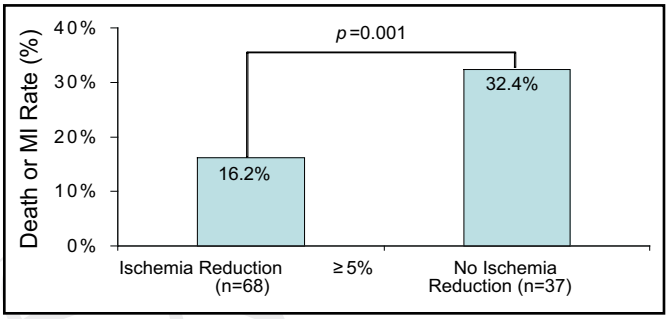
In addition, in an attempt to correlate the extent of myocardial ischemia to clinical outcomes, Dr. Shaw showed that the risk of death or MI was lower among patients who had a reduction in ischemia of at least 5% (13.4% vs 24.7%; p=0.037), particularly among patients with moderate-to-severe ischemia before treatment (16.2% vs 32.4%; p=0.001; Figure 2). The rates of death and MI ranged from 0-39% according to the amount of residual ischemia after PCI.

Figure 2. Risk of Death or MI Among Patients with Moderate-to-Severe Ischemia.



Dr. Shaw emphasized that although the findings suggest that MPS may be valuable for identifying patients at risk for death or MI, the prognostic findings in this substudy were exploratory with limited statistical power. Still, she said, "These findings suggest the potential value of MPS in identifying at-risk patients for targeting therapy and in guiding treatment strategies, particularly for patients with moderate-to-severe pre-treatment ischemia who may benefit with PCI as well as consideration of crossover to PCI for those patients with extensive residual ischemia following a course of medical management."

Duration of Eptifibatide Infusion after Uncomplicated PCI

This trial explored whether the infusion of eptifibatide after uncomplicated percutaneous intervention (PCI) with stenting could be safely shortened to <2 hours without increasing the risk of ischemic events and with the potential benefit of lowering the risk of major bleeding.

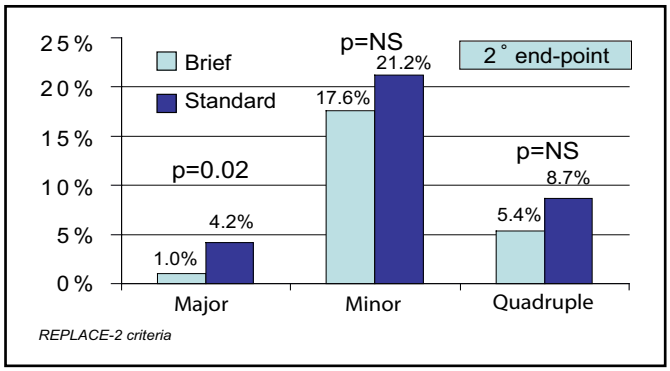
"This change in treatment [duration] reduces drug costs up to 37% of the standard regimen and significantly reduces the length of stay and associated costs," said Anthony Fung, MD, Vancouver General Hospital, Canada, who reported the findings of the Brief Infusion of Eptifibatide Following PCI (BRIEF-PCI) trial.

The BRIEF-PCI trial was designed to compare the standard 18-hour infusion of eptifibatide with a short infusion (<2 hours) after non-emergent PCI. Dr. Fung noted that contemporary PCI involves the use of dual oral antiplatelet therapy, including a loading dose of clopidogrel, and the routine use of coronary stents. The investigators' hypothesis, he said, was that this change in approach to PCI may obviate the need for prolonged infusion of eptifibatide.

The patients in the trial had stable angina, acute coronary syndromes, or recent (within <48 hours) ST-elevation myocardial infarction (STEMI). All patients received intravenous eptifibatide during PCI, and approximately two-thirds of the patients were treated with a loading dose of clopidogrel. After successful PCI, patients were randomly assigned to receive either standard eptifibatide (312 patients) or the short infusion (312 patients). The primary endpoint was ischemic myocardial injury within 24 hours after PCI, as determined by elevated levels of troponin-I and creatinine kinase MB at 6 and 18 hours compared with baseline. The trial was designed as a noninferiority study, with a reference event rate of the primary endpoint of 50% and an upper margin set at 10%. The study was powered at 80%, with a one-sided alpha of 0.05.

