

# German Asthma Net: Characterization of responders to anti-IL-5 and anti-IL-5(R) therapy

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German Asthma Net e.V.

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## Anti-IL-5 and anti-IL-5(R) therapy responders:

Treatments targeting interleukin 5 (IL-5) and the IL-5 receptor IL-5(R) include **mepolizumab, reslizumab, and benralizumab**. Previous real-life responder studies to anti-IL-5/IL-5(R) therapy suggest that indicators of good baseline disease control in severe asthma predict biologic treatment response.

We aimed to characterize responders to anti-IL-5/IL-5(R) therapy in patients from the **real-life, international registry German Asthma Net (GAN)**. Statistic tests used were Welch's ANOVA with Dunnett's corr., or  $\chi^2$  tests.

Baseline	Non-responders, n=47		Responders, n=274		Super-responders, n=183		Remission, n=124		p-value
Age, years	55.7 ± 12.2	47	56.9 ± 12.4	274	56.4 ± 11.9	183	55.2 ± 12.6	124	0.6
BMI, kg/m <sup>2</sup>	27.9 ± 5.7	47	26.8 ± 5.4	274	27.0 ± 5.2	183	26.3 ± 4.6	124	0.4
Blood eosinophils, G/L	0.3 ± 0.2	28	0.6 ± 1.0	213	0.6 ± 0.5	140	0.6 ± 0.5	98	<0.001
FeNO, ppb	40.5 ± 24.9	22	59.8 ± 57.9	155	54.2 ± 53.4	112	60.8 ± 53.9	77	0.032
Exacerbations/year	1.8 ± 2.7	45	4.7 ± 4.8	271	3.6 ± 4.0	179	3.6 ± 4.2	123	<0.001
Maintenance OCS, mg	3.1 ± 5.1	47	6.9 ± 12.4	274	3.6 ± 8.1	182	3.6 ± 7.8	123	0.001
Total IgE, IU/mL	473 ± 923	17	252 ± 325	144	263 ± 299	101	278 ± 318	71	0.8
Female, % of total*	61.7%		53.3%		52.5%		47.6%		0.086
CRSwNP, % of total*	61.7%		65.3%		64.5%		68.5%		0.8
Uncontrolled asthma (ACQ)†	81.4%		81.2%		76.3%		70.5%		0.2
Uncontrolled asthma (ACT)†	81.8%		80.9%		76.6%		67.5%		0.032
Poor quality of life (mAQLQ)†	83.3%		85.9%		83.3%		77.8%		0.4
Severe exacerbations*	34.5%		49.6%		44.2%		42.1%		0.3
Maintenance OCS use*	34.0%		50.4%		29.0%		31.5%		<0.001

p-values denote difference between 4 groups. \*: p-value from  $\chi^2$  test †: ACQ score  $\geq 1.5$ ;  $\chi^2$  test, ACT score < 20;  $\chi^2$  test, mAQLQ score < 5.4;  $\chi^2$  test. BMI, body mass index. CRSwNP, chronic sinusitis with nasal polyps. ICS: inhaled corticosteroids, in  $\mu\text{g}$  Beclomethasone equivalent.

### Definitions:

**Responder (R):**  $\geq 50\%$  reduction in exacerbation rate or corticosteroid dose after biologics start,  $\geq 1$  year and up to 7 years in the current cohort.

