

Table 1. Characteristics of included studies¹.

Author, Year	Study Design	Study Location	Follow-up Duration	Intervention: N of patients	Control: N of patients	Concomitant Diet/Exercise	Concomitant Medications	Concern for conflict of interest
Aithal, 2008	RCT, MC	UK	52 Weeks	Pioglitazone 30 mg/d N: 37	Placebo N: 37	Hypocaloric diet (500 kcal less), 53/week exercise	None	Low
Armstrong MJ, 2016	RCT, MC	UK	48 Weeks	Liraglutide subcutaneously 1.8 mg daily N: 26	Placebo N: 26	NR	NR	High (partial funding by Novo Nordisk)
Belfort, 2006	RCT, MC	USA	26 Weeks	Pioglitazone 45 mg/d N: 26	Placebo N: 21	Hypocaloric diet (500 kcal less)	None	Low
Bril, 2019	RCT, MC	USA	78 Weeks	Intervention 1: Vitamin E 400 BID N: 36 Intervention 2: Vitamin E 400 BID plus pioglitazone 45 mg/d N:37	Placebo N: 32	Lifestyle modification education	NR	Low
Cusi, 2016	RCT, SC	USA	78 Weeks	Pioglitazone 30 mg/d (titrated after 2 months to 45 mg/d) N: 50	Placebo N: 51	Lifestyle counseling and a hypocaloric diet	NR	Low
Harrison, 2018 (a bridging fibrosis)	RCT, MC	USA, France, Switzerland and Spain	96 Weeks	Intervention 1: Simtuzumab 75mg /week subcutaneous injection N: 74 Intervention 2: Simtuzumab 125 mg/week subcutaneous injection N: 74	Placebo N: 74	NR	NR	High (Funded by Gilead Sciences)
Harrison, 2003	RCT, SC	USA	26 Weeks	Vitamin E (1000 IU/d) plus Vitamin C (1,000 mg/d) N: 25	Placebo N: 24	NHLBI 1,600 cal and written exercise plan	NR	Low
Harrison, 2019	RCT, MC	USA	36 Weeks	Resmetirom 80 mg daily N: 84	Placebo N: 41	NR	Intervention group: PPI 39% , Statin 23%, Metformin 33%, Insulin 8%, ACEI 19%, Platelet aggregation inhibitors 20% Placebo group: PPI 24% , Statin 10%, Metformin 24%, Insulin	High (Funded by Madrigal Pharmaceuticals)

¹ RCT: Randomized Controlled Trial; MC: Multicenter; SC: Single center; NR: Not reported; NHLBI: National Heart, Lung, and Blood Institute; PPI: Proton Pump Inhibitors; ACEI: Angiotensin-converting-enzyme inhibitors; BID, Two Times a day; TID: Three Times a Day

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							7%, ACEI 24%, Platelet aggregation inhibitors 10%	
Harrison, 2020 (MSDC-0602K)	RCT, MC	USA	52 Weeks	Intervention 1: MSDC-0602K dose 62.5 mg daily N: 102 Intervention 2: MSDC-0602K dose 125 mg daily N: 99 Intervention 3: MSDC-0602K dose 250 mg daily N: 101	Placebo N: 100	None	None	High (Funded by Cirius Therapeutics)
Harrison, 2020 (Aldafermin)	RCT, MC	USA	24 Weeks	Aldafermin 1 mg daily by subcutaneous injection N:53	Placebo N:25	NR	Intervention group: Statin 20 (38%) Placebo group statin 5 (20%)	High (Funding for this study is provided by NGM Biopharmaceuticals)
Harrison, STELLAR 3 2020 (bridging fibrosis)	RCT, MC	26 countries	48 Weeks	Intervention 1: Selonsertib 18 mg daily N: 322 Intervention 2: Selonsertib 6 mg daily N: 321	Placebo N: 159	NR	NR	High (Funded by Gilead Sciences)
Loomba, 2018	RCT, MC	USA	24 Weeks	Selonsertib 18 mg daily +\- Simtuzumab self-subcutaneous injection once weekly N: 32	Simtuzumab self-subcutaneous injection once weekly N: 10	NR	NR	High (Multiple grants from pharmaceutical companies)
McPherson, 2017	RCT, MC	England	104 Weeks	Losartan 50 mg daily N: 24	Placebo N: 21	Standard advice with regard to diet, exercise and weight maintenance.	NR	Low
Navarro, 2019	RCT, MC	USA	48 Weeks	Silymarin TID N: 53 (26 pts 420 mg, 27 pts 700 mg)	Placebo N: 25	Education about healthy diet and lifestyle	NR	High (Some of the authors work in pharmaceutical companies)
Neuschwander-Tetri, 2015	RCT, MC	USA	72 Weeks	Obeticholic acid 25 mg daily N: 141	Placebo N: 142	Standardized recommendations on healthy eating habits, weight reduction, exercise,	None	Low
Newsome, 2020	RCT, MC	16 Countries	72 Weeks	Semaglutide 0.4 mg daily N: 82	Placebo N: 80	NR	NR	High (Sponsored by Novo Nordisk)

