

PROTOCOL SYNOPSIS

Product Name: Activase (Recombinant Tissue Plasminogen Activator, rt-PA)		Protocol Date: January 23, 2011	
Title: Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis (the ATTRACT Trial)			
Investigator/Sponsor: Suresh Vedantham, M.D.		Institution: Washington University in St. Louis	
<p>Primary Objective: Determine if the initial adjunctive use of Pharmacomechanical Catheter-Directed Thrombolysis (PCDT) in symptomatic patients with acute proximal deep vein thrombosis (DVT) reduces the occurrence of the Post-Thrombotic Syndrome (PTS) over 24 months follow-up.</p> <p>Secondary Objectives: 1) Compare resolution of acute DVT symptoms; venous disease-specific and general quality of life (QOL); safety; and cost-effectiveness between the two treatment arms; 2) Identify pre-treatment predictors of heightened therapeutic response to PCDT via correlation of PTS scores and QOL change scores with demographical variables, DVT risk factors, symptom duration, and anatomic thrombus extent; and 3) Determine if PTS scores and QOL change scores are correlated with post-treatment thrombus burden, recurrent DVT, and valvular reflux.</p>			
Number of Patients: 692		Number of Centers: 30-60	
<p>Experimental Arm Treatment: PCDT with intrathrombus delivery of rt-PA (maximum allowable total dose 35 mg) into the DVT over a period of up to 30 hours. Three methods of initial rt-PA delivery will be used: 1) Trellis-8 Peripheral Infusion System – maximum first-session rt-PA dose 25 mg; 2) AngioJet Rheolytic Thrombectomy System – maximum first-session rt-PA dose 25 mg; or 3) Catheter-directed rt-PA infusion for up to 30 hours at 0.01 mg/kg/hr (maximum 1.0 mg/hr) via a multisidehole infusion catheter. Before and after PCDT, patients will receive standard DVT therapy as in the Control Arm.</p> <p>Control Arm Treatment: Initial anticoagulant therapy with unfractionated heparin, enoxaparin, dalteparin, or tinzaparin, for at least 5 days, overlapped with long-term oral warfarin (target INR 2.0 – 3.0). Elastic compression stockings will be prescribed.</p>			
<p>Inclusion Criterion: Symptomatic proximal DVT involving the iliac, common femoral, and/or femoral vein.</p> <p>Exclusion Criteria: Active bleeding; bleeding diathesis including INR > 1.6 or platelets < 100,000/ml; severe liver dysfunction; recent (< 3 months) internal eye surgery, GI bleeding, or hemorrhagic retinopathy; history of stroke or intracranial lesion; recent (< 10 days) surgery, CPR, trauma, obstetrical delivery, cataract surgery, or other major invasive procedure; pregnancy; active cancer except for non-melanoma primary skin cancers; massive pulmonary embolism; acute limb threat from DVT; hemoglobin < 9.0 g/dl; age < 16 years or > 75 years; severe hypertension; allergy to heparin, rt-PA, or iodinated contrast; life-expectancy < 2 years; chronic non-ambulatory status; moderate (diabetics) or severe (non-diabetics) renal impairment; index DVT symptom duration > 14 days; established PTS or previous symptomatic DVT within the last 2 years in the index leg; contralateral symptomatic acute DVT involving the iliac and/or common femoral vein or for which thrombolysis is planned for initial DVT therapy; recent (<5 days) use of thienopyridine antiplatelet drugs (except clopidogrel); inability to tolerate PCDT, provide informed consent, or comply with study assessments (e.g. due to cognitive impairment).</p>			
Design: NIH-funded, Phase III, multicenter, randomized, open-label, assessor-blind, parallel two-arm, controlled clinical trial.			
<p>Primary Efficacy Outcome: Cumulative incidence of PTS within 24 months after randomization (Villalta PTS Scale).</p> <p>Secondary Efficacy Outcomes: Severity of PTS (Villalta PTS Scale, CEAP Clinical Class, Venous Clinical Severity Score); disease-specific (VEINES-QOL/Sym measure) and general (SF-36, Version 2) QOL; resolution of presenting DVT symptoms (Likert Scale, calf circumference measurements, Villalta PTS Scale); prevalence of valvular reflux and residual thrombus at 1 year (Duplex ultrasound); degree of clot lysis with PCDT (venography, Experimental Arm only); and cost-effectiveness.</p>			
Safety Endpoints: Major bleeding, symptomatic pulmonary embolism, recurrent venous thromboembolism, and death.			
<p>Data Analysis: The Ontario Clinical Oncology Group's Clinical Trials Methodology Group at McMaster University in Hamilton, Ontario (Canada) will be the Data Coordinating Center for the study. The primary data analysis will be an intent-to-treat comparison of the cumulative incidence of PTS within the 24 months after randomization. A Fisher's exact test will be used, testing will be two-sided, and a p value of 0.05 will be considered significant.</p>			
Trial Duration: 54 months	Start Date: February 2009	Stop Date: March 2013	Publication: Expected 2013