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14. ABSTRACT

In the fall of 2007, we started the Phase I dose escalation studies with 177Lu-DOTA-huJ591 monoclonal antibodies (mAb) using dose fractionation regimen. In patients with PCa and who have recurrent and/or metastatic disease, 177Lu dose (20-40 mCi/m2) was escalated in 5 different dose levels (3-6 patients at each dose level). So far we have recruited 17 patients in 5 groups. At each dose level, the patients received two doses of 177Lu-J591 mab, 2 weeks apart. The dose of huJ591 MAb remained fixed at 20 mg/dose. We hope to complete this first trial by June 2009 and start the combination therapy protocol almost immediately. The combination therapy protocol was approved by our IRB and was submitted to DOD HSRRB for review and approval. We started recruitment of subjects into the combination therapy protocol. Our goal is to complete the study in by September 2010. The revised SOW is attached.

15. SUBJECT TERMS
Radioimmunotherapy, Prostate cancer, 177Lu-DOTA-J591 antibody, Dose-Fractionation

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Introduction

We still lack a systemic treatment that clearly demonstrates improved survival in patients with disseminated hormone resistant prostate cancer (PC). Targeted radioimmunotherapy (RIT) utilizing radiolabeled monoclonal antibodies (mAbs) directed to cancer-related cell surface antigens has been clinically validated with the FDA approval of ^{90}Y and ^{131}I labeled anti-CD20 mAbs (Zevalin and Bexxar) for the treatment of lymphoma. Metastatic PC is a rational candidate for RIT since PC is radioresponsive, and typically develops as small-volume micro-metastatic sites of disease in marrow and lymph nodes that receive high levels of mAb. In PC, the most well established, prostate-restricted, cell surface antigen yet identified is prostate specific membrane antigen (PSMA). It is an ideal target for developing therapeutic agents as it is expressed by all the PCs and the expression levels progressively increase in more poorly differentiated, metastatic and hormone-refractory prostate cancers (HRPC).

J591 is a de-immunized mAb that binds with a very high affinity to the extracellular domain of PSMA on the viable tumor cells. In addition, the PSMA-J591 antibody complex is internalized, thereby delivering any antibody payload (radioisotope or drug) to the interior of the targeted cells. We have demonstrated radiolabeled J591 sensitively and specifically targets sites of metastatic PC in both bone and soft tissue**.** In a Phase I studies, we have determined that ^{90}Y-J591 (17.5 mCi/m^2) and ^{177}Lu-J591 (70 mCi/m^2) mAbs either decrease or stabilize serum PSA levels. We have selected ^{177}Lu-J591 as an agent of choice for further studies. ^{90}Y may be appropriate for larger tumors while ^{131}I may be more cytotoxic for smaller, micro-metastatic lesions typically seen in HRPC. ^{177}Lu behaves chemically like ^{90}Y and is stable in vivo. ^{177}Lu has low energy β- particles and suitable γ photons for dosimetric studies. Thus it has advantages of both ^{90}Y and ^{131}I, but none of their disadvantages. Therefore **^{177}Lu-J591 may be an ideal agent for RIT studies of PC**. The degree of anti-tumor response following RIT depends on several variables, especially total (cumulative) radiation dose to the tumor, dose-rate and tumor radiosensitivity. Also, myelotoxicity is the dose-limiting factor in RIT. Therefore strategies are needed to optimize dosimetry to the bone marrow and tumor. Dose-fractionation is a practical strategy to decrease the dose to bone marrow while increasing the cumulative radiation dose to the tumor at an optimal dose-rate. Preclinical studies strongly support this strategy. Combined modality radioimmunotherapy (CMRIT) is another strategy designed to enhance the cascade of molecular events required for apoptotic tumor cell death resulting from the continuous low dose-rate radiation. FDA approved anti-neoplastic agent Docetaxel can cause microtubular dysfunction and as a result cells are blocked in the G2/M phase of the cell cycle, thus increasing sensitivity of cells to radiation.

Therefore, **we propose to perform two independent phase I dose-escalation studies** in patients with HRPC. The first protocol is designed to determine the cumulative MTD of ^{177}Lu-J591, in a fractionated dose regimen of 2 low dose treatments given 2 weeks apart. A follow up protocol is designed to determine a safe dose of docetaxel to be given in combination with a fractionated dose regimen of ^{177}Lu-J591. This research proposal thus combines several important strategies for successful RIT of PC; a very specific and high affinity anti-PSMA mAb J591, an ideal radionuclide ^{177}Lu with useful γ and β- energies for imaging and therapy**, dose fractionation and CMRIT strategies (with docetaxel) to reduce myelotoxicity and to augment the anti-tumor response of RIT**. In the revised SOW attached here, we identified 4 major tasks.

