on the symptom score six months after start of the treatment in patients with CRSwNP.

	ATAD			Placebo				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI
Mortazavi 2017	7.95	3.4	19	11.89	4.2	19	48.5%	-3.94 [-6.37, -1.51]
Esmaeilzadeh 2015	7.5	3.2	16	10.6	3.6	16	51.5%	-3.10 [-5.46, -0.74]
Total (95% CI)			**35**			**35**	**100.0%**	**-3.51 [-5.20, -1.81]**

Heterogeneity: $Chi^2 = 0.24$, df = 1 (P = 0.63); $I^2 = 0\%$

Test for overall effect: Z = 4.06 (P < 0.0001)



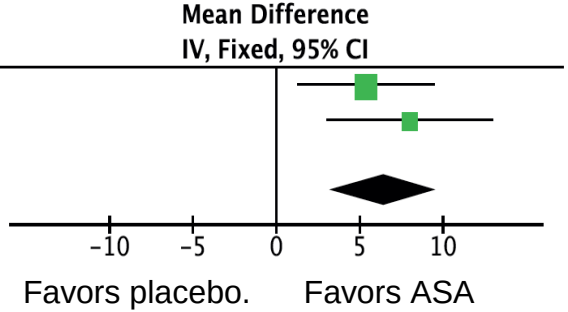
ASA DESENSITIZATION AND TX IN N-ERD
EFFECT ON FEV-1

Figure 6.1.12.3. Forest plot of the effect of ATAD versus standard treatment alone on the FEV1 six months after start of the treatment in patients with CRSwNP.

	Aspirin treatment			Placebo				Mean Difference	
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Fixed, 95% CI**	**Year**
Mortazavi 2017	85.37	5.9	19	80	7	19	59.6%	5.37 [1.25, 9.49]	2017
Esmaeilzadeh 2015	87.1	6.8	16	79.1	7.6	16	40.4%	8.00 [3.00, 13.00]	2015
Total (95% CI)			**35**			**35**	**100.0%**	**6.43 [3.26, 9.61]**	

Heterogeneity: $Chi^2 = 0.63$, df = 1 (P = 0.43); $I^2 = 0\%$

Test for overall effect: Z = 3.97 (P < 0.0001)



[ICAR CRS 2021]

TREATMENT OF CRS : 1A SYSTEMATIC REVIEWS

THERAPY	RECOMMENDATION	LEVEL OF EVIDENCE
ASA TX AFTER DESENSITIZATION WITH ORAL ASA IN N-ERD [CRSwNP]	• Consider Tx option in compliant patient • Reduced symptoms for 6 months after desensitization • Effective but does not reach "clinically important" mean difference • Significant adverse effects & patient burden	Moderate to high [Rec: A]

TREATMENT OF CRS: 1A(-) CAUTION

[ICAR CRS 2021]

THERAPY	RECOMMENDATION	QUALITY OF EVIDENCE
LOCAL & SYSTEMIC ANTI-FUNGAL AGENTS [CRSwNP]	• Only 1 controlled study • No improvement in symptoms, signs of dz., or QOL • **Do not use**	Moderate (?) [Strong Rec against: A-]
LONG-TERM ANTIBIOTICS (E.G. MACROLIDES) [CRSwNP]	• **Uncertain if any benefit** on symptoms • Patients with low IgE may respond better • **No advantage over INS** • Cardiovascular short/long-term adverse events a concern	Low Quality High heterogeneity **[Option: B]**

MACROLIDES USE IN CRS

Figure 6.1.2.1. Forest plot of the effect of macrolides versus placebo on responder scores in CRS patients.

Study or Subgroup	Macrolide Mean	Macrolide SD	Macrolide Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Std. Mean Difference IV, Random, 95% CI
Videler 2011	2.7	2.36	27	2.7	1.67	29	49.9%	0.00 [-0.52, 0.52]
Wallwork 2006	3.11	0.92	29	3.84	0.71	35	50.1%	-0.89 [-1.41, -0.37]
Total (95% CI)			**56**			**64**	**100.0%**	**-0.45 [-1.32, 0.43]**

Heterogeneity: $Tau^2 = 0.32$; $Chi^2 = 5.59$, df = 1 (P = 0.02); $I^2 = 82\%$
Test for overall effect: Z = 1.00 (P = 0.32)

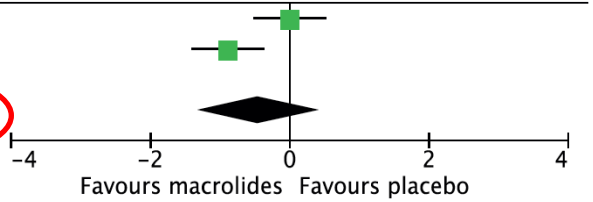
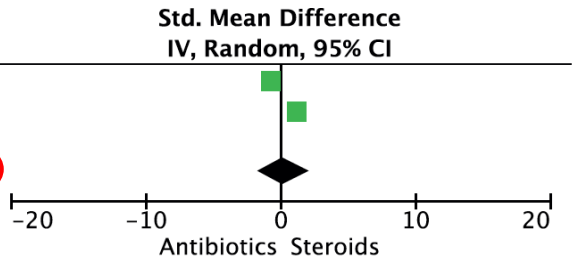


Figure 6.1.2.3. Forest plot of the effect of macrolides versus nasal corticosteroids on SNOT scores in CRS patients.

Study or Subgroup	Antibiotics Mean	Antibiotics SD	Antibiotics Total	Steroids Mean	Steroids SD	Steroids Total	Weight	Std. Mean Difference IV, Random, 95% CI
Amali 2015	0.27	0.12	20	0.46	0.29	40	50.0%	-0.76 [-1.31, -0.20]
Haxel 2014	0.95	0.13	29	0.79	0.14	29	50.0%	1.17 [0.61, 1.73]
Total (95% CI)			**49**			**69**	**100.0%**	**0.21 [-1.68, 2.09]**

Heterogeneity: $Tau^2 = 1.77$; $Chi^2 = 22.94$, df = 1 (P < 0.00001); $I^2 = 96\%$
Test for overall effect: Z = 0.21 (P = 0.83)



TREATMENT OF CRS: 1B RCTS

[ICAR CRS 2021]

THERAPY	RECOMMENDATION	QUALITY OF EVIDENCE
ANTIHISTAMINES	• No decrease in TNSS • Only 1 study • **Not enough evidence** to make recommendation	Very low **[Insufficient evidence]**
DECONGESTANTS + INCS VS. INCS	• Only 1 study showed increased benefit (without rebound) in CRSwNP • **EPOS recommended against use for CRS**, exception short-term for severe congestion	Very low **[Insufficient evidence]**
LOW SALICYLATE DIET IN NSAIDS ERD	• May improve endoscopic scores • **May reduce symptoms**	Low

TREATMENT OF CRS: 1B RCTS

[ICAR CRS 2021]

THERAPY	RECOMMENDATION	QUALITY OF EVIDENCE
HERBAL TREATMENT [ALL CRS]	• Mixed efficacy results (5 studies) • Adverse effects=placebo • **No recommendation for or against**	Low **[Insufficient evidence]**
MUCOLYTIC AGENTS [ALL CRS]	• Limited evidence • **No recommendation for or against**	Low **[Insufficient evidence]**
NASAL FUROSEMIDE [CRSwNP]	• 1 DBPCT showed reduced SNOTT, polyp size and nasal polyp score • **No recommendation for or against**	Very low [Option: B]
CAPSAICIN [ALL CRS]	• 2 small studies showed reduced polyp score & reduced nasal obstruction • **Consider in CRSwNP**	Low **[Insufficient evidence]**

TREATMENT OF CRS: 1B- RCTS (CAUTION)

[ICAR CRS 2021]

THERAPY	RECOMMENDATION	QUALITY OF EVIDENCE
SHORT-TERM ANTIBIOTICS FOR CRS OR ACUTE EXACERBATIONS [CRSwNP]	• 2 small placebo-controlled studies • **Unclear if there is any benefit** on symptoms • Adverse events with GI track	Very low **[Rec against: B-]**
ANTI-LEUKOTRIENES [CRSwNP]	• Limited studies, only 1 study blinded • Potential benefit uncertain • **Recommend not to use if INS tolerated** • **Option with or without INS**	Very low [Option: A]
TOPICAL ANTIBIOTICS [CRSwNP]	• No better than placebo in improving symptoms • **Uncertain if an impact on patient outcomes**	Very low **[Rec against: A-]**

TOPICAL ANTIBIOTICS FOR CRS

- 4 RCT trials with placebo control (3 CRSwNP) did not show any benefit for topical antibiotics
- A non-placebo controlled trial showed that high-volume irrigation with mupirocin vs. oral amoxicillin/clavulanic acid is superior to eradicating Staph aureus but SNOT-22 and endoscopy scores are not significantly better.

EPOS 2020 Position paper

[ICAR CRS 2021]

EPOS ADVICE ON OTHER TREATMENTS

RECOMMENDS AGAINST

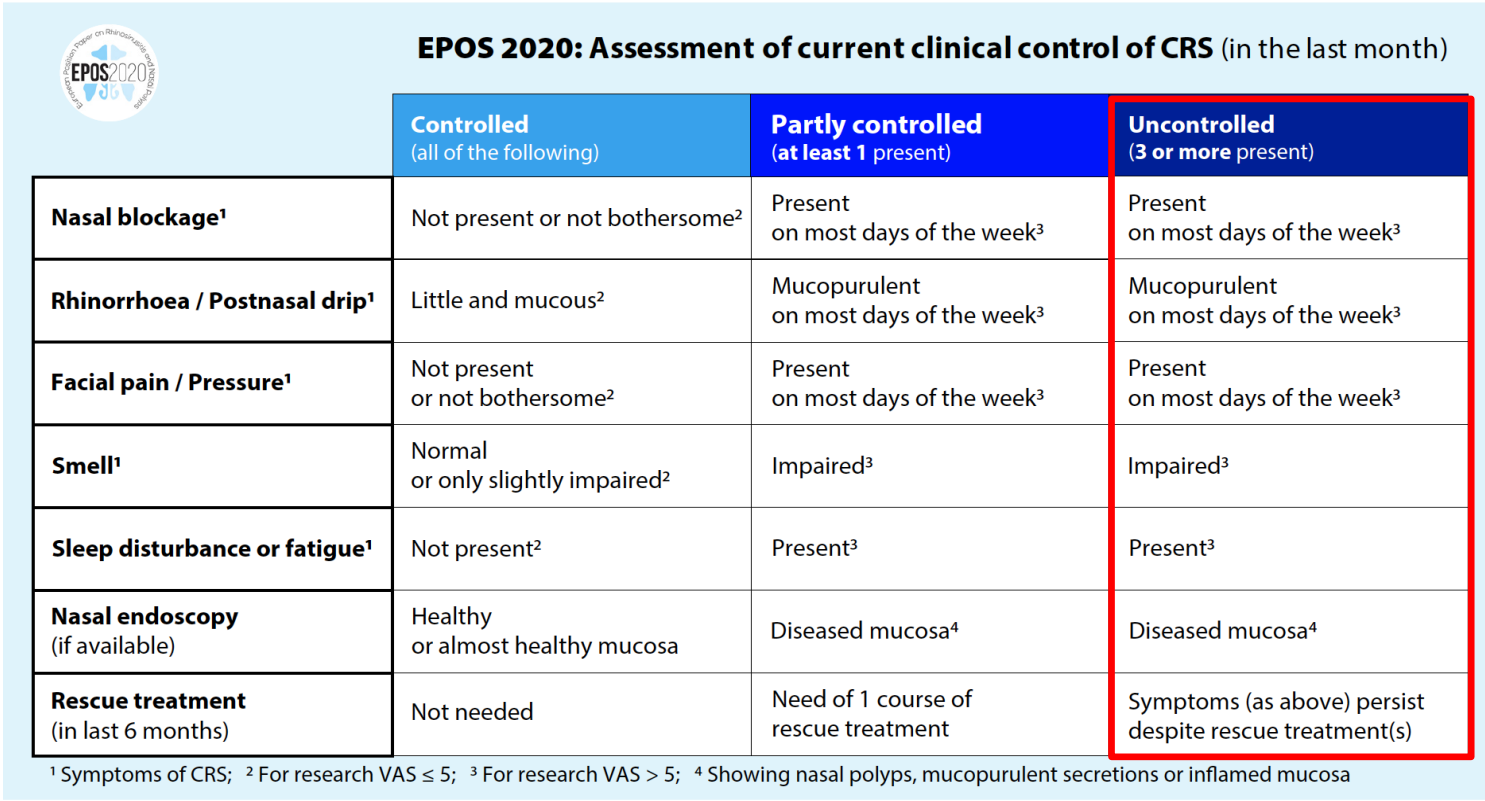
- Probiotics Ib (-) **[Insufficient evidence]**
- Acupuncture Ib (-)
- Traditional Chinese medicine Ib (-)
- Oral verapamil Ib
- Proton pump inhibitors Ib (-)
- Nasal lysine aspirin and platelet inhibitors (like Pradugrel) for N-ERD Ib (-)

