The Effect Of Acadesine On Reducing Cardiovascular and Cerebrovascular Adverse Events In Coronary Artery Bypass Graft (CABG) Surgery (Study P05633 AM1)(TERMINATED) (RED-CABG)

This study has been terminated.

Sponsor:
Merck Sharp & Dohme Corp.

Collaborator:
Duke Clinical Research Institute

Information provided by (Responsible Party):
Merck Sharp & Dohme Corp.

ClinicalTrials.gov Identifier:
NCT00872001

First received: March 27, 2009
Last updated: October 28, 2015
Last verified: October 2015
History of Changes

Purpose

The purpose of this study is to determine whether acadesine is effective in reducing the cardiovascular and cerebrovascular adverse events in high-risk participants undergoing CABG surgery.

Condition	Intervention	Phase
Coronary Artery Bypass Myocardial Infarction Ventricular Dysfunction, Left Stroke Cardiopulmonary Bypass	Drug: Acadesine Drug: Normal Saline	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Efficacy Study
Intervention Model: Parallel Assignment
Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor)
Primary Purpose: Prevention

Official Title: The Effect Of Acadesine On Clinically Significant Adverse Cardiovascular and Cerebrovascular Events In High-Risk Subjects Undergoing Coronary Artery Bypass Graft (CABG) Surgery Using Cardiopulmonary Bypass (Protocol No. P05633): RED-CABG Trial (Reduction in Cardiovascular Events by AcaDesine in Subjects Undergoing CABG)

Resource links provided by NLM:

MedlinePlus related topics: Coronary Artery Bypass Surgery

Drug Information available for: St. Thomas' Hospital cardioplegic solution Cardioplegic solution

U.S. FDA Resources

Further study details as provided by Merck Sharp & Dohme Corp.:

Primary Outcome Measures:

- Incidence of All-cause Death, Non-fatal Stroke, and Need for Mechanical Support for Severe Left Ventricular Dysfunction (SLVD) (Intent-to-Treat Population) [Time Frame: Up to Post-Operative Day 28] [Designated as safety issue: No]

  Incidence of all-cause death, non-fatal stroke, or need for mechanical support for SLVD (any component and composite) through post-operative Day 28 during and following CABG and administration of acadesine or placebo. Components defined as follows: All-cause death: Death from any cause, Non-fatal Stoke: occurrence of a stoke that was confirmed and adjudicated by Clinical Endpoints Committee that did not result in death, and Mechanical Support for SLVD: New use of any mechanical support for ≥1 hour for treatment of low cardiac output.

Secondary Outcome Measures:

- Incidence of Cardiovascular Death, Non-fatal Stroke, and Need for Mechanical Support for SLVD (Intent-to-Treat Population) [Time Frame: Up to Post-Operative Day 28] [Designated as safety issue: No]

  Incidence of cardiovascular death, non-fatal stroke, and need for mechanical support for SLVD (any component and composite) through post-operative Day 28 during and following CABG and administration of acadesine or placebo. Components defined as follows: Cardiovascular death: Death due to cardiovascular causes, Non-fatal Stroke: occurrence of a stroke that was confirmed and adjudicated by Clinical Endpoints Committee that did not result in death, and Mechanical Support for SLVD: New use of any mechanical support for ≥1 hour for treatment of low cardiac output.

Enrollment:	3080
Study Start Date:	April 2009
Study Completion Date:	October 2010
Primary Completion Date:	October 2010 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Active Comparator: Acadesine Acadesine intravenous (IV) infusion, plus cardioplegia solution with acadesine, and priming solution with acadesine in the heart lung machine during cardiopulmonary bypass (CPB)	Drug: Acadesine Acadesine 42 mg/kg diluted in normal saline to a total of 500 mL, delivered as an IV infusion over approximately 7 hours commencing within approximately 30 minutes before induction of anesthesia at a rate of 0.1 mg/kg/min (translating into 1.2 mL/min for a 500 mL solution). In addition, a 5 µg/mL cardioplegia solution of acadesine will be administered, and acadesine will be added to the priming solution (5 µg/mL) in the heart lung machine during CPB. Other Name: SCH 900395
Placebo Comparator: Placebo Normal saline, IV infusion, plus cardioplegia solution with added normal saline, and priming solution with added normal saline in the heart lung machine during CPB	Drug: Normal Saline Normal saline, 500 mL delivered as an IV infusion over approximately 7 hours commencing within approximately 30 minutes before induction of anesthesia at a rate of 1.2 mL/min for a 500 mL solution. In addition, standard cardioplegia solution with added normal saline will be administered, and placebo (normal saline) will also be added to the heart lung machine priming solution.

