EFFICACY AND SAFETY OF THE NEW PROGESTERONE RECEPTOR MODULATOR VILAPRISAN – DATA FROM THE PHASE 2 PROGRAM

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Introduction: Selective progesterone receptor modulators (SPRMs) in women with uterine fibroids (UFs) reduce heavy menstrual bleeding (HMB) and tumor size. We report the results of ASTEROID1, examining the efficacy and safety of the novel SPRM, vilaprisan, in women with UFs.
Materials/Patients and Methods: In this multicenter, randomized, double-blind, placebo-controlled, parallel-group study, women were randomized to oral placebo or vilaprisan 0.5 mg, 1 mg, 2 mg, 4 mg, once daily. Treatment began during the first week of the menstrual cycle and continued for 12 weeks, with a 24 week follow-up. The primary efficacy variable was amenorrhea. HMB was assessed using a daily bleeding diary, alkaline hematin method (except in Japan), and menstrual pictogram. UFs were assessed using transvaginal/abdominal ultrasound, and pelvic magnetic resonance imaging. Fibroid related symptoms and health-related quality of life (HRQoL) were assessed using different questionnaires, e.g. the UF-DSD (Uterine Fibroids Daily Symptom Diary) and the PGI-C (Patient Global Impression of Change). Safety parameters included adverse events (AEs), laboratory evaluations, and endometrial biopsies to assess progesterone receptor modulator-associated endometrial changes (PAEC). Statistical analyses were performed using Statistical Analysis Software (SAS Institute Inc, Cary, NC, USA). All variables were analyzed consistent with their type using descriptive statistics methods.
Results: 309 women were randomized equally to the 5 study arms; 286 women completed treatment. At doses ≥ 1 mg, controlled bleeding (< 80 ml in all subsequent 28-day intervals) was achieved within 3 days in the majority of patients; 97–100% of patients achieved controlled bleeding by the end of the treatment course; amenorrhea (<2 mL/28 days) was achieved in 87%–92% of patients by the end of the treatment course. Dose-dependent reductions in fibroid volume were seen with vilaprisan, up to approximately 40% at the highest dose. Fibroid related symptoms and HRQoL scores improved in all groups. Women also reported reduction in abdominal pain during treatment (UF-DSD). Proportion of patients reporting their symptoms to be ‘much better’ or ‘very much better’ was 67–75% at doses ≥ 1 mg (PGI-C).
The number of patients with treatment-emergent AEs was similar between the active and placebo groups, with no dose-dependent pattern. Laboratory parameters did not indicate any safety signal. No treatment-emergent critical endometrial findings were found in biopsies. As expected, class-specific effects on the endometrium (PAEC) were observed under vilaprisan treatment in the majority of patients, but were rapidly reversible to background levels during follow up.
Conclusions: In ASTEROID1, vilaprisan 1–4 mg effectively stops HMB, shrinks UFs, and improves quality of life. Vilaprisan was well tolerated. Expected PAECs were observed and were reversible after treatment. Further long-term studies of efficacy and safety are warranted.
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Keywords : vilaprisan, progesterone receptor modulator, fibroids, heavy menstrual bleeding, PAEC
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