



Correlation Between Product Parameters and Overall Survival in 3 Trials of Sipuleucel-T, an Autologous Active Cellular Immunotherapy for the Treatment of Prostate Cancer

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Methods

- The correlation between key product parameters and OS was assessed in patients who received ≥ 1 sipuleucel-T infusion (N=476) using a Cox regression model both unadjusted and adjusted for baseline prognostic variables (PSA [ln] and LDH [ln]), while stratifying by study. This integrated analysis included patients from three randomized studies of sipuleucel-T in metastatic castration-resistant (hormone refractory) prostate cancer: D9901 (n=82), D9902A (n=64) and D9902B (n=330).
- Parameters included cumulative CD54 upregulation, cumulative CD54+ cell count, and cumulative TNC count.¹ The product variables analyzed represent the sum of values infused into each patient (up to 3 infusions).
- CD54 upregulation is the fold increase in the average number of CD54 molecules expressed on final product APCs. CD54 was chosen as a biologically relevant marker because of its role in the immunologic synapse between APCs and T cells, and because its increased expression correlates with APC activation. Experiments have demonstrated that CD54+ APCs take up and present the PA2024 antigen to PAP-restricted T cell lines.

¹Sheikh N, Jones LA. Cancer Immunol. Immunother. 2008; 57: 1381-1390.

Results

Correlation between Overall Survival and Cell Product Parameters

Cell Product Parameters	Unadjusted		Adjusted for PSA and LDH	
	P-value ¹	HR (95% CI) ¹	P-value ²	HR (95% CI) ²
Cumulative CD54 ⁺ Cell Counts (x 10 ⁹)	0.016	0.812 (0.686, 0.962)	0.005	0.794 (0.675, 0.934)
Cumulative TNC Counts (x 10 ⁹)	< 0.001	0.675 (0.556, 0.818)	< 0.001	0.713 (0.588, 0.865)
Cumulative CD54 Upregulation	0.002	0.657 (0.503, 0.859)	0.041	0.760 (0.583, 0.989)

Hazard Ratios (HR) are per unit increase. PSA-prostate specific antigen. LDH-lactate dehydrogenase.

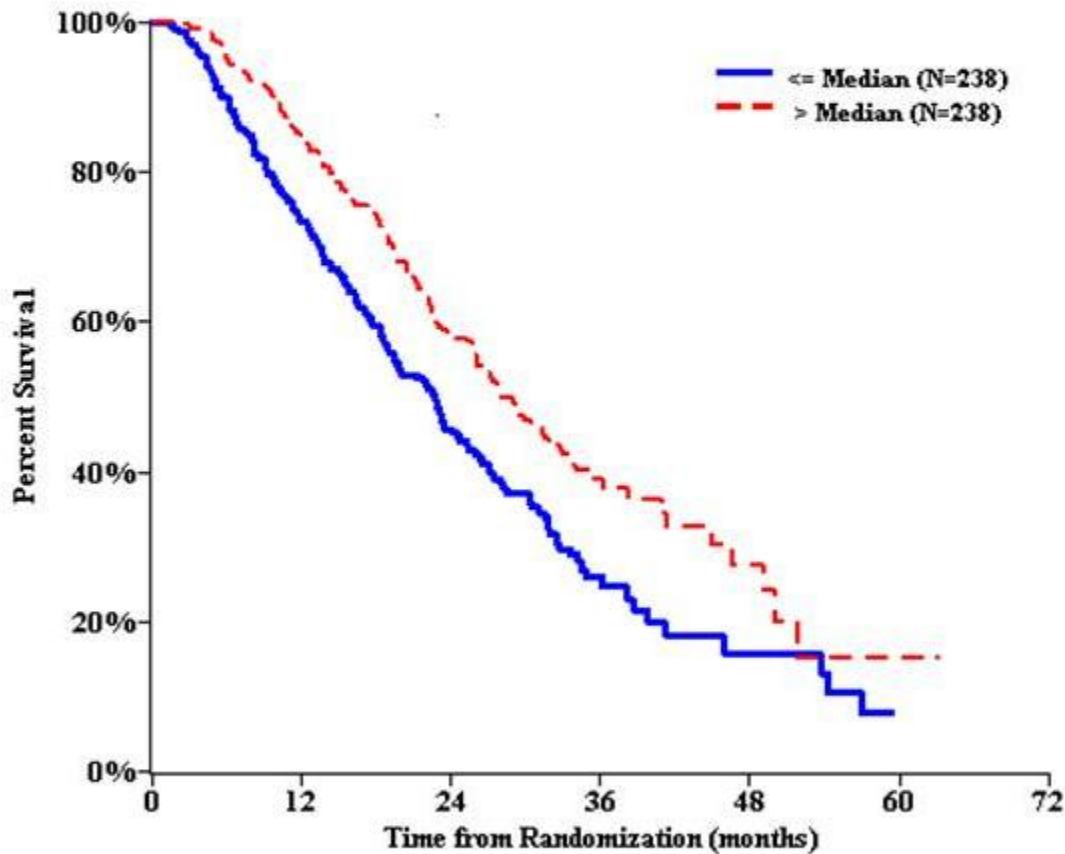
¹From 3 Cox regression models: Each cell product parameter

