ISPY

Overview

The I-SPY trial is a national study to identify biomarkers predictive of response to therapy throughout the treatment cycle for women with Stage 3 breast cancer. The I-SPY study is sponsored by the Specialized Programs of Research Excellence (SPORES) and includes participation from the Cancer and Leukemia Group B (CALGB) and American College of Radiology Imaging Network (ACRIN). The study involves the use of a contrast-enhanced breast MRI for the evaluation of locally-advanced breast cancer patients undergoing neoadjuvant treatment. The I-SPY study aims to correlate MRI results with molecular markers to identify the right surrogate marker for early response.

The I-SPY informatics effort involves providing informatics support for the I-SPY trial. This involves the integration, and analysis of diverse data types including clinical, MRI imaging, gene expression, Comparative Genome Hybridization (CGH), immunohistochemistry (IHC), Fluorescent In Situ Hybridization (FISH), and cell lysates throughout the breast cancer treatment cycle. By providing an integrative platform designed to correlate molecular data with MRI patterns, study researchers will be able to more effectively identify surrogate markers for early response which will ultimately result in more effective therapies for breast cancer patients.

To facilitate the integration and analysis of diverse data types, the NCICB caIntegrator data warehousing solution in conjunction with existing NCICB datamarts will be leveraged. caIntegrator data mining query and reporting tools will be accessible via a customized I-SPY application portal. The application portal will illustrate how research data is shared across study organizations and integrated in support of translational research.

Due to data access restrictions, the I-SPY data portal and the quality indicator portal are currently available only to I-SPY investigators.

Objectives

The main research objectives of the I-SPY trial are to:

- Identify biomarkers that predict response to therapy throughout the course of the cancer treatment cycle.
- Identify surrogate markers of response to preoperative chemotherapy that are predictive of survival and pathologic remission in Stage 3 breast cancer.
- Determine whether molecular markers alone or in conjunction with MRI will predict 3 year disease free survival and whether these markers are good predictors of residual disease at the time of surgery.
- Classify groups of participants with statistically different disease free survival.
- Determine the correlation between molecular markers and MRI imaging patterns.

The informatics objectives supporting the I-SPY trial are to:

- Collect and share biomedical research study results with study members, the SPORES community, and the NCI intramural/extramural community.
- Integrate biomedical research study results and analyze in support of translational research.
- Provide technologies supporting the capture and identification of biomarkers and surrogate markers that predict clinical outcome.
- Design technologies that can be re-used and customized to support a variety of cancer studies.

Potential Benefits

The information learned in the I-SPY effort will assist physicians in providing a better prognosis for breast cancer patients and selecting more effective treatments based on a patient's clinical and genomic signature. The I-SPY effort will also result in better integration of diverse data types across the research spectrum, directly supporting

translational research. Additionally, the informatics platform will facilitate data sharing and scientific collaboration amongst research shareholders including cancer centers, cooperative groups, SPORES, and the NCI community.

Detailed Scope

The scope of the I-SPY Informatics effort involves the capture and integration of I-SPY study data from Stage 3 breast cancer patients treated with neo-adjuvant chemotherapy in a phased implementation approach. Below are details of each Phase:

Phase 1: Requirements Analysis and Proof-of-Concept

The Phase 1 requirements analysis will include the development of use cases, wire frames, and workflow documentation supporting the capture and integration of select I-SPY data components.

The I-SPY proof-of-concept will demonstrate the capture of pre-analysis data (quality indicators) as well as the integration of clinical, gene expression, and CGH data via the caIntegrator data warehouse framework. This includes the development of an I-SPY data warehouse and customized caIntegrator query and reporting tools that will be shared among several participating organizations via the I-SPY data portal. Query and reporting tools will facilitate the analysis of proliferation markers, angiogenesis, apoptosis, hormone receptors, gene expression arrays, and MRI measurements.

The I-SPY requirements analysis effort for the prototype was completed in Q4 2004 and the proof-of-concept with support for gene expression, IHC, FISH and clinical outcomes was delivered to the ISPY investigator community in Q2 2005

Phase 2: Support for Additional Data types

The Phase 2 effort will involve support for additional data types MRI images, and cell lysates. This will involve extensions to the I-SPY data warehouse and ad hoc query and reporting tools.

Support for additional data types is scheduled for a Q2 2006 completion.

In addition to the data portal, a quality indicator portal was created to capture quality data for the frozen adn paraffin sections collected on this trial.

Integration

The I-SPY effort involves leveraging and extending existing NCICB infrastructure components and software applications. These components and applications will become part of the Cancer Bioinformatics Grid (caBIG) architecture as caBIG is developed and fully realized. The practical experience gained in supporting I-SPY will ensure that these components and applications are robust parts of caBIG as it is developed. Additionally, this experience can be leveraged in other studies throughout the NCI intramural and extramural community.