

**Bronchodilator reversibility in patients with severe asthma included in the GAN registry**

Katrin Milger<sup>1,2</sup>, Carlo Mümmler<sup>1,2</sup>, Dirk Skowasch<sup>3</sup>, Eckard Hamelmann<sup>4</sup>, Marco Idzko<sup>5</sup>, Christian Taube<sup>6</sup>, Hartmut Timmermann<sup>7</sup>, Roland Buhl<sup>8</sup>, Stephanie Korn<sup>9,10</sup>

<sup>1</sup>Medizinische Klinik und Poliklinik V, LMU Klinikum München, <sup>2</sup>Comprehensive Pneumology Center Munich (CPC-M), Member of the DZL, <sup>3</sup>Uniklinikum Bonn, Medizinische Klinik II, <sup>4</sup>Klinik für Kinder- und Jugendmedizin Bielefeld, <sup>5</sup>Universitätsklinik für Innere Medizin II; Abteilung für Pulmonologie, AKH Wien, <sup>6</sup>Universitätsklinikum Essen - Ruhrlandklinik; Klinik für Pneumologie, <sup>7</sup>Allergopraxis Hamburg <sup>8</sup>Universität Mainz; Med. Klinik; Schwerpunkt Pneumologie <sup>9</sup>IKF Pneumologie Mainz; Clinical Research Centre Respiratory Diseases <sup>10</sup>Thoraxklinik Heidelberg

**Background**

Positive bronchodilator reversibility (BDR) is a diagnostic criterion for asthma. However, patients with asthma may exhibit negative BDR test.

**Aim**

To describe frequency of positive and negative BDR in patients with severe asthma and associations with phenotypic characteristics.

**Methods**

We analysed severe asthma patients from the German Asthma Net (GAN) registry. The present analyses include the baseline visits of all registry patients as of January 1, 2021. Firstly, we selected patients with data on BDR test available. Then patients were stratified in positive and negative BDR test. Positive BDR was defined as FEV1 increase > 200 ml AND >12% upon testing with a short-acting beta-agonist (SABA). Patients who did not meet these criteria or only 1 of the 2 criteria were classified as negative.

**Results**

Out of 2013 patients with severe asthma included in the GAN registry, 793 had data on BDR. Herof, 250 (31.5%) had a positive BDR test, while 543 (68.5%) were classified as negative.

Item		Total N=793	Bronchodilator reversibility		p-value pos. vs. neg.
			Positive N=250	Negative N=543	
Sex- Female	n (%)	432 (54.5%)	129 (51.6%)	303 (55.8%)	0.27
Age - years	Mean (SD)	49.9 (16.3)	49.6 (15.6)	50.0 (16.5)	0.64
Age group - Children	n (%)	49 (6.2%)	15 (6.0%)	34 (6.3%)	0.88
BMI- kg/m <sup>2</sup>	Mean (SD)	27.4 (6.3)	27.2 (6.2)	27.5 (6.4)	0.68
Duration of asthma -years	Median	18.0 (0;80)	18.0 (0;72)	18.0 (0;80)	
Age at onset- years	Median	31.0	32.5 (0;69)	30.0 (0;84)	0.52
Age group at onset	Early (<12 years)	224 (28.4%)	62 (24.8%)	162 (30.0%)	0.13
	Late (> 12 years)	566 (71.6%)	188 (75.2%)	378 (70.0%)	
Asthma phenotype ICD10	predominantly allergic asthma	336 (42.4%)	104 (41.6%)	232 (42.7%)	0.95
	non-allergic asthma	249 (31.4%)	80 (32.0%)	169 (31.1%)	
	mixed forms of asthma	208 (26.2%)	66 (26.4%)	142 (26.2%)	
Smoking habits	never-smoker	447 (56.4%)	143 (57.2%)	304 (56.1%)	0.81
	Active smoker	19 (2.4%)	7 (2.8%)	12 (2.2%)	
	former smoker	326 (41.2%)	100 (40.0%)	226 (41.7%)	
Former smoker: packyears	N	322	96	226	
	Median (range)	10.00 (0.5; 80)	9.00 (0.5;75)	10.00 (0.5; 80)	
Active Smoker: packyears	N	18	7	11	
	Median (range)	7.35	6.50 (0.5; 30)	12.00 (0;56)	
COPD	N	791	250	541	
	yes	52 (6.6%)	13 (5.2%)	39 (7.2%)	0.29
Incapacity for work	No	437 (55.2%)	131 (52.4%)	306 (56.5%)	0.61
	Yes	235 (29.7%)	82 (32.8%)	153 (28.2%)	
	Unknown	50 (6.3%)	16 (6.4%)	34 (6.3%)	
	not applicable	70 (8.8%)	21 (8.4%)	49 (9.0%)	

**Table 1:** Clinical characteristics of patients with severe asthma and positive or negative bronchodilator responsiveness (BDR) test