Body of Text based on SOW

REVISED STATEMENT OF WORK (SOW) July 20, 2009

PageTask 1: Preparation of ^{177}Lu-DOTA-J591 mAB for clinical studies.

Under GMP conditions, monoclonal antibody HuJ591-GS Antibody was DOTA conjugated, vialed and labeled by Immunomedics Inc. which is the current manufacturer of record for the vialed DOTA-HuJ591 antibody drug product. The manufacturer's address and telephone number are:

Immunomedics Inc.
300 Americsn Road
Morris Plains, NJ 07950
Phone: 973-605-8200

The drug product consists of DOTA-HuJ591 antibody in 0.3 M ammonium acetate, pH 7.2, in 2 mL thermoplastic vials with gray butyl rubber stoppers and blue flip-off crimp seal closures. The nominal concentration is 8.0 mg/mL and the nominal fill volume is 1.3 mL. There are no other excipients added.

^{177}Lu-Labeling of DOTA-J591: 3 batches of the above lot of DOTA-J591 were labeled with ^{177}Lu to a specific activity of 10-20 mCi/mg. All the QC tests indicated that the material is suitable for clinical studies.

The above process was started around October and final tests were completed by March 2007.

Task 2: Obtain IRB approval of the Phase I dose escalation protocol using ^{177}Lu-J591 in a fractionated dose regimen

- After 16 months of interaction with HSRRB at DOD, the protocol was finally approved in May 2006. Subsequently, the protocol (modified by Cornell IRB and DOD HSRRB) was submitted to FDA for permission to start the clinical trial under an IND.
- In August 2006, the physician who is responsible for recruiting the patients and who is the PI on the institutional protocol left Cornell medical center. We subsequently replaced the physician and resubmitted the protocol for IRB approval and FDA approval.
- Finally in January 2007, we received the approval from FDA following minor modifications to the protocol as suggested by FDA.
- The revised protocol was resubmitted to Cornell IRB and then finally to HSRRB at DOD (in January 2007)
- After several communications, we were just informed that the protocol is finally approved. We are still waiting for the formal letter of approval from DOD.
- **The protocol was finally approved by HSRRB in July 2007 and clinical studies started**

Task 3: Phase I clinical trial with ^{177}Lu-J591 Dose fractionation regimen

- The Task 3 was started in the fall of 2007. We have recruited 16 patients in this protocol and we expect to complete this protocol over the next 6-9 months. We reported the preliminary results of dose fractionation protocol in a major conference.

- As of July 2009, we have studied 5 groups of subjects who received 2 doses (2 weeks apart) with 20, 25, 30, 35 mCi/m^2 ^{177}Lu-J591. The patients in the last group are under follow-up. We have not yet received the MTD.

- Preliminary data from this trial was presented at the Genitourinary Cancer symposium in 2009.

- In the month of August 09, we plan to start the next group with 45 mCi/m^2 and recruit 3 subjects over a period of 6-8 weeks.

Task 4: Phase 1 Clinical trial with combination therapy (177Lu-J591 and Docetaxel).

- The design of Phase 1 protocol of combination therapy was finalized. The protocol was formally submitted to IRB. We expect the IRB approval process will be completed in less that 2 weeks.

- Dr. Scott Tagawa (PI of the clinical protocol) submitted the protocol to DOD HSSRB for review. The goal is to study 5 groups starting with 20 mCi/m2. The patient would first received 4 weeks of Docetaxel and the on week 5 and 7 would also receive 177Lu-J591 dose.

- As of July 09, two patients were recruited into the trial and received the treatment dose.

- The plan is to recruit 3 patients in each group every 3 months.

- We hope to complete the recruitment and follow-up by October 2010. The final data analysis will be completed after the patient recruitment is finished.

The final data analysis will be completed after the patient recruitment is finished.

