Era of Hope Meeting Highlights Breast Cancer Research Advances

The US Department of Defense (DoD) Breast Cancer Research Program (BCRP) is the second largest funder of breast cancer research in the US. Since its inception in 1992, the BCRP has managed approximately $1.8 billion in peer-reviewed research.

Every few years, the DoD holds its “Era of Hope” meeting. The meeting provides a forum for scientists, physicians, breast cancer survivors and advocates, policymakers, and the general public to learn about recent breast cancer advances. The fourth Era of Hope meeting was held June 8–11, 2005, in Philadelphia.

Report and Highlights of the 2005 Era of Hope Meeting by Fran Visco

The 2005 Era of Hope was an extremely rewarding meeting. The fact that there were more consumers, representing more organizations than ever before, demonstrates that consumer involvement is key to the success of the BCRP and this meeting.

BCRP Background
The BCRP began as a result of the National Breast Cancer Coalition’s 1992 campaign to dramatically increase federal funding specifically targeted to breast cancer research. Through the efforts of the hundreds of organizations that make up NBCC, this program created an unprecedented partnership that unites the military, scientific, medical, and breast cancer survivor and advocacy communities to develop and carry out research to end breast cancer. It is the federal government’s only breast cancer research program that involves consumer advocates at both the scientific peer review and the programmatic review stages and at all levels of a scientific meeting.

The scientific peer review panels that evaluate each proposal for merit and the programmatic review panel have benefited from the voices (and votes) of 399 consumers, individuals that come from 255 separate organizations, providing an incredible reach into the world of breast cancer nationwide.

The Meeting
The purpose of the Era of Hope meeting is to have all research funded by the program in certain years presented to the public, through platform presentations and poster sessions. The Era of Hope program is designed by a Technical Planning Committee that includes scientists and consumers. The Committee reviews the reports of the funded research and chooses the themes and presentations. This year the themes were: Day One: Risk and Prevention; Day Two: Who Needs Treatment; Day Three: Focus on Treatment and Clinical Trials.

Advocate Involvement in Era of Hope
Consumer advocates were well represented at the Era of Hope meeting. There may be no other forum in the scientific community where such a diversity of scientific disciplines—basic scientists, clinicians, epidemiologists, nanotechnologists, mathematicians, physicists and more—come
together on an equal footing with consumers to look at the complexity of breast cancer research, challenge each other, explore controversial issues, and learn and plan together.

Key roles consumers played in every aspect of the Era of Hope meeting:

- The 21 members of the Technical Planning Committee included six consumer representatives.
- The 276 consumers from 95 organizations registered for Era of Hope represented one in six conference attendees, unprecedented for scientific meetings where consumers are usually a rarity.
- Each platform session was co-chaired by a consumer and a scientist.
- A consumer spoke at every plenary session.
- A consumer moderated every plenary session.
- A total of 39 consumers from 35 organizations participated as co-chairs and plenary speakers.
- Consumers at every session challenged the status quo and conventional wisdom, and offered what in many cases was an eye-opening perspective to the researchers whose laboratory careers may be far removed from real-world applications.

Other Unique Features of Era of Hope
There were eight plenaries, two innovator sessions, and 38 symposia that featured 226 research projects and more than 1,000 poster presentations at the Era of Hope meeting. Acceptance of DoD BCRP funding requires reporting of all findings, whether they are positive, negative, or inconclusive.

This is important because: more efficient use of resources can be made when researchers are able to learn from the mistakes and false starts of others who are investigating similar questions; it fosters development of collaborative relationships; it provides accountability to the public in terms of how research money is being spent.

This meeting maintains a strong focus on the broad vision of preventing and curing breast cancer, rather than on narrow and esoteric questions, and this focus was clear in all plenary sessions. One researcher noted, for example, that she has worked in the field of metastatic breast cancer for over 20 years and has given hundreds of presentations, but before this meeting she had never been asked to speak on what it will take to prevent breast cancer metastasis.

