i-Factor™ Bone Graft vs Autograft in Anterior Cervical Discectomy and Fusion: 2-Year Follow-up of the Randomized Single-Blinded Food and Drug Administration Investigational Device Exemption Study

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BACKGROUND: i-Factor™ Bone Graft (Cerapedics Inc, Westminster, Colorado) is a composite bone substitute material consisting of P-15 synthetic collagen fragment adsorbed onto anorganic bone mineral suspended in an inert biocompatible hydrogel carrier. A pivotal, noninferiority, US FDA Investigational Device Exemption study demonstrated the benefits of i-Factor™ compared to local autograft bone in single-level anterior cervical discectomy and fusion at 1-yr postoperative.

OBJECTIVE: To report 2-yr follow-up.

METHODS: Subjects randomly received either autograft (n = 154) or i-Factor™ (n = 165) in a cortical ring allograft and followed using radiological, clinical, and patient-reported outcomes.

RESULTS: At 2 yr, the fusion rate was 97.30% and 94.44% in i-Factor™ and autograft subjects, respectively ($P = .2513$), and neurological success rate was 94.87% (i-Factor™) and 93.79% (autograft; $P = .7869$). Neck Disability Index improved 28.30 (i-Factor™) and 26.95 (autograft; $P = .1448$); Visual Analog Scale arm pain improved 5.43 (i-Factor™) and 4.97 (autograft) ($p = .2763$); Visual Analog Scale neck pain improved 4.78 (i-Factor™) and 4.41 (autograft; $P = .1652$), Short Form-36 (SF-36v2) Physical Component Score improved 10.23 (i-Factor™) and 10.18 (autograft; $P = .4507$), and SF36v2 Mental Component Score improved 7.88 (i-Factor™) and 7.53 (autograft; $P = .9872$). The composite endpoint of overall success (fusion, Neck Disability Index improvement >15, neurological success, and absence of re-operations) was greater in i-Factor™ subjects compared to autograft subjects (69.83% and 56.35%, respectively, $P = .0302$). Twelve (7.45%) i-Factor™ subjects and 16 (10.53%) autograft subjects underwent re-operation ($P = .3411$). There were no allergic reactions associated with i-Factor™.

CONCLUSION: Use of i-Factor™ in anterior cervical discectomy and fusion is effective and safe, and results in similar outcomes compared to local autograft bone at 2 yr following surgery.

KEY WORDS: I-Factor™ bone graft, P-15 synthetic collagen fragment, Autograft, ACDF

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Anterior cervical discectomy and fusion (ACDF) is a standard-of-care treatment for cervical radiculopathy that does not respond to nonoperative care.[1-3] ACDF has traditionally been performed using iliac crest autograft, local

ABBREVIATIONS: ACDF, anterior cervical discectomy and fusion; **AE,** adverse event; **ANCOVA,** analysis of covariance; **CT,** computed tomography; **DDD,** degenerative disc disease; **FDA,** Food and Drug Administration; **IDE,** Investigational Device Exemption; **MCS,** mental component summary; **NDI,** Neck Disability Index; **PCS,** physical component summary; **SCB,** substantial clinical benefit; **SF-36,** Short Form 36; **VAS,** Visual Analog Scale

autograft, synthetic grafts, demineralized bone, ceramics, calcium phosphates, and bone morphogenetic proteins.[4-8] Local autograft bone may be of insufficient volume or of uncertain quality.

P-15 is a novel synthetic, 15-amino-acid polypeptide that mimics the cell-binding domain of type I collagen[9,10] and is able to signal a mechanical and biochemical communication pathway that ultimately results in new bone formation.[11,12] i-Factor™ Peptide Enhanced Bone Graft (Cerapedics Inc, Westminster, Colorado; i-Factor™) is a combination product consisting of P-15 which is adsorbed onto anorganic bone mineral and suspended in an inert biocompatible hydrogel carrier. It is approved by the US Food and Drug Administration (FDA) for single-level ACDF surgeries from C3 to C7.

The primary analysis of the pivotal multicenter FDA Investigational Device Exemption (IDE) noninferiority single-blinded clinical trial of i-Factor™ vs local autograft has demonstrated that i-Factor™ is safe and effective in single-level ACDF for the treatment of symptomatic cervical degenerative disc disease (DDD) based on a predetermined 12-mo patient follow-up.[13]

In this analysis, we report the 2-yr outcomes of i-Factor™ and autograft-treated subjects enrolled in the pivotal IDE study.

