

Opportunities in Cancer Immunotherapy

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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)

PMI – Oncology includes Immunotherapy

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)

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

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

	All grants/subprojects	Immunotherapy	% for ImmunoRx
SPORE (P50)*	52 grants	26 with ImmunoRx	50%
	209 subprojects	49 for ImmunoRx	23%
Program Grant (P01)	109 grants	24 with ImmunoRx	22%
	708 subprojects	66 with ImmunoRx	9%
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)
 - Cancer Immunotherapy Trials Network,
 - ETCTN (Early clinical trials)
 - Disease specific consortia (ABTC, PBTC)

		Any	ImmunoRx	% of ImmunoRx
All CTEP trials	# of clinical trials	11078	1274	12%
	(Phase 3)	(2137)	(128)	(6%)
<u>Before 2000</u>	# of clinical trials	8092	1002	12%
	(Phase 3)	(1670)	(111)	(6%)
Activated between <u>2000-2009</u>	# of clinical trials	2260	184	8%
	(Phase 3)	(344)	(10)	(3%)
Activated between <u>2010-2013</u>	# of clinical trials	556	51	9%
	(Phase 3)	(76)	(2)	(3%)
Activated between <u>2014- 2015</u>	# of clinical trials	170	37	22%
	(Phase 3)	(47)	(7)	(15%)
In review	# of clinical trials	63	11	
	(Phase 3)	(8)	(2)	

*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?