



Society for Immunotherapy of Cancer

Advances in Cancer Immunotherapy™

# Cancer Immunotherapy in Practice

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# Disclosures

- Advisory Board/Consultant: BMS, Jounce, Iovance, Merck, Immunocore, Regeneron, Replimmune, Sanofi, Novartis, Replimmune, Castle Biosciences
- Data Safety Monitoring Committee: Incyte, AstraZeneca
- Stock ownership: Bellicum, Asensus Surgical, Amarin
- Research support (all to institution): BMS, Merck, Celgene, Novartis, GSK, HUYA, Amgen, Regeneron, Replimmune
  
- I will not be discussing non-FDA approved indications during my presentation.

## CANCER DEATHS IN THE UNITED STATES

Cancer death rates dropped 27% from 2001 to 2020.

27%



[cdc.gov/cancer](https://cdc.gov/cancer)

## WHY DID CANCER DEATH RATES CHANGE FROM 2001 TO 2020?

- Educational campaigns to help people quit using tobacco.
- Vaccines to prevent viruses that can lead to cancer.
- Screening tests that can find cancer early, when treatment is likely to work best.
- New cancer treatments and therapies.

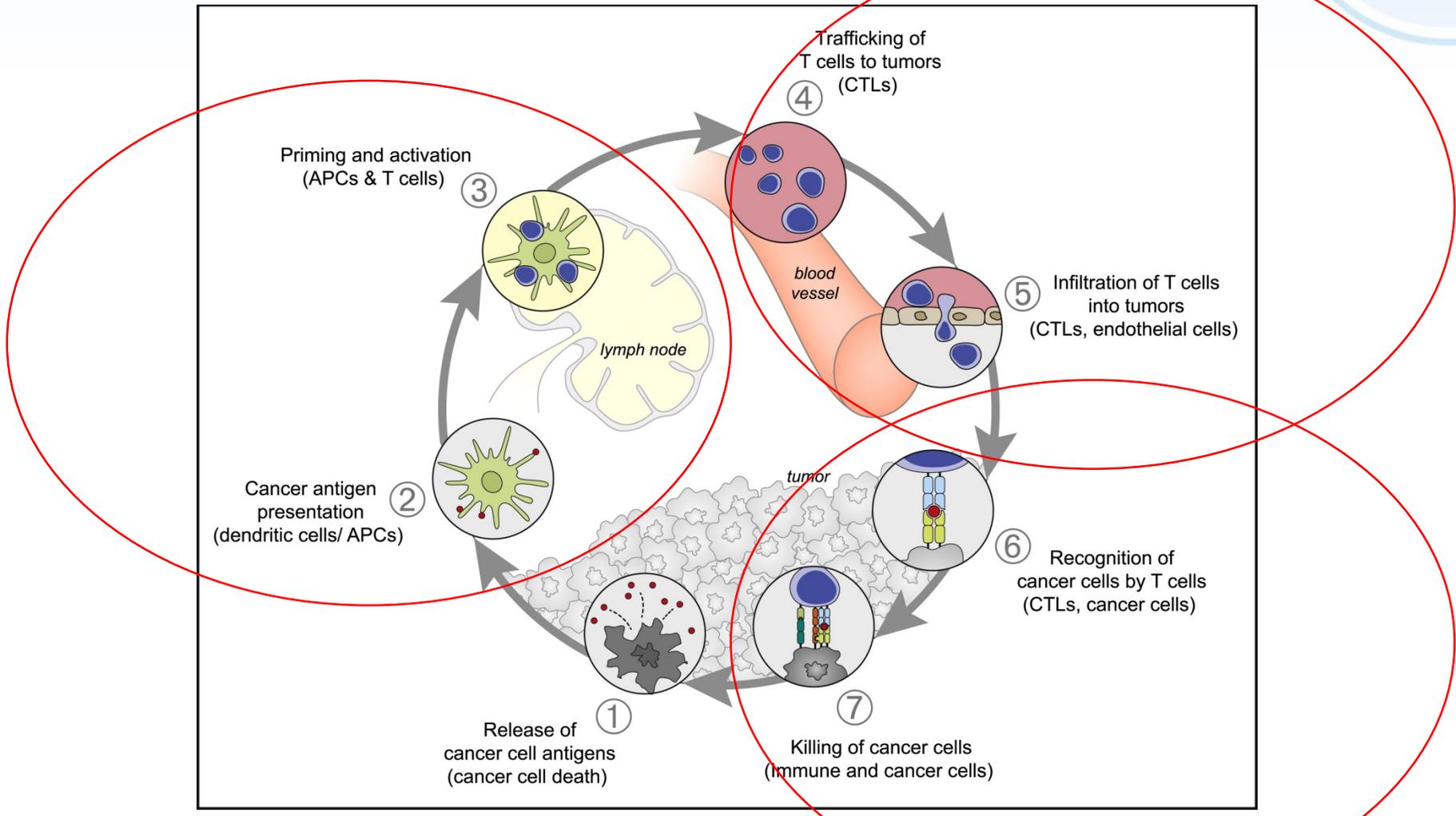


[cdc.gov/cancer](https://cdc.gov/cancer)