NO RECOMMENDATION FOR OR AGAINST

- Bacterial lysate Ib (-)
- Phototherapy Ib
- Filgastrim (r-met-HuG-CSF) Ib (-)
- Collodial silver nasal sp. Ib (-) [Rec. against :B-]
- Manuka honey **[Insufficient evidence]**
- **Surfactants [Insufficient evidence]**

UNCONTROLLED CRS

Figure 1.2.3. Assessment of current clinical control of CRS.

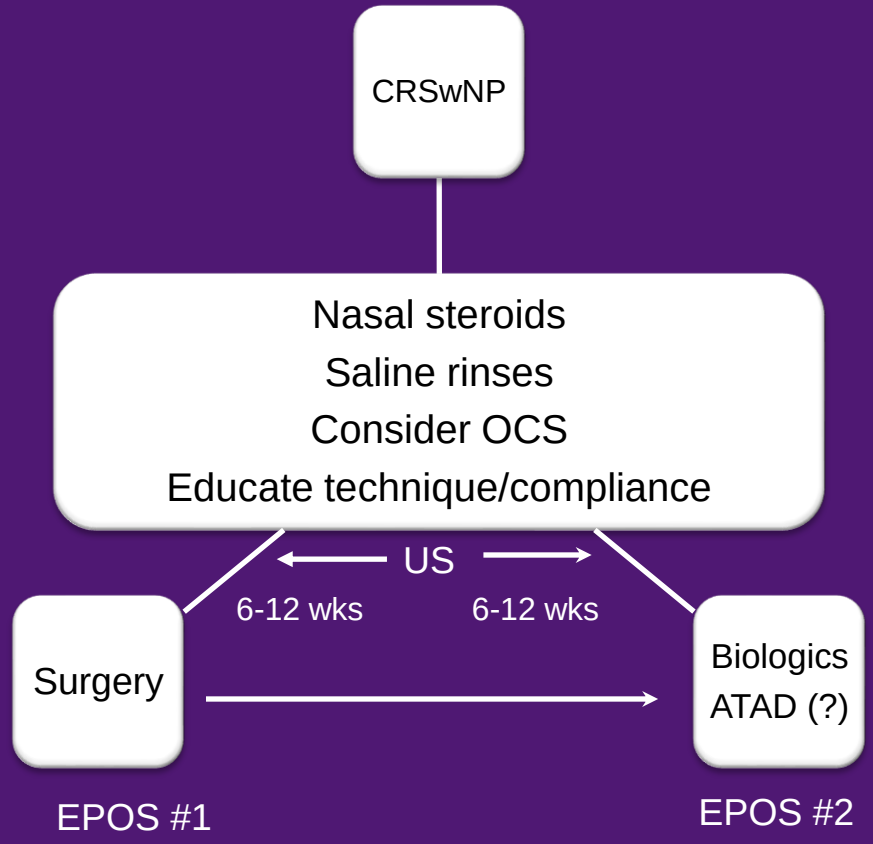


EPOS 2020: Assessment of current clinical control of CRS (in the last month)

	Controlled (all of the following)	**Partly controlled** (**at least 1** present)	**Uncontrolled** (**3 or more** present)
Nasal blockage[1]	Not present or not bothersome[2]	Present on most days of the week[3]	Present on most days of the week[3]
Rhinorrhoea / Postnasal drip[1]	Little and mucous[2]	Mucopurulent on most days of the week[3]	Mucopurulent on most days of the week[3]
Facial pain / Pressure[1]	Not present or not bothersome[2]	Present on most days of the week[3]	Present on most days of the week[3]
Smell[1]	Normal or only slightly impaired[2]	Impaired[3]	Impaired[3]
Sleep disturbance or fatigue[1]	Not present[2]	Present[3]	Present[3]
Nasal endoscopy (if available)	Healthy or almost healthy mucosa	Diseased mucosa[4]	Diseased mucosa[4]
Rescue treatment (in last 6 months)	Not needed	Need of 1 course of rescue treatment	Symptoms (as above) persist despite rescue treatment(s)

[1] Symptoms of CRS; [2] For research VAS ≤ 5; [3] For research VAS > 5; [4] Showing nasal polyps, mucopurulent secretions or inflamed mucosa

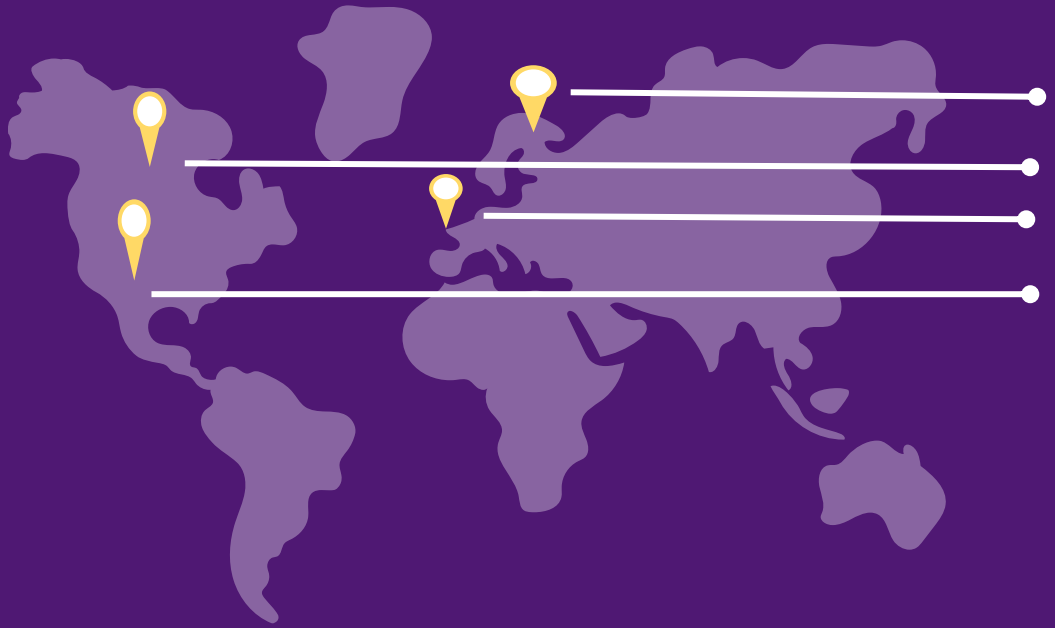
CRS, chronic rhinosinusitis; VAS, visual analogue scale.


CRSwNP
Nasal steroids
Saline rinses
Consider OCS
Educate technique/compliance
US
6-12 wks
6-12 wks
Surgery
Biologics
ATAD (?)
EPOS #1
EPOS #2

SURGERY

Functional Endoscopic Sinus Surgery (FESS)
Endoscopic Sinus Surgery (ESS)

ESS INTERVENTION RATES



FINLAND 0.71 [0.25-1,15)

CANADA 0.33/1000

UK 0.53/1000

US 0.94/1000 [0.5-1.8]

Recent trend

↓ Dx of CRS

↑ CRS surgery

EPOS 2020 position paper

WHEN IS ESS INDICATED?

- "**Failure of maximal medical treatment**" but what type and for how long?
- Systematic review (387 studies from 2009-2014) indicated only 21% reported requiring "max medical tx" prior to surgery. [1]
  - **91% used 8 wks. INS**
  - **89% used 3 wks. antibiotics**
  - 61% systemic corticosteroids for 18 days (same sNP or wNP)
  - 39% saline irrigations
- When, if ever, should the Lund-MacKay CT scan score be used?

1. Dautremont JF. Int Forum Allergy Rhinol. 2015;5(12):1095-103.

LUND-MACKEY CT SCORING SYSTEM

Lund–Mackey system.

Sinus	Right sinus	Left sinus
Frontal	0–2	0–2
Anterior ethmoids	0–2	0–2
Posterior ethmoids	0–2	0–2
Maxillary	0–2	0–2
Sphenoid	0–2	0–2
Ostiomeatal complex	0 or 2	0 or 2

For the sinuses: 0 = no inflammation; 1 = partial inflammation; 2 = 100% inflammation.
For the ostiomeatal complex: 0 = not occluded; 2 = occluded.
Maximum total score: 24.

LMS SCORING (0-24)

LMS of 2 or less= dx CRS has high neg predictive value

LMS of 5 or greater=dx CRS has high pos predictive value

EES PROPOSED MINIMAL CRITERIA FOR CRSwNP

1. **LMS of 1 (of 24) or greater**
2. **INS for 8 wks. or greater**
3. **Systemic corticosteroids (short course)**
4. **SNOTT-22 > 20 (of 110)**

1. Rudmik L. Int Forum Allergy Rhinol. 2016;6(6):557-67.

WHEN IS ESS INDICATED?

- “UK study 87 hospitals, 3128 pts having sinus surgery[1]
  - In CRSsNP **35%** had LMS <=4
  - In CRSwNP **8%** had LMS<=4
- Poor correlation between preoperative Lund-Mackay scores and QOL[2]
- Balloon dilatation RCT 57% had LMS <=4; **19% had LMS=0**.[3]
- 2014 JTFPP: “Consider endoscopic surgical intervention as an adjunct to medical treatment in patients with CRS that is poorly responsive to medical therapy. (Rec, C)”[4]

1. Hopkins C. Clin Otolaryngol. 2006;31(5):390-8. 2.Hopkins C. Otolaryngol Head Neck Surg. 2007;137(4):555-61. 3,Laury AM. Otolaryngol Head Neck Surg. 2018;159(1):178-84. 4. Peters, A.T. Ann Allergy Asthma Immunol 113(2014); 347-385.

