A pilot prospective longitudinal study comparing dupilumab to surgery in CRSwNP

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Abstract

Background: To date, there have not been any direct comparative studies assessing clinical outcomes in CRSwNP between biologic and surgical therapies. **Objective:** To directly compare the effect of dupilumab to FESS using subjective and objective outcomes of CRSwNP patients in a prospective longitudinal study. **Methods:** We prospectively enrolled 20 CRSwNP patients and counseled them on both biologic and surgical options. Patients were able to decide on either therapy, and data collected at baseline and 3-, 6-, 9-, and 12-months with subjective outcomes including the nasal congestion score (NCS) and SNOT-22 questionnaires, and objectively by degree of smell (UPSIT-40) and nasal polyp score (NPS). **Results:** All subjects met criteria for either biologic therapy or surgery, with NPS >5, Lund-Mackay score (LMK-CT)>16, SNOT-22>54, and were graded as anosmic/hyposmic. There were no significant differences in age, sex, comorbid asthma/Aspirin Exacerbated Respiratory Disease, or prior FESS between groups. Both dupilumab and FESS significantly improved outcomes by one year in patients with severe CRSwNP when compared to baseline. At one-year, patients on dupilumab had greater improvement in NCS, UPSIT and asthma control relative to one year post FESS. In a subgroup of patients with a history of prior sinus surgery and asthma, dupilumab had lower polyp recurrence rate compared to one year post FESS. **Conclusions:** Both dupilumab and FESS can significantly improve outcomes by one year in CRSwNP patients. However, in those with a history of asthma and prior surgery, dupilumab is more effective in reducing polyp recurrence and improving sinonasal outcomes than FESS.

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Conclusions: Both dupilumab and FESS can significantly improve outcomes by one year in CRSwNP patients. However, in those with a history of asthma and prior surgery, dupilumab is more effective in reducing polyp recurrence and improving sinonasal outcomes than FESS.

Keywords:

Nasal polyps, rhinosinusitis, sinus surgery, biologic, dupilumab, outcomes, type-2 inflammation.

Abbreviations: CRSwNP: Chronic rhinosinusitis with nasal polyps, FESS: Functional endoscopic sinus surgery, IL: interleukin, Ig: Immunoglobulin, NCS: Nasal congestion score: SNOT-22: 22-item Sinonasal outcome test, NPS: nasal polyps score, UPSIT-40: 40-item University of Pennsylvania Smell Identification Test, AERD: Aspirin exacerbated respiratory disease, LMK-CT: Lund Mackay computed tomography scoring system

Introduction

Chronic rhinosinusitis with nasal polyposis (CRSwNP) impacts approximately 2.6 million people in the United States, with a prevalence of 1 to 2.6% of the population.[1-4] Although the pathophysiology of CRSwNP is incompletely understood, in most Western and European countries, type 2-mediated inflammation is a significant contributor to the pathogenesis of the disease.[5] In CRSwNP, the type 2-mediated inflammatory cascade leads to a downstream increase in type-2 mediated cytokines, including interleukin(IL)-4, IL-5, and IL-13. This can culminate in epithelial injury, mucosal hypertrophy, and the formation of nasal polyps, potentially presenting as nasal obstruction, decreased olfaction, and excessive drainage.[6] Biologic therapies targeting type-2 inflammation have provided a novel option for physicians in treating CRSwNP. However, there have not been any prospective longitudinal studies comparing outcomes of biologic therapies to complete functional endoscopic sinus surgery (FESS) that may provide new insights into developing treatment algorithms for patients with CRSwNP.

