Figure 1. Landmark Analyses – Total Cohort.
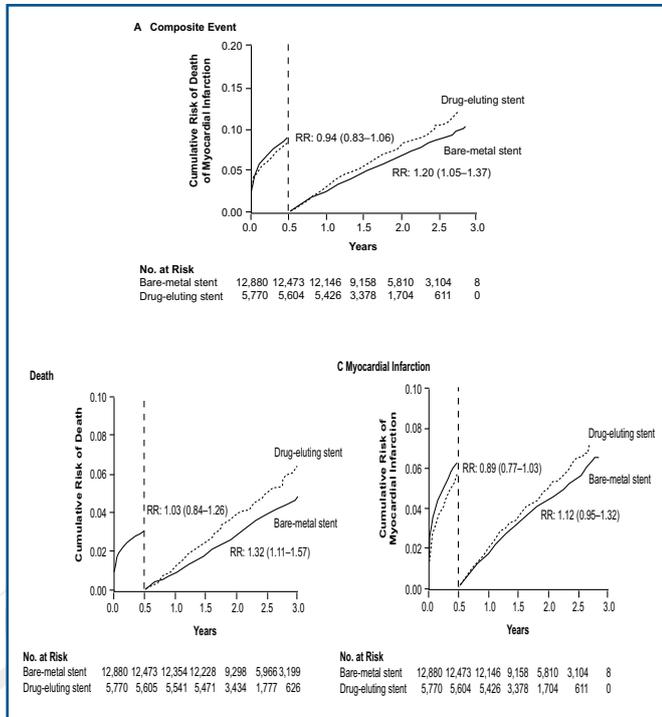
The continuous low risk of late stent thrombosis of 0.5% annually in patients treated with DES was more than offset by a 3.5% absolute reduction in the risk of restenosis with DES compared to BMS.

"The results are very positive for the 8 million patients worldwide who have received DES and are concerned by the risk of death and adverse events," said Prof. James. "But physicians should be concerned that we've not solved the problem of late stent thrombosis. They need to think carefully about patient selection." According to Prof. James, patients with larger vessels, increased risk of bleeding and compliance issues should receive BMS, while those with bifurcations, lesions longer than 8mm, narrow vessels, and those with diabetes may benefit from DES.

This study is based on observational data and there are a number of factors that may have affected the results including increased awareness of the risk of DES and prolonged antiplatelet therapy, improved techniques utilizing higher balloon pressures and more accurate stent sizing, and improved stent design. Large prospective randomized trials of DES versus BMS that include different durations of dual antiplatelet therapy are needed.

3-Year Clinical Data Continue to Show Superiority of Sirolimus-Eluting Versus Bare Metal Stents in STEMI Patients

Results of 3 years of clinical follow-up data presented by Marco Valgimigli, MD, University of Ferrara, Italy, continued to show superiority for a combination of tirofiban+sirolimus-eluting stent (SES) vs a combination of abciximab+bare-metal stent (BMS) in STEMI patients, as evidenced by significantly reduced target vessel revascularization (TVR) rates.

In the STRATEGY (Single High Dose Bolus Tirofiban and Sirolimus-Eluting Stent vs Abciximab and Bare Metal Stent in Myocardial Infarction) trial, 175 patients with STEMI were randomly assigned to receive a single high-dose bolus of tirofiban (25 μg/kg/3 min) and infusion (0.15 μg/kg/min for 18-24 hours) followed by SES implantation (n=87), or abciximab (bolus of 0.25 mg/kg/3-min with 0.125 mg/kg/min for12 hours) followed by BMS implantation (n=88).

The initial results through 8 months showed that treatment with tirofiban+SES was associated with a reduction in the primary endpoint (death, myocardial infarction (MI), stroke, or binary restenosis) vs the use of abciximab+BMS [Valgimigli M et al. *JAMA* 2005]. The 2-year study results published earlier this year [Valgimigli M et al. *J Am Coll Cardiol* 2007] showed a continued superiority of the tirofiban+ SES combination.

3-Year Results

A total of 74 (85%) patients in the tirofiban+SES and 77 (88%) in the abciximab+BMS arm were still being followed at 3 years. The primary endpoint was significantly lower in the tirofiban+SES group (p=0.008) (Figure 1).

Figure 1. Primary Endpoint at 3 Years.
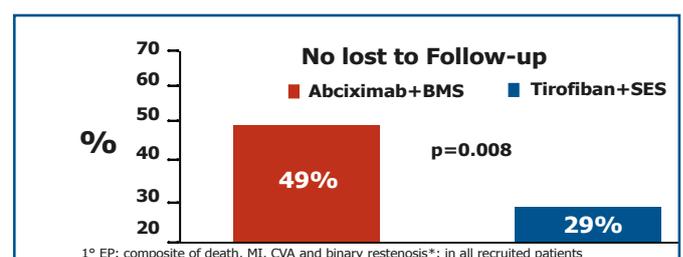
This difference was driven by an improvement in angiographic outcome leading to a significant reduction in the need for TVR in the tirofiban+SES group (p=0.01) (Figure 2).

