Diagnostic and Interventional Results from the CLIP Study

Presenter: Michael R. Jaff, D.O.
Assistant Professor of Medicine
Harvard Medical School
Medical Director, Vascular Diagnostic Laboratory
Vascular Ultrasound Core Laboratory
Massachusetts General Hospital
Boston, MA
Disclosure of Conflicts:

Michael Jaff: Nothing to disclose
James Hermiller: Nothing to disclose
Charles Simonton: Nothing to disclose
Tomoaki Hinohara: Abbott Labs stockholder
Michael Mooney: Nothing to disclose
Charles O’shaughnessy: Nothing to disclose
Louis Cannon: Nothing to disclose
CLIP Trial Management:

• Principal Investigator’s:
  James Hermiller, M.D and Charles Simonton, III, M.D.

• Ultrasound Core Laboratory:
  VasCore, Boston, MA; Michael Jaff, D.O., Director

• Clinical Events Committee & DSMB:
  Harvard Clinical Research Institute (HCRI), Boston, MA; Donald Cutlip, M.D., Director

• Data Management and Analysis:
  Harvard Clinical Research Institute (HCRI), Boston, MA; Donald Cutlip, M.D., Director

• Monitoring CRO:
  J. Tyson and Associates, Salem, WI
The CLIP Study

Objective:

The objective of the CLIP Study was to evaluate the safety and efficacy of the StarClose® Vessel Closure System in achieving hemostasis following diagnostic and interventional percutaneous procedures using a randomized and controlled study design.
The CLIP Study

Background:

• The StarClose VCS is a femoral access site closure technology that utilizes a flexible nitinol clip to complete a circumferential, extravascular arteriotomy close

• The CLIP Study was performed to evaluate safety and efficacy of the StarClose VCS as compared to standard compression following 5 & 6 French diagnostic or interventional percutaneous procedures

• StarClose is currently approved by the FDA for diagnostic and interventional indications
The CLIP Study

Methods:

- 483 subjects (208 diagnostic and 275 interventional) across 17 U.S. sites were randomized at a 2:1 ratio to receive either StarClose or compression

- A roll-in phase was conducted to provide the investigators experience with the StarClose VCS prior to pivotal enrollment

- A subset of 120 interventional subjects (79 StarClose; 41 standard compression) across 5 sites underwent an ultrasound exam at the 30-day follow up visit and telephone contact at 6 months to evaluate the femoral access site complications
The CLIP Study

Methods:

A subset of 120 interventional subjects (79 StarClose; 41 standard compression) across 5 sites underwent an ultrasound exam at the 30-day follow up visit and telephone contact at 6 months to evaluate the femoral access site complications

• The duplex ultrasound (DUS) protocol was developed and implemented by an independent vascular ultrasound core laboratory with extensive experience in vascular device trials
• DUS of the common femoral artery and vein, superficial femoral artery and vein, and the saphenofemoral venous confluence were evaluated
• Duplex imaging assessed vessel patency and determined the absence or presence of iatrogenic vascular injury: hematoma, pseudoaneurysm (PSA), arteriovenous fistula (AVF), and deep vein thrombosis

Clinical Follow-up

– 180 +/- 14 days
– Assessed for any access site related complications that may have manifested since 30 day clinic visit.
The CLIP Study – Primary Safety Endpoint

Major Vascular Complications:

1. Vascular injury requiring repair via surgery, angioplasty, or other percutaneous procedure
2. New ipsilateral lower extremity ischemia requiring intervention
3. Access site-related bleeding requiring transfusion
4. Access site-related infection requiring IV antibiotics or prolonged hospitalization
5. Access site-related nerve injury requiring intervention
The CLIP Study – Secondary Safety Endpoint

Minor Vascular Complications:

1. Pseudoaneurysm or Arteriovenous fistula (AVF) documented by ultrasound
2. Access site hematoma $\geq$ 6 cm
3. Late access site-related bleeding (following hospital discharge)
4. Transient lower extremity ischemia
5. Ipsilaterial deep vein thrombosis
6. Transient access site-related nerve injury
7. Access site-related vessel injury
8. Access site wound dehiscence
9. Access site-related bleeding requiring $\geq$ 30 minutes to re-achieve hemostasis
10. Localized access site infection treated with IM or oral antibiotics
The CLIP Study – Primary Efficacy Endpoint

• Time to Hemostasis – Elapsed time between sheath removal to first observed hemostasis
The CLIP Study – Secondary Efficacy Endpoints

