Assessing the Efficacy of Farnesoid X Receptor Agonists in the Management of Metabolic Dysfunction-Associated Steatotic Liver Disease: A Systematic Review and Meta-Analysis

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Background: Several randomized clinical trials have been conducted assessing the potential efficacy of X receptor (FXR) agonists in patients with metabolic dysfunction-associated liver disease (MASLD). A comprehensive review and analysis were needed to evaluate the findings of these trials. Hence, this systematic review and meta-analysis aim to study the association between FXR agonists and hepatic outcomes in patients with MASLD.

Introduction: Metabolic dysfunction-associated liver disease (MASLD) involves abnormal lipid accumulation in the liver, potentially progressing to metabolic dysfunction-associated steatohepatitis (MASH) with severe outcomes. X receptors (FXR), activated by bile acids, regulate liver metabolism and inflammation, offering a promising therapeutic target. Clinical trials with FXR agonists like obeticholic acid and tropifexor show potential in improving MASH histology. However, a comprehensive analysis of FXR modulation's impact on liver pathology and metabolism in MASLD and MASH is lacking. This systematic review aims to address this gap, informing future therapeutic approaches.

Methods: Systematic review and meta-analysis evaluating the efficacy of FXR agonists in 1,227 patients assigned to the FXR intervention group compared to 650 patients in the placebo group. Changes in liver enzymes and hepatic steatosis assessed by MRI-PDFF were evaluated.

Results: FXR agonist use was associated with a significant reduction in levels of AST, (WMD= -4.51, 95% CI=[-8.39,-0.63], P=0.02); ALT (WMD= -13.02, 95% CI=[-17.85,-8.19], P<0.00001); GGT (WMD= -32.20, 95% CI=[-38.63,-25.98], P<0.00001); MRI-PDFF, (SMD= -1.14, 95% CI=[-1.92,-0.35], P=0.005). FXR agonists did not significantly affect ALP levels, (WMD= 25.04, 95% CI= [19.22,30.87], P<0.00001}.

Conclusions: Results show promising evidence supporting the efficacy of FXR agonists in reducing hepatic steatosis and biomarkers of hepatic injury such as ALT, AST, and GGT.