Current treatment paradigms recommend surgical treatment if appropriate medical management fails to resolve CRSwNP.[7-11] The goal of FESS is to remove nasal polyps, enlarge the drainage pathways of the sinus cavities to restore normal mucosal and epithelial function as well as allow for the delivery of topical corticosteroids.[12] There are approximately 33,000 patients annually in the United States that undergo FESS for CRSwNP.[13] Despite its effectiveness, FESS has long-term limitations. Disease recurrence, particularly the regrowth of obstructive nasal polyps and worsening of symptoms, is a significant challenge in the management of CRSwNP. In a multi-center study, 38% of patients who underwent FESS for CRSwNP developed polyp recurrence at 12 months and 40% at 18 months.[14] Moreover, repeat FESS procedures for recurrent CRSwNP are not uncommon.[1]This may be due to failure of traditional therapies, including intranasal/oral steroids and antibiotics that target downstream inflammatory and infectious pathways, medication noncompliance, or failure of drug delivery to the sinonasal mucosa.[15]

Biologics are the first therapy in CRSwNP that target the major type-2 inflammatory molecular mechanisms of CRSwNP. Dupilumab is an IgG4 human monoclonal antibody that targets the IL-4 receptor alpha subunit. This blockade inhibits receptor signaling of both IL-4, IL-5 and IL-13, thereby reducing the recruitment of eosinophils and IgE.[16] Dupilumab is approved for the treatment of recalcitrant and severe CRSwNP in adults. Phase 3 trials, including SINUS 24 at six months and SINUS 52 at one year, have shown a significant decrease in nasal polyp size, radiographic disease severity, symptom severity, and improvement in olfaction.[17]Other biologics have since been approved for the management of CRSwNP, including omalizumab and mepolizumab.

To date, there is a lack of head-to-head prospective studies comparing the effectiveness of biologic therapy to FESS in treating CRSwNP.[18] In this manuscript, we present the findings of a one-year prospective longitudinal cohort directly comparing dupilumab to FESS in CRSwNP patients using subjective and objective outcome measures. At 3-,6-, 9-, and 12 months, the following outcomes were collected: patient symptoms and disease-specific quality of life (QoL) (SinoNasal Outcomes Test (SNOT-22), Nasal Congestion Score (NCS), Nasal Polyp Scores (NPS), University of Pennsylvania Smell Identification Test (UPSIT-40), and Asthma Control Questionnaire-5 (ACQ) for patients with comorbid asthma.

Methods

Patient recruitment

We recruited patients from the Banner-University Medical Center 'Allergy and Asthma' or 'Rhinology and Skull-based Surgery' clinics between February 2020 and January 2022. Eligible patients were adults ([?]18 years old) with severe CRSwNP with recurrent or persistent symptoms after appropriate medical therapy, including intranasal saline irrigations, a trial of oral corticosteroids (OCS), oral antibiotics, and continuous intranasal corticosteroids (INCS) use.[8, 9] The diagnosis of CRSwNP was made by two fellowship-trained rhinologists through history, nasal endoscopy, and radiographic studies according to established criteria.[19] The definition of severe CRSwNP was adapted from the European Forum for Research and Education in Allergy and Airway Diseases (EUFOREA) recommendations.[20] All patients met the criteria of bilateral nasal polyposis with a minimum total NPS (tNPS) of 4 according to the Meltzer clinical scoring system (0 = no polyps, 1 = polyps confined to the middle meatus, 2 = multiple polyps occupying the middle meatus,

3 = polyps extending beyond middle meatus, 4 = polyps completely obstructing the nasal cavity)[21] with a NPS of at least 1 in each nostril. Patients also had a minimum SNOT-22 score of [?]20.[22] Exclusion factors included patients with immunodeficiency, autoimmune disease, cystic fibrosis, and sinonasal tumors. Informed consent was obtained from all patients after a detailed explanation of the study procedures. The clinical study was approved by the University of Arizona Institutional Review Board (IRB: 1502660530).

Study longitudinal design and Outcome measures

Figure 1 depicts the study design. The physicians provided benefits and risks of biologic and FESS therapies using the patient-centered shared decision-making template provided by the American College of Allergy, Asthma, and Immunology in conjunction with the American Rhinologic Society.[23] Patients chose either dupilumab or FESS and were categorized according to their treatment. All patients had access to both treatments through insurance, and financial constraints did not influence the decision making. Demographics including age, sex, race & ethnicity, history of previous surgeries or biologic use, and comorbid conditions, including asthma, Aspirin Exacerbated Respiratory Disease (AERD), were obtained.