METHODS

Study Design

A prospective, randomized, controlled, multicenter clinical trial was conducted at 22 sites in North America to investigate the safety and efficacy of i-Factor™ compared to standard-of-care autograft (clinicaltrials.gov NCT00310440). Subjects underwent instrumented ACDF and randomly received either i-Factor™ (Cerapedics Inc) or local autograft in a cortical allograft ring implanted into the target vertebral interspace prior to placement of the cervical plate. The investigational protocol and statistical analysis plan were reviewed and approved by the FDA prior to study initiation, including the analysis of 2-yr data reported here. No changes occurred to the study design after trial commencement.

Objectives

Objectives of the analysis were to compare fusion, neurological outcomes, Neck Disability Index (NDI) functional outcomes, Visual Analog Scale (VAS) neck and arm/shoulder pain scores, Short Form-36 (SF-36v2) Physical (PCS) and Mental (MCS) Component Summary scores, overall success, and treatment complications between the i-Factor™ and local autograft subjects at 2 yr following instrumented single-level ACDF for symptomatic cervical DDD.

Inclusion and Exclusion Criteria

Inclusion and exclusion criteria were the same as in the 1-yr analysis.[13] Key inclusion criteria were as follows: age 18 to 70; failed to gain adequate relief from at least 6 wk of nonoperative treatment; radiographic evidence of single-level DDD of discogenic origin between C3 and C7 (including at least one of the following: degenerated/dark disc on MRI; decreased disc height compared to adjacent levels on radiographic film, CT, or MRI; or disc herniation on CT or MRI); radicular symptoms by history and physical examination; preoperative VAS pain level at neck or arm/shoulder > 4; and NDI > 30. Key exclusion criteria were as follows: multilevel symptomatic cervical DDD; previous cervical fusion and/or decompression at the index level; acute cervical injury or instability due to trauma (ie, subluxation > 3 mm on flexion/extension film); or presence of systemic infection, active malignancy, myelopathy, rheumatoid disease of the cervical spine, or severe osteoporosis or osteomalacia.

Surgical Technique

A traditional anterior cervical approach was performed with intraoperative radiographic identification of the symptomatic surgical level. Surgeons performed an anterior cervical discectomy with achievement of neural decompression. More than 85% of subjects underwent ACDFs at C5-C6 or C6-C7. Control subjects received a cortical allograft ring filled with autograft bone collected from osteophytes and endplate preparation during the procedure. Investigational subjects received a cortical allograft ring filled with an average of 0.78 cc of i-Factor™. Following placement of the ring in the interbody space, an anterior cervical plate was placed spanning the disc space level and fixed with a screw/plate construct. Subjects were discharged home based on the usual routine of the operating surgeon.

Endpoints

Successful fusion was based on roentgenographic examination (anteroposterior, lateral, flexion, and extension) showing evidence of bridging trabecular bone between the involved motion segments and translational motion < 3 mm and angular motion < 5°. This criterion was selected by the FDA. Qualitative evaluations of evidence of bridging bone were performed by 2 blinded radiologists from the central radiology laboratory (Medical Metrics Inc, Houston, Texas); a third radiologist was involved in cases of a tie. If there was a lack of evidence of bridging bone on 12-mo plain roentgenograms, a computed tomography (CT) scan was used to make the final determination of fusion status. The criteria for fusion on CT scan were trabecular bone formation patterns within the intervertebral disc space or bridging bone formation that crossed the interspace.

The NDI is a validated questionnaire that assesses the patient's disability during activities of daily living.[14] Neurological outcomes were assessed in motor, sensory, and reflex domains specific to the cervical spine. An independent, blinded adjudicator rated subjects as neurological success (maintenance or improvement) or failure (decline). VAS neck and arm/shoulder pain scores were collected on a 0 to 10 scale. SF-36v2 is an established general health survey.[15] The composite endpoint of overall success at 1 and 2 yr was defined as fusion success, neurological success, NDI success (NDI improvement of >15), and absence of re-operations and/or device-related serious adverse events (AEs).

Patient Population

A total of 319 subjects were enrolled between June 2006 and May 2013 at 19 sites in the United States and 3 sites in Canada. Four subjects were excluded from the investigational arm and 2 from the control arm for the efficacy analysis due to protocol deviations. Subjects were evaluated in person preoperatively and then postoperatively at 6 wk, 3 mo, 6 mo, 9 mo, 12 mo, 18 mo, and 24 mo and thereafter annually. Subjects were blinded to the treatment assignment and remained blinded through the study. Figure 1 shows patient flow. The 1-yr follow-up rate was 136/159 (85.53%) in the i-Factor™ group and 139/151 (92.05%) in the autograft group. The 2-yr follow-up rate was 117/150 (78.00%) in the i-Factor™ group and 127/149 (85.23%) in the autograft group.

