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Sipuleucel-T Immune Parameters and Correlation with Overall Survival

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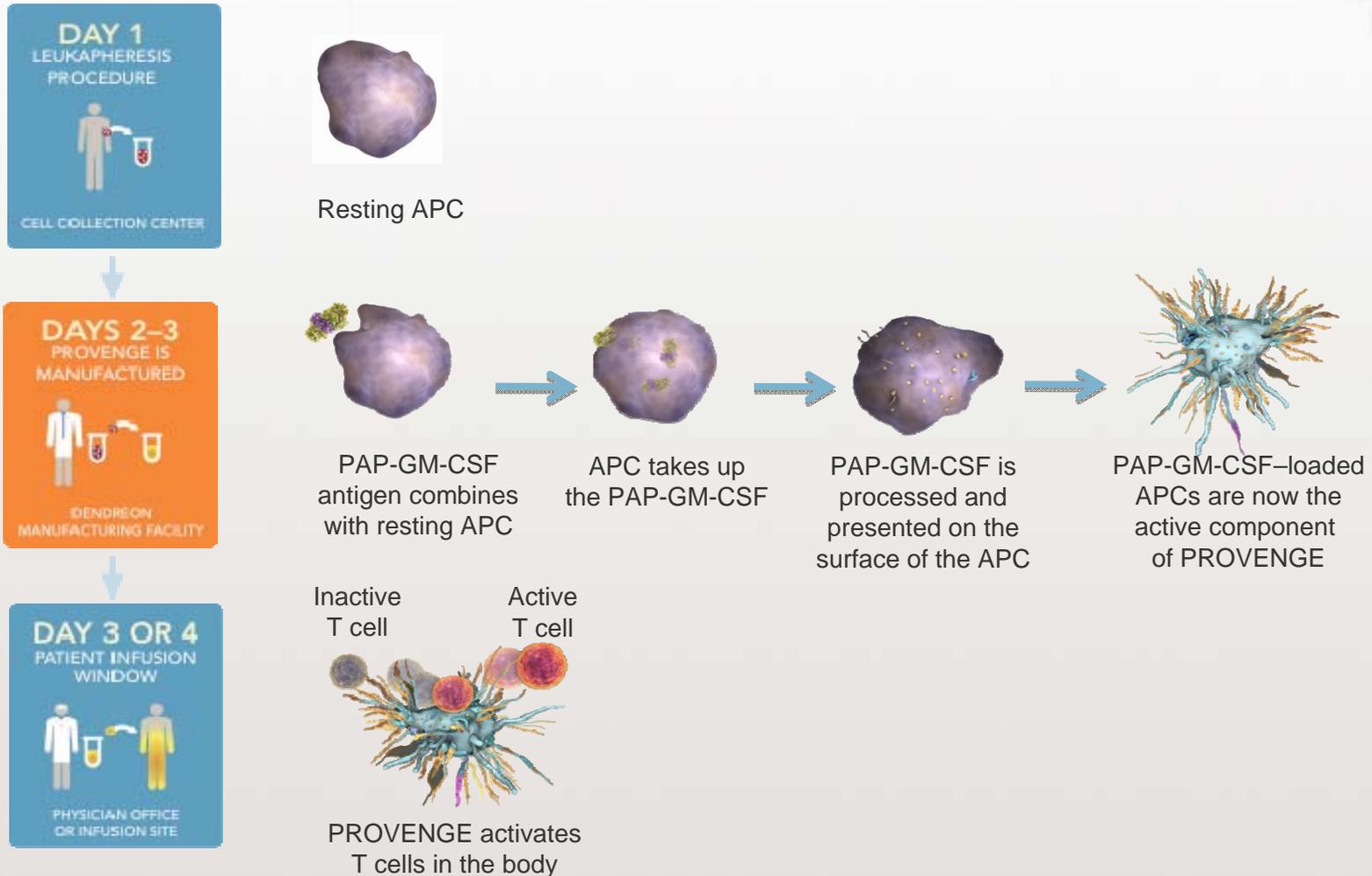
iSBTC "Immuno-Oncology Biomarkers 2010 and Beyond" Meeting

Sept. 30, 2010

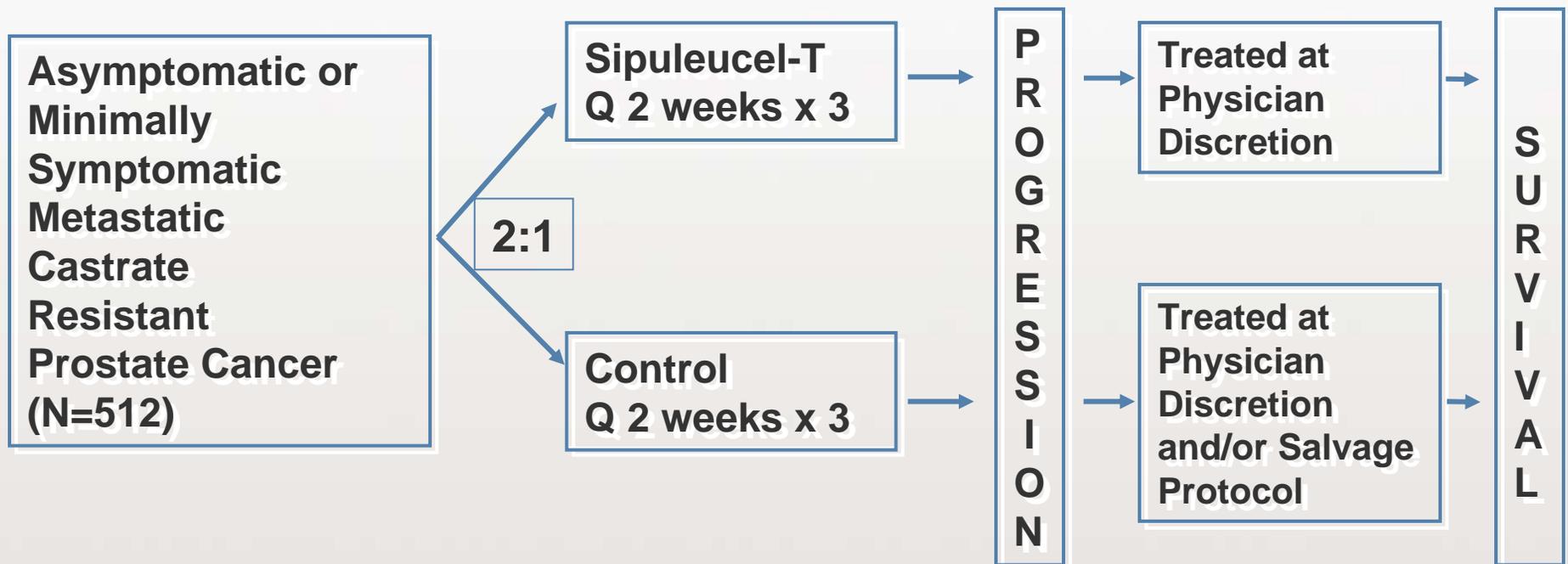
Disclosure

- Employment Dendreon Corporation
 - Chief Medical Officer
 - Salary & equity interest