Eligibility

Ages Eligible for Study:	50 Years and older
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

- A high risk participant undergoing non emergency CABG surgery requiring CPB and cardioplegia.
- Age: >=50 years

- At least one of the following risk factors:
  - Female (but not pregnant or lactating), or
  - History of prior CABG, or
  - History of myocardial infarction (MI), or
  - History of ischemic stroke, or
  - Left ventricular ejection fraction <=30%, or
  - Diabetes mellitus requiring insulin and/or antidiabetic agents.
- Significant coronary artery stenosis

Exclusion Criteria:

- Planned valve replacement, carotid artery or aortic surgery, distal coronary endarterectomy,surgical ablation for cardiac arrhythmia, or ventricular aneurysmectomy, alone or with CABG surgery (repair for mild to moderate mitral valve disease with concomitant CABG is not excluded).
- Planned or staged major surgery within 30 days of CABG surgery
- CABG surgery using intermittent aortic cross clamping without cardioplegia.
- Minimally invasive surgery (ie, without use of CPB).
- MI within 5 days prior to surgery.
- Pre-operative or planned intra operative/postoperative use of intra-aortic balloon pump (IABP), ventricular assist device (VAD), extra-corporeal membrane oxygenator (ECMO), or other mechanical hemodynamic assist device.
- History or presence of gout or uric acid nephrolithiasis.
- Serum creatinine >2 mg/dL (180 µmol/L).
- Serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >2 x Upper Limit of Normal (ULN).
- Adenosine, aminophylline, nicotinic acid, pentoxifylline, theophylline, and any cardioplegia solution containing adenosine, dipyridamole or lidoflazine within 24 hours before surgery:
- Dipyridamole within 2 days and allopurinol or febuxostat within 4 days before surgery
- Food and drinks containing caffeine, theobromines or methylxanthines (such as coffee, tea, colas, some 'energy' drinks or chocolate) within 12 hours before surgery.
- Pregnancy

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

No Contacts or Locations Provided

More Information

Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Weisel RD, Nussmeier N, Newman MF, Pearl RG, Wechsler AS, Ambrosio G, Pitt B, Clare RM, Pieper KS, Mongero L, Reece TL, Yau TM, Fremes S, Menasché P, Lira A, Harrington RA, Ferguson TB; RED-CABG Executive and Steering Committees. Predictors of contemporary coronary artery bypass grafting outcomes. J Thorac Cardiovasc Surg. 2014 Dec;148(6):2720-6.e1-2. doi: 10.1016/j.jtcvs.2014.08.018. Epub 2014 Aug 14.

Newman MF, Ferguson TB, White JA, Ambrosio G, Koglin J, Nussmeier NA, Pearl RG, Pitt B, Wechsler AS, Weisel RD, Reece TL, Lira A, Harrington RA; RED-CABG Steering Committee and Investigators. Effect of adenosine-regulating agent acadesine on morbidity and mortality associated with coronary artery bypass grafting: the RED-CABG randomized controlled trial. JAMA. 2012 Jul 11;308(2):157-64. doi: 10.1001/jama.2012.7633.

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT00872001 History of Changes
Other Study ID Numbers:	P05633 MK-8395 RED-CABG
Study First Received:	March 27, 2009
Results First Received:	November 20, 2012
Last Updated:	October 28, 2015
Health Authority:	United States: Food and Drug Administration

Additional relevant MeSH terms:

Myocardial Infarction
Ventricular Dysfunction
Ventricular Dysfunction, Left
Cardiovascular Diseases
Heart Diseases
Myocardial Ischemia
Vascular Diseases
Cardioplegic Solutions
Cardiovascular Agents
Pharmaceutical Solutions
Pharmacologic Actions
Therapeutic Uses

ClinicalTrials.gov processed this record on May 08, 2016

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Results First Received: November 20, 2012

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor); Primary Purpose: Prevention
Conditions:	Coronary Artery Bypass Myocardial Infarction Ventricular Dysfunction, Left Stroke Cardiopulmonary Bypass
Interventions:	Drug: Acadesine Drug: Normal Saline

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Acadesine	Acadesine IV infusion, plus cardioplegia solution with acadesine, and priming solution with acadesine in the heart lung machine during cardiopulmonary bypass (CPB)
Placebo (Normal Saline)	Placebo (normal saline) IV infusion, plus cardioplegia solution with added normal saline, and priming solution with added normal saline in the heart lung machine during CPB

Participant Flow: Overall Study

	Acadesine	Placebo (Normal Saline)
STARTED	1536	1544
COMPLETED	1400	1413
NOT COMPLETED	136	131
Adverse Event	34	23
Protocol Defined Clinical Event	5	7
Lost to Follow-up	13	12
Withdrawal by Subject	18	30
Protocol Violation	5	8
Did Not Meet Protocol Eligibility	38	36
Administrative	23	15

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Acadesine	Acadesine IV infusion, plus cardioplegia solution with acadesine, and priming solution with acadesine in the heart lung machine during cardiopulmonary bypass (CPB)
Placebo (Normal Saline)	Placebo (normal saline) IV infusion, plus cardioplegia solution with added normal saline, and priming solution with added normal saline in the heart lung machine during CPB
Total	Total of all reporting groups

Baseline Measures

	Acadesine	Placebo (Normal Saline)	Total

Number of Participants [units: participants]	**1536**	**1544**	**3080**
Age [units: years] Mean (Standard Deviation)	**66.2 (8.5)**	**66.7 (8.7)**	**66.5 (8.6)**
Gender [units: participants]			
Female	**519**	**523**	**1042**
Male	**1017**	**1021**	**2038**

Outcome Measures

Hide All Outcome Measures

1. Primary: Incidence of All-cause Death, Non-fatal Stroke, and Need for Mechanical Support for Severe Left Ventricular Dysfunction (SLVD) (Intent-to-Treat Population) [Time Frame: Up to Post-Operative Day 28]

