

# CONFIDENTIAL

CRCTU Birmingham

A 48-WEEK PHASE II, RANDOMISED, DOUBLE BLINDED  
PLACEBO CONTROLLED, PARALLEL-GROUP,  
MULTI-CENTRE TRIAL ON LIRAGLUTIDE'S SAFETY,  
EFFICACY AND ACTION ON LIVER HISTOLOGY AND  
METABOLISM IN OVERWEIGHT PATIENTS WITH  
NON-ALCOHOLIC STEATOHEPATITIS, WITH OR WITHOUT  
TYPE II DIABETES

Liraglutide Efficacy and Action in Non-alcoholic  
steatohepatitis

The word "LEAN" is written in a large, blue, serif font. The letters have a slight 3D effect with a darker blue shadow on the right side of each letter.

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Senior Statistician

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Data For Clinical Measurements

## Contents

# **1 Trial results for measurements**

## **1.1 Clinical Chemistry Data**

Table 1.1: Creatinine ( $\mu\text{mol/L}$ ) by treatment and Visit Number

Liraglutide (N=170)								
	1 (N=26)	3 (N=26)	4 (N=25)	5 (N=23)	6 (N=24)	7 (N=23)	8 (N=23)	Overall (N=170)
Creatinine (micro mol/L)								
N	26	26	24	23	24	23	23	169
Mean (SD)	83 (20)	81 (16)	80 (18)	79 (17)	81 (17)	83 (17)	79 (14)	81 (17)
Median	81	81	78	78	80	81	76	79
IQR	71, 91	70, 88	69, 89	69, 91	67, 89	72, 93	72, 86	71, 89
Range	54, 136	51, 122	41, 124	47, 129	48, 123	48, 121	50, 111	41, 136

Placebo (N=164)								
	1 (N=26)	3 (N=25)	4 (N=24)	5 (N=23)	6 (N=22)	7 (N=22)	8 (N=22)	Overall (N=164)
Creatinine (micro mol/L)								
N	26	25	24	23	22	22	19	161
Mean (SD)	71 (15)	73 (15)	68 (12)	72 (16)	73 (16)	71 (16)	70 (16)	71 (15)
Median	75	76	68	73	70	73	68	72
IQR	59, 81	58, 84	57, 80	57, 84	60, 85	60, 84	60, 82	59, 82
Range	48, 98	50, 103	50, 85	47, 100	47, 105	43, 94	47, 102	43, 105

Figure 1.1: Creatinine Charts

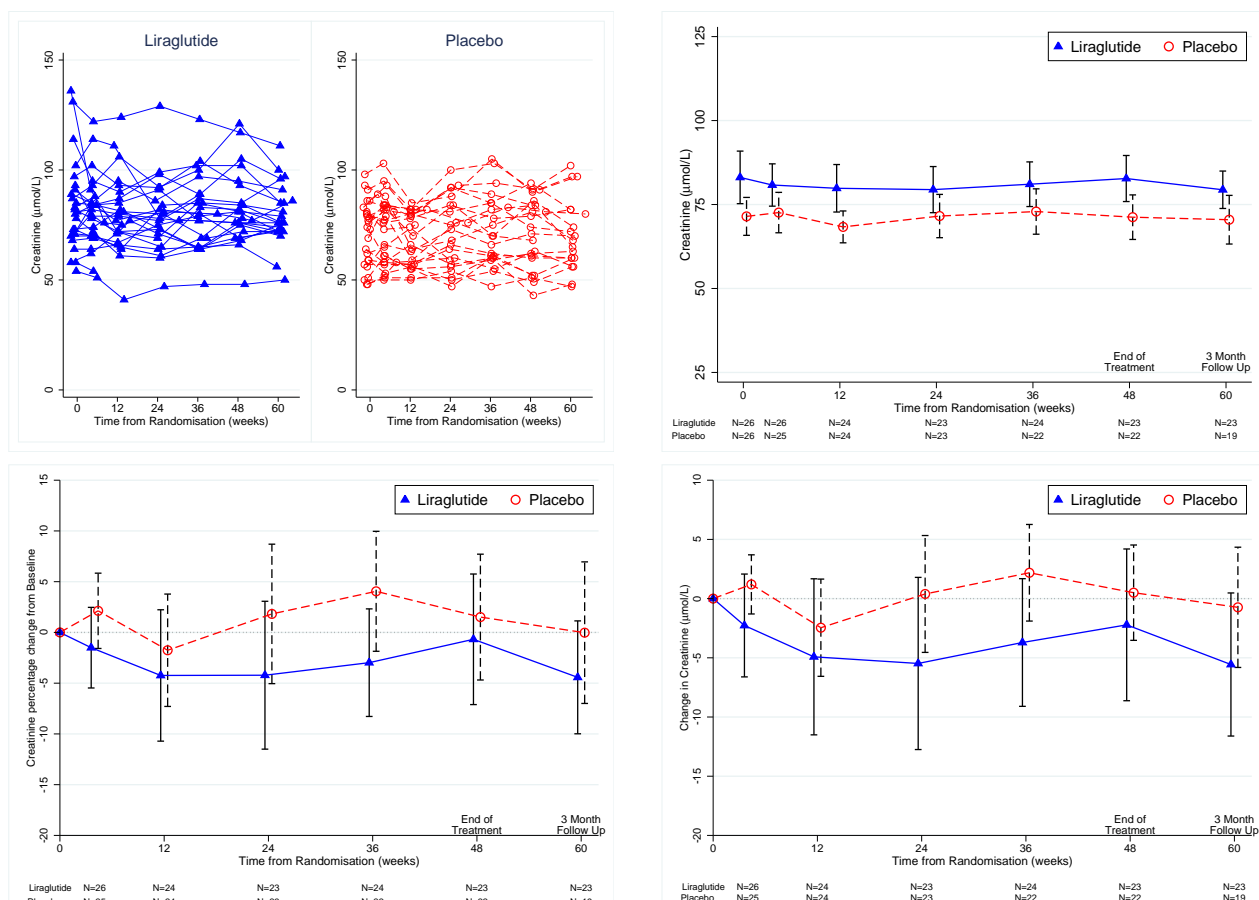


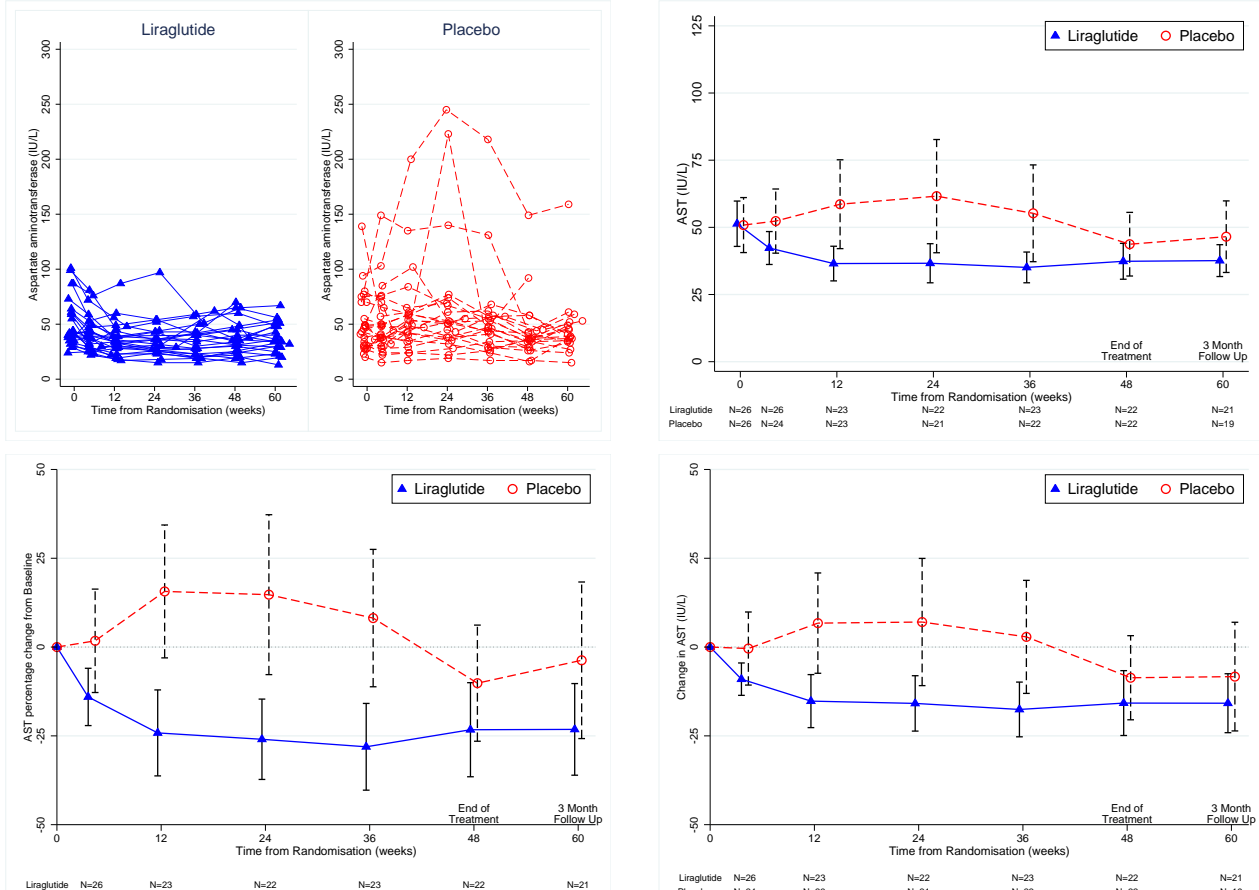
Table 1.2: AST (IU/L) by treatment and Visit Number

Liraglutide (N=170)								
	1 (N=26)	3 (N=26)	4 (N=25)	5 (N=23)	6 (N=24)	7 (N=23)	8 (N=23)	Overall (N=170)
<b>Aspartate aminotransferase (IU/L)</b>								
N	26	26	23	22	23	22	21	163
Mean (SD)	51 (22)	42 (16)	37 (16)	37 (17)	35 (14)	37 (16)	38 (14)	40 (17)
Median	42	40	34	34	34	35	35	36
IQR	35, 61	30, 49	28, 44	26, 43	23, 43	25, 45	29, 48	28, 48
Range	24, 101	22, 81	17, 87	15, 97	15, 62	15, 70	13, 67	13, 101

Placebo (N=164)								
	1 (N=26)	3 (N=25)	4 (N=24)	5 (N=23)	6 (N=22)	7 (N=22)	8 (N=22)	Overall (N=164)
<b>Aspartate aminotransferase (IU/L)</b>								
N	26	24	23	21	22	22	19	157
Mean (SD)	51 (27)	52 (30)	59 (40)	62 (49)	55 (43)	44 (28)	47 (30)	53 (36)
Median	47	45	49	51	47	37	39	44
IQR	31, 70	33, 68	35, 61	38, 67	30, 57	29, 44	34, 52	34, 58
Range	20, 139	15, 149	17, 200	19, 245	17, 218	16, 149	15, 159	15, 245

Figure 1.2: Aspartate aminotransferase Charts



This table for ALT does not include a value for one patient at visit 5 on placebo (presented on the individual data chart). A high value of 283 was reported but this was due to concomitant therapy.

Table 1.3: ALT (IU/L) by treatment and Visit Number

Liraglutide (N=170)								
	1 (N=26)	3 (N=26)	4 (N=25)	5 (N=23)	6 (N=24)	7 (N=23)	8 (N=23)	Overall (N=170)
<b>ALT</b>								
N	26	26	24	23	24	23	23	169
Mean (SD)	77 (34)	64 (26)	50 (21)	47 (21)	46 (21)	50 (24)	50 (28)	55 (27)
Median	74	65	46	43	51	45	52	53
IQR	43, 102	42, 78	35, 71	28, 56	26, 62	29, 71	28, 58	35, 73
Range	32, 151	23, 132	18, 91	14, 92	15, 88	14, 92	14, 126	14, 151

Placebo (N=164)								
	1 (N=26)	3 (N=25)	4 (N=24)	5 (N=23)	6 (N=22)	7 (N=22)	8 (N=22)	Overall (N=164)
<b>ALT</b>								
N	26	24	24	21	22	22	19	158
Mean (SD)	66 (42)	64 (34)	67 (42)	67 (52)	64 (37)	57 (34)	55 (28)	63 (39)
Median	56	56	65	56	56	50	50	55
IQR	44, 79	38, 79	36, 76	37, 75	42, 65	39, 64	41, 62	39, 73
Range	11, 209	14, 171	14, 211	12, 228	14, 168	18, 172	19, 155	11, 228

