

# Identification of a clear biologics case based on regular FeNO measurements

## Optimizing treatment decisions with biologics based on regular FeNO home measurement

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### Summary

The case study refers to a participant of the ongoing FeNO@home study. For the asthma patient, biologic therapy was indicated, but the confirmation of Type 2 inflammation was pending. FeNO home measurements were conducted over a period of 12 weeks under usual medication. The gathered data confirmed an existing Type 2 inflammation supporting the decision for dupilumab as biologic of choice for future asthma management. The case illustrates how frequent FeNO measurements can help to confirm inflammatory endotypes in severe asthmatics with active disease and exacerbations despite GINA step 5 inhaled therapy. **Frequent FeNO home measurement can lead to truly individualized asthma treatment.**

### Case history

A 55-year-old woman with severe asthma under maximum inhaled asthma treatment has been known as a patient for 5 years. She used to be a smoker (10 pack years). Her medical history included asthma diagnosed in adolescence, different allergies such as grass pollen and animal dander and an existing comorbidity with arterial hypertension. She showed frequent exacerbations with a need for oral corticosteroid (OCS) bursts; uncontrolled asthma symptoms according to the Asthma Control Questionnaire (ACQ score 1.6 units). The lung function was impaired despite maximal treatment (FEV1 approx. 60% of predicted). Fractional exhaled Nitric Oxide (FeNO) showed a low level (9 ppb) as measured in medical practice; no increased blood eosinophils. The patient received GINA (Global Initiative of Asthma) treatment step 5: high-dose inhaled corticosteroid plus

long-acting beta-agonist plus long-acting muscarinic antagonist which was frequently short-acting. Beta-agonist use daily. Antihypertensive combination treatment with AT1-Blocker/Thiazide.

#### Problem statement

The patient was not sufficiently medicated. Biologic therapy was indicated due to repeated OCS bursts. The selection and justification of an optimal biologic agent was found to be difficult in the absence of confirmed Type 2 inflammation. The expected outcome was that serial FeNO measurements provide the opportunity to identify patient characteristics (such as inflammatory endotype), to recognize potential asthma triggers and to detect exacerbations earlier.

### Investigation

The patient was included in the FeNO@home study<sup>1</sup> outside grass pollen season. The aim of the study was to investigate whether regular FeNO home measurements had an impact on patient compliance or behavior, variability of FeNO values over a longer period, correlation of FeNO values with symptoms, identification of asthma triggers, and treatment decisions. In this multicenter study, adult patients with diagnosed asthma performed FeNO measurements over a period of 12 weeks using the Vivatmo *me* measurement device for home use. They continued to take their currently prescribed asthma treatment, which could also be adapted. Daily symptoms, use of asthma medication, potential exacerbations, and Peak Expiratory Flow (PEF) were recorded in the device-associated Vivatmo *app*. After 12 weeks, the study ended with a final assessment of asthma control, symptoms, and lung function.

### Results and treatment

The prescribed medication for the patient was not adjusted during the study. The ACQ score reduced to 0.8 units. The expectations of serial FeNO measurements were fully met; an otherwise unreported significant asthma exacerbation was documented including confirmation of pronounced Type 2 inflammation during the exacerbation, but also outside the episode.

On 55 out of 89 days, the FeNO value exceeded the threshold of 25 ppb for recommended dupilumab prescription stated by GINA. An exacerbation trigger such as a virus infection was also confirmed.

The PEF was in the range of 190 to 350 l/min. Regular FeNO measurements helped to diagnose asthma endotype. Based on these results, the decision was made for dupilumab as optimal biologic therapy.