Sipuleucel-T: Designed to Stimulate a Patient's Immune System



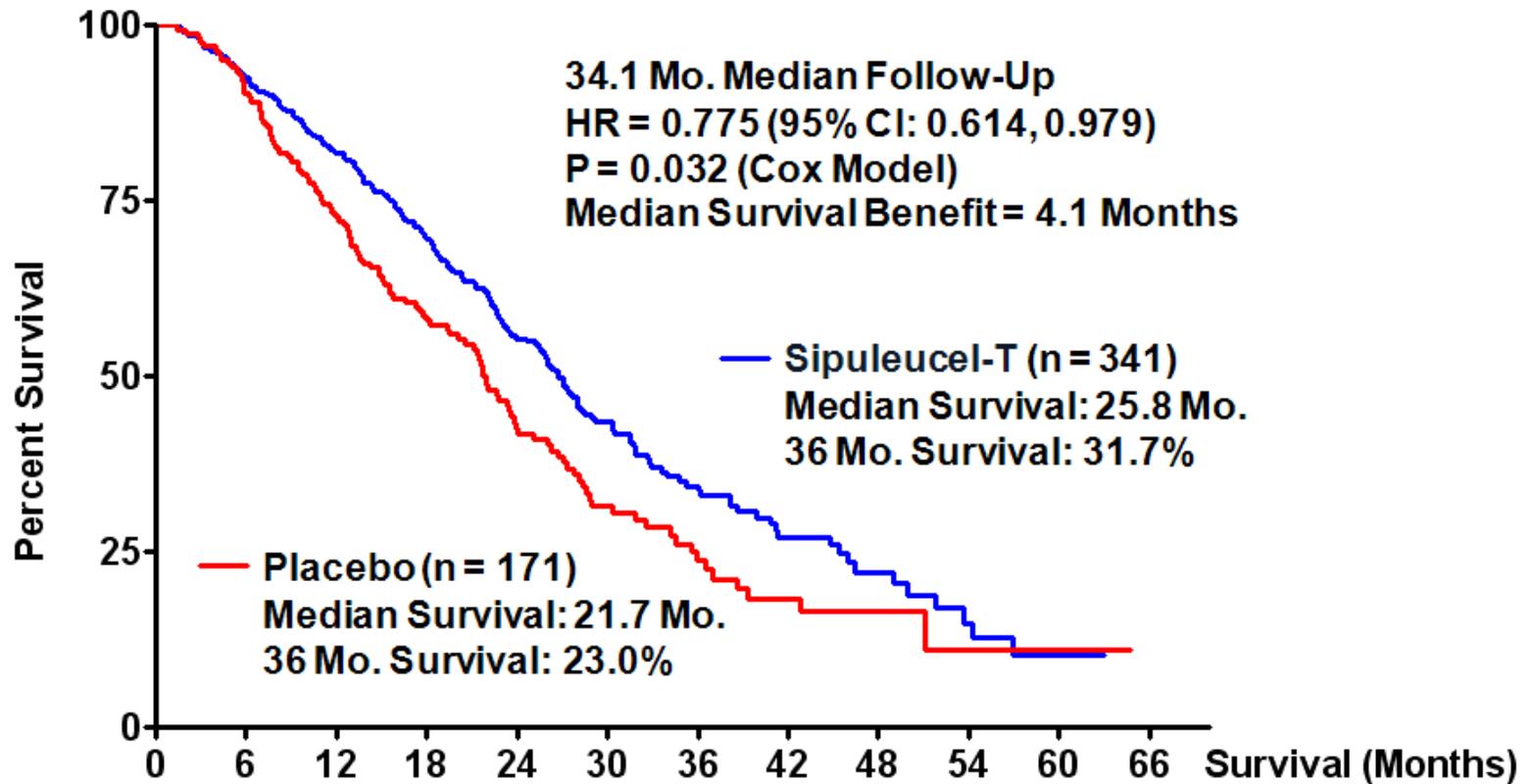
Randomized Phase 3 IMPACT Trial (IMmunotherapy Prostate AdenoCarcinoma Treatment)



Primary Endpoint: Overall Survival

Secondary Endpoint: Objective Disease Progression

IMPACT Overall Survival Intent-to-Treat Population (331 Events)



No. at Risk

Sipuleucel-T	341	274	129	49	14	1
Placebo	171	123	55	19	4	1

Adverse Events More Commonly¹ Reported in Sipuleucel-T Group

Preferred Term	Sipuleucel-T N = 338 %	Control N = 168 %
Chills	54.1	12.5
Pyrexia	29.3	13.7
Headache	16.0	4.8
Influenza-Like Illness	9.8	3.6
Myalgia	9.8	4.8
Hypertension	7.4	3.0
Hyperhidrosis	5.3	0.6
Groin Pain	5.0	2.4

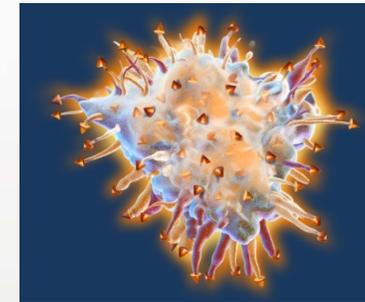
¹ Reported by $\geq 5\%$ of sipuleucel-T patients and having a ≥ 2 -fold difference from control. The majority of the most common AEs were mild or moderate in severity.

Safety results obtained from primary analysis did not substantively change with additional data obtained after study closure.

Sipuleucel-T Product Parameters

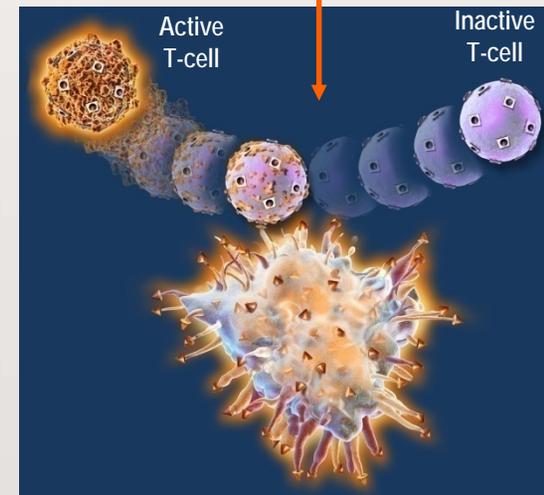
Key product attributes:

- Total nucleated cell count
- CD54 count
- CD54 'upregulation'



