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Mepolizumab: efficacia e sicurezza nella terapia dell'asma grave eosinofilico e comorbidità in età pediatrica

SIMRI
società italiana per le malattie respiratorie infantili

Bambino Gesù
OSPEDALE PEDIATRICO

Renato Cutrera

Direttore UOC Pneumologia e Fibrosi Cistica
Area Semintensiva Pediatrica Respiratoria
UOS Medicina del Sonno e Ventilazione a Lungo Termine
Centro Regionale - ERN Lung Center Malattie Rare Respiratorie

Area Pediatrica Universitaria Ospedaliera
Ospedale Pediatrico Bambino Gesù – IRCCS - Roma

R. Cutrera, 2024, renato.cutrera@opbg.net

Definizione di asma grave

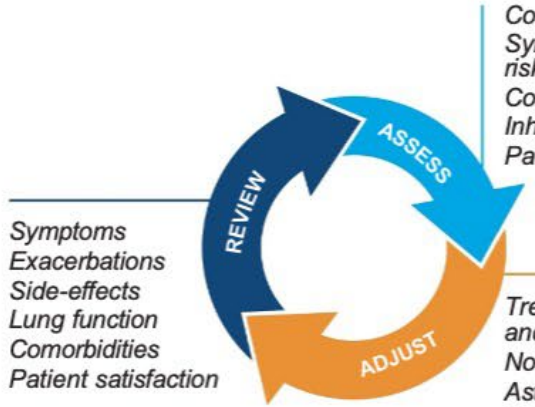
Ad oggi, non esiste una definizione universale di asma grave, tuttavia le diverse società scientifiche concordano nel valutare la gravità dell'asma in base al livello di trattamento richiesto per ottenere e mantenere un controllo adeguato.

Linee guida	Definizione	Scarso controllo dei sintomi	Elevate dosi di ICS
Global Initiative for the treatment of Asthma (GINA) 2022	- Richiede lo step 4 o lo step 5 di trattamento per raggiungere il controllo dei sintomi - Rimane non controllato nonostante l'aderenza a tali step terapeutici e la gestione dei fattori contribuenti	Si	Si
European Respiratory Society/American Thoracic Society (ERS/ATS) 2020	- Necessita di elevate dosi di ICS + un secondo farmaco (LABA, LTRA, teofillina) o OCS per ≥ 50% dell'anno per raggiungere il controllo dei sintomi - Rimane non controllato nonostante questo trattamento	Si	Si
British Thorac Society (BTS) 2016	- Gli attacchi di asma persistono nonostante l'elevato livello terapeutico (dosi moderate di ICS+LABA o LTRA, basse dosi di ICS+LABA o LTRA + una terapia addizionale, ricorso frequente agli OCS)	Si	Si

Votto M, De Filippo M, Licari A, et al. Biological Therapies in Children and Adolescents with Severe Uncontrolled Asthma: A Practical Review. Biologics. 2021.

GINA 2024 – Adults & adolescents 12+ years

Personalized asthma management
Assess, Adjust, Review
for individual patient needs



Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (see Box 2-2)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Comorbidities
Patient satisfaction

Treatment of modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications including ICS (as below)
Education & skills training

TRACK 1: PREFERRED CONTROLLER and RELIEVER
Using ICS-formoterol as the reliever* reduces the risk of exacerbations compared with using a SABA reliever, and is a simpler regimen

STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed-only low dose ICS-formoterol	Low dose maintenance ICS-formoterol	Medium dose maintenance ICS-formoterol	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-formoterol, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol*

See GINA severe asthma guide

TRACK 2: Alternative **CONTROLLER and RELIEVER**
Before considering a regimen with SABA reliever, check if the patient is likely to adhere to daily controller treatment

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
Take ICS whenever SABA taken*	Low dose maintenance ICS	Low dose maintenance ICS-LABA	Medium/high dose maintenance ICS-LABA	Add-on LAMA Refer for assessment of phenotype. Consider high dose maintenance ICS-LABA, ± anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP

RELIEVER: As-needed ICS-SABA*, or as-needed SABA

Other controller options (limited indications, or less evidence for efficacy or safety – see text)

Low dose ICS whenever SABA taken, or daily LTRA†, or add HDM SLIT*	*Medium dose ICS, or add LTRA†, or add HDM SLIT*	*Add LAMA or add LTRA† or add HDM SLIT, or switch to high dose ICS-only*	*Add azithromycin (adults) or add LTRA†. As last resort consider adding low dose OCS but consider side-effects*

*Anti-inflammatory reliever; †advise about risk of neuropsychiatric adverse effects

GINA 2024 Box 4-6

GINA 2024 – Children 6–11 years

Personalized asthma management:
Assess, Adjust, Review

Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (see Box 2-2)
Comorbidities
Inhaler technique & adherence
Child and parent/caregiver preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Comorbidities
Child and parent/ caregiver satisfaction

Treatment of modifiable risk factors & comorbidities
Non-pharmacological strategies
Asthma medications including ICS
Education & skills training

Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	Low dose ICS taken whenever SABA taken*	Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for children)	Low dose ICS-LABA, OR medium dose ICS, OR very low dose ICS-formoterol maintenance and reliever therapy (MART)	Refer for expert advice, OR medium dose ICS-LABA, OR low dose ICS-formoterol maintenance and reliever therapy (MART)	Refer for phenotypic assessment ± higher dose ICS-LABA or add-on therapy, e.g. anti-IgE, anti-IL4Rα, anti-IL5
Other controller options (limited indications, or less evidence for efficacy or safety)		*Daily leukotriene receptor antagonist (LTRA†), or low dose ICS taken whenever SABA taken**	*Low dose ICS + LTRA†*	*Add tiotropium or add LTRA†*	*As last resort, consider add-on low dose OCS, but consider side-effects*
RELIEVER	As-needed SABA (or ICS-formoterol reliever* in MART in Steps 3 and 4)				

*Anti-inflammatory reliever; †advise about risk of neuropsychiatric adverse effects

Adults and adolescents Inhaled corticosteroid	Total daily ICS dose (mcg) Low	Medium	High
BDP (pMDI*, HFA)	200–500	>500–1000	>1000
BDP (DPI or pMDI, extrafine particle, HFA)	100–200	>200–400	>400
Budesonide (DPI or pMDI*, HFA)	200–400	>400–800	>800
Ciclesonide (pMDI, extrafine particle, HFA)	80–160	>160–320	>320
Fluticasone furoate (DPI)	100		200
Fluticasone propionate (DPI)	100–250	>250–500	>500
Fluticasone propionate (pMDI*, HFA)	100–250	>250–500	>500
Mometasone furoate (DPI)	Depends on DPI device		
Mometasone furoate (pMDI*, HFA)	200–400		400
Children 6-11 years **Inhaled corticosteroid**	**Total daily ICS dose (mcg)** **Low**	**Medium**	**High**
BDP (pMDI*, HFA)	100–200	>200–400	>400
BDP (pMDI, extrafine particle, HFA)	50–100	>100–200	>200
Budesonide (DPI)	100–200	>200–400	>400
Budesonide (nebules)	250–500	>500–1000	>1000
Ciclesonide (pMDI, extrafine particle, HFA)	80	>80–160	>160
Fluticasone furoate (DPI)	50		n.a.
Fluticasone propionate (DPI)	50–100	>100–200	>200
Fluticasone propionate (pMDI*, HFA)	50–100	>100–200	>200
Mometasone furoate (pMDI*, HFA)	100		200

BDP: beclometasone dipropionate; DPI: dry powder inhaler; HFA: hydrofluoroalkane propellant; pMDI: pressurized metered dose inhaler. Table shows metered doses.
* standard (non-fine) particle. ICS by pMDI should preferably be used with a spacer..

Epidemiologia Asma in pediatria

Asma in Italia

9,5% - 10,4 %

(6-7 aa -13-14 aa)

Asma Grave:
Asma Grave non trattato
Asma Grave difficile da trattare
Asma grave resistente al trattamento

WHO document Bousquet, J. Et al.
J. Allergy Clin. Immunol. 126, 926–938.

Residenti 6- 18 anni 6.576.000
Asma 657.000
Asma Grave stimati 6.570 – 32.850

Asma Grave in Pediatria
1-5 % dei pazienti asmatici

SIDRIA
Studi italiani sui disturbi respiratori e l'ambiente

Bambino Gesù
OSPEDALE PEDIATRICO

R. Cutrera, 2024, renato.cutrera@opbg.net

SIMRI
società italiana per le malattie respiratorie infantili

Severe asthma features in children: a case–control online survey

Montella et al. Italian Journal of Pediatrics (2016) 42:9

	SA (41)	NSA (78)	P
Hospital admissions for asthma during the past year	12 (25%)	3	<0.001
Emergency-department visits for asthma during the past year	19 (45%)	8	<0.001
Oral steroids for asthma exacerbation in the past year	32 (75%)	34	<0.001
Nocturnal symptoms between exacerbations	22 (50%)	26	0.049
Asthmatic symptoms triggered by physical activity	36 (85%)	41	<0.001

Asma eosinofilico

Fenotipo asmatico caratterizzato da una **elevazione dei markers dell'infiammazione di tipo Th2** (eosinofili, eNo bronchiale su aria esalata, IL4, IL5, IL13).

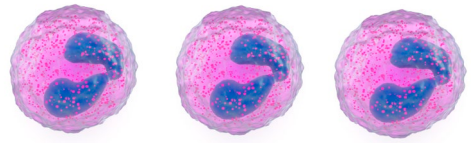
Circa il 70% delle forme di asma grave si caratterizza per una risposta infiammatoria tipo Th2.

E' più frequente tra le forme ad esordio tardivo.

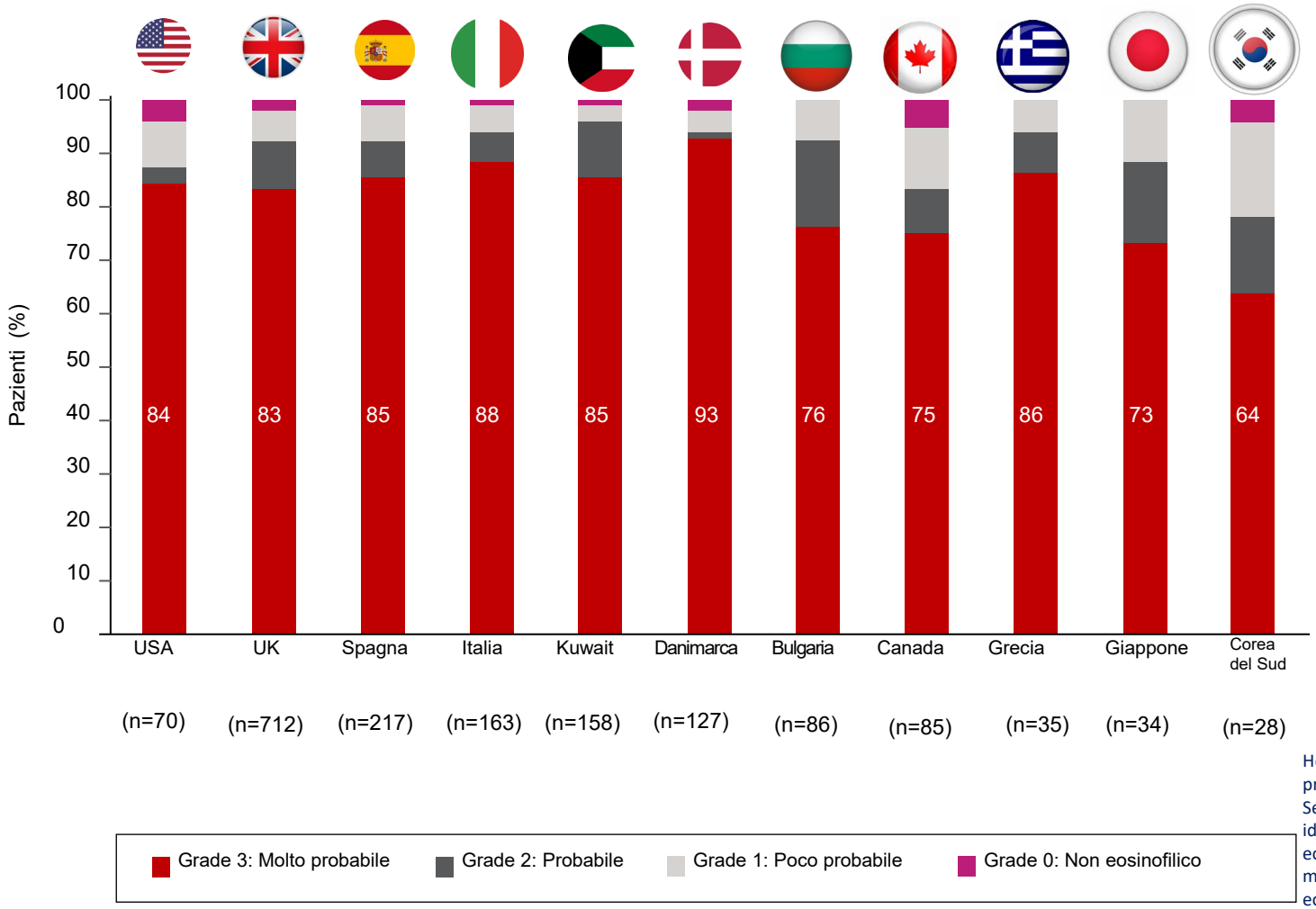
Il **fenotipo eosinofilico** si caratterizza per:

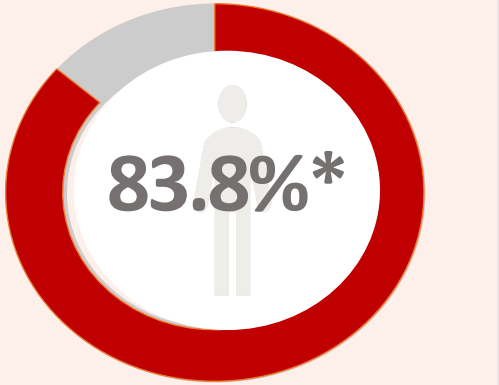
- livelli ematici di Eos compresi tra 200 and 300/microL
- o FeNO superiore a 24 ppb

Up to 84% of patients with severe asthma T2 have an eosinophilic phenotype [1,2]



Distribuzione del fenotipo asma severo eosinofilico per paese nella popolazione ISAR prospettica





Dei pazienti con asma severo hanno mostrato un **fenotipo eosinofilico[12]**

Elaborazione grafica fig. 1,2.

Heaney et al. (2021): studio di registro che coinvolgeva 1716 pazienti adulti con asma eosinofilico severo e presentava dati relativi alla conta eosinofilica ematica provenienti da 11 paesi arruolati nell' International Severe Asthma Registry dal 1 Gennaio 2015 al 30 Settembre 2019 . *83,8% di 1716 pazienti sono stati identificati come più probabili di avere un fenotipo eosinofilico (grado 3), 8,3% probabili di avere un fenotipo eosinofilico (grado 2) e 6,3% meno probabili di avere un fenotipo eosinofilico (grado 1) e 1,6% hanno mostrato un fenotipo non eosinofilico (grado 0). I pazienti con più probabilità di avere un fenotipo eosinofilico erano più anziani, avevano un asma ad insorgenza tardiva e mostravano una funzionalità polmonare peggiore rispetto a coloro con fenotipo non eosinofilico (1,6%).[12]

ISAR, International Severe Asthma Registry.

