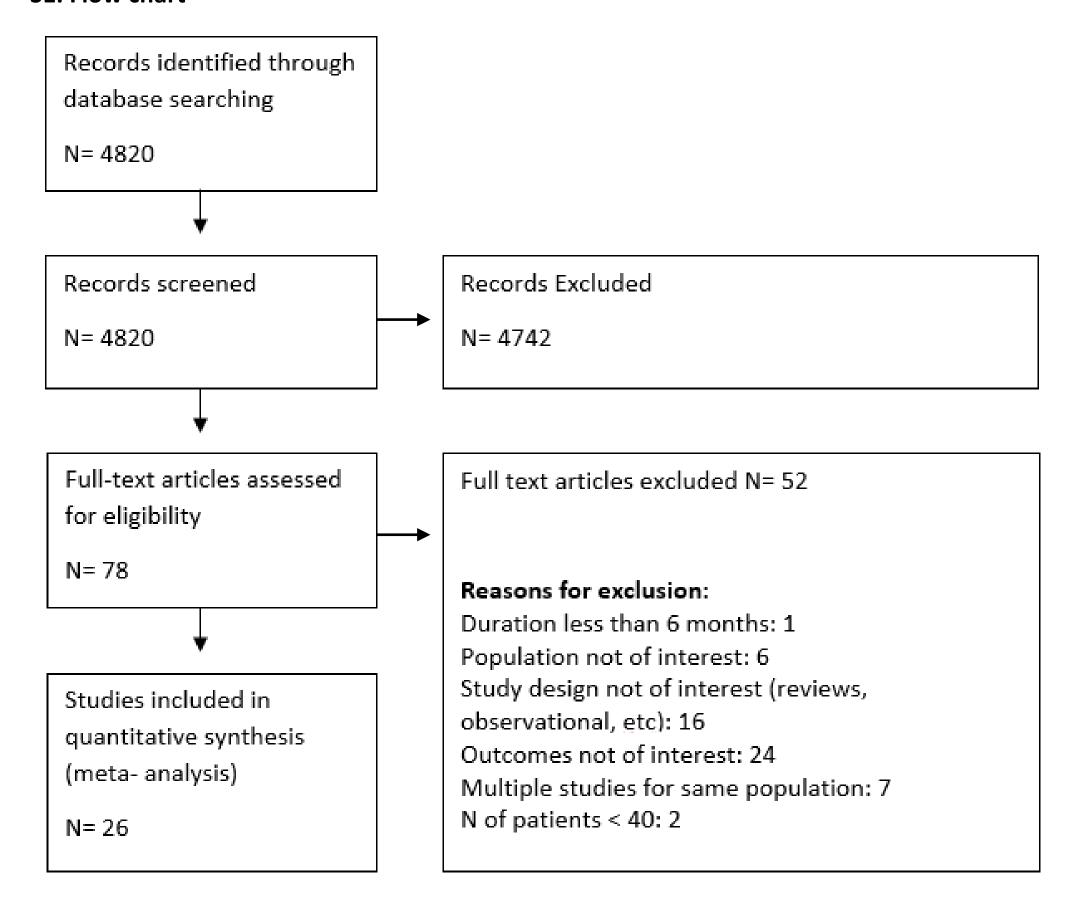
S1. Flow chart

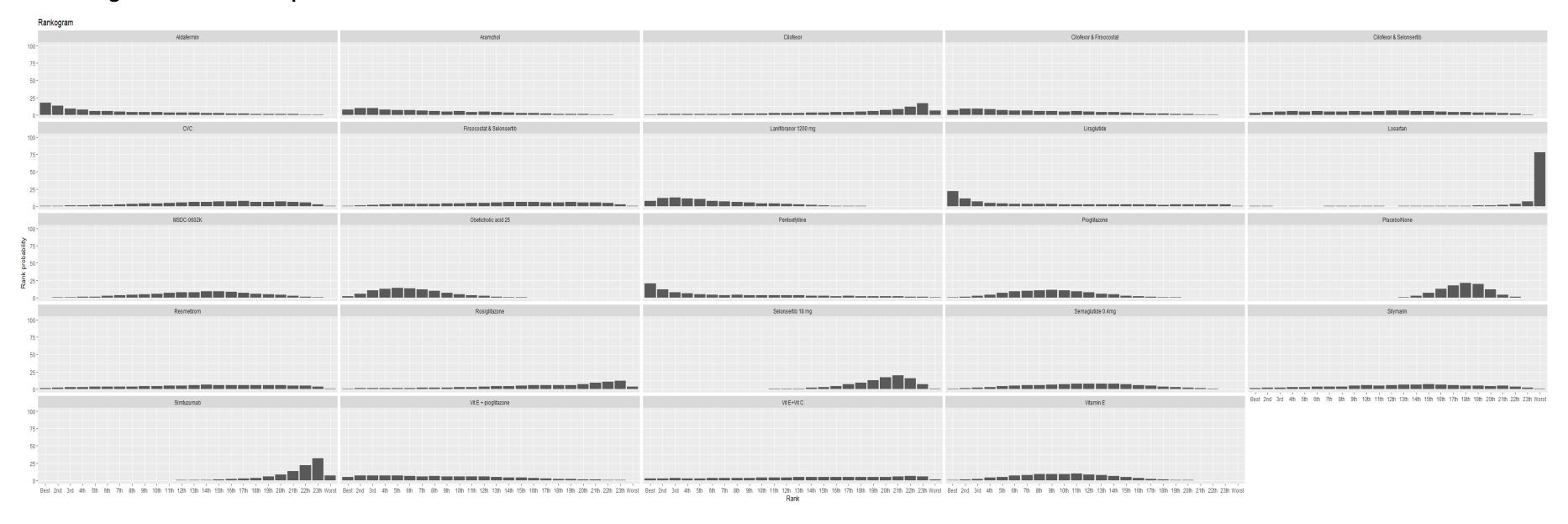


S2. Direct comparisons for fibrosis improvement

	Interven	tion1	Interven	ition2	>= 1-stage improvement		
Study Lanifibranor 1200 mg vs. Placebo Phase Ilb NATIVE clinical trial 2020	/None 35	83	Events 19	81	in fibrosis		95%-CI [1.21; 4.67]
Total Heterogeneity: not applicable Obeticholic acid 25 vs. Placebo/N Neuschwander-Tetri,2015	36	110	19	109	-	2.30	[1.21; 4.67]
Younossi 2019 Total Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $\rho = 0.92$ Aldafermin vs. Placebo/None		308 418	37 56	311 420	-		[1.44; 3.42] [1.57; 3.21]
Harrison 2020(Aldafermin) Total Heterogeneity: not applicable Pentoxifylline vs. Placebo/None	20 20	53 53	5	25 25			[0.79; 7.48] [0.79; 7.48]
Zein, 2011 Total Heterogeneity: not applicable	7	26 26	4	29 29			[0.59; 9.02] [0.59; 9.02]
Aramchol vs. Placebo/None Ratziu 2018 Total Heterogeneity: not applicable	29 29	98 98	8	48 48	-		[0.88; 5.04] [0.88; 5.04]
Cilofexor & Firsocostat vs. Placel Phase 2b ATLAS Trial 2020 Total Heterogeneity: not applicable	bo/None 16 16	78 78	4 4	39 39	-		[0.70; 7.29] [0.70; 7.29]
Liraglutide vs. Placebo/None Armstrong MJ 2016 Total Heterogeneity: not applicable	6 6	23 23	3	22 22	-		[0.48; 10.35] [0.48; 10.35]
Vit E + pioglitazone vs. Płacebo/N Bril 2019 Total Heterogeneity: not applicable	one 19 19	37 37	10 10	32 32	-		[0.87; 6.23] [0.87; 6.23]
Pioglitazone vs. Placebo/None Aithal, 2008 Belfort, 2006 Cusi 2016 Sanyal, 2010 (PIVENS) Total Heterogeneity: I^2 = 0%, τ^2 = 0, ρ = 0.99	9 12 20 35 76	50 80	6 7 13 26 52	37 21 51 83 192		1.71 1.95 1.71	[0.52; 5.26] [0.52; 5.64] [0.84; 4.54] [0.90; 3.24] [1.14; 2.72]
Vitamin E vs. Placebo/None Bril 2019 Sanyal, 2010 (PIVENS)	19 34	36 84	10 26	32 83	-	1.49	[0.91; 6.64] [0.79; 2.82]
Total Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0.41$ Cilofexor & Selonsertib vs. Place Phase 2b ATLAS Trial 2020	bo/None 13	120 77		115		1.78	[1.01; 2.95]
