

Supplementary data										
Additional file 1 Individual clinical data of 19 patients in PCSK9i group										
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10
Characteristics										
Age, years	71	63	64	60	59	65	44	61	50	64
Gender	M	M	F	M	F	M	M	F	M	F
Baseline NIHSS	3	0	3	0	6	0	0	0	6	0
Baseline mRS	3	0	3	0	4	0	0	0	3	0
Eligible artery	BA	BA	C7	C7	M1	BA	M1	BA	M1	M1
Risk factors/ medical history	HTN, CHD, smoking	HTN, diabetes,smoking, arthrolithiasis	HTN, diabetes	HTN	HTN	HTN	HTN	HTN, diabetes	HTN, diabetes	HTN
Medications										
Type of PCSK9 inhibitor	evolocumab	alirocumab	evolocumab	evolocumab	evolocumab	alirocumab	alirocumab	evolocumab	evolocumab	evolocumab
Antiplatelet agents	aspirin and	aspirin and	aspirin and	aspirin and	aspirin	aspirin and	aspirin and	aspirin and	aspirin	aspirin and
	clopidogrel	clopidogrel	clopidogrel	clopidogrel		clopidogrel	clopidogrel	clopidogrel		clopidogrel
Statin	atorvastatin 40mg	atorvastatin 40mg	atorvastatin 40mg	rosuvastatin 20mg	rosuvastatin 20mg	rosuvastatin 20mg	rosuvastatin 20mg	atorvastatin 40mg	rosuvastatin 20mg	rosuvastatin 20mg
Other medications	(-)	CCB, SU, DPP-4i	CCB, ARB, insulin, BGS	ARB	CCB	CCB	ACEI	CCB,alpha-GI	insulin	insulin
Laboratory parameters										
Glycosylated hemoglobin, % (baseline)	6.1	NA	NA	NA	NA	6.0	5.4	6.1	12.8	6.9

LDL-C, mmol/L (baseline)	3.18	4.29	2.36	3.09	2.06	2.71	2.18	1.89	3.32	2.15
LDL-C, mmol/L (1m)	0.46	1.01	0.46	1.56	NA	1.48	NA	0.28	0.45	NA
LDL-C, mmol/L (3m)	0.39	0.86	0.48	1.18	1.64	0.13	NA	0.79	0.55	0.58
LDL-C, mmol/L (6m)	NA	NA	NA	1.13	0.46	0.39	1.12	0.97	0.49	0.76
HDL-C, mmol/L (baseline)	1.23	0.94	1.26	1.11	0.9	0.8	0.97	1.16	0.87	0.79
Total cholesterol, mmol/L (baseline)	5.07	5.3	4.29	4.66	4.34	4.05	3.2	2.63	4.29	3.65
Triglycerides, mmol/L (baseline)	1.91	1.12	1.27	1.45	3.08	2.6	0.73	0.78	0.88	1.6
C-reactive protein, mg/L (baseline)	0.1	3.2	NA	NA	NA	NA	0.3	NA	0.9	2.5
Outcome										
NIHSS at follow-up (1m)	2	0	1	0	3	0	0	0	4	0
NIHSS at follow-up (3m)	1	0	1	0	2	0	0	0	3	0
NIHSS at follow-up (6m)	NA	0	0	0	1	0	0	0	1	0
mRS at last follow-up (1m)	3	0	2	0	3	0	0	0	2	0
mRS at last follow-up (3m)	2	0	1	0	2	0	0	0	2	0
mRS at last follow-up (6m)	6	0	1	0	2	0	0	0	2	0
Follow-up (mo)/Relapse	16/Yes	16/No	16/No	15/No	15/No	14/No	14/No	13/No	13/No	13/No

