American Association for Cancer Research®, April 8-13, 2022

GP2 immune response a predictor of recurrence in a phase IIb study evaluating HER2/neu peptide GP2 (GLSI-100) vs. GM-CSF alone after adjuvant trastuzumab in HER2 positive women with breast cancer

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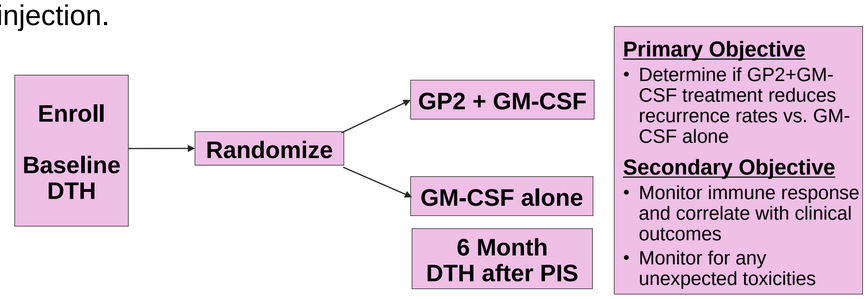
BACKGROUND

The results of a prospective, randomized, placebo-controlled, single-blinded, multicenter Phase IIb trial investigating GLSI-100 (GP2+GM-CSF) administered in the extended-adjuvant setting to node-positive and high-risk node-negative breast cancer patients with tumors expressing any degree of HER2 (immuno-histochemistry [IHC] 1-3+) (NCT00524277) have been reported. The trial enrolled HLA-A*02 patients randomized to receive GLSI-100 versus GM-CSF alone. It was previously reported that completion of the GLSI-100 Primary Immunization Series (PIS) reduced recurrence rates to 0% over a 5 year follow-up period in HER2 3+ (positive) patients, who received a standard course of trastuzumab after surgery. Interim analyses for this trial have been previously reported by Mittendorf et al.

METHODS

Enrolled and consented patients were randomly scheduled to receive a total of 6 GLSI-100 (500 mcg GP2: 125 mcg GM-CSF) or GM-CSF only intradermal injections every 3-4 weeks as part of the PIS for the first 6 months and 4 GLSI-100 or GM-CSF only booster intradermal injections every 6 months thereafter. Injection site reactions (ISR) were measured 48-72 hours after injection. Delayed-type hypersensitivity (DTH) to GP2 was measured at baseline and after 6 months of treatment. For the DTH test, 0.5 mL consisting of 100 mcg of GP2 reconstituted in bacteriostatic saline for injection was placed intradermally. The site of reaction was measured 48-72 hours after injection.



ACKNOWLEDGEMENTS

The authors have an ownership interest in Greenwich LifeSciences.

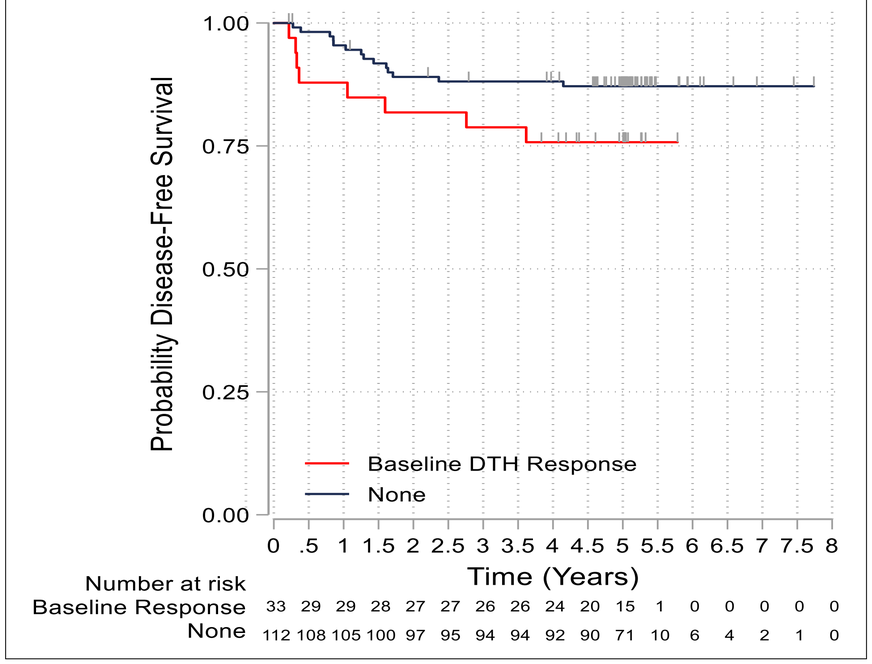
RESULTS

The study enrolled 180 patients with both HER2 3+ positive and low HER2 expressors (1-2+). After 5 years of follow-up, the Kaplan-Meier estimated 5-year DFS rate in the 46 HER2 3+ (positive) patients treated with GLSI-100, if the patients were treated, followed, and remained disease free over the first six months of treatment, was 100% versus 89.4% (95% CI:76.2, 95.5%) in the 50 placebo patients treated with GM-CSF (p = 0.0338).

A DTH reaction was used to assess in vivo immune responses in patients (n=150) prior to exposure to study medication and after 6 months of the first dose. The DTH orthogonal mean was measured 48-72 hours after injection using the sensitive ballpoint-pen method.

Previous publications have reported the increase in GP2 DTH response reported among patients after treatment with GLSI-100.

Figure 1: Disease Free Survival – Positive GP2 DTH Immune Response at Baseline versus No Response at Baseline



RESULTS (Continued)

Positive DTH immune responses to GP2 at baseline was defined as orthogonal mean induration larger than 5mm. It was previously reported that 22.8% (33/145) of patients reacted to GP2 at baseline and that in the subgroup of subjects with recurrence, 36.4% (8/22) had a positive baseline DTH.

Further analysis shows that a baseline DTH response may be predictive of disease-free survival. The Kaplan-Meier log-rank test depicted in Figure 1, in a pooled population of HER2 positive and HER2 low patients, shows a borderline effect (p = 0.0956) of baseline DTH response on disease-free survival. At year 4, 88% of all patients without a positive baseline GP2 DTH remained disease-free. The patients with a positive baseline GP2 DTH recurred 3.5 years earlier reaching a similar survival probability of 88% at 6 months.

In addition, the proportion of subjects recurring at any time was 24.2% (8/33) amongst those with a positive baseline GP2 DTH response versus 12.5% (14/112) amongst those with a negative baseline GP2 DTH response (p = 0.0984), suggesting that a positive baseline GP2 DTH may be associated with recurrence.

DISCUSSION AND CONCLUSIONS

The probability of recurrence is increased and recurrence is likely to occur years sooner in subjects with a positive GP2 DTH immune response at baseline versus those subjects without a positive GP2 DTH immune response at baseline.

Further studies assessing the prognostic value of GP2 immune response at baseline are planned. These studies may include additional measures of GP2 immune response by DTH as well as sequencing and identification of T cell profiles associated with residual disease, impending recurrence, or prior treatments.