CLINICAL STUDY OVERVIEW

SECURE-C®

Cervical Artificial Disc

IDE CLINICAL STUDY OVERVIEW

SECURE-C®

CLINICAL STUDY

OBJECTIVE

The objective of this Investigational Device Exemption (IDE) study was to evaluate the safety and effectiveness of the SECURE-C® Cervical Artificial Disc compared to anterior cervical discectomy and fusion (ACDF) surgery for reconstruction of the disc at one level from C3-C7 following single-level discectomy for intractable radiculopathy or myelopathy due to a single-level abnormality localized to the disc space in patients who have failed at least 6 weeks of conservative treatment.

STUDY DESIGN

The SECURE-C® IDE study was a prospective, two-arm, randomized, unmasked, concurrently controlled, non-inferiority multicenter clinical trial that was conducted at 18 investigational sites in the United States.

The investigational treatment was an anterior discectomy, followed by insertion of the SECURE-C® device. The control treatment was an anterior cervical discectomy and fusion (ACDF) procedure. Patients who were randomized to the control received an allograft spacer and an anterior cervical plate and screws.

- 18 U.S. sites
- 1:1 randomization applied
- 380 patients:
    - Investigational SECURE-C®
        - 89 non-randomized (up to 5 at each site)
        - 151 randomized
        - 240 total
    - Control ACDF
        - 140 randomized
- Single level treatment:
    - C3 – C7
- Postoperative follow-up:
    - 6 wk, 3 mo, 6 mo, 12 mo, 24 mo, annually

CLINICAL STUDY

INCLUSION CRITERIA	EXCLUSION CRITERIA
1. Symptomatic cervical disc disease (SCDD) in one vertebral level between C3-C7, defined as neck or arm (radicular) pain, or functional or neurologic deficit and radiographic confirmation (by CT, MRI, X-ray, etc.) of any of the following: • Herniated nucleus pulposus; • Radiculopathy or myelopathy; • Spondylosis (defined by presence of osteophytes); or • Loss of disc height 2. Age between 18 and 60 years 3. Failed at least 6 weeks of conservative treatment 4. Neck Disability Index (NDI) Questionnaire score of at least 30 (as percentage of 50 point total) 5. Able to understand and sign informed consent form 6. Psychosocially, mentally and physically able to fully comply with this protocol including adhering to follow-up schedule and filling out forms 7. Able to meet the proposed follow-up schedule at 6 weeks, 3 months, 6 months, 12 months and 24 months 8. Able to follow postoperative management program	1. More than one vertebral level requiring treatment 2. Prior fusion surgery adjacent to the level being treated 3. Prior surgery at the level to be treated 4. Clinically compromised vertebral bodies at the affected levels due to current or past trauma 5. Radiographic confirmation of facet joint disease or degeneration 6. Marked cervical instability on resting lateral or flexion/extension radiographs: • Translation greater than 3mm, and/or • More than 11° of rotational difference from that of either adjacent level 7. Severe spondylosis at the level to be treated as characterized by any of the following: • Bridging osteophytes; • A loss of disc height greater than 50%; or • Absence of motion (<2°) 8. Neck or arm pain of unknown etiology 9. Osteoporosis, osteopenia, Paget's disease, osteomalacia or any other metabolic bone disease 10. Pregnant or interested in becoming pregnant in the next 2 years 11. Active systemic or local infection 12. Known allergy to titanium, polyethylene, cobalt, chromium or molybdenum 13. Taking medications or any drug known to potentially interfere with bone/soft tissue healing (e.g., steroids) 14. Rheumatoid arthritis or other autoimmune disease 15. Systemic disease including AIDS, HIV, Hepatitis 16. Active malignancy: A patient with a history of any invasive malignancy (except non-melanoma skin cancer), unless he/she has been treated with curative intent and there has been no clinical signs or symptoms of the malignancy for at least 5 years 17. Neuromuscular disorders such as muscular dystrophy, spinal muscular atrophy, amyotrophic lateral sclerosis, etc. 18. Acute mental illness or substance abuse 19. Use of bone growth stimulator within past 30 days 20. Participation in other investigational device or drug clinical trials within 30 days of surgery 21. Prisoners

CLINICAL STUDY RESULTS

PATIENT ACCOUNTING AND DEMOGRAPHICS

Patient accounting includes the number and percentage of patients with any data and efficacy (primary endpoint) data. Demographics were similar for both the randomized SECURE-C® and ACDF treatment groups. A breakdown of the data for all randomized patients is provided in the tables below for comparison.

