ウゴービ皮下注
非アルコール性脂肪肝炎（NASH）

2.7.3.6 付録
1.サブグループ解析

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6.1 Subgroup analyses

6.1.1 Primary endpoints by sex - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Number of subjects	534	266
Sex	534	266
Resolution of steatohepatitis and no worsening of liver fibrosis		
Male	221(41.4)	122(45.9)
Week 72		
Yes	137 (62.0)	43 (35.2)
No	61 (27.6)	63 (51.6)
Missing	23 (10.4)	16 (13.1)
Female	313(58.6)	144(54.1)
Week 72		
Yes	177 (56.5)	34 (23.6)
No	94 (30.0)	84 (58.3)
Missing	42 (13.4)	26 (18.1)
Improvement in liver fibrosis and no worsening of steatohepatitis		
Male	221(41.4)	122(45.9)
Week 72		
Yes	79 (35.7)	22 (18.0)
No	119 (53.8)	84 (68.9)
Missing	23 (10.4)	16 (13.1)
Female	313(58.6)	144(54.1)
Week 72		
Yes	104 (33.2)	28 (19.4)
No	167 (53.4)	90 (62.5)
Missing	42 (13.4)	26 (18.1)

N: Number of subjects, %: Percentage of subjects.

6.1.2 Primary endpoints by age at baseline - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Number of subjects	534	266
Age at baseline	534	266
Resolution of steatohepatitis and no worsening of liver fibrosis		
<45 years	77(14.4)	49(18.4)
Week 72		
Yes	46 (59.7)	16 (32.7)
No	23 (29.9)	25 (51.0)
Missing	8 (10.4)	8 (16.3)
>=45 - <65 years	319(59.7)	153(57.5)
Week 72		
Yes	188 (58.9)	45 (29.4)
No	90 (28.2)	86 (56.2)
Missing	41 (12.9)	22 (14.4)
>=65 years	138(25.8)	64(24.1)
Week 72		
Yes	80 (58.0)	16 (25.0)
No	42 (30.4)	36 (56.3)
Missing	16 (11.6)	12 (18.8)
Improvement in liver fibrosis and no worsening of steatohepatitis		
<45 years	77(14.4)	49(18.4)
Week 72		
Yes	32 (41.6)	9 (18.4)
No	37 (48.1)	32 (65.3)
Missing	8 (10.4)	8 (16.3)
>=45 - <65 years	319(59.7)	153(57.5)
Week 72		
Yes	106 (33.2)	31 (20.3)
No	172 (53.9)	100 (65.4)
Missing	41 (12.9)	22 (14.4)

N: Number of subjects, %: Percentage of subjects.

Primary endpoints by age at baseline - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
>=65 years	138(25.8)	64(24.1)
Week 72		
Yes	45 (32.6)	10 (15.6)
No	77 (55.8)	42 (65.6)
Missing	16 (11.6)	12 (18.8)

N: Number of subjects, %: Percentage of subjects.

6.1.3 Primary endpoints by race - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Number of subjects	534	266
Race	527	265
Resolution of steatohepatitis and no worsening of liver fibrosis		
American Indian or Alaska Native	2(0.4)	0 (0.0)
Week 72		
Yes	2 (100.0)	0 (0.0)
No	0 (0.0)	0 (0.0)
Missing	0 (0.0)	0 (0.0)
Asian	142(26.9)	74(27.9)
Week 72		
Yes	83 (58.5)	25 (33.8)
No	44 (31.0)	41 (55.4)
Missing	15 (10.6)	8 (10.8)
Black or African American	3(0.6)	2(0.8)
Week 72		
Yes	3 (100.0)	2 (100.0)
No	0 (0.0)	0 (0.0)
Missing	0 (0.0)	0 (0.0)
Native Hawaiian or Other Pacific Islander	0 (0.0)	0 (0.0)
Week 72		
Yes	0 (0.0)	0 (0.0)
No	0 (0.0)	0 (0.0)
Missing	0 (0.0)	0 (0.0)
White	361(68.5)	179(67.5)
Week 72		
Yes	214 (59.3)	48 (26.8)
No	101 (28.0)	97 (54.2)
Missing	46 (12.7)	34 (19.0)

N: Number of subjects, %: Percentage of subjects.

Primary endpoints by race - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Other	19(3.6)	10(3.8)
Week 72		
Yes	7 (36.8)	2 (20.0)
No	8 (42.1)	8 (80.0)
Missing	4 (21.1)	0 (0.0)
Improvement in liver fibrosis and no worsening of steatohepatitis		
American Indian or Alaska Native	2(0.4)	0 (0.0)
Week 72		
Yes	1 (50.0)	0 (0.0)
No	1 (50.0)	0 (0.0)
Missing	0 (0.0)	0 (0.0)
Asian	142(26.9)	74(27.9)
Week 72		
Yes	49 (34.5)	16 (21.6)
No	78 (54.9)	50 (67.6)
Missing	15 (10.6)	8 (10.8)
Black or African American	3(0.6)	2(0.8)
Week 72		
Yes	1 (33.3)	2 (100.0)
No	2 (66.7)	0 (0.0)
Missing	0 (0.0)	0 (0.0)
Native Hawaiian or Other Pacific Islander	0 (0.0)	0 (0.0)
Week 72		
Yes	0 (0.0)	0 (0.0)
No	0 (0.0)	0 (0.0)
Missing	0 (0.0)	0 (0.0)

N: Number of subjects, %: Percentage of subjects.

Primary endpoints by race - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
White	361(68.5)	179(67.5)
Week 72		
Yes	128 (35.5)	29 (16.2)
No	187 (51.8)	116 (64.8)
Missing	46 (12.7)	34 (19.0)
Other	19(3.6)	10(3.8)
Week 72		
Yes	2 (10.5)	3 (30.0)
No	13 (68.4)	7 (70.0)
Missing	4 (21.1)	0 (0.0)

N: Number of subjects, %: Percentage of subjects.

6.1.4 Primary endpoints by ethnicity - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Number of subjects	534	266
Ethnicity	530	265
Resolution of steatohepatitis and no worsening of liver fibrosis		
Hispanic or Latino	95(17.9)	51(19.2)
Week 72		
Yes	53 (55.8)	17 (33.3)
No	23 (24.2)	24 (47.1)
Missing	19 (20.0)	10 (19.6)
Not Hispanic or Latino	420(79.2)	212(80.0)
Week 72		
Yes	248 (59.0)	60 (28.3)
No	128 (30.5)	120 (56.6)
Missing	44 (10.5)	32 (15.1)
Not Reported	15(2.8)	2(0.8)
Week 72		
Yes	9 (60.0)	0 (0.0)
No	4 (26.7)	2 (100.0)
Missing	2 (13.3)	0 (0.0)
Improvement in liver fibrosis and no worsening of steatohepatitis		
Hispanic or Latino	95(17.9)	51(19.2)
Week 72		
Yes	25 (26.3)	9 (17.6)
No	51 (53.7)	32 (62.7)
Missing	19 (20.0)	10 (19.6)
Not Hispanic or Latino	420(79.2)	212(80.0)
Week 72		
Yes	151 (36.0)	41 (19.3)
No	225 (53.6)	139 (65.6)
Missing	44 (10.5)	32 (15.1)

N: Number of subjects, %: Percentage of subjects.

Primary endpoints by ethnicity - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Not Reported	15(2.8)	2(0.8)
Week 72		
Yes	5 (33.3)	0 (0.0)
No	8 (53.3)	2 (100.0)
Missing	2 (13.3)	0 (0.0)

N: Number of subjects, %: Percentage of subjects.

6.1.5 Primary endpoints by diabetes status at baseline - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Number of subjects	534	266
Type 2 diabetes status at baseline	534	266
Resolution of steatohepatitis and no worsening of liver fibrosis		
NON-T2D	238(44.6)	115(43.2)
Week 72		
Yes	146 (61.3)	31 (27.0)
No	55 (23.1)	64 (55.7)
Missing	37 (15.5)	20 (17.4)
T2D	296(55.4)	151(56.8)
Week 72		
Yes	168 (56.8)	46 (30.5)
No	100 (33.8)	83 (55.0)
Missing	28 (9.5)	22 (14.6)
Improvement in liver fibrosis and no worsening of steatohepatitis		
NON-T2D	238(44.6)	115(43.2)
Week 72		
Yes	88 (37.0)	17 (14.8)
No	113 (47.5)	78 (67.8)
Missing	37 (15.5)	20 (17.4)
T2D	296(55.4)	151(56.8)
Week 72		
Yes	95 (32.1)	33 (21.9)
No	173 (58.4)	96 (63.6)
Missing	28 (9.5)	22 (14.6)

N: Number of subjects, %: Percentage of subjects, T2D: type 2 diabetes.

6.1.6 Primary endpoints by glyceamic status at baseline (non-T2D only) - summary - in-trial (72 weeks) - full analysis set (interim) (only subjects without type 2 diabetes at baseline) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Number of subjects	238	115
Glycaemic status at baseline	238	115
Resolution of steatohepatitis and no worsening of liver fibrosis		
Normo-glycemia (HbA1c<5.7%)	90(37.8)	42(36.5)
Week 72		
Yes	56 (62.2)	9 (21.4)
No	18 (20.0)	28 (66.7)
Missing	16 (17.8)	5 (11.9)
Pre-diabetes (HbA1c>=5.7%)	148(62.2)	73(63.5)
Week 72		
Yes	90 (60.8)	22 (30.1)
No	37 (25.0)	36 (49.3)
Missing	21 (14.2)	15 (20.5)
Improvement in liver fibrosis and no worsening of steatohepatitis		
Normo-glycemia (HbA1c<5.7%)	90(37.8)	42(36.5)
Week 72		
Yes	38 (42.2)	3 (7.1)
No	36 (40.0)	34 (81.0)
Missing	16 (17.8)	5 (11.9)
Pre-diabetes (HbA1c>=5.7%)	148(62.2)	73(63.5)
Week 72		
Yes	50 (33.8)	14 (19.2)
No	77 (52.0)	44 (60.3)
Missing	21 (14.2)	15 (20.5)

N: Number of subjects, %: Percentage of subjects, T2D: Type 2 diabetes.

6.1.7 Primary endpoints by fibrosis stage at baseline - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Number of subjects	534	266
Fibrosis stage at baseline	534	266
Resolution of steatohepatitis and no worsening of liver fibrosis		
F2	169(31.6)	81(30.5)
Week 72		
Yes	103 (60.9)	26 (32.1)
No	44 (26.0)	44 (54.3)
Missing	22 (13.0)	11 (13.6)
F3	365(68.4)	185(69.5)
Week 72		
Yes	211 (57.8)	51 (27.6)
No	111 (30.4)	103 (55.7)
Missing	43 (11.8)	31 (16.8)
Improvement in liver fibrosis and no worsening of steatohepatitis		
F2	169(31.6)	81(30.5)
Week 72		
Yes	62 (36.7)	13 (16.0)
No	85 (50.3)	57 (70.4)
Missing	22 (13.0)	11 (13.6)
F3	365(68.4)	185(69.5)
Week 72		
Yes	121 (33.2)	37 (20.0)
No	201 (55.1)	117 (63.2)
Missing	43 (11.8)	31 (16.8)

N: Number of subjects, %: Percentage of subjects.

6.1.8 Primary endpoints by BMI at baseline - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Number of subjects	534	266
Body mass index at baseline	534	265
Resolution of steatohepatitis and no worsening of liver fibrosis		
<27 kg/m^2	73(13.7)	32(12.1)
Week 72		
Yes	38 (52.1)	10 (31.3)
No	23 (31.5)	18 (56.3)
Missing	12 (16.4)	4 (12.5)
>=27 to <30 kg/m^2	79(14.8)	33(12.5)
Week 72		
Yes	48 (60.8)	11 (33.3)
No	18 (22.8)	15 (45.5)
Missing	13 (16.5)	7 (21.2)
>=30 to <35 kg/m^2	173(32.4)	79(29.8)
Week 72		
Yes	107 (61.8)	18 (22.8)
No	45 (26.0)	46 (58.2)
Missing	21 (12.1)	15 (19.0)
>= 35 kg/m^2	209(39.1)	121(45.7)
Week 72		
Yes	121 (57.9)	38 (31.4)
No	69 (33.0)	67 (55.4)
Missing	19 (9.1)	16 (13.2)

N: Number of subjects, %: Percentage of subjects, BMI: Body mass index.

Primary endpoints by BMI at baseline - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Improvement in liver fibrosis and no worsening of steatohepatitis		
<27 kg/m^2	73(13.7)	32(12.1)
Week 72		
Yes	23 (31.5)	9 (28.1)
No	38 (52.1)	19 (59.4)
Missing	12 (16.4)	4 (12.5)
>=27 to <30 kg/m^2	79(14.8)	33(12.5)
Week 72		
Yes	34 (43.0)	6 (18.2)
No	32 (40.5)	20 (60.6)
Missing	13 (16.5)	7 (21.2)
>=30 to <35 kg/m^2	173(32.4)	79(29.8)
Week 72		
Yes	64 (37.0)	14 (17.7)
No	88 (50.9)	50 (63.3)
Missing	21 (12.1)	15 (19.0)
>= 35 kg/m^2	209(39.1)	121(45.7)
Week 72		
Yes	62 (29.7)	21 (17.4)
No	128 (61.2)	84 (69.4)
Missing	19 (9.1)	16 (13.2)

N: Number of subjects, %: Percentage of subjects, BMI: Body mass index.

6.1.9 Primary endpoints by Lean NASH status at baseline - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Number of subjects	534	266
Lean NASH Status	527	264
Resolution of steatohepatitis and no worsening of liver fibrosis		
Yes	14(2.7)	8(3.0)
Week 72		
Yes	5 (35.7)	2 (25.0)
No	3 (21.4)	5 (62.5)
Missing	6 (42.9)	1 (12.5)
No	513(97.3)	256(97.0)
Week 72		
Yes	304 (59.3)	75 (29.3)
No	150 (29.2)	140 (54.7)
Missing	59 (11.5)	41 (16.0)
Improvement in liver fibrosis and no worsening of steatohepatitis		
Yes	14(2.7)	8(3.0)
Week 72		
Yes	2 (14.3)	1 (12.5)
No	6 (42.9)	6 (75.0)
Missing	6 (42.9)	1 (12.5)
No	513(97.3)	256(97.0)
Week 72		
Yes	179 (34.9)	49 (19.1)
No	275 (53.6)	166 (64.8)
Missing	59 (11.5)	41 (16.0)

N: Number of subjects, %: Percentage of subjects. Lean NASH is defined as a BMI <25 for non-Asians and < 23 for Asians. BMI: Body mass index.

6.1.10 Primary endpoints by ALT at baseline - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Number of subjects	534	266
ALT	534	266
Resolution of steatohepatitis and no worsening of liver fibrosis		
<=ULN	235(44.0)	116(43.6)
Week 72		
Yes	145 (61.7)	35 (30.2)
No	64 (27.2)	65 (56.0)
Missing	26 (11.1)	16 (13.8)
>ULN to <=3xULN	280(52.4)	138(51.9)
Week 72		
Yes	158 (56.4)	39 (28.3)
No	84 (30.0)	76 (55.1)
Missing	38 (13.6)	23 (16.7)
>3xULN	19(3.6)	12(4.5)
Week 72		
Yes	11 (57.9)	3 (25.0)
No	7 (36.8)	6 (50.0)
Missing	1 (5.3)	3 (25.0)
Improvement in liver fibrosis and no worsening of steatohepatitis		
<=ULN	235(44.0)	116(43.6)
Week 72		
Yes	76 (32.3)	24 (20.7)
No	133 (56.6)	76 (65.5)
Missing	26 (11.1)	16 (13.8)
>ULN to <=3xULN	280(52.4)	138(51.9)
Week 72		
Yes	101 (36.1)	23 (16.7)
No	141 (50.4)	92 (66.7)
Missing	38 (13.6)	23 (16.7)

N: Number of subjects, %: Percentage of subjects. ALT: Alanine Aminotransferase, ULN: Upper limit of normal range.

Primary endpoints by ALT at baseline - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
>3xULN	19(3.6)	12(4.5)
Week 72		
Yes	6 (31.6)	3 (25.0)
No	12 (63.2)	6 (50.0)
Missing	1 (5.3)	3 (25.0)

N: Number of subjects, %: Percentage of subjects. ALT: Alanine Aminotransferase, ULN: Upper limit of normal range.

6.1.11 Primary endpoints by AST at baseline - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Number of subjects	534	266
AST	534	266
Resolution of steatohepatitis and no worsening of liver fibrosis		
<=ULN	125(23.4)	60(22.6)
Week 72		
Yes	81 (64.8)	20 (33.3)
No	31 (24.8)	33 (55.0)
Missing	13 (10.4)	7 (11.7)
> ULN to <=3xULN	367(68.7)	185(69.5)
Week 72		
Yes	211 (57.5)	53 (28.6)
No	110 (30.0)	103 (55.7)
Missing	46 (12.5)	29 (15.7)
>3xULN	42(7.9)	21(7.9)
Week 72		
Yes	22 (52.4)	4 (19.0)
No	14 (33.3)	11 (52.4)
Missing	6 (14.3)	6 (28.6)
Improvement in liver fibrosis and no worsening of steatohepatitis		
<=ULN	125(23.4)	60(22.6)
Week 72		
Yes	42 (33.6)	12 (20.0)
No	70 (56.0)	41 (68.3)
Missing	13 (10.4)	7 (11.7)
> ULN to <=3xULN	367(68.7)	185(69.5)
Week 72		
Yes	126 (34.3)	35 (18.9)
No	195 (53.1)	121 (65.4)
Missing	46 (12.5)	29 (15.7)

N: Number of subjects, %: Percentage of subjects. AST: Aspartate Aminotransferase, ULN: Upper limit of normal range.

Primary endpoints by AST at baseline - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
>3xULN	42(7.9)	21(7.9)
Week 72		
Yes	15 (35.7)	3 (14.3)
No	21 (50.0)	12 (57.1)
Missing	6 (14.3)	6 (28.6)

N: Number of subjects, %: Percentage of subjects. AST: Aspartate Aminotransferase, ULN: Upper limit of normal range.

6.1.12 Primary endpoints by ALP at baseline - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Number of subjects	534	266
ALP	534	266
Resolution of steatohepatitis and no worsening of liver fibrosis		
<=ULN	510(95.5)	254(95.5)
Week 72		
Yes	307 (60.2)	75 (29.5)
No	145 (28.4)	139 (54.7)
Missing	58 (11.4)	40 (15.7)
>ULN	24(4.5)	12(4.5)
Week 72		
Yes	7 (29.2)	2 (16.7)
No	10 (41.7)	8 (66.7)
Missing	7 (29.2)	2 (16.7)
Improvement in liver fibrosis and no worsening of steatohepatitis		
<=ULN	510(95.5)	254(95.5)
Week 72		
Yes	177 (34.7)	50 (19.7)
No	275 (53.9)	164 (64.6)
Missing	58 (11.4)	40 (15.7)
>ULN	24(4.5)	12(4.5)
Week 72		
Yes	6 (25.0)	0 (0.0)
No	11 (45.8)	10 (83.3)
Missing	7 (29.2)	2 (16.7)

N: Number of subjects, %: Percentage of subjects. ALP: Alkaline Phosphatase, ULN: Upper limit of normal range.

6.1.13 Primary endpoints by renal function at baseline - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Number of subjects	534	266
Renal function at baseline	533	266
Resolution of steatohepatitis and no worsening of liver fibrosis		
Normal(eGFR >= 90 mL/min/1.73 m^2)	379(71.1)	193(72.6)
Week 72		
Yes	217 (57.3)	59 (30.6)
No	113 (29.8)	101 (52.3)
Missing	49 (12.9)	33 (17.1)
Mild Impairment(eGFR >= 60 to <90 mL/min/1.73 m^2)	135(25.3)	66(24.8)
Week 72		
Yes	86 (63.7)	17 (25.8)
No	35 (25.9)	42 (63.6)
Missing	14 (10.4)	7 (10.6)
Moderate Impairment(eGFR >= 30 to <60 mL/min/1.73 m^2)	19(3.6)	6(2.3)
Week 72		
Yes	10 (52.6)	1 (16.7)
No	7 (36.8)	4 (66.7)
Missing	2 (10.5)	1 (16.7)
Severe Impairment(eGFR >= 15 to < 30 mL/min/1.73 m^2)		1(0.4)
Week 72		
Yes	0 (0.0)	0 (0.0)
No	0 (0.0)	0 (0.0)
Missing	0 (0.0)	1 (100.0)
Improvement in liver fibrosis and no worsening of steatohepatitis		
Normal(eGFR >= 90 mL/min/1.73 m^2)	379(71.1)	193(72.6)
Week 72		
Yes	127 (33.5)	36 (18.7)
No	203 (53.6)	124 (64.2)
Missing	49 (12.9)	33 (17.1)

N: Number of subjects, %: Percentage of subjects, eGFR: Estimated glomerular filtration rate.

Primary endpoints by renal function at baseline - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Mild Impairment(eGFR >= 60 to <90 mL/min/1.73 m^2)	135(25.3)	66(24.8)
Week 72		
Yes	48 (35.6)	13 (19.7)
No	73 (54.1)	46 (69.7)
Missing	14 (10.4)	7 (10.6)
Moderate Impairment(eGFR >= 30 to <60 mL/min/1.73 m^2)	19(3.6)	6(2.3)
Week 72		
Yes	7 (36.8)	1 (16.7)
No	10 (52.6)	4 (66.7)
Missing	2 (10.5)	1 (16.7)
Severe Impairment(eGFR >= 15 to < 30 mL/min/1.73 m^2)		1(0.4)
Week 72		
Yes	0 (0.0)	0 (0.0)
No	0 (0.0)	0 (0.0)
Missing	0 (0.0)	1 (100.0)

N: Number of subjects, %: Percentage of subjects, eGFR: Estimated glomerular filtration rate.

6.1.14 Primary endpoints by trial product pen-injector - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Number of subjects	534	266
Trial product pen-injector	533	266
Resolution of steatohepatitis and no worsening of liver fibrosis		
DV3396	475(89.1)	234(88.0)
Week 72		
Yes	281 (59.2)	71 (30.3)
No	141 (29.7)	133 (56.8)
Missing	53 (11.2)	30 (12.8)
PDS290	58(10.9)	32(12.0)
Week 72		
Yes	33 (56.9)	6 (18.8)
No	14 (24.1)	14 (43.8)
Missing	11 (19.0)	12 (37.5)
Improvement in liver fibrosis and no worsening of steatohepatitis		
DV3396	475(89.1)	234(88.0)
Week 72		
Yes	166 (34.9)	48 (20.5)
No	256 (53.9)	156 (66.7)
Missing	53 (11.2)	30 (12.8)
PDS290	58(10.9)	32(12.0)
Week 72		
Yes	17 (29.3)	2 (6.3)
No	30 (51.7)	18 (56.3)
Missing	11 (19.0)	12 (37.5)

N: Number of subjects, %: Percentage of subjects.

6.1.15 Primary endpoints by region - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Number of subjects	534	266
Region	534	266
Resolution of steatohepatitis and no worsening of liver fibrosis		
Europe	143(26.8)	59(22.2)
Week 72		
Yes	81 (56.6)	12 (20.3)
No	47 (32.9)	38 (64.4)
Missing	15 (10.5)	9 (15.3)
North America	183(34.3)	97(36.5)
Week 72		
Yes	107 (58.5)	24 (24.7)
No	50 (27.3)	50 (51.5)
Missing	26 (14.2)	23 (23.7)
South America	41(7.7)	22(8.3)
Week 72		
Yes	25 (61.0)	9 (40.9)
No	11 (26.8)	11 (50.0)
Missing	5 (12.2)	2 (9.1)
Asia	132(24.7)	69(25.9)
Week 72		
Yes	79 (59.8)	24 (34.8)
No	38 (28.8)	38 (55.1)
Missing	15 (11.4)	7 (10.1)
Other	35(6.6)	19(7.1)
Week 72		
Yes	22 (62.9)	8 (42.1)
No	9 (25.7)	10 (52.6)
Missing	4 (11.4)	1 (5.3)

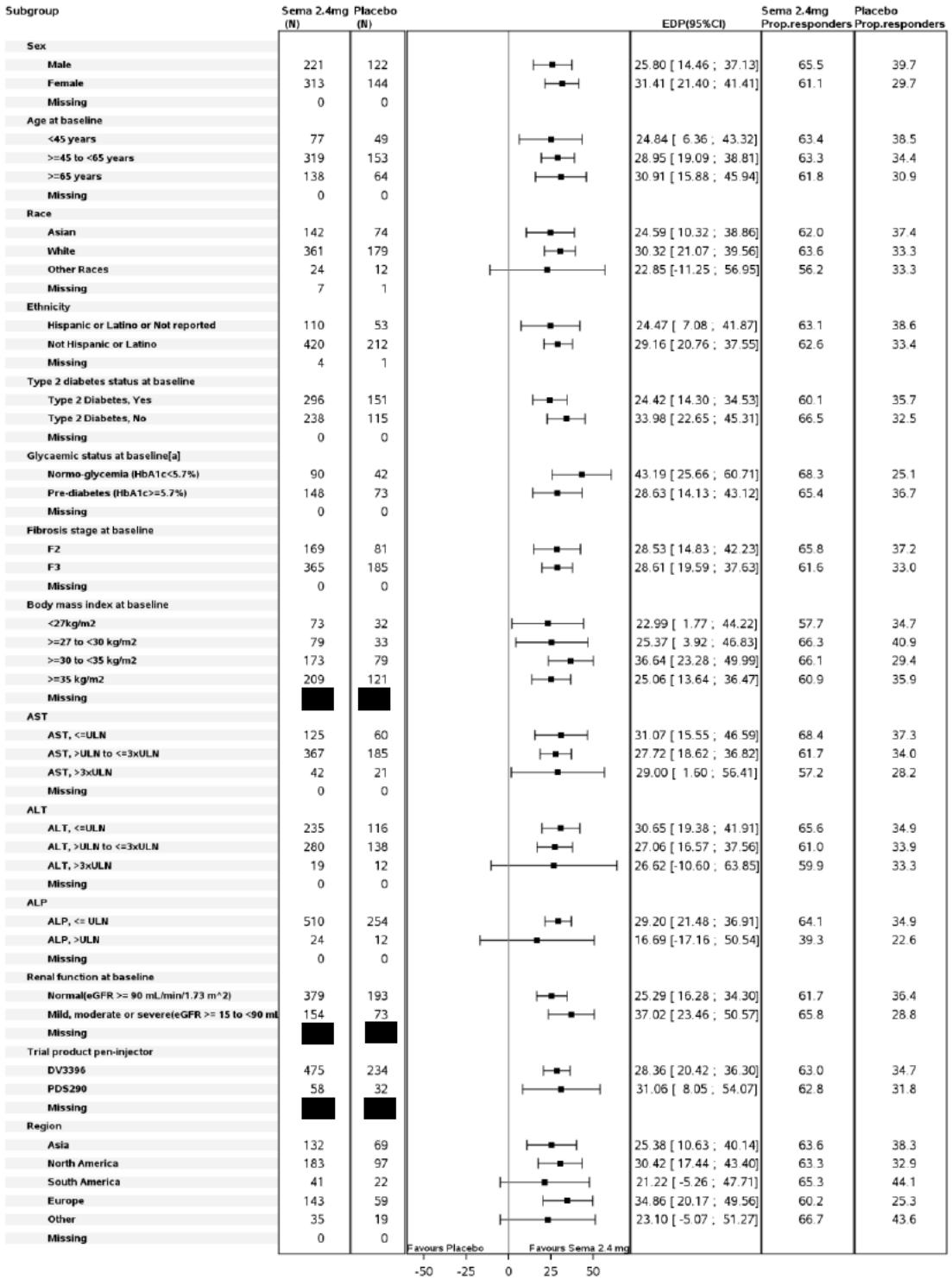
N: Number of subjects, %: Percentage of subjects.

Primary endpoints by region - summary - in-trial (72 weeks) - full analysis set (interim) - Trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Improvement in liver fibrosis and no worsening of steatohepatitis		
Europe	143(26.8)	59(22.2)
Week 72		
Yes	56 (39.2)	7 (11.9)
No	72 (50.3)	43 (72.9)
Missing	15 (10.5)	9 (15.3)
North America	183(34.3)	97(36.5)
Week 72		
Yes	60 (32.8)	15 (15.5)
No	97 (53.0)	59 (60.8)
Missing	26 (14.2)	23 (23.7)
South America	41(7.7)	22(8.3)
Week 72		
Yes	10 (24.4)	6 (27.3)
No	26 (63.4)	14 (63.6)
Missing	5 (12.2)	2 (9.1)
Asia	132(24.7)	69(25.9)
Week 72		
Yes	47 (35.6)	16 (23.2)
No	70 (53.0)	46 (66.7)
Missing	15 (11.4)	7 (10.1)
Other	35(6.6)	19(7.1)
Week 72		
Yes	10 (28.6)	6 (31.6)
No	21 (60.0)	12 (63.2)
Missing	4 (11.4)	1 (5.3)

N: Number of subjects, %: Percentage of subjects.

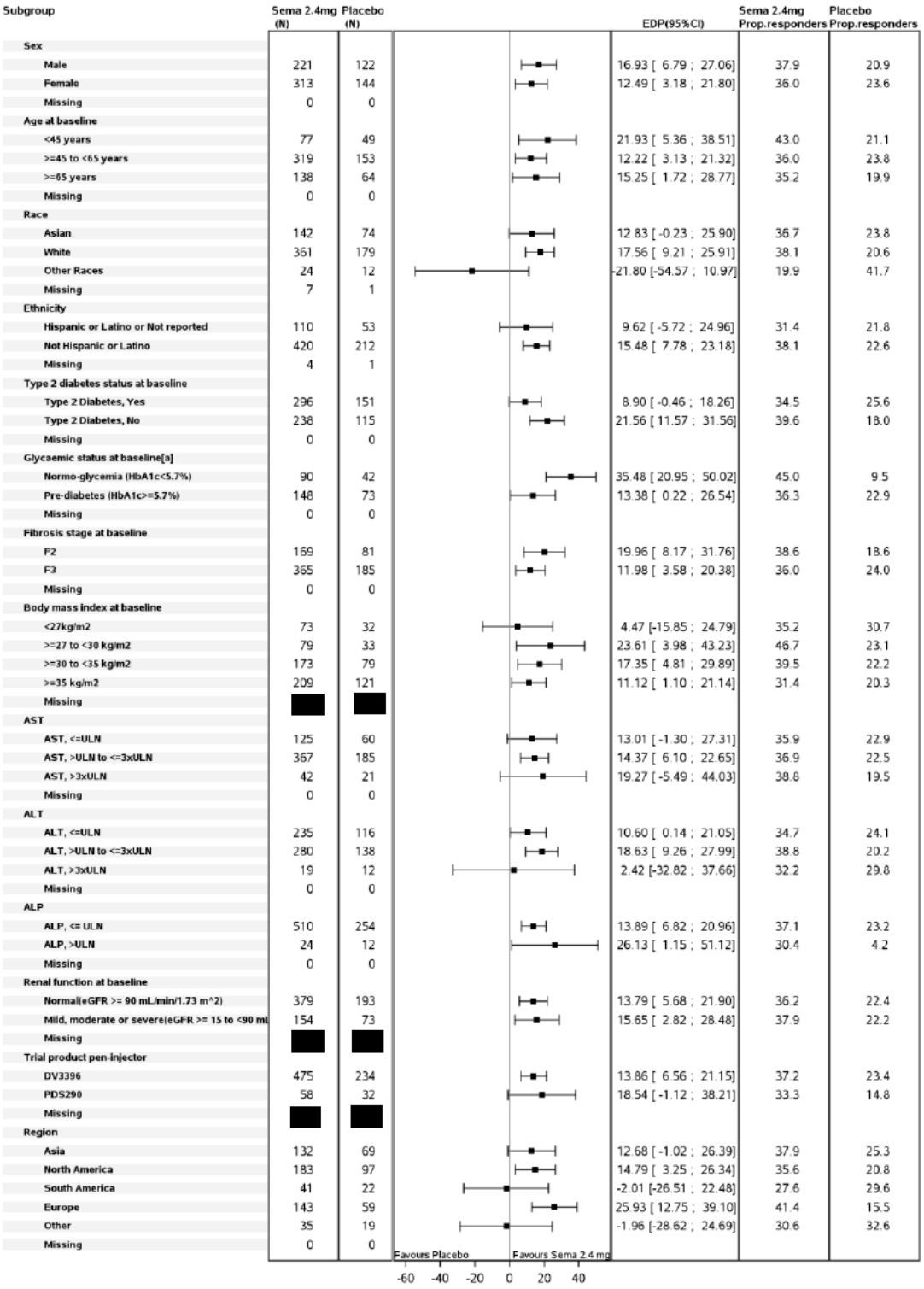
6.1.16 Resolution of steatohepatitis and no worsening of liver fibrosis by subgroups - Absolute difference - MI based on unconditional reference - forest plot - in-trial (72 weeks) - full analysis set (interim) - Trial 4553



a. The analyses included those without T2D at baseline. Unstratified CMH test. Missing data in any treatment group will be handled by MI that is informed by data from placebo subjects. Subjects who experience a liver-related clinical event before the week 72 visit will be handled as non-responders. Resolution of steatohepatitis is defined as a NAS of 0-1 for inflammation, 0 for ballooning and any value for steatosis according to NASH CRN. No worsening of liver fibrosis is defined as no increase in fibrosis score. Fibrosis is graded on the NASH CRN fibrosis scale from 0-4. AST: Aspartate Aminotransferase. ALT: Alanine Aminotransferase.
ALP: Alkaline Phosphatase, T2D: type 2 diabetes.

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6.1.17 Improvement in liver fibrosis and no worsening of steatohepatitis by subgroups - Absolute difference - MI based on unconditional reference - forest plot - in-trial (72 weeks) - full analysis set (interim) - Trial 4553



a: The analyses included those without T2D at baseline. Unstratified CMH test. Missing data in any treatment group will be handled by MI that is informed by data from placebo subjects. Subjects who experience a liver-related clinical event before the week 72 visit will be handled as non-responders. Improvement in fibrosis is defined as >= 1 grade improvement on the NASH CRN fibrosis scale. No worsening of steatohepatitis is defined as no increase from baseline in NAS score for ballooning, inflammation or steatosis. CI: Confidence interval, CMH: Cochran-Mantel-Haenszel, EDP: Estimated difference in responder proportions, N: Number of subjects, Prop. Responders %: proportion of responders in percentage, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, ALP: Alkaline Phosphatase, T2D: type 2 diabetes.

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6.1.18 Primary endpoints by dose at week 20 - summary - in-trial (72 weeks) - full analysis set (interim) - trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Number of subjects	534	266
Dose	499	254
Resolution of steatohepatitis and no worsening of liver fibrosis		
Not on trial product	15(3.0)	10(3.9)
Week 72		
Yes	5 (33.3)	5 (50.0)
No	6 (40.0)	4 (40.0)
Missing	4 (26.7)	1 (10.0)
Dose < 1.7 mg	56(11.2)	9(3.5)
Week 72		
Yes	37 (66.1)	5 (55.6)
No	13 (23.2)	3 (33.3)
Missing	6 (10.7)	1 (11.1)
Dose = 1.7 mg	59(11.8)	23(9.1)
Week 72		
Yes	34 (57.6)	9 (39.1)
No	19 (32.2)	12 (52.2)
Missing	6 (10.2)	2 (8.7)
Dose = 2.4 mg	369(73.9)	212(83.5)
Week 72		
Yes	232 (62.9)	57 (26.9)
No	109 (29.5)	126 (59.4)
Missing	28 (7.6)	29 (13.7)

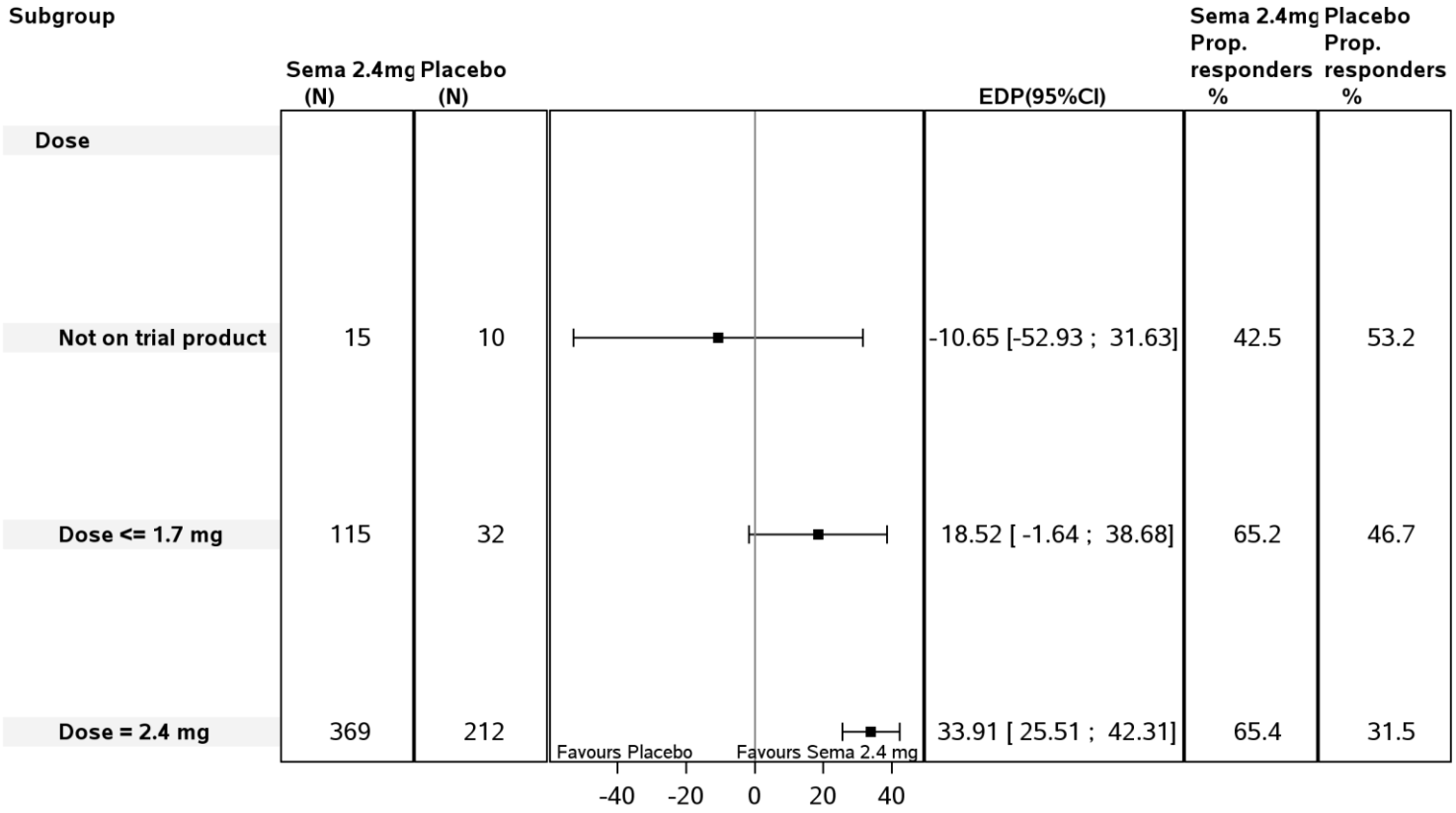
N: Number of subjects, %: Percentage of subjects.

Primary endpoints by dose at week 20 - summary - in-trial (72 weeks) - full analysis set (interim) - trial 4553

	Sema 2.4 mg N (%)	Placebo N (%)
Improvement in liver fibrosis and no worsening of steatohepatitis		
Not on trial product	15(3.0)	10(3.9)
Week 72		
Yes	2 (13.3)	3 (30.0)
No	9 (60.0)	6 (60.0)
Missing	4 (26.7)	1 (10.0)
Dose < 1.7 mg	56(11.2)	9(3.5)
Week 72		
Yes	24 (42.9)	4 (44.4)
No	26 (46.4)	4 (44.4)
Missing	6 (10.7)	1 (11.1)
Dose = 1.7 mg	59(11.8)	23(9.1)
Week 72		
Yes	18 (30.5)	2 (8.7)
No	35 (59.3)	19 (82.6)
Missing	6 (10.2)	2 (8.7)
Dose = 2.4 mg	369(73.9)	212(83.5)
Week 72		
Yes	135 (36.6)	41 (19.3)
No	206 (55.8)	142 (67.0)
Missing	28 (7.6)	29 (13.7)

N: Number of subjects, %: Percentage of subjects.

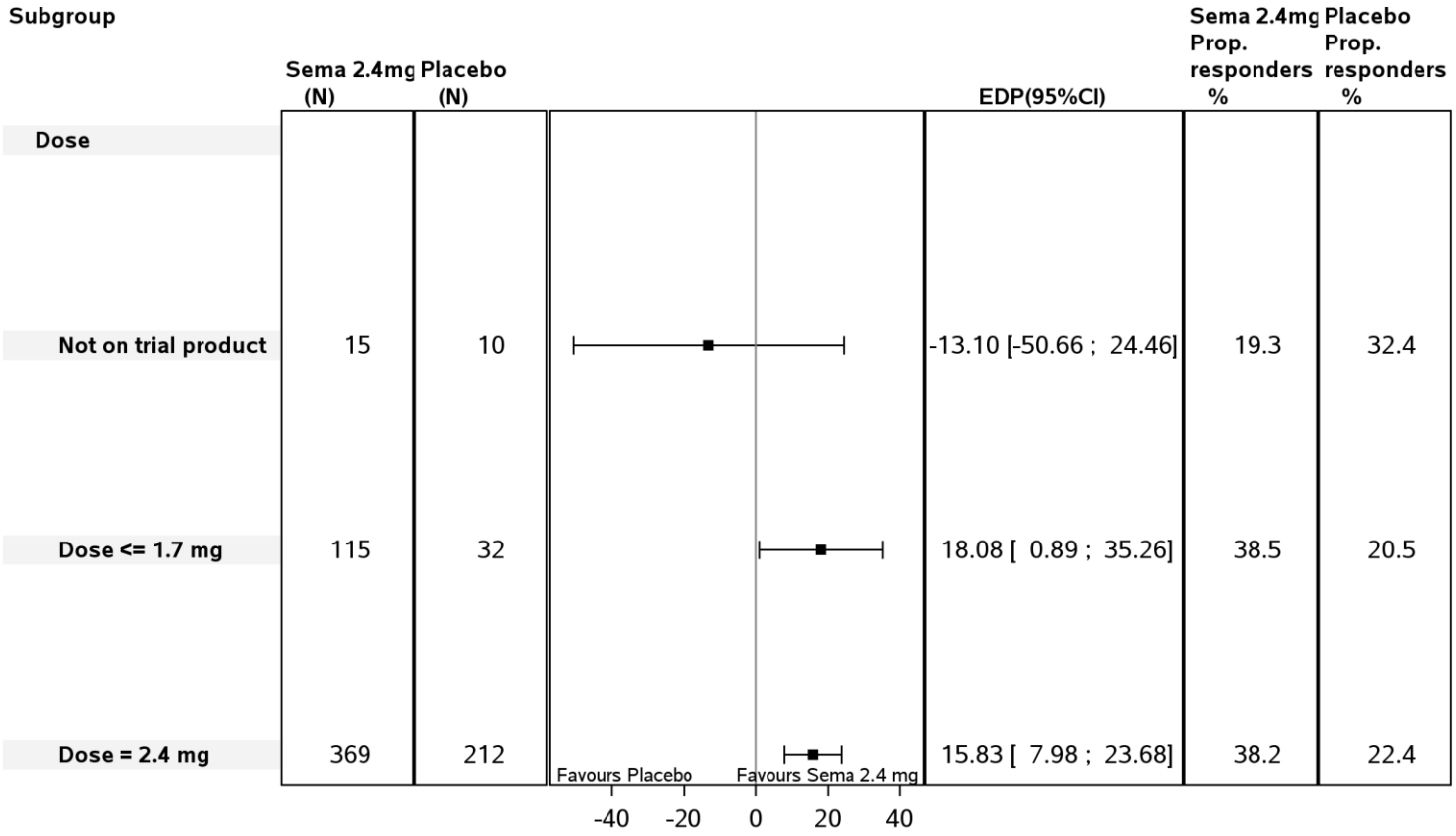
6.1.19 Resolution of steatohepatitis and no worsening of liver fibrosis by dose at week 20 - Absolute difference - MI based on unconditional reference - forest plot - in-trial (72 weeks) - full analysis set (interim) - trial 4553



Unstratified CMH test. Missing data in any treatment group will be handled by MI that is informed by data from placebo subjects. Subjects who experience a liver-related clinical event before the week 72 visit will be handled as non-responders. No worsening of liver fibrosis is defined as no increase in fibrosis score. Fibrosis is graded on the NASH CRN fibrosis scale from 0-4. Resolution of steatohepatitis is defined as a NAS of 0-1 for inflammation, 0 for ballooning and any value for steatosis according to NASH CRN. CI: Confidence interval, CMH: Cochran-Mantel-Haenszel, EDP: Estimated difference in responder proportions, N: Number of subjects, Prop. Responders %: proportion of responders in percentage.

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6.1.20 Improvement in liver fibrosis and no worsening of steatohepatitis by dose at week 20 - Absolute difference - MI based on unconditional reference - forest plot - in-trial (72 weeks) - full analysis set (interim) - trial 4553



Unstratified CMH test. Missing data in any treatment group will be handled by MI that is informed by data from placebo subjects. Subjects who experience a liver-related clinical event before the week 72 visit will be handled as non-responders. Improvement in fibrosis is defined as >= 1 grade improvement on the NASH CRN fibrosis scale. No worsening of steatohepatitis is defined as no increase from baseline in NAS score for ballooning, inflammation or steatosis. CI: Confidence interval, CMH: Cochran-Mantel-Haenszel, EDP: Estimated difference in responder proportions, N: Number of subjects, Prop. Responders %: proportion of responders in percentage.

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ウゴービ皮下注
非アルコール性脂肪肝炎（NASH）

2.7.3.6 付録
2.4296 試験における F2 及び F3 の被験者のデータに基づく事後解析

ノボ ノルディスク ファーマ株式会社

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6.2 Trial 4296 - F2-F3 efficacy analysis

6.2.1 Subjects disposition - overview - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N (%)	Sema 0.2 mg OD N (%)	Sema 0.4 mg OD N (%)	Placebo N (%)	Total N (%)
Randomised	80	78	82	80	320
Excluded subjects with fibrosis stage 1 at baseline	23 (28.8)	19 (24.4)	26 (31.7)	22 (27.5)	90 (28.1)
Included subjects with fibrosis stage 2 or 3 at baseline	57 (71.3)	59 (75.6)	56 (68.3)	58 (72.5)	230 (71.9)
Exposed subjects with fibrosis stage 2 or 3 at baseline	57 (71.3)	59 (75.6)	55 (67.1)	58 (72.5)	229 (71.6)
Analysis sets					
Full analysis set subjects with fibrosis stage 2 or 3 at baseline	57 (100)	59 (100)	56 (100)	58 (100)	230 (100)
Completed treatment [1]	53 (93.0)	48 (81.4)	51 (91.1)	53 (91.4)	205 (89.1)
With evaluable biopsy at week 72	52 (91.2)	46 (78.0)	48 (85.7)	51 (87.9)	197 (85.7)
Without evaluable biopsy at week 72	1 (1.8)	2 (3.4)	3 (5.4)	2 (3.4)	8 (3.5)
Premature treatment discontinuation	4 (7.0)	11 (18.6)	5 (8.9)	5 (8.6)	25 (10.9)
With evaluable biopsy at week 72	2 (3.5)	3 (5.1)	2 (3.6)	2 (3.4)	9 (3.9)
Without evaluable biopsy at week 72	2 (3.5)	8 (13.6)	3 (5.4)	3 (5.2)	16 (7.0)
Primary reason	4 (7.0)	11 (18.6)	4 (7.1)	5 (8.6)	24 (10.4)
Adverse event	2 (3.5)	10 (16.9)	1 (1.8)	3 (5.2)	16 (7.0)
Violation of inclusion and/or exclusion criteria	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Intention of becoming pregnant	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Participation in another clinical trial [2]	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Code break	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Surgical treatment for obesity	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Treatment with other GLP-1 receptor agonists, SGLT-2 inhibitors or bolus (fast-acting) insulin	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Lost to follow-up	0 (0.0)	0 (0.0)	1 (1.8)	1 (1.7)	2 (0.9)
Pregnancy	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Withdrawal of consent	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Other	1 (1.8)	0 (0.0)	1 (1.8)	1 (1.7)	3 (1.3)

[1]: subjects who completed treatment with trial product according to the end-of-trial form; [2]: simultaneous participation in any other clinical trial receiving an investigational medicinal product; [3]: subjects who attended the final scheduled visit. N: number of subjects; %: proportion of randomised subjects, OD: Once daily.

Subjects disposition - overview - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N (%)	Sema 0.2 mg OD N (%)	Sema 0.4 mg OD N (%)	Placebo N (%)	Total N (%)
Trial completers excluding deaths [3]	55 (96.5)	54 (91.5)	53 (94.6)	56 (96.6)	218 (94.8)
Completed treatment	53 (93.0)	48 (81.4)	51 (91.1)	53 (91.4)	205 (89.1)
Discontinued treatment	2 (3.5)	6 (10.2)	2 (3.6)	3 (5.2)	13 (5.7)
Withdrawal from trial or death	2 (3.5)	5 (8.5)	3 (5.4)	2 (3.4)	12 (5.2)
Primary reason					
Withdrawal by subject	1 (1.8)	5 (8.5)	1 (1.8)	1 (1.7)	8 (3.5)
Lost to follow-up	1 (1.8)	0 (0.0)	2 (3.6)	1 (1.7)	4 (1.7)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

[1]: subjects who completed treatment with trial product according to the end-of-trial form; [2]: simultaneous participation in any other clinical trial receiving an investigational medicinal product; [3]: subjects who attended the final scheduled visit. N: number of subjects; %: proportion of randomised subjects, OD: Once daily.

6.2.2 Demographics and baseline characteristics for categorical variables – summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
	N (%)	N (%)	N (%)	N (%)	N (%)
Number of subjects	57	59	56	58	230
Age group (years)					
18<= to <45	14 (24.6)	3 (5.1)	9 (16.1)	9 (15.5)	35 (15.2)
45<= to <65	28 (49.1)	40 (67.8)	36 (64.3)	39 (67.2)	143 (62.2)
65<=	15 (26.3)	16 (27.1)	11 (19.6)	10 (17.2)	52 (22.6)
Sex					
Female	35 (61.4)	41 (69.5)	32 (57.1)	35 (60.3)	143 (62.2)
Male	22 (38.6)	18 (30.5)	24 (42.9)	23 (39.7)	87 (37.8)
Race					
American Indian Or Alaska Native	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Asian	9 (15.8)	9 (15.3)	9 (16.1)	8 (13.8)	35 (15.2)
Black Or African American	1 (1.8)	1 (1.7)	0 (0.0)	0 (0.0)	2 (0.9)
Native Hawaiian or Other Pacific Islander	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
White	43 (75.4)	44 (74.6)	44 (78.6)	45 (77.6)	176 (76.5)
Other	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
N/A	4 (7.0)	5 (8.5)	2 (3.6)	4 (6.9)	15 (6.5)
Ethnicity					
Hispanic Or Latino	7 (12.3)	6 (10.2)	9 (16.1)	8 (13.8)	30 (13.0)
Not Hispanic Or Latino	46 (80.7)	48 (81.4)	45 (80.4)	46 (79.3)	185 (80.4)
N/A	4 (7.0)	5 (8.5)	2 (3.6)	4 (6.9)	15 (6.5)
Region					
Europe	29 (50.9)	33 (55.9)	27 (48.2)	26 (44.8)	115 (50.0)
North America	19 (33.3)	19 (32.2)	20 (35.7)	26 (44.8)	84 (36.5)
Japan	9 (15.8)	7 (11.9)	9 (16.1)	6 (10.3)	31 (13.5)
BMI group (kg/m^2)					
<25	1 (1.8)	0 (0.0)	2 (3.6)	1 (1.7)	4 (1.7)
25<= to <30	11 (19.3)	16 (27.1)	14 (25.0)	9 (15.5)	50 (21.7)
30<= to <35	16 (28.1)	17 (28.8)	18 (32.1)	17 (29.3)	68 (29.6)
35<=	29 (50.9)	26 (44.1)	22 (39.3)	31 (53.4)	108 (47.0)

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, N/A: Not Available, NAS: NASH activity score, SAF: Steatosis, Activity and Fibrosis, NFS: NAFLD Fibrosis Score, eGFR: Estimated glomerular filtration rate, FIB-4: Fibrosis-4.

Demographics and baseline characteristics for categorical variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
	N (%)	N (%)	N (%)	N (%)	N (%)
Type 2 diabetes					
Yes	36 (63.2)	41 (69.5)	34 (60.7)	39 (67.2)	150 (65.2)
No	21 (36.8)	18 (30.5)	22 (39.3)	19 (32.8)	80 (34.8)
Hypoglycaemic awareness					
Never	7 (12.3)	12 (20.3)	12 (21.4)	6 (10.3)	37 (16.1)
Rarely	4 (7.0)	4 (6.8)	1 (1.8)	2 (3.4)	11 (4.8)
Sometimes	4 (7.0)	2 (3.4)	1 (1.8)	5 (8.6)	12 (5.2)
Often	2 (3.5)	5 (8.5)	4 (7.1)	2 (3.4)	13 (5.7)
Always	19 (33.3)	16 (27.1)	16 (28.6)	24 (41.4)	75 (32.6)
History of gallbladder disease					
Yes	21 (36.8)	10 (16.9)	15 (26.8)	18 (31.0)	64 (27.8)
No	36 (63.2)	49 (83.1)	40 (71.4)	40 (69.0)	165 (71.7)
N/A	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Cholecystectomy					
Yes	13 (22.8)	6 (10.2)	9 (16.1)	12 (20.7)	40 (17.4)
No	44 (77.2)	53 (89.8)	47 (83.9)	46 (79.3)	190 (82.6)
Childbearing potential (only females)					
Yes	6 (10.5)	4 (6.8)	8 (14.3)	6 (10.3)	24 (10.4)
No	29 (50.9)	37 (62.7)	24 (42.9)	29 (50.0)	119 (51.7)
Smoking status					
Current Smoker	10 (17.5)	6 (10.2)	3 (5.4)	6 (10.3)	25 (10.9)
Previous Smoker	14 (24.6)	22 (37.3)	14 (25.0)	20 (34.5)	70 (30.4)
Never Smoked	33 (57.9)	31 (52.5)	39 (69.6)	32 (55.2)	135 (58.7)
Fibrosis stage (0-4)					
0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2	18 (31.6)	18 (30.5)	14 (25.0)	22 (37.9)	72 (31.3)
3	39 (68.4)	41 (69.5)	42 (75.0)	36 (62.1)	158 (68.7)
4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, N/A: Not Available, NAS: NASH activity score, SAF: Steatosis, Activity and Fibrosis, NFS: NAFLD Fibrosis Score, eGFR: Estimated glomerular filtration rate, FIB-4: Fibrosis-4.

Demographics and baseline characteristics for categorical variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
	N (%)	N (%)	N (%)	N (%)	N (%)
Hepatocyte ballooning (0-2)					
0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
1	37 (64.9)	32 (54.2)	35 (62.5)	39 (67.2)	143 (62.2)
2	20 (35.1)	27 (45.8)	21 (37.5)	19 (32.8)	87 (37.8)
Steatosis (0-3)					
0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
1	20 (35.1)	18 (30.5)	27 (48.2)	16 (27.6)	81 (35.2)
2	27 (47.4)	31 (52.5)	17 (30.4)	28 (48.3)	103 (44.8)
3	10 (17.5)	10 (16.9)	12 (21.4)	14 (24.1)	46 (20.0)
Lobular inflammation (0-3)					
0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
1	16 (28.1)	21 (35.6)	20 (35.7)	18 (31.0)	75 (32.6)
2	38 (66.7)	37 (62.7)	31 (55.4)	39 (67.2)	145 (63.0)
3	3 (5.3)	1 (1.7)	5 (8.9)	1 (1.7)	10 (4.3)
Total NAS (0-8)					
0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
4	21 (36.8)	21 (35.6)	25 (44.6)	22 (37.9)	89 (38.7)
5	21 (36.8)	23 (39.0)	19 (33.9)	18 (31.0)	81 (35.2)
6	13 (22.8)	10 (16.9)	9 (16.1)	14 (24.1)	46 (20.0)
7	1 (1.8)	5 (8.5)	2 (3.6)	4 (6.9)	12 (5.2)
8	1 (1.8)	0 (0.0)	1 (1.8)	0 (0.0)	2 (0.9)
Activity component of SAF score (0-4)					
0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
2	12 (21.1)	13 (22.0)	13 (23.2)	15 (25.9)	53 (23.0)
3	29 (50.9)	27 (45.8)	29 (51.8)	27 (46.6)	112 (48.7)
4	16 (28.1)	19 (32.2)	14 (25.0)	16 (27.6)	65 (28.3)

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, N/A: Not Available, NAS: NASH activity score, SAF: Steatosis, Activity and Fibrosis, NFS: NAFLD Fibrosis Score, eGFR: Estimated glomerular filtration rate, FIB-4: Fibrosis-4.

Demographics and baseline characteristics for categorical variables – summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
	N (%)	N (%)	N (%)	N (%)	N (%)
Classification of FIB4					
Fib-4 < 1.30	27 (47.4)	13 (22.0)	22 (39.3)	25 (43.1)	87 (37.8)
1.30 <= Fib-4 < 2.67	21 (36.8)	29 (49.2)	26 (46.4)	23 (39.7)	99 (43.0)
2.67 <= Fib-4	7 (12.3)	11 (18.6)	7 (12.5)	7 (12.1)	32 (13.9)
N/A	2 (3.5)	6 (10.2)	1 (1.8)	3 (5.2)	12 (5.2)
Classification of NFS					
NFS < -1.455	16 (28.1)	7 (11.9)	11 (19.6)	12 (20.7)	46 (20.0)
-1.455 <= NFS < 0.676	23 (40.4)	33 (55.9)	32 (57.1)	34 (58.6)	122 (53.0)
0.676 <= NFS	16 (28.1)	13 (22.0)	12 (21.4)	9 (15.5)	50 (21.7)
N/A	2 (3.5)	6 (10.2)	1 (1.8)	3 (5.2)	12 (5.2)
Classification of eGFR-CKD (mL/min/1.73m2)					
<30	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
30<= to <60	2 (3.5)	1 (1.7)	0 (0.0)	4 (6.9)	7 (3.0)
60<= to <90	18 (31.6)	25 (42.4)	13 (23.2)	10 (17.2)	66 (28.7)
90<=	37 (64.9)	33 (55.9)	43 (76.8)	44 (75.9)	157 (68.3)

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, N/A: Not Available, NAS: NASH activity score, SAF: Steatosis, Activity and Fibrosis, NFS: NAFLD Fibrosis Score, eGFR: Estimated glomerular filtration rate, FIB-4: Fibrosis-4.