Key Research Accomplishments

- Preparation of new lot of DOTA-J591 and optimization of ^{177}Lu labeling.
- Obtaining IRB approvals following repeated review of protocol by Cornell IRB, HSRRB and FDA
- Obtaining HSSRB approval for the trial
- Recruited the 16 subjects in Groups1-4 of the first phase I clinical study evaluating the dosefractionation.
- Submission of combination therapy (^{177}Lu-J591 + Docetaxel) protocol to Cornell IRB

Reportable Outcomes

Phase I trial of fractionated-dose ^{177}lutetium radiolabeled antiprostate-specific membrane antigen (PSMA) monoclonal antibody J591 (^{177}Lu-J591) in patients (pts) with metastatic castrate-resistant prostate cancer (metCRPC).

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172
Author(s):
S. T. Tagawa, S. Vallabhajosula, S. J. Goldsmith, K. Petrillo, D. Matulich, J. Kaplan, N. H. Bander, D. M. Nanus; Weill Cornell Medical College, New York, NY

Abstract:
Introduction: A phase II trial of single-dose ^{177}Lu-J591 radioimmunotherapy (RIT) in pts with metCRPC confirmed previously described anti-tumor activity, excellent targeting of met sites, and acceptable toxicity with an apparent dose-response relationship [Tagawa et al, ASCO 2008]. Dose fractionation of RIT may decrease toxicity (myelosuppression) while maintaining or increasing efficacy [DeNardo et al, 2002].
Methods: In this phase I study, cohorts of 3-6 pts with progressive metCRPC receive 2 fractionated doses of ^{177}Lu-J591 2 weeks apart: Cohort 1 (20 mCi/m$_2$ x2), dose escalation 5 mCi/m$_2$ per dose per cohort. The primary endpoint is to determine dose limiting toxicity (DLT) and the cumulative maximum tolerated dose (MTD) of fractionated ^{177}Lu-J591 RIT with pharmacokinetics and dosimetry and secondary endpoints of efficacy. DLT was defined as Gr >3 hematologic toxicity or Gr >2 non- hematologic toxicity.
Results: Median age of the 11 treated pts is 78 (range 63-86), median baseline PSA 49.5 (23.7-265.9), 91% with ECOG PS 1,9% ECOG 2. 82% had bone mets, 45% lymph node mets, and 36% extra-osseous visceral mets (lung). All pts had progressed after 1-3 hormonal therapies and 36% progressed on 1-4 lines of chemotherapy including docetaxel. No DLT's have been seen. 2 pts experienced reversible Gr 3 neutropenia and 1 Gr 3 thrombocytopenia; no growth factors or transfusions were needed. There was no Gr >1 non-hematologic toxicity. Overall, 5 of 11 pts experienced a PSA decline. Excluding the lowest dose-level, 63% experienced a PSA decline (with median time to progression of 20 weeks), 2 with >30% decline, 1 with >50% decline. Excellent targeting of known sites of PC metastases was seen in the majority of pts.
Conclusions: Fractionated dose ^{177}Lu-J591 is well tolerated, with reversible myelosuppression, demonstrating anti-tumor activity in pts with progressive metCRPC. The MTD has not yet been reached and enrollment continues on cohort 4 (35 mCi/m$_2$ x2) with plans to proceed to combination therapy with docetaxel.

1. Preparation of DOTA-J591 by Immunomedics Inc

Under GMP conditions, HuJ591-GS monoclonal Antibody was DOTA conjugated, vialed and labeled by Immunomedics Inc. which is the current manufacturer of record for the vialed DOTA-HuJ591 antibody drug product.

The drug product consists of DOTA-HuJ591 antibody in 0.3 M ammonium acetate, pH 7.2, in 2 mL thermoplastic vials with gray butyl rubber stoppers and blue flip-off crimp seal closures. The nominal concentration is 8.0 mg/mL and the nominal fill volume is 1.3 mL. There are no other excipients added.

Lot No: #0612012

Date of Manufacture: December 2006

Number of DOTA-J591 mAb vials: 165

Number of DOTAs/antibody: 3-4 (Tested by Immunomedics, Inc)

The batch release documents provided by Immunomedics, Inc are included in the Appendix-A

2. Acceptance testing of DOTA-J591

Upon the receipt of DOTA-J591 mAb vials from Immunomedics, Inc. the vials were accepted for clinical use following labeling with ^{177}Lu and quality control testing. 4 batches of ^{177}Lu-DOTA-J591 were prepared at different specific activities (10-20 mCi/mg). The QC results are shown in Table-1.

