Opportunities in Cancer Immunotherapy

James H. Doroshow
March 9, 2016
Agenda

- Inventory of NCI-funded immunotherapy projects and trials
  - Jim Doroshow

- Summary of the DCTD Cancer Immunotherapy Workshop
  - Helen Chen

- Discussion of opportunities in immunotherapy
  - CTAC Members with NCI panel (Jim Doroshow, Jeff Abrams, Helen Chen, Toby Hecht and Magdalena Thurin)
Rationale:

- Precision Medicine Initiative (PMI) - Oncology - 4 parts
  - NCI-supported clinical trials to advance precision oncology
    - Advanced sequencing for NCI-MATCH
    - Pediatric MATCH
    - Expand immunotherapy trials—combinations, molecular characterization, reagents
  - Develop better pre-clinical models for cancer treatment
  - Overcome therapeutic resistance in the clinic
  - Knowledge system for precision oncology
Inventory of NCI Funding for Cancer Immunology and Immunotherapy in Fiscal 2014

Definition of “Immunotherapy” used in this inventory –

• Agents with the primary MOA mediated through modulation of cancer immunity and effected through the immune system/cells (e.g. cytokines, check point inhibitors, vaccines, adoptive cell therapy)

• Antibodies or agents directed at tumor cell targets/angiogenesis, with the primary MOA uncertain, or mediated through signal transduction or cytotoxic payload were NOT included in this analysis (e.g. bevacizumab, trastuzumab, immunotoxin, radioimmunotherapy)
### NCI Extramural Funding for Immunotherapy –
A preliminary inventory of projects funded in FY 2014 (1)

#### Single-project grants (# of grants)

<table>
<thead>
<tr>
<th>Division</th>
<th>Description</th>
<th>All grants¹, ², ³</th>
<th>Grants related to Immunotherapy</th>
<th>% for immunotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCB (Division of Cancer Biology)</td>
<td>Mostly basic science</td>
<td>1894</td>
<td>114</td>
<td>6%</td>
</tr>
<tr>
<td>DCTD (Division of Cancer Treatment and Diagnosis)</td>
<td>Translational and clinical</td>
<td>1486</td>
<td>196</td>
<td>13%</td>
</tr>
<tr>
<td>SBIR (Small Business Innovation Research Program)</td>
<td></td>
<td>171</td>
<td>20</td>
<td>12%</td>
</tr>
<tr>
<td>CCT (Center for Cancer Training)</td>
<td>Training and Career Development Awards</td>
<td>977</td>
<td>79</td>
<td>8%</td>
</tr>
<tr>
<td>DCP (Division of Cancer Prevention)</td>
<td></td>
<td>391</td>
<td>4</td>
<td>1%</td>
</tr>
</tbody>
</table>

¹. Not included in this Table: Type 3’s
². Not included in this table – Multi-project grants - P01, P20, P30, P50, U19, U54, U10, UG1, UM1
³. Primary IC=CA
## NCI Extramural Funding for Immunotherapy –
A preliminary list of projects funded in FY 2014 (2)

### Multi-project grants or funding mechanisms

<table>
<thead>
<tr>
<th></th>
<th>All grants/subprojects</th>
<th>Immunotherapy</th>
<th>% for ImmunoRx</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SPORE (P50)</strong></td>
<td>52 grants</td>
<td>26 with ImmunoRx</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>209 subprojects</td>
<td>49 for ImmunoRx</td>
<td>23%</td>
</tr>
<tr>
<td><strong>Program Grant (P01)</strong></td>
<td>109 grants</td>
<td>24 with ImmunoRx</td>
<td>22%</td>
</tr>
<tr>
<td></td>
<td>708 subprojects</td>
<td>66 with ImmunoRx</td>
<td>9%</td>
</tr>
</tbody>
</table>
| **CTEP Clinical Trial Network**
New trials opened in 2014-2015 | 170 Trials (Phase 3: 47 trials) | 37 for ImmunoRx (Phase 3: 7 trials) | 22% (15%) |

*SPORE grants are based on FY 2015*
# Immunotherapy Trials in CTEP Clinical Trial Networks

## CTEP Clinical trial network:
- NCTN (Cooperative Groups)
- ETCTN (Early clinical trials)
- Cancer Immunotherapy Trials Network,
- Disease specific consortia (ABTC, PBTC)

<table>
<thead>
<tr>
<th></th>
<th>Any</th>
<th>ImmunoRx</th>
<th>% of ImmunoRx</th>
</tr>
</thead>
<tbody>
<tr>
<td>All CTEP trials</td>
<td># of clinical trials</td>
<td>11078</td>
<td>1274</td>
</tr>
<tr>
<td>(Phase 3)</td>
<td></td>
<td>(2137)</td>
<td>(128)</td>
</tr>
<tr>
<td>Before 2000</td>
<td># of clinical trials</td>
<td>8092</td>
<td>1002</td>
</tr>
<tr>
<td>(Phase 3)</td>
<td></td>
<td>(1670)</td>
<td>(111)</td>
</tr>
<tr>
<td>Activated between 2000-2009</td>
<td># of clinical trials</td>
<td>2260</td>
<td>184</td>
</tr>
<tr>
<td>(Phase 3)</td>
<td></td>
<td>(344)</td>
<td>(10)</td>
</tr>
<tr>
<td>Activated between 2010-2013</td>
<td># of clinical trials</td>
<td>556</td>
<td>51</td>
</tr>
<tr>
<td>(Phase 3)</td>
<td></td>
<td>(76)</td>
<td>(2)</td>
</tr>
<tr>
<td>Activated between 2014-2015</td>
<td># of clinical trials</td>
<td>170</td>
<td>37</td>
</tr>
<tr>
<td>(Phase 3)</td>
<td></td>
<td>(47)</td>
<td>(7)</td>
</tr>
<tr>
<td>In review</td>
<td># of clinical trials</td>
<td>63</td>
<td>11</td>
</tr>
<tr>
<td>(Phase 3)</td>
<td></td>
<td>(8)</td>
<td>(2)</td>
</tr>
</tbody>
</table>

*Trials without therapeutic interventions are excluded from the analysis*
Immunotherapy agents under CRADA agreement with CTEP
(a partial list)

**Check point inhibitors**
- Anti-CTLA-4 (Ipilimumab)
- Anti-PD-1 Nivolumab, Anti-PD-1 Pembrolizumab
- Anti-PD-L1 (MEDI4736 and MPDL3280A)

**Cytokine:**
- IL-15
- IL-12
- Others:

**T-cell engaging bispecific antibody**
- CD19 BiTE (Blinatumomab)

**Vaccine**
- CDX1401 (against NYSO-1)
- PSA PROSTVAC/TRICOM
- CEA TRICOM/PANVAC
- Other: peptide (gp100, HPV, RAS, P53, MART and others)

**Other immune modulators:**
- IDO (INDB0243360) ~ 2 trials
- Lenalidomide, Pomalidomide: - not counted in the analysis
- FLT3 ligands
- Anti-CD27 mAb (CellDex)

---

Types of trials sponsored by CTEP:
- Rare indications
- Special populations (Pediatric, HIV)
- Novel combinations
- Phase III and registration trials
- Biomarkers as the primary endpoints
Questions for CTAC

- What is limiting further success of cancer immunotherapy in the clinic?
  - Biology? Models? Biomarkers/Assays?

- What specific resources are lacking in the scientific community that contribute to these limitations? Are there critical scientific questions that are not being addressed or are not being supported sufficiently by industry or NCI?

- What specific initiatives should NCI support or create to accelerate the further success of immunotherapy?