6.2.3 Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Number of subjects	57	59	56	58	230
Age (years)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	54.9 (12.4)	60.0 (8.0)	55.6 (10.6)	53.6 (11.6)	56.1 (10.9)
Median (IQR)	58.0 (45.0;65.0)	59.0 (55.0;65.0)	55.0 (48.0;64.0)	55.0 (48.0;62.0)	57.5 (49.0;64.0)
Min ; Max	26.0; 75.0	38.0; 75.0	33.0; 75.0	22.0; 73.0	22.0; 75.0
Duration of Diabetes (years)					
N (%)	36 (63.2)	41 (69.5)	34 (60.7)	39 (67.2)	150 (65.2)
Mean (SD)	8.8 (5.6)	6.8 (6.2)	7.8 (8.0)	6.4 (6.0)	7.4 (6.5)
Median (IQR)	9.2 (5.0;11.4)	5.3 (3.0;8.4)	4.6 (2.4;10.5)	4.4 (2.1;10.5)	5.6 (2.6;10.6)
Min ; Max	0.0; 27.4	0.2; 25.5	0.0; 30.6	0.1; 23.7	0.0; 30.6
AUDIT score					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	1.4 (1.8)	1.5 (1.7)	1.6 (2.1)	1.2 (1.6)	1.4 (1.8)
Median (IQR)	1.0 (0.0;2.0)	1.0 (0.0;3.0)	0.5 (0.0;3.0)	1.0 (0.0;2.0)	1.0 (0.0;2.0)
Min ; Max	0.0; 7.0	0.0; 6.0	0.0; 8.0	0.0; 9.0	0.0; 9.0

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Weight-Related Parameters					
BMI (kg/m^2)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	35.9 (6.8)	35.0 (6.1)	34.5 (7.1)	35.8 (6.4)	35.3 (6.6)
Median (IQR)	35.4 (30.5;40.6)	34.6 (29.9;38.9)	32.8 (29.7;38.3)	35.7 (31.1;40.4)	34.5 (30.2;39.1)
Min ; Max	24.8; 51.3	25.1; 56.2	23.8; 57.9	24.5; 51.8	23.8; 57.9
Body Weight (kg)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	97.1 (21.6)	94.4 (22.5)	94.9 (21.0)	99.4 (21.8)	96.4 (21.7)
Median (IQR)	95.7 (82.0;108.8)	95.8 (75.2;108.0)	94.5 (78.0;107.9)	97.9 (82.1;111.0)	96.0 (80.2;108.6)
Min ; Max	56.1; 148.1	59.8; 162.3	55.0; 154.9	62.0; 150.0	55.0; 162.3
Height (m)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	1.6 (0.1)	1.6 (0.1)	1.7 (0.1)	1.7 (0.1)	1.6 (0.1)
Median (IQR)	1.6 (1.6;1.7)	1.6 (1.5;1.7)	1.7 (1.6;1.7)	1.6 (1.6;1.7)	1.6 (1.6;1.7)
Min ; Max	1.4; 1.9	1.4; 1.9	1.5; 1.9	1.5; 1.9	1.4; 1.9
Waist Circumference (cm)					
N (%)	56 (98.2)	58 (98.3)	56 (100.0)	57 (98.3)	227 (98.7)
Mean (SD)	114.6 (14.2)	111.4 (15.6)	110.5 (14.1)	114.3 (14.8)	112.7 (14.7)
Median (IQR)	113.0 (104.0;124.0	111.5 (98.0;121.0)	110.0 (101.8;119.3	114.0 (103.0;124.5	111.8 (103.0;122.2
Min ; Max	91.6; 149.3	86.0; 154.0	83.0; 147.3	86.0; 148.7	83.0; 154.0
Histology					
NAFLD Activity Score Calculated					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	4.9 (0.9)	5.0 (0.9)	4.8 (0.9)	5.0 (1.0)	4.9 (0.9)
Median (IQR)	5.0 (4.0;6.0)	5.0 (4.0;6.0)	5.0 (4.0;5.0)	5.0 (4.0;6.0)	5.0 (4.0;6.0)
Min ; Max	4.0; 8.0	4.0; 7.0	4.0; 8.0	4.0; 7.0	4.0; 8.0

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Fibroscan					
Liver Steatosis Fibroscan (dB/m)					
N (%)	27 (47.4)	29 (49.2)	25 (44.6)	31 (53.4)	112 (48.7)
Mean (SD)	321.5 (45.1)	343.2 (58.6)	327.8 (53.5)	345.5 (35.4)	335.2 (49.0)
Median (IQR)	324.0 (295.0;344.0	360.0 (317.0;394.0	340.0 (297.0;345.0	347.0 (326.0;373.0	341.0 (306.5;372.5
Min ; Max	214.0; 400.0	211.0; 400.0	199.0; 400.0	249.0; 400.0	199.0; 400.0
Liver Stiffness Fibroscan (kPa)					
N (%)	37 (64.9)	41 (69.5)	35 (62.5)	38 (65.5)	151 (65.7)
Mean (SD)	12.8 (6.8)	13.7 (5.5)	15.3 (11.8)	10.2 (3.9)	13.0 (7.6)
Geom. Mean (CV)	11.5 (76.9)	12.8 (68.0)	12.4 (93.7)	9.0 (92.8)	11.3 (85.0)
Median (IQR)	11.7 (8.0;15.3)	11.4 (9.8;18.2)	11.9 (8.0;16.1)	10.2 (7.9;12.8)	10.9 (8.6;15.3)
Min ; Max	5.6; 35.3	6.6; 30.1	2.4; 54.7	0.8; 17.8	0.8; 54.7

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Liver Enzymes					
Alanine Aminotransferase (U/L)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	68 (40)	60 (28)	66 (39)	65 (43)	65 (38)
Geom. Mean (CV)	58 (88.0)	53 (78.0)	57 (84.8)	55 (89.0)	56 (84.8)
Median (IQR)	59 (41;82)	53 (38;75)	60 (39;84)	55 (38;70)	55 (39;77)
Min ; Max	15; 222	13; 132	18; 199	16; 222	13; 222
Aspartate Aminotransferase (U/L)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	52 (23)	49 (22)	54 (29)	51 (34)	51 (27)
Geom. Mean (CV)	47 (77.6)	45 (72.3)	48 (77.9)	44 (85.0)	46 (78.2)
Median (IQR)	48 (34;69)	46 (31;61)	47 (33;66)	44 (30;60)	46 (31;63)
Min ; Max	14; 108	16; 135	21; 158	14; 229	14; 229
Gamma-glutamyltransferase (U/L)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	78 (62)	99 (133)	91 (86)	90 (117)	90 (104)
Geom. Mean (CV)	64 (90.6)	67 (108.1)	67 (105.4)	64 (101.9)	65 (101.4)
Median (IQR)	57 (41;90)	59 (39;105)	58 (41;105)	56 (38;92)	57 (39;97)
Min ; Max	18; 371	21; 905	19; 374	24; 739	18; 905

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Liver Synthesis Function					
Albumin (g/L)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	43 (3)	43 (3)	43 (3)	43 (3)	43 (3)
Geom. Mean (CV)	43 (27.3)	43 (26.2)	43 (26.1)	43 (25.8)	43 (26.3)
Median (IQR)	43 (41;45)	43 (42;45)	42 (41;44)	43 (41;45)	43 (41;45)
Min ; Max	35; 49	35; 50	34; 50	37; 50	34; 50
Albumin (g/dL)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	4.3 (0.3)	4.3 (0.3)	4.3 (0.3)	4.3 (0.3)	4.3 (0.3)
Geom. Mean (CV)	4.3 (27.3)	4.3 (26.2)	4.3 (26.1)	4.3 (25.8)	4.3 (26.3)
Median (IQR)	4.3 (4.1;4.5)	4.3 (4.2;4.5)	4.2 (4.1;4.4)	4.3 (4.1;4.5)	4.3 (4.1;4.5)
Min ; Max	3.5; 4.9	3.5; 5.0	3.4; 5.0	3.7; 5.0	3.4; 5.0
INR (ratio)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	1.10 (0.26)	1.07 (0.13)	1.18 (0.59)	1.08 (0.13)	1.11 (0.33)
Geom. Mean (CV)	1.08 (43.4)	1.06 (34.5)	1.12 (52.9)	1.07 (34.5)	1.08 (43.0)
Median (IQR)	1.04 (0.99;1.12)	1.06 (0.98;1.09)	1.06 (1.01;1.17)	1.05 (1.00;1.14)	1.06 (1.00;1.14)
Min ; Max	0.89; 2.60	0.86; 1.75	0.92; 5.37	0.88; 1.59	0.86; 5.37

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Exploratory Biomarkers					
CK 18 Fragments M30 (U/L)					
N (%)	57 (100.0)	59 (100.0)	55 (98.2)	58 (100.0)	229 (99.6)
Mean (SD)	653 (396)	568 (327)	990 (1221)	712 (599)	727 (730)
Geom. Mean (CV)	555 (89.1)	484 (89.8)	695 (106.1)	532 (110.0)	559 (100.1)
Median (IQR)	592 (351;848)	524 (289;736)	700 (405;996)	535 (322;836)	566 (352;840)
Min ; Max	170; 2201	79; 1699	216; 7654	41; 2871	41; 7654
CK 18 Fragments M65 (U/L)					
N (%)	57 (100.0)	59 (100.0)	55 (98.2)	58 (100.0)	229 (99.6)
Mean (SD)	1268 (763)	1133 (741)	1449 (957)	1371 (1190)	1303 (931)
Geom. Mean (CV)	1100 (84.1)	977 (83.2)	1220 (88.3)	1057 (100.1)	1083 (89.5)
Median (IQR)	1145 (901;1512)	959 (728;1373)	1170 (778;1626)	983 (700;1373)	1065 (767;1495)
Min ; Max	372; 5145	330; 4296	268; 4544	187; 5349	187; 5349
Fibroblast Growth Factor 21 Measurement (pg/mL)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	806.2 (669.4)	912.8 (1213.2)	700.2 (586.8)	796.2 (632.9)	805.2 (818.8)
Geom. Mean (CV)	603.4 (110.7)	591.5 (117.0)	529.0 (104.9)	621.5 (103.7)	585.8 (109.1)
Median (IQR)	565.3 (380.4;963.8	507.6 (312.9;1055.	475.2 (327.4;871.5	648.8 (411.2;1006.	556.3 (357.9;971.1
Min ; Max	31.3; 3313.0	117.1; 8057.0	92.4; 2624.0	101.5; 4213.0	31.3; 8057.0
N<LLOQ ; N>ULOQ	1; 0	0; 0	0; 0	0; 0	1; 0
IL-1R Antagonist (pg/mL)					
N (%)	57 (100.0)	57 (96.6)	55 (98.2)	57 (98.3)	226 (98.3)
Mean (SD)	1235 (1291)	897 (508)	952 (678)	1171 (734)	1065 (862)
Geom. Mean (CV)	939 (96.2)	785 (81.5)	785 (92.4)	968 (95.1)	866 (92.0)
Median (IQR)	773 (600;1234)	726 (580;1082)	743 (503;1236)	994 (624;1478)	788 (588;1272)
Min ; Max	376; 7800	301; 2664	254; 4364	229; 3472	229; 7800
Monocyte Chemotactic Protein 1 (MCP-1) (pg/mL)					
N (%)	57 (100.0)	59 (100.0)	55 (98.2)	58 (100.0)	229 (99.6)
Mean (SD)	381.0 (113.6)	385.2 (138.5)	417.3 (194.5)	417.2 (180.3)	400.0 (159.5)

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Geom. Mean (CV)	364.5 (59.5)	363.5 (63.7)	385.7 (69.1)	386.7 (68.3)	374.8 (65.2)
Median (IQR)	346.2 (302.9;455.1	360.5 (288.2;463.3	381.5 (307.9;497.2	396.2 (283.9;472.6	369.8 (295.2;472.6
Min ; Max	159.6; 679.5	175.1; 806.7	110.6; 1471.5	185.7; 1215.6	110.6; 1471.5

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Serum Enhanced Liver Fibrosis					
N (%)	57 (100.0)	58 (98.3)	55 (98.2)	57 (98.3)	227 (98.7)
Mean (SD)	9.9 (1.0)	10.0 (0.8)	10.1 (1.0)	9.8 (1.0)	9.9 (0.9)
Median (IQR)	9.8 (9.2;10.5)	9.9 (9.4;10.5)	10.2 (9.5;10.8)	9.7 (9.2;10.3)	9.8 (9.3;10.5)
Min ; Max	7.8; 12.6	8.3; 12.1	8.0; 12.6	7.9; 12.8	7.8; 12.8

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Glucose Metabolism By Diabetes Type					
Fasting Plasma Glucose (mmol/L) - NON-T2D					
N (%)	20 (35.1)	18 (30.5)	22 (39.3)	19 (32.8)	79 (34.3)
Mean (SD)	5.41 (0.65)	5.99 (1.42)	5.72 (0.73)	6.01 (1.46)	5.77 (1.11)
Median (IQR)	5.46 (4.79;5.86)	5.78 (4.94;6.68)	5.63 (5.11;6.34)	5.63 (5.19;6.18)	5.62 (5.09;6.16)
Min ; Max	4.34; 6.65	4.37; 10.26	4.78; 7.04	4.81; 11.25	4.34; 11.25
Fasting Plasma Glucose (mmol/L) - T2D					
N (%)	35 (61.4)	40 (67.8)	34 (60.7)	39 (67.2)	148 (64.3)
Mean (SD)	8.76 (2.49)	7.56 (2.01)	8.08 (2.85)	8.53 (2.36)	8.22 (2.45)
Median (IQR)	8.13 (6.83;10.69)	7.18 (6.23;8.73)	7.69 (5.68;9.50)	7.62 (6.82;9.80)	7.53 (6.48;9.52)
Min ; Max	5.54; 15.98	4.76; 12.27	4.86; 17.18	5.35; 14.65	4.76; 17.18
Glucagon (pg/mL) - NON-T2D					
N (%)	21 (36.8)	18 (30.5)	21 (37.5)	18 (31.0)	78 (33.9)
Mean (SD)	28 (14)	28 (16)	21 (11)	26 (20)	26 (15)
Geom. Mean (CV)	25 (77.8)	24 (89.3)	19 (79.5)	20 (113.0)	22 (90.8)
Median (IQR)	23 (18;34)	27 (14;40)	16 (14;25)	19 (11;36)	20 (15;33)
Min ; Max	9; 62	10; 61	6; 58	3; 78	3; 78
N<LLOQ ; N>ULOQ	0; 0	0; 0	0; 0	1; 0	1; 0
Glucagon (pg/mL) - T2D					
N (%)	35 (61.4)	40 (67.8)	34 (60.7)	38 (65.5)	147 (63.9)
Mean (SD)	38 (25)	34 (36)	37 (25)	37 (27)	37 (29)
Geom. Mean (CV)	32 (88.1)	26 (100.0)	30 (98.0)	29 (106.4)	29 (98.4)
Median (IQR)	32 (20;41)	25 (18;40)	30 (21;50)	29 (21;53)	30 (19;45)
Min ; Max	9; 125	3; 240	8; 111	6; 140	3; 240
N<LLOQ ; N>ULOQ	0; 0	1; 0	0; 0	0; 0	1; 0

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
HOMA Insulin Resistance Calculated - NON-T2D					
N (%)	20 (35.1)	18 (30.5)	20 (35.7)	19 (32.8)	77 (33.5)
Mean (SD)	5.36 (1.81)	8.14 (6.71)	6.19 (4.45)	9.72 (9.74)	7.30 (6.42)
Geom. Mean (CV)	5.08 (63.6)	6.40 (99.0)	5.15 (90.7)	6.85 (113.2)	5.79 (94.1)
Median (IQR)	5.12 (4.15;6.34)	5.72 (3.70;10.87)	5.20 (3.26;6.51)	5.61 (4.27;11.80)	5.29 (3.86;7.89)
Min ; Max	2.63; 10.20	2.34; 29.24	1.74; 21.11	1.89; 38.62	1.74; 38.62
HOMA Insulin Resistance Calculated - T2D					
N (%)	34 (59.6)	39 (66.1)	33 (58.9)	37 (63.8)	143 (62.2)
Mean (SD)	11.52 (6.83)	12.20 (19.55)	8.63 (5.83)	14.97 (14.00)	11.93 (13.25)
Geom. Mean (CV)	10.01 (82.7)	7.64 (111.3)	6.92 (100.4)	11.05 (106.8)	8.76 (103.5)
Median (IQR)	9.01 (7.30;13.24)	5.85 (4.47;12.32)	8.61 (4.28;10.20)	9.85 (6.53;16.15)	8.70 (5.18;13.24)
Min ; Max	3.92; 34.04	1.80; 95.67	1.60; 27.86	2.43; 70.68	1.60; 95.67
HbA1c (%) - NON-T2D					
N (%)	21 (36.8)	18 (30.5)	22 (39.3)	19 (32.8)	80 (34.8)
Mean (SD)	5.7 (0.4)	5.9 (0.5)	5.7 (0.4)	5.7 (0.8)	5.8 (0.5)
Median (IQR)	5.6 (5.4;6.0)	5.7 (5.6;6.1)	5.7 (5.5;5.9)	5.7 (5.4;5.9)	5.7 (5.5;5.9)
Min ; Max	5.2; 6.7	5.2; 7.2	4.9; 6.6	4.4; 8.4	4.4; 8.4
HbA1c (%) - T2D					
N (%)	36 (63.2)	41 (69.5)	34 (60.7)	39 (67.2)	150 (65.2)
Mean (SD)	7.4 (1.2)	7.0 (0.9)	7.2 (1.2)	7.3 (1.2)	7.2 (1.2)
Median (IQR)	7.3 (6.6;8.2)	6.8 (6.4;7.5)	7.1 (6.1;8.2)	6.9 (6.4;8.1)	7.0 (6.4;7.9)
Min ; Max	5.5; 10.6	5.6; 9.5	5.2; 10.0	5.5; 10.3	5.2; 10.6
HbA1c (mmol/mol) - NON-T2D					
N (%)	21 (36.8)	18 (30.5)	22 (39.3)	19 (32.8)	80 (34.8)
Mean (SD)	39.3 (4.5)	40.4 (5.5)	39.0 (4.3)	39.1 (8.5)	39.4 (5.8)
Median (IQR)	37.7 (35.5;42.1)	38.8 (37.7;43.2)	38.8 (36.6;41.0)	38.8 (35.5;41.0)	38.8 (36.6;41.0)
Min ; Max	33.3; 49.7	33.3; 55.2	30.1; 48.6	24.6; 68.3	24.6; 68.3

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
HbA1c (mmol/mol) - T2D					
N (%)	36 (63.2)	41 (69.5)	34 (60.7)	39 (67.2)	150 (65.2)
Mean (SD)	57.7 (13.2)	53.3 (10.2)	54.8 (13.6)	56.3 (13.6)	55.5 (12.6)
Median (IQR)	55.7 (48.6;65.6)	50.8 (46.5;58.5)	53.6 (43.2;66.1)	51.9 (46.5;65.0)	53.0 (46.5;62.8)
Min ; Max	36.6; 92.4	37.7; 80.3	33.3; 85.8	36.6; 89.1	33.3; 92.4

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Cardiovascular Risk Factors					
Calculated LDL-cholesterol (mmol/L)					
N (%)	53 (93.0)	54 (91.5)	54 (96.4)	57 (98.3)	218 (94.8)
Mean (SD)	2.83 (1.10)	2.86 (0.99)	2.82 (0.87)	2.91 (0.97)	2.86 (0.98)
Median (IQR)	2.72 (2.14;3.47)	2.80 (2.06;3.65)	2.82 (2.27;3.46)	2.92 (2.23;3.59)	2.82 (2.16;3.53)
Min ; Max	1.00; 6.64	0.65; 4.71	0.72; 5.45	0.73; 6.07	0.65; 6.64
Calculated LDL-cholesterol serum (mg/dL)					
N (%)	53 (93.0)	54 (91.5)	54 (96.4)	57 (98.3)	218 (94.8)
Mean (SD)	109.19 (42.50)	110.28 (38.19)	109.04 (33.55)	112.43 (37.60)	110.27 (37.82)
Median (IQR)	105.02 (82.63;133.9	108.11 (79.54;140.9	108.88 (87.64;133.5	112.74 (86.10;138.6	108.88 (83.40;136.2
Min ; Max	38.61; 256.37	25.10; 181.85	27.80; 210.42	28.19; 234.36	25.10; 256.37
Combined LDL cholesterol (mg/dL)					
N (%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)	226 (98.3)
Mean (SD)	108.40 (41.91)	109.58 (38.34)	110.92 (37.43)	113.03 (37.55)	110.51 (38.60)
Geom. Mean (CV)	100.61 (70.1)	101.77 (71.8)	104.52 (66.1)	106.24 (67.5)	103.29 (68.7)
Median (IQR)	103.47 (82.63;133.9	109.27 (79.54;137.0	108.88 (87.45;133.7	112.93 (86.10;139.7	108.88 (83.78;136.2
Min ; Max	38.61; 256.37	25.10; 181.85	27.80; 239.38	28.19; 234.36	25.10; 256.37
Combined LDL cholesterol (mmol/L)					
N (%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)	226 (98.3)
Mean (SD)	2.81 (1.09)	2.84 (0.99)	2.87 (0.97)	2.93 (0.97)	2.86 (1.00)
Geom. Mean (CV)	2.61 (70.1)	2.64 (71.8)	2.71 (66.1)	2.75 (67.5)	2.68 (68.7)
Median (IQR)	2.68 (2.14;3.47)	2.83 (2.06;3.55)	2.82 (2.27;3.47)	2.93 (2.23;3.62)	2.82 (2.17;3.53)
Min ; Max	1.00; 6.64	0.65; 4.71	0.72; 6.20	0.73; 6.07	0.65; 6.64

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Diastolic Blood Pressure (mmHg)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	80 (10)	82 (10)	81 (9)	81 (10)	81 (10)
Median (IQR)	80 (75;86)	81 (75;88)	81 (75;85)	82 (75;86)	81 (75;86)
Min ; Max	60; 99	68; 107	63; 103	57; 107	57; 107
Free Fatty Acids (mmol/L)					
N (%)	54 (94.7)	57 (96.6)	54 (96.4)	56 (96.6)	221 (96.1)
Mean (SD)	0.68 (0.27)	0.68 (0.36)	0.59 (0.21)	0.52 (0.28)	0.62 (0.29)
Geom. Mean (CV)	0.63 (69.5)	0.59 (82.2)	0.55 (67.4)	0.44 (88.2)	0.55 (79.5)
Median (IQR)	0.63 (0.51;0.86)	0.63 (0.44;0.78)	0.53 (0.46;0.71)	0.45 (0.30;0.71)	0.58 (0.42;0.76)
Min ; Max	0.29; 1.61	0.17; 2.01	0.21; 1.15	0.09; 1.40	0.09; 2.01
HDL Cholesterol (mg/dL)					
N (%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)	226 (98.3)
Mean (SD)	45.08 (11.97)	46.89 (10.60)	43.90 (10.85)	45.13 (11.55)	45.26 (11.23)
Geom. Mean (CV)	43.61 (54.3)	45.76 (50.0)	42.75 (50.6)	43.77 (52.9)	43.97 (52.0)
Median (IQR)	43.24 (36.29;54.44	43.63 (40.15;53.67	42.86 (37.45;48.46	41.51 (35.91;52.12	42.86 (37.07;51.35
Min ; Max	23.55; 83.78	26.25; 69.88	28.19; 88.42	27.80; 72.59	23.55; 88.42
HDL Cholesterol (mmol/L)					
N (%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)	226 (98.3)
Mean (SD)	1.17 (0.31)	1.21 (0.27)	1.14 (0.28)	1.17 (0.30)	1.17 (0.29)
Geom. Mean (CV)	1.13 (54.3)	1.19 (50.0)	1.11 (50.6)	1.13 (52.9)	1.14 (52.0)
Median (IQR)	1.12 (0.94;1.41)	1.13 (1.04;1.39)	1.11 (0.97;1.26)	1.08 (0.93;1.35)	1.11 (0.96;1.33)
Min ; Max	0.61; 2.17	0.68; 1.81	0.73; 2.29	0.72; 1.88	0.61; 2.29
LDL Cholesterol (mg/dL)					
N (%)	2 (3.5)	3 (5.1)	2 (3.6)	1 (1.7)	8 (3.5)
Mean (SD)	87.6 (3.8)	96.9 (47.6)	161.8 (109.8)	147.5 (.)	117.1 (59.1)
Geom. Mean (CV)	87.6 (21.1)	87.3 (90.3)	141.9 (104.6)	147.5 ( )	105.3 (80.2)
Median (IQR)	87.6 (84.9;90.3)	109.3 (44.4;137.1)	161.8 (84.2;239.4)	147.5 (147.5;147.5	99.8 (84.6;142.3)
Min ; Max	84.9; 90.3	44.4; 137.1	84.2; 239.4	147.5; 147.5	44.4; 239.4

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
LDL Cholesterol (mmol/L)					
N (%)	2 (3.5)	3 (5.1)	2 (3.6)	1 (1.7)	8 (3.5)
Mean (SD)	2.3 (0.1)	2.5 (1.2)	4.2 (2.8)	3.8 (.)	3.0 (1.5)
Geom. Mean (CV)	2.3 (21.1)	2.3 (90.3)	3.7 (104.6)	3.8 ( )	2.7 (80.2)
Median (IQR)	2.3 (2.2;2.3)	2.8 (1.2;3.6)	4.2 (2.2;6.2)	3.8 (3.8;3.8)	2.6 (2.2;3.7)
Min ; Max	2.2; 2.3	1.2; 3.6	2.2; 6.2	3.8; 3.8	1.2; 6.2
Systolic Blood Pressure (mmHg)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	133 (15)	137 (19)	133 (14)	130 (15)	133 (16)
Median (IQR)	135 (122;141)	135 (124;147)	130 (124;139)	130 (121;140)	133 (124;141)
Min ; Max	95; 164	104; 190	102; 163	93; 160	93; 190
Total Cholesterol (mg/dL)					
N (%)	56 (98.2)	57 (96.6)	56 (100.0)	58 (100.0)	227 (98.7)
Mean (SD)	186.1 (45.5)	190.6 (43.6)	186.7 (46.5)	194.5 (45.6)	189.5 (45.1)
Geom. Mean (CV)	180.5 (53.8)	185.4 (52.6)	181.0 (54.1)	189.2 (52.3)	184.0 (53.1)
Median (IQR)	185.3 (157.9;217.0	190.3 (154.8;224.3	184.9 (158.7;212.4	196.1 (159.1;226.3	190.3 (157.9;216.6
Min ; Max	93.4; 320.1	91.1; 274.9	73.4; 358.3	86.9; 352.5	73.4; 358.3
Total Cholesterol (mmol/L)					
N (%)	56 (98.2)	57 (96.6)	56 (100.0)	58 (100.0)	227 (98.7)
Mean (SD)	4.8 (1.2)	4.9 (1.1)	4.8 (1.2)	5.0 (1.2)	4.9 (1.2)
Geom. Mean (CV)	4.7 (53.8)	4.8 (52.6)	4.7 (54.1)	4.9 (52.3)	4.8 (53.1)
Median (IQR)	4.8 (4.1;5.6)	4.9 (4.0;5.8)	4.8 (4.1;5.5)	5.1 (4.1;5.9)	4.9 (4.1;5.6)
Min ; Max	2.4; 8.3	2.4; 7.1	1.9; 9.3	2.3; 9.1	1.9; 9.3
Triglycerides (mg/dL)					
N (%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)	226 (98.3)
Mean (SD)	170.2 (79.1)	180.8 (94.6)	169.5 (113.4)	187.5 (84.5)	177.1 (93.5)
Geom. Mean (CV)	155.6 (71.7)	162.9 (74.3)	148.1 (78.5)	168.8 (79.0)	158.8 (76.0)
Median (IQR)	150.4 (114.8;204.7	148.6 (118.4;213.6	146.0 (100.6;179.8	178.9 (134.4;216.3	153.5 (117.5;208.3
Min ; Max	71.2; 424.5	68.5; 506.4	61.4; 729.8	33.8; 454.8	33.8; 729.8

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Triglycerides (mmol/L)					
N (%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)	226 (98.3)
Mean (SD)	1.9 (0.9)	2.0 (1.1)	1.9 (1.3)	2.1 (0.9)	2.0 (1.1)
Geom. Mean (CV)	1.7 (71.7)	1.8 (74.3)	1.7 (78.5)	1.9 (79.0)	1.8 (76.0)
Median (IQR)	1.7 (1.3;2.3)	1.7 (1.3;2.4)	1.6 (1.1;2.0)	2.0 (1.5;2.4)	1.7 (1.3;2.3)
Min ; Max	0.8; 4.8	0.8; 5.7	0.7; 8.2	0.4; 5.1	0.4; 8.2
VLDL Cholesterol (mg/dL)					
N (%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)	226 (98.3)
Mean (SD)	32.64 (13.71)	34.17 (15.06)	31.91 (17.35)	36.35 (15.76)	33.80 (15.53)
Geom. Mean (CV)	30.17 (69.6)	31.40 (70.9)	28.62 (75.1)	32.84 (78.4)	30.74 (73.7)
Median (IQR)	29.34 (22.39;40.15	28.96 (23.17;41.70	28.38 (19.69;35.14	34.94 (26.25;42.08	29.92 (22.78;40.54
Min ; Max	13.90; 74.13	13.51; 79.15	11.97; 104.63	6.56; 73.75	6.56; 104.63
VLDL Cholesterol (mmol/L)					
N (%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)	226 (98.3)
Mean (SD)	0.85 (0.36)	0.89 (0.39)	0.83 (0.45)	0.94 (0.41)	0.88 (0.40)
Geom. Mean (CV)	0.78 (69.6)	0.81 (70.9)	0.74 (75.1)	0.85 (78.4)	0.80 (73.7)
Median (IQR)	0.76 (0.58;1.04)	0.75 (0.60;1.08)	0.74 (0.51;0.91)	0.91 (0.68;1.09)	0.78 (0.59;1.05)
Min ; Max	0.36; 1.92	0.35; 2.05	0.31; 2.71	0.17; 1.91	0.17; 2.71
hsCRP (mg/L)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	6.9 (7.5)	6.9 (8.0)	6.0 (7.9)	7.5 (9.2)	6.8 (8.1)
Geom. Mean (CV)	3.9 (149.3)	3.7 (152.2)	3.5 (131.7)	3.9 (152.5)	3.8 (146.1)
Median (IQR)	3.9 (2.0;9.4)	3.8 (1.9;8.5)	3.1 (1.8;8.3)	3.7 (1.8;11.2)	3.7 (1.9;9.0)
Min ; Max	0.2; 35.3	0.2; 33.7	0.5; 41.6	0.3; 39.9	0.2; 41.6

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Safety Parameters					
Alkaline Phosphatase (U/L)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	82 (25)	93 (30)	88 (42)	87 (33)	87 (33)
Geom. Mean (CV)	78 (59.4)	88 (60.8)	81 (65.6)	83 (59.7)	83 (61.6)
Median (IQR)	77 (67;95)	91 (69;105)	78 (63;101)	82 (69;94)	82 (66;100)
Min ; Max	34; 172	50; 181	44; 323	43; 253	34; 323
Amylase (U/L)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	56 (26)	67 (52)	52 (21)	58 (23)	58 (33)
Geom. Mean (CV)	51 (75.9)	57 (82.0)	48 (71.2)	54 (67.5)	52 (74.7)
Median (IQR)	52 (36;69)	48 (40;82)	48 (35;66)	54 (40;72)	52 (39;70)
Min ; Max	17; 130	24; 345	20; 102	25; 129	17; 345
Basophils Blood-Absolute (10^9/L)					
N (%)	55 (96.5)	54 (91.5)	55 (98.2)	55 (94.8)	219 (95.2)
Mean (SD)	0.06 (0.03)	0.05 (0.03)	0.06 (0.03)	0.06 (0.03)	0.06 (0.03)
Median (IQR)	0.05 (0.04;0.07)	0.05 (0.03;0.07)	0.06 (0.04;0.07)	0.06 (0.04;0.08)	0.05 (0.04;0.07)
Min ; Max	0.00; 0.18	0.00; 0.19	0.00; 0.15	0.01; 0.14	0.00; 0.19
Calcitonin (ng/L)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	2.0 (2.1)	1.8 (2.2)	2.2 (2.4)	2.2 (3.5)	2.0 (2.6)
Geom. Mean (CV)	1.4 (100.8)	1.3 (96.4)	1.5 (103.4)	1.4 (104.0)	1.4 (100.9)
Median (IQR)	1.0 (1.0;1.0)	1.0 (1.0;1.0)	1.0 (1.0;2.3)	1.0 (1.0;1.0)	1.0 (1.0;1.0)
Min ; Max	1.0; 9.2	1.0; 12.2	1.0; 11.6	1.0; 21.8	1.0; 21.8
N<LLOQ ; N>ULOQ	45; 0	48; 0	39; 0	45; 0	177; 0
Calcium (mg/dL)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	9.43 (0.40)	9.41 (0.35)	9.31 (0.39)	9.39 (0.35)	9.39 (0.37)
Geom. Mean (CV)	9.42 (20.8)	9.40 (19.3)	9.30 (20.4)	9.38 (19.4)	9.38 (20.0)
Median (IQR)	9.40 (9.16;9.72)	9.44 (9.16;9.64)	9.30 (9.04;9.52)	9.38 (9.12;9.60)	9.38 (9.12;9.60)

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Min ; Max	8.64; 10.48	8.68; 10.24	8.64; 10.48	8.72; 10.20	8.64; 10.48

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Calcium (mmol/L)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	2.36 (0.10)	2.35 (0.09)	2.33 (0.10)	2.35 (0.09)	2.35 (0.09)
Geom. Mean (CV)	2.36 (20.8)	2.35 (19.3)	2.33 (20.4)	2.35 (19.4)	2.34 (20.0)
Median (IQR)	2.35 (2.29;2.43)	2.36 (2.29;2.41)	2.33 (2.26;2.38)	2.35 (2.28;2.40)	2.35 (2.28;2.40)
Min ; Max	2.16; 2.62	2.17; 2.56	2.16; 2.62	2.18; 2.55	2.16; 2.62
Creatine Kinase (U/L)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	127 (99)	135 (87)	119 (86)	133 (115)	129 (97)
Geom. Mean (CV)	103 (94.4)	116 (83.3)	97 (93.8)	108 (90.6)	106 (90.6)
Median (IQR)	104 (68;145)	113 (76;156)	93 (61;141)	101 (66;154)	102 (68;149)
Min ; Max	31; 611	45; 547	27; 435	41; 757	27; 757
Creatinine (mg/dL)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	0.8 (0.2)	0.8 (0.2)	0.7 (0.2)	0.8 (0.2)	0.8 (0.2)
Geom. Mean (CV)	0.8 (51.2)	0.7 (52.8)	0.7 (49.5)	0.7 (53.8)	0.7 (51.8)
Median (IQR)	0.8 (0.6;0.9)	0.7 (0.6;0.8)	0.7 (0.6;0.8)	0.7 (0.6;0.9)	0.7 (0.6;0.9)
Min ; Max	0.5; 1.4	0.3; 1.4	0.4; 1.1	0.4; 1.3	0.3; 1.4
Creatinine (umol/L)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	68.2 (16.3)	66.9 (16.5)	63.8 (14.3)	67.6 (17.3)	66.6 (16.1)
Geom. Mean (CV)	66.4 (51.2)	64.9 (52.8)	62.3 (49.5)	65.5 (53.8)	64.8 (51.8)
Median (IQR)	68.6 (55.2;77.9)	65.9 (55.2;74.9)	63.7 (54.5;69.4)	65.6 (54.7;78.7)	65.5 (54.8;75.3)
Min ; Max	39.9; 120.0	29.2; 125.3	37.5; 100.4	35.3; 118.4	29.2; 125.3
Direct Bilirubin (umol/L)					
N (%)	39 (68.4)	39 (66.1)	39 (69.6)	41 (70.7)	158 (68.7)
Mean (SD)	4.6 (2.2)	4.4 (1.5)	5.0 (2.1)	3.8 (1.6)	4.4 (1.9)
Median (IQR)	4.0 (3.0;5.7)	4.1 (3.3;5.3)	4.3 (3.5;5.8)	3.5 (2.5;4.7)	3.9 (3.1;5.3)
Min ; Max	0.9; 10.6	2.2; 8.1	2.5; 10.7	1.8; 7.8	0.9; 10.7
N<LLOQ ; N>ULOQ	1; 0	0; 0	0; 0	0; 0	1; 0

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Direct Bilirubin Serum (mg/dL)					
N (%)	39 (68.4)	39 (66.1)	39 (69.6)	41 (70.7)	158 (68.7)
Mean (SD)	0.3 (0.1)	0.3 (0.1)	0.3 (0.1)	0.2 (0.1)	0.3 (0.1)
Median (IQR)	0.2 (0.2;0.3)	0.2 (0.2;0.3)	0.3 (0.2;0.3)	0.2 (0.1;0.3)	0.2 (0.2;0.3)
Min ; Max	0.1; 0.6	0.1; 0.5	0.1; 0.6	0.1; 0.5	0.1; 0.6
N<LLOQ ; N>ULOQ	1; 0	0; 0	0; 0	0; 0	1; 0
Eosinophils Blood-Absolute (10^9/L)					
N (%)	55 (96.5)	54 (91.5)	55 (98.2)	55 (94.8)	219 (95.2)
Mean (SD)	0.18 (0.11)	0.16 (0.11)	0.17 (0.10)	0.16 (0.12)	0.17 (0.11)
Median (IQR)	0.14 (0.11;0.22)	0.14 (0.09;0.20)	0.14 (0.10;0.22)	0.12 (0.08;0.20)	0.14 (0.10;0.21)
Min ; Max	0.04; 0.58	0.01; 0.68	0.01; 0.52	0.02; 0.62	0.01; 0.68
Erythrocytes (10^12/L)					
N (%)	55 (96.5)	54 (91.5)	55 (98.2)	55 (94.8)	219 (95.2)
Mean (SD)	4.67 (0.46)	4.58 (0.36)	4.70 (0.51)	4.67 (0.41)	4.66 (0.44)
Median (IQR)	4.71 (4.32;5.03)	4.57 (4.34;4.77)	4.67 (4.37;5.07)	4.68 (4.41;4.88)	4.64 (4.38;4.92)
Min ; Max	3.74; 5.54	3.81; 5.59	3.70; 6.36	3.59; 5.73	3.59; 6.36
Ferritin serum (ug/L)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	194.64 (158.87)	206.71 (211.61)	220.47 (265.60)	208.52 (214.51)	207.52 (214.46)
Geom. Mean (CV)	137.26 (126.9)	147.48 (109.5)	119.53 (149.2)	127.36 (141.8)	132.65 (132.1)
Median (IQR)	159.54 (94.23;260.7	134.93 (82.16;253.1	146.90 (42.81;254.4	126.70 (71.19;276.0	145.65 (77.74;260.7
Min ; Max	9.63; 898.44	36.66; 1278.67	12.96; 1237.19	6.98; 1252.71	6.98; 1278.67
Haematocrit in Blood (%)					
N (%)	55 (96.5)	54 (91.5)	55 (98.2)	55 (94.8)	219 (95.2)
Mean (SD)	44.4 (4.4)	43.5 (3.1)	44.4 (5.1)	43.7 (4.1)	44.0 (4.2)
Geom. Mean (CV)	44.2 (32.8)	43.4 (27.3)	44.1 (34.6)	43.5 (31.4)	43.8 (31.8)
Median (IQR)	45.5 (40.2;47.4)	43.8 (41.5;45.1)	43.3 (41.1;48.3)	43.5 (41.4;46.1)	44.1 (41.1;46.9)
Min ; Max	33.9; 53.8	36.9; 50.2	33.7; 60.9	35.1; 53.1	33.7; 60.9

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Haemoglobin in Blood (g/dL)					
N (%)	55 (96.5)	54 (91.5)	55 (98.2)	55 (94.8)	219 (95.2)
Mean (SD)	13.9 (1.6)	13.8 (1.1)	13.9 (1.7)	13.7 (1.4)	13.8 (1.5)
Geom. Mean (CV)	13.8 (36.2)	13.8 (29.1)	13.8 (36.5)	13.6 (33.0)	13.7 (34.0)
Median (IQR)	14.2 (13.0;15.1)	13.8 (13.1;14.5)	14.0 (12.8;14.9)	13.9 (12.8;14.8)	14.0 (12.9;14.7)
Min ; Max	9.3; 16.8	11.6; 16.1	9.8; 19.1	10.8; 16.3	9.3; 19.1
Haemoglobin in Blood (mmol/L)					
N (%)	55 (96.5)	54 (91.5)	55 (98.2)	55 (94.8)	219 (95.2)
Mean (SD)	8.6 (1.0)	8.6 (0.7)	8.6 (1.1)	8.5 (0.9)	8.6 (0.9)
Geom. Mean (CV)	8.6 (36.2)	8.5 (29.1)	8.6 (36.5)	8.4 (33.0)	8.5 (34.0)
Median (IQR)	8.8 (8.1;9.4)	8.6 (8.1;9.0)	8.7 (7.9;9.2)	8.6 (7.9;9.2)	8.7 (8.0;9.1)
Min ; Max	5.8; 10.4	7.2; 10.0	6.1; 11.8	6.7; 10.1	5.8; 11.8
Insulin Serum-Fasting (pmol/L)					
N (%)	54 (94.7)	57 (96.6)	54 (96.4)	57 (98.3)	222 (96.5)
Mean (SD)	196 (126)	216 (240)	201 (285)	287 (321)	226 (256)
Geom. Mean (CV)	170 (79.6)	165 (95.3)	150 (95.8)	209 (104.3)	172 (95.3)
Median (IQR)	161 (123;200)	156 (106;220)	154 (90;200)	187 (131;322)	164 (115;228)
Min ; Max	64; 651	59; 1393	44; 2153	55; 2153	44; 2153
N<LLOQ ; N>ULOQ	0; 0	0; 0	0; 1	0; 1	0; 2
Insulin Serum-Fasting (uIU/mL)					
N (%)	54 (94.7)	57 (96.6)	54 (96.4)	57 (98.3)	222 (96.5)
Mean (SD)	27 (17)	30 (33)	28 (40)	40 (45)	31 (35)
Geom. Mean (CV)	24 (79.6)	23 (95.3)	21 (95.8)	29 (104.3)	24 (95.3)
Median (IQR)	22 (17;28)	22 (15;30)	21 (12;28)	26 (18;45)	23 (16;32)
Min ; Max	9; 90	8; 193	6; 298	8; 298	6; 298
N<LLOQ ; N>ULOQ	0; 0	0; 0	0; 1	0; 1	0; 2
Leukocytes (10^9/L)					
N (%)	55 (96.5)	54 (91.5)	55 (98.2)	55 (94.8)	219 (95.2)

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Mean (SD)	7.07 (2.24)	6.77 (2.13)	6.58 (1.73)	7.16 (1.86)	6.90 (2.00)
Median (IQR)	6.93 (5.54;8.32)	6.31 (5.35;7.86)	6.60 (5.15;7.61)	7.05 (5.82;8.25)	6.62 (5.42;7.90)
Min ; Max	3.20; 14.54	3.58; 14.08	3.25; 10.72	3.53; 11.00	3.20; 14.54

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Lipase (U/L)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	39 (29)	51 (70)	42 (39)	41 (35)	43 (46)
Geom. Mean (CV)	32 (93.3)	37 (98.9)	33 (100.9)	34 (89.6)	34 (95.6)
Median (IQR)	32 (23;44)	35 (24;51)	32 (24;47)	33 (24;47)	33 (24;48)
Min ; Max	10; 156	10; 440	2; 277	10; 226	2; 440
N<LLOQ ; N>ULOQ	0; 0	0; 0	1; 0	0; 0	1; 0
Lymphocytes Blood - Absolute (10^9/L)					
N (%)	55 (96.5)	54 (91.5)	55 (98.2)	55 (94.8)	219 (95.2)
Mean (SD)	2.26 (0.91)	2.12 (0.63)	2.18 (0.66)	2.10 (0.64)	2.17 (0.72)
Median (IQR)	2.09 (1.68;2.64)	1.95 (1.63;2.45)	2.12 (1.68;2.68)	1.98 (1.51;2.65)	2.03 (1.64;2.64)
Min ; Max	1.09; 5.89	1.30; 4.40	0.84; 4.33	1.03; 3.76	0.84; 5.89
MELD Score Calculated (no unit)					
N (%)	56 (98.2)	59 (100.0)	56 (100.0)	58 (100.0)	229 (99.6)
Mean (SD)	5.8 (2.7)	5.3 (2.3)	6.3 (3.3)	5.0 (2.2)	5.6 (2.7)
Median (IQR)	6.0 (4.0;7.0)	5.0 (4.0;6.0)	6.0 (4.0;8.0)	5.0 (3.0;6.0)	5.0 (4.0;7.0)
Min ; Max	1.0; 14.0	-1.0; 11.0	2.0; 24.0	1.0; 9.0	-1.0; 24.0
Monocytes Blood - Absolute (10^9/L)					
N (%)	55 (96.5)	54 (91.5)	55 (98.2)	55 (94.8)	219 (95.2)
Mean (SD)	0.40 (0.18)	0.41 (0.19)	0.38 (0.12)	0.40 (0.13)	0.40 (0.16)
Median (IQR)	0.38 (0.28;0.50)	0.36 (0.27;0.51)	0.36 (0.30;0.45)	0.37 (0.30;0.48)	0.37 (0.29;0.49)
Min ; Max	0.05; 1.03	0.13; 1.26	0.13; 0.83	0.17; 0.85	0.05; 1.26
Neutrophils Blood-Absolute (10^9/L)					
N (%)	55 (96.5)	54 (91.5)	55 (98.2)	55 (94.8)	219 (95.2)
Mean (SD)	4.17 (1.50)	4.03 (1.77)	3.79 (1.27)	4.43 (1.46)	4.11 (1.52)
Median (IQR)	4.00 (3.17;5.04)	3.55 (2.97;4.54)	3.77 (3.02;4.35)	4.08 (3.29;5.36)	3.87 (3.14;4.74)
Min ; Max	1.47; 9.86	0.89; 10.07	1.39; 7.37	1.88; 7.99	0.89; 10.07

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Potassium (mEq/L)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	4.2 (0.3)	4.3 (0.3)	4.2 (0.3)	4.3 (0.3)	4.2 (0.3)
Geom. Mean (CV)	4.2 (27.8)	4.3 (28.5)	4.2 (28.8)	4.3 (27.9)	4.2 (28.4)
Median (IQR)	4.2 (4.0;4.4)	4.2 (4.1;4.5)	4.2 (4.0;4.4)	4.3 (4.1;4.6)	4.3 (4.0;4.4)
Min ; Max	3.3; 4.8	3.4; 5.0	3.3; 5.0	3.7; 5.0	3.3; 5.0
Potassium (mmol/L)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	4.2 (0.3)	4.3 (0.3)	4.2 (0.3)	4.3 (0.3)	4.2 (0.3)
Geom. Mean (CV)	4.2 (27.8)	4.3 (28.5)	4.2 (28.8)	4.3 (27.9)	4.2 (28.4)
Median (IQR)	4.2 (4.0;4.4)	4.2 (4.1;4.5)	4.2 (4.0;4.4)	4.3 (4.1;4.6)	4.3 (4.0;4.4)
Min ; Max	3.3; 4.8	3.4; 5.0	3.3; 5.0	3.7; 5.0	3.3; 5.0
Pulse (beats/min)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	75 (10)	75 (12)	73 (11)	76 (9)	75 (11)
Median (IQR)	75 (67;82)	75 (66;83)	72 (65;79)	74 (69;82)	74 (67;82)
Min ; Max	52; 97	52; 113	51; 102	62; 105	51; 113
Sodium (mEq/L)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	140 (2)	140 (2)	139 (2)	140 (2)	140 (2)
Geom. Mean (CV)	140 (12.1)	140 (12.9)	139 (11.8)	140 (11.9)	140 (12.2)
Median (IQR)	140 (138;141)	140 (139;142)	140 (139;141)	140 (139;141)	140 (139;141)
Min ; Max	135; 144	132; 144	133; 145	134; 144	132; 145
Sodium (mmol/L)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	140 (2)	140 (2)	139 (2)	140 (2)	140 (2)
Geom. Mean (CV)	140 (12.1)	140 (12.9)	139 (11.8)	140 (11.9)	140 (12.2)
Median (IQR)	140 (138;141)	140 (139;142)	140 (139;141)	140 (139;141)	140 (139;141)
Min ; Max	135; 144	132; 144	133; 145	134; 144	132; 145

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
Thrombocytes (10^9/L)					
N (%)	55 (96.5)	54 (91.5)	55 (98.2)	55 (94.8)	219 (95.2)
Mean (SD)	241 (99)	228 (60)	230 (68)	238 (67)	234 (75)
Median (IQR)	221 (174;272)	233 (181;274)	220 (191;261)	237 (189;270)	228 (186;270)
Min ; Max	122; 668	83; 383	64; 501	138; 419	64; 668
Total Bilirubin (mg/dL)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	0.7 (0.4)	0.7 (0.3)	0.7 (0.4)	0.6 (0.3)	0.7 (0.3)
Geom. Mean (CV)	0.7 (79.4)	0.6 (75.9)	0.7 (73.3)	0.5 (70.2)	0.6 (75.5)
Median (IQR)	0.6 (0.4;1.0)	0.6 (0.5;0.8)	0.7 (0.5;0.8)	0.6 (0.4;0.7)	0.6 (0.4;0.8)
Min ; Max	0.3; 1.9	0.2; 1.7	0.3; 1.9	0.3; 1.5	0.2; 1.9
Total Bilirubin (umol/L)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	12.6 (6.7)	11.3 (5.2)	12.8 (6.3)	10.0 (4.4)	11.7 (5.8)
Geom. Mean (CV)	11.2 (79.4)	10.2 (75.9)	11.6 (73.3)	9.2 (70.2)	10.5 (75.5)
Median (IQR)	10.9 (7.1;16.3)	10.3 (7.7;13.2)	11.4 (8.9;14.0)	9.5 (7.1;12.2)	10.6 (7.6;13.1)
Min ; Max	4.8; 33.0	2.7; 28.3	5.0; 32.3	4.3; 25.8	2.7; 33.0
Urea (mmol/L)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	5.1 (1.6)	5.4 (1.4)	4.7 (1.2)	5.1 (1.6)	5.1 (1.5)
Geom. Mean (CV)	4.9 (58.9)	5.2 (54.9)	4.6 (53.9)	4.8 (59.0)	4.9 (57.1)
Median (IQR)	4.6 (4.0;6.1)	5.2 (4.5;6.3)	4.3 (3.9;5.6)	4.8 (3.8;6.0)	4.8 (4.0;6.0)
Min ; Max	2.6; 10.0	2.3; 8.2	2.7; 7.5	2.8; 9.7	2.3; 10.0
eGFR (mL/min/1.73m2)					
N (%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)	230 (100.0)
Mean (SD)	95 (17)	91 (14)	98 (13)	96 (17)	95 (16)
Geom. Mean (CV)	93 (45.1)	90 (41.6)	98 (38.1)	94 (47.7)	94 (43.7)
Median (IQR)	95 (82;106)	93 (81;101)	98 (90;105)	98 (92;107)	97 (85;104)
Min ; Max	55; 139	51; 133	72; 132	49; 126	49; 139

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

Demographics and baseline characteristics for continuous variables - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo	Total
microRNA-122 (1/uL)					
N (%)	56 (98.2)	59 (100.0)	56 (100.0)	58 (100.0)	229 (99.6)
Mean (SD)	139 (134)	154 (172)	149 (147)	150 (197)	148 (164)
Geom. Mean (CV)	93 (123.3)	86 (150.2)	90 (140.2)	83 (145.8)	88 (139.7)
Median (IQR)	102 (40;176)	88 (46;225)	90 (44;241)	88 (38;181)	89 (43;187)
Min ; Max	16; 680	6; 798	9; 566	7; 1255	6; 1255
Liver Indices					
Fibrosis-4 Score Calculated					
N (%)	55 (96.5)	53 (89.8)	55 (98.2)	55 (94.8)	218 (94.8)
Mean (SD)	1.67 (0.93)	1.89 (0.94)	1.81 (1.19)	1.57 (0.92)	1.73 (1.00)
Geom. Mean (CV)	1.45 (83.7)	1.67 (80.9)	1.56 (83.3)	1.33 (90.0)	1.50 (84.9)
Median (IQR)	1.36 (1.03;2.08)	1.73 (1.34;2.28)	1.50 (1.00;2.25)	1.38 (0.97;1.93)	1.50 (1.04;2.15)
Min ; Max	0.42; 4.78	0.59; 4.49	0.63; 8.05	0.26; 4.94	0.26; 8.05
NAFLD Fibrosis Score Calculated					
N (%)	55 (96.5)	53 (89.8)	55 (98.2)	55 (94.8)	218 (94.8)
Mean (SD)	-0.635 (1.713)	-0.165 (1.122)	-0.503 (1.411)	-0.559 (1.405)	-0.468 (1.432)
Median (IQR)	-0.422 (-1.728;0.80	-0.049 (-0.977;0.43	-0.531 (-1.189;0.49	-0.417 (-1.179;0.39	-0.419 (-1.189;0.53
Min ; Max	-5.258; 2.274	-2.756; 2.279	-4.471; 2.915	-4.797; 2.283	-5.258; 2.915

N: Number of subjects, %: Percentage of subjects, OD: Once daily, BMI: Body mass index, T2D: Type 2 diabetes, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, LLOQ: Lower limit of quantification, ULOQ: Upper limit of quantification, hsCRP: High sensitivity C-reactive protein, NAFLD: Non-alcoholic fatty liver disease, INR: International normalized ratio, IL-1R antagonist: Interleukin-1 receptor agonist protein, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein, MELD: Model For End-Stage Liver Disease, eGFR: Estimated glomerular filtration rate.

6.2.4 Medical history at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N (%)	Sema 0.2 mg OD N (%)	Sema 0.4 mg OD N (%)	Placebo N (%)	Total N (%)
Number of Subjects	57	59	56	58	230
Any illness	36 (63.2)	26 (44.1)	30 (53.6)	28 (48.3)	120 (52.2)
Surgical and medical procedures	23 (40.4)	20 (33.9)	19 (33.9)	16 (27.6)	78 (33.9)
Hysterectomy	4 (7.0)	10 (16.9)	6 (10.7)	6 (10.3)	26 (11.3)
Appendicectomy	5 (8.8)	4 (6.8)	4 (7.1)	2 (3.4)	15 (6.5)
Female sterilisation	4 (7.0)	3 (5.1)	2 (3.6)	2 (3.4)	11 (4.8)
Tonsillectomy	0 (0.0)	3 (5.1)	3 (5.4)	3 (5.2)	9 (3.9)
Large intestinal polypectomy	1 (1.8)	2 (3.4)	1 (1.8)	1 (1.7)	5 (2.2)
Mammoplasty	1 (1.8)	1 (1.7)	2 (3.6)	1 (1.7)	5 (2.2)
Carpal tunnel decompression	1 (1.8)	1 (1.7)	1 (1.8)	1 (1.7)	4 (1.7)
Cataract operation	1 (1.8)	2 (3.4)	1 (1.8)	0 (0.0)	4 (1.7)
Thyroidectomy	2 (3.5)	0 (0.0)	0 (0.0)	1 (1.7)	3 (1.3)
Spinal operation	1 (1.8)	1 (1.7)	0 (0.0)	1 (1.7)	3 (1.3)
Abdominoplasty	1 (1.8)	1 (1.7)	1 (1.8)	0 (0.0)	3 (1.3)
Caesarean section	0 (0.0)	0 (0.0)	1 (1.8)	2 (3.4)	3 (1.3)
Hernia repair	1 (1.8)	1 (1.7)	0 (0.0)	1 (1.7)	3 (1.3)
Knee arthroplasty	1 (1.8)	1 (1.7)	0 (0.0)	1 (1.7)	3 (1.3)
Nasal septal operation	0 (0.0)	1 (1.7)	1 (1.8)	1 (1.7)	3 (1.3)
Polypectomy	1 (1.8)	2 (3.4)	0 (0.0)	0 (0.0)	3 (1.3)
Shoulder arthroplasty	1 (1.8)	2 (3.4)	0 (0.0)	0 (0.0)	3 (1.3)
Umbilical hernia repair	0 (0.0)	0 (0.0)	2 (3.6)	1 (1.7)	3 (1.3)
Oophorectomy	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)	2 (0.9)
Meniscus removal	0 (0.0)	0 (0.0)	1 (1.8)	1 (1.7)	2 (0.9)
Endometrial ablation	1 (1.8)	0 (0.0)	1 (1.8)	0 (0.0)	2 (0.9)
Mass excision	1 (1.8)	1 (1.7)	0 (0.0)	0 (0.0)	2 (0.9)
Meniscus operation	2 (3.5)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.9)
Sinus operation	0 (0.0)	1 (1.7)	1 (1.8)	0 (0.0)	2 (0.9)
Skin neoplasm excision	0 (0.0)	1 (1.7)	1 (1.8)	0 (0.0)	2 (0.9)
Abdominal hernia repair	1 (1.8)	0 (0.0)	0 (0.0)	1 (1.7)	2 (0.9)
Wisdom teeth removal	1 (1.8)	0 (0.0)	0 (0.0)	1 (1.7)	2 (0.9)
Shoulder operation	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Abscess drainage	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Anal fistula repair	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Arterial stent insertion	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)

Table contains events reported as medical history/concomitant illness with resolution prior to screening. MedDRA version 22.1. N: Number of subjects, %: Percentage of subjects, OD: Once daily.

Medical history at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N (%)	Sema 0.2 mg OD N (%)	Sema 0.4 mg OD N (%)	Placebo N (%)	Total N (%)
Arterial therapeutic procedure	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Bone lesion excision	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Breast tumour excision	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Debridement	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Epidermoid cyst excision	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Fracture treatment	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Finger amputation	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Gastric banding	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Haemorrhoid operation	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Intervertebral disc operation	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Neurectomy	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Hysterosalpingo-oophorectomy	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Oesophageal dilation procedure	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Oophorectomy bilateral	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Renal stone removal	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Eventration repair	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Rotator cuff repair	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Salpingectomy	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Salpingo-oophorectomy bilateral	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Colectomy	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Cardiac ablation	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Breast conserving surgery	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Bariatric gastric balloon insertion	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Atrial septal defect repair	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Aortic aneurysm repair	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Spinal laminectomy	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Stent placement	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Sterilisation reversal	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Tenoplasty	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Toe operation	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Transfusion	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Transurethral prostatectomy	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Tumour excision	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Uvulectomy	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Vasectomy	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)

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Medical history at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N (%)	Sema 0.2 mg OD N (%)	Sema 0.4 mg OD N (%)	Placebo N (%)	Total N (%)
Infections and infestations	8 (14.0)	10 (16.9)	7 (12.5)	7 (12.1)	32 (13.9)
Appendicitis	3 (5.3)	2 (3.4)	0 (0.0)	0 (0.0)	5 (2.2)
Herpes zoster	0 (0.0)	2 (3.4)	1 (1.8)	0 (0.0)	3 (1.3)
Pneumonia	1 (1.8)	1 (1.7)	1 (1.8)	0 (0.0)	3 (1.3)
Hepatitis B	0 (0.0)	0 (0.0)	2 (3.6)	1 (1.7)	3 (1.3)
Hepatitis C	1 (1.8)	0 (0.0)	2 (3.6)	0 (0.0)	3 (1.3)
Helicobacter infection	1 (1.8)	0 (0.0)	0 (0.0)	1 (1.7)	2 (0.9)
Tonsillitis	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)	2 (0.9)
Cellulitis	0 (0.0)	2 (3.4)	0 (0.0)	0 (0.0)	2 (0.9)
Urinary tract infection	1 (1.8)	0 (0.0)	0 (0.0)	1 (1.7)	2 (0.9)
Abscess limb	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Furuncle	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Postoperative wound infection	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Kidney infection	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Cytomegalovirus myocarditis	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Diverticulitis	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Staphylococcal infection	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Periorbital cellulitis	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Lyme disease	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Septic shock	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Varicella	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Gastrointestinal disorders	7 (12.3)	7 (11.9)	1 (1.8)	6 (10.3)	21 (9.1)
Large intestine polyp	1 (1.8)	3 (5.1)	0 (0.0)	2 (3.4)	6 (2.6)
Umbilical hernia	1 (1.8)	0 (0.0)	0 (0.0)	2 (3.4)	3 (1.3)
Diarrhoea	1 (1.8)	0 (0.0)	0 (0.0)	1 (1.7)	2 (0.9)
Rectal haemorrhage	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)	2 (0.9)
Diverticulum	0 (0.0)	2 (3.4)	0 (0.0)	0 (0.0)	2 (0.9)
Hernial eventration	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Hiatus hernia	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Nausea	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Inguinal hernia	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Diverticulum intestinal	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Gastrooesophageal reflux disease	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Diarrhoea haemorrhagic	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Anal fistula	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)

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Medical history at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N (%)	Sema 0.2 mg OD N (%)	Sema 0.4 mg OD N (%)	Placebo N (%)	Total N (%)
Abdominal distension	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Splenic artery aneurysm	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Intussusception	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Gastric ulcer	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Abdominal pain upper	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Colitis	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Haemorrhoids	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Constipation	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	5 (8.8)	6 (10.2)	4 (7.1)	4 (6.9)	19 (8.3)
Uterine leiomyoma	0 (0.0)	3 (5.1)	1 (1.8)	1 (1.7)	5 (2.2)
Breast cancer	1 (1.8)	1 (1.7)	0 (0.0)	1 (1.7)	3 (1.3)
Basal cell carcinoma	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Bladder cancer	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Breast cancer in situ	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Cervix carcinoma	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Melanocytic naevus	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Ovarian theca cell tumour	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Pituitary tumour benign	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Rectal neoplasm	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Squamous cell carcinoma of skin	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Skin cancer	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Ovarian cancer	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Investigations	4 (7.0)	5 (8.5)	4 (7.1)	5 (8.6)	18 (7.8)
Transient elastography	2 (3.5)	2 (3.4)	0 (0.0)	2 (3.4)	6 (2.6)
Biopsy liver	1 (1.8)	1 (1.7)	2 (3.6)	1 (1.7)	5 (2.2)
Colonoscopy	0 (0.0)	1 (1.7)	1 (1.8)	2 (3.4)	4 (1.7)
Ultrasound abdomen	1 (1.8)	2 (3.4)	0 (0.0)	0 (0.0)	3 (1.3)
Catheterisation cardiac	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)	2 (0.9)
Arthroscopy	1 (1.8)	0 (0.0)	0 (0.0)	1 (1.7)	2 (0.9)
Cardiac stress test	0 (0.0)	2 (3.4)	0 (0.0)	0 (0.0)	2 (0.9)
Endoscopy gastrointestinal	1 (1.8)	1 (1.7)	0 (0.0)	0 (0.0)	2 (0.9)
Oesophagogastroduodenoscopy	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Laparoscopy	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)

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Medical history at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N (%)	Sema 0.2 mg OD N (%)	Sema 0.4 mg OD N (%)	Placebo N (%)	Total N (%)
Echocardiogram	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Endoscopy	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Spinal X-ray	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Barium swallow	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Biopsy breast	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Biopsy breast normal	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Cyst aspiration	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Diagnostic aspiration	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Reproductive system and breast disorders	4 (7.0)	1 (1.7)	2 (3.6)	5 (8.6)	12 (5.2)
Menorrhagia	1 (1.8)	0 (0.0)	1 (1.8)	2 (3.4)	4 (1.7)
Endometriosis	0 (0.0)	1 (1.7)	1 (1.8)	1 (1.7)	3 (1.3)
Breast enlargement	1 (1.8)	0 (0.0)	0 (0.0)	1 (1.7)	2 (0.9)
Epididymal cyst	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Menstruation irregular	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Ovarian cyst	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Prostatitis	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Uterine polyp	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Musculoskeletal and connective tissue disorders	3 (5.3)	2 (3.4)	1 (1.8)	5 (8.6)	11 (4.8)
Back pain	1 (1.8)	0 (0.0)	0 (0.0)	1 (1.7)	2 (0.9)
Exostosis	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)	2 (0.9)
Intervertebral disc protrusion	1 (1.8)	0 (0.0)	0 (0.0)	1 (1.7)	2 (0.9)
Plantar fasciitis	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Rotator cuff syndrome	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Tendonitis	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Osteoarthritis	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Rheumatic fever	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Dupuytren's contracture	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Renal and urinary disorders	4 (7.0)	2 (3.4)	3 (5.4)	1 (1.7)	10 (4.3)
Nephrolithiasis	3 (5.3)	2 (3.4)	3 (5.4)	1 (1.7)	9 (3.9)
Haematuria	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Psychiatric disorders	2 (3.5)	4 (6.8)	2 (3.6)	1 (1.7)	9 (3.9)
Depression	1 (1.8)	2 (3.4)	1 (1.8)	0 (0.0)	4 (1.7)

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Medical history at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N (%)	Sema 0.2 mg OD N (%)	Sema 0.4 mg OD N (%)	Placebo N (%)	Total N (%)
Suicide attempt	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)	2 (0.9)
Alcohol abuse	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Alcoholism	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Drug dependence	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Insomnia	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Suicidal ideation	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Injury, poisoning and procedural complications	1 (1.8)	3 (5.1)	2 (3.6)	2 (3.4)	8 (3.5)
Ankle fracture	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)	2 (0.9)
Eye injury	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Meniscus injury	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Upper limb fracture	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Radius fracture	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Lower limb fracture	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Foot fracture	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Nervous system disorders	4 (7.0)	1 (1.7)	1 (1.8)	2 (3.4)	8 (3.5)
Carpal tunnel syndrome	0 (0.0)	1 (1.7)	0 (0.0)	1 (1.7)	2 (0.9)
Cerebrovascular accident	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Facial paralysis	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Ischaemic stroke	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Ruptured cerebral aneurysm	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Sciatica	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Syncope	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Transient ischaemic attack	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Paraesthesia	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Cardiac disorders	1 (1.8)	1 (1.7)	2 (3.6)	3 (5.2)	7 (3.0)
Atrial fibrillation	0 (0.0)	0 (0.0)	1 (1.8)	1 (1.7)	2 (0.9)
Acute myocardial infarction	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Left ventricular failure	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Myocardial infarction	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Myocarditis	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Angina pectoris	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Palpitations	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)

Table contains events reported as medical history/concomitant illness with resolution prior to screening. MedDRA version 22.1. N: Number of subjects, %: Percentage of subjects, OD: Once daily.

Medical history at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N (%)	Sema 0.2 mg OD N (%)	Sema 0.4 mg OD N (%)	Placebo N (%)	Total N (%)
Eye disorders	3 (5.3)	3 (5.1)	1 (1.8)	0 (0.0)	7 (3.0)
Cataract	2 (3.5)	1 (1.7)	0 (0.0)	0 (0.0)	3 (1.3)
Retinal detachment	0 (0.0)	2 (3.4)	0 (0.0)	0 (0.0)	2 (0.9)
Endocrine ophthalmopathy	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Vitreous haemorrhage	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Vascular disorders	0 (0.0)	1 (1.7)	3 (5.4)	1 (1.7)	5 (2.2)
Aortic aneurysm	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Deep vein thrombosis	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Orthostatic hypotension	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Phlebitis	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Varicose vein	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Endocrine disorders	1 (1.8)	1 (1.7)	2 (3.6)	0 (0.0)	4 (1.7)
Hyperthyroidism	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Thyroid mass	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Basedow's disease	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Goitre	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Respiratory, thoracic and mediastinal disorders	1 (1.8)	0 (0.0)	2 (3.6)	1 (1.7)	4 (1.7)
Dyspnoea	0 (0.0)	0 (0.0)	1 (1.8)	1 (1.7)	2 (0.9)
Pneumothorax	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Pulmonary hypertension	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Blood and lymphatic system disorders	1 (1.8)	1 (1.7)	1 (1.8)	0 (0.0)	3 (1.3)
Anaemia	1 (1.8)	1 (1.7)	1 (1.8)	0 (0.0)	3 (1.3)
General disorders and administration site conditions	0 (0.0)	1 (1.7)	0 (0.0)	2 (3.4)	3 (1.3)
Non-cardiac chest pain	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Oedema	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Polyp	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Metabolism and nutrition disorders	0 (0.0)	1 (1.7)	1 (1.8)	1 (1.7)	3 (1.3)
Dyslipidaemia	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Gout	0 (0.0)	1 (1.7)	0 (0.0)	0 (0.0)	1 (0.4)
Metabolic acidosis	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)

Table contains events reported as medical history/concomitant illness with resolution prior to screening. MedDRA version 22.1. N: Number of subjects, %: Percentage of subjects, OD: Once daily.

Medical history at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N (%)	Sema 0.2 mg OD N (%)	Sema 0.4 mg OD N (%)	Placebo N (%)	Total N (%)
Congenital, familial and genetic disorders	0 (0.0)	0 (0.0)	1 (1.8)	1 (1.7)	2 (0.9)
Atrial septal defect	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Ectopic kidney	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Immune system disorders	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.4)	2 (0.9)
Drug hypersensitivity	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Sarcoidosis	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Ear and labyrinth disorders	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Vertigo	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	1 (0.4)
Hepatobiliary disorders	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Hepatic cyst	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Pregnancy, puerperium and perinatal conditions	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Gestational diabetes	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Product issues	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Device dislocation	1 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Skin and subcutaneous tissue disorders	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)
Lichen planus	0 (0.0)	0 (0.0)	1 (1.8)	0 (0.0)	1 (0.4)

Table contains events reported as medical history/concomitant illness with resolution prior to screening. MedDRA version 22.1. N: Number of subjects, %: Percentage of subjects, OD: Once daily.

6.2.5 Concomitant illness at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N	(%)	Sema 0.2 mg OD N	(%)	Sema 0.4 mg OD N	(%)	Placebo N	(%)	Total N	(%)
Number of Subjects	57		59		56		58		230	
Any illness	57	(100.0)	59	(100.0)	56	(100.0)	58	(100.0)	230	(100.0)
Hepatobiliary disorders	55	(96.5)	52	(88.1)	53	(94.6)	52	(89.7)	212	(92.2)
Non-alcoholic steatohepatitis	50	(87.7)	48	(81.4)	45	(80.4)	45	(77.6)	188	(81.7)
Hepatic steatosis	8	(14.0)	4	(6.8)	11	(19.6)	8	(13.8)	31	(13.5)
Nonalcoholic fatty liver disease	6	(10.5)	2	(3.4)	4	(7.1)	5	(8.6)	17	(7.4)
Hepatic cyst	2	(3.5)	1	(1.7)	4	(7.1)	1	(1.7)	8	(3.5)
Steatohepatitis	1	(1.8)	0	(0.0)	1	(1.8)	0	(0.0)	2	(0.9)
Hepatomegaly	1	(1.8)	0	(0.0)	1	(1.8)	0	(0.0)	2	(0.9)
Hepatic lesion	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Liver disorder	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Metabolism and nutrition disorders	48	(84.2)	52	(88.1)	49	(87.5)	51	(87.9)	200	(87.0)
Type 2 diabetes mellitus	36	(63.2)	41	(69.5)	34	(60.7)	39	(67.2)	150	(65.2)
Obesity	22	(38.6)	19	(32.2)	16	(28.6)	19	(32.8)	76	(33.0)
Dyslipidaemia	18	(31.6)	16	(27.1)	10	(17.9)	12	(20.7)	56	(24.3)
Hyperlipidaemia	3	(5.3)	12	(20.3)	9	(16.1)	10	(17.2)	34	(14.8)
Hypercholesterolaemia	7	(12.3)	8	(13.6)	10	(17.9)	5	(8.6)	30	(13.0)
Hyperuricaemia	6	(10.5)	2	(3.4)	4	(7.1)	3	(5.2)	15	(6.5)
Vitamin D deficiency	3	(5.3)	3	(5.1)	3	(5.4)	4	(6.9)	13	(5.7)
Hypertriglyceridaemia	2	(3.5)	1	(1.7)	5	(8.9)	2	(3.4)	10	(4.3)
Gout	0	(0.0)	3	(5.1)	2	(3.6)	4	(6.9)	9	(3.9)
Glucose tolerance impaired	2	(3.5)	3	(5.1)	2	(3.6)	0	(0.0)	7	(3.0)
Cardiometabolic syndrome	3	(5.3)	1	(1.7)	1	(1.8)	1	(1.7)	6	(2.6)
Overweight	0	(0.0)	1	(1.7)	1	(1.8)	1	(1.7)	3	(1.3)
Insulin resistance	0	(0.0)	0	(0.0)	2	(3.6)	1	(1.7)	3	(1.3)
Hyperferritinaemia	0	(0.0)	0	(0.0)	0	(0.0)	2	(3.4)	2	(0.9)
Hyperhomocysteinaemia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Iron overload	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Magnesium deficiency	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Vitamin B complex deficiency	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Vitamin B12 deficiency	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Hyperinsulinaemia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Hypercalcaemia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)

Table contains events reported as medical history/concomitant illness either not resolved or resolved after screening. MedDRA version 22.1.
N: Number of subjects, %: Percentage of subjects, OD: Once daily.

