Immuno-Oncology Across Tumor Types:

Prostate Cancer

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Disclosures

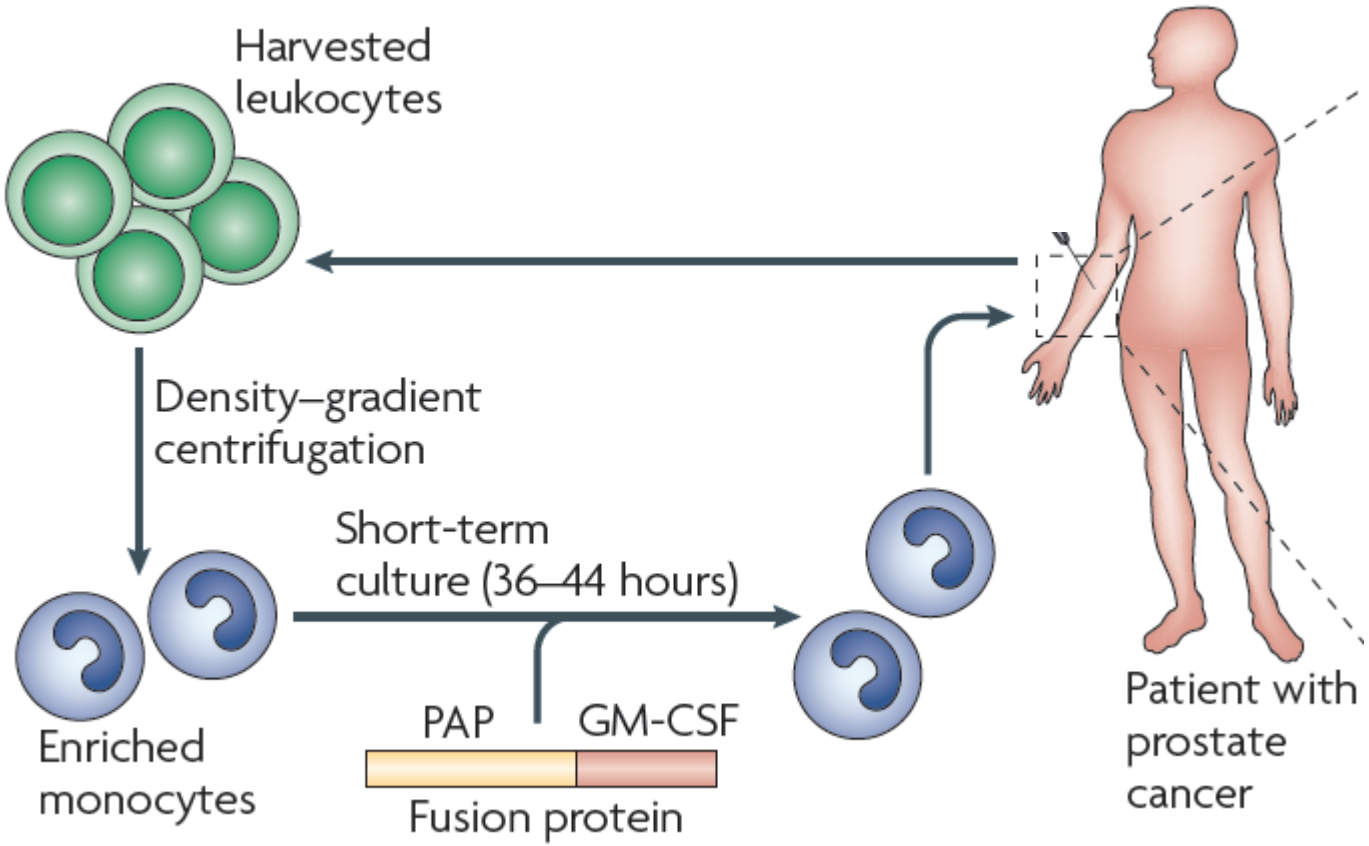
- Consulting: Bristol Myers Squibb, Compugen, Dendreon, ImmunExcite, Merck, NexImmune Novartis, Pfizer, Roche
- Research: Aduro Biotech, BMS
- Patents Licensed: AZ / Medimmune, Potenza

Outline

- Prostate Cancer Vaccines:
  - FDA-Approved Therapy (Sipuleucel-T) for Prostate Cancer
  - Vaccinia – Based Vaccine In Phase III
- Immune Checkpoint Blockade:
  - Anti-CTLA-4 (Ipilimumab) a Near Miss in Prostate Cancer
- Combining Immunotherapy with Hormonal Therapy
- Antigen-Spread following Sipuleucel-T Administration