PATIENT ACCOUNTING		
Patients/Data Accounting	**Randomized SECURE-C®**	**Randomized ACDF**
Patients Treated (Randomized)	151	140
Patients with Any Data at 24 Months	138	115
Follow-up Rate (Any Data) at 24 Months	93.2%	88.5%
Patients with Efficacy Data at 24 Months	138	98
Follow-up Rate (Efficacy) at 24 Months	93.2%	75.4%
Patients with Any Data at 84 Months	125	102
Follow-up Rate (Any Data) at 84 Months	86.8%	85.0%
Patients with Efficacy Data at 84 Months	124	101
Follow-up Rate (Efficacy) at 84 Months	86.1%	84.2%

DEMOGRAPHICS		
Category	**Randomized SECURE-C®**	**Randomized ACDF**
Male	53.6%	48.6%
Female	46.4%	51.4%
Mean Age (years)	43.4	44.4
Mean Height (inches)	68.1	67.3
Mean Weight (lbs.)	191.6	187.1
Mean BMI (kg/m2)	28.9	29.0
Race		
Caucasian	90.1%	90.0%
Black	6.6%	7.1%
Asian	0	0
Hispanic	1.3%	2.1%
Other	2.0%	0.7%
Current Tobacco Use (yes)	33.8%	37.9%
Average Symptom Duration (months)	16.6	19.8

SURGERY DATA

The mean blood loss and operative time was statistically higher for the SECURE-C® group, although the differences may not be clinically significant.

LEVELS TREATED		
Level	**Randomized SECURE-C®**	**Randomized ACDF**
C3-C4	3.3%	2.9%
C4-C5	5.3%	7.9%
C5-C6	49.7%	50.0%
C6-C7	41.7%	39.3%

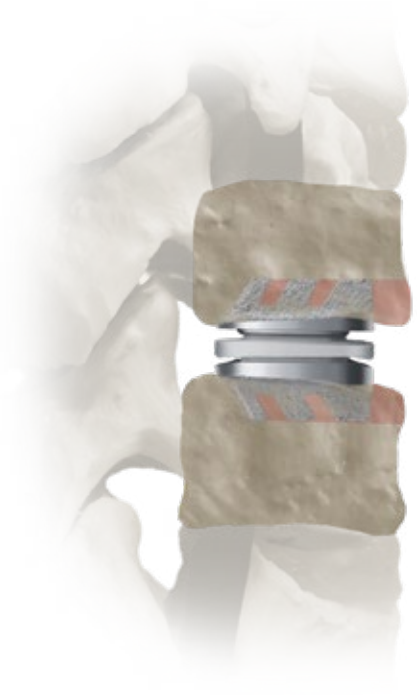
SURGERY DATA		
Data Type	**Randomized SECURE-C®**	**Randomized ACDF**
Mean Operative Time (min)	87.7	72.1
Mean Est. Blood Loss (mls)	55.2	45.6
Mean Length of Hospital Stay (days)	1.0	0.9
Mean Return to Work Time (days)	44.0	49.9

Please refer to the SECURE-C® Summary of Safety and Effectiveness Data (PMA P100003) at www.fda.gov for complete study results.

