

Supplemental Online Content

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eMethods 1. Search strategy

eMethods 2. Combined dataset

eMethods 3. Post hoc analyses

eTable 1. Definition of major adverse cardiac and cerebrovascular events in randomized trials included in the IPD meta-analysis

eTable 2. Patient characteristics for patients with saphenous vein grafts who did versus did not have per-protocol imaging

eTable 3. Patient characteristics for patients with saphenous vein grafts who underwent per-protocol imaging, by randomization group

eTable 4. Patient characteristics for patients with saphenous vein grafts who did not undergo per-protocol imaging, by randomization group

eTable 5. Sensitivity analyses for the primary outcome

eTable 6. Post hoc analyses for any graft failure

eTable 7. Net adverse events in patients receiving saphenous vein grafts

eTable 8. Comparison of outcomes for saphenous vein graft failure among patients randomized to ticagrelor monotherapy or aspirin

eTable 9. Comparison of bleeding events among patients randomized to ticagrelor monotherapy or aspirin

eFigure 1. Risk of bias in the included trials as assessed by the Cochrane risk of bias assessment tool 2

eFigure 2. PRISMA IPD Flow Diagram

eFigure 3. Individual and pooled estimates for bleeding events in the primary analysis

eFigure 4. Sensitivity analysis for saphenous vein graft failure per anastomosis

eFigure 5. Sensitivity analysis for the primary outcome in patients with 1-year imaging

eFigure 6. Post hoc analysis for saphenous vein graft occlusion

eFigure 7. Treatment-by-subgroup interaction for any graft failure

eFigure 8. BARC type 2, 3, or 5 bleeding in subgroups

eFigure 9. Forest plot for saphenous vein graft failure for aspirin, ticagrelor dual antiplatelet therapy, and ticagrelor monotherapy in the post hoc network meta-analysis

eReferences

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

eMethods 1. Search strategy

Ovid MEDLINE – ALL (1946 to present)

Searched on June 1, 2022

No language or publication date restrictions

Limited to RCTs with BMJ's validated study design search filter: <https://bestpractice.bmj.com/info/us/toolkit/learn-ebm/study-design-search-filters/>

Line #	Search
1	Ticagrelor/
2	(ticagrelor or brilinta or briliq or "AZD 6140" or "AZD6140" or "3-(7-((2-(3,4-difluorophenyl)cyclopropyl)amino)-5-(propylthio)-3H-(1-3)-triazolo(4,5-d)pyrimidin-3-yl)-5-(2-hydroxyethoxy)cyclopentane-1,2-diol" or "3 [7 [2 (3,4 difluorophenyl)cyclopropylamino] 5 propylthio 1,2,3 triazolo[4,5 d]pyrimidin 3 yl] 5 (2 hydroxyethoxy) 1,2 cyclopentanediol" or "3 [7 [2 (3,4 difluorophenyl)cyclopropylamino] 5 propylthio 1,2,3 triazolo[4,5 d]pyrimidin 3 yl] 5 hydroxymethoxy 1,2 cyclopentanediol" or possia).tw
3	1 or 2
4	Coronary Artery Bypass/ or Coronary Artery Bypass, Off-Pump/
5	(coronary adj2 (bypass* or graft* or surger*)).tw.
6	(CABG or aorticocoronary anastomosis or total arterial revasculari*ation* or multiple arterial revasculari*ation*).tw.
7	Internal Mammary-Coronary Artery Anastomosis/
8	((right internal mammary artery or RIMA or left internal mammary artery or LIMA or Coronary Internal Mammary Artery or arteria mammaria interna or arteria thoracica interna or internal thoracic artery or mammary internal artery) and (transplant* or graft* or anastomosis)).tw.
9	(surgical revasculari*ation* or cardiac muscle revasculari*ation* or coronary revasculari*ation* or heart muscle revasculari*ation* or heart myocardium revasculari*ation* or heart revasculari*ation* or internal mammary arterial anastomosis or internal mammary arterial implant* or internal mammary artery anastomosis or internal mammary artery graft* or internal mammary artery implant* or internal mammary-coronary artery anastomosis).tw.
10	Myocardial Revascularization/
11	(myocardial revasculari*ation* or myocardium revasculari*ation* or mammary artery implant* or mammary arterial implant* or mammary artery reimplant* or mammary arterial reimplant* or vineberg operation*).tw.
12	Transmyocardial Laser Revascularization/
13	(transmyocardial laser revasculari*ation* or trans-myocardial laser revasculari*ation*).tw.
14	or/4-13
15	3 and 14
16	"randomized controlled trial".pt.
17	(random* or single blind* or double blind* or triple blind*).ti,ab.
18	(retraction of publication or retracted publication).pt.
19	or/16-18
20	(animals not humans).sh.
21	((comment or editorial or meta-analysis or practice-guideline or review or letter) not "randomized controlled trial").pt.
22	(random sampl* or random digit* or random effect* or random survey or random regression).ti,ab. not "randomized controlled trial".pt.
23	19 not (20 or 21 or 22)
24	15 and 23

Ovid Embase (1974 to present)

Searched on June 1, 2022

No language or publication date restrictions

Limited to RCTs with BMJ's validated study design search filter: <https://bestpractice.bmj.com/info/us/toolkit/learn-ebm/study-design-search-filters/>

1	ticagrelor/
2	(ticagrelor or brilinta or briliq or "AZD 6140" or "AZD6140" or "3-(7-((2-(3,4-Difluorophenyl)cyclopropyl)amino)-5-(propylthio)-3H-(1-3)-triazolo(4,5-d)pyrimidin-3-yl)-5-(2-hydroxyethoxy)cyclopentane-1,2-diol" or "3 [7 [2 (3,4 difluorophenyl)cyclopropylamino] 5 propylthio 1,2,3 triazolo[4,5 d]pyrimidin 3 yl] 5 (2 hydroxyethoxy) 1,2 cyclopentanediol" or "3 [7 [2 (3,4 difluorophenyl)cyclopropylamino] 5 propylthio 1,2,3 triazolo[4,5 d]pyrimidin 3 yl] 5 hydroxymethoxy 1,2 cyclopentanediol" or possia).tw.
3	1 or 2
4	coronary artery bypass graft/ or off pump coronary surgery/
5	(coronary adj2 (bypass* or graft* or surger*)).tw.
6	(CABG or aorticocoronary anastomosis or total arterial revasculari*ation* or multiple arterial revasculari*ation*).tw.
7	heart muscle revascularization/
8	((right internal mammary artery or RIMA or left internal mammary artery or LIMA or Coronary Internal Mammary Artery or arteria mammaria interna or arteria thoracica interna or internal thoracic artery or mammary internal artery) and (transplant* or graft* or anastomosis)).tw.
9	(surgical revasculari*ation* or cardiac muscle revasculari*ation* or coronary revasculari*ation* or heart muscle revasculari*ation* or heart myocardium revasculari*ation* or heart revasculari*ation* or internal mammary arterial anastomosis or internal mammary arterial implant* or internal mammary artery anastomosis or internal mammary artery graft* or internal mammary artery implant* or internal mammary-coronary artery anastomosis).tw.
10	(myocardial revasculari*ation* or myocardium revasculari*ation* or mammary artery implant* or mammary arterial implant* or mammary artery reimplant* or mammary arterial reimplant* or vineberg operation*).tw.
11	(transmyocardial laser revasculari*ation* or trans-myocardial laser revasculari*ation*).tw.
12	or/4-11
13	3 and 12
14	(random\$ or placebo\$ or single blind\$ or double blind\$ or triple blind\$).ti,ab.
15	RETRACTED ARTICLE/
16	14 or 15
17	(animal\$ not human\$).sh,hw.
18	(book or conference paper or editorial or letter or review).pt. not exp randomized controlled trial/
19	(random sampl\$ or random digit\$ or random effect\$ or random survey or random regression).ti,ab. not exp randomized controlled trial/
20	16 not (17 or 18 or 19)
21	13 and 20

