RWD on Biologics in Severe Asthma

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Respiratory Medicine

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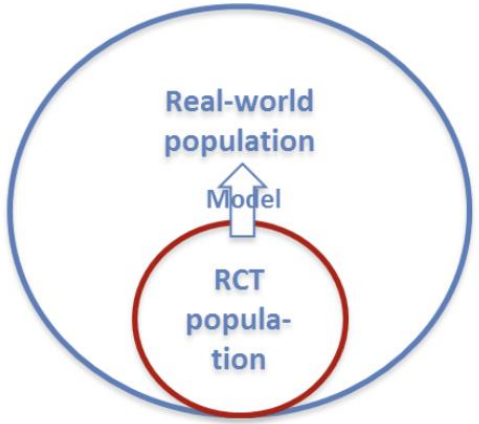
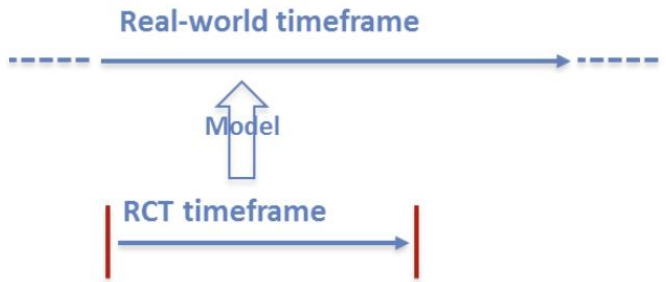
It is time to include real-world effectiveness data on medicinal product labels

Rafael Dal-Ré [a] ✉ · Raphaël Porcher [b] · Frits R Rosendaal [c] · Brigitte Schwarzer-Daum [d]

Affiliations & Notes Article Info



Prediction for new population



Prediction over time

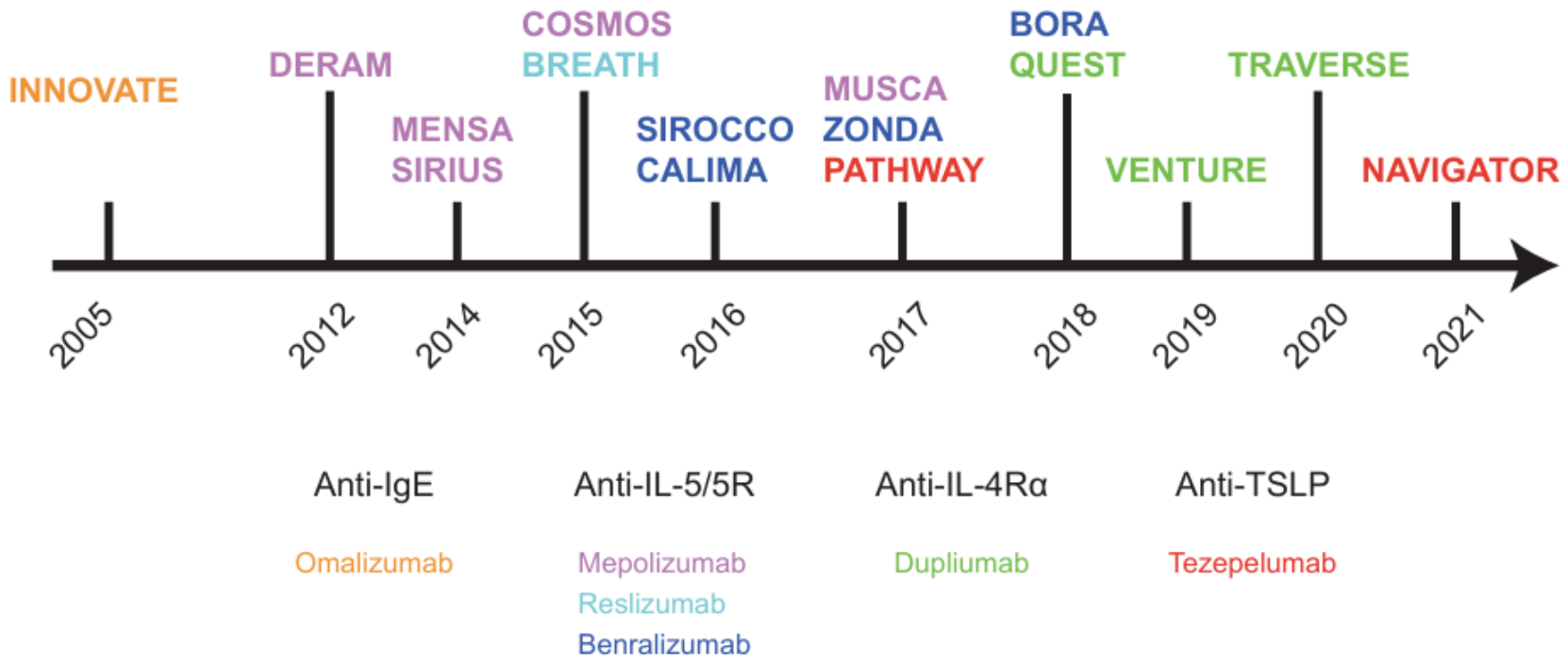


Image: https://rwe-navigator.eu/

Enrollment criteria of RCTs: IgE

Allergy 2005: 60: 309–316

ALLERGY
DOI: 10.1111/j.1398-9995.2004.00772.x

Original article

Benefits of omalizumab as add-on therapy in patients with severe persistent asthma who are inadequately controlled despite best available therapy (GINA 2002 step 4 treatment): INNOVATE

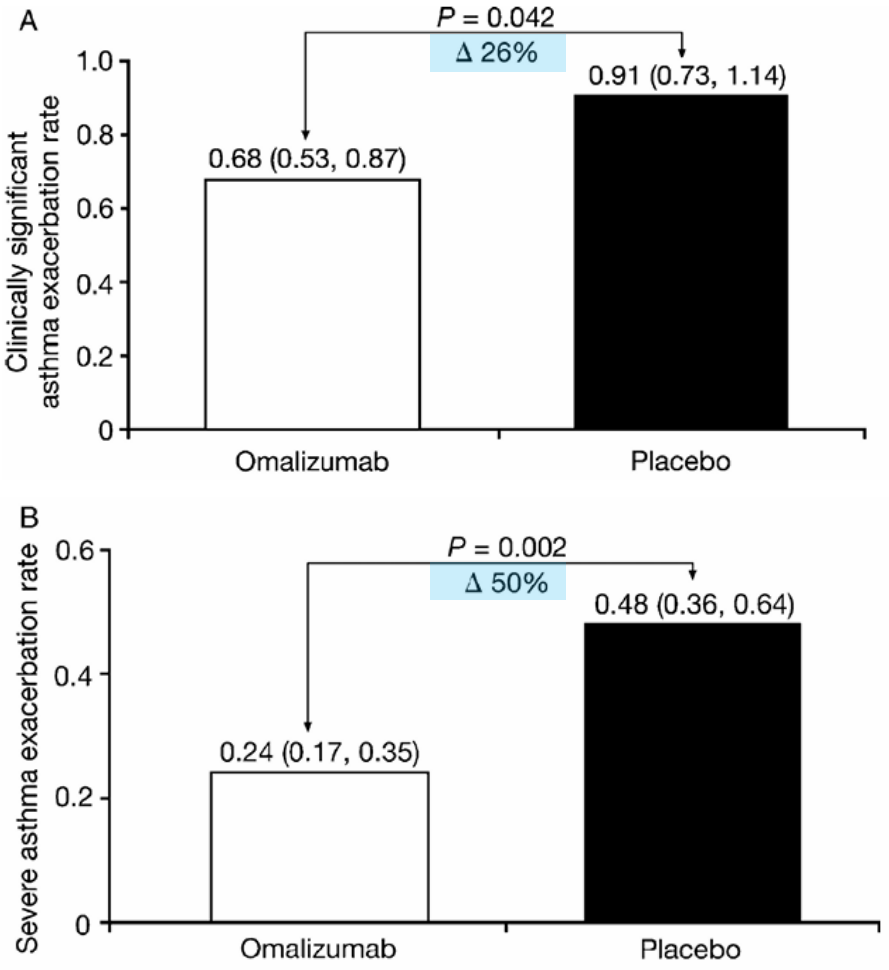
Exclusion

Smokers or smoking history of ≥10 pack-years.
Treatment for an exacerbation within 4 weeks of randomization (the run-in could be extended if necessary).
Use of methotrexate, gold salts, troleandomycin or cyclosporin within 3 months of the first visit.
Prior omalizumab treatment.

Inclusion

Positive skin prick test to at least one perennial aeroallergen likely to be encountered during the study. **Total serum IgE levels between 30 and ≤700 IU/mL.**
Requiring regular treatment with high-dose ICS (≥1000 µg/day beclomethasone dipropionate or equivalent) and LABA, aligning with GINA step 4 treatment.
FEV_1 between 40% and <80% of predicted normal, with ongoing asthma symptoms. FEV_1 reversibility of ≥12% from baseline within 30 minutes after inhaling up to 400 µg or nebulizing up to 5 mg of salbutamol.
Despite high-dose ICS and LABA use, at least two asthma exacerbations requiring systemic corticosteroids or at least one severe exacerbation within the past 12 months.
Severe exacerbation is defined as PEF or FEV_1 <60% of personal best, requiring systemic corticosteroids and leading to hospitalization or emergency room treatment.
Regular use of additional asthma medications for >4 weeks prior to randomization was allowed.
Maintenance oral corticosteroids (up to 20 mg/day) were permitted if the patient experienced at least one exacerbation while on this therapy in the previous 12 months.

Outcomes of RCTs: IgE



Type of visit	Statistic	Omalizumab (n = 209)	Placebo (n = 210)
Total emergency visits	Number	50	93
	Rate per treatment period	0.24	0.43
	Ratio of rates (95% CI)	0.561 (0.325–0.968)	
	P-value for ratio	0.038	
Hospital admissions	Number	13	25
	Rate per treatment period	0.06	0.12
	Ratio of rates (95% CI)	0.540 (0.250–1.166)	
	P-value for ratio	0.117	
Emergency room visits	Number	9	14
	Rate per treatment period	0.04	0.06
	Ratio of rates (95% CI)	0.659 (0.208–2.094)	
	P-value for ratio	0.480	
Unscheduled doctor visits	Number	28	54
	Rate per treatment period	0.13	0.24
	Ratio of rates (95% CI)	0.546 (0.271–1.100)	
	P-value for ratio	0.090	

Enrollment criteria of RCTs: IL-5

ORIGINAL ARTICLE

Mepolizumab Treatment in Patients with Severe Eosinophilic Asthma

Hector G. Ortega, M.D., Sc.D., Mark C. Liu, M.D., Ian D. Pavord, D.M., Guy G. Brusselle, M.D., J. Mark FitzGerald, M.D., Alfredo Chetta, M.D., Marc Humbert, M.D., Ph.D., Lynn E. Katz, Pharm.D., Oliver N. Keene, M.Sc., Steven W. Yancey, M.Sc., and Pascal Chanez M.D., Ph.D., for the MENSA Investigators*

Exclusion

Smoking history ≥10 pack years or other lung diseases (e.g., COPD, fibrosis, cancer).

Uncontrolled systemic conditions (e.g., cardiovascular, liver, autoimmune).

Eosinophilic disorders, immunodeficiency, or recent parasitic infection.

Recent biologic/investigational drugs or allergy to biologics.

Pregnant/breastfeeding, medication non-adherence, or prior study participation.

Inclusion

Age between 12 and 82 years.

Clinical diagnosis of asthma by a physician.

Adults: FEV_1 < 80% of predicted value.

At least one of the following test results:

- FEV_1 reversibility > 12%.
- Positive methacholine or mannitol challenge (current or within the past year).
- FEV_1 variability (≥20%) over two clinic visits in the past 12 months.

History of ≥2 asthma exacerbations in the past year treated with systemic glucocorticoids while on ≥880 µg/day of fluticasone or equivalent and at least 3 months of an additional controller.

Eosinophil count n≥150 cells/µL at screening or ≥300 cells/µL within the past year

Continuation of current asthma therapy allowed.

Outcomes of RCTs: IL-5

Outcome	Placebo (N=191)	Intravenous Mepolizumab (N=191)	Difference from Placebo (95% CI)	P Value	Subcutaneous Mepolizumab (N=194)	Difference from Placebo (95% CI)	P Value
Mean rate of clinically significant exacerbations	1.74	0.93	47 (28 to 60)†	<0.001	0.83	53 (36 to 65)†	<0.001
Mean rate of exacerbations requiring hospitalization or emergency department visit	0.20	0.14	32 (–41 to 67)†	0.30	0.08	61 (17 to 82)†	0.02
Mean rate of exacerbations requiring hospitalization	0.10	0.06	39 (–66 to 77)†	0.33	0.03	69 (9 to 89)†	0.03
Change from baseline in FEV_1 — ml							
Before bronchodilation	86±31	186±32	100 (13 to 187)	0.02	183±31	98 (11 to 184)	0.03
After bronchodilation	30±34	176±34	146 (50 to 242)	0.003	167±33	138 (43 to 232)	0.004
Change from baseline in score on Asthma Control Questionnaire	–0.50±0.07	–0.92±0.07	–0.42 (–0.61 to –0.23)	<0.001	–0.94±0.07	–0.44 (–0.63 to –0.25)	<0.001
Change from baseline in score on St. George's Respiratory Questionnaire	–9.0±1.2	–15.4±1.2	–6.4 (–9.7 to –3.2)	<0.001	–16.0±1.1	–7.0 (–10.2 to –3.8)	<0.001

Enrollment criteria of RCTs: IL-4Rα

ORIGINAL ARTICLE

Dupilumab Efficacy and Safety in Moderate-to-Severe Uncontrolled Asthma

M. Castro, J. Corren, I.D. Pavord, J. Maspero, S. Wenzel, K.F. Rabe, W.W. Busse, L. Ford, L. Sher, J.M. FitzGerald, C. Katelaris, Y. Tohda, B. Zhang, H. Staudinger, G. Pirozzi, N. Amin, M. Ruddy, B. Akinlade, A. Khan, J. Chao, R. Martincova, N.M.H. Graham, J.D. Hamilton, B.N. Swanson, N. Stahl, G.D. Yancopoulos, and A. Teper

Exclusion

Significant non-asthma lung diseases, unstable comorbidities, recent severe infections, or elevated eosinophils (>1500 cells/mm^3).

Recent biologics, immunosuppressants, or allergy to biologics; prohibited medications, recent live vaccines, and past bronchial thermoplasty.

Smoking history ≥10 pack-years, recent alcohol/drug abuse.

Non-adherence, pregnancy/breastfeeding, or inadequate contraception.

Inclusion

Age ≥12 years with physician-diagnosed persistent asthma for 12+ months per GINA 2014 guidelines.

Currently on medium-to-high-dose inhaled glucocorticoids (≥500 μg fluticasone equivalent) plus up to two additional controllers.

Pre-bronchodilator FEV_1 ≤80% of predicted (≤90% for ages 12-17) and FEV_1 reversibility of ≥12% and 200 ml.

ACQ-5 score ≥1.5 (indicating moderate or greater impairment).

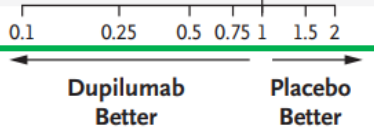
History of asthma worsening in the past year requiring hospitalization, emergency care, or systemic glucocorticoids for ≥3 days.

No minimum baseline eosinophil count or type 2 inflammation biomarker required.

Outcomes of RCTs: IL-4Rα

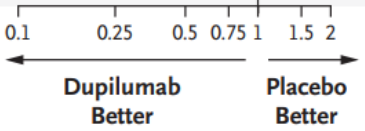
A Dupilumab, 200 mg Every 2 Wk, vs. Matched Placebo

Subgroup	No. of Patients		Relative Risk vs. Placebo (95% CI)
	Placebo	Dupilumab	
Overall	317	631	0.52 (0.41–0.66)
Eosinophil count			
≥300 cells/mm³	148	264	0.34 (0.24–0.48)
≥150 to <300 cells/mm³	84	173	0.64 (0.41–1.02)
<150 cells/mm³	85	193	0.93 (0.58–1.47)
FE_{NO}			
≥50 ppb	71	119	0.31 (0.18–0.52)
≥25 to <50 ppb	91	180	0.39 (0.24–0.62)
<25 ppb	149	325	0.75 (0.54–1.05)



B Dupilumab, 300 mg Every 2 Wk, vs. Matched Placebo

Subgroup	No. of Patients		Relative Risk vs. Placebo (95% CI)
	Placebo	Dupilumab	
Overall	321	633	0.54 (0.43–0.68)
Eosinophil count			
≥300 cells/mm³	142	277	0.33 (0.23–0.45)
≥150 to <300 cells/mm³	95	175	0.56 (0.35–0.89)
<150 cells/mm³	83	181	1.15 (0.75–1.77)
FE_{NO}			
≥50 ppb	75	124	0.31 (0.19–0.49)
≥25 to <50 ppb	97	186	0.44 (0.28–0.69)
<25 ppb	144	317	0.79 (0.57–1.10)



Enrollment criteria of RCTs: TSLP

ORIGINAL ARTICLE

Tezepelumab in Adults and Adolescents with Severe, Uncontrolled Asthma

Andrew Menzies-Gow, M.D., Jonathan Corren, M.D., Arnaud Bourdin, M.D., Geoffrey Chupp, M.D., Elliot Israel, M.D., Michael E. Wechsler, M.D., Christopher E. Brightling, F.Med.Sci., Janet M. Griffiths, Ph.D., Åsa Hellqvist, M.Sc., Karin Bowen, M.Sc., Primal Kaur, M.D., Gun Almqvist, M.Sc., Sandhia Ponnarambil, M.D., and Gene Colice, M.D.

