

# Biologika in der Therapie von schwerem Asthma: Wo stehen wir heute?



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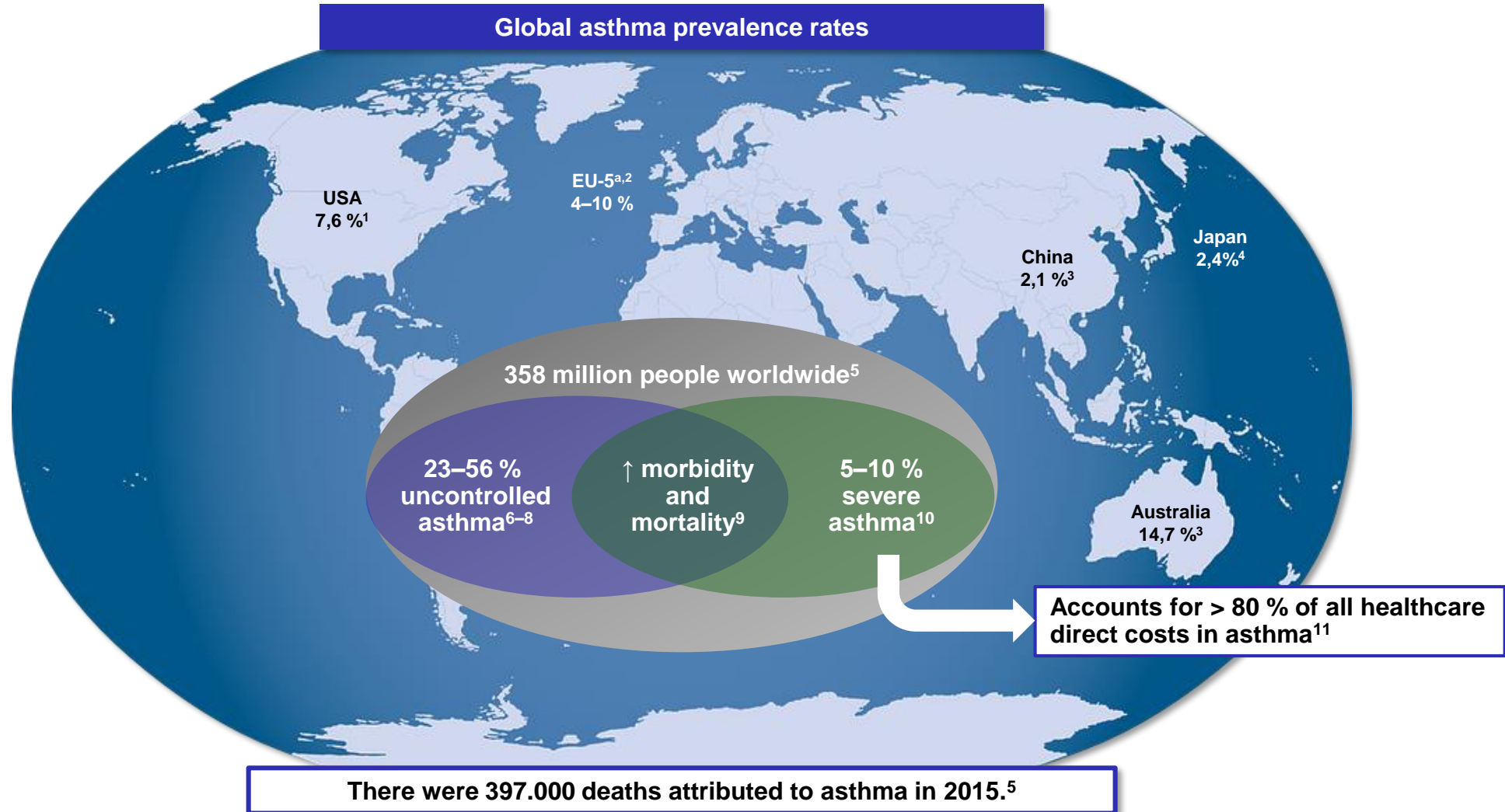


# Interessenskonflikt

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- Das Pneumologische Forschungsinstitut an der LungenClinic Grosshansdorf erhielt Kostenerstattungen für Beratung und Studiendurchführung von AB2BIO, AstraZeneca, Bayer Health Care, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Merck, Novartis, Pfizer, TEVA, Revotar, Sanofi, Sterna, Roche.
- Henrik Watz erhielt Honorare für Beratung und Vorträge sowie Erstattung von Reisekosten und Kongressgebühren der Firmen AstraZeneca, Boehringer Ingelheim, BerlinChemie, Chiesi, GlaxoSmithKline, Novartis, Sanofi, Roche.

# Global burden of asthma



# Unkontrolliert ... schwierig zu therapieren ... schweres Asthma

## Uncontrolled asthma

- **Poor symptom control** (frequent symptoms or reliever use, activity limited by asthma, night waking due to asthma)
- **Frequent exacerbations** ( $\geq 2$ /year) requiring OCS, or serious exacerbations ( $\geq 1$ /year) requiring hospitalization



## Difficult-to-treat asthma

- **Uncontrolled despite GINA Step 4–5 treatment** (e.g. medium or high dose ICS with a second controller; maintenance OCS), or such treatment to maintain good symptom control and reduce the risk of exacerbations
- Asthma may **appear difficult-to-treat because of modifiable factors** (incorrect inhaler technique, poor adherence, smoking or comorbidities, of incorrect diagnosis)



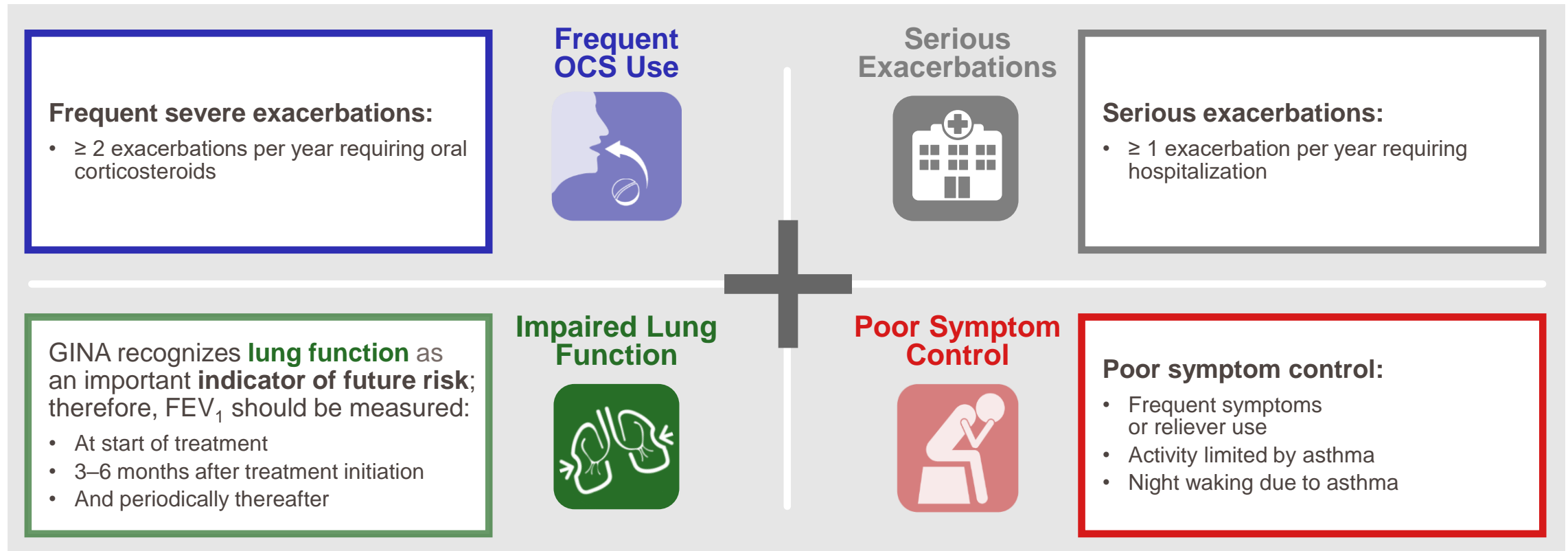
## Severe asthma

- **Uncontrolled despite GINA Step 4–5 treatment** (e.g. medium or high dose ICS with a second controller; maintenance OCS), **and good adherence and treatment of contributory factors** or asthma that **worsens when high-dose treatment is decreased**

# Kriterien der Asthmakontrolle

## GINA

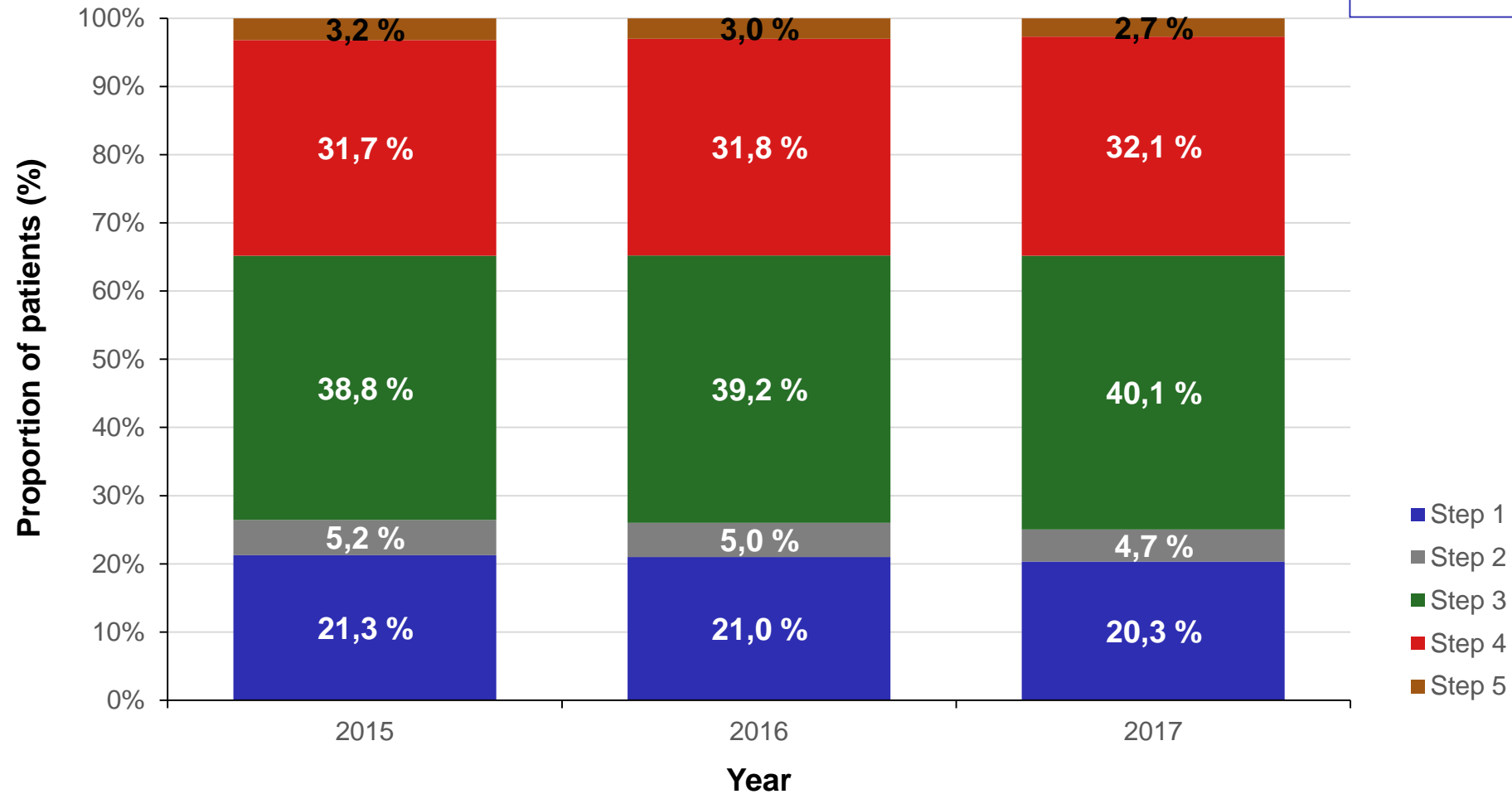
Any 1 of the following 4 criteria qualifies a patient as having uncontrolled asthma, despite therapy:



# Versorgungsrealität Deutschland I

## 1A. Severity of asthma according to treatment group

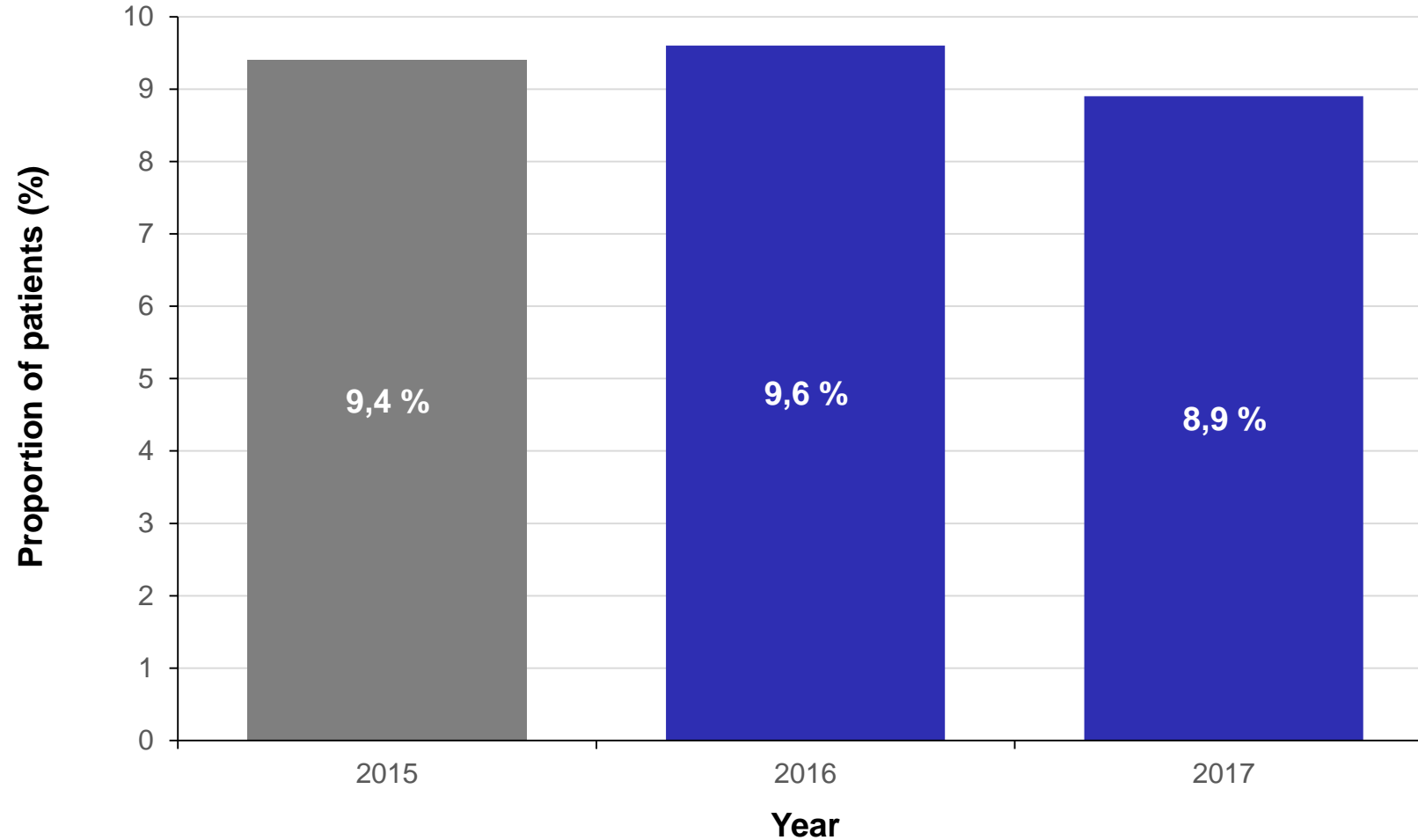
- n = 30.000
- 1039 Allgemeinpraxen



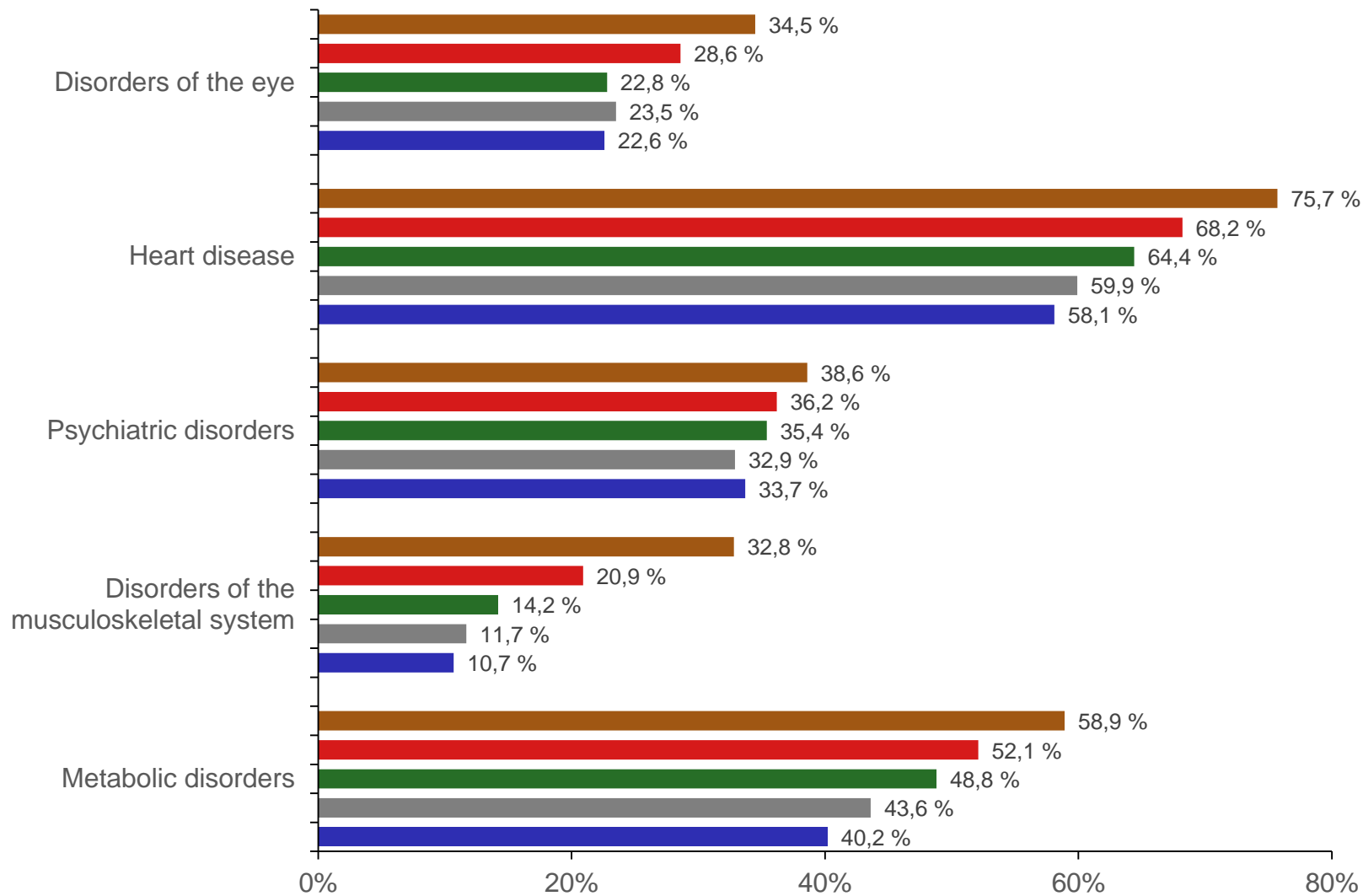
# Versorgungsrealität Deutschland I

2A. Proportion of patients with asthma receiving OCS > 30 d/y

- 10–15 mg Prednisolon
- 30 % nicht Stufe 5



# Versorgungsrealität Deutschland II (2015)



- Krankenkassendaten
- n = 4 Mio
- 7,3 % Asthmaprävalenz
- 8,7 % HD-ICS/LABA

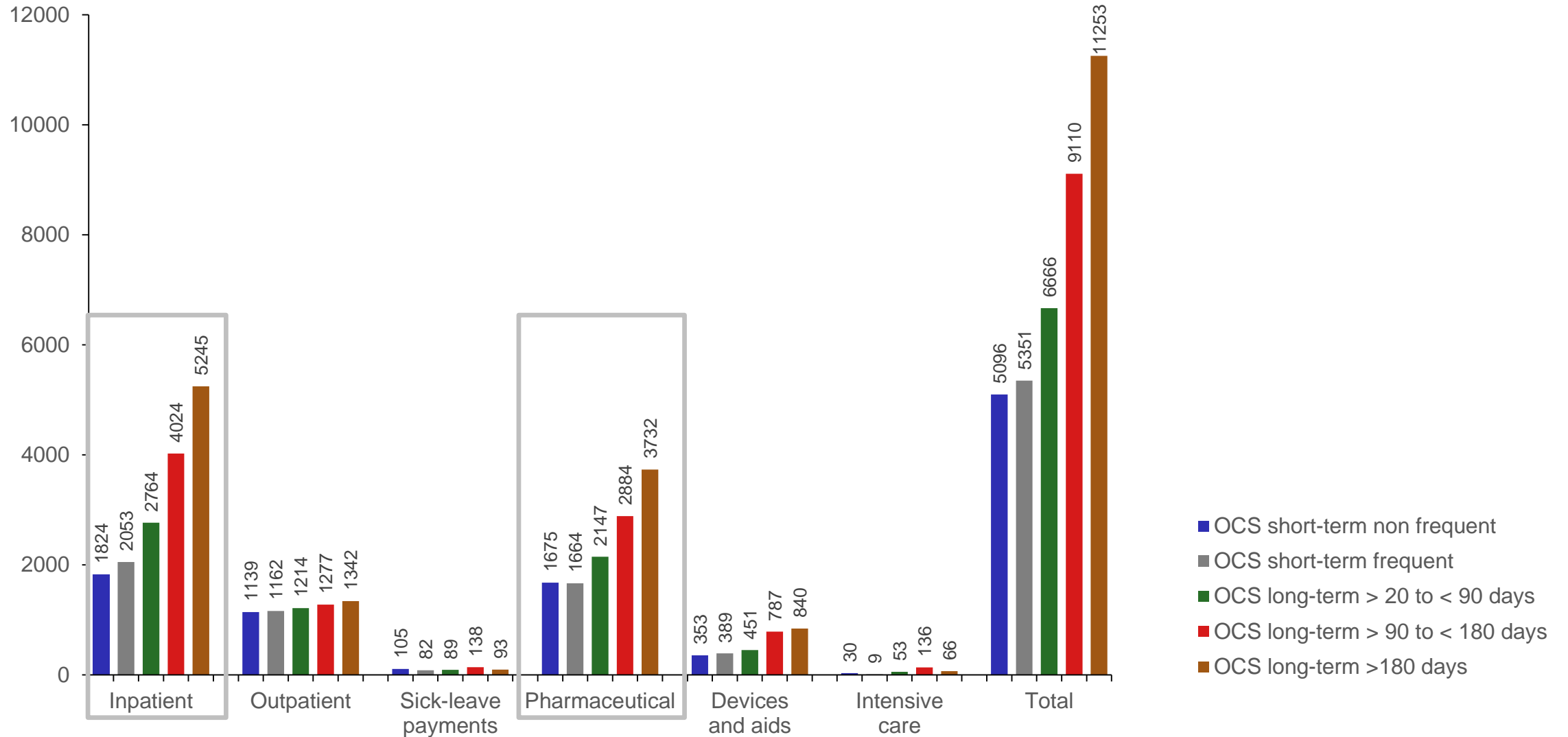
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17,3 % OCS (> 180 d/y)

