IMMUNOTHERAPY IN PROSTATE CANCER

NASPCC 15th Annual Meeting

2019

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Disclosures

- none

Acknowledgments

- James L. Gulley, MD, PhD
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Outline

- Prostate cancer immunotherapy- primer
- PD-1 and PDL-1 inhibition in prostate cancer
- Prostate Cancer Vaccines

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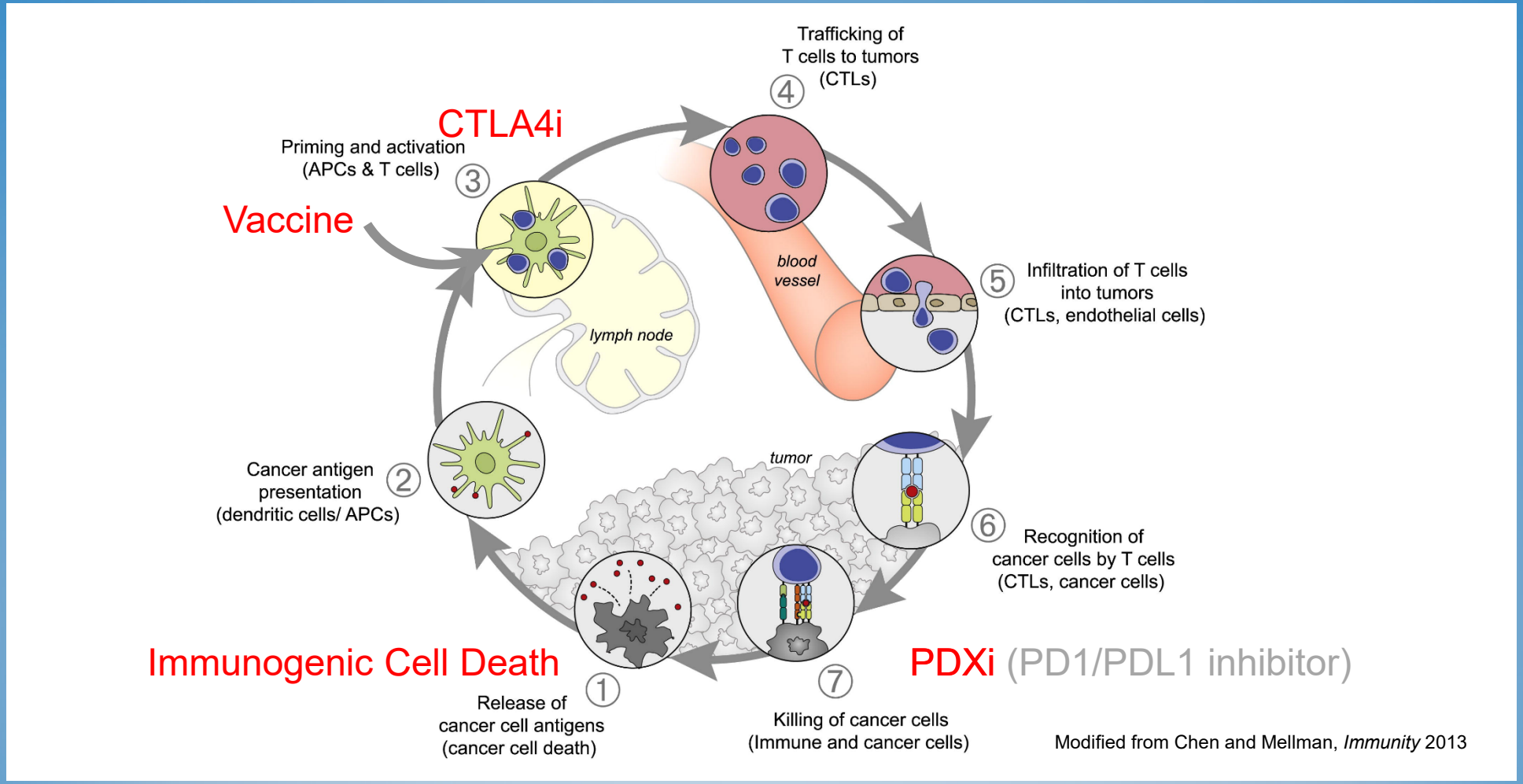
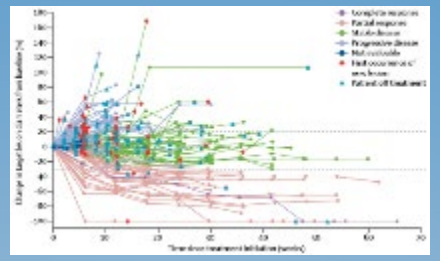
Sites for Therapeutic Intervention

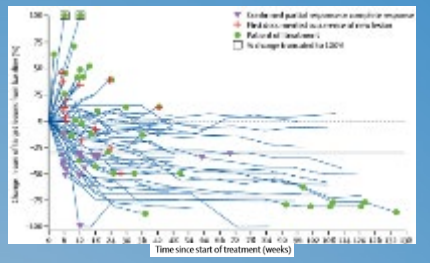


PDX Inhibition Shows Promise

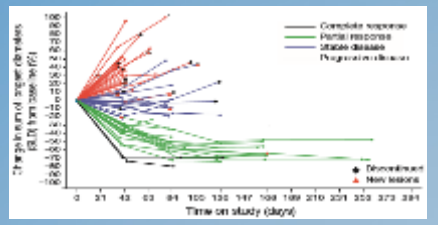
Rapid, deep, durable responses
Across a wide range of tumors
Seen in a subset of patients



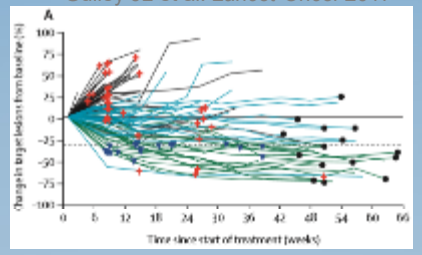
NSCLC: avelumab
Gulley JL et al. *Lancet Oncol* 2017



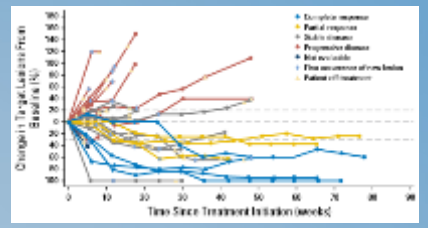
MSI hi CRC: nivolumab
Overman MJ et al. *Lancet Oncol* 2017



