ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
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# Clopidogrel Optimal Loading Dose Usage to Reduce Recurrent EveNTs/ Optimal Antiplatelet Strategy for InterventionS (CURRENT/OASIS7)

This study has been completed.

| | |
|---|---|
| Sponsor: | Sanofi |
| Collaborators: | Bristol-Myers Squibb |
| Information provided by: | Sanofi |
| ClinicalTrials.gov Identifier: | NCT00335452 |

## Purpose

The purpose of this study is to evaluate whether a higher dosage of clopidogrel with aspirin (two doses) will decrease the risk of ischemic complications (cardiac death (CV death), myocardial infarction (MI), stroke) after a percutaneous coronary intervention (PCI).

| Condition | Intervention | Phase |
|---|---|---|
| Acute Coronary Disease<br>Angina Unstable | Drug: Clopidogrel<br>Drug: acetylsalicyclic acid (ASA) | Phase 3 |

Study Type: Interventional
Study Design: Treatment, Factorial Assignment, Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor), Randomized, Efficacy Study
Official Title: Randomized, Multinational, Double-blind Study, Comparing a High Loading Dose Regimen of Clopidogrel Versus Standard Dose in Patients With Unstable Angina or Myocardial Infarction Managed With an Early Invasive Strategy.

Further study details as provided by Sanofi:

Primary Outcome Measure:

- First Occurrence of CV Death / MI / Stroke - Clopidogrel Treatment Regimen Comparison [Time Frame: 30 days] [Designated as safety issue: No]
  The primary endpoint is the first occurrence of any of the following events: - Cardiovascular death (any death with a clear cardiovascular or unknown cause), - Myocardial Infarction (diagnosis of new Myocardial Infarction (MI) - nonfatal or fatal) - Stroke (presence of a new focal neurologic deficit

thought to be vascular in origin, with signs or symptoms lasting more than 24 hours - nonfatal or fatal) reported between the randomization and Day 30 (inclusive), and validated by the blinded Event Adjudication Committee (EAC).

- First Occurrence of CV Death / MI / Stroke - ASA Dose Comparison [Time Frame: 30 days] [Designated as safety issue: No]
- First Occurrence of CV Death / MI / Stroke - Interaction Clopidogrel Treatment Regimen and ASA Dose Level [Time Frame: 30 days] [Designated as safety issue: No]
- First Occurrence of CV Death / MI / Stroke - Clopidogrel Treatment Regimen Comparison in PCI Subgroup [Time Frame: 30 days] [Designated as safety issue: No]

Secondary Outcome Measures:

- Occurrence of Major Bleeding - Clopidogrel Dose Regimen Comparison [Time Frame: 30 days] [Designated as safety issue: Yes]
  Major bleeding is defined as any severe bleeding (associated with any of the following: death, leading to a drop in hemoglobin ≥ 5 g/dl, significant hypotension with the need for inotropic agents, symptomatic intracranial hemorrhage, requirement for surgery or for a transfusion ≥ 4 units of red blood cells or equivalent whole blood) and other major bleeding (significantly disabling bleeding, or intraocular bleeding leading to significant loss of vision or bleeding requiring transfusion of 2-3 units of red blood cells or equivalent whole blood) after validation by the independent EAC.
- Occurrence of Major Bleeding - ASA Dose Level Comparison [Time Frame: 30 days] [Designated as safety issue: Yes]

Enrollment: 25086
Study Start Date: June 2006
Primary Completion Date: September 2009
Study Completion Date: September 2009

| Arms | Assigned Interventions |
|---|---|
| Experimental: Clopidogrel high dose treatment regimen + ASA high dose | Drug: Clopidogrel<br>oral administration<br><br>Other Names:<br>SR25990<br>Plavix<br>Drug: acetylsalicyclic acid (ASA)<br>oral administration |
| Experimental: Clopidogrel high dose treatment regimen + ASA low dose | Drug: Clopidogrel<br>oral administration<br><br>Other Names:<br>SR25990<br>Plavix<br>Drug: acetylsalicyclic acid (ASA)<br>oral administration |
| Active Comparator: Clopidogrel standard treatment regimen + ASA high dose | Drug: Clopidogrel<br>oral administration<br><br>Other Names:<br>SR25990<br>Plavix |

| Arms | Assigned Interventions |
|---|---|
| | Drug: acetylsalicyclic acid (ASA)<br>oral administration |
| Active Comparator: Clopidogrel standard treatment regimen + ASA low dose | Drug: Clopidogrel<br>oral administration<br><br>Other Names:<br>SR25990<br>Plavix<br>Drug: acetylsalicyclic acid (ASA)<br>oral administration |

## Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

### Criteria

Inclusion Criteria:

- Diagnosed with acute coronary disease with clinical symptoms and at least electrocardiogram changes or cardiac enzymes elevated

Exclusion Criteria:

- Use of anticoagulants within 10 days with an international normalized ratio (INR) > 1.5 or planned use during the hospitalisation period
- Administration of clopidogrel > 75 mg prior to randomization
- Contraindication to clopidogrel or aspirin
- Active bleeding or significant risk of bleeding

## Contacts and Locations

Locations
United States, New Jersey
sanofi-aventis administrative office
Bridgewater, New Jersey, United States, 08807
Argentina
sanofi-aventis administrative office
Buenos Aires, Argentina
Australia
sanofi-aventis Australia & New Zealand administrative office
Macquarie Park, Australia
Austria

sanofi-aventis administrative office
Vienna, Austria
Belgium
sanofi-aventis administrative office
Diegem, Belgium
Brazil
sanofi-aventis administrative office
Sao Paulo, Brazil
Bulgaria
sanofi-aventis administrative office
Sofia, Bulgaria
Canada
sanofi-aventis administrative office
Laval, Canada
Chile
sanofi-aventis administrative office
Santiago de Chile, Chile
China
sanofi-aventis administrative office
Beijing, China
Croatia
sanofi-aventis administrative office
Zagreb, Croatia
Czech Republic
sanofi-aventis administrative office
Praha, Czech Republic
Estonia
sanofi-aventis administrative office
Tallinn, Estonia
Finland
sanofi-aventis administrative office
Helsinki, Finland
France
sanofi-aventis administrative office
Paris, France
Germany
sanofi-aventis administrative office
Berlin, Germany
Greece
sanofi-aventis administrative office
Athens, Greece
India
sanofi-aventis administrative office
Mumbai, India
Ireland

sanofi-aventis administrative office
Dublin, Ireland
Israel
sanofi-aventis administrative office
Natanya, Israel
Italy
sanofi-aventis administrative office
Milano, Italy
Korea, Republic of
sanofi-aventis administrative office
Seoul, Korea, Republic of
Latvia
sanofi-aventis administrative office
Riga, Latvia
Lithuania
sanofi-aventis administrative office
Vilnius, Lithuania
Malaysia
sanofi-aventis administrative office
Kuala Lumpur, Malaysia
Mexico
sanofi-aventis administrative office
Mexico, Mexico
Netherlands
sanofi-aventis administrative office
Gouda, Netherlands
Poland
sanofi-aventis administrative office
Warszawa, Poland
Romania
sanofi-aventis administrative office
Bucuresti, Romania
Russian Federation
sanofi-aventis administrative office
Moscow, Russian Federation
Singapore
sanofi-aventis administrative office
Singapore, Singapore
Slovakia
sanofi-aventis administrative office
Brastislava, Slovakia
South Africa
sanofi-aventis administrative office
Midrand, South Africa
Spain

sanofi-aventis admnistrative office
Madrid, Spain
Sweden
sanofi-aventis administrative office
Bromma, Sweden
Switzerland
sanofi-aventis administrative office
Geneva, Switzerland
Turkey
sanofi-aventis administrative office
Istanbul, Turkey
United Kingdom
sanofi-aventis administrative office
Guildford, Surrey, United Kingdom

Investigators

| | | |
|---|---|---|
| Principal Investigator: | Shamir MEHTA, MD | Hamilton General Hospital,<br>McMaster University, CANADA |

## More Information

Results Publications:


CURRENT-OASIS 7 Investigators, Mehta SR, Bassand JP, Chrolavicius S, Diaz R, Eikelboom JW, Fox KA, Granger CB, Jolly S, Joyner CD, Rupprecht HJ, Widimsky P, Afzal R, Pogue J, Yusuf S. Dose comparisons of clopidogrel and aspirin in acute coronary syndromes. N Engl J Med. 2010 Sep 2;363(10):930-42. doi: 10.1056/NEJMoa0909475. Erratum in: N Engl J Med. 2010 Oct 14;363(16):1585.

