

Asthma remission : A New Target of Disease Control



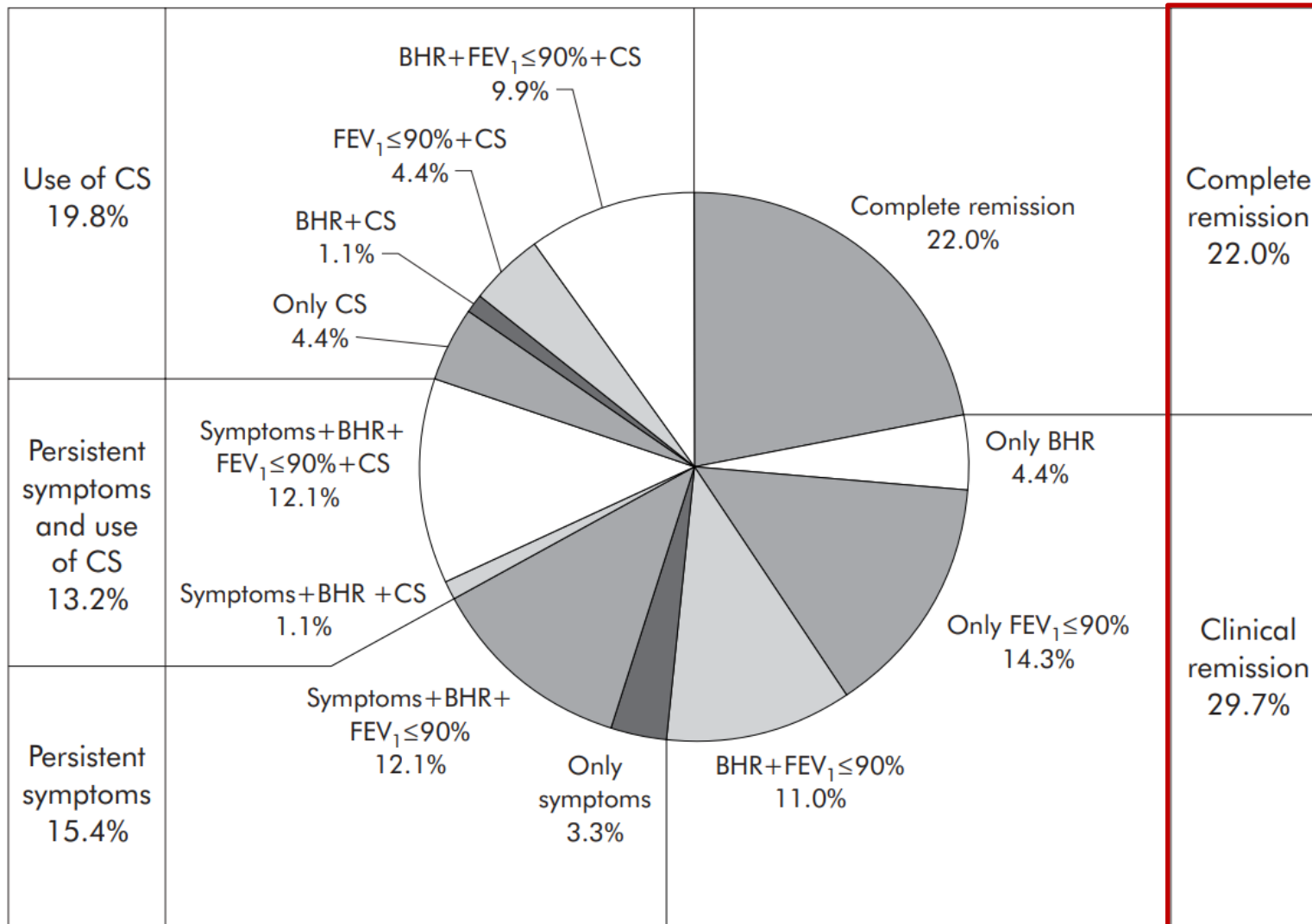
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Contents



- **Concept & definition of asthma remission**
- Real-world and registry-based studies
- Post-hoc analyses of RCTs on biologics
- Future perspectives
 - Earlier initiation of biologics to achieve remission?
 - Tapering or discontinuation of biologics after achieving remission?

Remission in childhood asthma



Outcome of childhood asthma at age 32–42 in a longitudinal study of 119 allergic asthmatic children after a follow up of 30 years

Spontaneous remission in adult asthma



First author [ref.]	Study characteristics	Remission definition	Remission
Adult-onset asthma			
ALMQVIST [38]	n=205; follow-up: 15.3 years; Sweden	No symptoms or asthma medications in past 12 months	11.2%
TUPPER [39]	n=78; mean follow-up: 33.3 years; Denmark	No symptoms or asthma medications in past 12 months; $F_{ENO} < 50$ ppb, no bronchodilator reversibility, no airway hyperresponsiveness and no airflow limitation	17%
WESTERHOF [40]	n=170; follow-up: 5 years; the Netherlands	No symptoms or asthma medications in past 12 months	15.9%
TUOMISTO [29]	n=203; follow-up: 12.2 years; Finland	No asthma symptoms, ACT score ≥ 25 , no asthma medication in last 6 months, no use of oral prednisolone in past 2 years; objective assessment of normal lung function	Clinical: 3%; normalisation of lung function: 2%
RÖNMARK [41]	n=250; follow-up: 5.8 years; Sweden	Clinical: no asthma symptoms and no asthma medications in past 12 months; complete: no medications, no symptoms, $FEV_1 > 80\%$ predicted and $PC_{20} > 8$ mg·mL ⁻¹	Clinical: 4.8%; complete: ~3%#

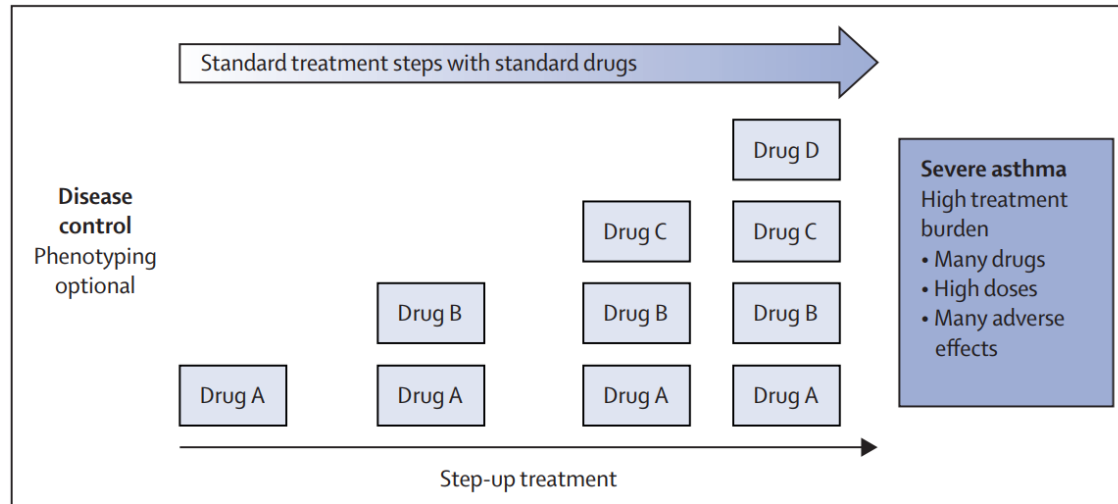
Prevalence

Spontaneous remission in adult asthma patients **2–52%**

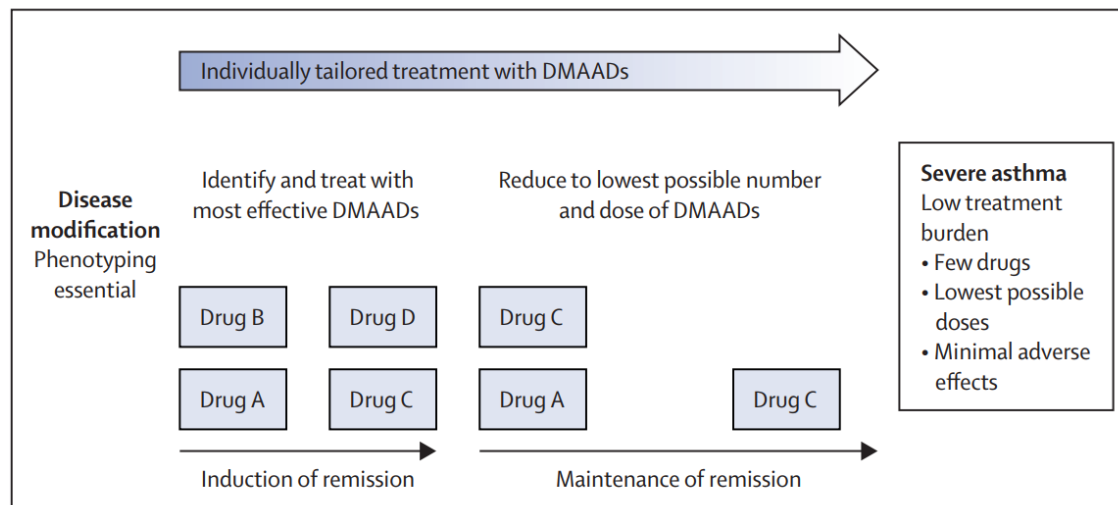
Remission is possible as part of the natural history of asthma, and the prevalence of remission in the adult asthma population varies between 2% and 52% (2% to 17% in adult-onset asthma).

Factors associated with remission
 : mild asthma, better lung function, better asthma control, younger age, early-onset asthma, shorter duration of asthma, milder bronchial hyperresponsiveness, fewer comorbidities and smoking cessation or never smoking

Paradigm shift in asthma management



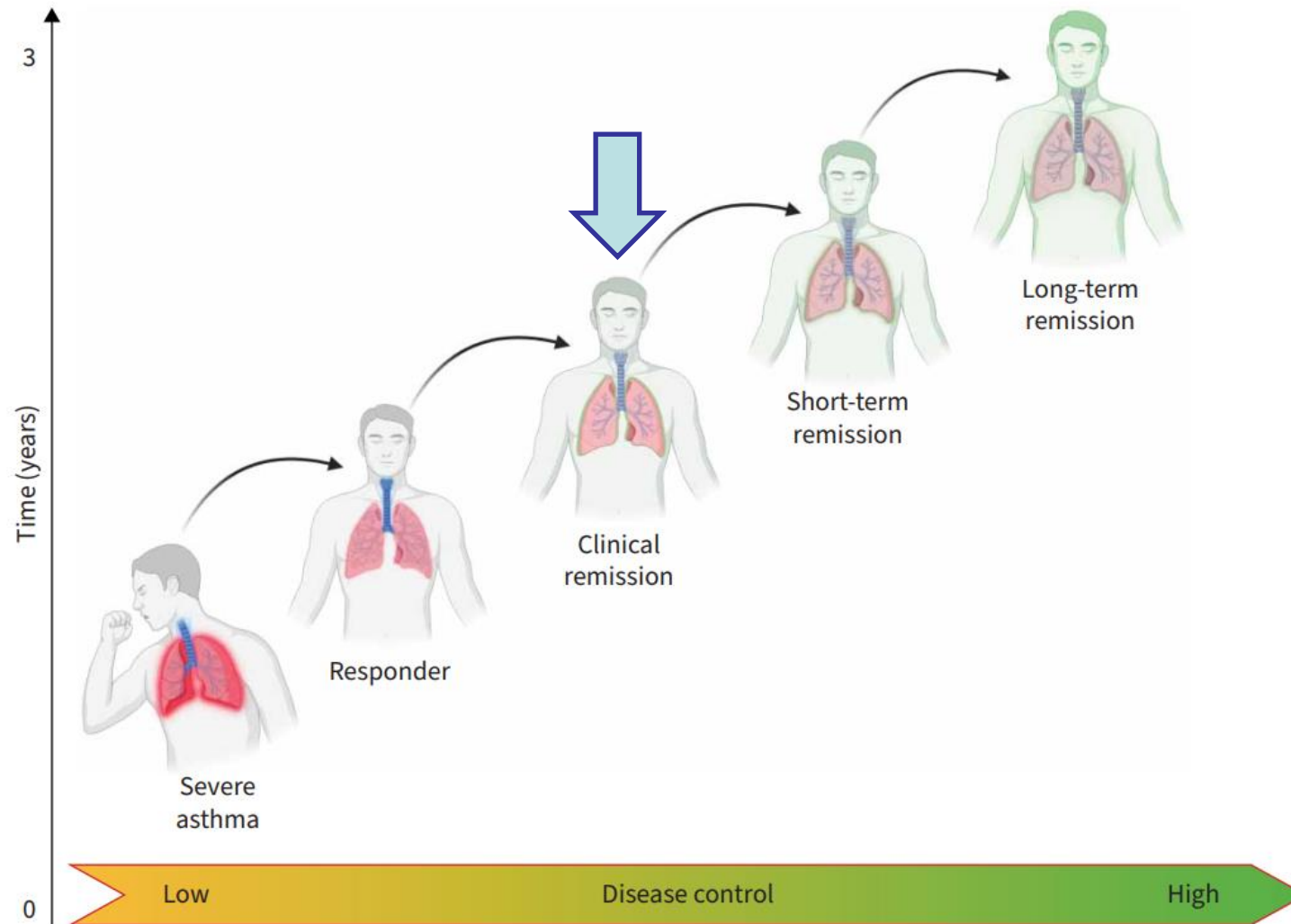
Short-term
Disease control
Reactive target treatment



Long-term
Disease modification
Proactive target treatment
Personalized

* disease-modifying anti-asthmatic drugs (DMAADs)

Concept of achieving clinical remission





Clinical Remission on Treatment

For ≥ 12 months:

- Sustained absence of significant asthma symptoms based on validated instrument, **and**
- Optimization and stabilization of lung function, **and**
- Patient and HCP agreement regarding disease remission, **and**
- No use of systemic corticosteroid therapy for exacerbation treatment or long-term disease control

Clinical Remission off Treatment

Same criteria maintained without asthma treatment for ≥ 12 months

Complete Remission on Treatment

Clinical remission plus the following:

- Current, objective evidence of the resolution of previously documented asthma-related inflammation (eg, reduced blood or sputum eosinophil counts, FENO, and/or other relevant measures), **and**
- In appropriate research settings: Current negative bronchial hyperresponsiveness

Complete Remission off Treatment

Same criteria maintained without asthma treatment for ≥ 12 months

Definition of Remission in the Biologic Era:

The only consensus is that there is no consensus

Country	Exacerbations + OCS	Symptom control	Lung function	Additional endpoints and terminology
Japan <i>Asthma practice guidelines</i>	No exacerbations + no OCS use	Absence of symptoms: ACT \geq 23	N/A	Lung function parameters not required, but should be evaluated after remission is reached
Germany <i>AWMF guidelines</i>		Absence of symptoms	stabilisation	N/A
Spain <i>GEMA guidelines</i>		Absence of symptoms	stabilisation and optimisation	<u>Complete Remission</u> <i>with CRSwNP</i> + No hyperresponsiveness and bronchial inflammation
Italy <i>SANI Delphi consensus</i>		Absence of symptoms: ACT \geq 20, ACQ <1.5	stabilisation	<u>Partial Clinical Remission</u> No OCS + 2/3 of the following criteria: - No symptoms - No exacerbations - Stable lung function
US <i>ACAAI, AAAAI, and ATS</i>		Absence of symptoms: ACT >20, AIRQ <2, ACQ <0.75	stabilisation and optimisation	No missed school or work due to asthma-related symptoms
	Symptoms requiring one-time reliever therapy no more than once a month	Continued use of controller therapies ONLY at low-medium dose of ICS, or less		

ACAAI, AAAAI and ATS (Modified Delphi)



Asthma Clinical Remission on Treatment Criteria

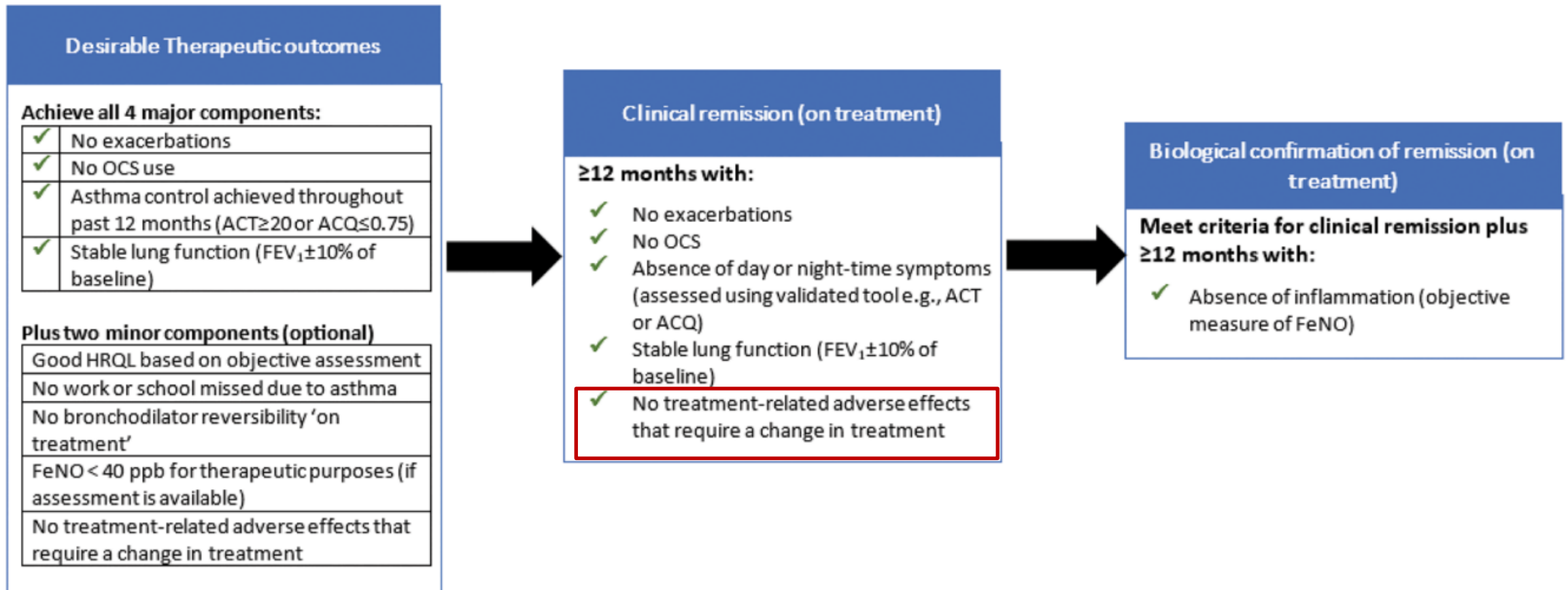
All the following criteria must be met over a 12-mo period and may be applied to those receiving monoclonal antibody therapy (biologic) for asthma:

1. **NO** exacerbations requiring a physician visit, emergency care, hospitalization, and/or systemic corticosteroid for asthma (ie, oral, injectable).
2. **NO** missed work or school over a 12-mo period due to asthma-related symptoms.
3. Stable and optimized pulmonary function results on all occasions, when measured over a 12-mo period, with ≥ 2 measurements during the y.
4. Continued use of controller therapies (ICS, ICS/LABA, leukotriene receptor antagonist) **ONLY** at low-medium dose of ICS, or less, as defined by most recent GINA strategy.
5. ACT > 20 , AirQ < 2 , ACQ < 0.75 on all occasions measured in the previous 12-mo period, with ≥ 2 measurements during the y.
6. Symptoms requiring 1-time reliever therapy (SABA, ICS-SABA, ICS-LABA) no more than once a mo.