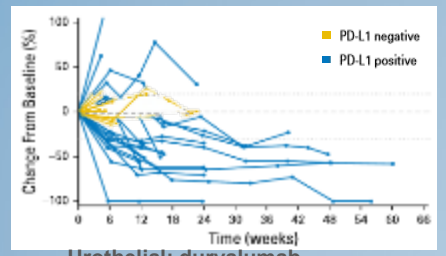
Urothelial: atezolizumab
Powles T et al. *Nature* 2014



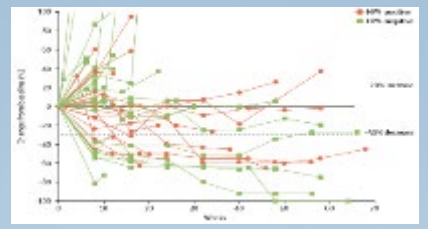
NSCLC (squamous only): nivolumab
Rizvi NA et al. *Lancet Oncol* 2015



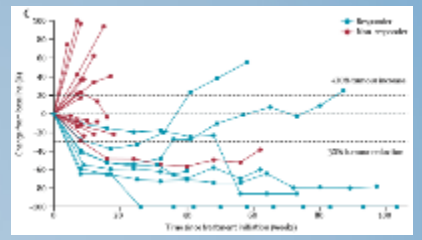
Urothelial: avelumab
Apolo AB et al. *J Clin Oncol* 2017



Urothelial: durvalumab
Massard C et al. *JCO* 2016



HNSCC: pembrolizumab
Seiwert TY et al. *Lancet Oncol* 2016



Urothelial: pembrolizumab
Plimack ER P et al. *Lancet Oncol* 2017

2018 Nobel Prize in Medicine

Jim Allison, MD Anderson

Tasuku Honjo, Kyoto University

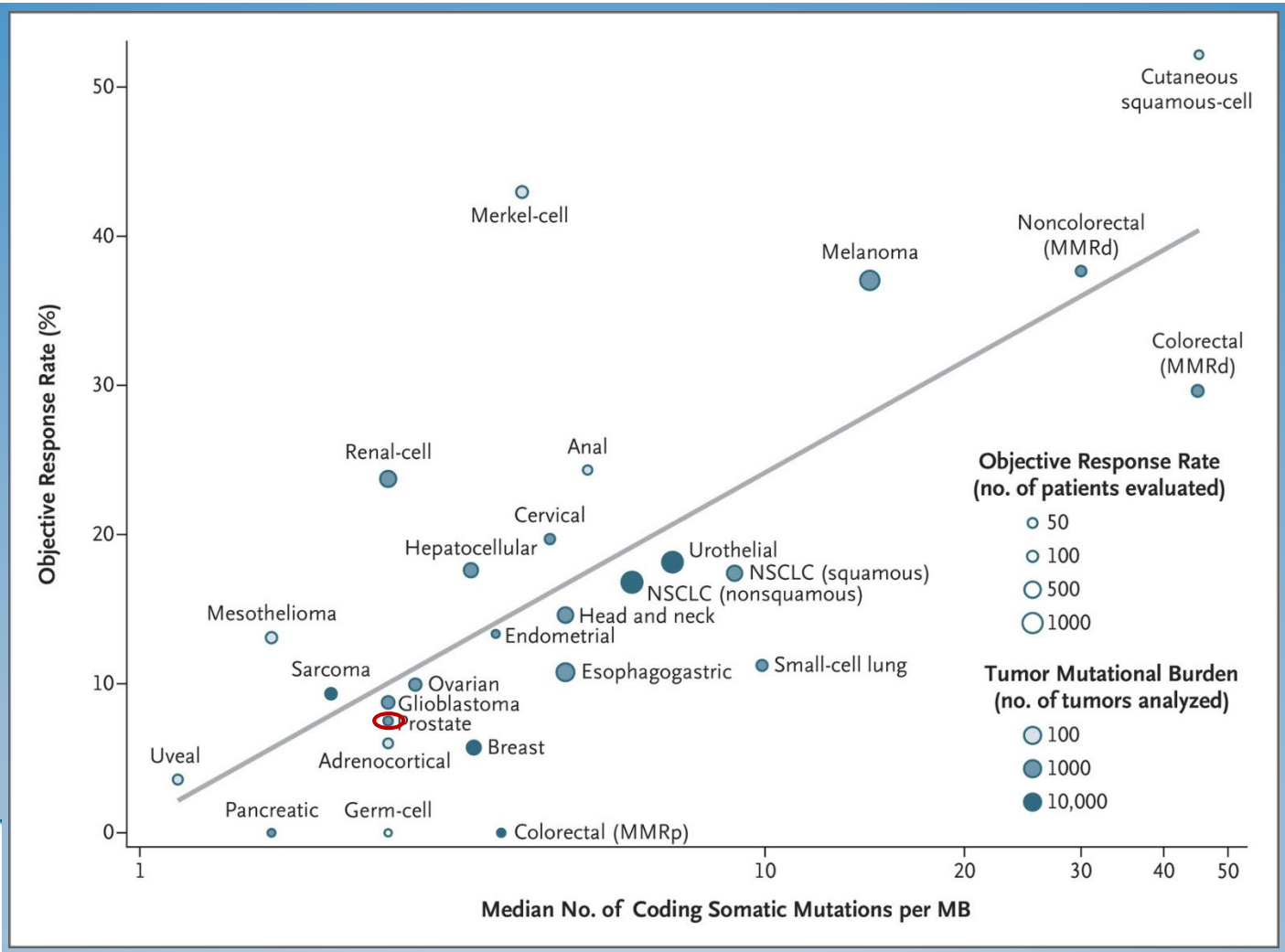
Immunotherapy Hits PRIMETIME!

