Table 1. Old and new glucose-lowering agents as potential treatments for adult patients with biopsy-proven NASH.

Drug target	Drug	Population	Intervention Use/Dosage/Patients	Duration	Hepatic Outcomes & Plasma Lipids			Metabolic Outcomes	Ref, (Year)
					Liver enzymes Plasma Lipids	Resolution of NASH without worsening of fibrosis	Improvement in fibrosis stage of ≥1 without worsening of NASH		
Pan-PPAR agonist	Lanifibranor	247 biopsy-proven NASH patients	Oral A: 1200 mg/d (n=83) B: 800 mg/d (n=83) C: placebo (n=81)	24 weeks	↓AST, ↓ALT, ↓γ-GT, ↓LDL ↓TG, ↑HDL-C	YES (49% 1200-mg lanifibranor vs. 22% placebo)	YES (48% 1200-mg lanifibranor vs. 29% placebo)	↓FPG ↓HOMA-IR ↓fasting insulin	46, (2021)
Dual PPARα/δ agonist	Elafibranor	276 biopsy-proven NASH patients (F0-F3 stages)	Oral A: 80 mg/d (n=93), B: 120 mg/d (n=91 C: placebo (n=92)	52 weeks	↓ALT, ↓γ-GT, ↓ALP, ↓TC, ↓LDL-C, ↑HDL-C	YES (19% 120-mg elafibranor vs. 12% placebo)	NO	↓FPG ↓HbA1c ↓HOMA-IR ↑Scr	49, (2016)
	Elafibranor (NCT02704403)	2157 biopsy-proven NASH patients (NAS score ≥4)	Oral A: 120 mg/d (n=717) B: placebo (n=253) (970 patients recruited)	72 weeks	-TC -HDL -LDL	NO	NO	-HOMA-IR -HbA1c	https://ir.genfit.com/news-releases/news-release-details/genfit-announces-results-interim-analysis-resolve-it-phase-3, (2020)
PPAR-γ agonist	Pioglitazone	101 biopsy-proven NASH patients with prediabetes or T2DM	Oral A: 45 mg/d (n=50) B: placebo (n=51)	18 months	↓AST, ↓ALT, ↓TG, ↑HDL-C	YES (51% 45-mg pioglitazone vs. 19% placebo)	NO	↑weight gain ↓FPG ↓HbA1c	57, (2016)
GLP-1RA	Semaglutide	320 biopsy-proven NASH patients (F1–F3 stages)	Subcutaneous A: 0.1 mg/d (n=80) B: 0.2 mg/d (n=78) C: 0.4 mg/d (n=82) D: placebo (n=80)	72 weeks	↓ALT, ↓AST	YES (59% 0.4-mg semaglutide vs.17% placebo)	NO	↓weight loss ↓HbA1c	72, (2021)
	Liraglutide	52 biopsy-proven NASH patients	Subcutaneous A: 1.8 mg/d (n=26) B: placebo (n=26)	48 weeks	↓AST, ↓γ-GT ↑HDL-C	YES (39% 1.8-mg liraglutide vs. 9% placebo)	NO	↓weight loss ↓HbA1c ↓FPG	74, (2016)

↓, decrease; ↑, increase; -, no change; \, unknown

Abbreviations: FPG, fasting plasma glucose; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; γ-GT, gamma-glutamyltransferase; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; TC, total cholesterol; TG, triglyceride, HOMA-IR; homeostasis model assessment of insulin resistance; T2DM, type 2 diabetes mellitus; PPAR, peroxisome proliferator–activated receptor; GIP, glucose-dependent insulinotropic polypeptide; GLP-1RA, glucagon-like peptide-1 receptor agonist.