

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Amarenco P, Kim JS, Labreuche J, et al. A comparison of two LDL cholesterol targets after ischemic stroke. *N Engl J Med* 2020;382:9-19. DOI: 10.1056/NEJMoa1910355

Comparison of 70 mg/dL and 100 mg/dL target LDL cholesterol levels after an ischemic stroke

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2. Trial Registration

Registration was through EUDRACT and ClinicalTrials.gov

2.1. An EUDRACT number was obtained on December 1, 2009 [EUDRACT Identifier number 2009-A01280-57]

2.2. Approval from French Authority (French drug agency, AFSSAPS) on December 9, 2009 [Identifier number B-91-44480]

2.3 IRB approval (centralized in France) on January 14, 2010 [Identifier Number P-081244-TST and 2009-A01280-57]

2.4. Registration on ClinicalTrials.gov [Identifier Number NCT01252875] finalized on December 3, 2010 after First patient included on March 15, 2010 and 330 patients randomized in-between. The delay was due to human error, believing the trial was fully uploaded before the first patient randomized, but the actual validation was 9 months late when the error was discovered.

2.5. All amendments to the protocol, between initially fully approved protocol by the French authorities, EUDRACT and IRB, and the end of the trial are listed in an online supplemental file including first and last version of the protocol (in French), protocol in English, table summarizing all amendments, statistical analysis plan.

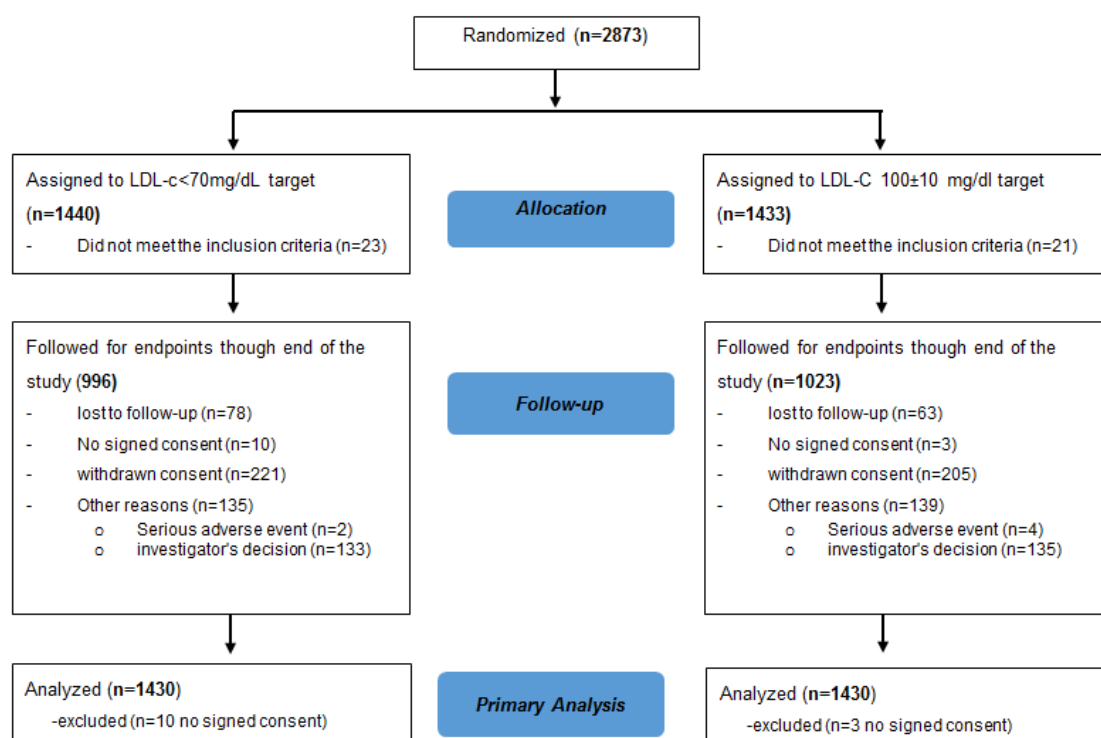
3. Data Safety Monitoring Board.

Since the study was performed under usual care, using drugs available on the market, prescribed by their doctors and reimbursed by the social security system, and that we did not anticipate unknown safety outcomes following LDL cholesterol lowering regardless of the LDL cholesterol level assigned by randomization, an independent Data Safety Monitoring Committee was not required

4. Conduct of the trial

In May 2019, the sponsor APHP decided to stop the trial because allocated funds had been used. The sponsor and investigators were masked to results of the study when the decision to stop the study has been taken.