Fuster V. Fine-tuning therapy for acute coronary syndromes. N Engl J Med. 2010 Sep 2;363(10):976-7. doi: 10.1056/NEJMe1008891.

Mehta SR, Tanguay JF, Eikelboom JW, Jolly SS, Joyner CD, Granger CB, Faxon DP, Rupprecht HJ, Budaj A, Avezum A, Widimsky P, Steg PG, Bassand JP, Montalescot G, Macaya C, Di Pasquale G, Niemela K, Ajani AE, White HD, Chrolavicius S, Gao P, Fox KA, Yusuf S; CURRENT-OASIS 7 trial investigators. Double-dose versus standard-dose clopidogrel and high-dose versus low-dose aspirin in individuals undergoing percutaneous coronary intervention for acute coronary syndromes (CURRENT-OASIS 7): a randomised factorial trial. Lancet. 2010 Oct 9;376(9748):1233-43. doi: 10.1016/S0140-6736(10)61088-4.

Stone GW. Acute coronary syndromes: finding meaning in OASIS 7. Lancet. 2010 Oct 9;376(9748):1203-5. doi: 10.1016/S0140-6736(10)61262-7.


| | |
|---|---|
| Responsible Party: | sanofi-aventis (ICD) |
| Study ID Numbers: | EFC5965<br>EUDRACT: 2006-000313-38 |
| Health Authority: | United States: Food and Drug Administration<br>Canada: Health Canada<br>Argentina: Administracion Nacional de Medicamentos, Alimentos y Tecnologia Medica |

## Participant Flow

| | |
|---|---|
| Recruitment Details | 25086 patients were enrolled and randomized between June 2006 and August 2009 in 597 sites in 39 countries. Because the observed overall blinded event rate was substantially lower than expected, the number of patients to be enrolled was increased from 18000 to 20000, then to 25000. |
| Pre-Assignment Details | Treatment assignment was performed through an automated voice randomization service (AreS). At the same time, the AReS provided allocation to a Clopidogrel treatment regimen according to a pre-defined randomization list and to a ASA dose according to a factorial design. |

Reporting Groups

| | Description |
|---|---|
| Clopidogrel 300/75/75 mg + ASA Low Dose | Day 1: Clopidogrel 300 mg loading dose + ASA ≥ 300 mg<br>Day 2 to Day 7: Clopidogrel 75 mg + ASA 75-100 mg<br>Day 8 to Day 30: Clopidogrel 75 mg + ASA 75-100 mg |
| Clopidogrel 300/75/75 mg + ASA High Dose | Day 1: Clopidogrel 300 mg loading dose + ASA ≥ 300 mg<br>Day 2 to Day 7: Clopidogrel 75 mg + ASA 300-325 mg<br>Day 8 to Day 30: Clopidogrel 75 mg + ASA 300-325 mg |
| Clopidogrel 600/150/75 mg + ASA Low Dose | Day 1: Clopidogrel 600 mg loading dose + ASA ≥ 300 mg<br>Day 2 to Day 7: Clopidogrel 150 mg + ASA 75-100 mg<br>Day 8 to Day 30: Clopidogrel 75 mg + ASA 75-100 mg |
| Clopidogrel 600/150/75 mg + ASA High Dose | Day 1: Clopidogrel 600 mg loading dose + ASA ≥ 300 mg<br>Day 2 to Day 7: Clopidogrel 150 mg + ASA 300-325 mg<br>Day 8 to Day 30: Clopidogrel 75 mg + ASA 300-325 mg |

Overall Study

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| Started | 6312 [1] | 6254 [1] | 6267 [1] | 6253 [1] |
| TREATED WITH CLOPIDOGREL | 6271 | 6218 | 6228 | 6217 |

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| TREATED WITH ASA | 6302 | 6251 | 6261 | 6247 |
| Completed | 6154 [2] | 6107 [2] | 6108 [2] | 6122 [2] |
| Not Completed | 158 | 147 | 159 | 131 |
| Death | 156 | 144 | 158 | 129 |
| Lost to Follow-up | 2 | 3 | 1 | 2 |

[1] Randomized
[2] Completed 30 days follow-up period

## Baseline Characteristics

Reporting Groups

| | Description |
|---|---|
| Clopidogrel 300/75/75 mg + ASA Low Dose | |
| Clopidogrel 300/75/75 mg + ASA High Dose | |
| Clopidogrel 600/150/75 mg + ASA Low Dose | |
| Clopidogrel 600/150/75 mg + ASA High Dose | |

Baseline Measures

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose | Total |
|---|---|---|---|---|---|
| Number of Participants | 6312 | 6254 | 6267 | 6253 | 25086 |
| Age, Continuous<br>[units: years]<br>Mean (Standard Deviation) | 61.3 (11.7) | 61.5 (11.7) | 61.2 (11.8) | 61.4 (11.9) | 61.3 (11.8) |
| Age, Customized<br>[units: participants] | | | | | |
| < 65 years | 3792 | 3740 | 3787 | 3735 | 15054 |

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose | Total |
|---|---|---|---|---|---|
| 65 - 74 years | 1573 | 1576 | 1543 | 1543 | 6235 |
| ≥ 75 years | 947 | 937 | 937 | 975 | 3796 |
| Missing | 0 | 1 | 0 | 0 | 1 |
| Gender, Male/Female [units: participants] | | | | | |
| Female | 1702 | 1756 | 1671 | 1742 | 6871 |
| Male | 4610 | 4498 | 4596 | 4511 | 18215 |
| Region of Enrollment [units: participants] | | | | | |
| Argentina | 182 | 159 | 162 | 174 | 677 |
| Australia | 97 | 100 | 96 | 95 | 388 |
| Austria | 41 | 35 | 35 | 40 | 151 |
| Belgium | 55 | 61 | 59 | 53 | 228 |
| Brazil | 292 | 275 | 270 | 288 | 1125 |
| Bulgaria | 111 | 122 | 125 | 112 | 470 |
| Canada | 349 | 379 | 373 | 347 | 1448 |
| Chile | 95 | 85 | 82 | 90 | 352 |
| China | 510 | 492 | 500 | 515 | 2017 |
| Croatia | 114 | 145 | 144 | 114 | 517 |
| Czech Republic | 257 | 275 | 277 | 258 | 1067 |
| Estonia | 1 | 0 | 0 | 1 | 2 |
| Finland | 132 | 127 | 127 | 132 | 518 |
| France | 177 | 163 | 165 | 175 | 680 |
| Germany | 471 | 450 | 453 | 470 | 1844 |
| Greece | 20 | 21 | 23 | 21 | 85 |
| India | 658 | 650 | 645 | 646 | 2599 |
| Ireland | 24 | 13 | 15 | 23 | 75 |

