Supplementary Online Content

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

eTable 1. Impact of Covariate Adjustment on Treatment Effect for Adherence, Systolic BP and LDL-Cholesterol

Covariate(s)	**Adherence**		**Systolic BP (mm Hg)**		**LDL-cholesterol (mg/dL)**	
	Relative Risk (95%CI)		**Difference (95% CI)**		**Difference (95% CI)**	
None	*1.33*	*(1.26; 1.41)*	-3.1	(-4.8; -1.3)	-5.3	(-8.1; -2.6)
Baseline value *	1.13	(1.08; 1.18)	*-2.6*	*(-4.0; -1.1)*	*-4.2*	*(-6.5; -1.9)*
Sex	1.33	(1.27; 1.41)	-3.1	(-4.8; -1.3)	-5.4	(-8.1; -2.7)
Age	1.34	(1.27; 1.41)	-3.3	(-5.0; -1.6)	-5.3	(-8.1; -2.6)
Site/country **	1.34	(1.27; 1.41)	-3.1	(-4.7; -1.5)	-5.3	(-8.1; -2.6)
Risk stratum	1.32	(1.25; 1.39)	-3.1	(-4.8; -1.4)	-5.3	(-8.1; -2.6)
Follow-up duration	1.33	(1.26; 1.41)	-3.1	(-4.8; -1.3)	-5.4	(-8.1; -2.6)
All	**1.13**	**(1.08; 1.18)**	**-2.7**	**(-4.1; -1.3)**	**-4.2**	**(-6.6; -1.9)**

Pre-specified primary analyses are in italics

* Baseline value: adjustment was conducted for the baseline value of the outcome measure for each of adherence, SBP or LDL-cholesterol separately.

** Indian sites were grouped; European sites were not grouped.

eTable 2. Effects on Secondary Outcomes: Other Laboratory Parameters at the End of Study

Parameter	FDC (N = 1002)	Usual care (N = 1002)	Total (N = 2004)
Sodium (mmol/L)			
N	929	908	1837
Mean (SD)	139.1 (3.5)	139.3 (3.2)	139.2 (3.4)
Median (IRQ)	139.0 (137.0, 141.0)	139.0 (138.0, 141.0)	139.0 (137.0, 141.0)
Potassium (mmol/L)			
N	926	904	1830
Mean (SD)	4.4 (0.5)	4.4 (0.5)	4.4 (0.5)
Median (IRQ)	4.4 (4.1, 4.7)	4.3 (4.1, 4.7)	4.3 (4.1, 4.7)
ALT IU/L			
N	924	906	1830
Mean (SD)	28.5 (14.6)	29.3 (21.7)	28.9 (18.5)
Median (IRQ)	25.0 (19.0, 34.0)	25.0 (19.0, 34.0)	25.0 (19.0, 34.0)
AST IU/L			
N	918	900	1818
Mean (SD)	27.2 (10.2)	27.9 (14.9)	27.6 (12.7)
Median (IRQ)	26.0 (21.0, 32.0)	26.0 (21.0, 31.0)	26.0 (21.0, 31.0)
Fasting glucose (mg/dL)			
N	927	908	1835
Mean (SD)	112.4 (39.1)	111.7 (36.5)	112.0 (37.8)
Median (IRQ)	100.9 (91.9, 118.9)	100.9 (91.9, 117.1)	100.9 (91.9, 118.0)

ALT = alanine transaminase
AST = aspartate aminotransferase

eTable 3. Effects on Secondary Outcomes: Weight, Waist Circumference, BMI and Lifestyle Factors at the End of Study

Parameter	FDC (N = 1002)	Usual care (N = 1002)	Total (N = 2004)
Weight (kgs)			
N	931	918	1849
Mean (SD)	76.2 (17.2)	76.5 (17.2)	76.4 (17.2)
Median (IRQ)	75.0 (64.0, 87.0)	75.0 (64.0, 87.0)	75.0 (64.0, 87.0)
Waist (cm)			
N	931	916	1847
Mean (SD)	97.1 (12.1)	97.2 (11.7)	97.2 (11.9)
Median (IRQ)	97.0 (89.2, 104.0)	96.9 (90.0, 104.1)	97.0 (89.6, 104.0)
BMI			
N	930	918	1848
Mean (SD)	27.0 (4.4)	26.9 (4.5)	27.0 (4.5)
Median (IRQ)	26.7 (23.9, 29.5)	26.6 (23.8, 29.7)	26.6 (23.8, 29.6)
Minutes spent doing moderate physical activities during last 7 days			
N	952	954	1906
Mean (SD)	156.9 (178.4)	140.5 (157.3)	148.7 (168.3)
Median (IRQ)	120.0 (0.0, 210.0)	120.0 (0.0, 210.0)	120.0 (0.0, 210.0)
Minutes spent doing vigorous physical activities during last 7 days			
N	952	954	1906
Mean (SD)	21.0 (72.9)	22.6 (68.5)	21.8 (70.7)
Median (IRQ)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)
Participant on an exercise programme	89/ 952 (9.3%)	76/ 954 (8.0%)	165/1906 (8.7%)
Participant seeing a dietician or on a weight control programme	36/ 952 (3.8%)	36/ 954 (3.8%)	72/1906 (3.8%)
Participant on a smoking cessation programme	10/ 952 (1.1%)	9/ 954 (0.9%)	19/1906 (1.0%)