Exclusion

Non-asthma lung diseases or systemic diseases with high eosinophils

Unstable systemic conditions or recent serious infections

Smoking history ≥10 pack-years or substance abuse

Recent biologics, immunosuppressants, or major surgery

Pregnancy, study non-compliance, or prior trial participation

Inclusion

12-80 years with a physician-diagnosed asthma for at least 12 months before screening.

On medium or high-dose inhaled glucocorticoids (≥500 µg fluticasone equivalent) for 12+ months before screening, plus an additional controller for at least 3 months.

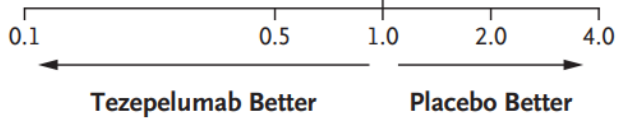
Pre-bronchodilator FEV_1 <80% of predicted; documented FEV_1 reversibility of ≥12% and 200 ml within the past 12 months.

At least two exacerbations requiring systemic glucocorticoids or hospitalization within the last 12 months.

Biologic Treatments: **Allowed if last dose taken over 4 months or five half-lives before screening.**

Outcomes of RCTs: TSLP

Subgroup	Tezepelumab	Placebo	Rate Ratio (95% CI)
	no. of patients/annualized rate of asthma exacerbations		
Overall	528/0.93	531/2.10	0.44 (0.37–0.53)
Eosinophil count at baseline (cells/μl)			
<300	309/1.02	309/1.73	0.59 (0.46–0.75)
≥300	219/0.79	222/2.66	0.30 (0.22–0.40)
Eosinophil count at baseline (cells/μl)			
<150	138/1.04	138/1.70	0.61 (0.42–0.88)
150 to <300	171/1.00	171/1.75	0.57 (0.41–0.79)
300 to <450	99/0.92	95/2.22	0.41 (0.27–0.64)
≥450	120/0.68	127/3.00	0.23 (0.15–0.34)
Eosinophil count at baseline (cells/μl)			
<150	138/1.04	138/1.70	0.61 (0.42–0.88)
≥150	390/0.89	393/2.24	0.39 (0.32–0.49)
FENO at baseline (ppb)			
<25	213/1.07	220/1.57	0.68 (0.51–0.92)
≥25	309/0.82	307/2.52	0.32 (0.25–0.42)
FENO at baseline (ppb)			
<25	213/1.07	220/1.56	0.68 (0.51–0.92)
25 to <50	158/0.87	151/2.20	0.40 (0.28–0.56)
≥50	151/0.75	156/2.83	0.27 (0.19–0.38)
Allergic status at baseline			
Positive for any perennial allergens	339/0.85	341/2.03	0.42 (0.33–0.53)
Negative for all perennial allergens	184/1.09	177/2.21	0.49 (0.36–0.67)



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Overview: anti-IgE

Study design	Patient	Patient numbers	Period	Main results Adverse effects	Ref
Retrospective, Italy, 2022	SAA	8	16 y	Exacerbation: 1.8 to 0.88/y Hospitalization: 0.3 to 0/y No adverse effects	136
Retrospective, Greece, 2021	Asthma	45	10.6 y	Exacerbation: 4.1 to 1.1/y (1 y) OCS:7.8 to 1.6 mg/d (8 y) No severe adverse events	137
Retrospective, Poland, 2020	SAA	854	4 y	Mini AQLQ: 2.9 to 5.0 points OCS: 10.8 to 2.7 mg/d (4 y)	138
Prospective, Germany, 2020	SAA	153	3 y	ACQ-6: 2.2 to 1.7 points (NS) No unexpected safety signals	139
Retrospective, Turkey, 2018	Asthma	465	>5 y	Exacerbation reduced to 54.8% (5 y) No hospitalization (5 y) Adverse effects: 12.7% (mild-to-moderate)	140
Observational, Kuwait, 2018	Poor- control asthma	65	4 y	OCS user: 99 to 17%, ACT: 15 to 23 points %FEV1 55.6 to 76.6%, Adverse effects: Mild 15%, Serious 4.6%	141
Observational, Italy, 2018	SAA	15	>5 y	ACT: 14.6 to 21.7 points, Exacerbation: 3.7 to 0.6/y (5 y) OCS: 22.5 to 1.7 mg/d (5 y) FEV1: 1.64 to 1.93 L (5 y)	39
Retrospective, United Kingdom, 2017	SAA	45	60.7 m	OCS: 25.8 to 6.0 mg/d, ACQ: 4.1 to 2.3, %FEV1: 59.2 to 75.7% No anaphylaxis or deaths	38
Retrospective, Italy, 2017	Difficult asthma	91	3.8 y	Adverse events: 6.6% discontinued No anaphylaxis	37
Retrospective, Italy, 2017	SAA	340	4 m to 120 m	Treatment duration was positively associated with a step down, did not affect ACT, exacerbations	36
Retrospective, Greece, 2012	SAA	60	4 y	%FEV1: +24.5%, ACT: +24% Exacerbation: −70% (4 y)	142

Anti-IL-5/5R: Mepolizumab

[Asthma Original Research]

CHEST Pulmonary

Prospective REALITI-A Study

2-Year Real-World Benefits of Mepolizumab in Severe Asthma

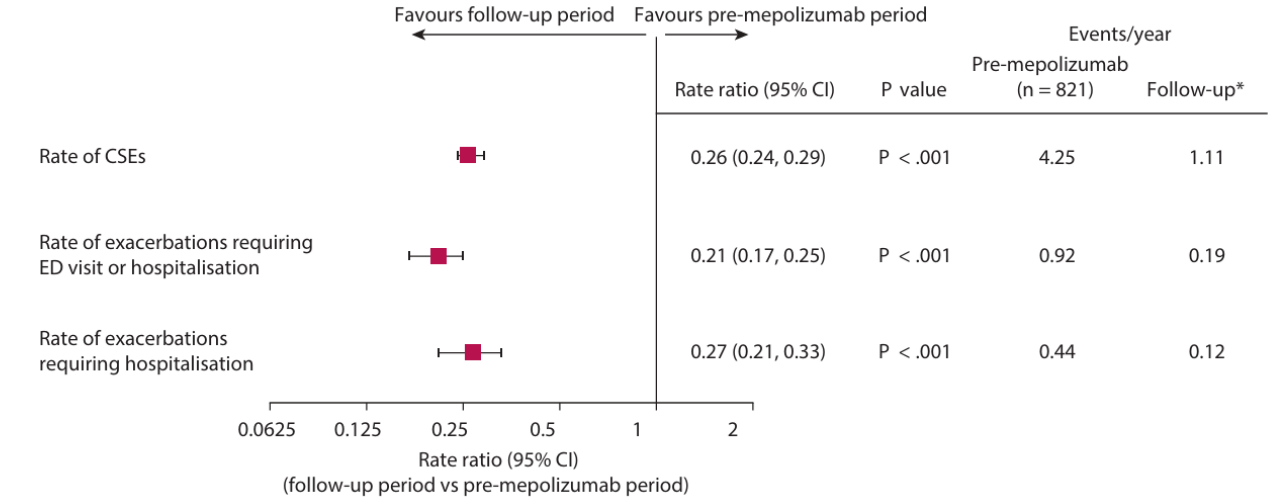
Cristiano Caruso, MD, PhD; G. Walter Canonica, MD; Manish Patel, MBChB, PhD; Andrew Smith, MBChB, PhD; Mark C. Liu, MD; Rafael Alfonso-Cristancho, MD, PhD; Robert G. Price, MSc; Rupert W. Jakes, PhD; Lydia Demetriou, MSc; Antonio Valero, MD; Thomas C. Köhler, MD; Charles Pilette, MD, PhD; Geoffrey Chupp, MD; Guy Brusselle, MD; and Peter Howarth, DM

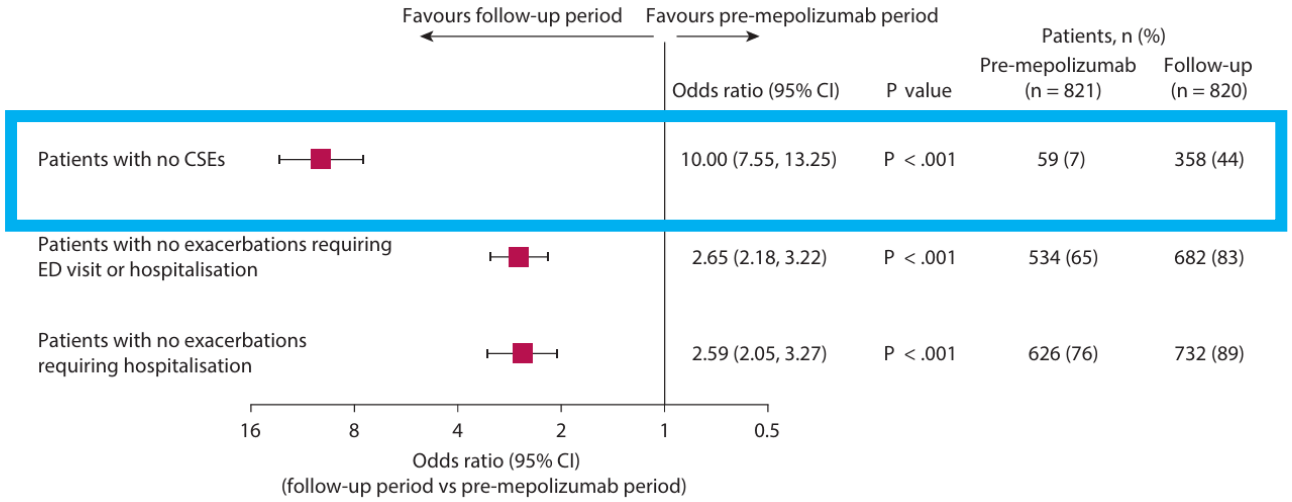
Baseline characteristics

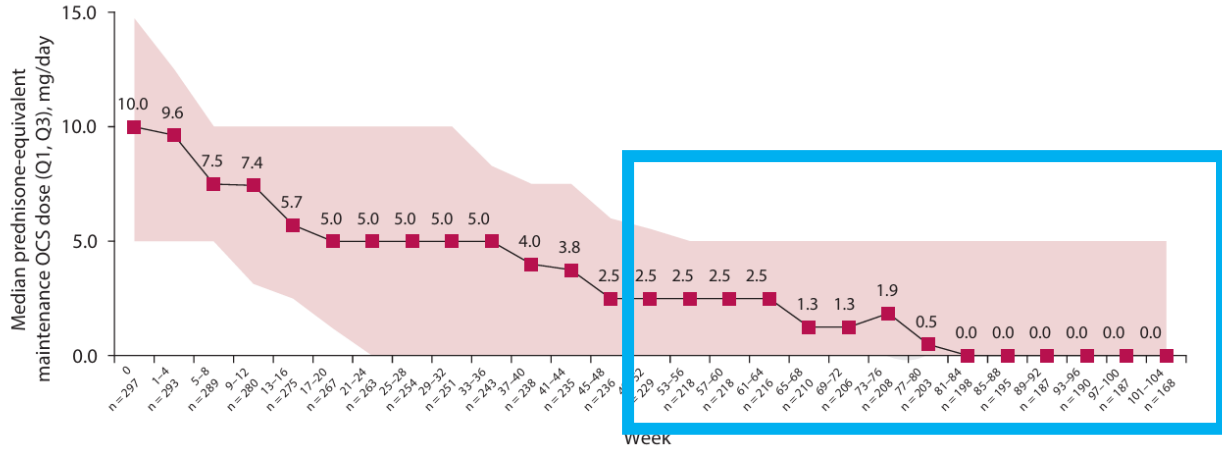
	Total Population (N = 822)	Did Not Discontinue Mepolizumab (n = 599)	Discontinued Mepolizumab (n = 223)
Age, y	54.0 [13.6]	55.2 [12.9]	51.1 [14.9]
Female	521 (63)	375 (63)	146 (65)
BMI, kg/m²	(n = 819) 29.0 [7.2]	(n = 598) 28.7 [7.0]	(n = 221) 30.1 [7.8]
Race			
- Asian or Pacific islander	34 (4)	20 (3)	14 (6)
- Black	25 (3)	15 (3)	10 (4)
- White	755 (92)	559 (93)	196 (88)
- Other	7 (<1)	4 (<1)	3 (<1)
Smoking history			
- Did not smoke	503 (62)	365 (61)	138 (62)
- Previous tobacco use	290 (36)	219 (37)	71 (32)
- Active tobacco use	23 (3)	11 (2)	12 (5)
Asthma duration, y	(n = 801) 19.7 [15.7]	(n = 587) 19.6 [15.7]	(n = 214) 19.7 [15.6]
Age at asthma diagnosis, y	(n = 801) 34.5 [19.4]	N/A	N/A

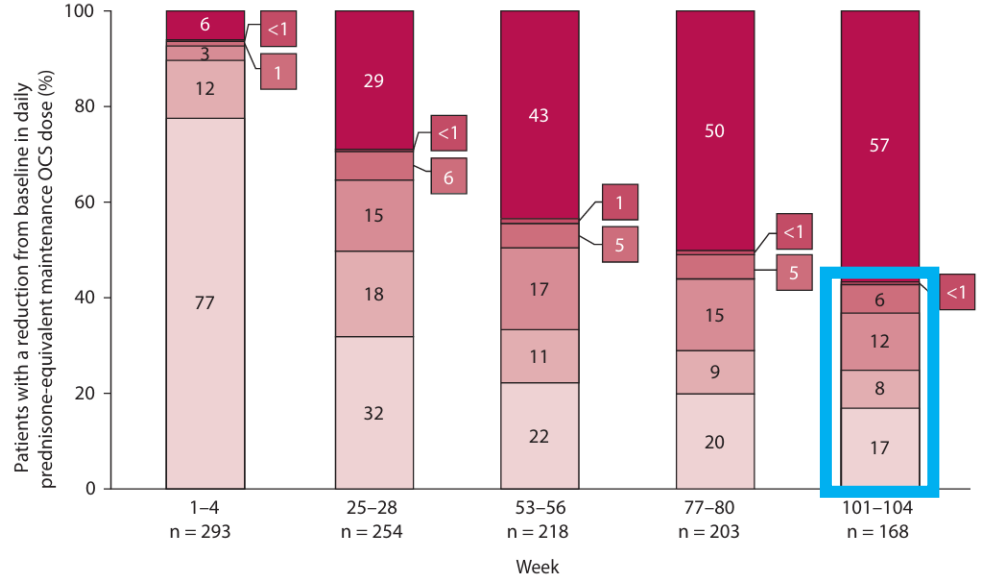
	Total Population (N = 822)	Did Not Discontinue Mepolizumab (n = 599)	Discontinued Mepolizumab (n = 223)
Blood eosinophil count, cells/mL	(n = 614) 350 [1.25]	(n = 449) 371 [1.24]	(n = 165) 299 [1.28]
Total IgE, KU/L	(n = 675) 168.6 [1.59]	(n = 490) 169.8 [1.53]	(n = 185) 165.6 [1.75]
Maintenance OCS	320 (39)	226 (38)	94 (42)
Dose, mg/d, median (Q1, Q3)	(n = 297) 10.0 (5.0, 14.7)	(n = 209) 8.1 (5.0, 10.2)	(n = 88) 10.7 (7.3, 20.0)
Patients with previous omalizumab treatment	151 (18)	100 (17)	51 (23)
Duration of omalizumab, mo	24.0 (6.0, 50.0)	24.0 (9.0, 52.5)	16.0 (5.0, 48.0)
Comorbidities			
- Hay fever	405 (49)	302 (50)	103 (46)
- Chronic sinusitis	331 (40)	252 (42)	79 (35)
- Nasal polyp	323 (39)	247 (41)	76 (34)
- Gastroesophageal reflux disease	310 (38)	228 (38)	82 (37)
- Drug hypersensitivity	269 (33)	187 (31)	82 (37)

Major outcomes: REALITI-A









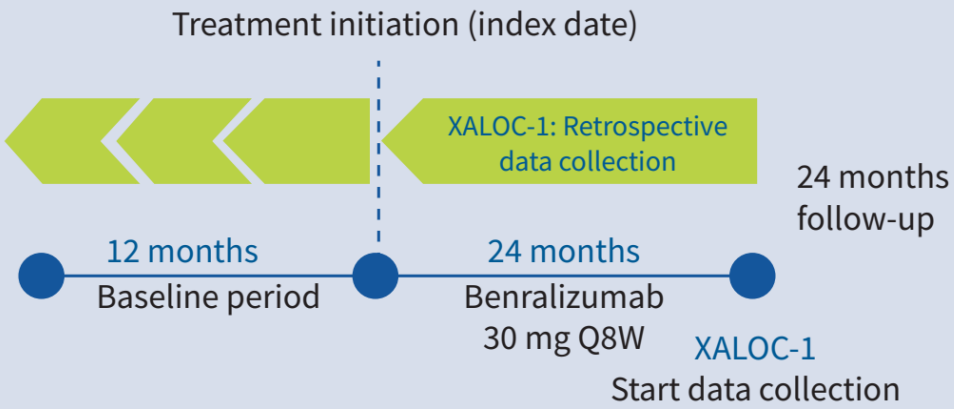
Anti-IL-5/5R: BENRALIZUMAB

EUROPEAN RESPIRATORY JOURNAL
ORIGINAL RESEARCH ARTICLE
D.J. JACKSON ET AL.

