Recent Advances in Biologics for Asthma

Jong Geol Jang, MD

Assistant Professor
Division of Pulmonary, Allergy, and Critical Care Medicine
Department of Internal Medicine
Yeungnam University Medical Center
Yeungnam University of Korea

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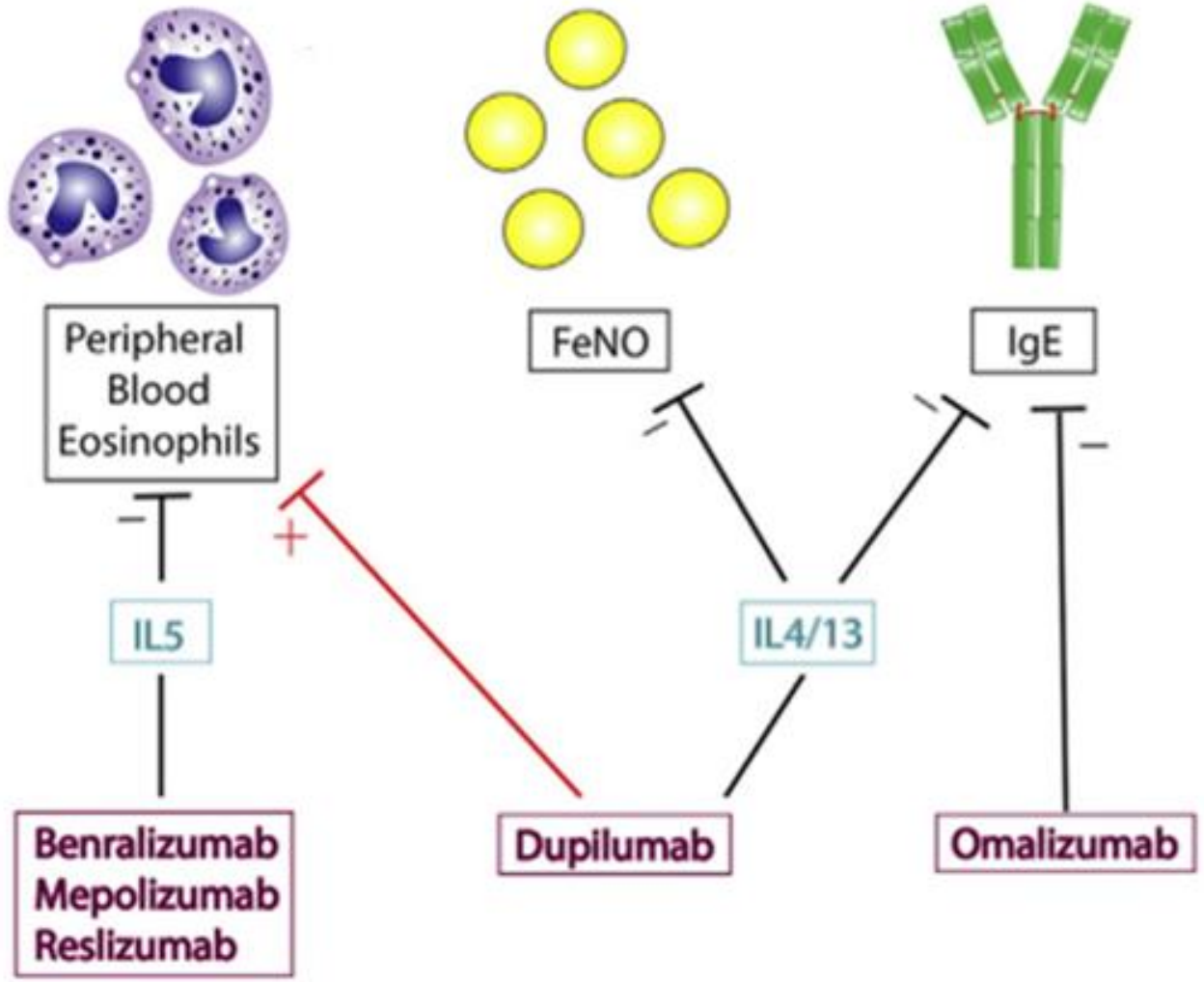
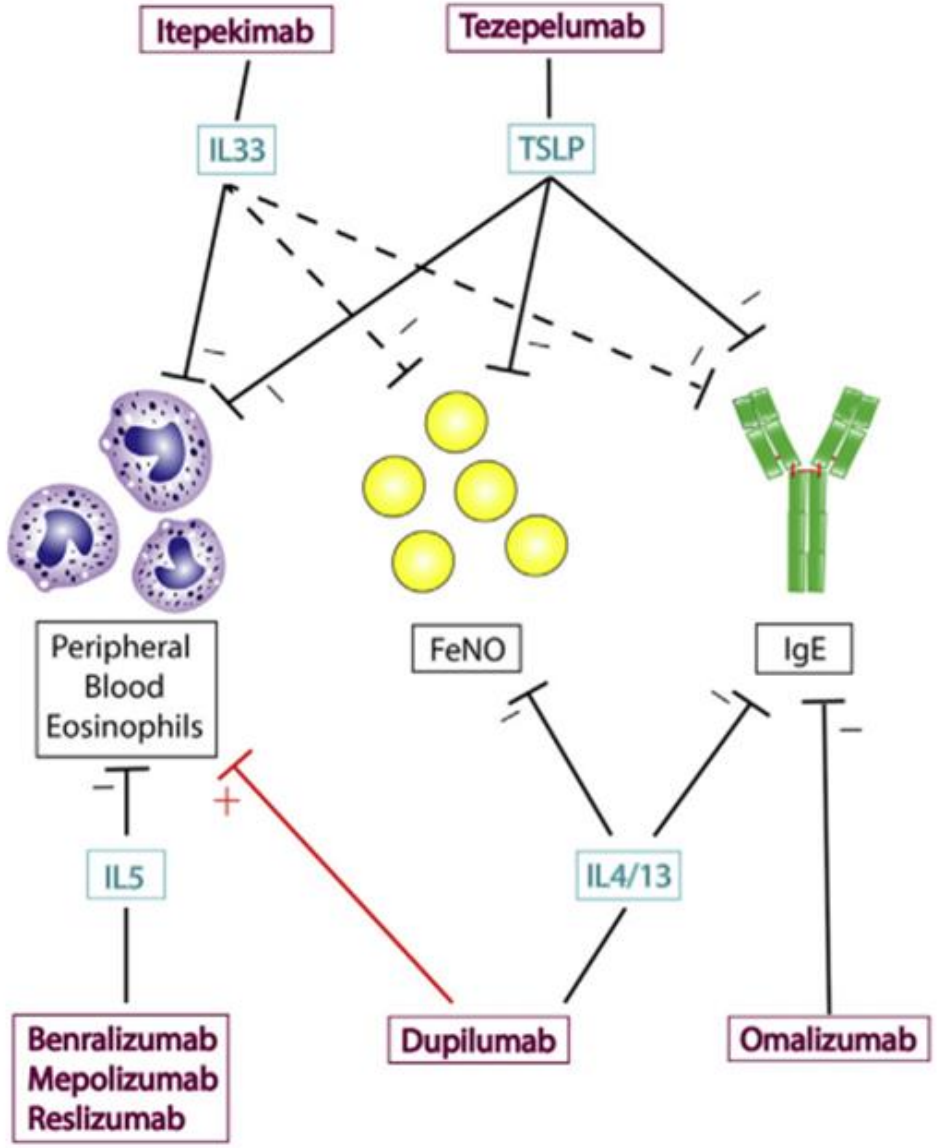
Brief review of biologics for Asthma



J Allergy Clin Immunol Pract 2022;10:1497-505

Brief review of biologics for Asthma



Exacerbations

FEV_1

Symptoms

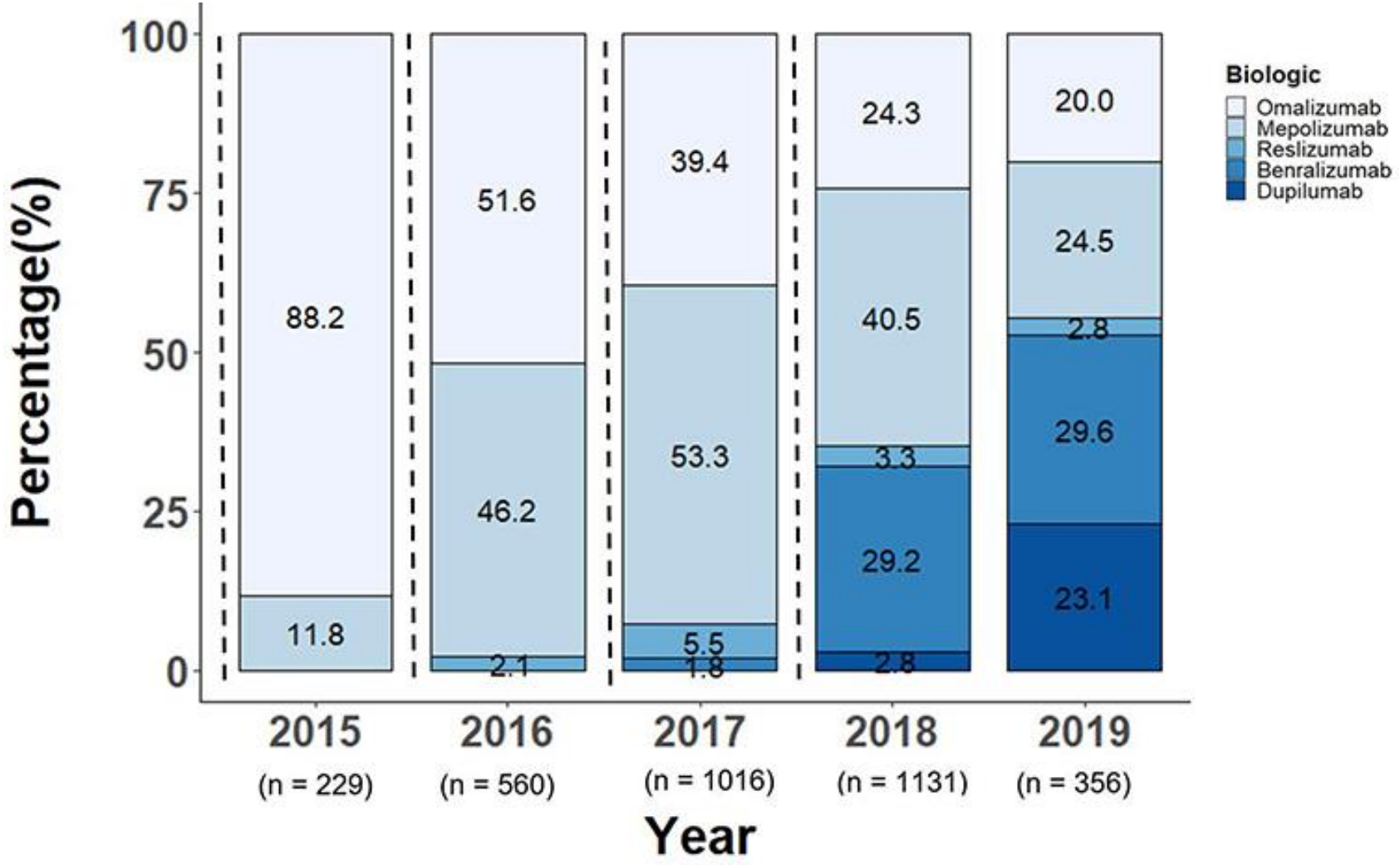
OCS sparing

Airway hyperresponsiveness

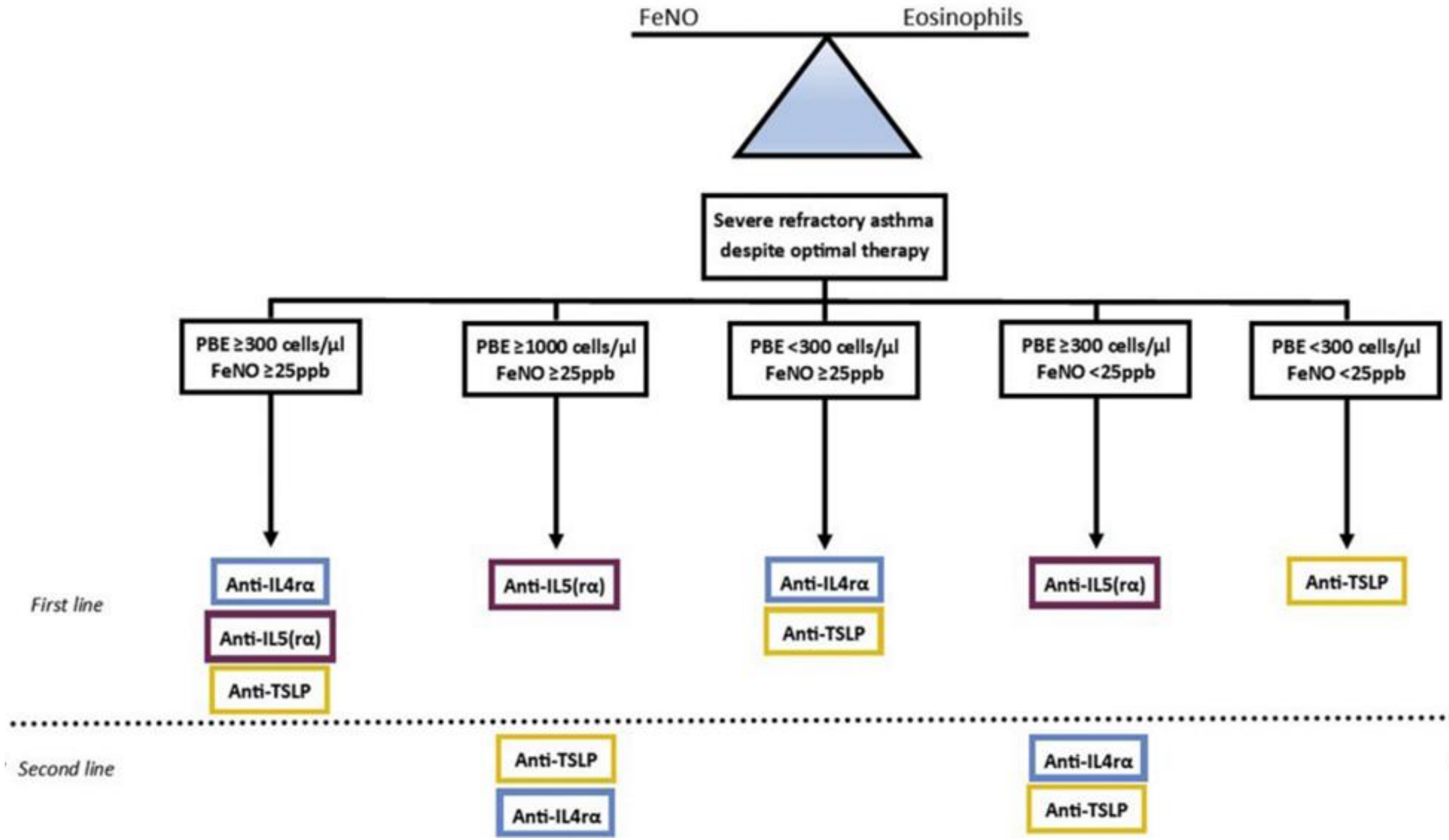
?Small airways dysfunction as R5-R20 or AX

J Allergy Clin Immunol Pract 2022;10:1497-505

Proportion of patients with severe asthma enrolled into ISAR or CHRONICLE (n= 3531) on each biologic (first use) by year



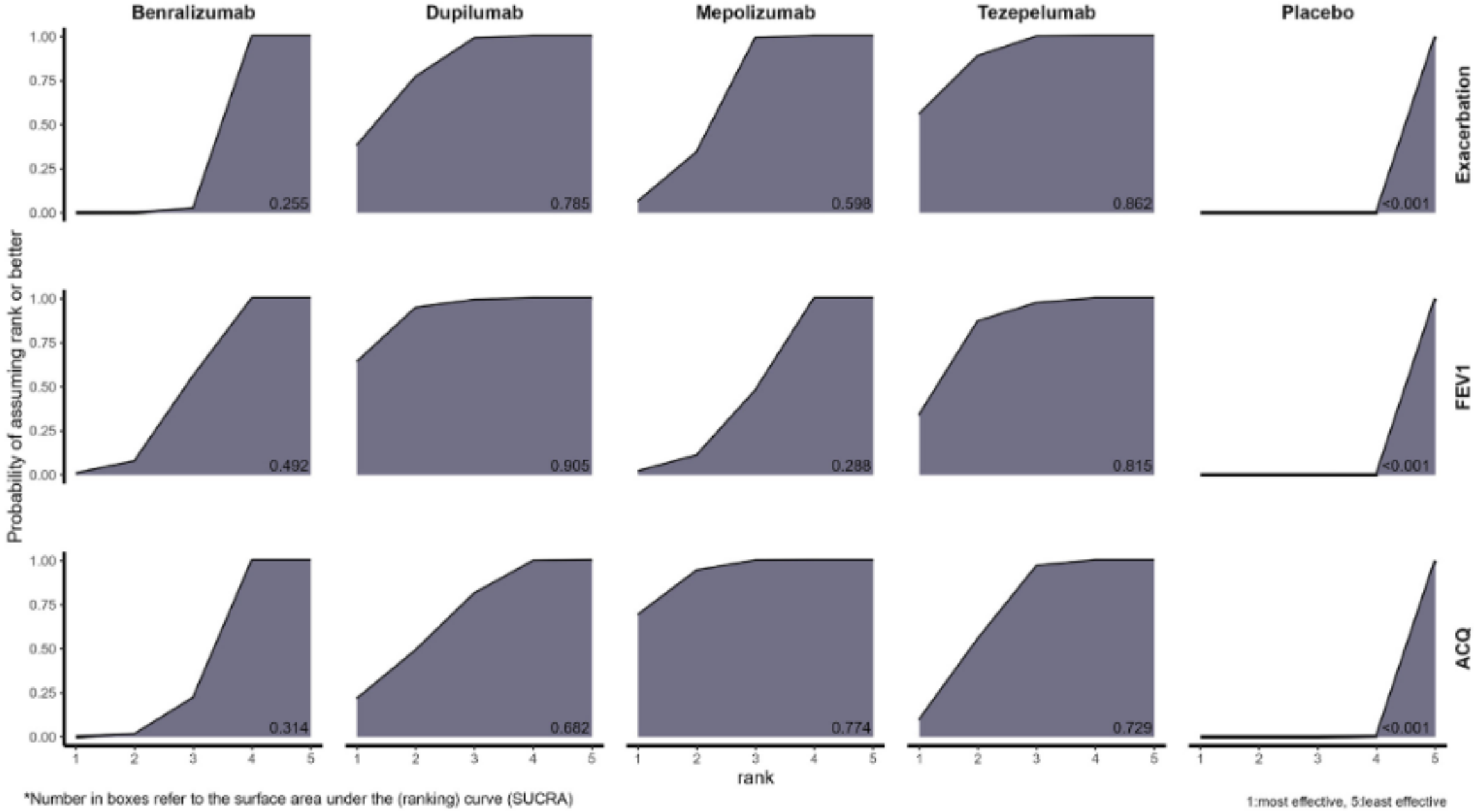
J Asthma Allergy. 2022 Jan 13;15:63-78



J Allergy Clin Immunol Pract 2022;10:1497-505

Comparative efficacy of tezepelumab to mepolizumab, benralizumab, and dupilumab in eosinophilic asthma: A Bayesian network meta-analysis

Tanawin Nopsopon, MD, MPH,[a,b,c] Grace Lassiter, MD, MPH,[d] Ming-Li Chen, MD,[b,e] G. Caleb Alexander, MD, MS,[f,g,h] Corinne Keet, MD, PhD,[i] Hwanhee Hong, PhD,[j] and Ayobami Akenroye, MBChB, MPH, PhD[a,f,k] *Boston, Mass; Bangkok, Thailand; New York, NY; Taichung, Taiwan; Baltimore, Md; and Chapel Hill and Durham, NC*



*Number in boxes refer to the surface area under the (ranking) curve (SUCRA)

1:most effective, 5:least effective

TABLE II. Summary of results of efficacy outcomes with GRADE criteria for certainty of evidence

	Tezepelumab	Dupilumab	Benralizumab	Mepolizumab[a]
Exacerbation: rate ratio, RR (95% CI)				
Tezepelumab	1.00	1.05 (0.69-1.61)***	1.59 (1.17-2.16)***	1.20 (0.85-1.68)**
FEV_1: mean difference in mL (95% CI)[b]				
Tezepelumab	0.00	20 (–78 to 120)**	–62 (–150 to 22)**	–66 (–170 to 33)*
ACQ: mean difference (95% CI)[c]				
Tezepelumab	0.00	0.01 (–0.37 to 0.39)**	0.17 (–0.02 to 0.37)**	–0.14 (–0.38 to 0.10)*

COMPARATIVE EFFECTIVENESS OF OMALIZUMAB, MEPOLIZUMAB, AND DUPILUMAB IN ASTHMA: A TARGET TRIAL EMULATION

Ayobami T. Akenroye, MBChB MPH PhD[1,2,3]; Jodi B. Segal, MD MPH[3,4,5]; Guohai Zhou, PhD[6]; Dinah Foer, MD[1,7]; Lily Li, MD[1]; G. Caleb Alexander, MD MS[3,4,5]; Corinne A. Keet, MD PhD[8]; John W. Jackson, ScD[3,5,9,10]

J Allergy Clin Immunol. 2023 Feb 3;S0091-6749(23)00144-6.
doi: 10.1016/j.jaci.2023.01.020.

Table 2: Incidence rate ratios (IRR) of exacerbations

EXACERBATION RATE RATIOS IRR (95% CI)	N=65 MEPOLIZUMAB	N=68 OMALIZUMAB	N=68 DUPILUMAB
MEPOLIZUMAB (reference)	1.00	0.78 (0.32 - 1.91)	0.28 (0.09 - 0.84)
OMALIZUMAB (reference)		1.00	0.36 (0.12 - 1.08)
DUPILUMAB (reference)			1.00

Dupilumab: 0.46 exacerbations per person-year

Omalizumab: 0.93 per person-year

Mepolizumab: 1.32 per person-year

J Allergy Clin Immunol. 2023 Feb 3;S0091-6749(23)00144-6.
doi: 10.1016/j.jaci.2023.01.020.

Table 3: Change from Baseline to 1 year in Pre-bronchodilator FEV1

MEAN DIFFERENCE IN LITERS (95% CI)	N=65 MEPOLIZUMAB	N=68 OMALIZUMAB	N=68 DUPILUMAB
MEPOLIZUMAB (reference)	0	0.028 (-0.083 to 0.140)	0.110 (-0.003 to 0.222)
OMALIZUMAB (reference)		0	0.082 (-0.040 to 0.204)
DUPILUMAB (reference)			0

J Allergy Clin Immunol. 2023 Feb 3;S0091-6749(23)00144-6.
doi: 10.1016/j.jaci.2023.01.020.

