Talk Outline

• **Immunotherapy progress in 2017**: 5 new approved PD-1/PD-L1 inhibitory agents
  – Pembrolizumab (Keytruda)
  – Atezolizumab (Tecentriq)
  – Nivolumab (Opdivo)
  – Durvalumab (Imfinzi)
  – Avelumab (Bavencio)

• **How to select the right agent for the right patient in the right setting**
  – Where do we still use chemotherapy?

• **Clinical trials**: combination approaches, use of immunotherapy in earlier disease settings
Bladder Cancer Epidemiology: 2018

US New Cases: 84,000
- Men – 64,000
  - 4th most common cancer diagnosis, #9 globally
- Women – 20,000

US Deaths: 18,000
- Men – 13,000
  - 8th most common cause of cancer-related death
- Women – 5,000

Siegel RL et al CA Cancer J Clin 2018
Mutation Frequency by Tumor Type

Higher mutational burden associated with benefit from PD-1 inhibitors

## Systemic Therapy for Bladder Cancer

### Pre-Immune Checkpoint Blockade

<table>
<thead>
<tr>
<th>Non-Muscle Invasive</th>
<th>Neoadjuvant Adjuvant</th>
<th>1st Line Metastatic</th>
<th>Next Line Metastatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>No systemic therapy</td>
<td>BCG</td>
<td>Gem + Cisplatin or A-MVAC (Cisplatin)</td>
<td>Gem + Cisplatin A-MVAC (Cisplatin) or Gem + Carbo</td>
</tr>
<tr>
<td></td>
<td>Gem + Cisplatin or A-MVAC (Cisplatin)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gem + Cisplatin or A-MVAC (Cisplatin)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gem + Cisplatin or A-MVAC (Cisplatin)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Cisplatin:**
- ORR: 50-60%
- Median OS: 15 mo.
- 1 year OS: 60%

**Carboplatin:**
- ORR: 36%
- Median OS: 9 mo.
- 1 year OS: 37%

**Next Line Metastatic:**
- Paclitaxel/Docetaxel
- Pemetrexed
- Vinflunin (ex-US)
- ORR: 12%
- Median OS: 7 mo.
- 1 year OS: 26%*

Evolution of Systemic Therapy for Urothelial Cancer

- **1997**: Standard MVAC
- **1999**: Gemcitabine + Cisplatin
- **2001**: Accelerated MVAC
- **2003**: Paclitaxel
- **2005**: Docetaxel
- **2007**: Vinflunine
- **2011**: Atezolizumab
- **2013**: Durvalumab breakthrough therapy designation Feb 17, 2016
- **2015**: Pembrolizumab
- **2016-2017**: Nivolumab, Avelumab, Pembrolizumab

**Key Events:**
- **1978**: Cisplatin USFDA Approved
- **1989**: MVAC
- **2009**: Vinflunine USFDA Approved for post-platinum advanced UC February 2, 2017
- **2016**: Nivolumab Feb 2017
- **2017**: Pembrolizumab May 2017

**References:**

http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm
Metastatic Urothelial Carcinoma: Prognostic Factors

MSKCC Risk Factors:
1. Karnofsky PS <80%
2. Visceral Mets:
   - Lung
   - Liver
   - Bone

Key decision points:
Front line, second line, beyond

Bajorin, JCO, 1999
T cell targets for immunoregulatory antibody therapy

I Mellman et al. Nature 480, 480-489 (2011) doi:10.1038/nature10673
Current Immunotherapy Targets

Lymph Node Microenvironment

- CTLA-4 Blockade (ipilimumab)

Tumor Microenvironment

- PD-1 Blockade (nivolumab)

Activation (cytokines, lysis, proliferation, migration to tumor)

Adapted from Wolchok, J. 2013 ASCO Annual Meeting.
# FDA-approved second-line ICIs

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

IMvigor210
Phase 2
Cohort 1: CIS ineligible (119)
Cohort 2: 2\textsuperscript{nd} Line (310)

GU-123
Phase 1b/2
2\textsuperscript{nd} Line NMIBC (70)

IMvigor130
Phase 3
1\textsuperscript{st} Line (1200)

IMvigor211
Phase 3
2\textsuperscript{nd} Line (931)

