

ADVANCES IN  
**Cancer**  
IMMUNOTHERAPY™



# Immunotherapy for the Treatment of Genitourinary Cancers

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Society for Immunotherapy of Cancer

# Disclosures

Consultant: Astra Zeneca, Genentech

Contracted Research: Astra Zeneca

Only FDA approved indications will be discussed



# Immunotherapy for Genitourinary Cancers

Prostate Cancer

Urothelial (bladder) Cancers

Renal Cell Carcinoma (RCC)



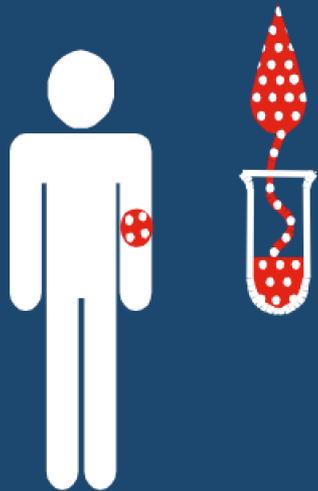
# Immunotherapy for Prostate Cancer

- Sipuleucel T (Provenge)



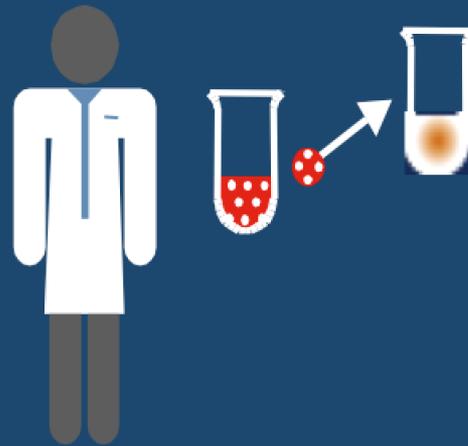
# Sipuleucel-T: A personalized immunotherapy

**Day 1**  
Blood draw



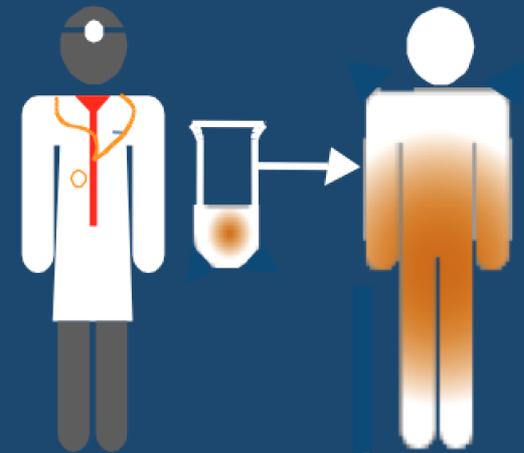
Infusion center

**Day 2-3**  
Blood immune cells activated



Lab

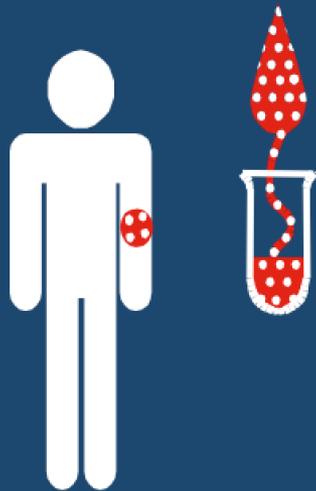
**Day 3-4**  
Provenge is infused



Doctor's Office

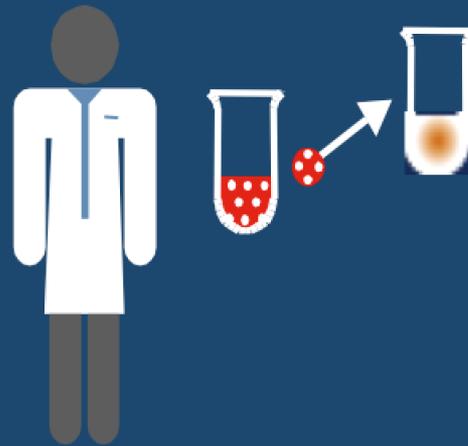
# Sipuleucel-T: A personalized immunotherapy

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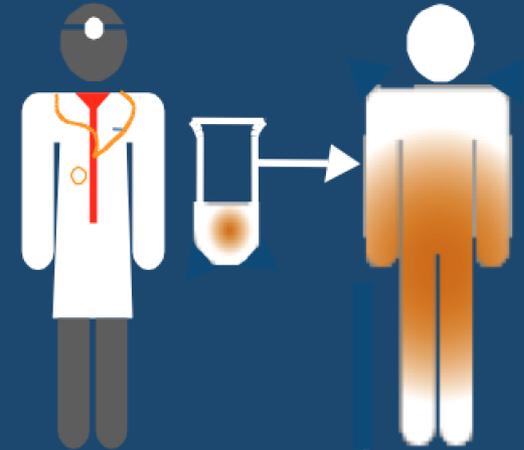
Infusion center