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose | Total |
|---|---|---|---|---|---|
| Israel | 286 | 272 | 275 | 282 | 1115 |
| Italy | 232 | 260 | 258 | 231 | 981 |
| Korea, Republic of | 161 | 149 | 152 | 165 | 627 |
| Latvia | 16 | 16 | 15 | 15 | 62 |
| Lithuania | 26 | 31 | 30 | 28 | 115 |
| Malaysia | 29 | 39 | 39 | 28 | 135 |
| Mexico | 16 | 17 | 19 | 17 | 69 |
| Netherlands | 46 | 48 | 48 | 46 | 188 |
| New Zealand | 36 | 31 | 29 | 29 | 125 |
| Poland | 365 | 322 | 325 | 362 | 1374 |
| Romania | 47 | 30 | 33 | 48 | 158 |
| Russian Federation | 132 | 137 | 138 | 131 | 538 |
| Singapore | 10 | 13 | 15 | 10 | 48 |
| Slovakia | 93 | 84 | 83 | 92 | 352 |
| South Africa | 24 | 14 | 14 | 23 | 75 |
| Spain | 264 | 276 | 283 | 263 | 1086 |
| Sweden | 10 | 11 | 9 | 10 | 40 |
| Switzerland | 51 | 64 | 64 | 48 | 227 |
| Turkey | 79 | 96 | 94 | 78 | 347 |
| United Kingdom | 28 | 29 | 34 | 28 | 119 |
| United States | 775 | 763 | 759 | 765 | 3062 |
| Qualifying condition<br>[units: participants] | | | | | |
| Suspected Unstable Angina (UA) | 1809 | 1771 | 1757 | 1877 | 7214 |
| Suspected MI without ST elevation (NSTEMI) | 2662 | 2662 | 2668 | 2539 | 10531 |
| MI with ST elevation (STEMI) | 1839 | 1817 | 1839 | 1832 | 7327 |

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose | Total |
|---|---|---|---|---|---|
| Missing | 2 | 4 | 3 | 5 | 14 |
| Intended PCI performed [1]<br>[units: participants] | | | | | |
| Yes | 4377 | 4326 | 4262 | 4298 | 17263 |
| No | 1935 | 1928 | 2005 | 1955 | 7823 |

[1] The intent to perform a PCI as early as possible and no later than 72 hours of randomization was part of the criteria for inclusion

## Outcome Measures

1. Primary Outcome Measure:

| | |
|---|---|
| Measure Title | First Occurrence of CV Death / MI / Stroke - Clopidogrel Treatment Regimen Comparison |
| Measure Description | The primary endpoint is the first occurrence of any of the following events:<br>• Cardiovascular death (any death with a clear cardiovascular or unknown cause),<br>• Myocardial Infarction (diagnosis of new Myocardial Infarction (MI) - nonfatal or fatal)<br>• Stroke (presence of a new focal neurologic deficit thought to be vascular in origin, with signs or symptoms lasting more than 24 hours - nonfatal or fatal)<br>reported between the randomization and Day 30 (inclusive), and validated by the blinded Event Adjudication Committee (EAC). |
| Time Frame | 30 days |
| Safety Issue? | No |

Analysis Population Description

The analysis is on the intent-to-treat population (ITT) that consists of all patients randomized irrespective of whether they received study medication, underwent a PCI, or otherwise complied with the study protocol.

Reporting Groups

| | Description |
|---|---|
| Clopidogrel 300/75/75 mg + ASA | Patients randomized to the Clopidogrel 300/75/75 mg dose regimen irrespective of the ASA dose |
| Clopidogrel 600/150/75 mg + ASA | Patients randomized to the Clopidogrel 600/150/75 mg dose regimen irrespective of the ASA dose |

Measured Values

| | Clopidogrel 300/75/75 mg + ASA | Clopidogrel 600/150/75 mg + ASA |
|---|---|---|
| Number of Participants Analyzed | 12566 | 12520 |
| First Occurrence of CV Death / MI / Stroke - Clopidogrel Treatment Regimen Comparison [units: participants] | | |
| CV death/MI/Stroke | 557 | 522 |
| - CV death | 222 | 226 |
| - MI (fatal or not) | 274 | 237 |
| - Stroke (fatal or not) | 61 | 59 |

Statistical Analysis 1 for First Occurrence of CV Death / MI / Stroke - Clopidogrel Treatment Regimen Comparison

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Clopidogrel 300/75/75 mg + ASA, Clopidogrel 600/150/75 mg + ASA |
| | Comments | [Not specified] |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.3037 |
| | Comments | The a priori threshold for statistical significance is ≤0.05. |
| | Method | Log Rank |
| | Comments | Two-sided stratified by ASA dose level (low or high) and qualifying condition (UA/NSTEMI or STEMI) log-rank test. |

| | | |
|---|---|---|
| Method of Estimation | Estimation Parameter | Other [Relative Risk Reduction (%)] |
| | Estimated Value | 6.1 |
| | Confidence Interval | (2-Sided) 95%<br>-5.8 to 16.6 |
| | Estimation Comments | The relative risk reduction (high dose treatment regimen (600/150/75 mg) versus standard treatment regimen (300/75/75 mg)) is estimated using stratified Cox proportional hazards model controlling for ASA dose level and qualifying condition. |

2. Primary Outcome Measure:

| | |
|---|---|
| Measure Title | First Occurrence of CV Death / MI / Stroke - ASA Dose Comparison |
| Measure Description | |
| Time Frame | 30 days |
| Safety Issue? | No |

Analysis Population Description

The analysis is on the the ASA treated population that consists of all patients randomized and having receiving at least one dose of ASA. All patients were included in the treatment group to which they were allocated by the AReS.

Reporting Groups

| | Description |
|---|---|
| Clopidogrel + ASA Low Dose | Patients treated with ASA low dose irrespective of the Clopidogrel treatment regimen |
| Clopidogrel + ASA High Dose | Patients treated with ASA high dose irrespective of the Clopidogrel treatment regimen |

Measured Values

| | Clopidogrel + ASA Low Dose | Clopidogrel + ASA High Dose |
|---|---|---|
| Number of Participants Analyzed | 12563 | 12498 |
| First Occurrence of CV Death / MI / Stroke - ASA Dose Comparison<br>[units: participants] | | |
| CV death/MI/Stroke | 546 | 527 |
| - CV death | 231 | 211 |
| - MI (fatal or not) | 260 | 251 |
| - Stroke (fatal or not) | 55 | 65 |

Statistical Analysis 1 for First Occurrence of CV Death / MI / Stroke - ASA Dose Comparison

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Clopidogrel + ASA Low Dose, Clopidogrel + ASA High Dose |
| | Comments | [Not specified] |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.6047 |
| | Comments | The a priori threshold for statistical significance is ≤0.05. |
| | Method | Log Rank |
| | Comments | Two-sided stratified by clopidogrel treatment regimen (300/75/75 mg or 600/150/75 mg) log-rank test. |

| | | |
|---|---|---|
| Method of Estimation | Estimation Parameter | Other [Relative Risk Reduction (%)] |
| | Estimated Value | 3.1 |
| | Confidence Interval | (2-Sided) 95%<br>-9.2 to 14.0 |
| | Estimation Comments | The relative risk reduction (ASA high dose versus ASA low dose) is estimated using stratified Cox proportional hazards model controlling for Clopidogrel treatment regimen. |

3. Primary Outcome Measure:

| | |
|---|---|
| Measure Title | First Occurrence of CV Death / MI / Stroke - Interaction Clopidogrel Treatment Regimen and ASA Dose Level |
| Measure Description | |
| Time Frame | 30 days |
| Safety Issue? | No |

Analysis Population Description

The analysis is on the intent-to-treat population (ITT) that consists of all patients randomized irrespective of whether they received study medication, underwent a PCI, or otherwise complied with the study protocol.