IMvigor010
Phase 3
Adjuvant MIBC (900)

PCD4989G
Phase 1
2\textsuperscript{nd} Line
IMvigor210: Phase 2 (Cohort 2), 2nd Line metastatic

**Figure D**: Intention-to-treat population (n=310)

<table>
<thead>
<tr>
<th>Group</th>
<th>Number at Risk</th>
<th>Median Overall Survival, months (95% CI)</th>
<th>12-month Overall Survival, % of patients (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IC2/3</td>
<td>100</td>
<td>11.4 (9.0-not estimable)</td>
<td>48% (38-58)</td>
</tr>
<tr>
<td>IC1</td>
<td>107</td>
<td>6.7 (5.1-8.8)</td>
<td>30% (20-39)</td>
</tr>
<tr>
<td>IC0</td>
<td>103</td>
<td>6.5 (4.4-8.3)</td>
<td>29% (20-39)</td>
</tr>
</tbody>
</table>

Rosenberg et al. Lancet 2016
IMvigor210: Phase 2 (Cohort 1)
1st Line metastatic, cisplatin ineligible

Balar AV et al. Lancet 2017
IMvigor211: Phase 3, 2nd Line metastatic

Overall ITT

<table>
<thead>
<tr>
<th></th>
<th>Events/Patients</th>
<th>Median OS (95% CI)</th>
<th>12-mo OS Rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atezolizumab</td>
<td>324/467</td>
<td>8.6 mo (7.8, 9.6)</td>
<td>39% (35, 44)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>350/464</td>
<td>8.0 mo (7.2, 8.6)</td>
<td>32% (28, 37)</td>
</tr>
</tbody>
</table>

IC2/3 (Primary endpoint)

<table>
<thead>
<tr>
<th></th>
<th>Events/Patients</th>
<th>Median OS (95% CI)</th>
<th>12-mo OS Rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atezolizumab</td>
<td>72/116</td>
<td>11.1 mo (8.8, 15.5)</td>
<td>46% (37, 56)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>88/118</td>
<td>10.6 mo (8.4, 12.2)</td>
<td>41% (32, 50)</td>
</tr>
</tbody>
</table>

Powles et al. EACR/AACR/SIC conference 2017
Pembrolizumab development

KEYNOTE-012
Phase 1b
2nd Line (33)

KEYNOTE-143
Phase 2
2nd Line (75)

KEYNOTE-057
Phase 2
2nd Line, NMIBC (260)

KEYNOTE-052
Phase 2
1st Line, CIS ineligible (350)

KEYNOTE-361
Phase 3
1st Line, with chemo (990)

KEYNOTE-045
Phase 3
2nd Line (542)
KEYNOTE-045: Phase 3, 2nd Line metastatic

Pembrolizumab as Second-Line Therapy for Advanced Urothelial Carcinoma


A Overall Survival

Hazard ratio for death, 0.73 (95% CI, 0.59–0.91)
P=0.002

B Progression-free Survival

Hazard ratio for disease progression or death, 0.98 (95% CI, 0.81–1.19)
P=0.42

Bellmunt et al. NEJM 2017
Durable Responses to Immunotherapy

72% ongoing response

35% ongoing response

Bellmunt et al. NEJM 2017
Who benefits the most from Pembrolizumab?

- No differences based on age, gender, functional status, histologic subtype
- Relatively greater benefits seen in current smokers, upper tract tumors, high PD-L1 expression, and node only disease

