口服類固醇依賴：如何利用生物製劑降低口服類固醇使用

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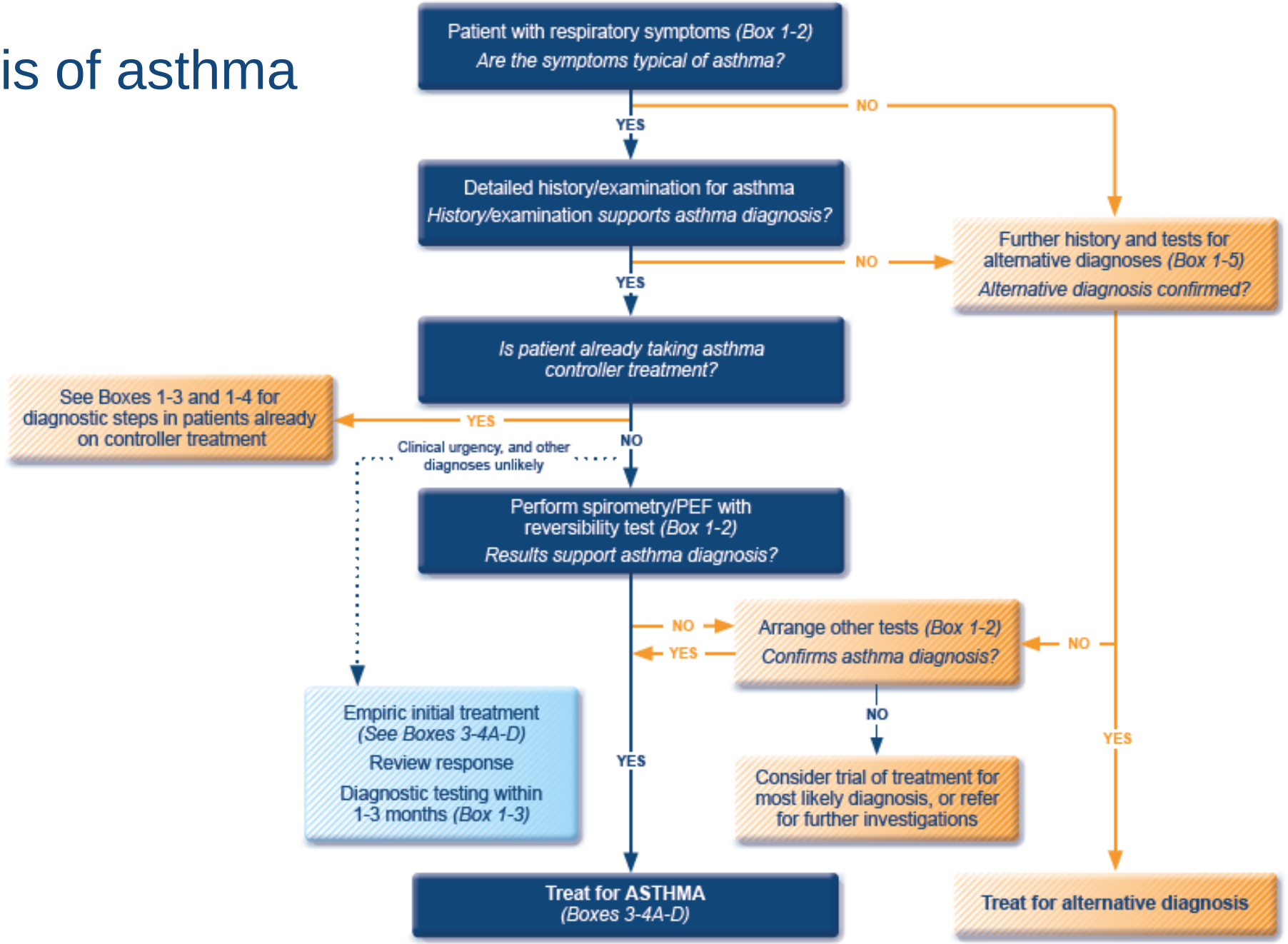
Global Initiative for Asthma (GINA)

What's new in GINA 2022?

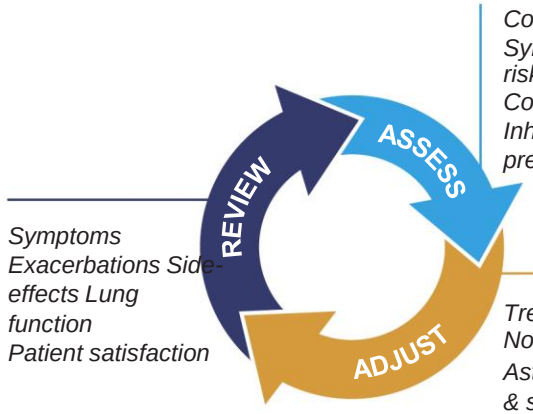
GINA Global Strategy for Asthma Management and Prevention

Diagnosis of asthma



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 2-2B)
Comorbidities
Inhaler technique & adherence Patient preferences and goals

Symptoms
Exacerbations Side-effects Lung function
Patient satisfaction

Treatment of modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications (adjust down/up/between tracks) Education & skills training

CONTROLLER and **PREFERRED RELIEVER** (Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever

STEPS 1 – 2	STEP 3	STEP 4	STEP 5
As-needed 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-IL4R, anti-TSLP

RELIEVER: As-needed low-dose ICS-formoterol

See GINA severe asthma guide

CONTROLLER and **ALTERNATIVE RELIEVER** (Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller

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-IL4R, anti-TSLP

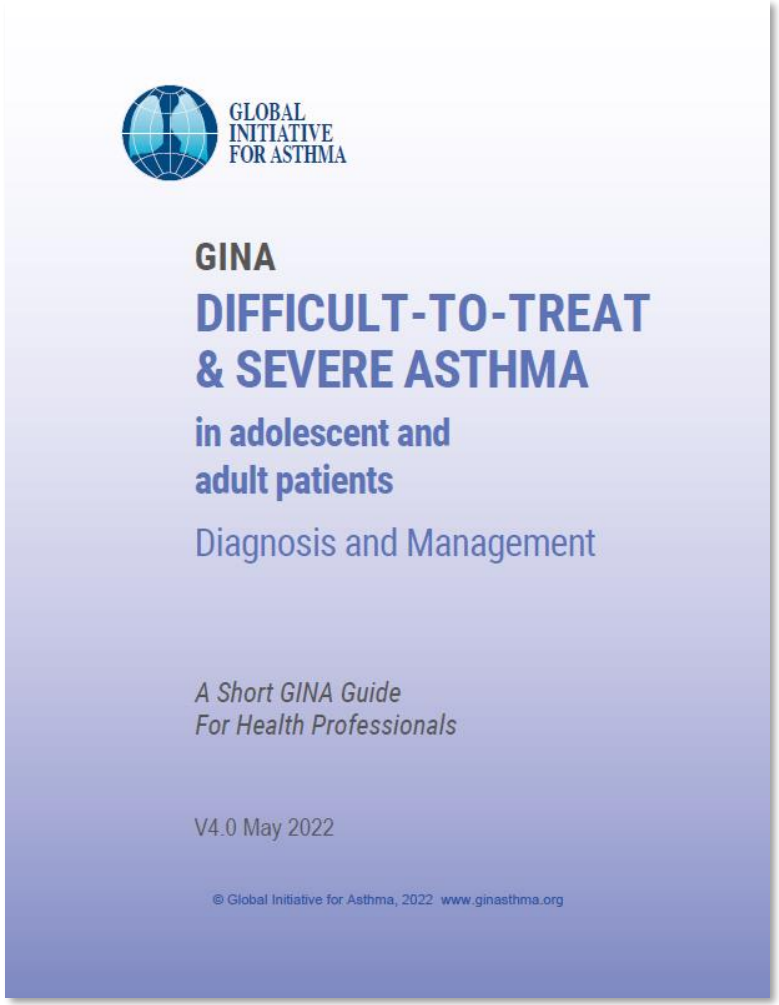
RELIEVER: As-needed short-acting beta$_2$-agonist

Other controller options for either track (limited indications, or less evidence for efficacy or safety)	*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 LTRA or HDM SLIT, or switch to high dose ICS*	*Add azithromycin (adults) or LTRA. As last resort consider adding low dose OCS but consider side-effects*

GINA 2022, Box 3-5A

Short GINA guide for difficult-to-treat and severe asthma in adults and adolescents, 2022

- Full size rather than ‘pocket’ size; easier to read
- Updated decision tree for assessment of adults and adolescents with difficult-to-treat asthma
  - Sections 1–4: primary or specialist care
  - Sections 5–8: specialist care
  - Sections 9–10: ongoing collaborative care with patient, GP, specialist, other health professionals
- Decision tree and text are also included in full GINA report (Chapter 3E)
- Slide set on GINA website



OCS Stewardship is helping change the landscape of inappropriate OCS use in asthma

Respiratory diseases account for ~70–80% of OCS prescriptions;[1] the continued inclusion of OCS in asthma treatment guidelines contributes to the ongoing use of OCS in severe asthma[2]

Globally, ~20–60% of patients with severe or uncontrolled asthma receive long-term OCS;[2] however, its use is associated with **significant morbidity and mortality**[3,4]

The availability of new treatment options and guideline reform has brought about a **paradigm shift in the use of OCS for RA and Crohn's disease**[5,6]

There is a need to drive a **similar transformation in asthma care** and relegate OCS to a **last-resort treatment**

Continued change in clinical practice is key to promoting OCS Stewardship and ensuring that patients are not exposed to inappropriate OCS use

OCS, oral corticosteroid(s); RA, rheumatoid arthritis

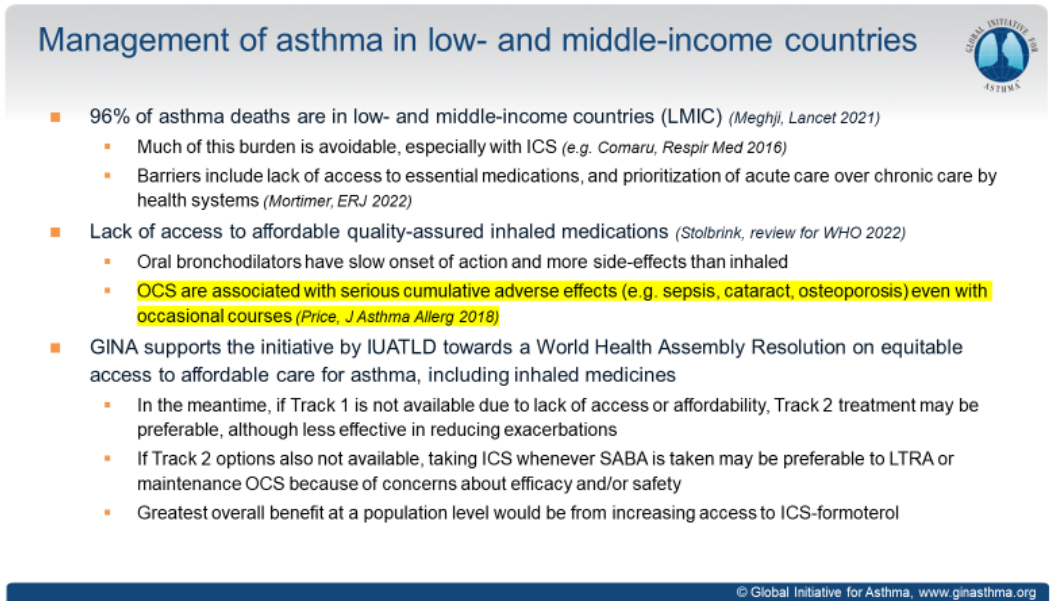
1. Menzies Gow A, et al. British Thoracic Society Winter Meeting 2021, 17 February 2021, London, UK, 24–25 February 2021 (Abstract S29);
2. Bleecker ER, et al. Am J Respir Crit Care Med 2020;201:276–293; 3. Price DB, et al. J Asthma Allergy 2018;11:193–204; 4. Lee H, et al. Eur Respir J 2019;54:1900804;
5. Chhaya V, et al. Aliment Pharmacol Ther 2016;44:482–494; 6. Black RJ, et al. Arthritis Res Ther 2017;19:253

