

9
NOVEMBRE
10



OTTICA RESPIRO

IL PAZIENTE AL CENTRO

VERONA **2018**
HOTEL LEON D'ORO

Nuovi approcci terapeutici nell'asma

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REGIONE DEL VENETO



ULSS9
SCALIGERA

Obiettivi a lungo termine della gestione dell'asma bronchiale

- Raggiungere un buon controllo dei sintomi e mantenere normali livelli di attività
- Minimizzare il rischio di esacerbazioni, limitazione fissa delle vie aeree ed effetti collaterali



The paradoxes of asthma management: time for a new approach?

Paul M. O'Byrne¹, Christine Jenkins² and Eric D. Bateman³

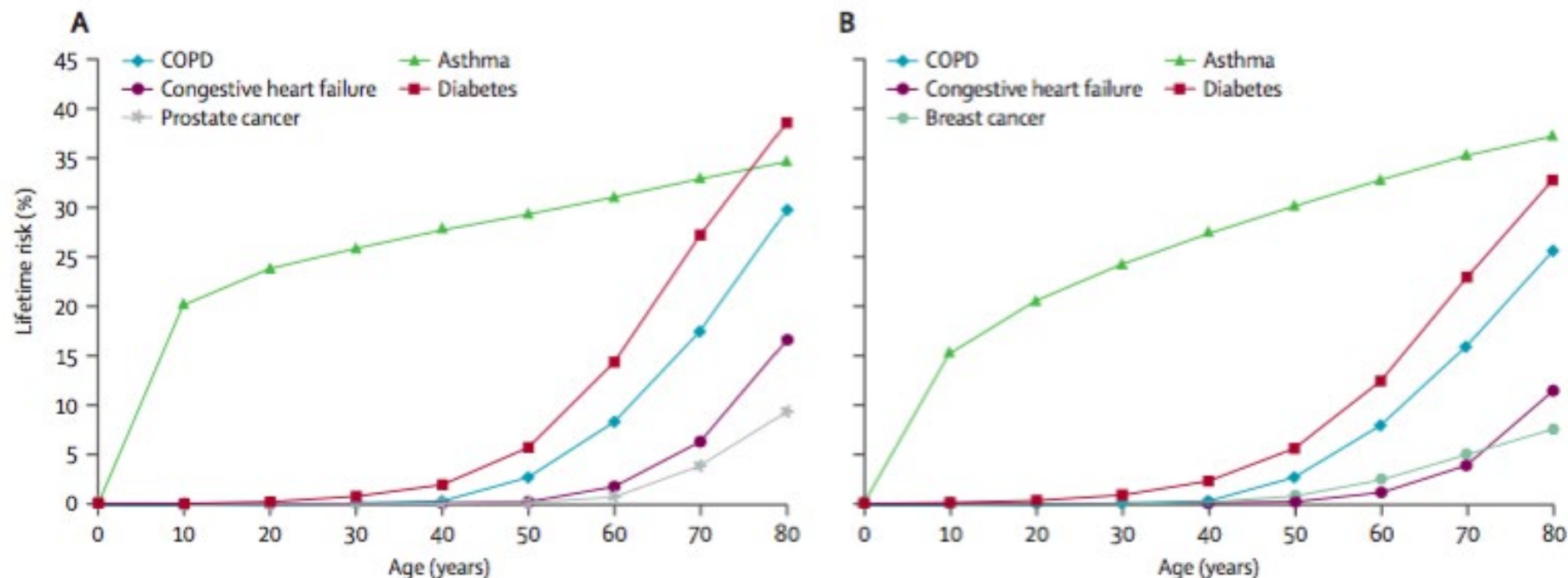


paradox ('parədɒks) - a statement or proposition which, despite sound (or apparently sound) reasoning from acceptable premises, leads to a conclusion that seems logically unacceptable or self-contradictory (Oxford Dictionary)

1) Inadeguato controllo

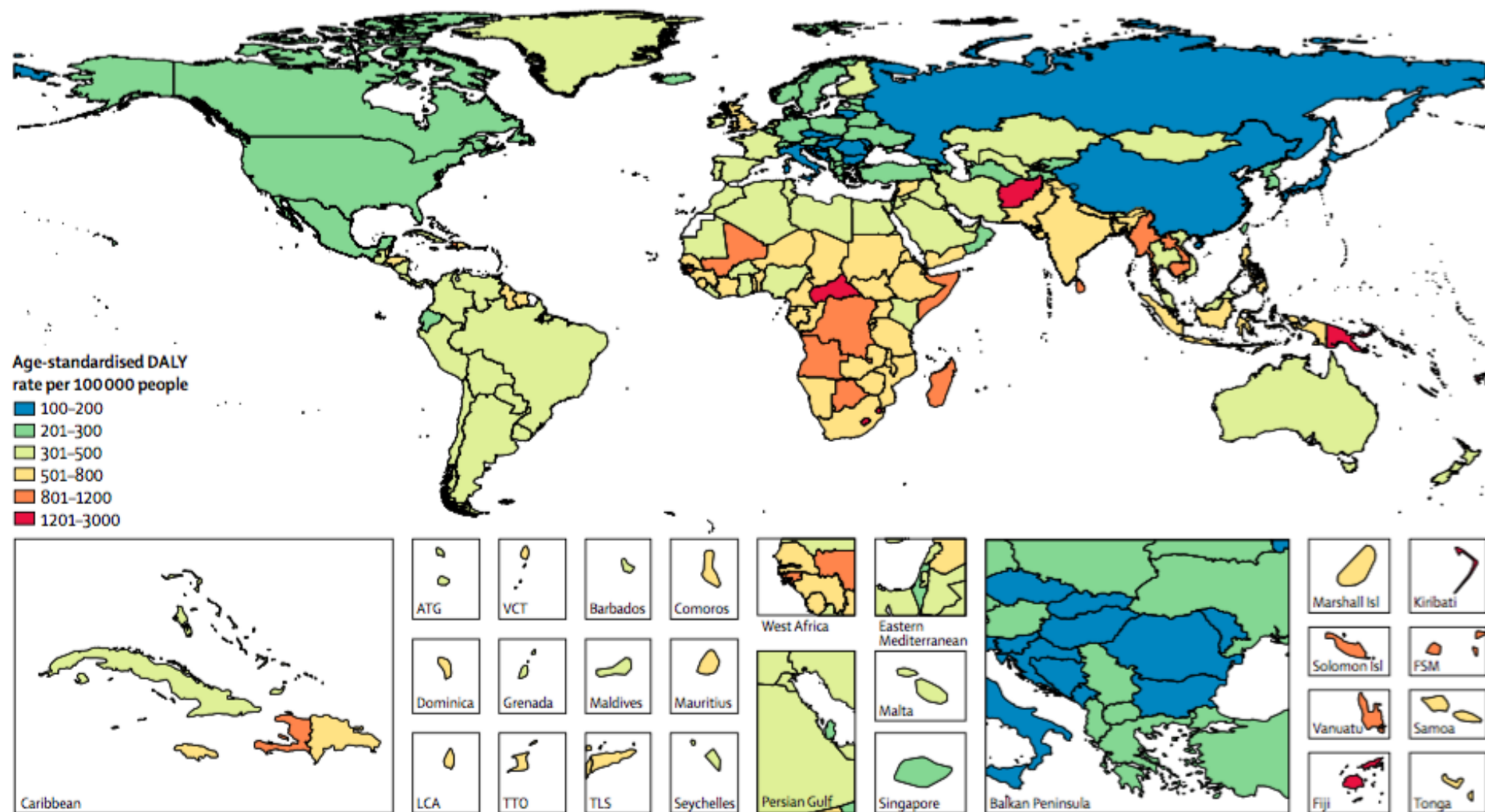
Asthma is one of the most common chronic diseases in the world, with a prevalence that is still growing in some developing countries. In recent decades, asthma mortality rates have fallen dramatically. However, despite this progress, national and international surveys continue to reveal inadequate asthma control in more than 50% of patients.

Lifetime risk of developing chronic obstructive pulmonary disease: a longitudinal population study



Lifetime risk of COPD, asthma, congestive heart failure, diabetes, prostate cancer, and breast cancer in men (A) and women (B)

Age-standardised DALY (disability-adjusted life years) rate per 100.000 people due to asthma

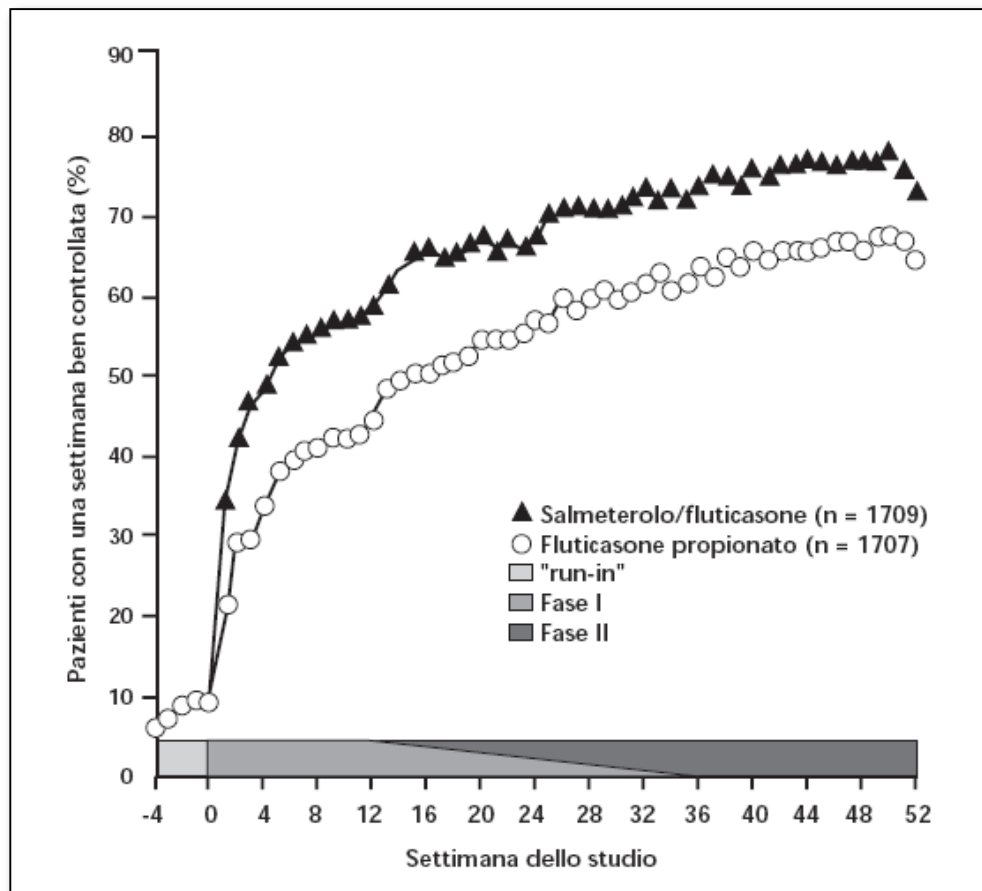


Can Guideline-defined Asthma Control Be Achieved?

The Gaining Optimal Asthma Control Study

Eric D. Bateman, Homer A. Boushey, Jean Bousquet, William W. Busse, Tim J. H. Clark, Romain A. Pauwels, and Søren E. Pedersen for the GOAL Investigators Group

La combinazione
SFC ha dimostrato
di permettere un
**buon controllo
dell'asma - come
definito nelle Linee
Guida – nel 77% dei
pazienti**

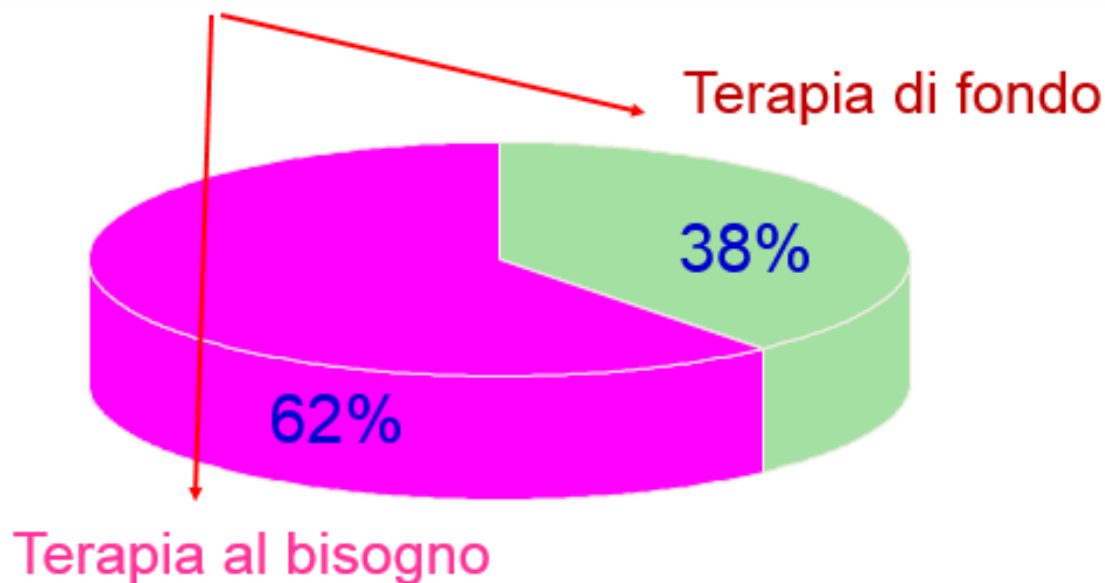


Asma non controllata nella vita reale

Pazienti asmatici in terapia nei 12 mesi precedenti

90,2 % in terapia

9,8 nessuna terapia

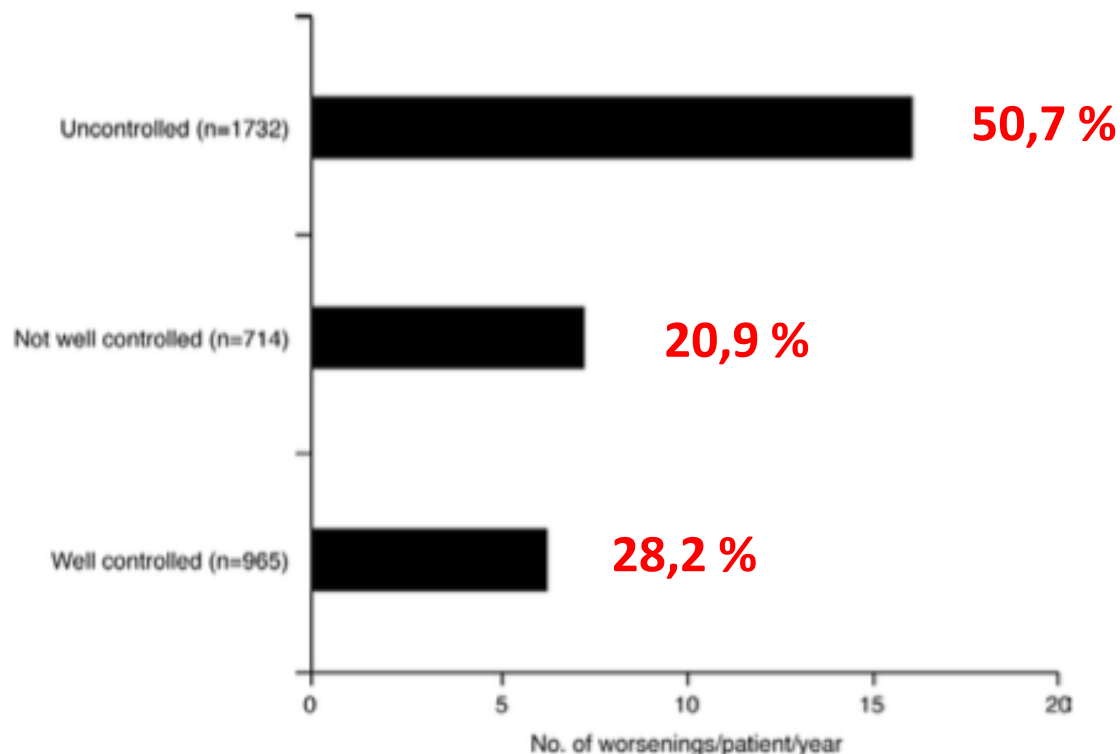


The control of asthma in Italy

Italian Study on Asthma in Young Adults - ISAYA

- Only 14% without AE o SFD in the last 12 months
- 20% had daily life activities impaired
- 8% had at least one hospital/emergency admission
- Only 10% had the disease under control
- They had a significantly higher percentage of drug use

Paradosso dell'asma bronchiale: percentuali ancora basse di pazienti controllati

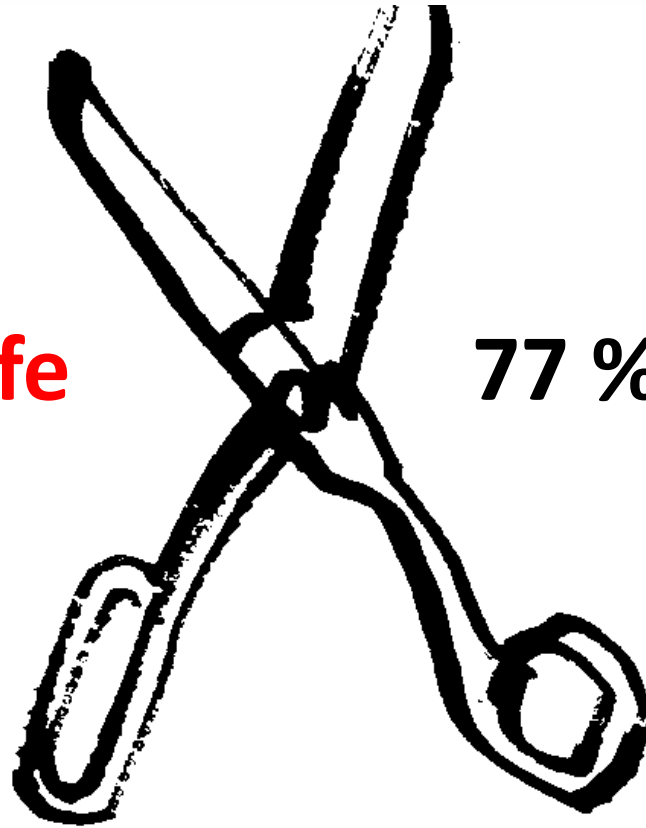


This study examined the attitudes and actions of 3415 physician-recruited adults aged ≥ 16 years with asthma in 11 countries who were prescribed regular maintenance therapy.

Paradosso dell'asma bronchiale: % pazienti controllati

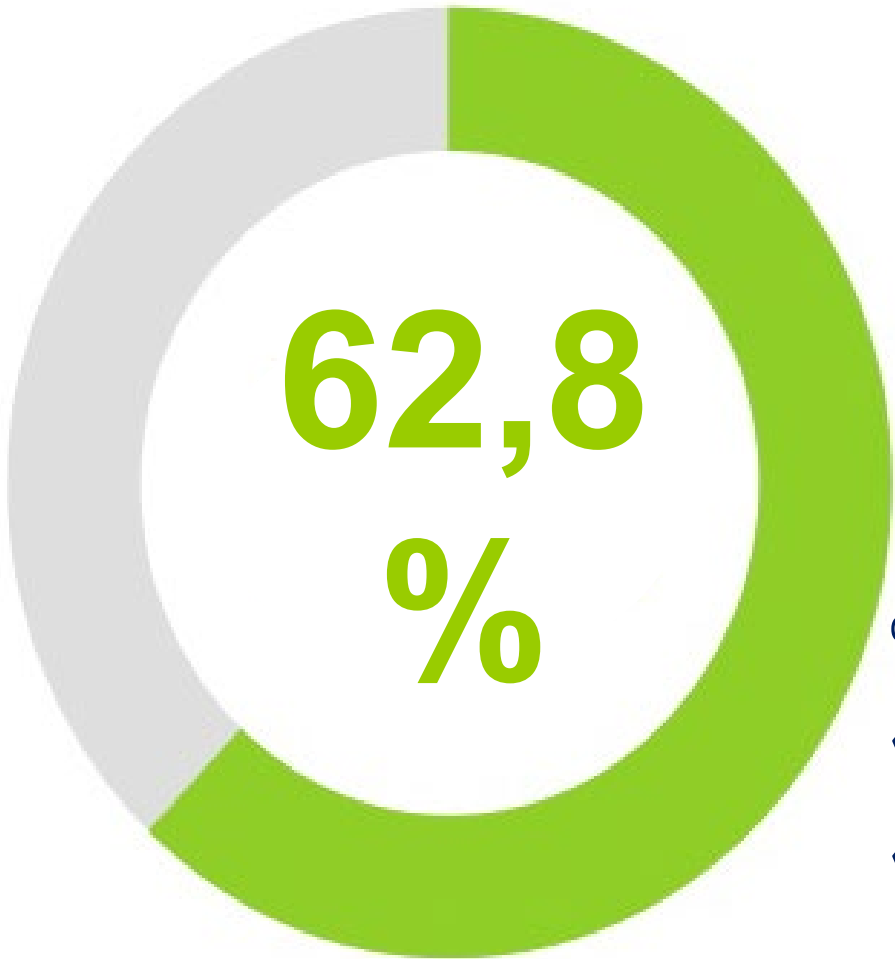
10-42 % real life

77 % studio clinico



2) Scarsa aderenza

As with all chronic diseases, poor adherence to regular maintenance medication is a reality in asthma. The most commonly observed pattern is the use of medication only when symptoms occur, and avoidance of treatment when it is perceived to be unnecessary.



