In this together.

Empowering Patients: The Crucial Role of Advocates in the I-SPY 2 Breast Cancer Trial

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I am excited to introduce the first quarterly feature in our e-newsletter spotlighting patient advocates. These individuals are making a real difference in the lives of cancer survivors and contributing significantly to advancements in cancer research. In this article, I will highlight how a dedicated group of advocates has been essential in ensuring the patient's voice is heard in one of the nation's largest adaptive breast cancer trials.

Having faced two breast cancer diagnoses five years apart, I learned a vital lesson: treatment decisions are rarely simple or straightforward. When seeking answers, I realized there was a gap between the questions I was asking and the information I received. While my caring physicians provided a "risk percentage" for cancer recurrence within five years, I wondered about the basis of that number. Was it derived from studies of people truly like me? How similar were their tumors to mine? How will the recommended treatments stop the cancer from returning? How would we know if they were working? What about side effects? Are there other treatment options? These questions are common—most patients need this information to make informed decisions.

For patient information the I-SPY2.2 trial visit: https://www.quantum-leaphealth.org/for-patients/i-spy-trials/about-i-spy-2/

Clinical trials are crucial for answering these questions for both patients and physicians. They provide strong scientific evidence on the safety and effectiveness of new treatments compared to existing standard options. Trials form the foundation for evaluating prevention, diagnosis, and treatment approaches, thereby guiding patients and clinicians toward the best available

therapies. However, traditional trial designs often prioritize scientific hypotheses over patient needs, which can limit their relevance to individual decisions. Increasingly, incorporating patient perspectives into clinical trials is recognized as essential for their success and relevance. Trials designed with patient input are more likely to produce results that truly benefit patients and lead to treatments that better address their needs.

I-SPY 2 Trial

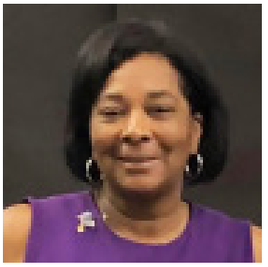
For the past 16 years, I and other patient advocates from the UCSF Breast Oncology Program's Breast Science Advocacy Core, along with others nationwide, have been involved in the initiation, development, and monitoring of the I-SPY trial, one of the first adaptive clinical trials for breast cancer. The I-SPY trial began at the University of California, San Francisco, in 2002. It evolved into I-SPY 2 in 2010 and is now the I-SPY 2 trial. This trial is conducted across 35 national institutions, encompassing 50 clinical sites. As the trial expanded, so did the number of advocates, with patient advocates involved at most trial sites.

The I-SPY 2 trial is an adaptive clinical trial for early-stage breast cancer where patients receive drug therapy before surgery (neoadjuvant). It evaluates new investigational drugs and combinations to determine if they are better, worse, or equivalent to standard treatments. Using personalized strategies based on biomarkers and imaging, the trial rapidly assesses treatment effectiveness. If a therapy is ineffective, patients may switch to alternative treatments within the trial. When the tumor responds well, patients can proceed directly to surgery, potentially avoiding additional therapy. This approach aims to identify the most effective and less toxic treatments faster than traditional trials.

I-SPY 2 advocates: right to left: Coleen Crespo, Amy Delson, Diane Heditsian, Thelma Brown, Carolyn Clark Beedle and Silver Alkhafaji.

Patient advocates have been involved in the I-SPY trial from its inception. They were invited by a visionary group of clinicians and scientists who recognized the importance of placing patients at the center of clinical research. Advocates became an integral part of the trial, helping to create a more patient-focused design and execution. Many advocates are former patients or trial participants themselves, providing valuable firsthand insight into the patient experience. Over the past 16 years, their role has grown substantially, influencing the trial in unexpected ways and contributing to improvements in communication, consent processes, and overall patient support throughout the study.

The I-SPY 2 trial follows several key steps designed to personalize and adapt treatment for early-stage breast cancer patients.



I-SPY 2 advocates: desending order: Susie Brain, Jan Tomlinson, Barbara LeStage, Jane Mortimor, Jane Perlmutter.

1. **Screening and Enrollment:** Patients with early-stage breast cancer are evaluated for eligibility and provide initial consent to participate in the trial.

2. **Biomarker and Imaging Assessment:** Patients undergo biomarker testing (to characterize their tumor) and imaging (such as MRI scans) to understand tumor features and predict treatment response. These results guide the initial treatment assignment.

3. **Randomization and Treatment Assignment:** Eligible patients are randomly assigned to receive either the standard-of-care therapy or one of several experimental drugs tested simultaneously under a master protocol.

4. **Adaptive Treatment Monitoring:** Using an adaptive design, treatment effectiveness is monitored early through imaging and biomarker analysis. If a treatment proves ineffective, patients may be switched to alternative therapies within the trial.

