

ELECTRONIC SUPPLEMENTARY MATERIAL

Efficacy and safety of evolocumab in individuals with type 2 diabetes mellitus: primary results of the randomised controlled BANTING study

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ESM Table 1 Percent change from baseline to week 12 in AUC stratified by baseline triglyceride levels (Baseline median triglyceride: 1.8 mmol/L)

	Percent change from baseline to week 12 in AUC (mean, SEM)			
	Baseline TG <1.8 mmol/L		Baseline TG ≥ 1.8 mmol/L	
	Placebo	Evolocumab	Placebo	Evolocumab
Total Cholesterol	n=64	n=124	n=64	n=133
	1.1 (2.2)	-31.1 (1.3)	2.2 (2.2)	-30.7 (1.6)
LDL-C	n=64	n=123	n=53	n=112
	0.9 (3.2)	-54.9 (2.0)	1.2 (3.1)	-53.5 (2.6)
HDL-C	n=64	n=124	n=64	n=133
	-2.5 (1.6)	5.4 (1.3)	1.6 (1.6)	11.7 (1.5)
Non-HDL-C	n=64	n=124	n=64	n=133
	2.7 (3.0)	-44.3 (1.8)	2.7 (2.7)	-41.1 (1.9)
Triglycerides	n=64	n=124	n=64	n=133
	15.7 (4.5)	0.9 (4.2)	3.8 (4.0)	-11.0 (3.2)
VLDL-C	n=64	n=123	n=53	n=116
	15.6 (4.5)	-1.6 (3.2)	-2.7 (3.3)	-10.3 (3.4)
Chylomicron triglycerides	n=47	n=91	n=49	n=92
	29.1 (10.2)	19.7 (9.7)	6.2 (7.0)	1.8 (8.4)
Chylomicron cholesterol	n=48	n=92	n=49	n=93
	8.5 (4.9)	-8.9 (3.8)	9.1 (6.0)	-18.3 (2.4)
ApoB48	n=62	n=121	n=63	n=131
	15.6 (5.7)	10.8 (7.7)	9.9 (8.3)	-7.5 (4.4)

Abbreviations: ApoB48, apolipoprotein B48; AUC, area under the curve; HDL-C, high-density

lipoprotein cholesterol; LDL-C, LDL cholesterol; n, number of patients in the full analysis set who

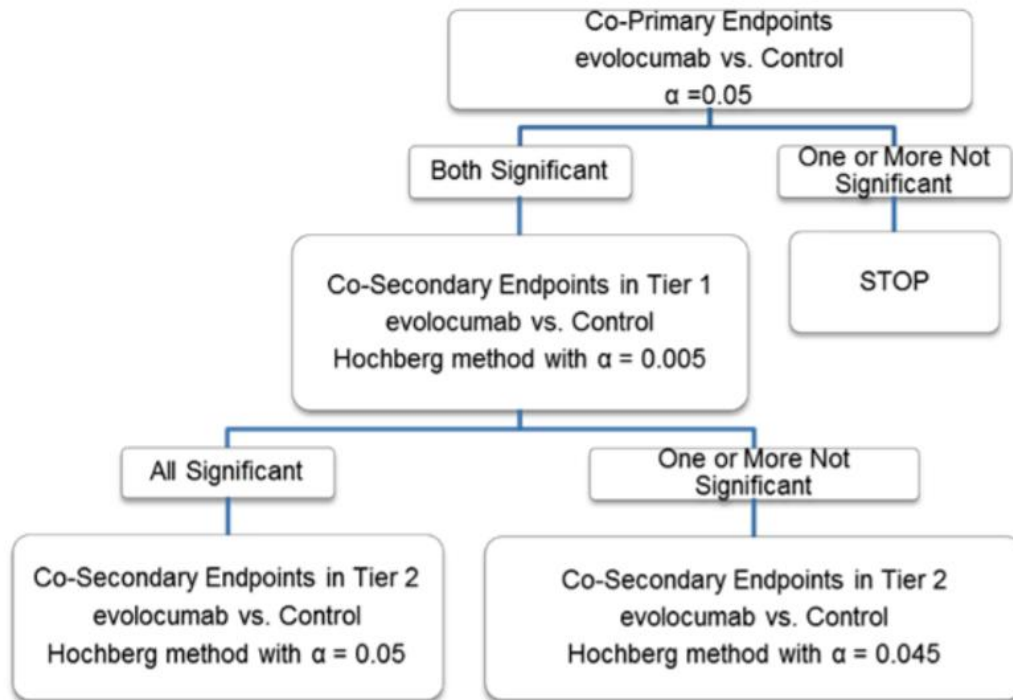
had AUC assessments; TG, triglycerides; VLDL-C, VLDL cholesterol

