No Benefit Shown for Facilitated PCI

Primary percutaneous coronary intervention (PCI) performed within 90 minutes of first medical contact is often difficult to achieve, especially when inter-hospital transfer is necessary. In light of this, investigators have evaluated the benefit of facilitated PCI, or PCI performed early after the administration of a fibrinolytic agent or GPIIb/IIIa inhibitor or a combination of these agents. The FINESSE (Facilitated Intervention with Enhanced Reperfusion Speed to Stop Events) study was designed to compare the outcomes of standard primary PCI with two different facilitated PCI strategies.

In the FINESSE trial, 2,452 patients with acute ST-elevation myocardial infarction (STEMI) were randomly assigned to 1 of 3 primary PCI strategies: facilitated PCI with reduced-dose reteplase and abciximab (reteplase/abciximab-facilitated PCI); facilitated PCI with upstream abciximab alone (abciximab-facilitated PCI); and abciximab administered in the catheterization laboratory just prior to PCI (in-lab axciximab). The primary endpoint was a composite of death (all-cause mortality), rehospitalization for heart failure, resuscitated ventricular fibrillation (within 48 hours after randomization), and cardiogenic shock at 90 days. The study was stopped prematurely (at 82% of its planned size) because of difficulty with enrollment and was therefore underpowered.

Stephen Ellis, MD, Cleveland Clinic, Ohio, reported that there were no significant differences among the three arms with respect to the primary endpoint; reteplase/abciximab-facilitated PCI 9.8%, abciximab-facilitated PCI 10.5%, and in-lab abciximab 10.7% (p=0.55). There were also no significant differences in the individual components of this endpoint among the three groups. Reteplase/abciximab-facilitated PCI significantly increased the patency of the infarct-related artery before PCI; the rate of TIMI 2/3 blood flow was 80% for this group vs 45% in abciximab-facilitated PCI group, and 37% in the in-lab abciximab group (p<0.0001). TIMI 3 blood flow did not differ among the three groups after PCI. The prevalence of TIMI major and minor bleeding was lower in the in-lab abciximab group (6.9%) than in the abciximab-facilitated PCI group (10.1%; p=0.008) or the reteplase/abciximab-facilitated PCI group (14.5%; p<0.001).

Dr. Ellis concluded, "Primary PCI with in-lab abciximab provides a better benefit-risk profile than the facilitated strategies in patients with STEMI who can undergo PCI within 4 hours of first medical contact."

In discussing the study, Frans van de Werf, MD, University of Leuven, Belgium, addressed the reasons for the negative results of the two facilitated PCI strategies tested in the FINESSE trial. "An important explanation could be suboptimal antithrombotic co-therapy," he said, noting that upfront clopidogrel was not given and upfront enoxaparin was given to only a subset of patients.

Prof. van de Werf concluded, "FINESSE does not support a strategy of facilitated PCI. Facilitation with either full-dose lytic [based on the ASSENT-4 study] or combination therapy cannot therefore be recommended" [ASSENT-4 PCI Investigators. *Lancet* 2006]. He added that a strategy of early lytic-based pharmacologic treatment preceding PCI may be beneficial in selected populations, such as those patients who present early (2-3 hours after symptom onset), with a large amount of viable myocardium, and who also receive adequate antithrombotic co-therapy. Another subgroup of patients with STEMI in whom an early lytic-based facilitated strategy should be studied include those in whom a long delay before PCI is anticipated, with the proviso that PCI be postponed if there is evidence of successful (TIMI 3) reperfusion after pharmacologic treatment.

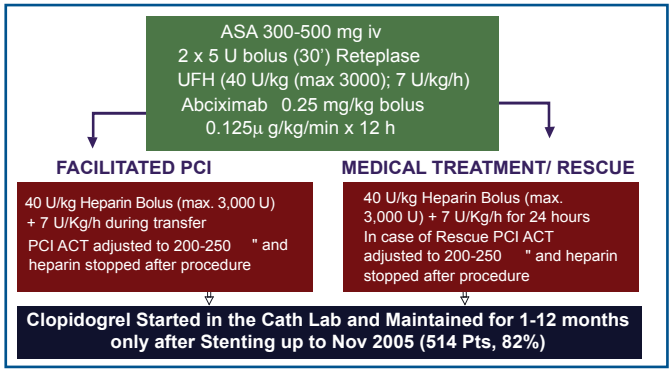
Immediate Angioplasty After Thrombolytic Therapy Can Save Lives and Reduce Recurrent Heart Attacks in AMI Patients

For patients with ST-elevation myocdardial infarction (STEMI), reperfusion with primary PCI is recommended if it can be performed within 90 minutes. However, treatment within this narrow window can not always be achieved, especially for patients who present to a hospital without a PCI facility. Fibrinolytic therapy is still the preferred treatment in this setting. The CARESS (Combined Abciximab Reteplase Stent Study in Acute Myocardial Infarction) in AMI trial was designed to compare a strategy of early transfer after fibrinolysis versus a strategy of medical treatment and transfer for PCI only if there was no evidence of reperfusion.

