Supplementary Table 2. Comparison between change in noninvasive serum biomarkers and change in liver fibrosis assessed by liver histology, in therapeutic trials of nonalcoholic steatohepatitis (NASH)

Study	Study design, duration & numbers recruited	Relevant drug for NASH	Patient group	Fibrosis marker	Fibrosis stage	Baseline	Follow-up	Change in mean	Change in serum biomarker score
Newsome et al.[1] (2021)	Phase 2, double-blind, randomised, placebo-controlled; 72 weeks; n=320	Semaglutide	0.1 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F0	n=0	n=13 (16%)		
					F1	n=23 (29%)	n=22 (28%)		
					F2	n=18 (22%)	n=19 (24%)		
					F3	n=39 (49%)	n=18 (23%)		
					F4	n=0	n=2 (3%)		
				Mean fibrosis stage[a] (SD)		2.2 (0.6)	1.6 (0.3)	−0.6	
				Mean ELF™ score[f,h]		9.8±1.0	9.42[d]		−0.34[e]
				Mean VCTE reading, kPa[g]		10.4±78.5	8.04[i]		−2.0[d]
			0.2 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F0	n=0	n=9 (14%)		
					F1	n=19 (26%)	n=19 (30%)		
					F2	n=18 (24%)	n=11 (17%)		
					F3	n=41 (55%)	n=23 (36%)		
					F4	n=0	n=2 (3%)		
				Mean fibrosis stage[a] (SD)		2.3 (0.7)	1.8 (0.4)	−0.5	
				Mean ELF™ score[f,h]		9.8±0.9	9.37[d]		−0.39[e]
				Mean VCTE reading, kPa[g]		12.3±74.0	7.55[i]		−4.75[d]
			0.4 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F0	n=0	n=11 (16%)		
					F1	n=26 (32%)	n=21 (30%)		
					F2	n=14 (17%)	n=17 (25%)		
					F3	n=42 (51%)	n=20 (29%)		
					F4	n=0	n=0		
				Mean fibrosis stage[a]		2.2 (0.6)	1.7 (0.4)	−0.5	
				Mean ELF™ score[f,h]		9.9±1.0	9.2[d]		−0.56[e]
				Mean VCTE reading, kPa[g]		11.5±87.1	7.68[i]		−3.82
			Placebo	Biopsy confirmed fibrosis using NASH CRN criteria	F0	n=0	n=8 (11%)		
					F1	n=22 (28%)	n=17 (24%)		
					F2	n=22 (28%)	n=16 (23%)		
					F3	n=36 (45%)	n=26 (37%)		
					F4	n=0	n=3 (4%)		
				Mean fibrosis stage[a] (SD)		2.2 (0.6)	2.0 (0.4)	−0.2	
				Mean ELF™ score[f,h]		9.6±0.9	9.77[d]		0.01e
				Mean VCTE reading, kPa[g]		8.7±90.0	10.84[i]		2.14d

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Supplementary Table 2. Continued