	Patient 11	Patient 12	Patient 13	Patient 14	Patient 15	Patient 16	Patient 17	Patient 18	Patient 19
Characteristics									
Age, years	64	59	42	43	67	46	64	50	58
Gender	M	M	M	M	F	M	M	M	M
Baseline NIHSS	0	5	3	1	10	3	3	3	0
Baseline mRS	0	2	2	2	4	3	1	2	0
Eligible artery type	BA	M1	M1	BA	M1	C4	M1	V4	V4
Risk factors/ medical history	HTN, smoking	arthrolithiasis	CHD, smoking	HTN, smoking	HTN, diabetes	HTN	HTN	HTN, diabetes, smoking	(-)
Medications									
Type of PCSK9 inhibitor	alirocumab	alirocumab	alirocumab	evolocumab	evolocumab	evolocumab	alirocumab	alirocumab	evolocumab
Antiplatelet agents	aspirin and clopidogrel	clopidogrel	aspirin and clopidogrel	aspirin and clopidogrel	aspirin	aspirin and clopidogrel	aspirin and clopidogrel	aspirin and clopidogrel	aspirin and clopidogrel
Statin	rosuvastatin 20mg	rosuvastatin 20mg	atorvastatin 40mg	atorvastatin 40mg	atorvastatin 40mg	atorvastatin 40mg	rosuvastatin 20mg	atorvastatin 40mg	atorvastatin 40mg
Other medications	CCB	(-)	(-)	(-)	ACEI, CCB, BGS	(-)	ACEI	(-)	(-)
Laboratory parameters									
Glycosylated hemoglobin, % (baseline)	NA	5.8	5.5	NA	7.1	5.6	5.4	NA	NA
LDL-C, mmol/L (baseline)	3.43	2.99	3.08	3.89	2.39	1.83	2.36	1.87	2.14
LDL-C, mmol/L (1m)	0.69	NA	0.56	0.82	NA	0.68	1.47	NA	0.97
LDL-C, mmol/L (3m)	1.51	0.93	0.43	0.85		0.88		1.04	0.38
LDL-C, mmol/L (6m)	0.48	1.19	0.82	1.09	0.65	NA	NA	NA	NA

HDL-C, mmol/L (baseline)	0.95	0.82	1.35	0.76	0.91	0.76	0.72	0.89	0.78
Total cholesterol, mmol/L (baseline)	6.09	4.7	5.62	4.54	3.97	1.29	3.47	2.88	3.63
Triglycerides, mmol/L (baseline)	1.83	2.95	3.65	0.97	2.13	0.87	1.44	0.77	2.73
C-reactive protein, mg/L (baseline)	NA	0.3	NA	2.5	3.1	NA	7.2	NA	NA
Outcome									
NIHSS at follow-up (1m)	0	3	2	1	8	2	2	1	0
NIHSS at follow-up (3m)	0	0	1	0	4	1	1	1	0
NIHSS at follow-up (6m)	0	0	0	0	1	0	0	0	0
mRS at last follow-up (1m)	0	0	1	1	4	2	1	1	0
mRS at last follow-up (3m)	0	0	1	1	2	1	1	1	0
mRS at last follow-up (6m)	0	0	0	1	1	0	0	1	0
Follow-up (mo)/Relapse	12/No	12/No	12/No	11/No	11/No	11/No	11/No	10/No	9/No

ACEI: angiotensin-converting enzyme inhibitor; alpha-GI: alpha-glucosidase inhibitor; ARB: angiotensin receptor blocker;

BA: basilar artery; BGS: biguanides; C: internal carotid artery; CCB: calcium channel blocker; CHD: coronary heart disease;

DPP-4i: dipeptidyl peptidase-4 inhibitor; HDL-C: high-density lipoprotein cholesterol; HTN: hypertension; LDL-C: low-density lipoprotein cholesterol; M: middle cerebral artery; mRS: the Modified Rankin Scale; mo: months; NIHSS: National Institutes of Health Stroke Scale; NA: not applicable; PCSK9i: proprotein convertase subtilisin/kexin type 9 inhibitor; SU: sulfonylureas

Additional file 2 Individual clinical data of 10 patients in control group

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Characteristics					
Age, years	63	54	64	68	46
Gender	M	F	F	M	M
Baseline NIHSS	3	9	9	1	0
Baseline mRS	2	3	3	1	1
Eligible artery	M1	P1	M1	BA	M1
Risk factors/ medical history	(-)	(-)	HTN	HTN, smoking	HTN, diabetes
Medications					
Type of PCSK9 inhibitor	evolocumab	alirocumab	evolocumab	evolocumab	evolocumab
Antiplatelet agents	aspirin and	aspirin	clopidogrel	aspirin and	aspirin and
	clopidogrel			clopidogrel	clopidogrel
Statin	atorvastatin 40mg	atorvastatin 40mg	atorvastatin 40mg	rosuvastatin 20mg	rosuvastatin 20mg
Other medications	(-)	ACEI, BGS, alpha-GI	(-)	CCB	BGS, alpha-GI
Laboratory parameters					
Glycosylated hemoglobin, % (baseline)	5.2	6.9	NA	7.2	8.6
LDL-C, mmol/L (baseline)	1.84	1.87	2.8	3.69	2.07
LDL-C, mmol/L (1m)	NA	NA	NA	3.17	0.97
LDL-C, mmol/L (3m)	NA	1.58	NA	2.47	1.32