Total Heterogeneity: not applicable Semaglutide 0.4mg vs. Placebo/N Newsome 2020	35	82	26	39	-	1.55	[0.54; 5.87]
Total Heterogeneity: not applicable Silymarin vs. Placebo/None Navarro 2019	35	53	26 7	80 25			[0.82; 2.93]
Wah Kheong 2017 Total Heterogeneity: I^2 = 81%, τ^2 = 1.6764, ρ Vit E+Vit C vs. Placebo/None		49 102	10	50 75			[1.18; 17.43] [0.22; 11.66]
Harrison, 2003 Total Heterogeneity: not applicable MSDC-0602K vs. Placebo/None	11 11	25 25	9	24 24	-		[0.42; 4.11] [0.42; 4.11]
Harrison 2020 (MSDC-0602K) Total Heterogeneity: not applicable Resmetirom vs. Placebo/None		252 252		74 74	-		[0.72; 2.49] [0.72; 2.49]
Harrison 2019 Total Heterogeneity: not applicable	21 21	73 73	8	34 34	-		[0.51; 3.36] [0.51; 3.36]
Firsocostat & Selonsertib vs. Plac Phase 2b ATLAS Trial 2020 Total Heterogeneity: not applicable	cebo/Non 11 11	79 79	4 4	39 39	-		[0.42; 4.77] [0.42; 4.77]
CVC vs. Placebo/None Ratziu 2020 Total Heterogeneity: not applicable		117 117	11 11	57 57	#		[0.54; 2.63] [0.54; 2.63]
Rosiglitazone vs. Placebo/None Ratziu, 2008 Total Heterogeneity: not applicable	9	32 32	9	31 31	=		[0.32; 2.85] [0.32; 2.85]
Cilofexor vs. Placebo/None Phase 2b ATLAS Trial 2020 Total Heterogeneity: not applicable	4	40 40	4	39 39	-		[0.23; 4.19] [0.23; 4.19]
Selonsertib 18 mg vs. Placebo/No Phase 2b ATLAS Trial 2020 STELLAR 3 2020 (bridging fibrosis) Total Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $\rho = 0.71$	4		4 26 30	39 159 198	-	0.75	[0.23; 4.32] [0.44; 1.27] [0.47; 1.27]
Simtuzumab vs. Placebo/None Harrison 2018 (a bridging fibrosis) Total Heterogeneity: not applicable		145 145		74 74	-		[0.35; 1.46] [0.35; 1.46]
Losartan vs. Placebo/None McPherson 2017 Total Heterogeneity: not applicable	1	24 24		21 · 21 ·			[0.02; 1.81] [0.02; 1.81]
Cilofexor vs. Cilofexor & Firsocos Phase 2b ATLAS Trial 2020 Total Heterogeneity: not applicable	stat 4 4	40 40	16 16	78 78	-		[0.13; 1.39] [0.13; 1.39]
Cilofexor vs. Cilofexor & Selonse Phase 2b ATLAS Trial 2020 Total	rtib 4 4	40 40	13 13	77 77	-		[0.17; 1.80] [0.17; 1.80]
