One-Year Analysis of the Prospective Multicenter SENTRY Clinical Trial: Safety and Effectiveness of the Novate Sentry Bioconvertible Inferior Vena Cava Filter

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ABSTRACT

Purpose: To prospectively assess the Sentry bioconvertible inferior vena cava (IVC) filter in patients requiring temporary protection against pulmonary embolism (PE).

Materials and Methods: At 23 sites, 129 patients with documented deep vein thrombosis (DVT) or PE, or at temporary risk of developing DVT or PE, unable to use anticoagulation were enrolled. The primary end point was clinical success, including successful filter deployment, freedom from new symptomatic PE through 60 days before filter bioconversion, and 6-month freedom from filter-related complications. Patients were monitored by means of radiography, computerized tomography (CT), and CT venography to assess filtering configuration through 60 days, filter bioconversion, and incidence of PE and filter-related complications through 12 months.

Results: Clinical success was achieved in 111 of 114 evaluable patients (97.4%, 95% confidence interval [CI] 97.1%–99.1%). The rate of freedom from new symptomatic PE through 60 days was 100% (n = 129, 95% CI 97.1%–100.0%), and there were no cases of PE through 12 months for either therapeutic or prophylactic indications. Two patients (1.6%) developed symptomatic caval thrombosis during the first month; neither experienced recurrence after successful interventions. There was no filter tilting, migration, embolization, fracture, or caval perforation by the filter, and no filter-related death through 12 months. Filter bioconversion was successful for 95.7% (110/115) at 6 months and for 96.4% (106/110) at 12 months.

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M.D.Dak. receives personal fees from Cook Medical (Bloomington, Indiana) and Novate Medical (Galway, Ireland). T.P.M. receives a research grant from Novate Medical. A.H.K receives personal fees and grants from Altura Medical (Menlo Park, California) and PQ Bypass (Sunnyvale, California). M.J.S. receives grants from ALN International (Miami, Florida), Argon Medical Devices (Frisco, Texas), B. Braun (Mesulungen, Germany), C.R. Bard (Murray Hill, New Jersey), Cook Medical, and Cordis Corporation (Milton, Florida), and personal fees from Avantec Vascular Corporation (Sunnyvale, California), Boston Scientific (Marlborough, Massachusetts), and Cook Medical. J.L.S. is an investor in Brightwater Medical (Murieta, California). G.M.A. is a paid consultant for Cook Medical, C.R. Bard, and Novate Medical. M.J.S. receives personal fees from Boston Scientific, Bristol Myers/Pfizer (Princeton, New Jersey), Cook Medical, and Gore Medical (Flagstaff, Arizona), grants from National Institutes of Health (Bethesda, Maryland), and is a board member of Cortego Medical (Raleigh, North Carolina). None of the other authors have identified a conflict of interest.

Appendices A–E can be found by accessing the online version of this article on www.jvir.org and clicking on the Supplemental Material tab.

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J Vasc Interv Radiol 2018; 29:1350–1361

https://doi.org/10.1016/j.jvir.2018.05.009
Pulmonary embolism (PE) leads to the hospitalization or death of approximately 225,000 Americans, 30,000 Canadians, and 300,000 Europeans per year, the incidence having increased during the past decade (1,2). In the United States, estimates of the nonfatal occurrence of PE range from 400,000 to 630,000 cases per year (3), and PE is the leading cause of preventable in-hospital mortality (4), with estimated annual cumulative costs ranging from $8.5 billion to $19.8 billion (5). Risk factors for PE include a history of deep vein thrombosis (DVT), recent surgical procedures, hospitalization for cancer and chronic conditions, prolonged inactivity or immobility, traumatic injury, obesity, and advanced age (6). The vast majority of PEs occur within 30 days of the index event (hospitalization, trauma, surgery) (7–9).

Whereas pharmacologic management with the use of anticoagulant agents is the established primary treatment for venous thromboembolic (VTE) disease, for many patients anticoagulation is ineffective, is contraindicated, or has to be discontinued during periods of high PE risk. Inferior vena cava (IVC) filters are recommended for these situations in accordance with careful selection criteria (3,10–12). In response to complications, such as IVC thrombosis, that have been associated with permanent IVC filters, retrievable devices have been available since 2003 for protection from PE during recognized periods of transient risk (13). However, even with the increased education and patient-tracking initiatives following the April 2010 US Food and Drug Administration (FDA) safety communication (updated in May 2014) advising prompt filter retrieval “as soon as protection from pulmonary embolism is no longer needed” (11,14,15), as many as 65%–80% of filters remain unretrieved, with an associated time-dependent increase in retrievable-filter–specific complications, including device tilting, fracture, migration, embolization, thrombosis, IVC perforation, surgery, and death (4,16–21). Prolonged indwelling time also increases the risk of failure and complications if filter retrieval is attempted (4,22).

The Sentry bioconvertible IVC filter (Novate Medical, Galway, Ireland) is designed to provide temporary protection against PE during transient high-risk periods and then to bioconvert, avoiding the need for a second (retrieval) intervention and leaving a patent IVC lumen. Bioconversion is defined as the release of filter arms from the filtering cone in the central portion of the IVC lumen after hydrolytic degradation of the bioabsorbable filament. Through 180 days in a preclinical study on the Sentry filter in an ovine model, there were no filter-related complications, and the devices were all bioconverted and stably incorporated, leaving all IVCs patent (23). Interim results are reported here from a prospective trial undertaken to evaluate the safety and efficacy of the Sentry IVC filter in patients with documented DVT or PE, or at temporary risk of developing DVT or PE, and with a contraindication to anticoagulation.

**MATERIALS AND METHODS**

**Study Design and Conduct**

The prospective, multicenter, nonrandomized, single-arm SENTRY Clinical Trial was conducted at 23 sites in the United States (n = 20), Belgium (n = 2), and Chile (n = 1). The protocol was approved by the appropriate Institutional Review Boards or Ethics Committees, and all study procedures were performed in accordance with the guidelines of good clinical practice and applicable regulations. Novate Medical was the sole sponsor of the study, which was conducted under an investigational device exemption (IDE G110111), in compliance with applicable provisions of 21 CFR Parts 50, 54, and 812 and in accordance with the ethical principles of the Declaration of Helsinki. The study was registered before the start of patient enrollment (ClinicalTrials.gov ID NCT01975090).

