

Relationship Between the Response to Antibody Therapy and Symptoms of Depression and Anxiety Disorders in Patients with Severe Asthma

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Purpose: Asthma is associated with a high prevalence of psychopathological disorders, especially depressive disorders or anxiety. In patients with uncontrolled severe asthma, monoclonal antibody (mAb)-therapy positively influenced control of mental disorders. Therefore, we evaluated the impact of antibody therapy on the burden of these mental diseases depending on responder status.

Patients and Methods: Data were collected retrospectively in patients with uncontrolled severe asthma (n = 82) prior to mAb-therapy ("baseline") (omalizumab, dupilumab, benralizumab or mepolizumab). Symptoms of Major Depressive Disorder (MDD) or General Anxiety Disorder (GAD) were detected at baseline using the Hospital Anxiety and Depression Scale (HADS), as well as general sociodemographic data and lung function parameters. At 6-month (±3 month) follow-up, the burden of psychopathological symptoms under mAb-therapy was assessed using the Patient Health Questionnaire-2 (PHQ-2) and Generalized Anxiety Disorder Scale-2 (GAD-2). Response status was classified using the Biologics Asthma Response Score (BARS), assessing exacerbations, oral corticosteroid usage and asthma control test (ACT) score. Predictors for non-response to mAb-therapy were identified using linear regression analysis.

Results: Patients with severe asthma suffered from symptoms of MDD/GAD more often compared to the general population, with a higher prevalence among mAb therapy non-responders. mAb-responders exhibited a declining burden of MDD, better quality of life (QoL), less exacerbations, better lung function and better disease control compared to non-responders. A history of symptoms of depression was identified as a predictor for non-response to mAb-therapy.

Conclusion: Asthma symptoms and psychological problems are linked and more prevalent in our cohort of severe asthma patients than in the general population. Patients with signs of MDD/GAD before mAb-therapy show less mAb therapy response suggesting a negative impact of prior psychological problems on treatment response. In some patients, the score on MDD/GAD was caused by severe asthma – here symptoms decreased after effective treatment.

Keywords: severe asthma, monoclonal antibody therapy, depression, anxiety, therapy response

Introduction

Asthma is a chronic airway inflammation characterized by varying respiratory symptoms and variable expiratory airflow limitation. In particular, patients with severe asthma suffer from exacerbations and variable impairment in exercise capacity.¹ Moreover, mental disorders like Major Depressive Disorder (MDD) and Generalized Anxiety Disorder (GAD) are more common in severe asthma patients than in the general population.^{2–6} MDD is characterized by a state of depressed mood, loss of interest and enjoyment, and reduced energy leading to increased fatigability and diminished

activity. GAD is characterized by persistent or recurring symptoms of apprehension, motor tension and autonomic dysregulation.^{7–9}

In patients with severe asthma insufficiently controlled by maximized conventional inhalator therapy and/or oral corticosteroids, monoclonal antibodies (mAb) like Omalizumab (anti-IgE), Benralizumab (anti-IL5 receptor alpha), Mepolizumab (anti-IL5) and Dupilumab (anti-IL4 receptor alpha), targeting underlying immunological pathways, have been established as additional treatment options.^{10–12} Previous research showed that disease management, perceived stress, anxiety and depressive symptoms improved significantly under mAb-therapy, independent of which mAb was used.^{13,14} While the reported responder rates vary, it is universally acknowledged that a significant subset of severe asthma patients do not respond to mAb therapy.^{15–17}

In this study, we aim to determine a possible relation between mAb-therapy response and mental health conditions, as well as to identify predictors for mAb-nonresponse or decline in mental status.

Methods

Study Aim, Design and Setting

In this single-centre, retrospective analysis, all patients beginning mAb-therapy in our centre between March 2020 and March 2022 were investigated using GAD and MDD questionnaires. All data were collected during routine appointments at our severe asthma outpatient clinic at Hannover Medical School, Hannover, Germany. The study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the local ethic committee of the Hannover Medical School (10539_BO_K_2022). All patients provided written informed consent allowing the use of their data for scientific research.