- Pre-clinical m
- Early stage h … n a variety of malignanc
- Nobel Prizes …

So wh … F

- An anti-PD/C … er is right around the c…

Response to anti-PD1 Therapy



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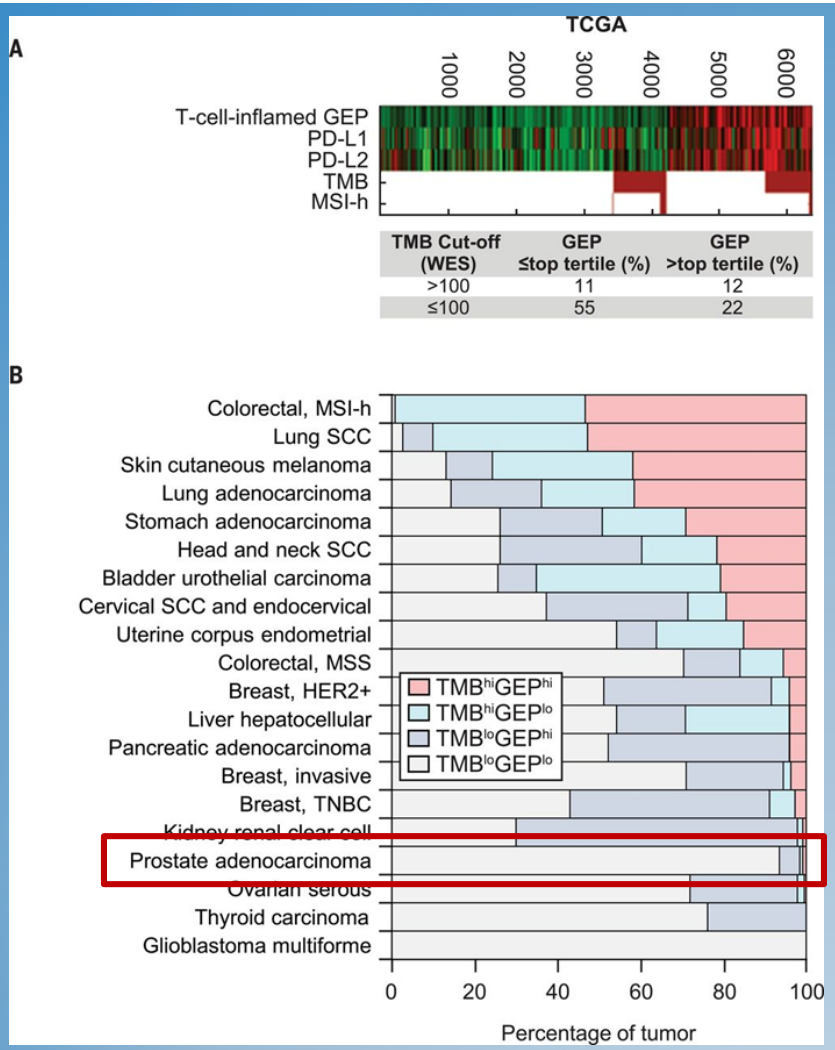
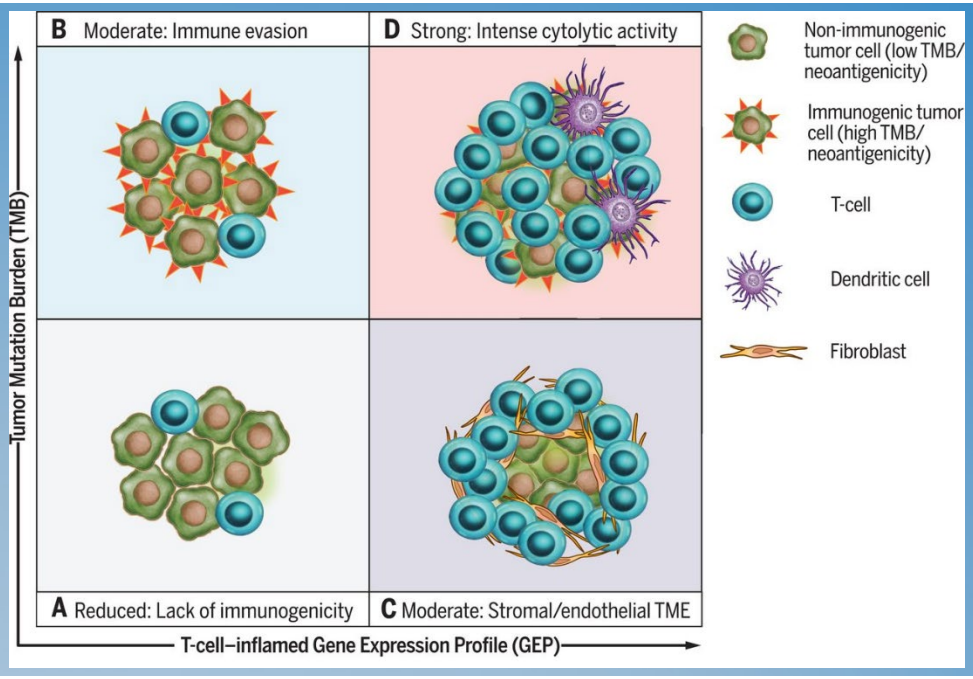
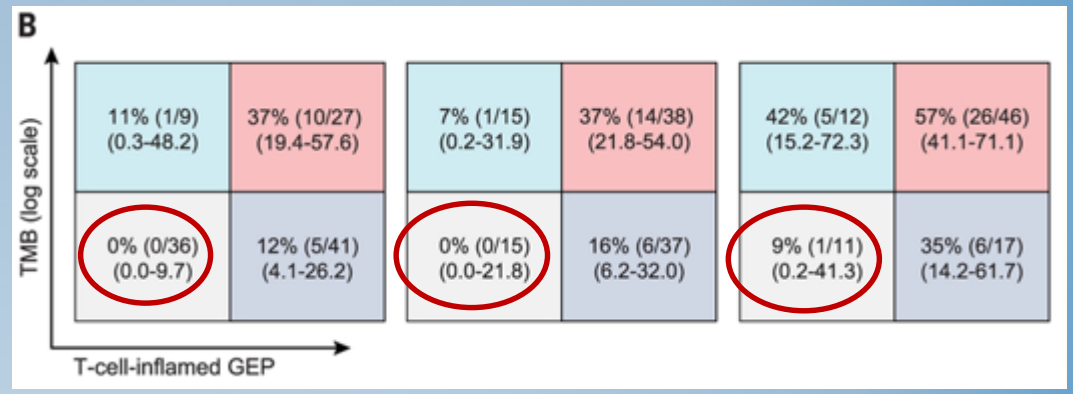
P<0.001

