

# PACCT-1 Trial: TAILORx

*A Clinical Trial Assigning Individualized  
Options for Treatment (Rx)*

## Community Education Slide Presentation *Script*

Note to users: ECOG developed these notes to use as a script or as reference when presenting the TAILORx to a lay audience. The notes are marked by slide for easy reference.

### *Slide 1 – Title Slide*

- Welcome. Today I'm going to be talking to you about a very exciting clinical trial called "TAILORx," which is an acronym for "Trial Assigning Individualized Options for Treatment."
- This is the first breast cancer trial that integrates a new molecular diagnostic test into the clinical decision-making process.
- The purpose of this presentation is to review the trial design, who is eligible to participate, the study endpoints, and how advocates have been involved in this trial from concept to implementation.

### *Slide 2 – Overview*

- Topics that will be reviewed include:
  - Information about the Program for the Assessment of Clinical Cancer Tests, also known as PACCT
  - Information regarding ER-positive, lymph-node negative breast cancer
  - A review of current treatment guidelines
  - Current prognostic and predictive factors
  - Information about the Oncotype DX test
  - And information about the rationale for TAILORx and its trial design
- Finally, I'll review involvement of patient advocates in the trial design.

### *Slide 3 – Program for the Assessment of Clinical Cancer Tests*

- This trial was developed as a result of the National Cancer Institute's "PACCT" Program, an acronym that stands for "Program for the Assessment of Clinical Cancer Tests."
- The purpose of PACCT is to translate innovative ideas, technologies, and concepts into clinical practice by convening strategy groups which plan initiatives, promote infrastructure development, and support working groups, workshops, and collaborative projects to achieve these goals.
- Many decisions for cancer treatments depend on information from clinical laboratory tests.
- New technologies are resulting in a variety of new laboratory tests, some of which involve complex tests that cannot be performed in clinical laboratories.
- The goals of PACCT are to ensure the translation of new knowledge about cancer and new technologies to clinical practice, and to develop more laboratory tools that give us valuable information to help make cancer treatments more effective.
- TAILORx is the first clinical trial that was developed as a result of the PACCT program.



# Community Education Slide Presentation *Script*

## ***Slide 4 – Management of ER-Positive, Lymph Node Negative Breast Cancer***

- The TAILORx trial will include patients with estrogen receptor-positive, lymph-node negative breast cancer.
- There are about 137,000 women diagnosed with this disease each year in the United States and Canada, accounting for more than one half of all new breast cancers.
- It is known that adding chemotherapy to hormonal therapy reduces the relative risk of recurrence by about 25 percent in this group.
- However, because the risk of recurrence is between 15-20 percent on average if treated with hormonal therapy, reducing the risk of recurrence by 25 percent in relative terms results in only a 3-5 percent absolute benefit, or less in some patients.
- Our current practice guidelines recommend chemotherapy for most patients, but about 80-85 percent are adequately treated with surgery, radiation, and hormonal therapy. This means that we are over-treating 80-85 percent of women who may have done well without chemotherapy.
- If the benefit from chemotherapy is very small, it may be overshadowed by the long-term and short-term side effects of treatment.
- If hormone therapy is enough for these women, they may be able to maintain a higher quality of life, with the same chances for disease-free survival, WITHOUT having chemotherapy.

## ***Slide 5 – NCCN Guidelines***

- In order to highlight this point, the National Comprehensive Cancer Center guidelines are shown on this slide. These practice guidelines were developed by breast cancer experts practicing at major National Cancer Institute-designated cancer centers in the U.S.
- The guidelines recommend adjuvant chemotherapy for women with tumors measuring more than one centimeter, or women with smaller tumors that have unfavorable pathological features, such as angiolymphatic invasion or poor nuclear and/or histologic grade.
- The important point here is that following these guidelines would result in administration of chemotherapy to about 90 percent of women with early stage breast cancer, most of whom might have been adequately treated with hormonal therapy alone.

## ***Slide 6 – NCCN Guidelines continued***

- There are certain caveats, however, which are stated here in the guidelines.
- First the panel stated that "... the absolute benefits of chemotherapy may be small."
- Second, the panel concluded that "The decision to add chemotherapy ...should be individualized, especially in those with a favorable prognosis and in women age 60 years or older where the incremental benefits of chemotherapy may be small."
- And third, the panel stated that "...there is insufficient data to make chemotherapy recommendations for those more than 70 years old."