Measure Type	Primary
Measure Title	Incidence of All-cause Death, Non-fatal Stroke, and Need for Mechanical Support for Severe Left Ventricular Dysfunction (SLVD) (Intent-to-Treat Population)
Measure Description	Incidence of all-cause death, non-fatal stroke, or need for mechanical support for SLVD (any component and composite) through post-operative Day 28 during and following CABG and administration of acadesine or placebo. Components defined as follows: All-cause death: Death from any cause, Non-fatal Stoke: occurrence of a stoke that was confirmed and adjudicated by Clinical Endpoints Committee that did not result in death, and Mechanical Support for SLVD: New use of any mechanical support for ≥1 hour for treatment of low cardiac output.
Time Frame	Up to Post-Operative Day 28
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The Intent-to-Treat Population included all participants randomly assigned to a treatment group and did not have to receive study drug. Each participant contributed to no more than one efficacy endpoint in any composite, i.e., a participant who experienced multiple components of an endpoint composite was counted only once in that composite.

Reporting Groups

	Description
Acadesine	Acadesine IV infusion, plus cardioplegia solution with acadesine, and priming solution with acadesine in the heart lung machine during cardiopulmonary bypass (CPB).
Placebo	Placebo (normal saline) IV infusion, plus cardioplegia solution with added normal saline, and priming solution with added normal saline in the heart lung machine during CPB.

Measured Values

	Acadesine	**Placebo**
Number of Participants Analyzed	**1536**	**1544**

[units: participants]		
Incidence of All-cause Death, Non-fatal Stroke, and Need for Mechanical Support for Severe Left Ventricular Dysfunction (SLVD) (Intent-to-Treat Population) [units: Percentage of Participants]		
Composite of All Events	**4.9**	**4.9**
All-Cause Death	**1.9**	**1.7**
Non-Fatal Stroke	**1.7**	**1.7**
Need for Mechanical Support for SLVD	**2.2**	**2.3**

No statistical analysis provided for Incidence of All-cause Death, Non-fatal Stroke, and Need for Mechanical Support for Severe Left Ventricular Dysfunction (SLVD) (Intent-to-Treat Population)

2. Secondary: Incidence of Cardiovascular Death, Non-fatal Stroke, and Need for Mechanical Support for SLVD (Intent-to-Treat Population) [Time Frame: Up to Post-Operative Day 28]

Measure Type	Secondary
Measure Title	Incidence of Cardiovascular Death, Non-fatal Stroke, and Need for Mechanical Support for SLVD (Intent-to-Treat Population)
Measure Description	Incidence of cardiovascular death, non-fatal stroke, and need for mechanical support for SLVD (any component and composite) through post-operative Day 28 during and following CABG and administration of acadesine or placebo. Components defined as follows: Cardiovascular death: Death due to cardiovascular causes, Non-fatal Stroke: occurrence of a stroke that was confirmed and adjudicated by Clinical Endpoints Committee that did not result in death, and Mechanical Support for SLVD: New use of any mechanical support for ≥1 hour for treatment of low cardiac output.
Time Frame	Up to Post-Operative Day 28
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
The Intent-to-Treat Population included all participants randomly assigned to a treatment group and did not have to receive study drug. Each participant contributed to no more than one efficacy endpoint in any composite, i.e., a participant who experienced multiple components of an endpoint composite was counted only once in that composite.

Reporting Groups

	Description
Acadesine	Acadesine IV infusion, plus cardioplegia solution with acadesine, and priming solution with acadesine in the heart lung machine during cardiopulmonary bypass (CPB)
Placebo (Normal Saline)	Placebo (normal saline) IV infusion, plus cardioplegia solution with added normal saline, and priming solution with added normal saline in the heart lung machine during CPB

Measured Values

	Acadesine	**Placebo (Normal Saline)**
Number of Participants Analyzed [units: participants]	**1536**	**1544**
Incidence of Cardiovascular Death, Non-fatal Stroke, and Need for Mechanical Support for SLVD (Intent-		

to-Treat Population) [units: Percentage of Participants]		
Composite of All Events	**4.8**	**4.7**
Cardiovascular Death	**1.7**	**1.6**
Non-Fatal Stroke	**1.7**	**1.7**
Need for Mechanical Support for SLVD	**2.2**	**2.3**

No statistical analysis provided for Incidence of Cardiovascular Death, Non-fatal Stroke, and Need for Mechanical Support for SLVD (Intent-to-Treat Population)

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Up to Post-Operative Day 28
Additional Description	The As-Treated Population was used as the safety population and included all subjects who were assigned randomized treatment and received any amount of study drug (ie, acadesine or placebo).