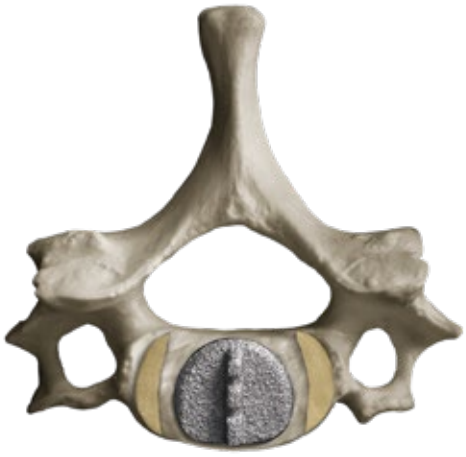
CLINICAL STUDY RESULTS

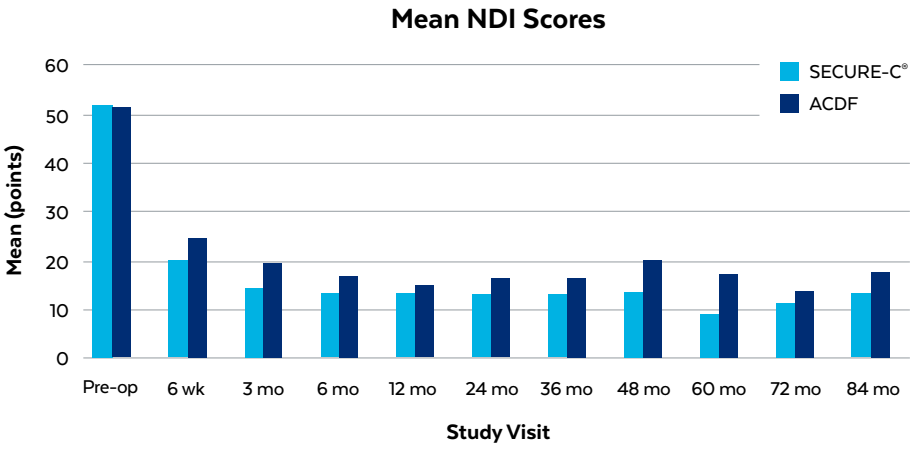
NECK DISABILITY INDEX

Both cohorts showed an improvement in their respective Neck Disability Index (NDI) scores from baseline to 24 months postoperative. Eighty-nine percent (89.2%) of randomized SECURE-C® patients demonstrated clinically significant (≥15 point) improvement in NDI compared to 84.5% of ACDF patients at the 24 month postoperative visit. Ninety-one percent (91.4%) of randomized SECURE-C® patients demonstrated at least a 25% improvement in NDI compared to 87.1% of ACDF patients at 24 months. By 84 months, 88.8% of randomized SECURE-C® patients demonstrated clinically significant improvement in NDI as compared to 84.1% of ACDF patients. Ninety percent (90.4%) of randomized SECURE-C® patients demonstrated at least a 25% improvement in NDI compared to 86.0% of ACDF patients at 84 months. Non-inferiority of the SECURE-C® group was demonstrated at the 24, 60 and 84 month postoperative visits for NDI.

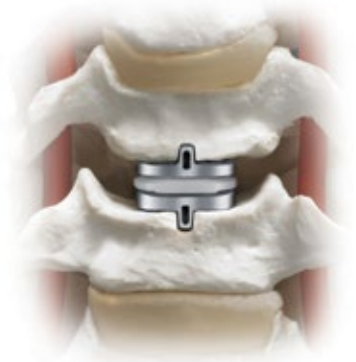


NECK DISABILITY INDEX		
NDI	Randomized SECURE-C®	Randomized ACDF
Mean Preoperative Score	51.8	51.5
Mean 24 Month Score	13.2	16.5
Patients with ≥15 point Improvement (at 24 months)	89.2%	84.5%
Patients with ≥25% Improvement (at 24 months)	91.4%	87.1%
Mean 84 Month Score	13.4	17.8
Patients with ≥15 point Improvement (at 84 months)	88.8%	84.1%
Patients with ≥25% Improvement (at 84 months)	90.4%	86.0%