62,8
%

real life

DELLA TERAPIA IN ASMA

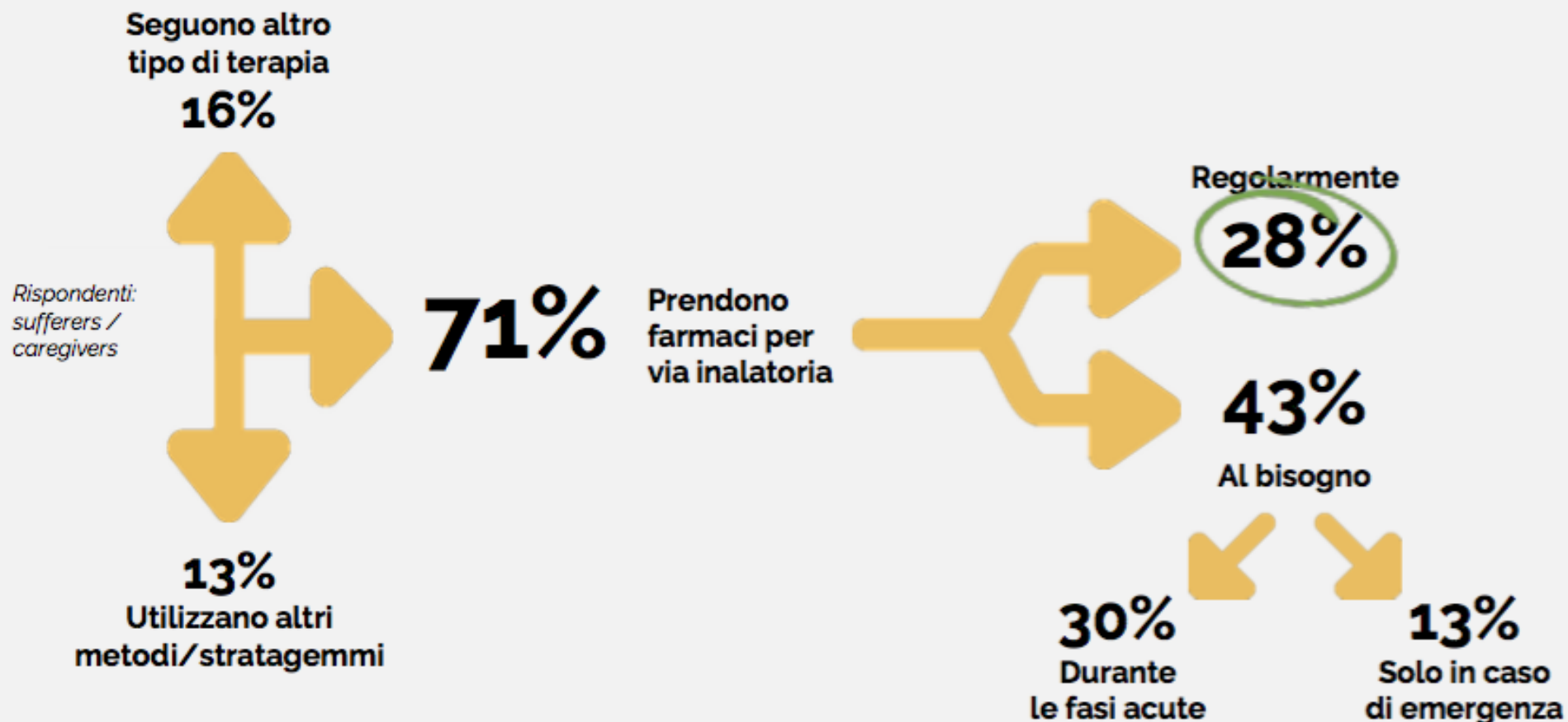
dei pazienti fa una terapia «**occasionale**»:
«*non regolare*», «*ciclica*»,
«*intermittente*»,
«*irregolare*», «*saltuaria*»

La maggior parte dei pazienti ha affrontato una crisi acuta, dovendo spesso ricorrere alla medicina d'urgenza



Rispondenti: sufferers / caregivers

I pazienti che seguono la terapia inalatoria in modo continuativo sono una minoranza



A prescindere dalla frequenza d'uso, l'inalatore ha un funzione rassicurante



**Solo una ristretta minoranza di pazienti
ammette di provare imbarazzo ad utilizzare
il device in pubblico, davanti ad altre persone**

Portano sempre con se'
l'erogatore
68%



Rispondenti: sufferers / caregivers

TABLE 1 Paradoxes in current asthma management

Paradox	Description
---------	-------------

- | | |
|---|---|
| 1 | In step 1 treatment, a SABA bronchodilator alone is recommended despite the fact that asthma is a disease of chronic airway inflammation with increased inflammation at the times of exacerbations. |
|---|---|

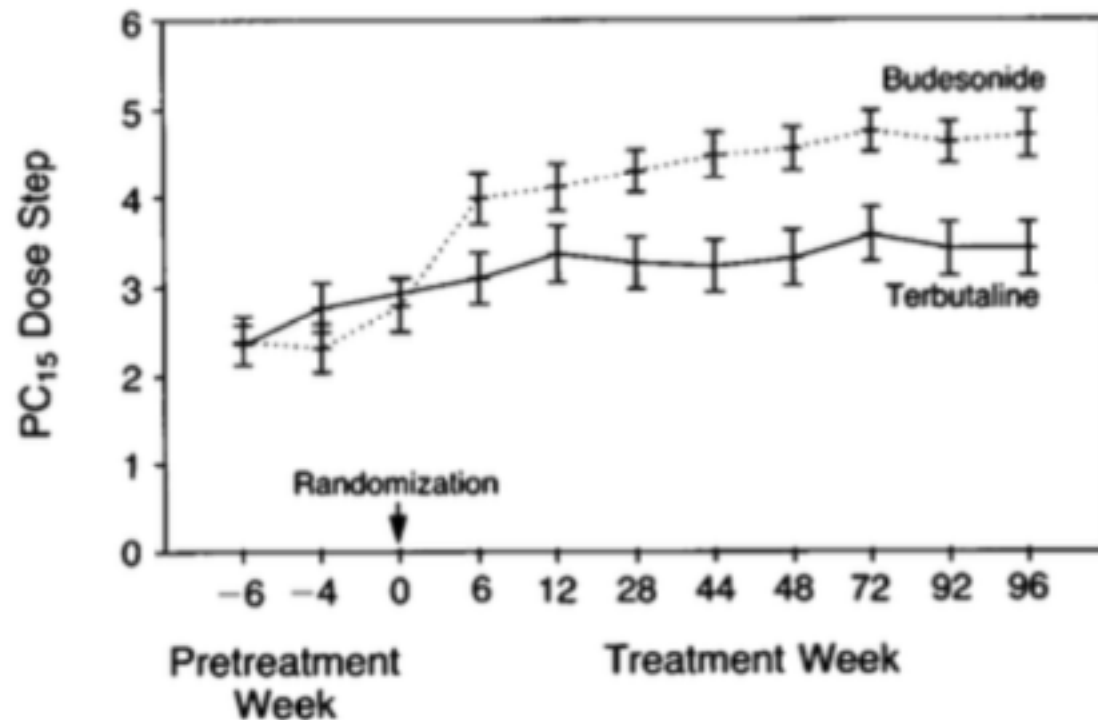
**L'asma è una malattia eterogenea,
di solito caratterizzata da infiammazione
cronica delle vie aeree.**

**È definita da una storia di sintomi respiratori,
quali respiro affannoso, dispnea, oppressione
toracica e tosse, che variano nel tempo
e d'intensità, associandosi ad una limitazione
variabile del flusso d'aria espiratorio¹**

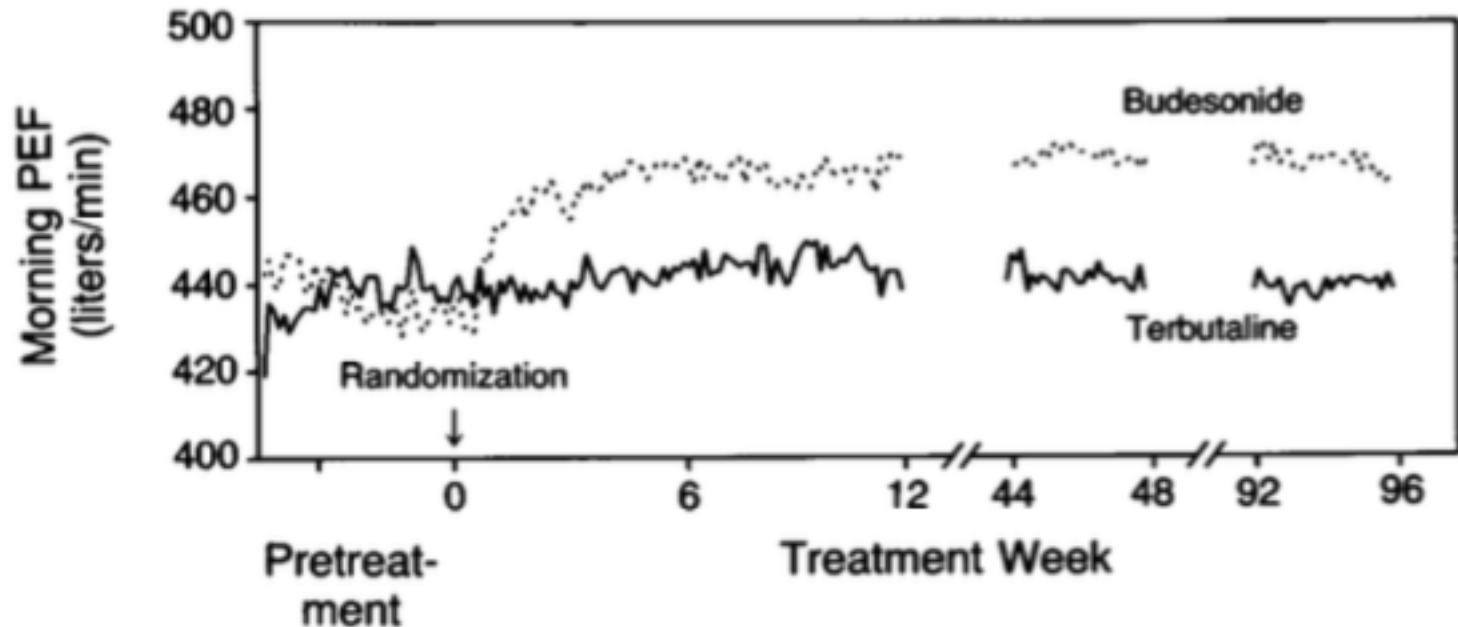


¹ GINA 2017

Comparison of a β_2 -agonist, terbutaline, with an inhaled corticosteroid, budesonide, in newly detected asthma



Comparison of a β_2 -agonist, terbutaline, with an inhaled corticosteroid, budesonide, in newly detected asthma



Budesonide was more effective in reducing:

- the symptoms of asthma
- the use of supplemental β_2 -agonist medication

Effects of Inhaled Beclomethasone Dipropionate in Clinical Asthma

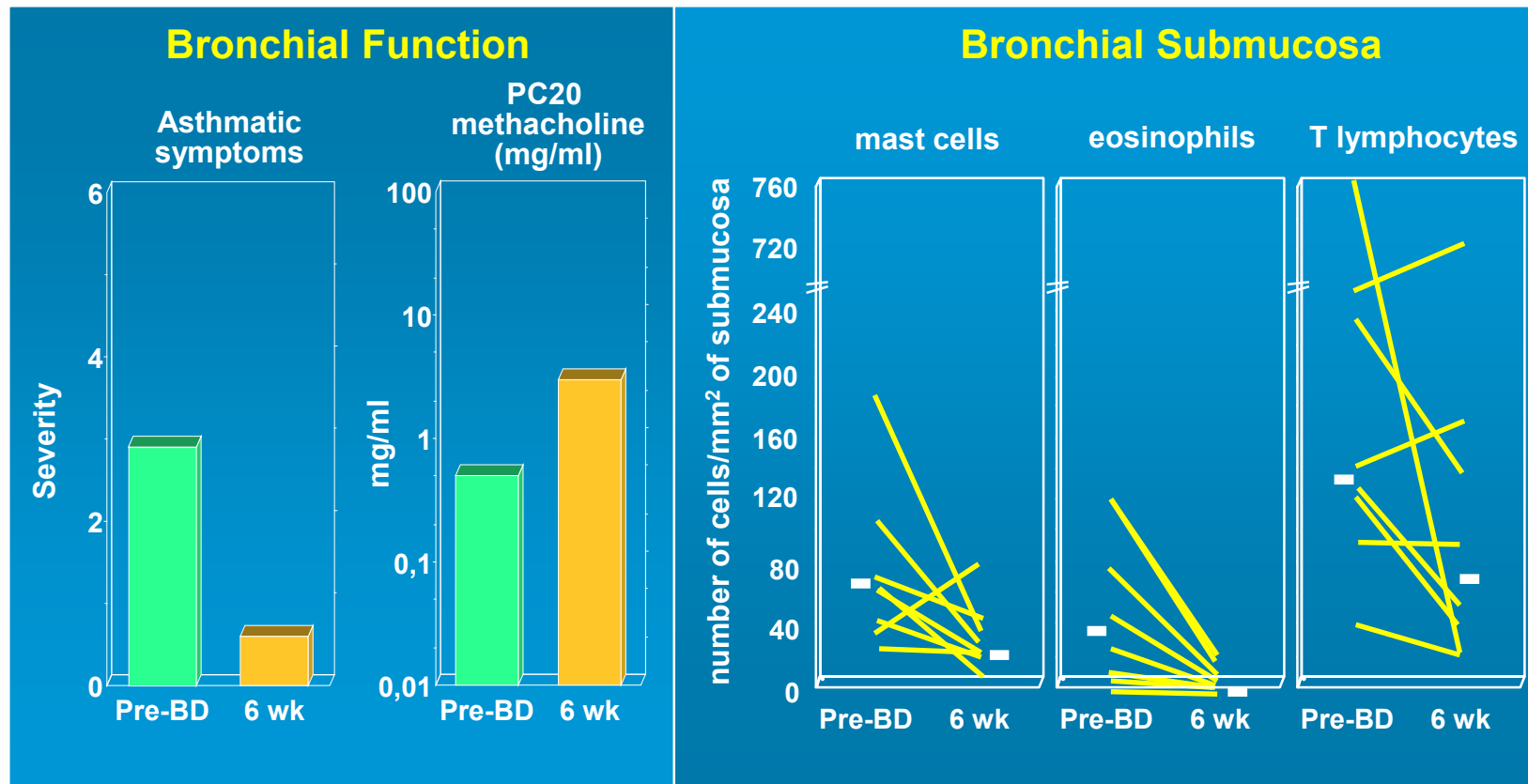


TABLE 1 Paradoxes in current asthma management

Paradox	Description
1	In step 1 treatment, a SABA bronchodilator alone is recommended despite the fact that asthma is a disease of chronic airway inflammation with increased inflammation at the times of exacerbations.
2	In step 1 treatment, the patient has autonomy and their perception of treatment as needed to control symptoms is accepted, whereas at higher asthma treatment steps it is assumed that patients will adopt a fixed-dose approach.
3	There is a switch in recommendation from using a SABA alone as-needed at step 1 to advising an ICS fixed-dose regimen at step 2 and minimising SABA use. The medication that treats the underlying disease, which patients are encouraged to take (the ICS) is not the one that the patient perceives is benefitting them (the SABA), which they are now discouraged from taking.
4	There is a different safety message in the advice given for the use of SABA and LABA within the guidelines; SABA alone being safe and LABA alone being unsafe.

Relationship between adherence to ICS and poor outcomes among adults with asthma

Overall adherence to ICS was approximately **50%**. Adherence to ICS was significantly and negatively correlated with the number of emergency department visits (correlation coefficient $[R] = 20.159$), the number of fills of an oral steroid ($R = 20.179$), and the total days' supply of oral steroid ($R = 20.154$).

Each **25% increase** in the proportion of time without ICS medication resulted in a doubling of the rate of asthma-related hospitalization (relative rate, 2.01; 95% CI, 1.06-3.79).

The salmeterol multicenter asthma research trial

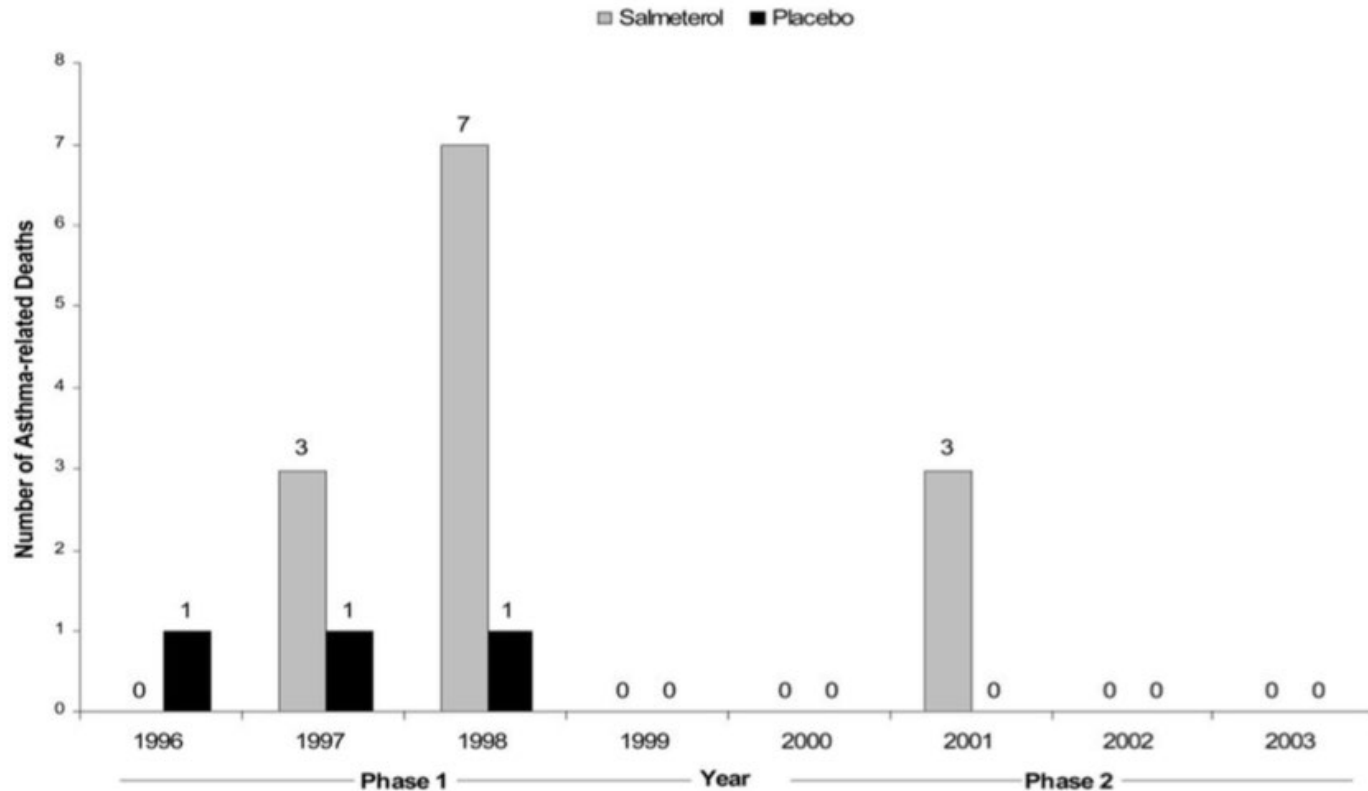


FIGURE 2. Occurrence of asthma-related deaths by phase and study year.

The use of beta₂-agonists and the risk of death and near death from asthma

Table 4. Adjusted Matched Odds Ratios for Inhaled Fenoterol or Inhaled Albuterol in the Subjects with Fatal or Near-Fatal Asthma during the 12 Months before the Index Date, According to an Ordinal Classification of Exposure.*

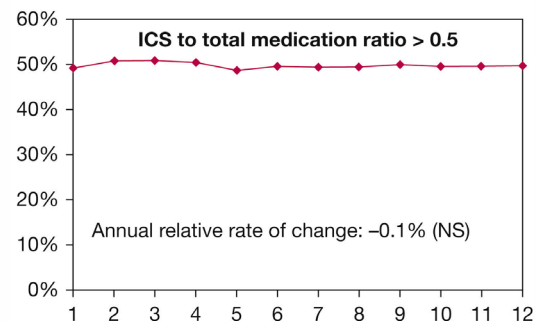
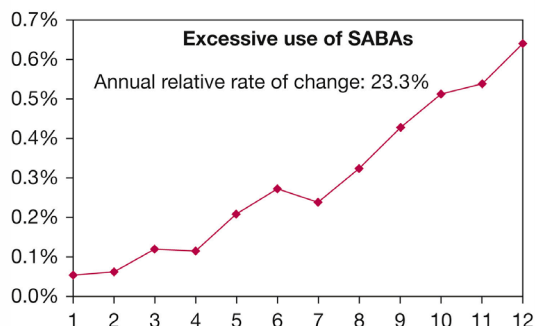
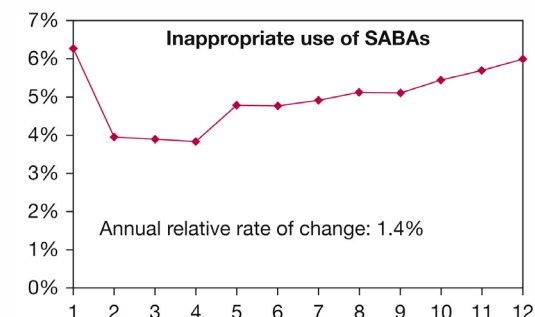
NO. OF INHALERS DISPENSED	EITHER OUTCOME		DEATHS ONLY	
	ODDS RATIO (95% CI)		ODDS RATIO (95% CI)	
Fenoterol				
0	1.0	—	1.0	—
1–12	4.1	(1.7–10.1)	4.7	(1.1–20.6)
13–24	19.8	(5.7–68.6)	40.5	(5.1–319)
≥25	21.5	(7.3–63.7)	113.2	(17.0–754)
Albuterol				
0	1.0	—	1.0	—
1–12	4.4	(2.0–9.8)	3.4	(0.9–13.3)
13–24	8.0	(3.2–19.8)	10.0	(2.1–46.5)
≥25	24.0	(9.0–64.1)	29.4	(5.1–171)
Fenoterol, adjusted for dose equivalence†				
0	1.0	—	1.0	—
1–6	3.2	(1.2–8.8)	3.1	(0.5–20.4)
7–12	7.8	(2.0–30.7)	9.0	(1.1–73.1)
≥13	22.7	(8.1–63.3)	90.0	(15.2–533)

Conclusions. An increased risk of death or near death from asthma was associated with the regular use of inhaled β_2 -agonist bronchodilators, especially fenoterol. Regardless of whether β -agonists are directly responsible for these adverse effects or are simply a marker for more severe asthma, heavy use of these agents should alert clinicians that it is necessary to reevaluate the patient's condition. (N Engl J Med 1992;326: 501-6.)

Has Asthma Medication Use Caught Up With the Evidence?

A 12-Year Population-Based Study of Trends

In 12 anni di osservazione l'aderenza nei confronti degli ICS non migliora, sale invece l'uso inappropriato e l'uso eccessivo di sabutamolo, che espone i Pazienti a severi rischi.