# Community Education Slide Presentation *Script*

## ***Slide 7 – Established Prognostic/Predictive Factors***

- Physicians typically rely on prognostic and predictive factors in clinical practice to make treatment recommendations.
- Prognostic factors are features of the cancer that are associated with an increased risk of relapse.
- Factors typically associated with a higher risk of relapse include having positive axillary lymph nodes, a larger tumor size (especially if lymph node negative), and the tumor cells having a poor grade.
- Predictive factors are features of the cancer that are associated with benefit from specific types of treatment.
- Examples include ER and PR expression, which predicts benefit from hormonal therapy, and HER2/neu expression, which predicts benefit from adjuvant trastuzumab (Herceptin).
- In other words, if the tumor is ER and PR negative, hormonal therapy is not effective, and is not used. Likewise, if the tumor is HER2/neu negative, Herceptin is not beneficial, and is not used.
- However, there is no predictive factor for chemotherapy – treatment selection here is based upon having a risk of recurrence that exceeds about 5-10 percent.

## ***Slide 8 – Background Information about Oncotype DX (ODX)***

- The Oncotype DX test is based not on a single gene or protein, but rather is a 21 gene test which evaluates genes involved in estrogen receptor signaling, proliferation, HER2/neu, and other pathways important for cancer cell growth and response to therapy.
- Oncotype DX predicts relapse more reliably than standard prognostic features in patients treated with tamoxifen who have ER-positive, lymph node negative disease.
- The test result is provided as a “Recurrence Score” ranging from 0-100 – higher score is associated with higher risk of relapse in tamoxifen-treated patients.
- The test is performed in a single laboratory (Genomic Health, Inc.) that is certified by regulatory agencies in the United States. The responsible agency is called CLIA.

## ***Slide 9 – Rationale for Selecting the Oncotype DX Test for TAILORx***

- There are several important reasons why Oncotype DX was selected for TAILORx.
- First, low Recurrence Score is associated with a low risk of recurrence if treated with tamoxifen alone.
- The risk of recurrence for this group is so low that adding chemotherapy is not likely to be beneficial.
- Second, high Recurrence Score is associated with an elevated risk of recurrence, and predicts greater benefit from chemotherapy.
- Third, Oncotype DX may be performed on routinely processed tissue that has already been collected and stored at surgery. No additional biopsies are needed.
- Finally, it is a commercially available test, and there is increasing precedent for third party reimbursement for the cost of the test.

# Community Education Slide Presentation *Script*

## ***Slide 10 – Trial Assigning Individualized Options for Treatment (Rx) TAILORx***

- The premise of the TAILORx is that integration of a molecular diagnostic test into clinical decision making may assist in making more informed treatment decisions.
- The implications are three-fold.
- First, it will reduce chemotherapy overtreatment in those with a low Recurrence Score who are likely to do well with hormonal therapy alone, and who might otherwise have received chemotherapy because of equivocal or poor risk clinical features.
- Second, it will reduce inadequate treatment by identifying individuals who derive great benefit from chemotherapy who might otherwise have received hormonal therapy alone because of equivocal or good risk clinical features.
- Third, it will evaluate the benefit of chemotherapy in patients with a mid-range Recurrence Score where uncertainty about its benefit remains.

## ***Slide 11 – PACCT-1: TAILORx Schema***

- The TAILORx schema is shown on this slide. It can look confusing at first. However, if we walk through it, the trial will become clearer.
- For those who meet the eligibility criteria and who have consented to participate, there is a pre-registration phase. A small amount of the tumor, which was already collected and stored at the time of surgery, will be sent to the Genomic Health laboratory and analyzed.
- When the result of the ODX are returned to the physician about 10-14 days later, the patient is registered and assigned to one of the study groups. The specific type of hormonal or chemotherapy treatment is up to the patient and her physician.
- At the time of registration, women will be able to provide several blood samples that will be stored in a tissue bank for evaluation of other cancer clinical tests in the future. The remaining tumor specimen will also be stored in that tumor bank after the Oncotype DX test has been completed.
- If the Recurrence Score is less than 11, women will be assigned to receive hormonal therapy alone. This group is called Secondary Study Group 1, or Arm A.
- If the Recurrence Score is more than 25, women will be assigned to chemotherapy plus hormonal therapy. This group is called Secondary Secondary Study Group 2, or Arm D.
- If the Recurrence Score ranges from 11 to 25, patients will be randomized to receive hormonal therapy alone, called Arm B, or chemotherapy plus hormonal therapy, called Arm C. Patients with a score of 11-25 in Arms B and C are considered the Primary Study Group.
- You can see here the proportion of patients expected to fall into each group. About 55 percent of patients with a low or high RS, those in Arms A and D, will have their treatment assigned on the basis of the test.
- For the approximately 45 percent of patients who have a mid-range score, the treatment will be randomly assigned. Randomization is a procedure that is commonly used in clinical trials when there is uncertainty about the best treatment option.

