

# ISCHAEMIC HEART DISEASE

## TRIALS

| NUMBER OF PARTICIPANTS | NUMBER OF WOMEN | PERCENTAGE OF WOMEN | MEAN AGE | MEAN FOLLOW-UP (YEARS) | TRIALS WITH ANALYSIS BY GENDER N, (%) |
|------------------------|-----------------|---------------------|----------|------------------------|---------------------------------------|
| 90,400                 | 24,756          | 27.3%               | 62.6     | 0.96                   | 5/13 (38.4%)                          |

| TRIAL   | YEAR     | POPULATION   | AGE   | N° OF SUBJECTS                           | FOLLOW UP | TREATMENT                         | DESCRIPTION OF END-POINT                               | PRIMARY END-POINT  | PRIMARY END-POINT HR   | NOTES   |
|---|----------|--|---|--|-----------|-----------------------------------|--|--|--|---|
|   |          | (Country)  | mean ± sd, range  | TOTAL (WOMEN n,%)                        | DURATION  |                                   |  | TOTAL (WOMEN n,%) (MEN n,%)  | (CI) P (WOMEN) (MEN)   |   |
| ASSENT-4 PCI (Van de Werf et al <sup>93</sup> ) | FEB 2006 | Patient with ST-segment elevation acute myocardial infarction (STEMI) scheduled to undergo primary PCI (International with significant European component) | 61±12.1 PCI+Tenecteplase; 60±12.0 PCI alone age ≥18 years | TOTAL: 1667 (WOMEN:386, 23%) (MEN: 1281) | 90 Days   | PCI+Tenecteplase versus PCI alone | Death, congestive heart failure, shock, within 90 days | PCI+Tenecteplase<br>TOTAL 151, 18.6%<br><br>(WOMEN 58/190, 30.5%) (MEN 93/620, 15.0%)<br><br>PCI alone<br>TOTAL: 110, 13.4%<br>(WOMEN: 29/182, 15.9%) (MEN: 81/637, 12.7%) | TOTAL<br>Relative Risk = 1.39 [95% CI: 1.11-1.74]<br>WOMEN<br>Relative Risk = 1.92 [95% CI: 1.29-2.85]<br>MEN<br>Relative Risk= 1.18 [95% CI: 0.89-1.56] | Tenecteplase was associated with more major adverse events particularly in women, but the interaction was not significant |

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|--|-------------|--|---|--|------------------|------------------------|--|--|--|---------------------------------------|
| CLARITY-TIMI 28 (Scirica et al <sup>94</sup> ) | JULY 2006   | Patients with ST-segment elevation myocardial infarction (STEMI) undergoing fibrinolysis (International with significant European component) | 57.6<br>Clopidogrel; 57.3<br>Placebo; age >65 years | Total: 3491, patients with Electrocardiograms valid for interpretation : 2431<br><b>(Women 462, 19%)</b><br>(Men 1969) | 30 days          | Clopidogrel vs placebo | Complete STResolution at 90 min, in-hospital death or recurrent MI, epicardial flow (TIMI flow grade 2 or 3) at late angiography | Complete STRes at 90 min<br>Clopidogrel 38.4%<br>Placebo 36.6%<br><br>TIMI flow grade 3<br>pt with complete STRes:<br>Placebo 434, 66.4%<br>Clopidogrel 474, 80.2%<br><br>in-hospital death or recurrent MI<br>pt with partial STRes:<br>Placebo 426, 6.6%<br>Clopidogrel 395, 2%<br><br>pt with complete STRes:<br>Placebo 434, 5.1%<br>Clopidogrel 474, 2.5% | OR <sub>ADJUSTED</sub> = 1.08<br>[95% CI: 0.91 -1.29]<br><br>OR <sub>ADJUSTED</sub> = 2.0<br>[95% CI: 1.5 -2.8]<br>P<0.001<br><br>OR <sub>ADJUSTED</sub> = 0.30<br>[95% CI: 0.13 - 0.67]<br>P= 0.003<br><br>OR <sub>ADJUSTED</sub> = 0.49<br>[95% CI: 0.24 - 1.02]<br>P= 0.056 | <b>Results by gender not reported</b> |