**Non-responder (NR):** <50% reduction

**Super responder (SR):** Like R, but: Zero systemic corticosteroids & exacerbations.

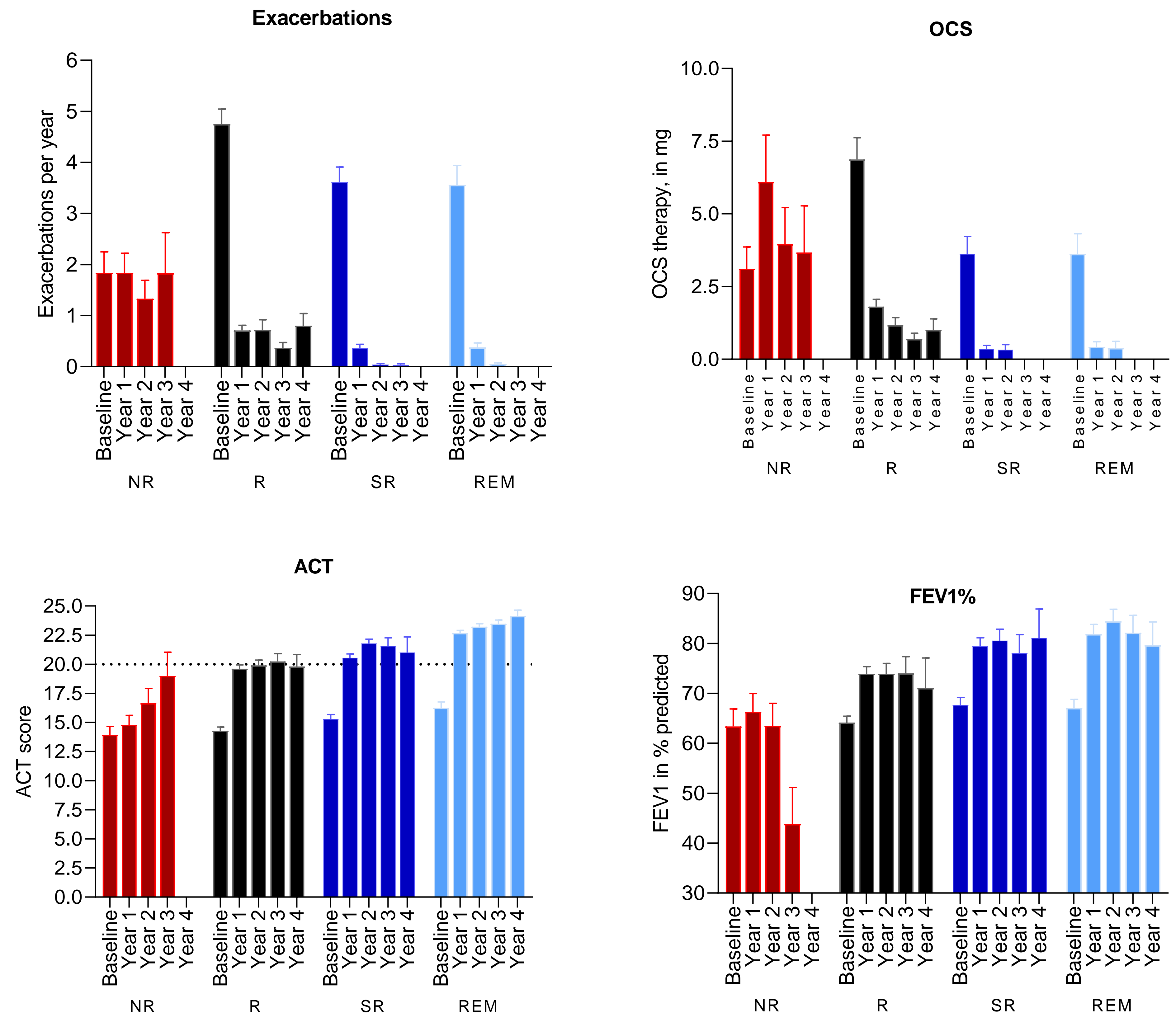
**Remission (REM):** Like SR, but plus ACT score  $\geq 20$ . (Milger et al. JACI:IP 2023)

**Type 2 inflammation biomarkers:** Blood eosinophil counts were highly significantly higher in responders, super-responders, and patients with remission at baseline, and FeNO was also significantly higher in these groups.

**Exacerbations and Corticosteroid therapy:** At baseline, non-responders had a significantly smaller exacerbation rate than all other groups. Furthermore, responders had significantly higher systemic corticosteroid doses at baseline than non-responders.

**Asthma control:** Asthma control (ACT) and quality of life (mAQLQ) were significantly different at baseline in the groups divided by therapy response.

**Over time:** Controlled asthma (ACT score  $\geq 20$ ) was seen at baseline in only 19-23% of non-to super-responders, but 33% of patients with remission. The **rate of asthma control improved over 3 years of therapy** in responders to 62-63%, in super-responders to 69-79%; whereas in non-responders it increased to only 20-35% in the first two years.



### Conclusion:

Anti-IL-5/IL-5(R) therapy improves exacerbations and corticosteroid dependency especially in patients with a high disease burden (high OCS and exacerbation rates), high blood eosinophil counts, and high FeNO.

Patients with super responders and remission outcomes show better asthma control and quality quality of life at baseline.