At their baseline visit, patients completed subjective symptom and disease-specific QoL assessments, including SNOT-22, NCS, and ACQ – for those with asthma. The physicians then recorded objective nasal endoscopy and Meltzer polyp scores, Lund-Mackay computed tomography scores (LMK-CT), and UPSIT-40 smell testing values. Once either dupilumab therapy was initiated or FESS performed, patients followed up at the 3-, 6-, 9-, and 12-month time points. During each visit, QoL and symptom instruments (NCS, SNOT-22, ACQ-5), nasal endoscopy (NPS), and UPSIT-40 olfactory testing were performed, and their values were recorded. Anosmia was defined as [?]18 on UPSIT-40.[24]The research team communicated with patients monthly to ensure 100% retention and all required instruments were completed in all visits. All patients were instructed to continue with saline irrigations and INCS, irrespective of the selected treatment throughout the entirety of the study.

Treatments – Dupilumab and FESS

In the dupilumab group, all patients received standard dosing of 300mg subcutaneously every two weeks with no adverse reactions recorded. The patients were then given the option of either clinic or at-home injections every other week. In the surgical group, all patients underwent full bilateral FESS as defined by the EPOS 2020 guidelines by two fellowship-trained rhinologists.[8] The patients were evaluated at the routine post-operative follow-ups. There were no perioperative complications reported. No patients in the dupilumab group experienced any adverse effects that necessitated stopping the therapy, no patients in the FESS group required revision surgery, and no patients in either group withdrew or switched treatments during the 12-month study period.

Statistical analysis

We reported frequencies and proportions for discrete data and mean ± standard deviation (SD) for continuous variables. Fisher's exact and chi-squared testing were used to analyze categorical differences. A two-tailed test was used to evaluate the statistical difference between groups and within groups in each treatment, followed by an ANOVA model with the baseline values to their corresponding endpoints. The effect size was determined using Hedge's g test (g). The 95% confidence level was used to set the confidence intervals (CI). An alpha level of 0.05 was determined a priori. All data were parametric. No missing data was reported as all subjects completed all subjective and objective measures. Statistical analyses were performed using Stata (BE 17).

Results

Patient characteristics

We assessed the first twenty patients with 1-year longitudinal data in our study. There was an even distribution of patients in the dupilumab (n=10) and FESS (n=10) groups with no significant differences in age, gender, or race. There was a high rate of comorbid asthma (>60%) and prior sinus surgery (>70%) in

both groups. There were no patients in either group that had failed a trial of biologic therapy. There were no significant differences in subject characteristics or outcome measures between the dupilumab and FESS groups at baseline (Table I). All patients met the criteria of severe CRS as defined by symptom scores, polyp size, smell impairment, and LMK-CT score.[20, 25, 26]

Changes in outcomes within and between groups

We first measured outcome measures from each time-point to baseline within each respective group. We then directly compared outcome effects between dupilumab and FESS by calculating the mean difference in scores between baseline and longitudinal time points.

Subjective outcomes (NCS, SNOT-22, ACQ)

Both dupilumab and FESS treatments showed significant improvements in subjective outcomes over 3-, 6-, 9-, and 12-months when compared to their baseline values for SNOT-22 and ACQ values (Fig 2 D,E,G,H). For NCS, patients in the dupilumab cohort showed steady improvement in NCS over time, while those in the FESS cohort showed sporadic improvement at 3 and 9 months (Fig 2A,B). When compared to each other, dupilumab had a steady decrease in symptoms over time for NCS, SNOT-22, and ACQ while FESS outcomes rapidly decreased by 3 months but then tended to plateau or regress (Fig 2 C,F,I). For patient-reported outcomes of nasal congestion, there were no significant differences at 3-, 6-, and 9-months. However, by 12-months dupilumab had a greater improvement compared to FESS (Fig 2C). For SNOT-22 questionnaires which measure global outcomes related to CRS, the FESS group reported significantly improved outcomes at 3 months compared to dupilumab, however this lost significance at the 6-, 9-, and 12-month timepoints (Fig 2F). In the group of patients with asthma, ACQ scores were improved at 3 months in the FESS group, but this difference shifted to the dupilumab group by 12 months (Fig 2I).