Figure 2. TVR at 3 Years.
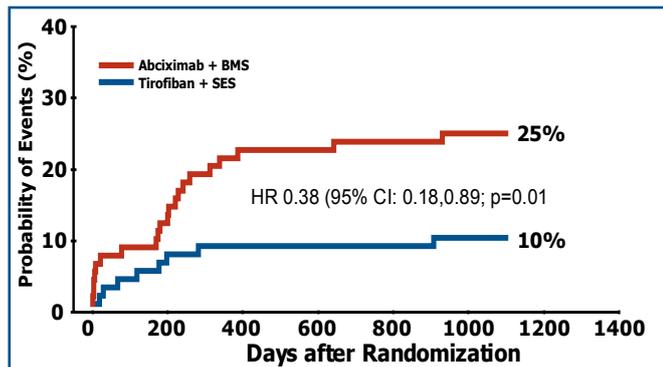
The cumulative incidence of major adverse cardiac events (death, MI or TVR) was lower in the tirofiban+SES group (28.7%) vs abciximab+BMS (40.9%) although the difference was not significant. All-cause mortality (16.0% vs 14.7%, p=0.85 and the composite of death/MI (19.5% vs 22.7%, p=0.57) were similar between the two treatment groups (tirofiban+SES and abciximab+BMS, respectively). There was no difference in the cumulative incidence of stent thrombosis (5.7% in the tirofiban+SES and 6.8% in the abciximab+BMS group, p=0.76).

"The results are reassuring given that the original results have not changed much over time," said Dr. Valgimigli. "Yet, we should not forget the number of patients in this study was very low." Further large scale trials are necessary to establish the role of this proposed strategy and to evaluate whether the observed differences in this study were related to the type of stent utilized or the selected GP IIb/IIIa antagonist. Future studies should also include data on the duration of dual antiplatelet treatment and the immediate consequences of its termination

Enoxaparin Continues to Show Clinical Benefit Vs Unfractionated Heparin for STEMI

One-year results of the ExTRACT-TIMI 25 trial presented by David A. Morrow, MD, Brigham and Women's Hospital, Boston, Massachusetts, continued to show significant benefits in favor of adjunctive treatment with enoxaparin vs unfractionated heparin in reducing the rate of death or nonfatal myocardial infarction (MI) in 20,479 patients with ST-elevation myocardial infarction (MI) (STEMI) treated with fibrinolysis.

The primary efficacy endpoint was the composite of death or nonfatal recurrent MI. The main secondary endpoint was the composite of death, nonfatal reinfarction, or recurrent myocardial ischemia leading to urgent revascularization. An additional secondary endpoint was the composite of death, nonfatal reinfarction, or nonfatal disabling stroke.

In the main study, treatment with enoxaparin for the duration of the index hospitalization was superior to the current strategy of infusing unfractionated heparin for 48 hours as adjunctive antithrombin therapy to fibrinolysis, reducing death or nonfatal MI by 17% (p<0.0001) at 30 days [Antman EM et al. *New Engl J Med* 2006].

At one year of follow-up, based on data from 99% of the original intent-to-treat population (enoxaparin n=10,153; unfractionated heparin n=10,122), treatment with enoxaparin continued to show significant reductions in death or nonfatal MI and for nonfatal MI alone compared to unfractionated heparin (Table 1). A significant benefit in favor of enoxaparin treatment was also seen for the secondary endpoint of death, MI, or disabling stroke. No statistical differences were seen for other study endpoints.

Table 1. Results at One Year.*

Endpoint	Enoxaparin (%)	Unfractionated Heparin (%)	HR	95 CI	P value
Death/MI	15.8	17.0	0.92	0.86 - 0.98	< 0.01
MI (nonfatal)	5.7	6.7	0.82	0.73 - 0.92	<0.001
Disabling Stroke	1.1	1.2	0.97	0.75 - 1.26	0.81
Death/MI/Nonfatal Disabling Stroke	16.0	17.3	0.91	0.85 - 0.98	0.007
Death	10.5	10.6	0.98	0.90 - 1.07	0.72

*Kaplan-Meier

The benefit in favor of enoxaparin was also evident when data were analyzed across major prespecified subgroups.

The one-year benefit of the enoxaparin strategy is accomplished through a reduction in the rate of nonfatal MI. Although through 30 days the rate of major bleeding was significantly higher with enoxaparin, net clinical benefit was significantly in favor of enoxaparin both early (30 days) and late (one year) after treatment (p<0.001).