Patient Selection and Treatment

All patients included in this study had already been diagnosed with severe asthma, according to American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines with an eosinophilic, allergic or combined phenotype.¹⁸ All patients received treatment following the step scheme for asthma with medium to high-dose inhaled glucocorticoids and a long-acting β 2-agonist and could receive a second or third controller and/or additional oral corticosteroid (OCS) therapy. Thus, all patients fulfilled preconditions for monoclonal antibody therapy in accordance with the Food and Drug Administration (FDA) and European Medicines Agency (EMA) and add-on therapy with either mepolizumab, benralizumab, dupilumab or omalizumab was initiated. The choice of antibody was made by the treating physician.

Data Collection at Baseline and Routine Follow-Up

Prior to initiation of mAb-therapy, patients' characteristics including age, sex, BMI, smoking status with calculation of pack years, alcohol consumption/abuse evaluated by Audit-C-Score¹⁹ (>4 (male) or >3 (female) were classified as "alcohol abuse"), pollutant exposure, allergies, education level, subdivided in academic education, vocational education and no completed education, family status and comorbidities were assessed. Additionally, Hospital Anxiety and Depression Scale (HADS-A, HADS-D), Patient Health Questionnaire-2 (PHQ-2) and Generalized Anxiety Disorder Scale-2 (GAD-2)^{20,21} were assessed at baseline prior to initiation of mAb-therapy. Both HADS subscales for anxiety (HADS-A) as well as depression (HADS-D) consist of 7 questions with a maximum score of 21 points. HADS scores were used as a screening test, all patients with a suspect (>10 points) or probable score (8–10 points) in HADS-A and HADS-D were classified as patients with signs of MDD and/or GAD.²² A positive AUDIT-C-Score and a suspect or probable HADS-A and HADS-D were considered to be a "current mental disorder". GAD-2 as well as PHQ-2 were developed as a valid ultra-short screening tool for anxiety (GAD-2) and depression (PHQ-2) and consist of two questions with a maximum score of 6 points. A higher score implies a higher probability for depression/anxiety with scores ≥ 3 indicating relevant symptoms of MDD and GAD.²⁰ Six months (± 3 month) after baseline, a routine follow-up appointment was conducted. Mental health under mAb-therapy was re-assessed using PHQ-2 and GAD-2 scores. Routine follow-up also included spirometry or body plethysmography standardised to ERS/ATS guidelines, capillary blood gas analysis, measurement of exhaled nitric oxide (eNO), and laboratory testing (differential blood count). Structured

questionnaires assessing pulmonary symptoms and asthma control (Asthma Control Test – ACT)²³ and changes in medication were assessed both at baseline and follow-up appointment. Exacerbations were defined as worsening of asthma symptoms requiring OCS for at least three days or an increase in the OCS dose. EQ5D questionnaire was used to evaluate quality of life (QoL) at both timepoints on a visual analogue scale (VAS) ranging from 0 points (worst imaginable health state) to 10 points (best imaginable health state).²⁴ Educational status was defined as low (no education), moderate (non-academic education) and high (academic education). Exacerbation rate was assessed for the last 12 months at baseline appointment and annualised for follow-up. It was defined as phases of progressive increase in asthma symptoms and/or decrease in lung function that exceed the patient's usual level of variability and that require modification or intensification of therapy over several days and the usage of oral corticosteroids over more than three days.

All pulmonary function tests (PFT) were performed under continued stable inhaled therapy. Responder status was assessed using Biologics Asthma Response Score (BARS) recently published by Milger et al.²⁵ Patients classified “responder” or “partial responder” were grouped in the “responder group”.

Statistical Analysis

For data analysis, IBM SPSS Statistics 28.0 (IBM Corp, Armonk, NY, USA) and R environment for statistical computing version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria) were used. Categorical variables are stated as numbers (n) and percentages (%). Depending on distribution, continuous variables are shown as median with interquartile ranges (IQR) or as mean \pm standard deviation (SD) unless indicated otherwise. Delta-values between the two time points were calculated for continuous variables in order to compare the slope. For group comparisons, Fisher's exact test, Chi-squared test, two-sided *t*-test or Mann–Whitney-*U*-test were used, as appropriate. For intergroup comparisons between time points paired *t*-test or Wilcoxon-signed-rank test were used as appropriate. Prevalence rates of GAD or MDD in patients with severe asthma and a representative German population (DEGS1-MH study)²⁶ were compared using χ^2 test. Point estimates with 95% confidence intervals (CI) and differences between the two populations were calculated. Simple- and multivariate logistic regression analysis was conducted to assess the impact on patients not responding to mAb-therapy. All reported p-values are two-sided. P-values <0.05 were considered statistically significant.

