The ATTRACT Trial

December 2015

Almost 7 Years
Almost 700 Patients
Almost Done
...What Will We Find?

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Disclosures

- NIH-NHLBI: ATTRACT Study (U01-HL088476), & C-TRACT Study Planning Grant (U34-HL123831)
- Research support to Wash U. from industry partners:
  - Bayer Healthcare (ATTRACT)
  - BSN Medical (ATTRACT)
  - Covidien (ATTRACT)
  - Genentech (ATTRACT)
  - Volcano (VIDIO), Cook (VIVO), Therakos Inc (unrelated)
- Off-label: rt-PA for DVT; stents for iliac vein

The ATTRACT Trial

Rationale

Management of DVT guided by international guidelines
- Most influential: Evidence based clinical practice guidelines...
  - American College of Chest Physicians
  - When ATTRACT initiated

Guidelines: [Thru June, 2008]

- We recommend against the routine use of catheter-directed thrombolysis (Grade 1C)
- CDT should be confined to selected patients requiring limb salvage (Grade 1C)

...In selected patients such as:
- those with massive iliofemoral DVT at risk of limb gangrene, we suggest IV thrombolysis (Grade 2C)
- IV delivery is minimally effective
The ATTRACT Trial

**Rationale**
- Despite therapeutic anticoagulation, post-thrombotic syndrome (PTS) occurs in 25-45% at 2 years
- PTS is lifelong
- Patients at increased risk for recurrence
- Recurrent DVT increases risk and severity of PTS 6X

**Predictors of Post-Thrombotic Syndrome**
- Common femoral or iliac vein thrombosis (OR 2.23, p<0.001)
- Post-thrombotic morbidity at 1 month (p<0.001)

**Objectives of Study Design**
- Results reflect actual use of PCDT in U.S. practice – get the accurate answer!
- Results credible to PCDT proponents and skeptics – "best fair test of PCDT"
- Focus $$ on items that affect clinical decisions
- Enroll a representative cohort & accommodate diversity in practice of AC and endovascular therapy
- Structural design promotes rigor, integrity, & balance
- Rigorously evaluate PTS, QOL, and safety; limited for secondary issues

**Study Population**
- Symptomatic proximal DVT involving the iliac, common femoral, and/or femoral vein
  - stratify randomization by thrombus extent
  - actual: 60% with “iliofemoral” DVT
- EXCLUDE patients with:
  - Higher bleeding risk, CNS lesions
  - Acute limb threat or massive PE
  - Symptom duration > 2 weeks
  - Same-leg PTS or DVT < 2 yrs
  - Active cancer

**Protocol**
- Symptomatic Proximal DVT
  - Iliofemoral DVT
  - Femoral-Popliteal DVT
  - Randomized
  - Catheter-Based Thrombus RemovalDEVICE
  - Anticoagulation

**Operational separation of PI from study data**
- Allocation concealed, explicit precautions to blind assessors
- Systematic Minimization of Bias
- Comparable use of AC, anti-platelet therapy, and filters
- Central randomization stratified by site and thrombus extent
- Equal surveillance of patients in both arms
The best-validated measure to diagnose incident PTS, evaluates 5 symptoms and 6 signs of PTS, highly sensitive to mild-moderate forms of PTS.

PTS = score $\geq 5$ or presence of ulcer in index leg

692 patients provides 80% power to detect 1/3 reduction in PTS over 2 years, alpha 0.05, 2-tailed, assuming 10% loss to follow-up of randomized pts.

Primary Measure

Villalta Scale

- PTS Severity (Villalta Scale, VCSS, CEAP Clinical Class)
- QOL (SF-36, VEINES-QOL)
- Relief of pain (Likert scale) & swelling (limb circumference)
- Safety (bleeding, VTE, death) & costs (dollars per QALY)
- Mechanism (obstruction and reflux by ultrasound - VSDS)

Secondary Outcomes

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<tr>
<th>PRESENT</th>
<th>ABSENT</th>
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<tr>
<td>PTS Severity (Villalta Scale, VCSS, CEAP Clinical Class)</td>
<td>What biomarkers of clot amplification/resolution, inflammation, vascular injury can predict which patients are best-suited?</td>
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<tr>
<td>QOL (SF-36, VEINES-QOL)</td>
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<tr>
<td>Relief of pain (Likert scale) &amp; swelling (limb circumference)</td>
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<td>Safety (bleeding, VTE, death) &amp; costs (dollars per QALY)</td>
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<tr>
<td>Mechanism (obstruction and reflux by ultrasound - VSDS)</td>
<td>Collaborative opportunity for valuable future studies</td>
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ATTRACT Community

Diverse Experts, NIH, Surgeon General, Organizations

“The Surgeon General is passionate for the ATTRACT Trial to go forward” - RADM James M. Galloway, Assistant U.S. Surgeon General – June 28, 2009

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