

**Table 1**  
**Summary of Various Clinical Trials**  
**(Study Comparison)**

Name of Study	Study Design	# of Subjects	Inclusion Criteria	Exclusion Criteria	Findings	Critique
The National Registry of MI (NRMI 3)	Voluntary, nationwide, uniform, prospective collection of data on the treatment of pts with Acute MI	37,320	Acute MI defined as hx and presentation suggestive of AMI, accompanied by either total creatine kinase, creatine kinase-MB or troponin levels > twice the upper limit of normal for the hospital's lab, or ECG evidence of AMI	Pts transferred to a participating registry hospital from any other hospital. Pts transferred out of a registry hospital.	No significant difference of the in-hospital rate of major bleeding, recurrent MI or in-hospital death between the LMWH and UFH patients. Major bleeding rates: LMWH arm – 4% UFH arm- 4.2%, OR 0.99, 95% CI 0.80 to 1.23. P=0.92 Dec. risk of recurrent AMI: LMWH arm – 1.5% UFH arm – 1.9%, OR of 0.74, 95% CI 0.53 to 1.05.	The registry collected only in-hospital data, and did not provide follow-up after hospital discharge. The study did not care about the treatment strategy and outcome of the participants, and so dosages of drugs used could have been different.
The National Investigators Collaborating on Enoxaparin-3 (NICE-3)	Prospective, open-label, nonrandomized observational study of subjects to receive active drug	671	Hx of unprovoked chest pain lasting at least 20mins within the previous 24hrs. CAD, documented by ECG changes, elevation in cardiac biomarkers, or hx of MI, PCI, or coronary angiogram, showing >50% luminal narrowing	Cardiogenic shock, acute or evolving ST-segment elevation MI, Angina precipitated by HF, severe valvular disease, hypertrophic cardiomyopathy, CABG within 2 mths or PCI within 7 days of enrollment and CrCL <30	Non-CABG major bleeding was 1.9%, (90% CI 1%-2.8%, 95% CI 0.8%-3%) and was not significantly higher than the pre-specified historical control rate of 2.0% Cumulative triple composite endpoint of death/MI/revascularization: Inhospital – 7% 30 days – 11.6%	Each institution had a choice of 1 of the 3 available GP ant., making the outcome not uniformed. Too small a sample size. The open-label design of the study, and the institutional use of protocols for CK monitoring
The ACUTE II Study	Prospective, randomized, 2-to-3 double-blind, study of subjects to receive active drug	525	Prolonged (>20mins) or episodes of angina at rest within previous 24hrs, evidenced by ECG of MI, or abnormal cardiac markers.	STEMI within 48hrs, CI to anticoagulants, hx of thrombocytopenia, allergy or intolerance to ASA, UFH, or Tirofiban, need for immediate invasive therapy, SCr >2, CrCl<30, or platelet count<150000/mm3	Incidence of total TIMI bleeding events: Tirofiban/UFH - 4.8% Tirofiban/Lovenox – 3.5% with OR of 1.4, CI 0.6-3.4 Transfusion: Tirifiban/UFH – 4.3% Tirofiban/Lovenox – 2.5% Refractory ischemia: UFH arm – 4.3% Lovenox arm – 0.6% Rehospitalizatio: UFH arm – 7.1% Lovenox arm – 1.6%	
The Platelet IIb/IIIa Antagonist for the Reduction of Acute Coronary Syndrome	Double-blind study, where the patients were randomized, but heparin type not	5225	Pts with ACS without ST-segment elevation, chest pain>20mins duration with onset within 12hrs,	N/A	Incidence of death/MI/SRI(30d UFH arm - 12.2%. LMWHarm -10.2%. Death/MI (30d): UFH arm – 10.9%	Pts in the LMWH group were older and sicker than in the UFH arm. The use of LMWH was not

Events in a Global Organization Network B (PARAGON B) Trial	randomized.		And either ECG evidence of ischemia, or a positive cardiac marker.		LMWH arm – 9%	randomized. Physician decision to start pt on LMWH depending on status of the patient
The Aggrastat to Zocor Trial (A-to-Z) Trial	Open-label, randomized, noninferiority study comparing enoxaparin with UFH in pts who received Tirofiban and Aspirin	3987	Non-ST segment elevation ACS presenting within 24hrs, after on set of ischemic symptoms at rest, lasting at least 10mins , and associated with 0.5mm ST segment depression or higher, elevated cardiac markers	Non-ischemic pain, shock, CI to study drugs, pts on lipid-lowering therapy, TC >250mg/dl, SCr >2mg/dl	8.4% of enoxaparin arm experienced death, MI, or refractory ischemia at 7 days vrs 9.4% of UFH arm-a 95% CI value. All components of composite primary and secondary end-points favored enoxaparin, except death. TIMI grade bleeding were 3% for enoxaparin and 2.5% for UFH- a significant bleeding	1. Being open-label. 2. There was a cross-over. 3. Pre-treatment with antithrombin.
The SYNERGY Trial	A prospective, randomized, open-label multicenter trial evaluating the efficacy and safety of enoxaparin vs. UFH when combined with GP IIb/IIIa inhibitor + ASA	10027	Pts >18yrs, ischemic pain at rest lasting >10mins and occurring within 24hrs before enrollment, plus 2 of the ff: ECG changes, >60yrs old, abnormal cardiac marker within 24hrs before enrollment.	Pregnant, allergy to pork, pork products, CI to UFH or LMWH, recent or planned spinal or epidural anesthesia, PCI within past 24hrs, ischemic or hemorrhagic stroke,tumor, intracranial aneurysm, active bleeding	Primary end point occurred in 14.0% of enoxaparin arm and 14.5% of UFH arm- a 95% CI. No diff. in ischemic events during PCI. More bleeding observed with enoxaparin- 9.1% vs 7.6% UFH using the TIMI scale	Problem of cross over, Inclusion in the study of pts pre-treated with antithrombin Use of GP IIb/IIIa inhibitors was not mandatory, but left to physician discretion. Fact that it was an open-label.

