# ICLIO National Conference

## Immuno-oncology In The Clinic Today

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**Philadelphia, Pa.**

ICLIO | INSTITUTE FOR CLINICAL IMMUNO-ONCOLOGY

AN INSTITUTE OF ACCC Association of Community Cancer Centers

accc-iclio.org

# Immunotherapy Approvals by FDA 2014-2016: Two years of remarkable progress

- September 4, 2014-Pembrolizumab approved for metastatic melanoma following Ipilumumab and BRAFi
- December 2014-Nivolumab approved for metastatic melanoma following Ipilumumab and BRAFi
- March 2015 – Nivolumab approved in squamous NSCLC following platinum-based therapy
- September 2015- Nivolumab + Ipilumumab approved in BRAF V600 WT metastatic melanoma
- October 2015 – Pembrolizumab approved in PD-L1 positive NSCLC following platinum-based therapy (companion diagnostic)
- October 2015 – Indication expanded to nonsquamous NSCLC for nivolumab (complementary diagnostic)
- October 2015-T-VAC approved for melanoma with injectable lesions
- October 2015-Ipilumumab approved for adjuvant treatment of LN+ melanoma

# Immunotherapy Approvals by FDA 2014-2016: Two years of remarkable progress

- November 2015- Nivolumab approved for Renal Cell Carcinoma after prior antioangiogenic therapy
- December 2015- Pembrolizumab approved in metastatic melanoma
- January 2016-Ipilumumab and Nivolumab approved for advanced malignant melanoma in BRAF WT or mutated
- May 2016-Nivolumab approved for classical Hodgkin's Disease after HSCT and brentuximab
- May 2016-Atezolizumab approved for urothelial cancers after cisplatin based therapy
- August 2016-Pembrolizumab approved for metastatic HNSCC after platinum based therapy
- September 13, 2016- Nivolumab dosing converted to fixed dose of 240 mg

# Immuno-oncology agents are being developed as both monotherapy and in combination with other agents to treat most tumor types

- Bladder
- Breast
- Colorectal
- Esophageal
- Gastric
- Head and Neck
- Hepatocellular
- Leukemia
- Lung
- Lymphoma
- Melanoma
- Ovarian
- Pancreatic
- Prostate
- Renal Cell Carcinoma

# WHERE ARE WE NOW?

# Experience with PD-1 Inhibitors at West Cancer Center 2014 to Present

- 2014: 2 patients treated
- 2015: 158 patients treated
- 2016 (through August): 306 patients treated

# Disease Types Treated with PD-1 Abs at West Cancer Center, 11/14-8/16

N=466

APPROVED DISEASES

| Disease Site | N | % |
|---|---|---|
| Non-small cell lung | 251 | 54 |
| Melanoma | 54 | 12 |
| Kidney | 37 | 8 |
| SCHNC | 27 | 6 |
| Bladder | 4 | 1 |
| | | |
| **TOTAL** | **373** | **81** |

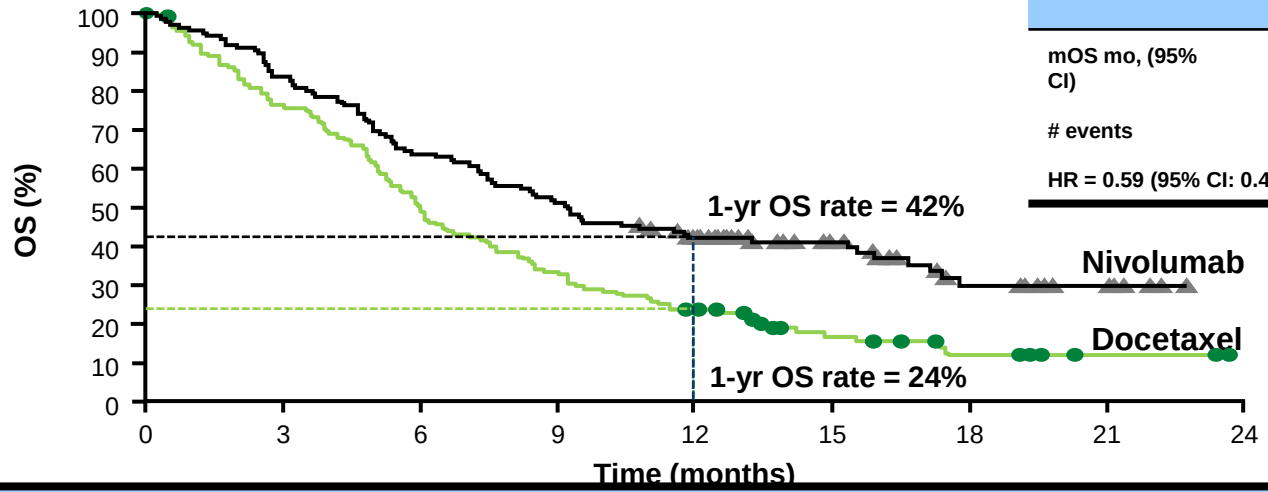
NON-APPROVED DISEASES

| Disease Site | N | % |
|---|---|---|
| GYN | 7 | |
| CNS | 6 | |
| Thymus | 3 | |
| Breast | 4 | |
| Lymphoma | 5 | |
| Anal | 2 | |
| Other skin | 5 | |
| Other | 15 | |
| ND | 19 | |