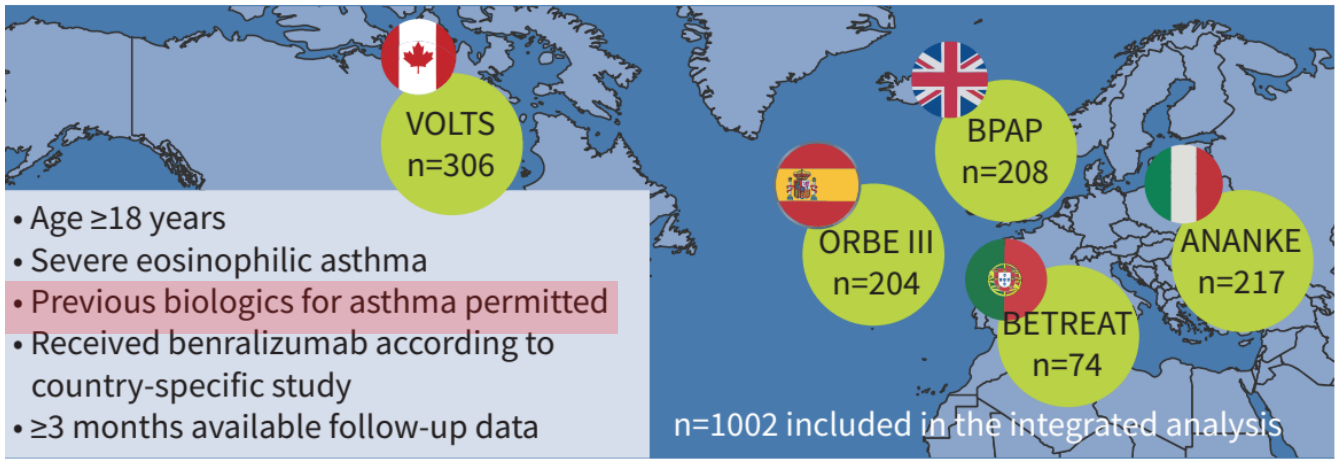
Benralizumab in severe eosinophilic asthma by previous biologic use and key clinical subgroups: real-world XALOC-1 programme

David J. Jackson, Girolamo Pelaia, Benjamin Emmanuel, Trung N. Tran, David Cohen, Vivian H. Shih, Anat Shavit, Douglas Arbetter, Rohit Katial, Adrian Paul J. Rabe, Esther Garcia Gil, Marisa Pardal, Javier Nuevo, Michael Watt, Silvia Boarino, Sheena Kayaniyil, Cláudia Chaves Loureiro, Alicia Padilla-Galo and Parameswaran Nair

Real-world observational study design

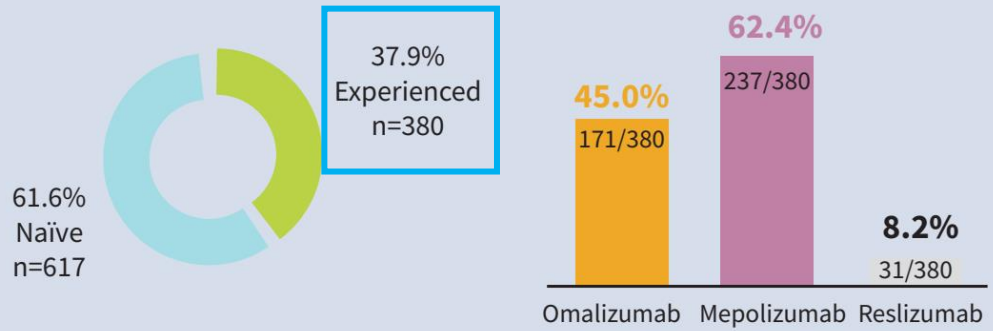


Study population



- Age ≥18 years
- Severe eosinophilic asthma
- Previous biologics for asthma permitted
- Received benralizumab according to country-specific study
- ≥3 months available follow-up data

Previous biologic experience



Previous biologic discontinued due to lack of efficacy	Omalizumab	Mepolizumab	Reslizumab
	57.3% 98/171	68.8% 163/237	**58.1%** 18/31

Baseline Characteristics

TABLE 1 Baseline demographics, overall and according to patients' previous biologic experience

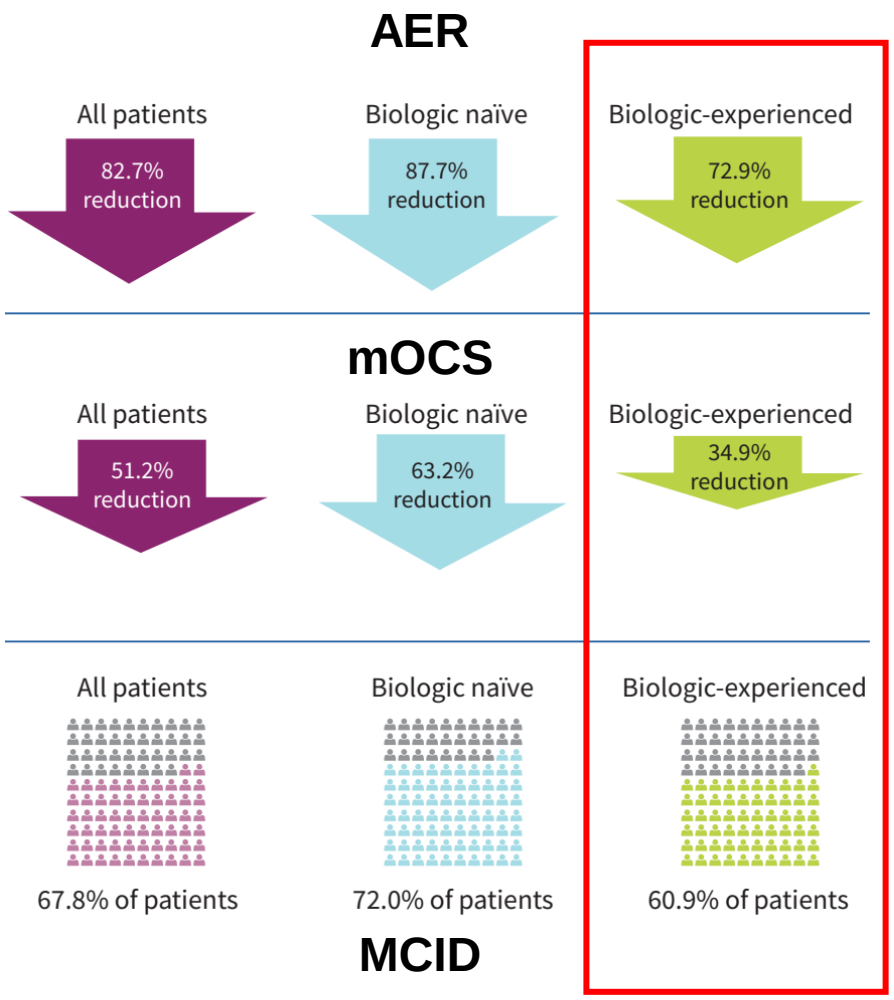
	All patients	Biologic-naïve patients	Biologic-experienced patients		
			All biologic-experienced patients[#]	Omalizumab-experienced patients	Mepolizumab-experienced patients
Patients	1002	617	380	171	237
Age at index date years	55.4±13.7	56.7±13.7	53.5±13.5	53.6±13.2	52.3±14.1
Age at asthma diagnosis years	38.2±18.2 (n=656)	38.9±18.9 (n=426)	37.1±16.8 (n=228)	34.7±16.0 (n=98)	36.5±17.9 (n=142)
<18 years[¶]	106 (10.6)	69 (11.2)	36 (9.5)	20 (11.7)	25 (10.5)
⩾18 years[¶]	550 (54.9)	357 (57.9)	192 (50.5)	78 (45.6)	117 (49.4)
Female[¶]	587 (58.6)	369 (59.8)	215 (56.6)	100 (58.5)	129 (54.4)
BMI[+] **kg·m**$^{-2}$	29.0±6.7 (n=904)	28.5±6.4 (n=557)	29.8±7.0 (n=343)	29.3±6.6 (n=146)	30.5±7.2 (n=221)
Smoking history[¶]					
Never-smoker	604 (60.3)	375 (60.8)	225 (59.2)	98 (57.3)	138 (58.2)
Current smoker	37 (3.7)	26 (4.2)	11 (2.9)	4 (2.3)	7 (3.0)
Ex-smoker	303 (30.2)	190 (30.8)	112 (29.5)	50 (29.2)	75 (31.6)
Positive atopic status[¶,§]	439 (43.8)	246 (39.9)	192 (50.5)	99 (57.9)	116 (48.9)
Concomitant CRSwNP[¶,§]	316 (31.5)	183 (29.7)	133 (35.0)	46 (26.9)	91 (38.4)
Concomitant allergic rhinitis[¶,§]	176 (17.6)	102 (16.5)	73 (19.2)	NA	NA

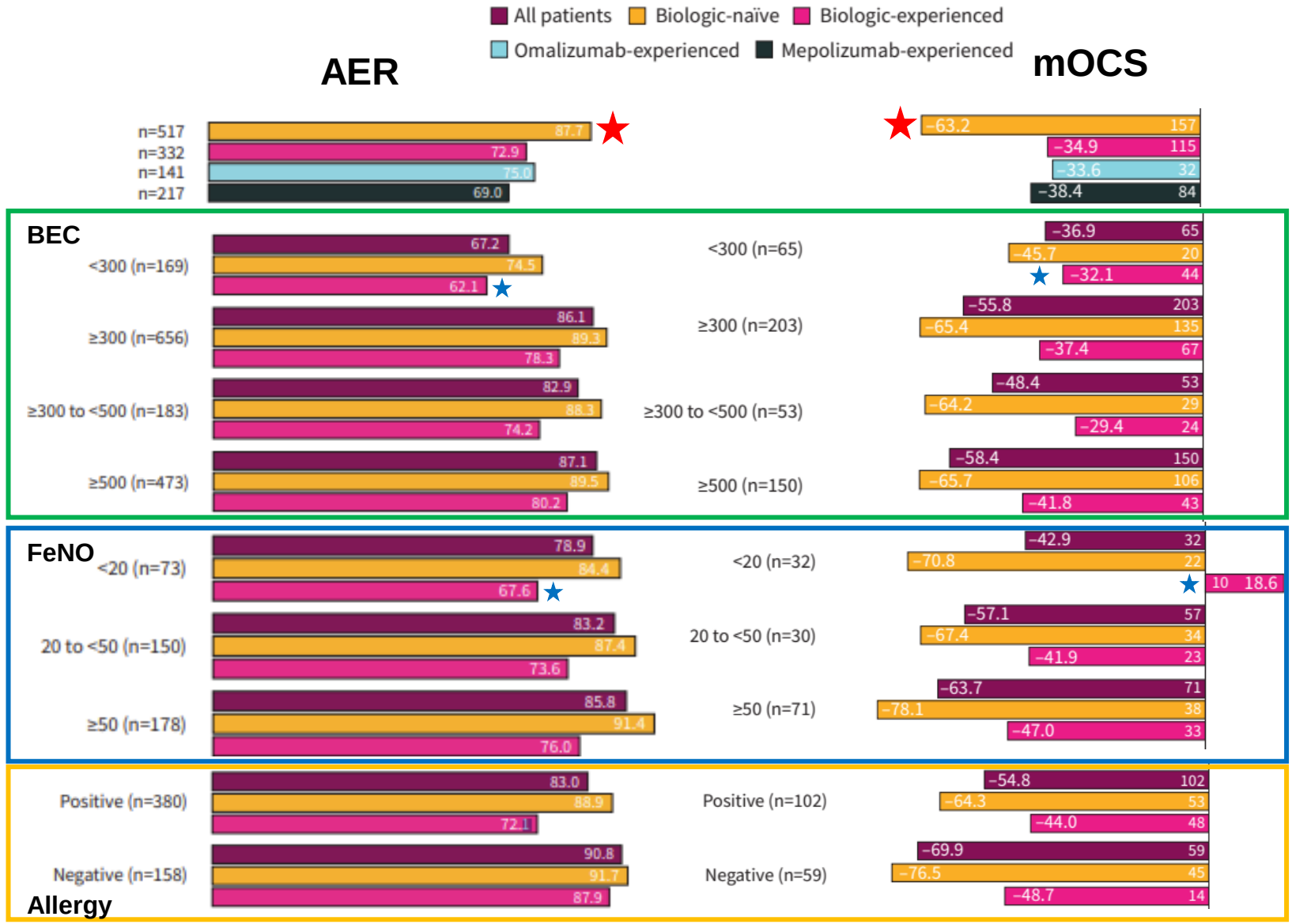
Baseline disease characteristics

TABLE 2 Baseline disease characteristics, overall and according to patients' previous biologic experience

	All patients	Biologic-naïve patients	Biologic-experienced patients		
			All biologic-experienced patients[#]	Omalizumab-experienced patients	Mepolizumab-experienced patients
Patients	1002	617	380	171	237
mOCS use at the index date[¶]	322 (32.1)	180 (29.2)	140 (36.8)	48 (28.1)	98 (41.4)
Daily mOCS dosage[¶] mg·day^{-1}	16.6±13.8	16.9±13.9	16.0±13.5	16.5±16.0	17.0±13.6
Daily mOCS dosage[¶] mg·day^{-1}	10.0 (5.0–25.0)	10.0 (5.0–25.0)	10.0 (5.0–21.0)	10.0 (5.0–21.0)	11.1 (5.0–25.0)
mOCS use during 12-month baseline period[+]	532 (53.1)	316 (51.2)	214 (56.3)	85 (49.7)	148 (62.4)
Pre-BD FEV_1 ⩾65% predicted	234 (56.8)	165 (59.1)	69 (51.9)	NA	NA
Pre-BD FEV_1[§] L	1.92±0.8 (n=395)	1.96±0.8 (n=274)	1.83±0.8 (n=121)	NA	NA
Post-BD FEV_1[§] L	1.96±0.8 (n=420)	2.01±0.8 (n=274)	1.87±0.9 (n=146)	2.05±0.9 (n=46)	1.78±0.8 (n=99)
AER during 12-month baseline period, mean (95% CI)	3.05 (2.86–3.25) (n=839)	3.29 (3.05–3.55) (n=506)	2.69 (2.39–3.02) (n=330)	2.31 (1.95–2.73) (n=140)	2.79 (2.42–3.21) (n=216)
Peak BEC during baseline period cells·µL^{-1}	510 (300–850) (n=965)	600 (400–1000) (n=603)	400 (190–700) (n=359)	461 (300–700) (n=162)	300 (100–680) (n=223)
Total serum IgE[§] IU·mL^{-1}	165.2 (60.1–462.0) (n=590)	127.5 (50.7–389.0) (n=410)	296.0 (96.3–607.0) (n=177)	354.7 (166.0–729.0) (n=106)	183.5 (71.0–473.0) (n=82)
F_{ENO}[§] ppb	55.2±48.2 (n=447)	51.5±46.2 (n=267)	60.8±50.7 (n=180)	NA	NA
ACQ-6 score[§]	2.93±1.4 (n=334)	3.04±1.4 (n=171)	2.83±1.5 (n=162)	2.92±1.3 (n=46)	2.88±1.5 (n=134)
ACT score[§]	14.31±5.0 (n=350)	14.19±4.9 (n=239)	14.58±5.2 (n=111)	15.31±5.28 (n=62)	13.46±5.38 (n=48)

Outcomes


AER
All patients
82.7% reduction
Biologic naïve
87.7% reduction
Biologic-experienced
72.9% reduction
mOCS
All patients
51.2% reduction
Biologic naïve
63.2% reduction
Biologic-experienced
34.9% reduction
All patients
67.8% of patients
Biologic naïve
72.0% of patients
Biologic-experienced
60.9% of patients
MCID


All patients
Biologic-naïve
Biologic-experienced
Omalizumab-experienced
Mepolizumab-experienced
AER
mOCS
n=517
n=332
n=141
n=217
87.7
72.9
75.0
69.0
−63.2
157
−34.9
115
−33.6
32
−38.4
84
BEC
<300 (n=169)
67.2
74.5
62.1
<300 (n=65)
−36.9
65
−45.7
20
−32.1
44
≥300 (n=656)
86.1
89.3
78.3
≥300 (n=203)
−55.8
203
−65.4
135
−37.4
67
≥300 to <500 (n=183)
82.9
88.3
74.2
≥300 to <500 (n=53)
−48.4
53
−64.2
29
−29.4
24
≥500 (n=473)
87.1
89.5
80.2
≥500 (n=150)
−58.4
150
−65.7
106
−41.8
43
FeNO
<20 (n=73)
78.9
84.4
67.6
<20 (n=32)
−42.9
32
−70.8
22
10
18.6
20 to <50 (n=150)
83.2
87.4
73.6
20 to <50 (n=30)
−57.1
57
−67.4
34
−41.9
23
≥50 (n=178)
85.8
91.4
76.0
≥50 (n=71)
−63.7
71
−78.1
38
−47.0
33
Allergy
Positive (n=380)
83.0
88.9
72.1
Positive (n=102)
−54.8
102
−64.3
53
−44.0
48
Negative (n=158)
90.8
91.7
87.9
Negative (n=59)
−69.9
59
−76.5
45
−48.7
14

Responder

SUPPLEMENTARY TABLE S7 Univariable analysis on baseline demographics and clinical characteristics in responders and non-responders at week 48.

