

# Castration-Resistant Prostate Cancer 2010 Update

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# Sipuleucel-T

- Autologous dendritic cells that have been exposed ex vivo to PA2024
- Composed of prostatic acid phosphatase (PAP) linked to granulocyte-macrophage colony stimulating factor (GM-CSF)
- Manufactured as recombinant protein antigen



## DAY 1 - LEUKAPHERESIS

The patient gets standard blood collection where white blood cells are extracted for treatment.

## DAY 2–3: PROVENGE MANUFACTURED

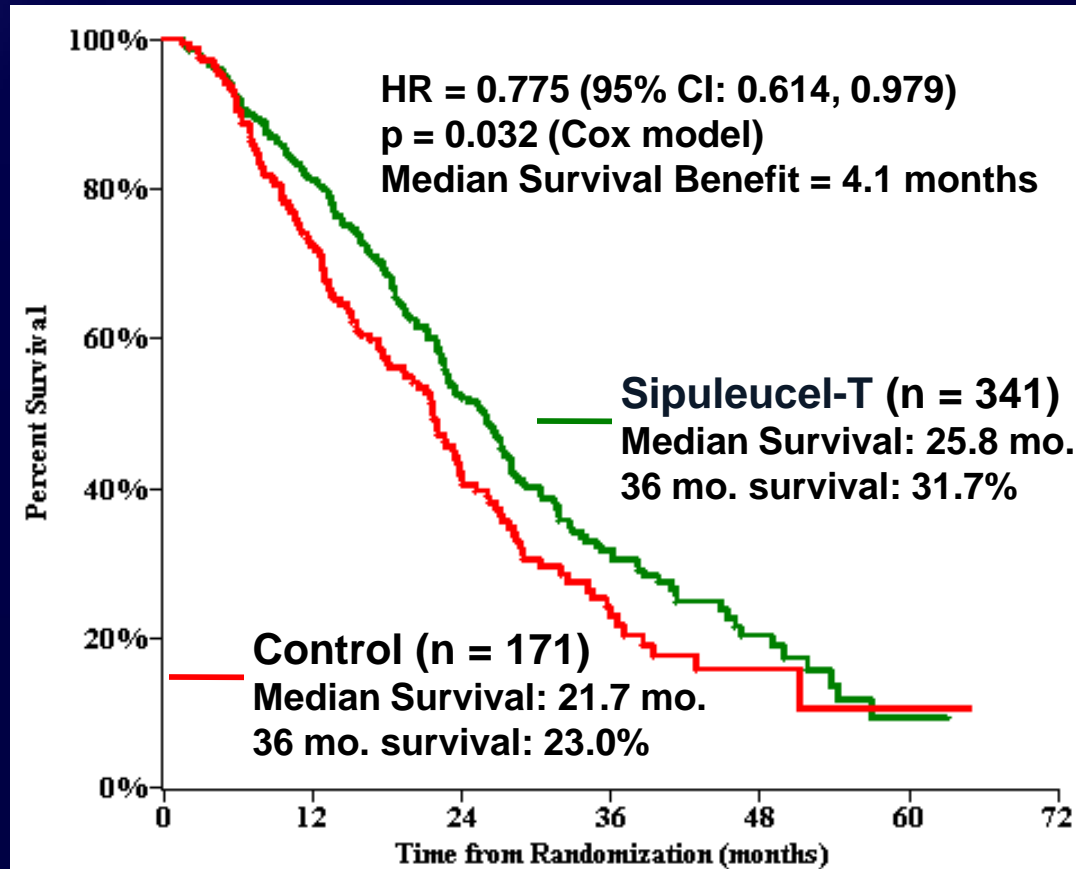
The patient's peripheral blood mononuclear cells (PMBCs) are separated from other white blood cells using proprietary technology.

## DAY 3–4: PATIENT INFUSED

The physician administers the pt's PROVENGE intravenously.  
*Complete course of therapy: 3 cycles*

# IMPACT: OS

## Primary Analysis (331 events)



### No. at Risk

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

# Sipuleucel-T: Common Adverse Events

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

# IMPACT: Did Differences in Post-Progression Treatment Impact Outcomes?

	<b>Sipuleucel-T</b> (n = 341)	<b>Control</b> (n =171)
<b>Any Intervention</b>	<b>81.8%</b>	<b>85.4%</b>
<b>Any Chemotherapy</b>	<b>65.4%</b>	<b>53.8%</b>
<b>Docetaxel</b>	<b>57.2%</b>	<b>50.3%</b>

- 63% placebo pts received salvage vaccine
- 40% as first post-progression therapy