Bellmunt et al. NEJM 2017
# Adverse Effects of Pembrolizumab

Bellmunt et al. NEJM 2017

<table>
<thead>
<tr>
<th>Event</th>
<th>Pembrolizumab Group (N = 266)</th>
<th>Chemotherapy Group (N = 255)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any event</td>
<td>Any Grade</td>
<td>Grade 3, 4, or 5</td>
</tr>
<tr>
<td>Treatment-related event†</td>
<td>162 (60.9)</td>
<td>40 (15.0)</td>
</tr>
<tr>
<td>Event leading to discontinuation of treatment</td>
<td>15 (5.6)</td>
<td>12 (4.5)</td>
</tr>
<tr>
<td>Event leading to death</td>
<td>4 (1.5)</td>
<td>4 (1.5)</td>
</tr>
<tr>
<td>Event occurring in ≥10% of patients in either group‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pruritus</td>
<td>52 (19.5)</td>
<td>0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>37 (13.9)</td>
<td>3 (1.1)</td>
</tr>
<tr>
<td>Nausea</td>
<td>29 (10.9)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>24 (9.0)</td>
<td>3 (1.1)</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>23 (8.6)</td>
<td>0</td>
</tr>
<tr>
<td>Asthenia</td>
<td>15 (5.6)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Anemia</td>
<td>9 (3.4)</td>
<td>2 (0.8)</td>
</tr>
<tr>
<td>Constipation</td>
<td>6 (2.3)</td>
<td>0</td>
</tr>
<tr>
<td>Peripheral sensory neuropathy</td>
<td>2 (0.8)</td>
<td>0</td>
</tr>
<tr>
<td>Neutrophil count decreased</td>
<td>1 (0.4)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>1 (0.4)</td>
<td>0</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Alopecia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Event of interest§</td>
<td>Any event</td>
<td>45 (16.9)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>17 (6.4)</td>
<td>0</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>10 (3.8)</td>
<td>0</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>11 (4.1)</td>
<td>6 (2.3)</td>
</tr>
<tr>
<td>Colitis</td>
<td>6 (2.3)</td>
<td>3 (1.1)</td>
</tr>
<tr>
<td>Infusion reaction</td>
<td>2 (0.8)</td>
<td>0</td>
</tr>
<tr>
<td>Nephritis</td>
<td>2 (0.8)</td>
<td>2 (0.8)</td>
</tr>
<tr>
<td>Severe skin reaction</td>
<td>2 (0.8)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Thyroiditis</td>
<td>2 (0.8)</td>
<td>0</td>
</tr>
<tr>
<td>Adrenal insufficiency</td>
<td>1 (0.4)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Myositis</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
First Line Pembrolizumab

Objective responses in:

24% including CR in 5%

47% in node only 23% in patients with visceral mets

38% if PD-L1+ (10%)

Keynote 052: Balar AV et al Lancet Oncol 2017
Nivolumab development

CHECKMATE-032
Phase 1/2
2nd Line (86)

CHECKMATE-275
Phase 2
2nd Line (386)
Avelumab development

**JAVELIN**: Phase 1b, 2nd Line metastatic

**A**

Median PFS: 11.6 weeks (95% CI, 6.1 to 17.4)
PFS rate at 48 weeks: 19.1% (95% CI, 8.5 to 32.8)

**B**

Median OS: 13.7 months (95% CI, 8.5 to ne)
OS rate at 12 months: 54.3% (95% CI, 37.9 to 68.1)

**JAVELIN**

Phase 1b

2nd Line (44)

*Apolo et al. J Clin Oncol 2017*
Avelumab Phase 2

ORR 17% (n=161 post-platinum), 6% CR’s
PFS higher in PD-L1 high patients (11.9 vs 6.1 months)
OS slightly higher (8.2 vs. 6.2 mo) in PD-L1 high patients

Patel MR et al
Lancet Oncol 2017
Update (n=191):
ORR 18%, 28% if PD-L1 high, PFS of 1.5 mo, OS 18.2 mo
Powles T et al JAMA Oncol 2017
**Therapeutic response: PD-L1 and PD-1**

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventana PD-L1</td>
<td>Atezolizumab (bladder, NSCLC)</td>
</tr>
<tr>
<td>(SP142)</td>
<td>11/2016</td>
</tr>
<tr>
<td>Ventana PD-L1</td>
<td>Nivolumab (NSCLC)</td>
</tr>
<tr>
<td>(SP263)</td>
<td>2017</td>
</tr>
<tr>
<td>Dako PD-L1</td>
<td>Nivolumab (NSCLC, melanoma)</td>
</tr>
<tr>
<td>(28-8)</td>
<td>1/2016</td>
</tr>
</tbody>
</table>

NCCN guidelines do not presently recommend PD-L1 testing given the lack of...
## Toxicities of ICIs