Heterogeneity: not applicable Cilofexor vs. Firsocostat & Selon: Phase 2b ATLAS Trial 2020 Total	sertib 4 4	40 40	11 11	79 79	-		[0.20; 2.31] [0.20; 2.31]
Heterogeneity: not applicable Cilofexor vs. Selonsertib 18 mg Phase 2b ATLAS Trial 2020 Total	4 4	40 40	4 4	39 39	-		[0.23; 4.19] [0.23; 4.19]
Heterogeneity: not applicable Cilofexor & Selonsertib vs. Cilofe Phase 2b ATLAS Trial 2020 Total	xor & Firs 13 13	socos 77 77	tat 16 16	78 78	=		[0.35; 1.77] [0.35; 1.77]
Heterogeneity: not applicable Cilofexor & Selonsertib vs. Firsoc Phase 2b ATLAS Trial 2020 Total	costat & 5 13 13		sertib 11 11	79 79	*		[0.52; 3.00] [0.52; 3.00]
Heterogeneity: not applicable Firsocostat & Selonsertib vs. Cilo Phase 2b ATLAS Trial 2020 Total	fexor & F 11 11	irsoc 79 79	ostat 16 16	78 78	-		[0.27; 1.45] [0.27; 1.45]
Heterogeneity: not applicable Selonsertib 18 mg vs. Simtuzuma Loomba 2018 Total	ib 13	32 32		10 10			[0.50; 15.02] [0.50; 15.02]
Heterogeneity: not applicable Selonsertib 18 mg vs. Cilofexor & Phase 2b ATLAS Trial 2020 Total	Firsocos 4 4	stat 39 39	16 16	78 78			[0.14; 1.43] [0.14; 1.43]
Heterogeneity: not applicable Selonsertib 18 mg vs. Cilofexor & Phase 2b ATLAS Trial 2020 Total	Selonse	ertib 39 39	13 13	77 77			[0.17; 1.86] [0.17; 1.86]
Heterogeneity: not applicable Selonsertib 18 mg vs. Firsocosta Phase 2b ATLAS Trial 2020 Total	t & Selon 4 4	39	11	79 79	_	0.71	[0.21; 2.38] [0.21; 2.38]
Heterogeneity: not applicable Vitamin E vs. Vit E + pioglitazone Bril 2019 Total	19 19	36	19	37 37	+	1.06	[0.42; 2.65] [0.42; 2.65]
Heterogeneity: not applicable Vitamin E vs. Pioglitazone Sanyal, 2010 (PIVENS) Total	34 34	84	35	80 80		0.87	[0.47; 1.63] [0.47; 1.63]
Heterogeneity: not applicable	34	04	20	00		0.07	[



S3. Rankogram for fibrosis improvement

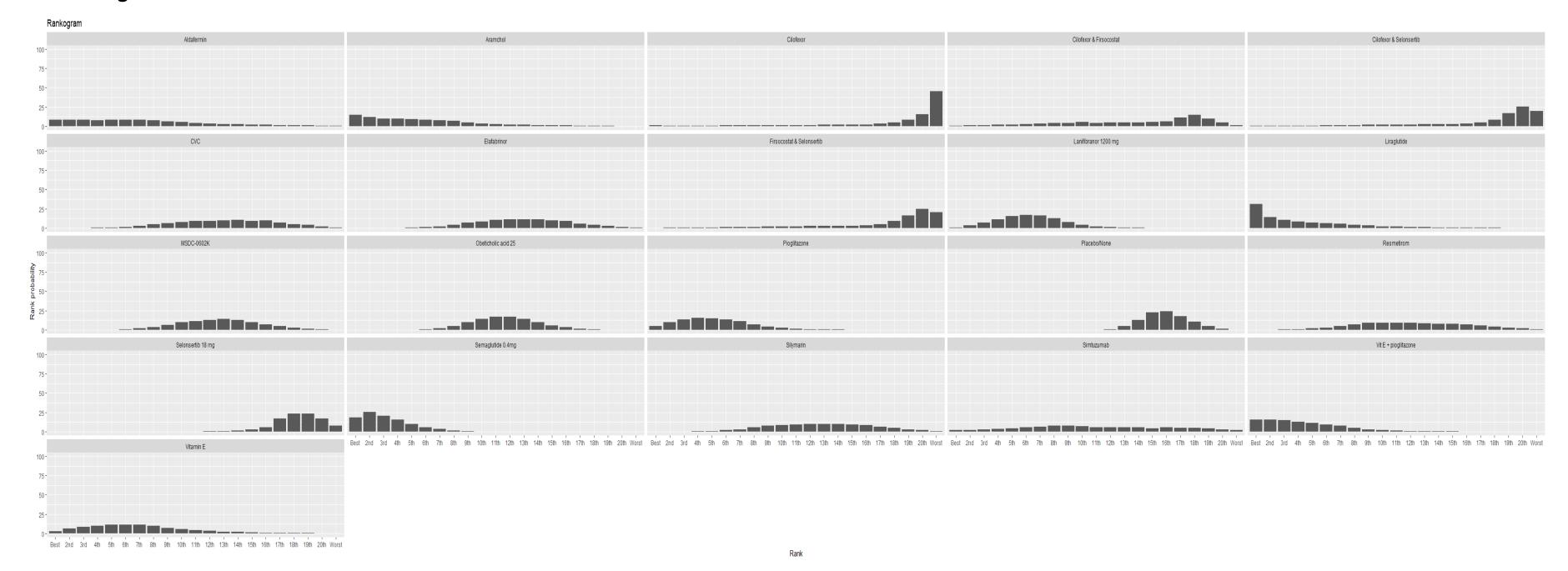


S4. Direct comparisons for NASH resolution

Study Eve		Total E		tion2 Total	Resolution of NASH	OR	95%-C