Asia, the Middle East, and South America



25 respiratory physicians from 7 countries (Argentina, Arabian Gulf, India, Mexico, Philippines, Thailand, and Vietnam)



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International Severe Asthma Registry (ISAR)



N = 3,717 from 23 countries

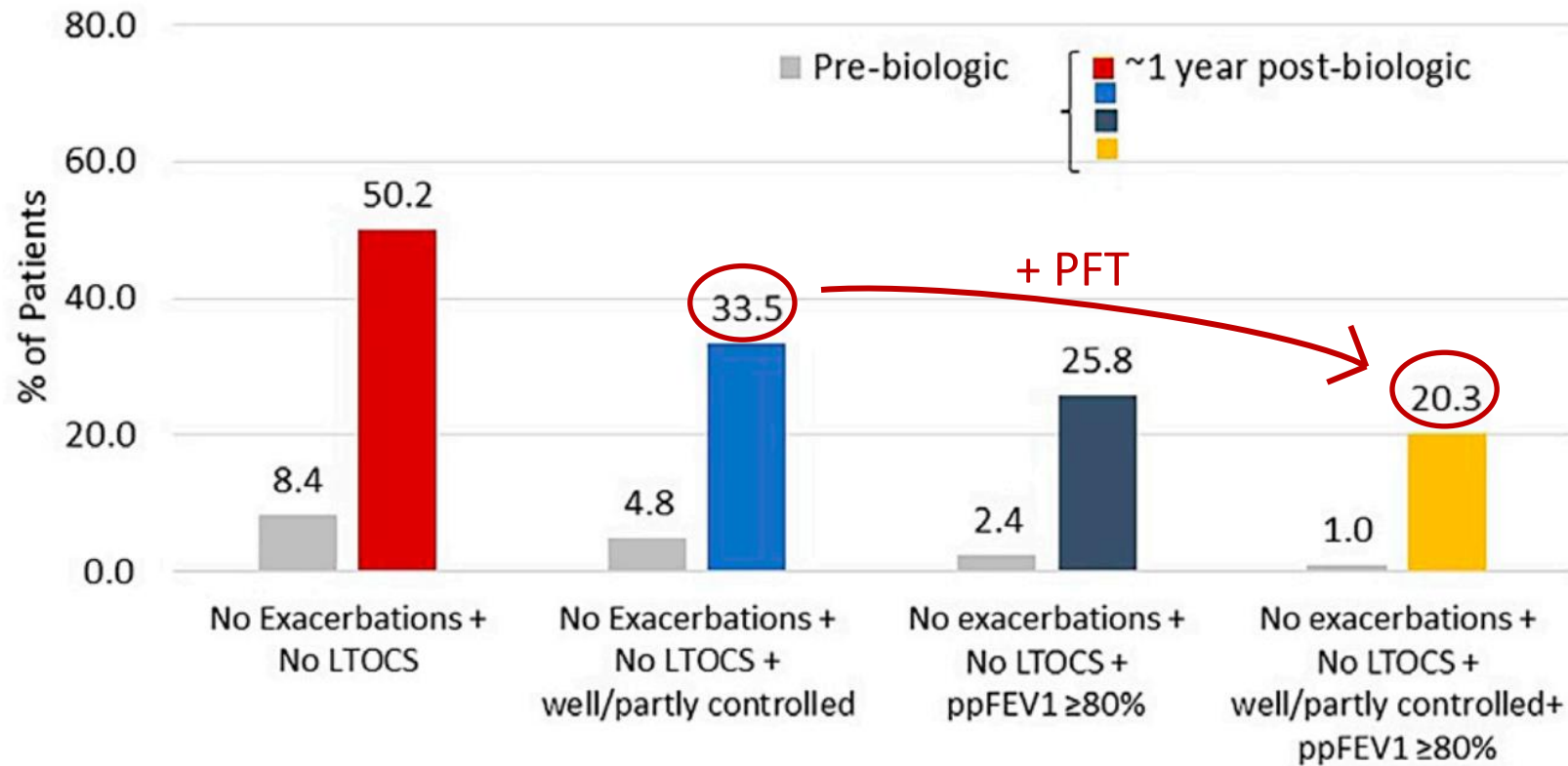
Longitudinal, before-to-after biologic initiation cohort study

→ Proportion of achieving multidomain-defined remission and factors associated with achieving remission

Outcome	Definition
Annualized exacerbation rate	<ul style="list-style-type: none"> • Asthma-related hospital attendance/admission, AND/OR • Asthma-related ER attendance, AND/OR
Asthma control*	<ul style="list-style-type: none"> • Acute OCS course ≥ 3 d • GINA control test (1), OR • ACT Test (48), OR • ACQ (49)
Daily LTOCS dose [†]	<ul style="list-style-type: none"> • Continuous OCS use ≥ 3 mo duration • Daily LTOCS (prednisolone equivalent) dose (mg)
Lung function [‡]	<ul style="list-style-type: none"> • ppFEV₁

Definitions	Exacerbations/year	LTOCS daily dose*	Asthma control [†]	ppFEV ₁ [‡]
Strict	0	0 mg	Partly/well controlled	$\geq 80\%$
Relaxed	≤ 1 (not requiring hospitalization)	≤ 5 mg		
2 domains				
3 domains				
3 domains				
4 domains				

Remission before and after treatment with biologics



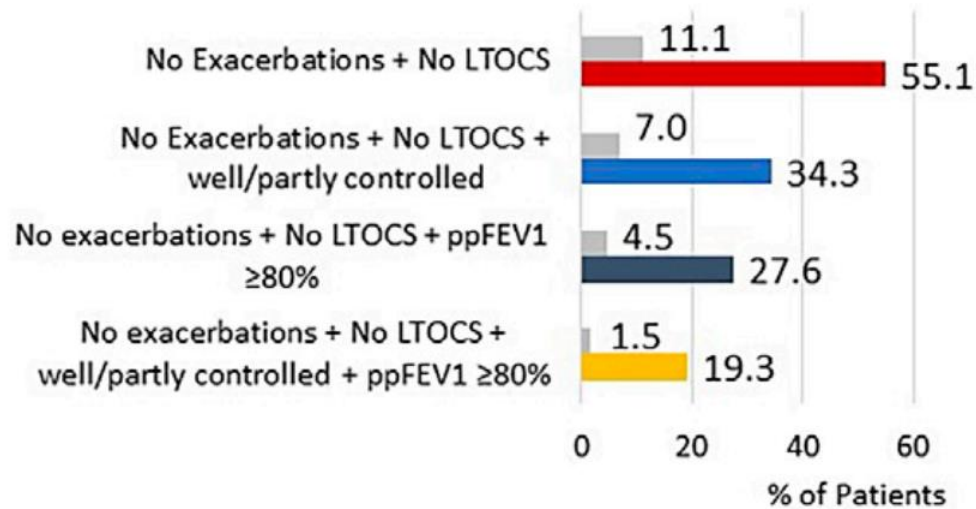
Remission before and after treatment with biologics



From May 1, 2017 to January 25, 2023

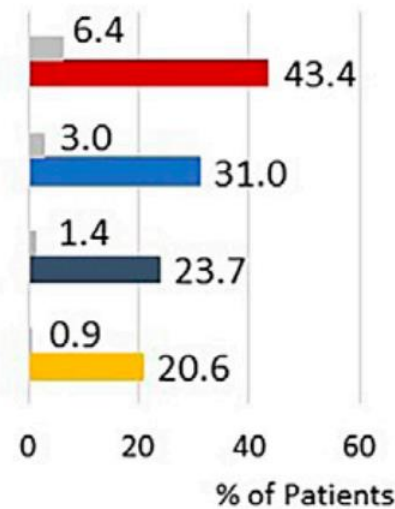
N = 1,390

Anti-IgE



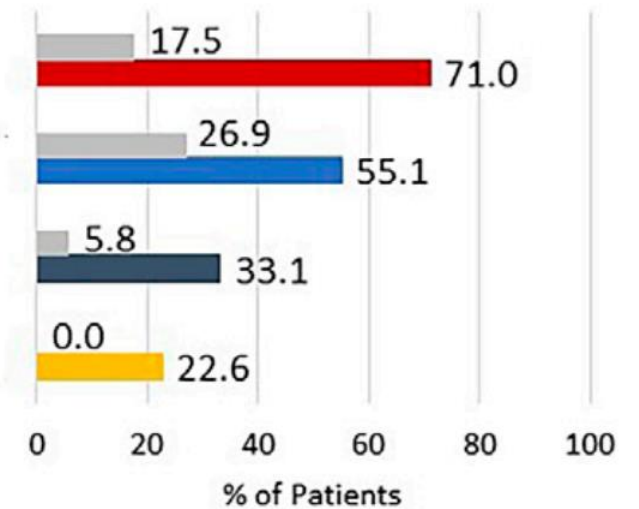
N = 2,021

Anti-IL5/5R



N = 306

Anti-IL4Rα

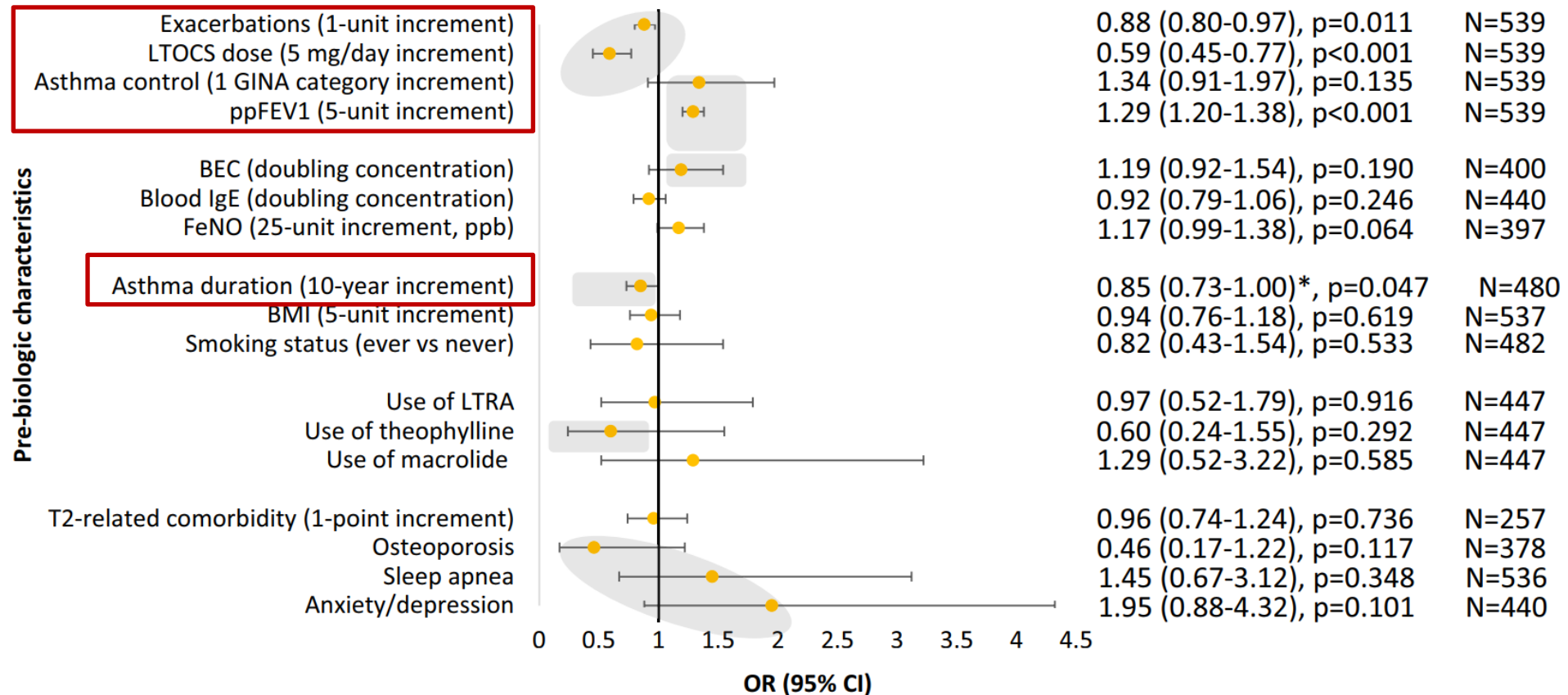


■ Pre-biologic ■ ~1-year post-biologic

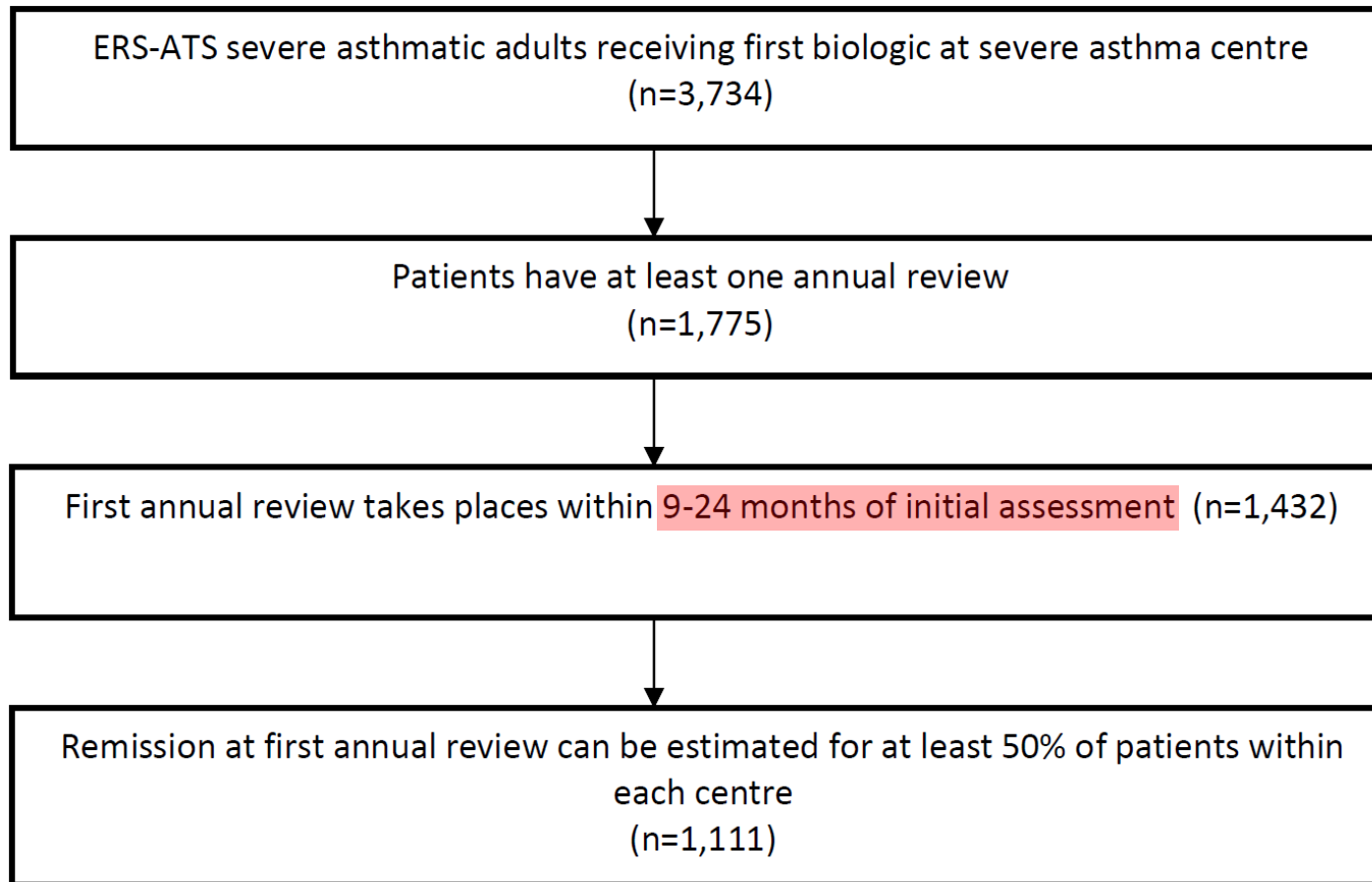
Prebiologic characteristics associated with remission