Yarchoan et al., *NEJM* 2017

Immunogenicity Profiles of Cancers







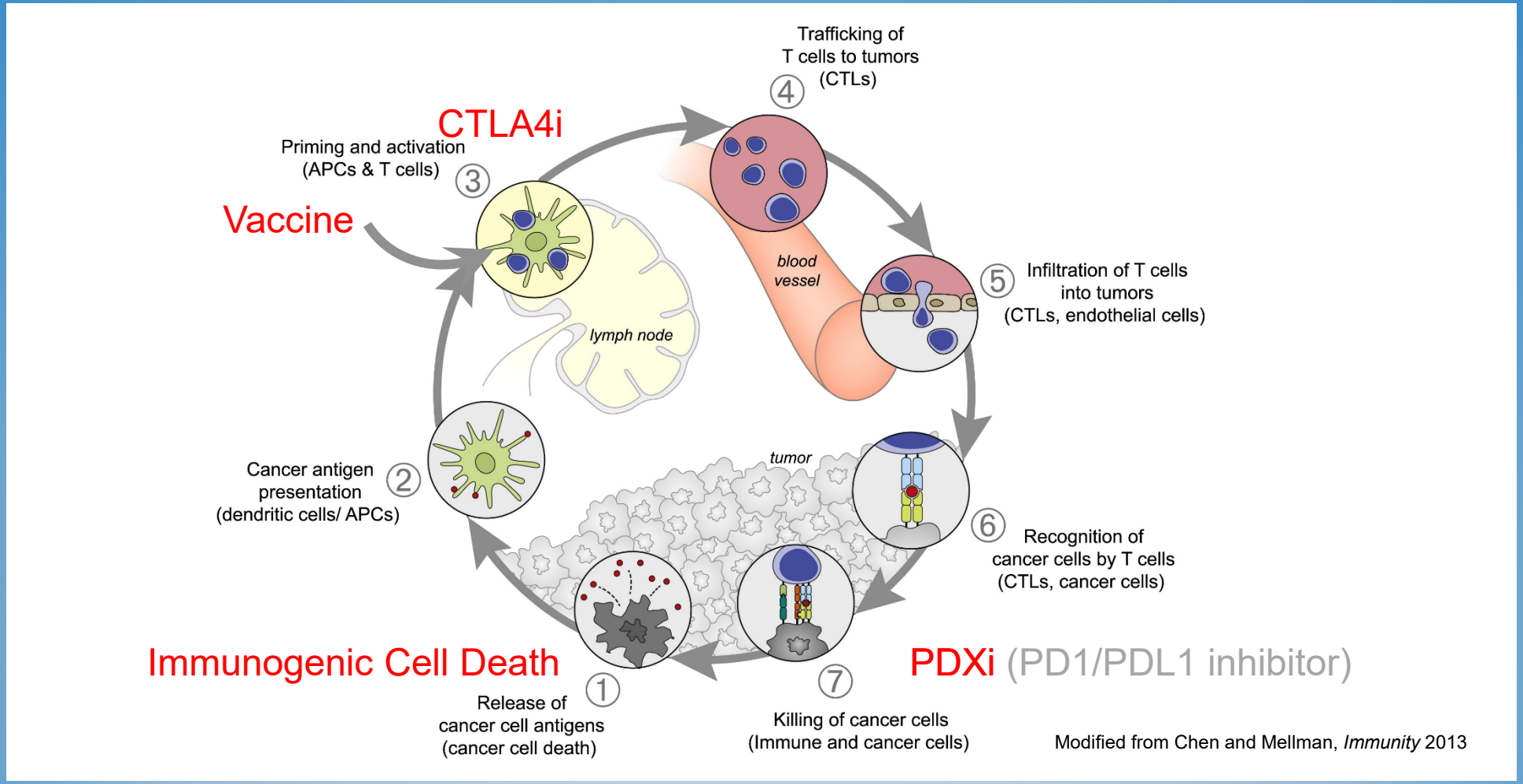
Cristescu et al., *Science* 2018

Prostate Cancer and anti-PD-1/PDL-1 Therapy

- PDL1 expression does not predict in prostate cancer
  - High TMB may be useful
- Predictive biomarkers for PD-1/PD-L1 inhibition are rapidly evolving
- At this time Prostate Cancer is generally believed to be relatively unresponsive to PD-1 inhibition.

Manogue et al *The Oncologist* 2019 p444-8

Sites for Therapeutic Intervention



Prostate Cancer Vaccines

- DNA based Vaccines
  - Elicit immune response by transfection to produce immunogenic tumor associated antigens (PSA, PSMA, PAP, PSCA, TARP)
    - Phase 1 trial: 9 of 22 responses; PSADT increased from 6.5mo to 9.3mo
    - Currently in Phase II
- Peptide based Vaccines
  - Immunize with tumor specific proteins to elicit cytotoxic T-cells
    - Targets are HLA-A24+, PAP, PSA, PSMA
    - Two Phase II studies showed improved PFS with combination therapy
    - Ongoing Phase III trial

Prostate Cancer Vaccines

- Viral Vector based Vaccines
  - Recombinant viral vectors carrying gene sequences to elicit immune responses against tumor antigens
    - Demonstrate anti-PSA antibiodies and T-cell responses
    - Phase II trials ongoing
- Cell based Vaccines
  - Autologous or allogenic whole cells including Antigen Presenting Cells (APCs) to induce anti-tumor immune response
    - GVAX is whole cell CaP cell lines engineered to overexpress GM-CSF to activate dendritic cells
      - Promising results in Phase I and II but no efficacy in Phase III