GINA acknowledges that occasional courses of OCS are associated with increased risk of AEs

The 'What's new in GINA 2022' slide deck acknowledges the risks associated with **occasional courses of OCS** and suggests considering maintenance OCS **only as a last resort because of serious cumulative AEs**[1]

> *OCS are associated with serious cumulative AEs (eg sepsis, cataract, osteoporosis) even with occasional courses*

This statement is referenced to Price et al (2018), which demonstrated that an increased risk of AEs begins at cumulative exposures of 0.5–<1 g, equivalent to 2–4 lifetime courses of OCS[2]



Management of asthma in low- and middle-income countries

- 96% of asthma deaths are in low- and middle-income countries (LMIC) *(Meghji, Lancet 2021)*
  - Much of this burden is avoidable, especially with ICS *(e.g. Comaru, Respir Med 2016)*
  - Barriers include lack of access to essential medications, and prioritization of acute care over chronic care by health systems *(Mortimer, ERJ 2022)*
- Lack of access to affordable quality-assured inhaled medications *(Stolbrink, review for WHO 2022)*
  - Oral bronchodilators have slow onset of action and more side-effects than inhaled
  - OCS are associated with serious cumulative adverse effects (e.g. sepsis, cataract, osteoporosis) even with occasional courses *(Price, J Asthma Allerg 2018)*
- GINA supports the initiative by IUATLD towards a World Health Assembly Resolution on equitable access to affordable care for asthma, including inhaled medicines
  - In the meantime, if Track 1 is not available due to lack of access or affordability, Track 2 treatment may be preferable, although less effective in reducing exacerbations
  - If Track 2 options also not available, taking ICS whenever SABA is taken may be preferable to LTRA or maintenance OCS because of concerns about efficacy and/or safety
  - Greatest overall benefit at a population level would be from increasing access to ICS-formoterol

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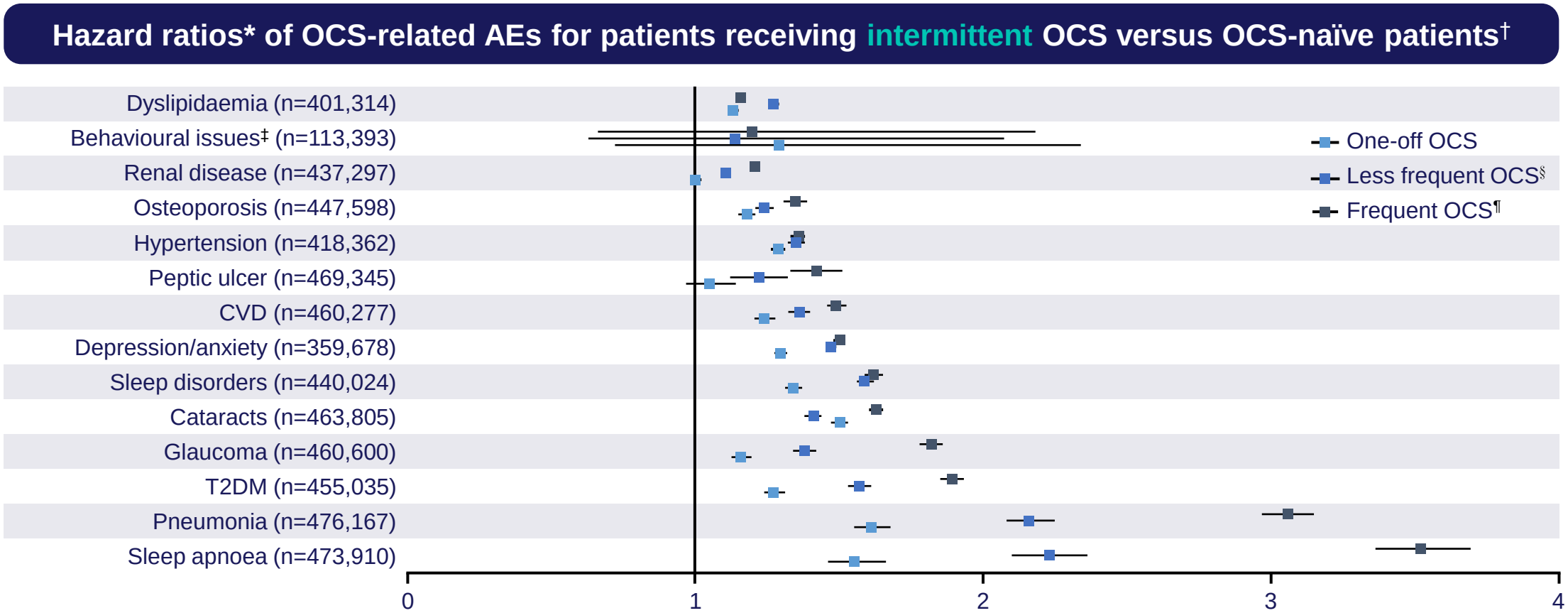
- AE, adverse effect; GINA, Global Initiative for Asthma; ICS, inhaled corticosteroid(s); IUATLD, International Union Against Tuberculosis and Lung Disease; LTRA, leukotriene receptor antagonist; OCS, oral corticosteroid(s); SABA, short-acting β_2-agonist

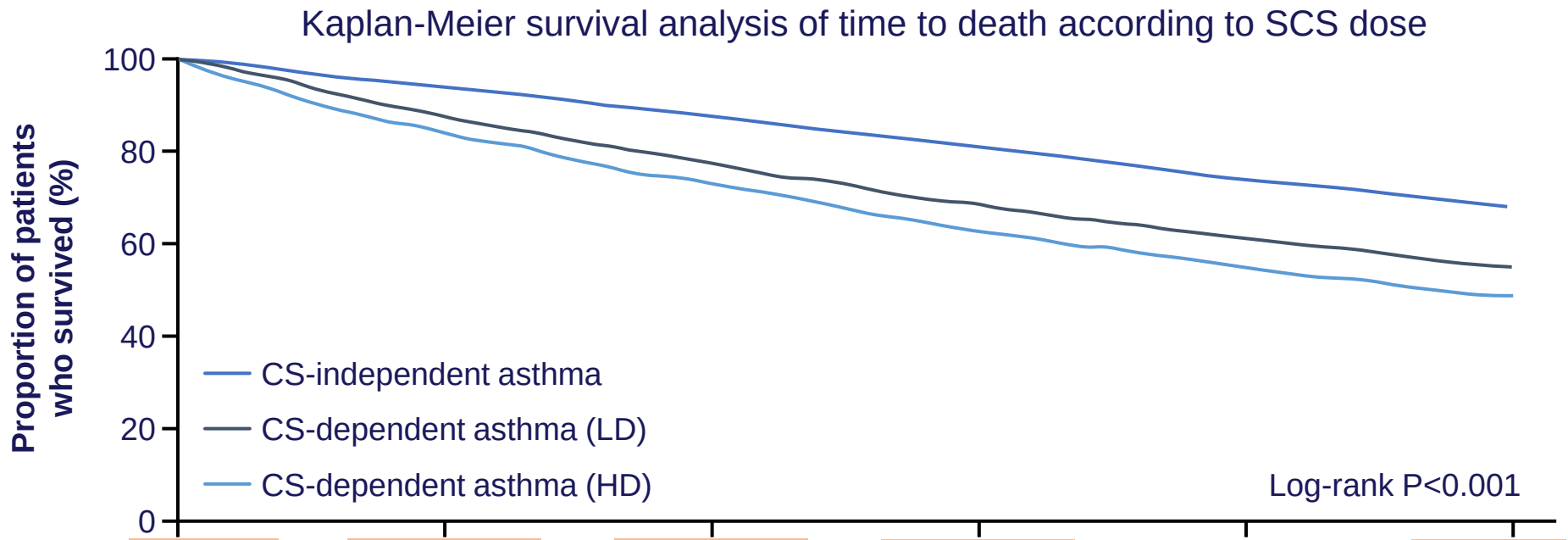
- 1. Global Initiative for Asthma (GINA). What's new in GINA 2022? Available from: https://ginasthma.org/gina-reports/ (Accessed 1 July 2022);
  2. Price DB, et al. J Asthma Allergy 2018;11:193–204

OCS Stewardship is needed to prevent AEs associated with intermittent OCS use



- *Hazard ratios were calculated using Cox regression analysis, adjusted for age, gender, BMI, smoking and time-varying OCS prescriptions; †OCS-naïve patients were matched with all patients receiving OCS prescriptions according to a 1:1 ratio; ‡behavioural issues include diagnosis for distress, agitation, nervousness, emotional problems, irritable and abnormal behaviour among patients <18 years; §patients with less frequent OCS use received all OCS prescriptions with a gap of ≥90 days; ¶patients with frequent OCS use received at least some OCS prescriptions with a gap of <90 days, allowing for other prescription gaps to be ≥90 days
- AE, adverse event; BMI, body mass index; CVD, cardiovascular diseases; OCS, oral corticosteroid(s); T2DM, Type 2 diabetes mellitus
- Heatley H, et al. Abstract accepted for presentation at IPCRG 2022

The risk of mortality associated with SCS use is dose-dependent



Follow-up duration, years	0	2	4	6	8	10
At risk, n:						
CS-independent asthma	8334	7904	7297	6735	6159	29
CS-dependent asthma (LD)	4197	3646	3220	2855	2544	18
CS-dependent asthma (HD)	4167	3483	3029	2607	2291	29

- CS, corticosteroid(s); HD, high dose; LD, low dose; SCS, systemic corticosteroid(s)
  Lee H, et al. Eur Respir J 2019;54:1900804

Key changes to GINA severe asthma guide in 2022
(continued)

- Anti-IL4R* (dupilumab) for severe eosinophilic/Type 2 asthma
  - Not suggested if blood eosinophils (current or historic) >1500/µl
  - Dupilumab now also approved for children ≥6 years with severe eosinophilic/Type 2 asthma, not on maintenance OCS *(Bacharier, NEJMed 2021)*
- Anti-TSLP* (tezepelumab) now approved for severe asthma (age ≥12 years)

Class	Name	Age*	Asthma indication*	Other indications*
Anti-IgE	Omalizumab (SC)	≥6 years	Severe allergic asthma	Nasal polyposis, chronic spontaneous urticaria
Anti-IL5	Mepolizumab (SC)	≥6 years	Severe eosinophilic/Type 2 asthma	Mepolizumab: EGPA, CRSwNP, hypereosinophilic syndrome
	Reslizumab (IV)	≥18 years		
Anti-IL5R	Benralizumab (SC)	≥12 years		
Anti-IL4R	Dupilumab (SC)	≥6 years	Severe eosinophilic/Type 2 asthma, or maintenance OCS	Moderate-severe atopic dermatitis, CRSwNP
Anti-TSLP	Tezepelumab (SC)	≥12 years	Severe asthma	