Concomitant illness at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N	(%)	Sema 0.2 mg OD N	(%)	Sema 0.4 mg OD N	(%)	Placebo N	(%)	Total N	(%)
Vascular disorders	41	(71.9)	43	(72.9)	34	(60.7)	35	(60.3)	153	(66.5)
Hypertension	37	(64.9)	41	(69.5)	34	(60.7)	31	(53.4)	143	(62.2)
Essential hypertension	3	(5.3)	2	(3.4)	0	(0.0)	2	(3.4)	7	(3.0)
Arteriosclerosis	1	(1.8)	1	(1.7)	0	(0.0)	2	(3.4)	4	(1.7)
Varicose vein	0	(0.0)	1	(1.7)	0	(0.0)	2	(3.4)	3	(1.3)
Peripheral vascular disorder	0	(0.0)	0	(0.0)	1	(1.8)	1	(1.7)	2	(0.9)
Angiopathy	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Diabetic vascular disorder	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Hot flush	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Post thrombotic syndrome	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
White coat hypertension	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Gastrointestinal disorders	27	(47.4)	30	(50.8)	26	(46.4)	28	(48.3)	111	(48.3)
Gastrooesophageal reflux disease	12	(21.1)	15	(25.4)	9	(16.1)	12	(20.7)	48	(20.9)
Gastritis	2	(3.5)	5	(8.5)	4	(7.1)	5	(8.6)	16	(7.0)
Irritable bowel syndrome	2	(3.5)	3	(5.1)	3	(5.4)	4	(6.9)	12	(5.2)
Constipation	5	(8.8)	3	(5.1)	3	(5.4)	1	(1.7)	12	(5.2)
Haemorrhoids	3	(5.3)	2	(3.4)	3	(5.4)	3	(5.2)	11	(4.8)
Chronic gastritis	3	(5.3)	3	(5.1)	3	(5.4)	1	(1.7)	10	(4.3)
Diverticulum	4	(7.0)	3	(5.1)	1	(1.8)	1	(1.7)	9	(3.9)
Hiatus hernia	1	(1.8)	3	(5.1)	2	(3.6)	2	(3.4)	8	(3.5)
Nausea	1	(1.8)	1	(1.7)	2	(3.6)	3	(5.2)	7	(3.0)
Dyspepsia	2	(3.5)	1	(1.7)	2	(3.6)	1	(1.7)	6	(2.6)
Abdominal pain upper	1	(1.8)	1	(1.7)	1	(1.8)	2	(3.4)	5	(2.2)
Gastric ulcer	2	(3.5)	2	(3.4)	1	(1.8)	0	(0.0)	5	(2.2)
Diarrhoea	2	(3.5)	0	(0.0)	2	(3.6)	0	(0.0)	4	(1.7)
Duodenitis	0	(0.0)	1	(1.7)	1	(1.8)	1	(1.7)	3	(1.3)
Abdominal distension	1	(1.8)	1	(1.7)	0	(0.0)	1	(1.7)	3	(1.3)
Colitis	0	(0.0)	1	(1.7)	2	(3.6)	0	(0.0)	3	(1.3)
Large intestine polyp	1	(1.8)	0	(0.0)	0	(0.0)	2	(3.4)	3	(1.3)
Pancreatic steatosis	1	(1.8)	0	(0.0)	1	(1.8)	1	(1.7)	3	(1.3)
Impaired gastric emptying	0	(0.0)	1	(1.7)	1	(1.8)	1	(1.7)	3	(1.3)
Oesophagitis	1	(1.8)	1	(1.7)	0	(0.0)	1	(1.7)	3	(1.3)
Gastric polyps	0	(0.0)	0	(0.0)	1	(1.8)	1	(1.7)	2	(0.9)
Dysphagia	1	(1.8)	1	(1.7)	0	(0.0)	0	(0.0)	2	(0.9)
Diverticulum intestinal	1	(1.8)	1	(1.7)	0	(0.0)	0	(0.0)	2	(0.9)

Table contains events reported as medical history/concomitant illness either not resolved or resolved after screening. MedDRA version 22.1.
N: Number of subjects, %: Percentage of subjects, OD: Once daily.

Concomitant illness at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N	(%)	Sema 0.2 mg OD N	(%)	Sema 0.4 mg OD N	(%)	Placebo N	(%)	Total N	(%)
Coeliac disease	1	(1.8)	0	(0.0)	0	(0.0)	1	(1.7)	2	(0.9)
Gastritis erosive	0	(0.0)	0	(0.0)	1	(1.8)	1	(1.7)	2	(0.9)
Dry mouth	2	(3.5)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.9)
Crohn's disease	0	(0.0)	0	(0.0)	1	(1.8)	1	(1.7)	2	(0.9)
Barrett's oesophagus	0	(0.0)	0	(0.0)	1	(1.8)	1	(1.7)	2	(0.9)
Abdominal pain	1	(1.8)	0	(0.0)	0	(0.0)	1	(1.7)	2	(0.9)
Abdominal hernia	1	(1.8)	0	(0.0)	0	(0.0)	1	(1.7)	2	(0.9)
Vomiting	1	(1.8)	0	(0.0)	1	(1.8)	0	(0.0)	2	(0.9)
Gastric mucosal hypertrophy	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Colitis ischaemic	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Appendiceal mucocoele	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Gastric disorder	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Colitis ulcerative	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Abdominal pain lower	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Gastroduodenal ulcer	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Epigastric discomfort	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Eructation	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Rectal haemorrhage	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Dental caries	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Chapped lips	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Duodenogastric reflux	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Abdominal tenderness	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Anal incontinence	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Flatulence	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Retching	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Umbilical hernia	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Duodenal ulcer	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Pelvic floor dyssynergia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Peptic ulcer	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Proctalgia	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Gastrointestinal pain	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Oral lichen planus	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Musculoskeletal and connective tissue disorders	24	(42.1)	33	(55.9)	26	(46.4)	28	(48.3)	111	(48.3)
Osteoarthritis	4	(7.0)	12	(20.3)	7	(12.5)	7	(12.1)	30	(13.0)
Back pain	6	(10.5)	7	(11.9)	4	(7.1)	7	(12.1)	24	(10.4)

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N: Number of subjects, %: Percentage of subjects, OD: Once daily.

Concomitant illness at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD		Sema 0.2 mg OD		Sema 0.4 mg OD		Placebo		Total	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
Arthralgia	3	(5.3)	3	(5.1)	2	(3.6)	6	(10.3)	14	(6.1)
Osteochondrosis	3	(5.3)	3	(5.1)	1	(1.8)	3	(5.2)	10	(4.3)
Arthritis	3	(5.3)	4	(6.8)	1	(1.8)	1	(1.7)	9	(3.9)
Osteoporosis	3	(5.3)	0	(0.0)	1	(1.8)	4	(6.9)	8	(3.5)
Spinal osteoarthritis	1	(1.8)	2	(3.4)	4	(7.1)	0	(0.0)	7	(3.0)
Fibromyalgia	2	(3.5)	1	(1.7)	0	(0.0)	3	(5.2)	6	(2.6)
Pain in extremity	1	(1.8)	3	(5.1)	0	(0.0)	2	(3.4)	6	(2.6)
Musculoskeletal pain	1	(1.8)	3	(5.1)	1	(1.8)	1	(1.7)	6	(2.6)
Muscle spasms	3	(5.3)	1	(1.7)	0	(0.0)	1	(1.7)	5	(2.2)
Myalgia	1	(1.8)	4	(6.8)	0	(0.0)	0	(0.0)	5	(2.2)
Neck pain	0	(0.0)	1	(1.7)	2	(3.6)	1	(1.7)	4	(1.7)
Intervertebral disc protrusion	2	(3.5)	0	(0.0)	2	(3.6)	0	(0.0)	4	(1.7)
Osteopenia	0	(0.0)	0	(0.0)	2	(3.6)	1	(1.7)	3	(1.3)
Rheumatoid arthritis	0	(0.0)	3	(5.1)	0	(0.0)	0	(0.0)	3	(1.3)
Trigger finger	1	(1.8)	1	(1.7)	0	(0.0)	1	(1.7)	3	(1.3)
Ankylosing spondylitis	1	(1.8)	0	(0.0)	1	(1.8)	0	(0.0)	2	(0.9)
Intervertebral disc degeneration	1	(1.8)	0	(0.0)	0	(0.0)	1	(1.7)	2	(0.9)
Periarthritis	1	(1.8)	1	(1.7)	0	(0.0)	0	(0.0)	2	(0.9)
Plantar fasciitis	0	(0.0)	0	(0.0)	2	(3.6)	0	(0.0)	2	(0.9)
Polyarthritis	0	(0.0)	1	(1.7)	1	(1.8)	0	(0.0)	2	(0.9)
Rotator cuff syndrome	0	(0.0)	0	(0.0)	2	(3.6)	0	(0.0)	2	(0.9)
Psoriatic arthropathy	1	(1.8)	0	(0.0)	1	(1.8)	0	(0.0)	2	(0.9)
Patellofemoral pain syndrome	0	(0.0)	0	(0.0)	1	(1.8)	1	(1.7)	2	(0.9)
Bursitis	0	(0.0)	1	(1.7)	1	(1.8)	0	(0.0)	2	(0.9)
Arthropathy	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Back disorder	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Cervical spinal stenosis	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Chondrocalcinosis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Dupuytren's contracture	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Flank pain	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Foot deformity	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Fracture pain	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Intervertebral disc compression	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Intervertebral disc disorder	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Metatarsalgia	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Muscle tightness	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)

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N: Number of subjects, %: Percentage of subjects, OD: Once daily.

Concomitant illness at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N	(%)	Sema 0.2 mg OD N	(%)	Sema 0.4 mg OD N	(%)	Placebo N	(%)	Total N	(%)
Musculoskeletal stiffness	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Osteochondritis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Osteoporosis postmenopausal	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Pain in jaw	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Scoliosis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Spinal pain	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Spondylitis	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Exostosis	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Tendonitis	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Sjogren's syndrome	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Respiratory, thoracic and mediastinal disorders	15	(26.3)	22	(37.3)	15	(26.8)	21	(36.2)	73	(31.7)
Asthma	6	(10.5)	6	(10.2)	8	(14.3)	9	(15.5)	29	(12.6)
Sleep apnoea syndrome	7	(12.3)	8	(13.6)	7	(12.5)	6	(10.3)	28	(12.2)
Dyspnoea	3	(5.3)	2	(3.4)	0	(0.0)	1	(1.7)	6	(2.6)
Cough	2	(3.5)	1	(1.7)	0	(0.0)	2	(3.4)	5	(2.2)
Rhinitis allergic	0	(0.0)	1	(1.7)	2	(3.6)	2	(3.4)	5	(2.2)
Chronic obstructive pulmonary disease	1	(1.8)	2	(3.4)	0	(0.0)	0	(0.0)	3	(1.3)
Bronchitis chronic	2	(3.5)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.9)
Pulmonary mass	1	(1.8)	1	(1.7)	0	(0.0)	0	(0.0)	2	(0.9)
Bronchial hyperreactivity	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Interstitial lung disease	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Nasal congestion	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Nasal septum deviation	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Snoring	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Vocal cord polyp	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Restrictive pulmonary disease	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Lung cyst	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Nervous system disorders	18	(31.6)	18	(30.5)	15	(26.8)	20	(34.5)	71	(30.9)
Diabetic neuropathy	7	(12.3)	5	(8.5)	1	(1.8)	5	(8.6)	18	(7.8)
Migraine	2	(3.5)	3	(5.1)	5	(8.9)	5	(8.6)	15	(6.5)
Headache	2	(3.5)	2	(3.4)	2	(3.6)	3	(5.2)	9	(3.9)
Neuropathy peripheral	0	(0.0)	2	(3.4)	4	(7.1)	1	(1.7)	7	(3.0)
Restless legs syndrome	2	(3.5)	1	(1.7)	3	(5.4)	1	(1.7)	7	(3.0)
Carotid arteriosclerosis	2	(3.5)	2	(3.4)	0	(0.0)	0	(0.0)	4	(1.7)

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N: Number of subjects, %: Percentage of subjects, OD: Once daily.

Concomitant illness at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N	(%)	Sema 0.2 mg OD N	(%)	Sema 0.4 mg OD N	(%)	Placebo N	(%)	Total N	(%)
Encephalopathy	1	(1.8)	2	(3.4)	0	(0.0)	1	(1.7)	4	(1.7)
Sciatica	1	(1.8)	1	(1.7)	0	(0.0)	2	(3.4)	4	(1.7)
Lacunar infarction	1	(1.8)	1	(1.7)	0	(0.0)	1	(1.7)	3	(1.3)
Carpal tunnel syndrome	0	(0.0)	0	(0.0)	1	(1.8)	1	(1.7)	2	(0.9)
Vascular encephalopathy	1	(1.8)	0	(0.0)	1	(1.8)	0	(0.0)	2	(0.9)
Autonomic nervous system imbalance	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Carotid artery disease	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Cervical radiculopathy	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Diabetic encephalopathy	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Dizziness	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Hyperaesthesia	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Hypoaesthesia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Meralgia paraesthetica	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Nerve compression	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Peripheral sensorimotor neuropathy	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Peripheral sensory neuropathy	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Seizure	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Neuralgia	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Memory impairment	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Peroneal nerve palsy	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Hemiparesis	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Somnolence	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Psychiatric disorders	18	(31.6)	16	(27.1)	16	(28.6)	15	(25.9)	65	(28.3)
Depression	7	(12.3)	9	(15.3)	8	(14.3)	13	(22.4)	37	(16.1)
Anxiety	8	(14.0)	3	(5.1)	4	(7.1)	9	(15.5)	24	(10.4)
Insomnia	4	(7.0)	6	(10.2)	5	(8.9)	3	(5.2)	18	(7.8)
Bipolar disorder	1	(1.8)	1	(1.7)	1	(1.8)	0	(0.0)	3	(1.3)
Anxiety disorder	0	(0.0)	0	(0.0)	2	(3.6)	0	(0.0)	2	(0.9)
Depressed mood	1	(1.8)	0	(0.0)	1	(1.8)	0	(0.0)	2	(0.9)
Tobacco abuse	1	(1.8)	1	(1.7)	0	(0.0)	0	(0.0)	2	(0.9)
Bipolar II disorder	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Borderline personality disorder	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Drug dependence	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Obsessive-compulsive disorder	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Panic disorder	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)

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Concomitant illness at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N	(%)	Sema 0.2 mg OD N	(%)	Sema 0.4 mg OD N	(%)	Placebo N	(%)	Total N	(%)
Post-traumatic stress disorder	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Stress	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Sleep disorder	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Claustrophobia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Eye disorders	13	(22.8)	18	(30.5)	17	(30.4)	14	(24.1)	62	(27.0)
Cataract	1	(1.8)	7	(11.9)	4	(7.1)	5	(8.6)	17	(7.4)
Myopia	2	(3.5)	3	(5.1)	4	(7.1)	3	(5.2)	12	(5.2)
Glaucoma	3	(5.3)	2	(3.4)	3	(5.4)	2	(3.4)	10	(4.3)
Dry eye	3	(5.3)	1	(1.7)	1	(1.8)	2	(3.4)	7	(3.0)
Presbyopia	1	(1.8)	2	(3.4)	2	(3.6)	1	(1.7)	6	(2.6)
Diabetic retinopathy	1	(1.8)	1	(1.7)	2	(3.6)	2	(3.4)	6	(2.6)
Retinopathy hypertensive	1	(1.8)	1	(1.7)	2	(3.6)	1	(1.7)	5	(2.2)
Non-proliferative retinopathy	1	(1.8)	1	(1.7)	0	(0.0)	0	(0.0)	2	(0.9)
Conjunctivitis allergic	0	(0.0)	0	(0.0)	1	(1.8)	1	(1.7)	2	(0.9)
Hypermetropia	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Eye irritation	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Conjunctival cyst	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Keratoconus	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Astigmatism	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Pterygium	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Retinal vascular disorder	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Cataract nuclear	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Normal tension glaucoma	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Ocular hypertension	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Choroiditis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Asthenopia	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Strabismus	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Macular degeneration	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Retinal degeneration	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Retinal tear	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Open angle glaucoma	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Arteriosclerotic retinopathy	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Endocrine disorders	20	(35.1)	15	(25.4)	7	(12.5)	13	(22.4)	55	(23.9)
Hypothyroidism	11	(19.3)	8	(13.6)	6	(10.7)	8	(13.8)	33	(14.3)

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Concomitant illness at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N	(%)	Sema 0.2 mg OD N	(%)	Sema 0.4 mg OD N	(%)	Placebo N	(%)	Total N	(%)
Goitre	6	(10.5)	3	(5.1)	0	(0.0)	2	(3.4)	11	(4.8)
Autoimmune thyroiditis	1	(1.8)	1	(1.7)	1	(1.8)	3	(5.2)	6	(2.6)
Hyperthyroidism	0	(0.0)	2	(3.4)	0	(0.0)	0	(0.0)	2	(0.9)
Thyroid mass	0	(0.0)	1	(1.7)	0	(0.0)	1	(1.7)	2	(0.9)
Adrenomegaly	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Hyperparathyroidism	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Thyroiditis	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Hypogonadism	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Adrenal mass	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Hypopituitarism	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Renal and urinary disorders	11	(19.3)	9	(15.3)	11	(19.6)	14	(24.1)	45	(19.6)
Renal cyst	6	(10.5)	4	(6.8)	6	(10.7)	3	(5.2)	19	(8.3)
Nephrolithiasis	2	(3.5)	1	(1.7)	2	(3.6)	5	(8.6)	10	(4.3)
Calculus urinary	0	(0.0)	0	(0.0)	1	(1.8)	2	(3.4)	3	(1.3)
Chronic kidney disease	1	(1.8)	0	(0.0)	0	(0.0)	2	(3.4)	3	(1.3)
Urinary incontinence	1	(1.8)	1	(1.7)	0	(0.0)	1	(1.7)	3	(1.3)
Diabetic nephropathy	1	(1.8)	0	(0.0)	0	(0.0)	1	(1.7)	2	(0.9)
Pollakiuria	0	(0.0)	0	(0.0)	0	(0.0)	2	(3.4)	2	(0.9)
Albuminuria	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Bladder prolapse	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Bladder spasm	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Cystitis interstitial	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Glomerulonephropathy	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Glomerulosclerosis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Hydrocalyx	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
IgA nephropathy	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Incontinence	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Micturition urgency	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Nocturia	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Proteinuria	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Renal colic	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Stress urinary incontinence	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Microalbuminuria	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Immune system disorders	10	(17.5)	11	(18.6)	10	(17.9)	12	(20.7)	43	(18.7)

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Concomitant illness at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N	(%)	Sema 0.2 mg OD N	(%)	Sema 0.4 mg OD N	(%)	Placebo N	(%)	Total N	(%)
Seasonal allergy	7	(12.3)	8	(13.6)	8	(14.3)	6	(10.3)	29	(12.6)
Drug hypersensitivity	2	(3.5)	2	(3.4)	2	(3.6)	6	(10.3)	12	(5.2)
Food allergy	1	(1.8)	1	(1.7)	0	(0.0)	1	(1.7)	3	(1.3)
Hypersensitivity	1	(1.8)	1	(1.7)	0	(0.0)	1	(1.7)	3	(1.3)
Multiple allergies	1	(1.8)	0	(0.0)	0	(0.0)	1	(1.7)	2	(0.9)
Allergy to arthropod bite	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Allergy to chemicals	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Perfume sensitivity	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Iodine allergy	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Reaction to preservatives	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Allergy to plants	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Skin and subcutaneous tissue disorders	8	(14.0)	9	(15.3)	9	(16.1)	14	(24.1)	40	(17.4)
Psoriasis	1	(1.8)	5	(8.5)	3	(5.4)	2	(3.4)	11	(4.8)
Dry skin	2	(3.5)	1	(1.7)	0	(0.0)	2	(3.4)	5	(2.2)
Pruritus	2	(3.5)	1	(1.7)	1	(1.8)	1	(1.7)	5	(2.2)
Drug eruption	0	(0.0)	0	(0.0)	1	(1.8)	2	(3.4)	3	(1.3)
Rosacea	0	(0.0)	1	(1.7)	1	(1.8)	1	(1.7)	3	(1.3)
Eczema	0	(0.0)	1	(1.7)	0	(0.0)	2	(3.4)	3	(1.3)
Alopecia	0	(0.0)	1	(1.7)	0	(0.0)	1	(1.7)	2	(0.9)
Hirsutism	0	(0.0)	1	(1.7)	1	(1.8)	0	(0.0)	2	(0.9)
Urticaria	0	(0.0)	0	(0.0)	1	(1.8)	1	(1.7)	2	(0.9)
Acanthosis nigricans	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Acne	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Actinic keratosis	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Dermal cyst	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Dermatitis atopic	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Dermatitis herpetiformis	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Dermatitis psoriasiform	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Erythema nodosum	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Hyperkeratosis	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Lichen planus	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Nail dystrophy	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Night sweats	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Rash	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Rash pruritic	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)

Table contains events reported as medical history/concomitant illness either not resolved or resolved after screening. MedDRA version 22.1.
N: Number of subjects, %: Percentage of subjects, OD: Once daily.

Concomitant illness at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N	(%)	Sema 0.2 mg OD N	(%)	Sema 0.4 mg OD N	(%)	Placebo N	(%)	Total N	(%)
Seborrhoeic dermatitis	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Umbilical haematoma	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Rhinophyma	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Lentigo	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Cardiac disorders	8	(14.0)	13	(22.0)	8	(14.3)	8	(13.8)	37	(16.1)
Cardiac failure chronic	3	(5.3)	3	(5.1)	0	(0.0)	1	(1.7)	7	(3.0)
Angina pectoris	3	(5.3)	3	(5.1)	0	(0.0)	1	(1.7)	7	(3.0)
Coronary artery disease	0	(0.0)	1	(1.7)	3	(5.4)	1	(1.7)	5	(2.2)
Atrial fibrillation	0	(0.0)	0	(0.0)	2	(3.6)	1	(1.7)	3	(1.3)
Myocardial ischaemia	1	(1.8)	2	(3.4)	0	(0.0)	0	(0.0)	3	(1.3)
Arrhythmia	0	(0.0)	2	(3.4)	0	(0.0)	1	(1.7)	3	(1.3)
Left ventricular hypertrophy	2	(3.5)	0	(0.0)	1	(1.8)	0	(0.0)	3	(1.3)
Diastolic dysfunction	0	(0.0)	0	(0.0)	0	(0.0)	2	(3.4)	2	(0.9)
Degenerative mitral valve disease	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Atrioventricular block first degree	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Arteriosclerosis coronary artery	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Bundle branch block right	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Left ventricular dysfunction	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Bundle branch block left	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Mitral valve prolapse	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Prinzmetal angina	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Ischaemic cardiomyopathy	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Sinus bradycardia	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Left atrial enlargement	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Myocardial infarction	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Palpitations	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Tricuspid valve incompetence	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Cardiac hypertrophy	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Supraventricular tachycardia	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Social circumstances	10	(17.5)	8	(13.6)	8	(14.3)	11	(19.0)	37	(16.1)
Menopause	5	(8.8)	5	(8.5)	4	(7.1)	7	(12.1)	21	(9.1)
Postmenopause	5	(8.8)	3	(5.1)	4	(7.1)	3	(5.2)	15	(6.5)
Corrective lens user	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)

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Concomitant illness at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N	(%)	Sema 0.2 mg OD N	(%)	Sema 0.4 mg OD N	(%)	Placebo N	(%)	Total N	(%)
General disorders and administration site conditions	9	(15.8)	2	(3.4)	6	(10.7)	10	(17.2)	27	(11.7)
Fatigue	5	(8.8)	0	(0.0)	1	(1.8)	2	(3.4)	8	(3.5)
Oedema peripheral	2	(3.5)	1	(1.7)	2	(3.6)	3	(5.2)	8	(3.5)
Cyst	0	(0.0)	0	(0.0)	1	(1.8)	2	(3.4)	3	(1.3)
Drug intolerance	1	(1.8)	1	(1.7)	0	(0.0)	1	(1.7)	3	(1.3)
Chest pain	1	(1.8)	0	(0.0)	1	(1.8)	0	(0.0)	2	(0.9)
Pain	0	(0.0)	0	(0.0)	1	(1.8)	1	(1.7)	2	(0.9)
Asthenia	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Hyperthermia malignant	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Pelvic mass	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Polyp	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Early satiety	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Ill-defined disorder	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Chronic fatigue syndrome	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Infections and infestations	6	(10.5)	6	(10.2)	7	(12.5)	7	(12.1)	26	(11.3)
Pyelonephritis chronic	1	(1.8)	1	(1.7)	1	(1.8)	1	(1.7)	4	(1.7)
Urinary tract infection	2	(3.5)	0	(0.0)	1	(1.8)	0	(0.0)	3	(1.3)
Nasopharyngitis	0	(0.0)	1	(1.7)	1	(1.8)	0	(0.0)	2	(0.9)
Onychomycosis	0	(0.0)	0	(0.0)	1	(1.8)	1	(1.7)	2	(0.9)
Abscess limb	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Chronic sinusitis	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Cystitis	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Ear infection	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Fungal skin infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Genital herpes	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Intervertebral discitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Lower respiratory tract infection	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Oral herpes	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Sinusitis	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Periodontitis	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Otitis media chronic	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Diverticulitis	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Tinea manuum	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Sialoadenitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Helicobacter infection	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)

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Concomitant illness at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N	(%)	Sema 0.2 mg OD N	(%)	Sema 0.4 mg OD N	(%)	Placebo N	(%)	Total N	(%)
Investigations	6	(10.5)	6	(10.2)	7	(12.5)	6	(10.3)	25	(10.9)
Hepatic enzyme increased	3	(5.3)	3	(5.1)	1	(1.8)	1	(1.7)	8	(3.5)
Blood cholesterol increased	1	(1.8)	1	(1.7)	1	(1.8)	2	(3.4)	5	(2.2)
Cardiac murmur	1	(1.8)	1	(1.7)	1	(1.8)	0	(0.0)	3	(1.3)
Serum ferritin increased	1	(1.8)	0	(0.0)	1	(1.8)	0	(0.0)	2	(0.9)
Blood creatine phosphokinase	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Blood creatine phosphokinase increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Blood potassium decreased	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Blood pressure increased	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Blood thyroid stimulating hormone increased	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Electrocardiogram abnormal	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Lipoprotein (a) increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Liver function test abnormal	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Blood testosterone decreased	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Ultrasound abdomen	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Serum ferritin decreased	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Heart rate irregular	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	8	(14.0)	3	(5.1)	5	(8.9)	6	(10.3)	22	(9.6)
Uterine leiomyoma	2	(3.5)	0	(0.0)	1	(1.8)	1	(1.7)	4	(1.7)
Adrenal adenoma	1	(1.8)	0	(0.0)	0	(0.0)	1	(1.7)	2	(0.9)
Seborrhoeic keratosis	0	(0.0)	2	(3.4)	0	(0.0)	0	(0.0)	2	(0.9)
Acrochordon	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Basosquamous carcinoma	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Benign neoplasm of thyroid gland	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Benign pancreatic neoplasm	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Essential thrombocythaemia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Eye naevus	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Fibroadenoma of breast	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Haemangioma of liver	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Haemangioma of skin	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Haemangioma of spleen	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Lipofibroma	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Lipoma	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Monoclonal gammopathy	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)

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Concomitant illness at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N	(%)	Sema 0.2 mg OD N	(%)	Sema 0.4 mg OD N	(%)	Placebo N	(%)	Total N	(%)
Pituitary tumour benign	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Prostatic adenoma	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Papilloma	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Intraductal papillary mucinous neoplasm	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Colon adenoma	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Haemangioma	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Blood and lymphatic system disorders	4	(7.0)	3	(5.1)	9	(16.1)	5	(8.6)	21	(9.1)
Splenomegaly	1	(1.8)	0	(0.0)	4	(7.1)	2	(3.4)	7	(3.0)
Iron deficiency anaemia	0	(0.0)	0	(0.0)	2	(3.6)	2	(3.4)	4	(1.7)
Anaemia	1	(1.8)	1	(1.7)	0	(0.0)	1	(1.7)	3	(1.3)
Thrombocytopenia	0	(0.0)	1	(1.7)	1	(1.8)	0	(0.0)	2	(0.9)
Lymphadenopathy	1	(1.8)	0	(0.0)	1	(1.8)	0	(0.0)	2	(0.9)
Polycythaemia	0	(0.0)	0	(0.0)	2	(3.6)	0	(0.0)	2	(0.9)
Thrombocytosis	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Hypergammaglobulinaemia	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Increased tendency to bruise	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Microcytic anaemia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Reproductive system and breast disorders	3	(5.3)	7	(11.9)	3	(5.4)	3	(5.2)	16	(7.0)
Benign prostatic hyperplasia	2	(3.5)	2	(3.4)	0	(0.0)	1	(1.7)	5	(2.2)
Polycystic ovaries	1	(1.8)	0	(0.0)	1	(1.8)	2	(3.4)	4	(1.7)
Ovarian cyst	0	(0.0)	2	(3.4)	1	(1.8)	0	(0.0)	3	(1.3)
Breast calcifications	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Erectile dysfunction	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Metrorrhagia	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Prostatitis	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Prostatomegaly	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Breast disorder	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Surgical and medical procedures	4	(7.0)	6	(10.2)	2	(3.6)	4	(6.9)	16	(7.0)
Hysterectomy	1	(1.8)	0	(0.0)	0	(0.0)	2	(3.4)	3	(1.3)
Bunion operation	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Cardiac pacemaker insertion	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Drain placement	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Hip arthroplasty	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)

Table contains events reported as medical history/concomitant illness either not resolved or resolved after screening. MedDRA version 22.1.
N: Number of subjects, %: Percentage of subjects, OD: Once daily.

Concomitant illness at screening by system organ class and preferred term - summary - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD N	(%)	Sema 0.2 mg OD N	(%)	Sema 0.4 mg OD N	(%)	Placebo N	(%)	Total N	(%)
Intraocular lens implant	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Knee operation	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Large intestinal polypectomy	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Nephrectomy	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Oesophagogastric fundoplasty	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Ovarian cystectomy	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Pterygium operation	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Middle ear prosthesis insertion	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Knee arthroplasty	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Female sterilisation	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Congenital, familial and genetic disorders	2	(3.5)	1	(1.7)	5	(8.9)	1	(1.7)	9	(3.9)
Gilbert's syndrome	1	(1.8)	0	(0.0)	2	(3.6)	0	(0.0)	3	(1.3)
Factor V Leiden mutation	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Mitochondrial myopathy	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Hyper IgE syndrome	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Type V hyperlipidaemia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Mayer-Rokitansky-Kuster-Hauser syndrome	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Dolichocolon	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Atrial septal defect	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Injury, poisoning and procedural complications	1	(1.8)	1	(1.7)	3	(5.4)	2	(3.4)	7	(3.0)
Thermal burn	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Meniscus injury	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Arthropod bite	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Epicondylitis	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)
Post procedural complication	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)	1	(0.4)
Rib fracture	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Scar	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Transurethral resection syndrome	0	(0.0)	0	(0.0)	1	(1.8)	0	(0.0)	1	(0.4)
Ear and labyrinth disorders	1	(1.8)	0	(0.0)	0	(0.0)	3	(5.2)	4	(1.7)
Vertigo	1	(1.8)	0	(0.0)	0	(0.0)	1	(1.7)	2	(0.9)
Hypoacusis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Tinnitus	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	1	(0.4)
Deafness bilateral	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.4)

Table contains events reported as medical history/concomitant illness either not resolved or resolved after screening. MedDRA version 22.1.
N: Number of subjects, %: Percentage of subjects, OD: Once daily.

6.2.6 Histological endpoints (regulatory guidance definition) - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - full analysis set - Trial 4296

	Sema 0.1 mg OD N	(%)	Sema 0.2 mg OD N	(%)	Sema 0.4 mg OD N	(%)	Placebo N	(%)
Number of subjects	57		59		56		58	
Resolution of steatohepatitis and no worsening of liver fibrosis								
Week 72 (EOT)								
Yes	23	(40.4)	21	(35.6)	33	(58.9)	10	(17.2)
No	31	(54.4)	28	(47.5)	17	(30.4)	43	(74.1)
Missing	3	(5.3)	10	(16.9)	6	(10.7)	5	(8.6)
Week 72 (EOT) (on-treatment)								
Yes	23	(40.4)	19	(32.2)	28	(50.0)	9	(15.5)
No	25	(43.9)	24	(40.7)	14	(25.0)	39	(67.2)
Missing	9	(15.8)	16	(27.1)	14	(25.0)	10	(17.2)
Improvement in fibrosis and no worsening in steatohepatitis								
Week 72 (EOT)								
Yes	27	(47.4)	19	(32.2)	24	(42.9)	15	(25.9)
No	27	(47.4)	30	(50.8)	26	(46.4)	38	(65.5)
Missing	3	(5.3)	10	(16.9)	6	(10.7)	5	(8.6)
Week 72 (EOT) (on-treatment)								
Yes	25	(43.9)	15	(25.4)	21	(37.5)	13	(22.4)
No	23	(40.4)	28	(47.5)	21	(37.5)	35	(60.3)
Missing	9	(15.8)	16	(27.1)	14	(25.0)	10	(17.2)

N: Number of subjects, %: Percentage of subjects, OD: Once daily, EOT: End of treatment.

6.2.7 Resolution of steatohepatitis and no worsening of liver fibrosis - Statistical analysis - CMH test - Absolute difference - MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - full analysis set - Trial 4296

	FAS	IMP	Estimate	95% CI	One-sided p-value	Two-sided p-value
Resolution of steatohepatitis and no worsening of liver fibrosis						
N (%) achieving target at week 72 (EOT)						
Sema 0.1 mg OD	57	3	24 (41.4)			
Sema 0.2 mg OD	59	10	23 (39.2)			
Sema 0.4 mg OD	56	6	35 (61.7)			
Placebo	58	5	11 (19.1)			
Difference in responder proportions (%-points) at week 72 (EOT)						
Sema 0.1 mg OD minus Placebo			22.54	[5.89; 39.20]	0.0040	0.0080
Sema 0.2 mg OD minus Placebo			20.55	[3.97; 37.13]	0.0076	0.0151
Sema 0.4 mg OD minus Placebo			42.80	[25.78; 59.81]	<.0001	<.0001

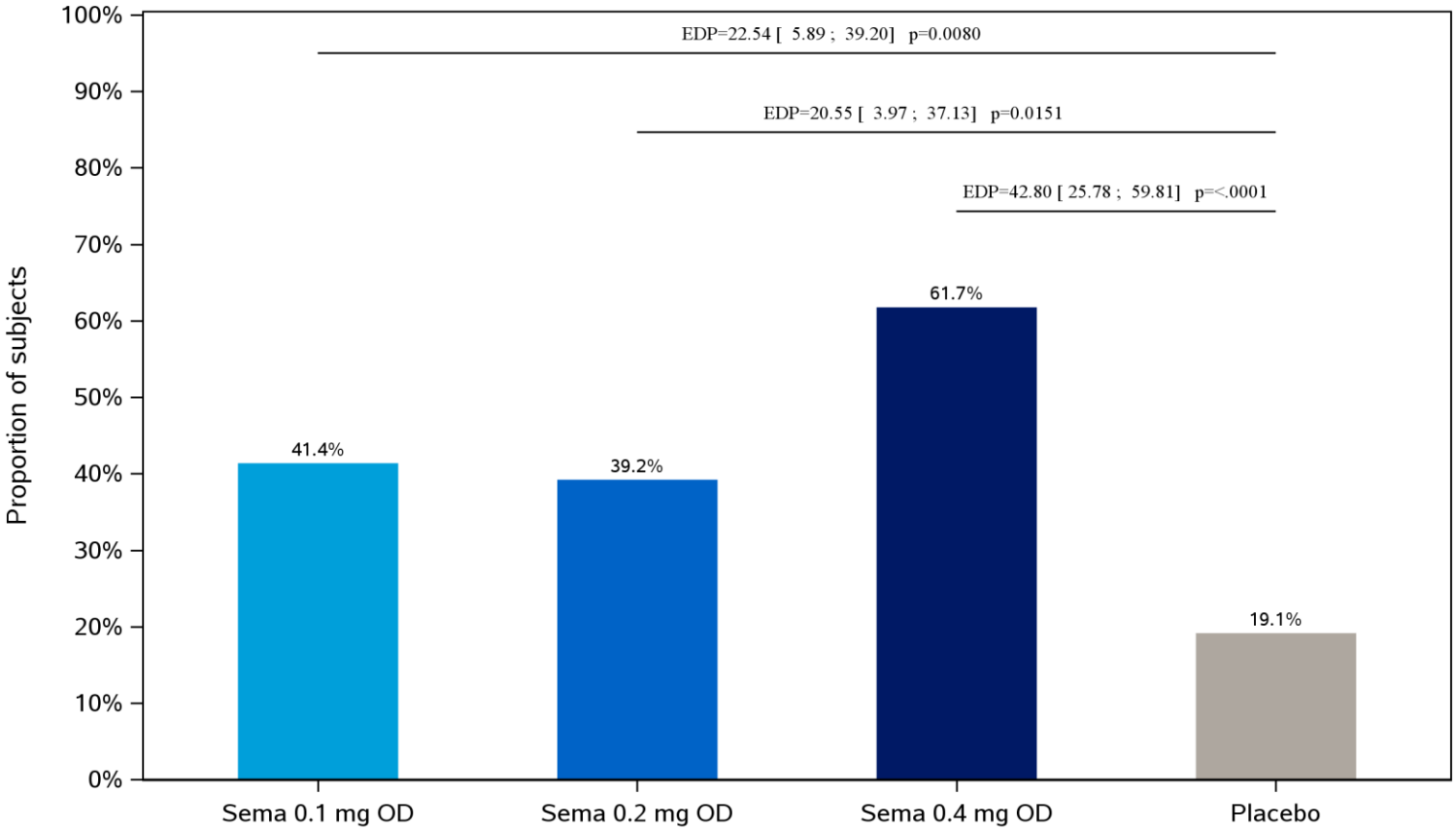
CMH test stratified by baseline diabetes status and baseline fibrosis stage. Missing data in any treatment group will be handled by MI that is informed by data from placebo subjects. Subjects who experience a liver-related clinical event before the week 72 visit will be handled as non-responders. No worsening of liver fibrosis is defined as no increase in fibrosis score. Fibrosis is graded on the NASH CRN fibrosis scale from 0-4. Resolution of steatohepatitis is defined as a NAS of 0-1 for inflammation, 0 for ballooning and any value for steatosis according to NASH CRN. CI: Confidence interval, CMH: Cochran-Mantel-Haenszel, FAS: Full analysis set for interim, IMP: Subjects with an imputed week 72 assessment, N (%): Number and percentage of subjects after imputation, OD: Once daily, EOT: End of treatment.

6.2.8 Resolution of steatohepatitis and no worsening of liver fibrosis - sensitivity analysis - CMH test - Absolute difference - Missing as non-responder - in-trial - subjects with fibrosis stage 2 or 3 at baseline - full analysis set - Trial 4296

	FAS	IMP	Estimate	95% CI	One-sided p-value	Two-sided p-value
Resolution of steatohepatitis and no worsening of liver fibrosis						
N (%) achieving target at week 72 (EOT)						
Sema 0.1 mg OD	57	3	23 (40.4)			
Sema 0.2 mg OD	59	10	21 (35.6)			
Sema 0.4 mg OD	56	6	33 (58.9)			
Placebo	58	5	10 (17.2)			
Difference in responder proportions (%-points) at week 72 (EOT)						
Sema 0.1 mg OD minus Placebo			23.46	[7.48; 39.44]	0.0020	0.0040
Sema 0.2 mg OD minus Placebo			18.67	[3.02; 34.33]	0.0097	0.0194
Sema 0.4 mg OD minus Placebo			41.83	[25.49; 58.17]	<.0001	<.0001

CMH test stratified by baseline diabetes status and baseline fibrosis stage. Missing data in any treatment group will be classified as non-responders according to a composite strategy. Subjects who experience a liver-related clinical event before the week 72 visit will be handled as non-responders. No worsening of liver fibrosis is defined as no increase in fibrosis score. Fibrosis is graded on the NASH CRN fibrosis scale from 0-4. Resolution of steatohepatitis is defined as a NAS of 0-1 for inflammation, 0 for ballooning and any value for steatosis according to NASH CRN. CI: Confidence interval, CMH: Cochran-Mantel-Haenszel, FAS: Full analysis set for interim, IMP: Subjects with an imputed week 72 assessment, N (%): Number and percentage of subjects after imputation, OD: Once daily, EOT: End of treatment.

6.2.9 Resolution of steatohepatitis and no worsening of liver fibrosis - proportion of subjects achieving target - bar plot - Absolute difference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



P-values are two-sided and taken from a CMH test stratified by baseline diabetes status and baseline fibrosis stage. Missing data in any treatment group will be handled by MI that is informed by data from placebo subjects. Subjects who experience a liver-related clinical event before the week 72 visit will be handled as non-responders CMH: Cochran-Mantel-Haenszel, OD: Once daily, EDP: Estimated difference in responder proportions.

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6.2.10 Improvement in liver fibrosis and no worsening of steatohepatitis (regulatory guidance definition) - statistical analysis - CMH test - Absolute difference - MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - full analysis set - Trial 4296

	FAS	IMP	Estimate	95% CI	One-sided p-value	Two-sided p-value
Improvement in fibrosis and no worsening in steatohepatitis						
N (%) achieving target at week 72 (EOT)						
Sema 0.1 mg OD	57	3	28 (48.8)			
Sema 0.2 mg OD	59	10	22 (37.0)			
Sema 0.4 mg OD	56	6	26 (46.2)			
Placebo	58	5	17 (28.4)			
Difference in responder proportions (%-points) at week 72 (EOT)						
Sema 0.1 mg OD minus Placebo			19.86	[1.67; 38.06]	0.0162	0.0324
Sema 0.2 mg OD minus Placebo			8.74	[-9.52; 27.00]	0.1740	0.3481
Sema 0.4 mg OD minus Placebo			16.04	[-2.46; 34.53]	0.0446	0.0893

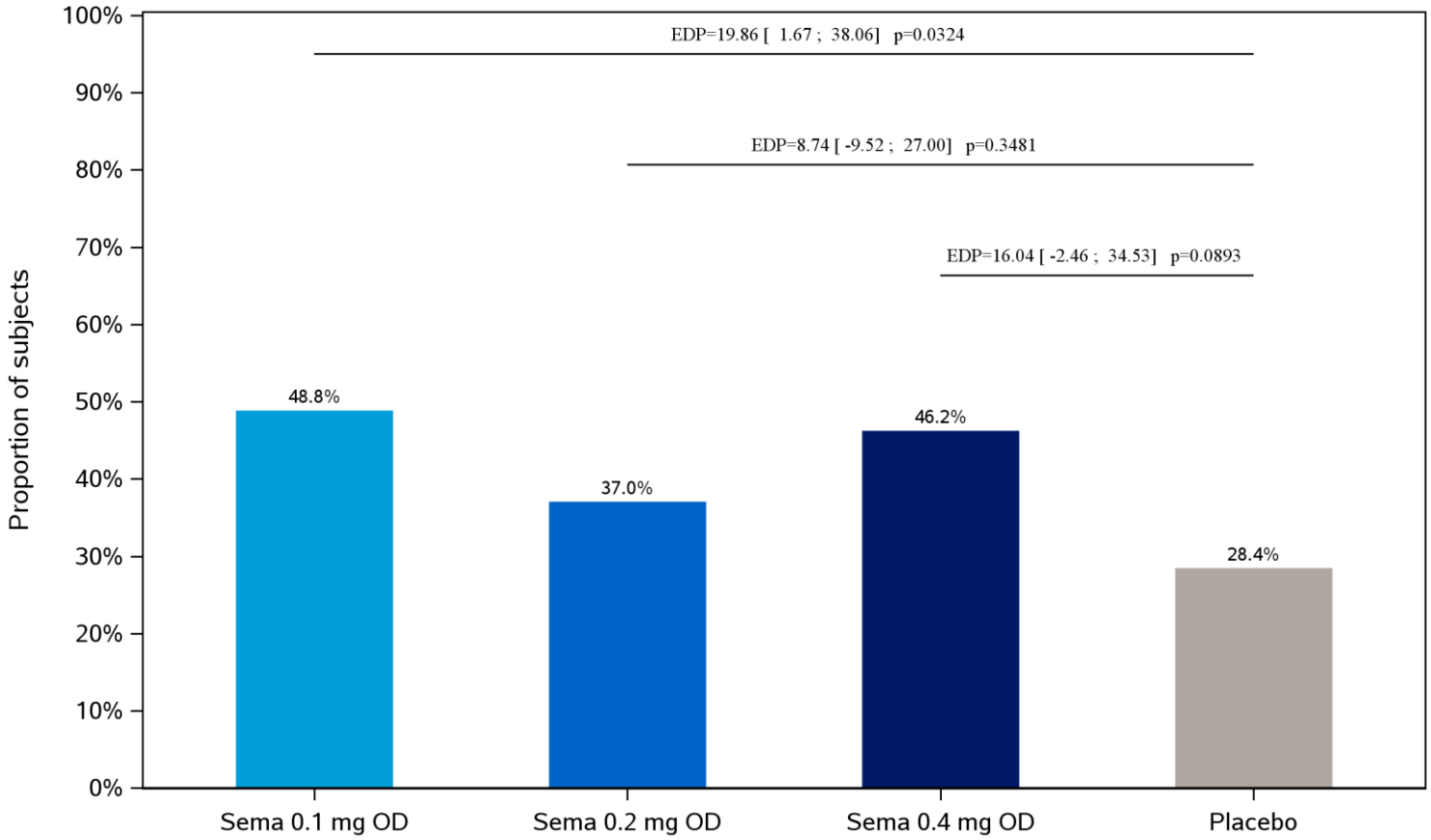
CMH test stratified by baseline diabetes status and baseline fibrosis stage. Missing data in any treatment group will be handled by MI that is informed by data from placebo subjects. Subjects who experience a liver-related clinical event before the week 72 visit will be handled as non-responders. Improvement in fibrosis is defined as >= 1 grade improvement on the NASH CRN fibrosis scale. No worsening of steatohepatitis is defined as no increase from baseline in NAS score for ballooning, inflammation or steatosis. CI: Confidence interval, CMH: Cochran-Mantel-Haenszel, FAS: Full analysis set for interim, IMP: Subjects with an imputed week 72 assessment, N (%): Number and percentage of subjects after imputation, OD: Once daily, EOT: End of treatment.

6.2.11 Improvement in liver fibrosis and no worsening of steatohepatitis (regulatory guidance defintion) - sensitivity analysis - CMH test - Missing as non-responder - in-trial - subjects with fibrosis stage 2 or 3 at baseline - full analysis set - Trial 4296

	FAS	IMP	Estimate	95% CI	One-sided p-value	Two-sided p-value
Improvement in fibrosis and no worsening in steatohepatitis						
N (%) achieving target at week 72 (EOT)						
Sema 0.1 mg OD	57	3	27 (47.4)			
Sema 0.2 mg OD	59	10	19 (32.2)			
Sema 0.4 mg OD	56	6	24 (42.9)			
Placebo	58	5	15 (25.9)			
Difference in responder proportions (%-points) at week 72 (EOT)						
Sema 0.1 mg OD minus Placebo			21.07	[3.64; 38.50]	0.0089	0.0178
Sema 0.2 mg OD minus Placebo			6.46	[-10.39; 23.32]	0.2261	0.4523
Sema 0.4 mg OD minus Placebo			15.35	[-2.16; 32.86]	0.0429	0.0858

CMH test stratified by baseline diabetes status and baseline fibrosis stage. Missing data in any treatment group will be classified as non-responders according to a composite strategy. Subjects who experience a liver-related clinical event before the week 72 visit will be handled as non-responders. Improvement in fibrosis is defined as >= 1 grade improvement on the NASH CRN fibrosis scale. No worsening of steatohepatitis is defined as no increase from baseline in NAS score for ballooning, inflammation or steatosis. CI: Confidence interval, CMH: Cochran-Mantel-Haenszel, FAS: Full analysis set for interim, IMP: Subjects with an imputed week 72 assessment, N (%): Number and percentage of subjects after imputation, OD: Once daily, EOT: End of treatment.

6.2.12 Improvement in liver fibrosis and no worsening of steatohepatitis (regulatory guidance definition) - proportion of subjects achieving target - bar plot - Absolute difference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



P-values are two-sided and taken from a CMH test stratified by baseline diabetes status and baseline fibrosis stage. Missing data in any treatment group will be handled by MI that is informed by data from placebo subjects. Subjects who experience a liver-related clinical event before the week 72 visit will be handled as non-responders CMH: Cochran-Mantel-Haenszel, OD: Once daily, EDP: Estimated difference in responder proportions.

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6.2.13 Fibrosis stage - shift table - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Baseline value		
	2 N (%)	3 N (%)	Total N (%)
Fibrosis Stage at week 72			
Sema 0.1 mg OD			
Number of subjects	18	39	57
0	5 (27.8)	1 (2.6)	6 (10.5)
1	7 (38.9)	8 (20.5)	15 (26.3)
2	5 (27.8)	9 (23.1)	14 (24.6)
3	0 (0.0)	17 (43.6)	17 (29.8)
4	0 (0.0)	2 (5.1)	2 (3.5)
Missing	1 (5.6)	2 (5.1)	3 (5.3)
Improvement	12 (66.7)	18 (46.2)	30 (52.6)
No change	5 (27.8)	17 (43.6)	22 (38.6)
Worsening	0 (0.0)	2 (5.1)	2 (3.5)
Sema 0.2 mg OD			
Number of subjects	18	41	59
0	3 (16.7)	2 (4.9)	5 (8.5)
1	6 (33.3)	6 (14.6)	12 (20.3)
2	4 (22.2)	4 (9.8)	8 (13.6)
3	0 (0.0)	22 (53.7)	22 (37.3)
4	0 (0.0)	2 (4.9)	2 (3.4)
Missing	5 (27.8)	5 (12.2)	10 (16.9)
Improvement	9 (50.0)	12 (29.3)	21 (35.6)
No change	4 (22.2)	22 (53.7)	26 (44.1)
Worsening	0 (0.0)	2 (4.9)	2 (3.4)

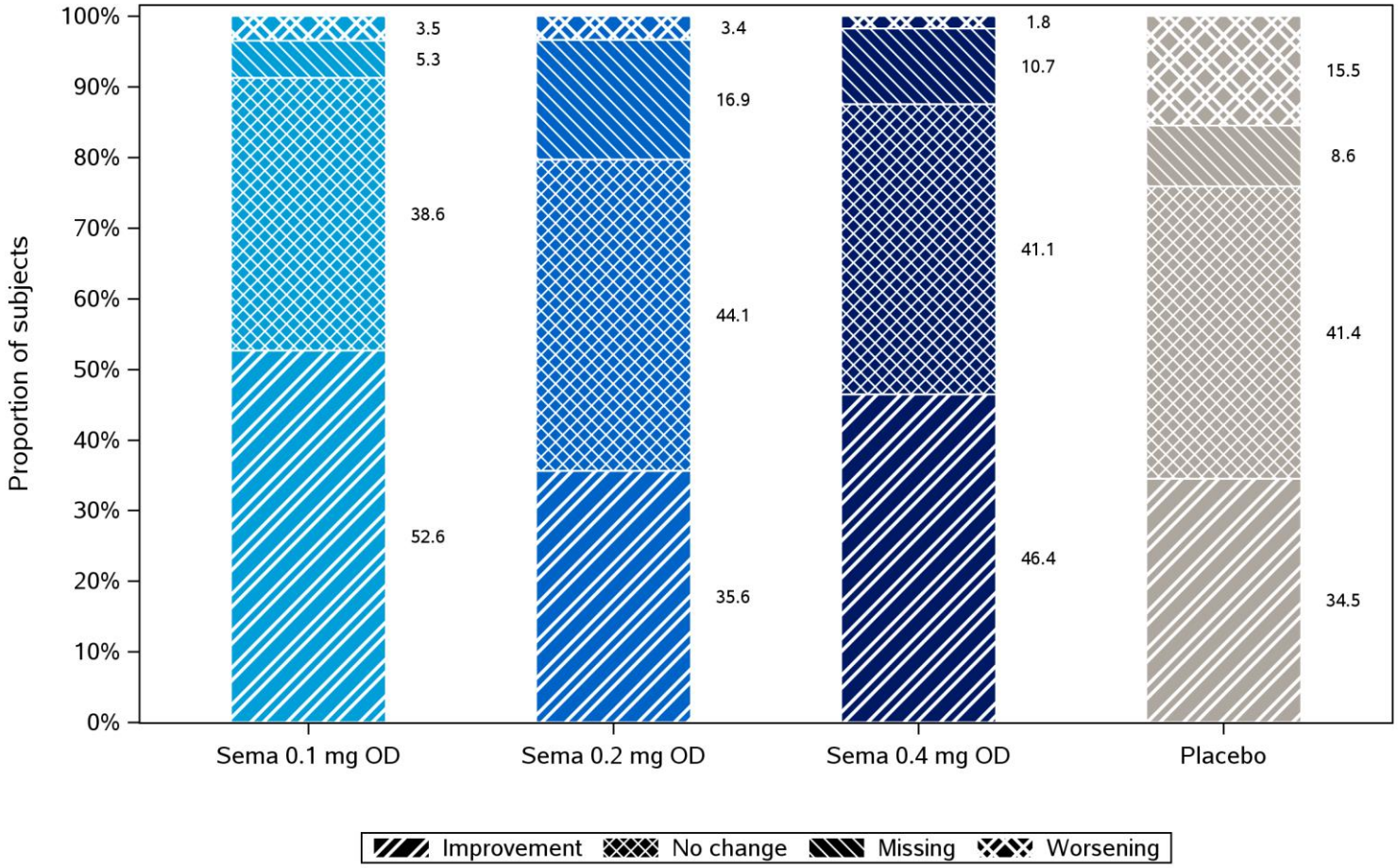
N: Number of subjects, %: Percentage of subjects, OD: Once daily.

Fibrosis stage - shift table - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Baseline value		
	2 N (%)	3 N (%)	Total N (%)
Sema 0.4 mg OD			
Number of subjects	14	42	56
0	0 (0.0)	2 (4.8)	2 (3.6)
1	5 (35.7)	9 (21.4)	14 (25.0)
2	5 (35.7)	10 (23.8)	15 (26.8)
3	1 (7.1)	18 (42.9)	19 (33.9)
4	0 (0.0)	0 (0.0)	0 (0.0)
Missing	3 (21.4)	3 (7.1)	6 (10.7)
Improvement	5 (35.7)	21 (50.0)	26 (46.4)
No change	5 (35.7)	18 (42.9)	23 (41.1)
Worsening	1 (7.1)	0 (0.0)	1 (1.8)
Placebo			
Number of subjects	22	36	58
0	2 (9.1)	1 (2.8)	3 (5.2)
1	4 (18.2)	7 (19.4)	11 (19.0)
2	6 (27.3)	6 (16.7)	12 (20.7)
3	6 (27.3)	18 (50.0)	24 (41.4)
4	1 (4.5)	2 (5.6)	3 (5.2)
Missing	3 (13.6)	2 (5.6)	5 (8.6)
Improvement	6 (27.3)	14 (38.9)	20 (34.5)
No change	6 (27.3)	18 (50.0)	24 (41.4)
Worsening	7 (31.8)	2 (5.6)	9 (15.5)

N: Number of subjects, %: Percentage of subjects, OD: Once daily.

6.2.14 Fibrosis stage - proportion of subjects by change from baseline - stacked bar plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



OD: Once daily.

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6.2.15 Steatosis - shift table - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Baseline value			
	1 N (%)	2 N (%)	3 N (%)	Total N (%)
Steatosis Grade at week 72				
Sema 0.1 mg OD				
Number of subjects	20	27	10	57
0	2 (10.0)	2 (7.4)	2 (20.0)	6 (10.5)
1	15 (75.0)	16 (59.3)	3 (30.0)	34 (59.6)
2	2 (10.0)	5 (18.5)	4 (40.0)	11 (19.3)
3	1 (5.0)	1 (3.7)	1 (10.0)	3 (5.3)
Missing	0 (0.0)	3 (11.1)	0 (0.0)	3 (5.3)
Improvement	2 (10.0)	18 (66.7)	9 (90.0)	29 (50.9)
No change	15 (75.0)	5 (18.5)	1 (10.0)	21 (36.8)
Worsening	3 (15.0)	1 (3.7)	0 (0.0)	4 (7.0)
Sema 0.2 mg OD				
Number of subjects	18	31	10	59
0	8 (44.4)	3 (9.7)	0 (0.0)	11 (18.6)
1	8 (44.4)	14 (45.2)	4 (40.0)	26 (44.1)
2	0 (0.0)	6 (19.4)	6 (60.0)	12 (20.3)
3	0 (0.0)	1 (3.2)	0 (0.0)	1 (1.7)
Missing	2 (11.1)	7 (22.6)	0 (0.0)	9 (15.3)
Improvement	8 (44.4)	17 (54.8)	10 (100.0)	35 (59.3)
No change	8 (44.4)	6 (19.4)	0 (0.0)	14 (23.7)
Worsening	0 (0.0)	1 (3.2)	0 (0.0)	1 (1.7)

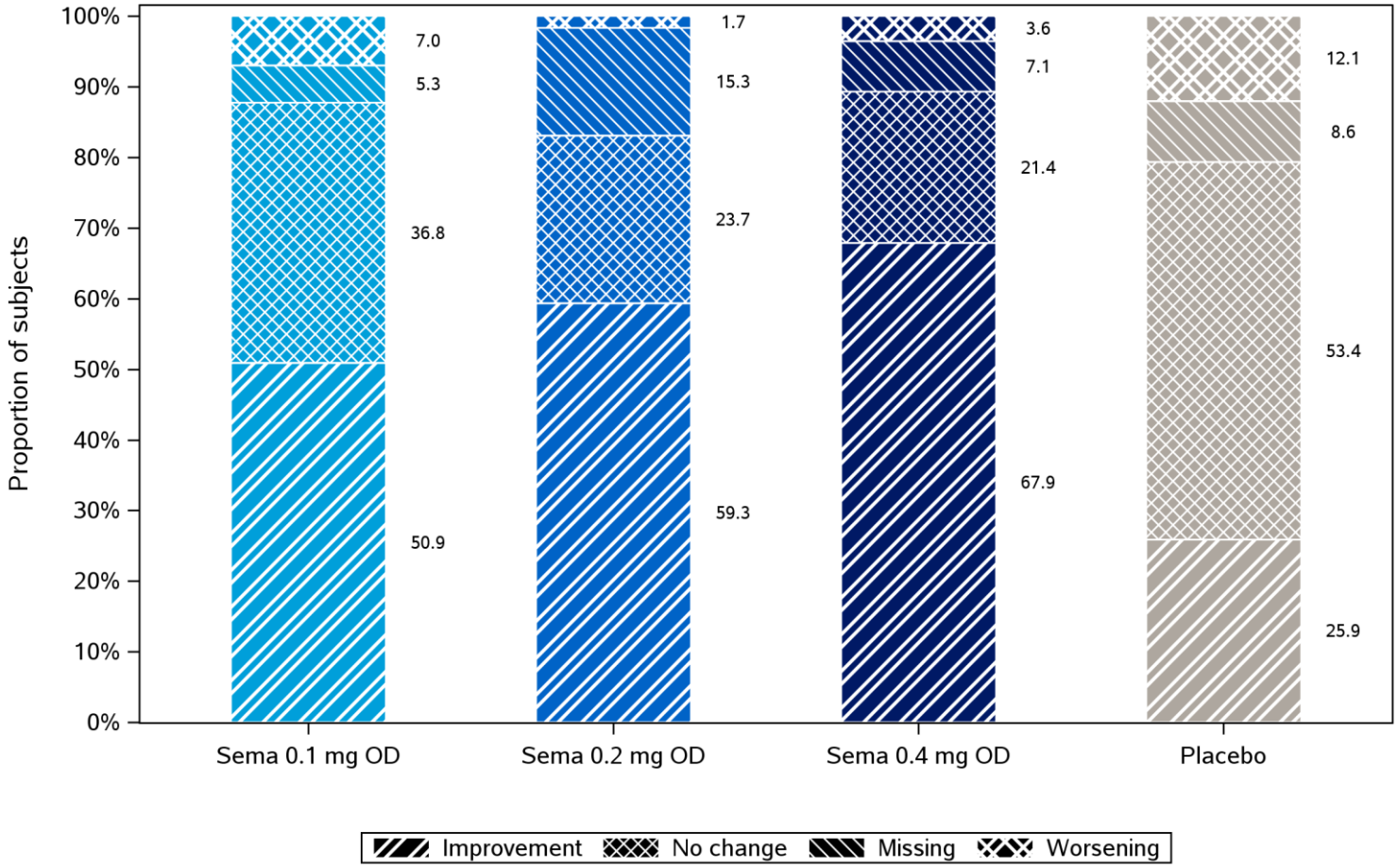
N: Number of subjects, %: Percentage of subjects, OD: Once daily.

Steatosis - shift table - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Baseline value			
	1 N (%)	2 N (%)	3 N (%)	Total N (%)
Sema 0.4 mg OD				
Number of subjects	27	17	12	56
0	13 (48.1)	6 (35.3)	1 (8.3)	20 (35.7)
1	9 (33.3)	10 (58.8)	6 (50.0)	25 (44.6)
2	2 (7.4)	1 (5.9)	2 (16.7)	5 (8.9)
3	0 (0.0)	0 (0.0)	2 (16.7)	2 (3.6)
Missing	3 (11.1)	0 (0.0)	1 (8.3)	4 (7.1)
Improvement	13 (48.1)	16 (94.1)	9 (75.0)	38 (67.9)
No change	9 (33.3)	1 (5.9)	2 (16.7)	12 (21.4)
Worsening	2 (7.4)	0 (0.0)	0 (0.0)	2 (3.6)
Placebo				
Number of subjects	16	28	14	58
0	1 (6.3)	1 (3.6)	0 (0.0)	2 (3.4)
1	10 (62.5)	7 (25.0)	2 (14.3)	19 (32.8)
2	2 (12.5)	14 (50.0)	4 (28.6)	20 (34.5)
3	0 (0.0)	5 (17.9)	7 (50.0)	12 (20.7)
Missing	3 (18.8)	1 (3.6)	1 (7.1)	5 (8.6)
Improvement	1 (6.3)	8 (28.6)	6 (42.9)	15 (25.9)
No change	10 (62.5)	14 (50.0)	7 (50.0)	31 (53.4)
Worsening	2 (12.5)	5 (17.9)	0 (0.0)	7 (12.1)

N: Number of subjects, %: Percentage of subjects, OD: Once daily.

6.2.16 Steatosis - proportion of subjects by change from baseline - stacked bar plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



OD: Once daily.