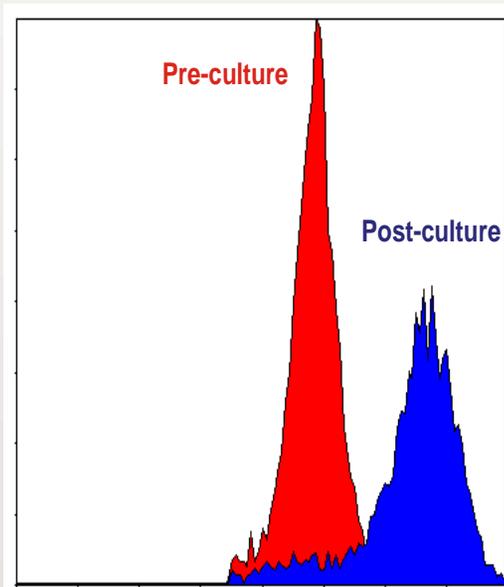
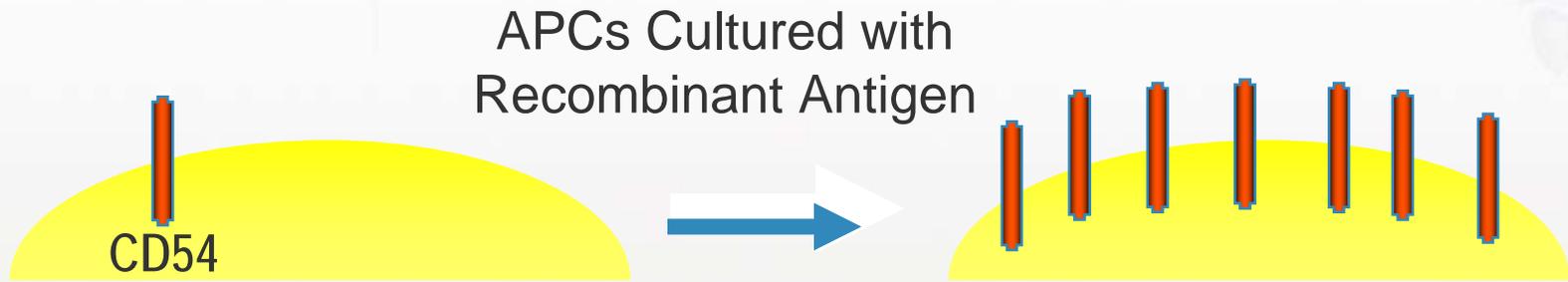
Fully activated, the APC is now sipuleucel-T

INFUSE PATIENT



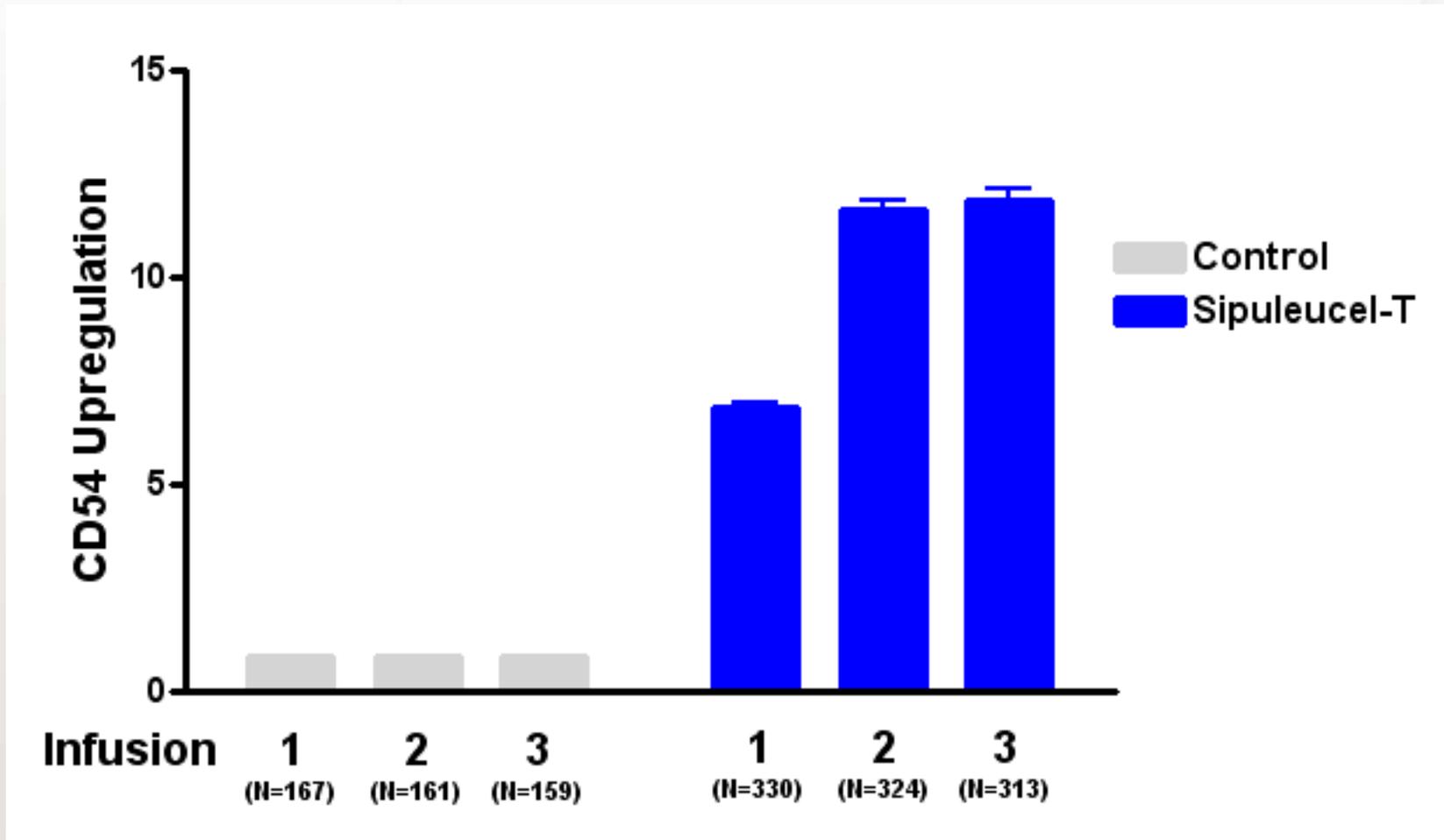
Sipuleucel-T
activates T cells in
the body

CD54 Upregulation Potency Assay for APCs

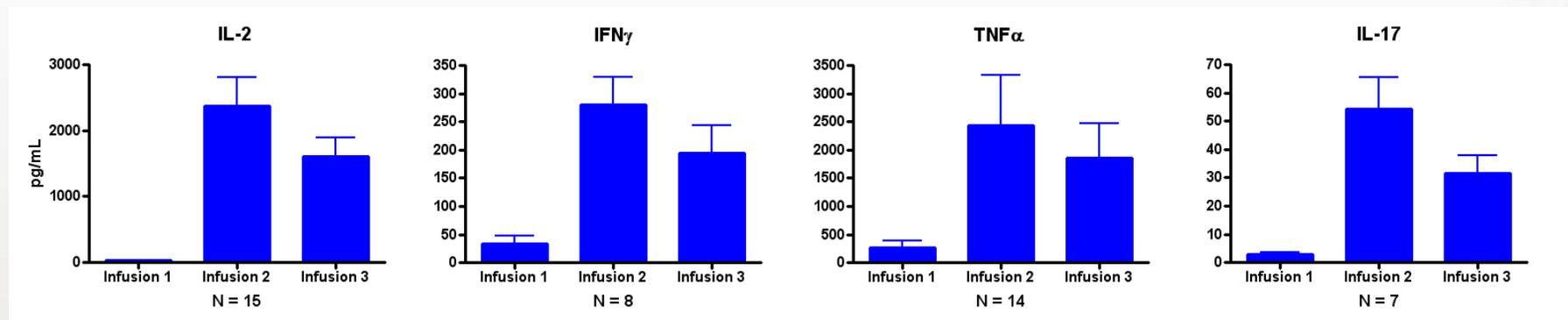


Mean Fluorescence Intensity

APC Activation Increases after Initial Sipuleucel-T Treatment



Cytokine Secretion in Culture Indicates Progressively Increased T Cell Activation



