

Supplementary Table 1. Baseline characteristics of included studies

Author, Year	Trial registration	Patient number for randomization	Study location	Medication	Target	Administration type	Intervention duration
Loomba R, 2023 ¹	NCT04929483	222	United States	Pegozafermin	FGF21 analogue	Subcutaneous injection weekly	24 weeks
Loomba R, 2024 ²	NCT03486899	197	United States and Japan	Pegbelfermin	FGF21 analogue	Subcutaneous injection weekly	48 weeks
Ratzu V, 2022 ³	NCT03421431	134	Canada, France, Germany, New Zealand, the United Kingdom, and the United States	EDP-305	FXR agonist	Oral daily	12 weeks
Harrison SA, 2022 ⁴	NCT03912532	171	United States	Aldafermin (NGM282 or M70)	FGF19 analogue	Subcutaneous injection daily	24 weeks
Kuchay MS, 2020 ⁵	NCT03590626	64	India	Dulaglutide	GLP-1RA	Subcutaneous injection weekly	24 weeks
Ratzu V, 2023 ⁶	NCT03812029	96 ^a	USA and Europe	Vonafexor	FXR agonist	Oral daily	12 weeks
Harrison SA, 2023 ⁷	NCT04321343	117	United States	PXL065	d-(R)-Pioglitazone	Oral daily	36 weeks
Harrison SA, 2021 ⁸	NCT03976401	80	United States	Efruxifermin	FGF21 analogue	Subcutaneous injection weekly	16 weeks
Huang JF, 2021 ⁹	NCT01068444	90	China	Pioglitazone	PPAR- γ agonist	Oral daily	24 weeks

Harrison SA, 2021 ¹⁰	NCT02443116	78	United States	Aldafermin	FGF19 analogue	Subcutaneous injection daily	24 weeks
Patel K, 2020 ¹¹	NCT02854605	140	United States, Canada, China, New Zealand, Switzerland, and the United Kingdom	Cilofexor (formerly GS-9674)	FXR agonist	Oral daily	24 weeks
Harrison SA, 2023 ¹²	NCT04197479	969 ^b	United States	Resmetirom	THR- β agonist	Oral daily	52 weeks
Loomba R, 2023 ¹³	NCT04048135	81	United States	Pegozafermin (BIO89-100)	FGF21 analogue	Subcutaneous injection weekly	12 weeks
Newsome PN, 2021 ¹⁴	NCT02970942	320	United States and other 15 countries	Semaglutide	GLP-1 RA	Subcutaneous injection daily	72 weeks
Calle RA, 2021 ¹⁵	NCT03248882	305 ^c	Australia, Canada, Israel, Poland, Taiwan and the United States	PF-05221304	dual ACC 1/2 inhibitor	Oral daily	16 weeks
Harrison SA, 2024 ¹⁶	NCT03900429	966	United States and other 14 countries	Resmetirom	THR- β agonist	Oral daily	52 weeks
Nakajima A, 2021 ¹⁷	NCT03071692	118	Japan	Pemafibrate	Selective PPAR- α modulator	Oral daily	72 weeks
Francque SM, 2021 ¹⁸	NCT03008070	247	United States and other 15 countries	Lanifibranor	Pan-PPAR agonist	Oral daily	24 weeks
Cusi K, 2016 ¹⁹	NCT00994682	101	United States	Pioglitazone	PPAR- γ agonist	Oral daily	18 months
Armstrong MJ,	NCT01237119	14	United Kingdom	Liraglutide	GLP-1 RA	Subcutaneous	12 weeks