[Cumulative Upregulation (ln), Cumulative TNC Counts (ln), and Cumulative CD54⁺ Cell Counts (ln)] incorporated as an independent variable in a Cox regression model stratified by study.

²From 3 Cox regression models: Each cell product parameter [Cumulative CD54⁺ Cell Count (ln), Cumulative TNC (ln), and Cumulative Upregulation (ln)] incorporated as an additional independent variable in the primary model with PSA (ln), and LDH (ln) as the common independent variables; all stratified by study.

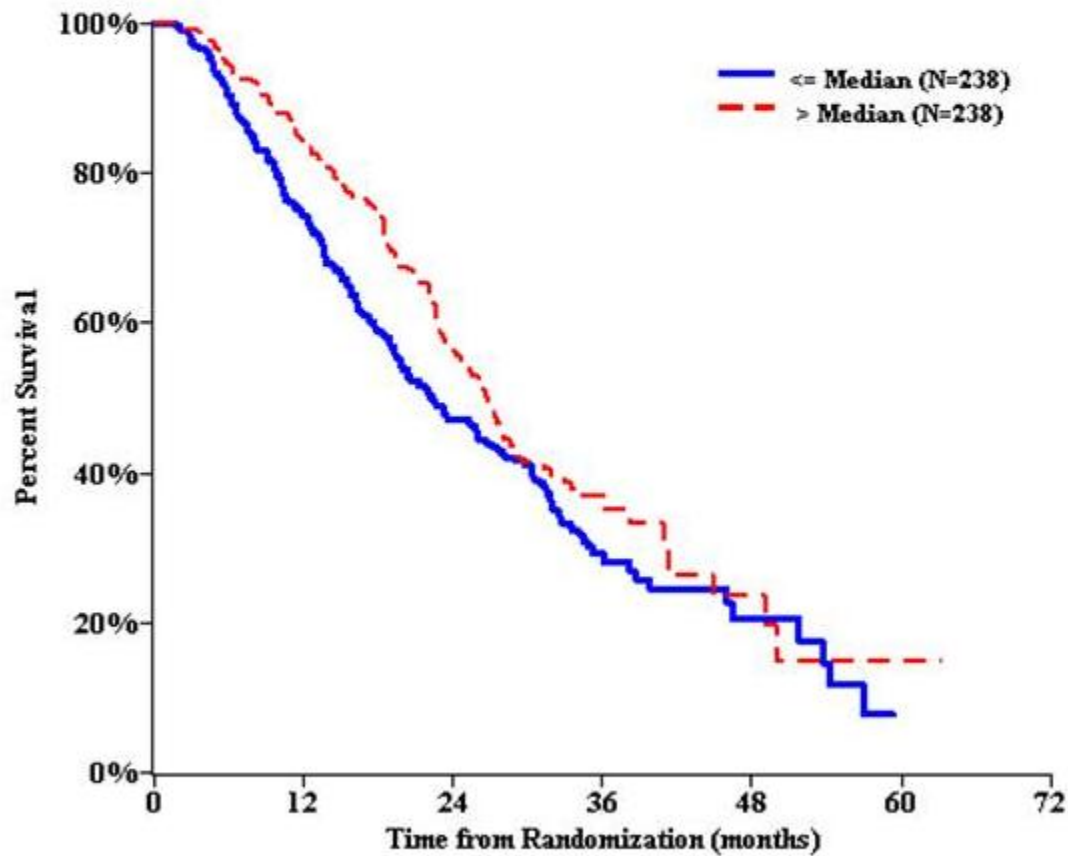
A correlation between each cell product parameter (natural log transformed) and overall survival was observed in both the unadjusted and adjusted Cox models.