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|--|----------|--|---|--|---|---|--|---|--|---------------------------------------|
| PRINCIPLE-TIMI 44 (Wiviott et al <sup>95</sup> ) | DEC 2007 | Patients undergoing cardiac catheterization for planned percutaneous coronary intervention (International with significant European component) | Prasugrel 64; Clopidogrel 163.8; age: >18 years | TOTAL. 201<br><b>(WOMEN: 51, 25%)</b><br>(MEN 150)       | 29 days                                 | Loading-dose: prasugrel 60 mg vs clopidogrel 600 mg; maintenance-dose: prasugrel 10 mg vs clopidogrel 150 mg            | For the loading-dose phase: IPA with 20 µmol/L ADP at 6 hours; for the maintenance-dose phase: IPA after 14 days | Loading-dose phase: Prasugrel 74.8±13.0%; clopidogrel 31.8± 21.1%;<br><br>maintenance-dose phase: Prasugrel 61.3±17.8%; clopidogrel 46.1± 21.3% | LS mean difference 43.2% [95% CI: 38.0- 48.4] P< 0.0001<br><br>LS mean difference 14.9% [95% CI: 10.6-19.3] P< 0.0001  | <b>Results by gender not reported</b> |
| PPCI (Kukreja et al <sup>96</sup> )              | OCT 2008 | Patients undergoing primary percutaneous coronary intervention (PCI) for a de novo lesion (Netherlands)  | 59.1± 11.9                                      | TOTAL: 1738<br><b>(WOMEN: 374, 21.5%)</b><br>(MEN: 1364) | median duration 1185 days (746 to 1675) | 3 sequential consecutive cohorts of bare metal stents (BMS), sirolimus-eluting (SES) or paclitaxel-eluting stents (PES) | 3 year All-cause death, nonfatal myocardial infarction, target vessel revascularization                          | Death<br>BMS: 16.4%<br>SES: 11.4%<br>PES: 12.9%<br><br>Composite MACE<br>BMS: 25.0%<br>SES: 17.8%<br>PES: 21.5%                                 | Death propensity score-adjusted SES vs BMS: adjusted HR = 0.63 [95% CI: 0.33-1.18]<br>SES vs PES: adjusted HR= 0.71 [95% CI: 0.40-1.26]<br><br>Composite MACE propensity score-adjusted SES vs PES adjusted HR= 0.62 [95% CI: 0.40-0.96] | <b>Results by gender not reported</b> |

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|---|-------------|---|------------|-----------------------|-------------------------------------|---|--|--|---|--|
| TRITON–TIMI 38 (Wiviott et al <sup>97</sup> ) | NOV 2007    | Patients with moderate-to-high-risk acute coronary syndromes with scheduled percutaneous coronary intervention<br><br>(North America 32%, Western Europe 26%, Eastern Europe 24.5, Middle East, Africa, or Asia–Pacific region 14%, South America 4%) | Median 61  | TOTAL: 13608          | Minimum 6 months, maximum 15 months | Prasugrel (60-mg loading dose and 10-mg daily maintenance dose) versus clopidogrel (300-mg loading dose and 75-mg daily maintenance dose) | Death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke | 12.1% clopidogrel<br>9.9% prasugrel<br><br>rates of myocardial infarction<br>9.7% clopidogrel vs. 7.4% prasugrel<br><br>urgent target-vessel revascularization<br>3.7% clopidogrel vs. 2.5% prasugrel<br><br>stent thrombosis<br>2.4% clopidogrel vs. 1.1% prasugrel | HR = 0.81 [95% CI: 0.73 - 0.90] P<0.001<br><br><br>P<0.001<br><br>P<0.001 | <b>Percentage of women enrolled not reported here but reported in the primary publication</b><br><br><b>Results by gender not reported</b> |

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|--|-------------|--|--|---|-------------------------------------|------------------------------|--|--|---|--|
| Analysis from the TRITON-TIMI 38 (Murphy et al <sup>98</sup> ) | OCT 2008    | Patient with acute coronary syndrome undergoing planned PCI<br><br>(International trial with significant European component) | 63<br>Prasugrel;<br>62<br>Clopidogrel: | TOTAL:<br>13608<br><b>(WOMEN: 3523, 26%)</b><br>(MEN:10085) | Minimum 6 months, maximum 15 months | Prasugrel versus Clopidogrel | Recurrence of CV death or MI or stroke | 3.7% Prasugrel;<br>7.1% Clopidogrel<br><br><b>(WOMEN 13.6% Prasugrel, 20.5% Clopidogrel)</b><br><br>(MEN 9.7% Prasugrel, 13.6 Clopidogrel) | HR = 0.46<br>[95%CI: 0.25-0.82]<br>P= 0.008 | <b>No significant interactions by subgroup, including gender</b><br><br><b>Women tended to have a higher incidence of subsequent event but the greater efficacy of prasugrel was observed in both gender</b> |