Table- 1: Evaluation of DOTA-J591 (lot #0612012)

Date	Batch	Incubation Time (min)	^{177}Lu-Labeling efficiency (%)	SA mCi/mg	Immuno-reactivity (%)
1/31/2007	1	15 min 30 min	94.3 100.0	10	90.6
	2	15 min 30 min 60 min	89.2 98.0 100.0	20	87.2
2/2/2007	3	15 min 30 min	70 100	5	94.1
2/22/2007	4	30 min	100	22.5	87.4
		Mean ± SD	**100**	**14.3 ± 8.2**	**89.8 ± 3.2**

Conclusion: The results in Table -1 indicate that DOTA-J591 mAb manufactured by Immunomedics, Inc was acceptable for clinical studies. Incubation of DOTA-J591 (10mg) with ^{177}Lu chloride (up to 225 mCi) will result in almost 100% labeling efficiency. The immunoreactivity was well preserved (90%). In addition to the above tests, the sterility and pyrogenicity tests have also indicated that ^{177}Lu-DOTA-J591 preparation is acceptable for clinical studies.

3. Phase 1 dose-escalation studies with ^{177}Lu-DOTA-J591: Dose fractionation regimen

In this phase I study, cohorts of 3-6 pts with progressive metastatic castrate-resistant prostate cancer (metCRP) received 2 fractionated doses of ^{177}Lu -J591, 2 weeks apart: Cohort 1 was started at 20 mCi/m^2 x 2 doses 2 weeks apart). Subsequently each cohort dose was escalated at 5 mCi/m^2 per dose increment.

The primary endpoint was to determine dose limiting toxicity (DLT) and the cumulative maximum tolerated dose (MTD) of fractionated ^{177}Lu -J591 RIT with pharmacokinetics and dosimetry and secondary endpoint of efficacy. DLT was defined as Grade >3 heme toxicity or Grade >2 non-heme toxicity.

Inclusion Criteria (summary)
- Histologically proven adenocarcinoma of prostate
- Radiographically evident metastatic disease
- Progression despite medical/surgical castration (testosterone < 50)
- Adequate bone marrow and organ function

Exclusion Criteria (summary)
- ECOG performance status > 2
- Prior radioisotopes (e.g. strontium, samarium)
- Bone scan with confluent lesions of axial/appendicular skeleton (superscan)
- Prior radiotherapy to > 25% of skeleton

Treatment

Cohorts of 3-6 subjects
- Cohort 1: initial dose of ^{177}Lu-J591 at 20 mCi/m^2 IV D1, D15
- Each subsequent cohort receives escalating doses of 5 mCi/m^2 per dose per cohort (i.e. cumulative dose escalation of 10 mCi/m^2 per cohort)
- No pre-medications given

Definition of Dose Limiting Toxicity (DLT)
- Platelet count < 15,000 or need for > 3 platelet transfusion in 30 days
- Gr 4 neutropenia
- Febrile neutropenia
- Attributable Gr $\geq$ 3 non-hematologic toxicity

(excluding infusion reactions)

Results

Patient recruitment and dose escalation cohorts

As of March 14th 2009, 16 patients were recruited in this protocol and received 4 dose levels; 20, 25, 30, and 35 mCi/m2; 2 doses given 2 weeks apart). The details of subject recruitment and doses received are shown in Table-2.

- Median age of the 16 treated pts is 75 (range 62-86)
- Median baseline PSA 49.8 (14.8 – 277.2)
- 6% with ECOG PS 0; 75% PS 1; 19% PS 2.
- 81% had bone mets, 56% lymph node mets, and 44% extra-osseous visceral mets (lung, liver)
- All pts had progressed after 1-3 hormonal therapies and 37% progressed on 1-4 lines of chemotherapy including docetaxel.