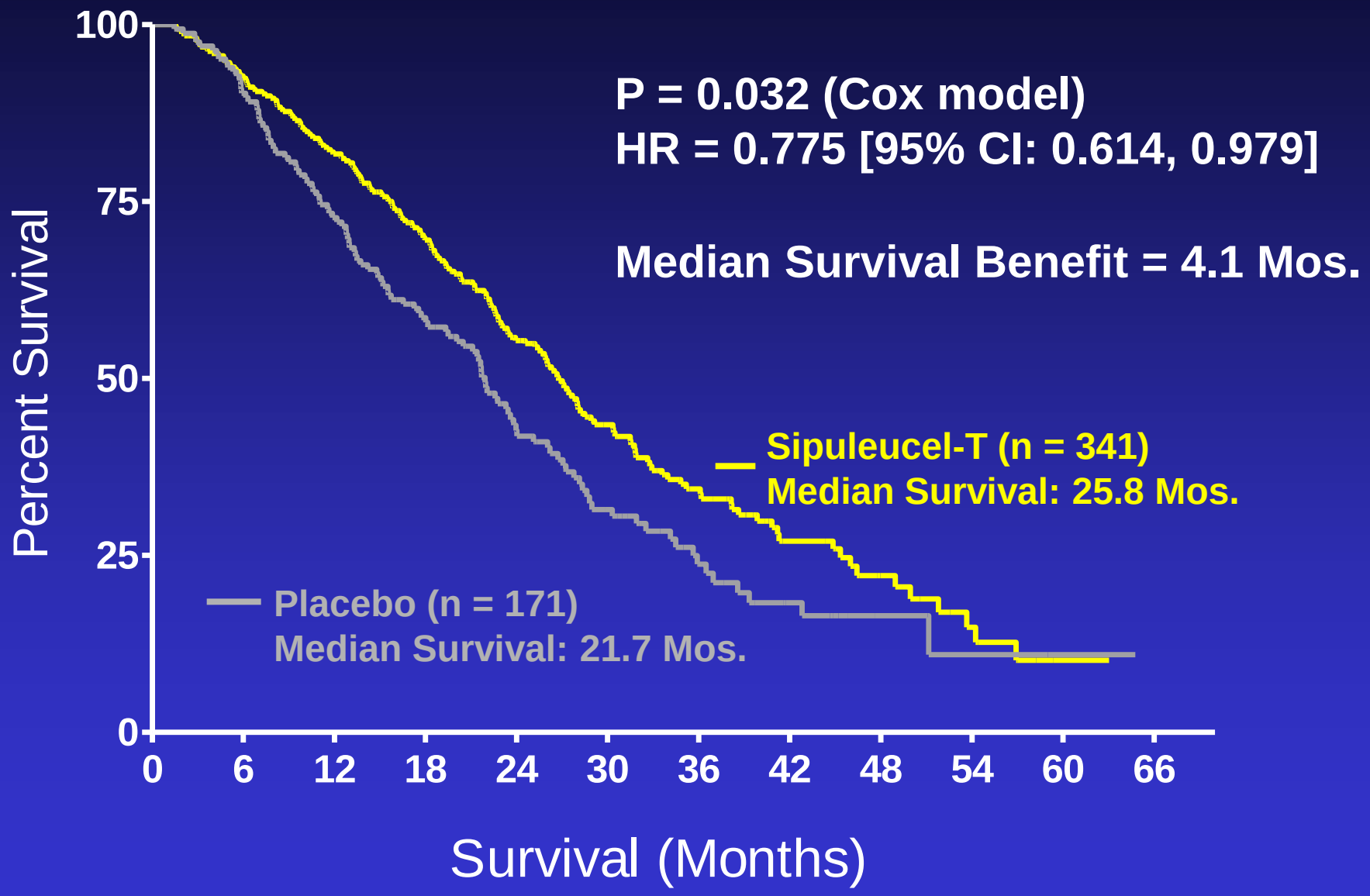
Vaccines

A “Dendritic Cell” Vaccine: Sipuleucel T

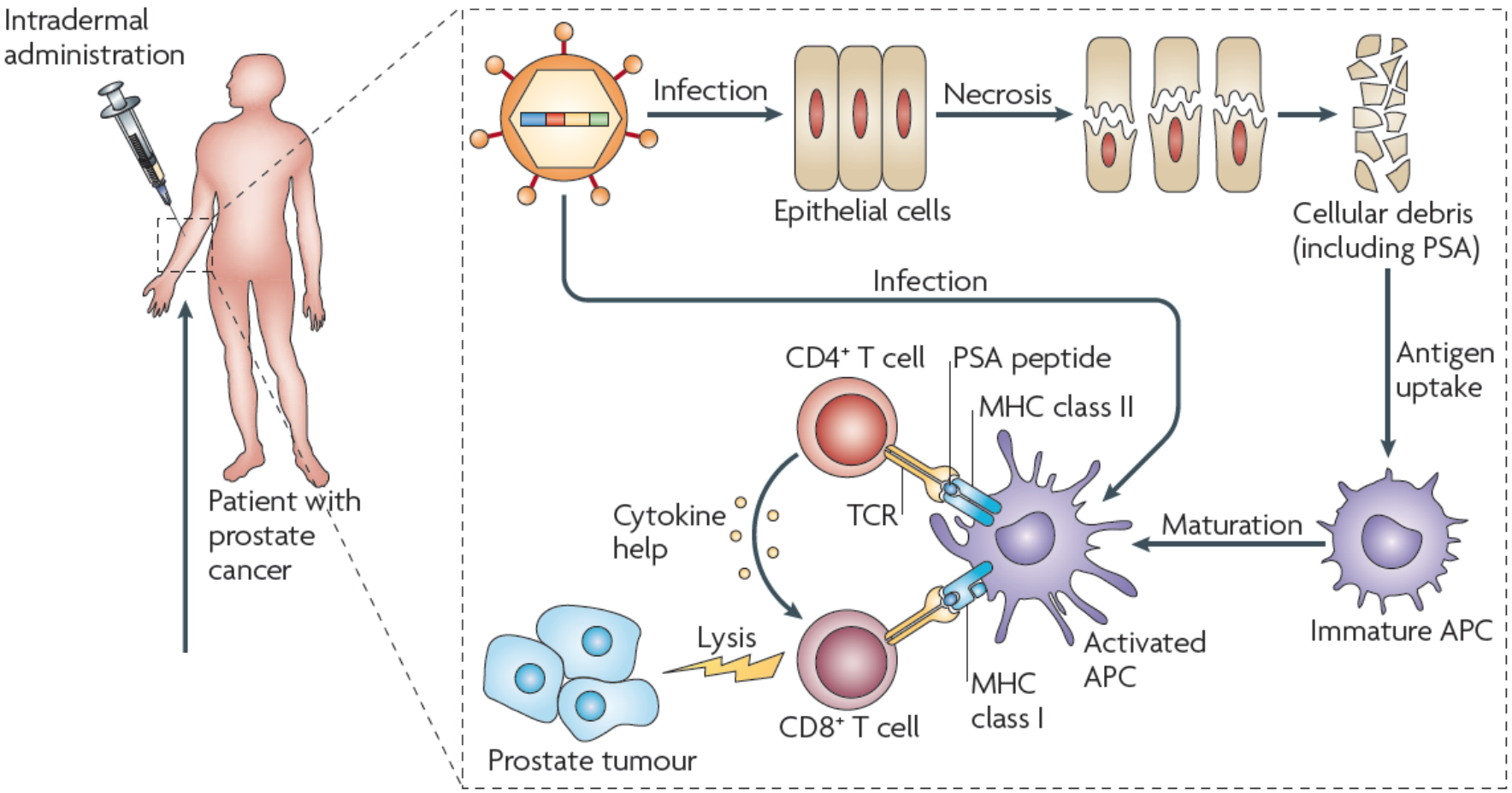


Drake CG *Nat Rev Immunol.* 2010;10:580-93.