Patients eligible for inclusion were at least 18 years of age and were determined by their physicians to be at a temporary (<60 days) risk of PE. All patients had documented DVT or PE or a high risk of developing DVT or PE and had a contraindication to or failure of anticoagulation. The indications for enrollment were consistent with American College of Radiology (ACR) and Society of Interventional Radiology (SIR) practice and quality improvement guidelines (3,12). The SENTRY trial administrative structure is summarized and the determination of patient eligibility is elaborated in Appendix A (available online on the article’s Supplemental Material page at www.jvir.org).

**Patient Population**

A total of 129 patients were enrolled from September 2014 to February 2016. Baseline patient characteristics and medical history are detailed in Table 1. The patient indications for filter placement and the reasons for inability to use anticoagulation therapy are summarized in Table 2. Of the 129 patients, 87 (67.4%) met the criteria for a therapeutic intervention—including current DVT and PE (14.0%), PE only (8.5%), and DVT only (45.0%)—whereas 42 (32.6%) met the criteria for a prophylactic filter placement. All 129 patients had

**Conclusions:** The Sentry IVC filter provided safe and effective protection against PE, with a high rate of intended bioconversion and a low rate of device-related complications, through 12 months of imaging-intense follow-up.

**ABBREVIATIONS**

CEC = clinical events committee, CI = confidence interval, DVT = deep vein thrombosis, FDA = US Food and Drug Administration, IDE = investigational device exemption, IVC = inferior vena cava, PE = pulmonary embolism, SAE = serious adverse event, VTE = venous thromboembolism
Visual Synopsis

Safety and effectiveness outcomes through 1 year with the Sentry Bioconvertible Inferior Vena Cava Filter

Enrollment
N = 129 patients

Therapeutic indication
n = 87

Prophylactic indication
n = 42

Percentage of patients

<table>
<thead>
<tr>
<th>Technical success¹</th>
<th>Freedom from symptomatic PE through 60 days²</th>
<th>Freedom from filter-related complications through 6 months¹²</th>
<th>Devices in full filtering configuration²</th>
<th>Devices bioconverted⁴</th>
<th>Freedom from symptomatic PE through 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>100%</td>
<td>98.2%</td>
<td>100%</td>
<td>95.3%</td>
<td>95.7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>96.4%</td>
<td>100%</td>
<td></td>
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</tbody>
</table>

Clinical success (the primary composite endpoint) was achieved in 111 of 114 evaluable patients (97.4%, 95% CI 92.5%–99.1%), and device deployment was successful in all patients. The Sentry IVC filter provided safe and effective protection against pulmonary embolism (PE), regardless of whether the indication for device placement was therapeutic or prophylactic, with a high rate of intended bioconversion and a low rate of device-related complications through 12 months of imaging-intense follow-up.

¹Component of the composite primary efficacy endpoint.

²Filter-related imaging complications could have included tilting, migration, perforation, embolization, or fracture. Filter-related symptomatic complications could have included filter-related death, symptomatic caval thrombosis, or other symptomatic complications requiring invasive intervention. The only reported filter-related complications were two cases of symptomatic caval thrombosis during the first month of follow-up, neither of which recurred after successful intervention.

³The device was in filtering configuration when all 6 pairs of arms were being held together in the central portion of the IVC lumen.

⁴Bioconversion was defined as the release of filter arms from the filtering cone in the central portion of the IVC lumen after hydrolytic degradation of the bioabsorbable filament.
permanent or temporary inability to use anticoagulation. Some patients had more than 1 contraindication.

Table 1. Baseline Patient Characteristics, Medical History, and Risk Factors (n = 129)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>Mean ± SD 62.6 ± 13.52</td>
</tr>
<tr>
<td></td>
<td>Range 21.0–88.0</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>73 (56.6%)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>Mean ± SD 30.5 ± 8.38</td>
</tr>
<tr>
<td></td>
<td>Range 17.3–78.1</td>
</tr>
<tr>
<td>WHO BMI category (kg/m²), n (%)</td>
<td>Underweight (&lt;18.5) 2 (1.6)</td>
</tr>
<tr>
<td></td>
<td>Normal weight (18.5 to &lt;25.0) 24 (18.6)</td>
</tr>
<tr>
<td></td>
<td>Overweight (25.0 to &lt;30.0) 45 (34.9)</td>
</tr>
<tr>
<td></td>
<td>Obese class I (30.0 to &lt;35.0) 29 (22.4)</td>
</tr>
<tr>
<td></td>
<td>Obese class II (35.0 to &lt;40.0) 18 (14.0)</td>
</tr>
<tr>
<td></td>
<td>Obese class III (≥40.0) 11 (8.5)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td>White (non-Hispanic) 107 (82.9)</td>
</tr>
<tr>
<td></td>
<td>Black 11 (8.5)</td>
</tr>
<tr>
<td></td>
<td>Hispanic 9 (7.0)</td>
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<tr>
<td></td>
<td>Unknown 2 (1.6)</td>
</tr>
<tr>
<td>Medical history/risk factors, n (%)</td>
<td>Hypertension 76 (58.9)</td>
</tr>
<tr>
<td></td>
<td>Recent surgery (≤30 d) 33 (25.6)</td>
</tr>
<tr>
<td></td>
<td>Diabetes 28 (21.7)</td>
</tr>
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<td></td>
<td>Malignancy 23 (17.8)</td>
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<td></td>
<td>Current smoker 21 (16.3)</td>
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<td></td>
<td>Morbid obesity 20 (15.5)</td>
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<tr>
<td></td>
<td>Chronic pulmonary disease 18 (14.0)</td>
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<tr>
<td></td>
<td>Gastrointestinal bleeding 17 (13.2)</td>
</tr>
<tr>
<td></td>
<td>Cerebrovascular event 16 (12.4)</td>
</tr>
<tr>
<td></td>
<td>Ischemic heart disease 15 (11.6)</td>
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<tr>
<td></td>
<td>Myocardial infarction 13 (10.1)</td>
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<tr>
<td></td>
<td>Congestive heart failure 12 (9.3)</td>
</tr>
<tr>
<td></td>
<td>Renal insufficiency/failure 11 (8.5)</td>
</tr>
<tr>
<td></td>
<td>Urogenital bleeding 8 (6.2)</td>
</tr>
<tr>
<td></td>
<td>Liver insufficiency/failure 6 (4.7)</td>
</tr>
<tr>
<td></td>
<td>Hormone replacement therapy 5 (3.9)</td>
</tr>
<tr>
<td></td>
<td>Respiratory failure 4 (3.1)</td>
</tr>
<tr>
<td></td>
<td>Pacemaker or defibrillator 4 (3.1)</td>
</tr>
</tbody>
</table>

BMI = body mass index; WHO = World Health Organization.

