ACCESS PTS:
How Do I Treat My PTS Patients

Mark J Garcia MD, FSIR, FACR
Vascular & Interventional Associates of Delaware
EndoVascular Consultants, LLC
Wilmington, DE USA
The ACCESS PTS Study

ACCElerated thrombolySiS for Post-Thrombotic Syndrome using the Acoustic Pulse Thrombolysis EkoSonic(r) Endovascular System –

1 Yr Results of a Multi-center Study
Disclosures

- IAC Vein Centers: Board of Directors
- BSC: speaker, research support
- BTG/EKOS: Speaker, consultant, research support
- Philips/Volcano: speaker, consultant
- Merit Medical: Chief Medical Officer, royalties
DVT & PTS - Prevalence

• Statistics:
  – DVT: 900,000 affected (1 to 2 per 1,000) each year
  – VTE Deaths: 100,000 Americans
  – PTS: 25-50% DVT pts treated with appropriate AC
    • 8-10% develop severe PTS including ulcers
    • 600,000 venous ulcers/yr @ 3B/yr
  – Likely MILLIONS suffering from PTS

https://www.cdc.gov/ncbddd/dvt/data.html
Kahn, SR. The Post Thrombotic Syndrome. Hematology 2016; 413-418
Current Standard Of Care for PTS

Those suffering from CVOD & PTS:

AC + ECS + elevation +/- wound care

NOT Sufficient

- Pts told “Nothing we can do about it… Have to live with it”
SeQUELAE of Chronic Venous Disease

Obstructive = Post Thrombotic

Non-Obstructive = Reflux

Venous permeability

Venenous HTN

SEQUELAE
Venous Hypertension
Rationale of Intervention

If you can:
• Reduce the luminal obstruction
• Restore flow

You should be able to:
• Reduce the venous HTN
• Reduce the severity of PTS sequelae
• Improve QOL

**CAN** be accomplished!!!
Case Selection: Reserved for

- Chronic Veno-Occlusive Disease
- Symptomatic w/ PTS
- Failed conservative Rx: AC + ECS
- QOL Limitations
Initial Evaluation

- **H & P**
  - Full DVT history & w/u: obtain Heme consult
  - Includes Villalta, VCSS & VEINES QOL data
- Pictures @ each visit
- Appropriate imaging (DUS, CTV, MRV)
Initial Evaluation
ACCESS PTS Protocol

- Wt-based enoxaparin pre-procedure - 1mg/kg BID (48 hrs pre) *
- Appropriate access to obtain complete direct in-line flow *
  - If pop clean: pop access
  - If pop diseased: tibial access
- Cross occlusion using standard CTO techniques/devices
- PTA to appropriate “normal” vessel size
- EKOS lysis @ 0.5-1.0 mg/hr overnight
- F/U w/ PTA +/- pelvic stenting (to lesser troch) as needed
- Discharged on Enoxaparin 1mg/kg BID x 1 mo & ECS
- Transition to oral agent @ 1 mo
- Initiate exercise program 2-3 days post-op
- F/U @ 30, 90, 180, 365 days w/ DUS
Discharge

• ABC’s
  – Activity – inc activity after 2 days
  – Bloodthinner – Enoxaparin (1mg/kg/ 2x day) x 1 mos -> OAC
  – Compression: ECS knee-hi 20-30 mmHg “out of bed” to “in bed”
The ACCESS PTS Trial:

**ACCElerated Thrombolysis for Post-Thrombotic Syndrome Using the EKOS System**

Catheter Based Therapy for Post-Thrombotic Venous Disease
Developing Evidence

ACCESS PTS : EKOS/BTG sponsored trial

Steering Committee:

- Mark J. Garcia MD - Study PI
- Michael R. Jaff DO – VasCore (Duplex US core lab)
- Ken Ouriel MD – Syntactx (venography core lab)
- Anthony Comerota MD – Safety Monitor
- Susan Kahn MD – Clinical Consultant
- Keith Sterling MD - Consultant
ACCESS PTS

- Prospective, **multicenter** study (29 sites enrolled).
- Patients with symptomatic LE DVT \( \geq 6 \) months
- **US documented** DVT \( \geq 6 \) mos.
- **Failed** minimum 3 mos conservative Rx (AC + ECS)
- Villalta \( \geq 8 \)
• Primary Endpoints:
  – **Clinical**: Reduction of 4 on Villalta scale @ 30 days compared to baseline in at least 50% of subjects
  
  – **Technical**: Increase in blood flow calculated by time to washout in the affected segments, Baseline vs Post-EkoS Treatment.