**Day 2-3**  
Blood immune cells activated



Lab

**Day 3-4**  
Provenge is infused



Doctor's Office

**COMPLETE COURSE OF THERAPY:**  
3 times over 6 weeks



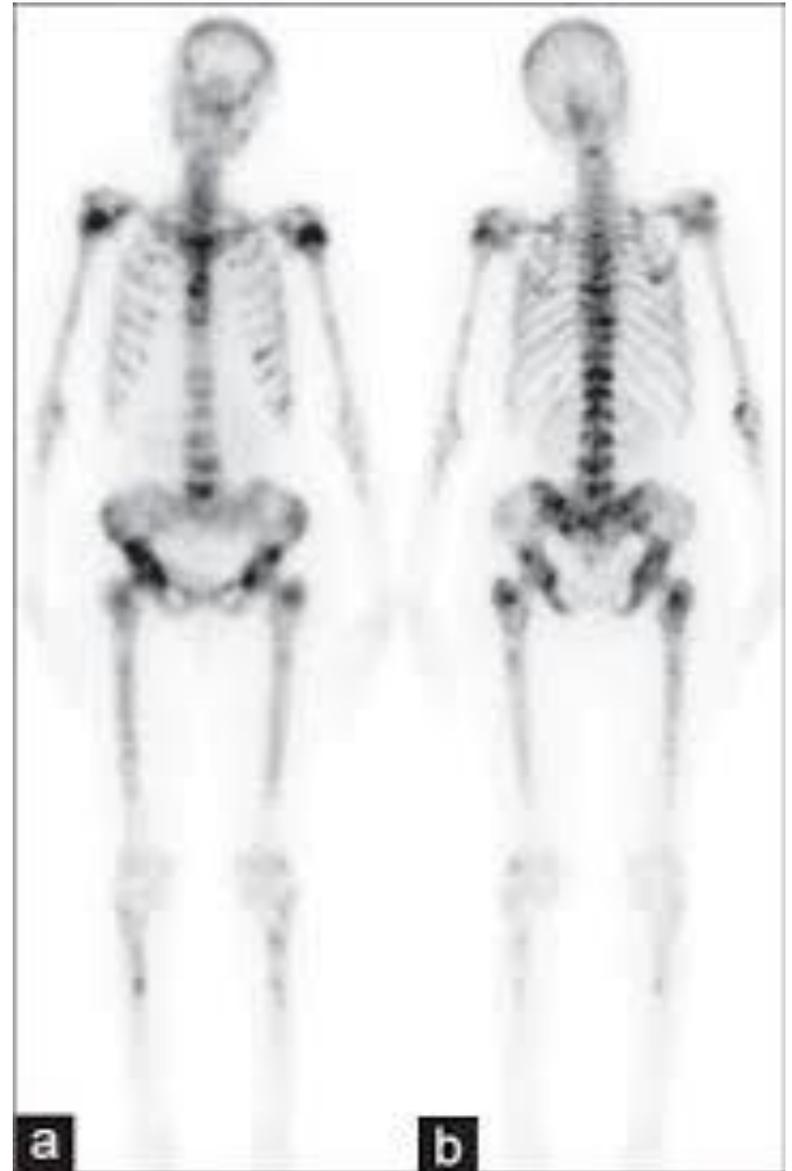
# Immunotherapy for Prostate Cancer

- Sipuleucel-T vs Placebo in men with asymptomatic metastatic castration-resistant prostate cancer
  - Survival benefit: 25.8 months vs. 21.7 month
  - Well tolerated
  - Few objective responses!
  - Few PSA declines!
- Likely “slows” progression of disease
  - No clear biomarker of response
- Ideal patient:
  - Metastatic prostate cancer
  - Rising PSA despite hormonal therapy
  - Mild-moderate disease burden
  - Not using opiates



# Case 1

- 69 year old M
- Prostatectomy 7 years ago
  - G1 4+3, pT3N0
- Develops multiple bony metastases
- Responds to androgen deprivation therapy for 3 years.
- PSA now rising, currently 15.4 ng/dL
- Feels well, denies pain





# What would you offer him?

**POSITION ARTICLE AND GUIDELINES**

**Open Access**



## The Society for Immunotherapy of Cancer consensus statement on immunotherapy for the treatment of prostate carcinoma

Douglas G. McNeel<sup>1</sup>, Neil H. Bander<sup>2</sup>, Tomasz M. Beer<sup>3</sup>, Charles G. Drake<sup>4</sup>, Lawrence Fong<sup>5</sup>, Stacey Harrelson<sup>6</sup>, Philip W. Kantoff<sup>7</sup>, Ravi A. Madan<sup>8</sup>, William K. Oh<sup>9</sup>, David J. Peace<sup>10</sup>, Daniel P. Petrylak<sup>11</sup>, Hank Porterfield<sup>12</sup>, Oliver Sartor<sup>13</sup>, Neal D. Shore<sup>6</sup>, Susan F. Slovin<sup>7</sup>, Mark N. Stein<sup>14</sup>, Johannes Vieweg<sup>15</sup> and James L. Gulley<sup>16\*</sup>





# What would you offer him?

- Hormonal therapy
  - Abiraterone
  - Enzalutamide
- Chemotherapy
  - Docetaxel
- Radiopharmaceutical Therapy
  - Radium-223
- Immunotherapy
  - Sipleucel T



- Why is Sipuleucel-T a reasonable choice now?
  - Diagnosis of prostate cancer
  - Evidence of metastatic disease
  - Rising PSA despite androgen deprivation therapy
  - Not requiring opiates
  - “Early” in the disease course
  
- Patient receives Sipuleucel-T without side effects
  - Goes on to start hormone therapy 2 months later, and has a prolonged response lasting more than 3 years.