Results

Patients Characteristics

Data from 82 patients diagnosed with severe asthma undergoing mAb-therapy were included, of which 38 patients (46%) showed a suspect or probable MDD and/or GAD. Overall, 61 (74%) were classified as responders and 21 (26%) as non-responders (Figure 1). Notably, 24/61 (39%) responders showed probable or suspect MDD/GAD, in contrast to 14/21 non-responder (67%) ($p = 0.030$). Further baseline characteristics are displayed in Table 1.

Treatment parameters at baseline and follow-up stratified by eventual treatment response are displayed in Figure 2. Responders showed significant improvements in FEV₁ ($p = 0.001$), QoL and ACT ($p < 0.001$) and exacerbation rate ($p < 0.001$), while non-responders did not.

Prevalence of Mental Disorders in Severe Asthma

53% of patients in our study cohort suffered from psychological problems at the time of mAb initiation, 38% from probable MDD, 37% from probable GAD as well as 9% from alcohol abuse. Compared to the German general population, this represents a drastically elevated prevalence among our severe asthma patient cohort ($p < 0.001$).²⁶ Of note, we observed 16- and 5-fold higher risks for signs of GAD and MDD, respectively, in patients with severe asthma in our cohort compared to the general population (Table 2).

Differences in Mental Disorders Dependant on mAb Responder Status

Monoclonal antibody responders showed a significantly declining PHQ-2-score (BL: 2 (IQR: 1–2), FU: 1 (IQR: 0–2), $p = 0.026$) and tended towards a decrease in GAD-2-score (BL: 2 (IQR: 0–2), FU: 1 (IQR: 0–2), $p = 0.051$), while mAb non-

