A Clinical Perspective

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Presenter Disclosure Information

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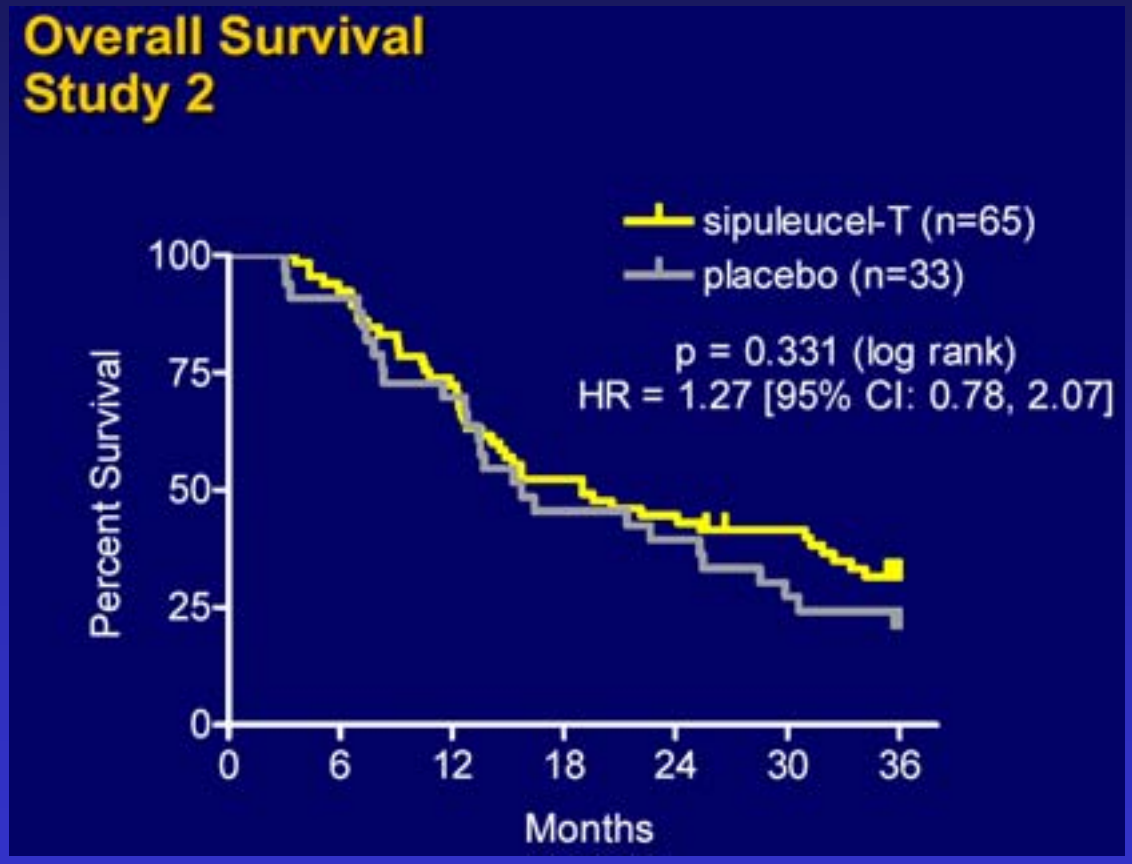
The following relationships exist related to this presentation:

Commercial Interest	**What I Received**	**My Role**
Bristol Meyers Squibb	Consulting Fee	Consultant
Amplimmune Inc	Consulting Fee	Consultant
Dendreon, Inc	Consulting Fee	Consultant
Pfizer, Inc	Consulting Fee	Consultant
Sanofi Aventis	Honorarium	Speakers' Bureau
Cell Genesys, Inc	Honorarium	Speakers' Bureau
Cell Genesys, Inc	Sponsored Research Agreement	Laboratory Investigator

"Doc, What happened to that ProVenge you promised me?"



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"Do you think it's SAFE?"

Adverse Drug Reactions: Severity of Events Integrated Studies 1 & 2

	sipuleucel-T N = 147		placebo N = 76	
Events	Grade 1 or 2 %	Grade 3 or 4 %	Grade 1 or 2 %	Grade 3 or 4 %
Chills	53.0	4.8	7.9	0.0
Pyrexia	29.9	2.0	6.6	0.0
Fatigue	41.5	1.4	28.9	0.0
Headache	17.7	1.4	6.6	0.0
Nausea	13.6	0.7	7.9	0.0
Asthenia	14.3	0.0	3.9	0.0
Dyspnea	7.5	3.4	1.3	1.3
Vomiting	10.2	0.7	2.6	0.0
Tremor	8.8	0.0	0.0	0.0

"Don't you think Immunotherapy is BETTER than Chemotherapy?"