Table - 2: Phase I: Lu-177 -J591 Dose Fractionation Studies

No.	TX Date	Pt.	Dose (mCi)	BSA	mCi/ m2	mCi	SA (mCi/mg)	RCP (%)	Immuno-reactivity	Sterility	Pyrogenicity
Cohort 1											
1	8/16/07	VC	37.40	1.87	20	38.5	12.6	100	94	Pass	Pass
	8/30/07	VC	37.40	1.87	20	39.7	12	99		Pass	Pass
2	8/30/07	WE	36.80	1.84	20	38	12.0	100		Pass	Pass
	9/13/07	WE	36.80	1.84	20	38.2	7.6	99.2	90.7	Pass	Pass
3	10/4/07	SH	47.00	2.34	20	48.6	11.2	99.5	81	Pass	Pass
	10/19/07	SH	47.00	2.34	20	47.8	10.8	>99.5	83.5	Pass	Pass
Cohort 2											
4	12/6/07	NL	52.50	2.1	25	53	11.9	99.7		Pass	Pass
	12/20/07	NL	52.50	2.1	25	53.1	12.89	98.45	89.4	Pass	Pass
5	12/13/07	JJP	48.00	1.92	25	48.5	13.24	>99.5	92.6	Pass	Pass
	12/27/07	JJP	48.00	1.92	25	49.3	11.29	>99.5	97.2	Pass	Pass
6	12/19/07	JE	49.25	1.97	25	51	10.31	99.38		Pass	Pass
	1/3/08	JE	49.25	1.97	25	53	10.87	99.77	84.7	Pass	Pass
Cohort 3											
7	3/19/08	TG	54.60	1.82	30	55.7	10.26	99.81	99.3	Pass	Pass
	4/2/08	TG	54.60	1.82	30	57.4	11.925	99.68	93.7	Pass	Pass
8	3/27/08	WB	70.20	2.34	30	69.3	9.88	99.9	97.8	Pass	Pass
	4/9/08	WB	70.20	2.34	30	71.5	12.5	100		Pass	Pass
9	5/15/08	PL	57.90	1.93	30	58.3	8.45	100		Pass	Pass
	5/29/08	PL	57.90	1.93	30	58.6	9.02	100		Pass	Pass
10	6/26/08	VM	57.30	1.91	30	59.8	9.07	99.93		Pass	Pass
	7/10/08	VM	57.30	1.91	30	59.1	8.8	99.61	99	Pass	Pass
Cohort 4											
11	8/26/08	DG	66.15	1.89	35	68.8	8.45	99.22	87	Pass	Pass
	9/10/08	DG	66.15	1.89	35	65.7	9.19	100		Pass	Pass
12	11/20/08	JG	79.8	2.28	35	79.6	9.45	99.86	102.4	Pass	Pass
	12/4/08	JG	79.8	2.28	35	82.8	9.02	99.85	84.9	Pass	Pass
13	12/10/08	BF	67.55	1.93	35	70.2	8.84	99.99	81.1	Pass	Pass
	12/24/08	BF	67.55	1.93	35	69.6	11.1	100	85.3	Pass	Pass
14	1/22/09	SS	59.15	1.69	35	63	9.78	99.97	94.7	Pass	Pass
	2/5/09	SS	59.15	1.69	35	61.1	8.35	100	93.1	Pass	Pass
15	2/4/09	MG	81.2	2.32	35	83.8	10.27	100	93.3	Pass	Pass
	2/18/09	MG	81.2	2.32	35	82.4	9.29	100	81	Pass	Pass
16	2/13/09	RPE	73.5	2.1	35	71.1	9.06	100	99.8	Pass	Pass
					Mean		**10.3**	**99.7**	**91.2**		
					SD		**1.5**	**0.4**	**6.7**		

Patient 16 had an allergic reaction and was not treated with the second dose

Toxicity

(individual subject worst grade to date)

- Infusion Reactions (n = 16 evaluable)
  6 (44%) overall (5 Gr 1, 1 Gr 3). All were transient, reversible

- Thrombocytopenia (n=12 evaluable)
  Gr 0 = 17%; Gr 1-2 = 75%; Gr 3 = 8%; Gr 4 = 0%