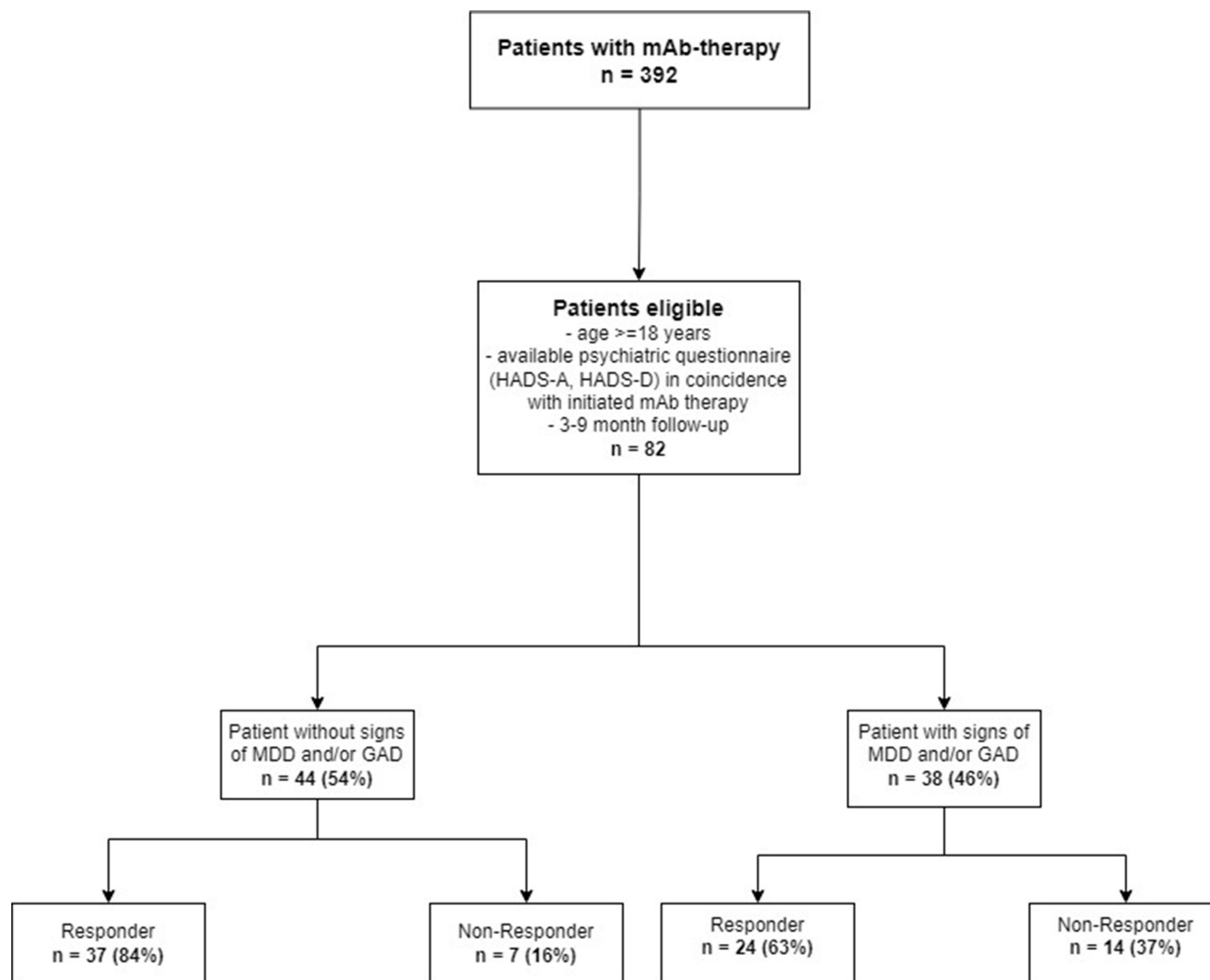


Figure 1 Flowchart of patient inclusion with consecutive subdivision in patients with and without signs of MDD/GAD and their respective responder-status.

responders showed no significant reduction in these scores [Table 3](#) and [Figure 2](#)). Comparison between responder and non-responder revealed a significantly lower PHQ-2-score ($p = 0.028$) and GAD-2-score ($p = 0.045$) for baseline and significantly lower PHQ-2-score for follow-up ($p = 0.003$). Responders exhibit significant lower scores in HADS-D ($p = 0.002$) with no significant differences in HADS-A ($p = 0.068$) as well as in further analysed characteristics ([Table 3](#)).

In logistic regression analysis, non-responding to mAb-therapy was associated with an OR of 1.23 (CI: 1.07–1.42), $p = 0.004$ per HADS-D point increase. Analysis for HADS-A revealed no significant impact ($p = 0.068$) in univariate analysis. Furthermore, an influence of alcohol (Audit C Score) on mAb non-response was detected with an OR of 0.65 (0.43–0.99) in multivariate analysis ($p = 0.043$). All further analysed variables did not show significant impact of psychological problems on mAb-therapy response ([Table 4](#)).

Discussion

To our knowledge, this is the first study to investigate changes in the burden and severity of psychological problems in patients with severe asthma receiving mAb-therapy and the impact on the patients' mAb responder status.

Patients that respond to mAb-therapy exhibit lower levels of MDD- or GAD-related symptoms and prevalence of probable MDD and GAD decreased significantly after initiation of mAb-therapy. Logistic regression analysis revealed pre-existing symptoms of depression as a major predictor for non-response to mAb-therapy.

Table I Characteristics of the Patients at Baseline

	All Patients n=82	No MDD or GAD n=44	MDD or GAD n=38	p-value
Age (years) – Median (IQR)	57 (50–63)	55 (49–64)	57 (50–62)	0.964
Female Sex – n (%)	49 (60%)	26 (59%)	23 (61%)	0.895*
BMI (kg/m²) – Median (IQR)	27.4 (24.2–32.5)	26.7 (23.9–31.1)	28.9 (24.8–34.9)	0.139
HADS-A – n (%)				
— Suspect	15 (18%)	0 (0%)	15 (40%)	
— Probable	15 (18%)	0 (0%)	15 (40%)	
— Unsuspectious	52 (63%)	44 (100%)	8 (21%)	
HADS-D – n (%)				
— Suspect	10 (12%)	0 (0%)	10 (26%)	
— Probable	21 (26%)	0 (0%)	21 (55%)	
— Unsuspectious	51 (62%)	44 (100%)	7 (18%)	
Smoking status – n (%)				0.496*
— Never	40 (49%)	23 (52%)	17 (45%)	
— Former	42 (51%)	22 (48%)	21 (55%)	
Pack years – Median (IQR)	14.5 (7.5–30)	10 (5.5–29)	19 (9–36)	0.281
Alcohol (Audit-C-Score Points) –Median (IQR)	2 (0–3.0)	2 (0–3.0)	1 (0–2.3)	0.374
Alcohol abuse - n (%)	7 (9%)	5 (11%)	2 (5%)	0.324*
Responder status – n (%)				0.030*
— Responder	61 (74%)	37 (84%)	24 (63%)	
— Non-Responder	21 (26%)	7 (16%)	14 (37%)	
Therapy – n (%):				0.051*
— Benralizumab	26 (32%)	14 (32%)	12 (32%)	
— Dupilumab	16 (20%)	9 (21%)	7 (18%)	
— Mepolizumab	33 (40%)	14 (32%)	19 (50%)	
— Omalizumab	7 (9%)	7 (16%)	0 (0%)	
Allergies – n (%)	54 (66%)	32 (59%)	22 (41%)	0.158*
Education category – n (%)^a				0.483*
— low	13 (16%)	5 (11%)	8 (21%)	
— moderate	58 (71%)	33 (75%)	25 (66%)	
— high	11 (13%)	6 (14%)	5 (13%)	
Family status – n (%)				0.088*
— Divorced	14 (17%)	4 (9%)	10 (26%)	
— Single	16 (20%)	12 (27%)	4 (11%)	