Reporting Groups

| | Description |
|---|---|
| Clopidogrel 300/75/75 mg + ASA Low Dose | |
| Clopidogrel 300/75/75 mg + ASA High Dose | |
| Clopidogrel 600/150/75 mg + ASA Low Dose | |
| Clopidogrel 600/150/75 mg + ASA High Dose | |

Measured Values

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| Number of Participants Analyzed | 6312 | 6254 | 6267 | 6253 |
| First Occurrence of CV Death / MI / Stroke - Interaction Clopidogrel Treatment Regimen and ASA Dose Level<br>[units: participants] | 267 | 290 | 282 | 240 |

Statistical Analysis 1 for First Occurrence of CV Death / MI / Stroke - Interaction Clopidogrel Treatment Regimen and ASA Dose Level

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Clopidogrel 300/75/75 mg + ASA Low Dose, Clopidogrel 600/150/75 mg + ASA Low Dose |
| | Comments | [Not specified] |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.4579 |
| | Comments | The a priori threshold for statistical significance is ≤0.05. |
| | Method | Log Rank |
| | Comments | Two-sided stratified by qualifying condition (UA/NSTEMI or STEMI) log-rank test. |

| | | |
|---|---|---|
| Method of Estimation | Estimation Parameter | Other [Relative Risk Reduction (%)] |
| | Estimated Value | -6.5 |
| | Confidence Interval | (2-Sided) 95%<br>-26.0 to 9.9 |
| | Estimation Comments | The relative risk reduction (high dose treatment regimen (600/150/75 mg) versus standard treatment regimen (300/75/75 mg)) is estimated using a stratified Cox proportional hazards model controlling for qualifying condition. |

Statistical Analysis 2 for First Occurrence of CV Death / MI / Stroke - Interaction Clopidogrel Treatment Regimen and ASA Dose Level

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Clopidogrel 300/75/75 mg + ASA High Dose, Clopidogrel 600/150/75 mg + ASA High Dose |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.0262 |
| | Comments | The a priori threshold for statistical significance is ≤0.05. |
| | Method | Log Rank |
| | Comments | Two-sided stratified by qualifying condition (UA/NSTEMI or STEMI) log-rank test. |

| | | |
|---|---|---|
| Method of Estimation | Estimation Parameter | Other [Relative Risk Reduction (%)] |
| | Estimated Value | 17.6 |
| | Confidence Interval | (2-Sided) 95%<br>2.2 to 30.5 |
| | Estimation Comments | The relative risk reduction (high dose treatment regimen (600/150/75 mg) versus standard treatment regimen (300/75/75 mg)) is estimated using a stratified Cox proportional hazards model controlling for qualifying condition. |

Statistical Analysis 3 for First Occurrence of CV Death / MI / Stroke - Interaction Clopidogrel Treatment Regimen and ASA Dose Level

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Clopidogrel 300/75/75 mg + ASA Low Dose, Clopidogrel 300/75/75 mg + ASA High Dose, Clopidogrel 600/150/75 mg + ASA Low Dose, Clopidogrel 600/150/75 mg + ASA High Dose |
| | Comments | [Not specified] |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.0355 |
| | Comments | The a priori threshold for statistical significance is ≤0.05. |
| | Method | Chi-squared |
| | Comments | Interaction chi-squared test of the Cox proportional hazards model. |

4. Primary Outcome Measure:

| | |
|---|---|
| Measure Title | First Occurrence of CV Death / MI / Stroke - Clopidogrel Treatment Regimen Comparison in PCI Subgroup |
| Measure Description | |
| Time Frame | 30 days |

| | |
|---|---|
| Safety Issue? | No |

Analysis Population Description

The intent-to-treat (ITT) analysis is done on the randomized patients who underwent PCI during the study.

Reporting Groups

| | Description |
|---|---|
| Clopidogrel 300/75/75 mg + ASA | Patients randomized to the Clopidogrel 300/75/75 mg dose regimen irrespective of the ASA dose |
| Clopidogrel 600/150/75 mg + ASA | Patients randomized to the Clopidogrel 600/150/75 mg dose regimen irrespective of the ASA dose |

Measured Values

| | Clopidogrel 300/75/75 mg + ASA | Clopidogrel 600/150/75 mg + ASA |
|---|---|---|
| Number of Participants Analyzed | 8703 | 8560 |
| First Occurrence of CV Death / MI / Stroke - Clopidogrel Treatment Regimen Comparison in PCI Subgroup<br>[units: participants] | | |
| CV death/MI/Stroke | 392 | 330 |
| - CV death | 132 | 130 |
| - MI (fatal or not) | 225 | 172 |
| - Stroke (fatal or not) | 35 | 28 |

Statistical Analysis 1 for First Occurrence of CV Death / MI / Stroke - Clopidogrel Treatment Regimen Comparison in PCI Subgroup

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Clopidogrel 300/75/75 mg + ASA, Clopidogrel 600/150/75 mg + ASA |
| | Comments | [Not specified] |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.0332 |
| | Comments | The a priori threshold for statistical significance is ≤0.05. |
| | Method | Log Rank |

| | | |
|---|---|---|
| | Comments | Two-sided stratified by ASA dose level (low or high) and qualifying condition (UA/NSTEMI or STEMI) Log-rank test. No adjustment was made. |

| | | |
|---|---|---|
| Method of Estimation | Estimation Parameter | Other [Relative Risk Reduction (%)] |
| | Estimated Value | 14.7 |
| | Confidence Interval | (2-Sided) 95%<br>1.2 to 26.3 |
| | Estimation Comments | The relative risk reduction (high dose treatment regimen (600/150/75 mg) versus standard treatment regimen (300/75/75 mg)) is estimated using a stratified Cox proportional hazards model controlling for ASA dose level and qualifying condition. |

5. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Occurrence of Major Bleeding - Clopidogrel Dose Regimen Comparison |
| Measure Description | Major bleeding is defined as any severe bleeding (associated with any of the following: death, leading to a drop in hemoglobin ≥ 5 g/dl, significant hypotension with the need for inotropic agents, symptomatic intracranial hemorrhage, requirement for surgery or for a transfusion ≥ 4 units of red blood cells or equivalent whole blood) and other major bleeding (significantly disabling bleeding, or intraocular bleeding leading to significant loss of vision or bleeding requiring transfusion of 2-3 units of red blood cells or equivalent whole blood) after validation by the independent EAC. |
| Time Frame | 30 days |
| Safety Issue? | Yes |

Analysis Population Description

The analysis is on the intent-to-treat population (ITT) that consists of all patients randomized irrespective of whether they received study medication, underwent a PCI, or otherwise complied with the study protocol.