Special Article

Global Variability in Administrative Approval Prescription Criteria for Biologic Therapy in Severe Asthma

J Allergy Clin Immunol Pract 2022;10:1202-16

TABLE II. Biologics license dates and reimbursement status in International Severe Asthma Registry countries with market authorization for their respective biologic (by April 2021)

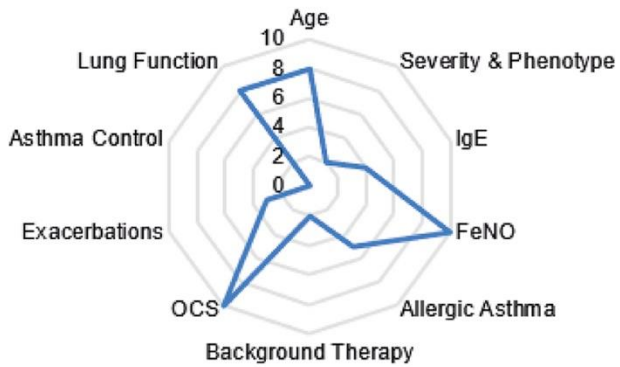
License date and reimbursement status	Omalizumab	Mepolizumab	Reslizumab	Benralizumab	Dupilumab
License dates					
European Medicines Agency license date	October 25, 2005	December 2, 2015	August 16, 2016	January 8, 2018	March 1, 2019*
US Food and Drug Administration license date	June 20, 2003	November 4, 2015	March 23, 2016	November 14, 2017	October 19, 2018†
Reimbursement status, n (%)					
No reimbursement	1 (3.6) SG	2 (7.1) SK, SG	4 (26.7) BR, CN, FR, SK	2 (7.1) SK, SG	5 (25.0) BR, IE, PT, SK, SG
Partial reimbursement	4 (14.3) CN, JP, RU, US	6 (21.4) AR, CN, JP, MX,‡ RU, US	2 (13.3) RU, US	5 (17.9) CN, JP, MX,‡ RU, US	4 (20.0) JP, MX,§ RU, US
Full reimbursement	23 (82.1) AR, AU, BR,‖ BG,¶ CO,# DK, DE, ES, EE, FI,§§ FR, GR, IS, IE,** IT, KW, MX,†† NL, PT, SA, SK, TW, UK	20 (71.4) AU, BR‖, BG,¶ CO,# DK, DE, ES, EE, FI,§§ FR, GR, IS, IE, IT, KW, NL, PT, SA, TW, UK	9 (60.0) DK, DE, ES, EE, FI,§§ IE,** NL, PT, UK	21 (75.0) AR‖‖, AU, BR,‡‡ BG,¶ CO,# DK, DE, ES, EE, FI,§§ FR, GR, IS, IE, IT, KW, NL, PT, SA, TW, UK	11 (55.0) AU, CO,# DK, DE, EE, FI,§§ FR, IT, KW, NL, SA
Total, n	28	28	15	28	20

J Allergy Clin Immunol Pract 2022;10:1202-16

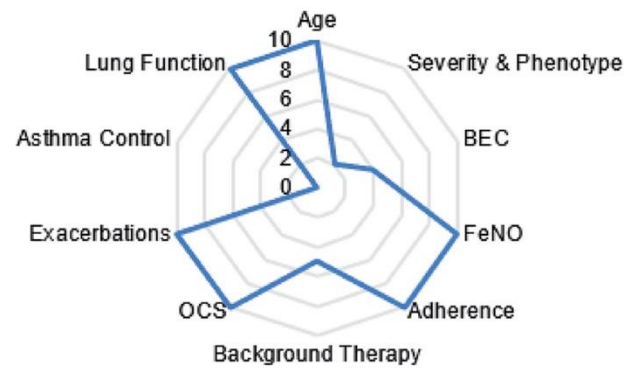
Biologic Accessibility Score

- Age
- Severity/phenotype
- Serum IgE (IU/mL)
- BEC (cells/mL)
- FeNO (parts per billion)
- Allergic asthma
- Background therapy
- OCS
- Exacerbations
- Asthma control
- Lung function
- Adherence

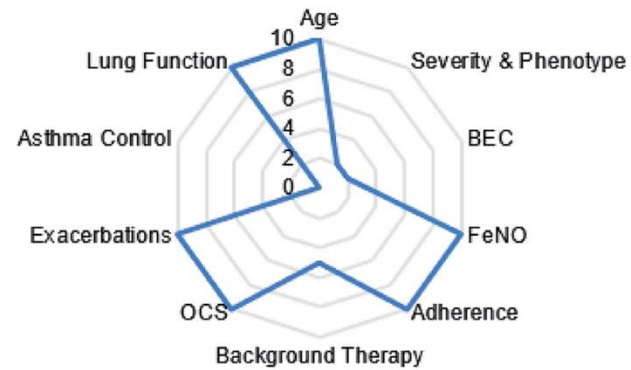
Omalizumab: South Korea - BACS 52



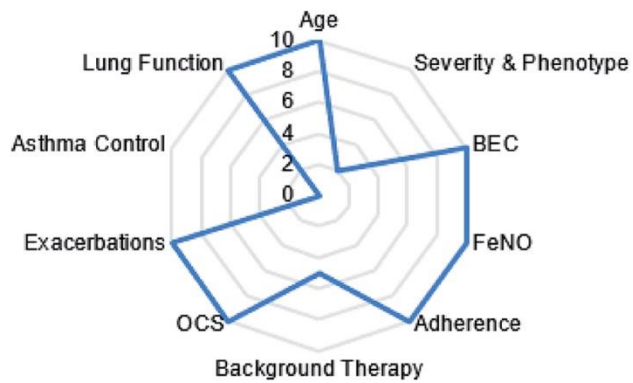
Mepolizumab: South Korea - BACS 71



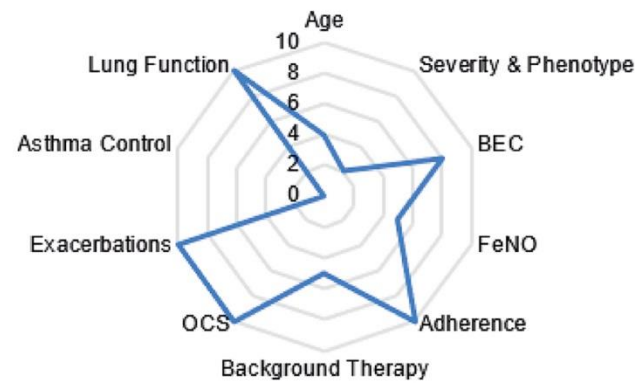
Reslizumab: South Korea - BACS 69



Benralizumab: South Korea - BACS 77



Dupilumab: South Korea - BACS 64



ERJ OPEN RESEARCH
ORIGINAL RESEARCH ARTICLE
A-N. FRIX ET AL.

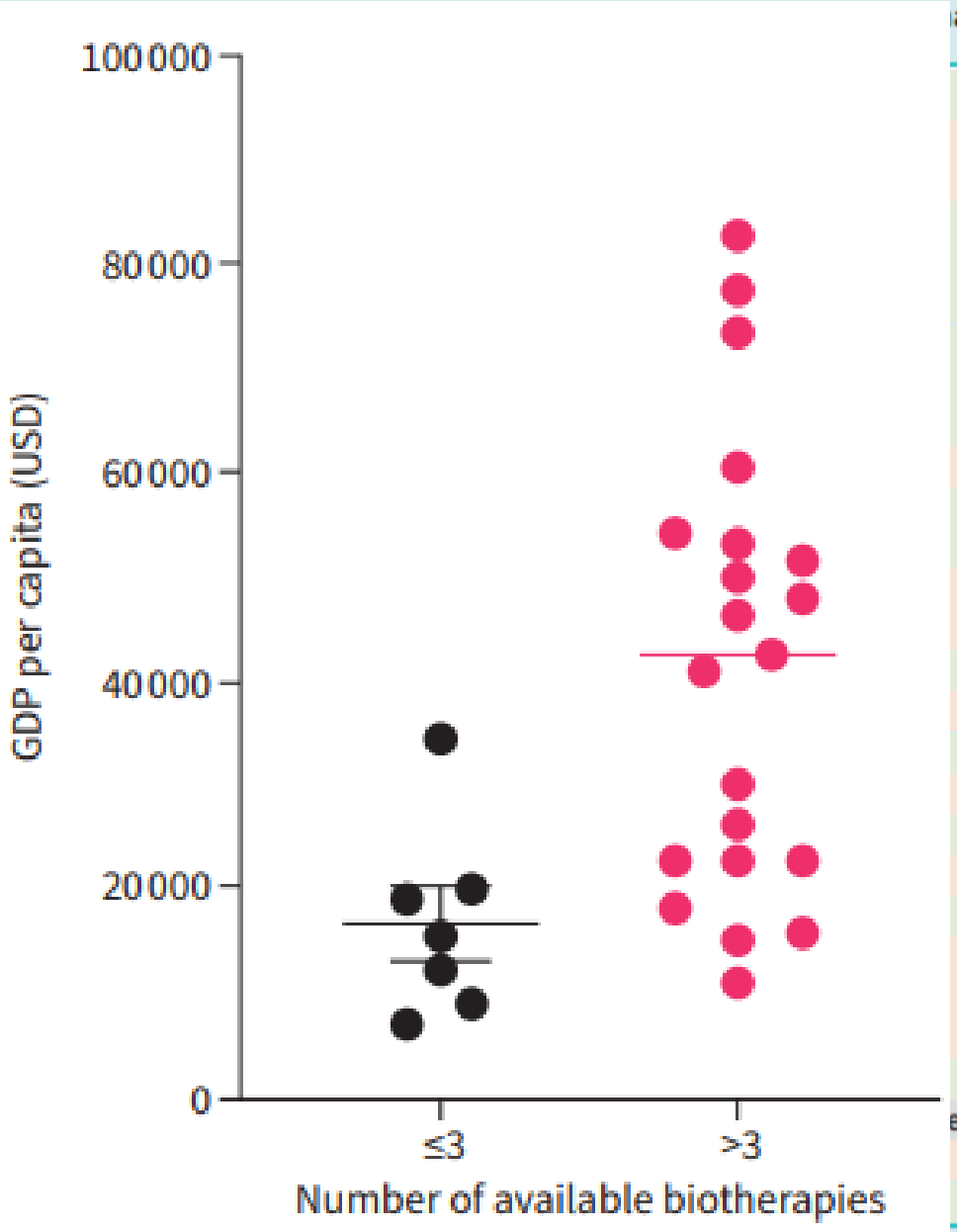
Heterogeneity in the use of biologics for severe asthma in Europe: a SHARP ERS study

Anne-Noelle Frix[1], Liam G. Heaney[2], Barbro Dahlén[3], Florin Mihaltan[4], Svetlana Sergejeva[5], Sanja Popović-Grle[6], Vratislav Sedlak[7], Lauri Lehtimäki[8], Arnaud Bourdin[9], Stephanie Korn[10], Eleftherios Zervas[11], Zsuzsanna Csoma[12], Dora Lúðvíksdóttir[13], Marcus Butler[14,15], Giorgio Walter Canonica[16], Ineta Grisle[17], Kristina Bieksiene[18], Anneke Ten Brinke[19], Piotr Kuna[20], Claudia Chaves Loureiro[21], Natalia M. Nenasheva[22], Zorica Lazic[23], Sabina Škrgat[24], David Ramos-Barbon[25], Joerg Leuppi[26,27], Bilun Gemicioglu[28], Apostolos Bossios[29], Celeste M. Porsbjerg[30], Elisabeth H. Bel[31], Ratko Djukanovic[32,33] and Renaud Louis[34]

ERJ Open Res 2022; 8: 00273-2022
DOI: 10.1183/ 23120541.00273-2022

TABLE 2 Availability of biologics in Europe (as of April 2021)

Country	Number of available biologics	Omalizumab	...ab
Austria	5	1	
Belgium	4	1	
Croatia	4	1	
Czech Republic	5	1	
Denmark	5	1	
Estonia	5	1	
Finland	5	1	
France	5	1	
Germany	5	1	
Greece	2	1	
Hungary	5	1	
Iceland	5	1	
Ireland	4	1	
Italy	3	1	
Latvia	5	1	
Lithuania	3	1	
Netherlands	5	1	
Poland	3	1	
Portugal	5	1	
Romania	2	1	
Russia	5	1	
Serbia	3	1	
Slovenia	4	1	
Spain	5	1	
Sweden	5	1	
Switzerland	5	1	...el
Turkey	2	1	
UK	5	1	



ERJ Open Res 2022; 8: 00273-2022
DOI: 10.1183/ 23120541.00273-2022

TABLE 3 Inclusion criteria for severe asthma biotherapies in Europe

Biotherapy	Common criteria	Disparities noted between countries	Additional criteria for some countries
Omalizumab (n=26 countries)	Severe asthma definition (ATS/ERS) (24/26) Exacerbation rate (24/26) • Four countries required >2 exacerbations/year • 20 countries considered ⩽2 exacerbations/year IgE levels (25/26), with very variable threshold (majority >30 or >76 $IU \cdot mL^{-1}$)	Age threshold: adults *versus* children for some countries FEV_1 levels: used as criterion in 13/26 countries (50%)	Adherence is an absolute criterion in two countries Non-smoking status is an absolute criterion in three countries Questionnaire for quality of life (QOL) was used as criterion in one country

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DOI: 10.1183/ 23120541.00273-2022

TABLE 3 Inclusion criteria for severe asthma biotherapies in Europe

Biotherapy	Common criteria	Disparities noted between countries	Additional criteria for some countries
Mepolizumab (n=24 countries)	Severe asthma definition (ATS/ERS) (21/24) Exacerbation rate (24/24) • Five countries required >2 exacerbations/year • 19 countries considered ⩽2 exacerbations/year Blood eosinophils (24/24), with a threshold variable between 150 and 500 cells·μL^{-1}) Of note, one country separated maintenance OCS patients and not on maintenance OCS patients to define threshold	Age: adult *versus* children. This was not clearly defined as criterion in some countries FEV_1 levels: used as criterion in 5/24 countries (20.8%)	Adherence is an absolute criterion in four countries Non-smoking status is an absolute criterion in three countries Questionnaire for QOL was used as criterion in one country Two countries offer the possibility of inclusion if sputum eosinophils are high, even if blood eosinophils are below the fixed threshold Cotinine level in saliva is a criterion in one country

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DOI: 10.1183/ 23120541.00273-2022

TABLE 3 Inclusion criteria for severe asthma biotherapies in Europe

Biotherapy	Common criteria	Disparities noted between countries	Additional criteria for some countries
Dupilumab (n=11 countries)	Severe asthma definition (ATS/ERS) (10/11) Exacerbation rate (10/11) • One country required >2 exacerbations/year • Nine countries considered ⩽2 exacerbations/year • One country had no threshold Blood eosinophils (11/11), with a threshold variable between 150 and 300 cells·μL^{-1})	Age: adult *versus* children. This was not clearly defined as criterion in some countries FEV_1 levels: used as criterion in 1/11 countries (9.1%) F_{ENO} levels: used in 5/11 countries (45.5%), with threshold >25 ppb for all countries	Adherence is an absolute criterion in two countries Non-smoking status is an absolute criterion in two countries Questionnaires for QOL were not used Three countries granted the biotherapy if patient was on OCS >50% of the year (without needing exacerbations or high blood eosinophilic count) Cotinine level in saliva is a criterion in one country

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DOI: 10.1183/ 23120541.00273-2022

TABLE 4 Assessment of effectiveness in biologics: ranking of objective criteria

Ranking	Patients on maintenance OCS	Item score	Patients not on maintenance OCS	Item score
National Leads Survey (n=28)				
1	Reduction of exacerbation rate by 75% over 1 year	3.4	Reduction of exacerbation rate by 75% over 1 year	2.5
2	Reduction of chronic dose of OCS by 50%	3.4	Reduction of exacerbation rate by 50% over 1 year	2.8
3	Stopping chronic maintenance OCS	3.5	Reduction of exacerbation rate by 25% over 1 year	4.8
4	Reduction of exacerbation rate by 50% over 1 year	4.1	Reduction in ACQ by 1 at 4/6 months	5
5	Reduction of exacerbation rate by 25% over 1 year	6	Increase in AQLQ by 1 at 4/6 months	5
6	Increase in AQLQ by 1 at 4/6 months	6.1	Reduction in ACQ by 0.5 at 4/6 months	5.5
7	Reduction in ACQ by 1 at 4/6 months	6.2	Increase in AQLQ by 0.5 at 4/6 months	5.7
8	Reduction in ACQ by 0.5 at 4/6 months	6.6	Reduction of chronic dose of ICS by 50%	6.2
9	Increase in AQLQ by 0.5 at 4/6 months	6.9	Improvement of 5% predicted FEV_1	7.6
10	Improvement of 5% predicted FEV_1	8.5		
Experts Broad Survey (n=263)				
1	Reduction of exacerbation rate by 75% over 1 year	2.6	Reduction of exacerbation rate by 75% over 1 year	1.9
2	Reduction of exacerbation rate by 50% over 1 year	3.1	Reduction of exacerbation rate by 50% over 1 year	3.1
3	Stopping chronic maintenance OCS	3.5	Reduction of exacerbation rate by 25% over 1 year	4.5
4	Reduction of chronic dose of OCS by 50%	4.1	Reduction in ACQ by 1 at 4/6 months	4.6
5	Reduction in ACQ by 1 at 4/6 months	4.8	Reduction in ACQ by 0.5 at 4/6 months	5.2
6	Reduction of exacerbation rate by 25% over 1 year	5.1	Reduction of chronic dose of ICS by 50%	5.6
7	Reduction in ACQ by 0.5 at 4/6 months	6.3	Increase in AQLQ by 1 at 4/6 months	6.3
8	Increase in AQLQ by 1 at 4/6 months	7.3	Increase in AQLQ by 0.5 at 4/6 months	6.8
9	Increase in AQLQ by 0.5 at 4/6 months	8.5	Improvement of 5% predicted FEV_1	7.8
10	Improvement of 5% predicted FEV_1	8.9		

ERJ Open Res 2022; 8: 00273-2022
DOI: 10.1183/ 23120541.00273-2022

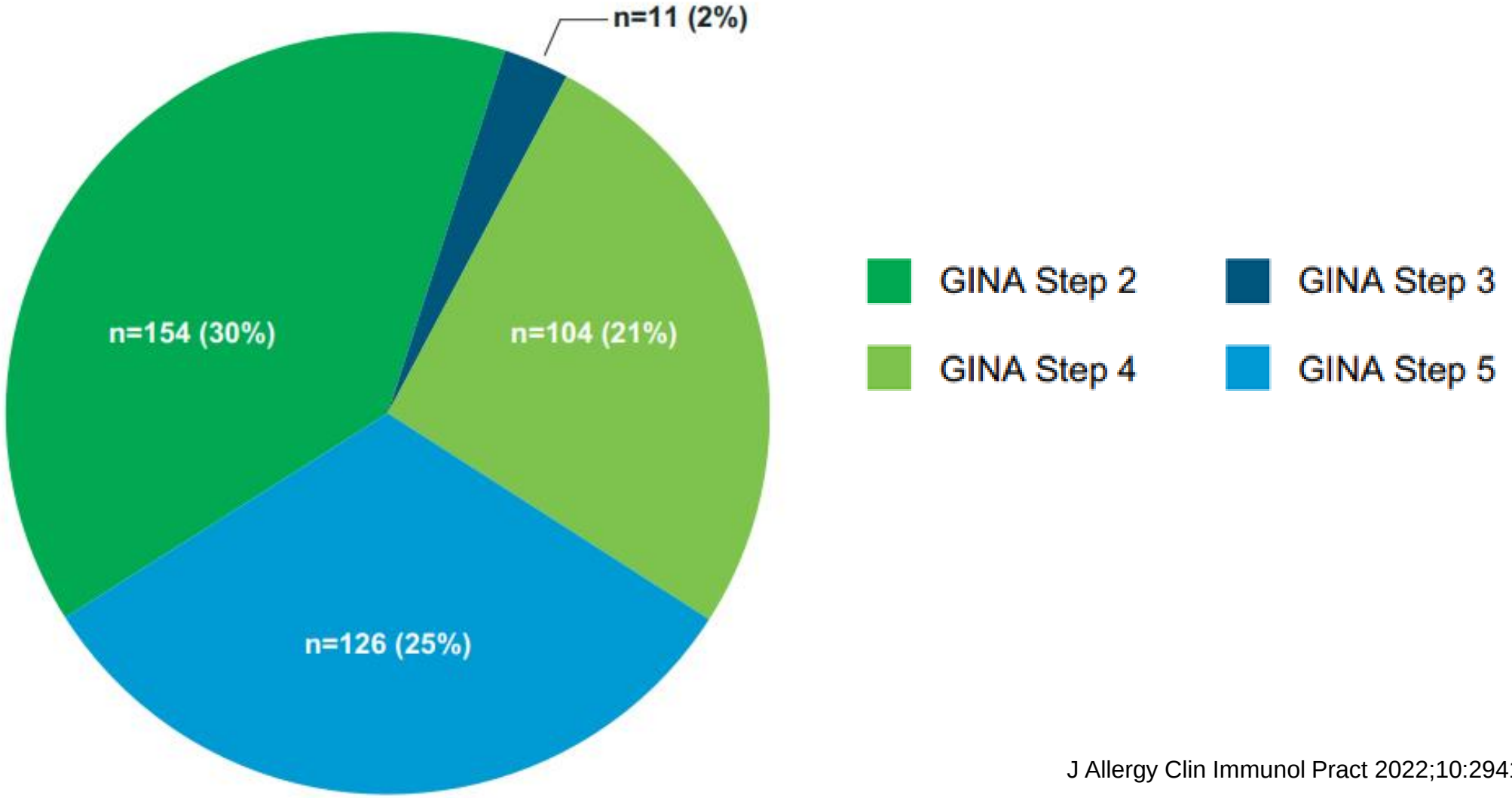
Original Article

Assessment of Real-World Escalation to Biologics in US Patients With Asthma

Bruce Bender, PhD[a], John Oppenheimer, MD[b,c], Maureen George, PhD, RN, AE-C[d], Randall Brown, MD, MPH, AE-C[e], Ayush Patel, PhD[e], Tanisha Hill, MPH[e], Amanda Boe, PhD[e], Ernesto Mayen Herrera, MSc[e], Zenobia Dotiwala, MS[f], Julian Casciano, BS[f], and Jonathan A. Bernstein, MD[g] *Denver, Colo; Newark, Cedar Knolls, and Parsippany, NJ; New York, NY; Delray Beach, Fla; and Cincinnati, Ohio*

