OPTALYSE PE Study

PROTOCOL SYNOPSIS

EKOS EkoSonic™ Endovascular System

Study Drug Name: Activase® (Genentech)

Primary Efficacy Objective: Determine the optimum dose of thrombolytic and duration of the Acoustic Pulse Thrombolysis™ as a treatment for acute submassive pulmonary embolism (PE). The primary efficacy objective is a change in the RV to LV diameter ratio.

Primary Safety Objective: Determine the frequency of major bleeding within 72 hours after the initiation of Acoustic Pulse Thrombolysis™ treatment in patients with submassive PE.

Study Patient Treatment: OPTALYSE Acoustic Pulse Thrombolysis™ treatment groups are listed below. A repeat CTA was obtained to measure RV/LV at 48 hours after the start of treatment.

Cohort 1: 2hr ultrasound; 2mg r-tPA/hr/catheter
Cohort 2: 4hr ultrasound; 1mg r-tPA/hr/catheter
Cohort 3: 6hr ultrasound; 1mg r-tPA/hr/catheter
Cohort 4: 6hr ultrasound; 2mg r-tPA/hr/catheter*

Inclusion Criteria: Age 18-75 inclusive; CTA evidence of proximal submassive PE (RV/LV diameter ratio ≥ 0.9 on CTA and hemodynamically stable); Symptom duration ≤14 days; Treated within 48 hours of diagnosis of PE by CTA.

Exclusion Criteria:

1. Stroke or transient ischaemic attack (TIA), head trauma, or other active intracranial or intraspinal disease within one year
2. Recent (within one month) or active bleeding from a major organ
3. Major surgery within seven days
4. Clinician deems high-risk for catastrophic bleeding
5. History of heparin-induced thrombocytopenia (HIT) or any haematologic disease potentially involving abnormal platelet number or function
6. Catheter-based pharmacomechanical treatment for pulmonary embolism within 3 days of study enrollment
7. Systolic blood pressure less than 90 mm Hg and/or use of vasopressors
8. Cardiac arrest (including pulseless electrical activity and asystole) requiring active cardiopulmonary resuscitation (CPR)
9. Evidence of irreversible neurological compromise
10. Life expectancy < 1 year
11. Use of thrombolytics or glycoprotein IIb/IIIa antagonists within 3 days prior to inclusion in the study
12. Out-of-Range Laboratory Values: Haematocrit < 30%, Platelets < 100 thousand/μL, INR > 3
13. Creatinine outside the normal range for the treating institution
14. Pregnancy
15. Active cancer (metastatic, progressive, or treated within the last 6 months). Exception: non-melanoma primary skin cancers
16. Known allergy, hypersensitivity, or thrombocytopenia from heparin, r-tPA, or iodinated contrast except for mild-moderate contrast allergies for which steroid pre-medication can be used

*Note: The steering committee closed Cohort 4 early.

INDICATIONS FOR USE: The EkoSonic™ Endovascular System is intended for controlled and selective infusion of physician-specified fluids, including thrombolytics, into the peripheral vasculature. The EkoSonic™ Endovascular System is CE Marked for the treatment of pulmonary embolism with a ≥50% clot burden in one or both main pulmonary arteries or lobar pulmonary arteries, and evidence of right heart dysfunction based on right heart pressures (mean pulmonary artery pressure ≥25 mmHg) or echocardiographic evaluation. **Contraindications:** Not designed for peripheral vasculature dilation purposes. This system is contraindicated when, in the medical judgment of the physician, such a procedure may compromise that patient's condition. Such conditions include but are not limited to: • Tortuous vascular anatomy compromising safe introduction of endovascular equipment • Conditions associated with increased risk of bleeding. See device instructions for use for complete prescribing information http://ekoscorp.com/international_enter.htm#Resources

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