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|---|-------------|---|---------------------------------------|---|------------------|---|--|---|--|---------------------------------------|
| TRITON-TIMI 38 (Montalescot et al <sup>99</sup> ) | FEB 2009    | Patients with ST-elevation myocardial infarction (STEMI)<br><br>(International with significant European component) | 58<br>Prasugrel;<br>59<br>Clopidogrel | TOTAL:<br>3534<br><b>(WOMEN 799, 22,6%)</b><br>(MEN 2735) | 15 months        | Prasugrel 60 mg loading, 10 mg maintenance versus clopidogrel 300 mg loading, 75 mg maintenance | Cardiovascular death, non-fatal myocardial infarction, non-fatal stroke at 30 days to 15 months. | At 30 days:<br>115, 6.5%<br>Prasugrel,<br>166, 9.5%<br>Clopidogrel;<br><br>At 15 months:<br>174, 10.0%<br>Prasugrel,<br>216, 12.4%<br>Clopidogrel | At 30 days:<br>HR= 0.68<br>[95% CI:<br>0.54–0.87]<br>P =0.0017<br><br>At 15 months:<br>HR = 0.79<br>[95% CI:<br>0.65–0.97]<br>P=0.0221 | <b>Results by gender not reported</b> |

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|---|------------------------------------|---|---|--|---|---|--|--|--|--|
| A substudy of the OASIS 5 and a meta-analysis of FRISC II, RITA 3, ICTUS, OASIS 5 TACTICS TIMI-18 (Swahn et al <sup>129</sup> ) | Advanced Access published FEB 2009 | women with non-ST-elevation acute coronary syndromes<br><br>(International with significant European component) | OASIS 5 substudy: Routine invasive 68.2+9.2 Selective invasive 67.8+8.8 age ≥21 years | OASIS 5 substudy: <b>WOMEN 184</b><br><br>meta-analysis: TOTAL: 7871 ( <b>WOMEN 2692, 34.2%</b> ) (MEN 5179) | OASIS 5 substudy : 2 years<br><br>meta-analysis: 1-year | OASIS 5 substudy: a routine coronary angiography versus a selective invasive strategy with coronary angiography only if they experienced symptoms or signs of severe ischaemia. | OASIS 5 substudy: death, MI, or stroke at 2 years<br><br>meta-analysis: 1-year death, MI | <i>OASIS 5 substudy:</i><br><b>Routine invasive 19 (21.0%)</b><br><b>Selective Invasive 14 (15.4%)</b><br><i>(deaths at 1 year</i><br><b>Routine invasive 8.8%</b><br><b>Selective invasive 1.1%</b><br><i>major bleeding at 30 days</i><br><b>Routine invasive 8.8 %</b><br><b>Selective invasive 1.1%))</b><br><i>Meta-analysis: Death, MI :</i><br><b>WOMEN Routine Invasive 10.4%</b><br><b>Selective Invasive 9.1%</b><br>MEN<br>Routine invasive 9.8%<br>Selective Invasive 12.1%<br><i>Death:</i><br><b>WOMEN Routine invasive 4.3%</b><br><b>Selective Invasive 2.9%</b><br>MEN<br>Routine invasive: 2.7%<br>Selective Invasive:3.9% | <b>HR= 1.46</b><br><b>[95% CI: 0.73–2.94]</b><br><br><i>(Deaths After 1 Year</i><br><b>HR = 9.01</b><br><b>[95% CI 1.11–72.90]</b><br><i>major bleeding at 30 days</i><br><b>HR = 11.45</b><br><b>[95% CI: 1.43–91.96]</b><br><br><i>Meta-analysis:</i><br><b>OR = 1.18</b><br><b>[95% CI: 0.92–1.53]</b><br><br>OR=0.78<br>[95% CI: 0.66–0.93]<br><br><b>OR =1.51</b><br><b>[95% CI: 1.00–2.29]</b><br><br>OR = 0.70<br>[95% CI: 0.51–0.96] | <b>No benefit of an early invasive strategy with greater mortality in women with ACS</b> |

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|--|-------------|---|---|--|-------------------------|---|--|---|---|---------------------------------------|
| PCI-CURE (Jolly et al <sup>100</sup> ) | APR 2009    | Patients with acute coronary syndromes undergoing PCI<br><br>(International with 48.8% Western Europe, 11.2% Eastern Europe, 21.4% Canada/USA, 10.4% Latin America, 8.0% Other) | Low dose 62.2±10.9<br>Medium dose 61.0 ±10.6<br>High dose 61.1±11.3 | TOTAL: 2658<br><b>(WOMEN 804, 30.2%)</b><br>(MEN 1854) | Mean follow-up 8 months | 3 aspirin dose groups:<br>≥200 mg (high)<br><br>101–199 mg (moderate)<br><br>≤100 mg (low). | Cardiovascular death, myocardial infarction, or stroke at 30 days and at long term follow-up | At 30 days:<br>43 (4.1%) low<br>17 (3.2%) moderate<br>43 (4.0%) high<br><br>long-term follow-up:<br>75 (7.1%) low<br>40 (7.4%) moderate<br>91 (8.6%) high | At 30 days:<br>HR = 0.99<br>[95% CI: 0.65–1.51]<br>High vs. low dose<br>HR = 0.77<br>[95% CI: 0.44–1.35]<br>Moderate vs. low dose<br><br>long-term follow-up:<br>HR = 1.21<br>[95% CI: 0.89–1.64]<br>High vs. low dose<br>HR = 1.04<br>[95% CI: 0.71–1.52]<br>Moderate vs. low dose | <b>Results by gender not reported</b> |



