NOVEL NEOADJUVANT DENDRITIC CELL VACCINE IN EARLY HER-2+ BREAST CANCER

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HER-2/neu Peptide Pulsed DC1 Vaccine for DCIS

**INNATE**

- CD86
- CD80
- CD83
- CD40

**ADAPTIVE**

- Pre-vaccination
- Post-vaccination

**DCIS**

- Pre-Vaccine HER-2/neu
- Post-Vaccine HER-2/neu
- Post-Vaccine CD45RO
Safety of DC1 Vaccines

- Grade I, II - fevers, chills, headache, fatigue, injection site soreness

- Cardiac 5/57 patients Asymptomatic declines in MUGA 10-20% within normal range all resolved on repeat 30 days

- No long term sequela patients out range 6 months – 84 months
HER2/neu pulsed-ICAIT DC1 activate anti-HER2/neu CD8 T cells in DCIS patients
Optimal induction of anti-tumor effector CD8+ T Cell responses requires multiple vaccinations

Optimal induction of anti-tumor effector CD8+ T Cell responses requires multiple vaccinations.
Induction of CD4 T cell anti-HER2 responses after ICAIT DC1 vaccination in DCIS patients
Induction of Complement fixing anti-HER2/neu ABs post-vaccine: Direct antibody-mediated tumor cell killing

% Cytotoxicity

HER2+ control
HER2+ control
Trastuzumab

DCIS
Ab coating

Pre-Vaccine
Post-Vaccine
Immune Response in the DCIS to DC1 Vaccination

Post-Vaccine Lymphocytes

Pre-Vaccine

Post-Vaccine

Post-Vaccine Lymphocytes
Lymphocyte Infiltration Within Residual DCIS Ducts Following Vaccination
Trafficking of Lymphocytes into breast post-vaccination of DCIS patients

CD4 T cells  CD8 T cells  CD20 B cells

Pre  Post
### Response to Vaccines

**Percent of cells staining HER-2/neu 2+ to 3+ Pre- and Post-vaccination**

Patients sorted by Phenotype and Pre-vaccination HER-2/neu expression

<table>
<thead>
<tr>
<th>% Pre-vaccine</th>
<th>% Post-vaccine</th>
<th>Percent Change</th>
<th>% Pre-vaccine</th>
<th>% Post-vaccine</th>
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<tbody>
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<td>ERpos HER-2/neu</td>
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<tr>
<td>ERneg HER-2/neu</td>
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<tr>
<td>100</td>
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</tbody>
</table>

*patient scored as HER-2/neu neg
**Induction of long-term anti-tumor immunity**

Robust anti-HER2 responses more than 4 yrs post vaccination

![Graph showing CD4 T cells IFN-γ](image)
Comparison of Absence of Disease Post DC1 Vaccine with Disease Free Recurrence
NSABP-B24: Outcomes of women with ER- DCIS

Allred, JCO, 2012

Department of Surgery, University of Pennsylvania Health System
Summary

- ICAIT DC1 Vaccines Induce Long Lasting Th1 CD4 and CD8 T cell responses
- They Induce Lymphocyte Migration into DCIS Ducts
- Induce Elimination of HER-2 Expressing DCIS
- Can Prevent Recurrence Of HER-2 Phenotype
- Suggest Vaccination Against Breast Cancer can be Effective if Targets are Right
- Caution that Multiple targets will be needed in true primary breast cancer prevention
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- Sara Matthews

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HER Family

Koutras et al. Onco Targets and Therapy 2008; 1: 5-19
HER Family Pre and Post-Vaccination