Cochrane Trials (Wiley)

Searched on June 1, 2022

ID	Search
#1	(ticagrelor or brilinta or brilique or "AZD 6140" or "AZD6140" or "3-(7-((2-(3,4-Difluorophenyl)cyclopropyl)amino)-5-(propylthio)-3H-(1-3)-triazolo(4,5-d)pyrimidin-3-yl)-5-(2-hydroxyethoxy)cyclopentane-1,2-diol" or "3 [7 [2 (3,4 difluorophenyl)cyclopropylamino] 5 propylthio 1,2,3 triazolo[4,5 d]pyrimidin 3 yl] 5 (2 hydroxyethoxy) 1,2 cyclopentenediol" or "3 [7 [2 (3,4 difluorophenyl)cyclopropylamino] 5 propylthio 1,2,3 triazolo[4,5 d]pyrimidin 3 yl] 5 hydroxymethoxy 1,2 cyclopentenediol" or possia):ti,ab
#2	(coronary NEAR/2 (bypass* or graft* or surger*)):ti,ab
#3	(CABG or aorticocoronary anastomosis or total arterial revasculari*ation* or multiple arterial revasculari*ation*):ti,ab
#4	((right internal mammary artery or RIMA or left internal mammary artery or LIMA or Coronary Internal Mammary Artery or arteria mammaria interna or arteria thoracica interna or internal thoracic artery or mammary internal artery) and (transplant* or graft* or anastomosis)):ti,ab
#5	(surgical revasculari*ation* or cardiac muscle revasculari*ation* or coronary revasculari*ation* or heart muscle revasculari*ation* or heart myocardium revasculari*ation* or heart revasculari*ation* or internal mammary arterial anastomosis or internal mammary arterial implant* or internal mammary artery anastomosis or internal mammary artery graft* or internal mammary artery implant* or internal mammary-coronary artery anastomosis):ti,ab
#6	(myocardial revasculari*ation* or myocardium revasculari*ation* or mammary artery implant* or mammary arterial implant* or mammary artery reimplant* or mammary arterial reimplant* or vineberg operation*):ti,ab
#7	(transmyocardial laser revasculari*ation* or trans-myocardial laser revasculari*ation*):ti,ab
#8	#2 OR #3 OR #4 OR #5 OR #6 OR #7
#9	#1 AND #8

eMethods 2. Combined dataset

Individual patient data were provided for the following variables: age, sex, acute coronary syndrome, smoking, diabetes, hypertension, dyslipidemia, prior myocardial infarction, prior percutaneous coronary intervention, prior stroke, left ventricular ejection fraction, creatinine, history of chronic kidney disease; use of cardiopulmonary bypass, saphenous vein graft harvest technique, number of saphenous vein grafts, sequential saphenous vein grafting, distal and sequential saphenous vein graft target vessel/territory, internal thoracic artery use, internal thoracic artery sequential grafting, internal thoracic artery distal and sequential target vessel/territory, radial artery use, radial artery sequential grafting, radial artery distal and sequential target vessel/territory; randomization allocation, duration of randomized treatment, per protocol randomized treatment, time to ticagrelor first dose, ticagrelor loading dose, time to aspirin first dose, aspirin total daily dose, aspirin discontinued preoperatively or aspirin-naïve; adverse events including date when available: all-cause death, cardiovascular death, non-fatal myocardial infarction, non-fatal stroke, repeat revascularization, Bleeding Academic research consortium (BARC) bleeding; follow-up time; protocol-directed imaging and timing, unscheduled imaging (type, timing), graft occlusion, graft stenosis >50%, graft segment (anastomosis) occlusion, graft segment (anastomosis) stenosis >50%.

eMethods 3. Post hoc analyses

Post hoc analyses for the primary analysis were performed using a multi-level logistic regression model with trial as a random effect (reported as odds ratios [OR] with 95% confidence intervals [CI]) or a Cox proportional hazards frailty model with trial as a random effect (reported as hazard ratio [HR] with 95% CI). These post-hoc analyses assessed the association of ticagrelor dual antiplatelet therapy (DAPT) (compared to aspirin) with saphenous vein graft occlusion at the graft level; the association of ticagrelor DAPT (compared to aspirin) with any graft failure (including arterial and saphenous vein grafts) at the patient, graft, and anastomosis level, and with the composite of any graft failure or cardiovascular death (patient-level).

These post hoc analyses also assessed the association of ticagrelor DAPT (compared to aspirin) with bleeding events, the individual components of MACCE, and MACE. Bleeding risk across important clinical subgroups (age, sex, diabetes, smoking, acute coronary syndrome) were assessed by inclusion of an interaction term between treatment and the subgroup of interest in the regression model.

Another post hoc analysis assessed the association of ticagrelor DAPT (compared to aspirin) with net adverse events, net adverse major clinical events, and overall net adverse events.

A post hoc frequentist random-effects network meta-analysis was performed with aspirin as the reference. Inconsistency between direct and indirect estimates was assessed by generalized Cochran's Q statistics for multivariate meta-analysis.¹

Post hoc analyses for the supplementary analysis were performed using a multi-level logistic regression model with trial as a random effect (reported as OR with 95% CI) to assess the association of ticagrelor monotherapy (compared to aspirin) with saphenous vein graft failure at the patient and anastomosis level, the composite of saphenous vein graft failure or cardiovascular death (patient-level), and bleeding events.

eTable 1. Definition of major adverse cardiac and cerebrovascular events in randomized trials included in the IPD meta-analysis

Event	TAP-CABG ²	DACAB ³	POPular CABG ⁴	TARGET ^{5 a}
Cardiovascular death	Death from cardiovascular or cerebrovascular causes, and any death without another known cause.	Death due to a cardiovascular etiology such as acute MI, sudden cardiac death, heart failure, stroke, cardiovascular procedure, cardiovascular hemorrhage, and other cardiovascular causes such as pulmonary embolism or PAD.	Defined as sudden death, death from acute myocardial infarction, arrhythmia, heart failure, cardiogenic shock, cerebrovascular event (ischemic stroke, hemorrhagic stroke ischemic stroke with hemorrhagic conversion, or intracranial hemorrhage), pulmonary embolism, peripheral arterial disease, bleeding and any death without another known cause.	
Myocardial infarction	Defined based on the universal definition of MI. ⁶ MI with CABG was defined as >5 x normal reference elevation of troponin-I within 72h after CABG, when associated with new pathological Q-waves or left bundle branch block, or angiographically documented new occlusion, or imaging evidence of new loss of myocardium.	Defined based on the third universal definition of MI. ⁷	Spontaneous MI: A rise and/or fall of cardiac biomarker values (preferably cardiac troponin (cTn)) occurring >48 hours following CABG, with at least two samples with a value above the 99th percentile upper reference limit (URL) and with at least one of the following: <ul style="list-style-type: none"> o Symptoms of ischemia o New or presumed new significant ST-segment–T wave (ST–T) changes or new left bundle branch block (LBBB) o Development of pathological Q waves in the ECG. 	