Reporting Groups

| | Description |
|---|---|
| Clopidogrel 300/75/75 mg + ASA | Patients randomized to the Clopidogrel 300/75/75 mg dose regimen irrespective of the ASA dose |
| Clopidogrel 600/150/75 mg + ASA | Patients randomized to the Clopidogrel 600/150/75 mg dose regimen irrespective of the ASA dose. |

Measured Values

| | Clopidogrel 300/75/75 mg + ASA | Clopidogrel 600/150/75 mg + ASA |
|---|---|---|
| Number of Participants Analyzed | 12566 | 12520 |
| Occurrence of Major Bleeding - Clopidogrel Dose Regimen Comparison<br>[units: participants] | | |

| | Clopidogrel 300/75/75 mg + ASA | Clopidogrel 600/150/75 mg + ASA |
|---|---|---|
| Major bleeding | 255 | 313 |
| - Severe bleeding | 195 | 236 |
| - Major but not severe bleeding | 65 | 83 |

Statistical Analysis 1 for Occurrence of Major Bleeding - Clopidogrel Dose Regimen Comparison

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Clopidogrel 300/75/75 mg + ASA, Clopidogrel 600/150/75 mg + ASA |
| | Comments | [Not specified] |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.012 |
| | Comments | The a priori threshold for statistical significance is ≤0.05. |
| | Method | Regression, Logistic |
| | Comments | logistic regression model including terms for ASA dose level (low or high) and qualifying condition (UA/NSTEMI or STEMI). |

6. Secondary Outcome Measure:

| | |
|---|---|
| Measure Title | Occurrence of Major Bleeding - ASA Dose Level Comparison |
| Measure Description | |
| Time Frame | 30 days |
| Safety Issue? | Yes |

Analysis Population Description

The analysis is on the treated patient population that consists of all patients randomized and having receiving at least one dose of ASA. All patients were included in the treatment group to which they were allocated by the AReS.

Reporting Groups

| | Description |
|---|---|
| Clopidogrel + ASA Low Dose | Patients treated with ASA low dose irrespective of the Clopidogrel treatment regimen |
| Clopidogrel + ASA High Dose | Patients treated with ASA high dose irrespective of the Clopidogrel treatment regimen |

Measured Values

| | Clopidogrel + ASA Low Dose | Clopidogrel + ASA High Dose |
|---|---|---|
| Number of Participants Analyzed | 12563 | 12498 |
| Occurrence of Major Bleeding - ASA Dose Level Comparison<br>[units: participants] | | |
| Major bleeding | 285 | 282 |
| - Severe bleeding | 215 | 216 |
| - Major but not severe bleeding | 74 | 73 |

Statistical Analysis 1 for Occurrence of Major Bleeding - ASA Dose Level Comparison

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Clopidogrel + ASA Low Dose, Clopidogrel + ASA High Dose |
| | Comments | [Not specified] |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.945 |
| | Comments | The a priori threshold for statistical significance is ≤0.05. |
| | Method | Regression, Logistic |
| | Comments | Logistic regression model including a term for Clopidogrel treatment regimen (300/75/75 mg or 600/150/75 mg). |

7. Post-Hoc Outcome Measure:

| | |
|---|---|
| Measure Title | Occurrence of Stent Thrombosis - Clopidogrel Treatment Regimen Comparison |
| Measure Description | This includes definite stent thrombosis (confirmed by angiography or evidence of recent thrombus determined at autopsy or by examination of tissue retrieved following thrombectomy) and probable stent thrombosis (unexplained death having occurred after intracoronary stenting or, MI related to acute ischemia in the territory of the implanted stent without angiographic confirmation and in the absence of any obvious cause) after validation by the EAC. |
| Time Frame | 30 days |
| Safety Issue? | No |

Analysis Population Description

The analysis is on the intent-to-treat population (ITT) that consists of all patients randomized irrespective of whether they received study medication, underwent a PCI, or otherwise complied with the study protocol.

Reporting Groups

| | Description |
|---|---|
| Clopidogrel 300/75/75 mg + ASA | Patients randomized to the Clopidogrel 300/75/75 mg dose regimen irrespective of the ASA dose |
| Clopidogrel 600/150/75 mg + ASA | Patients randomized to the Clopidogrel 600/150/75 mg dose regimen irrespective of the ASA dose |

Measured Values

| | Clopidogrel 300/75/75 mg + ASA | Clopidogrel 600/150/75 mg + ASA |
|---|---|---|
| Number of Participants Analyzed | 12566 | 12520 |
| Occurrence of Stent Thrombosis - Clopidogrel Treatment Regimen Comparison [units: participants] | | |
| Stent trombosis | 200 | 135 |
| - Definite | 111 | 58 |
| - Probable | 89 | 77 |

Statistical Analysis 1 for Occurrence of Stent Thrombosis - Clopidogrel Treatment Regimen Comparison

| | | |
|---|---|---|
| Statistical Analysis Overview | Comparison Groups | Clopidogrel 300/75/75 mg + ASA, Clopidogrel 600/150/75 mg + ASA |
| | Comments | [Not specified] |
| | Non-Inferiority or Equivalence Analysis? | No |
| | Comments | [Not specified] |

| | | |
|---|---|---|
| Statistical Test of Hypothesis | P-Value | 0.0004 |
| | Comments | The a priori threshold for statistical significance is ≤0.05. |
| | Method | Log Rank |
| | Comments | Two-sided stratified by ASA dose level (low or high) and qualifying condition (UA/NSTEMI or STEMI) log-rank test. |

| | | |
|---|---|---|
| Method of Estimation | Estimation Parameter | Other [Relative Risk Reduction (%)] |

| | | |
|---|---|---|
| | Estimated Value | 32.6 |
| | Confidence Interval | (2-Sided) 95%<br>16.2 to 45.8 |
| | Estimation Comments | The relative risk reduction (high dose treatment regimen (600/150/75 mg) versus standard treatment regimen (300/75/75 mg)) is estimated using a stratified Cox proportional hazards model controlling for ASA dose level and qualifying condition. |

## Reported Adverse Events

| | |
|---|---|
| Time Frame | 30 days |
| Additional Description | The analysis is on the intent-to-treat population (ITT). All patients were included in the treatment arm to which they were allocated by the AReS.<br><br>Any adverse event that developed or worsened on or after randomization up to the day of the final follow-up visit was included. |

Reporting Groups

| | Description |
|---|---|
| Clopidogrel 300/75/75 mg + ASA Low Dose | Day 1: Clopidogrel 300 mg loading dose + ASA ≥ 300 mg<br>Day 2 to Day 7: Clopidogrel 75 mg + ASA 75-100 mg<br>Day 8 to Day 30: Clopidogrel 75 mg + ASA 75-100 mg |
| Clopidogrel 300/75/75 mg + ASA High Dose | Day 1: Clopidogrel 300 mg loading dose + ASA ≥ 300 mg<br>Day 2 to Day 7: Clopidogrel 75 mg + ASA 300-325 mg<br>Day 8 to Day 30: Clopidogrel 75 mg + ASA 300-325 mg |
| Clopidogrel 600/150/75 mg + ASA Low Dose | Day 1: Clopidogrel 600 mg loading dose + ASA ≥ 300 mg<br>Day 2 to Day 7: Clopidogrel 150 mg + ASA 75-100 mg<br>Day 8 to Day 30: Clopidogrel 75 mg + ASA 75-100 mg |
| Clopidogrel 600/150/75 mg + ASA High Dose | Day 1: Clopidogrel 600 mg loading dose + ASA ≥ 300 mg<br>Day 2 to Day 7: Clopidogrel 150 mg + ASA 300-325 mg<br>Day 8 to Day 30: Clopidogrel 75 mg + ASA 300-325 mg |

