

ASMA GRAVE

Manuela Latorre , Mariaelisabetta Conte

1) Disease trajectory as a New Clinical paradigm in severe asthma management

Could biomarkers support a more timely identification of Step 4 patients who may be candidates for earlier biologic therapy?

2) Should the corticosteroid burden inform clinical decision-making?

3) Inhaled Therapy Step-Down Strategies in Severe Asthma Controlled on Biologic Treatment

4) Key principles of patient education in severe asthma.

Disease trajectory as a New Clinical paradigm in severe asthma management

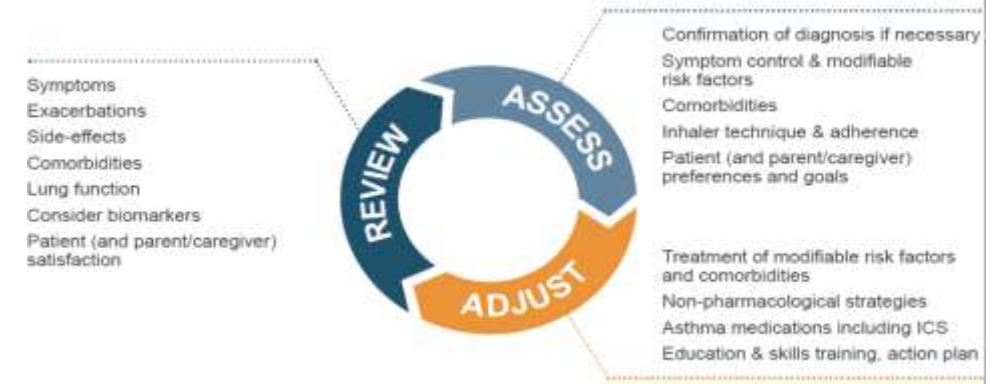
Symptom versus exacerbation control: an evolution in GINA guidelines?

Manuela Latorre, Riccardo Pistelli, Giovanna Elisiana Carpagnano, Alessandro Celi, Ilaria Puxeddu, Nicola Scichilone*, Antonio Spanevello, Giorgio Walter Canonica*^{1,2} and Pierluigi Paggiaro*^{1,2}

- Minimal (ideally no) chronic symptoms
- Minimal (infrequent) exacerbations
- No emergency visits
- Minimal (ideally no) need for «as needed» use of beta2-agonists
- No limitations on activities, including exercise
- PEF circadian variation of less than 20 percent

Figure 1. Control of asthma according to Global Initiative for Asthma (GINA) in documents between 2002 and 2005.

Adapted from Global Initiative for Asthma, www.ginasthma.org.



The goal of asthma management is to achieve the best possible long-term asthma outcomes for the patient:

- Long-term asthma symptom control, which may include:
 - Few/no asthma symptoms
 - No sleep disturbance due to asthma
 - Unimpaired physical activity
- Long-term asthma risk minimization, which may include:
 - No exacerbations
 - Improved or stable personal best lung function
 - No requirement for maintenance systemic corticosteroids
 - No medication side-effects.