# Immunotherapy for Bladder Cancer

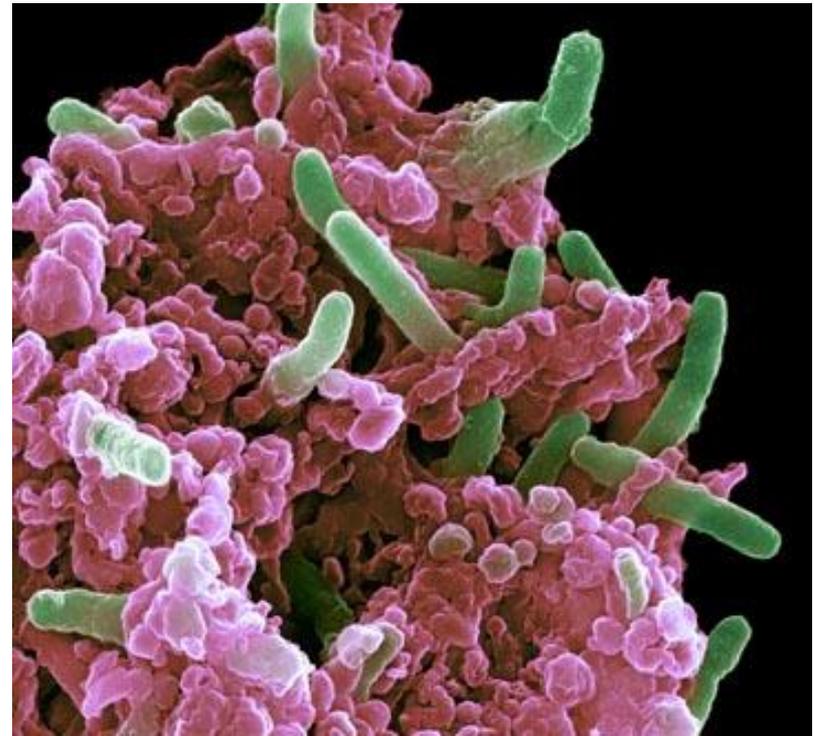
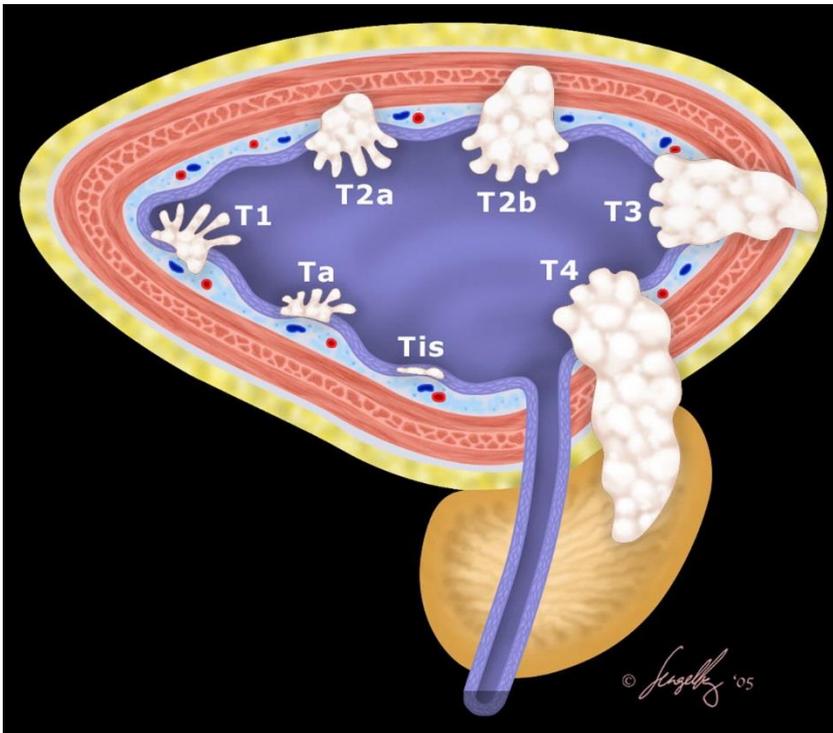
- Intravesical Bacille Calmette-Guerin (BCG)
  - Low stage bladder cancer
  
- PD-1/PD-L1 inhibitors
  - Metastatic bladder Cancer
    - Atezolizumab
    - Nivolumab
    - Others on deck





# Immunotherapy for Bladder Cancer

- Bacille Calmette-Guerin:
  - Attenuated (weakened) bovine tuberculosis strain
  - Given intravesically for superficial bladder tumors (Tis – T1)
  - Causes severe inflammation – effective in close to 60% of patients



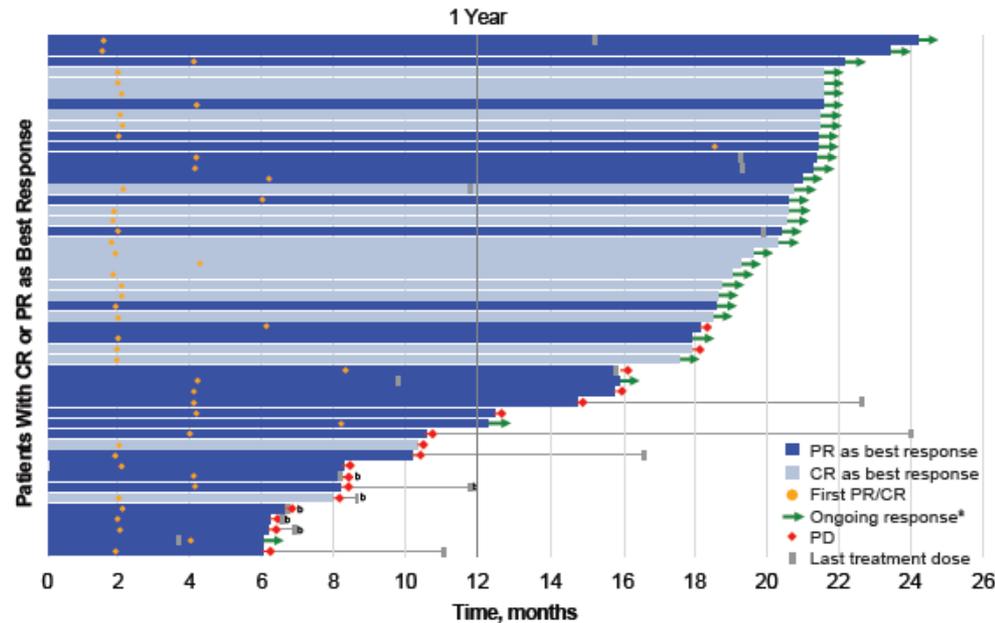
# PD-1 and PD-1 Inhibitors in Bladder Cancer

## Metastatic Bladder Cancer, platinum-refractory

	<b>Nivolumab</b>	<b>Atezolizumab</b>	<b>Pembrolizumab</b>
	Ph II, CheckMate 275 3 mg/kg q2w <sup>2</sup> (n=270)	Ph II, IMvigor 210, Cohort 2 1200 mg q3w <sup>3</sup> (n=310)	Ph III, KEYNOTE-045 200 mg q3w <sup>4</sup> (n=270)
Median follow-up, months	7	21	14
ORR, all-comers, %	19.6	16.0	21.1
CR rate, all-comers, %	2	6	7
ORR, PD-L1+	28%	28%	21.6%
ORR, PD-L1 negative	16%	10%	N/A
DOR	<b>NR</b>	<b>NR</b>	<b>NR</b>
OS, all-comers	8.7	7.9	10.3 (vs 7.4, HR=0.73)
OS, PD-L1+	11.3	11.9	8.0 (vs 5.2, HR=0.57)
Any grade / Gr 3/4 TRAE	66% / 15%	64% / 18%	61% / 14%
Discontinuation rate due to AEs	6%	5%	6%

