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EKOS™ Endovascular System
KNOCOUT PE

Prospective Multicenter International Registry of Ultrasound-Facilitated Catheter-Directed Thrombolysis in Intermediate-High and High-Risk Pulmonary Embolism (KNOCOUT PE)

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TRIAL OBJECTIVE

To understand the impact of the OPTALYSE PE study on various ultrasound-accelerated thrombolysis (USAT) protocols being used as the standard of care in the treatment of acute PE and associated long-term outcomes.

PATIENTS

489 prospective patients

CENTERS

64 international sites

Registry Design | Prospective Cohort

PATIENTS

489 patients
with intermediate-high risk and high-risk PE

Treated with EKOS from March 2018-June 2020

INCLUSION CRITERIA

- Male or female > 18 years of age and < 80 years of age
- Intermediate High-Risk or High-Risk PE
- RV/LV > 1.0 from diagnostic CTA or echocardiogram
- Symptom duration < 14 days
- Troponin elevation
- Investigator has selected the EKOS device to treat patient
- Infusion dose/duration per investigator's SOC

EXCLUSION CRITERIA

- Clinician deems subject high-risk for catastrophic bleeding
- Life expectancy < 1y

End Points

EFFICACY

- Thrombolytic dosing
- Thrombolytic infusion duration
- Adjuvant therapy
- Healthcare utilization: ICU and hospital length of stay (LOS)
- Quality of life as measured by PEmb-QoL and EQ-5D-5L VAS–365 days
- Echocardiogram
  - Change in RV:LV ratio from baseline
  - Tricuspid annular plane systolic excursion (TAPSE)
  - IVC collapse
  - Estimated right ventricular systolic pressure (RVSP)

SAFETY

- Recurrent VTE
- Major bleeding
- Mortality
- Diagnosis of chronic thromboembolic pulmonary hypertension (CTEPH)

Key Results
Safety (Within 30 Days)

0 ICH*
(0/489)

1.6% ISTH Major Bleeding
(8/489)

RECURRENT VTE
PE: 0.4%
(2/489)

Major Bleeding at 72 hours	8 (1.6%)
Gastrointestinal Hemorrhage	2 (0.4%)
Head Laceration	1 (0.2)
Vascular Access Site Hematoma	4 (0.8%)
Subdural Hematoma (pre-existing)	1 (0.2)

Recurrent VTE within 30 days	
Pulmonary Embolism	2 (0.4%)

*1 preexisting subdural hematoma (SDH)

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Key Results | Procedural

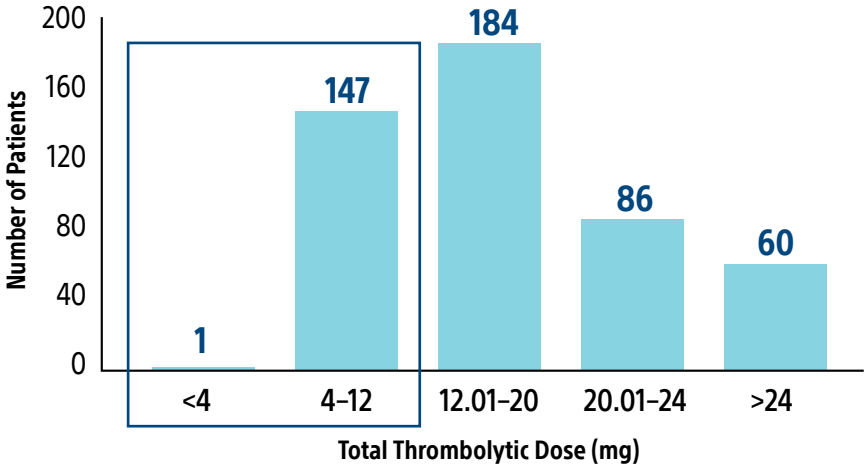
PROCEDURAL

- Mean dose of r-tPA: 18.1mg (SD 7.4)
- Mean infusion time: 10.5 hrs (SD 5.37)

