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Significant reduction in abdominal symptoms assessed with CFAbd score over 4 weeks of treatment with elexacaftor/tezacaftor/ivacaftor—First results from the RECOVER study

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Background: The novel, highly effective CFTR modulator combination elexacaftor/tezacaftor/ivacaftor for people with CF and the 508del mutation has the potential for substantial improvements in end organ function, including in the abdomen. The impact of previous modulator therapies, such as ivacaftor, on abdominal involvement, particularly abdominal symptoms, has not been sufficiently assessed. For this purpose, the Cystic Fibrosis Abdomen (CFAbd)-Score was developed and validated in line with FDA recommendations for development of a patient-reported outcome measure (PROM) with input from focus groups, multidisciplinary CF specialists, people with CF, and their families. CFAbd scores correlate well with clinical characteristics, ultrasound findings, and gut inflammation.
Methods: As part of the RECOVER study (NCT04602468), examining a wide array of outcome measures before and after elexacaftor/tezacaftor/ivacaftor introduction, gastrointestinal symptoms were reported at baseline and 1 month after elexacaftor/tezacaftor/ivacaftor using the CFAbd-Score. The PROM includes 28 items grouped in 5 domains.
Results: One hundred four participants completed the CFAbd-Score at baseline, and at submission of this abstract, 60 had completed the questionnaire after 1 month of therapy. Already in this cohort, total CFAbd-Score decreased significantly, from 14.0 ± 13.8 to 10.6 ± 10.6 ($P < 0.01$) (Figure 1). Furthermore, significant improvements were seen for the domains of pain (14.9 ± 20.9 to 9.1 ± 16.9; $P = 0.02$), GERD (14.7 ± 19.7 to 9.8 ± 15.5; $P < 0.01$), and impairment of quality of life (11.4 ± 19.1 to 6.7 ± 13.3; $P < 0.01$), although decline did not reach significance for disorders of bowel movements (18.9 ± 14.3 to 18.3 ± 13.9) or appetite (5.7 ± 9.2 to 4.2 ± 7.7). Final results will take into account differences in previous CFTR-modulating therapy, genotype, gender, and age.
Conclusion: Using the CFAbd-Score, the first PROM specifically developed for assessment of CF-related abdominal symptoms, we demonstrate comprehensive improvements in gastrointestinal symptoms after initiation of the highly effective modulator therapy elexacaftor/tezacaftor/ivacaftor. As part of RECOVER, in addition to longitudinal data on abdominal symptoms, markers of gut inflammation and pancreatic status will be collected over 2 years of therapy.

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Accelerated aging pathways are activated in cystic fibrosis airway disease

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Background: Cystic fibrosis (CF) is one of the most common single-gene disorders that affects multiple organ systems. CF is characterized by thick sticky mucus that plugs airways and leads to persistent bacterial infections and chronic inflammation. CF was once a disease of childhood, but advances in management and care have led to longer survival, with aging processes potentially contributing to disease progression. We have previously shown that FGF23/klotho signaling plays a role in CF-associated airway disease. FGF23 plasma levels are high in CF patients. We have also shown that high levels of circulating klotho downregulate 2 key proinflammatory markers in CF (IL-8 and TGF-β) in the bronchial

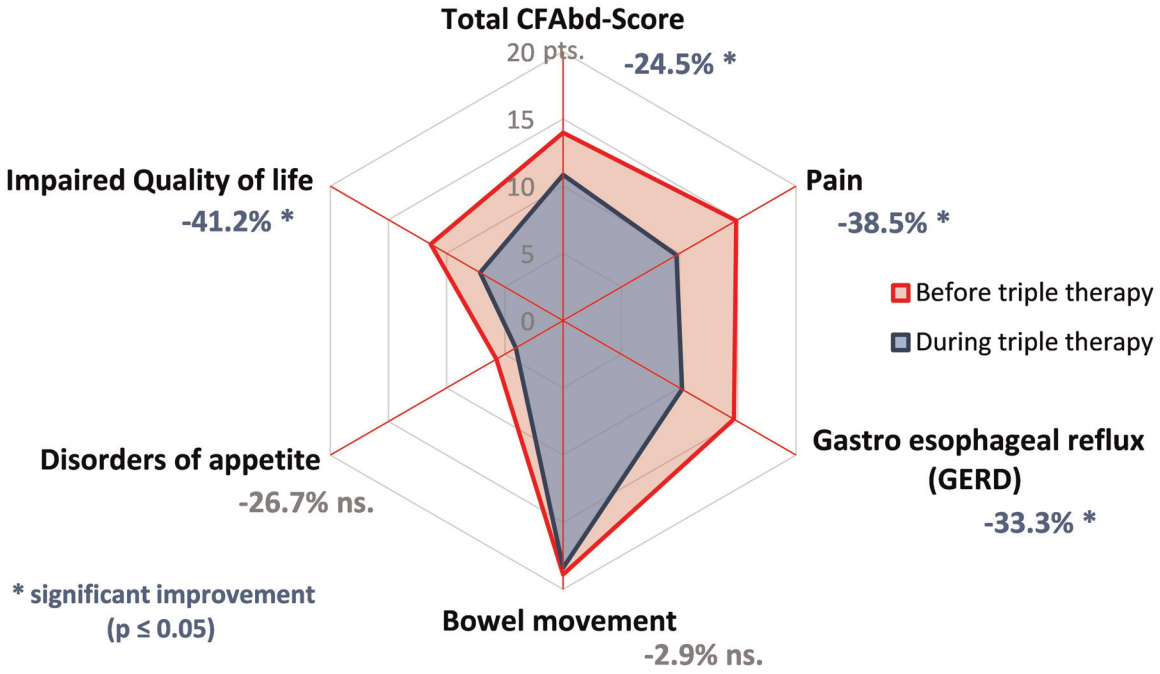

Figure 1. (abstract: 565): Changes in symptoms in total CFAbd-Score and in the respective 5 domains during the new triple modulating therapy (JG. Mainz, et al. RECOVER 2021, first results).