for use in CABG patients. Sub-group analyses investigating the effect of diabetes, age, on- versus off-pump, radial artery versus vein grafts, and ventricular function on outcomes will also be evaluated upon completion of the study. ART is expected to be completed in 2015 at which point long-term survival, quality of life, cost-effectiveness, and other analyses will be presented.

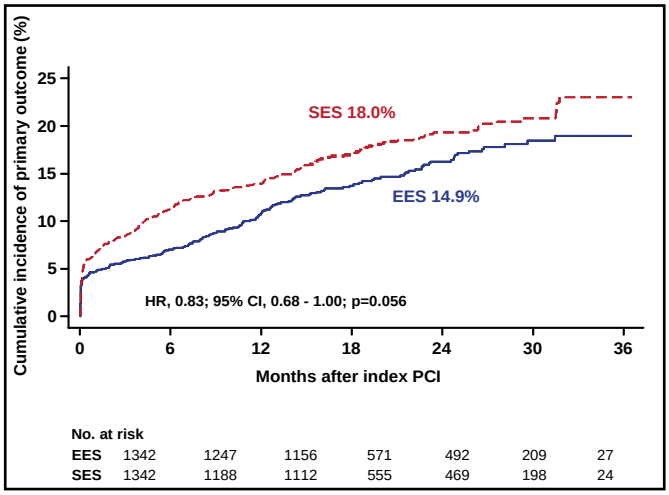
The Impact of EES Versus SES on Long-Term Clinical Outcome: Results from the LESSON-I Study

Long-term follow-up (up to 3 years) that compared everolimus-eluting (EES) and sirolimus-eluting stents (SES) for coronary revascularization revealed that the unrestricted use of EES was associated with lower risk of myocardial infarction (MI), target vessel revascularization (TVR), and stent thrombosis. The Long-term comparison of Everolimus-eluting and Sirolimus-eluting Stents for cOronary revascularizatioN (LESSON-I) data were presented by Stephan Windecker, MD, Bern University Hospital, Bern, Switzerland.

LESSON-I was a nonrandomized, observational study that included 3133 patients with stable angina and acute coronary syndromes who were undergoing percutaneous coronary intervention (PCI) at Bern University Hospital. After propensity score-matching, 2684 patients were included in the analysis (1342 matched pairs), with a median clinical follow-up of 1.3 years. Patients who were undergoing SES implantation prior to April 2003 and those who were previously included in the SIRTAX trial were excluded from this study. The primary endpoint was the patient-oriented composite of death, MI, and TVR through 3 years. The secondary endpoints included death, MI, TVR, TLR, cardiac death or MI, and stent thrombosis, according to the Academic Research Consortium (ARC). Patients who were treated with EES were more complex as compared with patients who were treated with SES. Multivessel treatment was performed in 24% of patients in the EES group (average number of stents was 2.0±1.1) and 16% of patients in the SES group (average number of stents was 1.8±0.9).

At 3 years, the rate of death, MI, or TVR was lower in the EES group than in the SES group (HR, 0.83; 95% CI, 0.68 to 1.00; p=0.056), while the rate of all-cause mortality was similar for both groups (Figure 1). The rates of MI and TVR at 3 years were significantly reduced in EES subjects as compared with SES recipients (3.3% vs 5.0% for MI; p=0.017 and 7.0% vs 9.6% for TVR; p=0.039 respectively). The incidence of definite stent thrombosis up to 3 years was lower in the EES group as well (0.5% vs 1.6% for SES; HR, 0.30; 95% CI, 0.12 to 0.75; p=0.01), and of note, not a single very late stent thrombosis occurred in the EES group. Prof. Windecker concluded that the differences in MI rates were driven by a 70% lower risk of QWMI and were present early but continued to increase during longer-term follow-up. The lower risk of MI in favor of EES was explained at least in part by the lower risk of definite stent thrombosis.

Figure 1. Primary Endpoint.



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The concept that EES was associated with lower rates of MI, partially owing to lower stent thrombosis risk, is interesting and may have clinical implications with regard to the duration of dual antiplatelet therapy. EES appears to be a safe and effective method for coronary revascularization in an all-comers population and may provide more favorable outcomes, particularly related to very late stent thrombosis, compared with SES. However, further investigation in the setting of a large-scale randomized clinical trial is needed in order to confirm these findings.

