

ADVANCES IN  
**Cancer**  
IMMUNOTHERAPY™



# Immunotherapy for the Treatment of Genitourinary Cancers

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Society for Immunotherapy of Cancer

# Disclosures

- Clinical trials and scientific studies: FDK Therapies, Genentech, Urogen, Dendreon, Nucleix, Abbott Laboratories, Combat Medical
- Consultant: AstraZeneca, BioCancell, Taris Biomedical
- I will be discussing non-FDA approved indications during my presentation.



## Learning Objectives:

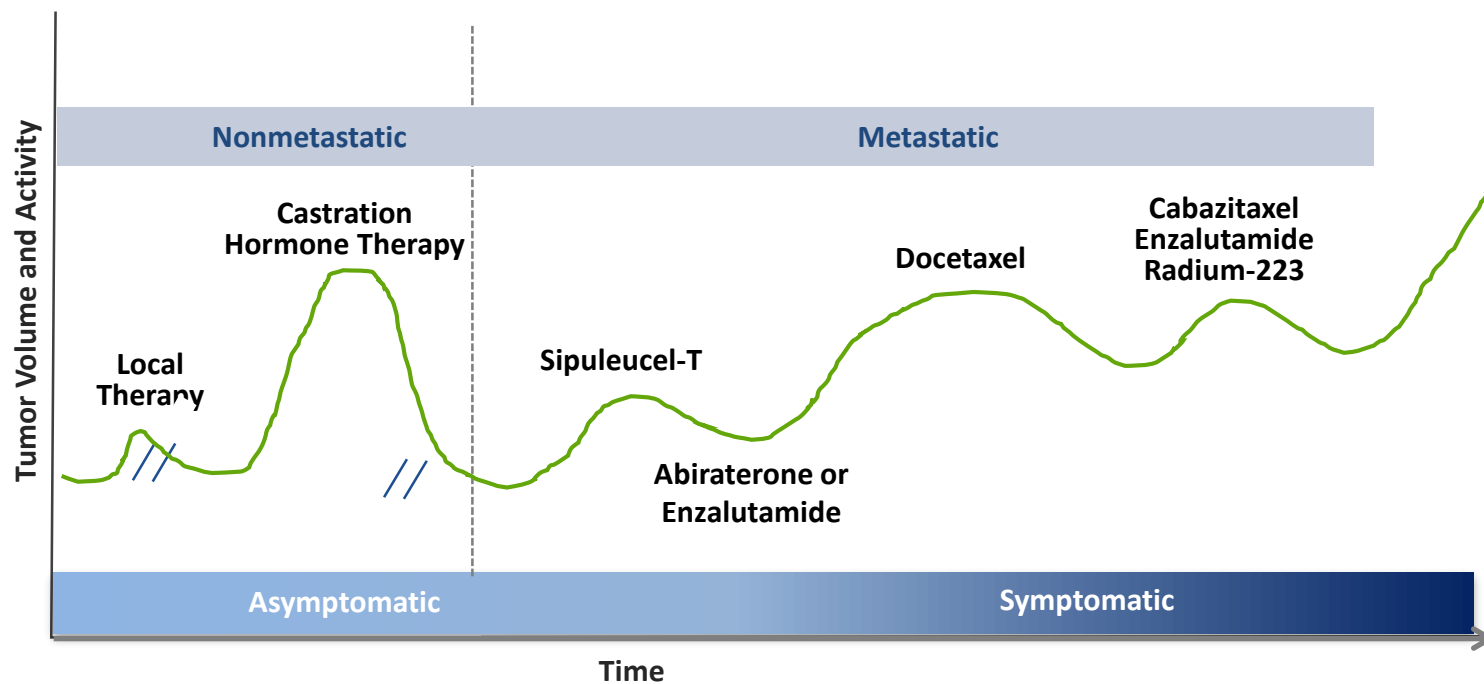
- Describe immunotherapy for prostate cancer, bladder cancer, and kidney cancer
- Review the clinical data of approved therapies
- Discuss patient selection criteria for approved therapies
- Review sequencing of approved therapies

## Prostate Cancer – Case #1:

- 68 y/o man with a Gleason 5+4 prostate cancer (2012).
- Bone & retroperitoneal node metastases: treated with leuprolide + bicalutamide
  - PSA nadir was 0.2 ng/mL, but began rising 2015. (Bicalutamide was discontinued)
  - PSA now 5 ng/mL and bone scan shows new metastases. Patient is asymptomatic.
  - What are appropriate immunotherapy treatment options?
    - A) Nivolumab
    - B) Sipuleucel-T
    - C) Ipilimumab
    - D) B or C



## Natural History of Lethal Prostate Cancer and Treatment Options



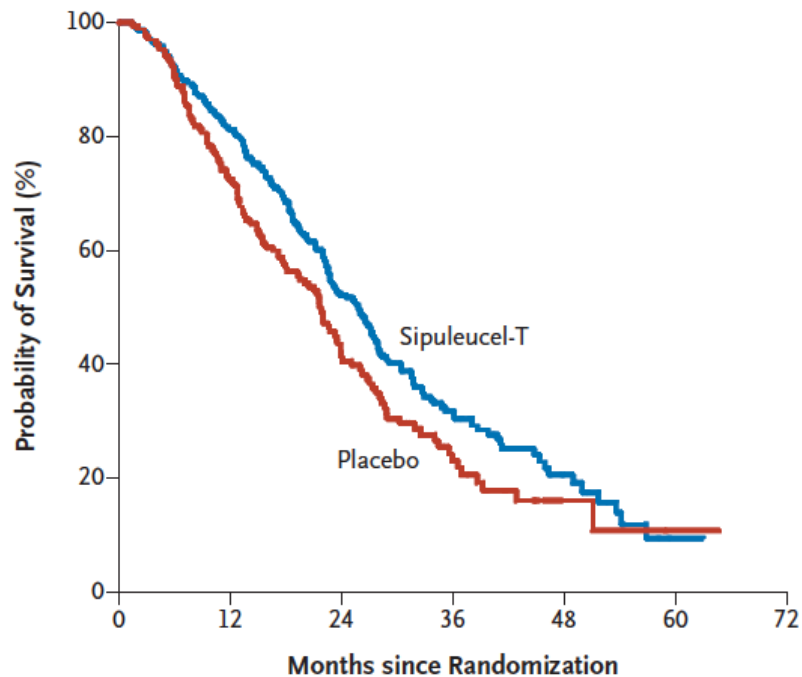
## Lessons learned for clinical trials:

### Prostate cancer:

- Not inflamed
- Not hyper-mutated
- Few abscopal effects
- No pseudoprogression
- Little response to checkpoint inhibitors
- $\uparrow$  vaccine dose  $\neq$   $\uparrow$  immunity