31.0% of patients received < 12mg r-tPA

69.5% of patients received < 20mg r-tPA

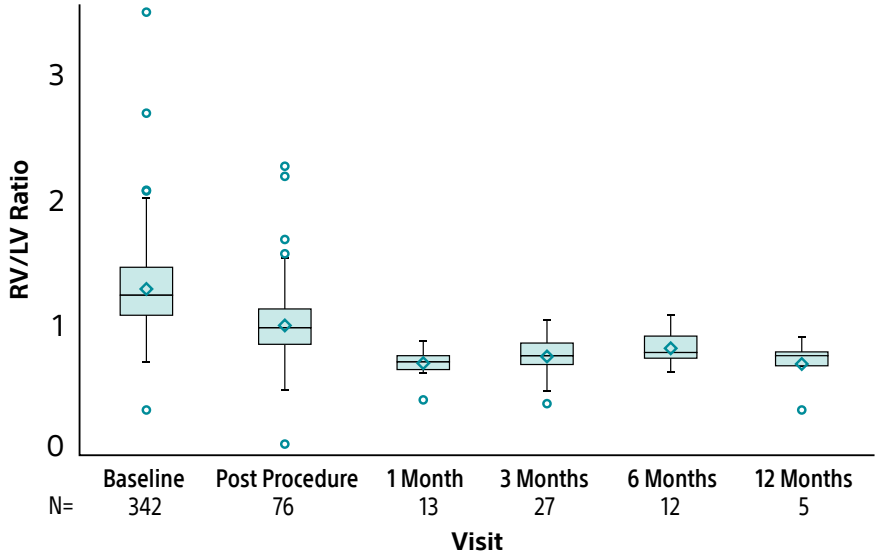
TOTAL THROMBOLYTIC DOSE



Key Results | Efficacy

RV/LV RATIO BY VISIT ON ECHO

Efficacy population in prospective patients



Key Results | Quality Of Life

QUALITY OF LIFE

- PEmb-QOL reduction at 3-months: 41%

QoL Measure	Post-Procedure Mean (SD)	3-Months Mean (SD)	Percent Change Mean (SD)	2-sided P-value
PEmb-QOL	38.5 (22.1)	16.0 (17.7)	41.1 (114.1)	<0.0001
VAS	63.1 (23.0)	75.5 (19.8)	56 (255.0)	0.0001

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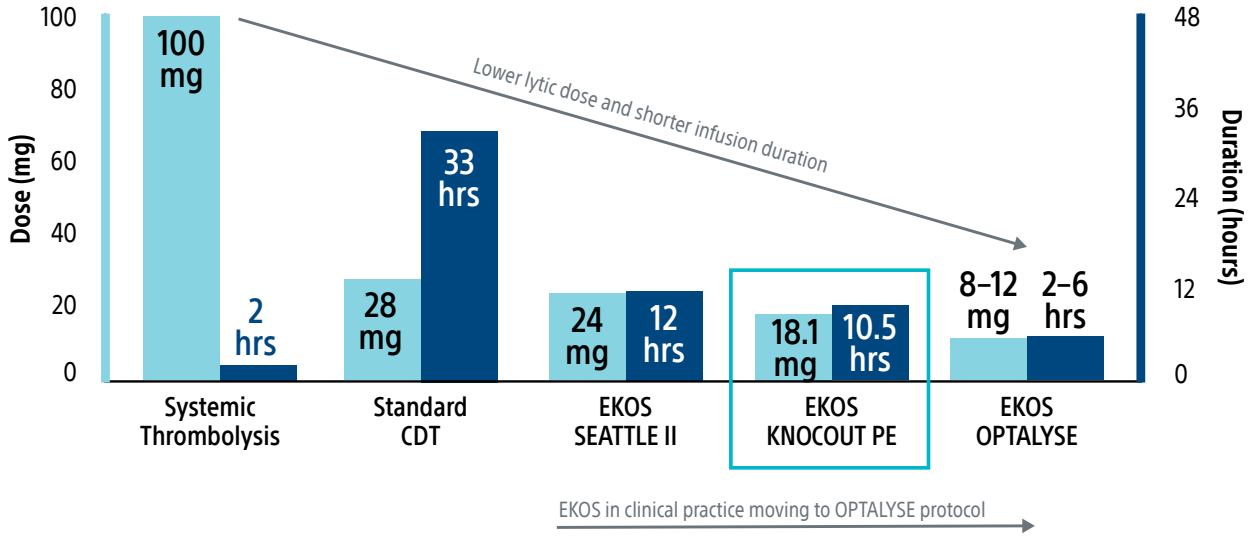
KNOCOUT PE CONCLUSIONS:

Results from this prospective multicenter registry reflect contemporary practice and demonstrate the performance of EKOS in the management of PE with lower total r-TPA dose and shorter infusion duration, marked clinical improvement in RV/LV ratio and low rates of major hemorrhagic complications with no intracerebral hemorrhagic events.

THROMBOLYTIC THERAPIES:

KNOCOUT PE shows that contemporary clinical practices are moving to low-dose, short duration OPTALYSE protocols. It adds to the growing evidence that EKOS is effective at treating intermediate risk and high risk PE with lower lytic doses and shorter infusion durations compared to other thrombolytic therapies.

DURATION AND DOSE BY THERAPY



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Standard CDT – Kuo W et al. CHEST 2015; 148(3):667 673.

SEATTLE II – Piazza G et al. A Prospective, Single-Arm, Multicenter Trial of Ultrasound-Facilitated, Catheter-Directed, Low-Dose Fibrinolysis for Acute Massive and Submassive Pulmonary Embolism. The SEATTLE II Study. J Amer Coll Cardiol: Cardiovasc Interventions 2015; 8(10):1382-1392.

