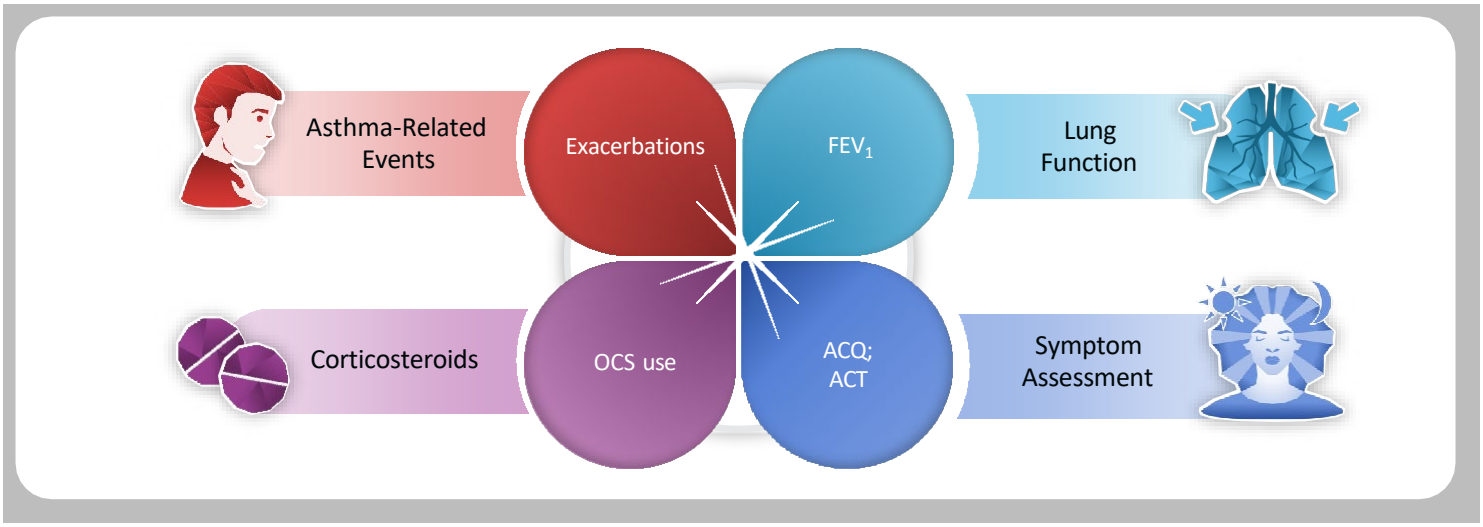
ON-TREATMENT ASTHMA REMISSION: MOVING BEYOND CONTROL

Proposed Framework for Remission[1-7]



Remission: A state or period with low to no disease activity that can be spontaneous or as a result of therapy[6]

Several Countries Have Recommended Clinical Remission Definitions[1-5]

For ≥12 months:	Germany[1]	Spain[2]*	Italy[3]	Japan[4]	US[5†]
1 Symptom assessment	Absence of symptoms	Absence of symptoms	ACT 20-25; ACQ <1.5	ACT ≥23	ACT >20; AirQ <2; ACQ <0.75
2 Lung function	Stabilized	Optimized and stabilized	Stabilized	Assessed if other criteria are achieved	Optimized and stabilized
3 No exacerbations	✓	✓	✓	✓	✓
4 No OCS use	✓	✓	✓	✓	✓
Other criteria	—	—	—	—	5 No missed work or school 6 Low-medium ICS dose 7 Reliever use ≤1 per month

*A broad consensus definition is being developed with over 120 experts and is expected in the GEMA 5.4 update.

†The US workgroup determined that symptom and lung function criteria must be met on all occasions measured in the previous 12-month period with a minimum of two measurements during the year.

The definition of on-treatment remission in asthma has not yet been established and further consensus among experts, guidelines, and societies is warranted.

This tool showcases the evolving evidence around asthma remission as of February 2024 and is intended for educational purposes only.

ACQ, Asthma Control Questionnaire; ACT, Asthma Control Test; AirQ, Asthma Impairment and Risk Questionnaire; FEV_1, forced expiratory volume in 1 second; ICS, inhaled corticosteroids; OCS, oral corticosteroids.