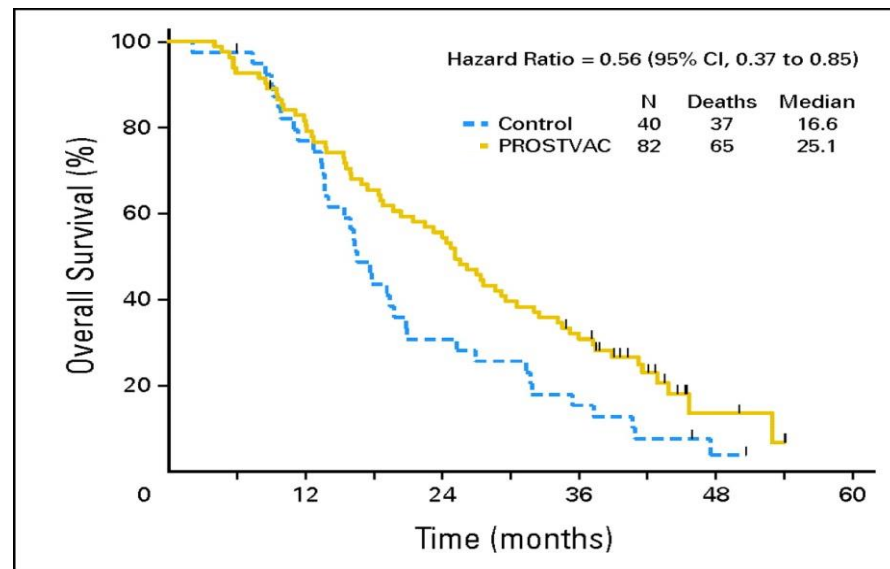
# Prostate cancer vaccines

## A Primary Efficacy



### No. at Risk

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



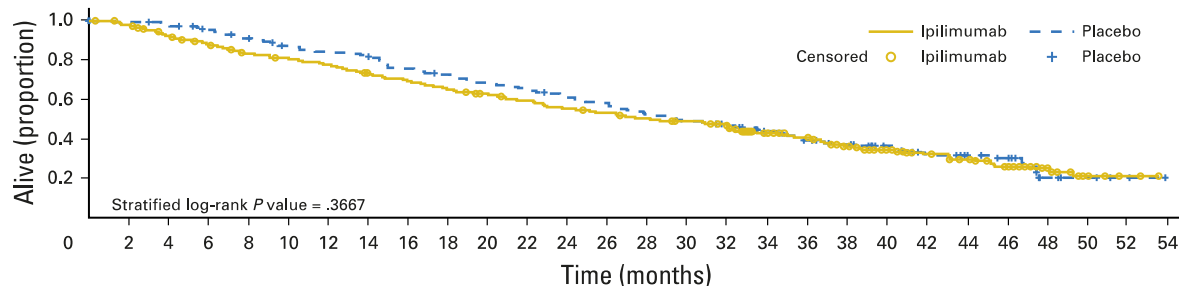
TRICOM: B7-1, ICAM-1 and LFA-3

## Sipuleucel-T: autologous cellular vaccine

- Indicated for CRPC with minimal symptoms
- Leukapheresis q 2 weeks x 3
  - Ex-vivo PBMC stimulation x 48 h
  - PA2024 antigen (fusion of PAP & GM-CSF)
- A/Es are generally mild and vague
  - Chills, fatigue, low-grade fever, flu-like achiness
  - Rare: infusion reactions, hypotension, thromboembolism

# Ipilimumab (anti-CTLA-4)

**A**



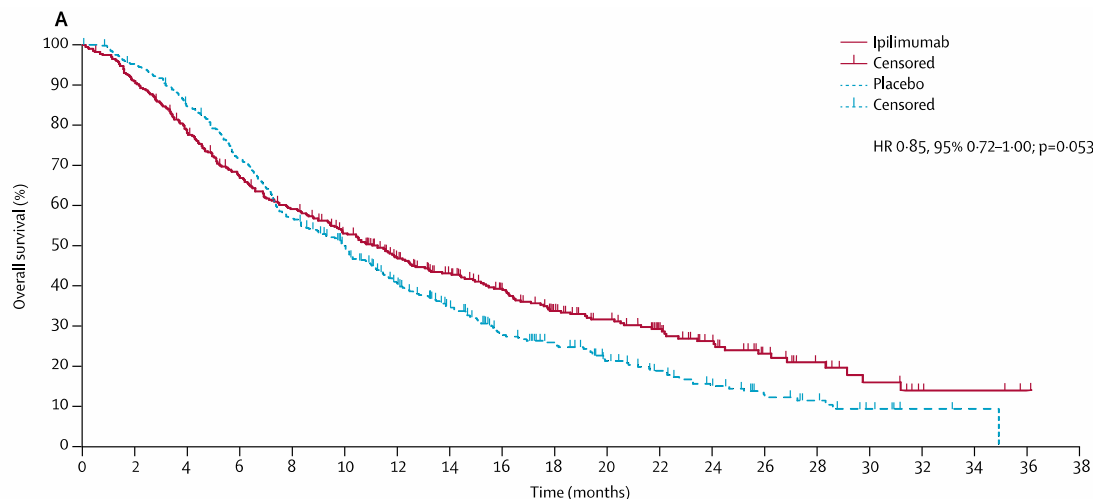
No. at risk

|            |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |    |    |    |    |    |    |   |   |   |
|------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|----|----|----|----|----|---|---|---|
| Ipilimumab | 400 | 389 | 364 | 342 | 320 | 310 | 298 | 279 | 265 | 250 | 236 | 223 | 208 | 197 | 186 | 179 | 166 | 136 | 116 | 94 | 78 | 64 | 46 | 32 | 18 | 7 | 3 | 0 |
| Placebo    | 202 | 198 | 195 | 186 | 175 | 166 | 161 | 155 | 142 | 136 | 128 | 122 | 113 | 108 | 98  | 92  | 85  | 74  | 59  | 53 | 41 | 33 | 25 | 19 | 6  | 4 | 2 | 0 |

CA-184-095 trial

Pre-chemo

No symptoms



Number at risk

|            |     |     |     |     |     |     |     |     |     |    |    |    |    |    |    |   |   |   |   |   |
|------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|----|----|----|----|----|---|---|---|---|---|
| Ipilimumab | 399 | 362 | 308 | 260 | 228 | 195 | 155 | 131 | 108 | 85 | 69 | 52 | 37 | 24 | 15 | 9 | 4 | 3 | 1 | 0 |
| Placebo    | 400 | 376 | 332 | 281 | 222 | 184 | 138 | 106 | 77  | 65 | 47 | 36 | 26 | 16 | 12 | 6 | 2 | 1 | 0 | 0 |

CA-184-043 trial

Post-chemo

No symptoms

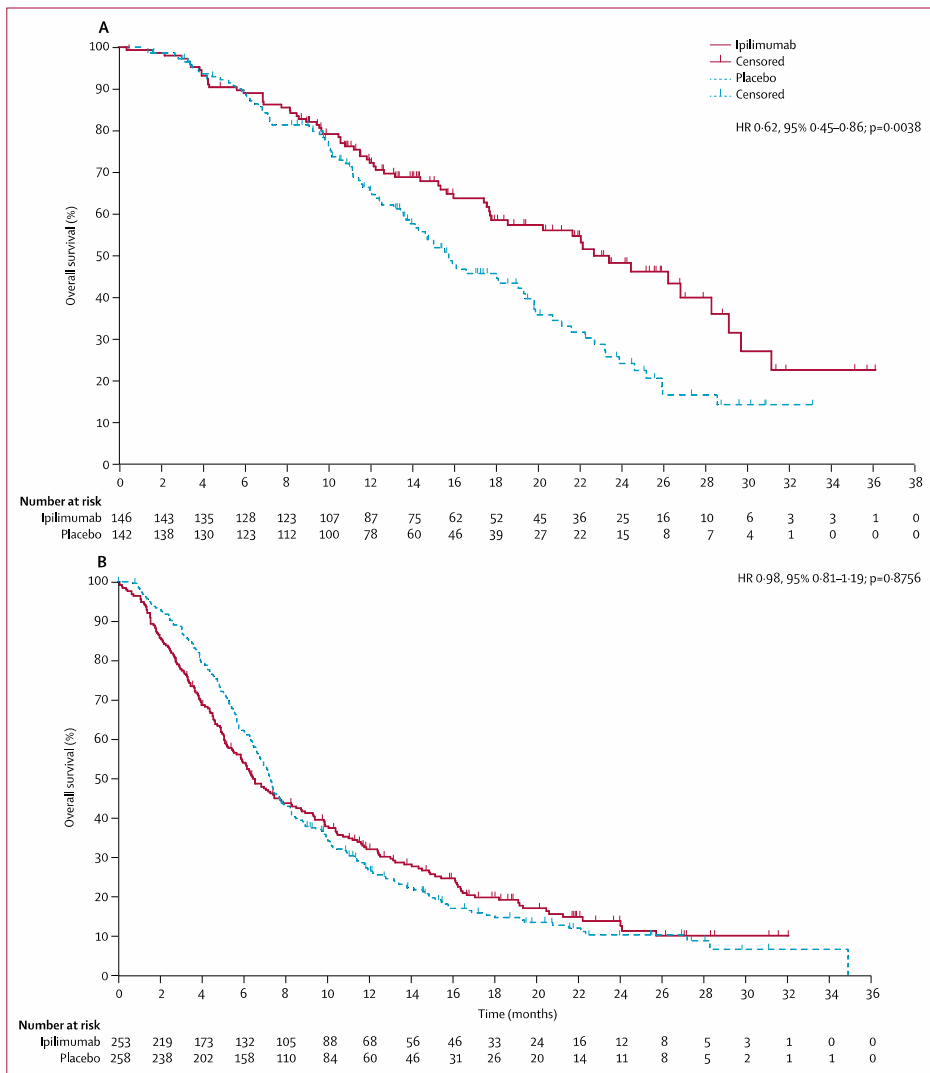
Radiation to bone met

Beer T, et al. J Clin Oncol 2017

Kwon ED, et al. Lancet Oncol 2014



# Ipilimumab (anti-CTLA-4)



Low risk men do better:

-ALP < 1.5X normal

-Hb > 11

-No visceral mets

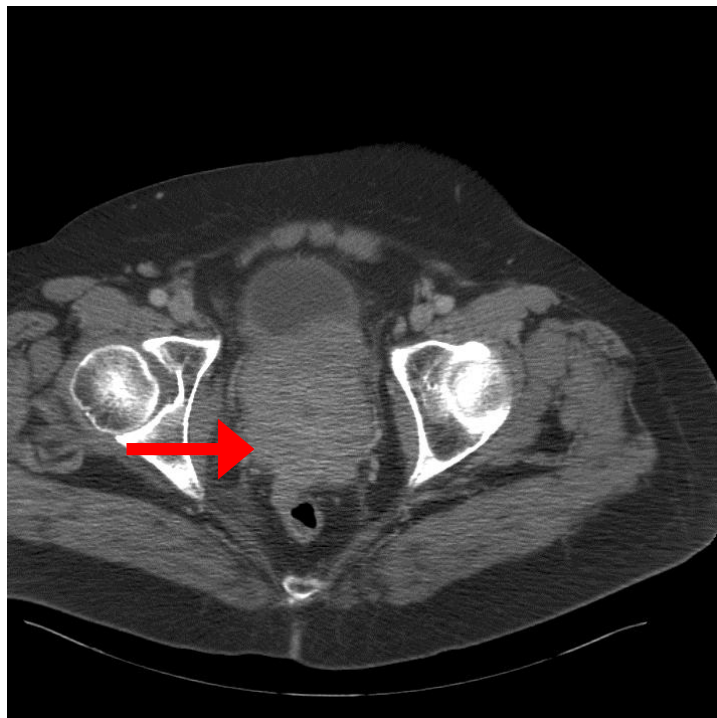
Lower disease burden probably matters



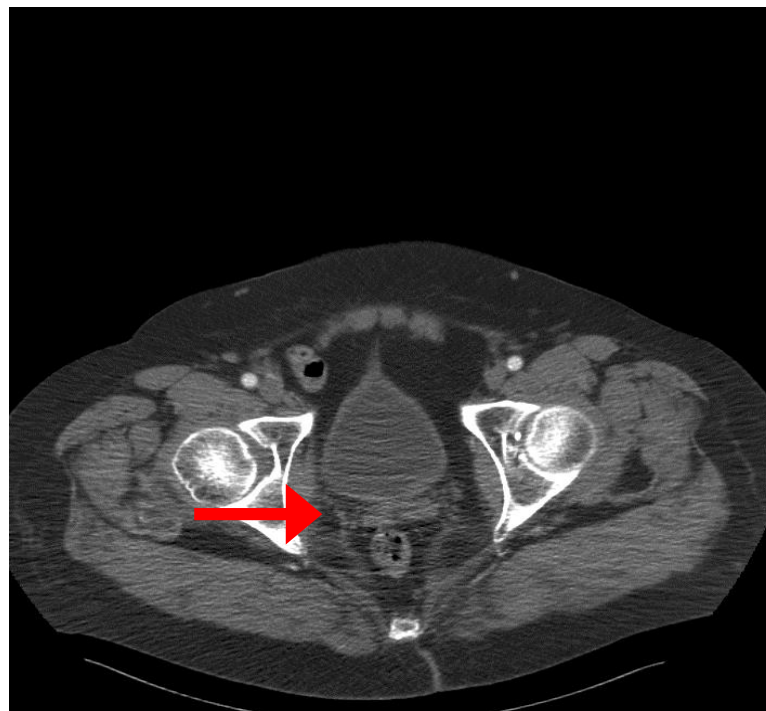


## Resolution of Prostate Mass

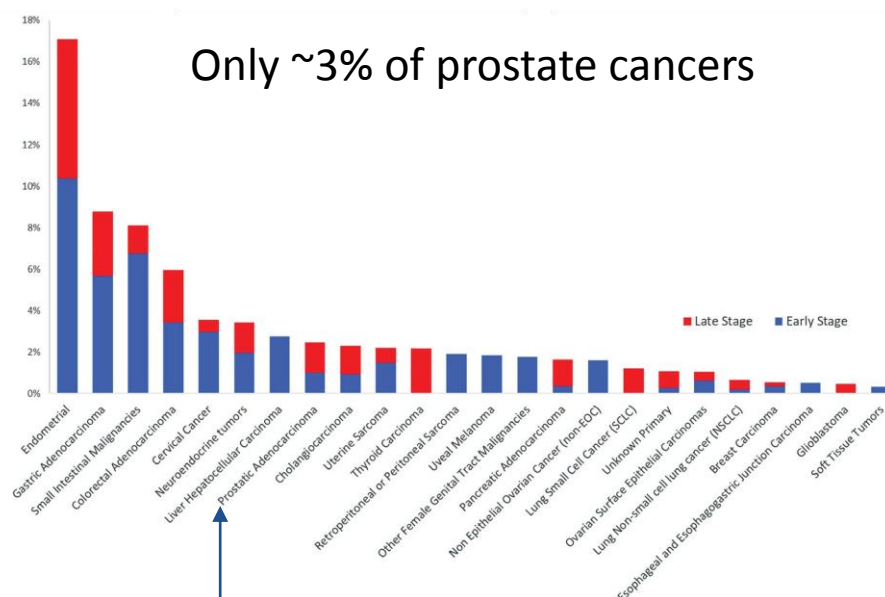
Screening



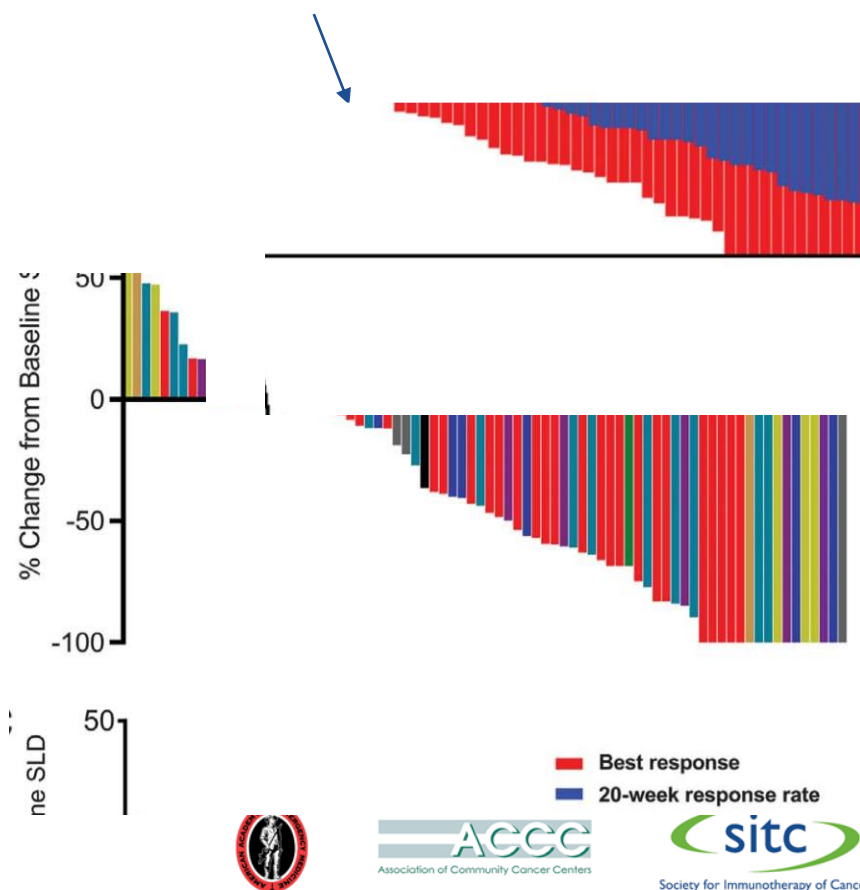
14 months

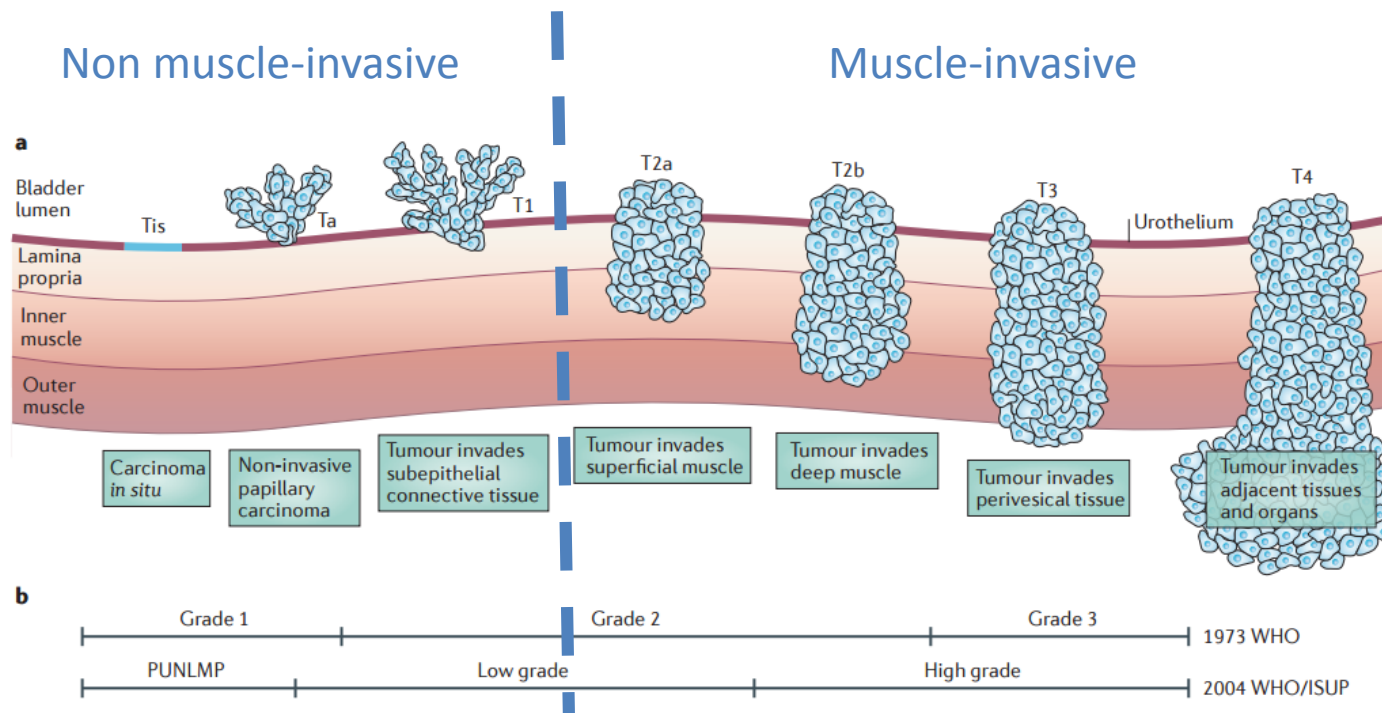


- Very little clinical activity in early phase trials
  - Exception: mismatch repair defect



Le D, et al. Science 2017





**Figure 1 | Bladder cancer grading and staging.** **a** | Staging of bladder cancer according to the Tumour–Node–Metastasis (TNM) system is shown<sup>3</sup>. **b** | Grading according to the 1973 World Health Organization (WHO) and 2004 WHO/ International Society of Urological Pathology (ISUP) criteria is shown<sup>4,5</sup>. The major difference is in the classification of papillary