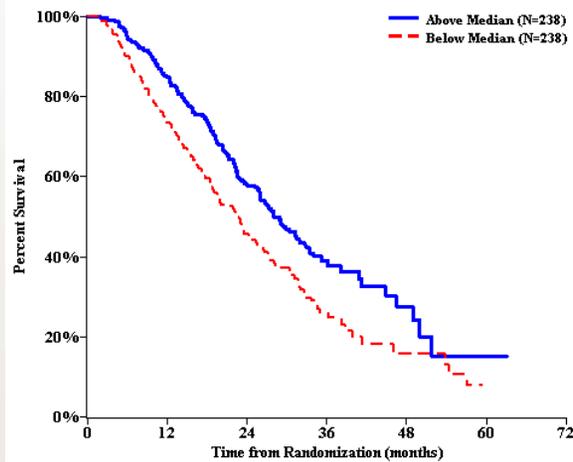
Correlation Between Overall Survival and Cell Product Parameters

Cell Product Parameters	P-Values	
	Unadjusted ¹	Adjusted for PSA and LDH ²
Cumulative TNC Counts (x 10 ⁹)	< 0.001	< 0.001
Cumulative CD54 ⁺ Cell Counts (x 10 ⁹)	0.016	0.005
Cumulative CD54 Upregulation	0.002	0.041

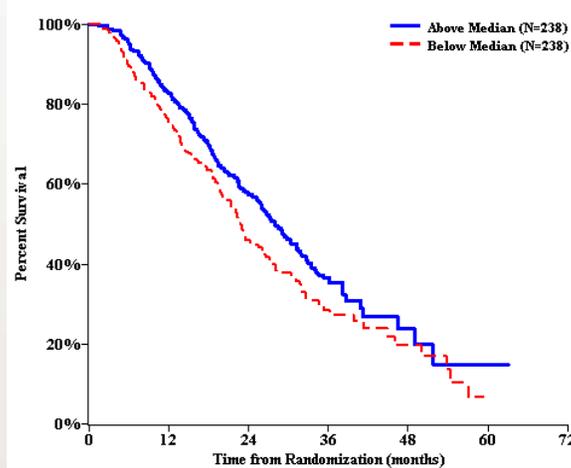
¹ From 3 Cox regression models. Each cell product parameter (cumulative CD54⁺ cell counts [ln], cumulative TNC counts [ln], and cumulative CD54 upregulation [ln]) incorporated as an independent variable in a Cox regression model stratified by study.

² From 3 Cox regression models. Each cell product parameter (cumulative CD54⁺ cell counts [ln], cumulative TNC counts [ln], and cumulative CD54 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.

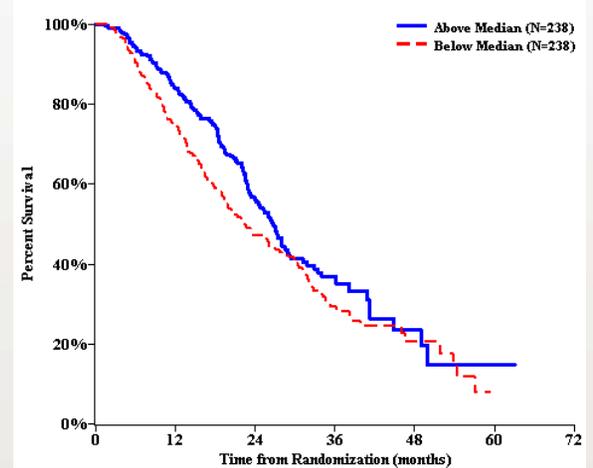
Overall Survival by Cumulative Product Parameter