**Check local eligibility criteria for specific biologic therapies; TSLP: thymic stromal lymphopoietin*

中央健康保險局修正：含omalizumab成分藥品(如Xolair)之藥品給付規定
（自103年10月1日起生效）

修正後給付規定	原給付規定
6.2.6.Omalizumab (如Xolair)：（97/6/1、100/6/1、103/10/1） 1. 限用於 （1）12歲以上之青少年或成人經胸腔內科或小兒科或過敏免疫專科醫師診斷為「重度持續性氣喘」病患，為非抽煙或正積極戒煙者，需符合下列條件。 I. (略) II.必須檢附「免疫球蛋白IgE檢驗結果」。免疫球蛋白Total IgE檢驗結果必須介於30~1300IU/mL，但使用抗IgE製劑後IgE值降低者不在此限(103/10/1)。 III.已接受高劑量類固醇藥物吸入劑 (青少年大於400 mcg belcomethasone dipropionate/day以上或他類固醇藥物吸入劑相等劑量；成人大於800mcg beclomethasone dipropionate/day以上或其他類固醇藥物吸入劑相等劑量) 及併用其他治療，如：長效乙二型作用劑 (β2-agonist)、口服類固醇治療、口服theophylline或抗白三烯素類藥品仍控制不良者，且過去四週氣喘控制仍不穩定者(包括:日間症狀每週超過2次、日常活動受到限制、有夜間氣喘症狀發作或到醒來、需要緩解型藥物每週超過2次或以上，符合上述條件2者或以上者) (103/10/1)。 IV.病歷記載有氣喘病史或需經證實為氣喘病患，支氣管擴張試驗顯示FEV1 reversibility超過12%與絕對值增加200mL以上，或使用類固醇後FEV1增加20%以上(103/10/1)。	6.2.6.Omalizumab (如Xolair)：（97/6/1、100/6/1） 1. 限用於 （1）12歲以上之青少年或成人經胸腔內科或小兒科或過敏免疫專科醫師診斷為「重度持續性氣喘」病患，為非抽煙或正積極戒煙者，需符合下列條件。 I. (略) II.必須檢附「免疫球蛋白IgE檢驗結果」。免疫球蛋白Total IgE檢驗結果必須介於70~700IU/mL，但使用抗IgE製劑後IgE值降低者不在此限。 III.已接受高劑量類固醇藥物吸入劑 (青少年大於400mcg beclomethasone dipropionate/day以上或其他類固醇藥物吸入劑相等劑量；成人大於800mcg beclomethasone dipropionate/day以上或其他類固醇藥物吸入劑相等劑量) 及併用其他治療，如：長效乙二型作用劑 (β2-agonist)、口服類固醇治療、口服theophylline或抗白三烯素類藥品仍控制不良者。 IV.需經證實為氣喘病患，支氣管擴張試驗顯示FEV1 reversibility超過12%與絕對值增加200mL以上，或使用類固醇後FEV1增加20%以上。

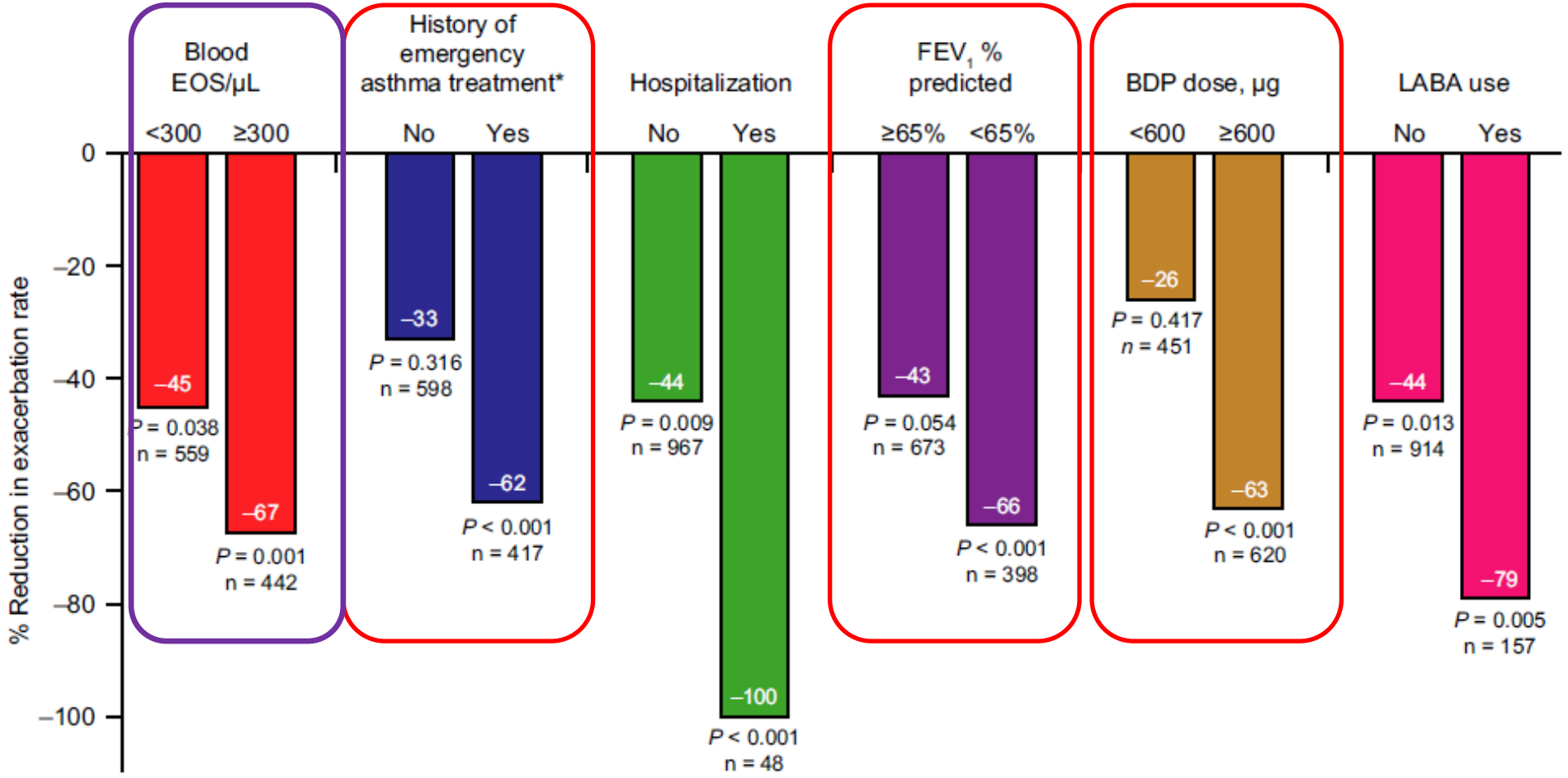
（2）6至12歲兒童經胸腔內科或小兒科或過敏免疫專科醫師診斷為「重度持續性氣喘」病患，需符合下列條件。（100/6/1）
I.及II. (略)
III.已接受高劑量類固醇藥物吸入劑 (大於400mcg Beclomethasone dipropionate/day以上或其他類固醇藥物吸入劑相等劑量) 及併用其他治療，如：長效乙二型作用劑 (β2-agonist)、口服類固醇治療、口服theophylline或抗白三烯素類藥品仍控制不良者，且過去四週氣喘控制仍不穩定者 (包括:日間症狀每週超過2次、日常活動受到限制、有夜間氣喘症狀發作或到醒來、需要緩解型藥物每週超過2次或以上，符合上述條件2者或以上者) (103/10/1)。
IV.病歷記載有氣喘病史或需經證實為氣喘病患，支氣管擴張試驗顯示FEV1 reversibility超過12%與絕對值增加200mL以上，或使用類固醇後FEV1增加20%以上(103/10/1)。

200mL以上，或使用類固醇後FEV1增加20%以上。
（2）6至12歲兒童經胸腔內科或小兒科或過敏免疫專科醫師診斷為「重度持續性氣喘」病患，需符合下列條件。（100/6/1）
I.及II. (略)
III.已接受高劑量類固醇藥物吸入劑 (大於400mcg Beclomethasone dipropionate/day以上或其他類固醇藥物吸入劑相等劑量) 及併用其他治療，如：長效乙二型作用劑 (β2-agonist)、口服類固醇治療、口服theophylline或抗白三烯素類藥品仍控制不良者。
IV.經證實為氣喘病患，支氣管擴張試驗顯示FEV1 reversibility超過12%，或使用類固醇後FEV1增加20%以上。

健保署公告：異動含mepolizumab成分（如Nucala）、benralizumab成分（如Fasenra）之藥品共2品項之支付價暨修訂其給付規定，並自109年11月1日起實施

修訂後給付規定	原給付規定
6.2.8.Mepolizumab (如Nucala)、Benralizumab (如Fasenra)（107/11/1、109/3/1、109/11/1）： 1. 限用於經胸腔專科或過敏免疫專科醫師診斷為嗜伊紅性(嗜酸性)白血球的嚴重氣喘且控制不良(severe refractory eosinophilic asthma)之18歲以上成人病患，投藥前12個月內的血中嗜伊紅性(嗜酸性)白血球≥300 cells/mcL，且需符合下列條件：(109/11/1) 1. 病患已遵循最適切的標準療法且過去6個月持續使用口服類固醇prednisolone每天至少5mg或等價當量(equivalence)。 2. 過去12個月內有2次或2次以上因氣喘急性惡化而需要使用全身性類固醇，且其中至少一次是因為氣喘惡化而需急診或住院治療。 2. 需經事前審查核准後使用。 3. 使用頻率： 4. Mepolizumab每4週使用不得超過1次。 5. Benralizumab第一個8週使用不得超過3次(第0、4、8週)，以後每8週使用不得超過1次。 6. 使用32週後進行評估，與未使用前比較，若「惡化」情形減少，方可繼續使用。 備註： 1.「惡化」的定義為必須使用口服/全身性類固醇治療、或住院治療、或送急診治療的氣喘惡化現象。 2.「最適切的標準療法」係指符合GINA治療指引Step 5之規範。(109/11/1)	6.2.8.Mepolizumab (如Nucala)、Benralizumab (如Fasenra)：（107/11/1、109/3/1） 1. 限用於經胸腔內科或過敏免疫專科醫師診斷為嗜伊紅性(嗜酸性)白血球的嚴重氣喘且控制不良(severe refractory eosinophilic asthma)之18歲以上成人病患，且需符合下列條件： 1. 病患同意且遵循最適切的標準療法且符合下述條件者： 2. 過去12個月有4次或4次以上因急性惡化而需要使用全身性類固醇，且其中至少一次是因為氣喘惡化而需急診或住院。 3. 過去6個月持續使用口服類固醇prednisolone至少每天5mg或等價當量(equivalent)。 1. 投藥前12個月內的血中嗜伊紅性(嗜酸性)白血球≥300 cells/mcL。 4. 需經事前審查核准後使用。 5. 使用頻率：（109/3/1） 6. Mepolizumab每4週使用不得超過1次。 7. Benralizumab第一個8週使用不得超過3次(第0、4、8週)，以後每8週使用不得超過1次。 8. 使用32週後進行評估，與未使用前比較，若「惡化」情形減少，方可繼續使用。 備註：「惡化」的定義為必須使用口服/全身性類固醇治療、或住院治療、或送急診治療的氣喘惡化現象。

