Efficacy and safety of the selective progesterone receptor modulator vilaprisan – 24-week outcomes from ASTEROID 2

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Introduction
In ASTEROID 2, 12 weeks' treatment with the selective progesterone receptor modulator vilaprisan (VPR) stopped heavy menstrual bleeding, induced amenorrhea, and reduced uterine fibroid (UF) volume. Here, we present the efficacy and safety of VPR treatment over 24 weeks in women with UF.

Materials/Patients and methods
ASTEROID 2 is a randomized, placebo- and active-controlled, phase 2 multicenter study, in which women with ≥1 UF ≥3 cm and heavy menstrual bleeding >80 mL documented by menstrual pictogram were randomized to receive VPR 2 mg once daily, ulipristal acetate (UPA) 5 mg once daily, or placebo. The 24-week outcomes for women randomized to VPR in either a 6/2 regimen (6 months' treatment followed by two bleeds), a 3/1 regimen (two 3-month treatment periods separated by a break of one bleed) or to UPA in a 3/2 regimen (two 3-month treatments followed by two bleeds) are presented. Amenorrhea (<2 mL during the last 28 days of the treatment course) was assessed by menstrual pictogram. Number of bleeding days was extrapolated to 365 days, enabling a fair comparison between treatment regimens that span different time periods. Change in volume of the three largest fibroids compared with baseline was measured by ultrasound. Adverse events and laboratory parameters were monitored. Safety variables included serum liver enzymes and endometrial assessments.

Results
A total of 145 women completed 24 weeks of treatment and the follow-up (VPR 6/2 n=33; VPR 3/1 n=30; UPA 3/2 n=34; the remaining women received placebo during parts of the treatment phase and were not included in this analysis). At 24 weeks, amenorrhea rates were 65.7% for women receiving VPR 6/2, 80.0% for VPR 3/1 and 75.7% for UPA 3/2. Mean (standard deviation [SD]) number of bleeding days during treatment periods and treatment breaks extrapolated to 365 days were 23.0 (22.1) days for VPR 6/2, 17.9 (7.7) for VPR 3/1, and 27.1 (14.1) for UPA 3/2. Pronounced changes in volume of the three largest fibroids were observed after 24 weeks treatment and –64.8% and VPR 3/1 (~50.2%), that were maintained to the end of follow-up (~61.1 and ~38.0%, respectively). Smaller changes were observed with UPA 3/2 (~33.7% after 24 weeks treatment and ~18.5% at the end of follow-up). Women self-reported decreases in symptom severity beyond bleeding and improvements in quality of life. No unexpected safety signals were observed and no signals for hepatotoxicity were observed. Evaluation of endometrial biopsies did not reveal any critical safety findings. Evaluation of expected progesterone receptor modulator-associated endometrial changes (PAECs) did not indicate any relevant difference in occurrence or reversibility of PAECs between women randomized to VPR 6/2, VPR 3/1 and UPA 3/2.

Conclusion
In ASTEROID 2, 24 weeks of VPR 2 mg treatment in 6/2 and 3/1 regimens effectively induced amenorrhea and decreased UF volume. VPR treatment was well tolerated and there were no unexpected safety findings. The treatment regimens explored here are being further investigated in phase 3 studies.

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