Comparison of the Asthma Control Questionnaire and patient diaries in uncontrolled asthma

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To the Editor:

The Asthma Control Questionnaire (ACQ) is a validated tool commonly used to assess therapeutic efficacy in asthma clinical trials, as it is responsive to changes in asthma control [1]. However, it depends on accurate recall since patients are asked about their symptoms, activities and rescue medication use over the previous week. Even if patients can accurately remember this period, this also means that data are averaged. Guidelines recommend that patients with asthma are trained to keep track of their symptoms (*e.g.* using a diary [2]) and clinical trials often require patients to complete a diary twice daily.

TRIMARAN and TRIGGER were two phase III, double-blind, 52-week studies in patients with uncontrolled asthma (seven-item Asthma Control Questionnaire (ACQ-7) score ⩾1.5) [3]. Both compared the efficacy and safety of single-inhaler triple therapy containing an extrafine formulation of the inhaled corticosteroid beclometasone dipropionate (BDP), the long-acting β_2-agonist formoterol fumarate (FF) and the long-acting muscarinic antagonist glycopyrronium *versus* BDP/FF, with TRIGGER including a third arm in which patients received open-label BDP/FF plus tiotropium. Patients completed an electronic diary (eDiary) twice daily (morning and evening), recording their symptom score and the number of puffs of rescue medication used during the day or night. The four daytime symptoms recorded were cough, wheeze, chest tightness and breathlessness, each rated by the patient from 0 (no symptoms) to 3 (severe symptoms); any night-time awakening due to asthma that resulted in rescue medication use was captured as "yes" or "no". At baseline and during clinic visits, they also completed the ACQ-7, which includes five questions on symptoms, one question on rescue medication use and forced expiratory volume in 1 s (FEV_1).

We tested the hypothesis that ACQ and eDiary assessments of asthma control may differ. Using TRIMARAN and TRIGGER data, we compared ACQ-6 results (*i.e.* excluding FEV_1) at baseline and weeks 26 and 52 with those from the eDiary (using data collected in the 7 days prior to the clinic visit). The analyses only included patients with complete eDiary data over that period. Data from the eDiary were mapped to the Global Initiative for Asthma (GINA) symptom control assessment [2], allocating a score of 1 to each of the following: 1) mild, moderate or severe daytime asthma symptoms (*i.e.* if at least one of the daytime eDiary symptoms scored 1, 2 or 3) on >2 days; 2) any night-time awakenings due to asthma; 3) rescue medication use on >2 days; and 4) as there is no direct question on activity limitation in the eDiary, patients who had moderate or severe daytime asthma symptoms (*i.e.* at least one of the daytime eDiary symptoms scored 2 or 3, both defined as impacting activity) on >2 days received an additional score of 1. These scores were then summed, consistent with the GINA assessment of asthma control, with a total of 3–4 indicating uncontrolled asthma. An ACQ-6 score ⩾1.5 indicates uncontrolled asthma [4, 5]. We used ACQ-6 rather than ACQ-7, since GINA does not include FEV_1 in the assessment of asthma control, although low FEV_1 is considered a risk factor for poor outcomes [2].

Overall, a higher proportion of patients in both studies met the ACQ-6 definition of uncontrolled asthma than met the eDiary definition at all three visits, with an improvement (*i.e.* reduction) from baseline in the proportion at weeks 26 and 52 with both measures (figure 1a). Given these results could be influenced by the cut-point selected to define "uncontrolled", we also conducted a series of analyses on the actual ACQ-6 and eDiary scores, by mapping the two sets of scores to each other (controlled asthma: ACQ-6 scores ⩽0.75 equalled eDiary total score of 0; poorly controlled: ACQ-6 >0.75–⩽1.5 equalled eDiary 1–2;