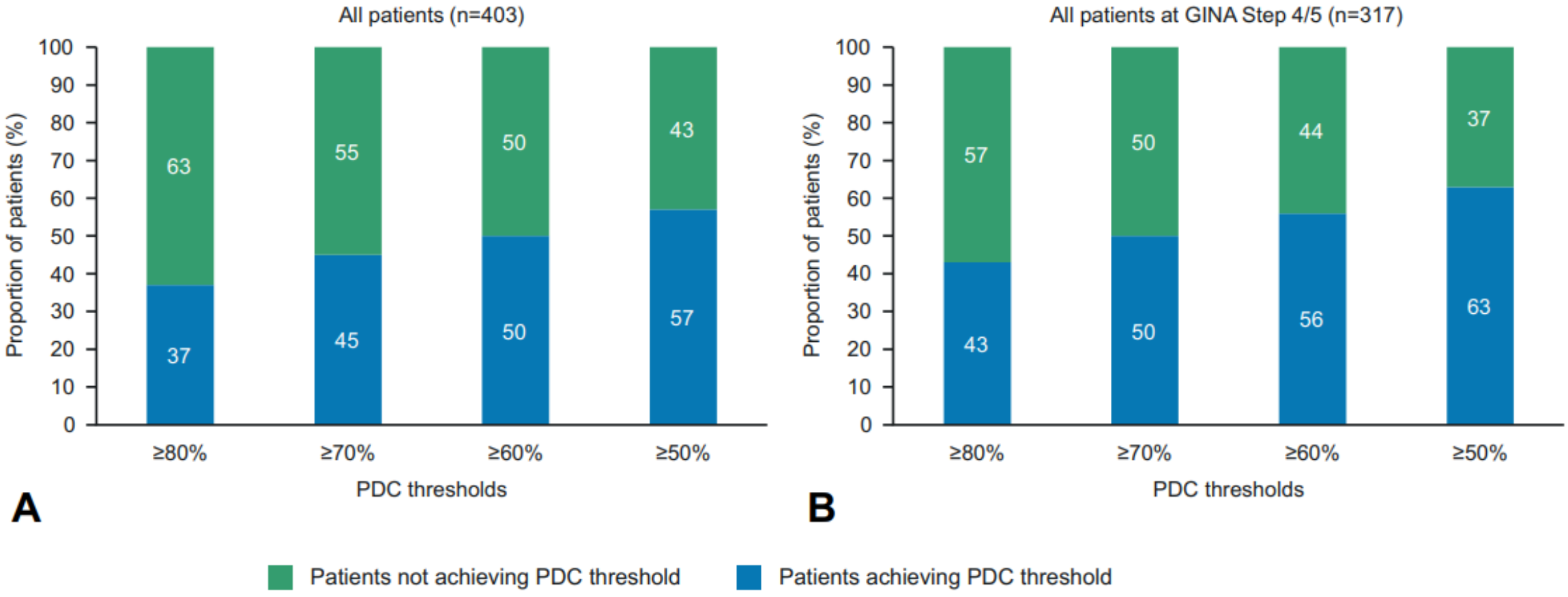
J Allergy Clin Immunol Pract 2022;10:2941-8

GINA step before biologic initiation



J Allergy Clin Immunol Pract 2022;10:2941-8

Proportion days covered level of patients who received maintenance treatment



J Allergy Clin Immunol Pract 2022;10:2941-8

Journal of Asthma and Allergy

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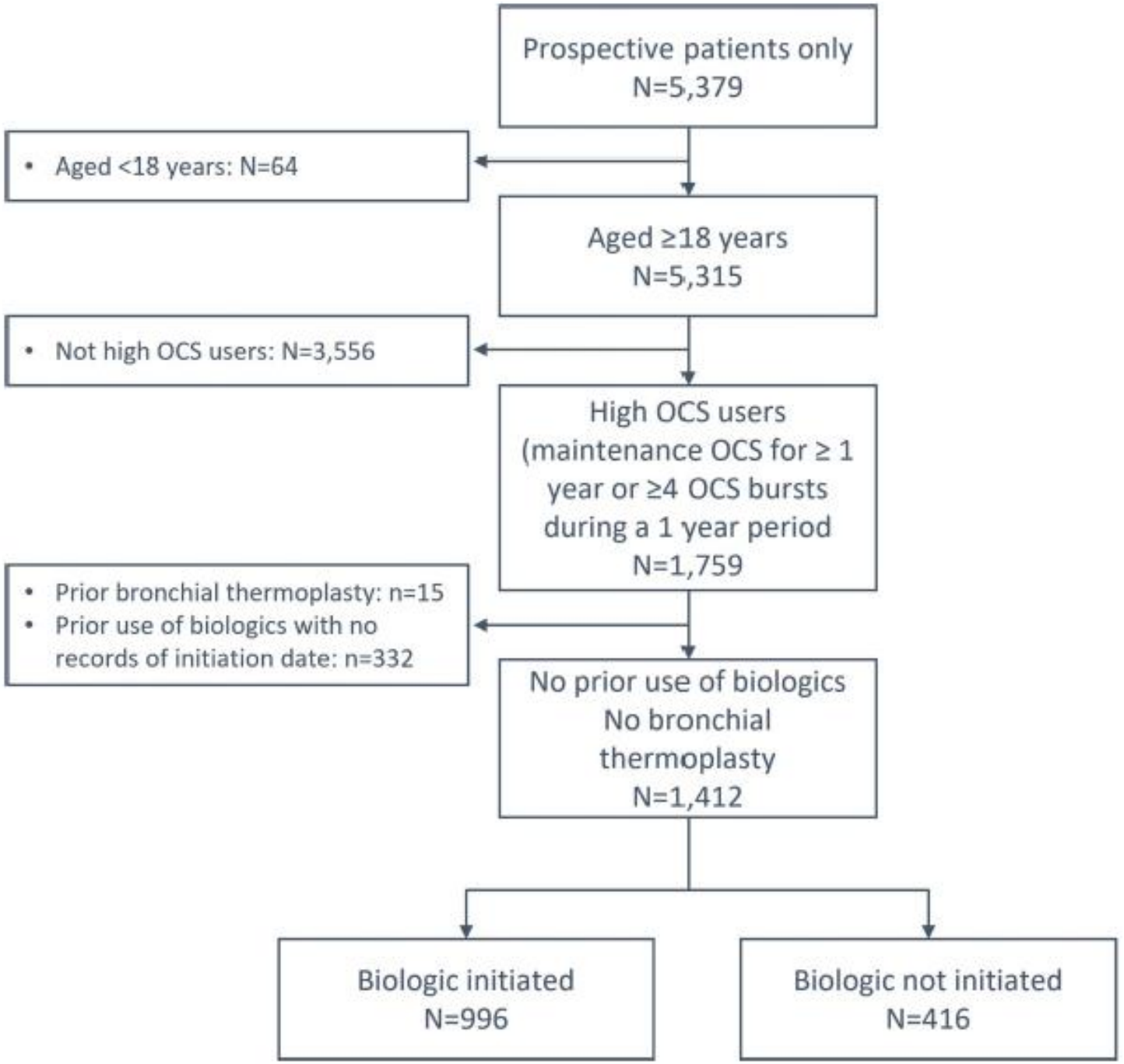
ORIGINAL RESEARCH

Characterization of Patients in the International Severe Asthma Registry with High Steroid Exposure Who Did or Did Not Initiate Biologic Therapy

J Asthma Allergy. 2022;15:1491-1510



Journal of Asthma and Allergy 2022:15 1491–1510


Canada
n=30
23.3%/76.7%
UK
n=623
23.1%/76.9%
Denmark
n=173
1.7%/98.3%
Bulgaria
n=10
60%/40%
Ireland
n=8
100%/0%
Kuwait
n=88
20.5%/79.5%
South Korea
n=20
71.4%/28.6%
Japan
n=21
71.4%/28.6%
Spain
n=10
30%/70%
UAE
n=3
100%/0%
Italy
n=237
42.6%/57.4%
Taiwan
n=22
81.8%/18.2%
Colombia
n=18
94.4%/5.6%
Greece
n=13
23.1%/76.9%
India
n=3
100%/0%
Mexico
n=16
43.8%/56.2%
Argentina
n=7
85.7%/14.3%
Saudi Arabia
n=27
44.4%/55.6%
Australia
n=83
48.2%/51.8%

Table 2 Baseline Clinical Characteristics for ISAR Patients with Severe Asthma and High Oral Corticosteroid Exposure Who Were and Were Not Initiated on Biologic (Bx) Therapy

	BX Not Initiated	BX Initiated	P-value	B-H Critical P value Threshold for Significance in Multiple Testing
Age of asthma onset Mean (SD)	N=402 29.5 (18.7)	N=876 27.9 (18.7)	0.150	0.057
Asthma duration Mean (SD)	N=394 23.8 (16.3)	N=859 23.7 (16.7)	0.910	0.098
Asthma control* Controlled, n (%) Partially controlled, n (%) Uncontrolled, n (%)	N=381 26 (6.8) 76 (20.0) 279 (73.2)	N=777 51 (6.6) 98 (12.6) 628 (80.8)	0.004	0.017
No. asthma exacerbations in the past year (excluding cases with 0 exacerbations) Mean (SD)	N=334 5.3 (4.0)	N=849 5.7 (3.9)	0.147	0.055
Healthcare resource utilization				
	N=416	N=996		
Emergency department visit, N (%)	157 (37.7)	321 (32.2)	0.046	0.038
Hospital admission, N (%)	131 (31.5)	286 (28.7)	0.297	0.069
Invasive ventilation (ever), N (%)	27 (6.5)	69 (6.9)	0.766	0.088

	BX Not Initiated	BX Initiated	P-value	B-H Critical P value Threshold for Significance in Multiple Testing
Adherence*	N=327	N=873		
Adherent, n (%)	249 (76.2)	774 (88.7)	<0.001	0.002
Poor: Clinical impression, n (%)	25 (7.7)	12 (1.4)		
Poor: Prescription records, n (%)	53 (16.2)	87 (10.0)		
BEC (/μL)	N=329	N=919		
Highest, Mean (SD)	398.9 (371.4)	482.8 (468.7)	0.003	0.014
FeNO, ppb	N=218	N=701	0.010	0.031
<25, n (%)	87 (39.9)	205 (29.2)		
25–50, n (%)	53 (24.3)	220 (31.4)		
>50, n (%)	78 (35.8)	276 (39.4)		

	BX Not Initiated	BX Initiated	P-value	B-H Critical P value Threshold for Significance in Multiple Testing
Co-morbidities				
Potential OCS-related co-morbidities				
Anxiety, n (%)	N=230 31 (13.5)	N=260 36 (13.9)	0.906	0.097
Depression, n (%)	N=227 25 (11.0)	N=254 23 (9.1)	0.474	0.079
Osteoporosis, n (%)	N=304 52 (17.1)	N=611 67 (11.0)	0.009	0.026
Peptic ulcer, n (%)	N=185 10 (5.4)	N=205 6 (2.9)	0.218	0.062
Type II diabetes, n (%)	N=170	N=210	0.239	0.064
T2 Comorbidities (ever)	N=416	N=996		
Allergic rhinitis, n (%)	168 (40.4)	313 (31.4)	0.001	0.010
Chronic rhinosinusitis, n (%)	83 (20.0)	246 (24.7)	0.054	0.043
Eczema, n (%)	38 (9.1)	98 (9.8)	0.682	0.084
Nasal polyps, n (%)	98 (23.6)	351 (35.2)	<0.001	0.005
Other				
Anaphylaxis event, n (%)	N=197 5 (2.5)	N=399 2 (0.5)	0.030	0.036
Cancer event, n (%)	N=199 13 (6.5)	N=393 8 (2.0)	0.005	0.019
Serious infection event, n (%)	N=196 26 (13.3)	N=396 194 (49.0)	<0.001	0.009

Journal of Asthma and Allergy

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ORIGINAL RESEARCH

Real World Biologic Use and Switch Patterns in Severe Asthma: Data from the International Severe Asthma Registry and the US CHRONICLE Study

J Asthma Allergy. 2022 Jan 13;15:63-78

Table 1 Pattern of Biologic Use Overall and by Country for Patients with Severe Asthma Enrolled into ISAR and CHRONICLE

Year in Which ≥2 Biologics Became Available	Population or Country	Continued n (%)	Stopped n (%)	Switched n (%)
Overall	Total (n=3531)	2791 (79.0)	356 (10.2)	384 (10.8)
	eCRF (n=2656)	2237 (84.2)	139 (5.3)	280 (10.5)
	USA only (n=2127)	1575 (74.1)	279 (13.1)	273 (12.8)
	Non-USA (n=1404)	1216 (86.6)	77 (5.5)	111 (7.9)

J Asthma Allergy. 2022 Jan 13;15:63-78. doi: 10.2147/JAA.S328653. eCollection 2022

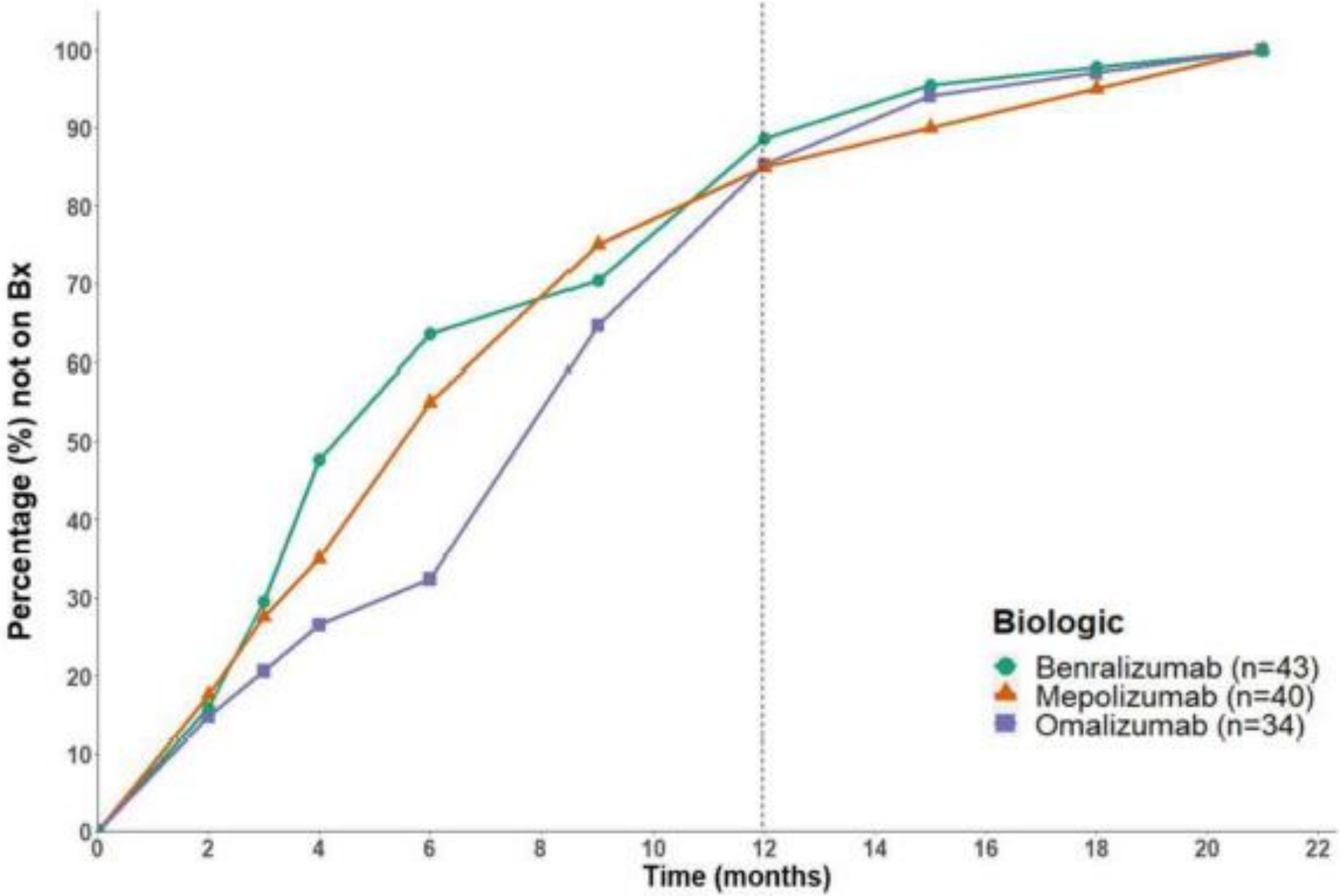

Figure 3 Time to biologic cessation for patients with severe asthma enrolled into ISAR or CHRONICLE who stopped or switched biologic (from 2018 onwards).
Abbreviation: ISAR, International Severe Asthma Registry.

Table 2 Demographic and Clinical Characteristics of Patients with Severe Asthma Enrolled into ISAR or CHRONICLE, Prior to First Biologic, According to Pattern of First Biologic Use

Biologic Utilisation Group	Continued 2791	Stopped 356	Switched 384	Stoppers vs Continuers: P-value[a]	Switchers vs Continuers: P-values[a]
Exacerbations[#]					
	728	46	73		
Not on long-term OCS, n (%)	503 (69.1)	39 (84.8)	62 (84.9)	0.002	0.004
Median (IQR)	4.0 (2, 6)	5.0 (4, 8)	4.5 (3, 8)		
Healthcare resource utilization					
Invasive Ventilation Episodes	715	42	67	0.002	0.079
≥1, n (%)	45 (6.3)	8 (19.0)	8 (11.9)		
Emergency Visits[#]	450	47	65	0.142	0.010
≥1, n (%)	180 (40.0)	24 (51.1)	37 (56.9)		
Hospitalizations[#]	639	45	63	0.004	<0.001
≥1, n (%)	136 (21.3)	18 (40.0)	29 (46.0)		

J Asthma Allergy. 2022 Jan 13;15:63-78

Table 2 Demographic and Clinical Characteristics of Patients with Severe Asthma Enrolled into ISAR or CHRONICLE, Prior to First Biologic, According to Pattern of First Biologic Use

Biologic Utilisation Group	Continued 2791	Stopped 356	Switched 384	Stoppers vs Continuers: P-value[a]	Switchers vs Continuers: P-values[a]
Allergic Rhinitis	514	109	77	0.026	1.000
Ever, n (%)	467 (90.9)	106 (97.2)	70 (90.9)		
CRS and NP	684	73	101	<0.001	0.020
CRSwNP, n (%)	411 (60.1)	28 (38.4)	63 (62.4)		
Biomarkers					
BEC (cells/μL)[#]	865	166	153		
Not on long-term OCS	771	150	134	0.411	0.011
<300, n (%)	326 (42.3)	58 (38.7)	41 (31.1)		
≥300, n (%)	445 (57.7)	92 (61.3)	93 (68.9)		
On long-term OCS	94	16	18	0.064	0.083
<300, n (%)	47 (50.0)	4 (25.0)	5 (27.8)		
≥300, n (%)	47 (50.0)	12 (75.0)	13 (72.2)		
FeNO (ppb)	**795**	**126**	**94**	0.663	0.007
0-<25, n (%)	357 (44.9)	62 (49.2)	28 (29.8)		
≥25 - <50, n (%)	250 (31.4)	37 (29.4)	32 (34.0)		
≥50, n (%)	188 (23.6)	27 (21.4)	34 (36.2)		

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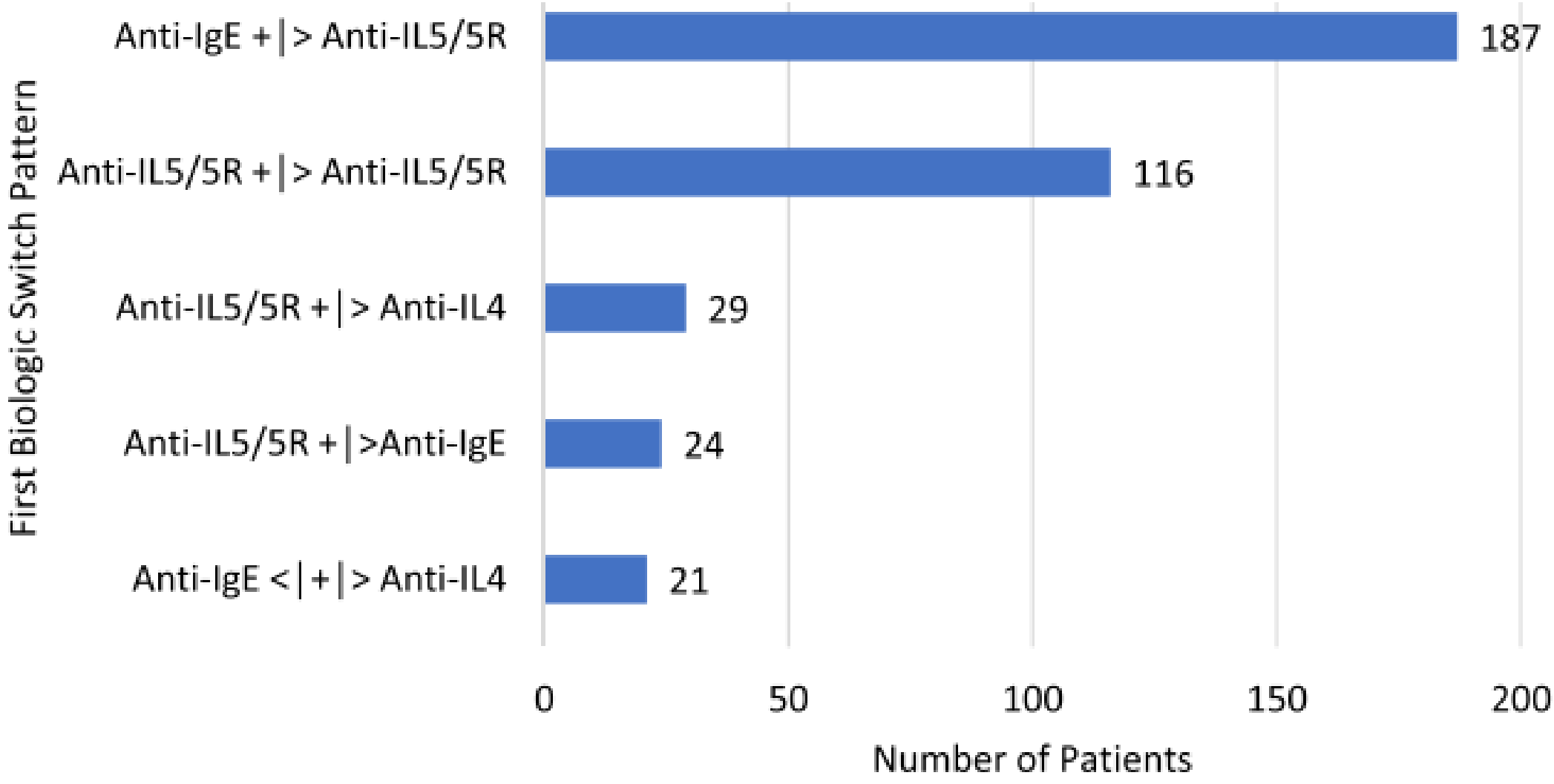
Table 3 Reasons Why eCRF Patients with Severe Asthma Enrolled into ISAR or CHRONICLE Stopped or Switched Their First Prescribed Biologic