TNC Count



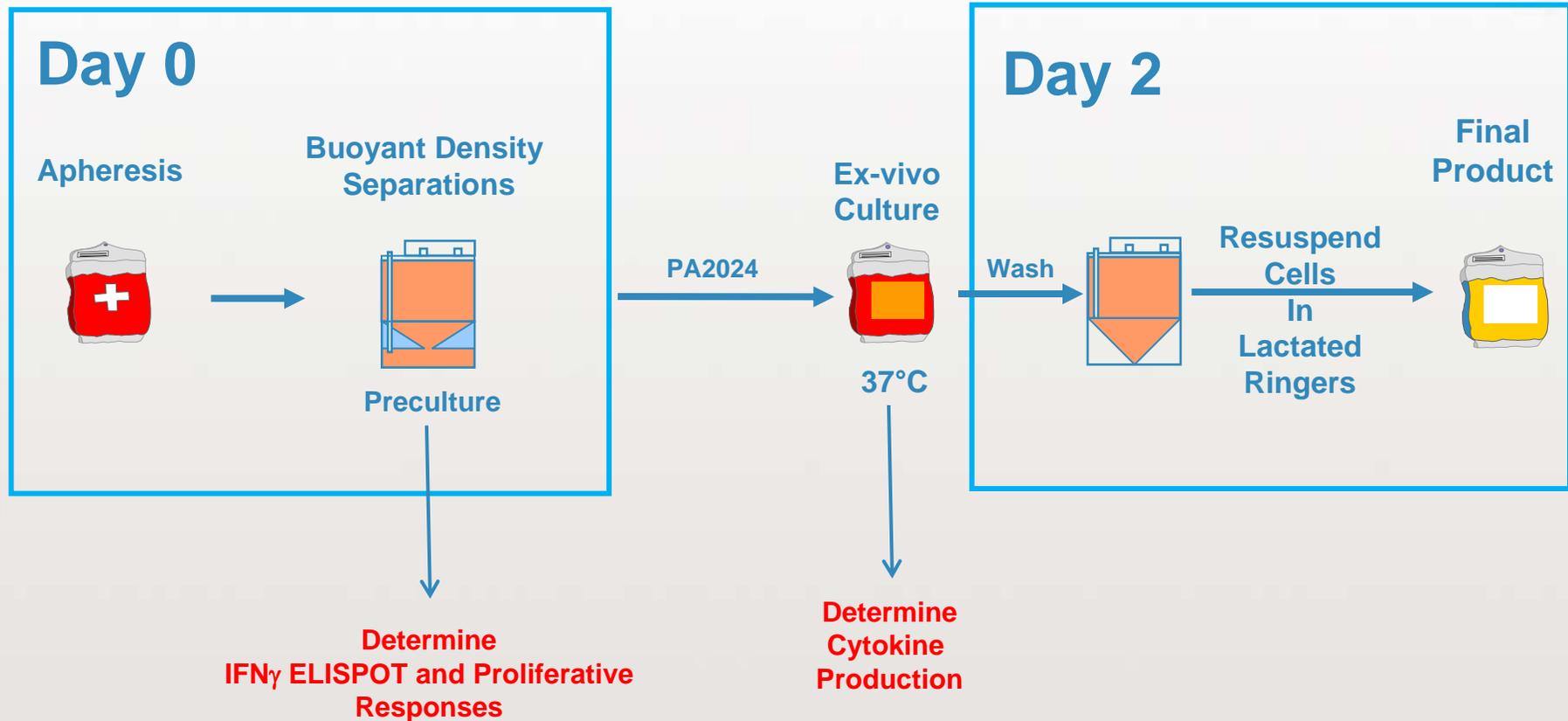
CD54+ Cell Count



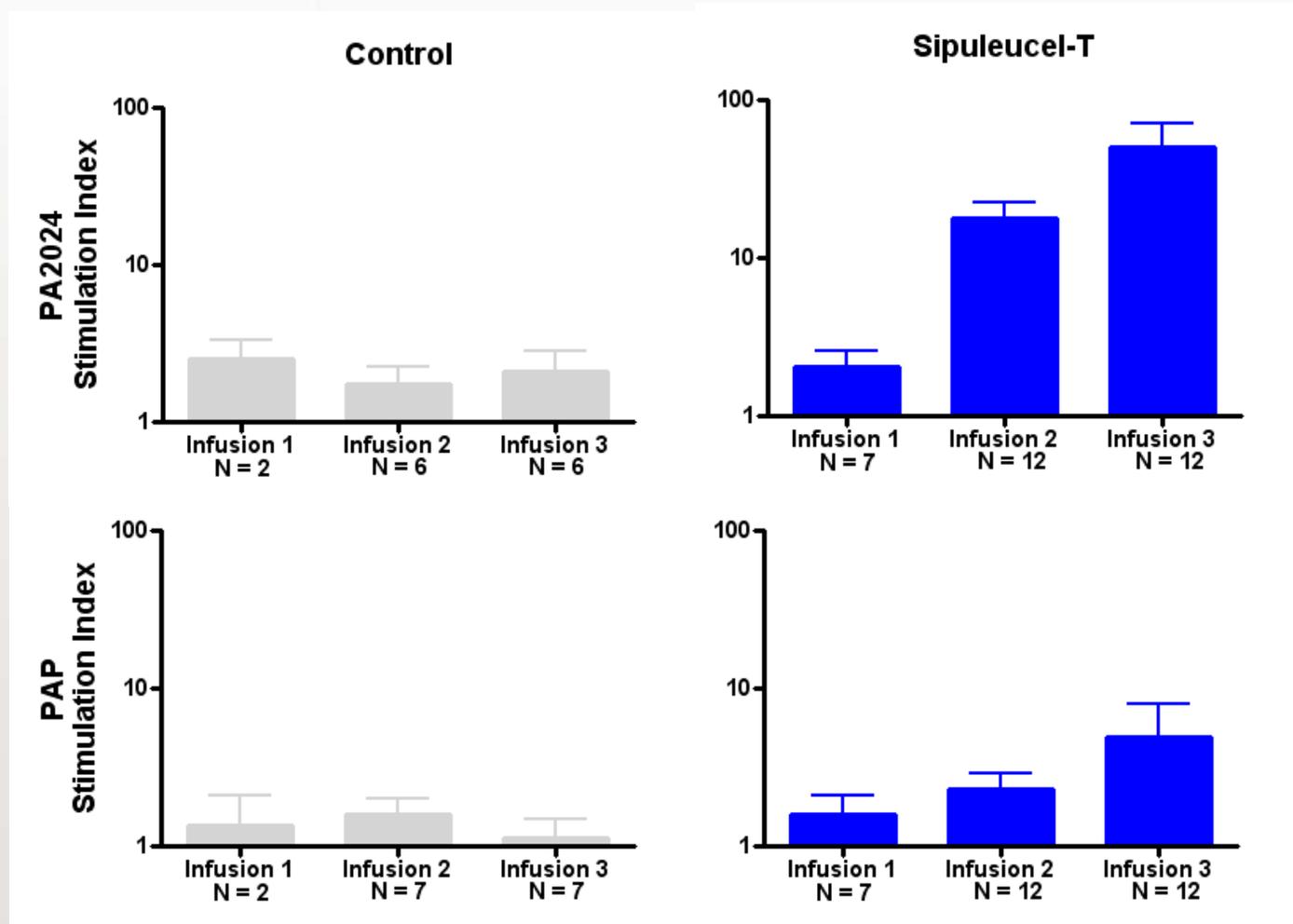
CD54 Upregulation

Sipuleucel-T patients with ≥ 1 infusion.

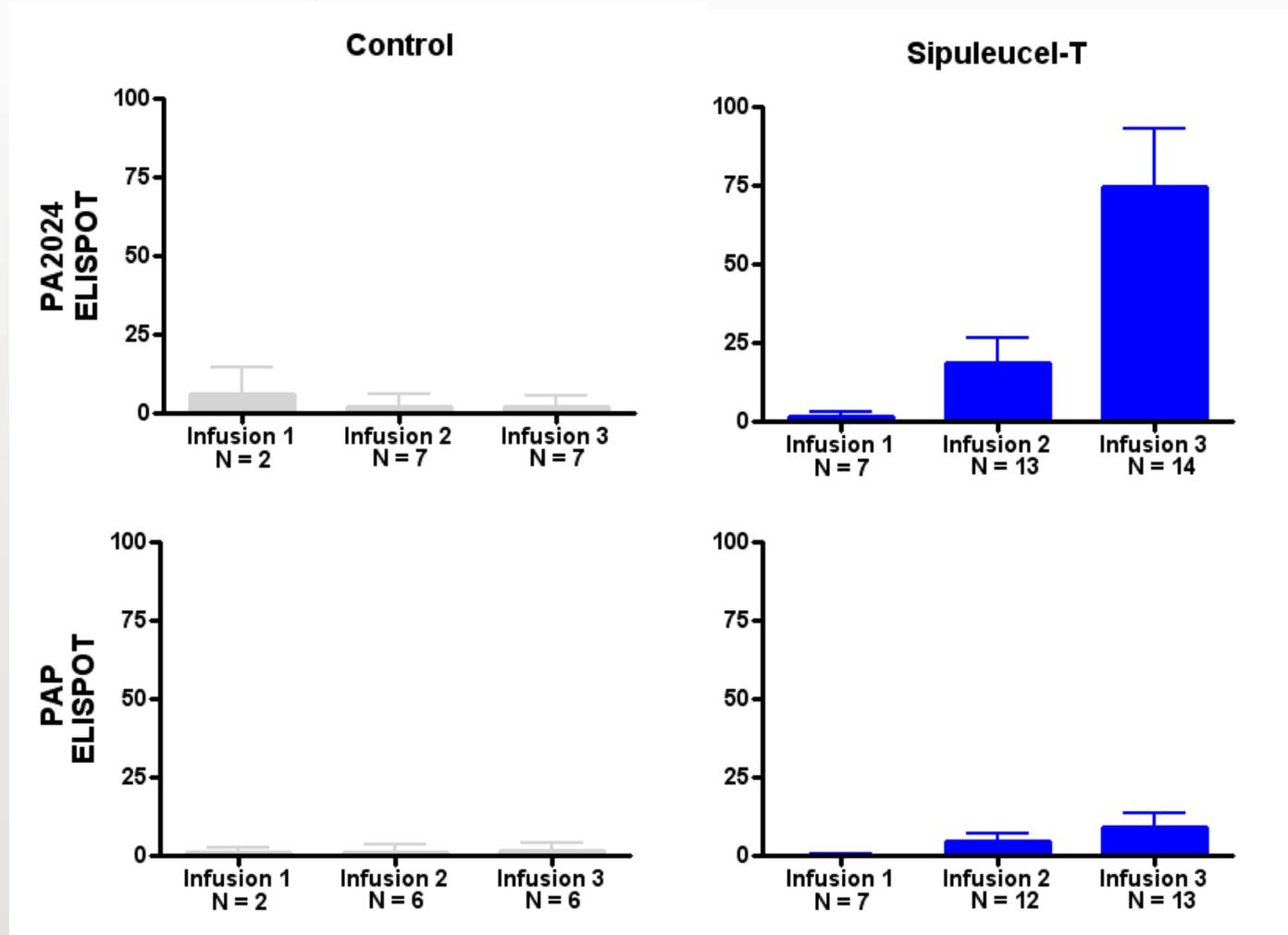
Evaluation of T Cell Activation and Immune Response During Treatment Phase



