Vaginal microflora and signs and symptoms of vaginal infection using a new disposable vaginal device for POP

Objective:

The aim of the study was to demonstrate that a new disposable vaginal device (ND) for the management of pelvic organ prolapse (POP) does not alter vaginal microflora in a clinically significant manner.

Methods:

A multi-center, open label, prospective, randomized, controlled, statistically powered (non-inferiority), cross over, home-use study, conducted in 7 sites (US & Israel) was performed. The ND is housed in small dimensions within an applicator and is self-inserted vaginally. Within the vagina the device opens to become a ring of up to 91 mm. Following insertion the applicator is discarded, and the device may remain within the vagina for up to 7 days. To remove the device the user pulls a string which collapses the device into small dimensions, for disposal.

Subjects were randomized into starting with the ND or with a commercially available ring pessary (CARP). The first usage phase of 30±2 days began after a 14-16 day washout period. This was followed by another 14-16 day washout period and then a second usage cross-over phase, where each group used the alternate device also for 30±2 days. The control pessary remained in situ during the entire study period. Swabs and cultures were taken before and after each study phase and sent to a single central lab for microflora analysis.

Vaginal microflora is variable and may show marked fluctuations of diverse microorganisms, even on a daily basis. In order to overcome influence of the daily fluctuations on lab results, clinical criteria were incorporated into the definition of failure. The primary endpoint was based on failure criteria defined as meeting at least 1 of the 3 failure parameters below:

1. Significant change in specific vaginal microflora (Lactobacillus spp*.*, *Gardnerella vaginalis*, Candida morphotypes, or*Staphylococcus aureus)* levels from baseline, where significant change was defined as (i) Nugent score ≥ 7, or (ii) > 1 scale unit increase in *Staphylococcus aureus* or Candida morphotype; or;
2. Vaginal symptoms that are bothersome to the subject, or;
3. Vaginal symptoms that require treatment.

Results

58 subjects who completed the study per-protocol used 350 devices over 1647 usage days. The total number of subjects who met at least one failure criterion was comparable between the ND and CARP. Nine subjects (15.5%) met the failure criteria for the primary endpoint for the ND and 9 (15.5%) for the CARP (p>0.999), with a 1-sided 97.5% upper limit of 13% (non-inferiority limit of 15%).

With the ND there were no vaginal infections, bothersome vaginal symptoms, or urinary infections. While using the CARP there was one case of overt vaginal infection which required treatment, two cases of UTI which required treatment, and 2 cases of bothersome vaginal complaints. Rate of spontaneous fluctuation of various microorganisms was 36-44%. Adverse events were minor, non-serious, mainly mild and anticipated.

Conclusions:

Study endpoints were successfully met, showing non-inferiority of the ND when compared to CARP. The minimal microflora changes and absence of clinical vaginal infections clearly demonstrate that there was no significant impact on vaginal microflora while using the ND and that the ND is comparable with the conventional pessary, with no additional microbiological safety concerns.