2016 ²⁰						injection daily	
Armstrong MJ, 2016 ²¹	NCT01237119	52	United Kingdom	Liraglutide	GLP-1 RA	Subcutaneous injection daily	48 weeks
Neuschwander-Tetri BA, 2015 ²²	NCT01265498	283	United States	Obeticholic acid	FXR agonist	Oral daily	72 weeks
Harrison SA, 2019 ²³	NCT02912260	125	United States	Resmetirom	THR- β agonist	Oral daily	36 weeks
Sanyal A, 2018 ²⁴	NCT02413372	75	United States	Pegbelfermin (BMS-986036)	FGF21 analogue	Subcutaneous injection daily or weekly	16 weeks
Loomba R, 2018 ²⁵	NCT02856555	126	United States	GS-0976 (Firsocostat)	dual ACC 1/2 inhibitor	Oral daily	12 weeks
Harrison SA, 2018 ²⁶	NCT02443116	82	Australia and United States	Aldafermin (NGM282)	FGF19 analogue	Subcutaneous injection daily	12 weeks
Ratzu V, 2016 ²⁷	NCT01694849	276	United States and European	Elafibranor (GFT505)	Dual PPAR α/δ agonist	Oral daily	52 weeks
Sanyal AJ, 2023 ²⁸	NCT02548351	2,477 ^d	United States and other 19 countries	Obeticholic acid	FXR agonist	Oral daily	18 months ^d
Alkhoury N, 2022 ²⁹	NCT03987074	108	United States	Semaglutide, Semaglutide+ Cilofexor, Semaglutide+ Firsocostat, Semaglutide+ Cilofexor+	GLP-1 RA; GLP-1 RA+FXR agonist GLP-1 RA+ACC inhibitor GLP-1 RA+FXR agonist+ACC	Semaglutide. subcutaneous injection weekly; Cilofexor and firsocostat were given orally once daily	24 weeks

				Firsocostat	inhibitor		
Younossi ZM, 2019 ³⁰	NCT02548351	1,968 ^d	United States and other 19 countries	Obeticholic acid	FXR agonist	Oral daily	18 months ^d
Mudaliar S, 2013 ³¹	NCT00501592	64	United States	Obeticholic acid	FXR agonist	Oral daily	6 weeks
V. Ratziu, 2008 ³²	n.a.	63	France	Rosiglitazone	PPAR γ agonist	Oral daily	12 months
Romero-Gómez M, 2023 ³³	NCT04944992	145	United States and other 15 countries	Efinopegdutide (MK-6024); Semaglutide	GLP-1/glucagon dual RA; GLP-1 RA	Subcutaneous injection weekly	24 weeks
Siddiqui MS, 2021 ³⁴	n.a.	16	n.a.	Saroglitazar	PPAR α/γ agonist	Oral daily	24 weeks
S. Gawrieh, 2021 ³⁵	NCT03061721	106	United States	Saroglitazar	PPAR- α/γ agonist	Oral daily	16 weeks
Harrison SA, 2024 ³⁶	NCT05006885	95	United States	Pemvidutide	GLP-1/GCG dual RA	Subcutaneous injection weekly	12 weeks
Sanyal AJ, 2024 ³⁷	NCT04771273	295	United States and other 24 countries	Survodutide	GLP-1/GCG dual RA	Subcutaneous injection weekly	48 weeks
Shankar SS, 2024 ³⁸	NCT04019561	74	United States and Puerto Rico	Cotadutide	GLP-1/GCG dual RA	Subcutaneous injection daily	19 weeks
Loomba R, 2024 ³⁹	NCT04166773	190	United States and other 9 countries	Tirzepatide	GLP-1/GIP dual RA	Subcutaneous injection weekly	52 weeks
Sanyal AJ, 2024 ⁴⁰	NCT04881760	98	United States	Retatrutide	GLP-1/GIP/GCG triple RA	Subcutaneous injection weekly	48 weeks

Newsome PN, 2024 ⁴¹	NCT04822181	800	United States and other 40 countries	Semaglutide	GLP-1 RA	Subcutaneous injection weekly	72 weeks ^d
Loomba R, 2024 ⁴²	NCT04173065	231	United States, Belgium, France, Mexico, Puerto Rico	VK2809	THR- β agonist	Oral daily	52 weeks
Noureddin M, 2024 ⁴³	NCT04880031	84	United States	Efimosfermin Alfa (BOS-580)	FGF21 analogue	Subcutaneous injection monthly	24 weeks
You H, 2024 ⁴⁴	NCT05193916	104	China's Mainland	Chiglitazar (Carfloglitazar)	Pan-PPAR agonist	Oral daily	18 weeks

Note: ACC, acetyl-coenzyme A carboxylase; FGF, fibroblast growth factor; FXR, farnesoid X receptor; GLP-1, glucagon-like peptide-1; GCG, glucagon; GIP, glucose-dependent insulintropic polypeptide; PPAR, peroxisome proliferator-activated receptor; THR, thyroid hormone receptor; RA, receptor agonist. n.a. not available. a. part B of this study; b. only for individuals in double-blind set; c. part A of this study; d. interim analysis.

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