4-domain remission: exacerbations + LTOCS + control + ppFEV1



UK Severe Asthma Registry (UKSAR)



Anti-IL-5	828 (84.4)
Anti-IgE	150 (15.3)
Anti-IL-4 receptor α	3 (0.3)

Remission definition

- 1) ACQ-5 <1.5
- 2) No OCS maintenance or OCS bursts
- 3) FEV₁ above LLN or Δ FEV₁ \geq - 100 mL

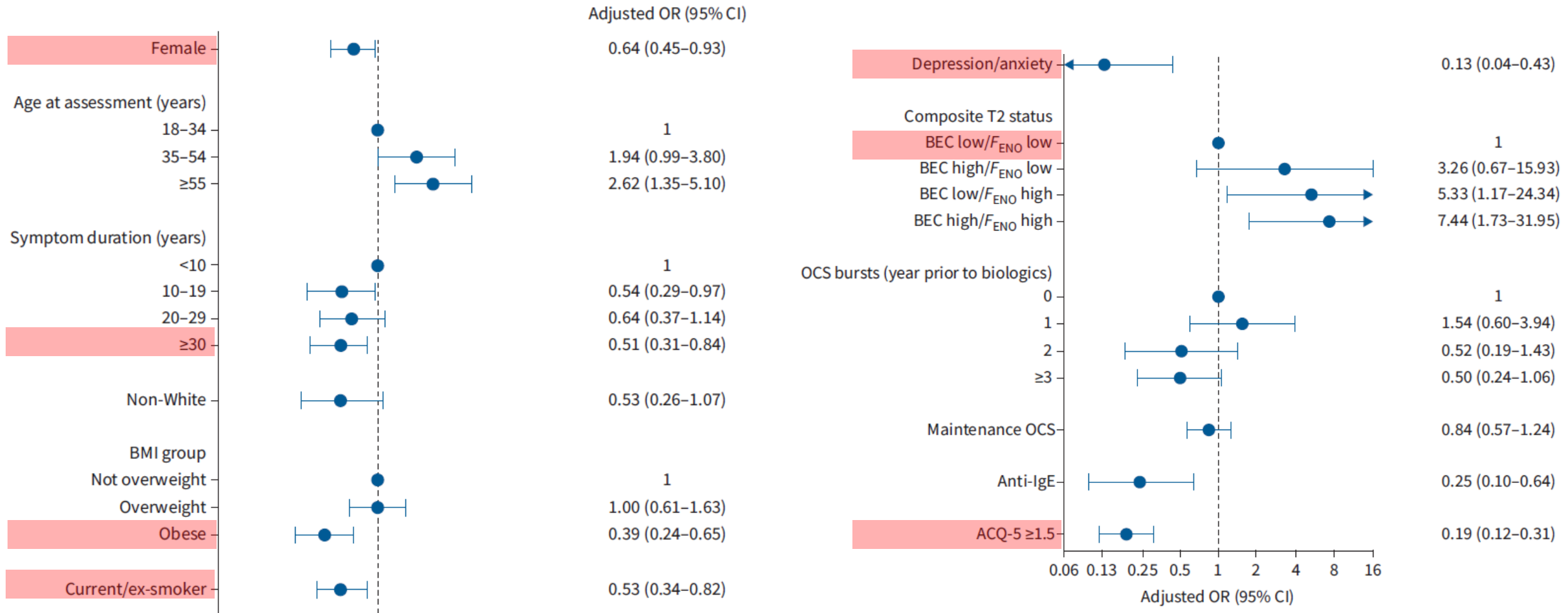
TABLE 1 Baseline demographics of the whole cohort at initial assessment prior to commencing biologics (n=1111)

	n	Category	Result
Time to first annual review (years)	1111		1.1 (1.0–1.3)
Sex	1111	Female	667 (60.0)
Age at first assessment (years)	1111		52.0 (41.0–61.0)
Ethnicity	1109	White	966 (87.1)
Smoking status	1083	Never	723 (66.8)
BMI (kg·m ⁻²)	1099		29.8 (26.1–34.8)
Atopic disease	1111		567 (51.0)
Depression/anxiety	1111		129 (11.6)
Gastro-oesophageal reflux	1111		224 (20.2)
Nasal polyps	1111		237 (21.3)
OCS bursts for exacerbation (last year)	1086		5 (3–8)
Any OCS bursts (last year)	1086		1020 (93.9)
FEV ₁ (L)	1089		2.0 (1.5–2.6)
FEV ₁ (% pred)	1077		66.9 (52.1–81.5)
FVC (L)	1062		3.1 (2.5–3.9)
FVC (% pred)	1026		85.9 (73.4–97.8)
FEV ₁ /FVC	1062		63.6 (53.7–72.1)
ACQ-5 score	954		3.2 (2.0–4.0)
Uncontrolled asthma	954	ACQ-5 ≥1.5	807 (84.6)
Maintenance OCS	1106		638 (57.7)
Maintenance OCS (mg) [¶]	1102		10 (8–15)
ICS	1111		1103 (99.3)
ICS dose (µg BDP-equivalent) ⁺	1025		2000 (1600–2000)

Factors related to Remission

Non-remission
(81.7% (n=678))

Remission
(18.3% (n=152))



Remission Rate Based On Different Criteria

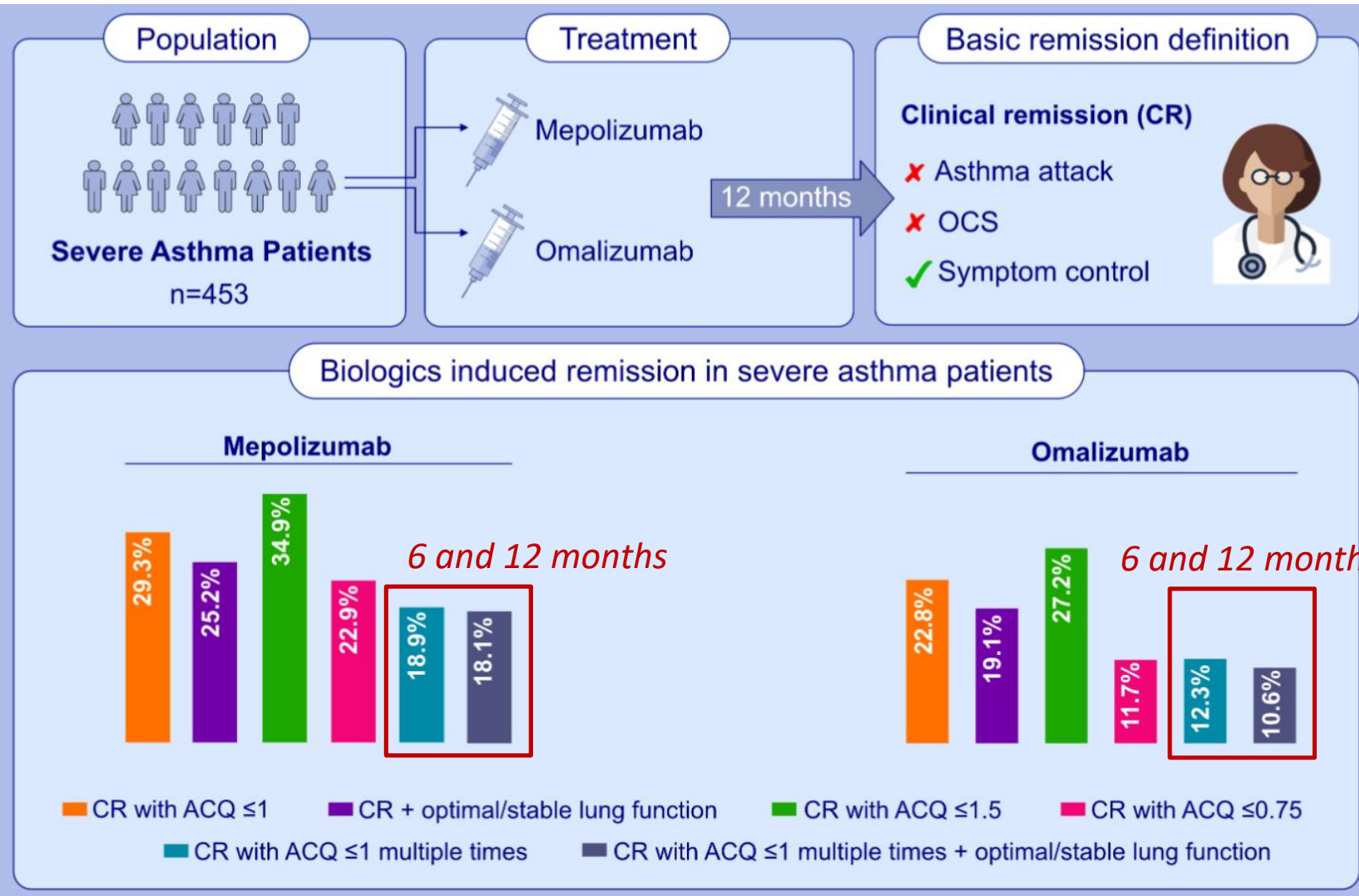


Non-remission (81.7% (n=678))	Remission (18.3% (n=152))
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Sensitivity analysis

- 1) ACQ-5 <1.5, and no OCS for disease control, and FEV₁ >LLN or ≤ 100mL FEV₁ reduction from baseline : **18.3%**
- 2) ACQ-5 <1.5, and no OCS for disease control, and FEV₁ >LLN or ≥ -5% FEV₁ reduction from baseline: **18.3%**
- 3) ACQ-5 <1.5, and no OCS for disease control, and FEV₁ >LLN or ≥ baseline FEV₁: **17.7%**
- 4) ACQ-5 <1.5, and no OCS for disease control : **21.2%**

Australian Xolair/Mepolizumab Registry (AXR/AMR)



Many of the longitudinal cohort studies report cross-sectional remission which is (in general) more forgiving than multiple time points

Importance of comorbidities

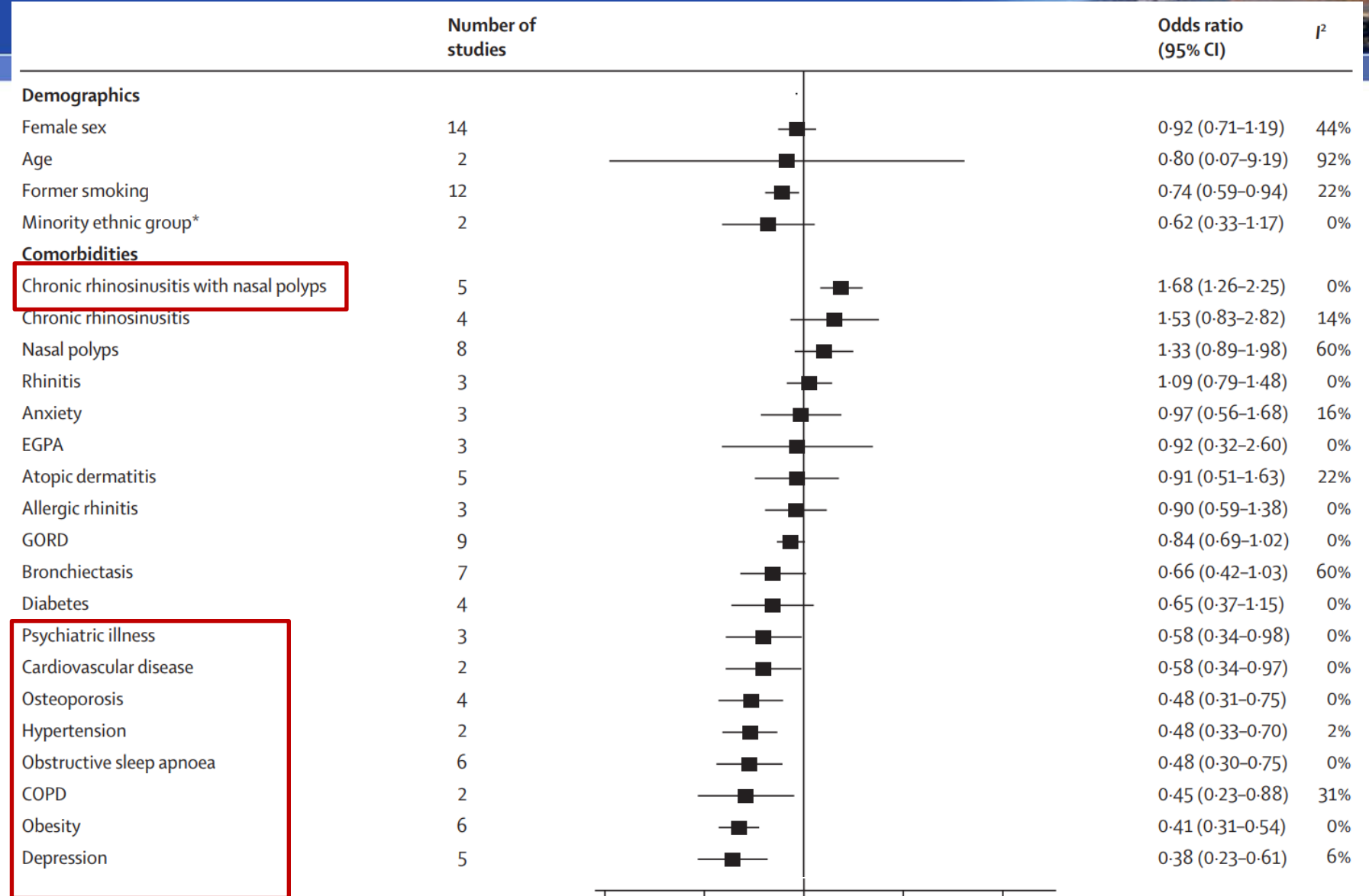


	No remission N=300*	Clinical remission N=110	p-value
Rhinitis	168 (56.0%)	67 (60.9%)	0.37
GERD	131 (43.7%)	50 (45.5%)	0.75
OSA	67 (22.3%)	14 (12.7%)	0.030
COPD	45 (15.0%)	11 (10.0%)	0.19
Nasal Polyps	84 (28.0%)	31 (28.2%)	0.97
Bronchiectasis	39 (13.0%)	11 (10.0%)	0.41
Vocal Cord Dysfunction	23 (7.7%)	3 (2.7%)	0.11
Anxiety	49 (16.3%)	12 (10.9%)	0.17
Depression	72 (24.0%)	10 (9.1%)	<0.001
Aspirin Sensitivity	25 (8.3%)	11 (10.0%)	0.60
Obesity	77 (25.7%)	12 (10.9%)	0.001
Osteoporosis	68 (22.7%)	10 (9.1%)	0.002
Other psychiatric illness	63 (21.0%)	12 (10.9%)	0.019

Variables	Odds ratio	p-value	95%CI
Gender (Male)	0.48	.071	0.21-1.06
BMI	0.91	.002	0.85-0.96
FEV1%predicted Post BD	1.02	.032	1.002-1.05
ACQ mean	0.58	.018	0.37-0.91
mOCS at baseline	0.35	.010	0.16-0.78
Hospitalization	0.32	.032	0.11-0.90
Comorbidities affecting remission			
Depression	0.40	.012	0.19-0.82
Obesity	0.41	.009	0.21-0.80
Osteoporosis	0.35	.004	0.17-0.72

Comorbidities

Meta-analysis of 25 studies
(RCTs and observational)

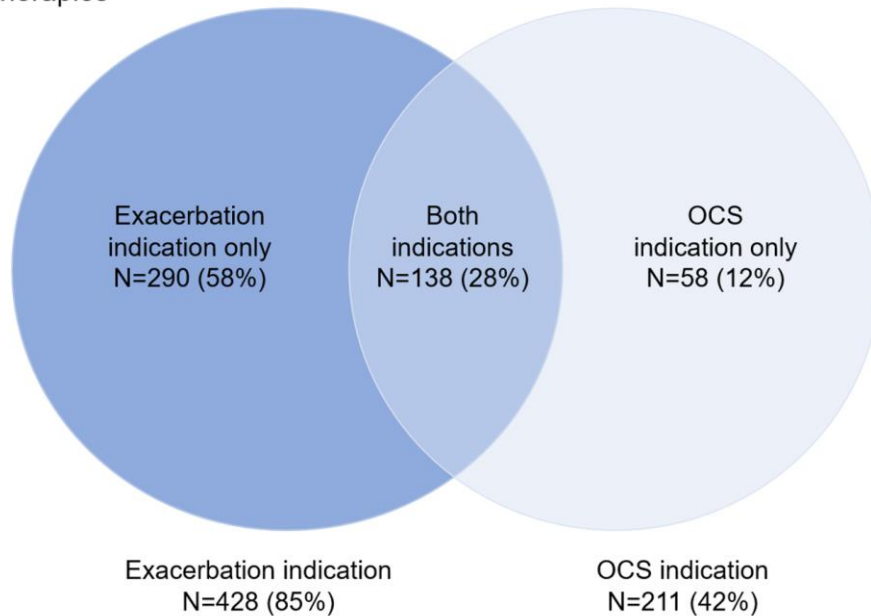


Danish Severe Asthma Registry (DSAR)



501 biologics naïve patients who initiated biologics

All biologic therapies
N=501



Clinical response (rate=79.2%)

- (1) Reduction of at least 50% in the annualized exacerbation rate if the indication was based on ≥ 2 exacerbations in the 12 months prior to treatment,
- (2) Reduction of at least 50% in the OCS dose from baseline if the indication was based on the need for mOCS.

