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AUTOLOGOUS MUSCLE CELL MEDIATED THERAPY FOR STRESS URINARY INCONTINENCE: COMBINED SAFETY & POTENTIAL EFFICACY RESULTS FROM TWO STUDIES

Hypothesis / aims of study
Two multicentre studies were conducted to assess the 12-month safety and potential efficacy of autologous muscle derived cells (AMDC) for treatment of stress urinary incontinence (SUI) in women.

Study design, materials and methods
This pooled analysis combines data from 2 studies of AMDC treatment for women with SUI. Both studies were conducted concurrently and intended to be evaluated together. Each protocol specified the same patient selection criteria and outcome measures. Enrolled patients had SUI refractory to prior treatment and had no symptom improvement over the past 6 months. Each patient underwent a needle biopsy of the quadriceps femoris during an out-patient procedure. At a cell processing facility, cells rich in myogenic content were isolated from biopsies and expanded *ex vivo* to produce AMDC. About 6 weeks following biopsy, patients underwent intrasphincteric injection of AMDC. Study I was a dose escalation study where 64 patients received 10 (n=16), 50 (n=16), 100 (n=24), or 200 x 10^6 (n=8) AMDC via a transurethral or periurethral injection. In Study II, 16 patients received 200 x 10^6 AMDC via a transurethral injection. The primary outcome measure was safety, determined by the incidence and severity of adverse events (AEs). Secondary outcomes of clinical efficacy were based on 3-day voiding diaries, 24-hour pad tests, and quality of life scores (e.g., UDI-6 and IIQ-7) at baseline and 12-month follow-up.

Results
Eighty-two patients underwent biopsy and, as planned, 80 patients underwent AMDC treatment; 72 patients completed diaries and pad tests at 12-month follow-up. At baseline, patients had a median of 7 stress leaks over 3 days and a mean pad weight of 51 g.
No serious procedure- or treatment-related AEs were reported and no AEs were adjudicated as AMDC product-related. All biopsy and injection procedure-related AEs self-resolved or were easily treated. Four patients experienced biopsy-related AEs, which included wound haematoma (2%), procedural dizziness with associated physiologic responses (2%), and post procedural haemorrhage (1%). Fourteen patients experienced 22 injection procedure-related AEs, which included dysuria (9%), pelvic/abdominal pain (5%), vulvovaginal pruritus (4%), micturition urgency (3%), haematuria (3%), vulvovaginal burning sensation (1%), sensation of foreign body in urethra (1%), increased urinary frequency (1%), and urinary tract infection (1%).
Compared to lower dose groups, the 100 and 200 x 10^6 dose groups had higher percentages of patients with ≥50% reduction in stress leaks and pad weight at 12-month follow-up (Table 1). Additionally, the lowest dose group (i.e., 10 x 10^6 AMDC) had the lowest percentages of patients with no stress leaks and negative pad tests. Nonetheless, all dose groups experienced statistically significant improvement in UDI-6 and IIQ-7 scores at 12-month follow-up (Table 2).

Table 1. Percentage of patients meeting endpoint at 12 months*

12-month outcomes	AMDC dose group			
	10 x 10^6	**50 x 10^6**	**100 x 10^6**	**200 x 10^6**
≥50% reduction in stress leaks	53% (8/15)	69% (9/13)	85% (17/20)	77% (17/22)
No stress leaks over 3 days	20% (3/15)	39% (5/13)	30% (6/20)	32% (7/22)
0-1 stress leaks over 3 days	40% (6/15)	54% (7/13)	50% (10/20)	55% (12/22)
≥50% reduction in pad weight	20% (3/15)	43% (6/14)	52% (11/21)	64% (14/22)
Negative pad tests (<1.3 g)	7% (1/15)	29% (4/14)	24% (5/21)	32% (7/22)

*Two patients who completed 12-month follow-up reported no stress leaks over 3 days at baseline and could not improve; therefore, they were excluded from the stress leak analysis.

Table 2. Mean UDI-6 and IIQ-7 scores

AMDC dose	Mean UDI-6 score ± std error		Mean IIQ-7 score ± std error	
	Baseline	**12-month**	**Baseline**	**12-month**
10 x 10^6	60.4 ± 4.1	30.3 ± 4.4*	39.6 ± 5.0	19.1 ± 3.6*
50 x 10^6	55.7 ± 4.8	26.8 ± 4.0*	38.7 ± 5.0	14.9 ± 5.0*
100 x 10^6	47.1 ± 3.5	32.5 ± 4.3*	37.7 ± 4.6	13.4 ± 2.3*
200 x 10^6	48.1 ± 4.3	33.9 ± 4.0*	44.3 ± 5.5	26.4 ± 5.5*

UDI-6 and IIQ-7 are scored 0-100, with lower scores indicating a higher quality of life.
Comparison of baseline and 12-month time points made by paired t-test; *p<0.05.

Interpretation of results
Intrasphincteric injection of AMDC at doses of 10, 50, 100, and 200 x 10^6 cells appears safe with no serious treatment-related AEs reported. No AMDC product-related AEs were reported and all procedure-related AEs self-resolved or were easily treated. Based on reduction of diary-reported stress leaks and 24-hour pad weight, more patients may be responsive to doses of ≥100 x

10^6 AMDC than to lower doses. However, all dose groups had statistically significant improvement in the validated quality of life surveys, IIQ-7 and UDI-6, 12 months following treatment.

Concluding message

Intrasphincteric injection of AMDC at doses of 10, 50, 100, and 200 x 10^6 cells appears safe with no serious treatment-related AEs reported. Efficacy data suggest that more patients may be responsive to doses of ≥100 x 10^6 AMDC, providing crucial information for a future placebo-controlled trial.

Disclosures

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