Moving beyond event-driven decisions



Focusing on future risk and prevention of loss of control

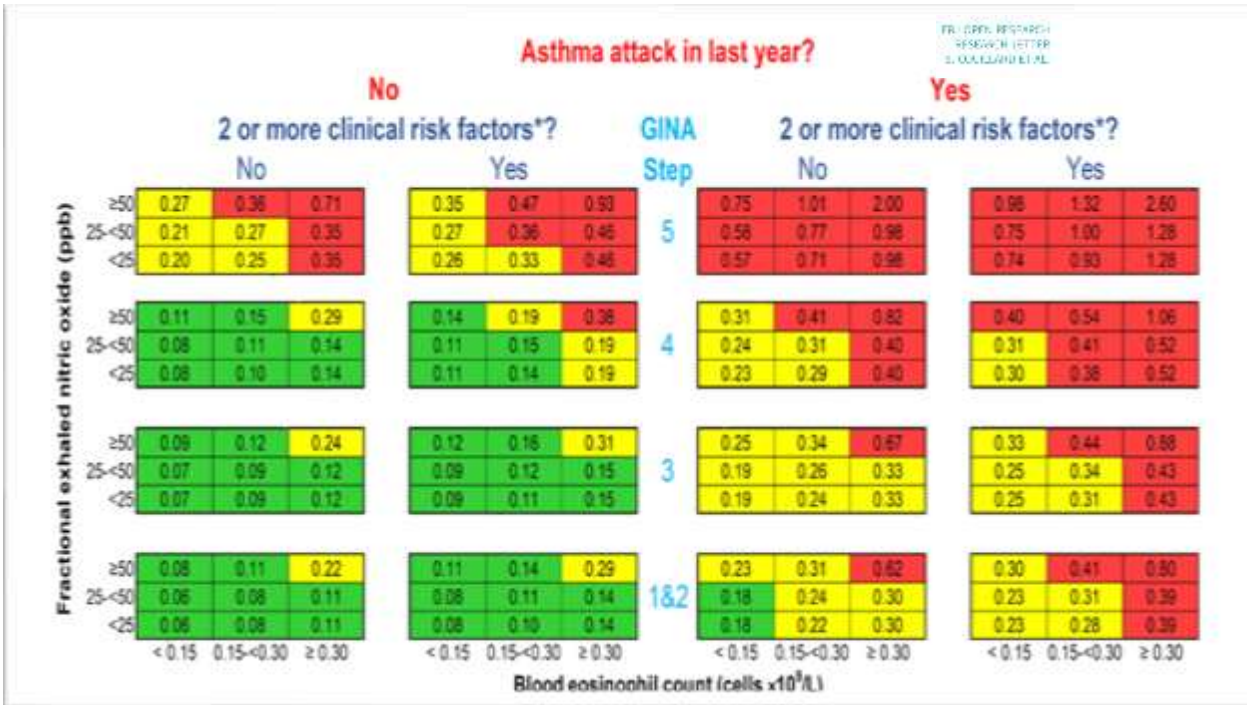
Biological risk' could offer a framework for selecting patients who may need intensified anti-inflammatory treatment

Evidence derives from the ORACLE 1 and ORACLE 2 models

Predicting the benefits of type-2 targeted anti-inflammatory treatment with the prototype Oxford Asthma Attack Risk Scale (ORACLE)



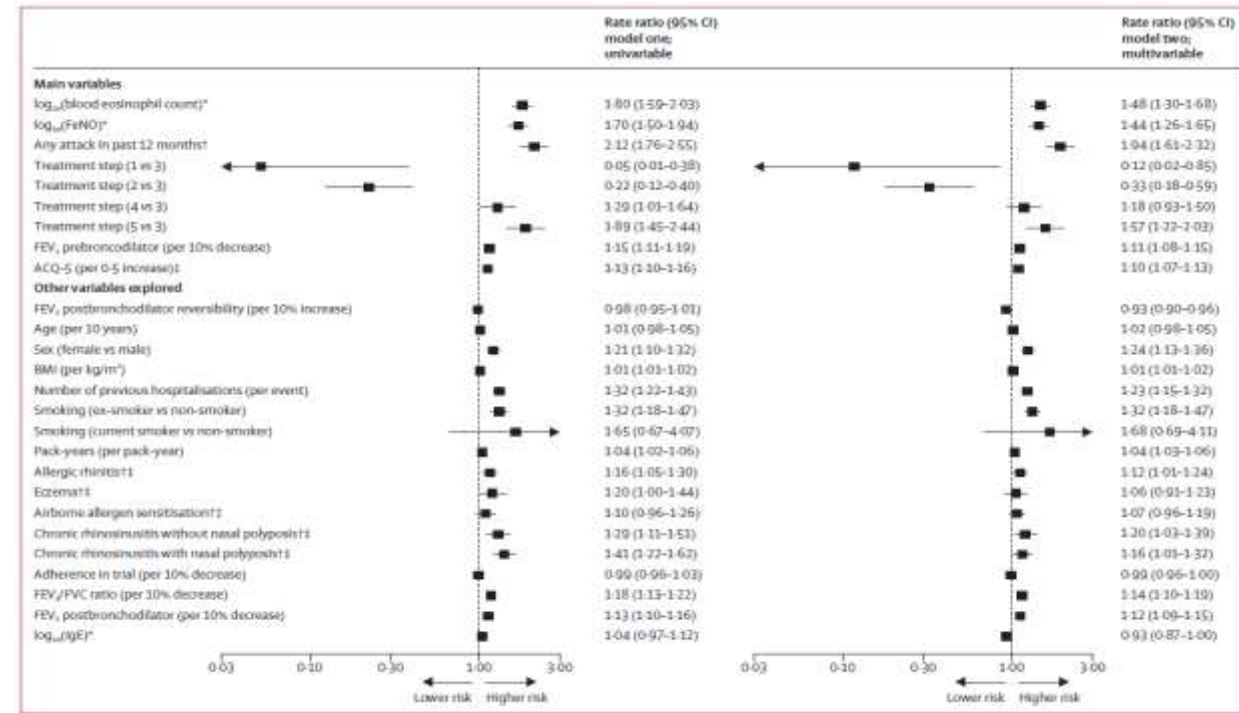
FRONTIERS IN ALLERGY AND ASTHMA RESEARCH LETTER S. GALLAND ET AL.