Crisi d'asma, muore a 12 anni

Tragedia nell'abitazione di un camionista a Tombolo ■ BERGAMIN E FAIS A PAGINA 25

TOMBOLO » MALATTIA KILLER

Stroncato a 12 anni da un attacco d'asma

Tombolo sotto choc per la morte di Filippo Bacchin, che ha donato le cornee. Oggi alle 15 l'ultimo saluto al «piccolo angelo»



Modena

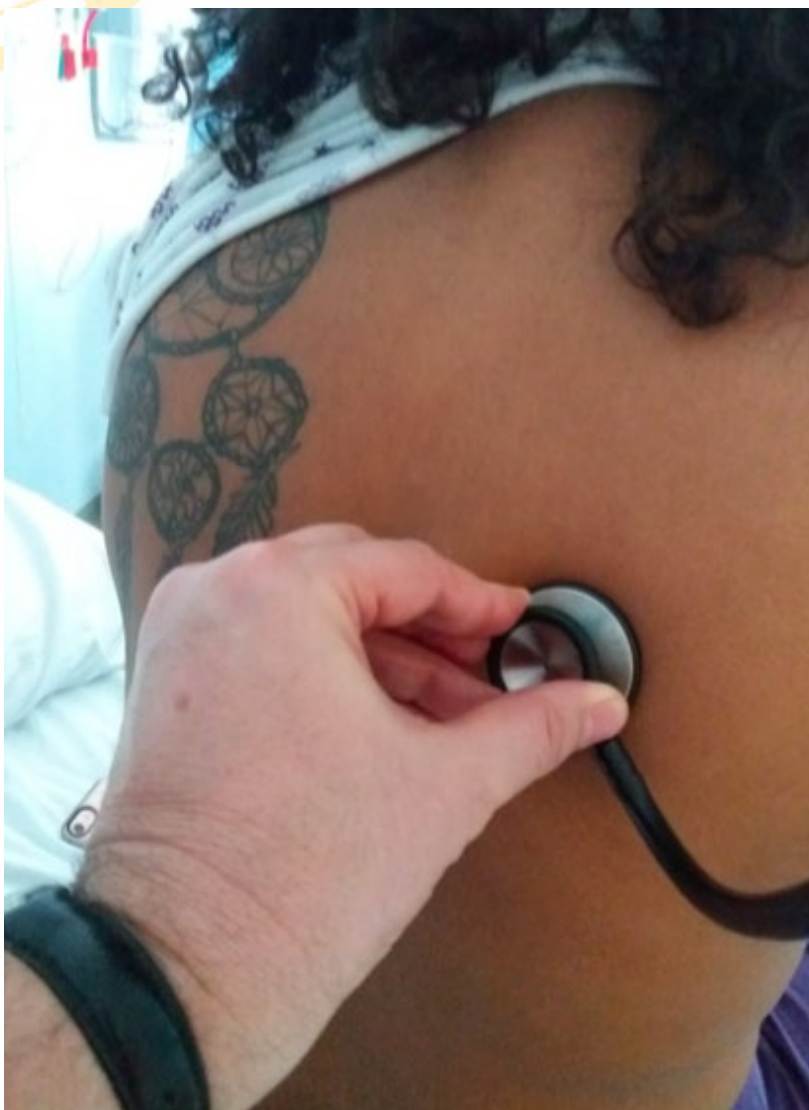
Attacco d'asma fatale, mamma muore a 49 anni

Addio a Margherita Cuoghi, tre figli, stroncata da una crisi: donati gli organi La madre Lucietta Righetti: «Era molto amata, commovente l'affetto che lascia»

Solo il tempo di affrettarsi a fare le scale di quattro piani, per recuperare il famoso, ma non sempre provvidenziale, Ventolin, per poi accasciarsi senza più forze e perdere conoscenza.

Coraggioso l'intervento di una quattordicenne che ha permesso, col massaggio cardiaco, di rimettere in moto il cuore della madre.

L'arrivo dell'ambulanza e la veloce corsa in ospedale, ma per Margherita Cuoghi non c'è stato più nulla da fare.



Sara, 19 anni

- asma atopico dall'infanzia
- Fuma 10 sigarette al giorno
- Incremento di 10 kg in 2 anni

Negli ultimi sei mesi:

- Sei confezioni di Ventolin prescritto dal MMG
- Quattro confezioni acquistate in farmacia senza prescrizione

Accesso al PS

Risultati

			Crit. Basso	Riferimento Basso Alto	Crit. Alto
Misurati (37.0°C)					
pH	7.42		[--	7.35 7.45	--]
pCO ₂	↓ 34	mmHg	[--	35 45	--]
pO ₂	↓ 59	mmHg	[--	80 100	--]
Na ⁺	136	mEq/L	[--	136 145	--]
Cl ⁻	105	mEq/L	[--	98 109	--]
Ca ⁺⁺	4.71	mg/dL	[--	4.50 5.30	--]
Hct	40	%	[--	36 49	--]
CO-Ossimetro					
tHb	12.7	g/dL	[--	12.3 17.5	--]
O ₂ Hb	92.2	%	[--	-- --	--]
COHb	2.0	%	[--	-- 3.0	--]
MethHb	1.3	%	[--	0.0 1.5	--]
HHb	4.6	%	[--	-- --	--]
sO ₂	95.2	%	[--	75.0 99.0	--]
Derivati					
BE(B)	-1.8	mmol/L	[--	-- --	--]
P/F Ratio	incalc	mmHg	[--	-- --	--]
O ₂ ct	16.5	mL/dL	[--	-- --	--]
HCO ₃ ⁻ (c)	22.1	mEq/L	[--	-- --	--]

*Con
somministrazione
di O₂ a 6 litri/min*

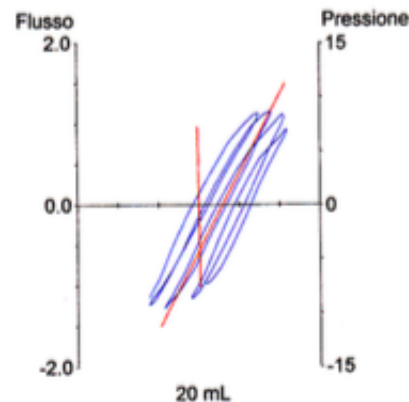
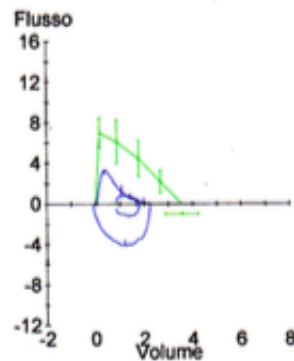


PLETISMOGRAFIA

VERONA
9-10 NOVEMBRE

		Ref	CI	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg
FVC	Litri	3.59	0.71	2.27	63			
FEV1	Litri	3.14	0.62	1.48	47			
FEV1/FVC	%	84	11	65				
FEF25-75%	L/sec	4.09	1.39	0.84	21			
FEF25%	L/sec	6.15	2.21	3.30	54			
FEF50%	L/sec	4.48	1.80	1.25	28			
FEF75%	L/sec	2.17	1.13	0.33	15			
PEF	L/sec	7.00	1.48	3.34	48			
FEV1/SVC	%	85	11	63				
FEF/FIF50				0.31				
MVV	L/min							
PEFT	Sec			0.15				
Vol Extrap	Litri			0.11				
FET100%	Sec			7.67				
VC	Litri	3.63	0.69	2.37	65			
ERV	Litri			0.48				
RV	Litri	1.31	0.57					
FRC PL	Litri	2.64	0.82					
TLC	Litri	4.84	0.98					
RV/TLC	%	27	10					
IC	Litri			1.85				
Vtg	Litri			0.65				
Raw	cmH2O/L/sec	1.64		30.62	1872			
Gaw	L/sec/cmH2O			0.033				

Dopo quattro giorni di
terapia steroidea ev,
antibiotico e
broncodilatatori
inalatori



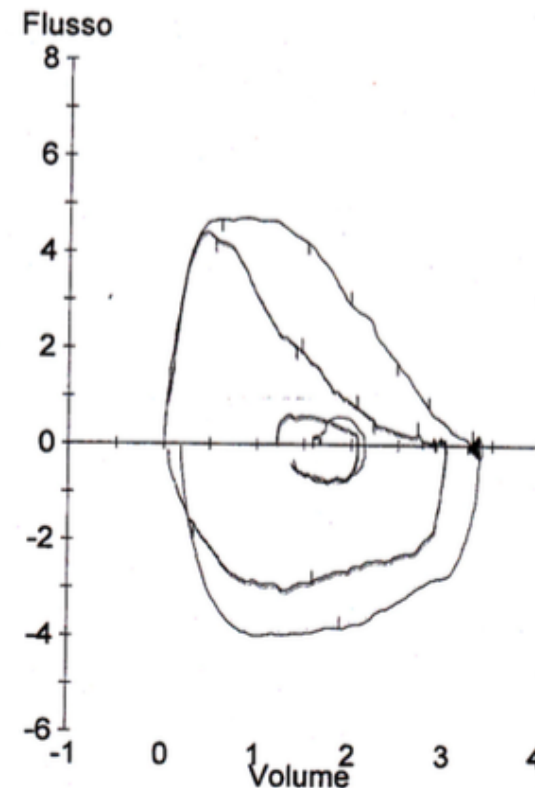
Spirometria eseguita nel 2015

Prescritto trattamento con ICS/LABA + antileucotrienico



Spirometria

		Ref	Pre Meas	Pre % Ref	Post Meas	Post % Chg
VC	Litri	3.34	3.02	90		
FVC	Litri	3.34	3.02	90	3.40	13
FEV1	Litri	3.19	2.09	66	2.85	36
FEV1/FVC %		86	69	81	84	21
FEV1/SVC %			69			
FEF50%	L/sec	4.22	1.94	46	4.17	115
PEF	L/sec	6.64	4.44	67	4.78	7
PEFT	Sec	▲	0.14		0.15	12
Vol Extrap	Litri		0.09		0.07	-24
FET100%	Sec		8.07		7.42	-8
FEF25-75%	L/sec	3.58	1.37	38	3.17	89

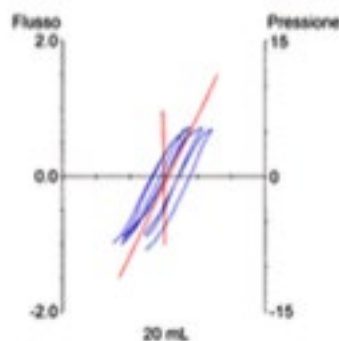
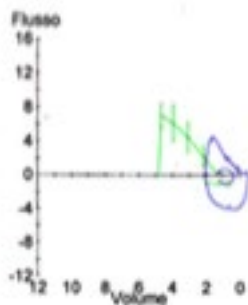




PLETISMOGRAFIA

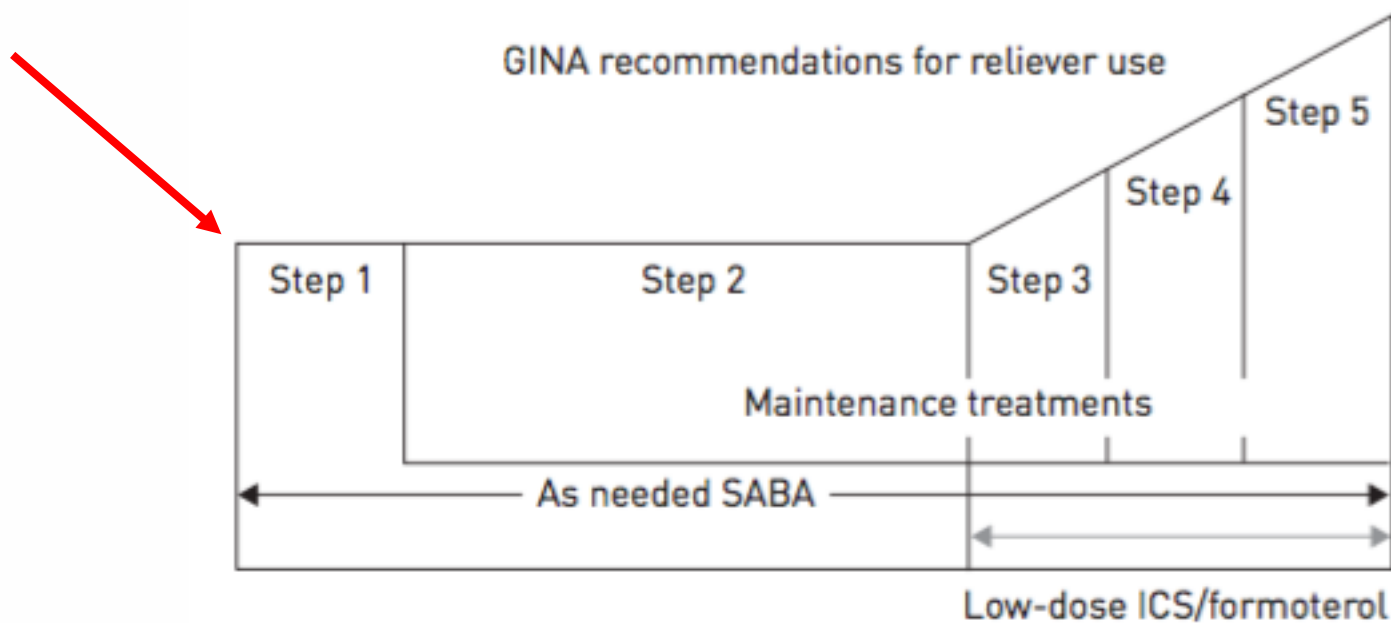
		Ref	CI	Pre Meas	Pre % Ref	Post Meas	Post % Ref	Post % Chg
FVC	Litri	3.59	0.71	2.64	74			
FEV1	Litri	3.14	0.62	2.01	64			
FEV1/FVC	%	84	11	76				
FEF25-75%	L/sec	4.09	1.39	1.68	41			
FEF25%	L/sec	6.15	2.21	4.50	73			
FEF50%	L/sec	4.48	1.80	2.15	48			
FEF75%	L/sec	2.17	1.13	0.70	32			
PEF	L/sec	7.00	1.48	4.53	65			
FEV1/SVC	%	85	11	76				
FEF/FIF50				0.55				
MVV	L/min							
PEFT	Sec			0.15				
Vol Extrap	Litri			0.08				
FET100%	Sec			6.90				
VC	Litri	3.63	0.69	2.64	73			
ERV	Litri			0.94				
RV	Litri	1.31	0.57	-0.55	-42			
FRC PL	Litri	2.64	0.82	0.44	17			
TLC	Litri	4.84	0.98	2.09	43			
RV/TLC	%	27	10	-26				
IC	Litri			1.66				
Vtg	Litri			0.94				
Raw	cmH2O/L/sec	1.64		19.53	1194			
Gaw	L/sec/cmH2O			0.051				

Dopo otto giorni di
terapia steroidea ev,
antibiotico e
broncodilatatori
inalatori

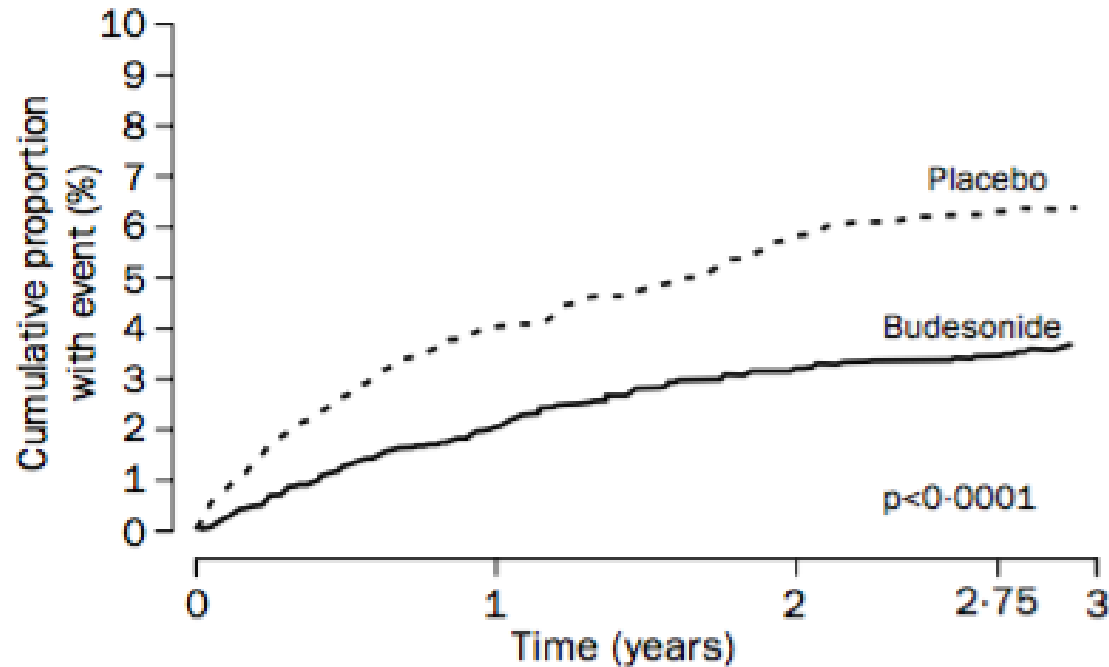


Possibili soluzioni

ICS ?



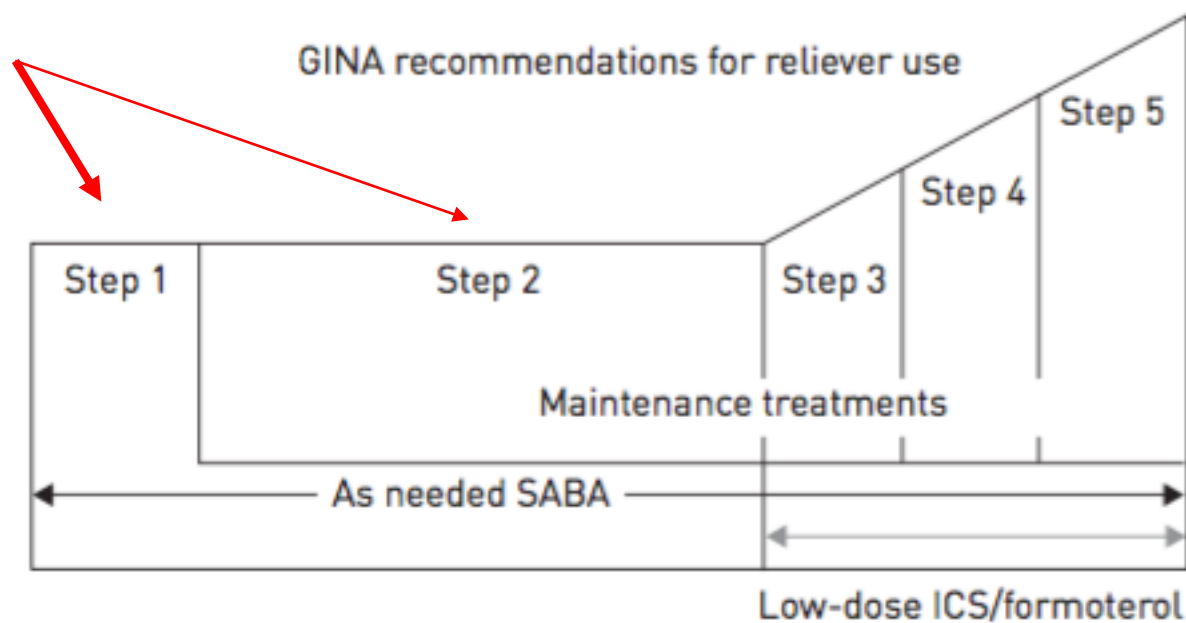
Early intervention with budesonide in mild persistent asthma



Interpretation Long-term, once-daily treatment with low-dose budesonide decreases the risk of severe exacerbations and improves asthma control in patients with mild persistent asthma of recent onset.

