Extended-Regimen OC Measures Up

BY HEIDI SPLETE
Senior Writer

WASHINGTON — Seasonale Lo, the 91-day extended-regimen low-dose oral contraceptive, was effective and well tolerated compared with a 28-day low-dose oral contraceptive, after both 1 year and 3 years of use.

The Seasonale Lo data from a randomized, multicenter study were presented in two posters at the annual meeting of the American College of Obstetricians and Gynecologists.

Dr. Andrew M. Kaunitz of the University of Florida Health Science Center in Jacksonville, Fla., monitored women aged 18-35 years who could potentially become pregnant. After 1 year, the overall cumulative failure rate of Seasonale Lo was 2.23% among 463 patients, compared with a 2.83% failure rate among 231 patients who took a traditional 28-day oral contraceptive (Levlite).

Compliance rates were high—98.1% in the Seasonale Lo group and 96.5% in the Levlite group. Among compliant patients, the Seasonale Lo failure rate was only 0.65%, compared with 4.14% among compliant Levlite patients. Although more Seasonale patients reported unscheduled bleeding days than the Levlite patients (6.1% vs. 3.3%), the number of scheduled bleeding or spotting days per cycle was approximately the same in both groups.

Breakthrough bleeding episodes were reported more frequently by the Seasonale Lo group than the Levlite group (13.8% vs. 1.3%), but the incidence of other adverse events was similar between the two groups. For example, headaches, the most common adverse event, were reported by 22% of the Seasonale Lo group and 21% of the Levlite group.

Each Seasonale Lo pill includes 0.02 mg of ethinyl estradiol and 0.1 mg of levonorgestrel. The regimen includes 84 days of active pills followed by 7 days of placebo pills. Dr. Kaunitz serves as a consultant to Barr Pharmaceuticals, the manufacturer of Seasonale, which also supported the study.

Seasonale continued to be safe and well tolerated in a subset of 161 women who participated in a 2-year extension of the study, reported Dr. David Portman of the Columbus Center for Women's Health Research in Columbus, Ohio.

Notably, the median number of unscheduled bleeding or spotting days decreased over the course of the study, from 2 days during the first cycle to 0 days by the eighth cycle. Patient exposure to the drug included 937 complete 91-day cycles. Patients reported their pill-taking, bleeding, and spotting data in electronic diaries, and they underwent clinical evaluation during quarterly visits. The overall discontinuation rates were similar to those for Seasonale Lo and Levlite in the original study, which were about 44% and 32%, respectively.

Dr. Portman serves on the speakers' bureau of Barr Pharmaceuticals. ■

Frovatriptan Appears to Offer Relief for Menstrual Migraines

BY HEIDI SPLETE
Senior Writer

WASHINGTON — Women who took 2.5 mg of frovatriptan either once or twice daily for 6 days at the time of menstruation had significantly fewer—and less severe—menstrual migraines, compared with women who took a placebo, reported Dr. Marie Pinizzotto and her colleagues at Endo Pharmaceuticals.

The women on either regimen of frovatriptan also reported significantly fewer headaches in general and less functional impairment compared with the placebo group. Data from the randomized, double-blind, three-way crossover study were presented in a poster at the annual meeting of the American College of Obstetricians and Gynecologists. The study was sponsored by Vernalis Development Ltd., and Endo Pharmaceuticals Inc.

Headaches occurred in 37.7% of the twice-daily frovatriptan group, versus 51.3% of the once-daily group and 67.1% of the placebo group.

Frovatriptan has been approved by the Food and Drug Administration for the acute treatment of migraines, both with and without aura, in adults, but it has not been approved for the prophylactic prevention of migraines. The manufacturers are seeking an additional indication for the prophylactic treatment of menstrual migraines.

The patients were randomized to receive each of the two treatment regimens or a placebo over the course of three different 6-day periods from 2 days before to 4 days after the onset of menstruation.

The incidence of pure menstrual migraines, defined as migraines that occurred during the time period from 2 days before to 3 days after the onset of menstruation, was significantly lower in both frovatriptan groups, compared with placebo. These distinctive headaches occurred in 37.7% of the twice-daily frovatriptan group, compared with 51.3% of the once-daily group and 67.1% of the placebo group. The intent-to-treat analysis included 179 women aged 18 years and older with at least a 1-year history of menstrually-related migraines. The mean age was 37 years, and 82% were white. On average, the study participants had a history of migraines greater than 10 years, and the average number of migraine attacks was one per month during the year prior to the study.