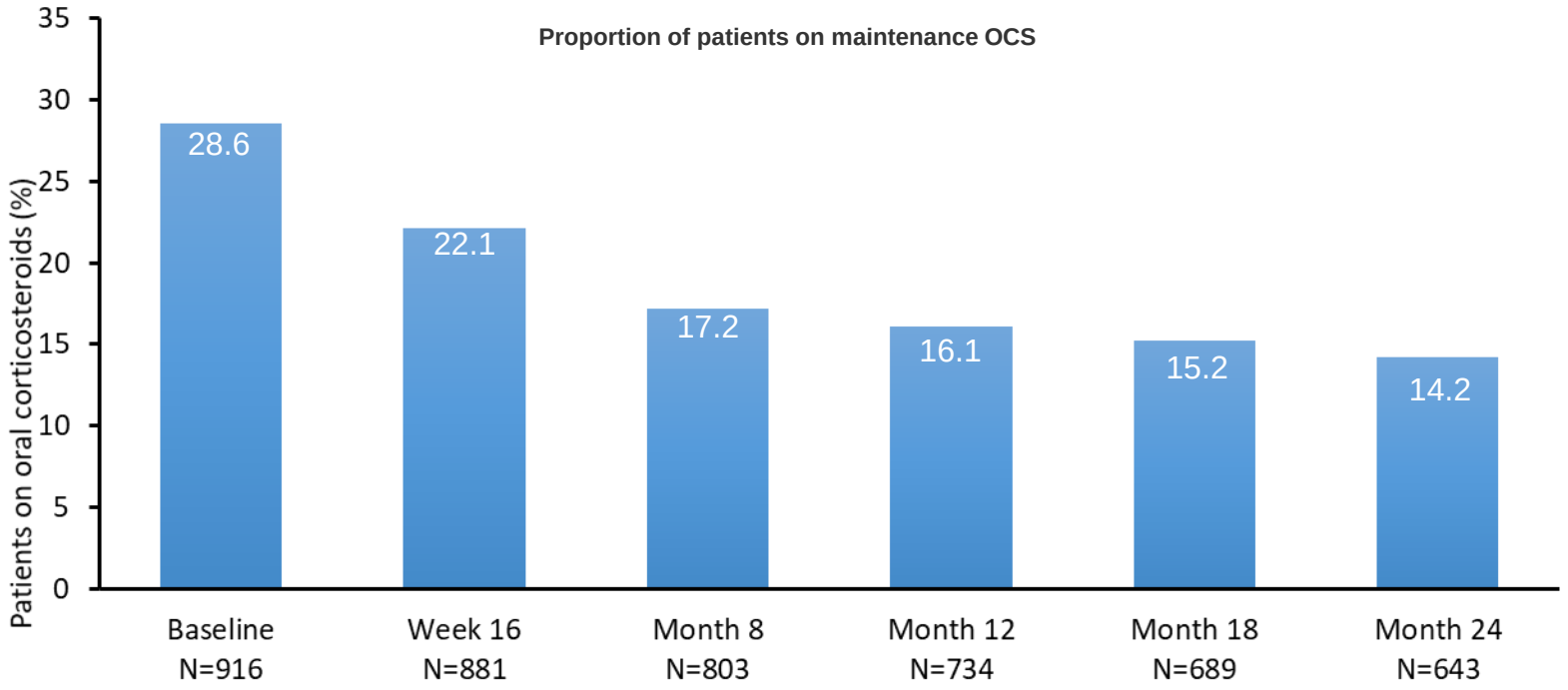
Percentage reduction in exacerbation rate with OMA V.S. placebo by blood EOS level and clinical indices of asthma severity



Casale TB, Chipps BE, Rosen K, et al. Allergy. 2017;00:1–8.

Omalizumab for severe asthma: oral corticosteroid-sparing effect

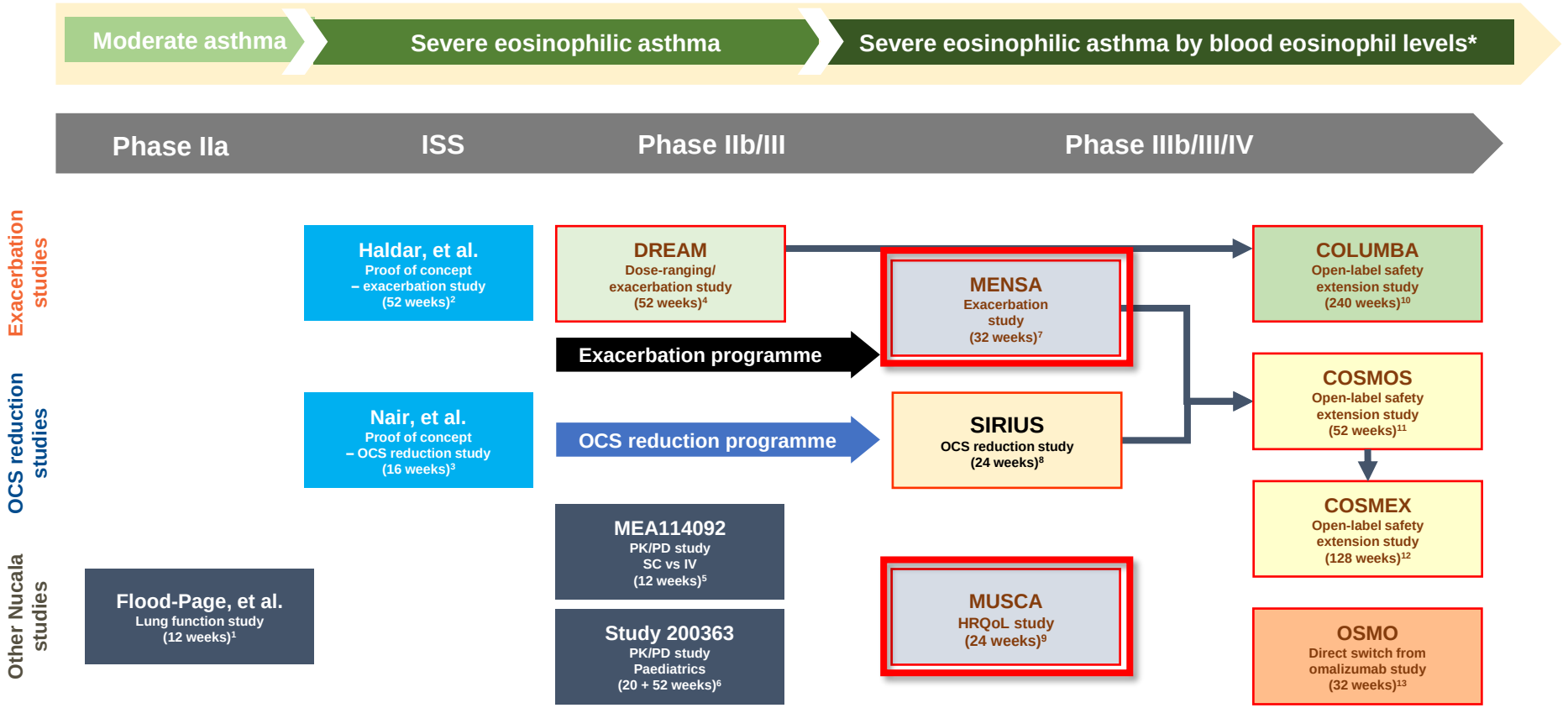
eXpeRience: A 2-year, multinational, non-interventional, observational registry of patients receiving omalizumab for uncontrolled allergic asthma in 943 patients



N = number of evaluable patients at each time point

Braunstahl G-J, et al. Allergy Asthma Clin Immunol 2013;9:47

Asthma clinical development programme for Nucala in adults



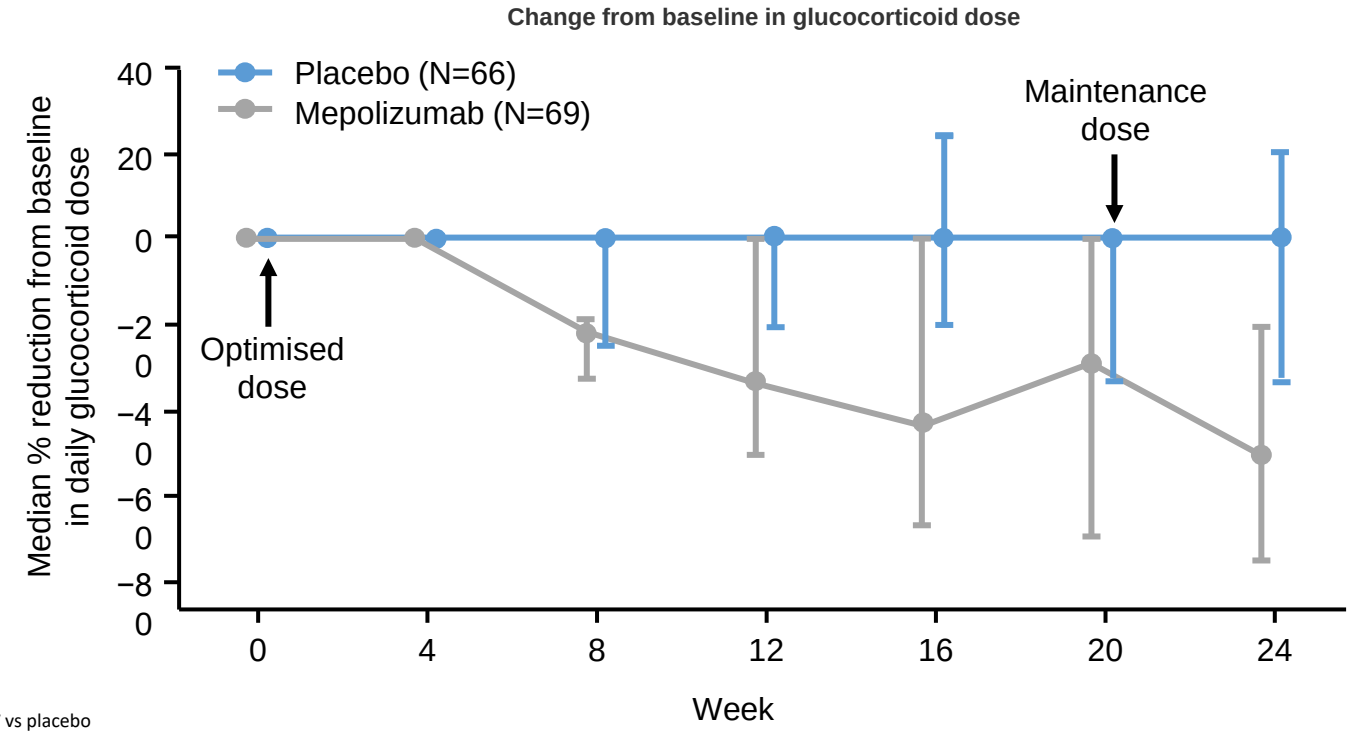
Note: Nucala is not licenced as an IV medication.

* Blood eosinophil levels of ≥150 cells/µL at study initiation or ≥300 cells/µL in previous 12 months. ISS, investigator-sponsored studies.

1. Flood-Page P, et al. *Am J Respir Crit Care Med*. 2007;176:1062–1071; 2. Haldar P, et al. *N Engl J Med.* 2009;360:973–984; 3. Nair P, et al. *N Engl J Med.* 2009;360:985–993; 4. Pavord ID, et al. *Lancet*. 2012;380:651–659;
5. NCT01366521. Available at: clinicaltrials.gov/ct2/show/NCT01366521 [accessed October 2018]; 6. GSK. Data on file. RF/NLA/0164/18; 7. Ortega HG, et al. *N Engl J Med.* 2014;371:1198–1207; 8. Bel EH, et al. *N Engl J Med.* 2014;371:1189–1197; 9. Chupp GL, et al. *Lancet Respir Med.* 2017;5;390–400; 10. Khatri S, et al. *J Allergy Clin Immunol*. 2018. [Epub ahead of print]. doi: https://doi.org/10.1016/j.jaci.2018.09.033; 11. Lugogo N, et al. *Clin Ther.* 2016;38:2058–2070; 12. NCT02135692. Available at: clinicaltrials.gov/ct2/show/ NCT02135692 [accessed October 2018]; 13. NCT02654145. Available at: clinicaltrials.gov/ct2/show/NCT02654145 [accessed October 2018].