Figure 1.3: Alanine aminotransferase Charts

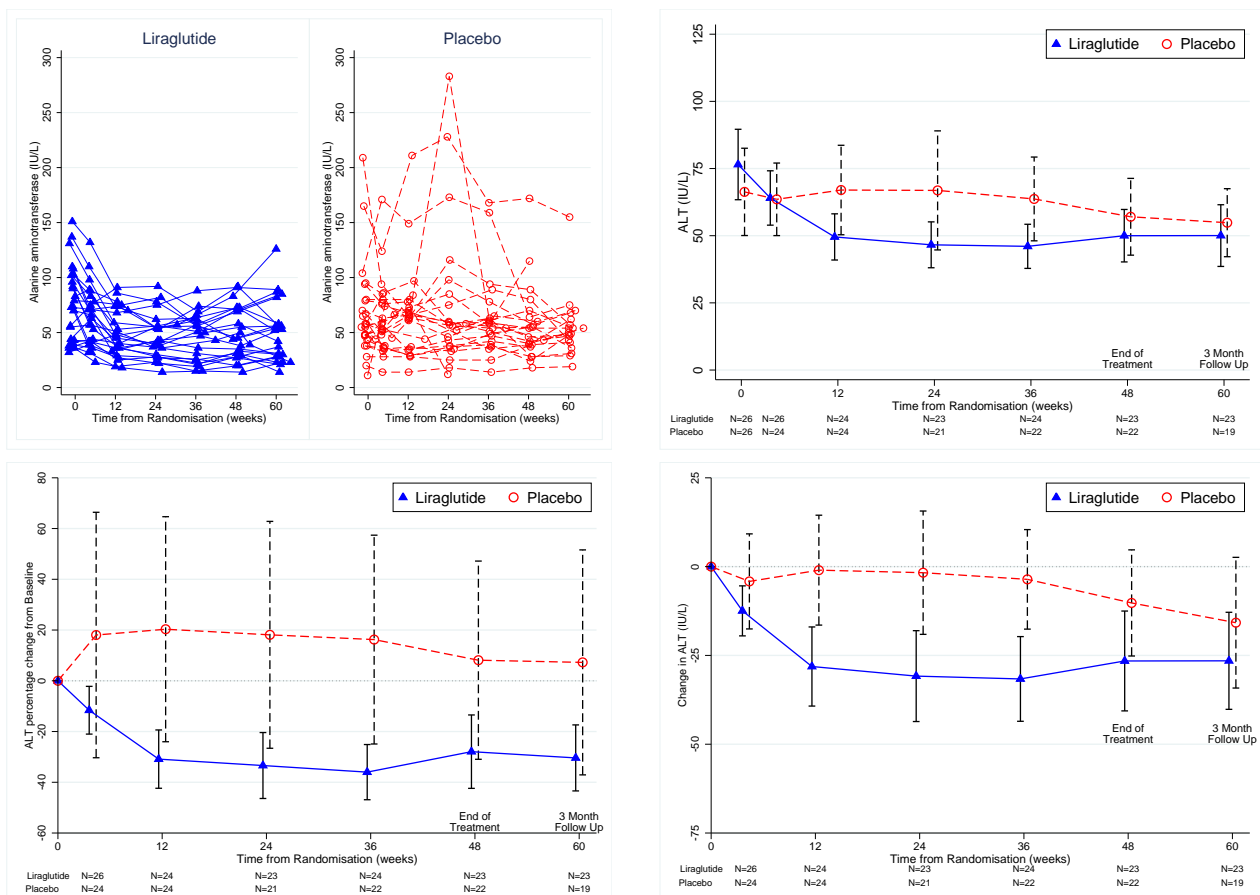


Table 1.4: ALP (IU/L) by treatment and Visit Number

Liraglutide (N=170)								
	1 (N=26)	3 (N=26)	4 (N=25)	5 (N=23)	6 (N=24)	7 (N=23)	8 (N=23)	Overall (N=170)
<b>Alkaline Phosphatase (IU/L)</b>								
N	26	26	24	23	24	23	23	169
Mean (SD)	76 (25)	74 (24)	67 (18)	69 (17)	68 (21)	69 (20)	71 (24)	71 (21)
Median	70	67	64	68	65	68	66	66
IQR	57, 87	56, 89	55, 78	56, 83	53, 77	53, 79	56, 77	55, 79
Range	43, 140	44, 143	43, 109	45, 105	44, 126	47, 126	41, 136	41, 143

Placebo (N=164)								
	1 (N=26)	3 (N=25)	4 (N=24)	5 (N=23)	6 (N=22)	7 (N=22)	8 (N=22)	Overall (N=164)
<b>Alkaline Phosphatase (IU/L)</b>								
N	26	25	24	23	22	22	19	161
Mean (SD)	87 (41)	83 (41)	81 (39)	87 (38)	82 (40)	81 (37)	83 (43)	83 (39)
Median	76	71	70	73	72	71	67	72
IQR	61, 88	58, 84	63, 83	66, 94	59, 86	59, 83	59, 77	61, 86
Range	39, 231	37, 216	17, 185	39, 195	37, 201	33, 188	37, 201	17, 231

Figure 1.4: Alkaline Phosphatase Charts

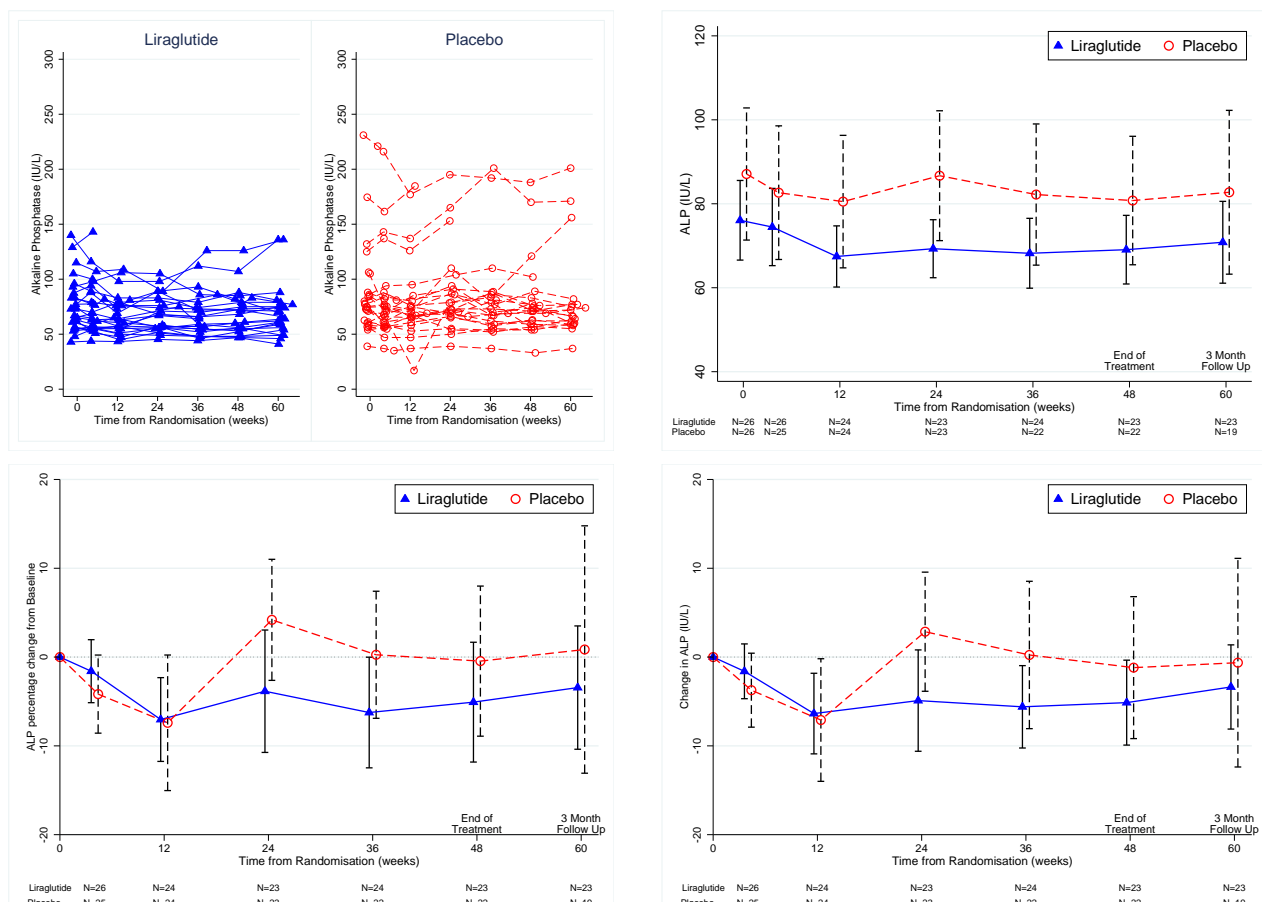


Table 1.5: GGT (IU/L) by treatment and Visit Number

Liraglutide (N=170)								
	1 (N=26)	3 (N=26)	4 (N=25)	5 (N=23)	6 (N=24)	7 (N=23)	8 (N=23)	Overall (N=170)
Gamma Glutamyltransferase (IU/L)								
N	25	26	22	21	21	22	23	160
Mean (SD)	91 (69)	65 (54)	60 (39)	52 (41)	55 (40)	58 (49)	56 (42)	63 (50)
Median	58	45	46	41	36	39	38	42
IQR	42, 125	32, 67	35, 93	28, 43	29, 77	28, 63	33, 73	31, 79
Range	25, 251	20, 237	19, 147	20, 169	16, 168	17, 218	15, 200	15, 251

Placebo (N=164)								
	1 (N=26)	3 (N=25)	4 (N=24)	5 (N=23)	6 (N=22)	7 (N=22)	8 (N=22)	Overall (N=164)
Gamma Glutamyltransferase (IU/L)								
N	25	24	23	21	22	22	19	156
Mean (SD)	115 (174)	111 (177)	105 (158)	108 (134)	75 (45)	74 (49)	76 (57)	96 (128)
Median	64	69	53	70	61	65	57	64
IQR	43, 140	40, 118	41, 121	42, 112	45, 101	31, 84	34, 102	41, 111
Range	16, 907	16, 915	19, 803	17, 636	14, 162	11, 182	12, 233	11, 915

Figure 1.5: Gamma Glutamyltransferase Charts

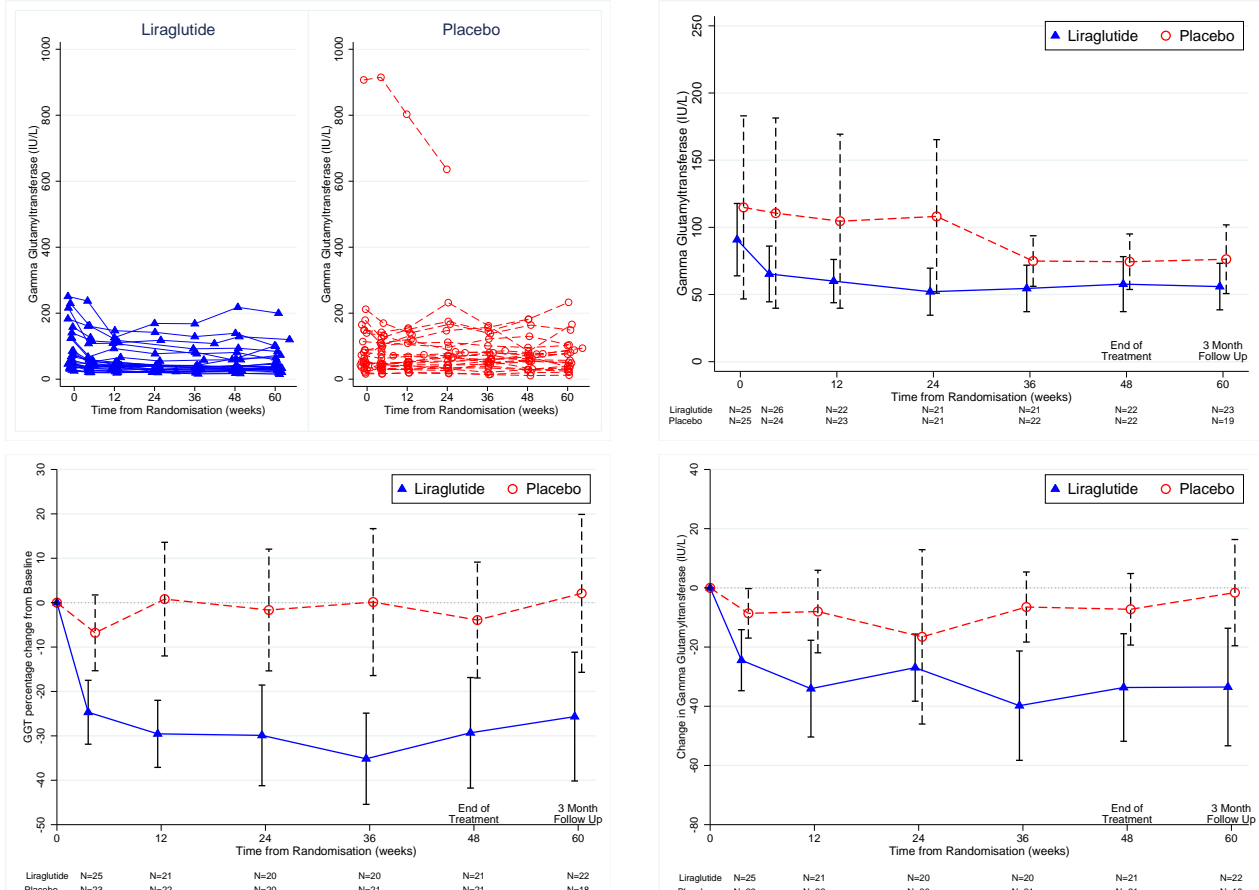




Table 1.6: Bilirubin ( $\mu\text{mol/L}$ ) by treatment and Visit Number

Liraglutide (N=170)								
	1 (N=26)	3 (N=26)	4 (N=25)	5 (N=23)	6 (N=24)	7 (N=23)	8 (N=23)	Overall (N=170)
Bilirubin (micro mol/L)								
N	26	26	24	23	24	23	23	169
Mean (SD)	13 (5)	11 (4)	12 (4)	12 (8)	12 (6)	12 (7)	13 (7)	12 (6)
Median	13	12	11	11	10	9	10	11
IQR	10, 16	9, 13	8, 15	7, 14	8, 17	7, 15	7, 15	8, 15
Range	3, 24	4, 20	4, 22	4, 37	4, 24	3, 26	4, 38	3, 38