Overall, moderate to severe headaches were reported by 25.3%, 32.3%, and 46% of women in the twice-daily frovatriptan, once-daily frovatriptan, and placebo groups; the incidence of functional impairment was 13.6%, 24.1%, and 35.4% in the twice-daily frovatriptan, once-daily frovatriptan, and placebo groups, respectively.

The overall symptoms of functional impairment—including light and sound sensitivity, nausea, and vomiting—were significantly reduced in women who took frovatriptan, and each of these symptoms individually were significantly reduced among patients in the twice-daily frovatriptan group, compared with the placebo group.

Adverse events included headache, nausea, dizziness, and nasopharyngitis, and the incidence of these events was similar between the two groups. ■

Topical Estrogen Best Treatment For Advanced Urogenital Atrophy

BY FRAN LOWRY
Contributing Writere

FORT LAUDERDALE, FLA. — Topical estrogen is important to the success of treatment for urogenital atrophy and also has therapeutic value for the management of urinary urgency, frequency, and, most importantly, nocturia, Dr. G. Willy Davila said at a symposium on pelvic floor disorders sponsored by the Cleveland Clinic Florida.

However, overcoming the fears of patients and oncologists about the safety of localized estrogen remains an uphill battle, said Dr. Davila, chairman of the department of gynecology, urology, and reconstructive pelvic surgery at the Cleveland Clinic Florida, Weston.

"Our task is to allay the fears of patients who come in and have this almost paranoid fear of any estrogen therapy. The main challenge is having the patient be compliant with therapy," he said.

Patients may be concerned that any form of estrogen might get into the bloodstream. But with vaginal estrogen, the dosage can be tailored so that it is not absorbed systemically, with the result that blood levels of estrogen are negligible, Dr. Davila said.

If vaginal atrophy is not treated, it will progress; advanced urogenital atrophy with increasing degrees of labial fusion is a common occurrence. The traditional treatment has been to lyse the labia, but this will be a stopgap measure only. "The most important issue is not that you lyse the labia, but rather that the patient continue using local estrogen. If the patient does not use local estrogen cream, this fusion will recur fairly promptly," he said.

Other conditions that respond well to local estrogen therapy include nocturia, dyspareunia, and stress incontinence. For the latter, adding an α-agonist to the estrogen preparation will have a synergistic effect and this can be very useful for stress incontinence in cases of significant atrophy. Local estrogen should also be applied if a woman is using a pessary to prevent erosion and ulceration, Dr. Davila said. Routine measurement of estradiol levels can reassure the patient that she is not absorbing estrogen systemically, he added.

Dr. Vincent Lucente of Temple University School of Medicine, Philadelphia, commented that there are no well-designed clinical trials that look specifically at topical applications of estrogen and urged continued investigation of the subject. ■

Bcl-2 Urine Test for Ovarian Ca Gets Good Results in Pilot Study

WASHINGTON — Elevated levels of the Bcl-2 protein in urine were associated with 92% of ovarian cancers in a pilot study of 95 women, Patricia Kruk, Ph.D., said at the annual meeting of the American Association for Cancer Research.

"Ovarian cancer has the highest mortality rate among gynecologic malignancies," said Dr. Kruk. "It is usually detected in the very late stages, because we don't have very good detection systems and the women are generally asymptomatic."

The average amount of Bcl-2 in the urine of 36 women with ovarian cancer was more than 2 ng/mL, which was significantly greater—at least 10 times greater in most cases—than Bcl-2 levels in the urine of 21 healthy women and 38 women with benign gynecologic disease.

Urinary levels of Bcl-2 decreased up to 100% after patients had debulking surgery, noted Dr. Kruk, who heads a cancer research team at the University of South Florida in Tampa. The Bcl-2 levels remained low during the course of chemotherapy, but increased significantly among patients whose disease recurred.

In contrast, urine samples from the healthy women showed almost no measurable Bcl-2. "All the women had normal renal function, so Bcl-2 was not suggestive of renal dysfunction," Dr. Kruk noted. Urinary levels of Bcl-2 were not related to tumor size, but increased levels of Bcl-2 were correlated with increased tumor stage and grade. In addition, only 65% of the patients with serious carcinomas were diagnosed using the standard method of blood test results for the tumor marker CA125. "We are cautiously optimistic and excited about our results," said Dr. Kruk.

—Heidi Splete