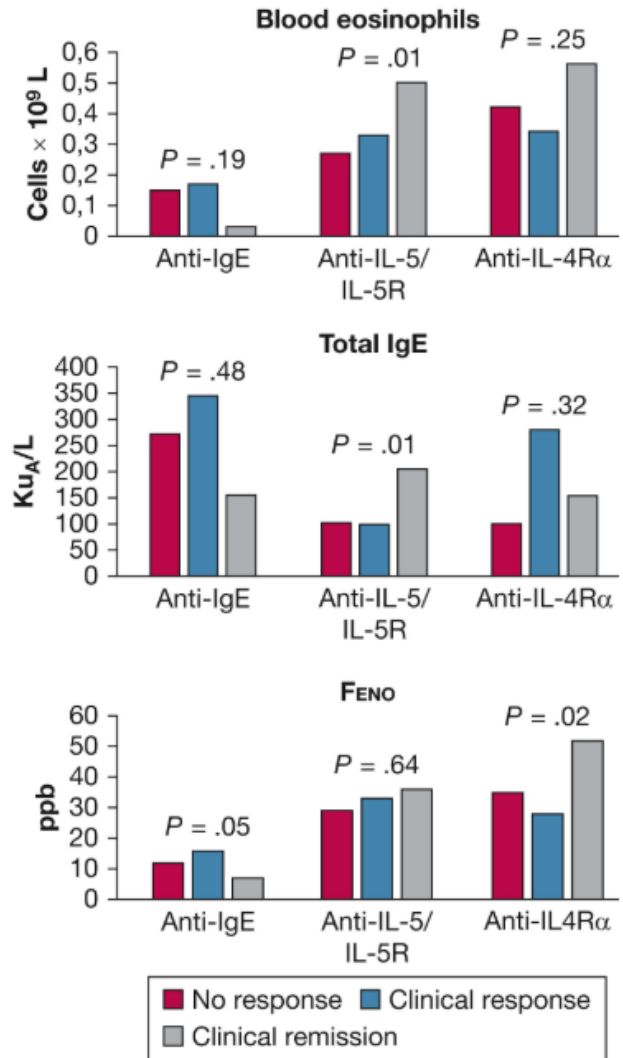
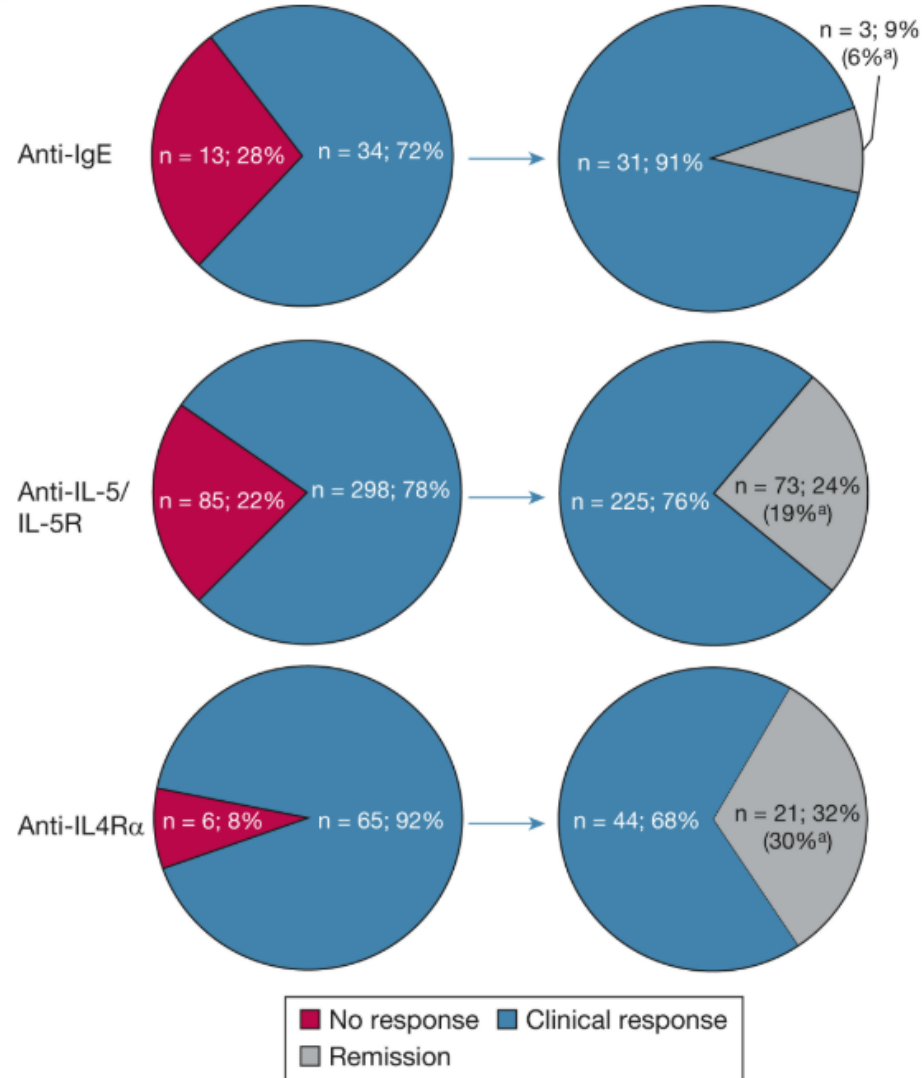
Clinical remission (rate=19.4%)

- (1) No AE
- (2) No mOCS
- (3) $ACQ-6 \leq 1.5$
- (4) $FEV_1 > 80\%$

Biomarkers and Efficacy of Biologics



Clinical remission rates varied widely by biologics



Baseline predictors of clinical remission



TABLE 4] Baseline Predictors of Clinical Remission After 12 Months of Biologic Therapy Analyzed in a Multivariate Logistic Regression Model With Remission as the Outcome

Predictors	OR (95% CI)	P Value
Sex		.13
Male	1.57 (0.88-2.83)	
Female	1.00 (Reference)	
BMI (kg/m ²) (1 unit increase)	0.92 (0.86-0.99)	.02
Duration of disease (1 y increase)	0.98 (0.97-0.99)	.047
Blood eosinophil count (doubling concentration)	1.18 (0.98-1.42)	.09
FENO (doubling concentration)	1.02 (0.81-1.27)	.88





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Definition of remission in clinical trials



Criteria for Remission	Dupilumab		Benralizumab		Tezepelumab	Mepolizumab	Multiple Biologics		
	2021 ¹ QUEST Phase 3	2022 ² TRAVERSE OLE	2022 ³ SIROCCO/ CALIMA Phase 3	2022 ⁴ ANDHI Phase 3b	2023 ⁵ XALOC-1	2022 ^{6,7} NAVIGATOR Phase 3	2022 ⁸ REDES	2022 ⁹ CHRONICLE	2022 ¹⁰ Danish Registry
 Absence of symptoms ^{a,b} and	ACQ-5 < 1.5	ACQ-5 < 1.5	ACQ-6 < 1.5" or ≤ 0.75	ACQ-6 < 1.5" or ≤ 0.75	ACQ-5 < 1.5 or ACT ≥ 16	ACQ-6 ≤ 1.5 ^{a,b}	ACT ≥ 20	Majority ≥ (50%) ACT ≥ 20	ACQ ≤ 1.5
 Optimized/ stabilized lung function and	Post-BD FEV _{1,pp} ≥ 80%	Post-BD FEV ₁ ≥ 80% OR pre-BD FEV ₁ ≥ 100 mL	Pre-BD FEV ₁ increase ≥ 100 mL	Pre-BD FEV ₁ increase ≥ 100 mL	Not included	Pre-BD FEV _{1,pp} > 80% OR Pre-BD FEV ₁ > 20% from baseline; FEV ₁ > 95% of baseline**	Not included	Not included	Post-BD FEV _{1,pp} ≥ 80%
 No exacerbations; no OCS ^c	✓	✓	✓	✓	✓	✓ ^d	✓	✓	✓
 Prevalence of clinical remission	31.7%	36.4%	26.3% ^e	28.7%	43%	14% ^f - 28.5% ^{g,h}	37%	35%	19%

Dupilumab

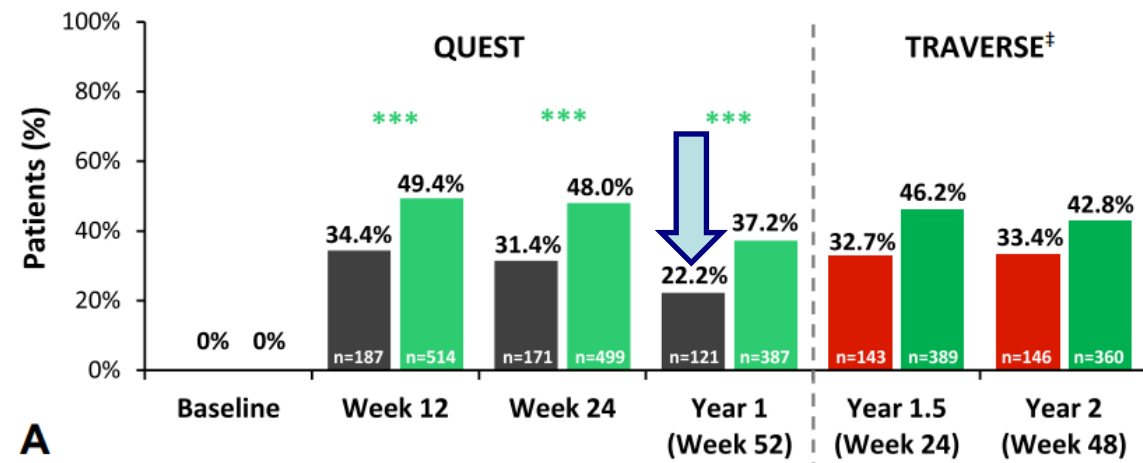


Clinical remission

- (1) No severe asthma exacerbations
- (2) Zero OCS use
- (3) Improved or stable lung function (decline from baseline FEV₁ by no more than 5%)
- (4) ACQ-5 score < 1.5

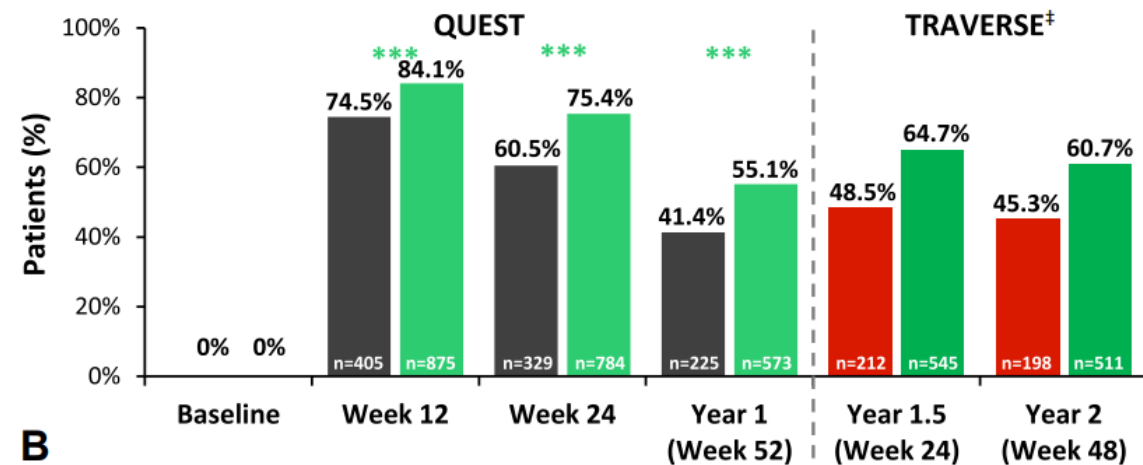
- Placebo (n=544)
- Dupilumab 200/300 mg q2w (n=1040)
- Placebo → dupilumab 300 mg q2w (n=437)
- Dupilumab → dupilumab 300 mg q2w (n=842)

Patients meeting all 4 criteria for on-treatment clinical remission[†]



A

Patients meeting ≥3 criteria for on-treatment clinical remission[†]

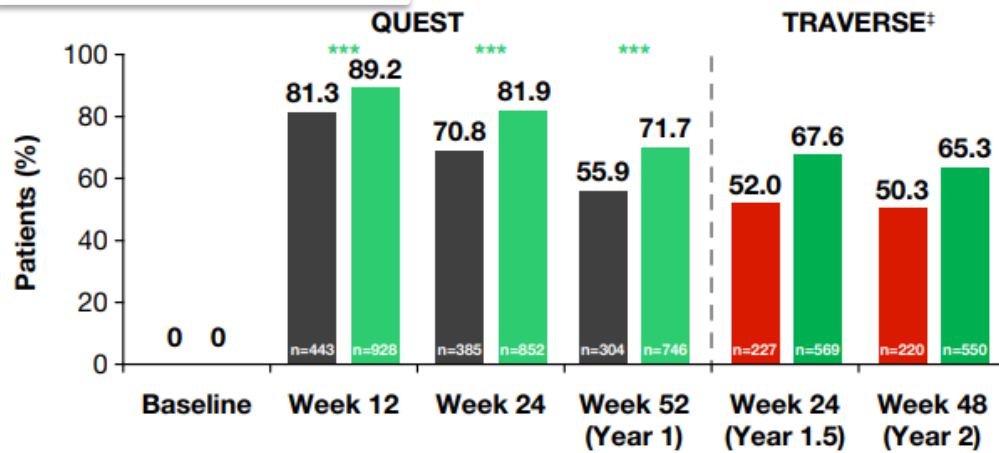


B

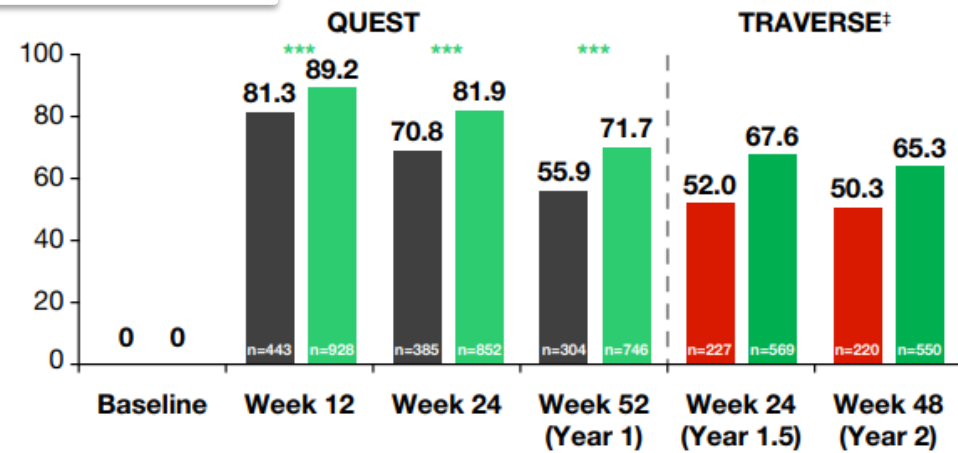
Individual criteria

patients receiving maintenance OCS were not enrolled in QUEST

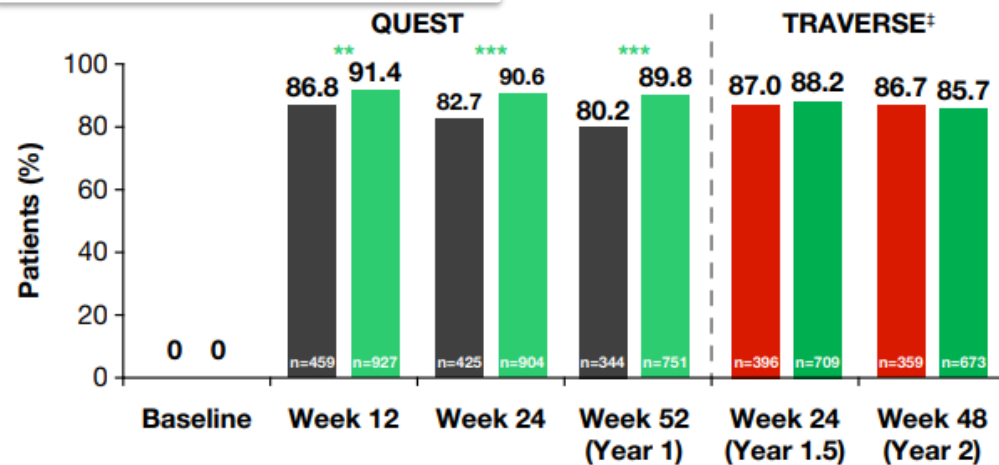
No exacerbations



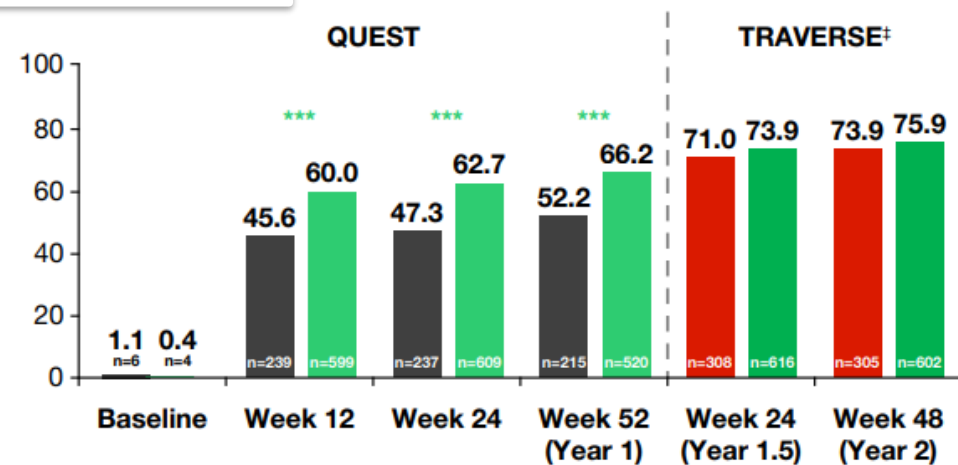
Zero OCS



Improved/Stable FEV₁



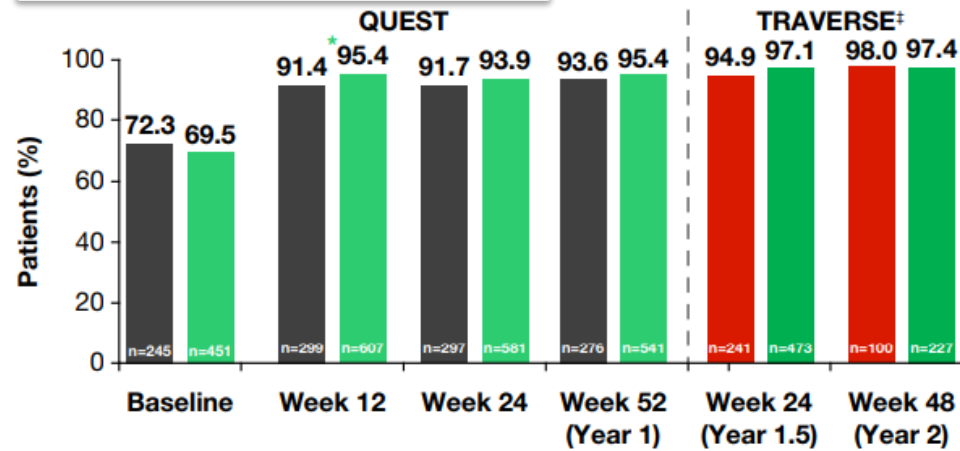
ACQ-5 < 1.5



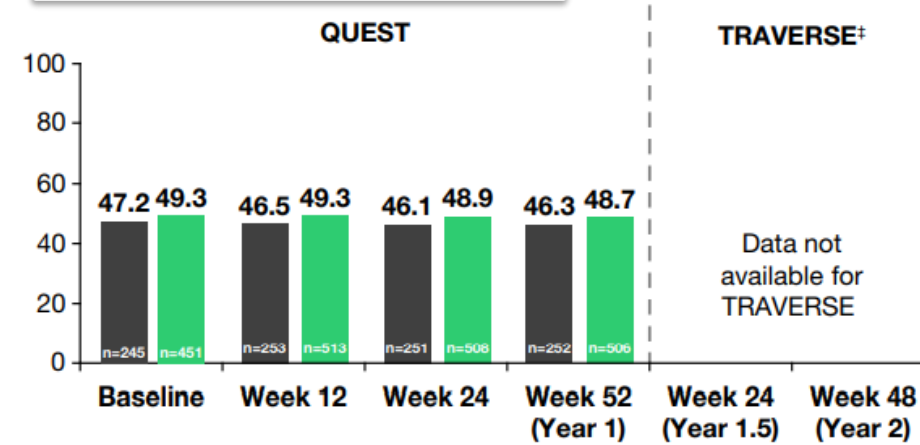
+ ACAAI, AAAAI and ATS consensus criteria



