Advances in Systemic Treatment of Bladder Cancer

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The Ottawa Hospital Cancer Centre
Cancer Treatment Across Eastern Ontario
TOHCC Research Network

Clinical Trials Program
New Drug (IND) Program

65 Oncologists
(23 Med, 20 Rad, 17 Surg, 5 Gyne)
1 Medical Director Clinical Research
1 Clinical Research Program Manager
1 Quality Supervisor
20 Study Coordinators
5 Start Up Specialists
6 Data Managers
1 Research Pharmacist
4 Pharmacy Research Technicians
1 Pharmacology Supervisor
3.5 Pharmacology Nurses
2 Laboratory Technicians

Site Chair
7 Investigators
2 Start Up Specialists
3 Study Coordinators
2 Data Managers
“Conventional” Cancer Treatments

- RADIATION
- SURGERY
- CHEMOTHERAPY
- TARGETED DRUG THERAPIES
10-years ago, bladder cancer research at a total standstill...
New Cancer Targets

Fibroblast Growth Factor

Immune Therapy

Nectin-4 ADC

Adapted from Hanahan and Weinberg, Cell 2011
Dr. James P. Allison

Dr. Takusu Honjo
Cancer Therapy by Inhibition of Negative Immune Regulation (CTLA4, PD1)
Metastatic Melanoma - FDG-PET images

October 2014

Anti-CTLA4
Anti-PD1

June 2015
Immunotherapy for Car Drivers

- PD-1
- CTLA-4
- Clutch
- Brake
- IL-2
- IFN-a
- Vaccines

Tumor Mutations?
Microenvironment?
Other “Checkpoints”?
More Cancer Mutations
= More “Foreign” to Immune System

Mean somatic mutation rate 8.2/Mb
(Median 5.8)

Linghua Wang, BCM 4/16
This study resulted in FDA approval of this immunotherapy!
## Options for Immunotherapy

### Bladder Cancer

#### NCCN Guidelines Version 5.2018

<table>
<thead>
<tr>
<th>Not Cisplatin Eligible</th>
<th>After Platinum Chemotherapy</th>
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<tr>
<td><strong>Preferred regimen</strong></td>
<td></td>
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<tr>
<td>• Pembrolizumab</td>
<td>• Pembrolizumab (category 1)&lt;sup&gt;18&lt;/sup&gt;</td>
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<tr>
<td>• Atezolizumab&lt;sup&gt;19&lt;/sup&gt;</td>
<td>• Atezolizumab&lt;sup&gt;19&lt;/sup&gt;</td>
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<tr>
<td>• Gemcitabine and carboplatin&lt;sup&gt;11&lt;/sup&gt;</td>
<td>• Nivolumab&lt;sup&gt;20&lt;/sup&gt;</td>
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**Alternative preferred regimens**

- • Durvalumab<sup>21</sup>
- • Avelumab<sup>22,23</sup>
Immunotherapy Use at The Ottawa Hospital

- Clinical Trial
- Standard Treatment

# Immunotherapy Infusions / Month

Year

- Lung CA
- Melanoma
- Genitourinary
- Gastrointestinal
- Head and Neck
- Breast
- Hematology
Does Immunotherapy have Side Effects?

- Encephalitis, aseptic meningitis
- Hypophysitis
- Uveitis
- Thyroiditis, hypothyroidism, hyperthyroidism
- Dry mouth, mucositis
- Pneumonitis
- Rash, vitiligo
- Thrombocytopenia, anemia
- Myocarditis
- Hepatitis
- Adrenal insufficiency
- Pancreatitis, autoimmune diabetes
- Nephritis
- Colitis
- Vasculitis
- Enteritis
- Arthralgia
- Neuropathy
Chemotherapy can be very effective

POUT Trial Results: Chemotherapy lowers chance of recurrence after surgery in upper-tract urothelial cancer by 51%!
Bladder Cancer Trials

Pembrolizumab
Atezolizumab
Durvalumab
+ many others

Rogaratinib
Erdafitinib

Enforumab
Vedotin

Ramucirumab
Enfortumab vedotin
(Antibody-Drug Conjugate)
Fibroblast Growth Factor Receptor Inhibitors (Rogaratinib, Erdafitinib)
Opportunities to test new treatments

Before Surgery

After Surgery

At recurrence

During Radiation