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The Coming 'Tsunami' of Older Breast Cancer Patients

BY ROBERT H. CARLSON

MIAMI BEACH—How to treat older women with breast cancer is becoming a critical question in the U.S., where the average age of a breast cancer patient is 61, and the vast majority of women who die of breast cancer are age 65 and older.

"That's frequently not the public's perception, though, or the perception of our colleagues," said Hyman B. Muss, MD, Director of Geriatric Oncology at Lineberger Comprehensive Cancer Center and Professor of Oncology at the University of North Carolina at Chapel Hill, speaking here at the Miami Breast Cancer Conference.

He called this the coming "tsunami" of older-age patients.

But age is not the key to choosing chemotherapy—rather it is the patient's life expectancy and overall health, he said. "The real issue in older people is whether cancer is the patient's most serious diagnosis, considering the common comorbid conditions in this population such as hypertension and diabetes. Even breast cancer patients with regional nodes usually die of non-cancer causes if they're over age 70."

The goal of adjuvant chemotherapy in elderly treatment is not always longevity, he explained.

"For the fit patient with good life expectancy, consider state-of-the-art chemotherapy. For the frail and very ill, consider endocrine therapy. For patients in the middle ground, the oncologist has to define the added value of chemotherapy, consider the expectations of the patient and family, and ask whether the potential toxicities are worth it.

Some patients may not consider therapy worth the toll on their bodies, Muss said, pointing to a survey of seriously ill patients asked to end the sentence: "I would rather die than have a treatment that causes…" The results:

- 11 percent said "high burden";
- 74 percent said "severe functional impairment"; and
- 89 percent said "severe cognitive loss."

Making the Chemotherapy Decision

Deciding whether to recommend chemotherapy to older patients is the most difficult decision, Muss said, since chemotherapy is associated with the greatest toxicity and the greatest potential for loss of function and adverse effects on quality of life.

Therefore, when considering whether to recommend chemotherapy, it is important to consider the life expectancy of the patient apart from the cancer. He said this can now be done accurately with available online models such as ePrognosis (**eprognosis.ucsf.edu**).

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Based on life expectancy, the potential benefits of different chemotherapy regimens can be shown using programs such as **Adjuvant!Online** and PREDICT (**www.predict.nhs.uk**)—these tools, though, have not been verified in older patients, Muss cautioned.

He said chemotherapy is likely to be most beneficial in older women with triple-negative breast cancer, and those with hormone-receptor-negative, HER2-positive breast cancers. Such therapy is likely to increase survival in most patients with these breast cancer phenotypes, provided that the patient's estimated survival is more than five years.

HYMAN B. MUSS, MD, said that age is not the key to choosing chemotherapy—rather it is the patient's life expectancy and overall health.

"The most difficult decision concerning chemotherapy use is in patients with hormone-receptor-positive, HER2-negative tumors," Muss said. "For these patients, if they have node-negative disease, and even if they have one to three positive nodes, the use of genetically based tests such as the 21-gene panel can be most helpful in making a treatment decision.

"For those with higher-risk hormone-receptor-positive, HER2-negative tumors, especially those with high-grade tumors and extensive nodes, chemotherapy is a major consideration."

Muss said adjuvant radiation after breast-conserving surgery and for patients with mastectomy who have high-risk tumors is generally well tolerated.

Breast radiation following breast conservation can be omitted without deleterious effects on survival in women with small hormone-receptor positive HER2-negative tumors, or those likely to be compliant with endocrine therapy.

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'Medical Crossfire Debate'

Is Genetic Susceptibility Panel Testing for Breast Cancer Ready for Prime Time?

BY ROBERT H. CARLSON

MIAMI BEACH—Genetic tests for breast cancer susceptibility that go beyond BRCA1/2 mutations are either a very bad idea or an idea whose time has come, depending on which speaker you listened to in a "Medical Crossfire" debate here at the Miami Breast Cancer Conference.

Not ready, said J. Michael Dixon, MD, Professor of Surgery, Consultant Surgeon, and Clinical Director of the Breakthrough Research Unit, Edinburgh Breast Unit, of Western General Hospital in Edinburgh, U.K., noting that there are limited data on the cancer risk for some of the genes in next-generation sequencing panel tests, and the interpretation of results is difficult. Getting informed consent is extremely problematic, he said, and there are huge issues surrounding variants of unknown significance (VUS).

"Patients at risk of breast cancer should have limited gene testing and not be exposed to the issues and concerns of multiplex gene testing," Dixon said.

The other debater, Pat Whitworth, MD, Director of the Nashville Breast Center, said: "If 'prime time' means access in practices delivering state-of-the-art care throughout the U.S., then panel testing is past 'ready for prime time.'" He said experienced cancer doctors and genetics specialists in leading programs have employed panel testing as a first-line approach for appropriate cases since 2013, and for much longer in certain cases.

J. MICHAEL DIXON, MD: Genetic Testing Not A Prime-Time Player

"So, I'm the curmudgeon," Dixon began, in his typically humorous style, promising to convince the audience that genetic susceptibility panel testing is not ready for prime time.

He began his story with the patenting of BRCA1/2 genes in 1995, by Myriad Genetics. After several rounds in various federal courts, the Supreme Court in 2013 upheld a lower court decision that human genes cannot be patented.

(At this point Dixon showed one of many humorous, and sometimes hilarious, video clips, which a written description cannot possibly do justice to.)

By 2014, there were nine labs offering BRCA1/2 testing, seven offering BRCA1/2 testing as part of a next-generation panel, 14 labs with tests that included BRCA1/2—"and an infinite number of genetic counselors pulling their hair out."

"Just because you can test for these tests doesn't mean you should," Dixon said.

World Health Organization criteria for genetic testing are that:

- The disease has to be an important health problem;
- The risk of the disease in the mutation-carrying disease is high in the general population and not just in the high-risk group;
- The mutations can be accurately identified, to avoid false positives, false negatives, and uncertainties; and
- Effective interventions have to exist.

"The reality is, only BRCA1/2 routinely fulfill those criteria," Dixon said.

Citing examples of what is currently available, he described tests from Ambry

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However, this does carry a small increased risk in local-regional recurrence, he said.

Adjuvant endocrine therapy is likely to be beneficial in reducing local-regional and distant recurrence in older women with hormone-receptor-positive breast cancers who have tumors larger than one centimeter and with estimated survival times exceeding five years, he said.

Triple-Negative Treatment Age Dependent

About 15 percent of elderly breast cancer patients have triple-negative breast cancer—"and it's just as bad in older people as in younger people," Muss said.

Most recurrences are within five years, so estimates of five-year survival are important. "More chemotherapy is better—usually with taxanes and anthracyclines—so estimating life expectancy and toxicity is key," he said. But even patients with a shorter life expectancy can benefit from treatment if the patient has large tumors or many involved nodes.

Anti-HER2 therapy in elderly patients depends on estimated survival, he said. "When there is an estimated survival of more than five years, I treat older patients like younger patients. But if the patient has cardiac comorbidities, order a cardiology consult."