Reason	Stopped (n=139)	Switched (n=280)
Reason available n (%)	113	183
Insufficient Clinical Efficacy	72 (63.7)	158 (86.3)
Potential adverse outcomes	18 (15.9)	14 (7.7)
Biologic Access Restriction	8 (7.1)	5 (2.7)
Patient Preference	4 (3.5)	3 (1.6)
Other	12 (10.6)	11 (6.0)

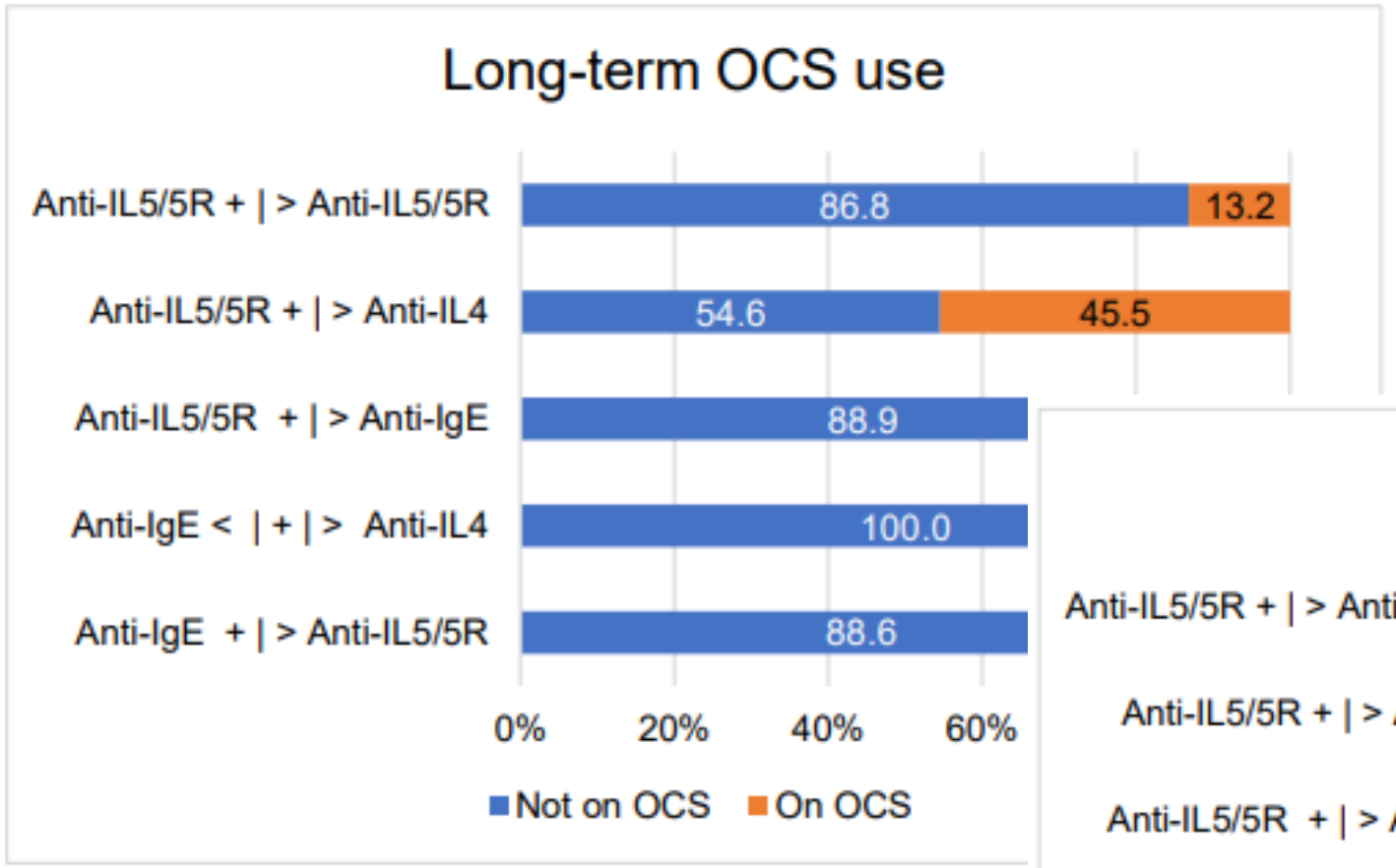
Abbreviations: eCRF, electronic case report form; ISAR, International Severe Asthma Registry.

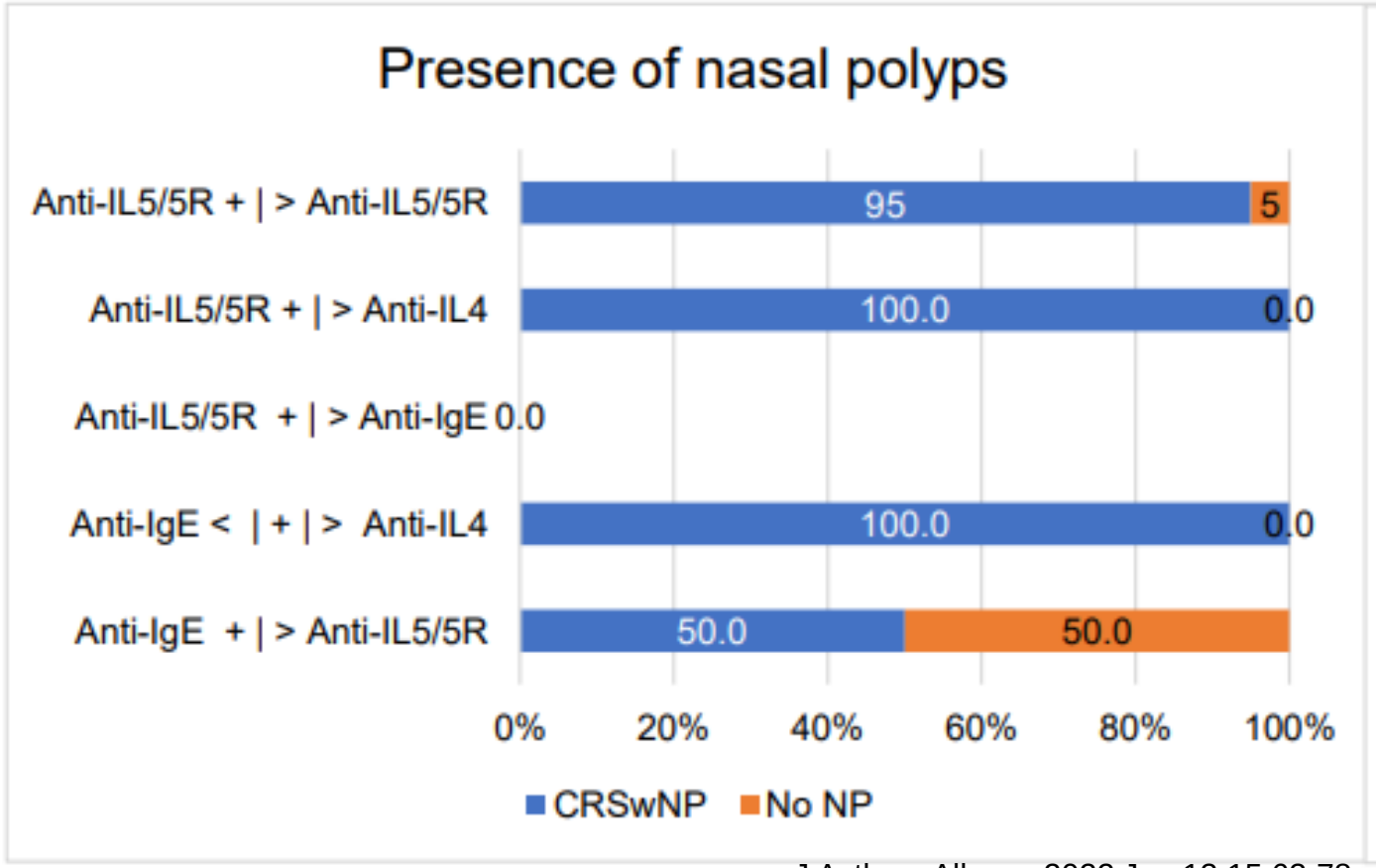
J Asthma Allergy. 2022 Jan 13;15:63-78

Patterns of Switching



J Asthma Allergy. 2022 Jan 13;15:63-78





J Asthma Allergy. 2022 Jan 13;15:63-78

Switch patterns in a cohort ofindividuals with asthma who received omalizumab or mepolizumab therapy

Ayobami Akenroye MBChB, MPH, PhD, Tessa Ryan BA, Alanna McGill BA, Guohai Zhou PhD, Jerome Shier MD and Jodi Segal MD, MPH

J Allergy Clin Immunol Pract. 2022 Nov 13;S2213-2198(22)01193-X. doi: 10.1016/j.jaip.2022.10.047.

TABLE I. Baseline characteristics of study population

Characteristic	Omalizumab	Mepolizumab	Mepolizumab patients eligible for omalizumab
N	65	62	38
Age, mean (SD)	45.6 (15.4)	54.7 (14.4)	54.6 (14.0)
Female sex, n (%)	51 (78.5)	42 (67.7)	25 (65.8)
Body mass index, mean (SD)	29.8 (7.0)	29.0 (6.8)	28.0 (6.1)
Race, n (%)			
White	48 (73.8)	48 (77.4)	33 (86.8)
Black	4 (6.2)	7 (11.3)	3 (7.9)
Asian	5 (7.7)	1 (1.6)	0 (0.0)
Ethnicity			
Hispanic, n (%)	2 (3.1)	1 (1.6)	0 (0.0)
Baseline eosinophil count (cells/μL), median (IQR)	310 (200-400)	425 (235-1005)	435 (255-848)
Baseline IgE (IU/mL), median (IQR)	144 (61-278)	182 (78-494)	146 (70-288)
Preindex annualized exacerbation rate, mean (SD)	1.8 (2.5)	2.6 (2.7)	2.7 (3.0)
Smoking status, n (%)			
Current	4 (6.2)	3 (4.8)	3 (7.9)
Former	16 (24.6)	9 (14.5)	5 (13.2)
Never	38 (58.5)	36 (58.1)	21 (55.3)
Unknown	7 (10.8)	14 (22.6)	9 (23.7)
Charlson comorbidity index, mean (SD)	1.2 (0.9)	1.3 (0.7)	1.3 (0.7)
Allergic rhinitis, n (%)	64 (98.5)	48 (77.4)	38 (100)

IQR, Interquartile range; *SD*, standard deviation.

J Allergy Clin Immunol Pract. 2022 Nov 13;S2213-2198(22)01193-X. doi: 10.1016/j.jaip.2022.10.047.

TABLE II. Frequency of switches and time to switch

Proportion of switches	Omalizumab	Mepolizumab	Mepolizumab patients eligible for omalizumab
	65	62	38
All-cause switch			
In first year, n (%)	7 (10.8)	6 (9.7)	3 (7.9)

J Allergy Clin Immunol Pract. 2022 Nov 13;S2213-2198(22)01193-X. doi: 10.1016/j.jaip.2022.10.047.

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In first year, n (%)	7 (10.8)	6 (9.7)	3 (7.9)
Over entire follow-up period, n (%)	12 (18.5)	24 (38.7)	14 (36.8)
Days to switch*, median (IQR)	300 (245-715)	669 (394-860)	774 (516-896)

J Allergy Clin Immunol Pract. 2022 Nov 13;S2213-2198(22)01193-X. doi: 10.1016/j.jaip.2022.10.047.

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Over entire follow-up period, n (%)	12 (18.5)	24 (38.7)	14 (36.8)
Days to switch*, median (IQR)	300 (245-715)	669 (394-860)	774 (516-896)
Effectiveness-related switches			
In first year, n (%)	6 (9.2)	4 (6.5)	2 (5.3)
Over entire follow-up period, n (%)	10 (15.4)	21 (33.9)	12 (31.6)
Days to switch*, median (IQR)	300 (258-618)	721 (460-871)	842 (620-906)

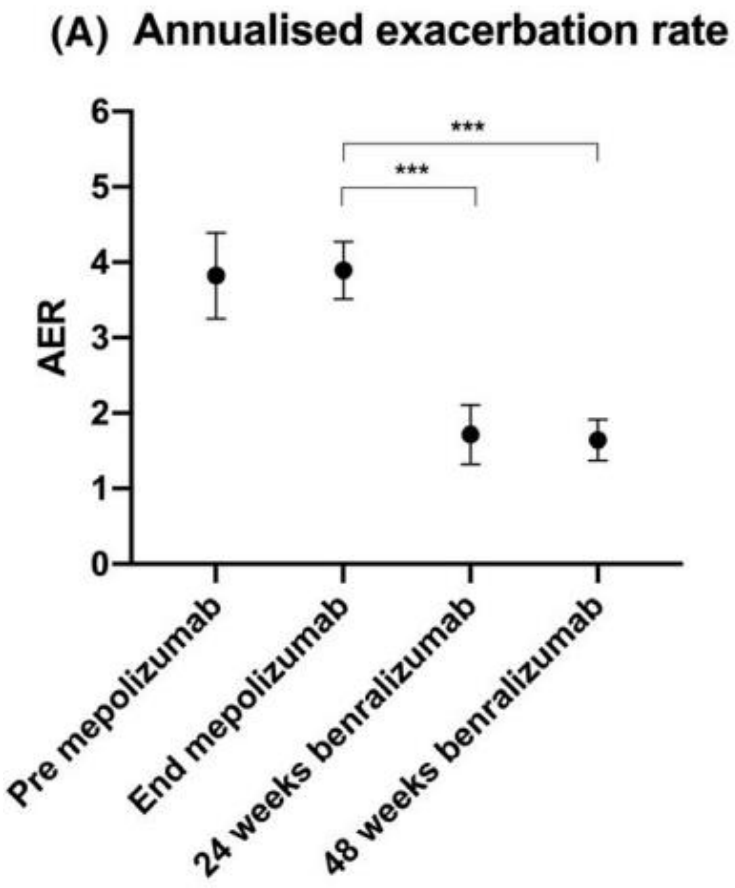
J Allergy Clin Immunol Pract. 2022 Nov 13;S2213-2198(22)01193-X. doi: 10.1016/j.jaip.2022.10.047.

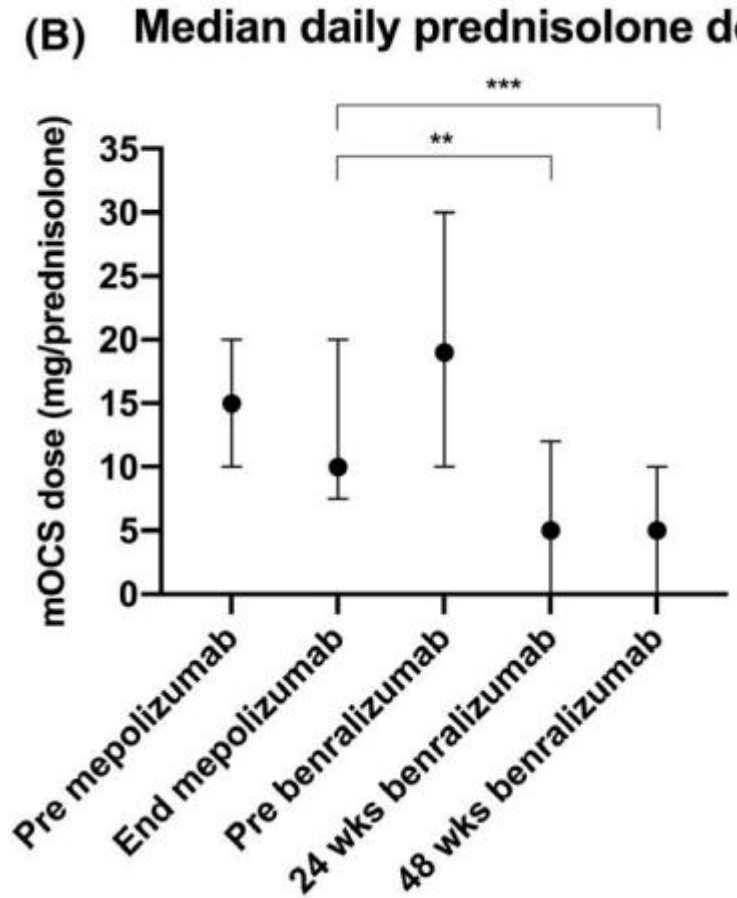
Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY EAACI

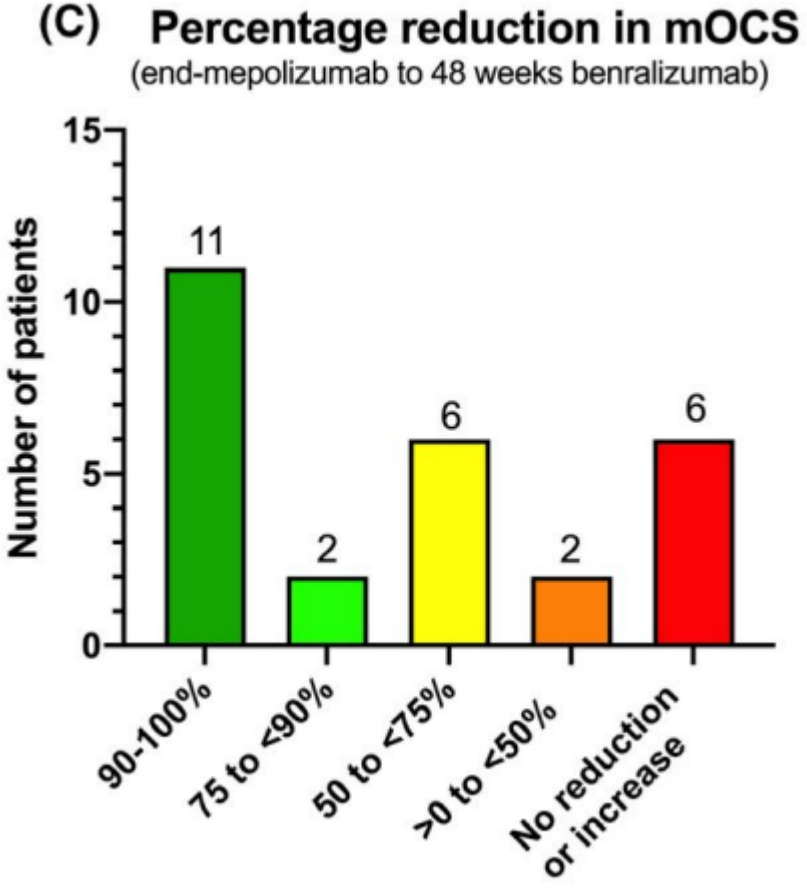
Benralizumab after sub-optimal response to mepolizumab in severe eosinophilic asthma

Machiko Matsumoto-Sasaki [1], Kaoruko Shimizu [1], Masanobu Suzuki [2], Masaru Suzuki [1], Yuji Nakamaru [2], Satoshi Konno [1]

Allergy. 2021 Jun;76(6):1890-1893.
doi: 10.1111/all.14693. Epub 2020 Dec 23.







3.89 (2.17) 1.64 (1.57)

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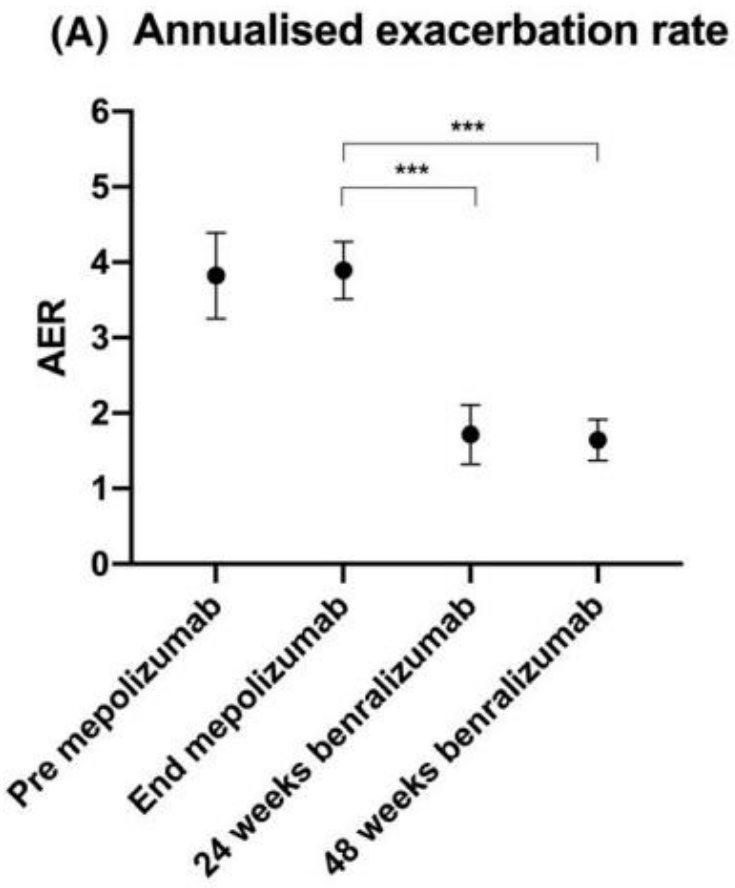