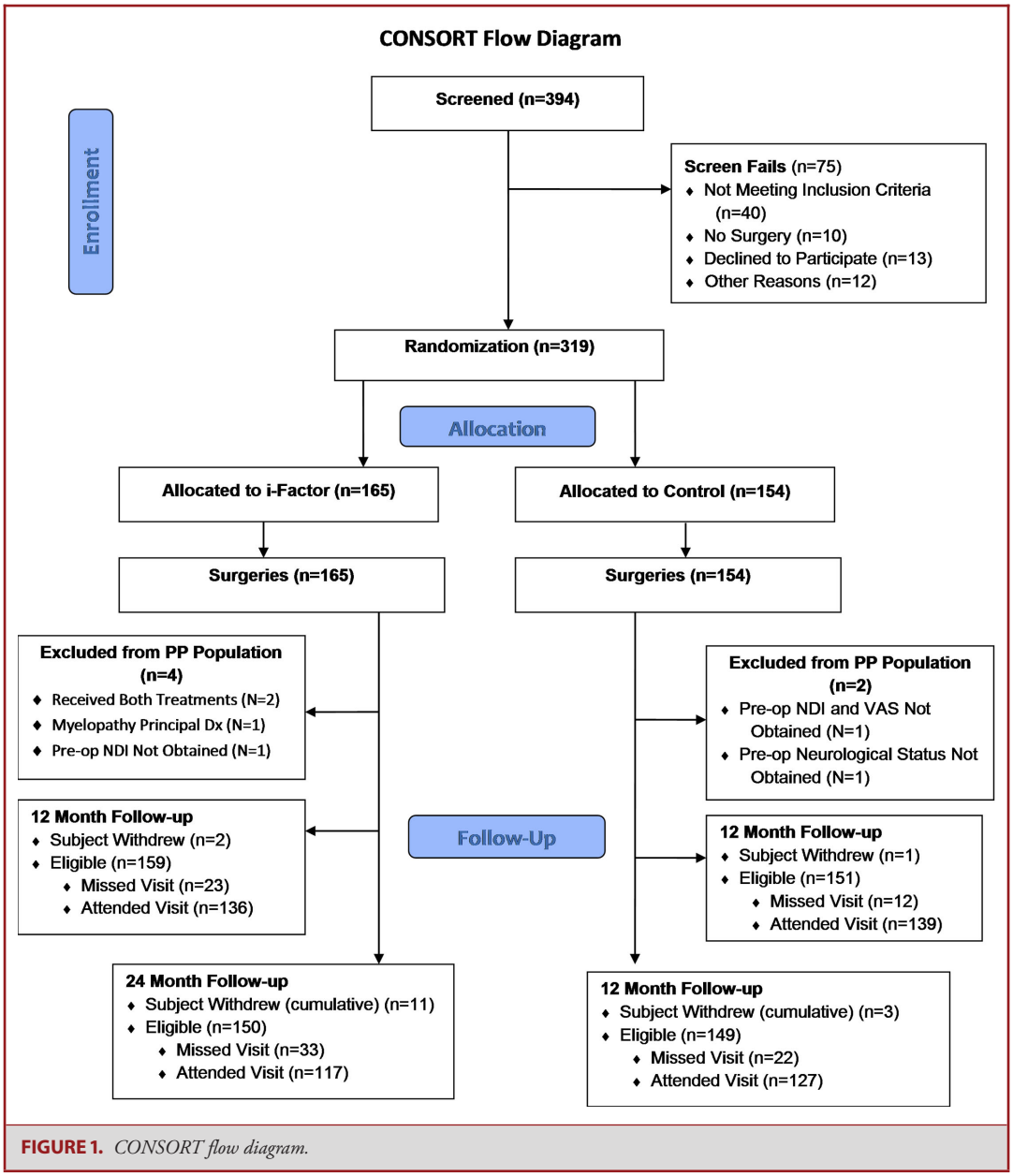

FIGURE 1. *CONSORT flow diagram.*

Data Processing and Statistical Methods

Randomization was performed using opaque sequenced envelopes using a 1:1 ratio. The sequence was generated centrally using random permuted blocks of sizes 2 and 4 and stratified by site. Data were collected using electronic case report forms. Data quality was monitored by independent study monitors to assure that the data were true, accurate, complete, and reliable. Additionally, the FDA performed several independent audits of the source data at various investigative sites and at the central data management center.

