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EKOS™ Endovascular System

KNOCOUT PE

International EkoSonic Registry of the Treatment and Clinical Outcomes of Patients with Pulmonary Embolism

Prospective Cohort 3-month Data Release

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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.

CENTERS:

83 international sites across the United States and Europe

PATIENTS:

Retrospective cohort: **991 patients**
Prospective cohort: **489 patients**

REGISTRY DESIGN | PROSPECTIVE COHORT

Patients	Inclusion Criteria	Exclusion Criteria
489 patients with intermediate-high risk and high-risk PE Treated with EKOS from March 2018-June 2020	• 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	• Clinician deems subject high-risk for catastrophic bleeding • Life expectancy < 1y

END POINTS

Efficacy	Safety
• Thrombolytic dosing • Thrombolytic infusion duration • Adjuvant therapy • Echocardiogram - Change in RV:LV ratio from baseline - Tricuspid annular plane systolic excursion (TAPSE) - IVC collapse - Estimated right ventricular systolic pressure (RVSP) • Healthcare utilization: ICU and hospital length of stay (LOS) • Quality of life as measured by PEmb-QoL and EQ-5D-5L VAS – 365 days	• Recurrent VTE • Major bleeding • Mortality • Diagnosis of chronic thromboembolic pulmonary hypertension (CTEPH)

KEY RESULTS

SAFETY (within 30 days)

0 ICH (0/489)	2.5% ISTH Major Bleeding (12/489)	Recurrent VTE	
		PE: 0.8% (4/489)	Confirmed Post-Procedure DVT: 0.2% (1/489)

Major Bleeding within 30 days	12 (2.5)
Anemia	1 (0.2)
Gastrointestinal Hemorrhage	1 (0.2)
Peritoneal Hemorrhage	1 (0.2)
Procedural Hemorrhage	1 (0.2)
Laceration	1 (0.2)
Compartment Syndrome	1 (0.2)
Hematoma	1 (0.2)
Lower Gastrointestinal Hemorrhage	1 (0.2)
Retinal Hemorrhage	1 (0.2)
Retroperitoneal Hemorrhage	1 (0.2)
Subdural Hematoma (pre-existing)	1 (0.2)
Vascular Access Site Hematoma	1 (0.2)
Recurrent VTE within 30 days	
Pulmonary Embolism	4 (0.8)
Confirmed Post-Procedure DVT	1 (0.2)*

*34 DVTs were reported, however; 33 of the 34 reported DVTs were identified on duplex ultrasound within 1-2 days of the USCDT procedure and were not differentiated from preexisting DVTs. 30 of the 34 DVTs were reported from one center.

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KEY RESULTS | PROCEDURAL

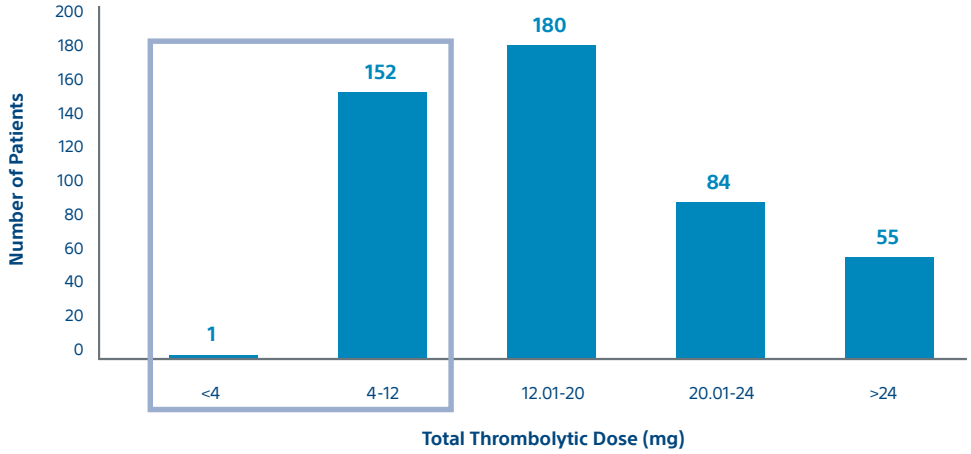
PROCEDURAL

- Mean dose of r-tPA: 17.9mg (SD 7.3)
- Mean infusion time: 10.4 hrs (SD 5.2)
- Mean time in ICU = 48.9hrs (SD 47.4)