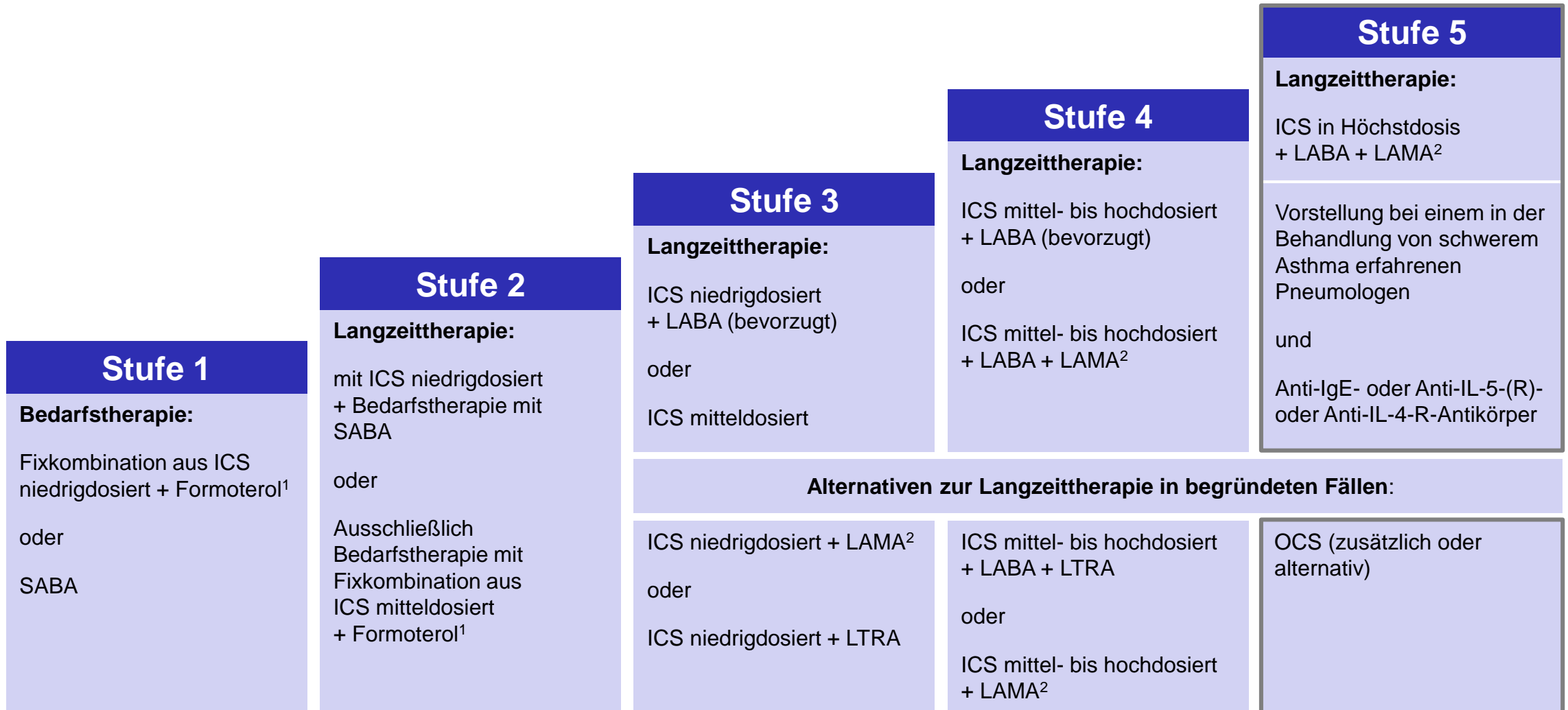
- OCS long-term >180 days
- OCS long-term >90 to <180 days
- OCS long-term >20 to <90 days
- OCS short-term frequent
- OCS short-term non frequent



# Versorgungsrealität Deutschland II (2015)



# Therapie-Empfehlung NVL Asthma



# Biomarker der Typ-2-Inflammation und klinische Kriterien zur Auswahl des Biologikums

Eligibility criteria

## Anti-IL4R $\alpha$ therapy

- FeNO  $\geq$  25 ppb
- Blood EOS  $\geq$  150/ $\mu$ L
- Exacerbation rate
- Maintenance OCS
- Comorbidities (CRSwNP/AD)

## Anti-IgE therapy

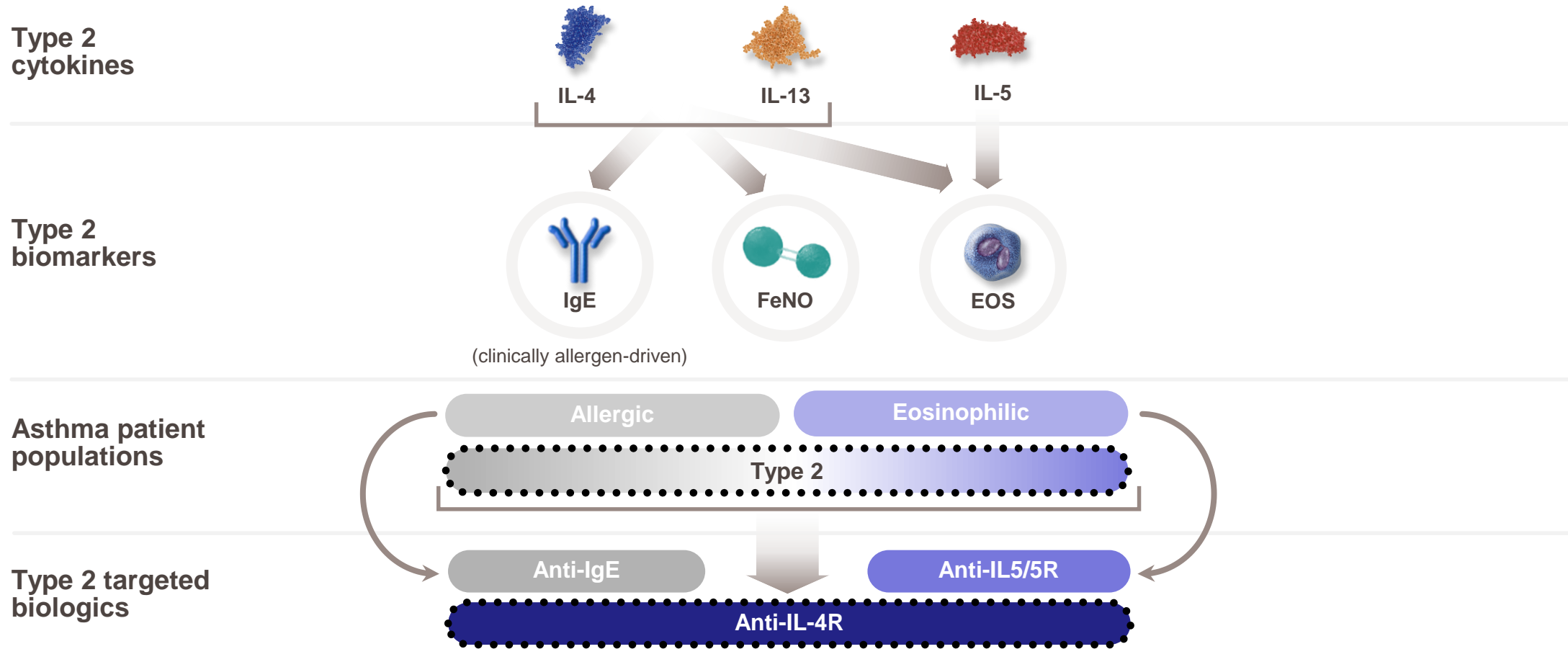
- Total and/or specific IgE
- Skin prick test (allergological evaluation)
- Clinical characteristics (eg, weight)
- Exacerbation rate
- Blood EOS  $\geq$  260/ $\mu$ L
- FeNO  $\geq$  20 ppb
- Childhood asthma

## Anti-IL-5/5R $\alpha$ therapies

- Blood EOS  $\geq$  300/ $\mu$ L
- Exacerbation rate
- Adult-onset asthma
- Maintenance OCS
- Comorbidities (CRSwNP)