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These *post hoc* analyses suggest that the Asthma Control Questionnaire and eDiary have different measurement properties, and it is therefore potentially valuable to include both in clinical trials
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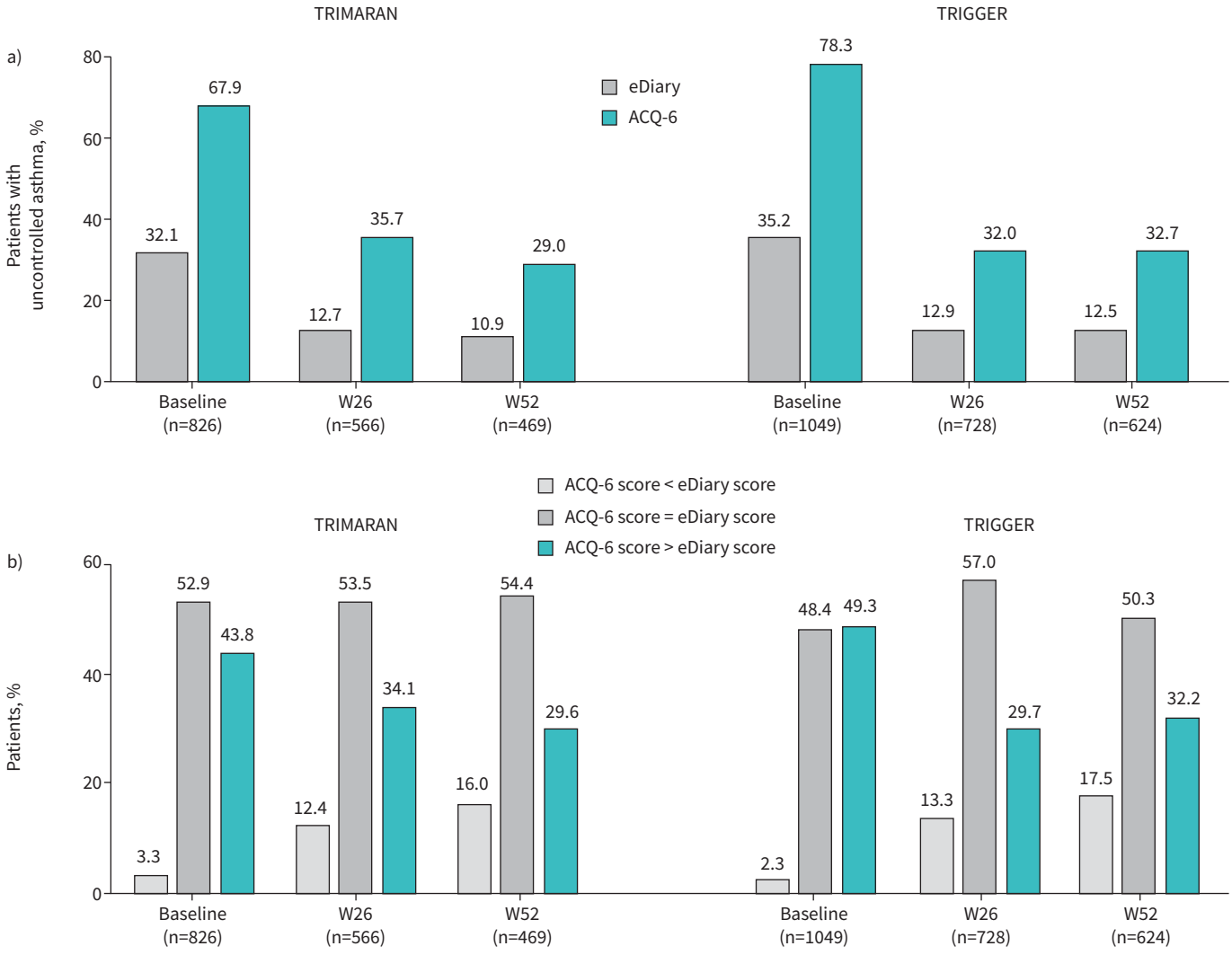

FIGURE 1 a) Proportion of patients with uncontrolled asthma according to the electronic diary (eDiary) (total score 3 or 4) or six-item Asthma Control Questionnaire (ACQ-6) (score ⩾1.5). b) Proportion of patients with ACQ-6 score less than, equal to or greater than eDiary total score. W: week.

uncontrolled: ACQ-6 >1.5 equalled eDiary 3–4). At baseline, 3.3% and 2.3% of patients had a lower ACQ-6 score than eDiary total score, indicating that asthma was rated as more controlled when using ACQ-6 than the eDiary (increasing to 12.4–17.5% during follow-up) (figure 1b). However, although 52.9% and 48.4% had their asthma rated similarly using the two scales at baseline, 43.8% and 49.3% had a higher ACQ-6 score than eDiary total score, indicating that asthma was rated as less controlled when using the ACQ than the eDiary, consistent with the first set of analyses. In terms of patient baseline characteristics, other than ACQ-6 (where the mean baseline value was higher in the groups with ACQ-6 score higher than the eDiary score) there were no consistent differences between these categories that could explain these results.

Both the ACQ and the eDiary combine objective parameters (*e.g.* rescue medication use) with subjective questions. We therefore conducted a further set of analyses specific to rescue medication use, where the eDiary data over the 7-day period prior to the ACQ assessment were averaged to allow a direct comparison between the two. The data matched for the ACQ and eDiary for 52.0–63.9% of patients (with a better match at weeks 26 and 52 than at baseline) but for approximately one-third of the patients (29.9–39.0%), the ACQ results were again higher than the eDiary.

Taken together, these results suggest that the two tools have different measurement properties and that asthma control tends to be rated worse when using the ACQ than the eDiary. It is possible that they are

measuring different components of asthma (given the questions are phrased differently). However, the main advantage of the eDiary is the twice-daily completion, whereas the ACQ is only completed at study visits and asks patients to recall their asthma symptoms over the previous 7 days. The rescue medication data suggest that the 7-day recall period of the ACQ may result in patients overestimating the impact of asthma on their day-to-day life and that the data collected twice-daily in the eDiary are more precise due to the absence of the recall period. The main limitation of these analyses is that whereas the ACQ is a validated endpoint, having demonstrated good cross-sectional validity to both the Asthma Quality of Life Questionnaire and the Short Form-36 [1], the eDiary was developed specifically for these studies and is not similarly validated. In addition, although the eDiary questions were mapped to the GINA symptom control assessment, the questions are not a perfect match and in future, it would perhaps be useful to include a direct question on activity limitation.

In conclusion, given the differing results from these two tools, it is potentially valuable to include both in clinical trials. Inclusion of the (validated) ACQ facilitates comparisons between trials (including of the patients recruited into different trials). However, the results (particularly the rescue medication data) highlight a potential limitation of the ACQ: the recall period. A daily eDiary, which by its nature, does not require patients to accurately recall their asthma control over a prolonged period (although more burdensome), perhaps more accurately reflects a patient's level of asthma control. Importantly, a twice-daily eDiary is more able to capture day-to-day variability in symptoms, which may be of particular interest in a disease such as asthma that is highly variable.

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