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FIGARO-BM, a Biomarker Study of FIGARO-DKD, Reveals New Insights Into the Mode-of-Action of Finerenone

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Abstract
Background: Mineralocorticoid receptor (MR) overactivation contributes to tissue fibrosis and end-organ damage found in cardiorenal disease.
Objective: The exploratory biomarker study, FIGARO-BM, aims to advance the understanding of the longitudinal pharmacodynamic response to finerenone, a non-steroidal, selective MR antagonist.
Methods: Samples were derived from the phase III parent trial FIGARO-DKD, which investigated finerenone's efficacy on cardiorenal outcomes and safety in patients with CKD and T2D. This substudy included 945 subjects from 21 countries, overall comparable to the total population; 2941 biomarkers in >4000 longitudinal post-randomization plasma samples were analyzed using Olink EXPLORE proteomics. Eligible subjects were on treatment with either placebo or finerenone for ≥24 months. Biomarkers with a significant difference ($p \leq 0.05$) between treatment arms at ≥1 study visit and with effect estimates above threshold were used for gene set enrichment analysis. Enriched terms were grouped into clusters based on membership similarities.
Results: 373 plasma protein biomarkers were modulated by finerenone treatment. Two clusters of extracellular matrix (ECM)-related pathways were identified, involving inflammation and fibrosis markers, e.g. fibronectin, osteopontin, and interleukin-17 family members, along with novel ECM remodeling markers. Other clusters linked directly to mineralocorticoid/aldosterone biology reflecting target modulation.
Conclusion: For the first time, FIGARO-BM provides human biomarker evidence that finerenone acts on inflammation and fibrosis pathways, one key driver of cardiorenal disease progression in T2D. The study supports preclinical findings from animal models and provides insights to mechanisms leading to clinical benefits in a broad cardiorenal patient population. Future studies are needed to validate these findings.

Key words: Biomarker, Finerenone, Inflammation, Fibrosis, Mineralocorticoid receptor
Abbreviations: Extracellular matrix (ECM), mineralocorticoid receptor (MR)
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Ethical approval:
FIGARO-BM was approved by ethical committees and regulatory authorities and complied with the Declaration of Helsinki. All patients provided written informed consent to the biomarker study.

Disclosures/Conflict of Interest:
This study was first presented on November 2nd 2023 at the American Society of Nephrology's (ASN) Kidney Week in Philadelphia, U.S.A.
MB is an employee of Bayer AG, Germany.
LC is an employee of Bayer UK, Great Britain.
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KR is an employee of Bayer AG, Germany.
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