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Loomba (Phase 2b ATLAS trial), 2020	RCT, MC	Multiple Countries	48 Weeks	<p>Intervention 1: Cilofexor 30 mg daily N: 40</p> <p>Intervention 2: Firsocostat 20 mg daily N: 40</p> <p>Inter3: Selonsertib 18 mg daily N: 39</p> <p>Inter4: Cilofexor & Selonsertib N: 77</p> <p>Inter5: Firsocostat & Selonsertib N: 79</p> <p>Inter6: Cilofexor & Firsocostat N: 78</p>	Placebo N: 39	NR	NR	High (Funded by Gilead Sciences)
Phase 2b NATIVE trial, 2020	RCT, MC	Multiple Countries	24 Weeks	<p>Intervention 1: Lanifibranor 800 mg daily N: 83</p> <p>Intervention 2: Lanifibranor 1200 mg daily N: 83</p>	Placebo N: 81	NR	NR	High (Funded by Inventiva)
Ratziu, 2008	RCT, SC	France	52 Weeks	Rosiglitazone 4 mg/d for 1 month, then 8 mg/day N: 32	Placebo N: 31	Healthy eating and twice weekly exercise (details NR)	None	Low
Ratziu 2016	RCT, MC	USA and 8 European countries	52 Weeks	<p>Intervention 1: Elafibranor 80 mg daily N: 93</p> <p>Intervention 2: Elafibranor 120 mg daily N: 91</p>	Placebo N: 92	NR	None	High (Funded by GENFIT)
Ratziu 2018	RCT, MC	11 countries from USA, Europe and Latin America	52 Weeks	Intervention 1: Aramchol 400 mg daily N: 101	Placebo N: 48	NR	NR	Unclear

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				Intervention 2: Aramchol 600 mg daily N: 98				
Ratzu, 2020 Friedman, 2018 ²	RCT, MC	81 sites across the United States, Australia, Hong Kong, and Europe	104 Weeks	Cenicriviroc (CVC) 150 mg daily N: 145	Placebo N: 72	NR	HMG CoA reductase inhibitors 35.4%, Biguanides 52.8 %,Angiotensin II inhibitors 22.9 %, Glucose lowering drugs excluding insulin 16.7%	High (Funded by tobira therapeutics)
Sanyal, 2010 (PIVENS)	RCT, MC	USA	96 Weeks	Intervention 1: Pioglitazone 30 mg/d N: 80 Intervention 2: Vitamin E daily N: 84	Placebo N: 83	Standardized diet and exercise	None	Low
Wah Kheong, 2017	RCT, SC	Malaysia	48 Weeks	Silymarin 700 mg TID N:49	Placebo TID N: 50	Lifestyle advice	NR	Low
Younossi, 2019	RCT, MC	20 Countries	78 Weeks (Interim analysis)	Obeticholic acid 25 mg daily N: 308	Placebo N: 311	NR	Intervention group: Lipid lowering 160 (52%) Statins 127 (41%) Antidiabetic medication 159 (52%) Thiazolidinediones 4 (1%) Vitamin E 32 (10%) Placebo group: Lipid lowering 175 (56%) Statins 144 (46%) Antidiabetic medication 167 (54%) Thiazolidinediones 5 (2%) Vitamin E 42 (14%)	High (Multiple grants from pharmaceutical companies)
Zein, 2011	RCT, MC	USA	52 Weeks	Pentoxifylline 400 mg TID N: 26	Placebo N: 29	Individualized nutritional counseling	None	Low