BEFORE ENDOSCOPIC SURGERY

- A CT scan is mandatory prior to ESS to confirm presence and extent of disease and to identify anatomical features that may increase risk of complications
  - Evaluate depth & asymmetry of cribriform niche
  - Examine lamina papyracea for dehiscence
  - Review sphenoid-ethmoidal cells
  - Examine sphenoid sinus for dehiscence of underlying optic nerve and carotid artery
  - Position of ethmoidal arteries relative to skull base
- If CRS diagnosed endoscopically, CT scan can be delayed until surgery is contemplated
- No need to repeat CT scan if previously obtained and no intervening surgery
- Use of preoperative steroids improves quality of surgical field, reduces duration of surgery, and reduces blood loss
- Oral steroids for 7-10 days (3 studies) or INS for 4 wks. (1 study) have both been effective but unclear if one or both are best

WHAT PREDICTS SUCCESSFUL ESS?

[ICAR CRS 2021]

- For patients, SNOT-22 most influential factor when they choose surgery[3]
  - ICAR CRS 2021 in agreement: Grade B
- Preoperative SNOT-22 predicts post-operative improvement[1]
  - SNOT-22 > 30= ↑ QOL; SNOT<20= No ↑ QOL
- Change at 3 & 12 months post-op vs. preop SNOT-22 predicts need for revision surgery [2]
- Systematic review/meta-analysis found improved SNOT-22 correlated with older age, asthma, prior ESS, and high preoperative SNOT-22.[4]
- Tobacco smokers had poorer SNOT-22 outcomes.[4]
- Delaying surgery results in reduced symptom improvement post-op
- Post-op sinus cavity debridement : ICAR CRS 2021 Rec: Grade B

1. Rudmik L. Laryngoscope. 2015;125(7):1517-22. 32. Rudmik L. Rhinology. 2016;54(2):111-6. 3.Soler ZM. Laryngoscope. 2013;123(10):2341-6.4. Le PT. Otolaryngol Head Neck Surg. 2018;159(3):414-23.

[ICAR CRS 2021]

SURGICAL PROCEDURES FOR CRS

- Antral washouts are not of value over medical treatment
- “Middle meatal antrostomy”(MMA) is enlargement of the maxillary sinus ostia
- MMA has better outcomes than Caldwell-Luc
- “Extended ESS” includes resection of middle/superior turbinates + total ethmoidectomy
- ”Radical antrectomy” includes medial maxillectomy with complete removal of the maxillary sinus mucosa, mega-antrostomy through the middle meatus and adjuvant canine fossa puncture, partial resection inferior turbinate
- Natural maxillary ostium must be patent but uncertain if enlargement is beneficial
- Careful debridement in olfactory cleft may improve olfactory function in CRSwNP
- Debate continues over minimally invasive vs. more aggressive surgical approach
  - iCAR CRS 2021 supports less invasive for milder dz Grade B
- Limited data on adjunctive septoplasty and turbinate surgery (1 or both used in 1/3 of sinus surgery cases)

EPOS 2020 position paper

[ICAR CRS 2021]

BALLOON SINUPLASTY

- In mild (and possibly moderate) CRSsNP equivalent results compared to ESS with fewer complications[1]
  - ICAR CRS 2021 in agreement: Grade B evidence
- For severe and/or complicated CRS or CRSwNP, ESS is usually preferred[1]
- Prospective RT of 12- patients with frontal sinusitis without polyps, balloon sinuplasty and ESS were equally effective based on Lund-Mackay score for both mild and moderate/severe disease. For mild disease balloon sinuplasty was equal to ESS for SNOT-22 but superior for moderate/severe dz.[2]

1. EPOS 2020 Position Paper. 2. Minni A. Eur Rev Med Pharmacol Sci. 2018;22(2):285-93.

[ICAR CRS 2021]

IMAGE GUIDANCE FOR ESS IS APPROPRIATE FOR:

- Revision sinus surgery.
- Distorted sinus anatomy of development, postoperative, or traumatic origin.
- **Extensive sino-nasal polyposis.**
- Pathology involving the frontal, posterior ethmoid and sphenoid sinuses.
- Disease abutting the skull base, orbit, optic nerve or carotid artery.
- CSF rhinorrhea or conditions where there is a skull base defect.
- Benign and malignant sino-nasal neoplasms.
- ICAR CRS 2021: ”Option, benefit>harm. Grade B evidence”

- International Consensus Statement on Allergy and Rhinology for Rhinosiusitis in 2016

PREDICTING TERTIARY DISEASE PREVENTION

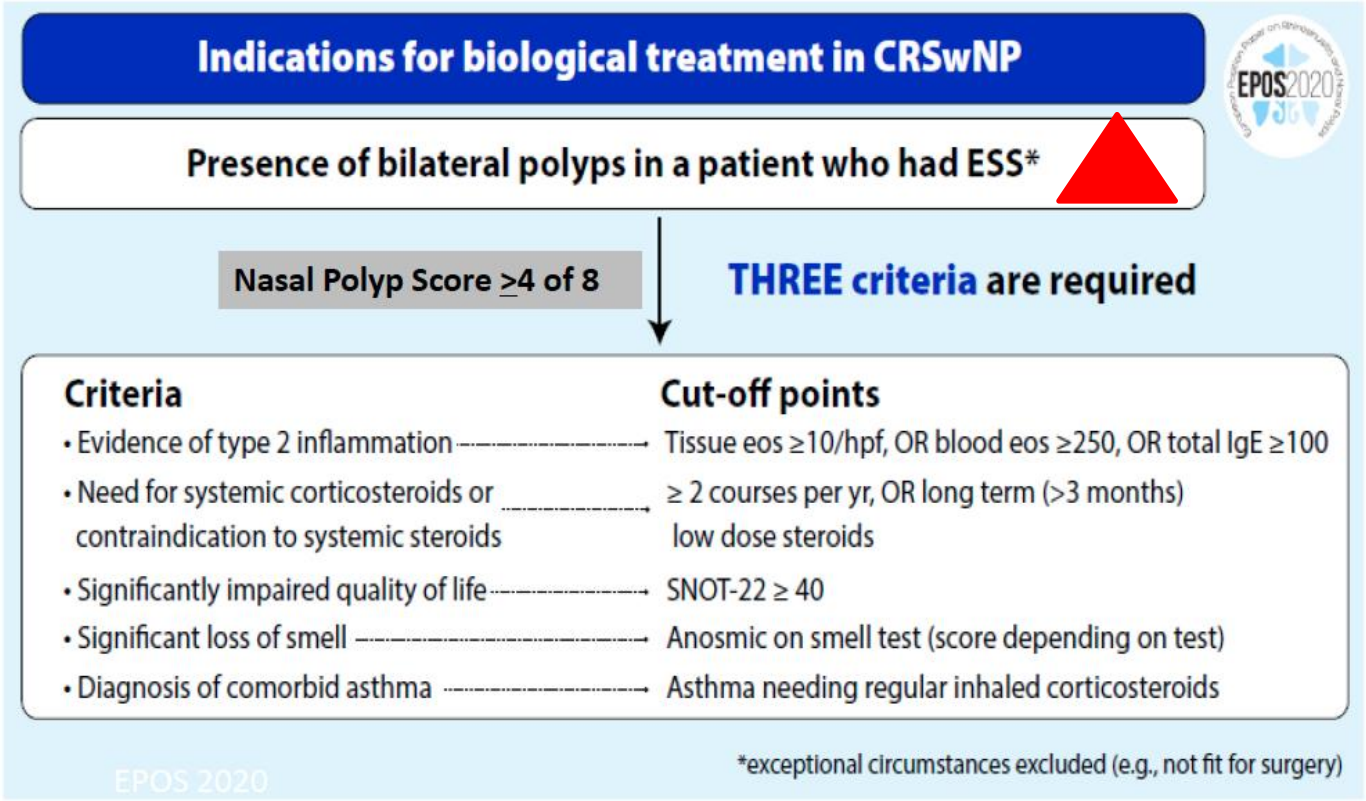
- Preoperative SNOT-22 score is best predictor of surgical success
- When loss of smell is major symptom, positive response to oral corticosteroids predicts better surgical outcome
- 12 months post FESS, 42% of patient stop INS even with regular phone contact– we must encourage adherence
- 40% CRS patients will have “uncontrolled dx” within 3-5 yrs. after ESS
- Tobacco smokers require higher rates of revision sinus surgery
- Occupational irritant exposure makes management more difficult
- In refractory CRS, consider co-existing immunodeficiency

EPOS 2020 Position paper

MONOCLONAL ANTIBODIES

EPOS 2020- Indications for Treatment with a Biologic

Figure 1.6.3. Indications for biological treatment in CRS.



BRITISH RHINOLOGICAL SOCIETY CONSENSUS GUIDANCE 2021 FOR CRSwNP

Biologics SHOULD be considered if the following conditions are met;

Patient with CRS with nasal polyps AND moderate symptom severity or more (SNOT22>=21 or VAS >=4) AND Lund-Mackay CT Score >= 8

AND a score of 5 points or more out of a possible 7;

Number of courses of OCS in last 12 months (to max of 2 points)
- 1 course in last 12 months = 1 point
- 2 or more courses in last 12 months = 2 points
- Unable to take OCS due to medical contraindications = 2 points

Number of previous surgeries for CRSwNP (to max of 3 points)
- 1 previous sinus surgery = 1 point
- 2 previous sinus surgeries = 2 points
- 3 or more previous sinus surgeries = 3 points
- If unfit for surgery = 3 points