# PD-1 and PD-1 Inhibitors in Bladder Cancer - Summary

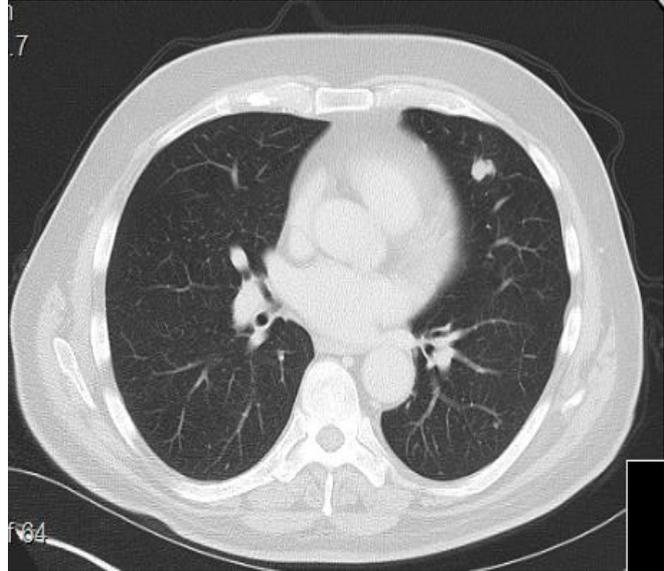
- Approved in the platinum-resistant metastatic setting
  - Atezolizumab
  - Nivolumab
- Overall well tolerated
- Durable responses in ~20% of patients
- Unanswered questions:
  - How long to treat?
  - Pseudoprogression?
  - Why do only some patients respond???





## Case 2

- 72 year old M
- Cystectomy 12 months ago
  - T3N0M0 urothelial cancer
- No perioperative chemotherapy
- Current GFR 70ml/ml
- CT: Multiple small pulmonary nodules.
- Biopsy: Metastatic TCC

