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EKOS™ Acoustic Pulse Thrombolysis Treatment

OPTALYSE STUDY

A Randomized Trial of the Optimum Duration of Acoustic Pulse Thrombolysis Procedure in Acute Intermediate-Risk Pulmonary Embolism: The OPTALYSE PE Trial.

Victor F. Tapson, Keith Sterling, Noah Jones, Mahir Elder, Uttam Tripathy, Jayson Brower, Robert L. Maholic, Charles B. Ross, Kannan Natarajan, Pete Fong, Lee Greenspon, Houman Tamaddon, Amir R. Piracha, Tod Engelhardt, John Katopodis, Vasco Marques, Andrew S.P. Sharp, Gregory Piazza and Samuel Z. Goldhaber. JACC: Cardiovascular Interventions Jul 2018; 11(14): 1401-1410; DOI: 10.1016/j.jcin.2018.04.008.

Piazza G, Sterling KM, Tapson VF, Ouriel K, Sharp ASP, Liu P-Y, Goldhaber SZ; OPTALYSE-PE Investigators. One-Year Echocardiographic, Functional, and Quality of Life Outcomes after Ultrasound-Facilitated Catheter-Based Fibrinolysis for Pulmonary Embolism. Circ Cardiovasc Interv. 2020;13:e009012. doi: 10.1161/CIRCINTERVENTIONS.120.009012

PATIENTS Acute PE with RV/LV ratio ≥0.9 (n= 101**; 17 centers)

Evaluate the optimal duration/dose of Acoustic Pulse Thrombolysis treatment using r-tPA administered via the EKOS system:

Efficacy - Change in RV/LV ratio on CTA at 48hrs | Safety – As measured by major bleeding within 72hrs

RANDOMIZATION

Cohort 1	Cohort 2	Cohort 3	Cohort 4
27 Patients***	27 Patients	28 Patients	18 Patients
2 (h) EKOS	4 (h) EKOS	6 (h) EKOS	6 (h) EKOS
4/8 mg r-tPA*	4/8 mg r-tPA*	6/12 mg r-tPA*	12/24 mg r-tPA*

*Total mg r-tPA: one/two catheters for unilateral or bilateral
**One of the randomized patients did not receive EKOS treatment
***One of the original 28 patients in this arm did not receive EKOS treatment

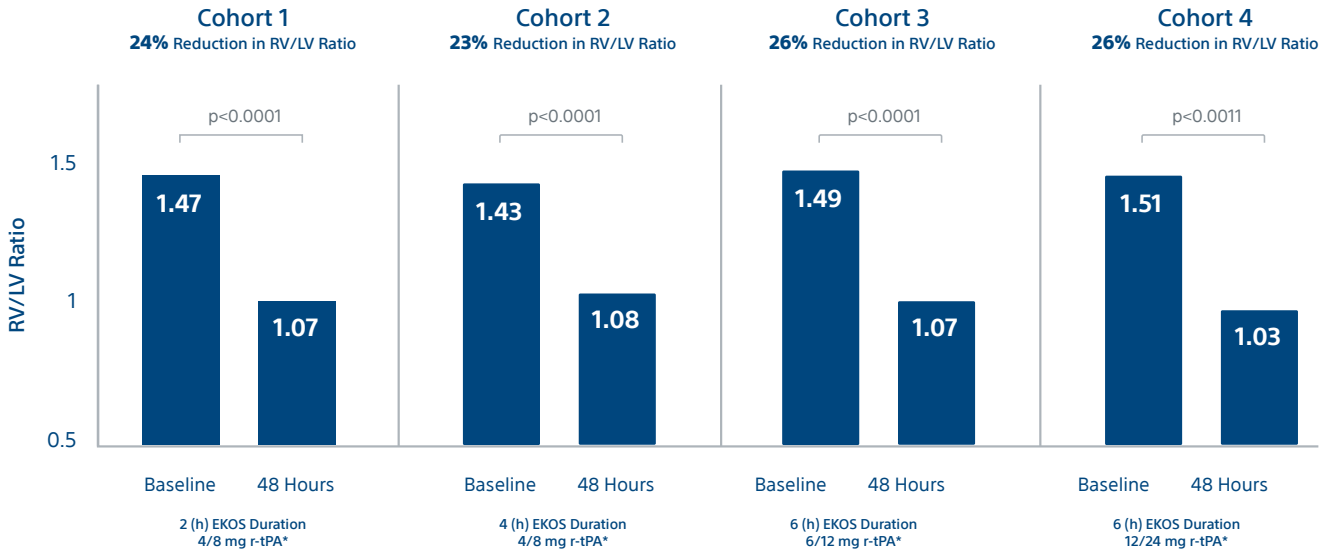
METHODS

- Anticoagulation therapy using heparin
- Acoustic Pulse Thrombolysis treatment using EKOS – following duration and dosage of randomly assigned study cohort
- Follow up at 48 hours post treatment start with CTA

