Dendreon
Targeting Cancer, Transforming Lives™

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Sipuleucel-T for the Active Cellular Immunotherapy of Prostate Cancer

Hot Topic Symposium; iSBTc Annual Meeting – October 31, 2009

Presenter Disclosure Information

David L. Urdal

The following relationships exist related to this presentation:

- *I am employed by Dendreon*
- *I own stock in Dendreon*
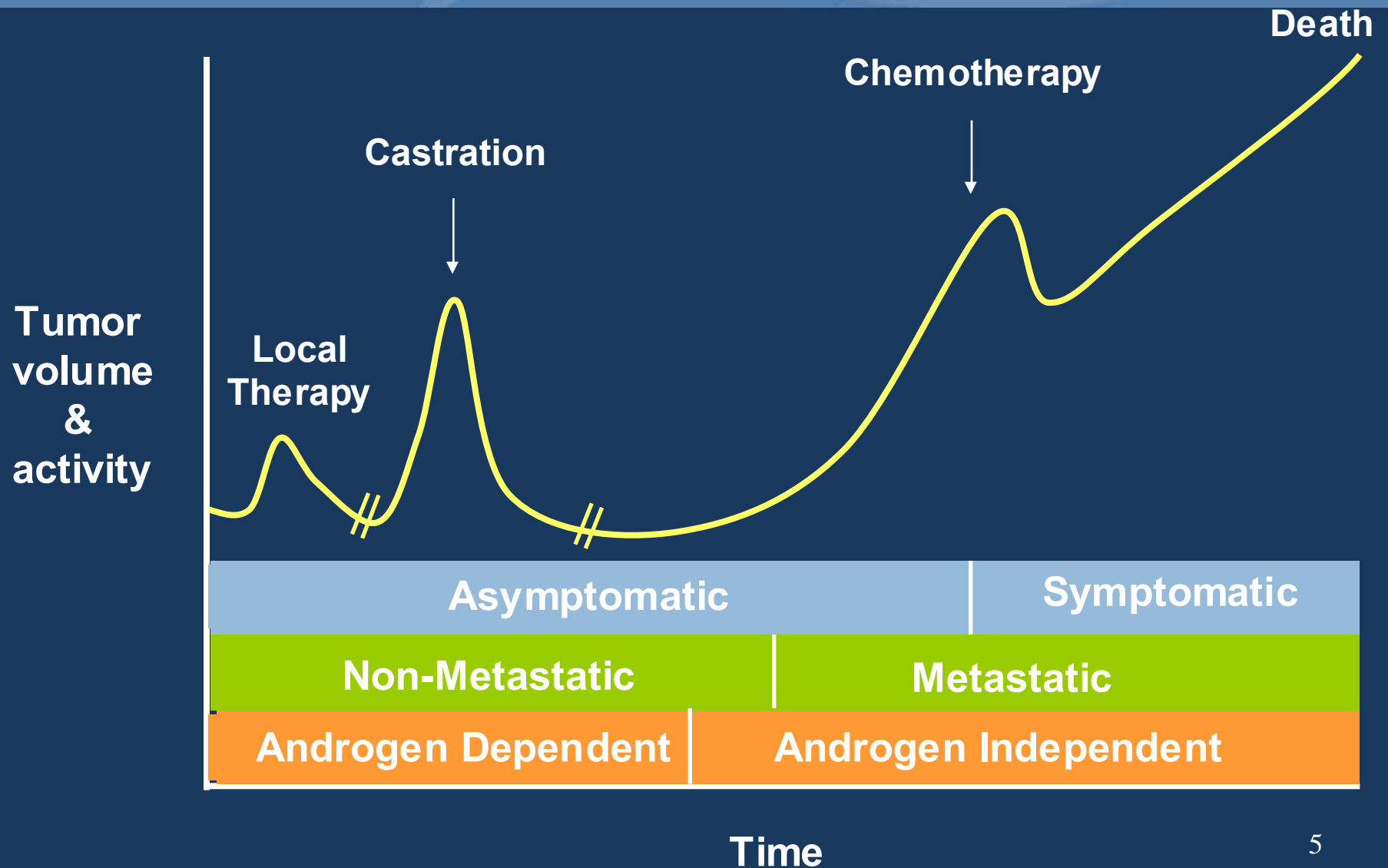- *I will be discussing development of a Dendreon product candidate*

Forward Looking Statements

This presentation includes forward looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Forward looking statements by their nature involve risks, uncertainties and assumptions inherent in discussing future events and trends. Information concerning risk factors that may affect such statements can be obtained in the Company's SEC filings.

