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Title: Efficacy and Safety of a Non-Animal Stabilized Hyaluronic Acid/Dextranomer (NASHA/Dx FI [Solesta®]) in Improving Fecal Incontinence: A Prospective, Single-arm, Multicenter, Clinical study with 36 Month Follow-up

Objective: Fecal incontinence (FI) affects up to 8.3% of non-institutionalized adults and leads to social withdrawal, embarrassment, and physical symptoms. Women with obstetric trauma, such as obstetric and sphincter injury (OASIS), are at greater risk of FI: up to 59% of women with OASIS experience FI. Surgical options are invasive compared to NASHA/Dx FI; a non-surgical, biocompatible injectable bulking agent. The primary aim of this study was to determine treatment efficacy, measured as a ≤50% re-intervention rate for FI at 36 months. Re-intervention was defined as sphincteroplasty, implantation of artificial bowel sphincter, retreatment with NASHA/Dx FI, graciloplasty, sacral neuromodulation (SN), or other surgical interventions. Secondary aims assessed FI-specific quality of life measures (FIQL, CCFIS), patient-reported global assessment of improvement, and time to re-intervention. The primary safety objective measured device-related adverse events (AEs) during injection, peri-injection, and through 36 months.

Methods: 283 subjects at 18 US sites were enrolled in a prospective, single-arm study (NCT#01647906). Patients with FI that failed conservative therapy were eligible. Participants received 1-2 NASHA/Dx FI treatments; the first within 30 days of baseline, and the second, if needed, 1-3 months after initial treatment. Other NASHA/Dx FI treatments were considered re-interventions. Enrolled subjects were followed for a minimum of 7 visits over 36-months following last treatment. The probability of re-intervention was estimated using a Bayesian multiple imputation approach.

Results: Of the 283 FI patients enrolled, the mean age was 64.6 (SD 13.0) and the average BMI of 27.8 (SD 7.72). Majority were female (85.5%), white (91.8%), and had FI for longer than 12 months (92.6%). The most common etiology of FI was obstetric (54.4%), followed by neurogenic (9.2%). Data for 192 patients (67.8%) was available at 36-month follow-up. Through 36-months, the Bayesian simulation estimation of the rate of re-intervention based on intention to treat was 18.9% (95% CI: 14.0%-24.4%); and the unadjusted proportion requiring re-intervention was 20.8% (40/192). Patients experienced improvement across all FIQL domains and a 4-point decrease in mean CCFIS, indicating improvement in QoL and reduction in symptom burden post-treatment (Table 1). 58 device-related AEs were reported; most were GI disorders that resolved quickly, and none were serious.

Conclusion: NASHA/Dx FI is efficacious in treating FI, with >80% of patients requiring no re-intervention over a 36-month period. NASHA/Dx FI demonstrates clinically significant improvement in efficacy, safety, durability and patient's QoL as a minimally invasive therapy option for FI patients.

Table 1: Change in FIQL and CCFIS from baseline to visit 7

Domain	**Change from Baseline** Mean (SD)	**Baseline Score** Mean (SD)	**Visit 7 Score** Mean (SD)
Fecal Incontinence Quality of Life (FIQL)			
Lifestyle sub-scale	**0.5 (0.77)**	2.6 (0.85)	3.2 (0.83)
Coping/Behavior sub-scale	**0.7 (0.84)**	1.9 (0.71)	2.7 (0.94)
Depression/Self-Perception sub-scale	**0.4 (0.69)**	2.6 (0.73)	3.0 (0.84)
Embarrassment sub-scale	**0.8 (0.92)**	1.9 (0.73)	2.7 (0.92)
Cleveland Clinic Fecal Incontinence Score (CCFIS)	**-4.0 (4.96)**	13.5 (3.52)	9.2 (5.09)

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