Variable	Responders (n=612)	Non-responders (n=78)	*P* value
Female, n (%)	369 /612 (60.3)	44/78 (56.4)	0.510
Age at start of benralizumab treatment, years, mean (SD)[a]	55.3 (13.4)	55.0 (14.0)	0.888
Asthma duration, years, mean (SD)[b]	(n=424) 17.7 (14.6)	(n=40) 16.4 (13.5)	0.584
BMI, kg/m^2, mean (SD)[c]	(n=571) 29.0 (6.5)	(n=67) 30.0 (7.7)	0.271
Smoking history, n/N (%)			
Ever smoker	204/581 (35.1)	29/69 (42.0)	0.258
Never smoker	377/581 (64.9)	40/69 (58.0)	
Peak baseline EOS count, cells/µL, mean (SD)[d]	(n=601) 704 (628)	(n=72) 663 (909)	0.006
Baseline IgE, IU/mL, mean (SD)[d]	(n=371) 353.1 (648.2)	(n=40) 734.1 (996.5)	0.132
FeNO, ppb, mean (SD)[e]	(n=329) 56.1 (48.5)	(n=29) 61.0 (60.9)	0.607
Positive atopic status, n/N (%)	275/410 (67.1)	32/38 (84.2)	0.035
Presence of CRSwNP, n/N (%)	204/612 (33.3)	16/78 (20.5)	0.024
Allergic rhinitis, n/N (%)	111/488 (22.7)	12/67 (17.9)	0.373
Any OCS related comorbidity[f], n/N (%)	293/612 (47.9)	45/78 (57.7)	0.104
Respiratory comorbidities (ABPA, EGPA, or eosinophilic pneumonia), n (%)	43/488 (8.8)	17/67 (25.4)	<0.001
Biologic-experience status, yes, n/N (%)	395/609 (64.9)	40/78 (51.3)	0.020
Exacerbations during the 12-month baseline period, mean (SD)[g]	(n=599) 4.0 (3.0)	(n=75) 1.5 (1.5)	<0.001
mOCS dose during the 12-month baseline period, mg/day, mean (SD)[h]	6.4 (12.1)	10.8 (13.2)	0.004
mOCS use at the index date, mg/day, mean (SD)	232/612 (37.9)	53/78 (67.9)	<0.001
Pre-BD FEV$_1$, L, mean (SD)[i]	(n=365) 2.0 (0.8)	(n=40) 1.8 (0.7)	0.361
Pre-BD FEV$_1$, % predicted, mean (SD)[c]	(n=362) 69.0 (21.4)	(n=39) 67.2 (21.5)	0.616
Controlled asthma (ACQ-6 score <1.5 or ACT score ≥16), n/N (%)	118/478 (24.7)	17/47 (36.2)	0.089
Participating country, n (%)			
Italy	151/612 (24.7)	5/78 (6.4)	0.002
Spain	123/612 (20.1)	11/78 (14.1)	0.551
Portugal	51/612 (8.3)	6/78 (7.7)	0.780
Canada	108/612 (17.6)	34/78 43.6)	<0.001
UK[j]	179/612 (29.2)	22/78 (28.2)	

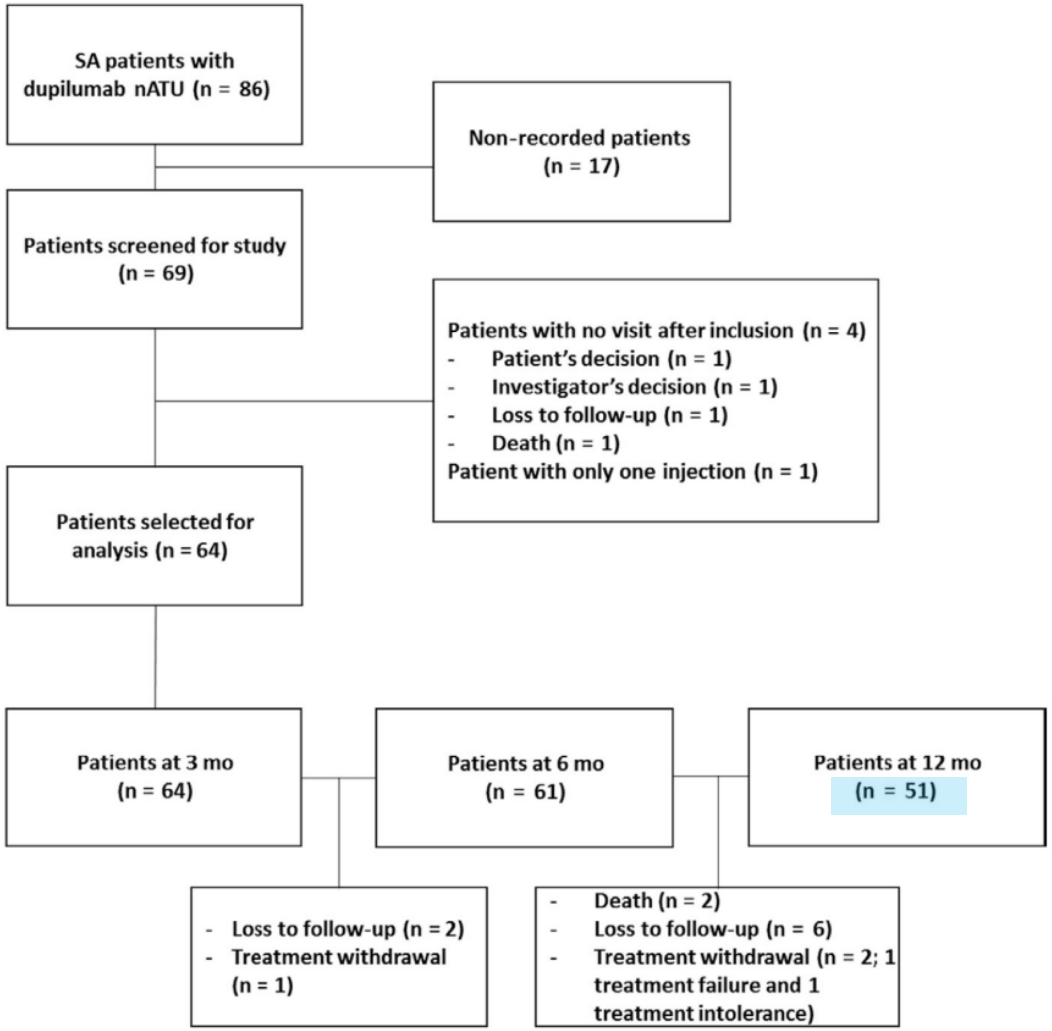
Multivariable
High BEC, Frequent AE

Anti-IL-4Rα: Dupilumab

Effectiveness and safety of dupilumab for the treatment of severe asthma in a real-life French multi-centre adult cohort

Clairelyne Dupin[1] | Drifa Belhadi[2,3] | Laurent Guilleminault[4,5,6] | Anne-Sophie Gamez[6,7] | Patrick Berger[6,8] | Frédéric De Blay[6,9] | Philippe Bonniaud[6,10,11,12] | Christophe Leroyer[13,14] | Guillaume Mahay[15] | Pierre-Olivier Girodet[6,8] | Chantal Raherison[6,8] | Stéphanie Fry[6,16] | Geneviève Le Bourdellès[17] | Alain Proust[18] | Lise Rosencher[19] | Gilles Garcia[6,20,21] | Arnaud Bourdin[6,7] | Cécile Chenivesse[6,16] | Alain Didier[4,5,6] | Camille Couffignal[2,3] | Camille Taillé[1,6]

Study population



Enrollment Requirement: Physicians needed to confirm to French Health authorities that patients had severe, uncontrolled asthma (SA) with no other treatment options

Criteria: Enrollment required evidence of poor asthma control or severe steroid side effects necessitating urgent intervention

Authorization: Both the French Health Authority and Sanofi had to approve patient entry into the program

Biomarkers: Eosinophilia or elevated FeNO were not required since Phase III RCT results were pending

Exclusion: Patients with past-year hypereosinophilia (>1500/mm^3) were excluded due to risks of symptomatic hypereosinophilia with dupilumab

Investigator Discretion: Investigators could set visit frequency and assessment tools based on standard practice.

Baseline characteristics

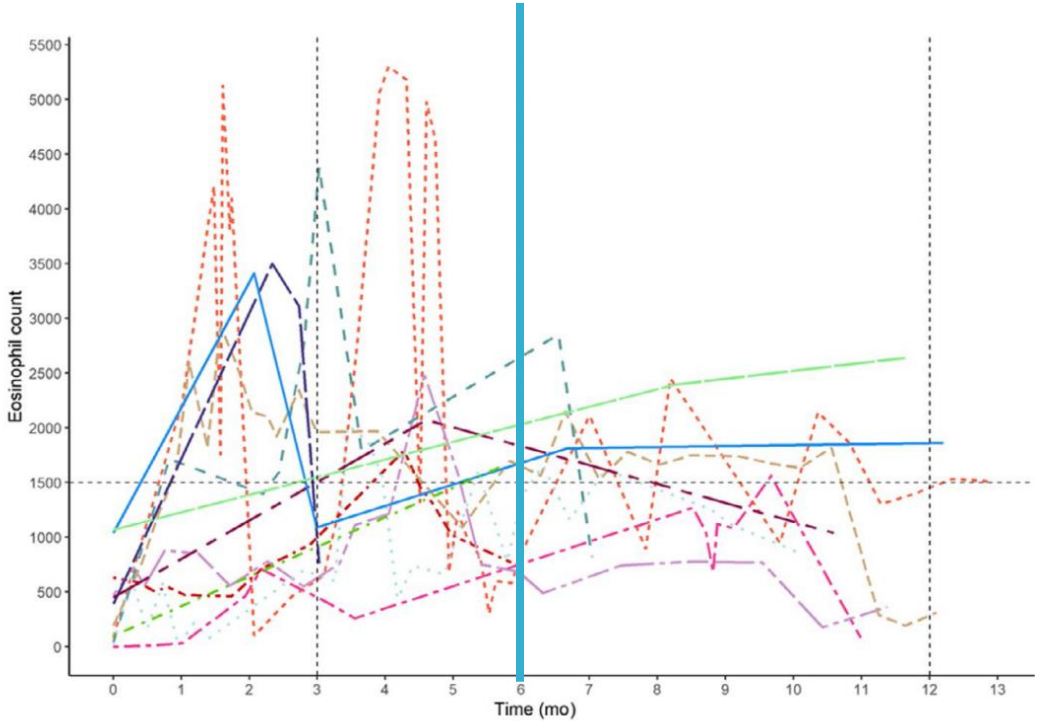
Demographics	Age (y), median [IQR]	64	51 [44-61]
	Sex: female, n (%)	64	34 (53.1)
	Age at diagnosis (y), median [IQR]	58	21 [10-40]
	BMI (Kg/m^2), median [IQR]	61	27 [23-31]
	Obesity, n (%)	61	20 (32.8)
	Current smokers, n (%)	62	1 (1.6)
	Former smokers, n (%)	62	30 (48.4)
Comorbidities	Atopy, n (%)	62	38 (61.3)
	Atopic dermatitis, n (%)	37	6 (16.2)
	Food allergy, n (%)	38	5 (13.2)
	Nasal polyps, n (%)	60	18 (30.0)
	AERD, n (%)	34	16 (47.1)
	GERD, n (%)	57	30 (52.6)
	Hypertension, n (%)	56	16 (28.6)
	OSA, n (%)	56	21 (37.5)
	Diabetes, n (%)	56	10 (17.9)
	Osteoporosis, n (%)	56	21 (37.5)
	Depression, n (%)	55	10/57 (17.5)
Ongoing treatments	Dose of ICS (µg/d), median [IQR]	60	800 [800-1600]
	LABA, n (%)	62	61 (95.2)
	Azithromycin, n (%)	62	11 (17.7)
	LAMA, n (%)	61	36 (59.0)
	LTRA, n (%)	62	28 (43.7)
	Daily OCS, yes, n (%)	62	47 (75.8)
	Dose of prednisone (mg/d), median [IQR]	47	20 [10-30]

Previous treatments	Omalizumab, n (%)	62	52 (83.9)
	Mepolizumab, n (%)	62	10 (16.7)
	Bronchial thermoplasty, n (%)	60	4 (6.7)
	Immunosuppressive drugs, n (%)	60	7 (11.7)
	Research protocol, n (%)	61	15 (24.6)
Asthma control	Exacerbations during the 12 previous months, median [IQR] (3 missing data)	57	4 [3-9]
	Hospitalization in the past 12 mo: yes, n (%)	58	28 (48.3)
	ICU stay: yes, n (%)	28	5 (17.9)
	Hospitalizations, med [IQR]	26	2 [1-3]
	Non-scheduled visits in the past 12 mo: yes, n (%)	60	40 (66.7)
	Non-scheduled visits, median [IQR]	38	3 [2-6]
	ACT score, median [IQR]	44	12 [7-16]
Pulmonary function tests	FEV1/FVC (%), median [IQR]	50	58 [51-72]
	FEV1 (% predicted)	56	59 [46-78]
	FEV1 (mL), median [IQR]	54	1785 [1160-2250]
	TLC (% predicted)	21	115 [103-128]
	RV (% predicted)	21	158 [143-207]
Blood test	Total IgE level (kU/L), median [IQR]	40	214 [61-437]
	Max blood eosinophil count in previous year (/mm^3), median [IQR]	52	365 [215-870]
	Blood eosinophil count at baseline (/mm^3), median [IQR]	54	240 [100-470]
	Blood eosinophil count at baseline ≥150/mm^3, n (%)	64	34 (53.1)
	Blood eosinophil count at baseline ≥300/mm^3, n (%)	64	20 (31.3)

Main outcomes

	Asthma Control Test score	Number of exacerbations	FEV1 (mL)	FEV1 (%)	OCS dose[a]	ICS dose[a]
Analysis at 3 mo (N = 64)						
N	30	/	32	34	49	60
Baseline	11 [7-15]		1690 [1030-2115]	53 [42-71]	20 [10-30]	800 [800-1600]
3 mo	19 [13-22]		1864 [1205-2490]	67 [45-81]	10 [7-15]	800 [400-800]
Difference	7 [1-11]		230 [10-610]	8 [1-18]	−5 [−18 to 0]	0 [−360 to 0]
P-value	*P* < .001		*P* < .001	*P* < .001	*P* < .001	*P* < .001
Analysis at 6 mo (N = 61)						
N	39	/	43	45	45	57
Baseline	11 [6-16]		1550 [1010-2250]	55 [45-76]	20 [10-30]	800 [800-1600]
6 mo	20 [12-22]		2060 [1290-2490]	66 [53-92]	7 [0-15]	800 [600-800]
Difference	6 [2-9]		180 [−30 to 530]	9 [2-17]	−10 [−20 to −5]	0 [−320 to 0]
P-value	*P* < .001		*P* < .001	*P* < .001	*P* < .001	*P* < .001
Analysis at 12 mo (N = 51)						
N	32	41	39	42	37	47
Baseline	14 [7-16]	4 [2-7]	1780 [1190-2170]	58 [47-76]	20 [10-30]	800 [800-1600]
12 mo	22 [17-24]	1 [0-2]	1940 [1250-2670]	68 [58-88]	5 [0-7]	800 [400-800]
Difference	9 [5-12]	−3 [−5 to −2]	200 [−30 to 620]	10 [1-19]	−13 [−20 to −5]	0 [−800 to 0]
P-value	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001	*P* < .001

