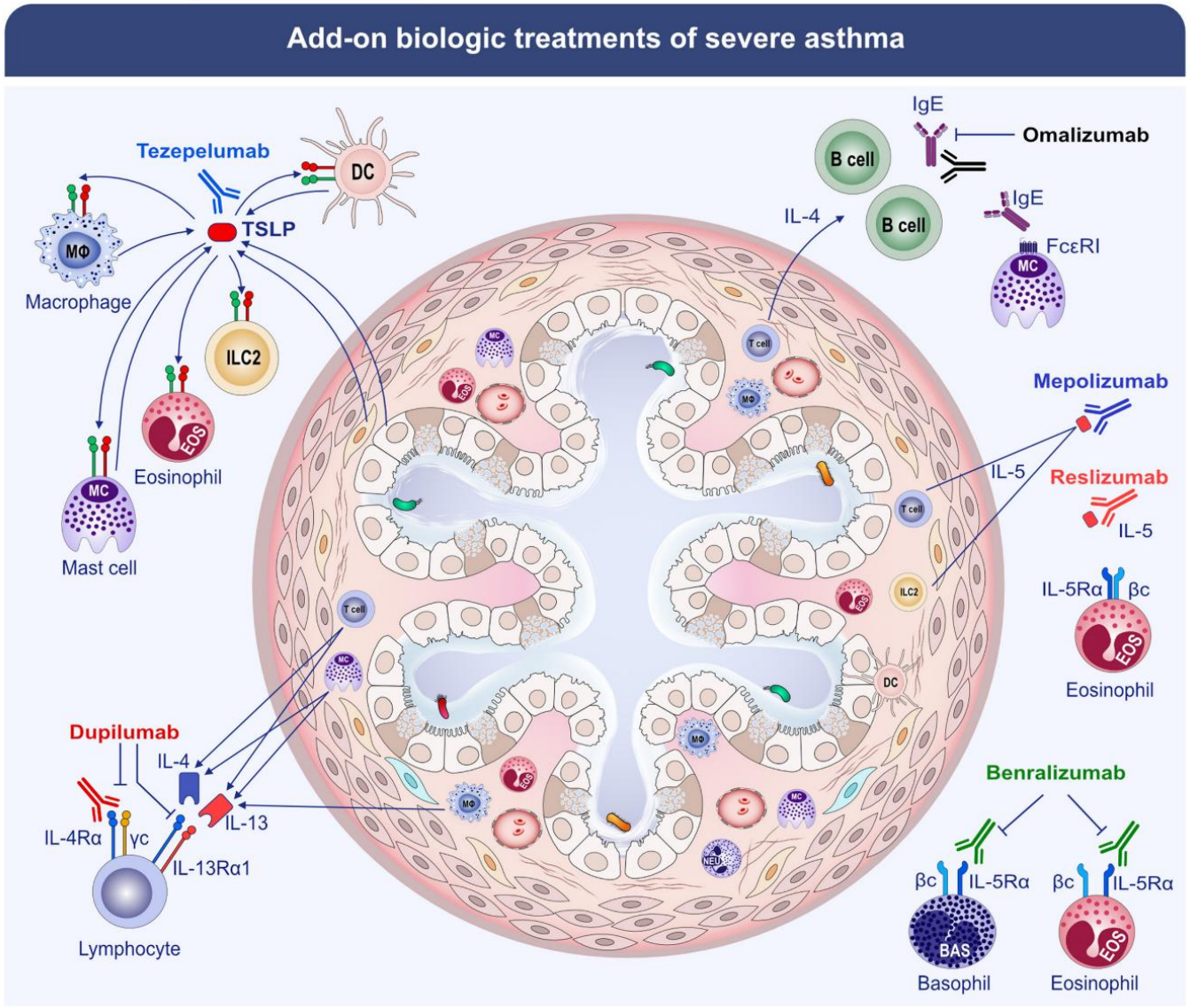
Severe Eosinophilic Asthma:

Endotyping and Comprehensive Treatment Strategies

가톨릭대학교
최준영

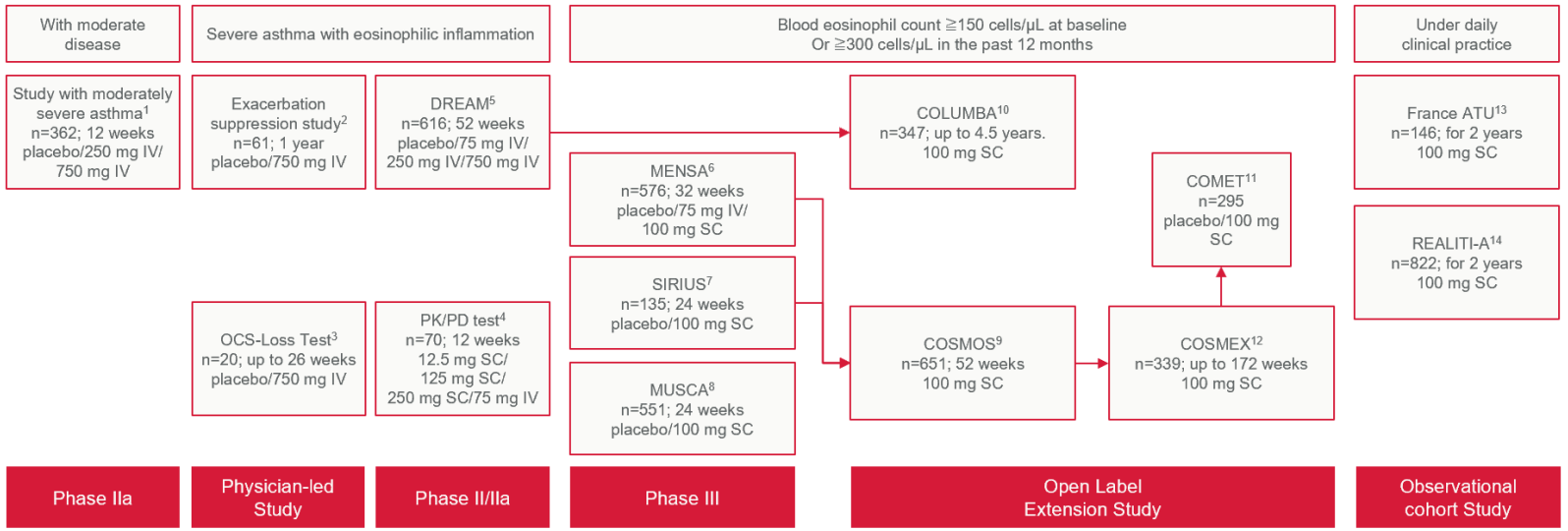
Success of T2-targeting biologics in asthma



Allergy. 2022 Dec;77(12):3538-3552.

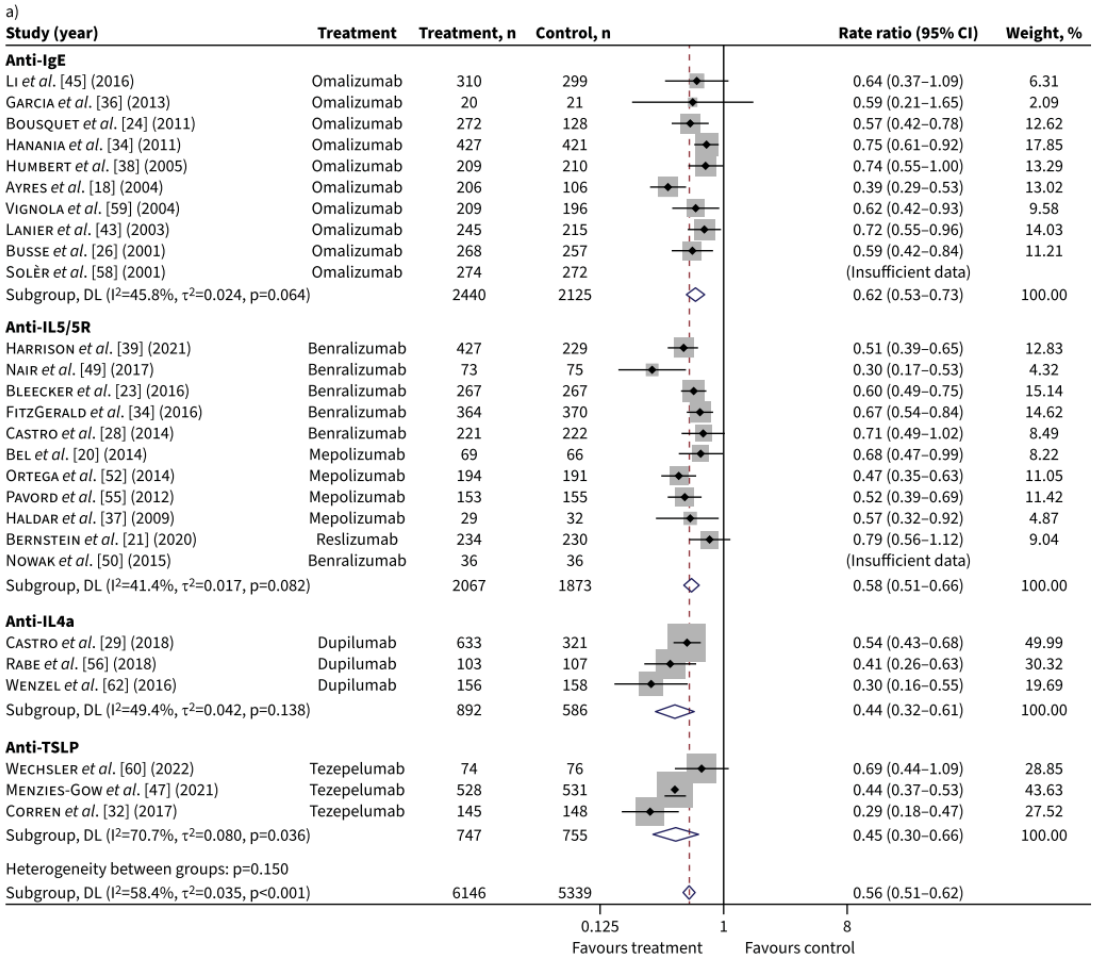
Mepolizumab

Benralizumab



Success of T2-targeting biologics in asthma

Exacerbation

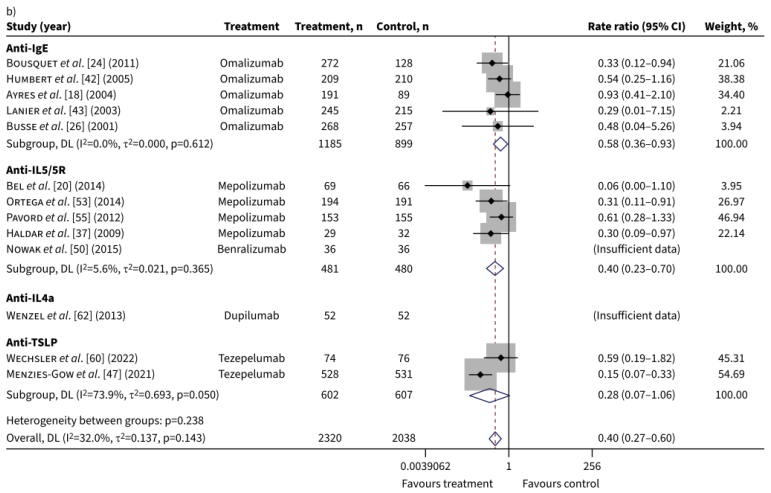


a)

Study (year)	Treatment	Treatment, n	Control, n	Rate ratio (95% CI)	Weight, %
Anti-IgE					
Li *et al.* [45] (2016)	Omalizumab	310	299	0.64 (0.37–1.09)	6.31
Garcia *et al.* [36] (2013)	Omalizumab	20	21	0.59 (0.21–1.65)	2.09
Bousquet *et al.* [24] (2011)	Omalizumab	272	128	0.57 (0.42–0.78)	12.62
Hanania *et al.* [34] (2011)	Omalizumab	427	421	0.75 (0.61–0.92)	17.85
Humbert *et al.* [38] (2005)	Omalizumab	209	210	0.74 (0.55–1.00)	13.29
Ayres *et al.* [18] (2004)	Omalizumab	206	106	0.39 (0.29–0.53)	13.02
Vignola *et al.* [59] (2004)	Omalizumab	209	196	0.62 (0.42–0.93)	9.58
Lanier *et al.* [43] (2003)	Omalizumab	245	215	0.72 (0.55–0.96)	14.03
Busse *et al.* [26] (2001)	Omalizumab	268	257	0.59 (0.42–0.84)	11.21
Solèr *et al.* [58] (2001)	Omalizumab	274	272	(Insufficient data)	
Subgroup, DL (I^2=45.8%, τ^2=0.024, p=0.064)		2440	2125	0.62 (0.53–0.73)	100.00
Anti-IL5/5R					
Harrison *et al.* [39] (2021)	Benralizumab	427	229	0.51 (0.39–0.65)	12.83
Nair *et al.* [49] (2017)	Benralizumab	73	75	0.30 (0.17–0.53)	4.32
Bleecker *et al.* [23] (2016)	Benralizumab	267	267	0.60 (0.49–0.75)	15.14
FitzGerald *et al.* [34] (2016)	Benralizumab	364	370	0.67 (0.54–0.84)	14.62
Castro *et al.* [28] (2014)	Benralizumab	221	222	0.71 (0.49–1.02)	8.49
Bel *et al.* [20] (2014)	Mepolizumab	69	66	0.68 (0.47–0.99)	8.22
Ortega *et al.* [52] (2014)	Mepolizumab	194	191	0.47 (0.35–0.63)	11.05
Pavord *et al.* [55] (2012)	Mepolizumab	153	155	0.52 (0.39–0.69)	11.42
Haldar *et al.* [37] (2009)	Mepolizumab	29	32	0.57 (0.32–0.92)	4.87
Bernstein *et al.* [21] (2020)	Reslizumab	234	230	0.79 (0.56–1.12)	9.04
Nowak *et al.* [50] (2015)	Benralizumab	36	36	(Insufficient data)	
Subgroup, DL (I^2=41.4%, τ^2=0.017, p=0.082)		2067	1873	0.58 (0.51–0.66)	100.00
Anti-IL4a					
Castro *et al.* [29] (2018)	Dupilumab	633	321	0.54 (0.43–0.68)	49.99
Rabe *et al.* [56] (2018)	Dupilumab	103	107	0.41 (0.26–0.63)	30.32
Wenzel *et al.* [62] (2016)	Dupilumab	156	158	0.30 (0.16–0.55)	19.69
Subgroup, DL (I^2=49.4%, τ^2=0.042, p=0.138)		892	586	0.44 (0.32–0.61)	100.00
Anti-TSLP					
Wechsler *et al.* [60] (2022)	Tezepelumab	74	76	0.69 (0.44–1.09)	28.85
Menzies-Gow *et al.* [47] (2021)	Tezepelumab	528	531	0.44 (0.37–0.53)	43.63
Corren *et al.* [32] (2017)	Tezepelumab	145	148	0.29 (0.18–0.47)	27.52
Subgroup, DL (I^2=70.7%, τ^2=0.080, p=0.036)		747	755	0.45 (0.30–0.66)	100.00
Heterogeneity between groups: p=0.150					
Subgroup, DL (I^2=58.4%, τ^2=0.035, p<0.001)		6146	5339	0.56 (0.51–0.62)	

0.125 1 8
Favours treatment Favours control

Hospitalization

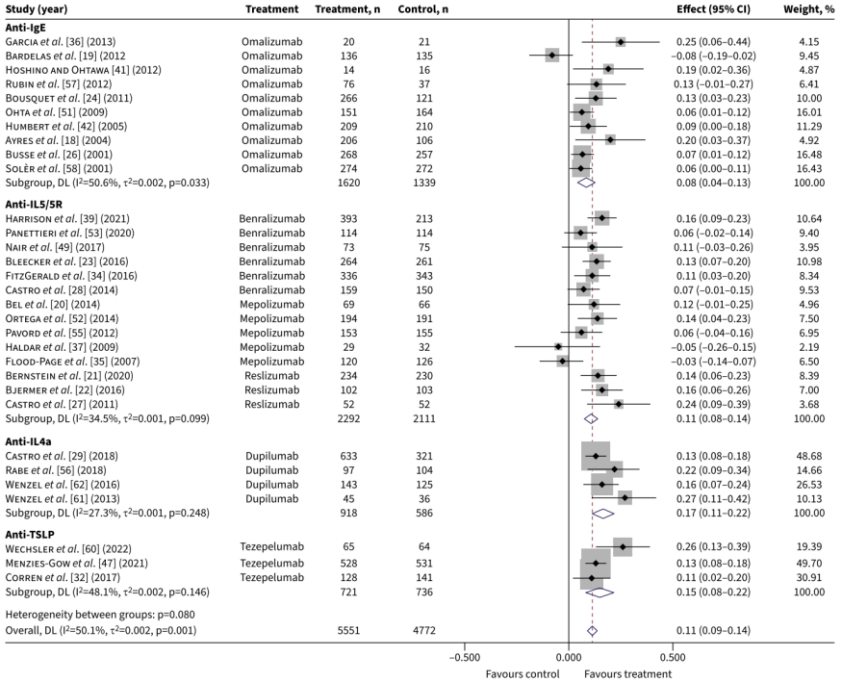


b)

Study (year)	Treatment	Treatment, n	Control, n	Rate ratio (95% CI)	Weight, %
Anti-IgE					
Bousquet *et al.* [24] (2011)	Omalizumab	272	128	0.33 (0.12–0.94)	21.06
Humbert *et al.* [42] (2005)	Omalizumab	209	210	0.54 (0.25–1.16)	38.38
Ayres *et al.* [18] (2004)	Omalizumab	191	89	0.93 (0.41–2.10)	34.40
Lanier *et al.* [43] (2003)	Omalizumab	245	215	0.29 (0.01–7.15)	2.21
Busse *et al.* [26] (2001)	Omalizumab	268	257	0.48 (0.04–5.26)	3.94
Subgroup, DL (I^2=0.0%, τ^2=0.000, p=0.612)		1185	899	0.58 (0.36–0.93)	100.00
Anti-IL5/5R					
Bel *et al.* [20] (2014)	Mepolizumab	69	66	0.06 (0.00–1.10)	3.95
Ortega *et al.* [53] (2014)	Mepolizumab	194	191	0.31 (0.11–0.91)	26.97
Pavord *et al.* [55] (2012)	Mepolizumab	153	155	0.61 (0.28–1.33)	46.94
Haldar *et al.* [37] (2009)	Mepolizumab	29	32	0.30 (0.09–0.97)	22.14
Nowak *et al.* [50] (2015)	Benralizumab	36	36	(Insufficient data)	
Subgroup, DL (I^2=5.6%, τ^2=0.021, p=0.365)		481	480	0.40 (0.23–0.70)	100.00
Anti-IL4a					
Wenzel *et al.* [62] (2013)	Dupilumab	52	52	(Insufficient data)	
Anti-TSLP					
Wechsler *et al.* [60] (2022)	Tezepelumab	74	76	0.59 (0.19–1.82)	45.31
Menzies-Gow *et al.* [47] (2021)	Tezepelumab	528	531	0.15 (0.07–0.33)	54.69
Subgroup, DL (I^2=73.9%, τ^2=0.693, p=0.050)		602	607	0.28 (0.07–1.06)	100.00
Heterogeneity between groups: p=0.238					
Overall, DL (I^2=32.0%, τ^2=0.137, p=0.143)		2320	2038	0.40 (0.27–0.60)	

0.0039062 1 256
Favours treatment Favours control

FEV1



Study (year)	Treatment	Treatment, n	Control, n	Effect (95% CI)	Weight, %
Anti-IgE					
Garcia *et al.* [36] (2013)	Omalizumab	20	21	0.25 (0.06–0.44)	4.15
Bardelas *et al.* [19] (2012	Omalizumab	136	135	−0.08 (−0.19–0.02)	9.45
Hoshino and Ohtawa [41] (2012)	Omalizumab	14	16	0.19 (0.02–0.36)	4.87
Rubin *et al.* [57] (2012)	Omalizumab	76	37	0.13 (−0.01–0.27)	6.41
Bousquet *et al.* [24] (2011)	Omalizumab	266	121	0.13 (0.03–0.23)	10.00
Ohta *et al.* [51] (2009)	Omalizumab	151	164	0.06 (0.01–0.12)	16.01
Humbert *et al.* [42] (2005)	Omalizumab	209	210	0.09 (0.00–0.18)	11.29
Ayres *et al.* [18] (2004)	Omalizumab	206	106	0.20 (0.03–0.37)	4.92
Busse *et al.* [26] (2001)	Omalizumab	268	257	0.07 (0.01–0.12)	16.48
Solèr *et al.* [58] (2001)	Omalizumab	274	272	0.06 (0.00–0.11)	16.43
Subgroup, DL (I^2=50.6%, τ^2=0.002, p=0.033)		1620	1339	0.08 (0.04–0.13)	100.00
Anti-IL5/5R					
Harrison *et al.* [39] (2021)	Benralizumab	393	213	0.16 (0.09–0.23)	10.64
Panettieri *et al.* [53] (2020)	Benralizumab	114	114	0.06 (−0.02–0.14)	9.40
Nair *et al.* [49] (2017)	Benralizumab	73	75	0.11 (−0.03–0.26)	3.95
Bleecker *et al.* [23] (2016)	Benralizumab	264	261	0.13 (0.07–0.20)	10.98
FitzGerald *et al.* [34] (2016)	Benralizumab	336	343	0.11 (0.03–0.20)	8.34
Castro *et al.* [28] (2014)	Benralizumab	159	150	0.07 (−0.01–0.15)	9.53
Bel *et al.* [20] (2014)	Mepolizumab	69	66	0.12 (−0.01–0.25)	4.96
Ortega *et al.* [52] (2014)	Mepolizumab	194	191	0.14 (0.04–0.23)	7.50
Pavord *et al.* [55] (2012)	Mepolizumab	153	155	0.06 (−0.04–0.16)	6.95
Haldar *et al.* [37] (2009)	Mepolizumab	29	32	−0.05 (−0.26–0.15)	2.19
Flood-Page *et al.* [35] (2007)	Mepolizumab	120	126	−0.03 (−0.14–0.07)	6.50
Bernstein *et al.* [21] (2020)	Reslizumab	234	230	0.14 (0.06–0.23)	8.39
Bjermer *et al.* [22] (2016)	Reslizumab	102	103	0.16 (0.06–0.26)	7.00
Castro *et al.* [27] (2011)	Reslizumab	52	52	0.24 (0.09–0.39)	3.68
Subgroup, DL (I^2=34.5%, τ^2=0.001, p=0.099)		2292	2111	0.11 (0.08–0.14)	100.00
Anti-IL4a					
Castro *et al.* [29] (2018)	Dupilumab	633	321	0.13 (0.08–0.18)	48.68
Rabe *et al.* [56] (2018)	Dupilumab	97	104	0.22 (0.09–0.34)	14.66
Wenzel *et al.* [62] (2016)	Dupilumab	143	125	0.16 (0.07–0.24)	26.53
Wenzel *et al.* [61] (2013)	Dupilumab	45	36	0.27 (0.11–0.42)	10.13
Subgroup, DL (I^2=27.3%, τ^2=0.001, p=0.248)		918	586	0.17 (0.11–0.22)	100.00
Anti-TSLP					
Wechsler *et al.* [60] (2022)	Tezepelumab	65	64	0.26 (0.13–0.39)	19.39
Menzies-Gow *et al.* [47] (2021)	Tezepelumab	528	531	0.13 (0.08–0.18)	49.70
Corren *et al.* [32] (2017)	Tezepelumab	128	141	0.11 (0.02–0.20)	30.91
Subgroup, DL (I^2=48.1%, τ^2=0.002, p=0.146)		721	736	0.15 (0.08–0.22)	100.00
Heterogeneity between groups: p=0.080					
Overall, DL (I^2=50.1%, τ^2=0.002, p=0.001)		5551	4772	0.11 (0.09–0.14)	

−0.500 0.000 0.500
Favours control Favours treatment

Kyriakopoulos et al. Eur Respir Rev. 2024;33(172).