Reporting Groups

	Description
Acadesine	Acadesine IV infusion, plus cardioplegia solution with acadesine, and priming solution with acadesine in the heart lung machine during cardiopulmonary bypass (CPB)
Placebo (Normal Saline)	Placebo (normal saline) IV infusion, plus cardioplegia solution with added normal saline, and priming solution with added normal saline in the heart lung machine during CPB

Serious Adverse Events

	Acadesine	**Placebo (Normal Saline)**
Total, serious adverse events		
# participants affected / at risk	**327/1442 (22.68%)**	**329/1457 (22.58%)**
Blood and lymphatic system disorders		
Anaemia † 1		
# participants affected / at risk	**6/1442 (0.42%)**	**2/1457 (0.14%)**
# events	**6**	**2**
Coagulopathy † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Heparin-Induced Thrombocytopenia † 1		
# participants affected / at risk	**2/1442 (0.14%)**	**1/1457 (0.07%)**
# events	**2**	**1**
Iron Deficiency Anaemia † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
† 1		

Leukocytosis		
# participants affected / at risk	**1/1442 (0.07%)**	**1/1457 (0.07%)**
# events	**1**	**1**
Thrombocytopenia † 1		
# participants affected / at risk	**2/1442 (0.14%)**	**1/1457 (0.07%)**
# events	**2**	**1**
Cardiac disorders		
Acute Myocardial Infarction † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Atrial Fibrillation † 1		
# participants affected / at risk	**44/1442 (3.05%)**	**41/1457 (2.81%)**
# events	**46**	**41**
Atrial Flutter † 1		
# participants affected / at risk	**2/1442 (0.14%)**	**6/1457 (0.41%)**
# events	**3**	**6**
Atrial Rupture † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**1/1457 (0.07%)**
# events	**1**	**1**
Atrioventricular Block Complete † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Bradycardia † 1		
# participants affected / at risk	**4/1442 (0.28%)**	**4/1457 (0.27%)**
# events	**4**	**4**
Cardiac Arrest † 1		
# participants affected / at risk	**12/1442 (0.83%)**	**7/1457 (0.48%)**
# events	**14**	**8**
Cardiac Failure † 1		
# participants affected / at risk	**5/1442 (0.35%)**	**1/1457 (0.07%)**
# events	**5**	**1**
Cardiac Failure Congestive † 1		
# participants affected / at risk	**11/1442 (0.76%)**	**12/1457 (0.82%)**
# events	**11**	**13**
Cardiac Tamponade † 1		
# participants affected / at risk	**4/1442 (0.28%)**	**4/1457 (0.27%)**
# events	**4**	**4**
Cardiac Valve Disease † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Cardio-Respiratory Arrest † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**4/1457 (0.27%)**
# events	**0**	**4**
Cardiogenic Shock † 1		
# participants affected / at risk	**4/1442 (0.28%)**	**3/1457 (0.21%)**
# events	**4**	**4**

Cardiopulmonary Failure † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**1/1457 (0.07%)**
# events	**1**	**1**
Electromechanical Dissociation † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**2/1457 (0.14%)**
# events	**1**	**2**
Nodal Rhythm † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**2/1457 (0.14%)**
# events	**0**	**2**
Pericardial Effusion † 1		
# participants affected / at risk	**2/1442 (0.14%)**	**4/1457 (0.27%)**
# events	**2**	**4**
Right Ventricular Failure † 1		
# participants affected / at risk	**2/1442 (0.14%)**	**0/1457 (0.00%)**
# events	**2**	**0**
Sick Sinus Syndrome † 1		
# participants affected / at risk	**4/1442 (0.28%)**	**4/1457 (0.27%)**
# events	**4**	**4**
Sinus Bradycardia † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Supraventricular Extrasystoles † 1		
# participants affected / at risk	**2/1442 (0.14%)**	**2/1457 (0.14%)**
# events	**2**	**2**
Tachyarrhythmia † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Tachycardia † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Ventricle Rupture † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Ventricular Arrhythmia † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**2/1457 (0.14%)**
# events	**1**	**2**
Ventricular Extrasystoles † 1		
# participants affected / at risk	**3/1442 (0.21%)**	**4/1457 (0.27%)**
# events	**3**	**4**
Ventricular Fibrillation † 1		
# participants affected / at risk	**5/1442 (0.35%)**	**6/1457 (0.41%)**
# events	**5**	**6**
Ventricular Tachycardia † 1		
# participants affected / at risk	**3/1442 (0.21%)**	**3/1457 (0.21%)**
# events	**3**	**3**

Endocrine disorders		
Inappropriate Antidiuretic Hormone Secretion † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Eye disorders		
Diabetic Retinopathy † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Gastrointestinal disorders		
Abdominal Adhesions † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Abdominal Distension † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Abdominal Pain † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Abdominal Pain Upper † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Ascites † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Colitis † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Colitis Ulcerative † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Diarrhoea † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Duodenal Ulcer Haemorrhage † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Dyspepsia † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**2/1457 (0.14%)**
# events	**0**	**2**
Dysphagia † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**1/1457 (0.07%)**
# events	**1**	**1**
Faecaloma † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**

Gastric Ulcer † 1		
# participants affected / at risk	**2/1442 (0.14%)**	**0/1457 (0.00%)**
# events	**2**	**0**
Gastritis † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**1/1457 (0.07%)**
# events	**1**	**1**
Gastrointestional Necrosis † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**2/1457 (0.14%)**
# events	**0**	**2**
Gastrointestinal Haemorrhage † 1		
# participants affected / at risk	**4/1442 (0.28%)**	**5/1457 (0.34%)**
# events	**4**	**5**
Haematemesis † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Ileus † 1		
# participants affected / at risk	**5/1442 (0.35%)**	**4/1457 (0.27%)**
# events	**5**	**4**
Ileus Paralytic † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Impaired Gastric Emptying † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Intestinal Ischaemia † 1		
# participants affected / at risk	**4/1442 (0.28%)**	**3/1457 (0.21%)**
# events	**4**	**3**
Intestinal Obstruction † 1		
# participants affected / at risk	**2/1442 (0.14%)**	**0/1457 (0.00%)**
# events	**2**	**0**
Large Intestine Perforation † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Lower Gastrointestinal Haemorrhage † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Mallory-Weiss Syndrome † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Malaena † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Nausea † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**2/1457 (0.14%)**
# events	**1**	**2**