# Sipuleucel-T: Questions

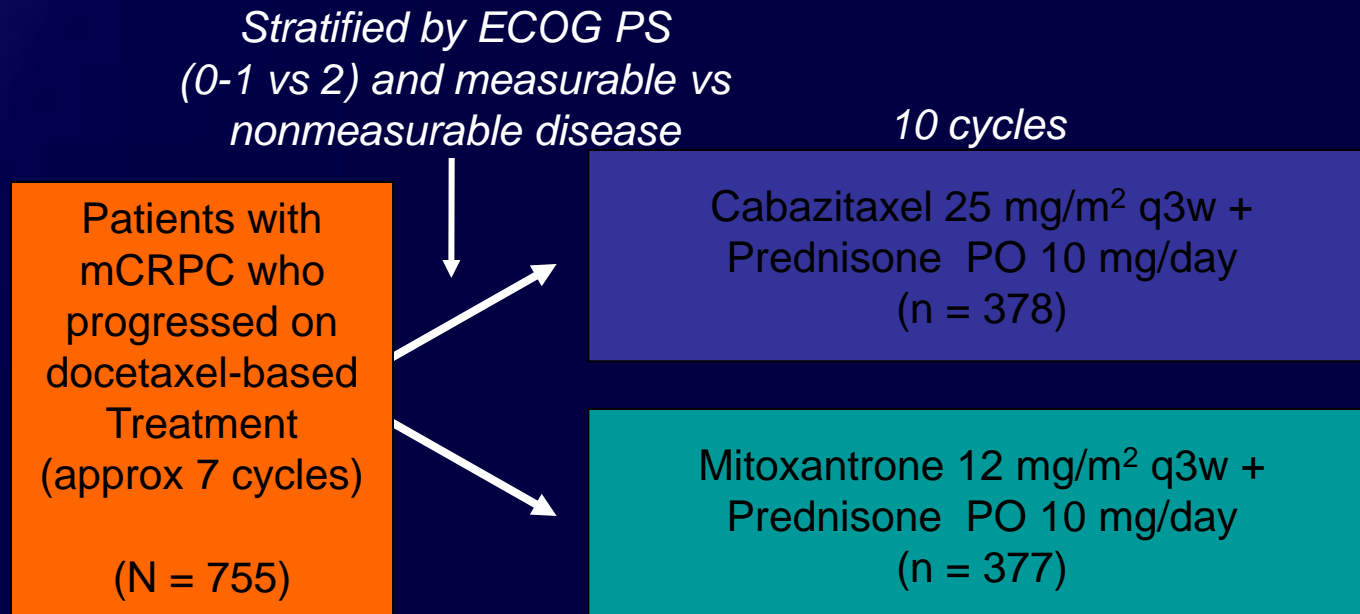
- ?Timing
- Biology
- Clinical Features
- Cost?, Reimbursement?

# Cabazitaxel

- Novel semisynthetic taxane developed to overcome taxane resistance
- Promotes tubulin assembly in vitro and stabilizes microtubules
- Minimal recognition with multi-drug resistance P-Glycoprotein
- 25 mg/m<sup>2</sup> every 3 weeks

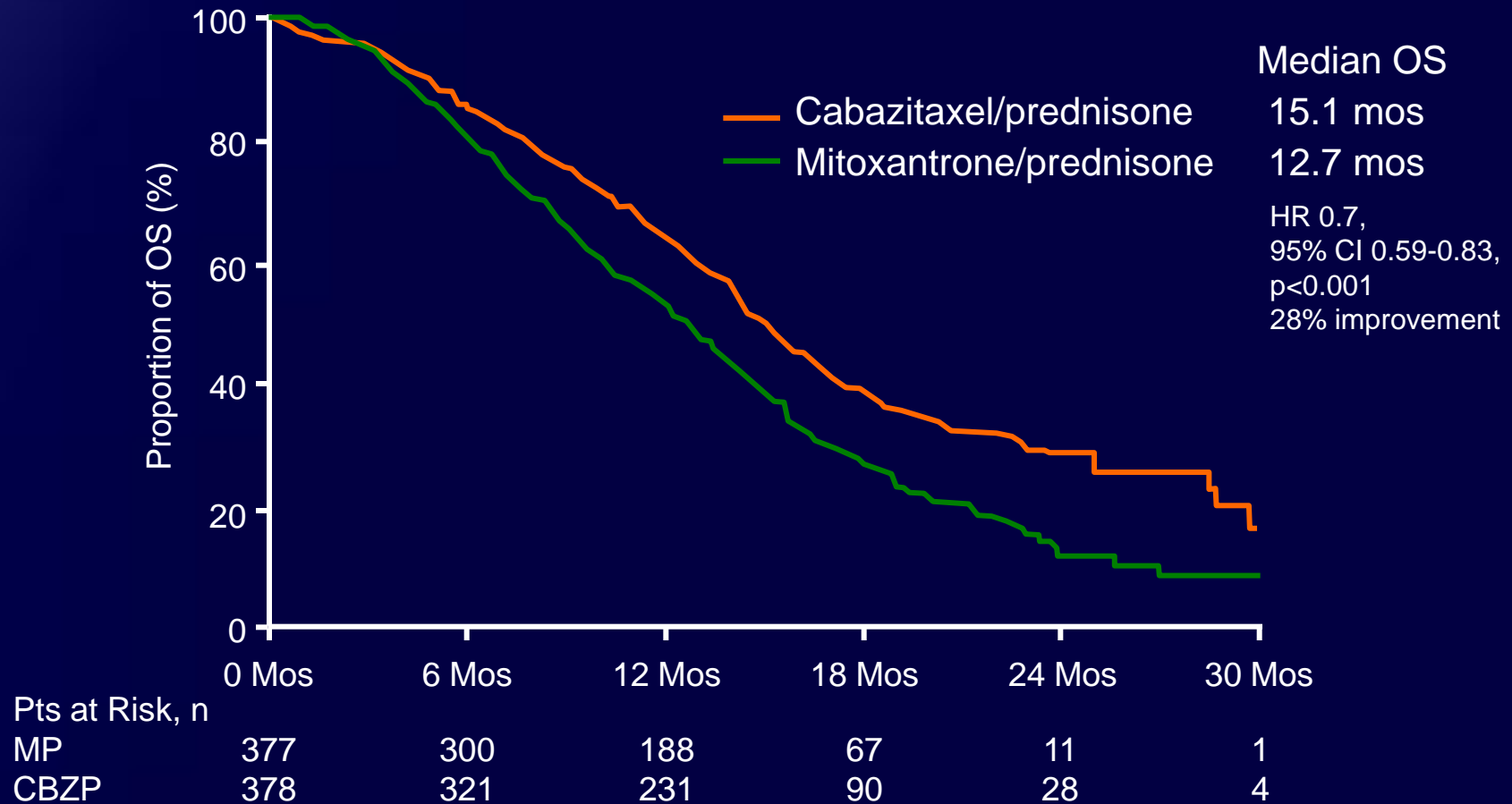
# TROPIC: Phase III Cabazitaxel vs Mitoxantrone in Docetaxel-Treated mCRPC