# Advances in Cancer Immunotherapy™

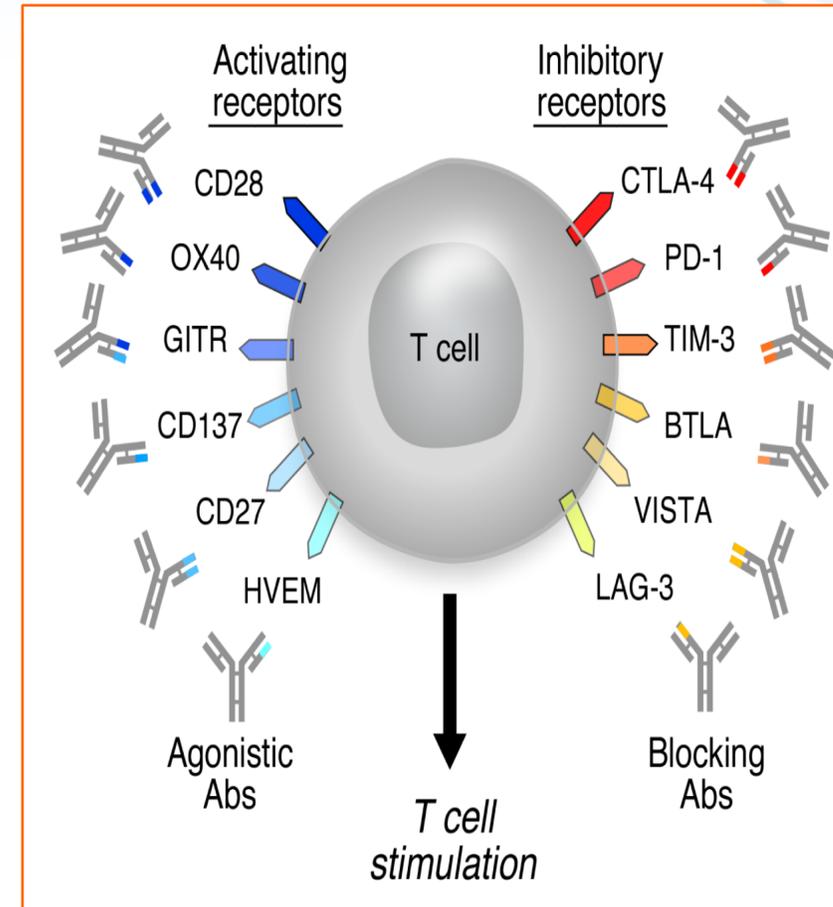
## Cancer – Immunity Cycle



# T-Cell Targets: A Balancing Act

## Treatment by Proxy

- Give a 'new' immune system
  - Allogeneic transplant
  - Adoptive cell therapy (LAK, TIL, CAR-T)
- 'Boost' immune response
  - IL-2, interferon
- 'Block' checkpoints
  - CTLA4, PD1, LAG3
- 'De novo' immunization

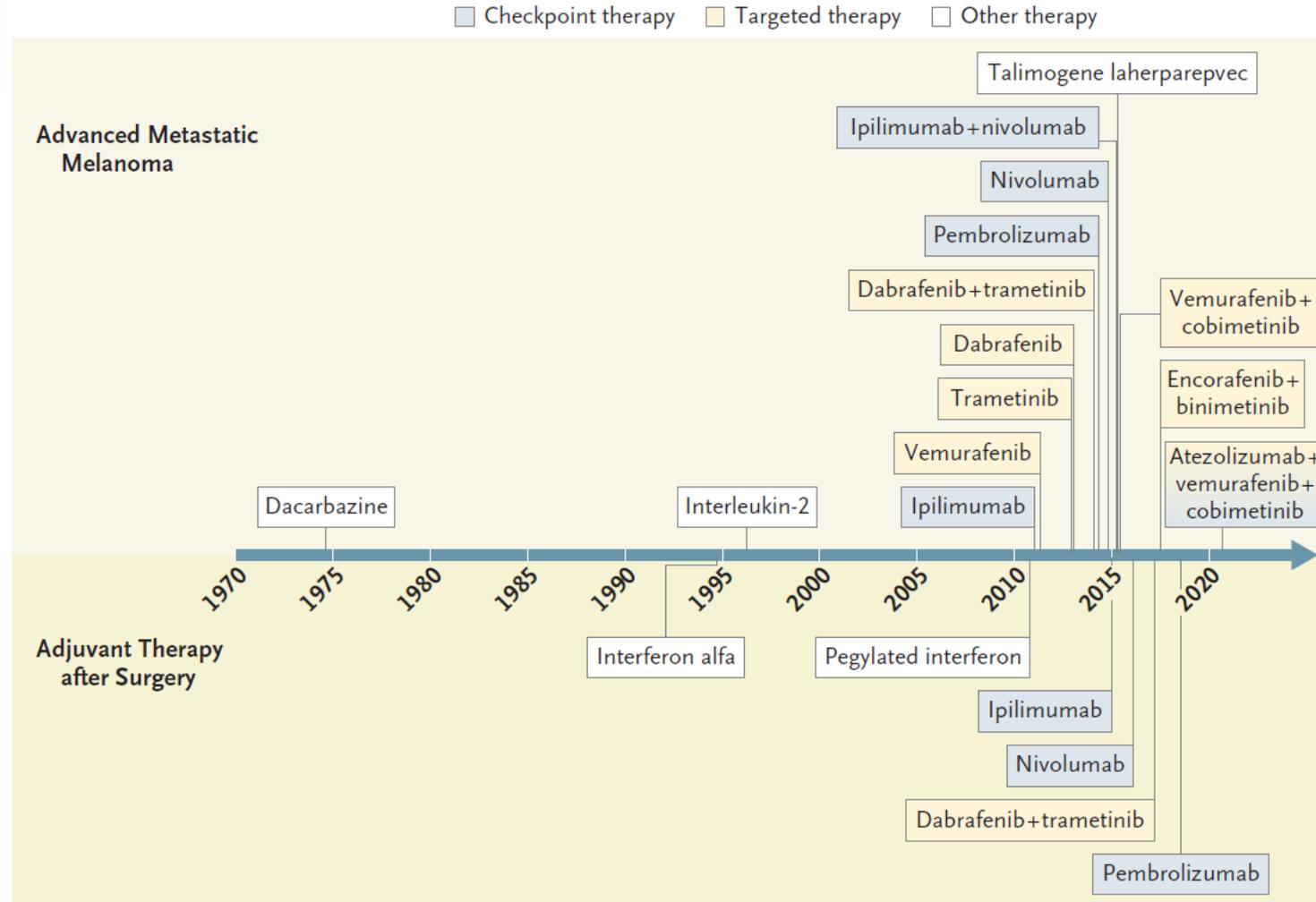


Mellman I, et al. *Nature*. 2011;480:480–489.