Study	Study design, duration & numbers recruited	Relevant drug for NASH	Patient group	Fibrosis marker	Fibrosis stage	Baseline	Follow-up	Change in mean	Change in serum biomarker score
Friedman et al.[2] (2018)	Phase 2b, double-blind, randomised, placebo-controlled; 52 weeks; n=288	Cenicriviroc	150 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F0	n=0	n=10 (7%)		
					F1	n=47 (32%)	n=44 (32%)		
					F2	n=42 (29%)	n=35 (25%)		
					F3	n=56 (39%)	n=47 (34%)		
					F4	n=0	n=2 (1%)		
				Mean fibrosis stage (SD)		2.1 (0.5)	1.9 (0.4)	−0.2	
				Median NFS score (min, max)		−0.942 (−4.55, 1.27)	−0.942 (−4.55, 1.27)		−0.942 (−4.55, 1.27)
				Mean NFS score for subjects with improvement (SD)		−1.28 (1.24)	−1.24 (1.21)		0.05 (0.52)
				Mean NFS score for subjects without improvement (SD)		−0.99 (1.09)	−0.80 (1.21)		0.19 (0.49)
				Median FIB-4 score (min, max)		1.239 (0.38, 4.20)	1.375 (0.42, 5.26)		0.080 (−1.81, 2.38)
				Mean FIB-4 for subjects with improvement (SD)		1.27 (0.59)	1.29 (0.63)		0.02 (0.41)
				Mean FIB-4 for subjects without improvement (SD)		1.44 (0.72)	1.61 (0.82)		0.16 (0.54)
				Median APRI score (min, max)		0.470 (0.20, 3.12)	0.539 (0.15, 3.45)		0.024 (−1.30, 1.49)
				Mean APRI for subjects with improvement (SD)		0.52 (0.29)	0.57 (0.49)		0.05 (0.41)
				Mean APRI for subjects without improvement (SD)		0.61 (0.43)	0.72 (0.50)		0.11 (0.38)
				Median ELF* (min, max)		−0.892 (−2.70, 1.27)	−0.828 (−2.50, 1.08)		0.023 (−1.98, 1.65)
				Mean ELF™ for subjects with improvement (SD)		−1.06 (0.65)	−1.10 (0.60)		−0.04 (0.66)
				Mean ELF™ for subjects without improvement (SD)		−0.72 (0.73)	−0.66 (0.76)		0.06 (0.53)
			Placebo	Biopsy confirmed fibrosis using NASH CRN criteria	F0	n=0	n=5 (4%)		
					F1	n=48 (35%)	n=42 (31%)		
					F2	n=40 (28%)	n=34 (25%)		
					F3	n=50 (38%)	n=50 (37%)		
					F4	n=0	n=5 (4%)		
				Mean fibrosis score (SD)		2.0 (0.5)	2.1 (0.4)	0.1	
				Median NFS score (min, max)		−1.223 (−4.81, 2.46)	−1.190 (−4.27, 2.34)		0.102 (−1.74, 1.37)
				Mean NFS score for subjects with improvement (SD)		−1.26 (1.46)	−1.24 (1.61)		0.02 (0.64)
				Mean NFS score for subjects without improvement (SD)		−1.13 (1.48)	−0.99 (1.41)		0.15 (0.48)

Supplementary Table 2. Continued

Study	Study design, duration & numbers recruited	Relevant drug for NASH	Patient group	Fibrosis marker	Fibrosis stage	Baseline	Follow-up	Change in mean	Change in serum biomarker score
				Median FIB-4 score (min, max)		1.303 (0.40, 4.14)	1.242 (0.36, 5.32)		0.006 (−1.18, 3.11)
				Mean FIB-4 for subjects with improvement (SD)		1.31 (0.63)	1.17 (0.60)		−0.14 (0.49)
				Mean FIB-4 for subjects without improvement (SD)		1.55 (0.76)	1.55 (0.76)		0.17 (0.73)
				Median APRI score (min, max)		0.568 (0.15, 2.26)	0.538 (0.13, 3.71)		−0.031 (−0.82, 3.46)
				Mean APRI for subjects with improvement (SD)		0.51 (0.26)	0.42 (0.26)		−0.09 (0.26)
				Mean APRI for subjects without improvement (SD)		0.70 (0.41)	0.81 (0.71)		0.11 (0.61)
				Median ELF™ (min, max)		−0.893 (−2.20, 1.62)	−1.003 (−2.53, 2.07)		−0.113 (−1.21, 1.60)
				Mean ELF™ for subjects with improvement (SD)		−1.10 (0.73)	−1.12 (0.68)		−0.02 (0.44)
				Mean ELF™ for subjects without improvement (SD)		−0.74 (0.73)	−0.81 (0.84)		−0.08 (0.59)
Francque et al.[3] (2021)	Phase 2b, double-blind, randomised, placebo-controlled; 24 weeks; n=247	Lanifibranor	800 mg	Mean fibrosis score (SD)[fj]		2.1±0.8	NR	NR	
				Median ELF™ score[i] (IQR)		NR	NR		−0.19 (−0.35 to −0.04)
				Median FIB-4[h] (IQR)		NR	NR		0 (−0.17 to 0.16)
				Median PRO-C3, μg/L (IQR)		NR	NR		−3.93 (−5.26 to −2.61)
				Mean VCTE reading, kPa (SD)		10.31 (4.73)	NR	−1.70 (3.23)	
			1,200 mg	Mean fibrosis score (SD)[fj]		2.1±0.8	NR	NR	
				Median ELF™ score[i] (IQR)		NR	NR		0.11 (−0.04 to 0.26)
				Median FIB-4[h] (IQR)		NR	NR		0.03 (−0.13 to 0.19)
				Median PRO-C3, μg/L (IQR)		NR	NR		−1.79 (−3.07 to −0.52)
				Mean VCTE reading, kPa (SD)		9.99 (5.46)	NR	−1.01 (3.88)	
			Placebo	Mean fibrosis score (SD)[fj]		2.0±0.8	NR	NR	
				Median ELF™ score[i] (IQR)		NR	NR		−0.08 (−0.23 to 0.06)
				Median FIB-4[h] (IQR)		NR	NR		0.03 (−0.19 to 0.13)
				Median PRO-C3, μg/L (IQR)		NR	NR		−1.01 (−2.30 to 0.28)
				Mean VCTE reading, kPa (SD)		9.96 (4.89)	NR	−0.66 (3.04)	