Semaglutide 0.4mg vs. Placebo/None Newsome 2020 Fotal Heterogeneity: not applicable	48 48	82 82	14 14	80 80	±		[3.22; 13.74 [3.22; 13.74
Liraglutide vs. Placebo/None Armstrong MJ 2016 Total Heterogeneity: not applicable	9	23 23	2 2	22 22			[1.20; 34.41 [1.20; 34.41
/it E + pioglitazone vs. Placebo/None Bril 2019 Total Jeterogeneity: not applicable	16 16	37 37	4	32 32	±		[1.55; 18.30 [1.55; 18.30
Pioglitazone vs. Placebo/None Cusi 2016 Total Leterogeneity: not applicable	26 26	50 50	10 10	51 51	±		[1.83; 10.78 [1.83; 10.78
Aramchol vs. Placebo/None Ratziu 2018 Total	16 16	98 98	2 2	48 48	-		[0.99; 20.39 [0.99; 20.39
eterogeneity; not applicable anifibranor 1200 mg vs. Placebo/None hase Ilb NATIVE clinical trial 2020 otal	37 37	83 83	15 15	81 81	±		[1.74; 7.19 [1.74; 7.19
/itamin E vs. Placebo/None Bril 2019 Fotal	12 12	36 36	4 4	32 32			[1.00; 12.29 [1.00; 12.29
leterogeneity; not applicable Aldafermin vs. Placebo/None Harrison 2020 (Aldafermin)	12	53 53	2	25 25		3.37	[0.69; 16.37
otal leterogeneity: not applicable simtuzumab vs. Placebo/None larrison 2018 (a bridging fibrosis)		145	2	74			[0.69; 16.37
Total Deterogeneity: not applicable Deterolic acid 25 vs. Placebo/None		145	2		-		[0.37; 9.02
Neuschwander-Tetri,2015 Younossi 2019 Total leterogeneity: $l^2 = 0\%$, $\tau^2 = 0$, $\rho = 0.67$	77.7	110 308 418	1 - 000	109 311 420	•	1.51	[0.88; 3.89 [0.89; 2.59 [1.05; 2.50
Resmetirom vs. Placebo/None Harrison 2019 Total Heterogeneity: not applicable	18 18	73 73	6 6	34 34	*		[0.55; 4.28 [0.55; 4.28
ASDC-0602K vs. Placebo/None Harrison 2020 Total Jeterogeneity: not applicable	67 67	252 252	15 15	74 74	=		[0.76; 2.68 [0.76; 2.68
Silymarin vs. Placebo/None Wah Kheong 2017 Fotal Heterogeneity: not applicable	14 14	49 49	11 11	50 50	-		[0.57; 3.53 [0.57; 3.53
Elafabrinor vs. Placebo/None Ratziu 2016 Total	29 29	182 182	11 11	92 92	#		[0.66; 2.94 [0.66; 2.94
leterogeneity: not applicable CVC vs. Placebo/None Friedman 2018 Total		145 145	9	144 144	-		[0.55; 3.32 [0.55; 3.32