Requires Prior Surgery

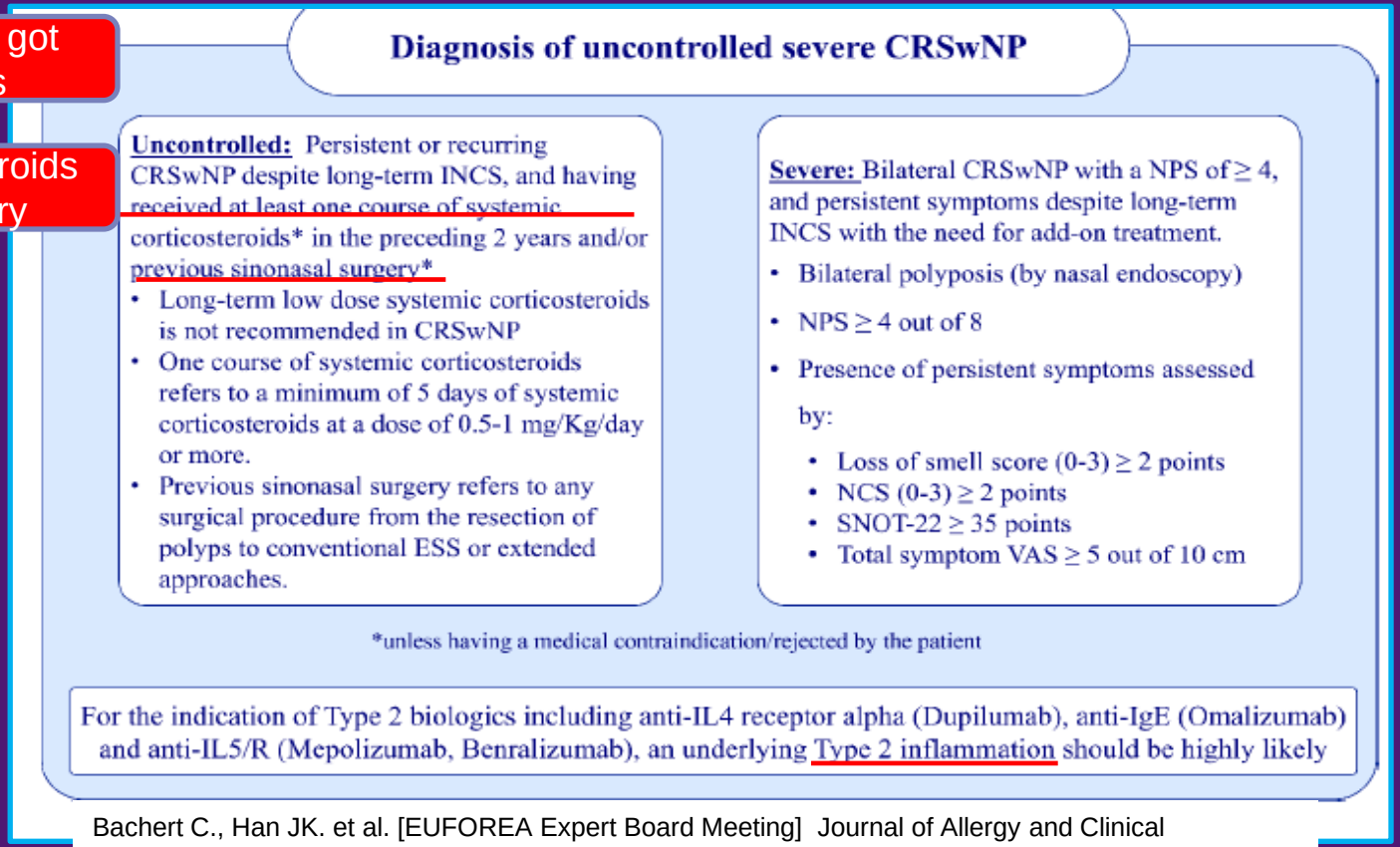
Comorbid asthma = 1 point

Comorbid N-ERD = 1 point in addition to 1 point for co-morbid asthma

THE EUROPEAN FORUM FOR RESEARCH AND EDUCATION IN ALLERGY AND AIRWAY DISEASES

Pt selection got Biologics

Systemic steroids OR surgery



Diagnosis of uncontrolled severe CRSwNP

Uncontrolled: Persistent or recurring CRSwNP despite long-term INCS, and having received at least one course of systemic corticosteroids* in the preceding 2 years and/or previous sinonasal surgery*

- Long-term low dose systemic corticosteroids is not recommended in CRSwNP
- One course of systemic corticosteroids refers to a minimum of 5 days of systemic corticosteroids at a dose of 0.5-1 mg/Kg/day or more.
- Previous sinonasal surgery refers to any surgical procedure from the resection of polyps to conventional ESS or extended approaches.

Severe: Bilateral CRSwNP with a NPS of ≥ 4, and persistent symptoms despite long-term INCS with the need for add-on treatment.

- Bilateral polyposis (by nasal endoscopy)
- NPS ≥ 4 out of 8
- Presence of persistent symptoms 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/rejected by the patient

For the indication of Type 2 biologics including anti-IL4 receptor alpha (Dupilumab), anti-IgE (Omalizumab) and anti-IL5/R (Mepolizumab, Benralizumab), an underlying Type 2 inflammation should be highly likely

Bachert C., Han JK. et al. [EUFOREA Expert Board Meeting] Journal of Allergy and Clinical Immunology. Vol. 147, Issue 1p29–36

WHEN TO USE BIOLOGIC TX FOR CRSwNP

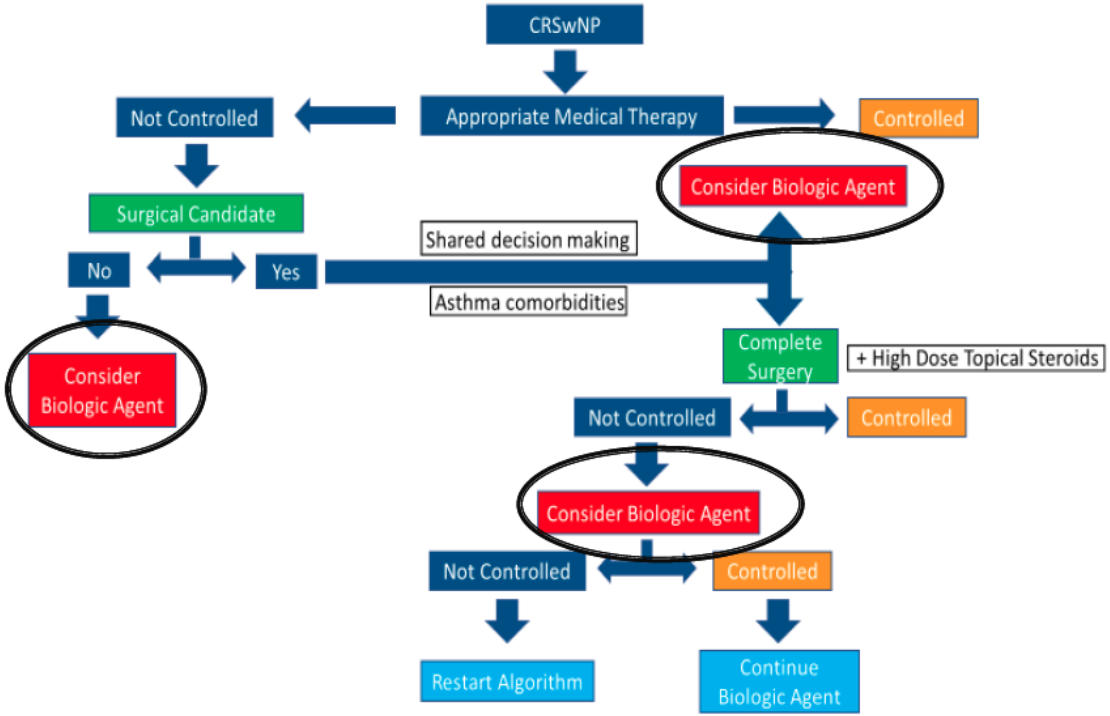
FDA

- May be used as add-on therapy for CRSwNP when **symptoms are "uncontrolled" with nasal corticosteroids**

INTERNATIONAL CONSENSUS STATEMENT ON RHINOSINUSITIS 2021

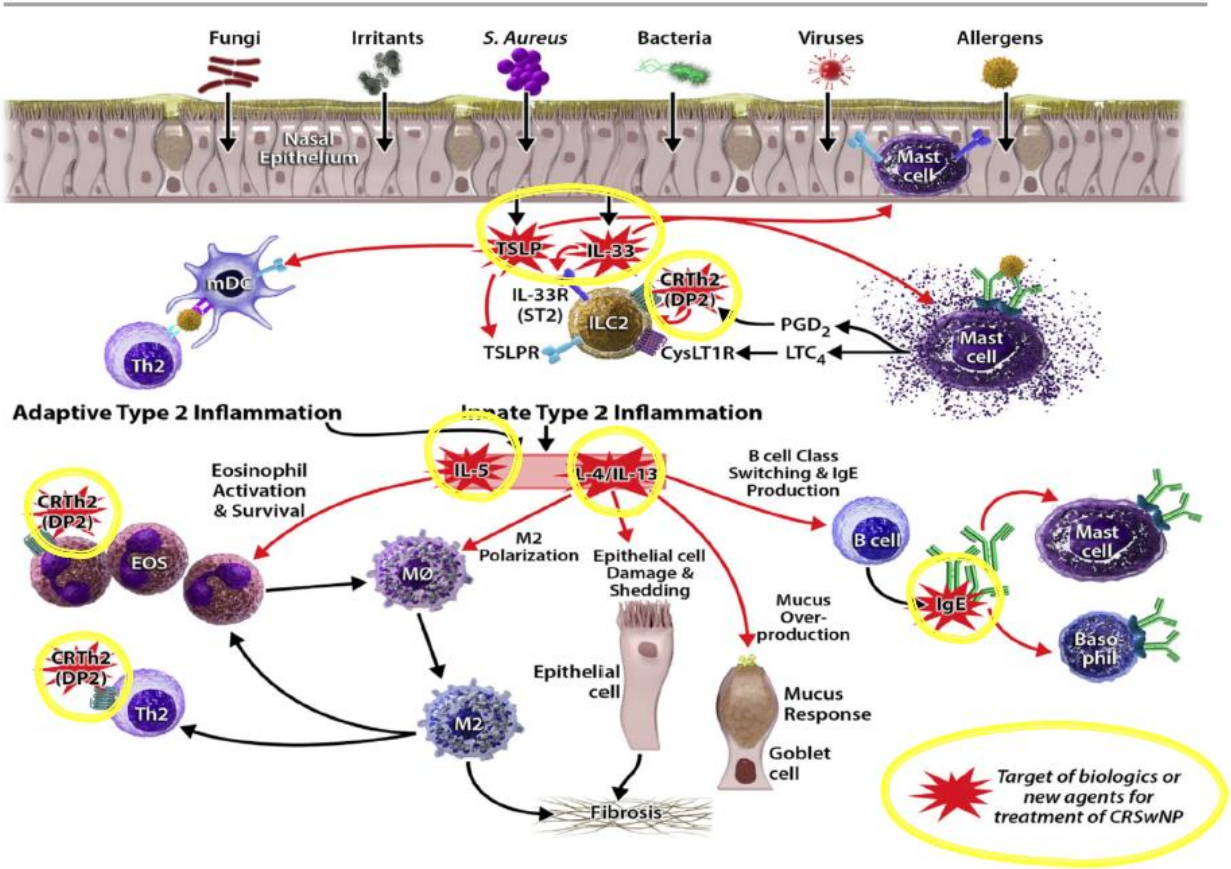
- Biologic therapy targeting type inflammation may also be considered an option for recalcitrant cases of CRS unwilling or unable to undergo surgical therapy

Proposed Pathway for the Treatment of CRSwNP



Damask CC, Ryan MW, Casale TB, Castro M, Franzese CB, Lee SE, Levy JM, Lin SY, Lio PA, Peters AT, Platt MP, White AA. Targeted Molecular Therapies in Allergy and Rhinology. Otolaryngol Head Neck Surg. 2021 Jan;164(1_suppl):S1-S21.

Pathophysiology and Targets of CRSwNP



T.M. Laidlaw and K.M. Buchheit / Ann Allergy Asthma Immunol 124 (2020) 326e332

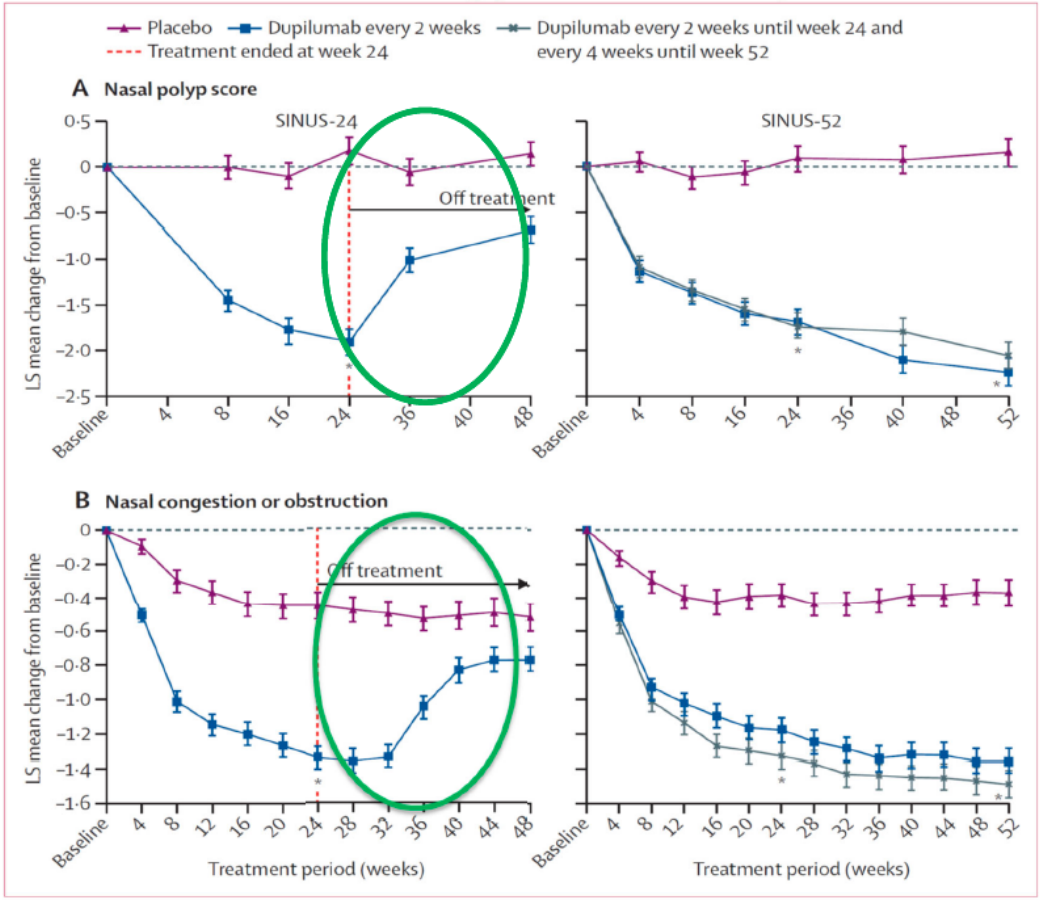
[ICAR CRS 2021]