Event	TAP-CABG ²	DACAB ³	POPular CABG ⁴	TARGET ⁵
			<ul style="list-style-type: none"> o Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality o Identification of an intracoronary thrombus by angiography or autopsy. 	
Stroke	Focal loss of neurological function caused by an ischemic or hemorrhagic event, with residual symptoms lasting ≥24h or leading to death.	Acute episode of focal or global neurological dysfunction persisting at least 24h with presence of acute infarction as demonstrated by imaging.	Defined as an acute new neurological deficit ending in death or lasting >24 hours not due to another readily identifiable cause such as trauma.	
Repeat revascularization	PCI or CABG.		Any coronary revascularization is defined as a PCI (balloon inflation with or without stent implantation) or CABG after the initial CABG. Target vessel revascularization is defined as revascularization, with CABG or PCI (balloon inflation with or without stent implantation), of a graft or a coronary vessel that provides blood flow to an artery that was grafted during the index CABG. An intervention in the LM after the index CABG that included a graft on the LAD or RCX counts as target vessel revascularization.	

Abbreviations: CABG, coronary artery bypass grafting; DACAB, Different Antiplatelet Therapy Strategy after Coronary Artery Bypass Graft Surgery; IPD, individual patient data; LAD, left anterior descending artery; LM, left main; MI, myocardial infarction; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; RCX, ramus circumflexus.

^a In TARGET,⁵ major adverse cardiovascular events were defined as cardiovascular death, myocardial infarction, cerebrovascular accident, hospitalization for coronary ischemia, need for coronary intervention, without further specification.⁸

eTable 2. Patient characteristics for patients with saphenous vein grafts who did versus did not have per-protocol imaging ^a

	Imaging	No Imaging	P value	SMD
Patients	n=794	n=77		
Age, median (IQR), years	66 (60-71)	73 (65-76)	<.001	.541
Age >65 years, No. (%)	433 (54.5)	0.57 (74.0)	.001	.414
Female sex, No. (%)	115 (14.5)	13 (16.9)	.690	.066
Dyslipidemia, No. (%)	501 (63.1)	40 (51.9)	.071	.227
Hypertension, No. (%)	538 (67.8)	50 (64.9)	.706	.060
Diabetes, No. (%)	260 (32.7)	26 (33.8)	.956	.022
Smoking, No. (%)	205 (25.8)	21 (27.3)	.887	.033
Chronic kidney disease, No. (%)	44 (5.5)	8 (10.4)	.144	.180
Previous myocardial infarction, No. (%)	161 (20.3)	22 (28.6)	.119	.194
Previous PCI, No. (%)	0.44 (0.50)	0.49 (0.50)	.330	.116
ACS at presentation, No. (%)	105 (13.2)	10 (13.0)	1.000	.007
LVEF, median (IQR), %	60 (51-65)	57 (51-63)	.416	.126
Use of cardiopulmonary bypass, No. (%)	541 (68.1)	57 (74.0)	.350	.130
Endoscopic saphenous vein graft harvest, No. (%) ^b	40/749 (5.3)	4/75 (5.3)	1.000	<.001
Sequential saphenous vein grafts, No. (%)	584 (73.6)	63 (81.8)	.148	.200

Abbreviations: ACS, acute coronary syndrome; IQR, interquartile range; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; SMD, standardized mean difference.

^a Includes patients from the TAP-CABG², DACAB³, and POPular CABG⁴ trials.

^b Changes in denominators indicate missing data.

eTable 3. Patient characteristics for patients with saphenous vein grafts who underwent per-protocol imaging, by randomization group^a

	Ticagrelor DAPT	Aspirin	<i>P</i> value	SMD
Patients	n=394	n=400		
Age, median (IQR), years	66 (60-71)	66 (61-72)	.789	.037
Age >65 years, No. (%)	216 (56.0)	217 (55.1)	.761	.022
Female sex, No. (%)	59 (15.0)	56 (14.0)	.772	.028
Dyslipidemia, No. (%)	256 (65.0)	245 (61.3)	.311	.077
Hypertension, No. (%)	268 (68.0)	270 (67.5)	.936	.011
Diabetes, No. (%)	129 (32.7)	131 (32.8)	1.000	<.001
Smoking, No. (%)	101 (25.6)	104 (26.0)	.971	.008
Chronic kidney disease, No. (%)	25 (6.3)	19 (4.8)	.408	.070
Previous myocardial infarction, No. (%)	81 (20.6)	80 (20.0)	.914	.014
Previous PCI, No. (%)	0.44 (0.50)	0.43 (0.50)	.742	.023
ACS at presentation, No. (%)	46 (11.7)	59 (14.8)	.240	.091
LVEF, median (IQR), %	59 (51-64)	60 (51-65)	.831	.018
Use of cardiopulmonary bypass, No. (%)	264 (67.0)	277 (69.2)	.547	.048
Endoscopic saphenous vein graft harvest, No. (%) ^b	18/374 (4.8)	22/375 (5.9)	.632	.047
Sequential saphenous vein grafts, No. (%)	284 (72.1)	300 (75.0)	.394	.066

Abbreviations: ACS, acute coronary syndrome; IQR, interquartile range; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; SMD, standardized mean difference.

^a Includes patients from the TAP-CABG², DACAB³, and POPular CABG⁴ trials.

^b Changes in denominators indicate missing data.

eTable 4. Patient characteristics for patients with saphenous vein grafts who did not undergo per-protocol imaging, by randomization group ^a

	Ticagrelor DAPT	Aspirin	<i>P</i> value	SMD
Patients	n=41	n=36		
Age, median (IQR), years	74 (68-76)	71 (62-75)	.230	.244
Age >65 years, No. (%)	32 (78.0)	25 (69.4)	.397	.194
Female sex, No. (%)	6 (14.6)	7 (19.4)	.797	.128
Dyslipidemia, No. (%)	19 (46.3)	21 (58.3)	.411	.242
Hypertension, No. (%)	26 (63.4)	24 (66.7)	.953	.068
Diabetes, No. (%)	14 (34.1)	12 (33.3)	1.000	.017
Smoking, No. (%)	13 (31.7)	8 (22.2)	.499	.215
Chronic kidney disease, No. (%)	3 (7.3)	5 (13.9)	.570	.215
Previous myocardial infarction, No. (%)	11 (26.8)	11 (30.6)	.914	.082
Previous PCI, No. (%)	0.51 (0.51)	0.47 (0.51)	.730	.079
ACS at presentation, No. (%)	4 (9.8)	6 (16.7)	.575	.205
LVEF, median (IQR), %	55 (51-61)	60 (55-63)	.568	.163
Use of cardiopulmonary bypass, No. (%)	33 (80.5)	24 (66.7)	.263	.317
Endoscopic saphenous vein graft harvest, No. (%) ^b	1/40 (2.5)	3/35 (8.6)	.514	.268
Sequential saphenous vein grafts, No. (%)	36 (87.8)	27 (75.0)	.247	.334

Abbreviations: ACS, acute coronary syndrome; IQR, interquartile range; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; SMD, standardized mean difference.

^a Includes patients from the TAP-CABG², DACAB³, and POPular CABG⁴ trials.

^b Changes in denominators indicate missing data.

eTable 5. Sensitivity analyses for the primary outcome

Outcome	Analysis	Odds Ratio (95% CI)
Saphenous vein graft failure <i>per graft</i>	As-treated ^{a,b}	0.53 (0.33-0.79)
Saphenous vein graft failure <i>per graft</i>	Per-protocol ^{a,c}	0.52 (0.33-0.80)
Saphenous vein graft failure <i>per graft</i>	Multiple imputation ^d	0.51 (0.35-0.74)

Abbreviations: CI, confidence interval.

^a The analysis population was saphenous vein grafts from patients with saphenous vein grafting who underwent protocol-defined imaging in the TAP-CABG², DACAB³ or POPular CABG⁴ trials.