Now, common story…….

- 65/F

- 과거 15년 전 천식 진단받고 타병원에서 치료받던 분
- 가정산소 치료하다가 현재 중단한 상태
- 4개월 전 호흡곤란 악화되어 2주간 타병원에서 입원치료 받음
- 이후 추적관찰 중 증상 악화 반복되어 전원됨
- Blood eosinophil count: 1140 (24.1%)
- Medication Hx.
  - IND/GLY/MOM
  - Roxithromycin (long-term)

PFT & FeNO

인천성모병원
폐기능검사실

Name: [redacted]
Gender: Female
Age: 64 Race: Asian
Height(cm): 156 Weight(kg): 63.0
Room: 호흡기내과(505)

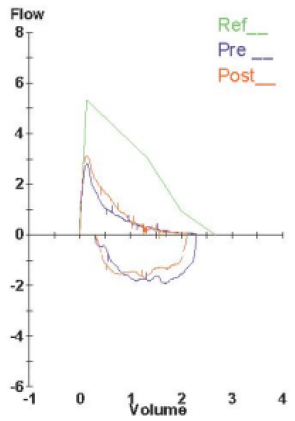
Id: [redacted] Vmax22-(1)
Date: 08/12/24
Temp: 27 PBar: 750
의뢰의사: 최준영
검 사 자 : 장은미

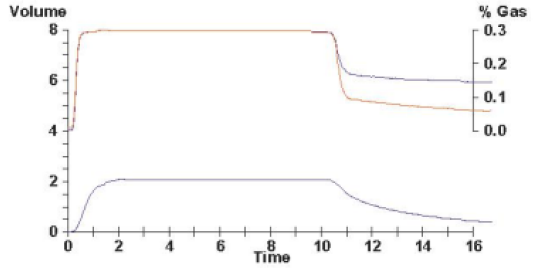
Spirometry

		Ref	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg
FVC	Liters	2.67	2.31	86	2.12	79	-8
FEV1	Liters	1.93	0.98	51	1.11	57	13
FEV1/FVC	%	73	42		52		
FEF25-75%	L/sec	2.31	0.31	13	0.33	14	6
FEF50%	L/sec	3.03	0.38	12	0.45	15	20
FEF75%	L/sec	0.91	0.14	15	0.10	11	-30
PEF	L/sec	5.30	3.32	63	3.12	59	-6
Vol Extrap	Liters		0.00		-0.01		
MVV	L/min	89	33	37			

Diffusion Hb: 13.4 gm/dL

		Ref	Pre Meas	Pre % Ref
DLCO	mL/mmHg/min	18.2	15.7	86
DL Adj	mL/mmHg/min	18.2	15.7	86
DLCO/VA	mL/mHg/min/L	3.73	4.32	116
DL/VA Adj	mL/mHg/min/L		4.32	
VA	Liters		3.64	





Comments:

NIOX®

FeNO Report

Patient Name : [redacted]
Patient Identity :
Technician :

Measurement table for measurement method FeNO

Date	NO-value	Mode	Comment	Signature
2024-08-12	53ppb	10s		

Reviewed by:

ACT score

ACT : 10 점

1. 지난 4주 동안 당신은 천식으로 인해 얼마나 많은 시간을 직장이나 학교나 집에서 평소 했던 : 2 : 대부분의 시간 동안 그랬다.

2. 지난 4주 동안 당신은 얼마나 자주 숨을 헐떡였거나 / 숨을 쉬기가 어려웠습니까? : 1 : 하루에 한 번 이상 그랬다.

3. 지난 4주 동안 당신은 천식 증상 (쌕쌕거리는 소리, 기침, 숨가쁨, 가슴 조임이나 통증)으로 인해 : 1 : 일주일에 4일 밤 이상을 그랬다.

4. 지난 4주 동안 당신은 응급약물 (예를 들면 살부타몰, 페노테롤, 벤토린, 베로텍 등)을 얼마나 : 1 : 하루에 3번 이상 사용했다.

5. 당신은 지난 4주 동안 천식을 얼마나 잘 조절 했다고 평가하겠습니까? : 5 : 완벽하게 조절했다.

→ **Benralizumab**

PFT & FeNO

인천성모병원
폐기능검사실

Name: [redacted]
Gender: Female
Age: 64 Race: Asian
Height(cm): 156 Weight(kg): 63.0
Room: 호흡기내과

[redacted]
Date: 08/20/24
Temp: 26 PBar: 749
의뢰의사: 최준영
검 사 자 : 장은미

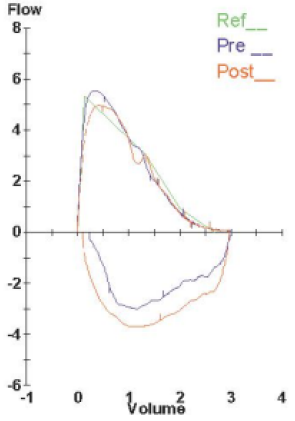
Vmax22-(1)

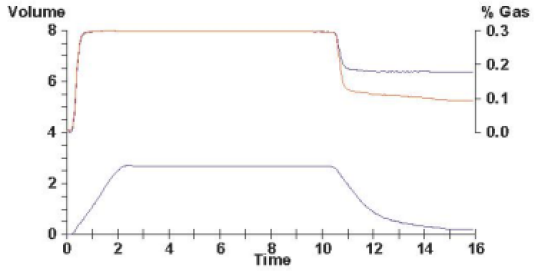
Spirometry

		Ref	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg
FVC	Liters	2.67	3.00	112	2.98	112	-1
FEV1	Liters	1.93	2.09	108	2.16	112	4
FEV1/FVC	%	73	70		73		
FEF25-75%	L/sec	2.31	1.23	53	1.36	59	11
FEF50%	L/sec	3.03	1.93	64	2.90	96	50
FEF75%	L/sec	0.91	0.39	43	0.40	44	2
PEF	L/sec	5.30	5.53	104	5.05	95	-9
Vol Extrap	Liters		0.02		0.03		39
MVV	L/min	89	61	69			

Diffusion Hb: 12.7 gm/dL

		Ref	Pre Meas	Pre % Ref
DLCO	mL/mmHg/min	18.2	14.1	78
DL Adj	mL/mmHg/min	18.2	14.4	79
DLCO/VA	mL/mHg/min/L	3.73	3.40	91
DL/VA Adj	mL/mHg/min/L		3.48	
VA	Liters		4.14	





NIOX®

FeNO Report

Patient Name
Patient Identity
Technician [redacted]

Measurement table for measurement method FeNO

Date	NO-value	Mode	Comment	Signature
2024-08-20	31ppb	10s		

Reviewed by:

ACT score

ACT : 21 점

1. 지난 4주 동안 당신은 천식으로 인해 얼마나 많은 시간을 직장이나 학교나 집에서 평소 했던 : 2 : 대부분의 시간 동안 그랬다.

2. 지난 4주 동안 당신은 얼마나 자주 숨을 헐떡였거나 / 숨을 쉬기가 어려웠습니까? : 5 : 전혀 그렇지 않았다.

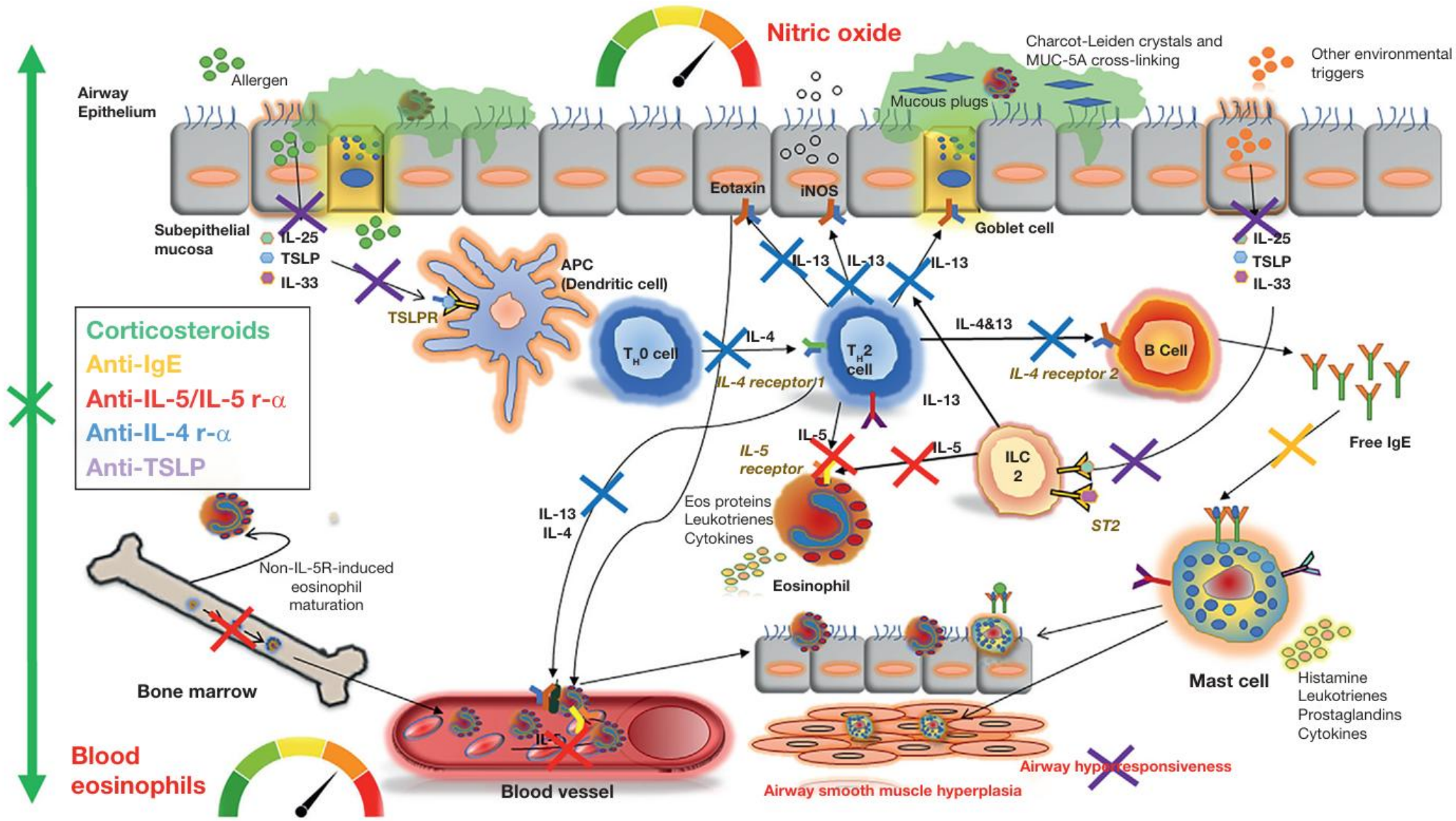
3. 지난 4주 동안 당신은 천식 증상 (쌕쌕거리는 소리, 기침, 숨가쁨, 가슴 조임이나 통증)으로 인해 : 5 : 전혀 그렇지 않았다.

4. 지난 4주 동안 당신은 응급약물 (예를 들면 살부타몰, 페노테롤, 벤토린, 베로텍 등)을 얼마나 : 5 : 전혀 사용하지 않았다.

5. 당신은 지난 4주 동안 천식을 얼마나 잘 조절 했다고 평가하겠습니까? : 4 : 잘 조절했다.

Contents

1. IL-5/IL-5Rα vs IL-4Rα

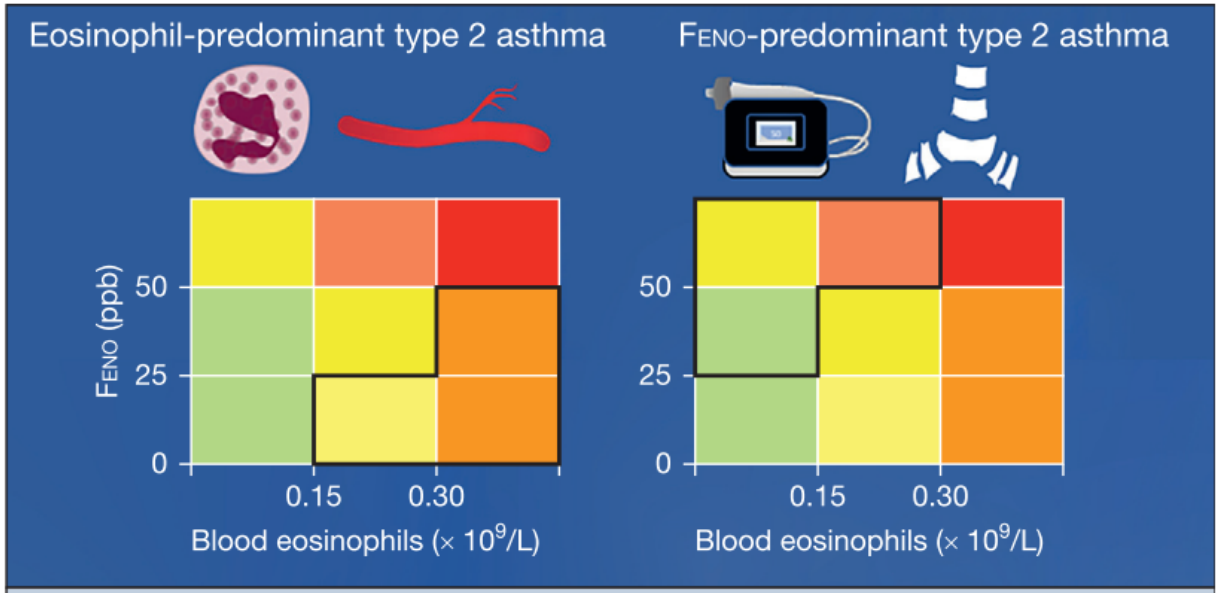


Couillard et al. Chest. 2025;167(2):330-42.

	Omalizumab	Mepolizumab	Reslizumab	Benralizumab	Dupilumab	Tezepelumab
Mechanism of action	Anti-IgE	Anti-IL5	Anti-IL5	Anti-IL5Rα	Anti-IL4Rα/13	Anti-TSLP
Criteria for initiation[a]	Uncontrolled symptoms of allergic asthma with sensitization to perennial aeroallergen despite ICS use	Eosinophilic asthma (AEC ≥ 150 cells/μL) with exacerbation (≥ 2 per year) despite use of ICS-LABA	Eosinophilic asthma (AEC ≥ 400) with exacerbation despite use of at least medium dose ICS	Eosinophilic asthma (AEC ≥ 300) with exacerbation (≥ 2 per year) despite use of medium to high dose ICS-LABA	Eosinophilic asthma (AEC ≥ 150) with steroid dependency or with exacerbation despite use of medium to high dose ICS-LABA	Uncontrolled asthma with exacerbation despite use of medium to high dose ICS-LABA, T2 high or low asthma
Mode of administration	Subcutaneous	Subcutaneous	IV	Subcutaneous	Subcutaneous	Subcutaneous
Dosing and dosing interval	Every 2 or 4 wks, based upon pre-dosing IgE level and body weight	100 mg every 4 wks	Weight based every 4 wks	30 mg every 4 wks × 3, then every 8 wks thereafter	200 mg or 300 mg every 2 wks (consider loading dose)	210 mg every 4 wks
Co-morbid conditions with FDA approval	CRSwNP; chronic spontaneous urticaria; IgE mediated food allergies	CRSwNP; EGPA/HES (300 mg monthly dosing regimen)	N/A	EGPA (monthly dosing regimen)	Atopic dermatitis; CRSwNP; eosinophilic esophagitis (300 mg weekly dosing for > 40 kg), COPD (AEC ≥ 300 cells/μL)	CRSwNP (FDA approval pending)

Couillard et al. Chest. 2025;167(2):330-42.

Measure blood eosinophils and FENO in all people with severe asthma



Greater % of late-onset asthma	Greater % of early onset
Less allergy	Allergy
Less AHR	AHR ++
Less atopic. More CRSwNP, EGPA	Eczema, atopic rhinitis > CRSwNP
Blood eos signal > FENO signal	FENO signal > blood eos signal
OCS > ICS sensitivity	ICS > OCS sensitivity
Anti-IL-5/-5R ~ Anti-IL-4R ~ Anti-TSLP response	Anti-IL-4R/Anti-TSLP > Anti-IL-5/-5R response
← Many patients have features of both →	

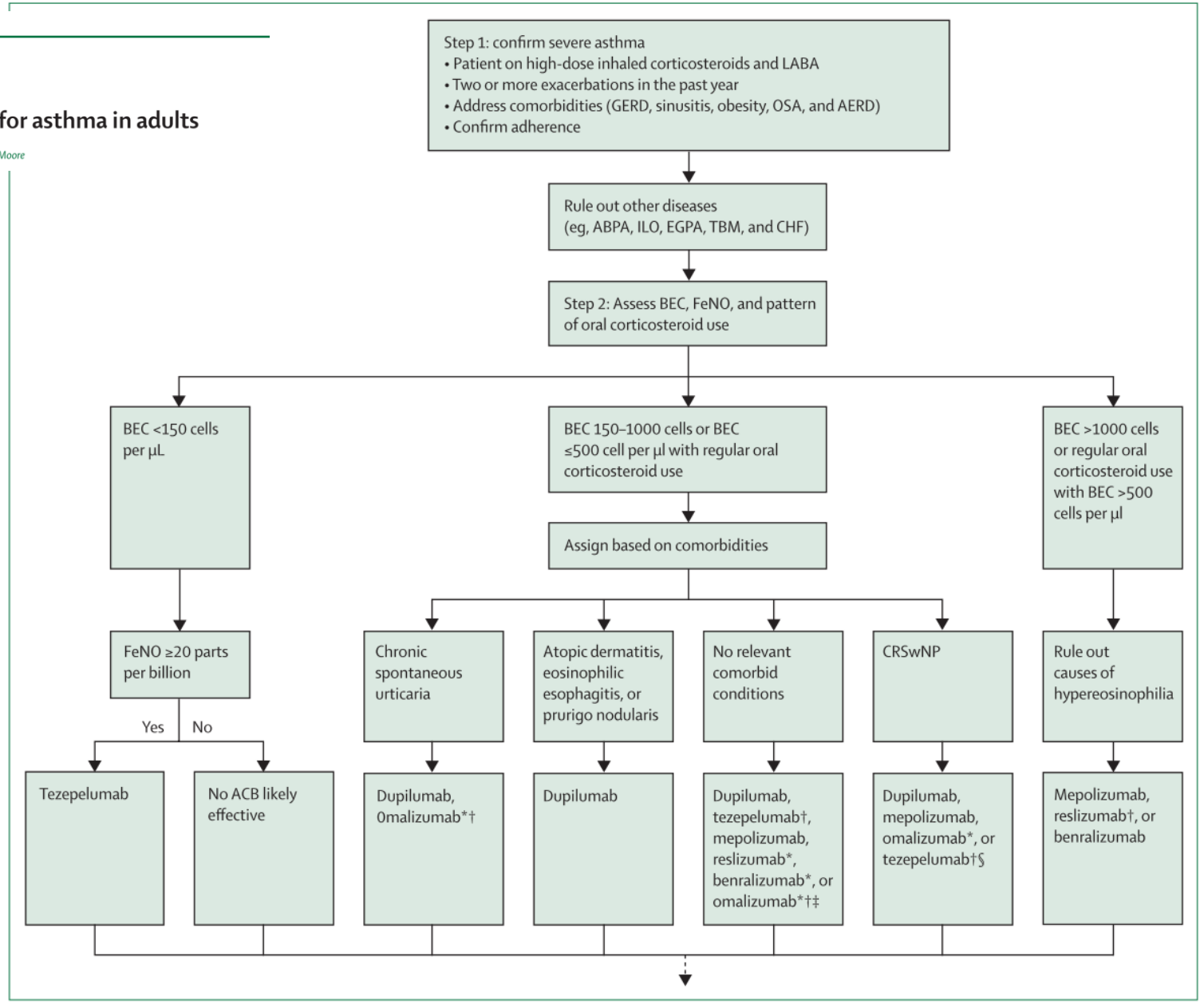
↑Eosinophils and/or ↑FENO = ↑risk of attacks, ↑response to biologics

Couillard et al. Chest. 2025;167(2):330-42.

Asthma 2

Anti-cytokine biologics for asthma in adults

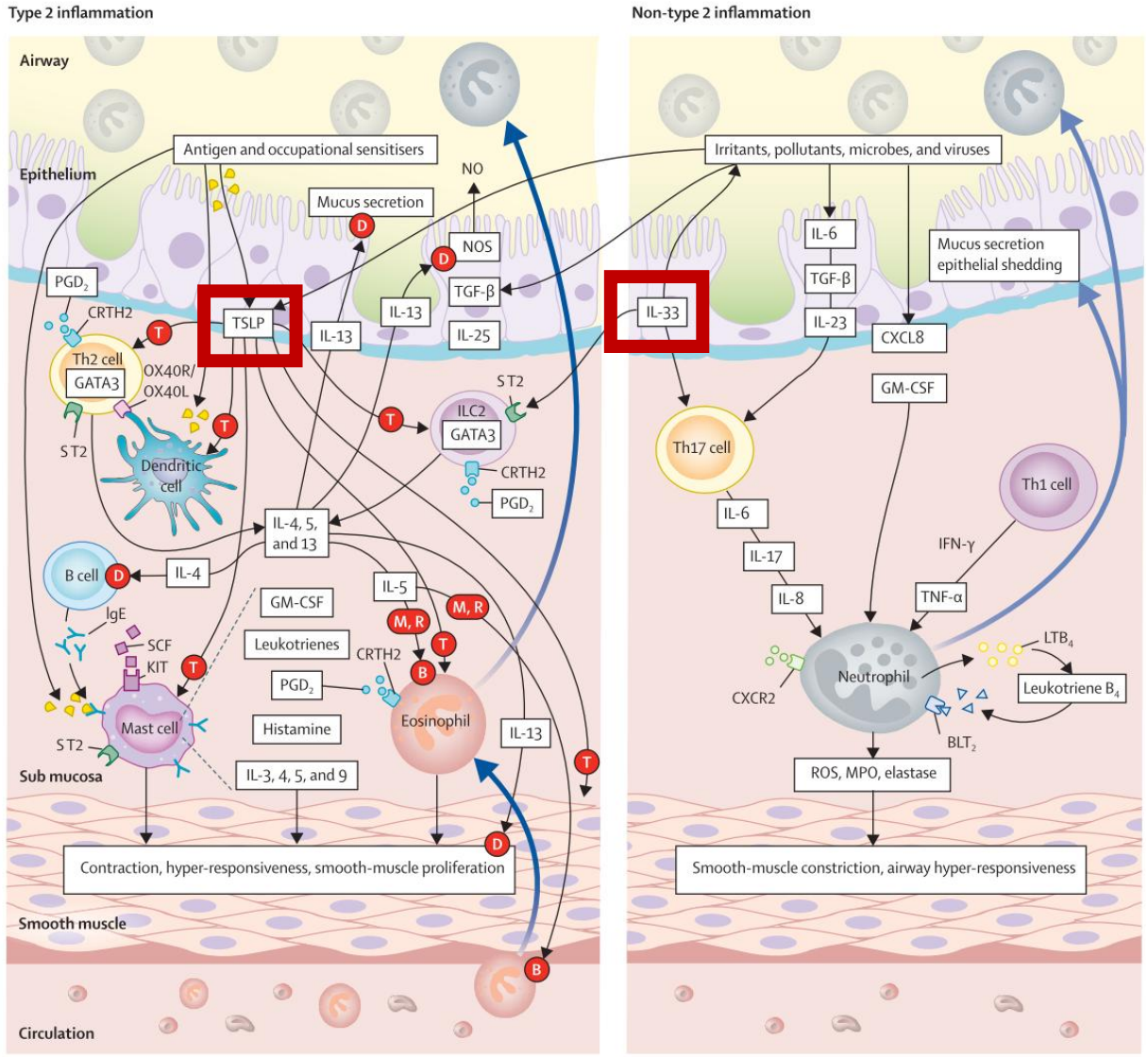
Elliot Israel, Michael E Wechsler, David J Jackson, Wendy C Moore



Israel et al. Lancet. 2025;406(10516):2282-94.

