San Antonio Breast Cancer Symposium® December 8-11, 2020

Greenwich LifeSciences

Five year median follow-up data from a prospective, randomized, placebo-controlled, single-blinded, multicenter, phase IIb study evaluating the reduction of recurrences using HER2/neu peptide GP2 + GM-CSF vs. GM-CSF alone after adjuvant trastuzumab in HER2 positive women with operable breast cancer

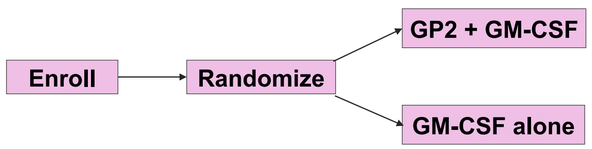
Snehal S Patel, David B McWilliams, Marisa S Patel, Christine T Fischette, Jaye Thompson and F Joseph Daugherty.
Greenwich LifeSciences, Stafford, TX

BACKGROUND

The final analysis of the GP2 prospective, randomized, placebo-controlled, single-blinded, multicenter Phase IIb trial investigating GP2+GM-CSF administered in the 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*) is now complete with 5 year follow-up. The trial enrolled HLA-A02 patients randomized to receive GP2+GM-CSF versus GM-CSF alone. The trial's primary objective was to determine if treatment with GP2, a HER2-derived peptide, reduces recurrence rates. Three and 4 year interim analyses for this trial and 3 Phase I studies showing GP2 to be safe and immunogenic have been previously reported by Mittendorf et al.

METHODS

Each enrolled and consented subject was randomized and scheduled to receive a total of 6 GP2+GM-CSF (500 mcg GP2:125 mcg GM-CSF) or placebo (125 mcg GM-CSF alone) intradermal injections every 3-4 weeks as part of the Primary Immunization Series (PIS) for the first 6 months and 4 GP2+GM-CSF booster or placebo intradermal injections every 6 months thereafter. Boosters were introduced during the trial, thus some patients did not receive all 4 boosters.



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

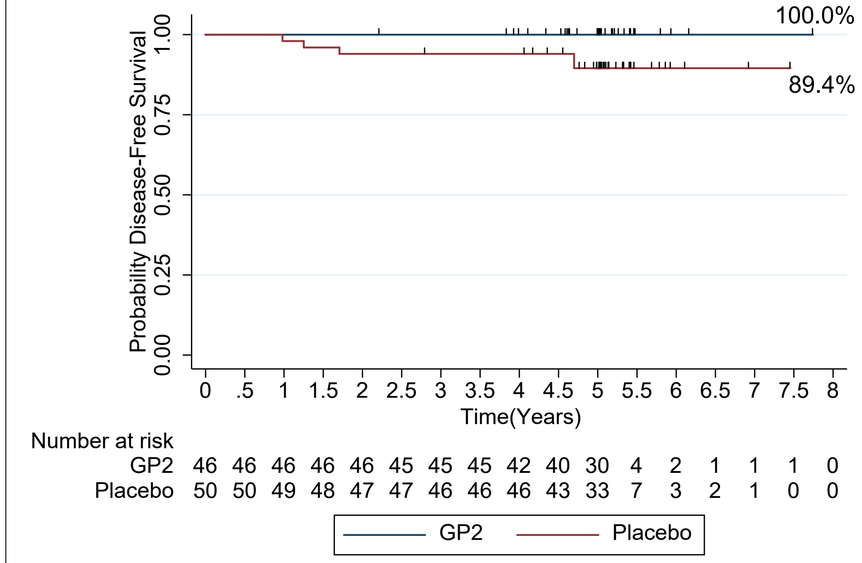
RESULTS

This 168 patient (ITT: n=180) basket trial across 16 clinical sites explored 96 HER2 3+ patients, who received a standard course of trastuzumab after surgery and subsequently completed the full PIS or placebo, starting the PIS at median 17.1 months after surgery, and 72 HER2 1-2+ patients, who did not receive trastuzumab after surgery and subsequently completed the full PIS or placebo, starting the PIS at median 10.8 months after surgery. Subject disease characteristics are described in Table 1.

