

## 9. Efficacy data

### 9.4 Secondary efficacy endpoint: MRI/MRS sub-study

Change in body fat redistribution as measured by MRI/MRS at T+24 weeks between telmisartan treated arm(s) and the control arm.

- Reduction in visceral fat at T+24 weeks between telmisartan treated arms and control arm
- Change in intrahepatic fat at T+24 weeks between telmisartan treated arms and control arm
- Change in lower leg muscle fat at T+24 weeks between telmisartan treated arms and control arm

**Note:** Internal visceral fat is the MRI outcome measure of interest (measured in dm<sup>3</sup>). The other MRI measures in Tables (b-e) are not of interest in terms of clinical hypotheses. Their summaries were added for completeness.

**Table 9-1 Summary statistics for the MRI and 1H MRS measurements (outcome x) at baseline and 24weeks by treatment group**

#### (a) Internal visceral fat (dm<sup>3</sup>)

	Baseline				Measurement at 24 weeks			
	Control: Non intervention N=13	20 mg daily N=10	40 mg daily N=10	80mg daily N=10	Control: Non intervention N=13	20 mg daily N=10	40 mg daily N=10	80mg daily N=10
n	8 (61.5%)	7 (70.0%)	6 (60.0%)	8 (80.0%)	8 (61.5%)	7 (70.0%)	5 (50.0%)	8 (80.0%)
Mean	3.53	5.15	3.58	4.10	3.74	5.18	4.42	4.74
Sd	1.08	2.20	2.70	2.71	1.43	2.67	2.06	2.59
Min	1.64	2.60	1.78	0.70	1.62	1.93	2.54	0.69
Max	5.06	8.33	8.79	8.04	5.69	9.55	7.04	8.98
Median	3.30	5.42	2.34	3.58	3.25	4.93	3.33	4.62
Q1	2.84	2.81	2.01	1.64	2.89	2.45	2.95	2.44
Q3	4.20	7.24	4.21	5.61	4.74	7.46	6.23	5.84
Missing	5 (38.5%)	3 (30.0%)	4 (40.0%)	2 (20.0%)	5 (38.5%)	3 (30.0%)	5 (50.0%)	2 (20.0%)

#### (b) External abdominal fat (dm<sup>3</sup>)

	Baseline				Measurement at 24 weeks			
	Control: Non intervention N=13	20 mg daily N=10	40 mg daily N=10	80mg daily N=10	Control: Non intervention N=13	20 mg daily N=10	40 mg daily N=10	80mg daily N=10
N	8 (61.5%)	7 (70.0%)	6 (60.0%)	8 (80.0%)	8 (61.5%)	7 (70.0%)	5 (50.0%)	8 (80.0%)
Mean	5.04	6.37	4.09	3.43	5.08	6.66	5.06	3.80
Sd	3.58	3.13	2.28	1.81	3.63	3.45	2.26	2.17
Min	1.72	2.56	1.31	0.76	1.22	2.23	1.75	0.77
Max	12.23	10.89	6.66	6.66	12.12	11.11	7.45	7.95
Median	3.76	6.14	4.66	3.24	3.79	7.39	5.01	3.16
Q1	1.91	2.61	1.51	2.36	1.98	2.44	4.25	2.86
Q3	6.85	8.75	5.90	3.56	7.14	9.10	6.84	3.79
Missing	5 (38.5%)	3 (30.0%)	4 (40.0%)	2 (20.0%)	5 (38.5%)	3 (30.0%)	5 (50.0%)	2 (20.0%)

**(c) Total internal fat (dm<sup>3</sup>)**

	Baseline				Measurement at 24 weeks			
	Control: Non intervention N=13	20 mg daily N=10	40 mg daily N=10	80mg daily N=10	Control: Non intervention N=13	20 mg daily N=10	40 mg daily N=10	80mg daily N=10
N	8 (61.5%)	7 (70.0%)	6 (60.0%)	8 (80.0%)	8 (61.5%)	7 (70.0%)	5 (50.0%)	8 (80.0%)
Mean	6.10	8.26	6.10	6.77	6.45	8.48	7.13	7.86
Sd	1.55	2.68	3.69	4.06	1.89	3.22	2.46	3.31
Min	3.07	5.35	3.57	2.51	3.16	5.45	4.73	2.91
Max	7.50	12.08	13.35	12.51	8.75	13.88	9.87	12.71
Median	6.75	8.72	4.73	5.96	6.26	7.50	6.73	7.78
Q1	4.72	5.76	3.92	3.03	4.96	5.56	4.85	4.98
Q3	6.98	10.77	6.27	9.35	7.87	11.87	9.48	9.30
Missing	5 (38.5%)	3 (30.0%)	4 (40.0%)	2 (20.0%)	5 (38.5%)	3 (30.0%)	5 (50.0%)	2 (20.0%)

