The clinical development of vilaprisan: The ASTEROID phase 3 program

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INTRODUCTION

- Vilaprisan (VPR) is a novel selective progesterone receptor modulator that has been shown in phase 2 studies to induce reversible amenorrhea, reduce heavy menstrual bleeding (HMB), and decrease the volume of uterine fibroids (UFs)[1–3]
- The ASTEROID (Assess Safety and Efficacy of Vilaprisan in Subjects with Uterine Fibroids) clinical development program is designed to evaluate the safety and efficacy of VPR in women with UFs
- To date, ASTEROID is the largest clinical development program initiated by Bayer Women's Health and the largest clinical trial program dedicated to UFs globally
- In addition to the completed phase 2 studies ASTEROID 1 and 2, the program currently comprises six phase 3 studies – ASTEROID 3 to 8 – which are planned to enroll >2700 women across approximately 850 centers in 40 countries

STUDY OBJECTIVES

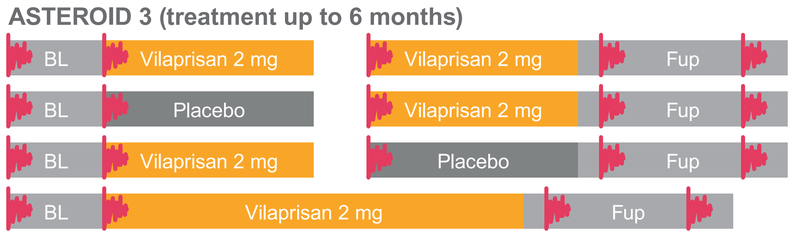
- ASTEROID 3, 4, and 7 aim to demonstrate the efficacy of VPR treatment at 3 months and/or 6 months compared with placebo, and are statistically powered for superiority versus placebo
- ASTEROID 5 aims to determine the efficacy of VPR at 3 and/or 9 months, and is statistically powered for non-inferiority versus active comparator (ulipristal acetate)
- ASTEROID 5 and 6 aim to show the efficacy and long-term safety of VPR for up to 2 years compared with ulipristal acetate and symptomatic, non-hormonal medical treatment, respectively
- ASTEROID 8 aims to assess the efficacy and safety of VPR treatment at 3 months and/or 6 months, with safety monitored for approximately 1 year of VPR treatment (no comparator/reference drug)

STUDY DESIGN[4–7]

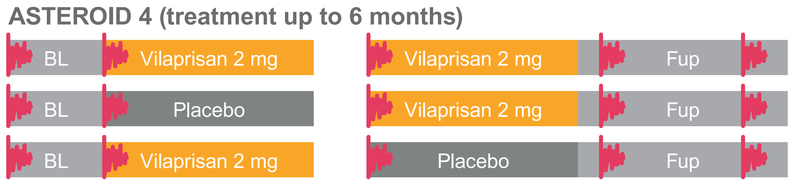
Figure 1. Phase 3 study designs

- ASTEROID 3 (NCT03400943) and 4 (NCT03400956) are randomized, parallel-group, double-blind, placebo-controlled multicenter trials
  - Estimated enrollment n=260 and n=156, respectively

ASTEROID 3 (treatment up to 6 months)

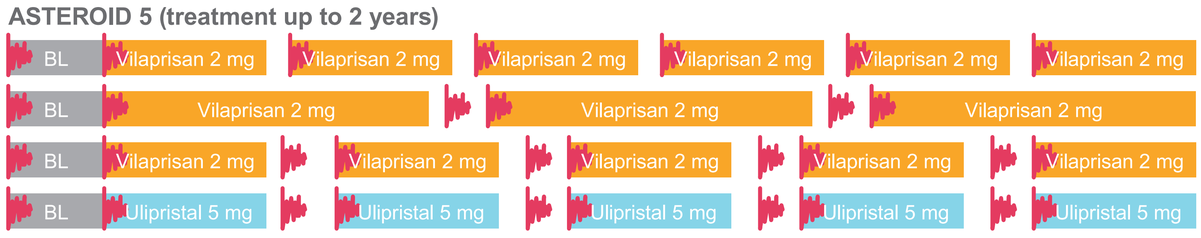


ASTEROID 4 (treatment up to 6 months)



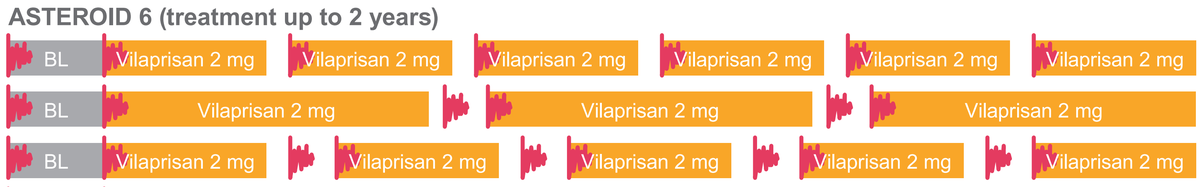
- ASTEROID 5 (NCT03240523) is a randomized, parallel-group, double-blind, double-dummy, active-controlled multicenter study
  - Estimated enrollment n=996

ASTEROID 5 (treatment up to 2 years)