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6.2.17 Lobular inflammation - shift table - in-trial (72 weeks) - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Baseline value			
	1 N (%)	2 N (%)	3 N (%)	Total N (%)
Lobular Inflammation at week 72				
Sema 0.1 mg OD				
Number of subjects	16	38	3	57
0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
1	11 (68.8)	22 (57.9)	1 (33.3)	34 (59.6)
2	4 (25.0)	14 (36.8)	2 (66.7)	20 (35.1)
3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	1 (6.3)	2 (5.3)	0 (0.0)	3 (5.3)
Improvement	0 (0.0)	22 (57.9)	3 (100.0)	25 (43.9)
No change	11 (68.8)	14 (36.8)	0 (0.0)	25 (43.9)
Worsening	4 (25.0)	0 (0.0)	0 (0.0)	4 (7.0)
Sema 0.2 mg OD				
Number of subjects	21	37	1	59
0	1 (4.8)	0 (0.0)	0 (0.0)	1 (1.7)
1	11 (52.4)	28 (75.7)	0 (0.0)	39 (66.1)
2	5 (23.8)	5 (13.5)	0 (0.0)	10 (16.9)
3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	4 (19.0)	4 (10.8)	1 (100.0)	9 (15.3)
Improvement	1 (4.8)	28 (75.7)	0 (0.0)	29 (49.2)
No change	11 (52.4)	5 (13.5)	0 (0.0)	16 (27.1)
Worsening	5 (23.8)	0 (0.0)	0 (0.0)	5 (8.5)

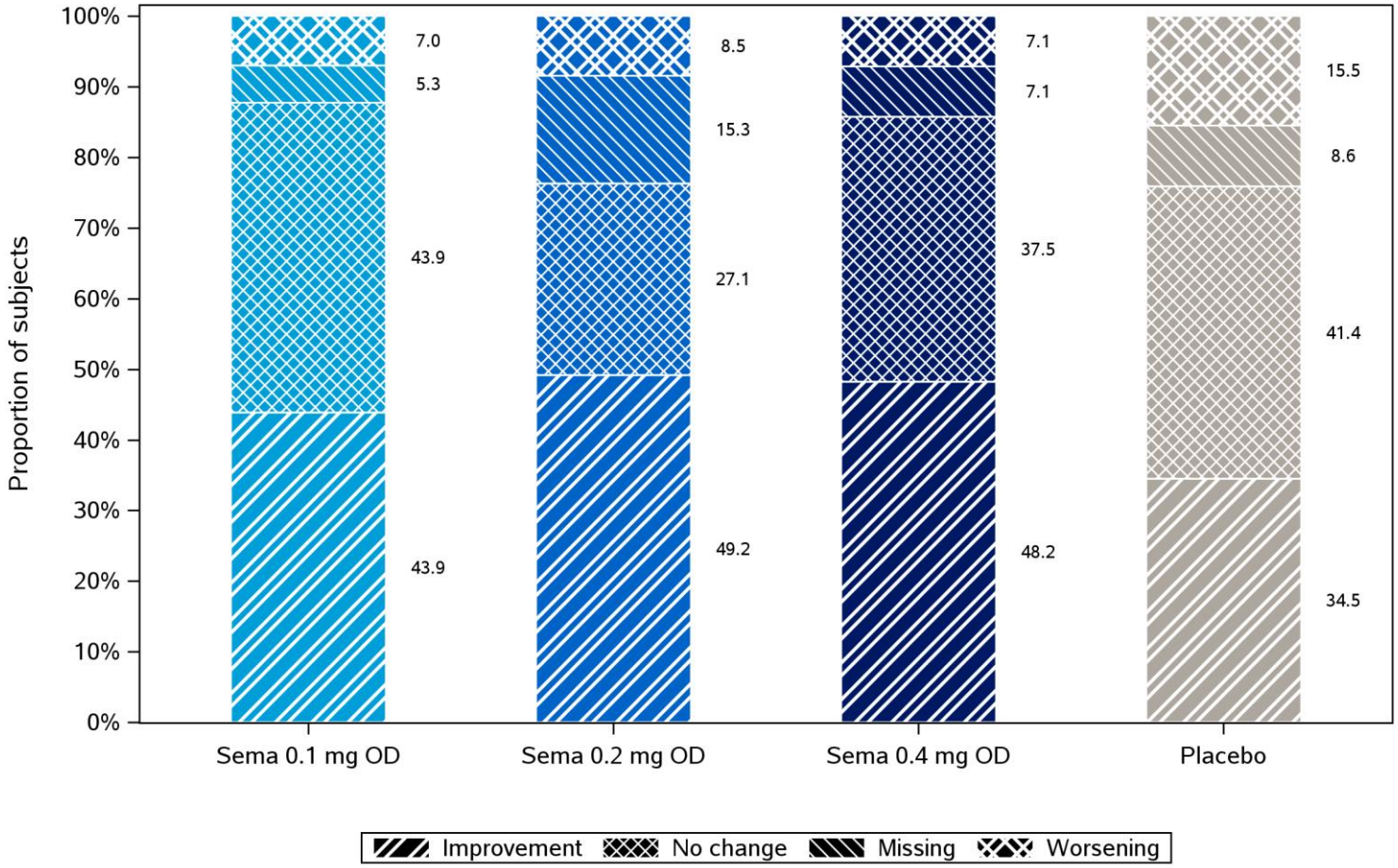
N: Number of subjects, %: Percentage of subjects, OD: Once daily.

Lobular inflammation - shift table - in-trial (72 weeks) - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Baseline value			
	1 N (%)	2 N (%)	3 N (%)	Total N (%)
Sema 0.4 mg OD				
Number of subjects	20	31	5	56
0	0 (0.0)	2 (6.5)	0 (0.0)	2 (3.6)
1	16 (80.0)	21 (67.7)	3 (60.0)	40 (71.4)
2	4 (20.0)	5 (16.1)	1 (20.0)	10 (17.9)
3	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0 (0.0)	3 (9.7)	1 (20.0)	4 (7.1)
Improvement	0 (0.0)	23 (74.2)	4 (80.0)	27 (48.2)
No change	16 (80.0)	5 (16.1)	0 (0.0)	21 (37.5)
Worsening	4 (20.0)	0 (0.0)	0 (0.0)	4 (7.1)
Placebo				
Number of subjects	18	39	1	58
0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
1	7 (38.9)	19 (48.7)	1 (100.0)	27 (46.6)
2	8 (44.4)	17 (43.6)	0 (0.0)	25 (43.1)
3	0 (0.0)	1 (2.6)	0 (0.0)	1 (1.7)
Missing	3 (16.7)	2 (5.1)	0 (0.0)	5 (8.6)
Improvement	0 (0.0)	19 (48.7)	1 (100.0)	20 (34.5)
No change	7 (38.9)	17 (43.6)	0 (0.0)	24 (41.4)
Worsening	8 (44.4)	1 (2.6)	0 (0.0)	9 (15.5)

N: Number of subjects, %: Percentage of subjects, OD: Once daily.

6.2.18 Lobular inflammation - proportion of subjects by change from baseline - stacked bar plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



OD: Once daily.

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6.2.19 Hepatocyte ballooning - shift table - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Baseline value		
	1 N (%)	2 N (%)	Total N (%)
Liver Cell Ballooning Injury at week 72			
Sema 0.1 mg OD			
Number of subjects	37	20	57
0	20 (54.1)	8 (40.0)	28 (49.1)
1	13 (35.1)	7 (35.0)	20 (35.1)
2	1 (2.7)	5 (25.0)	6 (10.5)
Missing	3 (8.1)	0 (0.0)	3 (5.3)
Improvement	20 (54.1)	15 (75.0)	35 (61.4)
No change	13 (35.1)	5 (25.0)	18 (31.6)
Worsening	1 (2.7)	0 (0.0)	1 (1.8)
Sema 0.2 mg OD			
Number of subjects	32	27	59
0	15 (46.9)	11 (40.7)	26 (44.1)
1	8 (25.0)	13 (48.1)	21 (35.6)
2	2 (6.3)	1 (3.7)	3 (5.1)
Missing	7 (21.9)	2 (7.4)	9 (15.3)
Improvement	15 (46.9)	24 (88.9)	39 (66.1)
No change	8 (25.0)	1 (3.7)	9 (15.3)
Worsening	2 (6.3)	0 (0.0)	2 (3.4)

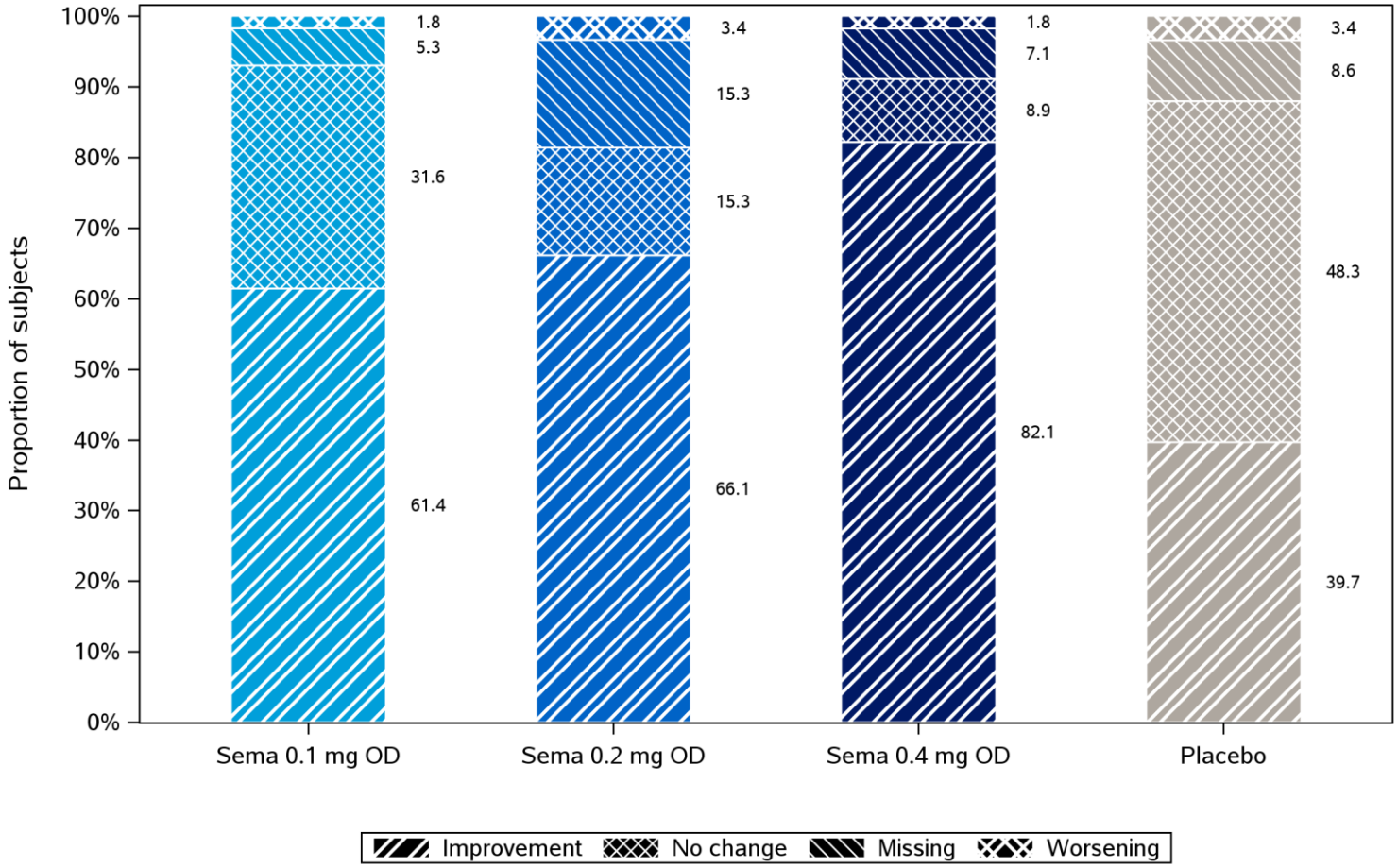
N: Number of subjects, %: Percentage of subjects, OD: Once daily.

Hepatocyte ballooning - shift table - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Baseline value		
	1 N (%)	2 N (%)	Total N (%)
Sema 0.4 mg OD			
Number of subjects	35	21	56
0	27 (77.1)	14 (66.7)	41 (73.2)
1	4 (11.4)	5 (23.8)	9 (16.1)
2	1 (2.9)	1 (4.8)	2 (3.6)
Missing	3 (8.6)	1 (4.8)	4 (7.1)
Improvement	27 (77.1)	19 (90.5)	46 (82.1)
No change	4 (11.4)	1 (4.8)	5 (8.9)
Worsening	1 (2.9)	0 (0.0)	1 (1.8)
Placebo			
Number of subjects	39	19	58
0	11 (28.2)	3 (15.8)	14 (24.1)
1	23 (59.0)	9 (47.4)	32 (55.2)
2	2 (5.1)	5 (26.3)	7 (12.1)
Missing	3 (7.7)	2 (10.5)	5 (8.6)
Improvement	11 (28.2)	12 (63.2)	23 (39.7)
No change	23 (59.0)	5 (26.3)	28 (48.3)
Worsening	2 (5.1)	0 (0.0)	2 (3.4)

N: Number of subjects, %: Percentage of subjects, OD: Once daily.

6.2.20 Hepatocyte ballooning - proportion of subjects by change from baseline - stacked bar plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



OD: Once daily.

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6.2.21 Total NAS - shift table - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Baseline value					
	4 N (%)	5 N (%)	6 N (%)	7 N (%)	8 N (%)	Total N (%)
NAFLD Activity Score at week 72						
Sema 0.1 mg OD						
Number of subjects	21	21	13	1	1	57
0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
1	2 (9.5)	0 (0.0)	3 (23.1)	0 (0.0)	0 (0.0)	5 (8.8)
2	7 (33.3)	8 (38.1)	4 (30.8)	0 (0.0)	0 (0.0)	19 (33.3)
3	5 (23.8)	2 (9.5)	2 (15.4)	0 (0.0)	0 (0.0)	9 (15.8)
4	2 (9.5)	2 (9.5)	2 (15.4)	0 (0.0)	1 (100.0)	7 (12.3)
5	3 (14.3)	6 (28.6)	2 (15.4)	0 (0.0)	0 (0.0)	11 (19.3)
6	1 (4.8)	1 (4.8)	0 (0.0)	1 (100.0)	0 (0.0)	3 (5.3)
7	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
8	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	1 (4.8)	2 (9.5)	0 (0.0)	0 (0.0)	0 (0.0)	3 (5.3)
Improvement	14 (66.7)	12 (57.1)	13 (100.0)	1 (100.0)	1 (100.0)	41 (71.9)
No change	2 (9.5)	6 (28.6)	0 (0.0)	0 (0.0)	0 (0.0)	8 (14.0)
Worsening	4 (19.0)	1 (4.8)	0 (0.0)	0 (0.0)	0 (0.0)	5 (8.8)
Sema 0.2 mg OD						
Number of subjects	21	23	10	5	0	59
0	1 (4.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
1	4 (19.0)	5 (21.7)	1 (10.0)	0 (0.0)	0 (0.0)	10 (16.9)
2	4 (19.0)	3 (13.0)	3 (30.0)	0 (0.0)	0 (0.0)	10 (16.9)
3	3 (14.3)	5 (21.7)	4 (40.0)	0 (0.0)	0 (0.0)	12 (20.3)
4	2 (9.5)	6 (26.1)	2 (20.0)	3 (60.0)	0 (0.0)	13 (22.0)
5	1 (4.8)	1 (4.3)	0 (0.0)	1 (20.0)	0 (0.0)	3 (5.1)
6	1 (4.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)
7	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
8	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	5 (23.8)	3 (13.0)	0 (0.0)	1 (20.0)	0 (0.0)	9 (15.3)
Improvement	12 (57.1)	19 (82.6)	10 (100.0)	4 (80.0)	0 (0.0)	45 (76.3)
No change	2 (9.5)	1 (4.3)	0 (0.0)	0 (0.0)	0 (0.0)	3 (5.1)
Worsening	2 (9.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.4)

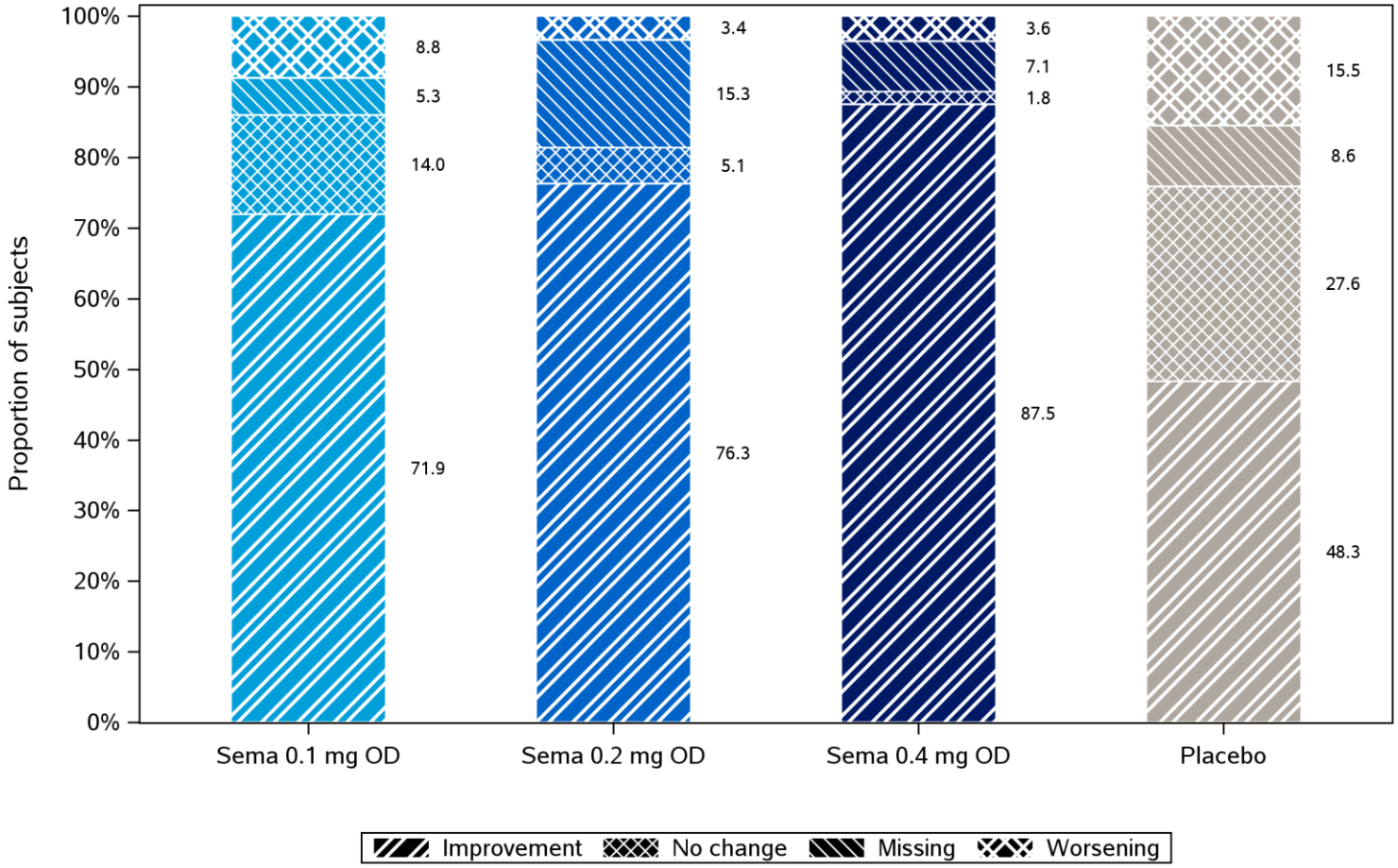
N: Number of subjects, %: Percentage of subjects, OD: Once daily.

Total NAS - shift table - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Baseline value					
	4 N (%)	5 N (%)	6 N (%)	7 N (%)	8 N (%)	Total N (%)
Sema 0.4 mg OD						
Number of subjects	25	19	9	2	1	56
0	0 (0.0)	1 (5.3)	1 (11.1)	0 (0.0)	0 (0.0)	2 (3.6)
1	7 (28.0)	5 (26.3)	1 (11.1)	1 (50.0)	0 (0.0)	14 (25.0)
2	9 (36.0)	7 (36.8)	3 (33.3)	1 (50.0)	0 (0.0)	20 (35.7)
3	5 (20.0)	2 (10.5)	0 (0.0)	0 (0.0)	1 (100.0)	8 (14.3)
4	0 (0.0)	3 (15.8)	2 (22.2)	0 (0.0)	0 (0.0)	5 (8.9)
5	1 (4.0)	1 (5.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.6)
6	1 (4.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
7	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
8	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	2 (8.0)	0 (0.0)	2 (22.2)	0 (0.0)	0 (0.0)	4 (7.1)
Improvement	21 (84.0)	18 (94.7)	7 (77.8)	2 (100.0)	1 (100.0)	49 (87.5)
No change	0 (0.0)	1 (5.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.8)
Worsening	2 (8.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.6)
Placebo						
Number of subjects	22	18	14	4	0	58
0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
1	2 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.4)
2	2 (9.1)	0 (0.0)	1 (7.1)	1 (25.0)	0 (0.0)	4 (6.9)
3	2 (9.1)	4 (22.2)	2 (14.3)	1 (25.0)	0 (0.0)	9 (15.5)
4	6 (27.3)	4 (22.2)	2 (14.3)	1 (25.0)	0 (0.0)	13 (22.4)
5	5 (22.7)	8 (44.4)	5 (35.7)	1 (25.0)	0 (0.0)	19 (32.8)
6	1 (4.5)	2 (11.1)	2 (14.3)	0 (0.0)	0 (0.0)	5 (8.6)
7	0 (0.0)	0 (0.0)	1 (7.1)	0 (0.0)	0 (0.0)	1 (1.7)
8	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	4 (18.2)	0 (0.0)	1 (7.1)	0 (0.0)	0 (0.0)	5 (8.6)
Improvement	6 (27.3)	8 (44.4)	10 (71.4)	4 (100.0)	0 (0.0)	28 (48.3)
No change	6 (27.3)	8 (44.4)	2 (14.3)	0 (0.0)	0 (0.0)	16 (27.6)
Worsening	6 (27.3)	2 (11.1)	1 (7.1)	0 (0.0)	0 (0.0)	9 (15.5)

N: Number of subjects, %: Percentage of subjects, OD: Once daily.

6.2.22 Total NAS - proportion of subjects by change from baseline - stacked bar plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



OD: Once daily.

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6.2.23 Liver stiffness assessed by transient elastography (FibroScan) by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Number of subjects	57	59	56	58
Liver Stiffness Fibroscan (kPa)				
Week 0 (Randomisation)				
N(%)	37 (64.9)	41 (69.5)	35 (62.5)	38 (65.5)
Geom. Mean (CV)	11.5 (49.1)	12.8 (39.4)	12.4 (69.8)	9.0 (68.7)
Mean (SD)	12.8 (6.8)	13.7 (5.5)	15.3 (11.8)	10.2 (3.9)
Median (IQR)	11.7 (8.0; 15.3)	11.4 (9.8; 18.2)	11.9 (8.0; 16.1)	10.2 (7.9; 12.8)
Min ; Max	5.6 ; 35.3	6.6 ; 30.1	2.4 ; 54.7	0.8 ; 17.8
Week 28				
N(%)	37 (64.9)	40 (67.8)	37 (66.1)	40 (69.0)
Geom. Mean (CV)	9.6 (41.3)	9.4 (46.1)	9.1 (53.1)	10.0 (46.7)
Mean (SD)	10.3 (4.0)	10.4 (5.6)	10.4 (6.3)	11.1 (5.7)
Median (IQR)	9.7 (7.0; 13.2)	9.2 (7.1; 11.9)	8.9 (6.5; 11.8)	9.7 (7.4; 12.1)
Min ; Max	4.4 ; 20.0	3.7 ; 34.6	3.8 ; 34.1	4.6 ; 32.4
Week 52				
N(%)	38 (66.7)	39 (66.1)	40 (71.4)	36 (62.1)
Geom. Mean (CV)	9.4 (45.7)	8.5 (46.1)	8.0 (51.8)	9.5 (46.7)
Mean (SD)	10.3 (5.0)	9.5 (6.3)	9.0 (4.9)	10.4 (4.8)
Median (IQR)	9.0 (6.8; 11.8)	8.1 (6.7; 10.1)	7.9 (5.9; 11.3)	9.0 (7.3; 13.2)
Min ; Max	4.9 ; 24.2	3.4 ; 40.9	2.6 ; 26.7	3.5 ; 22.6

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver stiffness assessed by transient elastography (FibroScan) by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 72 (EOT)				
N(%)	39 (68.4)	39 (66.1)	38 (67.9)	36 (62.1)
Geom. Mean (CV)	8.1 (49.0)	7.9 (47.8)	7.7 (51.9)	10.5 (52.4)
Mean (SD)	9.0 (4.7)	9.0 (5.8)	8.8 (5.5)	11.8 (6.0)
Median (IQR)	8.1 (6.3; 10.2)	7.2 (5.6; 9.8)	7.0 (5.5; 10.4)	10.7 (6.7; 15.3)
Min ; Max	2.8 ; 22.4	4.2 ; 35.9	3.4 ; 33.8	4.2 ; 31.3
Week 72 (EOT) (on-treatment)				
N(%)	37 (64.9)	34 (57.6)	35 (62.5)	33 (56.9)
Geom. Mean (CV)	7.9 (47.9)	8.2 (49.7)	7.7 (53.8)	10.3 (54.3)
Mean (SD)	8.8 (4.5)	9.4 (6.1)	8.8 (5.7)	11.7 (6.2)
Median (IQR)	7.9 (6.3; 10.2)	7.5 (6.0; 10.2)	7.0 (5.4; 10.4)	10.6 (6.6; 15.4)
Min ; Max	2.8 ; 22.4	4.2 ; 35.9	3.4 ; 33.8	4.2 ; 31.3

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

6.2.24 Liver stiffness assessed by transient elastography (FibroScan) - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Number of subjects	57	59	56	58
Liver Stiffness Fibroscan (kPa)				
Week 0 (Randomisation)				
N(%)	37 (64.9)	41 (69.5)	35 (62.5)	38 (65.5)
Geom. Mean (CV)	11.5 (49.1)	12.8 (39.4)	12.4 (69.8)	9.0 (68.7)
Mean (SD)	12.8 (6.8)	13.7 (5.5)	15.3 (11.8)	10.2 (3.9)
Median (IQR)	11.7 (8.0; 15.3)	11.4 (9.8; 18.2)	11.9 (8.0; 16.1)	10.2 (7.9; 12.8)
Min ; Max	5.6 ; 35.3	6.6 ; 30.1	2.4 ; 54.7	0.8 ; 17.8
Ratio to baseline in Liver Stiffness Fibroscan				
Week 28				
N(%)	35 (61.4)	36 (61.0)	32 (57.1)	36 (62.1)
Geom. Mean (CV)	0.81 (31.0)	0.72 (42.7)	0.75 (60.5)	1.13 (74.4)
Mean (SD)	0.84 (0.27)	0.81 (0.67)	0.88 (0.68)	1.56 (2.00)
Median (IQR)	0.75 (0.68; 0.99)	0.72 (0.55; 0.83)	0.79 (0.61; 0.98)	0.98 (0.74; 1.26)
Min ; Max	0.47 ; 1.63	0.35 ; 4.55	0.19 ; 4.13	0.45 ; 9.77
Week 52				
N(%)	33 (57.9)	35 (59.3)	32 (57.1)	31 (53.4)
Geom. Mean (CV)	0.76 (43.9)	0.66 (37.3)	0.71 (56.1)	1.05 (77.6)
Mean (SD)	0.83 (0.35)	0.70 (0.27)	0.80 (0.43)	1.52 (2.29)
Median (IQR)	0.77 (0.57; 1.04)	0.67 (0.55; 0.81)	0.76 (0.49; 0.99)	0.96 (0.68; 1.27)
Min ; Max	0.33 ; 1.58	0.32 ; 1.70	0.21 ; 2.25	0.40 ; 12.54

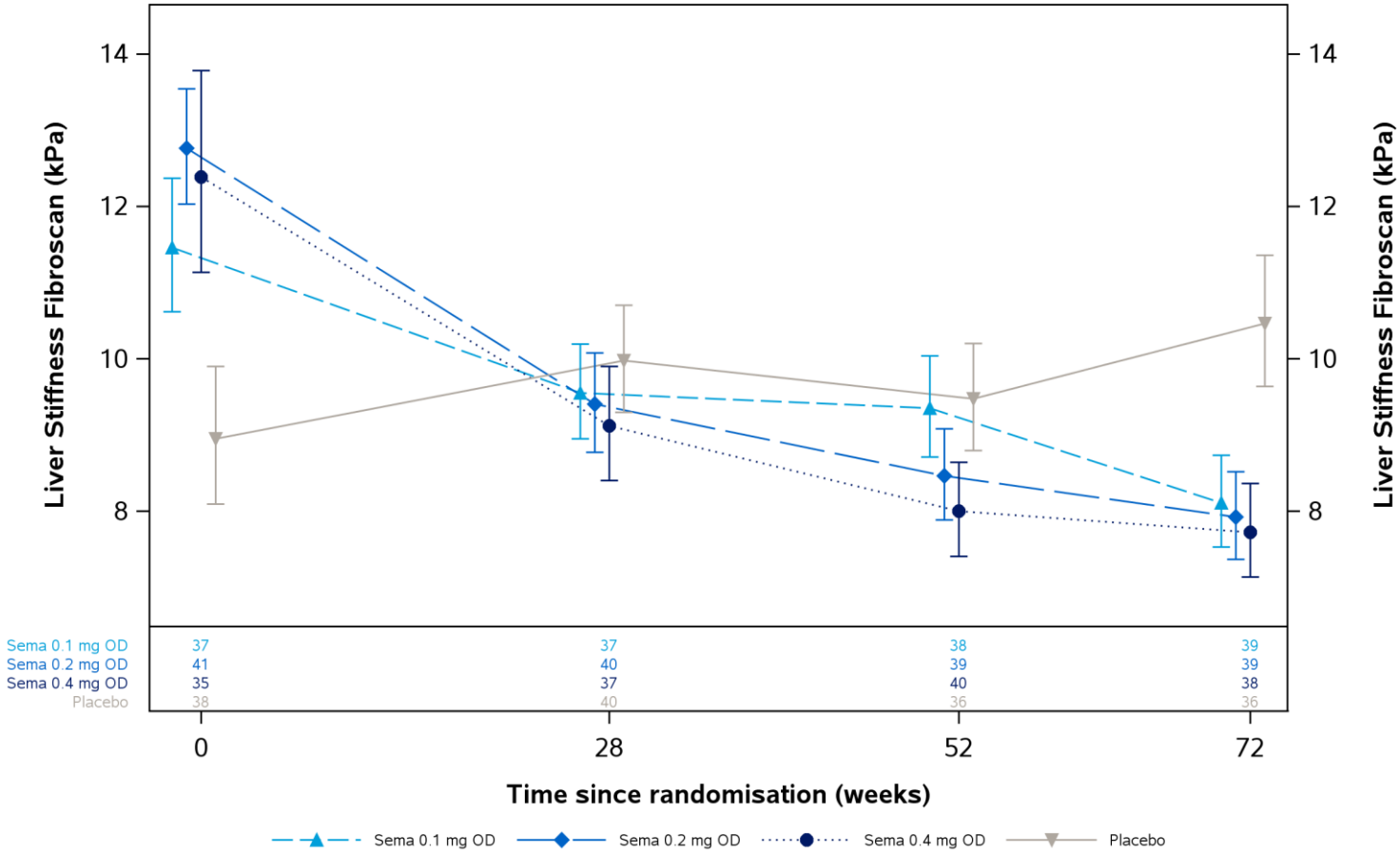
N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver stiffness assessed by transient elastography (FibroScan) - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 72 (EOT)				
N(%)	34 (59.6)	36 (61.0)	32 (57.1)	32 (55.2)
Geom. Mean (CV)	0.68 (47.6)	0.60 (58.4)	0.66 (61.3)	1.21 (83.8)
Mean (SD)	0.75 (0.35)	0.73 (0.73)	0.82 (0.87)	1.80 (2.75)
Median (IQR)	0.63 (0.56; 0.91)	0.55 (0.44; 0.83)	0.69 (0.52; 0.83)	1.00 (0.85; 1.44)
Min ; Max	0.23 ; 1.85	0.19 ; 4.72	0.23 ; 5.33	0.32 ; 15.00
Week 72 (EOT) (on-treatment)				
N(%)	33 (57.9)	31 (52.5)	30 (53.6)	29 (50.0)
Geom. Mean (CV)	0.68 (48.3)	0.60 (62.7)	0.65 (63.3)	1.21 (89.2)
Mean (SD)	0.75 (0.36)	0.75 (0.78)	0.82 (0.89)	1.86 (2.88)
Median (IQR)	0.64 (0.58; 0.91)	0.56 (0.43; 0.84)	0.65 (0.51; 0.83)	0.98 (0.83; 1.43)
Min ; Max	0.23 ; 1.85	0.19 ; 4.72	0.23 ; 5.33	0.32 ; 15.00

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

6.2.25 Liver stiffness assessed by transient elastography (FibroScan) by week - observed geometric mean plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



Number of observations per treatment group and visit is presented in the lower part of the plot. Mean +/- standard error calculated on log-scale and back-transformed to original scale. OD: Once daily.

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6.2.26 Liver stiffness assessed by transient elastography (FibroScan) - ratio to baseline - statistical analysis - ANCOVA - MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
Liver Stiffness Fibroscan (kPa)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	37	8.29		
Sema 0.2 mg OD	59	41	7.57		
Sema 0.4 mg OD	56	35	7.98		
Placebo	58	38	11.17		
Ratio to baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	37	0.73		
Sema 0.2 mg OD	59	41	0.67		
Sema 0.4 mg OD	56	35	0.71		
Placebo	58	38	0.99		
Treatment ratio at week 72 (EOT)					
Sema 0.1 mg OD / Placebo			0.74	[0.59; 0.93]	0.0094
Sema 0.2 mg OD / Placebo			0.68	[0.54; 0.85]	0.0006
Sema 0.4 mg OD / Placebo			0.71	[0.57; 0.90]	0.0039

ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval, OD: Once daily, EOT: End of treatment.

6.2.27 Liver steatosis assessed by transient elastography (FibroScan) by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Number of subjects	57	59	56	58
Liver Steatosis Fibroscan (dB/m)				
Week 0 (Randomisation)				
N(%)	27 (47.4)	29 (49.2)	25 (44.6)	31 (53.4)
Mean (SD)	321.5 (45.1)	343.2 (58.6)	327.8 (53.5)	345.5 (35.4)
Median (IQR)	324.0 (295.0; 344.0)	360.0 (317.0; 394.0)	340.0 (297.0; 345.0)	347.0 (326.0; 373.0)
Min ; Max	214.0 ; 400.0	211.0 ; 400.0	199.0 ; 400.0	249.0 ; 400.0
Week 28				
N(%)	27 (47.4)	31 (52.5)	30 (53.6)	33 (56.9)
Mean (SD)	318.7 (58.9)	297.9 (70.7)	280.6 (85.6)	340.7 (51.6)
Median (IQR)	322.0 (279.0; 362.0)	322.0 (250.0; 349.0)	294.0 (221.0; 355.0)	346.0 (304.0; 383.0)
Min ; Max	141.0 ; 400.0	100.0 ; 400.0	112.0 ; 400.0	197.0 ; 400.0
Week 52				
N(%)	30 (52.6)	33 (55.9)	32 (57.1)	32 (55.2)
Mean (SD)	328.6 (56.9)	301.9 (75.6)	265.0 (75.4)	333.3 (39.2)
Median (IQR)	328.0 (278.0; 377.0)	310.0 (252.0; 368.0)	293.5 (205.5; 322.5)	332.0 (302.5; 367.0)
Min ; Max	211.0 ; 400.0	129.0 ; 400.0	104.0 ; 397.0	249.0 ; 400.0
Week 72 (EOT)				
N(%)	31 (54.4)	32 (54.2)	31 (55.4)	31 (53.4)
Mean (SD)	319.3 (53.5)	301.8 (62.9)	267.9 (81.2)	325.1 (57.3)
Median (IQR)	316.0 (285.0; 350.0)	310.5 (275.0; 341.0)	271.0 (214.0; 330.0)	340.0 (304.0; 361.0)
Min ; Max	185.0 ; 400.0	163.0 ; 400.0	100.0 ; 400.0	133.0 ; 400.0

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

Liver steatosis assessed by transient elastography (FibroScan) by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 72 (EOT) (on-treatment)				
N(%)	29 (50.9)	30 (50.8)	30 (53.6)	29 (50.0)
Mean (SD)	322.5 (52.6)	300.1 (64.2)	264.9 (80.8)	322.8 (58.5)
Median (IQR)	320.0 (287.0; 350.0)	310.5 (274.0; 339.0)	262.5 (214.0; 318.0)	333.0 (304.0; 352.0)
Min ; Max	185.0 ; 400.0	163.0 ; 400.0	100.0 ; 400.0	133.0 ; 400.0

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

6.2.28 Liver steatosis assessed by transient elastography (FibroScan) - change from baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Number of subjects	57	59	56	58
Liver Steatosis Fibroscan (dB/m)				
Week 0 (Randomisation)				
N(%)	27 (47.4)	29 (49.2)	25 (44.6)	31 (53.4)
Mean (SD)	321.5 (45.1)	343.2 (58.6)	327.8 (53.5)	345.5 (35.4)
Median (IQR)	324.0 (295.0; 344.0)	360.0 (317.0; 394.0)	340.0 (297.0; 345.0)	347.0 (326.0; 373.0)
Min ; Max	214.0 ; 400.0	211.0 ; 400.0	199.0 ; 400.0	249.0 ; 400.0
Change from baseline in Liver Steatosis Fibroscan (dB/m)				
Week 28				
N(%)	25 (43.9)	26 (44.1)	23 (41.1)	29 (50.0)
Mean (SD)	-7.7 (41.2)	-49.5 (52.4)	-49.5 (64.8)	-9.2 (43.5)
Median (IQR)	-6.0 (-33.0; 16.0)	-50.5 (-79.0; -14.0)	-38.0 (-86.0; -3.0)	0.0 (-23.0; 21.0)
Min ; Max	-102.0 ; 76.0	-155.0 ; 67.0	-206.0 ; 55.0	-117.0 ; 73.0
Week 52				
N(%)	25 (43.9)	26 (44.1)	22 (39.3)	26 (44.8)
Mean (SD)	1.6 (60.1)	-47.7 (79.0)	-64.0 (58.7)	-14.5 (38.3)
Median (IQR)	-8.0 (-24.0; 49.0)	-41.5 (-89.0; 0.0)	-47.5 (-101.0; -25.0)	-15.0 (-45.0; 10.0)
Min ; Max	-117.0 ; 93.0	-261.0 ; 87.0	-181.0 ; 1.0	-79.0 ; 60.0
Week 72 (EOT)				
N(%)	25 (43.9)	26 (44.1)	22 (39.3)	25 (43.1)
Mean (SD)	-5.5 (47.3)	-53.7 (66.3)	-52.5 (68.0)	-15.2 (43.7)
Median (IQR)	0.0 (-47.0; 15.0)	-64.5 (-96.0; -3.0)	-38.0 (-91.0; -15.0)	-5.0 (-31.0; 9.0)
Min ; Max	-86.0 ; 115.0	-194.0 ; 87.0	-261.0 ; 50.0	-148.0 ; 45.0

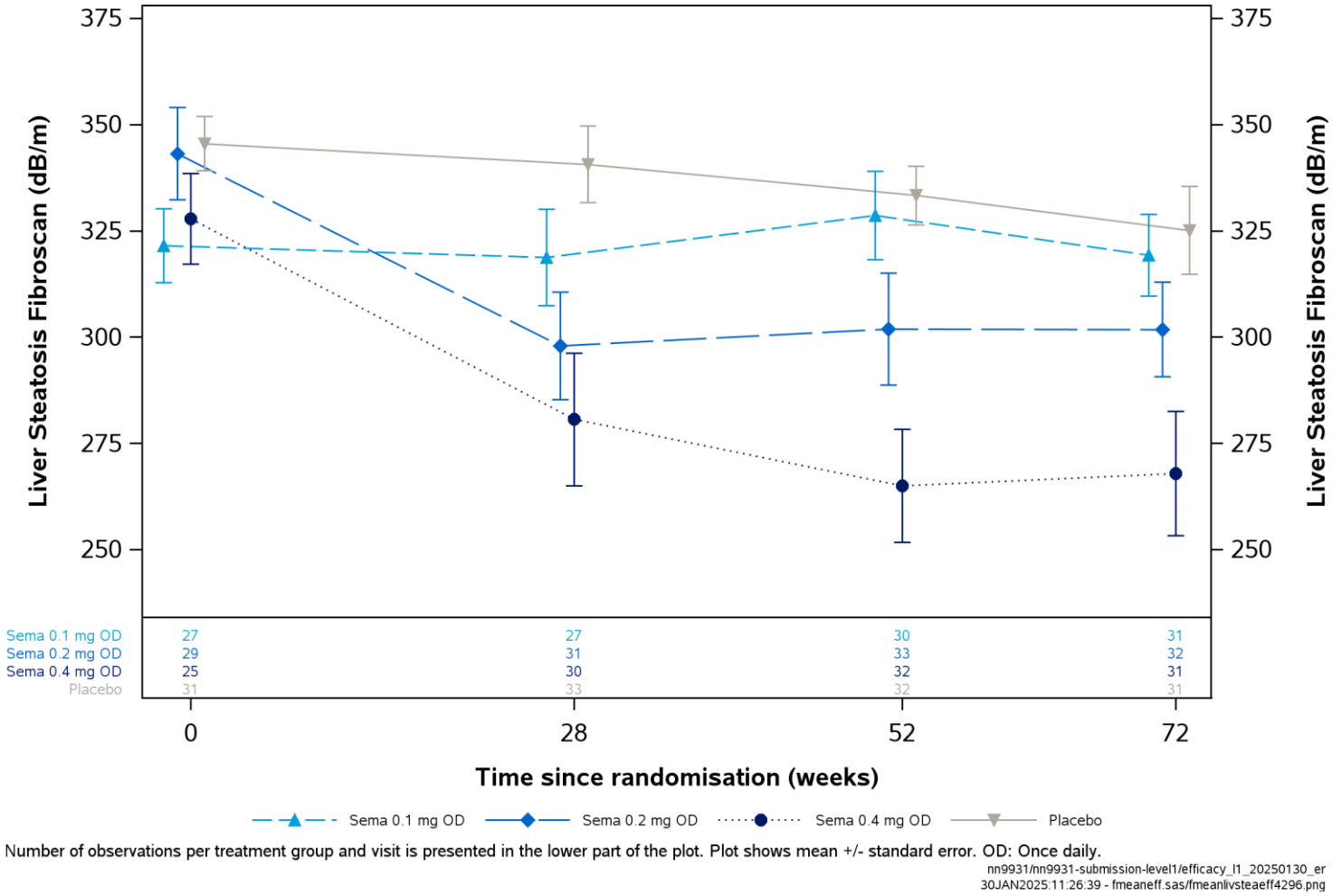
N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

Liver steatosis assessed by transient elastography (FibroScan) - change from baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 72 (EOT) (on-treatment)				
N(%)	24 (42.1)	24 (40.7)	21 (37.5)	23 (39.7)
Mean (SD)	-2.8 (46.4)	-54.0 (67.7)	-56.0 (67.7)	-14.2 (45.0)
Median (IQR)	1.5 (-43.5; 17.5)	-64.5 (-95.0; -6.5)	-43.0 (-91.0; -18.0)	-3.0 (-31.0; 13.0)
Min ; Max	-86.0 ; 115.0	-194.0 ; 87.0	-261.0 ; 50.0	-148.0 ; 45.0

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

6.2.29 Liver steatosis assessed by transient elastography (FibroScan) by week - observed mean plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



Number of observations per treatment group and visit is presented in the lower part of the plot. Plot shows mean +/- standard error. OD: Once daily.

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6.2.30 Liver steatosis assessed by transient elastography (FibroScan) - change from baseline - statistical analysis - ANCOVA with MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline

	FAS	N	Estimate	95% CI	Two-sided p-value
Liver Steatosis Fibroscan (dB/m)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	27	319.0		
Sema 0.2 mg OD	59	29	290.5		
Sema 0.4 mg OD	56	25	286.2		
Placebo	58	31	322.1		
Change from baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	27	-16.2		
Sema 0.2 mg OD	59	29	-44.7		
Sema 0.4 mg OD	56	25	-49.0		
Placebo	58	31	-13.0		
Treatment difference at week 72 (EOT)					
Sema 0.1 mg OD - Placebo			-3.2	[-32.90; 26.56]	0.8345
Sema 0.2 mg OD - Placebo			-31.6	[-60.36; -2.93]	0.0308
Sema 0.4 mg OD - Placebo			-35.9	[-66.31; -5.58]	0.0203

ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval, OD: Once daily, EOT: End of treatment.

6.2.31 Liver enzymes by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Number of subjects	57	59	56	58
Alanine Aminotransferase (U/L)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	58 (62.3)	53 (50.4)	57 (58.4)	55 (63.6)
Mean (SD)	68 (40)	60 (28)	66 (39)	65 (43)
Median (IQR)	59 (41; 82)	53 (38; 75)	60 (39; 84)	55 (38; 70)
Min ; Max	15 ; 222	13 ; 132	18 ; 199	16 ; 222
Week 4				
N(%)	57 (100.0)	57 (96.6)	54 (96.4)	58 (100.0)
Geom. Mean (CV)	52 (67.4)	49 (53.3)	53 (58.8)	52 (67.1)
Mean (SD)	62 (39)	56 (32)	61 (36)	63 (46)
Median (IQR)	56 (32; 78)	45 (35; 72)	54 (34; 76)	50 (37; 71)
Min ; Max	11 ; 216	15 ; 193	19 ; 178	14 ; 226
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	43 (62.7)	40 (51.1)	41 (60.5)	49 (72.4)
Mean (SD)	51 (38)	45 (22)	47 (25)	60 (43)
Median (IQR)	45 (31; 60)	40 (28; 56)	44 (27; 57)	49 (32; 79)
Min ; Max	12 ; 252	12 ; 114	7 ; 114	12 ; 254

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver enzymes by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 20				
N(%)	54 (94.7)	54 (91.5)	53 (94.6)	57 (98.3)
Geom. Mean (CV)	39 (70.2)	34 (53.2)	32 (64.4)	48 (69.9)
Mean (SD)	46 (26)	38 (22)	39 (27)	58 (41)
Median (IQR)	42 (26; 64)	33 (23; 49)	28 (22; 48)	46 (34; 61)
Min ; Max	7 ; 110	11 ; 132	10 ; 137	9 ; 202
Week 28				
N(%)	55 (96.5)	53 (89.8)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	39 (70.3)	33 (65.8)	28 (59.6)	47 (70.7)
Mean (SD)	48 (32)	40 (25)	32 (19)	58 (45)
Median (IQR)	42 (25; 59)	32 (21; 54)	26 (20; 40)	50 (31; 66)
Min ; Max	9 ; 157	10 ; 120	7 ; 90	14 ; 269
Week 36				
N(%)	53 (93.0)	52 (88.1)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	36 (77.6)	33 (69.8)	25 (57.5)	49 (68.2)
Mean (SD)	45 (29)	41 (35)	29 (20)	60 (48)
Median (IQR)	38 (22; 68)	31 (20; 49)	21 (16; 33)	47 (35; 67)
Min ; Max	8 ; 110	11 ; 237	10 ; 126	13 ; 312
Week 44				
N(%)	53 (93.0)	53 (89.8)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	34 (88.6)	30 (60.6)	24 (63.7)	47 (69.2)
Mean (SD)	44 (30)	35 (22)	29 (22)	58 (44)
Median (IQR)	40 (21; 55)	28 (19; 42)	21 (16; 37)	42 (31; 66)
Min ; Max	3 ; 158	10 ; 109	9 ; 137	14 ; 226
N<LLOQ ; N>ULOQ	1 ; 0			

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver enzymes by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 52				
N(%)	55 (96.5)	52 (88.1)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	35 (84.1)	30 (60.2)	24 (77.2)	47 (55.7)
Mean (SD)	45 (33)	36 (24)	30 (26)	53 (32)
Median (IQR)	38 (21; 64)	28 (19; 46)	23 (17; 30)	48 (32; 67)
Min ; Max	6 ; 140	13 ; 125	3 ; 146	17 ; 200
N<LLOQ ; N>ULOQ			1 ; 0	
Week 62				
N(%)	54 (94.7)	52 (88.1)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	32 (86.2)	28 (62.2)	26 (75.2)	46 (62.1)
Mean (SD)	42 (32)	34 (24)	34 (34)	54 (34)
Median (IQR)	31 (20; 55)	25 (18; 40)	23 (17; 36)	43 (32; 69)
Min ; Max	6 ; 139	10 ; 124	7 ; 205	13 ; 204
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	35 (89.4)	29 (63.8)	22 (76.2)	44 (59.7)
Mean (SD)	47 (38)	35 (22)	28 (23)	51 (30)
Median (IQR)	35 (21; 65)	26 (20; 46)	21 (14; 32)	43 (31; 63)
Min ; Max	7 ; 157	8 ; 109	3 ; 109	15 ; 145
N<LLOQ ; N>ULOQ			1 ; 0	
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	34 (87.2)	28 (64.1)	22 (72.3)	44 (60.1)
Mean (SD)	45 (35)	34 (22)	27 (21)	51 (30)
Median (IQR)	34 (21; 62)	26 (20; 44)	21 (14; 32)	42 (31; 63)
Min ; Max	7 ; 149	8 ; 109	3 ; 109	15 ; 145
N<LLOQ ; N>ULOQ			1 ; 0	

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver enzymes by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Aspartate Aminotransferase (U/L)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	47 (49.9)	45 (44.0)	48 (50.2)	44 (58.7)
Mean (SD)	52 (23)	49 (22)	54 (29)	51 (34)
Median (IQR)	48 (34; 69)	46 (31; 61)	47 (33; 66)	44 (30; 60)
Min ; Max	14 ; 108	16 ; 135	21 ; 158	14 ; 229
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	58 (100.0)
Geom. Mean (CV)	41 (47.3)	42 (46.4)	42 (45.4)	42 (59.5)
Mean (SD)	45 (21)	46 (22)	47 (21)	49 (30)
Median (IQR)	41 (30; 57)	42 (31; 55)	40 (32; 59)	41 (29; 56)
Min ; Max	14 ; 104	14 ; 115	18 ; 106	15 ; 148
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	35 (49.0)	35 (39.8)	35 (41.7)	40 (56.9)
Mean (SD)	40 (25)	38 (14)	38 (17)	45 (23)
Median (IQR)	36 (26; 47)	35 (27; 48)	32 (27; 45)	39 (27; 60)
Min ; Max	12 ; 187	12 ; 79	16 ; 101	12 ; 107

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver enzymes by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 20				
N(%)	53 (93.0)	54 (91.5)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	33 (52.2)	31 (45.7)	29 (43.2)	39 (49.5)
Mean (SD)	37 (17)	34 (17)	32 (15)	44 (21)
Median (IQR)	33 (24; 47)	29 (22; 41)	29 (22; 38)	40 (27; 54)
Min ; Max	10 ; 72	14 ; 101	14 ; 87	17 ; 108
Week 28				
N(%)	55 (96.5)	53 (89.8)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	34 (47.4)	32 (50.8)	26 (36.7)	39 (58.7)
Mean (SD)	37 (17)	36 (19)	28 (12)	45 (24)
Median (IQR)	36 (24; 45)	29 (23; 47)	26 (21; 31)	39 (24; 59)
Min ; Max	14 ; 111	12 ; 114	16 ; 73	13 ; 114
Week 36				
N(%)	53 (93.0)	52 (88.1)	53 (94.6)	57 (98.3)
Geom. Mean (CV)	31 (57.1)	30 (53.6)	24 (38.6)	41 (70.3)
Mean (SD)	35 (20)	35 (20)	26 (14)	51 (49)
Median (IQR)	29 (22; 40)	26 (22; 42)	24 (19; 30)	40 (26; 55)
Min ; Max	10 ; 88	13 ; 95	12 ; 108	11 ; 337
Week 44				
N(%)	53 (93.0)	54 (91.5)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	31 (57.1)	28 (47.1)	24 (35.9)	38 (58.4)
Mean (SD)	36 (18)	31 (19)	26 (12)	44 (25)
Median (IQR)	32 (22; 46)	26 (20; 35)	22 (19; 27)	35 (26; 59)
Min ; Max	11 ; 98	15 ; 127	13 ; 93	14 ; 111

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver enzymes by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 52				
N(%)	55 (96.5)	52 (88.1)	52 (92.9)	54 (93.1)
Geom. Mean (CV)	32 (57.8)	29 (50.5)	25 (41.1)	39 (50.7)
Mean (SD)	37 (25)	33 (23)	27 (15)	43 (20)
Median (IQR)	30 (22; 46)	28 (20; 36)	22 (20; 30)	40 (28; 52)
Min ; Max	10 ; 162	14 ; 161	12 ; 107	15 ; 98
Week 62				
N(%)	54 (94.7)	52 (88.1)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	30 (52.2)	27 (51.3)	26 (48.9)	37 (54.3)
Mean (SD)	34 (18)	32 (24)	30 (23)	42 (21)
Median (IQR)	30 (20; 40)	26 (19; 35)	22 (19; 30)	39 (25; 52)
Min ; Max	12 ; 94	12 ; 164	14 ; 156	12 ; 97
Week 72 (EOT)				
N(%)	55 (96.5)	51 (86.4)	53 (94.6)	54 (93.1)
Geom. Mean (CV)	32 (60.3)	28 (49.5)	23 (37.2)	37 (56.1)
Mean (SD)	37 (22)	31 (17)	25 (12)	42 (22)
Median (IQR)	29 (22; 48)	26 (20; 39)	21 (19; 26)	35 (26; 58)
Min ; Max	11 ; 89	11 ; 99	13 ; 67	14 ; 114
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	44 (74.6)	50 (89.3)	51 (87.9)
Geom. Mean (CV)	31 (59.3)	27 (49.3)	23 (33.6)	37 (57.2)
Mean (SD)	36 (21)	31 (17)	24 (11)	42 (23)
Median (IQR)	28 (22; 46)	25 (20; 36)	21 (19; 26)	34 (25; 58)
Min ; Max	11 ; 89	11 ; 99	15 ; 67	14 ; 114

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver enzymes by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Gamma-glutamyltransferase (U/L)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	64 (65.7)	67 (90.6)	67 (86.4)	64 (81.3)
Mean (SD)	78 (62)	99 (133)	91 (86)	90 (117)
Median (IQR)	57 (41; 90)	59 (39; 105)	58 (41; 105)	56 (38; 92)
Min ; Max	18 ; 371	21 ; 905	19 ; 374	24 ; 739
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	58 (100.0)
Geom. Mean (CV)	56 (66.2)	58 (83.7)	50 (71.3)	61 (81.2)
Mean (SD)	68 (52)	78 (77)	63 (50)	85 (105)
Median (IQR)	52 (37; 75)	56 (33; 86)	47 (31; 73)	53 (35; 82)
Min ; Max	16 ; 287	18 ; 411	16 ; 284	26 ; 644
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	51 (65.1)	50 (87.1)	44 (72.9)	61 (90.5)
Mean (SD)	61 (46)	71 (81)	54 (42)	89 (108)
Median (IQR)	47 (32; 75)	43 (28; 77)	41 (27; 69)	50 (36; 79)
Min ; Max	14 ; 282	18 ; 464	16 ; 232	12 ; 572

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver enzymes by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 20				
N(%)	54 (94.7)	54 (91.5)	53 (94.6)	57 (98.3)
Geom. Mean (CV)	51 (63.8)	46 (90.4)	37 (71.0)	61 (84.5)
Mean (SD)	62 (44)	65 (66)	46 (35)	87 (112)
Median (IQR)	48 (37; 69)	37 (27; 73)	37 (22; 62)	57 (36; 82)
Min ; Max	16 ; 222	14 ; 310	12 ; 216	19 ; 690
Week 28				
N(%)	55 (96.5)	53 (89.8)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	51 (73.8)	47 (90.0)	36 (69.7)	60 (84.8)
Mean (SD)	64 (49)	66 (71)	45 (36)	83 (93)
Median (IQR)	44 (32; 79)	41 (28; 75)	39 (22; 52)	56 (35; 81)
Min ; Max	14 ; 267	15 ; 365	12 ; 180	16 ; 537
Week 36				
N(%)	53 (93.0)	52 (88.1)	53 (94.6)	57 (98.3)
Geom. Mean (CV)	48 (69.9)	43 (96.9)	33 (75.4)	60 (80.7)
Mean (SD)	60 (47)	64 (73)	42 (39)	81 (84)
Median (IQR)	46 (30; 74)	39 (25; 66)	34 (20; 49)	55 (36; 89)
Min ; Max	12 ; 295	12 ; 300	12 ; 235	21 ; 500
Week 44				
N(%)	53 (93.0)	54 (91.5)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	50 (75.6)	44 (89.2)	32 (74.7)	61 (88.4)
Mean (SD)	64 (52)	63 (75)	42 (41)	86 (96)
Median (IQR)	46 (32; 74)	38 (25; 66)	30 (20; 46)	54 (36; 88)
Min ; Max	14 ; 300	12 ; 423	13 ; 265	20 ; 563

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver enzymes by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 52				
N(%)	55 (96.5)	52 (88.1)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	48 (74.0)	42 (95.6)	32 (87.2)	60 (83.6)
Mean (SD)	62 (65)	63 (86)	45 (53)	83 (94)
Median (IQR)	49 (29; 76)	39 (23; 65)	27 (18; 47)	56 (36; 84)
Min ; Max	14 ; 470	12 ; 490	11 ; 276	14 ; 609
Week 62				
N(%)	54 (94.7)	52 (88.1)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	46 (72.6)	40 (90.0)	31 (73.8)	59 (87.2)
Mean (SD)	58 (49)	59 (75)	40 (38)	83 (94)
Median (IQR)	43 (32; 65)	36 (25; 57)	29 (18; 51)	54 (37; 85)
Min ; Max	13 ; 301	12 ; 399	10 ; 254	13 ; 563
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	49 (84.8)	44 (91.0)	29 (70.3)	59 (92.1)
Mean (SD)	68 (70)	61 (61)	36 (31)	86 (99)
Median (IQR)	41 (30; 78)	42 (25; 70)	28 (16; 43)	52 (36; 86)
Min ; Max	14 ; 398	12 ; 313	10 ; 214	12 ; 538
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	49 (86.1)	42 (97.6)	28 (70.1)	59 (95.4)
Mean (SD)	67 (72)	61 (65)	36 (32)	87 (102)
Median (IQR)	41 (30; 73)	40 (23; 69)	28 (16; 43)	51 (36; 85)
Min ; Max	14 ; 398	12 ; 313	10 ; 214	12 ; 538

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

6.2.32 Liver enzymes - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Number of subjects	57	59	56	58
Alanine Aminotransferase (U/L)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	58 (62.3)	53 (50.4)	57 (58.4)	55 (63.6)
Mean (SD)	68 (40)	60 (28)	66 (39)	65 (43)
Median (IQR)	59 (41; 82)	53 (38; 75)	60 (39; 84)	55 (38; 70)
Min ; Max	15 ; 222	13 ; 132	18 ; 199	16 ; 222
Ratio to baseline in Alanine Aminotransferase				
Week 4				
N(%)	57 (100.0)	57 (96.6)	54 (96.4)	58 (100.0)
Geom. Mean (CV)	0.90 (24.5)	0.94 (31.0)	0.90 (27.2)	0.96 (25.8)
Mean (SD)	0.92 (0.22)	0.98 (0.28)	0.93 (0.22)	0.99 (0.26)
Median (IQR)	0.93 (0.77; 1.07)	0.99 (0.74; 1.20)	0.88 (0.76; 1.08)	0.95 (0.81; 1.10)
Min ; Max	0.48 ; 1.73	0.41 ; 1.65	0.32 ; 1.39	0.52 ; 1.72
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	0.74 (38.0)	0.77 (36.1)	0.68 (40.5)	0.88 (39.4)
Mean (SD)	0.79 (0.27)	0.82 (0.30)	0.74 (0.29)	0.94 (0.35)
Median (IQR)	0.76 (0.59; 1.00)	0.74 (0.59; 0.97)	0.67 (0.55; 0.84)	0.89 (0.70; 1.14)
Min ; Max	0.30 ; 1.41	0.37 ; 1.79	0.26 ; 1.58	0.38 ; 2.14

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver enzymes - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 20				
N(%)	54 (94.7)	54 (91.5)	53 (94.6)	57 (98.3)
Geom. Mean (CV)	0.68 (47.7)	0.65 (45.3)	0.54 (53.9)	0.86 (45.6)
Mean (SD)	0.75 (0.33)	0.71 (0.38)	0.61 (0.33)	0.93 (0.36)
Median (IQR)	0.73 (0.48; 0.91)	0.64 (0.49; 0.80)	0.58 (0.39; 0.76)	0.92 (0.68; 1.12)
Min ; Max	0.24 ; 1.43	0.27 ; 2.75	0.17 ; 1.89	0.15 ; 2.11
Week 28				
N(%)	55 (96.5)	53 (89.8)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	0.67 (47.0)	0.62 (58.7)	0.47 (53.8)	0.85 (48.7)
Mean (SD)	0.74 (0.30)	0.72 (0.42)	0.52 (0.24)	0.94 (0.44)
Median (IQR)	0.71 (0.50; 0.95)	0.68 (0.43; 0.83)	0.48 (0.35; 0.67)	0.86 (0.67; 1.16)
Min ; Max	0.23 ; 1.47	0.20 ; 2.50	0.12 ; 1.27	0.22 ; 2.70
Week 36				
N(%)	53 (93.0)	52 (88.1)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	0.63 (59.0)	0.61 (64.2)	0.41 (58.5)	0.88 (49.8)
Mean (SD)	0.72 (0.36)	0.73 (0.53)	0.47 (0.28)	0.98 (0.51)
Median (IQR)	0.63 (0.45; 0.97)	0.60 (0.46; 0.83)	0.38 (0.31; 0.58)	0.92 (0.71; 1.11)
Min ; Max	0.19 ; 1.75	0.18 ; 3.16	0.13 ; 1.34	0.27 ; 3.02
Week 44				
N(%)	53 (93.0)	53 (89.8)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	0.60 (56.9)	0.55 (51.5)	0.40 (63.5)	0.85 (55.8)
Mean (SD)	0.68 (0.31)	0.61 (0.28)	0.47 (0.25)	0.97 (0.58)
Median (IQR)	0.67 (0.42; 0.91)	0.62 (0.44; 0.74)	0.41 (0.29; 0.59)	0.81 (0.62; 1.13)
Min ; Max	0.15 ; 1.36	0.17 ; 1.71	0.08 ; 1.32	0.21 ; 3.44
N<LLOQ ; N>ULOQ	1 ; 0			

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver enzymes - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 52				
N(%)	55 (96.5)	52 (88.1)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	0.60 (65.8)	0.56 (55.9)	0.40 (62.6)	0.83 (52.0)
Mean (SD)	0.71 (0.42)	0.64 (0.32)	0.47 (0.25)	0.92 (0.40)
Median (IQR)	0.63 (0.41; 0.93)	0.59 (0.37; 0.79)	0.40 (0.28; 0.64)	0.89 (0.66; 1.10)
Min ; Max	0.14 ; 2.25	0.17 ; 1.52	0.12 ; 1.15	0.14 ; 2.36
N<LLOQ ; N>ULOQ			1 ; 0	
Week 62				
N(%)	54 (94.7)	52 (88.1)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	0.55 (66.3)	0.52 (55.7)	0.44 (77.8)	0.82 (57.9)
Mean (SD)	0.65 (0.38)	0.59 (0.31)	0.62 (1.05)	0.93 (0.45)
Median (IQR)	0.59 (0.40; 0.81)	0.55 (0.37; 0.75)	0.45 (0.29; 0.67)	0.82 (0.65; 1.20)
Min ; Max	0.11 ; 1.71	0.14 ; 1.85	0.10 ; 7.88	0.12 ; 2.08
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	0.60 (62.4)	0.55 (63.2)	0.38 (70.0)	0.79 (55.7)
Mean (SD)	0.70 (0.37)	0.65 (0.43)	0.45 (0.24)	0.89 (0.41)
Median (IQR)	0.67 (0.37; 0.91)	0.62 (0.41; 0.76)	0.38 (0.27; 0.63)	0.84 (0.63; 1.09)
Min ; Max	0.13 ; 1.81	0.16 ; 2.81	0.04 ; 0.97	0.11 ; 2.26
N<LLOQ ; N>ULOQ			1 ; 0	
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	0.60 (63.5)	0.53 (65.9)	0.37 (71.1)	0.80 (57.3)
Mean (SD)	0.70 (0.38)	0.64 (0.45)	0.44 (0.24)	0.90 (0.42)
Median (IQR)	0.67 (0.37; 0.91)	0.58 (0.36; 0.76)	0.37 (0.26; 0.62)	0.87 (0.63; 1.09)
Min ; Max	0.13 ; 1.81	0.16 ; 2.81	0.04 ; 0.97	0.11 ; 2.26
N<LLOQ ; N>ULOQ			1 ; 0	

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver enzymes - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Aspartate Aminotransferase (U/L)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	47 (49.9)	45 (44.0)	48 (50.2)	44 (58.7)
Mean (SD)	52 (23)	49 (22)	54 (29)	51 (34)
Median (IQR)	48 (34; 69)	46 (31; 61)	47 (33; 66)	44 (30; 60)
Min ; Max	14 ; 108	16 ; 135	21 ; 158	14 ; 229
Ratio to baseline in Aspartate Aminotransferase				
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	58 (100.0)
Geom. Mean (CV)	0.87 (27.5)	0.96 (30.3)	0.88 (37.0)	0.96 (24.5)
Mean (SD)	0.90 (0.24)	1.00 (0.31)	0.93 (0.26)	0.99 (0.28)
Median (IQR)	0.91 (0.78; 0.97)	0.98 (0.77; 1.15)	0.90 (0.76; 1.12)	0.98 (0.84; 1.10)
Min ; Max	0.41 ; 1.59	0.39 ; 2.10	0.14 ; 1.73	0.58 ; 2.48
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	0.74 (40.4)	0.79 (33.7)	0.72 (37.7)	0.91 (40.2)
Mean (SD)	0.80 (0.36)	0.84 (0.29)	0.77 (0.29)	0.97 (0.35)
Median (IQR)	0.77 (0.56; 0.91)	0.76 (0.62; 0.94)	0.70 (0.60; 0.88)	0.93 (0.71; 1.17)
Min ; Max	0.33 ; 2.67	0.37 ; 1.77	0.21 ; 1.95	0.19 ; 1.96