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|--|-------------|--|-------------------------------------|--|-----------------------------------|---|---|--|---|---|
| EASY Gender subanalysis (Tizon-Marcos et al <sup>101</sup> ) | APR 2009    | Patients with acute coronary syndrome undergoing transradial PCI | Women: 62.5±11.0<br>Men: 59.7±10.0; | TOTAL: 1348<br><b>(WOMEN. 298, 22%)</b><br>(MEN: 1050) | 30 days, 6 months, and 12 months. | Bolus-only abciximab to overnight hospitalization versus bolus followed by 12-hour infusion of abciximab after uncomplicated transradial coronary stenting. | Major adverse cardiac events including death, myocardial infarction, target vessel revascularization, major bleeding and local hematomas were evaluated at 30 days, 6 months, and 12 months | At 30 days:<br><b>WOMEN 10 (3.4%)</b><br>MEN 41 (3.9%)<br><br>at 6 months:<br><b>WOMEN 34 (11.5%)</b><br>MEN 82 (7.8%)<br><br>at 12 months:<br><b>WOMEN 42 (14.1%)</b><br>MEN 132(12.6%) | At 30 days:<br>P = 0.86<br><br>at 6 months:<br>P = 0.06<br><br>at 12 months<br>P = 0.49 | <b>Women tended to have more events than men at 6 months although the difference is not significant</b> |

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|---|-------------|---|---|---|------------------|---|--|---|---|---------------------------------------|
| Analysis from ACUITY (Ebrahimi et al <sup>102</sup> ) | MAY 2009    | Patients with NSTEMI-ACS undergoing early invasive management who received CABG | Clopidogrel Before CABG Median 65 (range 33–87)<br><br>No Clopidogrel Before CABG Median 64 (range 35–90) | Of 13819 pt 1539 (11.1%) underwent CABG<br><br><b>(WOMEN 353, 22.9%) (MEN 1186)</b> | 1 year           | Clopidogrel-exposed patients before CABG vs non-exposed | Ischemic events (death, myocardial infarction, or unplanned revascularization) | 30-day<br>Clopidogrel before CABG: 98 (12.7%)<br>No Clopidogrel before CABG: 129 (17.3%)<br><br>1-year<br>Clopidogrel before CABG: 142 (18.4%)<br>No Clopidogrel before CABG: 160 (21.4%) | P= 0.001<br><br><br>P = 0.14<br><br>Non-CABG-related major bleeding (3.4% vs. 3.2%, p= 0.87)<br>post-CABG major bleeding (50.3% vs. 50.9%, p =0.83) | <b>Results by gender not reported</b> |

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|-----------------------------------|-------------|--|--|--|------------------|---|--|---|---|---------------------------------------|
| HORIZONS-AMI<br>(Stone et al 103) | MAY 2009    | Patients presenting with ST-segment elevation myocardial infarction<br><br>(International with significant European component) | Median 59.9<br>Range 30.9–92.3<br>Paclitaxel-Eluting Stents<br><br>Median 59.3<br>Range 26.0–89.0<br>Bare-Metal Stents | TOTAL: 3006<br><b>(WOMEN 699, 23.5%)</b><br>(MEN 2307) | 12-month         | Paclitaxel-eluting stents versus identical bare-metal stents (in a 3:1 ratio) | 12-month rates of target-lesion revascularization for ischemia (analysis powered for superiority) and a composite safety outcome measure of death, reinfarction, stroke, or stent thrombosis (powered for noninferiority with a 3.0% margin) | 12-month rates target-lesion revascularization : 4.5%<br>Paclitaxel-Eluting Stents vs. 7.5% Bare-Metal Stents<br><br>target-vessel revascularization :<br>5.8% Paclitaxel-Eluting Stents vs. 8.7% Bare-Metal Stents<br><br>MACE:<br>8.1% Paclitaxel-Eluting Stents vs. 8.0% Bare-Metal Stents | HR = 0.59<br>[95% CI: 0.43 - 0.83]<br>P = 0.002<br><br>HR = 0.65<br>[95% CI: 0.48 - 0.89]<br>P = 0.006<br><br>HR = 1.02<br>[95% CI: 0.76 - 1.36]<br><br>absolute difference, 0.1 percentage point; [95% CI: 2.1-2.4]<br>P = 0.01 for noninferiority; P = 0.92 for superiority | <b>Results by gender not reported</b> |