REFERENCES

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EVOLUTION OF ON-TREATMENT REMISSION IN ASTHMA

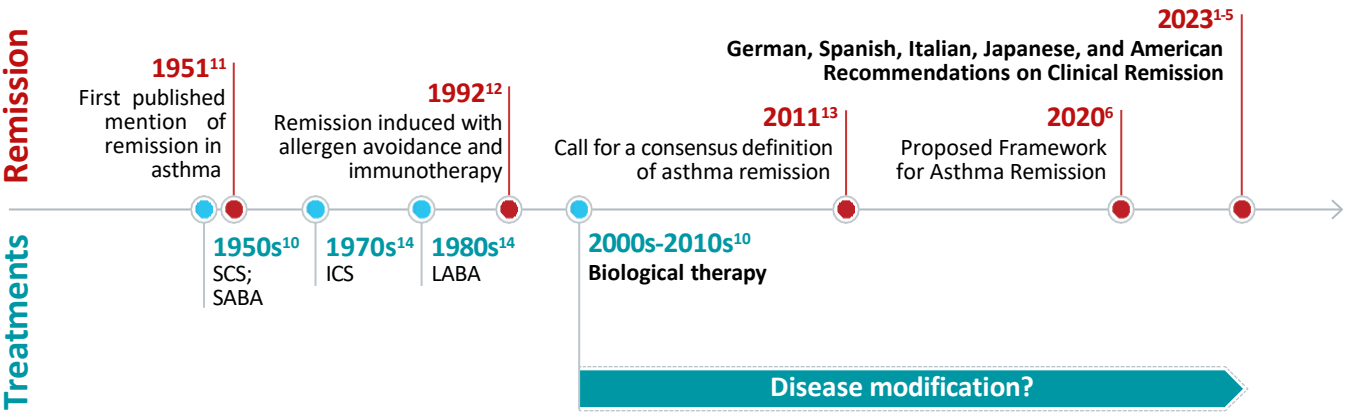
How Can Therapeutic Intervention Get Us to On-Treatment Clinical Remission?[6-10]

Natural Disease Course

Therapeutic Intervention

*Disease remission is broadly defined as a state or period with low to no disease activity and can be spontaneous or a result of therapy[1]
†Disease modification is an evolving topic in asthma and further study is required to demonstrate whether current interventions have the potential to modify disease.

Over 70-Years of On-Treatment Clinical Remission in Asthma



Remission may be achieved on or off treatment. Different definitions of remission have been proposed and implemented in various studies. Given this evolving framework for remission, further studies may provide a pathway to inform our understanding of disease modification in severe asthma.

This tool showcases the evolving evidence around asthma remission as of February 2024 and is intended for educational purposes only.

ICS, inhaled corticosteroids; LABA, long-acting beta agonist; SABA, short-acting beta agonist; SCS, systemic corticosteroids.

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REDUCING EXACERBATIONS IS A FUNDAMENTAL CRITERION OF ASTHMA REMISSION[1-7]

Asthma Control[15,16]*

- Zero exacerbations requiring hospitalization in previous 12 months

On-Treatment Clinical Remission[1-7]

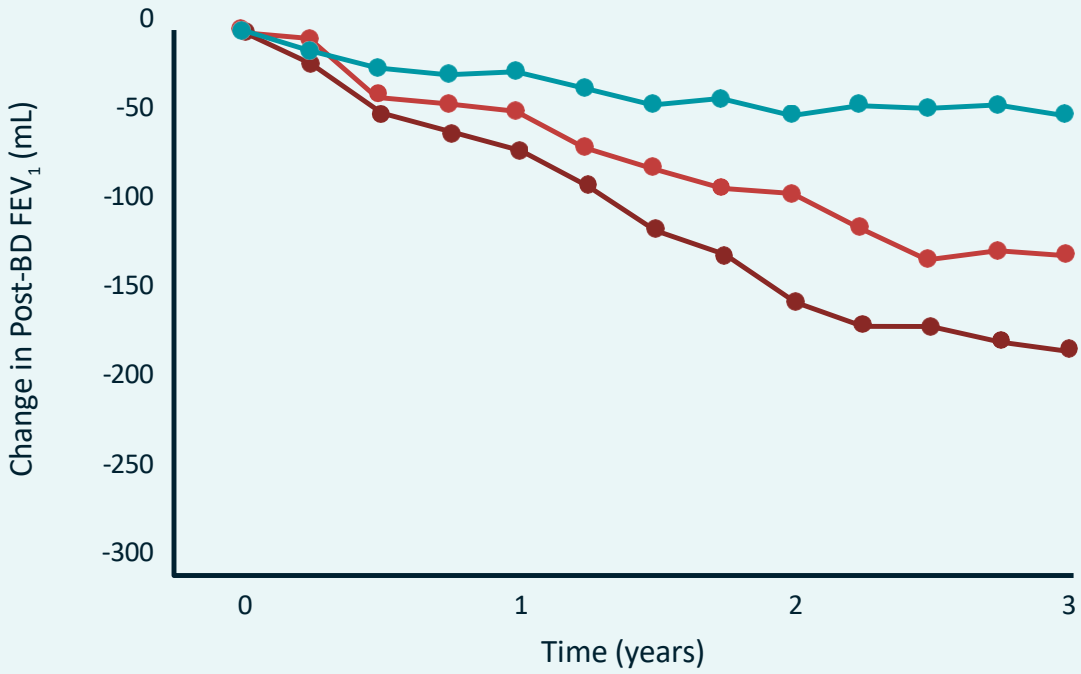
For ≥12 Months

- Zero exacerbations

Frequent Exacerbations Lead to Airflow Limitations[17]