At least BEC ≥ 1500 once: 25%



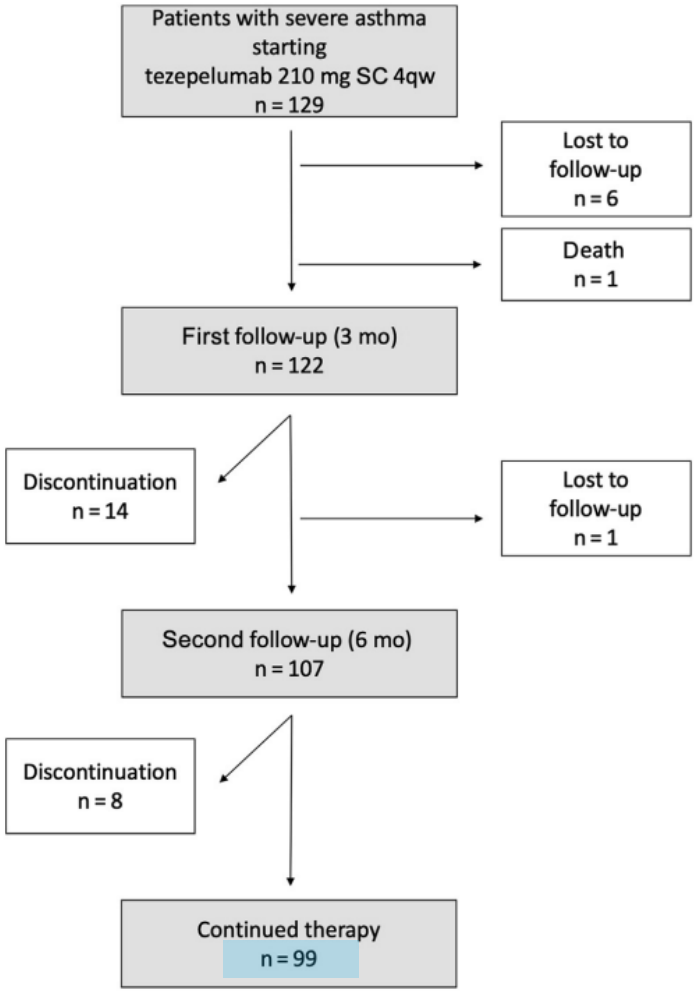
Anti-TSLP: Tezepelumab

Original Article

Real-World Data on Tezepelumab in Patients With Severe Asthma in Germany

Leonie Biener, MD[a,*], Carlo Mümmler, MD[b,*], Christopher Alexander Hinze, MD[c], Hendrik Suhling, MD[c], Stephanie Korn, MD[d], Christoph Fisser, MD[e], Arne Biener, MD[a], Carmen Pizarro, MD[a], Alexandra Lenoir, MD[b], Caroline Hackl, MD[b], Dirk Skowasch, MD[a,†], and Katrin Milger, MD[b,†] *Bonn, Munich, Hanover, Mainz, Heidelberg, and Regensberg, Germany*

Study population



Study Setup: Five German tertiary care centers
Timeframe: Patients started tezepelumab between November 1, 2022, and March 31, 2023;
Inclusion: No exclusion criteria
Treatment: All patients received 210 mg Tezepelumab SQ q4weeks
Data Points: Data were collected at four time points—before any biologic, baseline before tezepelumab, two months after starting tezepelumab, and six months after starting tezepelumab.

Outcomes measures: BARS

Variables	2 points	1 point	0 points
Reduction of exacerbations	Reduction ≥ 75% or 0 exacerbations	Reduction of 50%–74%	Reduction < 50%
Reduction of OCS	Reduction ≥ 75% or discontinuation	Reduction of 50%–74%	Reduction < 50%
Improvement in ACT	Improvement by 6 points or improvement ≥ 3 points and value ≥ 20 points	Improvement ≥ 3 points and value < 20 points	Improvement < 3 points
Second step: calculate mean value			
Good response	Mean value ≥ 1.5		
Response	Mean value 0.5 to < 1.5		
Insufficient response	Mean value < 0.5		

AE
OCS
ACT

Baseline characteristics

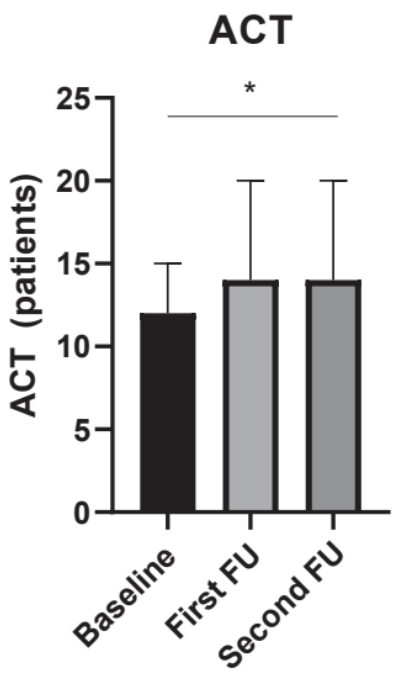
Age (y)	52.5 ± 13.1
Female	77 (59.7)
BMI (kg/m^2)	28.5 ± 6.3
Age at diagnosis (y)	28.9 ± 6.2
Smoking, pack-years	8.8 ± 12.3
Smoking: never	75 (58.1)
Smoking: ex	50 (38.8)
Smoking: current	4 (3.1)
Phenotypic characteristics	
T2-low	14 (10.9)
T2-high	111 (86.0)
T2-unknown	4 (3.1)
Nonallergic	41 (31.8)
Allergic	88 (68.2)
Eosinophilic	41 (31.8)
Adult-onset	77 (59.7)
Early-onset (<18 y of age)	42 (32.6)
Onset unknown	10 (7.8)

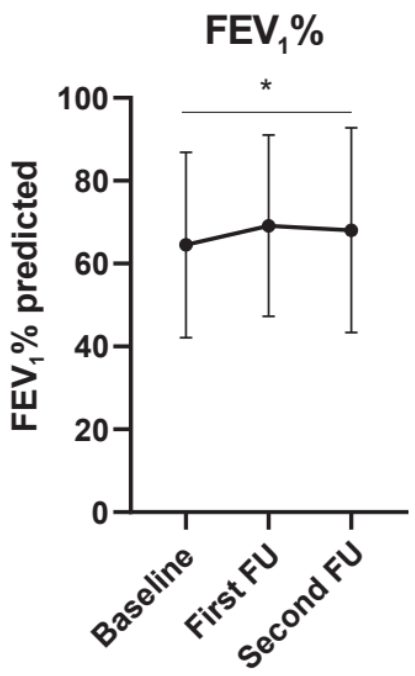
Comorbidities	
Atopic dermatitis	15 (11.6)
Allergic rhinitis	51 (39.5)
CRSwNP	23 (17.8)
CRSsNP	13 (10.1)
COPD	14 (10.9)
Bronchiectasis	15 (11.6)
ABPA	3 (2.3)
EAA	1 (0.8)
Number of previous biologics	
0	30 (23.3)
1	46 (35.7)
2	32 (24.8)
3	12 (9.3)
4	5 (3.9)
5	2 (1.6)

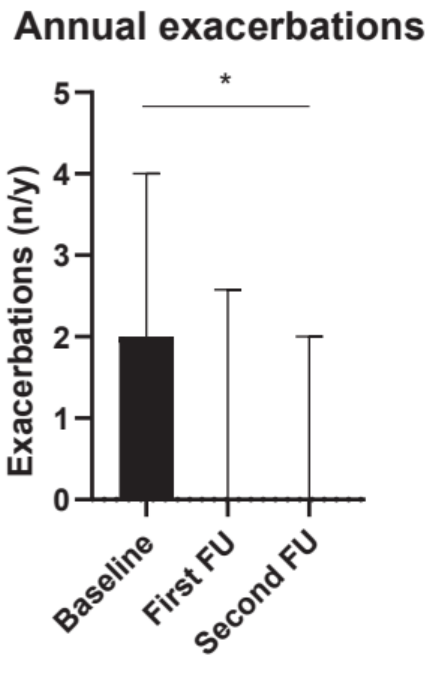
Baseline disease characteristics

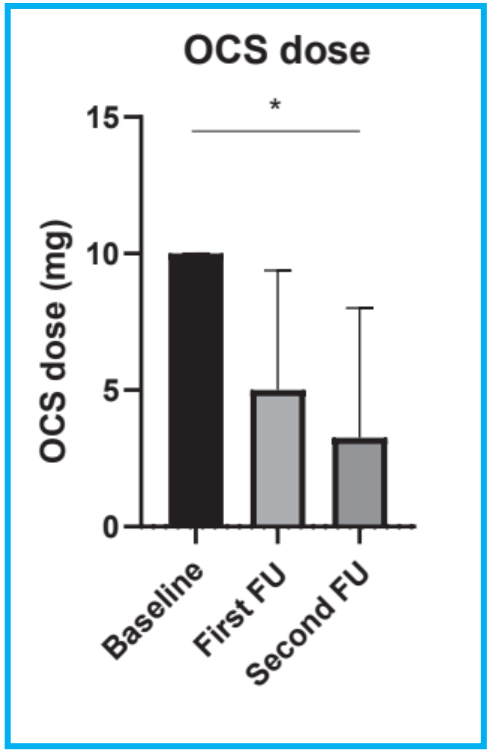
Pause between last biologic and tezepelumab (wk)	4 [2; 8]
ACT	12.0 [9.0; 15.5]
Annual exacerbations (overall)	1 [0; 4]
Annual exacerbations	
0	33 (25.6)
1	29 (22.5)
2	18 (14.0)
3	11 (8.5)
≥4	35 (27.1)
Missing	3 (2.3)
Pulmonary function test	
FEV_1 pre-BD (L)	2.1 ± 0.8
FEV_1 pre-BD (%)	64.8 ± 21.7
FVC (%)	74.9 ± 20.4
FEV_1/FVC	69.1 ± 15.4
RV (%)	133.1 ± 52.8
TLC (%)	96.6 ± 20.4
Laboratory findings	
Eosinophils (n/μL)†	120.0 [20.0; 310.0]
Eosinophils (%)†	1.4 [0.4; 3.6]
Neutrophils (n/μL)	5,736.7 ± 2,257.1
Basophils (n/μL)	62.0 ± 45.6
IgE (IU/mL)	157.5 [26.3; 362.0]
Medication	
Patients with long-term OCS therapy	48 (37.2)
OCS dose (prednisolone equivalent, mg)‡	10.0 [5.0; 10.0]
OCS duration (months)‡	24.0 [6.0; 90.0]
ICS low	3 (2.3)
ICS medium	18 (14.0)
ICS high	107 (82.9)
LABA	124 (96.1)
LAMA	111 (86.0)
Montelukast	46 (35.7)

Outcomes

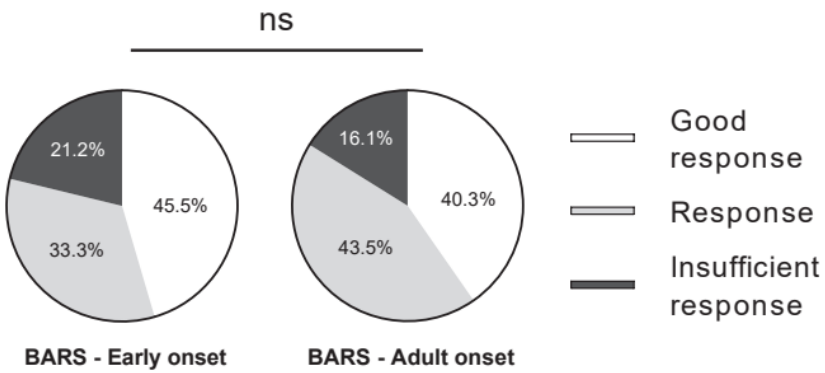

ACT
*
ACT (patients)
25
20
15
10
5
0
Baseline
First FU
Second FU

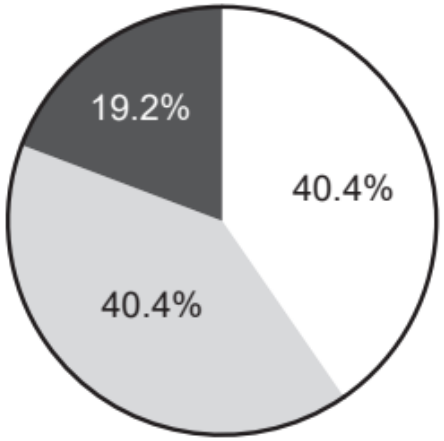

FEV1%
*
FEV1% predicted
100
80
60
40
20
0
Baseline
First FU
Second FU

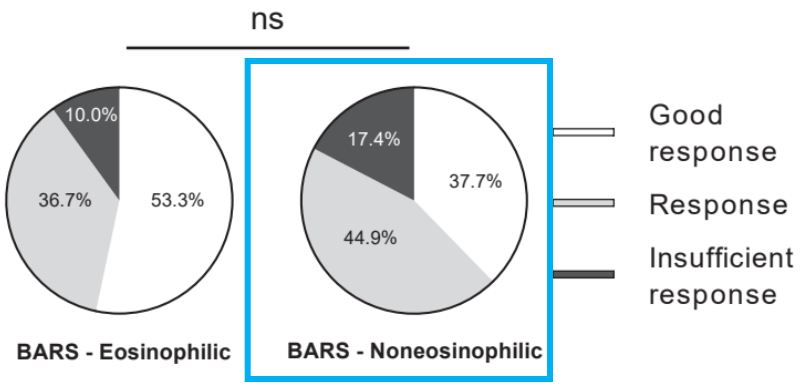

Annual exacerbations
*
Exacerbations (n/y)
5
4
3
2
1
0
Baseline
First FU
Second FU

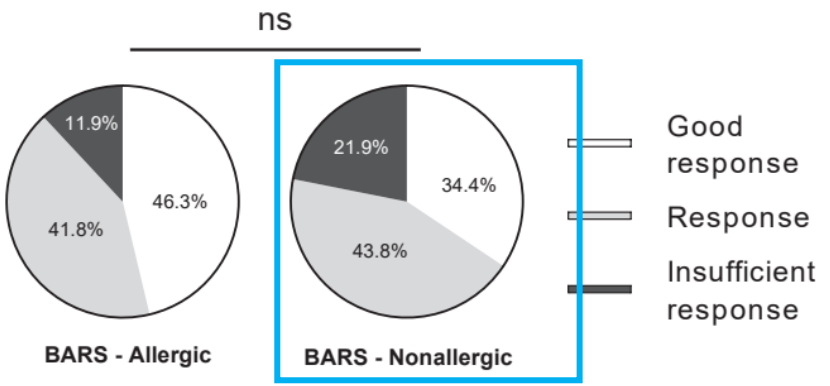

OCS dose
*
OCS dose (mg)
15
10
5
0
Baseline
First FU
Second FU

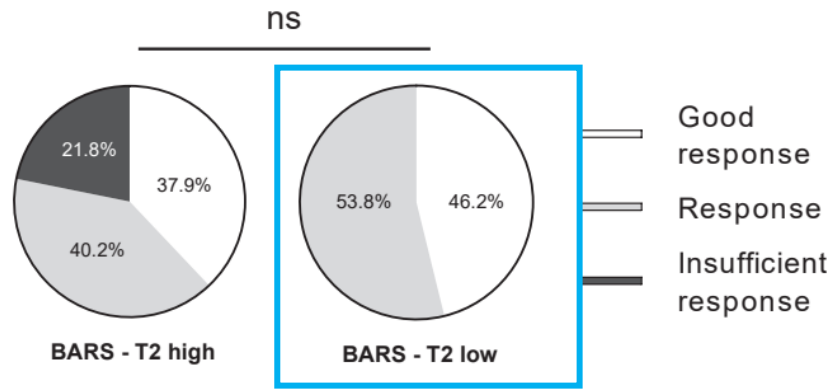
Outcomes

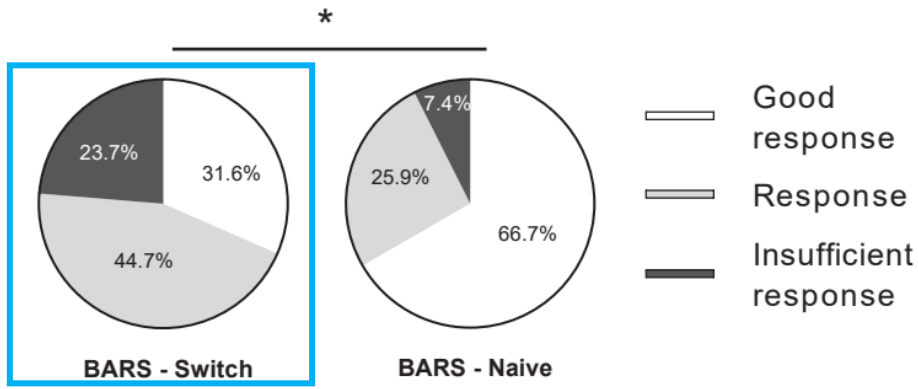

ns
21.2%
45.5%
33.3%
16.1%
40.3%
43.5%
BARS - Early onset
BARS - Adult onset
Good response
Response
Insufficient response


19.2%
40.4%
40.4%


ns
10.0%
36.7%
53.3%
17.4%
37.7%
44.9%
BARS - Eosinophilic
BARS - Noneosinophilic
Good response
Response
Insufficient response


ns
11.9%
46.3%
41.8%
21.9%
34.4%
43.8%
BARS - Allergic
BARS - Nonallergic
Good response
Response
Insufficient response


ns
21.8%
37.9%
40.2%
53.8%
46.2%
BARS - T2 high
BARS - T2 low
Good response
Response
Insufficient response


*
23.7%
31.6%
44.7%
7.4%
25.9%
66.7%
BARS - Switch
BARS - Naive
Good response
Response
Insufficient response

Contents

Omalizumab to Mepolizumab

ORIGINAL ARTICLE

Airway Diseases

Allergy EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY EAACI WILEY

The clinical benefit of mepolizumab replacing omalizumab in uncontrolled severe eosinophilic asthma

Kenneth R. Chapman[1] | Frank C. Albers[2] | Bradley Chipps[3] | Xavier Muñoz[4,5] | Gilles Devouassoux[6] | Miguel Bergna[7] | Dmitry Galkin[2] | Jay Azmi[8] | Dalal Mouneimne[9] | Robert G. Price[10] | Mark C. Liu[11]

Study population

Inclusion criteria

Patients aged ≥12 years (or ≥18 years if local regulations require).