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Supplementary Table 2. Continued

Study	Study design, duration & numbers recruited	Relevant drug for NASH	Patient group	Fibrosis marker	Fibrosis stage	Baseline	Follow-up	Change in mean	Change in serum biomarker score
Harrison et al.[4] (2020)	Phase 2b, double-blind, randomised, placebo-controlled; 52 weeks; n=392	MSDC-0602K	62.5 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F0	n=0	NR		Follow-up data was not recorded in the supplementary information. In the report the following information was provided regarding the performance of noninvasive biomarkers: The average effect of the combined highest doses relative to placebo on ELF™, FIB-4, FibroTest®, and CK-18 was a reduction of 0.21 (95% CI −0.39 to −0.03) SDs at 6 months and 0.17 (95% CI −0.37 to 0.02) SDs at 12 months.
					F1	n=37 (37.4%)	NR		
					F2	n=16 (16.2%)	NR		
					F3	n=47 (46.5%)	NR		
					F4	n=0	NR		
				Mean fibrosis stage[a] (SD)		2.12 (0.59)	NR	0.1	
				Mean APRI score (SD)		0.581 (0.3253)	NR		
				Mean ELF™ score (SD)		9.83 (0.986)	NR		
				Mean FIB-4 score (SD)		1.54 (0.686)	NR		
				Mean FibroTest® (SD)		0.31 (0.226)	NR		
			125 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F0	n=0	NR		
					F1	n=37 (36.7%)	NR		
					F2	n=16 (16.3%)	NR		
					F3	n=47 (45.9%)	NR		
					F4	n=0	NR		
				Mean fibrosis stage[a] (SD)		2.14 (0.59)	NR	−0.1	
				Mean APRI score (SD)		0.516 (0.2331)	NR		
				Mean ELF™ score (SD)		9.74 (0.953)	NR		
				Mean FIB-4 score (SD)		1.49 (0.755)	NR		
				Mean FibroTest® (SD)		0.31 (0.204)	NR		
			250 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F0	n=0	NR		
					F1	n=40 (40.6%)	NR		
					F2	n=16 (15.8%)	NR		
					F3	n=44 (43.6%)	NR		
					F4	n=0	NR		
				Mean fibrosis stage[a] (SD)		2.10 (0.53)	NR	−0.1	
				Mean APRI score (SD)		0.604 (0.4385)	NR		
				Mean ELF™ score (SD)		9.80 (1.052)	NR		
				Mean FIB-4 score (SD)		1.58 (0.909)	NR		
				Mean FibroTest® (SD)		0.33 (0.192)	NR		
			Placebo	Biopsy confirmed fibrosis using NASH CRN criteria	F0	n=0	NR		
					F1	n=36 (38.3%)	NR		
					F2	n=15 (16.0%)	NR		
					F3	n=43 (45.7%)	NR		
					F4	n=0	NR		
				Mean fibrosis stage[a] (SD)		2.2 (0.6)	NR	0.1	
				Mean APRI score (SD)		0.540 (0.2896)	NR		
				Mean ELF™ score (SD)		9.6 (0.850)	NR		
				Mean FIB-4 score (SD)		1.38 (0.688)	NR		
				Mean FibroTest® (SD)		0.31 (0.197)	NR		