- No exacerbations
- One exacerbation
- Two or more exacerbations

Lung Function Decline



- Post-BD FEV_1 13.6 mL/year
- Post-BD FEV_1 41.3 mL/year
- Post-BD FEV_1 58.3 mL/year

Each additional asthma exacerbation may cause irreversible lung function decline

*Adapted from GINA and ERS/ATS. †Severe exacerbation was defined as worsening asthma requiring at least 3 days of treatment with systemic corticosteroids, or a hospitalization due to asthma.
ATS, American Thoracic Society; BD, bronchodilator; ERS, European Respiratory Society; FEV_1, forced expiratory volume in 1 second; GINA, Global Initiative for Asthma.

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ZERO OCS USE IS REQUIRED FOR A STATE OF ASTHMA REMISSION[1-7]

Asthma Control[15,16]*

- **<2 exacerbations requiring OCS in previous 12 months**

On-Treatment Clinical Remission[1-7]

For ≥12 Months

- **Zero exacerbations requiring OCS**

Short-/Long-Term OCS Use Is Associated With AEs[15,18,19]

- Osteoporosis
  Fractures
- Anxiety
  Depression
- Type 2 diabetes
  Adrenal suppression
- Dyslipidemia
  Hypertension
  Thromboembolism
- Sleep disturbances
- GI bleeds/ulcers
- Obesity
- Increased risk of infection
- Cataracts
  Glaucoma

Risk of Adverse Events May Be Increased Following a Single OCS Burst[20]

Up to 2x
greater risk of fracture within 5-90 days

~3x
greater risk of venous thromboembolism within 5-30 days†

>3x
greater risk of sepsis within 5-30 days†

≥2 OCS bursts per year may indicate poor asthma control[15]

*Adapted from GINA and ERS/ATS. †$P<0.001$.[20]
AE, adverse event; ATS, American Thoracic Society; ERS, European Respiratory Society; GI, gastrointestinal; GINA, Global Initiative for Asthma; OCS, oral corticosteroids.

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ACHIEVING LUNG FUNCTION STABILIZATION OR IMPROVEMENT IS A KEY COMPONENT OF ASTHMA REMISSION[1-7]

Asthma Control[15,16]*

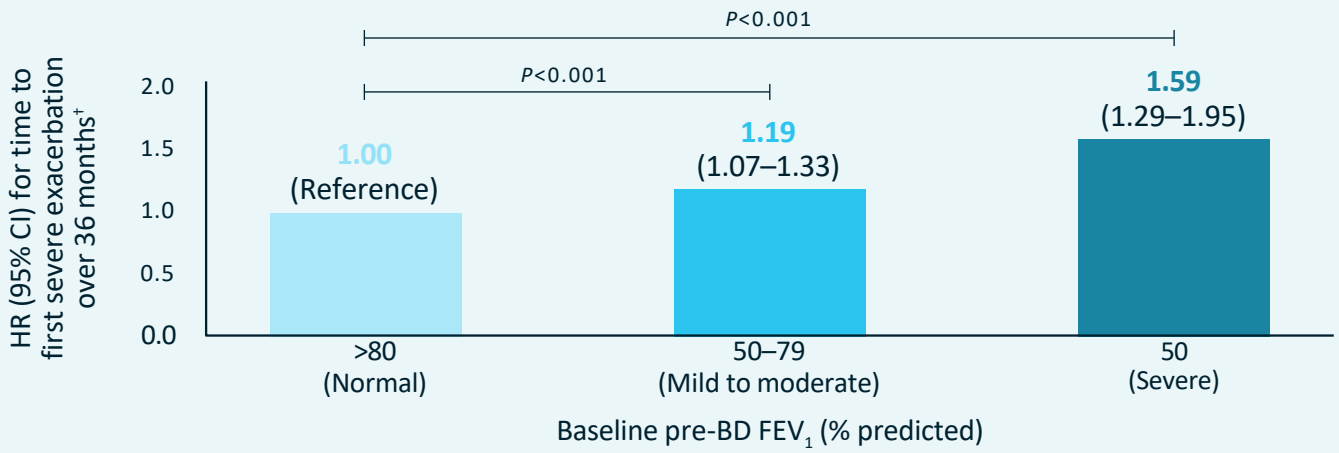
- FEV_1pp ≥80%

On-Treatment Clinical Remission[1-7]