Since GP2 is synergistic with trastuzumab, and the HER2 1-2+ patients did not receive trastuzumab, it was prespecified to compare recurrence rates ITT versus per protocol in these 2 distinct, independently reported populations, excluding those patients who did not complete the PIS. Figure 1 depicts evidence that DFS is more likely in HER2 3+ GP2-treated subjects (p = 0.0338). Figure 2 provides DFS for the HER2 1-2+ group.

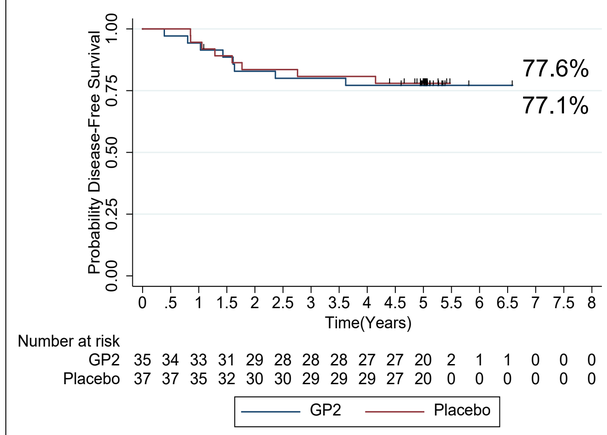
GP2 was shown to be well tolerated with no SAEs and elicited a potent immune response measured by local skin tests and immunological assays, which suggest peak immunity is reached at 6 months upon completion of the PIS.

Figure 1: HER2 3+ Subjects Who Completed PIS Following Trastuzumab



After 5 years of follow-up, the Kaplan-Meier estimated 5-year DFS rate in the 46 HER2 3+ patients treated with GP2+GM-CSF, if the patient completed the PIS, was 100% versus 89.4% (95% CI:76.2, 95.5%) in the 50 placebo patients treated with GM-CSF (*p = 0.0338*). As shown in Table 1, the treated versus placebo HER2 3+ patients were well-matched, where approximately 53% were stage T1, 41% were stages T2-T4, 55% were node positive, 58% were HR positive and received endocrine therapy, 77% received adjuvant radiation, 77% received adjuvant chemotherapy, and 89% received trastuzumab.

Figure 2: HER2 1-2+ Subjects Who Completed PIS without Trastuzumab



After 5 years of follow-up, the Kaplan-Meier estimated 5-year DFS rate in the 35 HER2 1-2+ patients treated with GP2+GM-CSF, if the patient completed the PIS, was 77.1% (95% CI:59.5, 87.9%) versus 77.6% (95% CI:60.1, 88.2%) in the 37 placebo patients treated with GM-CSF (*p = 0.9142*).

Table 1: Clinicopathologic Characteristics by Treatment Group for HER2 3+ and HER2 1-2+ Subjects Who Completed the PIS

