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## MULTICENTER RANDOMIZED CONTROLLED TRIAL TO EVALUATE URYX URETHRAL BULKING AGENT IN TREATING FEMALE STRESS URINARY INCONTINENCE: COMPARISON OF INITIAL AND EXPANSION PHASES OF TRIAL

### Hypothesis / aims of study

This study evaluated URYX® compared to Contigen® in treatment of female urinary incontinence. After 41 patients had been treated at six sites in an Initial Phase of the study, modifications were made to the recommended injection technique, addressing injection needle placement, rate of injection and injected volume per treatment. An additional 212 patients were treated at a total of 14 sites in an Expansion Phase of the study. We evaluated key efficacy and safety parameters in both phases to assess the impact of the technique changes on the outcomes, and to understand the importance of delivery technique in the use of injectables.

### Study design, materials and methods

URYX is an injectable solution of ethylene vinyl alcohol (EVOH) dissolved in dimethyl sulfoxide (DMSO) carrier. Contigen is glutaraldehyde cross-linked bovine collagen suspended in buffered saline. 237 females with genuine SUI were randomized and prospectively treated with either URYX or Contigen. A maximum of three treatments was allowed in the first 90 days. Mean age was 61 years. All patients had failed previous urinary incontinence treatment, with 46% failing at least one surgery. Efficacy was assessed at 12 months following the last treatment using pad weight and Stamey grade. The Incontinence Quality of Life (I-QOL) survey was utilized as well. Safety analysis was comprehensive.

### Results

In the overall population the mean total injected volume of URYX was 4.7ml, compared to 7.2ml for Contigen.

Primary effectiveness measures at one year were as follows:

| | INITIAL PHASE | | EXPANSION PHASE | |
|---|---|---|---|---|
| | **URYX (N=22)** | **Contigen (N=11)** | **URYX (N=89)** | **Contigen (N=46)** |
| **Pad Weight ≥50% Improvement** | 80% | 60% | 68% | 56% |
| **Pad Weight Dry** | 87% | 50% | 52% | 35% |
| **Stamey Grade Dry or Improved** | 55% | 82% | 61% | 50% |
| **Stamey Grade Dry** | 27% | 36% | 24% | 17% |

Key treatment-related adverse events reported were as follows:

| | INITIAL PHASE | | EXPANSION PHASE | |
|---|---|---|---|---|
| | **URYX (N=28)** | **Contigen (N=13)** | **URYX (N=146)** | **Contigen (N=66)** |
| **Dysuria** | 39% | 31% | 11% | 6% |
| **Hematuria** | 39% | 23% | 5% | 0% |
| **Delayed voiding** | 14% | 15% | 18% | 12% |
| **Urinary frequency** | 21% | 8% | 9% | 9% |
| **Urinary urgency** | 25% | 8% | 9% | 8% |
| **Urinary tract infection** | 18% | 0% | 10% | 5% |

**Interpretation of results**

On objective measures (Pad Weight), improvement in the URYX group was higher than in the Contigen group for both phases. On subjective measures (Stamey Grade), the Contigen group showed greater improvement in the Initial Phase, while the URYX group showed greater improvement in the Expansion Phase. However, there was generally no statistically significant (Fisher's Exact test, $p<.05$) difference between the groups within either phase. The only statistically significant difference between the Initial Phase and Expansion Phase within either group was for Dry Pad Weight in the URYX group.

A slightly higher incidence of complications and adverse events in the URYX group was associated with material exposure through the mucosa, which was observed in 16% of URYX treatments in the Initial Phase. Review of procedural videos suggested that placement of the URYX too shallow and/or too proximal to the bladder neck contributed to such exposure. After modification of recommended injection technique, the incidence of such exposure in the Expansion Phase declined to 6% of treatments. In all other subjects the complication rate was comparable between the two groups.

**Concluding message**

At one year after last treatment, improvement in both objective and subjective outcome measures was greater in the URYX group than in the Contigen group, though there was not a statistically significant difference between the groups. The URYX results were achieved using 36% less injected volume of material than used in the Contigen group. While there was no statistically significant difference in effectiveness outcomes within each group between the Initial Phase and the Expansion Phase, it appears that the modification of injection technique has successfully addressed the incidence of material exposure in the URYX group and the associated adverse events.

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