32.4% of patients received < 12mg r-tPA

70.6% of patients received < 20mg r-tPA

TOTAL THROMBOLYTIC DOSE

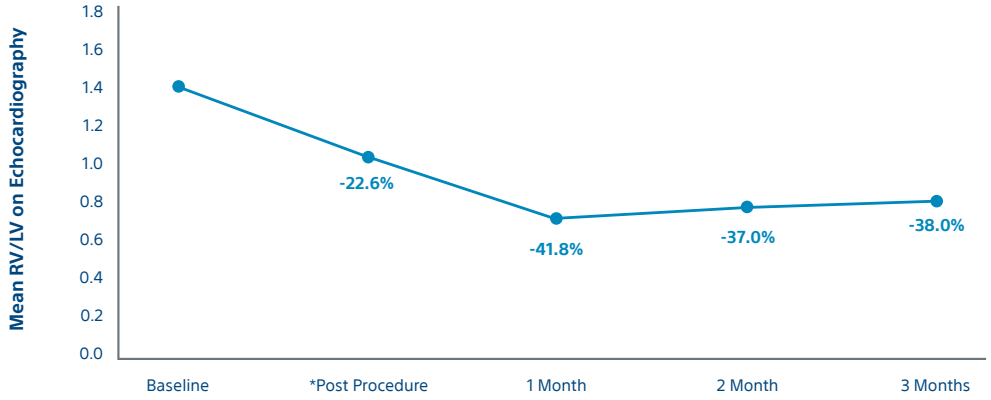


KEY RESULTS | EFFICACY

EFFICACY

- RV/LV Reduction from baseline
  - Post-Procedure: 23%
  - 3-months: 38%

CHANGE IN RV/LV



	Baseline	*Post Procedure	1 Month	2 Month	3 Months
Mean RV/LV	1.351	1.017	0.721	0.755	0.774
N	176	176	13	14	27

Significant decrease post-procedure that was sustained over time (P<0.0001)

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 (2.1)	16.0 (17.7)	41.1 (114.1)	<0.0001
VAS	63.1 (23.0)	75.5 (19.8)	56 (255.0)	0.0007

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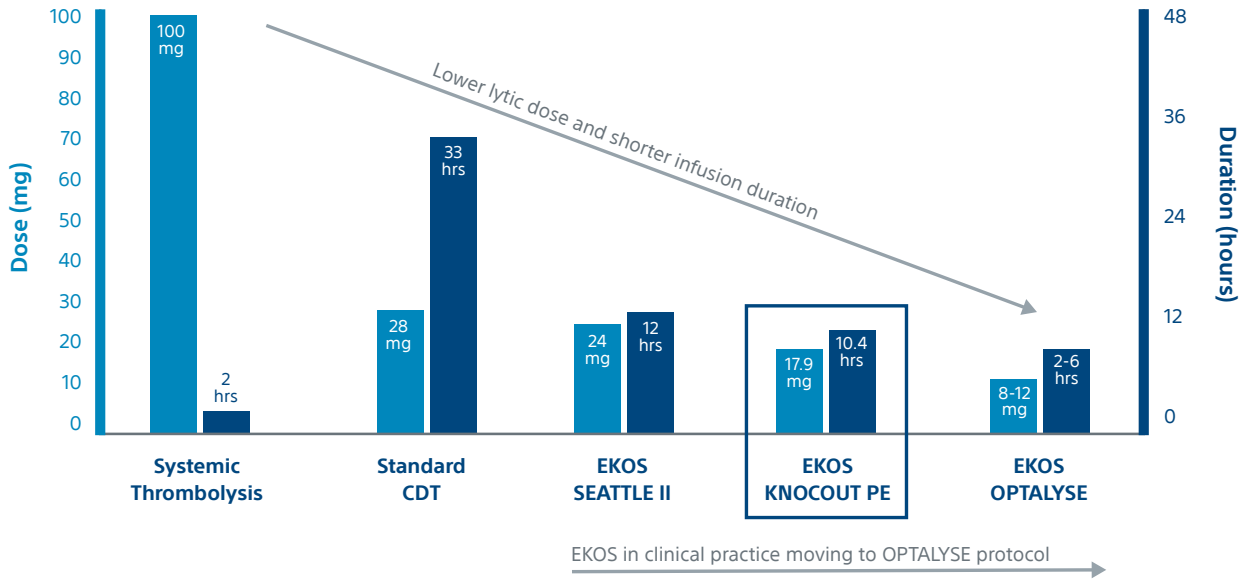
KNOCOUT PE CONCLUSIONS:

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



Systemic Thrombolysis – KonstantinidesS, GeibelA, HeuselG, et al. Heparin plus alteplase compared with heparin alone in patients with submassivepulmonary embolism. N EnglJ Med. 2002;347:1143–1150.

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 – 3-Month Prospective KNOCOUT Data Presentation at VIVA 2021.

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 Acoustic Pulse Thrombolysis Treatment

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 "Directions for Use" for more information on Indications, Contraindications, Warnings, Precautions, Adverse Events, and Operator's Instructions.

INDICATIONS FOR USE: The EkoSonic Endovascular System is indicated for the: Ultrasound facilitated, controlled and selective infusion of physician-specified fluids, including thrombolytics, into the vasculature for the treatment of pulmonary embolism. • Infusion of solutions into the pulmonary arteries. • Controlled and selective infusion of physician specified fluids, including thrombolytics, into the peripheral vasculature. All therapeutic agents utilized with the EkoSonic Endovascular System should be fully prepared and used according to the instruction for use of the specific therapeutic agent. 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 the patient's condition.

POTENTIAL COMPLICATIONS: Vessel perforation or rupture • Distal embolization of blood clots • Vessel spasm • Hemorrhage • Hematoma • Pain and tenderness • Sepsis/Infection • Thrombophlebitis • Tricuspid and pulmonic valve damage • Pulmonary infarct due to tip migration and spontaneous wedging, air embolism, and/or thromboembolism • Right bundle branch block and complete heart block • Intimal disruption • Arterial dissection • Vascular thrombosis • Drug reactions • Allergic reaction to contrast medium • Arteriovenous fistula • Thromboembolic episodes • Amputation • Pneumothorax • Perforation of the pulmonary artery. • Cardiac Arrhythmias – most frequently occurring during placement, removal or following displacement into the right ventricle. PI-726201-AA

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