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver enzymes - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 20				
N(%)	53 (93.0)	54 (91.5)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	0.70 (42.8)	0.69 (41.1)	0.61 (47.5)	0.90 (43.2)
Mean (SD)	0.76 (0.30)	0.75 (0.33)	0.67 (0.31)	0.97 (0.35)
Median (IQR)	0.74 (0.53; 0.95)	0.69 (0.55; 0.84)	0.63 (0.48; 0.81)	0.93 (0.79; 1.09)
Min ; Max	0.28 ; 1.65	0.25 ; 2.11	0.12 ; 2.09	0.22 ; 2.11
Week 28				
N(%)	55 (96.5)	53 (89.8)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	0.71 (41.3)	0.70 (43.4)	0.55 (44.1)	0.90 (43.5)
Mean (SD)	0.76 (0.29)	0.76 (0.34)	0.60 (0.24)	0.97 (0.39)
Median (IQR)	0.75 (0.56; 0.94)	0.75 (0.55; 0.85)	0.58 (0.44; 0.71)	0.95 (0.69; 1.19)
Min ; Max	0.23 ; 1.65	0.21 ; 2.34	0.15 ; 1.45	0.29 ; 2.16
Week 36				
N(%)	53 (93.0)	52 (88.1)	53 (94.6)	57 (98.3)
Geom. Mean (CV)	0.64 (57.7)	0.67 (46.7)	0.50 (45.1)	0.93 (53.3)
Mean (SD)	0.73 (0.37)	0.73 (0.32)	0.55 (0.25)	1.08 (0.91)
Median (IQR)	0.66 (0.48; 0.95)	0.69 (0.50; 0.89)	0.53 (0.38; 0.64)	0.92 (0.73; 1.15)
Min ; Max	0.15 ; 1.57	0.18 ; 1.80	0.19 ; 1.64	0.30 ; 7.17
Week 44				
N(%)	53 (93.0)	54 (91.5)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	0.66 (50.1)	0.61 (40.8)	0.50 (47.7)	0.87 (49.4)
Mean (SD)	0.73 (0.31)	0.66 (0.25)	0.55 (0.23)	0.97 (0.49)
Median (IQR)	0.76 (0.46; 0.87)	0.66 (0.50; 0.79)	0.53 (0.42; 0.66)	0.80 (0.66; 1.15)
Min ; Max	0.19 ; 1.36	0.18 ; 1.54	0.12 ; 1.32	0.30 ; 2.68

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver enzymes - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 52				
N(%)	55 (96.5)	52 (88.1)	52 (92.9)	54 (93.1)
Geom. Mean (CV)	0.67 (54.7)	0.64 (41.7)	0.52 (44.2)	0.88 (58.0)
Mean (SD)	0.76 (0.42)	0.68 (0.25)	0.56 (0.21)	0.98 (0.42)
Median (IQR)	0.70 (0.43; 0.98)	0.70 (0.47; 0.86)	0.57 (0.38; 0.73)	0.99 (0.67; 1.26)
Min ; Max	0.20 ; 2.53	0.21 ; 1.29	0.15 ; 1.05	0.08 ; 2.08
Week 62				
N(%)	54 (94.7)	52 (88.1)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	0.62 (53.2)	0.60 (43.0)	0.53 (64.7)	0.84 (57.5)
Mean (SD)	0.70 (0.36)	0.65 (0.27)	0.68 (0.89)	0.94 (0.39)
Median (IQR)	0.63 (0.43; 0.88)	0.60 (0.45; 0.79)	0.57 (0.37; 0.73)	0.89 (0.67; 1.16)
Min ; Max	0.16 ; 1.93	0.23 ; 1.43	0.11 ; 6.78	0.07 ; 2.11
Week 72 (EOT)				
N(%)	55 (96.5)	51 (86.4)	53 (94.6)	54 (93.1)
Geom. Mean (CV)	0.67 (55.9)	0.62 (48.0)	0.49 (46.9)	0.85 (62.5)
Mean (SD)	0.76 (0.39)	0.69 (0.32)	0.53 (0.22)	0.97 (0.49)
Median (IQR)	0.71 (0.42; 1.00)	0.63 (0.49; 0.85)	0.50 (0.36; 0.66)	0.91 (0.62; 1.19)
Min ; Max	0.19 ; 2.02	0.16 ; 1.91	0.15 ; 1.10	0.07 ; 2.69
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	44 (74.6)	50 (89.3)	51 (87.9)
Geom. Mean (CV)	0.66 (56.0)	0.60 (47.9)	0.48 (46.6)	0.85 (63.0)
Mean (SD)	0.75 (0.39)	0.66 (0.28)	0.52 (0.22)	0.97 (0.49)
Median (IQR)	0.71 (0.42; 1.00)	0.62 (0.47; 0.83)	0.50 (0.36; 0.64)	0.92 (0.62; 1.19)
Min ; Max	0.19 ; 2.02	0.16 ; 1.39	0.15 ; 1.10	0.07 ; 2.69

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver enzymes - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Gamma-glutamyltransferase (U/L)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	64 (65.7)	67 (90.6)	67 (86.4)	64 (81.3)
Mean (SD)	78 (62)	99 (133)	91 (86)	90 (117)
Median (IQR)	57 (41; 90)	59 (39; 105)	58 (41; 105)	56 (38; 92)
Min ; Max	18 ; 371	21 ; 905	19 ; 374	24 ; 739
Ratio to baseline in Gamma-glutamyltransferase				
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	58 (100.0)
Geom. Mean (CV)	0.88 (16.8)	0.87 (25.2)	0.78 (23.8)	0.95 (17.6)
Mean (SD)	0.89 (0.15)	0.90 (0.28)	0.80 (0.17)	0.97 (0.19)
Median (IQR)	0.88 (0.77; 1.00)	0.86 (0.75; 0.98)	0.80 (0.72; 0.89)	0.95 (0.87; 1.03)
Min ; Max	0.61 ; 1.26	0.40 ; 2.51	0.34 ; 1.18	0.59 ; 1.86
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	0.78 (26.5)	0.74 (26.4)	0.67 (42.6)	0.95 (26.5)
Mean (SD)	0.80 (0.21)	0.77 (0.21)	0.74 (0.43)	0.98 (0.27)
Median (IQR)	0.78 (0.66; 0.95)	0.76 (0.66; 0.86)	0.65 (0.51; 0.83)	0.96 (0.80; 1.07)
Min ; Max	0.44 ; 1.52	0.35 ; 1.73	0.25 ; 3.35	0.44 ; 2.04

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver enzymes - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 20				
N(%)	54 (94.7)	54 (91.5)	53 (94.6)	57 (98.3)
Geom. Mean (CV)	0.79 (29.0)	0.69 (39.4)	0.57 (40.9)	0.95 (31.4)
Mean (SD)	0.83 (0.24)	0.74 (0.34)	0.61 (0.25)	1.00 (0.36)
Median (IQR)	0.76 (0.66; 1.00)	0.68 (0.59; 0.85)	0.58 (0.46; 0.76)	0.93 (0.79; 1.10)
Min ; Max	0.43 ; 1.49	0.23 ; 2.70	0.24 ; 1.48	0.52 ; 2.37
Week 28				
N(%)	55 (96.5)	53 (89.8)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	0.78 (32.2)	0.67 (44.0)	0.55 (42.0)	0.93 (31.8)
Mean (SD)	0.82 (0.28)	0.74 (0.40)	0.59 (0.21)	0.98 (0.39)
Median (IQR)	0.78 (0.65; 0.97)	0.68 (0.55; 0.82)	0.58 (0.44; 0.74)	0.90 (0.73; 1.08)
Min ; Max	0.37 ; 1.93	0.22 ; 2.97	0.20 ; 0.98	0.56 ; 2.85
Week 36				
N(%)	53 (93.0)	52 (88.1)	53 (94.6)	57 (98.3)
Geom. Mean (CV)	0.77 (35.0)	0.62 (50.2)	0.50 (43.7)	0.94 (34.8)
Mean (SD)	0.81 (0.27)	0.70 (0.40)	0.54 (0.20)	1.00 (0.39)
Median (IQR)	0.76 (0.64; 0.92)	0.62 (0.48; 0.77)	0.52 (0.41; 0.67)	0.93 (0.77; 1.10)
Min ; Max	0.29 ; 1.65	0.22 ; 2.45	0.17 ; 1.09	0.46 ; 2.48
Week 44				
N(%)	53 (93.0)	54 (91.5)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	0.77 (34.7)	0.63 (46.9)	0.49 (47.1)	0.95 (40.1)
Mean (SD)	0.82 (0.29)	0.70 (0.35)	0.53 (0.21)	1.02 (0.45)
Median (IQR)	0.80 (0.68; 0.90)	0.66 (0.54; 0.81)	0.50 (0.38; 0.71)	0.93 (0.71; 1.15)
Min ; Max	0.33 ; 1.93	0.20 ; 2.38	0.13 ; 0.92	0.46 ; 2.73

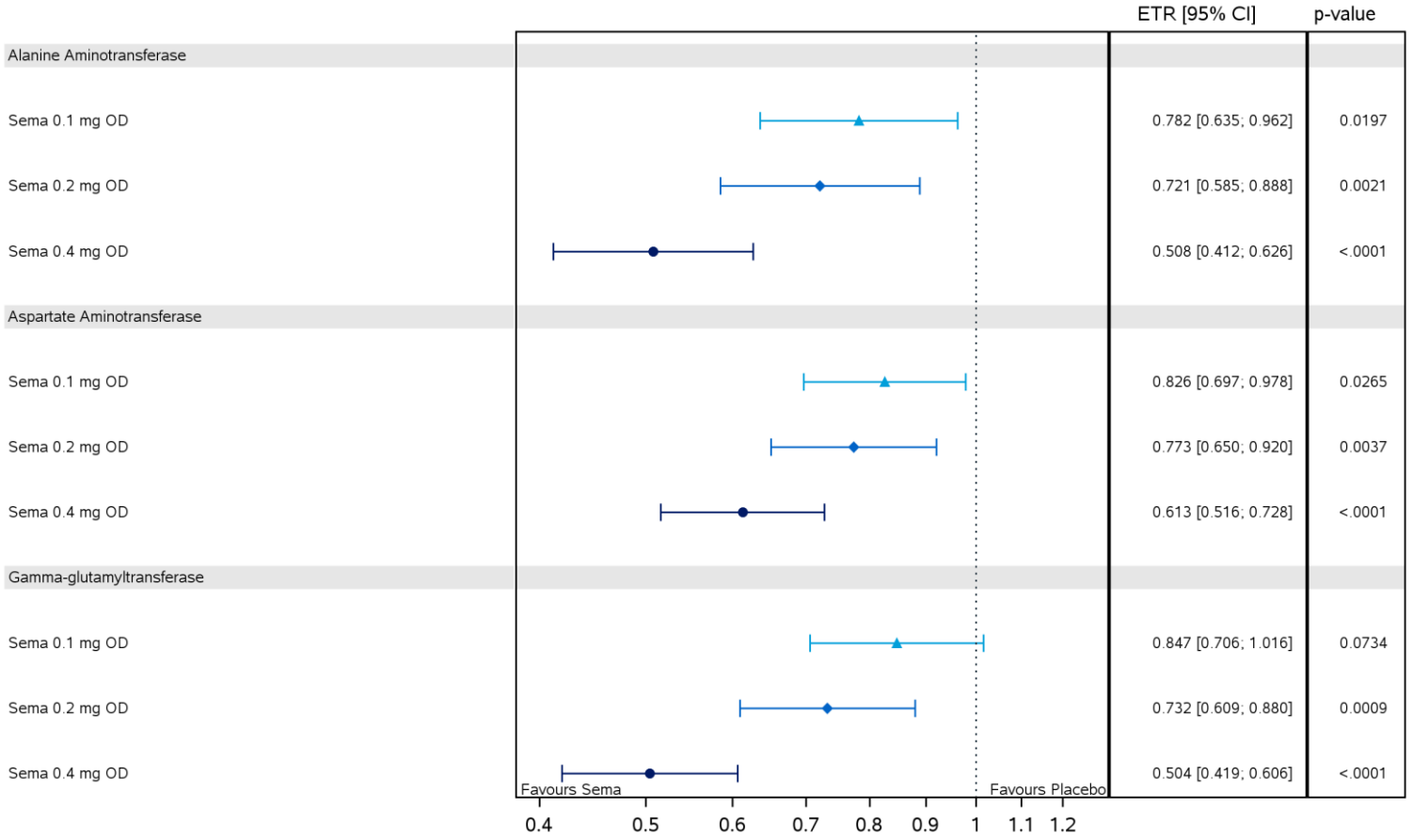
N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver enzymes - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 52				
N(%)	55 (96.5)	52 (88.1)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	0.74 (39.0)	0.58 (43.6)	0.49 (59.2)	0.92 (36.3)
Mean (SD)	0.79 (0.30)	0.63 (0.25)	0.57 (0.36)	0.97 (0.33)
Median (IQR)	0.79 (0.56; 0.92)	0.62 (0.48; 0.79)	0.49 (0.36; 0.71)	0.93 (0.73; 1.16)
Min ; Max	0.26 ; 1.99	0.18 ; 1.45	0.13 ; 2.16	0.32 ; 1.73
Week 62				
N(%)	54 (94.7)	52 (88.1)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	0.72 (40.9)	0.57 (42.9)	0.48 (56.7)	0.92 (44.6)
Mean (SD)	0.77 (0.29)	0.61 (0.26)	0.55 (0.37)	1.00 (0.45)
Median (IQR)	0.71 (0.60; 0.94)	0.60 (0.44; 0.77)	0.46 (0.35; 0.70)	0.97 (0.71; 1.14)
Min ; Max	0.18 ; 1.78	0.21 ; 1.67	0.16 ; 2.55	0.24 ; 2.87
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	0.76 (55.9)	0.63 (53.8)	0.43 (55.9)	0.91 (45.5)
Mean (SD)	0.89 (0.68)	0.72 (0.43)	0.49 (0.25)	0.99 (0.44)
Median (IQR)	0.70 (0.57; 1.00)	0.64 (0.50; 0.76)	0.45 (0.30; 0.64)	0.90 (0.67; 1.14)
Min ; Max	0.18 ; 4.17	0.18 ; 2.41	0.13 ; 1.16	0.23 ; 2.63
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	0.76 (56.9)	0.59 (48.1)	0.44 (56.2)	0.91 (46.9)
Mean (SD)	0.89 (0.69)	0.65 (0.31)	0.50 (0.25)	1.00 (0.45)
Median (IQR)	0.70 (0.57; 1.00)	0.63 (0.49; 0.72)	0.44 (0.30; 0.64)	0.91 (0.66; 1.14)
Min ; Max	0.18 ; 4.17	0.18 ; 1.71	0.13 ; 1.16	0.23 ; 2.63

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

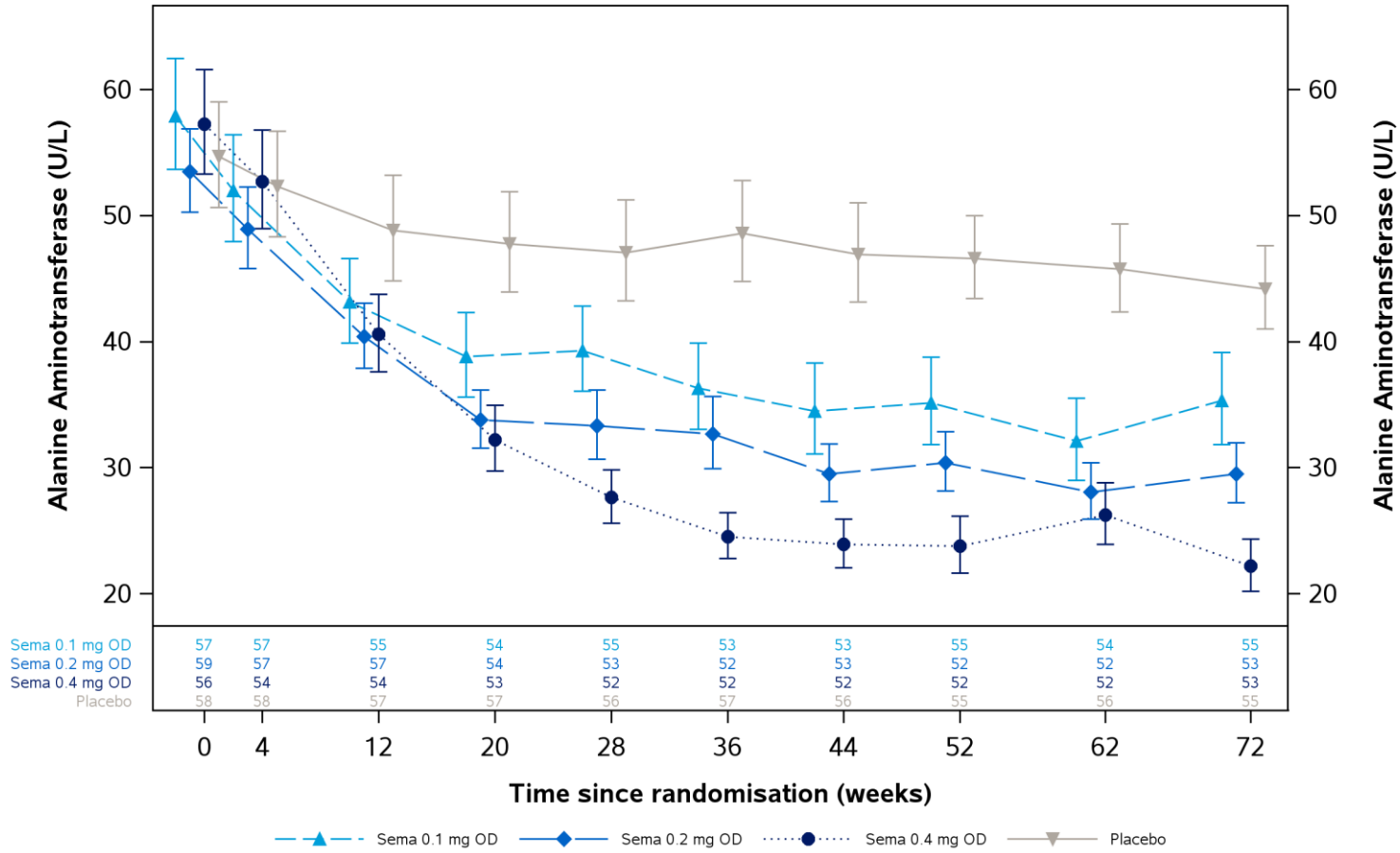
6.2.33 Liver enzymes - ratio to baseline - forest plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



ETRs with 95% CIs are from an ANCOVA on log-transformed data with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of the analysed parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. Treatment differences were estimated on the log-scale and back-transformed to original scale to give the ETRs. ETR: Estimated treatment ratio, CI: Confidence interval, ANCOVA: Analysis of covariance, OD: Once daily.

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6.2.34 ALT by week - observed geometric mean plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



Number of observations per treatment group and visit is presented in the lower part of the plot. Mean +/- standard error calculated on log-scale and back-transformed to original scale. ALT: Alanine Aminotransferase, OD: Once daily.

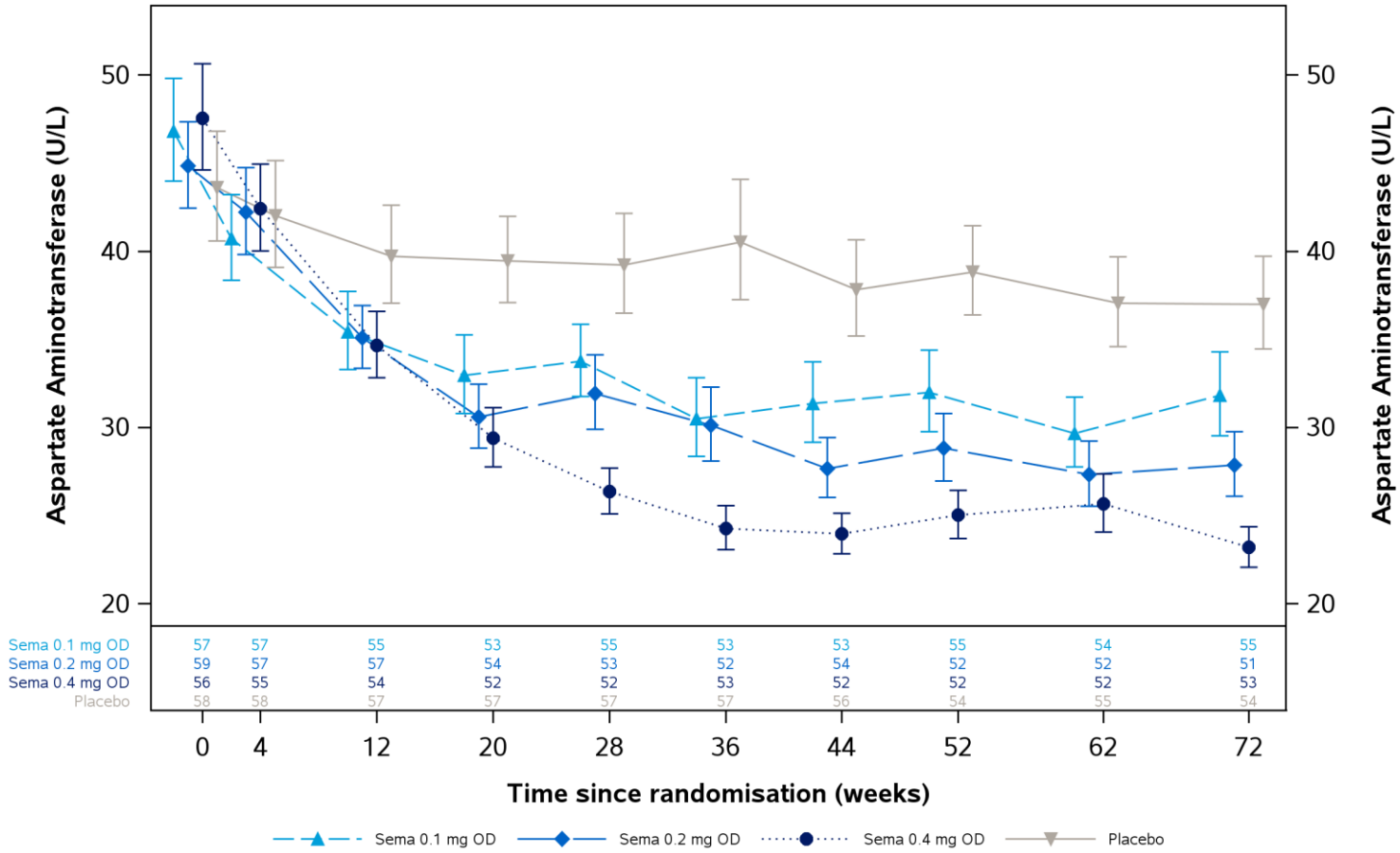
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6.2.35 ALT - ratio to baseline - statistical analysis - ANCOVA - MI based on unconditional reference - in-trial -subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
Alanine Aminotransferase (U/L)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	57	34.51		
Sema 0.2 mg OD	59	59	31.83		
Sema 0.4 mg OD	56	56	22.41		
Placebo	58	58	44.15		
Ratio to baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	57	0.62		
Sema 0.2 mg OD	59	59	0.57		
Sema 0.4 mg OD	56	56	0.40		
Placebo	58	58	0.79		
Treatment ratio at week 72 (EOT)					
Sema 0.1 mg OD / Placebo			0.78	[0.64; 0.96]	0.0197
Sema 0.2 mg OD / Placebo			0.72	[0.59; 0.89]	0.0021
Sema 0.4 mg OD / Placebo			0.51	[0.41; 0.63]	<.0001

ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval. ALT: Alanine Aminotransferase, OD: Once daily, EOT: End of treatment.

6.2.36 AST by week - observed geometric mean plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



Number of observations per treatment group and visit is presented in the lower part of the plot. Mean +/- standard error calculated on log-scale and back-transformed to original scale. AST: Aspartate Aminotransferase, OD: Once daily.

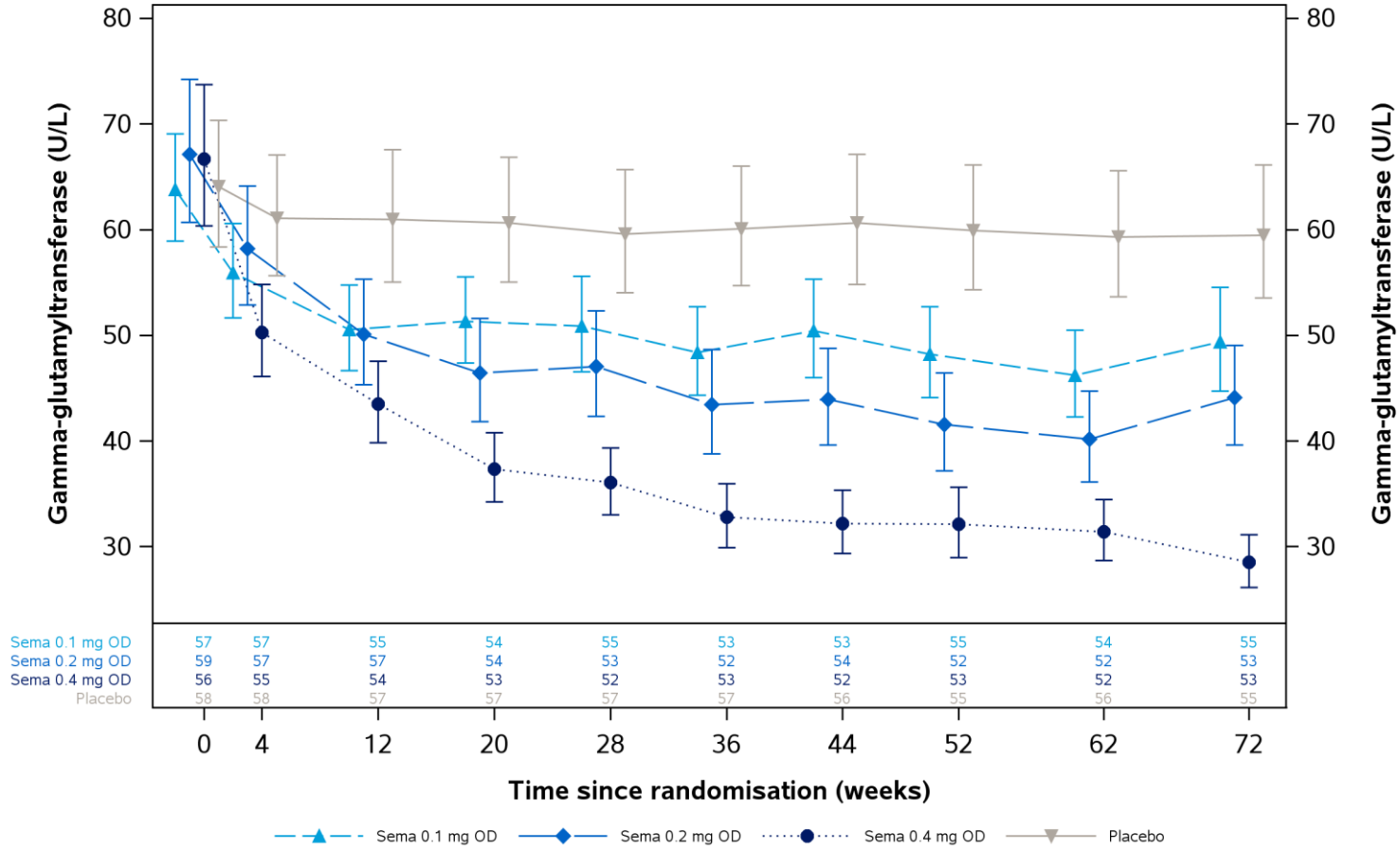
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6.2.37 AST - ratio to baseline - statistical analysis - ANCOVA - MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
Aspartate Aminotransferase (U/L)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	57	31.34		
Sema 0.2 mg OD	59	59	29.35		
Sema 0.4 mg OD	56	56	23.27		
Placebo	58	58	37.97		
Ratio to baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	57	0.69		
Sema 0.2 mg OD	59	59	0.64		
Sema 0.4 mg OD	56	56	0.51		
Placebo	58	58	0.83		
Treatment ratio at week 72 (EOT)					
Sema 0.1 mg OD / Placebo			0.83	[0.70; 0.98]	0.0265
Sema 0.2 mg OD / Placebo			0.77	[0.65; 0.92]	0.0037
Sema 0.4 mg OD / Placebo			0.61	[0.52; 0.73]	<.0001

ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval. AST: Aspartate Aminotransferase, OD: Once daily, EOT: End of treatment.

6.2.38 GGT by week - observed geometric mean plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



Number of observations per treatment group and visit is presented in the lower part of the plot. Mean +/- standard error calculated on log-scale and back-transformed to original scale. GGT: Gamma glutamyl transferase, OD: Once daily.

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6.2.39 GGT - ratio to baseline - statistical analysis - ANCOVA - MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
Gamma-glutamyltransferase (U/L)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	57	49.81		
Sema 0.2 mg OD	59	59	43.05		
Sema 0.4 mg OD	56	56	29.66		
Placebo	58	58	58.82		
Ratio to baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	57	0.76		
Sema 0.2 mg OD	59	59	0.66		
Sema 0.4 mg OD	56	56	0.45		
Placebo	58	58	0.90		
Treatment ratio at week 72 (EOT)					
Sema 0.1 mg OD / Placebo			0.85	[0.71; 1.02]	0.0734
Sema 0.2 mg OD / Placebo			0.73	[0.61; 0.88]	0.0009
Sema 0.4 mg OD / Placebo			0.50	[0.42; 0.61]	<.0001

ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval. GGT: Gamma glutamyl transferase, OD: Once daily, EOT: End of treatment.

6.2.40 Liver synthesis function by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Number of subjects	57	59	56	58
Albumin (g/dL)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	4.3 (7.2)	4.3 (6.7)	4.3 (6.6)	4.3 (6.5)
Mean (SD)	4.3 (0.3)	4.3 (0.3)	4.3 (0.3)	4.3 (0.3)
Median (IQR)	4.3 (4.1; 4.5)	4.3 (4.2; 4.5)	4.2 (4.1; 4.4)	4.3 (4.1; 4.5)
Min ; Max	3.5 ; 4.9	3.5 ; 5.0	3.4 ; 5.0	3.7 ; 5.0
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	58 (100.0)
Geom. Mean (CV)	4.3 (6.9)	4.3 (6.7)	4.3 (7.8)	4.3 (6.6)
Mean (SD)	4.3 (0.3)	4.3 (0.3)	4.3 (0.3)	4.3 (0.3)
Median (IQR)	4.3 (4.2; 4.4)	4.3 (4.2; 4.5)	4.3 (4.2; 4.4)	4.3 (4.2; 4.5)
Min ; Max	3.5 ; 4.9	3.6 ; 5.0	3.3 ; 5.3	3.7 ; 5.1
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	4.3 (6.6)	4.3 (5.8)	4.3 (7.3)	4.3 (7.9)
Mean (SD)	4.3 (0.3)	4.3 (0.2)	4.3 (0.3)	4.3 (0.3)
Median (IQR)	4.3 (4.1; 4.5)	4.3 (4.2; 4.5)	4.3 (4.2; 4.5)	4.4 (4.1; 4.6)
Min ; Max	3.7 ; 4.9	3.5 ; 4.9	3.4 ; 5.3	3.7 ; 5.0

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver synthesis function by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 20				
N(%)	54 (94.7)	54 (91.5)	53 (94.6)	57 (98.3)
Geom. Mean (CV)	4.3 (7.2)	4.3 (5.4)	4.3 (7.5)	4.3 (6.5)
Mean (SD)	4.3 (0.3)	4.3 (0.2)	4.3 (0.3)	4.3 (0.3)
Median (IQR)	4.3 (4.1; 4.5)	4.3 (4.1; 4.5)	4.3 (4.1; 4.5)	4.4 (4.2; 4.5)
Min ; Max	3.5 ; 5.0	3.8 ; 4.8	3.4 ; 5.0	3.8 ; 5.2
Week 28				
N(%)	55 (96.5)	53 (89.8)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	4.3 (6.9)	4.4 (7.0)	4.3 (7.3)	4.3 (6.7)
Mean (SD)	4.3 (0.3)	4.4 (0.3)	4.3 (0.3)	4.3 (0.3)
Median (IQR)	4.3 (4.1; 4.5)	4.4 (4.2; 4.5)	4.3 (4.1; 4.5)	4.3 (4.2; 4.6)
Min ; Max	3.5 ; 4.9	3.5 ; 5.0	3.4 ; 4.9	3.6 ; 5.0
Week 36				
N(%)	53 (93.0)	52 (88.1)	53 (94.6)	57 (98.3)
Geom. Mean (CV)	4.4 (6.6)	4.3 (7.1)	4.3 (7.2)	4.4 (7.4)
Mean (SD)	4.4 (0.3)	4.4 (0.3)	4.3 (0.3)	4.4 (0.3)
Median (IQR)	4.4 (4.1; 4.6)	4.4 (4.2; 4.6)	4.3 (4.1; 4.5)	4.4 (4.2; 4.6)
Min ; Max	3.8 ; 4.9	3.6 ; 5.1	3.4 ; 5.3	3.5 ; 5.0
Week 44				
N(%)	54 (94.7)	54 (91.5)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	4.3 (6.5)	4.3 (6.5)	4.3 (7.9)	4.4 (7.8)
Mean (SD)	4.3 (0.3)	4.3 (0.3)	4.3 (0.3)	4.4 (0.3)
Median (IQR)	4.3 (4.1; 4.5)	4.3 (4.2; 4.5)	4.4 (4.2; 4.6)	4.4 (4.2; 4.6)
Min ; Max	3.8 ; 4.8	3.6 ; 5.0	3.3 ; 5.4	3.5 ; 5.3

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver synthesis function by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 52				
N(%)	55 (96.5)	52 (88.1)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	4.3 (6.5)	4.4 (5.2)	4.3 (7.8)	4.4 (7.2)
Mean (SD)	4.3 (0.3)	4.4 (0.2)	4.4 (0.3)	4.4 (0.3)
Median (IQR)	4.4 (4.1; 4.5)	4.4 (4.3; 4.6)	4.4 (4.1; 4.6)	4.4 (4.2; 4.7)
Min ; Max	3.7 ; 5.1	3.9 ; 5.0	3.4 ; 5.1	3.7 ; 5.0
Week 62				
N(%)	54 (94.7)	52 (88.1)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	4.3 (6.8)	4.4 (6.5)	4.3 (7.5)	4.3 (7.1)
Mean (SD)	4.3 (0.3)	4.4 (0.3)	4.3 (0.3)	4.3 (0.3)
Median (IQR)	4.4 (4.2; 4.5)	4.5 (4.3; 4.6)	4.4 (4.2; 4.5)	4.4 (4.2; 4.6)
Min ; Max	3.7 ; 5.0	3.7 ; 5.0	3.4 ; 5.2	3.4 ; 4.8
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	4.3 (6.6)	4.3 (6.1)	4.3 (7.5)	4.4 (7.5)
Mean (SD)	4.4 (0.3)	4.3 (0.3)	4.3 (0.3)	4.4 (0.3)
Median (IQR)	4.4 (4.1; 4.5)	4.3 (4.2; 4.5)	4.3 (4.1; 4.6)	4.5 (4.2; 4.6)
Min ; Max	3.7 ; 4.9	3.8 ; 4.8	3.3 ; 4.8	3.3 ; 4.8
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	4.4 (6.5)	4.3 (5.7)	4.3 (7.6)	4.3 (7.5)
Mean (SD)	4.4 (0.3)	4.4 (0.2)	4.3 (0.3)	4.4 (0.3)
Median (IQR)	4.4 (4.1; 4.5)	4.4 (4.2; 4.5)	4.3 (4.1; 4.6)	4.4 (4.2; 4.6)
Min ; Max	3.7 ; 4.9	3.9 ; 4.8	3.3 ; 4.8	3.3 ; 4.8

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver synthesis function by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Albumin (g/L)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	43 (7.2)	43 (6.7)	43 (6.6)	43 (6.5)
Mean (SD)	43 (3)	43 (3)	43 (3)	43 (3)
Median (IQR)	43 (41; 45)	43 (42; 45)	42 (41; 44)	43 (41; 45)
Min ; Max	35 ; 49	35 ; 50	34 ; 50	37 ; 50
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	58 (100.0)
Geom. Mean (CV)	43 (6.9)	43 (6.7)	43 (7.8)	43 (6.6)
Mean (SD)	43 (3)	43 (3)	43 (3)	43 (3)
Median (IQR)	43 (42; 44)	43 (42; 45)	43 (42; 44)	43 (42; 45)
Min ; Max	35 ; 49	36 ; 50	33 ; 53	37 ; 51
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	43 (6.6)	43 (5.8)	43 (7.3)	43 (7.9)
Mean (SD)	43 (3)	43 (2)	43 (3)	43 (3)
Median (IQR)	43 (41; 45)	43 (42; 45)	43 (42; 45)	44 (41; 46)
Min ; Max	37 ; 49	35 ; 49	34 ; 53	37 ; 50

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver synthesis function by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 20				
N(%)	54 (94.7)	54 (91.5)	53 (94.6)	57 (98.3)
Geom. Mean (CV)	43 (7.2)	43 (5.4)	43 (7.5)	43 (6.5)
Mean (SD)	43 (3)	43 (2)	43 (3)	43 (3)
Median (IQR)	43 (41; 45)	43 (41; 45)	43 (41; 45)	44 (42; 45)
Min ; Max	35 ; 50	38 ; 48	34 ; 50	38 ; 52
Week 28				
N(%)	55 (96.5)	53 (89.8)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	43 (6.9)	44 (7.0)	43 (7.3)	43 (6.7)
Mean (SD)	43 (3)	44 (3)	43 (3)	43 (3)
Median (IQR)	43 (41; 45)	44 (42; 45)	43 (41; 45)	43 (42; 46)
Min ; Max	35 ; 49	35 ; 50	34 ; 49	36 ; 50
Week 36				
N(%)	53 (93.0)	52 (88.1)	53 (94.6)	57 (98.3)
Geom. Mean (CV)	44 (6.6)	43 (7.1)	43 (7.2)	44 (7.4)
Mean (SD)	44 (3)	44 (3)	43 (3)	44 (3)
Median (IQR)	44 (41; 46)	44 (42; 46)	43 (41; 45)	44 (42; 46)
Min ; Max	38 ; 49	36 ; 51	34 ; 53	35 ; 50
Week 44				
N(%)	54 (94.7)	54 (91.5)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	43 (6.5)	43 (6.5)	43 (7.9)	44 (7.8)
Mean (SD)	43 (3)	43 (3)	43 (3)	44 (3)
Median (IQR)	43 (41; 45)	43 (42; 45)	44 (42; 46)	44 (42; 46)
Min ; Max	38 ; 48	36 ; 50	33 ; 54	35 ; 53

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver synthesis function by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 52				
N(%)	55 (96.5)	52 (88.1)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	43 (6.5)	44 (5.2)	43 (7.8)	44 (7.2)
Mean (SD)	43 (3)	44 (2)	44 (3)	44 (3)
Median (IQR)	44 (41; 45)	44 (43; 46)	44 (41; 46)	44 (42; 47)
Min ; Max	37 ; 51	39 ; 50	34 ; 51	37 ; 50
Week 62				
N(%)	54 (94.7)	52 (88.1)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	43 (6.8)	44 (6.5)	43 (7.5)	43 (7.1)
Mean (SD)	43 (3)	44 (3)	43 (3)	43 (3)
Median (IQR)	44 (42; 45)	45 (43; 46)	44 (42; 45)	44 (42; 46)
Min ; Max	37 ; 50	37 ; 50	34 ; 52	34 ; 48
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	43 (6.6)	43 (6.1)	43 (7.5)	44 (7.5)
Mean (SD)	44 (3)	43 (3)	43 (3)	44 (3)
Median (IQR)	44 (41; 45)	43 (42; 45)	43 (41; 46)	45 (42; 46)
Min ; Max	37 ; 49	38 ; 48	33 ; 48	33 ; 48
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	44 (6.5)	43 (5.7)	43 (7.6)	43 (7.5)
Mean (SD)	44 (3)	44 (2)	43 (3)	44 (3)
Median (IQR)	44 (41; 45)	44 (42; 45)	43 (41; 46)	44 (42; 46)
Min ; Max	37 ; 49	39 ; 48	33 ; 48	33 ; 48

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver synthesis function by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
INR (ratio)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	1.08 (17.4)	1.06 (11.3)	1.12 (25.1)	1.07 (11.3)
Mean (SD)	1.10 (0.26)	1.07 (0.13)	1.18 (0.59)	1.08 (0.13)
Median (IQR)	1.04 (0.99; 1.12)	1.06 (0.98; 1.09)	1.06 (1.01; 1.17)	1.05 (1.00; 1.14)
Min ; Max	0.89 ; 2.60	0.86 ; 1.75	0.92 ; 5.37	0.88 ; 1.59
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	58 (100.0)
Geom. Mean (CV)	1.05 (9.5)	1.07 (13.6)	1.06 (8.6)	1.07 (13.5)
Mean (SD)	1.06 (0.10)	1.08 (0.17)	1.06 (0.09)	1.08 (0.18)
Median (IQR)	1.04 (1.00; 1.09)	1.05 (1.00; 1.11)	1.05 (1.00; 1.11)	1.05 (0.99; 1.11)
Min ; Max	0.87 ; 1.41	0.80 ; 1.95	0.87 ; 1.33	0.81 ; 2.15
Week 12				
N(%)	55 (96.5)	56 (94.9)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	1.05 (8.6)	1.08 (15.9)	1.05 (9.8)	1.05 (9.8)
Mean (SD)	1.06 (0.10)	1.09 (0.24)	1.06 (0.11)	1.05 (0.11)
Median (IQR)	1.05 (0.99; 1.10)	1.06 (0.98; 1.13)	1.04 (0.99; 1.09)	1.05 (0.97; 1.11)
Min ; Max	0.93 ; 1.43	0.91 ; 2.57	0.90 ; 1.49	0.85 ; 1.42

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver synthesis function by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 20				
N(%)	54 (94.7)	55 (93.2)	53 (94.6)	57 (98.3)
Geom. Mean (CV)	1.05 (11.4)	1.06 (9.9)	1.08 (10.2)	1.05 (9.3)
Mean (SD)	1.06 (0.14)	1.06 (0.11)	1.08 (0.11)	1.06 (0.10)
Median (IQR)	1.05 (1.00; 1.10)	1.05 (0.98; 1.12)	1.07 (1.02; 1.15)	1.04 (1.00; 1.10)
Min ; Max	0.85 ; 1.91	0.87 ; 1.33	0.83 ; 1.43	0.86 ; 1.40
Week 28				
N(%)	54 (94.7)	54 (91.5)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	1.05 (12.5)	1.03 (8.5)	1.06 (10.3)	1.06 (12.7)
Mean (SD)	1.06 (0.17)	1.04 (0.09)	1.06 (0.11)	1.06 (0.16)
Median (IQR)	1.03 (0.98; 1.09)	1.04 (0.96; 1.10)	1.05 (1.00; 1.11)	1.04 (0.97; 1.11)
Min ; Max	0.91 ; 2.17	0.87 ; 1.30	0.85 ; 1.46	0.89 ; 1.96
Week 36				
N(%)	53 (93.0)	52 (88.1)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	1.04 (8.3)	1.03 (7.9)	1.05 (8.5)	1.05 (11.3)
Mean (SD)	1.04 (0.09)	1.04 (0.08)	1.05 (0.09)	1.06 (0.13)
Median (IQR)	1.03 (0.99; 1.08)	1.04 (0.98; 1.08)	1.04 (0.99; 1.10)	1.04 (0.97; 1.12)
Min ; Max	0.86 ; 1.25	0.88 ; 1.37	0.88 ; 1.28	0.87 ; 1.56
Week 44				
N(%)	54 (94.7)	54 (91.5)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	1.01 (7.3)	1.05 (11.1)	1.05 (10.6)	1.06 (12.4)
Mean (SD)	1.02 (0.07)	1.05 (0.12)	1.05 (0.11)	1.07 (0.14)
Median (IQR)	1.01 (0.97; 1.06)	1.04 (0.97; 1.09)	1.04 (0.97; 1.13)	1.04 (1.01; 1.12)
Min ; Max	0.83 ; 1.21	0.85 ; 1.42	0.82 ; 1.39	0.79 ; 1.64

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver synthesis function by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 52				
N(%)	55 (96.5)	51 (86.4)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	1.04 (11.1)	1.01 (6.9)	1.04 (12.0)	1.03 (8.1)
Mean (SD)	1.05 (0.12)	1.02 (0.07)	1.04 (0.14)	1.04 (0.08)
Median (IQR)	1.02 (0.97; 1.11)	1.01 (0.96; 1.06)	1.02 (0.97; 1.10)	1.03 (0.99; 1.08)
Min ; Max	0.84 ; 1.47	0.88 ; 1.20	0.86 ; 1.62	0.83 ; 1.33
Week 62				
N(%)	53 (93.0)	52 (88.1)	51 (91.1)	54 (93.1)
Geom. Mean (CV)	1.03 (12.8)	1.01 (9.4)	1.02 (10.6)	1.03 (9.9)
Mean (SD)	1.03 (0.16)	1.01 (0.10)	1.03 (0.11)	1.04 (0.11)
Median (IQR)	1.01 (0.94; 1.07)	1.00 (0.95; 1.06)	1.00 (0.95; 1.09)	1.02 (0.97; 1.08)
Min ; Max	0.87 ; 1.88	0.88 ; 1.49	0.86 ; 1.41	0.85 ; 1.40
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	1.05 (10.9)	1.00 (7.8)	1.03 (9.9)	1.04 (13.2)
Mean (SD)	1.05 (0.12)	1.01 (0.08)	1.03 (0.11)	1.05 (0.16)
Median (IQR)	1.04 (0.96; 1.13)	1.00 (0.96; 1.05)	1.02 (0.97; 1.06)	1.02 (0.96; 1.07)
Min ; Max	0.88 ; 1.54	0.86 ; 1.24	0.84 ; 1.39	0.86 ; 1.79
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	51 (87.9)
Geom. Mean (CV)	1.05 (11.0)	1.00 (8.4)	1.03 (10.1)	1.02 (10.1)
Mean (SD)	1.05 (0.12)	1.01 (0.08)	1.03 (0.11)	1.03 (0.11)
Median (IQR)	1.04 (0.96; 1.13)	1.00 (0.95; 1.06)	1.02 (0.97; 1.07)	1.02 (0.96; 1.07)
Min ; Max	0.88 ; 1.54	0.86 ; 1.24	0.84 ; 1.39	0.86 ; 1.42

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

6.2.41 Liver synthesis function - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Number of subjects	57	59	56	58
Albumin (g/dL)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	4.3 (7.2)	4.3 (6.7)	4.3 (6.6)	4.3 (6.5)
Mean (SD)	4.3 (0.3)	4.3 (0.3)	4.3 (0.3)	4.3 (0.3)
Median (IQR)	4.3 (4.1; 4.5)	4.3 (4.2; 4.5)	4.2 (4.1; 4.4)	4.3 (4.1; 4.5)
Min ; Max	3.5 ; 4.9	3.5 ; 5.0	3.4 ; 5.0	3.7 ; 5.0
Ratio to baseline in Albumin				
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	58 (100.0)
Geom. Mean (CV)	1.00 (4.3)	1.01 (4.7)	1.01 (4.3)	1.01 (4.0)
Mean (SD)	1.00 (0.04)	1.01 (0.05)	1.01 (0.04)	1.01 (0.04)
Median (IQR)	1.00 (0.98; 1.02)	1.00 (0.98; 1.03)	1.02 (0.98; 1.05)	1.00 (0.98; 1.03)
Min ; Max	0.88 ; 1.10	0.91 ; 1.15	0.91 ; 1.10	0.93 ; 1.12
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	1.00 (4.4)	1.01 (4.4)	1.01 (4.5)	1.01 (5.3)
Mean (SD)	1.00 (0.04)	1.01 (0.04)	1.01 (0.05)	1.02 (0.05)
Median (IQR)	1.00 (0.98; 1.03)	1.00 (0.98; 1.05)	1.00 (0.98; 1.05)	1.02 (1.00; 1.05)
Min ; Max	0.89 ; 1.10	0.91 ; 1.11	0.89 ; 1.15	0.88 ; 1.12

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver synthesis function - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 20				
N(%)	54 (94.7)	54 (91.5)	53 (94.6)	57 (98.3)
Geom. Mean (CV)	1.01 (6.0)	1.00 (5.1)	1.01 (4.7)	1.01 (4.8)
Mean (SD)	1.01 (0.06)	1.00 (0.05)	1.01 (0.05)	1.02 (0.05)
Median (IQR)	1.00 (0.98; 1.05)	1.00 (0.98; 1.03)	1.00 (0.98; 1.05)	1.02 (0.98; 1.05)
Min ; Max	0.86 ; 1.17	0.88 ; 1.11	0.91 ; 1.10	0.90 ; 1.13
Week 28				
N(%)	55 (96.5)	53 (89.8)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	1.00 (5.0)	1.02 (6.2)	1.00 (4.8)	1.01 (4.9)
Mean (SD)	1.00 (0.05)	1.02 (0.06)	1.01 (0.05)	1.02 (0.05)
Median (IQR)	1.00 (0.98; 1.04)	1.02 (0.98; 1.07)	1.00 (0.98; 1.04)	1.02 (0.98; 1.05)
Min ; Max	0.87 ; 1.18	0.89 ; 1.21	0.89 ; 1.12	0.92 ; 1.11
Week 36				
N(%)	53 (93.0)	52 (88.1)	53 (94.6)	57 (98.3)
Geom. Mean (CV)	1.02 (5.2)	1.01 (6.6)	1.00 (4.4)	1.02 (5.5)
Mean (SD)	1.02 (0.05)	1.01 (0.07)	1.00 (0.04)	1.02 (0.06)
Median (IQR)	1.02 (0.98; 1.05)	1.01 (0.98; 1.05)	1.00 (0.96; 1.03)	1.02 (0.98; 1.07)
Min ; Max	0.89 ; 1.17	0.84 ; 1.21	0.93 ; 1.10	0.88 ; 1.11
Week 44				
N(%)	54 (94.7)	54 (91.5)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	1.00 (6.1)	1.00 (6.9)	1.02 (5.3)	1.02 (6.4)
Mean (SD)	1.01 (0.06)	1.01 (0.07)	1.02 (0.05)	1.02 (0.06)
Median (IQR)	1.00 (0.98; 1.05)	1.01 (0.96; 1.05)	1.02 (0.98; 1.05)	1.02 (0.98; 1.07)
Min ; Max	0.84 ; 1.12	0.84 ; 1.18	0.91 ; 1.15	0.84 ; 1.20

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver synthesis function - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 52				
N(%)	55 (96.5)	52 (88.1)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	1.01 (5.4)	1.02 (5.8)	1.02 (4.9)	1.03 (5.0)
Mean (SD)	1.01 (0.05)	1.03 (0.06)	1.02 (0.05)	1.03 (0.05)
Median (IQR)	1.00 (0.98; 1.05)	1.02 (1.00; 1.05)	1.02 (0.98; 1.05)	1.02 (0.98; 1.07)
Min ; Max	0.87 ; 1.11	0.90 ; 1.20	0.93 ; 1.15	0.93 ; 1.13
Week 62				
N(%)	54 (94.7)	52 (88.1)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	1.01 (6.3)	1.03 (6.4)	1.01 (5.3)	1.01 (5.5)
Mean (SD)	1.01 (0.06)	1.03 (0.07)	1.01 (0.05)	1.01 (0.06)
Median (IQR)	1.02 (0.96; 1.05)	1.02 (1.00; 1.07)	1.01 (0.99; 1.05)	1.02 (0.98; 1.05)
Min ; Max	0.86 ; 1.10	0.85 ; 1.20	0.90 ; 1.13	0.85 ; 1.12
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	1.02 (5.8)	1.01 (6.1)	1.00 (5.6)	1.02 (5.9)
Mean (SD)	1.02 (0.06)	1.01 (0.06)	1.00 (0.06)	1.02 (0.06)
Median (IQR)	1.00 (0.98; 1.06)	1.00 (0.96; 1.05)	1.00 (0.98; 1.05)	1.02 (0.98; 1.07)
Min ; Max	0.89 ; 1.17	0.88 ; 1.15	0.88 ; 1.12	0.83 ; 1.12
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	1.02 (5.8)	1.02 (6.0)	1.00 (5.7)	1.02 (6.0)
Mean (SD)	1.02 (0.06)	1.02 (0.06)	1.01 (0.06)	1.02 (0.06)
Median (IQR)	1.02 (0.98; 1.06)	1.02 (0.98; 1.07)	1.00 (0.98; 1.05)	1.02 (0.98; 1.07)
Min ; Max	0.89 ; 1.17	0.88 ; 1.15	0.88 ; 1.12	0.83 ; 1.12

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver synthesis function - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
INR (ratio)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	1.08 (17.4)	1.06 (11.3)	1.12 (25.1)	1.07 (11.3)
Mean (SD)	1.10 (0.26)	1.07 (0.13)	1.18 (0.59)	1.08 (0.13)
Median (IQR)	1.04 (0.99; 1.12)	1.06 (0.98; 1.09)	1.06 (1.01; 1.17)	1.05 (1.00; 1.14)
Min ; Max	0.89 ; 2.60	0.86 ; 1.75	0.92 ; 5.37	0.88 ; 1.59
Ratio to baseline in INR				
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	58 (100.0)
Geom. Mean (CV)	0.97 (17.9)	1.01 (15.6)	0.95 (25.3)	1.00 (15.5)
Mean (SD)	0.98 (0.14)	1.02 (0.19)	0.97 (0.16)	1.01 (0.18)
Median (IQR)	1.00 (0.96; 1.04)	0.99 (0.95; 1.06)	0.99 (0.92; 1.03)	1.00 (0.94; 1.06)
Min ; Max	0.40 ; 1.27	0.64 ; 2.14	0.19 ; 1.30	0.62 ; 2.03
Week 12				
N(%)	55 (96.5)	56 (94.9)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	0.97 (19.6)	1.01 (17.0)	0.94 (25.0)	0.98 (10.1)
Mean (SD)	0.98 (0.16)	1.03 (0.24)	0.96 (0.15)	0.98 (0.10)
Median (IQR)	1.01 (0.94; 1.05)	1.00 (0.96; 1.04)	0.98 (0.90; 1.04)	0.98 (0.94; 1.04)
Min ; Max	0.36 ; 1.38	0.59 ; 2.65	0.19 ; 1.30	0.72 ; 1.22

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver synthesis function - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 20				
N(%)	54 (94.7)	55 (93.2)	53 (94.6)	57 (98.3)
Geom. Mean (CV)	0.97 (18.4)	0.99 (9.8)	0.96 (25.9)	0.99 (8.6)
Mean (SD)	0.98 (0.17)	1.00 (0.09)	0.98 (0.17)	0.99 (0.08)
Median (IQR)	1.00 (0.92; 1.04)	1.00 (0.96; 1.04)	1.00 (0.94; 1.05)	1.00 (0.94; 1.05)
Min ; Max	0.40 ; 1.84	0.62 ; 1.16	0.20 ; 1.40	0.74 ; 1.15
Week 28				
N(%)	54 (94.7)	54 (91.5)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	0.96 (21.5)	0.97 (9.8)	0.95 (25.6)	0.99 (12.6)
Mean (SD)	0.98 (0.20)	0.97 (0.09)	0.97 (0.16)	1.00 (0.13)
Median (IQR)	1.00 (0.95; 1.04)	0.98 (0.93; 1.04)	0.96 (0.93; 1.06)	0.99 (0.94; 1.03)
Min ; Max	0.38 ; 2.05	0.67 ; 1.15	0.20 ; 1.27	0.61 ; 1.57
Week 36				
N(%)	53 (93.0)	52 (88.1)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	0.95 (18.8)	0.96 (10.3)	0.94 (23.8)	0.98 (13.5)
Mean (SD)	0.97 (0.14)	0.97 (0.09)	0.96 (0.15)	0.99 (0.14)
Median (IQR)	0.99 (0.92; 1.04)	0.97 (0.92; 1.02)	1.00 (0.90; 1.05)	0.99 (0.92; 1.04)
Min ; Max	0.38 ; 1.18	0.62 ; 1.16	0.22 ; 1.19	0.60 ; 1.71
Week 44				
N(%)	54 (94.7)	54 (91.5)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	0.93 (18.4)	0.98 (12.5)	0.94 (25.9)	1.00 (14.0)
Mean (SD)	0.94 (0.14)	0.99 (0.12)	0.96 (0.15)	1.01 (0.15)
Median (IQR)	0.95 (0.90; 1.03)	0.98 (0.93; 1.03)	0.98 (0.88; 1.04)	1.00 (0.93; 1.04)
Min ; Max	0.37 ; 1.16	0.58 ; 1.29	0.18 ; 1.17	0.64 ; 1.55

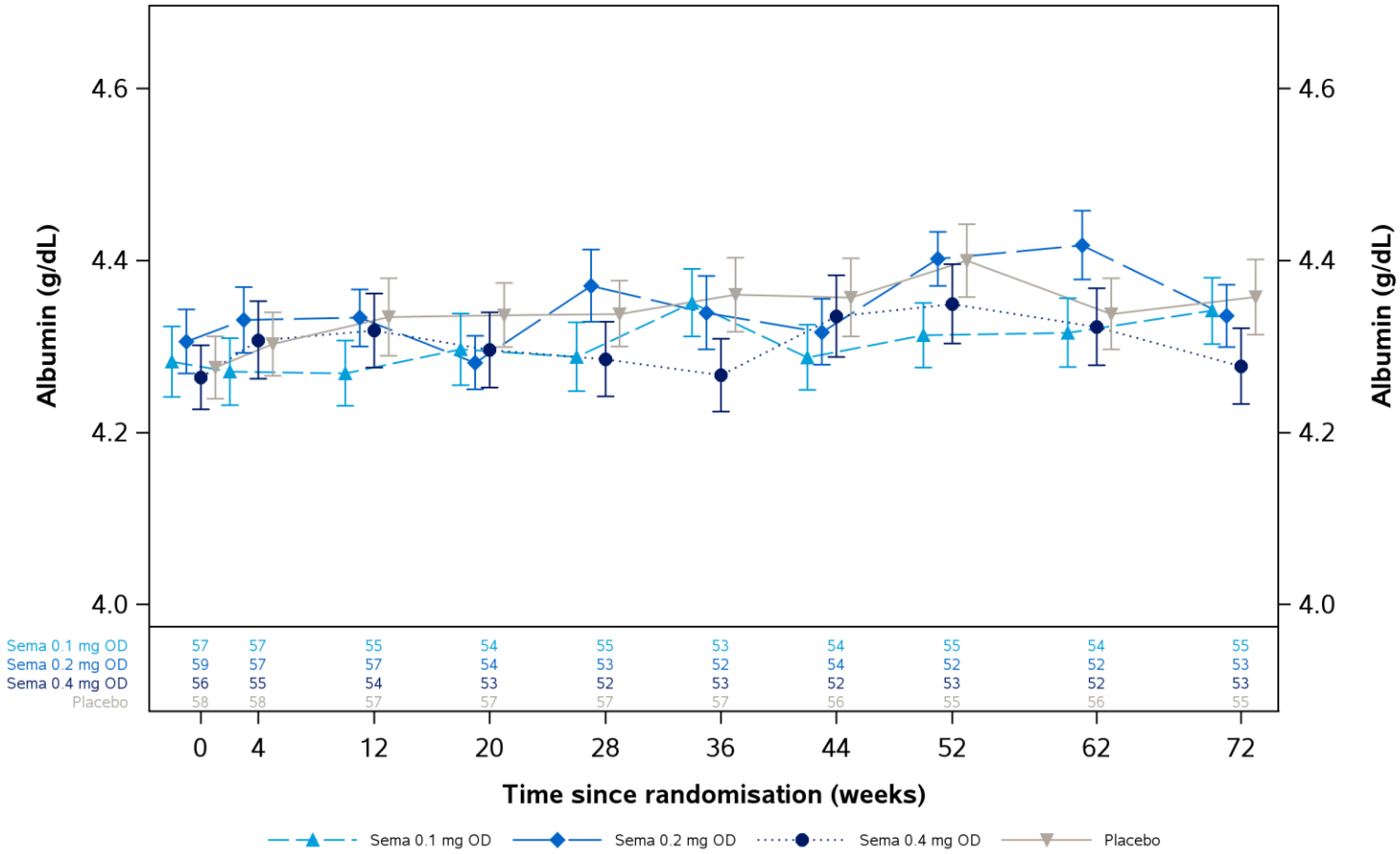
N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

Liver synthesis function - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 52				
N(%)	55 (96.5)	51 (86.4)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	0.96 (20.7)	0.95 (9.9)	0.93 (27.4)	0.97 (11.2)
Mean (SD)	0.97 (0.17)	0.96 (0.09)	0.95 (0.15)	0.97 (0.10)
Median (IQR)	1.00 (0.89; 1.07)	0.96 (0.91; 1.01)	0.97 (0.88; 1.02)	0.98 (0.89; 1.03)
Min ; Max	0.40 ; 1.36	0.62 ; 1.11	0.16 ; 1.20	0.64 ; 1.20
Week 62				
N(%)	53 (93.0)	52 (88.1)	51 (91.1)	54 (93.1)
Geom. Mean (CV)	0.94 (20.6)	0.95 (11.7)	0.91 (27.2)	0.97 (10.5)
Mean (SD)	0.96 (0.18)	0.95 (0.10)	0.93 (0.16)	0.97 (0.10)
Median (IQR)	0.97 (0.89; 1.01)	0.96 (0.90; 1.00)	0.95 (0.87; 1.00)	0.98 (0.91; 1.03)
Min ; Max	0.38 ; 1.77	0.57 ; 1.22	0.17 ; 1.20	0.65 ; 1.21
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	0.96 (21.0)	0.94 (11.9)	0.92 (26.3)	0.97 (15.7)
Mean (SD)	0.98 (0.17)	0.95 (0.11)	0.94 (0.15)	0.98 (0.17)
Median (IQR)	0.96 (0.92; 1.08)	0.96 (0.90; 1.00)	0.95 (0.89; 1.00)	0.96 (0.90; 1.04)
Min ; Max	0.35 ; 1.52	0.61 ; 1.29	0.17 ; 1.32	0.60 ; 1.81
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	51 (87.9)
Geom. Mean (CV)	0.96 (21.1)	0.94 (12.1)	0.92 (27.1)	0.95 (11.6)
Mean (SD)	0.98 (0.17)	0.95 (0.11)	0.94 (0.15)	0.96 (0.11)
Median (IQR)	0.96 (0.92; 1.07)	0.96 (0.90; 1.00)	0.95 (0.89; 1.02)	0.95 (0.90; 1.04)
Min ; Max	0.35 ; 1.52	0.61 ; 1.29	0.17 ; 1.32	0.60 ; 1.18

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

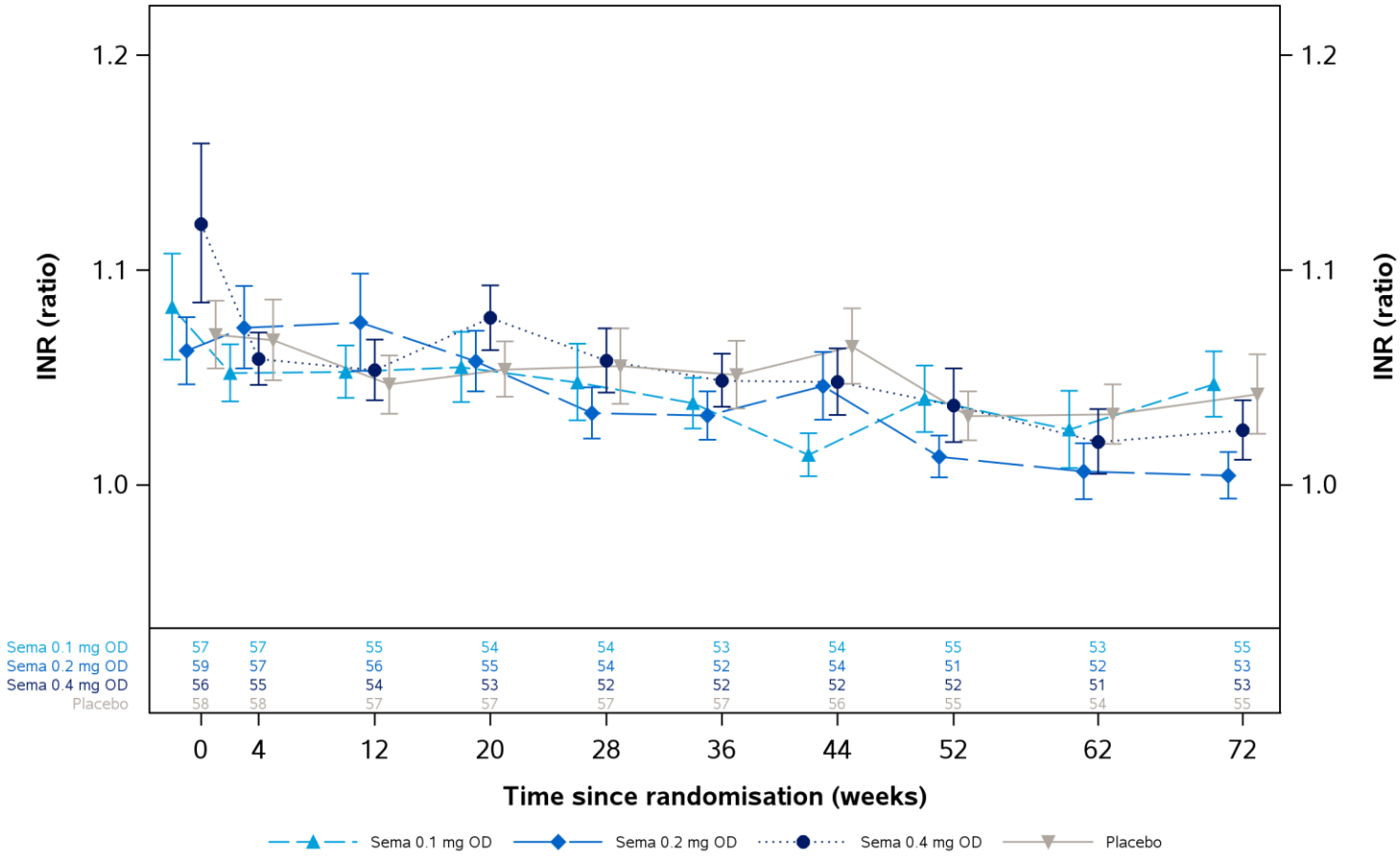
6.2.42 Albumin by week - observed geometric mean plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



Number of observations per treatment group and visit is presented in the lower part of the plot. Mean +/- standard error calculated on log-scale and back-transformed to original scale. OD: Once daily.