tumours, which are classified as grades 1, 2 and 3 in the older system and as papillary urothelial malignancy of low malignant potential (PUNLMP; equivalent to grade 1), low-grade papillary urothelial carcinoma or high-grade papillary urothelial carcinoma in the WHO/ISUP 2004 classification.

Knowles MA et al. *Nature Rev Cancer* 2015



## Bladder Cancer – Case #2:

60 y/o man NMIBC 5 years ago. After BCG + maintenance, develops a MIBC 2 years ago and underwent radical cystoprostatectomy. He then did well until 4 months ago when he was found to have lung and liver metastases. He started treatment with gemcitabine and cisplatin chemotherapy, but unfortunately had progressive disease after 3 cycles of therapy. What is the best immunotherapy treatment option for him?

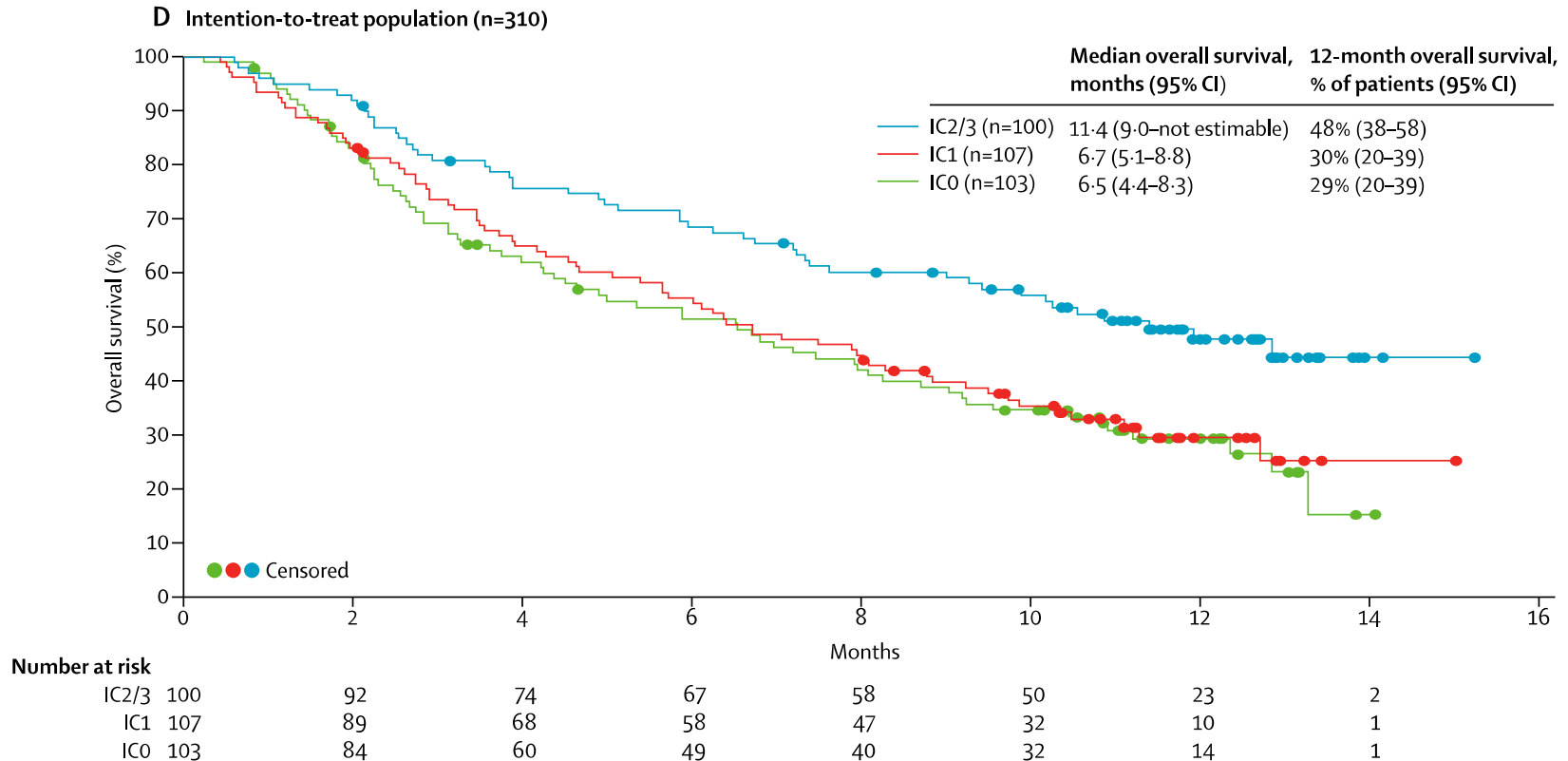
- A) IL-2
- B) Atezolizumab
- C) Pembrolizumab
- D) B or C