**Table 2**  
**Summary of various Clinical Trials**  
**(Study Comparison)**

<b>Name of Study</b>	<b>Treatment Regimens Evaluated</b>	<b>Outcome Variables Measured &amp; Method of Measurement</b>	<b>Study Location</b>	<b>Study Duration</b>
The NRMI-3	In-hospital events were compared between pts who received LMWH with GP IIb/IIIa inhibitors, and pts who received UFH with GP IIb/IIIa inhibitors through uniform data collection on the treatment of pts with AMI at the registry.	A combined end point was defined as the composite of major bleeding, recurrent ischemia, recurrent AMI, and hospital death, as reported by the over 1500 hospitals that participated.	National	2 years
The NICE-3	Pts received enoxaparin (1mg/kg SC q12h) with any of the 3 available GP IIb/IIIa antagonists, ie, Enoxaparin + Tirofiban + ASA (162.5 - 325mg) Enoxaparin + Eptifibatide + ASA(162.5-325mg) Enoxaparin + Abciximab + ASA 162.5-325mg)	Primary end point: Safety- measured by incidence of major bleeding not related to CABG, using TIMI bleeding criteria Secondary: Safety-measured by major or minor hemorrhage, and need for transfusions. Efficacy: All-cause death, MI, urgent revascularization	United States and Canada, at 56 sites.	5 months
The ACUTE II Study	Pts received 160-325mg ASA+ Tirofiban loading of 0.4mcg/kg/min for 30mins, followed by 0.1mcg/kg/min for 47.5hrs, and up to 107.5hrs + either UFH LD 5000u bolus, then 1000u/hr adjusted to therapeutic aPTT or + Lovenox 1mg/kg q12h SC	Primary: Major or minor bleeding according to site, severity, and cause, using TIMI trial bleeding criteria. Secondary: Transfusions of any type, clinical outcomes recorded for as long as 30 days, eg death, nonprocedure-related MI, peri-PCI-related MI, peri-CABG MI, refractory ischemia. Analyses conducted when 100 and 200 pts randomized	International, at 54 sites	N/A
PARAGON-B	Pts received either a renal-dosed Lamifiban, as a 500mcg bolus, then 72-hr infusion, or a placebo, together with daily doses of ASA, open-label heparin for at least, 3 days, at 5000u bolus, followed by 1000u/hr infusion. Per the protocol, in a selected, prespecified number of centers, LMWH instead of UFH was used.	Primary end point was a 30-day composite of death, MI, and severe recurrent ischemia requiring urgent revascularization. MI not associated with a revascularization procedure was defined as new pathological Q waves or creatine kinase (CK), or MB isoenzyme level >2, times the upper limit of normal (ULN) during the index hospital admission. SRI defined as >1 prolonged episode of chest pain at rest, for at least 20mins.	Multi-center, International, included North America, South America, Western Europe, and Australia	N/A
The Aggrastat to Zocor Trial (The A-to-Z Trial)	Enoxaparin at 1mg/kg q12h + tirofiban at 10mg/kg bolus, then 0.1mg/kg/min for a min of 48hrs, or 12hrs after intervention, and max of 120hrs + ASA 75-325mg Wt. adjusted UFH + tirofiban (same dose as above) + ASA 75-325mg	Primary: 1. Composite of all-cause death 2. New MI (MI-an increase of >50% in a marker associated with symptoms of ischemia. 3. Refractory ischemia within 7 days of tirofiban initiation Secondary: All-cause death, MI, Refractory ischemia, urgent coronary revasc. and multiple clinical MI events evaluated at 7 days individually, and as a composite. Tertiary- all primary and secondary endpoints and readmits for ACS at 48hrs and 30 days. Safety based on TIMI system of bleeding	International	2 ½ years
The SYNERGY Trial	UFH given according to a weight adjusted nomogram- bolus of 60u/kg to a max of 5000u, and initial infusion of 12u/kg/hr, to a max of 1000u/hr initially. Enoxaparin given as 1mg/kg q12h SQ.	Primary: Death, or MI at 30days. Secondary: Combined incidence of all-case mortality, nonfatal MI, Stroke or recurrent ischemia requiring revascularization, and individual components of the composite at 14 and 30 days.	International at 500 sites	2 years and 4 months