KEY RESULTS

Acute PE patients treated with EKOS showed the following improvements:

- Significant reduction in RV/LV ratios in all cohorts at 48 hours post initiation of procedure.
- RV/LV ratio reduced by 24% (P<0.0001) for the two-hour cohort using only 4mg of r-tPA per device.
- All cohorts had zero to very low bleeding rates.[1]



* Total mg r-tPA: one/two catheters
1. Cohorts 1 and 3 had zero major bleeding incidents, cohort 2 had one incident and cohort 4 had two incidents (including one ICH) two additional bleeds were not included due to additional tPA received outside of the study protocol.

Long-Term Results

Improved markers of RV remodeling

Improved QOL & functional performance

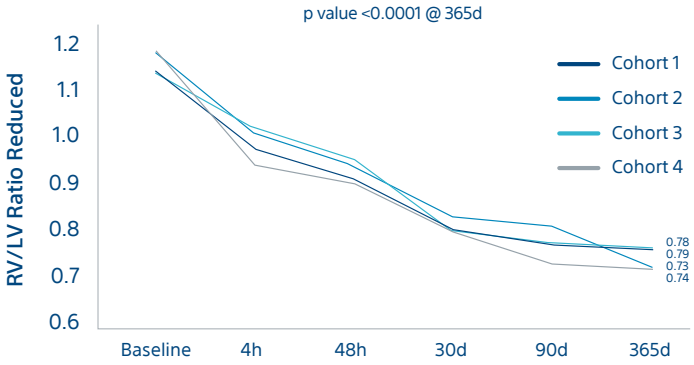
QOL & Functional scores mirrored RV recovery

ECHOCARDIOGRAPHIC RECOVERY

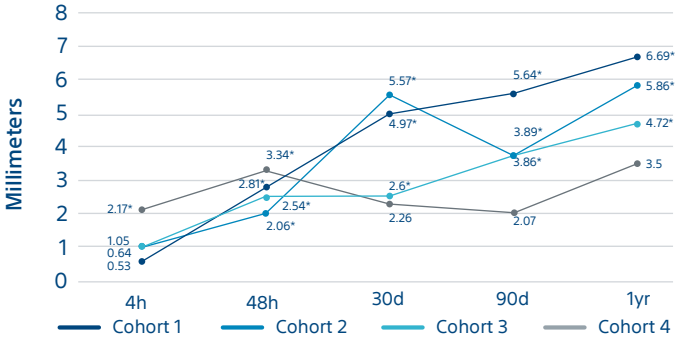
Marker of RV Remodeling Improves out to 1 Year:

- Echocardiographic markers of RV remodeling (e.g., RV/LV and TAPSE) improved in the short-, intermediate-, long-term follow-up
- Sustained ECHO improvement may be a determinant of post-PE syndrome prevention which enables more complete functional recovery