leterogeneity: not applicable Cilofexor & Firsocostat vs. Placebo/None Phase 2b ATLAS Trial 2020 Total	3	78 78	0	39 39	•		[0.18; 72.69 [0.18; 72.69
leterogeneity: not applicable Cilofexor & Selonsertib vs. Placebo/None Phase 2b ATLAS Trial 2020 Total	1	77 77	0	39 39		1.55	[0.06; 38.91 [0.06; 38.91
reterogeneity: not applicable Firsocostat & Selonsertib vs. Placebo/None Phase 2b ATLAS Trial 2020 Fotal	1	79 79	0	39 39		1.51	[0.06; 37.91 [0.06; 37.91
leterogeneity: not applicable Cilofexor vs. Placebo/None Phase 2b ATLAS Trial 2020	0	40	0	39		0.98	[0.02; 50.37
Total Heterogeneity: not applicable Selonsertib 18 mg vs. Placebo/None Harrison, STELLAR 3 2020 (bridging fibrosis)	16	40 322	14	159	-		[0.02; 50.37
Phase 2b ATLAS Trial 2020 Total leterogeneity: $I^2 = 6\%$, $\tau^2 = 0.0872$, $\rho = 0.30$	1 17	39 361	0 14	39 198			[0.12; 77.91 [0.25; 1.53
Cilofexor vs. Cilofexor & Firsocostat Phase 2b ATLAS Trial 2020 Fotal Teterogeneity: not applicable	0	40 40	3	78 - 78 -	-		[0.01; 5.28 [0.01; 5.28
Cilofexor vs. Cilofexor & Selonsertib Phase 2b ATLAS Trial 2020 Total leterogeneity: not applicable	0	40 40	1	77 77	-		[0.03; 15.81 [0.03; 15.81
Cilofexor vs. Firsocostat & Selonsertib Phase 2b ATLAS Trial 2020 Fotal Reterogeneity: not applicable	0	40 40	1	79 79	-		[0.03; 16.22 [0.03; 16.22
Cilofexor & Selonsertib vs. Cilofexor & Firsocos Phase 2b ATLAS Trial 2020 Total Jeterogeneity: not applicable	tat 1 1	77 77	3	78 78	-		[0.03; 3.23 [0.03; 3.23
Cilofexor & Selonsertib vs. Firsocostat & Selons Phase 2b ATLAS Trial 2020 Fotal Reterogeneity: not applicable	ertik 1 1	77 77	1	79 79			[0.06; 16.71 [0.06; 16.71
irsocostat & Selonsertib vs. Cilofexor & Firsoco Phase 2b ATLAS Trial 2020 Total	osta 1 1	79 79	3 3	78 78	-		[0.03; 3.15 [0.03; 3.15
Selonsertib 18 mg vs. Cilofexor Phase 2b ATLAS Trial 2020 Fotal	1	39 39	0	40 40			[0.12; 79.85 [0.12; 79.85
leterogeneity: not applicable Selonsertib 18 mg vs. Cilofexor & Firsocostat Phase 2b ATLAS Trial 2020 Total	1	39 39	3 3	78 78			[0.07; 6.54 [0.07; 6.54