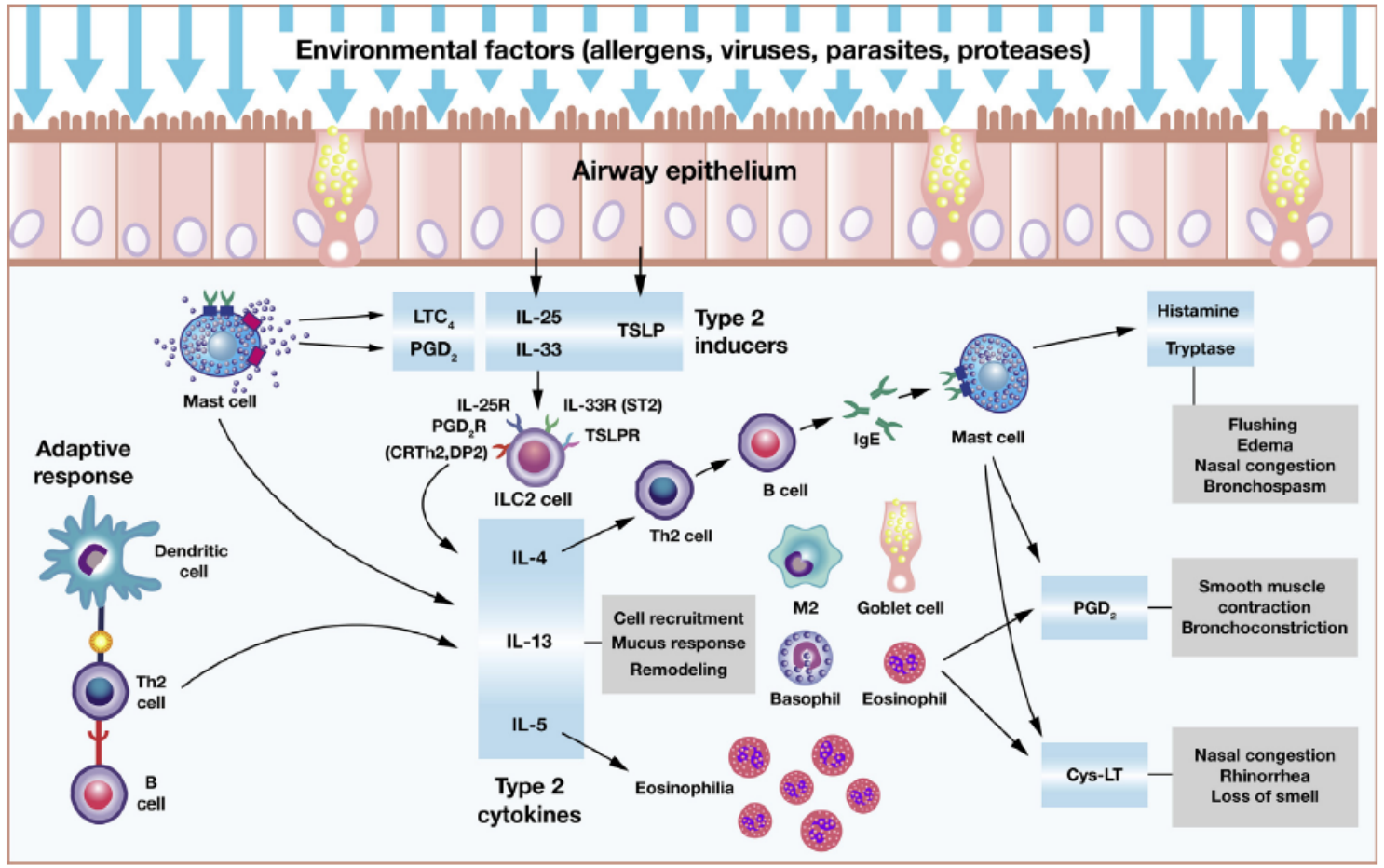
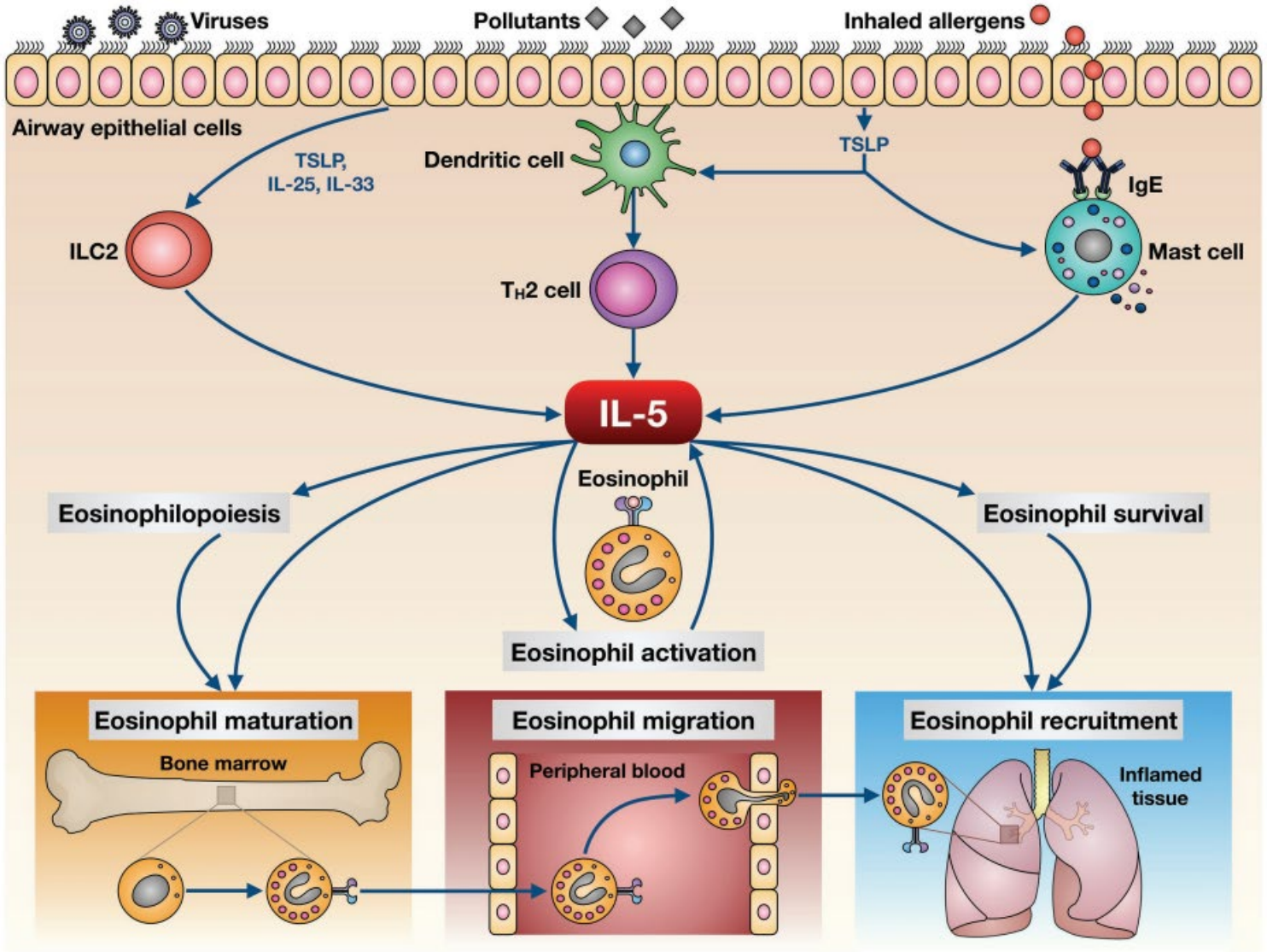


FIGURE 2. Type 2 inflammation pathway in upper and lower airway diseases. Antigen-presenting cells, including dendritic cells and B cells, activate Th2 cells to produce IL-4, IL-13, and IL-5. These cytokines are key and central drivers of type 2 inflammation, activating/recruiting mast cells, eosinophils, basophils, goblet cells, M2 macrophages, and B cells, and they are responsible for many inflammatory tissue responses. *Cys-LT*, Cysteinyl leukotriene; *ILC*, innate lymphoid cell; *LTC_4*, leukotriene C_4; PGD_2 ($CRTh_2$,DP_2), prostaglandin D_2; Th2, T helper 2; *TSLP*, thymic stromal lymphopoietin. Figure adapted with permission from Hulse et al.[23]

Infiammazione Th2 nelle alte e basse vie aeree



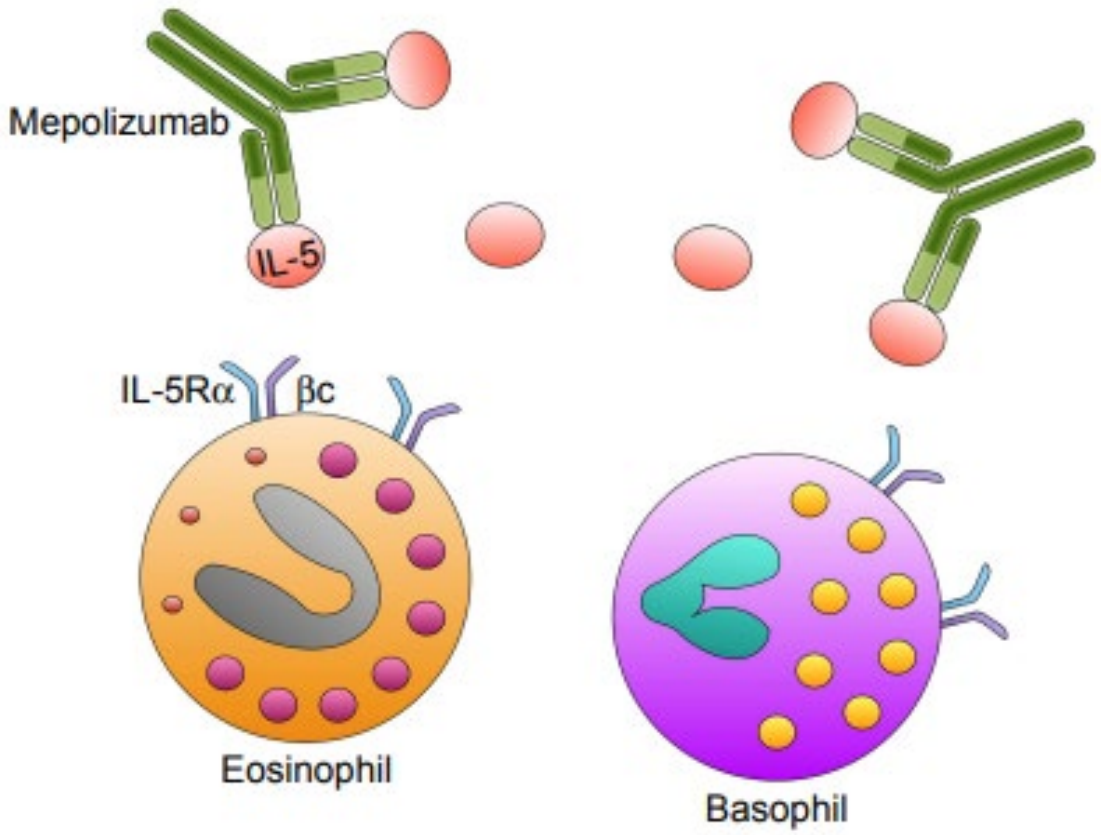
Pelaia C, Paoletti G, Puggioni F, et al. Interleukin-5 in the Pathophysiology of Severe Asthma. Frontiers in Physiology. 2019.

Mepolizumab: approvazione e meccanismo d'azione

Mepolizumab (Nucala, GlaxoSmithKline) è stato approvato dalla Food and Drug Administration e dall' European Medicines Agency nei pazienti di età superiore ai 12 anni a Novembre 2015 e a partire dai 6 anni a Settembre 2019, come terapia di mantenimento per l'asma grave eosinofilico.

Mepolizumab è un anticorpo monoclonale murino umanizzato appartenente alle IgG4 sottoclasse k.

Mepolizumab lega l'IL-5 circolante prevenendone l'interazione con il recettore alfa; tramite questo meccanismo d'azione inibisce la chemiotassi, l'attivazione e la sopravvivenza degli eosinofili.

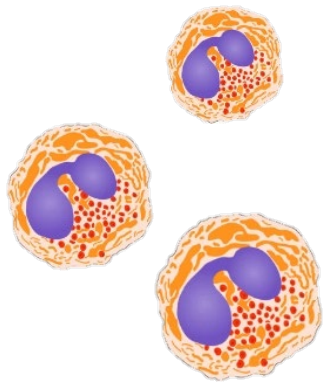


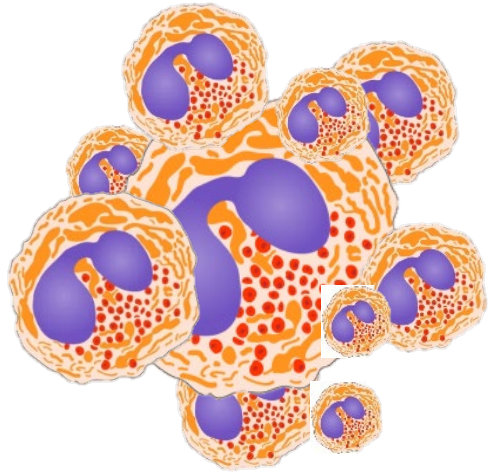
Pelaia C, Vatrella A, Busceti MT, et al. Severe eosinophilic asthma: from the pathogenic role of interleukin-5 to the therapeutic action of mepolizumab. Drug Design, Development and Therapy. 2017.

Role of eosinophils: two sides to the eosinophil story

Eosinofili giocano un ruolo importante:[1,2]

- Omeostasi del sistema immunitario
- Difesa contro i patogeni





Troppi eosinofili:[3]

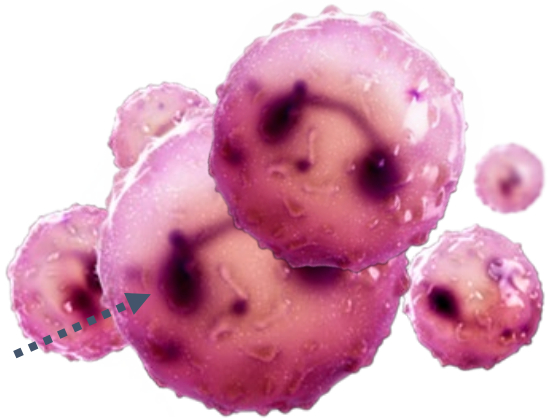
- Possono portare ad un danno tissutale

1. Wen T, Rothenberg ME. *Microbiol Spectr*. 2016;4:10.1128/microbiolspec.MCHD-0020-2015. **2. Weller PF, Spencer LA.** *Nat Rev Immunol*. 2017;7:746–60. **3. Baldini C, *et al*.** *Rheum Dis Clin North Am*. 2010;36:527–43.

R. Cutrera, 2024, renato.cutrera@opbg.net

Eosinofilo tra rischio e beneficio

Gli eosinofili omeostatici hanno ruoli variegati nell'omeostasi e nell'immunità



Tipo 1: Eosinofili regolatori omeostatici

Steady State

IL-5-dipendente

- **Intestino**
  - Risposta IgA mediata
  - Produzione di muco
- **Tessuto adiposo**
  - Mantenimento di AAMs
  - Sensibilità all'insulina
- **Utero**
  - *Preparazione dell'utero per la gravidanza*
  - *Ciclo mestruale*

IL-5-dipendente?

