HHS Public Access

Author manuscript

Ann Allergy Asthma Immunol. Author manuscript; available in PMC 2022 March 01.

Published in final edited form as:

Ann Allergy Asthma Immunol. 2021 March ; 126(3): 302–304. doi:10.1016/j.anai.2020.11.014.

Efficacy of type-2 targeted biologics in patients with asthma and bronchiectasis

Elizabeth Kudlaty, MD, MS[1], **Gayatri B. Patel, MD**[1], **Michelle L. Prickett, MD**[2], **Chen Yeh, MS**[3], **Anju T. Peters, MD, MS**[1]

[1]Division of Allergy and Immunology, Department of Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL 60611, United States

[2]Divison of Pulmonary and Critical Care, Department of Medicine, Feinberg School of Medicine, Northwestern University, Chicago IL, United States

[3]Division of Biostatistics, Department of Preventive Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL 60611, United States

Bronchiectasis is characterized by permanent, irreversible dilation of the bronchi due to inflammation and impaired mucus clearance and is associated with significant respiratory impairment. Bronchiectasis shares significant clinical characteristics with severe asthma, and they often coexist.[1] Although classically thought of as neutrophilic-predominant inflammation, emerging evidence suggests that the inflammation in bronchiectasis is heterogeneous with a subset of patients having an eosinophil-predominant type 2 inflammatory response. [2] Based on this observation, biologics that target type 2 inflammation may be a consideration for patients with bronchiectasis and severe asthma. However, evidence for this is limited to two small case reports, and patients with bronchiectasis were excluded from phase 3 biologic asthma clinical trials.[3,4] In this study, we report our real-world experience with an IL-4/IL-13 antagonist (dupilumab), anti-IgE (omalizumab) and extend the evidence for IL-5 (reslizumab)/ IL-5Rα antagonist (benralizumab) in patients with non-cystic fibrosis (CF) and non-allergic bronchopulmonary aspergillosis (ABPA) bronchiectasis.

This case series includes 12 patients with a radiographic diagnosis of bronchiectasis not due to cystic fibrosis (CF) or allergic bronchopulmonary aspergillosis (ABPA) who were treated with biologics targeting type 2 inflammation in an academic allergy-immunology clinic. All patients had chronic cough, sputum production, and a chest computed tomography (CT) scan documenting bronchiectasis. ABPA and CF diagnoses were excluded based on

Corresponding Author: Anju Peters, MD, MS, Division of Allergy and Immunology, Feinberg School of Medicine, Northwestern University, Chicago, IL 60611, Tel: 312-695-4000, Fax: 312-695-4141, Anjupeters@northwestern.edu.

Disclosures:

A. T. Peters is a consultant for Sanofi-Regeneron; consultant and receives research support from AstraZeneca and Optinose. The remaining authors have no disclosures.

documentation by the treating allergist/immunologist/pulmonologist. We characterized patient demographics, asthma controller medications, lung function, laboratory data (IgE and absolute eosinophil count (AEC)) respiratory exacerbations, systemic corticosteroids, and antibiotic courses for respiratory infections for the 12 months prior to initiation of the biologics. Respiratory exacerbation was defined as respiratory symptoms requiring systemic corticosteroids, or any increase in baseline dose if on chronic corticosteroids for ≥3 days or urgent care/emergency department visit for worsening respiratory symptoms. Respiratory exacerbations were considered distinct episodes if the interval between start dates was ≥21 days. The overall efficacy of the biologics was assessed through global physician assessment by the treating physicians (scale ranged from 1–5, Table 1). Outcomes were assessed during the use of biologics and compared to the 12 months prior to initiation of biologics and included 1) number of respiratory exacerbations; 2) number of systemic corticosteroid courses; 3) number of antibiotic courses for respiratory infections; and 4) global physician assessment. For those receiving dual biologics, outcomes were assessed after the second biologic was initiated.

Descriptive and categorical variables were calculated and summarized. Wilcoxon signed-rank test was performed to test the difference between pre- and post- biologic initiation. All analyses were conducted in R 3.6.1 and SAS version 9.4 (The SAS Institute; Cary, NC). This study was approved by the Institutional Review Board.

All patients had comorbid asthma. Clinical characteristics and global physician assessment during biologic treatment are described in Table 1. The etiology of bronchiectasis was post-infectious in three (25%), a combination of post-infectious and immunodeficiency in one (8%), and idiopathic in eight (67%). The average IgE (±SD) prior to biologic initiation was 576.83±856 kU/L, and AEC (±SD) was 479±470 K/uL. Based on chest CT scans, eight of the 12 patients had bronchiectasis that predominated in the lower lobes. The remainder had: upper lobe predominant (1/12), right middle lobe (2/12), and central bronchiectasis (1/12). High attenuated mucus was seen in one of the 12 patients. Nodules were seen in the majority of the scans (8/12), whereas tree-in-bud pattern was seen in 1/12.