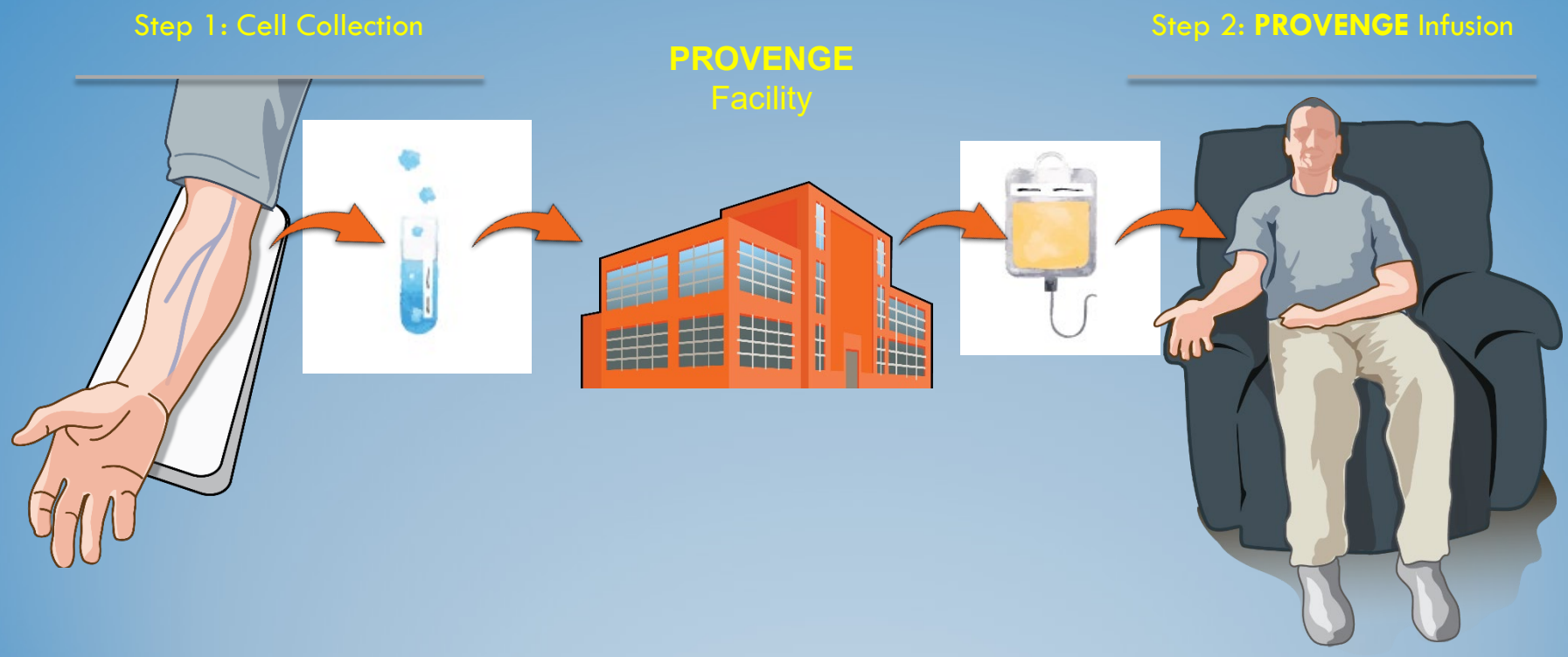
Cell Based Vaccine

- PROVENGE® (sipuleucel-T):
  - FDA approved for the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer[1]
    - The first FDA approved autologous cellular immunotherapy[1]
  - Designed to induce an immune response targeted against prostatic acid phosphatase (PAP), an antigen expressed in most prostate cancers[1,2]

1. PROVENGE® [package insert]. Dendreon Pharmaceuticals LLC 2017
2. Kantoff PW et al. *N Engl J Med*. 2010;363:411-422.

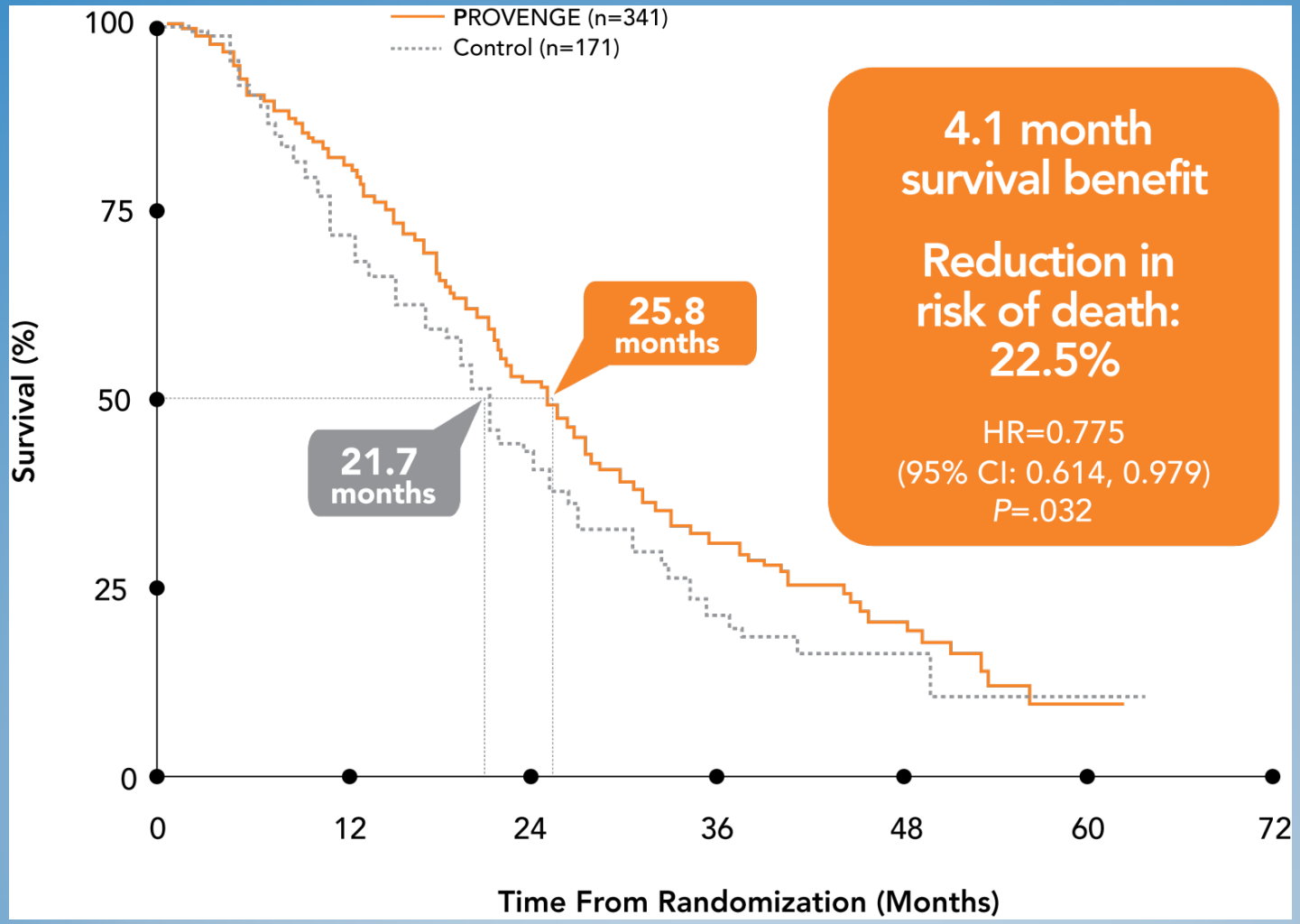
Cell Based Vaccine: Sipuleucel –T (PROVENGE)