ESM Table 2 Summary of Week 12 Absolute Values by MMTT Timepoints

	Week 12 at 0 minutes		Week 12 at 120 minutes	
	Placebo	Evolocumab	Placebo	Evolocumab
Total Cholesterol	n=134	n=269	n=133	n=269
(mmol/l)	4.88 (0.09)	3.30 (0.06)	4.83 (0.09)	3.26 (0.06)
LDL-C	n=124	n=256	n=123	n=253
(mmol/l)	2.7 (2.1, 3.4)	1.2 (0.8, 1.6)	2.5 (2.0, 3.4)	1.1 (0.7, 1.5)
HDL-C	n=134	n=269	n=133	n=269
(mmol/l)	1.16 (0.03)	1.19 (0.02)	1.12 (0.03)	1.17 (0.02)
Non-HDL-C	n=134	n=269	n=133	n=269
(mmol/l)	3.73 (0.09)	2.11 (0.06)	3.71 (0.09)	2.10 (0.05)
Triglycerides	n=134	n=269	n=133	n=269
(mmol/l)	1.7 (1.3, 2.5)	1.5 (1.1, 2.2)	1.9 (1.5, 2.8)	1.8 (1.3, 2.5)
VLDL-C	n=124	n=260	n=123	n=258
(mmol/l)	0.83 (0.03)	0.78 (0.02)	0.92 (0.03)	0.87 (0.02)
Chylomicron triglycerides	n=117	n=217	n=115	n=214
(mmol/l)	0.42 (0.27, 0.67)	0.40 (0.25, 0.66)	0.59 (0.36, 0.88)	0.53 (0.35, 0.80)
Chylomicron cholesterol	n=117	n=219	n=115	n=216
(mmol/l)	0.88 (0.73, 1.04)	0.70 (0.60, 0.88)	0.93 (0.80, 1.11)	0.70 (0.60, 0.91)
ApoB48	n=132	n=267	n=131	n=265
(g/l)	0.01 (0.006, 0.015)	0.008 (0.006, 0.013)	0.012 (0.009, 0.019)	0.012 (0.008, 0.016)
Plasma glucose	n=134	n=271	n=134	n=270
(mmol/l)	8.0 (6.3, 10.7)	8.4 (6.5, 10.8)	10.7 (8.1, 14.3)	10.7 (8.0, 13.5)
Insulin	n=133	n=266	n=133	n=264
(pmol/l)	117.4 (75.7, 191.7)	129.9 (72.2, 211.8)	254.2 (149.3, 385.5)	231.3 (141.3, 416.4)
Pro-insulin	n=133	n=268	n=132	n=268
(pmol/l)	21.5 (12.3, 40.2)	28.0 (13.8, 51.5)	47.1 (29.8, 75.9)	51.4 (28.4, 80.9)
C-peptide	n=133	n=264	n=133	n=263
(nmol/l)	1.10 (0.74, 1.49)	1.25 (0.81, 1.71)	1.96 (1.33, 2.56)	1.98 (1.34, 2.67)
Glucagon	n=128	n=264	n=128	n=264
(ng/l)	173.5 (110.1, 233.6)	153.3 (109.1, 231.0)	191.8 (127.7, 265.7)	180.4 (127.6, 245.0)
Free fatty acids	n=134	n=270	n=134	n=270
(mmol/l)	0.57 (0.42, 0.71)	0.51 (0.38, 0.67)	0.32 (0.21, 0.44)	0.31 (0.22, 0.44)
Interleukin-6	n=133	n=269	n=133	n=269
(pg/ml)	2.9 (2.1, 4.9)	3.4 (2.3, 5.6)	2.7 (1.9, 4.3)	3.1 (2.0, 4.9)
Adiponectin	n=132	n=268	n=132	n=267
(mcg/ml)	5.0 (3.4, 6.6)	4.4 (3.0, 7.1)	5.0 (3.3, 6.5)	4.5 (3.0, 7.0)

All data presented are median (Q1, Q3), except for total cholesterol, HDL-C, non-HDL-C, and VLDL-C, which are mean (SEM).

ESM Figure 1. Multiplicity Adjustment Methods



Tier 1 co-secondary endpoints: Change from baseline in LDL-C; percent change from baseline in non-HDL-C; percent change from baseline in ApoB, percent change from baseline in TC; achievement of target LDL-C <1.8 mmol/L; 50% reduction of LDL-C from baseline

Tier 2 co-secondary endpoints: Percent change from baseline in Lp(a); percent change from baseline in triglycerides; percent change from baseline in HDL-C; percent change from baseline in VLDL-C

Site Investigators by Country

Below is the list of principal investigators who have screened at least one patient.

Belgium: Ann Mertens (Leuven), André Scheen (Liege), Luc Van Gaal (Edegem).

Canada: Thomas Elliott (Vancouver), Pavel Hamet (Montreal), Yves Pesant (St-Jérôme), Eric St Amour (Gatineau).

Italy: Enzo Bonora (Verona), Andrea Palermo (Roma), Paolo Pozzilli (Roma).

Mexico: Luis Alejandro Nevarez Ruiz (Chihuahua).

Poland: Zbigniew Gaciong (Warszawa), Mateusz Sidor (Krakow), Krzysztof Strojek (Katowice), Malgorzata Zolcinska- Wilczynska ((Wroclaw).

Spain: Nuria Alonso Pedrol (Badalona), Ramon Gomis de Barbara (Barcelona), Pedro Mezquita Raya (Almeria), Manuel Muñoz Torres (Granada).

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