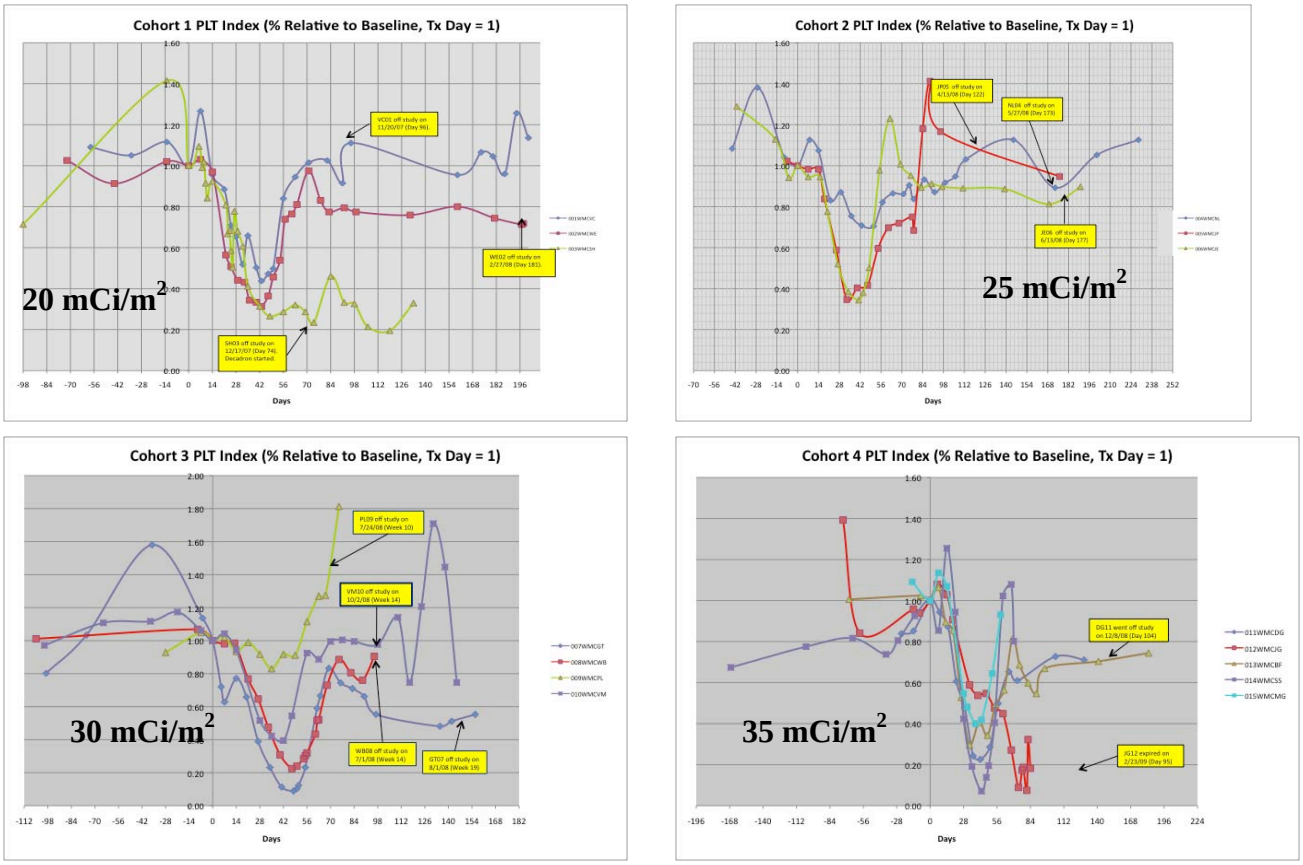
  No pts had significant bleeding or received platelet transfusions
  Thrombocytopenia following 177Lu-J591 treatment (20-35 mCi/m^2) is shown in **Figure-1**

- Neutropenia (n=12 evaluable)
  Gr 0 = 42%; Gr 1-2 = 42%; Gr 3 = 16%; Gr 4 = 0%

  No febrile neutropenia (no growth factor use)

- Transaminitis (n=12 evaluable)
  Transient Gr 1 17% (no Gr > 1)

Figure-1: Thrombocytopenia in 4 different groups of patients following ^{177}Lu-J591 treatment (20-35 mCi/m^2)



Preliminary Efficacy Results (n=11 evaluable)

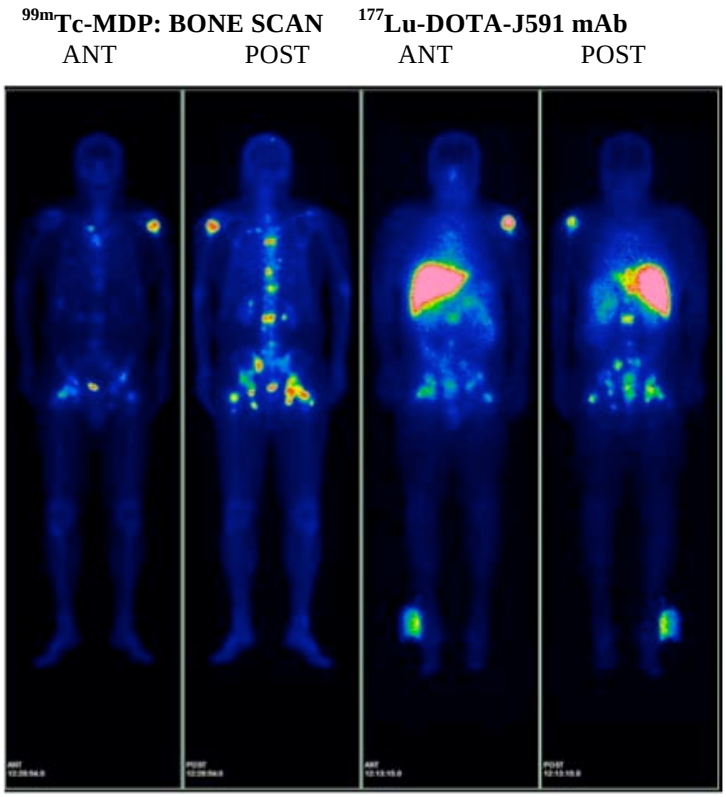
• Any PSA decline = 45% (all evaluable pts)
• Excluding cohort 1 (20 mCi/m^2 x2):
Any PSA decline = 63% (median time to progression = 20 weeks)
2 with > 30% PSA decline (including 1 with > 50%)