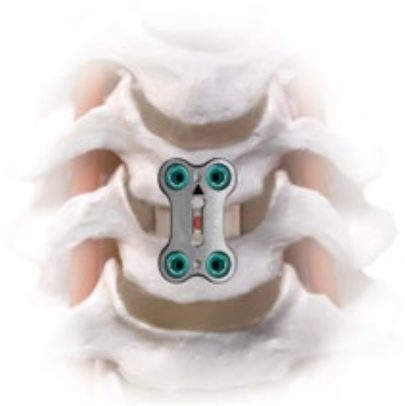




CLINICAL STUDY RESULTS



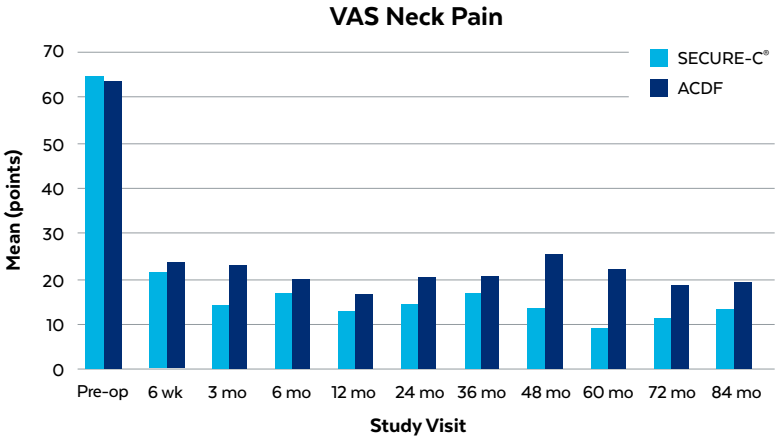
SECURE-C®

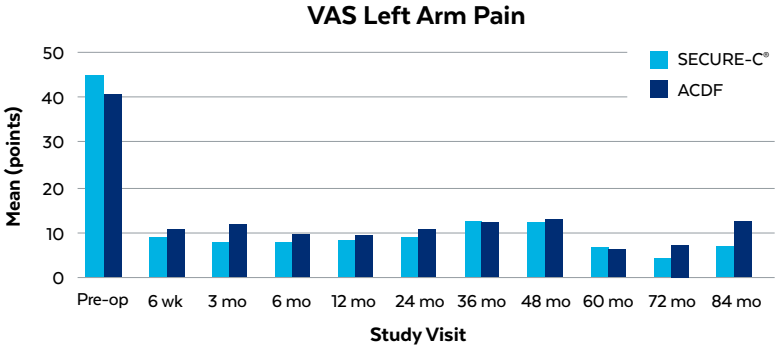


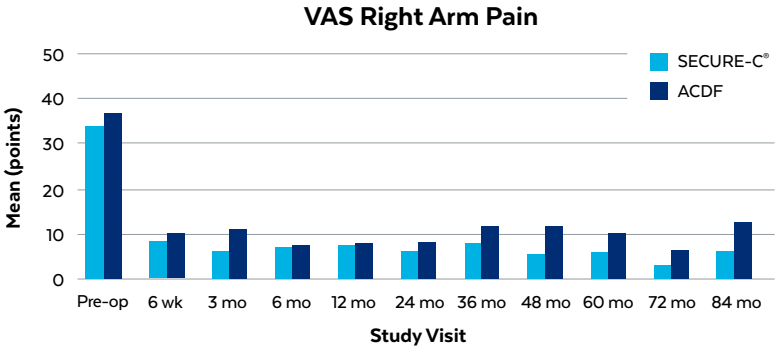
ACDF

VAS PAIN SCORES

Mean Visual Analog Scale (VAS) neck and arm pain scores improved in both SECURE-C® and ACDF treatment groups. Both cohorts demonstrated an improvement in neck and arm (right and left) VAS scores from baseline to the 84 month time point. For VAS improvement of at least 20mm (out of the 100mm scale) or zero postoperative pain, non-inferiority of SECURE-C® to ACDF was demonstrated for VAS neck, right and left arm pain at 24 and 84 months.