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



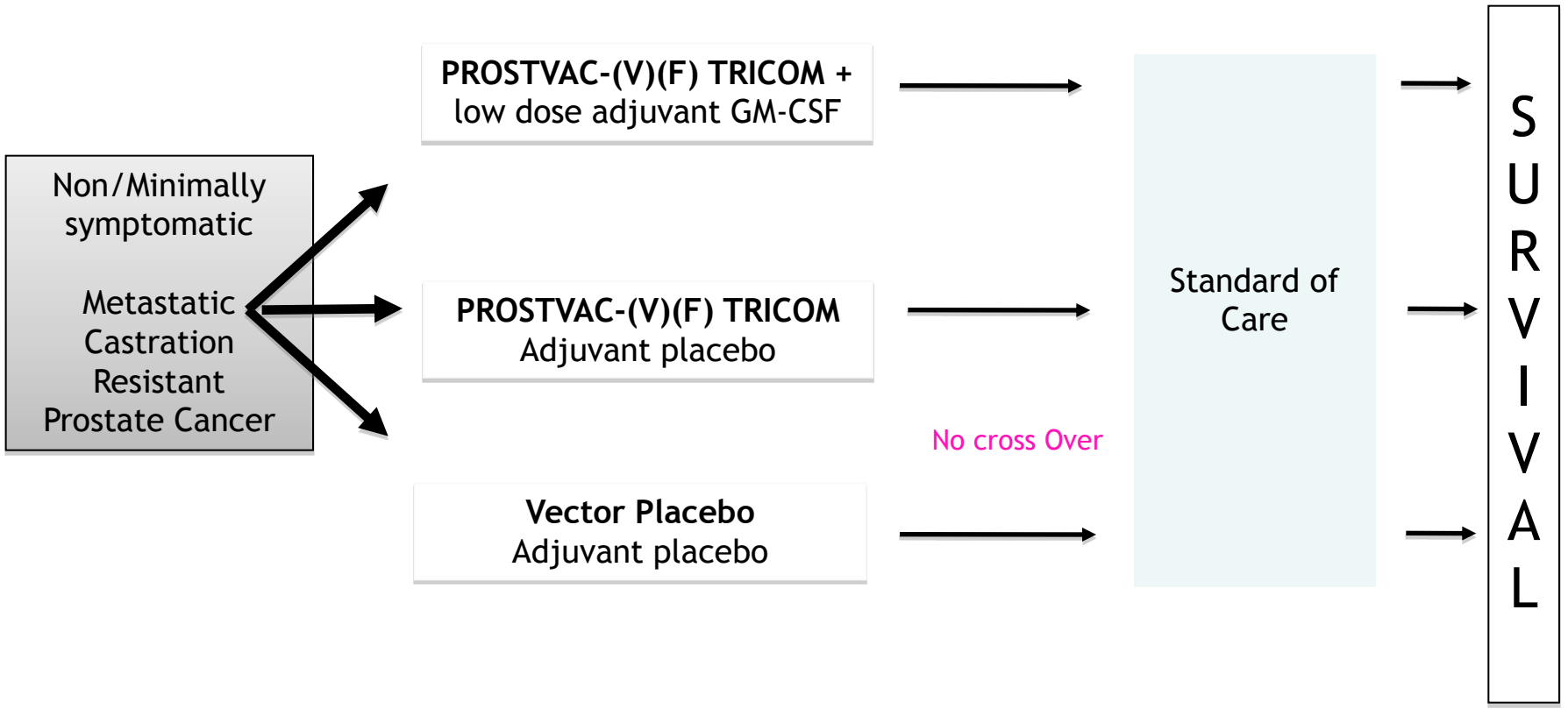
Prost Vac VF In Patients



Drake CG *Nat Rev Immunol.* 2010;10:580-93.

Prospect Trial: Design (SPA)

Phase 3 Global (US-CAN-AUS/WE/EE/Latin America)