Targeting: ^{177}Lu-J591 Imaging studies

Following the administration of the 1st dose whole body anterior and posterior scans were obtained 3-5 times over a period of 14 days. The ^{177}Lu uptake in tumor lesions was compared to the lesions identified in conventional bone scans (Figure -2).

• 11/13 evaluable scans (85%) had accurate imaging of known sites of metastatic disease.

Figure-2: Comparison of ^{177}Lu-J591 imaging with standard bone scans



Left panels: ^{99m}Tc-MDP bone scan images of pre-treatment bony metastases

Right panels: ^{177}Lu-J591 scan: total body images obtained via dual head gamma camera of sites of uptake 7 days after ^{177}Lu-J591 administration (^{177}Lu-J591 is cleared via the liver)

CONCLUSIONS

- Fractionated ^{177}Lu-J591 is well-tolerated, with reversible myelosuppression
- Successful targeting of known sites of metastatic disease occurs in the majority of patients
- PSA declines have been seen despite a potentially sub-optimal (for ^{177}Lu) pt population with bulky disease
- The MTD has not been reached, with enrollment ongoing on Cohort 5 with a cumulative dose exceeding the single dose MTD
- A phase I study in combination with docetaxel will begin enrollment in early 2009

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Appendix- A

DOTA-J591

Certificate of Analysis from Immunomedics, Inc.

CERTIFICATE OF ANALYSIS

J591 IgG-DOTA

P/N: 73406, C/N: 0612012

Assay	Specification*	Results
Potency	Report IgG-DOTA concentration and protein content.	7.5 mg/mL 10 mg/vial
Radiolabeling	Report Results	98.5% IgG-DOTA-^{111}In
Radiochemical Purity by ITLC	Report Results	99.0% IgG-DOTA-^{111}In
DOTA/IgG Ratio	Report results	3.4

Storage: 2-8 °C

Date of Manufacture: December 6, 2006

Date of Expiration: TBD

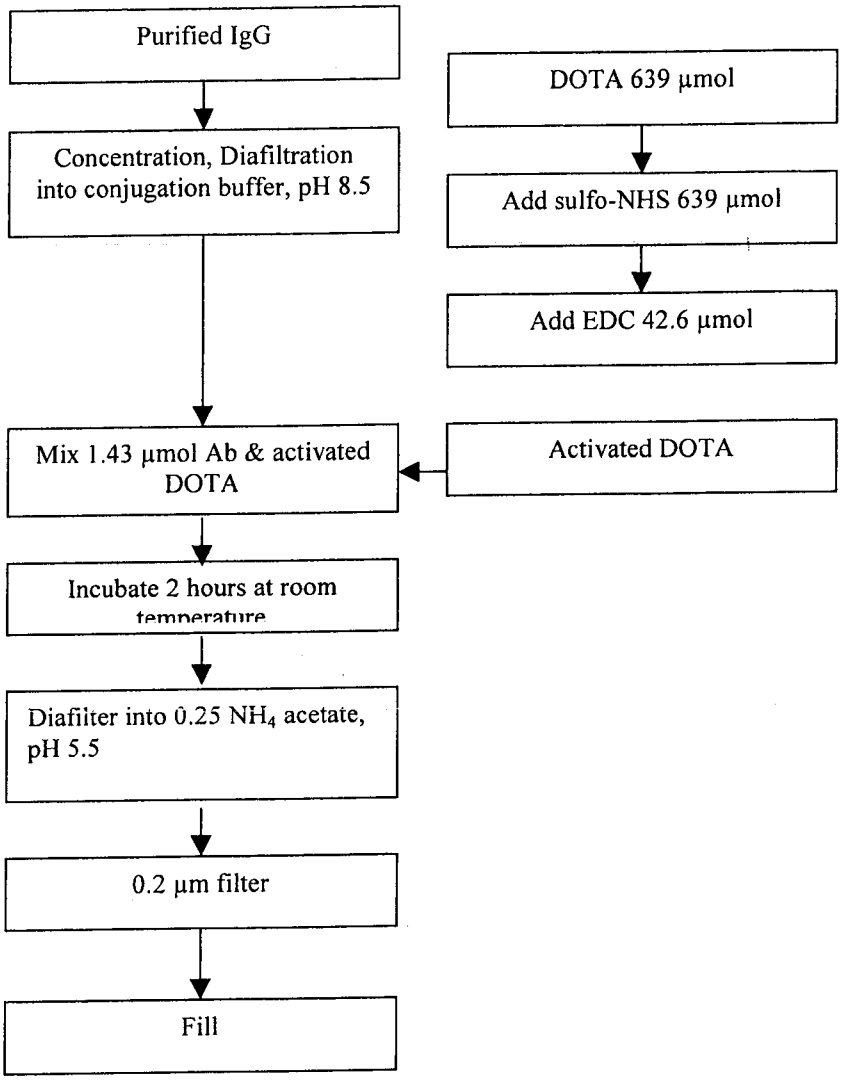
The above material meets all of the specifications.