# Typ-2-Inflammation

## Type 2 inflammation in asthma



# Kriterien der Typ-2- Inflammation und Schnittmengen

**GINA<sup>1</sup>**

## Criteria checklist: Type 2 inflammation

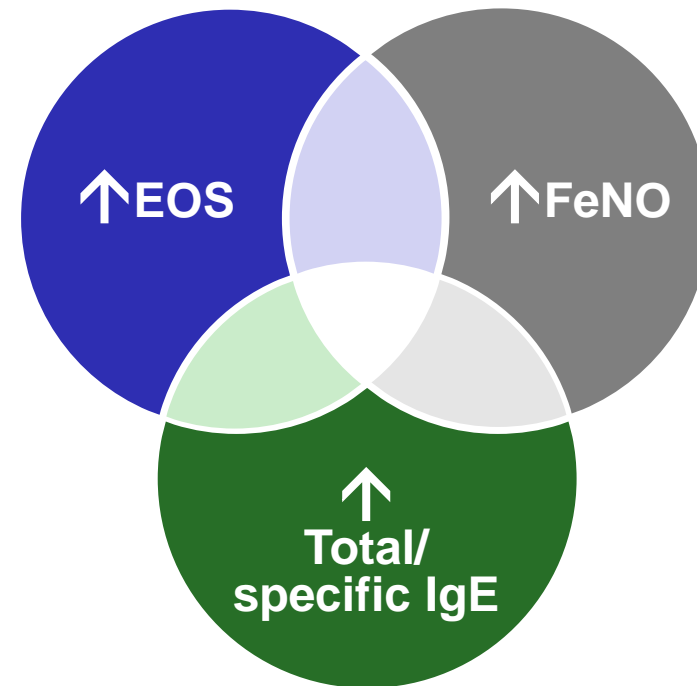
Blood EOS  $\geq$  150 cells/ $\mu$ l

FeNO  $\geq$  20 ppb

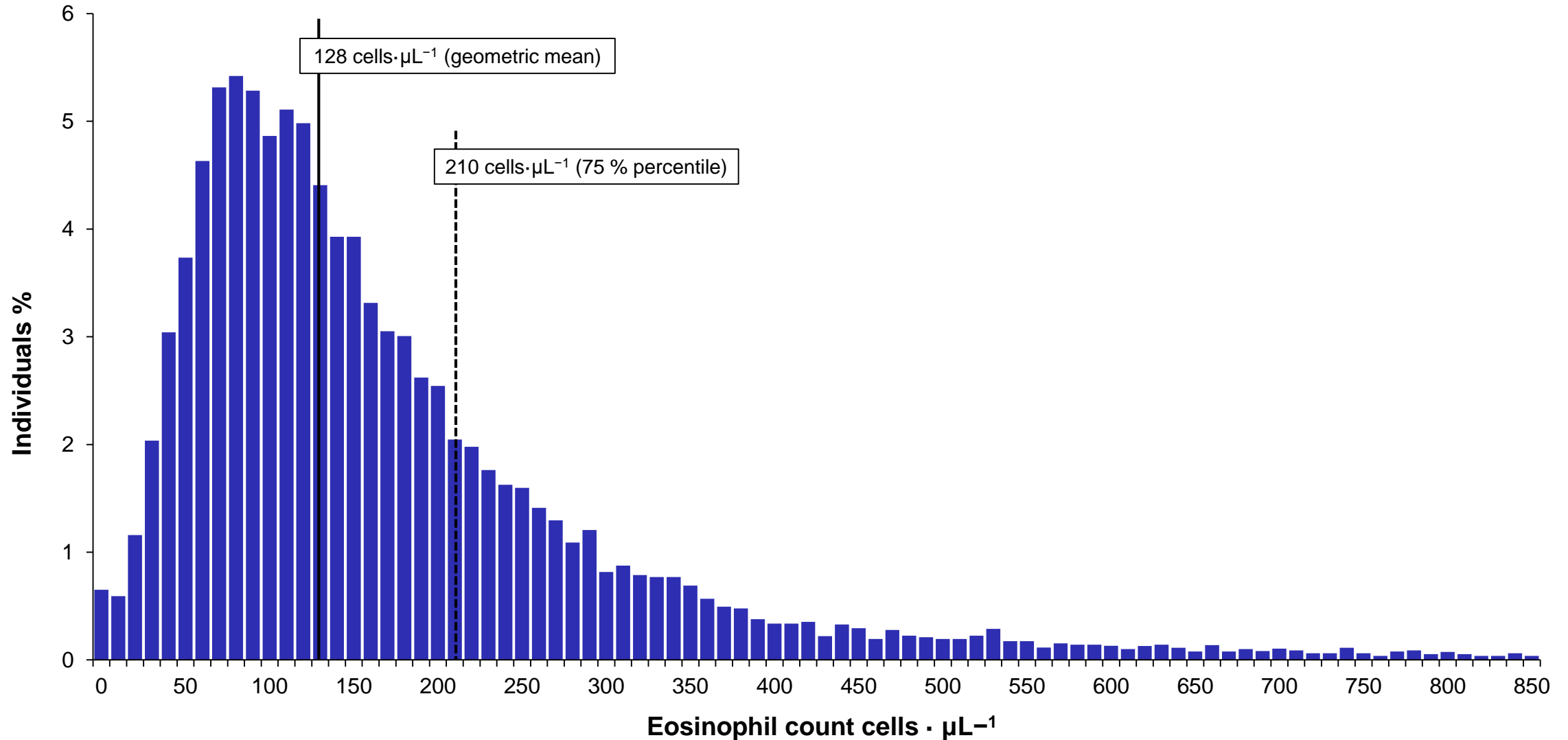
Sputum EOS  $\geq$  2%

Clinically allergen driven

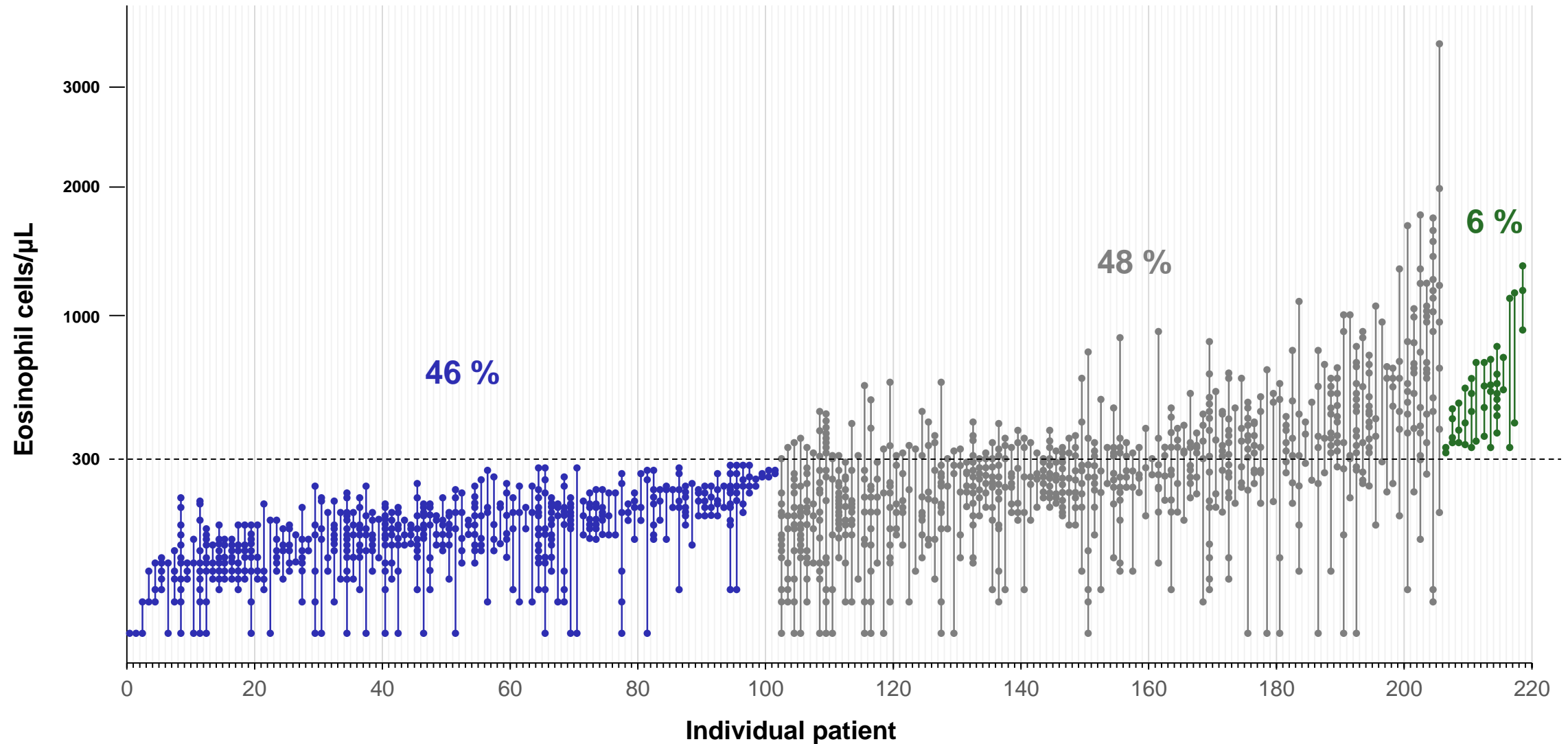
Need for maintenance OCS



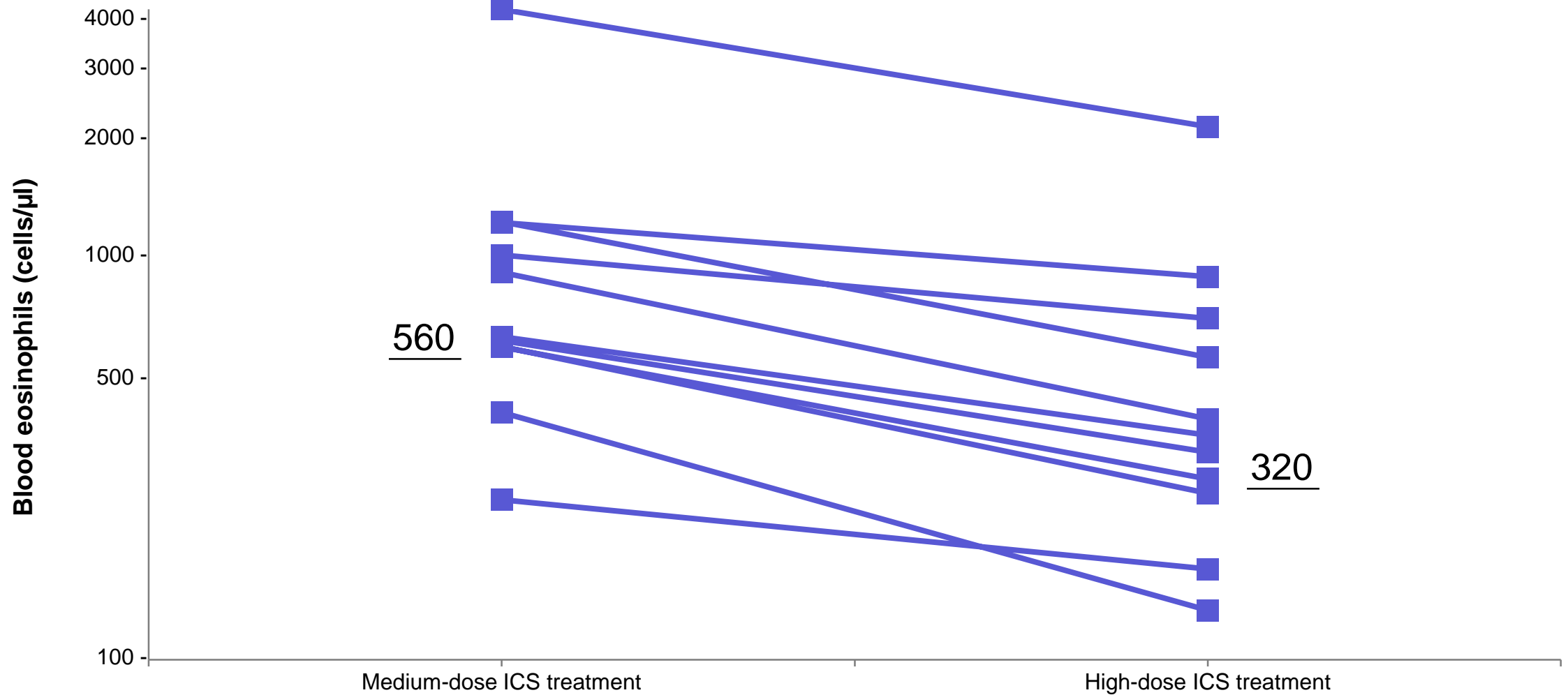
# Verteilung der EOS in der Allgemeinbevölkerung (Wien)