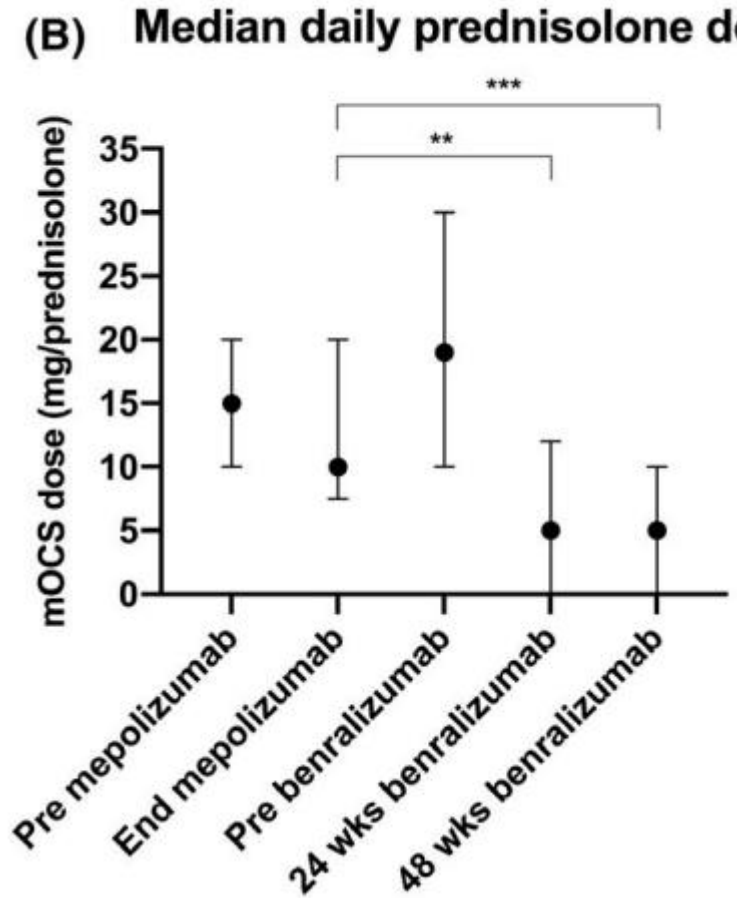

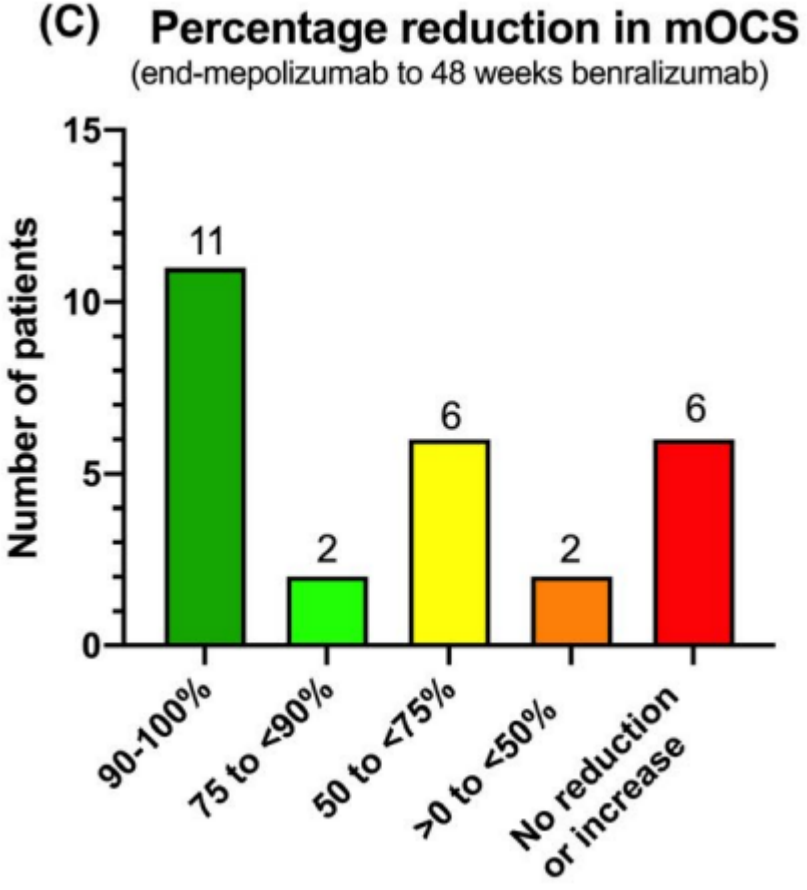

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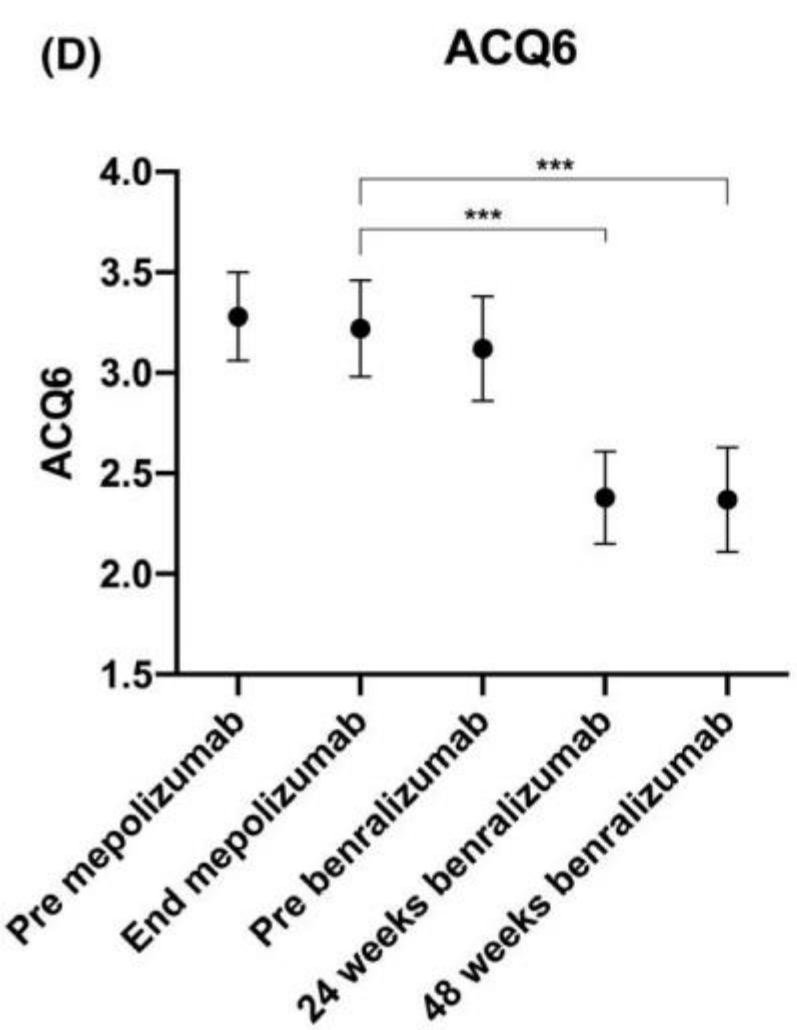
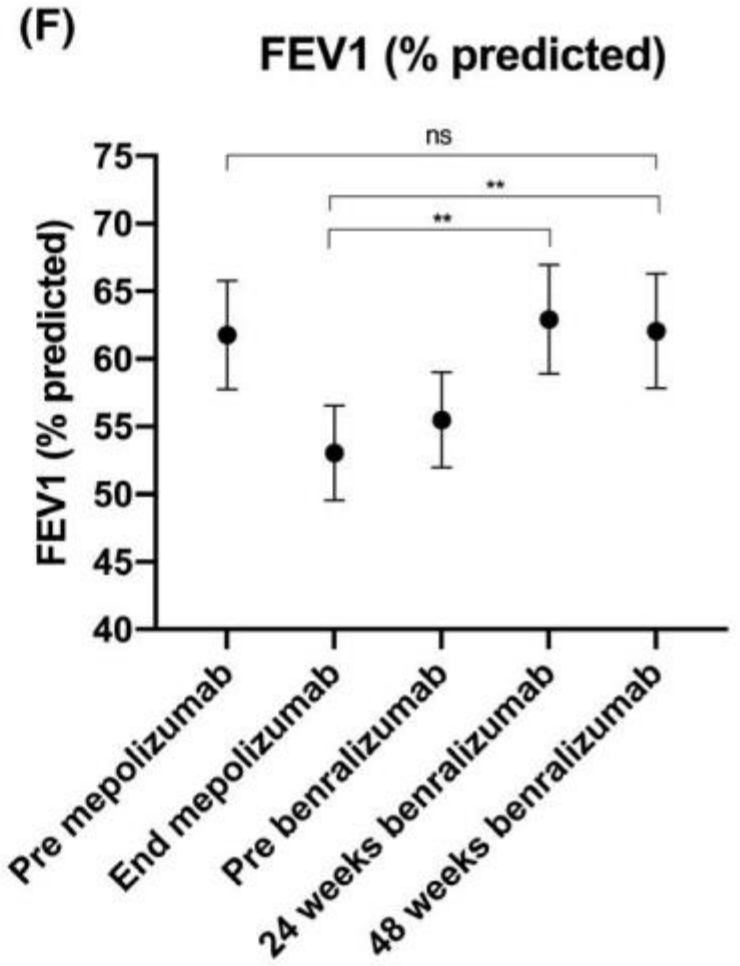




Allergy. 2021 Jun;76(6):1890-1893.
doi: 10.1111/all.14693. Epub 2020 Dec 23.

TABLE 1 Clinical outcome measures over time

	Baseline mepolizumab A	End of mepolizumab B	Baseline benralizumab C	48 weeks benralizumab D	Change B to D	*p* value A vs D	*p* value B vs D
Annualized exacerbation rate	3.82 (3.28)	3.89 (2.17)		1.64 (1.57)	−2.25	0.004	<0.001
On mOCS (number on ≥ 5 mg/day prednisolone)	26	26	26	14[a]	−12	0.120	0.090
Median mOCS dose (prednisolone, mg/day)	15.0 (10.0–20.0)	10 (7.5–20)	19.0 (10.0–30.0)	5.0 (0.0–10.0)	−5	0.001	<0.001
FEV1 (L)	1.72 (0.70)	1.51 (0.64)	1.58 (0.67)	1.78 (0.79)	0.27	0.474	0.008
FEV1 (% predicted)	61.78 (22.02)	53.05 (20.08)	55.48 (20.14)	62.06 (24.22)	9.01	0.747	0.007
Blood eosinophil count ($\times 10^9$)	0.20 (0.05–0.35)	0.00 (0.00–0.10)	0.10 (0.00–0.10)	0.00 (0.00–0.00)	0	<0.001	0.019
FeNO (ppb)	45 (30–84)	57 (33–81)	56 (27–77)	48 (29–83)	−9	0.636	0.221
ACQ-6	3.28 (1.24)	3.22 (1.36)	3.12 (1.52)	2.37 (1.51)	−0.85	<0.001	0.001
Mini-AQLQ	3.52 (1.28)	3.61 (1.48)	3.46 (1.44)	4.20 (1.59)	0.59	0.005	0.008

Allergy. 2021 Jun;76(6):1890-1893.
doi: 10.1111/all.14693. Epub 2020 Dec 23.

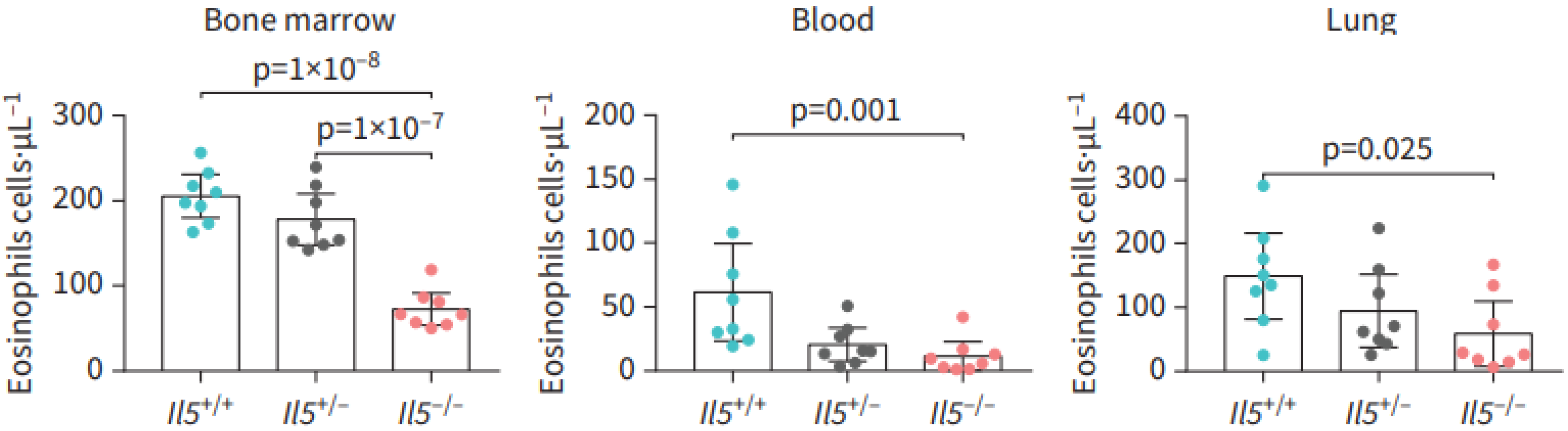
EUROPEAN RESPIRATORY JOURNAL
ORIGINAL RESEARCH ARTICLE
G. VAN HULST ET AL.

Anti-IL5 mepolizumab minimally influences residual blood eosinophils in severe asthma

Glenn Van Hulst [1,4], Joseph Jorssen[1,4], Nathalie Jacobs[1], Monique Henket[2], Renaud Louis[2], Florence Schleich[2], Fabrice Bureau[1,3,4] and Christophe J. Desmet [1,4]

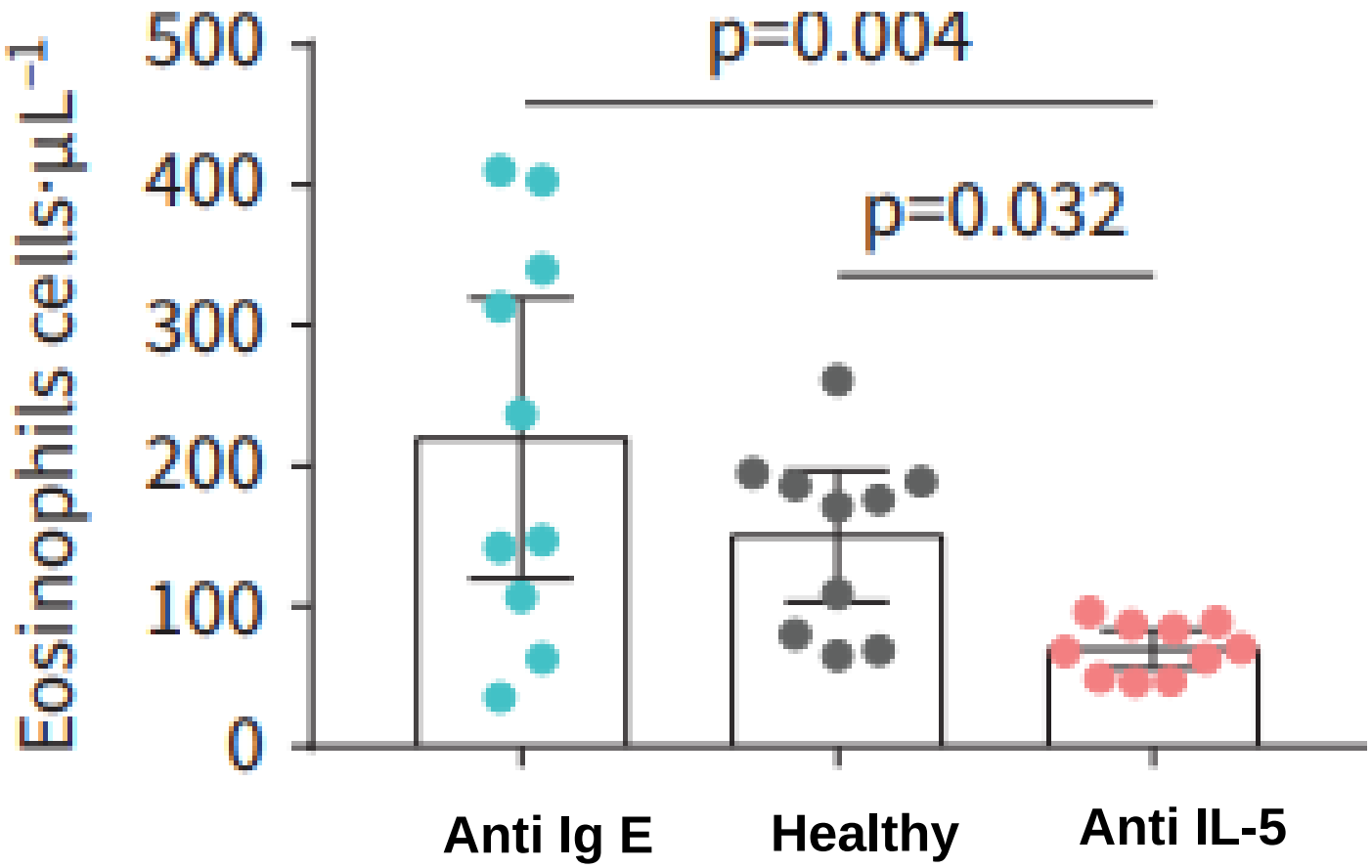
Eur Respir J 2022; 59: 2100935 [DOI: 10.1183/ 13993003.00935-2021]

Interleukin (*Il*)5-deficient mice



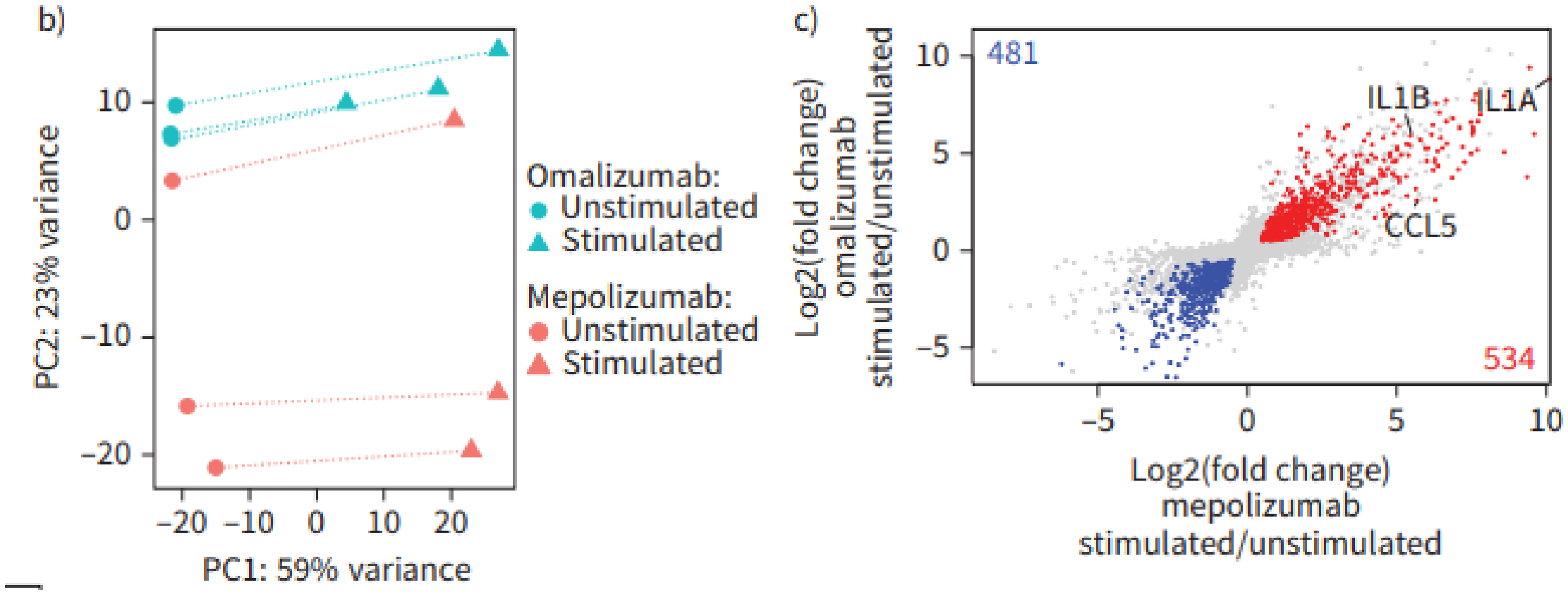
Eur Respir J 2022; 59: 2100935 [DOI: 10.1183/ 13993003.00935-2021]

Impact of mepolizumab on human blood eosinophils



Eur Respir J 2022; 59: 2100935 [DOI: 10.1183/ 13993003.00935-2021]

Transcriptomic response to stimulation of blood eosinophils from mepolizumab- or omalizumab-treated patient



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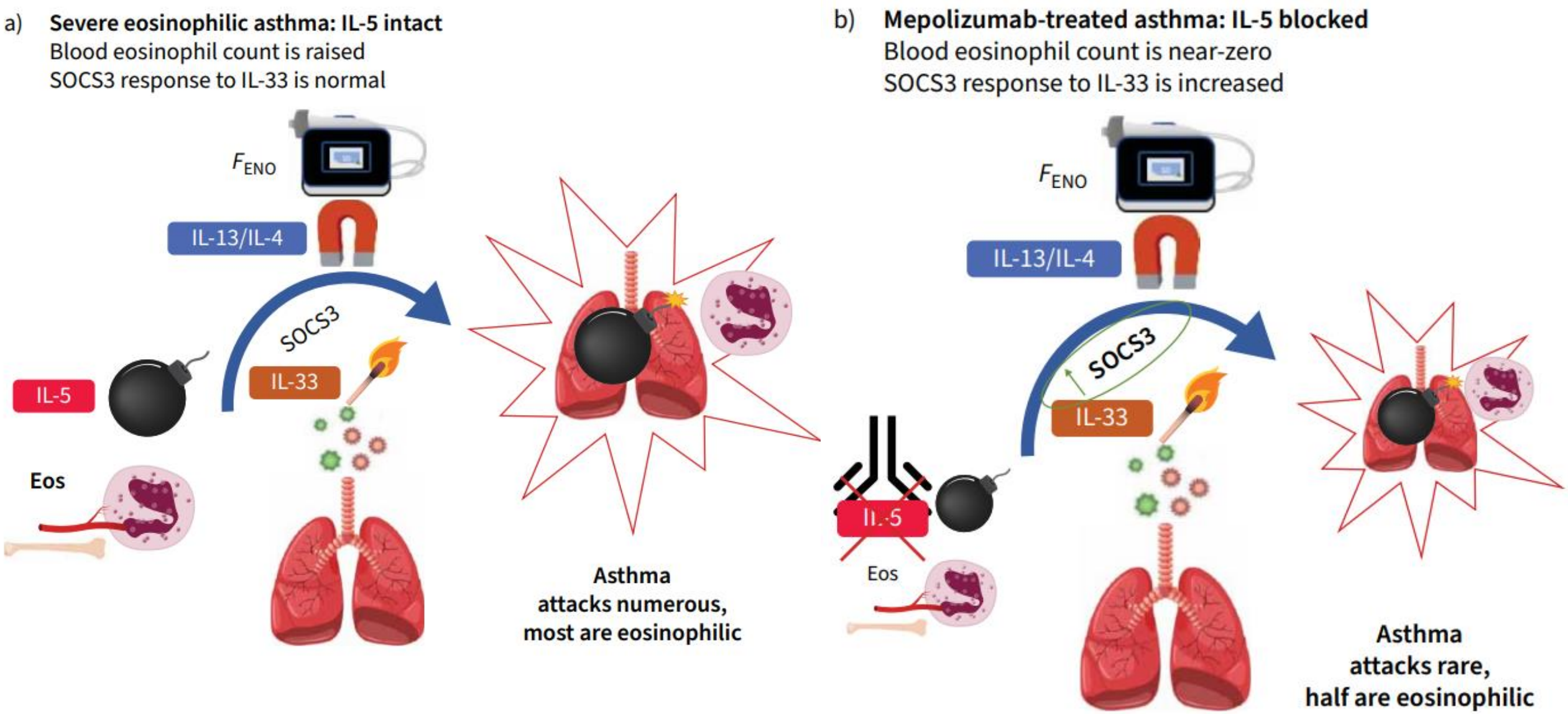


. Eur Respir J 2022; 60: 2200597 [DOI: 10.1183/13993003.00597-2022]