(Continued)

Table 1 (Continued).

	All Patients n=82	No MDD or GAD n=44	MDD or GAD n=38	p-value
— Married	42 (51%)	23 (52%)	19 (50%)	
— Widowed	10 (12%)	5 (11%)	5 (13%)	
Comorbidities— n (%)				
— Obesity	28 (34%)	13 (30%)	15 (40%)	0.344*
— Atopic dermatitis	8 (10%)	5 (11%)	3 (8%)	0.598*
— Chronic sinusitis	9 (11%)	5 (11%)	4 (11%)	0.904*
— Diabetes	8 (10%)	4 (9%)	4 (11%)	0.827*

Notes: ¹low, no vocational education; moderate, non-academic vocational education; high, academic degree. Continuous variables are stated as median and interquartile ranges (IQR) and categorical variables are stated as n and percent (%); * = χ^2 -Test. Statistically significant values in bold.

Abbreviations: MDD, Major Depression Disorder; GAD, General Anxiety Disorder; BMI, body mass index; HADS-A, Hospital Anxiety and Depression Scale—Anxiety; HADS-D, Hospital Anxiety and Depression Scale—Depression; IQR, interquartile range.

An increased prevalence of mental disorders, particularly MDD and GAD, in asthma patients as well as in other respiratory diseases is well documented in the literature: Previous studies about adolescents with asthma found a cumulative prevalence of 16.3% for anxiety and depressive disorder in an American population as well as a prevalence of 6.3% for depression disorder in a Taiwanese cohort.^{6,27} Fong et al identified a prevalence of 42.8% for depression and 38% for anxiety disorder in patients with severe asthma comparable to 37.8% for depression and 36.6% for anxiety in our cohort.¹⁴ Notably, another study found that 23% of patients suffering from idiopathic pulmonary hypertension exhibited depression disorder, whereas in patients with chronic thromboembolic pulmonary hypertension the prevalence of depression and anxiety resembled that of the general population, but panic disorders were more