TREATMENT OF CRSwNP : 1A SYSTEMATIC REVIEWS

THERAPY	RECOMMENDATION	LEVEL OF EVIDENCE
ANTI IL4/IL 13 (IL-4 RECEPTOR ALPHA) [CRSwNP]	• Improves nasal polyp score, CT score, SNOT-22 VAS, UPSIT, Lund-Mackay score, congestion at 4-6 months, olfaction, concomitant asthma and N-ERD • Recommends dupilumab use in patients fulfilling criteria for monoclonal antibody treatment	High (?) [May be considered for medical/surgical failure: A]

- Approved dose is 300 mg subcutaneously every 2 weeks
- Inhibits eosinophil migration into tissues
- May downregulate IgE and upregulate IgG

Dupilumab Reduces Nasal Polyp Size and Improves SNOT 22



Bachert et al. Lancet 2019; 394: 1638–50

Dupilumab Reduces Need For Systemic Steroids Or Sinus Surgery

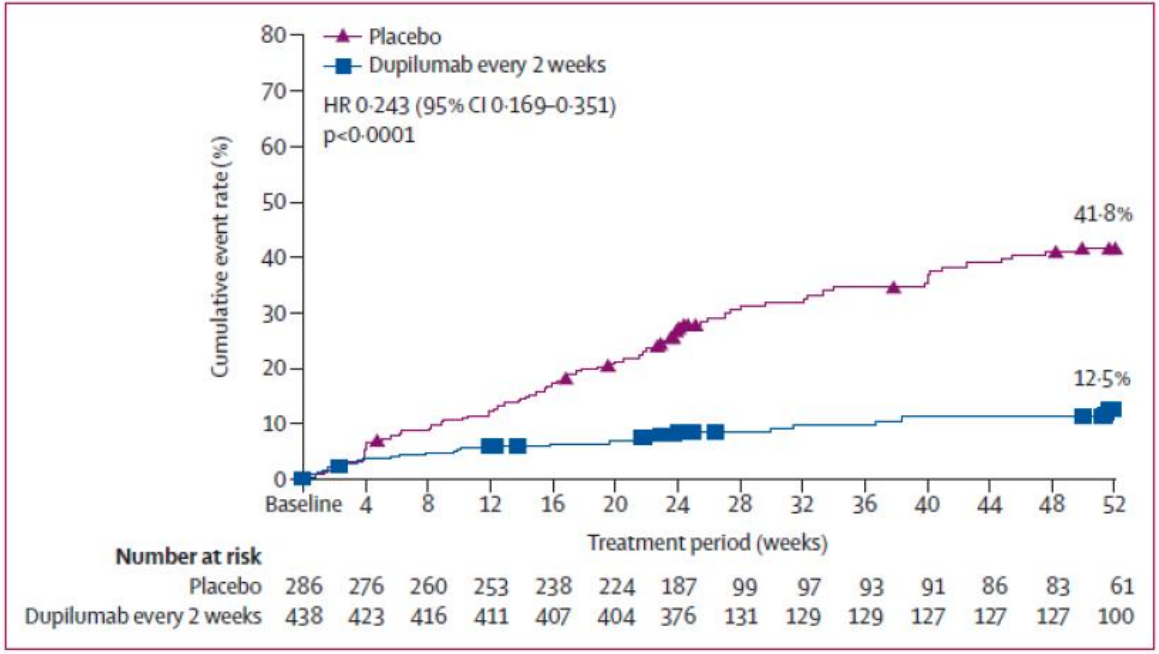


***Figure 3*: Time to first systemic corticosteroid use or nasal polyp surgery during the treatment period in the pooled analysis of SINUS-24 and SINUS-52**
HR=hazard ratio.

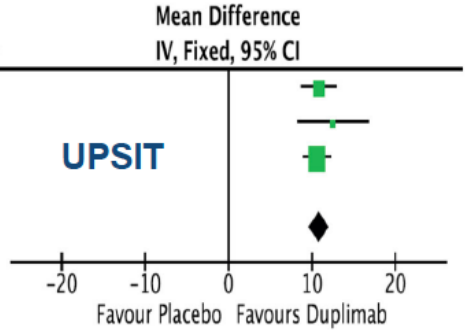
***Bachert et al. Lancet* 2019; 394: 1638–50**

Forest Plots on Effect of Dupilumab on UPSIT and Snot-22

Study or Subgroup	Experiment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
Bachert 2019 - SINUS 24	25.39	9.49	143	14.56	8.58	133	34.1%	10.83 [8.70, 12.96]	2019
Bachert 2016	28.7	8.2	30	16.2	8.7	30	8.5%	12.50 [8.22, 16.78]	2016
Bachert 2019 - SINUS 52	23.89	9.21	295	13.3	7.96	153	57.5%	10.59 [8.95, 12.23]	
Total (95% CI)			468			316	100.0%	10.83 [9.59, 12.08]	

Heterogeneity: $Chi^2 = 0.67$, $df = 2$ ($P = 0.72$); $I^2 = 0\%$

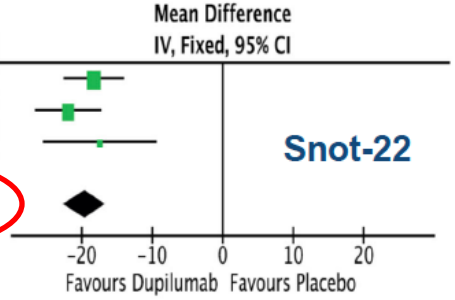
Test for overall effect: $Z = 17.06$ ($P < 0.00001$)



Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Bachert 2019 - SINUS 52	23.89	18.77	295	42.16	23.26	153	46.9%	-18.27 [-22.53, -14.01]
Bachert 2019 - SINUS 24	18.58	14.92	143	40.49	23.06	133	39.9%	-21.91 [-26.53, -17.29]
Bachert 2016	12.8	11	30	30.2	19.6	30	13.2%	-17.40 [-25.44, -9.36]
Total (95% CI)			468			316	100.0%	-19.61 [-22.53, -16.69]

Heterogeneity: $Chi^2 = 1.62$, $df = 2$ ($P = 0.44$); $I^2 = 0\%$

Test for overall effect: $Z = 13.17$ ($P < 0.00001$)



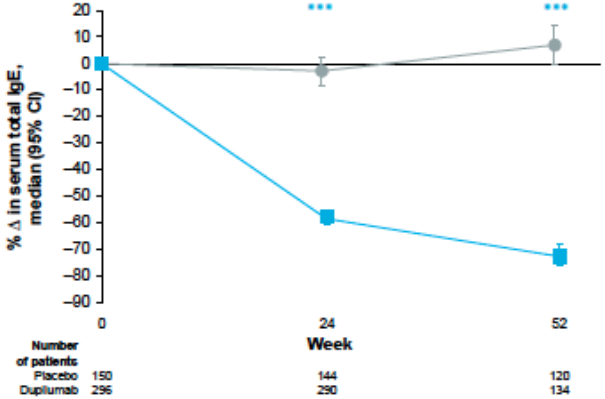
EPOS 2020

Dupilumab reduces IgE in patients with CRSwNP in blood and nasal secretions

Placebo Dupilumab 300 mg q2w

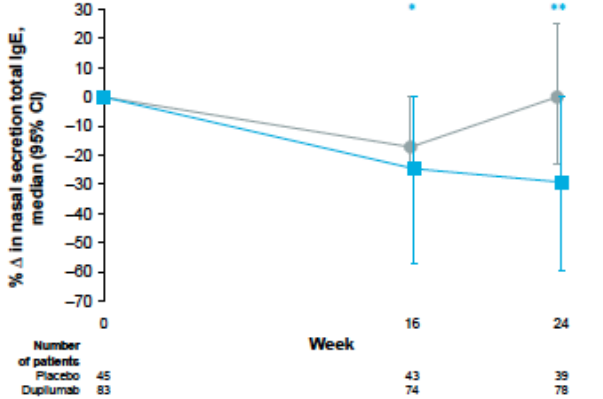
Serum total IgE, IU/mL

	Placebo	Dupilumab
BL, mean (SD)	228.59 (268.67)	245.54 (373.36)
BL, median (95% CI)	139.00 (104.00, 172.00)	122.00 (103.00, 145.00)
% Δ at Wk24, median (95% CI)	−3.13 (−8.33, 2.14)	−57.92 (−60.55, −56.20)
% Δ at Wk52, median (95% CI)	7.02 (0.00, 14.22)	−72.75 (−76.19, −67.70)



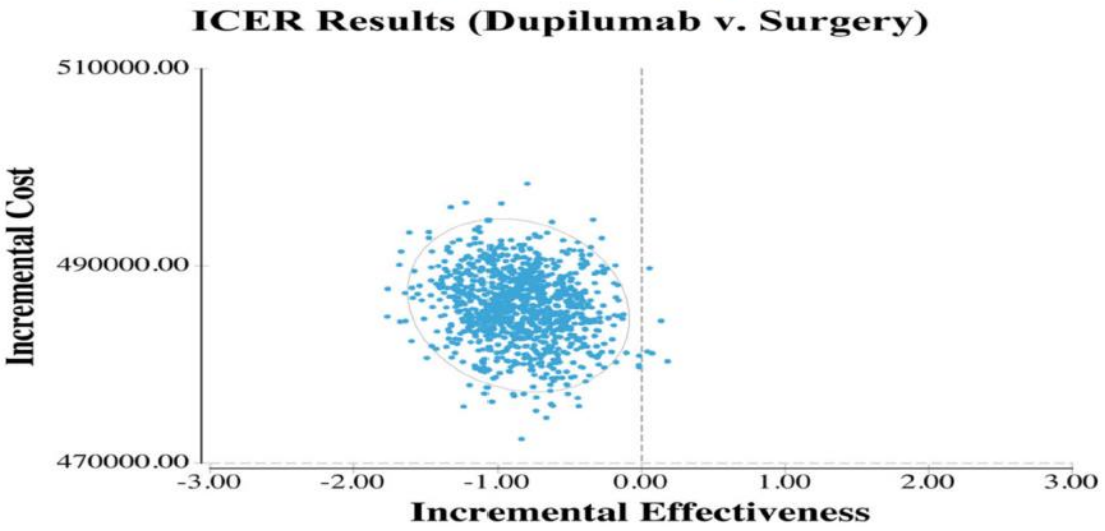
Nasal secretion total IgE, IU/mL

	Placebo	Dupilumab
BL, mean (SD)	19.91 (29.13)	49.43 (139.20)
BL, median (95% CI)	5.00 (4.00, 9.00)	6.00 (4.00, 12.00)
% Δ at Wk16, median (95% CI)	−17.39 (−26.97, 0.00)	−25.00 (−57.14, 0.00)
% Δ at Wk24, median (95% CI)	0.00 (−23.53, 25.00)	−29.17 (−60.00, 0.00)



*P < 0.05; **P < 0.01; ***P < 0.001. BL, baseline; CI, confidence interval; Wk, week.
Dupilumab 300 mg q2w includes pooled dupilumab 300 mg q2w and q2w–q4w arms to Week 24 and only 300 mg q2w arm up to Week 52. Biomarkers were summarized using descriptive statistics. Δ = change from baseline.