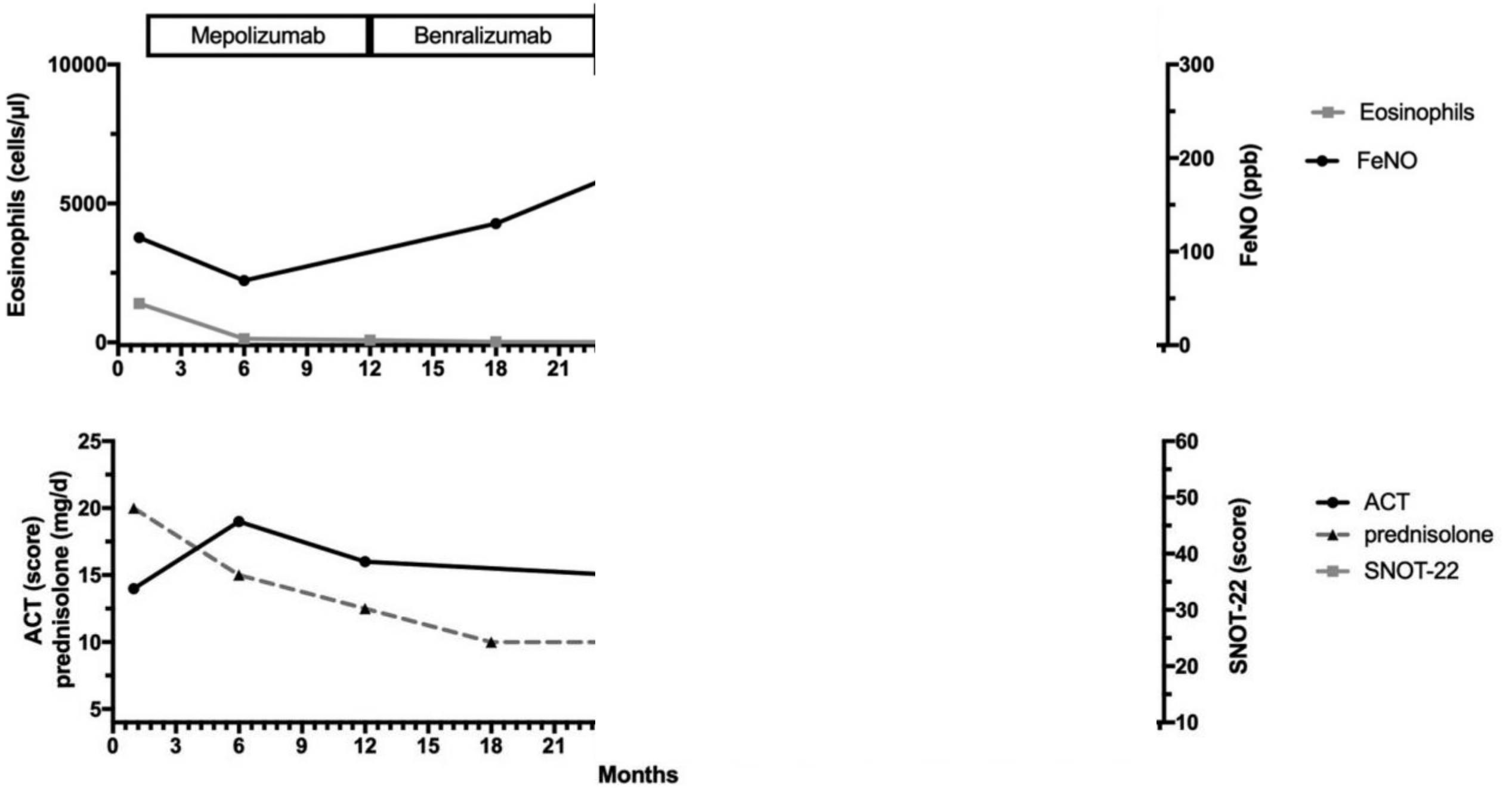
FULL TEXT ARTICLE

Hypereosinophilia with systemic manifestations under dupilumab and possibility of dual benralizumab and dupilumab therapy in patients with asthma and CRSwNP

Ignaz Briegel MD, Axelle Felicio-Briegel MD, Pontus Mertsch MD, Nikolaus Kneidinger MD, PhD, Frank Haubner MD and Katrin Milger MD

Journal of Allergy and Clinical Immunology: In Practice, 2021-12-01, Volume 9, Issue 12, Pages 4477-4479,

J Allergy Clin Immunol Pract. 2021 Dec;9(12):4477-4479.


Mepolizumab
Benralizumab
Eosinophils (cells/µl)
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FeNO (ppb)
300
200
100
0
Eosinophils
FeNO
ACT (score)
prednisolone (mg/d)
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20
15
10
5
0 3 6 9 12 15 18 21
Months
SNOT-22 (score)
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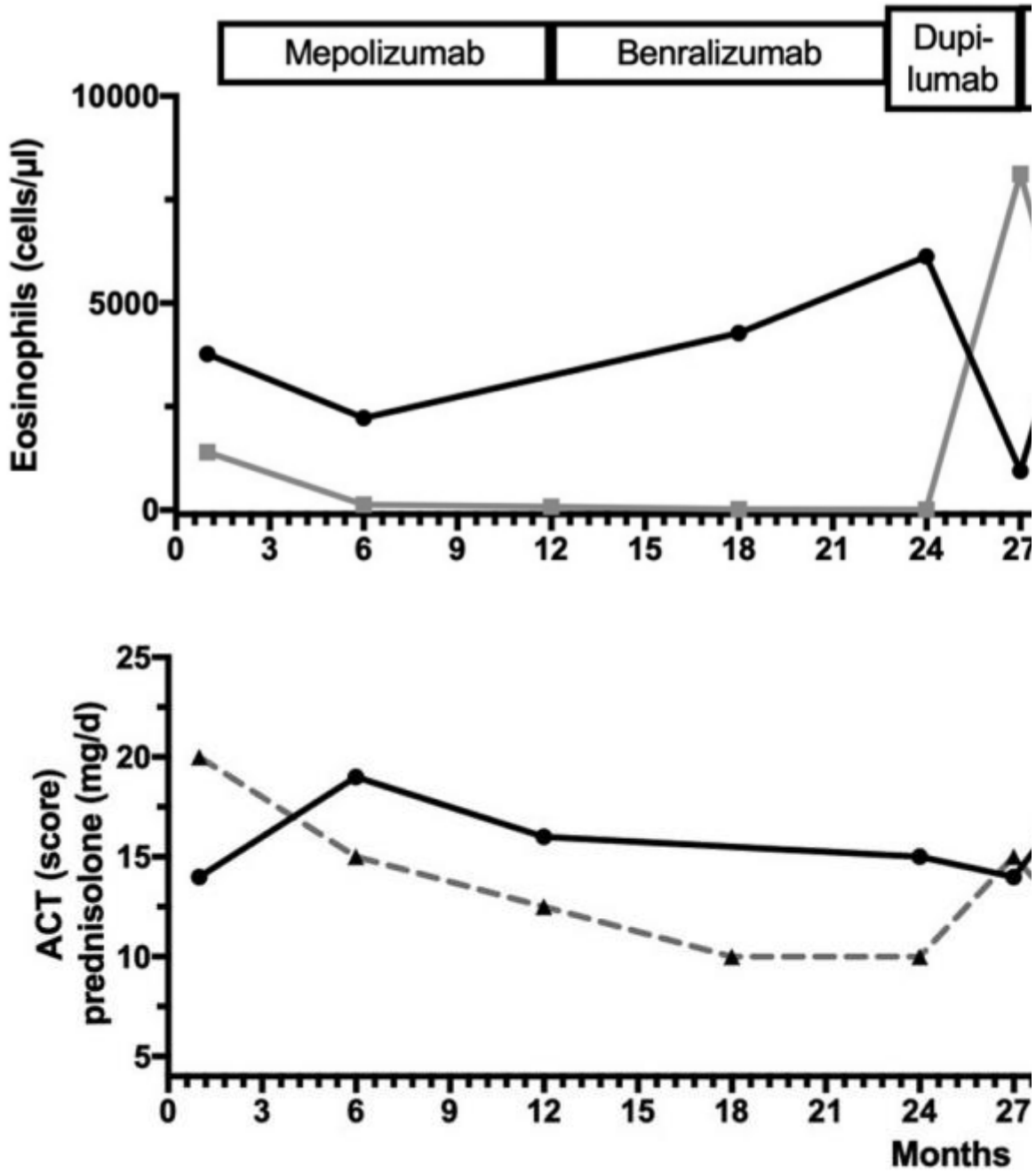
40
30
20
10
ACT
prednisolone
SNOT-22


Mepolizumab
Benralizumab
Dupi-
lumab
Eosinophils (cells/µl)
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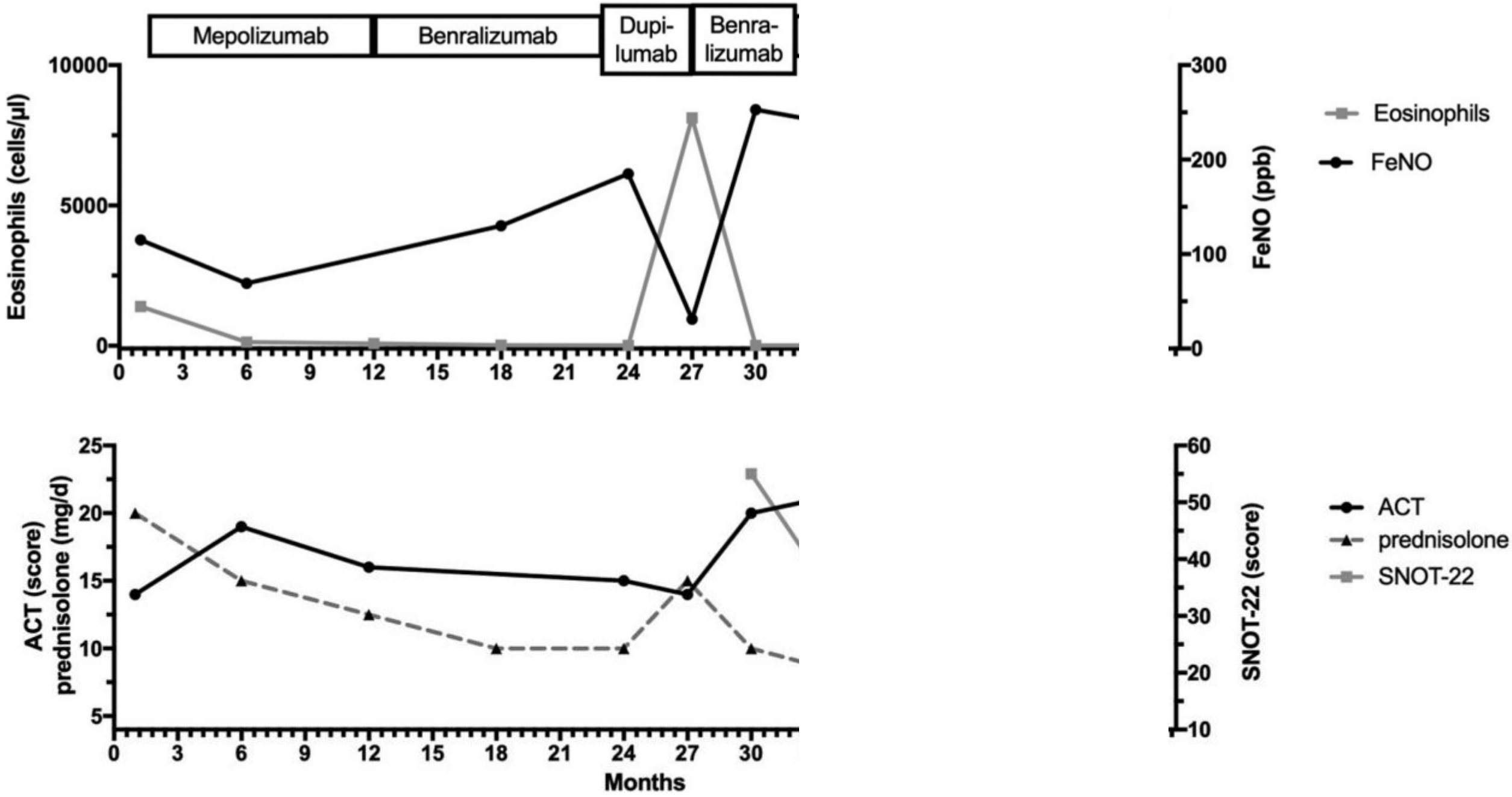
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Benralizumab
Dupi-lumab
Benra-lizumab
Eosinophils (cells/µl)
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Eosinophils
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ACT (score)
prednisolone (mg/d)
25
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Months
SNOT-22 (score)
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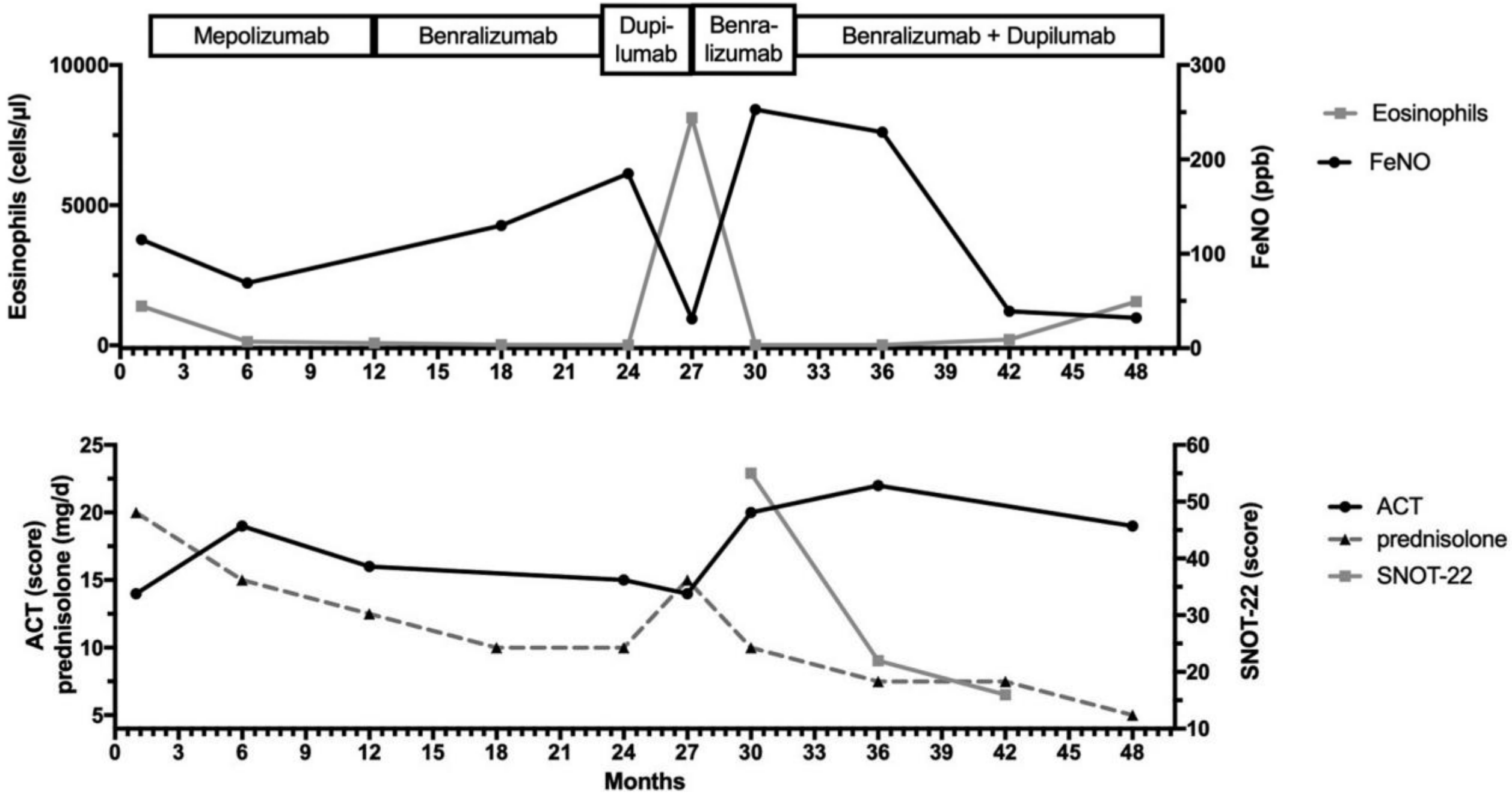
10
ACT
prednisolone
SNOT-22


Mepolizumab
Benralizumab
Dupi-
lumab
Benra-
lizumab
Benralizumab + Dupilumab
Eosinophils (cells/µl)
FeNO (ppb)
Eosinophils
FeNO
ACT (score)
prednisolone (mg/d)
SNOT-22 (score)
ACT
prednisolone
SNOT-22
Months

FULL TEXT ARTICLE

A case series of dual biologics therapy for severe asthma

Hana Serajeddini MD, FRCPC, Carmen Venegas Garrido MD, Anurag Bhalla MD, FRCPC, MSc, Melanie Kjarsgaard RRT, Chynna Huang RRT, Nicola LaVigne MLT, Katherine Radford MSc, Kayla Zhang BHSc, Terence Ho MD, FRCPC, MSc, Sarah Svenningsen PhD, Manali Mukherjee PhD and Parameswaran Nair MD, PhD, FRCP, FRCPC

Journal of Allergy and Clinical Immunology: In Practice, 2023-01-01, Volume 11, Issue 1, Pages 335-340.e2,

TABLE I. Participant demographics and clinical characteristics at baseline, after first biologic, and after second biologic

	All (n = 8)	N1	N2	N3	N4	N5	N6	N7	N8
Baseline characteristics									
Atopy, n (%)	7 (88)	Y	Y	Y	Y	Y	Y	N	Y
IgE (kU/L)*,†	262 (73-1925)	276	248	638	1925	81	591	73	160
Biologics									
First biologic	n/a	Benralizumab	Mepolizumab	Benralizumab	Dupilumab	Reslizumab	Mepolizumab	Benralizumab	Benralizumab
Second biologic	n/a	Dupilumab	Dupilumab	Dupilumab	Reslizumab	Dupilumab	Dupilumab	Dupilumab	Dupilumab
Duration first biologic (before second) (y)		2.5	4.7	1.8	1.7	2.9	0.8	0.8	2.2
Indication for second biologic (suboptimal control)		ACQ, OCS, FEV_1, CRS	ACQ, FEV_1, CRS, exacerbations	ACQ, CRS exacerbations,	OCS, FEV_1, exacerbations	OCS, FEV_1, exacerbations	ACQ, exacerbations	ACQ, exacerbations	ACQ, FEV_1, exacerbations

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IgE (kU/L)*,†	262 (73-1925)	276	248	638	1925	81	591	73	160
Biologics									
First biologic	n/a	Benralizumab	Mepolizumab	Benralizumab	Dupilumab	Reslizumab	Mepolizumab	Benralizumab	Benralizumab
Second biologic	n/a	Dupilumab	Dupilumab	Dupilumab	Reslizumab	Dupilumab	Dupilumab	Dupilumab	Dupilumab
Duration first biologic (before second) (y)		2.5	4.7	1.8	1.7	2.9	0.8	0.8	2.2
Indication for second biologic (suboptimal control)		ACQ, OCS, FEV_1, CRS	ACQ, FEV_1, CRS, exacerbations	ACQ, CRS exacerbations,	OCS, FEV_1, exacerbations	OCS, FEV_1, exacerbations	ACQ, exacerbations	ACQ, exacerbations	ACQ, FEV_1, exacerbations
ACQ‡									
Baseline	3.1 ± 1	3.2	3	3	3.6	1	4	1.8	5
After first biologic	2.4 ± 1	3	2.2	2.4	0.8	1	4.8	1.8	3.2
After second biologic	0.9 ± 1	0.5	1	0	0.8	0	1.8	0	2.8
OCS dose (mg/d)*									
Baseline	8.75 (5-30)	25	10	5	7.5	5	30	10	15
After first biologic	1.25 (0-20)	10	0	0	2.5	0	20	3	0
After second	0 (0-7.5)	5	0	0	0	0	7.5	0	0
Exacerbations /y (moderate-to- severe)									
Baseline		3	4	4	3	5	3	10	5
After first biologic		0	3	3	1	3	2	8	3
After second biologic		0	0	0	0	0	0	0	0
Sinus uncontrolled, n (%)									
Baseline	7 (88)	Y	Y	Y	N	Y	N	Y	Y
After first biologic		Y	Y	Y	N	Y	N	Y	Y
After second biologic		N	Y	N	Y	N	N	N	N

TABLE I. Participant demographics and clinical characteristics at baseline, after first biologic, and after second biologic

	All (n = 8)	N1	N2	N3	N4	N5	N6	N7	N8
Baseline characteristics									
Atopy, n (%)	7 (88)	Y	Y	Y	Y	Y	Y	N	Y
IgE (kU/L)*,†	262 (73-1925)	276	248	638	1925	81	591	73	160
Biologics									
First biologic	n/a	Benralizumab	Mepolizumab	Benralizumab	Dupilumab	Reslizumab	Mepolizumab	Benralizumab	Benralizumab
Second biologic	n/a	Dupilumab	Dupilumab	Dupilumab	Reslizumab	Dupilumab	Dupilumab	Dupilumab	Dupilumab
Duration first biologic (before second) (y)		2.5	4.7	1.8	1.7	2.9	0.8	0.8	2.2
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ACQ‡									
Baseline	3.1 ± 1	3.2	3	3	3.6	1	4	1.8	5
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After second	0 (0-7.5)	5	0	0	0	0	7.5	0	0
Exacerbations /y (moderate-to- severe)									
Baseline		3	4	4	3	5	3	10	5
After first biologic		0	3	3	1	3	2	8	3
After second biologic		0	0	0	0	0	0	0	0
Sinus uncontrolled, n (%)									
Baseline	7 (88)	Y	Y	Y	N	Y	N	Y	Y
After first biologic		Y	Y	Y	N	Y	N	Y	Y
After second biologic		N	Y	N	Y	N	N	N	N

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Exacerbations /y (moderate-to- severe)									
Baseline		3	4	4	3	5	3	10	5
After first biologic		0	3	3	1	3	2	8	3
After second biologic		0	0	0	0	0	0	0	0
Sinus uncontrolled, n (%)									
Baseline	7 (88)	Y	Y	Y	N	Y	N	Y	Y
After first biologic		Y	Y	Y	N	Y	N	Y	Y
After second biologic		N	Y	N	Y	N	N	N	N

TABLE I. Participant demographics and clinical characteristics at baseline, after first biologic, and after second biologic

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Duration first biologic (before second) (y)		2.5	4.7	1.8	1.7	2.9	0.8	0.8	2.2
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Exacerbations /y (moderate-to- severe)									
Baseline		3	4	4	3	5	3	10	5
After first biologic		0	3	3	1	3	2	8	3
After second biologic		0	0	0	0	0	0	0	0
Sinus uncontrolled, n (%)									
Baseline	7 (88)	Y	Y	Y	N	Y	N	Y	Y
After first biologic		Y	Y	Y	N	Y	N	Y	Y
After second biologic		N	Y	N	Y	N	N	N	N

