# Safety and Efficacy of the Selective Progesterone Receptor Modulator Asoprisnil for Heavy Menstrual Bleeding With Uterine Fibroids: Pooled Analysis of Two 12-Month, Placebo-Controlled, Randomized Trials

Abstract ID : 2395
Submitted by : Kristof Chwalisz the 2017-01-06 15:51:52
Category : SEUD CONGRESS
Typology : Communication orale / Oral communication
Status : Validated
Authorisation to disclose : Yes/Oui

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Introduction: Asoprisnil, a selective progesterone receptor modulator, effectively suppressed heavy menstrual bleeding (HMB), reduced uterine fibroid (UF) volume, and was well tolerated in shorter-term studies in women with UFs and HMB. In these two phase 3, North American, double-blind, placebo-controlled studies (NCT00152269/NCT00160381; ClinicalTrials.gov), the 12-month pooled efficacy and safety profile of asoprisnil 10 and 25 mg daily in women with UFs and HMB was assessed.

Materials/Patients and Methods: Premenopausal women ≥18 years with UF-associated HMB (n=907) were randomized 2:2:1 to 12 months of uninterrupted treatment with oral asoprisnil 10 mg, asoprisnil 25 mg, or placebo once daily. The composite primary efficacy endpoint was the percentage of women who met all 3 predefined criteria at 12 months/final visit: (1) ≥50% reduction in monthly blood loss (MBL), (2) hemoglobin concentration ≥11 g/dL or ≥1 g/dL increase from baseline at final visit, and (3) no surgical or invasive interventions for UFs. MBL was assessed by menstrual pictogram. Secondary efficacy endpoints included changes in other menstrual bleeding parameters, hemoglobin concentration, largest fibroid volume, uterine volume, and health-related quality of life (HRQoL). Endometrial biopsies taken at baseline, 6 and 12 months, and 3 months after cessation of treatment were assessed according to diagnostic categories developed by an expert panel specifically for asoprisnil trials.

Results: Overall, 90% and 93% of women in the asoprisnil 10- and 25-mg groups, respectively, met the primary endpoint (P<0.001 vs. 35% with placebo). Similar results were observed at month 6 (P<0.001). The mean MBL was consistently reduced to ≤21 mL and ≤13 mL by asoprisnil 10 and 25 mg, respectively, in month 1 through 12 of treatment; mean MBL with placebo was 170–204 mL. Amenorrhea (ie, no bleeding for that month) ranged from 66%–78% with asoprisnil 10 mg and 83%–93% with asoprisnil 25 mg, significantly more bleeding reduction vs. placebo (3%–12%, P<0.001). Hemoglobin increased rapidly with asoprisnil and was significantly higher vs. placebo throughout treatment. UF and uterine volumes were significantly reduced with asoprisnil vs. placebo at months 6 and 12 (P<0.001). Dose-dependent and significant improvements in HRQoL were observed with asoprisnil treatment. Asoprisnil was generally well tolerated. Endometrial biopsies indicated a dose- and time-dependent decrease in proliferative patterns and increase in diagnosis of “quiescent or minimally stimulated endometrium,” which was a dominant endometrial diagnosis at month 12. There was no significant change from baseline in mean endometrial thickness at month 6, but by month 12, an approximately 2-mm increase was present in both asoprisnil groups vs. placebo (P<0.01). This effect was associated with changes in endometrial texture (endometrial and subendometrial cysts, polypoid appearance) on magnetic resonance and ultrasonography images, which led to invasive diagnostic procedures in asoprisnil-treated women.

Conclusions: Uninterrupted treatment with asoprisnil for 12 months was effective in controlling HMB, improving anemia and HRQoL, and reducing fibroid and uterine volume; however, this treatment was associated with an increase in endometrial thickness and cystic changes after >6 months in some women and led to an increase in invasive diagnostic procedures.

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Keywords : asoprisnil, uterine leiomyomata, heavy menstrual bleeding, fibroids, selective progesterone receptor modulator
Authors :
References : , , ,

# Authors

**Elizabeth A. Stewart 1,** Michael P. Diamond 2, Alistair R. W. Williams 3, Bruce R. Carr 4, Walter Elger 5, Brittany M. Schwefel 6, Kristof Chwalisz 6,

1. Departments of Obstetrics & Gynecology and Surgery, Mayo Clinic and Mayo Medical School, Rochester, MN, UNITED STATES
2. Department of Obstetrics & Gynecology, Augusta University, Augusta, GA, UNITED STATES
3. Department of Pathology, University of Edinburgh, Edinburgh, UNITED KINGDOM
4. Department of Obstetrics & Gynecology, University of Texas Southwestern Medical Center, Dallas, TX, UNITED STATES
5. Evestra GmbH, Berlin-Dahlem, GERMANY
6. AbbVie Inc., North Chicago, IL, UNITED STATES

## Authors (raw format)

Stewart Elizabeth A. - email : stewart.izabeth@mayo.edu Institution : Mayo Clinic and Mayo Medical School Department : Departments of Obstetrics & Gynecology and Surgery City : Rochester, MN Country : UNITED STATES Speaker : Yes
Diamond Michael P. - email : mpdmd@aol.com Institution : Augusta University Department : Department of Obstetrics & Gynecology City : Augusta, GA Country : UNITED STATES Speaker : No
Williams Alistair R. W. - email : a.williams@ed.ac.uk Institution : University of Edinburgh Department : Department of Pathology City : Edinburgh Country : UNITED KINGDOM Speaker : No
Carr Bruce R. - email : Bruce.Carr@UTSouthwestern.edu Institution : University of Texas Southwestern Medical Center Department : Department of Obstetrics & Gynecology City : Dallas, TX Country : UNITED STATES Speaker : No
Elger Walter - email : w.elger@elger-berlin.de Institution : Evestra GmbH Department : City : Berlin-Dahlem Country : GERMANY Speaker : No
Schwefel Brittany M. - email : brittany.schwefel@abbvie.com Institution : AbbVie Inc. Department : City : North Chicago, IL Country : UNITED STATES Speaker : No
Chwalisz Kristof - email : Kristof.chwalisz@abbvie.com Institution : AbbVie Inc. Department : City : North Chicago, IL Country : UNITED STATES Speaker : No