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|--|----------|--|--|---|--------------------------------------|---|--|---|---|---|
| SCAAR<br>(James et al <sup>104</sup> )         | MAY 2009 | Patients who had received a coronary stent (Sweden)  | 66.2±11.0<br>Bare-Metal Stent<br>65.5±10.7<br>Drug-Eluting Stent | TOTAL:<br>47967<br><b>(WOMEN: 13344, 27.8%)</b><br>(MEN: 34623) | 1 to 5 years of follow-up (mean 2.7) | Drug eluting coronary stent versus bare-metal stent   | Death or myocardial infarction   | Death:<br>Total 2380<br>MI:<br>total 3198<br><br>no significant difference in outcome among subgroups   | RR = 0.96<br>[95% CI:<br>0.89-1.03]   | <b>Results by gender not reported</b>   |
| EARLY ACS<br>(Giugliano et al <sup>105</sup> ) | MAY 2009 | Patients who had acute coronary syndromes without ST-segment elevation and who were assigned to an invasive strategy. (International: Western Europe 40.3% Eastern Europe 10.8% North America 30.7% Middle East, Africa, or Asia-Pacific 18.15%) | Early eptifibatide: 67.4; delayed eptifibatide: 67.8             | TOTAL:<br>9406<br><b>(WOMEN 3009, 32%)</b><br>(MEN 6397)        | 30 days                              | Early eptifibatide (two boluses, each containing 180 µg per kilogram of body weight, administered 10 minutes apart, and a standard infusion ≥12 hours before angiography) versus a matching placebo infusion with provisional use of eptifibatide after angiography (delayed eptifibatide). | Composite of death, myocardial infarction, recurrent ischemia requiring urgent revascularization, or the occurrence of a thrombotic complication during percutaneous coronary intervention (thrombotic bailout) at 96 hours. | Early eptifibatide group: 439 (9.3%); delayed-eptifibatide group: 469 (10.0%)<br><br><b>WOMEN</b><br>Early eptifibatide group <b>9.7%</b><br>delayed-eptifibatide <b>10.4%</b><br><br>MEN<br>Early eptifibatide group 9.1%<br>delayed-eptifibatide 9.8% | OR = 0.92<br>[95% CI:<br>0.80 -1.06]<br>P = 0.23<br><br>Death/myocardial infarction (secondary endpoint)<br><br><b>WOMEN</b><br>Early eptifibatide group <b>10.7%</b><br>delayed-eptifibatide <b>13.0%</b><br><br>MEN<br>Early eptifibatide group 11.4%<br>delayed-eptifibatide 12.0% | <b>No significant difference between early or delayed eptifibatide in the primary endpoint in both gender.</b><br><br><b>Lower incidence of Death/MI (secondary endpoint) with early intervention in women than in men (p interaction =0.046)</b> |

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|--|-------------|--|---|---|------------------|---|---|---|---|--|
| SYNTAX (Serruys et al <sup>106</sup> ) | MAR 2009    | International trial conducted in 17 countries in Europe and the United States in patients with three-vessel or left main coronary artery disease   | PCI<br>65.2 ± 9.7<br>vs<br>CABG<br>65.0 ± 9.8         | TOTAL: 1800<br><b>(WOMEN 402, 23%)</b><br>MEN 1398        | 12 months        | Percutaneous coronary intervention (PCI) involving drug-eluting stents vs. coronary-artery bypass grafting (CABG)   | Major adverse cardiac and cerebrovascular events (i.e. death from any cause, stroke, myocardial infarction, or repeat revascularization) throughout the 12-month period after randomization | TOTAL<br>159 (17.8) PCI<br>vs<br>105 (12.4)<br>CABG   | RR = 1.44<br>[95% CI:<br>1.15 -1. 81 ]<br>P = 0.002   | <b>Results by gender not reported</b>                  |
| TIMACS (Mehta et al <sup>107</sup> )   | MAY 2009    | Patients with acute coronary syndromes undergoing either routine early intervention (coronary angiography ≤24 hours after randomization) or delayed intervention (coronary angiography ≥36 hours after randomization). (International with significant European component) | 65.0 Early Intervention,<br>65.7 Delayed Intervention | TOTAL: 3031<br><b>(WOMEN: 1051, 34.6%)</b><br>(MEN: 1980) | 6 Months         | Routine early intervention (coronary angiography ≤24 hours after randomization) versus delayed intervention (coronary angiography ≥36 hours after randomization). | Composite of death, myocardial infarction, or stroke at 6 months  | Early-intervention: 9.6%;<br>delayed intervention group: 11.3%<br><br><b>WOMEN:<br/>Early 9.6%<br/>Delayed 12.3%</b><br><br>MEN:<br>Early 9.6%<br>Delayed 10.7% | HR = 0.85<br>[95% CI:<br>0.68 - 1.06]<br>P = 0.15<br><br><b>WOMEN<br/>HR = 0.77<br/>[95% CI:<br/>0.53–1.12]</b><br><br>MEN<br>HR = 0.89<br>[95% CI:<br>0.68–1.18]<br>P for Interaction=<br>0.53 | <b>No benefit of early intervention in both gender</b> |