FeNO and Blood Eosinophils: The Map of Future Asthma Attack Risk
The ORACLE model demonstrates how Type-2 inflammatory activity—measured through FeNO and blood eosinophils—progressively increases the likelihood of severe asthma exacerbations.

Inflammatory and clinical risk factors for asthma attacks (ORACLE2): a patient-level meta-analysis of control groups of 22 randomised trials

Fleur L Meulmeester
 Lancet Respir Med. 2025
 Jun;13(6):505-516



The study shows that FeNO and eosinophils are independent and complementary predictors of exacerbation risk — even after adjustment for disease severity and clinical control

Assessing the Overall Corticosteroid Burden

Assessing cumulative corticosteroid exposure

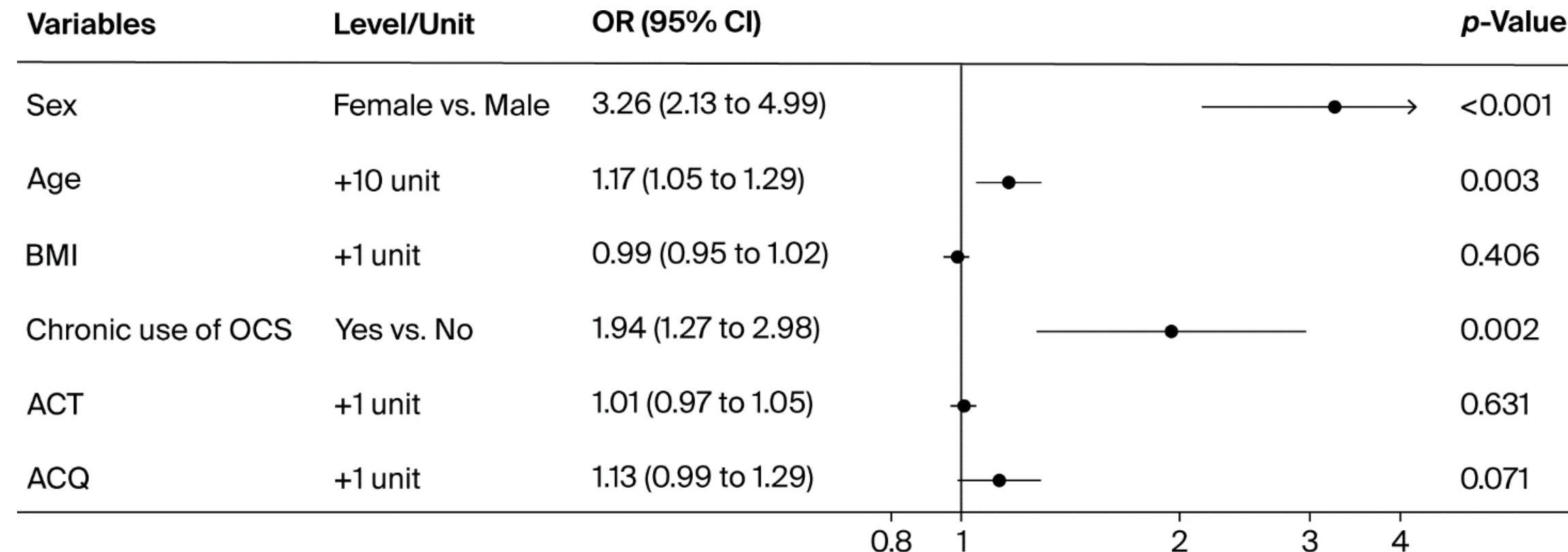
Evaluating the combined contribution of ICS and systemic corticosteroids (for asthma and comorbid conditions)

Considering the long-term risks of corticosteroid exposure, including osteoporosis, adrenal insufficiency, hypertension, weight gain, diabetes and increased cardiovascular risk.