Fusion and neurological success outcomes were tested using the Fisher exact test; NDI, VAS pain, and SF-36v2 outcomes were assessed using the repeated measures Analysis of Covariance (ANCOVA). Three factors were analyzed: ARM (i-Factor™ and autograft), TIME (6, 9, 12, 18, and 24 mo) and ARM*TIME interaction. The ARM*TIME interaction term tests if a degree of change between the follow-up observations varies between the 2 groups. The 2-sided alpha was set to 0.05. Differences between i-Factor™ and autograft groups at each time point were tested with the post hoc approach and Tukey adjustment. All analyses were performed using the imputed data and intent-to-treat approach.

Missing values for fusion outcome were imputed by last value carried forward starting with 9 mo of observation, if available. Missing

TABLE 1. Preoperative Demographics by Study Arm

Characteristic	i-Factor™ (n = 161)	Autograft (n = 152)	*P*-value[a]
Age (years)	47.7 ± 9.8	45.7 ± 9.4	.0653
Body mass index	28.6 ± 6.0	29.1 ± 5.7	.4970
Symptom duration (months)	18.5 ± 24.2	25.6 ± 35.7	.1779[b]
Gender (male)	42.24%	37.50%	.4201
Current tobacco use	20.50%	27.63%	.1472
Clinical			
VAS–neck	6.6 ± 2.4	6.7 ± 2.4	.6874
VAS–arm/shoulder	7.0 ± 2.0	6.9 ± 2.0	.8128
Functional			
NDI	50.6 ± 13.2	52.7 ± 14.4	.1955
SF-36v2 (PCS)	35.2 ± 7.4	34.3 ± 7.0	.2810
SF-36v2 (MCS)	40.6 ± 12.8	40.9 ± 13.1	.8253
Surgical level			.5376[c]
C3/C4 (%)	2.48%	2.63%	
C4/C5 (%)	11.18%	7.24%	
C5/C6 (%)	43.48%	50.00%	
C6/C7 (%)	42.86%	40.13%	

[a] *P*-values are for the independent 2-sample t-test for continuous variables and Fisher exact test for categorical variables, if not indicated otherwise.
[b] Wilcoxon signed-rank test.
[c] Chi-square test.

follow-up scores for NDI, SF-36v2, and VAS were assumed to be missing at random and were accounted for using a multiple imputations procedure. Neurological success was not imputed. After imputation, 2-yr fusion data were available for 148/161 (90.06%) of i-Factor™ subjects and 144/152 (92.76%) of autograft subjects, and neurological success was available for 117/161 (72.67%) and 127/152 (83.55%) of i-Factor™ and autograft subjects, respectively. NDI, VAS pain, and SF-36v2 were multiple imputed for all 313 subjects (100.0%).

The original sample size was determined for the primary noninferiority analysis at 1-yr follow-up and was described previously.[13] The current analysis had effective power exceeding 99% to detect a difference of 10 points in change in NDI under the common standard deviation of 20 using a t-test for independent samples.

Ethics

Approval from investigational review boards or research ethics boards was obtained at each site, and each subject provided written informed consent to participate in the study.

RESULTS

Demographics

Demographics, clinical metrics, functional metrics, and index surgical level data are presented in Table 1. Average age, symptom duration, gender, comorbidities, and evidence of current tobacco use were similar in both populations. Preoperative VAS neck and arm/shoulder pain scores, NDI scores, and SF-36v2 PCS and MCS scores were similar between the groups.

Efficacy Endpoints

NDI improved postoperatively in both the i-Factor™ (Cerapedics Inc) and autograft groups (TIME factor $P < .001$; Figure 2A). There were no differences between i-Factor™ subjects and autograft subjects in average NDI outcomes at any time point (ARM factor $P = .094$ and ARM*TIME factor $P = .561$; Table 2. The maximum improvement was reached at 6 mo; there were no differences at later follow-up time points and 6-mo follow-up in either group.

VAS pain arm/shoulder improved postoperatively in both i-Factor™ and autograft groups (TIME factor $P < .001$; Figure 2B). i-Factor™ subjects had superior outcomes compared to autograft subjects (ARM factor $P = .052$ and ARM*TIME factor $P = .031$). The difference in outcomes in the i-Factor™ subjects reached statistical significance at 3, 6, and 18 mo postoperatively. The maximum improvement was reached at 3 mo; there were no differences at later follow-up time points and 3-mo follow-up in either group.