- 755 pts, 146 centers, 26 countries



- Primary endpoint: OS;
- Secondary endpoints: PFS, Response, TTP, Safety

# TROPIC: Overall Survival



# TROPIC : Safety

DLT - Neutropenia

- Deaths from AEs more common with cabazitaxel vs mitoxantrone (4.9% vs 1.9%)

AE, %	Cabazitaxel/Prednisone (n = 371)		Mitoxantrone/Prednisone (n = 371)	
	All Grade	Grade ≥ 3	All Grade	Grade ≥ 3
Anemia	97.3	10.5	81.4	4.9
Leukopenia	95.7	68.2	92.5	42.3
Neutropenia	93.5	81.7	87.6	58.0
Thrombocytopenia	47.4	4.0	43.1	1.6
Diarrhea	46.6	6.2	10.5	0.3
Fatigue	36.7	4.9	27.5	3
Nausea	34.2	1.9	22.9	0.3
Vomiting	22.6	1.9	10.2	0
Asthenia	20.5	4.6	12.4	2.4
Hematuria	16.7	1.9	3.8	0.5
Back pain	16.2	3.8	12.1	3
Abdominal pain	11.6	1.9	3.5	0
Febrile neutropenia	7.5	7.5	1.3	1.3

# Cabazitaxel

- Improved OS, PFS, TTP (RECIST and PSA), Response rates
- Approved June 2010 for pts who failed docetaxel
- Concerns:
  - Death 4.9% vs 1.9%
  - Quality of Life
  - More Grade  $\geq 3$  toxicity
  - Neuropathy
  - Dose (25mg/m<sup>2</sup> vs 20 mg/m<sup>2</sup>)

# Aberaterone

- CB7630 – Aberaterone Acetate (Cougar)
- Castration-resistant Pr Ca cells continue to express high AR levels, mediate ongoing androgen signalling
- Androgen receptor antagonist
- Highly selective, irreversible inhibitor of cytochrome P-17A1 (17 alpha hydrolase and C17,20-lyase)
- Dual enzyme that blocks androgen production from adrenal glands

# A multicenter phase II study of abiraterone acetate in docetaxel pretreated CRPC pts

- 47 pts, abiraterone 1000 mg/ day, 28 day cycles
- Max PSA declines:
  - $\geq 30\%$  - 69%;  $\geq 50\%$  - 51%;  $\geq 90\%$  - 15%
- RECIST response: 17% PR, 66% SD
- Median duration treatment 167 days (95% CI 130-201).
- Toxicities: mainly grade 1-2
  - Hypokalemia 51%; HTN 17%; Edema 13%

# Abiraterone acetate plus prednisone in chemotherapy-naïve CRPC pts not exposed to ketoconazole: Results of a multicenter phase II study.

- 33 pts, progressive metastatic disease
- Median 2 prior hormonal therapies.
- 81% (17/21) showed decline in PSA levels.
- PSA declines:
  - $\geq 30\%$  - 76%,
  - $\geq 50\%$  - 76%,
  - $\geq 90\%$  - 43%;
  - 2 pts undetectable PSA levels

# Aberaterone

- Current phase III trial in men with castration-resistant prostate cancer who are chemotherapy naïve and asymptomatic / minimal symptomatic
- Phase III trial in men after chemotherapy has been completed, analysis pending
- Possible approval in future