

Use of Selective Estrogen Receptor Modulators Among Postmenopausal Women in the Managed Care Setting

Based on proceedings from a 1-day conference on the use of selective estrogen receptor modulators in the managed care setting.

Introduction

A group of multispecialty physicians (as listed on pages S138-S139) convened for a 1-day conference to discuss the emerging role of selective estrogen receptor modulators (SERMs) in the managed care setting. While the SERM tamoxifen has been used for breast cancer treatment for many years, there are new research data on its preventive role as well as on the emergence of other SERMs, such as raloxifene. These compounds may be particularly interesting to healthcare providers because of their potentially significant role in long-term disease prevention strategies. Although many questions about the future role of SERMs remain unanswered, the panelists engaged in a lively discussion about the characteristics of these agents and how they can be successfully integrated into the ongoing care of postmenopausal women. The panelists also speculated about the possible clinical impact of ongoing studies and identified areas that require further research.

Discussion topics focused on SERMs' differential effects on various tissues as well as their overall role in disease prevention among at-risk women. Throughout the day, panelists continually emphasized the importance of disease prevention efforts after menopause. While they agreed that successful preventive strategies must be implemented for the post-

menopausal population as a whole, they also emphasized the need to customize regimens for individual women to increase patient acceptance and promote long-term adherence.

Although the panel did not develop specific guidelines for use of SERMs among postmenopausal women, they did outline the characteristics of thorough preventive examinations and the role that SERMs can play as therapeutic options for many women in whom preventive intervention is appropriate. This article provides a summary of their recommendations.

Healthcare Trends and Postmenopausal Women

As baby boomers enter mid-life and life expectancy stretches into the eighth and ninth decades for many Americans, the United States population is increasingly being referred to as "aging." In addition to having other significant effects on society, the growing population of older Americans will result in increased healthcare spending for conditions that disproportionately affect them. Among women, the US population over age 50 will nearly double between 1998 and 2050.¹ Thus, conditions more likely to affect postmenopausal women, including cardiovascular disease, osteoporosis, and certain types of cancer, will become increasingly important to prevent and treat in their early stages. The impact of these trends on managed care

organizations can be only broadly estimated at this point. Female members, as primary household health-care decision makers, are likely to demand that managed care organizations allocate more resources toward women's health. By all estimates, the economic burden of an aging female population will be significant. Because many of the diseases affecting women after menopause can be prevented, the expert panel convened for this meeting suggested that managed care organizations should see these women's health issues as an opportunity to develop proactive disease prevention programs. In fact, turning these trends into disease prevention opportunities may be a successful approach to surviving the economic impact of the aging population on the healthcare system.

The panel suggested that managed care organizations may benefit from developing and implementing broad disease prevention guidelines for populations such as postmenopausal women, given current nationwide demands for cost-effective, measurable healthcare outcomes. They indicated that preventive interventions that effectively reduce the risk for conditions disproportionately affecting postmenopausal women could reduce overall expenditures and improve health. However, they cautioned that broad recommendations can be challenging to design and implement, and customized interventions also should be employed whenever possible. With this in mind, the group focused its suggestions on the need for disease prevention efforts, the key components of a successful prevention evaluation, and the current and future role of SERMs in disease prevention strategies. They also suggested ways to maintain focus on the needs of individual patients through effective patient-provider communication techniques. Differences of opinion among the expert panelists were voiced throughout the day and led to a

greater understanding of clinical issues that cannot be overlooked by individual healthcare providers. Areas of particular challenge to the group included determination of appropriate ages or intervals for conducting comprehensive evaluations, selection of specific tests or procedures, and identifying how physicians can maximize office time with patients as they seek to develop individual preventive programs. These differences also highlighted the need for ongoing discussion and debate.

Opportunities for Prevention

The perimenopausal transition presents a unique opportunity for disease prevention. Its symptoms (eg, hot flashes, night sweats, irregular bleeding) often prompt healthy women to schedule office visits, thus presenting an opportunity to conduct risk assessments and develop disease prevention strategies. This is an especially important time for clinicians to consider patients' risks for diseases that are affected by estrogen depletion, such as heart disease and osteoporosis.

