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TITLE: Vaccination with Dendritic Cell Myeloma Fusions in Conjunction With Stem Cell Transplantation and PD1 Blockade

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14. ABSTRACT
Most patients with multiple myeloma achieve a complete or near complete response following autologous transplantation. However, patients experience disease relapse from a persistent reservoir of chemotherapy resistant disease. There has been strong interest in developing immunotherapeutic strategies to eradicate residual disease following autologous transplantation. Our group has developed a tumor vaccine model whereby dendritic cells are fused with tumor cells. In clinical trials, vaccination with fusion cell results in anti-tumor immune and disease responses in a subset of patients. However, vaccine efficacy is blunted by tumor mediated immune suppression and the increased presence of regulatory T cells characteristic of patients with malignancy. An important element contributing to tumor mediated immune suppression is the PD-1/PDL-1 pathway. PD-L1 exerts a significant role in promoting T cell tolerance by binding PD-1 on activated T cells and suppressing their capacity to secrete stimulatory cytokines. We have demonstrated that blockade of this pathway results in enhanced immune responses to DC/myeloma fusion cells ex vivo. In the proposed study, we will examine toxicity, immunologic effect and clinical efficacy of CT-011 therapy following stem cell transplantation for patients with myeloma. These endpoints will then be assessed in patients undergoing combined therapy with the vaccine and antibody.

15. SUBJECT TERMS
DC/myeloma fusion vaccine, PD1 blockade, immunotherapy, multiple myeloma

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Table of Contents

A. INTRODUCTION

In this project, we are conducting a clinical trial in which patients with multiple myeloma are treated with an anti-PD1 antibody (CT-011) alone (Cohort 1) and in conjunction with a dendritic cell/myeloma fusion cell vaccine (Cohort 2) following autologous transplantation. The goal of the project is determine the effect of CT-011 alone, and in conjunction with a DC/myeloma fusion cell vaccine, to stimulate effective anti-tumor immunity and disease response.

B. BODY

Clinical Trial

The clinical study is being conducted in two stages. In the first stage, a pilot study is being conducted in which patients are treated with CT-011 alone following autologous transplant. The primary objective of this stage is to explore immunologic responses to CT-011 in the post-transplant period. The secondary objective is to assess the toxicity of treating patients with CT-011 in the post-transplant setting.

In the second stage, patients receive a combination of CT-011 and DC/myeloma fusion vaccination. The primary objective is to determine if cellular immunity is induced by treatment with monoclonal antibody CT-011 and DC/myeloma fusion cells in conjunction with stem cell transplant. The secondary objectives of this stage are: 1) To assess the toxicity associated with treating multiple myeloma patients with monoclonal antibody CT-O11 in combination with DC/myeloma fusion vaccine following autologous transplant, 2) To correlate levels of circulating activated and regulatory T cells with immunologic response, and 3) To define anti-tumor effects using serum markers, radiological studies, and time to disease progression.

The targeted study population includes patients with multiple myeloma who are potential candidates for high dose chemotherapy with stem cell rescue. In cohort 1, participants receive three infusions of CT-011 at doses of doses of 3mg/kg given at 6 week intervals beginning 1-3 months following autologous transplant. In cohort 2, participants receive three infusions of CT-

011 given at six week intervals, in conjunction with vaccination with DC/myeloma fusion cells. Vaccination is given one week before each infusion of CT-011 and is given in conjunction with GM-CSF on the day of vaccination and for three days thereafter.

Status: The protocol (DF-HCC protocol number 09-061) is open to accrual at the DF/HCC as of March 19, 2010. Rambam Medical Center (RMC) in Haifa, Israel was added on April 26, 2011. As of July 5 2012, 10 patients on cohort 1 became evaluable (having received 2 infusions of CT-011), and enrollment to cohort 2 was initiated. As of May 1, 2013, 50 patients have been screened. There have been eight screen failures: six patients did not meet eligibility criteria and two patients elected to pursue only standard of care therapy. To date, 43 participants have met eligibility criteria and have been enrolled: 27 patients on the first cohort (19 at DF/HCC and 8 at RMC) and 16 patients on the second cohort (14 at DF/HCC and 2 at RMC.) This is summarized in Table 2.

To date, 14 participants have come off study prior to initiation of study treatment, as outlined in Table 2.

Currently, 29 participants are enrolled to the study: 14 patients on the first cohort (9 at DF/HCC and 5 at RMC) and 15 patients on the second cohort (13 at DF/HCC and 2 at RMC.) Of the subjects who are enrolled onto the first cohort at DF/HCC, seven have completed both study treatment and active follow-up and are now in long-term follow-up; and two are undergoing stem cell collections in preparation for transplant. Of the five subjects enrolled onto the first cohort at RMC, four have completed treatment and active follow-up and are now in long-term follow-up; and one has completed treatment and is now in active follow-up.

Of the subjects enrolled onto the second cohort at DF/HCC, one is currently receiving treatment; three have undergone autologous stem cell transplant and will initiate treatment with vaccine and CT-011 within 100 days following autologous stem cell transplant; five have undergone tumor collection and dendritic cell collection for vaccine generation and are completing pre-transplant chemotherapy; and four have undergone tumor collection and cryopreservation but have not yet undergone dendritic cell collection. Of the subjects enrolled onto the second cohort at RMC, two subjects are completing standard of care pre-transplant therapy. Both of the subjects failed to

generate enough tumor and dendritic cells for vaccine generation and therefore will receive CT-011 alone, making them un-evaluable per protocol.

Subject Study Information

Table 1: Screen Failures

Subject Initials	Screening Number	Consent Date	Age	Gender	Race/ Ethnicity	Reason
ES	2	5/25/10	54	F	White	Failure to meet eligibility criteria
JP	5	7/16/10	51	M	Hispanic	Failure to meet eligibility criteria
GW	7	10/28/10	59	M	White	Failure to meet eligibility criteria
JD	13	5/3/2011	51	M	White	Failure to meet eligibility criteria
EB	18	7/25/11	62	F	African American	Elected to pursue standard of care therapy only
JH	19	8/15/11	72	F	White	Elected to pursue standard of care therapy only
JR	30	12/6/11	61	M	Hispanic	Failure to meet eligibility criteria
DA	45	1/10/13	59	M	White	Failure to meet eligibility criteria

Table 2: Subjects Enrolled

Subject Initials	Site	Screening Number	Enrollment Number	Consent Date	Registration Date	Age	Gender	Race/ Ethnicity	Off -Study Date	Reason Off-Study
LC	DF/HCC	1	1	5/10/2010	5/13/2010	48	M	White	8/14/2010	Disease Progression
RG	DF/HCC	3	2	6/23/2010	7/2/2010	70	M	White	11/5/2010	Death
RP	DF/HCC	4	3	7/1/2010	7/9/2010	52	F	Black	N/A	N/A
CC	DF/HCC	6	4	9/16/2010	9/29/2010	55	M	White	12/12/2011	Disease Progression
KF	DF/HCC	8	5	12/21/2010	12/30/2010	55	F	White	N/A	N/A
DW	DF/HCC	9	6	12/27/2010	1/7/2011	47	M	White	10/12/2011	Elected to pursue SOC therapy
DF	DF/HCC	10	7	12/29/2010	1/13/2011	63	M	White	N/A	N/A
GF	DF/HCC	11	8	1/3/2011	1/28/2011	73	F	White	10/19/2011	Elected to pursue SOC therapy
SM	DF/HCC	12	9	2/4/2011	2/15/2011	58	M	White	N/A	N/A
RR	DF/HCC	14	10	5/16/2011	5/18/2011	67	M	White	N/A	N/A
AG	DF/HCC	15	11	5/26/2011	6/6/2011	45	F	White	N/A	N/A

Subject Initials	Site	Screening Number	Enrollment Number	Consent Date	Registration Date	Age	Gender	Race/ Ethnicity	Off -Study Date	Reason Off-Study
KI	RMC	16	12	6/9/2011	6/14/2011	61	M	White	11/6/2011	Elected to pursue SOC therapy
BF	RMC	17	13	7/19/2011	7/21/2011	64	F	White	N/A	N/A
RB	DF/HCC	20	14	8/22/2011	8/26/2011	58	M	White	3/1/2012	Elected to pursue SOC therapy
SMM	RMC	21	15	9/5/2011	9/12/2011	55	M	White	N/A	N/A
FM	DF/HCC	22	16	10/12/2011	10/26/2011	50	M	Hispanic	N/A	N/A
ES	DF/HCC	23	17	11/3/2011	11/10/2011	55	F	White	N/A	N/A
KM	DF/HCC	24	18	10/21/2011	11/10/2011	49	M	Black	1/19/2012	Death
KM	DF/HCC	25	19	11/17/2011	11/21/2011	56	F	White	N/A	N/A
KR	RMC	26	20	11/22/2011	11/30/2011	47	M	White	N/A	N/A
NP	DF/HCC	27	21	12/16/2011	12/21/2011	62	F	White	N/A	N/A
RT	RMC	28	22	1/5/2012	1/9/2012	66	F	White	N/A	N/A
BB	DF/HCC	29	23	1/20/2012	1/30/2012	60	M	White	N/A	N/A
TB	RMC	32	24	2/2/2012	2/3/2012	60	M	White	N/A	N/A
IC	DF/HCC	31	25	1/5/12	2/17/12	66	F	Hispanic	N/A	N/A
LY	PM26	33	26	5/4/2012	5/8/2012	64	M	White	N/A	N/A
HH	PM27	34	27	6/19/2012	6/21/2012	30	M	White	N/A	N/A
CG	PM28	35	28	7/17/2012	7/23/2012	61	F	White	N/A	N/A
SF	PM29	36	29	8/3/2012	8/7/2012	47	M	White	N/A	N/A
PLL	PM30	37	30	10/11/2012	10/18/2012	66	M	White	3/21/2013	Not receiving transplant
FH	PM31	38	31	10/11/2012	11/1/2012	66	M	White	N/A	N/A
WP	PM32	39	32	11/26/2012	12/11/2012	63	M	White	N/A	N/A
EH	PM33	40	33	11/27/2012	12/13/2012	68	F	White	N/A	N/A
AW	PM34	41	34	12/13/2012	12/17/2012	53	F	White	N/A	N/A
MS	PM35	42	35	12/18/2012	12/21/2012	68	M	White	N/A	N/A
JG	PM36	43	36	11/28/2012	1/4/2013	70	F	White	N/A	N/A
HB	PM37	44	37	2/4/2013	2/7/2013	75	M	White	N/A	N/A
SA	PM38	46	39	2/3/2013	2/7/2013	47	F	White	N/A	N/A
MAG	PM38	47	38	2/5/2013	2/12/2013	66	F	White	N/A	N/A
DP	PM40	48	40	3/1/2013	3/7/2013	71	F	White	N/A	N/A
DH	PM41	49	41	3/6/2013	3/21/2013	59	M	White	N/A	N/A
SS	PM42	50	42	3/21/2013	3/25/2013	69	M	White	N/A	N/A
CK	PM43	51	43	4/17/2013	4/26/2013	49	F	White	N/A	N/A

TABLE 3: PARTICIPANTS WHO HAVE RECEIVED TREATMENT

SUBJECT ID	Cohort and Dose Administered	Treatment Dates	Clinical Outcome
RP/PM3 (DF/HCC)	Cohort 1: CT-011 Alone 3 doses at 3mg/kg	#1. 2/14/11 #2. 3/28/11 #3. 5/9/11	Best response at the end of transplant was complete response. Since completing treatment, the participant has remained in a complete response.
CC/PM4 (DF/HCC)	Cohort 1: CT-011 Alone 3 doses at 3mg/kg	#1. 5/4/11 #2. 6/15/11 #3. 7/27/11	Best response at the end of transplant was complete response. The participant developed disease progression at five months following last treatment.
KF/PM5 (DF/HCC)	Cohort 1: CT-011 Alone 3 doses at 3mg/kg	#1 6/28/11 #2. 8/9/11 #3. 9/20/11	Best response at the end of transplant was complete response. Since completing treatment, the participant has remained in a complete response.
DF/PM7 (DF/HCC)	Cohort 1: CT-011 Alone 3 doses at 3mg/kg	#1. 3/6/12 #2. 4/26/12 #3. TBD	Best response at the end of transplant was very good partial response. Best response after receiving treatment was a very good partial response. Since completing treatment, the participant has remained in a very good partial response.
SM/PM9 (DF/HCC)	Cohort 1: CT-011 Alone 3 doses at 3mg/kg	#1. 9/19/11 #2. 10/31/11 #3. 12/12/11	Best response at the end of transplant was very good partial response. Since completing treatment, the participant has remained stable at his best response.
RR/PM10 (DF/HCC)	Cohort 1: CT-011 Alone 3 doses at 3mg/kg	#1. 1/31/12 #2. 3/13/12 #3. 4/24/12	Best response at the end of transplant was complete response. Since completing treatment, the participant has remained in a complete response.
BF/PM13 (RMC)	Cohort 1: CT-011 Alone 3 doses at 3mg/kg	#1. 1/19/11 #2. 3/1/12 #3. 4/11/12	Best response at the end of transplant was complete response. Since completing treatment, the participant has remained in a complete response.
SMM/PM15 (RMC)	Cohort 1: CT-011 Alone 3 doses at 3mg/kg	#1. 4/5/12 #2. 5/15/12 #3. 6/28/12	Best response at the end of transplant was very good partial response. Since completing treatment, the participant has remained in a very good partial response.
FM/PM16 (DF/HCC)	Cohort 1: CT-011 Alone 3 doses at 3mg/kg	#1. 5/24/12 #2. 7/5/12 #3. 8/16/12	Best response at the end of transplant was very good partial response. Since completing treatment, the participant has remained in a very good partial response.
KM/PM19 (DF/HCC)	Cohort 1: CT-011 Alone 3 doses at 3mg/kg	#1. 5/21/12 #2. 7/2/12 #3. 8/13/12	Best response at the end of transplant was a partial response. Note: in the early post-transplant period prior to initiation of CT-011, her paraprotein increased to 1400 mg/dl from a nadir of 1000 mg/dl pre-transplant. At the time of her second CT-011 infusion, her paraprotein was 1650mg/dl, and on follow up 2 weeks later, was stable at 1600 mg/dl. The participant continued to receive treatment and her paraprotein has remained stable since completing treatment.
KR/PM20 (RMC)	Cohort 1: CT-011 Alone 3 doses at 3mg/kg	#1. 5/30/12 #2. 7/12/12 #3. 8/22/12	Best response at the end of transplant was very good partial response. The participant developed progressive disease four months following completion of study treatment and was removed from study.
TR/PM22 (RMC)	Cohort 1: CT-011 Alone 3 doses at 3mg/kg	#1. 8/23/12 #2. 9/27/12 #3. 11/7/12	Best response at the end of transplant was complete response. Since completing treatment, the participant has remained in a complete response.
TB/PM24 (RMC)	Cohort 1: CT-011 Alone 3 doses at 3mg/kg	#1. 7/18/12 #2. 9/6/12 #3. 10/11/12	Best response at the end of transplant was complete response. Since completing treatment, the participant has remained in a complete response.

SUBJECT ID	Cohort and Dose Administered	Treatment Dates	Clinical Outcome
LY/PM26 (RMC)	Cohort 1: CT-011 Alone 3 doses at 3mg/kg	#1. 12/6/12 #2. 1/17/13 #3. 3/4/13	Best response at the end of transplant was complete response. Since completing treatment the participant has remained in a complete response.
SF/PM29	Cohort 2: DC/MM Fusion Vaccine 3 doses at 5x10^6 cells + CT-011 3 doses at 3mg/kg	Vac #1. 3/7/13 Inf #1. 3/14/13 Vac #2. 4/18/13 Inf #2. 4/25/13 Vac #3. TBD Inf #3. TBD	Best response at the end of transplant was complete response. The participant will have his disease reassessed at one month following completion of treatment.

In total, 14 participants have initiated treatment on cohort one and are evaluable for response. Of these 14 participants, 12 remain without disease progression: seven participants have achieved a CR, four participants have achieved a VGPR and one participant has achieved a PR. In addition, two participants developed progressive disease: one progressed four months following completion of treatment (7.9 months following transplant) and one progressed five months following completion of treatment (10.5 months following transplant.) Both were subsequently removed from study. The median time without disease progression for the 14 evaluable participants is 16.5 months from transplant.

Immunological Responses to Date: Immunologic response was determined by quantifying circulating tumor reactive T cells at each time point as defined by the percent T cells expressing IFNg in response to ex vivo exposure to autologous tumor lysate. Results are presented as the percentage of CD4 or CD8 T cells expressing IFNg.

Pt #	IFNg (REN)	Pre-Mobilization	Pre-Infusion #1	Pre-Infusion #2	Pre-Infusion #3	Post 1 month	Post 3 month	Post 6 month
PM03	CD4/IFNg	0.21	0.39	1.23	3.27	1	1.85	3.42
	CD8/IFNg	0.42	3.43	11.33	13.3	3.34	4.61	9.22
PM05	CD4/IFNg	0.07	0.33	0.39	4.08	3.82	0.19	0.31
	CD8/IFNg	0.49	0.39	1.25	11.99	11.76	1.4	0.86
PM05	CD4/IFNg	0.07	0.33	0.39	4.08	3.82	0.19	0.31
	CD8/IFNg	0.49	0.39	1.25	11.99	11.76	1.4	0.49
PM09	CD4/IFNg	0.55	5.2	1.27	2.53	1.2	0.67	0.35
	CD8/IFNg	0.7	2.6	10.63	6.68	7.31	5.1	3.61
PM10	CD4/IFNg	0.23	0.20	0.50	0.17	0.42	0.56	0.52
	CD8/IFNg	2.30	3.20	5.47	0.71	4.20	3.69	4.32

0.39 1.25

TREATMENT RELATED ADVERSE EVENTS

Subject ID	AE	Start Date	CTC Grade	Relationship to CT-011	Relationship toVaccine	Action Taken Regarding TX	Outcome
PM03	Leukopenia	3/14/11	1	POSSIBLE	N/A	NONE	RESOLVED
PM03	Leukopenia	5/2/11	1	POSSIBLE	N/A	NONE	RESOLVED
PM03	Leukopenia	5/23/11	1	POSSIBLE	N/A	NONE	RESOLVED
PM03	Leukopenia	7/11/11	2	POSSIBLE	N/A	NONE	RESOLVED
PM03	Leukopenia	7/13/11	1	POSSIBLE	N/A	NONE	ONGOING
PM03	ANC	5/9/11	1	POSSIBLE	N/A	NONE	RESOLVED
PM03	ANC	5/23/11	1	POSSIBLE	N/A	NONE	RESOLVED
PM03	ANC	6/10/11	2	POSSIBLE	N/A	NONE	RESOLVED
PM03	ANC	7/11/11	3*	POSSIBLE	N/A	NONE	RESOLVED
PM03	ANC	7/13/11	1	POSSIBLE	N/A	NONE	RESOLVED
PM03	ANC	9/2/11	2	POSSIBLE	N/A	NONE	RESOLVED
PM03	ANC	9/30/11	1	POSSIBLE	N/A	NONE	RESOLVED
PM03	Allergic Rhinitis	7/11/11	1	POSSIBLE	N/A	NONE	RESOLVED
PM04	Diarrhea	5/5/11	1	PROBABLE	N/A	NONE	RESOLVED
PM04	Diarrhea	7/27/11	1	POSSIBLE	N/A	NONE	RESOLVED
PM04	Diarrhea	9/5/11	1	POSSIBLE	N/A	NONE	RESOLVED
PM04	Pain, Joint	8/27/11	2	POSSIBLE	N/A	NONE	RESOLVED
PM04	Night Sweats	9/3/11	1	POSSIBLE	N/A	NONE	RESOLVED
PM04	Fatigue	8/27/11	2	POSSIBLE	N/A	NONE	RESOLVED
PM04	Fatigue	9/18/11	1	POSSIBLE	N/A	NONE	RESOLVED
PM05	Diarrhea	7/7/11	1	POSSIBLE	N/A	NONE	RESOLVED
PM05	Diarrhea	7/31/11	1	POSSIBLE	N/A	NONE	RESOLVED
PM05	Diarrhea	9/27/11	1	POSSIBLE	N/A	NONE	RESOLVED
PM05	Diarrhea	10/19/11	1	POSSIBLE	N/A	NONE	RESOLVED
PM07	diarrhea	3/6/12	1	POSSIBLE	N/A	NONE	RESOLVED
PM09	Diarrhea	10/10/11	1	POSSIBLE	N/A	NONE	RESOLVED
PM09	Rash	10/1/11	2	POSSIBLE	N/A	NONE	RESOLVED
PM09	Thyroid Function, Low	10/31/11	1	POSSIBLE	N/A	NONE	RESOLVED
PM09	Eosinophils, Elevated	12/12/11	1	POSSIBLE	N/A	NONE	RESOLVED
PM10	Diarrhea	2/2/12	1	PROBABLY	N/A	NONE	RESOLVED
PM10	Diarrhea	2/13/12	1	POSSIBLE	N/A	NONE	RESOLVED
PM10	Diarrhea	2/23/12	1	PROBABLY	N/A	NONE	RESOLVED
PM10	Diarrhea	4/27/12	1	PROBABLY	N/A	NONE	RESOLVED
PM10	Nausea	2/1/12	1	PROBABLY	N/A	NONE	RESOLVED

Subject ID	AE	Start Date	CTC Grade	Relationship to CT-011	Relationship toVaccine	Action Taken Regarding TX	Outcome
PM10	Thyroid Function, Low	3/13/12	1	POSSIBLE	N/A	NONE	RESOLVED
PM15	Weakness	4/5/12	1	POSSIBLE	N/A	NONE	RESOLVED
PM15	Periorbital Swelling	4/5/12	1	POSSIBLE	N/A	NONE	RESOLVED
PM19	Leukopenia	6/4/2012	1	POSSIBLE	N/A	NONE	RESOLVED
PM19	Leukopenia	7/2/2012	1	POSSIBLE	N/A	NONE	RESOLVED
PM19	Leukopenia	7/23/2012	1	POSSIBLE	N/A	NONE	RESOLVED
PM19	Leukopenia	9/4/2012	1	POSSIBLE	N/A	NONE	RESOLVED
PM19	Diarrhea	7/15/2012	1	POSSIBLE	N/A	NONE	RESOLVED
PM19	Diarrhea (intermittent)	8/14/2012	2	POSSIBLE	N/A	NONE	RESOLVED
PM19	Diarrhea (intermittent)	11/2012	1	POSSIBLE	N/A	NONE	RESOLVED
PM19	Lymphopenia	7/23/2012	1	POSSIBLE	N/A	NONE	RESOLVED
PM19	Arthralgia, hands	11/2012	1	POSSIBLE	N/A	NONE	RESOLVED
PM29	Myalgias	3/7/2013	1	UNRELATED	POSSIBLE	NONE	RESOLVED
PM29	Arthralgia, R ankle	3/11/2013	1	UNRELATED	POSSIBLE	NONE	RESOLVED
PM29	Vaccine Site Reaction	3/11/2013	1	UNRELATED	DEFINITELY	NONE	RESOLVED
PM29	Ecchymosis, vaccine site	3/13/2013	1	UNRELATED	DEFINITELY	NONE	RESOLVED
PM29	Facial Flushing	3/10/2013	1	UNRELATED	POSSIBLE	NONE	RESOLVED
PM29	ANC	3/14/2013	1	UNRELATED	POSSIBLE	NONE	RESOLVED
PM29	Leukopenia	3/14/2013	1	UNRELATED	POSSIBLE	NONE	RESOLVED
PM29	Flu-like Symptoms	3/14/2013	1	POSSIBLE	UNRELATED	NONE	RESOLVED
PM29	Leukopenia	4/4/2013	1	POSSIBLE	UNRELATED	NONE	RESOLVED
PM29	ANC	4/4/2013	1	POSSIBLE	UNRELATED	NONE	RESOLVED

*The episode of grade 3 low ANC resolved to grade 1 after two days without growth factor support. This event did not meet TLT criteria.

Treatment Related Serious Adverse Events:

There have been no serious adverse events related to study treatment.

Treatment Summary of Subjects that Died While on Study:

There have been two unrelated deaths on study. The participants had not initiated study treatment. One participant died on 11/5/10 after suffering a cardiac arrest in his home; the event was reported to the Dana Farber Harvard Cancer Center IRB on 11/11/10. Another participant committed suicide on 1/19/12; the event was reported to the Dana Farber Harvard Cancer Center

IRB on 1/20/12. Although the unrelated deaths did not meet reporting criteria to the FDA, both were nevertheless communicated to the FDA as the events were representative of deaths on study (FDA1571: S268 sent on 11/15/10, and FDA1571: S295 sent on 1/20/12,). At RMC, one participant came off study prior to initiating study treatment to pursue only standard of care therapy.

C. REPORTABLE OUTCOMES

There are no updated reportable outcomes since last year.

D. CONCLUSIONS

The clinical trial (DF-HCC protocol 09-061) is open to accrual at both the Dana Farber Harvard Cancer Center (Boston), and Rambam Medical Center (Haifa, Israel). To date, 27 patients have been enrolled into Cohort 1, and 16 patients have been enrolled to Cohort 2. 14 patients have received at least two infusions of CT-011. The remaining patients are undergoing pre-transplant therapy/transplant. CT-011 has been well tolerated, with possibly related adverse events consisting of transient grade 1-2 leukopenia, diarrhea, fatigue, arthralgia, rash, and peri-orbital edema. One patient developed grade 3 neutropenia, which resolved after two days without growth factor. Immunologic response was determined by quantifying circulating tumor reactive T cells prior to each dose of CT-011 and at 1, 3, 6 months following the last infusion, as defined by the percentage of T cells expressing IFNg in response to ex vivo exposure to autologous tumor lysate. 12 patients have completed 6 months of follow up after the third dose of CT-011, and 5 have been evaluated for immune response. CT-011 therapy was associated with the dramatic expansion of myeloma specific T cells. We are currently enrolling to the second cohort in which patients receive CT-011 in addition to the DC/MM fusion vaccine. Clinical and immunological response to the study treatment will be assessed.