*Per FDA, VAS data excludes one site in which some scores were reported verbally rather than written.

Patient Satisfaction

Overall, patients who received the SECURE-C® implant were satisfied with their results and would undergo the surgery again. By 84 months, 95% of the SECURE-C® group was definitely or mostly satisfied, compared to 89% for the ACDF control group.

Ninety-two percent (92%) of patients treated with the investigational device responded definitely or mostly when asked whether they felt the surgery helped as much as they thought it would as compared to 88% of those who received the control treatment. Ninety-five percent (95%) of SECURE-C® patients responded that they definitely or mostly agreed when asked whether they would undergo the same surgery again, whereas 88% of those treated with ACDF would have the operation again.

CLINICAL STUDY RESULTS

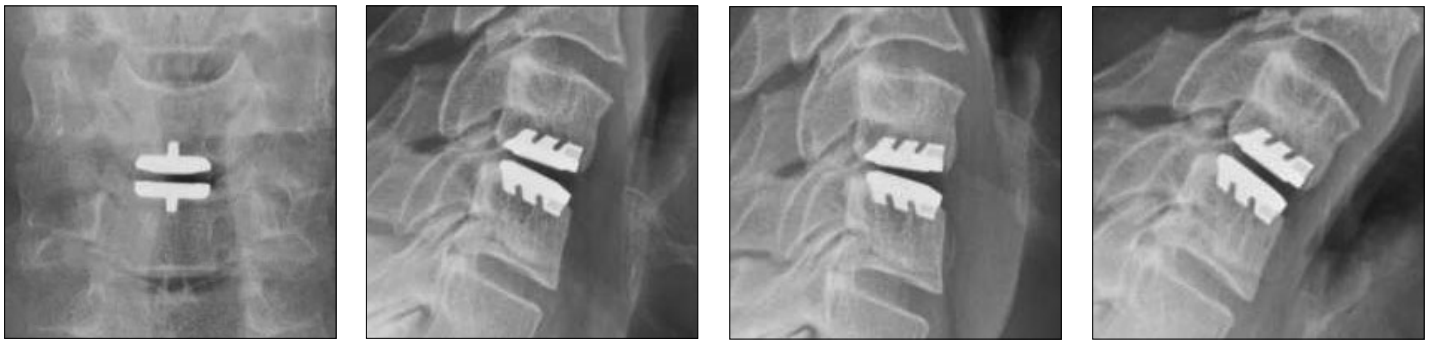
RADIOLOGICAL ASSESSMENT

Radiographic evaluations were performed at each time point for both treatment groups. Anterior-posterior (AP), lateral and flexion-extension films were evaluated at 6 months, 12 months and 24 months postoperative and annually thereafter through 84 months.

Radiographic fusion, defined radiographically as bridging trabecular bone and range of motion ≤3mm in translation and ≤2° in rotation, was assessed for ACDF patients. Radiographic fusion was exhibited in 89% of ACDF patients at 24 months, 97% at 60 months, and 97% at 84 months.

Radiographic data for provided evidence of motion (≥4°) at the treated level in 85%, 82% and 85% of all SECURE-C® patients at 24, 60 and 84 months, respectively. No displacement or migration (including superior-inferior subsidence) was recorded for the investigational group at any time point. Additionally, no radiolucencies were observed in SECURE-C® patients at any time point except one patient at 6 months, which was not seen at subsequent visits.