# Almost ubiquitous use of PD1/PD-L1 AB in 2022

Nivolumab	Pembrolizumab	Atezolizumab	Durvalumab	Avelumab
NSCLC, Melanoma, HCC, RCC, Urothelial, Hodgkin's, MSI-H CRC H/N SCC, Mesothelioma, Esophagus, Gastric/GEJ	Melanoma, NSCLC, HNSCC, Hodgkin's, PMBCL, Gastric, Esophagus, Cervical, Urothelial, MSI-H CRC, Gastric, Esophageal, Cervical, HCC, RCC, TNBC, Endometrial, CSCC, Merkel, TMB-High Cancer. MSI-H Cancer	NSCLC, ES-SCLC, Urothelial, Melanoma, HCC	NSCLC, ES-SCLC	Merkel Urothelial, RCC

# Drug Approvals in Melanoma

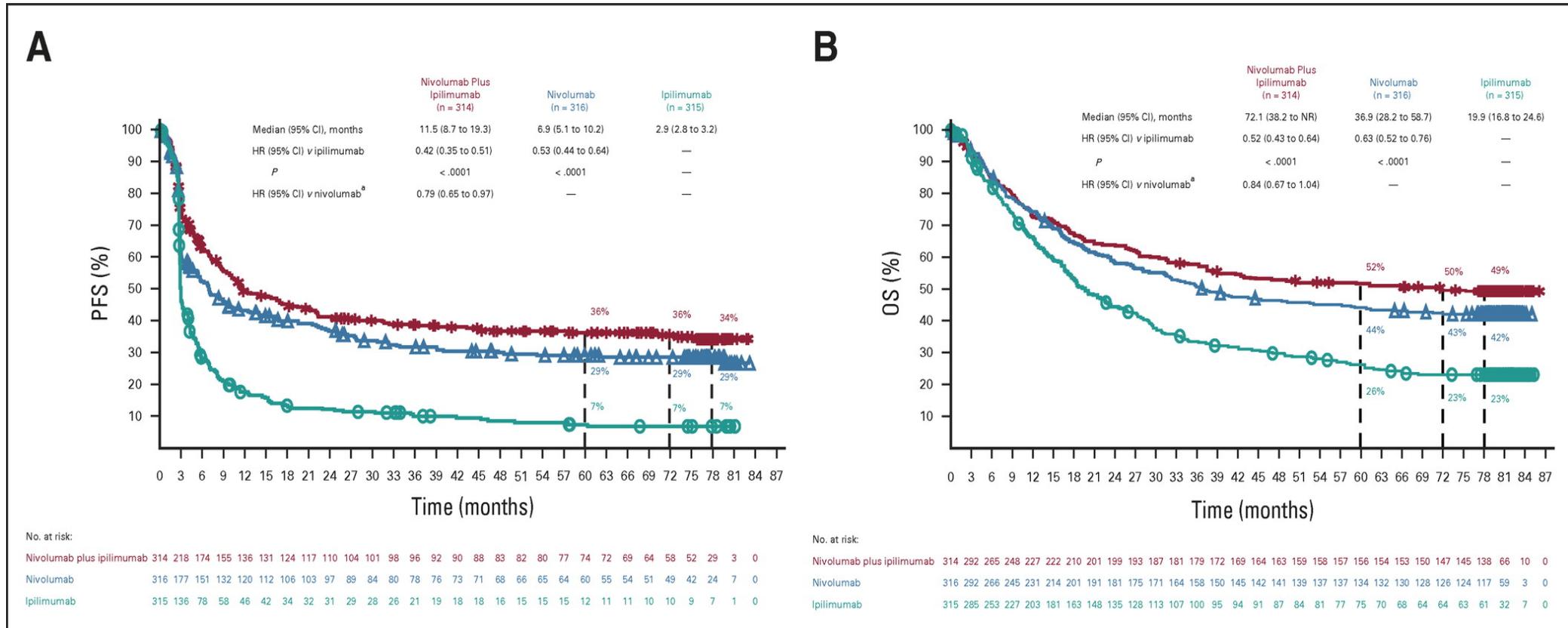


Nivolumab +  
Relatlimab

2022

Curti and Faries, *N Engl J Med* 2021;384:2229

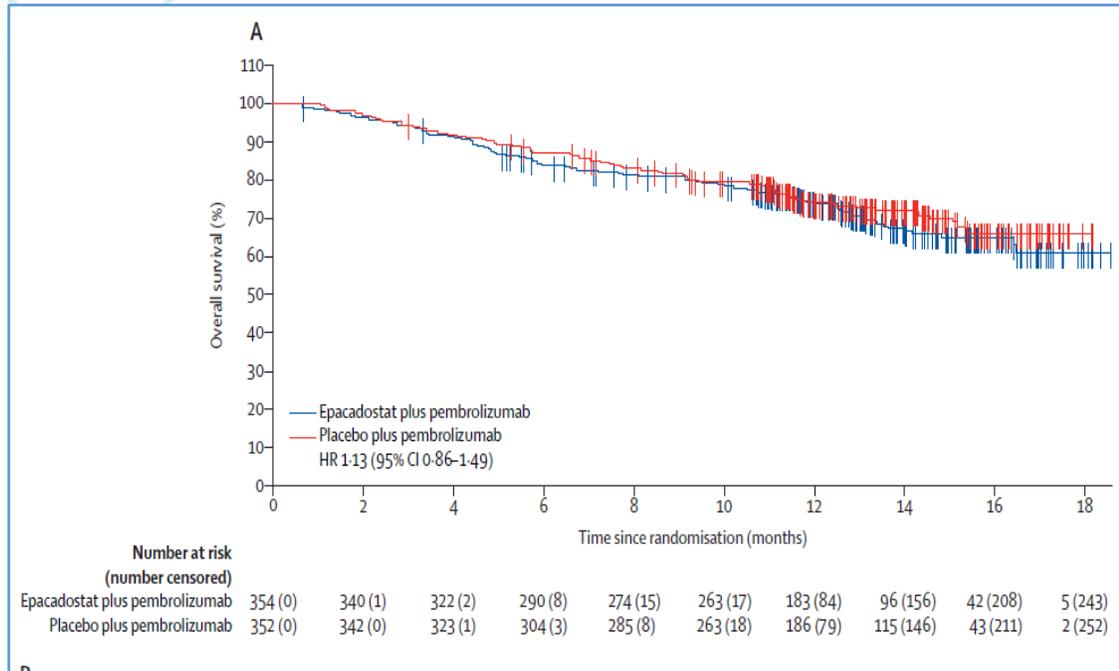
# CHECKMATE-067: 6.5-year Survival in Melanoma



49%

Wolchok et al. *J Clin Oncol* 2022 40:127-137.

# But other sobering phase 3 results...

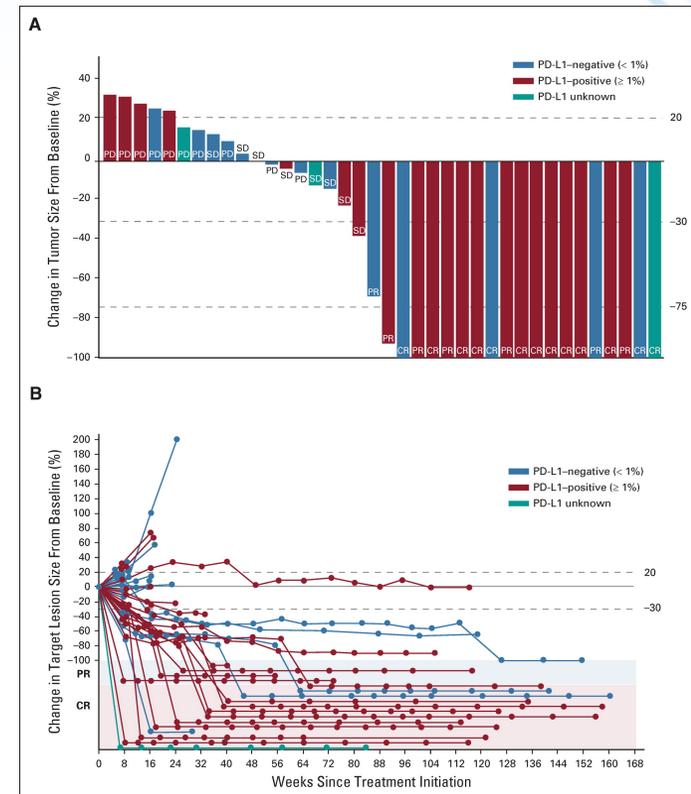


Long et al. *Lancet Oncol* 2019;20:1083.