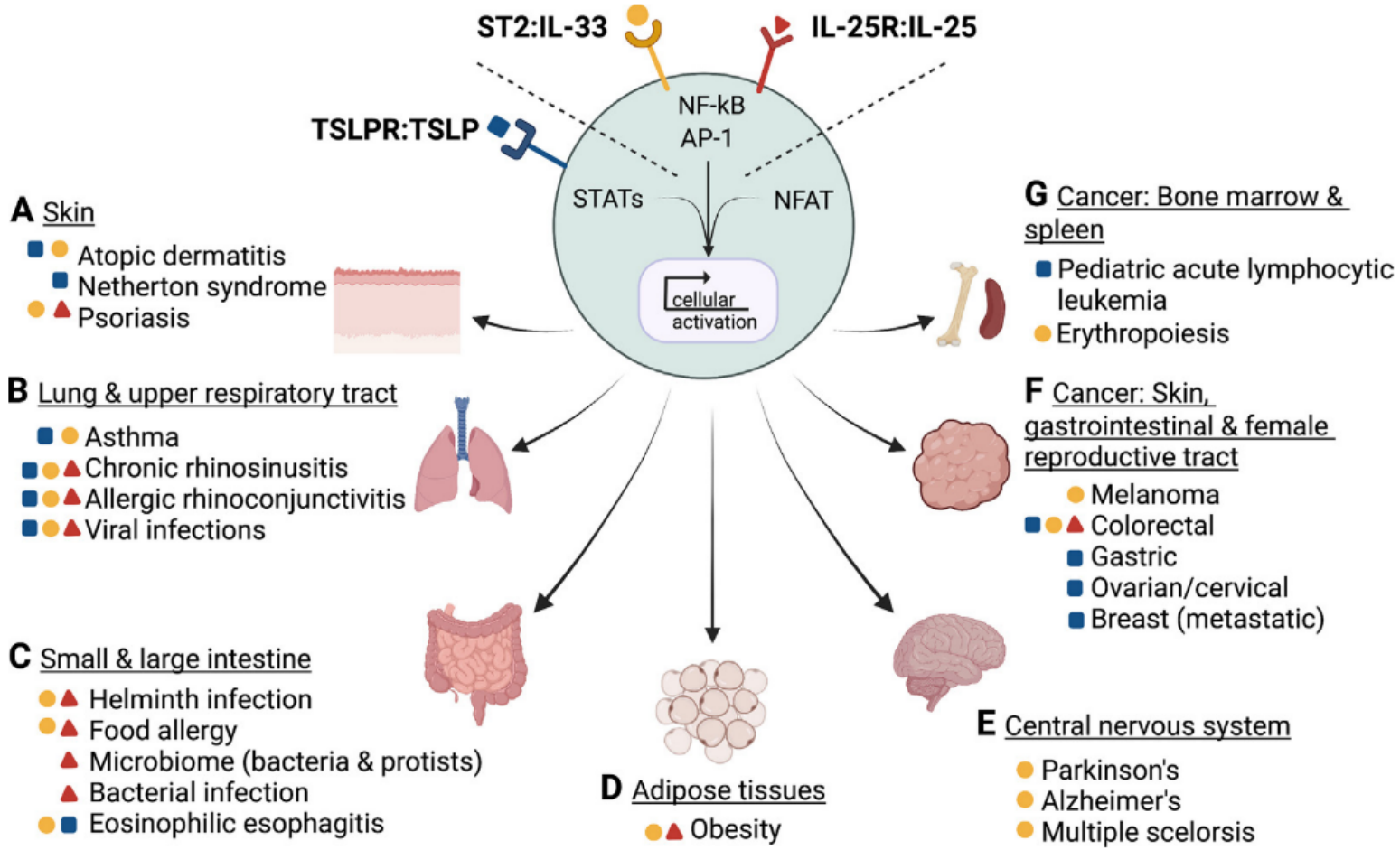
2. Alarmin-targeting agents

Alarmins are not all the same.



Israel et al. Lancet. 2025;406(10516):2282-94

Alarmins are not all the same.



Bagnasco et al. Int J Mol Sci. 2024;25(11).

Tezepelumab and T2-high endotype

The NEW ENGLAND JOURNAL of MEDICINE

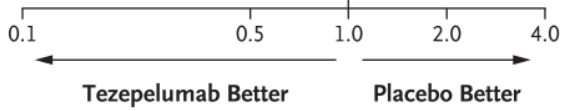
ORIGINAL ARTICLE

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.

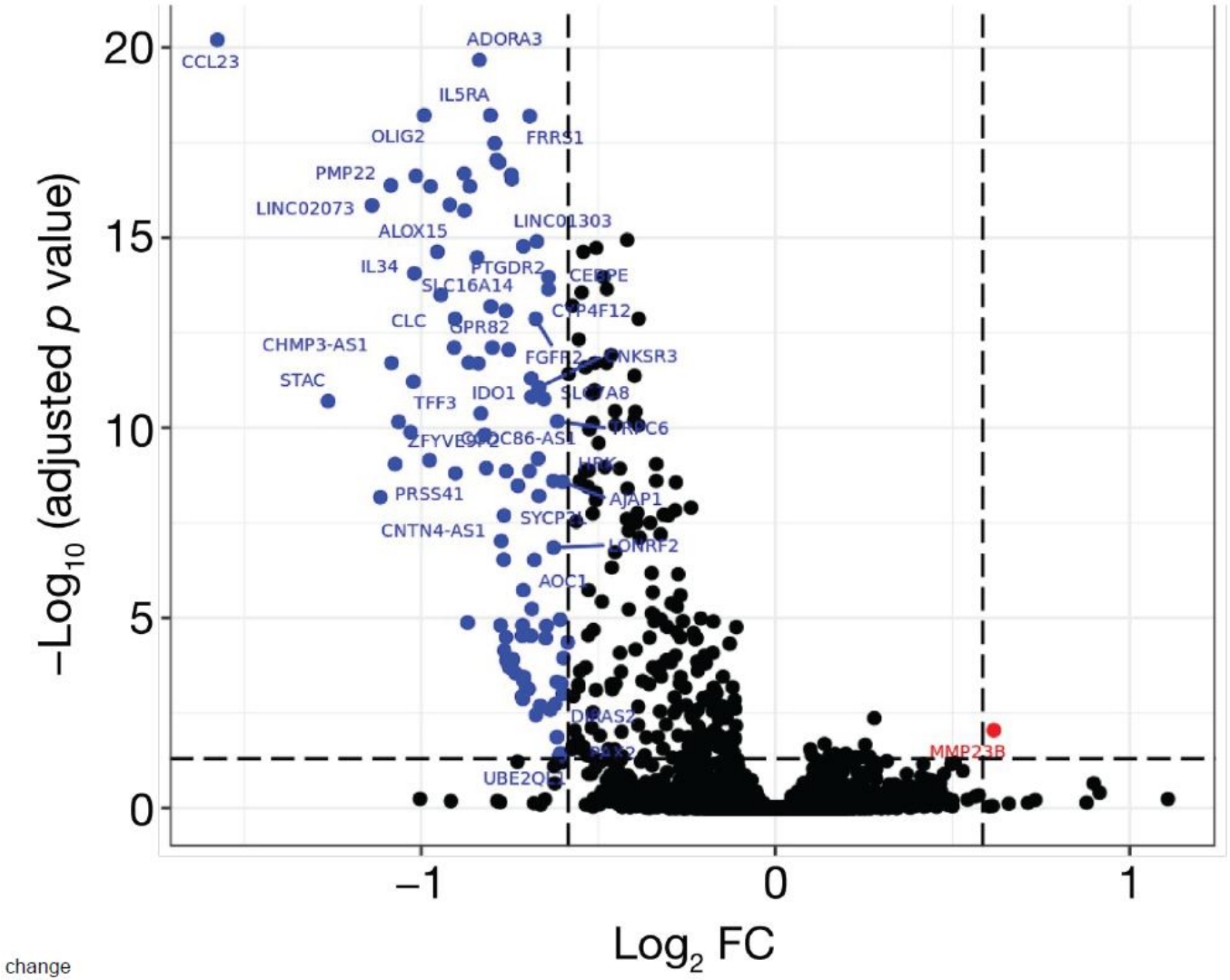
NAVIGATOR

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)



Menzies-Gow et al. N Engl J Med. 2021;384(19):1800-9.

Tezepelumab treatment - RNA sequencing



- Downregulated genes
- No change in expression
- Upregulated genes

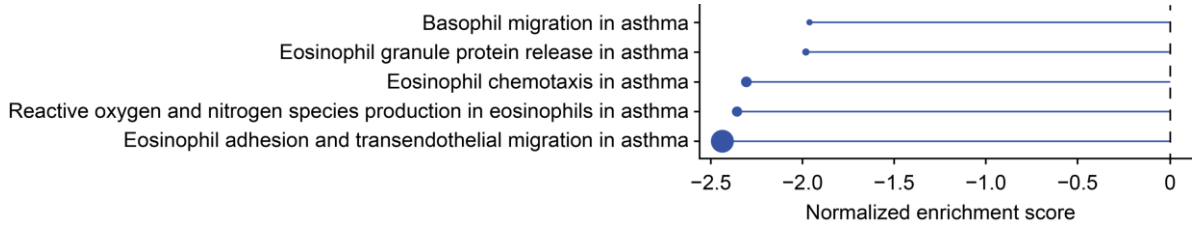
100 genes were downregulated and one gene was upregulated

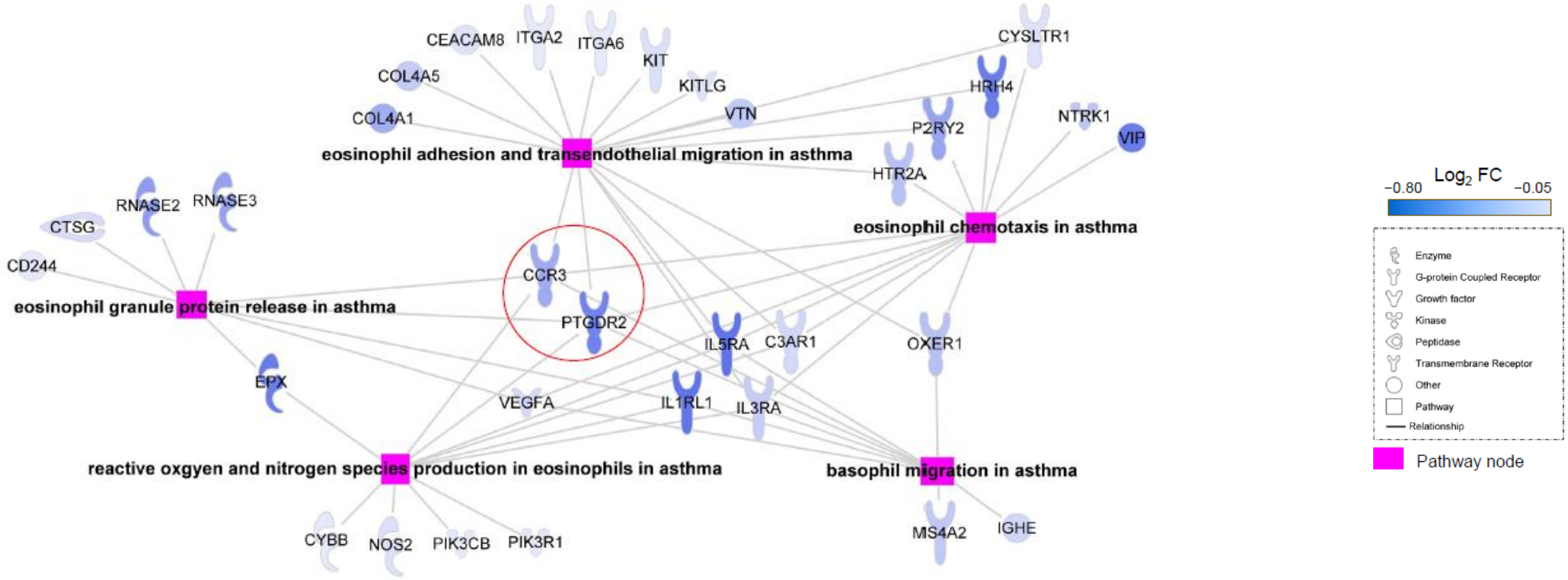
Sherrill et al. Poster presented at: ATS 2026; Orlando, FL. May 15–20, 2026.

Most enriched pathways - associated with reduced eosinophilic inflammation

The 5 most enriched downregulated pathways (adjusted p < 0.01) were associated with eosinophil migration and activation.

The pathway network displaying the 33 leading edge genes from the 5 most enriched down-regulated pathways

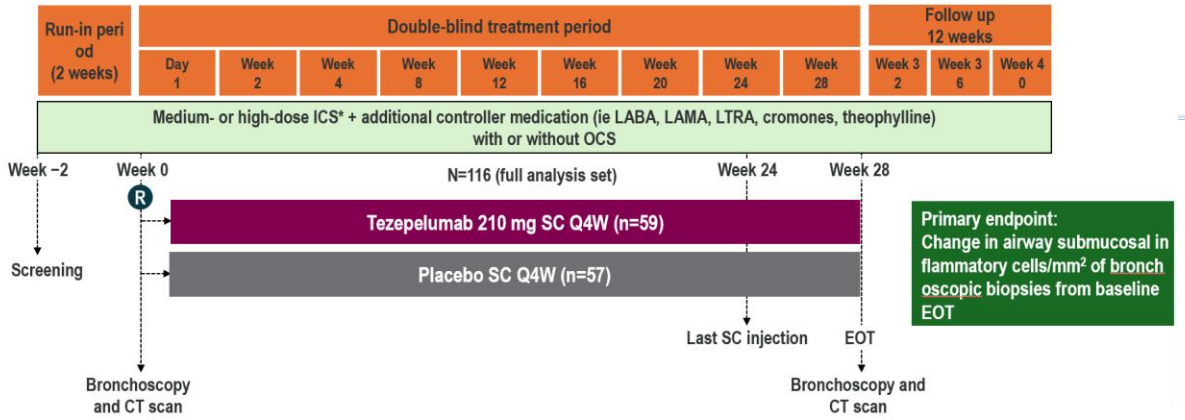


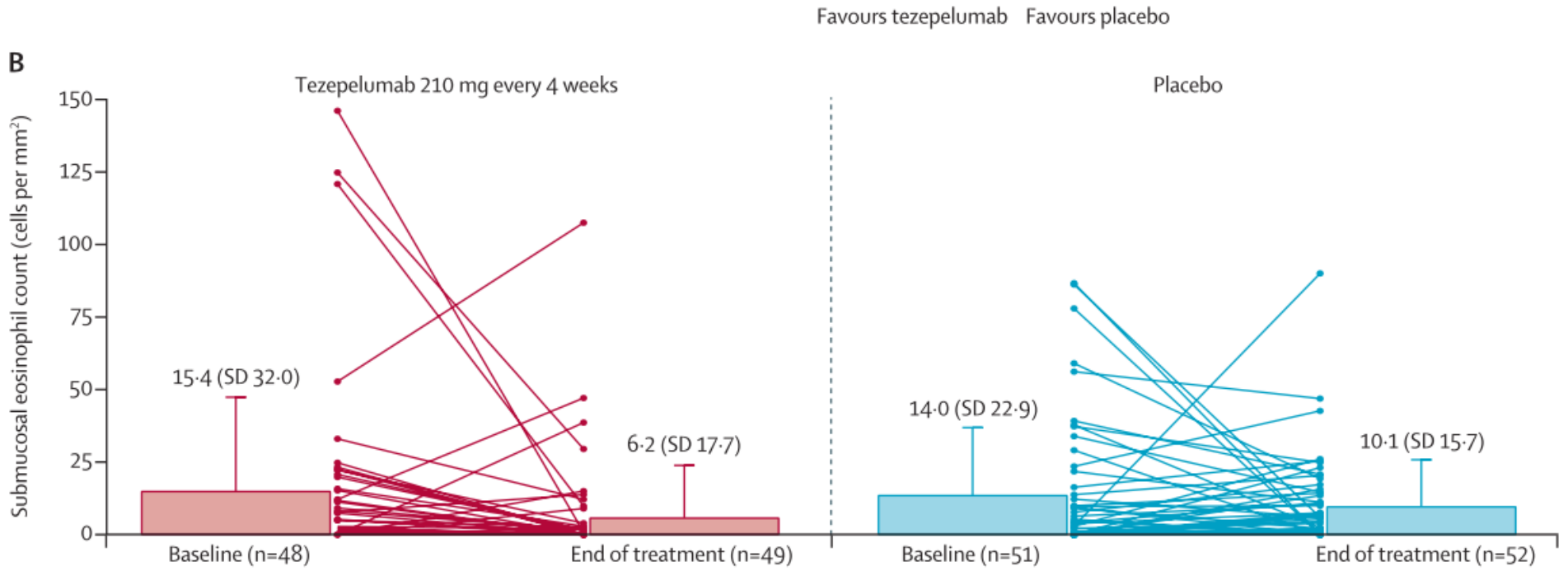


Sherrill et al. Poster presented at: ATS 2026; Orlando, FL. May 15–20, 2026.

Effect of tezepelumab on airway inflammatory cells, remodelling, and hyperresponsiveness in patients with moderate-to-severe uncontrolled asthma (CASCADE): a double-blind, randomised, placebo-controlled, phase 2 trial

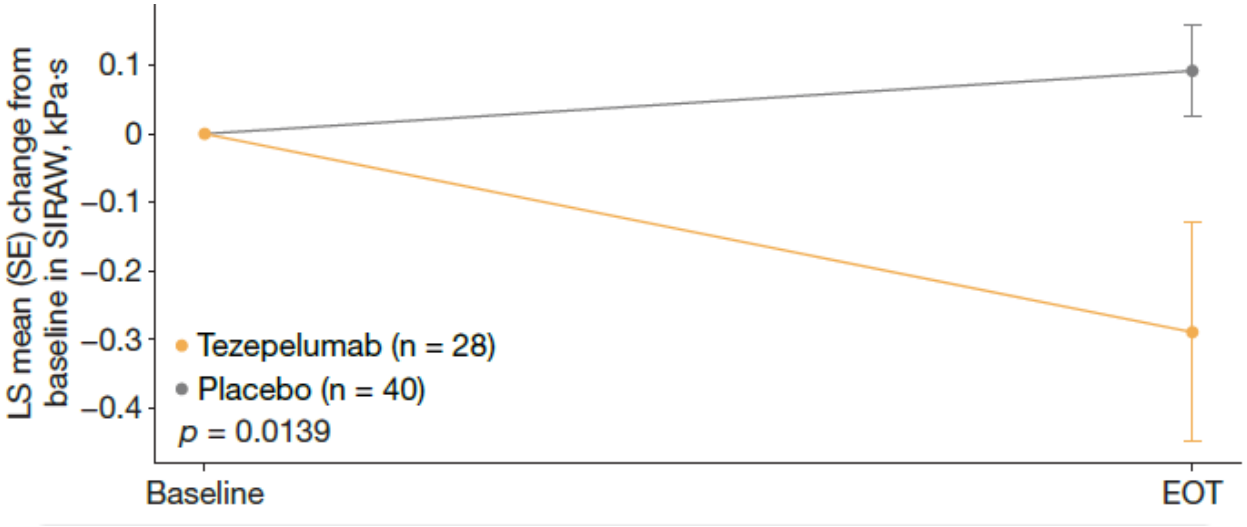
Sarah Diver, Latifa Khalfaoui*, Claire Emson*, Sally E Wenzel, Andrew Menzies-Gow, Michael E Wechsler, James Johnston, Nestor Molfino, Jane R Parnes, Ayman Megally, Gene Colice†, Christopher E Brightling†, on behalf of the CASCADE study investigators‡*





Diver S et al. Lancet Respir Med. 2021;9(11):1299-312.

CASCADE: post-hoc analysis

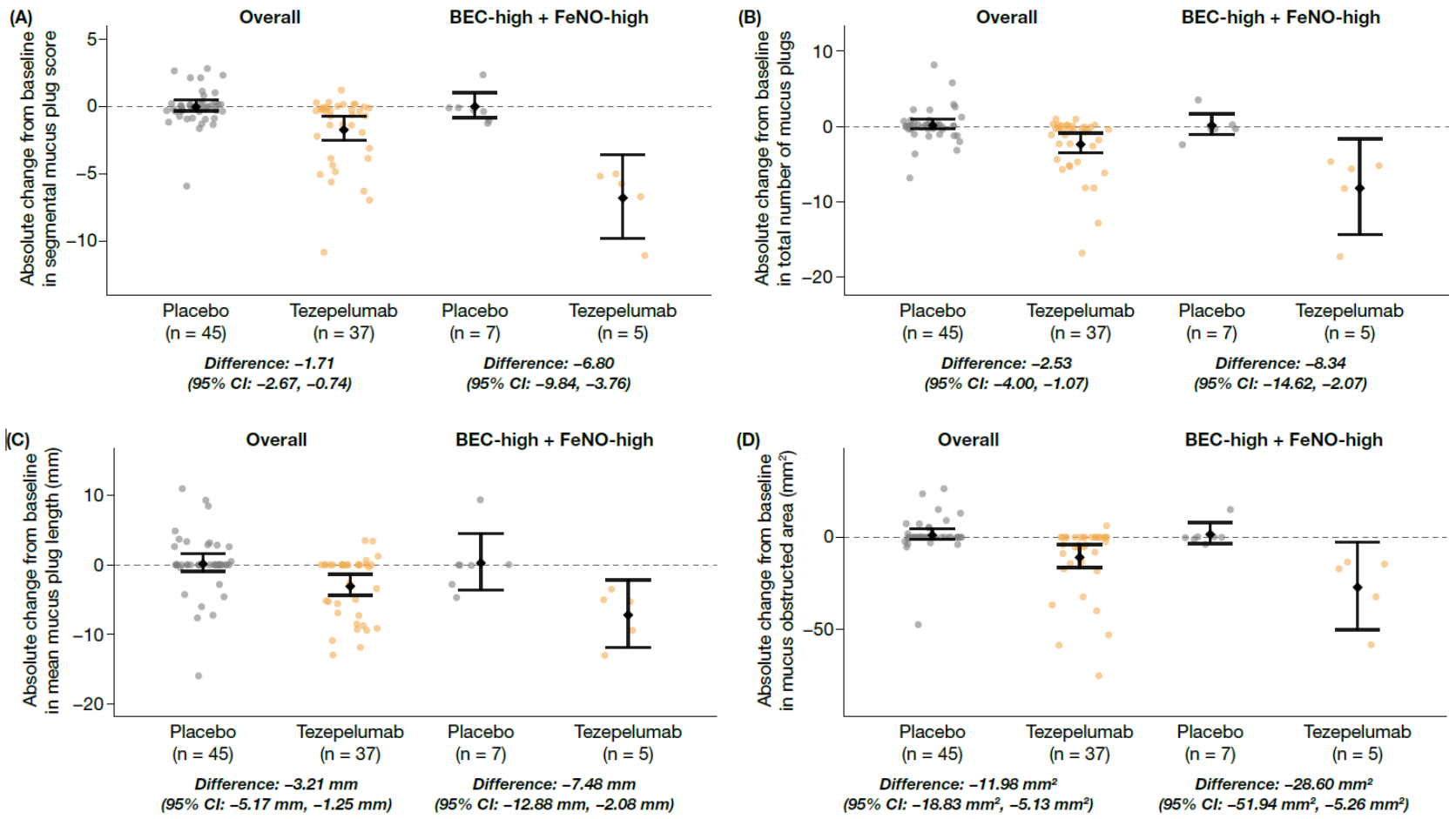


Subgroup	Mean (SD) sIRAW, kPa·s				
	Placebo (n)	Placebo Mean (SD)	Tezepelumab (n)	Tezepelumab Mean (SD)	p-value
Overall	40	0.092 (0.420)	28[a]	-0.289 (0.848)	0.0139
BEC-high	16	0.109 (0.434)	9	-0.857 (0.705)	0.0001
BEC-low	24	0.080 (0.419)	19	-0.021 (0.787)	0.7075
FeNO-high	15	0.146 (0.509)	13	-0.467 (0.624)	0.0052
FeNO-low	25	0.059 (0.364)	14	-0.175 (1.025)	0.2633
BEC-high + FeNO-high	7	0.038 (0.216)	5	-0.818 (0.729)	0.0051
BEC-high + FeNO-low	9	0.165 (0.557)	4	-0.906 (0.782)	0.0112
BEC-low + FeNO-high	8	0.241 (0.675)	8	-0.247 (0.468)	0.1605
BEC-low + FeNO-low	16	0.000 (0.191)	10	0.118 (0.991)	0.6227

Poster presented at: ATS 2026; Orlando, FL. May 15–20, 2026. Poster #1383

CASCADE: post-hoc analysis

Tezepelumab reduced mucus plugging and obstruction metrics from baseline to EOT versus placebo, with **greater reductions in the BEC-high + FeNO-high** population.