In general, adherence to long-term therapies is low, particularly when the medication is for the prevention of an asymptomatic condition (eg, osteoporosis) or is associated with side effects (eg, estrogen and hormone replacement therapies [ERT and HRT]). Many women avoid estrogen-based therapies because they are concerned about increasing their risk for breast or uterine cancer. In addition, they often discontinue therapy because of side effects, including uterine bleeding and breast pain or bloating. However, these issues do not diminish the importance of preventive regimens for at-risk populations. Building a successful physician-patient partnership may be one key to increasing long-term adherence. A successful partnership begins with a comprehensive assessment to identify and prioritize each patient's risks and potential benefits. Then, individual

preventive regimens can be developed that take a woman's lifestyle, preferences, health history, and family history into consideration. The expanding utility of SERMs for disease prevention may help clinicians to further partner with their female patients by expanding options for long-term therapy and customizing the regimen to meet the needs of individual women.

Comprehensive Assessment

The panel advocated adoption of a "well-woman" prevention evaluation to identify women who may benefit from preventive intervention. This evaluation can be conducted before, during, or after a woman enters perimenopause. When discussing timing, the panel did not come to conclusions about the ideal age for this first evaluation or subsequent visits. However, they did agree that periodic screening, risk assessment and stratification, and adjustment of the preventive regimen should be continued throughout the postmenopausal years. They also suggested that emphasis always be placed on dis-

eases that have modifiable risk factors and/or established treatment options. This approach fit well with the group's focus on estrogen depletion and the role of SERMs.

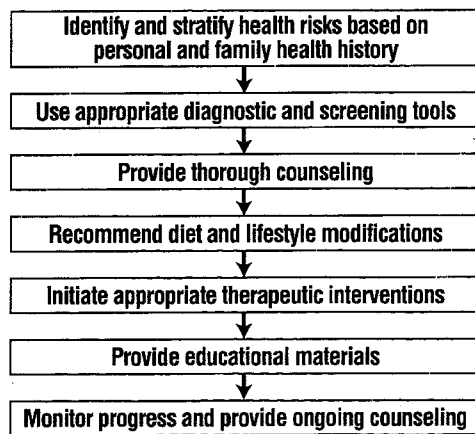
Fundamental components of a comprehensive evaluation for disease prevention, as described by the panel, can be summarized in the following steps (Figure).

Identify and Stratify Health Risks. A detailed personal and family health history should be part of a comprehensive evaluation. Because it is neither possible nor desirable to test each patient for every condition, historical risk factors can be used to select appropriate screening tests by identifying which patients are likely to be at highest risk for certain conditions. Then, clinicians can stratify a patient's risk factors to determine which problems must be addressed immediately. Part of the challenge is to evaluate the woman's overall health and potential health risks rather than considering only certain aspects of her current health.

Numerous organizations, such as the National Osteoporosis Foundation, the American College of Obstetricians and Gynecologists, the American Cancer Society, and the American Heart Association, provide a wealth of information, including suggested screening guidelines and other care recommendations (see the Table for a list of such specialty organizations). Clinicians can use these guidelines to better identify women who are at high risk and should be screened. Thus, physicians and healthcare organizations do not have to devise original guidelines in all instances. In addition to assisting physicians with decisions to screen, these organizations offer other resources, such as consensus opinions and publications regarding new research findings as well as diagnostic and treatment techniques.

Use Appropriate Diagnostic and Screening Tools. Based on the results of a complete physical examination

Figure. Fundamental Components of a Comprehensive Evaluation for Disease Prevention



and history, appropriate diagnostic and screening tools can be employed. Utilization of specific tests lies at the discretion of the clinician, and guidelines from specialty organizations may be helpful in selecting appropriate diagnostic measurements. In addition to providing needed information, the results of these tests may motivate patients to begin a preventive regimen. Some studies have found that patients who understand their test results, such as their bone mineral density measurements, are more likely to initiate appropriate preventive regimens.²

Provide Thorough Counseling. Physician counseling is an important source of patient information, and surveys have shown that women respond positively to physician recommendations.^{3,4} In addition, women who understand their risks and the reasons for their specific treatment regimens are more likely to take responsibility for their healthcare, to initiate changes, and to begin and continue a prevention regimen.