COST EFFECTIVE ANALYSIS OF DUPILUMAB VS. ESS



- 100% of individual ICER outcomes (dots) favored ESS vs dupilumab at a willingness to pay threshold of $100,000/QUALY.
- ESS cost-effective vs dupilumab regardless of frequency of revision ESS and at any annual cost of dupilumab >$855!

ESS: $50,436.99 and produced 9.80 QALYs
Dupilumab: $536,420.22 and produced 8.95 QALYs

.

Scangas GA. Laryngoscope. 2021;131(1):E26-E33.

TREATMENT OF CRSwNP: 1B RCTS

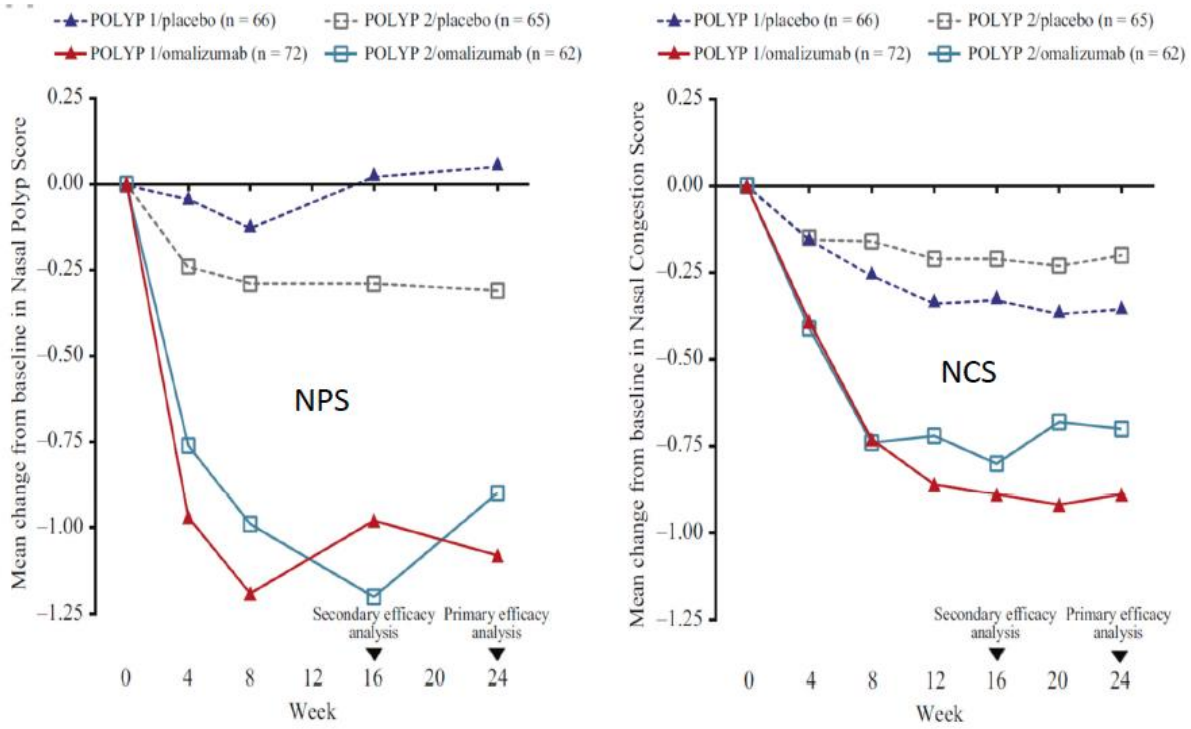
[ICAR CRS 2021]

THERAPY	RECOMMENDATION	QUALITY OF EVIDENCE
ANTI-IGE [CRSWNP]	• Small study (2010) in CRS did not show significant change on Sinus CT[1] • 2 Phase III studies (2020) showed benefit for CRSwNP[2] • 1 case-control of asthmatics with CRSwNP[3] • 1 RT single blind allergic fungal rhinosinusitis[4] • Studies showed benefit in reducing symptoms, AHRQ, nasal polyp size on endoscopy/CT • "Insufficient studies to recommend for or against"	Not rated [Consider for pts with concomitant asthma: Grade B]

1. Pinto JM, Rhinology. 2010;48(3):318-24. 2. Gevaert P. J Allergy Clin Immunol. 2020;146(3):595-605.3. Bidder T. Rhinology. 2018;56(1):42-5. 4. Mostafa BE. Eur Arch Otorhinolaryngol. 2020;277(1):121-8.

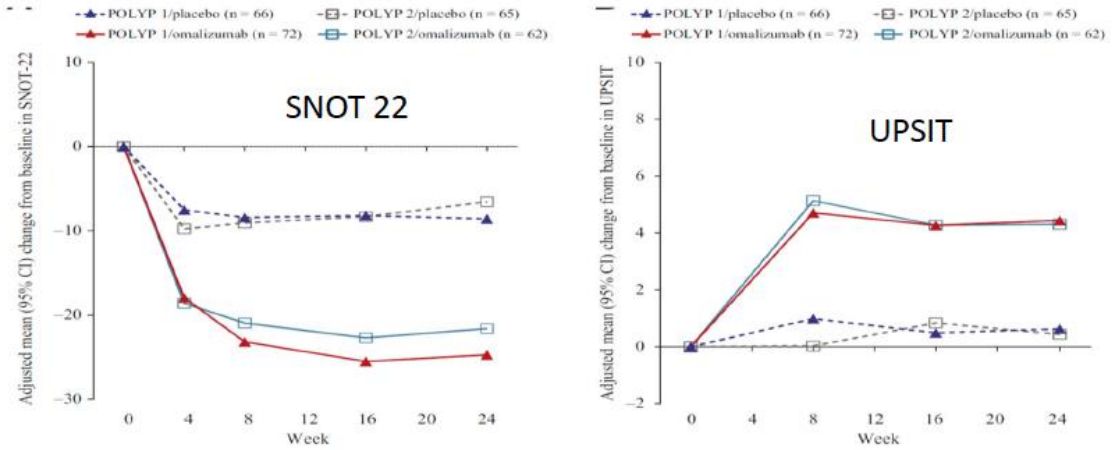
Omalizumab Improvements in NPS and NCS

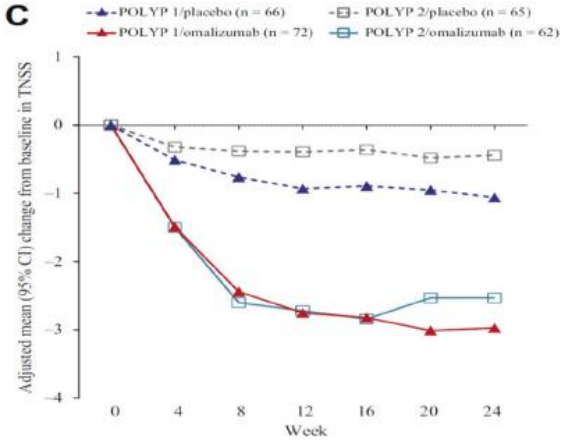
Polyp Study 1 & 2 Clinical Phase 3 trials



Gevaert et al, JACI, 2020

Omalizumab Improvements in Key Secondary Endpoints





TNSS

Gevaert et al, JACI, 2020

TREATMENT OF CRSwNP: 1B RCTS

[ICAR CRS 2021]

THERAPY	RECOMMENDATION	QUALITY OF EVIDENCE
ANTI-IL-5 MEPOLIZUMAB	• Reduced symptoms & need for surgery • **Recommend use if patient qualifies for monoclonal Tx** • **[Only 2 small trials of IV mepolizumab]**	Not rated [Option for patients with concomitant uncontrolled eosinophilic asthma: Grade C]

1. Weinstein SF. JACI in Pract. 2019;72(2):589.

MEPOLIZUMAB CLINICAL TRIALS

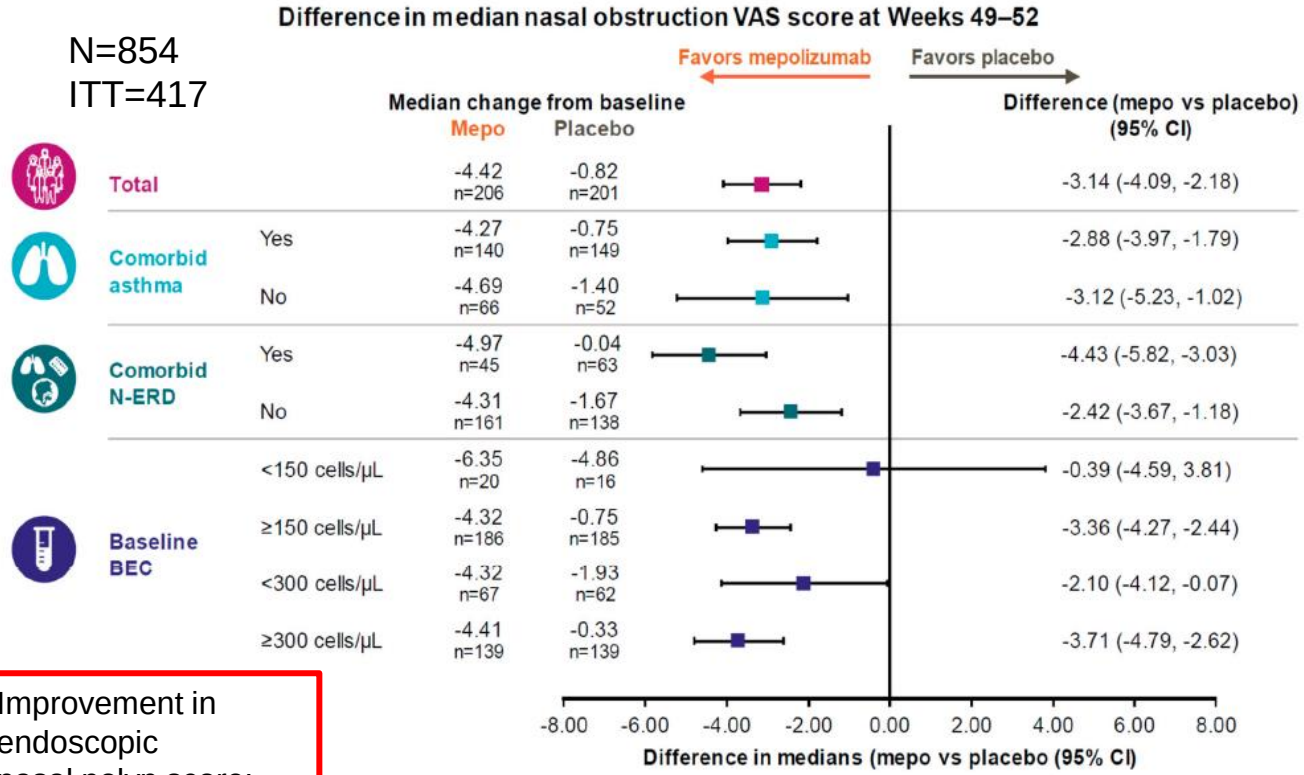
- RCT 30 patients with severe CRSwNP received mepolizumab **750 mg IV** q 4 wks. for 2 doses[1]
  - At 8 wks. 12/20 had improved NP score and CT score vs. 1/10 patients receiving placebo
- DBPCT 105 patients with severe CRSwNP received mepolizumab **750 mg IV** q 4 weeks for 6 doses[2]
  - At week 25, reduced need for surgery, NP severity VAS score, endoscopic NP score, and improved Sino-Nasal Outcome Test
  - Mepolizumab's safety profile was comparable with that of placebo.