^b Analyzed according to which treatment was received.

^c Analyzed according to whether the randomized treatment was administered in accordance with the individual trial protocols.

^d The analysis population was all saphenous vein grafts in the TAP-CABG², DACAB³ or POPular CABG⁴ trials, with imputation of the outcome for saphenous vein grafts of patients who did not undergo protocol-defined imaging.

eTable 6. Post hoc analyses for any graft failure

Outcome	Ticagrelor DAPT	Aspirin	Difference, % (95% CI) ^a	Odds Ratio (95% CI) ^a	P value
	No./total No. (%)	No./total No. (%)			
Graft failure <i>per graft</i>					
TAP-CABG ²	8/73 (11.0)	28/94 (29.8)	-18.8 (-31.3 to -6.4)	0.29 (0.12-0.69)	.006
DACAB ³	23/362 (6.3)	57/352 (16.2)	-10.2 (-15.1 to -5.2)	0.35 (0.20-0.60)	<.001
POPular CABG ⁴	37/469 (7.9)	42/486 (8.6)	-0.8 (-4.3 to 2.8)	0.91 (0.57-1.44)	.67
Overall	68/904 (7.5)	127/932 (13.6)	-5.9 (-8.8 to -3.1)	0.52 (0.38-0.72)	<.001
Graft failure <i>per patient</i>	65/401 (16.2)	110/408 (27.0)	-10.4 (-16.0 to -4.9)	0.52 (0.37-0.74)	<.001
Graft failure or cardiovascular death	68/404 (16.8)	112/410 (27.3)	-10.1 (-15.7 to -4.6)	0.52 (0.37-0.74)	<.001
Graft failure <i>per anastomosis</i>	98/1501 (6.5)	178/1548 (11.5)	-4.6 (-7.1 to -2.2)	0.55 (0.40-0.76)	<.001

The analysis population consisted of patients with protocol-defined imaging. For the composite of graft failure or cardiovascular death, the analysis population consisted of patients with protocol-defined imaging or cardiovascular death.

Abbreviations: CI, confidence interval; DAPT, dual antiplatelet therapy.

^a Adjusted by trial.

eTable 7. Net adverse events in patients receiving saphenous vein grafts

Outcome	Ticagrelor DAPT	Aspirin	Difference, % (95% CI) ^a	Odds Ratio (95% CI) ^a	P value
	No./total No. (%)	No./total No. (%)			
Net adverse events ^b					
TAP-CABG ²	6/19 (31.6)	15/23 (65.2)	-33.6 (-63.9 to -3.4)	0.25 (0.07-0.93)	.04
DACAB ³	23/157 (14.7)	49/153 (32.0)	-17.4 (-26.6 to -8.1)	0.36 (0.21-0.64)	<.001
POPular CABG ⁴	38/218 (17.4)	47/224 (21.0)	-3.6 (-10.9 to 3.8)	0.80 (0.49-1.28)	.34
Overall	67/394 (17.0)	111/400 (27.8)	-10.6 (-16.3 to -4.9)	0.53 (0.38-0.75)	<.001
Net adverse major clinical events ^c					
TAP-CABG ²	0/19 (0.0)	1/23 (4.4)	-	-	-
DACAB ³	6/167 (3.6)	8/166 (4.8)	-1.2 (-5.6 to 3.1)	0.74 (0.25-2.18)	.58
POPular CABG ⁴	22/249 (8.8)	16/247 (6.5)	2.4 (-2.3 to 7.1)	1.40 (0.72-2.74)	.33
Overall	28/435 (6.4)	25/436 (5.7)	0.7 (-2.5 to 3.9)	1.13 (0.65-1.97)	.67
Overall net adverse events ^d					
TAP-CABG ²	7/19 (36.8)	15/23 (65.2)	-28.4 (-2.4 to 59.1)	0.31 (0.08-1.15)	.08
DACAB ³	67/157 (42.1)	63/153 (40.4)	1.8 (-9.2 to 12.7)	1.08 (0.69-1.69)	.75
POPular CABG ⁴	81/225 (33.9)	60/224 (36.8)	9.2 (0.6 to 17.8)	1.54 (1.03-2.30)	.04
Overall	155/403 (38.5)	138/403 (34.2)	4.3 (-2.3 to 10.9)	1.21 (0.90-1.61)	.20

Abbreviations: CI, confidence interval; DAPT, dual antiplatelet therapy.

^a Adjusted by trial.

^b Included graft failure (failure of arterial and/or saphenous vein grafts) and BARC \geq type 3 bleeding. Subset to patients with protocol-defined imaging.

^c Included all-cause death, myocardial infarction, stroke, and BARC \geq type 3 bleeding.

^d Included graft failure, MACCE, and BARC \geq type 2 bleeding. Subset to patients with protocol-defined imaging or death.

eTable 8. Comparison of outcomes for saphenous vein graft failure among patients randomized to ticagrelor monotherapy or aspirin

Outcome	Ticagrelor Monotherapy	Aspirin	Difference, % (95% CI) ^a	Odds Ratio (95% CI) ^a	P value
	No./total No. (%)	No./total No. (%)			
Primary outcome					
Saphenous vein graft failure <i>per graft</i>					
DACAB ³	40/219 (18.3)	50/223 (22.4)	-4.5 (0.04 to 13.3)	0.77 (0.46-1.30)	.33
TARGET ⁵	31/149 (20.8)	33/159 (20.8)	0.0 (-9.8 to 9.7)	1.00 (0.56-1.81)	.99
Overall	71/368 (19.3)	83/382 (21.7)	-2.6 (-9.1 to 3.9)	0.86 (0.58-1.27)	.44
Saphenous vein graft failure <i>per patient</i>	64/254 (25.2)	75/256 (29.3)	-4.1 (-11.9 to 3.7)	0.81 (0.55-1.20)	.30
Saphenous vein graft failure or cardiovascular death	64/254 (28.3)	79/260 (32.7)	-5.2 (-13.0 to 2.6)	0.77 (0.52-1.14)	.19
Saphenous vein graft failure <i>per anastomosis</i>	88/622 (14.2)	113/620 (18.2)	-3.1 (-8.3 to 2.2)	0.77 (0.52-1.14)	.19

The analysis population consisted of patients with saphenous vein grafts who underwent protocol-defined imaging. For the composite of saphenous vein graft failure or cardiovascular death, the analysis population consisted of patients with protocol-defined imaging or cardiovascular death.

Abbreviations: CI, confidence interval.

^a Adjusted by trial.

eTable 9. Comparison of bleeding events among patients randomized to ticagrelor monotherapy or aspirin

Outcome	Ticagrelor Monotherapy (n=293)	Aspirin (n=289)	Difference, % (95% CI) ^a	Odds Ratio (95% CI) ^a	P value
	No. of events (%)	No. of events (%)			
BARC bleeding type 2 - 5					
DACAB ³	20/166 (12.1)	16/166 (9.6)	2.4 (-4.3 to 9.1)	1.28 (0.64-2.58)	.48
TARGET ⁵	6/127 (4.7)	5/123 (4.1)	0.7 (-4.5 to 5.8)	1.17 (0.35-3.96)	.80
Overall	26/293 (8.9)	21/289 (7.3)	1.7 (-2.8 to 6.1)	1.25 (0.69-2.29)	.46
BARC bleeding type 2, 3 or 5					
DACAB ³	20/166 (12.1)	16/166 (9.6)	2.4 (-4.3 to 9.1)	1.28 (0.64-2.58)	.48
TARGET ⁵	6/127 (4.7)	5/123 (4.1)	0.7 (-4.5 to 5.8)	1.17 (0.35-3.96)	.80
Overall	26/293 (8.9)	21/289 (7.3)	1.7 (-2.8 to 6.1)	1.25 (0.69-2.29)	.46
BARC bleeding type 3 or 5					
DACAB ³	1/166 (0.6)	0/166 (0.0)	-	-	-
TARGET ⁵	2/166 (1.6)	0/123 (0.0)	-	-	-
Overall	3/293 (1.0)	0/289 (0.0)	-	-	-

The analysis population consisted of patients with saphenous vein grafts.