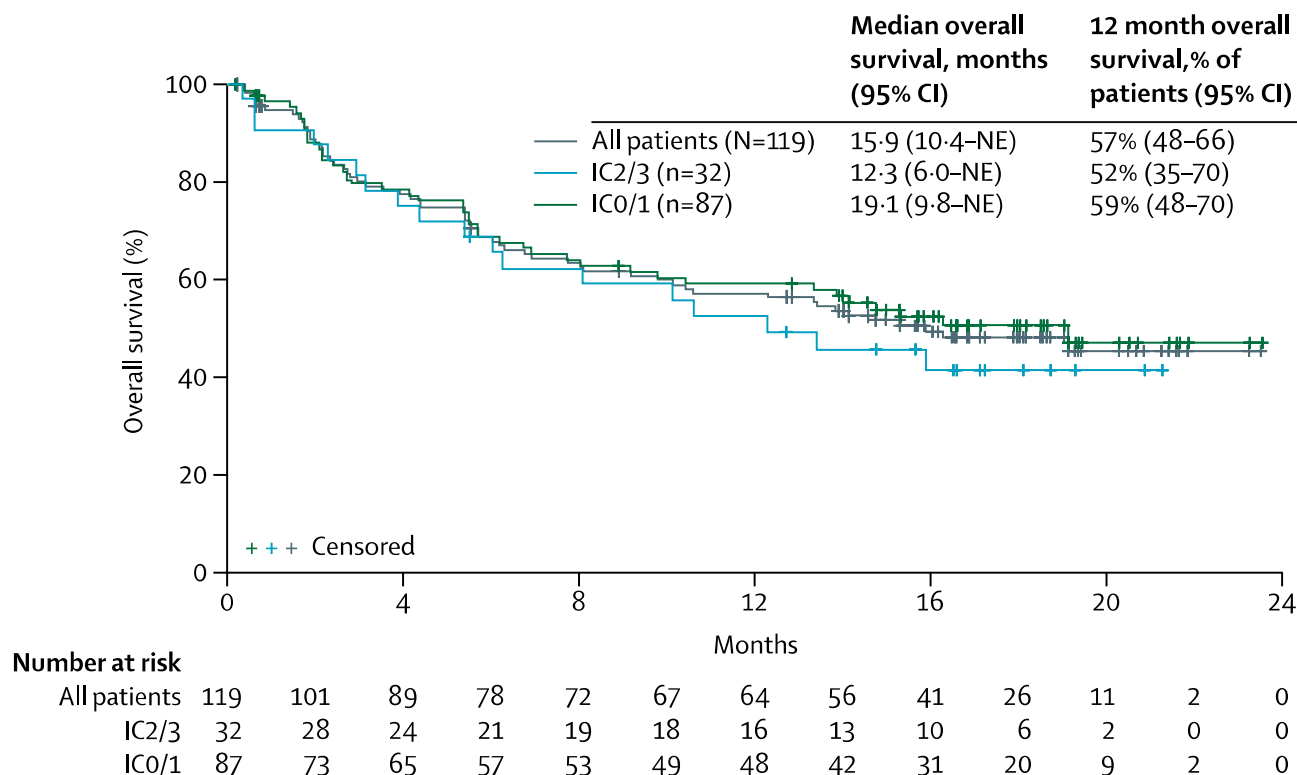
# PD-L1 / PD-1 blockade

| Drug                        | Target | FcγR-binding | ORR | CR  | PFS             | OS               |
|-----------------------------|--------|--------------|-----|-----|-----------------|------------------|
| Atezolizumab<br>(Tecentriq) | PD-L1  | No           | 13% | 3%  | -               | 9 m<br>39% @1y   |
| Avelumab<br>(Bavencio)      | PD-L1  | Yes          | 18% | 11% | 12 w<br>19% @1y | 14 m<br>54% @ 1y |
| Durvalumab<br>(Imfinzi)     | PD-L1  | No           | 31% | -   | -               | -                |
| Nivolumab<br>(Opdivo)       | PD-1   | No           | 20% | 2%  | 8 w             | 9 m<br>40% @ 1y  |
| Pembrolizumab<br>(Keytruda) | PD-1   | No           | 21% | 7%  | 8 w<br>17% @ 1y | 10 m<br>44% @ 1y |

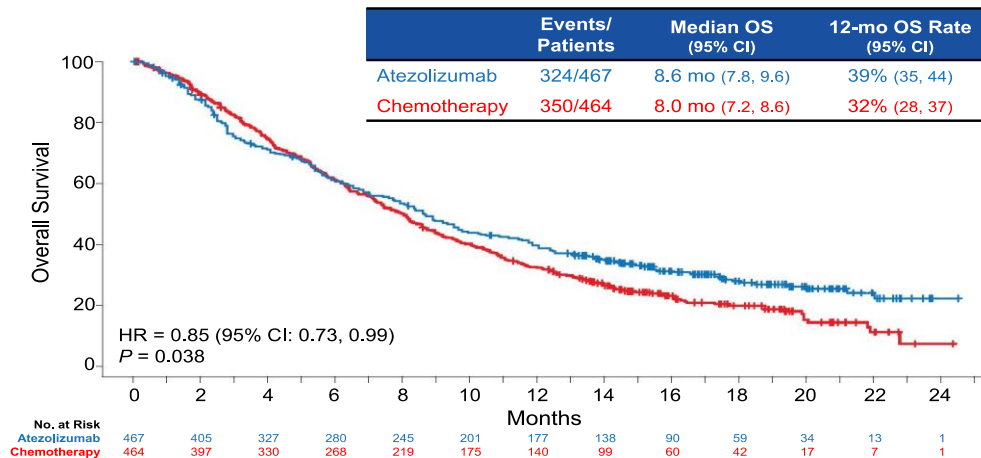
## IMvigor210: Phase 2 (Cohort 2), 2<sup>nd</sup> Line metastatic



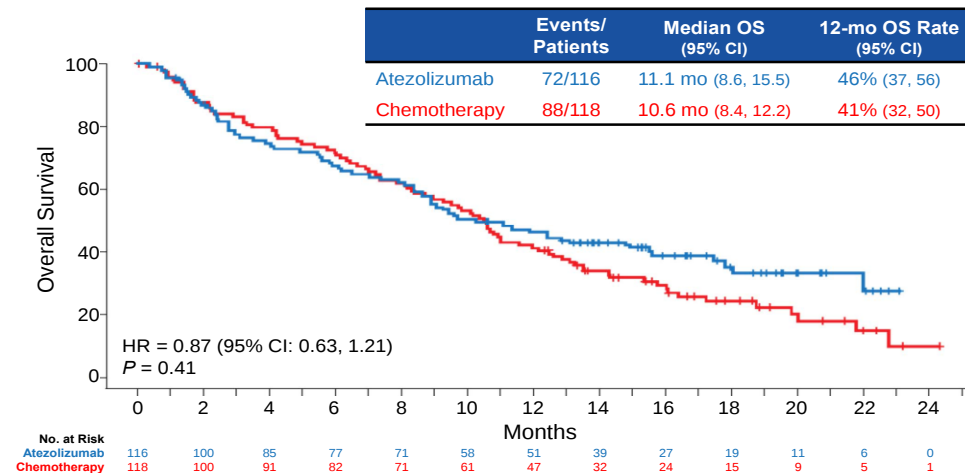
## IMvigor210: Phase 2 (Cohort 1), 1<sup>st</sup> Line metastatic, cisplatin ineligible