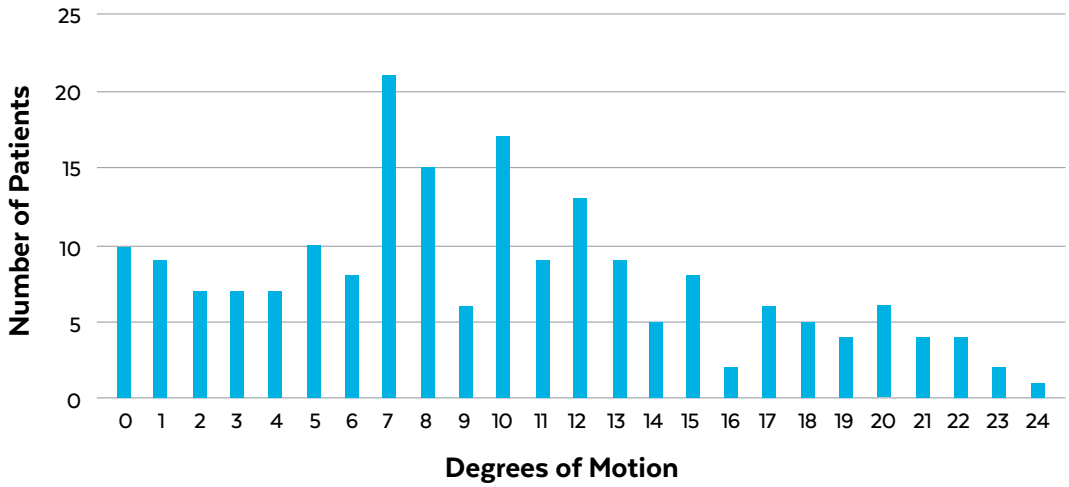
Sample SECURE-C® Patient Radiographs at 24 Months



AP | Lateral | Extension | Flexion

Flexion-Extension Range of Motion at 24 Months

for all SECURE-C® patients (randomized and non-randomized)



CLINICAL STUDY RESULTS

RANGE OF MOTION AND DISC HEIGHT

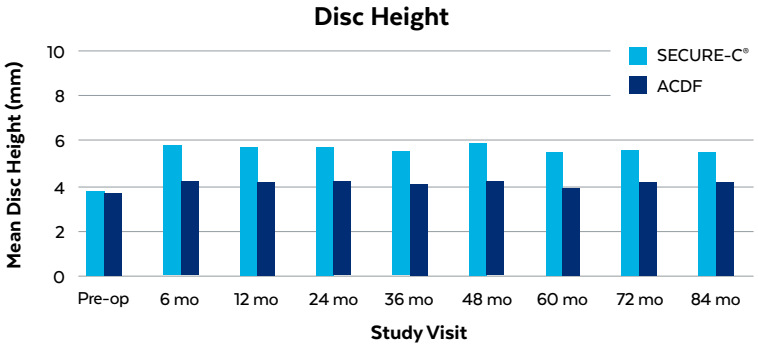
SECURE-C® is designed to allow motion in the cervical spine. Randomized SECURE-C® patients exhibited a mean range of motion (ROM) of 9.3°, 8.6°, and 9.1° in flexion-extension at 24, 60 and 84 months, respectively. In patients treated with SECURE-C® who returned for follow-up, 85%, 82% and 85% had ≥4° of flexion-extension motion or maintenance of motion at 24, 60 and 84 months, respectively, relative to their preoperative baseline.

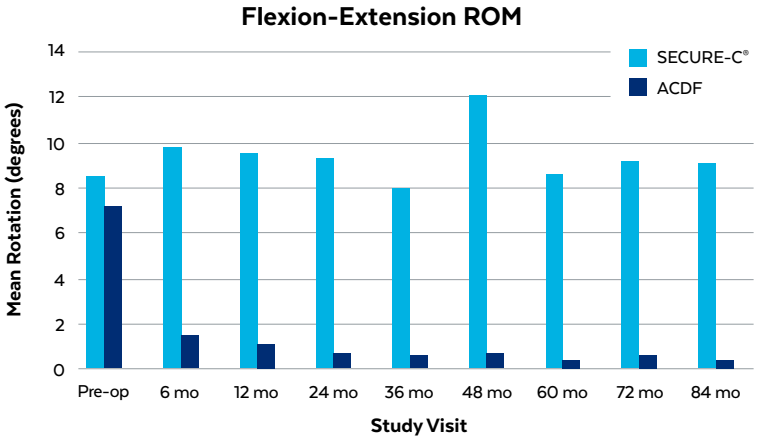
SECURE-C® is also designed to allow for AP translation during motion. The randomized SECURE-C® group demonstrated a mean ROM of 1.2mm, 1.1mm, and 1.1mm in translation at 24, 60 and 84 months after surgery, respectively. Mean disc height was 5.7mm, 5.5mm and 5.5mm for the randomized SECURE-C® group, compared to 4.2mm, 3.9mm and 4.2mm for the ACDF group, at 24, 60 and 84 months, respectively.