- **Timo**
  - *Selezione negativa delle Cellule T?*
- **Ghiandola mammaria**
  - Sviluppo della ghiandola mammaria

IL-5-indipendente

- **Polmone**
  - Prevenzione della risposta allergica T_H2 mediata

La funzione descritta *in corsivo* è stata suggerita, ma manca ancora una dimostrazione chiara.

AAM: alternatively activated macrophage

Abdala-Valencia H, et al. *J Leukoc Biol.* 2018;104:95–108; **Marichal T, et al.** *Front Med (Lausanne).* 2017;4:101.

The Journal of Clinical Investigation jci.org Volume 126 Number 9 September 2016 3185

A hidden residential cell in the lung

Marc E. Rothenberg

Division of Allergy and Immunology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA.

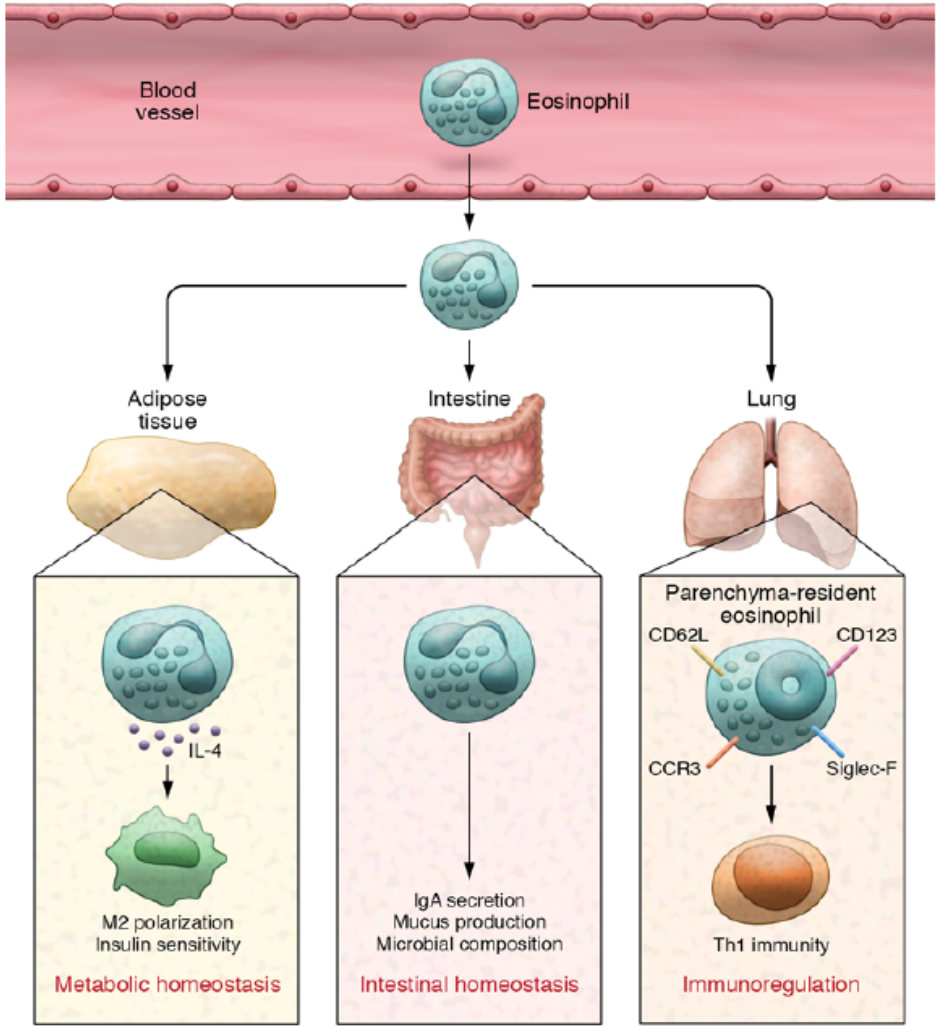
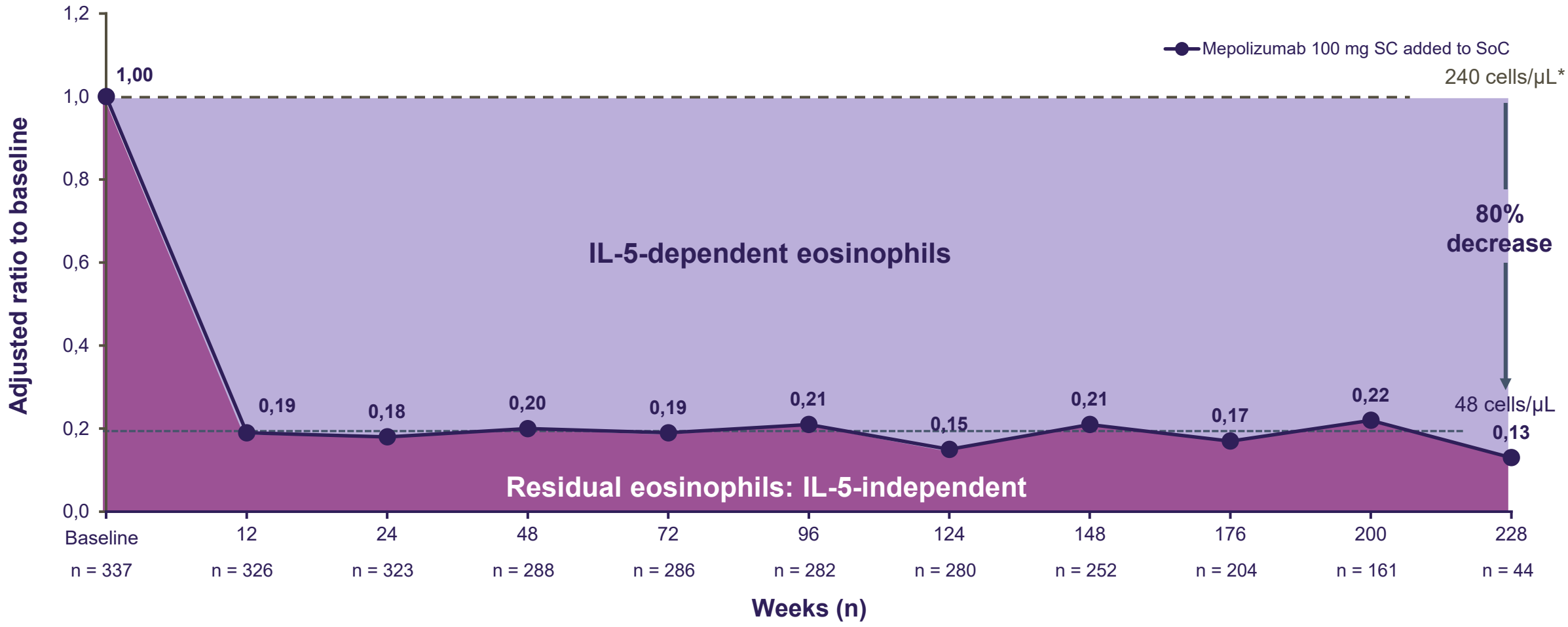


Table 1. Differential properties of rEos and iEos

Property	rEos	iEos
Location	Lung parenchyma	Peribronchial
Nucleus	Ringed	Segmented
Allergen induced	No	Yes
Siglec-F levels	Intermediate	High
CD62L levels	High	Low
CD101 levels	Low	High
IL-5 dependent	No	Yes
Role	Immunosuppressive	Proinflammatory

Mepolizumab reduces eosinophils to within the normal range: suggestive of two human eosinophil populations: IL-5-dependent and IL-5-independent



*Geometric mean at baseline. **Note:** Where a result of zero was recorded, a small value (i.e. minimum all non-missing results/2) was added prior to log transformation.

1. Khatri S, *et al.* *J Allergy Clin Immunol*. 2019;143:1742–51. **2. Mesnil C, *et al.*** *J Clin Invest*. 2016;126:3279–95.

Mepolizumab: criteri di efficacia

I dati sull'efficacia di Mepolizumab sono stati raccolti da diversi trials clinici condotti in adulti e bambini di età superiore ai 12 anni, tra i quali si ricordano lo studio Dose-Ranging Efficacy And Safety With Mepolizumab In Severe Asthma (DREAM), lo studio Mepolizumab As Adjunctive Therapy In Patients With Severe Asthma (MENSA), lo studio Steroid Reduction With Mepolizumab Study (SIRIUS) e lo studio Mepolizumab Adjunctive Therapy In Subjects With Severe Eosinophilic Asthma (MUSCA).

Più recentemente un multinazionale, non-randomizzato, studio in aperto è stato condotto da Gupta et al. in pazienti di età compresa tra i 6 e gli 11 anni.

Comberiati P, McCormack K, Malka-Rais J, et al. Proportion of Severe Asthma Patients Eligible for Mepolizumab Therapy by Age and Age of Onset of Asthma. The Journal of Allergy and Clinical Immunology: in Practice. 2019.

Lancet 2012; 380: 651–59

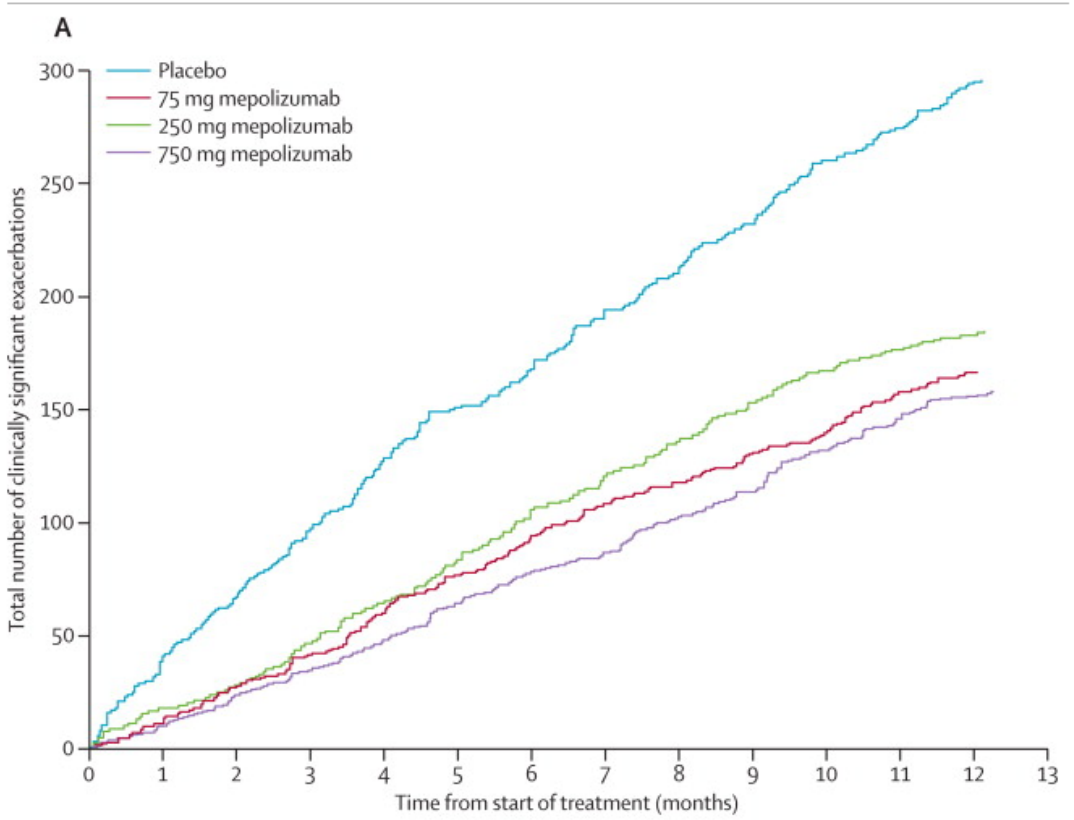
Mepolizumab for severe eosinophilic asthma (DREAM): a multicentre, double-blind, placebo-controlled trial

Ian D Pavord, Stephanie Korn, Peter Howarth, Eugene R Bleecker, Roland Buhl, Oliver N Keene, Hector Ortega, Pascal Chanez

STUDIO DREAM

Gruppo di studio:
616 soggetti di età 12-74 anni trattati con Mepolizumab
per 52 settimane vs placebo

Risultati:
- le riacutizzazioni si sono ridotte significativamente rispetto al placebo
- gli AQLQ e ACQ scores non hanno mostrato differenze significative rispetto al placebo
- il FEV1 non ha mostrato differenze significative rispetto al placebo



ORIGINAL ARTICLE

N Engl J Med 2014;371:1198-207

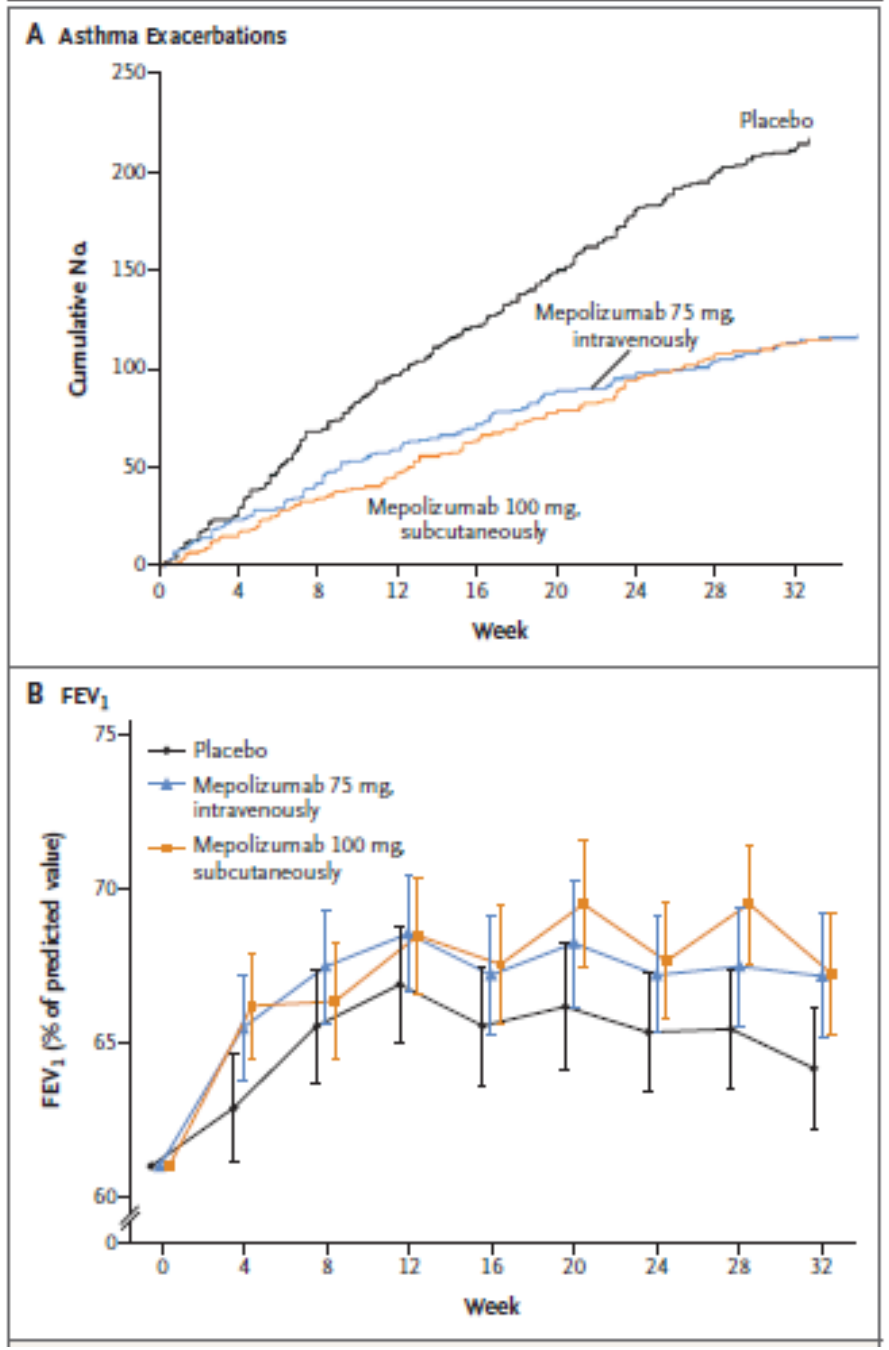
Mepolizumab Treatment in Patients with Severe Eosinophilic Asthma