# Variabilität der Bluteosinophilen schweres Asthma (n = 219; 5-Jahres-Zeitraum)



# Einfluss der inhalativen Kortikosteroide





# FeNO-Interpretation: populationsbasierte Daten Deutschland

**Table 5 predicted FeNO values at the age of 50 y.**

Smoking	-	-	-	-	+	+	+	+
Infection	-	-	+	+	-	-	+	+
Allergy	-	+	-	+	-	+	-	+
Height [cm]								
150	11,0	12,2	12,0	13,2	8,4	9,2	9,1	10,1
160	12,1	13,4	13,2	14,6	9,2	10,2	10,0	11,1
170	13,4	14,8	14,6	16,1	10,2	11,3	11,1	12,3
180	14,8	16,4	16,1	17,8	11,3	12,5	12,2	13,6
190	16,4	18,1	17,8	19,7	12,4	13,8	13,5	15,0

# Biologika zur Therapie des schweren Asthmas

## Eligibility criteria

### Anti-IL4R $\alpha$ therapy

- FeNO  $\geq$  25 ppb
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### Anti-IgE therapy

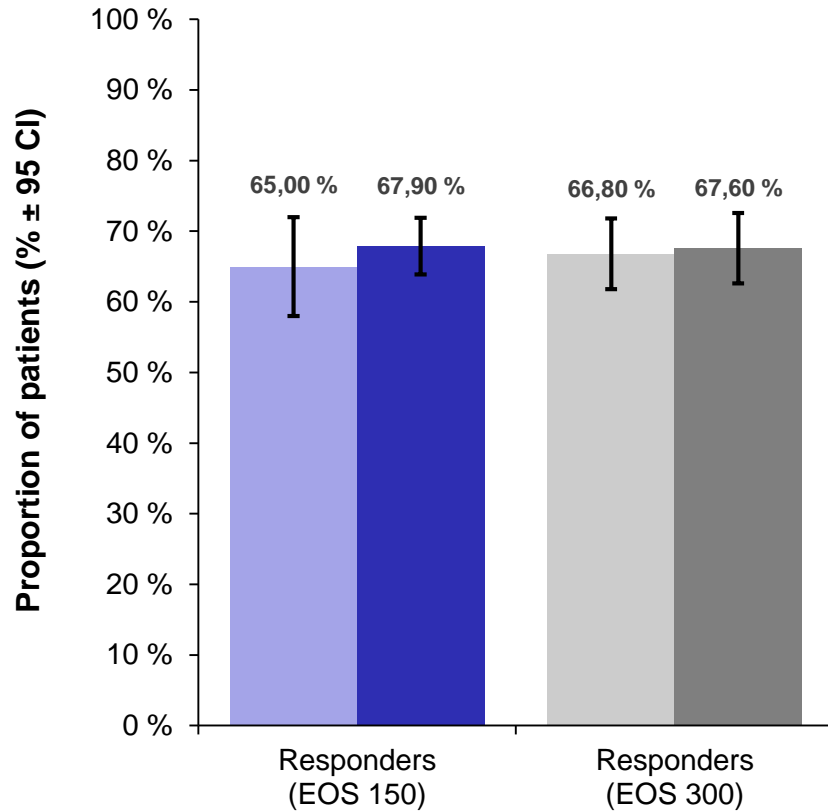
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### Anti-IL-5/5R $\alpha$ therapies

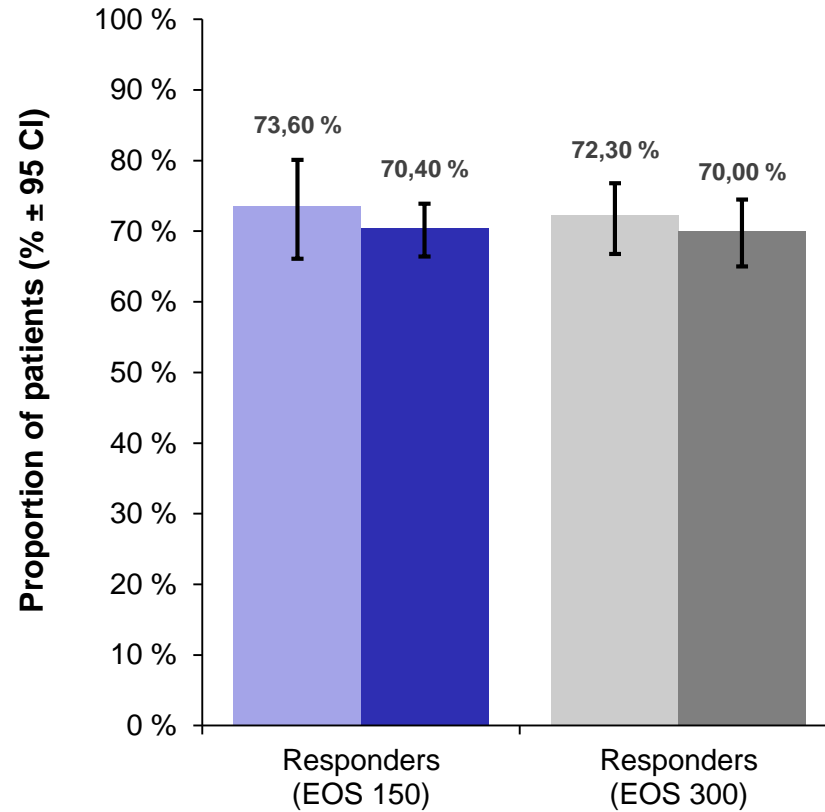
- Blood EOS  $\geq$ 300/ $\mu$ L
- Exacerbation rate
- Adult-onset asthma
- Maintenance OCS
- Comorbidities (CRSwNP)

# Anti-IgE: Real World Omalizumab (STELLAIR)

**A – Responders based on physician’s global evaluation (GETE)**



**B – Responders based on 40 % decrease in the annual exacerbation rate**



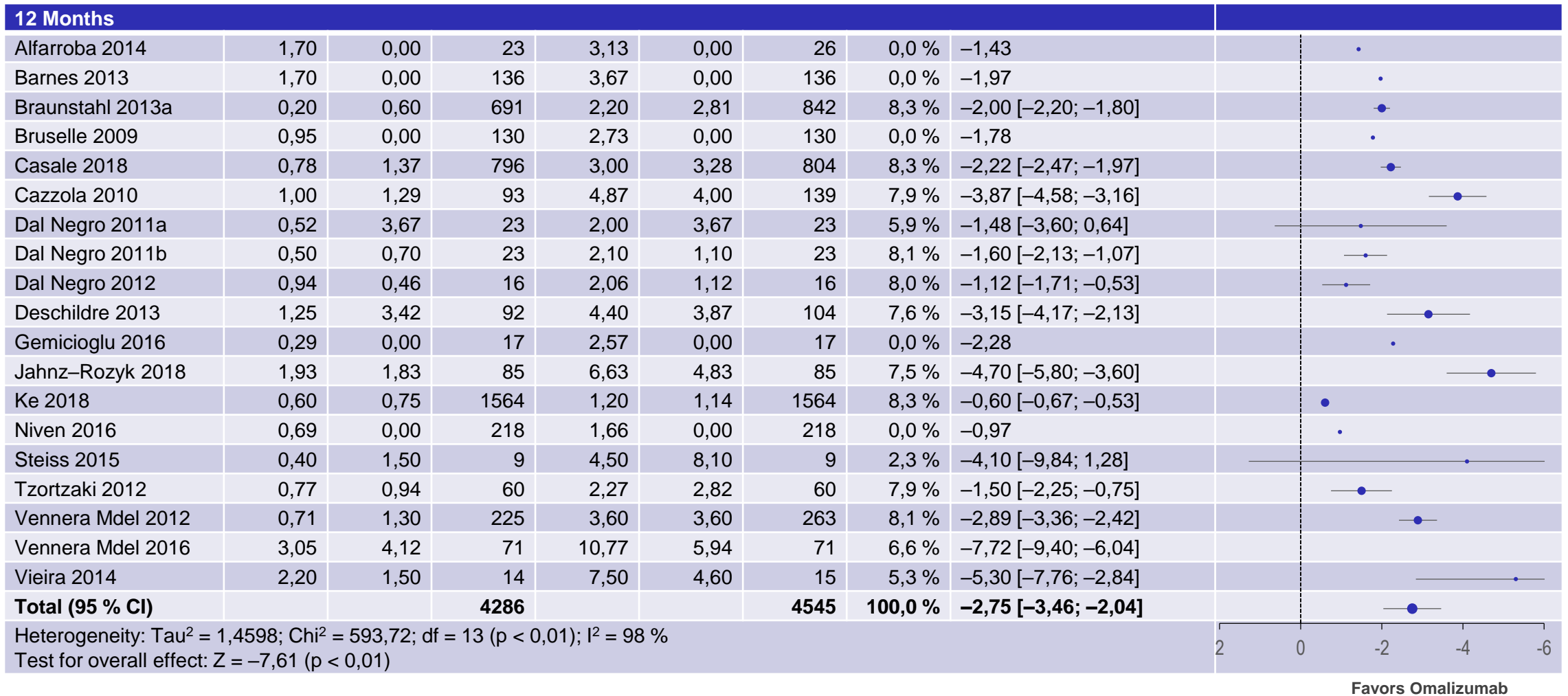
- n = 872
- 28 % OCS
- 20 mg Pred.