Sipuleucel-T for the Active Cellular Immunotherapy of Prostate Cancer

- Introduction to prostate cancer

- Development of sipuleucel-T

  ➢ Clinical results

  ➢ Regulatory milestones

  ➢ IMPACT clinical trial results

- Conclusions

Natural History of Prostate Cancer

Death

Chemotherapy

Castration

Tumor volume & activity

Local Therapy

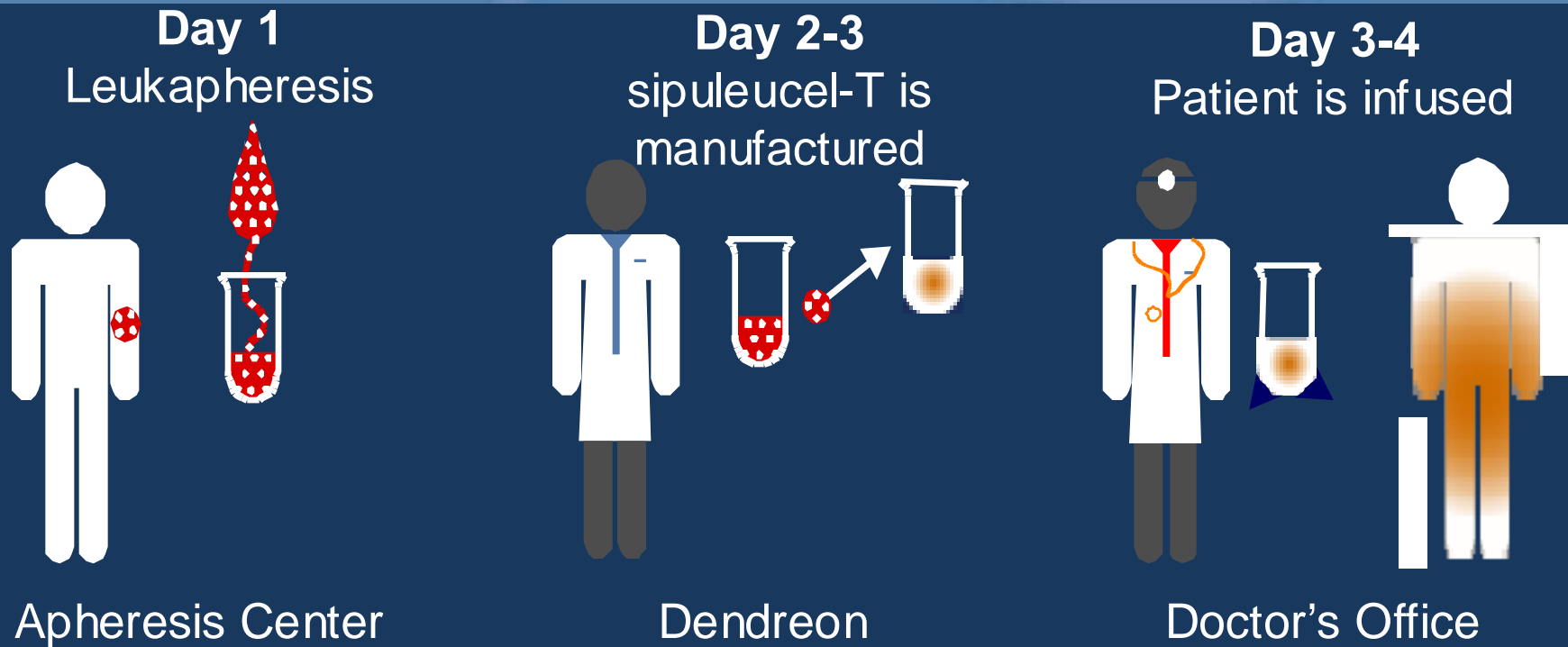| Asymptomatic		Symptomatic
Non-Metastatic	Metastatic	
Androgen Dependent	Androgen Independent	

Time

5

Androgen-Independent (Castration Resistant) Prostate Cancer Remains Unmet Medical Need

- Deadly disease

- Modest survival advantage seen with docetaxel-based regimens

- Majority of patients reject chemotherapy due to QOL impact

- Novel treatment approaches with acceptable safety profiles are needed

Development of sipuleucel-T

Sipuleucel-T is an autologous investigational active cellular immunotherapy product that activates the immune system against prostate cancer
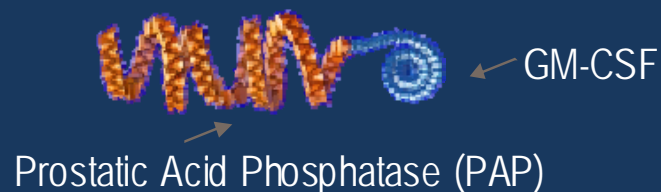
Sipuleucel-T: Patient-Specific Product

Day 1
Leukapheresis

Day 2-3
sipuleucel-T is
manufactured

Day 3-4
Patient is infused

Apheresis Center

Dendreon

Doctor's Office

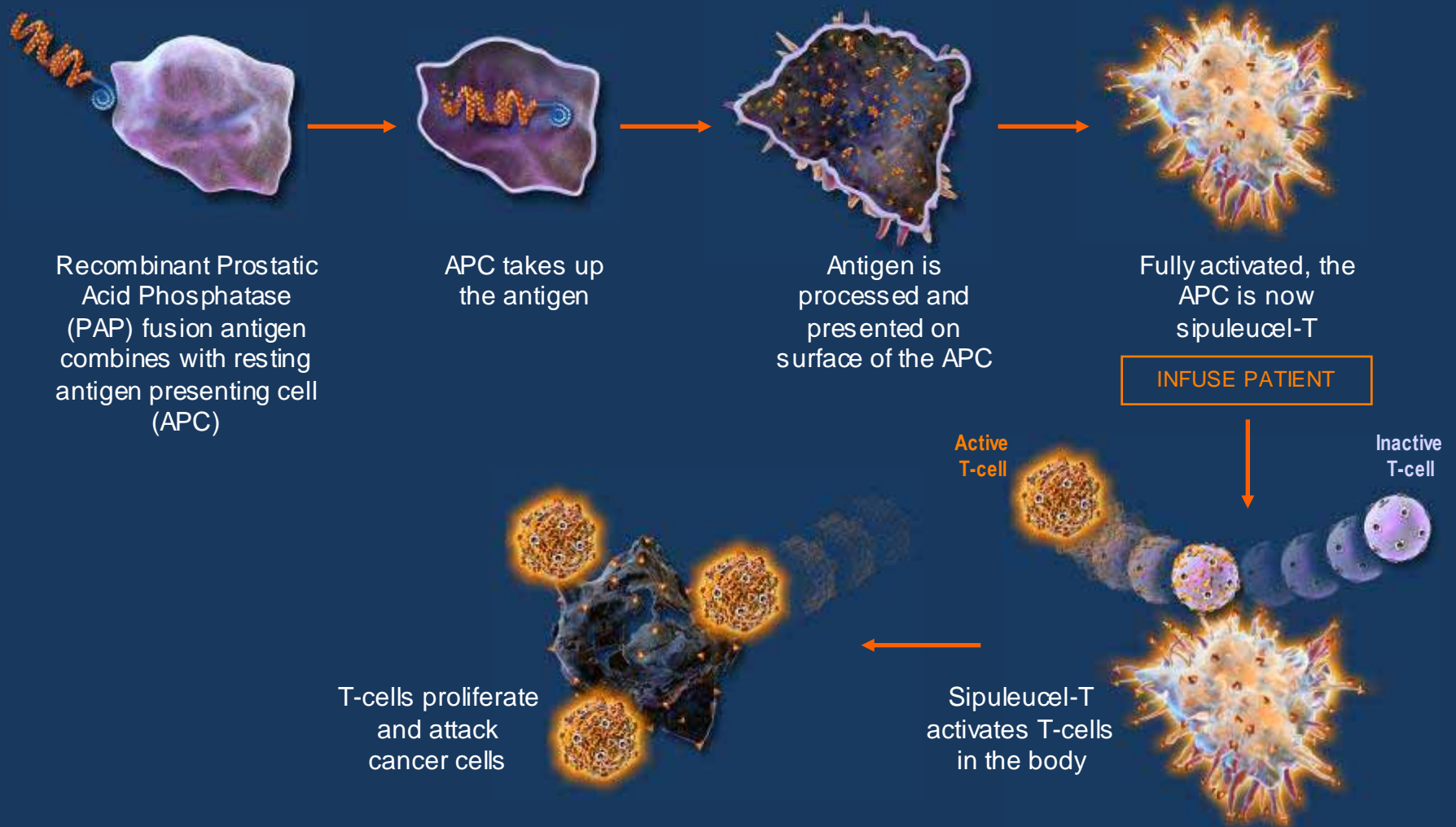COMPLETE COURSE OF THERAPY:
Weeks 0, 2, 4