Oesophageal Spasm † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Oesophageal Varices Haemorrhage † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Peritonitis † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Small Intestinal Obstruction † 1		
# participants affected / at risk	**2/1442 (0.14%)**	**1/1457 (0.07%)**
# events	**2**	**1**
General disorders		
Adverse Drug Reaction † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Asthenia † 1		
# participants affected / at risk	**4/1442 (0.28%)**	**0/1457 (0.00%)**
# events	**4**	**0**
Catheter Site Haemorrhage † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Chest Pain † 1		
# participants affected / at risk	**6/1442 (0.42%)**	**1/1457 (0.07%)**
# events	**6**	**1**
Device Occlusion † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Extravasation † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Fatigue † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Gait Disturbance † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
General Physical Health Deterioration † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Impaired Healing † 1		
# participants affected / at risk	**3/1442 (0.21%)**	**1/1457 (0.07%)**
# events	**3**	**1**
Multi-Organ Failure † 1		
# participants affected / at risk	**4/1442 (0.28%)**	**2/1457 (0.14%)**

# events	4	2
Non-Cardiac Chest Pain † 1		
# participants affected / at risk	1/1442 (0.07%)	1/1457 (0.07%)
# events	1	1
Oedema † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Oedema Peripheral † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Organ Failure † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Sudden Cardiac Death † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Systemic Inflammatory Response Syndrome † 1		
# participants affected / at risk	1/1442 (0.07%)	2/1457 (0.14%)
# events	1	2
Hepatobiliary disorders		
Cholecystitis † 1		
# participants affected / at risk	2/1442 (0.14%)	0/1457 (0.00%)
# events	2	0
Cholecystitis Acute † 1		
# participants affected / at risk	1/1442 (0.07%)	2/1457 (0.14%)
# events	1	2
Cholelithiasis † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Hepatic Failure † 1		
# participants affected / at risk	1/1442 (0.07%)	1/1457 (0.07%)
# events	1	1
Hydrocholecystis † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Immune system disorders		
Anaphylactic Reaction † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Anaphylactoid Reaction † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Infections and infestations		
Abscess Limb † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)

# events	1	0
Bacterial Sepsis † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Bronchitis † 1		
# participants affected / at risk	3/1442 (0.21%)	0/1457 (0.00%)
# events	3	0
Bronchopneumonia † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Cellulitus † 1		
# participants affected / at risk	5/1442 (0.35%)	8/1457 (0.55%)
# events	5	8
Cholecystitis Infective † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Clostridial Infection † 1		
# participants affected / at risk	1/1442 (0.07%)	2/1457 (0.14%)
# events	1	2
Drug Related Sepsis † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Escherichia Bacteraemia † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Gangrene † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Gastroenteritis † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Gastroenteritis Viral † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Haematoma Infection † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Incision Site Infection † 1		
# participants affected / at risk	3/1442 (0.21%)	3/1457 (0.21%)
# events	3	3
Infection † 1		
# participants affected / at risk	9/1442 (0.62%)	9/1457 (0.62%)
# events	9	10
Mediastinal Abscess † 1		
# participants affected / at risk	1/1442 (0.07%)	1/1457 (0.07%)

# events	1	1
Mediastinitis † 1		
# participants affected / at risk	2/1442 (0.14%)	2/1457 (0.14%)
# events	2	2
Pharyngitis Streptococcal † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Pneumonia † 1		
# participants affected / at risk	10/1442 (0.69%)	14/1457 (0.96%)
# events	10	14
Postoperative Wound Infection † 1		
# participants affected / at risk	2/1442 (0.14%)	2/1457 (0.14%)
# events	2	2
Pyelonepritis † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Pyothorax † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Respiratory Tract Infection † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Sepsis † 1		
# participants affected / at risk	7/1442 (0.49%)	6/1457 (0.41%)
# events	7	6
Septic Shock † 1		
# participants affected / at risk	4/1442 (0.28%)	2/1457 (0.14%)
# events	4	2
Staphylococcal Infection † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Staphylococcal Mediastinitis † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Urinary Tract Infection † 1		
# participants affected / at risk	2/1442 (0.14%)	4/1457 (0.27%)
# events	2	4
Wound Infection † 1		
# participants affected / at risk	6/1442 (0.42%)	6/1457 (0.41%)
# events	6	6
Wound Infection Pseudomonas † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Wound Infection Staphylococcal † 1		
# participants affected / at risk	0/1442 (0.00%)	2/1457 (0.14%)
# events	0	2