PRIMARY ENDPOINT: Overall Survival

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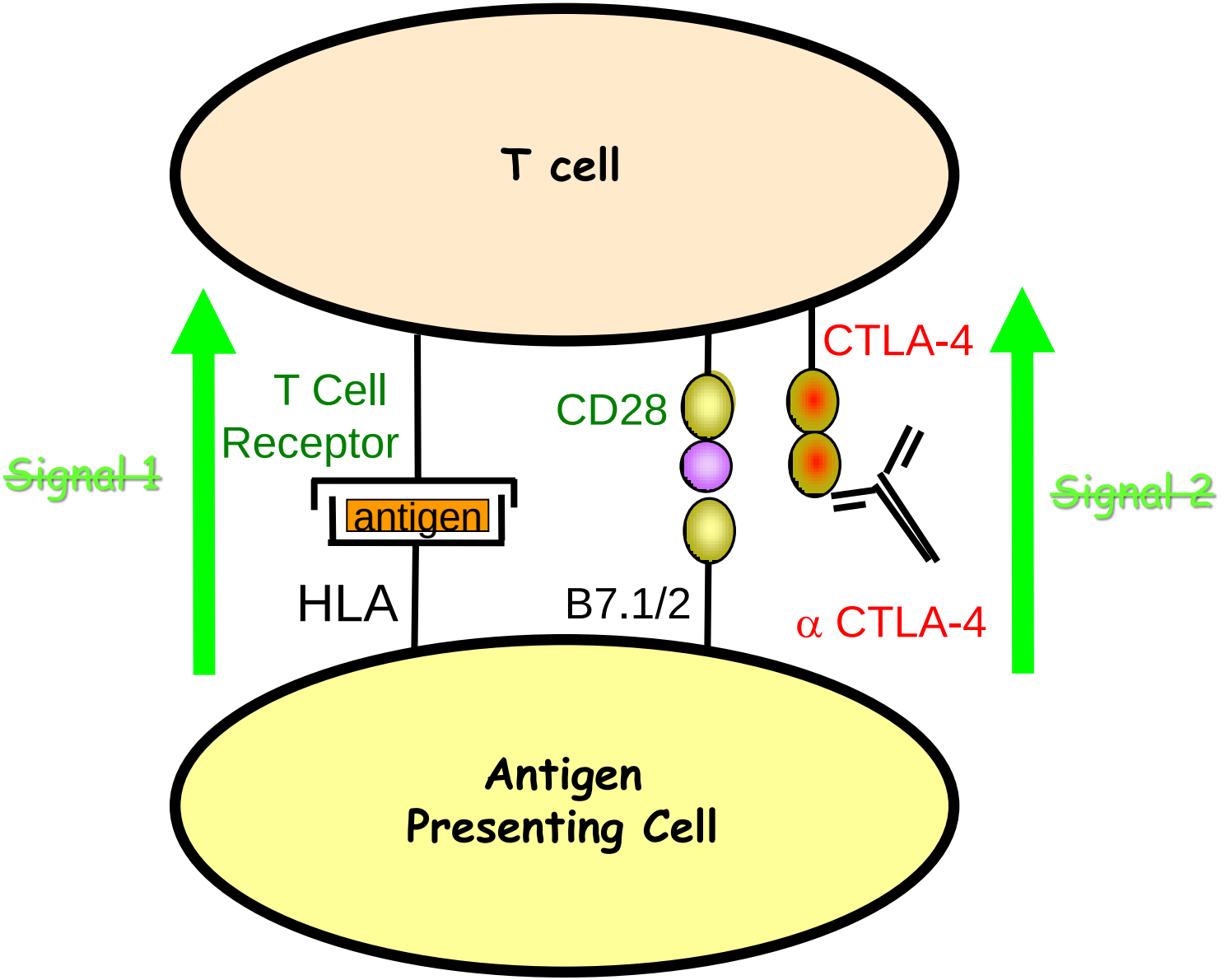
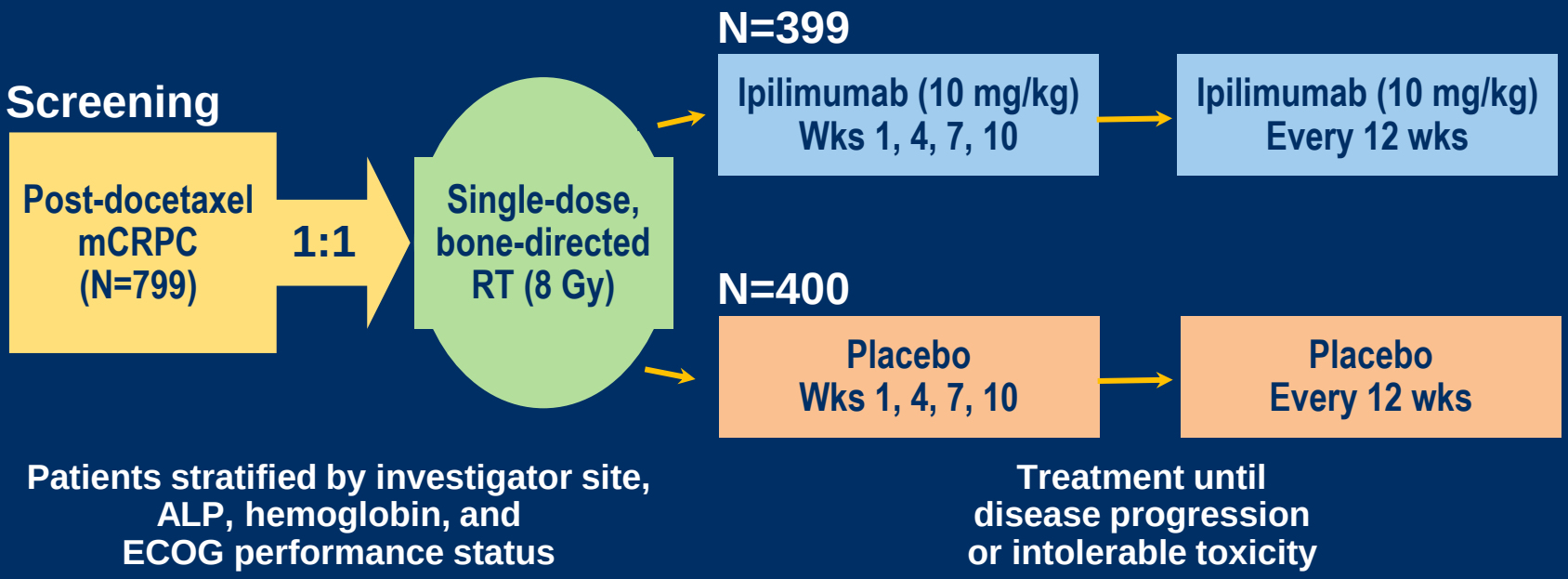
Immune Checkpoint Blockade: CTLA-4

Ipilimumab (Anti-CTLA-4) Blocks the CTLA-4 Checkpoint, RestoringT Cell Activation



Phase 3 Study of Ipilimumab in Post-Docetaxel mCRPC (CA184-043): Study Design*[1]