PROVENGE treatment is 3 cycles, each comprising 2 steps



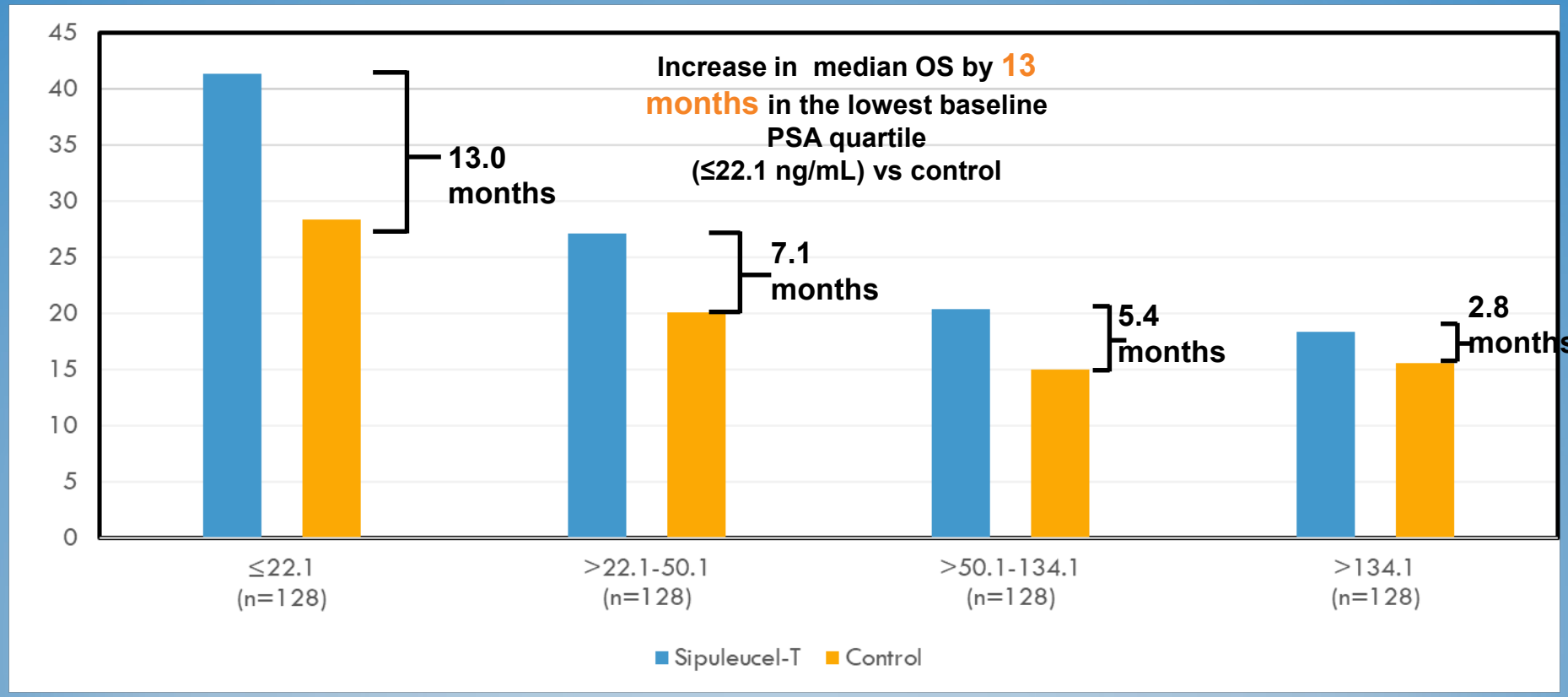
Provenge [prescribing information]. Seal Beach, CA: Dendreon Pharmaceuticals LLC; 2017.

Cell Based Vaccine: Sipuleucel –T (PROVENGE)



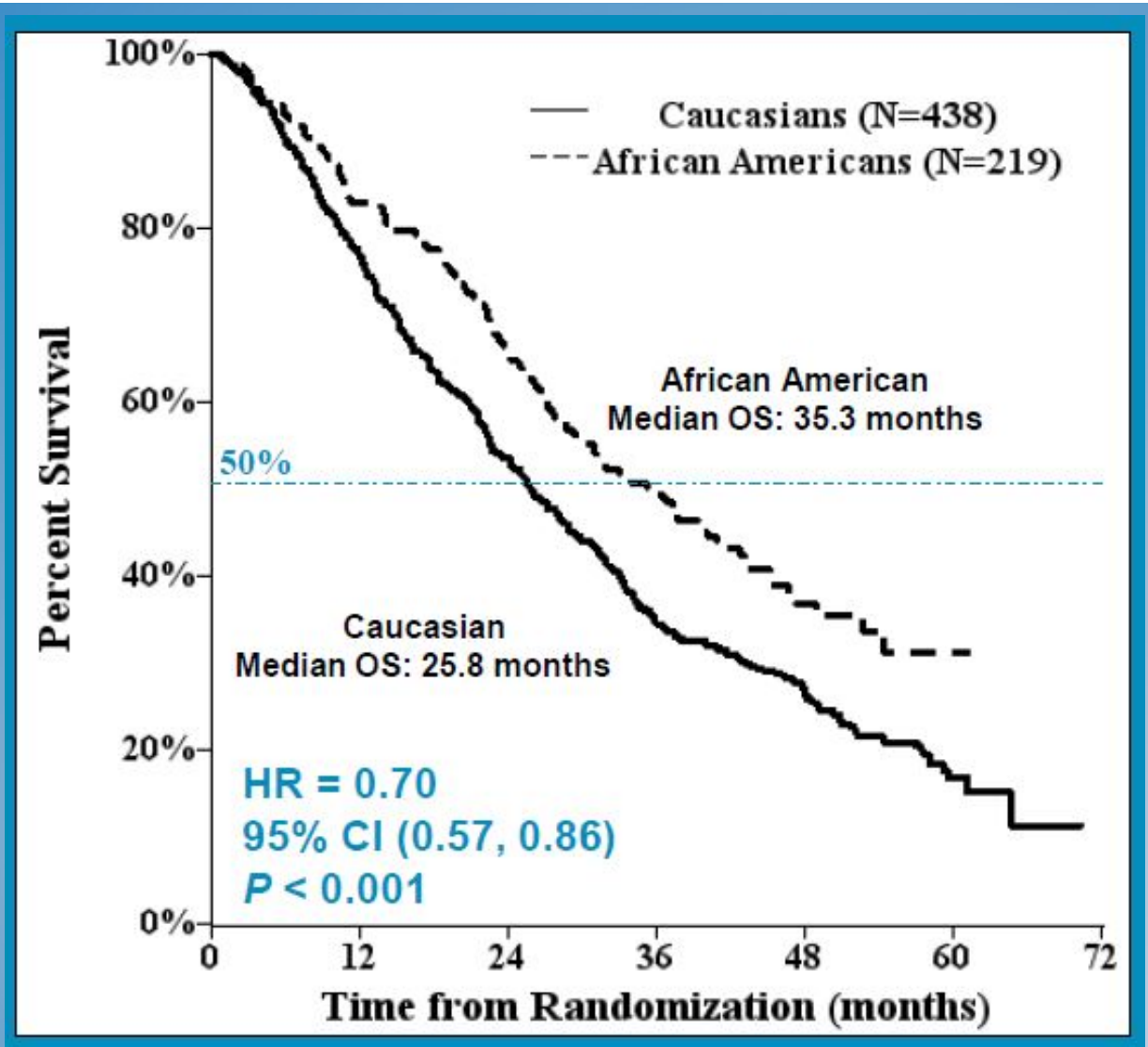
Kantoff PW, et al. New Engl J Med. 2010; 363:411-22

Immunotherapy as an Early Step mCRPC?