leterogeneity: not applicable Selonsertib 18 mg vs. Cilofexor & Selonsertib Phase 2b ATLAS Trial 2020 Total	1	39 39	1	77 77			[0.12; 32.86 [0.12; 32.86
leterogeneity: not applicable Selonsertib 18 mg vs. Firsocostat & Selonsertib Phase 2b ATLAS Trial 2020 Total	1 1	39 39	1	79 79		2.05	[0.12; 33.71 [0.12; 33.71
leterogeneity: not applicable /itamin E vs. Vit E + pioglitazone Bril 2019	12	36	16	37	_	0.66	[0.25; 1.70
Total Teterogeneity: not applicable	12	36	16	37			[0.25; 1.70



S5. Rankogram for NASH resolution



S6. Direct and Indirect comparisons for fibrosis improvement

Comparison	Number of Studies	Direct Evidence	Random effects model	OR	95%-CI
Cilofexor vs Plac Direct estimate Indirect estimate Network estimate	1	0.78		0.63 [0	.23; 4.19] .04; 9.64] .24; 3.20]
Cilofexor vs Selo Direct estimate Indirect estimate Network estimate	1	0.78		1.50 [0.	.23; 4.19] 10; 22.99] .30; 3.89]
Cilofexor & Firso Direct estimate Indirect estimate Network estimate	1	ocebo/None 0.65	*	1.71 [0	.70; 7.29] .34; 8.51] .80; 5.28]
Cilofexor & Firso Direct estimate Indirect estimate Network estimate	1	lonsertib 18 0.65	mg	2.99 [0.	.70; 7.29] 60; 14.87] .97; 6.41]
Cilofexor & Selor Direct estimate Indirect estimate Network estimate	1	o.67	*	1.33 [0	.54; 5.87] .25; 7.17] .61; 4.27]
Cilofexor & Selor Direct estimate Indirect estimate Network estimate	1	lonsertib 18 0.67	mg	2.38 [0.	.54; 5.87] 44; 12.81] .74; 5.19]
Firsocostat & Sel Direct estimate Indirect estimate Network estimate	1	Placebo/Non 0.68	10	1.05 [0	.42; 4.77] .18; 6.09] .47; 3.49]
Firsocostat & Sel Direct estimate Indirect estimate Network estimate	1	Selonsertib 0.68	18 mg	1.91 [0.	.42; 4.77] 33; 11.10] .57; 4.24]
Pioglitazone vs P Direct estimate Indirect estimate Network estimate	4	0.96		— 4.43 [0.	.14; 2.72] 51; 38.26] .19; 2.80]
Pioglitazone vs V Direct estimate Indirect estimate Network estimate	1	0.75		0.85 [0	.62; 2.13] .29; 2.51] .62; 1.82]