# WHY THE DRAMATIC UPTAKE?

# BECAUSE IT WORKS!!!!

# Second Line Non Small Cell Lung Cancer Overall Survival – CheckMate 017




| | Nivolumab N = 135 | Docetaxel N = 137 |
|---|---|---|
| mOS mo, (95% CI) | 9.2 (7.3, 13.3) | 6.0 (5.1, 7.3) |
| # events | 86 | 113 |

HR = 0.59 (95% CI: 0.44, 0.79), *P* = .00025

| Number of Patients at Risk: | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Nivolumab | 135 | 113 | 86 | 69 | 52 | 31 | 15 | 7 | 0 |
| Docetaxel | 137 | 103 | 68 | 45 | 30 | 14 | 7 | 2 | 0 |

Symbols represent censored observations

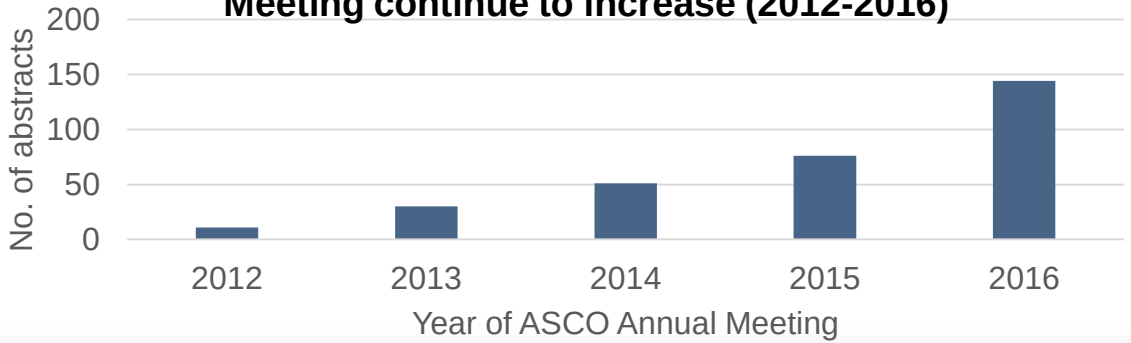


**Brahmer J, et al. *N Engl J Med.* 2015;373:123-135.**

# 2016 ASCO Annual Meeting
# June 3-7, 2016, Chicago, Illinois

| Abstracts on Immunotherapy in 2016 ASCO | |
|---|---|
| Checkpoint inhibition | 216 |
| Anti-PD-1/PD-L1 | 144 |
| Adoptive cell transfer | 36 |

**Number of abstracts on the anti-PD-1 pathway at the ASCO Annual Meeting continue to increase (2012-2016)**



# Considerations for healthcare providers and patients when using immunotherapy to treat patients with cancer:

***Response patterns to immunotherapy may differ compared to the responses observed with cytotoxic agents***

***Novel therapies with novel mechanisms of action can result in specific treatment-related adverse events (i.e. immune-related Adverse Events (irAEs))***

# Considerations for healthcare providers and patients when using immunotherapy to treat patients with cancer:

***Response patterns to immunot***
***compared to the responses ob***
***agents***

Is my cancer getting better or worse?

***Novel therapies with novel m***
***result in specific treatment-***
***immune-related Adverse Events (irAEs))***

What kind of side effects can I expect?

# Biomarkers for Anti PD-1’s

- As monotherapy, only a fraction of patients derive benefit in most cancers
- Clear need for biomarkers to distinguish best populations for treatment

# Current putative biomarkers for selecting PD-1s

- PD-L1 expression in tumor cells
- Total Mutation Burden
- MSI-High/MMR-D

# PD-L1 Expression correlated with Response to Pembrolizumab in NSCLC: KEYNOTE-010

- Analysis of outcomes with PD-L1 categorized as a tumor proportion score (TPS)[1]
  - Phase III randomized study: pembrolizumab improved OS over

| Pembro/Doce | TPS 1%-24% | TPS 25%-49% | TPS 50%-74% | TPS ≥75% |
|---|---|---|---|---|
| mOS (mo) | 9.7/8.5 | 9.8/9.9 | 15.8/8.2 | 16.6/8.2 |
| mPFS (mo) | 2.6/4.0 | 2.9/3.8 | 4.3/4.3 | 6.2/4.0 |
| ORR (%) | 8.6/10.9 | 15.8/9.1 | 22.6/9.6 | 33.7/7.0 |