Placebo (N=164)								
	1 (N=26)	3 (N=25)	4 (N=24)	5 (N=23)	6 (N=22)	7 (N=22)	8 (N=22)	Overall (N=164)
Bilirubin (micro mol/L)								
N	26	24	24	22	22	22	19	159
Mean (SD)	13 (7)	12 (6)	14 (6)	15 (6)	16 (9)	13 (7)	14 (8)	14 (7)
Median	13	11	14	15	15	11	12	13
IQR	8, 16	8, 13	10, 16	12, 18	9, 18	9, 16	8, 20	9, 17
Range	5, 35	5, 27	6, 24	5, 30	6, 42	4, 34	6, 32	4, 42

Figure 1.6: Bilirubin Charts

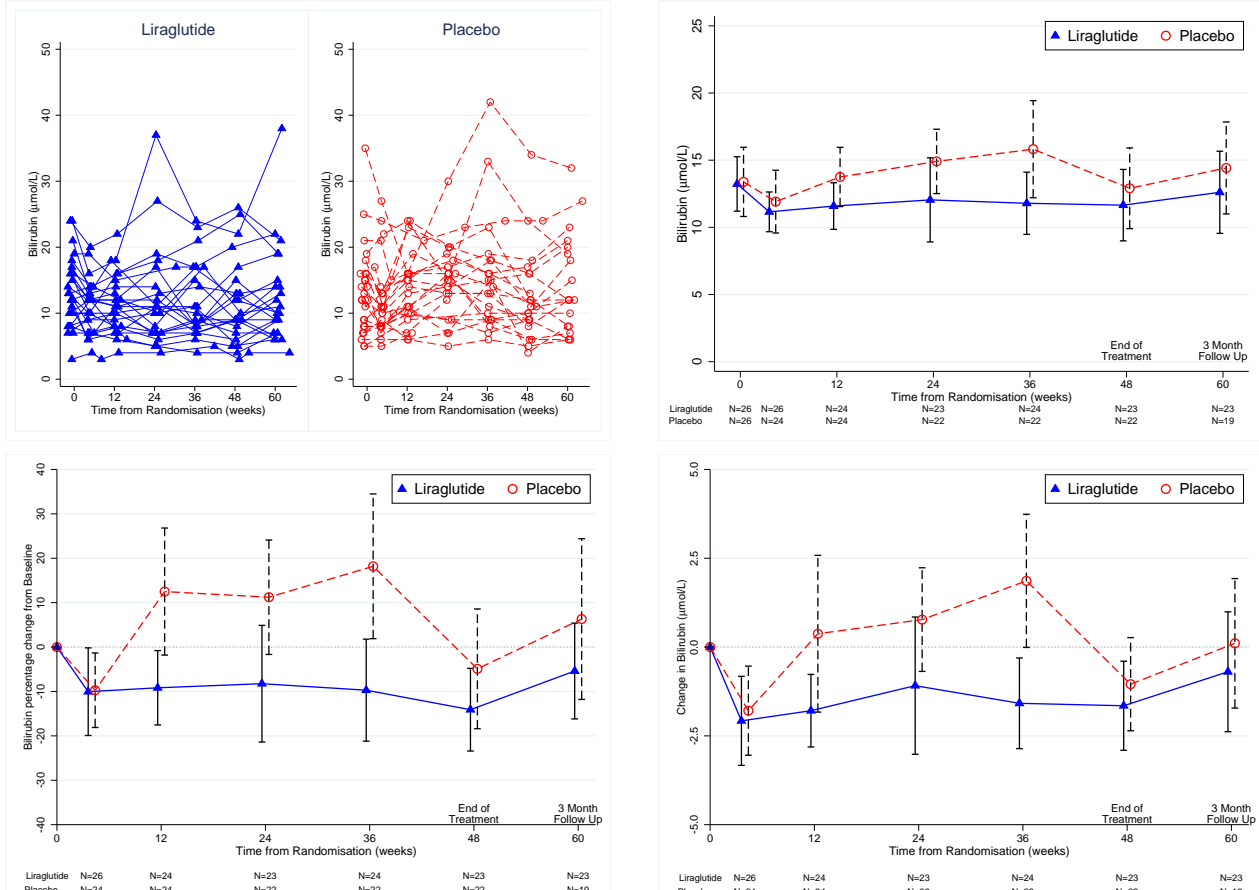


Table 1.7: Albumin (g/L) by treatment and Visit Number

Liraglutide (N=170)								
	1 (N=26)	3 (N=26)	4 (N=25)	5 (N=23)	6 (N=24)	7 (N=23)	8 (N=23)	Overall (N=170)
Albumin (g/L)								
N	26	26	24	23	24	23	23	169
Mean (SD)	45 (6)	44 (5)	43 (4)	44 (4)	44 (5)	45 (5)	45 (5)	44 (5)
Median	47	45	43	45	45	46	44	45
IQR	42, 48	42, 48	40, 48	39, 47	42, 48	43, 48	42, 48	41, 48
Range	34, 55	36, 51	37, 52	35, 48	34, 51	34, 52	36, 52	34, 55

Placebo (N=164)								
	1 (N=26)	3 (N=25)	4 (N=24)	5 (N=23)	6 (N=22)	7 (N=22)	8 (N=22)	Overall (N=164)
Albumin (g/L)								
N	26	24	24	23	22	22	19	160
Mean (SD)	43 (5)	42 (4)	42 (4)	42 (4)	43 (4)	42 (5)	43 (5)	42 (4)
Median	43	42	43	44	44	44	42	43
IQR	41, 46	42, 45	39, 45	41, 45	40, 45	38, 45	39, 47	39, 45
Range	34, 51	32, 48	36, 52	35, 50	34, 49	32, 49	35, 51	32, 52

Figure 1.7: Albumin Charts

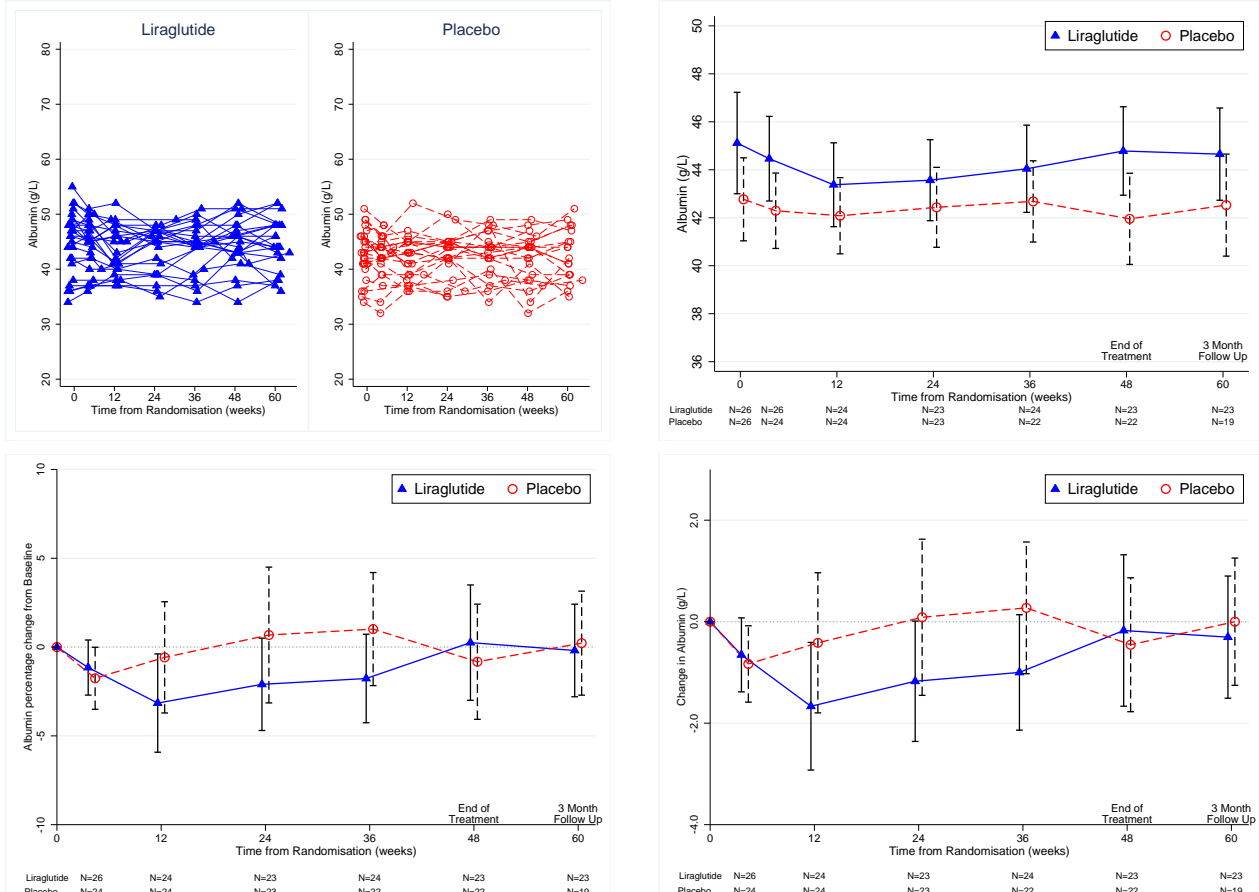


Table 1.8: Total Cholesterol (mmol/L) by treatment and Visit Number

Liraglutide (N=120)						
	1 (N=26)	4 (N=25)	5 (N=23)	7 (N=23)	8 (N=23)	Overall (N=120)
Total Cholesterol (mmol/L)						
N	26	23	23	22	23	117
Mean (SD)	4.50 (1.06)	3.99 (1.24)	4.05 (1.21)	4.43 (1.31)	4.43 (1.19)	4.28 (1.20)
Median	4.35	3.90	3.90	4.30	4.20	4.20
IQR	4.00, 5.30	3.20, 4.80	3.10, 5.10	3.90, 5.40	3.80, 5.50	3.50, 5.20
Range	2.00, 6.40	1.80, 6.50	1.90, 6.20	1.90, 7.30	1.70, 6.40	1.70, 7.30

Placebo (N=117)						
	1 (N=26)	4 (N=24)	5 (N=23)	7 (N=22)	8 (N=22)	Overall (N=117)
Total Cholesterol (mmol/L)						
N	24	24	22	21	19	110
Mean (SD)	4.97 (1.18)	4.96 (1.35)	5.00 (1.28)	4.85 (1.17)	4.97 (1.35)	4.95 (1.24)
Median	4.85	4.80	5.00	4.80	4.80	4.80
IQR	4.10, 5.75	4.05, 5.70	4.10, 5.50	4.10, 5.40	4.00, 5.60	4.10, 5.70
Range	3.20, 8.10	2.40, 9.10	2.60, 8.30	2.20, 7.20	2.70, 8.90	2.20, 9.10

Figure 1.8: Total Cholesterol Charts

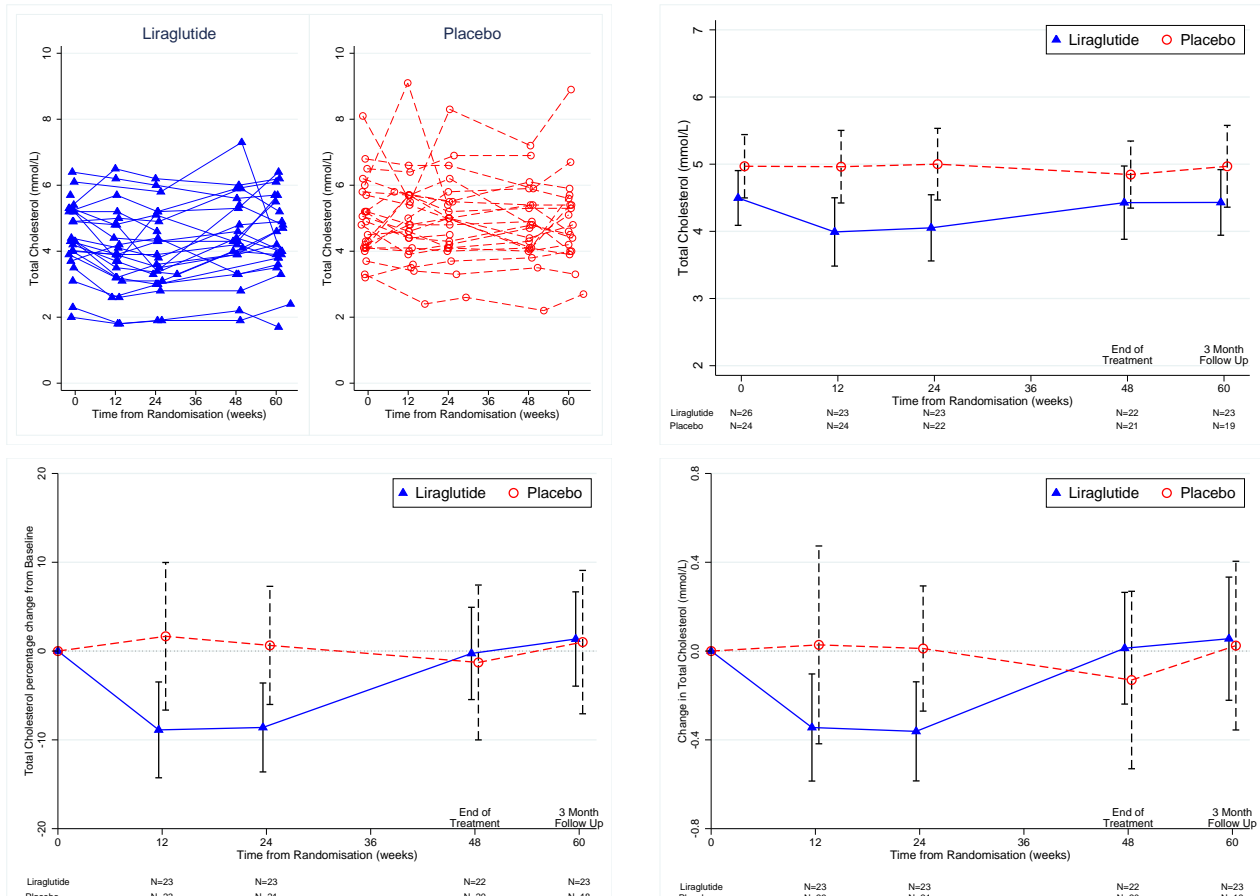


Table 1.9: Triglycerades (mmol/L) by treatment and Visit Number

Liraglutide (N=120)						
	1 (N=26)	4 (N=25)	5 (N=23)	7 (N=23)	8 (N=23)	Overall (N=120)
Triglycerides (mmol/L)						
N	26	23	23	22	23	117
Mean (SD)	1.93 (1.05)	1.69 (0.75)	1.56 (0.67)	1.74 (0.87)	1.78 (0.69)	1.75 (0.82)
Median	1.60	1.47	1.41	1.50	1.70	1.58
IQR	1.20, 2.40	1.10, 2.20	1.10, 1.80	1.10, 2.08	1.30, 2.00	1.20, 2.03
Range	0.70, 5.15	0.60, 3.35	0.70, 3.30	0.80, 4.30	0.80, 3.90	0.60, 5.15

