8-9-2023

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Received: 17 April 2023 | Accepted: 24 July 2023

DOI: 10.1002/nau.25256

CLINICAL ARTICLE

Neurourology Urodynamics | SUFU | WILEY

Management of female stress urinary incontinence with single-incision mini-sling (Altis®): 36 month multicenter outcomes

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Abstract

Purpose: To assess noninferiority of the safety and effectiveness of the Altis® Single Incision Sling (SIS) with standard midurethral transobturator and/or retropubic slings through 36 months in a prospective, longitudinal, nonrandomized US Food and Drug Administration (FDA) 522 cohort study.

Materials and Methods: Adult females with confirmed predominant stress urinary incontinence (UI) through cough stress test (CST) or urodynamics and failed two noninvasive incontinence therapies. Effectiveness endpoints included objective dryness, negative CST, adverse events, and revision/resurgery through 36 months. The primary effectiveness endpoint was reduction from baseline in 24-h pad weight of ≥50% at 6 months, as requested by the FDA, and is included as a study point in this paper. Primary safety endpoint was rate of related serious adverse events (SAE) through 36 months. Noninferiority margins of 15% and 10% were prespecified for the effectiveness and safety endpoints. Due to the observational nature of the cohort study, a propensity methodology was conducted to assess the effect of potential confounding variables on the primary endpoints between groups.

Results: Three hundred fifty-five women underwent the sling procedure ($n = 184$ Altis; $n = 171$ Comparator). One hundred fourty (76%) Altis subjects and 101 (59%) Comparator subjects completed follow-up through 36 months. At 36 months, for the effectiveness endpoint, the difference in proportions of −0.005 for Altis versus Comparator (95% confidence interval [CI]: −0.102 to 0.092) was statistically significant ($p = 0.002$), supporting the hypothesis that Altis is noninferior to Comparator. Furthermore, both groups demonstrated high objective efficacy; in the

Abbreviations: ADJOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; CST, cough stress test; FDA, US Food and Drug Administration; MUI, mixed urinary incontinence; MUS, midurethral sling; OAB, overactive bladder; OR, odds ratio; PVR, postvoid residual; PWT, pad weight test; RMUS, retropubic midurethral sling; SAE, serious adverse event; SIS, single incision sling; SUI, stress urinary incontinence; TMUS, transobturator midurethral sling; TP, treated population; UI, urinary incontinence.

Altis arm $n = 99$ (81.8%) subjects were a success, and in the Comparator arm, $n = 79$ (82.3%) subjects were a success. Additionally, regarding the CST, Altis was found to be noninferior to the Comparator at every study visit, and the rate of negative CST remained above 80% for both groups ($p < 0.001$). At 36 months, Altis ($n = 2$; 1.1%) and Comparator ($n = 4$; 2.3%) subjects experienced a device and/or procedure-related SAE. The difference in proportions of 0.013 for Altis versus Comparator (95% CI: −0.023 to 0.048) was statistically significant ($p < 0.001$), demonstrating that Altis is noninferior to Comparator with respect to the primary safety endpoint throughout the study. There were 62 (36.3%) retropubic midurethral slings (RMUS), 96 (56.1%) transobturator midurethral slings (TMUS), and 13 (7.6%) SIS slings in the Comparator group. For the 36 month effectiveness endpoint, assessing the noninferiority of Altis versus RMUS and Altis versus TMUS, 99 (81.8%) Altis and 37 (90.2%) RMUS were a success, trending toward statistical significance, however, it cannot be determined to be noninferior ($p = 0.092$). Ninty-nine (81.8%) Altis and 33 (71.7%) TMUS were a success; this was statistically significant ($p < 0.001$), demonstrating Altis was noninferior to TMUS. Rates of negative CST were 122 (87.1%) Altis, 40 (93.0%) RMUS ($p < 0.001$), and 44 (91.7%) TMUS ($p < 0.001$). CST demonstrated that Altis was noninferior to RMUS and Altis was noninferior to TMUS at 36 months.

Conclusion: Altis single-incision sling was noninferior to standard midurethral sling for treatment of stress UI, throughout the study and at 36 months. Furthermore, adverse event rates were low.