Possibili soluzioni

**Combination
ICS/SABA
or ICS/LABA ?**

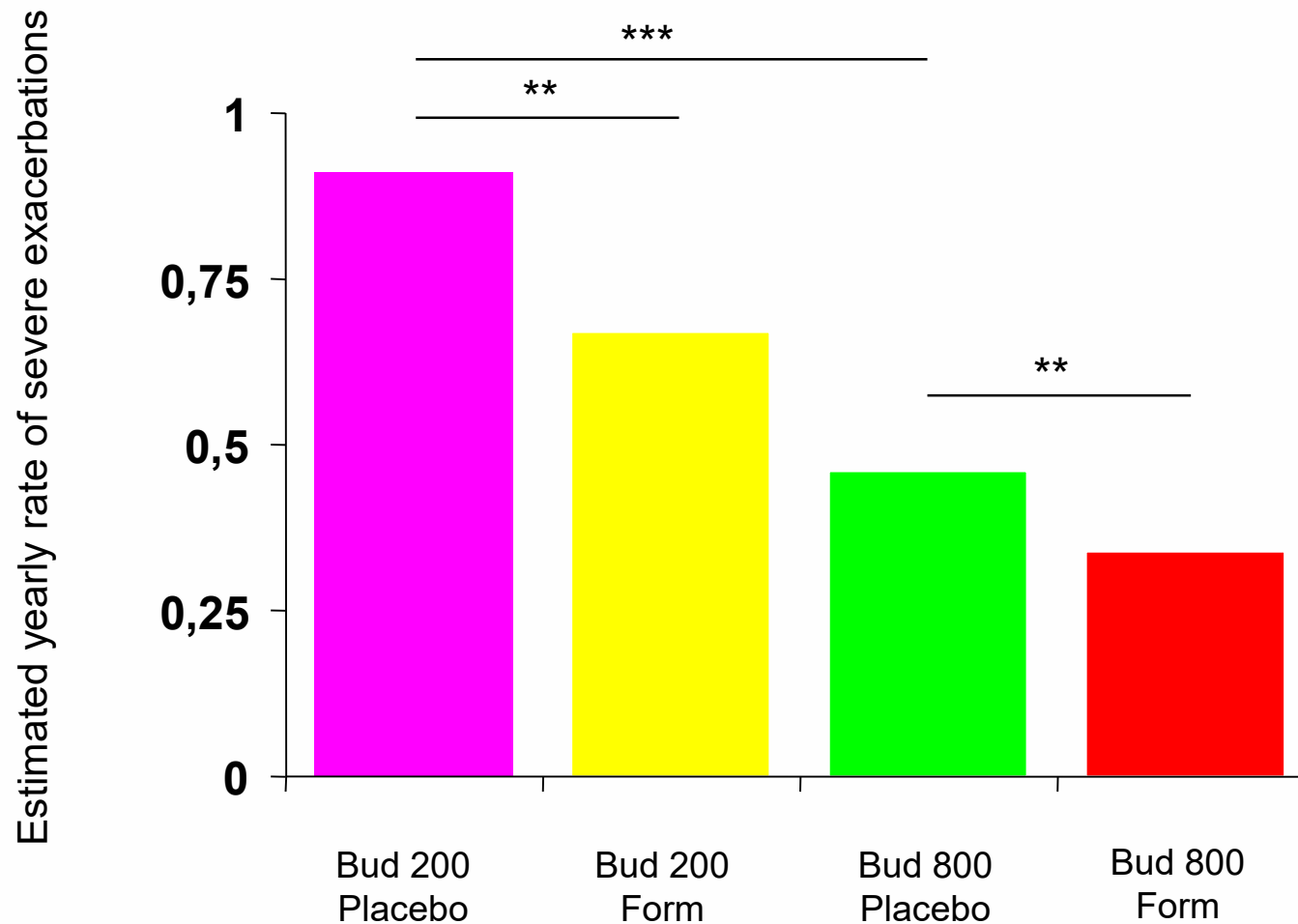


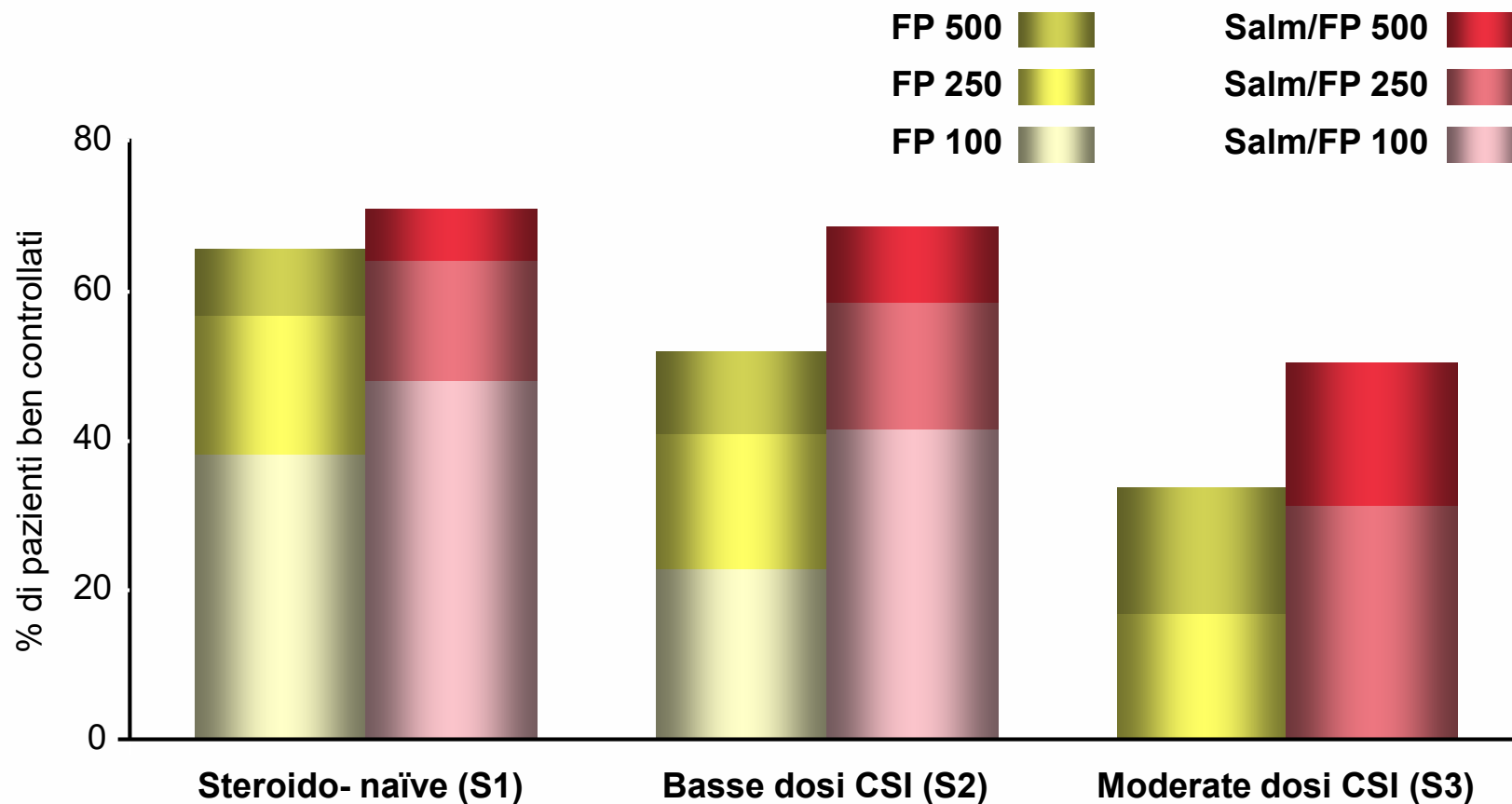
Due strategie alternative per mantenere il controllo dell'asma

“montagna piatta” mantenuta da trattamento regolare



Combination therapy in asthma

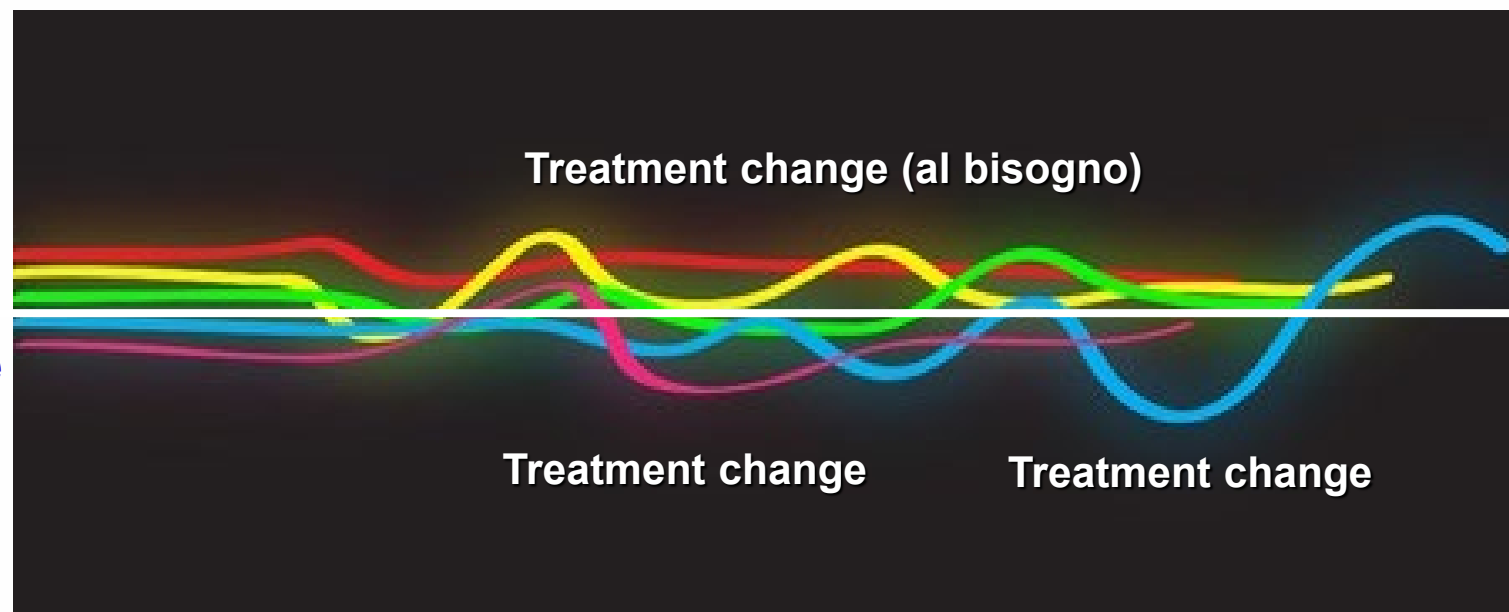




Strategia alternativa per mantenere il controllo dell'asma: Terapia adattabile

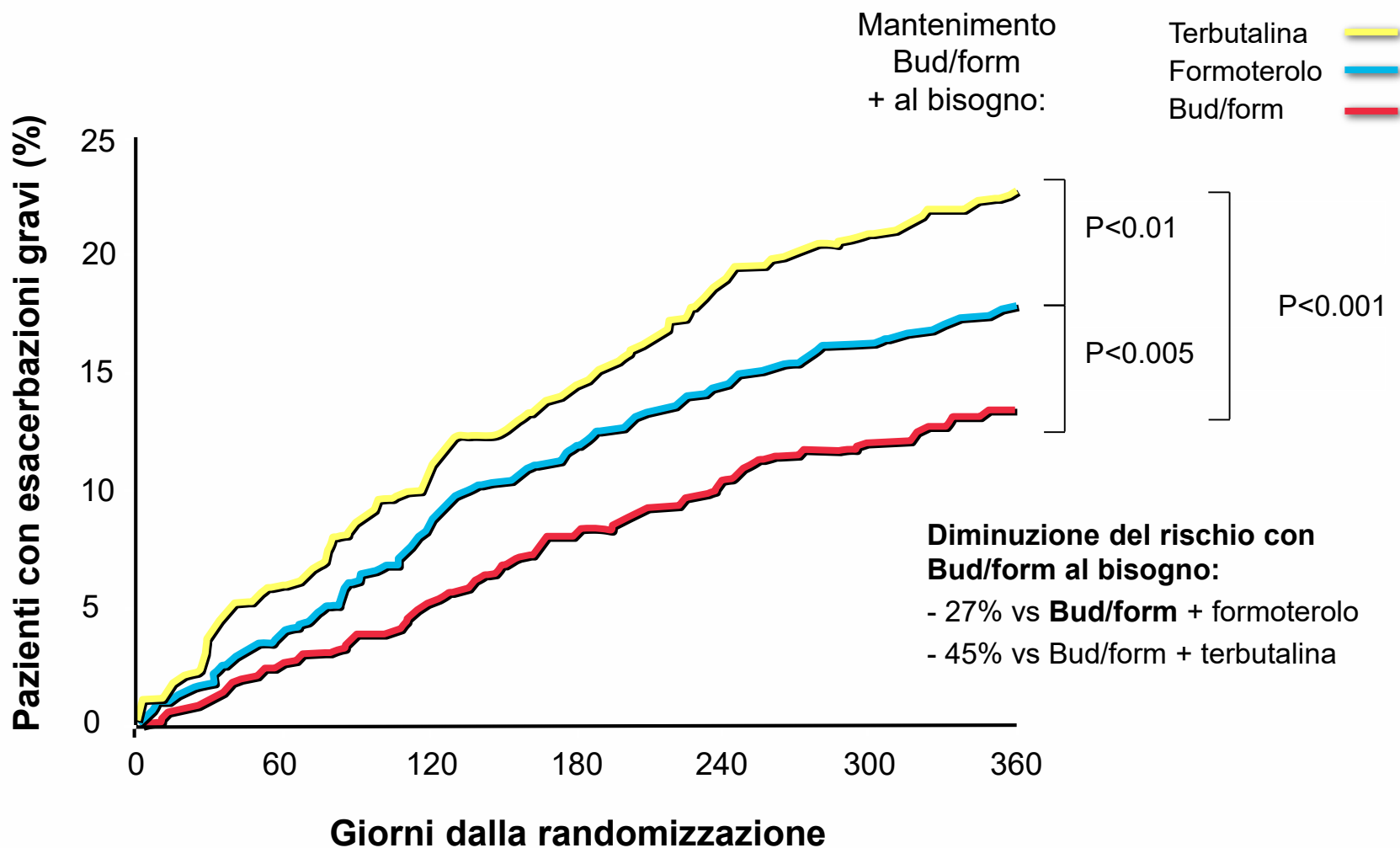
Terreno ondulato

Terapia
regolare



Studio SMILE

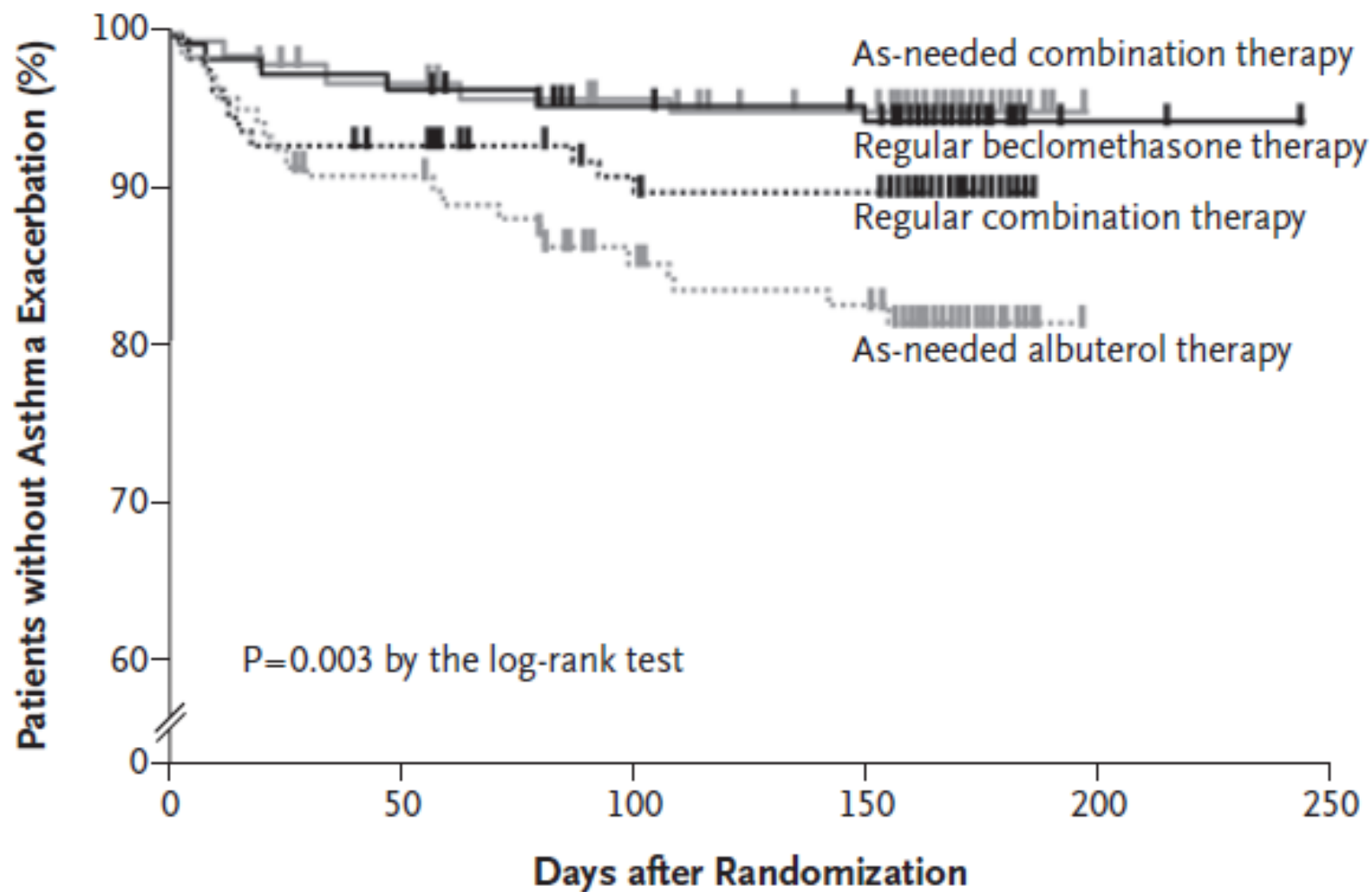
Tempo alla prima riacutizzazione grave



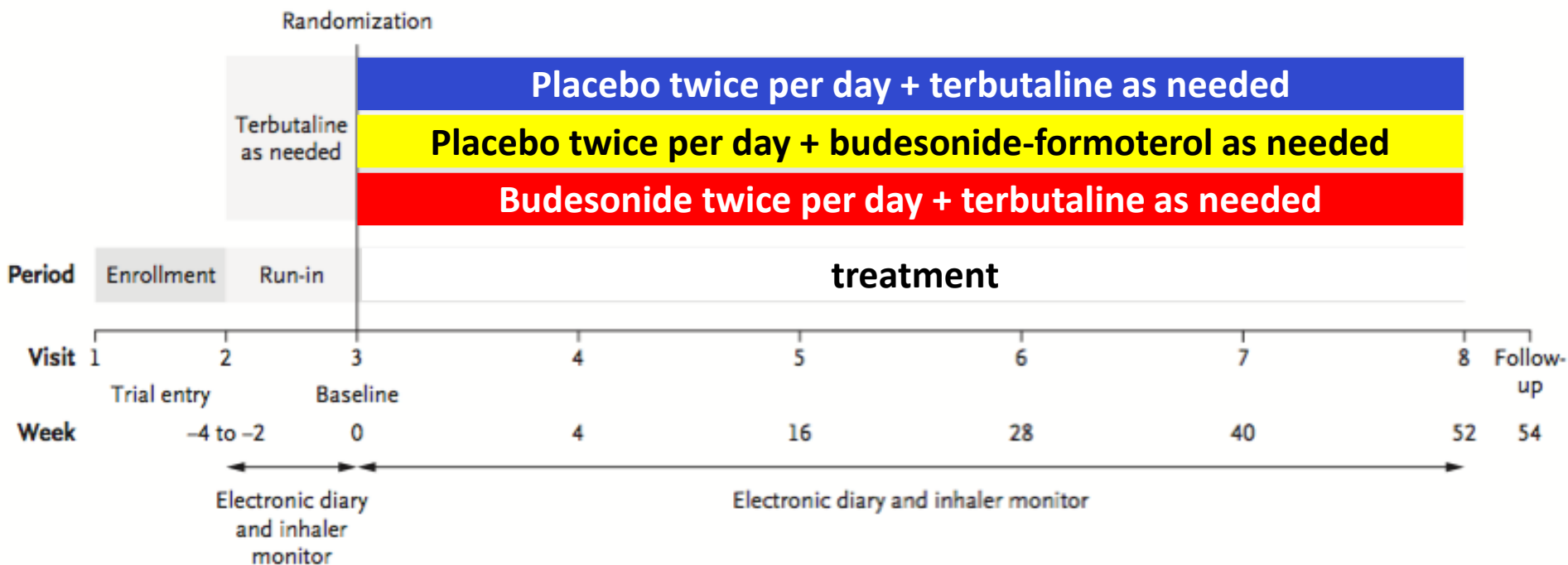
Possibili strategie terapeutiche

- Terapia regolare + β_2 stimolante a rapida azione al bisogno
- Terapia «al bisogno» (guidata dai sintomi)
- Terapia adattabile (mantenimento e al bisogno)



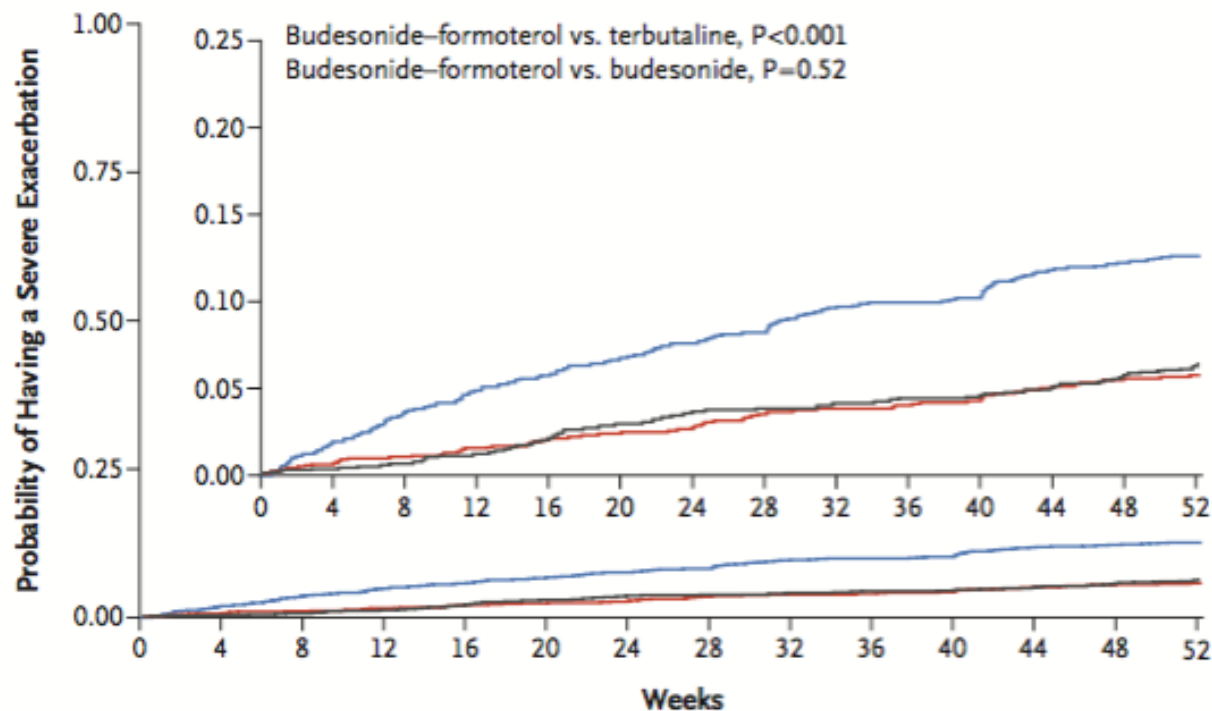


Inhaled combined Budesonide-Formoterol as needed in mild asthma



— Terbutaline as needed (N=1277) — Budesonide-formoterol as needed (N=1277) — Budesonide maintenance (N=1282)

A Severe Exacerbation



- 64 %

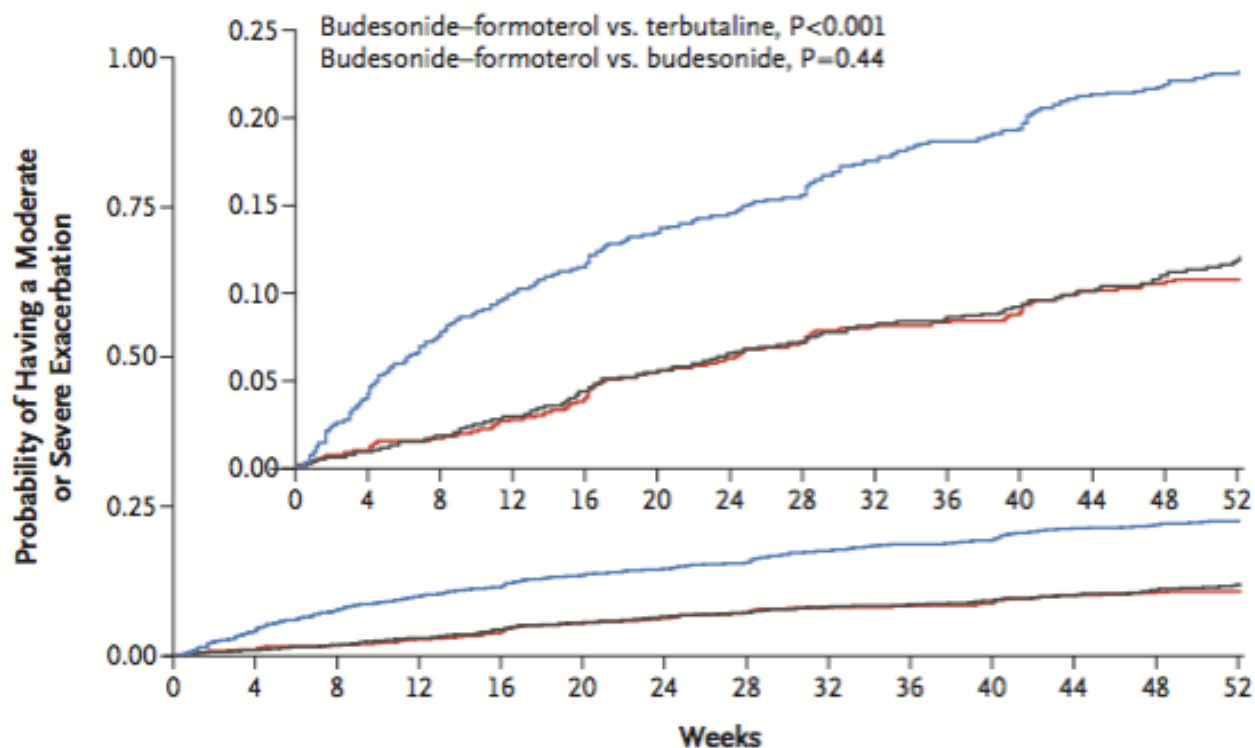
0.20

0.07

0.09

— Terbutaline as needed (N=1277) — Budesonide-formoterol as needed (N=1277) — Budesonide maintenance (N=1282)

