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**Title: Real-life biomarker response to anti-IL5 and anti-IgE therapies in severe asthma patients**

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**Introduction/Background:** Biologics (Bx) are known to decrease biomarker levels: anti-IL5 reduces blood eosinophils (BEC) and anti-IgE reduces FeNO. Bx are thought to have limited effect on serum IgE (IgE).

**Aims and Objectives:** To assess the proportions of severe asthma patients whose biomarkers (BEC, FeNO and IgE) decrease following Bx (Anti-IL5 and Anti-IgE) initiation.

**Methods:** Eligible patients in the International Severe Asthma Registry (ISAR) with biomarker and Bx data were included. For each time window from pre-Bx initiation to Bx treatment of up to 3+ years, the proportion of patients with a clinically meaningful (>25%) decrease in biomarkers was determined.

**Results:** BEC reduced by >25% over 2-3 years in 80.7% of anti-IL5 and 41.6% of anti-IgE patients. FeNO reduced by >25% over 2-3 years in 41.6% of anti-IL5 and 47.8% of anti-IgE patients. IgE reduced by >25% over 2-3 years in 41.7% of anti-IL5 and 15.6% of anti-IgE patients.

**Figure:** Median (IQR) biomarker changes and patient proportions with decreased biomarkers in response to Bx

Time window (from pre-biologic baseline)	BEC (cells/ $\mu$ L)			FeNO (ppb)			IgE (IU/mL)		
	N	Median (IQR) change	Patients (n [%]) with >25% drop in BEC	N	Median (IQR) change	Patients (n [%]) with >25% drop in FeNO	N	Median (IQR) change	Patients (n [%]) with >25% drop in IgE
<b>Anti-IL5 patients</b>									
0 to 3 months	234	-400 (-900 to -100)	187 (82)	113	-1 (-20 to 12)	45 (39.8)	37	-23 (-97 to 0)	16 (43.2)
3 to 12 months	516	-400 (-750 to -100)	414 (82.1)	327	0 (-21 to 14)	117 (35.8)	121	0 (-101 to 12)	40 (33.1)
1 to 2 years	442	-345 (-600 to -100)	344 (78.7)	309	-4 (-25 to 10)	121 (39.2)	85	-3 (-68 to 26)	29 (34.1)
2 to 3 years	218	-340 (-620 to -90)	171 (80.7)	154	-3.5 (-21 to 10)	64 (41.6)	24	-1.2 (-113.7 to 10.5)	10 (41.7)
3+ years	71	-420 (-660 to -190)	110 (45.6)	57	-1 (-12 to 20)	19 (33.3)	11	-84 (-256 to 3)	6 (54.6)
<b>Anti-IgE patients</b>									
0 to 3 months	82	-114.5 (-450 to 0)	48 (60)	49	-17 (-51 to 1)	29 (59.2)	35	180 (46 to 478)	-
3 to 12 months	176	-22 (-200 to 25)	73 (42.2)	81	-7 (-24 to 4)	37 (45.7)	70	77.2 (-12 to -394.5)	9 (12.9)
1 to 2 years	178	-10 (-200 to 100)	71 (40.8)	75	-4 (-31 to 3)	35 (46.7)	71	160 (-34 to 480)	14 (19.7)
2 to 3 years	103	-30 (-200 to 100)	42 (41.6)	46	-3.5 (-28 to 4)	22 (47.8)	45	126 (-17 to 349.3)	7 (15.6)
3+ years	175	0 (-130 to 100)	51 (29.8)	40	0.5 (-10.5 to 10.5)	12 (30)	118	171.7 (14 to 377)	16 (13.6)

**Conclusions:** In real life, >80% of anti-IL5 patients had decreased BEC over 2-3 years; ~40% of anti-IgE patients had decreased FeNO over 2-3 years. Further research on the association between limited biomarker response to Bx and asthma outcomes is needed.

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