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Antigen Delivery Cassette™

- Composed of prostatic acid phosphatase (PAP) linked to granulocyte-macrophage colony stimulating factor (GM-CSF)

- Manufactured as recombinant protein antigen

- Robust, reproducible, well-characterized immune responses

GM-CSF

Prostatic Acid Phosphatase (PAP)

Sipuleucel-T: Autologous APC Cultured with Antigen Delivery Cassette

Recombinant Prostatic Acid Phosphatase (PAP) fusion antigen combines with resting antigen presenting cell (APC)

APC takes up the antigen

Antigen is processed and presented on surface of the APC

Fully activated, the APC is now sipuleucel-T

INFUSE PATIENT

Active T-cell

Inactive T-cell

T-cells proliferate and attack cancer cells

Sipuleucel-T activates T-cells in the body

*The precise mechanism of sipuleucel-T in prostate cancer has not been established.*

Pre-Clinical Rationale

- Antigen-loaded APCs isolated from peripheral blood showed clinical promise in lymphoma

- Prostatic acid phosphatase (PAP) highly expressed in prostate tissue

- Granulocyte Macrophage Colony Stimulating Factor (GM-CSF) activates APCs

- Rat APCs, loaded with PAP+GM-CSF fusion protein, induced prostatitis

Hsu et al., (1996) Nat. Med. 2:52-58
Laus et al., (2001) Can. Res. Ther. Cont. 11:1-10

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The Phase 3 Plan

- Two identical Phase 3 multi-center, double-blind, randomized, placebo controlled trials
    - D9901
    - D9902A
- Target population: asymptomatic, metastatic androgen independent prostate cancer
- Well-defined manufacturing process
- Potency and other release specifications established

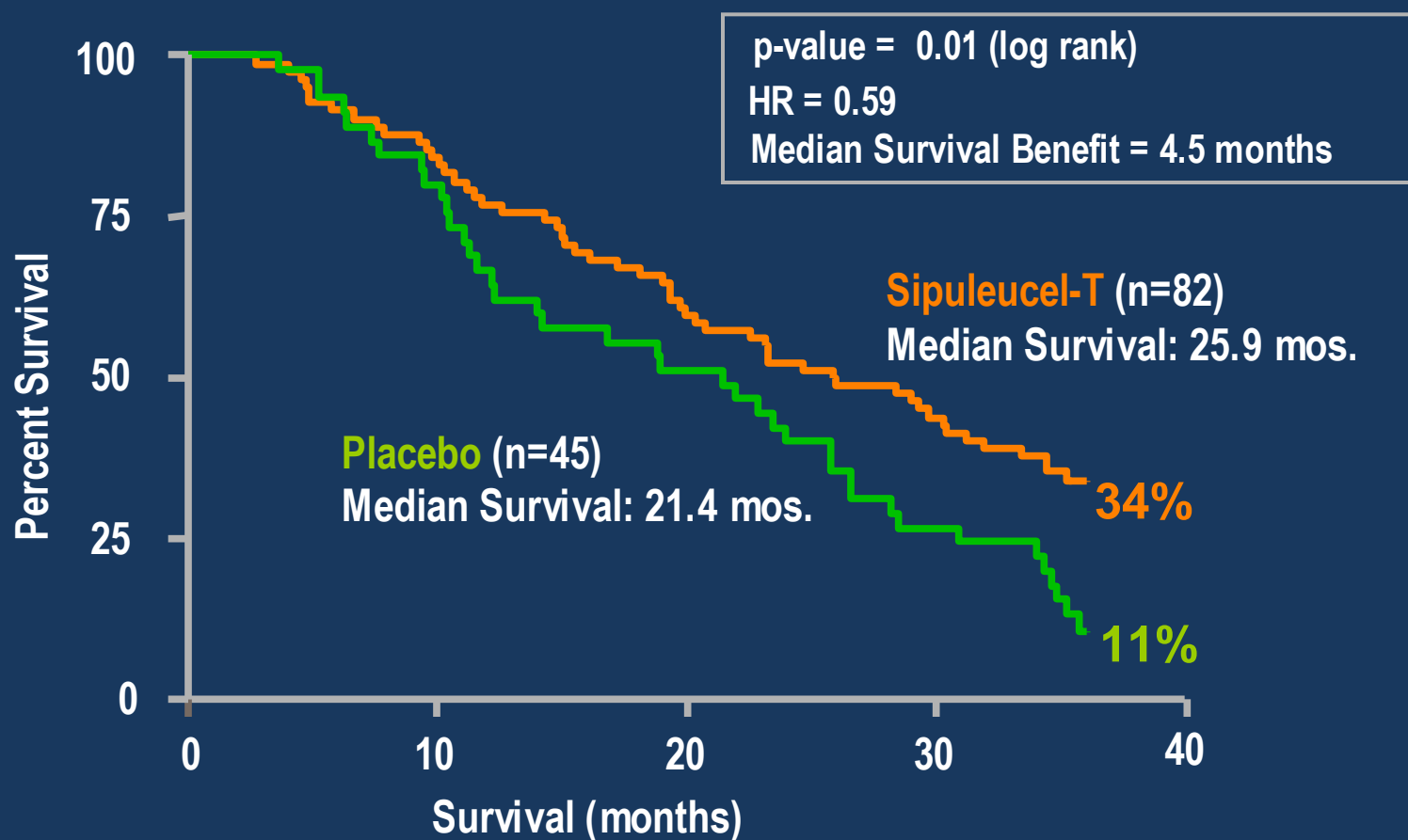# Randomized, Double Blind, Placebo-Controlled Trials, Studies D9901 and D9902
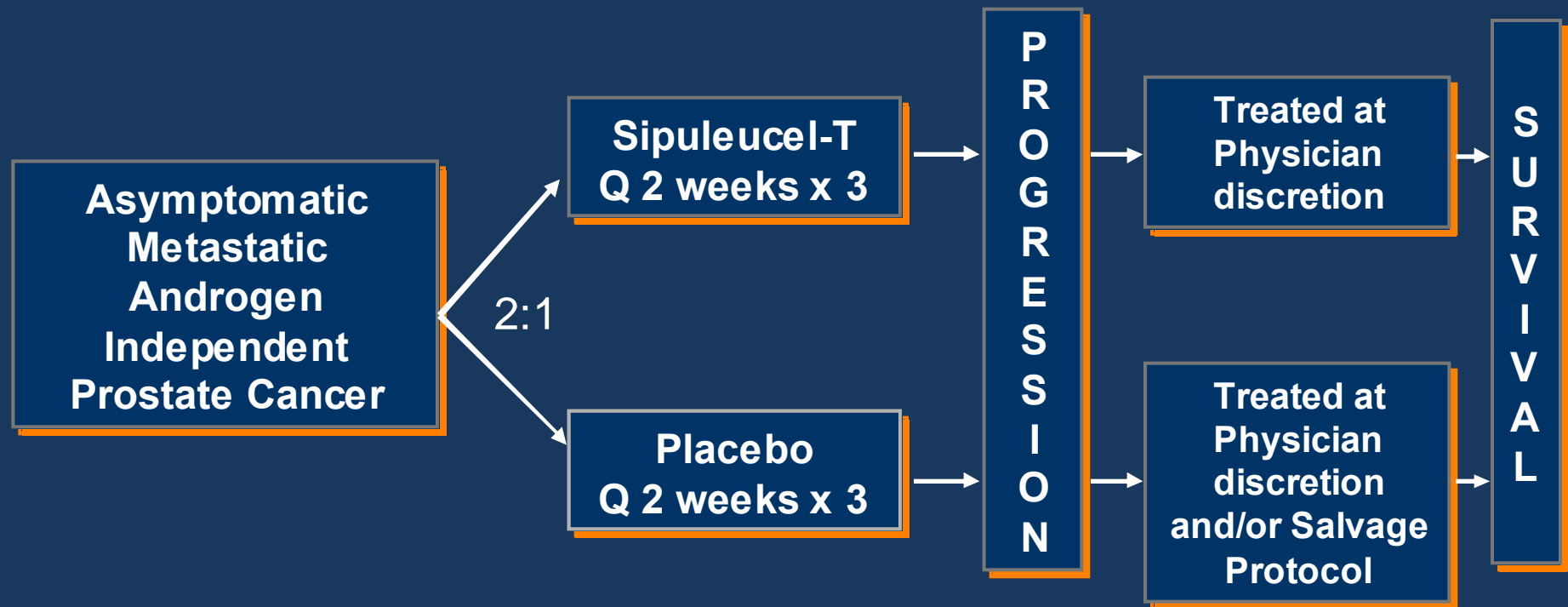
Primary endpoint: Time to Disease Progression
  - Radiographic, Clinical or Pain
  - Not PSA

