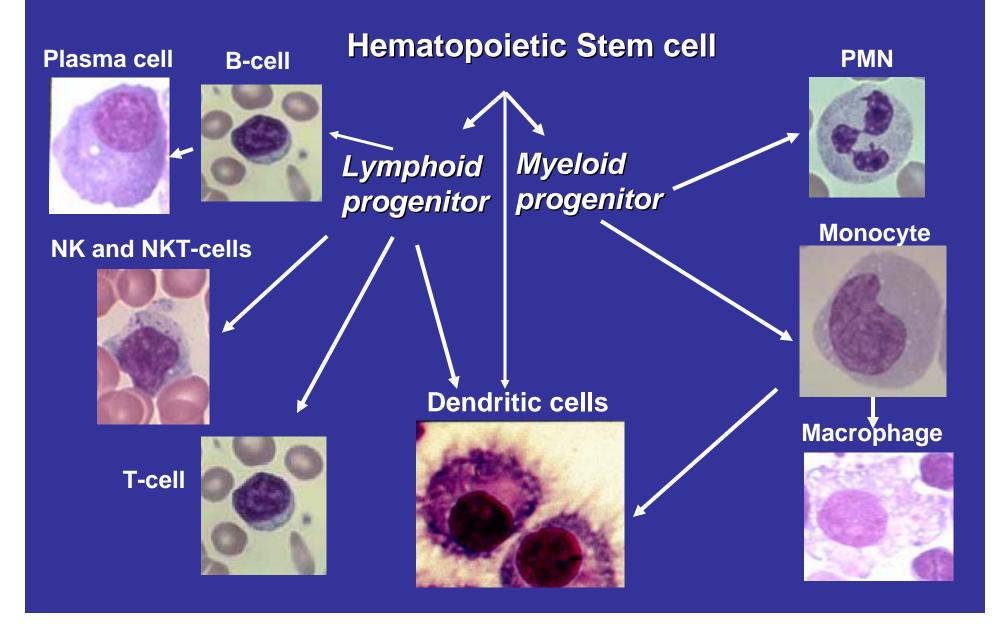
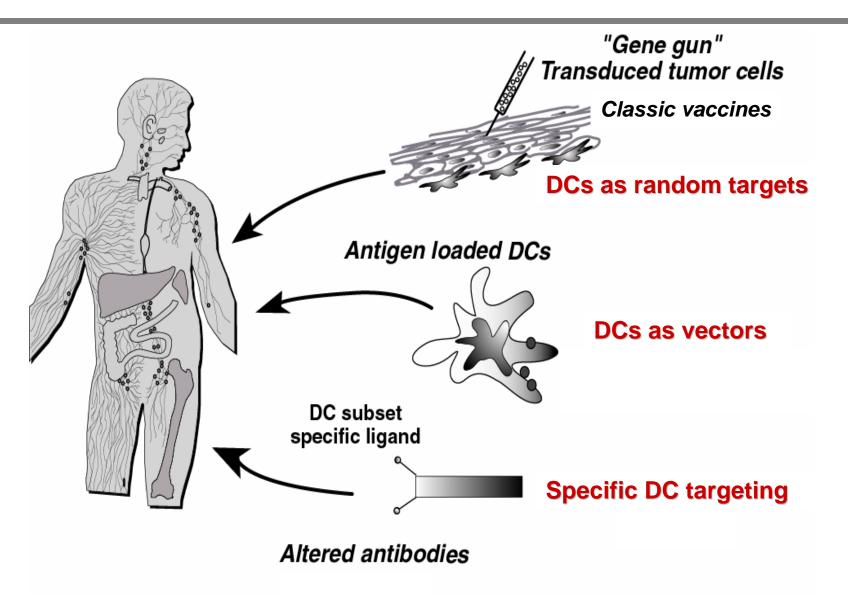


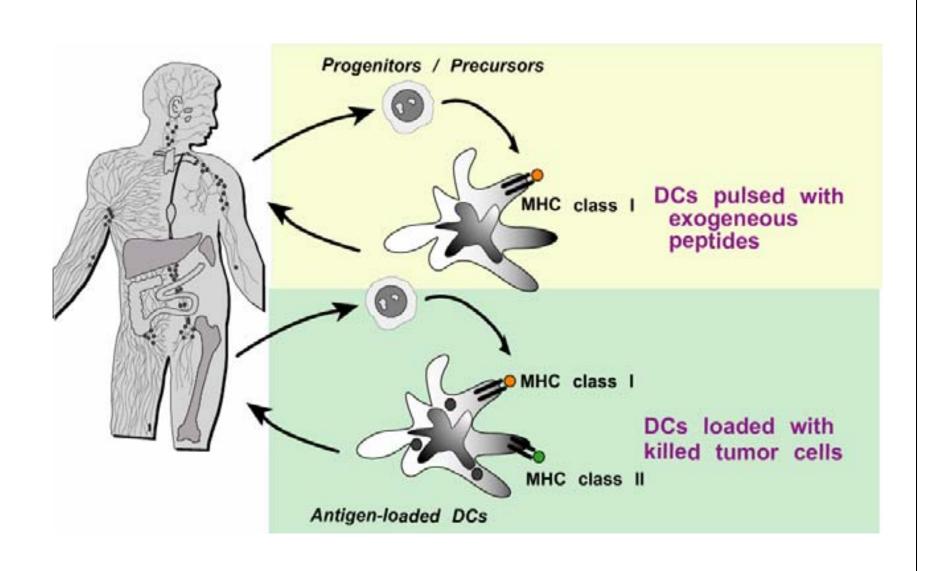
The Immune System



THE CENTRAL ROLE OF DENDRITIC CELLS IN VACCINATION



Ex vivo generated DCs can be loaded with either tumor peptide or with killed tumor cells



Tumor antigen preparations

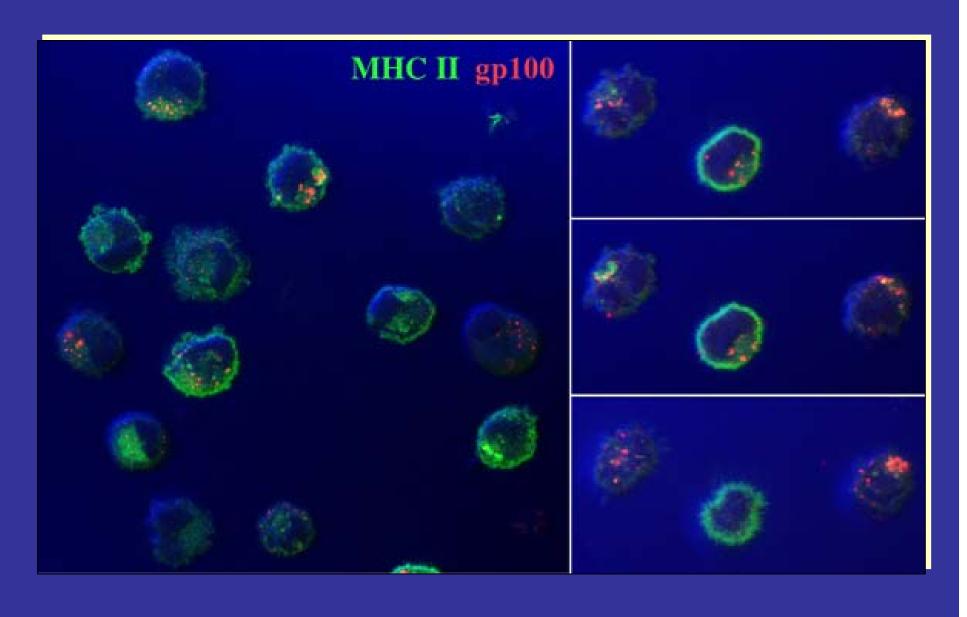
Synthetic peptides

- HLA restriction
- Response limited to few CTL cell clones
- Few MHC class II epitopes
- True tumor rejection antigens ?

