THE USE OF FENO IN CLINICAL TRIALS WITH GENERIC ICS IN ASTHMATIC PATIENTS AS PRIMARY ENDPOINT TO SHOW BIOEQUIVALENCE: CAN THE US PERSPECTIVE BE IMPLEMENTED IN THE EUROPEAN GUIDELINE?

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Designing clinical trials in asthma it is crucial to find the perfect primary endpoint for showing bioequivalence. Especially if the investigational medicinal product is not a bronchodilator, but a substance, which suppresses the inflammatory process, e. g. inhalative corticosteroids (ICS). In the past, lung function parameters were used as the primary endpoint, which entails a long study duration and hundreds of patients. Chowdhury from FDA stated, that FeNO is a good marker for bioequivalence measurements in the market approval process of generic ICS products.[1]He has good reasons to do that, since the measurement of fractional exhaled nitric oxide (FeNO) is established as a non-invasive marker for eosinophilic inflammation, and several guidelines focus on that diagnosis.[2, 3, 4]FeNO is a surrogate measure of eosinophilic inflammation and at the same time, eosinophilic airway inflammation is usually steroid responsive.[5,]It originates mostly from the epithelium, as inducible nitric oxide (NO) synthase, which is sensitive to steroids.[6]National Jewish Health published 2009 a consensus statement on the clinical use of FeNO measurement. They state that FeNO should be a part of the clinical management of asthma in ambulatory settings in conjunction with other conventional methods of asthma assessment. Furthermore, FeNO should be used to determine the presence or absence of eosinophilic airway inflammation, to determine the likelihood of steroid responsiveness, to measure response to steroid therapy and level of inflammation control. In addition, FeNO is a useful tool to monitor patient ICS treatment adherence and allergen exposure.[7]Therefore, FeNO may be used to predict steroid responsiveness and as a measure to determine the optimal treatment of airway inflammation. At the same time, Kim et al, also from FDA provides suggestions for the study design, beginning with a pilot, to establish the response in FeNO to the respective ICS in its different dose strength. The next step is a pivotal trial, in which bioequivalence will be shown.[9] If good care is taken to design the clinical trial in terms of patient population, concomitant medication, equipment and other factors, which can influence the measurement, then efficient clinical trials can be performed, with a relatively short treatment time of 2-4 weeks and 50 to 100 patients.[9, 10]

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