Planned analysis: Overall Survival

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Sipuleucel-T Overall 3-Year Survival Intent-to-Treat Study D9901

p-value = 0.01 (log rank)
HR = 0.59
Median Survival Benefit = 4.5 months

Sipuleucel-T (n=82)
Median Survival: 25.9 mos.

Placebo (n=45)
Median Survival: 21.4 mos.

34%

11%

Percent Survival

Survival (months)

100 — 75 — 50 — 25 — 0

0   10   20   30   40

Small EJ, Schellhammer PF, Higano CS, et. al. Placebo-Controlled Phase III Trial of Immunologic Therapy with Sipuleucel-T (APC8015) in Patients with Metastatic, Asymptomatic Hormone Refractory Prostate Cancer. *J Clin Oncol* 24:3089-3094, 2006

Survival Results Robust

- Treatment effect consistent across subpopulations

- Survival results confirmed by multiple sensitivity analyses

  – Adjustment for prognostic factors

  – Adjustment for Docetaxel

  – PCa specific mortality

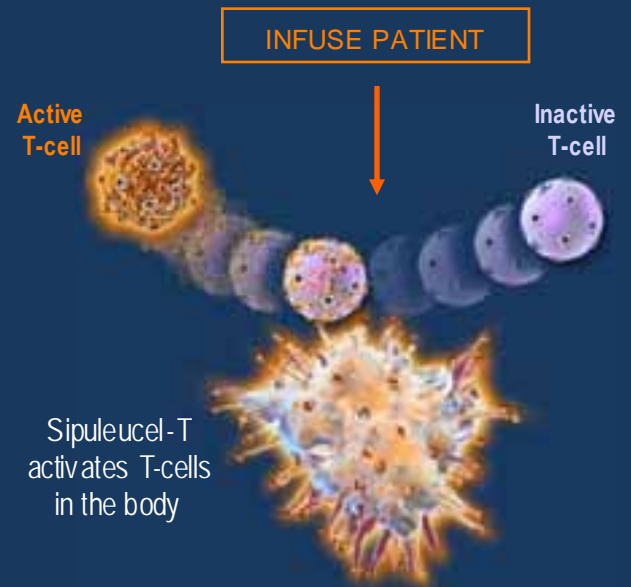 – Integrated analysis of D9901 and D9902A

Sipuleucel-T Laboratory/Clinical Correlations

Key product attributes:

- **Total nucleated cell count**

- **CD54 count**

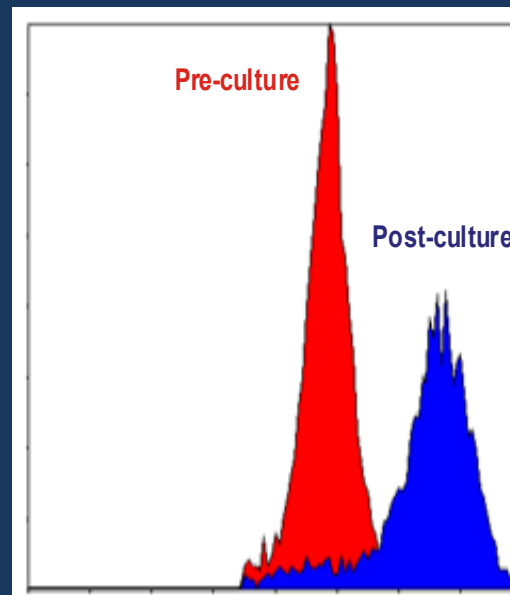- **CD54 'upregulation'**
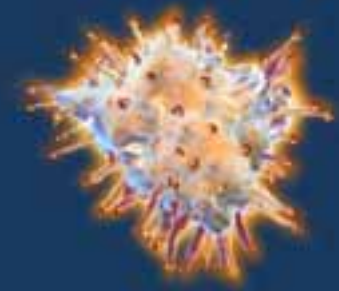
Fully activated, the APC
is now sipuleucel-T

INFUSE PATIENT

**Active
T-cell**

**Inactive
T-cell**

Sipuleucel-T
activates T-cells
in the body

The precise mechanism of sipuleucel-T in prostate cancer has not been established.