VAS pain neck improved postoperatively in both i-Factor™ and autograft groups (TIME factor $P < .001$; Figure 2C). There were no differences between i-Factor™ subjects and autograft subjects in VAS pain neck outcomes at any time point (ARM factor $P = .146$ and ARM*TIME factor $P = .462$). The maximum improvement was reached at 3 mo; there were no differences at later follow-up time points and 6-mo follow-up in either group.

SF-36v2 PCS improved postoperatively in both i-Factor™ and autograft subjects (TIME factor $P < .001$; Figure 2D). There were no differences between i-Factor™ subjects and autograft subjects in SF-36v2 PCS outcomes at any time point (ARM factor $P = .286$ and ARM*TIME factor $P = .646$). The maximum improvement was reached at 6 mo; there were no differences at later follow-up time points and 6-mo follow-up in either group.

SF-36v2 MCS improved postoperatively in both i-Factor™ and autograft subjects (TIME factor $P < .001$; (Figure 2E). There were no differences between i-Factor™ subjects and autograft subjects in SF-36v2 MCS outcomes at any time point (ARM factor $P = .83$ and ARM*TIME factor $P = .90$). The maximum improvement was reached at 6 mo; there were no differences at later follow-up time points and 6-mo follow-up in either group.

At 1 yr, 88.97% of i-Factor™ subjects and 85.82% of autograft subjects met the criteria for successful fusion ($P = .42$; Table 3). At 2 yr, 97.30% of i-Factor™ subjects and 94.44% of autograft subjects met the criteria for successful fusion ($P = .22$; Table 3). At 1 yr, 93.71% of i-Factor™ subjects and 93.01% of autograft subjects were adjudicated as neurological success ($P = .81$). At 2 yr, 94.87% of i-Factor™ subjects and 93.79% of autograft subjects were neurological success ($P = .69$).

The composite endpoint of overall success rate was higher in i-Factor™ subjects at 1 and 2 yr compared to autograft subjects (Table 3). At 1 yr, 99/144 (68.75%) of i-Factor™ subjects and 82/144 (56.94%) of autograft subjects were classified as overall success ($P = .038$). At 2 yr, 81/116 (69.83%) of i-Factor™ subjects and 71/126 (56.35%) of autograft subjects were classified as overall success ($P = .03$).

