MRI models by response predictive subtype for predicting pathologic complete response

**BACKGROUND**

- MRI predictive modeling is a key component of the pre-RCB (Predicted Residual Cancer Burden) clinical workflow for re-directing ‘excellent responders’ to skip AC (anthracycline) and proceed to surgery early in I-SPY 2 TRIAL.
- Drug allocation by the new response-predictive subtype (RPS) could lead to a higher pathologic complete response (pCR) rate than allocation based on HR+HER2 subtype. The purpose of this study is to optimize MRI prediction model based on RPS.

**METHODS – MRI models by subtype**

Subtype-specific MRI prediction models were performed by:
- **Receptor subtype** - defined by HR+HER2 status
- **RPS** - defined by immune, DNA repair deficiency (DRD), HER2, Blueprint (Agenda)

Sankey diagram of receptor subtype and RPS

**RESULTS – MRI models by subtype**

<table>
<thead>
<tr>
<th>Subtype</th>
<th>N</th>
<th>pCR rate</th>
<th>AUC</th>
<th>FTV predictions improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full</td>
<td>854</td>
<td>30.1 (15%)</td>
<td>0.71</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td>HR+HER2</td>
<td>338</td>
<td>65 (10%)</td>
<td>0.71</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td>HR+ER2+</td>
<td>141</td>
<td>58 (39%)</td>
<td>0.68</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td>HR-HER2+</td>
<td>74</td>
<td>49 (66%)</td>
<td>0.73</td>
<td>✓ ✓ ✓</td>
</tr>
<tr>
<td>Triple negative</td>
<td>303</td>
<td>133 (44%)</td>
<td>0.74</td>
<td>✓ ✓ ✓</td>
</tr>
</tbody>
</table>

**Distribution of RPS within receptor subtypes**

- **HR+HER2**: n=336
  - 53% HER2/Immune-DRD
  - 39% HER2/Immune+DRD
  - 9% HER2/Immune+DRD
- **HR-HER2+**: n=431
  - 62% HER2+/B+HER2_or_Basal
  - 38% HER2+/B-Luminal
- **HR-HER2-**: n=74
  - 67% HER2-HPHER2_or_Basal
  - 3% HER2+/B-Luminal
- **Triple negative**: n=303
  - 63% HER2-/B+/HER2_or_Basal
  - 25% HER2-/Immune-DRD
  - 12% HER2-/Immune+DRD

**Statistical analysis**

1. Logistic regression model of predicting pCR
2. Best models were chosen by achieving the highest AUC
3. Models were optimized using data from the full cohort of 854 patients or within subtype-defined cohort

**RESULTS – Individually patient prediction**

Scatter plot of individual patient’s predicted probability of pCR by HR+HER2 versus by RPS

**CONCLUSIONS**

- Wider range of performances were observed when MRI models were optimized by RPS compared to models optimized by receptor subtype
- Improved predictive performance was observed using RPS-specified MRI model in HR+ breast cancer
- RPS-specific MRI models will be implemented in treatment re-direction algorithms in the ongoing I-SPY 2.2 TRIAL

**Advocate statement**

Predicting patients’ probability of pCR by RPS can improve the effectiveness of MRI in measuring treatment response. Early prediction of responders will increase treatment optimization by giving responders the option of omitting AC chemotherapy and going to direct surgery after their first treatment regimen avoiding the side and late effects of AC and likely improving their quality of life.

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