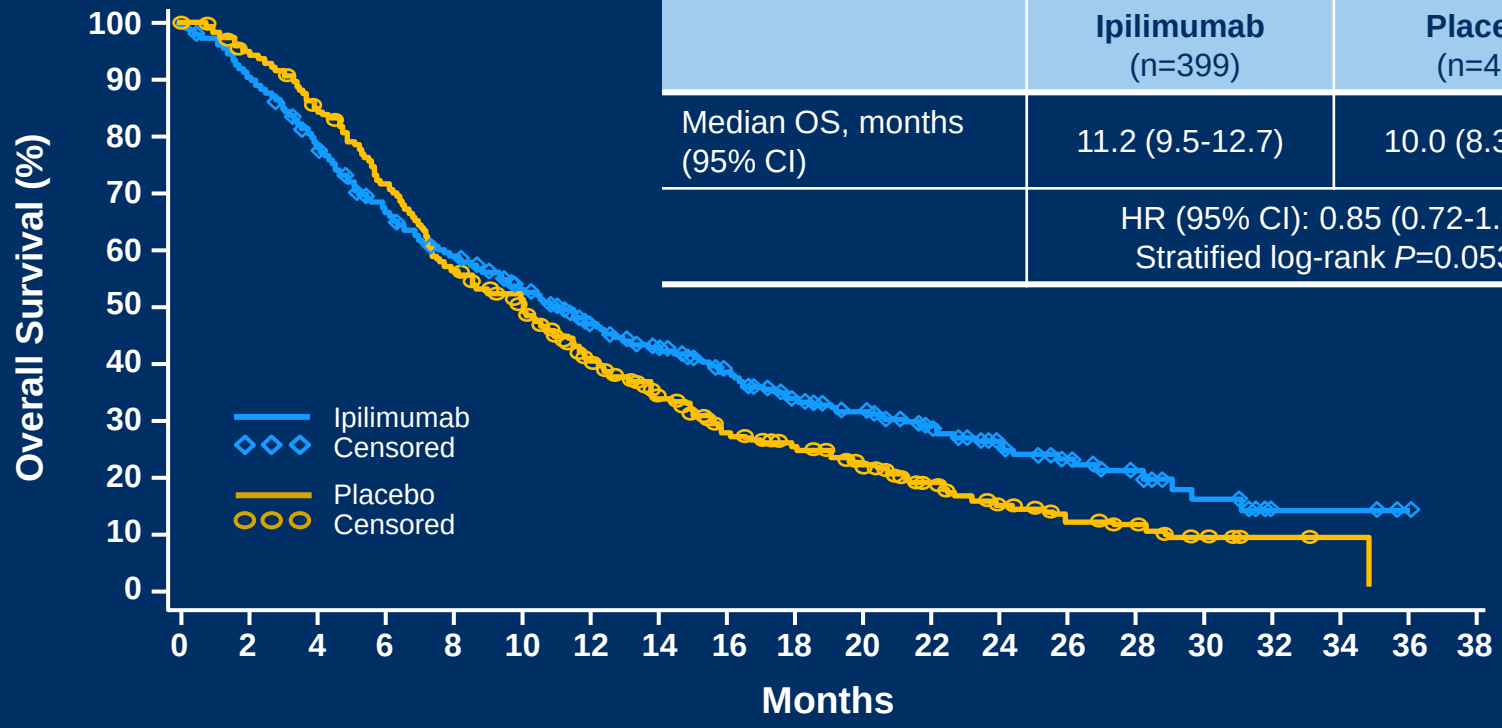
- Primary endpoint: overall survival (OS)
- Secondary endpoints: progression-free survival (PFS), safety
- Exploratory endpoint: prostate-specific antigen (PSA) response rate

*ClinicalTrials.gov Identifier: NCT00861614.
ALP=alkaline phosphatase; ECOG=Eastern Cooperative Oncology Group; RT=radiotherapy.
[1]Gerritsen WR et al. Paper presented at: European Cancer Congress 2013; Amsterdam, The Netherlands. Abstract 2850.

Phase 3 Study of Ipilimumab in Post-Docetaxel mCRPC (CA184-043)[1]

Primary Endpoint: OS (Intent to Treat [ITT] Population)

	Ipilimumab (n=399)	Placebo (n=400)
Median OS, months (95% CI)	11.2 (9.5-12.7)	10.0 (8.3-11.0)
	HR (95% CI): 0.85 (0.72-1.00) Stratified log-rank *P*=0.0530	



Safety

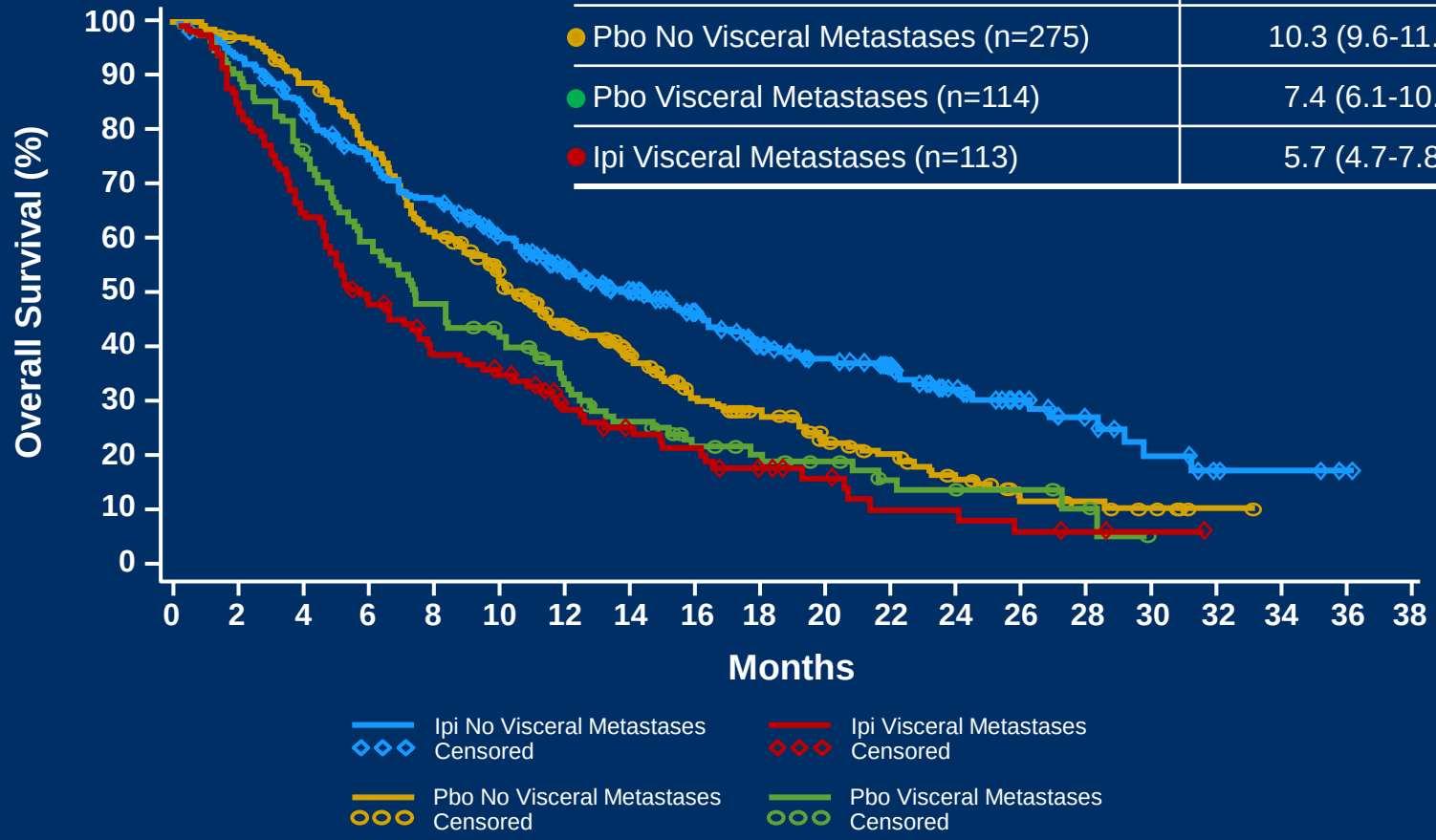
- Adverse event (AE) profile was consistent with that previously reported for ipilimumab*
  - The most frequent severe immune-related AEs were diarrhea and colitis

*See poster presentation at this meeting: Beer et al. Abstract ID: 52.