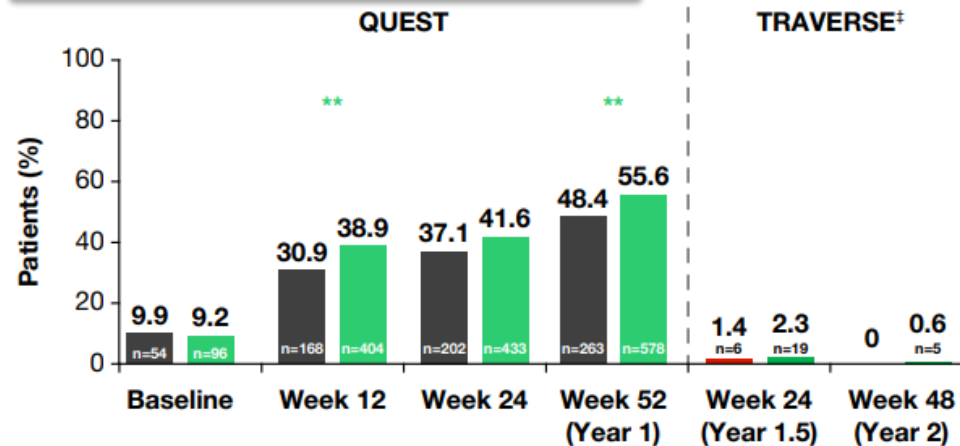
No missed work/school



On low- or medium ICS



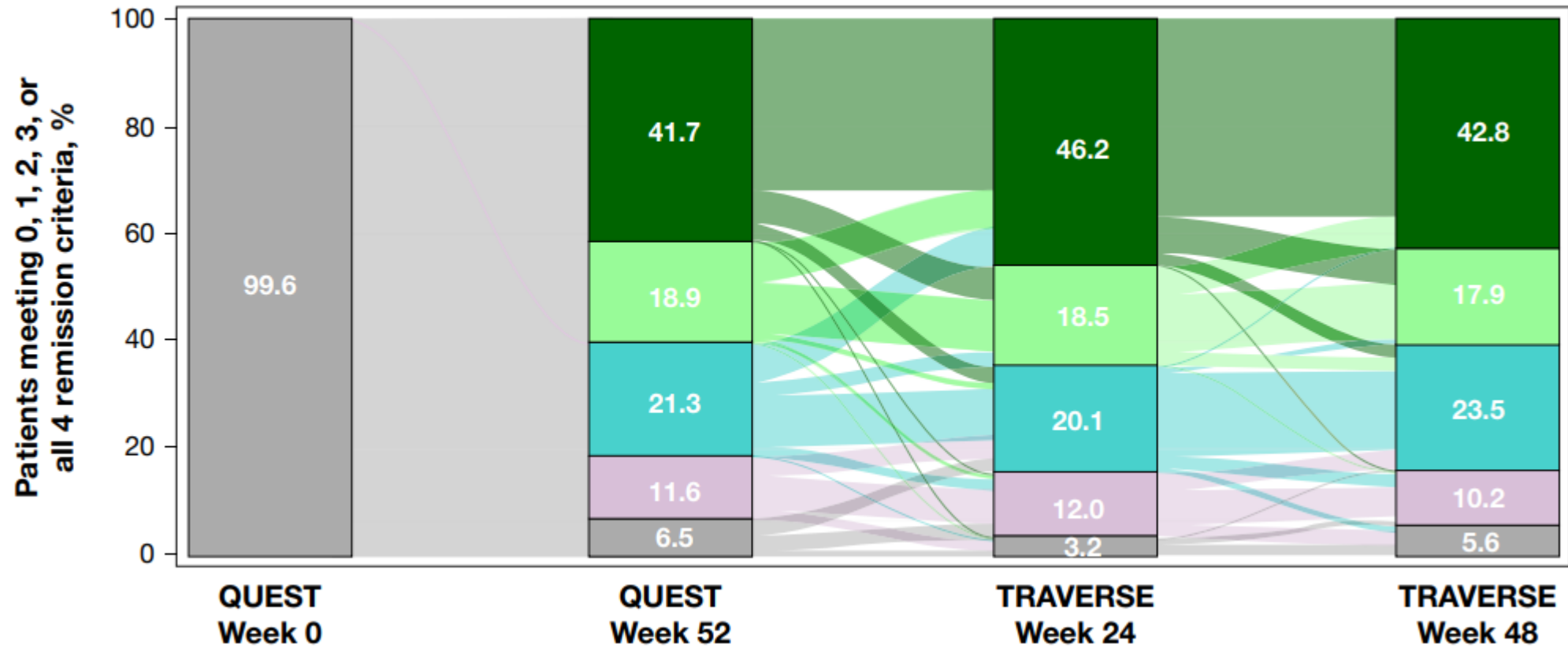
Reliever use ≤ 1/month



Stay in remission for up to 2 years

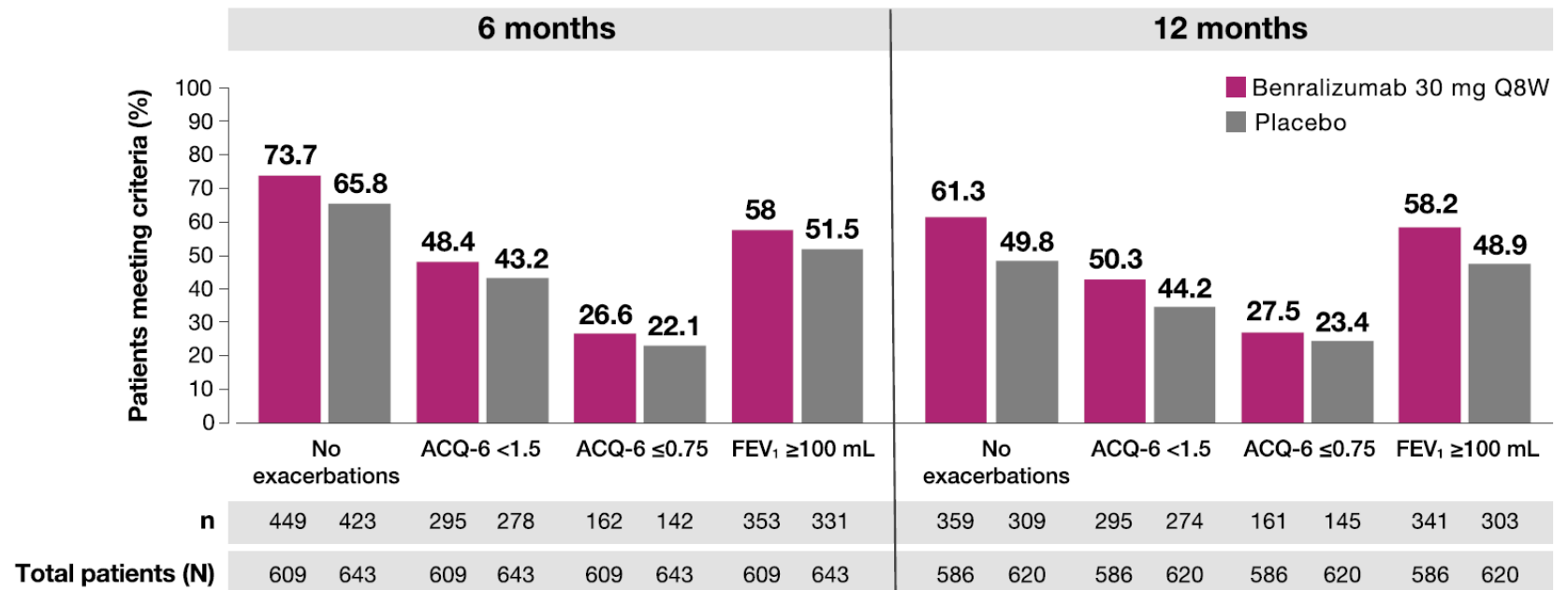
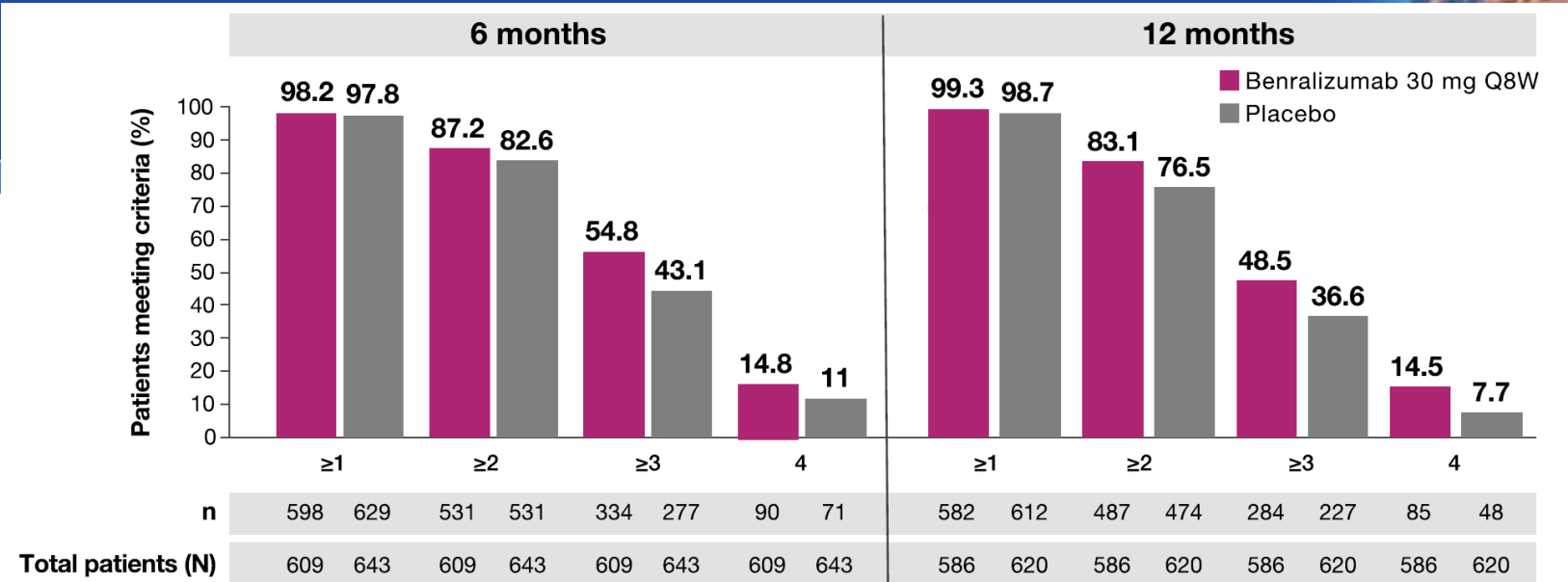


Dupilumab/dupilumab treatment arm (exposed population)



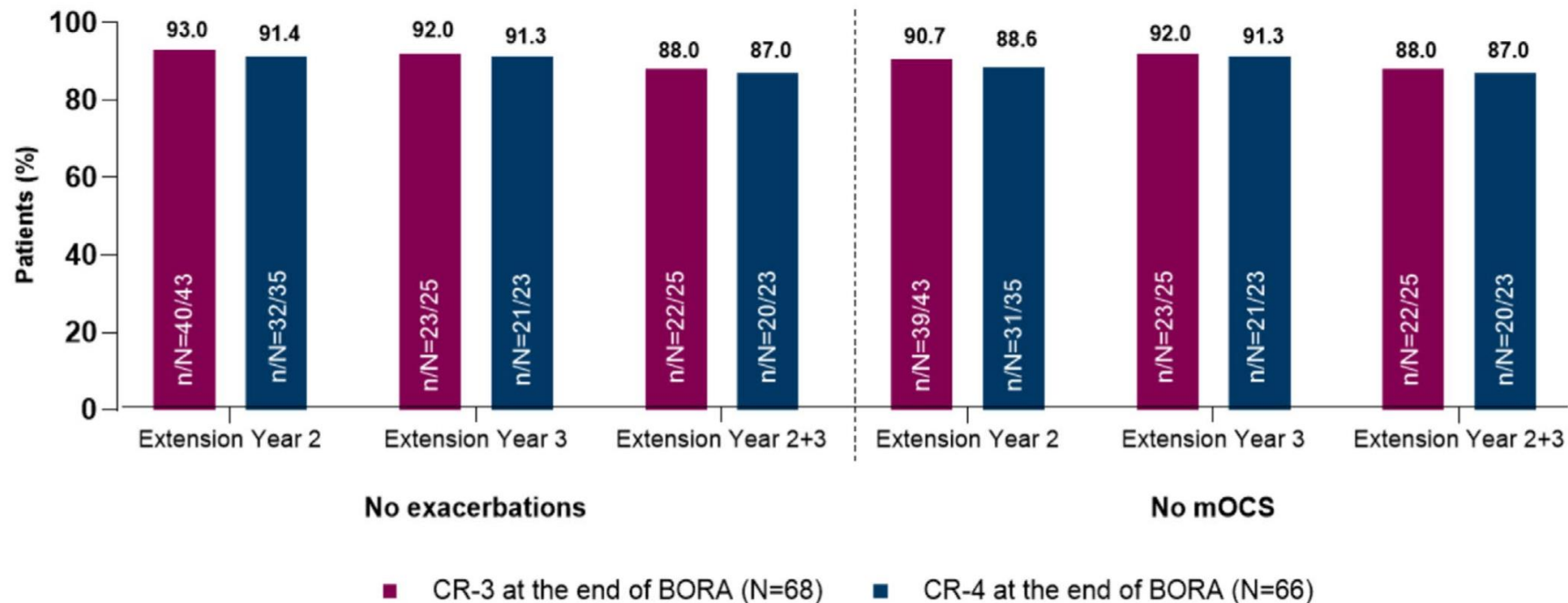
Benralizumab

SIROCCO/CALIMA

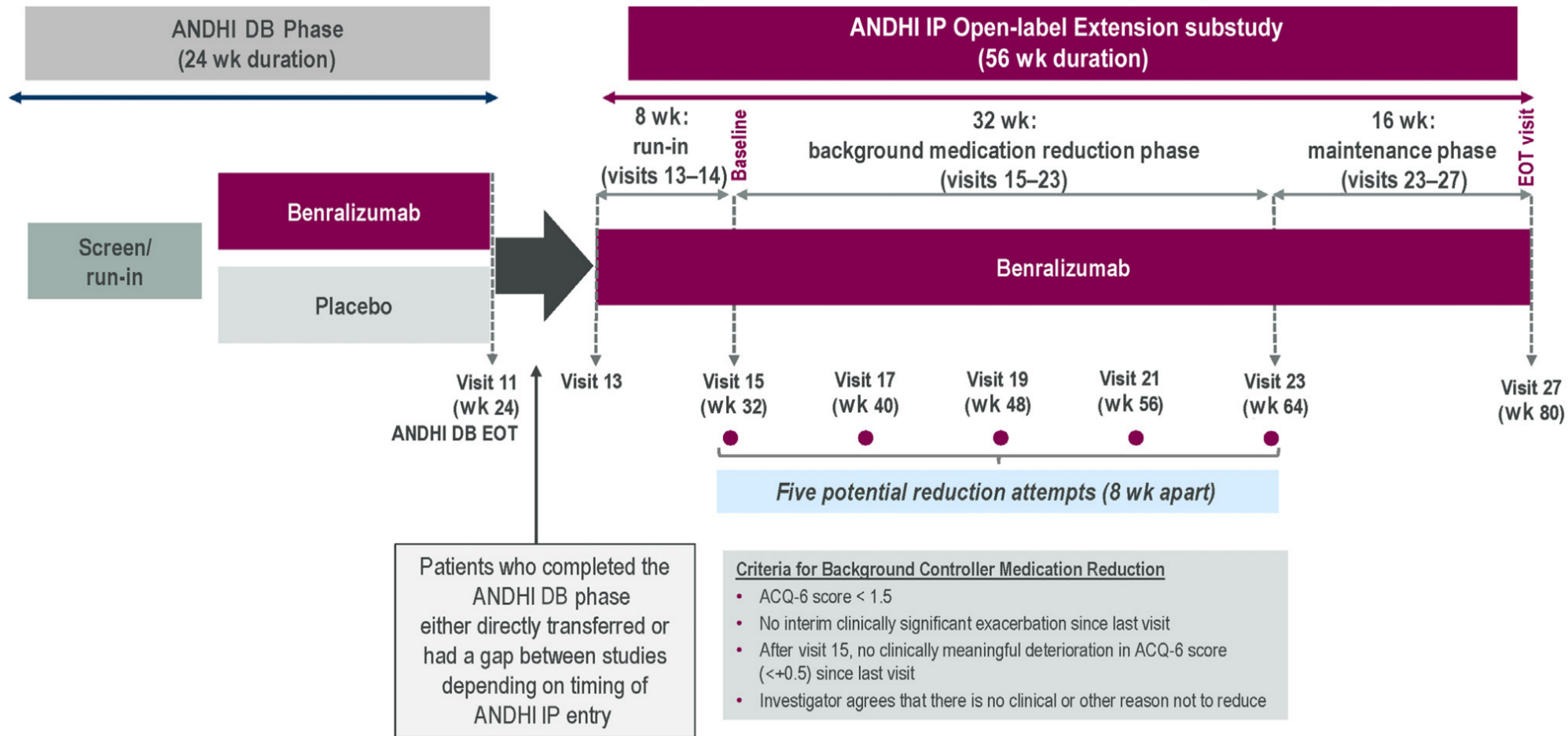


Benralizumab (SIRROCCO/CALIMA → BORA/MELTEMI)

remission at 24 months. Additionally, 31.7% and 25.8% of patients who did not achieve remission at the end of SIROCCO and CALIMA subsequently achieved three- and four-component remission criteria, respectively, at 24 months after 12 months' additional treatment with benralizumab in BORA.