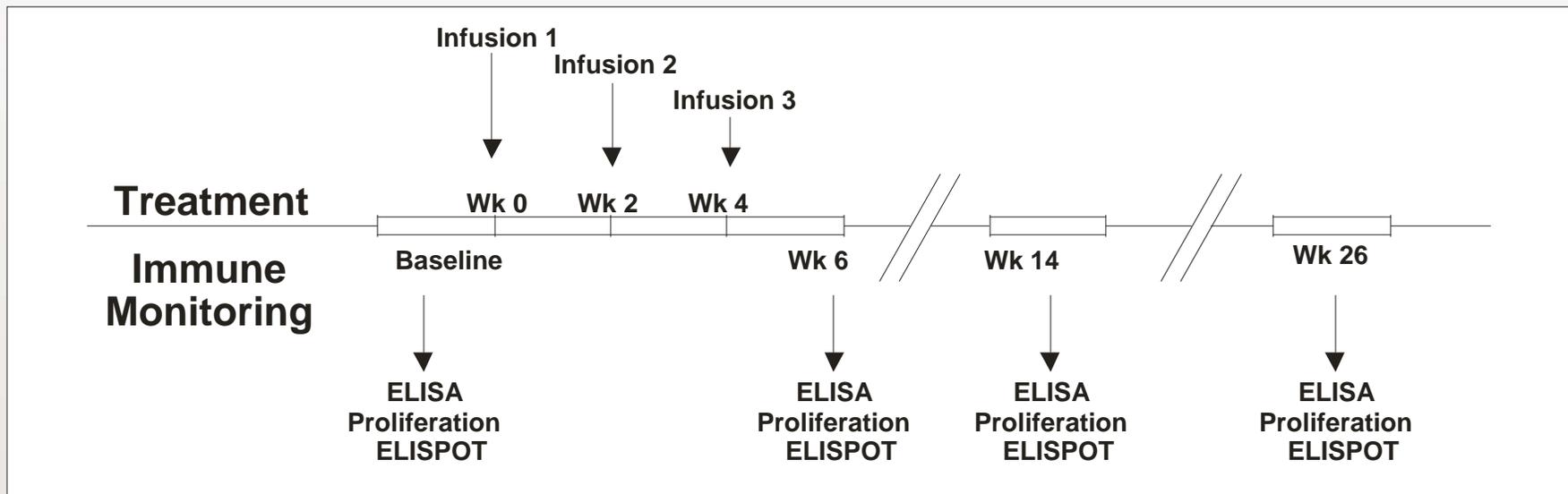
Pre-Culture Proliferative Responses are Increased During the Treatment Cycle



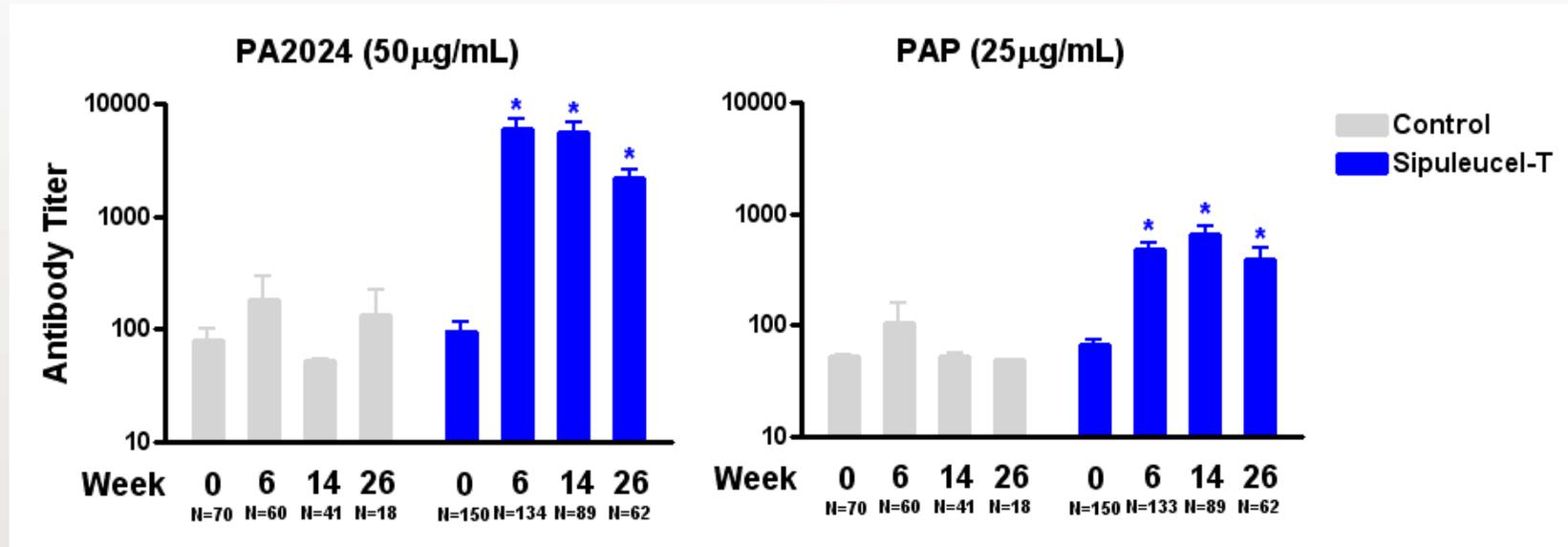
Pre-Culture ELISPOT Responses are Increased During the Treatment Cycle