B Moderate or Severe Exacerbation



- 60 %

Bud/For 57 µg
Bud 340 µg

17 %

As needed Budesonide-Formoterol versus maintenance Budesonide in mild asthma

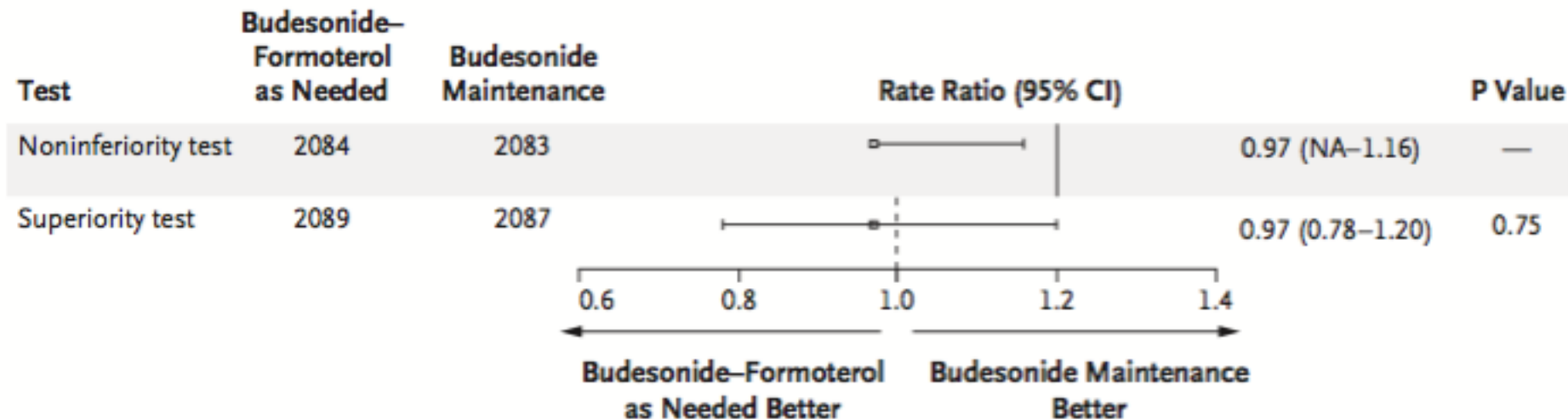
Placebo twice per day + budesonide-formoterol as needed

0.11

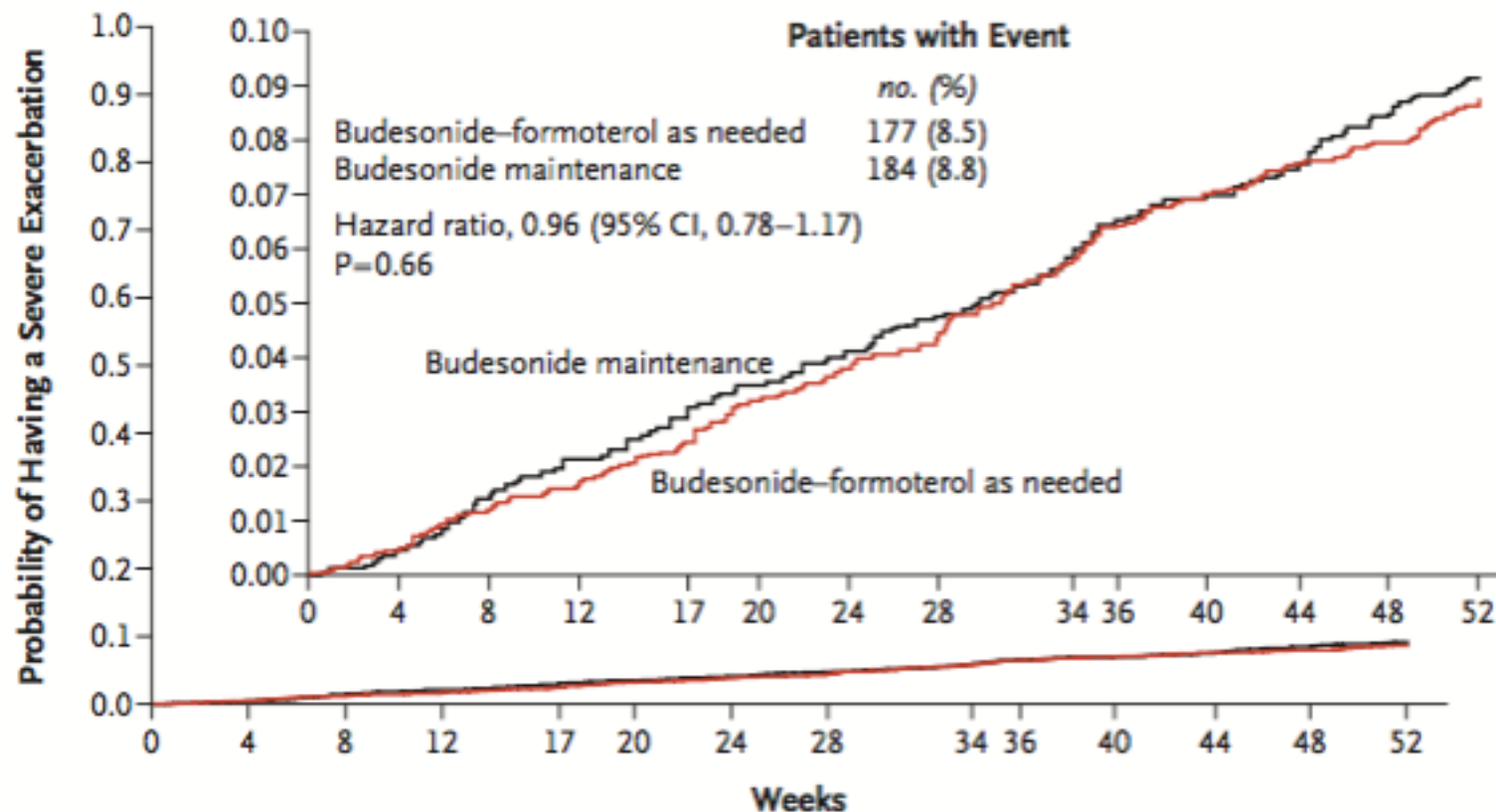
Budesonide twice per day + terbutaline as needed

0.12

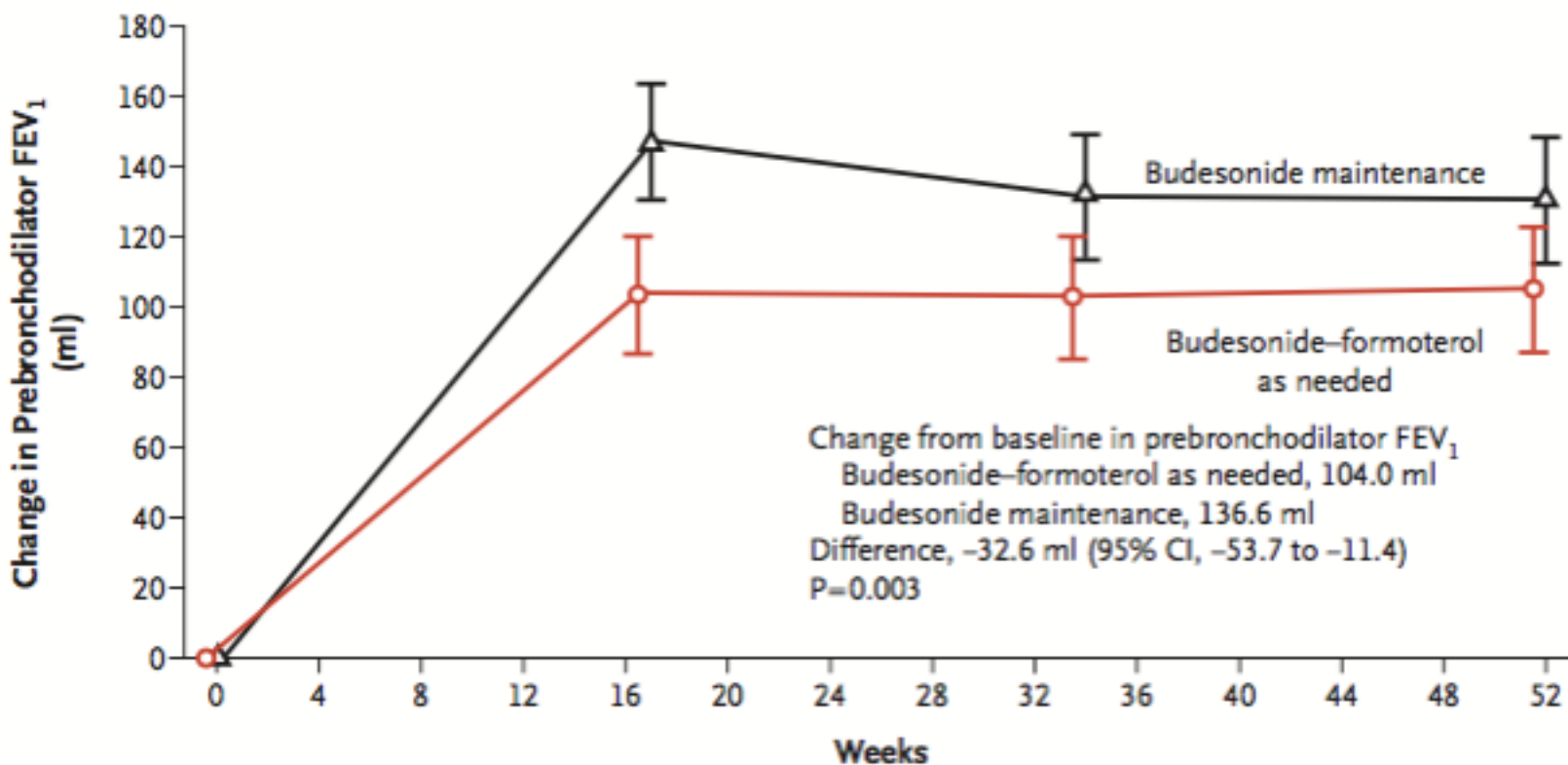
A Annualized Rate of Severe Asthma Exacerbations



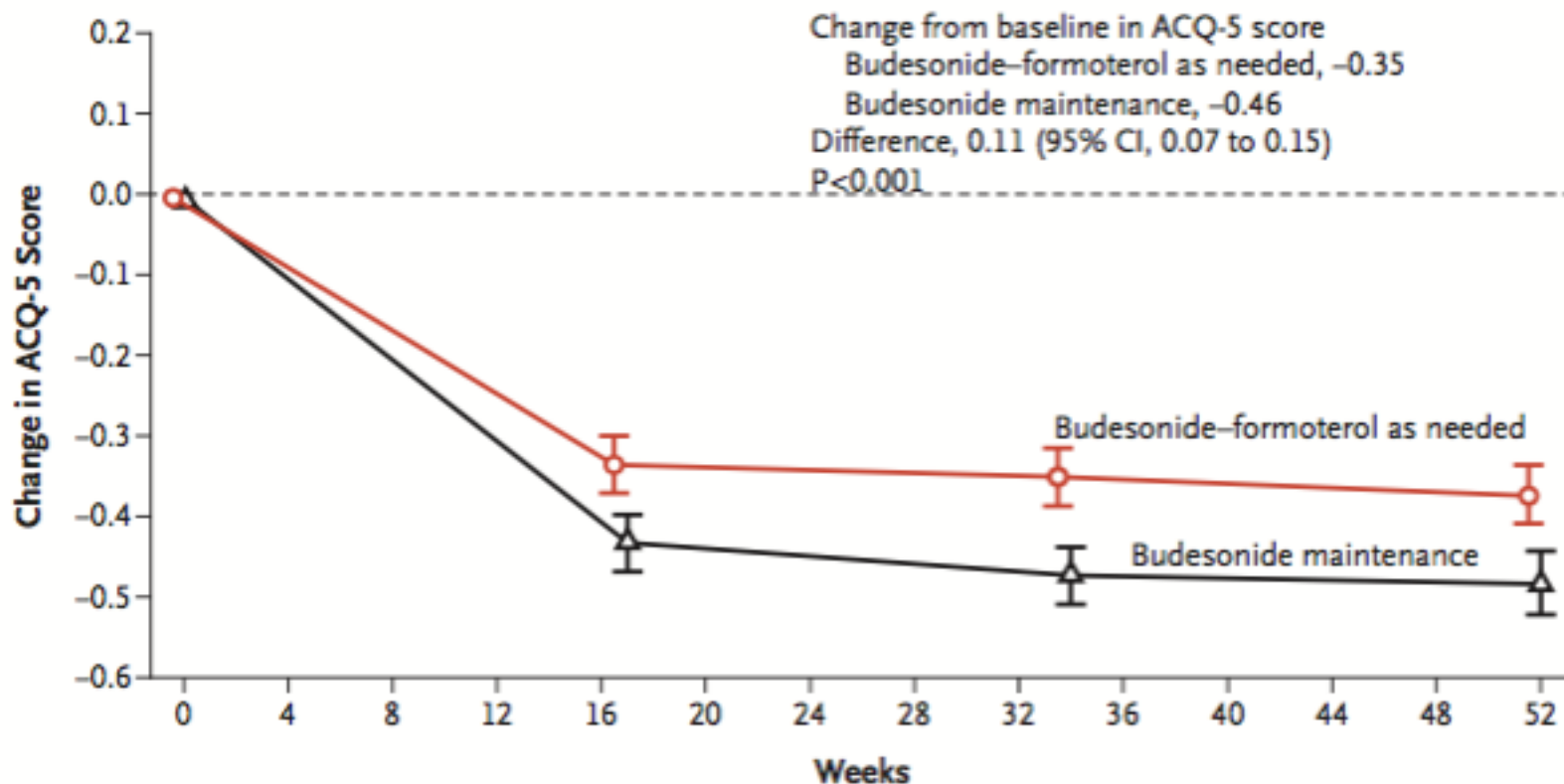
Time to First Severe Exacerbation



Change in Prebronchodilator FEV₁ from Baseline

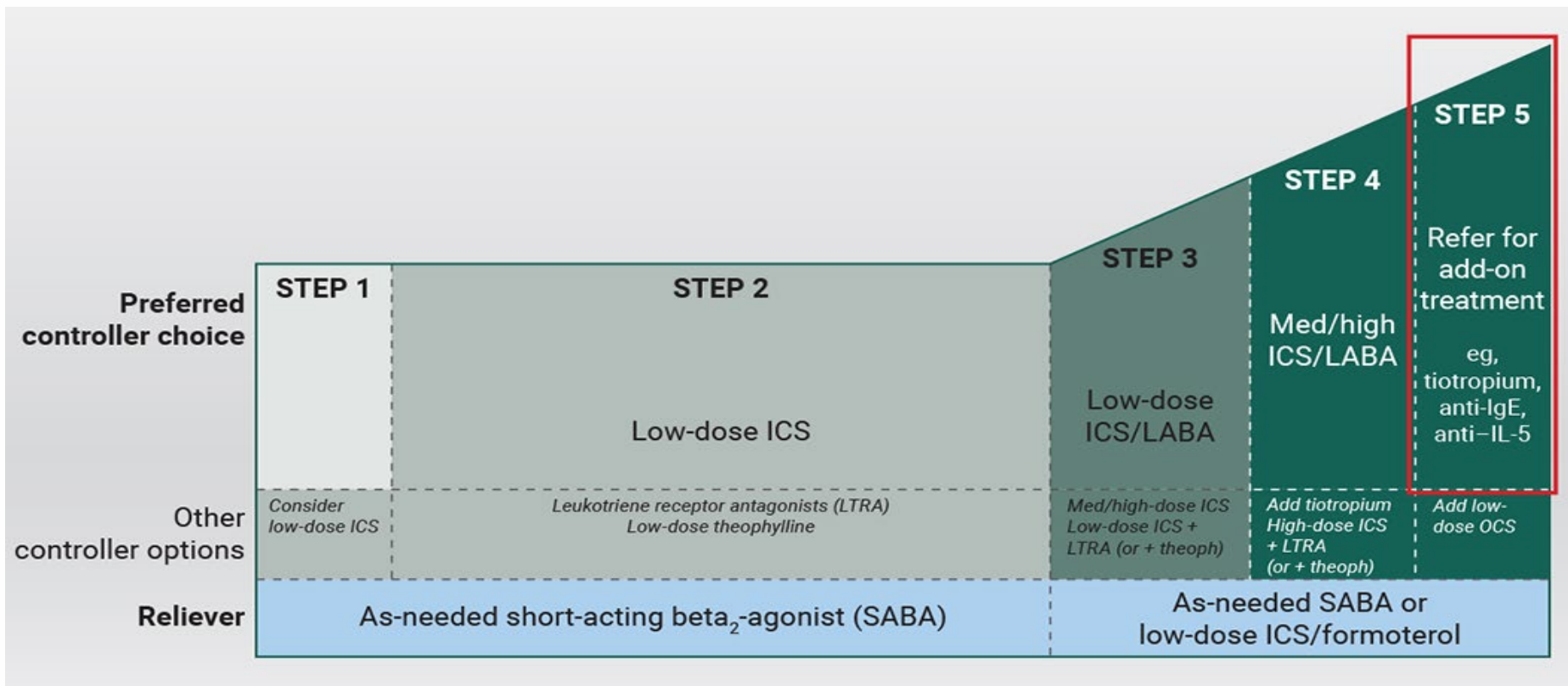


Change in ACQ-5 Score from Baseline



However, the potential role of an antiinflammatory reliever used as needed is to address the more common scenario of reliance on and overuse of SABAs, which is associated with worsening asthma, exacerbations,^{6,19,20} and potentially death, which are often closely associated with poor adherence to the use of inhaled glucocorticoids.²¹

GINA-Based treatment Steps



Identifying Severe Asthma: GINA and ERS/ATS Definitions of Severe Asthma

GINA¹

(In children ≥ 6 years of age, adolescents, and adults)

- Severe asthma is asthma that requires Step 4 or Step 5 treatment with medium- or high-dose ICS/LABA (+/- additional controllers) in order to prevent asthma from becoming uncontrolled
- Asthma that remains uncontrolled despite Step 4 or Step 5 treatment

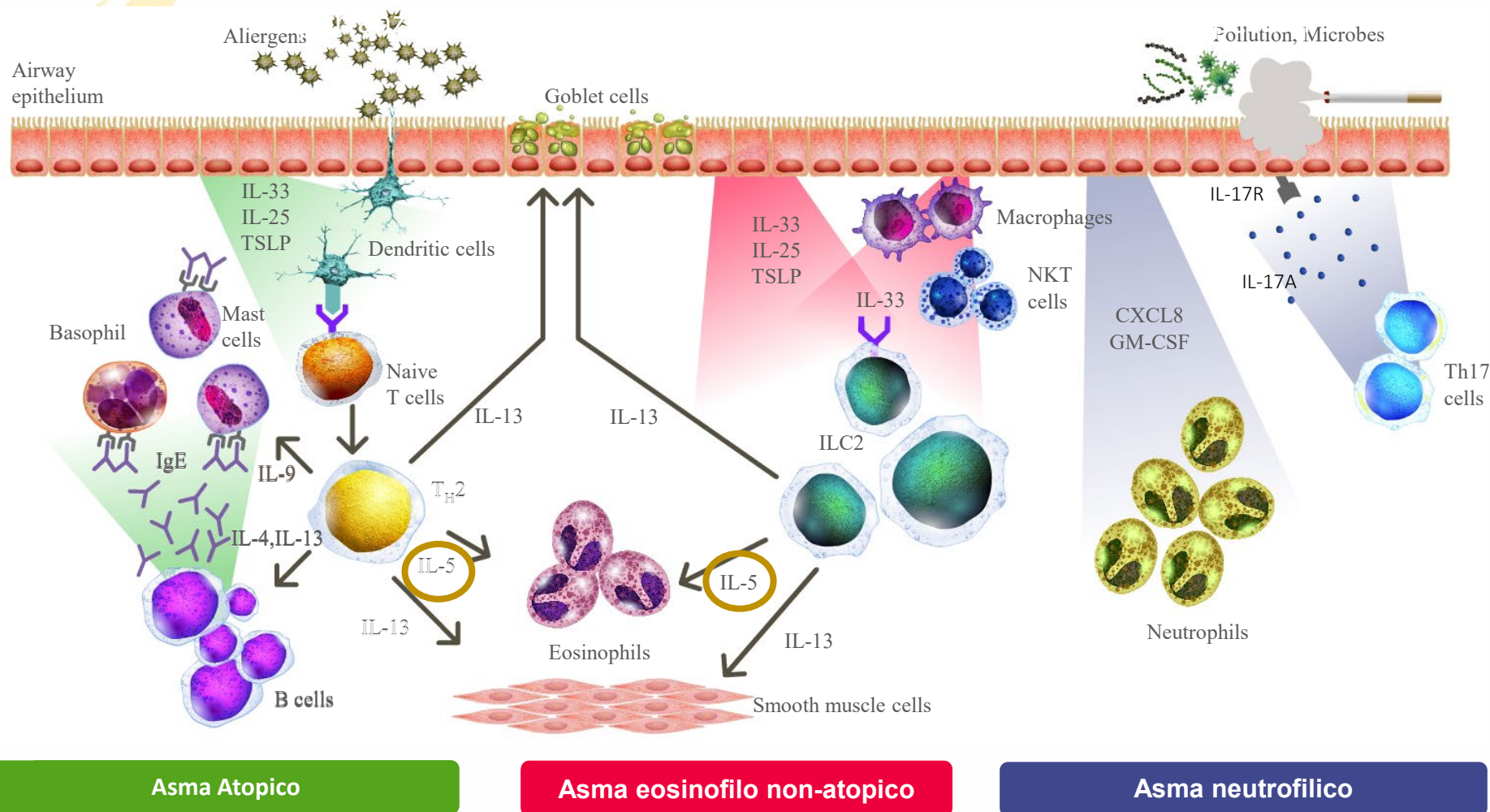
ERS/ATS Guidelines²

(In youths ≥ 6 years of age and adults)

- Severe asthma is asthma that requires treatment with GINA Step 4 or Step 5 therapy for the previous year
- Or asthma that requires systemic corticosteroids $\geq 50\%$ of the previous year in order to maintain control or asthma that remains uncontrolled despite therapy