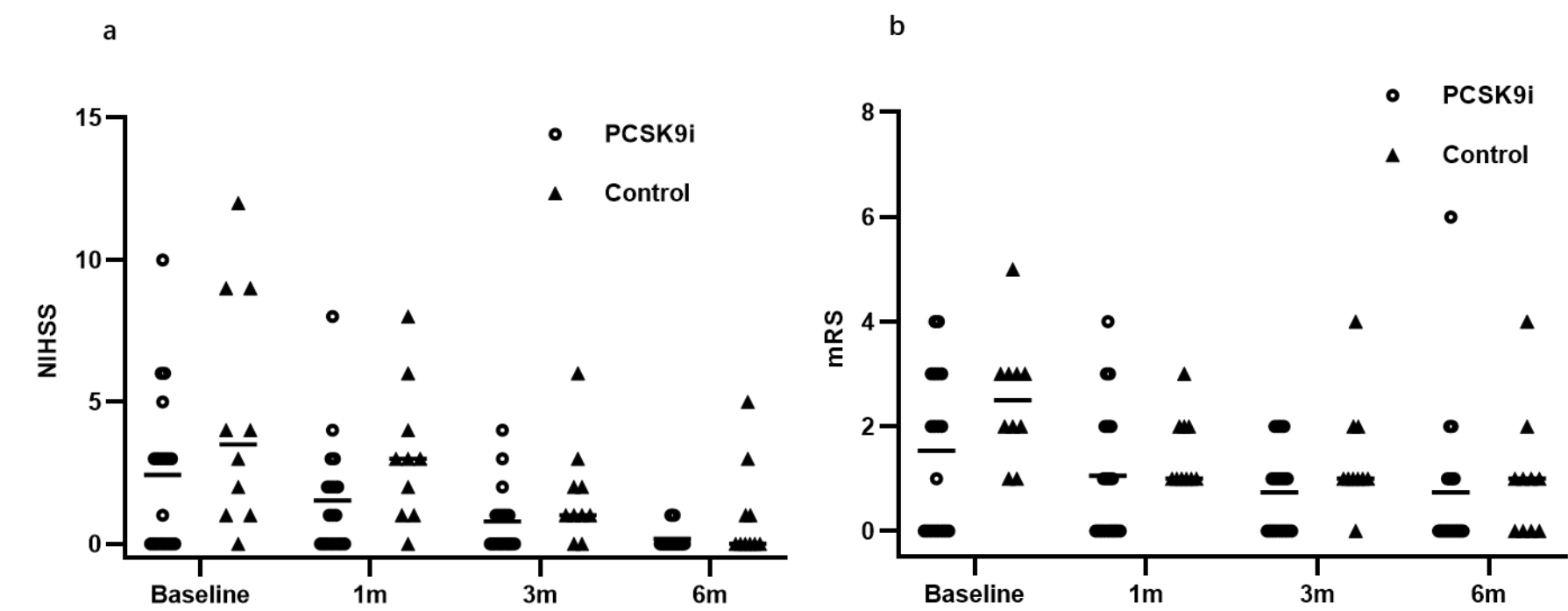
LDL-C, mmol/L (6m)	NA	NA	NA	1.13	0.46
HDL-C, mmol/L (baseline)	0.87	0.92	1.18	0.84	0.74
Total cholesterol, mmol/L (baseline)	2.84	2.98	4.32	4.61	3.08
Triglycerides, mmol/L (baseline)	1.99	0.97	1.64	1.36	1.17
C-reactive protein, mg/L (baseline)	0.6	15.4	6.4	0.4	1.5
Outcome					
NIHSS at follow-up (1m)	3	4	6	1	0
NIHSS at follow-up (3m)	1	2	3	1	0
NIHSS at follow-up (6m)	0	1	3	0	0
mRS at last follow-up (1m)	2	1	1	1	1
mRS at last follow-up (3m)	1	2	2	1	1
mRS at last follow-up (6m)	0	1	2	1	1
Follow-up (mo)/Relapse	16/Yes	16/No	16/No	15/No	15/No

	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10
Characteristics					
Age, years	51	62	54	55	55
Gender	M	F	M	M	M
Baseline NIHSS	1	12	4	4	2
Baseline mRS	2	5	2	3	3
Eligible artery type	M1	M1	M1	M2	M1
Risk factors/ medical history	smoking	diabetes	HTN, smoking	HTN, smoking	HTN, CHD, smoking
Medications					
Type of PCSK9 inhibitor	alirocumab	alirocumab	alirocumab	evolocumab	evolocumab
Antiplatelet agents	aspirin and clopidogrel	clopidogrel	aspirin and clopidogrel	aspirin and clopidogrel	aspirin and clopidogrel
Statin	rosuvastatin 20mg	rosuvastatin 20mg	atorvastatin 40mg	atorvastatin 40mg	atorvastatin 40mg
Other medications	(-)	ACEI, alpha-GI	CCB, insulin	CCB	(-)
Laboratory parameters					
Glycosylated hemoglobin, % (baseline)	5.2	7.54	4.77	5	4.4
LDL-C, mmol/L (baseline)	2.97	1.83	3.27	2.75	3.81
LDL-C, mmol/L (1m)	2.01	NA	1.44	1.49	2.13
LDL-C, mmol/L (3m)	2.11	0.96	NA	1.56	1.8
LDL-C, mmol/L (6m)	2.99	0.94	NA	NA	2.14