Abbreviations: BARC, Bleeding Academic Research Consortium; CI, confidence interval.

^a Adjusted by trial.

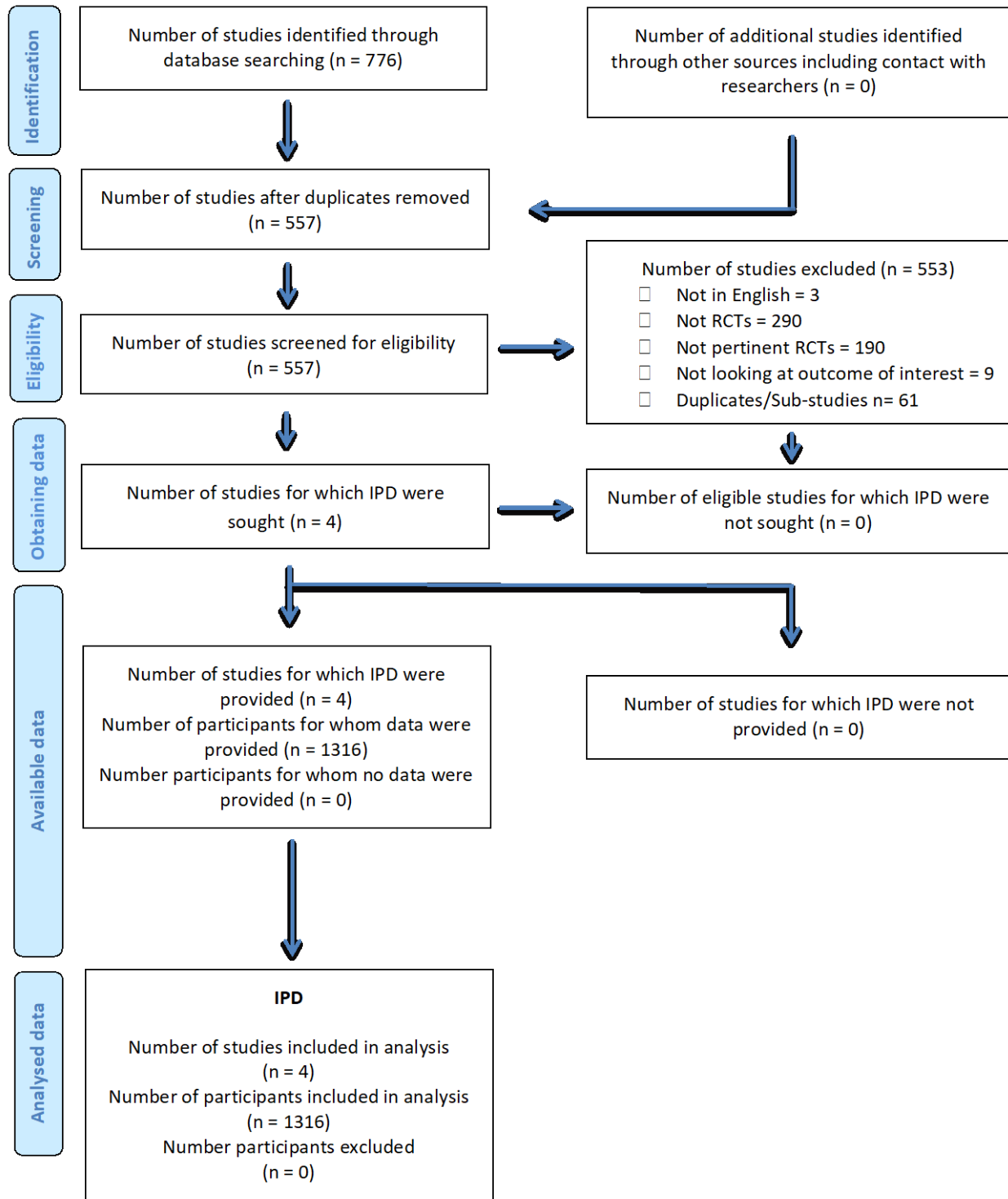
eFigure 1. Risk of bias in the included trials as assessed by the Cochrane risk of bias assessment tool 2

Intention-to-treat	Study ID	Experimental	Comparator	Outcome	D1	D2	D3	D4	D5	Overall		
	TAP-CABG	Ticagrelor DAPT	Aspirin monotherapy	Saphenous vein graft patency								Low risk
	DACAB	Ticagrelor DAPT and Ticagrelor monotherapy	Aspirin monotherapy	Saphenous vein graft patency							Some concerns	
	POPular CABG	Ticagrelor DAPT	Aspirin monotherapy	Saphenous vein graft patency								High risk
	TARGET	Ticagrelor monotherapy	Aspirin monotherapy	Saphenous vein graft patency								

D1	Randomisation process
D2	Deviations from the intended interventions
D3	Missing outcome data
D4	Measurement of the outcome
D5	Selection of the reported result

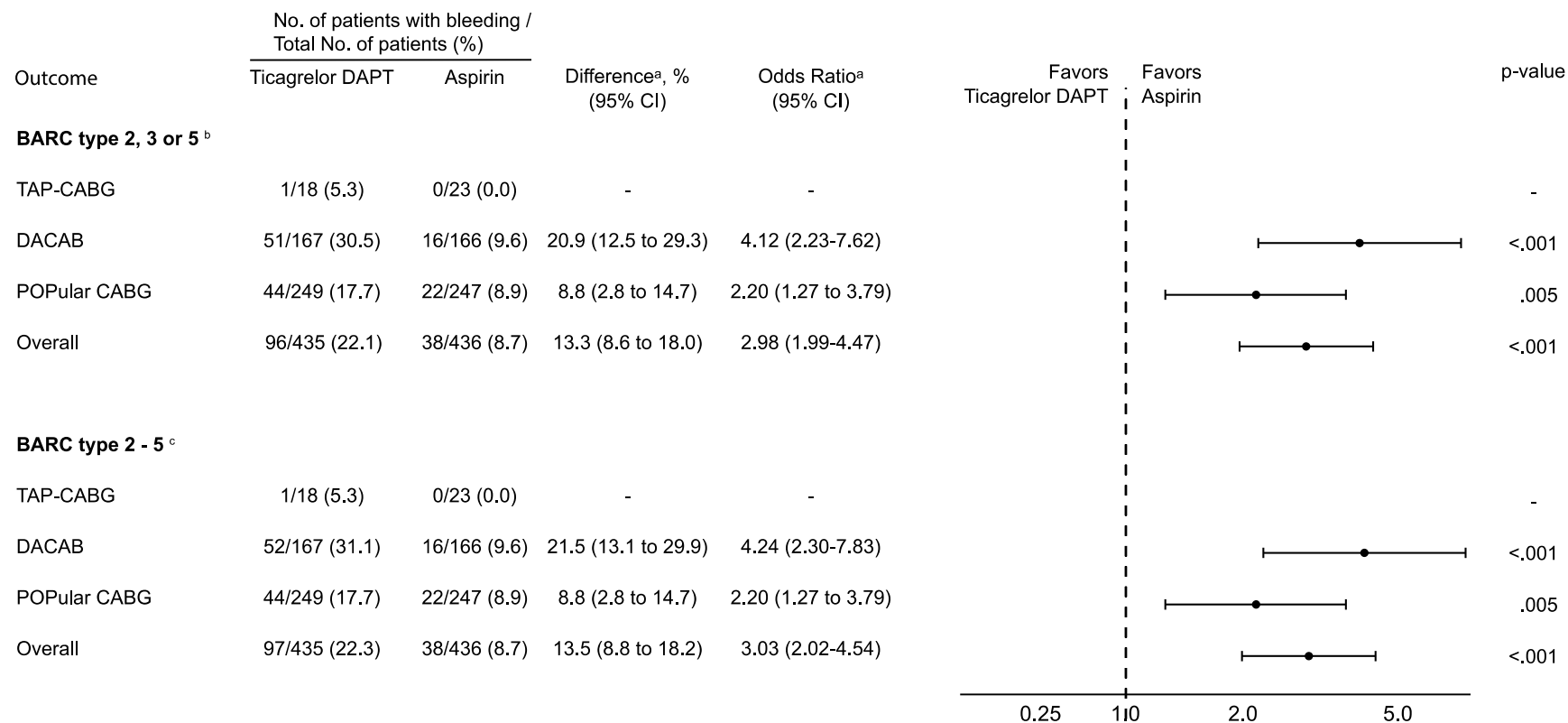
TAP-CABG, Ticagrelor and Aspirin for the Prevention of Cardiovascular Events after Coronary Artery Bypass Graft Surgery; DACAB, Different Antiplatelet Therapy Strategy after Coronary Artery Bypass Graft Surgery; DAPT, dual antiplatelet therapy; POPular CABG, Effect of Ticagrelor on Saphenous Vein Graft Patency in Patients undergoing Coronary Artery Bypass Grafting Surgery; TARGET, Ticagrelor Antiplatelet Therapy to Reduce Graft Events and Thrombosis.