² Both studies have same population but reported different outcomes

Table 2. Patients' characteristics³

Study, year	Intervention	Age (Mean)	Sex (% male)	Diabetes n, %	NAFLD activity score (Mean)	Fibrosis score (Mean)	Advanced fibrosis n, %	BMI (Mean)	ALT (Mean)	AST (Mean)
Aithal, 2008	Pioglitazone	52	70%	0	NR	1.7	7, 19%	29.8	93.6	NR
	Placebo	55	51%	0	NR	2.3	11, 30%	30.8	84.1	NR
Armstrong MJ, 2016	Liraglutide	50	69%	9, 35%	4.9	2.3	12, 46%	34.2	77	51
	Placebo	52	50%	8, 31%	4.8	2.3	15, 58%	37.7	66	51
Belfort, 2006	Pioglitazone	51	54%	26, 100%	NR	1.75	2, 10%	33.5	67	47
	Placebo	51	33%	21, 100%	NR	1.25	7, 27%	32.9	61	42
Bril, 2019	Vitamin E	60	93%	36, 100%	3.9	1.6	NR	33.8	53	41
	Vitamin E plus pioglitazone	60	81%	37, 100%	3.7	1.4	NR	35.2	40	32
	Placebo	57	93%	32, 100%	4.2	1.5	NR	33.6	53	40
Cusi, 2016	Pioglitazone	52	72%	24, 48%	4.5	1.1	NR	34.3	62	47
	Placebo	49	69%	28, 55%	4.5	0.9	NR	34.5	57	43
Harrison, 2018 (a bridging fibrosis)	Simtuzumab 75mg	56	39%	48, 68%	4.6	2.8	70, 98.6%	34.2	47	41
	Simtuzumab 125 mg	55	36%	50, 68%	4.9	3	74, 100%	34.1	54	41
	Placebo	56	35%	49, 66%	4	3	74, 100%	32.7	50	42
Harrison, 2003	Vitamin E plus Vitamin C	52	39%	14, 61%	3.1	NR	4, 18%	35	92	63.2
	Placebo	50	50%	5, 23%	3	NR	6, 26%	30.8	109	80.2
Harrison, 2019	Resmetirom	51	45%	36, 43%	4.9		18, 21%	35.8	50	35.1
	Placebo	47.3	59%	13, 32%	4.8	NR	7, 17%	33.6	60.1	38
Harrison, 2020 (MSDC-0602K)	MSDC-0602K dose 62.5 mg	56.9	43%	57,55.6%	5.5	2.1	47, 46.5%	34.7	58.3	44.9
	MSDC-0602K dose 125 mg	56	35%	51, 52%	5.2	2.1	45, 45.9%	35.9	50.9	42.7
	MSDC-0602K dose 250 mg	56.8	43%	52,51.5%	5.4	2	44, 43.6%	35	59.3	46.4

³ Phase 2b NATIVE trial, 2020: Press release. Patients' characteristics and risk of bias assessment could not be abstracted

