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REVIEW AND ANALYSIS METHODOLOGY OF THREE PIVOTAL URETHRAL BULKING AGENT TRIALS: ARE THE ANALYSES TREATED EQUAL?

Hypothesis / aims of study

There are four urethral bulking agents (UBAs) in the United States approved for the treatment of adult female stress urinary incontinence. Contigen® was the first FDA approved UBA to which Coaptite®, Macroplastique® and Durasphere® have been compared. All three studies used different methods of analysis making it difficult to compare treatment outcomes. Intent-to-treat using last observation carried forward (ITT LOCF) was used for Coaptite, ITT for Macroplastique and as-followed for Durasphere [1, 2, 3]. The aim of this review and methods analysis is to compare published FDA data by using the same intent-to-treat and as-followed analyses.

Study design, materials and methods

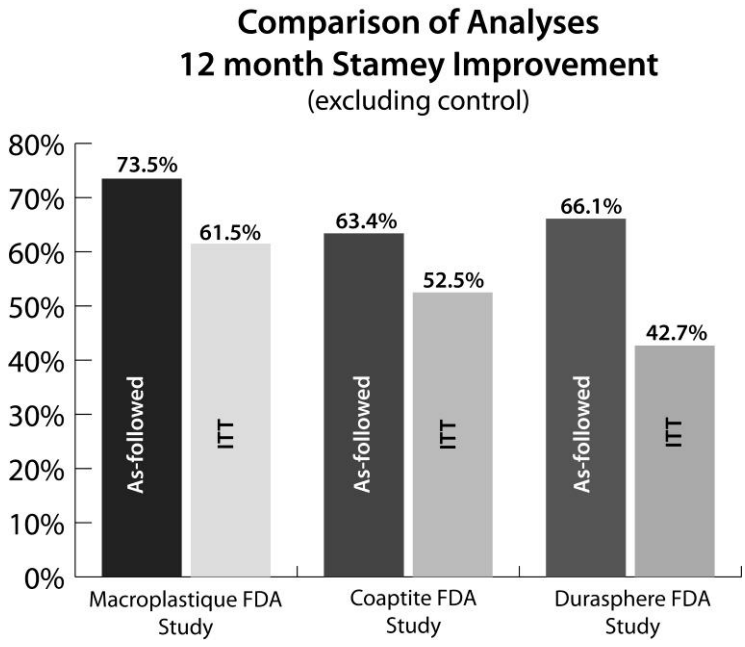
Study inclusion criteria across all UBA pivotal trials were homogenous including adult women with major complaint of stress urinary incontinence secondary to ISD. Techniques for injection were similar and used either periurethral or transurethral technique. The primary endpoint for all studies was improvement of ≥1 Stamey grade from baseline to 12 months. Using the same ITT and as-followed methodology, a reanalysis of Stamey improvement was conducted in the three studies.

Results

Mean total volumes injected per patient were: 4.0, 6.8 and 7.6 cc for Coaptite, Macroplastique and Durasphere, respectively. Contigen volumes (controls) were 6.8, 7.2 and 9.6 cc, respectively. Mean number of treatments per patients were 1.9, 1.5, 1.7 for Coaptite, Macroplastique and Durasphere, compared to 2.0, 1.6 and 1.6 for Contigen.

Only Macroplastique had statistically significant treatment outcomes compared to Contigen using ITT analysis. None of the UBAs were inferior to Contigen. See table and figure.

12-Month Pivotal Trial	≥1 Stamey Grade Improvement			
	ITT	p-value	As-followed	p-value
Macroplastique Contigen	75/122 (61.5%) 60/125 (48.0%)	**0.03**	75/102 (73.5%) 60/94 (63.8%)	0.14
Coaptite Contigen	83/158 (52.5%) 57/138 (41.3%)	0.054	83/131 (63.4%) 57/100 (57.0%)	0.33
Durasphere Contigen	76/178 (42.7%) 79/177 (44.6%)	0.71	76/115 (66.1%) 79/120 (65.8%)	0.97



Interpretation of results

These results emphasize the importance of analytic method when critically comparing treatment outcomes. The ITT analysis demonstrates all UBAs are statistically equivalent to Contigen, excluding Macroplastique, which demonstrated statistically significant improvement of Stamey's grade at 12 months compared to control (Contigen).

Concluding message

Although this study is limited by not being a head-to-head clinical study, the similarities of design allows for a reasonable comparison of the efficacy of UBAs.

References

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