- ASTEROID 6 (NCT03194646) is a randomized, open-label, parallel-group multicenter study
  - Estimated enrollment n=1050

ASTEROID 6 (treatment up to 2 years)



- ASTEROID 7 will be a randomized double-blind trial (study planned)
  - Estimated enrollment n=100

ASTEROID 7 (treatment up to 6 months)*

*design currently under evaluation

- ASTEROID 8 will be a randomized open-label trial
  - Estimated enrollment n=150

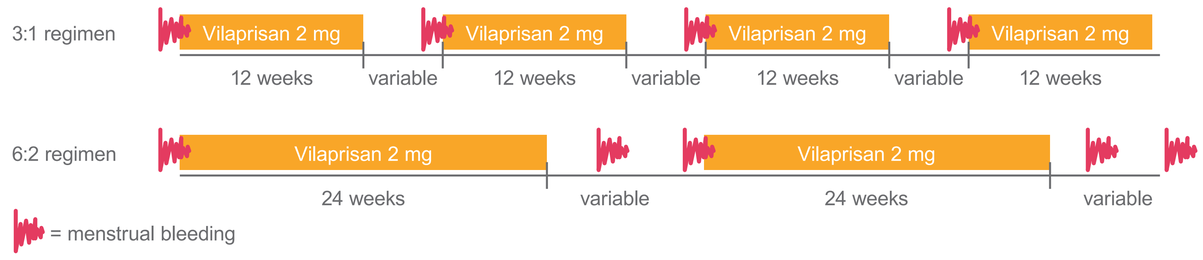
ASTEROID 8 (treatment up to 1 year)

- The phase 3 program will enroll patients from across Europe and from other countries, including Brazil, Canada, China, Japan, Korea, Mexico, Russia, Taiwan, USA and Vietnam

BL, baseline; FUP, follow up

TREATMENT REGIMENS

Figure 2. Vilaprisan treatment regimens



- Two optimized VPR regimens will be investigated in these trials
  - A 3/1 VPR regimen – 3 months' continuous treatment with a break of one menstrual bleed
  - A 6/2 regimen – 6 months' continuous treatment with a break of two bleeds

KEY INCLUSION CRITERIA

- The ASTEROID 3, 4, 5 and 7 study populations consist of female adults with ≥1 UFs measuring ≥3 cm in diameter (as diagnosed by ultrasound)
  - Women must be experiencing HMB (defined as blood loss of >80 mL) and be willing to use a non-hormonal method of contraception
  - Key exclusion criteria include women with abnormal endometrial biopsies and/or UFs with largest diameter >12 cm
- ASTEROID 6 will enroll women with UFs and/or those at high risk of recurrence following recent surgery, with one or more symptoms of UFs (i.e. HMB, pelvic pressure/pain)
- ASTEROID 8 will enroll women with UFs and HMB

KEY ENDPOINTS

- The primary outcome measure in ASTEROID 3, 4, 5 and 7 is the induction of amenorrhea (defined as menstrual blood loss of <2 mL during the last 28 days of treatment). The secondary outcomes include time to onset of amenorrhea, time to onset of controlled bleeding, HMB response, absence of bleeding (spotting allowed), endometrial histology and endometrial thickness
- Additional secondary outcomes in ASTEROID 5 are the number of bleeding days and the change in volume of largest fibroid compared with baseline
- The primary outcome in ASTEROID 6 is percentage change in bone mineral density of lumbar spine and the secondary outcome measure is the number of bleeding days
- The primary outcome in ASTEROID 8 is the incidence of treatment-emergent adverse events and the secondary outcome measure is the number of bleeding days from Day 1 of the first treatment period until the day before start of a new treatment period

RESULTS

- The phase 3 ASTEROID study program began in 2017
- Patient recruitment is actively ongoing

CONCLUSIONS

- The phase 3 ASTEROID clinical development program is intended to comprehensively evaluate VPR for the long-term treatment of UFs, addressing endpoints that are relevant to patients, clinicians, health authorities, and society

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DISCLOSURES

- KGD serves on advisory boards and has been an invited speaker at scientific meetings for Bayer AG, MSD/Merck, HRA-Pharma, Exelgyn, Gedeon Richter on an ad-hoc basis. Her institution has received grants for conducting clinical trials on vilaprisan
- AA has provided consulting services to AbbVie, Bayer, Allergan, MD Stem Cells, and has received a grant from the National Institutes of Health for fibroid-related research (R01 ES 028615-01, R01HD 087417, R01 HD 094378, R01 HD 094380). In addition, he holds a patent for 'Methods for novel diagnostics and therapeutics for uterine sarcoma' (US Pat No. 9,790,562 B2)
- LDB receives PI grant support from Bayer and has served on Scientific Advisory Boards for Bayer, AbbVie, Allergan and PCORI. She has earned book royalties from Elsevier and Wolters Kluwer
- JS has provided consulting services for Bayer and is a PI for Bayer and a study of uterine fibroids sponsored by Biospecifics, Inc. He is a board member for the American Society for Reproductive Medicine and American Board of Obstetrics and Gynecology
- UM, SP, KP and CS are employees of Bayer AG

Asteroid