

# A cluster analysis of bleeding/spotting patterns in women using a novel 24/4 regimen of Drospirenone 4 mg as a progestin only oral contraceptive

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**Objectives:** Progestin-only hormonal contraceptives are estrogen free and have an excellent safety profile. The incidence of unscheduled endometrial bleeding associated with progestinonly contraception remains a significant barrier to their widespread use. A novel Drospirenone 4 mg (DRSP) only regimen of 24/4 days per month has been developed to improve consumer acceptability and compliance. A further analysis of our complete clinical protocol study 301 was performed to identify patterns and acceptability of unscheduled bleeding/spotting.

**Methods:** The 301 clinical trial included 713 healthy sexually active women who were at risk for pregnancy. The data set had information on demographic and gynaecological and medical history with laboratory and vital signs assessments, prior/concomitant medications/contraceptive use and daily bleeding and spotting information that was obtained during the clinical trial. A total of 74 baseline (BL) and 77 performance (PERF) parameters were selected to characterise the participants at baseline and the effect of the treatment, respectively. The variables were organised by type: for example, 16 BL variables were related to patient and demographic characteristics and 15 PERF variables were related to change in vital signs during the study. Three bleeding related endpoints were captured: total number of bleeding/spotting days per cycle, total number of scheduled bleeding/spotting days per cycle and total number of unscheduled bleeding/spotting days per cycle. Hierarchical clustering analysis was performed for each participant and correlations were sought between these parameters and the total number of scheduled bleeding/spotting days per cycle and the total number of unscheduled bleeding/spotting days per cycle.

**Results:** Four cluster patterns were identified based on bleeding information obtained from cycles 2 to 13. Cluster 1 Optimal Bleeding Pattern – Baseline parameters not sufficient for characterization. Cluster 2 Frequent Unscheduled bleeding/spotting – High level of education, <20 years of age, smokers. Cluster 3 Slight to no Bleeding or spotting – Higher BMI, higher blood pressure, higher cholesterol levels. Cluster 4 Very unfavorable Bleeding/spotting – Prior heavy menstrual bleeding (association is not very strong due to small sample size). More than 85% of the participants fell in clusters 1, 2 and 3, which correlated with treatment acceptability rated as excellent or good by more than 85% of them.

**Conclusion:** The results of this innovative analysis identified women with high BMI, blood pressure and higher cholesterol levels as having the best unscheduled bleeding/spotting profile. The reasons for this new finding are unknown at this time.