Figure S1. Flow Diagram of Study Participants



Supplemental Table S1. Baseline characteristics in French and South Korean Patients

Characteristics	France (N=2148)	South Korea (N=712)
Age, years	67.4 (11.1)	64.5 (11.2)
Male sex, no/total no, (%)	1468/2148 (68.3)	466/712 (65.5)
Body-mass index, median (IQR)	26.2 (23.8-29.1)	24.4 (22.4-26.2)
Entry event		
Ischemic stroke	1777/2142 (83.0)	672/712 (94.4)
TIA	365/2142 (17.0)	40/712 (5.6)
Time since entry event, days, median (IQR)	6.0 (3.0-9.0)	8.0 (4.0-18.0)
Medical history		
Hypertension, no/total no, (%)	1420/2143 (66.2)	448/703 (63.7)
Diabetes, no/total no, (%)	386/2139 (18.0)	257/702 (36.6)
Dyslipidemia, no/total no, (%)	1321/2139 (61.8)	419/699 (59.9)
Former smoker, no/total no, (%)	517/2139 (24.2)	138/702 (19.7)
Current smoker, no/total no, (%)	648/2139 (30.3)	211/702 (30.1)
Stroke or TIA, no/total no, (%)	238/2139 (11.1)	84/700 (12.0)
Coronary artery disease, no/total no, (%)	419/2138 (19.6)	71/699 (10.2)
Statin naïve	1269/2139 (59.3)	300/699 (42.9)
Lipids, mg/dL		
LDL-c, mean (sd)	137 (37)	129 (39)
HDL-c, mean (sd)	51 (19)	46 (15)
Total cholesterol, mean (sd)	214 (49)	194 (44)
Triglycerides, median (IQR)	121.0 (90.0-161.0)	127.0 (92.0-177.0)
Systolic blood pressure, mmHg, mean (sd)	143 (22)	135 (19)
Diastolic blood pressure, mmHg, mean (sd)	80 (13)	79 (12)
Glucose, mg/dL, median (IQR)	5.5 (4.9-6.3)	6.3 (5.3-8.2)
Hemoglobin A1c, %, mean (sd)	6.2 (2.3)	6.6 (1.5)

Table S2. Persistence: medication use

Medications	At 6 months		At 1 year		At 2 years		At 3 years	
	<70 mg/dL	100±10 mg/dL	<70 mg/dL	100±10 mg/dL	<70 mg/dL	100±10 mg/dL	<70 mg/dL	100±10 mg/dL
	(N=1181)	(N=1181)	(N=1024)	(N=1037)	(N=924)	(N=926)	(N=623)	(N=649)
≥1 antiplatelet agent	999/1168 (85.5)	1014/1167 (86.9)	863/1004 (86.0)	896/1029 (87.1)	797/920 (86.6)	791/917 (86.3)	522/616 (84.7)	526/639 (82.3)
Aspirin	614/999 (61.5)	630/1014 (62.1)	489/863 (56.7)	508/896 (56.7)	457/797 (57.3)	426/791 (53.9)	290/522 (55.6)	264/526 (50.2)
Other antiplatelet agent	620/999 (62.1)	622/1014 (61.3)	537/863 (62.2)	564/896 (62.3)	476/797 (59.7)	501/791 (63.3)	284/522 (54.4)	320/526 (60.8)
Dual therapy	239/999 (23.9)	244/1014 (24.1)	168/863 (19.5)	181/896 (20.2)	141/797 (17.7)	138/791 (17.4)	61/522 (11.7)	57/526 (10.8)
≥1 anticoagulant agent	165/905 (18.2)	159/900 (17.7)	140/784 (17.9)	139/788 (17.6)	128/714 (17.9)	132/708 (18.6)	99/532 (18.6)	108/555 (19.5)
≥1 antihypertensive agent	878/1066 (82.3)	912/1062 (85.9)	772/919 (84.0)	837/949 (88.2)	714/838 (85.2)	758/843 (90.0)	502/586 (85.7)	547/613 (89.2)
1	386/1066 (36.2)	373/1062 (35.1)	324/919 (35.2)	323/949 (34.1)	284/838 (33.9)	288/843 (34.2)	202/586 (34.5)	201/613 (32.8)
2	290/1066 (27.2)	309/1062 (29.1)	257/919 (28.0)	287/949 (30.2)	245/838 (29.2)	271/843 (32.2)	161/586 (27.5)	200/613 (32.6)
≥3	202/1066 (18.9)	230/1062 (21.7)	191/919 (20.8)	227/949 (23.9)	185/838 (22.1)	199/843 (23.6)	139/586 (23.7)	146/613 (23.8)
≥1 lipid-lowering agent	1167/1181 (98.8)	1174/1181 (99.4)	996/1024 (97.3)	1036/1037 (99.9)	898/924 (97.2)	911/926 (98.4)	570/623 (91.5)	579/649 (89.2)
Statin only	871/1167 (74.6)	1113/1174 (94.8)	664/996 (66.7)	977/1036 (94.3)	566/898 (63.0)	857/911 (94.1)	337/570 (59.3)	536/579 (92.6)
Intense statin therapy*	147/774 (19.0)	62/937 (6.6)	120/591 (20.3)	54/814 (6.6)	117/500 (23.4)	53/702 (7.6)	73/310 (23.6)	38/446 (8.5)
Moderate intensity statin therapy**	621/774 (80.2)	625/937 (66.7)	470/591 (79.5)	546/814 (67.1)	381/500 (76.2)	488/702 (69.5)	235/310 (75.8)	315/446 (70.6)
Low intensity statin therapy***	6/774 (0.8)	250/937 (26.7)	1/591 (0.2)	214/814 (26.3)	2/500 (0.4)	161/702 (22.9)	2/310 (0.6)	93/446 (20.9)
Statin + Ezetimibe	292/1167 (25.0)	57/1174 (4.9)	329/996 (33.0)	56/1036 (5.4)	330/898 (36.8)	51/911 (5.6)	231/570 (40.5)	41/579 (7.1)
Ezetimibe only	4/1167 (0.4)	4/1174 (0.3)	3/994 (0.3)	3/1036 (0.3)	2/898 (0.2)	3/911 (0.3)	1/570 (0.2)	2/579 (0.3)

