PRESERVE Study Update
VEITH meeting

Predicting the Safety and Effectiveness of Inferior Vena Cava Filters

Disclosures
- Cook, Cordis
  - Consultant
- PRESERVE study
  - Cook
  - Cordis
  - BBraun
  - ALN
  - Bard
  - Argon
  - Volcano

IVC Filters - Why Is The FDA So Concerned

Beyond whether filters are indicated in any clinical setting, their safety remains a major question.

Few of the currently used filters have had a large multicenter safety study performed.

Most studies used as the basis for FDA clearance of the newer retrievable filters may be of insufficient size to detect unusual adverse events.

IVC Filters - Why Is The FDA So Concerned

- Caudal migrations were observed in 12% of cases
  - (10 of 85 patients with a complete data set)
- Filter fracture (1/85, 1.2%)
- Filter tilt of more than 15° (15/85, 18%)
- Leg penetration (16/61, 26%)

The FDA warning of August 2010 reported 146 cases of filter migration and 56 filter fractures among a variety of filter designs, including the G2.

Currently available studies have not pointed to these potential more severe complications of filter placement.

The FDA communication expressed the concern that these mechanical failures may be associated with the long-term placement of retrievable filters.

Unfortunately, the FDA adverse events reports cannot provide the frequency of these complications and their incidence is unknown.
Given the potential severe consequences of
- filter fracture
- filter embolisation
- vena cava penetration of filter parts
- the marked growth in their use
the SVS/SIR/FDA have designed this study
- to better understand the current use of vena filters
- and the adverse events associated with their use.

The overall goals
- Characterize current practice
- the indications
- filter type
- frequency and success of filter removal
- safety of placement initially and in the long term
- filter mechanical stability
- caval patency
- frequency of subsequent episodes of pulmonary embolism
- recurrence of deep vein thrombosis
The first steps are to identify the characteristics of use in a broad range of clinical practice settings in the US.

The PRESERVE Trial
A Prospective, Single Arm, Evaluation of the Safety and Effectiveness of Inferior Vena Cava Filters
The PRESERVE Trial

The study is a multi-center, prospective, open-label, non-randomized investigation of all commercially available inferior vena cava filters placed in subjects for the prevention of death from fatal or symptomatic PE. This study will enroll approximately 1800 IVC filter subjects at up to 60 sites in the United States. All treated subjects will be evaluated at procedure, 3-months, 6-months (phone), 12-months, 18-months (phone), and 24-months post-procedure. All subjects in whom the IVC filter is removed will be followed for 1-month post-retrieval.

Primary Safety Endpoint is a composite endpoint at 12-months that includes:
1. Freedom from clinically significant perforation after successful filter placement;
2. Freedom from filter embolization;
3. Freedom from caval thrombotic occlusion;
4. Freedom from new deep vein thrombosis (DVT); and
5. Freedom from serious adverse events (SAEs) within the peri-operative period

Primary Effectiveness Endpoint is a composite endpoint at 12-months in situ or 1-month post-retrieval (whichever comes first) that includes:
- Procedural and technical success
- Freedom from clinically significant pulmonary embolism (PE)

Secondary endpoints include the following:
- Mechanical Stability, defined by the absence of the following at the time of retrieval or at each follow up:
  - Migration: cephalad movement of the filter >20mm relative to fixed anatomic landmarks compared to the time of placement
  - Migration: caudal migration of the filter >20mm relative to fixed anatomic landmarks compared to the time of placement
  - Perforation: >5mm outside apparent cava wall as determined by CT or perforation of adjacent viscera or major vessel
  - Filter fracture: any loss of a filter’s structural integrity (i.e. breakage or separation) documented by imaging or autopsy
  - Filter embolization: post-deployment movement of the filter or its components to a distant anatomic site completely out of the target zone

Secondary endpoints include the following:
- Procedure-related complications, in the judgment of the Principal Investigator at 3-months
- Major adverse events (composite and individual components) defined as death, PE, caval thrombotic occlusion, DVT, clinically significant perforation, retroperitoneal hematoma, or adjacent organ penetration at 3-months, 6-months, 12-months, 18-months, and 24-months
- Filter tilting >15° at any time-point as determined by appropriate imaging;

Secondary endpoints include the following:
- Filter retrieval at any time
  - Attempted retrieval
  - Successful retrieval
  - Failed retrieval
  - Percentage of retrieval success
  - Complications associated with filter retrieval
  - Reasons for failed retrieval
- Secondary Effectiveness Endpoint will be calculated for each individual filter and includes freedom from PE at 12 months.

Study Design

The PRESERVE Trial
Study Design

- Multi-center, prospective, open label, non-randomized
- 60 sites in US
- 2,100 subjects
  - 300 subjects enrolled for each IVC filter from participating manufacturers
  - Site Limits: 45 subjects per filter; 210 subjects overall
- Secondary Effectiveness Endpoint
  - Will allow potential labeling expansion

Impact of PRESERVE

- Largest dataset on IVC Filters
- Major paradigm-shift from traditional trial design & data collection
- Real world evidence to support regulatory decision-making for medical devices

Enrollment update

Enrollment Accrual as of 11/09

Enrollment by Filter Type as of 11/09

Site Updates
Top Enrolling Sites as of 11/09

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<th># Subjects</th>
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<td>Sarasota Memorial Hospital</td>
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Leader Board by Filter as of 11/09

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<th>Filter</th>
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<th>Specialty</th>
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Study Updates

- 4 of 6 filters have reached their enrollment goal of 300 subjects.
- Accrual rate for other two filters is 1-3 per month combined.
- Loss to follow-up is currently running at approximately 6 subjects per month.
- PRESERVE plans to end enrollment into the study in December 2018. All subjects enrolled at that time will be followed for 2 years, per protocol.

Study Updates

- Power calculations based on current lost to follow-up rates and projected sample sizes at end of study, show we would have sufficient power to test the primary and secondary hypotheses of interest for the 4 filters that have enrolled 300 subjects.
- Calculations assume current lost to follow-up rates do not worsen.

Study Updates

- For the remaining 2 filters, there will be insufficient power to assess the secondary effectiveness endpoint, that may allow a labeling change.
- For these 2 filters, further data collection outside of PRESERVE may be a way forward.
- The FDA has been made aware of the planned change. Since the analysis will not changed, the Agency has stated they do not need to approve the change.
Save the Date!

SIR Annual Meeting 2019
Austin, Texas

- PRESERVE Investigator Meeting
  - Saturday, March 23, 2019
  - Time TBD

Please RSVP at: PRESERVE@neriscience.com