Relationship of Symptom State to Benefit from Docetaxel (TAX 327)

	Docetaxel Q 3 wks median survival (months)	Mitoxantrone median survival (months)	Δ (months)	Hazard Ratio
Asymptomatic (N = 367)	23.0	19.8	3.2	0.73 (p = 0.009)

Overall Survival Summary Study 1

		Survival Percentiles (months)		
	N	75%	50%	25%
sipuleucel-T	**82**	**14.3**	**25.9**	**≥ 36.0**
placebo	**45**	**10.5**	**21.4**	**30.9**

Δ = 4.5 Months

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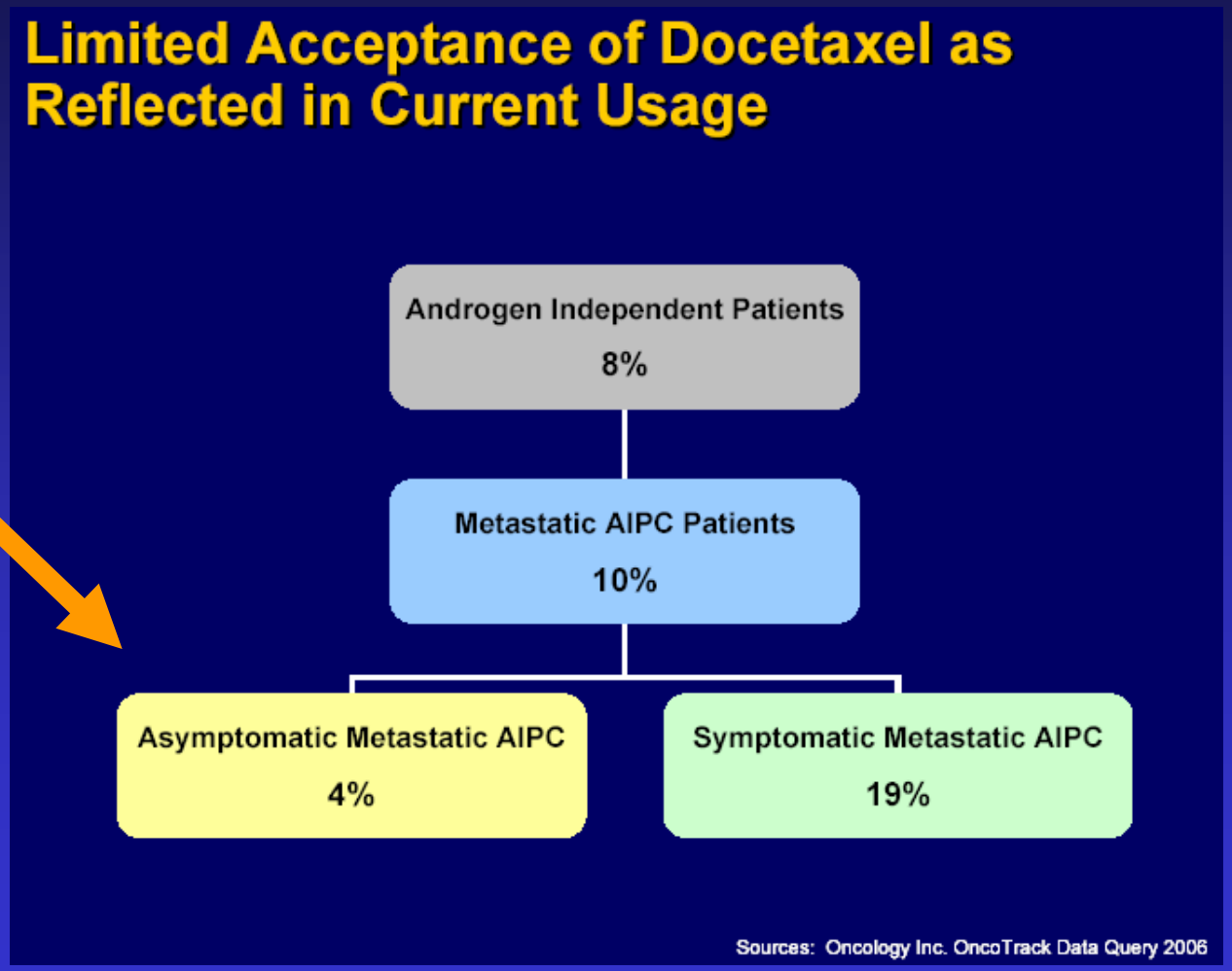
"Chemo? …. I've heard chemo is bad bad bad"