Serious Adverse Events

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Total | 322/6312 (5.1%) | 329/6254 (5.26%) | 372/6267 (5.94%) | 332/6253 (5.31%) |
| Blood and lymphatic system disorders | | | | |
| Anaemia [A] * | 5/6312 (0.08%) | 1/6254 (0.02%) | 3/6267 (0.05%) | 5/6253 (0.08%) |
| Anaemia of chronic disease [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Disseminated intravascular coagulation [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Eosinophilia [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Haemorrhagic anaemia [A] * | 7/6312 (0.11%) | 5/6254 (0.08%) | 4/6267 (0.06%) | 6/6253 (0.1%) |
| Heparin-induced thrombocytopenia [A] * | 0/6312 (0%) | 2/6254 (0.03%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Iron deficiency anaemia [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Lymphadenopathy [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Microcytic anaemia [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Nephrogenic anaemia [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 2/6253 (0.03%) |
| Normochromic normocytic anaemia [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Splenic infarction [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Thrombocytopenia [A] * | 2/6312 (0.03%) | 3/6254 (0.05%) | 4/6267 (0.06%) | 2/6253 (0.03%) |
| White blood cell disorder [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Cardiac disorders | | | | |
| Acute left ventricular failure [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Atrial thrombosis [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Bradyarrhythmia [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Cardiac arrest [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Cardiac failure [A] * | 0/6312 (0%) | 2/6254 (0.03%) | 0/6267 (0%) | 0/6253 (0%) |
| Cardiac failure congestive [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Cardiac perforation [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Cardiac tamponade [A] * | 2/6312 (0.03%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Cardio-respiratory arrest [A] * | 2/6312 (0.03%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Cardiogenic shock [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Cardiopulmonary failure [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Coronary artery thrombosis [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Dressler's syndrome [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Haemorrhage coronary artery [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Interventricular septum rupture [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Intracardiac thrombus [A] * | 1/6312 (0.02%) | 2/6254 (0.03%) | 1/6267 (0.02%) | 5/6253 (0.08%) |
| Left ventricular failure [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Mitral valve incompetence [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Myocardial infarction [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Myocarditis [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Myopericarditis [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Palpitations [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Pericardial effusion [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Pericardial haemorrhage [A] * | 15/6312 (0.24%) | 12/6254 (0.19%) | 18/6267 (0.29%) | 11/6253 (0.18%) |
| Pericarditis [A] * | 3/6312 (0.05%) | 1/6254 (0.02%) | 2/6267 (0.03%) | 1/6253 (0.02%) |

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Right ventricular dysfunction [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Congenital, familial and genetic disorders | | | | |
| Atrial septal defect [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Gastrointestinal angiodysplasia haemorrhagic [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Phimosis [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Ventricular septal defect [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Ear and labyrinth disorders | | | | |
| Deafness [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Hypoacusis [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Vertigo [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Endocrine disorders | | | | |
| Pituitary cyst [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Eye disorders | | | | |
| Diplopia [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Glaucoma [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Retinal detachment [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Gastrointestinal disorders | | | | |
| Abdominal discomfort [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Abdominal pain [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Abdominal pain upper [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 3/6253 (0.05%) |
| Acute abdomen [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Colitis ischaemic [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 1/6253 (0.02%) |

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Colonic pseudo-obstruction [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Constipation [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 2/6253 (0.03%) |
| Diarrhoea [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Diverticular perforation [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Diverticulum intestinal haemorrhagic [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Duodenal ulcer [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Duodenal ulcer haemorrhage [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 2/6253 (0.03%) |
| Dysphagia [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Enterocolitis haemorrhagic [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Gastric haemorrhage [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 3/6253 (0.05%) |
| Gastric polyps [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Gastric ulcer [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Gastric ulcer haemorrhage [A] * | 2/6312 (0.03%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Gastritis [A] * | 2/6312 (0.03%) | 3/6254 (0.05%) | 2/6267 (0.03%) | 3/6253 (0.05%) |
| Gastritis erosive [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Gastritis haemorrhagic [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Gastrointestinal haemorrhage [A] * | 13/6312 (0.21%) | 12/6254 (0.19%) | 15/6267 (0.24%) | 15/6253 (0.24%) |
| Gastrointestinal ischaemia [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Gastrointestinal pain [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Gastrointestinal ulcer haemorrhage [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 2/6267 (0.03%) | 3/6253 (0.05%) |
| Gastrooesophageal reflux disease [A] * | 0/6312 (0%) | 3/6254 (0.05%) | 2/6267 (0.03%) | 0/6253 (0%) |

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Haematemesis [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Haemorrhagic erosive gastritis [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Haemorrhoidal haemorrhage [A] * | 0/6312 (0%) | 2/6254 (0.03%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Hiatus hernia [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Ileus [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Intestinal ischaemia [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Intestinal obstruction [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Large intestinal haemorrhage [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Lumbar hernia [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Melaena [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Mesenteric vein thrombosis [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Nausea [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Oesophagitis haemorrhagic [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Pancreatitis [A] * | 0/6312 (0%) | 4/6254 (0.06%) | 2/6267 (0.03%) | 0/6253 (0%) |
| Pancreatitis acute [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 2/6253 (0.03%) |
| Peptic ulcer [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 2/6253 (0.03%) |
| Peptic ulcer haemorrhage [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Periodontitis [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Peritonitis [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Rectal haemorrhage [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Reflux oesophagitis [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Retroperitoneal haematoma [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 2/6267 (0.03%) | 2/6253 (0.03%) |
| Retroperitoneal haemorrhage [A] * | 2/6312 (0.03%) | 4/6254 (0.06%) | 9/6267 (0.14%) | 8/6253 (0.13%) |
| Small intestinal obstruction [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Tongue haemorrhage [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Upper gastrointestinal haemorrhage [A] * | 3/6312 (0.05%) | 6/6254 (0.1%) | 3/6267 (0.05%) | 6/6253 (0.1%) |
| Vomiting [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| General disorders | | | | |
| Application site erosion [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Catheter site haematoma [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Catheter site haemorrhage [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Chest pain [A] * | 2/6312 (0.03%) | 3/6254 (0.05%) | 5/6267 (0.08%) | 1/6253 (0.02%) |
| Fatigue [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Gait disturbance [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Implant site haematoma [A] * | 2/6312 (0.03%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Implant site haemorrhage [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Inflammation [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Mechanical complication of implant [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Multi-organ failure [A] * | 1/6312 (0.02%) | 2/6254 (0.03%) | 3/6267 (0.05%) | 1/6253 (0.02%) |
| Necrosis [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Non-cardiac chest pain [A] * | 4/6312 (0.06%) | 2/6254 (0.03%) | 2/6267 (0.03%) | 1/6253 (0.02%) |
| Oedema peripheral [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Puncture site haemorrhage [A] * | 17/6312 (0.27%) | 21/6254 (0.34%) | 22/6267 (0.35%) | 31/6253 (0.5%) |
| Pyrexia [A] * | 1/6312 (0.02%) | 5/6254 (0.08%) | 0/6267 (0%) | 4/6253 (0.06%) |
| Systemic inflammatory response syndrome [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Vessel puncture site haematoma [A] * | 2/6312 (0.03%) | 2/6254 (0.03%) | 1/6267 (0.02%) | 2/6253 (0.03%) |
| Hepatobiliary disorders | | | | |
| Acute hepatic failure [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Bile duct obstruction [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Biliary colic [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Cholangitis [A] * | 2/6312 (0.03%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Cholecystitis [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Cholecystitis acute [A] * | 3/6312 (0.05%) | 4/6254 (0.06%) | 1/6267 (0.02%) | 2/6253 (0.03%) |
| Cholelithiasis [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Hepatic failure [A] * | 2/6312 (0.03%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Hepatitis [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Hyperbilirubinaemia [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Immune system disorders | | | | |
| Anaphylactic reaction [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Anaphylactic shock [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Drug hypersensitivity [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Hypersensitivity [A] * | 3/6312 (0.05%) | 0/6254 (0%) | 1/6267 (0.02%) | 3/6253 (0.05%) |
| Infections and infestations | | | | |