BMI = body mass index

eTable 4. Quality of Life Scores and Overall EQ-5D Index at the End of the Study

Score	FDC (N = 1002) LS Mean (se)	Usual care (N = 1002) LS Mean (se)	Difference Polypill-Usual care Mean difference (95% CI)	P-value
Mobility score	1.27 (0.02)	1.26 (0.02)	0.01 (-0.04; 0.06)	0.67
Personal care score	1.07 (0.01)	1.11 (0.01)	-0.04 (-0.07; -0.00)	0.04
Usual activities score	1.18 (0.02)	1.19 (0.02)	-0.02 (-0.06; 0.03)	0.46
Pain/discomfort score	1.45 (0.02)	1.45 (0.02)	-0.01 (-0.07; 0.05)	0.84
Anxiety/depression	1.24 (0.02)	1.29 (0.02)	-0.05 (-0.11; -0.00)	0.05
VAS score	76.12 (0.56)	73.69 (0.57)	2.43 (0.87; 3.99)	<.01
EQ-5D summary index	0.82 (0.01)	0.81 (0.01)	0.01 (-0.01; 0.02)	0.43

Higher scores indicate poorer functioning for the five dimensions (mobility, self-care, activities, pain, anxiety/depression) (range: 1-3), while higher ratings on the visual analogue scale (VAS) (0-100) and summary index (0-1) represent better health.

eTable 5. Reported Use of FDC and Other Cardiovascular Medications in the FDC Group, by Study Visit

	Month 1		Month 6		Month 12		Month 18		Month 24	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Number of patients assessed (denominator)	993		977		935		524		34	
Adherent to FDC	940	94.7%	833	85.3%	757	81.0%	398	76.0%	22	64.7%
Not adherent to FDC	53	5.3%	144	14.7%	178	19.0%	126	24.0%	12	35.3%
Of those not taking FDC, no. taking other meds										
Not on statin, antiplatelet or BP lowering drugs	4	7.5%	17	11.8%	23	12.9%	26	20.6%	2	16.7%
On BP-lowering drug	49	92.5%	121	84.0%	146	82.0%	99	78.6%	11	91.7%
On statin	42	79.2%	112	77.8%	127	71.3%	86	68.3%	9	75.0%
On antiplatelet	47	88.7%	120	83.3%	140	78.7%	88	69.8%	8	66.7%
On combination of 1+1+1 *	39	73.6%	101	70.1%	111	62.4%	73	57.9%	7	58.3%
On combination of 1+1+2 **	26	49.1%	66	45.8%	70	39.3%	54	42.9%	4	33.3%

* 1+1+1 combination = 1 statin + 1 antiplatelet + 1 BP-lowering drug

** 1+1+2 combination = 1 statin + 1 antiplatelet + 2 BP-lowering drugs

Adherence defined as taking a drug at least 4 days in the week preceeding the visit

eTable 6. Cardiovascular Events in FDC and Usual Care Groups

Event or event category	FDC (N = 1002)	Usual care (N = 1002)
Coronary heart disease	33	23
Death from coronary heart disease	7	7
Sudden death	0	0
Myocardial infarction	8	6
Coronary artery bypass graft	2	2
Percutaneous coronary intervention	19	14
Hospitalisation for unstable angina	5	2
Heart failure	4	0
Cerebrovascular disease	8	5
Peripheral vascular disease*	8	11
Total cardiovascular events	**50**	**35**
Nonfatal	38	30
Fatal	14	8
Non-Cardiovascular deaths	3	7
All deaths	17	15

Some patients had more than one event. Patients may be included in the same column more than once, but not in the same row more than once.

*All peripheral arterial events were defined as death due to peripheral vascular disease, new symptomatic claudication, amputation due to ischaemia, dissection, and peripheral arterial revascularisation procedures (such as: carotid endarterectomy or stent, open repair or stenting of aortic aneurysm or dissection, limb revascularisation, e.g. femoral–popliteal bypass surgery) or chronic leg ulceration due to arterial insufficiency.

FDC = fixed dose combination.

eTable 7. Serious Adverse Events in FDC and Usual Care Groups

Event type	**FDC (N = 1002)**	**Usual care (N = 1002)**
Total number of serious adverse events	154	142
Patients with at least one SAE	118 (11.8%)	102 (10.2%)
Cardiac disorders	42 (4.2%)	27 (2.7%)
Infections and infestations	16 (1.6%)	10 (1.0%)
Neoplasms benign and malignant	13 (1.3%)	11 (1.1%)
Vascular disorders	11 (1.1%)	12 (1.2%)
Nervous system disorders	9 (0.9%)	13 (1.3%)
Gastrointestinal disorders	10 (1.0%)	11 (1.1%)
General disorders and administration site conditions	8 (0.8%)	8 (0.8%)
Injury, poisoning and procedural complications	7 (0.7%)	5 (0.5%)
Musculoskeletal and connective tissue disorders	3 (0.3%)	6 (0.6%)
Metabolism and nutrition disorders	3 (0.3%)	5 (0.5%)
Renal and urinary disorders	5 (0.5%)	3 (0.3%)
Respiratory, thoracic and mediastinal disorders	5 (0.5%)	3 (0.3%)
Reproductive system and breast disorders	1 (0.1%)	6 (0.6%)
Surgical and medical procedures	3 (0.3%)	2 (0.2%)
Psychiatric disorders	1 (0.1%)	2 (0.2%)
Hepatobiliary disorders	1 (0.1%)	1 (0.1%)
Blood and lymphatic system disorders	1 (0.1%)	0
Congenital, familial and genetic disorders	0	1 (0.1%)
Immune system disorders	0	1 (0.1%)
Investigations	1 (0.1%)	0
Skin and subcutaneous tissue disorders	0	1 (0.1%)

Numerators are patients who experience an adverse event at least once

Denominators are all patients randomised

Serious adverse events (SAE) (defined as any untoward medical occurrence that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or requires intervention to prevent permanent impairment or damage) categorised by major system order class (SOC, MedDRA coding). FDC = fixed dose combination.