Osteoporosis in severe asthmatic patients: data from the Severe Asthma Network in Italy (SANI) registry

Latorre M. ¹, Costanzo G. ², Ledda A.G. ², Sambugaro G. ², Cardini C. ³, Sala I. ^{4,5}, Oriecua C. ^{6,7}, Bagnardi V. ⁴, Blasi F. ^{8,9}, Paggiaro P. ¹⁰, Canonica G.W. ^{11,12}, Heffler E. ^{11,12}, Senna G. ¹³, Firinu D. ², Puxeddu I. ¹⁴, Pini L. ¹⁵, Del Giacco S. ² on behalf of the SANI study group *

Variables	Level/Unit	OR (95% CI)	<i>p</i> -Value
Sex	Female vs. Male	3.26 (2.13 to 4.99)	<0.001
Age	+10 unit	1.17 (1.05 to 1.29)	0.003
BMI	+1 unit	0.99 (0.95 to 1.02)	0.406
Chronic use of OCS	Yes vs. No	1.94 (1.27 to 2.98)	0.002
ACT	+1 unit	1.01 (0.97 to 1.05)	0.631
ACQ	+1 unit	1.13 (0.99 to 1.29)	0.071



Inhaled Therapy Step-Down Strategies in Severe Asthma Controlled on Biologic Treatment

In patients with severe asthma who achieve clinical remission on biologic therapy, a gradual and structured reduction of inhaled corticosteroids (ICS) can be considered, prioritizing safety and maintaining control.

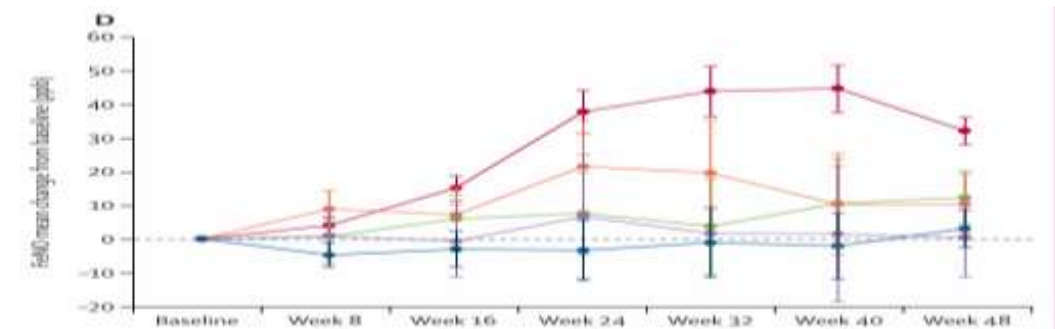
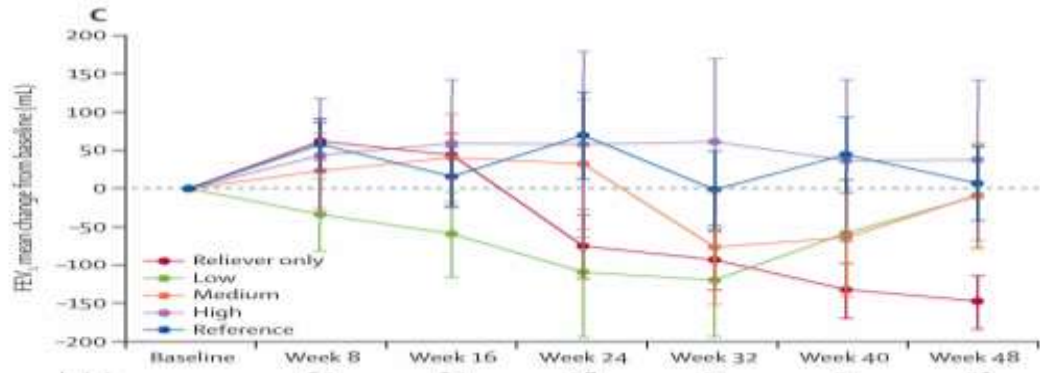
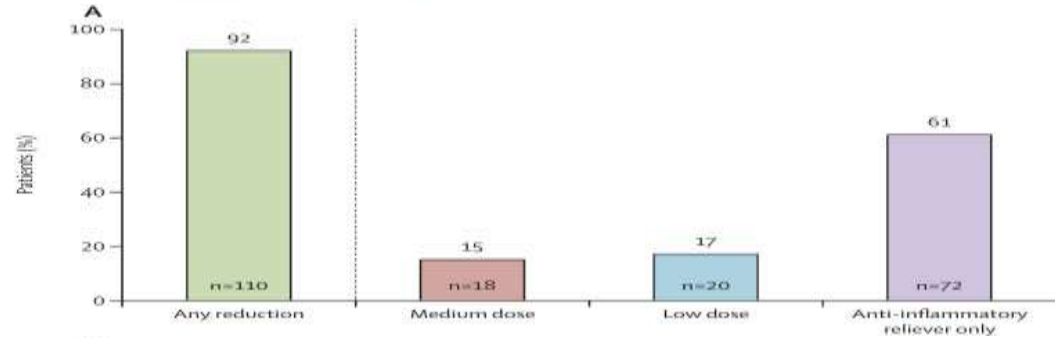
How to approach step-down:

Key Questions for Step-Down Strategy:

- 1) When should ICS step-down be initiated?
- 2) How should step-down be performed and which control parameters should be evaluated?
- 3) At what intervals should ICS dose reductions be made?
- 4) Which biomarkers should be assessed to support further reduction?
- 5) When should step-down be stopped, and what is the minimal effective ICS dose?
- 6) How should LAMA be managed during step-down? Reduce ICS to medium doses first, then withdraw LAMA?

Reduction of daily maintenance inhaled corticosteroids in patients with severe eosinophilic asthma treated with benralizumab (SHAMAL): a randomised, multicentre, open-label, phase 4 study

David J Jackson, Liam G Heaney, Marc Humbert, Brian D Kent, Anat Shavit, Lina Hiljemark, Lynda Olinger, David Cohen, Andrew Menzies-Gow, Stephanie Korn, on behalf of the SHAMAL Investigators*



ICS use trajectories in severe asthma patients on benralizumab: real-life data from 3-years follow-up

Laura Pini^{a,b}, Marco Caminati^{c,d,*}, Matteo Maule^{c,d}, Diego Bagnasco^e, Bianca Beghè^e, Benedetta Bondi^e, Fulvio Braido^e, Paolo Cameli^g, Cristiano Caruso^h, Claudia Crimiⁱ, Yehia El Masri^b, Jordan Giordani^b, Gabriella Guarnieri^j, Manuela Latorre^k, Andrea Mastrototaro^c, Francesco Menzella^l, Claudio Micheletto^m, Alessandro Piniⁿ, Stefano Piras^b, Antonio Spanevello^{o,p}, Andrea Vianello^j, Dina Visca^{o,p}, Martina Zappa^o, Marco Zurlo^{c,d}, Pierluigi Paggiaro^q, Francesco Blasi^{r,s}, Giorgio Walter Canonica^{t,u}, Gianenrico Senna^{f,g,1}, Roberto Benoni^{v,1}, On behalf of the SANI study group