Diagnosis of asthma for ≥1 year, as per National Heart, Lung, and Blood Institute or GINA guidelines.

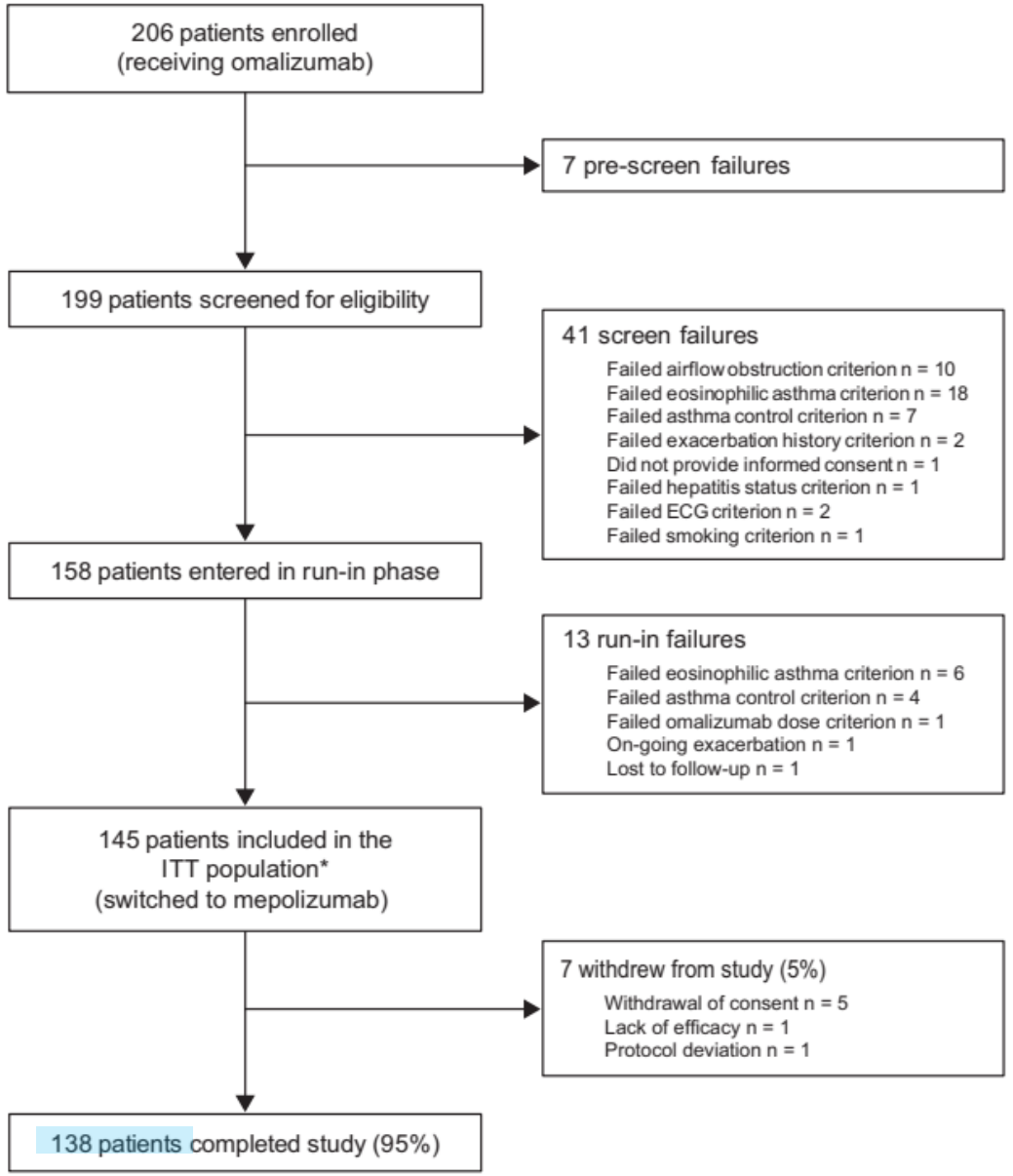
Peripheral blood eosinophil count of ≥150 cells/μL at Visit 1 or ≥300 cells/μL in the 12 months before Visit 1.

Asthma not optimally controlled with omalizumab treatment.

Exclusion criteria

Patients who achieved optimal asthma control within the last 12 months with omalizumab.

Patients who experienced fewer than two exacerbations while on omalizumab in the last year.



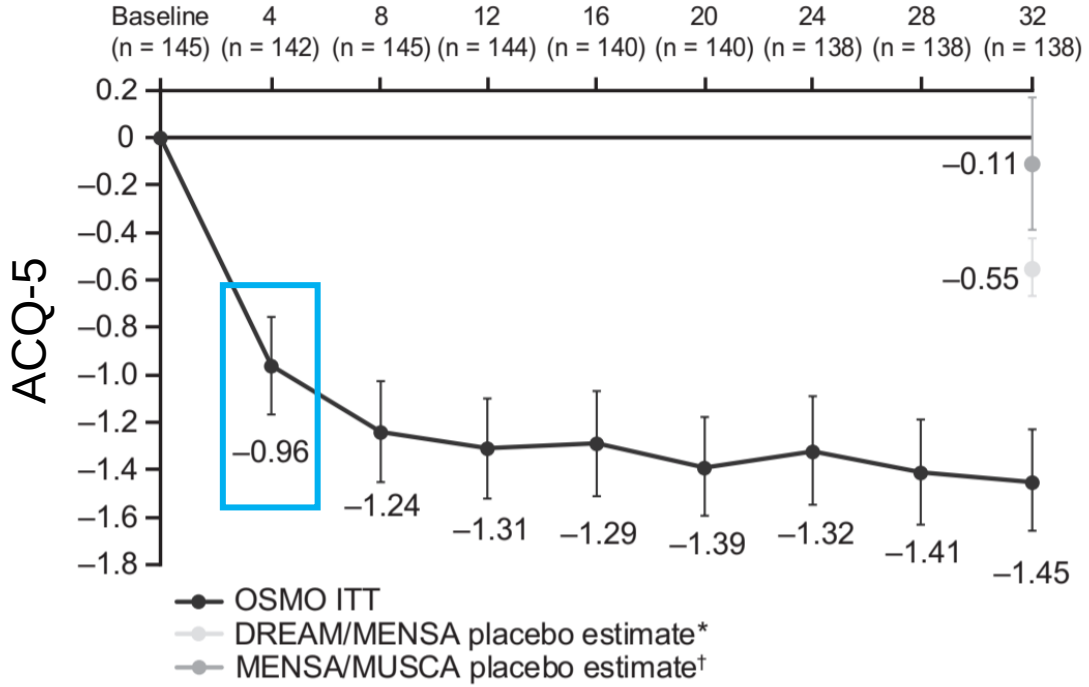
Baseline characteristics

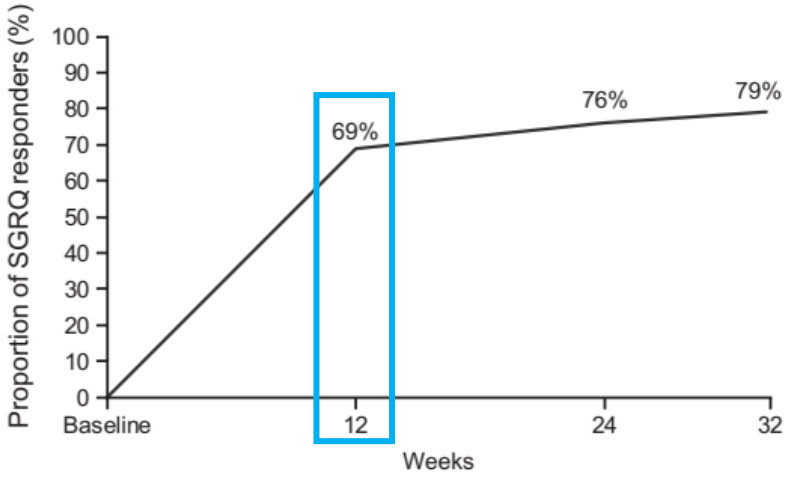
Age, years	
12-17, n (%)	2 (1)
18-64, n (%)	112 (77)
≥65, n (%)	31 (21)
Mean (SD)	53.6 (13.83)
Gender, female, n (%)	86 (59)
Race, n (%)	
White	128 (88)
Asian	5 (3)
Black or African American	11 (8)
Mixed	1 (<1)
Ethnicity, n (%)	
Non-Hispanic/Latino	107 (74)
Body mass index, kg/m^2, mean (SD)	30.2 (6.27)
Duration of asthma, years, mean (SD)	25.6 (16.81)
Allergy comorbidities	
Allergic rhinitis	29 (20)
Nasal polyps	20 (14)
Maintenance OCS use at baseline, n (%)	35 (24)
Median (range) dose, mg/day prednisolone equivalent	10 (4, 40)

Concurrent therapy use at baseline, n (%)	
ICS[a]	145 (100)
Mean (SD) dose, mcg/day fluticasone propionate (DPI) equivalent	997 (574)
LABA[b]	145 (100)
SABA	125 (86)
LTRA	70 (48)
LAMA	62 (43)
Xanthine	14 (10)
Exacerbations[c] in the past 12 mo	
Clinically significant exacerbations, mean (SD)	3.3 (2.65)
Exacerbations requiring ER/hospitalization, n (%)	43 (30)
Exacerbations requiring hospitalization, n (%)	17 (12)
Spirometry assessments at baseline, mean (SD)	
Prebronchodilator % of predicted FEV_1	59.5 (17.94)
Prebronchodilator FEV_1, L	1.76 (0.68)
Postbronchodilator FEV_1, L[d]	1.99 (0.80)
Prebronchodilator FEV_1/FVC	0.62 (0.13)
Postbronchodilator FEV_1/FVC[d]	0.65 (0.13)
FEV_1 reversibility, L	0.22 (0.26)

Baseline ACQ-5 score[e], mean (SD)	3.19 (0.937)
Baseline SGRQ total score[f], mean (SD)	56.6 (17.36)
Baseline blood eosinophil count, cells/µL	
Geometric mean (SD logs)	290 (1.135)
≥150 cells/µL at screening, n (%)	125 (86)
≥300 cells/µL in previous 12 mo, n (%)	96 (66)
Omalizumab therapy prior to treatment[g]	
Duration, months, median (range)	29.6 (4, 161)
Frequency of dose, n (%)	
Every 2 wk	75 (52)
Monthly	69 (48)
Monthly dose, mg, median (range)[h]	450.0 (100, 1200)

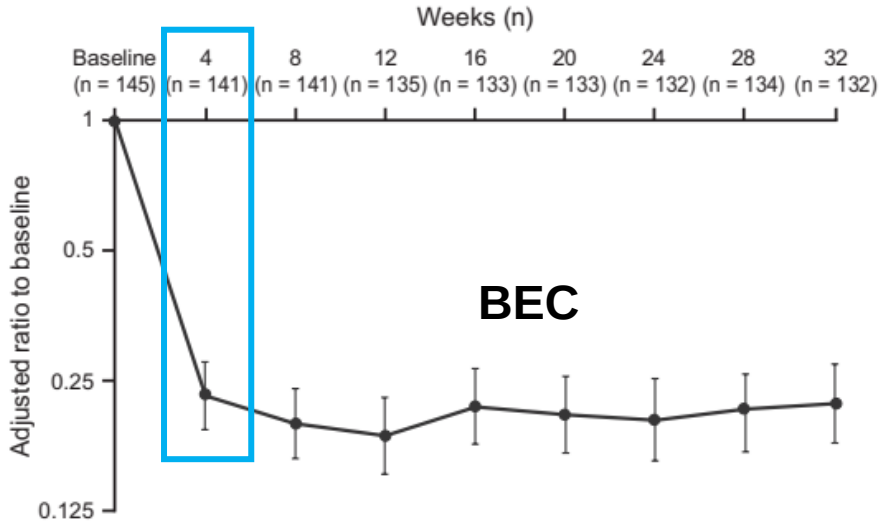
Symptoms





AE/BEC

	Mepolizumab 100 mg SC N = 145
Clinically significant exacerbations	
Pretreatment[c] annualized exacerbation rate	3.26
On-treatment[d] annualized exacerbation rate	1.18
Rate Ratio [On/Pretreatment] (95% CI)	0.36 (0.28, 0.47)[b]
Exacerbations requiring ER visit or hospitalization	
Pretreatment[c] annualized exacerbation rate	0.63
On-treatment[d] annualized exacerbation rate	0.19
Rate ratio [On/Pretreatment] (95% CI)	0.31 (0.18, 0.53)[b]
Exacerbations requiring hospitalization	
Pretreatment[c] annualized exacerbation rate	0.17
On-treatment[d] annualized exacerbation rate	0.12
Rate ratio [On/Pretreatment] (95% CI)	0.74 (0.40, 1.37)



Omalizumab to Benralizumab

biomedicines

MDPI

Article

Switch from Omalizumab to Benralizumab in Allergic Patients with Severe Eosinophilic Asthma: A Real-Life Experience from Southern Italy

Corrado Pelaia [1], Claudia Crimi [2], Santi Nolasco [2], Giovanna Elisiana Carpagnano [3], Raffaele Brancaccio [4], Enrico Buonamico [3], Raffaele Campisi [2], Claudia Gagliani [5], Vincenzo Patella [4], Girolamo Pelaia [1,*], Giuseppe Valenti [5] and Nunzio Crimi [2]

Study population

Inclusion criteria

Adults with severe, uncontrolled asthma

High BEC and high-dose ICS/LABA use with suboptimal symptom control on omalizumab

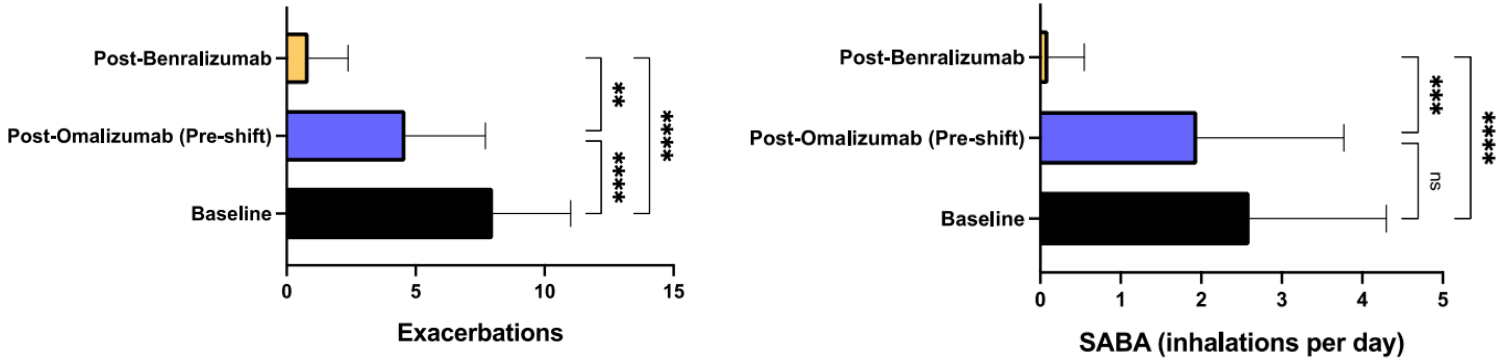
High serum IgE levels (30–1500 IU/mL) and sensitivity to perennial aeroallergens