# Community Education Slide Presentation *Script*

## *Slide 12 – Study Design*

- The two primary objectives of the trial are shown on this slide. The trial was designed to address these issues.
- The first primary objective is to determine whether adjuvant hormonal therapy is not inferior to adjuvant chemohormonal therapy in patients who have a mid-range Recurrence Score of 11-25.
- Only patients who meet standard clinical criteria for chemotherapy are eligible for the trial. For this reason, hormonal therapy is considered the experimental arm and chemohormonal therapy is considered the standard treatment arm.
- Another way of stating the primary objective is that the study will determine whether hormonal therapy is as effective as chemohormonal therapy.
- Another primary objective is to create a tissue and specimen bank in order to evaluate new “clinical cancer tests.” This is extremely important because it will allow researchers to evaluate new tests as they are developed and compare them to Oncotype DX without having to perform another large trial.

## *Slide 13 – Definition of Risk Groups for TAILORx*

- It is important to point out that the definitions of low, intermediate or mid-range, and high risk have been modified for the TAILORx trial, and are different than the original definitions reported for the assay.
- The definitions were modified in order to reduce the risk of under-treatment in the trial. In other words, an effort was made to minimize the risk that patients who are truly benefiting from chemotherapy would not receive it.
- It is currently unclear at what Recurrence Score benefit from chemotherapy occurs. It is clear that chemotherapy is not likely to be beneficial if the Recurrence Score is less than 11. It is also clear that chemotherapy is very beneficial if the Recurrence Score is more than 25. The trial will determine whether there is any chemotherapy benefit if the Recurrence Score is 11-25, and if so, at what level this benefit can be detected.
- For the low Recurrence Score group, the upper bound was reduced from 18 to 11. In TAILORx, this is called Secondary Study Group 1. This was done because at Recurrence Score of 10 or lower, there is a less than 5-10 percent chance of relapsing with hormonal therapy alone. This 5-10 percent threshold is typically used for recommending adjuvant chemotherapy. Therefore, women with a Recurrence Score of less than 11 will receive hormonal therapy alone.
- For the high Recurrence Score group, the upper bound was reduced from 30 to 25. In TAILORx, this is called Secondary Study Group 2. A RS of 30 is associated with a 20 percent risk of recurrence. This group will receive chemotherapy in addition to hormonal therapy. Lowering the threshold to 25 will reduce the risk of under-treating this group.
- Finally, the definition of the intermediate or mid-range group was adjusted from 18-30 down to a range of 11-25. This is called the Primary Study Group because it is in this group we are evaluating whether chemotherapy is beneficial. Changing this definition reduces the risk of under-treatment at the upper range of this mid-range group.

# Community Education Slide Presentation *Script*

## *Slide 14 – Key Eligibility Criteria*

- Key eligibility characteristics required for participation in the trial are shown on this slide.
- These are the characteristics of a tumor for which established clinical guidelines would recommend chemotherapy.
- First, the tumor must be ER positive and/or PR positive.
- Second, the axillary lymph nodes must be negative, obtained either by sentinel lymph node biopsy or axillary dissection.
- Third the tumor must be HER2 negative. This is for two reasons. First, most HER2/neu positive tumors will have a high Recurrence Score. Second, most patients who have HER2/neu positive tumors will require chemotherapy and may also benefit from Herceptin.
- Finally, the tumor must be 1.1 to 5.0 cm in size, or 0.5 to 1.0 cm plus having unfavorable histologic features. Unfavorable histologic features are determined by the pathologist's analysis of the specimen using a microscope.

