San Antonio Breast Cancer Symposium, December 7-10, 2021

For Audio Recording, Please Visit: https://greenwichlifesciences.com/clinical-trials/

Greenwich LifeSciences

Analysis of GP2 immune response and relationship to recurrence in a prospective, randomized, placebo-controlled, single-blinded, multicenter, phase IIb study evaluating the use of HER2/neu peptide GP2+GM-CSF (GLSI-100) vs. GM-CSF alone after adjuvant trastuzumab operable in HER2 positive women with breast cancer

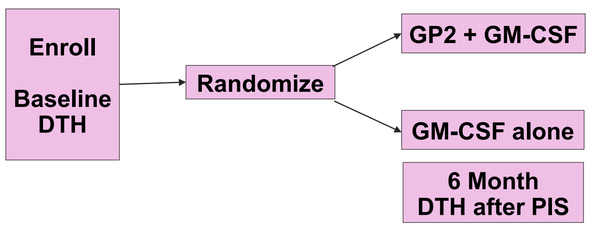
Snehal S Patel, David B McWilliams, Christine T Fischette, Jaye Thompson, Mira Patel, F Joseph Daugherty.
Greenwich LifeSciences, Stafford, TX

BACKGROUND

The results of a prospective, randomized, placebo-controlled, single-blinded, multicenter Phase IIb trial investigating GP2+GM-CSF (GLSI-100) 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+ patients, who received a standard course of trastuzumab after surgery. Interim analyses for this trial have been previously reported by Mittendorf et al.

METHODS

Each enrolled and consented patient was 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. Delayed-type hypersensitivity to GP2 was performed at baseline and after 6 months of treatment. In this test 0.5 ml consisting of 100 mcg of GP2 reconstituted in bacteriostatic saline for injection in 0.5ml is placed intradermally. The site of reaction is measured after 48 to 72 hours.



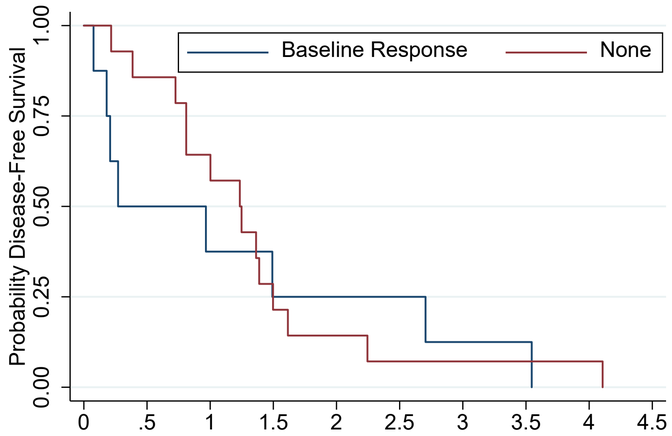
Primary Objective
- Determine if GP2+GM-CSF treatment reduces recurrence rates vs. GM-CSF alone

Secondary Objective
- Monitor immune response and correlate with clinical outcomes
- Monitor for any unexpected toxicities

RESULTS

This trial explored HER2 3+ positive patients, who received a standard course of trastuzumab after surgery, and HER2 1-2+ patients, who did not receive trastuzumab after surgery. 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 presentations have reported an increase in DTH reactions after the PIS compared to baseline DTH reactions. In addition, the DTH reactions after the PIS were significantly greater in GLSI-100 treated patients than in control patients (10.8 mm vs. 0.0 mm, p = 0.009).

Figure 1: Time to Recurrence by Baseline DTH Response in Subgroup of Patients Experiencing Breast Cancer Recurrence



Number at Risk

Baseline Response	8	4	3	2	2	2	1	1	0	0
None	14	12	9	3	2	1	1	1	1	0

Median Time to Recurrence

Baseline DTH Response	0.27 years
None: No Baseline DTH Response	1.2 years
	p = 0.7140

It was noted that some patients reported significant DTH responses at baseline, prior to exposure to GP2. It was found that 22.8% of patients reacted to GP2 at baseline with induration of 5 mm of greater in the baseline DTH test. A positive response is defined as a site measurement of 5 mm of larger.

A Kaplan-Meier analysis in the subgroup of patients who experienced a recurrence of breast cancer over the course of the study investigates time to recurrence by baseline DTH response (positive = Baseline Response / negative = None). Although the survival curves become quite similar after 1.5 years, which makes the two curves statistically the same, p = 0.7140, the early effect of baseline response to GP2 assessed by DTH creates an obvious effect on early recurrence. The median time to recurrence of those with a baseline DTH response is 99 days (0.27 years) while those with no baseline DTH took 438 days (1.2 years) to recur by life table analysis techniques. These summary statistics by standard methods are 0.6 years for those with a baseline response and 1.2 years for those with none.

Note, these analysis are conducted independent of the treatment group assigned as the interest was how baseline DTH results might predict early recurrence.

Tables 1: Data Listing of Baseline and 6 Month DTH in Patients Experiencing Breast Cancer Recurrence

Patient	Treatment	Node Status	T Stage	Tumor Size (cm)	HER2 Status	Time to Recurrence (days)	Baseline DTH (mm)	6 Month DTH (mm)
PG66V66	GP2	N1a	T1	2.0	1	76	43	
AG45V45	Placebo	N3	T2	2.1	2	353	29	44
PG23V23	GP2	N1a	T3	5.0	1	1295	13	25
AG8V8	Placebo	N0	T1a	1.3	2	988	10	30
AG1V1	Placebo	N2a	T1a	1.4	2	545	9	34
BR-02	GP2	N3a	T2	2.5	3	28	9	
PG47V47	GP2	N1a	T1	0.7	2	99	8	
PG25V25	GP2	N1a	ypT0	0.0	3	66	7	
PG4V4	GP2	i+	T2	2.3	1	820	0	24
PG2V2	GP2	N0	T2	4.5	1	265	0	20
PG9V9	GP2	N1a	T4	1.5	1	498	0	16
BR-103	GP2	N3a	T1	2.0	2	507	0	15
AG26V26	Placebo	N2a	T2	2.4	2	1500	0	6
BR-119	Placebo	N1a	T1	0.9	3	451	0	6
BR-109	GP2	N3a	T3	5.5	1	366	0	3
AG28V28	Placebo	N0	T2	2.2	1	456	0	0
AG39V39	Placebo	N2a	T3	9.0	1	296	0	0
AG3V3	Placebo	N0	T2	2.3	1	296	0	0
PG42V42	GP2	N0	T2	2.2	2	590	0	0
BR-129	GP2	N2a	T3	5.3	1	141	0	
BR-45	Placebo	Nx	T1b	0.8	3	547	0	
PG53V53	GP2	N0	T2	4.6	1	79	0	
AG10V10	Placebo	N3c	T4	5.0	3	326		0

The table above lists the raw data for the subjects who recurred over the course of follow-up and their baseline and 6 month DTH assessments.

DISCUSSION AND CONCLUSIONS

This data suggests that a baseline immune response to GP2 through a positive response to a DTH skin test could suggest that the patient is at higher risk of imminent recurrence. It is theorized that a positive baseline DTH skin test to GP2 may be evidence of an existing immune response to GP2 associated with residual disease, impending recurrence, or prior treatments.

Further studies assessing if GP2 immune response is an important prognosticator of cancer disease state or recurrence are planned.

ACKNOWLEDGEMENTS

The authors have an ownership interest in Greenwich LifeSciences.