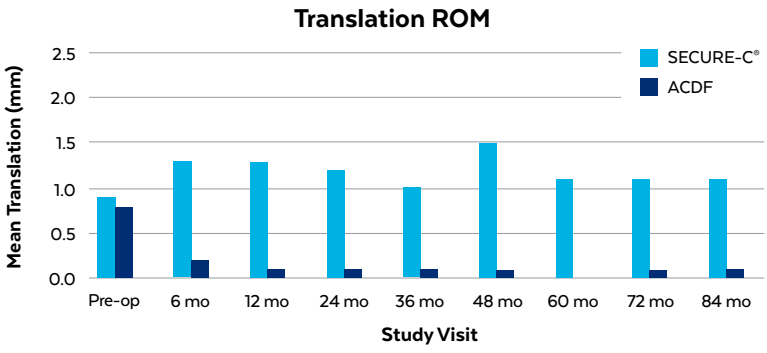
Flexion

Extension

Translation







CLINICAL STUDY RESULTS

ADVERSE EVENTS

Adverse events were reported throughout the duration of the entire study. The adverse event rate was similar for both treatment groups. Approximately 87% of all SECURE-C® patients experienced one or more adverse events, compared to approximately 90% of all ACDF patients.

SECONDARY SURGERIES

All secondary surgical procedures at the index level were recorded for the duration of the study. The incidence of secondary surgery at the index level was 4.2% for SECURE-C® patients as compared to 15.3% for the ACDF patients.

TREATMENT	LEVEL	REASON	PROCEDURE
ACDF	C5-6	Left C5 radiculopathy	Removal
ACDF	C4-5	Device revision	Removal
ACDF	C4-5	Myelopathy	Removal
ACDF	C5-6	Neck pain and right arm pain	Removal
ACDF	C6-7	Right shoulder pain	Removal
ACDF	C6-7	Neck pain and thumb paresthesia	Reoperation
ACDF	C5-6	Neck pain and numbness	Removal
ACDF	C5-6	C4-5 and C6-7 disc herniation	Removal
ACDF	C6-7	Neck and left arm pain	Removal
ACDF	C5-6	Neck pain	Removal
ACDF	C4-5	Neck pain, C5-6 disc herniation	Removal
ACDF	C6-7	Left arm pain, numbness	Removal
ACDF	C5-6	Neck/shoulder pain, C4-5 disc degeneration	Removal
ACDF	C5-6	Neck and right upper extremity pain	Removal
ACDF	C6-7	Adjacent segment disease	Revision
ACDF	C6-7	Neck and arm pain, C5-6 disc degeneration	Removal
ACDF	C6-7	Neck and left arm pain	Removal
ACDF	C5-6	Left arm pain	Removal
ACDF	C5-6	Neck and shoulder pain	Removal
ACDF	C6-7	Cervical spondylosis and myelopathy	Removal
ACDF	C5-6	Neck and left arm pain	Removal
ACDF	C5-6	Neck and arm pain and numbness	Removal
SECURE-C®*	C5-6	Neck and shoulder pain	Removal
SECURE-C®*	C5-6	Arm/parascapular pain	Removal
SECURE-C®*	C5-6	Neck and upper extremity pain	Removal
SECURE-C®*	C6-7	Neck and upper extremity pain	Removal
SECURE-C®	C5-6	Neck pain	Removal
SECURE-C®	C6-7	Neck pain	Removal
SECURE-C®	C5-6	C5-7 radiculopathy	Reoperation
SECURE-C®	C5-6	C5-6 stenosis	Reoperation
SECURE-C®	C5-6	Left C4-5 and left C5-6 stenosis	Reoperation
SECURE-C®	C6-7	Neck and left arm pain	Supplemental Fixation