Mepolizumab for severe asthma: oral corticosteroid-sparing effect

SIRIUS: A randomised, double-blind trial in patients (N=135) with severe eosinophilic asthma on long-term oral corticosteroids



0% reduction in dose (from baseline)

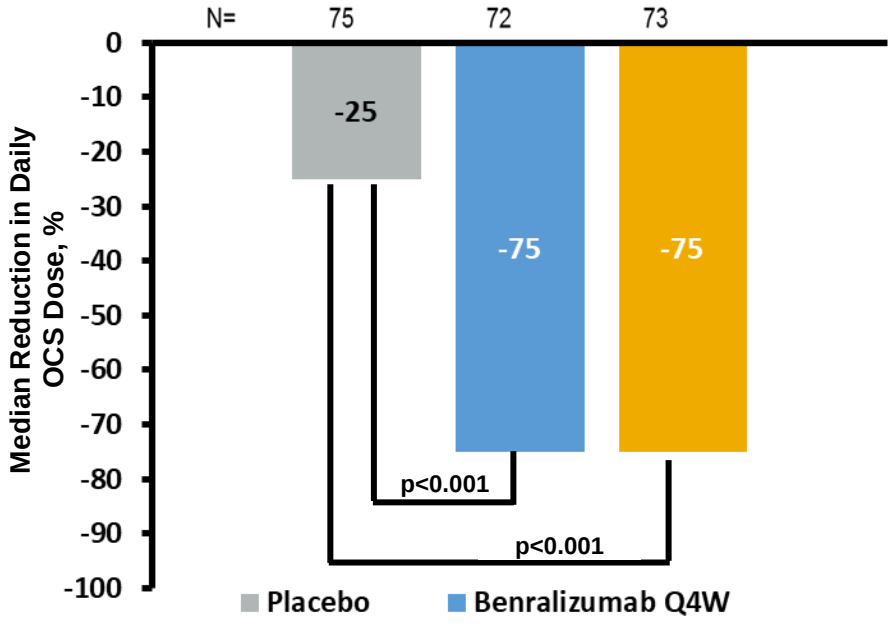
50% reduction in dose (from baseline)*

*p=0.007 vs placebo

Bel EH, et al. N Engl J Med 2014;371:1189–1197

ZONDA: Benralizumab Significantly Reduced Final OCS Doses at Week 28 While Maintaining Asthma Control vs. Placebo (Full Analysis Set)

Primary Analysis



Categorical Analysis

Reduction in Final OCS Dose, n (%)	Placebo N=75	Benra 30 mg Q4W N=72	Benra 30 mg Q8W N=73
≥90%	9 (12)	24 (33)	27 (37)
≥75%	15 (20)	38 (53)	37 (51)
≥50%	28 (37)	48 (67)	48 (66)
>0%	40 (53)	55 (76)	58 (79)
No change or any increase in OCS dose	35 (47)	17 (24)	15 (21)
OR (95 % CI)	–	**4.09 (2.22–7.57)**	**4.12 (2.22–7.63)**
p-value	–	<0.001	<0.001

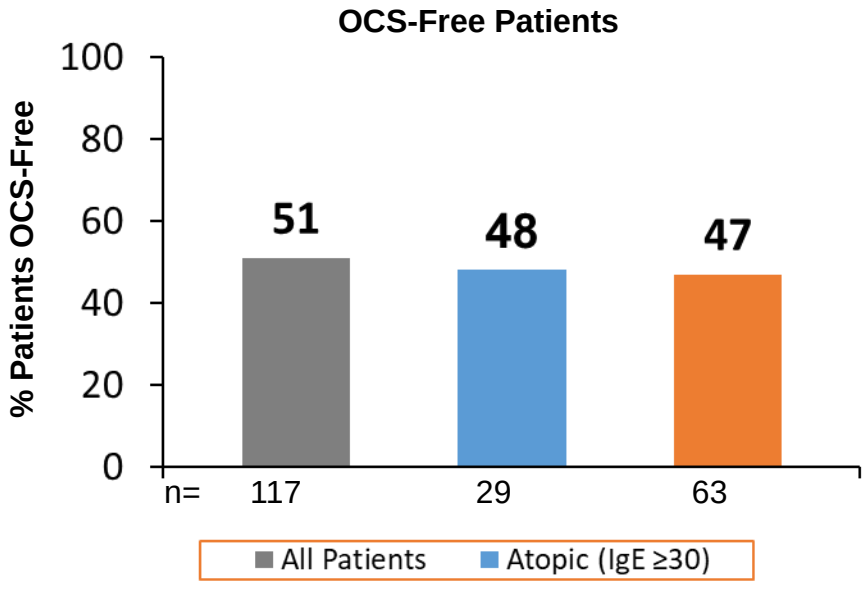
- **Reduction in final OCS daily dose was 4X greater with benra vs. placebo (median baseline OCS dose was 10 mg/d in all groups)**

benra = benralizumab; CI = confidence interval; OCS = oral corticosteroid; OR = odds ratio; Q4W = every 4 weeks; Q8W = every 8 weeks.

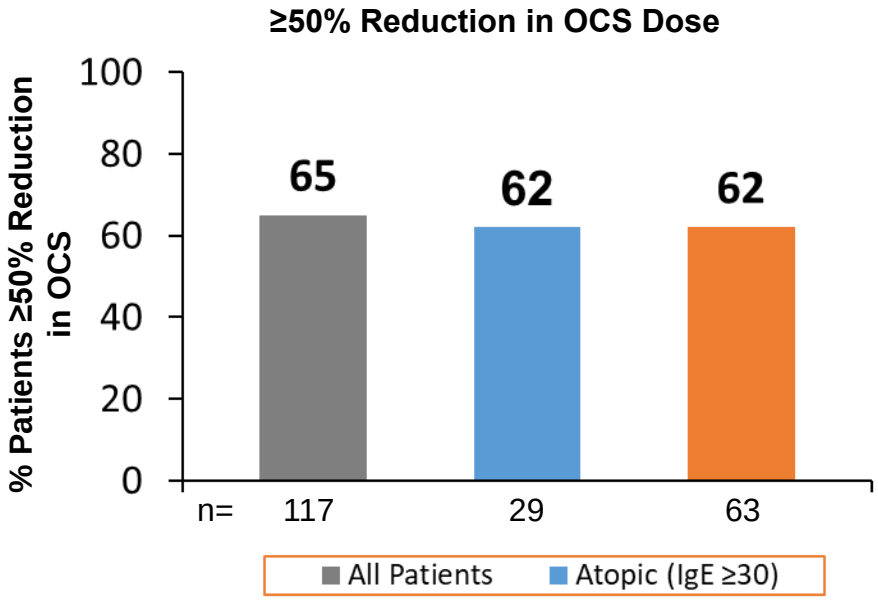
Nair P et al. *N Engl J Med*. 2017;376:2448-2458.

OCS Elimination and Dose Reduction at Week 48

接受benralizumab的治療48週後，有51%的病人已完全停止口服類固醇的治療



相較baseline, 高達65%的病患, 使用FASENRA治療至第48週時, 已顯著降低口服類固醇紀量達50%以上



Note: Patients with a sensitisation to any perennial aero-allergens but with a total IgE measure <30 IU/mL were excluded from the sub-group comparison.

N = number of patients; OCS = oral corticosteriod.

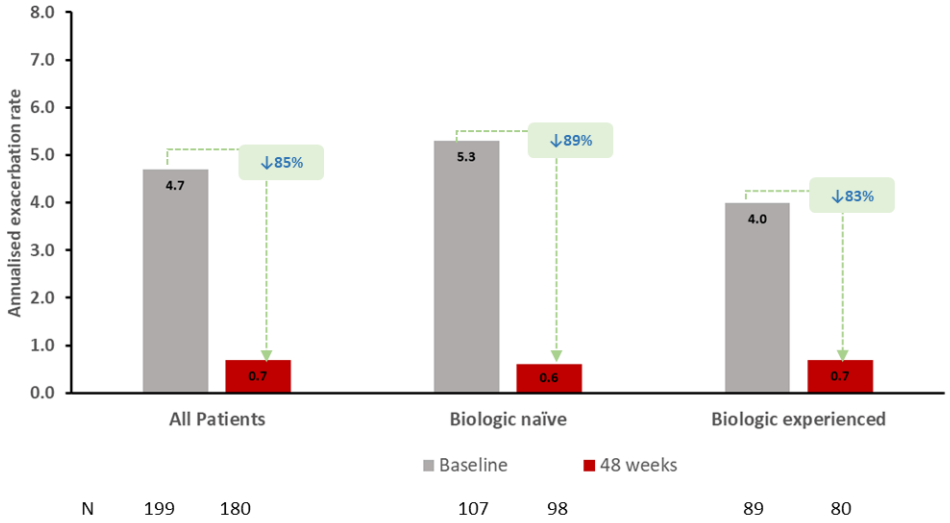
Jackson DJ et al. Presented at: EAACI International Digital Congress; June 6-8, 2020; London, UK.

5 Appendix: Key findings in biologic naïve vs experienced patients

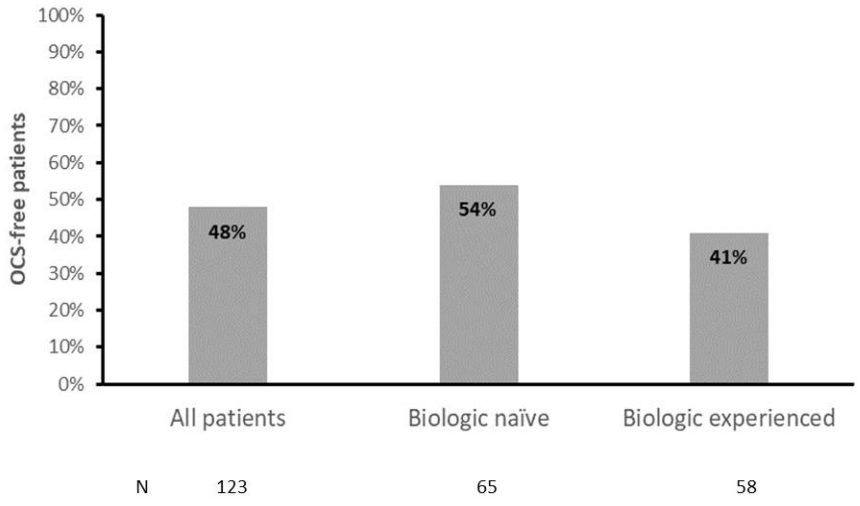
Benralizumab demonstrated substantial effect on all key clinical outcomes in both biologic-naive patients and those failing on previous biologic.

- 44% (89/202) of patients were biologic experienced; 75% of these (67/89) were mepolizumab and 10% (9/89) omalizumab experienced.