It is important to recognize that women gather health information from a variety of sources. In a Gallup survey, only one third of the women surveyed received information about menopause from their physicians, and many of these women were dissatisfied with the information that was provided.⁵ A majority of the survey participants reported relying on news media, such as magazines, journals, books, and television, and friends or family members for information. Thus, women may develop their opinions based on inaccurate or incomplete information, and these beliefs may have important implications for healthcare decisions. For example, a 1995 Gallup survey demonstrated that women perceived breast cancer to be the leading cause of death among their sex; in reality, heart disease is the leading cause of death, followed by all types of cancer, including breast cancer.⁶

Recommend Diet and Lifestyle Modifications. Several universal preventive measures, such as healthy diet, regular exercise, and smoking cessation, are important for all women and should be recommended for the prevention of heart disease, osteoporosis, and other diseases. Certain lifestyles and behaviors can

Table. Organizations Providing Screening Guidelines or Other Resources

Organization	Phone Number	Website Address
American Association of Clinical Endocrinologists	904/353-7878	http://www.aace.com
American Cancer Society	800/227-2345	http://www.cancer.org
American College of Cardiology	800/253-4636	http://www.acc.org
American College of Physicians	800/523-1546 215/351-2600	http://www.acponline.org
American College of Obstetricians and Gynecologists	202/638-5577	http://www.acog.org
American Diabetes Association	703/549-1500	http://www.diabetes.org
American Heart Association	800/242-8721	http://www.americanheart.org
American Society for Bone and Mineral Research	202/857-1161	http://www.asbmr.org
American Society for Reproductive Medicine	205/978-5000	http://www.asrm.org
Centers for Disease Control and Prevention	800/311-3435 404/639-3311	http://www.cdc.gov
Cochrane Collaboration	401/863-9950	http://www.cochrane.org
Endocrine Society	301/941-0200	http://www.endo-society.org
National Cancer Institute	301/496-9228	http://www.nci.nih.gov
National Institutes of Health	301/435-3848	http://www.nih.gov
National Osteoporosis Foundation	202/223-2226	http://www.nof.org
North American Menopause Society	216/844-8748	http://www.menopause.org

be important considerations as risk factors are stratified and a prevention program is developed.

Initiate Appropriate Therapeutic Interventions. Appropriate pharmacologic therapy should be initiated after a complete risk assessment, thorough counseling, and consideration of possible dietary and lifestyle changes. With this accomplished, the clinician and the patient are in a better position to evaluate the complete range of treatment options. Ideally, the selected regimen will be appropriate for and accepted by the patient. Thus, the woman's preferences and tolerances will have been taken into consideration to increase the probability that the regimen will be continued long term.

Provide Educational Materials. Educational materials for women, such as newsletters, brochures, and on-line information, can help women understand their risk factors, ways to diminish risk, and the need for prevention or treatment strategies. These materials also help to reinforce concepts covered during an office visit. When patients are well informed, they can participate more actively in the development of their preventive regimen and may be more likely to continue the program.

Monitor Progress and Provide Ongoing Counseling. Monitoring progress and providing ongoing counseling are important parts of building a physician-patient partnership to support the prevention strategy. In addition to providing the physician with feedback on treatment efficacy and adherence, such follow-up and counseling may promote other healthy behaviors and strengthen the woman's overall commitment to the prevention program. Sharing and discussing test results may be another way to increase long-term adherence. Because a woman's risk factors will change as she grows older, periodic reassessments and ongoing counseling are also needed to ensure that new risks are identified and addressed.

Tools to Maximize Office Visit Time. Like patients, physicians can benefit from the use of tools developed to suit their practices, including standardized questionnaires that provide assistance with patient and family history taking or forms to streamline organizational guidelines for screening. For example, physicians who want to maximize their office time may have nonphysician staff members take detailed personal and family health histories. Another alternative is to develop a health history questionnaire that the patients can complete on their own before their appointments. One potential advantage of a questionnaire is that physicians and allied healthcare providers have an opportunity to review the information before seeing the patient.