1.Gevaert P. J Allergy Clin Immunol. 2011;128(5):989-95 e1-8.2. Bachert C. J Allergy Clin Immunol. 2017;140(4):1024-31 e14.

SYNAPSE Phase 3 Trial (100 mg subcutaneous)

Mepolizumab improved nasal obstruction VAS score compared with placebo, especially in patients with comorbid N-ERD or a baseline BEC ≥150 cells/µL

N=854
ITT=417

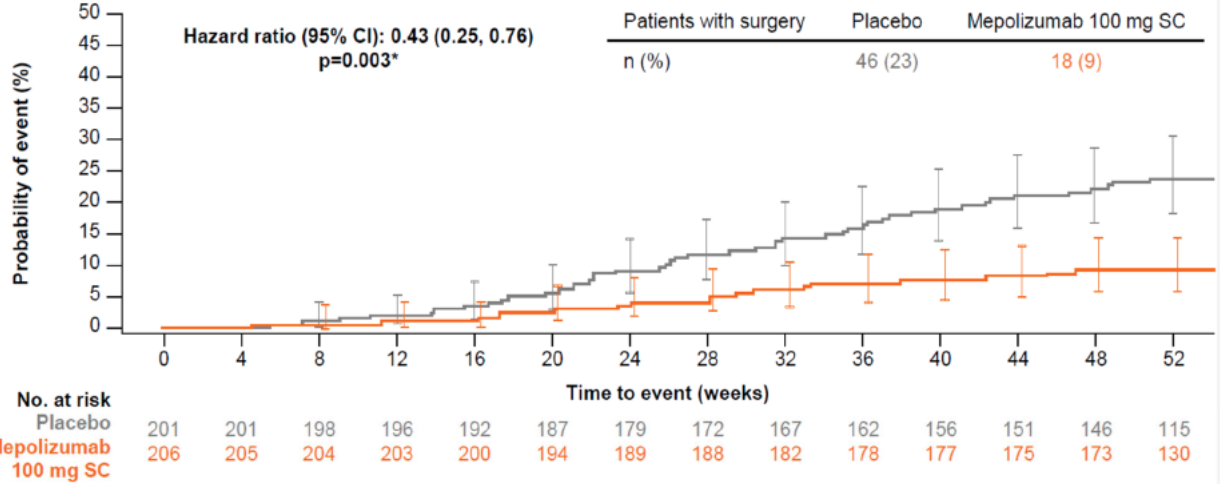


Improvement in endoscopic nasal polyp score:
- 0.73, P=<0.0001

Han JK., Bachert C. et al. Lancet Respir. Med. In press 4.16.21

Significantly fewer nasal surgeries were observed and fewer patients required OCS with mepolizumab treatment versus placebo

Time-to-first actual nasal surgery (key secondary endpoint)



Proportion of patients requiring OCS

Odds ratio to placebo (95% CI): 0.58 (0.36, 0.92)
p=0.020*

Patients with ≥ 1 OCS course	Placebo	Mepolizumab 100 mg SC
n (%)	74 (37)	52 (25)

Han JK., Bachert C. et al. Lancet Respir. Med. In press 4.16.21

COCHRANE 2020 SYSTEMATIC REVIEW ANTI IL-5 MAB

Chong LY, et al. *Cochrane Database of Systematic Reviews* 2020, Issue 2.

Biologic	# RCTs	# Patients	Positive Outcome	Certainty of Evidence	Conclusion
Dupilumab	3 3 2 3	784 784 725 374	SNOT-22 VAS Surgery avoidance CT score	High Moderate Moderate High	Improves SNOT-22, CT, probably improves symptoms, may reduce the need for further surgery
Mepolizumab	1 1 2	105 72 135	SNOT-22 VAS Surgery avoidance	Low Low Very low	May improve SNOT-22 & symptoms, uncertain if reduces surgery or CT score
Omalizumab	1 1 2	105 72 125	SNOT-22 VAS Surgery avoidance	LOW Very low Very low	Uncertain about benefits/harms

COCHRANE 2020 SYSTEMATIC REVIEW ANTI IL-5 MAB

Chong LY, et al. *Cochrane Database of Systematic Reviews* 2020, Issue 2.

Improvement in SNOT-22

Dupilumab (top)
Mepolizumab (bottom)

Analysis 1.1. Comparison 1 Anti-IL-4Rα mAb (dupilumab) versus placebo (on top of topical steroids), Outcome 1 HRQL - disease-specific (SNOT-22, 0 to 110, lower = better).

Study or subgroup	Dupilumab N	Dupilumab Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.1.1 Up to 24 weeks							
Bachert 2016	30	12.8 (11)	30	30.2 (19.6)		13.21%	-17.4[-25.44,-9.36]
LIBERTY SINUS 24	143	18.6 (14.9)	133	40.5 (23.1)		40.05%	-21.91[-26.53,-17.29]
LIBERTY SINUS 52	295	23.9 (18.8)	153	42.2 (23.4)		46.73%	-18.27[-22.55,-13.99]
Subtotal ***	**468**		**316**			**100%**	**-19.61[-22.54,-16.69]**
Heterogeneity: Tau²=0; Chi²=1.62, df=2(P=0.44); I²=0%							
Test for overall effect: Z=13.15(P<0.0001)							
1.1.2 At 52 weeks							
LIBERTY SINUS 52	150	21.7 (19.2)	153	44.1 (22.7)		100%	-22.38[-27.1,-17.66]
Subtotal ***	**150**		**153**			**100%**	**-22.38[-27.1,-17.66]**
Heterogeneity: Not applicable							
Test for overall effect: Z=9.29(P<0.0001)							
Test for subgroup differences: Chi²=0.95, df=1 (P=0.33), I²=0%							

MD=-22.38

Favours dupilumab -50 -25 0 25 50 Favours placebo

Analysis 2.1. Comparison 2 Anti-IL-5 mAb (mepolizumab) versus placebo (on top of topical steroids), Outcome 1 HRQL - SNOT-22 (1 to 100, lower = better) up to 25 weeks.

Study or subgroup	Mepolizumab N	Mepolizumab Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Bachert 2017	54	27.1 (21.8)	51	40.4 (24.2)		100%	-13.26[-22.08,-4.44]
Total ***	**54**		**51**			**100%**	**-13.26[-22.08,-4.44]**
Heterogeneity: Tau²=0; Chi²=0, df=0(P<0.0001); I²=100%							
Test for overall effect: Z=2.95(P=0)							

MD=-13.26

Favours mepolizumab -100 -50 0 50 100 Favours placebo

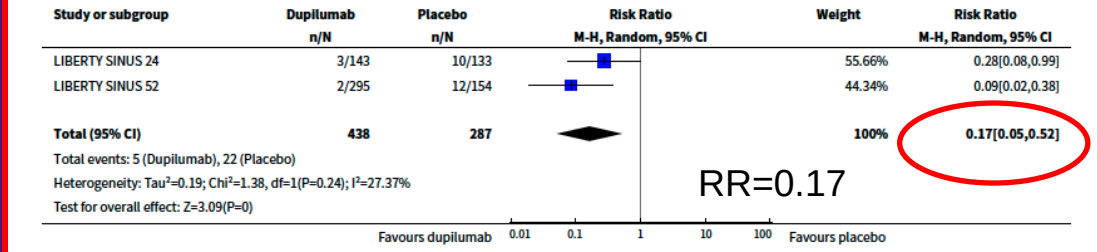
COCHRANE 2020 SYSTEMATIC REVIEW ANTI IL-5 MAB

Avoidance of surgery

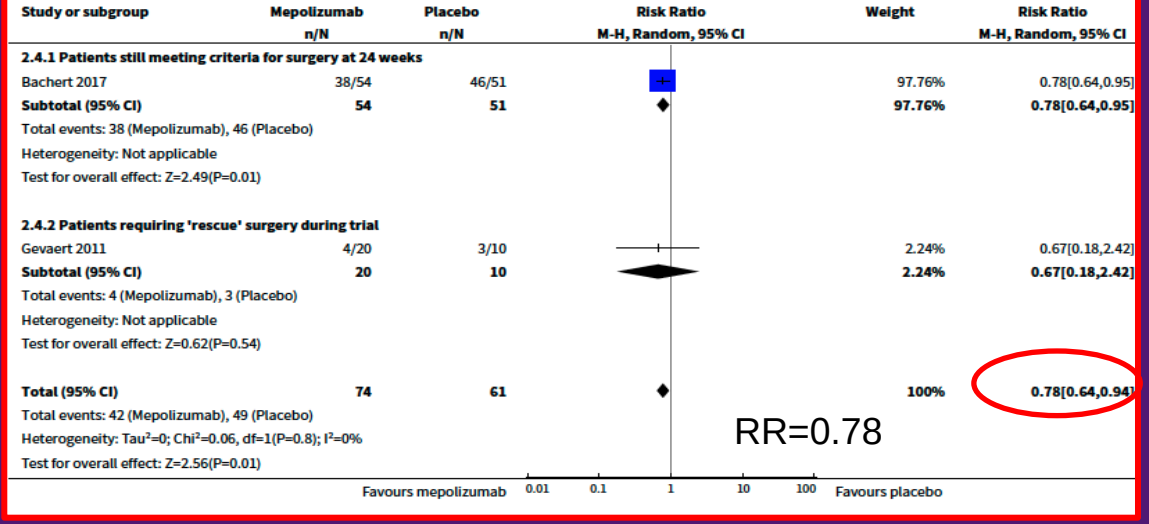
Dupilumab (top)
Mepolizumab (bottom)

Chong LY, et al.
Cochrane Database of Systematic Reviews
2020, Issue 2.

Analysis 1.4. Comparison 1 Anti-IL-4Rα mAb (dupilumab) versus placebo (on top of topical steroids), Outcome 4 Avoidance of surgery - number of patients who had surgery as rescue treatment.



Analysis 2.4. Comparison 2 Anti-IL-5 mAb (mepolizumab) versus placebo (on top of topical steroids), Outcome 4 Avoidance of surgery - patients no longer meeting criteria for surgery at end of follow-up.



