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SAFETY AND POTENTIAL EFFECTIVENESS OF COOK MYOSITE AUTOLOGOUS MUSCLE DERIVED CELLS FOR TREATMENT OF STRESS URINARY INCONTINENCE: PRELIMINARY RESULTS FROM A DOSE ESCALATION STUDY

Hypothesis / aims of study

This prospective, dose escalation study is designed to assess the 12-month safety and potential effectiveness of 4 different doses of Cook MyoSite Autologous Muscle Derived Cells (CMI-AMDC) for treatment of stress urinary incontinence (SUI) in women. This preliminary report describes the 6-month follow-up results for all dose groups and the 12-month follow-up results for the two lowest dose groups.

Study design, materials and methods

Women, aged 18 years or more, with symptoms of SUI were included in the study. Each patient had failed a prior treatment for SUI (e.g., behavioral, medication, bulking, or surgery) and had not shown improvement in incontinence symptoms over the previous 6 months.

Patients received trans- or periuretheral administration of 10 million, 50 million, 100 million, or 200 million CMI-AMDC, which were derived from biopsies of the quadriceps femoris. Multiple injections were used to distribute the total dose of cells circumferentially around the urinary sphincter. Local anesthesia was used for the biopsy and during the CMI-AMDC injection. Patient evaluation occurred at baseline and at 1, 3, 6, and 12 months following treatment.

Safety of the CMI-AMDC therapy, which is the primary outcome of the study, is based on the incidence of adverse events. The study is not powered to assess effectiveness of the therapy; however, potential effectiveness is gauged with quantitative and qualitative measures of SUI assessed before and after CMI-AMDC injection. Outcome measures include a 3-day diary of incontinence episodes, 24-hour pad weight, and quality of life scores (i.e., Urogenital Distress Inventory (UDI-6) and the Incontinence Impact Questionnaire (IIQ-7)). Patients serve as their own controls. Per study design, the statistical significance of changes in outcome measures will be tested at study completion.

Results

Sixty-four (64) women received intrasphincter delivery of either 10 million (n=16), 50 million (n=16), 100 million (n=24), or 200 million (n=8) CMI-AMDC (Table 1). To date, 1 patient from the 10 million dose group has been lost to follow-up while 1 patient from the 50 million dose group and 2 patients from the 100 million dose group have withdrawn from the study. All remaining patients in the 10 million and 50 million dose groups have completed 12-month follow-up, while 86.4% (19/22) of remaining patients in the 100 million dose group and 75.0% (6/8) of patients in the 200 million dose group have completed 6-month follow-up.

Table 1. Baseline patient characteristics for each CMI-AMDC dose group

	CMI-AMDC dose			
Characteristic (Mean±std error)	10 million (n=16)	50 million (n=16)	100 million (n=24)	200 million (n=8)
Age	55.8±2.8	51.6±1.6	54.3±2.3	53.8±2.3
Body mass index	27.4±1.3	27.6±1.3	27.8±0.9	27.6±1.8
3-day stress leaks	10.1±1.9	8.6±2.8	9.9±1.7	15.9±7.3
24-hr pad weight	24.2±4.9	33.5±18.1	45.3±20.6	27.2±15.9

No serious adverse events related to CMI-AMDC treatment have been reported. Treatment-related adverse events occurring within 30 days of CMI-AMDC injection were limited to pelvic/abdominal pain or cramping (4.7%, 3/64), dysuria (4.7%, 3/64), gross haematuria (3.1%, 2/64), vaginal and/or urethral itching (3.1%, 2/64), haematoma at the biopsy site (3.1%, 2/64), increased frequency (1.6%, 1/64), and transient sensation of a foreign object in the urethra (1.6%, 1/64). All events were easily treated or self-resolved.

Compared to baseline, some patients in each dose group reported ≥50% improvement in the incidence of stress leaks and ≥50% improvement in the amount of urine leakage during a 24-hour pad test (Table 2). Some patients also reported 0 or 1 stress leaks or <1.3 g of pad weight at 6 and 12 months (Table 2). Improvement may be dose dependent since a higher proportion of patients in the 2 highest dose groups experienced ≥50% improvement in stress leaks and pad weight compared to patients in the 2 lowest dose groups. Patient quality of life was also assessed using 2 validated surveys, the UDI-6) and the IIQ-7. Compared to baseline, improvement in mean UDI-6 and IIQ-7 scores was observed for all dose groups (Table 3).

Table 2. Percentage of patients reporting ≥50% improvement or dry status (i.e., 0 or 1 stress leaks over 3 days and <1.3 g pad weight) based on diary reported stress leaks and the 24-hour pad test*

	Stress leaks reported over 3 days				**24-hour pad test**			
	≥50% improvement		**0 or 1 stress leaks**		**≥50% improvement**		**<1.3 g pad weight**	
Dose group	**6-month**	**12-month**	**6-month**	**12-month**	**6-month**	**12-month**	**6-month**	**12-month**
10 million	66.7% (10/15)	53.3% (8/15)	46.7% (7/15)	40.0% (6/15)	50.0% (7/14)	20.0% (3/15)	7.1% (1/14)	6.7% (1/15)
50 million	66.7% (10/15)	66.7% (8/12)	46.7% (7/15)	58.3% (7/12)	35.7% (5/14)	46.2% (6/13)	14.3% (2/14)	30.8% (4/13)

100 million	77.8% (14/18)	—	50.0% (9/18)	—	73.7% (14/19)	—	36.8% (7/19)	—
200 million	83.3% (5/6)	—	66.7% (4/6)	—	83.3% (5/6)	—	66.7% (4/6)	—

*NOTE: Incomplete/missing diary and pad weight data were excluded from the analysis.

Table 3. Mean quality of life scores for each CMI-AMDC dose group

Dose group	**Mean UDI-6 scores**			**Mean IIQ-7 scores**		
	Baseline	**6-month**	**12-month**	**Baseline**	**6-month**	**12-month**
10 million	60.4±4.1	37.8±4.8	30.3±4.4	39.6±5.0	28.6±6.4	19.0±3.6
50 million	55.7±4.8	25.3±4.3	26.8±4.0	38.7±5.0	14.0±5.1	14.9±5.0
100 million	47.0±3.5	31.8±4.3	–	37.7±4.6	13.6±3.2	–
200 million	41.7±8.3	29.2±9.3	–	35.7±10.0	24.6±12.4	–

Interpretation of results

These preliminary results suggest that intrasphincter injection of CMI-AMDC is safe at doses ranging from 10 million to 200 million CMI-AMDC. No treatment-related serious adverse events were reported and all minor complications associated with CMI-AMDC treatment occurred at low rates and either self-resolved or were easily treated. Preliminary effectiveness data suggest that treatment reduced the amount of leakage during a 24-hour pad test, lowered the incidence of diary-reported stress leaks over 3 days, and improved the quality of life for some patients.

Concluding message

Intrasphincter injection of CMI-AMDC at doses of 10 million, 50 million, 100 million, and 200 million cells is safe. Additionally preliminary effectiveness data from this small feasibility study suggest that CMI-AMDC treatment may improve both symptoms and quality of life in adult women with SUI.

Specify source of funding or grant	**This study was sponsored by Cook Myosite.**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**Yes**
Specify Name of Public Registry, Registration Number	**This study is registered at ClinicalTrials.gov (Registration number: NCT00847535).**
Is this a Randomised Controlled Trial (RCT)?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**This study has been approved by Beaumont Hospital Human Investigation Committee, Vanderbilt University Institutional Review Board, and Sunnybrook Health Sciences Centre Research Ethics Board.**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**