IMPACT Trial Time Points for Sipuleucel-T Treatment and Immune Monitoring

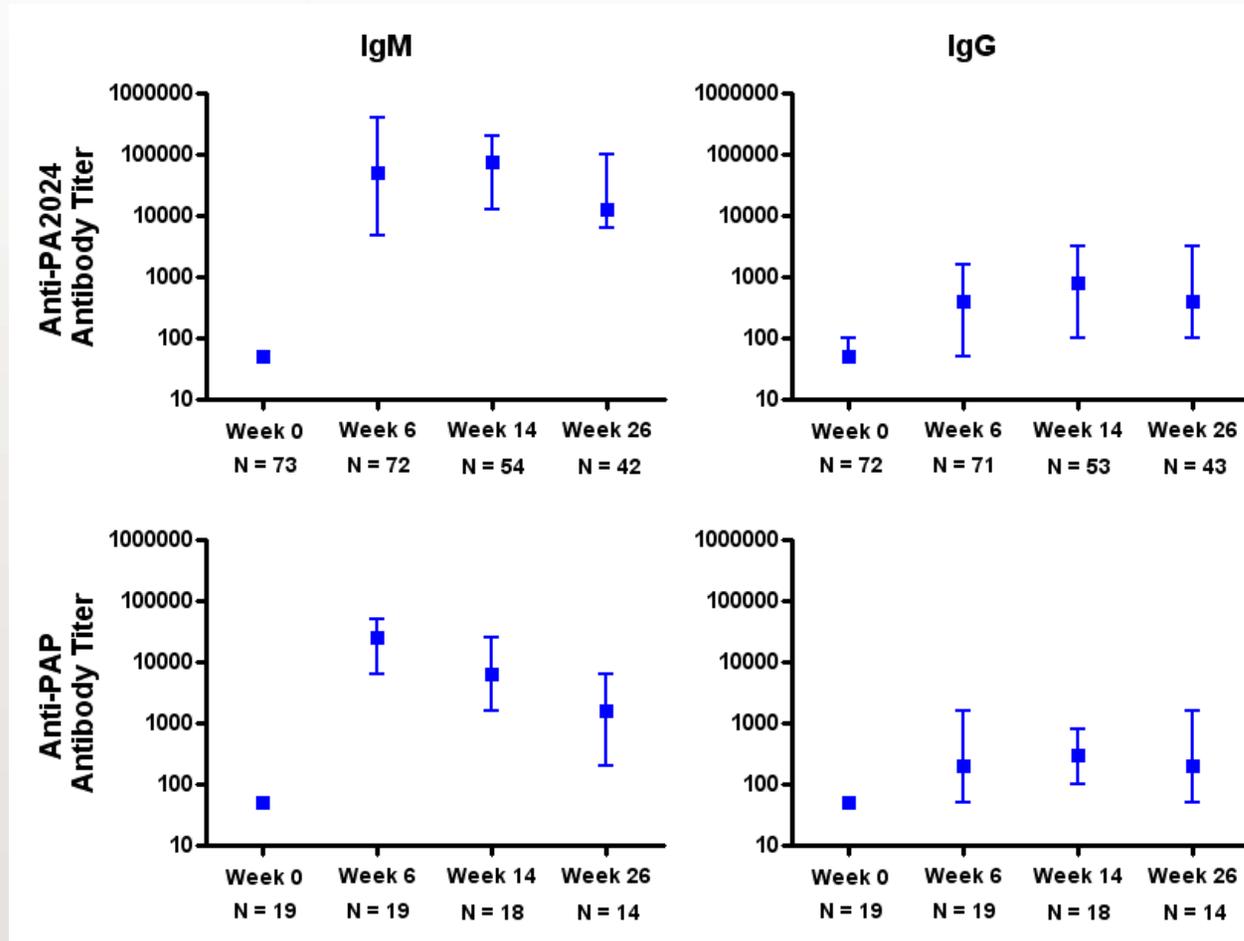


Sipuleucel-T Generates Persistent Antigen-Specific Humoral Responses

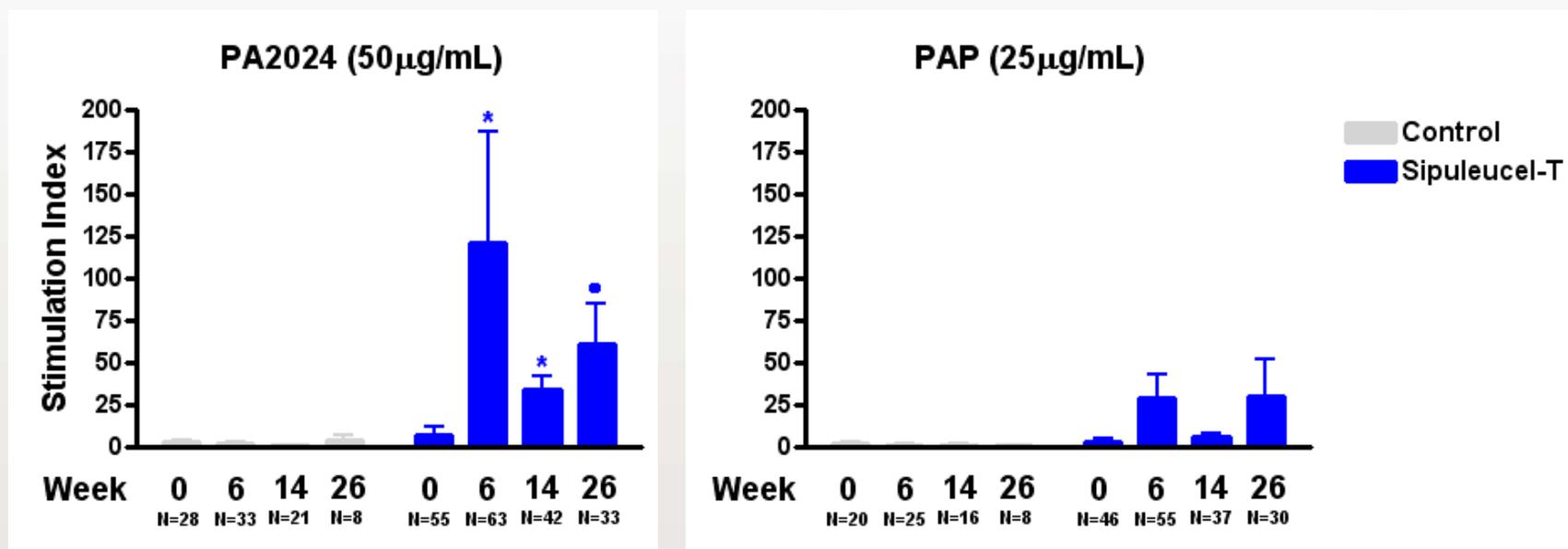


* P < 0.001 compared with control.