Dr. Fung reported that ischemic myocardial injury occurred in 30.1% of the patients who received the short infusion and in 28.3% of those who received the standard infusion (noninferiority margin, 1.8% [95% CI, 7.8%]; p<0.012 for noninferiority). There was also no difference between the two groups in the rate of the individual secondary endpoints of death, nonfatal MI, urgent target vessel revascularization, or a composite of these events. The incidence of minor bleeding did not differ between the two groups (17.6% vs 21.2%), but major bleeding occurred less frequently among patients who received the short infusion (1.0% vs 4.2%; p=0.02; Figure 1).

Figure 1. Bleeding and Quadruple Endpoints.



"Many institutions have shortened the infusion of eptifibatide already," noted Dr. Fung. "The findings of our trial confirm that this change is safe and has the benefit of lower rates of major bleeding." Because the overall sample size was relatively modest (624 patients) and the trial was designed as a non-inferiority comparison with a 10% absolute difference boundary, larger confirmatory trials are needed to validate these results.

Comparison of Eptifibatide and Abciximab as Adjunct to Primary PCI

The EVA-AMI trial compared two intravenous glycoprotein IIb/IIIa inhibitors (GPI), eptifibatide and abciximab, as adjuncts to primary percutaneous coronary intervention (PCI) with respect to several measures of myocardial perfusion. The study represents the first head-to-head comparison of two GPIs in primary PCI for ST-elevation myocardial infarction (STEMI).

EVA-AMI involved 430 STEMI patients with fewer than 12 hours of symptoms and who were scheduled for primary PCI. The patients were randomly assigned to either eptifibatide (double bolus followed by 24-hour infusion; 226 patients) or abciximab (bolus followed by 12-hour infusion; 201 patients). All patients received aspirin, clopidogrel, and unfractionated heparin or enoxaparin.

The primary endpoint was ST resolution at 1 hour after PCI. ST resolution is a marker of myocardial perfusion and has been closely linked to short- and long-term mortality after STEMI, thus making it an ideal surrogate endpoint for comparing adjunctive therapies in reperfusion. Electrocardiograms were performed at baseline and 1 hour after PCI; ST resolution of more than 70% was considered to be complete, and resolution between 30% and 70% was considered to be partial.

Myocardial perfusion, as assessed by TIMI flow grade after PCI, did not differ significantly between eptifibatide and abciximab (82.4% vs 84.3%). Electrocardiographic data after PCI were available for 220 patients. The rates of complete ST resolution between the two groups were similar (63.1% for the eptifibatide group and 59.6% for the abciximab group) and met the criteria for noninferiority (Table 1). However, significantly more patients in the abciximab group had no ST resolution (14.7% vs 5.4%; p=0.021). With regard to in-hospital clinical events, the two GPIs did not differ significantly with respect to rates of death, myocardial infarction, heart failure, target vessel revascularization, or minor or major bleeding (Table 1).

Table 1. Comparison of Eptifibatide and Abciximab in the EVA-AMI Trial.

	Eptifibatide	Abciximab
TIMI grade 3 flow	82.4%	84.3%
ST resolution		
>70%	63.1%	59.6%
≥30%	31.5%	25.7%
None	5.4%*	14.7%*
Death	3.5%	3.5%
Myocardial infarction	1.5%	0
Heart failure	6.4%	8.5%
Target vessel revascularization	2.7%	4%
Major bleeding	1.8%	0
Minor bleeding	4.1%	4.5%

*p=0.021; all of the other comparisons were not statistically significant.

Uwe Zeymer, MD, Herzzentrum Ludwigshafen, Germany, who reported the findings of the study, noted that processing of the study data has not been completed. The study's clinical events committee has not yet evaluated the clinical events and serious adverse events, and collection of 6-month follow-up data is still ongoing.

"Because eptifibatide is less expensive than abciximab, it may be a valid alternative to abciximab for patients with STEMI undergoing primary PCI," said Dr. Zeymer.

Quality of Life and Cost-Effectiveness Associated with the Late Opening of a Total Occluded Artery

Quality-of-life and cost-effectiveness analyses of data from patients in the Occluded Artery Trial (OAT) have shown that a strategy of routine percutaneous coronary intervention (PCI) has modest symptom benefits that diminish over time. The strategy is also more expensive than optimal medical therapy alone.

In OAT, high-risk asymptomatic patients with a total occluded coronary artery 3-28 days after myocardial infarction (MI) were randomly assigned to either PCI or medical therapy alone and followed for up to 4