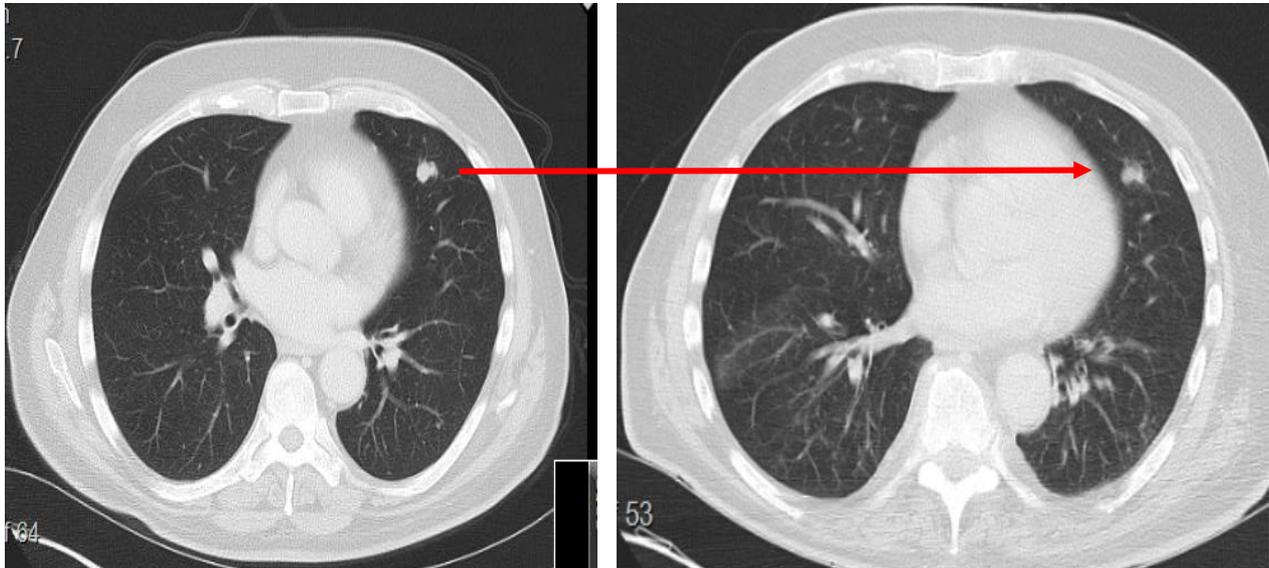


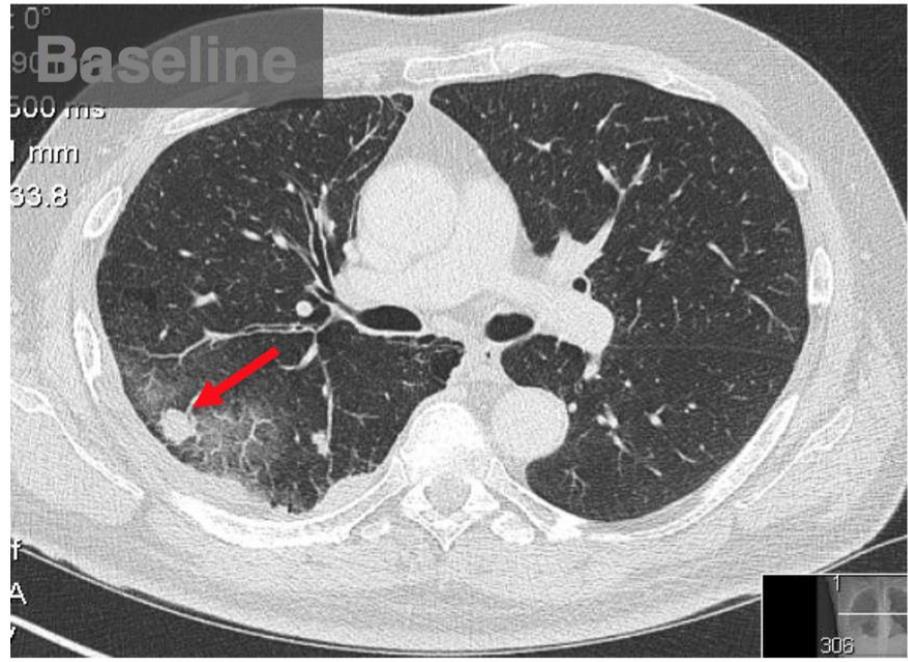


# Starts Cisplatin-based chemotherapy

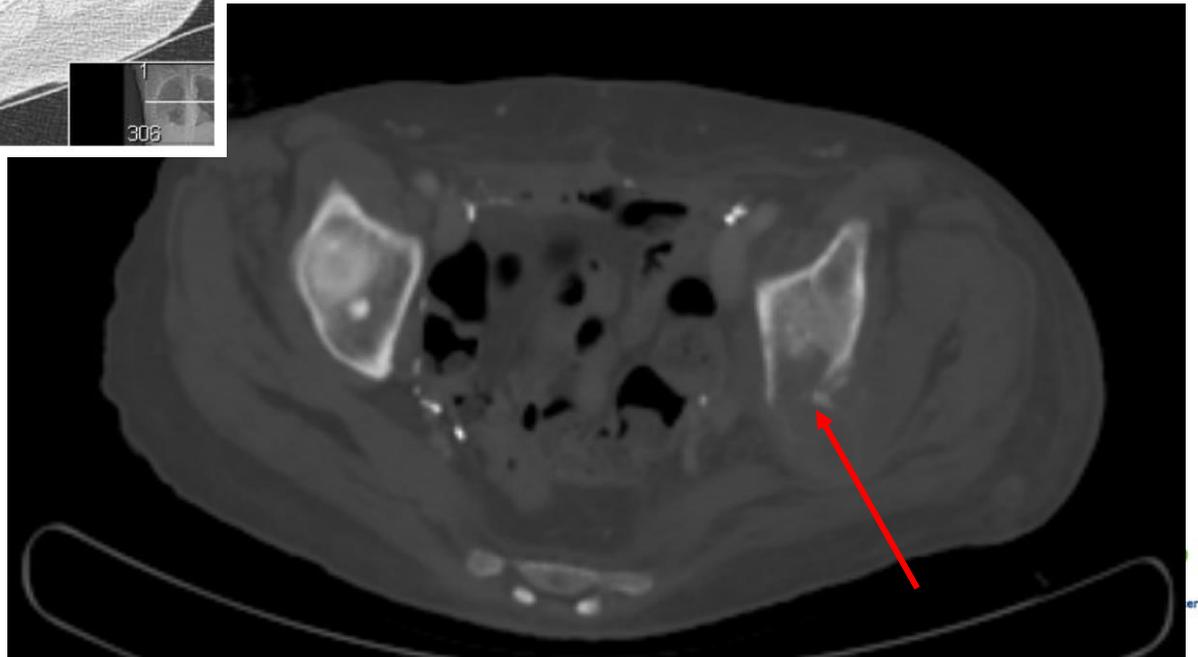
## Cisplatin + Gemcitabine x 6 cycles

- Grade 2 mucositis
- Grade 2 infection
- Grade 3 low neutrophils and neutropenic fever
- CT Chest: Slight regression of nodules



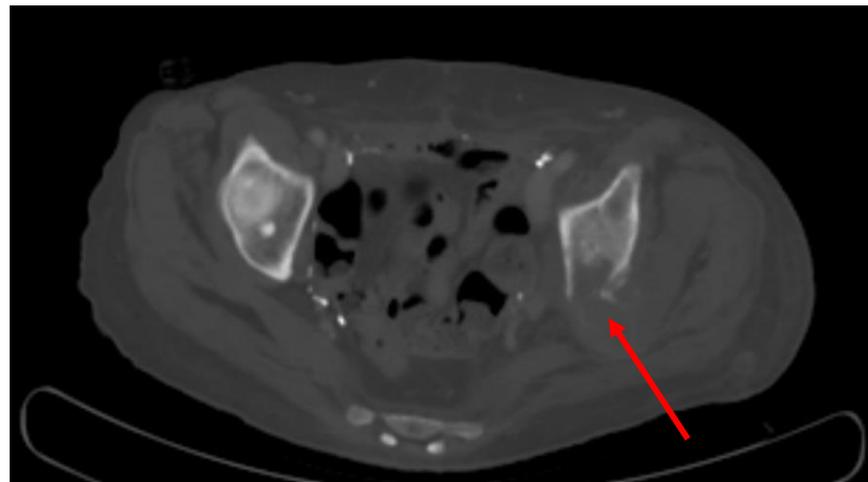
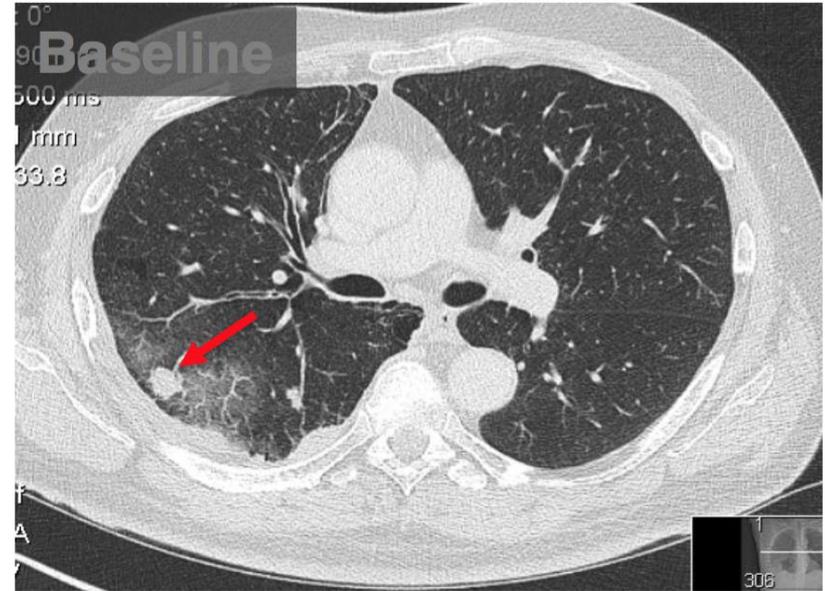