***Echoes of a failure:  
what lessons can we learn?***

**Sondak, Khushalani**

**Lancet Oncol 2019;20:1037**



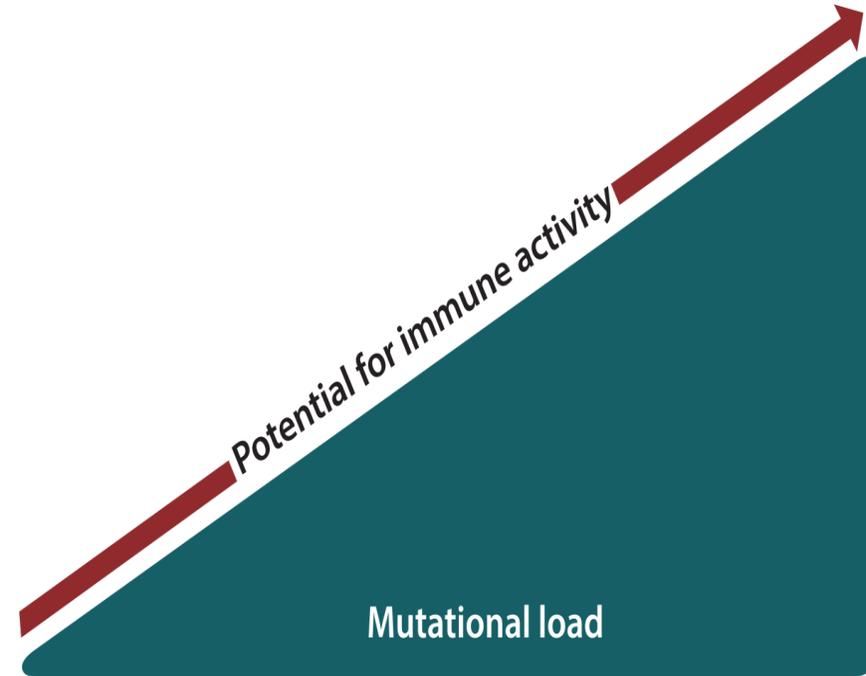
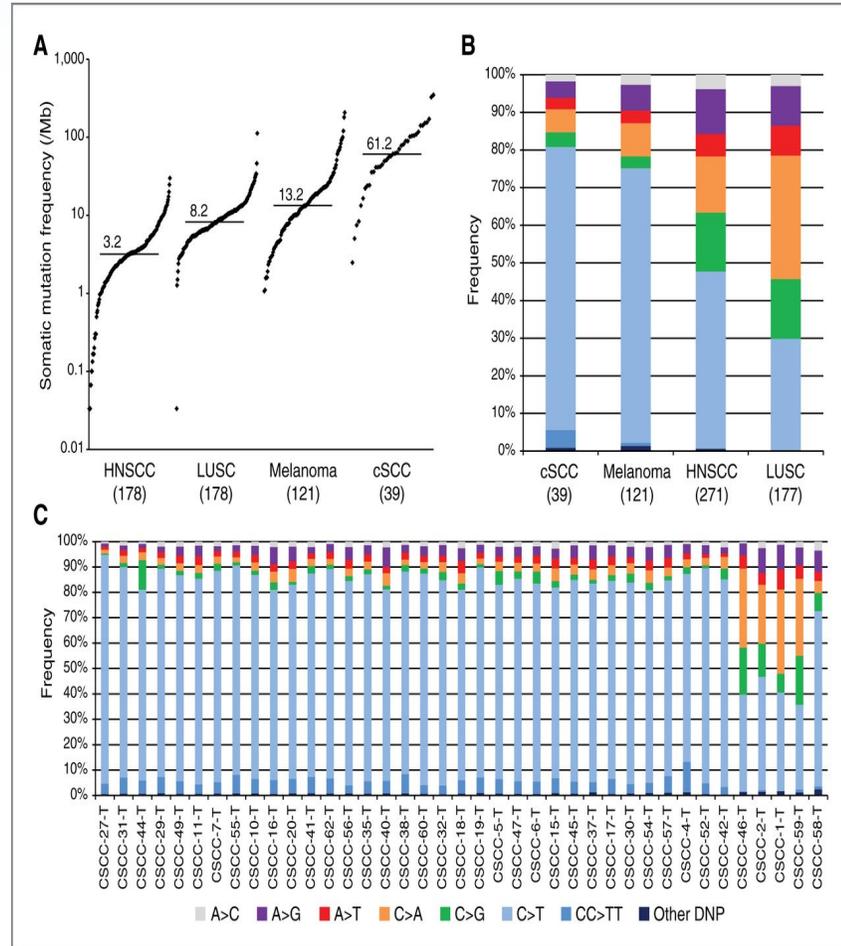
Diab et al. *J Clin Oncol* 2021;39:2914.