Table 2. Treatment.*

Variable	Docetaxel Every 3 Wk	Weekly Docetaxel	Mitoxantrone Every 3 Wk
No. randomized	335	334	337
No. treated with chemotherapy	332	330	335
No. treated with prednisone	332	330	335
No. of cycles			
Median	9.5	4	5
Range	1–11	1–6	1–11
≥1 Infusion delayed (%)	24	34	21
Dose reduction (%)	12	9	8
Major protocol violation (%)	7	8	7
Reasons for stopping treatment (%)			
Completed treatment	46	35	25
Progression of disease	38	35	56
Adverse event	11	16	10
Withdrawal of consent	1	6	3
Death	1	2	2
Other	4	6	5
Crossover to other drug (%)	27	24	20

N ENGL J MED 351;15 WWW.NEJM.ORG OCTOBER 7, 2004

"If it's not so bad – then why doesn't anyone want it?"



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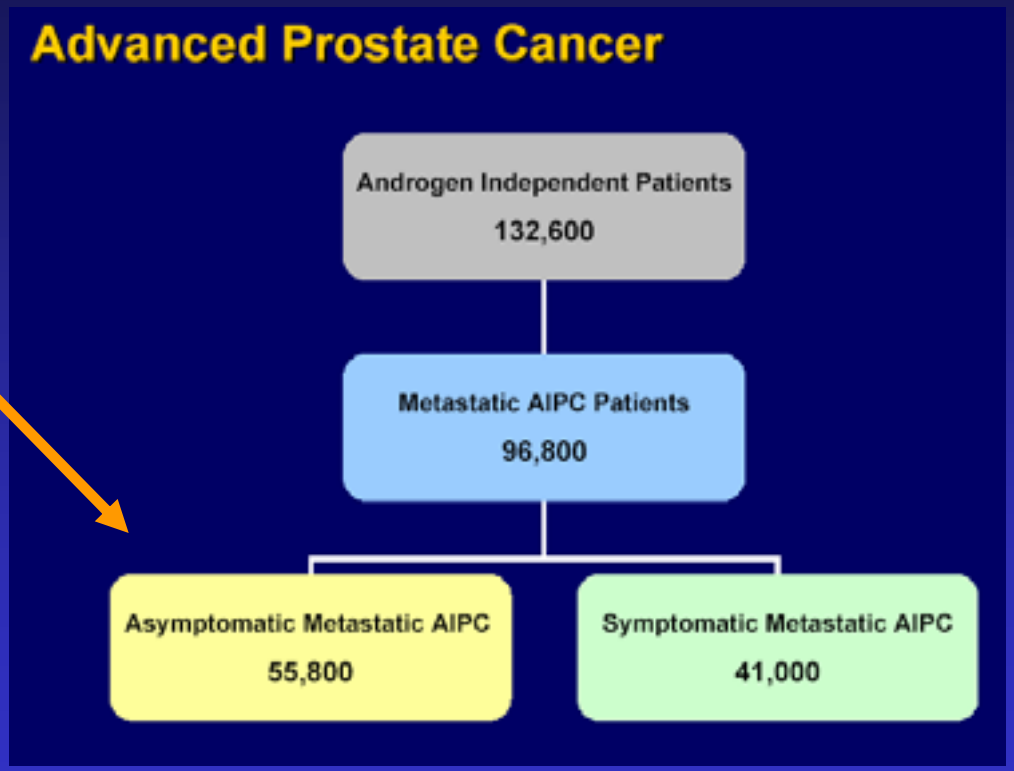
From the back of my napkin ….



50% of ASYMPTOMATIC HRPC Patients = 29,000

X 3 months EACH

= 87,000 months of life saved

= 7000 patient years

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Conclusions

- IMPACT (D9902B) Closed to Accrual in August
  - Interim analysis next year
  - End of survival discussion …

- Inappropriate for biologics to "Dis" conventional therapy
  - Docetaxel has documented survival benefit in asymptomatic HRPC
  - Sipuleucel T benefit is similar (4.5 versus 3.2 months)
  - Unclear whether Sipuleucel alone would achieve same benefit
    - About 50% of patients in D9901 got both sipuleucel T + chemo

- INSTEAD
  - Clinical Reality = many patients will get BOTH
    - Sipuleucel T -> Docetaxel or other way?
    - Co-administration
    - More creative combinations
      - Sipuleucel + Ipilimumab
      - Sipuleucel + Immunomodulatory Cyclophosphamide