

## **Breast Cancer Updates**

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Breast cancer research is advancing at an electrifying pace. This past year has seen many advances with approvals of several drugs active in breast cancer and some real insight into our understanding how breast cancer behaves.

One of the things we have learned over the past few years is that breast cancer is not just one disease but probably at least a dozen distinct entities. Probably the only thing they have in common is that are found in the breast. Since the completion of the human genome project several years ago, this has enabled scientists to really understand breast cancer on a molecular level which, in my opinion, is the reason for so many advances.

So let's look at some examples of some of these advances. Trying to exploit differences among different types of breast cancer is a test that is becoming integrated in how we take care of breast cancer that has not spread to the lymph nodes under the arm (node negative breast cancer) and uses estrogen to grow (hormone receptor positive breast cancer). This test is comprised of a set of genes (made up of DNA, the building blocks of life) that estimates the risk of recurrence of breast cancer and response to hormonal therapy. Many breast cancers use estrogen to grow and one way to tackle stray cells that are floating around in the blood stream is to block these cancer cells ability to use estrogen as food to grow- this is called hormonal (really anti-hormonal) therapy. Well, this test (called a 21 gene recurrence score or Oncotype) seems like it is pretty good at predicting the response of tumors to tamoxifen (a hormonal therapy used to treat breast cancer). We are trying to learn if this test can be useful in predicting behavior of tumors that have spread to the lymph nodes under the arm. The goal of this is to be able to figure out what patients with breast cancer might be able to avoid having chemotherapy and who may absolutely need it. There is a large clinical trial underway trying to evaluate this question and it is called the TAILORX trial. It is estimated that over 10,000 women will be enrolled in this trial.

Another advance over the past year has been the FDA approval of three drugs. They are called lapatinib (Tykerb), bevacizumab (Avastin) and ixabepilone (Ixempra). Lapatinib is called a tyrosine kinase inhibitor and this is used to shrink breast cancer that is HER2neu positive. HER 2 neu is a growth accelerator present of breast cancer cells but is also a target for drugs (i.e. trastuzumab or Herceptin). The studies showed that laptinib was very good at keeping cancer under control longer when combined with another chemotherapy pill called capecitabine (Xeloda) as compared to capecitabine alone. This is a real advance for patients who have HER 2 neu positive tumors because it gives them another option. It might also be really important because we are learning so much about HER2neu and it might be that all HER2neu is not created equal and lapatinib may exploit this fact.

The other biologic that was approved in the past year was bevacizumab (avastin). This is an interesting drug because we think it affects blood vessels that feed tumors. Blood vessel formation is critical for tumors and normal tissue development. The bevacizumab sops up VEGF-A which is critical for blood vessel growth and maintenance. We don't know if bevacizumab just cuts off blood vessel formation or if it allows the tumor blood vessels to become less tortuous so that we get better delivery of chemotherapy (vascular normalization hypothesis). Either way, we know that when breast cancer patients receive chemotherapy (Taxol) and bevacizumab together, it is twice as good in shrinking the breast cancer and keeping it under control for double the time as Taxol alone. This is a very important finding.

Ixabepilone is a chemotherapy drug which was approved by the FDA in October 2007. It is the first in class of a new family of chemotherapy drugs called the epothilones. Our group was very involved in developing this drug so we are particularly happy it was approved. This drug is very good at shrinking tough to treat (refractory) breast cancer. Our expectation is that once the clinical trials are done, we hope to find that it is equally good at preventing breast from spreading. These adjuvant trials are underway in Europe right now.

The oncology health care team is always looking at ways to try to prevent cancer from coming back. The Breast Cancer Research Program at Weill Cornell has two really interesting projects aimed at exactly this concept. One of our studies is a Phase II trial of tetrathiomolybdate (TM) in patients with breast cancer who have a moderate to high risk of breast cancer coming back. We know that blood vessels are critical in promoting a dormant tumor to transform into an actively growing entity. Studies have shown that copper is a key component of angiogenesis (blood vessel formation) so armed with a lot of background studies, we have embarked on clinical trial of providing a copper depletion compound (TM pills) to patients who have completed standard therapy but are looking to do something extra- with the hope of decreasing the risk of tumor recurrence. This trial is actively accruing and we are seeing some interesting results.

Because we are trying to understand how breast cancer behaves and why it may be predestined to spread at diagnosis, we several studies underway with our colleagues in Pediatrics, Dr David Lyden and Dr. Rosie Kaplan. Our studies are looking to ultimately predict who has the "kind" of breast cancer that is pre-determined to spread. We are looking to develop a strategy that can prevent this from happening. In our study, a simple blood test over time provides us with the raw material we need to study and try to figure out this important issue. In support of this concept and project, we were awarded a Komen for the Cure Grant to study this whole area. What this could potentially mean for our patients is that we would be able to tailor therapy for all our patients' particular tumor.

So as you can see, these are exciting times in breast cancer research and the best is yet to come.