RV/LV ratio continued to reduce after 48h



Mean Differences – TAPSE Compared with Baseline

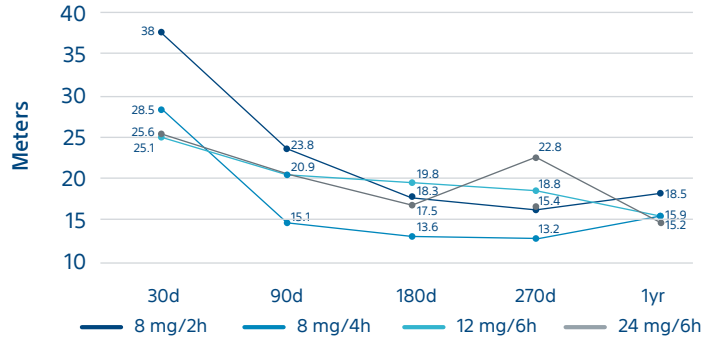


QUALITY OF LIFE AND FUNCTIONAL PERFORMANCE

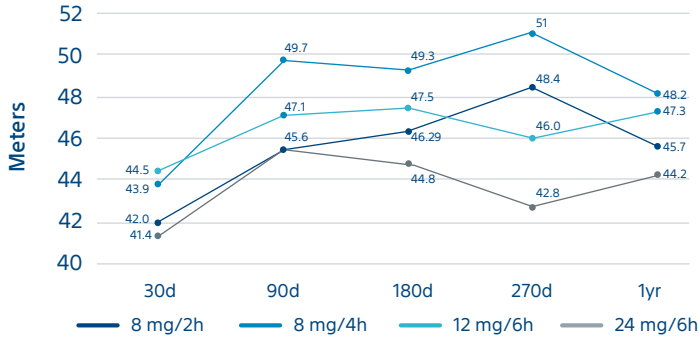
Pemb-QOL Score + PROMIS-PF:

- Although OPTALYSE PE did not have a control arm, one-year improvement in QOL and functional status scores mirrored RV recovery as assessed by serial ECHO
- No other study has performed a similarly rigorous and extensive echocardiographic evaluation and assessment after therapy for PE thus far

Mean PEmb – QOL Scores



Mean PROMIS-PF-6b Scores



Mean 6-Minute Walk (6-MW) Test Distance:

- From one month to one year after initial therapy:
  - Patients walked further on their 6-MW test
  - Greater proportion of patients without symptoms of dyspnea or fatigue after their 6-MW test
  - Overall improved functional performance scores

Borg Scale Score for Dyspnea and Fatigue – 365 days:

- Analysis of the 6-MW tests using the Borg Scale showed that the proportion of patients reporting zero fatigue or zero dyspnea both before and after their 6-MW Test increased from 30 days to 365 days, signifying that these patients continue to improve their 6-MW performance over time.

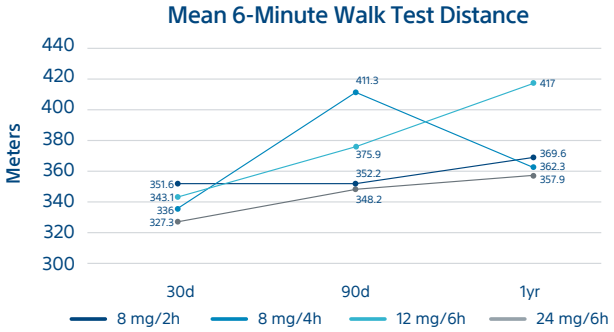
LONG-TERM RESULTS

The EKOS System's very low dose and short duration regimens in the OPTALYSE PE trial, resulted in rapid improved measures of right-heart function and continue to improve out to one year for all treatment arms. Additionally, the favorable mortality rates, recurrent PE rates, quality of life scores, and functional status scores demonstrate long-term benefits of EKOS therapy.

ACUTE RESULTS

The EKOS™ system's very low dose and short-duration regimens in the OPTALYSE PE trial, prove to be as acutely effective as the regimens in previous EKOS studies (ULTIMA and SEATTLE II), pointing to a paradigm-changing approach for PE treatment.

These data further prove the PE clinical efficacy and safety of the OPTALYSE PE treatment protocols. No other study has performed a similarly rigorous and extensive echocardiographic evaluation and assessment after therapy for PE thus far.



Long-term OPTALYSE safety & efficacy at 365d		
	Mortality	Recurrent PE
OPTALYSE PE	2%	2%
PEITHO-AC[3]	8%	N/A
PEITH-TNK[3]	10%	N/A
Baglin-AC[4]	N/A	3.7%

2. Sterling, K. "Long-term Results of the OPTALYSE PE trial" as presented at the International Symposium on Endovascular Therapy (ISET) meeting, Hollywood, FL Feb 2018.
3. Konstantinides, MD, et al, "Impact of Thrombolytic Therapy on the Long-Term Outcome of Intermediate-Risk Pulmonary Embolism" Journal of the American College of Cardiology; vol 69, pp.1536-1544, 2017.
4. Baglin, et al., "Does the clinical presentation and extent of venous thrombosis predict likelihood and type of recurrence? A patient-level meta-analysis," Journal of Thrombosis and Haemostasis, vol. 8, no. 11, pp. 2436-2442, 2010. 3.

PI-818407-AB

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