Use of biologics decreased median (IQR) monthly respiratory exacerbations (pre: 0.13[0–0.29] vs post: 0.0[0–0.11], P=0.02) and corticosteroid courses (pre: 0.17[0.04–0.29] vs post: 0.0[0.0–0.11], P=0.008). Systemic antibiotic courses for respiratory infections also were decreased, although it was not statistically significant (pre: 0.17[0.08–0.23] vs. post: 0.04[0.0–0.16], P=0.13). FEV1 (L) pre- vs post-biologic was not different (1.42[1.08–2.23] vs 1.75[1.05–2.19], P=0.2). On overall global physician assessment, eight patients (80%) had somewhat or significant improvement, and two (20%) were unchanged. Two patients on therapy less than 3 months were excluded from the evaluation.

Previous studies have reported that an allergic (i.e. allergic rhinitis, elevated IgE) and/or eosinophilic (i.e. CRS) phenotype may predispose to bronchiectasis, a relationship also observed in this study.[5,6] In this case series, biologics were effective for treating patients with non-CF and non-ABPA bronchiectasis with an eosinophilic phenotype and/or coexisting allergic diseases. Our results add to the two reports from Europe, which observed benefit with mepolizumab and benralizumab in a small number of bronchiectasis patients

with severe asthma.[3,4] Our study demonstrates that this is more likely a general class effect of anti-type 2 biologics as our series included patients treated with dupilumab and omalizumab in addition to anti-IL-5 agents.

This study has several limitations. It is a single-center retrospective case series, and our study population may not be generalizable. Second, bronchiectasis is recognized as a heterogeneous disease, and the etiology of bronchiectasis was not uniform in this study. There was significant referral bias in our cohort as patients with bronchiectasis and type 2 comorbid diseases were specifically referred to our clinic for consideration of biologic therapy. Finally, asthma and bronchiectasis are both obstructive lung diseases and have considerable overlap. In our cohort of patients with bronchiectasis and concomitant asthma, it cannot be precisely determined how much of the observed effect from the biologic was due to the treatment of asthma versus bronchiectasis. This is an important group to analyze, and imaging with a high-resolution chest CT scan should be considered integral in the work-up of severe asthma as bronchiectasis is associated with significant morbidity and is increasingly recognized in patients with severe asthma. [1,7,8]

Bronchiectasis guidelines highlight the heterogeneous nature of bronchiectasis, and experts suggest an endotype-targeted approach for the treatment of bronchiectasis.[9] This case series is one of the first to show that treatment with biologics targeting type 2 inflammation leads to clinical improvement including reduction in corticosteroid courses, respiratory exacerbations, and systemic antibiotic courses in a subset of patients with bronchiectasis. While additional studies are needed to further elucidate the role of biologics in patients with bronchiectasis, this study suggests that biologics are a potential treatment option for the subgroup of patients with type 2 bronchiectasis not controlled with standard of care therapy.

Acknowledgments

Funding Sources: Division of Allergy and Immunology, Department of Medicine, Northwestern University Feinberg School of Medicine; Chronic Rhinosinusitis Integrative Studies Program (NIH P01AI145818); NIH T32AI083216; Ernest Bazley Foundation.

References

1. Coman I, Pola-Bibian B, Barranco P, et al. Bronchiectasis in severe asthma: Clinical features and outcomes. Ann Allergy Asthma Immunol. 2018;120(4):409–413. [PubMed: 29496464]
2. Tsikrika S, Dimakou K, Papaioannou AI, et al. The role of non-invasive modalities for assessing inflammation in patients with non-cystic fibrosis bronchiectasis. Cytokine. 2017;99:281–286. [PubMed: 28863927]
3. Rademacher J, Konwert S, Fuge J, Dettmer S, Welte T, Ringshausen FC. Anti-IL5 and anti-IL5Ralpha therapy for clinically significant bronchiectasis with eosinophilic endotype: a case series. Eur Respir J. 2020;55(1).
4. Carpagnano GE, Scioscia G, Lacedonia D, Curradi G, Foschino Barbaro MP. Severe uncontrolled asthma with bronchiectasis: a pilot study of an emerging phenotype that responds to mepolizumab. J Asthma Allergy. 2019;12:83–90. [PubMed: 30881051]
5. Somani SN, Kwah JH, Yeh C, et al. Prevalence and characterization of chronic rhinosinusitis in patients with non-cystic fibrosis bronchiectasis at a tertiary care center in the United States. Int Forum Allergy Rhinol. 2019;9(12):1424–1429. [PubMed: 31589811]
6. Shteinberg M, Nassrallah N, Jrbashyan J, Uri N, Stein N, Adir Y. Upper airway involvement in bronchiectasis is marked by early onset and allergic features. ERJ Open Res. 2018;4(1).