Overall Survival by Cumulative Total Nucleated Cell Counts*



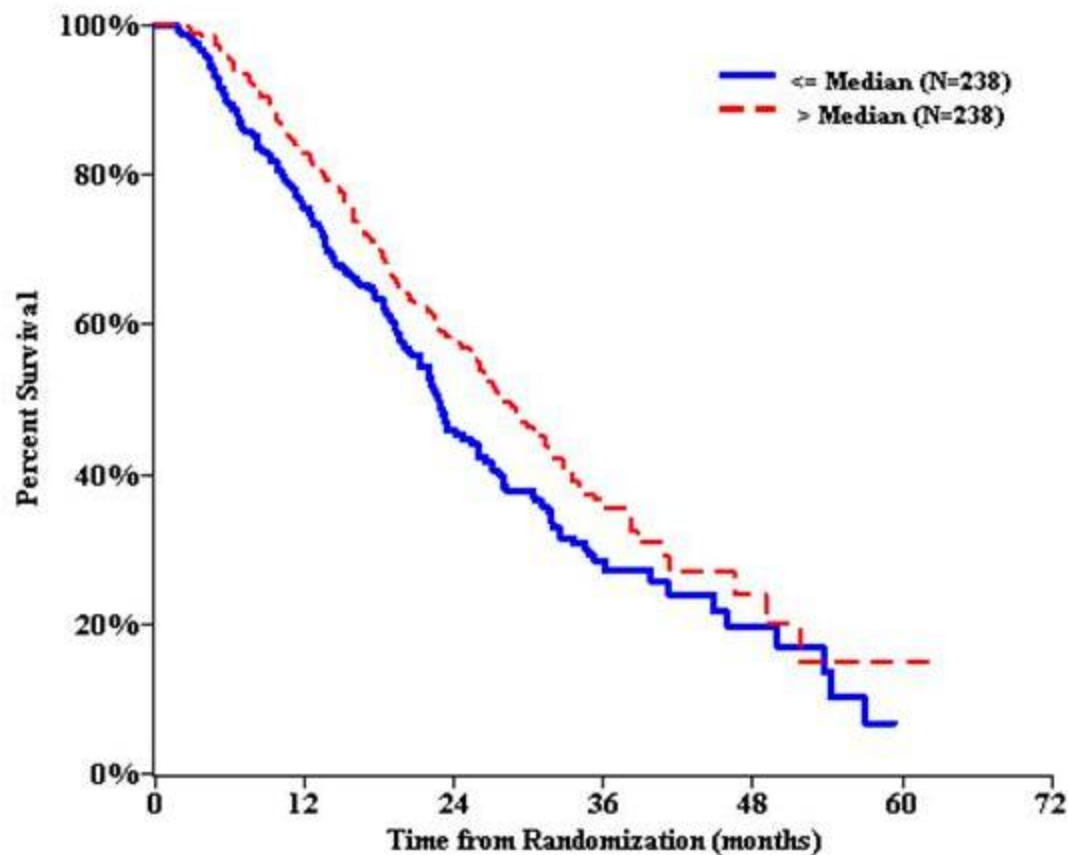
*Sipuleucel-T Patients with ≥ 1 Infusion

Overall Survival by Cumulative CD54 Upregulation*



*Sipuleucel-T Patients with ≥ 1 Infusion

Overall Survival by Cumulative CD54+ Cell Counts*



*Sipuleucel-T Patients with ≥ 1 Infusion

Conclusions

- **There was a significant positive correlation between OS and each of the 3 cell product parameters.**
- **The correlation between overall survival and product parameters appeared to be independent of baseline prognostic factors.**
- **These data support the finding that engagement of the immune system may contribute to the sipuleucel-T survival findings.**