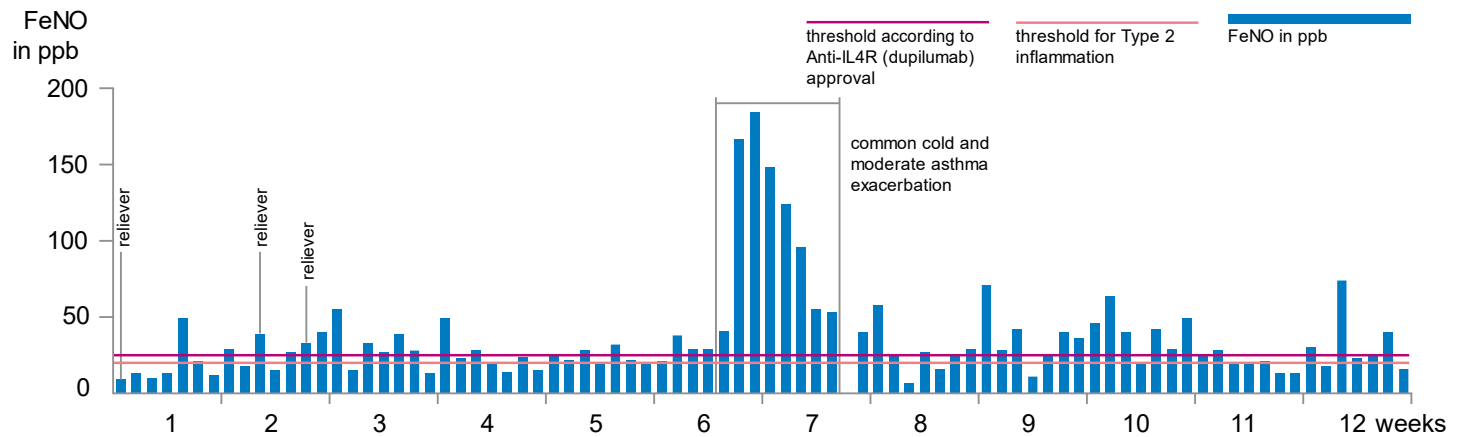


Figure: Course of the FeNO values based on regular home measurements by patients, thresholds according to GINA<sup>2</sup>

## Discussion

Asthma is known to be a heterogenous disease consisting of multiple overlapping phenotypes driven by different endotypes.<sup>3-6</sup> Identifying these phenotypes, including the broad definition of Type 2 and Non-type 2 asthma,<sup>7</sup> allows for better understanding of disease mechanisms and the personalization of treatment.<sup>6,8</sup> Elevated FeNO levels in combination with a clinical history, spirometry, and other biomarkers can aid with asthma diagnosis, predicting responsiveness to ICS, and stratifying add-on biologic therapies in severe asthma.<sup>2,9,10,11</sup> For the prescription of dupilumab as indicated by the GINA report, a specified number of severe exacerbations in the last year and Type 2 biomarkers such as eosinophils or FeNO above a specified level should be given.<sup>2</sup>

Although eosinophil counts in induced sputum or bronchial biopsies are considered as the gold standard for the assessments of Type 2 inflammation, these tests require specific expertise, resources, and do not allow continued monitoring.<sup>12</sup> Consequently, FeNO is an additional indicator of Type 2 inflammation that is noninvasive, repeatable, safe, and can be delivered at the point of care<sup>9</sup> or, since recently, even at the patient's home using the Vivatmo *me*. In this study, patients were trained in how to use the device upon study inclusion. They continued to measure their FeNO values at home. The course of FeNO values was evaluated after 12 weeks. Asthma therapy could be adjusted at two intermediate contacts. The use of a measurement device for home use in this clinical study allowed for continuous FeNO monitoring with limited effort on the part of physicians and patients.

These are some preliminary results since the study is still ongoing. Thus, only a single patient case is reported. The completion of the study is needed to strengthen the beneficial effects of FeNO home measurement for physicians and asthma patients.

## Conclusion

Overall, the patient can be considered as a relevant example for beneficial FeNO home measurements.

Severe asthmatic with high symptom load and active inflammation, documentation of significant exacerbation that otherwise would have remained unreported, consistent demonstration of Type 2 inflammatory pattern in stable periods and during asthma worsening (in contrast to low FeNO values during single practice measurement), supporting the decision for dupilumab as biologic of choice for future asthma management.

Single cross-sectional practice observations may underestimate the prevalence of Type 2 inflammation in severe asthmatics. This has implications on the choice of optimal biologic treatment. This case illustrates how frequent FeNO home measurements can help to confirm inflammatory endotypes in severe asthmatics with active disease and exacerbations despite GINA step 5 inhaled therapy, ultimately leading to truly individualized treatment decisions (biologic/dupilumab).

## References

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