Reduction in annualized exacerbation rates

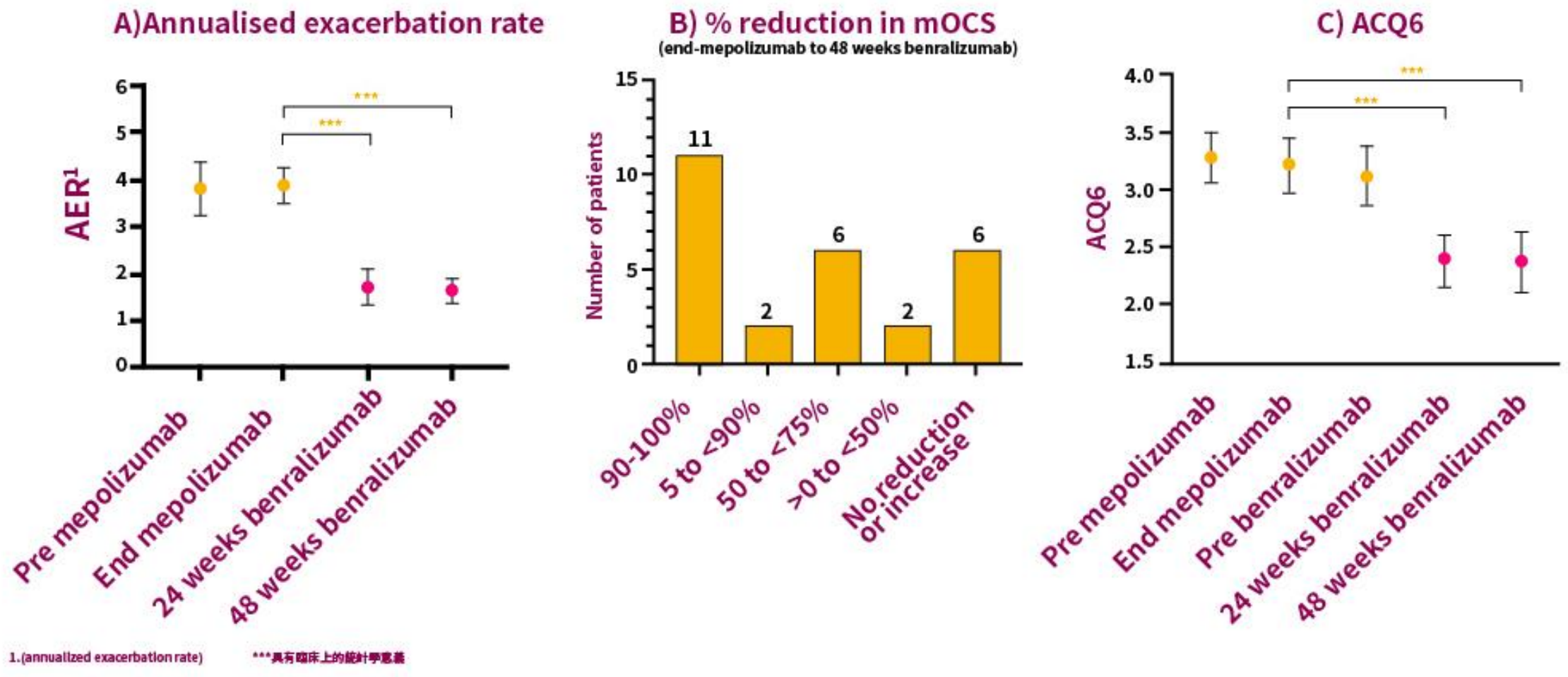


Percentage of patients OCS-free at 48 weeks



Data in the Appendix presented at ATS 2020. Reference Jackson et al 2020, abstract #12147

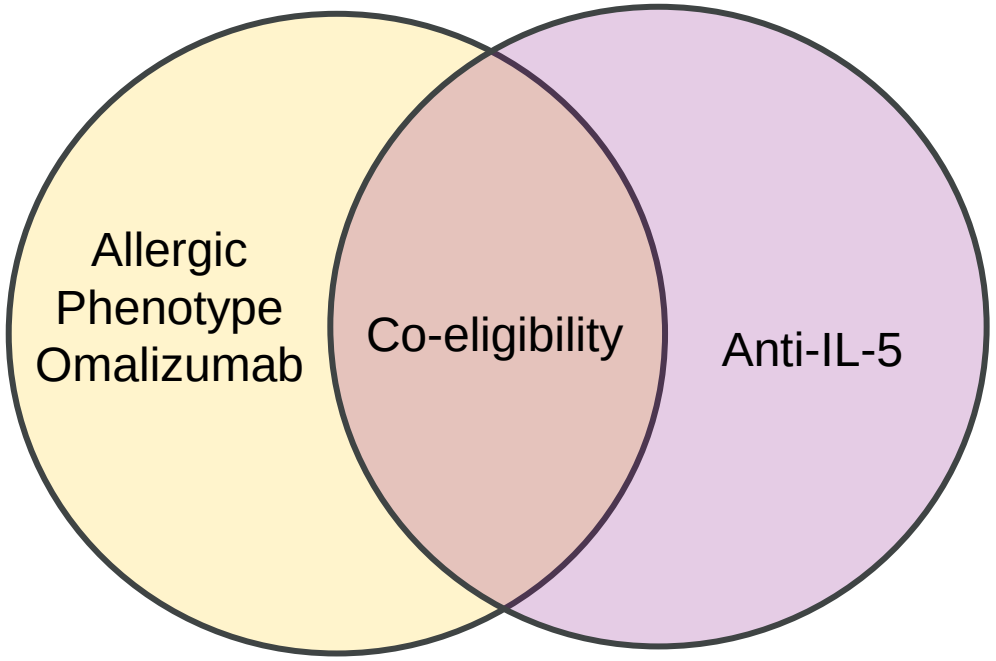
Response to benralizumab after sub-optimal response to mepolizumab in severe eosinophilic (a retrospective study)



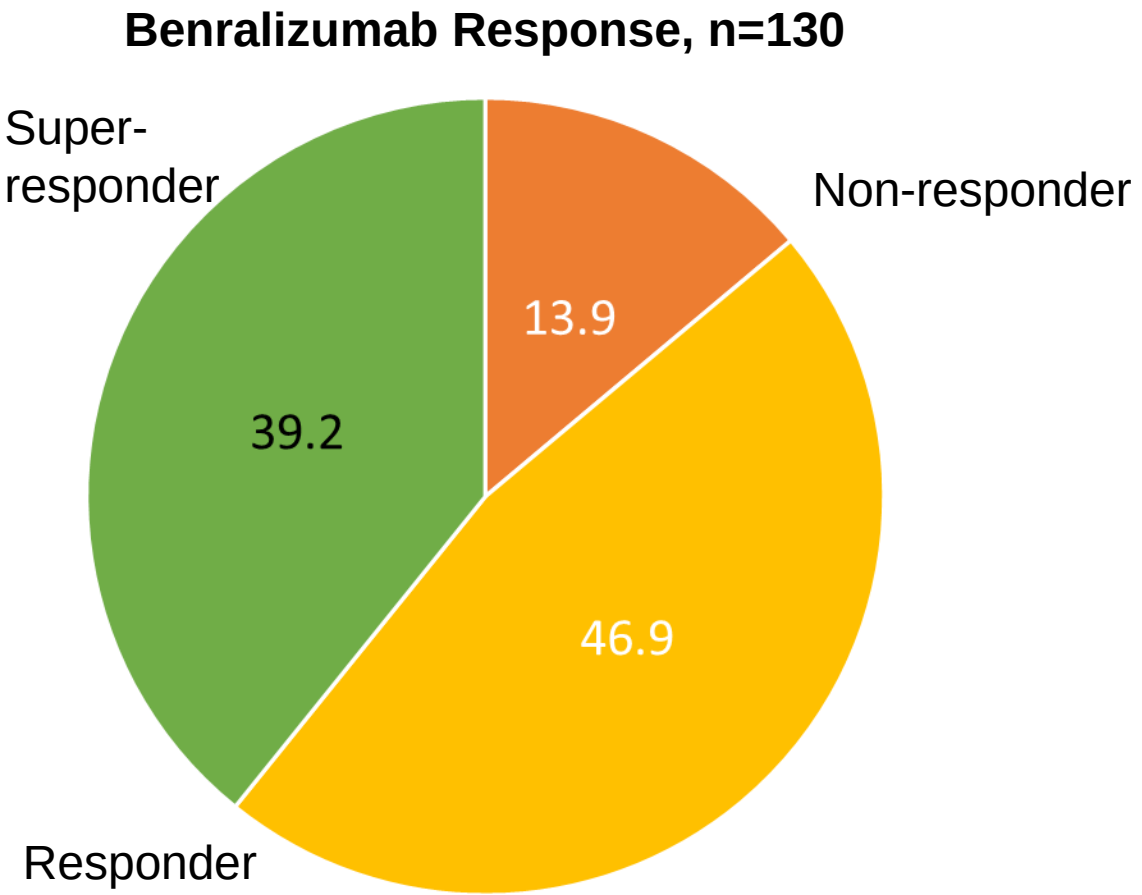
Kavanagh J et al. Allergy 2020;00:1–4.

The data is based upon Real World Evidence (RWE) data and is subject to potential confounding bias usually associated with observational research.

How do severe atopic patients eligible for anti-IgE respond to anti-IL-5/5R mAbs?



Real world effectiveness of benralizumab



Response to treatment was defined as a reduction of ≥ 50% in annualized exacerbation rate (AER) or in mOCS dose after 48 weeks of treatment.

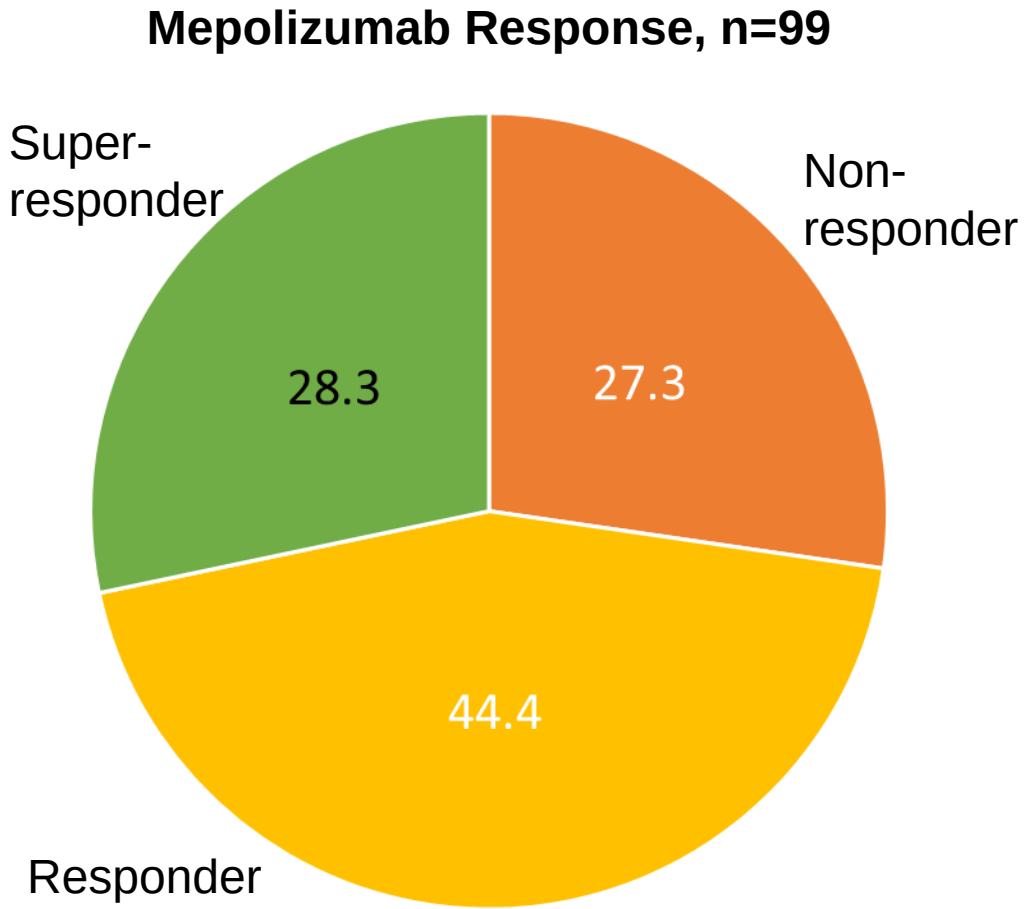
Super response was defined as zero exacerbations and no mOCSs for asthma.

Please note that as head-to-head studies were not conducted between these products, it is inappropriate to draw any comparisons and/or make any conclusions as the study design, demographics and other criteria may be different.

Kavanagh J et al . CHEST 2021; 159(2):496 506

The data is based upon Real World Evidence (RWE) data and is subject to potential confounding bias usually associated with observational research.

Real world effectiveness of mepolizumab



Response to treatment was defined as a reduction of ≥ 50% in annualized exacerbation rate (AER) or in mOCS dose after 48 weeks of treatment.

Super response was defined as zero exacerbations and no mOCSs for asthma.

Please note that as head-to-head studies were not conducted between these products, it is inappropriate to draw any comparisons and/or make any conclusions as the study design, demographics and other criteria may be different.