Hector G. Ortega, M.D., Sc.D., Mark C. Liu, M.D., Ian D. Pavord, D.M., Guy G. Brusselle, M.D., J. Mark FitzGerald, M.D., Alfredo Chetta, M.D., Marc Humbert, M.D., Ph.D., Lynn E. Katz, Pharm.D., Oliver N. Keene, M.Sc., Steven W. Yancey, M.Sc., and Pascal Chanez M.D., Ph.D., for the MENSA Investigators*

STUDIO MENSA

Gruppo di studio:
576 soggetti di età 12-82 anni trattati con Mepolizumab
per 32 settimane vs placebo

Risultati:
- le riacutizzazioni si sono ridotte significativamente rispetto al placebo
- l'ACQ score è migliorato significativamente rispetto al placebo
- il FEV1 pre e post-broncodilatazione è aumentato significativamente rispetto al placebo



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 25, 2014 VOL. 371 NO. 13

Oral Glucocorticoid-Sparing Effect of Mepolizumab in Eosinophilic Asthma

Elisabeth H. Bel, M.D., Ph.D., Sally E. Wenzel, M.D., Philip J. Thompson, M.D., Charlene M. Prazma, Ph.D., Oliver N. Keene, M.Sc., Steven W. Yancey, M.Sc., Hector G. Ortega, M.D., Sc.D., and Ian D. Pavord, D.M., for the SIRIUS Investigators*

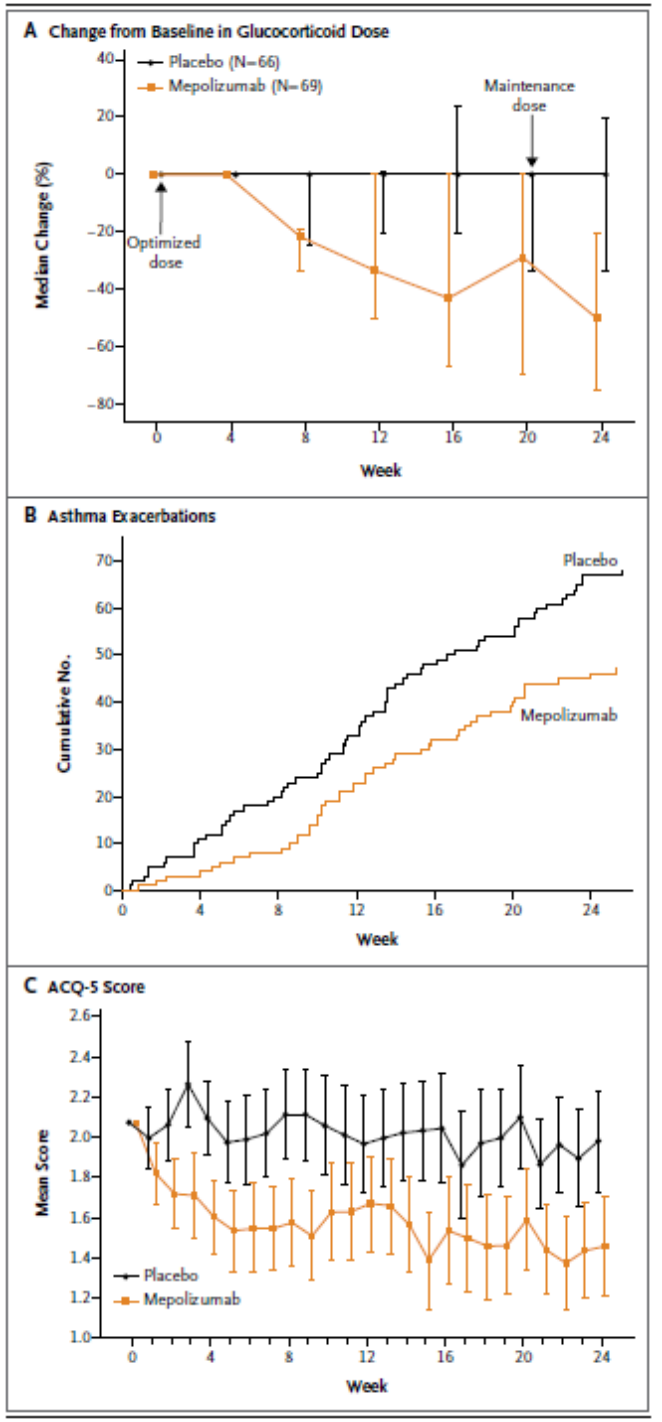
STUDIO SIRIUS

Gruppo di studio:

135 soggetti di età 16-74 anni trattati con Mepolizumab per 20 settimane vs placebo

Risultati:

- Il consumo giornaliero di corticosteroidi orali e le riacutizzazioni si sono ridotte significativamente rispetto al placebo
- l'ACQ score è migliorato significativamente rispetto al placebo
- il FEV1 non ha mostrato differenze significative rispetto al placebo



Lancet Respir Med 2017

Efficacy of mepolizumab add-on therapy on health-related quality of life and markers of asthma control in severe eosinophilic asthma (MUSCA): a randomised, double-blind, placebo-controlled, parallel-group, multicentre, phase 3b trial

Geoffrey L Chupp, Eric S Bradford, Frank C Albers, Daniel J Bratton, Jie Wang-Jairaj, Linda M Nelsen, Jennifer L Trevor, Antoine Magnan, Anneke ten Brinke

STUDIO MUSCA

Gruppo di studio:

551 soggetti di età > 12 anni trattati con Mepolizumab per 24 settimane vs placebo

Risultati:

- il SGRQ score è migliorato significativamente rispetto al placebo
- le riacutizzazioni si sono ridotte significativamente rispetto al placebo
- il FEV1 pre-broncodilatazione è aumentato significativamente rispetto al placebo

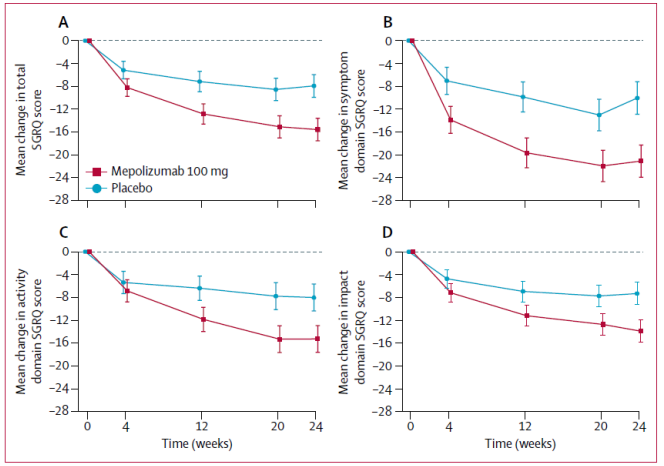


Figure 3: **St George's Respiratory Questionnaire (SGRQ) scores at each visit**
Figure shows adjusted mean changes (95% CI) from baseline in (A) total SGRQ score, (B) symptom domain SGRQ score, (C) activity domain SGRQ score, and (D) impacts domain SGRQ score.

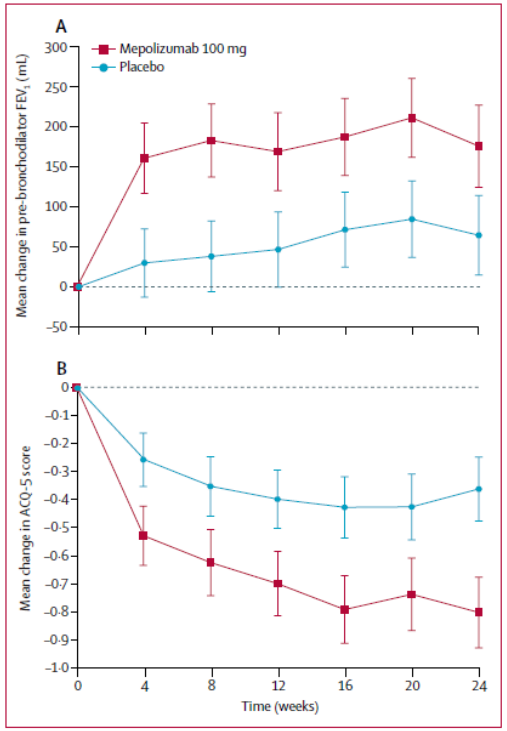


Figure 4: **Secondary endpoints at each visit**
Data are adjusted mean changes (95% CI) from baseline in (A) pre-bronchodilator FEV_1 and (B) Asthma Control Questionnaire (ACQ)-5 scores.

R. Cutrera, 2024, renato.cutrera@opbg.net

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Check for updates

ORIGINAL ARTICLE: ASTHMA
Pediatric Pulmonology. 2019;54:1957–1967

Subcutaneous mepolizumab in children aged 6 to 11 years with severe eosinophilic asthma

Atul Gupta MD(Res)[1] | Isabelle Pouliquen PharmD[2] | Daren Austin PhD[2] | Robert G. Price MSc[3] | Rodger Kempsford PhD[4] | Jonathan Steinfeld MD[5] | Eric S. Bradford MD[6] | Steven W. Yancey MSc[6]

STUDIO di Gupta et. al

Gruppo di studio:
36 soggetti di età 6-11 anni trattati con Mepolizumab per 12 settimane vs placebo

Risultati:
- le riacutizzazioni si sono ridotte significativamente rispetto al placebo
- l'ACQ score è migliorato significativamente rispetto al placebo
- il FEV1 non ha mostrato differenze significative rispetto al placebo

TABLE 4 Summary of secondary and other endpoints: ACQ-7 and C-ACT total scores and exacerbations

	Mean (95% CI)		
	Mepolizumab 40 mg SC (weight <40 kg) (N = 26)	Mepolizumab 100 mg SC (weight ≥40 kg) (N = 10)	Total (N = 36)
Blood eosinophil counts, cells/μL			
Ratio to baseline at week 4	0.19 (0.13, 0.28)	0.22 (0.08, 0.61)	0.20 (0.14, 0.29)
Ratio to baseline at week 8	0.11 (0.08, 0.16)	0.14 (0.07, 0.29)	0.12 (0.09, 0.16)
Ratio to baseline at week 12	0.12 (0.07, 0.20)	0.17 (0.09, 0.32)	0.13 (0.09, 0.19)
% reduction from baseline at week 12	88.5	83.4	87.1
ACQ-7 score[a]			
Change from baseline at week 4	−0.55 (−1.01, −0.09)	−0.47 (−1.16, 0.21)	−0.53 (−0.89, −0.16)
Change from baseline at week 8	−0.65 (−1.15, −1.16)	−0.30 (−1.19, 0.59)	−0.55 (−0.97, −0.14)
Change from baseline at week 12	−0.41 (−0.91, 0.08)	0.08 (−0.88, 1.04)	−0.26 (−0.69, 0.16)
≥0.5 point reduction from baseline, n/N (%)	11/23 (48)	5/10 (50)	16/33 (48)
C-ACT score[b]			
Change from baseline at week 4	1.8 (0.2, 3.5)	2.4 (−0.9, 5.7)	2.0 (0.6, 3.4)
Change from baseline at week 8	3.0 (0.7, 5.4)	1.5 (−1.6, 4.6)	2.6 (0.8, 4.4)
Change from baseline at week 12	2.1 (0.2, 4.1)	−0.3 (−4.0, 3.4)	1.4 (−0.3, 3.1)
Prebronchodilator FEV_1 (mL)			
Change from baseline at week 4	93 (−19, 206)	55 (−52, 162)	83 (−1, 167)
Change from baseline at week 8	90 (−17, 198)	−63 (−314, 188)	48 (−52, 148)
Change from baseline at week 12	72 (−37, 181)	2 (−175, 179)	51 (−37, 139)
Patients with on-treatment exacerbations (weeks 0–12), n (%)			
Any	8 (31)	2 (20)	10 (28)
1 exacerbation	6 (23)	1 (10)	7 (19)
2 exacerbations	2 (8)	1 (10)	3 (8)

Data are mean (95% CI) unless stated otherwise; [a]decreased scores, or [b]increased scores, from baseline indicate improvement in asthma control.
Abbreviations: ACQ-7, Asthma Control Questionnaire; C-ACT, Childhood Asthma Control Test; CI, confidence interval; FEV_1, forced expiratory volume in 1 s; SC, subcutaneous.

Evolving evidence suggests IL-5 also has an impact beyond eosinophils, leading to epithelial barrier dysfunction, airways remodelling and disease progression[1–8]

IL-5 signalling

Downregulates genes relating to tight junctions and barrier function in **ciliated epithelial cells**[1,2]

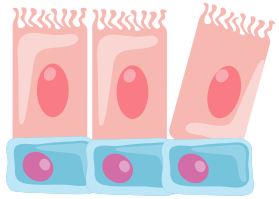
Enhanced proliferation and activation of **fibroblasts**[3]

Differentiation, proliferation and survival of **eosinophils**,[9] contributing to increased eosinophil protein signalling and downstream airway remodelling effects[4]

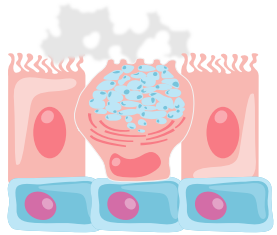
IL-5 signalling stimulates expression of functional IL-5Rα on **plasma cells**[1,5]

Mediate **T_{reg} cell** production[6]

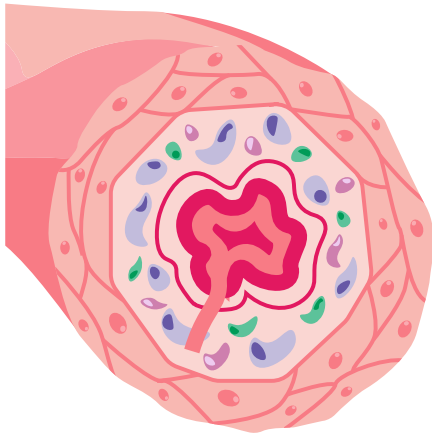
Mediate **ILC2** activity[7]



Promotes **epithelial barrier dysfunction and fibrosis**[1–3]



Role in **immune responses**[1,4–7,9] and formation of **mucus plugs**[10]



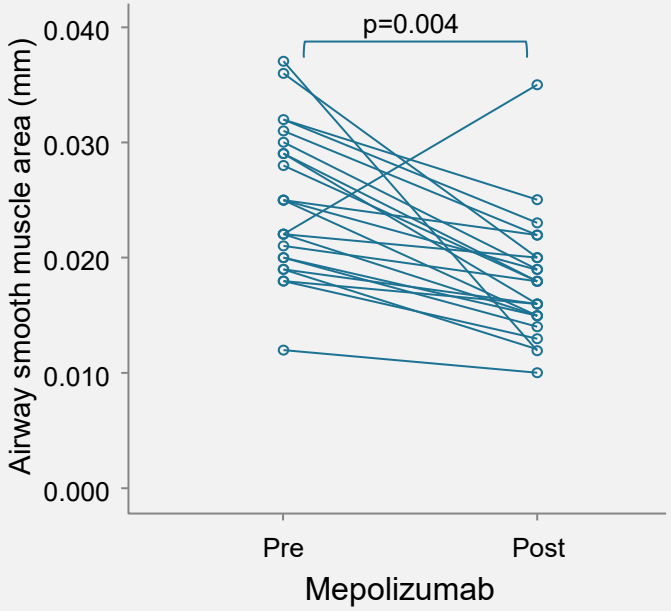
Leads to **airway remodelling**[8] **and disease progression**[11]

IL, interleukin; IL-5Rα, interleukin-5 receptor alpha; ILC, innate lymphoid cell; T_{reg}, regulatory T cell.