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Appendicitis [A] * | 0/6312 (0%) | 2/6254 (0.03%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Application site infection [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Bacteraemia [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Bronchiolitis [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Bronchitis [A] * | 2/6312 (0.03%) | 2/6254 (0.03%) | 1/6267 (0.02%) | 2/6253 (0.03%) |
| Bronchopneumonia [A] * | 0/6312 (0%) | 0/6254 (0%) | 2/6267 (0.03%) | 2/6253 (0.03%) |
| Catheter related infection [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Catheter sepsis [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Cellulitis [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 2/6267 (0.03%) | 1/6253 (0.02%) |
| Dengue fever [A] * | 0/6312 (0%) | 2/6254 (0.03%) | 0/6267 (0%) | 0/6253 (0%) |
| Diverticulitis [A] * | 1/6312 (0.02%) | 2/6254 (0.03%) | 0/6267 (0%) | 2/6253 (0.03%) |
| Endocarditis [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Endocarditis bacterial [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Erysipelas [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Escherichia sepsis [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Gallbladder empyema [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Gangrene [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Gastroenteritis [A] * | 4/6312 (0.06%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 2/6253 (0.03%) |
| Gastrointestinal infection [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Graft infection [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Haematoma infection [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Incision site infection [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Infected skin ulcer [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Influenza [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Liver abscess [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Lobar pneumonia [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 2/6253 (0.03%) |
| Lower respiratory tract infection [A] * | 3/6312 (0.05%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Lower respiratory tract infection viral [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Lung infection [A] * | 2/6312 (0.03%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Mediastinitis [A] * | 0/6312 (0%) | 3/6254 (0.05%) | 0/6267 (0%) | 0/6253 (0%) |
| Meningitis coxsackie viral [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Myocarditis infectious [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Necrotising fasciitis [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Osteomyelitis [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Peridiverticulitis [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Peritoneal infection [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Pneumonia [A] * | 21/6312 (0.33%) | 11/6254 (0.18%) | 22/6267 (0.35%) | 16/6253 (0.26%) |
| Pneumonia primary atypical [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Post procedural infection [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Post procedural pneumonia [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Post procedural sepsis [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Postoperative wound infection [A] * | 3/6312 (0.05%) | 3/6254 (0.05%) | 2/6267 (0.03%) | 3/6253 (0.05%) |

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Pseudomembranous colitis [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Pulmonary sepsis [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Puncture site infection [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Pyelonephritis [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Pyelonephritis acute [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Respiratory tract infection [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Sepsis [A] * | 4/6312 (0.06%) | 3/6254 (0.05%) | 5/6267 (0.08%) | 0/6253 (0%) |
| Septic shock [A] * | 4/6312 (0.06%) | 2/6254 (0.03%) | 5/6267 (0.08%) | 4/6253 (0.06%) |
| Sinusitis [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Staphylococcal mediastinitis [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Upper respiratory tract infection [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Urinary tract infection [A] * | 3/6312 (0.05%) | 0/6254 (0%) | 3/6267 (0.05%) | 3/6253 (0.05%) |
| Urosepsis [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Viral infection [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Wound infection [A] * | 1/6312 (0.02%) | 4/6254 (0.06%) | 3/6267 (0.05%) | 0/6253 (0%) |
| Injury, poisoning and procedural complications | | | | |
| Agitation postoperative [A] * | 0/6312 (0%) | 2/6254 (0.03%) | 0/6267 (0%) | 0/6253 (0%) |
| Anaemia postoperative [A] * | 2/6312 (0.03%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Anaesthetic complication pulmonary [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Cardiac procedure complication [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Chest injury [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Collapse of lung [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Complication of device removal [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Compression fracture [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Confusion postoperative [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Deep vein thrombosis postoperative [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Facial bones fracture [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Fall [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Fat embolism [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Femur fracture [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Haematuria traumatic [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Haemolytic transfusion reaction [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Hepatic haematoma [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Hip fracture [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Incision site haemorrhage [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 2/6267 (0.03%) | 0/6253 (0%) |
| Incisional hernia, obstructive [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Joint dislocation [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Lower limb fracture [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Mechanical ventilation complication [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Operative haemorrhage [A] * | 39/6312 (0.62%) | 50/6254 (0.8%) | 57/6267 (0.91%) | 48/6253 (0.77%) |
| Overdose [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Post procedural haematoma [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Post procedural haemorrhage [A] * | 12/6312 (0.19%) | 16/6254 (0.26%) | 18/6267 (0.29%) | 6/6253 (0.1%) |
| Postoperative fever [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Postpericardiotomy syndrome [A] * | 0/6312 (0%) | 2/6254 (0.03%) | 0/6267 (0%) | 0/6253 (0%) |
| Procedural hypotension [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Rib fracture [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Subcutaneous haematoma [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Subdural haematoma [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Subdural haemorrhage [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Tibia fracture [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Traumatic haemorrhage [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Vascular pseudoaneurysm [A] * | 7/6312 (0.11%) | 8/6254 (0.13%) | 7/6267 (0.11%) | 9/6253 (0.14%) |
| Vascular pseudoaneurysm ruptured [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Wound [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Wound dehiscence [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 2/6253 (0.03%) |
| Investigations | | | | |
| Blood creatinine increased [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Haemoglobin decreased [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 5/6267 (0.08%) | 2/6253 (0.03%) |
| Hepatic enzyme increased [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Platelet count decreased [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Metabolism and nutrition disorders | | | | |
| Dehydration [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 3/6253 (0.05%) |
| Diabetes mellitus [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Diabetes mellitus inadequate control [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Fluid overload [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Fluid retention [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Gout [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Hydraemia [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Hyperglycaemia [A] * | 0/6312 (0%) | 0/6254 (0%) | 2/6267 (0.03%) | 0/6253 (0%) |
| Hyperkalaemia [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Hypocalcaemia [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Hypoglycaemia [A] * | 4/6312 (0.06%) | 2/6254 (0.03%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Hyponatraemia [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 2/6267 (0.03%) | 0/6253 (0%) |
| Musculoskeletal and connective tissue disorders | | | | |
| Compartment syndrome [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Gouty arthritis [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Gouty tophus [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Intervertebral disc protrusion [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Muscle haemorrhage [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Muscular weakness [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Musculoskeletal chest pain [A] * | 2/6312 (0.03%) | 1/6254 (0.02%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Musculoskeletal pain [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Myalgia [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Osteoarthritis [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Osteochondrosis [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | | |
| Acute leukaemia [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Benign hepatic neoplasm [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Breast cancer [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Bronchial carcinoma [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Colon cancer [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Gastric cancer [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Laryngeal cancer [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Lung adenocarcinoma [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Lung adenocarcinoma metastatic [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Lung neoplasm malignant [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Metastases to lung [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Metastatic carcinoma of the bladder [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Metastatic gastric cancer [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Pancreatic carcinoma [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Pituitary tumour benign [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Rectosigmoid cancer [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Tumour associated fever [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Nervous system disorders | | | | |
| Anoxic encephalopathy [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Brain stem syndrome [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Carotid artery stenosis [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Convulsion [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Critical illness polyneuropathy [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Dizziness [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Drop attacks [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Dysarthria [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Encephalomalacia [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Grand mal convulsion [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Haemorrhage intracranial [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 2/6253 (0.03%) |
| Haemorrhagic stroke [A] * | 1/6312 (0.02%) | 3/6254 (0.05%) | 2/6267 (0.03%) | 1/6253 (0.02%) |
| Headache [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Hypertensive encephalopathy [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Loss of consciousness [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Migraine without aura [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Multiple sclerosis [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Neurological symptom [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Optic neuritis [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Paraesthesia [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Presyncope [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Spinal cord infarction [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Spinal cord ischaemia [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |

