US AneuRx Clinical Trial

10 year experience
1996-2006

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For the AneuRx clinical investigators

MEET 2007
Cannes
US AneuRx Clinical Trial
1996-1999

- Largest, prospective multicenter EVAR clinical trial
  - 1193 patients
  - 19 clinical sites
- Longest monitored follow up
  - 600 patients at 5 years
- All patients included
  - No exclusions for device changes, emergency, high-risk or off-protocol use
- Includes initial EVAR learning curve
- Follow up concluded in 2006

Inclusion criterion: aortic neck length 10 mm
## U.S. AneuRx Clinical Trial

### Patient entry 1996 - 1999

<table>
<thead>
<tr>
<th>Phase</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1</td>
<td>40 patients</td>
</tr>
<tr>
<td>Phase 2</td>
<td>424 stent graft vs. 66 open surgery</td>
</tr>
<tr>
<td>Phase 3</td>
<td>639 patients</td>
</tr>
<tr>
<td>Phase 2/3</td>
<td>90 high risk / compassionate use</td>
</tr>
<tr>
<td>TOTAL</td>
<td>1193 patients</td>
</tr>
</tbody>
</table>

Initial EVAR experience for almost all investigators in trial
# Primary Outcome Measures

**AneuRx U.S. Clinical Trial (n = 1193)**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>≤30 days</th>
<th>&gt;30 days</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aneurysm Rupture</td>
<td>5 (0.4%)</td>
<td>21 (1.8%)</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td>Aneurysm-related death</td>
<td>23 (1.9%)</td>
<td>15 (1.3%)</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td>Conversion to surgical repair</td>
<td>15 (1.2%)</td>
<td>52 (4.4%)</td>
<td>6 (0.6%)</td>
</tr>
<tr>
<td>Death (all causes)</td>
<td>23 (1.9%)</td>
<td>379 (31.8%)</td>
<td>34 (3.4%)</td>
</tr>
</tbody>
</table>

Operative mortality (30 day) 1.9 %

Includes patient data as of December 31, 2006
Freedom from Rupture

*Kaplan-Meier Analysis, n=1193*

Freedom from Intra-op, Peri-op, and Post-op Rupture

All Phase I, II, III/EU/Misc/HR Patients

97% at 5 years

599 pts. at risk at 5 years

Includes patient data as of April 27, 2007
Freedom from AAA death

*Kaplan-Meier Analysis, n=1193*

Freedom from Aneurysm-related Mortality

All Phase I,II,III/EU/Misc/HR Patients

96 %

at 5 years

601 pts. at risk at 5 years
Includes patient data as of April 27, 2007
Freedom from Surgical Conversion

*Kaplan-Meier Analysis, n=1193*

600 pts. at risk at 5 years
Includes patient data as of April 27, 2007

92% at 5 years
Freedom From Death (all cause)

*Kaplan-Meier Analysis, n=1193*

**Freedom from Death**

All Phase I,II,III/EU/Misc/HR Patients

- **60% at 5 years**

601 pts. at risk at 5 years

Includes patient data as of April 27, 2007
## Secondary Outcome Measures

**AneuRx U.S. Clinical Trial  n = 1193**

<table>
<thead>
<tr>
<th></th>
<th>1 yr</th>
<th>2 yrs</th>
<th>3 yrs</th>
<th>4 yrs</th>
<th>5 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Endoleak</strong></td>
<td>14 %</td>
<td>16 %</td>
<td>14 %</td>
<td>13 %</td>
<td>14 %</td>
</tr>
<tr>
<td><strong>Enlargement</strong></td>
<td>7 %</td>
<td>9 %</td>
<td>11 %</td>
<td>14 %</td>
<td>17 %</td>
</tr>
<tr>
<td><strong>Migration</strong></td>
<td>2 %</td>
<td>5 %</td>
<td>6 %</td>
<td>8 %</td>
<td>6 %</td>
</tr>
<tr>
<td><strong>Patency</strong></td>
<td>99%</td>
<td>98 %</td>
<td>98 %</td>
<td>95 %</td>
<td>92 %</td>
</tr>
</tbody>
</table>

Rate at each interval
Includes patient data as of December 31, 2006
Lessons learned

- Patient selection
- Technique of implantation
- Rupture and migration
- Endoleak
- Importance of proximal and distal fixation
- Device improvements
Rupture analysis

- Rupture first reported in 2000, after completion of clinical trial
- Not directly related to endoleak
  - the primary efficacy endpoint in the trial
- Related to inadequate stent graft fixation
  - Proximal aortic neck
  - Iliac limbs
  - Modular junctions
- Higher risk of rupture with 1st generation ‘stiff device’

J Vasc Surg 2001;33:S135-45
Low initial device placement

- No endoleak
- Angio at 4 months
- No treatment
- Rupture after auto accident at 9 months

Short angulated neck, device placement low, loss of proximal fixation
Initial deployment below neck

No endoleak

Migration and Rupture at 20 months

Begin Stent Ring 1.5cm below RA

Full Stent Ring 2.5cm below RA
Iliac limb fixation
Rupture at 21 months
Rupture due to poor iliac fixation
Type I endoleak

A) PRE-OP  
B) 1 MONTH  
C) 16 MONTHS  
D) 24 MONTHS  
RUPTURE

Accesory Left renal
Type II endoleak Short iliac fixation length
Left iliac Type I endoleak
Rupture due to Lack of iliac fixation
Migration analysis (n=1119)

- Predictors of AneuRx migration multivariate analysis
  - Renal-to-stent graft distance $p=.01$
  - Length of stent graft fixation $p=.04$
  - Clinical implant site $p=.007$

JVS 2003; 38: 1264
Iliac fixation not measured by Core Lab

Elimination of endoleak was primary endpoint for procedural success during AneuRx trial (1996-1999)

Iliac extenders used only to treat endoleak

No endoleak

Poor iliac fixation
Iliac fixation prevents migration

- Importance of proximal and distal fixation
- No migration if iliac fixation is good, even with suboptimal proximal fixation
Kaplan-Meier analysis

Four year freedom from migration with good iliac fixation = 100 %
The AneuRx Stent Graft: improvements in design

1st-generation
- Stiff Body design
- Pre-RPM graft material
- “Bullet” delivery system

2nd-generation
- Flex-body stent design
- RPM Graft Material

3rd-generation
- Xpedient Delivery System

4th-generation
- Resilient Graft Material

5th-generation
- Xcelerant Delivery System

AAAdvantage
- Enhanced, strategically placed RO markers
- Extended aortic body
- Contoured stent ring
- Longer, larger and flared iliac limbs

Advances since completion of clinical trial

- Device and delivery system improvements
- Understanding importance of fixation rather than primary focus on endoleak
- Advances in imaging
- Refinement of technique of insertion
AneuRx clinical trial

*a decade of experience*

1996

Elimination of endoleak

2006

renals to hypogastrics