March 14, 2022 – Press Release

**Phase 3 PIVOT IO-001**

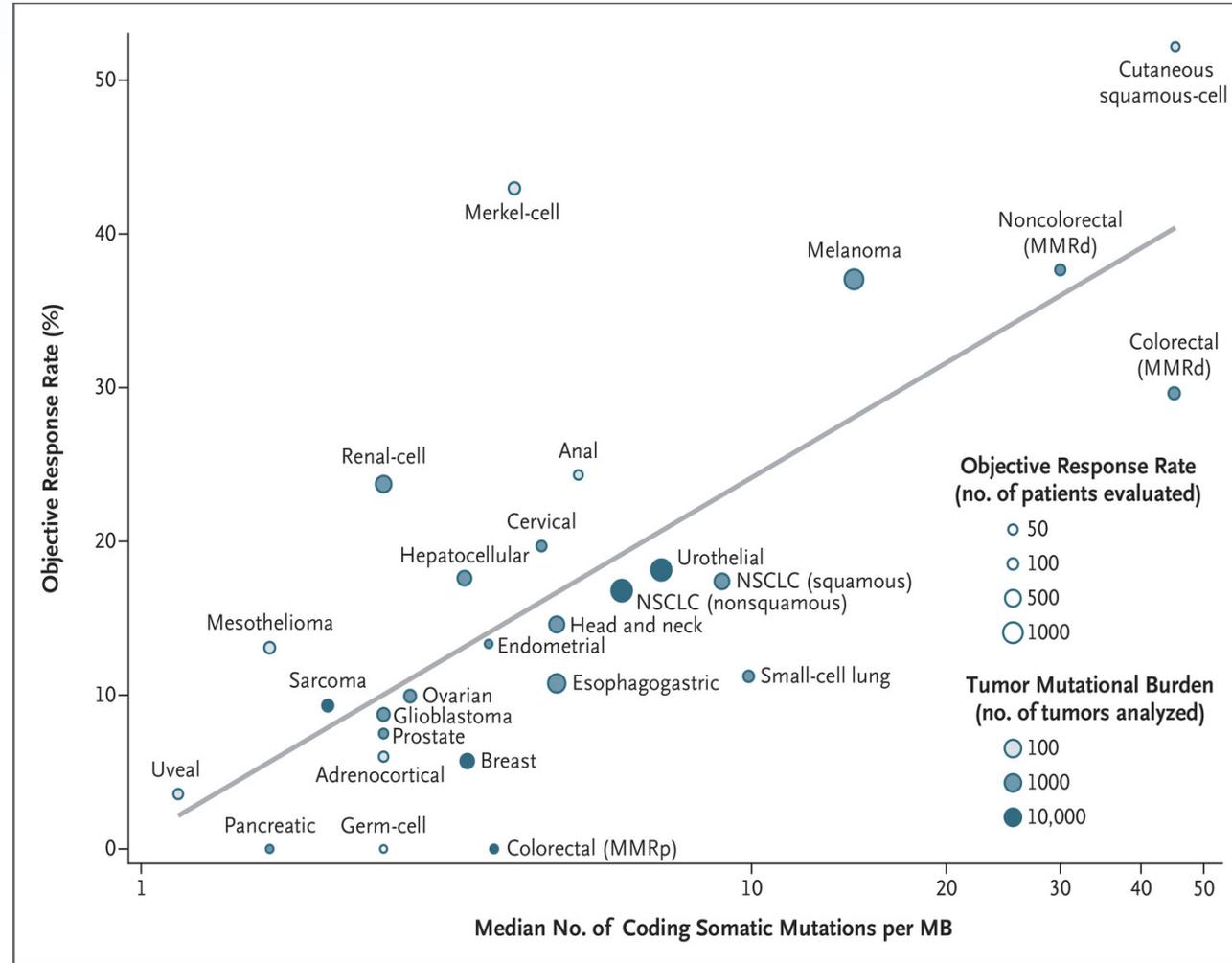
*.....study did not meet the primary end-points of progression-free survival and overall response rate by blinded independent central review.....*