TREATMENT OF CRSwNP: 1B RCTS

[ICAR CRS 2021]

THERAPY	RECOMMENDATION	QUALITY OF EVIDENCE
ANTI-IL-5 RESILIZUMAB	• 1 small RCT showed inconsistent results in the two IV doses studied[1] • Reduced polyp size • Anaphylaxis a risk	[Consider an Option for patients with concomitant uncontrolled eosinophilic asthma: Grade C]

1. Weinstein SF. JACI in Pract. 2019;72(2):589.

New Biological Agents Under Development

INNATE CYTOKINES DRIVE TH2 INFLAMMATION

CRTH2 ANTAGONIST

- **Oral antagonist of prostaglandin D_2 receptor 2**
- Fevipiprant Phase 3b international trial NCT03681093
  - 150 mg, 450 mg, or placebo daily tablet
  - 16 wk. study of 98 subjects
  - Preliminary results (clinicaltrials.gov) show that primary endpoint was not met

- 3 additional Phase 2 studies

INNATE CYTOKINES DRIVE TH2 INFLAMMATION

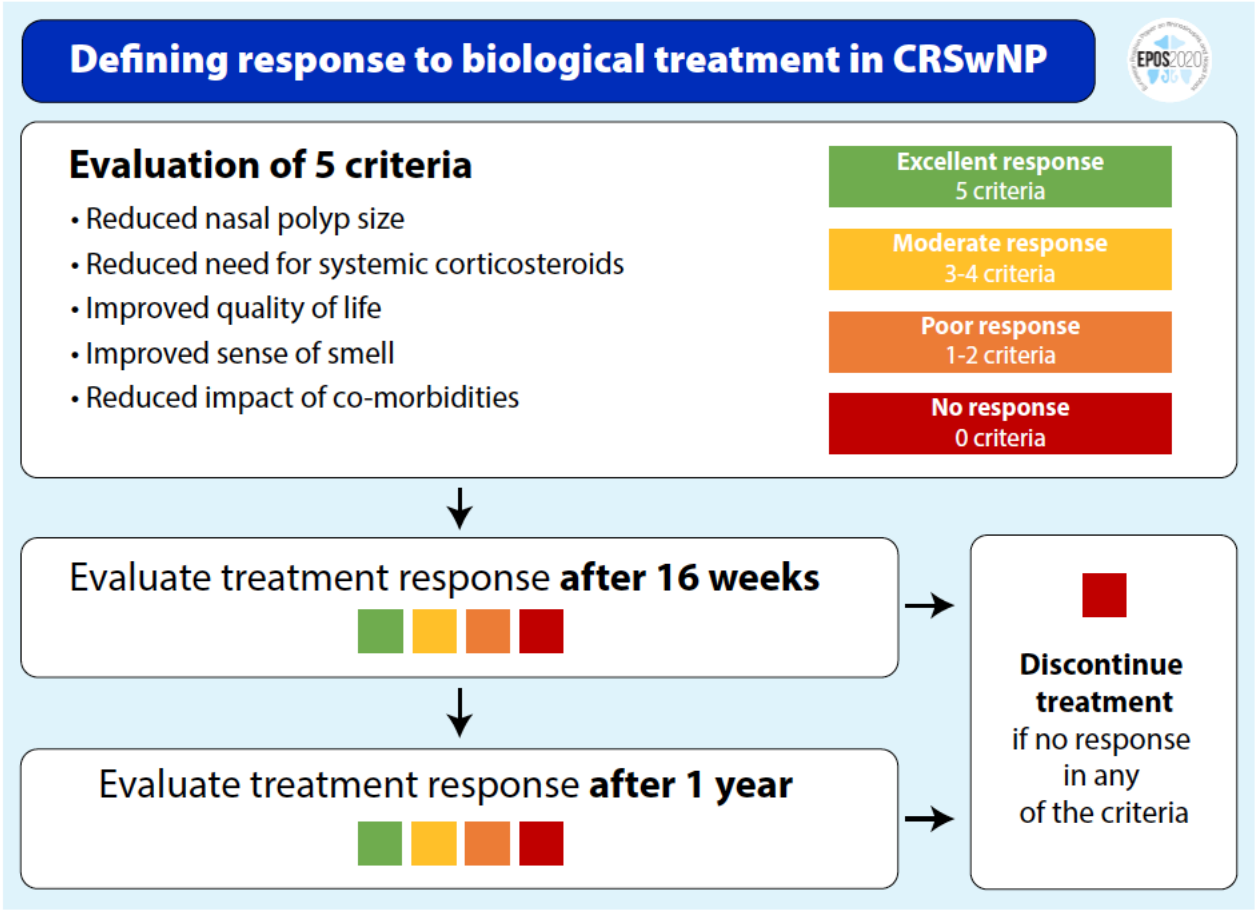
ANTI-IL-33

- **May be very important for AERD + CRSwNP patients**
- **Phase 2 study** (100 pts)Etokimab NXT03614923– NPS, SNOT-22
- Phase 1 study (41 pts) AMG 282-NCT02170337-safety study
- No results posted clinicaltrials.gov
- Has also been studied for asthma

TSLP

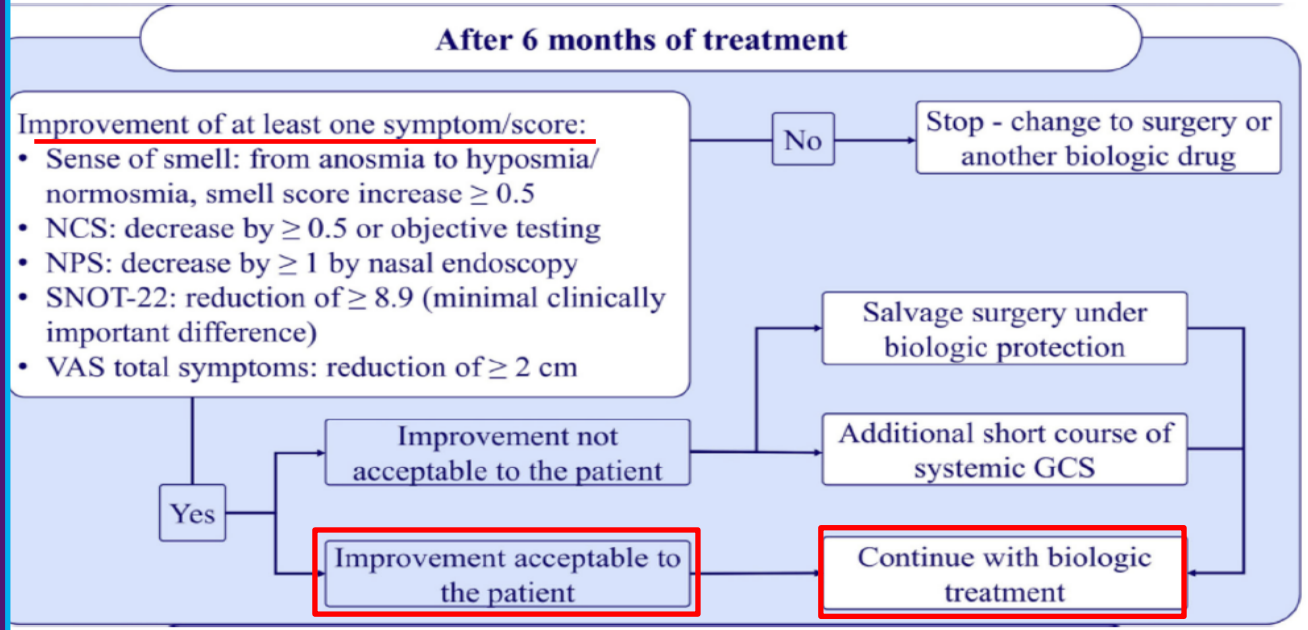
- No CRSwNP trials yet
- **Asthma Phase 3 study** Tezepelumab/AMG 157
- Reduces asthma exacerbations
- + results in eosinophil low subgroup
- Likely suited for AERD

Figure 1.6.4. Response criteria for biologicals in the treatment of CRS.



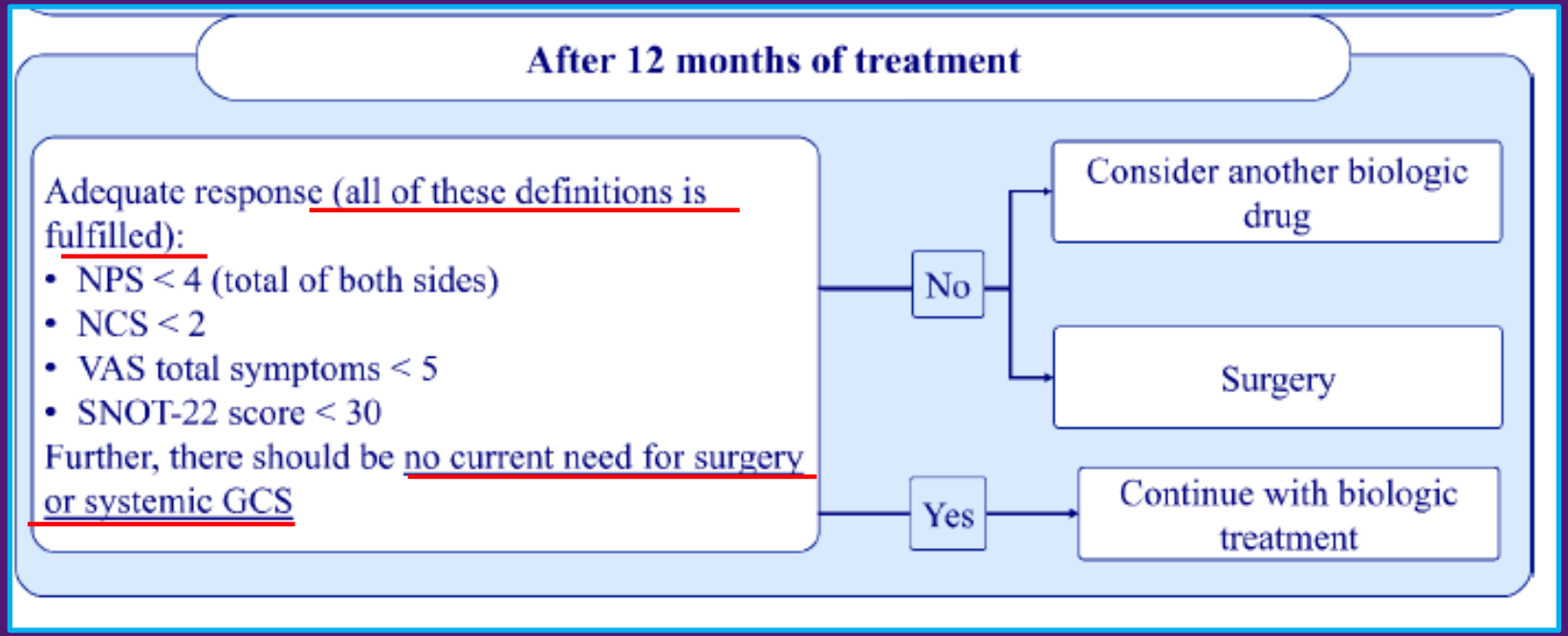
THE EUROPEAN FORUM FOR RESEARCH AND EDUCATION IN ALLERGY AND AIRWAY DISEASES

Treatment Assessment



Bachert C., Han JK. et al. [EUFOREA Expert Board Meeting] Journal of Allergy and Clinical Immunology.Vol. 147, Issue 1p29–36

THE EUROPEAN FORUM FOR RESEARCH AND EDUCATION IN ALLERGY AND AIRWAY DISEASES



Bachert C., Han JK. et al. [EUFOREA Expert Board Meeting] Journal of Allergy and Clinical Immunology. Vol. 147Issue 1p29–36

THANKS

Drdanawallace@gmail.com