Study Device and Procedure
The Sentry IVC filter (Fig 1) is made from a single piece of laser-cut nitinol, which is formed into a cylindrical frame with an integral filter cone consisting of 6 pairs of arms held together in the center of the IVC by means of a bioabsorbable filament composed of poly-p-dioxanone, a biodegradable synthetic polymer. During bioconversion, the bioabsorbable filament hydrolyzes, releasing the filtering arms from the filtering cone. The filtering arms then retract to the IVC wall into a nonfiltering configuration. This design allows temporary protection against PE followed by restoration of IVC lumen patency. The Sentry is indicated for use in IVCs with diameters of 16–28 mm and has a maximum deployed length of 57.7 mm. Detailed description of the Sentry filter and the implantation procedure is provided in Appendix B (available online on the article’s Supplemental Material page at www.jvir.org).

Study Follow-up and Imaging Evaluation
After device implantation, according to an intensive FDA-approved schedule, patients were evaluated at 1 month (range 30–44 days), 2 months (60–67 days), 6 months (150–210 days), and 12 months (335–395 days). Each follow-up visit included clinical assessment for symptoms of PE and DVT, monitoring of adverse events, and assessment of VTE risk factors. Imaging for filter configuration and...
complications was performed with the use of ultrasonography of the lower extremities and computerized tomographic (CT) venography at 1 month and anterior-posterior and lateral x-ray (or by CT venography if thrombus was observed at 1 month) at 2 months. Imaging for filter bioconversion status and complications was performed with the use of CT at 6 months, anterior-posterior and lateral x-ray at 12 months, and CT venography at 24 months. The study core laboratory reviewed all CT imaging for filtering status, the presence of thrombus, and filter-related complications.

Study End Points
Study end points were formulated in accordance with SIR reporting standards (24) and ACR guidelines (3) and with reference to recent IDE studies (25–28). The predefined primary end point was clinical success at 6 months, a composite of technical success (filter deployment as intended without acute events), freedom from symptomatic PE through 60 days, and 6-month freedom from filter-related complications, including tilting, migration, embolization, fracture, perforation, symptomatic caval thrombosis, any other symptomatic filter-related complication requiring invasive intervention, or filter-related death.

Secondary efficacy end points included: the technical success rate at day 0; filter status at months 1 and 2 (the percentage of patients with devices in filtering configuration, based on all 6 pairs of arms being held together in the central portion of the IVC lumen, and the percentage in nonfiltering configuration with arms separated from the central portion of the lumen); bioconversion status at months 6, 12, and 24 (the percentages bioconverted and the percentages not converted); and new symptomatic PE through 6, 12, and 24 months. Secondary and safety end points are further specified and defined in Appendix C (available online on the article’s Supplemental Material page at www.jvir.org).

Statistical Analysis
For the statistical analysis on the primary end point of clinical success at 6 months, the observed rate was tested against the acceptance criterion by means of the 2-sided 95% Wilson confidence interval (CI) for the binomial proportion. If the lower confidence limit for the true proportion was ≥ 80%, the end point was deemed to be successfully achieved. In accordance with the calculation outlined in the study protocol, a sample size of 108 patients at 6 months was determined to be sufficient to test the primary end point statistical hypothesis. For the secondary end points and other clinical outcomes data, the number and percentage of observed patients for each end point were determined, and where appropriate the 2-sided 95% CI using the Wilson score interval around the proportion was calculated. Baseline patient characteristics and medical history were summarized with the use of statistics including frequency counts and percentages for categorical variables and means and SDs for continuous variables.

RESULTS
A total of 63 investigators performed the implantations of the Sentry IVC filter in 129 patients at 23 sites. Study patient disposition through 12 months is detailed in Figure 2.

Filter Placement Procedures
A Sentry device was successfully implanted in all 129 patients. In 1 patient the filter could not be advanced through the introducer sheath (owing to resistance experienced by the investigator) in the left femoral vein. In that case, a second Sentry filter was successfully deployed via the same left femoral vein, and there were no clinical sequelae
Filter Efficacy Outcomes

Results for the composite primary filter efficacy end point of clinical success at 6 months are detailed in Table 3. All 3 of the component criteria were met by 111 (97.4%) of 114 patients evaluable for the composite end point (95% CI 92.5%–99.1%). Because the 92.5% lower limit of the 95% CI exceeds 80%, the Sentry IVC filter passed the predefined acceptance criteria for demonstrating efficacy on the clinical success end point. Technical success of deployment was achieved in 99.2% (129/130) of deployment attempts (95% CI 95.8%–99.9%). The rate of freedom from new symptomatic PE through 60 days was 100% (n = 129; 95% CI 97.1%–100.0%), regardless of whether the indication for device placement was therapeutic or prophylactic. The rate of freedom from IVC filter–related complications through 6 months was 98.2% (112/114, 95% CI 93.8%–99.5%), based on findings of symptomatic caval thrombosis in 2 patients—1 with a therapeutic indication and 1 with a prophylactic indication—during the first month of follow-up. The 2 cases of caval thrombosis were adjudicated by the the clinical events committee (CEC) as serious adverse events having an unknown relationship to the device and procedure, because it was not possible to determine whether the thrombus was captured by or generated by the filter. After successful treatment with thrombectomy and thrombolysis in both cases of symptomatic caval thrombosis, the 2-month follow-up confirmed that the filter was in correct filtering configuration, and there was no recurrence of the caval thrombosis in either patient (Appendix D [available online on the article’s Supplemental Material page at www.jvir.org]). Through 12-month follow-up, no further cases of symptomatic caval thrombosis were noted.

No new symptomatic PEs were noted (Table 3), and there were no other imaging or symptomatic filter-related complications at the scheduled follow-up visits through 12 months. There were no deaths adjudicated to be filter related.

Filter Configuration and Bioconversion Results

The Sentry is designed to provide filtering protection for a minimum duration of 60 days and then to bioconvert to a nonfiltering configuration when the bioabsorbable filament hydrolyzes, releasing the filter arms for retraction to the IVC wall. Table 4 summarizes the filter status for all patients with imaging assessment at 1 and 2 months and the bioconversion status for all patients with imaging assessment at 6 and 12 months. Figure 3 presents representative CT imaging for a single patient. At the 1-month follow-up, 100% of the devices (119/119) were in filtering configuration, and at the 2-month follow-up, 95.3% (101/106) remained in filtering configuration. Through follow-up of ≥12 months, there were no device-related adverse events or new symptomatic PE in the 5 patients whose devices were not in full filtering
configuration at the 2-month follow-up (which occurred from days 61 to 67).