Injury, poisoning and procedural complications		
Collapse of Lung † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Drug Toxicity † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Femur Fracture † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Graft Haemorrhage † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Incision Site Haemorrhage † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Operative Haemorrhage † 1		
# participants affected / at risk	**3/1442 (0.21%)**	**2/1457 (0.14%)**
# events	**3**	**2**
Post Procedural Haemorrhage † 1		
# participants affected / at risk	**16/1442 (1.11%)**	**17/1457 (1.17%)**
# events	**16**	**17**
Postoperative Ileus † 1		
# participants affected / at risk	**2/1442 (0.14%)**	**1/1457 (0.07%)**
# events	**2**	**1**
Postoperative Renal Failure † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Postoperative Respiratory Distress † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**3/1457 (0.21%)**
# events	**1**	**3**
Postoperative Thoracic Procedure Complication † 1		
# participants affected / at risk	**8/1442 (0.55%)**	**3/1457 (0.21%)**
# events	**8**	**3**
Postpericardiotomy Syndrome † 1		
# participants affected / at risk	**2/1442 (0.14%)**	**4/1457 (0.27%)**
# events	**2**	**4**
Renal Injury † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Shunt Thrombosis † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Traumatic Lung Injury † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**

# events	0	1
Vascular Graft Occlusion † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Vascular Graft Complication † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Vasoplegia Syndrome † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Weaning Failure † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Wound Complication † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Wound Dehiscence † 1		
# participants affected / at risk	1/1442 (0.07%)	2/1457 (0.14%)
# events	1	2
Investigations		
Cardiac Output Decreased † 1		
# participants affected / at risk	3/1442 (0.21%)	0/1457 (0.00%)
# events	3	0
Electrocardiogram Change † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
International Normalised Ratio Increased † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Pulse Absent † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
White Blood Cell Count Increased † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Metabolism and nutrition disorders		
Dehydration † 1		
# participants affected / at risk	0/1442 (0.00%)	2/1457 (0.14%)
# events	0	2
Diabetes Mellitus † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Diabetes Mellitus Inadequate Control † 1		
# participants affected / at risk	2/1442 (0.14%)	0/1457 (0.00%)
# events	2	0

Electrolyte Imbalance † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Fluid Overload † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**2/1457 (0.14%)**
# events	**0**	**2**
Hyperglycaemia † 1		
# participants affected / at risk	**2/1442 (0.14%)**	**2/1457 (0.14%)**
# events	**3**	**2**
Hypoglycaemia † 1		
# participants affected / at risk	**6/1442 (0.42%)**	**0/1457 (0.00%)**
# events	**6**	**0**
Metabolic Acidosis † 1		
# participants affected / at risk	**2/1442 (0.14%)**	**1/1457 (0.07%)**
# events	**2**	**1**
Metabolic Disorder † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Musculoskeletal and connective tissue disorders		
Back Pain † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Costochondritis † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Fracture Delayed Union † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Musculoskeletal Chest Pain † 1		
# participants affected / at risk	**2/1442 (0.14%)**	**2/1457 (0.14%)**
# events	**2**	**2**
Pain in Extremity † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		
Renal Cancer † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Squamous Cell Carcinoma † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Nervous system disorders		
Anoxic Encephalopathy † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**

# events	0	1
Carpal Tunnel Syndrome † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Cerebrovascular Incident † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Convulsion † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Depressed Level of Consciousness † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Encephalopathy † 1		
# participants affected / at risk	3/1442 (0.21%)	0/1457 (0.00%)
# events	3	0
Hypoxic Encephalopathy † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Metabolic Encephalopathy † 1		
# participants affected / at risk	2/1442 (0.14%)	1/1457 (0.07%)
# events	2	1
Paresis † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Presynope † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Syncope † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Psychiatric disorders		
Affective Disorder † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Depression † 1		
# participants affected / at risk	1/1442 (0.07%)	1/1457 (0.07%)
# events	1	1
Disorientation † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Hallucination, Visual † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Mental Status Changes † 1		

# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Suicidal Ideation † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Transient Psychosis † 1		
# participants affected / at risk	1/1442 (0.07%)	1/1457 (0.07%)
# events	1	1
Renal and urinary disorders		
Acute Prerenal Failure † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Haematuria † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Renal Failure † 1		
# participants affected / at risk	20/1442 (1.39%)	14/1457 (0.96%)
# events	21	14
Renal Failure Acute † 1		
# participants affected / at risk	9/1442 (0.62%)	10/1457 (0.69%)
# events	10	10
Renal Tubular Necrosis † 1		
# participants affected / at risk	0/1442 (0.00%)	2/1457 (0.14%)
# events	0	2
Urinary Retention † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Respiratory, thoracic and mediastinal disorders		
Acute Pulmonary Oedema † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Acute Respiratory Distress Syndrome † 1		
# participants affected / at risk	6/1442 (0.42%)	3/1457 (0.21%)
# events	7	3
Acute Repiratory Failure † 1		
# participants affected / at risk	4/1442 (0.28%)	8/1457 (0.55%)
# events	4	8
Asphyxia † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Bronchospasm † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Chronic Obstructive Pulmonary disease † 1		
# participants affected / at risk	4/1442 (0.28%)	2/1457 (0.14%)

# events	4	2
Cough † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Dyspnoea † 1		
# participants affected / at risk	3/1442 (0.21%)	0/1457 (0.00%)
# events	3	0
Epistaxis † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Haemothorax † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Hydropneumothorax † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Hypoxia † 1		
# participants affected / at risk	2/1442 (0.14%)	4/1457 (0.27%)
# events	2	4
Lung Disorder † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Pleural Effusion † 1		
# participants affected / at risk	28/1442 (1.94%)	26/1457 (1.78%)
# events	31	27
Pleural Fistula † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Pleuritic Pain † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Pneumothorax † 1		
# participants affected / at risk	9/1442 (0.62%)	4/1457 (0.27%)
# events	9	4
Pulmonary Embolism † 1		
# participants affected / at risk	14/1442 (0.97%)	12/1457 (0.82%)
# events	14	12
Pulmonary Fibrosis † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Pulmonary Haematoma † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Pulmonary Haemorrhage † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1