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6.2.43 INR by week - observed geometric mean plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



Number of observations per treatment group and visit is presented in the lower part of the plot. Mean +/- standard error calculated on log-scale and back-transformed to original scale. INR: International normalized ratio, OD: Once daily.

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6.2.44 INR - ratio to baseline - statistical analysis - ANCOVA - MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
INR (ratio)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	57	1.05		
Sema 0.2 mg OD	59	59	1.01		
Sema 0.4 mg OD	56	56	1.02		
Placebo	58	58	1.04		
Ratio to baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	57	0.97		
Sema 0.2 mg OD	59	59	0.93		
Sema 0.4 mg OD	56	56	0.94		
Placebo	58	58	0.96		
Treatment ratio at week 72 (EOT)					
Sema 0.1 mg OD / Placebo			1.00	[0.96; 1.05]	0.8950
Sema 0.2 mg OD / Placebo			0.97	[0.93; 1.01]	0.1009
Sema 0.4 mg OD / Placebo			0.98	[0.94; 1.02]	0.3493

ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval. INR: International normalized ratio, OD: Once daily, EOT: End of treatment.

6.2.45 ELF - change from baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Number of subjects	57	59	56	58
Serum Enhanced Liver Fibrosis				
Week 0 (Randomisation)				
N(%)	57 (100.0)	58 (98.3)	55 (98.2)	57 (98.3)
Mean (SD)	9.9 (1.0)	10.0 (0.8)	10.1 (1.0)	9.8 (1.0)
Median (IQR)	9.8 (9.2; 10.5)	9.9 (9.4; 10.5)	10.2 (9.5; 10.8)	9.7 (9.2; 10.3)
Min ; Max	7.8 ; 12.6	8.3 ; 12.1	8.0 ; 12.6	7.9 ; 12.8
Change from baseline in Serum Enhanced Liver Fibrosis				
Week 28				
N(%)	55 (96.5)	53 (89.8)	51 (91.1)	56 (96.6)
Mean (SD)	-0.4 (0.7)	-0.4 (0.6)	-0.7 (0.7)	-0.0 (0.6)
Median (IQR)	-0.5 (-0.8; 0.2)	-0.5 (-0.8; -0.1)	-0.7 (-1.2; -0.2)	0.0 (-0.3; 0.3)
Min ; Max	-2.2 ; 0.8	-1.9 ; 1.1	-2.9 ; 0.7	-1.2 ; 1.3
Week 52				
N(%)	55 (96.5)	51 (86.4)	52 (92.9)	54 (93.1)
Mean (SD)	-0.5 (0.8)	-0.6 (0.6)	-0.6 (0.8)	0.0 (0.6)
Median (IQR)	-0.4 (-0.9; 0.1)	-0.4 (-1.0; -0.1)	-0.7 (-1.3; -0.1)	0.0 (-0.3; 0.3)
Min ; Max	-2.3 ; 1.0	-2.3 ; 0.8	-2.1 ; 1.8	-2.1 ; 1.5
Week 72 (EOT)				
N(%)	55 (96.5)	52 (88.1)	52 (92.9)	55 (94.8)
Mean (SD)	-0.5 (0.7)	-0.5 (0.7)	-0.7 (0.8)	0.1 (0.8)
Median (IQR)	-0.5 (-1.0; 0.1)	-0.5 (-0.9; -0.0)	-0.6 (-1.2; -0.2)	0.1 (-0.3; 0.6)
Min ; Max	-1.8 ; 1.2	-2.4 ; 1.8	-2.8 ; 1.1	-1.8 ; 2.5

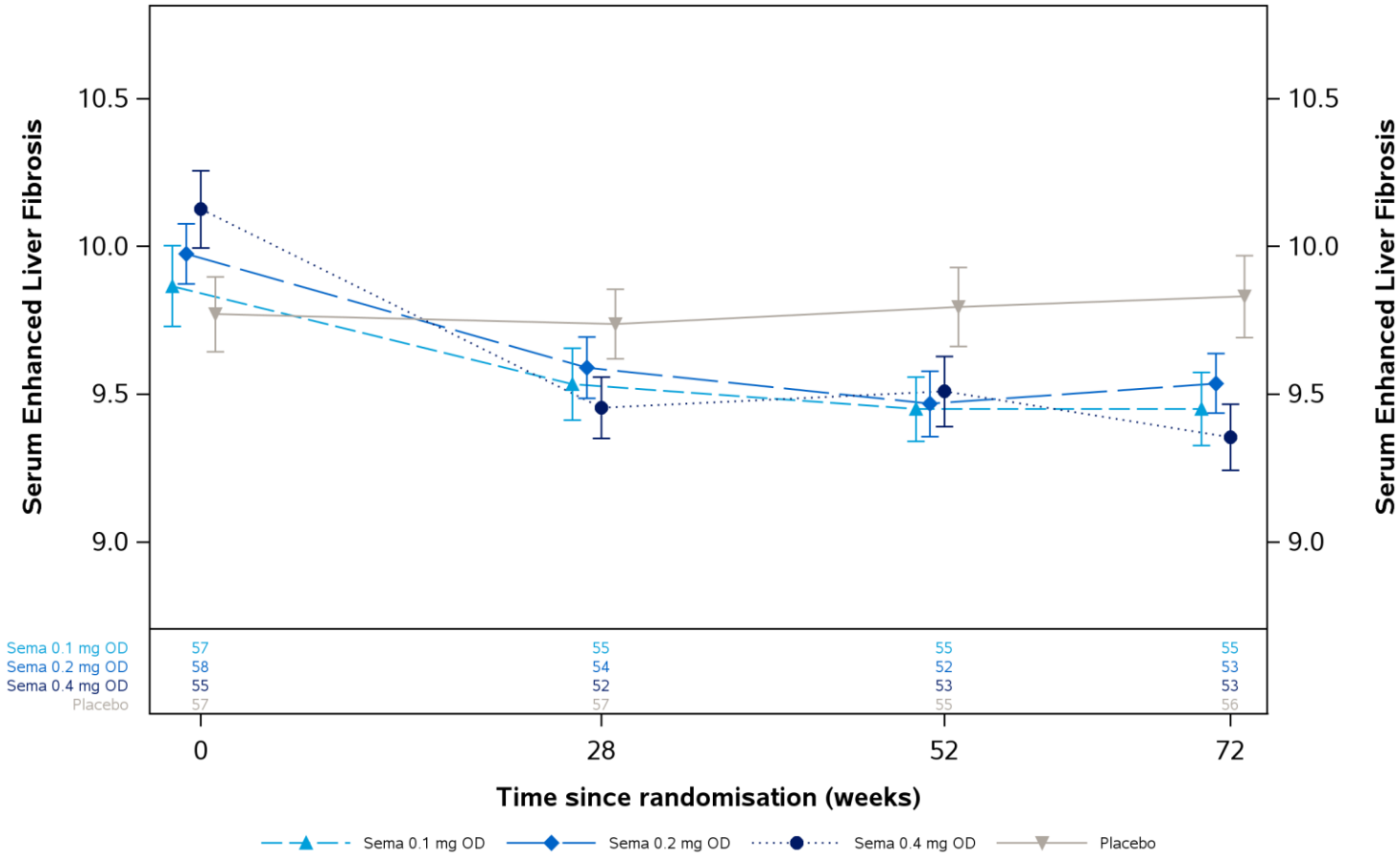
N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment, ELF: Enhanced liver fibrosis test.

ELF - change from baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	45 (76.3)	49 (87.5)	51 (87.9)
Mean (SD)	-0.5 (0.7)	-0.6 (0.7)	-0.8 (0.8)	0.0 (0.7)
Median (IQR)	-0.5 (-1.0; 0.0)	-0.5 (-0.9; -0.1)	-0.6 (-1.2; -0.3)	0.1 (-0.3; 0.6)
Min ; Max	-1.8 ; 1.2	-2.4 ; 0.9	-2.8 ; 1.1	-1.8 ; 1.9

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment, ELF: Enhanced liver fibrosis test.

6.2.46 ELF by week - observed mean plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



Number of observations per treatment group and visit is presented in the lower part of the plot. Plot shows mean +/- standard error. ELF: Enhanced liver fibrosis test, OD: Once daily.

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6.2.47 ELF - change from baseline - statistical analysis - ANCOVA - MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
Serum Enhanced Liver Fibrosis					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	57	9.47		
Sema 0.2 mg OD	59	58	9.51		
Sema 0.4 mg OD	56	55	9.30		
Placebo	58	57	9.94		
Change from baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	57	-0.46		
Sema 0.2 mg OD	59	58	-0.42		
Sema 0.4 mg OD	56	55	-0.63		
Placebo	58	57	0.01		
Treatment difference at week 72 (EOT)					
Sema 0.1 mg OD - Placebo			-0.46	[-0.73; -0.20]	0.0006
Sema 0.2 mg OD - Placebo			-0.43	[-0.70; -0.16]	0.0020
Sema 0.4 mg OD - Placebo			-0.64	[-0.91; -0.36]	<.0001

ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval. ELF: Enhanced liver fibrosis test, OD: Once daily, EOT: End of treatment.

6.2.48 Weight-related parameters by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Number of subjects	57	59	56	58
Body Weight (kg)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Mean (SD)	97.1 (21.6)	94.4 (22.5)	94.9 (21.0)	99.4 (21.8)
Median (IQR)	95.7 (82.0;108.8)	95.8 (75.2;108.0)	94.5 (78.0;107.9)	97.9 (82.1;111.0)
Min ; Max	56.1 ; 148.1	59.8 ; 162.3	55.0 ; 154.9	62.0 ; 150.0
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	58 (100.0)
Mean (SD)	96.2 (21.6)	92.0 (22.5)	92.4 (20.8)	98.9 (22.1)
Median (IQR)	95.0 (81.5;109.5)	93.2 (73.5;104.8)	92.2 (75.2;105.0)	97.4 (80.5;110.6)
Min ; Max	54.1 ; 147.0	58.7 ; 161.1	53.3 ; 154.2	61.4 ; 154.0
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Mean (SD)	94.8 (21.6)	88.7 (21.6)	88.5 (20.7)	98.9 (22.2)
Median (IQR)	93.2 (79.0;107.6)	91.5 (70.5;102.2)	89.4 (72.0; 99.5)	96.4 (82.0;110.2)
Min ; Max	53.4 ; 146.5	55.7 ; 150.6	51.0 ; 146.6	61.5 ; 154.0
Week 20				
N(%)	54 (94.7)	55 (93.2)	53 (94.6)	57 (98.3)
Mean (SD)	93.6 (21.7)	87.5 (21.4)	85.2 (20.8)	98.9 (22.5)
Median (IQR)	91.3 (78.2;105.7)	88.8 (68.0;102.2)	86.6 (70.0; 96.4)	97.0 (82.2;110.3)
Min ; Max	52.8 ; 149.2	52.4 ; 145.5	48.7 ; 144.7	61.4 ; 154.0

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, BMI: Body mass index, EOT: End of treatment.

Weight-related parameters by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	54 (94.7)	54 (91.5)	52 (92.9)	57 (98.3)
Mean (SD)	93.1 (21.9)	87.1 (21.8)	84.0 (21.0)	99.2 (22.1)
Median (IQR)	90.5 (78.6;107.0)	87.6 (67.0;100.8)	84.6 (67.3; 94.3)	96.3 (82.7;110.7)
Min ; Max	52.7 ; 150.1	50.5 ; 144.4	45.6 ; 144.2	61.5 ; 151.0
Week 36				
N(%)	53 (93.0)	52 (88.1)	53 (94.6)	57 (98.3)
Mean (SD)	93.2 (22.3)	86.2 (22.0)	82.8 (21.6)	99.5 (22.1)
Median (IQR)	91.9 (78.8;106.0)	85.0 (66.7;100.7)	84.8 (65.7; 91.6)	96.3 (83.1;112.5)
Min ; Max	52.0 ; 150.6	51.7 ; 142.4	44.8 ; 147.0	61.7 ; 150.0
Week 44				
N(%)	54 (94.7)	54 (91.5)	52 (92.9)	56 (96.6)
Mean (SD)	93.0 (22.2)	86.2 (21.6)	82.2 (21.1)	98.7 (21.4)
Median (IQR)	91.9 (77.9;108.0)	85.5 (66.3;100.7)	84.8 (66.2; 92.8)	96.2 (82.6;111.8)
Min ; Max	53.6 ; 151.5	51.3 ; 142.3	43.4 ; 141.7	61.4 ; 149.0
Week 52				
N(%)	55 (96.5)	52 (88.1)	53 (94.6)	55 (94.8)
Mean (SD)	92.5 (21.8)	85.6 (22.2)	81.9 (21.2)	98.2 (21.1)
Median (IQR)	89.8 (77.2;106.7)	85.5 (67.0; 99.0)	83.7 (67.0; 92.2)	96.1 (81.5;111.9)
Min ; Max	51.6 ; 143.8	50.7 ; 145.2	42.2 ; 143.0	61.7 ; 150.0

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, BMI: Body mass index, EOT: End of treatment.

Weight-related parameters by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 62				
N(%)	54 (94.7)	52 (88.1)	51 (91.1)	56 (96.6)
Mean (SD)	92.9 (22.4)	85.4 (22.7)	82.1 (22.0)	98.2 (21.2)
Median (IQR)	91.9 (76.5;107.0)	85.5 (67.3; 99.1)	82.8 (68.0; 93.0)	96.6 (81.2;111.5)
Min ; Max	51.6 ; 142.9	50.7 ; 147.5	41.3 ; 149.9	62.0 ; 149.0
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	56 (96.6)
Mean (SD)	93.0 (22.5)	85.0 (22.7)	81.3 (22.1)	98.3 (21.3)
Median (IQR)	91.9 (77.5;107.1)	85.5 (66.0; 98.5)	80.7 (69.0; 90.9)	96.4 (82.0;111.4)
Min ; Max	51.4 ; 146.5	51.9 ; 148.3	41.1 ; 153.7	61.8 ; 147.0
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Mean (SD)	93.1 (22.8)	84.7 (22.8)	81.8 (22.6)	98.9 (21.6)
Median (IQR)	91.9 (77.5;107.1)	85.1 (65.5; 98.5)	81.6 (69.0; 91.0)	98.0 (83.9;111.4)
Min ; Max	51.4 ; 146.5	51.9 ; 148.3	41.1 ; 153.7	61.8 ; 147.0

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, BMI: Body mass index, EOT: End of treatment.

Weight-related parameters by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
BMI (kg/m^2)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Mean (SD)	35.9 (6.8)	35.0 (6.1)	34.5 (7.1)	35.8 (6.4)
Median (IQR)	35.4 (30.5; 40.6)	34.6 (29.9; 38.9)	32.8 (29.7; 38.3)	35.7 (31.1; 40.4)
Min ; Max	24.8 ; 51.3	25.1 ; 56.2	23.8 ; 57.9	24.5 ; 51.8
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	58 (100.0)
Mean (SD)	35.6 (7.0)	34.2 (6.2)	33.6 (6.9)	35.6 (6.6)
Median (IQR)	34.6 (30.1; 41.3)	33.6 (29.5; 38.3)	32.1 (28.9; 37.0)	35.1 (30.9; 40.7)
Min ; Max	23.9 ; 51.5	23.9 ; 55.7	23.5 ; 57.6	24.9 ; 51.6
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Mean (SD)	35.2 (6.8)	33.0 (5.9)	32.3 (6.8)	35.5 (6.6)
Median (IQR)	34.5 (30.3; 40.7)	31.5 (28.5; 37.1)	31.1 (27.8; 35.2)	34.8 (31.0; 40.6)
Min ; Max	23.6 ; 50.6	23.6 ; 52.1	22.1 ; 54.8	24.8 ; 50.4
Week 20				
N(%)	54 (94.7)	55 (93.2)	53 (94.6)	57 (98.3)
Mean (SD)	34.8 (6.7)	32.4 (5.8)	31.0 (6.8)	35.5 (6.7)
Median (IQR)	34.3 (30.1; 40.0)	31.1 (27.6; 36.8)	30.0 (26.1; 33.9)	34.7 (31.1; 40.9)
Min ; Max	22.3 ; 49.6	23.5 ; 50.3	21.6 ; 54.1	24.4 ; 51.6

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, BMI: Body mass index, EOT: End of treatment.

Weight-related parameters by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	54 (94.7)	54 (91.5)	52 (92.9)	57 (98.3)
Mean (SD)	34.6 (6.8)	32.2 (6.0)	30.5 (6.9)	35.6 (6.8)
Median (IQR)	34.0 (29.8; 38.8)	30.9 (27.9; 37.0)	28.9 (25.7; 33.9)	34.6 (31.2; 41.3)
Min ; Max	22.8 ; 52.1	23.8 ; 50.0	20.1 ; 53.9	24.1 ; 53.6
Week 36				
N(%)	53 (93.0)	52 (88.1)	53 (94.6)	57 (98.3)
Mean (SD)	34.7 (7.1)	31.7 (5.8)	30.1 (7.0)	35.7 (6.8)
Median (IQR)	33.8 (29.4; 39.3)	30.6 (27.3; 36.3)	28.7 (25.7; 34.0)	34.6 (31.2; 41.3)
Min ; Max	21.6 ; 52.4	22.9 ; 49.3	19.9 ; 54.9	24.3 ; 54.3
Week 44				
N(%)	54 (94.7)	54 (91.5)	52 (92.9)	56 (96.6)
Mean (SD)	34.6 (7.1)	31.9 (6.0)	29.8 (6.8)	35.4 (6.6)
Median (IQR)	33.8 (29.4; 39.9)	30.8 (27.9; 36.1)	28.5 (25.6; 33.6)	34.5 (30.7; 40.6)
Min ; Max	22.2 ; 53.7	22.8 ; 49.2	19.3 ; 53.0	24.3 ; 53.7
Week 52				
N(%)	55 (96.5)	52 (88.1)	53 (94.6)	55 (94.8)
Mean (SD)	34.4 (7.2)	31.6 (6.0)	29.6 (6.9)	35.4 (6.4)
Median (IQR)	33.4 (29.2; 40.4)	30.4 (27.1; 36.1)	28.6 (24.5; 33.7)	34.6 (31.0; 40.8)
Min ; Max	22.1 ; 53.4	22.3 ; 50.2	19.0 ; 53.4	24.4 ; 48.2

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, BMI: Body mass index, EOT: End of treatment.

Weight-related parameters by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 62				
N(%)	54 (94.7)	52 (88.1)	51 (91.1)	56 (96.6)
Mean (SD)	34.4 (7.3)	31.5 (6.2)	29.7 (7.1)	35.2 (6.3)
Median (IQR)	33.4 (29.5; 40.4)	29.9 (27.1; 36.4)	28.4 (25.5; 33.2)	34.0 (30.7; 40.7)
Min ; Max	21.8 ; 53.4	22.0 ; 51.0	18.2 ; 56.0	24.6 ; 48.8
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	56 (96.6)
Mean (SD)	34.5 (7.3)	31.3 (6.3)	29.4 (7.2)	35.3 (6.2)
Median (IQR)	34.0 (29.5; 40.8)	30.3 (27.4; 35.9)	28.2 (25.0; 32.1)	34.5 (31.2; 40.0)
Min ; Max	21.6 ; 52.6	21.4 ; 51.3	18.5 ; 57.4	24.5 ; 48.6
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Mean (SD)	34.6 (7.4)	31.4 (6.3)	29.6 (7.3)	35.5 (6.1)
Median (IQR)	34.0 (29.5; 40.8)	29.9 (27.4; 36.2)	28.3 (25.5; 32.9)	34.9 (31.2; 40.0)
Min ; Max	21.6 ; 52.6	21.4 ; 51.3	18.5 ; 57.4	24.6 ; 48.6

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, BMI: Body mass index, EOT: End of treatment.

Weight-related parameters by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Waist Circumference (cm)				
Week 0 (Randomisation)				
N(%)	56 (98.2)	58 (98.3)	56 (100.0)	57 (98.3)
Mean (SD)	114.6 (14.2)	111.4 (15.6)	110.5 (14.1)	114.3 (14.8)
Median (IQR)	113.0 (104.0;124.0)	111.5 (98.0;121.0)	110.0 (101.8;119.3)	114.0 (103.0;124.5)
Min ; Max	91.6 ; 149.3	86.0 ; 154.0	83.0 ; 147.3	86.0 ; 148.7
Week 4				
N(%)	56 (98.2)	57 (96.6)	55 (98.2)	58 (100.0)
Mean (SD)	113.3 (14.9)	110.6 (15.5)	109.1 (14.2)	113.3 (15.0)
Median (IQR)	109.5 (103.0;124.8)	110.0 (97.0;121.0)	107.0 (101.0;119.0)	110.5 (102.5;124.5)
Min ; Max	88.0 ; 150.2	87.0 ; 153.0	82.8 ; 143.5	87.5 ; 148.5
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Mean (SD)	112.2 (14.3)	107.4 (15.3)	106.4 (14.0)	112.7 (15.5)
Median (IQR)	110.0 (105.0;121.5)	105.4 (95.3;117.0)	106.6 (98.0;113.0)	112.0 (100.0;124.0)
Min ; Max	87.0 ; 149.8	84.0 ; 151.2	81.0 ; 142.2	82.0 ; 148.7
Week 20				
N(%)	54 (94.7)	54 (91.5)	53 (94.6)	57 (98.3)
Mean (SD)	111.6 (14.8)	106.4 (15.2)	102.9 (13.9)	113.4 (15.6)
Median (IQR)	110.8 (101.6;121.7)	103.7 (94.0;115.0)	103.5 (95.0;111.0)	112.0 (100.5;124.0)
Min ; Max	86.0 ; 148.5	83.0 ; 145.0	78.0 ; 137.2	80.0 ; 147.0

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, BMI: Body mass index, EOT: End of treatment.

Weight-related parameters by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	53 (93.0)	54 (91.5)	52 (92.9)	57 (98.3)
Mean (SD)	111.4 (15.0)	105.9 (15.9)	101.0 (13.7)	113.1 (15.3)
Median (IQR)	110.5 (101.0;123.4)	105.5 (91.0;114.5)	102.8 (92.8;111.0)	112.5 (101.6;124.6)
Min ; Max	85.0 ; 144.8	83.0 ; 144.0	72.0 ; 132.1	82.0 ; 146.5
Week 36				
N(%)	53 (93.0)	52 (88.1)	53 (94.6)	57 (98.3)
Mean (SD)	111.2 (15.3)	105.0 (16.0)	100.8 (14.6)	113.5 (15.3)
Median (IQR)	109.2 (100.0;119.1)	104.0 (92.0;113.3)	102.0 (92.0;109.0)	111.0 (102.0;125.0)
Min ; Max	83.4 ; 143.5	83.5 ; 142.5	74.8 ; 138.4	82.0 ; 146.5
Week 44				
N(%)	54 (94.7)	54 (91.5)	51 (91.1)	56 (96.6)
Mean (SD)	111.0 (15.5)	105.6 (15.9)	99.5 (13.7)	112.6 (14.9)
Median (IQR)	109.1 (99.0;118.5)	105.3 (93.0;114.0)	100.2 (89.0;105.0)	110.8 (101.3;123.8)
Min ; Max	85.0 ; 148.6	83.0 ; 141.5	75.0 ; 132.5	85.0 ; 147.0
Week 52				
N(%)	55 (96.5)	52 (88.1)	53 (94.6)	55 (94.8)
Mean (SD)	110.7 (15.4)	105.4 (16.4)	99.4 (14.3)	112.7 (14.8)
Median (IQR)	110.0 (99.0;120.5)	105.0 (91.5;114.3)	100.0 (89.0;107.0)	110.6 (103.5;123.5)
Min ; Max	83.5 ; 142.3	81.5 ; 143.3	72.1 ; 128.3	82.0 ; 148.0

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, BMI: Body mass index, EOT: End of treatment.

Weight-related parameters by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 62				
N(%)	54 (94.7)	51 (86.4)	51 (91.1)	56 (96.6)
Mean (SD)	111.0 (15.4)	105.4 (16.9)	98.7 (13.9)	112.2 (14.2)
Median (IQR)	108.4 (100.0;123.0)	105.5 (90.2;114.0)	100.0 (88.9;106.5)	112.4 (101.0;122.5)
Min ; Max	82.5 ; 146.7	77.5 ; 144.0	72.5 ; 129.5	84.5 ; 146.8
Week 72 (EOT)				
N(%)	55 (96.5)	52 (88.1)	53 (94.6)	56 (96.6)
Mean (SD)	110.7 (15.4)	104.9 (17.1)	98.1 (14.9)	112.5 (15.3)
Median (IQR)	108.7 (99.0;121.0)	105.5 (89.8;114.8)	99.2 (88.0;104.0)	111.5 (100.2;124.2)
Min ; Max	84.5 ; 146.6	77.0 ; 142.5	71.0 ; 134.6	82.5 ; 145.7
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	45 (76.3)	50 (89.3)	53 (91.4)
Mean (SD)	110.7 (15.6)	104.6 (17.5)	98.4 (15.0)	112.5 (15.3)
Median (IQR)	108.7 (99.0;121.0)	105.0 (88.5;113.0)	99.4 (89.0;104.0)	111.0 (100.3;122.0)
Min ; Max	84.5 ; 146.6	77.0 ; 142.5	71.0 ; 134.6	82.5 ; 145.7

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, BMI: Body mass index, EOT: End of treatment.

6.2.49 Body weight - change from baseline by week - summary - in-trial - full analysis set

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Number of subjects	57	59	56	58
Body Weight (kg)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Mean (SD)	97.1 (21.6)	94.4 (22.5)	94.9 (21.0)	99.4 (21.8)
Median (IQR)	95.7 (82.0;108.8)	95.8 (75.2;108.0)	94.5 (78.0;107.9)	97.9 (82.1;111.0)
Min ; Max	56.1 ; 148.1	59.8 ; 162.3	55.0 ; 154.9	62.0 ; 150.0
Change from baseline in Body Weight (kg)				
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	58 (100.0)
Mean (SD)	-0.9 (2.3)	-1.8 (2.1)	-2.0 (1.9)	-0.5 (2.0)
Median (IQR)	-1.0 (-1.8; -0.2)	-1.5 (-2.4; -0.5)	-1.9 (-2.7; -0.9)	-0.4 (-1.4; 0.8)
Min ; Max	-5.6 ; 10.0	-10.5 ; 2.3	-8.5 ; 2.5	-7.0 ; 4.6
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Mean (SD)	-2.6 (3.2)	-4.7 (3.4)	-5.6 (3.1)	-0.7 (2.7)
Median (IQR)	-2.3 (-4.6; -0.6)	-3.9 (-6.3; -2.4)	-5.3 (-8.0; -3.6)	-0.4 (-2.3; 1.1)
Min ; Max	-10.3 ; 7.6	-14.7 ; 2.2	-12.1 ; 2.2	-9.5 ; 4.0
Week 20				
N(%)	54 (94.7)	55 (93.2)	53 (94.6)	57 (98.3)
Mean (SD)	-3.9 (3.8)	-6.7 (4.7)	-9.0 (4.2)	-0.7 (2.9)
Median (IQR)	-3.4 (-6.0; -1.9)	-5.4 (-9.9; -3.6)	-8.4 (-11.8; -6.7)	-0.6 (-1.9; 0.8)
Min ; Max	-14.9 ; 5.9	-18.9 ; 1.8	-18.1 ; 1.2	-13.1 ; 4.7

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

Body weight - change from baseline by week - summary - in-trial - full analysis set

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	54 (94.7)	54 (91.5)	52 (92.9)	57 (98.3)
Mean (SD)	-4.4 (5.1)	-7.5 (5.6)	-10.9 (5.2)	-0.4 (3.6)
Median (IQR)	-3.5 (-6.8; -0.9)	-6.2 (-10.4; -3.4)	-10.5 (-14.1; -7.8)	-0.5 (-2.2; 2.1)
Min ; Max	-18.2 ; 7.0	-21.6 ; 0.4	-23.2 ; 0.9	-14.4 ; 5.6
Week 36				
N(%)	53 (93.0)	52 (88.1)	53 (94.6)	57 (98.3)
Mean (SD)	-4.3 (5.1)	-8.2 (5.8)	-11.4 (5.9)	-0.1 (4.2)
Median (IQR)	-3.6 (-6.5; -1.9)	-7.2 (-11.2; -4.2)	-11.0 (-15.9; -6.9)	0.0 (-1.4; 2.1)
Min ; Max	-17.0 ; 7.3	-22.6 ; 0.8	-24.7 ; 2.8	-14.0 ; 7.6
Week 44				
N(%)	54 (94.7)	54 (91.5)	52 (92.9)	56 (96.6)
Mean (SD)	-4.4 (5.7)	-8.4 (6.0)	-12.6 (6.4)	-0.4 (4.4)
Median (IQR)	-3.5 (-6.4; -1.5)	-7.4 (-11.8; -4.4)	-12.1 (-17.2; -8.1)	-0.1 (-1.6; 2.4)
Min ; Max	-20.4 ; 8.2	-23.6 ; 1.1	-26.6 ; 2.9	-14.0 ; 6.7
Week 52				
N(%)	55 (96.5)	52 (88.1)	53 (94.6)	55 (94.8)
Mean (SD)	-4.9 (6.0)	-8.7 (6.1)	-13.2 (7.5)	-0.2 (3.8)
Median (IQR)	-4.3 (-9.3; -1.2)	-7.3 (-12.3; -3.5)	-11.9 (-17.5; -7.8)	-0.1 (-2.1; 2.0)
Min ; Max	-22.0 ; 8.0	-24.7 ; -0.2	-38.8 ; 0.9	-10.8 ; 7.8

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

Body weight - change from baseline by week - summary - in-trial - full analysis set

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 62				
N(%)	54 (94.7)	52 (88.1)	51 (91.1)	56 (96.6)
Mean (SD)	-4.7 (6.1)	-8.8 (6.3)	-13.1 (7.6)	-0.8 (4.6)
Median (IQR)	-3.6 (-7.0; -0.5)	-7.4 (-12.5; -4.3)	-12.4 (-17.7; -8.4)	-0.2 (-2.9; 2.1)
Min ; Max	-26.0 ; 7.0	-24.1 ; 1.6	-31.1 ; 0.6	-12.1 ; 7.5
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	56 (96.6)
Mean (SD)	-4.4 (6.2)	-9.4 (7.2)	-13.8 (8.9)	-0.6 (4.9)
Median (IQR)	-3.2 (-7.1; -0.4)	-7.9 (-12.4; -4.1)	-12.0 (-17.4; -8.1)	-0.6 (-3.4; 2.5)
Min ; Max	-26.0 ; 7.5	-33.1 ; 0.2	-40.0 ; 1.1	-13.2 ; 8.7
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Mean (SD)	-4.6 (6.3)	-9.2 (6.4)	-13.5 (8.2)	-0.6 (4.7)
Median (IQR)	-3.5 (-7.1; -1.0)	-8.1 (-12.4; -4.4)	-13.0 (-17.4; -8.1)	-0.8 (-3.4; 2.2)
Min ; Max	-26.0 ; 7.5	-23.9 ; 0.2	-33.8 ; 1.1	-13.2 ; 8.7

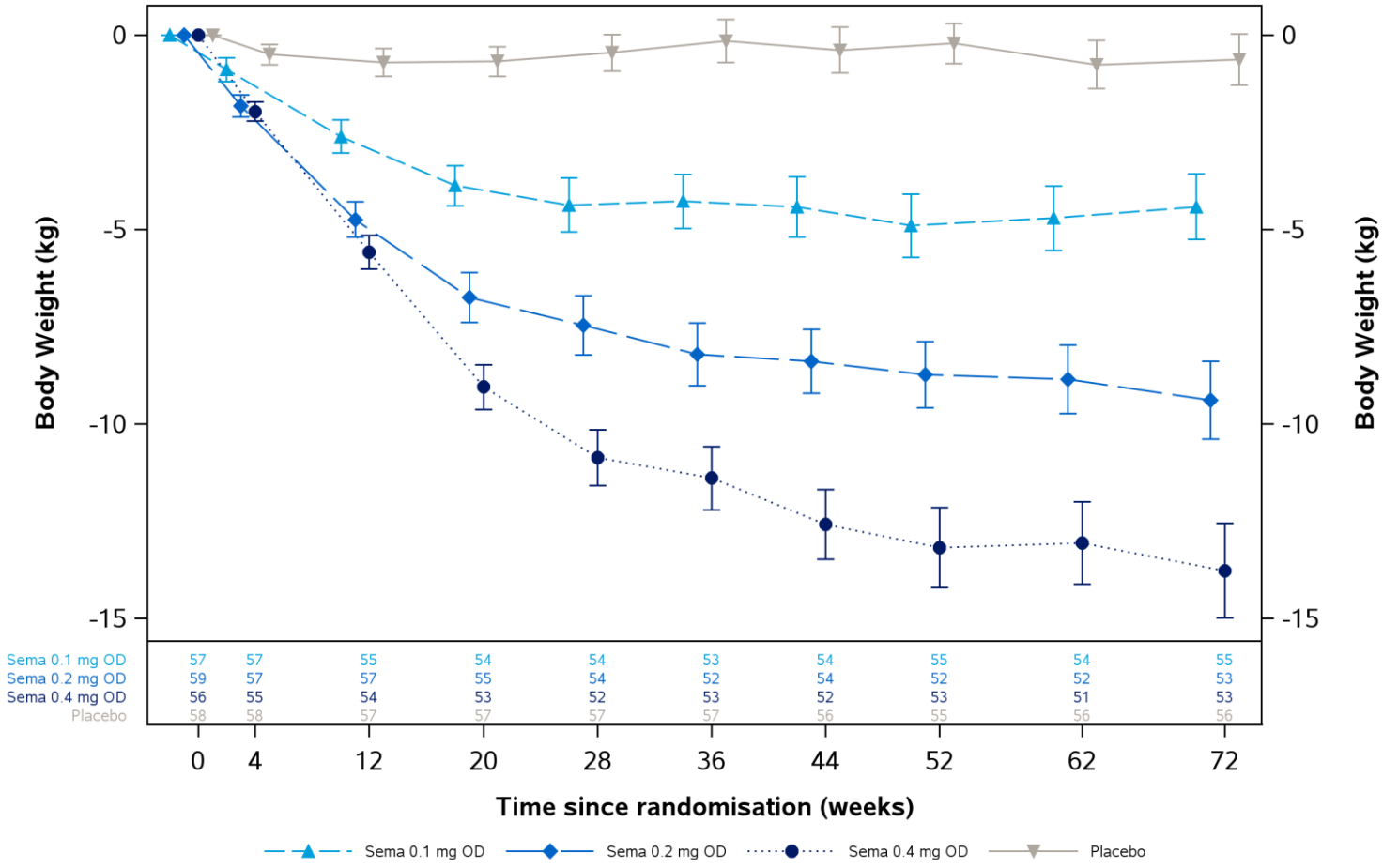
N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

6.2.50 Body weight - change from baseline - statistical analysis - ANCOVA - MI based on unconditional reference -in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
Body Weight (kg)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	57	92.14		
Sema 0.2 mg OD	59	59	87.80		
Sema 0.4 mg OD	56	56	83.15		
Placebo	58	58	96.13		
Change from baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	57	-4.30		
Sema 0.2 mg OD	59	59	-8.63		
Sema 0.4 mg OD	56	56	-13.28		
Placebo	58	58	-0.30		
Treatment difference at week 72 (EOT)					
Sema 0.1 mg OD - Placebo			-3.99	[-6.60; -1.39]	0.0026
Sema 0.2 mg OD - Placebo			-8.33	[-10.93; -5.72]	<.0001
Sema 0.4 mg OD - Placebo			-12.98	[-15.61;-10.34]	<.0001

ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval, OD: Once daily, EOT: End of treatment.

6.2.51 Body weight - change from baseline by week - observed mean plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



Number of observations per treatment group and visit is presented in the lower part of the plot. Plot shows mean +/- standard error. OD: Once daily.

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6.2.52 Systolic and diastolic blood pressure by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Number of subjects	57	59	56	58
Diastolic Blood Pressure (mmHg)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Mean (SD)	80 (10)	82 (10)	81 (9)	81 (10)
Median (IQR)	80 (75; 86)	81 (75; 88)	81 (75; 85)	82 (75; 86)
Min ; Max	60 ; 99	68 ; 107	63 ; 103	57 ; 107
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	58 (100.0)
Mean (SD)	81 (10)	80 (12)	82 (10)	80 (9)
Median (IQR)	81 (75; 87)	79 (71; 85)	80 (76; 85)	80 (75; 85)
Min ; Max	56 ; 103	57 ; 118	60 ; 117	60 ; 104
Week 8				
N(%)	55 (96.5)	59 (100.0)	54 (96.4)	57 (98.3)
Mean (SD)	79 (10)	78 (11)	80 (8)	81 (11)
Median (IQR)	80 (72; 86)	78 (72; 83)	80 (75; 86)	80 (74; 88)
Min ; Max	59 ; 99	48 ; 119	62 ; 108	56 ; 110
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Mean (SD)	80 (11)	80 (10)	78 (9)	79 (12)
Median (IQR)	79 (72; 85)	79 (73; 86)	77 (71; 83)	79 (70; 86)
Min ; Max	60 ; 105	66 ; 105	55 ; 102	55 ; 110

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

Systolic and diastolic blood pressure by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 16				
N(%)	55 (96.5)	54 (91.5)	53 (94.6)	57 (98.3)
Mean (SD)	80 (10)	79 (12)	78 (9)	81 (10)
Median (IQR)	80 (72; 87)	80 (70; 86)	78 (73; 84)	80 (75; 87)
Min ; Max	60 ; 104	55 ; 114	57 ; 99	60 ; 109
Week 20				
N(%)	54 (94.7)	55 (93.2)	53 (94.6)	57 (98.3)
Mean (SD)	79 (10)	77 (11)	78 (10)	81 (11)
Median (IQR)	79 (72; 86)	78 (70; 84)	80 (72; 84)	80 (76; 87)
Min ; Max	58 ; 110	57 ; 115	55 ; 102	58 ; 106
Week 28				
N(%)	54 (94.7)	54 (91.5)	52 (92.9)	57 (98.3)
Mean (SD)	80 (9)	79 (9)	78 (9)	79 (9)
Median (IQR)	80 (74; 85)	79 (72; 86)	77 (72; 84)	80 (71; 85)
Min ; Max	60 ; 100	62 ; 104	59 ; 105	60 ; 105
Week 36				
N(%)	53 (93.0)	52 (88.1)	53 (94.6)	57 (98.3)
Mean (SD)	78 (10)	78 (10)	77 (9)	82 (10)
Median (IQR)	79 (70; 84)	78 (71; 86)	78 (70; 84)	82 (77; 86)
Min ; Max	58 ; 102	60 ; 102	58 ; 100	63 ; 106

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

Systolic and diastolic blood pressure by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 44				
N(%)	54 (94.7)	53 (89.8)	52 (92.9)	56 (96.6)
Mean (SD)	80 (10)	77 (10)	78 (8)	79 (10)
Median (IQR)	80 (72; 85)	77 (72; 82)	78 (73; 82)	79 (73; 84)
Min ; Max	59 ; 112	60 ; 105	56 ; 98	50 ; 107
Week 52				
N(%)	55 (96.5)	52 (88.1)	53 (94.6)	55 (94.8)
Mean (SD)	79 (10)	77 (12)	79 (9)	80 (9)
Median (IQR)	78 (73; 85)	76 (70; 84)	78 (74; 84)	82 (72; 87)
Min ; Max	57 ; 105	55 ; 116	62 ; 100	57 ; 96
Week 62				
N(%)	54 (94.7)	52 (88.1)	52 (92.9)	56 (96.6)
Mean (SD)	81 (11)	80 (9)	79 (8)	80 (11)
Median (IQR)	79 (73; 87)	80 (75; 87)	79 (75; 84)	80 (74; 86)
Min ; Max	59 ; 113	60 ; 100	48 ; 100	54 ; 110
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	56 (96.6)
Mean (SD)	81 (10)	80 (9)	78 (8)	79 (10)
Median (IQR)	80 (75; 89)	78 (74; 86)	77 (74; 82)	80 (72; 86)
Min ; Max	60 ; 118	60 ; 100	56 ; 94	50 ; 100

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

Systolic and diastolic blood pressure by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	53 (91.4)
Mean (SD)	81 (11)	80 (9)	78 (8)	79 (10)
Median (IQR)	80 (75; 89)	78 (73; 86)	78 (74; 82)	80 (70; 86)
Min ; Max	60 ; 118	60 ; 100	56 ; 94	50 ; 97

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

Systolic and diastolic blood pressure by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Systolic Blood Pressure (mmHg)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Mean (SD)	133 (15)	137 (19)	133 (14)	130 (15)
Median (IQR)	135 (122; 141)	135 (124; 147)	130 (124; 139)	130 (121; 140)
Min ; Max	95 ; 164	104 ; 190	102 ; 163	93 ; 160
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	58 (100.0)
Mean (SD)	131 (14)	132 (16)	129 (13)	128 (14)
Median (IQR)	130 (122; 140)	131 (124; 138)	128 (119; 138)	129 (116; 136)
Min ; Max	100 ; 157	102 ; 190	96 ; 165	100 ; 172
Week 8				
N(%)	55 (96.5)	59 (100.0)	54 (96.4)	57 (98.3)
Mean (SD)	129 (14)	127 (14)	126 (15)	131 (13)
Median (IQR)	130 (118; 140)	126 (117; 136)	126 (119; 137)	131 (122; 137)
Min ; Max	100 ; 155	100 ; 160	92 ; 161	107 ; 173
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Mean (SD)	129 (14)	126 (16)	123 (13)	129 (14)
Median (IQR)	130 (119; 140)	124 (110; 137)	122 (112; 132)	130 (120; 138)
Min ; Max	100 ; 155	94 ; 162	99 ; 154	104 ; 179

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

Systolic and diastolic blood pressure by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 16				
N(%)	55 (96.5)	54 (91.5)	53 (94.6)	57 (98.3)
Mean (SD)	129 (14)	126 (15)	122 (12)	129 (12)
Median (IQR)	128 (121; 138)	125 (115; 135)	124 (113; 129)	130 (120; 138)
Min ; Max	96 ; 159	95 ; 156	92 ; 144	108 ; 156
Week 20				
N(%)	54 (94.7)	55 (93.2)	53 (94.6)	57 (98.3)
Mean (SD)	126 (15)	127 (14)	123 (13)	129 (14)
Median (IQR)	125 (115; 134)	127 (115; 135)	121 (117; 132)	130 (121; 136)
Min ; Max	101 ; 186	93 ; 155	85 ; 151	99 ; 168
Week 28				
N(%)	54 (94.7)	54 (91.5)	52 (92.9)	57 (98.3)
Mean (SD)	129 (13)	128 (14)	122 (14)	129 (14)
Median (IQR)	128 (120; 139)	129 (120; 136)	121 (110; 134)	128 (121; 137)
Min ; Max	100 ; 160	93 ; 157	98 ; 150	101 ; 180
Week 36				
N(%)	53 (93.0)	52 (88.1)	53 (94.6)	57 (98.3)
Mean (SD)	130 (15)	128 (15)	124 (14)	131 (12)
Median (IQR)	132 (120; 139)	128 (118; 137)	123 (114; 133)	131 (123; 140)
Min ; Max	102 ; 175	99 ; 157	99 ; 149	109 ; 160

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

Systolic and diastolic blood pressure by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 44				
N(%)	54 (94.7)	53 (89.8)	52 (92.9)	56 (96.6)
Mean (SD)	129 (14)	128 (14)	123 (12)	129 (13)
Median (IQR)	130 (122; 136)	128 (120; 136)	123 (114; 131)	130 (121; 136)
Min ; Max	103 ; 176	97 ; 160	98 ; 147	94 ; 174
Week 52				
N(%)	55 (96.5)	52 (88.1)	53 (94.6)	55 (94.8)
Mean (SD)	128 (15)	126 (14)	126 (12)	130 (12)
Median (IQR)	126 (115; 136)	127 (115; 133)	126 (118; 134)	130 (122; 140)
Min ; Max	98 ; 171	102 ; 169	93 ; 151	98 ; 159
Week 62				
N(%)	54 (94.7)	52 (88.1)	52 (92.9)	56 (96.6)
Mean (SD)	129 (16)	127 (16)	124 (12)	129 (15)
Median (IQR)	127 (118; 140)	129 (115; 133)	124 (113; 134)	130 (119; 139)
Min ; Max	100 ; 164	102 ; 171	99 ; 152	90 ; 175
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	56 (96.6)
Mean (SD)	133 (16)	130 (15)	126 (12)	128 (14)
Median (IQR)	132 (121; 146)	127 (121; 142)	126 (118; 134)	130 (118; 135)
Min ; Max	100 ; 168	95 ; 165	100 ; 165	93 ; 168

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

Systolic and diastolic blood pressure by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	53 (91.4)
Mean (SD)	133 (16)	130 (15)	125 (11)	128 (13)
Median (IQR)	132 (121; 145)	127 (121; 142)	125 (117; 134)	130 (118; 134)
Min ; Max	100 ; 168	95 ; 165	100 ; 144	93 ; 159

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

6.2.53 Systolic and diastolic blood pressure - change from baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Number of subjects	57	59	56	58
Diastolic Blood Pressure (mmHg)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Mean (SD)	80 (10)	82 (10)	81 (9)	81 (10)
Median (IQR)	80 (75; 86)	81 (75; 88)	81 (75; 85)	82 (75; 86)
Min ; Max	60 ; 99	68 ; 107	63 ; 103	57 ; 107
Change from baseline in Diastolic Blood Pressure (mmHg)				
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	58 (100.0)
Mean (SD)	1 (9)	-2 (9)	1 (8)	-1 (8)
Median (IQR)	1 (-5; 6)	-1 (-8; 2)	0 (-5; 5)	-1 (-6; 4)
Min ; Max	-22 ; 29	-23 ; 36	-15 ; 27	-18 ; 24
Week 8				
N(%)	55 (96.5)	59 (100.0)	54 (96.4)	57 (98.3)
Mean (SD)	-0 (8)	-4 (11)	-1 (10)	1 (9)
Median (IQR)	-2 (-6; 4)	-4 (-8; 2)	-2 (-6; 3)	0 (-5; 5)
Min ; Max	-16 ; 24	-37 ; 18	-20 ; 40	-17 ; 24
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Mean (SD)	0 (9)	-2 (10)	-4 (12)	-2 (9)
Median (IQR)	0 (-8; 6)	-1 (-8; 4)	-3 (-10; 1)	-3 (-7; 3)
Min ; Max	-16 ; 25	-38 ; 23	-43 ; 39	-20 ; 27

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

Systolic and diastolic blood pressure - change from baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD		Sema 0.2 mg OD		Sema 0.4 mg OD		Placebo	
Week 16								
N(%)	55 (96.5)		54 (91.5)		53 (94.6)		57 (98.3)	
Mean (SD)	1 (10)		-2 (11)		-3 (9)		-0 (8)	
Median (IQR)	1 (-5;	7)	-4 (-8;	5)	-4 (-8;	2)	0 (-6;	3)
Min ; Max	-23 ; 20		-29 ; 27		-26 ; 32		-15 ; 27	
Week 20								
N(%)	54 (94.7)		55 (93.2)		53 (94.6)		57 (98.3)	
Mean (SD)	-0 (10)		-5 (10)		-3 (11)		-0 (10)	
Median (IQR)	0 (-6;	7)	-4 (-11;	1)	-2 (-10;	4)	-2 (-5;	5)
Min ; Max	-25 ; 20		-31 ; 17		-24 ; 39		-20 ; 37	
Week 28								
N(%)	54 (94.7)		54 (91.5)		52 (92.9)		57 (98.3)	
Mean (SD)	0 (8)		-3 (10)		-3 (9)		-2 (9)	
Median (IQR)	-2 (-6;	5)	-3 (-9;	2)	-3 (-8;	2)	-2 (-8;	4)
Min ; Max	-15 ; 25		-34 ; 20		-22 ; 25		-30 ; 21	
Week 36								
N(%)	53 (93.0)		52 (88.1)		53 (94.6)		57 (98.3)	
Mean (SD)	-1 (9)		-4 (10)		-4 (9)		1 (10)	
Median (IQR)	0 (-9;	6)	-4 (-10;	2)	-4 (-10;	0)	0 (-5;	8)
Min ; Max	-26 ; 17		-42 ; 17		-27 ; 25		-20 ; 24	

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

Systolic and diastolic blood pressure - change from baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 44				
N(%)	54 (94.7)	53 (89.8)	52 (92.9)	56 (96.6)
Mean (SD)	0 (9)	-5 (10)	-4 (10)	-2 (10)
Median (IQR)	1 (-6; 7)	-4 (-11; 1)	-4 (-11; 1)	-3 (-9; 3)
Min ; Max	-26 ; 17	-34 ; 17	-20 ; 35	-20 ; 28
Week 52				
N(%)	55 (96.5)	52 (88.1)	53 (94.6)	55 (94.8)
Mean (SD)	-0 (9)	-4 (8)	-2 (8)	-1 (8)
Median (IQR)	0 (-6; 5)	-5 (-10; 0)	-2 (-7; 3)	0 (-6; 4)
Min ; Max	-26 ; 17	-19 ; 17	-22 ; 20	-18 ; 24
Week 62				
N(%)	54 (94.7)	52 (88.1)	52 (92.9)	56 (96.6)
Mean (SD)	1 (11)	-1 (10)	-2 (10)	-1 (9)
Median (IQR)	0 (-5; 8)	-3 (-7; 4)	-1 (-8; 3)	-2 (-6; 4)
Min ; Max	-21 ; 36	-23 ; 29	-32 ; 23	-21 ; 20
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	56 (96.6)
Mean (SD)	2 (10)	-3 (10)	-3 (9)	-2 (9)
Median (IQR)	2 (-4; 8)	-3 (-8; 4)	-3 (-10; 1)	-3 (-8; 4)
Min ; Max	-20 ; 23	-29 ; 21	-22 ; 24	-19 ; 27

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

Systolic and diastolic blood pressure - change from baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	53 (91.4)
Mean (SD)	2 (9)	-2 (9)	-3 (9)	-2 (8)
Median (IQR)	2 (-4; 8)	-3 (-8; 4)	-3 (-10; 1)	-3 (-8; 4)
Min ; Max	-20 ; 23	-19 ; 21	-22 ; 24	-19 ; 21

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

Systolic and diastolic blood pressure - change from baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Systolic Blood Pressure (mmHg)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Mean (SD)	133 (15)	137 (19)	133 (14)	130 (15)
Median (IQR)	135 (122; 141)	135 (124; 147)	130 (124; 139)	130 (121; 140)
Min ; Max	95 ; 164	104 ; 190	102 ; 163	93 ; 160
Change from baseline in Systolic Blood Pressure (mmHg)				
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	58 (100.0)
Mean (SD)	-2 (13)	-5 (19)	-4 (12)	-3 (13)
Median (IQR)	-5 (-10; 4)	-2 (-14; 5)	-1 (-16; 5)	-5 (-12; 5)
Min ; Max	-31 ; 31	-64 ; 66	-25 ; 25	-25 ; 31
Week 8				
N(%)	55 (96.5)	59 (100.0)	54 (96.4)	57 (98.3)
Mean (SD)	-4 (13)	-10 (20)	-6 (13)	0 (13)
Median (IQR)	-3 (-10; 5)	-6 (-20; 2)	-6 (-13; 0)	0 (-9; 5)
Min ; Max	-42 ; 19	-85 ; 22	-38 ; 21	-30 ; 30
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Mean (SD)	-4 (12)	-11 (18)	-9 (14)	-1 (14)
Median (IQR)	-5 (-11; 5)	-11 (-20; 1)	-8 (-16; 0)	-2 (-10; 5)
Min ; Max	-35 ; 27	-84 ; 20	-53 ; 10	-26 ; 41

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

Systolic and diastolic blood pressure - change from baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 16				
N(%)	55 (96.5)	54 (91.5)	53 (94.6)	57 (98.3)
Mean (SD)	-3 (13)	-11 (20)	-10 (15)	-1 (14)
Median (IQR)	-5 (-12; 7)	-11 (-20; 0)	-8 (-19; 0)	-2 (-7; 5)
Min ; Max	-35 ; 26	-73 ; 46	-71 ; 13	-36 ; 47
Week 20				
N(%)	54 (94.7)	55 (93.2)	53 (94.6)	57 (98.3)
Mean (SD)	-6 (16)	-12 (19)	-9 (14)	-1 (15)
Median (IQR)	-9 (-16; 4)	-9 (-24; 3)	-10 (-17; 0)	-2 (-12; 6)
Min ; Max	-44 ; 45	-68 ; 15	-64 ; 20	-27 ; 51
Week 28				
N(%)	54 (94.7)	54 (91.5)	52 (92.9)	57 (98.3)
Mean (SD)	-3 (13)	-10 (18)	-10 (14)	-1 (14)
Median (IQR)	-5 (-13; 6)	-11 (-17; 0)	-11 (-19; 0)	-2 (-10; 5)
Min ; Max	-31 ; 24	-78 ; 22	-48 ; 11	-29 ; 36
Week 36				
N(%)	53 (93.0)	52 (88.1)	53 (94.6)	57 (98.3)
Mean (SD)	-3 (15)	-11 (21)	-9 (15)	0 (13)
Median (IQR)	-4 (-12; 6)	-9 (-24; 4)	-8 (-18; 0)	1 (-9; 9)
Min ; Max	-40 ; 34	-89 ; 26	-54 ; 25	-29 ; 30

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

Systolic and diastolic blood pressure - change from baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 44				
N(%)	54 (94.7)	53 (89.8)	52 (92.9)	56 (96.6)
Mean (SD)	-3 (15)	-11 (17)	-9 (15)	-1 (15)
Median (IQR)	-5 (-12; 6)	-9 (-19; 0)	-11 (-21; 0)	-2 (-11; 7)
Min ; Max	-34 ; 32	-63 ; 20	-50 ; 21	-35 ; 43
Week 52				
N(%)	55 (96.5)	52 (88.1)	53 (94.6)	55 (94.8)
Mean (SD)	-5 (16)	-11 (15)	-6 (15)	-1 (13)
Median (IQR)	-5 (-13; 6)	-11 (-21; -2)	-8 (-14; 2)	-1 (-10; 6)
Min ; Max	-35 ; 31	-47 ; 25	-70 ; 19	-25 ; 30
Week 62				
N(%)	54 (94.7)	52 (88.1)	52 (92.9)	56 (96.6)
Mean (SD)	-5 (18)	-10 (16)	-8 (16)	-2 (13)
Median (IQR)	-3 (-15; 4)	-10 (-21; 2)	-8 (-14; 0)	-2 (-12; 8)
Min ; Max	-55 ; 33	-55 ; 20	-56 ; 37	-27 ; 28
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	56 (96.6)
Mean (SD)	-0 (16)	-9 (19)	-7 (15)	-3 (15)
Median (IQR)	-1 (-9; 12)	-10 (-20; 3)	-5 (-15; 2)	-2 (-12; 5)
Min ; Max	-38 ; 33	-59 ; 30	-51 ; 34	-42 ; 33

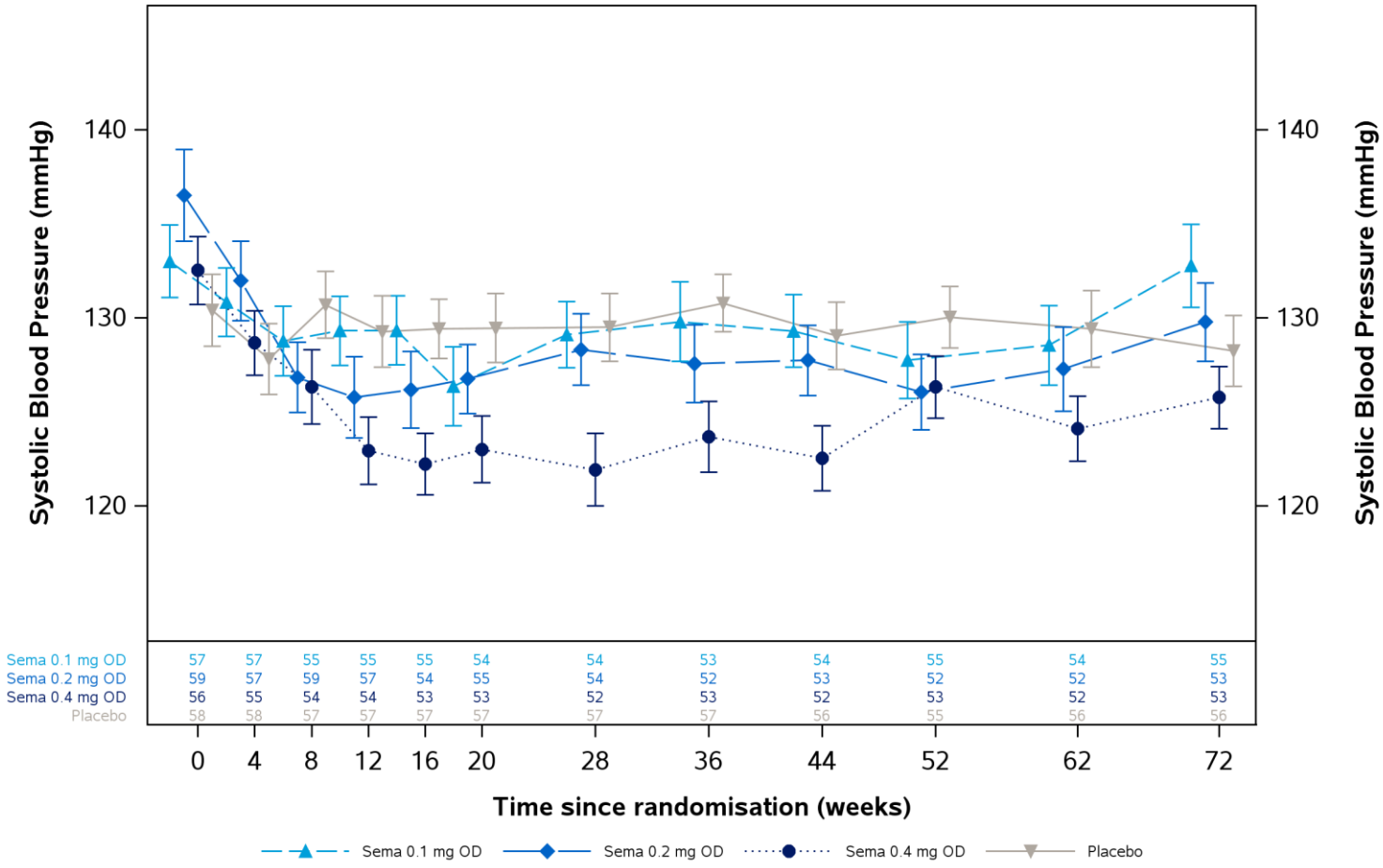
N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

Systolic and diastolic blood pressure - change from baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	53 (91.4)
Mean (SD)	-0 (16)	-8 (17)	-7 (14)	-4 (14)
Median (IQR)	-1 (-9; 12)	-11 (-20; 3)	-6 (-15; 2)	-2 (-11; 5)
Min ; Max	-38 ; 33	-42 ; 25	-51 ; 19	-42 ; 22

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

6.2.54 Systolic blood pressure by week - observed mean plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



Number of observations per treatment group and visit is presented in the lower part of the plot. Plot shows mean +/- standard error. OD: Once daily.

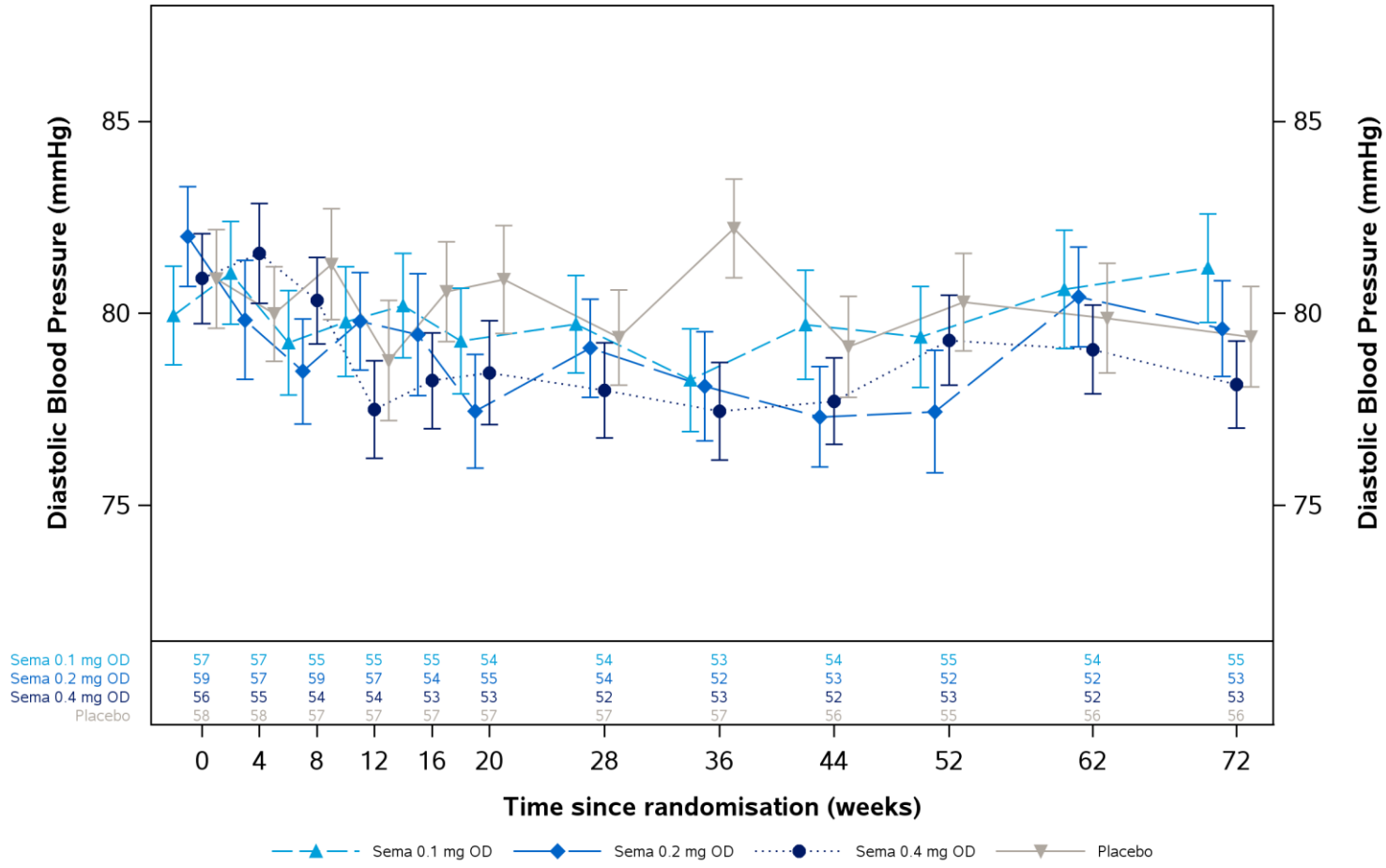
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6.2.55 Systolic blood pressure - change from baseline - statistical analysis - ANCOVA - MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
Systolic Blood Pressure (mmHg)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	57	132.74		
Sema 0.2 mg OD	59	59	127.59		
Sema 0.4 mg OD	56	56	126.10		
Placebo	58	58	129.40		
Change from baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	57	-0.39		
Sema 0.2 mg OD	59	59	-5.54		
Sema 0.4 mg OD	56	56	-7.03		
Placebo	58	58	-3.73		
Treatment difference at week 72 (EOT)					
Sema 0.1 mg OD - Placebo			3.34	[-1.64; 8.32]	0.1889
Sema 0.2 mg OD - Placebo			-1.81	[-6.92; 3.30]	0.4874
Sema 0.4 mg OD - Placebo			-3.30	[-8.35; 1.75]	0.2001

ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval, OD: Once daily, EOT: End of treatment.

6.2.56 Diastolic blood pressure by week - observed mean plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



Number of observations per treatment group and visit is presented in the lower part of the plot. Plot shows mean +/- standard error. OD: Once daily.

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6.2.57 Diastolic blood pressure - change from baseline - statistical analysis - ANCOVA - MI based on unconditional reference - in-trial – subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
Diastolic Blood Pressure (mmHg)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	57	81.85		
Sema 0.2 mg OD	59	59	78.96		
Sema 0.4 mg OD	56	56	78.19		
Placebo	58	58	79.29		
Change from baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	57	0.90		
Sema 0.2 mg OD	59	59	-1.99		
Sema 0.4 mg OD	56	56	-2.76		
Placebo	58	58	-1.66		
Treatment difference at week 72 (EOT)					
Sema 0.1 mg OD - Placebo			2.56	[-0.52; 5.64]	0.1033
Sema 0.2 mg OD - Placebo			-0.33	[-3.44; 2.77]	0.8330
Sema 0.4 mg OD - Placebo			-1.10	[-4.22; 2.02]	0.4901

ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval, OD: Once daily, EOT: End of treatment.