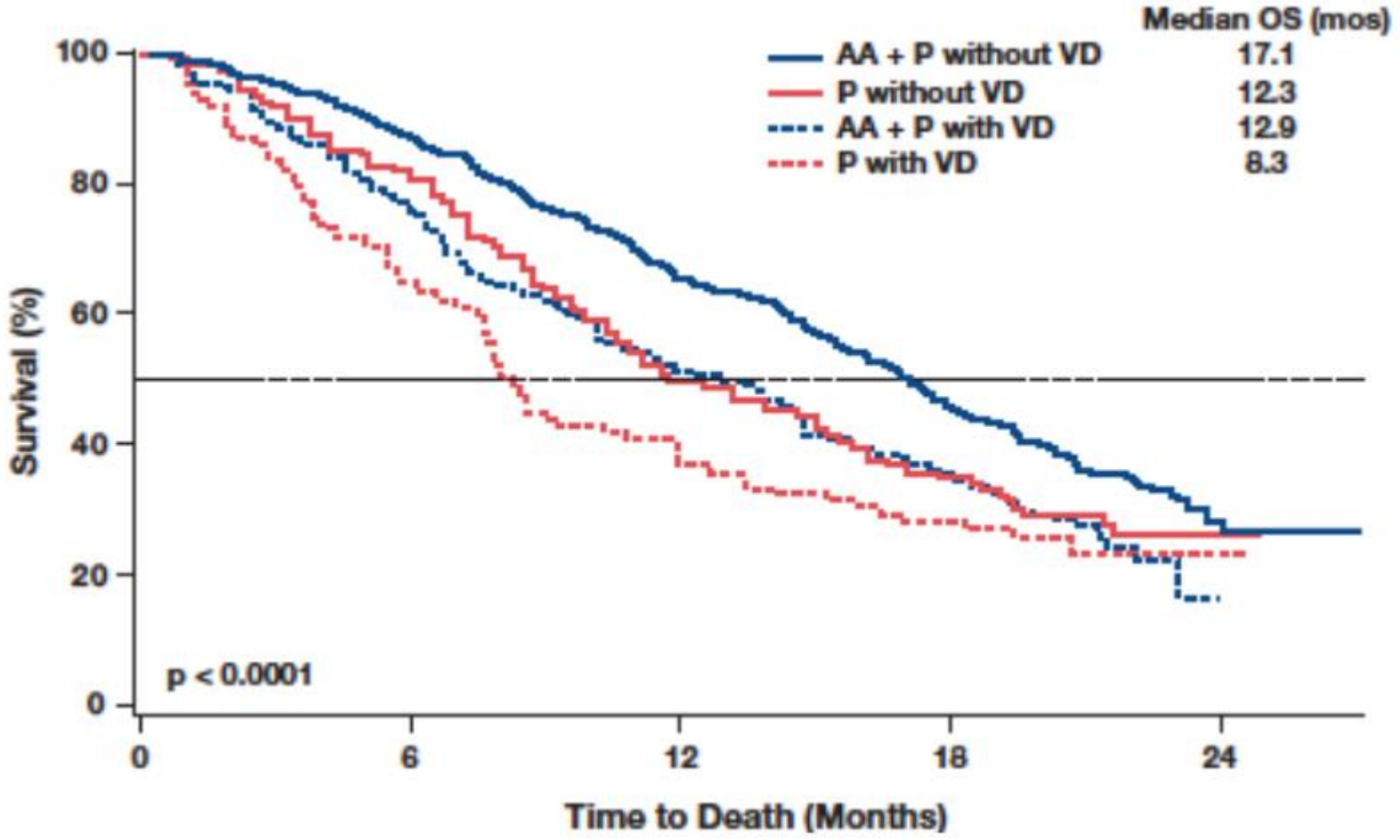
[1]Gerritsen WR et al. Paper presented at: European Cancer Congress 2013; Amsterdam, The Netherlands. Abstract 2850.

OS by the Presence of Visceral Metastases at Baseline

Group	Median OS, months (95% CI)
Ipi No Visceral Metastases (n=280)	14.4 (11.5-16.4)
Pbo No Visceral Metastases (n=275)	10.3 (9.6-11.7)
Pbo Visceral Metastases (n=114)	7.4 (6.1-10.2)
Ipi Visceral Metastases (n=113)	5.7 (4.7-7.8)



