

New Treatment Approved for Endometriosis Pain

Depo subQ provera 104 is as effective as leuprolide acetate and is associated with fewer side effects.

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

Subcutaneous medroxyprogesterone acetate has been approved for the treatment of endometriosis-related pelvic pain. It is the first new treatment to be approved for this indication in 15 years.

Depo subQ provera 104 (DMPA-SC), which contains 104 mg medroxyprogesterone acetate, treats endometriosis pain as effectively as leuprolide acetate, but is associated with significantly less bone loss and fewer vasomotor symptoms, according to data provided by Pfizer Inc., which manufactures the agent.

The Food and Drug Administration granted approval for the endometriosis pain indication in March. Depo subQ provera 104 received FDA approval for use as a contraceptive in December 2004. Pfizer said depo subQ provera 104 would be widely available this month.

Depo subQ provera 104 is a new formulation of medroxyprogesterone acetate, which is the active ingredient in Depo-Provera Contraceptive Injection (medroxyprogesterone acetate injectable suspension), but with 30% less hormone.

Depo subQ provera 104 is available in prefilled syringes each containing 0.65 mL (104 mg) of medroxyprogesterone acetate sterile aqueous suspension.

Administered by subcutaneous injection four times a year (every 12-14 weeks), DMPA-SC halts menstruation, which results in thinner, more compact endometrial tissue, the company said. This in turn halts the growth of endometrial implants, relieving endometriosis-associated pain.

The package insert contains a black box warning concerning possible bone loss: Women who use DMPA-SC may lose significant bone mineral density. Bone loss is greater with increasing duration of use and may not be completely reversible. It is unknown if use of depo subQ provera 104 during adolescence or early adulthood, a critical period of bone accretion, will reduce peak bone mass and increase the risk of osteoporotic fracture in later life. Depo subQ provera 104 should be used as a long-term birth control method (that is, longer than 2 years) only if other birth control methods are inadequate.

Pfizer's phase III randomized controlled trial showed that DMPA-SC is associated with significantly less bone loss than le-

uprolide acetate for depot suspension, the only other drug approved for treatment of endometriosis-related pain.

The 18-month study included 274 women aged 18-49 years who had diagnoses of endometriosis-associated pelvic pain. They were randomized to 6 months of treatment with either DMPA-SC (104 mg every 3 months) or leuprolide (11.25 mg IM every 3 months), and 12 months of follow-up.

There were no significant differences in pain symptom reduction. Women in both groups showed some bone mineral density declines at the end of treatment, but the mean losses were significantly less for women taking DMPA-SC in both the femur (0.3% vs. 1.65%) and the spine (1.1% vs. 3.95%).

In women who had been taking DMPA-SC, bone mineral density return to pre-treatment levels 12 months after discontinuing treatment. Those who had been taking leuprolide showed continued bone mineral density losses of 1.3% in the femur and 1.7% in the spine.

DMPA-SC was also associated with significantly fewer vasomotor symptoms, especially hot flashes.

It's important to remember that the only cure for endometriosis is aggressive surgical excision, David Redwine, M.D., Endometriosis Association advisor, said

in an interview. Surgery has been repeatedly shown to have a cure rate of about 60% in even resistant cases.

"Excision is the only treatment which has documentation of cure, although this information is typically withheld from patients as they consider their treatment options. The result is that patients undergo repeated rounds of medical therapies without eradication of their disease," Dr. Redwine said. "Depo subQ 104 adds another form of medical therapy for endometriosis to be used by physicians who cannot treat the disease effectively by surgery."

The bone loss associated with any hormonal therapy for symptoms is worrisome, he said, especially in women who are still actively laying down bone. "I am concerned about young women being exposed to medicines that do not treat a disease and that can produce systemic side effects, the permanency of which are not fully known," said Dr. Redwine, medical director of the endometriosis treatment program at St. Charles Medical Center in Bend, Ore.

Daniel Watts, a Pfizer spokesman, said depo subQ provera 104 will offer a much-needed alternative to women who don't elect surgery.

"Not all patients are appropriate candidates for surgery," Watts said in an interview with this newspaper. ■

Fibroid Treatment Maintains Favorable 5-Year Track Record

BY HEIDI SPLETE
Senior Writer

BETHESDA, MD. — Follow-up data for women who underwent uterine artery embolization for the treatment of fibroids show that 73% still reported improved symptoms 5 years later.

Of 182 women who completed 5-year follow-up, 25 had undergone hysterectomies, 6 had undergone myomectomies, and 3 had undergone repeat embolizations. None of the hysterectomies were performed due to complications of embolization, and at least four were due to a condition other than recurrent fibroids. The failure rate after 5 years was 20%.