Poster presented at: ATS 2026; Orlando, FL. May 15–20, 2026. Poster #P1390

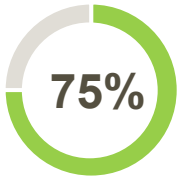
OCS reduction in cortico-dependent patients across SC biologics

Mepolizumab

SIRIUS[1]

Reduction in median mOCS dose vs. PBO
at 24 weeks
(median 3.1 mg/day; n=69), vs. baseline (12.5 mg/day; n=69)[1]

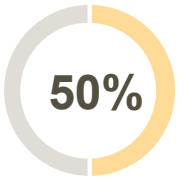
REALITI-A[5]



Reduction in mOCS dose vs. baseline
at 1 year
(median 2.5 mg/day; n=222), vs. baseline (10 mg/day; n=298)[6]

Benralizumab

ZONDA[2]



Reduction in median mOCS dose vs. PBO
at 28 weeks
(median 5.0 mg/day; n=73), vs. baseline (10.0 mg/day; n=73)[2]

Dupilumab

VENTURE[3]

Reduction in median mOCS dose vs. PBO
at 24 weeks
(baseline 10.75 mg/day; n=103)[4]

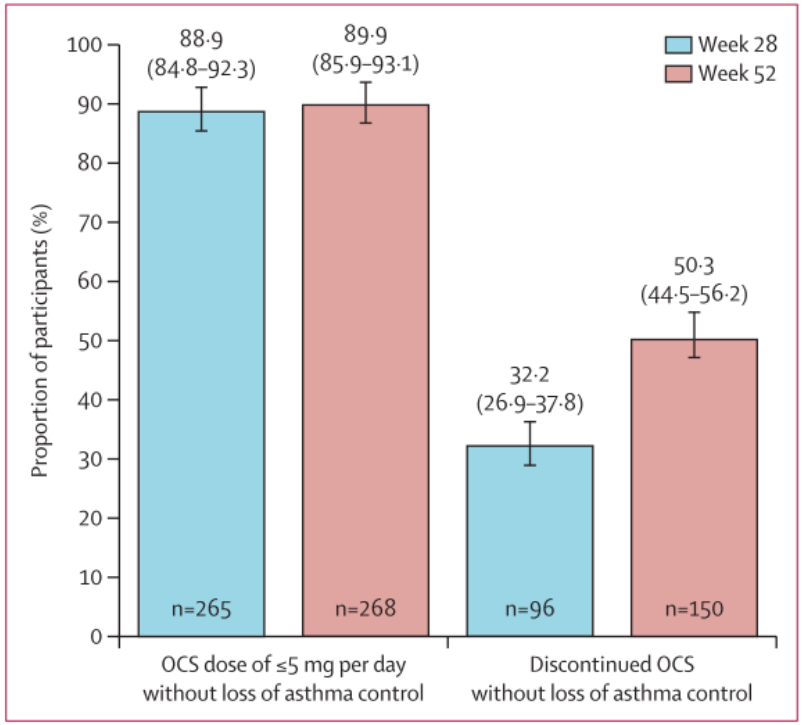
CI, confidence interval; mg, milligram; mOCS, maintenance oral corticosteroid; OR, odds ratio; PBO, placebo; SC, subcutaneous.

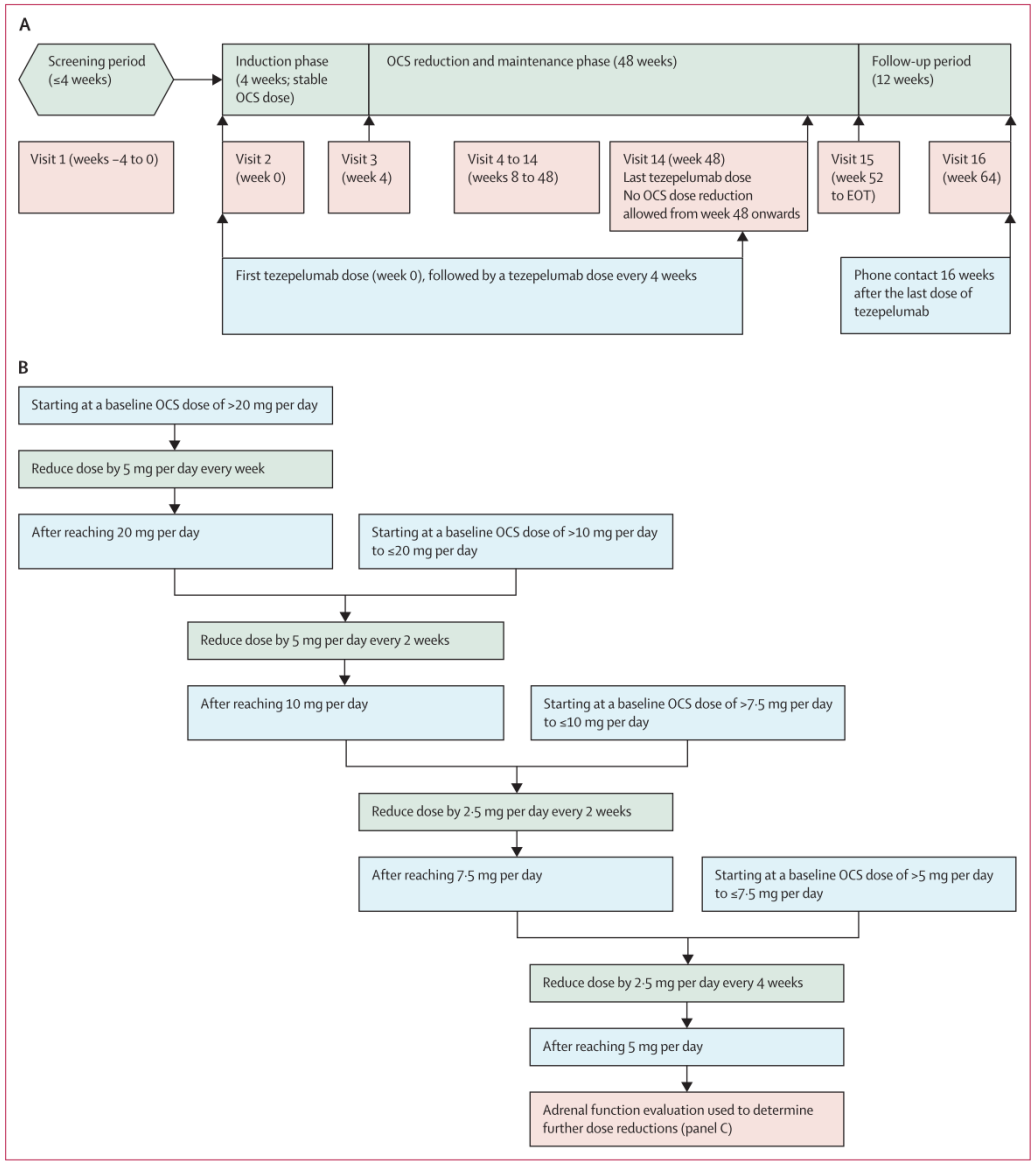
1. Bel EH, Wenzel SE, M. (2014). Oral glucocorticoid–sparing effect of benralizumab in severe asthma. *New England journal of medicine*, *376*(25), 2448-2458. 2. Nair, P., Wenzel, S., Rabe, K. F., Bourdin, A., Lugogo, N. L., Kuna, P., ... & Goldman, M. (2017). Oral glucocorticoid–sparing effect of benralizumab in severe asthma. New England journal of medicine, 376(25), 2448-2458; 3. Rabe KF, Nair P, Brusselle G, Maspero JF, Castro M, Sher L,..., & Teper A. Efficacy and Safety of Dupilumab in Glucocorticoid-Dependent Severe Asthma. N Engl J Med. 2018;378(26):2475-2485; 4. Rabe et al. N Engl J Med 2018 supplementary data; 6. Pilette, C., Canonica, G. W., Chaudhuri, R., Chupp, G., Lee, F. E. H., Lee, J. K., ... & Howarth, P. (2022). REALITI-A Study: Real-World Oral Corticosteroid-Sparing Effect of Mepolizumab in Severe Asthma. *The Journal of Allergy and Clinical Immunology: In Practice*, *10*(10), 2646-2656.

OCS reduction in Tezepelumab – WAYFINDER : single-arm evidence

Oral corticosteroid reduction and discontinuation in adults with corticosteroid-dependent, severe, uncontrolled asthma treated with tezepelumab (WAYFINDER): a multicentre, single-arm, phase 3b trial

David J Jackson, Njira L Lugogo, Mark Gurnell, Liam G Heaney, Stephanie Korn, Guy Brusselle, Pascal Chanez, Ricardo del Olmo, Jean-Pierre Llanos, Nanna Keeling, Kinga Sałapa, Bill Cook, Amit D Parulekar, Konstantinos Kostikas, Robert Fogel, Neil Martin, Shradha N Chandarana



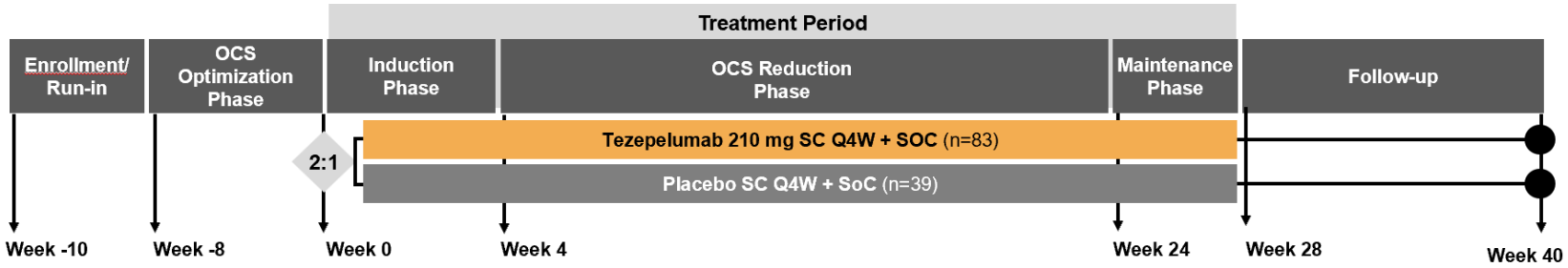


Jackson et al. Lancet Respir Med. 2026;14(2):129-40.

OCS reduction in Tezepelumab – SUNRISE :placebo-controlled evidence

Efficacy and safety of tezepelumab versus placebo in reducing oral corticosteroid use in adults with severe, oral corticosteroid-dependent asthma (SUNRISE): a multicentre, placebo-controlled, double-blind, phase 3 trial

Michael E Wechsler, Christopher E Brightling, Guy Brusselle, Marco Caminati, Tamara Soler, Efrain Montaño González, Narongwit Nakwan, Iwona Capala-Szczurko, Gillian Hunter, Gun Almqvist, Harbans Lal, Piotr Kabelis, Paola Scrigner, Yuko Matsunaga, Nestor Molfino, Sandhia S Ponnarambil, on behalf of the SUNRISE study investigators



- **This study has been terminated due to slow enrollment, resulting from evolving clinical practices that reduced the use of maintenance OCS for severe asthma treatment.**
- **The planned enrollment was for 207 patients: 138 to tezepelumab and 69 to placebo.**

Asthma Control Criteria for OCS Reduction

Patient must meet at least 1:[a]

- Mean morning PEF ≥80% of baseline
- An increase of no more than 2 nights with asthma-related awakenings (requiring rescue medication) over a 7-day period compared to baseline
- Mean use of SABA rescue medication: no more than 4 inhalations/day above baseline
- Pre-BD FEV_1 ≥80% of baseline
- No requirement to increase systemic corticosteroids dose for asthma symptoms/ exacerbations since last visit
- Non-asthma criterion: no signs or symptoms of adrenal insufficiency

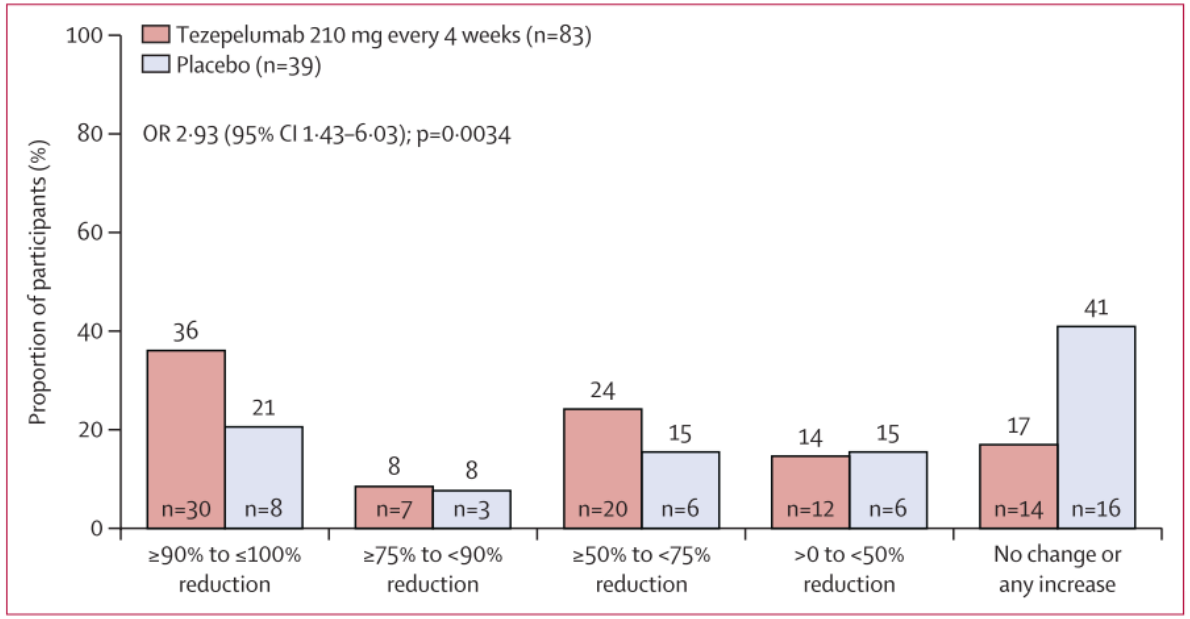
OCS Titration Schedule

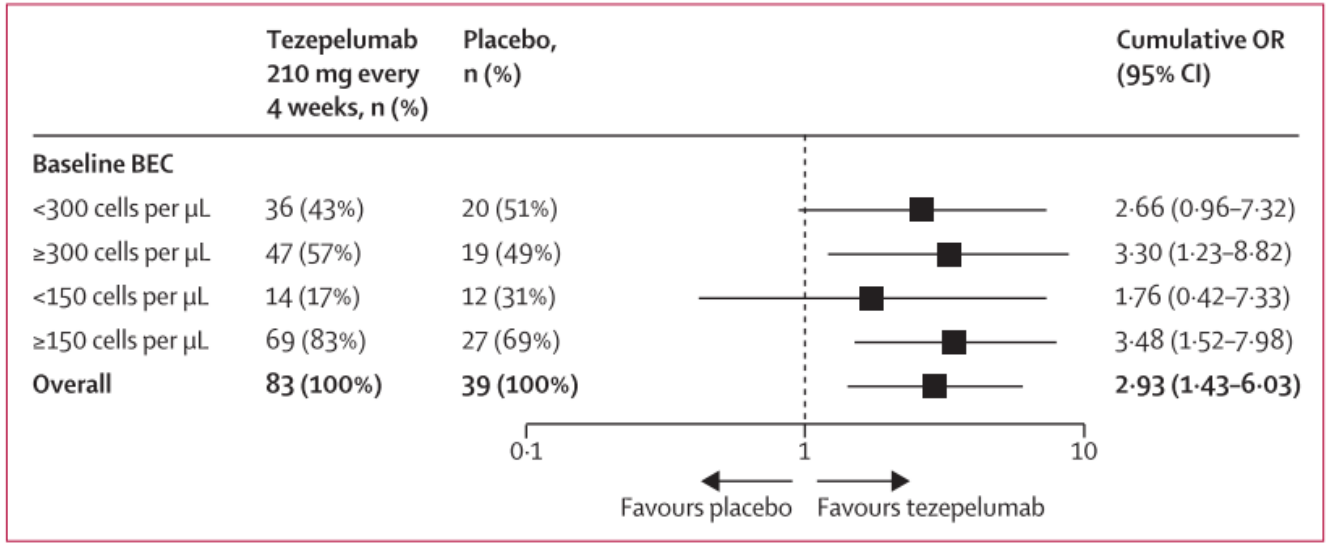
Starting OCS dose at each visit	Dose reduction	OCS optimization phase (8 weeks)	OCS reduction phase (20 weeks)[b]
>10-30 mg/day	5 mg of the daily dose	Q2W	Q4W
7.5-10[b] mg/day	2.5 mg of the daily dose	Q2W	Q4W

During the optimization phase, participants were excluded if asthma was controlled at an OCS dose of <7.5 mg/day or >30 mg/day and/or they had three consecutive dose reductions without losing asthma control

Wechsler et al. Lancet Respir Med. 2026;14(6):481-92.

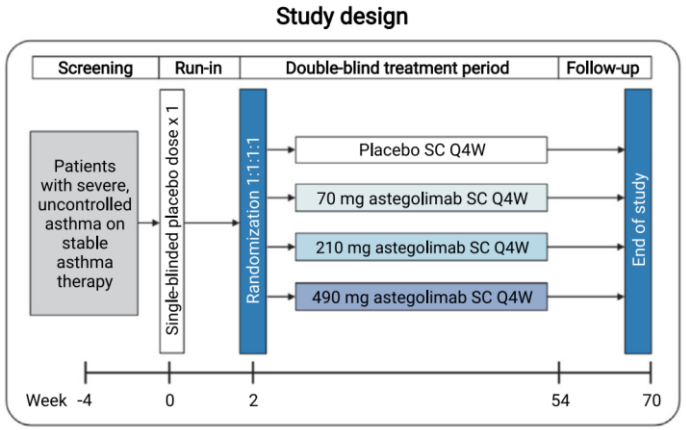
OCS reduction in Tezepelumab – SUNRISE :placebo-controlled evidence

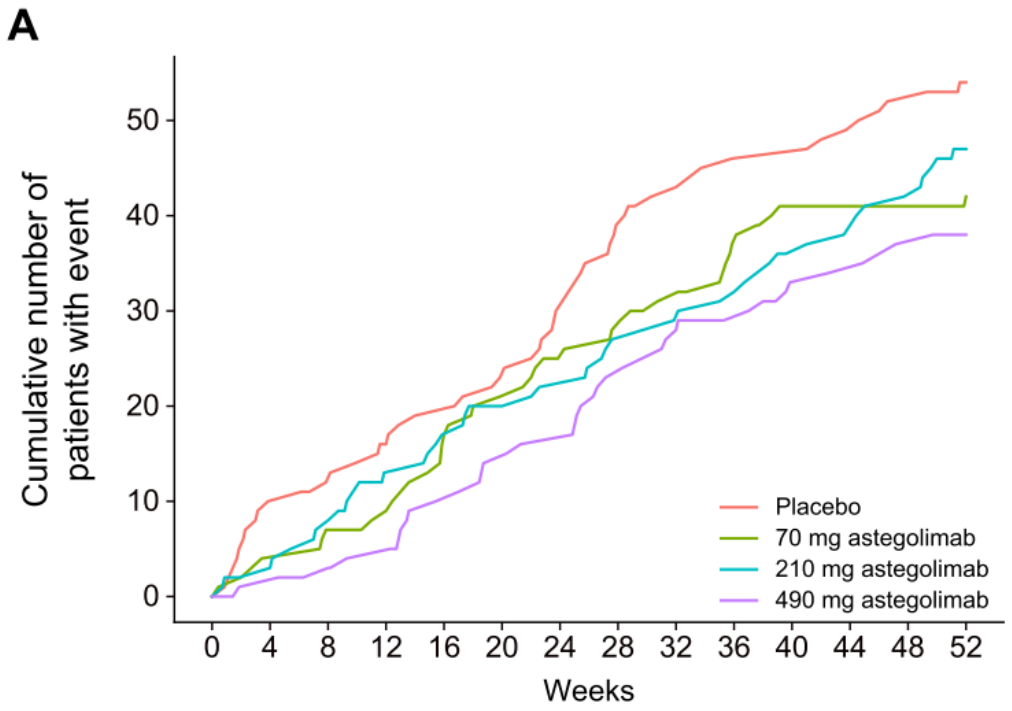


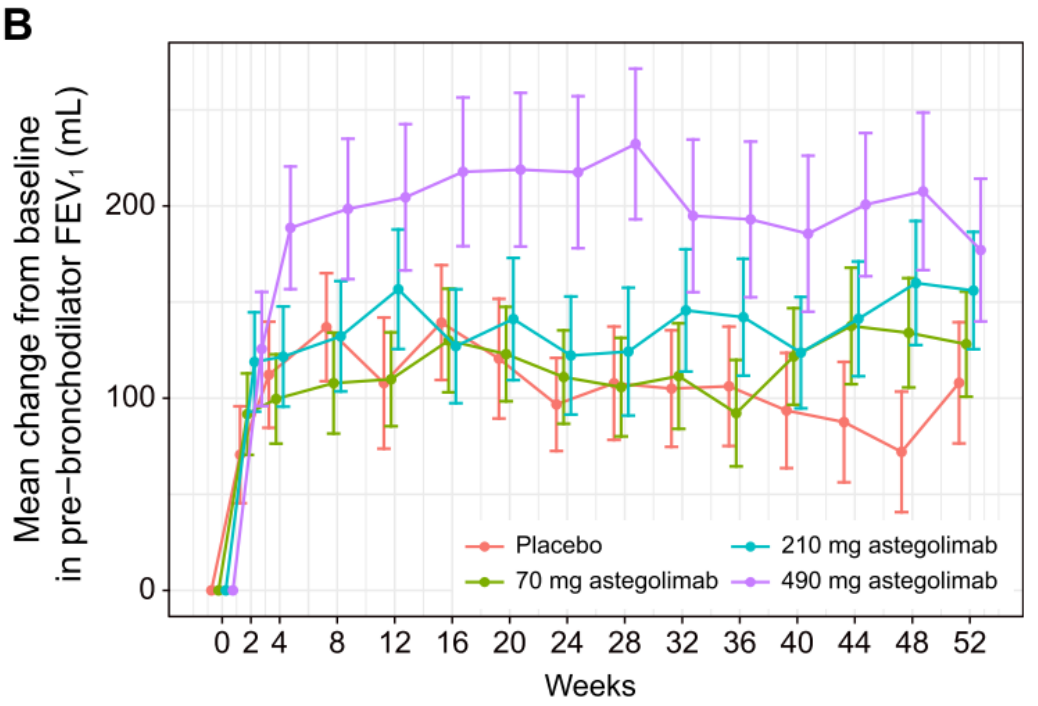


Wechsler et al. Lancet Respir Med. 2026;14(6):481-92.