KEYWORDS

adjustable sling, midurethral sling, mini-sling, single-incision sling, stress urinary incontinence

1 | INTRODUCTION

Urinary incontinence (UI) affects nearly 50% of all women; among these, 50−80% are identified as having stress UI (SUI). SUI is prevalent, with 13.6% of women in the United States having had at least one surgical procedure for SUI in their lifetime, resulting in 260 000 continence surgical procedures annually.[1] This rate has increased steadily in the past 20 years.[2] Additionally, it is commonly assumed by healthcare professionals that UI is an underreported condition, indicating the actual incidence rate may be much higher.[3]

Surgical treatment is indicated for SUI after failure of conservative treatment. Midurethral sling (MUS) procedures are considered the mainstay of SUI treatment. Examples include retropubic or transobturator MUS (RMUS, TMUS). However, despite their high success rates, these procedures are associated with significant complications, including bladder perforation and vessel injuries with RMUS[4] and postoperative groin and thigh pain with TMUS.[4–6] To minimize these complications, a new generation of slings emerged: single incision slings (SIS). These slings are characterized by a shorter tape length with fixation to either the obturator membrane (Altis®) or obturator internus muscle (Solyx™, Desara® One), without penetration into the lateral adductor muscles. Furthermore, there are two types of SIS: adjustable during insertion (Altis®) and nonadjustable.

In 2012, the US Food and Drug Administration (FDA) mandated post-market surveillance studies for all SIS to provide efficacy and safety data. Following the FDA's 522 order, a prospective cohort study was initiated to compare the safety and efficacy of Altis SIS with FDA cleared RMUS and/or TMUS for the treatment of SUI (Altis 522 Study NCT02348112). Given the paucity of comparative data on the efficacy and safety of SIS, our prospective cohort study aimed to determine whether the use of the Altis SIS System (Coloplast) was noninferior to RMUS and/or TMUS through 36 months follow-up.

2 | MATERIALS AND METHODS

The aim of the Altis 522 Study was to assess the noninferiority of the safety and effectiveness of the Altis® SIS with standard RMUS and/or TMUS through 36 months of follow-up. The study was a prospective, post-market, nonrandomized, cohort study comparing Altis SIS and FDA cleared RMUS and/or TMUS slings in the surgical treatment of SUI in adult female patients. This cohort study was registered (NCT02348112). Four hundred and sixteen women enrolled between January 2015 and May 2018. Written informed consent was obtained. The study was conducted at 23 sites across the United States and Canada with 7 sites in the Altis group, 10 sites in the Comparator group, and 6 sites in both groups. This cohort study was conducted in accordance with the Helsinki Declaration and approved by independent institutional review boards or ethics committees for each site. To optimally reflect physician and patient directed choice in real clinical practice, a nonrandomized study was performed. The selection of the surgical intervention was based on surgeon expertize and shared decision-making between the patient and physician. Methods have been described previously in the initial 12-month publication.[7]

Patients were eligible if SUI was their predominant incontinence symptom and confirmed through Cough Stress Test (CST) or urodynamics. Eligible patients were required to have failed two noninvasive continence therapies (e.g., Kegel exercise, behavior modification, pad use, biofeedback) for >6 months. Exclusion criteria included stage 2 or greater pelvic organ prolapse (POP) determined by the POP quantification (POP-Q) system, prior SUI surgery, a concomitant surgical procedure, active urogenital/skin infection, incontinence due to neurogenic causes, history of radiation or brachytherapy, postvoid residual (PVR) > 100 cc on ≥2 occasions, and patient planning a future pregnancy. Preoperative baseline assessments included urogynecological history, physical examination, CST performed in lithotomy or standing position, PVR test, 24-h pad weight test (PWT), and validated patient questionnaires consisting of the UDI-6 for assessment of distress caused by urinary symptoms, IIQ-7 for evaluation of the psychosocial impact of incontinence and VAS for Pain.

The Altis SIS, with one static anchor and one dynamic bidirectional anchor allowing intraoperative tensioning, was implanted per the manufacturer's instructions for use (IFU). Collected intraoperative data included anesthesia method, procedure setting, duration, and complications. All FDA-cleared commercially available RMUS and TMUS were allowed in the Comparator group. All implanted slings were Amid type 1. By allowing the comparator group to include a variety of commercially available RMUS and TMUS, in a patient population with variable characteristics, we intended to include a diverse group of surgical patients with the aim to reflect actual clinical practice. Surgeons followed the IFU associated with the device of choice. Cystoscopy was routinely performed, and the Foley catheter removed according to local protocol.

Subjects were evaluated postoperatively at 6, 12, 18, 24, and 36 months. Twenty-four hour PWT, CST, UDI-6, IIQ-7, and PGI-I questionnaires assessed efficacy.

