OPTALYSE PE STUDY

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


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

**Objectives**
Evaluate the optimal duration and dose of Acoustic Pulse Thrombolysis™ (APT) 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**

<table>
<thead>
<tr>
<th>Cohort 1</th>
<th>Cohort 2</th>
<th>Cohort 3</th>
<th>Cohort 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>27 Patients***</td>
<td>27 Patients</td>
<td>28 Patients</td>
<td>18 Patients</td>
</tr>
<tr>
<td>2 (h) EKOS™</td>
<td>4 (h) EKOS™</td>
<td>6 (h) EKOS™</td>
<td>6 (h) EKOS™</td>
</tr>
<tr>
<td>4/8 mg r-tPA*</td>
<td>4/8 mg r-tPA*</td>
<td>6/12 mg r-tPA*</td>
<td>12/24 mg r-tPA*</td>
</tr>
</tbody>
</table>

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

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

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.

¹ Total mg r-tPA: one/two catheters
**Key Results: Long Term**

Patients continued to improve through 365d$^2$ follow up:

- RV/LV ratio improved significantly across all four cohorts long-term.$^2$
- Multiple Quality of Life (QOL) metrics showed valuable improvements from 30d following EKOS™ therapy to 365d post-treatment.
- Very low all-cause mortality and recurrent PE rates of 2% each for all cohorts.

<table>
<thead>
<tr>
<th>RV/LV ratio continued to reduce after 48h</th>
<th>Long-term OPTALYSE safety &amp; efficacy at 365d</th>
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<tbody>
<tr>
<td>p value &lt;0.0001 @ 365d</td>
<td>Mortality</td>
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<tr>
<td></td>
<td>OPTALYSE PE</td>
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<tr>
<td></td>
<td>PEITHO-AC$^1$</td>
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<tr>
<td></td>
<td>PEITHO-TNK$^3$</td>
</tr>
<tr>
<td></td>
<td>Baglin - AC$^4$</td>
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</table>

**Quality of Life**

Two unique measurements of quality of life show significant improvements from 30d to 365d following EKOS™ therapy.

<table>
<thead>
<tr>
<th>PEmb-QOL score decreased for all cohorts</th>
<th>PROMIS-PF score increased for all cohorts</th>
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$^2$ - 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.


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 & SEATTLE II), pointing to a paradigm-changing approach for PE treatment.

LONG-TERM RESULTS:
The EKOS™ System's very low dose and short duration regimens, in the OPTALYSE PE trial, resulted in rapidly improved measures of right-heart function that were maintained for one year. Additionally, the favorable mortality rates, recurrent PE rates, and quality of life results demonstrate long-term benefits of EKOS™ therapy. This data further proves the PE clinical efficacy and safety of the OPTALYSE PE treatment protocols.