KNOCOUT PE – Sterling KM, Goldhaber SZ, Sharp ASP, et al. Prospective Multicenter International Registry of Ultrasound-Facilitated Catheter-Directed Thrombolysis in Intermediate-High and High-Risk Pulmonary Embolism (KNOCOUT PE). Circ Cardiovasc Interv. 2024;17:e013448. doi: 10.1161/CIRCINTERVENTIONS.123.013448

OPTALYSE – TapsonVF, Sterling K, Jones N, et al. A randomized trial of the optimum duration of acoustic pulse thrombolysis procedure in acute intermediate-risk pulmonary embolism: the OPTALYSE PE trial. JACC Cardiovasc Interv. 2018;11:1401-1410. doi: 10.1016/j.jcin.2018.04.008

EKOS™ Endovascular Device

CAUTION: Federal law (USA) restricts this device to sale by or on the order of a physician. Rx only. Prior to use, please see the complete "Instructions for Use" for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator's Instructions. **INTENDED USE / INDICATIONS FOR USE** The EkoSonic Endovascular Device is intended to be used with EKOS-branded control systems to employ high frequency (2 MHz to 3 MHz), low-power ultrasound to facilitate the infusion of physician-specified fluids, including procedural fluids and thrombolytics, into the pulmonary and/or peripheral vasculature of adults. It is intended to be used by physicians experienced in endovascular interventional procedures. The EkoSonic Endovascular System is not intended for use in the neurovasculature. Refer to the product insert supplied with the physician-specified fluid for fluid-specific preparation, contraindications, side effects, warnings, and precautions. The EkoSonic Endovascular System, consisting of the Infusion Catheter and the Ultrasonic Core, is indicated for the: • Ultrasound facilitated, controlled and selective intravascular infusion of physician-specified fluids, including thrombolytics, for the treatment of pulmonary embolism and/or deep vein thrombosis. • Controlled and selective infusion of physician-specified fluids, including thrombolytics, into the pulmonary arteries and/or peripheral vasculature. **CONTRAINDICATIONS** The EkoSonic Endovascular Device is contraindicated for use in: • Patients in whom thrombolytic and/or anticoagulation therapy is contraindicated. • Any situation in which the medical judgment of the physician determines such a procedure may compromise the patient's condition. **WARNINGS** • Never aspirate blood back into the drug lumens as perfusion pores and/or drug lumens may become occluded. • Never activate ultrasound energy with the Infusion Catheter or Ultrasonic Core's working length exposed to the air. The device should be placed within the patient anatomy, with physician-specified fluids running through the drug lumen and coolant flowing through the coolant lumen. Otherwise, overheating may occur, potentially causing burns, damage to the Ultrasonic Core, and/or interrupting therapy. • Never attempt to use the Ultrasonic Core with any catheter except the compatible EKOS Infusion Catheter. • Do not attempt to use non-compatible working lengths (i.e., 135 cm Infusion Catheter and 106 cm Ultrasonic Core and vice-versa). Incorrect size matching may be harmful to the patient and require additional intervention or surgery. • The EkoSonic Endovascular System is not intended for use in the neurovasculature. **PRECAUTIONS** Carefully read all Instructions for Use prior to use. • The EkoSonic device is designed to provide optimum acoustic output during the first 24 hours of operation. • The EkoSonic device should only be used to infuse physician-specified fluids, including thrombolytics. Other types of fluids, outside of thrombolytics and procedural fluids (heparinized saline, saline, contrast media, etc.), have not been evaluated for use with the EkoSonic Endovascular Device. • This device is not designed for use as a peripheral vascular dilator. • During normal use, ultrasound energy may cause a temperature rise in the treatment zone. The catheter surface temperature is limited to a maximum of 43 °C. • Therapeutic agents, such as thrombolytics, should be administered through the drug port whereas the procedural fluids (such as saline and contrast agent) should be administered through the coolant port or central lumen. **ADVERSE EVENTS** Potential adverse events which may be associated with use of the EkoSonic Endovascular System when used as indicated include, but are not limited to: • Allergic Reaction (contrast, device, or other) • Arrhythmia • Burn • Cardiac Tamponade • Cardiac Trauma • Death • Embolism (air, device, plaque, thrombus, tissue, or other) • Hematoma • Hemorrhage • Hypotension • Infection/Sepsis • Ischemia/Necrosis • Need for additional intervention or surgery • Pain • Pneumothorax • Renal Insufficiency/Failure • Respiratory Failure • Thrombosis/Thrombus • Vasospasm • Vessel Occlusion • Vessel Trauma (AV fistula, dissection, perforation, pseudoaneurysm, rupture or injury) **92844459 V A.1**

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