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Cycle Control and Bleeding Patterns for a New Contraceptive Vaginal Ring Containing 150 µg Nestorone® and 15µg Ethinyl Estradiol Daily: Results from a Multi-Center, Multi- National Open Label Phase 3 Clinical

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A Collaborative Effort:

- USAID Cooperative Agreement
- NIH/NICHD
- World Health Organization
- Population Council

The Active Treatment Portion for the Phase III trial of the NES/EE CVR has successfully been completed , goals & objectives have been met or were exceeded

Phase III Trial Objectives:

1. Evaluate 1 year data on contraceptive efficacy and safety of the CVR as the basis for regulatory approval
2. Evaluate cycle control (bleeding patterns), return to fertility, side effects, and acceptability of the CVR

Conducting the Phase III Trial

300B Study was supported by USAID & WHO

- 12 study sites: Europe, Latin America, Australia, and US
- Acceptability study was conducted to identify characteristics of the CVR that appeal or are problematic for women & partners. To identify characteristics of women who are satisfied and successful users of the CVR

FDA requirements for number of cycles & number of women with one (1) full year of usage have been met or exceeded.

CVR Phase III Enrollment

	Protocol 300B
Screened with data*	1516
Enrolled with data	1135
Completed 13 cycles (>360 days)	470
Cycles	10,659

•Phase III Data Requirements for FDA approval
20,000 cycles in 1st year of use
400 women with I full year of usage

*Protocol modified after study commencement to exclude women above 29.0 BMI as in Nuva Ring Phase III study

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Demographics

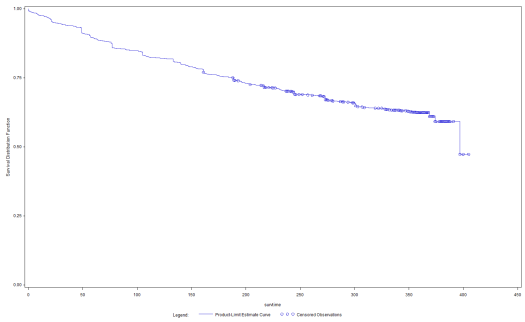
	300B n=1135
Race	
Caucasion	78.9%
Black	6.2%
Other	3.5%
Asian	2.6%
Ethnicity	
Non-Hispanic	55.8%
Hispanic	44.2%
Education	
< 12 Years	10.7%
HS Grad	26.5%
Some College	26.6%
College Degree or +	36.1%

Sample Characteristics

	300B n=1135
Age	26.7 ± 5.21
Weight	63.16 ± 9.82
BMI	23.75 ± 3.59
Gravidity	1.04 ± 1.36
Smoking	16.0%

Continuation Rates

Survival Curve for Ring Discontinuation

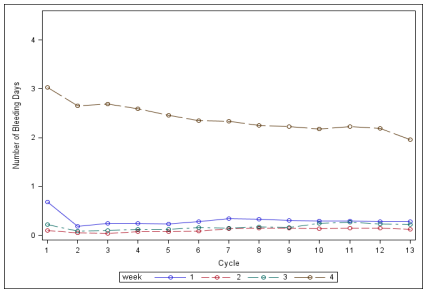


- Excludes women originally enrolled with BMI > 29.0

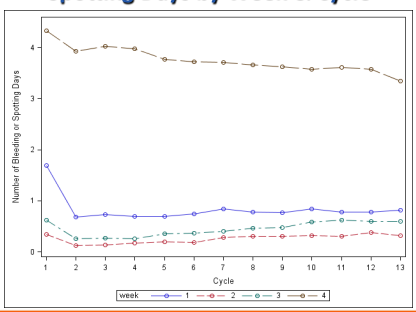
Bleeding Control of the CVR

- The mean and median number of bleeding and/or spotting days per cycle remained relatively constant across all cycles
- Overall, for all cycles combined in 1054 subjects, the mean and median number of scheduled bleeding and/or spotting days per cycle per subject were both 4.6 (SD=1.4)

NES/EE Ring: Mean Number of Bleeding Days by Week & Cycle



NES/EE Ring: Mean Number of Bleeding & Spotting Days by Week & Cycle



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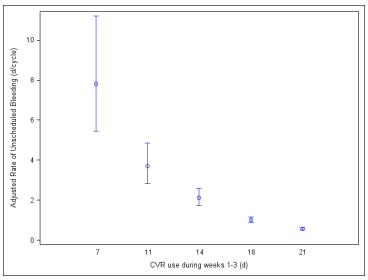
Bleeding Control of the CVR

- During the ring in period, when bleeding was not expected (Days 1-21, total of 273 days), the mean number of bleeding and/or spotting days per cycle varied with no trend observed across cycles
- For all cycles combined, the mean number of unscheduled bleeding and/or spotting days per cycle per subject was 0.7 (SD=1.46) and the median was 0

Bleeding Patterns with the NES/EE CVR

- 2.0% (21/1034) of subjects never bled and/or spotted on scheduled bleeding days during all of their cycles
- 3.5% (36/1034) of subjects never bled on scheduled bleeding days during all of their cycles
- <1% of subjects discontinued from the study due to bleeding and/or spotting issues (scheduled or unscheduled)

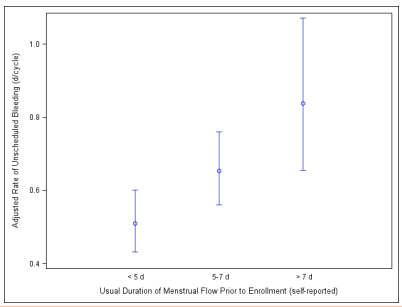
Unscheduled Bleeding and CVR Use/ Compliance During Days 1-21 of Cycle



Results: CVR meets qualifying standards set by the FDA

- Cycle requirements were met
- Requirements for use of CVR for 1 year were exceeded,
- Pearl Index for all women is comparable to recently approved contraceptives
- Bleeding Patterns (scheduled and unscheduled) are favorable
- Safety profile consistent with currently available hormonal contraceptives
- User satisfaction high

Menstrual History and Unscheduled Bleeding



The CVR is an effective, convenient, easily-used new contraceptive method.

Strengths

- **Monthly ring-good for one year**
  - Daily action not required
  - Not coitus dependent
  - Eliminates need for repeated visits to doctor & pharmacy
- **Effective**
- **Lack of androgen effect**
  - Weight /lipids favorable
- **High level of user satisfaction**
- **Under a woman's control**
  - She decides when to stop & start
  - No need for a trained health provider
  - Rapid return to fertility if desired

Challenges

- Medical risks & side effects similar to currently available hormonal contraceptives
- Manufacturing process is currently changing to a commercial process, development is underway

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