**Background**

- Ductal carcinoma in situ (DCIS) of the breast is a pre-malignant condition that represents a heterogeneous collection of lesions.
- Characteristics of DCIS that have been associated with a high risk of progression and recurrence include: large size, high grade with comedo necrosis, Her2 positivity, and hormone receptor negativity.
- The biology of high risk DCIS shows a high proportion of macrophages and suppressed T cells.
- Re-educating the tumor immune micro-environment could be a potential treatment for high risk DCIS.

**Objectives**

**Primary objectives of the dose escalation cohort:**
- Determine the maximum tolerated dose
- Define the dose limiting toxicities, tolerability, and feasibility of intralesionally administered pembrolizumab

**Primary objectives of the dose expansion cohort:**
- Determine the response rate to intralesional pembrolizumab as measured by an increase in intralesional CD8+ T cells from baseline to post treatment compared to the control group

**Exploratory objectives:**
- Characterize changes in the immune microenvironment of DCIS
- Determine whether changes are seen in tumor volume on MRI imaging following intralesional pembrolizumab

**Trial Design**

**Agent:** Pembrolizumab

**Administration:** Intralesional injection directly into tumor

**How often:** Two doses, three weeks apart

### Dose Escalation Cohort

3+3 dose escalation cohort design: 3 subjects will be enrolled into each cohort unless a dose limiting toxicity is observed.

**Dose Expansion Cohort**

Dose determined by the maximum tolerated dose in dose escalation cohort. 30 subjects randomized to the control group (10 patients) or the treatment group (20 patients)

**Pembrolizumab**

Pembrolizumab is a humanized monoclonal antibody that blocks the interaction between programmed death 1 (PD-1) and its ligands programmed death ligands 1 and 2 (PD-L1 and PD-L2), a pathway used by tumors to suppress immune control.

**Main Eligibility Criteria**

Patient has at least 2 of the following high risk features associated with her DCIS:
- High-grade
- Palpable mass
- Hormone receptor negative (less than 1%)
- Her2 positive
- Young age (less than 45 years old)
- Large size (greater than 5 cm)

**Accrual Goals and Status**

We plan to accrue 18-48 patients.

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Dose Received</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose Escalation - 1</td>
<td>2 mg</td>
<td>3-6</td>
</tr>
<tr>
<td>Dose Escalation - 2</td>
<td>4 mg</td>
<td>3-6</td>
</tr>
<tr>
<td>Dose Escalation - 3</td>
<td>8 mg</td>
<td>3-6</td>
</tr>
<tr>
<td>Dose Expansion - Treatment</td>
<td>Maximum tolerated dose</td>
<td>20</td>
</tr>
<tr>
<td>Dose Expansion - Control</td>
<td>No treatment</td>
<td>10</td>
</tr>
</tbody>
</table>

One patient has been enrolled into the 2 mg dose escalation cohort. The patient has received the two injections and is awaiting surgery.