Supplementary Table 2. Continued

Study	Study design, duration & numbers recruited	Relevant drug for NASH	Patient group	Fibrosis marker	Fibrosis stage	Baseline	Follow-up	Change in mean	Change in serum biomarker score
Armstrong et al.[5] (2016)	Phase 2, double-blind, randomised, placebo-controlled; 48 weeks; n=52	Liraglutide	1.8 mg	Biopsy confirmed fibrosis stages using Kleiner scoring system	F0–F2	n=14 (54%)	NR		
					F3–F4	n=12 (46%)	NR		
				Mean fibrosis stage (SD)		2.3 (0.9)	NR	−0.2 (0.8)	
				Mean ELF™ score (SD)		9.3 (SD)			−0.3 (0.8)
			Placebo	Biopsy confirmed fibrosis stages using Kleiner scoring system	F0–F2	n=11 (42%)	NR		
					F3–F4	n=15 (58%)	NR		
				Mean fibrosis stage (SD)		2.3 (1.3)	NR	0.2 (1.0)	
				Mean ELF™ score (SD)		9.4 (1.3)			0.1 (0.8)
Chalasani et al.[6] (2020)	Phase 2b, double-blind, randomised, placebo-controlled; 52 weeks; n=162	Belapectin	2 mg/kg	Biopsy confirmed cirrhosis using Ishak scoring system	F3	0	n=15[m] (31.5%)		
					F4	n=54 (100%)	n=31[m] (68.5%)		
				Mean fibrosis stagea (SD)		4.0[d]	3.7[a] (1.2)	−0.3[d]	
				Mean ELF™ score (SD)		10.73 (1.26)	NR		0.49 (0.83)
				Mean Fibrotest® score (SD)					0.02 (0.02)
				Mean VCTE reading, kPa (SD)		32.4 (17.7)	NR		−1.3 (12.5)
			8 mg/kg	Biopsy confirmed cirrhosis using Ishak scoring system	F3	n=0	n=10[m] (24.1%)		
					F4	n=54 (100%)	n=31[m] (75.9%)		
				Mean fibrosis stagea (SD)		4.0[d]	3.75[a] (1.3)	−0.25[d]	
				Mean ELF™ score (SD)		10.64 (1.16)			0.50 (0.78)
				Mean Fibrotest® score (SD)					0.01 (0.02)
				Mean VCTE reading, kPa (SD)		29.3 (14.9)			−2.34 (10.8)
			Placebo	Biopsy confirmed cirrhosis using Ishak scoring system	F3	n=0	n=12[m] (1.3)		
					F4	n=54 (100%)	n=33[m] (74.1%)		
				Mean fibrosis stagea (SD)		4.0[d]	3.7[a] (1.3)	−0.3[d]	
				Mean ELF™ score (SD)		10.81 (1.1)	NR		0.37 (0.63)
				Mean Fibrotest® score (SD)		NR	NR		0.03 (0.02)
				Mean VCTE reading, kPa (SD)		29.9 (17.8)	NR		−0.47 (18.6)
Harrison et al.[7] (2021)	Phase 2, double blind, randomised, placebo-controlled; 24 weeks; n=78	Aldafermin	1 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F2	n=29 (55%)	NR		
					F3	n=24 (45%)	NR		
				Mean fibrosis stage (SD)		2.5[a] (0.7)	NR	NR[n]	
				Mean ELF™ score (SD)		9.8 (0.8)	NR		−0.2 (0.5)
				Mean PRO-C3 score, µg/L (SD)		17.5 (8.4)	NR		−5.4 (6.2)
			Placebo	Biopsy confirmed fibrosis using NASH CRN criteria	F2	n=15 (60%)	NR	NR[n]	
					F3	n=10 (40%)	NR		
				Mean fibrosis stagea (SD)		2.4 (0.7)	NR		
				Mean ELF™ score (SD)		9.9 (1.0)	NR		0 (0.6)
				Mean PRO-C3 score, µg/L (SD)		17.1 (7.0)	NR		−1.2 (6.2)

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Supplementary Table 2. Continued