ISCHAEMIC HEART DISEASE

**META-ANALYSIS**

| TRIAL   | YEAR     | POPULATION   | AGE  | N° OF SUBJECTS  | FOLLOW UP     | TREATMENT  | DESCRIPTION OF END-POINT  | PRIMARY END-POINT   | PRIMARY END-POINT HR  | NOTES                                 |
|---|----------|--|--|---|---------------|--|---|---|---|---------------------------------------|
|   |          | (Country)  | mean ± sd, range   | TOTAL (WOMEN n,%)   | DURATION      |  |   | TOTAL (WOMEN n,%) (MEN n,%)   | (CI) P (WOMEN (MEN )  |                                       |
| Analysis of 9 trials on Bare--Metal stents (BMS), Sirolimus-eluting stents (SES) or Paclitaxel-eluting stents (PES) (Stone et al <sup>108</sup> ) | MAR 2007 | Patients with a single previously untreated native coronary-artery lesion<br><br>(International with significant European component) | SES 61.9±11.1<br><br>BMS 61.9±10.7<br><br>PES 62.4±10.8<br><br>BMS 62.2±10.6 | Pt from 4 Trials<br>TOTAL: 1748<br><b>(WOMEN:497, 28.4%)</b><br>(MEN: 1251)<br><br>Pt from 5 Trials<br>TOTAL: 3513<br><b>(WOMEN: 964, 27.4%)</b><br>(MEN: 2549) | Up to 5 years | Pt from 4 Trials Sirolimus-eluting stents (SES) or Bare--Metal stents (BMS)<br><br>Pt from 5 Trials Paclitaxel-eluting stents (PES) or bare-metal stents (BMS) | 4-year rates of stent thrombosis, 4-year rates of target-lesion revascularization | 4-year rates of stent thrombosis:<br>BMS group 0.6% versus SES group 1.2%<br><br>BMS group 0.9% versus PES group 1.3%<br><br>4-year rates of target-lesion revascularization<br>BMS 23.6%<br>SES 7.8%<br><br>BMS 20.0%<br>PES 10.1% | HR = 2.00<br>[95% CI: 0.68 -5.85]<br>P = 0.20<br><br>HR = 1.44<br>[95% CI: 0.73-2.84]<br>P = 0.30<br><br>HR = 0.29<br>[95%CI: 0.22-0.39]<br>P<0.001<br><br>HR = 0.46<br>[95%CI: 0.38-0.55]<br>P<0.001 | <b>Results by gender not reported</b> |

**ISCHAEMIC HEART DISEASE**

| TRIAL  | YEAR      | POPULATION   | AGE  | N° OF SUBJECTS   | FOLLOW UP | TREATMENT   | DESCRIPTION OF END-POINT                            | PRIMARY END-POINT   | PRIMARY END-POINT HR  | NOTES   |
|--|-----------|--|--|--|-----------|---|---|---|---|---|
| SES versus BMS Analysis from 4 randomized trials (Solinas et al <sup>137</sup> )   | NOV 2007  | Patients undergoing percutaneous coronary intervention using sirolimus-eluting stents<br><br>(International with significant European component) | SES<br><b>WOMEN 65.7 ± 10.9</b><br>MEN 60.3 ± 10.9<br>BMS<br><b>WOMEN 65.42 ± 10.53</b><br>MEN 60.52 ± 10.41 | TOTAL: 1748<br><b>(WOMEN: 497, 28.4%)</b><br>(MEN: 1251)   | 12 months | Sirolimus-eluting stents (SES) versus bare-metal stents (BMS) | MACE<br>Binary restenosis at angiographic follow-up | In-segment binary restenosis rate<br><b>WOMEN SES 6.3% vs. BMS 43.8%</b><br>MEN SES 6.4% vs. BMS 35.6%<br><br>1-year MACE<br><b>WOMEN SES 20 (8.1%) BMS 55 (22.3%)</b><br>MEN SES 48 (7.7%) BMS 143 (23.1%) | P<0.0001<br><br>P<0.0001<br><br>P<0.0001<br><br>P<0.0001  | <b>Clinical outcomes were similar in both gender</b>  |
| Early Invasive vs. Conservative Treatment Strategies in Women and Men With Unstable Angina and Non-ST-Segment Elevation Myocardial Infarction (O'Donoghue et al <sup>130</sup> ) | JULY 2008 | Meta-analysis of 8 randomized trials to compare the effects of an invasive vs conservative strategy in women and men with NSTEMI ACS             | weighted mean age:<br><br><b>WOMEN 64.1 years</b><br>MEN 61.3 years  | TOTAL: 10412<br><b>(WOMEN: 3075, 30.3%)</b><br>(MEN: 7075) | 12 months |   | Death, nonfatal MI, or rehospitalization with ACS   | OVERALL: CONSERVATIVE 1313/5067 (25.9%)<br>vs. INVASIVE 1075/5083 (21.1%)<br><br><b>WOMEN: 709/3075 (23%) CONSERVATIVE 385/1537 (25.0%)</b><br>vs. INVASIVE 324/1538 (21.1%)                                | OR <sub>OVERALL</sub> = 0.78 [95% CI: 0.61-0.98]<br><br><b>OR<sub>WOMEN</sub> = 0.81 [95% CI: 0.65 -1.01]</b> | <b>No gender significant interaction, overall.</b><br><br><b>In women the benefit of invasive strategy is significant only in those at high risk, with positive biomarkers.</b> |

