Appendix

TRILOGY ACS Efficacy Adjustment Models

The TRILOGY ACS efficacy outcome adjustment models were constructed using a comprehensive list of patient characteristics and risk factors selected based on clinical knowledge (for a complete list, see the table below). Missing values were imputed using a multiple imputation approach that applies an MCMC method to create a monotone missing pattern and then uses a multivariate normal distribution to impute missing values. The imputation method replaces each missing value with a representative sample of plausible values by creating *m* complete data sets. As a result, the uncertainty due to the missingness is appropriately accounted for and analyses on the imputed data result in valid statistical inference. The *m* complete data sets can be analyzed using standard statistical procedures; the results are then aggregated across all simulated data sets. In this work, *m* was taken to be 25. Because a comparison of descriptive statistics from the first complete data set and the aggregation of the 25 complete data sets revealed negligible differences, only the first complete data set was used when fitting the adjustment for ease of computation. When fitting the adjustment model, the proportional hazards assumption was checked for each covariate and the linearity assumption was checked for each continuous covariate at alpha-level 0.05. If the proportional hazard assumption was violated, an interaction of the variable with log-transformed time was included in the model. If the linearity assumption was violated, a restricted cubic spline was used to approximate the non-linear relationship of the variable with the outcome. All analyses were performed using SAS 9.3 (SAS Institute Inc., Cary, NC) and R 2.14.1 (R Foundation for Statistical Computing, Vienna, Austria).

Table S1. TRILOGY ACS efficacy adjustment models

Characteristic	CV death, MI, stroke	CV death	MI	Stroke	All-cause death
Randomised treatment	✓	✓	✓	✓	✓
Weight (kg)	✓	✓	✓	✓	✓
Age (y)	✓	✓	✓	✓	✓
Female sex	✓	✓	✓	✓	✓
NSTEMI	✓	✓	✓	✓	✓
NSTEMI*log(time)	✓	-	-	-	-
Killip class I on presentation	✓	✓	✓	✓	✓
Time from presentation until start of study drug (h)	✓	✓	✓	✓	✓
Cardiovascular risk factors					
Family history of CAD	✓	✓	✓	✓	✓
Hypertension	✓	✓	✓	✓	✓
Hyperlipidaemia	✓	✓	✓	✓	✓
Diabetes mellitus	✓	✓	✓	✓	✓
Current/recent smoke	✓	✓	✓	✓	✓
Cardiovascular disease history					
Previous myocardial infarction	✓	✓	✓	✓	✓
Previous PCI	✓	✓	✓	✓	✓
Previous CABG	✓	✓	✓	✓	✓
Previous peripheral artery disease	✓	✓	✓	✓	✓
Previous atrial fibrillation	✓	✓	✓	✓	✓
Previous heart failure	✓	✓	✓	✓	✓
At randomisation					
Systolic blood pressure (mm Hg)	✓*	✓	✓	✓*	✓
Heart rate (bpm)	✓	✓	✓	✓*	✓
Heart rate*log(time)	✓	✓	-	-	✓
Clopid stratum 2: started in hosp ≤72 h	✓	✓	✓	✓	✓
Clopid stratum 3: started at home	✓	✓	✓	✓	✓
Angiography performed?	✓	✓	✓	✓	✓
Haemoglobin (g/dL)	✓	✓	✓	✓	✓

Characteristic	CV death, MI, stroke	CV death	MI	Stroke	All-cause death
Creatinine (mg/dL)	✓*	✓	✓*	✓	✓
Baseline concomitant medications					
Beta-blocker	✓	✓	✓	✓	✓
ACE inhibitor/ARB	✓	✓	✓	✓	✓
Statin	✓	✓	✓	✓	✓
Proton-pump inhibitor	✓	✓	✓	✓	✓
Region†					
East Asia	✓	✓	✓	✓	✓
Indian Subcontinent	✓	✓	✓	✓	✓
Latin America	✓	✓	✓	✓	✓
Mediterranean Basin	✓	✓	✓	✓	✓
North America	✓	✓	✓	✓	✓
Western Europe/Scandinavia	✓	✓	✓	✓	✓
Rest of world	✓	✓	✓	✓	✓

*A restricted cubic spline was used to account for the non-linear relationship of the variable with the outcome.
†Region was left out of the adjusted analyses due to collinearity with HDI.
ARB, angiotensin receptor blocker; BPM, beats per minute; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CV, cardiovascular, MI, myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention

Table S2. Classification of participating countries according to Human Development Index and gross national income

Human Development Index (2010)			Gross National Income (2010)		
Medium (*n*=1898)	**High (*n*=3744)**	**Very High (*n*=3659)**	**Lower Middle (*n*=2107)**	**Upper Middle (*n*=3353)**	**High (*n*=3841)**
India (n=1141)	Turkey (n=200)	Poland (n=393)	India (n=1141)	Tunisia (n=47)	Poland (n=393)
South Africa (n=77)	Tunisia (n=47)	Portugal (n=54)	Philippines (n=127)	Thailand (n=93)	Hungary (n=260)
Egypt (n=132)	Colombia (n=123)	Hungary (n=260)	Egypt (n=132)	China (n=328)	Croatia (n=182)
Philippines (n=127)	Brazil (n=362)	Malta (n=22)	Ukraine (n=707)	Peru (n=156)	Slovakia (n=162)
Thailand (n=93)	Ukraine (n=707)	Slovakia (n=162)		Colombia (n=123)	Czech Republic (n=138)
China (n=328)	Russian Federation (n=299)	Czech Republic (n=138)		Serbia (n=91)	Malta (n=22)
	Peru (n=156)	Singapore (n=13)		South Africa (n=77)	South Korea (n=82)
	Costa Rica (n=10)	United Kingdom (n=106)		Bulgaria (n=528)	Portugal (n=54)
	Serbia (n=91)	Austria (n=23)		Costa Rica (n=10)	Greece (n=43)
	Bulgaria (n=528)	Italy (n=232)		Panama (n=70)	Israel (n=214)
	Malaysia (n=84)	Greece (n=43)		Romania (n=257)	New Zealand (n=26)
	Mexico (n=109)	Spain (n=43)		Malaysia (n=84)	Spain (n=43)
	Panama (n=70)	Denmark (n=55)		Argentina (n=357)	Italy (n=232)
	Croatia (n=182)	Belgium (n=29)		Mexico (n=109)	United Kingdom (n=106)
	Romania (n=257)	Finland (n=13)		Brazil (n=362)	Singapore (n=13)
	Argentina (n=357)	France (n=99)		Turkey (n=200)	France (n=99)
	Chile (n=89)	Israel (n=214)		Russian Federation (n=299)	Ireland (n=18)
	Lithuania (n=73)	Switzerland (n=20)		Chile (n=89)	Canada (n=146)
		South Korea (n=82)		Lithuania (n=73)	Germany (n=133)
		Germany (n=133)			Australia (n=41)
		Sweden (n=14)			Belgium (n=29)
		Canada (n=146)			Austria (n=23)
		Netherlands (n=155)			Finland (n=13)

Human Development Index (2010)			Gross National Income (2010)		
Medium (*n*=1898)	**High (*n*=3744)**	**Very High (*n*=3659)**	**Lower Middle (*n*=2107)**	**Upper Middle (*n*=3353)**	**High (*n*=3841)**
		Ireland (n=18)			US/Puerto Rico (n=1125)
		US/Puerto Rico (n=1125)			Netherlands (n=155)
		New Zealand (n=26)			Sweden (n=14)
		Australia (n=41)			Denmark (n=55)
					Switzerland (n=20)