Study	Study design, duration & numbers recruited	Relevant drug for NASH	Patient group	Fibrosis marker	Fibrosis stage	Baseline	Follow-up	Change in mean	Change in serum biomarker score
Harrison et al.[8] (2021)	Phase 2a, double blind, randomised, placebo-controlled; 12 weeks; n=80	Efruxifermin	28 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F1	n=7 (37%)	NR		
					F2	n=7 (37%)	NR		
					F3	n=5 (26%)	NR		
				Mean fibrosis stage[a] (SD)		1.9 (0.4)	NR	NR[n]	
				Mean ELF™ score (SD)		9.5 (0.6)	NR		8.8[d,o]
				Mean PRO-C3 score, µg/L (SD)		19.2 (10.7)	NR		12.0[d,o]
			50 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F1	n=7 (35%)	NR	NR[n]	
					F2	n=8 (40%)	NR		
					F3	n=5 (25%)	NR		
				Mean fibrosis stage[a] (SD)		1.9 (0.4)	NR		
				Mean ELF™ score (SD)		9.5 (0.9)	NR		8.8[d,o]
				Mean PRO-C3 score, µg/L (SD)		16.2 (5.8)	NR		11.0[d,o]
			70 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F1	n=7 (35%)	NR	NR[n]	
					F2	n=6 (30%)	NR		
					F3	n=7 (35%)	NR		
				Mean fibrosis stage[a] (SD)		2.0 (0.4)	NR		
				Mean ELF™ score (SD)		9.5 (0.8)	NR		9.3[d,o]
				Mean PRO-C3 score, µg/L (SD)		17.2 (5.9)	NR		10.0[d,o]
			Placebo	Biopsy confirmed fibrosis using NASH CRN criteria	F1	n=8 (38%)	NR	NR[n]	
					F2	n=5 (24%)	NR		
					F3	n=8 (38%)	NR		
				Mean fibrosis stage[a] (SD)		2.0 (0.5)	NR		
				Mean ELF™ score (SD)		9.5 (1.0)	NR		9.5[d,o]
				Mean PRO-C3 score, µg/L (SD)		16.1 (6.7)	NR		15.0[d,o]

Supplementary Table 2. Continued

Study	Study design, duration & numbers recruited	Relevant drug for NASH	Patient group	Fibrosis marker	Fibrosis stage	Baseline	Follow-up	Change in mean	Change in serum biomarker score
Loomba et al.[9] (2021)	Phase 2b, double blind, randomised, placebo-controlled; 48 weeks; n=392	Cilofexor Firsocostat and Selonsertib	Selonsertib 18 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F0–F2	n=0	Study arm discontinued		
					F3	n=18 (46%)			
					F4	n=21 (54%)			
				Median ELF™ score (IQR)		9.6 (8.9, 11.4)			
				Median VCTE reading, kPa (IQR)		16.3 (12.3, 23.2)			
			Firsocostat 20 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F0–F2	n=2 (5%)	NR	Data not available to calculate change	
					F3	n=16 (40%)	NR		
					F4	n=22 (55%)	NR		
				Median ELF™ score (IQR)		10.2 (9.7, 10.6)	NR		−0.1 (−0.4, 0.1)
				Median VCTE reading, kPa (IQR)		17.1 (13.2, 22.2)	NR		−6.3 (−9.6, −3.0)
			Cilofexor 30 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F0–F2	n=1 (3%)	NR	Data not available to calculate change	
					F3	n=17 (43%)	NR		
					F4	n=22 (55%)	NR		
				Median ELF™ score (IQR)		10.1 (9.7, 10.7)	NR		0.2 (−0.1, 0.4)
				Median VCTE reading, kPa (IQR)		16.0 (12.8, 21.7)	NR		−4.3 (−7.5, −1.0)
			Firsocostat 20 mg Selonsertib 18 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F0–F2	n=1 (1%)	NR	Data not available to calculate change	
					F3	n=32 (42%)	NR		
					F4	n=46 (58%)	NR		
				Median ELF™ score (IQR)		10.0 (9.4, 10.9)	NR		0.1 (−0.1, 0.20)
				Median VCTE reading, kPa (IQR)		16.5 (11.0, 25.1)	NR		−2.4 (−4.7, −2.0)
			Cilofexor 30 mg Selonsertib 18 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F0–F2	n=2 (3%)	NR	Data not available to calculate change	
					F3	n=29 (38%)	NR		
					F4	n=46 (60%)	NR		
				Median ELF™ score (IQR)		10.1 (9.6, 10.8)	NR		0.1 (−0.1, 0.30)
				Median VCTE reading, kPa (IQR)		14.9 (10.2, 20.6)	NR		−3.1 (−5.5, −0.7)
			Cilofexor 30 mg Firsocostat 20 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F0–F2	n=2 (3%)	NR	Data not available to calculate change	
					F3	n=34 (44%)	NR		
					F4	n=42 (54%)	NR		
				Median ELF™ score (IQR)		10.0 (9.4, 10.7)	NR		−0.0 (−0.2, 0.20)
				Median VCTE reading, kPa (IQR)		15.7 (10.9, 22.2)	NR		−4.2 (−6.5, −1.9)
			Placebo	Biopsy confirmed fibrosis using NASH CRN criteria	F0–F2	n=0	NR	Data not available to calculate change	
					F3	n=17 (44%)	NR		
					F4	n=22 (56%)	NR		
				Median ELF™ score (IQR)		10.1 (9.2, 11.0)	NR		0.3 (0.1, 0.6)
				Median VCTE reading, kPa (IQR)		17.1 (14.3, 23.2)	NR		−1.2 (−4.1, 1.8)