Placebo (N=117)						
	1 (N=26)	4 (N=24)	5 (N=23)	7 (N=22)	8 (N=22)	Overall (N=117)
Triglycerides (mmol/L)						
N	24	24	22	21	19	110
Mean (SD)	1.77 (0.81)	1.96 (1.51)	1.55 (0.62)	1.81 (1.53)	1.52 (0.74)	1.73 (1.11)
Median	1.64	1.75	1.60	1.60	1.40	1.60
IQR	1.30, 2.05	1.15, 2.10	1.10, 1.94	1.20, 1.85	1.10, 1.80	1.10, 2.00
Range	0.57, 4.70	0.72, 8.50	0.53, 3.30	0.50, 8.00	0.60, 4.00	0.50, 8.50

Figure 1.9: Triglycerades Charts

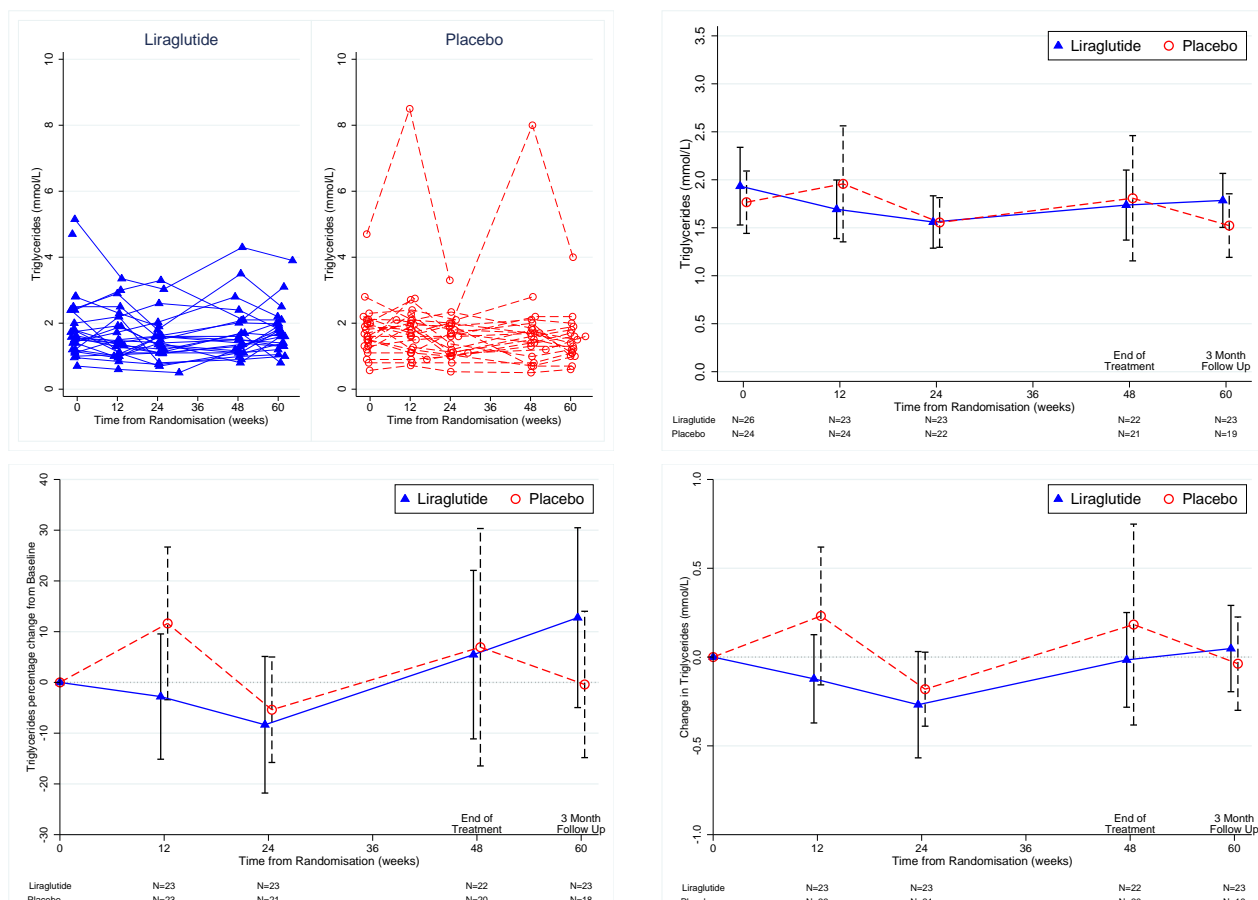


Table 1.10: High Density Lipoprotein (mmol/L) by treatment and Visit Number

Liraglutide (N=120)						
	1 (N=26)	4 (N=25)	5 (N=23)	7 (N=23)	8 (N=23)	Overall (N=120)
High Density Lipoprotein (mmol/L)						
N	25	22	23	22	21	113
Mean (SD)	1.10 (0.38)	1.00 (0.27)	1.12 (0.33)	1.24 (0.47)	1.24 (0.44)	1.14 (0.39)
Median	1.03	0.97	1.06	1.13	1.02	1.03
IQR	0.90, 1.15	0.80, 1.20	0.90, 1.32	0.90, 1.50	0.90, 1.60	0.90, 1.30
Range	0.61, 2.20	0.61, 1.60	0.63, 1.70	0.61, 2.40	0.70, 2.40	0.61, 2.40

Placebo (N=117)						
	1 (N=26)	4 (N=24)	5 (N=23)	7 (N=22)	8 (N=22)	Overall (N=117)
High Density Lipoprotein (mmol/L)						
N	25	23	21	19	17	105
Mean (SD)	1.27 (0.22)	1.17 (0.28)	1.28 (0.28)	1.26 (0.26)	1.24 (0.22)	1.24 (0.25)
Median	1.20	1.19	1.20	1.20	1.26	1.20
IQR	1.15, 1.40	0.97, 1.30	1.10, 1.47	1.05, 1.43	1.10, 1.40	1.08, 1.40
Range	0.88, 1.83	0.66, 1.80	0.85, 1.87	0.73, 1.77	0.90, 1.59	0.66, 1.87

Figure 1.10: High Density Lipoprotein Charts

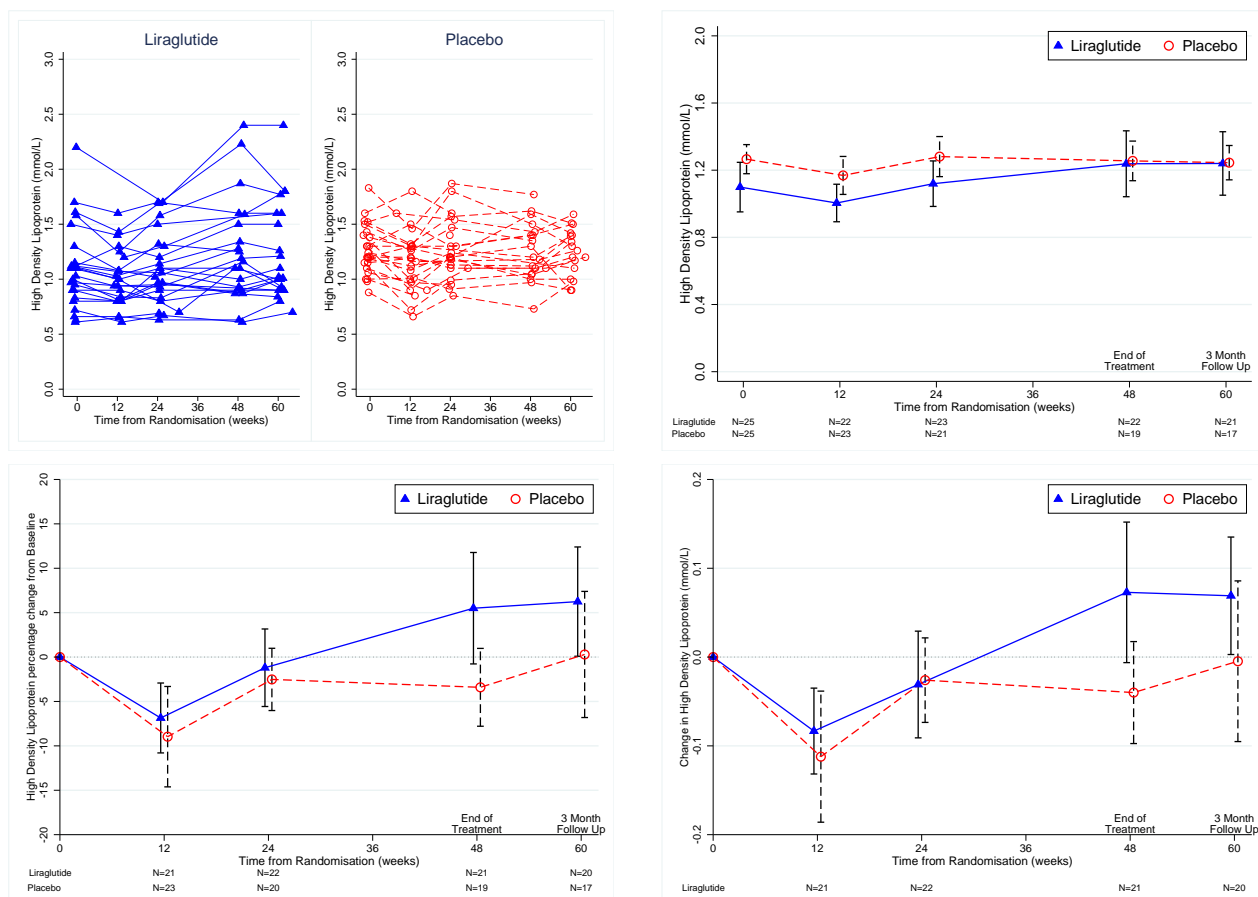


Table 1.11: Low Density Lipoprotein (mmol/L) by treatment and Visit Number

Liraglutide (N=120)						
	1 (N=26)	4 (N=25)	5 (N=23)	7 (N=23)	8 (N=23)	Overall (N=120)
Low Density Lipoprotein (mmol/L)						
N	23	21	22	20	20	106
Mean (SD)	2.61 (0.81)	2.35 (0.96)	2.33 (0.95)	2.51 (0.91)	2.51 (1.01)	2.46 (0.92)
Median	2.65	2.37	2.44	2.40	2.53	2.44
IQR	2.14, 3.31	1.74, 2.79	1.43, 3.04	1.95, 3.01	1.86, 3.39	1.83, 3.19
Range	0.38, 4.02	0.50, 3.96	0.50, 3.88	0.52, 4.40	0.34, 4.05	0.34, 4.40

Placebo (N=117)						
	1 (N=26)	4 (N=24)	5 (N=23)	7 (N=22)	8 (N=22)	Overall (N=117)
Low Density Lipoprotein (mmol/L)						
N	23	23	21	18	17	102
Mean (SD)	2.88 (1.03)	2.85 (0.89)	3.09 (1.10)	2.80 (0.90)	2.91 (0.93)	2.91 (0.96)
Median	2.86	2.94	2.94	2.67	2.94	2.90
IQR	2.12, 3.50	2.12, 3.55	2.34, 3.44	2.38, 3.37	2.56, 3.57	2.22, 3.50
Range	1.24, 5.22	1.09, 4.67	1.00, 5.79	0.55, 4.22	0.77, 4.50	0.55, 5.79

