Phase 1 clinical trial of a therapeutic prostate cancer vaccine containing PSA/IL-2/GM-CSF in PSA defined biochemical recurrent prostate cancer patients

Jonathan F. Head, Gregory A. Daniels, Michelle McKinney, Weg Ongkeko, Jessica Wang-Rodriguez, Kyoko Sakamoto, Robert L. Elliott

VA San Diego Healthcare System, San Diego, CA; VA Medical Center, San Diego, CA; Oncbiomune, Baton Rouge, LA

Navy Cancer Vaccine Program (NCVP) with OncBioMune

- Naval Health Research Center (NHRC), San Diego, CA
- Veterans Administration Medical Center (VAMC), La Jolla, CA
- UCSD Medical School, La Jolla, CA
- OncBioMune, LLC, Baton Rouge, LA

PSA Vaccine Components

- Antigens
  - PSA — 50 micrograms
- "Biological" Adjuvants
  - IL-2 — 2×10^4 IU
  - GM-CSF — 16.7 micrograms

NCVP Patient Group

- Prostate Cancer Patients at Relapse (defined by rising PSA) after initial treatment (surgery, radiation or seeds)

NCVP Phase 1a Clinical Trial

Vaccinate 20 patients to confirm minimal toxicity of the PSA vaccine

NCVP Phase 1b Clinical Trial

- Enroll 28 additional patients
- Add Boosters, #7-12, every month, alternating IL-2 (11 million units) and PSA vaccine

INDICATIONS TO BE STUDIED

Men with PSA-only recurrent prostate cancer will be enrolled equally between hormone naïve patients (Cohort 1), and hormone-independent patients (Cohort 2).

SAFETY ANALYSIS

The safety of PSA/IL-2/GM-CSF vaccine will be assessed by the Investigator and the Sponsor using the NCI Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0 to grade adverse events and laboratory abnormalities. Conventional clinical parameters will be assessed in all patients.

Table 1 (Updated 4/15/15)

PATIENT #	WEEK 1 LBA	WEEK 7 LBA AFTER 3 VACCINES	WEEK 19 LBA AFTER 6 VACCINES
1	------	------	------
2	1.56	1.72	0.91
3	0.76	1.12	1.21
4	2.08	1.41	1.52
5	1.60	1.75	1.64
6	3.27	3.57	1.46
7	1.10	------	------
8	1.16	1.31	1.93
9	1.43	40.16	1.72
10	0.82	1.19	1.00
11	1.24	0.89	1.05
12	1.49	0.90	------

TRIAL DESIGN

Phase 1A. All patients will receive the 6 induction vaccinations at a single dose. Enrollment will be suspended after 20 patients accrue and an interim safety analysis will occur 30 days after the 20th patient receives the last vaccine. If 3 or more DLAEs have occurred among the first 20 patients, the study will terminate. Otherwise, the study will proceed to Phase 1B.

Phase 1B. Should the safety analysis of Phase 1A demonstrate the safety of the vaccine according to the above-mentioned criterion, 28 additional patients will be recruited to the Phase 1B and receive induction vaccination (same as in Phase 1A). Patients who tolerate therapy and have an increase in PSADT of greater than 50% will proceed to receive maintenance vaccination. If at any time 3 or more DLAEs have occurred among these 28 patients, the study will terminate.

KEY INCLUSION CRITERIA

- Adenocarcinoma of the prostate.
- Rising serum PSA levels documented by 3 values over the last 6 months prior to study enrollment. Each value must be > 2 weeks from the previous value.
- Patients with rising PSA must have had either 1) prior definitive therapy including surgery or radiation therapy (hormone-naïve, defined as hormone-naïve patients and patients who received hormone therapy in the past who currently have total testosterone > 50 ng/dL), OR 2) hormone suppressive therapy as documented by surgical castration or a serum testosterone value < 50 ng/dL (hormone-independent). Patients must have completed these therapies for at least 6 months but no longer than 20 years prior to enrollment.
- PSA value within 4 weeks of starting therapy < 20 ng/mL for hormone-naïve (defined as hormone-naïve patients and patients who received hormone therapy in the past who currently have total testosterone > 50 ng/dL) patients or < 60 ng/mL for hormone-independent patients.
- NO radiographically measurable disease.

PRIMARY OBJECTIVE

- To evaluate the safety and tolerability of the induction vaccination (Phase 1A), and if acceptable, the maintenance vaccination (Phase 1B).