• Interim analysis confirmed study safety
Patient Enrollment

- 1216 pts screened
- 113 pts consented
- 81 pts enrolled w/ ITT
  - 32 did not meet eligibility
  - 3 failed to cross
- 78 pts treated
- 73 pts evaluable by protocol
  - 5 pts non-evaluable per protocol @ 30d
- 85 limbs enrolled
  - 4 bilateral pts
- 82 limbs treated
- 77 limbs evaluable
# Demographics

<table>
<thead>
<tr>
<th></th>
<th>N (pts)</th>
<th>Mean</th>
<th>Median</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (yrs)</strong></td>
<td>78</td>
<td>54.6</td>
<td>54.5</td>
<td>26</td>
<td>76</td>
</tr>
<tr>
<td><strong>Weight (lbs.)</strong></td>
<td>78</td>
<td>218.4</td>
<td>219.0</td>
<td>111</td>
<td>330</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>78</td>
<td>32.1</td>
<td>31.7</td>
<td>18.2</td>
<td>48.5</td>
</tr>
</tbody>
</table>

<p>| | | | | | |</p>
<table>
<thead>
<tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td>F = 25</td>
<td>(32.1%)</td>
<td>M = 53</td>
<td>(67.9%)</td>
<td></td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td>W = 58</td>
<td>(74.4%)</td>
<td>AA = 12</td>
<td>(15.4%)</td>
<td>H = 5</td>
</tr>
</tbody>
</table>

* 78 Pts that had Rx initiated  (77 pts had 30d f/u)
### Demographics

<table>
<thead>
<tr>
<th></th>
<th>N Limbs (%)</th>
<th>Mean (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of DVT</td>
<td>82</td>
<td><strong>13.2</strong></td>
</tr>
<tr>
<td>Hx of PE</td>
<td><strong>25 (32.1%)</strong></td>
<td></td>
</tr>
<tr>
<td>Left Leg*</td>
<td>49 (60%)</td>
<td></td>
</tr>
<tr>
<td>Right Leg*</td>
<td>33 (40%)</td>
<td></td>
</tr>
</tbody>
</table>

* 78 Pts & 82 Limbs   (4 Pts had BLE DVT Treated)
DVT Location: 2/3 infrainguinal only

<table>
<thead>
<tr>
<th>Location</th>
<th>N Limbs (82)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVC</td>
<td>6</td>
<td>7.3</td>
</tr>
<tr>
<td>CIV</td>
<td>26</td>
<td>31.7</td>
</tr>
<tr>
<td>EIV</td>
<td>29</td>
<td>35.3</td>
</tr>
<tr>
<td>CFV</td>
<td>54</td>
<td>65.9</td>
</tr>
<tr>
<td>PFV</td>
<td>7</td>
<td>8.5</td>
</tr>
<tr>
<td>Pr-FV</td>
<td>63</td>
<td>76.8</td>
</tr>
<tr>
<td>Di-FV</td>
<td>69</td>
<td>84.1</td>
</tr>
<tr>
<td>Pop</td>
<td>58</td>
<td>70.7</td>
</tr>
<tr>
<td>Tibial</td>
<td>22</td>
<td>26.8</td>
</tr>
</tbody>
</table>