Changes in Olfaction

Ninety percent of patients in both groups were classified as anosmic at baseline. The improvement in olfaction with dupilumab was gradual and consistent, improving by 5 points at 3 months and up to 17.4 points by 12 months. All patients transitioned to non-anosmia and 50% were classified as normosmic (normal smell) (Fig 3A). The improvement in olfaction with FESS was more immediate with an improvement of 12 points by 3-, 6-, and 9-months with a slight regression by 12-months. 70% of patients transitioned to non-anosmia and 50% were classified as normosmic (Fig 3B). By 12 months, the mean improvement in UPSIT-40 score was significantly greater in the dupilumab group compared to the FESS group (Fig 3C).

Changes in total nasal polyp score

Both FESS and dupilumab groups showed significant reductions in tNPS compared to baseline and at all follow-up visits, with a mean decrease of approximately 5-points by 12 months compared to baseline (Fig 3 D,E). The dupilumab group showed continued improvement in tNPS over time, with nearly all patients achieving complete resolution of nasal polyps by 12 months. The one patient in the dupilumab group with persistent nasal polyps had comorbid asthma and AERD. In comparison, there was a significant decrease in nasal polyp scores in the FESS group compared to dupilumab at 3- and 6-months. However, by 12 months there was no statistical difference in mean change in polyp scores between dupilumab and FESS groups (Fig 3F).

Subgroup analysis of patients with polyp recurrence

A diagnosis of polyp recurrence was given if patients had a history of no visible polyps (tNPS=0) at a time-point during the study and then had documented polyp regrowth bilaterally (tNPS>=1). In the dupilumab group, no subject experienced polyp recurrence, whereas four patients in the FESS group had mild polyp recurrence by 12 months. Further analysis of the FESS group revealed that all patients with polyp recurrence had asthma and a history of prior sinus surgery at enrollment. Compared to FESS without polyp recurrence, this subgroup demonstrated poorer outcomes in NCS and ACQ scores by 12 months (Table 2). We then compared patients in the FESS and dupilumab groups who also had risk factors of asthma and a history

of prior sinus surgery. When we compared outcomes of these patients in this high-risk group, dupilumab therapy had a large magnitude of effect on NCS, SNOT-22, UPSIT scores, and ACQ (Table 3).

Discussion

In our one-year prospective longitudinal cohort study, dupilumab and FESS were effective in reducing subjective sinonasal symptoms, improving smell, and reducing nasal polyp size.

By 3 month followup, we found that FESS had more immediate effects on sinonasal symptoms and asthma control however, by 12-month followup, we found that dupilumab had a greater improvement on nasal congestion symptoms, olfactory discrimination scores, and asthma control compared to FESS. This comparative effect was magnified when assessing a high-risk group of patients with previous sinus surgery and comorbid asthma.

We hypothesize that this finding is due to the specific and prolonged targeting of type-2 inflammatory markers by dupilumab compared to the initial effect of the removal of obstructive nasal polyps and creation of patent sinus drainage pathways by FESS. Type-2 mediated cytokines including IL-4, IL-5, and IL-13 are important mediators of type-2 inflammation and have been found to be elevated in CRSwNP.[6, 27] Dupilumab blocks IL-4/IL-13 induction and downstream effector cells and cytokines including IL-5 that likely provides durable effects on CRS symptoms, olfaction, and nasal polyp growth.[16] Nasal polyps are composed of group 2 innate lymphoid cells (ILC2) that contribute to type 2 inflammation, and their removal by FESS likely contribute to the significant improvements seen in SNOT-22 and ACQ scores at 3 months compared to dupilumab.[28] However, persistent type-2 inflammation in the sinonasal cavities likely resulted in these comparisons losing significance by 12 months. Similarly, increased levels of type-2 cytokines,[29] and in particular IL-5 in the olfactory tissues have been found to be associated with decreased olfaction and taste in CRSwNP.[30] Although complete removal of diseased mucosa through "reboot" surgery has been shown to provide durable olfaction at 12 months, this aggressive surgery must be balanced by the potential risk of scarring and subsequent loss of olfactory epithelia.[30]