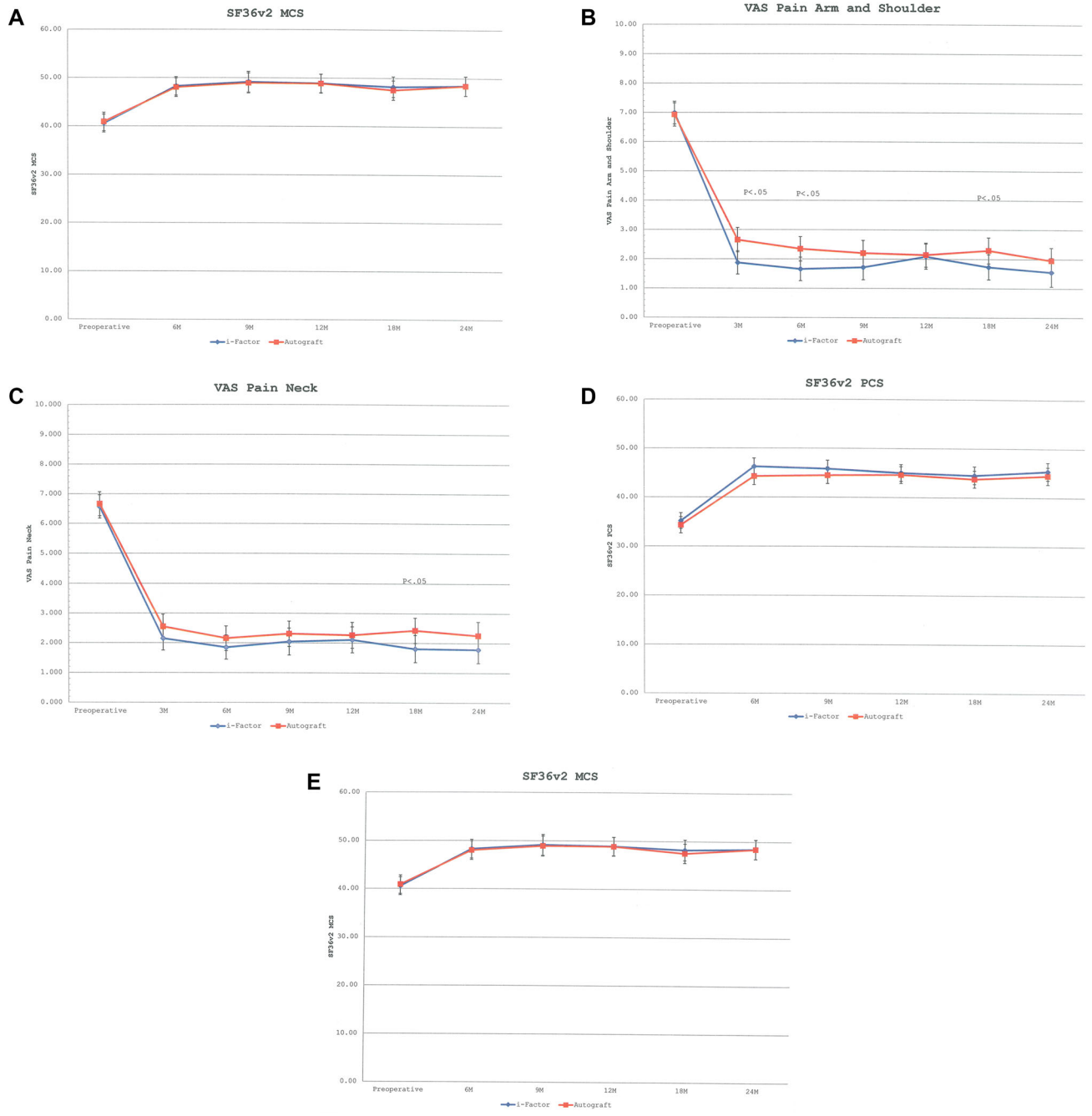

FIGURE 2. **A**, *NDI by study arm and follow-up.* **B**, *VAS for pain arm/shoulder by study arm and follow-up.* **C**, *VAS for pain neck by study arm and follow-up.* **D**, *Short Form 36v2 Physical Component Score (SF-36v2 PCS) by study arm and follow-up.* **E**, *Short Form 36v2 Mental Component Score (SF-36v2 MCS) by study arm and follow-up. Bars represent 95% confidence intervals.*

TABLE 2. Two-Year Outcomes by Treatment Arm

	i-Factor™ (n = 161) Preoperative	24 M	Autograft (n = 152) Preoperative	24 M	ARM	TIME	ARM*TIME
NDI	50.63 (47.71 to 53.55)	22.33 (18.90 to 25.76)	52.61 (49.61 to 55.62)	25.66 (22.55 to 28.78)	0.0941	<.0001	0.5607
VAS arm/shoulder	6.99 (6.60 to 7.38)	1.56 (1.06 to 2.05)	6.93 (6.53 to 7.33)	1.95 (1.51 to 2.39)	0.0516	<.0001	0.0306
VAS neck pain	6.57 (6.17 to 6.96)	1.79 (1.33 to 2.24)	6.66 (6.25 to 7.07)	2.25 (1.78 to 2.72)	0.1455	<.0001	0.4619
SF-36v2 PCS	35.17 (33.56 to 36.78)	45.40 (43.60 to 47.21)	34.29 (32.63 to 35.95)	44.47 (42.70 to 46.24)	0.2859	<.0001	0.6461
SF-36v2 MCS	40.56 (38.70 to 42.42)	48.43 (46.43 to 50.44)	40.88 (38.97 to 42.79)	48.41 (46.42 to 50.40)	0.8265	<.0001	0.9040

Numbers in parentheses are 95% confidence intervals.

Adverse Events

The most common complication in both groups was axial pain (44.72% and 42.11% in the i-Factor™ and autograft groups, respectively [$P = .65$]), postoperative residual radiculopathy (21.12% and 20.39% in the i-Factor™ and autograft groups, respectively [$P = .89$]), and dysphagia (19.25% and 19.74% in the i-Factor™ and autograft groups, respectively [$P = 1.0$]; Table 4). New radiculopathy was more common in autograft subjects compared to i-Factor™ subjects (25.0% and 13.66%, respectively [$P = .014$]). There were 6 cases of superficial infection in i-Factor™ subjects and none in autograft subjects ($P = .03$) There were no reports of allergic reactions associated with i-Factor™. Regarding other complications, 2 autograft subjects developed chronic lymphocytic leukemia: 1 i-Factor™ subject developed a bone hemangioma in the lumbar spine and another i-Factor™ subject developed renal cancer.