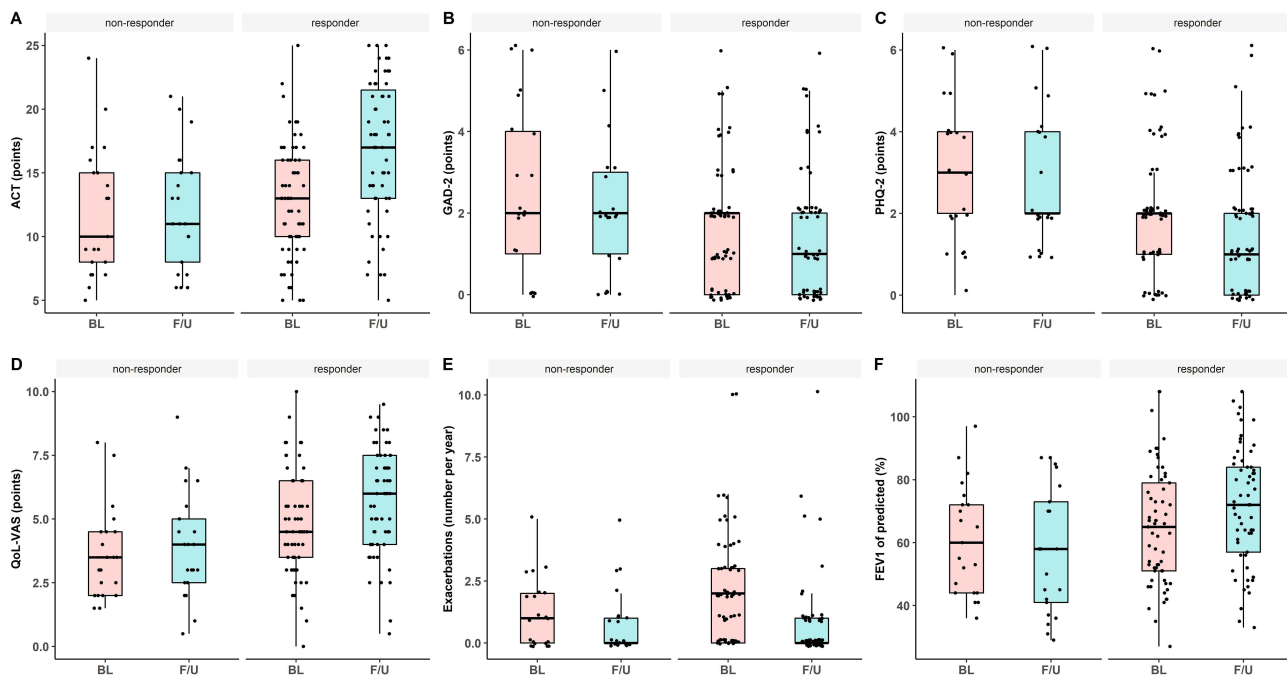


Figure 2 Comparison between baseline (BL) and follow-up (F/U) for (A) Asthma-Control Test (ACT), (B) Generalized Anxiety Disorder (GAD)-2 score, (C) Patients Health Questionnaire (PHQ)-2 score, (D) Quality of Life on Visual Analogue Scale (QoL-VAS), (E) Exacerbation counts and (F) Forced expiratory volume in one second (FEV₁) subdivided in Responder and Non-Responder. Data are presented as boxplots. The bars show the median value, the lower and upper ends correspond to the first and third quartiles (25th and 75th percentiles). The upper whisker extends from the upper edge of the boxplot to the highest value, the lower whisker extends from the lower edge of the boxplot to the smallest value.

Table 2 Psychological Disorder Prevalence Rates in Patient with Severe Asthma Compared to German Population

	Severe Asthma n=82	DEGSI-MH n=5318	p-value	Risk Ratio
Any current mental disorder	52.5% (41.2–63.5)	27.7% (26.3–29.2)	<0.001	1.90
Alcohol abuse	8.5% (3.8–17.4)	1.8% (1.4–2.3)	<0.001	4.72
Major Depressive Disorder	37.8% (27.5–49.2)	7.7% (6.9–8.6)	<0.001	4.91
Generalized Anxiety Disorder	36.6% (26.4–48.0)	2.2% (1.8–2.8)	<0.001	16.6

Notes: Any current mental disorder is defined by a positive AUDIT-C-Score or a probable or suspect HADS-D or HADS-A Score. Statistically significant values in bold. Data are shown as percent (%) and 95% confidence intervals (CI) and risk ratios.

Abbreviations: CI, confidence interval; DEGSI-MH, Studie zur Gesundheit Erwachsener in Deutschland (German study of health status in adults) – Mental Health.