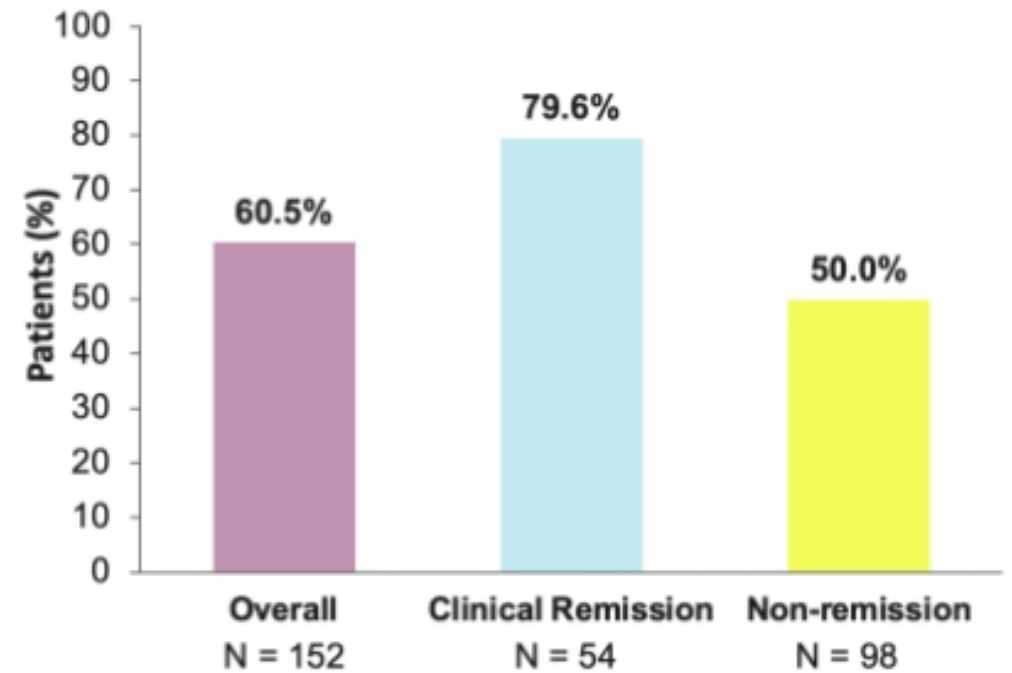
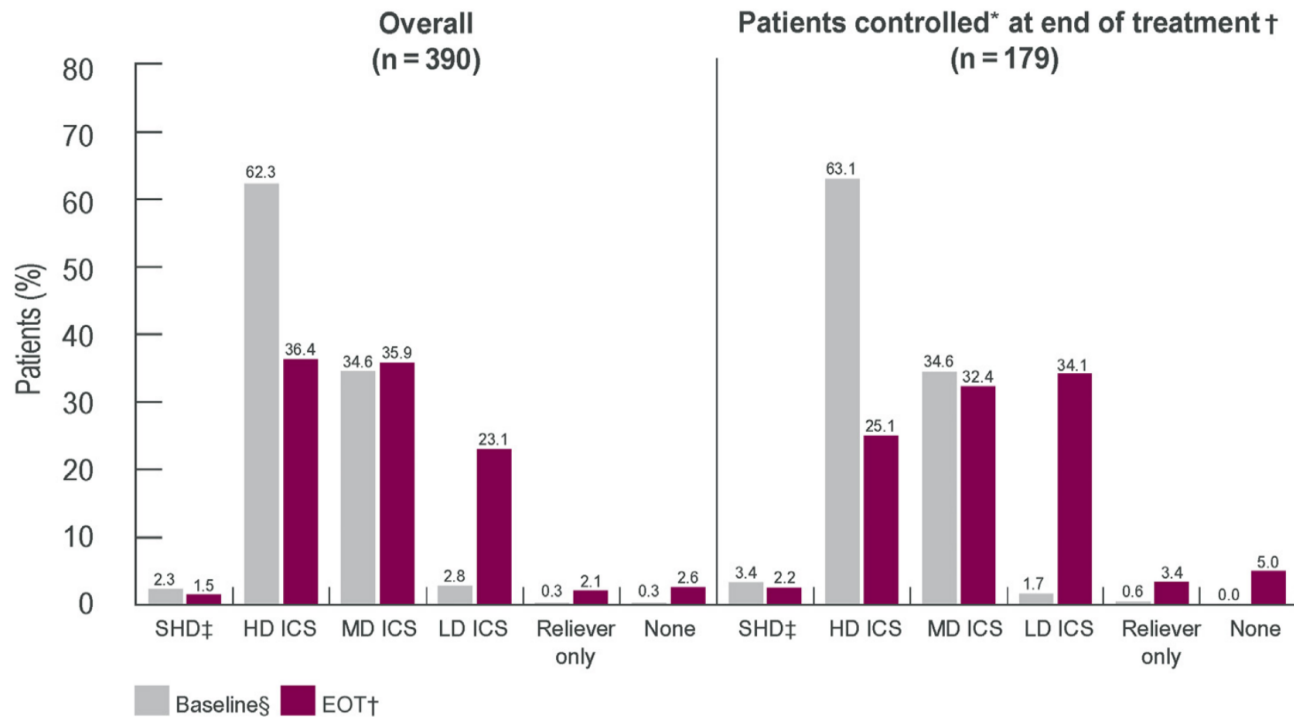
Benralizumab (ANDHI in Practice study)



ICS reduction in clinical remission



Patients with background Tx reduction at the end of ANDHI IP (18 months)



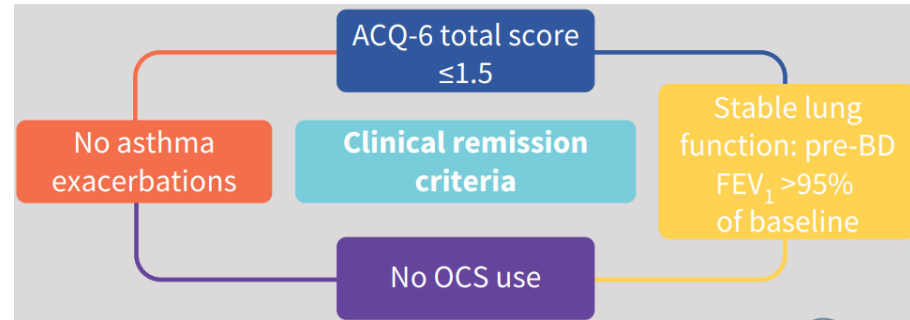
*Controlled

ACQ-6 score <1.5 + no clinically significant exacerbations since week 72

Tezepelumab



NAVIGATOR → DESTINATION study

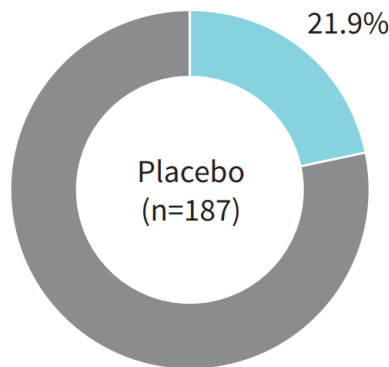
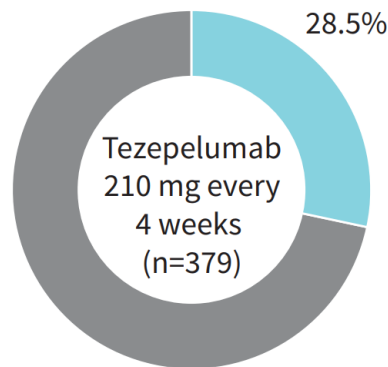


Weeks 0–52

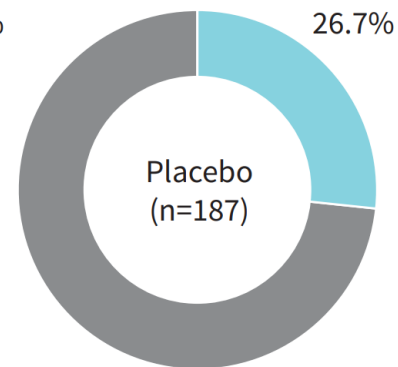
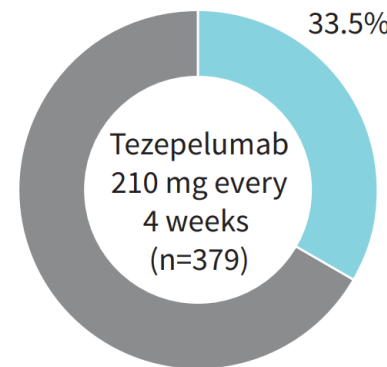
Weeks >52–104

■ Achieved clinical remission

■ Did not achieve clinical remission



OR (95% CI)
1.44 (0.95–2.19)



OR (95% CI)
1.44 (0.97–2.14)

While remission was associated with improvements in blood eosinophils and FENO, these biomarkers alone did not fully predict remission, suggesting the need for broader clinical markers used for predicting remission on treatment.

	Achieved complete clinical response	Achieved on-treatment clinical remission
Patients	199	108
Age years	48.3±16.9	48.3±17.6
Female	119 (59.8)	58 (53.7)
BMI kg·m⁻²	28±6.3	28±6.1
ICS dose group^a		
Medium	45 (22.6)	29 (26.9)
High	154 (77.4)	79 (73.1)
Maintenance OCS use	18 (9.0)	0 (0.0)
Pre-BD FEV₁ L	1.80±0.69	2.03±0.70
Pre-BD FEV₁ % predicted	60.6±17.5	66.3±16.6
Exacerbations in the 12 months before enrolment in NAVIGATOR		
2	109 (54.8)	71 (65.7)
>2	90 (45.2)	37 (34.3)
F_{ENO} level ppb		
Mean±SD	47.7±38.9	43.7±36.4
Median (min–max)	35.0 (5.0–213.0)	34.0 (5.0–213.0)
F_{ENO} group ppb		
<25	65 (32.8)	37 (34.6)
≥25 to <50	61 (30.8)	35 (32.7)
≥50	72 (36.4)	35 (32.7)
BEC cells·μL⁻¹		
Mean±SD	406±363	375±412
Median (min–max)	340 (20–3650)	290 (0–3650)
BEC group cells·μL⁻¹		
<150	35 (17.6)	22 (20.4)
150 to <300	53 (26.6)	34 (31.5)
<300	88 (44.2)	56 (51.9)
≥300	111 (55.8)	52 (48.1)
300 to <450	44 (22.1)	21 (19.4)
≥450	67 (33.7)	31 (28.7)
Serum total IgE IU·mL⁻¹		
Mean±SD	514.4±756.4	591.9±1339.7
Median (min–max)	206.1 (1.5–4357.4)	237.4 (1.5–12 823.2)
FEIA positive for any perennial aeroallergen⁺	116 (58.3)	69 (63.9)
Nasal polyps	43 (21.6)	23 (21.3)

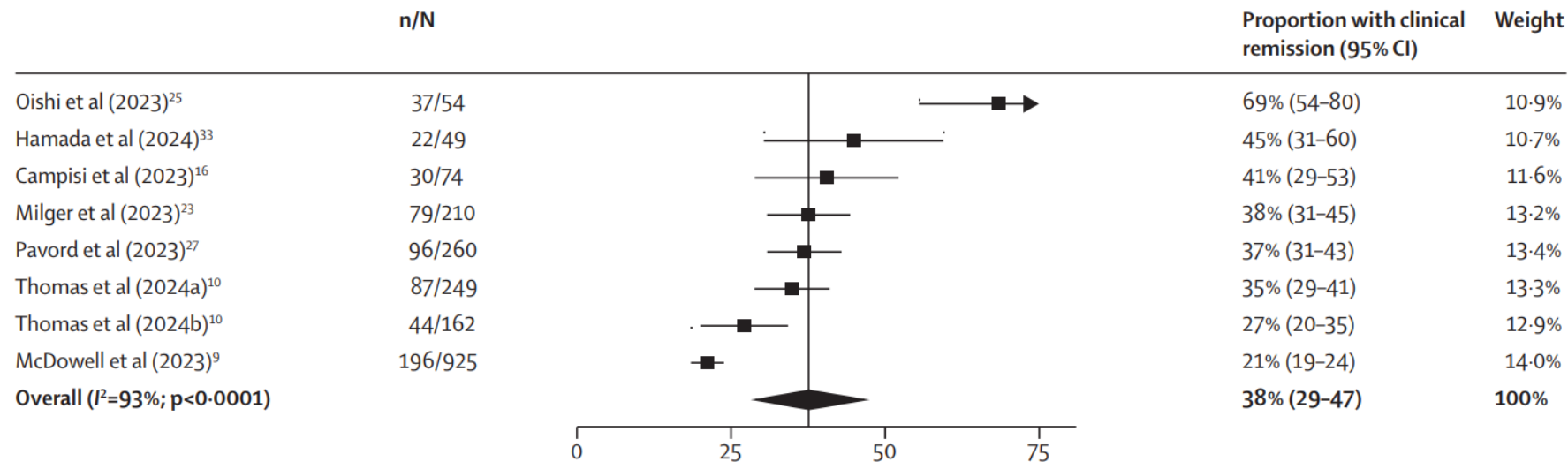
Meta-analysis (RCT + observational studies)



Clinical remission attainment, definitions, and correlates among patients with severe asthma treated with biologics: a systematic review and meta-analysis

Amy Shackleford, Liam G Heaney, Charlene Redmond, P Jane McDowell, John Busby

A Three-component definition of clinical remission

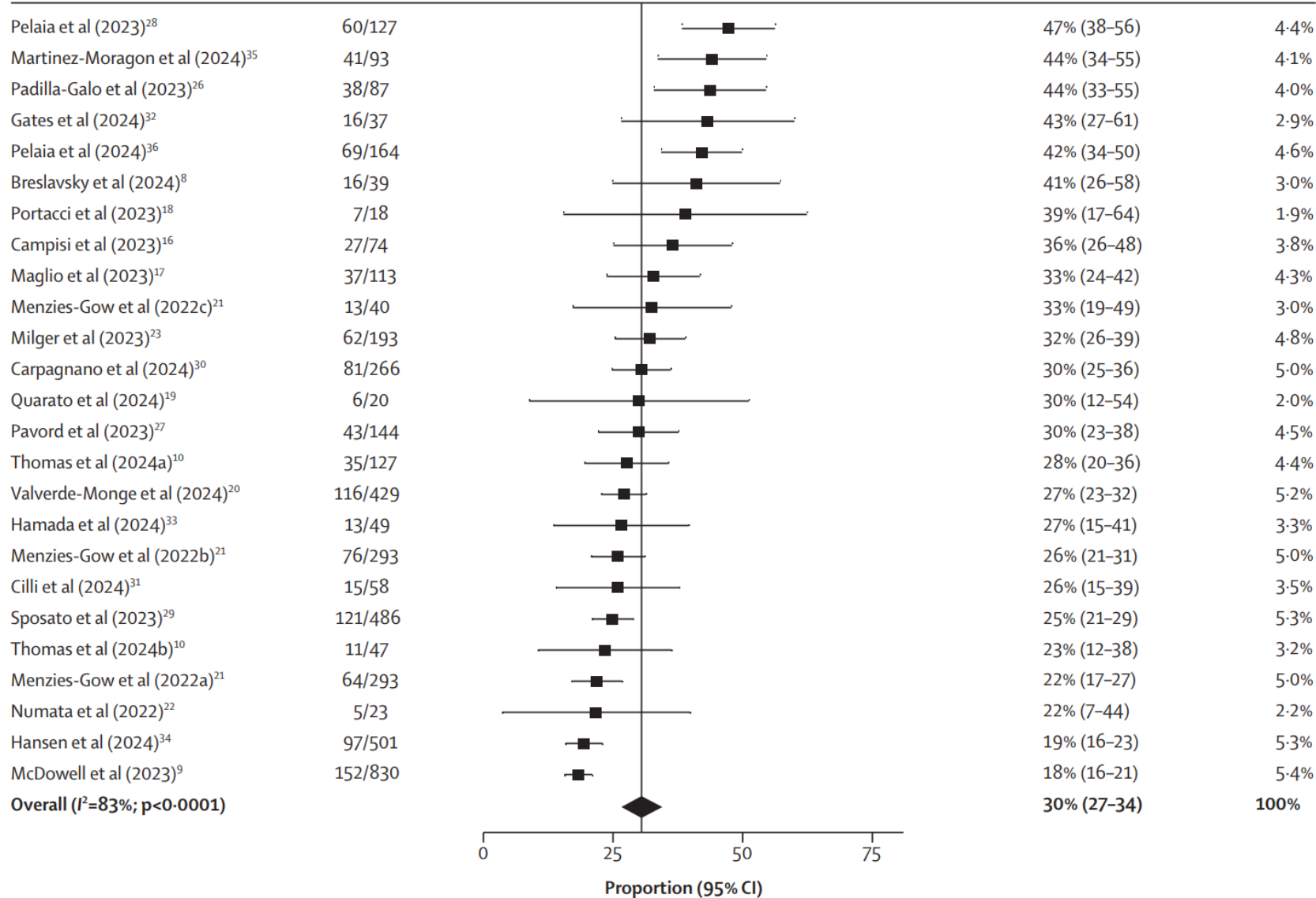


AE + OCS + Sx control
→ 38%

Meta-analysis (RCT + observational studies)



B Four-component definition of clinical remission



**AE + OCS + Sx control + PFT
→ 30%**

Contents



- Concept & definition of asthma remission
- Real-world and registry-based studies
- Post-hoc analyses of RCTs on biologics
- **Future perspectives**
 - Earlier initiation of biologics to achieve remission?
 - Tapering or discontinuation of biologics after achieving remission?