Figure 1.11: Low Density Lipoprotein Charts

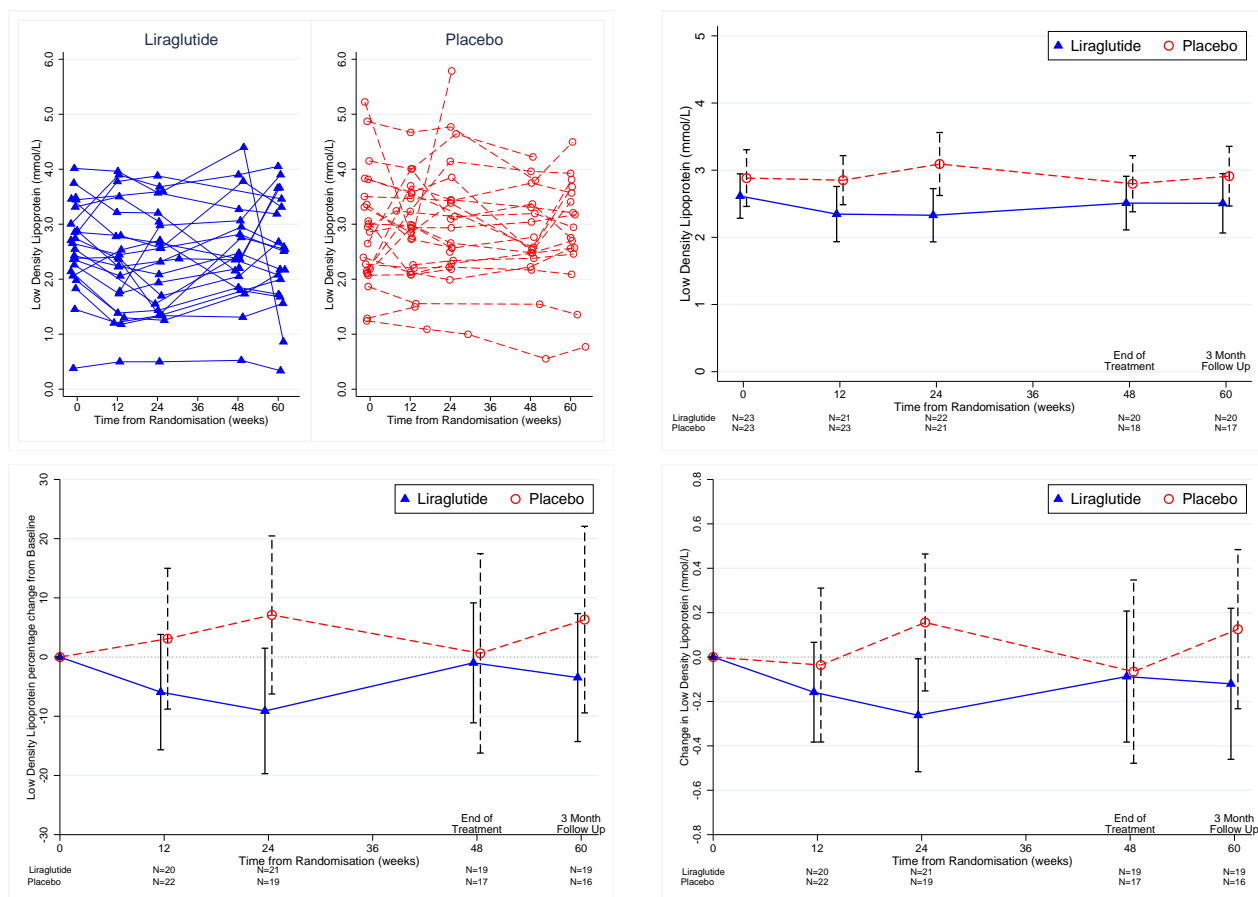


Table 1.12: Clinical chemistry change from baseline to 48 weeks (end of treatment visit)

	Liraglutide (N=26)	Placebo (N=26)	*Adjusted Change from baseline (95%CI)	p-value
Urea (mmol/L)	0.035 (0.823) N=23	-0.191 (1.359) N=22	0.427 (-0.256, 1.110)	0.21
Creatinine (micro mol/L)	-2.217 (15.681) N=23	0.500 (9.635) N=22	2.362 (-5.065, 9.789)	0.52
Potassium (mmol/L)	0.077 (0.329) N=23	-0.083 (0.259) N=22	0.128 (-0.028, 0.284)	0.11
Sodium (mmol/L)	-0.652 (2.822) N=23	0.136 (2.031) N=22	-0.626 (-1.772, 0.521)	0.28
Calcium (mmol/L)	0.024 (0.088) N=23	-0.018 (0.103) N=21	0.045 (-0.003, 0.094)	0.07
Magnesium (mmol/L)	0.017 (0.058) N=18	-0.002 (0.073) N=17	0.026 (-0.008, 0.061)	0.13
Phosphate (mmol/L)	0.052 (0.134) N=23	-0.033 (0.164) N=19	0.083 (-0.002, 0.168)	0.06
Aspartate aminotransferase (IU/L)	-15.8 (21.8) N=22	-8.6 (28.3) N=22	-6.7 (-19.3, 5.9)	0.29
Alanine aminotransferase (IU/L)	-26.6 (34.4) N=23	-10.2 (35.8) N=22	-10.7 (-25.9, 4.5)	0.16
Alkaline Phosphatase (IU/L)	-5.13 (11.70) N=23	-1.19 (19.13) N=22	-5.46 (-14.36, 3.43)	0.22
Gamma Glutamyltransferase (IU/L)	-33.7 (42.5) N=21	-7.2 (28.3) N=21	-22.8 (-40.4, -5.2)	<b>0.01</b>
Bilirubin (micro mol/L)	-1.65 (3.07) N=23	-1.05 (3.14) N=22	-0.63 (-2.52, 1.26)	0.51
Albumin (g/L)	-0.174 (3.651) N=23	-0.455 (3.158) N=22	1.138 (-0.707, 2.982)	0.22
Amylase (IU/L)	7.55 (16.47) N=20	2.55 (11.77) N=20	6.44 (-2.78, 15.66)	0.17
Total Cholesterol (mmol/L)	0.013 (0.602) N=22	-0.130 (0.912) N=20	0.066 (-0.427, 0.560)	0.79
Triglycerides (mmol/L)	-0.016 (0.638) N=22	0.183 (1.290) N=20	-0.197 (-0.834, 0.439)	0.53
High Density Lipoprotein (mmol/L)	0.073 (0.185) N=21	-0.040 (0.128) N=19	0.134 (0.029, 0.238)	<b>0.01</b>
Low Density Lipoprotein (mmol/L)	-0.088 (0.656) N=19	-0.066 (0.868) N=17	-0.126 (-0.622, 0.371)	0.61

Data are Mean (SD) and N numbers.

\*Change from baseline and p-values determined from linear regression analysis using the baseline characteristic score and treatment as covariates

## **1.2 Glucose, ELF, ELISA Data**



Table 1.13: Serum Glucose (mmol/L) by treatment and Visit Number

Liraglutide (N=170)								
	1 (N=26)	3 (N=26)	4 (N=25)	5 (N=23)	6 (N=24)	7 (N=23)	8 (N=23)	Overall (N=170)
Serum Glucose (mmol/L)								
N	25	26	24	23	22	23	23	166
Mean (SD)	6.0 (1.7)	5.2 (1.1)	5.0 (0.8)	5.0 (0.8)	5.0 (0.4)	5.0 (0.7)	5.5 (1.1)	5.3 (1.1)
Median	5.5	5.0	5.0	4.7	5.0	4.9	5.3	5.0
IQR	4.9, 6.7	4.6, 5.3	4.4, 5.5	4.6, 5.3	4.7, 5.3	4.3, 5.5	4.8, 5.5	4.6, 5.5
Range	3.9, 11.9	3.6, 8.0	3.7, 7.1	4.1, 7.3	4.2, 5.8	3.6, 6.4	4.1, 9.5	3.6, 11.9

Placebo (N=164)								
	1 (N=26)	3 (N=25)	4 (N=24)	5 (N=23)	6 (N=22)	7 (N=22)	8 (N=22)	Overall (N=164)
Serum Glucose (mmol/L)								
N	26	25	24	23	22	22	19	161
Mean (SD)	6.1 (1.5)	5.9 (1.6)	6.1 (1.6)	5.8 (1.6)	5.8 (1.2)	6.5 (2.8)	6.5 (2.9)	6.1 (1.9)
Median	5.6	5.4	5.6	5.5	5.6	5.8	5.5	5.6
IQR	5.1, 6.7	4.8, 6.5	5.2, 6.7	4.7, 6.3	4.8, 6.9	4.7, 7.4	5.0, 6.4	5.0, 6.5
Range	4.3, 10.1	4.4, 10.3	4.1, 10.3	4.2, 12.0	4.2, 8.3	4.1, 16.4	4.6, 16.1	4.1, 16.4

Figure 1.12: Serum Glucose (mmol/L) Charts

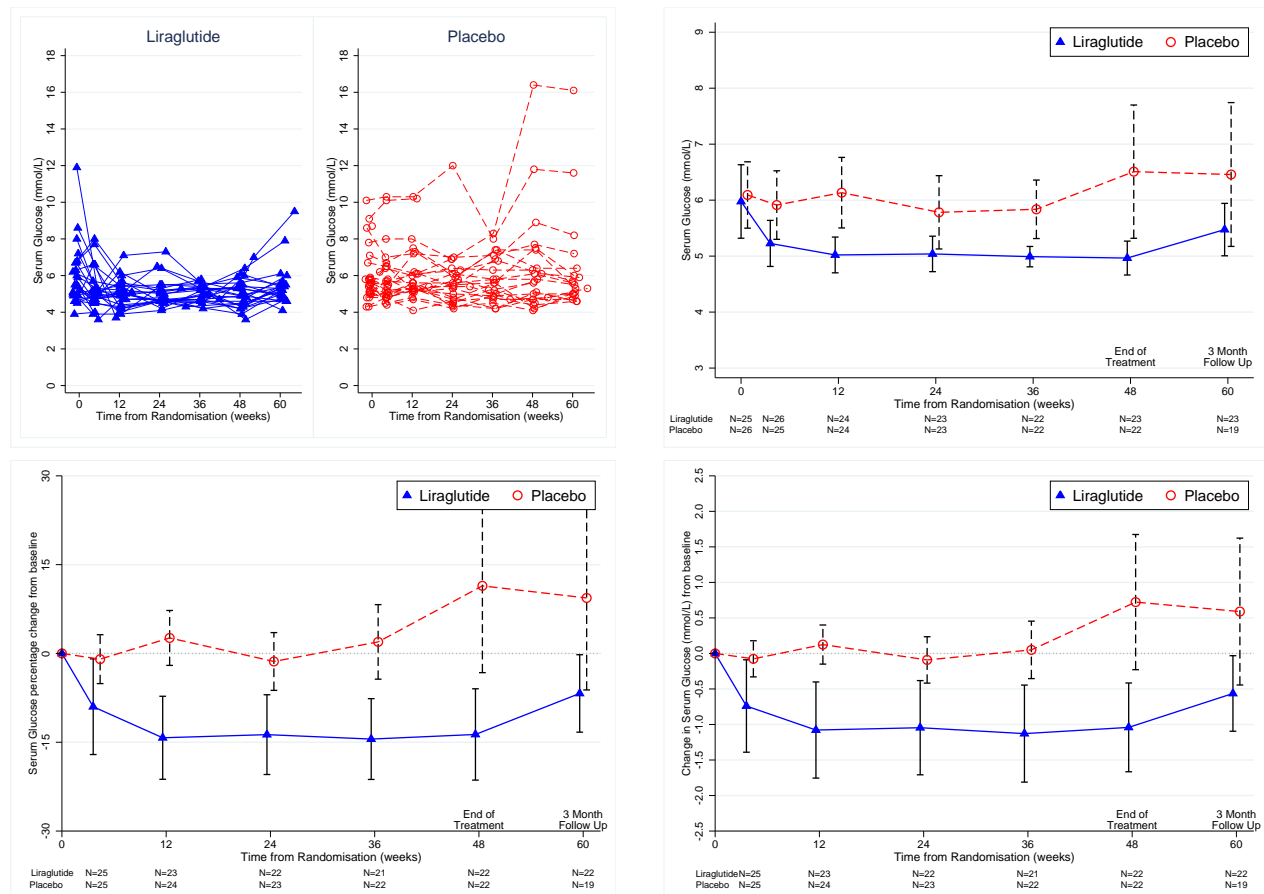


Table 1.14: HbA<sub>1C</sub> (%) Charts by treatment and Visit Number

Liraglutide (N=144)							
	1 (N=26)	4 (N=25)	5 (N=23)	6 (N=24)	7 (N=23)	8 (N=23)	Overall (N=144)
<b>HbA<sub>1C</sub> (%)</b>							
N	26	22	23	23	22	22	138
Mean (SD)	5.9 (0.7)	5.5 (0.5)	5.4 (0.5)	5.5 (0.4)	5.4 (0.4)	5.8 (0.7)	5.6 (0.6)
Median	5.8	5.5	5.4	5.5	5.4	5.8	5.5
IQR	5.3, 6.3	5.1, 5.6	5.1, 5.6	5.2, 5.7	5.1, 5.6	5.2, 6.1	5.2, 5.8
Range	5.0, 7.4	4.6, 6.8	4.7, 6.9	4.9, 6.5	4.8, 6.3	4.9, 7.5	4.6, 7.5

Placebo (N=139)							
	1 (N=26)	4 (N=24)	5 (N=23)	6 (N=22)	7 (N=22)	8 (N=22)	Overall (N=139)
<b>HbA<sub>1C</sub> (%)</b>							
N	26	23	23	19	21	16	128
Mean (SD)	6.0 (0.9)	6.2 (1.1)	6.0 (0.8)	5.9 (0.6)	5.8 (1.1)	6.2 (1.5)	6.0 (1.0)
Median	5.8	5.8	5.8	5.8	5.6	5.8	5.8
IQR	5.5, 6.3	5.5, 6.3	5.4, 6.6	5.5, 6.3	5.2, 5.9	5.3, 6.7	5.4, 6.3
Range	5.0, 8.3	5.2, 9.7	4.7, 8.1	5.2, 7.5	3.7, 9.1	4.6, 10.8	3.7, 10.8