Pulmonary Hypertension † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Pulmonary Oedema † 1		
# participants affected / at risk	**2/1442 (0.14%)**	**2/1457 (0.14%)**
# events	**2**	**2**
Respiratory Alkalosis † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Respiratory Arrest † 1		
# participants affected / at risk	**5/1442 (0.35%)**	**3/1457 (0.21%)**
# events	**5**	**3**
Respiratory Distress † 1		
# participants affected / at risk	**5/1442 (0.35%)**	**3/1457 (0.21%)**
# events	**5**	**3**
Respiratory Failure † 1		
# participants affected / at risk	**33/1442 (2.29%)**	**23/1457 (1.58%)**
# events	**34**	**25**
Tracheal Stenosis † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Skin and subcutaneous tissue disorders		
Angioedema † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Diabetic Ulcer † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Linear IGA Disease † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Subcutaneous Emphysema † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Urticaria † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Surgical and medical procedures		
Aortic Bypass † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Incisional Drainage † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
† 1		

Mechanical Ventilation		
# participants affected / at risk	**3/1442 (0.21%)**	**0/1457 (0.00%)**
# events	**3**	**0**
Thoracic Cavity Drainage † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**3/1457 (0.21%)**
# events	**0**	**3**
Vascular disorders		
Air Embolism † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Aortic Rupture † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Arterial Thrombosis Limb † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Arteriovenous Fistula † 1		
# participants affected / at risk	**0/1442 (0.00%)**	**1/1457 (0.07%)**
# events	**0**	**1**
Deep Vein Thrombosis † 1		
# participants affected / at risk	**9/1442 (0.62%)**	**5/1457 (0.34%)**
# events	**9**	**5**
Embolism † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Exsanguination † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Haematoma † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Haemodynamic Instability † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Haemorrhage † 1		
# participants affected / at risk	**2/1442 (0.14%)**	**0/1457 (0.00%)**
# events	**2**	**0**
Hypertension † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Hypertensive Crisis † 1		
# participants affected / at risk	**1/1442 (0.07%)**	**0/1457 (0.00%)**
# events	**1**	**0**
Hypotension † 1		
# participants affected / at risk	**14/1442 (0.97%)**	**18/1457 (1.24%)**

# events	16	18
Jugular Vein Thrombosis † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Labile Blood Pressure † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Lymphatic Fistula † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Orthostatic Hypotension † 1		
# participants affected / at risk	0/1442 (0.00%)	2/1457 (0.14%)
# events	0	2
Peripheral Arterial Occlusive Disease † 1		
# participants affected / at risk	2/1442 (0.14%)	0/1457 (0.00%)
# events	2	0
Peripheral Embolism † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	2	0
Peripheral Ischaemia † 1		
# participants affected / at risk	2/1442 (0.14%)	2/1457 (0.14%)
# events	2	2
Peripheral Vascular Disorder † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
Shock † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Shock Haemorrhagic † 1		
# participants affected / at risk	1/1442 (0.07%)	0/1457 (0.00%)
# events	1	0
Thrombophlebitis Superficial † 1		
# participants affected / at risk	1/1442 (0.07%)	1/1457 (0.07%)
# events	1	1
Venous Thrombosis † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1
White Clot Syndrome † 1		
# participants affected / at risk	0/1442 (0.00%)	1/1457 (0.07%)
# events	0	1

† Events were collected by systematic assessment

1 Term from vocabulary, MedDRA 13.0

Other Adverse Events

Hide Other Adverse Events

Time Frame	Up to Post-Operative Day 28
Additional Description	The As-Treated Population was used as the safety population and included all subjects who were assigned randomized treatment and received any amount of study drug (ie, acadesine or placebo).

Frequency Threshold

Threshold above which other adverse events are reported	5%

Reporting Groups

	Description
Acadesine	Acadesine IV infusion, plus cardioplegia solution with acadesine, and priming solution with acadesine in the heart lung machine during cardiopulmonary bypass (CPB)
Placebo (Normal Saline)	Placebo (normal saline) IV infusion, plus cardioplegia solution with added normal saline, and priming solution with added normal saline in the heart lung machine during CPB

Other Adverse Events

	Acadesine	**Placebo (Normal Saline)**
Total, other (not including serious) adverse events		
# participants affected / at risk	**1154/1442 (80.03%)**	**1189/1457 (81.61%)**
Blood and lymphatic system disorders		
Anaemia † 1		
# participants affected / at risk	**384/1442 (26.63%)**	**383/1457 (26.29%)**
# events	**388**	**387**
Leukocytosis † 1		
# participants affected / at risk	**114/1442 (7.91%)**	**95/1457 (6.52%)**
# events	**117**	**95**
Thrombocytopenia † 1		
# participants affected / at risk	**119/1442 (8.25%)**	**129/1457 (8.85%)**
# events	**123**	**129**
Cardiac disorders		
Atrial Fibrillation † 1		
# participants affected / at risk	**290/1442 (20.11%)**	**328/1457 (22.51%)**
# events	**303**	**346**
Sinus Tachycardia † 1		
# participants affected / at risk	**81/1442 (5.62%)**	**67/1457 (4.60%)**
# events	**82**	**67**
Gastrointestinal disorders		
Constipation † 1		
# participants affected / at risk	**207/1442 (14.36%)**	**244/1457 (16.75%)**
# events	**209**	**245**
Nausea † 1		