Carlo Di Mario, MD, Imperial College, London, UK, reported the findings of the CARESS in AMI study, which was carried out in hospitals in Italy, Poland, and France that did not have PCI facilities. Six hundred patients with

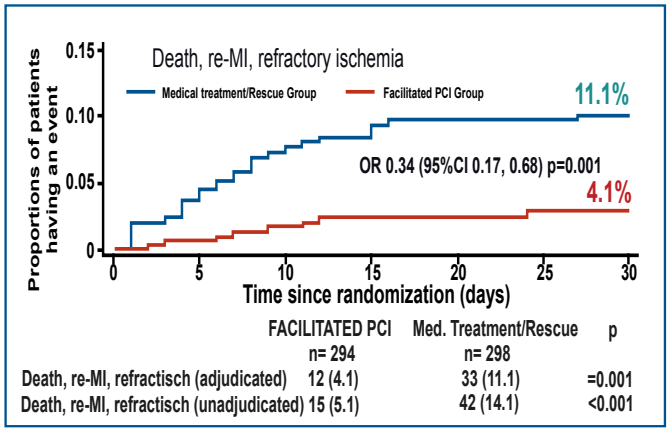
STEMI who presented less than 12 hours after symptom onset were randomly assigned to either facilitated PCI or medical treatment/rescue after fibrinolysis with half-dose reteplase and abciximab (Figure 1). The primary outcome was the composite of all-cause mortality, reinfarction, or refractory ischemia at 30 days. Of the patients in the medical treatment/rescue group, 36% were subsequently referred for PCI.

Figure 1. CARESS Treatment Summary.



Prof. Di Mario reported that facilitated PCI (with half-dose reteplase + abciximab) led to a 67% reduction in the incidence of the composite endpoint (Figure 2) compared to medical treatment with half-dose reteplase + abciximab followed by rescue PCI as needed. When the components of the primary endpoint were assessed individually, refractory ischemia was significantly less frequent in the facilitated PCI group (0.7% vs 5.0%; p<0.002). The incidences of death and reinfarction were also lower in the facilitated PCI group, but these differences did not reach statistical significance (3.1% vs 4.4%, p=0.403, and 0.3% vs 1.7%, p=0.104, respectively). Severe bleeding was rare in both groups, and Prof. Di Mario suggested that this was because the study excluded older patients and patients at high risk for bleeding.

Figure 2. Primary Outcome at 30 Days.



"In our view," concluded Prof. Di Mario, "this trial confirms and expands the indication of the current ESC guidelines to perform early angioplasty, within 24 hours after lysis, and suggests that high-risk STEMI patients should be immediately transferred for angiography after lysis."

Professor Freek Verheugt, Nijmegen University, the Netherlands, who discussed the study, noted that the results of CARESS confirmed the findings of other studies that have indicated the benefit of immediate PCI. He said that one of the remaining questions is how the results would have differed if all patients had been given clopidogrel. In addition, he noted that an important factor to determine is the optimal time interval between fibrinolysis and PCI. This interval has ranged from 2.3-17 hours in trials showing benefit of facilitated PCI.

One of the limitations of the CARESS trial was the absence of a standard strategy (eg, full-dose fibrinolytic or primary PCI without preceding fibrinolysis) as the comparator. Without such an "anchor" to serve as the gold-standard, it is possible that neither of the strategies tested in CARESS would be superior to currently recommended reperfusion strategies. Such a scenario would be consistent with the findings of the GUSTO-V (half-dose rPA + abciximab was not superior to full-dose rPA) and FINESSE (half-dose rPA + abciximab prior to PCI was less beneficial than primary PCI with abciximab in the catheterization laboratory) studies, thus emphasizing the importance of including existing standard treatments in trials that are evaluating novel therapies.

Study Supports Anti-Arrhythmic Effects of Ranolazine in Patients with Acute Coronary Syndrome

Ranolazine, an anti-ischemic agent approved for use in the treatment of chronic angina, has also been shown to have anti-arrhythmic effects in experimental models. The MERLIN-TIMI 36 trial was the first study in which the anti-arrhythmic effects of ranolazine were evaluated in humans.

MERLIN-TIMI 36 involved 6,560 patients with unstable angina/non-ST-elevation acute coronary syndrome who were randomly assigned to receive ranolazine or placebo in addition to standard therapy. The primary results of the study were recently published [Morrow DA et al.