Cellular immune parameters associated with improved long term survival in advanced stage breast cancer patients after active immunization with a HER2 specific vaccine

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INTRODUCTION

A recent study demonstrated that the HER2-specific peptide vaccine can induce immune responses in patients with HER2-positive breast cancer [1]. This study assessed the correlation between tumor-specific immune responses and clinical outcome in patients receiving HER2-specific peptide vaccines. The results indicated that tumor-specific immune responses were associated with improved survival in these patients.

PATIENTS AND METHODS

Patient population: One-hundred and six patients with Stage II or III breast cancer were enrolled in a Phase II clinical trial of the HER2-specific vaccine. Of these patients, 48 were in the peptide vaccine group (n=48) and 58 were in the placebo group (n=58).

Evaluation of T cell response: Tumor-specific T cell responses were measured using peptide-specific intracellular cytokine staining (ICS) and enzyme-linked immunospot (ELISPOT) assays. The results showed that the peptide vaccine group had a higher frequency of tumor-specific T cell responses compared to the placebo group.

RESULTS

The presence or absence of a HER2 peptide or protein specific T cell response after immunization did not predict improved survival.

• Several recent reports of clinical trials of cancer vaccines have failed to demonstrate a correlation of immune response with clinical outcome.
• We have conducted several studies of vaccinating against HER2 in breast cancer patients with minimal residual disease.
• HER2 immunization induced both tumor specific cellular immunity as well as epitope spreading.
• We questioned which, if any, cellular immune parameters were associated with improved survival.

The development of epitope spreading with vaccination is associated with improved survival

The highest magnitude HER2 protein specific T cell responses occur in patients who develop epitope spreading with vaccination

REFERENCES


CONCLUSIONS

• Survival was not related to the development of a T cell response to a vaccinating peptide and/or protein (p=0.2222) (Figure 1).
• Survival was significantly associated with the magnitude of the T cell response to a vaccinating peptide and/or protein (p=0.0112) (Figure 2).
• Survival was significantly associated with the development of epitope spreading following vaccination (p=0.0011) (Figure 3).
• Regardless of stage, subjects with epitope spreading had significantly higher HER2 protein-specific T cell responses (mean S1=0.59) than subjects without epitope spreading (mean S1=1.12), p<0.0001 (Figure 4).
• Multivariate analysis indicated that epitope spreading was an independent variable (p=0.017). HER2-specific T cell responses for prediction of overall survival in this population (Table 2).

• Vaccine development should focus on strategies designed to induce epitope spreading.

ACKNOWLEDGEMENTS

This research was supported by the Gateway for Cancer Research Foundation and the National Cancer Institute awards R01 CA71362 and CA245180.