



## Managing the fallout from the Women's Health Initiative

**B**y now, I am sure, you are quite familiar with the Women's Health Initiative (WHI), the hormone replacement therapy (HRT) trial whose estrogen-progestin arm was discontinued when it became clear that risks exceeded benefits.<sup>1</sup> Chances are you've been inundated with questions about it. And since it received so much media attention, and its findings were so contrary to expectations, there are questions aplenty.

Among the talents we will have to employ in counseling patients on this issue are toler-

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ance and understanding. Tolerance of the questions. Understanding about why they are directed primarily at us. After all, we are America's menopause experts. And because physicians traditionally have served as arbiters of moral and health-related issues, the public expects definitive answers. As Alexander Pope wondered more than 300 years ago, "Who shall decide when doctors disagree?"

The truth is, like most other aspects of contemporary life, medicine is colored increasingly in grays, rather than definite blacks and whites. And one task facing us at this juncture is helping our patients understand that there is no single answer—no magic formula—that applies to all women. Rather, the solutions to the challenges of menopause are as varied and diverse as the women we treat. And so goes the ques-

tion of HRT. (For more on interpreting the WHI findings, see our cover story on page 72.)

At first glance, the study appears to be filled with bad news, making it necessary for each physician and patient to reevaluate the long-term use of estrogen-progestin for conditions related to menopause. Nevertheless, some general conclusions can be drawn:

- While risks clearly exceeded benefits in the trial, for most women the overall health risk is extremely low, and there is no urgency to stop treatment.
- Estrogen-progestin therapy should not be used for the primary or secondary prevention of heart disease. Rather, patients should focus on lifestyle factors such as weight, diet and exercise, control of blood pressure, and the use of cholesterol-lowering agents, low-dose aspirin, beta blockers, and angiotensin-converting enzyme (ACE) inhibitors.
- For women taking estrogen-progestin therapy for osteoporosis prevention or treatment, other medications—such as raloxifene, alendronate, risedronate, or calcitonin—should be considered. Women also should be sure to get adequate daily exercise and maintain healthy calcium and vitamin D intakes.
- Estrogen-progestin therapy should not be used to prevent colon cancer, a stance supported by the National Cancer Institute. Instead, screening programs that rely on fecal occult blood testing, sigmoidoscopy, and colonoscopy should be the mainstays of prevention.

One important aspect of the WHI trial is that it clearly defines the main indication for

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estrogen-progestin therapy: the treatment of menopausal symptoms such as hot flashes, sleep disorders, and cognitive disturbances. It also suggests that naturally menopausal women should use combined estrogen-progestin therapy for less than 5 years. These 2 conclusions alone add a great deal of clarity to patient counseling. In fact, the indications for estrogen-progestin use in naturally menopausal women have never been clearer.

The WHI trial should motivate Ob/Gyns to consider an array of nonestrogen therapies for menopausal symptoms. The antidepressant venlafaxine, for example, was shown to be clearly effective for the treatment of menopausal hot flashes in 1 randomized controlled trial. In this study, 221 women with breast cancer and vasomotor symptoms were randomized to receive placebo or 3 different doses of venlafaxine: 37.5 mg, 75 mg, or 150 mg daily. After 4 weeks, mean hot-flush scores were reduced from baseline by 27%, 31%, 61%, and 61%, respectively.<sup>2</sup>

Further, we are likely to discover that the effects of estrogen-progestin therapy are dose-, time-, and agent-specific. The WHI trial probably will spur intensive investigation of other doses of estrogen and alternative progestins (e.g., natural micronized progestin, progestin patches), as well as the development of an array of new estrogens and progestins.

Although the data yielded by the WHI trial may at first appear to be less than helpful, we should be grateful for this information. Not only does it advance the field of women's health, it points the way to an exciting future in menopause medicine. The challenge is conveying this fact to our patients. ■



REFERENCES

1. Writing Group for the Women's Health Initiative Randomized Controlled Trial. Risks and benefits of estrogen plus progestin in healthy postmenopausal women. Principal results from the Women's Health Initiative randomized controlled trial. *JAMA*. 2002; 288:321-333.
2. Loprinzi CL, Kugler JW, Sloan JA, et al. Venlafaxine in management of hot flashes in survivors of breast cancer: a randomized controlled trial. *Lancet*. 2000;356:2059-2063.