HDL-C, mmol/L (baseline)	1.1	0.91	0.93	1.14	0.84
Total cholesterol, mmol/L (baseline)	4.35	3.04	4.42	4.09	5.11
Triglycerides, mmol/L (baseline)	1.57	1.64	1.17	1.08	1.68
C-reactive protein, mg/L (baseline)	NA	1.8	0.1	2.6	1.1
Outcome					
NIHSS at follow-up (1m)	1	8	3	3	2
NIHSS at follow-up (3m)	0	6	1	2	1
NIHSS at follow-up (6m)	0	5	0	1	0
mRS at last follow-up (1m)	1	3	1	2	2
mRS at last follow-up (3m)	0	4	1	1	1
mRS at last follow-up (6m)	0	4	0	1	0
Follow-up (mo)/Relapse	12/No	12/No	12/No	11/No	11/No

ACEI: angiotensin-converting enzyme; alpha-GI: alpha-glucosidase inhibitor; ARB: angiotensin receptor blocker; BA: basilar artery; BGS: biguanides; C: internal carotid artery; CCB: calcium channel blocker; CHD: coronary heart disease; DPP-4i: dipeptidyl peptidase-4 inhibitor; HDL-C: high-density lipoprotein cholesterol; HTN: hypertension; LDL-C: low-density lipoprotein cholesterol; M: middle cerebral artery; mRS: the Modified Rankin Scale; mo: months; NIHSS: National Institutes of Health Stroke Scale; NA: not applicable; P: posterior cerebral artery; PCSK9i: proprotein convertase subtilisin/kexin type 9 inhibitor; SU: sulfonylureas

Additional file 3 Clinical outcomes over time



Temporal changes of NIHSS (a) and mRS (b) scores in the two study groups.

Additional file 4: Changes in intracranial artery plaque features on high resolution MR vessel wall imaging

	PCSK9i patients (n=12)	Controls (n=3)	P value between groups
Plaque area, mm ²			
Baseline	13.07±10.72	12.99±14.87	0.990
Follow-up	11.53±8.65	14.87±2.88	0.106
Norminal change, %	-8.0 (-19.5 to 3.6)	17.0 (-22.3 to 56.3)	0.050
P value from baseline	0.216	0.221	
Plaque burden, %			
Baseline	0.89 (0.71, 0.96)	0.90 (0.90, 0.92)	0.470
Follow-up	0.85 (0.71, 0.92)	0.92 (0.88, 0.92)	0.727
Norminal change, %	-2.6 (-7.3 to 2.0)	-1.5 (-9.0 to 5.9)	0.774
P value from baseline	0.184	0.465	
Enhancement ratio			
Baseline	1.84±0.57	1.97±0.90	0.760
Follow-up	1.53±0.50	2.28±0.06	0.018*
Norminal change, %	-13.7 (-27.2 to 0.3)	37.7 (-14.6 to 221)	0.024*
P value from baseline	0.183	0.673	
Degree of stenosis, %			
Baseline	0.67±0.19	0.57±0.16	0.442
Follow-up	0.60±0.24	0.64±0.20	0.036*
Norminal change, %	-11.7 (-23.3 to -0.1)	16.0 (-7.6 to 39.6)	0.027*
P value from baseline	0.047*	0.095	

Percent wall volume, PWV			
Baseline	0.81±0.12	0.81±0.04	0.962
Follow-up	0.81±0.11	0.79±0.03	0.626
Norminal change, %	0.2 (-5.1 to 5.4)	-2.3 (-8.3 to 3.7)	0.515
P value from baseline	0.960	0.578	
Eccentricity			
Baseline	0.64±0.20	0.72±0.11	0.564
Follow-up	0.56±0.16	0.81±0.07	0.027*
Norminal change, %	-7.9 (-26.6 to 10.8)	13.7 (-3.1 to 30.5)	0.105
P value from baseline	0.327	0.051	

MR: magnetic resonance; PCSK9i: proprotein convertase subtilisin/kexin type 9 inhibitor. * P<0.05