Kavanagh J et al. CHEST 2020; 158(2):491-500

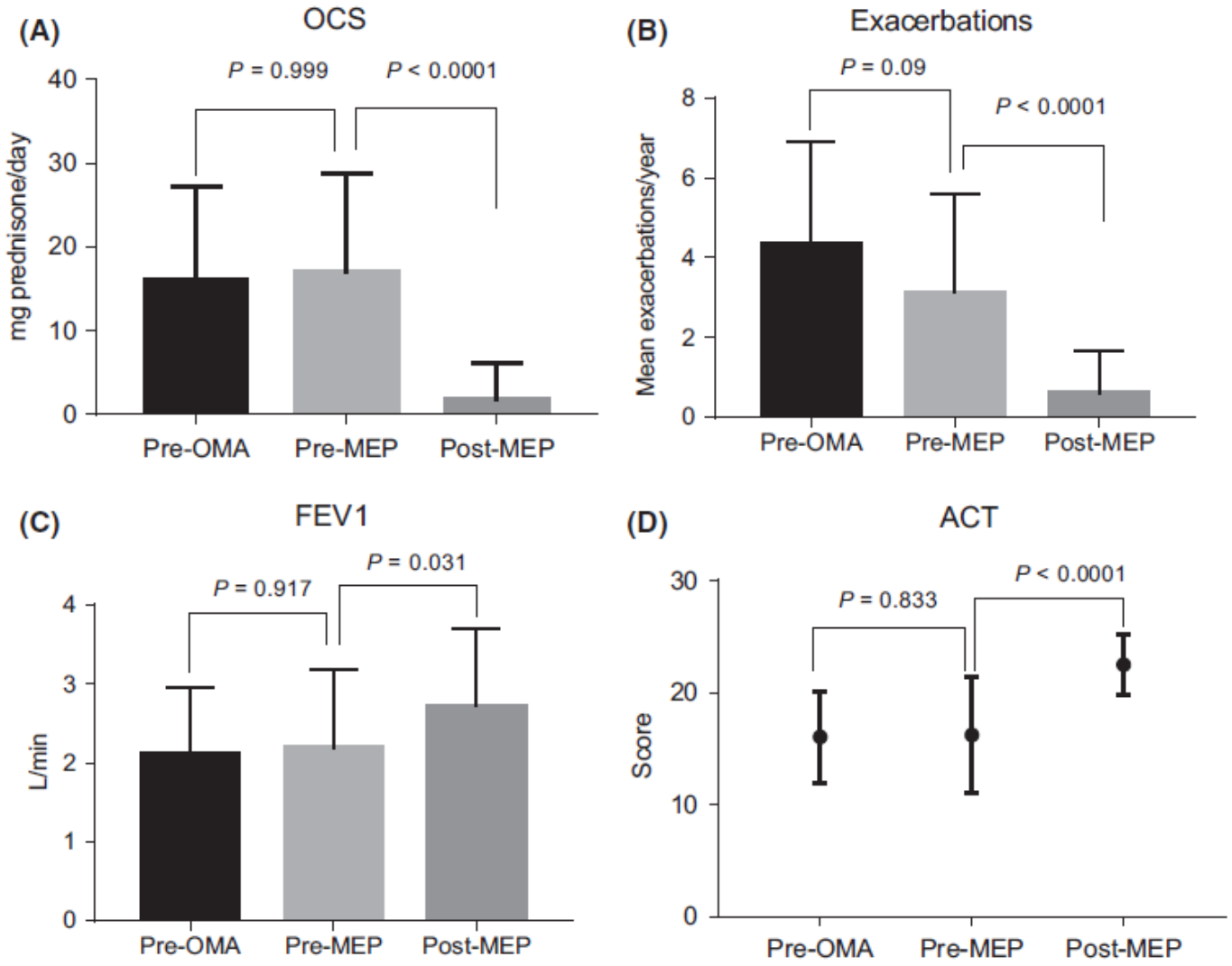
The data is based upon Real World Evidence (RWE) data and is subject to potential confounding bias usually associated with observational research.

The present results suggest that, when the anti-IgE-strategy fails and severe asthma maintains a high-eosinophil profile, a switch to IL-5 antagonists is a reasonable choice.

Retrospective analysis:

- Severe asthma patients, N=27
- Age: 57±11.7 years
- Non-responder to OMA:

  Unable to discontinue or escalate daily dose of OCS, who persisted with 2 or more exacerbations/year or needed at least 1 hospitalization.
- Washout period: 1 month



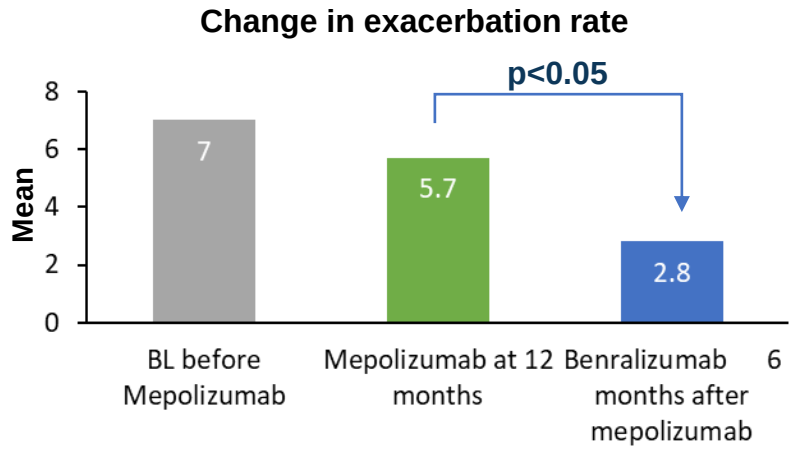
Allergy. 2019;74(12):2539-2541.

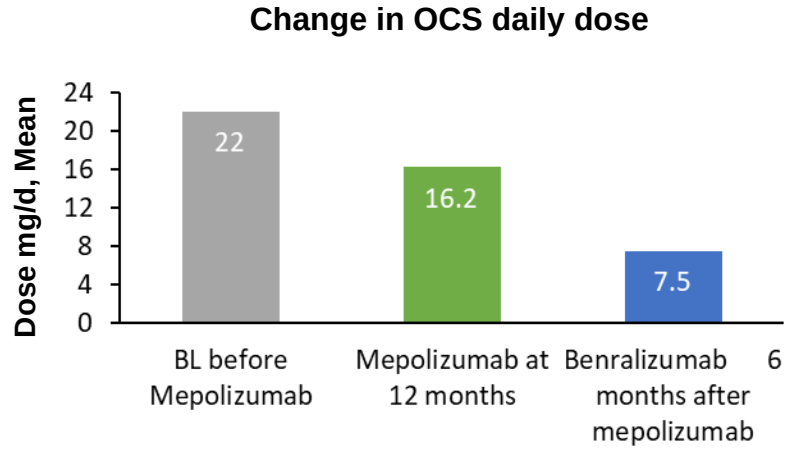
Retrospective Study: Benralizumab at 6 Months After Switching From 12 Months of Mepolizumab Treatment

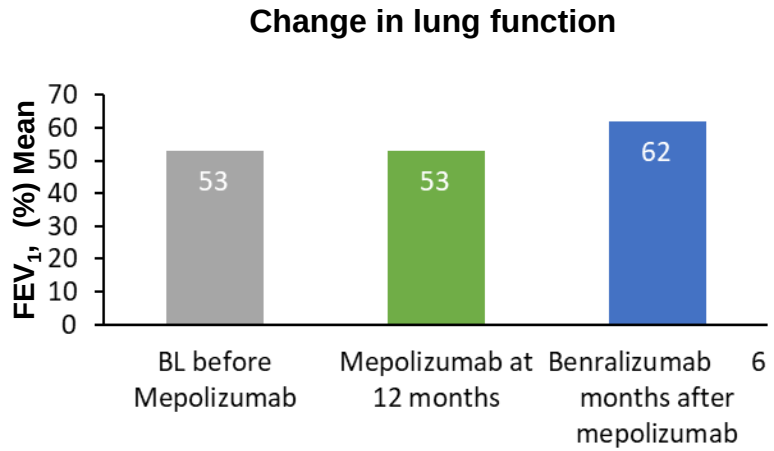
Direct Switching
(No washout period)

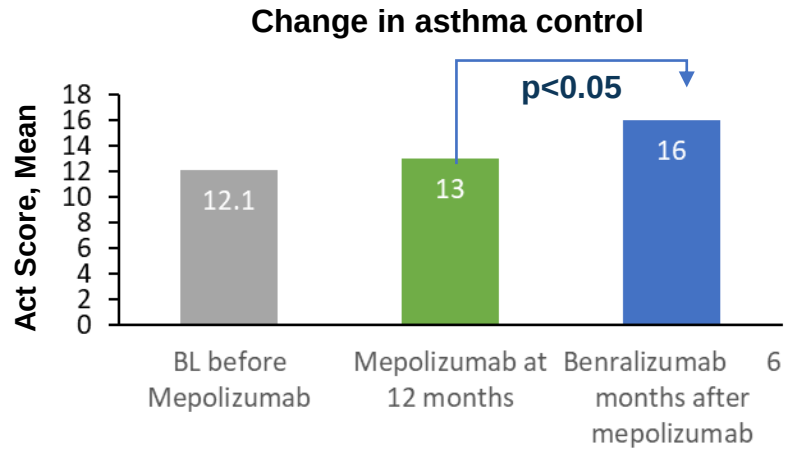
Patients treated with benralizumab for 6 months after intermediate/poor response to mepolizumab, 48% were observed to have an GETE score of 1-2 (p=0.012)

Retrospective analysis:
- SEA patients, N=22
- Age: 49±11 years
- History of NP, 55%
- bEOS 12 months after mepo vs. 6 months after benra 186 cells/µL vs. 0 cells/µL (p<0.05)
- Intermediate or poor response to mepo (GETE score of 3-4 at 12 months)









Good or excellent response had GETE scores of 1-2.

ACT = Asthma Control Test; BL = baseline; bEOS = blood eosinophils; GETE = Global Evaluation for Treatment Efficiency; NP = nasal polyps; OCS = oral corticosteriod; SEA = severe eosinophilic asthma.

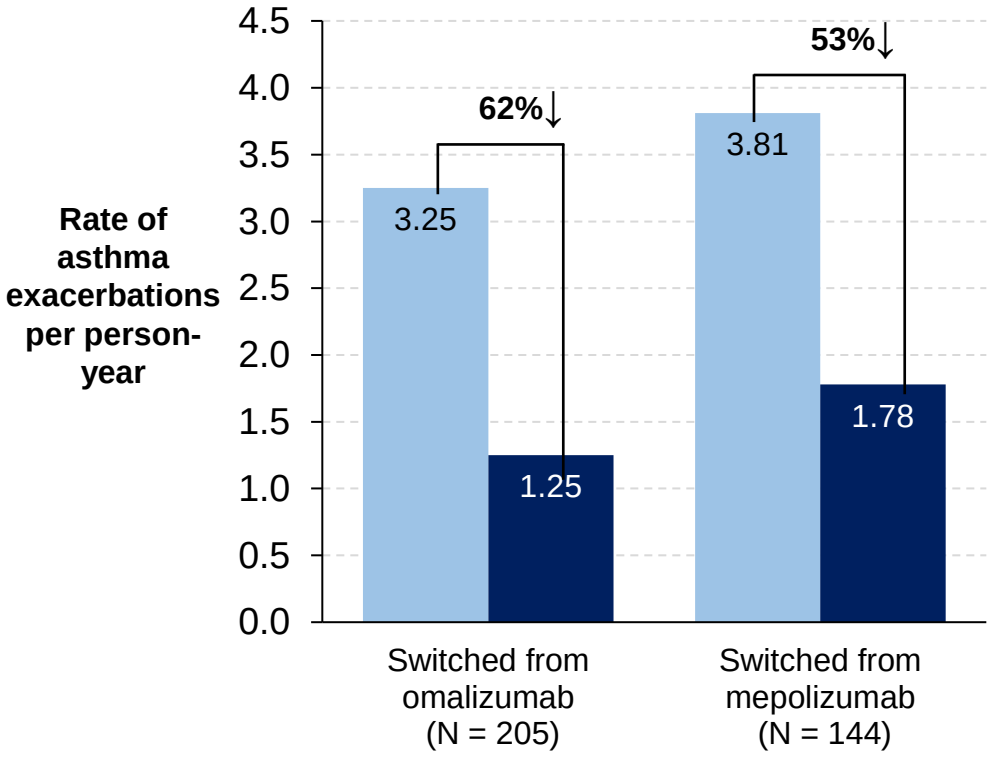
Luzietoso MF et al. *Eur Respir J.* 2020;56:2258.