Efficacy and safety endpoints included: Objective dryness (defined as 24-h PWT ≤ 4.0 gm per protocol and ≤1.3 gm per FDA advisory), negative CST, adverse events, and revision/resurgery through 36 months. The primary efficacy endpoint, as required by the FDA and included as a study point in this paper, was an assessment of improvement in SUI at 6 months; treatment success defined as a 50% reduction from baseline in 24-h pad weight. The primary safety endpoint was the rate of device and/or procedure-related serious adverse events (SAE) through 36 months. Preliminary results of the primary effectiveness and safety endpoints, including patient selection, sample size estimation, baseline and surgical characteristics, have been previously published.[7] Statistically validated endpoint analysis data are presented in this manuscript. Secondary safety endpoints included comparative assessments of relevant device and procedure-related non-SAEs. Adverse events identified as relevant were required by FDA within the 522 order and included observed rates of organ perforation, bleeding, mesh exposure in the vagina, mesh erosion, pelvic pain, infection, de novo dyspareunia, urinary retention, recurrent incontinence, other urinary problems, and neuromuscular problems.

2.1 | Statistical considerations

The sample size was calculated to assess noninferiority of the primary efficacy and safety endpoints at 80% power with a type I error rate of 0.05 for each primary endpoint analysis. The sample size for the primary efficacy and safety endpoints was calculated to detect a noninferiority margin of 15% assuming a 6-month success rate of 75% in each group, and to detect a noninferiority limit of 10% assuming an underlying rate of device and procedure related SAEs of 10% in each group, respectively. The final sample size was determined to be the maximum of these sample size calculations for the primary endpoints with a 20% loss to follow-up at the end of the study. Assuming an equal allocation, this required a minimum of 328 subjects.

Noninferiority was assessed using a normal approximation test for a difference in binomial proportions at 80% power with a type-I error rate of 0.05 (two-sided; equivalent to one-sided 0.025) and was considered achieved if the upper limit of the 95% confidence interval (CI) for the difference in proportions (between Altis and Comparator arms) was less than 0.15 and 0.10 for efficacy and safety endpoints, respectively. Subjects were enrolled in the study once signed informed consent was obtained. The treated population (TP) included all enrolled subjects that underwent the surgical sling procedure. Data analysis was performed on the TP analysis set.

Due to the observational nature of the cohort study, for long-term safety evaluation, a propensity methodology was conducted to assess the effect of potential confounding variables on the primary endpoints given baseline factors: age, parity, BMI, smoking status, diabetes, hysterectomy status, history of multiple urinary tract infections.[8,9] The obtained propensity score was then applied in an adjusted logistic regression for each primary endpoint to determine whether the odds of treatment success were impacted by the propensity score when compared to an unadjusted logistic regression model. All analyses were performed using the SAS statistical software (version 9.4, SAS Institute).

3 | RESULTS

Four hundred and sixteen women enrolled between January 2015 and May 2018, 61 withdrew before treatment, and 355 underwent the sling procedure (TP); 184 were implanted with an Altis device, and 171 with a Comparator device. One-hundred forty (76%) Altis subjects and 101 (59%) Comparator subjects completed follow-up through 36 months (Figure 1).

The baseline patient characteristics are shown in Table 1. Patients in the Altis group were older and had a higher proportion of postmenopausal women. Patients in the Comparator group had a higher BMI, a higher urinary distress score, a higher proportion of current smokers, and a higher proportion of premenopausal women. History of previous pelvic surgery, sexually active and dyspareunia rates were comparable between groups. MUI diagnosis was more frequent in the Comparator group.

For the 36 months effectiveness endpoint measure, in the Altis arm, $n = 99$ (81.8%) were a success, and in the Comparator arm, $n = 79$ (82.3%) were a success. Using a noninferiority margin of 0.15, the difference in proportions of −0.005 for Altis versus Comparator (95% CI: −0.102 to 0.092) was statistically significant ($p = 0.002$). For the effectiveness endpoint measures, when assessing the noninferiority of Altis versus Comparator in 24-h pad weight success (≥50% reduction), the null hypothesis was rejected at every study visit through 36 months. Additional effectiveness analyses defined success as a dry pad (24-h pad weight ≤ 4.0 gm and ≤1.3 gm). Noninferiority was affirmed for all study visits through 36 months. The proportion of Altis subjects with dry pad weight was greater than or equal to Comparator subjects at all visits for both ≤ 4.0 gm and ≤1.3 gm (Table 2). Additionally, regarding the CST, Altis was found to be noninferior to the Comparator arm at every study visit, and the rate of negative CST remained above 80% for both groups ($p < 0.001$; Figure 2).

Post hoc analyses were performed to assess the noninferiority of Altis versus RMUS only and Altis versus TMUS only for 36 months efficacy. This study was not designed to determine noninferiority of Altis to RMUS or TMUS.

When assessing noninferiority of Altis versus RMUS at 36-month effectiveness endpoints, 99 (81.8%) Altis and 37 (90.2%) RMUS subjects were a success, trending toward statistical significance, however, it cannot be determined to be noninferior ($p = 0.092$). When assessing the noninferiority of Altis versus TMUS, 99 (81.8%) Altis and 33 (71.7%) TMUS subjects were a success, was statistically significant ($p < 0.001$), and thus Altis was noninferior.