■ < 150 cells/μL, n = 163    ■ ≥ 150 cells/μL, n = 560  
■ < 300 cells/μL, n = 346    ■ ≥ 300 cells/μL, n = 377

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■ < 300 cells/μL, n = 346    ■ ≥ 300 cells/μL, n = 377

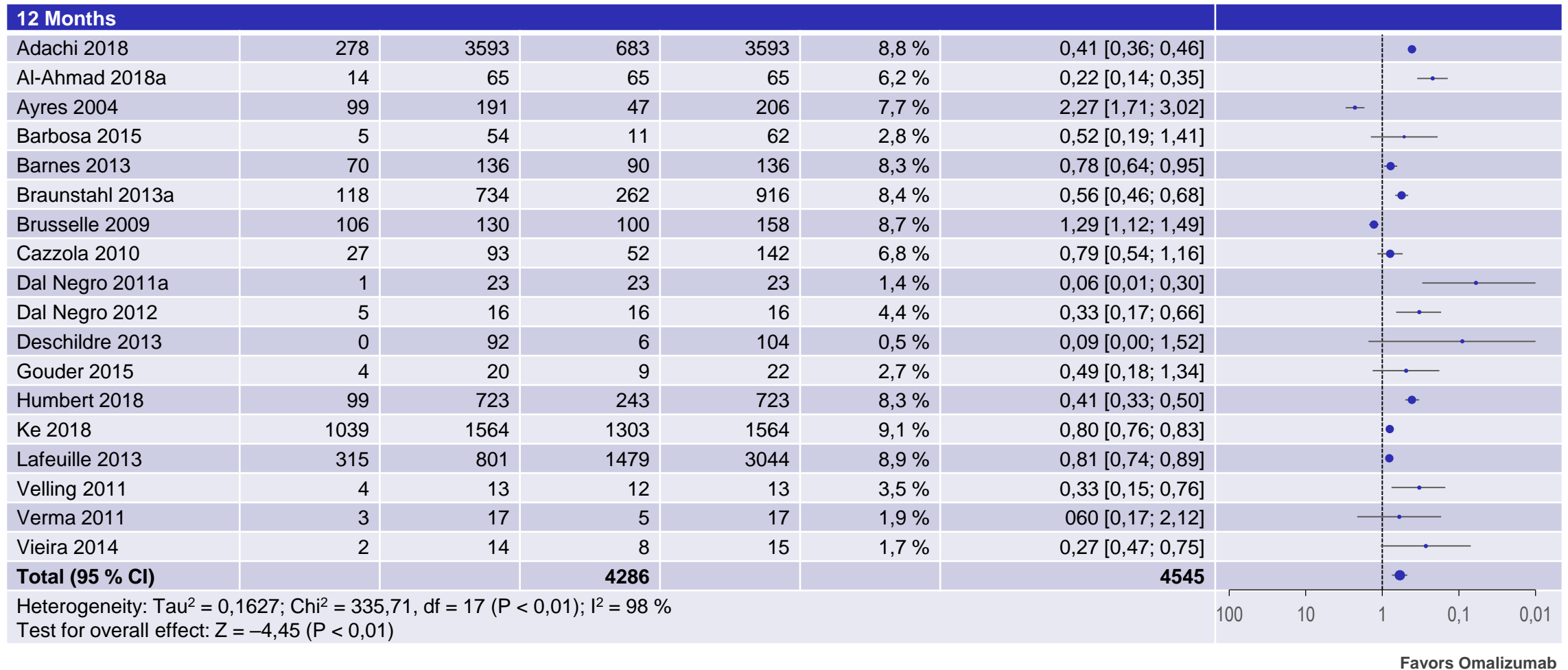
# Anti-IgE: Omalizumab

## Meta-Analyse der Real-World-Studien – Reduktion der Exazerbationen

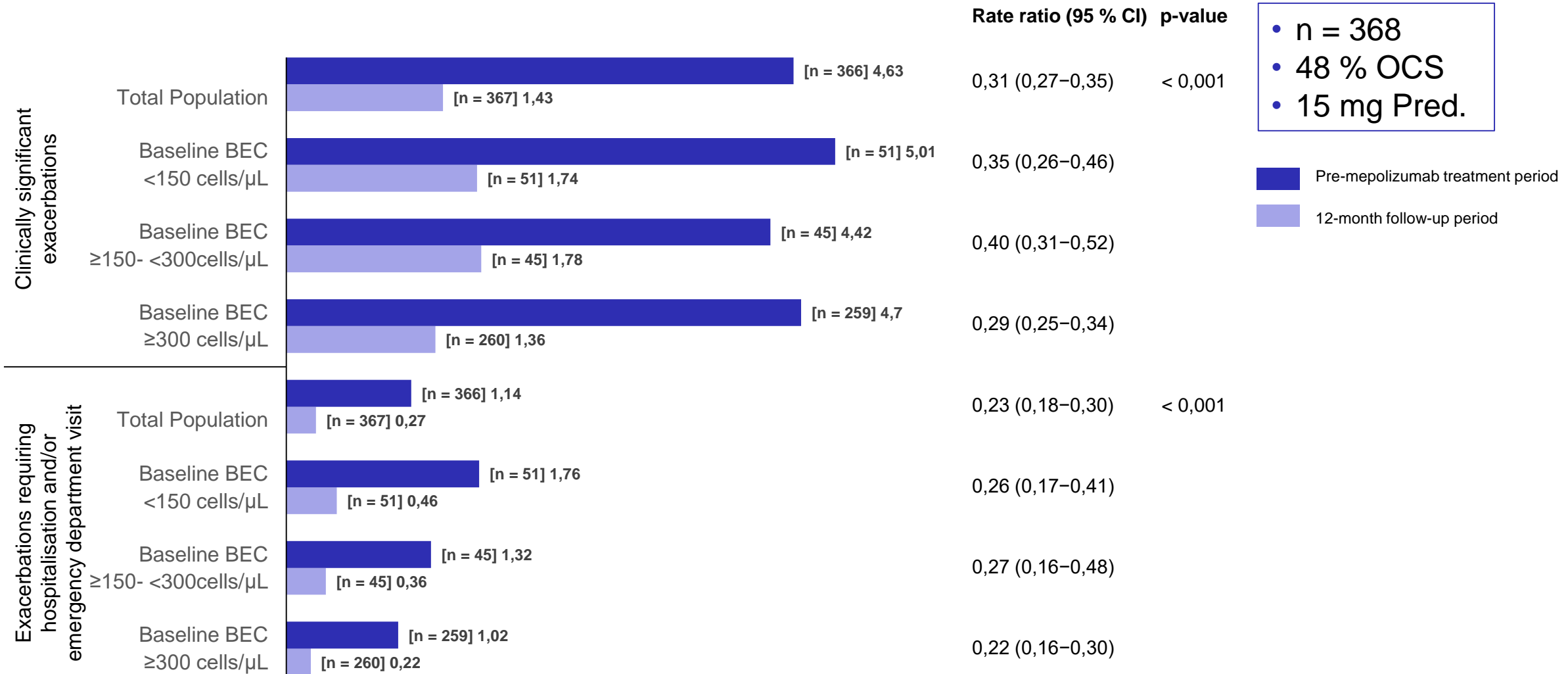


# Anti-IgE: Omalizumab

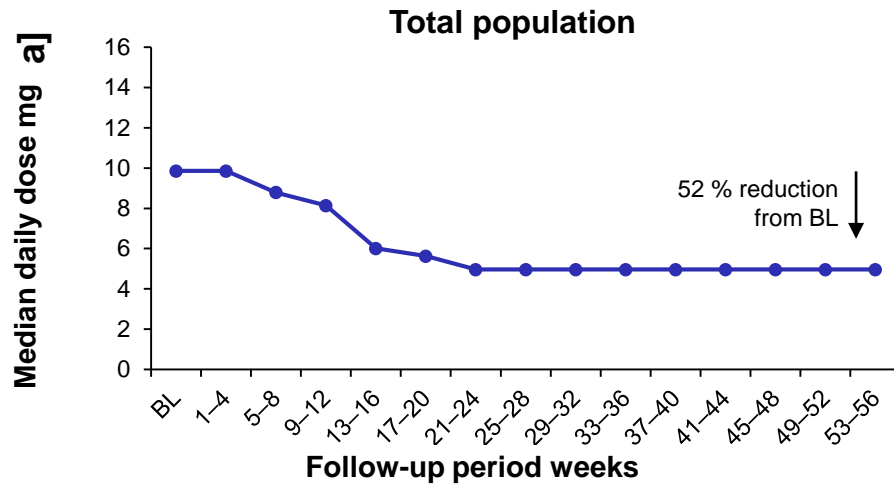
## Meta-Analyse der Real-World-Studien – Reduktion der oralen Steroide



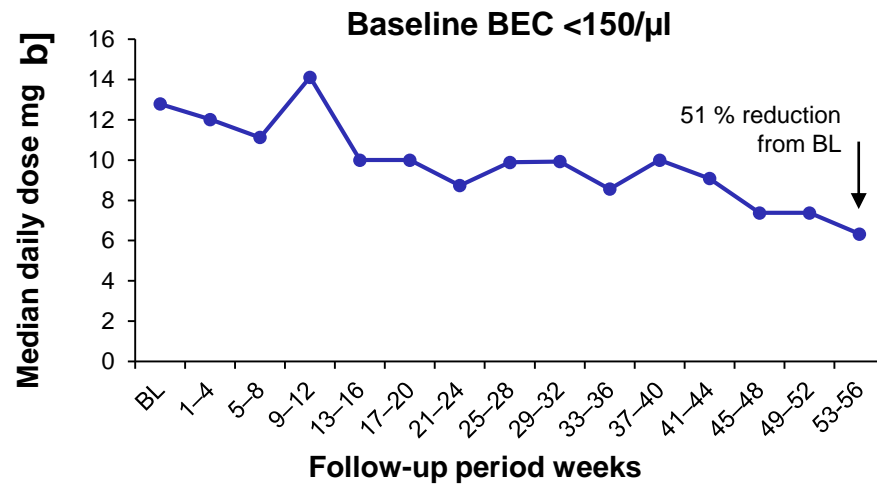
# Anti-IL-5: Real World Mepolizumab (REALITI-A)



# Anti-IL-5: Real World Mepolizumab (REALITI-A)

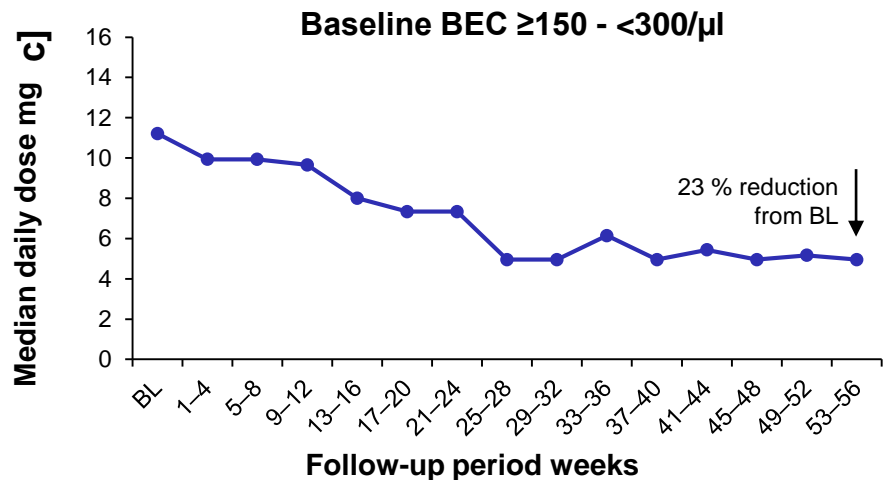


n: 159 158 156 156 154 153 153 152 151 150 149 146 143 143 143

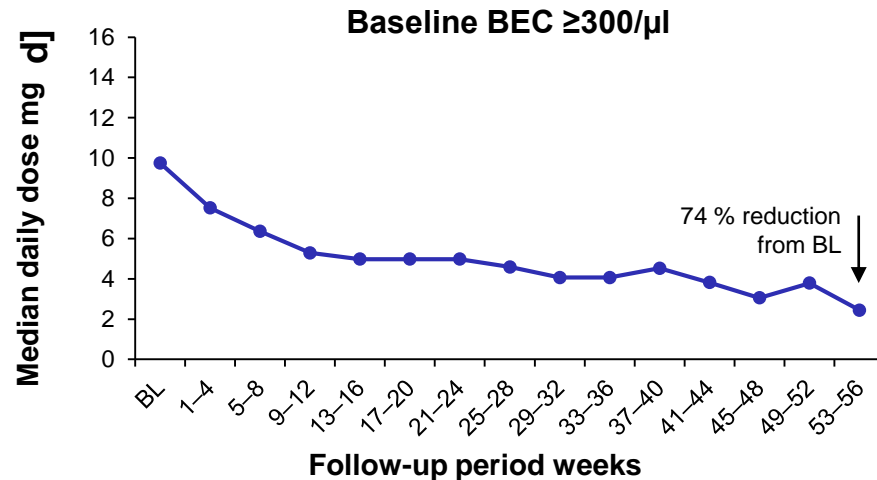


n: 28 28 28 28 28 27 27 27 27 27 27 26 24 24 24

- n = 368
- 48 % OCS
- 15 mg Pred.