Table 3 Comparison Between Responders and Non-Responders

	Non-Responder n = 21	Responder n = 61	p-value
Age (years) – Median (IQR)	56 (51–67)	57 (49–63)	0.504
Female Sex – n (%)	13 (62%)	36 (59%)	0.816
BMI (kg/m²) – Median (IQR)	27.1 (24.1–37.1)	27.6 (24.1–32)	0.862
HADS-A – n (%)			0.336*
Suspect	4 (19%)	11 (18%)	
Probable	11 (52%)	41 (67%)	
Unsuspectious	6 (29%)	9 (15%)	
HADS-A Score – Median (IQR)	7 (3–12)	5 (2–9)	0.063
HADS-D – n (%)			0.018*
Suspect	3 (14%)	7 (12%)	
Probable	8 (38%)	43 (71%)	
Unsuspectious	10 (48%)	11 (18%)	
HADS-D-Score – Median (IQR)	10 (6–13)	4 (2–9)	0.002
Smoking status – n (%)			0.902*
Never	10 (48%)	31 (51%)	
Former	11 (52%)	30 (49%)	
Pack years – Median (IQR)	15 (9–38)	14 (6–30)	0.361
Alcohol (Audit-C-Score Points) –Median (IQR)	1 (0–2)	2 (1–3)	0.035
Alcohol abuse - n (%)	0 (0%)	1 (12%)	0.105
BL PHQ2 – Median (IQR)	3 (2–4)	2 (1–3)	0.028
FU PHQ2 – Median (IQR)	2 (2–4)	1 (0–2)	0.003
BL GAD2 – Median (IQR)	2 (1–5)	2 (0–2)	0.045
FU GAD2 – Median (IQR)	2 (1–3)	1 (0–2)	0.191

Notes: Continuous variables are stated as median and interquartile ranges (IQR), Statistically significant values in bold. * = χ^2 -Test.

Abbreviations: PHQ-2, Patient Health Questionnaire-2; GAD-2, General Anxiety Disorder-2; BL, Baseline; FU, Follow-Up; BMI, body mass index; HADS-A, Hospital Anxiety and Depression Scale—Anxiety; HADS-D, Hospital Anxiety and Depression Scale—Depression.

Table 4 Multivariate Analysis of Impact on Non-Responding to mAb-Therapy

	Univariate OR (95% CI)	p-value	Multivariate OR (95% CI)	p-value
HADS-A	1.11 (0.99–1.24)	0.068		
HADS-D	1.19 (1.06–1.33)	0.004	1.23 (1.07–1.42)	0.004
Male Sex	0.89 (0.23–2.45)	0.816		
Pollutants exposure, any	0.87 (0.27–2.81)	0.812		
Education category	0.90 (0.36–2.25)	0.819		
Audit-C-Score	0.67 (0.46–0.98)	0.040	0.65 (0.43–0.99)	0.043
BMI	1.0 (0.93–1.09)	0.86		
Age	1.02 (0.97–1.06)	0.499		
Smoking status	1.07 (0.40–2.87)	0.902		
Allergies, any	0.95 (0.33–2.72)	0.927		
FEV ₁	0.99 (0.96–1.02)	0.406		
Marital status	0.37 (0.13–1.05)	0.062		

Note: Statistically significant values in bold.

Abbreviations: CI, confidence interval; OR, Odds-ratio; HADS-A, Hospital Anxiety and Depression Scale—Anxiety; HADS-D, Hospital Anxiety and Depression Scale – Depression; Audit-C, Alcohol Use Disorders Identification Test; BMI, Body mass index; FEV₁, Forced expiratory volume.

common.^{28,29} Concerning patients with chronic obstructive pulmonary disease (COPD), meta-analysis showed a prevalence of 24.6% for depression³⁰ and 40% for anxiety.³¹ Both the cause for the general elevation in prevalence of mental disorders and the cause for the wide spread of prevalence among patients suffering from respiratory diseases remain unclear. The aforementioned studies analysed cohorts differing greatly in age, origin and stage of illness, so the weighting of mental illness is certainly related to this and thus an individualized approach must be taken to identify affected patients. Either way, the connection between psychological problems and asthma therapy remains to be elucidated.

A positive effect of mAb-therapy on anxiety and depression disorders in patients with severe asthma has been reported previously, without differentiation between mAb-therapy responders and non-responders.¹³ Comparable to our approach, one part of the above-mentioned WATCH study by Fong et al examined the relation between the response to Omalizumab/Mepolizumab and MDD/GAD evaluated by HADS-A/D. Non-responders suffered from mental disorders more frequently. Furthermore, depression was identified as a potential influence factor for mAb-therapy nonresponse,¹⁴ matching our own findings. Additionally, our study includes patients with omalizumab and mepolizumab as well as those with dupilumab and benralizumab. In fact, effects of mAb-therapy response on mental health have not only been described for severe asthma but also for other chronic diseases, particularly rheumatoid arthritis.^{32–34} While an association between GAD/MDD and mAb-therapy non-response is well-established, the underlying mechanisms remain unclear: One possible explanation is the well-described decreased therapy adherence in patients with psychiatric comorbidities.^{35,36} To date, there are no specific data on the adherence of patients with severe asthma and mAb-therapy, so we can only draw on empirical values from our daily work. For example, a regular application of the therapy can be indirectly deduced from falling values of IgE and/or eosinophils. Moreover, cytokine imbalances were identified in psychiatric patients, possibly affecting the efficacy of immunomodulation.³⁷ For example, elevated production of disease-related Th2 and Th17 cytokines has been detected in asthmatic patients suffering from MDD,³⁸ whereas the influence of these elevated cytokines on the success of mAb-therapy remains unclear. Thus, this issue needs further investigation.

