Prospective Multicenter Trial of Pharmaco-mechanical Catheter-Directed Thrombolysis with the Bashir Endovascular Catheter for Acute Pulmonary Embolism

The RESCUE Study

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On Behalf of RESCUE Investigators

Funding support: NHLBI – SBIR, Commonwealth of Pennsylvania Department of Health and Thrombolex Inc.
Disclosure Statement of Financial Interest

I, Riyaz Bashir MD have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Co-Inventor
Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grant/Research Support</td>
<td>Thrombolex Inc.</td>
</tr>
<tr>
<td>Consulting Fees/Honoraria</td>
<td>Thrombolex Inc.</td>
</tr>
<tr>
<td>Major Stock Shareholder/Equity</td>
<td>Thrombolex Inc.</td>
</tr>
<tr>
<td>Royalty Income</td>
<td>Thrombolex Inc.</td>
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<tr>
<td>Ownership/Founder</td>
<td>Thrombolex Inc.</td>
</tr>
<tr>
<td>Intellectual Property Rights</td>
<td>Thrombolex Inc.</td>
</tr>
<tr>
<td>Other Financial Benefit</td>
<td>Thrombolex Inc.</td>
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Faculty disclosure information can be found on the app.
Study Rationale

Improve the safety and efficacy by delivering a small dose of thrombolytic within the thrombus with a device designed for use in large vessels (pulmonary arteries).

First-in-Human study of Pharmaco-mechanical Catheter-Directed Thrombolysis (PM-CDT) with Bashir Endovascular Catheter has shown promising early results.
Study Objective

Assess safety and efficacy of Pharmaco-Mechanical Catheter-directed thrombolysis (PMCDT) using the Bashir Endovascular Catheter in patients with intermediate-risk acute pulmonary embolism.

- **Design**: Multicenter, prospective Single arm clinical trial
Pharmaco-Mechanical Catheter Directed Thrombolysis with Bashir Endovascular Catheter

The Bashir Endovascular Catheter is not yet cleared for the treatment of Pulmonary Embolism
Potential Advantages of the Bashir Endovascular Catheter

- Wider cross-sectional distribution
- No blood loss
- Prompt restoration of blood flow
- Ease of use
- Continuous monitoring of PA pressures
- Low profile - 7F compatible

**Potential Implications:**
- Reduced duration of therapy
- Reduced dose of thrombolytics
- Reduced Major bleeding rates
- Greater efficacy
METHODS - Key Eligibility Criteria

- **Inclusion Criteria**
  1. 18 years to ≤ 75 years of age;
  2. PE symptom duration ≤ 14 days
  3. Filling defect in at least one main or lobar pulmonary artery
  4. RV/LV end diastolic diameter ratio ≥ 0.9

- **Exclusion Criteria**
  1. Active COVID 19 within last two months.
  2. CVA or TIA within one (1) year
  3. Head trauma, active intracranial or intraspinal disease
  4. Active bleeding
  5. Intracranial condition(s) that may increase the risk of bleeding
METHODS - Primary End-points

• Primary efficacy end-point:
  ▪ Reduction in CTA derived RV/LV ratio at 48 hours from the baseline.

• Primary safety end-point:
  ▪ Major bleeding and device related adverse events at 72 hours
METHODS

Secondary Efficacy End-point
PA obstruction reduction at 48 hours

*Refined Modified Miller Index* as measured on CTA within 48 hours after the completion of the r-tPA infusion compared to baseline as evaluated by core lab.
METHODS
Secondary Safety End-points

- Device related adverse events.
- All-cause mortality at 30-day follow-up.
- SAEs through 30-day follow-up.
- Recurrent PE through 30-day follow-up.