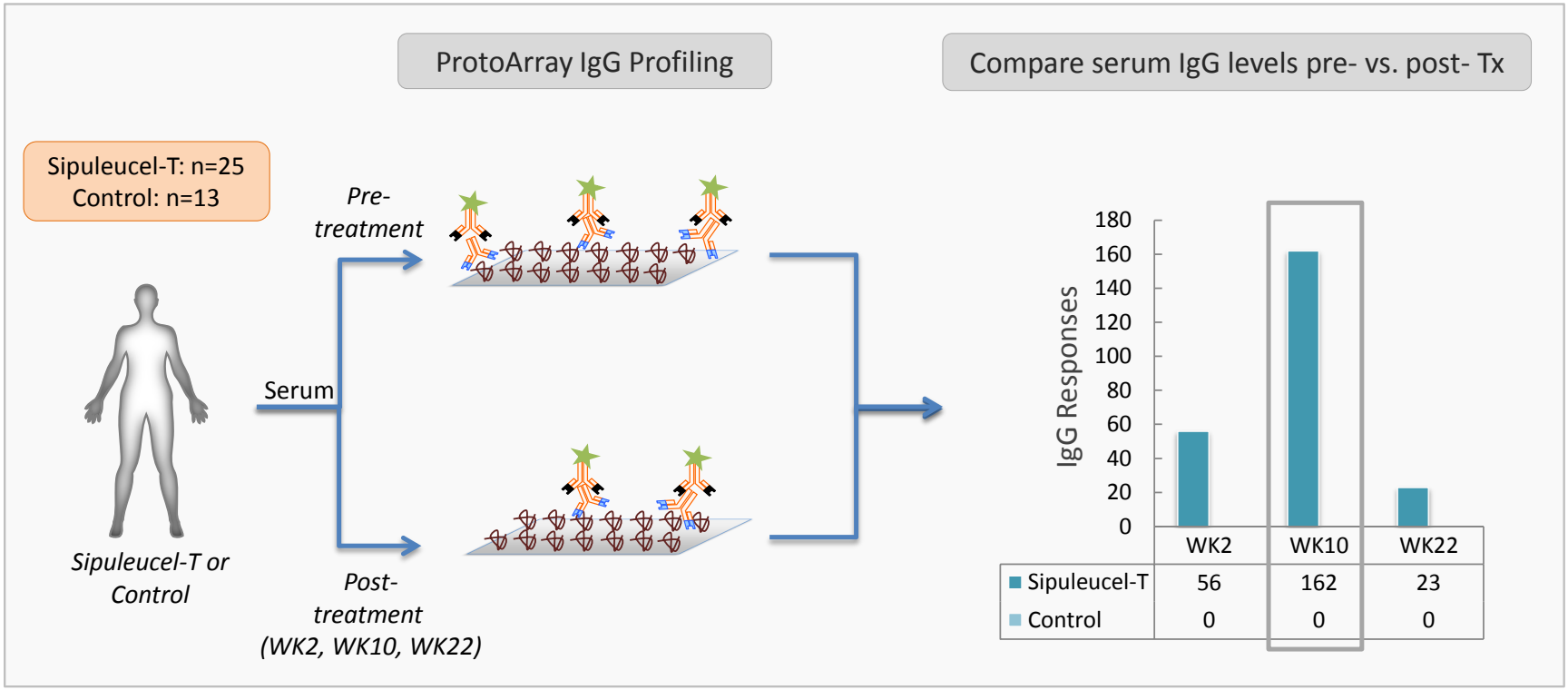
Visceral Mets Don't Seem to Affect Efficacy Of Abiraterone Acetate