The data is based upon Real World Evidence (RWE) data and is subject to potential confounding bias usually associated with observational research.

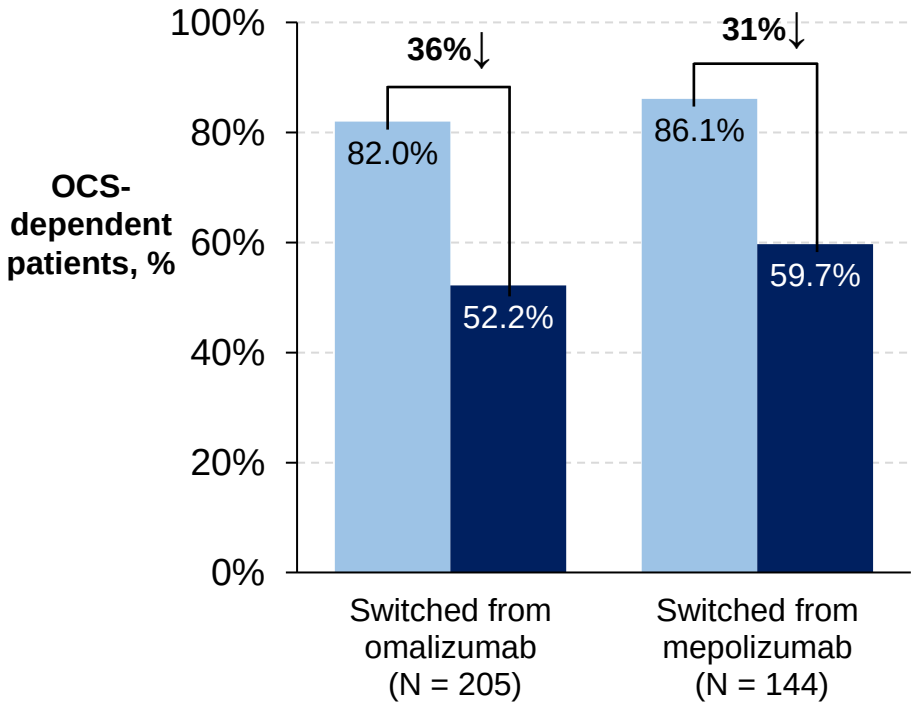
ZEPHYR 2 study: The reduction of exacerbation rate and OCS-dependent patients were observed in the switch cohort.

These are observational data. The efficacy and safety of benralizumab has not been evaluated in head-to-head trials vs omalizumab or mepolizumab.

Exacerbation rate



OCS-dependent patients (%)



N = number.

- Across the eosinophil and switch cohorts, there was a reduction in asthma exacerbation rates in the post-index period

Maselli DJ et al. Poster Presentation at American College of Allergy, Asthma, and Immunology Meeting 2021; November 4-8, 2021.

The data is based upon Real World Evidence (RWE) data and is subject to potential confounding bias usually associated with observational research.

Assess and treat severe asthma phenotypes *cont'd*

Continue to optimize management as in section **3** (including inhaler technique, adherence, comorbidities, non-pharmacologic strategies)

8 Consider *add-on biologic Type 2-targeted* treatments

- Consider add-on Type 2-targeted biologic therapy for patients with exacerbations or poor symptom control on high dose ICS-LABA, who have evidence of Type 2 inflammation*
- Consider **local payer eligibility criteria***, **comorbidities** and **predictors of response** when choosing between available therapies
- Also consider cost, dosing frequency, route (SC or IV), patient preference

Which biologic is appropriate to start first?

Eligibility | *Predictors of asthma response*

Anti-IgE *(omalizumab)*

*Is the patient eligible for **anti-IgE** for severe allergic asthma?**
- Sensitization on skin prick testing or specific IgE
- Total serum IgE and weight within dosage range
- Exacerbations in last year

What factors may predict good asthma response to anti-IgE?
- Blood eosinophils ≥260/µl ++
- FeNO ≥20 ppb +
- Allergen-driven symptoms +
- Childhood-onset asthma +

no / *no*

Anti-IL5 / Anti-IL5R *(benralizumab, mepolizumab, reslizumab)*

*Is the patient eligible for **anti-IL5 / anti-IL5R** for severe eosinophilic asthma?**
- Exacerbations in last year
- Blood eosinophils, e.g. ≥150/µl or ≥300/µl

What factors may predict good asthma response to anti-IL5/5R?
- Higher blood eosinophils +++
- More exacerbations in previous year +++
- Adult-onset of asthma ++
- Nasal polyposis ++

no / *no*

Anti-IL4R *(dupilumab)*

*Is the patient eligible for **anti-IL4R** for severe eosinophilic/Type 2 asthma?**
- Exacerbations in last year
- Blood eosinophils ≥150 and ≤1500/µl, or FeNO ≥25 ppb, or taking maintenance OCS

What factors may predict good asthma response to anti-IL4R?
- Higher blood eosinophils +++
- Higher FeNO +++

no / *no*

Anti-TSLP *(tezepelumab)*

*Is the patient eligible for **anti-TSLP** for severe asthma?**
- Exacerbations in last year

What factors may predict good asthma response to anti-TSLP?
- Higher blood eosinophils +++
- Higher FeNO +++

Eligible for none? Return to section **7**

Choose one if eligible*; trial for at least 4 months and assess response

*Good asthma response?**

unclear → Extend trial to 6-12 months*

yes → Good response to T2-targeted therapy

no → **STOP add-on**

Consider switching to a different Type 2-targeted therapy, if eligible*

no → Little/no response to T2-targeted therapy

No evidence of Type 2 airway inflammation

No evidence of Type 2 airway inflammation. Go to section **10**

* *Check local eligibility criteria for specific biologic therapies as these may vary from those listed*

8 Consider *add-on biologic Type 2-targeted* treatments

pharmacologic strategies)

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Predictors of asthma response

What factors may predict good asthma response to anti-IgE?
- Blood eosinophils ≥260/µl ++
- FeNO ≥20 ppb +
- Allergen-driven symptoms +
- Childhood-onset asthma +

What factors may predict good asthma response to anti-IL5/5R?
- Higher blood eosinophils +++
- More exacerbations in previous year +++
- Adult-onset of asthma ++
- Nasal polyposis ++

What factors may predict good asthma response to anti-IL4R?
- Higher blood eosinophils +++
- Higher FeNO +++

What factors may predict good asthma response to anti-TSLP?
- Higher blood eosinophils +++
- Higher FeNO +++

Choose one if eligible*; trial for at least 4 months and assess response

*Good asthma response?**

unclear → Extend trial to 6-12 months*

yes → Good response to T2-targeted therapy

no → **STOP add-on**

Consider switching to a different Type 2-targeted therapy, if eligible*

no → Little/no response to T2-targeted therapy

No evidence of Type 2 airway inflammation

No evidence of Type 2 airway inflammation. Go to section 10

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8 Consider *add-on biologic Type 2-targeted* treatments

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Which biologic is appropriate to start first?

Eligibility

Anti-IgE *(omalizumab)*

*Is the patient eligible for **anti-IgE** for severe allergic asthma?**

- Sensitization on skin prick testing or specific IgE
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- Exacerbations in last year

no / *no*

Anti-IL5 / Anti-IL5R *(benralizumab, mepolizumab, reslizumab)*

*Is the patient eligible for **anti-IL5 / anti-IL5R** for severe eosinophilic asthma?**

- Exacerbations in last year
- Blood eosinophils, e.g. ≥150/µl or ≥300/µl

no / *no*

Anti-IL4R *(dupilumab)*

*Is the patient eligible for **anti-IL4R** for severe eosinophilic/Type 2 asthma?**

- Exacerbations in last year
- Blood eosinophils ≥150 and ≤1500/µl, or FeNO ≥25 ppb, or taking maintenance OCS

no / *no*

Anti-TSLP *(tezepelumab)*

*Is the patient eligible for **anti-TSLP** for severe asthma?**

- Exacerbations in last year

Eligible for none? Return to section 7

Choose one if eligible*; trial for at least 4 months and assess response

*Good asthma response?**

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Consider switching to a different Type 2-targeted therapy, if eligible*

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Assess and treat severe a

Continue to optimize management as in

8 Consider ***add-on biologi***

- Consider add-on Type 2-targeted biologic therapy for patients with exacerbations or poor symptom control on high dose ICS-LABA, who have evidence of Type 2 inflammation*
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Eligibility	*Predictors of asthma response*
Anti-IgE *(omalizumab)* *Is the patient eligible for **anti-IgE** for severe allergic asthma?** • Sensitization on skin prick testing or specific IgE • Total serum IgE and weight within dosage range • Exacerbations in last year	*What factors may predict good asthma response to anti-IgE?* • Blood eosinophils ≥260/µl ++ • FeNO ≥20 ppb + • Allergen-driven symptoms + • Childhood-onset asthma +
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no / *no*	
Anti-IL4R *(dupilumab)* *Is the patient eligible for **anti-IL4R** for severe eosinophilic/Type 2 asthma?** • Exacerbations in last year • Blood eosinophils ≥150 and ≤1500/µl, or FeNO ≥25 ppb, or taking maintenance OCS	*What factors may predict good asthma response to anti-IL4R?* • Higher blood eosinophils +++ • Higher FeNO +++
no / *no*	
Anti-TSLP *(tezepelumab)* *Is the patient eligible for **anti-TSLP** for severe asthma?** • Exacerbations in last year	*What factors may predict good asthma response to anti-TSLP?* • Higher blood eosinophils +++ • Higher FeNO +++

Eligible for none? Return to section **7**

end trial to 2 months*

unclear

*Good asthma sponse?**

yes

Good response to T2-targeted therapy

no

P add-on

der switching ifferent Type eted therapy, ble*

no

Little/no response to T2-targeted therapy

SPECIALIST CARE; SEVERE ASTHMA CLINIC IF AVAILABLE

Assess and treat severe asthma phenotypes *cont'd*

Continue to optimize management as in section **3** (including inhaler technique, adherence, comorbidities, non-pharmacolo

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Anti-IL4R *(dupilumab)*

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no / *no*

Anti-TSLP *(tezepelumab)*

*Is the patient eligible for **anti-TSLP** for severe asthma?**

- Exacerbations in last year

Eligible for none? Return to section **7**

No evidence of Type 2 airway inflammation

Choose one if eligible*; trial for at least 4 months and assess response

*Good asthma response?**

yes → **Good response to T2-targeted therapy**

unclear → Extend trial to 6-12 months*

no → **STOP add-on**

Consider switching to a different Type 2-targeted therapy, if eligible*

no → **Little/no response to T2-targeted therapy**

* *Check local eligibility criteria for specific biologic therapies as these may vary from those listed*

Conclusion

- Reduce OCS is an important work
  - Avoid mortality and mobidity
  - Avoie OCS related side effect
- Biologic agent can reduce OCS usage, in step 5
  - Anti-IgE
  - Anti-IL5
  - Anti-IL5R
- Refer to specialist when severe asthma

Thanks