*All end-points are adjudicated by the DSMB/CEC Committee*
Rescue protocol

Unilateral PE – Total 7 mgs of rt-PA with Single device (2mgs pulse Spray and 5mgs over 5 hours)

Bilateral PE – Total 14 mgs of rt-PA with two devices (2 mgs pulse Spray and 5 mgs infusion into each PA over 5 hours)
Pulmonary Angiogram Post PM-CDT

CTA
Pre PM-CDT
RESULTS

• A total of 109 patients
• 18 U.S. sites
• October 2020 to May 2022
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristics (N=109)</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57 ± 13.3</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>33.3 ± 6.05</td>
</tr>
<tr>
<td>Male</td>
<td>67 (61.5%)</td>
</tr>
<tr>
<td>Female</td>
<td>42 (38.5%)</td>
</tr>
<tr>
<td>Caucasian/Non-Hispanic</td>
<td>64 (58.7%)</td>
</tr>
<tr>
<td>African American</td>
<td>32 (29.4%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>10 (9.2%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (2.8%)</td>
</tr>
<tr>
<td>BNP</td>
<td>1101 ± 1950 pg/ml</td>
</tr>
<tr>
<td>Troponin</td>
<td>0.52 ± 2.1 ng/ml</td>
</tr>
<tr>
<td>History of Cancer</td>
<td>17 (15.6%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>27 (24.7%)</td>
</tr>
<tr>
<td>Previous DVT</td>
<td>28 (25.7%)</td>
</tr>
<tr>
<td>History of Pulmonary Embolism</td>
<td>15 (13.8%)</td>
</tr>
</tbody>
</table>
### Pulmonary Embolism Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral Pulmonary Embolism</td>
<td>7 (6.4%)</td>
</tr>
<tr>
<td>Bilateral Pulmonary Embolism</td>
<td>102 (93.6%)</td>
</tr>
<tr>
<td>Elevated Troponin or BNP</td>
<td>98/109 (89.9%)</td>
</tr>
<tr>
<td>Elevated Troponin</td>
<td>78/109 (66.1%)</td>
</tr>
<tr>
<td>Elevated BNP</td>
<td>78/105 (74.3%)</td>
</tr>
<tr>
<td>Negative Biomarkers</td>
<td>69/109 (8.3%)</td>
</tr>
</tbody>
</table>

90% patients had both elevated biomarkers as well as right ventricular dilatation.
## RESULTS: Procedural Characteristics

### Characteristics (N=109)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total dose of rt-PA, mg</td>
<td></td>
</tr>
<tr>
<td>Unilateral PE (Pulse spray + infusion)</td>
<td>7 (2+5)</td>
</tr>
<tr>
<td>Bilateral PE (Pulse spray + infusion)</td>
<td>14 (4+10)</td>
</tr>
<tr>
<td>Total procedure time in minutes (Median ± SD)</td>
<td>64.2±28.8</td>
</tr>
<tr>
<td>Catheter placement time in minutes (Median ± SD)</td>
<td>15±14</td>
</tr>
<tr>
<td>No. of devices per patient</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>7 (6.4%)</td>
</tr>
<tr>
<td>2</td>
<td>103 (93.6%)</td>
</tr>
<tr>
<td>Completed r-tPA infusion (N=61)</td>
<td>109 (100%)</td>
</tr>
</tbody>
</table>
RESULTS

Primary Efficacy Outcome - RV/LV Ratio

33.3 % Reduction

Reduction of 0.56 ± 0.41 (95% CI: 0.48 – 0.64) p < 0.0001
## RESULTS: Primary Safety Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedural Success (n=109)</td>
<td>109 (100%)</td>
</tr>
<tr>
<td>Major Bleeding within 72 hours (ISTH) (n=109)</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>Major Device related adverse events (n=109)</td>
<td>1 (0.9%)</td>
</tr>
</tbody>
</table>
Pulmonary Artery Obstructive Index Reduction

Refined Modified Miller Index (Core Lab.)