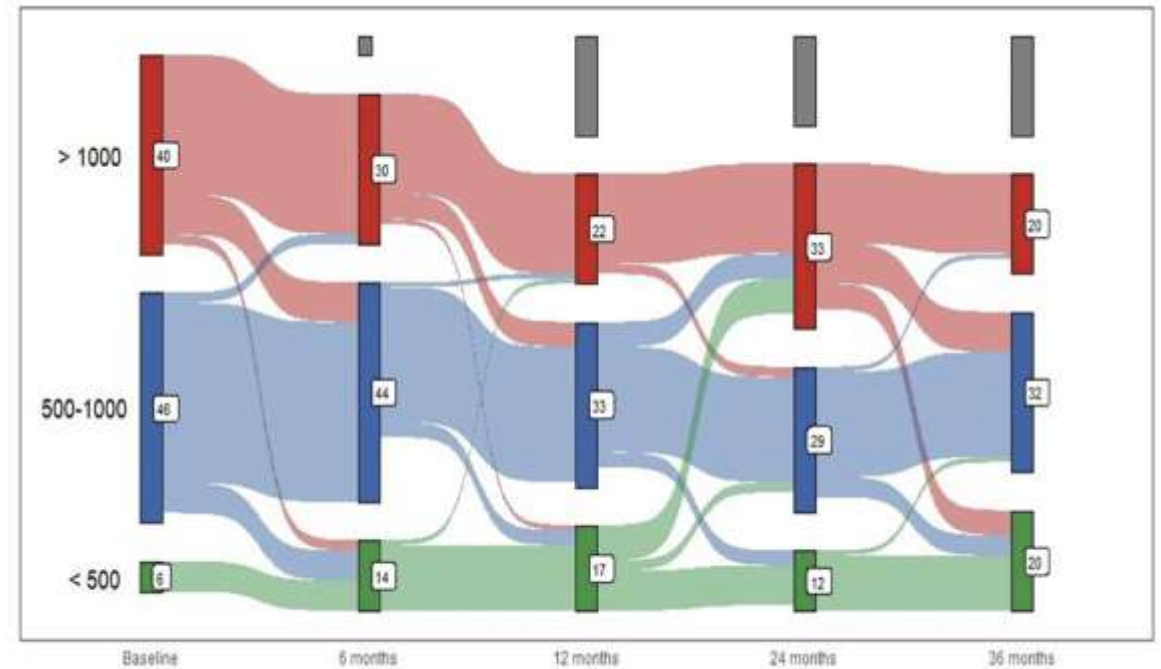
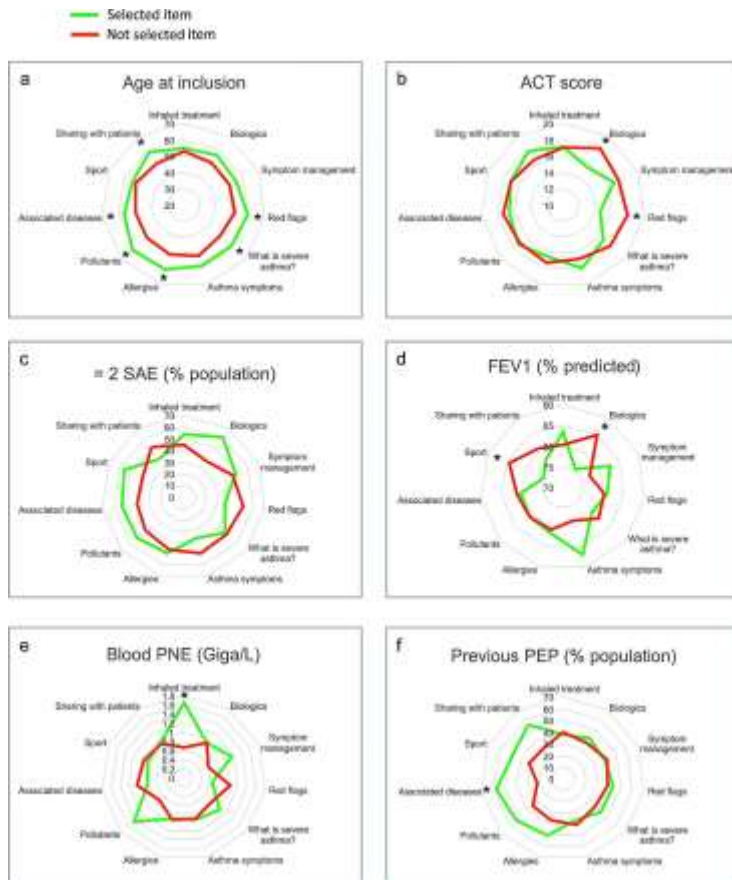


Fig. 1. - Sankey plot of the number of patients at each follow-up time point based on Inhaled corticosteroids dosage. Grey bars represent the missing values.

Key principles of patient education in severe asthma.

Patient education needs in severe asthma, a pilot study

Rodolphe Laurence¹, Julien Ancel¹, Maëva A. Devilliers², Sophie Carre^{1,3}, Sandra Dury¹, Valérian Dormoy², Gaëtan Deslée^{1,2} and Jeanne-Marie Perotin^{1,2,4*}



Main educational topics:

- 1. Security needs** (treatment use, inhaled and corticosteroid treatment, biologics, symptom and exacerbation management, asthma control, red flags)
- 2. Pathology's knowledge** (what is severe asthma?, asthma symptoms)
- 3. Living with asthma** (comorbidities, sports, nutrition/diet, pollutants, allergies, emotion, social rights, family)
- 4. Sharing with fellow patients** (group therapy, partner patient)

Different educational needs are expressed by three main phenotypes of severe asthma:

- 1. Uncontrolled asthma and/or reduced FEV1**
- 2. Higher blood eosinophils**
- 3. Older age**

Age at diagnosis, time from severe asthma diagnosis, BMI, occupation category seem not to be associated with clinically relevant selected topics.