Twelve (7.45%) i-Factor™ subjects and 16 (10.53%) autograft subjects had subsequent cervical spine surgery ($P = .34$). Among the 12 subsequent surgeries in i-Factor™ subjects, there were 6 surgeries that involved a different cervical level, 3 surgeries that involved the index and a different level, and 3 surgeries that involved the index level only. Overall, there were 6 (3.73%) subsequent surgeries involving index level in i-Factor™ subjects. In the 16 subsequent surgeries in autograft subjects, there were 3 involving a different level only, 7 involving a different and the index level, and 6 involving the index level only. In total, 13 (8.44%) autograft subjects had re-operation at the index level.

TABLE 3. Composite Endpoint of Overall Success at 12 and 24 mo by Component

Component	i-Factor™	Autograft	*P*-value[a]
12 mo			
Overall success	99/144 (68.75%)	82/144 (56.94%)	.0382
Fusion success	129/145 (88.97%)	121/141 (85.82%)	.4220
NDI success	112/141 (79.43%)	103/139 (74.10%)	.2907
Neurological success	134/143 (93.71%)	133/143 (93.01%)	.8123
Safety success	157/161 (97.52%)	145/152 (95.39%)	.3085
24 mo			
Overall success	81/116 (69.83%)	71/126 (56.35%)	.0302
Fusion success	144/148 (97.30%)	136/144 (94.44%)	.2195
NDI success	89/116 (76.72%)	87/126 (69.05%)	.1804
Neurological success	111/117 (94.87%)	119/127 (93.70%)	.6944
Safety success	153/161 (95.03%)	137/151 (90.73%)	.1379

[a]Chi-square test.

DISCUSSION

The results of this analysis are an extended report of the previous 1-yr outcomes of the FDA IDE pivotal investigation on the effectiveness and safety of i-Factor™ (Cerapedics Inc) in single-level ACDF for symptomatic cervical DDD.[13] The current analysis shows the continuous safety and effectiveness of i-Factor™ at 2 yr following surgical treatment for symptomatic radiculopathy due to single-level cervical DDD as compared to local autologous bone. Specifically, at 2 yr, fusion outcomes improved compared to 1-yr outcomes and reached 97.3% in the i-Factor™ subjects and 94.4% in the autologous bone group. Patient-reported symptoms and functional and health-related quality of life outcomes were sustained at 2 yr in both groups.

At both 12- and 24-mo follow-up, the rate of the composite endpoint of overall success was higher in i-Factor™ subjects compared to autograft subjects. Other outcomes in i-Factor™ subjects were similar to those in autograft subjects on all evaluated measures.

The rate of AEs was similar between i-Factor™ and autograft subjects with a few exceptions. The incidence of new radiculopathy was approximately twice as high in the autograft group. On the other hand, 6 i-Factor™ subjects had superficial infection compared to none in the autograft group.

PCS improvement of 10 points exceeds the substantial clinical benefit (SCB) threshold of 6.5, and VAS pain neck of 5.4 points and arm/shoulder of 4.8 points exceed the SCB threshold of 3.5.[16] Improvement in outcomes in i-Factor™ and autologous bone subjects at two years were clinically relevant. NDI improvement of 28 points in the i-Factor™ subjects exceeds the substantial clinical benefit (SCB) threshold of 9.5; SF36 PCS improvement of 10 points exceeds the SCB threshold of 6.5, and VAS pain neck of 5.4 points and arm/shoulder of 4.8 points exceed the SCB threshold of 3.5.16.

TABLE 4. Complications by Treatment Group

	i-Factor™ (N = 165)		Autograft (N = 154)		*P*-value[a]
	n	%	n	%	
Pseudarthrosis/nonunion	21	12.73	25	16.23	.3790
Screw malposition	0	0.00	1	0.66	.4856
Postoperative radiculopathy/radiculitis	34	21.12	31	20.39	.8901
Axial pain (nuchal or periscapular pain or neck fatigue)	72	44.72	64	42.11	.6500
New intractable neck pain	14	8.70	22	14.47	.1149
Adjacent segment degeneration	21	13.04	25	16.45	.4274
Dural tear	1	0.62	0	0.00	1.0000
Retropharyngeal hematoma/airway obstruction	0	0.00	1	0.66	.4856
Horners syndrome	0	0.00	1	0.66	.4856
Partial or complete vocal cord paralysis (hoarseness)	4	2.48	1	0.66	.3720
Superficial infection	6	3.73	0	0.00	.0301
Dysphagia	31	19.25	30	19.74	1.0000
Dysphonia	1	0.62	2	1.32	.6132
Progression of myelopathy	1	0.62	0	0.00	1.0000
New radiculopathy	22	13.66	38	25.00	.0142
Cardiopulmonary event	1	0.62	0	0.00	1.0000
Worsening of neurological status	1	0.62	3	1.97	.3587

[a]Fisher exact test.