Reduction of 8.0 ± 3.9
(95% CI: 7.3 – 8.8)

p < 0.0001

35.9% Reduction
### RESULTS: Secondary Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinically Relevant Non-Major bleeding (n=109)</td>
<td>1 (0.92%)</td>
</tr>
<tr>
<td>Non major procedure related AE <em>(n=109)</em></td>
<td>2 (1.8%)</td>
</tr>
<tr>
<td>Recurrent PE through 30-day follow-up (n=104)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>SAEs through 30-day follow up (n=104)</td>
<td>7 (6.7%)</td>
</tr>
<tr>
<td>All-cause mortality at 30 days (n=104)</td>
<td>1 (0.92%)</td>
</tr>
<tr>
<td>Intracranial Hemorrhage</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Median Hospital Length of stay in days ± SD (n=109)</td>
<td>2.88 ± 1.6</td>
</tr>
</tbody>
</table>

*epistaxis, non-access site hematoma with anemia*
Hemodynamics at 5 hours

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Baseline mean ± SD</th>
<th>Post PM-CDT mean ± SD</th>
<th>Difference mean ± SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic PA pressure, mmHg (n=93)</td>
<td>49.53 ± 13.39</td>
<td>43.74 ± 13.51</td>
<td>5.94 ± 10.69</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cardiac output, L/min (n=98)</td>
<td>4.81 ± 1.43</td>
<td>5.31 ± 1.59</td>
<td>0.49 ± 1.59</td>
<td>0.0029</td>
</tr>
<tr>
<td>Cardiac index, L/min per m² (n=98)</td>
<td>2.29 ± 0.60</td>
<td>2.47 ± 0.71</td>
<td>0.19 ± 0.76</td>
<td>0.0156</td>
</tr>
</tbody>
</table>
DISCUSSION
Thrombolytic Efficiency (Core Lab. Data)

The thrombolytic efficiency of one mg of r-tPA is higher with PM CDT
Reduction in RV/LV Ratio parallels that seen with systemic thrombolysis
DISCUSSION

Reduction in Pulmonary Artery Obstruction parallels that seen with systemic thrombolysis

DISCUSSION

Safety

Major Bleeding rates with PM-CDT parallels that seen with anticoagulation alone

Contemporary Intermediate risk PE Trials

- PETHO (ST) 11.50%
- SEATTLE II (IR) 7.00%
- OPTALYSE 3.90%
- PETHO (AC) 2.40%
- EXTRACT PE 1.70%
- FLARE 0.96%
- RESCUE 0.92%

Conclusion

The RESCUE trial showed that PMCDT with the Bashir Endovascular Catheter met its primary efficacy and safety endpoints and demonstrated:

- Reduction in RV/LV ratio by 33.3% at 48 hours (p<0.0001)
- Reduction in PA obstruction index by 35.9% at 48 hours (p<0.0001)
- There were fewer than 1% major bleeding or device related adverse events
Future perspective

- RCT to compare PM-CDT with:
  - Anticoagulation in Intermediate-risk PE patients
  - Systemic thrombolysis in high-risk PE patients.

- PE-TRACT and Hi PEITHO trials will inform us about longer term clinical and functional outcomes
RESCUE STUDY

Management team

- Steering Committee
  - Dr Akhilesh Sista (National Co-PI)
  - Dr Kenneth Rosenfield (National Co-PI)
  - Dr Anthony Comerota
- DSMB/CEC
  - Dr Gregory Piazza (Chairperson)
  - Dr Raghu Kolluri
  - Dr Robert Lookstein
  - Dr Melissa S. Martinson (Statistician)

Imaging Core lab

NAMSA/Syntactx Inc. New York NY

Enrollment by sites

Clinical Research Organization

Eminence Inc.
References

Synergistic Effect Of Endogenous And Exogenous Fibrinolysis

Rapid flow restoration
Endogenous

- Luminal filling and blood velocity
- Endogenous lytic activity\(^1,2\)

Multichannel infusion
Exogenous

- Exposure of fibrin receptors to t-PA
- Exogenous lytic activity

**Synergistic effect demonstrated in an in vitro model\(^3\)**

**FIGURE 1** Synergistic Clot Lysis by t-PA and Pro-uPA In Vitro

- Lysis by the combination of t-PA and pro-uPA
- Lysis by each alone