Astegolimab - ZENYATTA trial

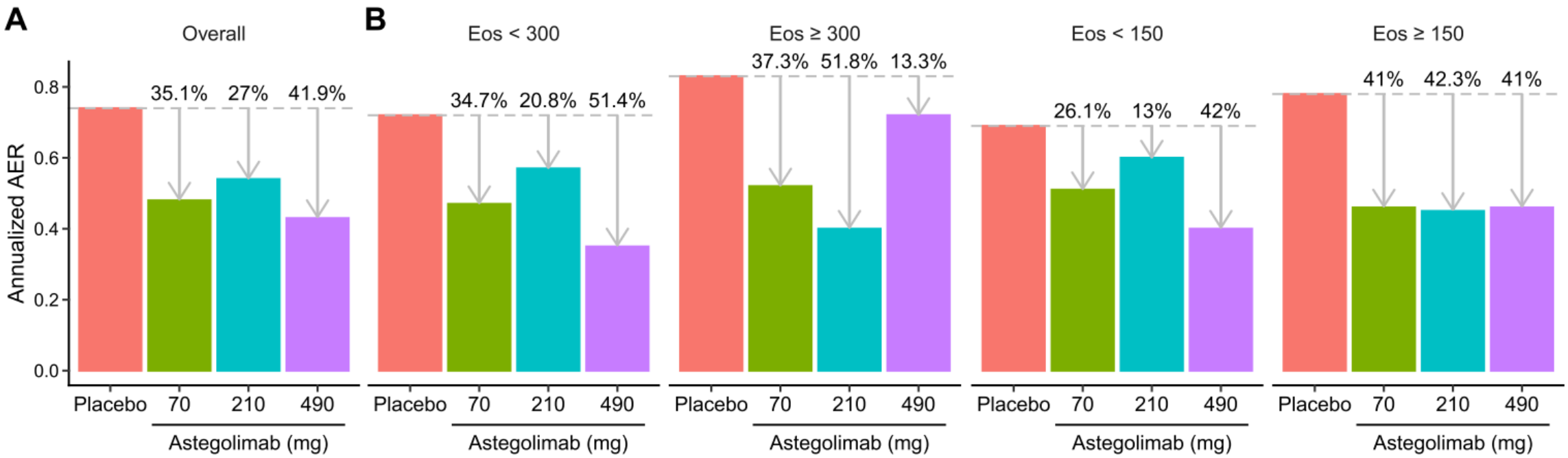






Kelsen et al. J Allergy Clin Immunol. 2021;148(3):790-8.

Astegolimab - ZENYATTA trial



Kelsen et al. J Allergy Clin Immunol. 2021;148(3):790-8.

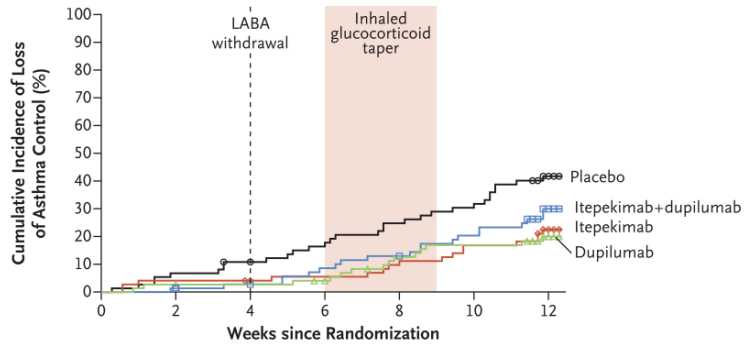
Itepekimab

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

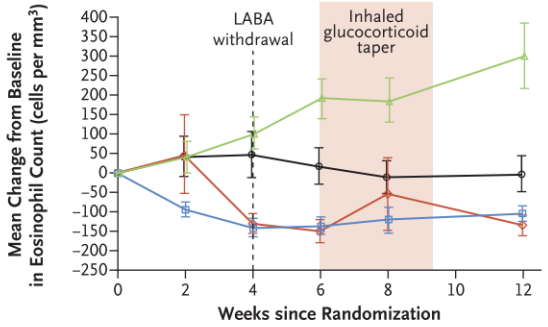
Efficacy and Safety of Itepekimab in Patients with Moderate-to-Severe Asthma

A Primary End Point: Loss of Asthma Control



No. of Patients							
Placebo	74	69	65	60	54	50	31
Itepekimab	73	70	69	67	64	59	48
Itepekimab+dupilumab	74	73	68	63	60	54	32
Dupilumab	74	72	71	69	61	58	43

C Change in Blood Eosinophil Count



No. of Patients						
Placebo	74	69	67	61	54	52
Itepekimab	73	68	65	62	65	62
Itepekimab+ dupilumab	74	66	68	62	58	56
Dupilumab	74	71	67	68	69	56

End Point	Placebo (N=74)	Itepekimab (N=73)	Itepekimab plus Dupilumab (N=74)	Dupilumab (N=74)
Primary end point: event indicating loss of asthma control during 12-wk intervention period — no. (%)	30 (41)	16 (22)	20 (27)	14 (19)
Odds ratio vs. placebo (95% CI)		0.42 (0.20 to 0.88)	0.52 (0.26 to 1.06)	0.33 (0.15 to 0.70)
P value vs. placebo		0.02	0.07	NA†
Patients with baseline eosinophils <300 cells per mm³ — no.	33	37	42	43
Primary end-point event — no. (%)	11 (33)	7 (19)	13 (31)	10 (23)
Odds ratio vs. placebo (95% CI)		0.46 (0.15 to 1.41)	0.92 (0.33 to 2.56)	0.62 (0.22 to 1.77)
Patients with baseline eosinophils ≥300 cells per mm³ — no.	41	36	32	31
Primary end-point event — no. (%)	19 (46)	9 (25)	7 (22)	4 (13)
Odds ratio vs. placebo (95% CI)		0.39 (0.14 to 1.05)	0.30 (0.10 to 0.87)	0.17 (0.05 to 0.58)

Wechsler et al. N Engl J Med. 2021;385(18):1656-68.

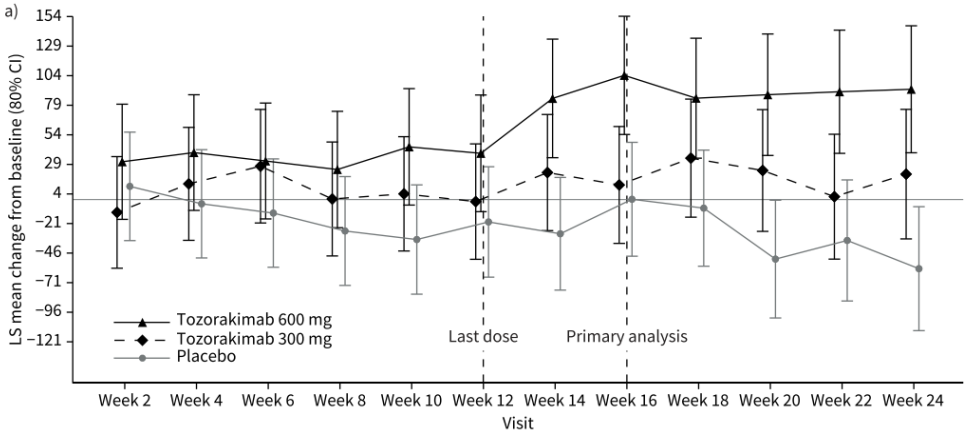
Tozorakimab

ERJ OPEN RESEARCH
ORIGINAL RESEARCH ARTICLE
J. CORREN ET AL.

FRONTIER-3: a randomised phase 2a study to investigate tozorakimab, an anti-interleukin-33 monoclonal antibody, in early-onset asthma

TABLE 2 Change from baseline to week 16 in pre-BD FEV_1 in the ITT population and stratified by exacerbation history

Treatment group	n	LS mean change from baseline mL, mean±SE	LS mean difference from placebo, mL	80% CI	One-sided p-value
Tozorakimab 600 mg	77	116±48	4	−71–79	0.473
Tozorakimab 300 mg	76	148±47	36	−38–111	0.267
Placebo	81	112±46	–	–	–
Patients with ⩾2 exacerbations in the previous 12 months					
Tozorakimab 600 mg	30	194±65	212	102–322	0.007
Tozorakimab 300 mg	31	59±67	77	−34–187	0.186
Placebo	29	−18±69	–	–	–



Corren et al. ERJ Open Res. 2026;12(1).

Tozorakimab

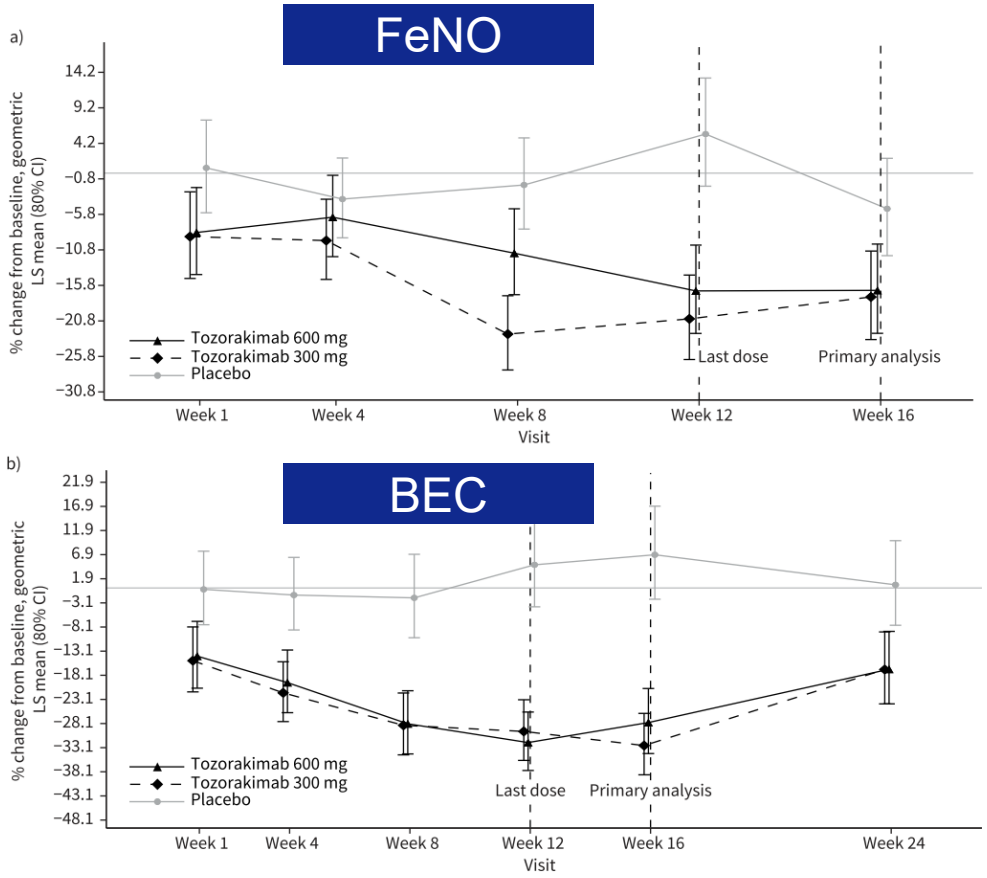


FIGURE 3 % change from baseline in concentration of a) fractional exhaled nitric oxide (to week 16), and b) blood eosinophil count (to week 24). LS: least-squares.

Table 1. Reduced levels of T2 and T1 chemokines and cytokines were observed in nasal lining fluid from participants who received tozorakimab relative to those receiving placebo

T2 cytokines associated with the recruitment of T2 immune cells (e.g. mast cells, eosinophils, T cells) and airway mucus hypersecretion[8–10]

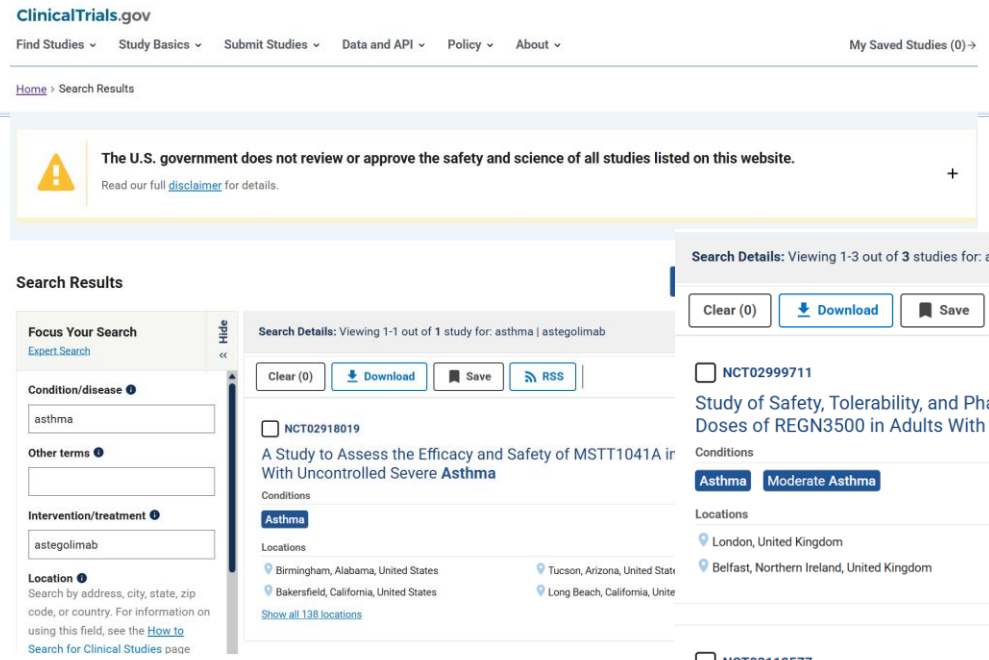
T1 inflammatory chemokines associated with NK and Th1 cell recruitment[11,12]

Mixed T2 and T1 cell recruitment[13]

Biomarker	Tozorakimab 300 mg				Tozorakimab 600 mg			
	Week 4		Week 16		Week 4		Week 16	
	Fold change	*p* value[a]	Fold change	*p* value[a]	Fold change	*p* value[a]	Fold change	*p* value[a]
IL-4	0.50	0.008	0.68	0.136	0.64	0.084	0.71	0.184
IL-5	0.25	0.001	0.32	0.007	0.37	0.015	0.42	0.062
IL-9	0.38	0.099	0.34	0.067	0.57	0.327	0.59	0.363
IL-13	0.44	0.002	0.42	0.001	0.56	0.025	0.48	0.004
CCL1	0.93	0.038	0.92	0.028	0.67	0.265	0.71	0.342
CCL3	0.64	0.064	0.87	0.557	0.65	0.067	0.96	0.867
CCL4	0.57	0.020	0.73	0.187	0.64	0.067	0.79	0.320
CCL5	0.85	0.346	0.74	0.076	0.83	0.285	0.67	0.017

Samples are from nasal lining fluid collected from FRONTIER-3 participants. Presented data are placebo-adjusted relative expression and measured by NULISA proteomics. Placebo sample number per time point: baseline, n = 70; week 4, n = 68; week 16, n = 70. Tozorakimab 300 mg, sample number per time point: baseline, n = 61; week 4, n = 59; week 16, n = 57. Tozorakimab 600 mg, sample number per time point: baseline, n = 64; week 4, n = 60; week 16, n = 60.
[a]Raw *p* values were not statistically significant after FDR correction.

Corren et al. ERJ Open Res. 2026;12(1).; Rytelewski et al. Poster presented at: ATS 2026; Orlando, FL. May 15–20, 2026.
Poster ID: ATS_3268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A Study to Assess the Efficacy and Safety of MSTT1041A in With Uncontrolled Severe Asthma
Conditions
Asthma
Locations
Birmingham, Alabama, United States
Tucson, Arizona, United State
Bakersfield, California, United States
Long Beach, California, Unite
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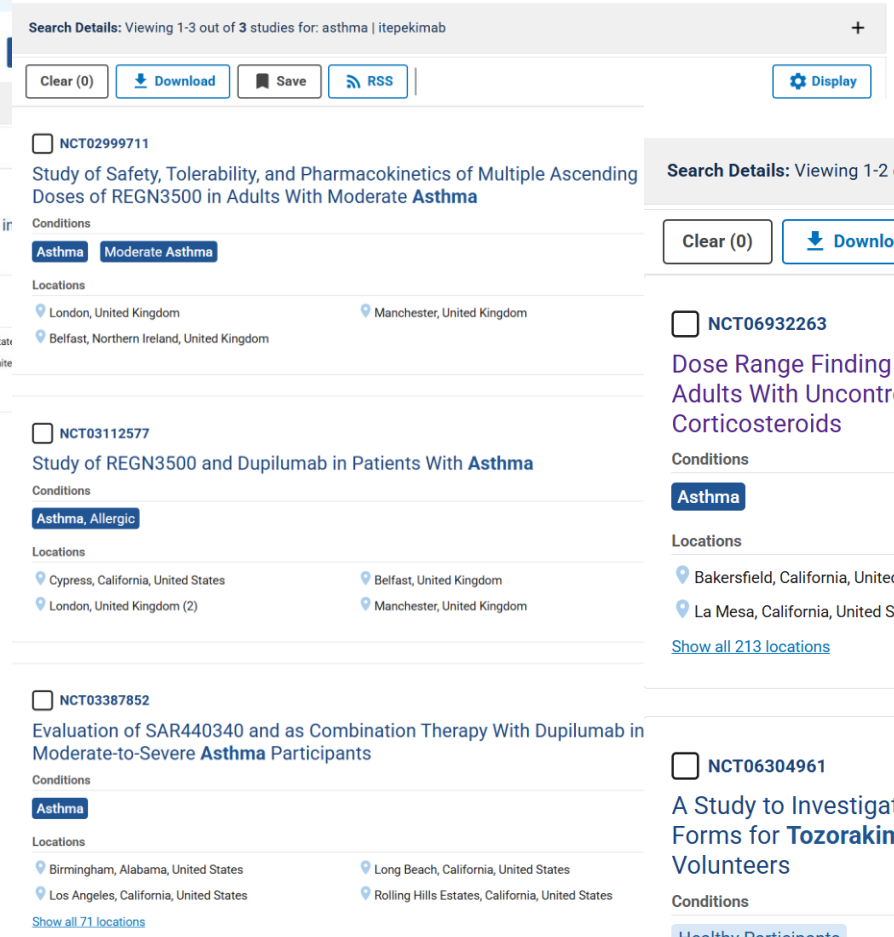
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Study of Safety, Tolerability, and Pharmacokinetics of Multiple Ascending Doses of REGN3500 in Adults With Moderate Asthma
Conditions
Asthma
Moderate Asthma
Locations
London, United Kingdom
Manchester, United Kingdom
Belfast, Northern Ireland, United Kingdom
NCT03112577
Study of REGN3500 and Dupilumab in Patients With Asthma
Conditions
Asthma, Allergic
Locations
Cypress, California, United States
Belfast, United Kingdom
London, United Kingdom (2)
Manchester, United Kingdom
NCT03387852
Evaluation of SAR440340 and as Combination Therapy With Dupilumab in Moderate-to-Severe Asthma Participants
Conditions
Asthma
Locations
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Long Beach, California, United States
Los Angeles, California, United States
Rolling Hills Estates, California, United States
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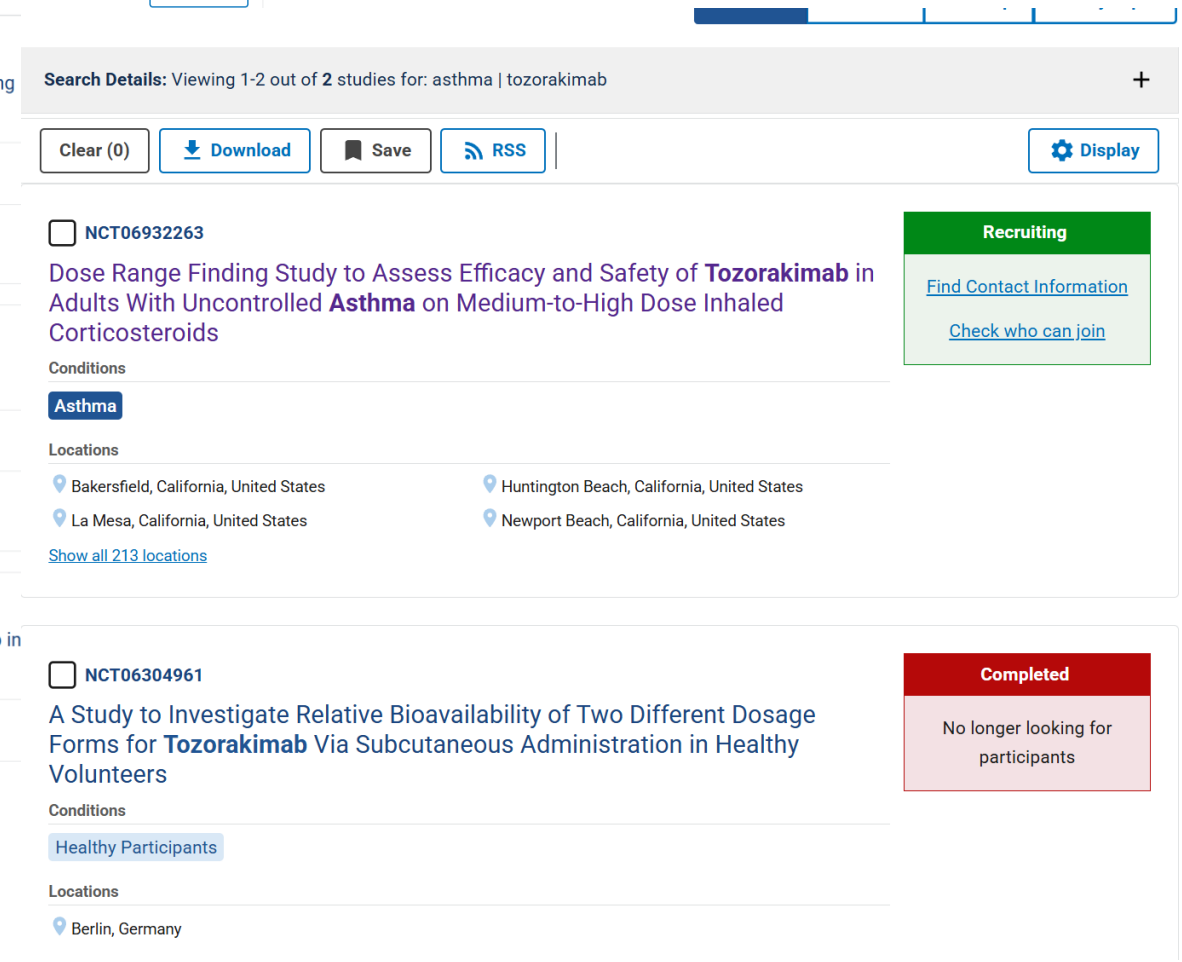
Search Details: Viewing 1-2 out of 2 studies for: asthma | tozorakimab
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NCT06932263
Dose Range Finding Study to Assess Efficacy and Safety of Tozorakimab in Adults With Uncontrolled Asthma on Medium-to-High Dose Inhaled Corticosteroids
Conditions
Asthma
Locations
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Huntington Beach, California, United States
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NCT06304961
A Study to Investigate Relative Bioavailability of Two Different Dosage Forms for Tozorakimab Via Subcutaneous Administration in Healthy Volunteers
Conditions
Healthy Participants
Locations
Berlin, Germany
Completed
No longer looking for participants

What comes next?