## IMvigor211: Phase 3, 2<sup>nd</sup> Line metastatic



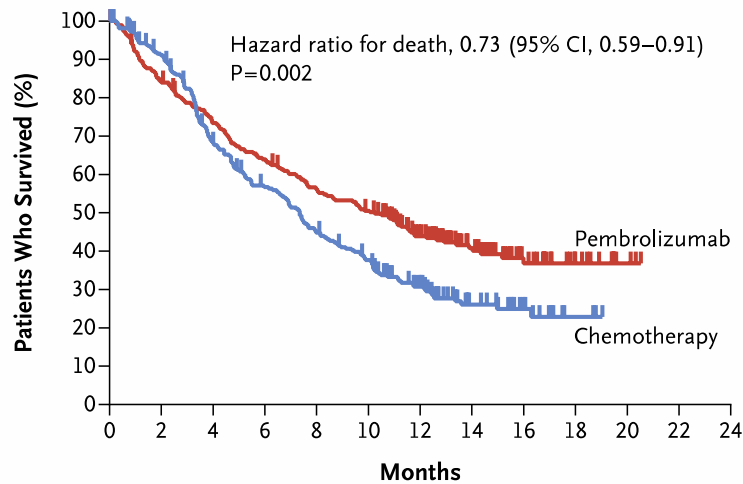
Overall ITT



IC2/3 (Primary endpoint)

## KEYNOTE-045: Phase 3, 2<sup>nd</sup> Line metastatic

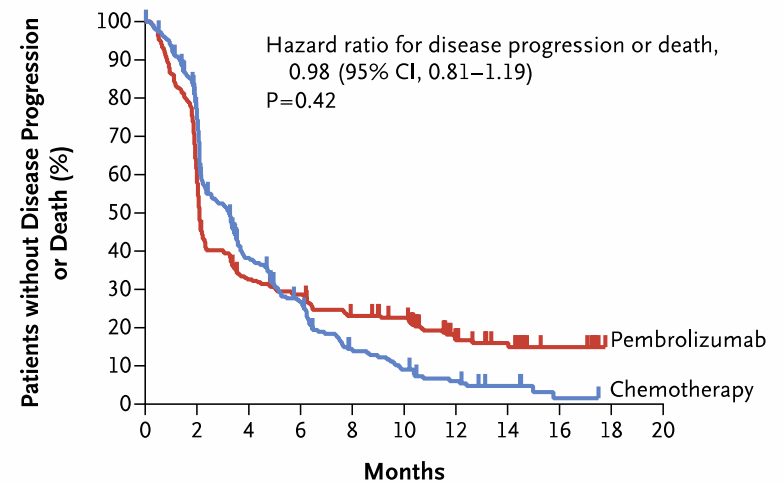
**A Overall Survival**



**No. at Risk**

|               |     |     |     |     |     |     |    |    |    |    |   |   |   |
|---------------|-----|-----|-----|-----|-----|-----|----|----|----|----|---|---|---|
| Pembrolizumab | 270 | 226 | 194 | 169 | 147 | 131 | 87 | 54 | 27 | 13 | 4 | 0 | 0 |
| Chemotherapy  | 272 | 232 | 171 | 138 | 109 | 89  | 55 | 27 | 14 | 3  | 0 | 0 | 0 |

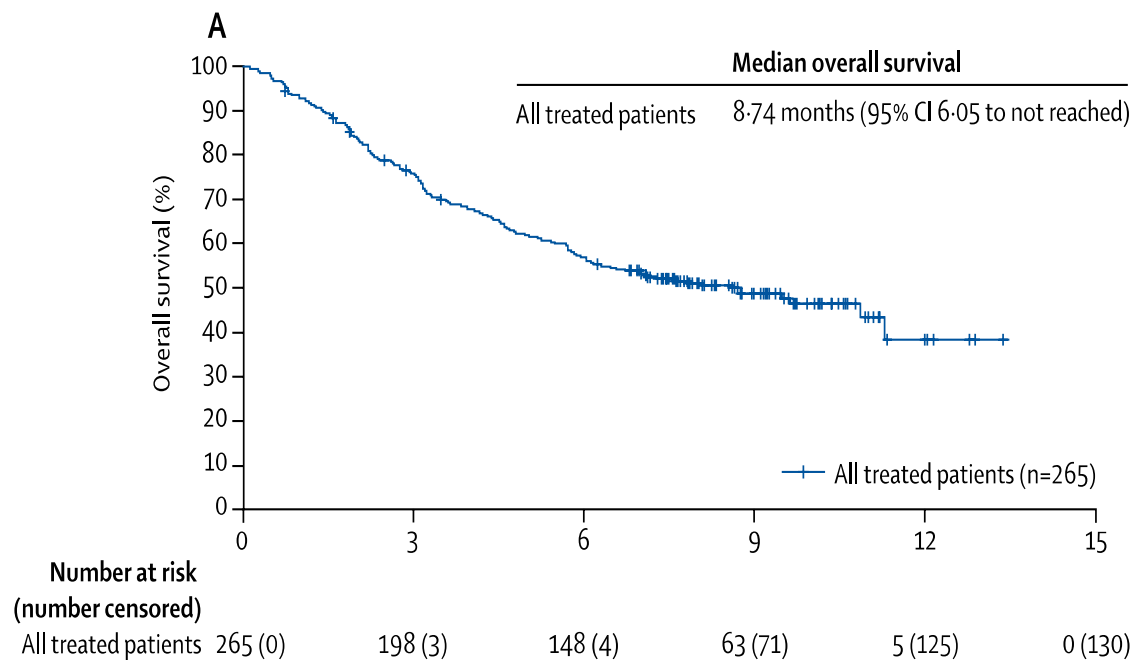
**B Progression-free Survival**



**No. at Risk**

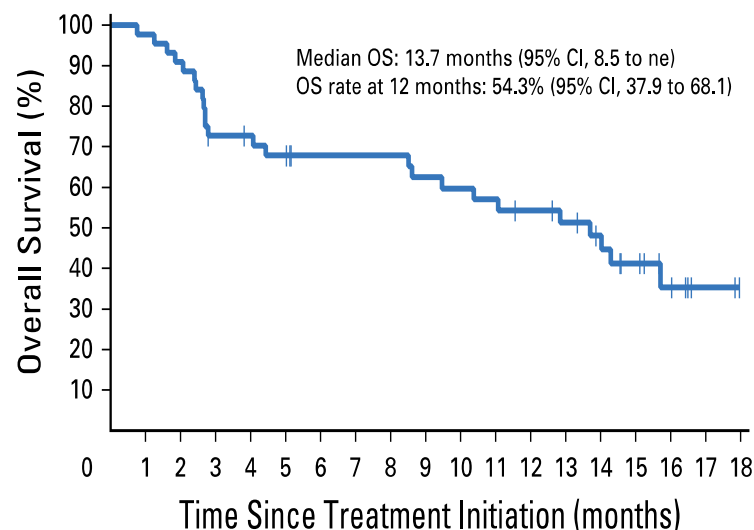
|               |     |     |    |    |    |    |    |    |   |   |   |
|---------------|-----|-----|----|----|----|----|----|----|---|---|---|
| Pembrolizumab | 270 | 165 | 85 | 73 | 56 | 51 | 23 | 16 | 7 | 0 | 0 |
| Chemotherapy  | 272 | 188 | 85 | 56 | 27 | 17 | 10 | 5  | 1 | 0 | 0 |