At the 6-month follow-up, 95.7% of the filters (110/115) were confirmed by the core laboratory to be bioconverted. Through 12 months there were no new DVT, PE, or IVC filter–related complications reported in any of the 5 patients whose devices were not bioconverted at 6 months, and by 12-month follow-up 3 of the 5 devices had bioconverted. On all CT imaging performed at any time point, there were no instances of filter perforation of the IVC wall.

### Secondary VTE Outcomes

All patients available for follow-up were reported to be free from new symptomatic PE through 60 days (n = 126), 6 months (n = 117), and 12 months (n = 111). Ultrasonography of the lower extremities was performed ≤7 days before the index procedure and at 1-month follow-up to assess for the presence of DVT. After 1 month, there was no protocol-mandated lower-extremity imaging, and DVT status was assessed based on symptoms and any site-performed imaging that was part of follow-up of high-risk patients. Through 60 days, the rate of new or worsening DVT was 7.8% (10/129). There were 8 cases of new DVT and 3 cases of worsening DVT confirmed by the CEC in 10 patients. One patient experienced both a new and a worsening DVT (Appendix E [available online on the article’s Supplemental Material page at www.jvir.org]). The protocol-mandated 1-month CT venography revealed the presence of thrombus in the filters of 18 (15.8%) of 114 patients with core laboratory review. The thrombus was symptomatic only in the 2 noted cases of symptomatic caval thrombosis (Appendix E [available online on the article’s Supplemental Material page at www.jvir.org]).

In 2 cases in which patients developed new transient VTE risks after the 60-day protection period, the placement of a second IVC filter (a Günther Tulip [Cook Medical, Bloomington, Indiana]) was required above the bioconverted study device. In the first of these 2 cases, the patient was readmitted for epistaxis 125 days after the index procedure, and warfarin was stopped and reversed. In this patient, the new implantation was adjudicated to be due not to the study device or the index procedure but to the new VTE risk (contraindication to anticoagulation due to epistaxis). The

### Table 3. Filter Efficacy Outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>n (%)</th>
<th>95% CI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary composite end point of clinical success at 6 months</td>
<td>111/114 (97.4)</td>
<td>92.5–99.1</td>
</tr>
</tbody>
</table>

#### Components of the primary composite end point

| Technical success per filter deployment attempt* | 129/130 (99.2) | 95.8–99.9 |

#### Through 60 days

| Symptomatic PE | 0/129 (0) | 0/126 (0) | 0/117 (0) |

#### 61–210 days

| Symptomatic PE | 0/129 (0) | 0/126 (0) | 0/117 (0) |

#### 211–395 days

| Symptomatic PE | 0/114 (0) | 0/114 (0) | 0/114 (0) |

#### Filter-related imaging complication

| Tilting | 0 (0) | 0 (0) | 0 (0) |
| Migration | 0 (0) | 0 (0) | 0 (0) |
| Perforation | 0 (0) | 0 (0) | 0 (0) |
| Embolization | 0 (0) | 0 (0) | 0 (0) |
| Fracture | 0 (0) | 0 (0) | 0 (0) |
| Any imaging complication | 0 (0) | 0 (0) | 0 (0) |

#### Filter-related symptomatic complication

| Filter-related death | 0 (0) | 0 (0) | 0 (0) |
| Symptomatic caval thrombosis† | 2 (1.6) | 0 (0) | 0 (0) |
| Other symptomatic complications requiring invasive intervention | 0 (0) | 0 (0) | 0 (0) |

CI = confidence interval; PE = pulmonary embolism.

*One deployment failure occurred when the filter could not be advanced through the introducer sheath in the left femoral vein; a second Sentry filter was successfully deployed via the same left femoral vein, and there were no clinical sequelae.

†Two cases of symptomatic caval thrombosis developed and were successfully treated during the first month of follow-up.

‡Of the 115 patients who underwent the protocol-mandated 6-month imaging, 1 patient was imaged 2 days before the beginning of the window for 6-month imaging and was not included in the denominator for this end point.
second patient had been originally enrolled after an open cystoprostatectomy for small-cell bladder cancer and recent gastrointestinal bleeding. The new filter implantation was performed when a hemorrhagic brain metastasis was identified 137 days after the index procedure. This event also was considered to be due to a new VTE risk involving contraindication to anticoagulation and not to the study device or index procedure.

Safety
In the entire safety analysis population of 129 patients, ≥1 adverse events were experienced by a total of 85 (65.9%) through 210 days after implantation (the end of the window for 6-month follow-up) and by 58 (49.6%) from 211 to 395 days (the end of the window for 12-month follow-up). One or more serious adverse events were experienced by 47 patients (36.4%) through 210 days after implantation and by 16 patients (13.7%) from 211 to 395 days (Table 5). None of the serious adverse events were confirmed by the CEC as being related to the filter. One case of a new symptomatic DVT—swelling in the right leg, with ultrasonography showing clotting extending from the filter down into the right iliac vein and to the right calf—with onset 8 days after the index filter implantation was adjudicated to be procedure related, due to access site thrombosis. After treatment with anticoagulation, the Sentry device was in filtering configuration at 1- and 2-months follow-ups and was confirmed to be bioconverted at 6 months, with the patient experiencing no further clinical events. None of the 12 deaths through 12 months (due to cancer [n = 3], cardiopulmonary arrest [n = 2], respiratory failure [n = 3], multiorgan failure, hypertensive cardiovascular disease, liver failure, and myasthenia gravis) were related to the Sentry filter or to the index procedure, as reported by the sites and confirmed by CEC adjudication.

At study baseline, all 129 enrolled patients were reported by the sites to have permanent, temporary, or predicted contraindications to anticoagulation. The overall anticoagulation status of the patients changed as their conditions progressed during the course of the study, and when there was no longer a contraindication, the decision whether to administer anticoagulation was left to each individual physician (Table 6).