* Atorvastatin 40-80, Rosuvastatin 10-40; ** Atorvastatin 10-20, Rosuvastatin 5-10, Simvastatin 20-40, Pravastatin 40-80, Fluvastatin 40-80, Pitavastatin 2-4; *** Simvastatin 10, Pravastatin 10-20, Fluvastatin 20-40, Pitavastatin 1

Figure S2. Blood pressure evolution

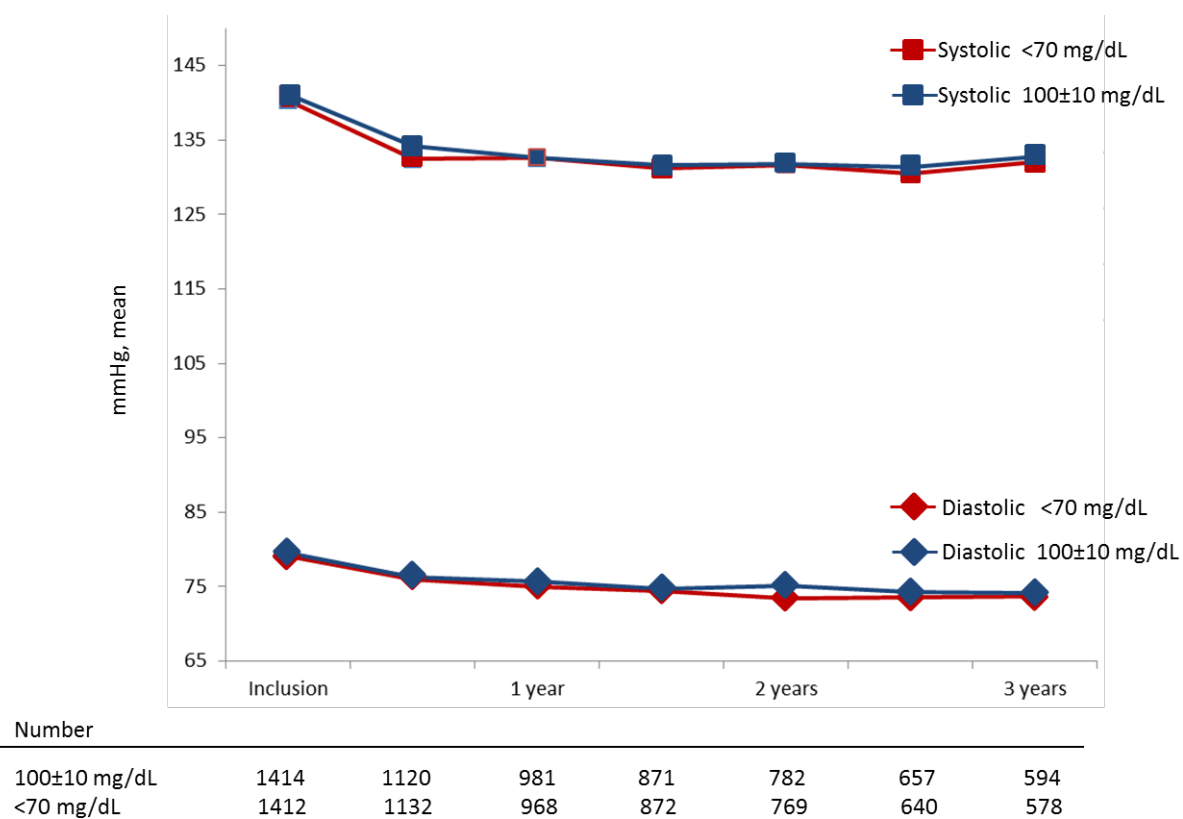


Figure S3. Current smokers : smoking cessation

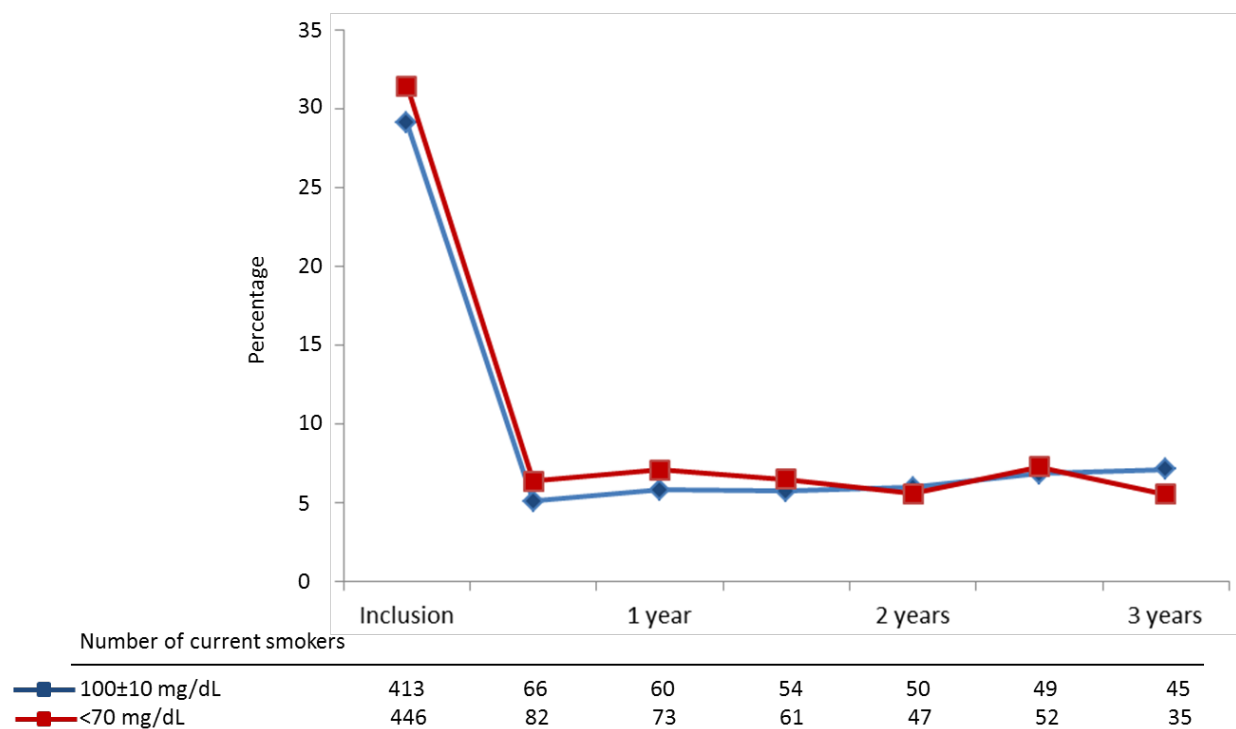


Figure S4. HbA1c evolution in diabetic patients at baseline.