## CHECKMATE-275: Phase 2, 2<sup>nd</sup> Line metastatic



## JAVELIN: Phase 1b, 2<sup>nd</sup> Line metastatic

**B**

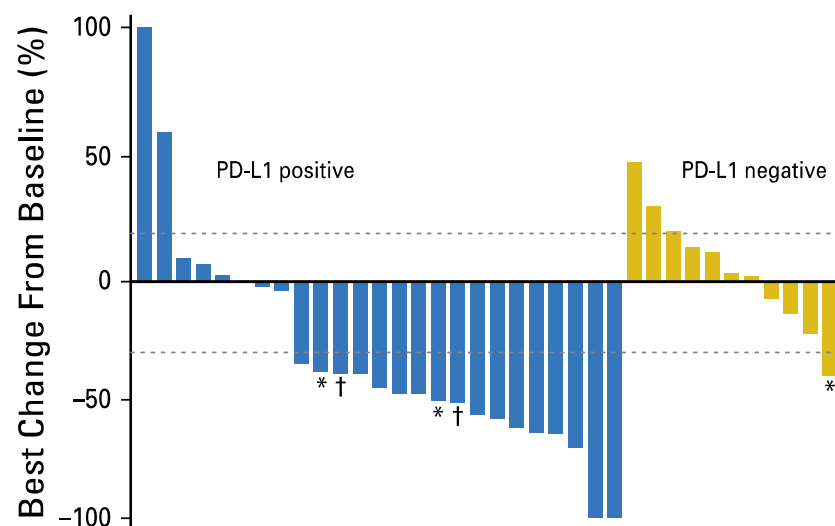


No.  
at risk

|    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |   |   |   |
|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|---|---|---|
| 44 | 43 | 40 | 31 | 30 | 28 | 25 | 25 | 25 | 23 | 22 | 21 | 19 | 17 | 14 | 10 | 6 | 2 | 0 |
|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|---|---|---|

## CD-ON-MEDI4736-1108: Phase 1/2, 2<sup>nd</sup> Line metastatic

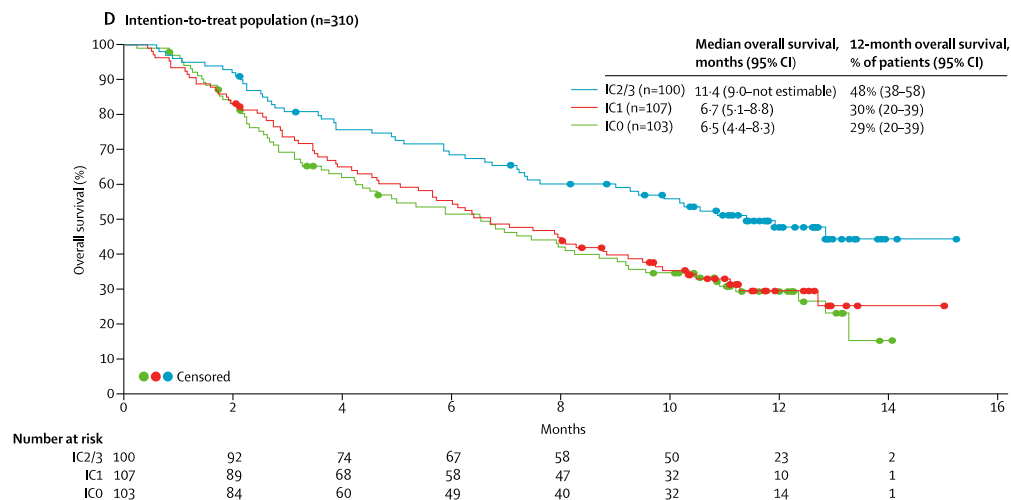
**A**



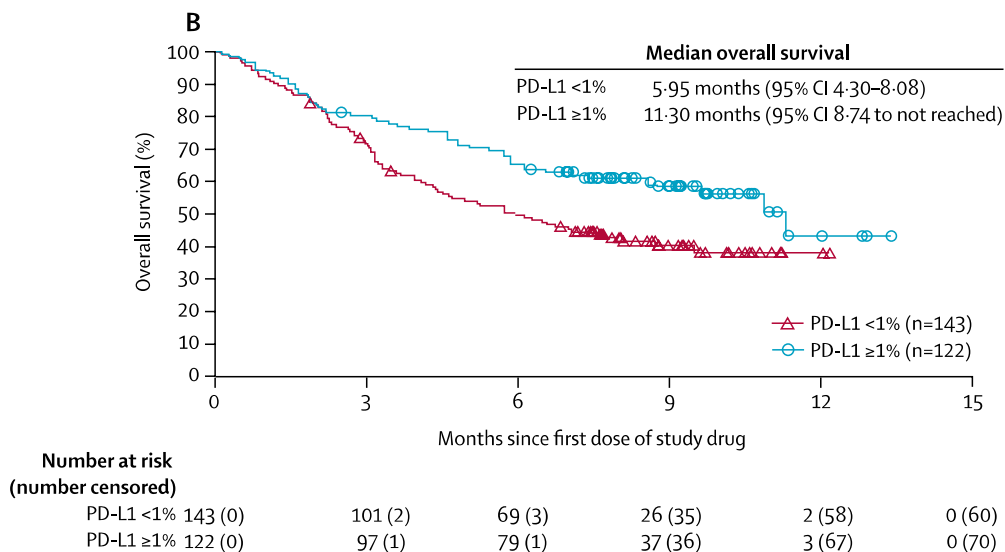
Apolo et al. J Clin Oncol 2017  
Massard et al. J Clin Oncol 2016



# PD-L1 status and response



Atezolizumab  
(PD-L1)



Nivolumab  
(PD-1)

Rosenberg et al. Lancet 2016  
Sharma et al. Lancet Oncol 2017



# Biomarkers of response

| Biomarker             |         | Uses                          |
|-----------------------|---------|-------------------------------|
| Ventana PD-L1 (SP142) | 11/2016 | Atezolizumab (bladder, NSCLC) |
| Ventana PD-L1 (SP263) | 2017    | Nivolumab (NSCLC)             |
| Dako PD-L1 (28-8)     | 1/2016  | Nivolumab (NSCLC, melanoma)   |

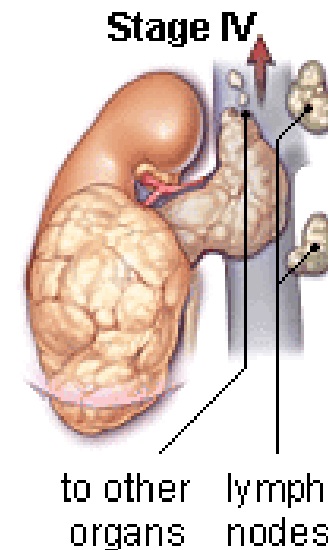
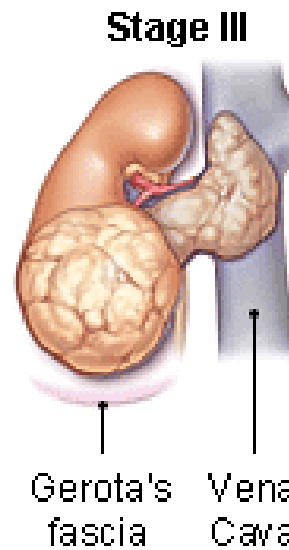
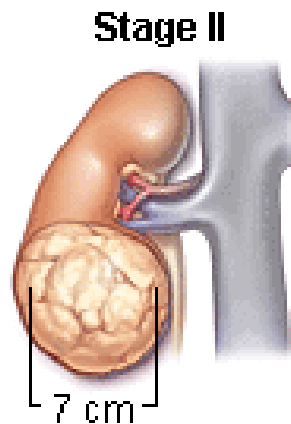
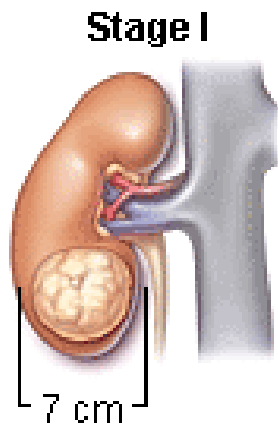
Word of caution: remember ImVigor211...biomarkers can mislead you