<table>
<thead>
<tr>
<th>Immune-related toxicities</th>
<th>No. trials</th>
<th>No. events</th>
<th>Incidence, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All grades</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colitis</td>
<td>16</td>
<td>206/5,442</td>
<td>2.3 (1.3–3.9)</td>
</tr>
<tr>
<td>AST</td>
<td>14</td>
<td>330/3,855</td>
<td>6.5 (3.3–12.4)</td>
</tr>
<tr>
<td>Rash</td>
<td>19</td>
<td>952/5,777</td>
<td>13.9 (10.6–18.0)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>15</td>
<td>244/4,622</td>
<td>5.1 (3.8–6.8)</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>15</td>
<td>119/4,599</td>
<td>2.6 (2.0–3.7)</td>
</tr>
<tr>
<td>High grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colitis</td>
<td>16</td>
<td>119/5,442</td>
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<tr>
<td>AST</td>
<td>14</td>
<td>94/3,855</td>
<td>1.5 (0.7–3.4)</td>
</tr>
<tr>
<td>Rash</td>
<td>18</td>
<td>50/5,299</td>
<td>1.1 (0.7–1.7)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>14</td>
<td>5/4,144</td>
<td>0.3 (0.2–0.5)</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>15</td>
<td>42/4,599</td>
<td>1.1 (0.7–1.7)</td>
</tr>
</tbody>
</table>
## NCCN Guidelines 2018

### PRINCIPLES OF SYSTEMIC THERAPY

**Subsequent systemic therapy for locally advanced or metastatic disease (Stage IV) (post-platinum)**

Participation in clinical trials of new agents is recommended.

<table>
<thead>
<tr>
<th>Preferred regimen</th>
<th>Other recommended regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pembrolizumab (category 1)</td>
<td>Nab-paclitaxel</td>
</tr>
<tr>
<td></td>
<td>Paclitaxel or docetaxel</td>
</tr>
<tr>
<td></td>
<td>Gemcitabine</td>
</tr>
<tr>
<td></td>
<td>Pemetrexed</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Alternative preferred regimens</th>
<th>Useful in certain circumstances based on prior medical therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atezolizumab</td>
<td>Ifosfamide</td>
</tr>
<tr>
<td>Nivolumab</td>
<td>Methotrexate</td>
</tr>
<tr>
<td>Durvalumab</td>
<td>Ifosfamide, doxorubicin, and gemcitabine</td>
</tr>
<tr>
<td>Avelumab</td>
<td>Gemcitabine and paclitaxel</td>
</tr>
<tr>
<td></td>
<td>Gemcitabine and cisplatin</td>
</tr>
<tr>
<td></td>
<td>DDMVAC with growth factor support</td>
</tr>
</tbody>
</table>

**Subsequent systemic therapy for locally advanced or metastatic disease (Stage IV) (post-checkpoint inhibitor)**

Participation in clinical trials of new agents is recommended.

<table>
<thead>
<tr>
<th>Preferred regimen for cisplatin ineligible, chemotherapy naïve</th>
<th>Other recommended regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemcitabine/carboplatin</td>
<td>Nab-paclitaxel</td>
</tr>
<tr>
<td></td>
<td>Paclitaxel or docetaxel</td>
</tr>
<tr>
<td></td>
<td>Gemcitabine</td>
</tr>
<tr>
<td></td>
<td>Pemetrexed</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Preferred regimens for cisplatin eligible, chemotherapy naïve</th>
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</thead>
<tbody>
<tr>
<td>Gemcitabine and cisplatin</td>
<td>Ifosfamide</td>
</tr>
<tr>
<td>DDMVAC with growth factor support</td>
<td>Methotrexate</td>
</tr>
<tr>
<td></td>
<td>Ifosfamide, doxorubicin, and gemcitabine</td>
</tr>
<tr>
<td></td>
<td>Gemcitabine and paclitaxel</td>
</tr>
</tbody>
</table>
Overall Response Rates: Post-Platinum

Historical Control w Chemo ~ 12%

- Atezolizumab Phase II
  - n=310
- Atezolizumab
  - n=87
- Avelumab
  - n=44
- Durvalumab
  - n=42
- Nivolumab
  - n=78
- Pembrolizumab
  - n=29