**ISCHAEMIC HEART DISEASE**

| <b>TRIAL</b>  | <b>YEAR</b> | <b>POPULATION</b> | <b>AGE</b> | <b>N° OF SUBJECTS</b> | <b>FOLLOW UP</b> | <b>TREATMENT</b> | <b>DESCRIPTION OF END-POINT</b> | <b>PRIMARY END-POINT</b>  | <b>PRIMARY END-POINT HR</b>   | <b>NOTES</b> |
|---|-------------|-------------------|------------|-----------------------|------------------|------------------|---------------------------------|---|---|--------------|
| Early Invasive vs. Conservative treatment strategies in women and men with unstable angina and non-ST-segment elevation myocardial infarction |             |                   |            |                       |                  |                  |                                 | <p>MEN:<br/>1679/7075 (24%)<br/>CONSERVATIVE<br/>928/3530<br/>(26.3%)<br/>vs.<br/>INVASIVE<br/>751/3545<br/>(21.2%)</p> <p><i>BIOMARKER STATUS:</i><br/>OVERALL<br/>Biomarker Positive (high risk)<br/>CONSERVATIVE<br/>538/1903<br/>INVASIVE<br/>378/1942</p> <p>Biomarker Negative (low risk)<br/>CONSERVATIVE<br/>463/1911<br/>INVASIVE<br/>381/1869</p> <p><b>WOMEN:</b><br/>Biomarker Positive<br/>CONSERVATIVE<br/>156/550<br/>INVASIVE<br/>118/550</p> | <p>OR<sub>MEN</sub> = 0.73<br/>[95% CI:<br/>0.55-0.98]</p> <p><b>P<sub>INTERACTION</sub> = 0.26</b></p> <p>OR<sub>OVERALL</sub> = 0.59<br/>[95% CI:<br/>0.51-0.69]</p> <p>OR<sub>OVERALL</sub> = 0.79<br/>[95% CI:<br/>0.58-1.06]</p> <p><b>OR<sub>WOMEN</sub> = 0.67</b><br/>[95% CI:<br/>0.50-0.88]</p> |              |



**ISCHAEMIC HEART DISEASE**

| <b>TRIAL</b>  | <b>YEAR</b> | <b>POPULATION</b> | <b>AGE</b> | <b>N° OF SUBJECTS</b> | <b>FOLLOW UP</b> | <b>TREATMENT</b> | <b>DESCRIPTION OF END-POINT</b>   | <b>PRIMARY END-POINT</b>   | <b>PRIMARY END-POINT HR</b>                                | <b>NOTES</b> |
|---|-------------|-------------------|------------|-----------------------|------------------|------------------|---|--|--|--------------|
| Early Invasive vs. Conservative Treatment Strategies in Women and Men With Unstable Angina and Non-ST-Segment Elevation Myocardial Infarction |             |                   |            |                       |                  |                  |   | Biomarker Negative<br><b>CONSERVATIVE</b><br>163/743<br><b>INVASIVE</b><br>152/743 | <b>OR<sub>WOMEN</sub> = 0.94</b><br>[95% CI:<br>0.61-1.44] |              |
|   |             |                   |            |                       |                  |                  | MEN<br>Biomarker Positive<br><b>CONSERVATIVE</b><br>382/1353<br><b>INVASIVE</b><br>260/1392 | OR <sub>MEN</sub> = 0.56<br>[95% CI:<br>0.46-0.67]                                 |  |              |
|   |             |                   |            |                       |                  |                  | Biomarker Negative<br><b>CONSERVATIVE</b><br>300/1168<br><b>INVASIVE</b><br>229/1126        | OR <sub>MEN</sub> = 0.72<br>[95% CI:<br>0.51-1.01]                                 |  |              |