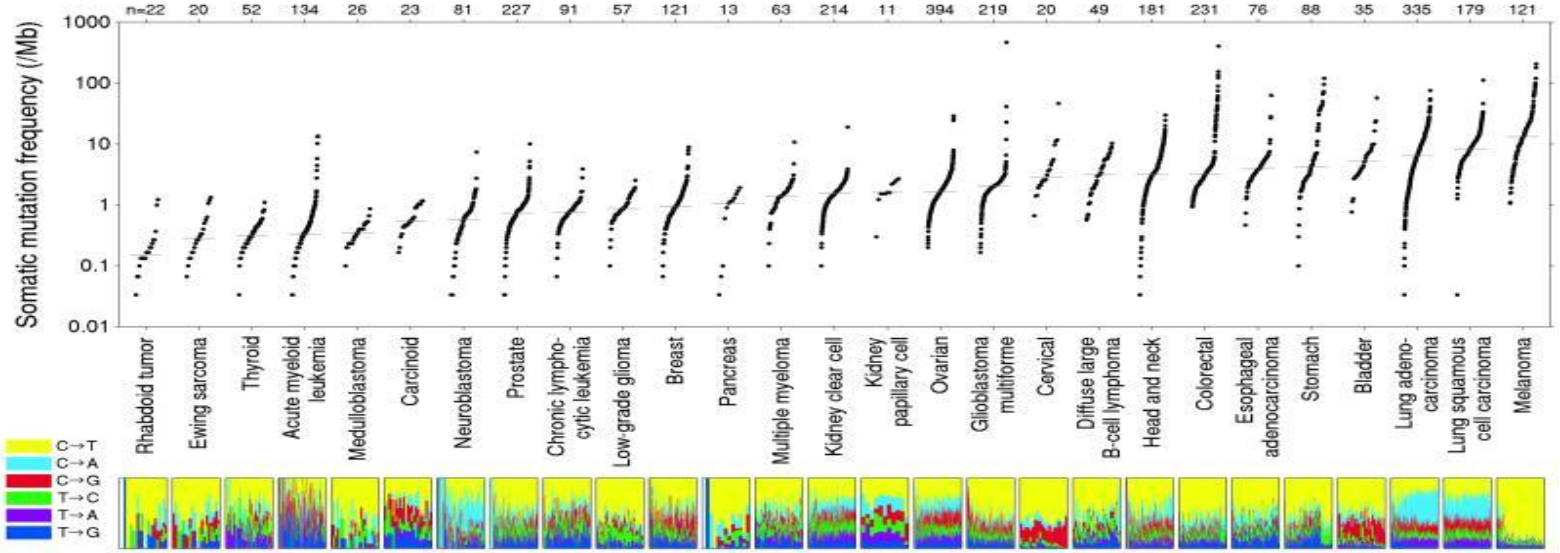
- Increasing PD-L1 expression was associated with more favorable outcomes with pembrolizumab, but not with docetaxel

Doce: docetaxel; mOS: median overall survival; mPFS: median progression-free survival; ORR: objective response rate.

1. Baas P, et al. J Clin Oncol. 2016;34 (suppl); Abstract 9015; 2. Herbst RS, et al. Lancet. 2016; 9; 387(10027):1540-50.

# Tumor Mutation Burden (TMB) in Different Cancer Types

**Somatic mutation frequencies observed in exomes from 3,083 tumor-normal pairs**




Each dot corresponds to a tumor-normal pair, with vertical position indicating the total frequency of somatic mutations in the exome.

Lawrence MS, et al. Nature. 2013 Jul 11;499(7457):214-218.

# Managing patient side effects takes care coordination

- Communication between treatments
  - Phone calls by nurses to assess for irAEs
  - Symptom algorithm trigger
  - Monitor response to supportive care
- Communication after treatment
  - Long-term follow-up visits
  - Assessment and management of chronic irAEs
  - Survivorship issues

# PATIENT ACCESS To State-of-the-art I-O Care

## “There’s no referring it away….”

Community oncologist/trialist with experience in Immuno-Oncology

**But-will there be different levels of care?**

# Variation among sites of care for I-O

| AMCs | Large community practice :10-50 MDs | Small community practice: 1-9 MDs |
|---|---|---|
| Sub-sub specialists | Some sub-subspecialization | Generalists |
| External referrals | Internal/external referrals | External referrals |
| Research/practice | Practice/research | Practice |
| High expertise | Variable expertise | Lesser expertise |
| Innovators | Early Adopters | Late Adopter |
| Few night coverage issues | High night coverage issues | Few night coverage issues |
| Reimbursement concerns low/moderate | Reimbursement issues mod but manageable | Reimbursement issues severe |

# Access to I-O Agents

- Reimbursement for approved agents excellent
- Drug replacement for unapproved uses excellent to date
- Long term cost a problem-will access be a problem?
- Value proposition requires different tools
  - QALY?
  - How to measure the tail?

# Lots of Clinical Questions….

How Long Should Patients Receive I-O Agents:

- CTLA4: 4 treatments?
- PD-1 Abs: Forever? 1 year? 2 years? After progression?

Can I-O be combined with chemotherapy?

What combinations should be advanced?