**(d) Total external fat (dm<sup>3</sup>)**

	Baseline				Measurement at 24 weeks			
	Control: Non intervention N=13	20 mg daily N=10	40 mg daily N=10	80mg daily N=10	Control: Non intervention N=13	20 mg daily N=10	40 mg daily N=10	80mg daily N=10
N	8 (61.5%)	7 (70.0%)	6 (60.0%)	8 (80.0%)	8 (61.5%)	7 (70.0%)	5 (50.0%)	8 (80.0%)
Mean	18.09	20.37	13.30	12.21	18.35	20.94	16.38	13.26
Sd	10.97	7.31	5.40	5.37	11.11	8.32	5.36	5.14
Min	8.14	9.71	5.60	4.99	6.47	8.68	7.58	5.51
Max	41.12	30.35	17.58	22.76	40.01	32.29	20.94	22.40
Median	14.96	22.25	15.96	12.00	14.89	22.71	16.93	12.57
Q1	9.02	11.41	7.23	7.32	9.38	12.08	16.05	9.40
Q3	20.81	24.35	17.46	12.80	22.05	27.82	20.40	14.92
Missing	5 (38.5%)	3 (30.0%)	4 (40.0%)	2 (20.0%)	5 (38.5%)	3 (30.0%)	5 (50.0%)	2 (20.0%)

**(e) Total body fat (dm<sup>3</sup>)**

	Baseline				Measurement at 24 weeks			
	Control: Non intervention N=13	20 mg daily N=10	40 mg daily N=10	80mg daily N=10	Control: Non intervention N=13	20 mg daily N=10	40 mg daily N=10	80mg daily N=10
N	8 (61.5%)	7 (70.0%)	6 (60.0%)	8 (80.0%)	8 (61.5%)	7 (70.0%)	5 (50.0%)	8 (80.0%)
Mean	24.19	28.64	19.39	18.99	24.80	29.41	23.51	21.08
Sd	11.49	9.52	7.37	8.35	11.60	11.17	5.91	7.56
Min	11.20	15.47	9.52	7.50	9.63	14.13	14.31	8.06
Max	47.74	41.21	29.48	32.10	45.90	44.15	29.88	31.70
Median	21.50	30.98	20.57	19.78	22.20	30.05	25.79	21.48
Q1	15.90	16.76	12.38	10.41	16.00	17.63	21.66	15.26
Q3	25.53	36.43	23.85	24.33	27.01	41.69	25.92	25.84
Missing	5 (38.5%)	3 (30.0%)	4 (40.0%)	2 (20.0%)	5 (38.5%)	3 (30.0%)	5 (50.0%)	2 (20.0%)

**f) <sup>1</sup>H MRS Liver (intrahepatic and intramyocellular triglyceride content in liver)**

	Baseline				Measurement at 24 weeks			
	Control: Non intervention N=13	20 mg daily N=10	40 mg daily N=10	80mg daily N=10	Control: Non intervention N=13	20 mg daily N=10	40 mg daily N=10	80mg daily N=10
N	12 (92.3%)	10 (100.0%)	8 (80.0%)	10 (100.0%)	8 (62.0%)	7 (70.0%)	4 (40.0%)	8 (80.0%)
Mean	8.21	6.70	1.90	2.24	3.01	7.30	1.23	1.60
Sd	18.23	10.40	2.08	4.17	4.07	10.13	0.46	2.26
Min	0.40	0.40	0.30	0.10	0.10	0.20	0.70	0.30
Max	64.80	30.70	6.40	14.00	12.80	25.10	1.70	6.90
Median	1.65	1.55	1.15	1.00	1.80	2.50	1.25	0.60
Q1	0.60	0.40	0.40	0.60	0.80	0.40	0.70	0.30
Q3	3.00	8.40	2.00	1.50	2.40	18.30	1.50	1.30
Missing	1 (7.7%)	0 (0.00%)	2 (20.0%)	0 (0.00%)	5 (38.0%)	3 (30.0%)	6 (60.0%)	2 (20.0%)