Asthma factors related to clinical remission



Asthma characteristics

Later asthma onset	3	1.49 (0.67-3.32)	35%
Atopy	11	0.89 (0.71-1.12)	12%
Any family history of asthma	2	0.70 (0.33-1.50)	0%
Longer asthma duration	3	0.49 (0.32-0.76)	22%
Worse asthma symptoms	5	0.23 (0.17-0.33)	0%
Worse FEV ₁	2	0.09 (0.01-0.92)	87%

Atopy

Non-steroidal anti-inflammatory drug sensitivity	6	1.55 (1.10-2.19)	0%
House dust mite sensitisation	2	0.66 (0.43-1.02)	0%

Biomarkers

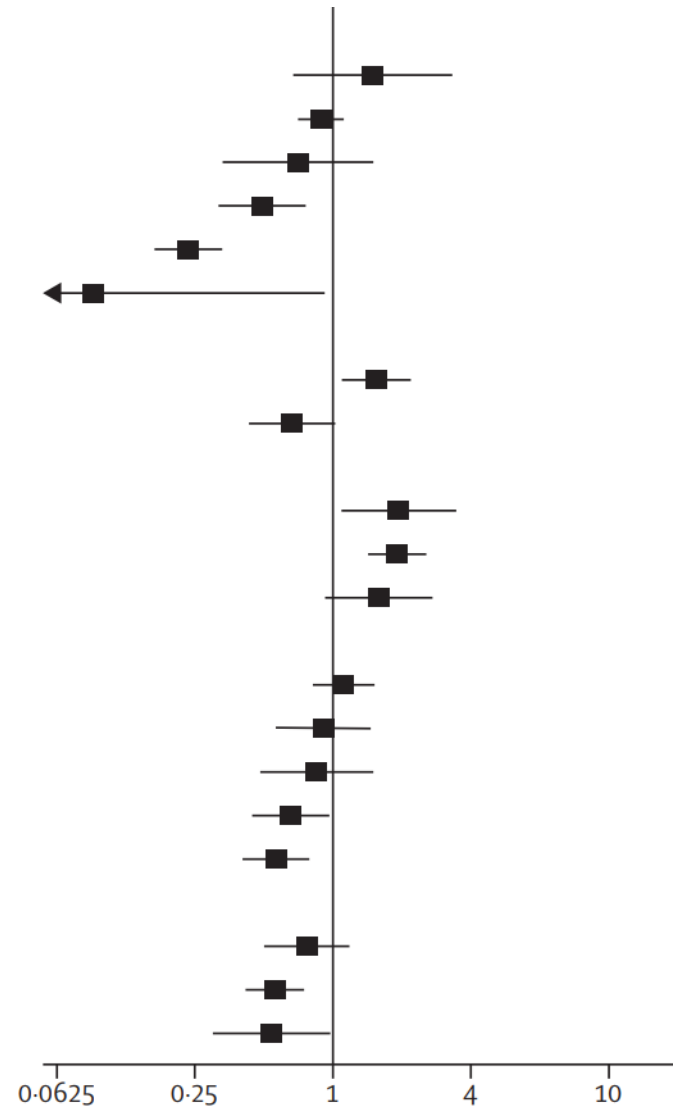
Higher FeNO	2	1.94 (1.09-3.46)	45%
Higher blood eosinophils	7	1.91 (1.42-2.56)	0%
Higher IgE	2	1.59 (0.92-2.72)	0%

Asthma treatment

Leukotriene receptor antagonists	3	1.12 (0.82-1.52)	0%
Short-acting β -agonists	2	0.91 (0.56-1.46)	0%
Long-acting muscarinic antagonists	5	0.85 (0.48-1.50)	60%
Previous use of biologics	5	0.66 (0.44-0.97)	0%
Maintenance oral corticosteroids	13	0.57 (0.40-0.79)	49%

Health-care resource use in past year

Exacerbations	7	0.77 (0.50-1.18)	0%
Attended emergency department	5	0.56 (0.42-0.75)	0%
Admission to hospital	2	0.54 (0.30-0.97)	32%



Early intervention? No evidence yet.



Asthma Remission

What is asthma remission?

A high level of disease control – the absence of signs and symptoms of asthma for ≥ 12 months

Types of asthma remission

Types	Either on or off treatment:
Clinical remission	<ul style="list-style-type: none">• No symptoms• No attacks• Optimisation of lung function
Complete remission	<ul style="list-style-type: none">• Clinical remission plus normalisation of underlying pathology

Prevalence

Spontaneous remission in adult asthma patients

2–52%

Potential treatments to induce remission

Biologics

- Highly effective in eosinophilic asthma



Macrolides

- Treat eosinophilic and non-eosinophilic asthma



Treatable traits approach

- Many underlying treatable traits contribute to the multifaceted aetiology of asthma
 - Identifying and treating all underlying traits may improve asthma outcomes



Early intervention

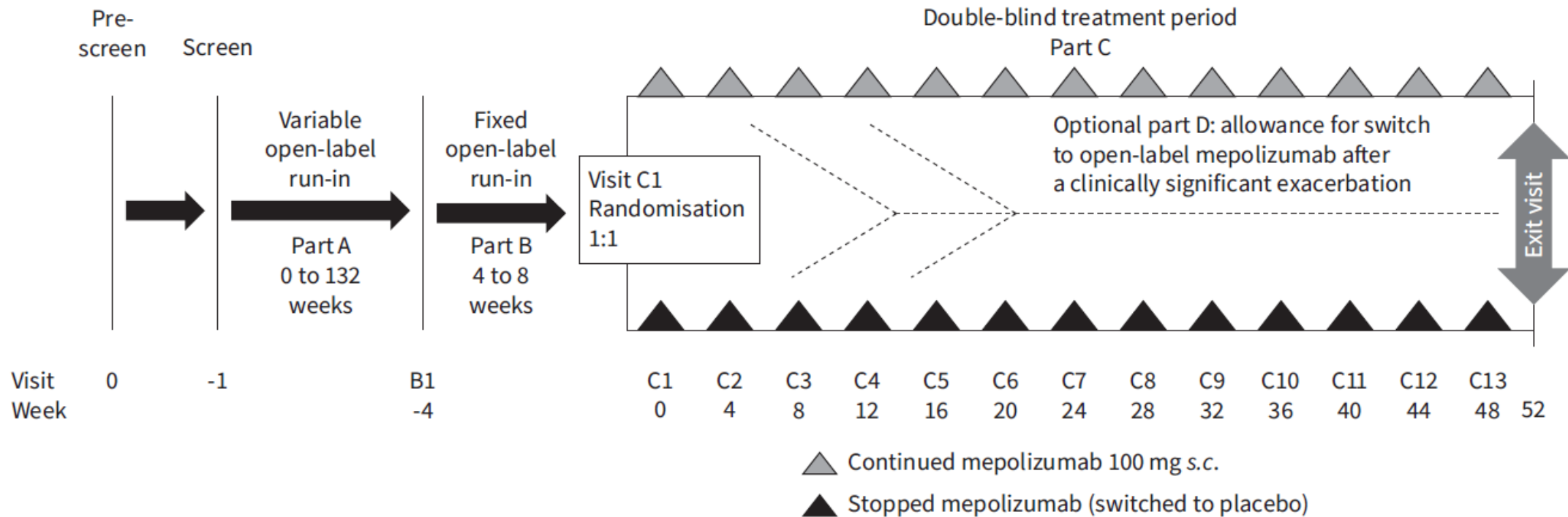
- People accumulate health and psychological issues over time, including iatrogenic issues
- Timely targeted intervention might halt asthma progression



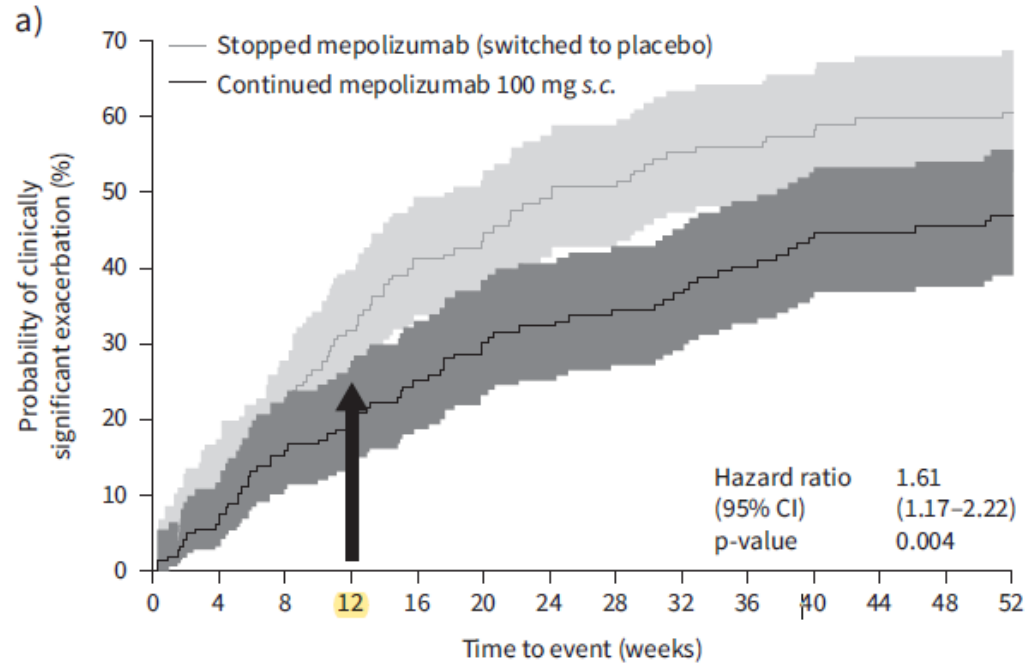
Discontinuation of biologics



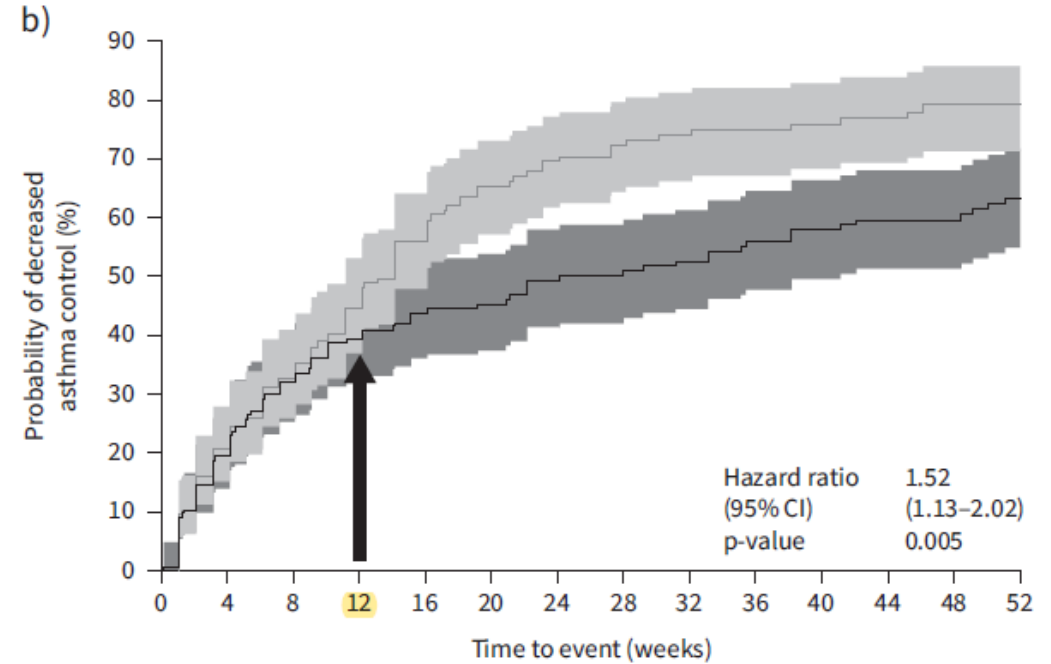
COMET study : Stopping vs. Continuing long-term (≥ 3 years, median 44.1 months) mepolizumab treatment



Discontinuation leads to exacerbation



	Number at risk													
	0	4	8	12	16	20	24	28	32	36	40	44	48	52
Placebo	151	134	120	103	86	78	69	66	59	57	55	52	49	42
Mepolizumab 100 mg s.c.	144	135	122	115	104	97	94	91	87	80	75	74	73	55



	Number at risk													
	0	4	8	12	16	20	24	28	32	36	40	44	48	52
Placebo	151	119	100	76	58	42	35	31	28	26	24	23	20	19
Mepolizumab 100 mg s.c.	144	116	96	84	73	70	62	60	57	50	48	46	45	32

Similar risk of exacerbation within 6 months of biologics discontinuation

Claim data analysis in the US

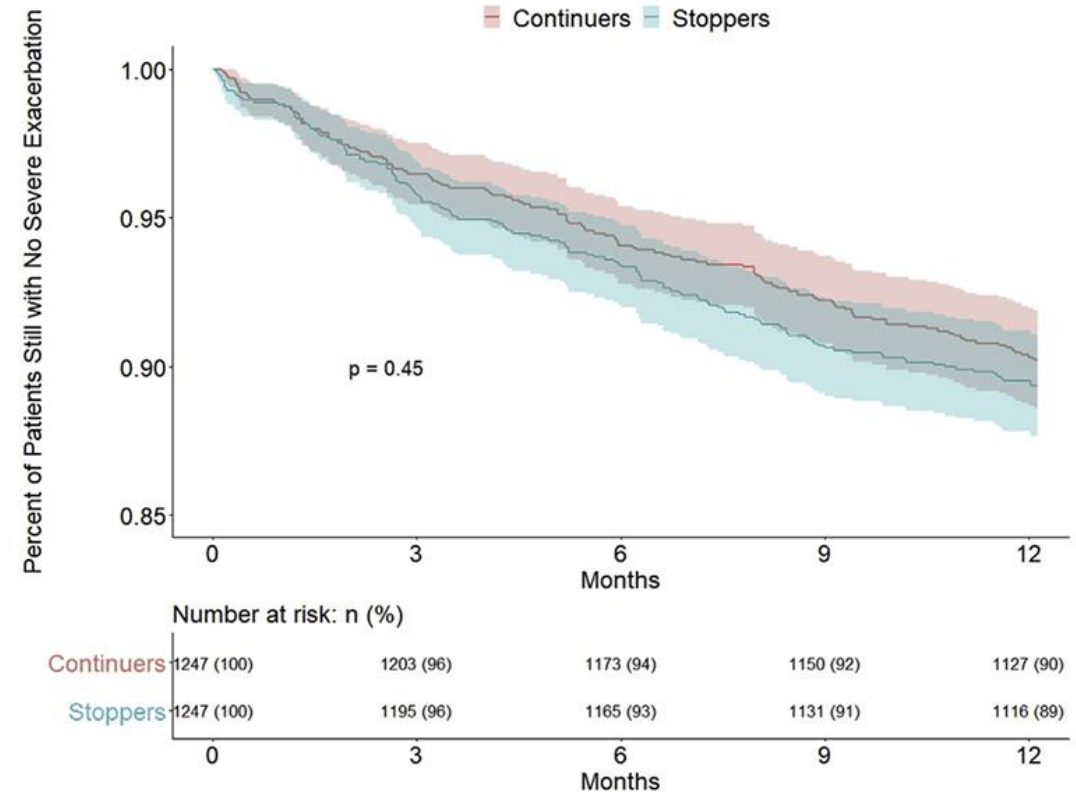
4,960 asthma biologic users → 1,249 discontinued (after 6-12 mo use)

1:1 PSM with continuers (at least 18 mo)

Primary outcome

= Discontinuation failure (50% increase in exacerbation)

