Urolon™

24-month

Clinical Study Data

urolon™ *perspectives*

In September 2016, a European multicenter clinical trial was initiated to support the safety and efficacy of Urolon™, a bioresorbable urethral implant for the treatment of mild to moderate female stress urinary incontinence (SUI). 50 female subjects, recruited between September 2016 and July 2017, were treated by transurethral sub-mucosal Urolon™ injection. All subjects had attempted and failed prior pelvic floor muscle training.

SUI symptoms and treatment success (efficacy) were assessed with the Stamey Grading System (SGS), Patient Global Impression of Severity (PGI-S) and Patient Global Impression of Improvement (PGI-I). Whilst SGS is used as an objective measure of efficacy, PGI-S and PGI-I represent subjective measures of efficacy. The PGI-S is a single question asking the patient to rate how their urinary tract condition is now on a scale of 1 - *Normal* to 4 - *Severe*. PGI-I is a transition scale from a single question asking the patient to rate their urinary tract condition now, as compared with how it was before beginning treatment, on a scale from 1 - *Very much better* to 7 - *Very much worse*.

Quality of life (QoL) was assessed using both the International Consultation on Incontinence Questionnaire – Short Form (ICIQ-SF) and Incontinence Quality of Life (I-QoL) scale. ICIQ-SF severity is divided into the following categories: *slight* (1-5), *moderate* (6-12), *severe* (13-18) and *very severe* (19-21). I-QoL is a disease-specific instrument designed to measure the impact of urinary incontinence on quality of life. QoL measures are an essential end-point in evaluating the efficacy of incontinence treatments. Safety was assessed via reported adverse events and an additional cystoscopic examination at the 12-month follow-up.

EFFICACY SUMMARY FOR UROLON™

Distribution of SGS scores before treatment (baseline) and at the follow-up visits are shown in *figure 1*. A higher grade indicates a higher SUI severity. Results show a shift to a lower grade and therefore an improvement in SUI after treatment with Urolon™.

Total improvement of SGS-scores are shown in *figure 2*. Total improvement at 3-month follow-up was 63%, at 6-month follow-up 54%, at 12-month follow-up 58%, at 18-month follow-up 47% and at 24-months follow-up 50%. Of note is that at baseline, the majority of subjects started with a SGS 1 (mild) which is very difficult to reduce to a SGS 0 (due to the low sensitivity of the SGS). For example, a subject with both a SGS of 1 at baseline and at 24-month follow-up can still have a considerable improvement on other endpoints that may have more impact on the quality of life of the subject. Therefore SGS results are likely an underestimation of perceived improvement. This is supported by the results of other endpoints that were recorded during the trial as shown below.

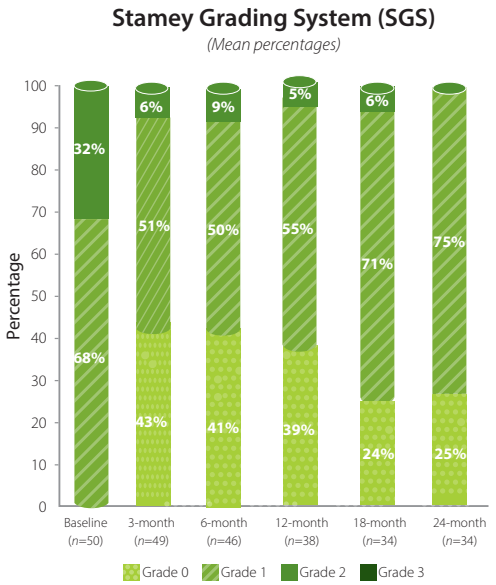


Figure 1: SGS at baseline, 3-, 6-, 12-, 18-, and 24-month follow-up. A higher grade indicates a higher SUI severity. Results show a shift to a lower grade and therefore an improvement in SUI after treatment with Urolon™. Note: percentages are rounded numbers.

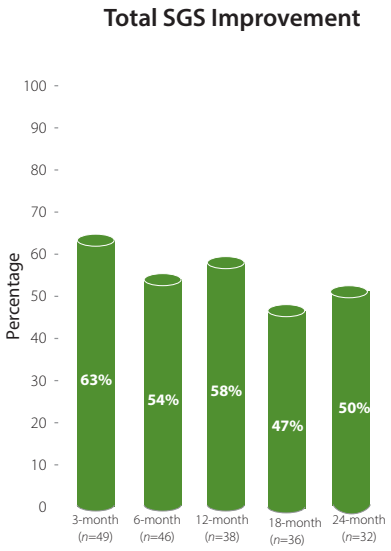


Figure 2: SGS total improvement results showing improvement in SGS at all time-points.