Another potential tool for enhancing the use of office time is a standardized well-woman examination form. These forms would be similar to the prenatal forms that many healthcare providers currently use and could incorporate organizational guidelines for age-appropriate examinations and screening tests. To assist physicians who see a large number of patients each day, single-page forms that focus on risk stratification and disease prevention may be helpful tools. In addition, managed care organizations could also provide guidelines or other resources to help physicians understand the disease prevention choices available for each stage of a patient's life.

Preventive Use of SERMs

After a comprehensive examination, risk assessment and stratification, and appropriate lifestyle and dietary recommendations, pharmacologic intervention may be necessary. SERMs, such as tamoxifen, toremifene, and raloxifene, may prove to be pharmacologic options for long-term health maintenance among postmenopausal women. These compounds behave as estrogen agonists in some tissues and estrogen antagonists

in others. Like estrogen, some of these agents may protect against osteoporosis and heart disease without some of the negative effects of ERT and HRT, such as increased risk of certain cancers or undesirable side effects in the uterus or breast. Long-term studies are underway to assess how well certain SERMs prevent heart disease and breast cancer, both of which are associated with significant morbidity and mortality. In addition, SERMs may encourage long-term adherence among certain women if they are not associated with increased cancer risks or side effects such as uterine bleeding or breast pain. These compounds may also increase adherence if they prove to be effective for the prevention of multiple diseases and can simplify a woman's treatment regimen.

Current and Future Uses of SERMs

At this time, tamoxifen is indicated for the prevention and treatment of breast cancer; toremifene is indicated for treatment of metastatic breast cancer; and raloxifene is indicated for the prevention of osteoporosis. SERMs as a group appear to have many of the benefits of estrogen, including positive effects on bone mineral density and lipid levels, without some of the negative effects, such as the possibility of an increased risk for breast cancer. However, SERMs also carry risks, including an increased risk for deep vein thrombosis that is comparable to the risk associated with ERT/HRT; certain SERMs also increase risk for endometrial cancer. The varying effects of SERMs seem to be associated with their classification as either benzothiophenes (raloxifene) or triphenylethylenes (tamoxifen and its analogs). For these reasons, the risks and benefits of each compound should be considered.

The panel concluded that they would like to see continuation of controlled clinical trials to demonstrate the ongoing safety and efficacy of

SERMs for long-term prevention of osteoporotic fractures as well as breast cancer and heart disease. The group cautioned, however, that therapeutic decisions must be based on the best clinical evidence available at the time treatment begins, with the understanding that new data may result in changing treatment plans in the future. While they emphasized the importance of ongoing research,

Ultimately, trials such as the Study of Tamoxifen and Raloxifene (STAR) and Raloxifene Use for the Heart (RUTH) may provide the long-term clinical data needed to assess the effectiveness of these agents for the prevention of breast cancer and heart disease.

they discouraged clinicians from waiting to initiate therapy until data from completed long-term clinical studies are available.

Ultimately, trials such as the Study of Tamoxifen and Raloxifene (STAR) and Raloxifene Use for the Heart (RUTH) may provide the long-term clinical data needed to assess the effectiveness of these agents for the prevention of breast cancer and heart disease. In addition, the Multiple Outcomes of Raloxifene Evaluation (MORE) study already has shown a reduction in vertebral fracture risk among postmenopausal women with osteoporosis after 2 years of raloxifene treatment.⁷ The results of these trials may also have important implications for selecting appropriate candidates for SERM therapy. In the future, healthcare providers may select a SERM for patients who are at risk for several diseases (eg, breast cancer, osteoporosis, and heart disease). Based on emerging data, the panel expressed optimism that

SERMs may add significant new treatment options that will allow a larger number of postmenopausal women to reduce their risk for the three diseases that often affect this population: osteoporosis, breast cancer, and heart disease.

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