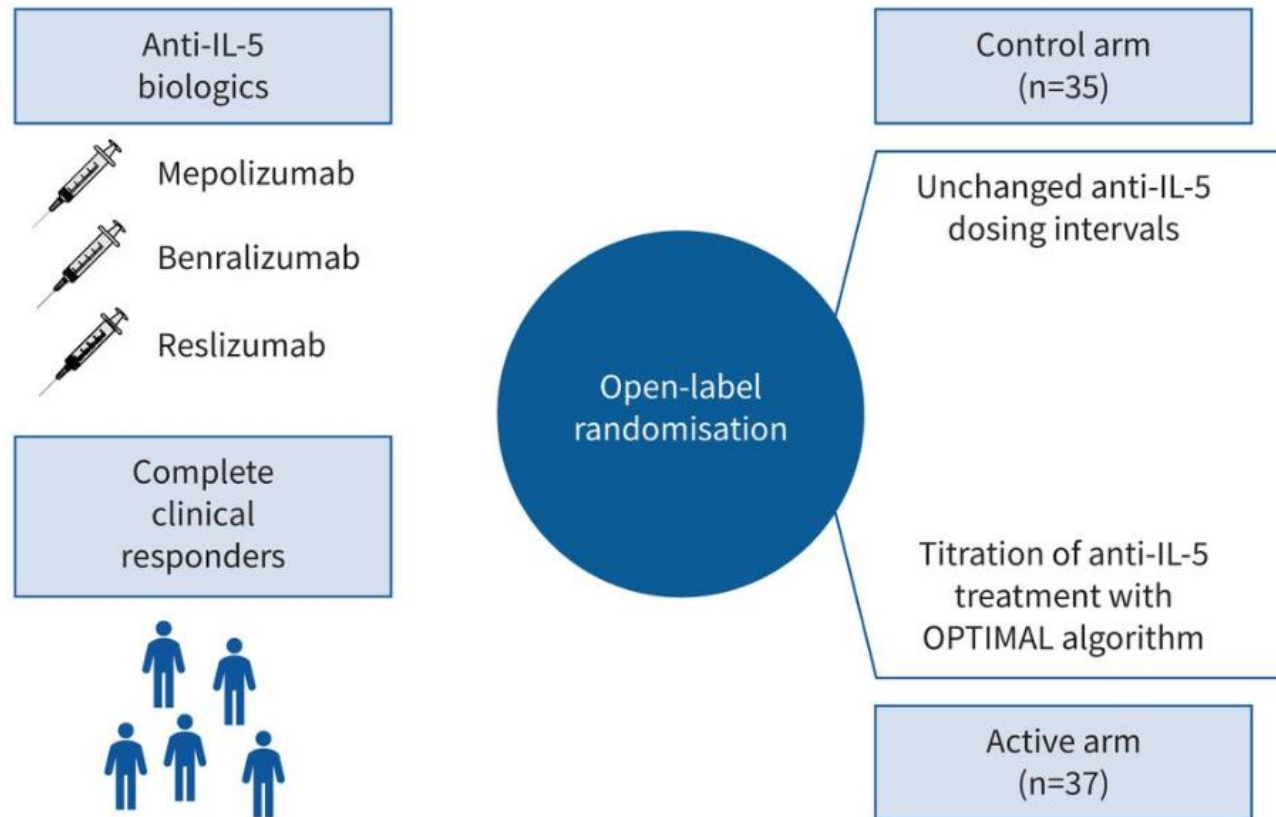
10.2% of stoppers and 9.5% of continuers



Titration of anti-IL-5 biologics interval in severe asthma

The OPTIMAL study

*No AE, No mOCS
for at least 12 months
of biologics
+ Eos < 300*



Titration protocol

Mepolizumab, Reslizumab

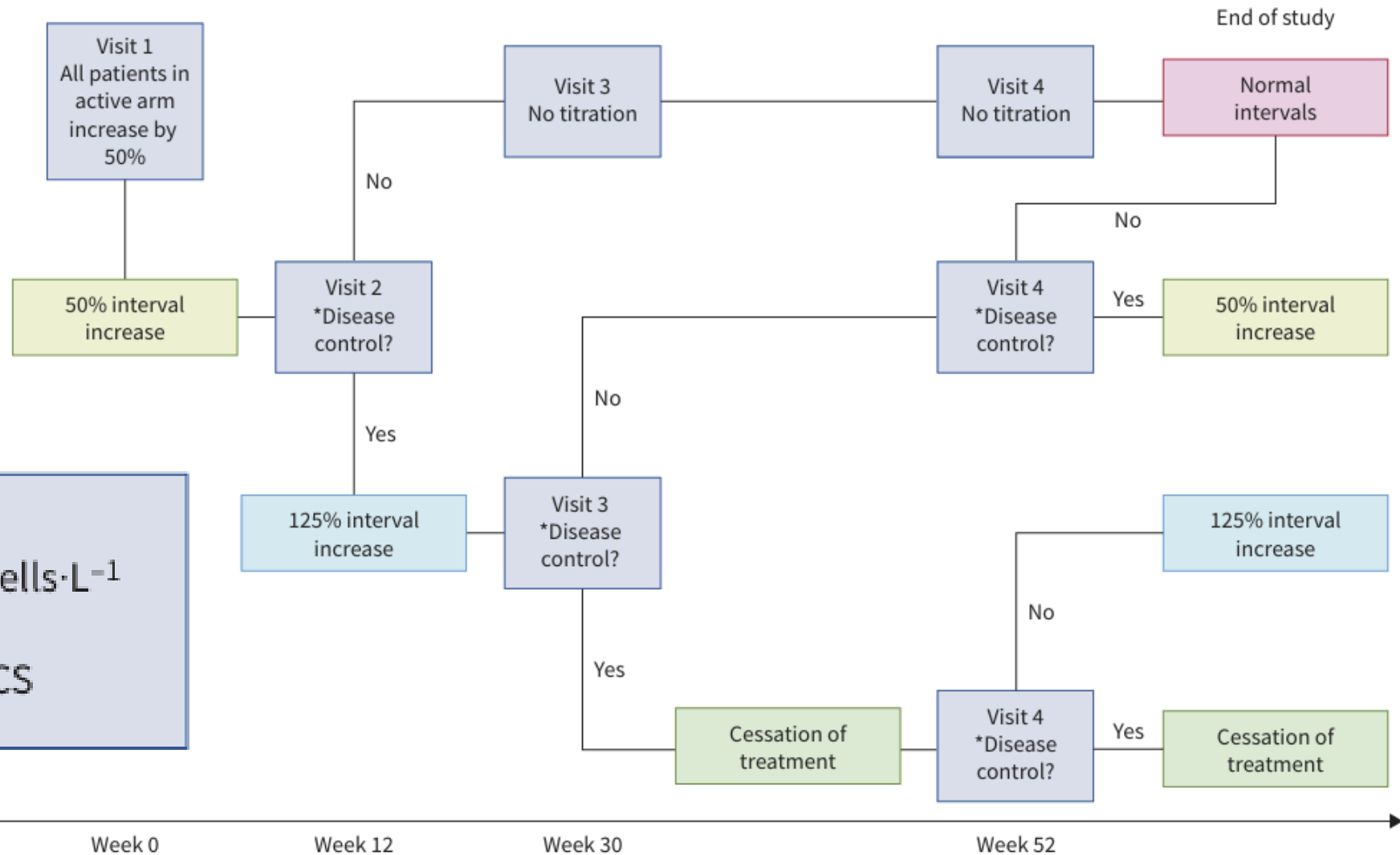
: 4wk → 6wk → 9wk → DC

Benralizumab

: 8wk → 12wk → 18wk → DC

*Disease control?

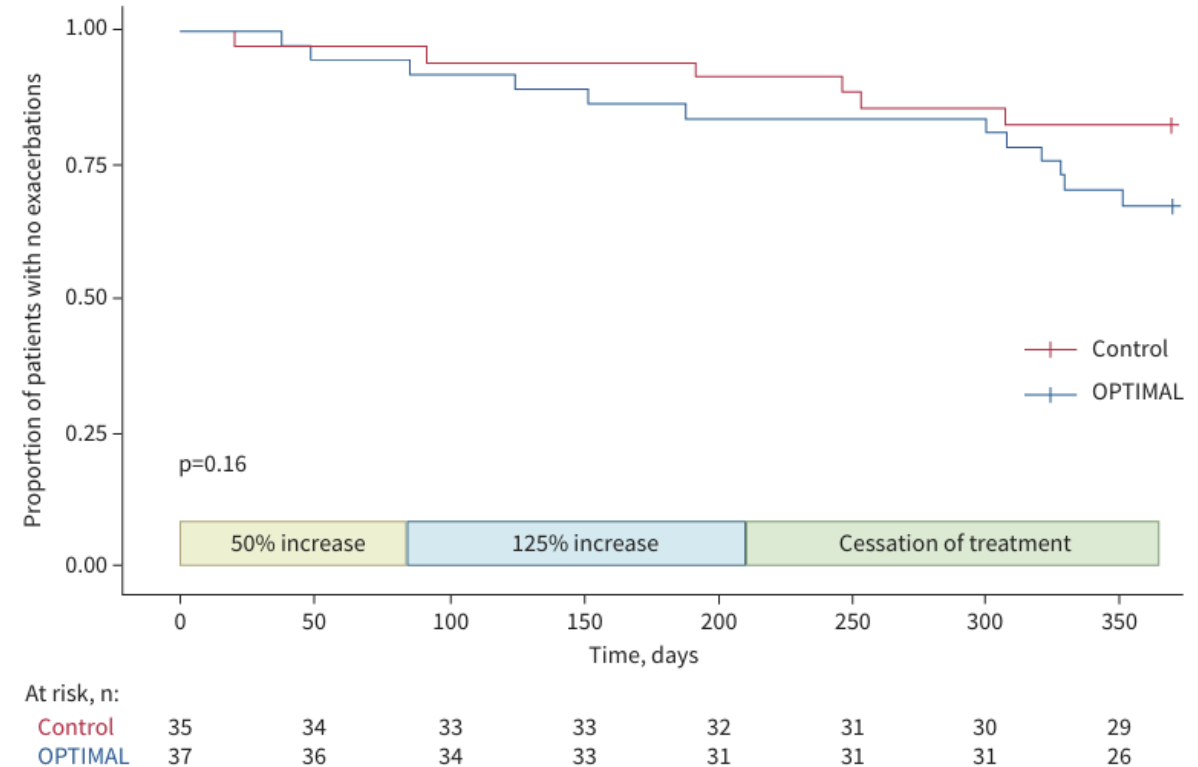
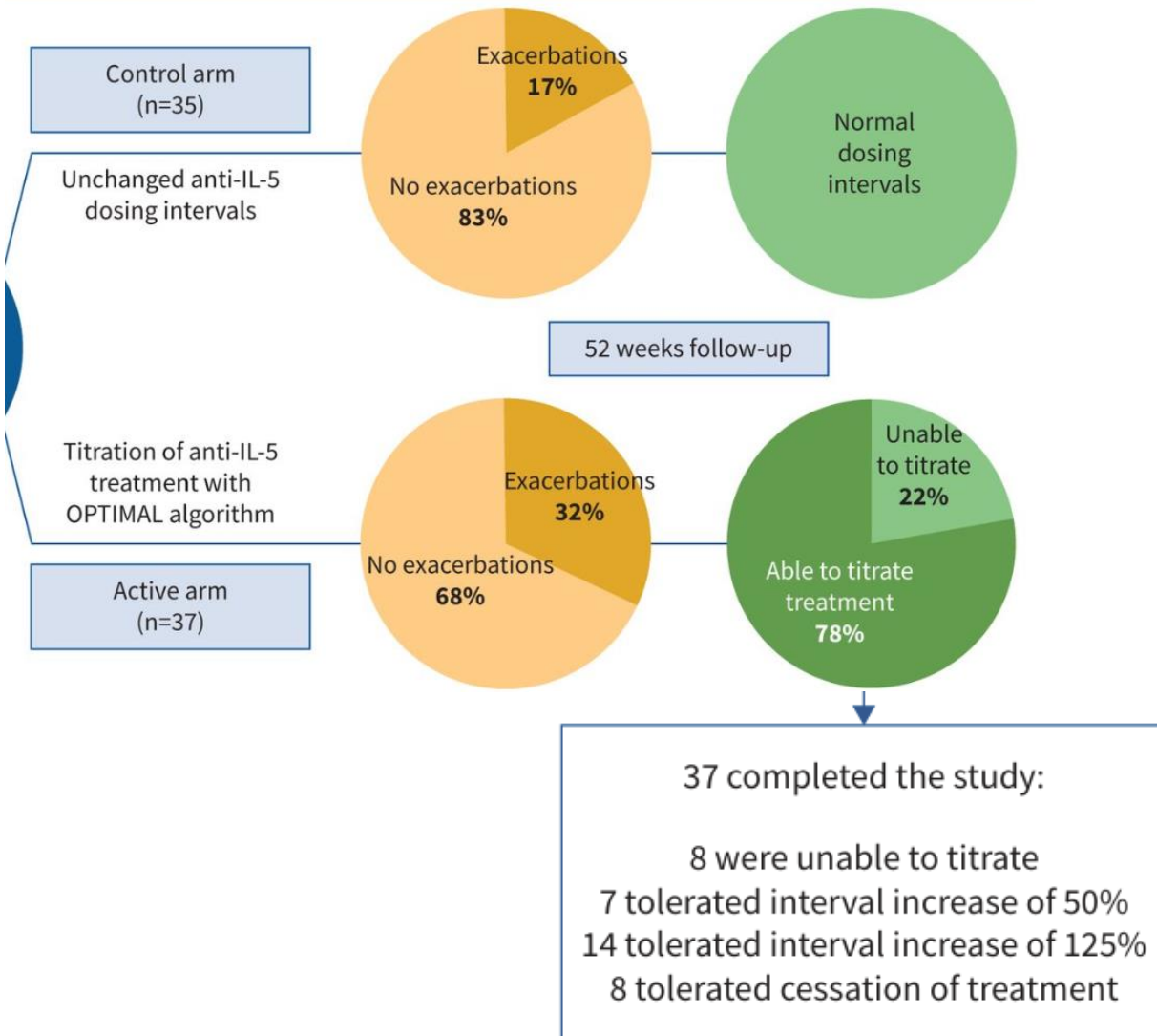
- Blood eosinophils $\leq 0.3 \times 10^9 \text{ cells} \cdot \text{L}^{-1}$
- FEV₁ decline $\leq 15\%$
- No exacerbation requiring OCS



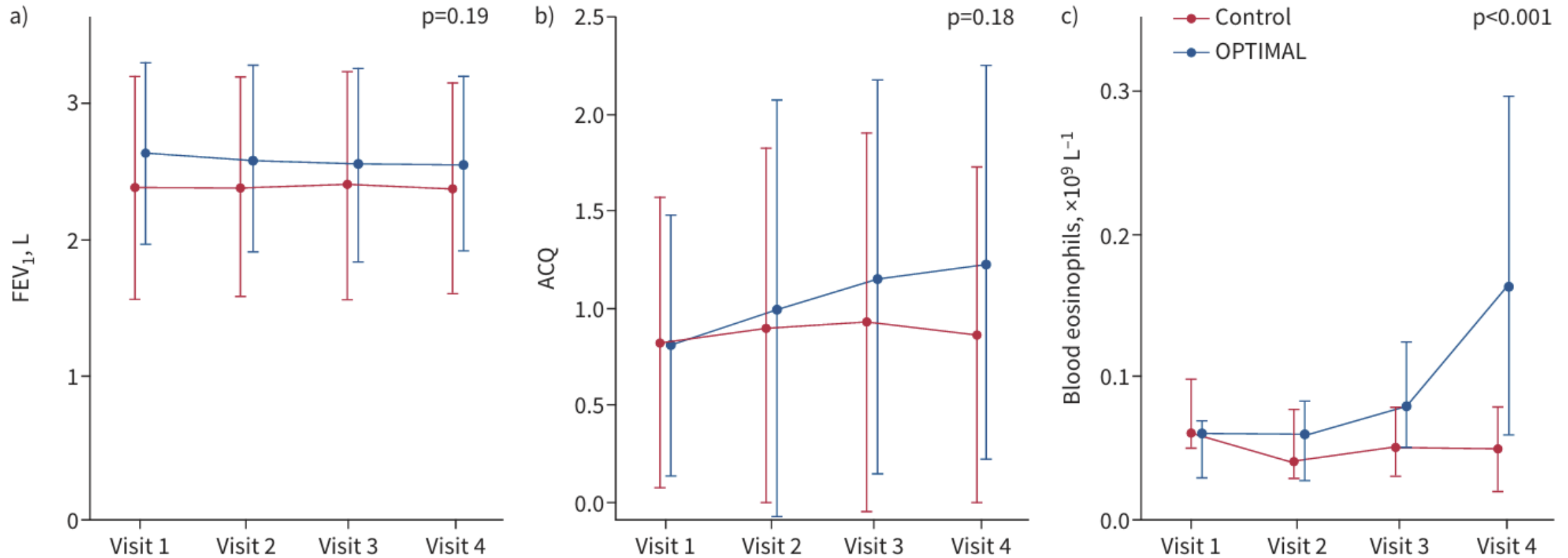
Non-significant increase in exacerbation



The OPTIMAL study



Titration of anti-IL-5 biologics in severe asthma



Summary



- Definition of remission in asthma : Clinical vs. Complete
- Clinical remission on biologics treatment = New goal of asthma management
 - ✓ **Meta-analysis : 30%** (Four component : AE + OCS + Sx control + PFT)
 - ✓ Related factors: Male, Short duration of disease, Low BMI, Never smoker, T2 high biomarker, Low symptom, Comorbidities...
- Unsolved questions
 - Consensus of definition of remission
 - Tapering/Discontinuation of controller medication or biologics?
 - Earlier intervention with biologics
 - Role of biomarkers to assess disease activity



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