*Non-Randomized SECURE-C®

NEUROLOGIC STATUS

Overall neurologic status was maintained or improved for 96%, 96%, and 94% of all SECURE-C® patients as compared to 93%, 97% and 87% of ACDF patients at 24, 60 and 84 months, respectively.

OVERALL SUCCESS AND CONCLUSIONS

OVERALL SUCCESS

A patient was considered a success at 24 or 84 months if all of the following criteria were met:

- Pain/disability improvement of at least 25% in NDI compared with the score at baseline
- No device failures requiring revision, reoperation, removal, or supplemental fixation
- Absence of major complications defined as major vessel injury, neurologic damage or nerve injury
- For fusion control patients only, radiographic fusion, as defined radiographically by the presence of bridging trabecular bone and range of motion ≤3mm in translation and ≤2° in rotation

Overall success results at 24 and 84 months demonstrate that the SECURE-C® Cervical Artificial Disc is statistically superior to ACDF for the indications studied.

OVERALL SUCCESS	24 MONTHS		84 MONTHS	
Criteria	SECURE-C®	ACDF	SECURE-C®	ACDF
NDI Improvement (≥25% from baseline)	91.4%	87.1%	90.4%	86.0%
No Device Failures	98.0%	92.7%	94.7%	84.3%
Absence of Major Complications	100.0%	100.0%	100.0%	100.0%
Radiographic Fusion	N/A	89.1%	N/A	97.1%
Overall Success	**90.1%**	**71.1%**	**86.3%**	**70.0%**

In addition, FDA requested that overall success data at 24 and 84 months be analyzed and reported using the following criteria:

- Pain/disability improvement of at least 15 points in NDI compared with the score at baseline
- Maintenance or improvement in all components of neurologic status
- No secondary surgery at the index level including revision, reoperation, removal, or supplemental fixation
- No potentially device-related adverse events
- No intraoperative changes in treatment (SECURE-C® group only)

Overall success (FDA-defined) results at 24 and 84 months demonstrate that the SECURE-C® Cervical Artificial Disc is statistically superior to ACDF for the indications studied.

OVERALL SUCCESS (FDA-DEFINED)	24 MONTHS		84 MONTHS	
Criteria	SECURE-C®	ACDF	SECURE-C®	ACDF
NDI Improvement (≥15 points from baseline)	89.2%	84.5%	88.8%	84.1%
Maintenance of Neurologic Status	96.0%	93.9%	93.5%	87.6%
No Secondary Surgery at the Index Level	98.0%	92.7%	94.7%	84.3%
No Potentially Device-Related Adverse Events	97.3%	92.0%	94.7%	82.6%
No Intraoperative Changes in Treatment	98.0%	N/A	98.0%	N/A
Overall Success	**83.8%**	**71.4%**	**79.2%**	**63.6%**

CONCLUSIONS

The SECURE-C® Cervical Artificial Disc is a safe and effective treatment for reconstruction of the disc at one level from C3-C7 following single-level discectomy for intractable radiculopathy or myelopathy due to a single-level abnormality localized to the disc space in patients who have failed at least 6 weeks of conservative treatment. This device is as good as the current standard of care (ACDF), in providing pain relief and satisfaction with fewer reoperations. Patients treated with the SECURE-C® implant exhibited significant postoperative improvement in pain and disability with a high rate of satisfaction, and fewer secondary procedures. Clinical data demonstrate that SECURE-C® is statistically superior to ACDF at 24 and 84 months after surgery.

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