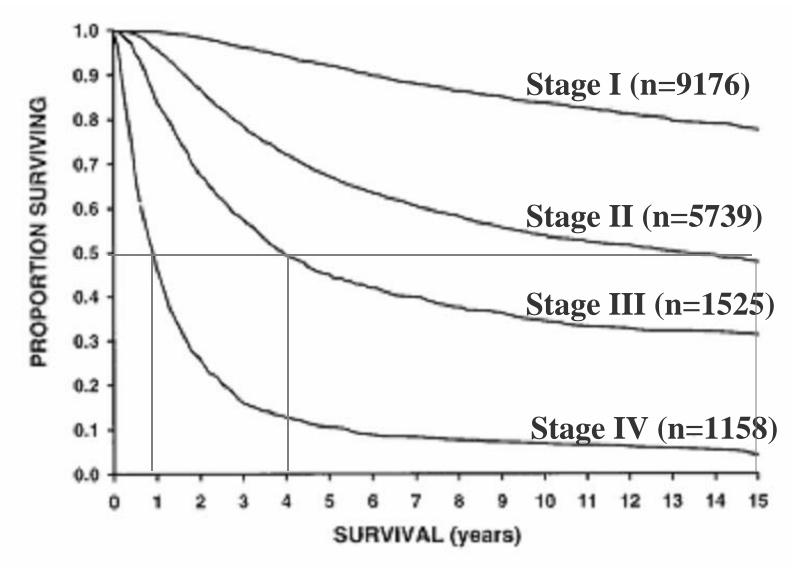
Killed allogeneic tumor cells

- No HLA restriction
- Multiple epitopes and CTL clones
- MHC class II epitopes and CD4 T cells
- Potential Identification of true *in vivo* tumor rejection antigens.

DENDRITIC CELLS CAPTURE MELANOMA CELL BODIES



Melanoma 15-Year Survival versus Stage



From: Balch et al JCO 19:3635, 2001

Stage IV Melanoma M categories and One-Year Survival

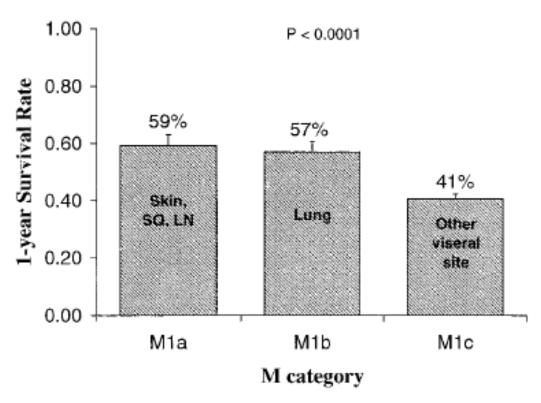


Fig 6. One-year survival rates from the AJCC melanoma staging database comparing the different M categories. There is a significant difference comparing skin, subcutaneous, and lung metastases to all other sites (P < .0001).

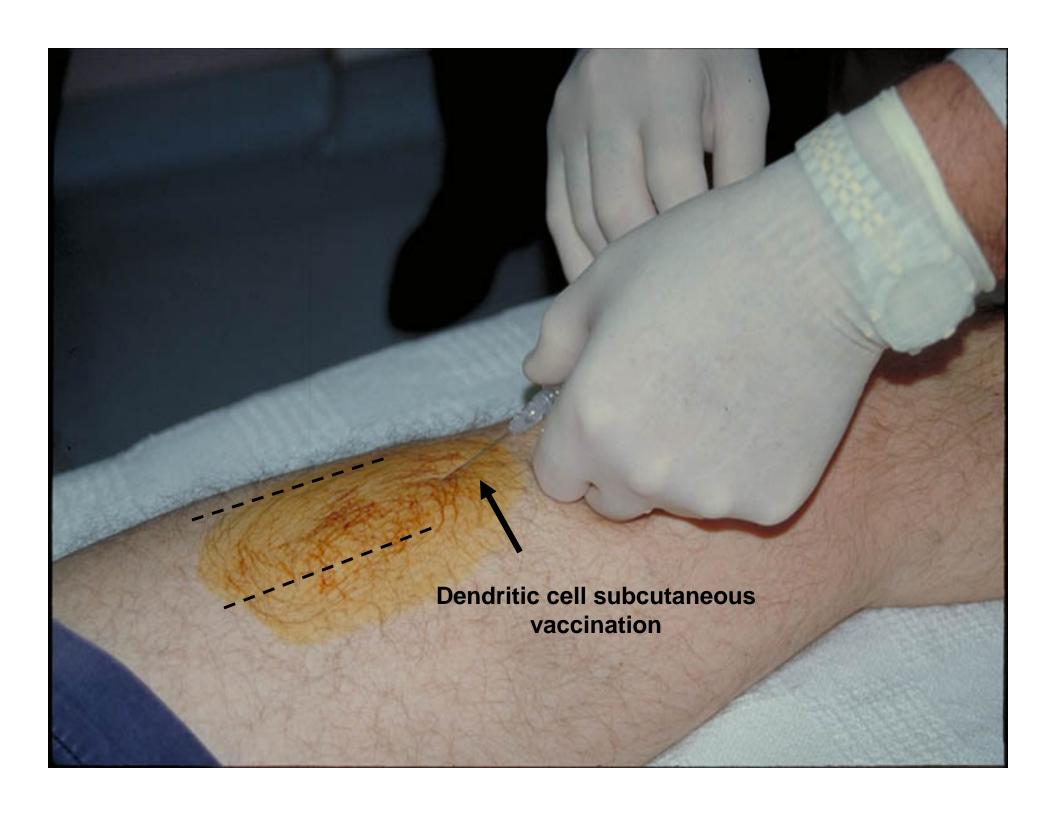
Balch et al JCO 19:3635, 2001

Dendritic Cell Vaccines Trials for Stage IV Melanoma

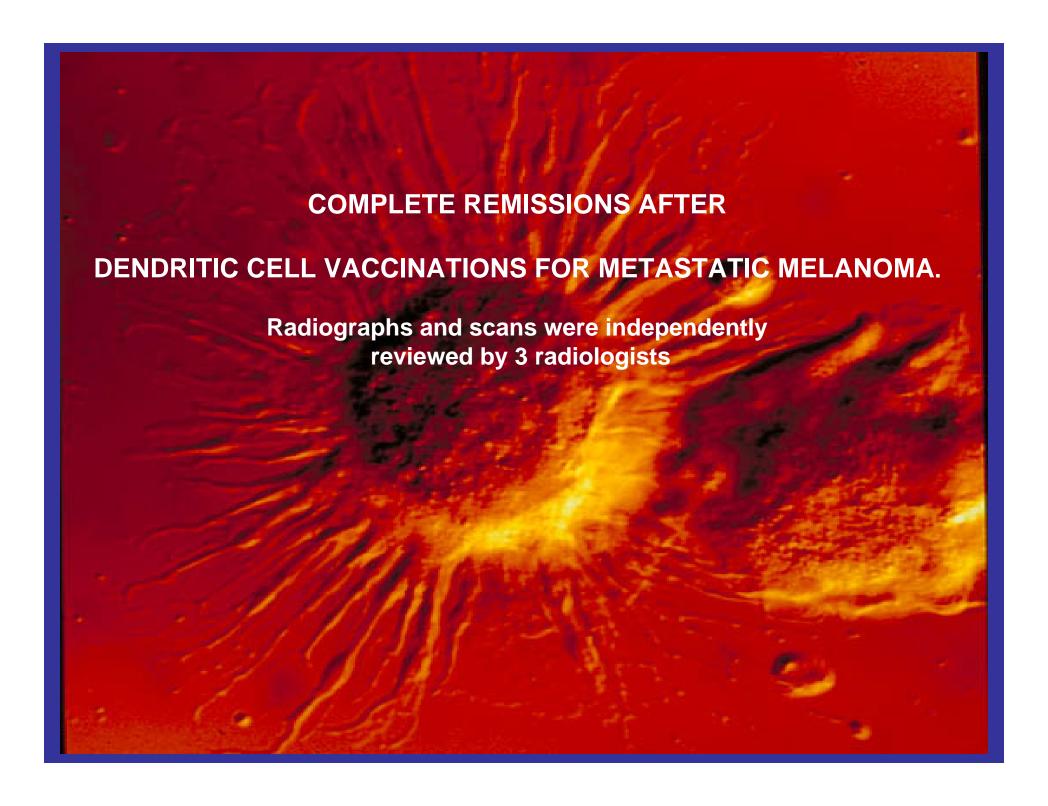
- Trial 1 (098) DCs derived from CD34
 progenitors cultured with Flt-3 L, GM-CSF, TNF α and loaded with HLA-A*0201 melanoma
 peptides and KLH
- Trial 2 (000) DCs as in 098 plus INF-α
- Trial 3 (002) DCs derived from monocytes cultured with IL-4, GM-CSF, TNF-α, CD40-L and loaded with Colo829 melanoma cell line and KLH
- Trial 4 (003) DCs derived from monocytes cultured with GM-CSF, TNF-α and CD40-L loaded with HLA-A*0201 melanoma peptides and KLH

Patient Characteristics

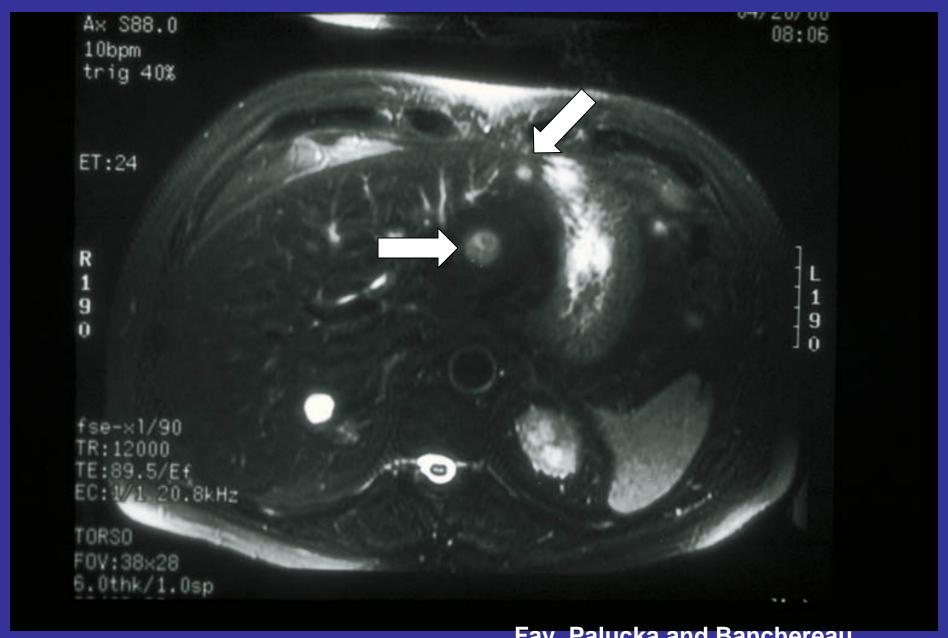
Number of patients	64		
Median age, years (range)	55 (28-75)		
Gender (male/female)	40 (63%)		
Substage of Stage IV, n (%)		Time to Stage IV, n (%)	
M1a	10 (16)	more than 12 months	31 (48)
M1b	19 (30)	12 months or less	33 (52)
M1c	35 (55)		
LDH (elevated/normal)	18 (28%)		
Chemotherapy (yes/no)	26 (41%)		
Response, n (%)		Duration, months	
CR	5 (8)	31, 61+, 87+, 93+, 100+	
PR	2 (3)	8, 53+	
SD	27 (42)	7- 21	
NR/PD	30 (47)		
NE	1 (2)		





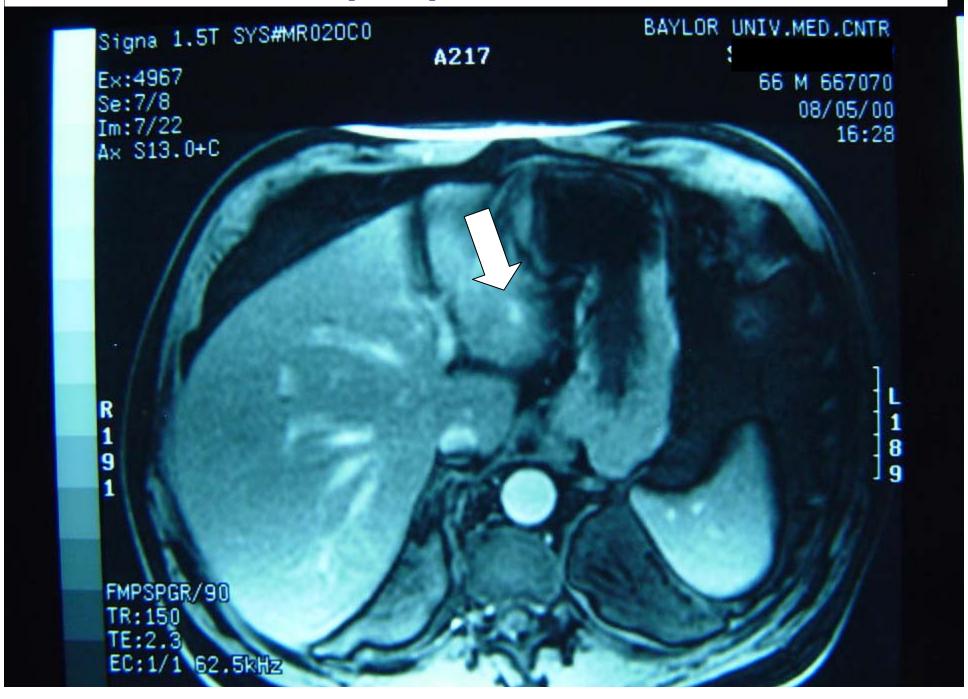


098-004-18 [Mel 21] GS 4-20-00 MRI baseline



Fay, Palucka and Banchereau

098-004-18 [Mel 21] GS 8-5-00 after 4 vaccines



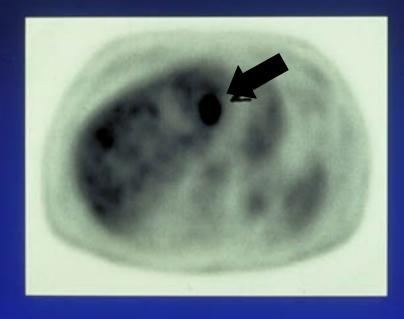
0908-004-18 [Mel 21] GS 12-27-00 MRI post 8 vaccines



Fay, Palucka and Banchereau

4-14-2000

1-15-2001

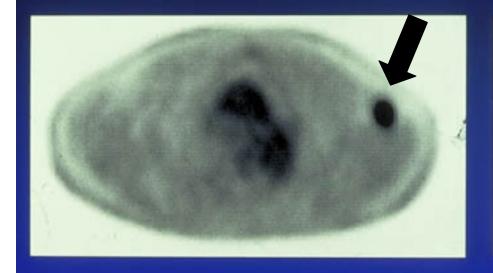


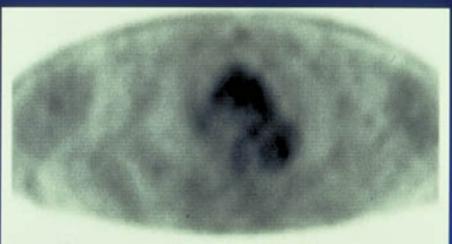


Fay, Palucka and Banchereau

4-14-2000

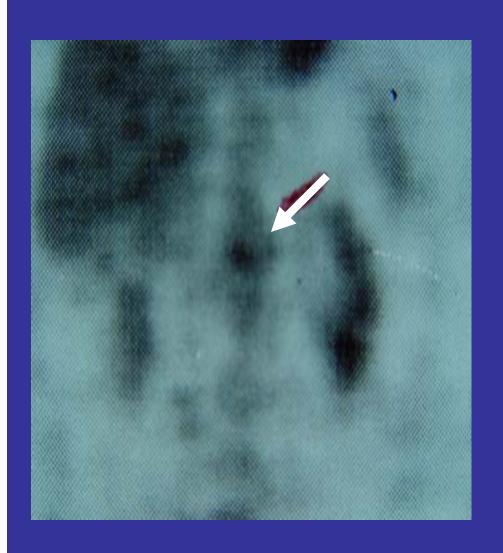
1-15-2001

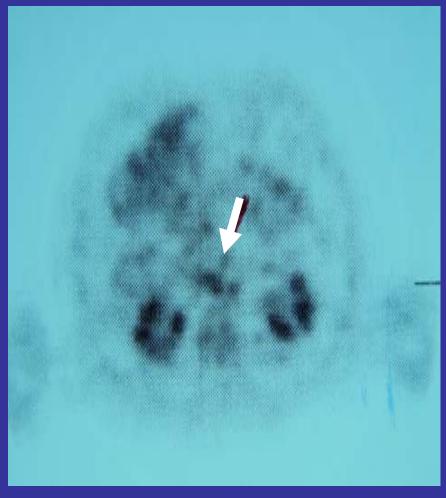




Fay, Palucka and Banchereau

098-004-1 BASELINE PET SCANS (UCSF)



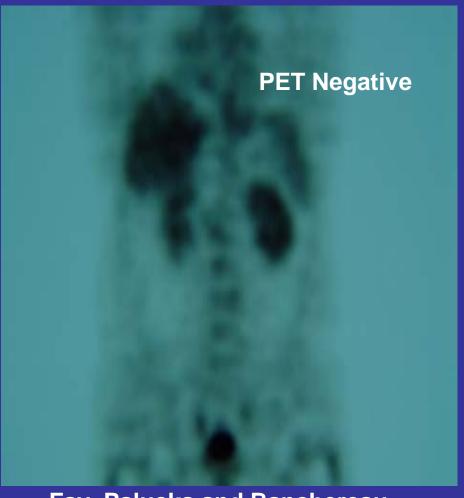


098-004-1 PET SCANS

Baseline at UCSF

After 4 DC Vaccines at BUMC





Fay, Palucka and Banchereau



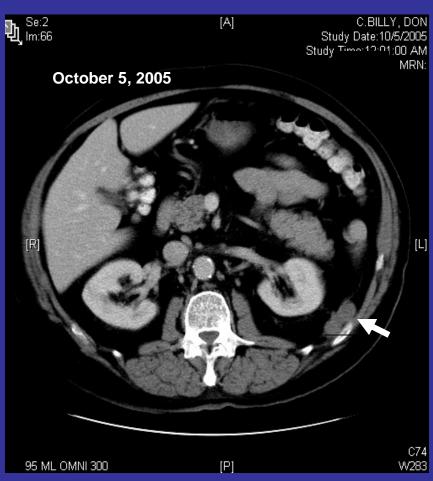


002-094-004

Baseline

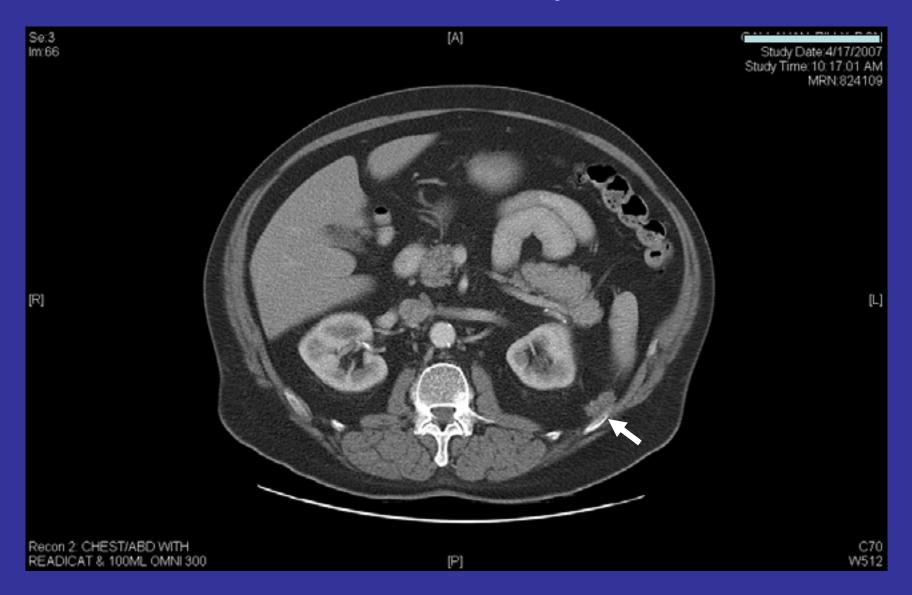


After 8 DC Vaccinations



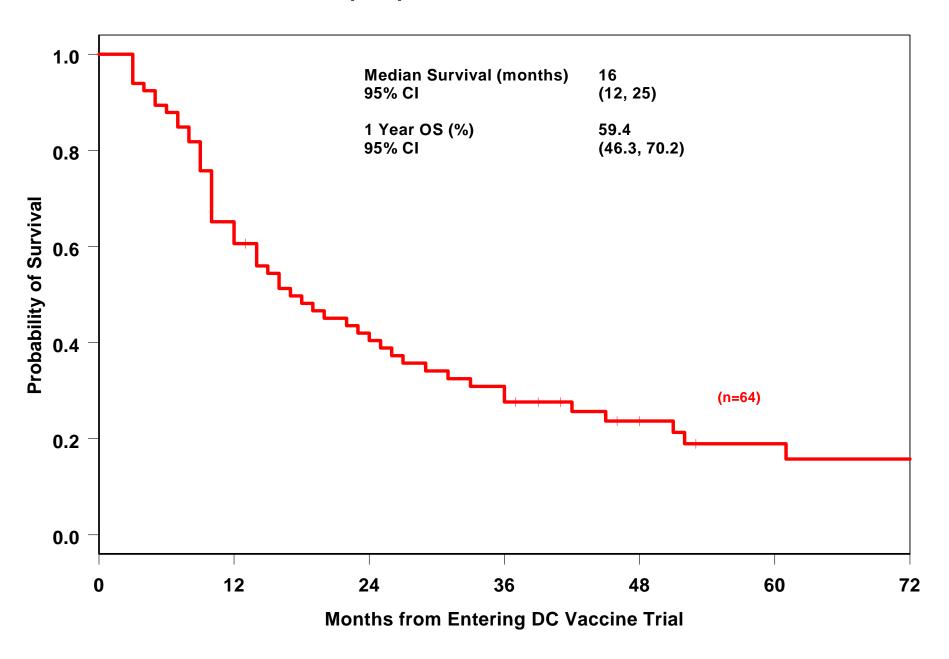
Fay, Palucka and Banchereau

Most Recent Scan April 2007

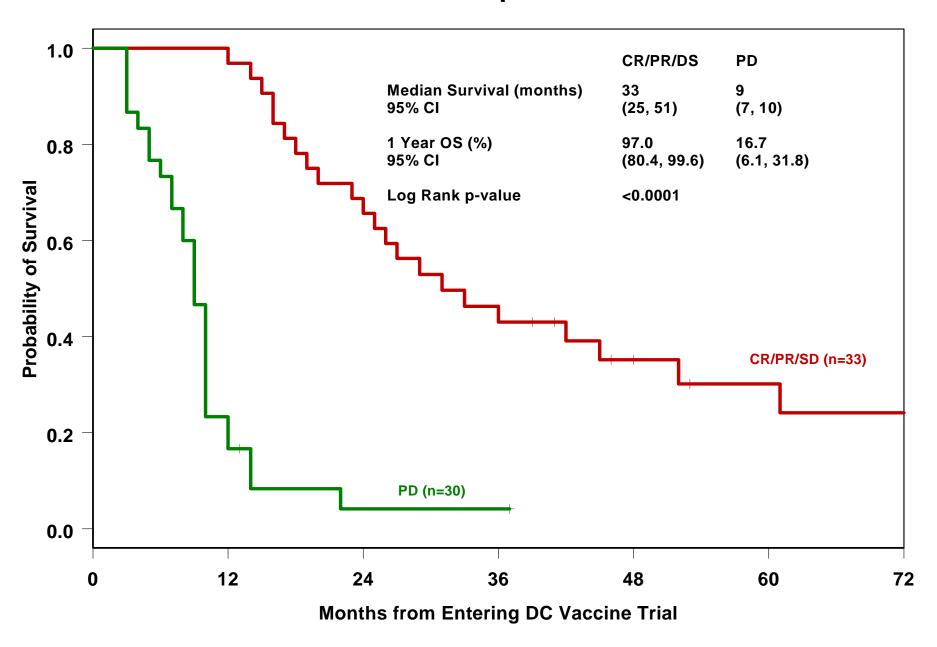


Fay, Palucka and Banchereau

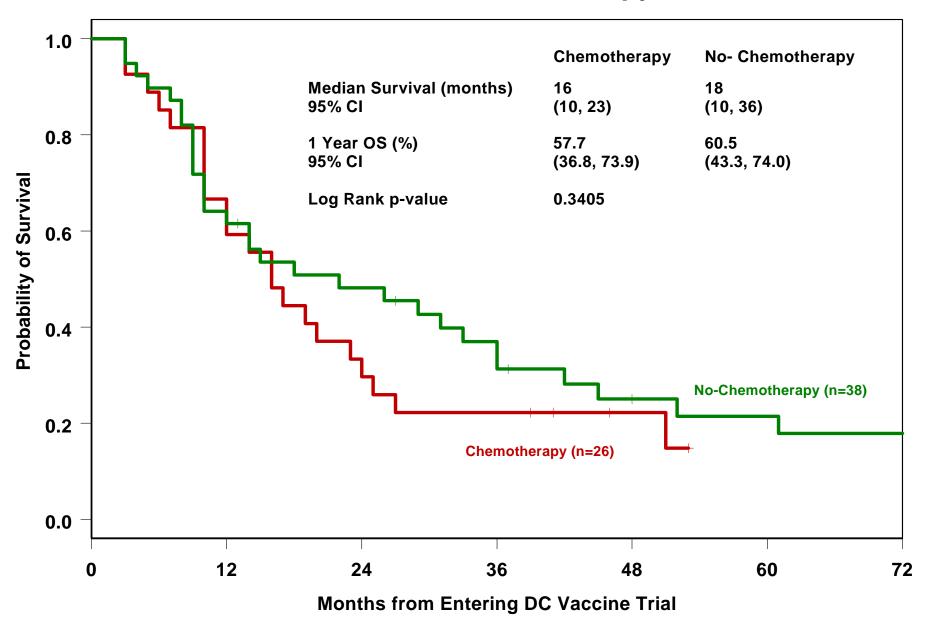
Overall Survival (OS) for Metastatic Melanoma Patients



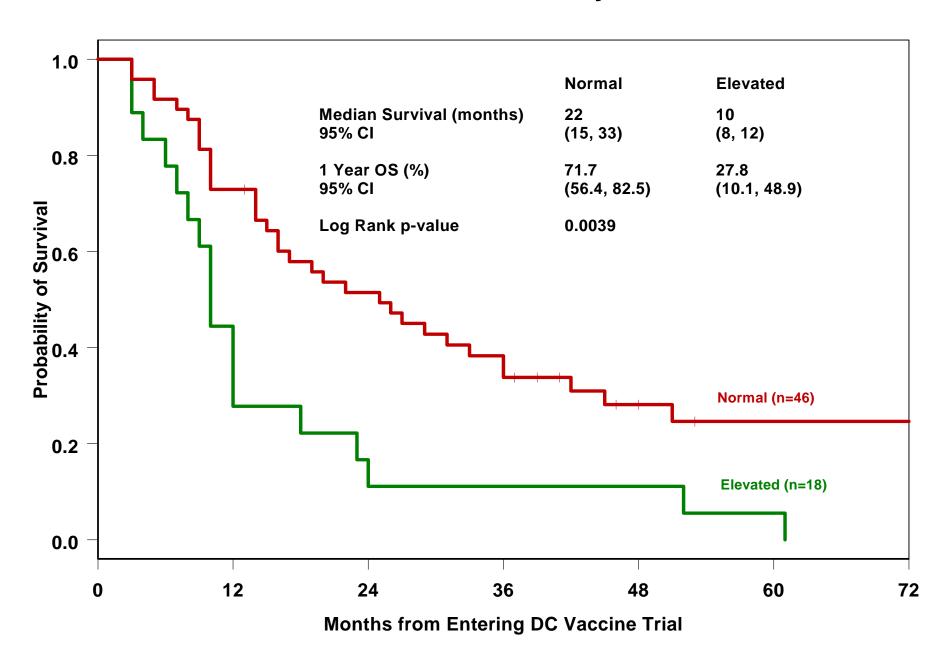
OS: Best Response



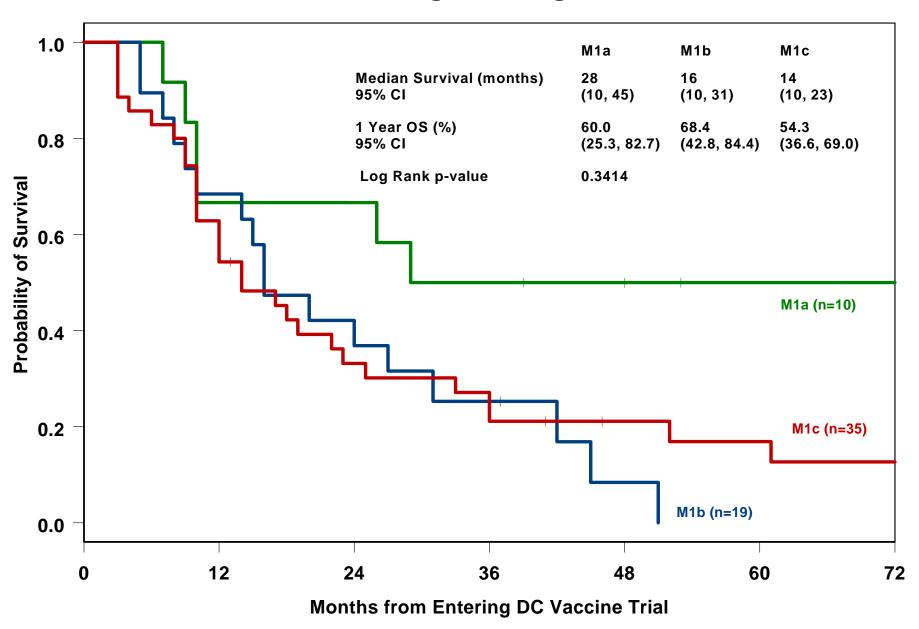
OS: Prior Chemotherapy



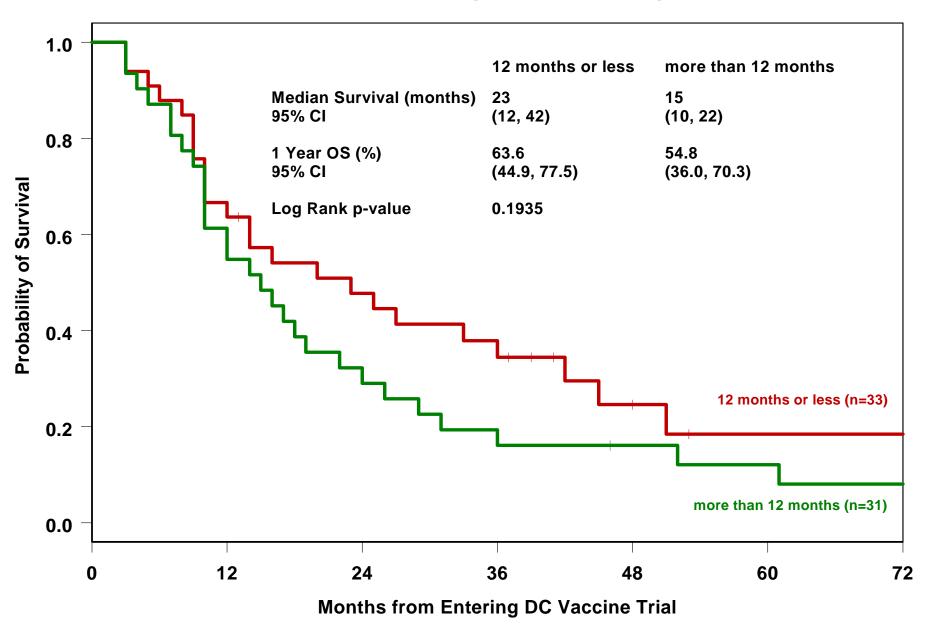
OS: LDH at entry



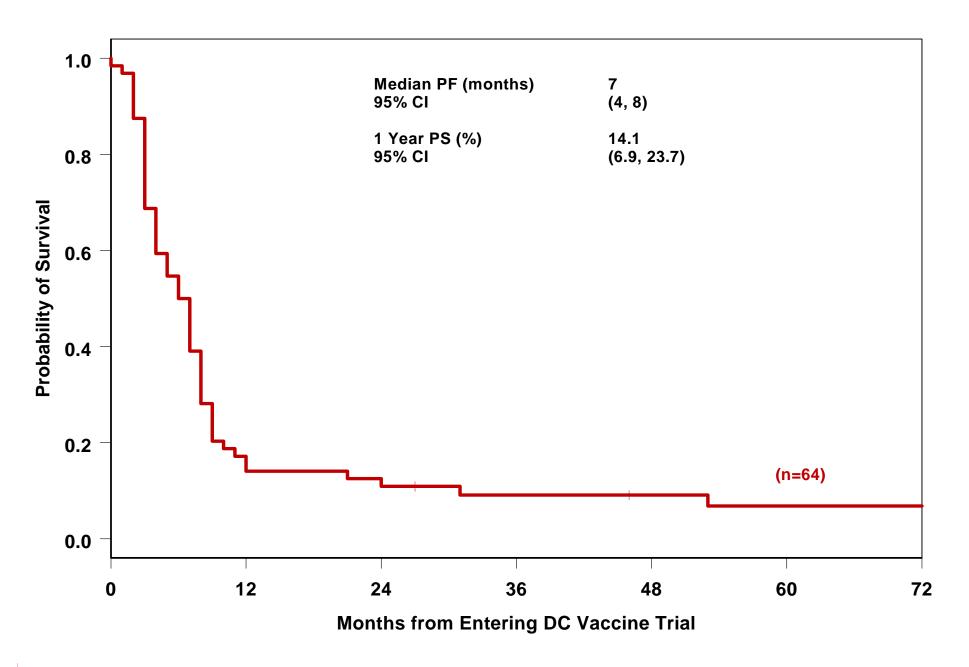
OS: Substage of Stage IV



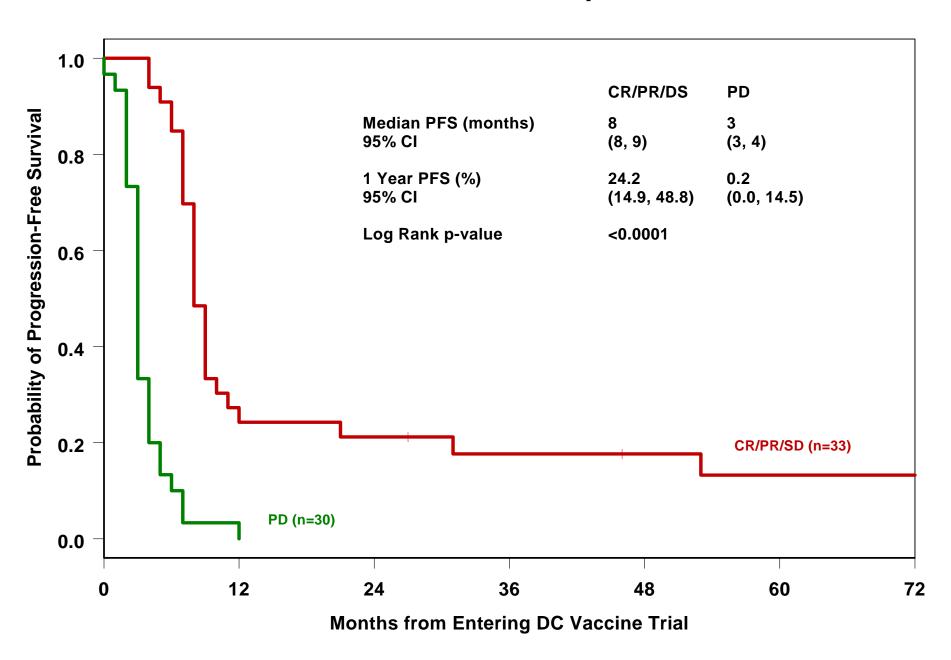
OS: Time from Diagnosis to Stage IV



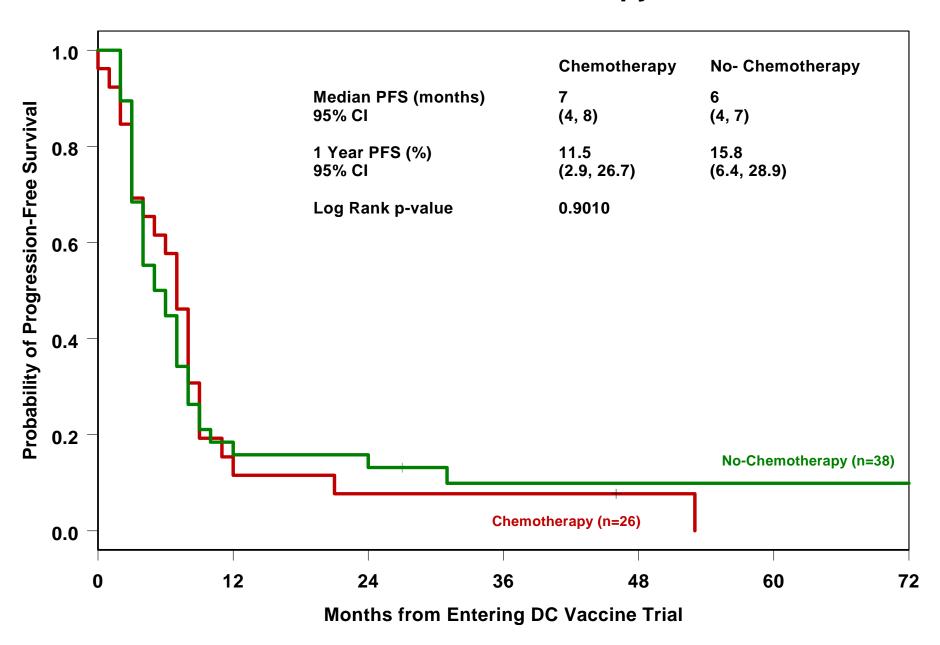
Progression-Free Survival (PFS) for Metastatic Melanoma Patients



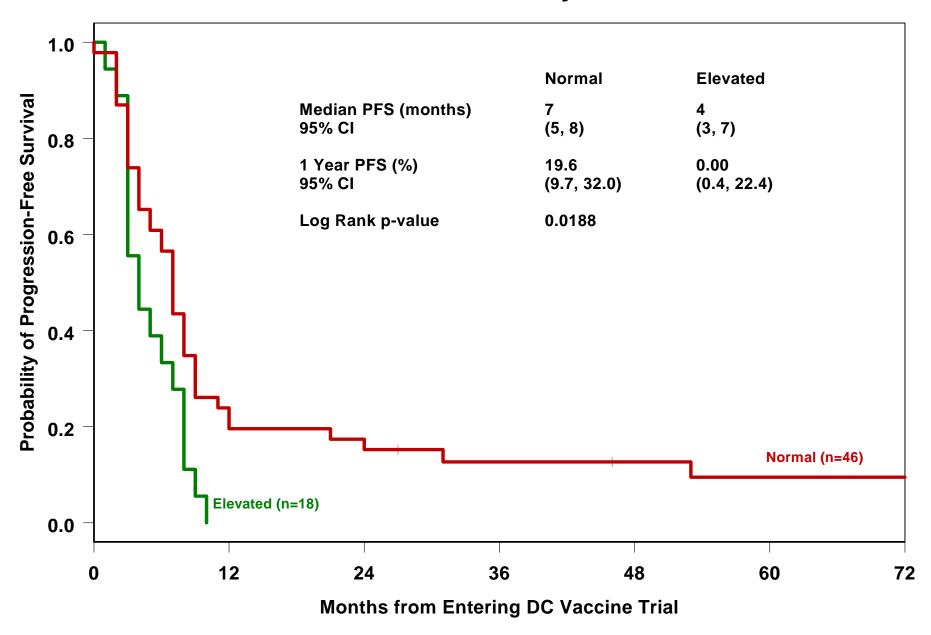
PFS: Best Response



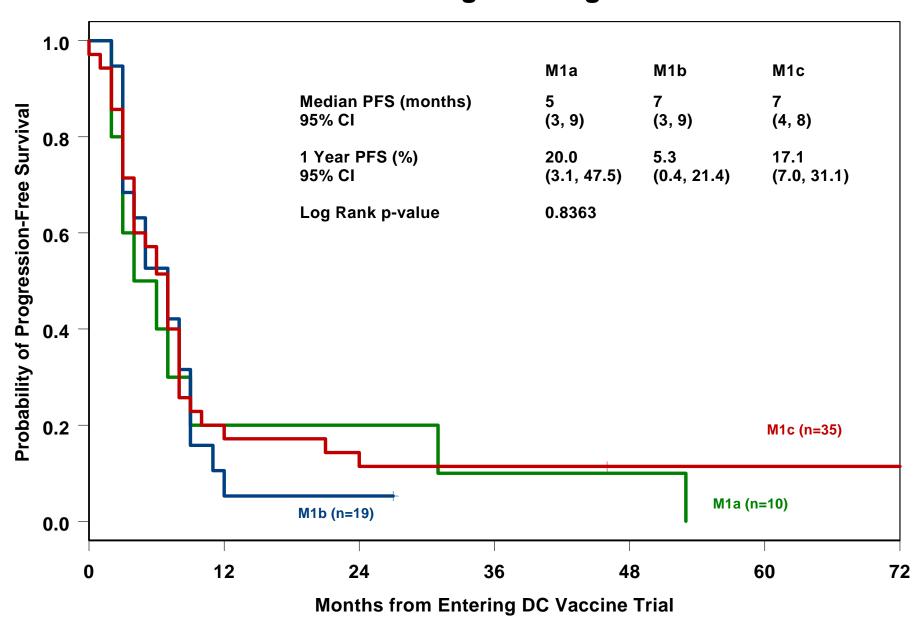
PFS: Prior Chemotherapy



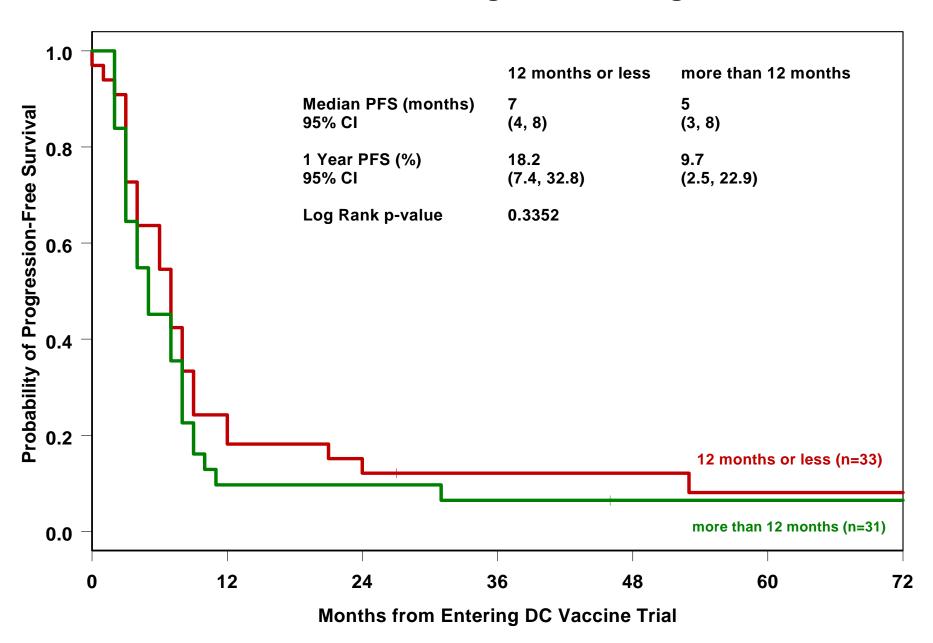
PFS: LDH at entry



PFS: Substage of Stage IV



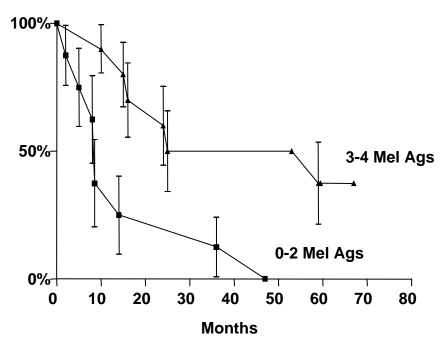
PFS: Time from Diagnosis to Stage IV

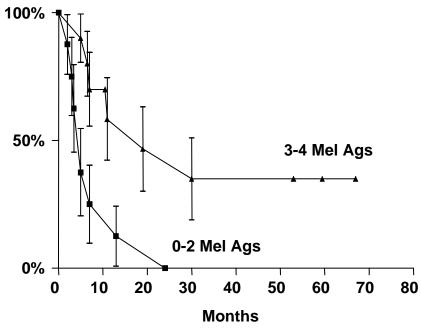


098-004 Clinical Trial

Overall survival from study entry

Progression-free survival from study entry





0-2 Mel Ags - median: 8.5 months; at risk: 5; events: 8
3-4 Mel Ags - median: 42 months; at risk: 5; events: 6
Logrank test p=0.0065
ratio 0.2; 95%Cl -0.14 to 0.55

hazard ratio 3.7; 95%CI 1.6 to 19

0-2 Mel Ags - median: 5 months; at risk: 5; events: 8
3-4 Mel Ags - median: 19 months; at risk: 5; events: 6
Logrank test p=0.01
ratio 0.26; 95%CI -0.08 to 0.6
hazard ratio 3.4; 95%CI 1.45 to 17

Conclusions

- Vaccination of patients with Stage IV melanoma with DCs loaded with melanoma antigens is associated with long term survival in approximately 20 % of patients
- Clinical factors associated with prolonged overall survival in this study include:

disease regression or stable disease during the trial, normal LDH at baseline, M1a Substage

Thanks to our patients

Baylor Foundation, NCI, J. Fordtran, M. Ramsay, BRI M. Stone, Sammons Cancer Center

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 - cGMP Lab:
 - N. Taquet
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 - J. Shay
 - L.Vence
 - J. Connolly
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 - P. Blanco
 - P. Dubsky
 - S. Paczesny
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