Clinical Associations of Mucus Plugging in Moderate to Severe Asthma

TABLE II. Odds ratios (ORs) (95% CIs) for spirometry, type 2 biomarkers, and exacerbations in association with the presence of mucus plugging score of ≥1 using logistic regression modeling adjusted for confounding variables

	Mucus plug	
Clinical feature	**Crude OR (95% CI)**	**Adjusted OR (95% CI)**
FEV_1 (44%)	3.06 (1.46-6.41)†	2.45 (0.95-6.31)
Forced expiratory flow at 25% to 75% of FVC (68%)	5.18 (2.27-11.83)‡	2.64 (0.92-7.55)
FEV_1/FVC (51%)	4.02 (1.91-8.45)‡	3.01 (1.14-7.97)*
Exacerbations (61%)	4.58 (2.03-10.31)‡	5.00 (1.55, 16.11)†
Peripheral blood eosinophils (62%)	2.95 (1.37-6.37)†	3.23 (1.16-8.96)*
FeNO (48%)	2.30 (1.01-5.27)*	2.09 (0.66-6.56)
Total IgE (57%)	2.73 (1.29-5.80)†	3.20 (1.09-9.37)*
Aspergillus fumigatus IgE (22%)	3.91 (1.35-11.33)*	9.37 (1.82-48.20)†
A fumigatus IgG (12%)	1.42 (0.45-4.54)	1.99 (0.45-8.79)

J Allergy Clin Immunol Pract 2023;11:195-9

CHEST

Asthma Control, Airway Mucus, and ^{129}Xe MRI Ventilation After a Single Benralizumab Dose

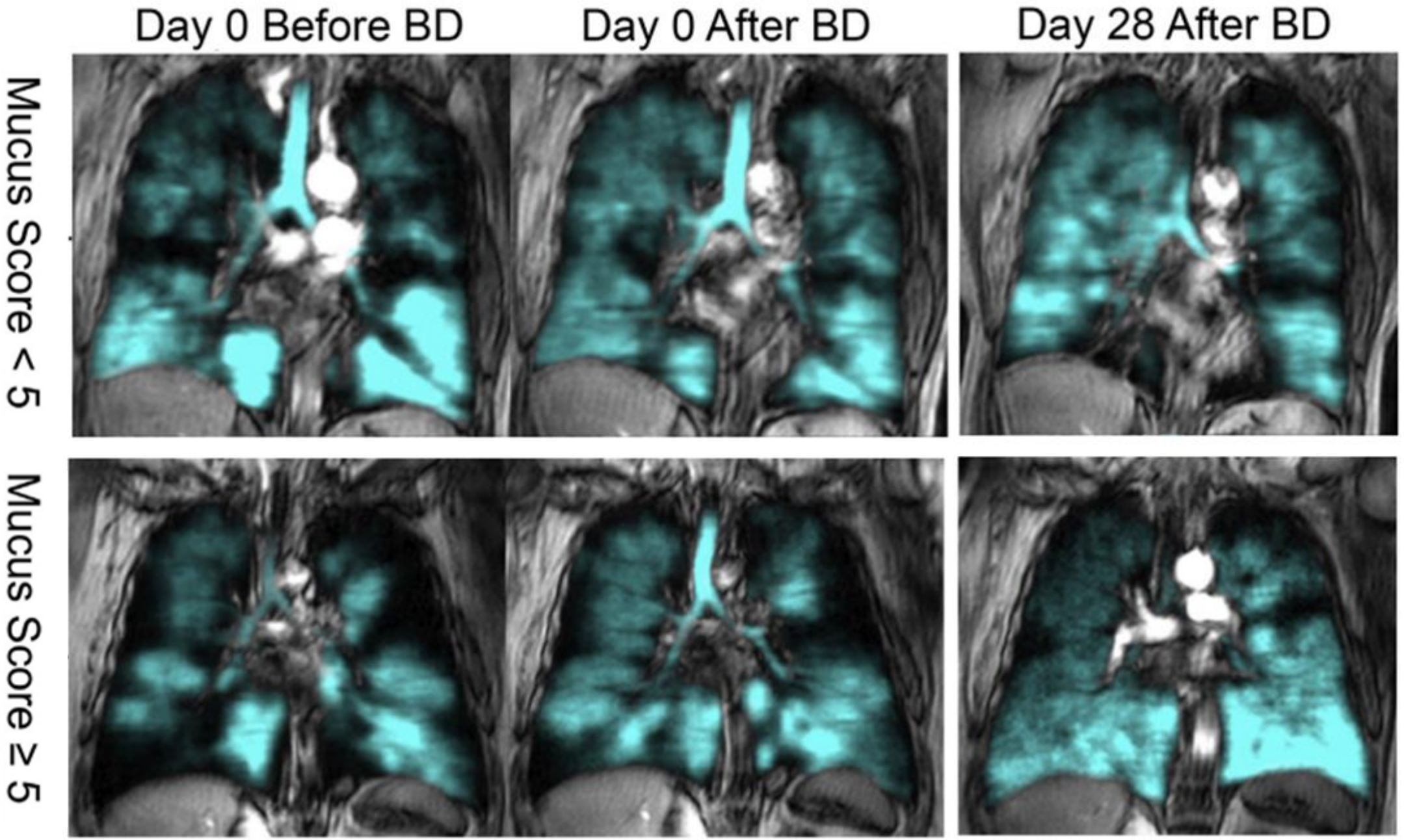
Marrissa J. McIntosh, BSc; Harkiran K. Kooner, BSc; Rachel L. Eddy, PhD; Samira Jeimy, MD; Christopher Licskai, MD; Constance A. Mackenzie, MD; Sarah Svenningsen, PhD; Parameswaran Nair, MD, PhD; Cory Yamashita, MD; and Grace Parraga, PhD

Chest. 2022 Sep;162(3):520-533.
doi: 10.1016/j.chest.2022.03.003.

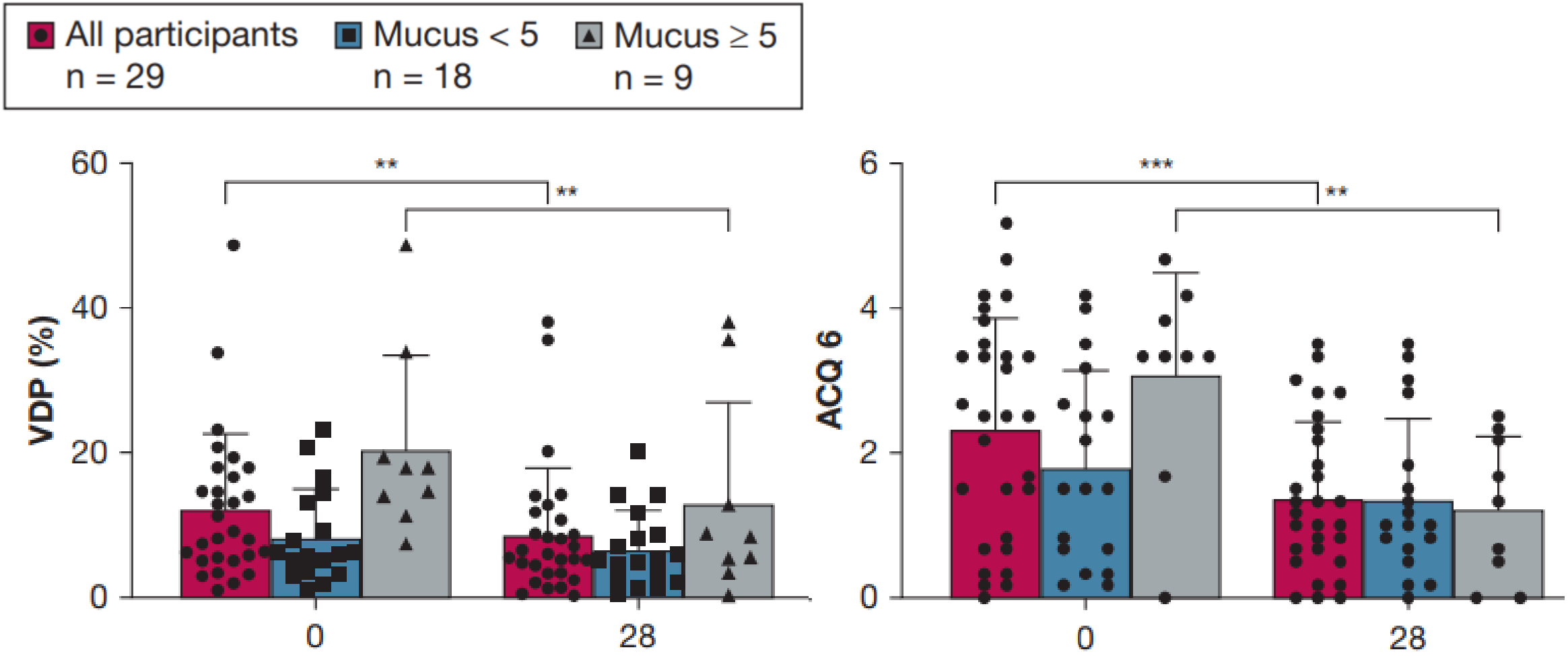
TABLE 1] Baseline Demographic Characteristics

Characteristic	All Participants (n = 29)	Mucus Plug Score < 5 (n = 18)	Mucus Plug Score ≥ 5 (n = 9)	*P* Value
Age, y	59 ± 12	62 ± 8	55 ± 17	—
Female sex	16 (69)	11 (61)	5 (55)	—
BMI, kg/m^2	29 ± 5	30 ± 6	27 ± 3	—
Inflammatory markers				
Eos, cells/μL	630 ± 380	520 ± 270	920 ± 420	.04
FENO, ppb	48 ± 35[a]	51 ± 37	45 ± 34[b]	1.0
CT imaging findings[a]				
TAC	140 ± 50	130 ± 23	160 ± 80	.9
Mucus plug score	5 ± 9	1 ± 2	13 ± 11	—
MRI findings				
VDP before bronchodilator	17 ± 10	13 ± 7	25 ± 11	.008
VDP after bronchodilator	12 ± 10	8 ± 7	21 ± 13	.02

CHEST 2022; 162(3):520-533



Chest. 2022 Sep;162(3):520-533. doi: 10.1016/j.chest.2022.03.003.



Chest. 2022 Sep;162(3):520-533.
doi: 10.1016/j.chest.2022.03.003.

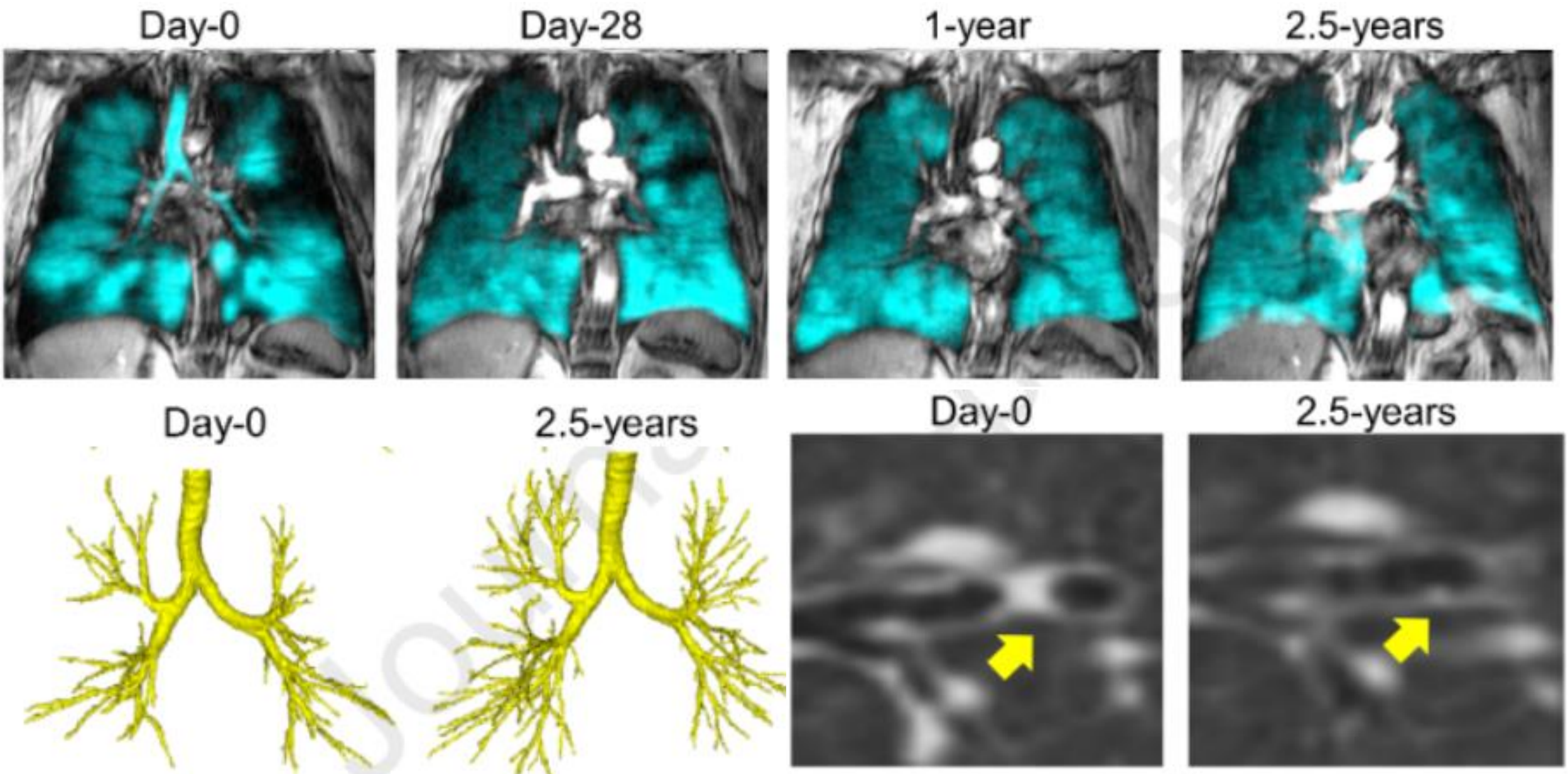
CT Mucus Score and 129Xe MRI Ventilation Defects after 2.5-years anti-IL-5Rα in Eosinophilic Asthma

Marrissa J McIntosh [1], Harkiran K Kooner [1], Rachel L Eddy [2], Angela Wilson [3], Hana Serajeddini [4], Anurag Bhalla [5], Christopher Licskai [5], Constance A Mackenzie [6], Cory Yamashita [5], Grace Parraga [7]

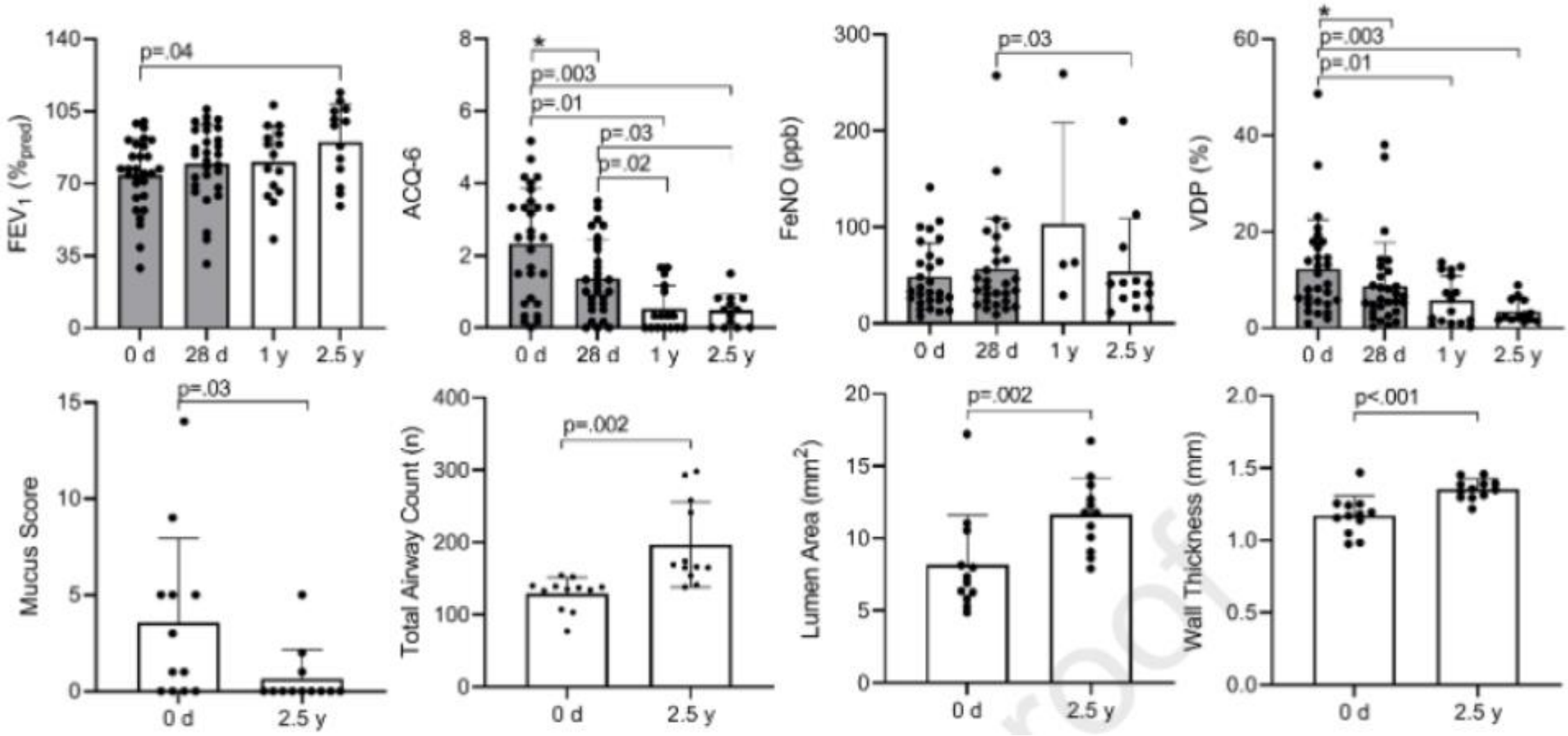
Affiliations + expand

PMID: 36781102 DOI: 10.1016/j.chest.2023.02.009

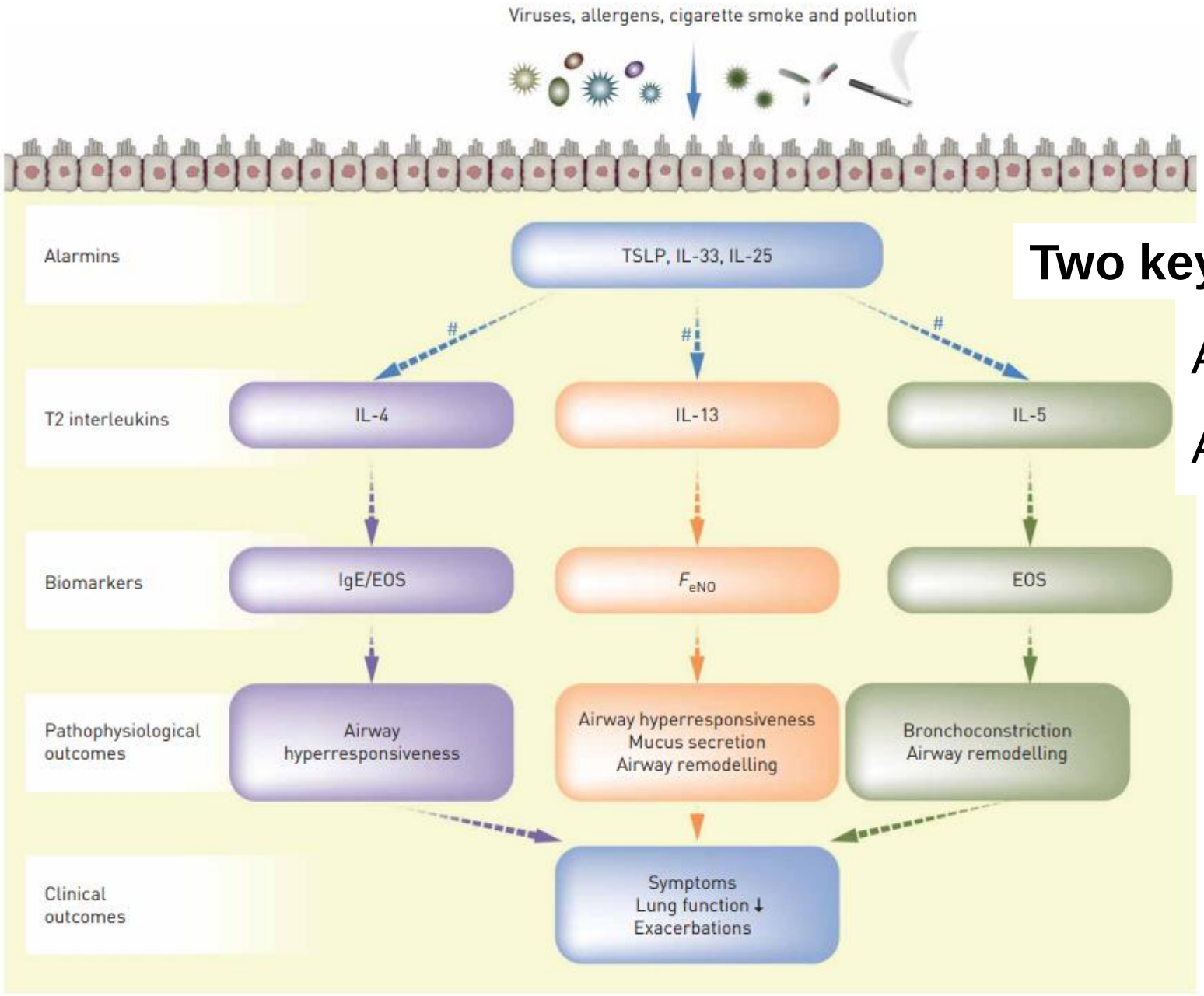
Chest. 2023 Feb 11;S0012-3692(23)00189-7.
Doi: 10.1016/j.chest.2023.02.009.



Chest. 2023 Feb 11;S0012-3692(23)00189-7.
Doi: 10.1016/j.chest.2023.02.009.



Chest. 2023 Feb 11;S0012-3692(23)00189-7.
Doi: 10.1016/j.chest.2023.02.009.