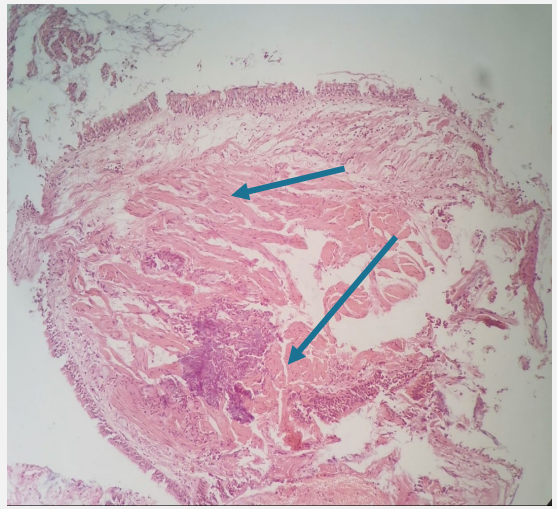
1. Buchheit KM, et al. *J Allergy Clin Immunol* 2021;148:574–584; 2. Barretto KT, et al. *Allergy* 2020;75:2127–2130; 3. Bajbouj K, et al. *Allergy* 2023;78:882–885;
4. Siddiqui S, et al. *J Allergy Clin Immunol* 2023;152:841–857; 5. Buchheit KM, et al. *J Allergy Clin Immunol* 2020;145:1574–1584; 6. Bergantini L, et al. *Scand J Immunol* 2021;94:e13031;
7. Malik B, et al. *Respirology* 2023;28:758–766; 8. Abstract OA3152 - Domvri K;European Respiratory Journal;2023;62;1-5; 9. Pelaia C, et al. *Front Physiol* 2019;10:1514; 10. Dunican EM, et al. *J Clin Invest* 2018;128:997–1009; 11. Huang Y, et al. *Ann Transl Med* 2022;10:1023.

MESILICO: anti-IL-5 treatment was associated with a reduction in smooth muscle area in endobronchial biopsies

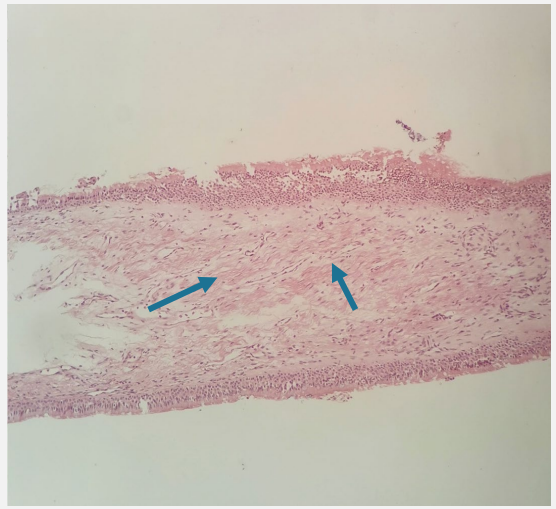
H&E staining (x10) showing airway smooth muscle layer in endobronchial biopsies



Pre-treatment



After 12 months of mepolizumab treatment



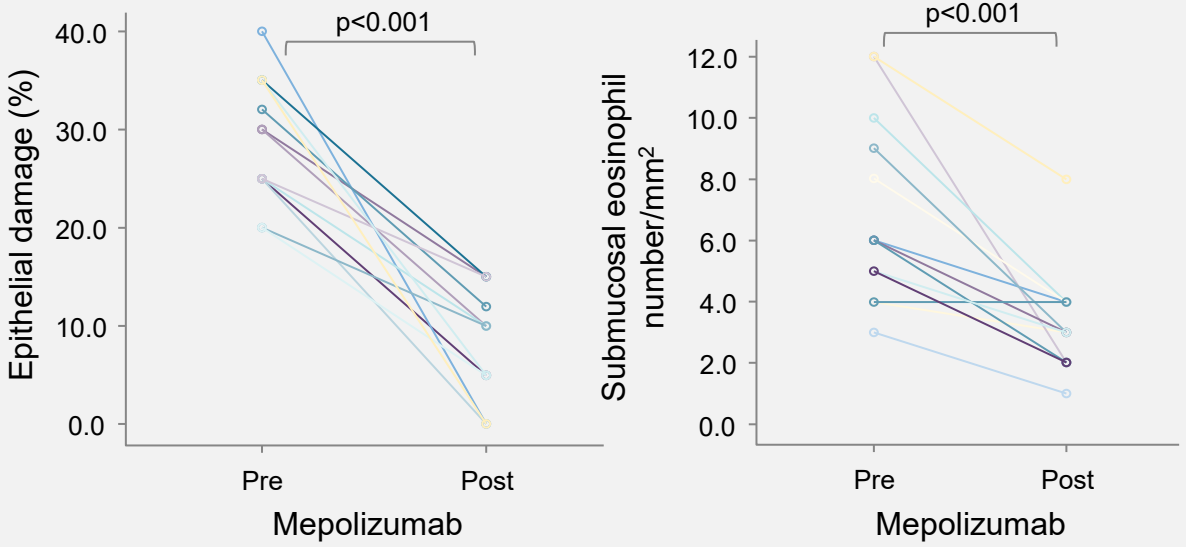
Treatment with mepolizumab resulted in a significant reduction (mean 27%) in airway smooth muscle area (p=0.004)

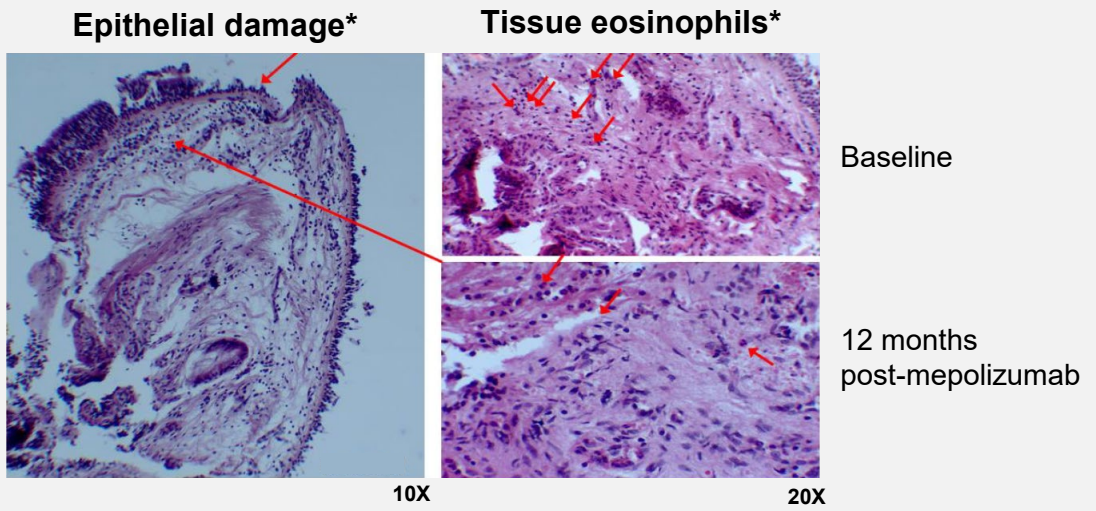
No equivalent data with reslizumab or benralizumab.
H&E, haematoxylin and eosin; IL, interleukin.
1. Domvri K, et al. ERS 2023. Poster #3152, 2. Domvri et al OA3152 European Respiratory Journal, DOI: 10.1183/13993003.congress-2023..

Bambino Gesù
OSPEDALE PEDIATRICO

SIMRI
società italiana per le malattie respiratorie infantili

MESILICO: anti-IL-5 treatment was associated with a significant improvement in bronchial epithelial integrity





Improvement in epithelial integrity with mepolizumab was associated with a decrease in submucosal eosinophils

No equivalent data with reslizumab or benralizumab. *Representative images; H&E stained.
H&E, haematoxylin and eosin; IL, interleukin; SD, standard deviation.
1. Domvri K, et al. ERS 2023. Poster #3152, 2. Domvri et al OA3152 European Respiratory Journal, DOI: 10.1183/13993003.congress-2023..

Bambino Gesù OSPEDALE PEDIATRICO

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Since 2014, the Global Initiative for Asthma(GINA) has focused on asthma control and personalized management of patients'modifiable risk factors, including comorbidities. [1,2]

Investigation for the presence of comorbidities is recommended at every part of the asthma management journey, and multimorbidity is recognized as a common problem in patients with asthma.[1]

Some of these comorbidities can:
- Complicate asthma treatment ,considerably increase the risk of poor asthma-related outcomes,[3-5]
- Are associated with significant productivity losses.[6]
- Overall comorbidity-attributable health care costs are 5 times- higher than costs attributable to asthma alone.[7]

Type 2 (T2) inflammatory comorbidities	Comorbidities potentially related to oral corticosteroid (OCS) exposure	Comorbidities that mimic-raggravate asthma symptoms ,with some overlap between categories

1GlobalInitiativeforAsthma.Globalstrategyforasthmamanagementandpreven-tion.2023.Availableat:https://ginasthma.org/wp-content/uploads/2023/05/GINA-2023-Full-Report-2023-WMS.pdf.AccessedSeptember22,2023. 2.GlobalInitiativeforAsthma.Globalstrategyforasthmamanagementandpreven-tion.Revised2014.Availableat:https://ginasthma.org/wp-content/uploads/2019/01/2014-GINA.pdf.AccessedSeptember22,2023.
3.PatelGB,PetersAT.Comorbiditiesassociatedwithsevereasthma.JPrecisRespirMed.2019;2(1):5–9.
4.ChanoineS,SanchezM,PinI,TemamS,LeMoualN,FournierA,etal.Multimorbid-itymedicationsandpoorasthmaprognosis.EurRespirJ.2018;51(4):1702114.
5.PriceD,Menzies-GowA,BachertC,CanonicaGW,KocksJ,KhanAH,etal.Associa-tionbetweenatype2inflammatorydiseaseburdenscoreandoutcomesamongpatientswithasthma.JAsthmaAllergy.2021;14:1173–1183.
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7.ChenW,LyndLD,FitzGeraldJM,MarraCA,BalshawR,ToT,etal.Excessmedicalcostsinpatientswithasthmaandtheroleofcomorbidity.EurRespirJ.2016;48(6):1584–1592.
8.ChungKF.Definingphenotypesinasthma:asteptowardspersonalizedmedicine.Drugs.2014;74(7):719–728.
9.PorsbjergC,Menzies-GowA.Co-morbiditiesinsevereasthma:clinicalimpactandmanagement.Respirology.2017;22(4):651–661.

Table 1
Prevalence of 30 Comorbid Conditions in Patients With Severe Asthma

Comorbidities	Number of contributing countries	Sample size[a]	N[b]	Prevalence
Potentially T2-related categories				
Allergic rhinitis	22	11,281	5525	49%
Chronic rhinosinusitis[c]	21 (all −AU)	11,223	5151	46%
Nasal polyposis	22	11,613	2413	21%
Eczema or atopic dermatitis	22	11,600	1199	10%
Urticaria	4 (AU, ES, UK, USA)	6849	243	3.5%
Food allergy	5 (AU, ES, PT, UK, USA)	6977	230	3.3%
Aspirin sensitivity	7 (AU, CA, DK, ES, PT, UK, USA)	7498	122	1.6%
Eosinophilic esophagitis	3 (AU, UK, USA)	6149	32	0.52%
Potentially OCS-related comorbidities				
Obesity	22	11,583	4893	42%
Hypertension	12 (AU, ES, IT, JP, MX, PL, PT, SK, TW, UAE, UK, USA)	9252	2104	23%
Sleep apnea	21 (all −IT)	10,094	2256	22%
Dyslipidemia	4 (AU, ES, UK, USA)	6849	1083	16%
Anxiety or depression[d]	21 (all −DK)	11,019	1565	14%
Osteoporosis	21 (all −DK)	10,742	1371	13%
Diabetes	22	11,422	1336	12%
Coronary heart disease	22	11,039	984	8.9%
Pneumonia	20 (all −DK, −ES)	10,300	877	8.5%
Other significant infections	20 (all −IE, −PT)	6918	560	8.1%
Peptic ulcer	20 (all −DK, -ES)	10,323	266	2.6%
Pulmonary embolism or VTE	20 (all −DK, −ES)	9972	246	2.5%
Cataract	21 (all −DK)	10,923	258	2.4%
Chronic kidney disease	21 (all −DK)	11,032	164	1.5%
Adrenal insufficiency	3 (AU, UK, USA)	6149	80	1.3%
Glaucoma	21 (all −DK)	10,888	139	1.3%
Cerebrovascular accident	20 (all −DK, −ES)	9968	63	0.63%
Comorbidities mimicking or aggravating asthma				
GERD[e]	7 (AU, CA, DK, ES, PT, UK, USA)	7400	3243	44%
COPD	7 (AU, CA, DK, ES, PT, UK, USA)	7508	1045	14%
Bronchiectasis	7 (AU, CA, DK, ES, PT, UK, USA)	7509	799	11%
VCD or laryngeal spasms	5 (AU, DK, ES, UK, USA)	7199	758	11%
Dysfunctional breathing	6 (AU, CA, DK, ES, UK, USA)	7389	234	3.2%

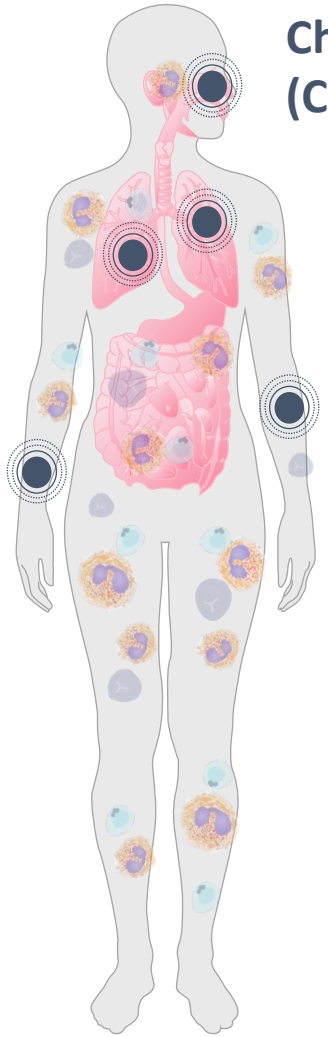
Abbreviations: AU, Australia; CA, Canada; COPD, chronic obstructive pulmonary disease; DK, Denmark; ES, Spain; GERD, gastroesophageal reflux disease; IE, Ireland; IT, Italy; JP, Japan; MX, Mexico; OCS, oral corticosteroid' PL, Poland; PT, Portugal; SK, South Korea; T2, type 2; TW, Taiwan; UAE, United Arab Emirates; UK, United Kingdom; USA, United States of America; VCD, vocal cord dysfunction; VTE, venous thromboembolism.
[a]Variations in sample size are because of missing values for individual patients and/or at the country level.
[b]Number of patients with comorbidity.
[c]With or without nasal polyposis.
[d]Can also mimic or aggravate asthma.
[e]Can also be OCS related.