Goodman et. al, *PCAN* 2014

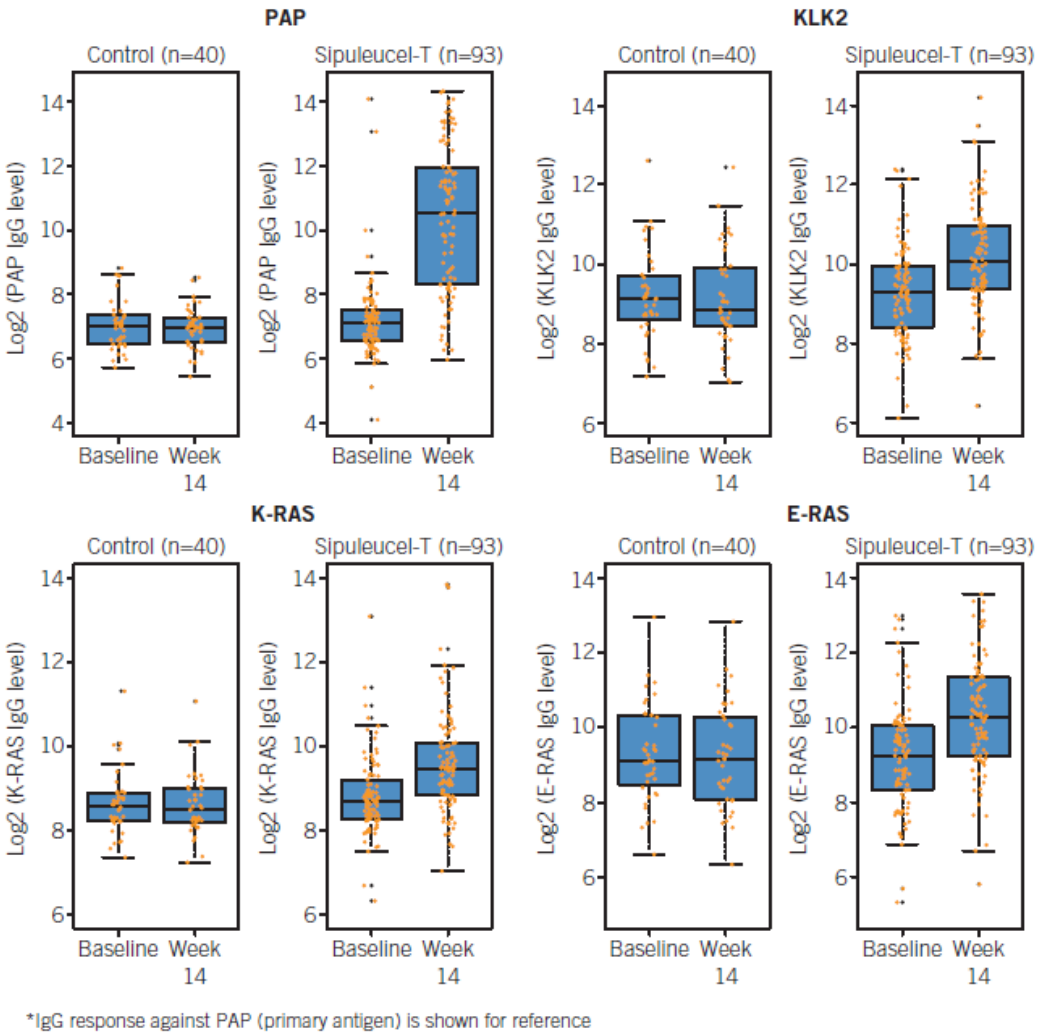
Antigen Spread

Testing for Antigen Spread



Thakurta et. al. *Cancer Immunology* Research, in submission

IgG Responses to Non-Targeted Antigens



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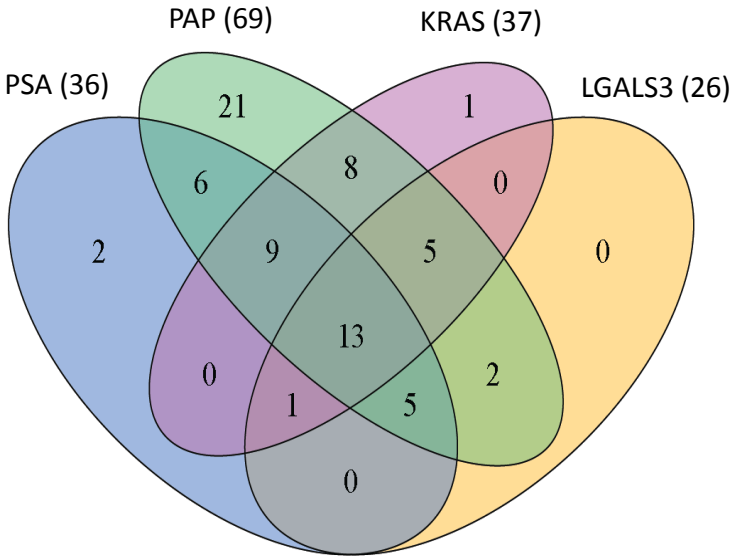
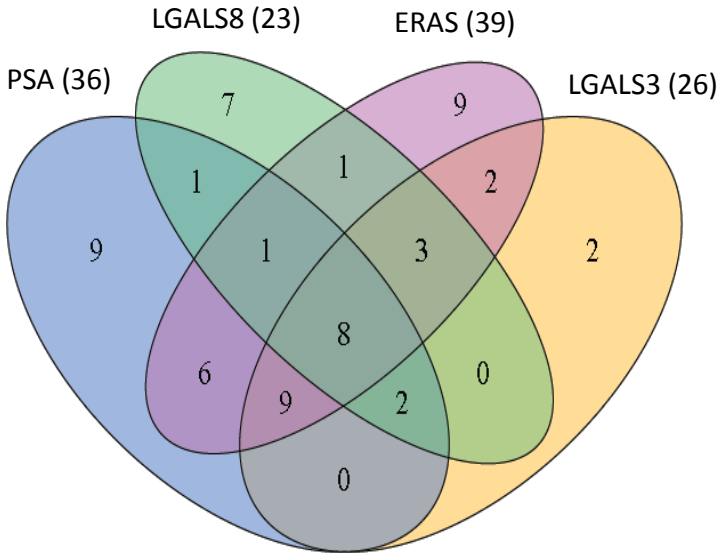
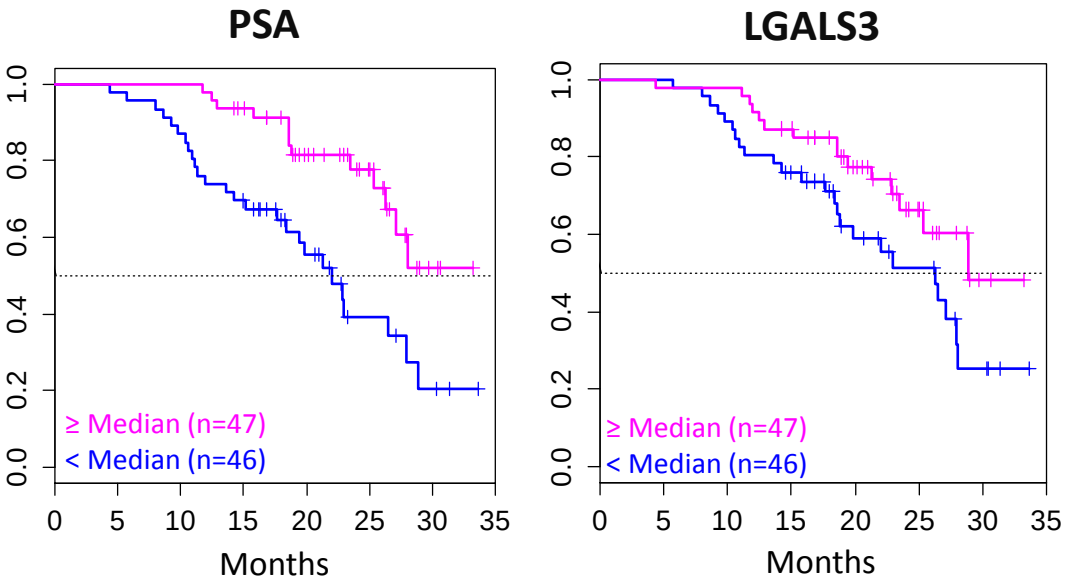
Responses Overlap

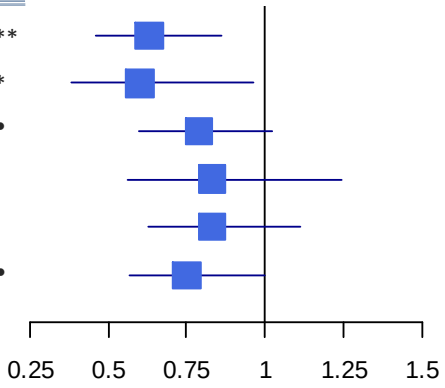




And Correlate With Survival



ANTIGEN	HR	P-VALUE
PSA	0.63	0.003**
LGALS3	0.60	0.035*
ERAS	0.79	0.075•
LGALS8	0.83	0.369
KRAS	0.83	0.218
KLK2	0.75	0.051•



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Summary

- One cancer vaccine that is US FDA-approved for treating prostate cancer
- Ongoing Phase III Vaccine Trials in Prostate Cancer
  - ProstVac VF
- Immune Checkpoint Blockade is not FDA-approved to treat prostate cancer
  - Phase III trial of anti-CTLA-4 (ipliimumab) pre-chemotherapy prostate cancer
  - Not much activity for anti-PD-1 in advanced prostate cancer
- Are visceral mets in prostate cancer immunologically different
  - Resistant to immune attack?
  - Hostile microenviroment?
  - Systemic immune suppression (cytokine-mediated?)
- Antigen Spread