DISCUSSION
In the present imaging-intense IDE trial of the Sentry bioconvertible IVC filter, the composite primary end point of clinical success at 6 months was achieved in 97.4% of evaluable patients (111/114), with the 92.5% lower limit of the 95% CI surpassing the 80% SIR trial performance objective. The 3 failures on the composite end point included the need for a second (successful) implantation attempt in 1 patient and the occurrence within the first month of symptomatic caval thrombosis in 1 patient with a therapeutic indication and in 1 with a prophylactic indication (both cases adjudicated to have an unknown relationship to the device and procedure, successfully treated with thrombectomy and thrombolysis, and subsequently showing no recurrence). The 99.2% rate of deployment technical success exceeded the established 97% SIR threshold value (12).

There were no cases of new symptomatic PE through 60 days before filter bioconversion and this extended through the 12-month follow-up. This outcome compares favorably with 6-month PE rates ranging from 1% to 8% in recent trials of retrievable IVC filters (25–29). Through 60 days, the incidence of new or worsening DVT was 7.8% (10/129), similar to recent findings for retrievable filters (25–29) and considerably better than the rates reported for permanent filters in the PREPIC study (30); none of the DVTs were confirmed to be device related, and 1 that occurred at 8 days was considered to be procedure related. Of the 18 patients with confirmed thrombus in their filters at protocol-mandated 1-month CT venography, only 2 (the cases of caval thrombosis) were symptomatic, and there were no further VTE-related events, symptomatic PE, or adverse events either before or after the bioconversion of their filters for those patients.

Through the scheduled follow-ups at 1, 2, 6, and 12 months, there was no filter tilting, migration, perforation, embolization, fracture, or filter-related death noted. Allowing

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Filtering status through 60 days</td>
<td>126</td>
</tr>
<tr>
<td>Filters in filtering configuration</td>
<td>129 (100.0)</td>
</tr>
<tr>
<td>95% CI (%)</td>
<td>97.1–100.0</td>
</tr>
<tr>
<td>1-month imaging</td>
<td>119</td>
</tr>
<tr>
<td>Filters in filtering configuration</td>
<td>119 (100.0)</td>
</tr>
<tr>
<td>95% CI (%)</td>
<td>96.9–100.0</td>
</tr>
<tr>
<td>2-month imaging</td>
<td>106</td>
</tr>
<tr>
<td>Filters in filtering configuration</td>
<td>101 (95.3)</td>
</tr>
<tr>
<td>95% CI (%)</td>
<td>89.4–98.0</td>
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</tbody>
</table>

Filter bioconversion status

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filtering configuration at 1- and 2-months follow-ups</td>
<td>101 (95.3)</td>
</tr>
<tr>
<td>Filters remaining held in the central portion = 106; not bioconverted = 5 (4.3)</td>
<td></td>
</tr>
<tr>
<td>95% CI (%)</td>
<td>90.2–98.1</td>
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<tr>
<td>12 months = 106 (96.4); not bioconverted = 4 (3.6)</td>
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<tr>
<td>95% CI (%)</td>
<td>91.0–98.6</td>
</tr>
<tr>
<td>6 months = 90 (95.7); not bioconverted = 5 (4.3)</td>
<td></td>
</tr>
<tr>
<td>95% CI (%)</td>
<td>91.9–98.0</td>
</tr>
<tr>
<td>12 months = 106 (96.4); not bioconverted = 4 (3.6)</td>
<td></td>
</tr>
<tr>
<td>95% CI (%)</td>
<td>94.9–98.0</td>
</tr>
</tbody>
</table>

CI = confidence interval.

*Filtering configuration: all 6 filter arms held in the central portion of the IVC lumen.
†Bioconverted: ≥1 filter arm separated from the central portion of the IVC lumen; not bioconverted: all 6 filter arms remaining held in the central portion of the IVC lumen.
for the 2 successfully resolved cases of symptomatic caval thrombosis, the rate of freedom from IVC filter-related complications through 6 months was 98.2% (112/114), and there were no further cases of symptomatic caval thrombosis through 12 months. In comparison, device-related complications have been a matter of increasing concern with indwelling retrievable IVC filters and have been found to occur at a greater rate than with permanent filters (17,19,22). The need to develop devices that will effectively trap emboli and preserve retrievability has resulted in design compromises that appear to be associated with less secure implantation than the permanent filters (21), leading to complications such as tilting, migration, embolization, perforation, and fracture (21,31). Although the majority of retrievable IVC filters are placed to provide short-term protection against PE after index events including surgery, trauma, and hospitalization, rates of retrieval vary widely between centers and are often as low as 20%–35% (20,21), despite the 2010 FDA safety communication about the potential for long-term complications, which was updated in 2014 (4,7,16,27,32). The factors that have been noted as responsible for retrievable filters being left in place for long periods or permanently include technical failure during retrieval attempts, endothelialization, and lack of patient compliance (4,11,14,22). Whereas the rate of filter retrieval may not have increased appreciably since the FDA advisory, a recent study has documented a 29.0% decrease in IVC filter placement from 2010 to 2014 while the rate of hospitalizations related to VTE remained steady (33).

Regarding the design concept and rationale for the Sentry IVC filter to provide protection until bioconversion after 60 days after implantation, contemporary data support the premise that the period of highest risk for PE in

Figure 3. Representative CT imaging for a single patient. (a) Coronal image acquired as part of helical dataset 1 month after filter placement, showing the Sentry device in filtering configuration. (b) Coronal image at 6-month follow-up showing the device in bioconverted configuration. (c-e) Axial views of the bioconverted device at 6-month follow-up, with the images keyed to the coronal view in (b).
patients with temporary contraindications to anticoagu-
lants occurs early. In one study in a group of trauma pa-
tients, the average time from injury to PE was determined
to be 7.9 days (34), and other studies have found that the
majority of trauma-related PE occur < 30 days after
the index event (7–9). In studies of postoperative PE, the
mean time from surgery to PE was 3–20 days (10,35,36).
The majority of inpatient PE after orthopedic surgery
occur by 35 days after the procedure (37,38). According to
a decision analysis with mathematical modeling developed
by the FDA, if the transient risk for PE has passed, the
risk/benefit profile begins to favor removal of a retrievable
filter from 29 to 54 days after the index implantation (14).
The protection period of up to 60 days offered by the
Sentry filter extends comfortably beyond the term of risk
demonstrated by these data. Indeed, in this trial no patients
required an extension of the protection period, and no
patients suffered a new symptomatic PE at any time point
through the current 12-month follow-up.