eFigure 2. PRISMA IPD Flow Diagram



Abbreviations: IPD, individual patient data; RCTs, randomized clinical trials.

eFigure 3. Individual and pooled estimates for bleeding events in the primary analysis



The analysis population included patients who received saphenous vein grafts.

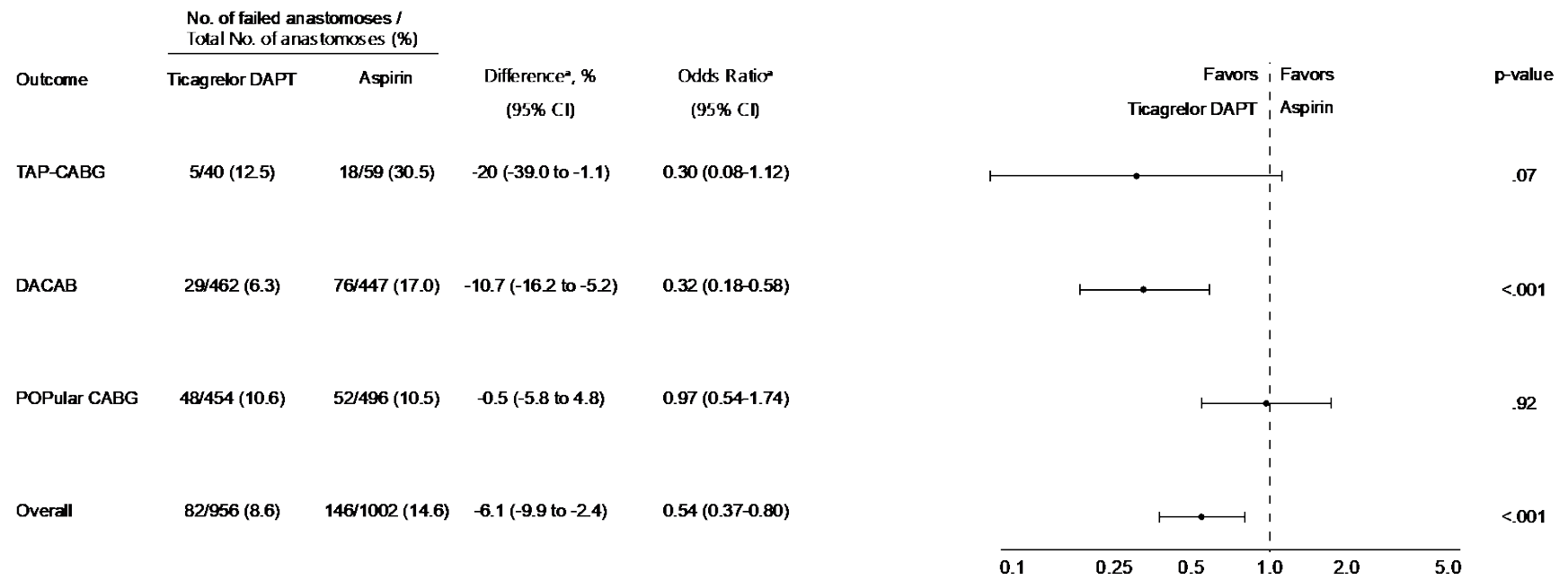
Abbreviations: BARC, Bleeding Academic Research Consortium; CI, confidence interval, DAPT, dual antiplatelet therapy.

^a Adjusted by trial.

^b Secondary outcome.

^c Post hoc outcome.

eFigure 4. Sensitivity analysis for saphenous vein graft failure per anastomosis

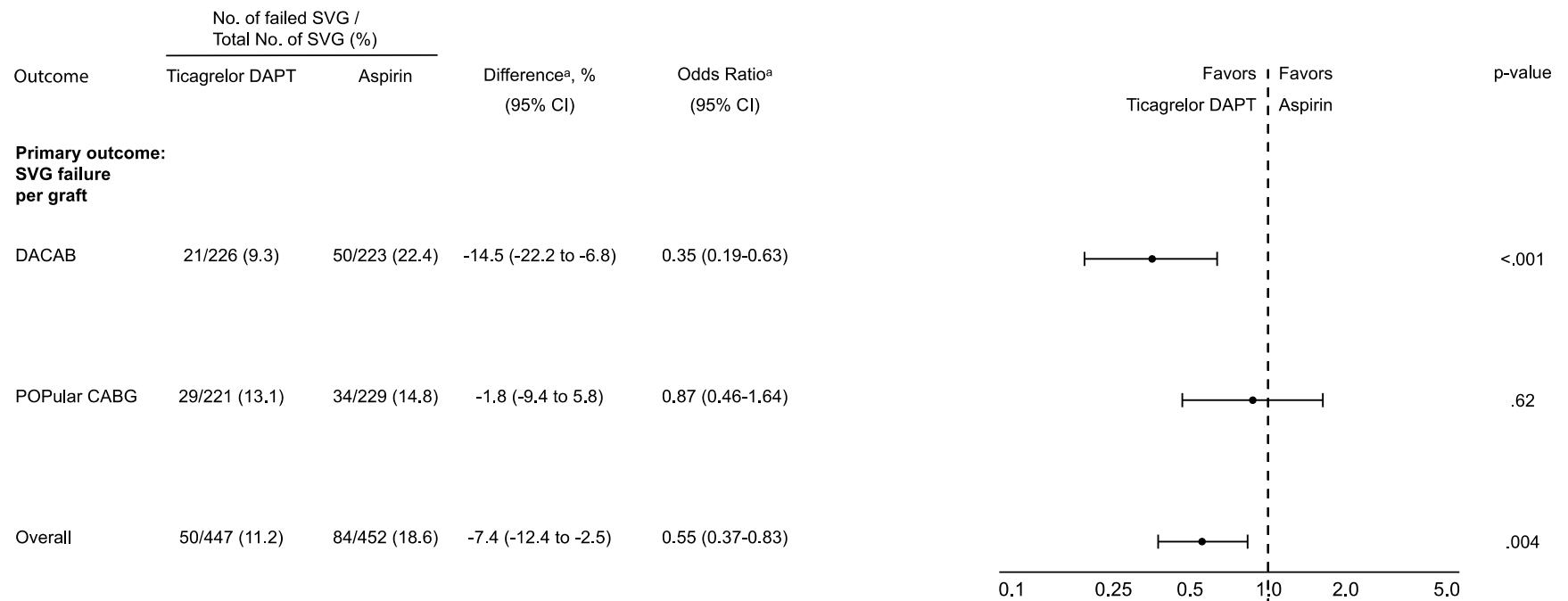


The analysis included saphenous vein grafts from patients who underwent protocol-defined imaging.