Study, year	Intervention	Age (Mean)	Sex (% male)	Diabetes n, %	NAFLD activity score (Mean)	Fibrosis score (Mean)	Advanced fibrosis n, %	BMI (Mean)	ALT (Mean)	AST (Mean)
	Placebo	54.6	43%	50, 50%	5.3	2.1	46, 45.7%	35.03	58.6	42.7
Harrison, 2020 (Aldafermin)	Aldafermin	53	51%	32, 60%	5.7	NR	24, 45%	35.8	73.3	54.5
	Placebo	54.1	36%	16, 64%	5.4	NR	10, 40%	36.8	55.1	44.3
Harrison, STELLAR 3 2020 (bridging fibrosis)	Selonsertib 18 mg	59	44%	224, 70%	NR	-0.2	322, 100%	32.4	56	48
	Selonsertib 6 mg	59	39%	223, 69%	NR	-0.13	321, 100%	32.4	52	46
	Placebo	59	52%	116, 73%	NR	-0.19	159, 100%	32.2	56	43
Loomba, 2018	Selonsertib 18 mg daily +\- Simtuzumab	55	31%	21, 66%	NR	NR	21, 66%	33	69	48
	Simtuzumab	57	40%	8, 80%	NR	NR	6, 60%	37	61	56
McPherson, 2017	Losartan	58	54.1%	15,62.50%	5.5	2.07	5/15, 33%	32.8	52.5	35
	Placebo	45	57.1%	12,57.14%	5.5	2.41	8/17, 47%	34.1	65	46
Navarro, 2019	Silymarin	48.2	67 %	14 (27%)	4.4	1.4	19%	33.5	61	46
	Placebo	49.5	56%	7 (28%)	4.4	1	16%	33.4	65	51
Neuschwander-Tetri, 2015	Obeticholic acid	52	30%	75, 53%	5.3	1.9	NR	35	83	64
	Placebo	51	37%	74, 52%	5.1	1.8	NR	34	82	58
Newsome, 2020	Semaglutide	54.3	43%	49, 60%	4.8	Enhanced liver fibrosis test score 9.9	42, 51%	35.2	54	44
	Placebo	52.4	45%	50, 62%	4.9	9.6	36, 45%	36.1	55	42
Loomba (Phase 2b ATLAS trial), 2020	Cilofexor	59	27%	27, 68%	NR	NR	39, 98%	32	50	49
	Firsocostat	63	37%	30, 75%	NR	NR	38, 95%	33	47	41
	Selonsertib	60	38%	26, 67%	NR	NR	39, 100%	32	42	44
	Cilofexor & Selonsertib	61	34%	58, 75%	NR	NR	75, 98%	33	45	41
	Firsocostat & Selonsertib	59	38%	57, 72%	NR	NR	78, 99%	35	43	44
	Cilofexor & Firsocostat	62	38%	57, 73%	NR	NR	76, 98%	34	42	46
	Placebo	59	31%	27, 69%	NR	NR	39, 100%	35	44	41
Ratziu, 2008	Rosiglitazone	53	19%	9, 28%	4	NR	5, 16%	31.5	69	46
	Placebo	54	18%	11, 35%	3	NR	15, 48%	30.5	84	61
Ratziu 2016	Elafibranor 80 mg	52.7	53%	37, 40%	5	1.5	23, 24.7%	31.8	60.7	40.9

Study, year	Intervention	Age (Mean)	Sex (% male)	Diabetes n, %	NAFLD activity score (Mean)	Fibrosis score (Mean)	Advanced fibrosis n, %	BMI (Mean)	ALT (Mean)	AST (Mean)
	Elafibranor 120 mg	52.4	53%	37, 42%	4.9	1.7	20, 22.5%	31	63.8	41.7
	Placebo	52.4	60%	33, 36%	5	1.5	20, 21.7%	30.9	63.8	44.5
Ratziu 2018	Aramchol	53.9	35%	All patients are either prediabetic or diabetic	5.06	NR	47.5%	32.4	68.1	NR
	Aramchol	54.9	35%		5.21	NR	36.7%	33	55.9	NR
	Placebo	54.4	47.9%		5.06	NR	33%	32.6	67.7	NR
Ratziu, 2020 Friedman, 2018	CENICRIVIROC	54.9	55.4%	73, 60%	≥5: 85 (70.2%)	2	46, 38%	33.32	58.9	42.49
	Placebo	52	48.3%	25, 41.7%	≥5: 45 (75.0%)	2.1	24, 40%	34.47	64.15	47.04
Sanyal, 2010 (PIVENS)	Pioglitazone	47	38%	0	5.1	1.4	NR	34	82	54
	Vitamin E	46.6	38%	0	5.1	1.5	NR	34	86	59
	Placebo	45	42%	0	4.8	1.6	NR	35	81	55
Wah Kheong, 2017	Silymarin	49.6	49%	23, 46.9%	5	1	14, 28.6%	30	88	52
	Placebo	50.1	44%	30, 60%	5	1	10, 20%	31	73	46
Younossi, 2019	Obeticholic acid	55	43%	171, 56%	NAS ≥6: 68%	NR	NR	NR	80.2	57.0
	Placebo	55	40%	175, 56%	NAS ≥6: 70%	NR	NR		79.6	58.9
Zein, 2011	Pentoxifylline	50.5	69.2%	1, 3.8%	5.7	NR	5, 19.2%	32.9	81.5	58
	Placebo	49.6	69%	4, 13.8%	5.4	NR	9, 31%	34	55	43