CD54 Upregulation Potency Assay for APCs

APCs cultured with recombinant antigen
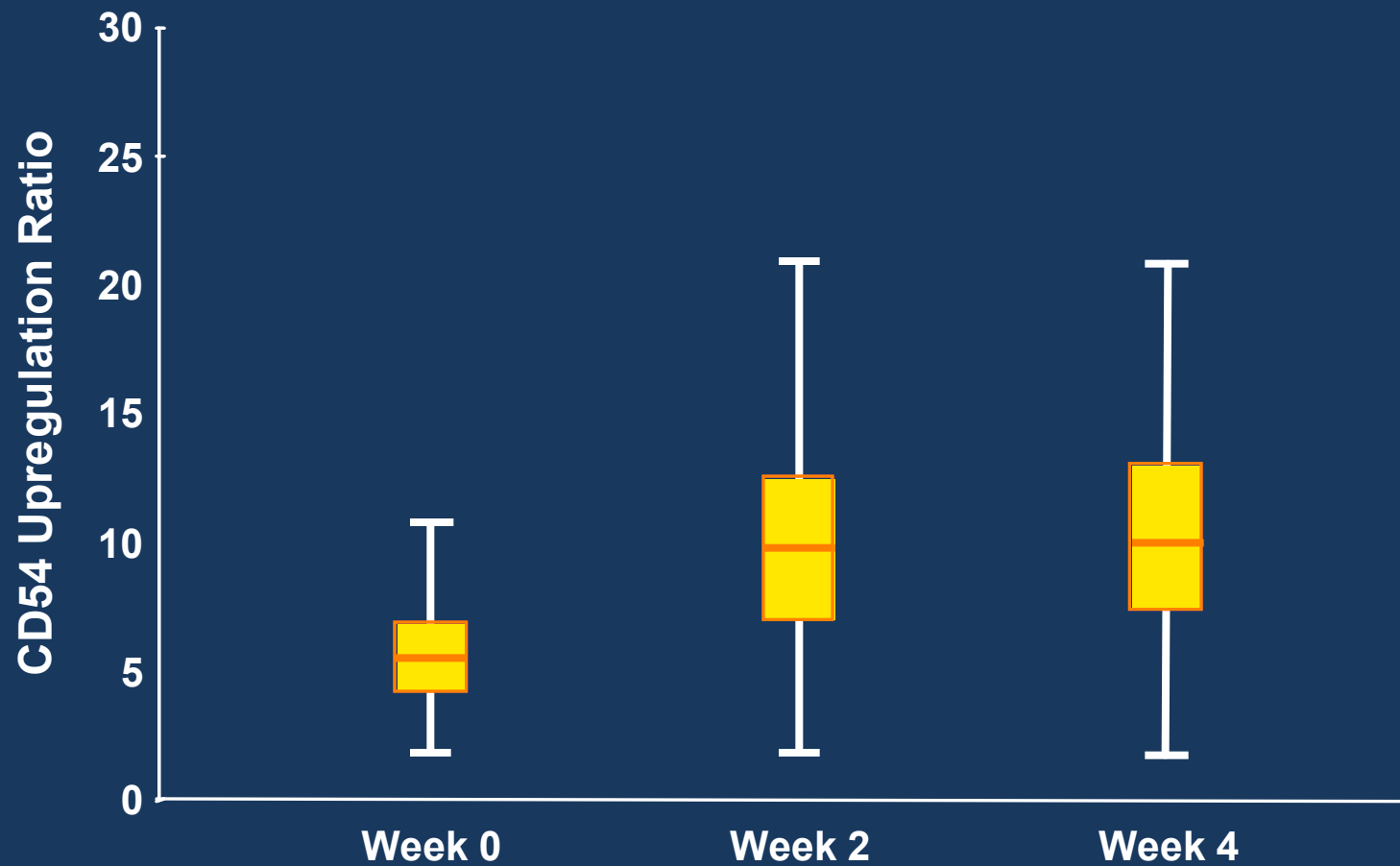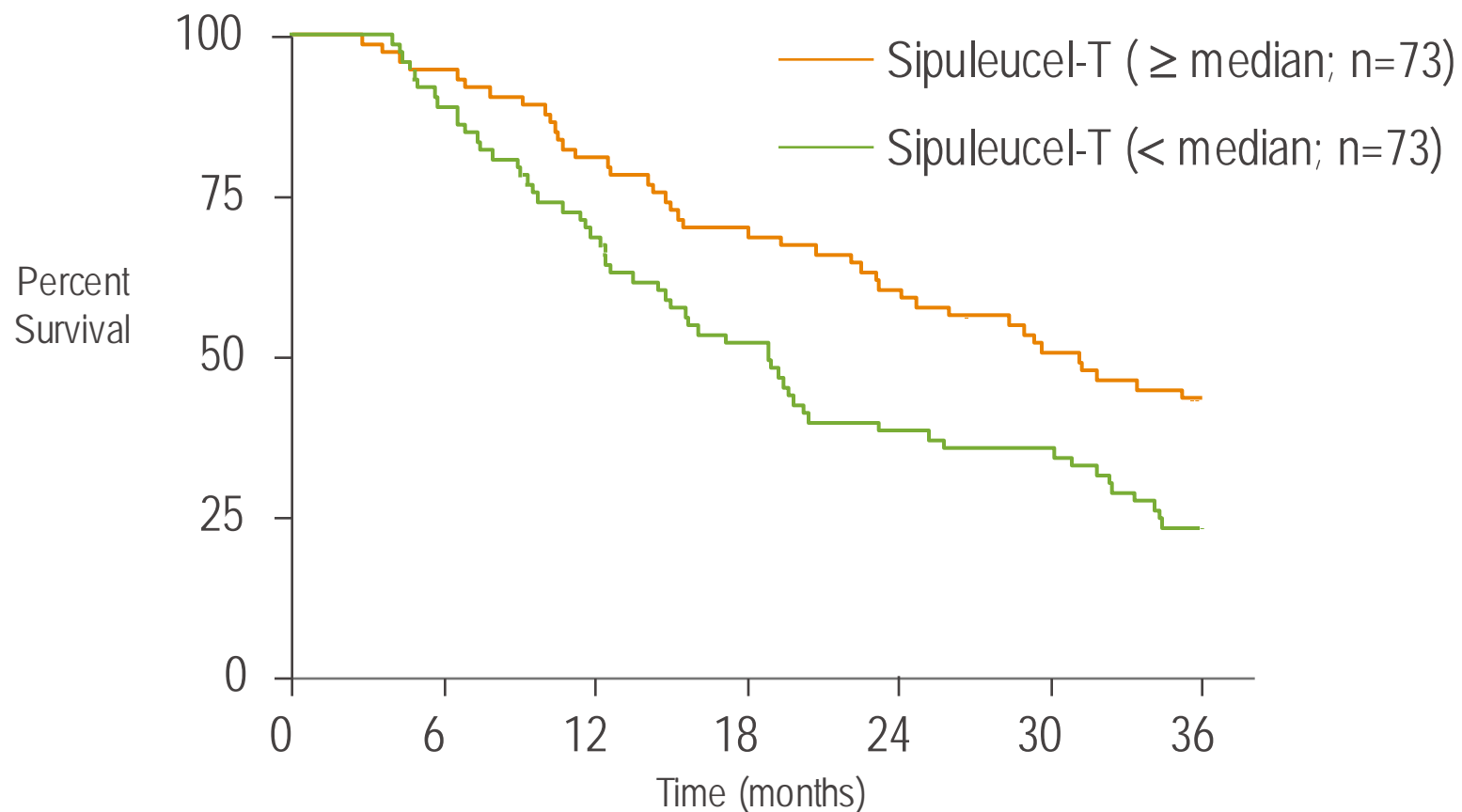
CD54