Selonsertib 18 m Direct estimate Indirect estimate Network estimate	2	0.93		1.97 [0.	.47; 1.27] 31; 12.43] .51; 1.34]
Simtuzumab vs F Direct estimate Indirect estimate Network estimate	1	9 0.86		0.28 [0	.35; 1.46] .05; 1.66] .33; 1.22]
Vit E + pioglitazor Direct estimate Indirect estimate Network estimate	1	o/None 0.76		1.00 [0	.87; 6.23] .17; 5.77] .80; 4.48]
Vitamin E vs Place Direct estimate Indirect estimate Network estimate	2	0.89	*	1.67 [0	.01; 2.95] .37; 7.58] .04; 2.85]
Selonsertib 18 m Direct estimate Indirect estimate Network estimate	1	ımab 0.21		1.07 [0	50; 15.02] .45; 2.55] .60; 2.82]
Vit E + pioglitazor Direct estimate Indirect estimate Network estimate	1	0.84	0.1 0.5 1 2 10	2.45 [0.	.38; 2.37] 31; 19.60] .48; 2.56]



S7. Direct and Indirect comparisons for NASH resolution

Comparison	Number of Studies	Direct Evidence	Random effects model	OR		95%-CI
Cilofexor vs Plac Direct estimate Indirect estimate Network estimate	1	0.65		0.98 0.03 0.29	[0.02; [0.00; [0.01;	50.37] 6.23] 6.79]
Cilofexor vs Selo Direct estimate Indirect estimate Network estimate	1	0.94		0.32 - 289.31 [0 0.48	[0.01; 0.00; 85859 [0.02;	486.08]
Cilofexor & Firso Direct estimate Indirect estimate Network estimate	1	ocebo/None 0.38	-	3.66 0.50 1.07	[0.18; [0.05; [0.17;	•
Cilofexor & Firso Direct estimate Indirect estimate Network estimate	1	lonsertib 18 ı 0.83	mg	1.19 14.32 1.81	[0.17; [0.19; 1 [0.31;	084.14]
Cilofexor & Selor Direct estimate Indirect estimate Network estimate	1	o.47	*	1.55 0.15 0.45	[0.06; [0.01; [0.05;	38.91] 3.17] 4.13]
Cilofexor & Selor Direct estimate Indirect estimate Network estimate	1	lonsertib 18 i 0.88	mg	0.50 15.74 0.77	[0.05; [0.03; 7 [0.09;	418.07]
Firsocostat & Se Direct estimate Indirect estimate Network estimate	1	Placebo/None 0.47	e	1.51 0.15 0.44	[0.06; [0.01; [0.05;	3.09]
Firsocostat & Se Direct estimate Indirect estimate Network estimate	1	Selonsertib 1 0.88	8 mg 0.001 1101000	0.49 15.33 0.75	[0.05; [0.03; 7 [0.09;	211.51]