• Time to Ambulation – Elapsed time between sheath removal and when subjects stands and walks 20 ft without re-bleeding

• Time to Dischargeability – Elapsed time between sheath removal and when subject is medically able to be discharged based solely on the assessment of the access site

• Device Success – Attainment of final hemostasis using StarClose alone or with adjunctive compression ≤ 5 minutes and freedom from major vascular complications

• Procedure Success – Attainment of final hemostasis using any method and freedom from major vascular complications
StarClose Vascular Closure System

- Designed to close 5F and 6F puncture sites in the femoral artery following catheterization procedures
- Delivers a Nitinol clip directly to the arteriotomy for a secure, extravascular close
- Single-operator procedure
- Allows closure through the sheath, minimizing risk of infection
- Primary healing of tissue planes
StarClose Clip

- Nitinol clip
- 4mm diameter
- .008” thick
The CLIP Study - Results

30-Day Results
Diagnostic Arm
## CLIP Results: Diagnostic ITT Subjects

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>StarClose VCS N=136</th>
<th>Compression (Control) N=72</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Vascular Complications</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Minor Vascular Complications</td>
<td>2.2% (3/136)</td>
<td>1.4% (1/72)</td>
<td>1.00</td>
</tr>
<tr>
<td>Mean Time to Hemostasis (Mins)</td>
<td>1.5</td>
<td>15.5</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Time to Ambulation – Mean (Mins)</td>
<td>163</td>
<td>269</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Time to Dischargeability (Hrs)</td>
<td>3.5</td>
<td>5.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Device Success</td>
<td>89.7%</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Procedure Success</td>
<td>100%</td>
<td>100%</td>
<td>NS</td>
</tr>
</tbody>
</table>
The CLIP Study - Results

Results

Interventional Arm
## CLIP Results: Interventional ITT Subjects

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>StarClose VCS N=184</th>
<th>Compression (Control) N=91</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Vascular Complications</td>
<td>1.1% (2/184)</td>
<td>1.1% (1/91)</td>
<td>1.00</td>
</tr>
<tr>
<td>Minor Vascular Complications</td>
<td>4.3% (8/184)</td>
<td>7.7% (7/91)</td>
<td>0.107</td>
</tr>
<tr>
<td>Mean Time to Hemostasis (Mins)</td>
<td>8</td>
<td>29.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Median Time to Hemostasis (Mins)</td>
<td>.33</td>
<td>19.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Time to Ambulation – Mean (Mins)</td>
<td>407</td>
<td>466</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Device Success</td>
<td>86.8%</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Procedure Success</td>
<td>98.9%</td>
<td>98.7%</td>
<td>NS</td>
</tr>
</tbody>
</table>
The CLIP Study - Results

6 Month Results
Ultrasound Sub-study
The CLIP Study – 6 Month Results

Results: 30 Day Ultrasound

- Subject accountability was 80% (96/120) for the 30 day DUS exam
- Duplex ultrasound of 96 subjects randomized to StarClose (n=71) and compression (n=25) revealed no evidence of hematoma, PSA, or AVF in the StarClose group
- All 96 subjects demonstrated patency of the access site artery and vein without thrombosis or stenosis through 30 days
- Through 6 months there was no indication of iatrogenic vascular injury or vessel thrombosis
The CLIP Study

Results: 6 Month Clinical Results

• Subject accountability was 95.8% (115/120) at 180 days

• Rate of major vascular complications at 6 months was 1.3% (1/79) for the StarClose group and 2.4% (1/41) for the compression group (p=NS)*

• Rate of minor vascular complications at 6 months was 1.3% (1/79) for the StarClose group and 9.8% (4/41) for the compression group (p=0.046)*

• Two deaths occurred in the control group (compression) between days 30 and 180, but these were unrelated to the femoral access site

* Calculations based on number of subjects experiencing events
Ultrasound image of extravascular StarClose device
Conclusion:

- Clinical results of the CLIP Study indicate that StarClose Vascular Closure System provides a safe and effective means for closing arteriotomies in subjects undergoing percutaneous diagnostic and interventional procedures.

- StarClose VCS demonstrated a statistically significant reduction in times to hemostasis, ambulation and discharge (diagnostic population only) when compared to standard compression.

- Clinical follow-up of the ultrasound sub-study population at 6 months demonstrated that StarClose maintained its safety profile as compared to standard compression with a reduction in major (p=NS) and minor (p<.05) vascular complications.
References:

