Influence of anti-interleukin (IL)-5/anti-IL-5 receptor-α treatment on work productivity in patients with severe eosinophilic asthma

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To the Editor:

~3–10% of asthma patients suffer from severe asthma, representing a substantial burden for affected patients due to distinct symptoms, frequent exacerbations and numerous medication side-effects [1]. Despite the rather small percentage, patients with severe asthma are responsible for up to 50% of direct and indirect costs associated with bronchial asthma [2]. Hospitalisations and medications are the main driver for high economic costs, but indirect costs including lost work days or loss in productivity due to sickness also lead to steadily increasing healthcare expenses [3]. Over the last years monoclonal antibodies (mepolizumab, reslizumab, benralizumab) interfering directly with the interleukin-5 (IL-5) or IL-5 receptor-α (IL-5Rα) have been approved for use in patients with severe eosinophilic asthma (SEA). Treatment with these antibodies is highly clinically effective and an inherent part of Global Initiative for Asthma (GINA) guidelines for treatment of bronchial asthma [4], but leads to high treatment costs. Antibody treatment can lead to improvement of lung function, reduction of exacerbations and reduction of oral corticosteroid intake, but little information concerning the impact on lost work days or loss in productivity exists.

In this retrospective, single-centre study we investigated the effect of anti-IL-5/IL-5Rα antibody treatment on lost work days or loss in productivity in patients with SEA. All patients were treated in our severe asthma outpatient clinic of Hannover Medical School, Germany, and were included in the study between October 2019 and April 2020. Patients were treated with maximised inhaler therapy and were started on treatment with either mepolizumab (anti-IL-5) or benralizumab (anti-IL-5Rα) within the last 10 months prior to questionnaire assessment. Patients provided written informed consent and analyses were performed with approval of the local institutional review board of Hannover Medical School (No. 8050_BO_K_2018).

During follow-up, participating patients were asked to fill out an asthma and work questionnaire including the visual analogue scale (VAS) from the Work Productivity and Activity Impairment Questionnaire (WPAI) ranging from 0 (asthma does not influence my productivity) to 10 points (I am not able to work due to my asthma disease) to assess the impact asthma has on work productivity and the occupational status as well as missed days at work. The questionnaire considered patients' employment situation retrospectively for 12 months prior to antibody therapy and the current timepoint under treatment. Positive and negative changes induced by antibody treatment, such as more or less problems with co-workers/employer, were assessed. Continuous variables are stated as median (interquartile range (IQR)), and categorical variables are shown as n (%). Comparisons between timepoints were conducted using Wilcoxon-test, paired t-test or McNemar's test, as appropriate. A p-value of <0.05 was considered statistically significant.

23 patients were included and the median treatment duration at timepoint of assessment was 7 months (IQR 6–10). Median patient age was 56 years (IQR 50–64), 65% of patients were female and the most frequent comorbidities were obesity (39%) and chronic rhinosinusitis with nasal polyps (30%). 12 patients (52%) were treated with mepolizumab and 11 patients (48%) with benralizumab. Asthma control test (ACT) scores increased from 11.5 (IQR 9–16) to 17.5 (IQR 13–21) points under therapy, p=0.002. ACT

Shareable abstract (@ERSpublications)
This retrospective study shows that treatment with anti-eosinophilic antibodies in patients with severe eosinophilic asthma is associated with an increase in work productivity and a decrease in missed days at work https://bit.ly/3IIPppR

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and WPAI correlated with a Pearson correlation coefficient of −0.612, p=0.015. Patients described their employment situation prior to therapy start as follows: fulltime employed (eight patients, 35%), part-time employed (seven patients, 30%) and not employed (eight patients, 35%). Reasons for not working were: old age pension (n=5, 22%), disability (n=2, 9%), unemployment (n=1, 4%). After treatment initiation, employment situation remained stable in all patients except two, who reduced working hours due to partial retirement unrelated to their bronchial asthma. Employed patients stated a median of 4 (IQR 2–14) missed days at work per month prior to treatment start and 0 (IQR 0–2) after therapy initiation (p=0.015). WPAI-VAS was 6 (IQR 4–7) prior to treatment and 3 (IQR 2–4) after therapy initiation (p=0.002). Changes of the WPAI-VAS and missed days at work from baseline (prior to therapy) to follow-up are depicted in figure 1. Patients stated positive changes such as fewer problems with co-workers/employer and reduced symptoms during work after therapy initiation. The number of patients negatively affected at work by their asthma decreased from 16 (70%) to 6 (26%), p=0.057.

In this retrospective study we could show that treatment with anti-eosinophilic antibodies is associated with an increase in work productivity and a decrease in missed days at work. Severe asthma leads to substantial impairment of daily activity and a reduction of work productivity based on the WPAI score, with higher levels of impairment in patients with a more severe grade of disease activity [5]. Furthermore, Chen *et al.* [5] showed that an impairment of work productivity of >10% predicted is associated with an increased number of emergency visits and hospitalisations. Using data from the MENSA and MUSCA licensing trials for mepolizumab, Albers *et al.* [6] also showed that according to the WPAI scale, work impairment decreases under treatment with mepolizumab, indicating that antibody treatment could lead to an increase in work productivity in patients with SEA. In the real-world prospective CHRONICLE trial, asthma patients under therapy with systemic corticosteroids showed the highest work impairment, whereas patients with biological treatment showed the lowest grade of impairment [7]. This finding is supported by our results, showing a significant decrease on the WPAI-VAS after initiation of antibody therapy, indicating a significant improvement in subjective productivity at work. Despite its broad use in clinical practice, the WPAI questionnaire has not been validated specifically for use in patients with asthma. Referring to other chronic conditions, changes in the WPAI of 20% or more are considered clinically relevant [8, 9]. Besides the increase in work productivity, patients also stated a significant decrease in missed days at work per month under antibody treatment. Furthermore, the number of patients negatively affected by their disease decreased and patients described positive effects of the antibody treatment on their daily working experience.

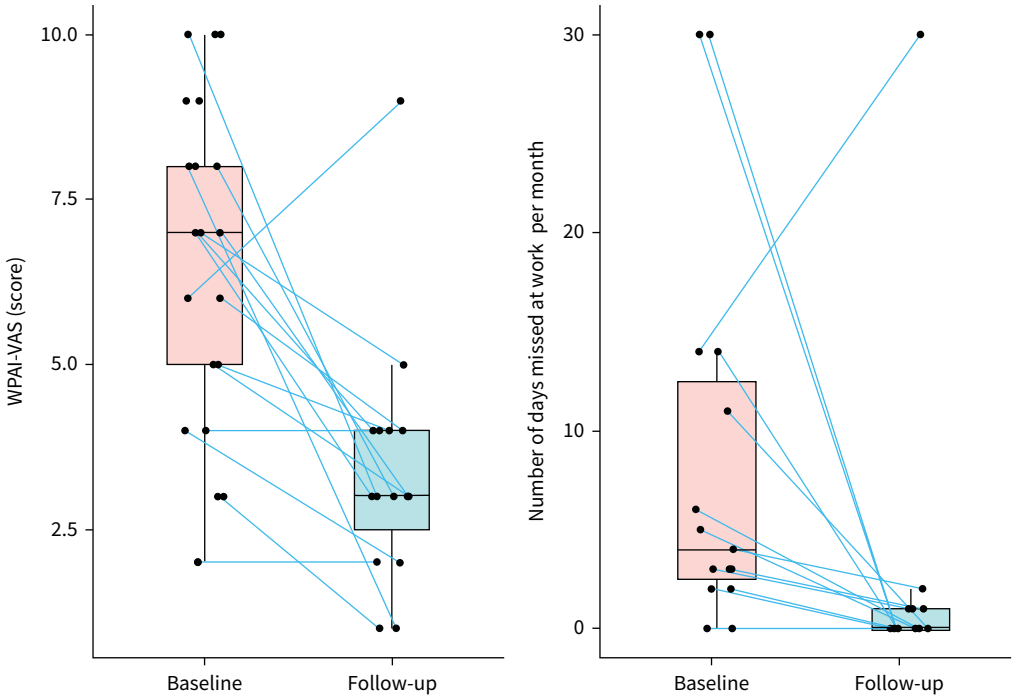

FIGURE 1 Change of the WPAI-VAS and missed days at work from baseline (prior to treatment) to follow-up (control under anti-IL-5/anti-IL-5Rα treatment). WPAI: work productivity and activity impairment; VAS: visual analogue scale; IL: interleukin.

Besides the influence severe asthma has on the patients' activity and work productivity, severe bronchial asthma also leads to high healthcare costs with hospitalisations and medication being the main cost driver for directs costs [3, 10]. Padilla-Galo *et al*. [11] recently showed that treatment with benralizumab is expensive but cost-effective as it decreases healthcare costs by reducing exacerbations and medication use and increases overall disease control and lung function. The results of our study and the conclusion that a reduction of the exacerbation rate and adequate symptom control in patients with SEA leads to an increase in productivity and a reduction of missed days at work could support the finding that antibody treatment is cost-effective despite high treatment costs and could improve acceptance of treatment.

Our study is primarily limited by the small number of patients included and the retrospective design. As a result, a recall bias cannot be excluded. Furthermore, parts of the questionnaire used are not validated. Certain patient data were only assessed at baseline, therefore analysis of confounding factors such as comorbidities could not be performed. In summary, our results lead to the conclusion that anti-eosinophilic treatment in patients with SEA could lead to an improvement in work productivity. Whether observed effects of anti-eosinophilic treatment are followed by a decrease in indirect healthcare costs needs to be analysed in further research.

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