Abbreviations: CI, confidence interval; DAPT, dual antiplatelet therapy; SVG, saphenous vein graft.

^a Adjusted by trial.

eFigure 5. Sensitivity analysis for the primary outcome in patients with 1-year imaging

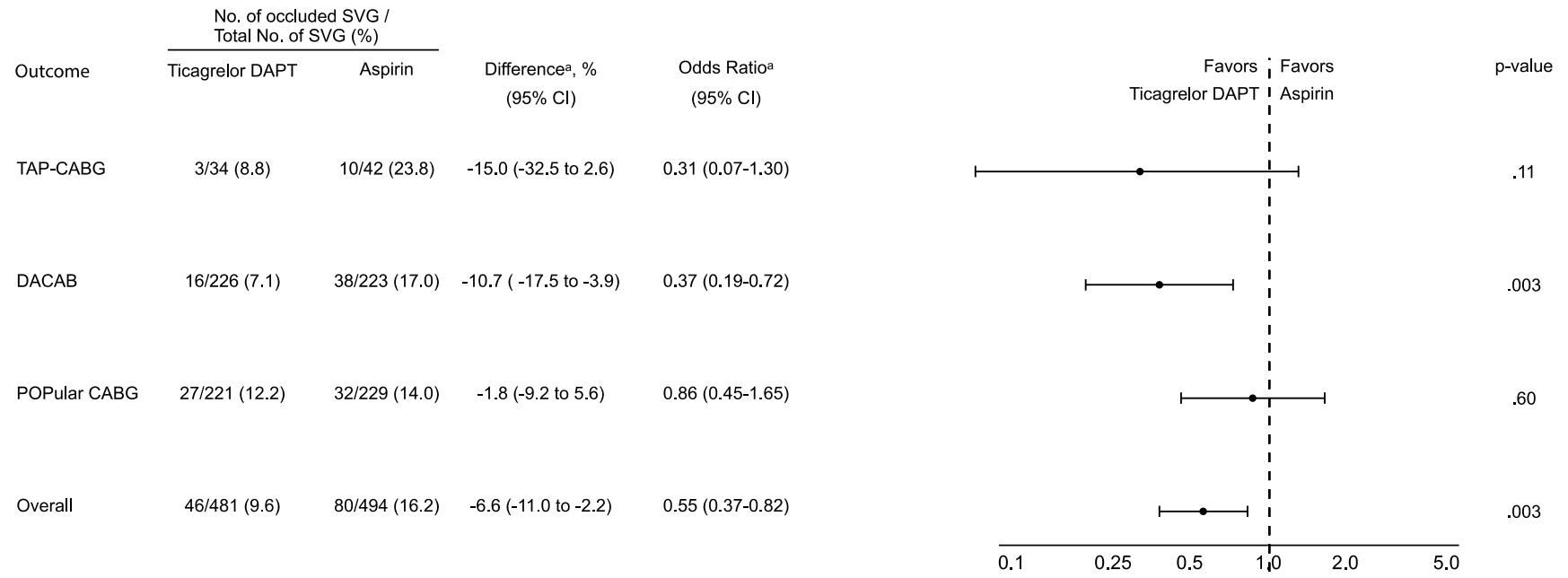


The analysis included saphenous vein grafts from patients who underwent protocol-defined imaging in the trials that had protocol-defined imaging at 1-year (DACAB, POPular CABG).

Abbreviations: CI, confidence interval; DAPT, dual antiplatelet therapy; SVG, saphenous vein graft.

^a Adjusted by trial.

eFigure 6. Post hoc analysis for saphenous vein graft occlusion

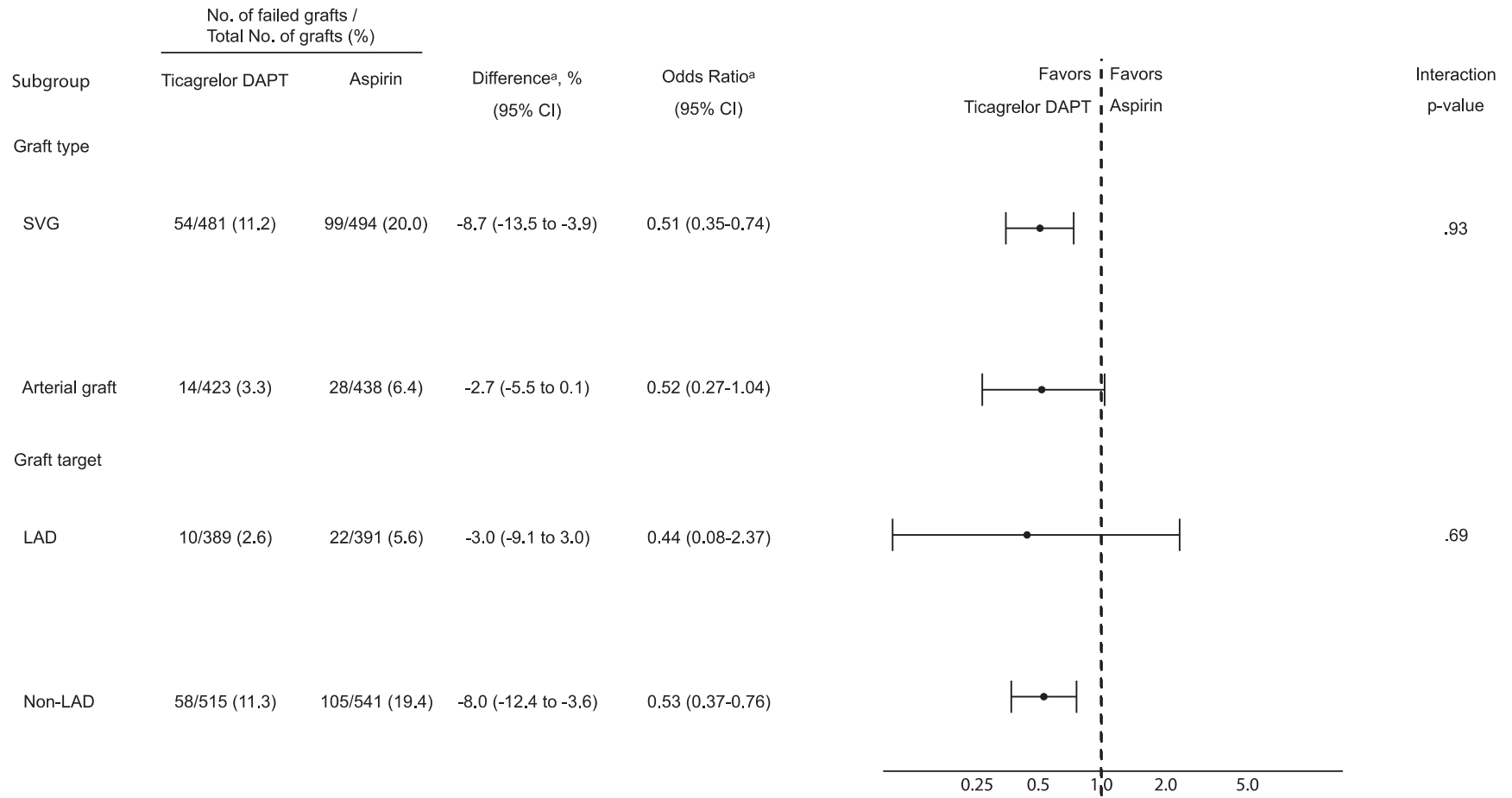


The analysis included saphenous vein grafts from patients who underwent protocol-defined imaging.