In the present study, 100% of the filters were in stable
filtering configuration at the 1-month protocol-mandated
imaging, and 95.3% remained so at 2 months. Then
95.7% had successfully bioconverted by 6 months, and at
the 12-month follow-up 96.4% (106/110) were con-
firmed to be bioconverted. The rate of bioconversion for the Sentry
filter contrasts favorably with the retrieval rates (as noted
above) for retrievable filters. The efficacy and safety out-
comes for the Sentry through 12 months contrast favorably
with the noted occurrence of long-term complications
associated with indwelling retrievable filters.

As with recent interim reports on trials of retrievable IVC
filters, limitations of the present study include the

*Anticoagulants included heparin, factor Xa inhibitors, direct thrombin inhibitor, factor II inhibitor, and Coumadin derivatives. A pa-
tient could use >1 anticoagulant medication within the same time interval.
nonrandomized single-arm design and the inherent potential for bias in a manufacturer-funded regulatory device trial. Although the rate of freedom from symptomatic PE was 100% through 60 days before filter bioconversion and then extending through the 12-month follow-up for the full patient cohort, it is possible that instances of asymptomatic PE may have gone undetected (which is consistent with other IVC filter studies) because imaging was performed only in patients with suggestive clinical symptoms. Whereas the currently reported 1-year outcomes support the viability of this novel approach to providing temporary protection against PE, longer-term follow-up in a broader patient population will be important to confirm the durability of efficacy and safety outcomes and to ensure that the benefit of avoiding the need for device retrieval does not come with as yet unforeseen costs. The 24-month follow-up, which will be separately reported, includes CT venography, and any further filter-related complications will be described, including loss of IVC patency after capture of thrombus or any thrombogenicity associated with retracted filter arms. IVC diameter at the level of filter placement was not evaluated in 60-day imaging but will be reported for the 24-month follow-up.

In this 1-year interim analysis of the SENTRY clinical trial data, for patients requiring temporary protection against PE and unable to use anticoagulation, the SENTRY IVC filter showed high rates of technical and clinical success and minimal complications, within the efficacy and safety thresholds suggested by SIR and comparing favorably with outcomes reported for retrievable IVC filters. The results of this trial suggest that this bioconvertible device may provide an alternative to existing retrievable IVC filters that often remain indwelling long after the period of transient PE risk has passed and that are associated with relatively high complication rates.

ACKNOWLEDGMENTS

ClinicalTrials.gov ID NCT01975090.

The study was funded by Novate Medical (Galway, Ireland). Writing support services were provided by Galen Press (Austerlitz, New York) and paid for by the study sponsor. The authors thank Diane Gargus for clinical trial management.

The following investigators and institutions participated in the SENTRY Clinical Trial (Michael D. Dake, MD, principal investigator) in addition to the authors: Robert Feezor, MD (University of Florida, Gainesville, Florida); Sanjeeva Kalva, MD (UT Southwestern Medical Center, Dallas, Texas); Darren Kies, MD (Emory University, Atlanta, Georgia); Marc Bosiers, MD (AZ Sint-Blasius, Denderemonde, Belgium); Werner Ziegler, MD (Memorial Hospital of Colorado Springs, Colorado Springs, Colorado); Mark Farber, MD (University of North Carolina, Chapel Hill, North Carolina); David Paolini, MD (Jobst Vascular Institute, Toledo, Ohio); Robert Spillane, MD (Hartford Hospital, Hartford, Connecticut); Steven Jones, MD (Cardiovascular Associates of the Southeast, Birmingham, Alabama); and Patrick Peeters, MD (Imelda Hospital, Bonheiden, Belgium).

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CME TEST QUESTIONS: OCTOBER 2018

Examination available at http://learn.sirweb.org/. To take the online JVIR CME tests, please log into the SIR Learning Center with your SIR user name and password. Nonmembers: If you do not already have an SIR username and password, please click on “Create an Account” to gain access to the SIR Learning Center. Once in the Learning Center, click on the “Publication” activity type for a listing of all available JVIR CME tests. Each test will be available online for 3 years from the month/date of publication.

The CME questions in this issue are derived from the article “One-Year Analysis of the Prospective Multicenter SENTRY Clinical Trial: Safety and Effectiveness of the Novate Sentry Bioconvertible Inferior Vena Cava Filter” by Dake et al.

In this study, the authors prospectively assess the bioconvertible Sentry inferior vena cava (IVC) filter in patients requiring temporary protection against pulmonary embolism (PE).

1. Based on prior published data, approximately what percentage of filters remain unretrieved, thus risking an increase in filter-specific complications?
   a. 10–20%.
   b. 25–50%.
   c. 60–80%.
   d. > 90%.

2. Based on the results of this study, what percentage of patients were free from IVC filter related complications at 6 months?
   a. 20%.
   b. 50%.
   c. 70%.
   d. > 95%.

3. Based on the results published in this study, what was the incidence of filter migration and/or perforation of the caval wall by 1 or more filter struts at 1 year following implantation?
   a. 0%.
   b. 1%.
   c. 2%.
   d. > 5%.

4. The IVC filter use in this study is designed to provide filtering protection for a minimum duration of 60 days and then bioconvert to a nonfiltering configuration. What was the reported success rate of filter bioconversion at 60 days in this study?
   a. 2.1%.
   b. 3.5%.
   c. 4.3%.
   d. 5.2%.

1. The IVC filter use in this study is designed to provide filtering protection for a minimum duration of 60 days and then bioconvert to a nonfiltering configuration.
APPENDIX A. STUDY DESIGN

Study Administration

The prospective, multicenter, nonrandomized, single-arm SENTRY Clinical Trial was conducted at 23 sites in the United States (n = 20), Belgium (n = 2), and Chile (n = 1). The protocol was approved by the appropriate Institutional Review Boards or Ethics Committees, and all study procedures were performed in accordance with the guidelines of good clinical practice and applicable regulations. Novate Medical was the sole sponsor of the study, which was conducted under an investigational device exemption (IDE G1101111), in compliance with applicable provisions of 21 CFR Parts 50, 54, and 812 and in accordance with the ethical principles of the Declaration of Helsinki. Data were collected on case report forms (with supervision by Vitruvian Clinical Research, San Ramon, California) and reviewed and adjudicated by an independent data monitoring committee and a clinical events committee (CEC). Global Institute for Research (Richmond, Virginia) served as the imaging core laboratory, providing independent measurement and analysis in accordance with the predefined study protocols. QST Consultations (Allendale, Michigan) developed the statistical hypothesis for the study, and Advanced Research Associates (Santa Clara, California) defined the statistical analysis plan and methods and provided statistical analysis support. The study was registered before the start of patient enrollment (ClinicalTrials.gov ID NCT01975090).