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Supplementary Table 2. Continued

Study	Study design, duration & numbers recruited	Relevant drug for NASH	Patient group	Fibrosis marker	Fibrosis stage	Baseline	Follow-up	Change in mean	Change in serum biomarker score
Harrison et al.[10] (2019)	Phase 2, double blind, randomised, placebo-controlled; 36 weeks; n=125	Resmetriom	80 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F0	n=1 (1%)	NR	Reported as Fibrosis responder=28.8%	
					F1	n=47 (56%)	NR		
					F2	n=18 (21%)	NR		
					F3	n=18 (21%)	NR		
					F4	n=0	NR		
				Mean fibrosis stage[a] (SD)		1.6 (0.3)	NR		
				Mean ELF™ score (SD)		9.2 (0.9)	NR		−0.38[q] (0.09)
				Mean PRO-C3 score, µg/L (SD)		17.8 (10.3)	NR		−2.2[t] (2.1); −6.5[u] (3.5)
			Placebo	Biopsy confirmed fibrosis using NASH CRN criteria	F0	n=2 (5%)		Reported as Fibrosis responders=16.7%	
					F1	n=19 (46%)			
					F2	n=13 (32%)			
					F3	n=7 (17%)			
					F4	n=0			
				Mean fibrosis stage[a] (SD)		1.6 (0.3)			
				Mean ELF™ score (SD)		9.2 (1.0)			0.02[p] (0.12)
				Mean PRO-C3 score, µg/L (SD)		16.2 (59.0)			7.4[r] (3.1); 14.9[s] (5.6)
Ratziu et al.[11] (2016)	Phase 2, double blind, randomised, placebo-controlled; 52 weeks; n=276	Elafibranor	80 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F0	n=20 (21.5%)		Data not available to calculate change	
					F1	n=28 (30.1%)			
					F2	n=22 (23.7%)			
					F3[v]	n=23 (24.7%)			
					F4	n=0			
				Mean fibrosis stage (SD)		1.5 (1.1)			
				Mean NFS score (SD)		NR	NR		
				Mean Fibrotest® (SD)		NR	NR		
			120 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F0	n=5 (5.6%)		Mean change: Responders=−0.7[d] Non-responders=0.25[d]	
					F1	n=39 (43.8%)			
					F2	n=25 (28.1%)			
					F3[v]	n=20 (22.5%)			
					F4	n=0			
				Mean fibrosis stage (SD)		1.7 (0.9)			
				Mean NFS score (SD)		NR	NR		−0.25[d]
				Mean Fibrotest® (SD)		NR	NR		−0.07[d]
			Placebo	Biopsy confirmed fibrosis using NASH CRN criteria	F0	n=15 (16.3%)		Data not available to calculate change	
					F1	n=32 (34.8%)			
					F2	n=25 (27.2%)			
					F3[v]	n=20 (21.7%)			
					F4	n=0			
				Mean fibrosis stage (SD)		1.5 (1.0)			
				Mean NFS score (SD)		NR	NR		−0.01[d]
				Mean Fibrotest® (SD)		NR	NR		−0.01[d]

Supplementary Table 2. Continued

Study	Study design, duration & numbers recruited	Relevant drug for NASH	Patient group	Fibrosis marker	Fibrosis stage	Baseline	Follow-up	Change in mean	Change in serum biomarker score
Harrison et al.[12] (2020)	Phase III (STELLAR-4), double blind, randomised, placebo-controlled; 48 weeks; n=877	Selonsertib	6 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F0	n=0	n=1 (0.3%)		
					F1	n=0	n=1 (0.3%)		
					F2	n=0	n=2 (0.6%)		
					F3	n=0	n=55 (15.7%)		
					F4	n=351 (100%)	n=292 (83.2%)		
				Mean fibrosis stage[a] (SD)		4.0 (1.8)	3.8 (1.4)		
				Median ELF™ score (IQR)		10. 64 (10.01–11.34)	10.84 (10.08–11.52)		−0.2[d]
				Median Fibrotest® (IQR)		0.58 (0.41–0.73)	0.58 (0.39–0.73)		NC
				Median APRI score (IQR)		0.8 (0.5–1.3)	0.8 (0.5–1.3)		NC
				Median FIB-4 score (IQR)		2.48 (1.74–3.65)	2.58 (1.65–3.99)		0.10[d]
				Median NFS score (IQR)		0.629 (−0.215 to 1.629)	0.984 (−0.031 to 1.814)		0.355[d]
				Median VCTE reading, kPa (IQR)		21.30 (14.0–29.8)	20.40 (13.9–29.8)		−0.9[d]
			18 mg	Biopsy confirmed fibrosis using NASH CRN criteria	F0	n=0	n=0		
					F1	n=0	n=2 (0.6%)		
					F2	n=0	n=1 (0.3%)		
					F3	n=0	n=64 (18.1%)		
					F4	n=354 (100%)	n=281 (81.1%)		
				Mean fibrosis stage[a] (SD)		4.0 (1.8)	3.7 (1.4)	−0.3[d]	
				Median ELF™ score (IQR)		10.61 (10.04–11.34)	10.73 (10.07–10.51)		0.10[d]
				Median Fibrotest® (IQR)		0.58 (0.44–0.73)	0.58 (0.40–0.75)		NC
				Median APRI score (IQR)		0.8 (0.6-1.2)	0.8 (0.5–1.3)		NC
				Median FIB-4 score (IQR)		2.55 (1.76–3.62)	2.65 (1.74–3.76)		0.10[d]
				Median NFS score (IQR)		0.659 (−0.119 to 1.472)	0.816 (0.031–1.574)		0.157[d]
				Median VCTE reading, kPa (IQR)		21.10 (14.7–28.8)	19.4 (14.3–27.3)		−1.7[d]
			Placebo	Biopsy confirmed fibrosis using NASH CRN criteria	F0	n=0	n=0		
					F1	n=0	n=0		
					F2	n=0	n=0		
					F3	n=1 (0.6%)	n=27 (15.7%)		
					F4	n=171 (99.4%)	n=145 (84.3%)		
				Mean fibrosis stage[a] (SD)		3.7 (1.4)	3.8 (1.5)		0.10[d]
				Median ELF™ score (IQR)		10.67 (10.05–11.16)	10.66 (10.14–11.26)		−0.01[d]
				Median Fibrotest® (IQR)		0.59 (0.40–0.77)	0.57 (0.39–0.73)		−0.02[d]
				Median APRI score (IQR)		0.8 (0.6–1.2)	0.7 (0.5–1.2)		−0.1[d]
				Median FIB-4 score (IQR)		2.50 (1.81–3.66)	2.50 (1.65–3.67)		NC
				Median NFS score (IQR)		0.682 (−0.304 to 1.450)	0.774 (−0.241 to 1.595)		0.092[d]
				Median VCTE reading, kPa (IQR)		20.00 (14.4–26.7)	19.30 (13.8–26.7)		0.70[d]

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Supplementary Table 2. Continued