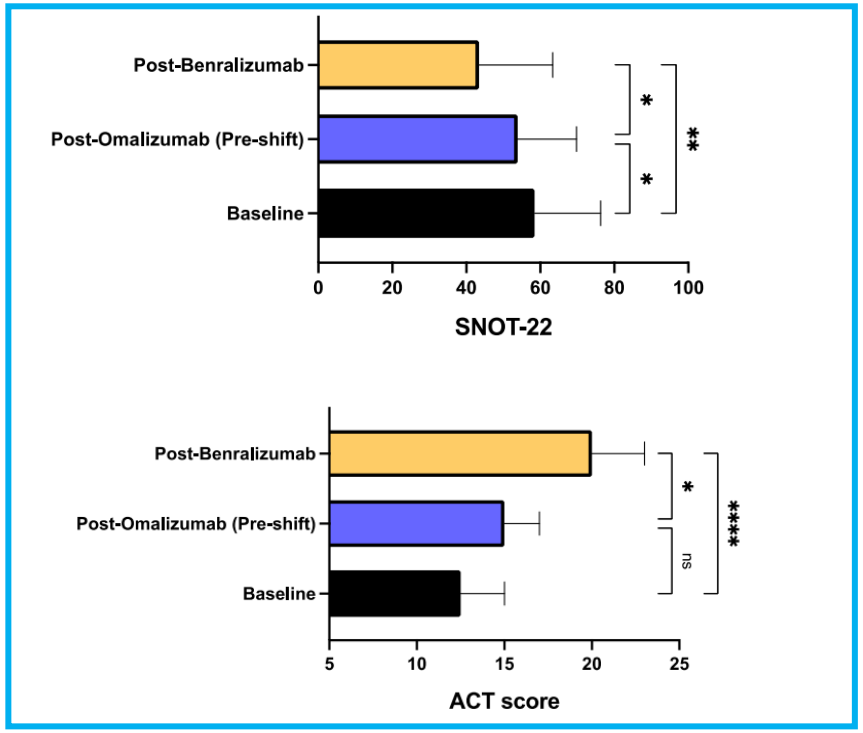
CRSwNP in some patients

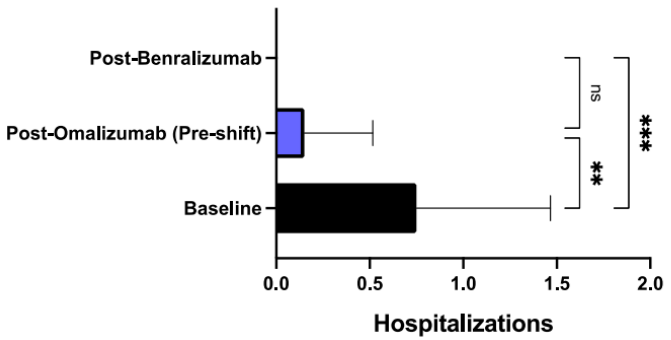
Defined omalizumab failure as lack of satisfactory control after ≥12 months, with recurrent exacerbations or ongoing symptoms

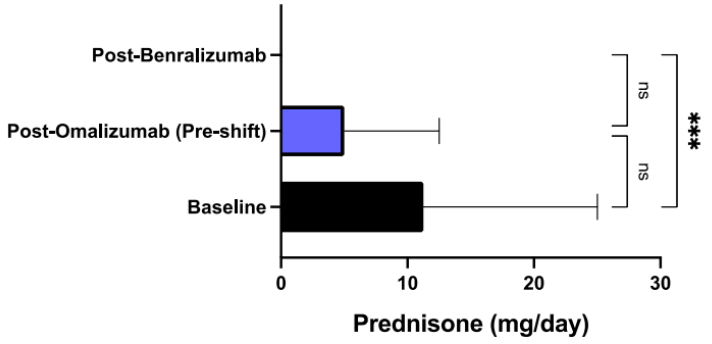
Characteristics	Total Population (N = 20)
Female gender, N (%)	13 (65)
Male gender, N (%)	7 (35)
Age, mean (±SD), years	52.85 ± 9.39
Asthma onset age, mean (±SD), years	31.40 ± 14.34
Duration of asthma, mean (±SD), years	21.85 ± 15.90
BMI, mean (±SD), % predicted	23.47 ± 3.54
FEV_1, mean (±SD), % predicted	62.47 ± 13.84
FEV_1/FVC, mean (±SD), %	61.15 ± 11.65
Blood eosinophils, median value (IQR), cells/μL	543.5 (360.0–1048)
Total serum IgE, median value (IQR), IU/mL	274.5 (198.8–412.8)
Gastro-esophageal reflux disease, N (%)	11 (55)
Chronic rhinosinusitis with nasal polyps, N (%)	9 (45)
Bronchiectasis, N (%)	7 (35)
Atopic dermatitis, N (%)	3 (15)
Obstructive sleep apnea syndrome, N (%)	2 (10)
On treatment with ICS/LABA, N (%)	20 (100)
On treatment with LAMA, N (%)	15 (75)
On treatment with LTRA drugs, N (%)	14 (70)

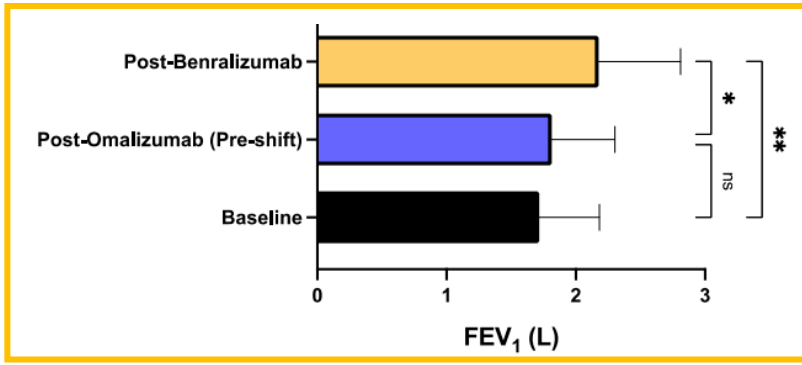
Outcomes

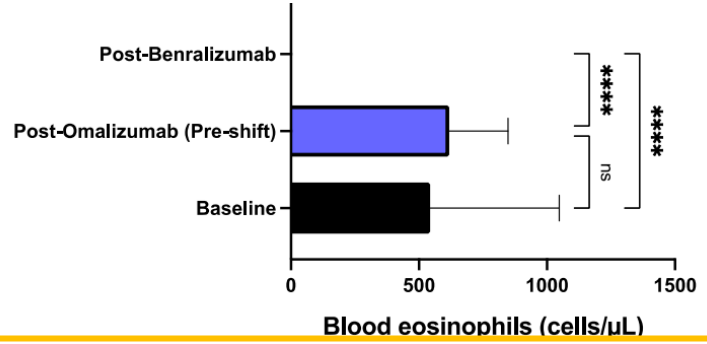

Post-Benralizumab
Post-Omalizumab (Pre-shift)
Baseline
0
5
10
15
Exacerbations
**
****
****
Post-Benralizumab
Post-Omalizumab (Pre-shift)
Baseline
0
1
2
3
4
5
SABA (inhalations per day)
***
ns
****


Post-Benralizumab
Post-Omalizumab (Pre-shift)
Baseline
0
20
40
60
80
100
SNOT-22
*
*
**
Post-Benralizumab
Post-Omalizumab (Pre-shift)
Baseline
5
10
15
20
25
ACT score
*
ns
****


Post-Benralizumab
Post-Omalizumab (Pre-shift)
Baseline
0.0
0.5
1.0
1.5
2.0
Hospitalizations
ns
**
***


Post-Benralizumab
Post-Omalizumab (Pre-shift)
Baseline
0
10
20
30
Prednisone (mg/day)
ns
ns
***


Post-Benralizumab
Post-Omalizumab (Pre-shift)
Baseline
0
1
2
3
FEV1 (L)
*
ns
**


Post-Benralizumab
Post-Omalizumab (Pre-shift)
Baseline
0
500
1000
1500
Blood eosinophils (cells/µL)
****
ns
****

Mepolizumab to Benralizumab

DOI: 10.1111/all.14693

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

Study population

We retrospectively assessed **33 patients** with SEA treated at our specialist centre, who were switched from mepolizumab to benralizumab following a sub-optimal response

Sub-optimal response

Failing to 1) ≥50% reduction in mOCS dose; 2) ≥50% reduction in annualized exacerbation rate (AER);

Ongoing requirement of ≥ 7.5 mg PD/day or an AER of ≥3

Clinical outcomes

	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

Anti-IgE/IL-5/IL-5R to Dupilumab

Original Article

Dupilumab Improves Asthma Control and Lung Function in Patients with Insufficient Outcome During Previous Antibody Therapy

Carlo Mümmler, MD[a,b], Dieter Munker, MD[a,b], Michaela Barnikel, MD[a,b], Tobias Veit, MD[a,b], Moritz Z. Kayser, MD[c], Tobias Welte, MD, PhD[c], Jürgen Behr, MD[a,b], Nikolaus Kneidinger, MD, PhD[a,b], Hendrik Suhling, MD[c,*], and Katrin Milger, MD[a,b,*] *Munich and Hanover, Germany*

Study population/Baseline characteristics

Retrospective Single Center Study

Of 454 severe asthmatics treated with biologics,

38 patients (8.4%) were enrolled

Inclusion Criteria

Severe asthma-ATS/ERS

Former anti-IgE or anti-IL-5/anti-IL-5R ≥ 3 months

Switch to dupilumab < 6 months

Age (y), mean ± SD	55 ± 12
Female, n (%)	22 (58)
Male, n (%)	16 (42)
BMI (kg/m^2), median (IQR)	25 (22-31)
Age at asthma diagnosis (y), median (IQR)*	25 (10-47)
Time since asthma diagnosis (y), median (IQR)*	27 (10-42)
Allergies, n (%)	29 (76)
Polysensitization, n (%)	19 (50)
Former smokers, n (%)	10 (26)
Comorbidities, n (%)	
ENT comorbidities	28 (74)
Nasal polyposis	18 (47)
Allergic rhinitis	18 (47)
Chronic sinusitis without nasal polyps	10 (26)
Atopic dermatitis	12 (32)
Aspirin intolerance	7 (18)
Steroid-induced side effects	16 (42)

Clinical Characteristics

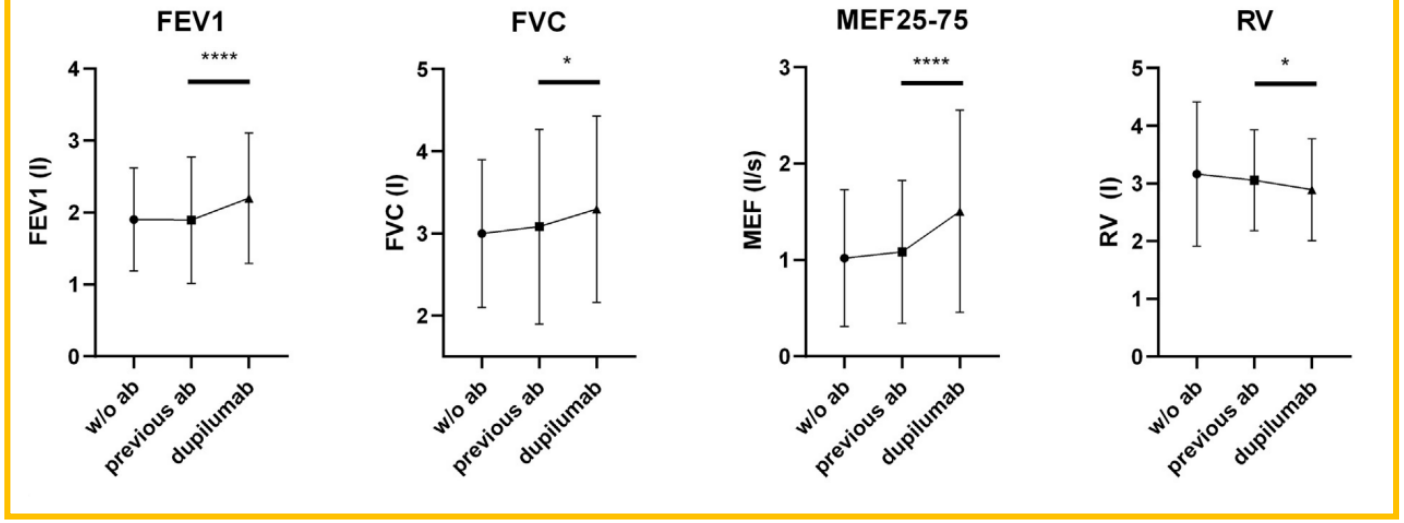
	Pre-antibody	During antibody (IgE, IL5/5R)
Medication, n (%)		
ICS/LABA (high)	27 (75)*	31 (82)
ICS/LABA (medium)	9 (25)*	7 (18)
LAMA	29 (81)*	33 (87)
LTRA	22 (61)*	23 (61)
OCS	23 (64)*	15 (39)
Dose of prednisolone (mg), median (IQR) in patients with baseline OCS	10 (5-15)	4 (0-10)
Previous biologic, n (%)	—	
Mepolizumab	—	11 (29)
Benralizumab	—	19 (50)
Reslizumab	—	2 (5)
Omalizumab	—	6 (16)
Duration of previous biological therapy (mo), median (IQR)		10 (7-14)
Asthma control and exacerbations		
ACT score, mean ± SD	12 ± 5†	14 ± 5‡
Number of patients with exacerbations before/during previous antibody therapy, n (%)	23 (60)§	21 (55)
Calculated number of annualized exacerbations during previous antibody therapy, median (IQR)	2 (1-4)	0.8 (0.0-2.4)

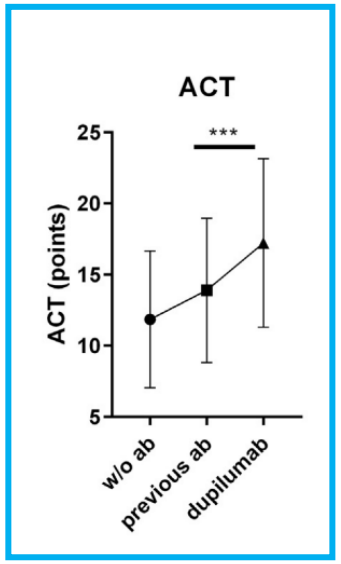
Clinical Characteristics

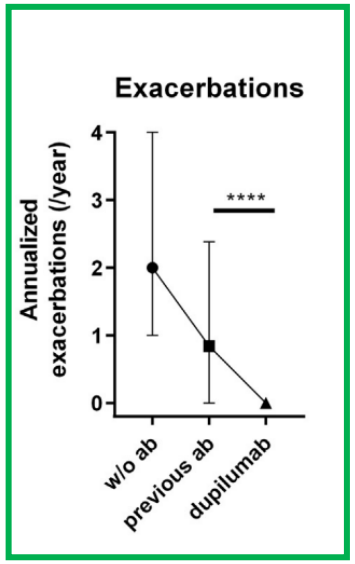
	Pre-antibody	During antibody (IgE, IL5/5R)
Lung function, mean ± SD		
FEV_1 (L)	1.90 ± 0.70*	1.89 ± 0.87
FEV_1 % predicted	62% ± 20%*	60% ± 22%
FVC (L)	3.00 ± 0.89*	3.08 ± 1.2
FVC % predicted	80.3% ± 18%*	81% ± 20%
RV (L)	3.17 ± 1.23*	3.06 ± 0.86
RV % predicted	158% ± 58%*	144% ± 34%
TLC (L)	6.38 ± 1.37	6.34 ± 1.34
TLC % predicted	107 ± 20	105 ± 14
FEV_1/FVC, mean ± SD	0.62 ± 0.12	0.60 ± 0.12
MEF25-75 (L/s)	1.02 ± 0.70*	1.08 ± 0.73*
MEF25-75 % predicted	33% ± 29%*	32% ± 21%*
Reff (kPa × s/L)	NA	0.50 ± 0.35‖
Reff % predicted	NA	163% ± 115%‖
Biomarker		
FENO (ppb), median (IQR)	52 (30-129)¶	55 (29-99)‡
Eosinophils (G/L), median (IQR)—all patients	0.41 (0.21-0.62)	0.04 (0.00-0.18)‡
Eosinophils (G/L), in patients with anti−IL-5/anti−IL-5Rα therapy, median (IQR)#	0.48 (0.23-0.68)	0.0 (0.0-0.13)
Eosinophils (G/L), median (IQR) in patients with anti-IgE therapy**	0.21 (0.15-0.62)	0.2 (0.16-0.42)
IgE (IU/mL), median (IQR)—all patients	333 (53-534)	
IgE (IU/mL), in patients with anti−IL-5/anti−IL-5Rα therapy, median (IQR)§	148 (52-496)	186 (49-365)
IgE (IU/mL), in patients with anti-IgE therapy, median (IQR)**	344 (55-4340)	