The rates of negative CST at 36 months were 122 (87.1%) Altis, 40 (93.0%) RMUS ($p < 0.001$), and 44 (91.7%) TMUS ($p < 0.001$). CST demonstrated that Altis was noninferior to RMUS and Altis was noninferior to TMUS at 36 months.

A total of $n = 2$ Altis (1.1%) and $n = 4$ Comparator (2.3%) subjects experienced a device and/or procedure-related SAE within the 36-month study window. One Altis case of urinary/retention obstruction was defined as a SAE due to the need for surgery. The unadjusted logistic regression showed no significant increase or decrease in the odds ratio (OR = 0.46; $p = 0.372$). Inclusion of the propensity score did not demonstrate a shift in estimated odds or hypothesis test results (AdjOR = 0.43; $p = 0.345$). The results demonstrate that Altis is noninferior to the Comparator group with respect to primary safety endpoints through 36 months (Table 3).

The proportion of subjects in each arm experiencing device and/or procedure–related adverse events were also compared: 25/184 Altis (13.6%) subjects compared to 21/171 Comparator (12.3%) subjects experienced a secondary safety endpoint through 36 months following the index procedure ($p < 0.001$). Therefore, there is sufficient evidence to conclude that Altis is noninferior to the Comparator with respect to secondary safety endpoints through 36 months.

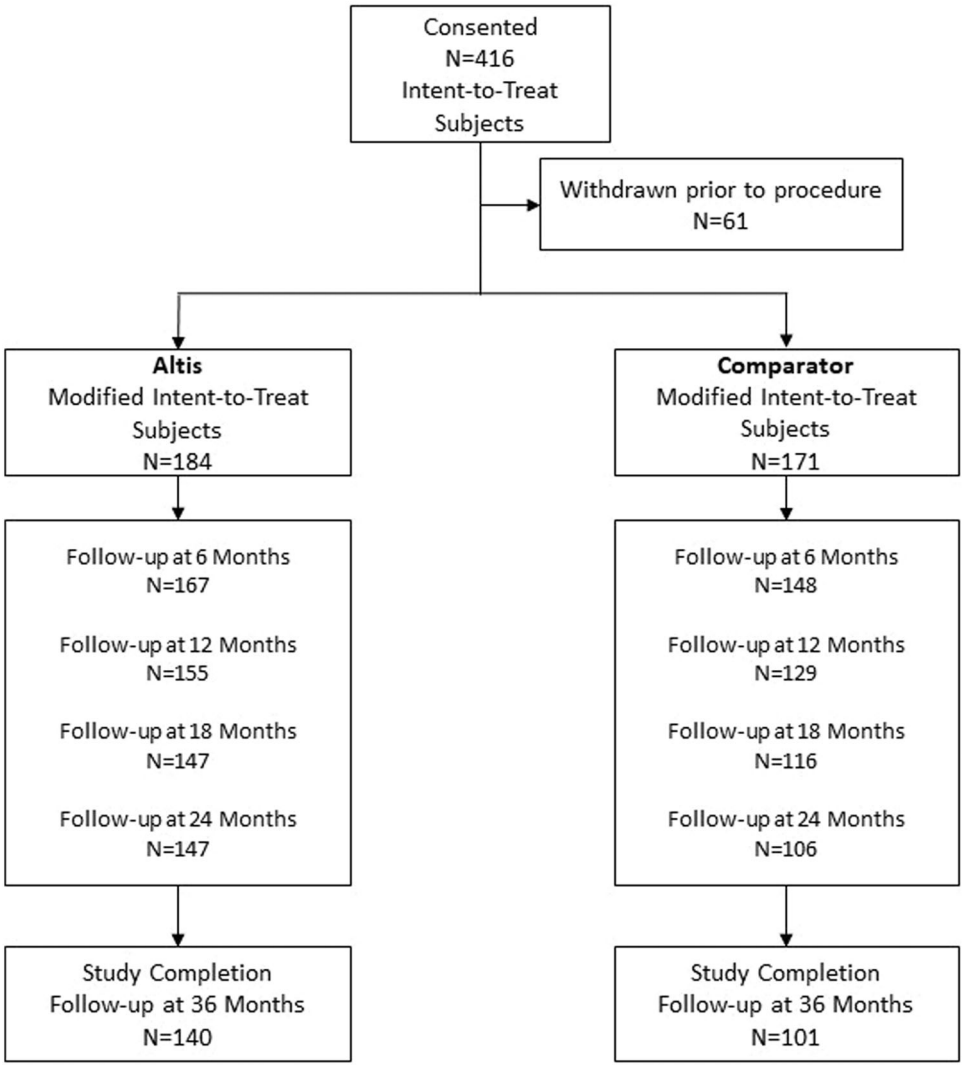

FIGURE 1 Enrollment and follow-up flow chart. CONSORT diagram of subjects completing study procedures and follow-up visits.