Ding Shieh
Quality Control Director

12/13/06
Date

8 mg/ml
x 1.3 ml/vial = 10.4 mg/vial
161 vials = 1,674 mg
Remainder 200 mg released Ab
~85% efficiency

Process Flow Chart for DOTA-Conjugation of J591 Antibody



Immunomedics®, Inc.	Shipping Request Form	Appendix A Document: M401 Revision: 12 Effective Date: MAY 2 0 2006

Should be received by QA 48-hours prior to shipment. No Friday shipments.

Today's Date: 1/9/07	**Date to be Shipped:** 1/9/07
Shipping Address: Dr. Neil H. Bander Laboratory of Urologic Oncology Weill Medical College of Cornell University 1300 ~~York~~ R4 1/9/07 York Avenue, E300 New York, NY 10021	
Telephone #: 212-746-5493	
Protocol #: N/A	Lot #: N/A
FDA on File: N/A	Investigator's Name: Neil H. Bander
Product to be Shipped ~~16 vials~~ 16 vials of J591 IgG-DOTA CN: 061202	
Initial Shipment? ☑ Yes ☐ No ☐ Coded ☐ Uncoded *(Please Check)*	
ITLC Strips Needed? ☐ Yes ☑ No	
Approval Signatures and Date	
Requisitioner: L M. Le 1/9/07	
Manager Approval: L M Le 1/9/07	
Regulatory Affairs Approval: [signature] 1/9/07	
QA Approval: R Yee 1/9/07	
Dispatched By: Jay Wells 1/9/07	

ORIGINAL COPY

IMMUNOMEDICS, INC.	**Temperature Recorder Activation Form** (For shipments *from* Immunomedics)	Appendix A Document: Q408 Revision:. 5 Effective Date: 10/30/04

Part I: To be completed by Immunomedics

Product Shipped: hLL1 IgG-DOTA

Storage Condition of Product Shipped: ☑ 2-8°C ☐ <-20 °C ☐ <-70 °C ☐ Ambient

Part Number: 73406 Control Number: 06/2012

Number of temperature recorder(s) in this shipment: 2 S/N: 3403628758

Time temperature recorder(s) activated and placed into package:

Time: 2:30 PM EST Date: 1/9/07

Performed by: RY Date: 1/9/07

NOTE: Please Complete the Part II and RETURN This Document and All the Temperature Recorders to Immunomedics, Inc., by Overnight Carrier.

Part II: Shipment Receipt, To be completed by the RECEIVER

Date Package Received: 1/10/07 Time Received: p.m. Received By: VN

Condition of outside container: ☑ Good ☐ Damaged

If damaged, describe damage: _____

Performed By: Vincent NAVARRO Date: 1/10/07

Time temperature recorder(s) removed from shipment container:

Time: 3pm EST Date: 1/10/07

Performed by: VN Date: 1/10/07

Note: Once Shipment container is opened upon receipt, temperature recorder(s) & product must be promptly removed and properly stored at the specified temperature.

ORIGINAL