An important second endpoint that was recorded is the PGI-S showing that 76%, 72%, 63%, 75% and 72% of the subjects were improved at 3-, 6-, 12-, 18- and 24-month follow-up, respectively. This represents sustained improvement up to 24-month follow-up.

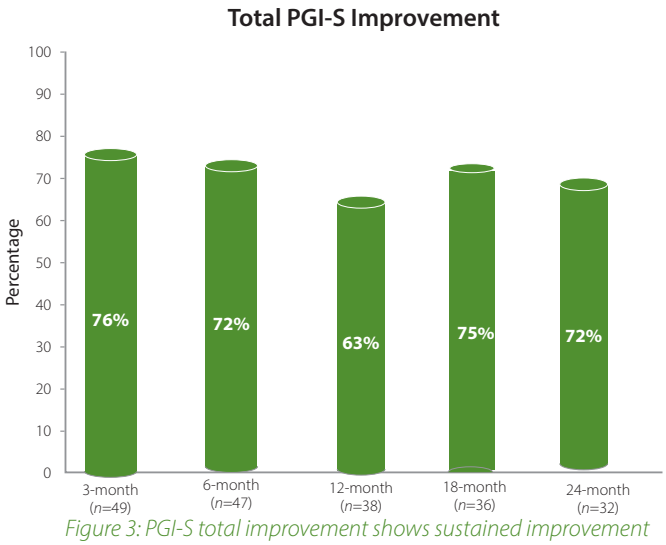


Figure 3: PGI-S total improvement shows sustained improvement up to 24-month follow-up.

Subjects were also asked how they experienced their current state of incontinence during follow-up, compared to how it was before they were treated with Urolon™. Results were recorded with the PGI-I showing that 86%, 74%, 79%, 81% and 81% of the subjects were satisfied with the treatment at 3-, 6-, 12-, 18-, and 24-month time-points, respectively. This shows that the treatment was experienced with high satisfaction by the subjects with a sustained improvement up to 2 years post-treatment.

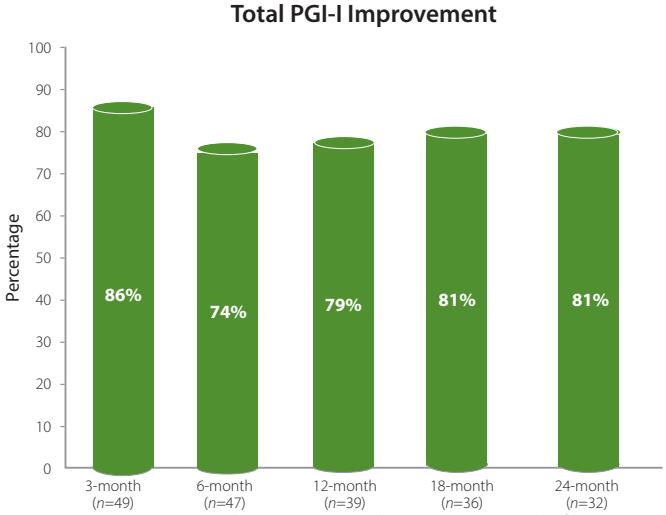
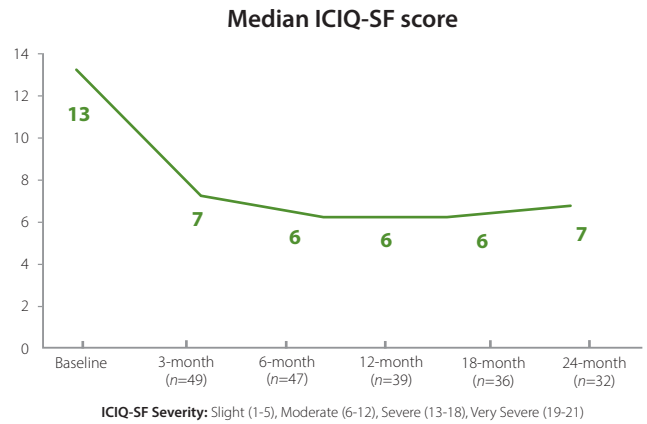


Figure 4: PGI-I total improvement showing sustained efficacy.