4 months later  
however... new  
lesions appear in  
lungs and bone



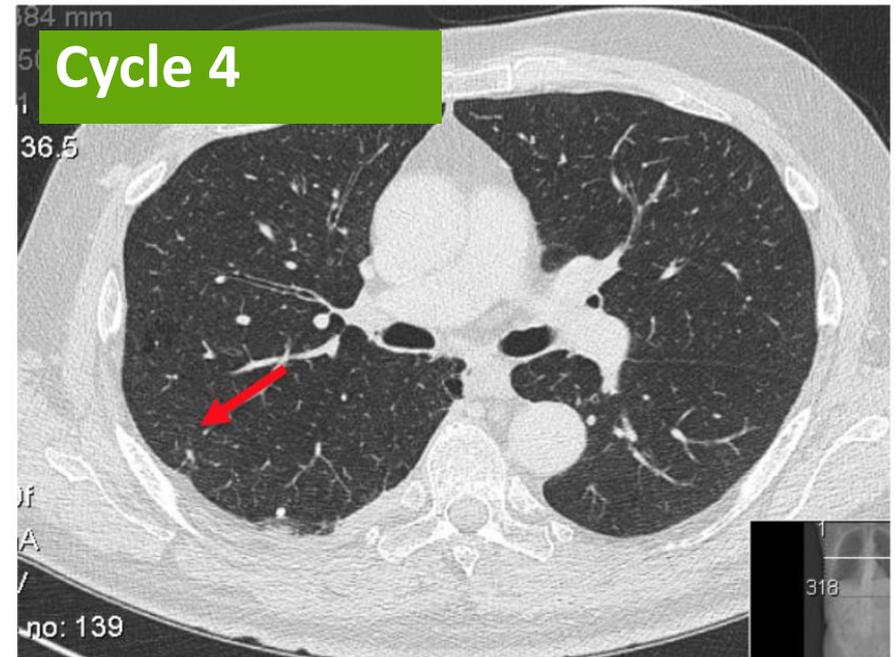
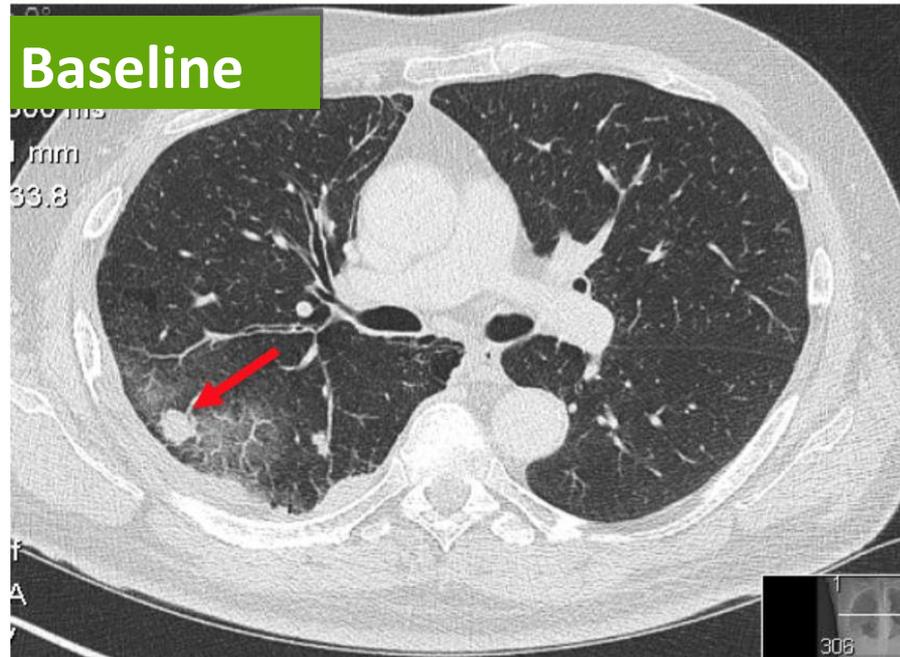
# What would you offer him?

- | ■ Chemotherapy | Response Rate |
|----------------|---------------|
| - Pemetrexed   | 27%           |
| - Docetaxel    | 11%           |
| - Vinflunine   | 8.6%          |
- 
- | ■ Immunotherapy | Response Rate |
|-----------------|---------------|
| - Atezolizumab  | 16%           |
| - Nivolumab     | 19%           |
- 
- |                      |  |
|----------------------|--|
| ■ Clinical Trials??? |  |
|----------------------|--|





# Patient starts Atezolizumab 1200mg IV q3 weeks

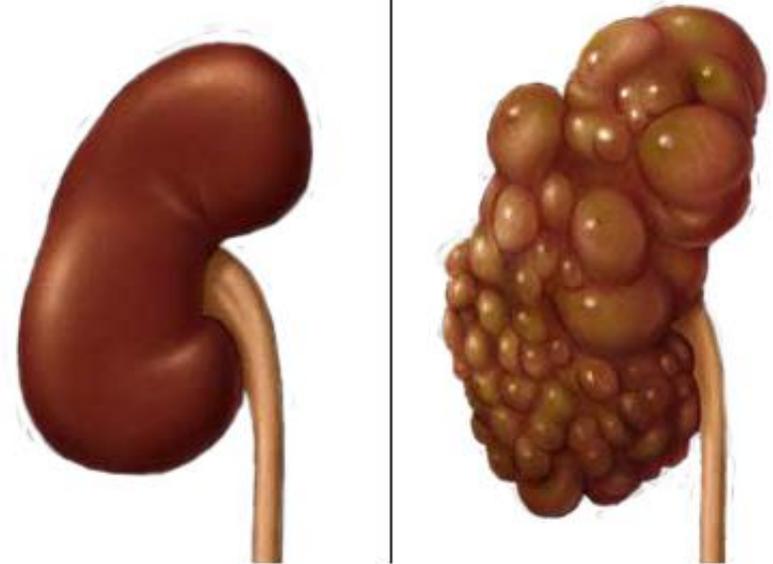


- And has an excellent clinical response!
- Ongoing 9 months later
- Adverse events: Grade 2 hypothyroidism



# Immunotherapy for Kidney Cancer

- “Old School”: Cytokines
  - Interferon-alfa2b
  - High dose interleukin 2
- “New School”: PD-1/PD-L1 inhibitors
  - Nivolumab