Patient Eligibility Determination

Patients eligible for inclusion were ≥ 18 years of age and were determined by their physicians to be at a temporary (< 60 days) risk of pulmonary embolism (PE). All patients had documented deep vein thrombosis (DVT) or PE, or a high risk of developing DVT or PE, and had a contraindication to or failure of anticoagulation. The trial allowed enrollment of up to 40% of patients with a prophylactic indication (no current PE or DVT but high risk of PE). The indications for enrollment were consistent with American College of Radiology and Society of Interventional Radiology practice and quality improvement guidelines. Patients were required to have an average inferior vena cava (IVC) diameter of 16–28 mm and an infrarenal IVC length ≥ 9 cm. Patients were excluded if they were pregnant or planning to become pregnant within 12 months, had impaired renal function (serum creatinine ≥ 2.0 mg/dL), had life expectancy < 12 months, had a malignancy extending the PE period of risk > 60 days, had a known hypercoagulable state, or had an inherited or acquired hemostatic disorder. Venographic and/or procedural exclusion criteria included presence of a caval stent or IVC filter or history of IVC filter (< 1 month after retrieval), inability to gain femoral or internal jugular vein access or infection at the only available access site, duplicated or left-sided IVC, renal vein thrombosis or IVC thrombosis extending to the renal veins, occlusive or free-floating IVC thrombus, or known allergy or hypersensitivity to study device materials or to contrast media (not amenable to premedication). Baseline assessment on consented patients was performed ≤ 7 days before the index procedure, and patient enrollment occurred with insertion of the Sentry IVC filter introducer sheath.

APPENDIX B. THE SENTRY IVC FILTER AND IMPLANTATION TECHNIQUE

Device Design and Mechanism

The Sentry inferior vena cava (IVC) filter is made from a single piece of laser-cut nitinol, which is formed into a cylindrical frame with an integral filter cone consisting of 6 pairs of arms held together in the center of the IVC by means of a bioabsorbable filament composed of poly-p-dioxanone, a biodegradable synthetic polymer. The nitinol frame is designed to concentrically and longitudinally distribute radial force to decrease device tilting, migration, perforation, and fracture. Six fixation barbs (4 in the cranial direction and 2 in the caudal direction) are located on the nitinol frame to minimize device migration. On deployment, the cylindrical frame expands to appose the IVC wall, inciting incorporation of portions of the filter into the caval wall by means of neointimal healing. The Sentry filter was designed to support clot-trapping efficacy similar to that of the currently marketed IVC filters, as confirmed by FDA-mandated in vivo and in vitro bench testing. The device is nonmagnetic. It is sterilized by ethylene oxide.

During bioconversion, the bioabsorbable filament hydrolyzes, releasing the filtering arms from the filtering cone. The filtering arms then retract to the IVC wall into a nonfiltering configuration, where they are endothelialized along with the device frame. The mechanism of the filter-arm retraction is a function of the shape memory properties of the nitinol. The entire filter is cut from a single piece of nitinol and expanded to its finished diameter; during this process the filter arms are oriented in the nonfiltering position adjacent to the frame elements. When the bioabsorbable filament hydrolyzes during bioconversion and releases the arms, then due to the nitinol properties the arms return to their set position. This design allows temporary protection against pulmonary embolism followed by restoration of IVC lumen patency. The Sentry is indicated for use in IVC with diameters from 16 to 28 mm and has a maximum deployed length of 57.7 mm.

Device Implantation

The study investigators were instructed to obtain a cavigram with the use of an IVC sizing catheter to determine the diameter of the IVC and the infrarenal length at the implantation site (the cranial end of the filter to be landed ≥ 2 cm below the caudal renal vein). The IVC diameter was measured in both the anterior-posterior and lateral planes, with the mean diameter confirmed to be within the specified range of 16–28 mm. The infrarenal IVC length was
measured between the caudal renal vein and the iliac confluence and was required to be > 9 cm.

The Sentry filter comes preloaded in a bidirectional cartridge, which can be inserted through the custom 7-F introducer sheath for deployment by means of a femoral or jugular approach. Upon attainment of vascular access, a guidewire is advanced into the IVC over which the introducer sheath and dilator are advanced to the intended deployment site, with the cranial marker band used for positioning ≥ 2 cm below the most caudal renal vein. After removal of the dilator and guidewire and the confirmatory cavogram measurement, the loading tool (containing the preloaded filter) is oriented according to the access route with reference to the femoral and jugular labels and inserted into the hub of the introducer sheath. The device pusher is then used to advance the filter through the loading tool and into the introducer sheath to the intended deployment location (when the deployment indicator on the pusher approaches the loading tool, the loaded filter is approaching the tip of the introducer sheath). Deployment is performed by slowly retracting the outer sheath over the pusher (which is held stationary).

Following deployment, biplanar venograms were required in the study to verify that the device was in the intended location and in the filtering configuration. The device instructions for use specify that it should not be placed in a suprarenal position. When the filter implantation was transjugular, a catheter was placed cranial to the filter, and a retrograde injection of contrast was used to show the section of the IVC containing the filter. The study sites were instructed to not cross the filter in performing the postdeployment venography.

APPENDIX C. STUDY END POINTS AND DEFINITIONS

Study end points were formulated in accordance with the Society of Interventional Radiology reporting standards and the American College of Radiology guidelines and with reference to recent investigational device exemption studies. The predefined primary end point was clinical success at 6 months, a composite of technical success (filter deployment as intended without acute events), freedom from symptomatic pulmonary embolism (PE) through 60 days, and 6-month freedom from symptomatic PE. Filter-related complication requiring intervention, or filter-related death. Secondary end points included: technical success at 6 months, a composite of technical success (filter deployment as intended without acute events), freedom from symptomatic PE through 6, 12, and 24 months.

An adverse event was considered to be a serious adverse event if it resulted in death, was life-threatening, required or prolonged hospitalization, resulted in persistent or significant disability/incapacity, or was an important medical event that jeopardized the subject and required medical or surgical intervention.

A sensitivity analysis of the primary end point of clinical success at 6 months was performed on the full analysis set with all missing data considered to be failures. This approach presented a worst-case scenario.

