Pembrolizumab Plus Standard Neoadjuvant Therapy for High-Risk Breast Cancer: Results From the I-SPY 2 Trial

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BACKGROUND

• Tumors can co-opt the PD-1 pathway to evade immune surveillance

• Pembrolizumab is a humanized monoclonal antibody against PD-1
  - Modest single-agent activity seen in heavily pretreated breast cancer

• Safety of pembrolizumab plus paclitaxel available prior to inclusion
  - KEYNOTE 021 trial in advanced NSCLC

• The I-SPY 2 Trial tested the ability of pembrolizumab to improve pathologic complete response (pCR) rates over standard therapy

STUDY METHODS AND PATIENTS

Primary endpoint: pCR (ypT0/is and ypN0)

"Graduation" for efficacy requires an 85% predicted possibility of success in a 1:1 randomized 300-patient phase III trial.

RESULTS

Pembrolizumab graduated in all HER2- signatures: Both HR+/HER2- and triple negative.

Table 1. Results

<table>
<thead>
<tr>
<th>Signature</th>
<th>Estimated pCR Rate (%: 90% Probability Interval)</th>
<th>Probability Pembrolizumab to Superior to Control</th>
<th>Predictive Probability of Success in Phase III</th>
</tr>
</thead>
<tbody>
<tr>
<td>All HER2-</td>
<td>0.46 (0.34-0.58)</td>
<td>0.16 (0.06-0.27)</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>TNBC</td>
<td>0.60 (0.43-0.78)</td>
<td>0.20 (0.06-0.33)</td>
<td>&gt;99%</td>
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<tr>
<td>HR+/HER2-</td>
<td>0.34 (0.20-0.53)</td>
<td>0.13 (0.03-0.24)</td>
<td>&gt;99%</td>
</tr>
</tbody>
</table>

The Bayesian model estimated pCR rates appropriately adjusted to characteristics of the I-SPY 2 population. The raw pCR rates (not shown) are higher than the model estimates of 0.604 in triple-negative breast cancer.

Table 2. Select Treatment-Related Adverse Events

Table 3. Adverse Events of Special Interest

- Pembrolizumab x 4 cycles plus paclitaxel has graduated for all HER2-signatures studied
  - Tripling of the estimated pCR rate in triple-negative breast cancer (60% vs 20%)
  - Near tripling of the estimated pCR rate in HR+/HER2- (34% vs 13%)
  - First agent to graduate in HR+/HER2- signature

- Adrenal insufficiency was observed at a higher rate than previously reported in advanced cancer

CONCLUSIONS

REFERENCES