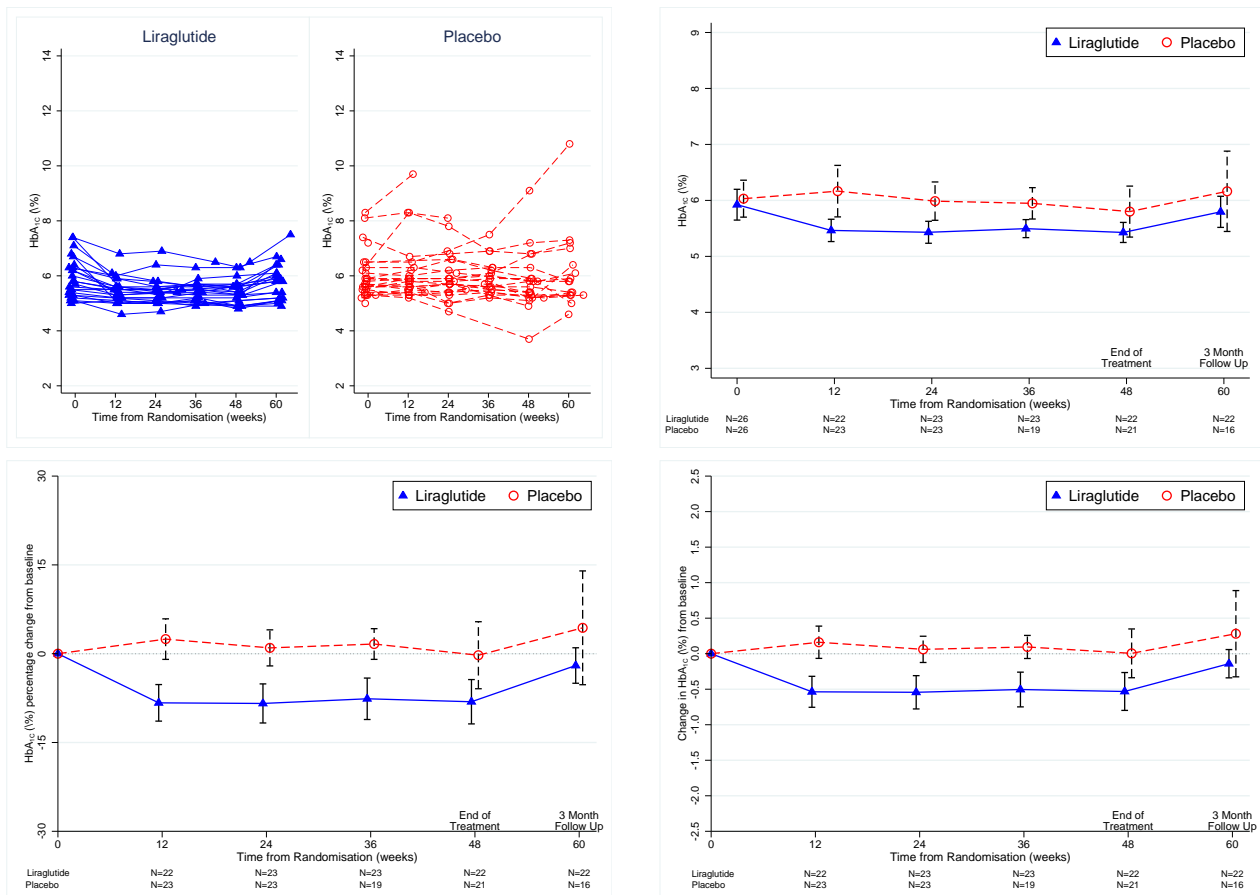
Figure 1.13: HbA<sub>1C</sub> (%) Charts

Table 1.15: HbA<sub>1C</sub> (mmol/mol) by treatment and Visit Number

Liraglutide (N=144)							
	1 (N=26)	4 (N=25)	5 (N=23)	6 (N=24)	7 (N=23)	8 (N=23)	Overall (N=144)
<b>HbA<sub>1C</sub> (mmol/mol)</b>							
N	26	22	23	23	22	22	138
Mean (SD)	41.2 (7.8)	36.2 (5.3)	35.9 (5.3)	36.6 (4.4)	35.8 (4.7)	39.8 (7.4)	37.7 (6.3)
Median	40.0	36.5	36.0	37.0	36.0	40.0	37.0
IQR	34.0, 45.0	32.0, 38.0	32.0, 38.0	33.0, 39.0	32.0, 38.0	33.0, 43.0	33.0, 40.0
Range	31.0, 57.0	27.0, 51.0	28.0, 52.0	30.0, 48.0	29.0, 45.0	30.0, 59.0	27.0, 59.0

Placebo (N=139)							
	1 (N=26)	4 (N=24)	5 (N=23)	6 (N=22)	7 (N=22)	8 (N=22)	Overall (N=139)
<b>HbA<sub>1C</sub> (mmol/mol)</b>							
N	26	23	23	19	21	16	128
Mean (SD)	42.4 (9.3)	44.0 (12.3)	42.0 (9.2)	41.5 (6.7)	39.9 (11.7)	43.8 (16.1)	42.2 (10.9)
Median	39.5	40.0	40.0	40.0	38.0	40.0	40.0
IQR	37.0, 45.0	37.0, 45.0	36.0, 49.0	37.0, 45.0	33.0, 41.0	34.0, 49.5	36.0, 45.0
Range	31.0, 67.0	33.0, 83.0	28.0, 65.0	33.0, 58.0	17.0, 76.0	27.0, 95.0	17.0, 95.0

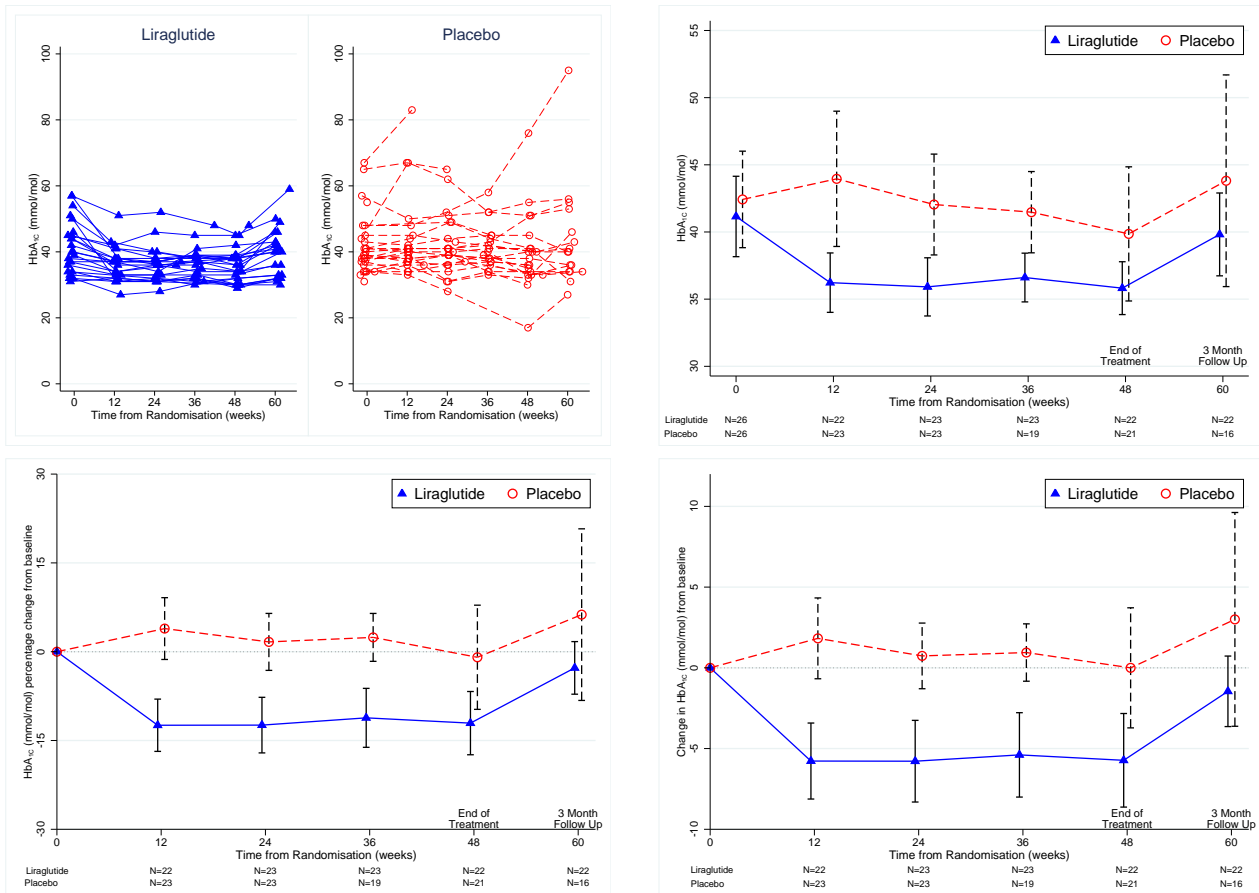
Figure 1.14: HbA<sub>1C</sub> (mmol/mol) Charts

Table 1.16: Serum Insulin (pmol/L) by treatment and Visit Number

<b>Liraglutide</b> (N=120)						
	<b>1</b> (N=26)	<b>4</b> (N=25)	<b>5</b> (N=23)	<b>7</b> (N=23)	<b>8</b> (N=23)	<b>Overall</b> (N=120)
<b>Serum Insulin (pmol/L)</b>						
N	26	23	22	23	23	117
Mean (SD)	166 (80)	176 (113)	168 (189)	149 (84)	152 (98)	162 (116)
Median	135	130	117	135	111	130
IQR	114, 198	93, 206	77, 190	77, 223	81, 190	91, 203
Range	42, 351	64, 453	44, 960	36, 331	48, 407	36, 960

<b>Placebo</b> (N=117)						
	<b>1</b> (N=26)	<b>4</b> (N=24)	<b>5</b> (N=23)	<b>7</b> (N=22)	<b>8</b> (N=22)	<b>Overall</b> (N=117)
<b>Serum Insulin (pmol/L)</b>						
N	26	21	20	22	20	109
Mean (SD)	257 (289)	222 (220)	170 (137)	246 (290)	165 (85)	215 (225)
Median	169	158	110	152	167	153
IQR	99, 232	99, 214	91, 181	95, 292	100, 187	96, 209
Range	45, 1166	59, 995	67, 557	32, 1396	84, 463	32, 1396

Figure 1.15: Serum Insulin (pmol/L) Charts

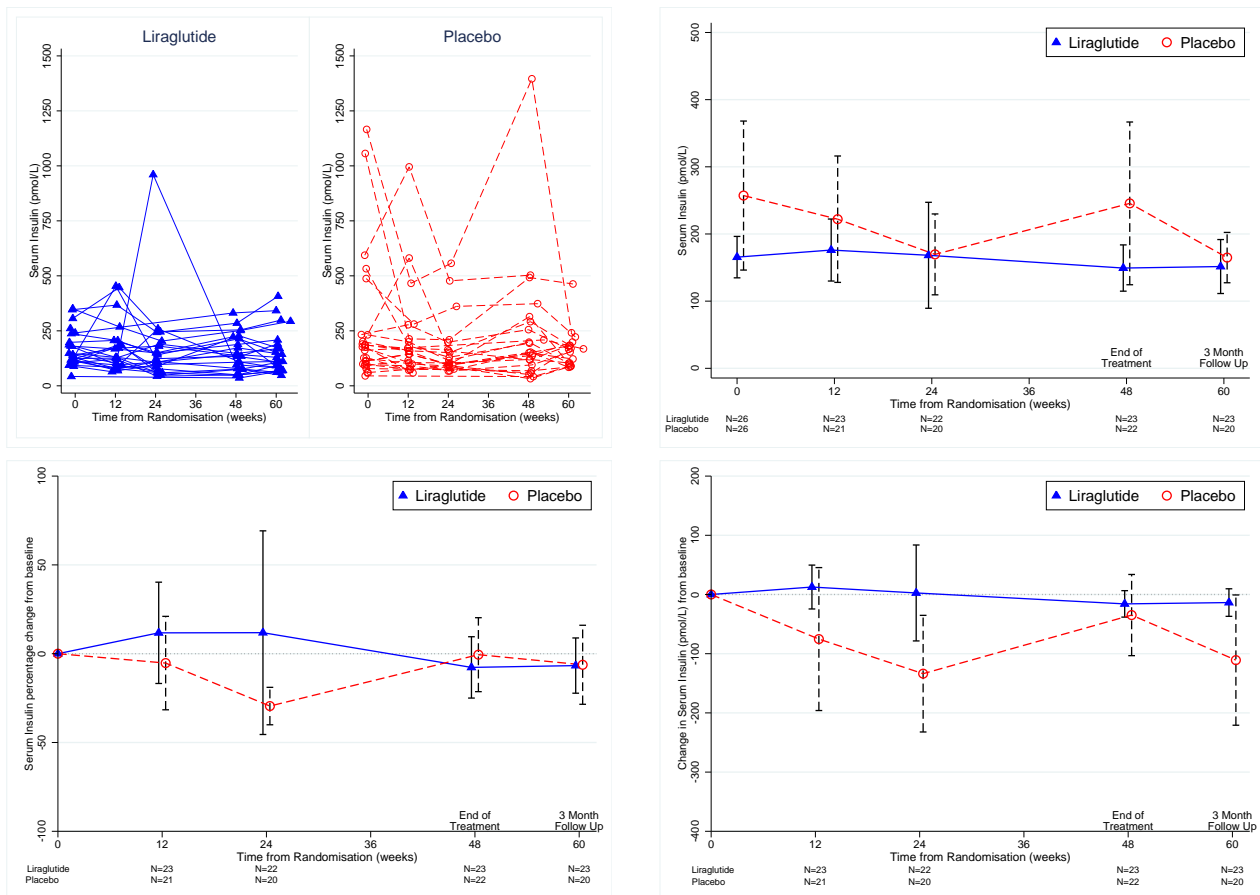


Table 1.17: HOMA-IR (mmol.IU.L) by treatment and Visit Number

Liraglutide (N=120)						
	1 (N=26)	4 (N=25)	5 (N=23)	7 (N=23)	8 (N=23)	Overall (N=120)
HOMA-IR (mmol.IU.L)						
N	25	22	22	23	23	115
Mean (SD)	6.7 (4.7)	5.8 (4.4)	5.9 (8.0)	4.9 (3.1)	5.6 (4.5)	5.8 (5.1)
Median	5.1	4.2	3.9	4.6	4.2	4.6
IQR	4.1, 7.3	2.8, 6.7	2.1, 5.8	2.4, 7.7	2.4, 6.5	2.8, 6.9
Range	3.0, 23.3	1.5, 18.0	1.3, 39.9	1.0, 11.2	1.4, 17.8	1.0, 39.9