* 78 Pts & 82 Limbs (4 Pts had BLE DVT Treated)
# Procedural Data: EKOS & Lysis

<table>
<thead>
<tr>
<th>r-TPA</th>
<th>N (L)</th>
<th>Mean</th>
<th>Std</th>
<th>Median</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total dose (mg)</td>
<td>82</td>
<td>18.5</td>
<td>7.59</td>
<td>19.3</td>
<td>6</td>
<td>46</td>
</tr>
<tr>
<td>TPA Duration (hr)</td>
<td>82</td>
<td>22.8</td>
<td>5.70</td>
<td>22.4</td>
<td>6</td>
<td>48</td>
</tr>
<tr>
<td>US Duration (hr)</td>
<td>82</td>
<td>23.0</td>
<td>5.38</td>
<td>22.4</td>
<td>16</td>
<td>48</td>
</tr>
</tbody>
</table>

* 78 Pts w/ 82 Limbs (4 Pts had BLE DVT Treated)
## Hospitalization Data

<table>
<thead>
<tr>
<th></th>
<th>N (Pts)</th>
<th>Mean (d)</th>
<th>Std</th>
<th>Median</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU</td>
<td>25 (32%)</td>
<td>1.4</td>
<td>0.64</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>No ICU</td>
<td>53 (68%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital Stay (days)</td>
<td>78</td>
<td>3.4</td>
<td>6.11</td>
<td>2</td>
<td>1</td>
<td>38</td>
</tr>
</tbody>
</table>
Revascularization Events
(w/in 30 days)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>N Limbs (82)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 Limbs</td>
<td>(1 RT, 4 LT)</td>
<td>6.1</td>
</tr>
<tr>
<td>CDT</td>
<td>2</td>
<td>2.4</td>
</tr>
<tr>
<td>PTA</td>
<td>3</td>
<td>3.7</td>
</tr>
<tr>
<td>Stent</td>
<td>3</td>
<td>3.7</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>2.4</td>
</tr>
</tbody>
</table>

* 78 Pts w/ 82 Limbs treated
ACCESS PTS: Primary Endpoint Results

1° Endpoint Analysis:

- **Goal:** ≥ 4 pt reduction in Villalta @ 30d in 50% treated
- **Actual:** 4 pt reduction was seen in 67% of pts treated

\[ p = 0.003 \quad (95\% \text{ CI}) \]
Villalta Results

mean improvement 47.9% from baseline @ 360d

Baseline vs post treatment follow up intervals: $p \leq 0.0001$

Intent to Treat Population

Villalta Score

Baseline  | 30 Days Post | 90 Days Post | 180 Days Post | 365 Days Post
--- | --- | --- | --- | ---
15.5 | 9.7 | 8.7 |  |  

Baseline Score
## Results: Villalta Scale

<table>
<thead>
<tr>
<th></th>
<th>N (L)</th>
<th>Mean</th>
<th>Δ from Baseline</th>
<th>% Change</th>
<th>P from baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>82</td>
<td>15.5</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>30 d Post</td>
<td>79</td>
<td>9.7</td>
<td>-5.9</td>
<td>34.8%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>90 d Post</td>
<td>74</td>
<td>8.7</td>
<td>-7.0</td>
<td>42.5%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>180 d Post</td>
<td>69</td>
<td>8.0</td>
<td>-7.9</td>
<td>48.6%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>365 d Post</td>
<td>64</td>
<td>8.0</td>
<td>-8.5</td>
<td>47.9%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Change in Villalta Score: $p < 0.0001$ (95% CI) at each interval (using Mixed Model Repeated Measure - MMRM)
VCSS Results

mean improvement 42.3% from baseline @ 365d

Baseline vs post treatment follow up intervals: \( p < 0.0001 \)

Intent to Treat Population

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>30 Days Post</th>
<th>90 Days Post</th>
<th>180 Days Post</th>
<th>365 Days Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>VCSS Score</td>
<td>12.0</td>
<td>8.3</td>
<td>7.7</td>
<td>6.9</td>
<td>7.0</td>
</tr>
</tbody>
</table>
## Results: VCSS