Conversely, chronic diseases such as severe asthma may also cause or aggravate affective mood disorders and anxiety in affected patients, who consequentially avoid enjoyable activities and social contacts.^{39,40} In chronic respiratory diseases, repetitive breathlessness as well as frequent exacerbations can cause a loss of self-control and engulfment of daily routine. Thus, these factors favour mental distress with consecutive depression and anxiety disorder.^{40,41} The improvement of depression in PHQ2 test in mAb-responders shows the direct influence of pulmonary improvement on psychological status.

The cited literature in the preceding sections matches our results with regard to a negative impact of pre-existing depression on mAb-response but also with a positive effect of disease control on symptoms of depression. However, it has to be mentioned that our and the cited results just base on statistical observation without proof of a causal relationship. It remains unclear whether severe asthma and MDD/GAD are at all related in our patients. Consideration of risk factors and reasons of these mental disorders^{42,43} reveals a complexity that is not restricted to severe asthma. In patient cohorts suffering from asthma and other chronic diseases, risk factors for psychiatric morbidities (eg, history of depression, older age) are more prevalent.^{27,44} Given the complex and incompletely understood pathogenesis of asthma and the multitude of factors influencing its course and severity,⁴⁵ further research concerning its interplay with mental illness is necessary.

The main advantage of our study is the classification of our treated patients in responder and non-responder according to the novel BARS Score that is universally applicable to classify mAb-therapy response.²⁵

Limitations: The generalizability of our study is limited by its monocentric and retrospective design as well as the relatively small sample size. Further, using HADS in combination with PHQ-2 and GAD-2 scores to estimate the follow-up to classify patients with probable MDD and/or GAD does not allow diagnosis of mental disorders. Additionally, there are no values for the minimum clinically important difference (MCID) for these questionnaires, making a clinical appraisal of changes more difficult. Nevertheless, they prove useful as a reliable screening tool with the benefit of being able to discriminate between severity of symptoms.^{20,46} Our study also focuses on two of the most prevalent mental disorders, but does not consider the wide range of all mental illnesses.

Conclusion

This is the first study evaluating the impact of anxiety or depression on mAb-therapy response in severe asthma patients. Patients responding to mAb-therapy showed less signs of MDD/GAD. Conversely, a history of depression, but not anxiety, was a negative predictor for mAb-therapy success. Taken together, our findings highlight the need for a subsequent psychiatric evaluation in patients suffering most probably from mental disorders and severe asthma as well as for further research regarding possible causal connections between asthma and mental diseases.

Abbreviations

mAb, monoclonal antibody; MDD, Major Depression Disorder; GAD, General Anxiety Disorder; HADS, Hospital Anxiety and Depression Scale; PHQ-2, Patient Health Questionnaire-2; GAD-2, General Anxiety Disorder-2; CTEPH, Chronic thromboembolic pulmonary hypertension; QoL, Quality of Life; ACT, Asthma Control Test; ERS, European respiratory society; ATS, American thoracic society; FDA, Food and Drug agency; EMA, European Medicines agency; COPD, Chronic obstructive pulmonary disease; OCS, Oral corticosteroids; Audit-C-Score, Alcohol Use Disorders Identification Test; CI, Confidence interval; OR, Odds ratio; BMI, Body Mass Index; FEV₁, Forced expiratory volume; IgE, Immunoglobulin E; MCID, minimum clinically important difference; BL, Baseline; FU, Follow-Up; IQR, Interquartile range.

Data Sharing Statement

Data used in this study are available on reasonable request by the corresponding author.

Ethics Approval and Consent to Participate

Approval of the local ethic committee of the Hannover Medical School (10539_BO_K_2022) was given and all patients provided written informed consent allowing the use of their data for scientific research.

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