There have been two reported studies that evaluated outcomes for FESS against published biologic trials. Dharmarajan et al. compared the outcomes of FESS to dupilumab in a retrospective, matched group of 54 patients in each group at 6- and 12 months.[31] FESS was favored in terms of NPS scores, while dupilumab was favored in terms of SNOT-22 scores specific to olfaction, cough, and post-nasal drainage. Of those that had FESS, 43% exhibited polyp recurrence after surgery. Limitations of this study included the retrospective nature and, therefore, the lack of matched time points where the average follow-up periods for FESS and dupilumab were 17.9 and 12.2 months, respectively. Moreover, their outcomes were limited to symptomatic scores derived from SNOT-22 without objective outcome measures. Miglani et al. conducted a comparative analysis that included 111 patients with CRSwNP who underwent FESS and compared their outcomes to those reported in biologic trials of dupilumab, omalizumab, and mepolizumab.[32]They evaluated SNOT-22, NPS, and olfaction. Compared to dupilumab, their findings indicate that at six months, smell improvement was similar in both groups. They also reported that FESS had better NCS and comparable SNOT-22 scores at 6 and 12 months. Notably, there was incomplete data from the FESS group, with nearly half lost in follow-up. There were also some inconsistencies between the comparative measures (e.g., UPSIT vs. Sniffin' sticks, NPS vs. Lund-Kennedy Endoscopy-derived polyp score, etc.) that made analyses, particularly for polyp size, challenging.[21, 32-34]

Our one-year prospective longitudinal pilot study aimed to provide evidence to enhance clinical therapeutic recommendations for CRSwNP by directly comparing the efficacy of dupilumab and FESS in patients with severe CRSwNP. By reporting consistent outcome points at matched time points, we minimized outcome heterogeneity. To our knowledge, this is the first head-to-head comparison study between dupilumab and FESS in CRSwNP.

There were several limitations of our study. We compared FESS patients to dupilumab, one of three biologic therapies FDA-approved for CRSwNP. We chose to compare to dupilumab alone to reduce the heterogeneity of therapies as it is currently the most effective biologic for CRSwNP as shown in a recently published

meta-analysis.[35] In this pilot study we recruited a small group of patients however all twenty patients completed 12-month follow-up. Although we acknowledge the possibility of selection bias due to patients self-selecting their treatments, we provided detailed counselling for each option in accordance with published guidelines regardless of their insurance coverage or socioeconomic status. .[23] The equal distribution of subjects across therapy groups and absence of significant differences between them suggest that our counseling was unbiased towards either treatment. Due to ethical and cost concerns, we were unable to perform blinding, randomization, or have a blinded assessor of the outcome measures. We also did not perform molecular endotyping of these patients, because these are not currently the standard of care in the workup of CRSwNP patients for either surgery or biologic therapy. Future studies assessing local and systemic type-2 biomarkers would be beneficial in understanding the specific treatment response of CRSwNP. While all patients continued the use INCS/irrigations as part of their standard medical therapy after dupilumab and post-FESS, the absence of objective methods of quantifying medical therapy adherence is another potential limitation to our study. Finally, our study assessed longitudinal outcomes over one year and it would be beneficial to investigate if patients with polyp recurrence required followup surgery or initiation of biologic therapy long-term.

The findings from our study reinforce and support current clinical algorithms for patients with CRSwNP. First, shared decision-making tools can be very effective for both patients and physicians in weighing the advantages and disadvantages of therapies for CRSwNP, including biologic versus sinus surgery. The shifting paradigm of CRSwNP management was evidenced by the fact that half of our patients chose biologic therapy compared to FESS. In our study, patients undergoing FESS had significant improvements in SNOT-22 and total nasal polyp scores compared to baseline. This reinforces the guidelines published by Han et al. in which patients without a history of prior sinus surgery, FESS should be a first-line therapy given that it removes the mechanical obstruction of nasal polyps, enlarges sinus cavities for improved local drug delivery, and is significantly less expensive compared to biologic therapy. However, when we evaluated a subgroup of patients with a history of asthma and prior sinus surgery, the comparative effect of dupilumab had greater improvements to FESS for SNOT-22, NCS, ACQ, UPSIT scores, and reduced polyp recurrence. In this high-risk group, biologic therapies should be considered given they meet the criteria established by the EUFOREA guidelines.