Positive change in asthma control using therapeutic patient education in severe uncontrolled asthma: a one-year prospective study

Xiaoxian Zhang^{1†}, Zhengdao Lai^{2†}, Rihuang Qiu³, E Guo⁴, Jing Li¹, Qingling Zhang¹ and Najjian Li^{1*}

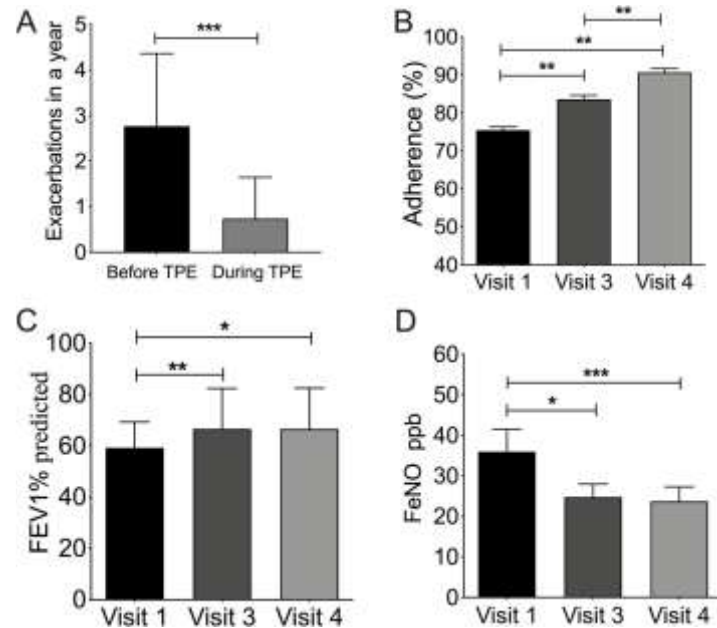


Fig. 1 Changes in participant total exacerbations, spirometry, and fractional exhaled nitric oxide (FeNO) over the course of the study. **A** Asthma exacerbations decreased significantly after therapeutic patient education (TPE). **B–D** Measurements were conducted on day 1 (visit 1) and after 6 months (visit 3) and 12 months (visit 4). Predicted forced expiratory volume in 1 s (FEV₁) increased significantly and FeNO decreased over time. Medication adherence was calculated as the percentage of prescribed doses taken each week. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Therapeutic patient educational intervention may address:

1. Asthma pathophysiology
2. Illness perceptions
3. Medication skills
4. Self-monitoring techniques
5. Environmental control
6. Avoidance strategies

Therapeutic patient education can be an effective and collaborative tool to improve asthma control and decrease exacerbations in patients with severe uncontrolled asthma

Educational objectives for patients with severe asthma

«Severe asthma can be unpredictable, and everyone's symptoms are different. This can make it difficult to explain to people around you»

- Educate patients, family members, and, in some cases, employers and co-workers about the disease, symptoms, and treatments (including side effects).
- Direct patients to patient associations to share experiences and guide them to severe asthma centers.
- Provide emotional support and help them to manage physical challenges.
- Spread awareness of severe asthma to treat people at the earliest opportunity for the greatest benefit and get them back to living the life they want to live.

Key Topics to Explore for the GINA 2026 Update

1. Disease trajectory as a New Clinical paradigm in severe asthma management

Severe asthma management is shifting from an event-driven approach toward a model centered on **future risk prediction and prevention of loss of control**.

Biomarkers such as **FeNO and blood eosinophils** provide meaningful insight into a patient's *biological risk*, potentially helping to identify which **Step 4 patients** may benefit from earlier initiation of biologic therapy.

2. Corticosteroid burden matters

Clinical decision-making should account for the patient's **cumulative corticosteroid exposure**, including ICS and systemic corticosteroids, while considering potential complications such as **osteoporosis, adrenal insufficiency, hypertension, weight gain, diabetes and increased cardiovascular risk**.

3. Step-down of inhaled therapy in patients controlled on biologics

For patients with severe asthma who achieve stable control on biologic therapy, a **gradual and structured ICS step-down** can be considered although **the optimal approach and criteria for step-down remain to be fully defined**.

4. Key principles of patient education in severe asthma

Patient education can be effective to improve asthma control and decrease exacerbations in patients with severe uncontrolled asthma. It is essential to define **standard educational programs and procedures** that address not only **therapeutic targets** but also **individual expectations and specific personal needs and satisfactions**.