APPENDIX D. COMPOSITE PRIMARY FILTER EFFICACY END POINT OUTCOMES

Primary Efficacy End Point Components

The predefined primary end point was clinical success at 6 months, a composite of technical success (filter deployment as intended without acute events), freedom from symptomatic...
pulmonary embolism (PE) through 60 days, and 6-month freedom from filter-related complications, including tilting, migration, embolization, fracture, perforation, symptomatic caval thrombosis, any other symptomatic filter-related complication requiring invasive intervention, or filter-related death.

All 3 of the component criteria were met by 111 (97.4%) of 114 patients evaluable for the composite end point (95% CI 92.5%–99.1%). Because the 92.5% lower limit of the 95% CI exceeds 80%, the Sentry IVC filter passed the predefined acceptance criteria for demonstrating efficacy on the clinical success end point. Technical success of deployment was achieved in 99.2% (129/130) of deployment attempts (95% CI 95.8%–99.9%). The rate of freedom from new symptomatic PE through 60 days was 100% (n = 129; 95% CI 97.1%–100.0%), regardless of whether the indication for device placement was therapeutic or prophylactic. The rate of freedom from inferior vena cava (IVC) filter–related complications through 6 months was 98.2% (112/114, 95% CI 93.8%–99.5%).

Technical Success of Deployment—One Failure
In one patient the filter could not be advanced through the introducer sheath (owing to resistance experienced by the investigator) in the left femoral vein, which the investigator had determined to be the most appropriate access route. When the investigator noted difficulty in advancing the device, the entire apparatus was withdrawn. Before that system was discarded, the filter was deployed from the kinked introducer sheath, and it was found to be intact with no apparent damage. After the withdrawal of the first system, a new system (new introducer sheath, new device) was successfully deployed through the same left femoral approach as originally intended. There were no clinical sequelae.

Filter-Related Complications through 6 Months—Two Cases of Symptomatic Caval Thrombosis
One of the 2 cases of symptomatic caval thrombosis occurred, following a protocol deviation, in a prophylactic-indication patient who had 2 separate underlying congenital prothrombotic conditions and a history of recurrent PE despite adequate anticoagulation and who was scheduled for major spinal surgery, with anticoagulation contraindicated. After the patient resumed anticoagulation, he developed the symptomatic caval thrombosis (at 8 days after the index filter implantation), which was successfully treated with the use of thrombectomy (Angiojet Thrombectomy System; Boston Scientific), ultrasound-enhanced thrombolysis, and percutaneous transluminal angioplasty of the iliac veins, common femoral vein, and IVC.

The other case of symptomatic caval thrombosis occurred in a therapeutic-indication patient who had developed bilateral deep vein thrombosis while recovering from subdural hematoma and a subsequent burr-hole procedure, and who was not a candidate for anticoagulation. The patient developed a symptomatic caval thrombosis 32 days after the filter implantation, which was successfully treated with the use of thrombolysis (Ekosonic Endovascular System; EKOS) and mechanical thrombectomy.

The 2 cases of caval thrombosis were both adjudicated by the study clinical events committee as serious adverse events having an unknown relationship to the device and procedure, because it was not possible to determine whether the thrombus was captured by or generated by the filter. In both cases of symptomatic caval thrombosis, the 2-month follow-up confirmed that the filter was in correct filtering configuration, and there was no recurrence of the caval thrombosis in either patient.

Three Cases of Incorrect Device Orientation Not Classified as Deployment Failures
Three different investigators at 3 different institutions deviated from the Sentry instructions for use, the study protocol, and the site training when they attached the loading tool to the introducer sheath in the incorrect orientation—resulting in the 3 devices being deployed upside down, with the apex of the filter directed caudally. No second filter was deployed in any of these cases, and there were no adverse events associated with any of the deviations. The incorrect deployments were reviewed by Novate and attributed to user error.

Per protocol, these 3 cases were not classified as deployment failures. Had they been adjudicated as deployment failures, the rate of deployment technical success would have been 96.9% (126/130). After completion of the trial, the printed arrows and text on the loading tool of the Sentry IVC filter were modified to more clearly identify the correct orientation for femoral and jugular approaches. Additional warnings have also been included in the device instructions for use.

APPENDIX E. SECONDARY VTE OUTCOMES

Cases of New or Worsening Deep Vein Thrombosis
After 1 month, there was no protocol-mandated lower-extremity imaging, and deep vein thrombosis (DVT) status was assessed based on symptoms and any site-performed imaging that was part of the follow-up of high-risk patients. Through 60 days, the rate of new or worsening DVT was 7.8% (10/129). There were 8 cases of new DVT and 3 cases of worsening DVT confirmed by the study clinical events committee (CEC) in 10 patients. One patient experienced both a new and a worsening DVT.

The DVT noted within the first 2 months of follow-up were symptomatic in 5 cases. None of the DVTs noted in the first 2 months were confirmed as being device related. One case of a new symptomatic DVT—swelling in the right leg, with ultrasound showing clotting extending from the filter down into the right iliac vein and to the right calf—with onset 8 days after the index filter implantation was adjudicated to be
procedure related due to access site thrombosis. After treat-
ment with anticoagulation, the Sentry device was in filtering
configuration at 1- and 2-month follow-ups and was
confirmed to be bioconverted at 6 months, with the patient
experiencing no further clinical events.

One new symptomatic DVT was reported at 158 days and
was adjudicated as not related to the procedure and as
having an unknown relationship to the study device. One
additional new symptomatic DVT was reported at 224 days
and was adjudicated as being not related to the procedure or
the study device. Through 12 months, there were 2 site-
reported cases of DVT that the CEC determined to be
continuing (1 reported at 7 days, 1 at 287 days).

**Findings of Thrombus in Filters**

The protocol-mandated 1-month computerized tomographic
(CT) venography revealed the presence of thrombus in the
filters of 18 (15.8%) of 114 patients with core laboratory
review. The thrombus was symptomatic only in the 2 noted
cases of symptomatic caval thrombosis. In CT venography
follow-up that was available at 2 months for 10 of these 18
patients, the thrombus was completely resolved in 3, the
thrombus size had been reduced in 5, the thrombus was
slightly larger in 1 (< 4 mm increase in length while the clot
width decreased), and in 1 the imaging quality did not allow
accurate determination of size although the presence of
thrombus was confirmed. No patient with thrombus in the
filter at 1 month had experienced a pulmonary embolism
(PE) at 2 months, and PE did not occur after bioconversion
of any of the filters that contained thrombus at 1 month. In
13 of these patients who completed follow-up to 12 months,
the filters were reported by the investigators to be bio-
converted in 12. Follow-up through 24 months will be re-
ported for all of these patients.