Schellhammer PF, et al. *Urology*. 2013;81:1297-1302.
This exploratory analysis suggests that patients with lower baseline PSA levels experience the greatest magnitude of benefit with PROVENGE

PROCEED: Overall OS of PSA-matched AA and CAU Patients Treated with Sipuleucel-T



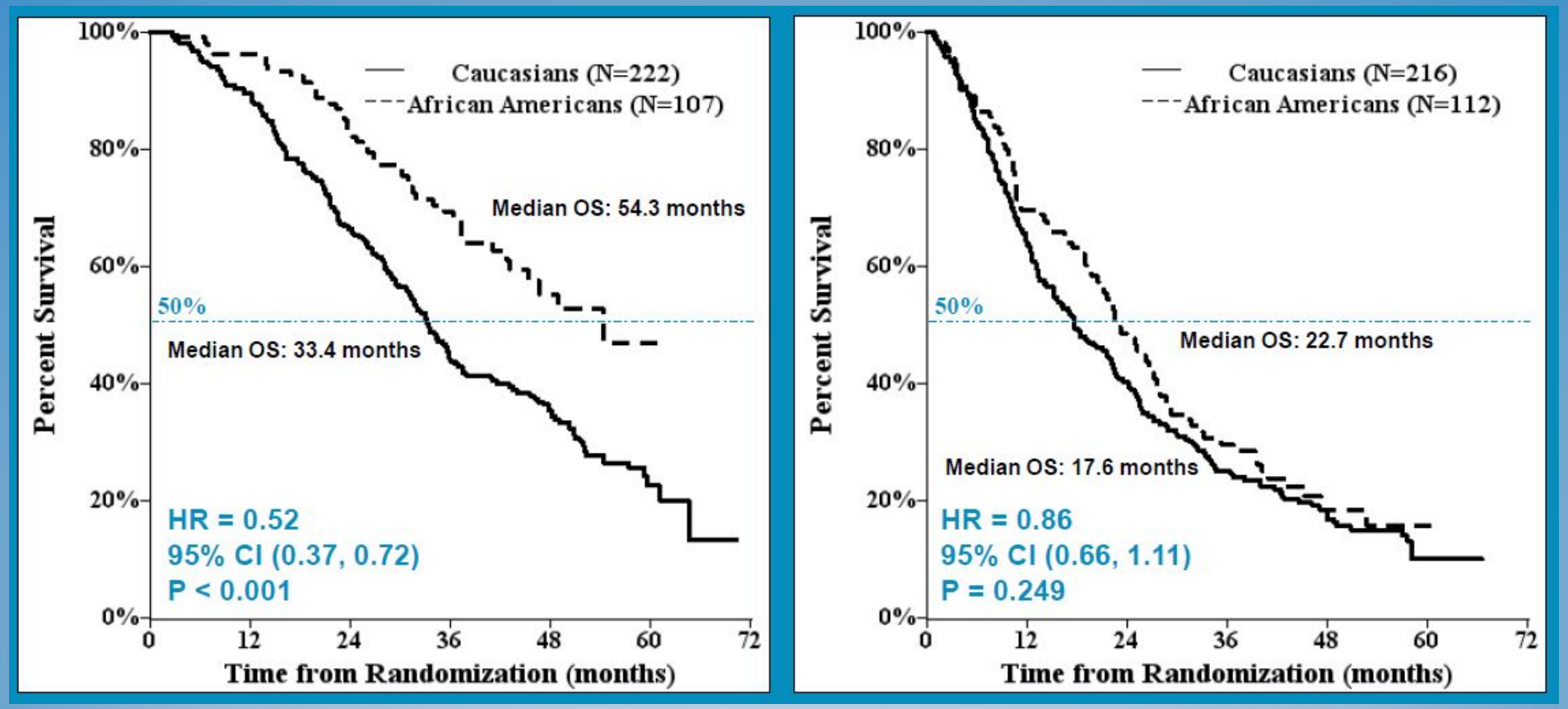
- **Median PSA = 29.48 ng/ml**

AA = African American;
CAU = Caucasian;
CI = confidence interval;
HR = hazard ratio;
OS = overall survival;
PSA = prostate-specific antigen

ASCO poster presentation #147 by Oliver Sartor MD 2019

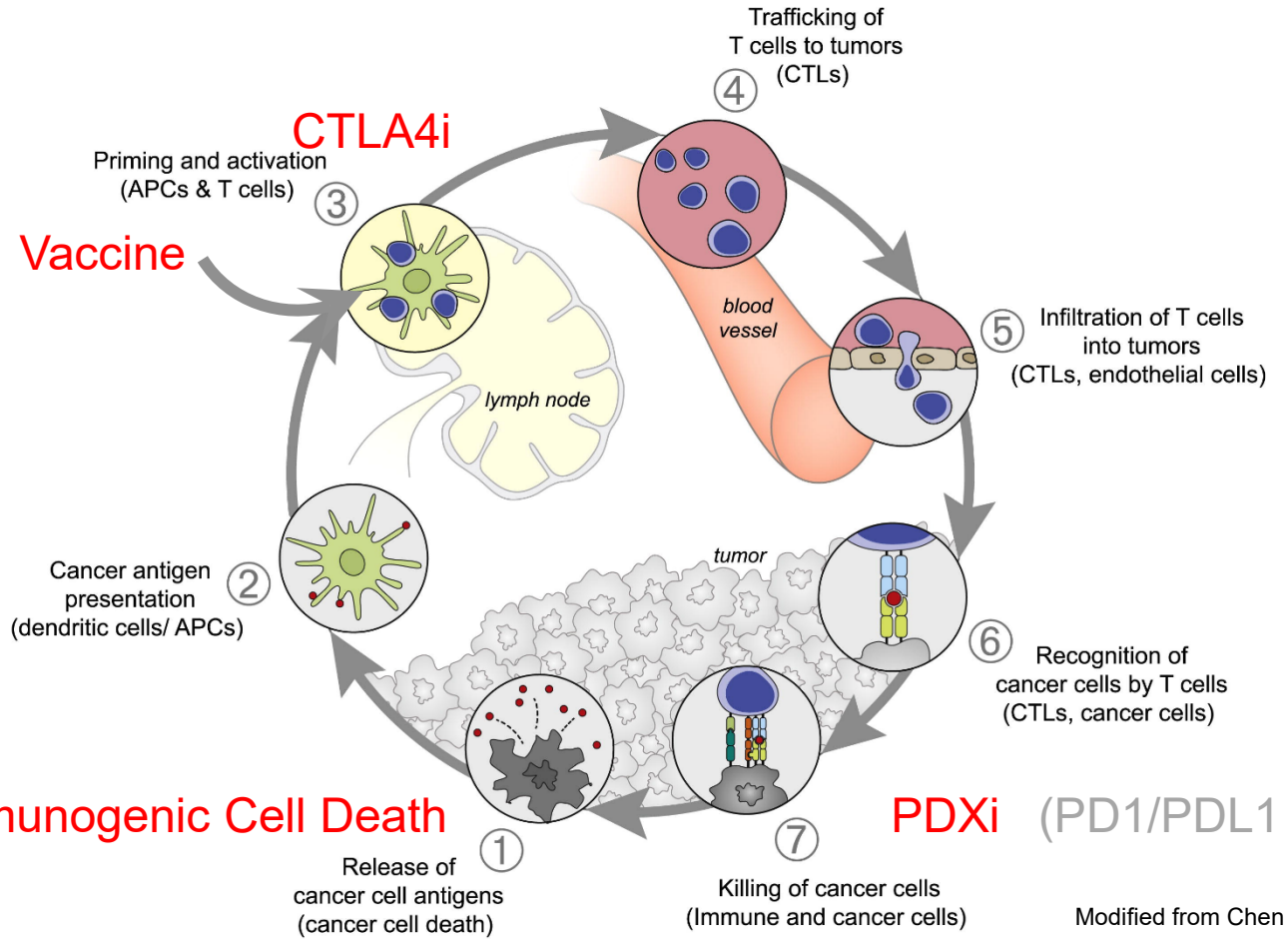
PROCEED: OS of PSA-matched AA and CAU Patients Treated with Sipuleucel-T