The most relevant events are listed in Table 4. There were no cases of mesh exposure, extrusion, or erosion associated with Altis through 36 months. One case of mesh exposure in the Comparator arm, not from the study sling, was associated with a second implanted nonstudy MUS ($p = 0.482$). One subject (0.5%) in the Altis arm experienced revision/resurgery compared to 7 subjects (4.1%) in the Comparator arm for recurrent incontinence ($n = 6$) and urinary retention ($n = 1$) over the course of 36 months. Seven (7) subjects (3.8%) in the Altis arm experienced hip pain due to position during the procedure, with the majority of pain resolving in less than 31 days. The most relevant events were statistically significant only for revision/resurgery ($p < 0.001$) in favor of Altis and hip pain ($p = 0.015$) in favor of the Comparator and, therefore, provides additional evidence supporting the claim that Altis is noninferior to the Comparator.

4 | DISCUSSION

Our findings indicate the safety and efficacy of Altis SIS are noninferior to MUS through 36 months. In both groups, objective measures demonstrated high efficacy. Furthermore, adverse event rates were low and the Altis cohort had significantly fewer revisions than the Comparator cohort.

The emphasis of real world choice, by allowing the surgeon and patient to select what they desire best, allowed this trial to have both RMUS and TMUS slings. In the Comparator group, there were 62 (36.3%) RMUS slings, 96 (56.1%) TMUS slings, and 13 (7.6%) SIS slings. The effectiveness endpoint demonstrated noninferiority between Altis and TMUS, however, between Altis and RMUS, noninferiority cannot be determined. CST demonstrated noninferiority between Altis and RMUS, and Altis and TMUS.

TABLE 1 Baseline characteristics.

Characteristic	Altis	Comparator	*p* Value[a]
Age, years[b]	56.2 ± 11.4	53.3 ± 12.3	0.024
BMI, kg/m^2[b]	30.0 ± 5.8	31.8 ± 7.7	0.014
Parity[c]	2 (1–7)	2 (1–7)	0.898
Menopause status			
Premenopausal	32 (17.4%)	60 (35.1%)	0.004
Postmenopausal	134 (72.8%)	101 (59.1%)	0.031
Previous pelvic surgery	129 (70.1%)	116 (67.8%)	0.644
Previous prolapse surgery	6 (3.3%)	6 (3.5%)	0.897
Previous incontinence surgery	0 (0.0%)	0 (0.0%)	-
Previous hysterectomy	74 (40.2%)	69 (40.4%)	0.980
Other pelvic surgery	82 (44.6%)	68 (39.8%)	0.360
Ethnicity			
Hispanic/Latino	38 (20.7%)	17 (9.9%)	0.005
Non-Hispanic/Latino	146 (79.3%)	154 (90.1%)	
Race			
White or Caucasian	179 (97.3%)	156 (91.2%)	0.013
Black or African American	4 (2.2%)	12 (7.0%)	
American Indian or Alaska Native	0 (0.0%)	2 (1.2%)	
Asian	0 (0.0%)	1 (0.6%)	
Native Hawaiian or Other	1 (0.5%)	1 (0.6%)	
Not disclosed	1 (0.5%)	2 (1.2%)	
Smoking history			
Current	17 (9.2%)	33 (19.3%)	0.023
Former	61 (33.2%)	53 (31.0%)	
Never	106 (57.6%)	85 (49.7%)	
Diabetes	24 (13.0%)	28 (16.4%)	0.375
Baseline incontinence diagnosis			
SUI	74 (40.2%)	31 (18.1%)	<0.001
MUI	110 (59.8%)	140 (81.9%)	<0.001
OAB wet	71/110 (64.5%)	89/140 (63.6%)	0.874
UDI-6 score[b]	50.3 ± 20.0	56.4 ± 21.1	0.006
IIQ-7 score[b]	56.7 ± 27.0	59.3 ± 24.7	0.355
Sexually active	129 (70.1%)	113 (66.1%)	0.416
Dyspareunia	27/51 (52.9%)	22/48 (45.8%)	0.480

Note: Data for the treated population are presented as numbers (%), unless otherwise noted. Significance $p \leq 0.050$.

[a]*p* Value for continuous variables is from a *t*-test, for categorical variables *p* Value is from a chi-square test;

[b]Mean ± standard deviation;

[c]Median (range).

TABLE 2 Effectiveness endpoint measures through 36 months.