6.2.58 Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Number of subjects	57	59	56	58
Total Cholesterol (mg/dL)				
Week 0 (Randomisation)				
N(%)	56 (98.2)	57 (96.6)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	180.5 (25.8)	185.4 (24.8)	181.0 (26.1)	189.2 (24.5)
Mean (SD)	186.1 (45.5)	190.6 (43.6)	186.7 (46.5)	194.5 (45.6)
Median (IQR)	185.3 (157.9; 217.0)	190.3 (154.8; 224.3)	184.9 (158.7; 212.4)	196.1 (159.1; 226.3)
Min ; Max	93.4 ; 320.1	91.1 ; 274.9	73.4 ; 358.3	86.9 ; 352.5
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	57 (98.3)
Geom. Mean (CV)	169.0 (27.4)	174.1 (25.8)	164.5 (24.8)	186.1 (24.3)
Mean (SD)	174.8 (44.1)	179.3 (41.6)	169.2 (40.1)	191.3 (46.3)
Median (IQR)	178.8 (144.0; 204.2)	178.8 (152.9; 204.2)	173.0 (142.9; 191.5)	185.7 (159.1; 224.7)
Min ; Max	76.1 ; 274.1	75.3 ; 278.8	70.7 ; 310.4	105.0 ; 342.1
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	171.6 (24.9)	169.8 (26.4)	160.2 (28.5)	186.3 (24.1)
Mean (SD)	176.5 (41.2)	175.2 (42.9)	166.0 (43.8)	191.5 (45.6)
Median (IQR)	174.9 (147.5; 200.8)	172.2 (142.5; 201.2)	165.6 (140.9; 182.2)	193.8 (151.7; 220.5)
Min ; Max	83.0 ; 295.0	79.5 ; 272.6	55.6 ; 337.8	97.3 ; 331.3

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	53 (93.0)	52 (88.1)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	178.2 (26.4)	176.1 (26.3)	167.0 (25.4)	183.0 (25.6)
Mean (SD)	184.0 (46.1)	181.9 (46.8)	172.1 (42.8)	188.7 (47.9)
Median (IQR)	179.5 (154.4; 214.7)	177.6 (145.2; 214.3)	166.8 (147.7; 195.2)	188.4 (159.1; 214.7)
Min ; Max	93.1 ; 315.8	96.9 ; 331.3	76.4 ; 332.4	90.7 ; 358.3
Week 52				
N(%)	55 (96.5)	51 (86.4)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	173.9 (24.5)	180.7 (25.8)	171.4 (24.3)	175.9 (26.0)
Mean (SD)	178.8 (41.2)	186.4 (46.6)	176.0 (39.7)	181.6 (46.1)
Median (IQR)	176.8 (145.9; 205.4)	188.4 (155.6; 214.7)	170.3 (153.7; 190.3)	176.1 (145.6; 207.3)
Min ; Max	86.9 ; 275.7	98.5 ; 333.6	73.0 ; 310.0	96.1 ; 328.2
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	174.2 (26.0)	184.2 (21.5)	169.1 (22.7)	175.8 (26.5)
Mean (SD)	179.8 (45.7)	188.4 (40.4)	173.1 (36.4)	181.8 (48.9)
Median (IQR)	175.3 (147.9; 206.2)	180.3 (158.3; 208.1)	166.4 (151.0; 199.2)	178.8 (147.9; 208.9)
Min ; Max	93.4 ; 305.4	109.3 ; 294.6	84.6 ; 257.1	91.9 ; 374.9
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	175.4 (26.2)	183.2 (21.5)	169.2 (23.1)	179.0 (25.3)
Mean (SD)	181.1 (46.0)	187.3 (39.6)	173.3 (36.9)	184.7 (48.2)
Median (IQR)	175.7 (149.8; 206.2)	182.2 (157.5; 215.1)	166.8 (150.2; 199.2)	180.9 (154.4; 210.2)
Min ; Max	93.4 ; 305.4	109.3 ; 271.0	84.6 ; 257.1	113.5 ; 374.9

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Total Cholesterol (mmol/L)				
Week 0 (Randomisation)				
N(%)	56 (98.2)	57 (96.6)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	4.7 (25.8)	4.8 (24.8)	4.7 (26.1)	4.9 (24.5)
Mean (SD)	4.8 (1.2)	4.9 (1.1)	4.8 (1.2)	5.0 (1.2)
Median (IQR)	4.8 (4.1; 5.6)	4.9 (4.0; 5.8)	4.8 (4.1; 5.5)	5.1 (4.1; 5.9)
Min ; Max	2.4 ; 8.3	2.4 ; 7.1	1.9 ; 9.3	2.3 ; 9.1
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	57 (98.3)
Geom. Mean (CV)	4.4 (27.4)	4.5 (25.8)	4.3 (24.8)	4.8 (24.3)
Mean (SD)	4.5 (1.1)	4.6 (1.1)	4.4 (1.0)	5.0 (1.2)
Median (IQR)	4.6 (3.7; 5.3)	4.6 (4.0; 5.3)	4.5 (3.7; 5.0)	4.8 (4.1; 5.8)
Min ; Max	2.0 ; 7.1	2.0 ; 7.2	1.8 ; 8.0	2.7 ; 8.9
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	4.4 (24.9)	4.4 (26.4)	4.1 (28.5)	4.8 (24.1)
Mean (SD)	4.6 (1.1)	4.5 (1.1)	4.3 (1.1)	5.0 (1.2)
Median (IQR)	4.5 (3.8; 5.2)	4.5 (3.7; 5.2)	4.3 (3.7; 4.7)	5.0 (3.9; 5.7)
Min ; Max	2.2 ; 7.6	2.1 ; 7.1	1.4 ; 8.8	2.5 ; 8.6

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	53 (93.0)	52 (88.1)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	4.6 (26.4)	4.6 (26.3)	4.3 (25.4)	4.7 (25.6)
Mean (SD)	4.8 (1.2)	4.7 (1.2)	4.5 (1.1)	4.9 (1.2)
Median (IQR)	4.7 (4.0; 5.6)	4.6 (3.8; 5.6)	4.3 (3.8; 5.1)	4.9 (4.1; 5.6)
Min ; Max	2.4 ; 8.2	2.5 ; 8.6	2.0 ; 8.6	2.4 ; 9.3
Week 52				
N(%)	55 (96.5)	51 (86.4)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	4.5 (24.5)	4.7 (25.8)	4.4 (24.3)	4.6 (26.0)
Mean (SD)	4.6 (1.1)	4.8 (1.2)	4.6 (1.0)	4.7 (1.2)
Median (IQR)	4.6 (3.8; 5.3)	4.9 (4.0; 5.6)	4.4 (4.0; 4.9)	4.6 (3.8; 5.4)
Min ; Max	2.3 ; 7.1	2.6 ; 8.6	1.9 ; 8.0	2.5 ; 8.5
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	4.5 (26.0)	4.8 (21.5)	4.4 (22.7)	4.6 (26.5)
Mean (SD)	4.7 (1.2)	4.9 (1.0)	4.5 (0.9)	4.7 (1.3)
Median (IQR)	4.5 (3.8; 5.3)	4.7 (4.1; 5.4)	4.3 (3.9; 5.2)	4.6 (3.8; 5.4)
Min ; Max	2.4 ; 7.9	2.8 ; 7.6	2.2 ; 6.7	2.4 ; 9.7
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	4.5 (26.2)	4.7 (21.5)	4.4 (23.1)	4.6 (25.3)
Mean (SD)	4.7 (1.2)	4.9 (1.0)	4.5 (1.0)	4.8 (1.2)
Median (IQR)	4.6 (3.9; 5.3)	4.7 (4.1; 5.6)	4.3 (3.9; 5.2)	4.7 (4.0; 5.4)
Min ; Max	2.4 ; 7.9	2.8 ; 7.0	2.2 ; 6.7	2.9 ; 9.7

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Combined LDL cholesterol (mg/dL)				
Week 0 (Randomisation)				
N(%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	100.61 (41.6)	101.77 (43.5)	104.52 (37.5)	106.24 (38.9)
Mean (SD)	108.40 (41.91)	109.58 (38.34)	110.92 (37.43)	113.03 (37.55)
Median (IQR)	103.47 (82.63;133.98)	109.27 (79.54;137.07)	108.88 (87.45;133.78)	112.93 (86.10;139.77)
Min ; Max	38.61 ; 256.37	25.10 ; 181.85	27.80 ; 239.38	28.19 ; 234.36
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	57 (98.3)
Geom. Mean (CV)	91.39 (48.7)	93.44 (62.6)	93.78 (36.4)	105.00 (38.2)
Mean (SD)	100.49 (41.61)	103.56 (36.34)	99.15 (31.50)	111.53 (36.42)
Median (IQR)	93.82 (69.50;130.12)	105.02 (85.71;123.55)	97.68 (75.29;118.15)	113.90 (87.26;131.66)
Min ; Max	28.19 ; 213.13	3.86 ; 182.63	31.27 ; 193.44	35.52 ; 216.22
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	95.14 (40.4)	90.34 (50.4)	89.80 (43.7)	103.35 (43.1)
Mean (SD)	101.95 (36.98)	99.00 (37.61)	96.71 (35.45)	111.31 (39.85)
Median (IQR)	100.77 (72.20;124.32)	100.39 (73.75;118.15)	92.08 (74.90;114.29)	111.97 (79.92;135.52)
Min ; Max	33.20 ; 222.39	13.90 ; 186.49	16.60 ; 230.50	31.66 ; 223.55

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	53 (93.0)	52 (88.1)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	97.61 (41.9)	97.83 (43.6)	96.41 (36.0)	100.88 (45.6)
Mean (SD)	105.31 (41.11)	106.05 (42.17)	102.04 (34.68)	109.38 (41.00)
Median (IQR)	98.84 (79.54;132.05)	96.72 (78.38;135.14)	99.61 (79.73;118.73)	110.42 (81.08;135.14)
Min ; Max	41.70 ; 244.79	34.36 ; 243.63	28.19 ; 225.10	23.94 ; 250.97
Week 52				
N(%)	55 (96.5)	51 (86.4)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	94.40 (41.4)	98.38 (44.0)	96.45 (37.0)	93.64 (47.8)
Mean (SD)	101.33 (36.32)	106.15 (39.72)	102.06 (33.03)	102.18 (39.37)
Median (IQR)	100.39 (79.54;123.17)	103.09 (83.40;124.71)	96.33 (84.36;113.51)	102.70 (70.27;128.96)
Min ; Max	32.82 ; 199.23	21.62 ; 236.29	28.96 ; 206.56	19.31 ; 213.90
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	96.52 (41.1)	101.41 (37.8)	97.15 (33.0)	94.81 (42.3)
Mean (SD)	103.45 (36.37)	107.90 (37.31)	101.86 (30.52)	102.23 (39.14)
Median (IQR)	99.61 (78.38;124.71)	102.70 (79.15;136.29)	97.30 (81.47;116.22)	102.32 (83.40;123.17)
Min ; Max	28.57 ; 177.61	37.45 ; 197.68	32.43 ; 174.52	30.50 ; 257.91
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	97.78 (41.3)	100.41 (39.2)	97.24 (33.3)	97.91 (39.4)
Mean (SD)	104.76 (36.40)	107.24 (37.84)	102.02 (30.70)	104.71 (38.41)
Median (IQR)	101.16 (79.92;124.71)	100.97 (78.76;138.61)	97.49 (81.47;116.22)	105.02 (86.10;123.36)
Min ; Max	28.57 ; 177.61	37.45 ; 197.68	32.43 ; 174.52	44.79 ; 257.91

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Combined LDL cholesterol (mmol/L)				
Week 0 (Randomisation)				
N(%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	2.61 (41.6)	2.64 (43.5)	2.71 (37.5)	2.75 (38.9)
Mean (SD)	2.81 (1.09)	2.84 (0.99)	2.87 (0.97)	2.93 (0.97)
Median (IQR)	2.68 (2.14; 3.47)	2.83 (2.06; 3.55)	2.82 (2.27; 3.47)	2.93 (2.23; 3.62)
Min ; Max	1.00 ; 6.64	0.65 ; 4.71	0.72 ; 6.20	0.73 ; 6.07
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	57 (98.3)
Geom. Mean (CV)	2.37 (48.7)	2.42 (62.6)	2.43 (36.4)	2.72 (38.2)
Mean (SD)	2.60 (1.08)	2.68 (0.94)	2.57 (0.82)	2.89 (0.94)
Median (IQR)	2.43 (1.80; 3.37)	2.72 (2.22; 3.20)	2.53 (1.95; 3.06)	2.95 (2.26; 3.41)
Min ; Max	0.73 ; 5.52	0.10 ; 4.73	0.81 ; 5.01	0.92 ; 5.60
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	2.46 (40.4)	2.34 (50.4)	2.33 (43.7)	2.68 (43.1)
Mean (SD)	2.64 (0.96)	2.56 (0.97)	2.50 (0.92)	2.88 (1.03)
Median (IQR)	2.61 (1.87; 3.22)	2.60 (1.91; 3.06)	2.39 (1.94; 2.96)	2.90 (2.07; 3.51)
Min ; Max	0.86 ; 5.76	0.36 ; 4.83	0.43 ; 5.97	0.82 ; 5.79

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	53 (93.0)	52 (88.1)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	2.53 (41.9)	2.53 (43.6)	2.50 (36.0)	2.61 (45.6)
Mean (SD)	2.73 (1.06)	2.75 (1.09)	2.64 (0.90)	2.83 (1.06)
Median (IQR)	2.56 (2.06; 3.42)	2.51 (2.03; 3.50)	2.58 (2.07; 3.08)	2.86 (2.10; 3.50)
Min ; Max	1.08 ; 6.34	0.89 ; 6.31	0.73 ; 5.83	0.62 ; 6.50
Week 52				
N(%)	55 (96.5)	51 (86.4)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	2.44 (41.4)	2.55 (44.0)	2.50 (37.0)	2.43 (47.8)
Mean (SD)	2.62 (0.94)	2.75 (1.03)	2.64 (0.86)	2.65 (1.02)
Median (IQR)	2.60 (2.06; 3.19)	2.67 (2.16; 3.23)	2.50 (2.19; 2.94)	2.66 (1.82; 3.34)
Min ; Max	0.85 ; 5.16	0.56 ; 6.12	0.75 ; 5.35	0.50 ; 5.54
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	2.50 (41.1)	2.63 (37.8)	2.52 (33.0)	2.46 (42.3)
Mean (SD)	2.68 (0.94)	2.79 (0.97)	2.64 (0.79)	2.65 (1.01)
Median (IQR)	2.58 (2.03; 3.23)	2.66 (2.05; 3.53)	2.52 (2.11; 3.01)	2.65 (2.16; 3.19)
Min ; Max	0.74 ; 4.60	0.97 ; 5.12	0.84 ; 4.52	0.79 ; 6.68
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	2.53 (41.3)	2.60 (39.2)	2.52 (33.3)	2.54 (39.4)
Mean (SD)	2.71 (0.94)	2.78 (0.98)	2.64 (0.80)	2.71 (0.99)
Median (IQR)	2.62 (2.07; 3.23)	2.62 (2.04; 3.59)	2.53 (2.11; 3.01)	2.72 (2.23; 3.20)
Min ; Max	0.74 ; 4.60	0.97 ; 5.12	0.84 ; 4.52	1.16 ; 6.68

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
HDL Cholesterol (mg/dL)				
Week 0 (Randomisation)				
N(%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	43.61 (26.3)	45.76 (22.6)	42.75 (23.1)	43.77 (25.1)
Mean (SD)	45.08 (11.97)	46.89 (10.60)	43.90 (10.85)	45.13 (11.55)
Median (IQR)	43.24 (36.29;54.44)	43.63 (40.15;53.67)	42.86 (37.45;48.46)	41.51 (35.91;52.12)
Min ; Max	23.55 ; 83.78	26.25 ; 69.88	28.19 ; 88.42	27.80 ; 72.59
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	57 (98.3)
Geom. Mean (CV)	42.18 (24.6)	43.91 (24.0)	41.43 (22.1)	44.47 (24.4)
Mean (SD)	43.47 (11.47)	45.08 (10.12)	42.44 (9.79)	45.77 (11.32)
Median (IQR)	40.93 (35.91;49.42)	43.24 (39.77;50.97)	40.93 (35.52;47.88)	41.70 (36.29;53.28)
Min ; Max	25.87 ; 93.44	18.92 ; 72.20	26.64 ; 79.92	28.57 ; 73.36
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	42.29 (23.3)	43.40 (21.6)	41.83 (22.7)	46.43 (21.8)
Mean (SD)	43.43 (10.45)	44.35 (9.21)	42.86 (9.48)	47.54 (10.98)
Median (IQR)	42.08 (36.68;49.03)	43.63 (38.61;47.88)	41.31 (36.68;49.42)	45.17 (39.38;52.12)
Min ; Max	23.17 ; 81.08	20.85 ; 73.36	20.85 ; 69.88	33.20 ; 81.08

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	53 (93.0)	52 (88.1)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	43.93 (25.5)	46.02 (24.6)	42.88 (24.1)	44.40 (26.6)
Mean (SD)	45.36 (12.21)	47.36 (11.49)	44.05 (10.14)	45.91 (11.99)
Median (IQR)	43.24 (37.45;50.19)	43.82 (38.42;57.34)	44.21 (36.10;50.77)	45.56 (37.07;52.90)
Min ; Max	23.17 ; 85.71	25.48 ; 77.99	23.17 ; 72.20	26.25 ; 77.22
Week 52				
N(%)	55 (96.5)	51 (86.4)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	45.64 (25.5)	48.24 (23.6)	47.84 (23.5)	45.43 (27.1)
Mean (SD)	47.11 (12.48)	49.55 (11.79)	49.09 (11.04)	47.05 (12.79)
Median (IQR)	46.72 (37.45;52.90)	46.72 (41.31;57.53)	50.39 (40.93;56.95)	44.79 (36.29;56.37)
Min ; Max	25.87 ; 84.56	30.50 ; 76.06	28.19 ; 79.54	26.64 ; 80.31
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	44.84 (27.1)	47.21 (23.9)	46.58 (24.1)	44.37 (21.7)
Mean (SD)	46.49 (13.24)	48.52 (11.61)	47.88 (11.36)	45.40 (10.12)
Median (IQR)	42.86 (36.29;53.28)	45.56 (40.15;56.37)	47.10 (37.84;54.05)	44.02 (38.22;50.19)
Min ; Max	25.48 ; 86.49	27.03 ; 74.52	27.41 ; 82.63	30.12 ; 76.06
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	44.78 (27.5)	47.65 (24.0)	46.51 (24.4)	44.17 (22.1)
Mean (SD)	46.48 (13.43)	48.95 (11.47)	47.85 (11.55)	45.24 (10.35)
Median (IQR)	42.86 (36.29;53.28)	47.30 (40.93;57.92)	47.10 (36.68;54.05)	43.63 (38.03;50.00)
Min ; Max	25.48 ; 86.49	27.03 ; 73.75	27.41 ; 82.63	30.12 ; 76.06

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
HDL Cholesterol (mmol/L)				
Week 0 (Randomisation)				
N(%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	1.13 (26.3)	1.19 (22.6)	1.11 (23.1)	1.13 (25.1)
Mean (SD)	1.17 (0.31)	1.21 (0.27)	1.14 (0.28)	1.17 (0.30)
Median (IQR)	1.12 (0.94; 1.41)	1.13 (1.04; 1.39)	1.11 (0.97; 1.26)	1.08 (0.93; 1.35)
Min ; Max	0.61 ; 2.17	0.68 ; 1.81	0.73 ; 2.29	0.72 ; 1.88
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	57 (98.3)
Geom. Mean (CV)	1.09 (24.6)	1.14 (24.0)	1.07 (22.1)	1.15 (24.4)
Mean (SD)	1.13 (0.30)	1.17 (0.26)	1.10 (0.25)	1.19 (0.29)
Median (IQR)	1.06 (0.93; 1.28)	1.12 (1.03; 1.32)	1.06 (0.92; 1.24)	1.08 (0.94; 1.38)
Min ; Max	0.67 ; 2.42	0.49 ; 1.87	0.69 ; 2.07	0.74 ; 1.90
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	1.10 (23.3)	1.12 (21.6)	1.08 (22.7)	1.20 (21.8)
Mean (SD)	1.12 (0.27)	1.15 (0.24)	1.11 (0.25)	1.23 (0.28)
Median (IQR)	1.09 (0.95; 1.27)	1.13 (1.00; 1.24)	1.07 (0.95; 1.28)	1.17 (1.02; 1.35)
Min ; Max	0.60 ; 2.10	0.54 ; 1.90	0.54 ; 1.81	0.86 ; 2.10

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	53 (93.0)	52 (88.1)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	1.14 (25.5)	1.19 (24.6)	1.11 (24.1)	1.15 (26.6)
Mean (SD)	1.17 (0.32)	1.23 (0.30)	1.14 (0.26)	1.19 (0.31)
Median (IQR)	1.12 (0.97; 1.30)	1.14 (1.00; 1.48)	1.15 (0.94; 1.32)	1.18 (0.96; 1.37)
Min ; Max	0.60 ; 2.22	0.66 ; 2.02	0.60 ; 1.87	0.68 ; 2.00
Week 52				
N(%)	55 (96.5)	51 (86.4)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	1.18 (25.5)	1.25 (23.6)	1.24 (23.5)	1.18 (27.1)
Mean (SD)	1.22 (0.32)	1.28 (0.31)	1.27 (0.29)	1.22 (0.33)
Median (IQR)	1.21 (0.97; 1.37)	1.21 (1.07; 1.49)	1.31 (1.06; 1.48)	1.16 (0.94; 1.46)
Min ; Max	0.67 ; 2.19	0.79 ; 1.97	0.73 ; 2.06	0.69 ; 2.08
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	1.16 (27.1)	1.22 (23.9)	1.21 (24.1)	1.15 (21.7)
Mean (SD)	1.20 (0.34)	1.26 (0.30)	1.24 (0.29)	1.18 (0.26)
Median (IQR)	1.11 (0.94; 1.38)	1.18 (1.04; 1.46)	1.22 (0.98; 1.40)	1.14 (0.99; 1.30)
Min ; Max	0.66 ; 2.24	0.70 ; 1.93	0.71 ; 2.14	0.78 ; 1.97
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	1.16 (27.5)	1.23 (24.0)	1.20 (24.4)	1.14 (22.1)
Mean (SD)	1.20 (0.35)	1.27 (0.30)	1.24 (0.30)	1.17 (0.27)
Median (IQR)	1.11 (0.94; 1.38)	1.23 (1.06; 1.50)	1.22 (0.95; 1.40)	1.13 (0.99; 1.30)
Min ; Max	0.66 ; 2.24	0.70 ; 1.91	0.71 ; 2.14	0.78 ; 1.97

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
VLDL Cholesterol (mg/dL)				
Week 0 (Randomisation)				
N(%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	30.17 (41.1)	31.40 (42.4)	28.62 (47.0)	32.84 (50.8)
Mean (SD)	32.64 (13.71)	34.17 (15.06)	31.91 (17.35)	36.35 (15.76)
Median (IQR)	29.34 (22.39; 40.15)	28.96 (23.17; 41.70)	28.38 (19.69; 35.14)	34.94 (26.25; 42.08)
Min ; Max	13.90 ; 74.13	13.51 ; 79.15	11.97 ; 104.63	6.56 ; 73.75
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	57 (98.3)
Geom. Mean (CV)	28.57 (40.1)	28.14 (41.4)	24.95 (45.9)	31.25 (44.2)
Mean (SD)	30.81 (12.58)	30.68 (14.66)	27.59 (13.82)	34.05 (14.76)
Median (IQR)	28.19 (20.85; 38.61)	26.25 (21.62; 33.59)	25.48 (18.15; 31.66)	29.73 (25.48; 39.00)
Min ; Max	13.90 ; 66.02	13.90 ; 82.24	11.97 ; 73.75	7.34 ; 76.45
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	28.65 (43.1)	28.66 (46.4)	23.67 (49.0)	29.73 (44.9)
Mean (SD)	31.17 (13.35)	31.84 (17.18)	26.47 (13.92)	32.68 (15.45)
Median (IQR)	27.41 (21.24; 37.07)	26.64 (21.62; 38.22)	22.59 (18.15; 28.96)	28.19 (22.01; 36.68)
Min ; Max	12.36 ; 70.66	10.81 ; 111.97	9.27 ; 71.81	10.42 ; 76.83

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	53 (93.0)	52 (88.1)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	30.13 (46.3)	26.11 (42.7)	23.35 (46.8)	29.98 (51.1)
Mean (SD)	33.24 (15.68)	28.47 (13.09)	25.99 (13.94)	33.46 (16.15)
Median (IQR)	27.80 (22.39; 42.08)	25.87 (19.11; 32.24)	22.20 (17.18; 28.38)	29.73 (23.17; 38.61)
Min ; Max	13.51 ; 76.45	10.42 ; 70.66	9.65 ; 72.59	6.18 ; 77.22
Week 52				
N(%)	55 (96.5)	51 (86.4)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	27.94 (44.1)	27.32 (50.1)	22.43 (51.2)	29.62 (43.0)
Mean (SD)	30.35 (12.19)	30.69 (16.18)	25.53 (15.16)	32.35 (15.27)
Median (IQR)	28.19 (22.01; 37.45)	25.48 (18.53; 35.52)	19.69 (16.60; 26.45)	28.19 (24.32; 37.84)
Min ; Max	8.49 ; 59.07	10.42 ; 76.45	9.65 ; 75.68	12.36 ; 101.16
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	27.07 (45.8)	28.52 (49.5)	20.88 (49.6)	30.91 (48.3)
Mean (SD)	29.83 (14.32)	31.94 (16.67)	23.41 (12.38)	34.12 (15.56)
Median (IQR)	25.48 (20.46; 36.68)	27.03 (20.46; 36.68)	20.08 (13.90; 28.19)	30.50 (23.55; 40.15)
Min ; Max	10.42 ; 81.85	11.58 ; 76.45	8.11 ; 61.39	6.56 ; 78.38
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	27.05 (46.4)	27.75 (49.5)	20.84 (50.6)	31.50 (48.1)
Mean (SD)	29.88 (14.50)	31.06 (16.25)	23.46 (12.65)	34.73 (15.68)
Median (IQR)	25.48 (20.46; 35.91)	27.80 (20.08; 36.68)	20.08 (13.90; 28.19)	30.69 (24.52; 41.70)
Min ; Max	10.42 ; 81.85	11.58 ; 76.45	8.11 ; 61.39	6.56 ; 78.38

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
VLDL Cholesterol (mmol/L)				
Week 0 (Randomisation)				
N(%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	0.78 (41.1)	0.81 (42.4)	0.74 (47.0)	0.85 (50.8)
Mean (SD)	0.85 (0.36)	0.89 (0.39)	0.83 (0.45)	0.94 (0.41)
Median (IQR)	0.76 (0.58; 1.04)	0.75 (0.60; 1.08)	0.74 (0.51; 0.91)	0.91 (0.68; 1.09)
Min ; Max	0.36 ; 1.92	0.35 ; 2.05	0.31 ; 2.71	0.17 ; 1.91
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	57 (98.3)
Geom. Mean (CV)	0.74 (40.1)	0.73 (41.4)	0.65 (45.9)	0.81 (44.2)
Mean (SD)	0.80 (0.33)	0.79 (0.38)	0.71 (0.36)	0.88 (0.38)
Median (IQR)	0.73 (0.54; 1.00)	0.68 (0.56; 0.87)	0.66 (0.47; 0.82)	0.77 (0.66; 1.01)
Min ; Max	0.36 ; 1.71	0.36 ; 2.13	0.31 ; 1.91	0.19 ; 1.98
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	0.74 (43.1)	0.74 (46.4)	0.61 (49.0)	0.77 (44.9)
Mean (SD)	0.81 (0.35)	0.82 (0.44)	0.69 (0.36)	0.85 (0.40)
Median (IQR)	0.71 (0.55; 0.96)	0.69 (0.56; 0.99)	0.59 (0.47; 0.75)	0.73 (0.57; 0.95)
Min ; Max	0.32 ; 1.83	0.28 ; 2.90	0.24 ; 1.86	0.27 ; 1.99

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	53 (93.0)	52 (88.1)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	0.78 (46.3)	0.68 (42.7)	0.60 (46.8)	0.78 (51.1)
Mean (SD)	0.86 (0.41)	0.74 (0.34)	0.67 (0.36)	0.87 (0.42)
Median (IQR)	0.72 (0.58; 1.09)	0.67 (0.50; 0.84)	0.58 (0.45; 0.74)	0.77 (0.60; 1.00)
Min ; Max	0.35 ; 1.98	0.27 ; 1.83	0.25 ; 1.88	0.16 ; 2.00
Week 52				
N(%)	55 (96.5)	51 (86.4)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	0.72 (44.1)	0.71 (50.1)	0.58 (51.2)	0.77 (43.0)
Mean (SD)	0.79 (0.32)	0.79 (0.42)	0.66 (0.39)	0.84 (0.40)
Median (IQR)	0.73 (0.57; 0.97)	0.66 (0.48; 0.92)	0.51 (0.43; 0.69)	0.73 (0.63; 0.98)
Min ; Max	0.22 ; 1.53	0.27 ; 1.98	0.25 ; 1.96	0.32 ; 2.62
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	0.70 (45.8)	0.74 (49.5)	0.54 (49.6)	0.80 (48.3)
Mean (SD)	0.77 (0.37)	0.83 (0.43)	0.61 (0.32)	0.88 (0.40)
Median (IQR)	0.66 (0.53; 0.95)	0.70 (0.53; 0.95)	0.52 (0.36; 0.73)	0.79 (0.61; 1.04)
Min ; Max	0.27 ; 2.12	0.30 ; 1.98	0.21 ; 1.59	0.17 ; 2.03
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	0.70 (46.4)	0.72 (49.5)	0.54 (50.6)	0.82 (48.1)
Mean (SD)	0.77 (0.38)	0.80 (0.42)	0.61 (0.33)	0.90 (0.41)
Median (IQR)	0.66 (0.53; 0.93)	0.72 (0.52; 0.95)	0.52 (0.36; 0.73)	0.80 (0.64; 1.08)
Min ; Max	0.27 ; 2.12	0.30 ; 1.98	0.21 ; 1.59	0.17 ; 2.03

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Triglycerides (mg/dL)				
Week 0 (Randomisation)				
N(%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	155.6 (43.3)	162.9 (46.2)	148.1 (50.9)	168.8 (51.5)
Mean (SD)	170.2 (79.1)	180.8 (94.6)	169.5 (113.4)	187.5 (84.5)
Median (IQR)	150.4 (114.8; 204.7)	148.6 (118.4; 213.6)	146.0 (100.6; 179.8)	178.9 (134.4; 216.3)
Min ; Max	71.2 ; 424.5	68.5 ; 506.4	61.4 ; 729.8	33.8 ; 454.8
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	57 (98.3)
Geom. Mean (CV)	146.2 (40.2)	145.8 (45.5)	129.1 (49.1)	160.7 (45.2)
Mean (SD)	157.6 (64.4)	162.7 (95.1)	145.6 (87.1)	176.1 (81.6)
Median (IQR)	143.3 (105.9; 198.5)	134.4 (110.4; 171.8)	130.8 (92.6; 162.9)	152.2 (130.8; 199.4)
Min ; Max	71.2 ; 337.3	70.3 ; 581.2	60.5 ; 553.6	38.3 ; 488.6
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	146.6 (43.1)	149.2 (51.5)	121.2 (49.0)	152.1 (44.9)
Mean (SD)	159.4 (68.2)	171.5 (120.7)	135.6 (71.3)	167.2 (79.1)
Median (IQR)	140.6 (109.5; 189.6)	136.2 (110.4; 195.8)	116.1 (92.6; 148.6)	143.3 (112.1; 188.7)
Min ; Max	62.3 ; 362.2	55.2 ; 839.3	47.2 ; 367.6	54.3 ; 392.5

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	53 (93.0)	52 (88.1)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	154.7 (47.0)	136.3 (47.8)	120.3 (49.6)	154.4 (52.0)
Mean (SD)	171.3 (83.4)	152.9 (87.9)	136.4 (85.8)	173.3 (87.7)
Median (IQR)	142.4 (113.9; 214.5)	132.2 (97.5; 164.7)	113.0 (88.1; 146.0)	153.1 (119.3; 196.7)
Min ; Max	68.5 ; 429.0	54.3 ; 474.4	49.0 ; 548.2	32.0 ; 414.7
Week 52				
N(%)	55 (96.5)	51 (86.4)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	145.3 (47.6)	141.5 (53.3)	114.8 (51.3)	156.7 (52.0)
Mean (SD)	160.7 (77.0)	161.8 (96.0)	130.7 (77.8)	180.9 (132.5)
Median (IQR)	143.3 (112.1; 191.4)	129.9 (95.2; 182.5)	101.0 (85.0; 135.7)	143.3 (123.7; 194.0)
Min ; Max	43.6 ; 421.9	52.5 ; 499.3	49.8 ; 388.0	63.2 ; 936.3
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	138.7 (46.6)	148.9 (54.1)	107.5 (51.4)	159.4 (49.5)
Mean (SD)	153.6 (77.7)	171.2 (104.8)	121.9 (71.2)	177.1 (84.8)
Median (IQR)	130.8 (104.1; 186.9)	138.8 (105.0; 187.8)	103.2 (72.1; 143.3)	156.6 (121.0; 205.6)
Min ; Max	52.5 ; 479.7	59.6 ; 497.5	40.9 ; 424.5	33.8 ; 421.9
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	138.7 (47.2)	145.4 (54.9)	107.3 (52.5)	162.5 (49.3)
Mean (SD)	153.9 (78.7)	167.9 (106.2)	122.3 (72.8)	180.3 (85.6)
Median (IQR)	130.8 (104.1; 183.3)	142.8 (103.2; 187.8)	102.8 (71.2; 143.3)	157.5 (125.0; 213.2)
Min ; Max	52.5 ; 479.7	59.6 ; 497.5	40.9 ; 424.5	33.8 ; 421.9

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Triglycerides (mmol/L)				
Week 0 (Randomisation)				
N(%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	1.7 (43.3)	1.8 (46.2)	1.7 (50.9)	1.9 (51.5)
Mean (SD)	1.9 (0.9)	2.0 (1.1)	1.9 (1.3)	2.1 (0.9)
Median (IQR)	1.7 (1.3; 2.3)	1.7 (1.3; 2.4)	1.6 (1.1; 2.0)	2.0 (1.5; 2.4)
Min ; Max	0.8 ; 4.8	0.8 ; 5.7	0.7 ; 8.2	0.4 ; 5.1
Week 4				
N(%)	57 (100.0)	57 (96.6)	55 (98.2)	57 (98.3)
Geom. Mean (CV)	1.6 (40.2)	1.6 (45.5)	1.5 (49.1)	1.8 (45.2)
Mean (SD)	1.8 (0.7)	1.8 (1.1)	1.6 (1.0)	2.0 (0.9)
Median (IQR)	1.6 (1.2; 2.2)	1.5 (1.2; 1.9)	1.5 (1.0; 1.8)	1.7 (1.5; 2.2)
Min ; Max	0.8 ; 3.8	0.8 ; 6.5	0.7 ; 6.2	0.4 ; 5.5
Week 12				
N(%)	55 (96.5)	57 (96.6)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	1.6 (43.1)	1.7 (51.5)	1.4 (49.0)	1.7 (44.9)
Mean (SD)	1.8 (0.8)	1.9 (1.4)	1.5 (0.8)	1.9 (0.9)
Median (IQR)	1.6 (1.2; 2.1)	1.5 (1.2; 2.2)	1.3 (1.0; 1.7)	1.6 (1.3; 2.1)
Min ; Max	0.7 ; 4.1	0.6 ; 9.4	0.5 ; 4.1	0.6 ; 4.4

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	53 (93.0)	52 (88.1)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	1.7 (47.0)	1.5 (47.8)	1.4 (49.6)	1.7 (52.0)
Mean (SD)	1.9 (0.9)	1.7 (1.0)	1.5 (1.0)	1.9 (1.0)
Median (IQR)	1.6 (1.3; 2.4)	1.5 (1.1; 1.9)	1.3 (1.0; 1.6)	1.7 (1.3; 2.2)
Min ; Max	0.8 ; 4.8	0.6 ; 5.3	0.6 ; 6.2	0.4 ; 4.7
Week 52				
N(%)	55 (96.5)	51 (86.4)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	1.6 (47.6)	1.6 (53.3)	1.3 (51.3)	1.8 (52.0)
Mean (SD)	1.8 (0.9)	1.8 (1.1)	1.5 (0.9)	2.0 (1.5)
Median (IQR)	1.6 (1.3; 2.2)	1.5 (1.1; 2.1)	1.1 (1.0; 1.5)	1.6 (1.4; 2.2)
Min ; Max	0.5 ; 4.7	0.6 ; 5.6	0.6 ; 4.4	0.7 ; 10.5
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	1.6 (46.6)	1.7 (54.1)	1.2 (51.4)	1.8 (49.5)
Mean (SD)	1.7 (0.9)	1.9 (1.2)	1.4 (0.8)	2.0 (1.0)
Median (IQR)	1.5 (1.2; 2.1)	1.6 (1.2; 2.1)	1.2 (0.8; 1.6)	1.8 (1.4; 2.3)
Min ; Max	0.6 ; 5.4	0.7 ; 5.6	0.5 ; 4.8	0.4 ; 4.7
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	1.6 (47.2)	1.6 (54.9)	1.2 (52.5)	1.8 (49.3)
Mean (SD)	1.7 (0.9)	1.9 (1.2)	1.4 (0.8)	2.0 (1.0)
Median (IQR)	1.5 (1.2; 2.1)	1.6 (1.2; 2.1)	1.2 (0.8; 1.6)	1.8 (1.4; 2.4)
Min ; Max	0.6 ; 5.4	0.7 ; 5.6	0.5 ; 4.8	0.4 ; 4.7

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Free Fatty Acids (mg/dL)				
Week 0 (Randomisation)				
N(%)	54 (94.7)	57 (96.6)	54 (96.4)	56 (96.6)
Geom. Mean (CV)	17.90 (41.0)	16.76 (55.3)	15.50 (38.8)	12.52 (62.7)
Mean (SD)	19.30 (7.68)	19.05 (10.25)	16.55 (5.88)	14.57 (7.92)
Median (IQR)	17.63 (14.38;24.25)	17.77 (12.41;22.00)	14.95 (12.97;20.02)	12.69 (8.32;19.88)
Min ; Max	8.18 ; 45.40	4.79 ; 56.68	5.92 ; 32.43	2.54 ; 39.48
Week 4				
N(%)	54 (94.7)	57 (96.6)	55 (98.2)	57 (98.3)
Geom. Mean (CV)	15.99 (39.9)	16.05 (41.4)	15.74 (49.3)	13.68 (50.4)
Mean (SD)	17.11 (6.25)	17.37 (7.33)	17.58 (9.28)	15.07 (6.08)
Median (IQR)	16.36 (13.25;19.74)	16.07 (13.25;20.87)	14.95 (11.28;21.43)	14.95 (11.28;19.18)
Min ; Max	4.23 ; 38.63	7.33 ; 45.68	4.23 ; 60.07	3.38 ; 29.33
Week 12				
N(%)	54 (94.7)	57 (96.6)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	13.59 (48.4)	15.57 (50.5)	14.95 (42.4)	13.40 (55.3)
Mean (SD)	14.99 (6.66)	17.26 (7.62)	16.22 (7.07)	15.02 (6.78)
Median (IQR)	13.82 (10.72;18.33)	16.92 (11.28;22.00)	14.95 (11.70;20.45)	14.10 (10.15;20.59)
Min ; Max	3.67 ; 34.97	3.67 ; 37.22	6.49 ; 48.50	1.97 ; 33.56

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	53 (93.0)	52 (88.1)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	13.52 (60.1)	14.37 (61.2)	15.14 (55.3)	13.64 (59.3)
Mean (SD)	15.35 (7.18)	16.15 (7.00)	17.03 (8.50)	15.75 (8.99)
Median (IQR)	14.38 (11.28;20.02)	16.50 (11.00;19.74)	16.22 (11.42;20.30)	15.51 (9.02;19.18)
Min ; Max	2.26 ; 37.22	0.99 ; 37.79	2.54 ; 53.02	3.95 ; 57.81
N<LLOQ ; N>ULOQ		1 ; 0		
Week 52				
N(%)	55 (96.5)	49 (83.1)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	13.91 (50.4)	15.47 (37.1)	12.13 (57.4)	15.25 (52.7)
Mean (SD)	15.38 (6.68)	16.49 (6.20)	13.74 (6.44)	17.05 (7.90)
Median (IQR)	14.38 (10.43;18.89)	14.66 (12.13;20.59)	13.25 (8.74;18.05)	15.79 (10.72;23.97)
Min ; Max	3.10 ; 35.53	7.61 ; 35.53	3.38 ; 27.07	3.38 ; 40.33
Week 72 (EOT)				
N(%)	53 (93.0)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	14.92 (49.9)	16.16 (47.7)	10.55 (74.8)	13.36 (76.5)
Mean (SD)	16.48 (7.10)	17.93 (8.87)	12.56 (7.33)	15.94 (8.24)
Median (IQR)	16.07 (11.28;19.46)	16.36 (11.00;21.15)	11.28 (7.90;15.23)	14.38 (9.59;22.28)
Min ; Max	4.51 ; 35.25	6.20 ; 51.89	0.99 ; 45.97	0.99 ; 32.43
N<LLOQ ; N>ULOQ			2 ; 0	1 ; 0
Week 72 (EOT) (on-treatment)				
N(%)	51 (89.5)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	14.75 (50.5)	16.54 (42.4)	10.38 (72.2)	13.99 (64.2)
Mean (SD)	16.33 (7.19)	17.96 (7.58)	12.08 (5.73)	16.22 (8.10)
Median (IQR)	16.07 (10.15;19.46)	17.06 (11.56;21.71)	11.28 (7.90;15.23)	15.51 (9.59;22.28)
Min ; Max	4.51 ; 35.25	7.33 ; 37.22	0.99 ; 26.23	2.54 ; 32.43
N<LLOQ ; N>ULOQ			2 ; 0	

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Free Fatty Acids (mmol/L)				
Week 0 (Randomisation)				
N(%)	54 (94.7)	57 (96.6)	54 (96.4)	56 (96.6)
Geom. Mean (CV)	0.63 (41.0)	0.59 (55.3)	0.55 (38.8)	0.44 (62.7)
Mean (SD)	0.68 (0.27)	0.68 (0.36)	0.59 (0.21)	0.52 (0.28)
Median (IQR)	0.63 (0.51; 0.86)	0.63 (0.44; 0.78)	0.53 (0.46; 0.71)	0.45 (0.30; 0.71)
Min ; Max	0.29 ; 1.61	0.17 ; 2.01	0.21 ; 1.15	0.09 ; 1.40
Week 4				
N(%)	54 (94.7)	57 (96.6)	55 (98.2)	57 (98.3)
Geom. Mean (CV)	0.57 (39.9)	0.57 (41.4)	0.56 (49.3)	0.49 (50.4)
Mean (SD)	0.61 (0.22)	0.62 (0.26)	0.62 (0.33)	0.53 (0.22)
Median (IQR)	0.58 (0.47; 0.70)	0.57 (0.47; 0.74)	0.53 (0.40; 0.76)	0.53 (0.40; 0.68)
Min ; Max	0.15 ; 1.37	0.26 ; 1.62	0.15 ; 2.13	0.12 ; 1.04
Week 12				
N(%)	54 (94.7)	57 (96.6)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	0.48 (48.4)	0.55 (50.5)	0.53 (42.4)	0.48 (55.3)
Mean (SD)	0.53 (0.24)	0.61 (0.27)	0.58 (0.25)	0.53 (0.24)
Median (IQR)	0.49 (0.38; 0.65)	0.60 (0.40; 0.78)	0.53 (0.42; 0.73)	0.50 (0.36; 0.73)
Min ; Max	0.13 ; 1.24	0.13 ; 1.32	0.23 ; 1.72	0.07 ; 1.19

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	53 (93.0)	52 (88.1)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	0.48 (60.1)	0.51 (61.2)	0.54 (55.3)	0.48 (59.3)
Mean (SD)	0.54 (0.25)	0.57 (0.25)	0.60 (0.30)	0.56 (0.32)
Median (IQR)	0.51 (0.40; 0.71)	0.59 (0.39; 0.70)	0.58 (0.41; 0.72)	0.55 (0.32; 0.68)
Min ; Max	0.08 ; 1.32	0.04 ; 1.34	0.09 ; 1.88	0.14 ; 2.05
N<LLOQ ; N>ULOQ		1 ; 0		
Week 52				
N(%)	55 (96.5)	49 (83.1)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	0.49 (50.4)	0.55 (37.1)	0.43 (57.4)	0.54 (52.7)
Mean (SD)	0.55 (0.24)	0.58 (0.22)	0.49 (0.23)	0.60 (0.28)
Median (IQR)	0.51 (0.37; 0.67)	0.52 (0.43; 0.73)	0.47 (0.31; 0.64)	0.56 (0.38; 0.85)
Min ; Max	0.11 ; 1.26	0.27 ; 1.26	0.12 ; 0.96	0.12 ; 1.43
Week 72 (EOT)				
N(%)	53 (93.0)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	0.53 (49.9)	0.57 (47.7)	0.37 (74.8)	0.47 (76.5)
Mean (SD)	0.58 (0.25)	0.64 (0.31)	0.45 (0.26)	0.57 (0.29)
Median (IQR)	0.57 (0.40; 0.69)	0.58 (0.39; 0.75)	0.40 (0.28; 0.54)	0.51 (0.34; 0.79)
Min ; Max	0.16 ; 1.25	0.22 ; 1.84	0.04 ; 1.63	0.04 ; 1.15
N<LLOQ ; N>ULOQ			2 ; 0	1 ; 0
Week 72 (EOT) (on-treatment)				
N(%)	51 (89.5)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	0.52 (50.5)	0.59 (42.4)	0.37 (72.2)	0.50 (64.2)
Mean (SD)	0.58 (0.25)	0.64 (0.27)	0.43 (0.20)	0.58 (0.29)
Median (IQR)	0.57 (0.36; 0.69)	0.61 (0.41; 0.77)	0.40 (0.28; 0.54)	0.55 (0.34; 0.79)
Min ; Max	0.16 ; 1.25	0.26 ; 1.32	0.04 ; 0.93	0.09 ; 1.15
N<LLOQ ; N>ULOQ			2 ; 0	

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

6.2.59 Lipids - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Number of subjects	57	59	56	58
Total Cholesterol (mmol/L)				
Week 0 (Randomisation)				
N(%)	56 (98.2)	57 (96.6)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	4.7 (25.8)	4.8 (24.8)	4.7 (26.1)	4.9 (24.5)
Mean (SD)	4.8 (1.2)	4.9 (1.1)	4.8 (1.2)	5.0 (1.2)
Median (IQR)	4.8 (4.1; 5.6)	4.9 (4.0; 5.8)	4.8 (4.1; 5.5)	5.1 (4.1; 5.9)
Min ; Max	2.4 ; 8.3	2.4 ; 7.1	1.9 ; 9.3	2.3 ; 9.1
Ratio to baseline in Total Cholesterol				
Week 4				
N(%)	56 (98.2)	55 (93.2)	55 (98.2)	57 (98.3)
Geom. Mean (CV)	0.94 (11.5)	0.93 (11.2)	0.91 (13.0)	0.98 (15.5)
Mean (SD)	0.94 (0.10)	0.94 (0.11)	0.92 (0.12)	0.99 (0.14)
Median (IQR)	0.95 (0.89; 0.99)	0.93 (0.87; 1.00)	0.91 (0.86; 0.99)	0.99 (0.93; 1.05)
Min ; Max	0.59 ; 1.19	0.68 ; 1.42	0.56 ; 1.44	0.55 ; 1.39
Week 12				
N(%)	54 (94.7)	55 (93.2)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	0.95 (14.5)	0.91 (14.3)	0.89 (15.6)	0.98 (14.0)
Mean (SD)	0.96 (0.14)	0.92 (0.13)	0.90 (0.13)	0.99 (0.13)
Median (IQR)	0.95 (0.87; 1.05)	0.91 (0.85; 1.00)	0.89 (0.81; 0.98)	0.99 (0.92; 1.08)
Min ; Max	0.59 ; 1.37	0.60 ; 1.36	0.47 ; 1.25	0.63 ; 1.25

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	53 (93.0)	51 (86.4)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	0.99 (14.4)	0.94 (20.6)	0.93 (15.3)	0.96 (17.8)
Mean (SD)	1.00 (0.14)	0.96 (0.19)	0.94 (0.14)	0.98 (0.15)
Median (IQR)	0.99 (0.93; 1.05)	0.95 (0.82; 1.07)	0.93 (0.84; 1.02)	1.00 (0.92; 1.05)
Min ; Max	0.67 ; 1.39	0.50 ; 1.46	0.56 ; 1.33	0.48 ; 1.37
Week 52				
N(%)	54 (94.7)	49 (83.1)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	0.96 (16.9)	0.97 (14.8)	0.95 (12.4)	0.93 (22.1)
Mean (SD)	0.97 (0.15)	0.98 (0.15)	0.96 (0.11)	0.95 (0.19)
Median (IQR)	0.97 (0.88; 1.06)	0.96 (0.87; 1.05)	0.97 (0.88; 1.04)	0.95 (0.87; 1.07)
Min ; Max	0.54 ; 1.47	0.66 ; 1.38	0.72 ; 1.19	0.44 ; 1.45
Week 72 (EOT)				
N(%)	54 (94.7)	51 (86.4)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	0.96 (18.5)	1.00 (20.0)	0.94 (16.1)	0.93 (20.4)
Mean (SD)	0.98 (0.17)	1.02 (0.23)	0.95 (0.15)	0.95 (0.19)
Median (IQR)	0.96 (0.90; 1.06)	1.02 (0.89; 1.07)	0.95 (0.87; 1.04)	0.95 (0.87; 1.03)
Min ; Max	0.54 ; 1.59	0.61 ; 2.05	0.58 ; 1.31	0.48 ; 1.74
Week 72 (EOT) (on-treatment)				
N(%)	52 (91.2)	45 (76.3)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	0.97 (18.8)	0.98 (19.1)	0.94 (16.2)	0.93 (20.9)
Mean (SD)	0.98 (0.18)	1.00 (0.22)	0.95 (0.15)	0.95 (0.19)
Median (IQR)	0.97 (0.91; 1.07)	0.98 (0.89; 1.05)	0.94 (0.87; 1.04)	0.95 (0.87; 1.03)
Min ; Max	0.54 ; 1.59	0.61 ; 2.05	0.58 ; 1.31	0.48 ; 1.74

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Combined LDL cholesterol (mmol/L)				
Week 0 (Randomisation)				
N(%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	2.61 (41.6)	2.64 (43.5)	2.71 (37.5)	2.75 (38.9)
Mean (SD)	2.81 (1.09)	2.84 (0.99)	2.87 (0.97)	2.93 (0.97)
Median (IQR)	2.68 (2.14; 3.47)	2.83 (2.06; 3.55)	2.82 (2.27; 3.47)	2.93 (2.23; 3.62)
Min ; Max	1.00 ; 6.64	0.65 ; 4.71	0.72 ; 6.20	0.73 ; 6.07
Ratio to baseline in Combined LDL cholesterol				
Week 4				
N(%)	55 (96.5)	55 (93.2)	55 (98.2)	57 (98.3)
Geom. Mean (CV)	0.91 (18.4)	0.90 (38.1)	0.90 (18.2)	0.98 (24.4)
Mean (SD)	0.92 (0.16)	0.94 (0.22)	0.92 (0.18)	1.01 (0.21)
Median (IQR)	0.93 (0.84; 1.01)	0.93 (0.81; 1.04)	0.90 (0.81; 0.97)	1.02 (0.90; 1.12)
Min ; Max	0.47 ; 1.34	0.09 ; 1.78	0.51 ; 1.78	0.38 ; 1.54
Week 12				
N(%)	53 (93.0)	55 (93.2)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	0.94 (22.7)	0.88 (26.9)	0.86 (23.5)	0.97 (29.0)
Mean (SD)	0.96 (0.21)	0.91 (0.21)	0.88 (0.19)	1.00 (0.22)
Median (IQR)	0.95 (0.85; 1.07)	0.90 (0.82; 1.03)	0.87 (0.82; 0.99)	1.02 (0.92; 1.09)
Min ; Max	0.48 ; 1.65	0.31 ; 1.59	0.33 ; 1.48	0.29 ; 1.39

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	52 (91.2)	51 (86.4)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	0.97 (22.1)	0.96 (31.4)	0.93 (24.4)	0.94 (34.5)
Mean (SD)	0.99 (0.22)	1.00 (0.29)	0.96 (0.25)	0.99 (0.25)
Median (IQR)	0.98 (0.89; 1.09)	0.97 (0.84; 1.11)	0.92 (0.84; 1.01)	1.00 (0.88; 1.14)
Min ; Max	0.55 ; 1.64	0.35 ; 1.92	0.48 ; 1.82	0.22 ; 1.57
Week 52				
N(%)	53 (93.0)	49 (83.1)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	0.93 (26.7)	0.96 (23.1)	0.92 (18.8)	0.88 (38.3)
Mean (SD)	0.96 (0.24)	0.98 (0.23)	0.94 (0.16)	0.93 (0.27)
Median (IQR)	0.97 (0.84; 1.08)	0.92 (0.83; 1.14)	0.93 (0.86; 1.04)	0.94 (0.78; 1.14)
Min ; Max	0.39 ; 1.85	0.48 ; 1.59	0.48 ; 1.35	0.18 ; 1.61
Week 72 (EOT)				
N(%)	53 (93.0)	51 (86.4)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	0.95 (24.6)	1.00 (31.2)	0.94 (23.7)	0.90 (33.0)
Mean (SD)	0.98 (0.24)	1.06 (0.41)	0.96 (0.23)	0.94 (0.28)
Median (IQR)	0.95 (0.89; 1.05)	1.00 (0.85; 1.14)	0.97 (0.81; 1.06)	0.92 (0.81; 1.08)
Min ; Max	0.48 ; 1.88	0.44 ; 3.14	0.48 ; 1.63	0.32 ; 2.14
Week 72 (EOT) (on-treatment)				
N(%)	51 (89.5)	45 (76.3)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	0.96 (24.9)	0.97 (29.8)	0.93 (24.2)	0.90 (33.8)
Mean (SD)	0.98 (0.24)	1.02 (0.39)	0.96 (0.23)	0.94 (0.29)
Median (IQR)	0.96 (0.89; 1.06)	0.99 (0.85; 1.10)	0.97 (0.80; 1.06)	0.92 (0.81; 1.07)
Min ; Max	0.48 ; 1.88	0.44 ; 3.14	0.48 ; 1.63	0.32 ; 2.14

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
HDL Cholesterol (mmol/L)				
Week 0 (Randomisation)				
N(%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	1.13 (26.3)	1.19 (22.6)	1.11 (23.1)	1.13 (25.1)
Mean (SD)	1.17 (0.31)	1.21 (0.27)	1.14 (0.28)	1.17 (0.30)
Median (IQR)	1.12 (0.94; 1.41)	1.13 (1.04; 1.39)	1.11 (0.97; 1.26)	1.08 (0.93; 1.35)
Min ; Max	0.61 ; 2.17	0.68 ; 1.81	0.73 ; 2.29	0.72 ; 1.88
Ratio to baseline in HDL Cholesterol				
Week 4				
N(%)	55 (96.5)	55 (93.2)	55 (98.2)	57 (98.3)
Geom. Mean (CV)	0.97 (10.5)	0.97 (11.5)	0.98 (12.6)	1.02 (11.6)
Mean (SD)	0.97 (0.10)	0.97 (0.11)	0.98 (0.12)	1.03 (0.13)
Median (IQR)	0.97 (0.91; 1.05)	0.97 (0.91; 1.03)	0.97 (0.90; 1.04)	1.00 (0.96; 1.06)
Min ; Max	0.69 ; 1.14	0.72 ; 1.25	0.66 ; 1.33	0.78 ; 1.46
Week 12				
N(%)	53 (93.0)	55 (93.2)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	0.97 (12.3)	0.95 (13.8)	0.99 (15.0)	1.06 (12.1)
Mean (SD)	0.98 (0.12)	0.96 (0.13)	1.00 (0.15)	1.07 (0.13)
Median (IQR)	0.99 (0.91; 1.05)	0.94 (0.89; 1.04)	0.99 (0.93; 1.08)	1.05 (0.97; 1.15)
Min ; Max	0.71 ; 1.25	0.71 ; 1.29	0.64 ; 1.44	0.74 ; 1.34

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	52 (91.2)	51 (86.4)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	1.01 (12.7)	1.00 (13.8)	1.01 (16.5)	1.01 (13.3)
Mean (SD)	1.02 (0.13)	1.01 (0.15)	1.03 (0.17)	1.02 (0.14)
Median (IQR)	1.01 (0.95; 1.09)	0.97 (0.91; 1.09)	1.01 (0.92; 1.12)	0.99 (0.93; 1.10)
Min ; Max	0.74 ; 1.51	0.78 ; 1.49	0.63 ; 1.59	0.78 ; 1.43
Week 52				
N(%)	53 (93.0)	49 (83.1)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	1.06 (11.4)	1.05 (13.1)	1.13 (16.9)	1.03 (14.3)
Mean (SD)	1.06 (0.12)	1.06 (0.14)	1.14 (0.19)	1.04 (0.15)
Median (IQR)	1.06 (0.98; 1.13)	1.04 (0.97; 1.15)	1.11 (1.04; 1.24)	1.03 (0.94; 1.13)
Min ; Max	0.77 ; 1.39	0.81 ; 1.52	0.62 ; 1.64	0.71 ; 1.49
Week 72 (EOT)				
N(%)	53 (93.0)	51 (86.4)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	1.04 (13.9)	1.04 (13.6)	1.10 (17.9)	1.01 (12.8)
Mean (SD)	1.04 (0.14)	1.05 (0.14)	1.11 (0.21)	1.02 (0.13)
Median (IQR)	1.04 (0.95; 1.14)	1.04 (0.95; 1.17)	1.09 (0.97; 1.20)	1.02 (0.93; 1.12)
Min ; Max	0.75 ; 1.36	0.77 ; 1.40	0.79 ; 1.77	0.75 ; 1.28
Week 72 (EOT) (on-treatment)				
N(%)	51 (89.5)	45 (76.3)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	1.04 (13.3)	1.03 (13.6)	1.10 (18.4)	1.00 (12.9)
Mean (SD)	1.04 (0.14)	1.04 (0.14)	1.12 (0.21)	1.01 (0.13)
Median (IQR)	1.04 (0.95; 1.14)	1.06 (0.95; 1.16)	1.09 (0.97; 1.22)	1.01 (0.92; 1.12)
Min ; Max	0.75 ; 1.36	0.77 ; 1.40	0.79 ; 1.77	0.75 ; 1.28

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
VLDL Cholesterol (mmol/L)				
Week 0 (Randomisation)				
N(%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	0.78 (41.1)	0.81 (42.4)	0.74 (47.0)	0.85 (50.8)
Mean (SD)	0.85 (0.36)	0.89 (0.39)	0.83 (0.45)	0.94 (0.41)
Median (IQR)	0.76 (0.58; 1.04)	0.75 (0.60; 1.08)	0.74 (0.51; 0.91)	0.91 (0.68; 1.09)
Min ; Max	0.36 ; 1.92	0.35 ; 2.05	0.31 ; 2.71	0.17 ; 1.91
Ratio to baseline in VLDL Cholesterol				
Week 4				
N(%)	55 (96.5)	55 (93.2)	55 (98.2)	57 (98.3)
Geom. Mean (CV)	0.94 (25.0)	0.89 (27.9)	0.86 (25.4)	0.95 (29.8)
Mean (SD)	0.97 (0.26)	0.92 (0.25)	0.89 (0.23)	0.99 (0.29)
Median (IQR)	0.96 (0.80; 1.13)	0.91 (0.77; 1.06)	0.88 (0.70; 0.99)	0.99 (0.80; 1.11)
Min ; Max	0.58 ; 2.20	0.44 ; 1.60	0.56 ; 1.48	0.47 ; 2.00
Week 12				
N(%)	53 (93.0)	55 (93.2)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	0.92 (29.0)	0.91 (39.1)	0.81 (26.8)	0.91 (29.8)
Mean (SD)	0.96 (0.29)	0.98 (0.46)	0.84 (0.23)	0.94 (0.27)
Median (IQR)	0.95 (0.76; 1.09)	0.92 (0.73; 1.09)	0.79 (0.66; 0.97)	0.92 (0.80; 1.02)
Min ; Max	0.53 ; 1.81	0.32 ; 3.28	0.48 ; 1.41	0.34 ; 1.77

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	52 (91.2)	51 (86.4)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	0.96 (30.6)	0.83 (28.4)	0.80 (33.9)	0.91 (28.4)
Mean (SD)	1.01 (0.31)	0.86 (0.24)	0.85 (0.29)	0.95 (0.28)
Median (IQR)	0.95 (0.82; 1.17)	0.82 (0.65; 1.00)	0.75 (0.65; 1.06)	0.92 (0.76; 1.05)
Min ; Max	0.48 ; 2.10	0.46 ; 1.56	0.40 ; 1.64	0.40 ; 1.78
Week 52				
N(%)	53 (93.0)	49 (83.1)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	0.90 (27.9)	0.87 (28.2)	0.78 (30.0)	0.90 (33.5)
Mean (SD)	0.93 (0.27)	0.90 (0.26)	0.82 (0.24)	0.94 (0.32)
Median (IQR)	0.90 (0.75; 1.03)	0.88 (0.69; 1.05)	0.75 (0.64; 0.99)	0.87 (0.73; 1.10)
Min ; Max	0.43 ; 1.82	0.51 ; 1.58	0.38 ; 1.40	0.43 ; 1.88
Week 72 (EOT)				
N(%)	53 (93.0)	51 (86.4)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	0.87 (31.4)	0.90 (37.1)	0.73 (39.6)	0.93 (37.6)
Mean (SD)	0.91 (0.30)	0.97 (0.41)	0.78 (0.29)	0.99 (0.35)
Median (IQR)	0.85 (0.73; 1.04)	0.83 (0.72; 1.13)	0.73 (0.55; 0.97)	0.93 (0.72; 1.16)
Min ; Max	0.39 ; 1.81	0.45 ; 2.51	0.26 ; 1.42	0.34 ; 1.88
Week 72 (EOT) (on-treatment)				
N(%)	51 (89.5)	45 (76.3)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	0.87 (31.3)	0.88 (35.8)	0.72 (40.0)	0.93 (37.4)
Mean (SD)	0.91 (0.30)	0.93 (0.39)	0.77 (0.30)	0.99 (0.35)
Median (IQR)	0.85 (0.73; 1.04)	0.83 (0.69; 1.00)	0.70 (0.53; 0.95)	0.93 (0.74; 1.15)
Min ; Max	0.39 ; 1.81	0.45 ; 2.51	0.26 ; 1.42	0.34 ; 1.88

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Triglycerides (mmol/L)				
Week 0 (Randomisation)				
N(%)	55 (96.5)	57 (96.6)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	1.7 (43.3)	1.8 (46.2)	1.7 (50.9)	1.9 (51.5)
Mean (SD)	1.9 (0.9)	2.0 (1.1)	1.9 (1.3)	2.1 (0.9)
Median (IQR)	1.7 (1.3; 2.3)	1.7 (1.3; 2.4)	1.6 (1.1; 2.0)	2.0 (1.5; 2.4)
Min ; Max	0.8 ; 4.8	0.8 ; 5.7	0.7 ; 8.2	0.4 ; 5.1
Ratio to baseline in Triglycerides				
Week 4				
N(%)	55 (96.5)	55 (93.2)	55 (98.2)	57 (98.3)
Geom. Mean (CV)	0.94 (25.1)	0.89 (29.5)	0.86 (24.9)	0.95 (29.9)
Mean (SD)	0.97 (0.26)	0.93 (0.28)	0.89 (0.23)	0.99 (0.29)
Median (IQR)	0.95 (0.79; 1.11)	0.90 (0.76; 1.05)	0.88 (0.70; 0.99)	0.99 (0.81; 1.11)
Min ; Max	0.58 ; 2.21	0.44 ; 1.97	0.57 ; 1.47	0.47 ; 2.01
Week 12				
N(%)	53 (93.0)	55 (93.2)	54 (96.4)	57 (98.3)
Geom. Mean (CV)	0.92 (28.9)	0.91 (40.0)	0.80 (28.0)	0.90 (29.9)
Mean (SD)	0.95 (0.29)	0.99 (0.46)	0.83 (0.23)	0.94 (0.28)
Median (IQR)	0.92 (0.76; 1.09)	0.92 (0.74; 1.10)	0.78 (0.65; 0.97)	0.90 (0.80; 1.02)
Min ; Max	0.53 ; 1.79	0.31 ; 3.27	0.48 ; 1.41	0.34 ; 1.76