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Tables

Table I. Patients' Baseline Characteristics

Baseline Characteristic	**Dupilumab** (n=10)	**FESS** (n=10)	**p-value**
Age	59.5± 11.2	54.3± 14.5	0.38
White	6 (60)	8 (80)	0.17
Female	6 (60)	6 (60)	1.00
Comorbid Asthma	7 (70)	6 (60)	0.65
Comorbid AERD	2 (20)	1 (10)	0.54
Previous Sinus Surgery	8 (80)	7 (70)	0.31
Failed previous Biologic	0 (0)	0 (0)	1.00
LMK-CT	16.7± 2.6	17.8± 3.1	0.40
NCS	2.1± 1.2	2.3± 0.7	0.65

Baseline Characteristic	**Dupilumab** (n=10)	**FESS** (n=10)	**p-value**
SNOT-22	54.4± 20.5	64.5± 24.6	0.33
UPSIT	14.3± 8.3	15.6±10.6	0.76
NPS	5.0± 1.1	6.2±1.7	0.08
Anosmia*	9 (90)	9 (90)	1.00
ACQ**	1.2± 0.5	1.6± 0.4	0.09

Data reported as mean ± SD or n (%).

* Anosmia defined as UPSIT-40 score [?]18

** ACQ completed in patients with asthma

Table 2: Comparison between attributes and outcomes for CRSwNP patients who underwent FESS and developed polyp recurrence (0, 12 months)

Characteristic	**FESS (no recurrence)** (n=6)	**FESS (recurrence)** (n=4)	**p-value**
White	4 (66.7)	4 (100)	0.22
Female	3 (50)	3 (75)	0.45
Comorbid Asthma	2 (33.3)	4 (100)	**0.04**
Comorbid AERD	0 (0)	1 (25)	0.22
Previous Sinus Surgery	2 (50)	4 (100)	0.10
Baseline LMK-CT	17.8± 4.4	19.8± 2.2	0.43
NCS (0M)	2.1± 0.8	2.5± 0.6	0.42
NCS (12M)	1.2± 0.4	2±0	**0.004**
SNOT-22 (0M)	61.5± 21.3	69.5± 31.8	0.64
SNOT-22 (12M)	25.3± 7.1	29.5± 6.8	0.38
UPSIT (0M)	14.8± 9.9	11.8± 4	0.58
UPSIT (12M)	22.3± 7.3	25.0± 0.8	0.49
Anosmia (0M)*	5 (83.3)	4 (100)	0.41
Anosmia (12M)*	3 (50)	0 (0)	0.11
NPS (0M)	5.7± 1.7	7.5± 1	0.09
NPS (12M)	0±0	2±0	**<0.0001**
ACQ (0M) **	0.9± 0.1	1.9± 0.3	**<0.0001**
ACQ (12M)**	0.5± 0	1.3± 0.4	**0.001**

Continuous data reported as mean ± SD. Categorical data reported as n (%)

* Anosmia defined as UPSIT-40 score [?]18

** ACQ completed in patients with asthma.

Table 3: Sub-group comparison between treatment outcomes for CRSwNP patients with history of Asthma and previous sinus surgery (0, 12 months)

Characteristic	**Dupilumab** (n=6)	**FESS** (n=6)	**p-value**	**Effect size**
White	5 (83.3%)	5 (83.3%)	1	
Female	5 (83.3%)	3 (50%)	0.24	
Comorbid AERD	2 (33.2%)	1 (16.7%)	0.52	