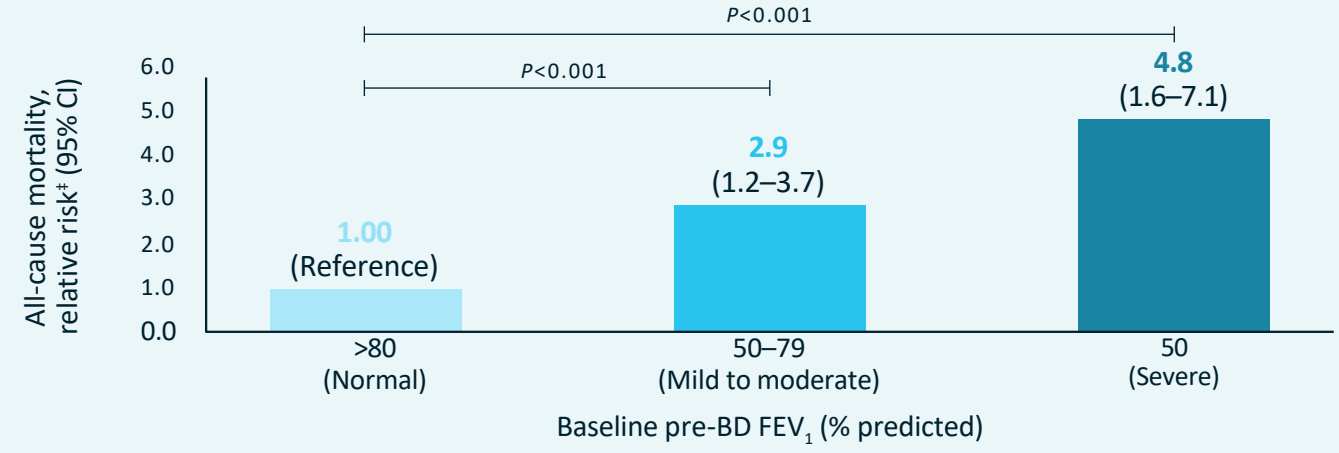
For ≥12 Months

- Stable or optimized lung function

Low FEV_1 Is a Predictor of Future Severe Exacerbations[21]



Impaired Lung Function Is Associated With Increased Risk of Mortality[22]



*Adapted from GINA and ERS/ATS. †n=1865; Cox proportional hazard model analysis adjusted for age at index date, smoking status, body mass index, gender, rhinitis, chronic sinusitis, nasal polyps, atopic dermatitis, diabetes, anaphylaxis, ischemic heart disease, heart failure, food allergy, anxiety, depression, and psoriasis.[8] ‡n=1075; relative risk of death from asthma during 25 years of follow-up.[9] ATS, American Thoracic Society; BD, bronchodilator; CI, confidence interval; ERS, European Respiratory Society; FEV_1, forced expiratory volume in 1 second; FEV_1pp, FEV_1 percent predicted; GINA, Global Initiative for Asthma; HR, hazard ratio.

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LONG-TERM SYMPTOM CONTROL IS AN IMPORTANT PATIENT-REPORTED COMPONENT OF ASTHMA REMISSION[1-7]

Asthma Control[15,16]*

- ACQ ≤1.5 or ACT ≥20

On-Treatment Clinical Remission[1-7]

For ≥12 Months

- ACQ ≤1.5 or ≤0.75; or ACT ≥20

ACQ Score Is Calculated as the Average of 5, 6, or 7 Items Over 1 Week[23,24]

ACQ-5	ACQ-6	ACQ-7
Night Awakenings	ACQ-5 criteria + reliever use	ACQ-5 criteria + reliever use + pre-BD FEV_1
Symptoms on Waking		
Activity Limitation		
Shortness of Breath		
Wheezing		

Minimal Clinically Important Difference = 0.5[25]

- **≤0.75** well-controlled asthma
- **0.75–1.5** partly controlled asthma
- **≥1.5** poorly controlled asthma

The ACT Is a Validated Composite of Five Domains Related to Asthma Control Assessed Over 4 Weeks[23,26]

ACT Score Criteria

- Impact on Daily Activities
- Shortness of Breath
- Nighttime Awakenings
- Rescue Treatment Frequency
- Asthma Control Rating

Minimal Clinically Important Difference = 3[27]

- **≥20** well-controlled asthma
- **16-19** partly controlled asthma
- **≤15** poorly controlled asthma

*Adapted from GINA and ERS/ATS.

ACQ, Asthma Control Questionnaire; ACT, Asthma Control Test; ATS, American Thoracic Society; BD, bronchodilator; ERS, European Respiratory Society; FEV_1, forced expiratory flow in 1 second; GINA, Global Initiative for Asthma.

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