Two key defining features of asthma

Airway inflammation

Airway hyperresposiveness

Eur Respir J 2020; 56: 2000260
[https://doi.org/10.1183/ 13993003.00260-2020]

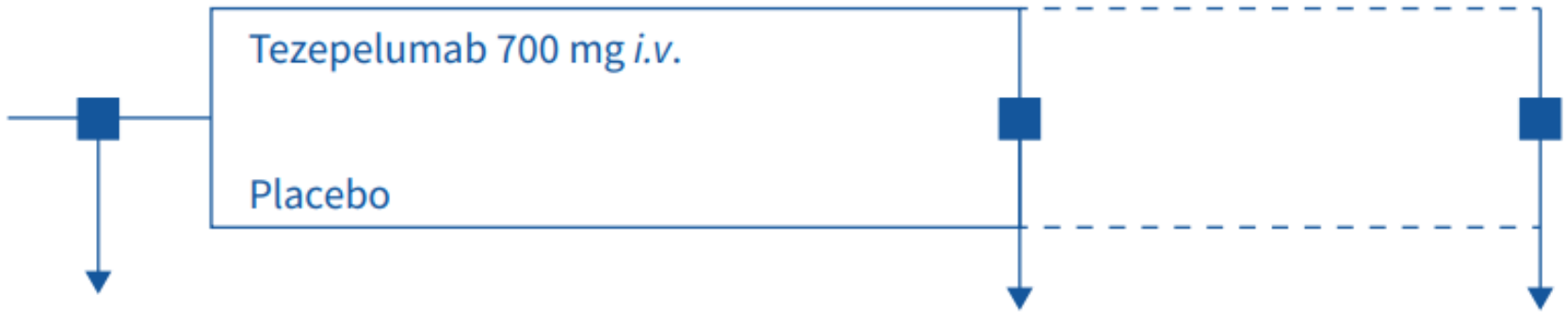
EUROPEAN RESPIRATORY JOURNAL
ORIGINAL RESEARCH ARTICLE
A. SVERRILD ET AL.

The effect of tezepelumab on airway hyperresponsiveness to mannitol in asthma (UPSTREAM)

Asger Sverrild[1], Susanne Hansen[1,2], Morten Hvidtfeldt[1], Carl-Magnus Clausson[3], Olga Cozzolino[3], Samuel Cerps[3], Lena Uller[3], Vibeke Backer[4], Jonas Erjefält[3] and Celeste Porsbjerg[1]

Eur Respir J 2022; 59: 2101296
[DOI: 10.1183/ 13993003.01296-2021]

Week	−2	0	4	8	12	21
Visit	1/2	3	4	5	6/7	8
IP dose		1st dose	2nd dose	3rd dose		



Baseline
- AHR to mannitol
- Lung function
- F_{ENO}
- Skin prick test
- Blood samples
- Sputum count
- ACQ, AQLQ

Bronchoscopy

Week 12
- AHR to mannitol
- Lung function
- F_{ENO}
- Skin prick test
- Blood samples
- Sputum count
- ACQ, AQLQ

Bronchoscopy

Follow-up
- AHR to mannitol
- Lung function
- F_{ENO}
- Blood samples
- ACQ, AQLQ

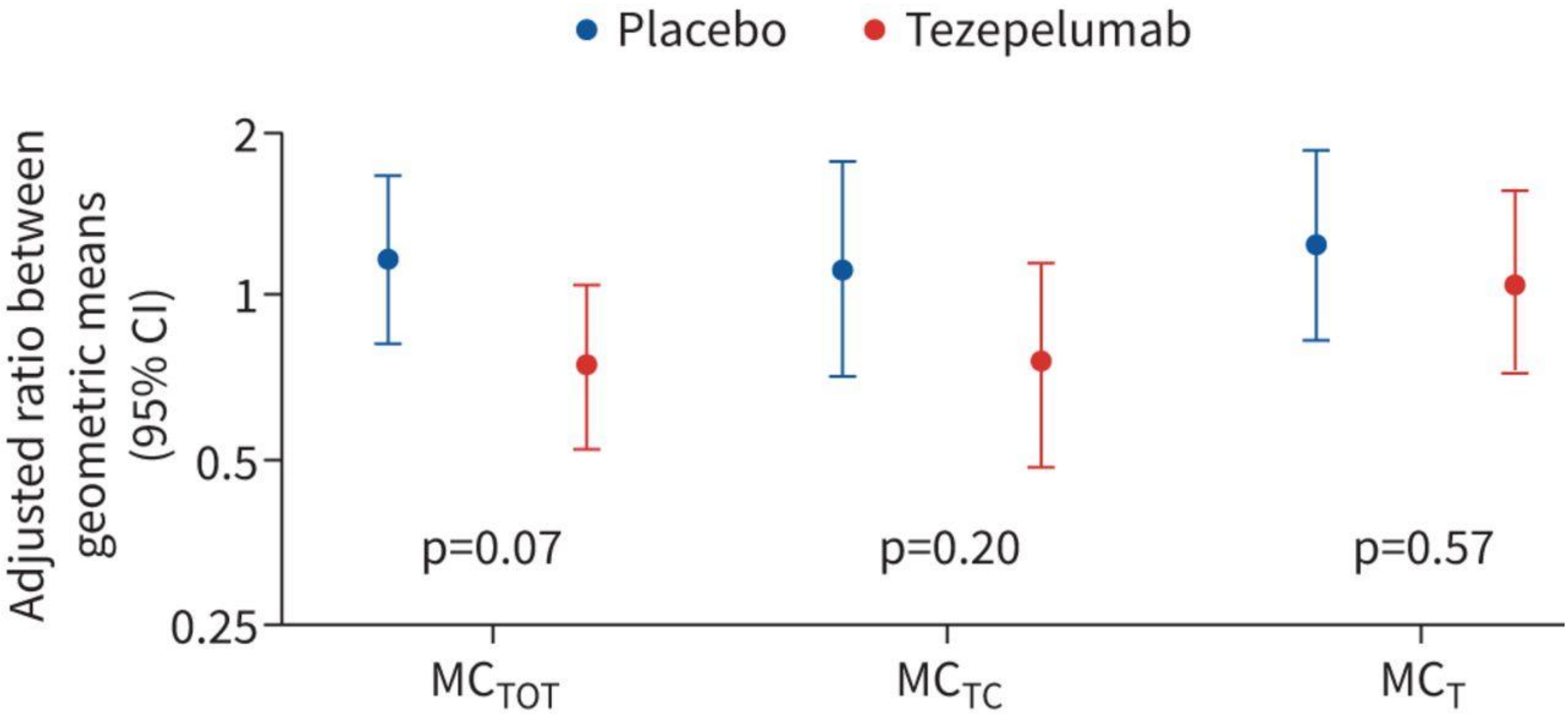

Placebo
Tezepelumab
Adjusted ratio between geometric means (95% CI)
2
1
0.5
0.25
p=0.07
p=0.20
p=0.57
MC_TOT
MC_TC
MC_T

TABLE 2 Change in airway hyperresponsiveness from baseline to week 12

	Overall		Eosinophil high[#]		Eosinophil low[¶]	
	Placebo (n=20)	Tezepelumab (n=20)	Placebo (n=13)	Tezepelumab (n=10)	Placebo (n=7)	Tezepelumab (n=10)
PD_{15}[+]						
Baseline, mg geometric mean (range)	69.5 (4.0–297.2)	134.7 (23.4–278.7)	71.0 (10.4–286.6)	121.1 (23.4–278.7)	66.9 (4.0–297.2)	149.9 (67.6–195.7)
Adjusted mean change (DD) from baseline to week 12 (95% CI)	1.0 (0.3–1.6)	1.9 (1.2–2.5)	0.8 (0.02–1.7)	1.9 (0.9–2.8)	1.1 (−0.03–2.2)	1.8 (0.9–2.7)
Treatment difference (DD) compared with placebo (95% CI)		0.9 (0.0–1.9)		1.0 (−0.2–2.3)		0.7 (−0.8–2.2)
p-value		0.06		0.10		0.35
Test negatives						
Test negative at week 12, n (%)	3 (15)	9 (45)				
p-value for comparison with placebo		0.04				

PD_{15}: provoking dose of inhaled mannitol causing a 15% reduction in forced expiratory volume in 1 s; DD: doubling doses. [#]: blood eosinophils $\geqslant 0.25\times10^9$ L^{-1} and/or sputum eosinophils ⩾3%; [¶]: blood eosinophils $<0.25\times10^9$ L^{-1} and sputum eosinophils <3%; [+]: model adjusted for baseline value of $\log_2 PD_{15}$ and baseline inhaled corticosteroid use (high/low). Multiple imputation used for missing data at visit 6 (n=1).

Eosinophil depletion with benralizumab is associated with attenuated mannitol airway hyperresponsiveness in severe uncontrolled eosinophilic asthma

Rory Chan, MBChB, Chris RuiWen Kuo, MBChB, Sunny Jabbal, MD, and Brian J. Lipworth, MD *Dundee, United Kingdom*

J Allergy Clin Immunol. 2022 Nov 16;S0091-6749(22)01510-X.
doi: 10.1016/j.jaci.2022.10.028.

TABLE I. Mean values for mannitol PD_{10}, RDR, spirometry, oscillometry, ACQ, mini-AQLQ, and type 2 biomarkers at weeks 0, 2, 4, 8, 12, and 24

Characteristic	Baseline (after run-in)	Week 2	Week 4	Week 8	Week 12 (after benralizumab)	Geometric mean fold difference (CI) at week 12	Week 24
Mannitol PD_{10} (mg)	67	142	157	185*	266**	4.0 (1.9, 8.3)	169*
Mannitol RDR (%/mg)	0.1418	0.0679	0.0630	0.0490*	0.0345**	0.2 (0.1, 0.5)	0.0435*

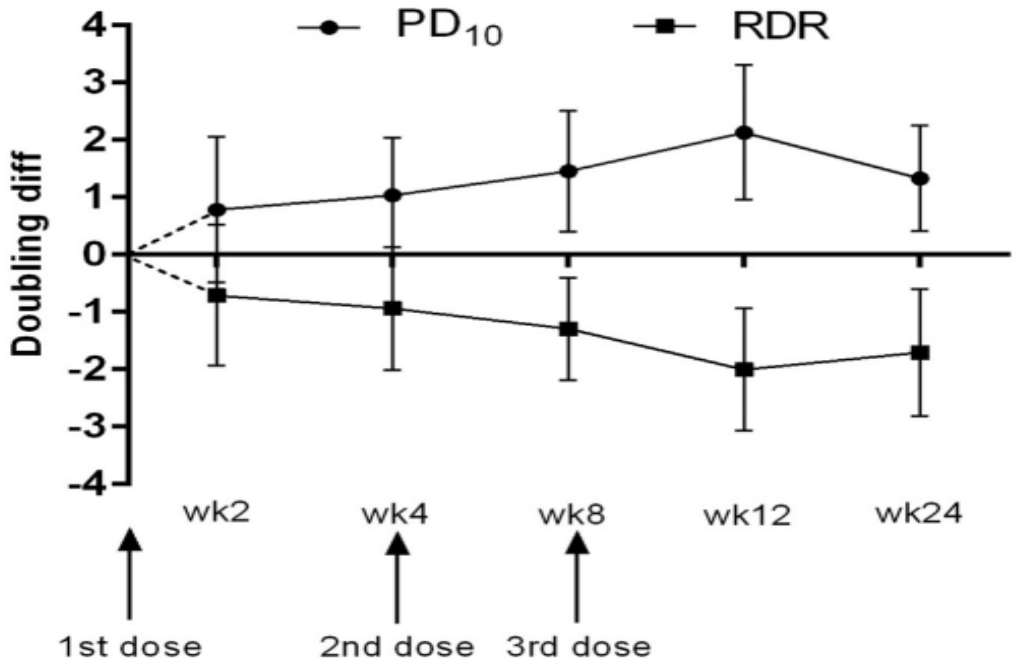


FIG 1. Mean (95% CI) DD for PD_{10} and RDR at serial time points after benralizumab therapy.

J Allergy Clin Immunol. 2022 Nov 16;S0091-6749(22)01510-X.
doi: 10.1016/j.jaci.2022.10.028.

TABLE II. Mean PEF rate, patient subjective symptoms, and relief therapy in the 7 days before each respective visit

Characteristic	Baseline	Week 2	Week 4	Week 8	Week 12	Mean difference (95% CI) at week 12	Week 24
PEF (L/min)	357	388*	400**	398**	404**	48 (21, 74)	404*
Symptoms	1.7	1.3*	1.3**	1.1***	1.0****	−0.7 (−0.9, −0.5)	0.9***
Relief therapy	3	2*	2*	1**	1*	−2 (−3, −0)	2*

Bonferroni-corrected *P* values versus baseline: **P* < .05, ***P* < .01, ****P* < .001, *****P* < .0001.

J Allergy Clin Immunol. 2022 Nov 16;S0091-6749(22)01510-X.
doi: 10.1016/j.jaci.2022.10.028.

EUROPEAN RESPIRATORY JOURNAL
ORIGINAL RESEARCH ARTICLE
P.J. MCDOWELL ET AL.

Glucocorticoid toxicity reduction with mepolizumab using the Glucocorticoid Toxicity Index

P. Jane McDowell [1], John H. Stone[2], Yuqing Zhang[2], Kirsty Honeyford[3], Louise Dunn[3], R. Jayne Logan[3], Lorcan P.A. McGarvey[1], Claire A. Butler[3] and Liam G. Heaney[1]

Glucocorticoid Toxicity Index

Toxicity domain		Points	Number (%)
Body mass index (BMI)	BMI <27	0	31 (30.7)
	BMI ≥27 but <30	21	15 (14.9)
	BMI ≥30	36	55 (54.5)
Glucose metabolism	HgbA1c <5.7	0	35 (34.7)
	HgbA1c <5.7 but on medication	32	53 (52.5)
	HgbA1c ≥5.7	32	
	HgbA1c ≥5.7 and on medication	44	13 (12.9)
	Diabetic retinopathy, nephropathy, or neuropathy (count only one)	44	
Blood pressure	Normotensive: systolic ≤120 and diastolic ≤85 no medications	0	33 (32.7)
	Systolic ≤120 and diastolic ≤85 but on medications	19	51 (50.5)
	Systolic >120 or diastolic >85 on no medications	19	
	Systolic >120 or diastolic >85 and on medications	44	17 (16.8)
	Hypertensive emergency or PRES (count only one)	44	
Lipid metabolism	LDL ≤ target	0	43 (42.6)
	LDL ≤ target but on medications	10	51 (50.5)
	LDL > target on no medications	10	
	LDL > target on treatment	30	7 (6.9)
Bone/tendon	Normal BMD or no known history of osteoporosis		94 (93.1)
	Osteoporosis	29	7 (6.9)
	Insufficiency fracture secondary to osteoporosis	29	
	Osteonecrosis	29	
	Tendon rupture while on corticosteroids	29	
Glucocorticoid myopathy	No myopathy	0	95 (94.1)
	Minor GC myopathy	11	2 (2)
	Moderate GC myopathy	63	4 (4)
	Severe GC myopathy	63	

J Allergy Clin Immunol Pract 2021;9:365-72

Glucocorticoid Toxicity Index

Toxicity domain		Points	Number (%)
Skin	No skin toxicity	0	21 (20.8)
	*Minor skin toxicity (1 or more than 1 minor skin item)	8	50 (49.5)
	*Moderate skin toxicity (1 or more than 1 moderate skin item)	26	30 (29.7)
	*Severe skin toxicity (1 or more than 1 moderate skin item)	26	
	*Select only 1 (minor, moderate, or severe)		
Neuropsychiatric	No neuropsychiatric toxicity	0	19 (18.8)
	*Minor (1 or more than 1 minor NP item: insomnia, mania, depression, cognitive)	11	16 (15.8)
	*Moderate (1 or more than 1 moderate NP item: insomnia, mania, depression, cognitive)	74	66 (65.3)
	*Severe (1 or more than 1 severe NP item: insomnia, mania, depression, cognitive)	74	
	Psychosis	74	
	Glucocorticoid-induced violence	74	
	*Select only 1 (minor, moderate, or severe)		
Infection	No GTI-relevant infections within the prebaseline GTI interval of the study	0	59 (58.4)
	Oral or vaginal candidiasis or noncomplicated zoster (<grade 3) within the prebaseline GTI interval of the study	19	20 (19.8)
	Grade 3 or grade 4 infection within the prebaseline GTI interval of the study	93	21 (20.8)
Ocular	No ocular pathology	0	88 (87.1)
	Increased IOP	33	13 (12.9)
	Posterior subcapsular cataract	33	
	Central serous retinopathy	33	
Gastrointestinal	No GI pathology	0	98 (97.0)
	GI perf absence of NSAIDs	33	3 (3)
	PUD without *Helicobacter pylori*	33	
Endocrine	No endocrine pathology	0	100 (99)
	Symptomatic adrenal sufficiency	33	1 (1)

J Allergy Clin Immunol Pract 2021;9:365-72

TABLE 2 Clinical and patient reported outcomes at baseline (V1) and after 12 months mepolizumab treatment (V2)

	V1	V2	Toxicity change at V2 (95% CI)	p-value
Total ED attendances past 12 months	120/39 patients	15/10 patients	−1.05 (−1.55–−0.55)	<0.001
Hospital admissions past 12 months	60/29 patients	17/11 patients	−0.42 (−0.71–−0.14)	0.004
FEV_1 % predicted	68.9±19.0	70.1±21.7	1.16 (−1.69–4.01)	0.42
FVC % predicted	85.9±16.0	86.5±17.4	0.79 (−1.66–3.25)	0.52
FEV_1/FVC	61.9±14.6	62.1±16.9	0.23 (−2.51–2.97)	0.87
F_{eNO} (ppb)	35 (20–57)	38 (24–68)	0.01 (−9.56–9.58)	0.99
Blood eosinophils (cells·μL^{-1})	280 (100–600)	60 (40–100)	−280 (−340–−210)	<0.001
BMI (kg·m^{-2})	30.5±5.8	29.9±5.5	−0.66 (−0.27–−1.06)	0.002
BP systolic (mmHg)	130.3±16.1	129.3±18.0	−0.96 (−3.58–1.66)	0.003
LDL (mmol·L^{-1})	2.8±0.9	2.6±0.9	−0.14 (−0.25–−0.02)	0.02
Total cholesterol (mmol·L^{-1})	5.3±1.1	5.0±1.1	−0.31 (−0.45–−0.17)	0.006
HbA1c (mmol·mol^{-1})	41 (37–46)	39 (35–43)	−2.68 (−3.75–−1.62)	<0.001
Mini AQLQ overall[#]	3.6±1.4	4.5±1.6	0.88 (0.61–1.16)	<0.01
SGRQ overall[¶]	55.8±20.9	43.4±23.2	−12.81 (−16.50–−9.12)	<0.01
ACQ5 total[#]	2.6±1.3	1.7±1.2	−0.89 (−1.15–−0.63)	<0.01
HADS anxiety[+]	8 (5–13.5)	7 (4–11)	−1.02 (−1.68–−0.36)	<0.01
HADS depression[+]	6 (3–11)	5 (2–10)	−1.04 (−1.76–−0.32)	<0.01
EuroQoL-5L5D index	0.63 (0.4–0.8)	0.71 (0.4–0.9)	0.05 (0.003–0.10)	0.04
EuroQoL-5L5D health scale	65 (50–75)	75 (56–85)	9.68 (5.87–13.50)	<0.01

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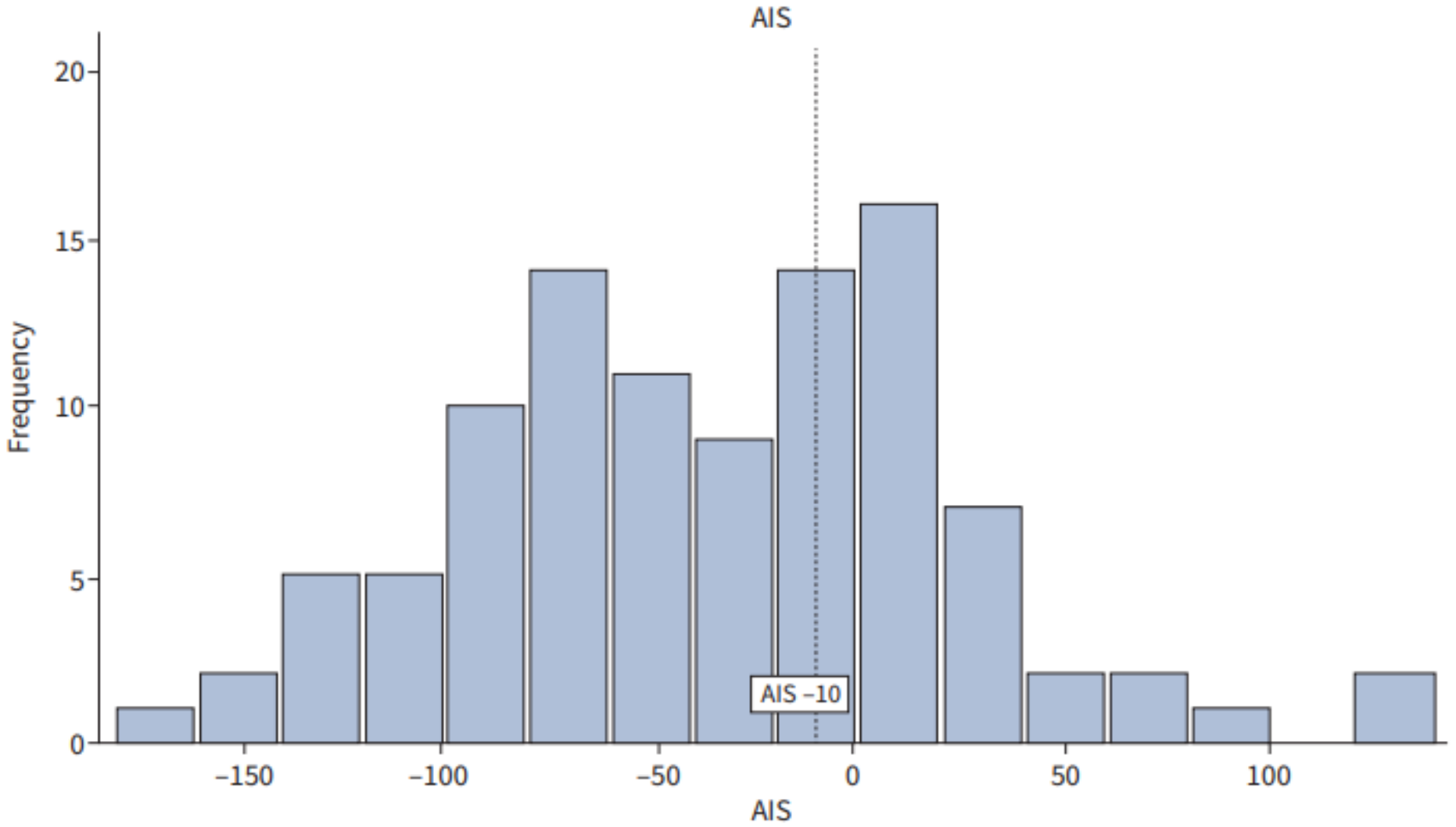
Distribution of aggregate improvement score



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Summary

- Comparison between biologics
- Switch of biologics
- Dual biologics
- Mucus plugs
- Airway hyperresponsiveness
- Steroid toxicity