Visit	Altis	Comparator	Difference in proportions (95% CI)	*p* Value[a]
Pad weight success (≥ 50% reduction from baseline)				
6 months	130 (77.8%)	119 (83.2%)	−0.054 (−0.139 to 0.031)	0.013
12 months	127 (79.9%)	99 (79.2%)	0.007 (−0.083 to 0.096)	<0.001
18 months	125 (83.3%)	93 (81.6%)	0.018 (−0.068 to 0.104)	<0.001
24 months	125 (83.9%)	84 (80.8%)	0.031 (−0.056 to 0.118)	<0.001
36 months	99 (81.8%)	79 (82.3%)	−0.005 (−0.102 to 0.092)	0.002
Dry (≤ 4 gm) pad weights				
6 months	98 (58.7%)	75 (52.4%)	0.062 (−0.047 to 0.172)	<0.001
12 months	96 (61.5%)	58 (46.4%)	0.151 (0.036−0.267)	<0.001
18 months	96 (65.3%)	66 (58.9%)	0.064 (−0.052 to 0.180)	<0.001
24 months	109 (74.7%)	52 (50.5%)	0.242 (0.125−0.359)	<0.001
36 months	78 (66.1%)	62 (66.0%)	0.001 (−0.124 to 0.126)	0.009
Dry (≤ 1.3 gm) pad weights				
6 months	64 (38.3%)	45 (31.5%)	0.069 (−0.038 to 0.175)	<0.001
12 months	59 (37.8%)	37 (29.6%)	0.082 (−0.029 to 0.194)	<0.001
18 months	53 (36.1%)	42 (37.5%)	−0.014 (−0.133 to 0.104)	0.012
24 months	57 (39.0%)	34 (33.0%)	0.060 (−0.061 to 0.182)	<0.001
36 months	45 (38.1%)	38 (40.4%)	0.023 (−0.107 to 0.152)	0.004

Note: Data for the treated population are presented as count (%), unless otherwise noted. Significance $p \leq 0.050$.

Abbreviation: CI, confidence interval.

[a]*p* Value for categorical variables is a difference in proportions noninferiority test between groups with a noninferiority margin of 0.15.

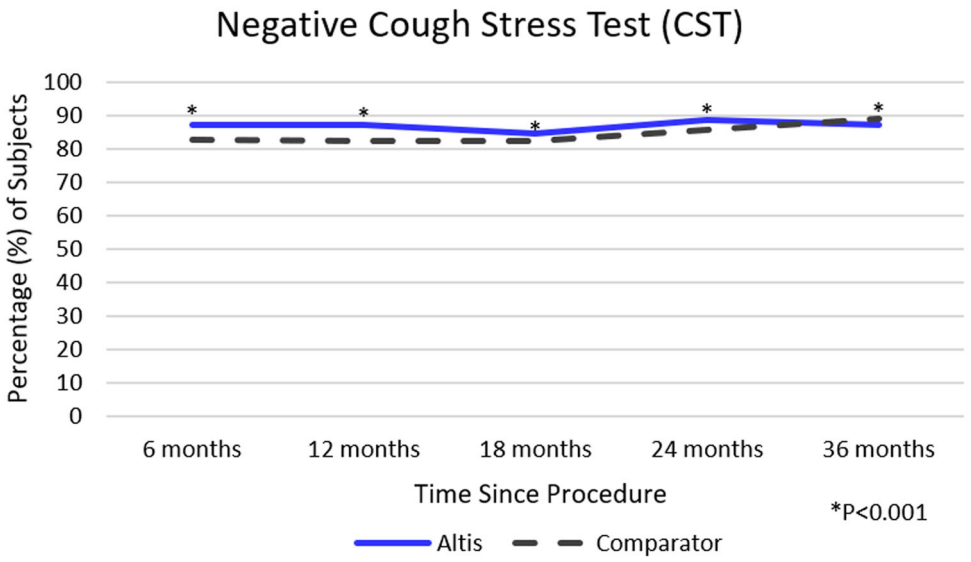

FIGURE 2 Negative cough stress test (CST) through 36 months. Data for the treated population are presented as numbers (%). Significance $p \leq 0.050$. **p* Value for categorical variables is a difference in proportions noninferiority test between groups with a noninferiority margin of 0.15.

TABLE 3 Safety endpoint measure—device and/or procedure-related serious adverse events through 36 months.

	Altis	Comparator	Difference in proportions (95% CI)	*p* Value[a]
Device and/or procedure-related SAEs through 36 months	2/184 (1.1%)	4/171 (2.3%)	0.013 (−0.023 to 0.048)	<0.001
Propensity score analysis[b]	Odds ratio for device and/or procedure-related SAEs		95% CI for odds ratio	*p* Value[c]
Unadjusted logistic regression model	0.46	(0.083−2.537)	0.372	
Adjusted logistic Regression model	0.43	(0.075−2.477)	0.345	

Note: Data for the treated population are presented as count/sample size (%), unless otherwise noted. Significance $p \leq 0.050$.