# Kidney cancer

Surgically  
resectable

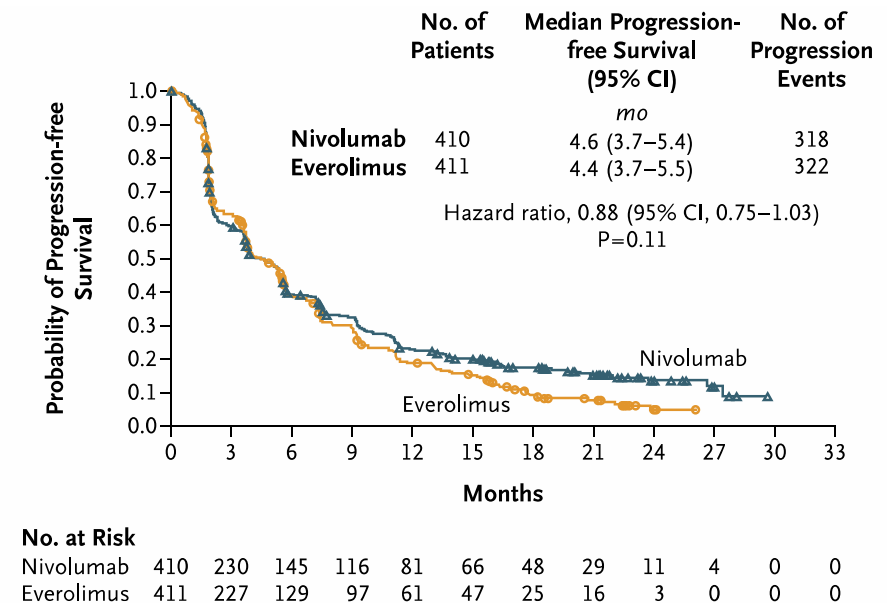
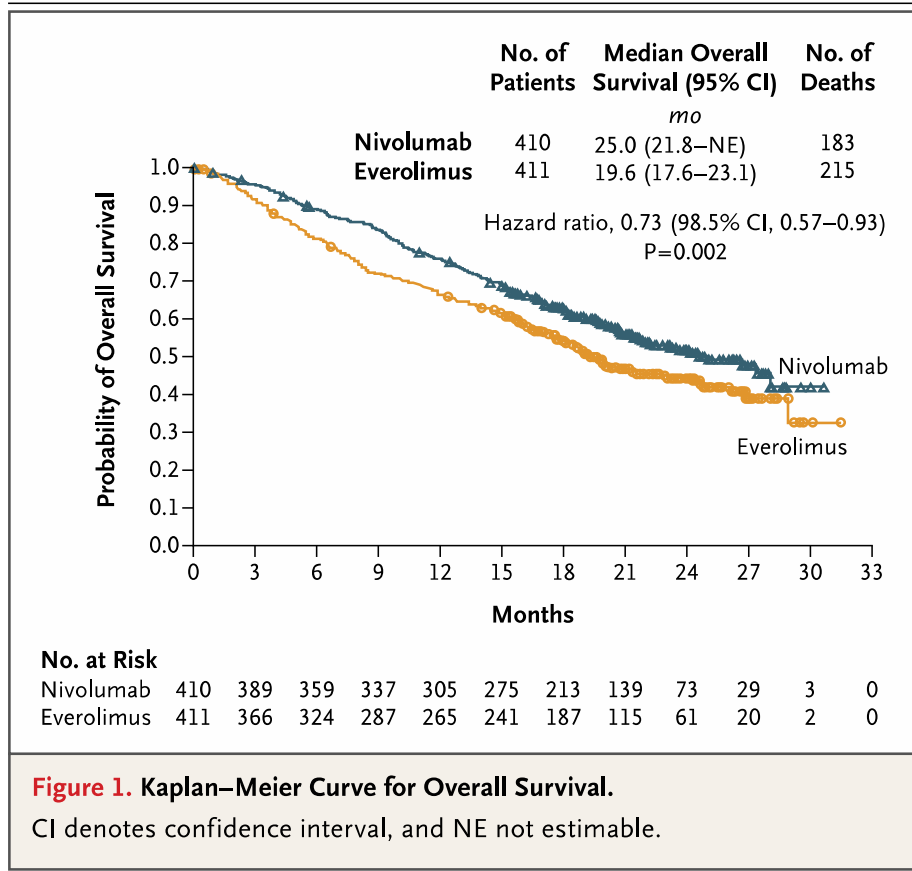
Metastatic



reemakeup.blogspot.com

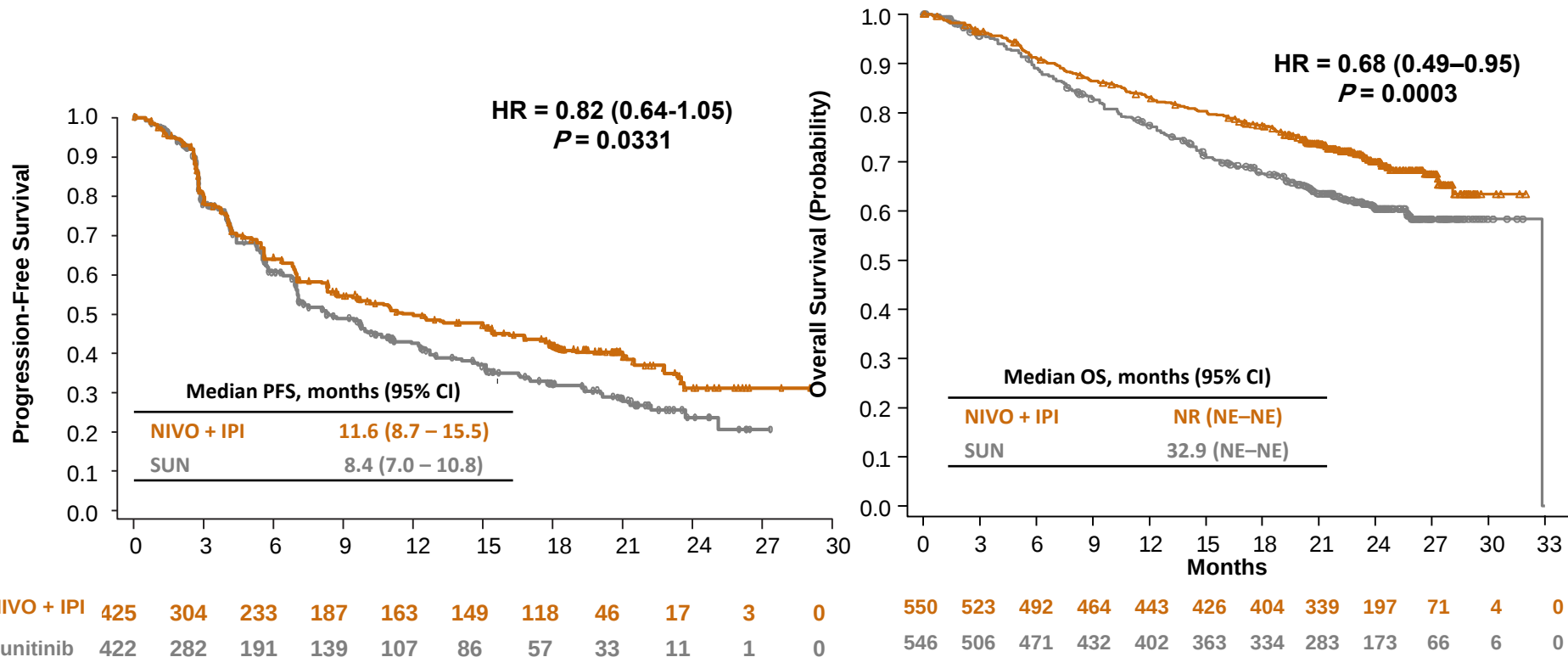


## CheckMate 025: Phase 3, 2<sup>nd</sup> line metastatic



FDA approved

## CheckMate 214: Phase 3, 1<sup>st</sup> line metastatic



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>

POSITION ARTICLE AND GUIDELINES

Open Access



## 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>

# SITC guidelines

POSITION ARTICLE AND GUIDELINES

Open Access



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

Ashish M. Kamat<sup>1\*</sup>, Joaquim Bellmunt<sup>2</sup>, Matthew D. Galsky<sup>3</sup>, Badrinath R. Konety<sup>4</sup>, Donald L. Lamm<sup>5</sup>, David Langham<sup>6</sup>, Cheryl T. Lee<sup>7</sup>, Matthew I. Milowsky<sup>8</sup>, Michael A. O'Donnell<sup>9</sup>, Peter H. O'Donnell<sup>10</sup>, Daniel P. Petrylak<sup>11</sup>, Padmanee Sharma<sup>12</sup>, Eila C. Skinner<sup>13</sup>, Guru Sonpavde<sup>14</sup>, John A. Taylor III<sup>15</sup>, Prasanth Abraham<sup>16</sup> and Jonathan E. Rosenberg<sup>17</sup>