SECONDARY ANALYSIS

- Secondary endpoints will be analyzed by cohort, i.e., hormone-naïve patients and hormone independent patients.
- Prostate-specific antigen doubling time (PSADT) will be analyzed descriptively using a repeated measures longitudinal model. The percentage of change from baseline will be given at each time point. An increase from baseline in PSADT > 50% will be considered clinically significant. The percent of subjects who achieve a clinically significant change will be calculated and compared to historical controls at our institution.
- Time to measurable disease, time to subsequent therapy, disease-specific survival, and overall survival will be calculated and compared with historical controls at our institution using Kaplan-Meier curves and log-rank tests.
- vaccine-induced immune response.

Progress

- Recombinant PSA has been manufactured cGMP
- Engaged Theradex as our CRO for putting together our IND submission and as Medical Monitor
- FDA IND approved
- UCSD Medical School IRB approved
- Fully funded Phase 1 Clinical Trial initiated 1st quarter 2013

Patient Number	PSA Doubling Time Before Vaccine (Days)	PSA Doubling Time After Vaccine (Days)	Improvement in Doubling Time	Increase in Immunity to PSA After Vaccine
1p	121	54	NO	---
2	478	302	NO	YES
3	522	1235	YES	YES
4	324	429	YES	NO
5pr	259	807	YES	YES
6	659	672	YES	YES
7*	---	---	---	---
8	314	511	YES	YES
9	76	70	NO	YES
10	463	657	YES	YES
11	579	167	NO	YES
12**	---	---	---	---
			6/10	8/9

*Patient Withdrew **No Data Yet

RESULTS

- Twelve of twenty patients in the Phase 1a portion of the trial have received at least one vaccine injection and 10 patients have received all 6 vaccines.
- None of the 12 patients who have had at least one vaccine have had a DLAE.
- None of the 10 patients who have received all 6 vaccines in the Phase 1a have had a DLAE.
- Seven of the 10 patients who have received 3 vaccines have had increased immune responses to PSA as determined with a Lymphocyte Blastogenesis Assay.
- Five of the 9 patients who have received 6 vaccines have had increased immune responses to PSA as determined with a Lymphocyte Blastogenesis Assay.
- Eight of 9 patients at 31 weeks post first vaccine have had an increased immune response to PSA as determined with a Lymphocyte Blastogenesis Assay.

Phase 1 Highlights

- Trial at University of California San Diego Moore's Cancer Center and the Veterans' Hospital, La Jolla, CA
- Trial in patients with recurrent disease
- 11 biochemically progressing patients enrolled, 3 dropped out of study for progression (2 PSA,1 radiological) and 8 remain on study
- OBM plans to ask the FDA to allow us to initiate a Phase 2 Trial due to lack of toxicity of the PSA therapeutic vaccine

Phase 2

- Patient Number will be 120 (80 vaccinated prostate cancer patients and 40 control prostate cancer patients)
- Patient population will be in the active surveillance category, where standard surgical or radiation therapy are not yet indicated

CONTACT

Jonathan F. Head, Ph.D.
OncBioMune Pharmaceuticals
11441 Industriplex Blvd.
Suite 190
Baton Rouge, LA 70809
(225) 227-2384

Patient Number	PSA Doubling Time Before Vaccine (Days)	PSA Doubling Time After Vaccine (Days)	Improvement in Doubling Time	Increase in Immunity to PSA After Vaccine	Increase in Immunity to PAP After Vaccine	Increase in Immunity to PSMA After Vaccine	Increase in Immunity to CEA After Vaccine	Increase in Immunity to CA-125 After Vaccine
1p	121	54	NO	---	---	---	---	---
2	478	302	NO	YES	YES	YES	YES	YES
3	522	1235	YES	YES	YES	YES	YES	YES
4	324	429	YES	NO	YES	YES	NO	NO
5pr	259	807	YES	YES	YES	YES	NO	YES
6	659	672	YES	YES	YES	YES	YES	NO
7*	---	---	---	---	---	---	---	---
8	314	511	YES	YES	YES	NO	NO	
9	76	70	NO	YES	YES	NO	YES	YES
10	463	657	YES	YES	YES	YES	YES	YES
11	579	167	NO	YES	YES	NO	NO	NO
12**	---	---	---	---	---	---	---	---
			6/10	8/9	9/9	6/9	5/9	5/8

*Patient Withdrew **No Data Yet