Abbreviations: CI, confidence interval; DAPT, dual antiplatelet therapy; SVG, saphenous vein graft.

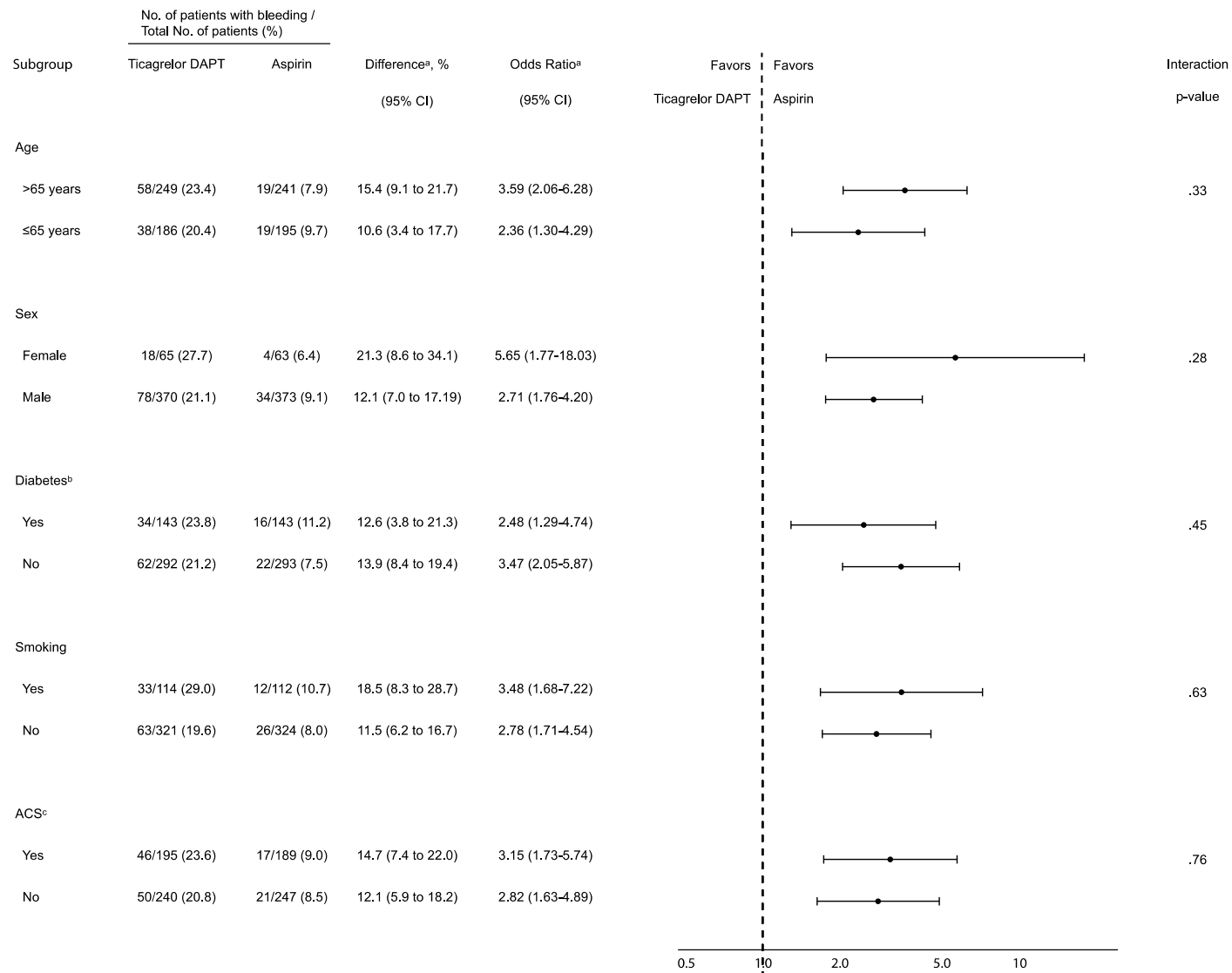
^a Adjusted by trial.

eFigure 7. Treatment-by-subgroup interaction for any graft failure



The analysis population included patients in the TAP-CABG, DACAB or POPularCABG trials who had protocol-defined imaging.
 Abbreviations: CI, confidence interval; DAPT, dual antiplatelet therapy; LAD, left anterior descending artery; SVG, saphenous vein graft.

eFigure 8. Bleeding Academic Research Consortium (BARC) type 2, 3, or 5 bleeding in subgroups



The analysis population included patients who received saphenous vein grafts in the TAP-CABG, DACAB or POPular CABG trials.

Abbreviations: CI, confidence interval; ACS, acute coronary syndrome; DAPT, dual antiplatelet therapy.

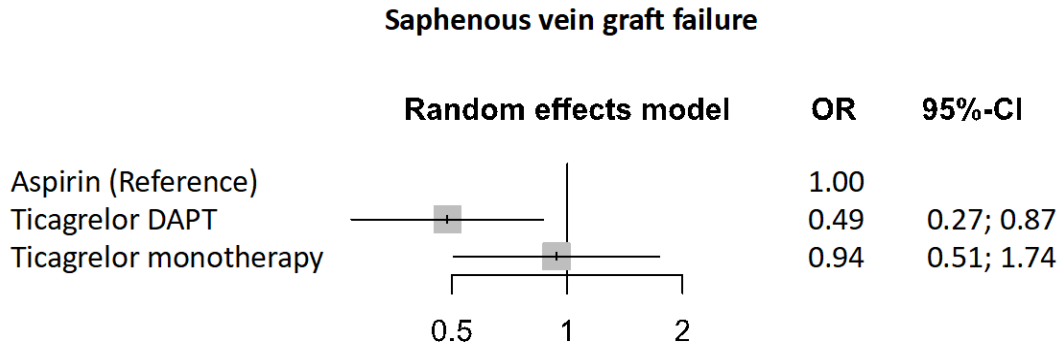
^a Adjusted by trial.

^b Defined as self-reported diagnosis, elevated HbA1c, or active therapy.

^c Defined as STEMI, NSTEMI-ACS, or unstable angina.

^{b-c} Definitions varied by trial.

eFigure 9. Forest plot for saphenous vein graft failure for aspirin, ticagrelor dual antiplatelet therapy, and ticagrelor monotherapy in the post hoc network meta-analysis



The analysis population included saphenous vein grafts from patients who underwent protocol-defined imaging in any of the randomization groups in the 4 trials.

Abbreviations: CI, confidence interval; DAPT, dual antiplatelet therapy; OR, odds ratio.

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