1. Switching
2. Long-interval
3. Combination

Switching biologics

Journal of Asthma and Allergy

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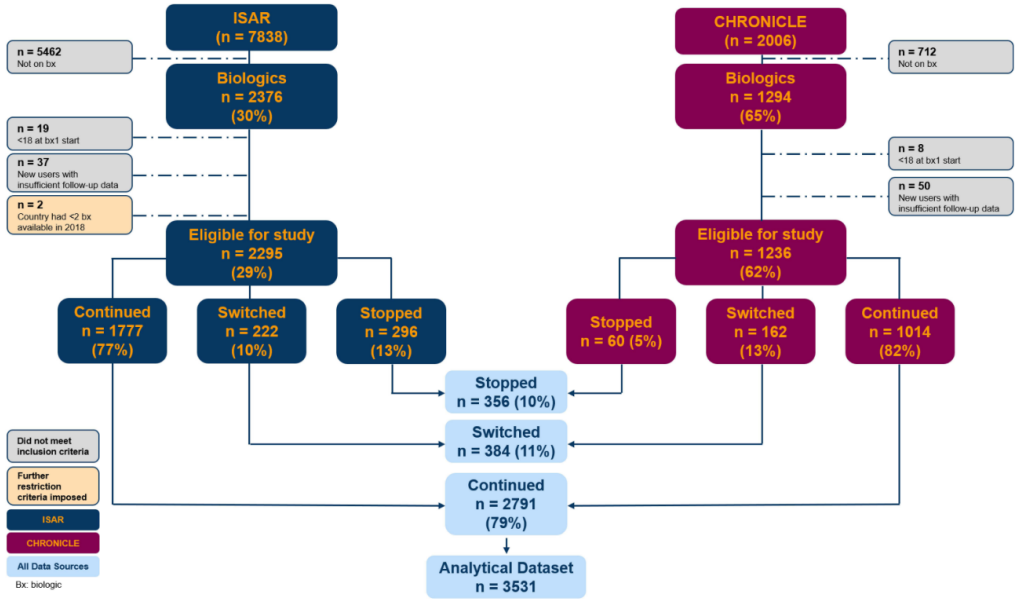
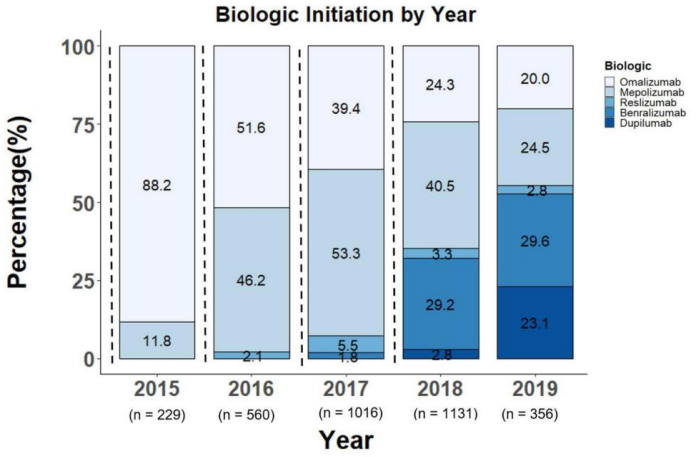
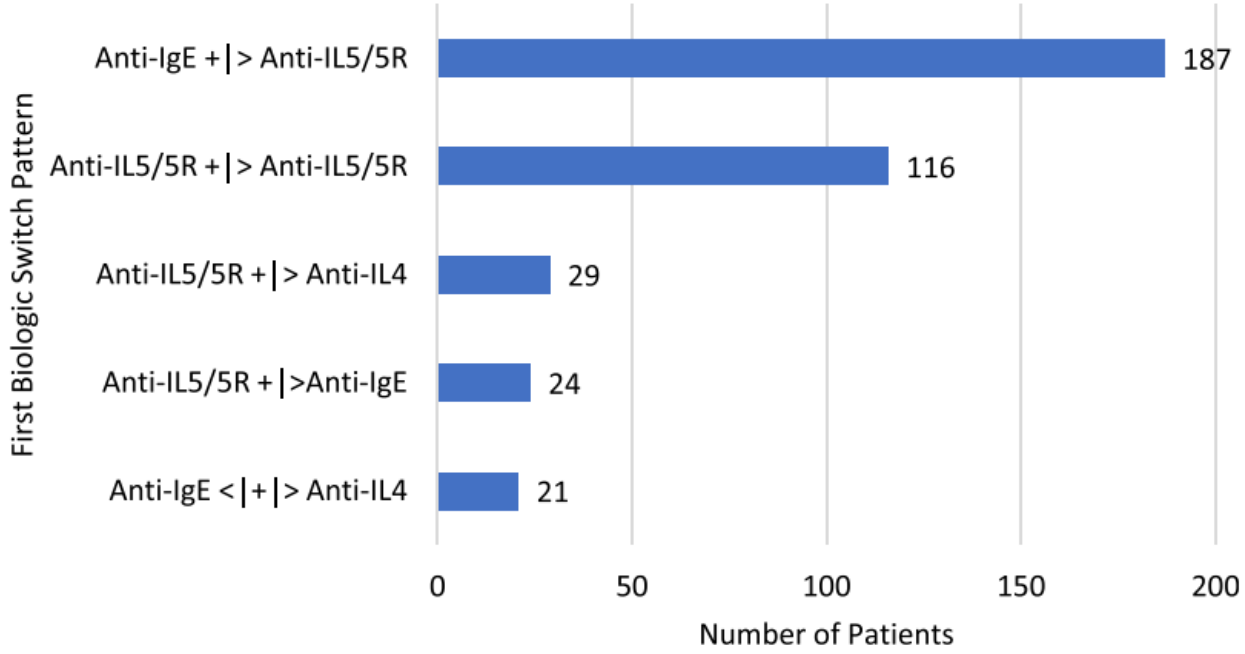
ORIGINAL RESEARCH

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

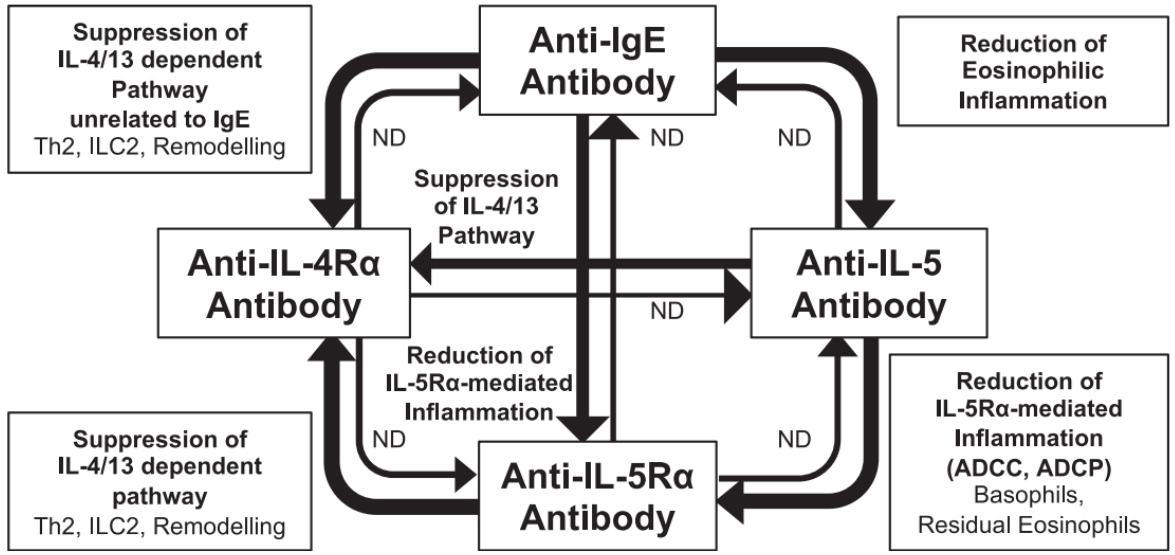


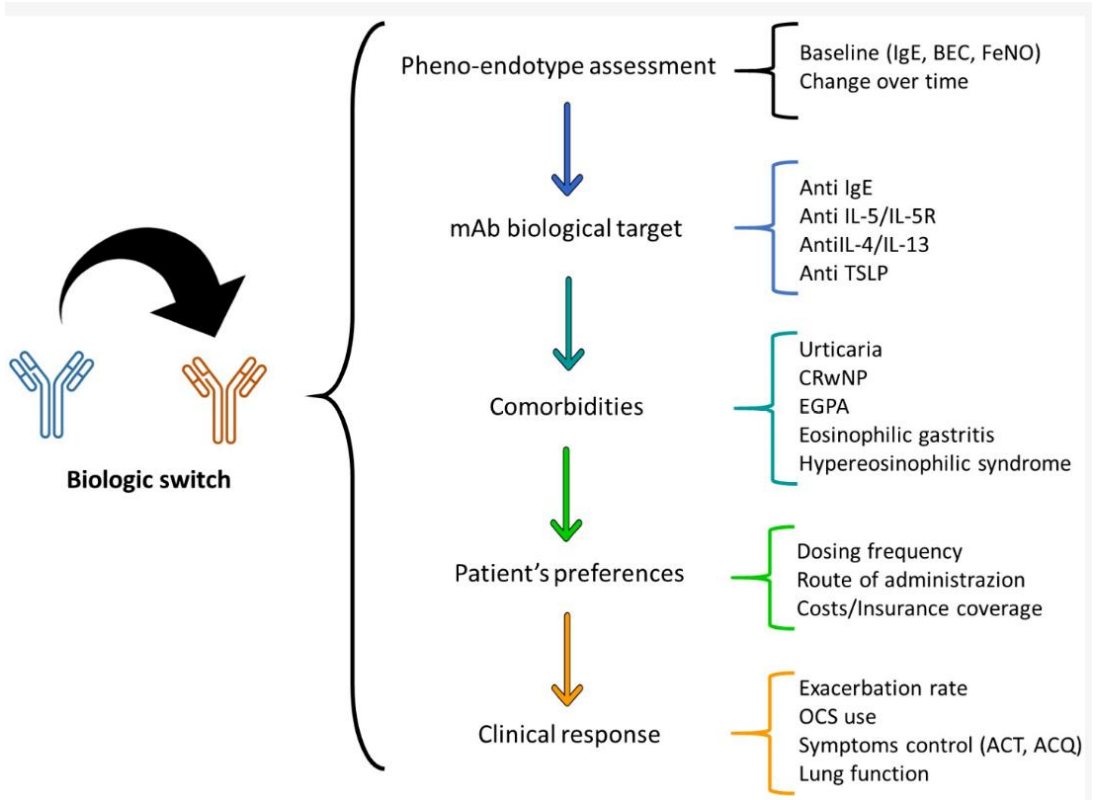




Menzies-Gow et al. J Asthma Allergy. 2022;15:63-78.

Switching biologics





Dragonieri et al. Adv Respir Med. 2024;92(2):110-22.Nagase et al. Allergol Int. 2023;72(1):11-23.

Switching biologics

Respir Investig. 2025 Jul;63(4):592-599. doi: 10.1016/j.resinv.2025.04.022. Epub 2025 May 8.

Switching to tezepelumab from other biologics in patients with severe asthma: a retrospective study

Toshiyuki Sumi [1], Taiki Ishigooka [2], Keigo Matsuura [2], Takumi Ikeda [2], Yuta Koshino [2], Keito Suzuki [2], Yuichi Yamada [3], Hirofumi Chiba [4]

Affiliations + expand

PMID: 40339469 DOI: 10.1016/j.resinv.2025.04.022

J Asthma Allergy. 2025 Aug 5:18:1161-1166. doi: 10.2147/JAA.S516225. eCollection 2025.

Evaluating Safety and Effectiveness of Switching Biologics in Managing Severe Asthma Patients

Leena Al Awn [1 2 3], Maha AlAmmari [1 2 3], Dalal AlAbdulkarim [1 2 3], Reem AlAhmed [3 4 5], Bijesh Yadav [3 5], Hamdan Al-Jahdali [3 4 5]

Affiliations + expand

PMID: 40787082 PMCID: PMC12335250 DOI: 10.2147/JAA.S516225

Biomedicines. 2025 Aug 28;13(9):2096. doi: 10.3390/biomedicines13092096.

Biomarker-Associated Remission After Switching to Dupilumab in Severe Asthma Following Failure of Prior Biologics

Fabio Romano Selvi [1], David Longhino [1], Gabriele Lucca [1], Ilaria Baglivo [1], Maria Antonietta Zavarella [1], Chiara Laface [1], Laura Bruno [1], Arianna Delfino Spiga [1], Sara Gamberale [1], Ludovica Fabbroni [1], Angela Rizzi [1], Arianna Aruanno [1], Marina Curci [1], Alessandro Buonomo [1], Stefania Colantuono [2], Marinella Viola [1], Gianluca Ianiro [3], Antonio Gasbarrini [3], Cristiano Caruso [1]

BMC Pulm Med. 2025 Nov 26;26(1):4. doi: 10.1186/s12890-025-04044-7.

Clinical outcomes after switching from omalizumab to anti-IL-5/IL-5R biologics in severe asthma: a retrospective cohort study

Fatma Arzu Akkuş [1], Fatih Çölkesen [2], Tuğba Önalan [3], Mehmet Emin Gerek [2], Mehmet Kılınç [4], Şevket Arslan [2]

Asia Pac Allergy. 2025 Dec;15(4):281-285. doi: 10.5415/apallergy.0000000000000244. Epub 2025 Dec 2.

The frequency and predictability of switching biologic agents in severe asthma: A real-world perspective

Ali Can [1], Özge Atik [1]

J Asthma Allergy. 2025 Sep 3:18:1229-1237. doi: 10.2147/JAA.S523832. eCollection 2025.

Clinical and Healthcare Cost Characteristics of Severe Asthma Patients with Long-Term Control on Omalizumab: A Comparative Analysis with Patients Who Switched to Other Biologics

Hironobu Sunadome [1 2], Hisako Matsumoto [2 3], Tadao Nagasaki [2 4], Yusuke Hayashi [2], Satoru Terada [2], Kenta Nishi [2], Natsuko Nomura [2], Mariko Kogo [2], Chie Morimoto [2], Tsuyoshi Oguma [2 5], Susumu Sato [1 2], Toyohiro Hirai [2]

J Clin Med. 2026 May 27;15(11):4149. doi: 10.3390/jcm15114149.

Biologic Switching in Patients with Severe Asthma: Effects on Exacerbations, Corticosteroid Use and Lung Function

Fatma Dindar Çelik [1], Kurtuluş Aksu [1]

Allergy. 2026 Apr;81(4):1289-1292. doi: 10.1111/all.70205. Epub 2025 Dec 24.

Dupilumab Effectiveness in Biologic-Naïve and Switched Severe Asthma in Real Life

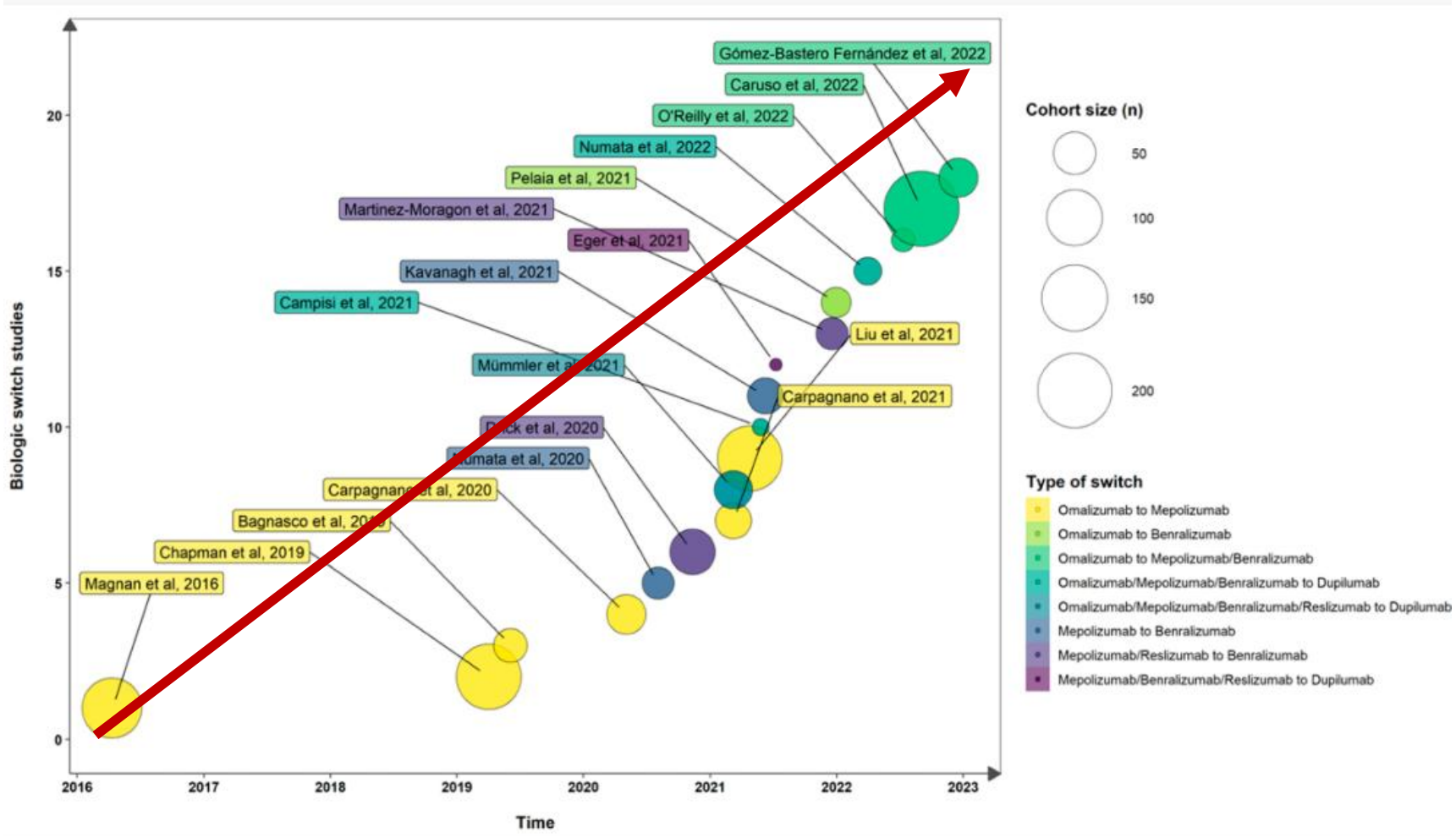
Catherine Moermans [1 2], Mare Sabbe [1 2], Adrien Onssels [1], Noémie Bricmont [1], Romane Bonhiver [1], France Regnier [2], Sophie Graff [2], Sara Gerday [1], Makon-Sébastien Njock [1], Adeline Rosu [1], Virginie Paulus [2], Françoise Guissard [2], Stéphanie Ziant [2], Carole Sanchez [2], Marie Ernst [3], Christophe Desmet [4], Renaud Louis [1 2], Florence Schleich [1 2 5]

J Asthma Allergy. 2022 Feb 9:15:187-195. doi: 10.2147/JAA.S348513. eCollection 2022.

Clinical Characteristics of Patients and Factors Associated with Switching Biologics in Asthma

Machiko Matsumoto-Sasaki [1], Kaoruko Simizu [1], Masanobu Suzuki [2], Masaru Suzuki [1], Hirokazu Kimura [1], Yuji Nakamaru [2], Yoichi M Ito [3], Akihiro Honma [2], Satoshi Konno [1]

Switching biologics



Scioscia et al. Int J Mol Sci. 2023;24(11).

Switching biologics

Allergy

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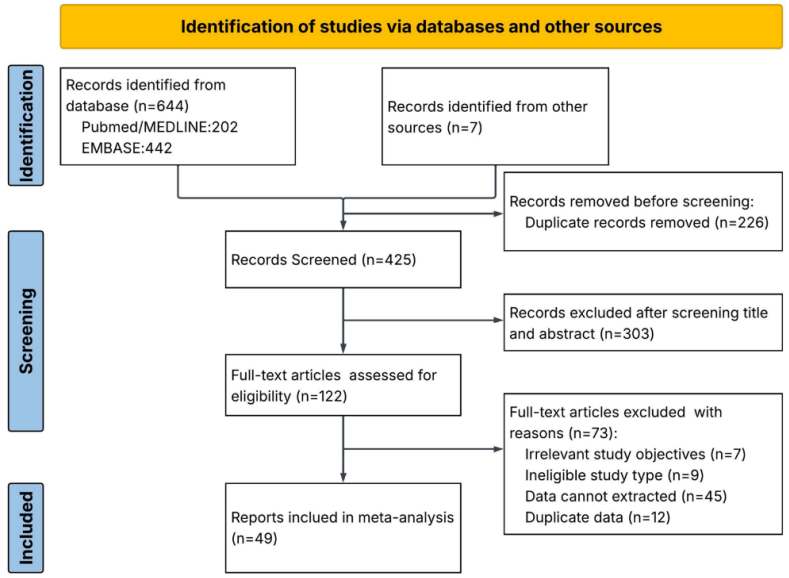
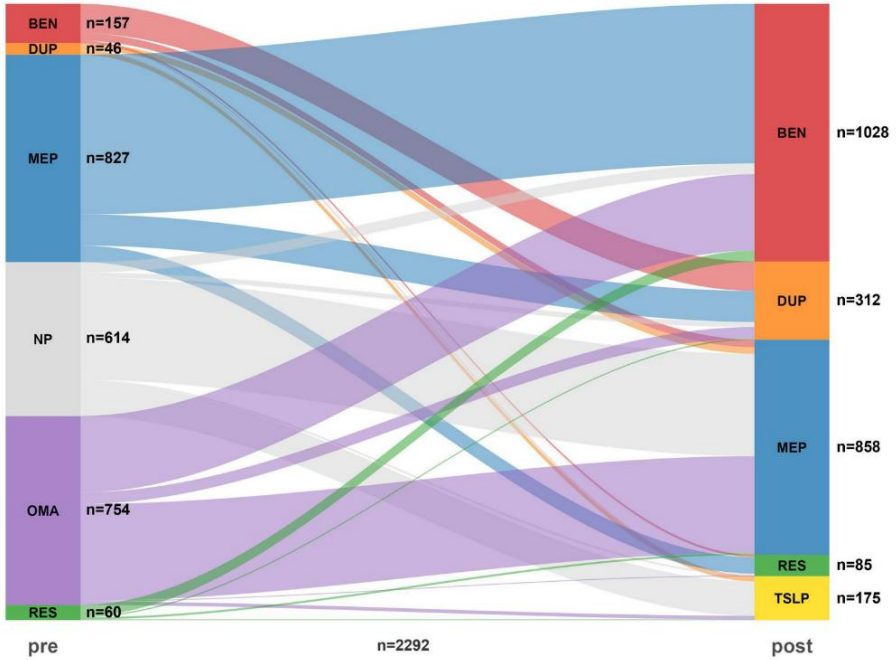
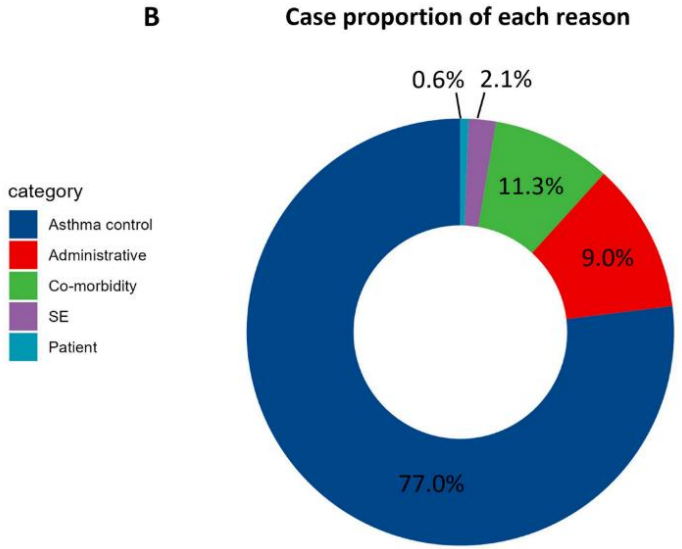
ORIGINAL ARTICLE OPEN ACCESS