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|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Syncope [A] * | 2/6312 (0.03%) | 0/6254 (0%) | 2/6267 (0.03%) | 0/6253 (0%) |
| Transient ischaemic attack [A] * | 0/6312 (0%) | 0/6254 (0%) | 2/6267 (0.03%) | 1/6253 (0.02%) |
| Psychiatric disorders | | | | |
| Alcohol withdrawal syndrome [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Anxiety [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Bipolar i disorder [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Completed suicide [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Confusional state [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Delirium [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Depression [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Generalised anxiety disorder [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Major depression [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Mental disorder due to a general medical condition [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Mental status changes [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Post-traumatic stress disorder [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Psychotic disorder [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Suicide attempt [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Renal and urinary disorders | | | | |
| Calculus ureteric [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 2/6253 (0.03%) |
| Cystitis haemorrhagic [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Haematuria [A] * | 5/6312 (0.08%) | 4/6254 (0.06%) | 4/6267 (0.06%) | 5/6253 (0.08%) |

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|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Hydronephrosis [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Nephrolithiasis [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Nephropathy [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Nephropathy toxic [A] * | 2/6312 (0.03%) | 2/6254 (0.03%) | 2/6267 (0.03%) | 0/6253 (0%) |
| Renal colic [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Renal cyst [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Renal failure [A] * | 7/6312 (0.11%) | 7/6254 (0.11%) | 8/6267 (0.13%) | 8/6253 (0.13%) |
| Renal failure acute [A] * | 11/6312 (0.17%) | 9/6254 (0.14%) | 18/6267 (0.29%) | 10/6253 (0.16%) |
| Renal failure chronic [A] * | 2/6312 (0.03%) | 2/6254 (0.03%) | 0/6267 (0%) | 3/6253 (0.05%) |
| Renal impairment [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Urethral stenosis [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Reproductive system and breast disorders | | | | |
| Menorrhagia [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Ovarian haemorrhage [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Prostatitis [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Respiratory, thoracic and mediastinal disorders | | | | |
| Acute pulmonary oedema [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Acute respiratory distress syndrome [A] * | 2/6312 (0.03%) | 0/6254 (0%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Acute respiratory failure [A] * | 1/6312 (0.02%) | 2/6254 (0.03%) | 2/6267 (0.03%) | 0/6253 (0%) |
| Apnoea [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Atelectasis [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 3/6253 (0.05%) |
| Chronic obstructive pulmonary disease [A] * | 2/6312 (0.03%) | 4/6254 (0.06%) | 5/6267 (0.08%) | 2/6253 (0.03%) |

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|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Cough [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Dyspnoea [A] * | 2/6312 (0.03%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Emphysema [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Epistaxis [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 2/6253 (0.03%) |
| Haemoptysis [A] * | 1/6312 (0.02%) | 2/6254 (0.03%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Haemothorax [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 2/6253 (0.03%) |
| Hypoxia [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Idiopathic pulmonary fibrosis [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Laryngospasm [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Lung disorder [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Pleural effusion [A] * | 3/6312 (0.05%) | 0/6254 (0%) | 3/6267 (0.05%) | 1/6253 (0.02%) |
| Pleural haemorrhage [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 2/6267 (0.03%) | 0/6253 (0%) |
| Pleurisy [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Pneumonia aspiration [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Pneumonitis [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Pneumothorax [A] * | 5/6312 (0.08%) | 1/6254 (0.02%) | 2/6267 (0.03%) | 2/6253 (0.03%) |
| Pulmonary alveolar haemorrhage [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Pulmonary congestion [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Pulmonary embolism [A] * | 5/6312 (0.08%) | 7/6254 (0.11%) | 5/6267 (0.08%) | 10/6253 (0.16%) |
| Pulmonary oedema [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Respiratory arrest [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 2/6253 (0.03%) |

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|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Respiratory depression [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Respiratory distress [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Respiratory failure [A] * | 3/6312 (0.05%) | 4/6254 (0.06%) | 4/6267 (0.06%) | 2/6253 (0.03%) |
| Sleep apnoea syndrome [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Thoracic haemorrhage [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Upper respiratory tract congestion [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Skin and subcutaneous tissue disorders | | | | |
| Angioedema [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Dermatitis allergic [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Drug eruption [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Erythema [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Haemorrhage subcutaneous [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Henoch-schonlein purpura [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Palmar-plantar erythrodysaesthesia syndrome [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Rash [A] * | 2/6312 (0.03%) | 0/6254 (0%) | 0/6267 (0%) | 3/6253 (0.05%) |
| Rash maculo-papular [A] * | 0/6312 (0%) | 0/6254 (0%) | 2/6267 (0.03%) | 0/6253 (0%) |
| Skin haemorrhage [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Urticaria [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Vascular disorders | | | | |
| Aortic aneurysm rupture [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Aortic dissection [A] * | 2/6312 (0.03%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 0/6253 (0%) |

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|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Arterial haemorrhage [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Arterial occlusive disease [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Arterial rupture [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Arterial thrombosis limb [A] * | 0/6312 (0%) | 2/6254 (0.03%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Arteriovenous fistula [A] * | 0/6312 (0%) | 3/6254 (0.05%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Artery dissection [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Deep vein thrombosis [A] * | 3/6312 (0.05%) | 1/6254 (0.02%) | 6/6267 (0.1%) | 7/6253 (0.11%) |
| Femoral artery dissection [A] * | 2/6312 (0.03%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Femoral artery occlusion [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Haematoma [A] * | 1/6312 (0.02%) | 1/6254 (0.02%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Haemorrhage [A] * | 3/6312 (0.05%) | 5/6254 (0.08%) | 5/6267 (0.08%) | 2/6253 (0.03%) |
| Hypertension [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 2/6267 (0.03%) | 1/6253 (0.02%) |
| Hypertensive crisis [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Hypotension [A] * | 3/6312 (0.05%) | 0/6254 (0%) | 2/6267 (0.03%) | 1/6253 (0.02%) |
| Iliac artery occlusion [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Orthostatic hypotension [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Peripheral arterial occlusive disease [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |
| Peripheral embolism [A] * | 0/6312 (0%) | 0/6254 (0%) | 2/6267 (0.03%) | 0/6253 (0%) |
| Peripheral ischaemia [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 1/6267 (0.02%) | 1/6253 (0.02%) |
| Peripheral vascular disorder [A] * | 0/6312 (0%) | 0/6254 (0%) | 2/6267 (0.03%) | 0/6253 (0%) |
| Phlebitis [A] * | 0/6312 (0%) | 0/6254 (0%) | 1/6267 (0.02%) | 0/6253 (0%) |

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Shock [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Shock haemorrhagic [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Thrombosis [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Vena cava thrombosis [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Venous haemorrhage [A] * | 1/6312 (0.02%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |
| Venous thrombosis [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |
| Venous thrombosis limb [A] * | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 1/6253 (0.02%) |
| Wound haemorrhage [A] * | 0/6312 (0%) | 1/6254 (0.02%) | 0/6267 (0%) | 0/6253 (0%) |

* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA (12.0)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

| | Clopidogrel 300/75/75 mg + ASA Low Dose | Clopidogrel 300/75/75 mg + ASA High Dose | Clopidogrel 600/150/75 mg + ASA Low Dose | Clopidogrel 600/150/75 mg + ASA High Dose |
|---|---|---|---|---|
| | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) | Affected/At Risk (%) |
| Total | 0/6312 (0%) | 0/6254 (0%) | 0/6267 (0%) | 0/6253 (0%) |

## Limitations and Caveats

[Not specified]

## More Information

Certain Agreements:

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

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

Publication of the study is made jointly in the name of all wholehearted collaborators. Other papers are authored based on the contributions of the individuals to the overall study. Sub-studies with scientific merit which have received prior approvals of the Steering Committee may be published separately in the names of contributing Investigators. A copy of all manuscripts are provided to the Sponsors for their review and the final decision to publish is made by the Steering Committee.

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