

WEB EXCLUSIVES

New Ways of Studying Drugs are Needed to Succeed in Developing New Agents

BY BEVERLY A. CALEY

A plethora of molecularly targeted agents have the potential to be effective new treatments for breast cancer, Jose Baselga, MD, told an overflow crowd at an educational session held Wednesday evening. He cautioned, however, that to take full advantage of many of the promising new agents, it may be necessary to change the way new drugs are studied and developed.

Baselga described dozens of new cancer treatments currently being investigated. He said researchers have never before been in a similar position in terms of the wide variety of individual drugs and drug classes in development. “Clearly, we can no longer see breast cancer as one [disease],” he said. In fact, he added, even presently established subtypes of breast cancer are now known to have their own subtypes. “Whenever possible, we have to design our clinical trials based on the best molecular profiling that we can,” Baselga urged.

So many potential new treatments are available that “if we try to develop them in a classical way, we will fail,” Baselga said. “We will need to select these patients, we will need to do biopsies, we will need to check biomarkers. The way I see the future going is to try to implement more trials in the neoadjuvant setting.”

An audience member asked whether focusing studies on the neoadjuvant setting would have treatment implications for patients with advanced cancers. Baselga responded that it is already increasingly difficult to enroll patients in the advanced setting.

“Since Herceptin has done so well in preventing recurrences, the number of patients enrolling in trials has been diminishing. It will be easier and faster to do neoadjuvant studies than first- and second-line treatment” in the advanced setting. Eventually, he explained, new agents could be studied in a broader patient population.

Baselga said he does not expect new molecularly targeted agents to replace

traditional chemotherapy drugs that have proven effectiveness in treating breast cancer. “There is no need to make a choice between them,” he said. “We need everything we have against cancer.”

In the second half of the session, Douglas Yee, MD, focused on the promise shown by cancer treatments that target a group of hormone receptors known as insulin-like growth factors receptors (IGFRs). The hormones, IGFs, that bind to this receptor are similar to estrogen in their contribution to the growth of cancer cells.

The way in which IGF and its receptor help breast cancer cells survive and reproduce is complicated, so it is difficult to determine the best way to use the anti-IGFR agents that are now being developed. In his presentation, Yee said the unknowns about how IGFR inhibition will work are analogous to the questions that had to be answered before determining what are now established targeted therapies in breast cancer.

His example was that tamoxifen and Herceptin (trastuzumab) are used very differently with chemotherapy. Tamoxifen is usually given after chemotherapy, whereas Herceptin is often given concurrently with chemotherapy. It is not yet known whether IGFR inhibition will be more like tamoxifen or could be more like Herceptin. There is preclinical data to support the idea that treating with an IGFR inhibitor after chemotherapy increases the effectiveness of chemotherapy, but on the other hand, if the IGFR inhibitor is given first, followed by cytotoxic chemotherapy, cytotoxic chemotherapy is less effective.

In an interview with *CURE*, Yee said, “It might be true that anti-IGFR agents will be effective as single agents, but I don’t think that is where we are going to start. We will be starting in combination with things that we know work.

“We are working on improving therapies based on biology,” Yee continued. “There are a huge amount of data suggesting the IGF/IGFR system is relevant to breast cancer. But we could say that all day, and you couldn’t prove it to be true until the drugs become available.” Yee went on to explain that now that the drugs are available for clinical study, researchers are beginning to sort out the best ways to use them.

Read more of *CURE*'s coverage of the 31st annual San Antonio Breast Cancer Symposium at <http://media.curetoday.com/htmlmail/sabcs>.