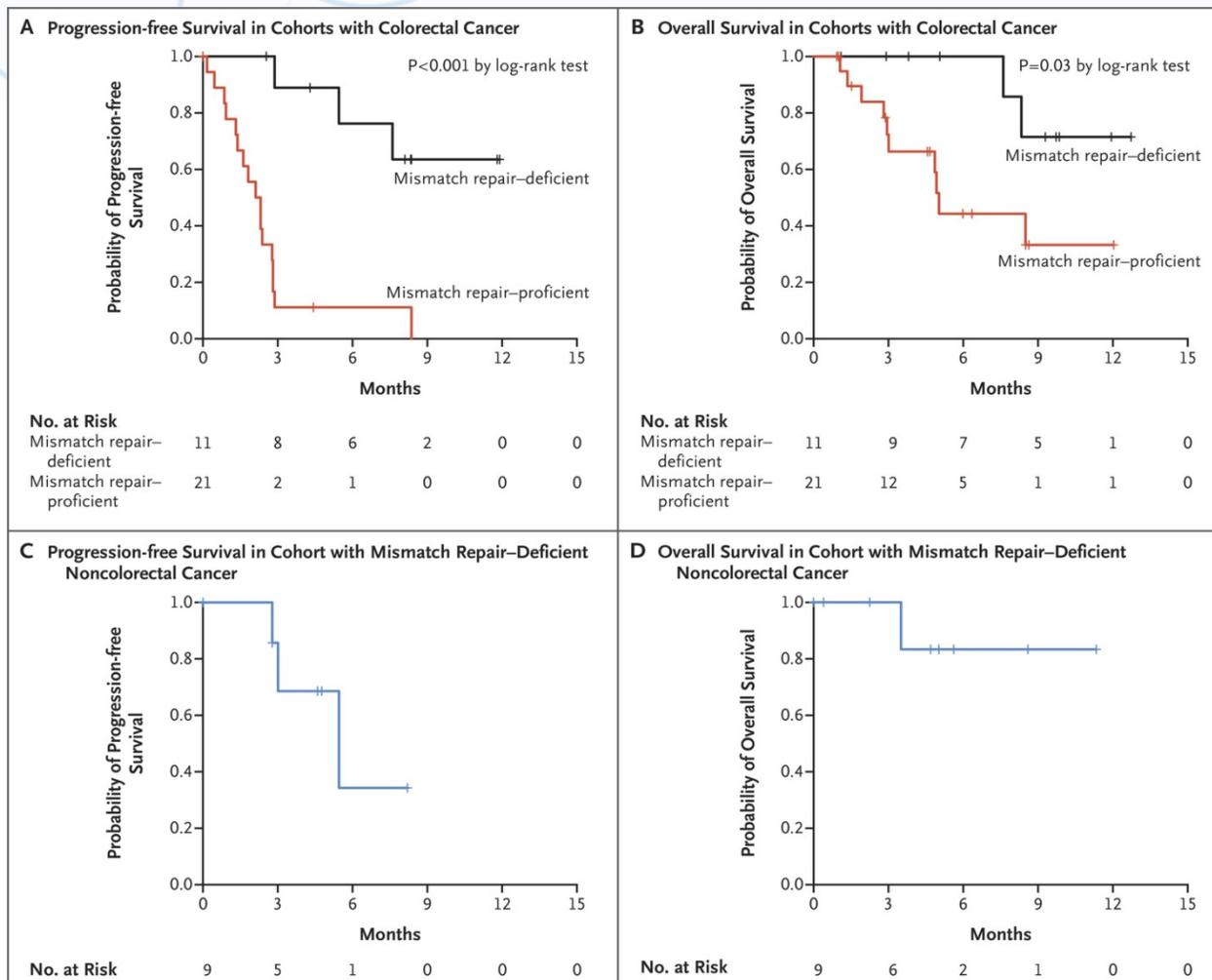
# Mutation Frequency in Tumors



Pickering CR, et al. *Clin Cancer Res.* 2014;20:6582-6592.

# TMB and Response to Anti-PD-1/PD-L1 Therapy





- **First tumor agnostic biomarker-based approval (May 23, 2017)**
- **High unmet need**
- **High response rate (40%)**
- **Established safety profile**
- **Extended to pediatric solid tumors**
- **No companion diagnostic to identify MSH-H or dMMR cancers**

Le DT et al. *N Engl J Med* 2015;372:2509-2520.