## *Slide 15 – Key Eligibility Criteria continued*

- Another important criterion is that the patient and the doctor must agree to use standard chemotherapy and hormonal therapy. "Standard" means the treatment is recommended by clinical guidelines.
- An important thing to remember about the TAILORx trial is that the doctor and the patient choose which hormonal therapy and which chemotherapy will be used in treatment.
- Since having the ODX is a requirement of being in the study, a tissue specimen from the primary breast cancer must be shipped to the appropriate laboratory after consent is obtained.
- Most women in this clinical trial will have the ODX test after they are pre-registered. To accommodate women who have had the ODX and have a RS of 11-25 will be allowed to enter the Primary Study Group. The primary study group will help us answer the primary endpoint question of this trial.

## *Slide 16 – Key Points*

- An important feature of this study is, as mentioned before, that the physician and patient may use the hormonal or chemotherapy of their choice, as long as it is consistent with NCCN guidelines. This allows the choice of a more or less aggressive chemotherapy regimen based on the individual patient's needs.
- The other important feature is the patient will not be responsible for the cost of the test. GHI will work with the patient to secure reimbursement for patients who have health insurance. This includes appeals if necessary. For those who are uninsured or partially insured, patients will not be responsible for the cost of the Oncotype DX Assay.

# Community Education Slide Presentation *Script*

## ***Slide 17 – Advocate Involvement in TAILORx***

- Advocates have been involved in all stages of the development of the TAILORx trial.
- A patient advocate sat on the PACCT Breast Cancer Working Group that chose the test to be used in the trial.
- Advocates serve on the North American Intergroup, which oversees clinical trials conducted by the cooperative groups.
- The Data Monitoring Committee (DMC) oversees the conduct of the trial. It is an independent group with no members directly associated with the trial. It periodically reviews adverse events and the findings of the trial to that date. An advocate currently serves as a standing member of the DMC.

## ***Slide 18 – Advocate Involvement in TAILORx continued***

- The Research Advocacy Network (RAN), a non-profit organization dedicated to involving advocates in all aspects of medical research, collaborated with ECOG, a cooperative group funded by the NCI, and the NCI to conduct two focus groups that discussed trial design.
- There was concern that the trial might not be able to recruit the needed number of participants.
- RAN held two focus groups.
- One consisted of patients who met eligibility requirements.
- The other consisted of breast cancer advocates.
- RAN also interviewed key thought leaders.

## ***Slide 19 – Key Findings of Focus Groups***

- One of the key findings from RAN's work with focus groups was that there was a lot of interest in the ODX test.
- However, it was also found that randomization to treatment was problematic for many members of the focus groups.
- Some thought that the commercial availability of the test could affect accrual.
- The willingness by physicians to enroll patients is a key to success.
- RAN also learned key points of the trial that needed to be included in the patient education material.

## ***Slide 20 – Outcome of Focus Groups***

- The outcomes of the focus groups were impressive.
- It was the first time Eastern Cooperative Oncology Group (ECOG) used focus groups to inform the design of a Phase III trial it was proposing to conduct.
- The research leadership found the information helpful and they hope to continue using market research techniques as they develop concepts and protocols in the future.
- Researchers would like to use this technique earlier in the process – at the concept stage before too much time and money has been spent.
- George Sledge, MD, Professor of Medicine and Pathology, Indiana University School of Medicine and Chair of the ECOG Breast Committee, captures the essence of the outcome: "It (the market research) did have an effect. Not on the basic question but on how we thought about the design. We broadened our criteria and became more realistic about our accrual goals."

# Community Education Slide Presentation *Script*

## *Slide 21 – If You Participate In TAILORx*

- If you participate in TAILORx, you may be randomized to receive hormonal therapy alone or hormonal therapy plus chemotherapy.
- There will be no additional biopsy required. The test will be conducted on tissue that has already been taken for diagnostic purposes.
- Joining TAILORx will not make you ineligible for other trials. For information on other trials that you may be eligible for go to [www.CancerTrialsHelp.org](http://www.CancerTrialsHelp.org).

## *Slide 22 – Key Points*

- TAILORx was activated 4/7/2006.
- List of active sites and patient education material can be found at [www.ecog.org/general/tailorx.html](http://www.ecog.org/general/tailorx.html)