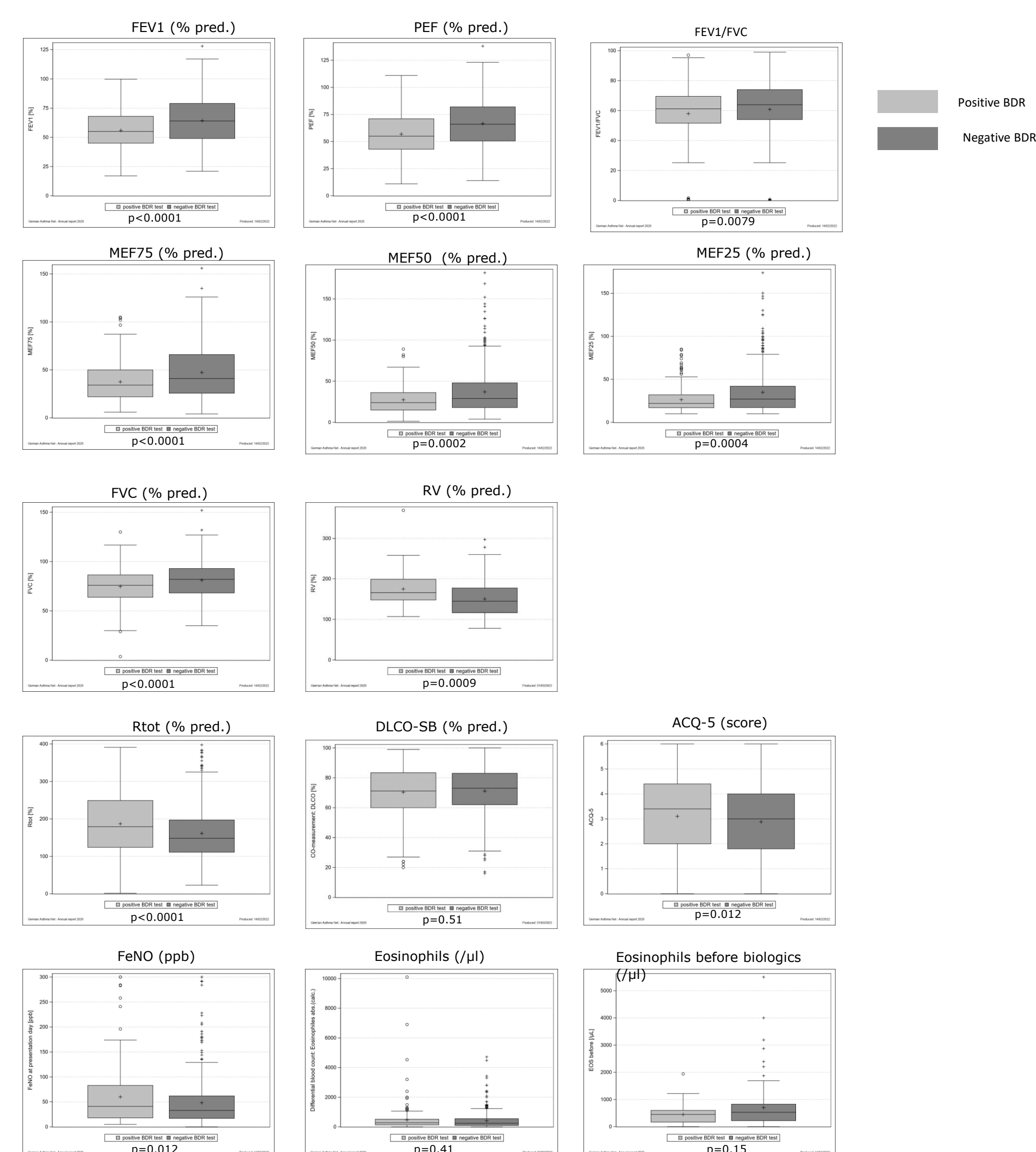
**Results**

**Table 2: Comparison for selected dichotomous parameters in positive vs negative BDR**

Item		Bronchodilator reversibility			p-value
		Total	Positive	Negative	
Resting dyspnea	N	792	250	542	<b>0.0006*</b>
	yes	156 (19.7%)	67 (26.8%)	89 (16.4%)	
Chest tightness / chest pain	N	792	250	542	<b>0.0034*</b>
	Yes	233 (29.4%)	91 (36.4%)	142 (26.2%)	
Gastroesophageal reflux (GERD)	N	790	250	540	<b>0.0011*</b>
	Yes	286 (36.2%)	70 (28.0%)	216 (40.0%)	
Chronic sinusitis	N	791	250	541	0.1233*
	Yes	364 (46.0%)	105 (42.0%)	259 (47.9%)	
Nasal polyps	N	118	273	391	0.77*
	Yes	41 (34.7%)	99 (36.3%)	140 (35.8%)	
EGPA	N	791	250	541	<b>0.0211*</b>
	Yes	17 (2.1%)	1 (0.4%)	16 (3.0%)	
- Systemic therapies OCS - biologics	N	793	250	542	0.0130*
	without OCS and without biologics	321 (40.5%)	105 (42.0%)	216 (39.9%)	
	with OCS and without biologics	221 (27.9%)	82 (32.8%)	139 (25.6%)	
	without OCS and with biologics	162 (20.5%)	35 (14.0%)	127 (23.4%)	
	with OCS and with biologics	88 (11.1%)	28 (11.2%)	60 (11.1%)	

\*p-value by Chi-square test, #p-value by U-test.

**Figure 1**



**Figure 1: Comparison of selected parametric variables in patients with positive versus negative BDR test** including pre-bronchodilator pulmonary function tests, ACQ-5, FeNO and blood eosinophil count. p-values by U-test. All n = 793 except for eosinophils before biologics n=134

Multivariate linear regression analysis identified association of lower baseline FEV1% (p<0.001) and chest tightness (p<0.05) with positive, and GERD (p<0.05) with negative BDR.

**Conclusions**

In this real-life setting the majority of patients with severe asthma exhibited negative BDR. Interestingly, this was not associated with smoking history or COPD, but with lower FeNO and presence of GERD.