Phase I Basket Studies:
- Dreicer ASCO 2016
- Petrylak ASCO 2015
- Apolo GUASCO 2016
- Massard ASCO 2016
- Sharma ASCO 2016
- Plimack ASCO 2015

Plimack ER, ASCO 2016
12 month OS: Post Platinum

- **Atezolizumab Phase II**
  - n=310
  - Dreicer ASCO 2016

- **Atezolizumab**
  - n=87
  - Petrylak ASCO 2015

- **Avelumab**
  - n=44
  - Apolo GUASCO 2016

- **Durvalumab**
  - n=42
  - Massard ASCO 2016

- **Nivolumab**
  - n=78
  - Sharma ASCO 2016

- **Pembrolizumab**
  - n=29
  - Plimack ASCO 2015

Historical Control w Chemo ~ 26%

Plimack ER, ASCO 2016
Frontline Therapy for UC: Cis-Ineligible

**Gem Carbo**

Randomized Phase II/III Trial Assessing Gemcitabine/Carboplatin and Methotrexate/Carboplatin/Vinblastine in Patients With Advanced Urothelial Cancer Who Are Unfit for Cisplatin-Based Chemotherapy: EORTC Study 30986

**Atezolizumab**

<table>
<thead>
<tr>
<th>Cisplatin ineligibility criteria</th>
<th>N = 119</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal impairment</td>
<td>70%</td>
</tr>
<tr>
<td>GFR &lt; 60 mL/min but &gt; 30</td>
<td></td>
</tr>
<tr>
<td>Hearing loss, 25 dB*</td>
<td>14%</td>
</tr>
<tr>
<td>Peripheral neuropathy, ≥ Grade 2</td>
<td>6%</td>
</tr>
<tr>
<td>ECOG PS2</td>
<td>20%</td>
</tr>
<tr>
<td>Renal impairment and ECOG PS2</td>
<td>7%</td>
</tr>
</tbody>
</table>

**Balar A, et al. IMvigor210: 1L atezolizumab in cisplatin-ineligible mUC. ASCO 2016**
Future development of PD1 inhibitors in UC

1st line
- Non-muscle-invasive bladder cancer
  - Low grade
    - Pembrolizumab + BCG
  - High grade
    - Pembrolizumab + BCG
    - Atezolizumab Pembro + Chemo
- Neoadjuvant
  - Atezolizumab
  - Pembrolizumab
- Adjuvant
  - Atezolizumab Ph III
  - Nivolumab Ph III
- Cisplatin-eligible
  - Durvalumab + Tremelimumab (Ph III)
- Cisplatin-ineligible
  - Pembrolizumab

2nd line and beyond
- Muscle-invasive bladder cancer
  - Trimodality
    - Pembrolizumab + RT
  - Maintenance
    - Avelumab (Ph III)
      - Pembrolizumab
      - Platinum-refractory
        - Pembrolizumab (Ph III vs chemo)
        - Atezolizumab (Ph III vs chemo)

- Metastatic urothelial cancer
  - Platinum +/- pembro (Ph III)
  - Pembrolizumab
Microbiome and IC

- Recent data support a direct mechanistic role of the gut microbiome in mediating immune tone in distant sites (tumors)
- “Good bacteria” can mediate tumor rejection reversible with antibiotics
- Associated with greater T cell infiltration
- Duke is studying the role of the microbiome during IC therapy in RCC and TCC patients
- Suggests role for prebiotics for these specific bacteria such as Akkermansia muciniphila, a gram negative anaerobic bacteria which is enriched in responding patients and these responses are fecally transferable

Routy B et al Science 2017
Key Takeaways

- PD-1 and PD-L1 inhibitors are all active in metastatic UC
- Only Pembrolizumab has level 1 survival evidence
- In platinum ineligible patients, tolerability and durability of responses suggest reasonable alternatives to chemotherapy, many options to choose from
- Given lower response rates than chemotherapy, at this time single agent pembrolizumab is probably best in the 2nd line setting
- Currently being evaluated in all stages of disease and in combinations with chemotherapy
- Relatively well tolerated
- Biomarker enrichment possible but not sufficient for clinical use at this time
- No head-to-head comparisons