7. Lujan M, Gallardo X, Amengual MJ, Bosque M, Mirapeix RM, Domingo C. Prevalence of bronchiectasis in asthma according to oral steroid requirement: influence of immunoglobulin levels. Biomed Res Int. 2013;2013:109219.
8. Mao B, Yang JW, Lu HW, Xu JF. Asthma and bronchiectasis exacerbation. Eur Respir J. 2016;47(6):1680–1686. [PubMed: 27076584]
9. Chalmers JD, Chotirmall SH. Bronchiectasis: new therapies and new perspectives. The Lancet Respiratory Medicine. 2018;6(9):715–726. [PubMed: 29478908]

Ann Allergy Asthma Immunol. Author manuscript; available in PMC 2022 March 01.

Table 1

Patient Characteristics and Global Physician Assessment with Use of Type 2-Targeted Biologics

ID#	Age	Sex	Race	Smoking history	Allergic rhinitis (allergen sensitization)	Asthma controller medications	CRS	Asthma	FEV1 baseline % predicted	IgE(kU/L)	AEC (K/uL)	Biologic	Duration on biologic (months)	Global physician assessment[≠]
1	73	F	Asian	Never	Yes (tree, grass, dust mite, cockroach, fusarium)	ICS, LABA, LAMA	CRSwNP	Yes	67	2622	1.1	benralizumab	27	5
2	47	F	Black	Never	Yes (tree, grass, cockroach, cat, dog, fusarium, helminthosporium, epicoccum, aspergillus)	ICS, LABA, LAMA, LTRA	CRSwNP (AERD)	Yes	49	345	0.1	dupilumab	11	5
3	76	F	Black	Never	Yes (ragweed, dust mite, cockroach)	ICS, LABA, LAMA. LTRA	No	Yes	28	12	0	dupilumab	1	Excluded (<3months of biologic)
4	51	M	Caucasian	Never	Yes (tree, dust mite, cat, dog, alternaría, fusarium, helminthosporium, pénicillium, hormodendrum, aspergillus)	ICS, LABA	No	Yes	57	357	0.05	dupilumab	7	4
5	58	M	Declined	Former	Yes (tree, grass, ragweed, dust mite, cockroach, cat, dog, mouse, pénicillium, aspergillus)	ICS, LABA	CRSsNP	Yes	23	1872	0.4	benralizumab + omalizumab	1[*]	Excluded (<3months of biologic)
6	65	F	Caucasian	Never	Not performed	ICS, LTRA	CRSsNP	Yes	64	7.8	0.8	dupilumab	4	5
7	54	F	Hispanic	Never	Yes (dust mite)	ICS, LABA LAMA. LTRA	No	Yes	44	83	0.3	benralizumab	9	4
8	57	F	Caucasian	Never	Yes (tree, grass, ragweed, dust mite, cat, dog, aspergillus)	ICS, LABA, LTRA	CRSsNP	Yes	57	11.5	0	benralizumab	22	3
9	73	F	Caucasian	Former	No (skin test negative)	ICS, LABA	No	Yes	100	43.7	1.5	reslizumab	33	4
10	49	F	Caucasian	Never	Yes (grass, ragweed, dust mite, cat, dog, alternaría, aspergillus)	ICS, LABA. LTRA	CRSwNP	Yes	79	1144	0.8	benralizumab + omalizumab	23[**]	4

ID#	Age	Sex	Race	Smoking history	Allergic rhinitis (allergen sensitization)	Asthma controller medications	CRS	Asthma	FEV1 baseline % predicted	IgE(kU/L)	AEC (K/uL)	Biologic	Duration on biologic (months)	Global physician assessment[≠]
11	57	M	Declined	Former	Yes (aspergillus)	ICS, LABA, LTRA	CRSwNP (AERD)	Yes	65	381	0.3	reslizumab	28	5
12	81	M	Caucasian	Former	Yes (tree, ragweed, cat, dog, pénicillium, alternaría, helminthosporium, aspergillus)	ICS, LABA, LAMA	No	Yes	51	43	0.1	dupilumab + omalizumab	6***	5

F: female, M: male

ICS: inhaled corticosteroid, LABA: long-acting beta-agonist, LAMA: long-acting muscarinic antagonist, LTRA: leukotriene receptor antagonists

CRS: chronic rhinosinusitis, CRSwNP: chronic rhinosinusitis with nasal polyps, CRSsNP: chronic rhinosinusitis without nasal polyps, AERD: aspirin exacerbated respiratory disease

FEV: forced expiratory volume, AEC: absolute eosinophil count

[≠]: 1= significantly worse, 2= somewhat worse, 3= same, 4= somewhat improved, 5= significantly improved

* omalizumab: 26 months, benralizumab: 1 month,

** omalizumab: 13.9 years, benralizumab: 23 months,

*** omalizumab: 4 years, dupilumab: 6 months

Ann Allergy Asthma Immunol. Author manuscript; available in PMC 2022 March 01.