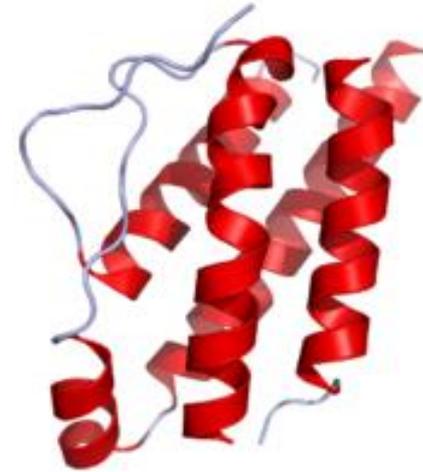


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# Cytokines in Kidney Cancer

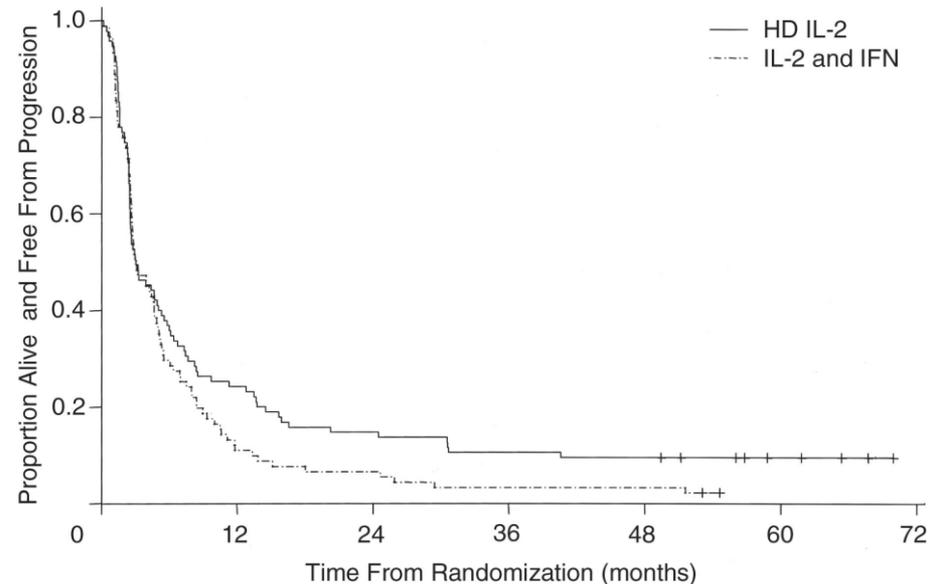
- Interferon alfa (+bevacizumab)

- Daily SQ injection
- Tested in metastatic setting
- Modest response rate (<25%)
- Significant toxicity (flu like symptoms, depression)
- Rarely used anymore



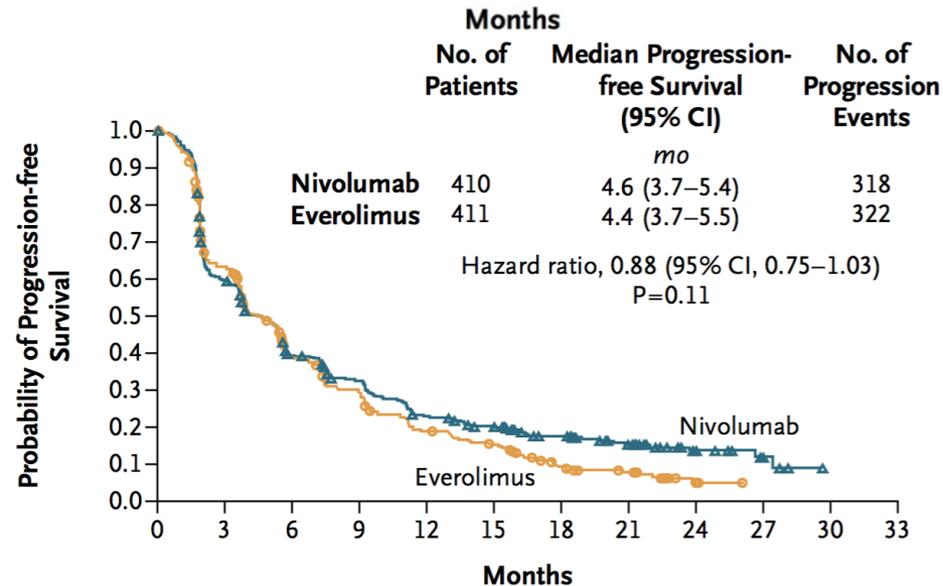
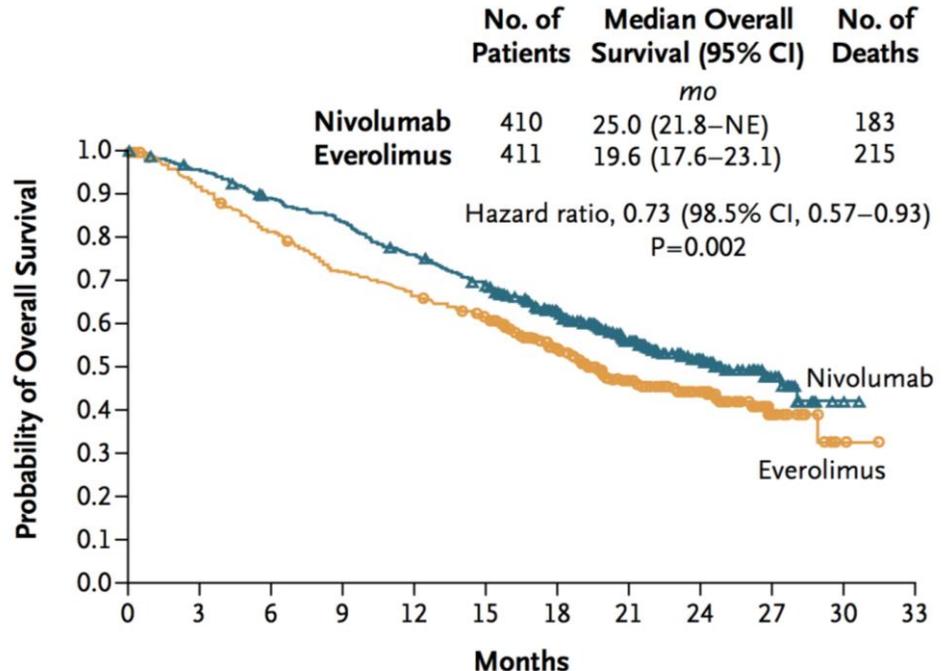
- High dose Interleukin-2