ATOLL Study Shows Intravenous Enoxaparin is Associated with Better Ischemic Outcomes in Primary PCI for STEMI than UHF

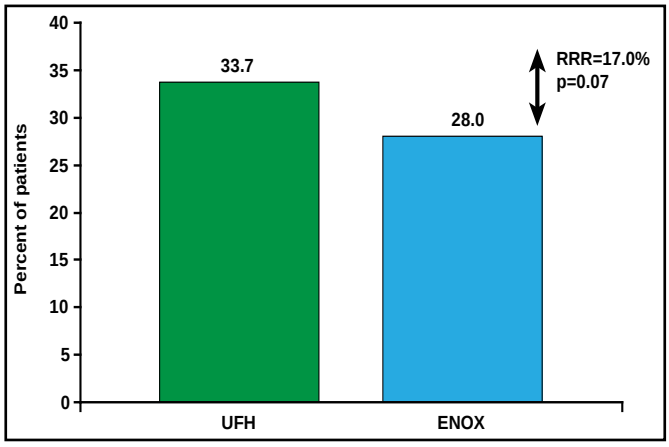
Although the study failed to meet its primary endpoint, results from the ATOLL study, presented by Gilles Montalescot, MD, Pitié-Salpétrière Hospital, Paris, France, indicate that the low-molecular-weight heparin enoxaparin may provide better clinical outcomes than unfractionated heparin (UFH) in ST-elevation myocardial infarction (STEMI) patients who are undergoing primary percutaneous coronary intervention (PCI).

The Acute STEMI Treated with primary PCI and intravenous enoxaparin Or UFH to Lower ischemic and bleeding events at short- and Long-term follow-up study (ATOLL; NCT00718471) was an investigator-driven study that was designed to compare intravenous (IV) enoxaparin and IV UFH in patients who were undergoing primary PCI for STEMI. The study population comprised patients aged ≥18 years who presented within 12 hours of symptom onset. A total of 910 patients from 43 sites were randomly assigned to receive IV enoxaparin (n=450; 0.5 mg/kg; same dose with or without GPIIb/IIIa inhibitors) or IV-UFH (n=460; 50-70 IU/kg with GPIIb/IIIa inhibitors; 70-100 IU without GPIIb/IIIa inhibitors) before coronary angiography. All subjects received aspirin (160-500 mg/day according to local practice) and clopidogrel (300-900 mg as loading dose according to local practice). Approximately 18% of subjects were aged over 75 years.

The primary study endpoint was the composite of all-cause mortality at 30 days, complications of MI at 30 days (eg, resuscitated cardiac arrest, recurrent myocardial infarction/acute coronary syndrome (MI/ACS), urgent revascularization), procedure failure (eg, definite stent thrombosis), and non-CABG major bleeding during hospitalization. The main safety endpoint was major bleeding during hospitalization (STEEPLE definitions). The main secondary endpoint was the composite of all-cause mortality, recurrent MI/ACS, or urgent revascularization at 30 days.

At 30 days, the primary endpoint of death, MI, procedural failure, or noncoronary artery bypass grafting major bleeding was reduced but did not reach statistical significance—28% of subjects received enoxaparin and 33.7% received UFH (relative risk reduction 17%; 95% CI, 0.68 to 1.01; p=0.07; Figure 1).

Figure 1. Primary Endpoint.



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For the main secondary endpoint, there was a significant (p=0.01) 41% reduction with enoxaparin (11.3% for UFH vs 6.7% for enoxaparin). All results for the other secondary endpoints favored enoxaparin IV (Table 1).

Table 1: Other Secondary Endpoints.

Endpoint	Enoxaparin	UFH	p value
Death or complications of MI	7.8%	12.4%	p=0.02
Death, reinfarction, urgent revascularization	5.1%	8.5%	p=0.04
All-cause death	3.8%	6.3%	p=0.08
Death or resuscitated cardiac arrest	4.0%	7.0%	p=0.05
Death, complication of MI or major bleeding	10.2%	15%	p=0.03

The main safety endpoint occurred in 4.9% of patients who were on enoxaparin and 4.5% of patients who were on UFH (nonsignificant).

Commenting on the ATOLL study results, Harvey White, MD, Auckland City Hospital, Auckland, New Zealand, noted, "The ATOLL trial investigators have shown that enoxaparin is safe for patients undergoing primary PCI and likely has a clinically relevant effect in reducing ischemic complications compared with unfractionated heparin. They have moved us closer to the goal of further improving the outcomes of patients suffering an ST-elevation myocardial infarction."

ISAR-REACT 3A: Low-Dose UFH Better for Elective PCI

Unfractionated heparin (UFH), at a dose of 100 U/kg, is preferable to standard higher-dose treatment in patients who are undergoing elective percutaneous coronary intervention (PCI), according to new findings from the Intracoronary Stenting and Antithrombotic Regimen-Rapid Early Action for Coronary Treatment 3A (ISAR-REACT 3A; NCT00735280) trial.

Although 140 U/kg has been the standard dose for UFH in interventional cardiology for decades, physicians have started to use lower doses of UFH to decrease the risk of bleeding, said Stefanie Schulz, MD, Deutsches Herzzentrum, Munich, Germany. Dr. Schulz presented results of the ISAR-REACT 3A trial, which confirmed the benefits of lower-dose UFH in patients who are undergoing elective PCI.

In the ISAR-REACT 3A trial, 2505 biomarker-negative patients who were undergoing elective PCI were treated with a bolus dose of UFH 100 U/kg without activated clotting time (ACT) monitoring. This treatment group