Anti-PA2024 Humoral Response Undergoes Class Switching

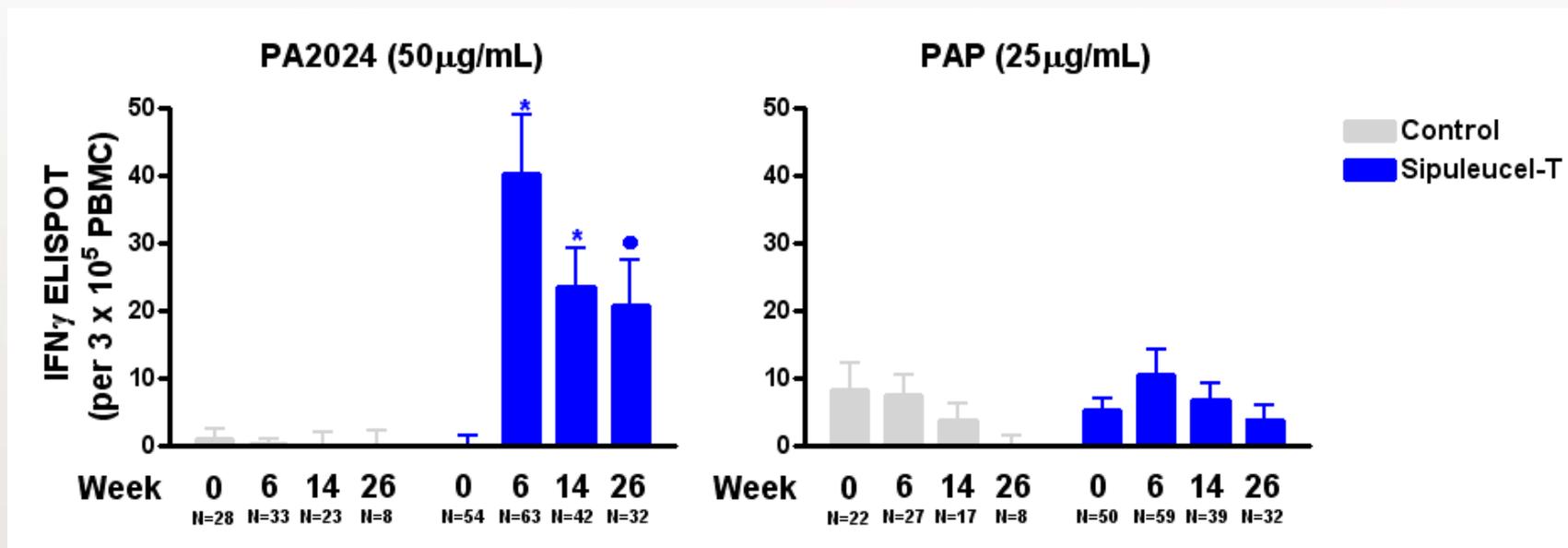


Sipuleucel-T Induces Long-Lasting Proliferative Responses to PA2024 and PAP



- * P < 0.001 compared with control.
- P = 0.009 compared with control.

Sipuleucel-T Induces Long-Lasting ELISPOT Responses to PA2024 and PAP

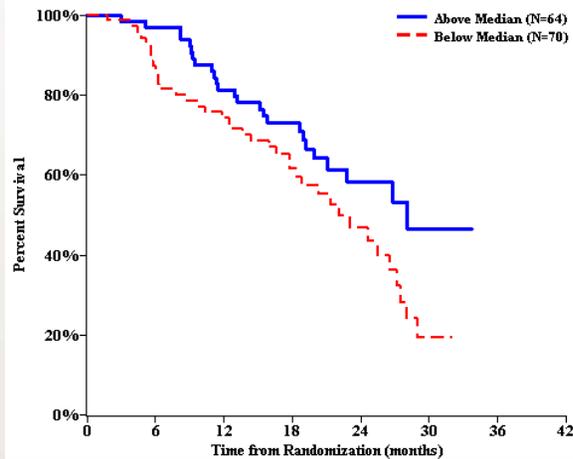


- * P < 0.001 compared with control.
- P = 0.020 compared with control.

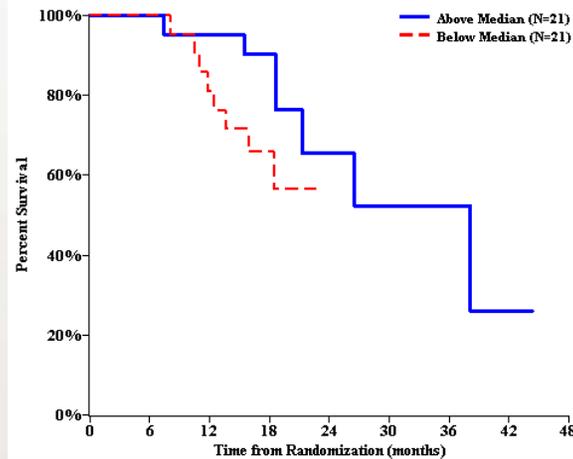
Immune Response to PA2024 and Overall Survival

		Time Point		
Response		Week 6	Week 14	Week 26
ELISA	N	134	89	62
	p-value	0.079	0.744	0.610
Proliferation	N	63	42	33
	p-value	0.712	0.057	0.874
ELISPOT	N	63	42	32
	p-value	0.824	0.885	0.049

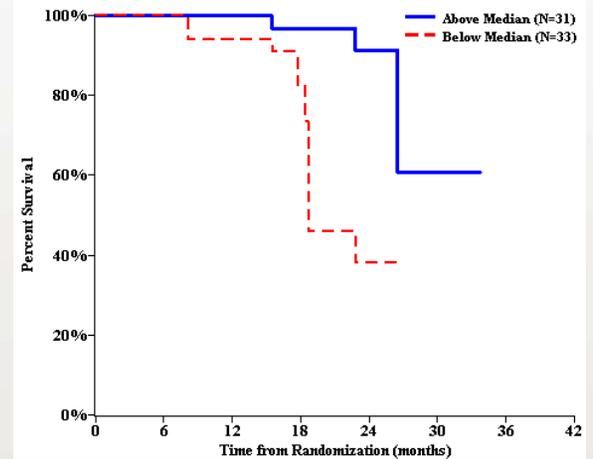
Overall Survival by Magnitude of Immune Response Above vs Below Median



**ELISA
Week 6**



**Proliferation
Week 14**



**ELISPOT
Week 26**

Conclusions

- APC activation and cytokine profile of product suggests immunologic prime-boost
- Sipuleucel-T generates robust cellular and humoral immune responses *in vivo*
- IgM to IgG humoral responses consistent with class switching
- Response durations suggest immunological memory
- Correlations between immunologic parameters and overall survival
- Immunologic parameters in product and peripheral blood are candidate biomarkers for clinical activity of sipuleucel-T

Acknowledgements

We are indebted to the following:

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