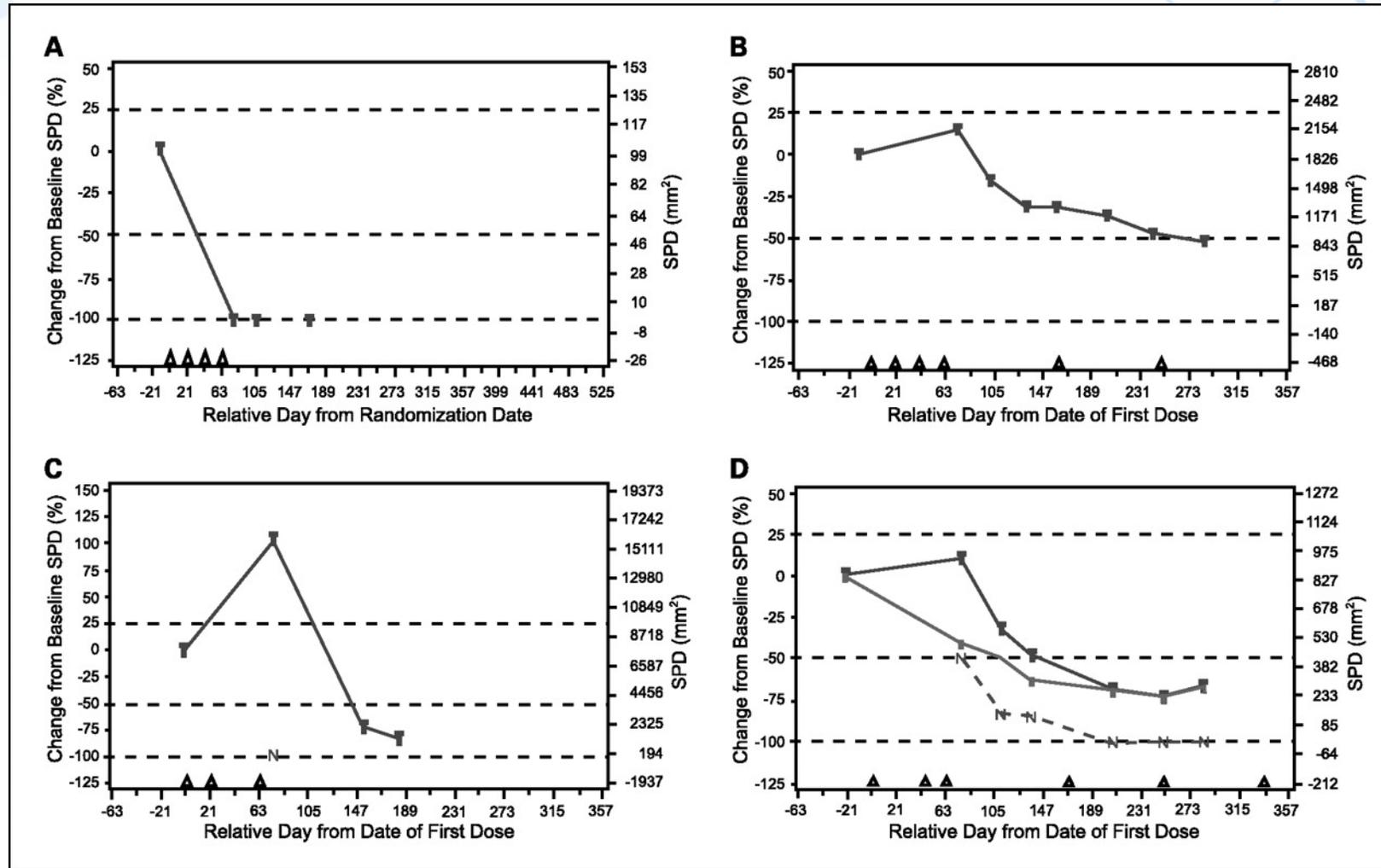
# Tips for the Team (I call this *ETA*)

- **E**valuate co-morbidities and potential contra-indications to immune checkpoint inhibition
  - Age is NOT a contra-indication, but tolerance of toxicity needs attention
- **T**hink about goals and duration of treatment
  - Is this predicated on depth of response in a given tumor type?
- **A**nticipate toxicities
  - Almost all toxicity is immune in nature
  - Provider and patient education and communication is key to early recognition and treatment
  - Infusion reactions are uncommon

## General Principles of AE Management

- Treat early and treat aggressively
- ≥ grade 3 toxicity
  - Steroids, including intravenous if necessary
  - Slow taper over 4-6 weeks
  - **Interrupt checkpoint inhibitor dosing (This is important!)**
  - Add infliximab if toxicity does not improve within 3-7 days (for hepatitis, use mycophenolate)
- Steroid use not believed to hamper therapeutic effect

# Be patient yourself: Patterns of response to ipilimumab



Wolchok JD et al. *Clin Cancer Res* 2009;15:7412-7420



*“Not everything that matters can be measured, and not everything that is measured matters”*

Albert Einstein

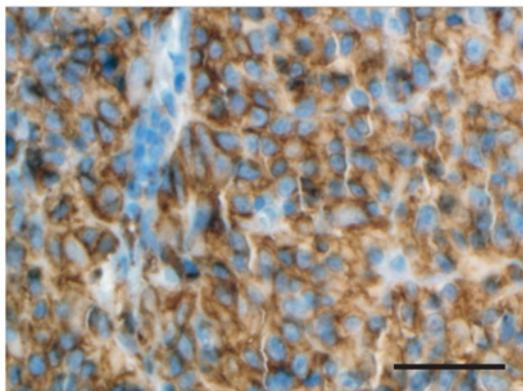
# The Need for Biomarkers

- Response to anti-PD1 therapy is not universal
  - Melanoma (40%), NSCLC (20%), RCC (22%)
- Adverse events to IO can range from mild to severe, yet do not necessarily correlate with response
- High drug costs