<table>
<thead>
<tr>
<th></th>
<th>N (L)</th>
<th>Mean</th>
<th>( \Delta ) from Baseline</th>
<th>% Change</th>
<th>( P ) from baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td>82</td>
<td>12.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>30 d Post</strong></td>
<td>79</td>
<td>8.3</td>
<td>-3.8</td>
<td>27.0%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>90 d Post</strong></td>
<td>73</td>
<td>7.7</td>
<td>-4.5</td>
<td>31.4%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>180 d Post</strong></td>
<td>70</td>
<td>6.9</td>
<td>-5.2</td>
<td>40.7%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>365 d Post</strong></td>
<td>63</td>
<td>7.0</td>
<td>-5.7</td>
<td>42.3%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Change in VCSS Score: \( p < 0.0001 \) (95% CI) at each interval (using Mixed Model Repeated Measure -MMRM)
VEINES-QOL Results

mean improvement 36.2% @ 365 d

Baseline vs post treatment follow up intervals: \( p \leq 0.0001 \)

Intent to Treat Population

Baseline 61,1
30 days 71,5
90 days 78,4
180 days 80,9
365 days 79,8
## Results: VEINES-QOL

<table>
<thead>
<tr>
<th></th>
<th>N (L)</th>
<th>Mean</th>
<th>Δ from Baseline</th>
<th>% Change</th>
<th>P from baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>63</td>
<td>61.1</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>30 d Post</td>
<td>62</td>
<td>71.5</td>
<td>10.5</td>
<td>21.3%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>90 d Post</td>
<td>58</td>
<td>78.4</td>
<td>16.5</td>
<td>32.5%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>180 d Post</td>
<td>55</td>
<td>80.9</td>
<td>19.2</td>
<td>36.5%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>365 d Post</td>
<td>52</td>
<td>79.8</td>
<td>19.7</td>
<td>36.2%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Change in VEINES-QOL Score: \( p < 0.0001 \) (95% CI) at each interval (using Mixed Model Repeated Measure - MMRM)
Safety Endpoint

N = 78 Pts

- 1 Major Bleed - Epistaxis w/in 72 hrs of EKOS Rx (1.3%)
  - Related to AC
  - (died at 32 days of multi-organ failure)
- Recurrent DVT N = 3 (3.8%)
- PE N = 1 in 30 days (1.3% - 0 during hospitalization)
Study Patient 1

- 53 yo AA M w/ DVT LLE since 2009 (7 yrs)
- Non-healing ulcer x 6.5 yrs
- Baseline Villalta: 15 (ulcer), 20 total score
- EKOS CFV => Pop
- r-TPA dose 24.4 mg x 24 hrs
Study Patient 1: 30d Villalta = 15

Baseline

Post treatment
Study Patient 2

- 75 yo F w/ DVT Rt leg since Feb 2010 (>5 yrs)
- Baseline Villalta: 15 no ulcer
- R-TPA dose 20.4 mg x 22 hrs
- Adjuvant PTA
Study Patient 2

Baseline

Post Treatment
Study patient 2: 30d Villalta = 7

Baseline (15)  Post Treatment (7)
Conclusions:

- ACCESS PTS is a statistically significant Study:
  - 67% reached $1^0$ endpoint of Villalta reduction of 4 ($p = 0.003$)
  - Villalta improvement @ 30d = 6 pts & 35% ($p < 0.0001$)
  - Villalta improvement @ 365d = 8.0 pts & 48% ($p < 0.0001$)
  - VCSS improvement @ 30d = 3.8 pts & 27% ($p < 0.0001$)
  - VCSS improvement @ 365d = 5.7 pts & 42% ($p < 0.0001$)
  - VEINES QOL improvement @ 30d = 10 pts & 21% ($p < 0.0001$)
  - VEINES QOL improvement @ 365d = 19 pts & 36% ($p < 0.0001$)

** Final valuation will include DUS patency & venographic improvement
Conclusions

For Pts suffering from Chronic Veno-Occlusive Disease & PTS:

- Endovascular intervention using USCDT with PTA
  - safe & effective treatment for recanalizing chronic venous occlusions
- ACCESS PTS treatment protocol:
  - Statistically improves PTS scores & sequelae (Villalta & VCSS)
  - Statistically improves QOL (VEINES-QOL)

There is hope for PTS patients who have failed standard of care therapy
Thank You

markmd@viad.co