STUDENTS' CORNER
LETTER TO THE EDITOR

Resmetirom in fatty liver disease: A promising step ahead in metabolic dysfunction-associated steatotic liver disease treatment

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Dear Editor, Metabolic dysfunction-associated steatotic liver disease (MASLD, previously NAFLD) affects approximately 25–30% of adults globally.[1,2] Its inflammatory and progressive variant, metabolic dysfunction-associated steatohepatitis (MASH), is strongly associated with obesity and type 2 diabetes. In 2023, the nomenclature was formally updated to MASLD/MASH by international liver societies to better reflect the central role of metabolic dysregulation.[2] The rising epidemic of MASLD/MASH already imposes a staggering public health burden (>$100 billion) in the United States alone,[2] underscoring for an urgent need for pharmacological treatments.

Resmetirom (MGL-3196) is a novel, oral thyroid hormone receptor-β agonist that selectively enhances thyroid hormone signalling in the liver. This action reduces hepatic steatosis and fibrosis without producing systemic thyromimetic effects.[2] In landmark MAESTRO phase 3 trials, resmetirom demonstrated significant reductions in liver fat content and improved metabolic parameters Observed ~30–38% relative reduction in hepatic MRI-PDFF at 52 weeks on resmetirom with both 80 and 100 mg doses.[3] Crucially, a significantly greater proportion of patients treated with resmetirom achieved histologic resolution of MASH without worsening fibrosis, compared to placebo.[2] These findings align with the drug's mechanism, indicating resmetirom potentially changes the disease course. MRI-PDFF is a non-invasive biomarker, validated by the US Food and Drug Administration (FDA), which correlates closely with biopsy- assessed steatosis.[4]

The recent FDA approval of resmetirom for adult patients with non-cirrhotic MASH and moderate to advanced liver fibrosis marks a breakthrough in MASLD management.[5] As the first liver-directed pharmacotherapy for this condition, it provides a new targetted strategy to complement foundational lifestyle and metabolic interventions. Its use requires accurate staging—typically via elastography or other non-invasive tests—to exclude cirrhosis.[5] In clinical practice, resmetirom should augment, not replace, therapies addressing obesity and insulin resistance, such as diet, exercise, GLP-1 receptor agonists, or bariatric surgery, to optimise both hepatic and cardiometabolic outcomes. Long-term studies will be essential to clarify its effects on fibrosis progression and hard clinical endpoints.

Resmetirom's approval in March 2024 represents a milestone in hepatometabolic therapeutics.[6] However, further evaluation in South Asians is needed, given the increasing Pakistani burden of MASLD and the underrepresentation in clinical trials in this region. We call on local researchers, clinicians, and policymakers to make equitable access to such novel therapies as resmetirom and to fund population-specific metabolic health initiatives.

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