Abbreviation: CI, confidence interval.

[a]*p* Value for a noninferiority test is between groups using a normal approximation (*Z*-test) where the noninferiority margin for a difference is 0.10;

[b]Propensity score calculated as odds of treatment assignment given age, parity, BMI, smoking status, diabetes, hysterectomy status, and history of multiple UTIs;

[c]*p* Value for the odds ratio from a logistic regression where the outcome is the Device and/or Procedure-Related SAEs events through 36 Months.

Our results are consistent with published literature on Altis SIS. CST procedures were performed in six studies, with negative CST results ranging 50−92%.[10–15] Viruega-Cuaresma et al. reported negative CST of 50% at 6 years based on two patients.[15] Up to the 4-year mark, where the attrition rate was reasonable, negative CST rates ranged between 96.8% and 85.7% from years 1 to 4, respectively.[15] Two publications (same patient cohort) used 24-h Pad Weight Testing, with results of 90.1% and 90.0% meeting the performance goal of 50% decrease and "dry" (pad weight ≤ 4 gm) measured at 77.2% and 81.1% at 12 and 24 months follow-up respectively.[11,12] Another study that defined cure as pad weight ≤ 8 grams was achieved in 72.0% at 36 months.[16]

Furthermore, observed adverse event rates in the Altis 522 Study are similar or better than published literature. Reported complications include urinary tract infections, 0.9−9.8%[12,13,15,17,18]; dyspareunia, 0.9−11.7%[12,13,16,19]; and urinary retention, 1.8−10.6%.[10,12,13,17–19] In general, these complication rates were lower in this study, particularly for dyspareunia for both the Altis and Comparator groups. The de novo dyspareunia (Altis = 1.6%; Comparator = 1.2%) and worsening dyspareunia rates were low (Altis = 0.5%; Comparator = 0.6%). Similarly low rates of dyspareunia have been reported elsewhere for the Solyx 522 study.[20] There were no cases of mesh exposure, extrusion, or erosion due to the study sling observed in the Altis 522 Study, which is consistent with the low event rates described in the literature (0.7−5.2%).[12–19] Interestingly, the first paper published on Altis had an extrusion rate of 3.5%.[12] In that IDE trial there could be no prior experience of the surgeons using Altis since all patients had to be enrolled in the trial. Some of the surgeons participated in both studies. The 0% (522 Study) versus 3.5% (IDE) extrusion rate may be an example of Performance Bias, where the skill and experience of the surgeon impacts the results. We suggest it is important to attempt to control Performance Bias in study design. Readers should consider the conclusions and impact of Performance Bias as they evaluate any paper with results substantially different from other published literature.

At baseline, there was a difference in the incontinence diagnosis between groups. However, in both arms a majority of patients were diagnosed with stress-predominant MUI (Altis 59.8% vs. Comparator arm 81.9%) or SUI (Altis 40.2% vs. Comparator 18.1%). Furthermore, the proportion of patients with urgency-related incontinence (i.e., OAB wet) was similar ($p = 0.874$). This study did not restrict treatment for OAB symptoms. Patients in both groups may have received treatment for OAB over the study duration.

One study limitation is, at 36 months, the attrition rate for the Altis arm was 23.9%, whereas the attrition rate for the Comparator arm was 40.9%. The largest source of attrition within the Comparator arm was a single site where the principal investigator left the institution with no available replacement. The site was forced to terminate the study and all 32/171 (18.7%) subjects were withdrawn. This site closure example highlights the impact a single site can have, and the importance of stability within the research site, ensuring collateral flow in case of a change in research personnel.

Study strengths include the large number of study participants, prospective, multicenter approach, duration of 36 months, and use of standardized and validated instruments to measure subjective outcomes. Due to the real-world study design, lack of randomization between treatment arms may be considered an inherent

TABLE 4 Device and/or procedure-related adverse events through 36 months.