Eosinophilic inflammation is an important component of the pathogenesis of T2 eosinophilic disease and related co-morbidities [1-6]

Chronis rhinosinusitis with nasal polyps (CRSwNP)

Chronic obstructive pulmonary disease (COPD)[a]

Severe Eosinophilic Asthma (SEA)



Hypereosinophilic syndrome (HES)

Eosinophilic granulomatosis with polyangiitis (EGPA)

Elevated eosinophil numbers are a common thread among several conditions [1]

The presence of multiple comorbidities may be an indicator of underlying eosinophilic-driven inflammation [1,7,8]

[a] Mepolizumab non è indicato nel trattamento della COPD

1. Wechsler ME, et al. *Mayo Clin Proc*. 2021;96:2694-2707; 2. Schleimer RP. *Annu Rev Pathol*. 2017;12:331-357; 3. Travers J & Rothenberg ME. *Mucosal Immunol*. 2015;8:464-475; 4. Tworek D & Antczak A. *Adv Respir Med*. 2017;85:271-276; 5. Furuta S et al. *Allergol Int*. 2019;68:430–436; 6. Sastre B et al. *J Investig Allergol Clin Immunol*. 2018;28:289–304; 7. Lambrecht BN, Hammad H. *Nat Immunol.* 2015;16:45–56; 8. de Groot JC, et al. *ERJ Open Res*. 2015;1(1):00024-2015.

Bambino Gesù OSPEDALE PEDIATRICO

R. Cutrera, 2024, renato.cutrera@opbg.net

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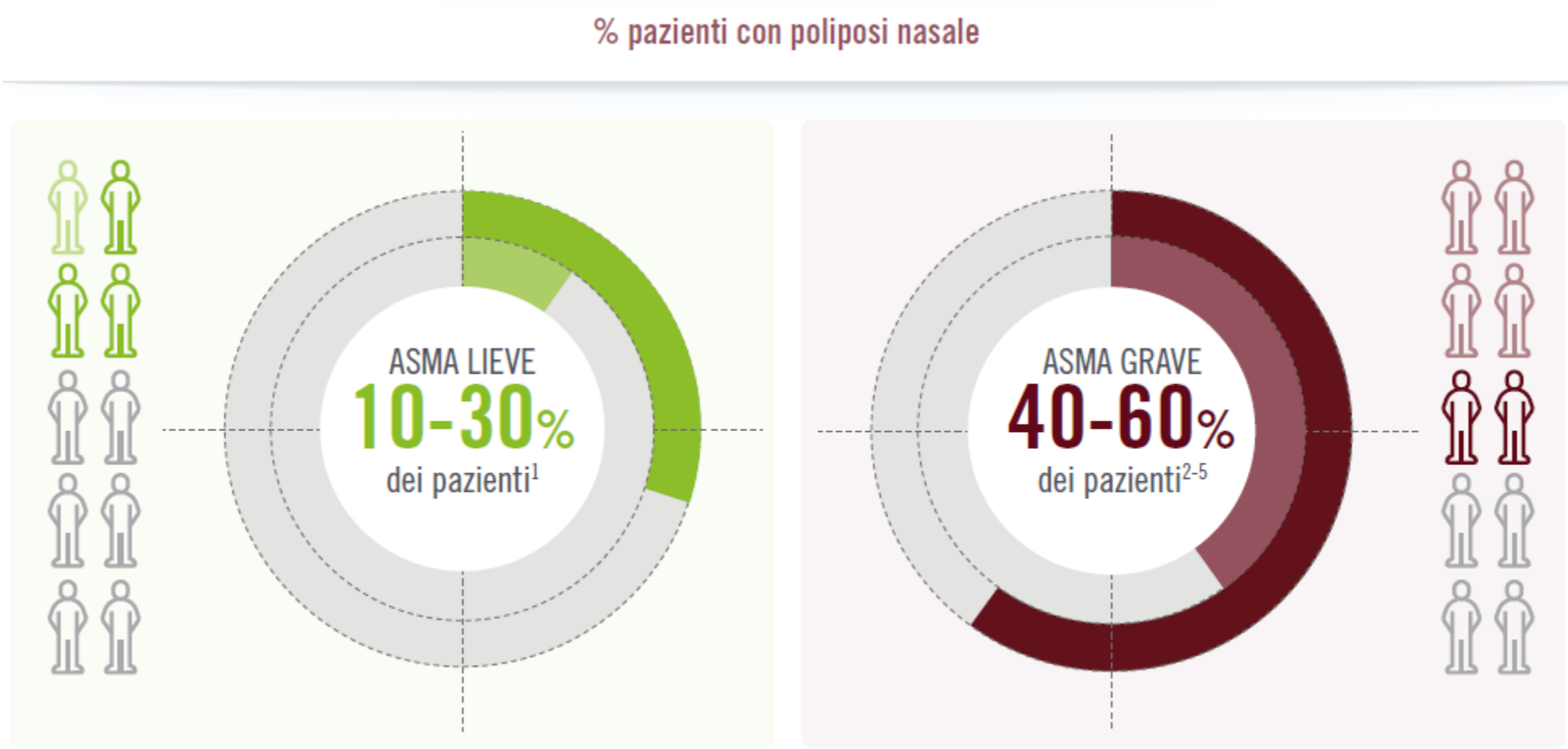
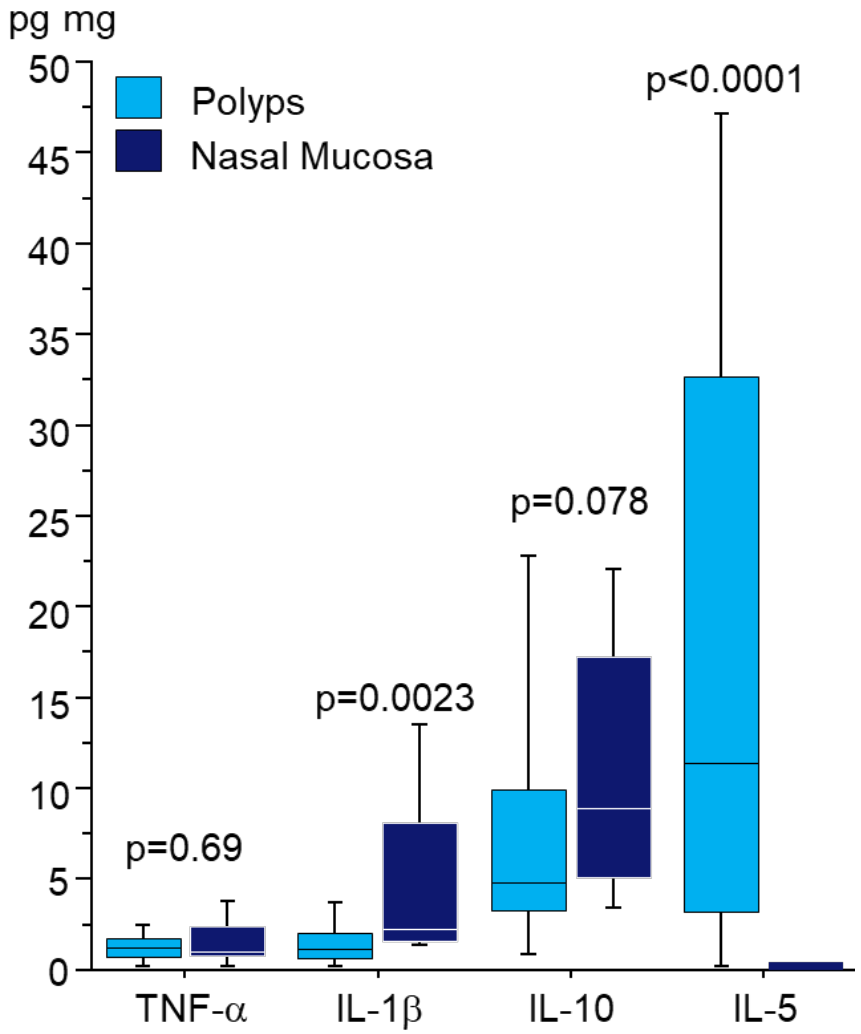
The presence of CRSwNP as a comorbidity of asthma is associated with the severity of the asthma itself[1]

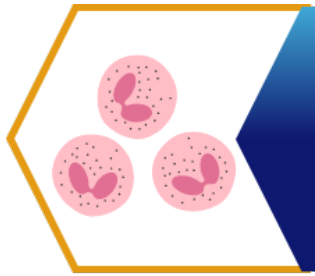


Elaborazione grafica di dati da testo, Rif. 1-5

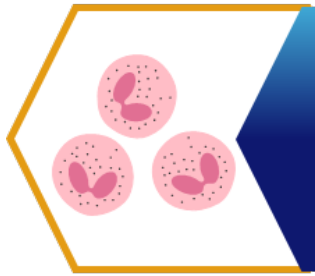
1. Fokkens WJ et al. Allergy. 2019;74(12):2312–2319. **2. Canonica et al.**, Respir Med 2020 May;166:105947. **3.Lombardi et al.**, Pulm Pharmacol Ther. 2019;54:87-89. **4.Bagnasco Pulm Pharmacol Ther.** 2019;58:101836. **5. Pelaia et al.**, Clin Exp Allergy. 2020;10.1111/cea.13613.

Up to 90% of all polyps are eosinophilic with significant levels of IL-5 present in polyp tissue





Within polyps, EOS may contribute to inflammation by releasing chemotactic and vasoactive substances



- Prolonged survival of EOS

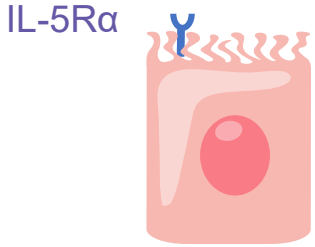
The presence of EOS in polyps may be related to:

- Increased migration of EOS

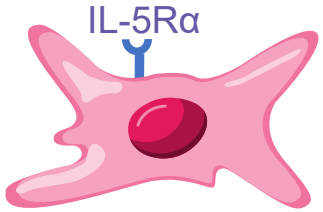
Bachert C, et al. *The Journal of allergy and clinical immunology*;1997;99;837-42

New evidence has shown that the IL-5 receptor is present on multiple cell types in sinus and airway tissue*[1–3]

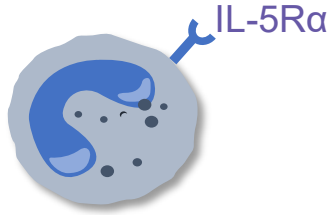
Ciliated epithelial cells†



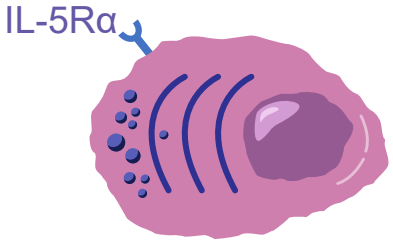
Fibroblasts‡



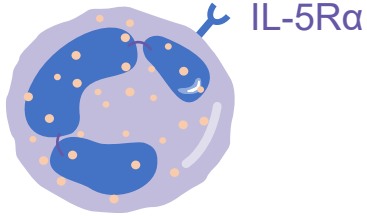
Eosinophils



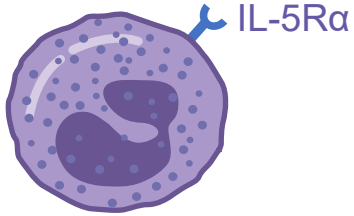
Plasma cells†



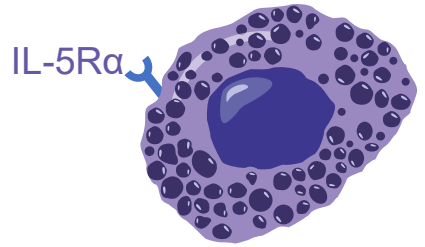
Neutrophils‡



Basophils



Mast cells†



The highest expression of IL-5Rα was found **in sinus tissue plasma cells, mast cells and ciliated epithelial cells, compared with fibroblasts, endothelial and myeloid cells**[1]

*18,036 surgically excised sinus tissue cells from subjects with AERD (n=3), CRSsNP (n=5) and CRSwNP (n=3); †Found in sinus tissue; ‡Found in airway tissue.[2]
AERD, aspirin-exacerbated respiratory disease; CRSsNP, chronic rhinosinusitis without nasal polyps; CRSwNP, chronic rhinosinusitis with nasal polyps; IL, interleukin; IL-5Rα, interleukin-5 receptor alpha.

1. Buchheit KM, et al. *J Allergy Clin Immunol* 2021;148:1574–1584; 2. Bajbouj K, et al. *Allergy* 2023;78:882–885; 3. Gorski SA, et al. *PLoS ONE* 2019;14:1–13.

