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Prevention of estrogen-independent breast cancer using her family targeted dendritic cell vaccines

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Introduction: HER-2/neu over-expression in breast cancer is associated with high risk of recurrence and poorer outcomes. HER-2/neu expression has been identified in breast cancer stem cells. Elimination of HER-2/neu-expressing cells may therefore improve breast cancer outcomes.

Methods: Twenty-seven patients with HER-2/neu over-expressing ductal carcinoma in situ (DCIS) were enrolled in a phase I neoadjuvant trial to determine whether HER-2/neu peptide-pulsed DC vaccines were safe and could eliminate HER-2/neu over-expressing cells. Pre- and post- vaccination immune monitoring and histopathological analysis were conducted to assess results.

Results: Post-immunization, anti-HER-2/neu $CD4^{pos}$ and $CD8^{pos}$ T cells were identified in >88% of subjects, with evidence of durable (>2 yr) responses and inter-molecular epitope spreading. Five of 27 (18.5%) vaccinated subjects had no evidence of remaining disease. Detectable HER-2/neu was eliminated (i.e. immunoedited) in 11 of 22 (50%) patients with residual DCIS. Comparing the 10 ERneg with the17 ER^{pos} subjects we observed: no residual DCIS in 40% vs. 5.9% of patients, and sustained HER-2/neu expression in 10% vs. 47.1%, suggesting vaccination was more effective against hormone-independent DCIS (p=0.04). Post-vaccination DCIS phenotypes also differed significantly between ERpos and ER^{neg} subjects (p=0.01). Seven of 16 patients (43.8%) initially presenting with the more aggressive ER^{pos} HER-2/neu^{pos} phenotype demonstrated ER^{pos} HER-2/neu^{neg} phenotype after vaccination, while 3 of 6 (50%) starting with ER^{neg} HER-2/neu^{pos} DCIS became ER^{neg} HER-2/neu^{neg}.

Conclusions: This targeted immunoediting approach appeared effective for reducing HER-2/neu-expressing cells in DCIS, suggesting that targeting HER-2/neu and other stem cell-associated molecules should be explored for preventing primary and recurrent breast cancer.