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	52 (91.2)	51 (86.4)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	0.96 (31.1)	0.83 (35.0)	0.80 (34.3)	0.92 (29.3)
Mean (SD)	1.00 (0.32)	0.89 (0.39)	0.84 (0.29)	0.95 (0.28)
Median (IQR)	0.92 (0.81; 1.14)	0.82 (0.64; 1.00)	0.75 (0.63; 1.06)	0.93 (0.76; 1.05)
Min ; Max	0.48 ; 2.10	0.46 ; 3.05	0.39 ; 1.64	0.40 ; 1.76
Week 52				
N(%)	53 (93.0)	49 (83.1)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	0.91 (29.1)	0.87 (30.8)	0.77 (31.5)	0.92 (37.3)
Mean (SD)	0.94 (0.28)	0.91 (0.29)	0.81 (0.25)	0.99 (0.43)
Median (IQR)	0.91 (0.74; 1.03)	0.84 (0.70; 1.05)	0.73 (0.63; 0.99)	0.92 (0.74; 1.17)
Min ; Max	0.43 ; 1.83	0.51 ; 1.86	0.38 ; 1.39	0.43 ; 3.19
Week 72 (EOT)				
N(%)	53 (93.0)	51 (86.4)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	0.87 (33.2)	0.91 (38.0)	0.72 (42.1)	0.93 (37.4)
Mean (SD)	0.91 (0.32)	0.98 (0.44)	0.78 (0.31)	0.99 (0.35)
Median (IQR)	0.85 (0.71; 1.04)	0.84 (0.72; 1.08)	0.73 (0.52; 0.98)	0.94 (0.73; 1.16)
Min ; Max	0.39 ; 1.91	0.45 ; 2.88	0.26 ; 1.47	0.34 ; 1.88
Week 72 (EOT) (on-treatment)				
N(%)	51 (89.5)	45 (76.3)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	0.86 (33.2)	0.89 (37.0)	0.71 (42.5)	0.94 (37.2)
Mean (SD)	0.91 (0.32)	0.95 (0.42)	0.77 (0.31)	1.00 (0.35)
Median (IQR)	0.85 (0.71; 1.04)	0.84 (0.69; 1.00)	0.71 (0.50; 0.95)	0.94 (0.74; 1.15)
Min ; Max	0.39 ; 1.91	0.45 ; 2.88	0.26 ; 1.47	0.34 ; 1.88

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Free Fatty Acids (mmol/L)				
Week 0 (Randomisation)				
N(%)	54 (94.7)	57 (96.6)	54 (96.4)	56 (96.6)
Geom. Mean (CV)	0.63 (41.0)	0.59 (55.3)	0.55 (38.8)	0.44 (62.7)
Mean (SD)	0.68 (0.27)	0.68 (0.36)	0.59 (0.21)	0.52 (0.28)
Median (IQR)	0.63 (0.51; 0.86)	0.63 (0.44; 0.78)	0.53 (0.46; 0.71)	0.45 (0.30; 0.71)
Min ; Max	0.29 ; 1.61	0.17 ; 2.01	0.21 ; 1.15	0.09 ; 1.40
Ratio to baseline in Free Fatty Acids				
Week 4				
N(%)	52 (91.2)	55 (93.2)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	0.92 (37.4)	0.94 (51.1)	1.01 (47.7)	1.09 (69.4)
Mean (SD)	0.98 (0.35)	1.06 (0.54)	1.13 (0.61)	1.34 (0.98)
Median (IQR)	0.92 (0.70; 1.22)	0.95 (0.67; 1.32)	1.00 (0.77; 1.41)	0.99 (0.65; 1.56)
Min ; Max	0.29 ; 2.00	0.25 ; 3.35	0.32 ; 4.10	0.32 ; 5.36
Week 12				
N(%)	51 (89.5)	55 (93.2)	50 (89.3)	55 (94.8)
Geom. Mean (CV)	0.75 (44.7)	0.90 (51.0)	0.97 (49.7)	1.05 (81.8)
Mean (SD)	0.82 (0.31)	1.01 (0.50)	1.09 (0.60)	1.38 (1.28)
Median (IQR)	0.76 (0.60; 1.06)	0.96 (0.69; 1.27)	0.93 (0.72; 1.20)	0.96 (0.70; 1.42)
Min ; Max	0.22 ; 1.55	0.32 ; 2.67	0.42 ; 3.18	0.14 ; 7.50

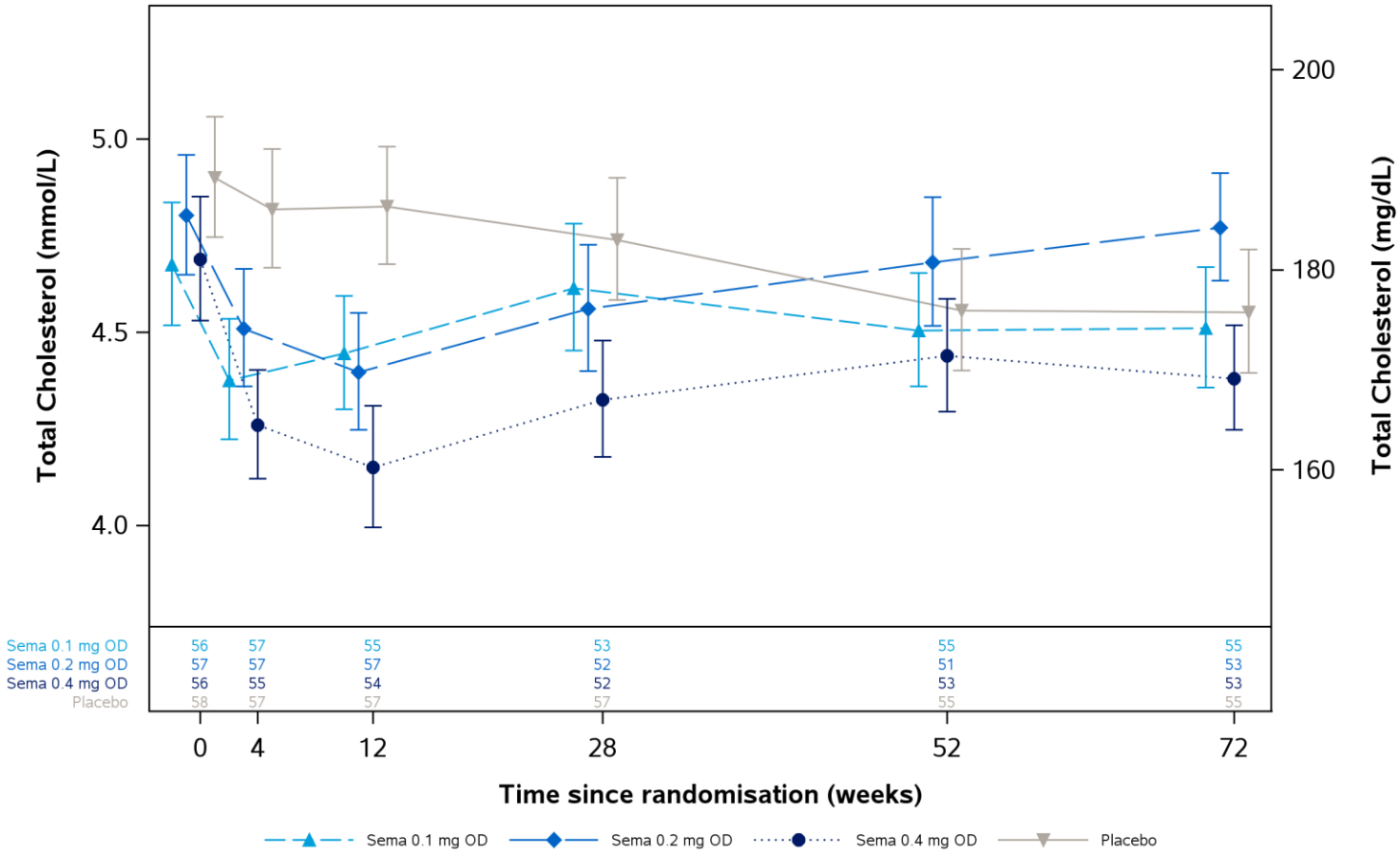
N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

Lipids - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 28				
N(%)	51 (89.5)	50 (84.7)	50 (89.3)	55 (94.8)
Geom. Mean (CV)	0.75 (51.6)	0.84 (70.4)	0.96 (49.6)	1.07 (70.5)
Mean (SD)	0.83 (0.37)	1.01 (0.68)	1.08 (0.65)	1.32 (1.00)
Median (IQR)	0.75 (0.63; 1.00)	0.82 (0.65; 1.11)	0.91 (0.79; 1.14)	1.03 (0.72; 1.58)
Min ; Max	0.17 ; 2.18	0.16 ; 3.59	0.30 ; 4.18	0.20 ; 5.86
N<LLOQ ; N>ULOQ		1 ; 0		
Week 52				
N(%)	52 (91.2)	47 (79.7)	51 (91.1)	53 (91.4)
Geom. Mean (CV)	0.75 (55.6)	0.91 (67.8)	0.77 (59.7)	1.18 (83.8)
Mean (SD)	0.85 (0.44)	1.07 (0.59)	0.88 (0.46)	1.56 (1.33)
Median (IQR)	0.77 (0.55; 1.09)	0.99 (0.64; 1.44)	0.76 (0.53; 1.11)	1.06 (0.76; 1.58)
Min ; Max	0.14 ; 2.26	0.15 ; 2.88	0.19 ; 2.00	0.28 ; 6.00
Week 72 (EOT)				
N(%)	51 (89.5)	51 (86.4)	51 (91.1)	53 (91.4)
Geom. Mean (CV)	0.83 (58.5)	0.96 (68.6)	0.68 (85.9)	1.07 (78.6)
Mean (SD)	0.96 (0.55)	1.16 (0.74)	0.84 (0.53)	1.35 (1.08)
Median (IQR)	0.85 (0.66; 1.12)	0.94 (0.73; 1.31)	0.71 (0.47; 0.99)	1.01 (0.71; 1.60)
Min ; Max	0.22 ; 2.79	0.21 ; 3.06	0.04 ; 2.25	0.13 ; 5.44
N<LLOQ ; N>ULOQ			2 ; 0	1 ; 0
Week 72 (EOT) (on-treatment)				
N(%)	49 (86.0)	44 (74.6)	48 (85.7)	50 (86.2)
Geom. Mean (CV)	0.82 (59.1)	0.94 (68.0)	0.67 (86.0)	1.11 (72.3)
Mean (SD)	0.95 (0.56)	1.13 (0.73)	0.83 (0.51)	1.38 (1.09)
Median (IQR)	0.85 (0.66; 1.10)	0.91 (0.76; 1.24)	0.72 (0.49; 0.96)	0.98 (0.71; 1.66)
Min ; Max	0.22 ; 2.79	0.21 ; 3.06	0.04 ; 2.25	0.32 ; 5.44
N<LLOQ ; N>ULOQ			2 ; 0	

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment, LDL: Low density lipoprotein, HDL: High density lipoprotein, VLDL: Very low density lipoprotein.

6.2.60 Total cholesterol by week - observed geometric mean plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



Number of observations per treatment group and visit is presented in the lower part of the plot. Mean +/- standard error calculated on log-scale and back-transformed to original scale. OD: Once daily.

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6.2.61 Total cholesterol - ratio to baseline - statistical analysis - ANCOVA - MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
Total Cholesterol (mmol/L)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	56	4.57		
Sema 0.2 mg OD	59	57	4.73		
Sema 0.4 mg OD	56	56	4.47		
Placebo	58	58	4.45		
Ratio to baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	56	0.96		
Sema 0.2 mg OD	59	57	0.99		
Sema 0.4 mg OD	56	56	0.94		
Placebo	58	58	0.93		
Treatment ratio at week 72 (EOT)					
Sema 0.1 mg OD / Placebo			1.03	[0.96; 1.10]	0.4142
Sema 0.2 mg OD / Placebo			1.06	[1.00; 1.14]	0.0687
Sema 0.4 mg OD / Placebo			1.00	[0.94; 1.07]	0.9017
Total Cholesterol (mg/dL)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	56	176.49		
Sema 0.2 mg OD	59	57	182.81		
Sema 0.4 mg OD	56	56	172.42		
Placebo	58	58	171.70		
Ratio to baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	56	0.96		
Sema 0.2 mg OD	59	57	0.99		
Sema 0.4 mg OD	56	56	0.94		
Placebo	58	58	0.93		

ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval, OD: Once daily, EOT: End of treatment.

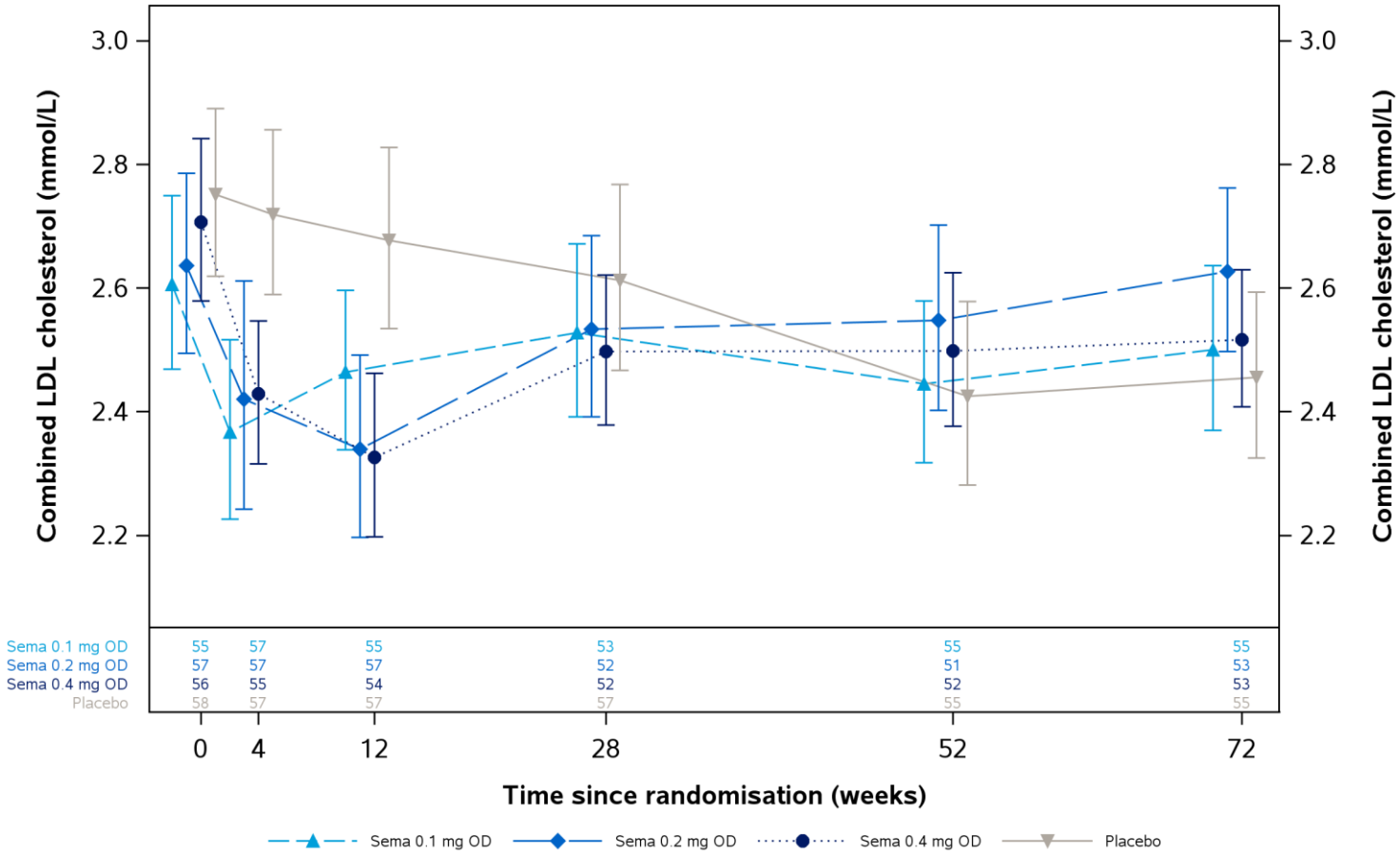
Total cholesterol - ratio to baseline - statistical analysis - ANCOVA - MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
Treatment ratio at week 72 (EOT)					
Sema 0.1 mg OD / Placebo			1.03	[0.96; 1.10]	0.4142
Sema 0.2 mg OD / Placebo			1.06	[1.00; 1.14]	0.0687
Sema 0.4 mg OD / Placebo			1.00	[0.94; 1.07]	0.9017

ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval, OD: Once daily, EOT: End of treatment.

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6.2.62 LDL cholesterol by week - observed geometric mean plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



Number of observations per treatment group and visit is presented in the lower part of the plot. Mean +/- standard error calculated on log-scale and back-transformed to original scale. LDL: Low density lipoprotein, OD: Once daily.

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6.2.63 LDL cholesterol - ratio to baseline - statistical analysis - ANCOVA - MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
Combined LDL cholesterol (mmol/L)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	55	2.53		
Sema 0.2 mg OD	59	57	2.65		
Sema 0.4 mg OD	56	56	2.52		
Placebo	58	58	2.39		
Ratio to baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	55	0.94		
Sema 0.2 mg OD	59	57	0.99		
Sema 0.4 mg OD	56	56	0.94		
Placebo	58	58	0.89		
Treatment ratio at week 72 (EOT)					
Sema 0.1 mg OD / Placebo			1.06	[0.96; 1.17]	0.2727
Sema 0.2 mg OD / Placebo			1.11	[1.00; 1.23]	0.0435
Sema 0.4 mg OD / Placebo			1.06	[0.96; 1.17]	0.2817
Combined LDL cholesterol (mg/dL)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	55	97.50		
Sema 0.2 mg OD	59	57	102.38		
Sema 0.4 mg OD	56	56	97.44		
Placebo	58	58	92.23		
Ratio to baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	55	0.94		
Sema 0.2 mg OD	59	57	0.99		
Sema 0.4 mg OD	56	56	0.94		
Placebo	58	58	0.89		

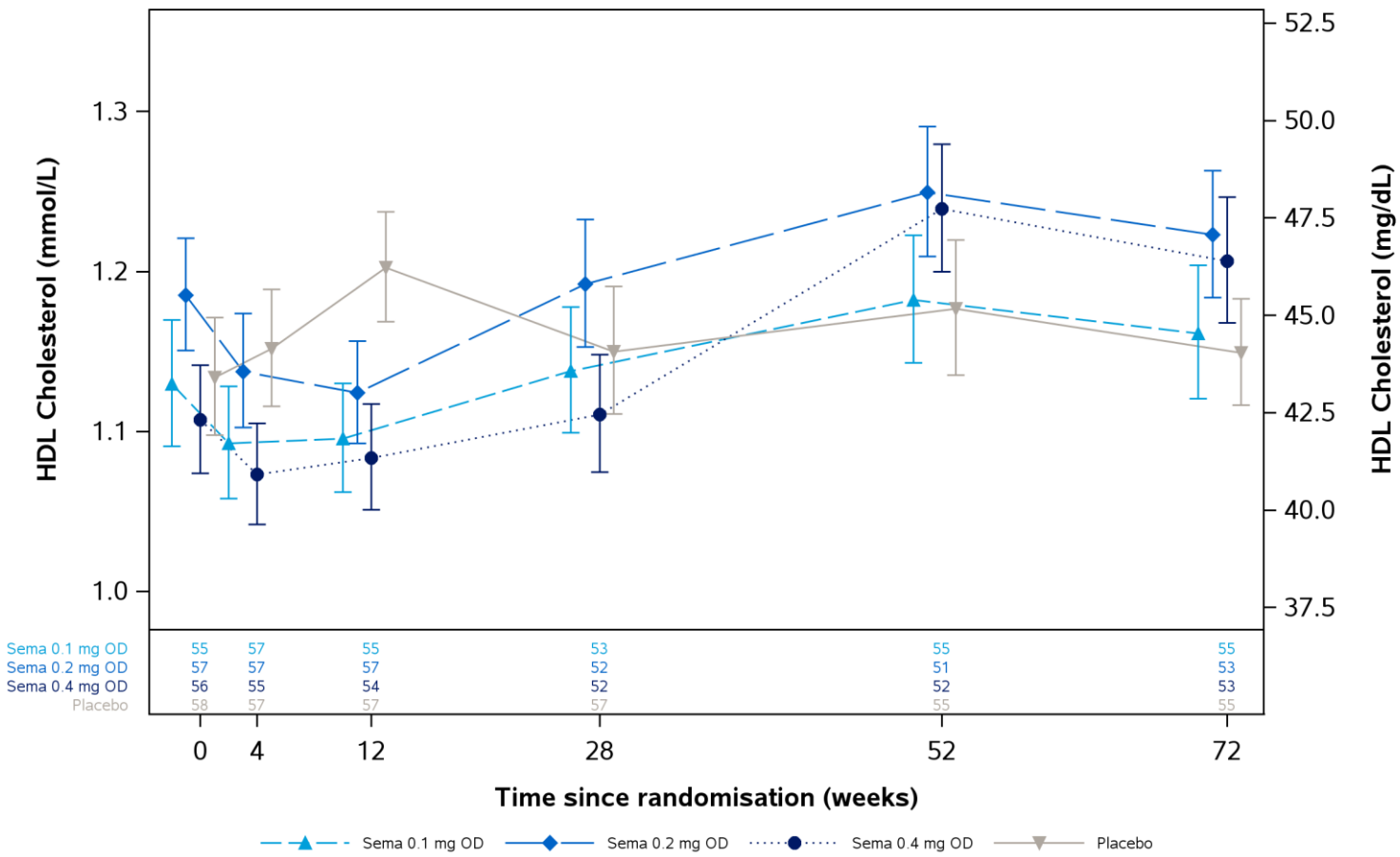
ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval. LDL: Low density lipoprotein, OD: Once daily, EOT: End of treatment.

LDL cholesterol - ratio to baseline - statistical analysis - ANCOVA - MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
Treatment ratio at week 72 (EOT)					
Sema 0.1 mg OD / Placebo			1.06	[0.96; 1.17]	0.2727
Sema 0.2 mg OD / Placebo			1.11	[1.00; 1.23]	0.0435
Sema 0.4 mg OD / Placebo			1.06	[0.96; 1.17]	0.2817

ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval. LDL: Low density lipoprotein, OD: Once daily, EOT: End of treatment.

6.2.64 HDL cholesterol by week - observed geometric mean plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



Number of observations per treatment group and visit is presented in the lower part of the plot. Mean +/- standard error calculated on log-scale and back-transformed to original scale. HDL: High density lipoprotein, OD: Once daily.

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6.2.65 HDL cholesterol - ratio to baseline - statistical analysis - ANCOVA - MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
HDL Cholesterol (mmol/L)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	55	1.18		
Sema 0.2 mg OD	59	57	1.19		
Sema 0.4 mg OD	56	56	1.23		
Placebo	58	58	1.15		
Ratio to baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	55	1.03		
Sema 0.2 mg OD	59	57	1.04		
Sema 0.4 mg OD	56	56	1.08		
Placebo	58	58	1.01		
Treatment ratio at week 72 (EOT)					
Sema 0.1 mg OD / Placebo			1.02	[0.97; 1.08]	0.4187
Sema 0.2 mg OD / Placebo			1.03	[0.98; 1.09]	0.2316
Sema 0.4 mg OD / Placebo			1.07	[1.02; 1.13]	0.0106
HDL Cholesterol (mg/dL)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	55	45.38		
Sema 0.2 mg OD	59	57	45.85		
Sema 0.4 mg OD	56	56	47.54		
Placebo	58	58	44.41		
Ratio to baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	55	1.03		
Sema 0.2 mg OD	59	57	1.04		
Sema 0.4 mg OD	56	56	1.08		
Placebo	58	58	1.01		

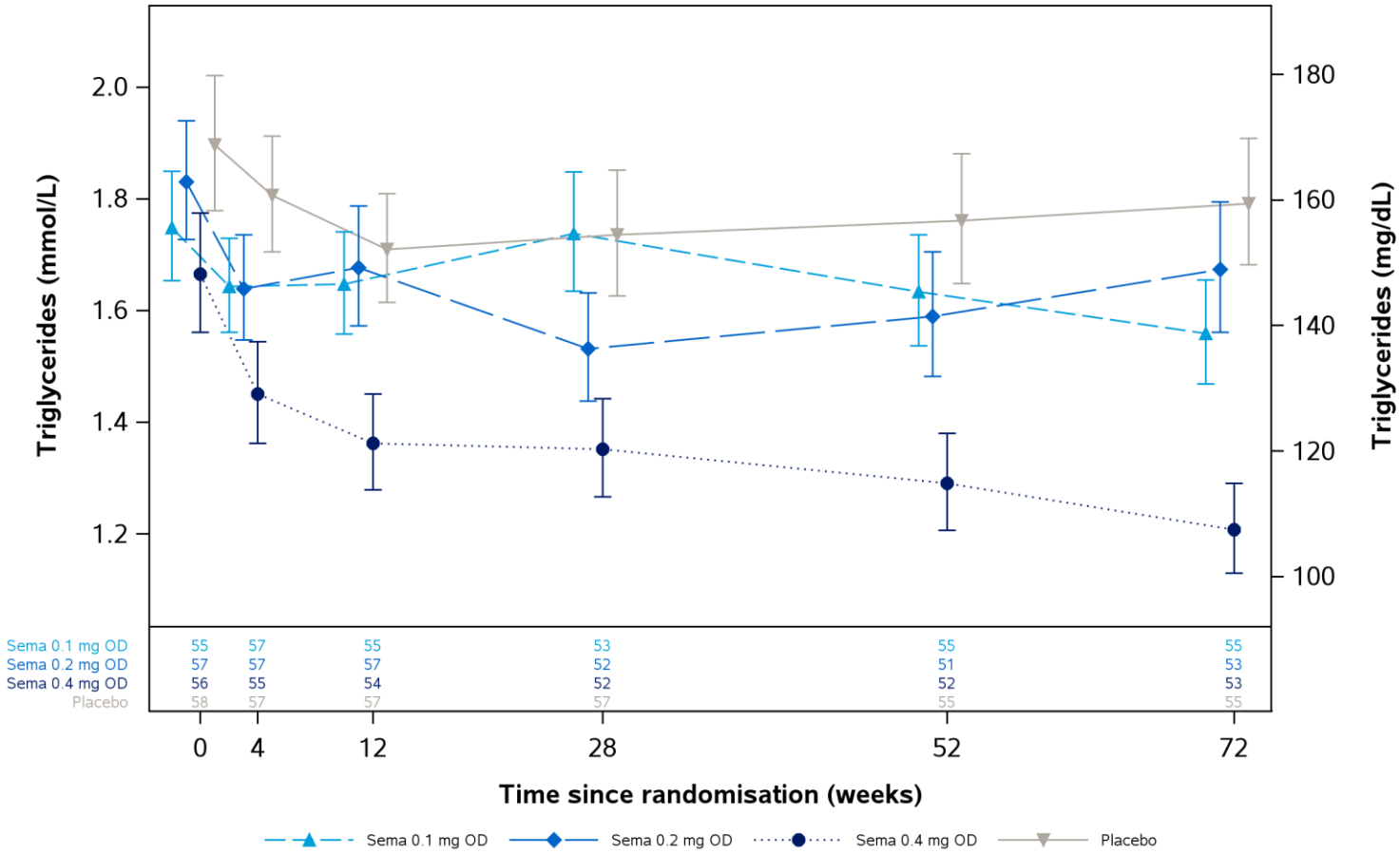
ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval. HDL: High density lipoprotein, OD: Once daily, EOT: End of treatment.

HDL cholesterol - ratio to baseline - statistical analysis - ANCOVA - MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
Treatment ratio at week 72 (EOT)					
Sema 0.1 mg OD / Placebo			1.02	[0.97; 1.08]	0.4187
Sema 0.2 mg OD / Placebo			1.03	[0.98; 1.09]	0.2316
Sema 0.4 mg OD / Placebo			1.07	[1.02; 1.13]	0.0106

ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval. HDL: High density lipoprotein, OD: Once daily, EOT: End of treatment.

6.2.66 Triglycerides by week - observed geometric mean plot - in-trial -subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



Number of observations per treatment group and visit is presented in the lower part of the plot. Mean +/- standard error calculated on log-scale and back-transformed to original scale. OD: Once daily.

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6.2.67 Triglycerides - ratio to baseline - statistical analysis - ANCOVA - MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
Triglycerides (mmol/L)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	55	1.55		
Sema 0.2 mg OD	59	57	1.63		
Sema 0.4 mg OD	56	56	1.29		
Placebo	58	58	1.70		
Ratio to baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	55	0.87		
Sema 0.2 mg OD	59	57	0.91		
Sema 0.4 mg OD	56	56	0.72		
Placebo	58	58	0.96		
Treatment ratio at week 72 (EOT)					
Sema 0.1 mg OD / Placebo			0.91	[0.80; 1.03]	0.1444
Sema 0.2 mg OD / Placebo			0.96	[0.84; 1.09]	0.4978
Sema 0.4 mg OD / Placebo			0.76	[0.66; 0.86]	<.0001
Triglycerides (mg/dL)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	55	137.64		
Sema 0.2 mg OD	59	57	144.93		
Sema 0.4 mg OD	56	56	114.75		
Placebo	58	58	151.71		
Ratio to baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	55	0.87		
Sema 0.2 mg OD	59	57	0.91		
Sema 0.4 mg OD	56	56	0.72		
Placebo	58	58	0.96		

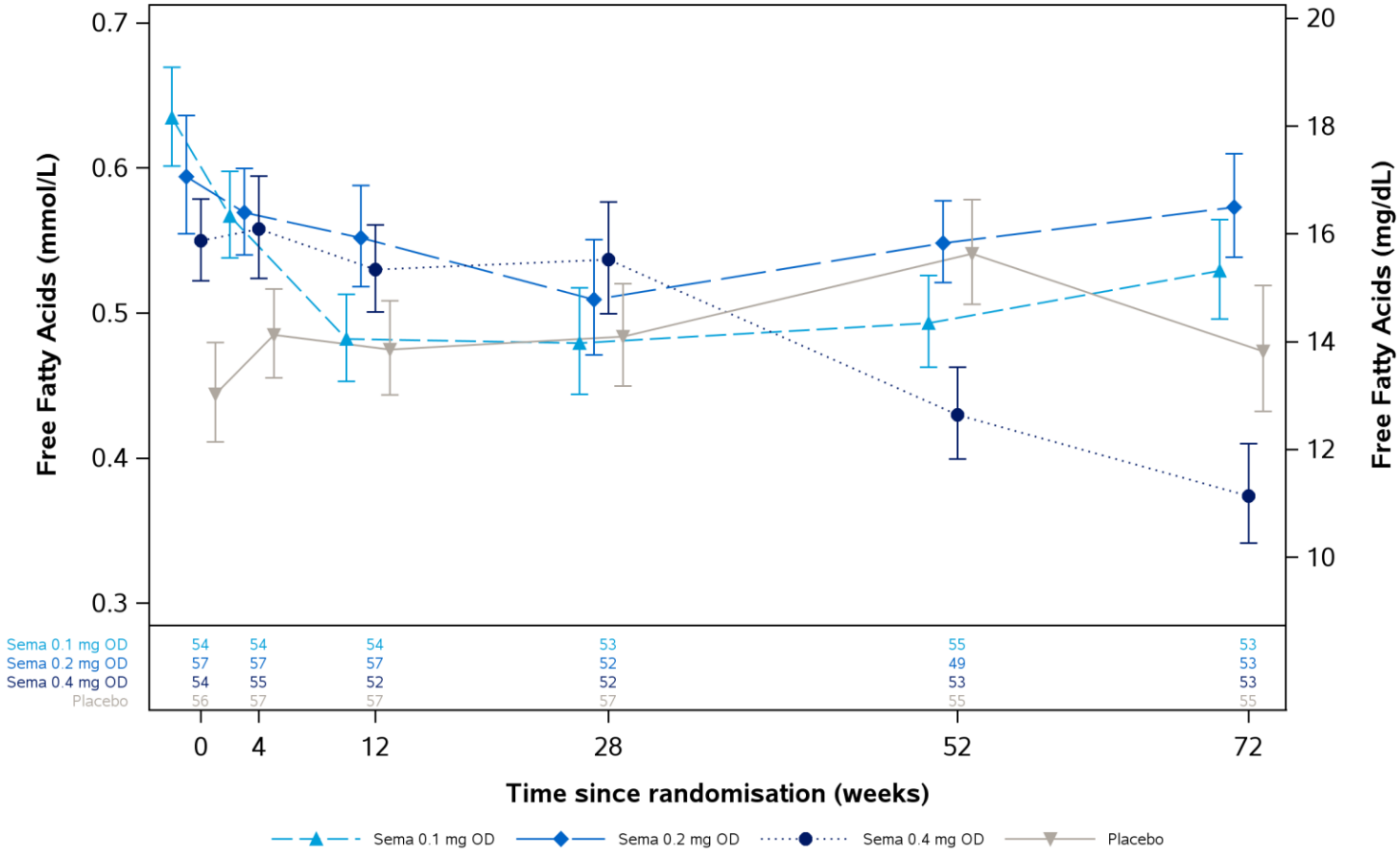
ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval, OD: Once daily, EOT: End of treatment.

Triglycerides - ratio to baseline - statistical analysis - ANCOVA - MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
Treatment ratio at week 72 (EOT)					
Sema 0.1 mg OD / Placebo			0.91	[0.80; 1.03]	0.1444
Sema 0.2 mg OD / Placebo			0.96	[0.84; 1.09]	0.4978
Sema 0.4 mg OD / Placebo			0.76	[0.66; 0.86]	<.0001

ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval, OD: Once daily, EOT: End of treatment.

6.2.68 Free fatty acids by week - observed geometric mean plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



Number of observations per treatment group and visit is presented in the lower part of the plot. Mean +/- standard error calculated on log-scale and back-transformed to original scale. OD: Once daily.

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6.2.69 Free fatty acids - ratio to baseline - statistical analysis - ANCOVA - MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
Free Fatty Acids (mmol/L)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	54	0.51		
Sema 0.2 mg OD	59	57	0.55		
Sema 0.4 mg OD	56	54	0.38		
Placebo	58	56	0.51		
Ratio to baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	54	0.92		
Sema 0.2 mg OD	59	57	1.00		
Sema 0.4 mg OD	56	54	0.69		
Placebo	58	56	0.92		
Treatment ratio at week 72 (EOT)					
Sema 0.1 mg OD / Placebo			1.00	[0.79; 1.26]	0.9982
Sema 0.2 mg OD / Placebo			1.08	[0.86; 1.36]	0.5054
Sema 0.4 mg OD / Placebo			0.75	[0.59; 0.94]	0.0115
Free Fatty Acids (mg/dL)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	54	14.31		
Sema 0.2 mg OD	59	57	15.48		
Sema 0.4 mg OD	56	54	10.67		
Placebo	58	56	14.31		
Ratio to baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	54	0.92		
Sema 0.2 mg OD	59	57	1.00		
Sema 0.4 mg OD	56	54	0.69		
Placebo	58	56	0.92		

ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval, OD: Once daily, EOT: End of treatment.

Free fatty acids - ratio to baseline - statistical analysis - ANCOVA - MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
Treatment ratio at week 72 (EOT)					
Sema 0.1 mg OD / Placebo			1.00	[0.79; 1.26]	0.9982
Sema 0.2 mg OD / Placebo			1.08	[0.86; 1.36]	0.5054
Sema 0.4 mg OD / Placebo			0.75	[0.59; 0.94]	0.0115

ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval, OD: Once daily, EOT: End of treatment.

6.2.70 High sensitivity C-reactive protein by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Number of subjects	57	59	56	58
hsCRP (mg/L)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	3.9 (171.8)	3.7 (179.1)	3.5 (132.3)	3.9 (179.9)
Mean (SD)	6.9 (7.5)	6.9 (8.0)	6.0 (7.9)	7.5 (9.2)
Median (IQR)	3.9 (2.0; 9.4)	3.8 (1.9; 8.5)	3.1 (1.8; 8.3)	3.7 (1.8; 11.2)
Min ; Max	0.2 ; 35.3	0.2 ; 33.7	0.5 ; 41.6	0.3 ; 39.9
Week 4				
N(%)	55 (96.5)	57 (96.6)	55 (98.2)	58 (100.0)
Geom. Mean (CV)	2.9 (226.8)	2.8 (162.4)	2.5 (106.7)	3.8 (133.9)
Mean (SD)	6.3 (8.3)	5.3 (7.3)	3.6 (3.5)	6.2 (6.7)
Median (IQR)	2.8 (1.1; 7.5)	2.7 (1.3; 7.1)	2.4 (1.2; 5.1)	3.6 (1.7; 7.4)
Min ; Max	0.1 ; 35.1	0.1 ; 35.5	0.5 ; 20.2	0.5 ; 30.7
Week 12				
N(%)	55 (96.5)	57 (96.6)	53 (94.6)	57 (98.3)
Geom. Mean (CV)	3.1 (223.7)	2.3 (211.8)	2.0 (111.7)	3.6 (173.6)
Mean (SD)	6.2 (7.3)	5.1 (7.7)	3.0 (2.8)	6.6 (7.3)
Median (IQR)	3.0 (1.3; 8.8)	2.7 (1.0; 5.5)	1.8 (1.1; 3.7)	3.8 (1.4; 8.9)
Min ; Max	0.1 ; 36.5	0.1 ; 39.8	0.2 ; 12.1	0.4 ; 27.1
N<LLOQ ; N>ULOQ	1 ; 0	1 ; 0		

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

High sensitivity C-reactive protein by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD		Sema 0.2 mg OD		Sema 0.4 mg OD		Placebo	
Week 20								
N(%)	54 (94.7)		54 (91.5)		52 (92.9)		57 (98.3)	
Geom. Mean (CV)	3.4 (209.1)		2.3 (247.3)		1.8 (132.3)		3.5 (155.3)	
Mean (SD)	7.3 (10.0)		5.7 (8.9)		3.0 (3.4)		6.1 (6.7)	
Median (IQR)	3.1 (1.4;	8.8)	2.6 (0.7;	4.9)	1.7 (0.9;	3.7)	4.1 (1.5;	7.0)
Min ; Max	0.1 ; 47.1		0.1 ; 38.0		0.2 ; 16.2		0.4 ; 25.0	
N<LLOQ ; N>ULOQ			1 ; 0					
Week 28								
N(%)	55 (96.5)		53 (89.8)		52 (92.9)		57 (98.3)	
Geom. Mean (CV)	3.0 (209.8)		2.1 (199.1)		1.7 (144.6)		3.5 (149.6)	
Mean (SD)	5.7 (6.4)		4.7 (7.5)		2.9 (3.4)		5.8 (5.8)	
Median (IQR)	3.1 (1.4;	7.8)	2.1 (0.8;	4.8)	1.9 (0.9;	3.6)	3.4 (1.6;	7.9)
Min ; Max	0.1 ; 29.2		0.2 ; 38.7		0.2 ; 19.3		0.2 ; 27.2	
N<LLOQ ; N>ULOQ	1 ; 0							
Week 36								
N(%)	53 (93.0)		52 (88.1)		53 (94.6)		57 (98.3)	
Geom. Mean (CV)	2.6 (217.2)		1.8 (326.9)		1.4 (135.8)		3.8 (164.6)	
Mean (SD)	5.3 (6.4)		10.0 (39.3)		2.3 (2.9)		7.2 (10.0)	
Median (IQR)	2.8 (1.2;	7.4)	1.7 (0.6;	3.7)	1.2 (0.6;	3.2)	3.5 (2.1;	8.4)
Min ; Max	0.1 ; 30.0		0.1 ; 279.5		0.2 ; 16.6		0.3 ; 55.3	
N<LLOQ ; N>ULOQ			1 ; 0					
Week 44								
N(%)	53 (93.0)		54 (91.5)		52 (92.9)		56 (96.6)	
Geom. Mean (CV)	2.9 (278.0)		1.9 (278.0)		1.7 (166.4)		3.7 (168.4)	
Mean (SD)	8.0 (17.2)		5.8 (11.0)		4.0 (8.9)		7.1 (10.3)	
Median (IQR)	2.8 (1.4;	7.5)	1.9 (0.7;	4.5)	1.6 (0.7;	3.3)	3.7 (1.4;	9.0)
Min ; Max	0.1 ; 117.0		0.1 ; 53.2		0.3 ; 54.7		0.4 ; 64.5	
N<LLOQ ; N>ULOQ	1 ; 0		1 ; 0					

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

High sensitivity C-reactive protein by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 52				
N(%)	55 (96.5)	52 (88.1)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	2.9 (208.0)	1.5 (183.2)	1.4 (181.0)	3.4 (166.5)
Mean (SD)	5.7 (6.8)	3.1 (4.8)	2.7 (3.4)	6.2 (6.9)
Median (IQR)	3.3 (1.3; 9.3)	1.6 (0.6; 3.0)	1.3 (0.6; 2.9)	3.0 (1.5; 8.5)
Min ; Max	0.1 ; 29.6	0.1 ; 28.5	0.1 ; 18.1	0.3 ; 27.3
Week 62				
N(%)	54 (94.7)	52 (88.1)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	3.0 (258.6)	1.5 (217.5)	1.4 (123.5)	3.0 (143.3)
Mean (SD)	7.3 (10.5)	3.3 (5.0)	2.2 (2.6)	5.1 (5.7)
Median (IQR)	3.3 (1.3; 6.7)	1.4 (0.6; 3.3)	1.1 (0.8; 2.8)	2.6 (1.4; 6.9)
Min ; Max	0.1 ; 46.8	0.1 ; 26.0	0.2 ; 11.8	0.3 ; 30.1
N<LLOQ ; N>ULOQ		2 ; 0		
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	3.3 (228.1)	1.7 (252.7)	1.3 (165.4)	3.6 (146.5)
Mean (SD)	7.4 (9.6)	4.4 (9.0)	2.3 (2.9)	6.1 (6.2)
Median (IQR)	3.2 (1.2; 9.2)	1.8 (0.5; 5.0)	1.1 (0.6; 3.0)	3.7 (1.8; 8.9)
Min ; Max	0.1 ; 44.6	0.1 ; 60.8	0.1 ; 14.7	0.4 ; 29.6
N<LLOQ ; N>ULOQ		1 ; 0	1 ; 0	
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	3.5 (231.0)	1.6 (280.1)	1.2 (159.5)	3.7 (143.7)
Mean (SD)	7.6 (9.7)	4.6 (9.6)	2.1 (2.4)	6.1 (6.2)
Median (IQR)	3.2 (1.4; 9.2)	1.7 (0.5; 5.0)	1.1 (0.5; 3.0)	3.9 (1.8; 8.9)
Min ; Max	0.1 ; 44.6	0.1 ; 60.8	0.1 ; 12.5	0.4 ; 29.6
N<LLOQ ; N>ULOQ		1 ; 0	1 ; 0	

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

6.2.71 High sensitivity C-reactive protein - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Number of subjects	57	59	56	58
hsCRP (mg/L)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Geom. Mean (CV)	3.9 (171.8)	3.7 (179.1)	3.5 (132.3)	3.9 (179.9)
Mean (SD)	6.9 (7.5)	6.9 (8.0)	6.0 (7.9)	7.5 (9.2)
Median (IQR)	3.9 (2.0; 9.4)	3.8 (1.9; 8.5)	3.1 (1.8; 8.3)	3.7 (1.8; 11.2)
Min ; Max	0.2 ; 35.3	0.2 ; 33.7	0.5 ; 41.6	0.3 ; 39.9
Ratio to baseline in hsCRP				
Week 4				
N(%)	55 (96.5)	57 (96.6)	55 (98.2)	58 (100.0)
Geom. Mean (CV)	0.75 (52.6)	0.76 (82.0)	0.73 (83.3)	0.96 (81.0)
Mean (SD)	0.86 (0.56)	0.96 (0.95)	1.13 (2.07)	1.24 (1.18)
Median (IQR)	0.76 (0.56; 0.96)	0.80 (0.61; 0.99)	0.67 (0.48; 1.04)	0.93 (0.77; 1.26)
Min ; Max	0.27 ; 3.91	0.02 ; 7.42	0.18 ; 13.90	0.08 ; 6.41
Week 12				
N(%)	55 (96.5)	57 (96.6)	53 (94.6)	57 (98.3)
Geom. Mean (CV)	0.77 (58.5)	0.63 (92.6)	0.64 (84.7)	0.90 (68.2)
Mean (SD)	0.91 (0.71)	0.84 (0.81)	0.97 (1.91)	1.05 (0.56)
Median (IQR)	0.75 (0.60; 1.00)	0.65 (0.44; 0.95)	0.60 (0.45; 0.88)	0.97 (0.69; 1.23)
Min ; Max	0.23 ; 5.04	0.02 ; 4.77	0.06 ; 14.26	0.08 ; 2.74
N<LLOQ ; N>ULOQ	1 ; 0	1 ; 0		

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

High sensitivity C-reactive protein - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 20				
N(%)	54 (94.7)	54 (91.5)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	0.83 (66.5)	0.61 (102.1)	0.55 (81.3)	0.89 (64.7)
Mean (SD)	1.03 (0.83)	0.83 (0.83)	0.71 (0.65)	1.03 (0.55)
Median (IQR)	0.78 (0.58; 1.14)	0.63 (0.43; 0.96)	0.54 (0.39; 0.86)	0.88 (0.72; 1.18)
Min ; Max	0.23 ; 4.37	0.02 ; 5.69	0.07 ; 4.28	0.11 ; 3.00
N<LLOQ ; N>ULOQ		1 ; 0		
Week 28				
N(%)	55 (96.5)	53 (89.8)	52 (92.9)	57 (98.3)
Geom. Mean (CV)	0.73 (64.7)	0.56 (90.2)	0.53 (76.0)	0.88 (64.3)
Mean (SD)	0.89 (0.70)	0.68 (0.38)	0.66 (0.51)	1.00 (0.47)
Median (IQR)	0.70 (0.50; 1.02)	0.64 (0.43; 0.86)	0.57 (0.32; 0.79)	0.92 (0.68; 1.28)
Min ; Max	0.28 ; 4.34	0.02 ; 1.80	0.09 ; 2.63	0.09 ; 2.30
N<LLOQ ; N>ULOQ	1 ; 0			
Week 36				
N(%)	53 (93.0)	52 (88.1)	53 (94.6)	57 (98.3)
Geom. Mean (CV)	0.65 (57.2)	0.51 (144.4)	0.42 (75.8)	0.97 (111.0)
Mean (SD)	0.73 (0.37)	1.12 (3.49)	0.54 (0.46)	2.53 (11.00)
Median (IQR)	0.68 (0.50; 0.87)	0.54 (0.37; 0.86)	0.37 (0.26; 0.63)	1.02 (0.69; 1.18)
Min ; Max	0.10 ; 2.07	0.01 ; 25.57	0.13 ; 2.48	0.07 ; 83.98
N<LLOQ ; N>ULOQ		1 ; 0		
Week 44				
N(%)	53 (93.0)	54 (91.5)	52 (92.9)	56 (96.6)
Geom. Mean (CV)	0.71 (75.0)	0.53 (174.8)	0.52 (159.4)	0.96 (112.5)
Mean (SD)	1.01 (1.67)	5.45 (35.54)	2.11 (9.14)	1.59 (2.85)
Median (IQR)	0.71 (0.52; 0.87)	0.51 (0.36; 0.75)	0.43 (0.30; 0.75)	0.93 (0.67; 1.51)
Min ; Max	0.22 ; 11.63	0.01 ; 261.74	0.10 ; 65.40	0.06 ; 18.70
N<LLOQ ; N>ULOQ	1 ; 0	1 ; 0		

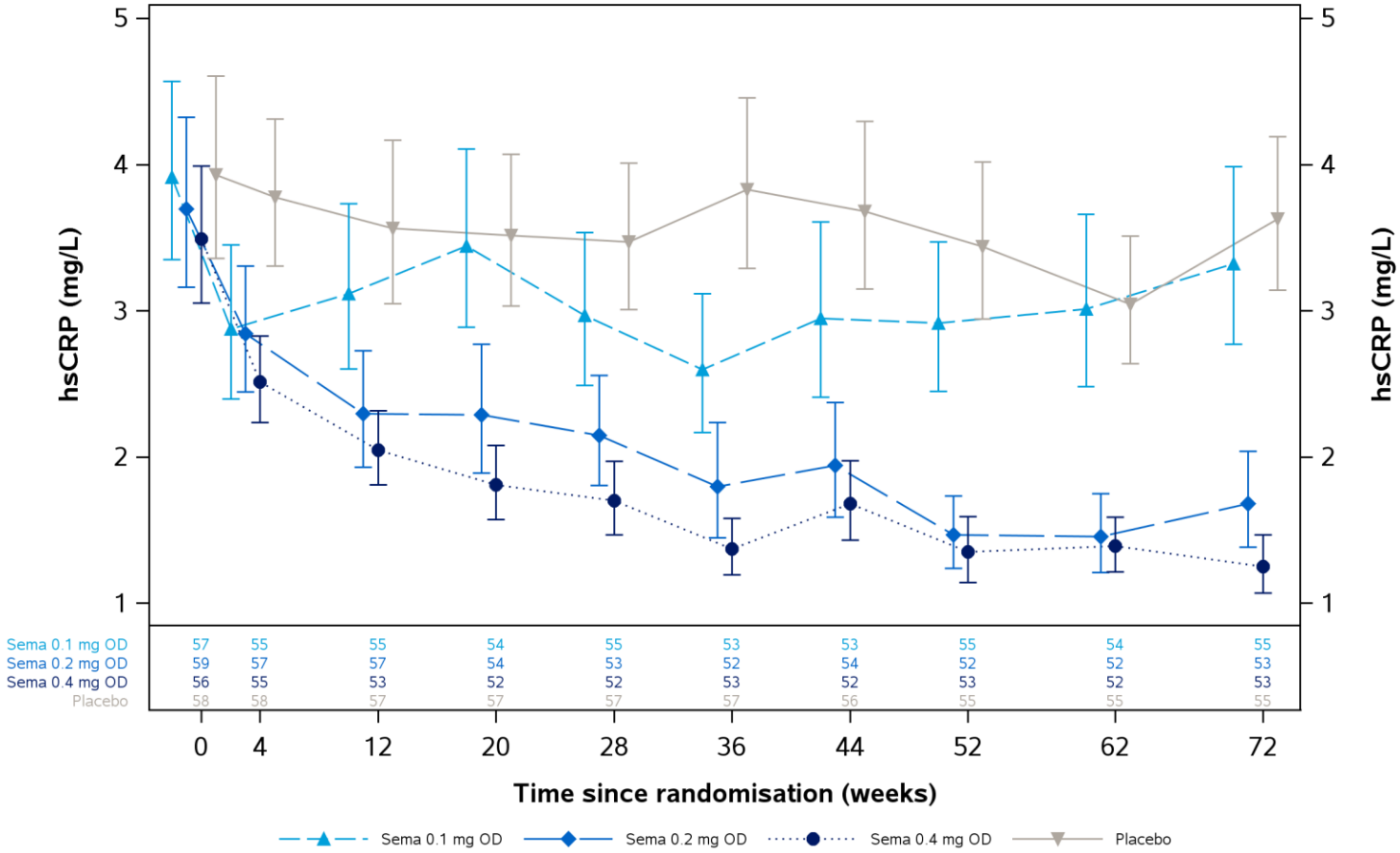
N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

High sensitivity C-reactive protein - ratio to baseline by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 52				
N(%)	55 (96.5)	52 (88.1)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	0.72 (69.0)	0.43 (98.0)	0.40 (72.9)	0.88 (84.2)
Mean (SD)	0.90 (0.83)	0.54 (0.32)	0.49 (0.33)	1.12 (0.93)
Median (IQR)	0.74 (0.44; 1.06)	0.51 (0.29; 0.65)	0.39 (0.24; 0.65)	0.90 (0.64; 1.30)
Min ; Max	0.24 ; 5.84	0.01 ; 1.58	0.10 ; 1.48	0.07 ; 6.22
Week 62				
N(%)	54 (94.7)	52 (88.1)	52 (92.9)	55 (94.8)
Geom. Mean (CV)	0.74 (114.4)	0.42 (79.8)	0.43 (98.7)	0.77 (80.8)
Mean (SD)	1.66 (4.57)	0.54 (0.45)	0.70 (1.38)	0.94 (0.60)
Median (IQR)	0.61 (0.44; 0.98)	0.41 (0.27; 0.70)	0.41 (0.26; 0.70)	0.81 (0.57; 1.11)
Min ; Max	0.21 ; 31.41	0.04 ; 3.08	0.10 ; 10.00	0.05 ; 3.07
N<LLOQ ; N>ULOQ		2 ; 0		
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Geom. Mean (CV)	0.82 (121.0)	0.47 (129.0)	0.37 (108.2)	0.88 (80.0)
Mean (SD)	1.51 (2.71)	0.73 (0.86)	0.53 (0.49)	1.08 (0.70)
Median (IQR)	0.69 (0.47; 1.16)	0.51 (0.27; 0.75)	0.36 (0.24; 0.62)	0.94 (0.62; 1.38)
Min ; Max	0.07 ; 15.71	0.01 ; 4.58	0.04 ; 2.71	0.10 ; 4.02
N<LLOQ ; N>ULOQ		1 ; 0	1 ; 0	
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Geom. Mean (CV)	0.83 (122.2)	0.46 (138.9)	0.37 (112.6)	0.88 (82.3)
Mean (SD)	1.54 (2.75)	0.74 (0.90)	0.53 (0.50)	1.10 (0.72)
Median (IQR)	0.69 (0.47; 1.16)	0.50 (0.26; 0.75)	0.36 (0.23; 0.64)	0.94 (0.62; 1.39)
Min ; Max	0.07 ; 15.71	0.01 ; 4.58	0.04 ; 2.71	0.10 ; 4.02
N<LLOQ ; N>ULOQ		1 ; 0	1 ; 0	

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, CV: Coefficient of variation, IQR: Inter-quartile range, EOT: End of treatment.

6.2.72 High sensitivity C-reactive protein by week - observed geometric mean plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



Number of observations per treatment group and visit is presented in the lower part of the plot. Mean +/- standard error calculated on log-scale and back-transformed to original scale. OD: Once daily.

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6.2.73 High sensitivity C-reactive protein - ratio to baseline - statistical analysis - ANCOVA - MI based on unconditional reference - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
hsCRP (mg/L)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	57	3.13		
Sema 0.2 mg OD	59	59	1.86		
Sema 0.4 mg OD	56	56	1.44		
Placebo	58	58	3.37		
Ratio to baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	57	0.83		
Sema 0.2 mg OD	59	59	0.50		
Sema 0.4 mg OD	56	56	0.38		
Placebo	58	58	0.90		
Treatment ratio at week 72 (EOT)					
Sema 0.1 mg OD / Placebo			0.93	[0.68; 1.28]	0.6632
Sema 0.2 mg OD / Placebo			0.55	[0.40; 0.76]	0.0003
Sema 0.4 mg OD / Placebo			0.43	[0.31; 0.59]	<.0001

ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval, OD: Once daily, EOT: End of treatment.

6.2.74 SF-36 bodily pain by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Number of subjects	57	59	56	58
SF36 Std Score NBS Bodily Pain (score)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Mean (SD)	47.9 (12.1)	47.7 (9.4)	49.5 (10.4)	47.8 (10.8)
Median (IQR)	50.7 (38.2; 62.0)	46.7 (42.2; 55.6)	51.5 (44.5; 55.6)	46.7 (42.2; 55.6)
Min ; Max	21.7 ; 62.0	30.1 ; 62.0	21.7 ; 62.0	21.7 ; 62.0
Week 28				
N(%)	54 (94.7)	54 (91.5)	52 (92.9)	57 (98.3)
Mean (SD)	50.0 (10.3)	47.0 (10.4)	50.7 (10.3)	46.1 (11.5)
Median (IQR)	51.1 (38.6; 62.0)	46.7 (38.2; 55.6)	51.5 (44.5; 62.0)	46.7 (38.6; 55.6)
Min ; Max	21.7 ; 62.0	26.5 ; 62.0	21.7 ; 62.0	21.7 ; 62.0
Week 52				
N(%)	55 (96.5)	52 (88.1)	53 (94.6)	53 (91.4)
Mean (SD)	51.3 (10.4)	47.6 (9.5)	49.4 (11.5)	46.7 (12.4)
Median (IQR)	53.9 (42.2; 62.0)	46.7 (38.2; 53.5)	51.5 (38.2; 62.0)	46.7 (38.2; 55.6)
Min ; Max	21.7 ; 62.0	30.6 ; 62.0	21.7 ; 62.0	21.7 ; 62.0
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Mean (SD)	49.4 (11.9)	49.0 (9.8)	53.0 (10.1)	45.7 (11.8)
Median (IQR)	50.7 (38.2; 62.0)	50.7 (42.2; 55.6)	55.6 (46.7; 62.0)	42.6 (38.2; 55.6)
Min ; Max	25.7 ; 62.0	30.6 ; 62.0	26.5 ; 62.0	21.7 ; 62.0

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

SF-36 bodily pain by week - summary - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Mean (SD)	49.3 (12.0)	50.1 (9.5)	53.0 (10.2)	46.4 (11.5)
Median (IQR)	50.7 (38.2; 62.0)	50.7 (42.2; 62.0)	55.6 (46.7; 62.0)	46.7 (38.2; 55.6)
Min ; Max	25.7 ; 62.0	30.6 ; 62.0	26.5 ; 62.0	21.7 ; 62.0

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

6.2.75 SF-36 bodily pain - change from baseline by week - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Number of subjects	57	59	56	58
SF36 Std Score NBS Bodily Pain (score)				
Week 0 (Randomisation)				
N(%)	57 (100.0)	59 (100.0)	56 (100.0)	58 (100.0)
Mean (SD)	47.9 (12.1)	47.7 (9.4)	49.5 (10.4)	47.8 (10.8)
Median (IQR)	50.7 (38.2; 62.0)	46.7 (42.2; 55.6)	51.5 (44.5; 55.6)	46.7 (42.2; 55.6)
Min ; Max	21.7 ; 62.0	30.1 ; 62.0	21.7 ; 62.0	21.7 ; 62.0
Change from baseline in SF36 Std Score NBS Bodily Pain (score)				
Week 28				
N(%)	54 (94.7)	54 (91.5)	52 (92.9)	57 (98.3)
Mean (SD)	1.8 (9.4)	-0.7 (11.5)	1.2 (9.2)	-1.7 (7.3)
Median (IQR)	0.0 (0.0; 7.7)	0.0 (-7.7; 6.5)	0.0 (-3.8; 7.1)	0.0 (-4.8; 0.0)
Min ; Max	-17.3 ; 31.5	-23.8 ; 31.9	-31.5 ; 20.2	-29.8 ; 19.8
Week 52				
N(%)	55 (96.5)	52 (88.1)	53 (94.6)	53 (91.4)
Mean (SD)	2.8 (8.2)	-0.2 (11.1)	-0.1 (9.9)	-2.1 (8.5)
Median (IQR)	0.0 (0.0; 8.1)	0.0 (-7.5; 6.5)	0.0 (-6.5; 6.5)	0.0 (-6.5; 4.0)
Min ; Max	-19.4 ; 27.8	-23.8 ; 31.9	-23.8 ; 19.8	-25.0 ; 15.3
Week 72 (EOT)				
N(%)	55 (96.5)	53 (89.8)	53 (94.6)	55 (94.8)
Mean (SD)	1.0 (9.9)	1.3 (10.4)	3.5 (7.7)	-2.0 (9.9)
Median (IQR)	0.0 (-4.0; 6.5)	0.0 (-4.0; 8.5)	0.0 (0.0; 9.3)	-0.4 (-8.5; 0.4)
Min ; Max	-23.8 ; 31.5	-31.5 ; 23.8	-10.5 ; 25.0	-27.8 ; 35.5

N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

SF-36 bodily pain - change from baseline by week - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	Sema 0.1 mg OD	Sema 0.2 mg OD	Sema 0.4 mg OD	Placebo
Week 72 (EOT) (on-treatment)				
N(%)	53 (93.0)	46 (78.0)	50 (89.3)	52 (89.7)
Mean (SD)	1.2 (10.0)	2.2 (9.7)	3.5 (7.8)	-1.1 (9.2)
Median (IQR)	0.0 (-3.6; 6.5)	0.0 (-4.0; 8.5)	0.0 (0.0; 9.3)	0.0 (-8.1; 0.4)
Min ; Max	-23.8 ; 31.5	-15.7 ; 23.8	-10.5 ; 25.0	-16.9 ; 35.5

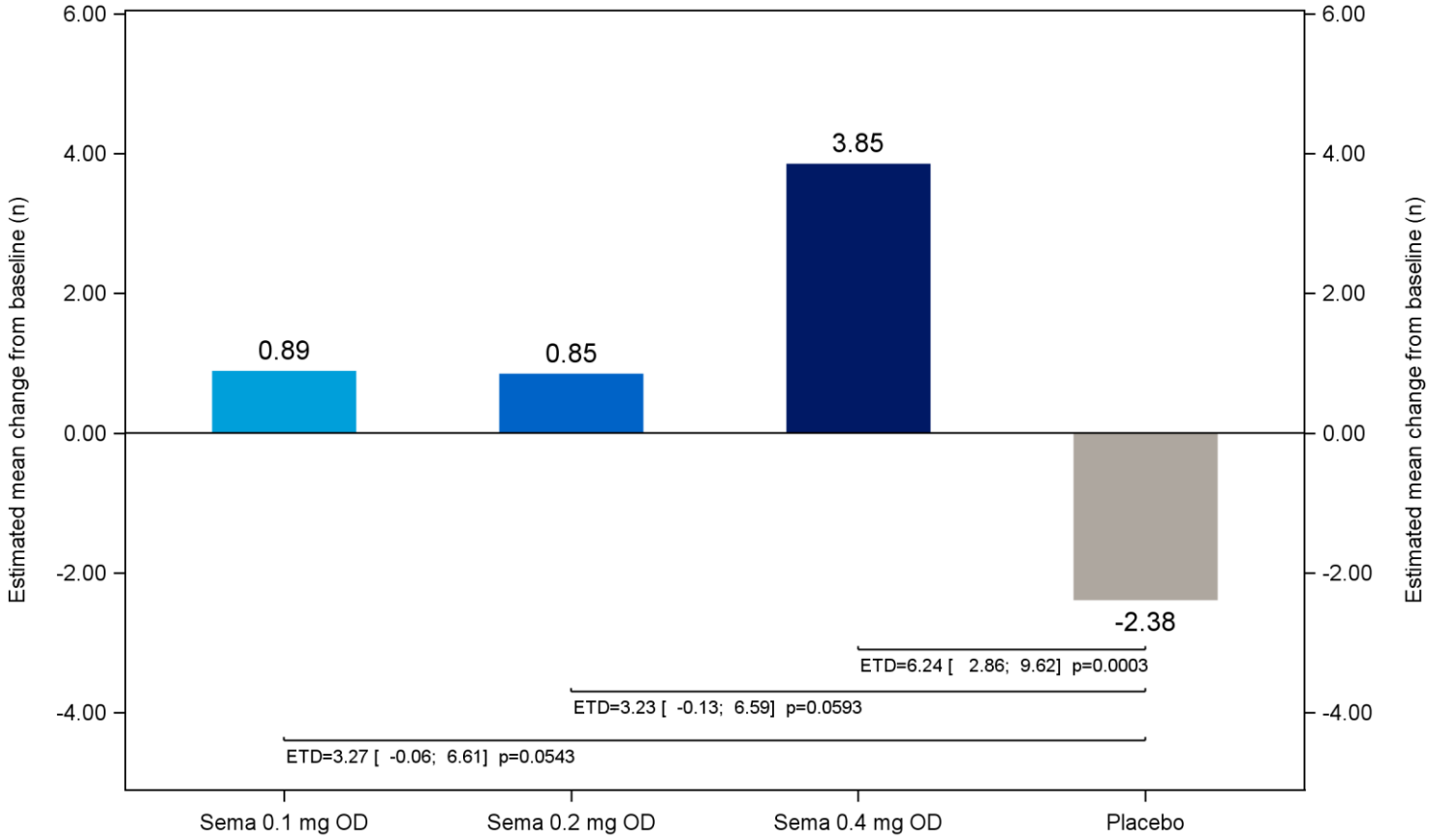
N: Number of subjects, %: Percentage of subjects, OD: Once daily, SD: Standard deviation, IQR: Inter-quartile range, EOT: End of treatment.

6.2.76 SF-36 bodily pain - change from baseline - statistical analysis - ANCOVA - MI based on unconditional reference -in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296

	FAS	N	Estimate	95% CI	Two-sided p-value
SF36 Std Score NBS Bodily Pain (score)					
Mean at week 72 (EOT)					
Sema 0.1 mg OD	57	57	49.11		
Sema 0.2 mg OD	59	59	49.07		
Sema 0.4 mg OD	56	56	52.07		
Placebo	58	58	45.83		
Change from baseline at week 72 (EOT)					
Sema 0.1 mg OD	57	57	0.89		
Sema 0.2 mg OD	59	59	0.85		
Sema 0.4 mg OD	56	56	3.85		
Placebo	58	58	-2.38		
Treatment difference at week 72 (EOT)					
Sema 0.1 mg OD - Placebo			3.27	[-0.06; 6.61]	0.0543
Sema 0.2 mg OD - Placebo			3.23	[-0.13; 6.59]	0.0593
Sema 0.4 mg OD - Placebo			6.24	[2.86; 9.62]	0.0003

ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, FAS: Full analysis set, N: Number of subjects with baseline assessment, CI: Confidence interval, OD: Once daily, EOT: End of treatment.

6.2.77 SF-36 bodily pain - change from baseline - bar plot - in-trial - subjects with fibrosis stage 2 or 3 at baseline - Trial 4296



ANCOVA with treatment, baseline diabetes status, baseline fibrosis stage and diabetes-by-fibrosis interaction as factors, and baseline body weight and baseline value of parameter as covariates. Missing data were imputed from the observed data in the placebo group using the same ANCOVA model but without treatment as factor. ANCOVA: Analysis of covariance, MI: Multiple imputation, N: Number of subjects with baseline assessment, CI: Confidence interval, OD: Once daily, ETD: Estimated treatment difference.

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