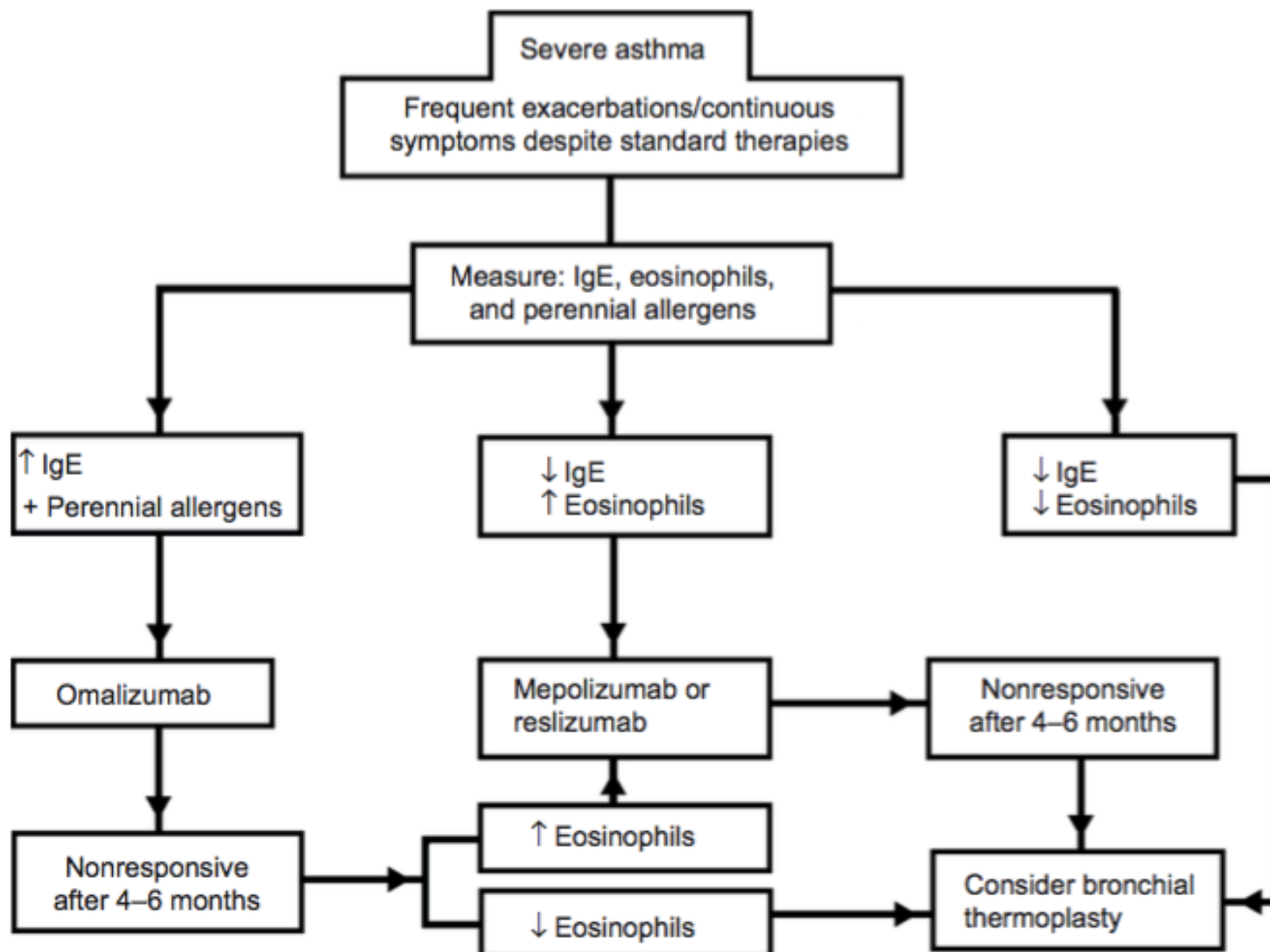
ATS=American Thoracic Society; ERS=European Respiratory Society; GINA=Global Initiative for Asthma; ICS=inhaled corticosteroids; LABA=long-acting beta₂ agonist.
1. Adapted from GINA. Global Strategy for Asthma Management and Prevention. 2018. <http://ginasthma.org/2018-gina-report-global-strategy-for-asthma-management-and-prevention/>. Accessed April 9, 2018. 2. Chung KF, et al. *Eur Respir J*. 2014;43(2):343-373.

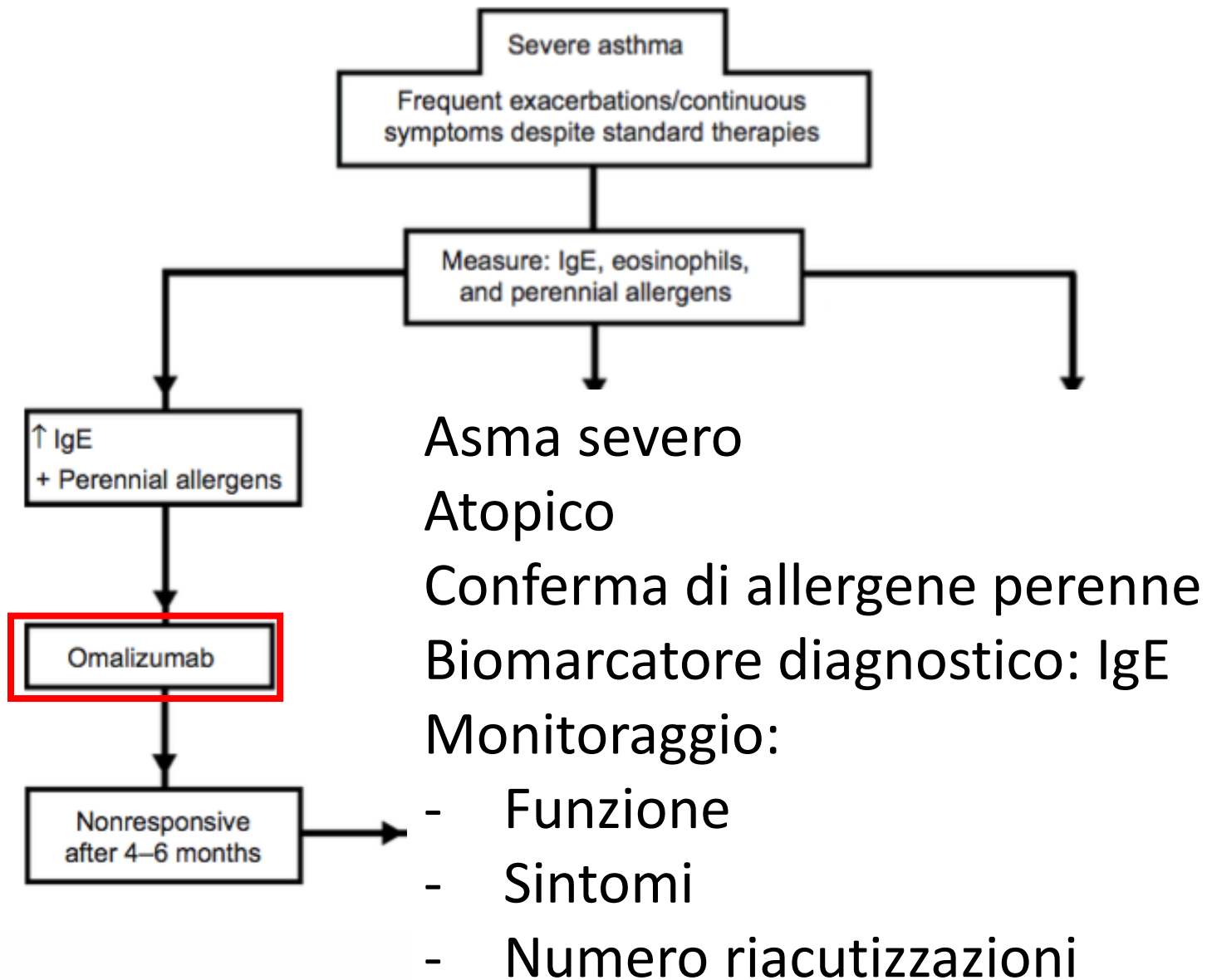
Indentificazione di un TARGET molecolare



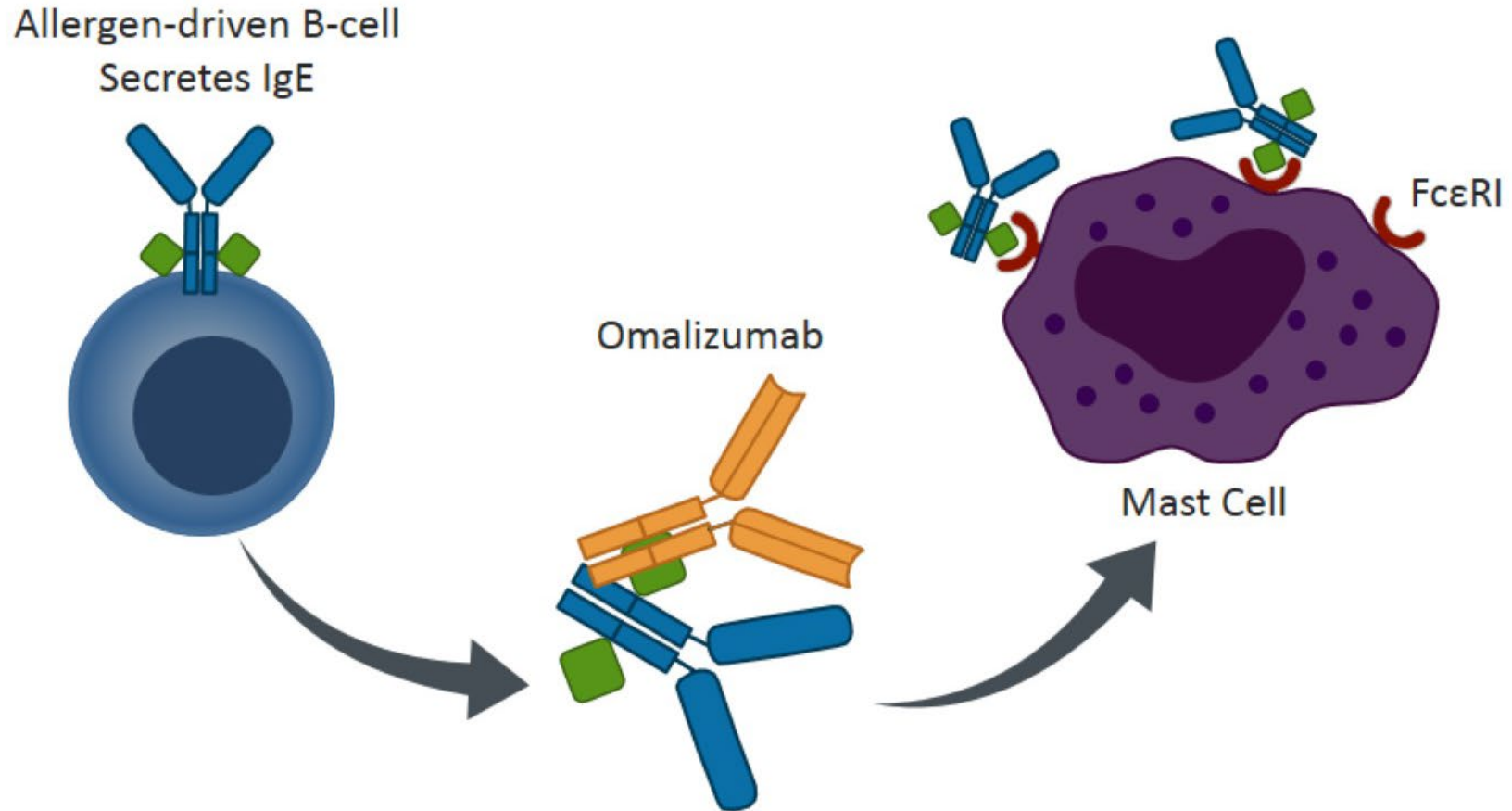
Ig = immunoglobulin; IL = interleukin; NKT cells = natural killer T cells;

TSLP = thymic stromal lymphopoietin; TSLPR = thymic stromal lymphopoietin receptor



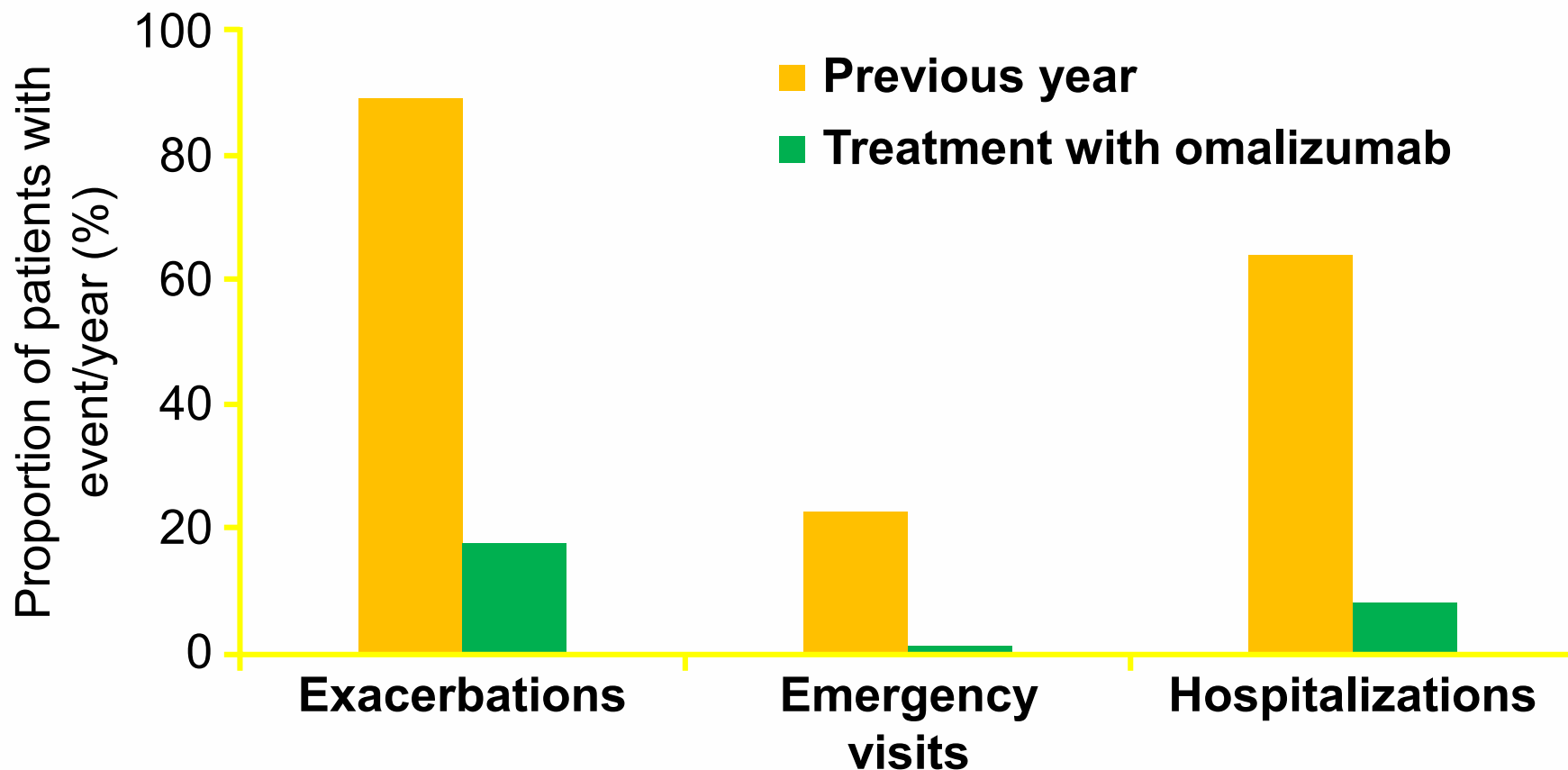


Blocking the allergic cascade by omalizumab



Italian real – life experience of Omalizumab

Reduction in asthma-related events

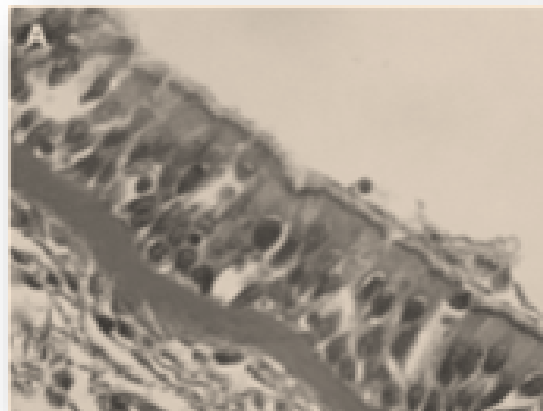


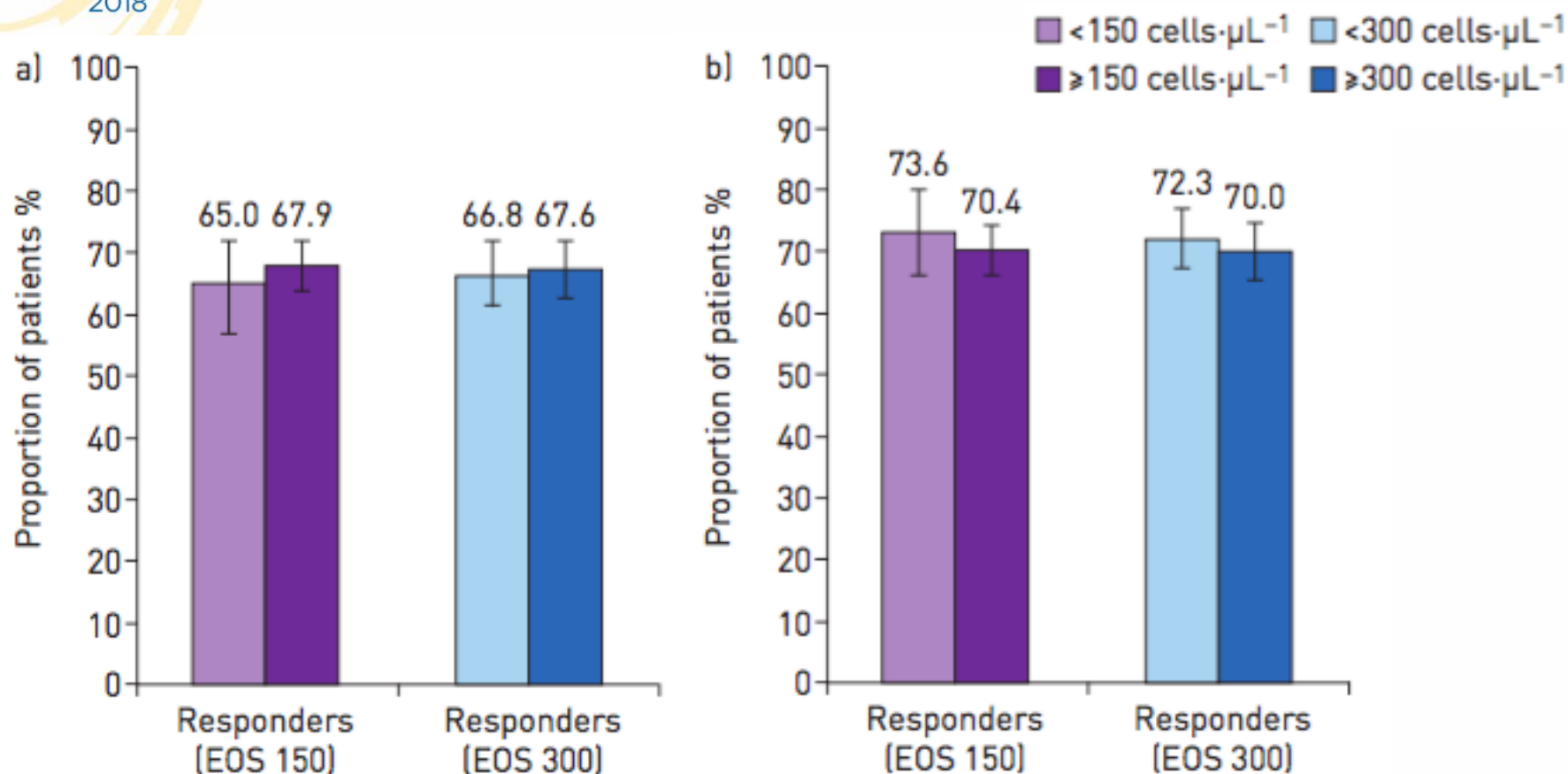
Omalizumab modulates bronchial reticular basement membrane thickness and eosinophil infiltration in severe persistent allergic asthma patients.

Riccio AM, Dal Negro RW, Micheletto C, De Ferrari L, Folli C, Chiappori A, Canonica GW.