**ISCHAEMIC HEART DISEASE**

| <b>TRIAL</b>  | <b>YEAR</b> | <b>POPULATION</b>   | <b>AGE</b>   | <b>N° OF SUBJECTS</b> | <b>FOLLOW UP</b> | <b>TREATMENT</b>               | <b>DESCRIPTION OF END-POINT</b>  | <b>PRIMARY END-POINT</b>   | <b>PRIMARY END-POINT HR</b>  | <b>NOTES</b>  |
|---|-------------|---|--------------|-----------------------|------------------|--------------------------------|--|--|--|---|
| β blockers meta-analysis of 33 randomised controlled trials (Bangalore et al <sup>109</sup> ) | DEC 2008    | Patients having non-cardiac surgery (International with significant European component) | 32.9 to 74.5 | TOTAL: 12306          | 30 days          | β-blocker versus control group | 30-day all-cause mortality, cardiovascular mortality, non-fatal myocardial infarction, non-fatal stroke, heart failure, and myocardial ischaemia | Non-fatal myocardial infarction: control group 268/5775<br>β-blocker 179/6040<br><br>Myocardial ischaemia: control group 137/1384<br>β-blocker 74/1479<br><br>Non-fatal stroke: control group 17/5523<br>β-blocker 38/5710 | OR = 0.65<br>[95% CI: 0.54–0.79]<br>(number needed to treat [NNT] 63)<br><br>OR = 0.36<br>[95% CI: 0.26–0.50] (NNT 16)<br><br>OR = 2.16<br>[95% CI : 1.27–3.68]<br>(number needed to harm [NNH] 293) | <b>Percentage of women enrolled not reported</b><br><br><b>Results by gender not reported</b> |

**ISCHAEMIC HEART DISEASE**

| <b>TRIAL</b>  | <b>YEAR</b> | <b>POPULATION</b>  | <b>AGE</b>        | <b>N° OF SUBJECTS</b>   | <b>FOLLOW UP</b>   | <b>TREATMENT</b>                                   | <b>DESCRIPTION OF END-POINT</b>  | <b>PRIMARY END-POINT</b>   | <b>PRIMARY END-POINT HR</b>  | <b>NOTES</b>                          |
|---|-------------|--|-------------------|---|--|--|--|--|--|---------------------------------------|
| Drug-Eluting Stents in Acute Myocardial Infarction (Brar et al <sup>110</sup> ) | MAY 2009    | Patients with ST-segment elevation myocardial infarction (STEMI) Meta-Analysis of 13 randomized trials and 18 registries | Mean age 62 years | TRIALS:<br>Total: 7352<br><br>REGISTRIES:<br>Total: 26521<br><br><b>WOMEN 23%</b> | TRIALS:<br>Mean follow-up, 6-24 months<br>REGISTRIES:<br>6-36 months | Drug Eluting Stent (DES) or Bare Metal Stent (BMS) | Death, myocardial infarction (MI), target vessel revascularization (TVR), and stent thrombosis | TRIALS:<br>TVR<br>DES 241/4515<br>BMS 326/2837<br><br>Death<br>DES 167/4515<br>BMS 121/2837<br><br>MI<br>DES 153/4515<br>BMS 121/2837<br><br>Stent thrombosis<br>DES 128/4825<br>BMS 82/3147 | TRIALS:<br>RR = 0.44;<br>[95%CI:<br>0.35 - 0.55]<br><br>RR = 0.89<br>[95%CI:<br>0.70 - 1.14]<br><br>RR = 0.82<br>[95%CI:<br>0.64 - 1.05]<br><br>RR = 0.97<br>[95% CI:<br>0.73-1.28]<br><br>REGISTRIES – 1 year:<br><i>TVR</i><br>RR = 0.54<br>[95%CI:<br>0.40 - 0.74]<br>P<0.01<br><i>MI</i><br>RR = 0.87<br>[95% CI:<br>0.62 - 1.23]<br>P=0.44<br><br><i>Death</i><br>RR = 0.68<br>[95% CI:<br>0.54 - 0.86]<br>P<0.01<br><br><i>Death -2 years</i><br>RR = 0.89<br>[95% CI:<br>0.64 - 1.22]<br>P=0.45 | <b>Results by gender not reported</b> |