Placebo (N=117)						
	1 (N=26)	4 (N=24)	5 (N=23)	7 (N=22)	8 (N=22)	Overall (N=117)
HOMA-IR (mmol.IU.L)						
N	26	21	20	22	19	108
Mean (SD)	9.6 (9.8)	9.0 (9.5)	6.3 (5.1)	10.8 (14.3)	6.5 (3.3)	8.6 (9.4)
Median	5.5	5.7	3.8	6.0	5.8	5.7
IQR	3.5, 11.1	3.6, 8.8	2.9, 7.7	3.8, 13.9	3.3, 8.4	3.4, 9.6
Range	1.7, 41.8	2.5, 38.3	1.9, 21.0	0.9, 66.1	2.8, 13.7	0.9, 66.1

Figure 1.16: HOMA-IR (mmol.IU.L) Charts

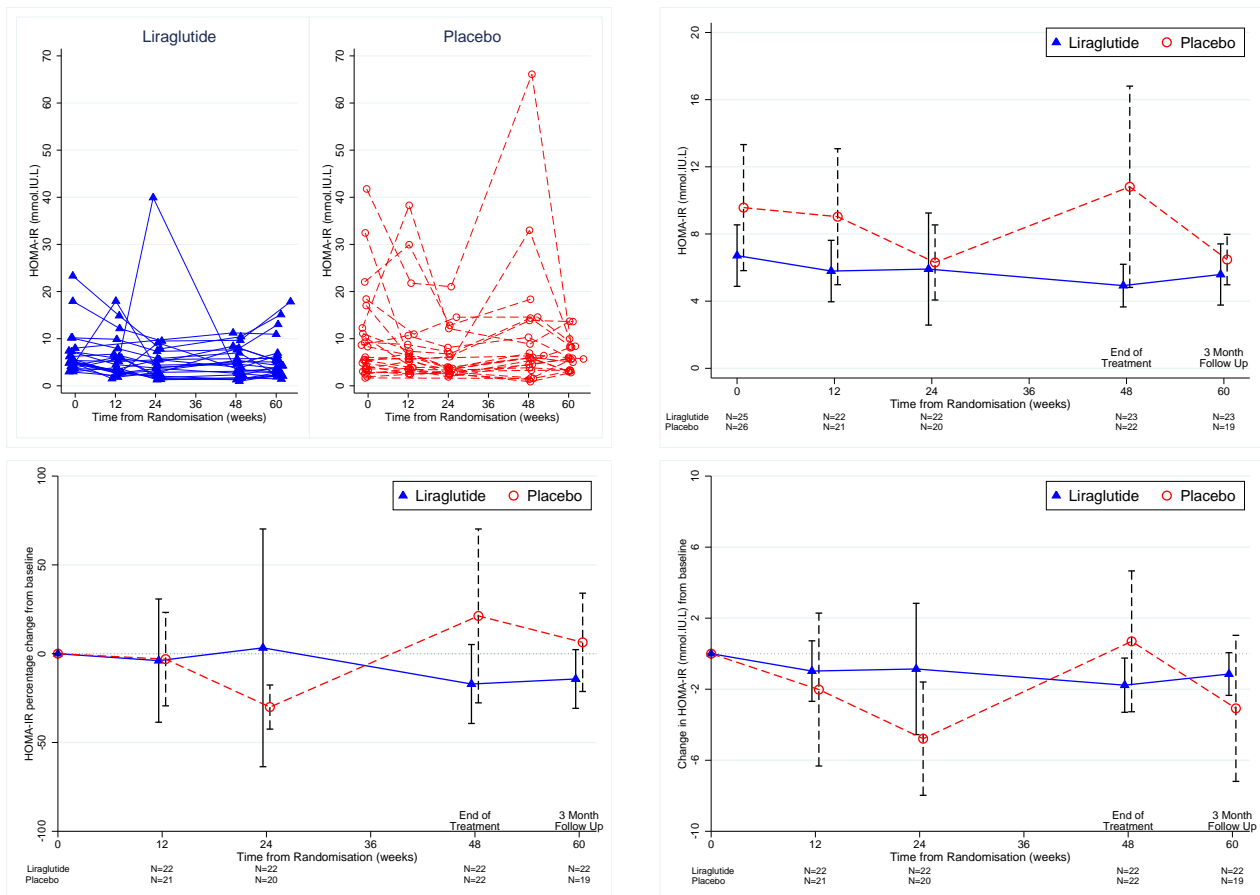


Table 1.18: NEFA ( $\mu\text{mol.L}$ ) by treatment and Visit Number

Liraglutide (N=120)						
	1 (N=26)	4 (N=25)	5 (N=23)	7 (N=23)	8 (N=23)	Overall (N=120)
NEFA ( $\mu\text{mol.L}$ )						
N	26	23	23	23	22	117
Mean (SD)	967 (535)	773 (361)	852 (432)	727 (398)	821 (368)	832 (428)
Median	895	797	793	641	823	801
IQR	730, 1094	491, 913	557, 1028	488, 870	629, 920	557, 967
Range	360, 3219	237, 1772	173, 1900	282, 2067	273, 1865	173, 3219

Placebo (N=117)						
	1 (N=26)	4 (N=24)	5 (N=23)	7 (N=22)	8 (N=22)	Overall (N=117)
NEFA ( $\mu\text{mol.L}$ )						
N	26	22	21	22	20	111
Mean (SD)	836 (368)	1002 (466)	793 (363)	703 (268)	841 (471)	835 (397)
Median	835	983	706	599	721	774
IQR	516, 1078	721, 1203	548, 849	468, 960	490, 1074	540, 1018
Range	392, 1707	16, 1980	406, 1621	223, 1150	157, 2097	16, 2097

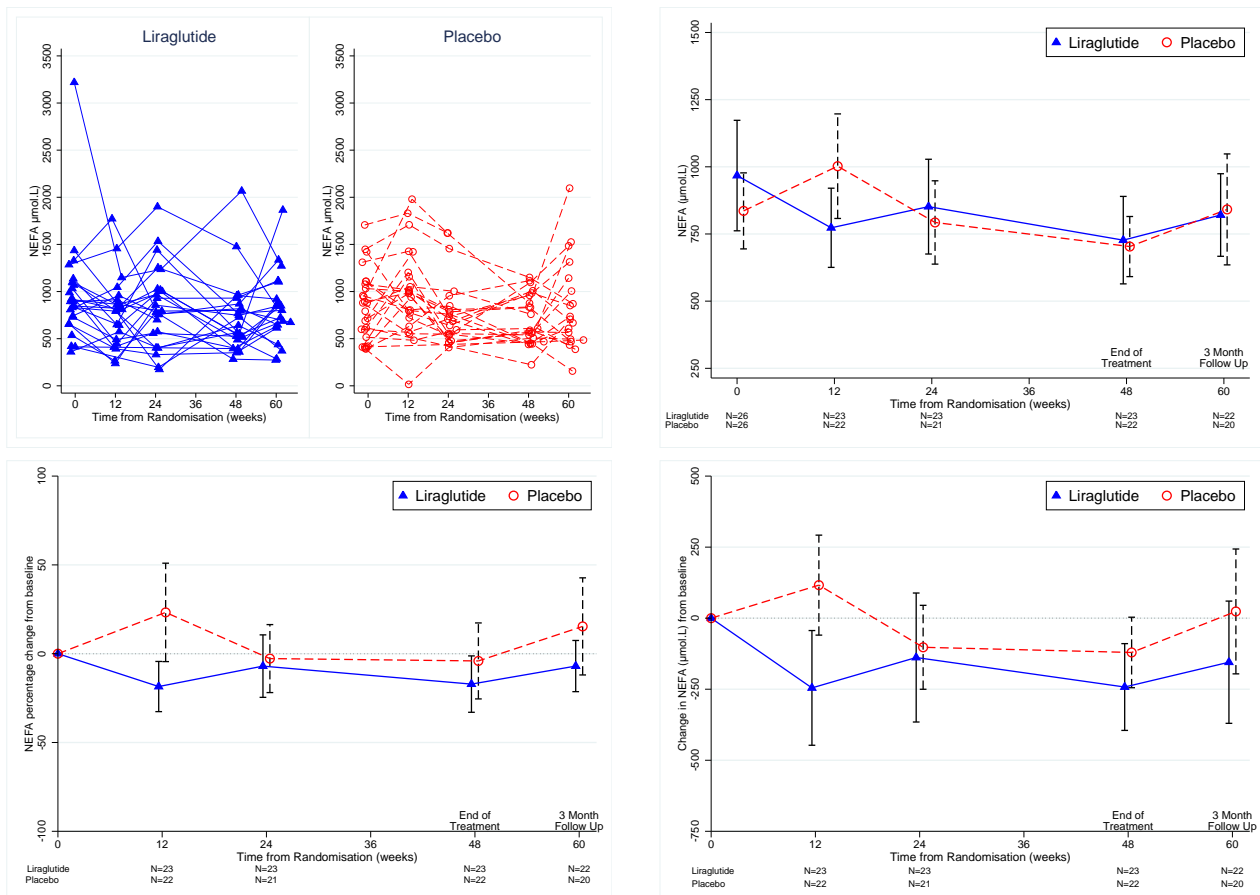
Figure 1.17: NEFA ( $\mu\text{mol.L}$ ) Charts

Table 1.19: ADIPO-IR (mmol.IU.L) by treatment and Visit Number

Liraglutide (N=120)						
	1 (N=26)	4 (N=25)	5 (N=23)	7 (N=23)	8 (N=23)	Overall (N=120)
ADIPO-IR (mmol.IU.L)						
N	26	23	22	23	22	116
Mean (SD)	22.2 (12.7)	18.3 (12.1)	18.4 (15.9)	14.2 (8.8)	17.9 (14.0)	18.3 (12.9)
Median	17.6	14.4	15.8	11.1	16.1	15.7
IQR	14.4, 28.2	9.4, 24.1	8.5, 23.2	7.2, 19.1	8.7, 22.3	9.1, 23.4
Range	2.6, 51.5	2.9, 51.7	4.5, 77.0	3.7, 38.1	2.5, 65.5	2.5, 77.0

Placebo (N=117)						
	1 (N=26)	4 (N=24)	5 (N=23)	7 (N=22)	8 (N=22)	Overall (N=117)
ADIPO-IR (mmol.IU.L)						
N	26	21	20	22	20	109
Mean (SD)	30.5 (42.7)	32.3 (33.0)	18.8 (14.3)	25.0 (27.4)	18.6 (12.3)	25.4 (29.4)
Median	18.8	20.7	11.0	16.2	16.3	17.5
IQR	11.2, 30.1	12.7, 28.3	9.9, 26.0	8.9, 31.1	11.5, 21.1	10.6, 29.0
Range	2.6, 220.2	8.2, 141.3	5.4, 53.9	2.1, 112.3	4.5, 58.0	2.1, 220.2