Int J Immunopathol Pharmacol 2012; 25(2):475-84

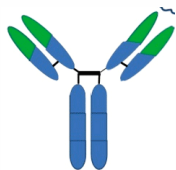
Applying stereology to measure thickness of the basement membrane zone in bronchial biopsy





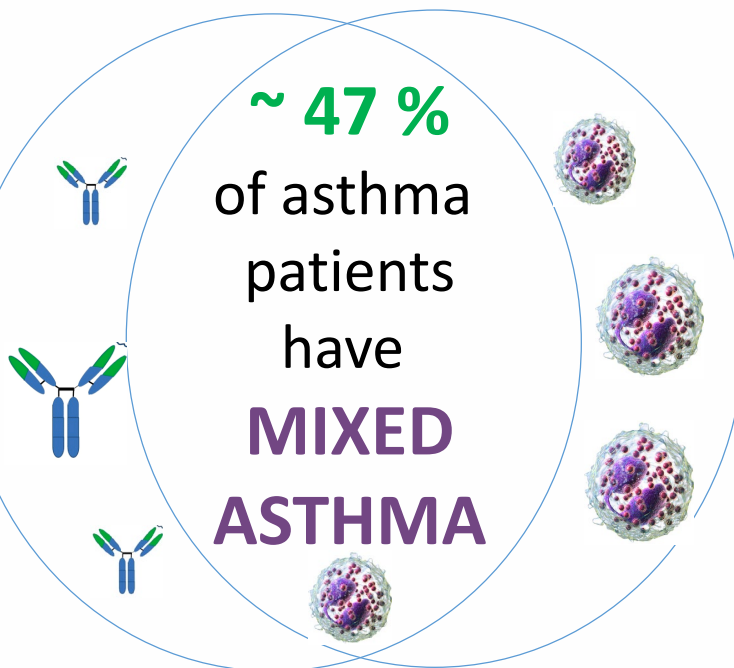
Responders to omalizumab treatment in adults at time of first effectiveness assessment after 4–6 months of treatment according to blood eosinophil count cut-off at 150 cells·μL⁻¹ (“EOS 150”: <150 cells·μL⁻¹, n=163; ≥150 cells·μL⁻¹, n=560) and 300 cells·μL⁻¹ (“EOS 300”: <300 cells·μL⁻¹, n=346; ≥300 cells·μL⁻¹, n=377). a) Responders based on physician’s global evaluation of Treatment Effectiveness). b) Responders based on a ≥40% decrease in the annual exacerbation rate

Patients have a spectrum of asthma including allergic, eosinophilic, and mixed asthma



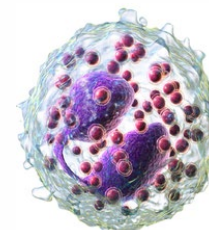
~ 14 %

of asthma patients
have **ALLERGIC
ASTHMA**

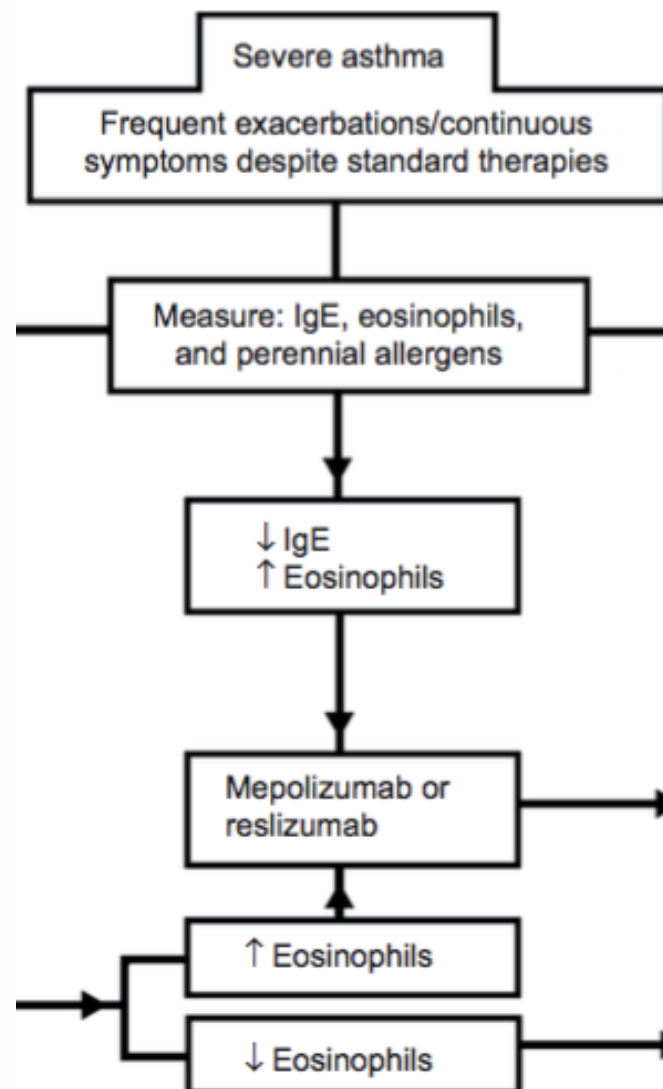


~ 22 %

of asthma patients
have
**EOSINOPHILIC
ASTHMA**



- Asma severo
- eosinofilico
- Atopico e non-atopico
- Biomarcatore diagnostico:
 - eosinofilia ematica
- Monitoraggio:
 - Funzione
 - Sintomi
 - Numero riacutizzazioni
 - eosinofilia



Maselli DJ, et al. J of Asthma 2016

Clinical profile of late-onset eosinophilic asthma



Can be late onset



Equal gender distribution



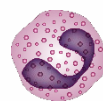
No or limited allergies to common allergens



Risk of severe exacerbations



Low FEV₁ with persistent airflow limitation



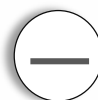
Elevated blood eosinophils



Normal or moderately elevated IgE



Rhinosinusitis with nasal polyps



May be aspirin sensitive



Dynamic hyperinflation and air trapping

**Patients
with asthma**

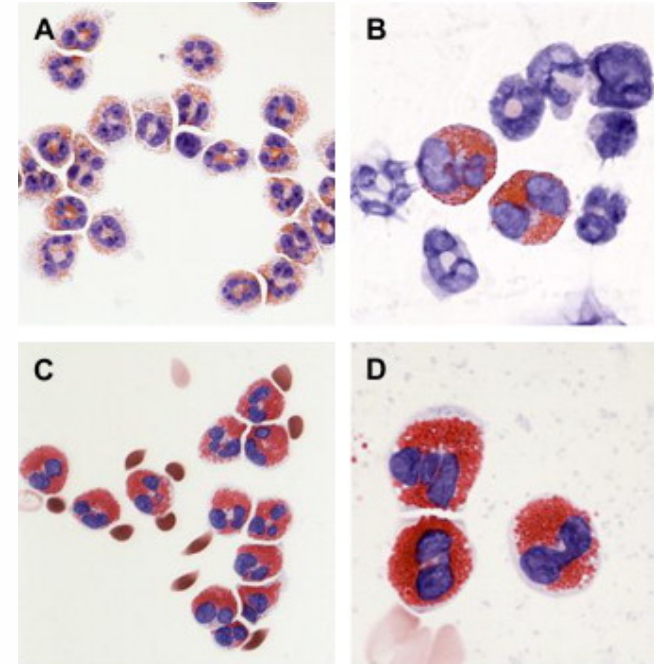
**Uncontrolled
with ICS**

**Dependent on
oral steroids**

**Targeted biologic therapies can help
patients achieve asthma control and
limit their use of oral steroids**

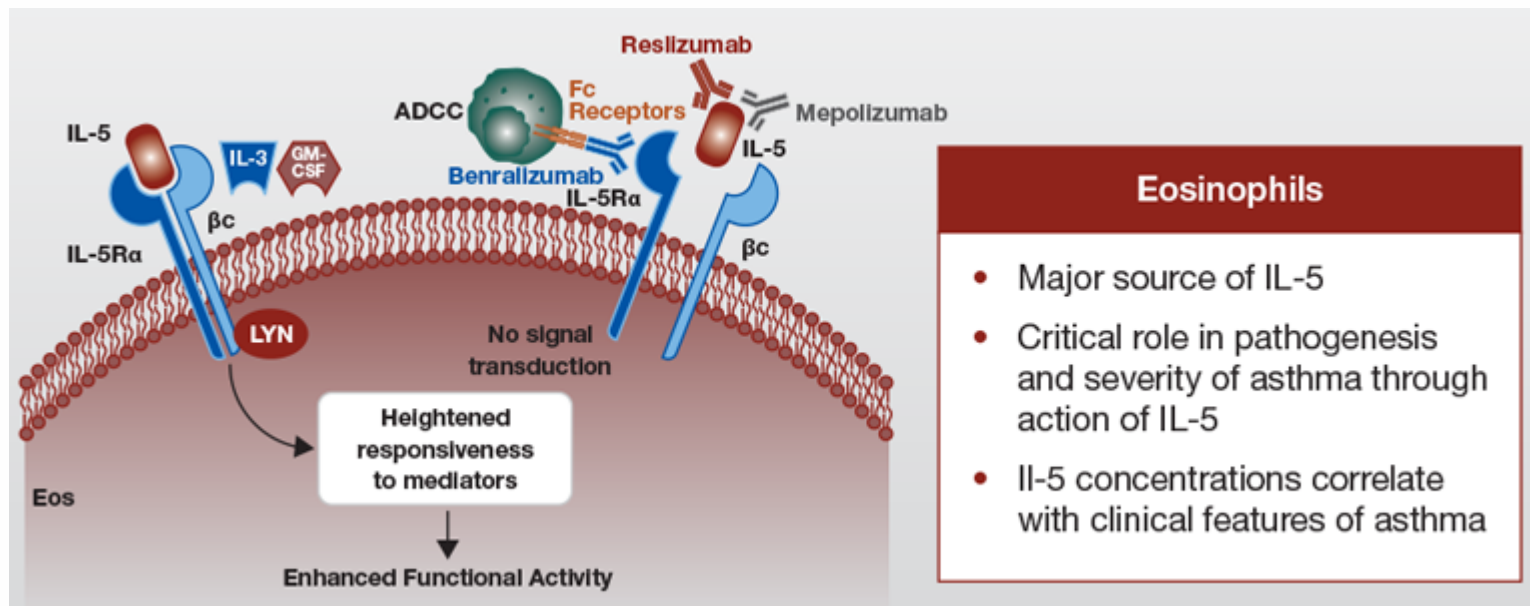
Interleukin-5

IL-5 is primarily produced by activated Th2 cells, but also Mast cells and eosinophils. It promotes:



- eosinophil maturation
- eosinophil migration and chemotaxis
- eosinophil activation and survival

IL-5 pathways inhibition in severe eosinophilic asthma

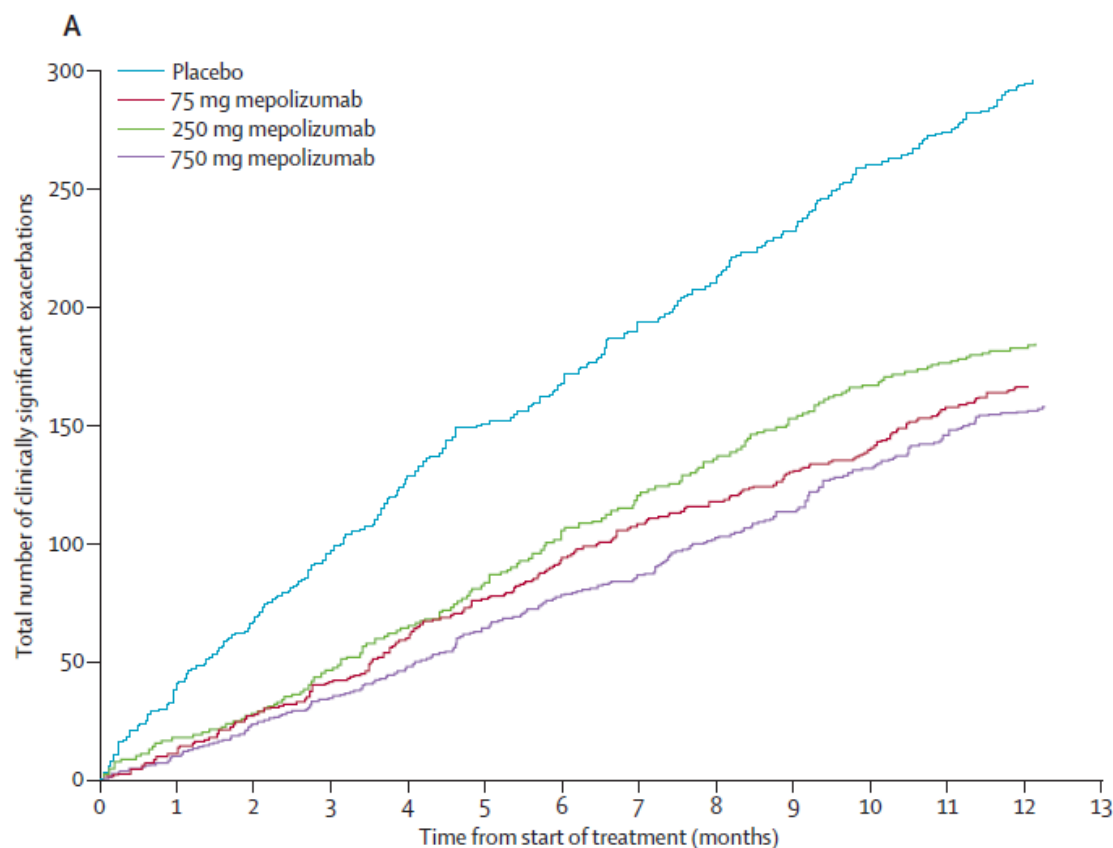


Agent	Target/MOA
Mepolizumab	Binds to epitope of IL-5, blocks binding with IL-5Rα
Reslizumab	Binds to epitope of IL-5, blocks binding with IL-5Rα
Benralizumab	Inhibition of IL-5Rα activation, leading to enhanced antibody-dependent cell-mediated cytotoxicity

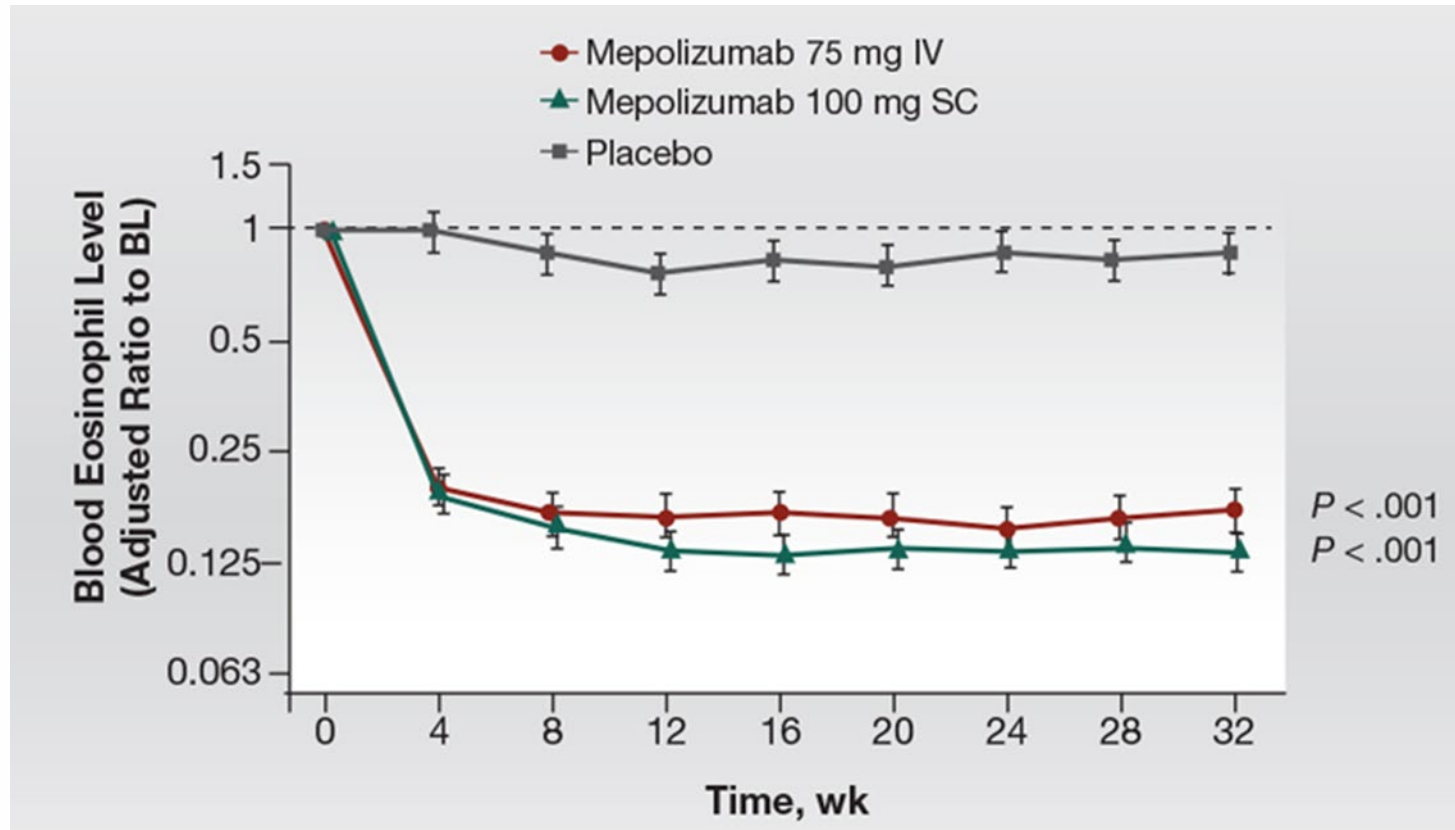
DREAM study: inclusion criteria

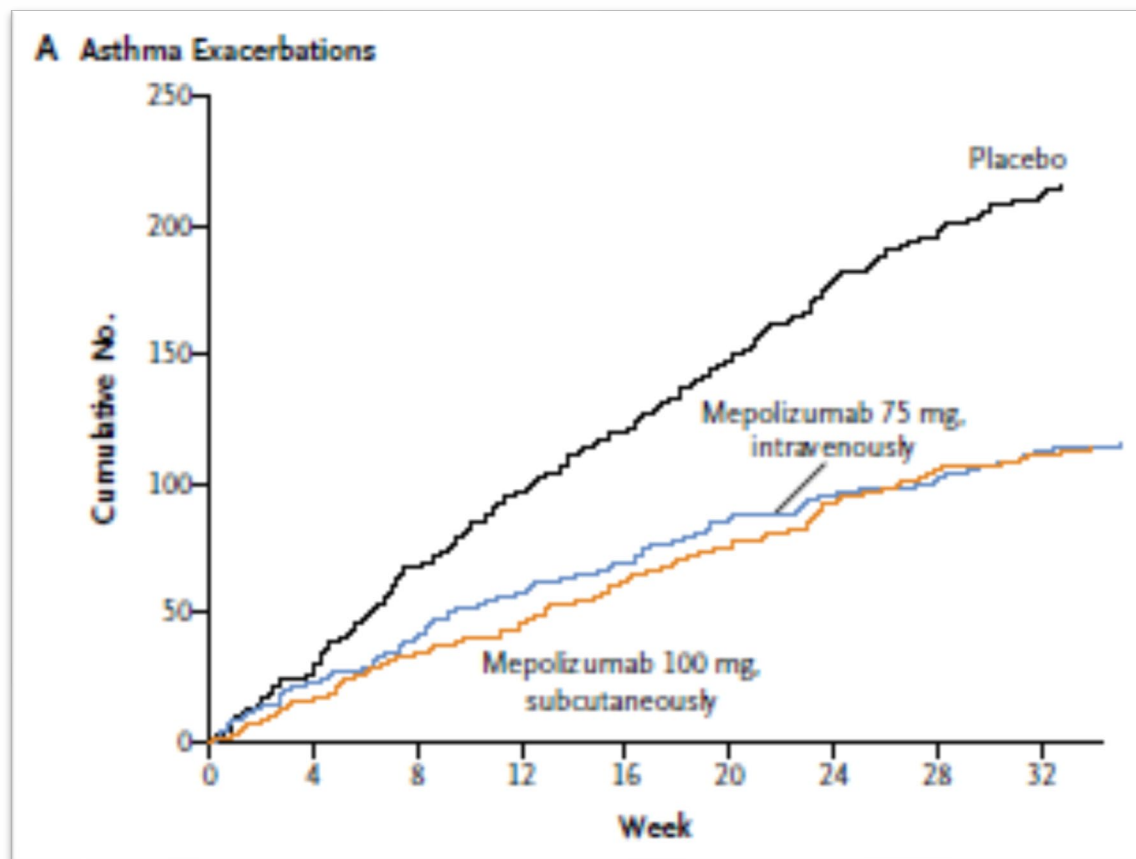
- Age 12-74 years
- Clinical diagnosis of asthma (refractory)
- History of two or more exacerbations / year
- **Evidence of eosinophilic inflammation:**
 - 1) sputum eosinophil count $\geq 3\%$, *or*
 - 2) blood eosinophil count $\geq 300/\mu\text{L}$, *or*
 - 3) $\text{FE}_{\text{NO}} \geq 50$ ppb.

Mepolizumab in severe eosinophilic asthma: impact on exacerbations

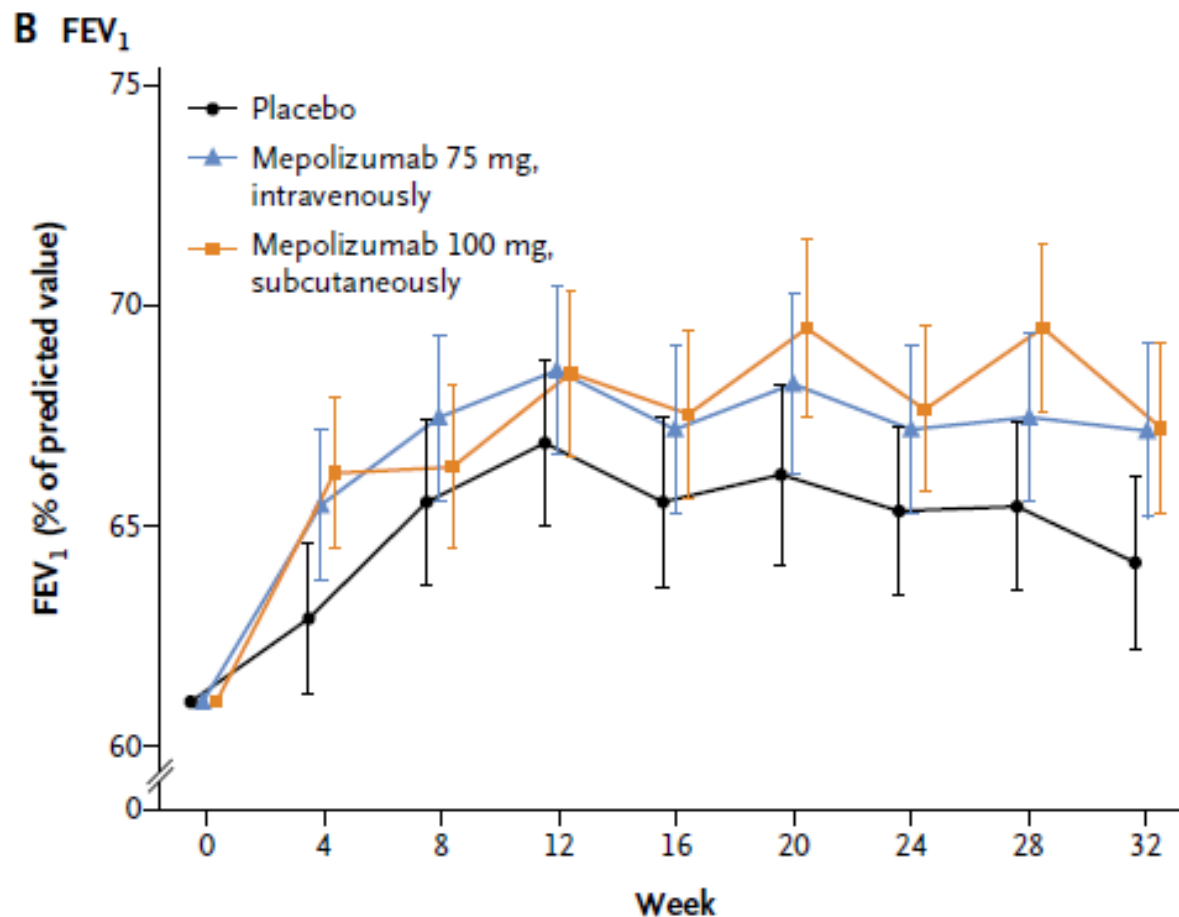


The effect of IL-5 targeted treatment on blood eosinophils levels: Mepolizumab

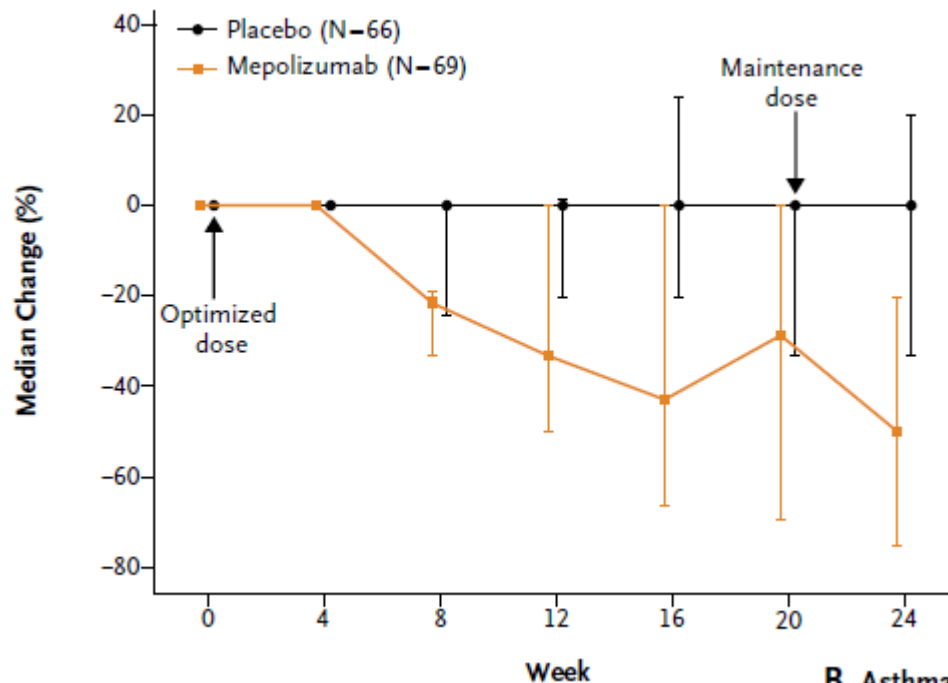




The rate of exacerbations was reduced by **47 %** among patients receiving intravenous mepolizumab and by **53 %** among those receiving subcutaneous mepolizumab, as compared with those receiving placebo ($P < 0.001$).