	HER2 3+			HER2 1-2+		
Characteristic	**GP2 (n = 46)**	**Placebo (n = 50)**	***p* value[1]**	**GP2 (n = 35)**	**Placebo (n = 37)**	***p* value[1]**
Age (median, [min, max])	50.5 (26.9-72.3)	52.1 (33.7-72.1)	*0.4011*	50.8 (36.7-76.7)	49.9 (26.3-69.2)	*0.8146*
T Stage						
T0/is	2 (4.4%)	1 (2.0%)		0 (0.0%)	0 (0.0%)	
T1	23 (50.0%)	28 (56.0%)		14 (40.0%)	11 (29.7%)	
T2	17 (37.0%)	14 (28.0%)	*0.874*	14 (40.0%)	17 (46.0%)	*0.654*
T3	1 (2.2%)	2 (4.0%)		5 (14.3%)	8 (21.6%)	
T4	2 (4.4%)	3 (6.0%)		2 (5.7%)	1 (2.7%)	
Other	1 (2.2%)	2 (4.0%)		0 (0.0%)	0 (0.0%)	
Node Status						
Negative	22 (47.8%)	20 (40.0%)	*0.496*	12 (34.3%)	11 (29.7%)	*0.679*
Positive	24 (52.2%)	29 (58.0%)		23 (65.7%)	26 (70.3%)	
Not done	0 (0.0%)	1 (2.0%)		0 (0.0%)	0 (0.0%)	
Histology						
Ductal	44 (95.7%)	48 (96.0%)	*0.996*	33 (94.3%)	32 (86.5%)	*0.415*
Lobular	1 (2.2%)	1 (2.0%)		1 (2.9%)	1 (2.7%)	
Other	1 (2.2%)	1 (2.0%)		1 (2.9%)	4 (10.8%)	
Grade						
Moderate	15 (32.6%)	16 (32.0%)	*0.795*	16 (45.7%)	13 (35.1%)	*0.143*
Poorly Differentiated	29 (63.0%)	33 (66.0%)		17 (48.6%)	16 (43.2%)	
Well Differentiated	2 (4.4%)	1 (2.0%)		2 (5.7%)	8 (21.6%)	
ER/PR Status						
Negative	18 (39.1%)	22 (44.0%)	*0.629*	12 (34.3%)	8 (21.6%)	*0.230*
Positive	28 (60.9%)	28 (56.0%)		23 (65.7%)	29 (78.4%)	
Surgery						
Lumpectomy	21 (45.7%)	20 (40.0%)	*0.362*	13 (37.1%)	12 (32.4%)	*0.675*
Mastectomy	25 (54.4%)	28 (56.0%)		22 (62.9%)	25 (67.6%)	
Other	0 (0.0%)	2 (4.0%)		0 (0.0%)	0 (0.0%)	
Radiation						
Adjuvant	34 (73.9%)	40 (80.0%)	*0.478*	26 (74.3%)	31 (83.8%)	*0.434*
Neoadjuvant	0 (0.0%)	0 (0.0%)		1 (2.9%)	0 (0.0%)	
None	12 (26.1%)	10 (20.0%)		8 (22.9%)	6 (16.2%)	
Chemotherapy						
Adjuvant	37 (80.4%)	37 (74.0%)		25 (71.4%)	26 (70.3%)	
Neoadjuvant	6 (13.0%)	7 (14.0%)	*0.753*	6 (17.1%)	8 (21.6%)	*0.123*
Both	1 (2.2%)	1 (2.0%)		0 (0.0%)	1 (2.7%)	
None	2 (4.4%)	5 (10.0%)		4 (11.4%)	0 (0.0%)	
Not Specified	0 (0.0%)	0 (0.0%)		0 (0.0%)	2 (5.4%)	
Endocrine Therapy						
None	17 (37.0%)	21 (42.0%)	*0.614*	12 (34.3%)	11 (29.7%)	*0.679*
Yes	29 (63.0%)	29 (58.0%)		23 (65.7%)	26 (70.3%)	
Trastuzumab Use						
None	3 (6.5%)	7 (14.0%)	*0.294*	35 (100.0%)	35 (94.6%)	*0.163*
Yes	43 (93.5%)	42 (84.0%)		0 (0.0%)	2 (5.4%)	
Unknown	0 (0.0%)	1 (2.0%)		0 (0.0%)	0 (0.0%)	

[1] Continuous variables difference between treatment groups assessed by t-test. Categorical variables difference between treatment group distribution assessed by chi-square test.

CONCLUSIONS

This study demonstrated that completion of the GP2+GM-CSF PIS safely elicited a potent immune response and reduced recurrence rates to 0% in HER2 3+ patients, who received a standard course of trastuzumab after surgery. A pivotal Phase III trial is being initiated to treat HER2 3+ patients in the neoadjuvant setting. GP2 also may be effective when used in parallel to trastuzumab based therapeutics or in combination with trastuzumab based therapeutics in HER2 1-2+ or other HER2 expressing cancers.

ACKNOWLEDGEMENTS

The authors have an ownership interest in Greenwich LifeSciences.