Asthma and Lower Airway Disease

Patterns and Clinical Efficacy of Biologics Switching in Patients With Severe Asthma: A Systematic Review and Meta-Analysis

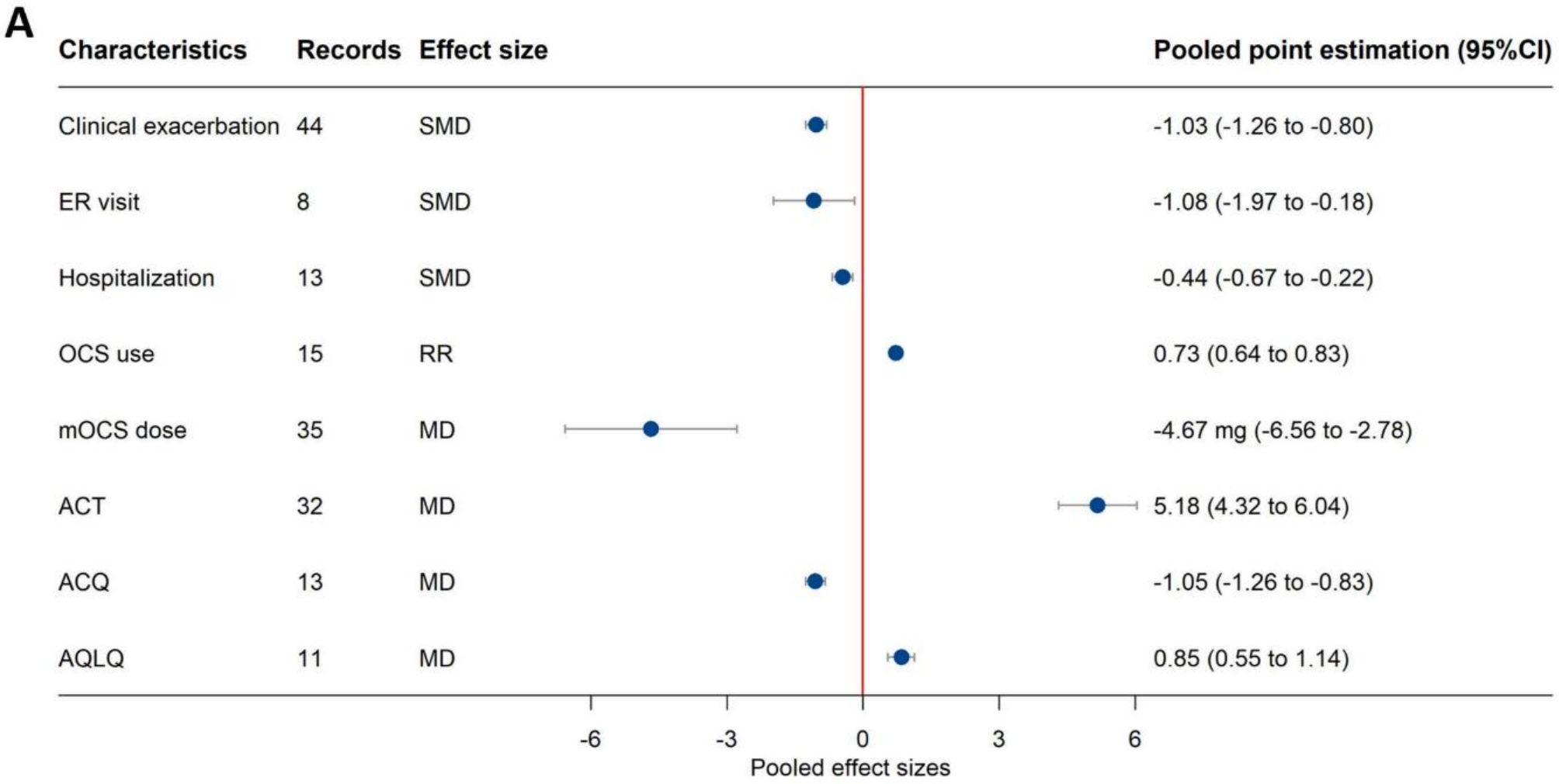






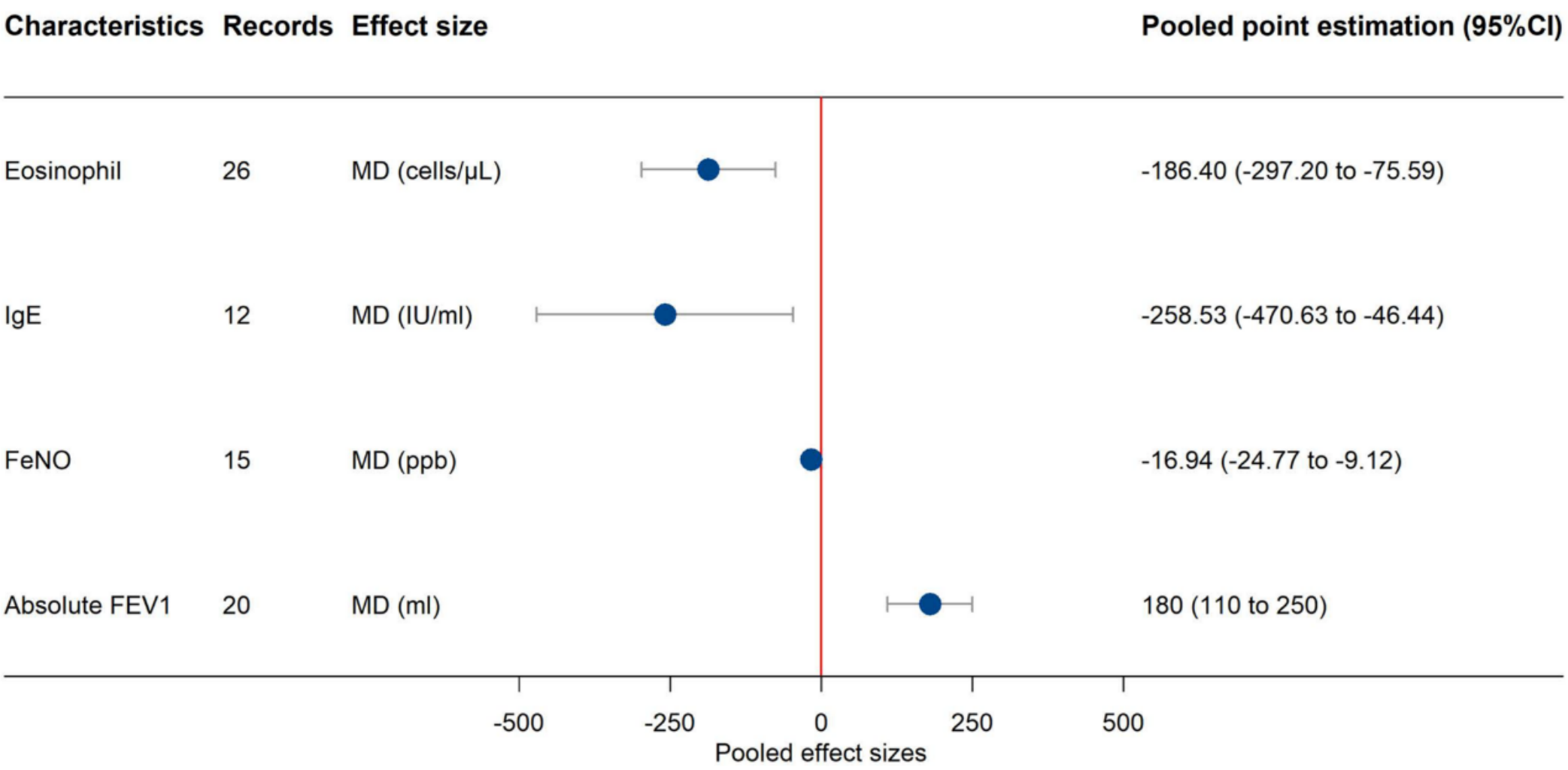
Zheng et al. Allergy. 2026;81(5):1548-70.

Clinical and symptomatic outcomes

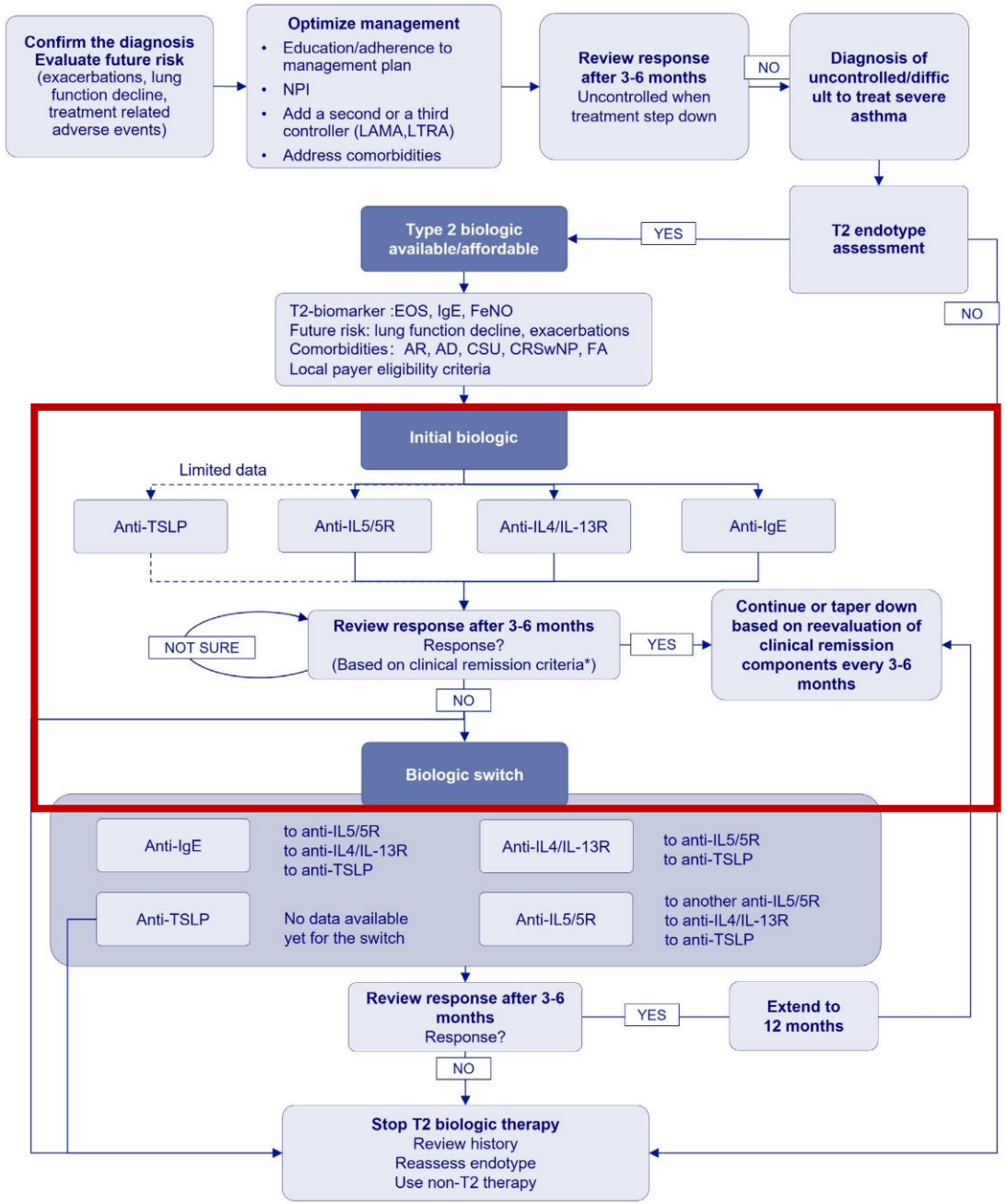


Zheng et al. Allergy. 2026;81(5):1548-70.

Laboratory indicators



Zheng et al. Allergy. 2026;81(5):1548-70.



Review response to an initial trial of add-on Type 2-targeted therapy

- At present, there are no well-defined criteria for a good asthma response, but consider exacerbations, symptom control, lung function, treatment intensity (including OCS dose), and patient satisfaction.
- Also consider the patient's biomarkers (interval and during exacerbations, if available), and response of any comorbid Type 2 conditions (atopic dermatitis, nasal polyps, etc). Review response as above.
- If the response is unclear, consider extending the trial to a total of 6–12 months. If there is only a partial response, or a differential response between asthma and comorbid conditions, re-evaluate these diagnoses.
- Monitor for potential adverse events, including for infections
- If there is no response, stop the biologic therapy, and consider switching to a trial of a different Type 2-targeted therapy, if available and if the patient is eligible.

GINA 2026; Zheng et al. Allergy. 2026;81(5):1548-70.

Long-interval

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Twice-Yearly Depemokimab in Severe Asthma with an Eosinophilic Phenotype

Depemokimab is an ultra-long-acting biologic therapy with enhanced binding affinity for interleukin-5, which potentially enables effective 6-month dosing intervals for patients with asthma.

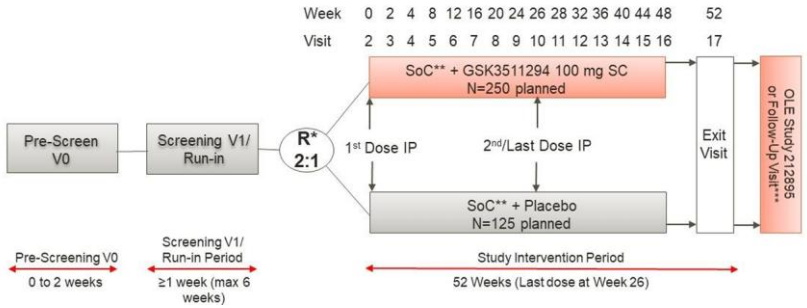
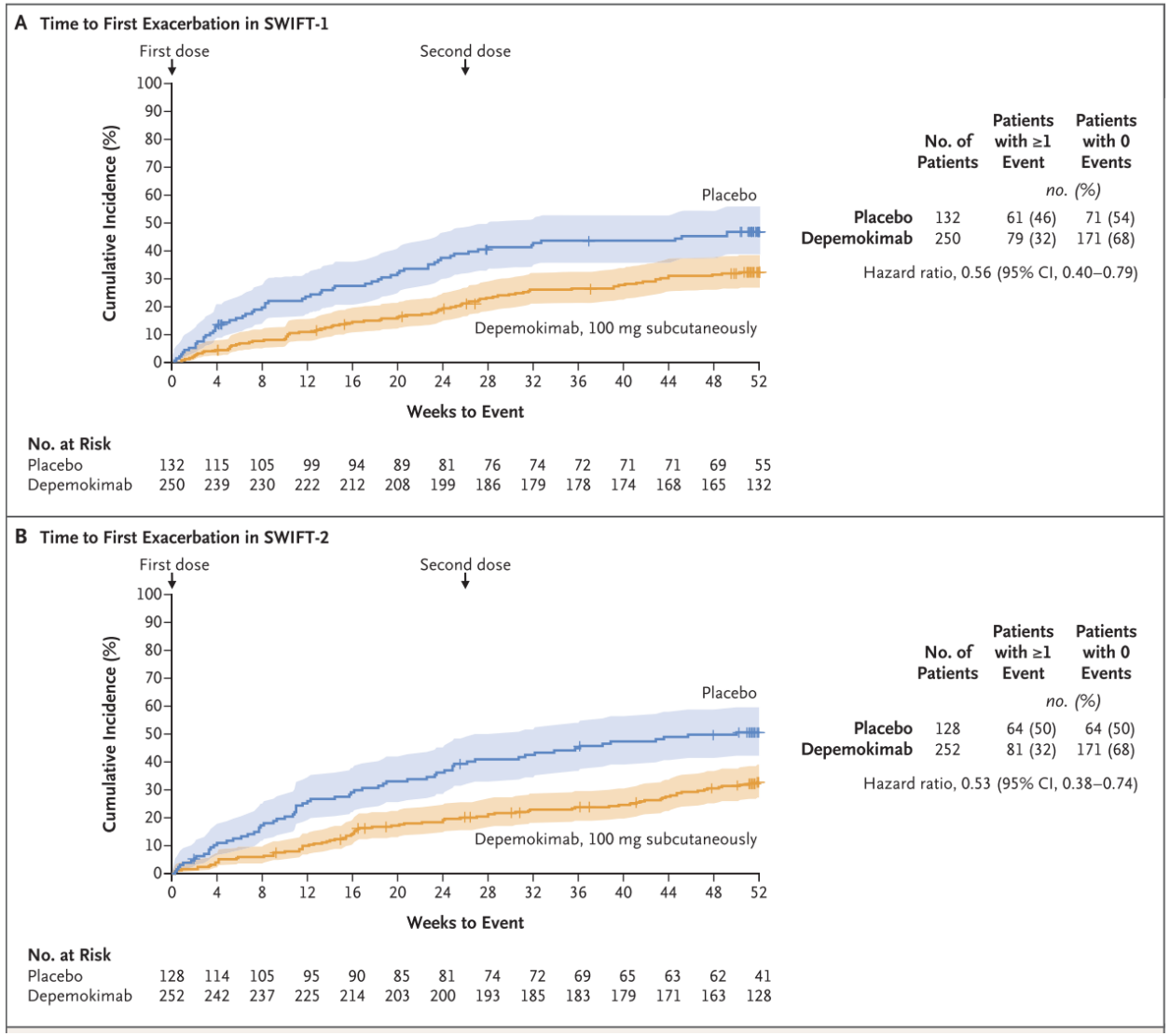
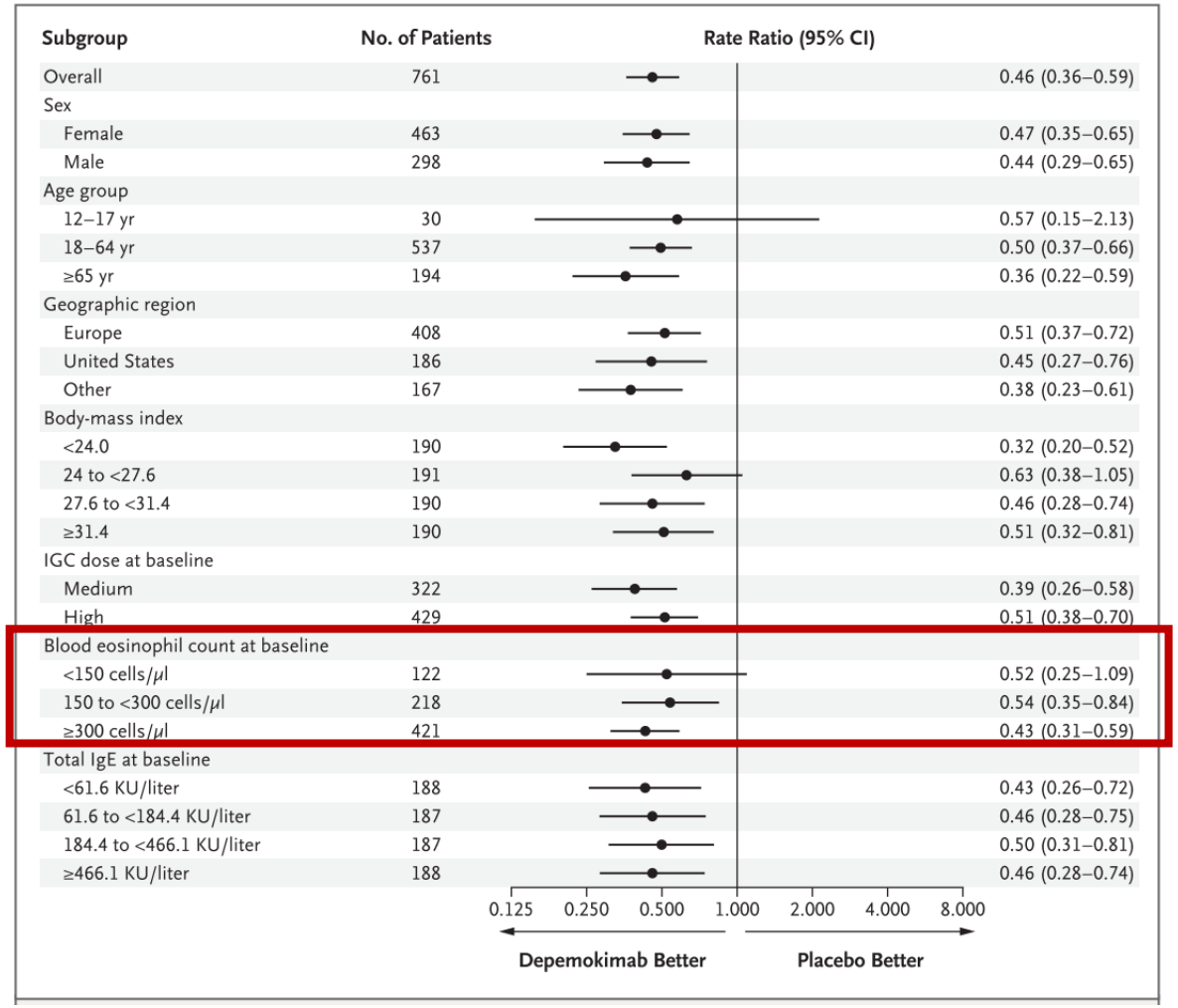


Table 2. Summary of Primary and Secondary End Points.*

End Point	SWIFT-1			SWIFT-2			Pooled Trials	
	Depemokimab (N=250)	Placebo (N=132)	P Value†	Depemokimab (N=252)	Placebo (N=128)	P Value†	Depemokimab (N=502)	Placebo (N=260)
Primary end point								
Annualized rate of exacerbations at 52 wk (95% CI)	0.46 (0.36 to 0.58)	1.11 (0.86 to 1.43)	<0.001	0.56 (0.44 to 0.70)	1.08 (0.83 to 1.41)	<0.001	0.51 (0.43 to 0.60)	1.11 (0.92 to 1.33)
Rate ratio (95% CI)	0.42 (0.30 to 0.59)			0.52 (0.36 to 0.73)			0.46 (0.36 to 0.59)	
Percent between-group difference in annual rate (95% CI)	58 (41 to 70)			48 (27 to 64)			54 (41 to 64)	
No. of exacerbations‡	120	150		153	167		273	317
Secondary end points								
Change from baseline in SGRQ score at 52 wk§	−13.03±1.11	−9.67±1.54	0.08	−14.80±1.04	−12.49±1.46	0.20	−13.92±0.76	−11.04±1.06
Treatment difference (95% CI)	−3.36 (−7.11 to 0.39)			−2.31 (−5.84 to 1.23)			−2.88 (−5.43 to −0.32)	
Change from baseline in ACQ-5 score at 52 wk¶	−0.82±0.07	−0.77±0.09		−0.81±0.07	−0.70±0.09		−0.81±0.05	−0.73±0.06
Treatment difference (95% CI)	−0.04 (−0.27 to 0.18)			−0.11 (−0.33 to 0.11)			−0.08 (−0.24 to 0.07)	
Change from baseline in prebronchodilator FEV_1 at 52 wk — liter	0.16±0.03	0.16±0.04		0.24±0.03	0.18±0.04		0.20±0.02	0.17±0.03
Treatment difference (95% CI)	−0.01 (−0.089 to 0.088)			0.06 (−0.04 to 0.15)			0.03 (−0.04 to 0.09)	
Change from baseline in asthma nightly symptom diary at 52 wk‖	−1.39±0.12	−1.30±0.17		−1.18±0.09	−0.97±0.13		NA	
Treatment difference (95% CI)	−0.09 (−0.50 to 0.31)			−0.21 (−0.52 to 0.09)				
Change from baseline in asthma daily symptom diary at 52 wk‖	−1.33±0.10	−1.25±0.14		−1.13±0.08	−0.93±0.11		NA	
Treatment difference (95% CI)	−0.08 (−0.42 to 0.26)			−0.21 (−0.48 to 0.07)				
Annualized rate of exacerbations leading to hospitalization or ED visit at 52 wk (95% CI)**	NA			0.05 (0.02 to 0.09)	0.11 (0.05 to 0.22)		0.02 (0.01 to 0.04)	0.09 (0.05 to 0.15)
Rate ratio (95% CI)	NA			0.42 (0.16 to 1.13)			0.28 (0.13 to 0.61)	
Percent reduction in annual rate (95% CI)	NA			58 (−13 to 84)			72 (39 to 87)	
Number of exacerbations	5	13		16	18		21	31

Jackson et al. N Engl J Med. 2024;391(24):2337-49.