	Altis	Comparator	*p* Value[1]
Serious device and/or procedure-related adverse events			
Pelvic/urogenital pain (groin)	1 (0.5%)	0 (0.0%)	1.000
Urinary retention/obstruction requiring surgery	1 (0.5%)	0 (0.0%)	1.000
Bleeding, hematoma or hemorrhage	0 (0.0%)	1 (0.6%)	0.482
Delayed wound healing	0 (0.0%)	1 (0.6%)	0.482
Mesh exposure (extrusion)	0 (0.0%)	1 (0.6%)	0.482
Perforation, bladder	0 (0.0%)	1 (0.6%)	0.482
Revision/Resurgery	1 (0.5%)	7 (4.1%)	<0.001
Relevant nonserious device and/or procedure-related adverse events			
Urinary retention/obstruction	9 (4.9%)	3 (1.8%)	0.142
Recurrent incontinence	2 (1.1%)	7 (4.1%)	0.094
Vaginal blood spotting	1 (0.5%)	1 (0.6%)	1.000
Delayed wound healing	0 (0.0%)	1 (0.6%)	0.482
"Button hole" in Fornix	0 (0.0%)	1 (0.6%)	0.482
Infection	0 (0.0%)	1 (0.6%)	0.482
Other urinary problems			
Voiding dysfunction	1 (0.5%)	0 (0.0%)	1.000
Urgency worsening	0 (0.0%)	2 (1.2%)	0.231
Dysuria	1 (0.5%)	1 (0.6%)	1.000
Pain			
Pelvic/urogenital (groin) pain	7 (3.8%)	4 (2.3%)	0.546
Dyspareunia, de novo	3 (1.6%)	2 (1.2%)	1.000
Dyspareunia, worsening	1 (0.5%)	1 (0.6%)	1.000
Vaginal pain	1 (0.5%)	0 (0.0%)	1.000
Pain at incision site	0 (0.0%)	1 (0.6%)	0.482
Extremity pain			
Hip pain	7 (3.8%)	0 (0.0%)	0.015
Leg pain	4 (2.2%)	0 (0.0%)	0.124
Hip and leg pain	3 (1.6%)	0 (0.0%)	0.249
Sciatica	1 (0.5%)	0 (0.0%)	1.000
Calf pain	0 (0.0%)	1 (0.6%)	0.482
Abdominal pain			
Lower abdominal pain	1 (0.5%)	0 (0.0%)	1.000
Lower abdomen cramping	0 (0.0%)	1 (0.6%)	0.482

Note: Data for the treated population are presented as the number of subjects (%). Significance $p \leq 0.05$.

[1]*p* Value is for a Fisher's exact test for the proportions between groups.

limitation; therefore, propensity score matching was performed to control for baseline patient factors.

One further limitation of the study design is that it did not account for race and ethnicity representation as a component of the inclusion criteria and therefore resulted in a population, based on baseline demographics, which does not adequately reflect minority groups. As recently indicated, race and ethnicity representation should increase in priority for clinical trial design and execution.[21]

Consideration of new sling technology requires the approach demonstrate noninferiority to existing options and provide an alternative that satisfies some unmet need. Potential benefits of the Altis® SIS mini-sling are unique in that it provides surgeons with the ability to tighten and loosen the sling during implantation,[22] utilizes less mesh volume than full-length slings, and is less invasive into the retropubic and groin spaces. Without reimbursement constraints Altis SIS can be performed under local anesthesia in an outpatient or office setting providing value and reduced cost in the surgical treatment of female SUI.[11] In addition, Altis reduces the risk of blind needle passage through the groin or abdomen. Small bowel injury has been reported in full-length retropubic slings at a rare rate of 0.005%, with a death rate of 25%.[23] This risk is eliminated with SIS. Finally, anchoring inside the body eliminates thigh or abdominal muscle passage and exit wounds required for full-length slings.

5 | CONCLUSIONS

Our study demonstrates noninferiority between Altis SIS mini-sling and MUS in terms of treatment success and adverse events at 36 months. This study answered the scientific needs of safety and midterm efficacy on the noninferiority of the Altis SIS compared to the standard MUS.

AUTHOR CONTRIBUTIONS

Le Mai Tu, Edward Gheiler, Craig E. Hanson, Mark Jalkut, Rebecca McCrery, Mitesh Parekh, Mohamad Parva and Ty Erickson contributed to the implementation of the research; Le Mai Tu and Ty Erickson contributed to the analysis of the results and to the writing of the manuscript.

ACKNOWLEDGMENT

Sponsored by Coloplast Corp. This study was sponsored by Coloplast; the sponsor assembled a team of collaborators to design this study in accordance with the Food and Drug Administration 522 mandate and provided statistical analysis of data. Authors independently completed the writing of the report and submitted article for publication.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The participants of this study did not give written consent for their data to be shared publicly, so due to the sensitive nature of the research supporting data is not available.

ETHICS STATEMENT

This cohort study was conducted in accordance with the Helsinki Declaration and approved by independent institutional review boards or ethics committees for each site. Written informed consent was obtained. Permission to reproduce material from other sources: N/A.

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How to cite this article: Tu LM, Gheiler E, Hanson CE, et al. Management of female stress urinary incontinence with single-incision mini-sling (Altis®): 36 month multicenter outcomes. *Neurourol Urodyn*. 2023;1-11. doi:10.1002/nau.25256