Pre-culture

Post-culture

Mean Fluorescence Intensity

CD54 Upregulation by Treatment Week
Phase 3 Manufacturing Data

APC Activation Correlates with Survival (D9901 and D9902A)

Sipuleucel-T Potency Correlates with Survival

- Biologically relevant product measurement

- Independent of prognostic factors

- May support the efficacy findings

Sipuleucel-T is Well Tolerated

Event [n(%)]	Sipuleucel-T (n=82)		Placebo (n=45)		p-value
	Grade 1-2	Grade 3-4	Grade 1-2	Grade 3-4	
Rigors (chills)	45 (54.9)	4 (4.9)	4 (8.9)	0 (0.0)	<0.001
Pyrexia (fever)	22 (26.8)	2 (2.4)	1 (2.2)	0 (0.0)	0.0001
Tremor	8 (9.8)	0 (0.0)	0 (0.0)	0 (0.0)	0.0497
Feeling Cold	7 (8.5)	0 (0.0)	0 (0.0)	0 (0.0)	0.0505

Phase 3 Trial D9901

Regulatory Milestones

- The Center for Biologics Evaluation and Research (CBER)
    - Office of Cellular, Tissue and Gene Therapies (OCTGT)

- September 2005: Pre-BLA Meeting held with FDA:
    - Survival benefit observed in Study D9901
    - Supported by D9902A and the absence of significant toxicity
    - Will serve as the clinical basis of a BLA for sipuleucel-T
- November 2005: FDA granted Fast Track Status for sipuleucel-T

Regulatory Milestones (continued)

- August – November 2006: Submit rolling BLA

- January 2007: BLA accepted
  for Priority Review

- March 2007: FDA's Cell, Tissue and Gene Therapies Advisory Committee

Cell, Tissue and Gene Therapy Advisory Committee

- Key Questions to the Committee

  – Is sipuleucel-T reasonably safe for the intended patient population?
    17 yes – 0 no

  – Has substantial evidence of efficacy been established?
    13 yes – 4 no

The Preliminary Outcome

- Complete Response Letter – May 8, 2007

- Request for additional clinical and CMC information

IMPACT Phase 3 Study (D9902B)
IMmunotherapy for Prostate AdenoCarcinoma Treatment

- Randomized 2:1, double-blind, placebo-controlled

- ~500 men with minimally symptomatic, metastatic AIPC

- Enrolled at ~70 sites in North America

- Primary endpoint: Survival

- Secondary endpoint: Time to objective disease progression

- Special Protocol Assessment

- Positive interim or final survival analysis sufficient to amend BLA

Sipuleucel-T Immunotherapy for Advanced Prostate Cancer: A Randomized, Double-Blind, Placebo-Controlled Phase 3 Trial
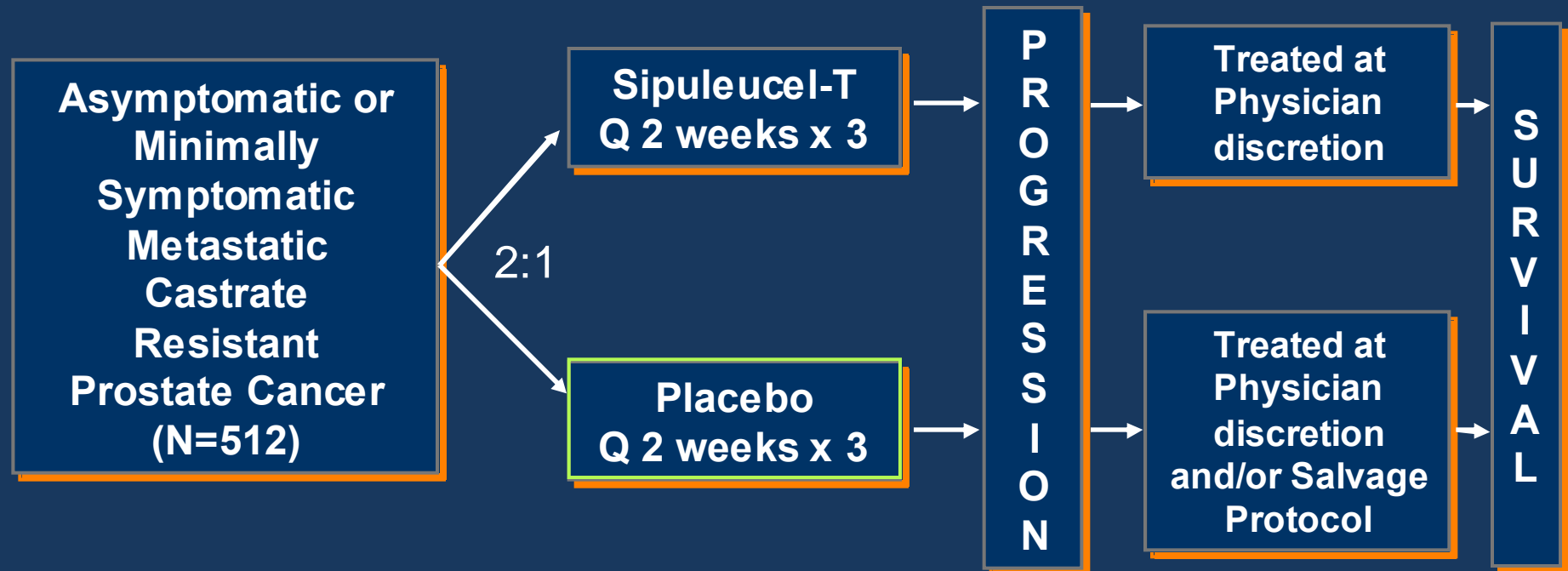
IMPACT STUDY