# participants affected / at risk	354/1442 (24.55%)	365/1457 (25.05%)
# events	362	373
Vomiting † 1		
# participants affected / at risk	80/1442 (5.55%)	86/1457 (5.90%)
# events	81	86
General disorders		
Generalized Oedema † 1		
# participants affected / at risk	87/1442 (6.03%)	85/1457 (5.83%)
# events	87	85
Oedema Peripheral † 1		
# participants affected / at risk	108/1442 (7.49%)	124/1457 (8.51%)
# events	112	134
Pain † 1		
# participants affected / at risk	100/1442 (6.93%)	119/1457 (8.17%)
# events	100	123
Pyrexia † 1		
# participants affected / at risk	117/1442 (8.11%)	105/1457 (7.21%)
# events	122	105
Injury, poisoning and procedural complications		
Incision Site Pain † 1		
# participants affected / at risk	218/1442 (15.12%)	205/1457 (14.07%)
# events	221	211
Procedural Pain † 1		
# participants affected / at risk	560/1442 (38.83%)	525/1457 (36.03%)
# events	572	543
Metabolism and nutrition disorders		
Hyperglycaemia † 1		
# participants affected / at risk	180/1442 (12.48%)	165/1457 (11.32%)
# events	181	165
Hypocalcaemia † 1		
# participants affected / at risk	85/1442 (5.89%)	74/1457 (5.08%)
# events	86	74
Hypokalaemia † 1		
# participants affected / at risk	139/1442 (9.64%)	126/1457 (8.65%)
# events	143	127
Psychiatric disorders		
Anxiety † 1		
# participants affected / at risk	75/1442 (5.20%)	88/1457 (6.04%)
# events	75	89
Insomnia † 1		
# participants affected / at risk	89/1442 (6.17%)	87/1457 (5.97%)
# events	89	87
Respiratory, thoracic and mediastinal disorders		
Atelectasis † 1		

# participants affected / at risk	**257/1442 (17.82%)**	**241/1457 (16.54%)**
# events	**265**	**252**
Pleural Effusion † 1		
# participants affected / at risk	**323/1442 (22.40%)**	**336/1457 (23.06%)**
# events	**340**	**352**
Pulmonary Oedema † 1		
# participants affected / at risk	**59/1442 (4.09%)**	**76/1457 (5.22%)**
# events	**59**	**76**
Vascular disorders		
Hypertension † 1		
# participants affected / at risk	**74/1442 (5.13%)**	**74/1457 (5.08%)**
# events	**76**	**76**
Hypotension † 1		
# participants affected / at risk	**280/1442 (19.42%)**	**280/1457 (19.22%)**
# events	**286**	**283**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA 13.0

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data

No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.

There **IS** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The agreement is:

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **less than or equal to 60 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

☐ The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is **more than 60 days but less than or equal to 180 days**. The sponsor cannot require changes to the communication and cannot extend the embargo.

Other disclosure agreement that restricts the right of the PI to discuss or publish trial results after the trial is completed.

☑ **Restriction Description:**
The investigator agrees not to publish or publicly present any interim results of the study without the prior written consent of the sponsor. The investigator further agrees to provide to the sponsor 45 days prior to submission for publication or presentation, review copies of abstracts or manuscripts for publication (including, without limitation, slides and texts of oral or other public presentations and texts of any transmission through any electronic media that report any study results).

Results Point of Contact:

Name/Title: Senior Vice President, Global Clinical Development
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Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Weisel RD, Nussmeier N, Newman MF, Pearl RG, Wechsler AS, Ambrosio G, Pitt B, Clare RM, Pieper KS, Mongero L, Reece TL, Yau TM, Fremes S, Menasché P, Lira A, Harrington RA, Ferguson TB; RED-CABG Executive and Steering Committees. Predictors of contemporary coronary artery bypass grafting outcomes. J Thorac Cardiovasc Surg. 2014 Dec;148(6):2720-6.e1-2. doi: 10.1016/j.jtcvs.2014.08.018. Epub 2014 Aug 14.

Newman MF, Ferguson TB, White JA, Ambrosio G, Koglin J, Nussmeier NA, Pearl RG, Pitt B, Wechsler AS, Weisel RD, Reece TL, Lira A, Harrington RA; RED-CABG Steering Committee and Investigators. Effect of adenosine-regulating agent acadesine on morbidity and mortality associated with coronary artery bypass grafting: the RED-CABG randomized controlled trial. JAMA. 2012 Jul 11;308(2):157-64. doi: 10.1001/jama.2012.7633.

Responsible Party:	Merck Sharp & Dohme Corp.
ClinicalTrials.gov Identifier:	NCT00872001 History of Changes
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Study First Received:	March 27, 2009
Results First Received:	November 20, 2012
Last Updated:	October 28, 2015
Health Authority:	United States: Food and Drug Administration

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