Jackson et al. N Engl J Med. 2024;391(24):2337-49.

Switching to Long-interval agent

American Journal of Respiratory and Critical Care Medicine, 2026, 212(5), 921–935
https://doi.org/10.1093/ajrccm/aamag031
Published: February 11, 2026
Original Research | Asthma and Allergy

ATS American Thoracic Society
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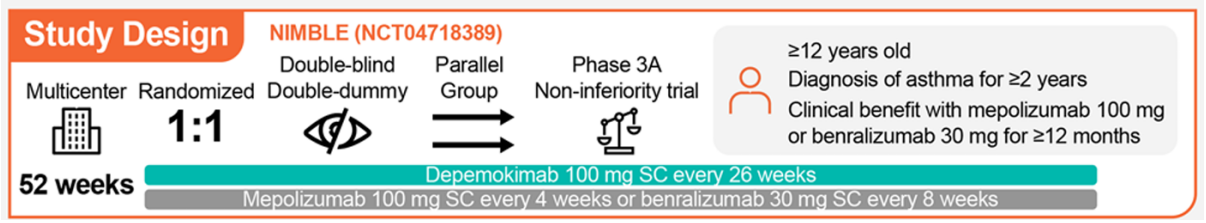
Switching to twice-yearly depemokimab from mepolizumab/benralizumab in severe asthma: a multicenter, randomized, double-blind, phase 3A clinical trial (NIMBLE)



Endpoint	Depemokimab (*n* = 848)	Active comparator (mepolizumab/ benralizumab) (*n* = 839)
Primary endpoint: annualized rate of clinically significant exacerbations over 52 weeks		
No.	813	803
Annualized rate (95% CI)	0.57 (0.50 to 0.64)	0.49 (0.43 to 0.55)
RR (95% CI)	1.16 (0.98 to 1.38)	
Primary endpoint (supplementary estimand): annualized rate of clinically significant exacerbations over 52 weeks		
No.	775	757
Annualized rate (95% CI)	0.51 (0.45 to 0.58)	0.45 (0.39 to 0.52)
RR (95% CI)	1.13 (0.94 to 1.36)	
Secondary endpoint: weighted mean change from baseline to week 52 in SGRQ total score		
No.	765	755
LS mean (SE)	25.94 (0.48)	25.76 (0.49)
LS mean change (SE)	-0.69 (0.48)	-0.86 (0.49)
Treatment difference (95% CI)	0.17 (-0.85 to 1.20)	
Secondary endpoint: weighted mean change from baseline to week 52 in ACQ-5		
No.	773	758
LS mean (SE)	0.94 (0.03)	0.97 (0.03)
LS mean change (SE)	0.03 (0.03)	0.06 (0.03)
Treatment difference (95% CI)	-0.03 (-0.09 to 0.02)	
Secondary endpoint: weighted mean change from baseline to week 52 in FEV_1		
No.	795	782
LS mean (SE)	2.20 (0.009)	2.19 (0.010)
LS mean change (SE)	-0.014 (0.009)	-0.018 (0.010)
Treatment difference (95% CI)	0.004 (-0.016 to 0.024)	

While statistical non-inferiority was not met (the upper limit of the 95% CI exceeded 1.28), exacerbation rates were low in both treatment groups

Chupp et al. BLUE 2026;212(5):921-35.

Switching to Long-interval agent

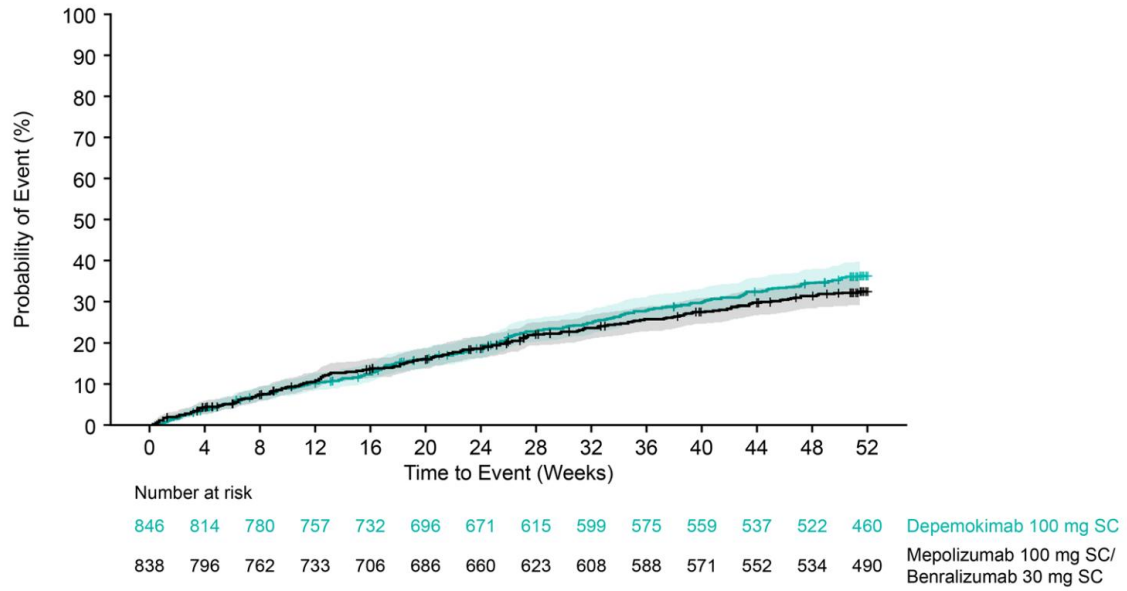


Table 4 Summary of adverse events in the safety population on treatment and posttreatment.

Event	Depemokimab (*n* = 848)	Active comparator (*n* = 839)
AEs, No. (%)		
Any AE	717 (85)	691 (82)
Related to study treatment	78 (9)	82 (10)
Leading to permanent discontinuation of study treatment or study withdrawal	13 (2)	12 (1)
Leading to dose interruption or delay	11 (1)	22 (3)
SAEs, No. (%)		
Any SAE	80 (9)	75 (9)
Related to study treatment	0	3 (<1)
Fatal	0	1 (<1)
Fatal, related to study treatment	0	0

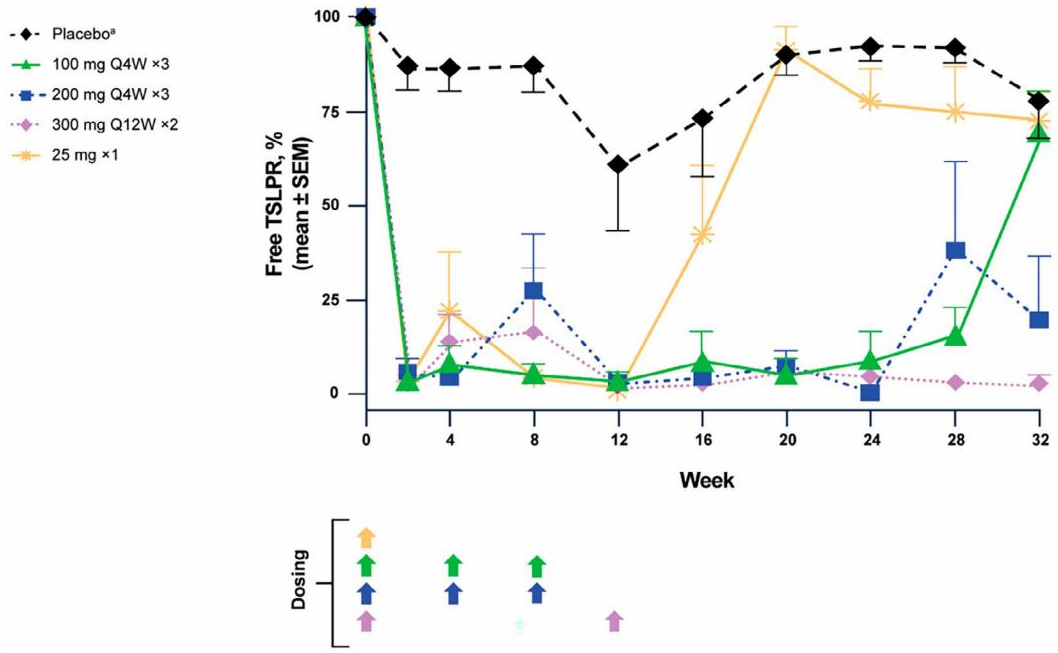
Chupp et al. BLUE 2026;212(5):921-35.

Long-interval

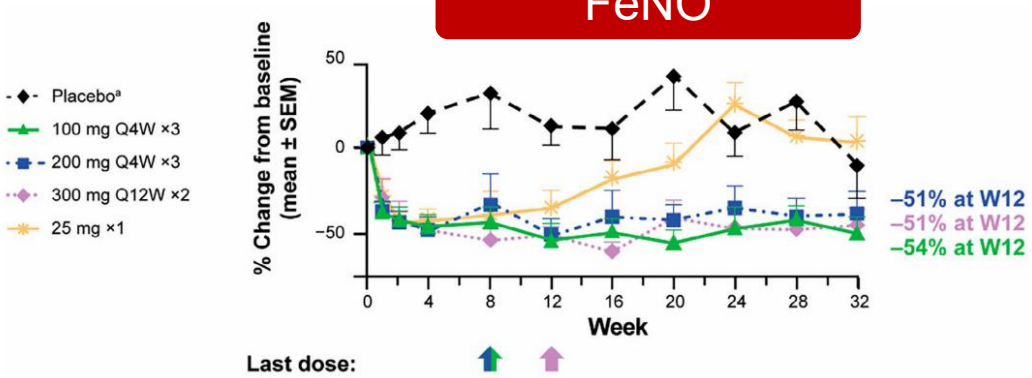
ARTICLE

Verekitug, a Novel Antibody Antagonist to the TSLP Receptor in Adults with Asthma: A 32-Week Randomized Phase 1b Multiple Ascending-Dose Trial

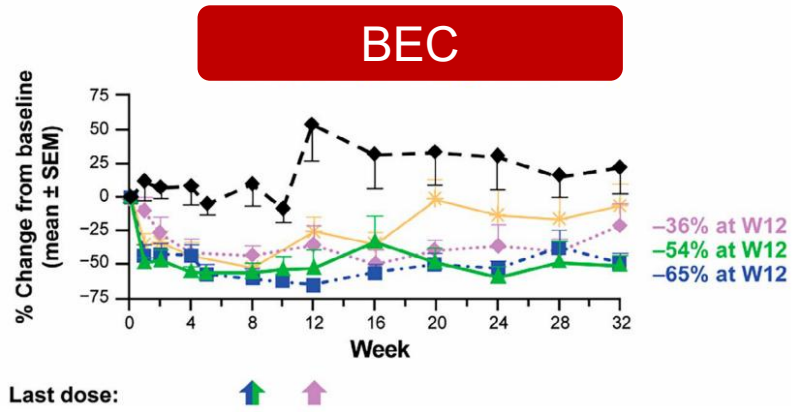
TSLP



FeNO



BEC



Singh et al. Clin Pharmacol Ther. 2026;119(3):782-90.

Combination

Journal of Asthma and Allergy

Dovepress
Taylor & Francis Group

Open Access Full Text Article

CASE SERIES

Combining Dual Biologics Therapy for Severe Asthma: A Series of Ten Cases

Yan Chen*, Lu Wang*, Jiaxing Xie

- All 10 patients exhibited
  - Good tolerance to the combined biologic therapies
  - improvements in asthma and comorbidity management
  - Reduction in OCS usage.
- No serious adverse events were reported.

Table 1 Demographics and Clinical Characteristics of Patients at Baseline and After Dual Biologic

	All	N1	N2	N3	N4	N5	N6	N7	N8	N9	N10
Baseline characteristics											
Age (y)	56±15	80	45	59	55	34	82	57	47	59	45
Female sex, n (%)	6 (60%)	M	M	F	F	F	F	M	M	F	F
Diagnosis	N/A	SEA	SEA	SEA	SEA	SEA	SEA	SEA	SEA	SEA	SEA
Comorbidities	N/A	AR, COPD	CRS, localized-EGPA	CRS, AD	EGPA, CRS, EOM	localized-EGPA, EOM, CRSwNP	CRS	localized-EGPA, CRS, EOM	AR, CSU	localized-EGPA, AR, CRS	EGPA, AR, CRS, CSU
Atopy, n (%)	6 (60%)	N	Y	Y	Y	Y	N	Y	N	N	Y
Biologics	N/A	Dupi+Mepo	Benra→Dupi→Dupi +Mepo	Dupi→Dupi +Mepo	Dupi→Mepo→Dupi +Mepo	Benra→Dupi→Dupi +Mepo	Mepo→Mepo +Dupi	Oma→Benra→Benra +Dupi	Oma→Oma +Mepo→Mepo	Oma→Oma +Mepo→Mepo	Oma→ Mepo→Dupi→Mepo +Dupi
Combined reason		advanced age, asthma-COPD overlap, severe airflow restriction, OCS dependence and exacerbations	CRW and respiratory function improved a little with Benra alone, switched to Dupi alone led to symptoms controlled and no exacerbations, but OCS still required 15–20mg/d	elevated blood eosinophils with Dupi	blood eosinophils elevated with Dupi alone, switched to Mepo alone led to CRS and EOM relapsed	CRW and EOM uncontrolled with Benra alone, switched to Dupi improved CRW and EMO, but led to exacerbation induced by significant increase in blood eosinophils	exacerbations still persist and OCS could not discontinue with Mepo alone	asthma symptom uncontrolled with Oma alone, CRS and EOM uncontrolled with Benra alone, Dupi induced elevated blood eosinophils	asthma symptom uncontrolled with Oma alone, reserve Oma for CUS, but urticaria repeated relapses	asthma symptom uncontrolled with Oma alone and resulted in blood eosinophils elevation	symptom uncontrolled with Oma or Mepo alone, elevated blood eosinophils and diagnosis EGPA with Dupi
Combined benefits		no exacerbations, no OCS and symptoms controlled	Symptoms good controlled and OCS reduced to 5–10 mg/d	no nasal inhalers, no ICS+LABA, achieved clinical remission	Asthma, CRS and EOM controlled, and blood eosinophils not elevated	Asthma, CRS and EOM controlled, and blood eosinophils not elevated	Symptoms controlled, no exacerbations and OCS discontinued	CRS and EOM controlled and blood eosinophils not elevated	discontinuation of Oma and mepo alone did not result in relapse	discontinuation of Oma and mepo alone did not result in relapse	Symptoms controlled and blood eosinophils not elevated

Chen et al. J Asthma Allergy. 2025;18:507-17.

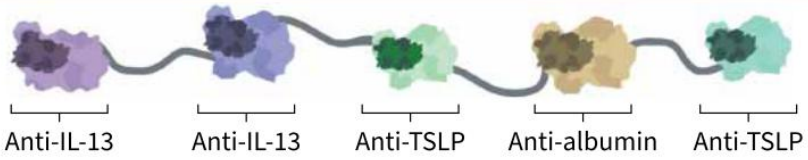
Combination

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

A proof-of-mechanism trial in asthma with lunsekimig, a bispecific NANOBODY molecule

Annemie Deiteren, Emmanuel Krupka, Lieselot Bontinck, Karine Imberdis, Griet Conickx, Selcuk Bas, Naimish Patel, Heribert W. Staudinger and Benjamin T. Suratt

Lunsekimig, a novel bispecific NANOBODY construct, antagonises the function of two cytokines TSLP and IL-13



- NANOBODY building blocks are highly stable, high-affinity (nM–pM) variable domains, ~10 times smaller than monoclonal antibodies, that can be fused together in a mix-and-match manner to generate multivalent, multispecific molecules

Phase 1b, single-dose, randomised (2:1), double-blind, proof-of-mechanism study

Participants

- 36 adults aged 18–60 years with controlled mild-to-moderate asthma for ≥12 months as defined in the GINA 2020 guidelines
- Elevated F_{ENO} (≥25 ppb)
- FEV_1 ≥60% predicted
- ICS-naive or on stable treatment (≥3 months) with low- or medium-dose ICS

Two sites

- Germany
- UK

Single subcutaneous injection of lunsekimig 400 mg or placebo

Screening	Admission		Discharge			Visits						EOS visit
D–28 to D–2	D–1	D1	D2	D3	D4	D5	D6	D8	D15	D29	D57	D71

- **Primary end-point**: Safety and tolerability through day 71
- **Main pharmacodynamic secondary end-point**: Change from baseline in F_{ENO} at day 29

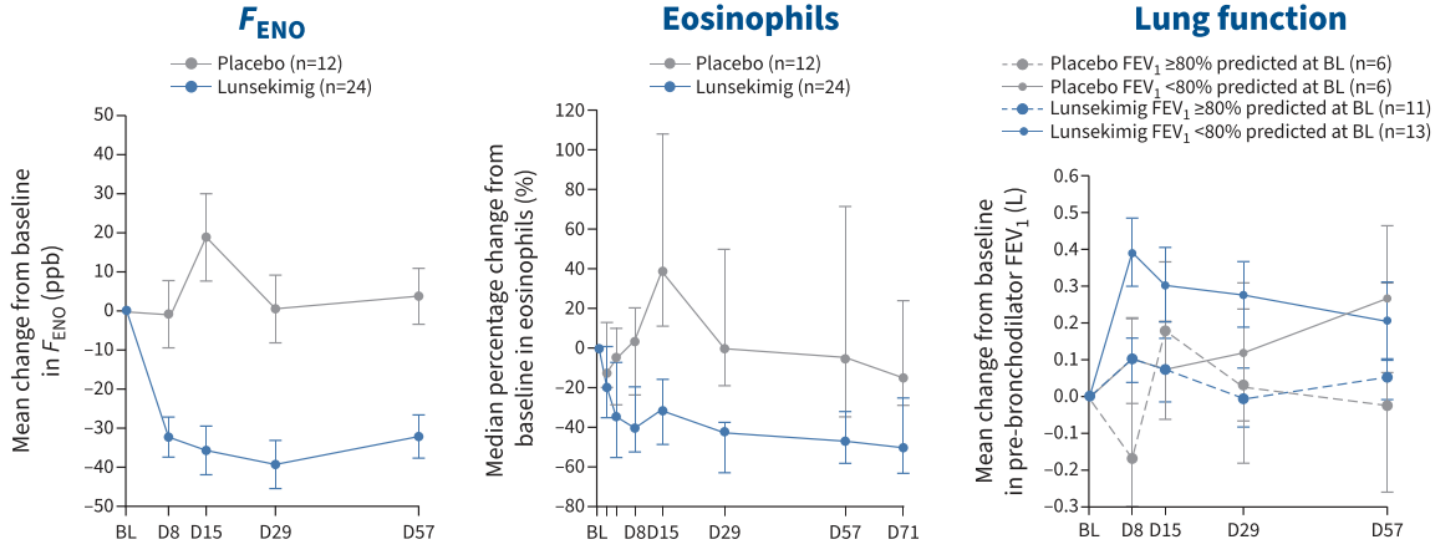
Deiteren et al. Eur Respir J. 2025;65(4).

Results

Safety

- A single dose of lunsekimig was well tolerated, with no serious TEAEs
- TEAEs were reported in 75% of participants in both treatment groups; all were mild or moderate in severity

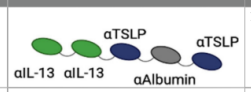
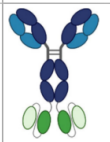
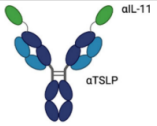
Most common TEAEs (>10%) (n (%))	Lunsekimig 400 mg (n=24)	Placebo (n=12)
Nasopharyngitis	7 (29.2)	4 (33.3)
Headache	5 (20.8)	4 (33.3)
Injection site reaction	5 (20.8)	0

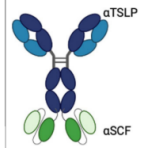
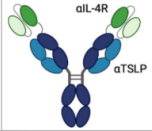
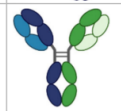


- Lunsekimig reduced F_{ENO}
- Lunsekimig reduced the type 2 asthma blood biomarkers eosinophils, IL-5, eotaxin-3/CCL26, TARC/CCL17 and IgE
- Lunsekimig improved lung function and small airway dysfunction in those with impaired lung function at baseline

Deiteren et al. Eur Respir J. 2025;65(4).

Combination

Therapeutic	Sponsor	Targets	Structure	Half-life ext?	ROA	Indication	Current development stage	Study ID	Study status	Estimated primary completion
Lunsekimig	Sanofi	TSLP, IL-13		No	SC	Asthma (moderate-to-severe)	Phase 2	NCT06102005	Active, not recruiting	March 2026
					SC	Asthma (high risk)	Phase 2	NCT06676319	Recruiting	October 2027
					SC	CRSwNP	Phase 2	NCT06454240	Recruiting	January 2027
PF-07275315	Pfizer	TSLP, IL-4, IL-13		No	SC	Asthma (moderate-to-severe)	Phase 2	NCT06977581	Recruiting	March 2027
CM512	Keymed, Belenos	TSLP, IL-13			SC	Asthma (moderate-to-severe)		NCT07011524	Not yet recruiting	July 2027
					SC	COPD	Phase 2	NCT06980142	Not yet recruiting	March 2028
					SC	CRSwNP	Phase 2	NCT06930612	Not yet recruiting	September 2026
IBI3002	Innovent	TSLP, IL-4RA			IV, SC	Asthma	Phase 1b	NCT06947408	Recruiting	April 2026
HB0056	Huabo	TSLP, IL-11					Phase 1	NCT06612970	Recruiting	June 2025

Therapeutic	Sponsor	Targets	Structure	Half-life ext?	ROA	Indication	Current development stage	Study ID	Study status	Estimated primary completion
CDX-622	Celldex	TSLP, SCF					Phase 1	NCT06650761	Recruiting	January 2026
APG333	Apogee	TSLP, combo					Phase 1	ACTRN12624001358538	Active, not recruiting	December 2025
ATI-052	Aclaris	TSLP, IL-4RA					Phase 1			
ZW1528	Zymeworks	IL-33, IL-4RA					Preclinical			
HXN-1012	Helixon	TSLP, IL-13					Preclinical			
HXN-1013	Helixon	TSLP, IL-33					Preclinical			
PX-128	Johnson & Johnson	TSLP, IL-13					Preclinical			
BD9	Teva	TSLP, IL-13					Preclinical			
Undisclosed	Novarock Bio	IL-25, IL-4RA					Preclinical			

Komori et al. Front Allergy. 2025;6:1700060.

Take home messages

1. Anti–IL-5/IL-5Rα and anti–IL-4Rα biologics target overlapping T2-high populations, but blood eosinophils better predict IL-5 pathway responses, whereas FeNO and IL-4/IL-13–related comorbidities favor IL-4Rα blockade.
2. TSLP inhibition has shown the most consistent efficacy among alarmin-targeting therapies, including OCS-sparing effects.
3. IL-33/ST2 blockade remains promising but is less clinically advanced.
4. Biologic switching may benefit patients when better aligned with inflammatory phenotype or comorbidities. Long-interval, combination, and multispecific biologics are emerging