David Penson, MD, MPH

Professor of Urology
Vanderbilt University
For the IMPACT Study Investigators

American Urological Association Annual Meeting
April 28, 2009

Randomized Phase 3 IMPACT Trial
(IMmunotherapy Prostate AdenoCarcinoma Treatment)

Primary endpoint: Overall Survival
Secondary endpoint: Time to Objective Disease Progression

Statistical Analysis Plan

- Stratification Factors
  - Bisphosphonate use
  - Primary Gleason score
  - Number of bone metastases
- HR and P-values
  - Calculated from Cox model
    - Adjusted for PSA and LDH
  - 2 sided p-values
  - Log rank as sensitivity analysis
- Analyses
  - Interim: one
  - Final: $p < 0.043$ required for statistical significance

Patient Demographics and Baseline Characteristics

	Sipuleucel-T (N = 341)	Placebo (N = 171)
Age, median yrs (range)	72 (49 – 91)	70 (40 – 89)
Race, white (%)	89.4	91.2
ECOG status, 0 (%)	82.1	81.3
Gleason Score ≤ 7 (%)	75.4	75.4
Disease localization		
Bone only (%)	50.7	43.3
Soft tissue only (%)	7.0	8.2
Bone & soft tissue (%)	41.9	48.5
>10 bone mets (%)	42.8	42.7
Bisphosphonate use	48.1	48.0
Prior docetaxel (%)	15.5	12.3

Baseline Median Laboratory Values

	Sipuleucel-T (N = 341)	Placebo (N = 171)
Serum PSA, ng/mL	51.7	47.2
Serum PAP, U/L	2.7	3.2
Alk. Phosphatase, U/L	99.0	109.0
Hemoglobin, g/dL	12.9	12.7
LDH, U/L	194.0	193.0
WBC, $10^3/\mu L$	6.2	6.0

IMPACT Overall Survival: Primary Endpoint
Intent-to-Treat Population

P = 0.032 (Cox model)
HR = 0.775 [95% CI: 0.614, 0.979]

Median Survival Benefit = 4.1 Mos.

Sipuleucel-T (n = 341)
Median Survival: 25.8 Mos.

Placebo (n = 171)
Median Survival: 21.7 Mos.

Percent Survival
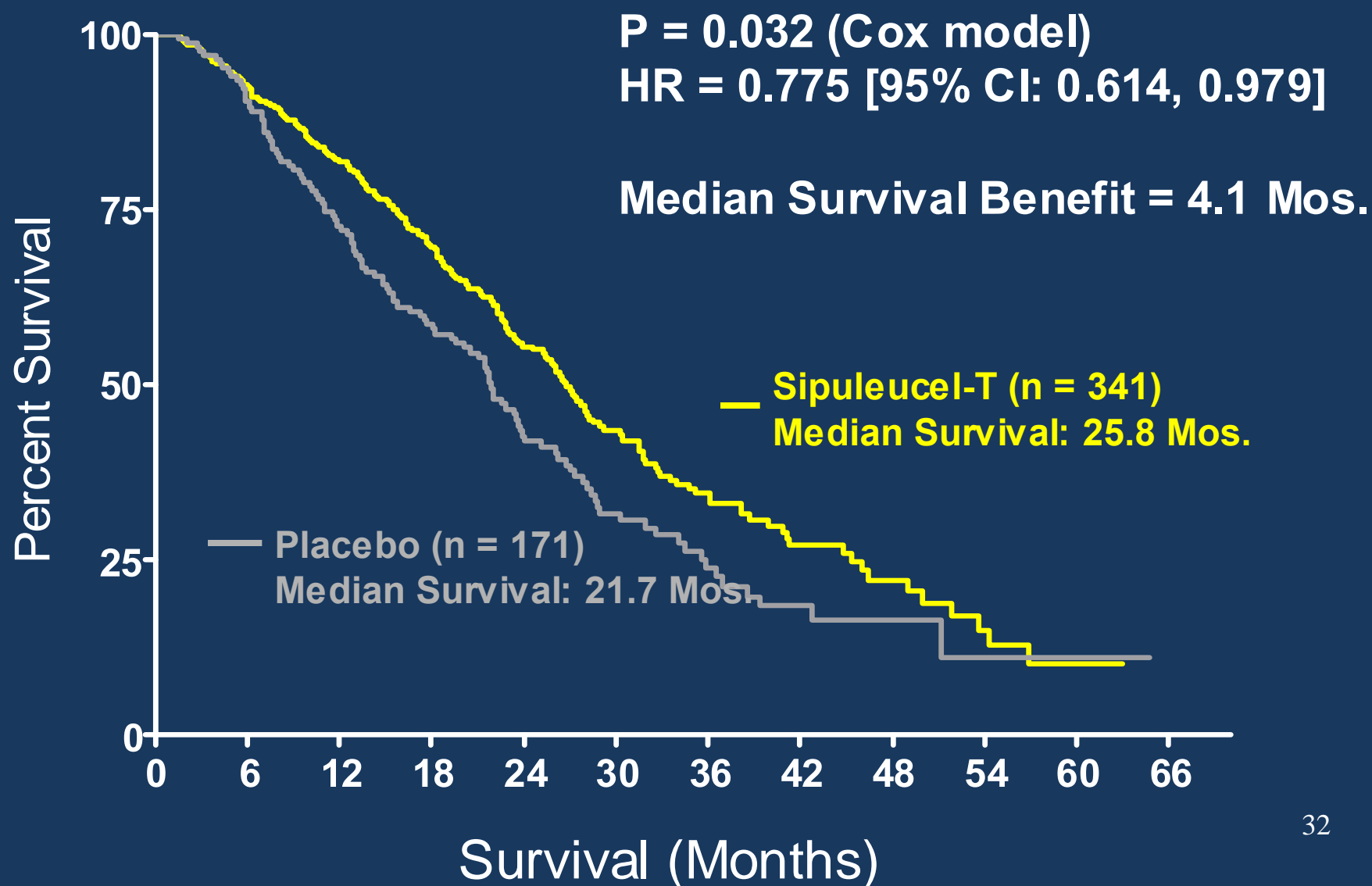
Survival (Months)

Overall Survival Summary

	N	Survival Percentiles (months)		
		75%	**50%**	**25%**
Sipuleucel-T	341	15.1	**25.8**	41.3
Placebo	171	11.0	**21.7**	35.6

	% Survival (K-M estimates)		
	24 Mos.	**36 Mos.**	**48 Mos.**
Sipuleucel-T	52.1	**31.7**	20.5
Placebo	41.2	**23.0**	16.0