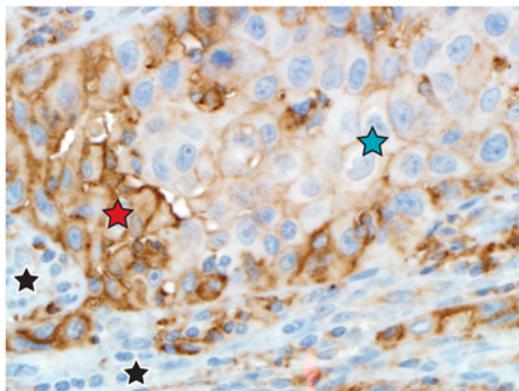
*Giving an (expensive) IO drug to a patient who develops severe toxicity, and fails to respond – failure on all fronts*

# PD-L1 Expression and Response in Different Cancers

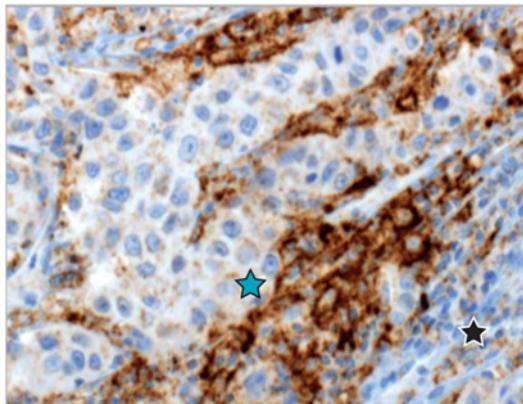
Melanoma



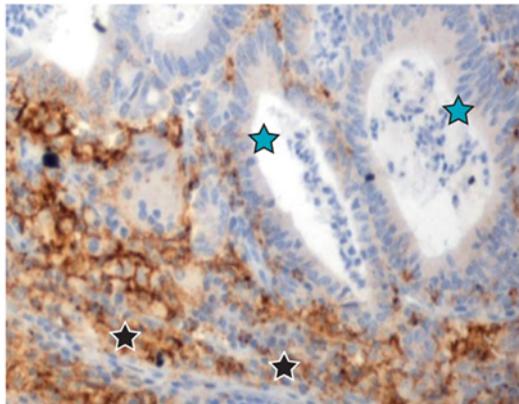
SCCHN



Breast carcinoma

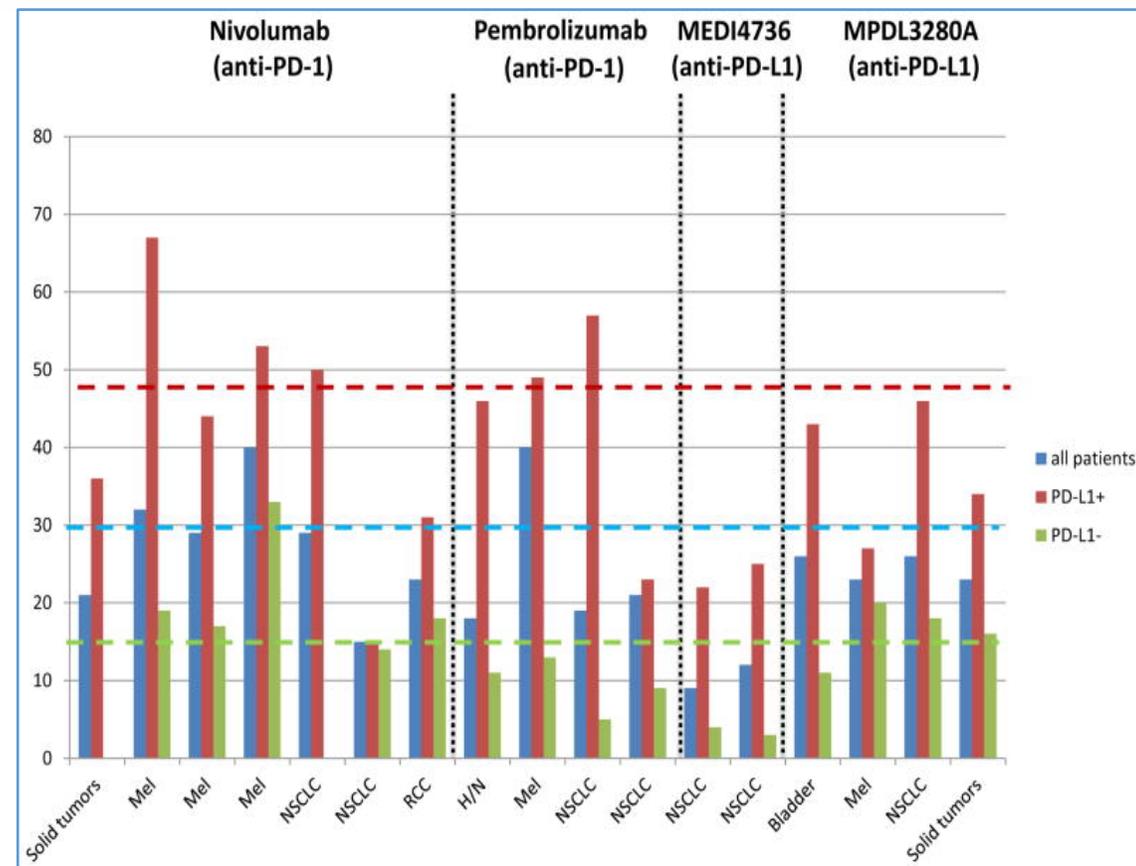


Gastric carcinoma



Topalian et al. *Nat Reviews Cancer*. 2016;16:275  
Sunshine J et al. *Curr Opin Pharmacol*. 2015;23:32

Nature Reviews | [Cancer](#)



# Multi-disciplinary Care



# Summary

- Immune checkpoint inhibitor therapy has transformed the landscape of cancer management
- Immunotherapy can be potentially curative in some cancers, yet not all will benefit
- Toxicity management requires anticipation and intervention, sometimes with long term needs
- Biomarker discovery and validation is paramount to realize the goal of ‘precision medicine’