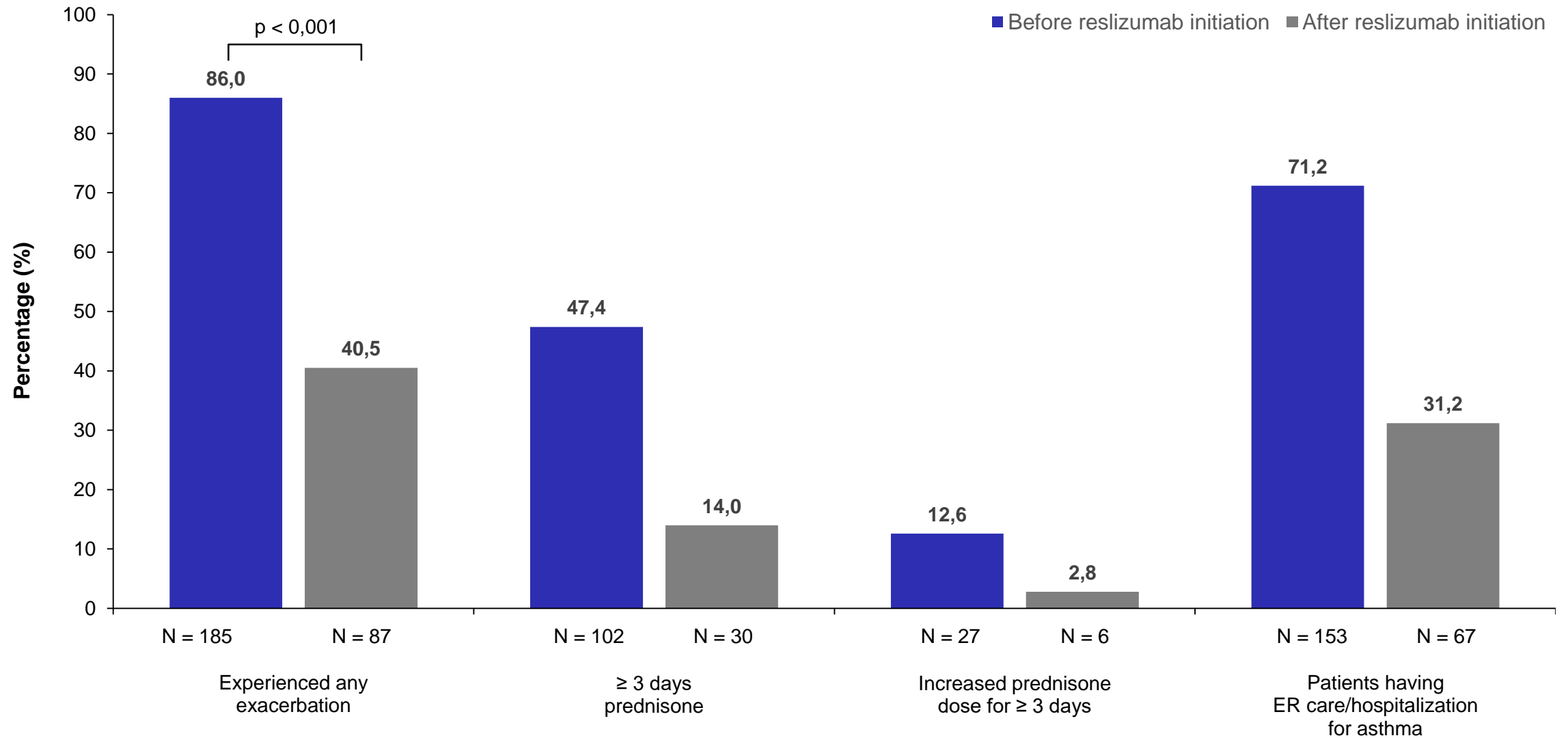


n: 32 32 32 32 31 31 31 31 31 31 31 30 30 30 30



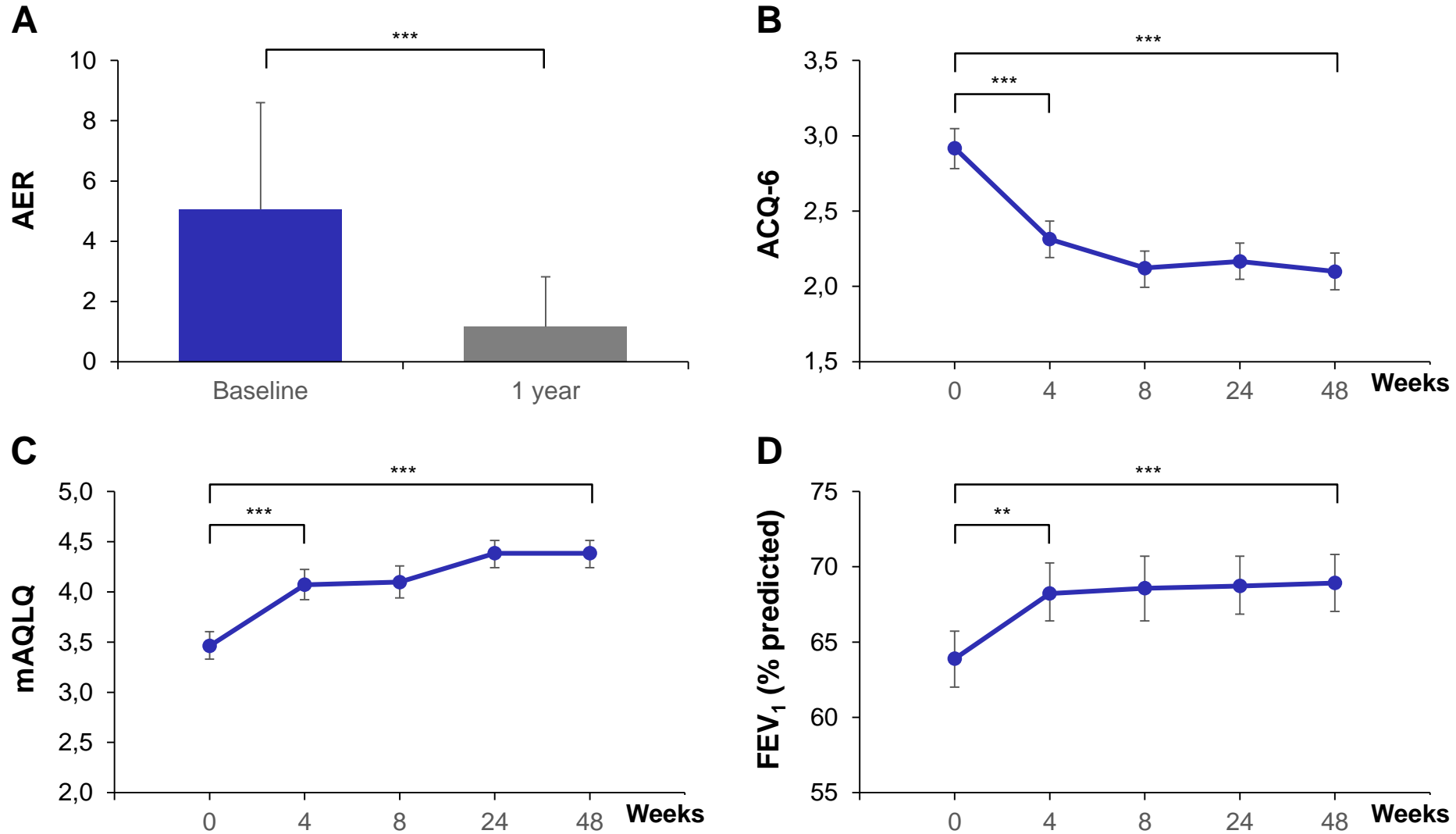
n: 98 97 95 95 94 94 94 93 92 91 90 89 88 88 88

# Anti-IL-5: Real World Reslizumab





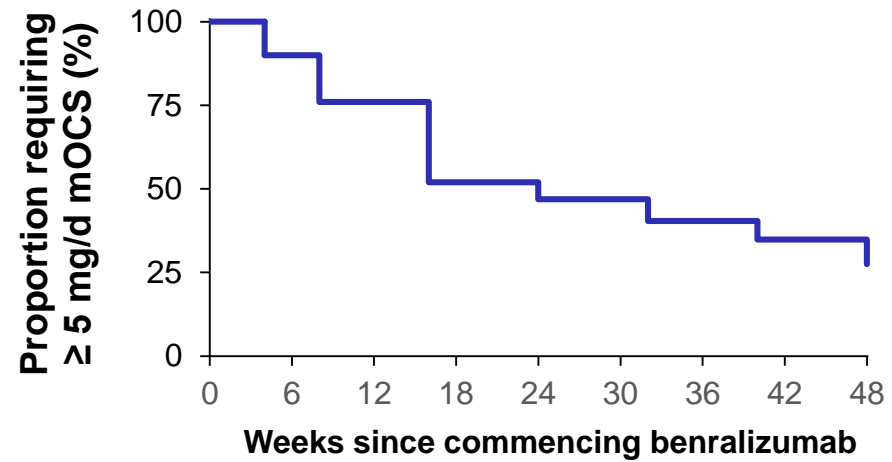
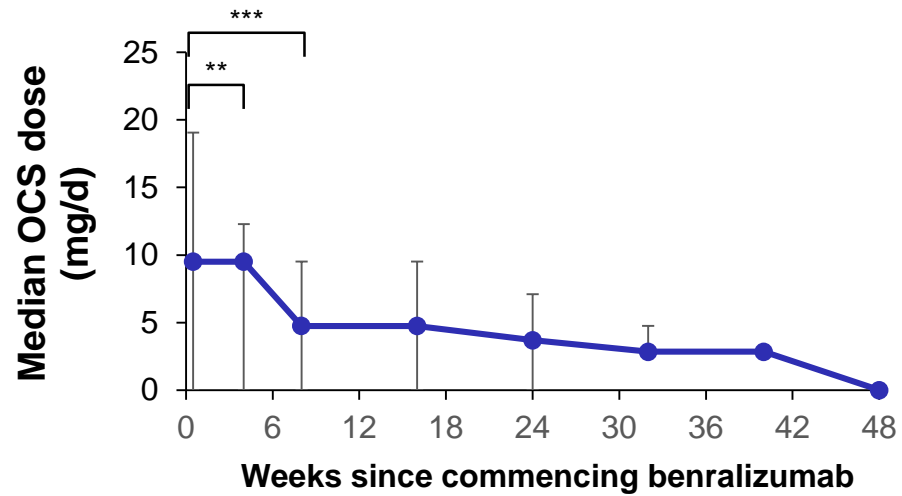
# Anti-IL5-R $\alpha$ : Real World Benralizumab