Study	Study design, duration & numbers recruited	Relevant drug for NASH	Patient group	Fibrosis marker	Fibrosis stage	Baseline	Follow-up	Change in mean	Change in serum biomarker score
Loomba et al.[13] (2018)	Phase 2, double blind, randomised, de facto placebo-controlled; 24 weeks; n=72	Selonsertib ±Simtuzumab	Selonsertib 6 mg ±Simtuzumab	Biopsy confirmed F3 using NASH CRN criteria		n=20 (67%)	Improvement n=8 (30%) Cirrhosis n=2 (7%)		
				Median ELF™ score (IQR)		NR	NR		−0.07 (−0.46 to 0.36)
				Median Fibrotest® (IQR)		NR	NR		0.02 (−0.03 to 0.08)
				Median VCTE reading, kPa (IQR)		NR	NR		−0.80 (−1.90 to 2.30)
			Selonsertib 18 mg ±Simtuzumab	Biopsy confirmed F3 using NASH CRN criteria		n=21 (66%)	Improvement n=13 (43%) Cirrhosis n=1 (3%)		
				Median ELF™ score (IQR)		NR	NR		0.02 (−0.34 to 0.52)
				Median Fibrotest® (IQR)		NR	NR		−0.01 (−0.03 to 0.03)
				Median VCTE reading, kPa (IQR)		NR	NR		0.2 (−3.50 to 1.40)
			Simtuzumab	Biopsy confirmed F3 using NASH CRN criteria		n=6 (60%)	Improvement n=2 (20%) Cirrhosis n=2 (20%)		
				Median ELF™ score (IQR)		NR	NR		−0.13 (−0.35 to 0.05)
				Median Fibrotest® (IQR)		NR	NR		0.01 (−0.04 to 0.05)
				Median VCTE reading, kPa (IQR)		NR	NR		−0.50 (−3.80 to 3.4)
Ratziu et al.[15] (2018)	Phase 2b, double blinde, randomised, placebo-controlled; 52 weeks; n=247	Aramachol	400 mg	Biopsy confirmed fibrosis using NASH CRN staging system	F2 F3	18.8% 45.7%	NR NR		
				FIB-4 change from baseline to week 52		NR	NR		−0.05±0.06
				NFS change from baseline to week 52		NR	NR		−0.12±0.08
			600 mg	Biopsy confirmed fibrosis using NASH CRN staging system	F2 F3	22.4% 36.7%			
				FIB-4 change from baseline to week 52		NR	NR		−0.10±0.06
				NFS change from baseline to week 52		NR	NR		−0.04±0.08
			Placebo	Biopsy confirmed fibrosis using NASH CRN staging system	F2 F3	16.7% 33.3%			
				FIB-4 change from baseline to week 52		NR	NR		−0.12±0.08
				NFS change from baseline to week 52		NR	NR		0.23±0.11

NR, not reported; NC, no change; ELF™, enhanced liver fibrosis; FIB-4, fibrosis-4; NFS, NAFLD fibrosis score; APRI, aspartate transaminase to platelet ratio index; PRO-C3, Type III collagen marker of the N-terminal pro-peptide; SD, standard deviation; IQR, interquartile range; VCTE, vibration controlled transient elastography; CI, confidence interval.

[a]Mean not provided, calculation made using data provided in the manuscript tables and supplementary information. [b]Manufacturers published cut off thresholds for fibrosis.[14] [c]Biopsy validated cut-off thresholds for fibrosis.[3] [d]No standard deviation/IQR reported. [e]Change in biomarker score is the change reported in the research paper and not the exact difference between baseline and follow-up. [f]Plus-minus values are means±SD. [g]Plus-minus values are geometric means±coefficient of variation. [h]An ELF™ score greater than 9.8 indicates a moderate risk of advanced fibrosis, and a score of greater than 11.3 denotes a high risk of advanced fibrosis. [i]No geometric means±coefficient of variation reported. [j]Fibrosis stage was classified according to the SAF-NASH CRN staging system. [k]A Fibrosis-4 index score of less than 1.45 indicates low probability of stage F3 or F4 fibrosis, and a score greater than 3.25 indicates a high probability of stage F3 or F4 fibrosis. [l]An ELF™ score of less than 7.7 indicates none to mild fibrosis, and a score of 11.3 or greater indicates cirrhosis. [m]*n* value is approximate and was calculated from the % improvement recorded in Table 4 of the manuscript.[6] [n]Improvement/no improvement or worsening reported, unable to calculate changes in fibrosis stage as data is not provided. [o]Estimated values only, exact values not recorded, data taken from manuscript[8] Figure 3, (f) and (g). [p]Mean difference reported for subjects with ELF™≥9.0 only (n=21) at week 12. [q]Mean difference reported for subjects with ELF™ ≥9.0 only (n=40) at week 12. [r]Mean difference reported for subjects with Baseline ≥10.00 ng/mL (n=25). [s]Mean difference reported for subjects with Baseline ≥17.50 ng/mL (n=12). [t]Mean difference reported for subjects with Baseline ≥10.00 ng/mL (n=53). [u]Mean difference reported for subjects with Baseline ≥17.50 ng/mL (n=29). [v]Bridging fibrosis.

*Data for baseline, follow-up and change in ELF™ score taken from Supplmentary Table 6.[2]

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