The fusion rates reported in the literature vary due to poorly defined fusion criteria, low patient numbers, and variable time periods at which fusion is assessed.[17,18] The fusion rate for i-Factor™ observed in this study (97.3%) is higher than the rates reported for control groups in comparable pivotal studies using similar methodology and definitions to those used in our study. In a Secure-C study, Vaccaro et al[19] reported the fusion rate of 89.1% at 2-yr following single-level ACDF using a plate and allograft bone. In a study of PCM® cervical disc, Phillips et al[20] reported the fusion rate of 92.1% at 2 yr. Cheng et al[21] reported a fusion rate of 92.9% at 3-yr follow-up and Fernandez-Fairen et al[22] reported fusion rate of 84.8%.

Lubelski et al[18] reported a re-operation rate associated with ACDF of 4.8% (the use of autograft or allograft was not specified), which is similar to the 3.7% re-operation rate observed in i-Factor™ subjects.[23]

Limitations

There are limitations to our study. Our study involved subjects who met detailed inclusion and exclusion criteria and were willing to participate in a randomized controlled trial; therefore, subjects in clinical practice may differ from the subjects enrolled in this study. Next, some subjects were not available at 2-yr follow-up. We accounted for such data by using prespecified imputation approaches. We also performed multiple statistical sensitivity analyses to address this issue and arrived at the conclusion that missing follow-ups did not bias our results. For practical reasons, surgeons were not blinded to the treatment assignment. However, assessment of fusion and neurological success was performed by independent blinded adjudicators, and assessment of functional and quality of life outcomes was self-reported by blinded subjects. Criteria for fusion, determined by the FDA, were less stringent than in some other studies.[24] Nevertheless, the presence of continuous bridging bone was an absolute requirement determining whether fusion had occurred. Fusion assessment was blinded, and the criteria were the same in both arms of the study.

CONCLUSION

ACDF is an effective and safe treatment for cervical radiculopathy due to cervical DDD. Use of i-Factor™ (Cerapedics Inc) in ACDF is effective and safe, and results in similar outcomes compared to local autograft bone at 2 yr following surgery.

Disclosures

Cerapedics, Inc provided research funding to investigator sites to conduct this FDA IDE trial, including the research departments of the authors of this manuscript. No funding was received for other purposes. Utilization of i-Factor™ Putty (ABM/P-15™) in the application described in this investigation was performed as part of an FDA investigational trial. Drs Sasso and Janssen report receiving nonstudy-related clinical or research support from Cerapedics, Inc. Dr Janssen reports receiving stock/stock options from Cerapedics, Inc. Dr Kopjar and his company were contracted by Cerapedics, Inc to design and manage the clinical study. The remaining authors report no other conflicts of interest, including consultancy agreements, royalties, gifts received, intellectual property with regard to the products (i-Factor™ Putty) or company (Cerapedics, Inc) involved in this scientific investigation.

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COMMENT

This is a prospective study comparing i Factor™ vs local autograft placed within a cortical allograft ring. They found that i Factor™ is non-inferior and actually was statistically superior to local autograft for multiple parameters. while the study is well-done, there is a methodological error that was mandated by the FDA that results in partial invalidation of their fusion results. They chose >3 mm of motion, lack of bridging bone and >5° of angular motion as their definition of pseudarthrosis. Unfortunately, these criteria have been invalidated. the accepted criteria according to a number of publications, including a study done by the Cervical Spine Research Society, are: 1) less than 1 mm of interspinous process motion at the index level 2) >4 mm at a non-fused level to make sure that the flex-ex was adequate, and 3) use of a magnified image to make sure that identical points are chose on the flex and extension views. Using a >3 mm criterion will underestimate the pseudarthrosis rate and increase the success rate of the operation. Therefore, readers should not rely on the data as it pertains to the fusion rates, as the fusion.

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