Below Median PSA *Median PSA 29.48 ng/ml* **Above Median PSA**



ASCO poster presentation #147 by Oliver Sartor MD 2019

Combination Therapy?



Modified from Chen and Mellman, *Immunity* 2013

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1-800-4-CANCER Live Chat

From 1995 to 2014, in fact, there was a sharp increase in the launch price of new cancer drugs—that is, the cost of a new drug being introduced to the market for the first time. Most cancer drugs launched between 2009 and 2014 were priced at more than $100,000 per patient for one year of treatment. More recently, we've seen launch prices of more than $400,000 for a year of treatment.

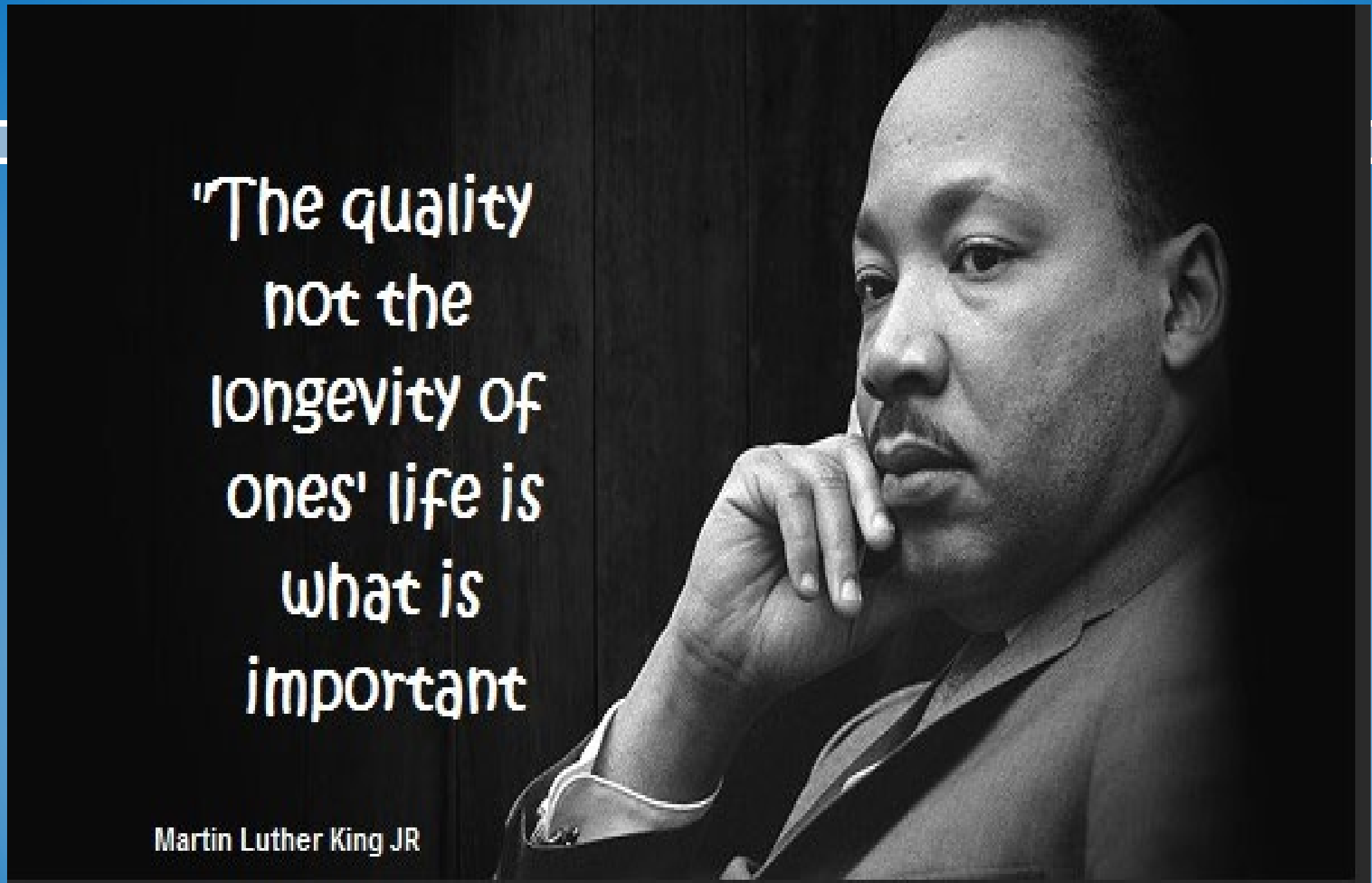
As a consequence of these increasing prices, according to one recent analysis, some patients may face out-of-pocket costs of nearly $12,000 a year for one drug .

The President's Cancer Panel is an independent panel that was established under the National Cancer Act of 1971. The panel's charge under the law is to identify high-priority issues that are impeding progress against cancer, engage the relevant stakeholders, and develop recommendations for addressing each respective issue. The recommendations are included in a report that is submitted to the President.

Barbara K. Rimer, Dr.P.H., dean of the University of North Carolina's Gillings School of Global Public Health, is the panel's chair.

Conclusions

- Substantial progress being made in understanding the immuno-biology of prostate cancer
  - New therapeutic targets are being discovered
  - Combination approaches will be needed to enhance immune responses in prostate cancer patients
  - Interesting overall survival differences in AA patients in the sipuleucel-T analyses present exciting questions and areas for investigation
- Clearly more research is needed
- Economic feasibility research is needed as well


"The quality not the longevity of ones' life is what is important
Martin Luther King JR

THANK YOU!

Prostate Cancer Immunotherapy Update 2019