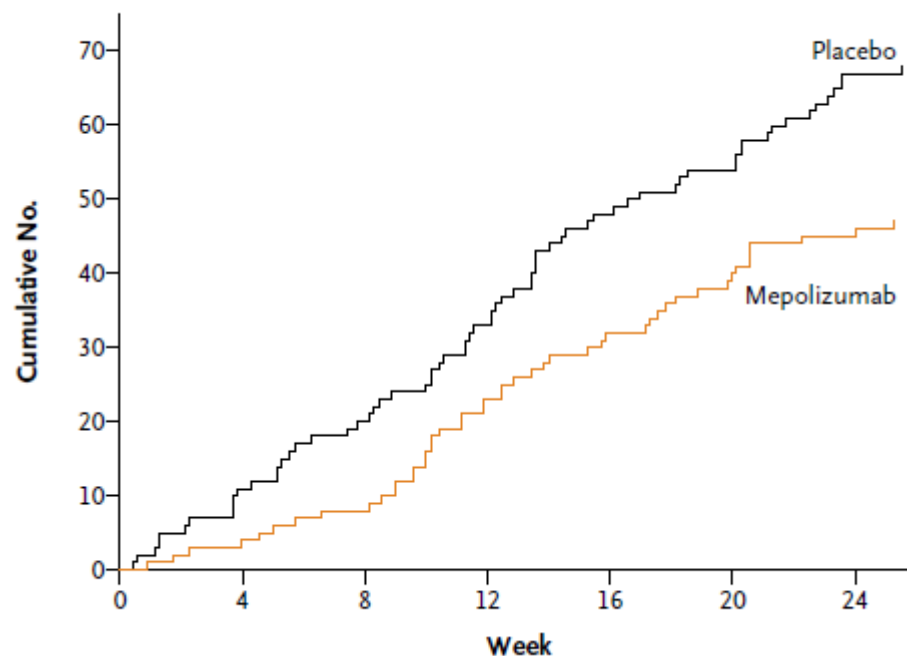
At week 32, the mean increase from baseline in FEV₁ was 100 ml greater in patients receiving intravenous mepolizumab than in those receiving placebo ($P = 0.02$) and **98 ml** greater in patients receiving subcutaneous mepolizumab than in those receiving placebo ($P=0.03$).



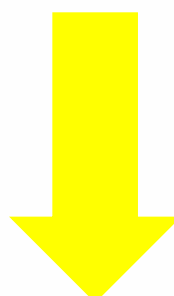
- 50 %



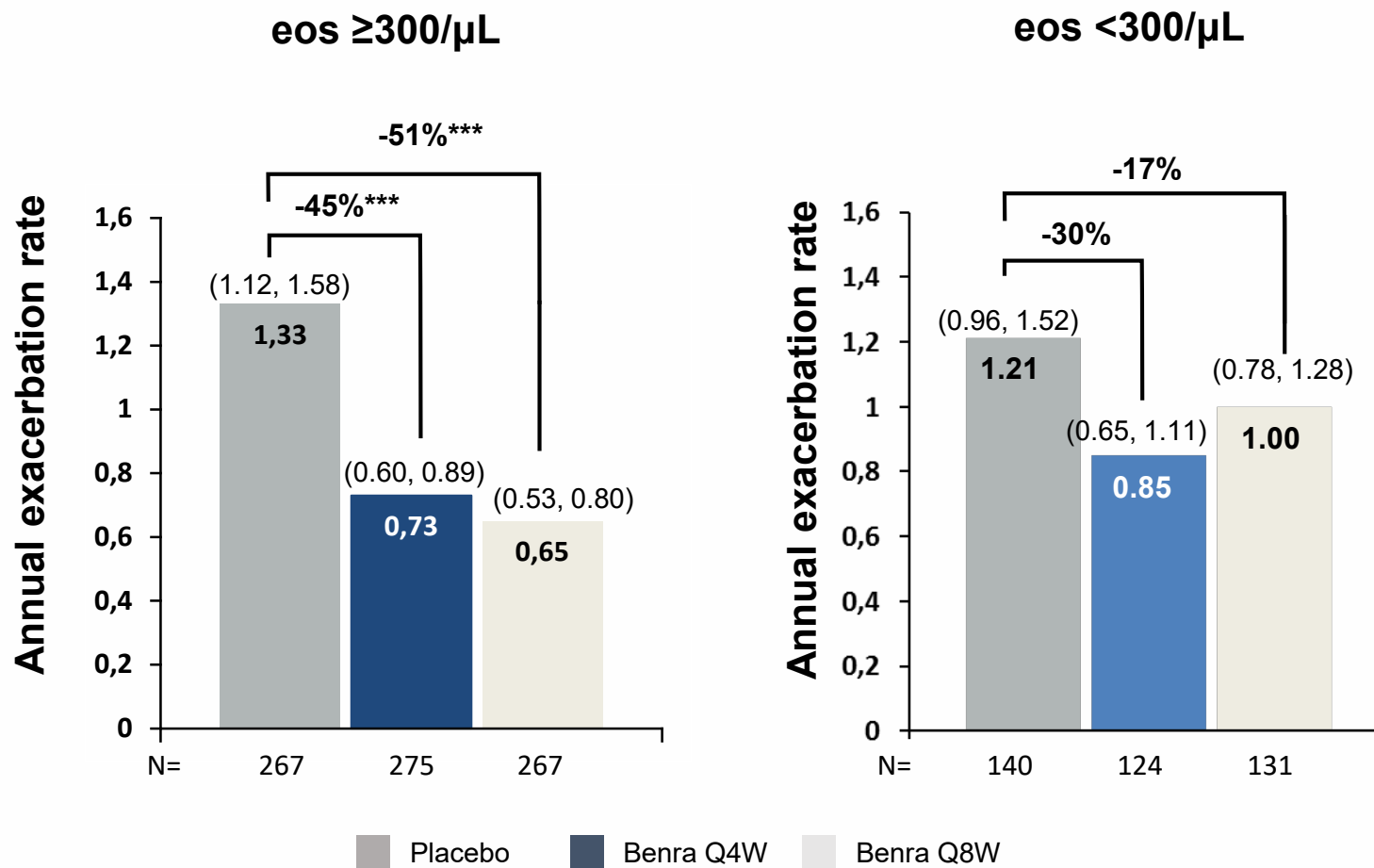
B Asthma Exacerbations



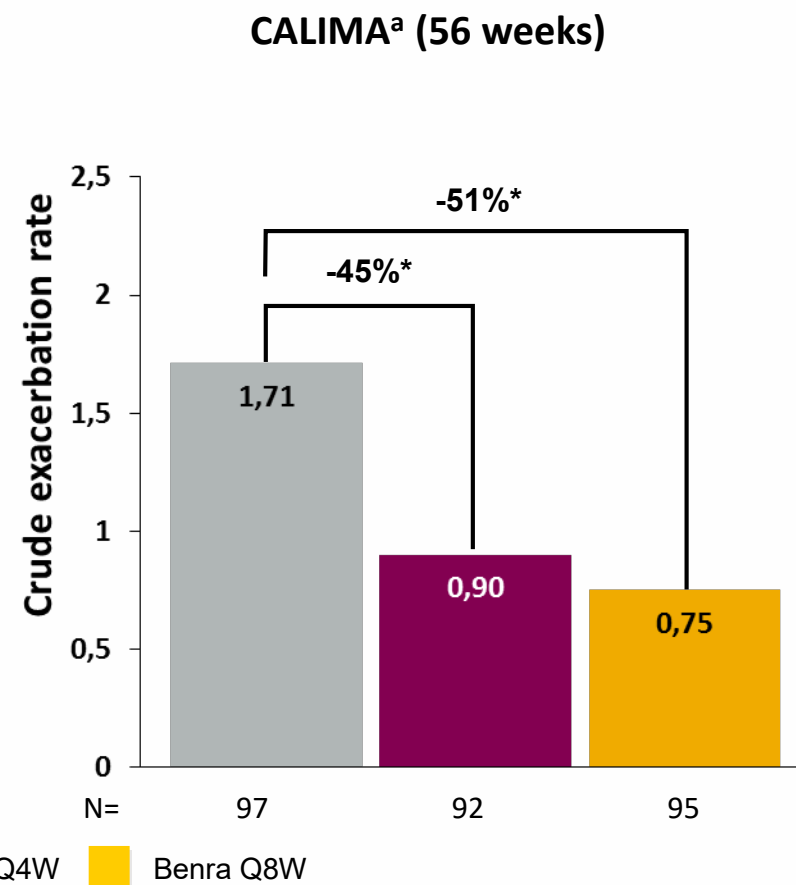
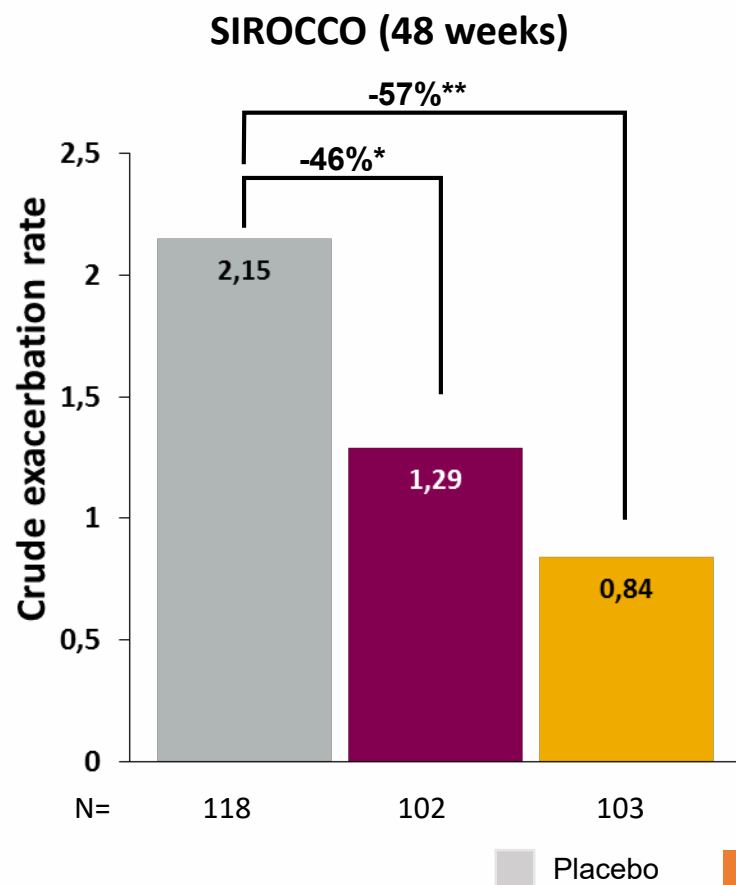
- 32 %



SIROCCO: Benralizumab Reduced the Annual Exacerbation Rate (AER) Compared with Placebo (FAS, eos $\geq 300/\mu\text{L}$)



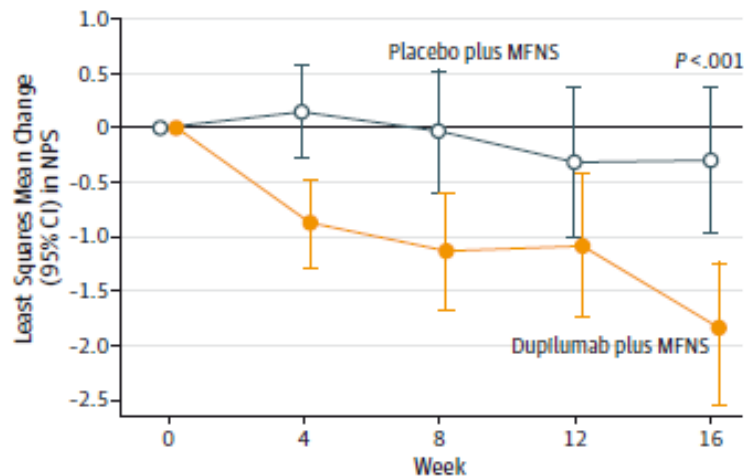
SIROCCO and CALIMA: AER in Patients with ≥ 3 Prior Exacerbations ($\text{eos} \geq 300/\mu\text{L}$)



In both studies Benralizumab produced a similar magnitude reduction of exacerbation

Effect of Subcutaneous Dupilumab on Nasal Polyp Burden in Patients With Chronic Sinusitis and Nasal Polyposis

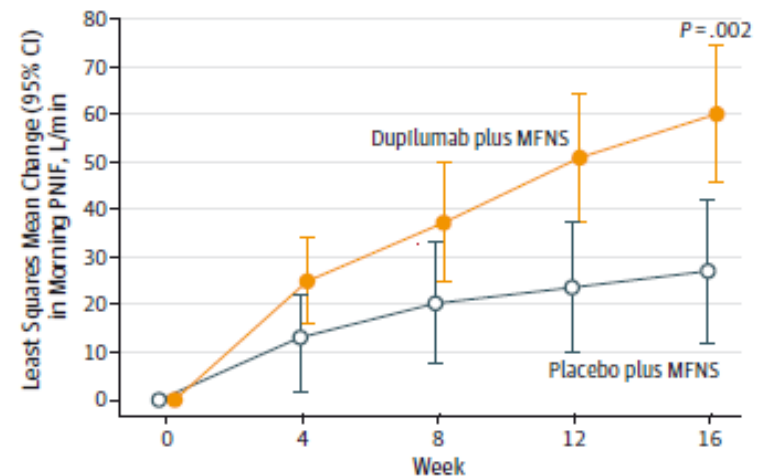
A Endoscopic nasal polyp score (NPS) by treatment group



No. of patients

Placebo plus MFNS	30	29	26	25	23
Dupilumab plus MFNS	30	30	27	26	29

B Morning peak nasal inspiratory flow (PNIF) by treatment group^a

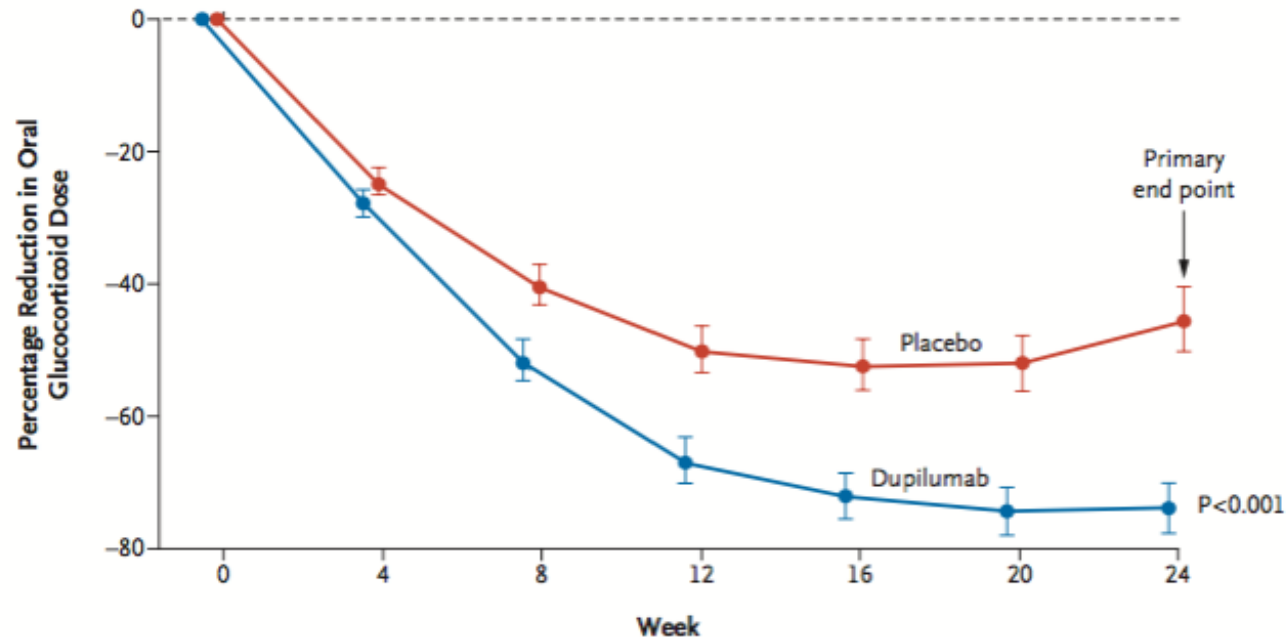


No. of patients

Placebo plus MFNS	30	30	28	26	23
Dupilumab plus MFNS	30	30	29	29	29

Efficacy and Safety of Dupilumab in Glucocorticoid-Dependent Severe Asthma

A Percentage Reduction in Oral Glucocorticoid Dose

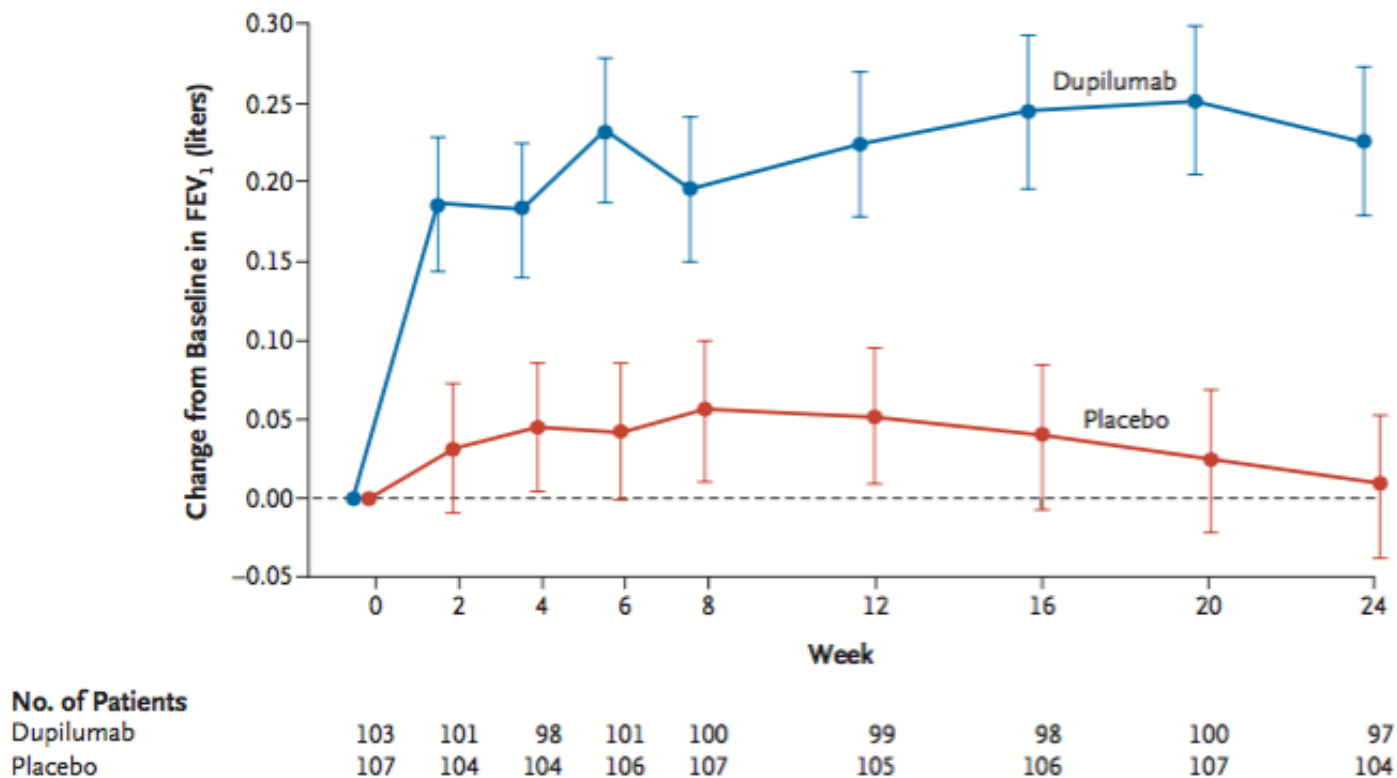


- 71 % oral glucocorticoid dose

No. of Patients

Placebo	107	107	107	107	107	107	106
Dupilumab	103	103	102	101	101	101	101

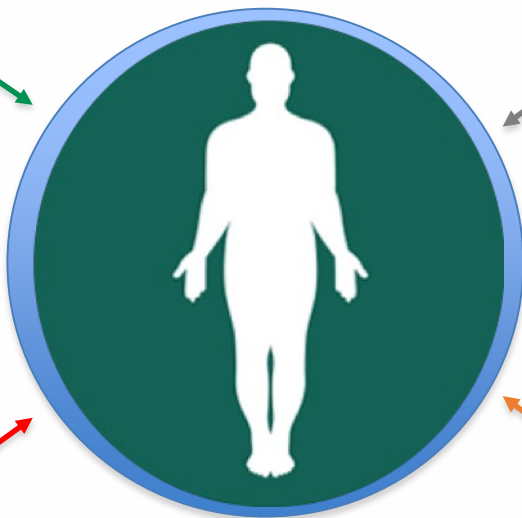
B Change from Baseline in FEV₁ before Bronchodilator Use



Considerazioni cliniche per la terapia biologica nell'asma severa

Quale paziente ?

Quale
biomarcatore ?



Come
monitorare ?

Quale biologico ?