- Tested in treatment-naïve metastatic setting
- Rare durable complete responses (<5% of patients)!
- Significant toxicity
  - Mimics sepsis
  - Requires ICU admission and blood pressure support



# PD-1 Inhibition in Kidney Cancer

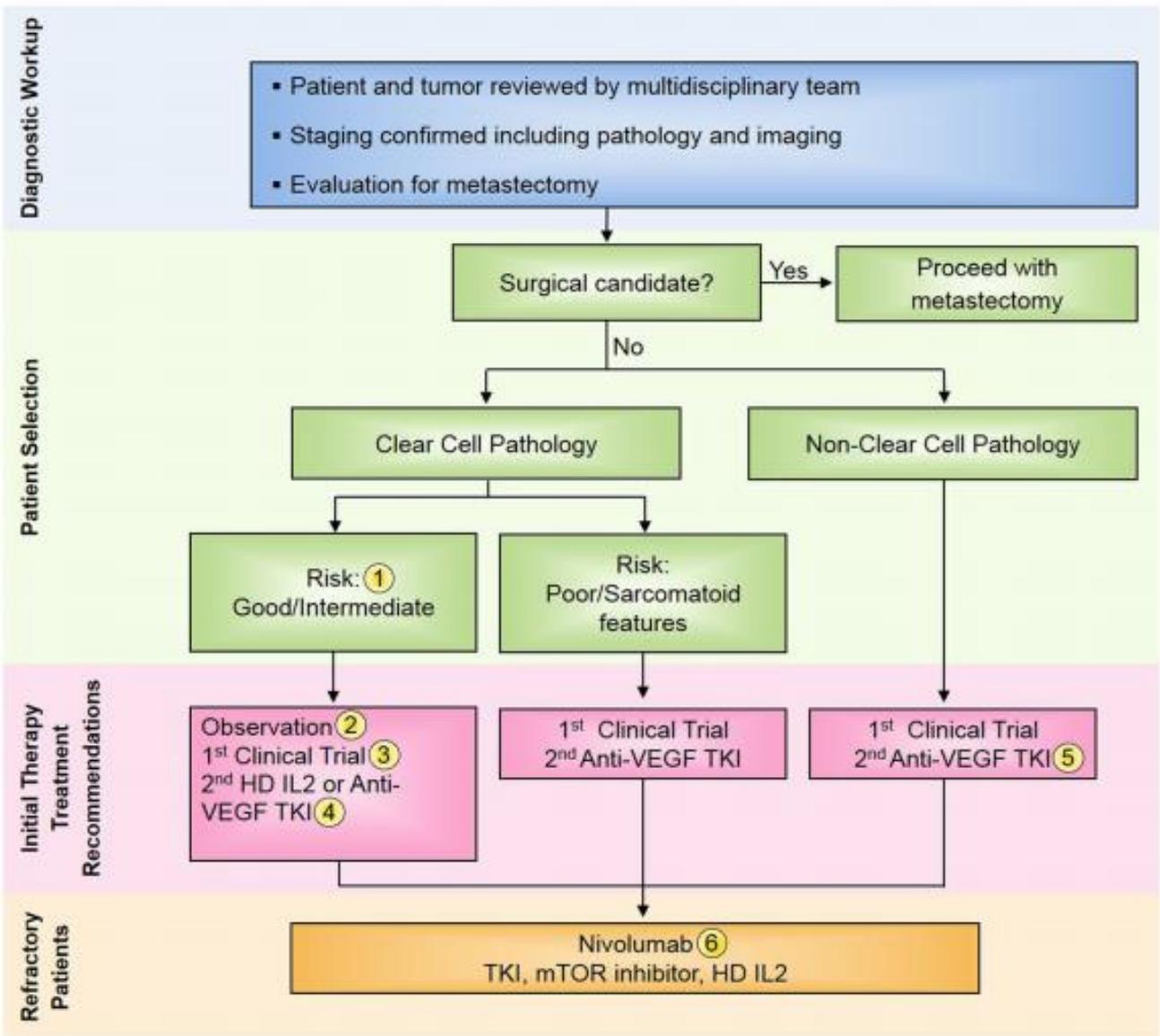
- Phase III Nivolumab vs Everolimus
  - Metastatic clear cell RCC
  - 1-2 prior antiangiogenics (TKIs)
- Results
  - 5.4 median survival benefit
  - No difference in median PFS
  - Well tolerated with rare grade 3 or 4 events.
- Establishes nivolumab as a option for TKI-treated, metastatic RCC.





# Society for Immunotherapy of Cancer consensus statement on immunotherapy for the treatment of renal cell carcinoma

Brian I. Rini<sup>1</sup>, David F. McDermott<sup>2</sup>, Hans Hammers<sup>3</sup>, William Bro<sup>4</sup>, Ronald M. Bukowski<sup>5</sup>, Bernard Faba<sup>6</sup>, Jo Faba<sup>6</sup>, Robert A. Figlin<sup>7</sup>, Thomas Hutson<sup>8</sup>, Eric Jonasch<sup>9</sup>, Richard W. Joseph<sup>10</sup>, Bradley C. Leibovich<sup>11</sup>, Thomas Olencki<sup>12</sup>, Allan J. Pantuck<sup>13</sup>, David I. Quinn<sup>14</sup>, Virginia Seery<sup>2</sup>, Martin H. Voss<sup>15</sup>, Christopher G. Wood<sup>9</sup>, Laura S. Wood<sup>1</sup> and Michael B. Atkins<sup>16\*</sup>



# What's next for Immune therapies?

## Prostate

- Recombinant viruses (Prostvac), bacteria (Listeria)
- Bispecific antibodies (CD3 – PSMA)
- PD-1/PD-L1
- CTLA-4 combinations
- DNA-based vaccines

## Bladder/Kidney

- PD-1/PD-L1 in different stages of disease
  - Neoadjuvant, adjuvant etc.
- Combination PD-1 or PD-L1 with:
  - Other immune agents (CTLA-4, IDO, A2A, 4-1BB etc)
  - TKIs (axitinib)
  - Anti-angiogenics (bevacizumab)
  - Other targeted therapies