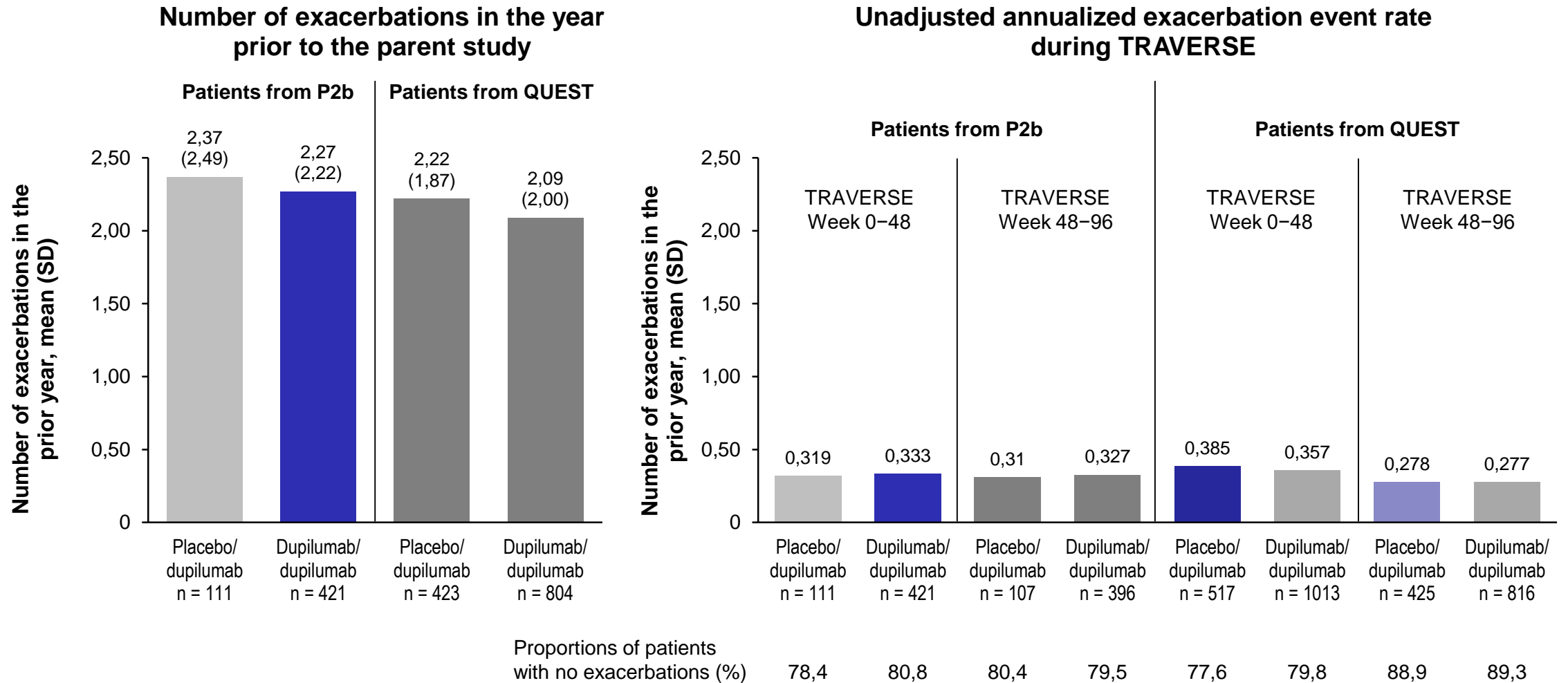
- n = 130
- 74 % OCS
- 10 mg Pred.

# Anti-IL5-R $\alpha$ : Real World Benralizumab

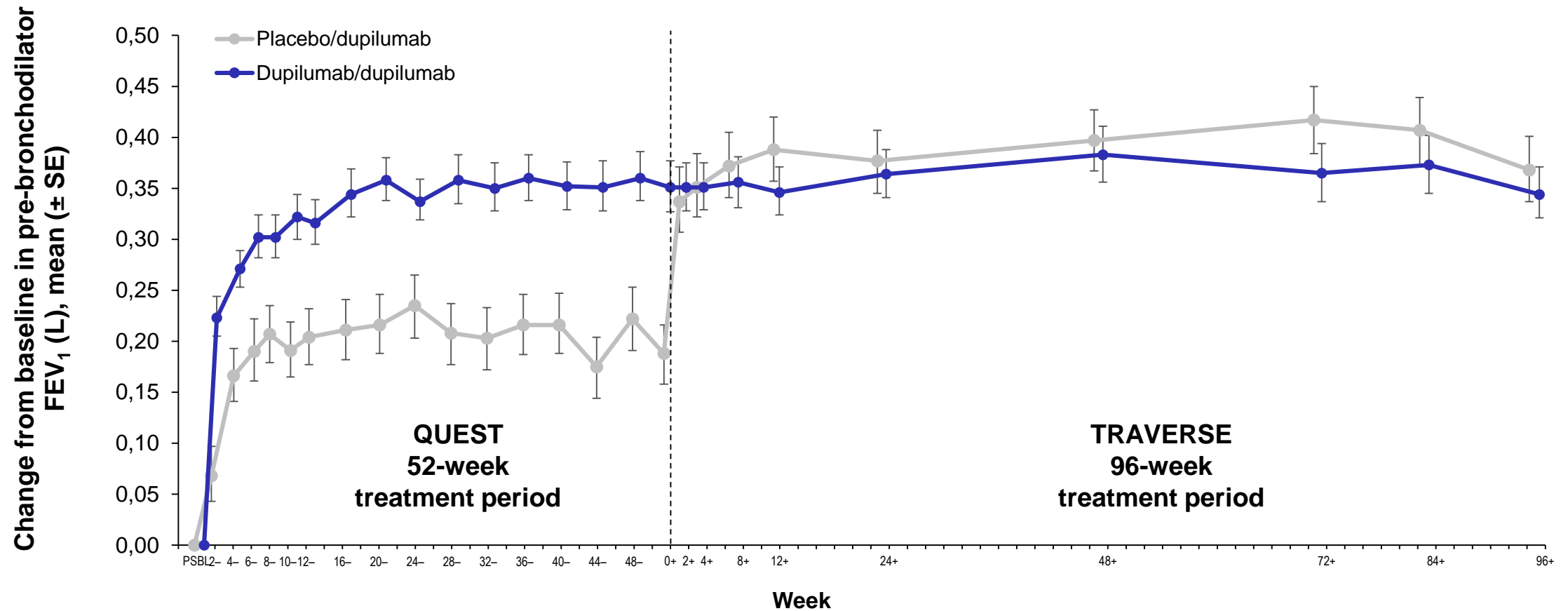
- n = 130
- 74 % OCS
- 10 mg Pred.



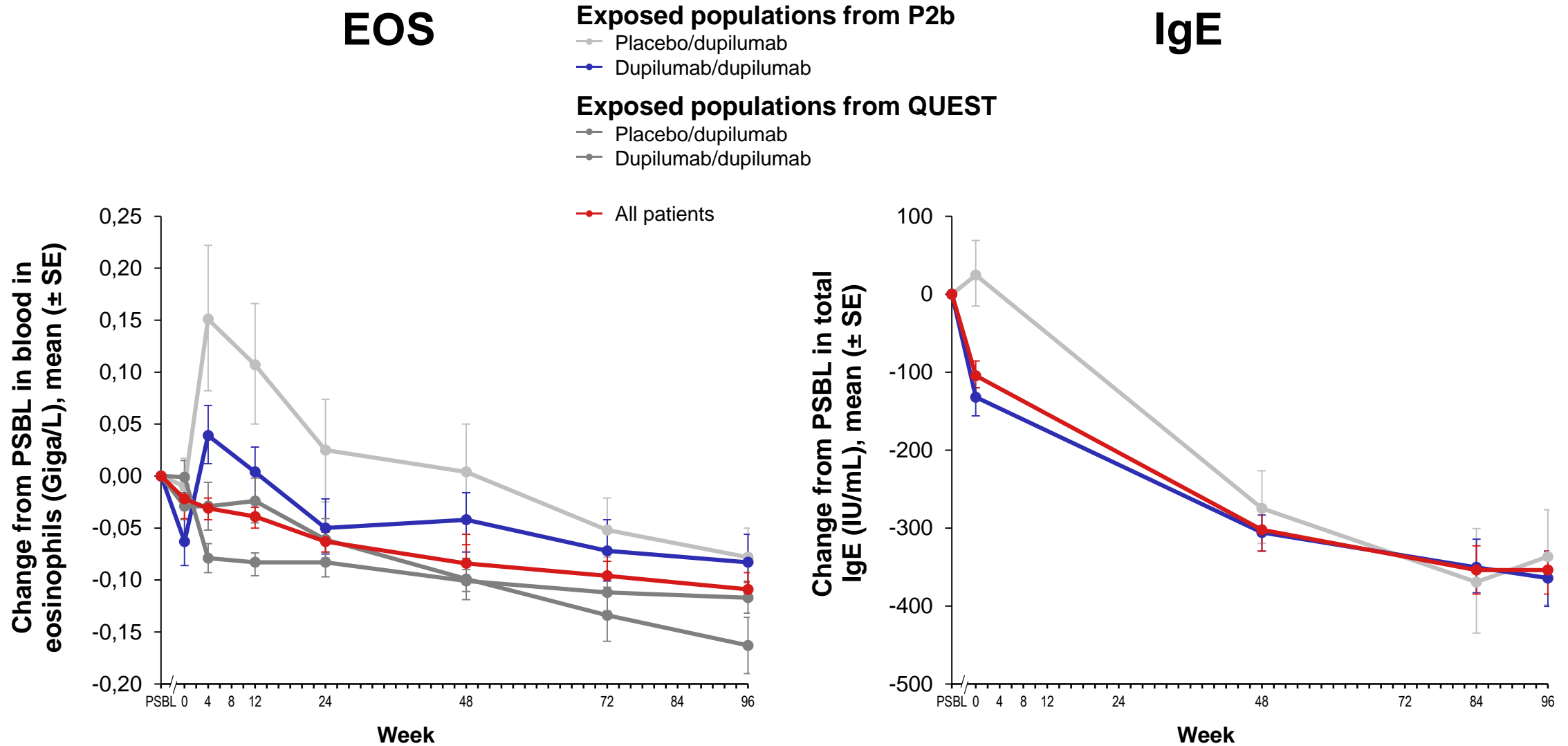
# Anti-IL4-R $\alpha$ : TRAVERSE (Exacerbation) Dupilumab



# Anti-IL4-R $\alpha$ : TRAVERSE (Lungenfunktion) Dupilumab



# Anti-IL4-R $\alpha$ : TRAVERSE (Biomarker) Dupilumab



# Zusammenfassung

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- 5–10 % der Asthmatiker haben ein schweres unkontrolliertes Asthma.
- Systemische Steroidgaben zur Dauertherapie dieser Patienten sind nur noch in begründeten Ausnahmefällen indiziert.
- Biologika zur Therapie der Typ-2-Inflammation können die Asthmakontrolle bei Patienten mit schwerem Asthma substantziell bessern.

Vielen Dank für Ihre Aufmerksamkeit!

Diese CME wird Ihnen mit freundlicher Unterstützung von Sanofi-Aventis auf [cme.medlearning.de](http://cme.medlearning.de) angeboten (€ 12.750,00).