5. **Pathological Complete Response (pCR) Evaluation:** pCR is defined as the complete elimination of invasive cancer cells in the breast and underarm lymph nodes after neoadjuvant therapy. Achieving pCR strongly indicates effective systemic therapy and is linked to a favorable prognosis.

6. **Continuous Learning and Drug Selection:** A working group—including patient advocates—regularly reviews accumulating data to add promising investigational drugs or remove ineffective ones from the trial.

7. **Early Surgery Option:** If the tumor responds exceptionally well and no cancer is detected, patients may proceed to surgery early, avoiding unnecessary additional treatment.

Together, these steps enable the I-SPY 2 trial to rapidly identify effective, less toxic treatments tailored to individual patients while maintaining a patient-centered approach.

▶ For more information and graphic explainations on the trial visit: https://www.quantumleaphealth.org/for-investigators/i-spy-trials/i-spy-2-2-trial/

I-SPY 2 advocates: desending order: Bev Parker, Crystal Kretzer, Carol Simmons, Deborah Romer, and Sandy Finestone.

Patient advocates have contributed to the I-SPY2 trial in several key ways:

Identifying Meaningful Outcomes: Patient advocates highlight what truly matters to them regarding treatment benefits—such as quality of life, pain reduction, and the ability to perform daily activities. Their input helps select study endpoints that are more relevant to patients than solely clinical measures.

Optimizing Study Procedures: Advocates provide insights into practical challenges of trial participation, including visit frequency, complex procedures, and travel difficulties. This feedback leads to more patient-friendly protocols, making trials less intimidating and easier to navigate.

Improving Communication: Advocates continuously assist in developing clear, easy-to-understand language for patient materials, including the trial website and result reports, ensuring information is accessible and consistent for all participants.

Enhancing the Consent Process: They lead efforts to shorten and simplify consent forms using understandable language, ensuring participants fully comprehend what they agree to before enrolling.

Participating in Trial Design and Execution: Advocates actively contribute to all 14 working groups within the trial, influencing biomarker development, data analysis, policy changes, drug safety, surgical outcomes, and the creation of communication tools for patients and physicians.

Patient-Reported Outcomes (PROs): I-SPY 2 patient advocates enhance PROs by ensuring outcomes reflect patient priorities like quality of life and symptoms. They clarify survey questions, foster trust to increase participation, and guide researchers in designing relevant trials. They also ensure meaningful return of results, amplifying the patient voice throughout the research process.

Enhanced Recruitment and Retention: Advocate engagement improves patient retention, builds trust and transparency between researchers and participants, and helps reach diverse populations, leading to more complete, robust, and meaningful study results.

I-SPY 2 advocates: desending order: Kelly Wilkinson, and Joan Venticinque.

Final thoughts on I-SPY 2

Having been involved in the I-SPY trial and participating in its development over the years I have learned a great deal. First how important it is to have such a forward-thinking physician scientist, Laura Esserman, MD. She had the vision to change the way clinical trials are done, to get treatments to patients faster and safer, and for inviting advocate involvement. Finally, by involving patients as partners, I-SPY 2 shifts from research done ***to*** patients to research done ***with*** them—making the process more ethical, efficient, and impactful. ❒

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Glossary

Adaptive design: An adaptive clinical trial is a study that allows for modifications to the trial procedures—such as dosage, sample size, or treatment arms—based on interim data analysis without compromising the study's validity or integrity.

Neoadjuvant: In the I-SPY 2 trial, neoadjuvant treatment refers to therapy given before surgery. This preoperative therapy can include chemotherapy, HER2-targeted therapy, immunotherapy, or hormone therapy.

Biopsy: A biopsy is a procedure where a small sample of tissue is taken from the body to be examined under a microscope to check for disease.

Biomarker: Something in the body that is measured as an indicator of personal health or disease.

IRB: An Internal Reveiw Board is a team of people who review studies to protect the rights and welfare of study participants.

MRI: An MRI (Magnetic Resonance Imaging) is a scan that uses magnets and radio waves to take detailed pictures of the inside of your body. pCR: is defined as the complete elimination of invasive cancer cells in the breast and axillary lymph nodes following neoadjuvant therapy (treatment given before surgery).

Patient-Centered: Patient-centered means focusing on the patient's needs, preferences, and values when making healthcare decisions and providing care.

Patient Reported Outcomes: The information that patients share about their own health or well-being to answer questions in a study.

Policy: Healthcare policy is a set of rules and decisions made by governments or organizations to guide how healthcare is provided, paid for, and improved.

Protocol: A complete description of the research plan and procedures.

Return of Results: Return of results means giving patients or participants the findings or outcomes from medical tests or research studies that were done on them.

Screening: Tests and questions to find out if a person can join a study.