Mepolizumab improved clinical outcomes in patients with severe asthma and comorbidities

- Analisi post-hoc degli studi DREAM, MENSA, SIRIUS e MUSCA
- Endpoint primario: tasso annuale delle riacutizzazioni clinicamente significative
- Endpoint secondari: ACQ-5, SGRQ; pre-FEV1

TASSO DI RIACUTIZZAZIONI

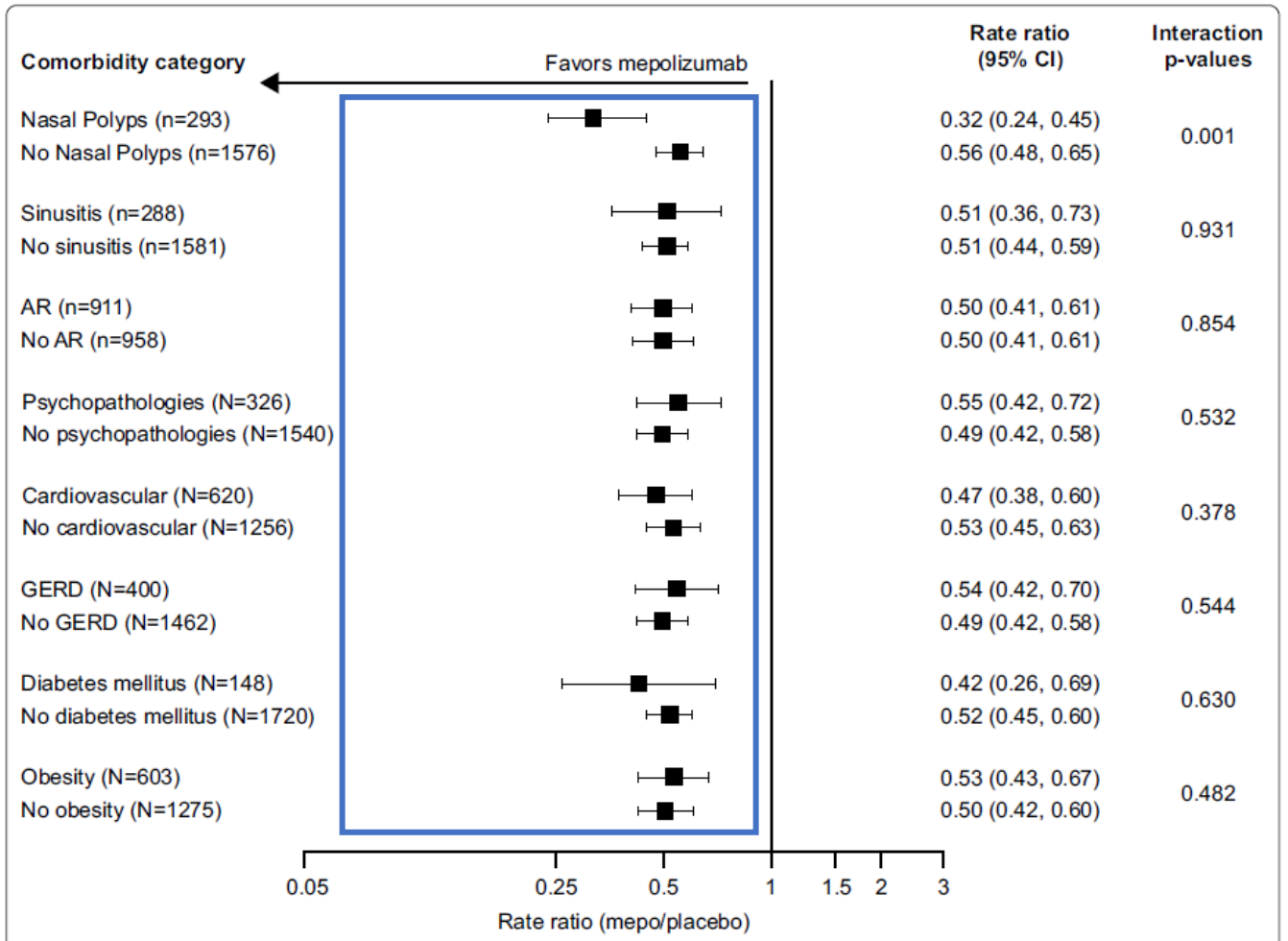


Fig. 1 Rate of clinically significant exacerbations by comorbidity category. The rate of clinically significant exacerbations was analyzed using a negative binomial generalized linear model with a log-link function, including log of time on treatment as an offset variable. p-interaction < 0.1. *AR* allergic rhinitis/hay fever; *CI* confidence interval; *GERD* gastroesophageal reflux disease; *mepo* mepolizumab

Bambino Gesù OSPEDALE PEDIATRICO

Gibson et al. Respir Res . 2021 Jun 7;22(1):171.

SIMRI società italiana per le malattie respiratorie infantili

Mepolizumab improved clinical outcomes in patients with severe asthma and comorbidities

Gibson et al., 2021

PUNTEGGIO ACQ-5

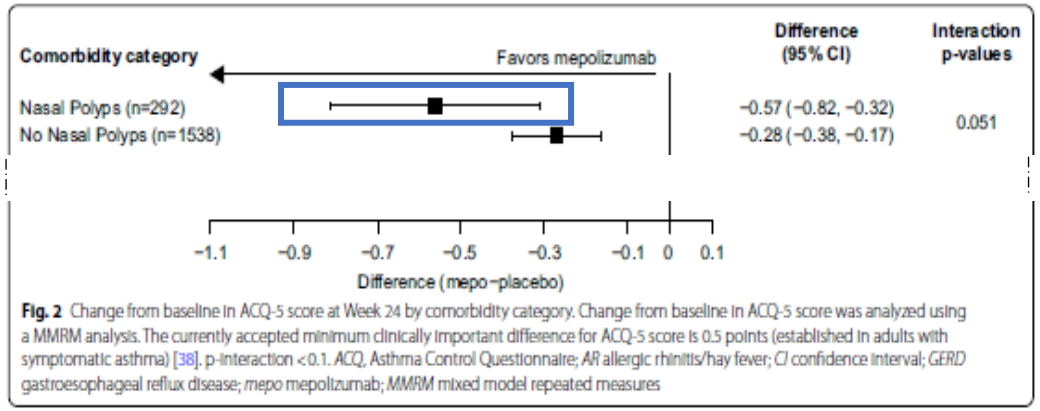


Fig. 2 Change from baseline in ACQ-5 score at Week 24 by comorbidity category. Change from baseline in ACQ-5 score was analyzed using a MMRM analysis. The currently accepted minimum clinically important difference for ACQ-5 score is 0.5 points (established in adults with symptomatic asthma) [38]. p-interaction < 0.1. *ACQ*, Asthma Control Questionnaire; *AR* allergic rhinitis/hay fever; *CI* confidence interval; *GERD* gastroesophageal reflux disease; *mepo* mepolizumab; *MMRM* mixed model repeated measures

FEV_1

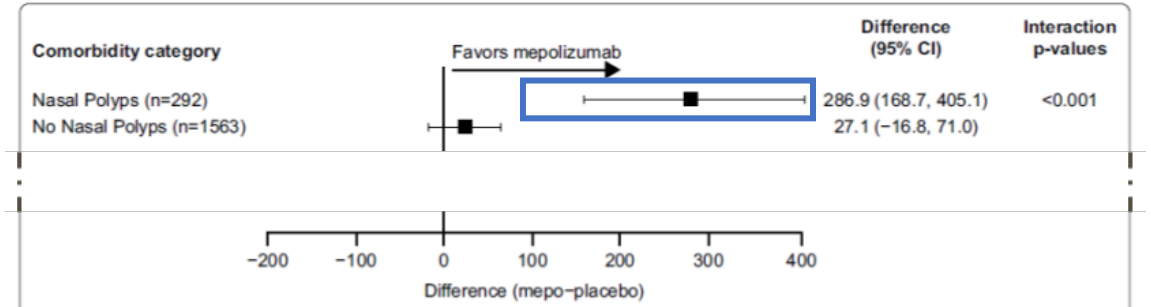


Fig. 4 Change from baseline in pre-bronchodilator FEV_1 (mL) at Week 24 by comorbidity category. Change from baseline in pre-bronchodilator FEV_1 was analyzed using a MMRM analysis. p-interaction < 0.1. *AR* allergic rhinitis/hay fever; *CI* confidence interval; FEV_1 forced expiratory volume in 1 s; *GERD* gastroesophageal reflux disease; *mepo* mepolizumab; *MMRM* mixed model repeated measures

PUNTEGGIO SGRQ

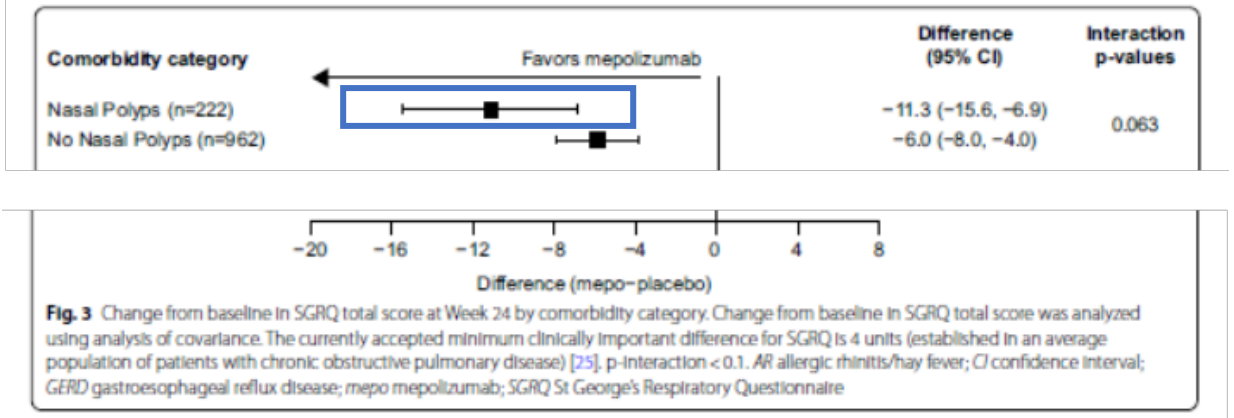


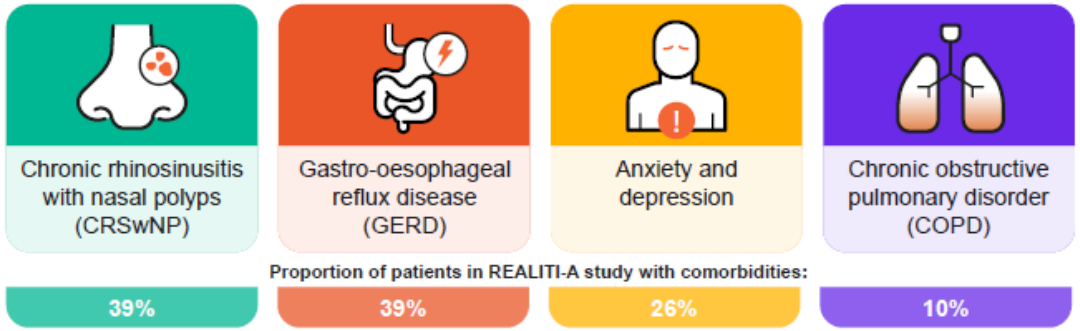
Fig. 3 Change from baseline in SGRQ total score at Week 24 by comorbidity category. Change from baseline in SGRQ total score was analyzed using analysis of covariance. The currently accepted minimum clinically important difference for SGRQ is 4 units (established in an average population of patients with chronic obstructive pulmonary disease) [25]. p-interaction < 0.1. *AR* allergic rhinitis/hay fever; *CI* confidence interval; *GERD* gastroesophageal reflux disease; *mepo* mepolizumab; *SGRQ* St George's Respiratory Questionnaire

Gibson et al. Respir Res . 2021 Jun 7;22(1):171.

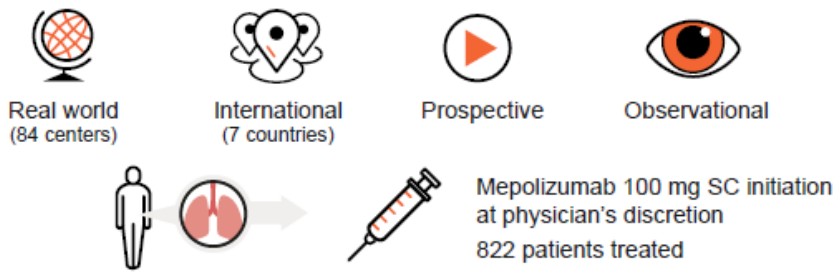
Mepolizumab in Patients With Severe Asthma and Comorbidities: 1-Year REALITI-A Analysis

In real-world clinical practice, patients with severe asthma and a range of comorbidities had reduced CSEs and mOCS dose following 1 year of mepolizumab treatment, with additional improvements for patients with CRSwNP

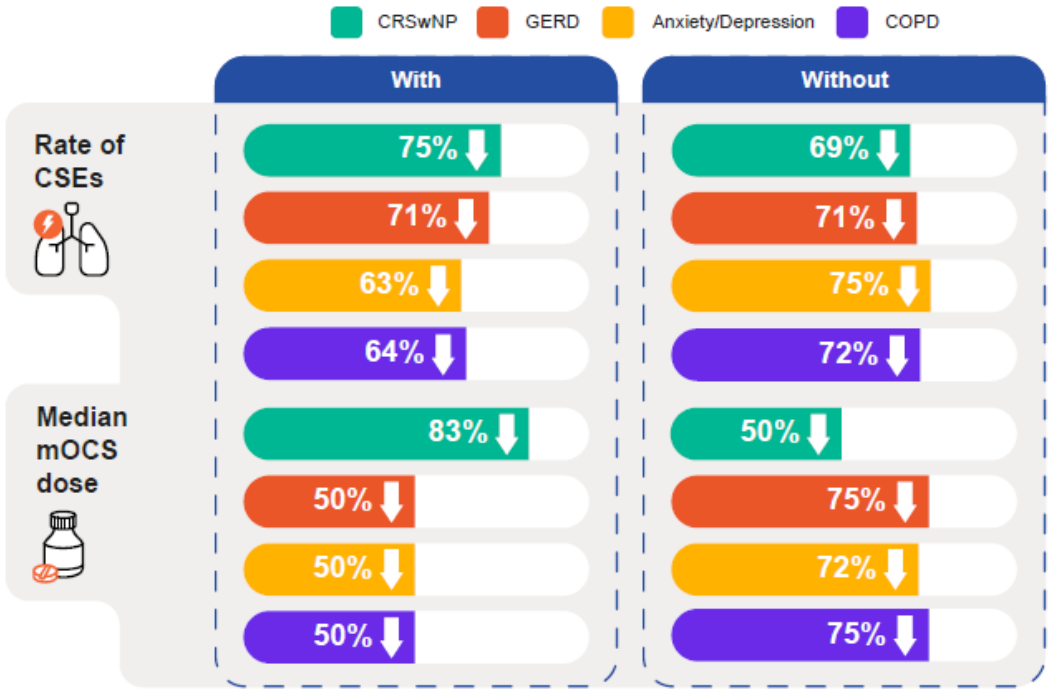
Common comorbities in patients with severe asthma that add to disease burden:



REALITI-A (GSK ID: 204710)



1 year following mepolizumab initiation*



*percentage change (reduction) versus pre-mepolizumab treatment. This study was funded by GSK (GSK IS:204710); please refer to the associated manuscript for additional disclosures. COPD, chronic obstructive pulmonary disorder; CRSwNP, chronic rhinosinusitis with nasal polyps; CSE, clinically significant asthma exacerbation; GERD, gastro-oesophageal reflux disease; mOCS, maintenance oral corticosteroids; SC subcutaneous

R. Cutrera, 2024, renato.cutrera@opbg.net

Respiratory comorbidities in severe asthma: focus on the pediatric age

- Respiratory asthma comorbidities are frequent treatable traits whose management can significantly improve outcomes in difficult-to-treat asthma.

- Children and adolescents possess unique characteristics in terms of clinical presentation, endotyping, and therapeutic approach

- Regarding the pediatric population, a newly published, monocentric, cross- sectional Italian study detected comorbidities in up to 87% of the 508 asthmatic children (aged 5 to 17 years). Mainly, **respiratory comorbidities alone affected 37%** of them, whereas **joined respiratory and non-respiratory comorbidities were found in another 40% .**

Licari et al. EXPERT REVIEW OF RESPIRATORY MEDICINE 2023, VOL. 17, NO. 1, 1-13
https://doi.org/10.1080/17476348.2023.2168261

R. Cutrera, 2024, renato.cutrera@opbg.net

children Children **2022**, 9, 1001.