Characteristic	**Dupilumab** (n=6)	**FESS** (n=6)	**p-value**	**Effect size**
Baseline	16.3± 2.1	18.5± 2.3	0.11	
LMK-CT				
NCS (0M)	2.2± 1.1	2± 0.6	0.7	0.208
NCS (12M)	0.0± 0.0	1.7± 0.5	**<0.0001**	4.436
SNOT-22 (0M)	48± 22.1	64.3± 27.4	0.28	0.604
SNOT-22 (12M)	0.5± 0.6	28± 6.1	**<0.0001**	5.855
UPSIT (0M)	15.1± 10.1	12.17± 4.1	0.52	0.351
UPSIT (12M)	32.2± 4.7	23.5± 3.7	**0.005**	1.898
Anosmia (0M)*	5 (83.3)	6 (100)	0.32	
Anosmia (12M)*	0 (0)	1 (16.7)	0.32	
NPS (0M)	5± 1.3	6.7± 1.5	0.06	1.117
NPS (12M)	0.4± 1.1	1.5± 0.8	0.06	1.055
ACQ (0M) **	1.4± 0.3	1.6± 0.4	0.38	0.521
ACQ (12M)**	0.0± 0.0	1±0.5	**0.0007**	2.609

Continuous data reported as mean ± SD. Categorical data reported as n (%). Effect sizes calculated with Hedge's g.

* Anosmia defined as UPSIT-40 score [?]18

** ACQ completed in patients with asthma.

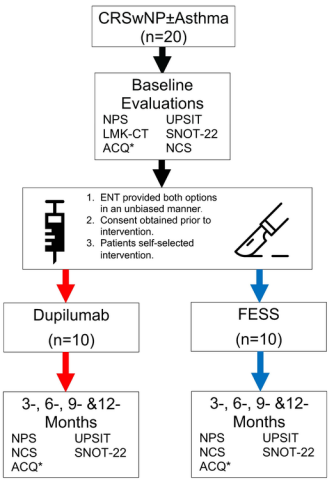
Figure Legends

Figure 1: Longitudinal Study Design. CRSwNP: Chronic rhinosinusitis with nasal polyps, FESS: Functional endoscopic sinus surgery, NCS: Nasal congestion score: SNOT-22: 22-item Sinonasal outcome test, NPS: nasal polyps score, UPSIT-40: 40-item University of Pennsylvania Smell Identification Test, LMK-CT: Lund Mackay computed tomography scoring system,

Figure 2: Longitudinal subjective outcomes within and between groups. The effect of dupilumab and FESS over time within groups for NCS (A,B), SNOT-22 (D,E), and ACQ (G,H). Dupilumab n=10, FESS n=10, except for ACQ (Dupilumab n=7, FESS n=6). Comparisons of the mean change from baseline to timepoint between dupilumab and FESS for NCS (C), SNOT-22 (F), and ACQ (I). * p<=.05, ** p<=.01, *** p<=.001, ****p<=.0001

Figure 3: Longitudinal objective outcomes within and between groups. The effect of dupilumab and FESS over time within groups for UPSIT (A,B) and NPS (D,E). Dupilumab n=10, FESS n=10. Comparisons of the mean change from baseline to timepoint between dupilumab and FESS for UPSIT (C) and NPS (F). * p<=.05, ** p<=.01, *** p<=.001, ****p<=.0001

Figure 1



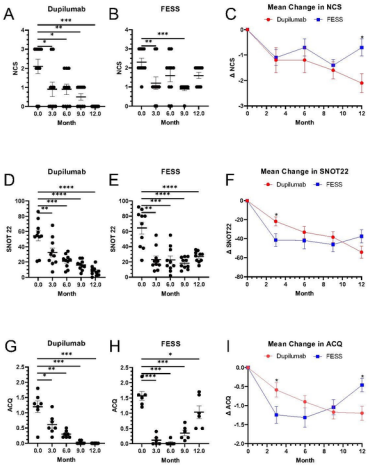


Figure 2

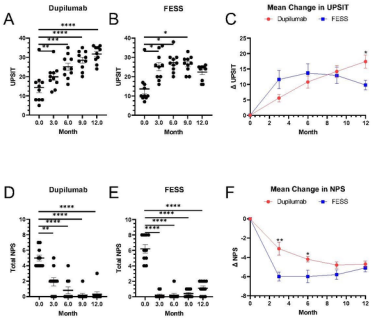


Figure 3