Figure 1.18: ADIPO-IR (mmol.IU.L) Charts

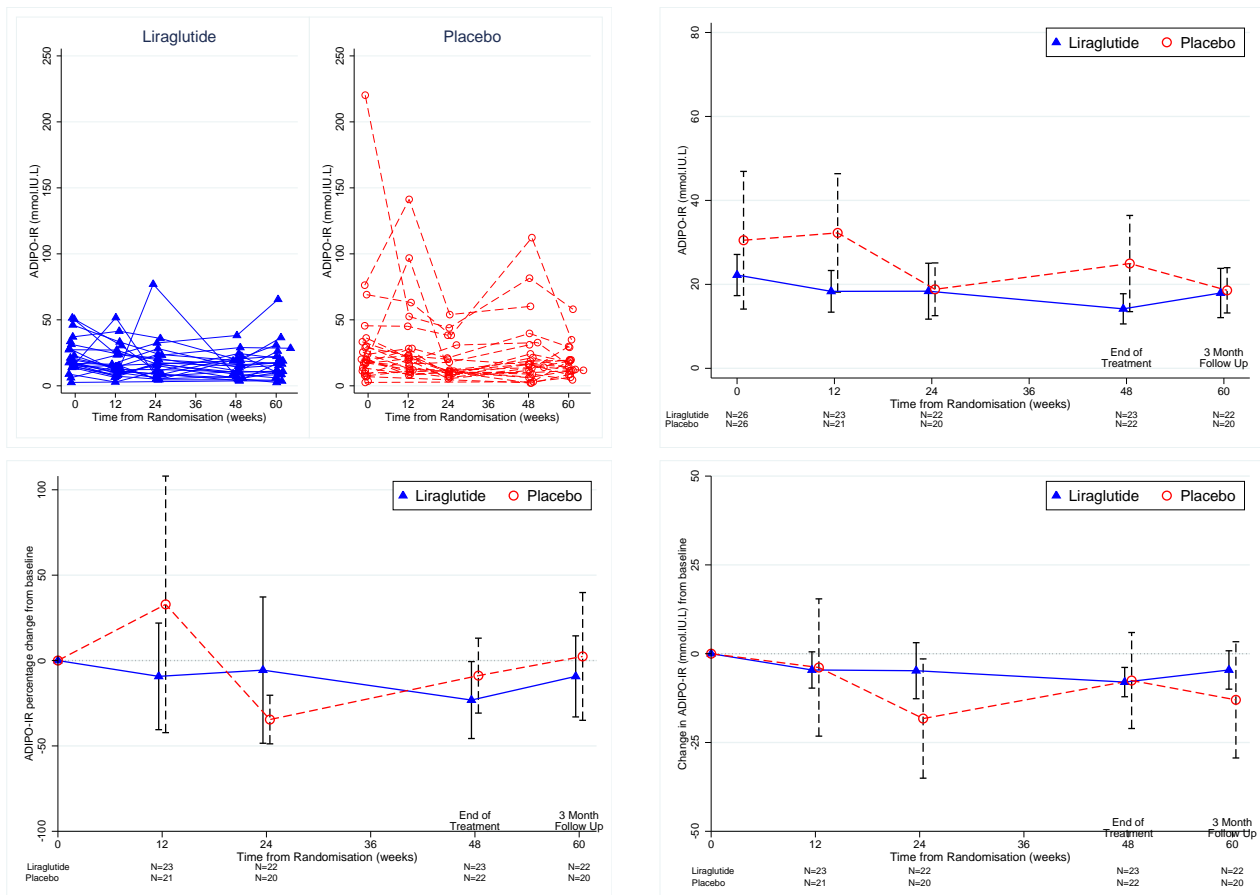


Table 1.20: Enhanced Liver Fibrosis (ELF) test result by treatment and Visit Number

Liraglutide (N=72)				
	1 (N=26)	7 (N=23)	8 (N=23)	Overall (N=72)
Enhanced Liver Fibrosis (ELF) test				
N	26	23	22	71
Mean (SD)	9.3 (0.9)	9.1 (0.8)	9.3 (0.8)	9.2 (0.8)
Median	9.2	9.1	9.3	9.2
IQR	8.6, 9.7	8.7, 9.4	8.9, 9.6	8.8, 9.6
Range	7.9, 12.2	6.9, 10.8	7.2, 10.8	6.9, 12.2

Placebo (N=70)				
	1 (N=26)	7 (N=22)	8 (N=22)	Overall (N=70)
Enhanced Liver Fibrosis (ELF) test				
N	26	22	20	68
Mean (SD)	9.4 (1.3)	9.6 (1.2)	9.4 (1.3)	9.5 (1.3)
Median	9.3	9.5	9.0	9.2
IQR	8.4, 10.4	8.9, 10.1	8.4, 10.0	8.5, 10.2
Range	7.1, 12.1	8.0, 12.4	7.4, 12.5	7.1, 12.5

Figure 1.19: Enhanced Liver Fibrosis (ELF) test Charts

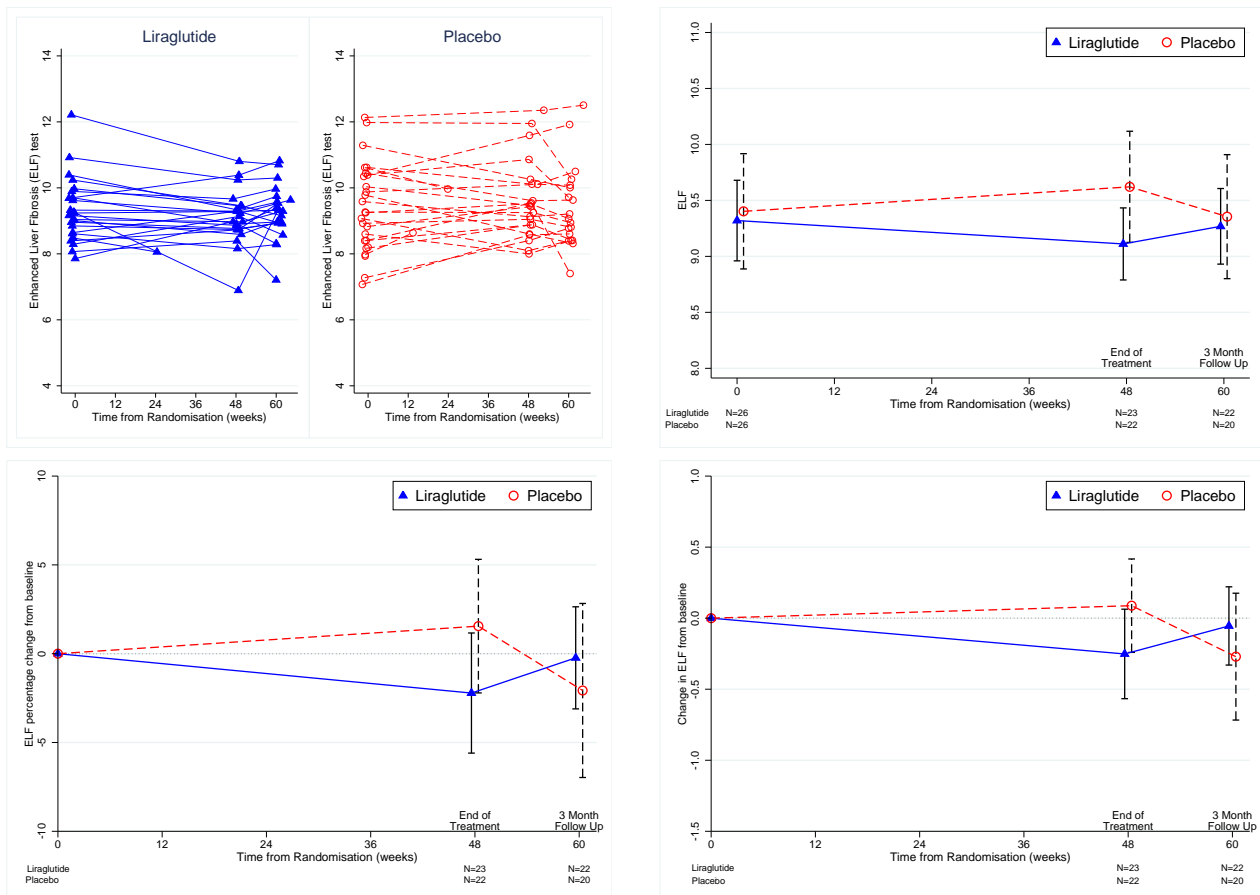




Table 1.21: Cytokeratin-18 M30 (IU/L) by treatment and Visit Number

Liraglutide (N=72)				
	1 (N=26)	7 (N=23)	8 (N=23)	Overall (N=72)
Cytokeratin-18 M30 (IU/L)				
N	26	23	23	72
Mean (SD)	394 (304)	190 (168)	259 (287)	286 (272)
Median	311	111	136	186
IQR	163, 509	77, 277	65, 234	87, 335
Range	65, 1175	44, 668	47, 1070	44, 1175

Placebo (N=70)				
	1 (N=26)	7 (N=22)	8 (N=22)	Overall (N=70)
Cytokeratin-18 M30 (IU/L)				
N	25	22	20	67
Mean (SD)	352 (370)	274 (204)	283 (287)	306 (297)
Median	163	236	203	204
IQR	125, 447	93, 380	118, 267	109, 418
Range	54, 1371	64, 857	57, 1216	54, 1371

Figure 1.20: Cytokeratin-18 M30 (IU/L) Charts

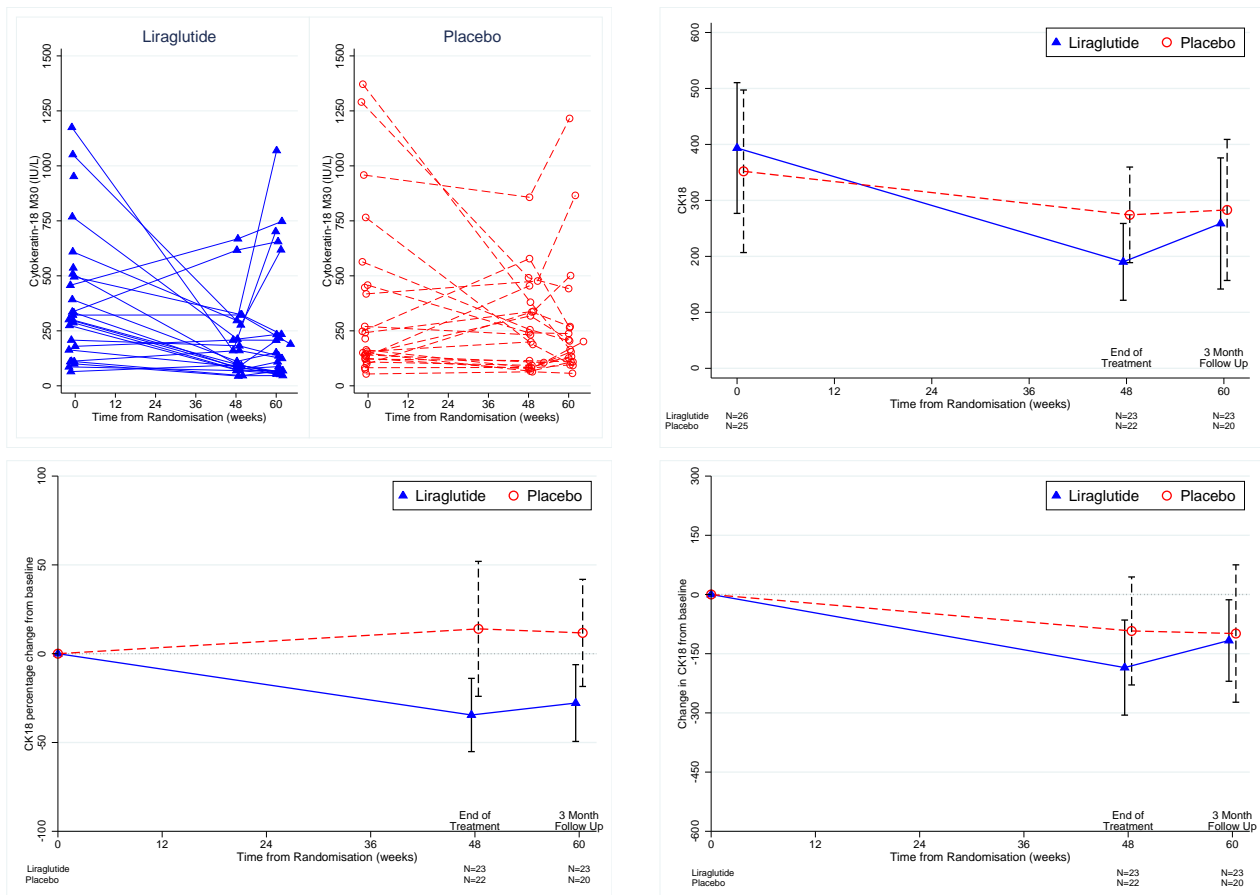


Table 1.22: Further sample results change from baseline to 48 weeks (end of treatment visit)

	Liraglutide (N=26)	Placebo (N=26)	*Adjusted Change from baseline (95%CI)	p-value
Glucose (mmol/L)	-1.04 (1.49) N=22	0.72 (2.28) N=22	-1.67 (-2.81, -0.53)	<b>0.005</b>
HbA <sub>1C</sub> (%)	-0.53 (0.64) N=22	0.00 (0.80) N=21	-0.48 (-0.91, -0.05)	<b>0.03</b>
HbA <sub>1C</sub> (mmol/mol)	-5.73 (6.94) N=22	0.00 (8.69) N=21	-5.18 (-9.91, -0.44)	<b>0.03</b>
Insulin (pmol/L)	-15.9 (54.7) N=23	-34.7 (164.1) N=22	-4.0 (-75.0, 67.0)	0.91
HOMA-IR (mmol.IU.L)	-1.77 (3.65) N=22	0.70 (9.49) N=22	-2.74 (-7.24, 1.76)	0.23
NEFA ( $\mu$ mol.L)	-242 ( 374) N=23	-121 ( 297) N=22	-49 ( -200, 101)	0.51
ADIPO-IR (mmol.IU.L)	-7.99 (10.09) N=23	-7.55 (32.34) N=22	-6.34 (-15.09, 2.41)	0.15
Cytokeratin-18 (IU/L)	-185 ( 295) N=23	-92 ( 327) N=22	-86 ( -188, 16)	0.10
Enhanced Liver Fibrosis (ELF) test	-0.25 (0.77) N=23	0.09 (0.79) N=22	-0.40 (-0.80, 0.00)	0.05

Data are Mean (SD) and N numbers.

\*Change from baseline and p-values determined from linear regression analysis using the baseline characteristic score and treatment as covariates