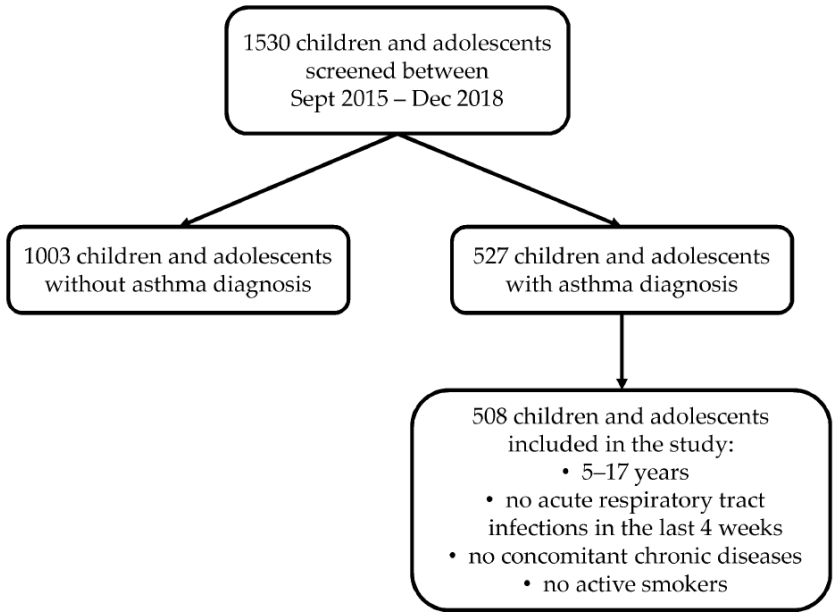
MDPI

Article

Asthma Comorbidities: Frequency, Risk Factors, and Associated Burden in Children and Adolescents

Salvatore Fasola [1,*,†], Giuliana Ferrante [2,†], Giovanna Cilluffo [3], Velia Malizia [1], Pietro Alfano [1], Laura Montalbano [1], Giuseppina Cuttitta [1,‡] and Stefania La Grutta [1,‡]

Reference Group	
A	asthma only
Comorbidity Group	
AR	asthma AND (rhinitis OR sinusitis OR snoring)
AER	asthma AND (food allergy OR gastroesophageal reflux OR eczema OR urticaria OR angioedema OR anaphylaxis)
ARER	asthma AND (rhinitis OR sinusitis OR snoring) AND (food allergy OR gastroesophageal reflux OR eczema OR urticaria OR angioedema OR anaphylaxis)



	Overall *n* = 508 (100%)	A *n* = 68 (13%)	AR *n* = 188 (37%)	AER *n* = 50 (10%)	ARER *n* = 202 (40%)	*p*-Value
Asthma severity						0.666
Intermittent	246 (48)	32 (47)	93 (49)	25 (50)	96 (48)	
Mild persistent	170 (33)	27 (40)	65 (35)	15 (30)	63 (31)	
Moderate/severe persistent	92 (18)	9 (13)	30 (16)	10 (20)	43 (21)	
Asthma control						0.220
Well controlled	195 (38)	34 (50)	64 (34)	21 (42)	76 (38)	
Partly controlled	107 (21)	8 (12)	46 (24)	8 (16)	45 (22)	
Uncontrolled	206 (41)	26 (38)	78 (41)	21 (42)	81 (40)	
Exacerbations last 12 months	2.6 (3.4)	2.0 (3.2)	3.0 (3.4)	2.2 (3.4)	2.6 (3.3)	**0.009**
FEV_1 % predicted	96.5 (13.2)	95.9 (14.6)	96.2 (12.0)	93.8 (13.3)	97.8 (13.7)	0.193
eNO, ppb	13.2 (10.1)	13.0 (8.9)	14.9 (11.9)	11.5 (7.4)	12.2 (9.1)	0.185
C-ACT/ACT [1]	20.6 (4.1)	21.8 (2.7)	19.7 (4.8)	20.9 (3.7)	20.8 (3.8)	0.215
PSQI [1]	2.1 (1.9)	1.5 (1.3)	2.3 (1.8)	1.4 (0.8)	2.3 (2.2)	**0.034**
PAQLQ [1]	5.3 (1.2)	5.5 (1.0)	5.2 (1.2)	5.4 (1.1)	5.4 (1.2)	0.635
VAS [1]	8.3 (1.8)	8.7 (1.5)	8.1 (1.9)	8.5 (1.8)	8.2 (1.7)	0.404

Data are presented as *n* (%) or mean (SD). A: asthma only. AR: asthma with respiratory comorbidities. AER: asthma with extra-respiratory comorbidities. ARER: asthma with both respiratory and extra-respiratory comorbidities. FEV_1: forced expiratory volume in 1 s. eNO: exhaled nitric oxide. Significant *p*-values are in bold. [1] Available for 225 subjects providing their consent for symptom assessment.

Mepolizumab: Indicazioni terapeutiche e posologia

ASMA EOSINOFILICO SEVERO[1,2]

indicato come terapia aggiuntiva per l'asma eosinofilico refrattario severo negli adulti, adolescenti e bambini di età pari o superiore a 6 anni.

Adulti e adolescenti>12 anni: 100mg ogni 4 settimane
Bambini 6-11 anni: 40mg una volta ogni 4 settimane

RINOSINUSITE CRONICA CON POLIPOSI NASALE (CRSwNP)[1,2]

indicato come terapia aggiuntiva a corticosteroidi intranasali per il trattamento di adulti con CRSwNP severa per i quali la terapia con corticosteroidi sistemici e/o la chirurgia non forniscono un controllo adeguato della malattia.

GRANULOMATOSI EOSINOFILICA CON POLIANGITE (EGPA)[1,2]

indicato come terapia aggiuntiva per pazienti di età pari o superiore a 6 anni con granulomatosi eosinofilica con poliangite (EGPA) recidivante/remittente o refrattaria.

Adulti e adolescenti>12 anni: 300mg ogni 4 settimane
Bambini 6-11 anni >40kg: 200mg una volta ogni 4 settimane
Bambini 6-11 anni <40kg: 100mg una volta ogni 4 settimane

SINDROME IPEREOSINOFILA (HES)[1,2]

indicato come terapia aggiuntiva per pazienti adulti con sindrome ipereosinofila non adeguatamente controllata senza una causa secondaria non ematologica identificabile.

R. Cutrera, 2024, renato.cutrera@opbg.net

Piano terapeutico mepolizumab (GU 13.01.2024)

Indicazione rimborsata SSN

Trattamento limitato ai pazienti con asma eosinofilico refrattario severo negli adulti, adolescenti e bambini di età pari o superiore a 6 anni che presentano, alla prima prescrizione, le seguenti caratteristiche:

☐ >150 eosinofili/mmc attuale in assenza di trattamento steroideo sistemico e almeno un valore > 300 eosinofili/mmc nell'anno precedente

e (indicare almeno una delle due condizioni sotto specificate)

☐ Ha avuto almeno 2 riacutizzazioni di asma nonostante la massima terapia inalatoria (trattate con steroide sistemico o che hanno richiesto ricovero) nei 12 mesi precedenti (Step 4-5 di GINA, dai 12 anni), o nonostante la massima terapia inalatoria tollerata (dai 6 agli 11 anni)

oppure

☐ Ha ricevuto terapia continuativa con steroidi per via orale in aggiunta alla terapia inalatoria massimale per almeno 6 mesi nell'ultimo anno (condizione applicabile solo per gli adulti dai 18 anni di età)

Condizioni cliniche e criteri di rimborsabilità

Il/la Paziente soddisfa tutte le condizioni sottostanti:

☐ età ≥6 aa
☐ >150 eosinofili/mmc attuale in assenza di trattamento steroideo sistemico e almeno un valore > 300 eosinofili/mmc nell'anno precedente

e (indicare almeno una delle due condizioni sotto specificate)

☐ Ha avuto almeno 2 riacutizzazioni di asma nonostante la massima terapia inalatoria (trattate con steroide sistemico o che hanno richiesto ricovero) nei 12 mesi precedenti (Step 4-5 di GINA, dai 12 anni), o nonostante la massima terapia inalatoria tollerata (dai 6 agli 11 anni)

oppure

☐ Ha ricevuto terapia continuativa con steroidi per via orale in aggiunta alla terapia inalatoria massimale per almeno 6 mesi nell'ultimo anno (condizione applicabile solo per gli adulti dai 18 anni di età)

Prescrizione

☐ Prima prescrizione	☐ Prosecuzione terapia: ☐ con modifiche ☐ senza modifiche
Farmaco	**Posologia**
☐ 1 penna preriempita SC 100 mg 1 ml ☐ 1 siringa preriempita SC 100 mg 1 ml ☐ 1 flaconcino SC 100 mg ☐ 1 siringa preriempita SC 40 mg/0,4 ml	Adulti e adolescenti di età pari o superiore a 12 anni ☐ 100 mg somministrati per via sottocutanea una volta ogni 4 settimane. Bambini di età compresa tra 6 e 11 anni ☐ 40 mg somministrati per via sottocutanea una volta ogni 4 settimane.

R. Cutrera, 2024, renato.cutrera@opbg.net

Mepolizumab - forme farmaceutiche

Mepolizumab 100 mg polvere per soluzione iniettabile[1]

- Dopo la ricostituzione, ogni mL di soluzione contiene 100 mg di mepolizumab
- Deve essere somministrato solo tramite iniezione sottocutanea da parte di un operatore sanitario
- Una volta ogni 4 settimane
- L'iniezione può essere fatta nella parte superiore del braccio, nella coscia o nell'addome

Mepolizumab 40 mg soluzione iniettabile in penna preriempita[2]

- Ogni penna preriempita da 1 mL contiene 40 mg di mepolizumab
- Solo per iniezione sottocutanea
- Può essere somministrato da un prestatore di cure
- Una volta ogni 4 settimane
- Per l'autosomministrazione i siti di iniezione raccomandati sono l'addome o la coscia

Nei bambini di età tra 6 e 11 anni la dose raccomandata di mepolizumab è 40 mg una volta ogni 4 settimane.

Mepolizumab 100 mg soluzione iniettabile in siringa preriempita[2]

- Ogni siringa preriempita da 1 mL contiene 100 mg di mepolizumab
- Solo per iniezione sottocutanea
- Può essere auto-somministrato dal paziente o somministrato da un prestatore di cure
- Una volta ogni 4 settimane
- Per l'autosomministrazione i siti di iniezione raccomandati sono l'addome o la coscia

Mepolizumab 100 mg soluzione iniettabile in penna preriempita[2]

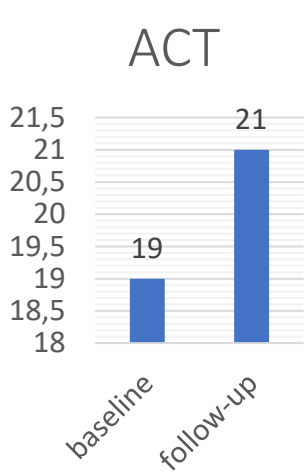
- Ogni penna preriempita da 1 mL contiene 100 mg di mepolizumab
- Solo per iniezione sottocutanea
- Può essere auto-somministrato dal paziente o somministrato da un prestatore di cure
- Una volta ogni 4 settimane
- Per l'autosomministrazione i siti di iniezione raccomandati sono l'addome o la coscia

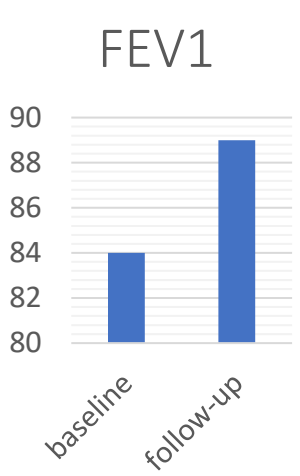
Somministrabile in adulti e adolescenti > 12 anni

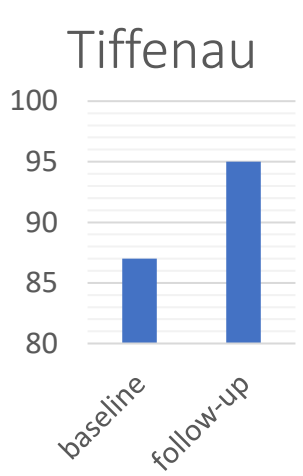
1. Nucala 100 mg polvere per soluzione iniettabile. Riassunto delle Caratteristiche del Prodotto. **2. Nucala 100 mg soluzione iniettabile in penna preriempita Nucala 100 mg.** Riassunto delle Caratteristiche del Prodotto.

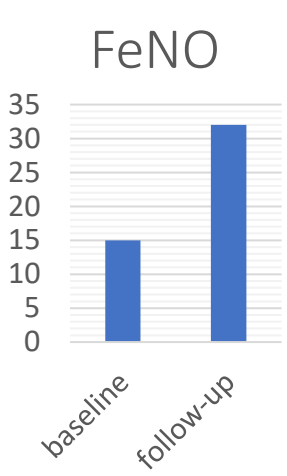
R. Cutrera, 2024, renato.cutrera@opbg.net

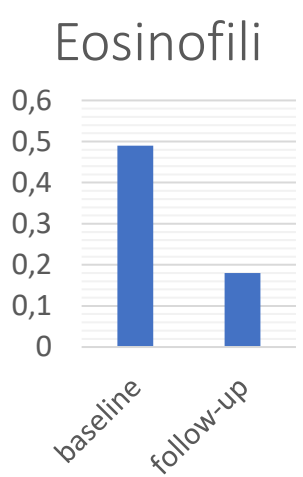
Pazienti in terapia con Mepolizumab dopo 1 anno (7 pazienti)
U.O.C. Pneumologia & Fibrosi Cistica – Ospedale Pediatrico Bambino Gesù IRCCS Roma

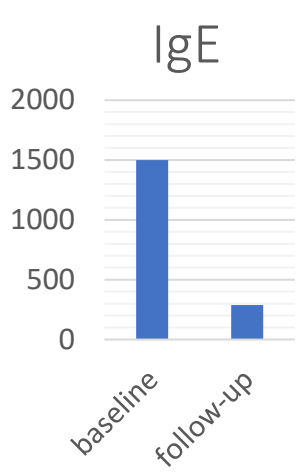


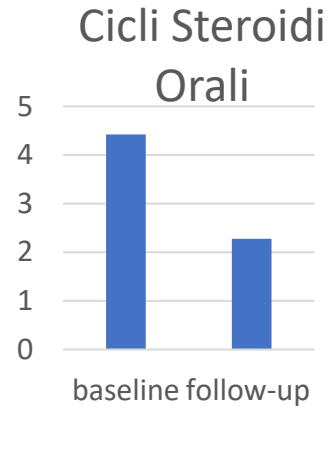












	ACT	FEV1	Tiffenau	FeNO	Eosinofili	IgE	Cicli steroidi orali
Baseline	19 [18-21]	84 [73-101.7]	87 [67-92]	15 [5-26]	0.49 [0.2-0.61]	1500 [800-2263]	4.42 [3.29-5.57]
Follow-up	21 [18-21.2]	89 [85-92]	94.5 [80-105]	32 [5-61]	0.18 [0.03-0.22]	287 [139-300]	2.28 [0.14-4.7]
P value	0.42	0.7	0.45	0.88	0.06	0.02	0.001

Bambino Gesù
OSPEDALE PEDIATRICO

R. Cutrera, 2024, renato.cutrera@opbg.net

SIMRI

Conclusioni and Take Home Messages

L'asma grave ha una prevalenza del 1-5 % dei pazienti pediatrici asmatici (sotto diagnosticato?)

Fenotipizzazione dell'Asma Grave

Asma grave eosinofilico e ruolo del Mepolizumab

Mepolizumab efficace e sicuro nei pazienti pediatrici con asma grave eosinofilico

Hot topics nell'età di transizione: altre patologie ipereosinofiliche

R. Cutrera, 2024, renato.cutrera@opbg.net