In addition to a reduction in severity of SUI symptoms and sustained efficacy, the data also show an important endpoint that measures the improvement in Quality of Life (QoL). Results show that the median ICIQ-SF score improved from "severe" at baseline to "moderate" at all follow-up visits for 2 years (*figure 5*).



ICIQ-SF Severity: Slight (1-5), Moderate (6-12), Severe (13-18), Very Severe (19-21)

Figure 5: Results show an improvement in median ICIQ-SF scores from "severe" at baseline to "moderate" up-to 2 years post initial treatment.

The improvement in QoL is further reflected in *figure 6* which shows the percentage of subjects that were improved in their I-QoI scores at 3-, 6-, 12- and 18-month follow-up as compared to baseline.

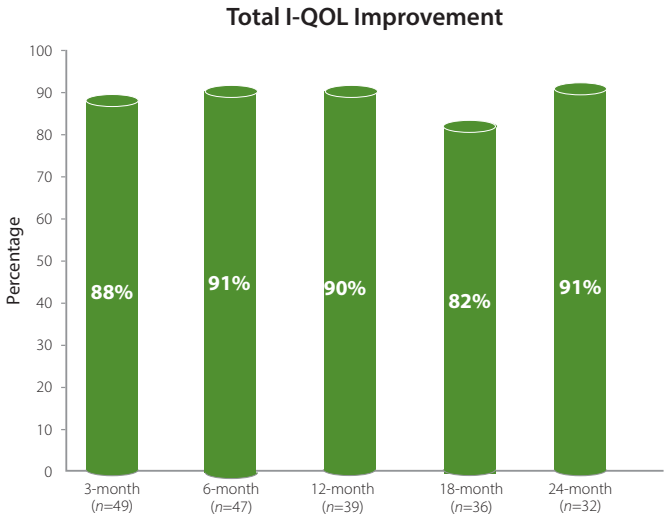


Figure 6: Percentage of subjects that had an I-QoL improvement at follow-up visits as compared to baseline.

SAFETY SUMMARY FOR UROLON™

Six subjects reported a total of 8 adverse events (AE) which were mild in nature and resolved spontaneously by providing relevant medication and/or catheterization. At 12-month follow-up, all subjects received an additional cystoscopic examination. No abnormalities were found at the injection sites.

Data show 35% of subjects were re-treated, which is favorable when compared to currently available (permanent) urethral bulking agents which show re-treatment rates of 35% - 77%[1-6]. Because re-treatments are also common with permanent bulking agents, the bioresorption of Urolon™ is a unique advantage from a safety perspective. Re-treatments cause an accumulation of bulking agent material at the injection site over the years. With Urolon™ the accumulation is expected to be limited as the product

bioresorbes over time and eventually is removed from the body completely. In contrast, (accumulated) permanent materials will remain forever in the tissue as foreign bodies, potentially eliciting a delayed inflammatory response years after injection. This is a well-known and common problem with equivalent permanent bulking agent materials used in dermal tissue. Here, complications associated with permanent materials regularly become permanent problems and are especially difficult to treat.

The mean (± sd) initial injection volume was 1.5 ± 0.5ml with a median of 1.6ml. The mean (± sd) re-treatment injection volume was 1.3 ± 0.4ml and a median of 1.3ml. Total mean injection volume (initial volume + re-treatment) was 1.8 ± 0.9ml and a median of 1.6ml showing Urolon™ is cost-effective. All injection volumes are corrected for loss of needle priming volume (0.4ml; Cook® Medical, Williams cystoscopic needle, 35cm, 5Fr, 23G, reference part number 090001).

CONCLUDING MESSAGE

In summary, the intermediate analysis shows Urolon™ as a safe and effective treatment option for females with mild to moderate SUI who have attempted or failed pelvic floor muscle training. Results show improvements in both SUI severity and QoL with only 6 subjects that reported treatment-related AE's which supports a high safety profile. Anecdotal reports from all clinical study sites confirms the performance of Urolon™ as superior in comparison to current urethral bulking agents. The bioresorption profile of Urolon™ is an attractive characteristic and feedback from urologists, gynecologists and urogynecologists alike, suggest this is a highly sought-after feature.

Urolon™ Benefits
• High biocompatibility
• Excellent safety profile
• Bioresorbable, low-risk procedure
• Sustained efficacy up to 18-month follow-up
• Cost-effective (low injection volume)
• High patient satisfaction

REFERENCES

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NOTES

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