ACRIN 6698 Protocol:

Diffusion-weighted MR Imaging Biomarkers for Assessment of Breast Cancer Response to Neoadjuvant Treatment: A sub-study of the ISPY-2 TRIAL

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DWI QC Director: Tom Chenevert, PhD
ACRIN 6698

**Purpose:** To test diffusion-weighted MRI (DWI) for ability to predict breast tumor response to neoadjuvant therapy.

- This study will be performed in coordination with the ongoing ISPY-2 adaptive phase II trial of neoadjuvant treatment of breast cancer (PIs: L. Esserman, D. Berry)
- The accrual target is **304** consecutive ISPY-2 patients enrolled at sites eligible to participate in ACRIN 6698.
Primary Aim:

To determine if the percentage change in tumor ADC value measured from baseline to early treatment time point is predictive of pathologic complete response.

Secondary Aims:

Multiple secondary aims will investigate ADC change relative to, and in combination with change in tumor volume and DCE-MRI parameters.
Quantitative DWI Protocol

• 4 b-value acquisition (0, 100, 600, 800)
• Performed prior to contrast injection
• Bilateral, axial acquisition
• Phantom QC procedure will be performed for site qualification and ongoing, biannual QA (*Chenevert lab*)
• Test-retest DWI will be performed in 60 patients
Accrual Target

- The accrual target is 304 consecutive ISPY-2 patients enrolled at sites eligible to participate in ACRIN 6698. This assumes:
  - Detected difference of 0.15 between the AUC for ADC prediction of pCR non-responders, versus the null hypothesis
  - 90% power and type I error rate of 5%
  - 10% drop out rate
  - 27% loss due to patients with MammaPrint low at screening
  - 20% of cases not analyzable (ie., missing MRI$_1$ or MRI$_2$, poor image quality)
Test-Retest

- Reproducibility of ADC measurements will be evaluated by performing “test-retest” DWI scans for a subset of 60 patients.

- Two DWI scans using identical scan protocols, prior to injection of contrast agent. Patients leave and return to the scan table between DWI scans.

- Test-retest scans will only be performed at one MRI visit. It is preferable for this to be performed at baseline; however, test-retest can be performed at the early treatment time point (MR visit 2) if unable to perform at MR 1.
<table>
<thead>
<tr>
<th>Site</th>
<th>Status</th>
<th>Accrual</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loyola University</td>
<td>Pending</td>
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<tr>
<td>University of Texas MD Anderson</td>
<td>Active</td>
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</tr>
<tr>
<td>Oregon Health &amp; Science University</td>
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<tr>
<td>Swedish Cancer Institute</td>
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<td>University of Alabama</td>
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<td>University of Southern California</td>
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<tr>
<td>University of Washington</td>
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</table>

Total 7
## I-SPY2 / 6698 Workflow

<table>
<thead>
<tr>
<th>Baseline Biomarker Collection</th>
<th>Early Treatment Biomarker Collection</th>
<th>Inter-regimen Biomarker Collection</th>
<th>Pre-surgical Biomarker Collection</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Screening</strong></td>
<td><strong>Paclitaxel</strong> <em>(12 weekly cycles)</em></td>
<td><strong>AC</strong> <em>(4 cycles)</em></td>
<td><strong>Surgery</strong></td>
</tr>
<tr>
<td><strong>Randomize</strong></td>
<td><strong>Paclitaxel</strong> + Investigational Drug A** <em>(12 weekly cycles)</em></td>
<td><strong>AC</strong> <em>(4 cycles)</em></td>
<td></td>
</tr>
<tr>
<td><strong>ON STUDY</strong></td>
<td><strong>Paclitaxel</strong> + Investigational Drug B** <em>(12 weekly cycles)</em></td>
<td><strong>AC</strong> <em>(4 cycles)</em></td>
<td></td>
</tr>
<tr>
<td><strong>Consent #2 Treatment Consent</strong></td>
<td><strong>MRI Blood Draw</strong></td>
<td><strong>MRI Blood Draw</strong></td>
<td><strong>Tissue</strong></td>
</tr>
</tbody>
</table>

*If you are Her2 positive you will also receive Trastuzumab.*

**An investigational drug may be used instead of Trastuzumab if you are Her2 positive.**

- ACRIN 6698 Repeat DW-MRI
- ACRIN 6698 Repeat DW-MRI *(if not performed at T1)*

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**ACRIN**

American College of Radiology Imaging Network
Workflow

Consent & Registration

- I-SPY2/6698 screening consent
- Register patient to I-SPY2 via TRANSCEND
  - I-SPY2 DCC will forward registration data to ACRIN
- I-SPY2 team to notify 6698 team (if different) of patient consent & registration
- 6698 DWI retest consent
  - with the screening consent or separately
  - before scheduling MR1 or at MR1 visit
MRI Time Points

Pre-Treatment
  MRI-1
  DWI-retest (if consented)

If patient is eligible/randomized to treatment...

Early Treatment
  MRI-2
  DWI-retest (if ≠ MR-1)

Inter-regimen
  MRI-3

Pre-surgery
  MRI-4
Thank You