

# Levy et al. “Repletion of factor XIII following cardiopulmonary bypass using a recombinant A-subunit homodimer – a preliminary report” (Thromb Haemost 2009; 102.4)

## Appendix

*Inclusion Criteria:* Informed consent obtained before any trial-related activities; age between 35 and 75 years of age; undergoing first myocardial revascularisation; adequate renal and hepatic function defined as creatinine  $\leq 1.4$  mg/dl, bilirubin  $\leq 1.5$  times upper limit of normal, alkaline phosphatase  $\leq 2$  times upper limit of normal and AST  $\leq 1.5$  times upper limit of normal; a haematocrit  $\geq 34\%$  for females and  $39\%$  for males and haemoglobin  $\geq 11.8$  g/dl for females and  $13.5$  g/dl for males; a negative serum pregnancy test within 3 days of enrolment if female and of child-bearing potential; agreement to use a medically accepted form of contraception if applicable; a negative history for drug abuse.

*Exclusion Criteria:* Previous participation (randomisation and dosing) in the trial; known antibodies or hypersensitivity to FXIII; known hereditary bleeding diathesis or coagulopathy; known allergy to yeast or yeast-derived proteins; need for an emergent ( $\leq 24$ -hour) myocardial revascularisation procedure; undergoing a procedure that requires deep hypothermic circulatory arrest  $< 28^\circ$  C, or had deep hypothermic cardiac arrest  $< 32^\circ$  C during current procedure; any surgical procedure in the 30 days prior to enrolment (excluding angiogram); a previous history of autoimmune disorder involving autoantibodies, e.g., systemic lupus erythematosus; a history of cerebrovascular event (including thrombotic or haemorrhagic stroke or transient ischaemic attack) and/or extra-myocardial thromboembolic events, e.g., deep vein thrombosis or pulmonary embolus; history or family history of heritable coagulopathy, including Factor V Leiden, Protein C deficiency, Protein S deficiency; type I diabetes or type 2 diabetes requiring insulin treatment at the time of screening, and/or having a history of diabetic retinopathy; a history of peripheral vascular disease requiring surgical correction, including carotid endarterectomy (CEA) or femoral-popliteal bypass, or is currently experiencing claudication; a body mass index (BMI)  $\geq 37$ ; a history of heparin-induced thrombocytopenia; acute myocardial infarction (MI)  $< 24$  hours prior to surgery, or has suspected or confirmed intra-operative MI; pre-operative (within 30 days) transfusion of any blood and/or blood product; atrial fibrillation or history of atrial fibrillation; receipt of clopidogrel (Plavix<sup>®</sup>)  $< 5$  days prior to surgery; receipt of abciximab (ReoPro<sup>®</sup>)  $< 24$  hours prior to surgery; receipt of other GP IIb/IIIa inhibitors  $< 12$  hours prior to surgery; receipt of tPA or fibrinolytics  $< 24$  hours prior to surgery; receipt of low molecular weight heparin (LMWH) within 3 days of surgery; preoperative heparin exposure for  $> 3$  days; preoperative heparin exposure for  $\leq 3$  days and a prior history of therapeutic heparin exposure (defined as subcutaneous or intravenous administration) within the preceding 6 months; receipt or expected receipt of aprotinin (Trasylo<sup>®</sup>), epsilon-amino caproic acid (Amicar<sup>®</sup>), tranexamic acid (Cyklokapron<sup>®</sup>) or factor VIIa (NovoSeven<sup>®</sup>); a preoperative (within 30 days) ejection fraction of  $< 30\%$  or current signs and symptoms of congestive heart failure; haemodynamic instability during or following bypass requiring placement of a left ventricular assist device or intra-aortic balloon pump or administration of  $\geq 2$  inotropic agents, excluding vasopressors; requirement for surgical procedures in addition to myocardial revascularisation, e.g., valve repair or replacement; ventricular arrhythmia post-CPB cannula removal that requires therapeutic intervention; prior treatment with any experimental agent within 30 days prior to enrolment; prior treatment with rFXIII; pregnancy, breast feeding or intention of becoming pregnant; concurrent serious chronic or acute illness or infection, as per the investigator’s judgment; medical, social or psychosocial factors expected to impact upon compliance or safety; weight  $> 140$  kg.