New hormone therapy shows promise for menopausal symptoms in animal model

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Investigators at Wake Forest Baptist Medical Center have concluded research on a new postmenopausal hormone therapy that shows promise as an effective treatment for menopausal symptoms and the prevention of osteoporosis without increasing the risk for heart disease or breast cancer.

Traditional forms of hormone therapy (HT) provide the benefits of symptom relief, prevention of osteoporosis and prevention of atherosclerosis, but increase the risk of uterine cancer (with estrogens alone) or breast cancer (with combined estrogens and progestins). Thus, the risk-benefit ratio of traditional HT is not ideal. Less potent plant-derived estrogens are relatively safe, but less effective. Selective estrogen receptor modulators (SERMs) provide both beneficial effects and adverse effects, but the ideal treatment has proven elusive, said J. Mark Cline, D.V.M., Ph.D., one of the co-authors.

The Wake Forest Baptist team worked in partnership with the pharmaceutical company Pfizer to explore a new strategy, termed a Tissue Selective Estrogen Combination (TSEC). Using this strategy, a conventional estrogen (CEE) was combined with a bone-protective SERM-like drug, bazedoxifene acetate (BZA), to produce a complementary pattern of tissue effects that maximize the benefits of HT while avoiding the risk. The study involved a 20-month randomized, parallel-arm trial – which has a comparison group and at least one new or active therapy group – in postmenopausal nonhuman primates, designed to determine the effect of TSEC treatment on the breast, uterus and

cardiovascular system.

The TSEC strategy has been evaluated in the Selective estrogens, Menopause, And Response to Therapy (SMART) phase 3 trials involving more than 6,000 women. Cline said the Wake Forest Baptist nonhuman primate trials are important because they can address tissue responses directly, whereas studies in women use clinical outcomes that may require many years to provide conclusive results.

The Wake Forest Baptist findings are discussed in separate papers, both published recently in *Menopause: The Journal of The North American Menopause Society*.

Prior work by Cline in the 1990s demonstrated the adverse effect of a widely used estrogens and estrogen-progestin combination on the breast, a finding that was predictive of the breast cancer patterns later found in the Women's Health Initiative. In contrast to that finding, the TSEC strategy is anticipated to reduce breast cancer risk. "Remarkably, BZA overrides the adverse effects of CEE at the level of gene expression in the breast, suppressing abnormal tissue growth," Cline said.

Lead investigator Thomas B. Clarkson, D.V.M., is hopeful about the promise of this new approach. "The findings are encouraging for postmenopausal women," he said. "We believe that women can be given CEE along with BZA to protect against breast cancer and uterine cancer, without adversely affecting the cardiovascular system, but more research is necessary."

Provided by Wake Forest University Baptist Medical Center