Survival Consistency Between Population Subsets

Favors sipuleucel-T

Hazard Ratio (95% Confidence Interval)

Bisphosphonate Use: Yes
No
Primary Gleason Grade: ≥ 4
≤ 3
No. Bone Metastases: > 10
≤ 10
Disease Localization: Single
Bone + Soft Tissue
ECOG Performance Status: 1
0
Age: Above Median
Below Median
PSA: Above Median
Below Median
LDH: Above Median
Below Median
Alkaline Phos: Above Median
Below Median
Hemoglobin: Above Median
Below Median

0.0   0.5   1.0   1.5

Survival Results Confirmed by Multiple Sensitivity Analyses

Favors sipuleucel-T

	Hazard Ratio	P-value
Primary Model (Adj. for PSA, LDH)	0.775	P = 0.032
Unadjusted/Log Rank	0.766	P = 0.023
Adjusted for Docetaxel Use	0.763	P = 0.036
PCa-Specific Survival	0.772	P = 0.036

Hazard Ratio (95% Confidence Interval)

0.0   0.5   1.0   1.5

Time to Objective Disease Progression

- Secondary endpoint

- Result

  – Independent radiologic review

  – HR=0.951 (95% CI: 0.77,1.17); P=0.628 (log rank)

- Consistent with other trials in advanced prostate cancer

- Difficult endpoint to measure reliably and doesn't correlate with overall survival

Most Common Adverse Events (≥ 5%)
Higher Rate in Sipuleucel-T (p ≤ 0.05)

Preferred Term	Sipuleucel-T N = 338 %	Placebo N = 168 %
Chills	54.1	12.5
Pyrexia	29.3	13.7
Headache	16.0	4.8
Influenza-like illness	9.8	3.6
Hypertension	7.4	3.0
Hyperhidrosis	5.3	0.6

Consistency Across Phase 3 Studies

|	D9901* (N = 127)	D9902A* (N = 98)	IMPACT ** (N = 512)	Integrated** (N=737)
Hazard Ratio	0.586	0.786	0.775	0.735
p-value	p = 0.010	p = 0.331	p = 0.032	p < 0.001
Median Survival Benefit (months)	4.5	3.3	4.1	3.9
36-Month survival (%)				
sipuleucel-T	34%	32%	32%	33%
placebo	11%	21%	23%	20%

*Unadjusted Cox model & log rank
**Cox model adjusted for PSA and LDH

Summary

- Confirms improvement in overall survival for advanced prostate cancer

- Highly favorable benefit to risk profile

- Short duration of therapy

- Potential to create new treatment paradigm in oncology

- Amend BLA November 2009

Active Cellular Immunotherapy: A Potential New Treatment for Prostate Cancer
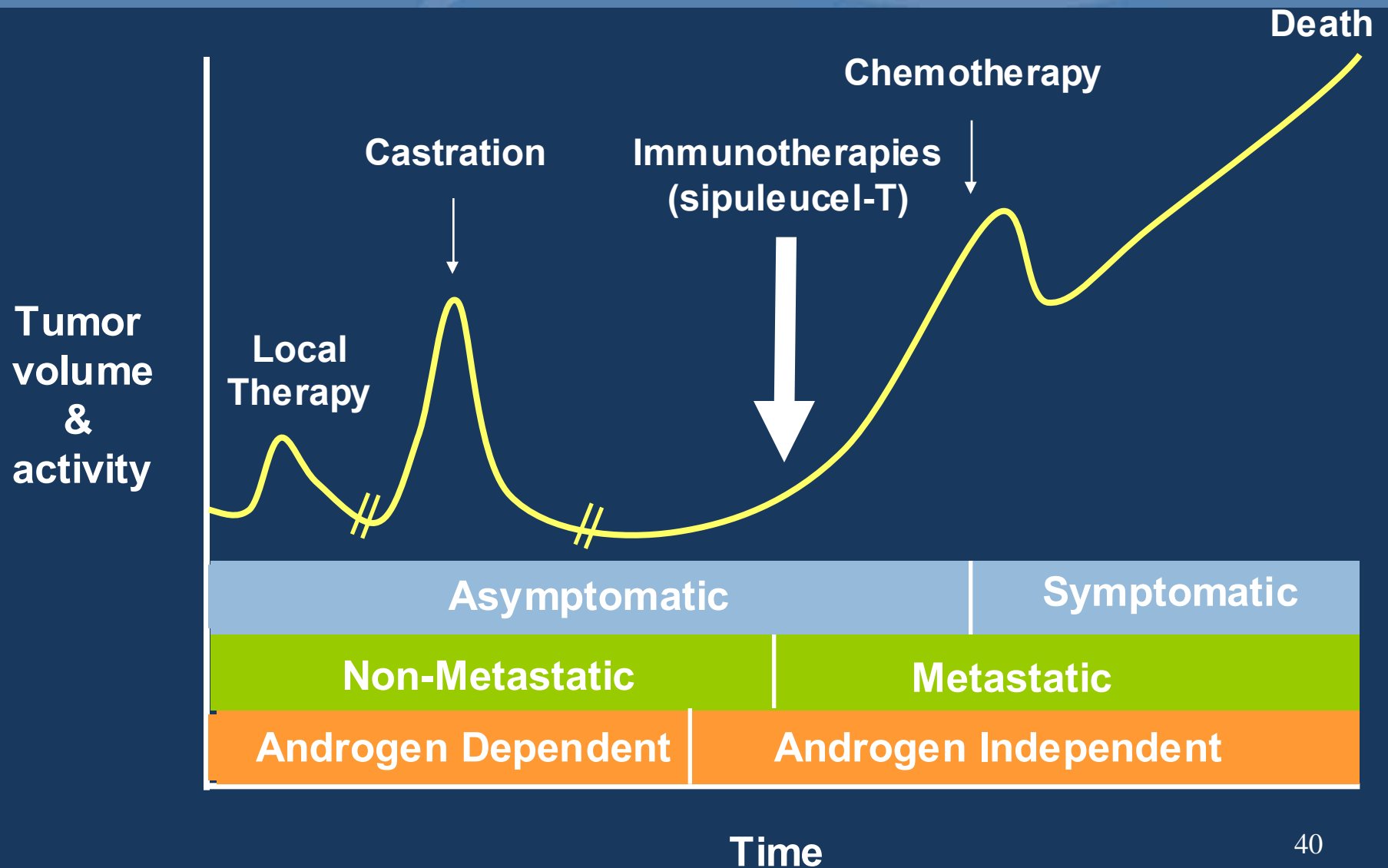
Acknowledgements

We are indebted to the patients who volunteered for this trial.

IMPACT Study Investigators

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Dendreon Personnel

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