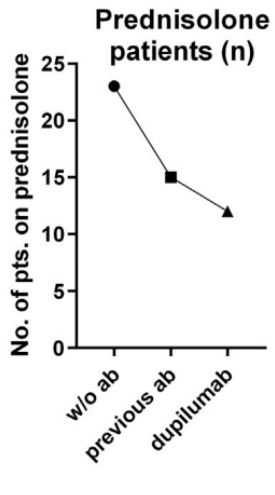
Switching Indication & Results

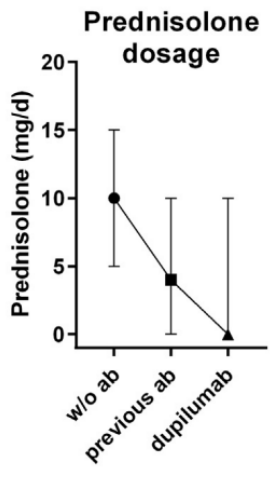
Indication for switch to dupilumab, n (%)	n = 38
Insufficient subjective response	32 (84)
Insufficient reduction in exacerbations	18 (47)
Insufficient change in lung function	26 (68)
Insufficient response of comorbidities	11 (29)
Insufficient change in symptoms of nasal polyposis	8 (21)
Insufficient reduction in OCS	12 (32)
Persistent eosinophilia	5 (13)
Persistent allergic symptoms	2 (5)
Side effect of previous antibody	1 (3)

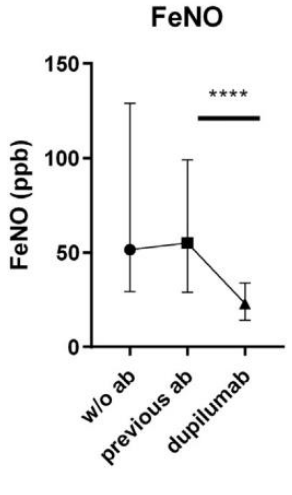


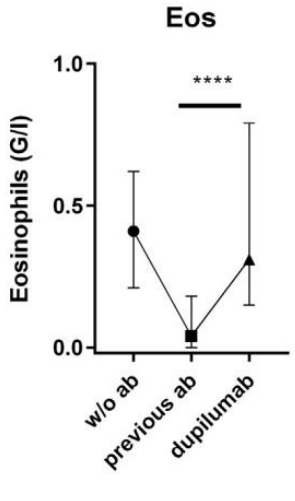


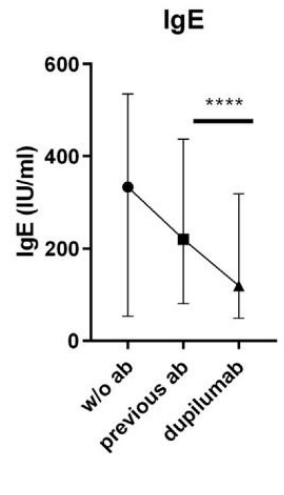






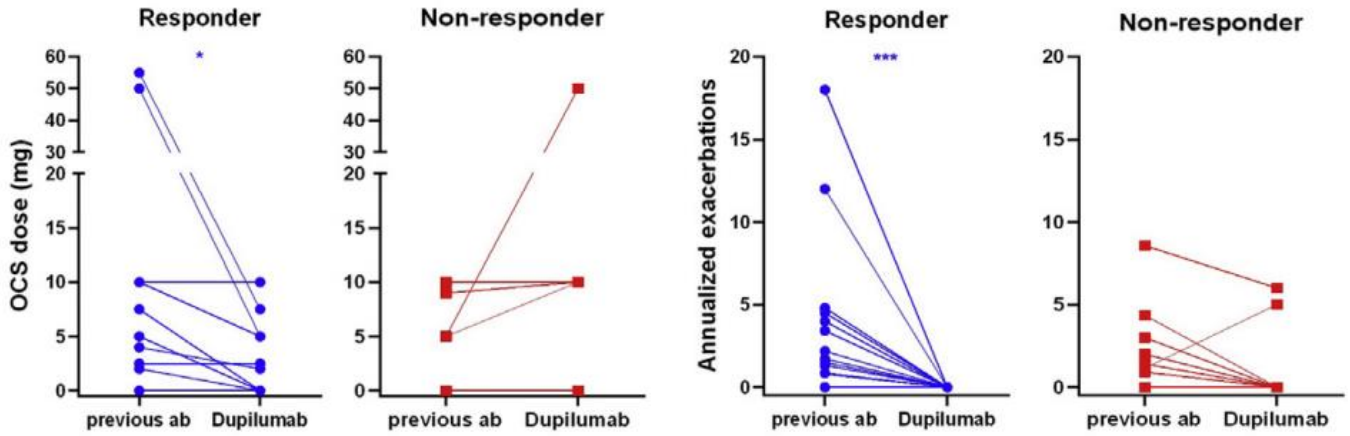


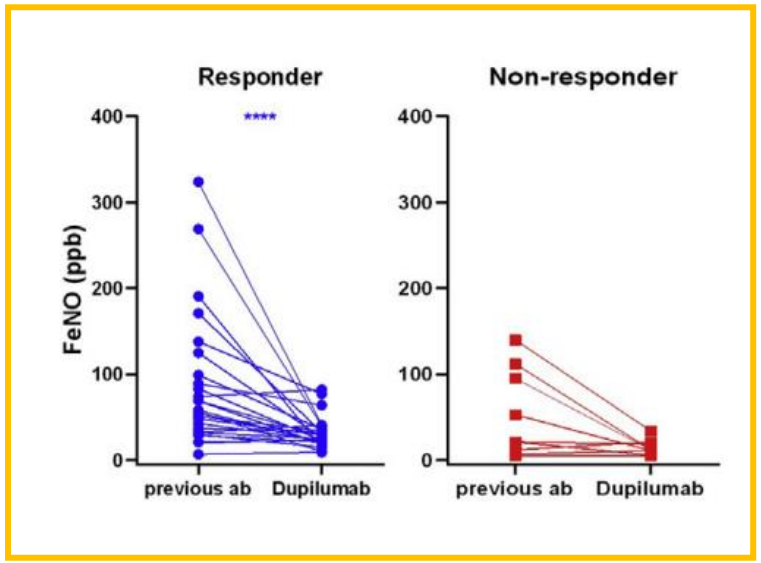


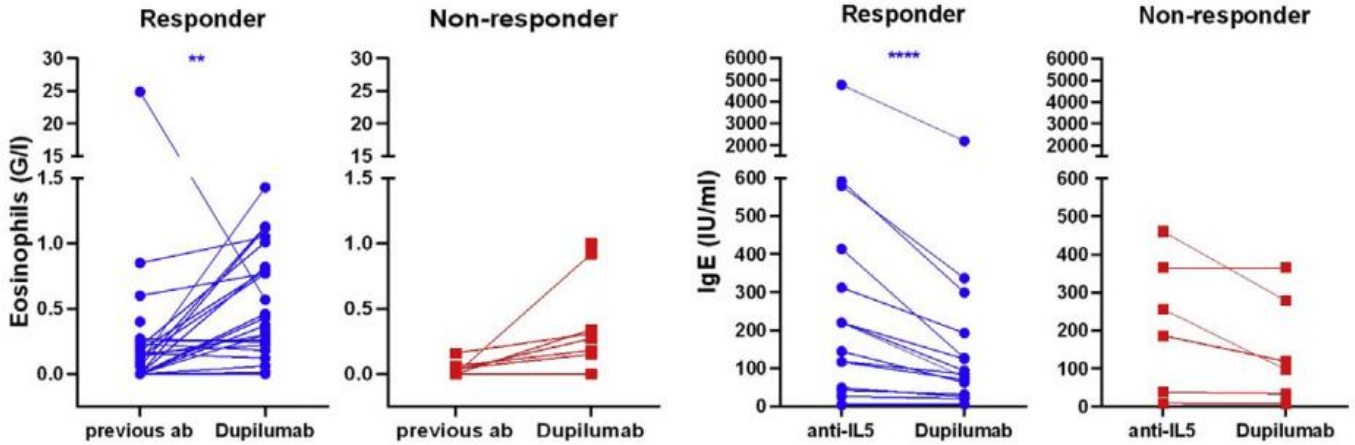


Response indication/responders

Classification of response to dupilumab	
Group	**n = 38**
Responder group, n (% of all patients)	n = 29 (76%)
ACT score increase (≥3 points),	12 (32)
FEV_1 increase (≥150 mL)	24 (63)
OCS reduction (≥50%)	7 (47)
Response of comorbidities	10 (26)
Nonresponder group	n = 9 (24%)
ACT score reduction (≥3 points)	2 (5)
FEV_1 reduction (≥150 mL)	3 (8)
OCS increase (>50%)	4 (27)
Increase in exacerbations	1 (3)







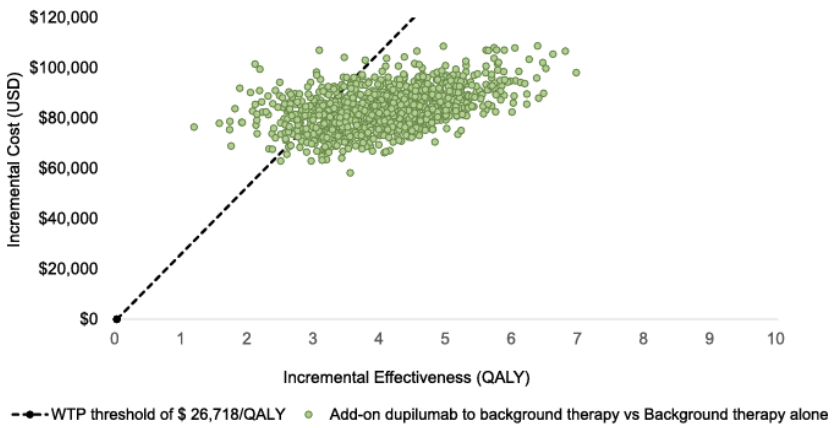
Contents

Biologics – cost issue

RESEARCH Open Access

Cost-effectiveness analysis of dupilumab among patients with uncontrolled severe asthma using LIBERTY ASTHMA QUEST Korean data

Sung-Hee Oh[1], Chin Kook Rhee[2], Eun Jin Bae[3] and Hyemin Ku[4*]



"중증 천식 환자, 급여제한으로 부작용 높은 약물 의존"

방혜림 기자 | 입력 2024.11.06 06:01 | 댓글 0

호산구성 천식 생물학적 제제 세부 급여기준

① 치료 시작 전 12개월 이내에 혈중 호산구 수치가 300cells/㎕ 이상이면서 치료 시작 전 12개월 이내에 전신 코르티코스테로이드가 요구되는 천식 급성악화가 4번 이상 발생했거나, 치료 시작 6개월 전부터 프레드니솔론(prednisolone) 5㎎/day와 동등한 수준 이상의 경구용 코르티코스테로이드를 지속 투여한 경우

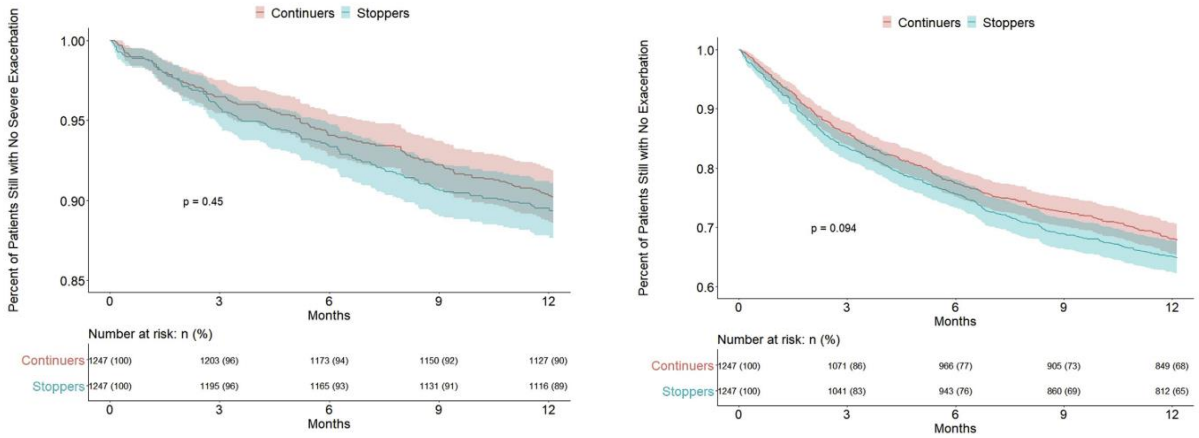
② 치료 시작 전 12개월 이내에 혈중 호산구 수치가 400cells/㎕ 이상이면서 치료 시작 전 12개월 이내에 전신 코르티코스테로이드가 요구되는 천식 급성 악화가 3번 이상 발생한 경우

Biologics – Duration/Discontinuation

Original Article

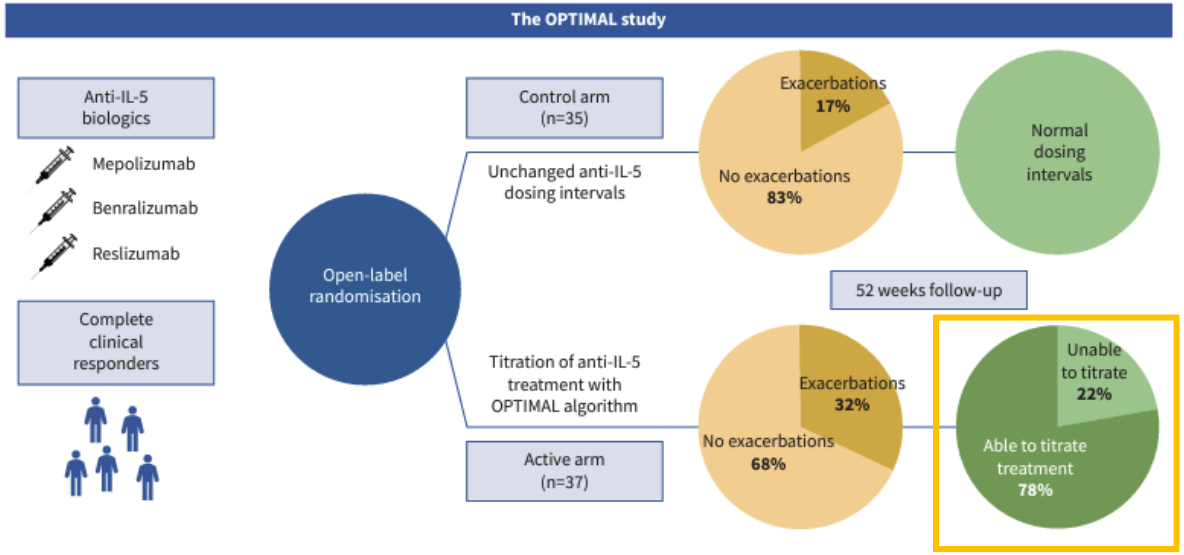
Asthma Patients Who Stop Asthma Biologics Have a Similar Risk of Asthma Exacerbations as Those Who Continue Asthma Biologics

Molly M. Jeffery, PhD[a], Jonathan W. Inselman, MS[b], Jacob T. Maddux, MD[c], Regina W. Lam, BA[d], Nilay D. Shah, PhD[a,b,e], and Matthew A. Rank, MD[b,f,g] *Rochester, Minn; Phoenix and Scottsdale, Ariz; and Cambridge, Mass*



Titration of anti-IL-5 biologics in severe asthma: an open-label randomised controlled trial (the OPTIMAL study)

Marianne Baastrup Soendergaard, Anne-Sofie Bjerrum, Linda Makowska Rasmussen, Sofie Lock-Johansson, Ole Hilberg, Susanne Hansen, Anna von Bulow and Celeste Porsbjerg



Summary

RCTs vs. RWDs

Duration/Inclusion criteria

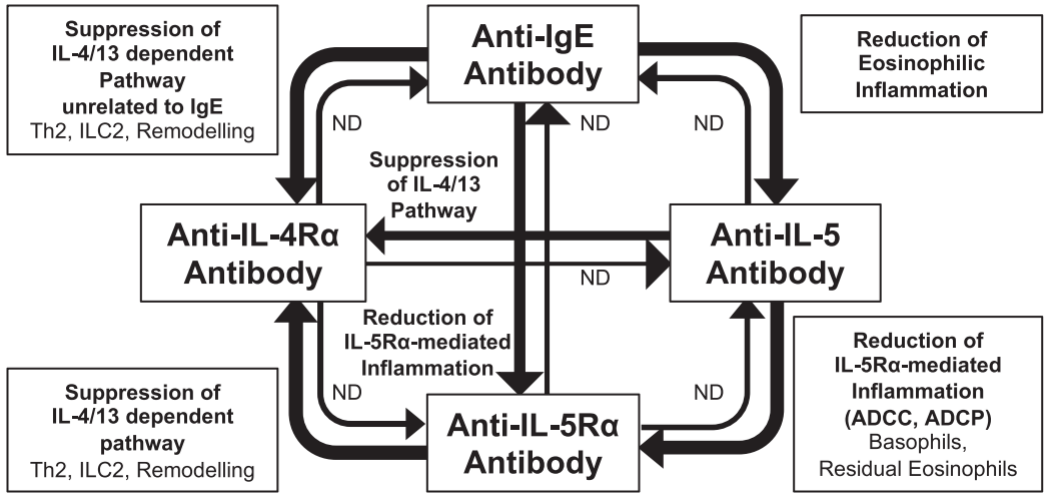
Other biologics permitted

Findings from RWDs

Mostly positive over 52 weeks

Previous biologics use: can be candidates

Biologics switching



Future RWDs

Cost & Dose interval