The Science
Scientific themes that were at the heart of several presentations:

*Breast cancer as a heterogeneous disease*
Gene expression profiling technologies have allowed researchers to identify several breast cancer "types" that include those dubbed Luminal A and Luminal B (tumors that are positive for hormone receptors and arise from luminal cells); HER2 (tumors that test positive for HER2 and negative for hormone receptors); BRCA (tumors that arise from mutations of the BRCA1 or BRCA2 genes); and Basal (tumors that are negative for estrogen and progesterone receptors and for HER2 [also sometimes referred to as HER-2 or Her-2/neu or erb-b2]). Recognition of the heterogeneous character of breast cancer will allow for better selection of patient subgroups for clinical trials testing targeted therapies. Without taking this into account, we dilute risk among our test populations, and we obscure recognition of real risk factors and effective treatments.
**Tumor progenitor cells**
Several researchers presented on their investigations of the role of tumor progenitor or breast cancer stem cells. This line of investigation hypothesizes that a tumor is an abnormal organ growing within the breast from abnormal progenitor cells. The implication is that the cancer cannot be finally arrested unless and until the stem cells underlying it are killed. Choosing stem-cell specific targets for future treatments may therefore prove far more effective in stopping cancer from progressing. This type of hypothesis could explain:

- Why tumor regression does not correlate with survival if chemotherapy is killing differentiated cells but sparing cancer stem cells;
- Why the real disease is carcinogenesis, not cancer;
- Why some micro-metastatic cells never develop into metastasis and others, the ones that are stem cells, do;
- How negative environmental exposures during late puberty (such as atomic bomb fallout after World War II) can lead to breast cancer 20, 30, or 40 years later; and
- Why a small percentage of estrogen receptor (ER)-positive tumors that arise from ER-negative stem cells remain refractory to tamoxifen treatment, while those that arise from ER-positive stem cells are completely arrested.

This model could explain why even early diagnosis is, in fact, late diagnosis. It also opens the door for more biologic, rather than chemotoxic, treatments that have fewer side effects.

**Nanotechnology applications**
Because biological systems are well defended, more sophisticated means of defeating them will be required in order to interrupt cancer processes and pathways. Nanotechnologies that involve ultra-small particles can be used to move drugs across membranes or into intracellular spaces that would otherwise not be accessible. Nanotechnology can, for example, deliver drugs directly to the target without exposing other body tissues to cytotoxic effects. These methods can also be exploited to visualize and to destroy tumor cells without impacting surrounding tissue.

**Rethinking clinical trials**
Several sessions and presentations dealt with issues of adapting and improving clinical trial design and analysis in the age of targeted therapies, when there are more targeting agents to be tested than there are patients. One problem is keeping ahead of fast-changing technologies so that trial results are not obsolete before they are released. The need for collection of more and more samples, more and more data from each patient must not interfere with the priority of delivery of quality cancer care.

Also discussed in several contexts was the expectation that new treatments will be added to old treatments, while finding simpler and less toxic treatments to replace the toxic ones are rarely considered. Careful pharmaco-diagnostics and patient selection will help ensure that beneficial treatments are not lost to noise in the analysis phase.

**Individual presentations**
A few of the projects presented at the meeting are summarized below:

- Without treatment, about 50 percent of ductal carcinoma in situ (DCIS) will progress to invasive breast cancer. This means that 50 percent of the women treated with radiotherapy for breast cancer do not benefit from the treatment. One presenter proposed...
that we abandon the one-size-fits-all approach to DCIS treatment, and start tailoring treatments based on ER and HER2 status.

- A ratio of two-gene genes (HOXB13 and IL17BR) can be used to predict tamoxifen resistance in ER-positive tumors. The method was developed by comparing gene profiles of tumors from women treated with tamoxifen alone who had or had not recurred. Accuracy of this prediction method was reported to be 78 percent.
- One presenter proposed chronic treatments that target biomarkers tied to angiogenesis to produce long-term inhibition of cancer progression. This would lead to management of cancer as a chronic disease, analogous, perhaps, to the use of statin drugs against cardiac disease.
- Levels of two estrogen metabolites (4-hydroxyestradiol and estrogen-3, 4-quinone conjugates) were found to be nearly four times higher in women with breast cancer than in women who did not have the disease, suggesting that problems in estrogen metabolism may lie at the root of breast cancer. Specifically, the researchers hypothesize that catechol estrogen quinine reacts with DNA to produce specific mutations that may trigger cancer in the breast or prostate, and other common forms of human cancer.

Please visit the NBCCF website at www.stopbreastcancer.org for additional analysis of the Breast Cancer Research Program and Era of Hope.