**g) Soleus anterior**

	Baseline				Measurement at 24 weeks			
	Control: Non intervention N=13	20 mg daily N=10	40 mg daily N=10	80mg daily N=10	Control: Non intervention N=13	20 mg daily N=10	40 mg daily N=10	80mg daily N=10
N	12 (92.3%)	10 (100.0%)	8 (80.0%)	10 (100.0%)	8 (62.0%)	7 (70.0%)	4 (40.0%)	8 (80.0%)
Mean	19.50	19.01	12.60	17.29	19.45	17.07	22.23	16.63
Sd	10.78	17.77	5.83	11.77	13.25	9.17	21.01	8.97
Min	6.20	6.10	5.00	7.40	5.20	7.70	4.80	8.20
Max	41.80	65.10	22.40	44.50	40.00	33.70	51.90	33.60
Median	17.80	12.40	11.80	13.70	16.65	15.80	16.10	14.50
Q1	11.10	6.80	7.20	9.20	5.30	7.80	4.80	8.20
Q3	23.20	25.60	15.20	21.10	21.60	21.50	21.80	17.50
Missing	1 (7.7%)	0 (0.00%)	2 (20.0%)	0 (0.00%)	5 (38.0%)	3 (30.0%)	6 (60.0%)	2 (20.0%)

**h) Tibialis anterior**

	Baseline				Measurement at 24 weeks			
	Control: Non intervention N=13	20 mg daily N=10	40 mg daily N=10	80mg daily N=10	Control: Non intervention N=13	20 mg daily N=10	40 mg daily N=10	80mg daily N=10
N	11 (84.6%)	10 (100.0%)	8 (80.0%)	9 (100.0%)	8 (62.0%)	7 (70.0%)	4 (40.0%)	8 (80.0%)
Mean	6.25	8.10	5.34	7.82	8.10	10.21	5.08	7.41
Sd	3.10	3.71	2.13	2.79	4.97	6.25	1.35	2.73
Min	0.00	1.40	3.00	3.00	2.60	2.50	3.80	3.40
Max	11.00	13.90	9.60	11.00	18.60	17.70	6.60	11.20
Median	5.90	8.55	4.90	7.70	7.40	9.80	4.95	7.80
Q1	4.90	5.90	3.60	7.30	3.50	2.80	3.80	3.90
Q3	9.10	10.50	5.40	9.70	8.40	17.60	5.80	8.80
Missing	2 (15.4%)	0 (0.00%)	2 (20.0%)	1 (0.00%)	5 (38.0%)	3 (30.0%)	6 (60.0%)	2 (20.0%)

**Table 9-2 Model estimates for Internal visceral fat at 24 weeks (n=8 and 8 for groups 'control' and '80 mg daily', respectively)**

Variable	Parameter Estimate	Standard Error	95% confidence interval	p-value
Intercept	0.219	0.281	(-0.393, 0.831)	0.4510
Baseline value (internal visceral fat)	0.992	0.063	(0.854, 1.129)	<0.0001
Relative change in total external fat*	3.837	1.257	(1.100, 6.575)	0.0100
Treatment D vs control	0.043	0.278	(-0.563, 0.650)	0.8790

\* Relative changes in total external fat is calculated as (baseline measurement - 24 weeks measurement)/baseline measurement, and is taken into account when modelling internal visceral fat as discussed by the sub-study team.

**Table 9-3 Model estimates for Intrahepatic triglyceride content in liver at 24 weeks (n=8 and 8 for groups 'control' and '80 mg daily', respectively)**

Variable	Parameter Estimate	Standard Error	95% confidence interval	p-value
Intercept	1.186	0.513	(0.079,2.293)	0.0377

Baseline value	0.689	0.080	(0.516,0.862)	<0.0001
Treatment D vs control	-1.309	0.660	(-2.734,0.116)	0.0688

**Table 9-4 Model estimates for Intramyocellular triglyceride content in the soleus and tibialis anterior at 24 weeks (n=8 and 8 for groups 'control' and '80 mg daily', respectively)**

**Multivariate test**

<b>Two-dimensional variable: Soleus &amp; Tibialis</b>	<b>Approx. F</b>	<b>Numerator Df</b>	<b>Denominator Df</b>	<b>p-value</b>
Intercept	184.238	2	10	<0.0001
Baseline values	4.892	4	22	0.0056
Treatment D vs control	0.249	2	10	0.7839

**Univariate models (ANCOVA)**

<b>Variable: Soleus</b>	<b>Parameter Estimate</b>	<b>Standard Error</b>	<b>95% confidence interval</b>	<b>p-value</b>
Intercept	3.589	2.917	(-2.767,9.945)	0.2420
Baseline value	0.841	0.109	(0.602,1.074)	<0.0001
Treatment D vs control	-2.977	2.433	(-8.278,2.324)	0.2450
<b>Variable: Tibialis</b>	<b>Parameter Estimate</b>	<b>Standard Error</b>	<b>95% confidence interval</b>	<b>p-value</b>
Intercept	9.884	2.958	(3.440,16.329)	0.0059
Baseline value	-0.246	0.402	(-1.121,0.632)	0.5546
Treatment D vs control	-0.442	2.348	(-5.557,4.673)	0.8539