Changing Breast Cancer Outcomes

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Better Outcomes Due To More Screening and More Medical Therapy

Goals For Medical Adjuvant Therapy

• Identify patients with highest likelihood of dissemination of micrometastatic disease to distant organs

• Exploit known targets in breast cancer
  – Estrogen receptor-α – “hormone” therapy
  – DNA synthesis - chemotherapy
  – HER2 oncogene – trastuzumab

• Identify individual risk for each patient to provide appropriate therapy
  – De-escalate therapy for low risk patients
  – Precision therapy for high risk patients
Oncotype DX 21 Gene Recurrence Score (RS) Assay

16 Cancer and 5 Reference Genes From 3 Studies

\[ \text{RS} = +0.47 \times \text{HER2 Group Score} - 0.34 \times \text{ER Group Score} + 1.04 \times \text{Proliferation Group Score} + 0.10 \times \text{Invasion Group Score} + 0.05 \times \text{CD68} - 0.08 \times \text{GSTM1} - 0.07 \times \text{BAG1} \]

**PROLIFERATION**
- Ki-67
- STK15
- Survivin
- Cyclin B1
- MYBL2

**ESTROGEN**
- ER
- PR
- Bcl2
- SCUBE2

**INVASION**
- Stromolysin 3
- Cathepsin L2

**HER2**
- GRB7
- HER2

**GSTM1**

**BAG1**

**CD68**

**REFERENCE**
- Beta-actin
- GAPDH
- RPLPO
- GUS
- TFRC

**Category** | **RS (0 – 100)**
---|---
Low risk | RS < 18
Int risk | RS ≥ 18 and < 31
High risk | RS ≥ 31

TAILORx Methods: Treatment Assignment & Randomization

Accrued between April 2006 – October 2010

Preregister - Oncotype DX RS (N=11,232)

Register (N=10,273)

ARM A: Low RS 0-10 (N=1629 evaluable)
ASSIGN
Endocrine Therapy (ET)

ARM B: Experimental Arm (N=3399)
ET Alone

ARM C: Standard Arm (N=3312)
ET + Chemo

Mid-Range RS 11-25
(N=6711 evaluable)

RANDOMIZE

Stratification Factors: Menopausal Status, Planned Chemotherapy, Planned Radiation, and RS 11-15, 16-20, 21-25

ARM D: High RS 26-100
(N=1389 evaluable)
ASSIGN
ET + Chemo

TAILORx Results - ITT Population: All Arms (A,B,C & D)

9-Year Event Rates

- **RS 0-10 (Arm A)**
  - 3% distant recurrence with ET alone

- **RS 11-25 (Arms B & C)**
  - 5% distant recurrence rate overall
  - ≤ 1% difference for all endpoints
    - IDFS (83.3 vs. 84.3%)
    - DRFI (94.5 vs. 95.0%)
    - RFI (92.2 vs. 92.9%)
    - OS (93.9 vs. 93.8%)

- **RS 26-100 (Arm D)**
  - 13% distant recurrence despite chemo + ET
Investigation of Serial studies to Predict Your Therapeutic Response with Imaging and Molecular Analysis

P.I. – Laura Esserman, M.D. UCSF
HR+/HER2- patients with low-risk 70-gene (MammaPrint) Scores are not enrolled in I-SPY2 Agilent 44K IDE
EFS Dataset

Updated I-SPY 2 EFS/DRFS data
- 950 patients
- 3.8 years median follow-up

pCR rates differ by subtype
- HR+ rates have lowest pCR

Yee, SABCS 2017
11 Agent Combinations Included in this analysis, including control

Yee, et al. submitted
pCR is a highly significant predictor of EFS and DRFS

**EFS**

- EFS at 3yr: 95%
- EFS at 3yr: 78%

**DRFS**

- DRFS at 3yr: 95%
- DRFS at 3yr: 81%

Yee, et al. submitted
I-SPY 2+ Draft Design: Maximizing the chance of achieving pCR

Program Project 2017-2022

ARC (Adaptive Rapid Cycle) Learning Arm

REG (Regulatory Evidence Generation) Arm

Block A

Block B

Block C

I-SPY  |  The right drug. The right patient. The right time. Now.
Potential Cancer Disparities In Minnesota

Special Populations

• Largest urban population of Hmong in the world (~90,000) is in the Twin Cities
• Largest Somali-American population in the country (~40,000)
• 11 Federally recognized American Indian tribes (~68,000)
• 26% rural – rural/mix
Minnesota Cancer Clinical Trials Network

- Supported through MNDrive - $4M year
- Engaged
  - Mayo Clinic Cancer Center
  - Metro MN NCORP
  - Sanford Health NCORP
  - Essentia Health CCRP
  - Mille Lacs Band Ojibwe
  - Hormel Institute
  - Fairview Health Services
- Enrolled 317 patients to date
  - 12% rural
  - 43% town/rural
  - 45% urban/town/rural
What’s Next For Breast Cancer?

• Better individualized markers of:
  – Risk to aid mammographic screening
    • WISDOM trial
  – Predictive factors to select “right sized” treatment
• New and novel drugs
• Innovation in clinical trial design
• Inclusion of “ignored” populations