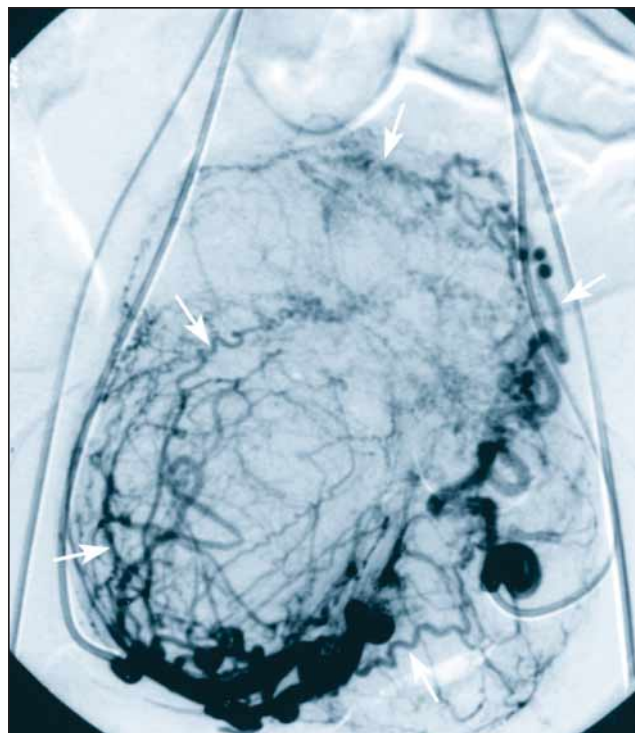
"The women most likely to go on to subsequent intervention were those with single, very large fibroids," James Spies, M.D., the study's lead investigator, said in an interview. On the other hand, the women with large numbers of smaller fibroids were less likely to fail.

The initial cohort included 200 women: 95% completed follow-up at 1 year, 80% at 2 years, 91% at 3 years, 89% at four years, and 91% at 5 years. Three patients died during the 5-year follow-up—two from unrelated cancer and one from heart disease.

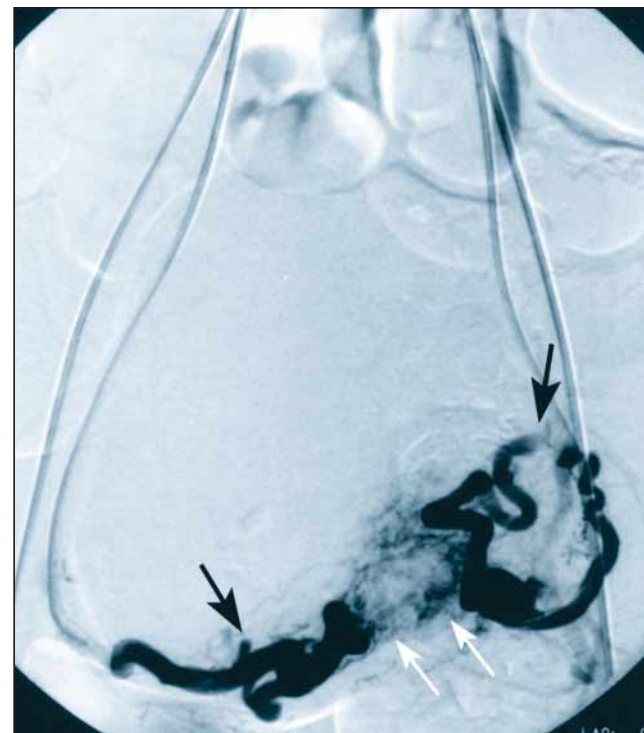
Dr. Spies, professor of radiology at Georgetown University, Washington, and his associates presented data on the 5-year follow-up in a poster presentation at an international congress on uterine leiomyoma research sponsored by the National Institutes of Health.

Dr. Spies and his colleagues also presented a poster on 1-year follow-up data on 1,701 women of the 3,166 who initially registered with the Fibroid Registry for Outcomes Data (FIBROID).

The registry is a collaborative effort of the Society of Interventional Radiology Foundation, the Duke Clinical Research Institute, the Food and Drug Administration, and corporate supporters, including Biosphere, a com-



This angiogram shows fibroids as they appeared before uterine artery embolization was performed.



Normal branches (white arrows) and uterine arteries (black) are open after the procedure is completed.

pany that produces the particles used in uterine artery embolization. Dr. Spies, a member of the medical advisory board for Biosphere, said the company had no input into the gathering of data or analysis of the registry.

Overall, the women demonstrated a significant improvement in symptoms. Compared with baseline scores, 90% showed an improvement of greater than 10% on symptom scores on the Health-Related Quality of Life scale at both 6 months and 1 year.

After 1 year, the mean HRQoL score was 86.5, and the mean symptom score on the Uterine Fibroid Symptom Quality of Life scale was 19.2; both represented signifi-

cant improvements from baseline and were in the range of scores for normal subjects.

"There was a striking and marked improvement in both symptom and quality of life scores, there is stable improvement between 6 and 12 months, there were relatively few complications and hospitalizations, and in general most patients were satisfied with the outcome," said Dr. Spies, a member of the Steering Committee of FIBROID.

Most women reported a dramatic improvement in sexual function, although some reported no significant change, and 6%-7% reported a decrease. ■