The integrated analysis of the two clinical studies of a flexible-extended regimen of ethinylestradiol/drospirenone for the treatment of Japanese patients with endometriosis and/or dysmenorrhea

Abstract ID : 2379
Submitted by : Shigetomo Yamamoto the 2017-01-05 03:20:59
Category : SEUD CONGRESS
Typology : Poster
Status : Validated
Authorisation to disclose : Yes/Oui

Introduction
In patients using a low-dose estrogen/progestin (EP) combination, menstruation (withdrawal bleeding) is induced by a tablet-free interval. In patients using a 28-day cyclic regimen of low-dose EP combination, the withdrawal bleeding comes in monthly cycles. An extended cycle regimen of EP combination is expected to suppress ovarian function more reliably compared with a 28-day cyclic regimen and to improve symptoms associated with menstruation.
Pain, the major subjective symptom in patients with endometriosis or dysmenorrhea, is most severe during menstruation (withdrawal bleeding). A Flexible extended regimen, which allows women to extend their menstrual cycle and manage intracyclic (breakthrough) bleeding, may alleviate the burden on patients with dysmenorrhea by decreasing the frequency of withdrawal bleeding during treatment as compared with 28-day cyclic regimens or the menstrual periods every 4 weeks of a natural menstrual cycle.
Therefore, clinical trials for endometriosis and/or dysmenorrhea were conducted in Japan.
Materials/Patients and methods
The safety of a combination of ethinylestradiol and drospirenone (EE/DRSP) in a flexible extended regimen in patients with endometriosis and/or dysmenorrhea was evaluated based on the each clinical studies (Studies 15457 (NCT0169711; multi-center, randomized, double-blind, placebo-controlled) and 16114 (NCT01892904; multi-center, randomized, open-label, active-controlled (28-day cyclic regimen))). This time, we evaluated the long-term safety of the EE/DRSP flexible extended regimen by the integrated analysis of the two studies.
Results
The numbers of subjects used for safety evaluation were 235 subjects receiving the EE/DRSP flexible extended regimen in the integrated analysis, including 163 subjects entering the long-term treatment phase.
At Week 24, 84.3 % (198/235) experienced at least 1 treatment emergent adverse event (TEAE), and 62.6% (147/235) experienced at least 1 study drug-related TEAE. Serious TEAEs were reported in 0.4% (1/235) of the subjects (pulmonary embolism and deep vein thrombosis simultaneously occurring in 1 subject). Most of the reported TEAEs were mild or moderate in their maximum intensity. No deaths were reported. At Week 52, 92.8% (218/235) experienced at least 1 TEAE and 70.6% (166/235) experienced at least 1 study drug-related TEAE. Serious TEAEs were reported in 0.9% (2/235) of the subjects (same case as the above and appendicitis (unrelated to the study medication)). Most of the reported TEAEs were mild or moderate in their maximum intensity. Severe TEAEs were reported in 1 subject (same case as the above). No deaths were reported. Common TEAEs were genital haemorrhage, nasopharyngitis, headache, plasminogen increased, nausea, metrorrhagia and thrombin-antithrombin III complex increased. Common study drug-related TEAE were genital haemorrhage, plasminogen increased, nausea, metrorrhagia, headache and thrombin-antithrombin III complex increased. There were consistent with those expected in patients using EP combinations, and were not notably different from the common TEAEs and their incidences reported in 4 phase III studies including flexible-extended regimen of EE/DRSP conducted outside of Japan.
Conclusion
The safety profile of EE/DRSP did not differ from the known safety profile of EP combinations. No safety concerns were newly noted for application of EE/DRSP to the new patient population, endometriosis patients, and the new treatment regimen of EE/DRSP, flexible extended regimen.

Keywords : low-dose estrogen/progestin, endometriosis, dysmenorrhea, clinical traial, flexible extended regimen
Authors :
References : , , ,

Authors

Mikio Momoeda 1, Masami Kondo 2, Joerg Elliesen 3, Masanobu Yasuda 2, Shigetomo Yamamoto 4, Harada Tasuku 5,

1. Integrated Women’s Health, St. Luke’s International Hospital, Tokyo, JAPAN
2. Product Development, Bayer Yakuhin, Ltd., Osaka, JAPAN
3. Global Clinical Development, Bayer Pharma AG, Berlin, GERMANY
4. Medical Affairs, Bayer Yakuhin, Ltd., Osaka, JAPAN
5. Obstetrics and Gynecology, Tottori University, Yonago, JAPAN

Authors (raw format)

Momoeda Mikio - email : momoeda-tky@umin.ac.jp Institution : St. Luke's International Hospital Department : Integrated Women's Health City : Tokyo Country : JAPAN Speaker : Yes
Kondo Masami - email : masami.kondo@bayer.com Institution : Bayer Yakuhin, Ltd. Department : Product Development City : Osaka Country : JAPAN Speaker : No
Elliesen Joerg - email : joerg.elliesen@bayer.com Institution : Bayer Pharma AG Department : Global Clinical Development City : Berlin Country : GERMANY Speaker : No
Yasuda Masanobu - email : masanori.yasuda@bayer.com Institution : Bayer Yakuhin, Ltd. Department : Product Development City : Osaka Country : JAPAN Speaker : No
Yamamoto Shigetomo - email : shigetomo.yamamoto@bayer.com Institution : Bayer Yakuhin, Ltd. Department : Medical Affairs City : Osaka Country : JAPAN Speaker : No
Tasuku Harada - email : tasuku@med.tottori-u.ac.jp Institution : Tottori University Department : Obstetrics and Gynecology City : Yonago Country : JAPAN Speaker : No