Breast cancer subtype specific pCR with MRI assessed tumor volume progression during NAC in the I-SPY 2 TRIAL

**Methods**

- **I-SPY 2 TRIAL**
  - A multicenter, phase 2 trial using response-adaptive randomization within biomarker subtypes to evaluate novel agents as neoadjuvant therapy for high-risk breast cancer
- **Inclusion criteria:** Tumor Size ≥ 2.5 cm; hormone receptor (HR)+HER2-; patients with FTV increase + visual confirmation of progression
- **Primary Endpoint:** Pathologic complete response (pCR)
- **Goal:** To investigate (graduate) regimens that have ≥ 85% predictive probability of success in a 300-patient phase 3 neoadjuvant trial defined by HR and HER2 status, and MP
- **Regimens may leave the trial for one of four reasons:**
  - Futility (≤ 10% probability of success)
  - Maximum sample size accrual (with probability ≤ 10% and ≤ 40%)
  - Graduation (≥ 85% probability of success)
  - As recommended by the independent DSMB

To date: 11 experimental regimens have been evaluated for efficacy

**Background**

It is important to be able to identify patients who are progressing in an adaptive randomized trial as I-SPY 2 so their treatment can be changed to a different therapeutic regimen. MRI is an accurate and non-invasive imaging method to monitor treatment response.

**Purpose:** To study retrospectively the accuracy of identifying patients not achieving pCR using MRI assessed tumor volume at 3 different treatment time points by breast cancer subtype.

**Conclusions**

- Overall, very few MRI assessed progression found in the analysis cohort
- 100% of MRI assessed progression in HR+/HER2+ were non-pCRs
- over 90% of MRI assessed progression at T2 were non-pCRs

**Summary table**

<table>
<thead>
<tr>
<th>Analysis cohort</th>
<th>MRI assessed pCRs (%)</th>
<th>T2</th>
<th>T3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full cohort</td>
<td>909/660 (13%)</td>
<td>43 (40)</td>
<td>5 (100)</td>
</tr>
<tr>
<td>HR+/HER2+</td>
<td>380/316 (119%)</td>
<td>53 (48)</td>
<td>14 (133)</td>
</tr>
<tr>
<td>HR-</td>
<td>156/98 (63%)</td>
<td>7 (7)</td>
<td>1 (100)</td>
</tr>
<tr>
<td>HER2+</td>
<td>89</td>
<td>33 (33%)</td>
<td>2 (100)</td>
</tr>
<tr>
<td>HER2-</td>
<td>363/217 (100%)</td>
<td>26 (24)</td>
<td>3 (300)</td>
</tr>
</tbody>
</table>

**MRI assessed progression**

- **MRI assessed progression = FTV increase + visual confirmation

**Figure 1**

- Functional tumor volume (FTV)
- Patients with any amount of FTV increase at early treatment (after 3 weeks, T1, inter-regime (T2), and pre-surgery (T3) and visual confirmation to eliminate the possibilities of false progressions due to strong BPE, enhanced vessels, motion, or insufficient image quality

**Figure 2**

- Distribution of progression by subanalysis

**Figure 3**

- T1 may be too early for triple negative disease
- MRI assessed progression identifies non-responders more accurately at later treatment points

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The University of Chicago Medical Center, Department of Biostatistics and Bioinformatics: Sincere thanks to our DSMB, Independent Agent Selection Committee, our patients, advocates and investigators.