

Precision Medicine for Oncology: Current Scope & Future Opportunities

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Precision Medicine Initiative


FY16 Support

Agency	\$ Million
NIH	200
• <i>Cancer</i>	70
• <i>Cohort</i>	130
FDA	10
Office of the National Coordinator for Health Information Technology	5
TOTAL	\$215

Precision Medicine Initiative: Oncology

Goal: Increase Genomics-Based Clinical and Preclinical Studies of Cancer Treatment

1. Expand genomics-based clinical trials of targeted agents and immunotherapy
2. Understand & overcome resistance to targeted drugs, drug combinations, and immunotherapy
3. Improve pre-clinical models for evaluating targeted therapeutics and immunotherapy
4. Create national cancer database to integrate genomic information with clinical response and outcome



NCI-MATCH trial (Molecular Analysis for Therapy Choice)

- Foundational treatment/discovery trial that forms a platform for future PMI oncology clinical trials
- Assigns therapy based on molecular abnormalities, not site of tumor origin, for patients without available standard therapy
- Regulatory umbrella for 24 phase II efficacy studies using 24 drugs from > 20 companies (May 2016); as single agents or combinations
- Greatly increases the proportion of patients who can receive experimental treatment because open nationwide (2400 sites)
- Fastest accruing clinical trial in history of NCI (800 patients in 3 months!)

Precision Medicine Initiative for Oncology:

1. Increase genomics-based clinical trials of targeted agents and immunotherapy

A). Expanded the NCI-MATCH umbrella: new trials, new agents, and combinations to confirm initial 'hits' across the 'long tail' of low prevalence mutations:

- ✓ Increased accrual from 3000 to 5000 patients to attain a 20-25% estimated 'MATCH' rate
- ✓ Resourced WES, RNA seq, copy # determinations for all pts treated on NCI-MATCH
- ✓ Funded Pediatric-MATCH accrual, tissue acquisition, and sequencing

Precision Medicine Initiative for Oncology:

1. Increase genomics-based clinical trials of targeted agents and immunotherapy

B). Expanded support for molecular characterization of immunotherapy trials (input from 2 NCI workshops):

- ✓ “Administrative supplements (for CCSG, P50, and U01/U10 grantees) to support biomarker development and correlative studies associated with clinical trials of immunotherapy”—issued April 15, 2016
- ✓ “Administrative supplements (for CCSG, P50, or P01 grantees) to support studies of how the microenvironment of pancreatic ductal adenocarcinoma affects immunotherapy”—issued April 26, 2016
- ✓ STAY TUNED
- ✓ NCI Virtual Drug Formulary

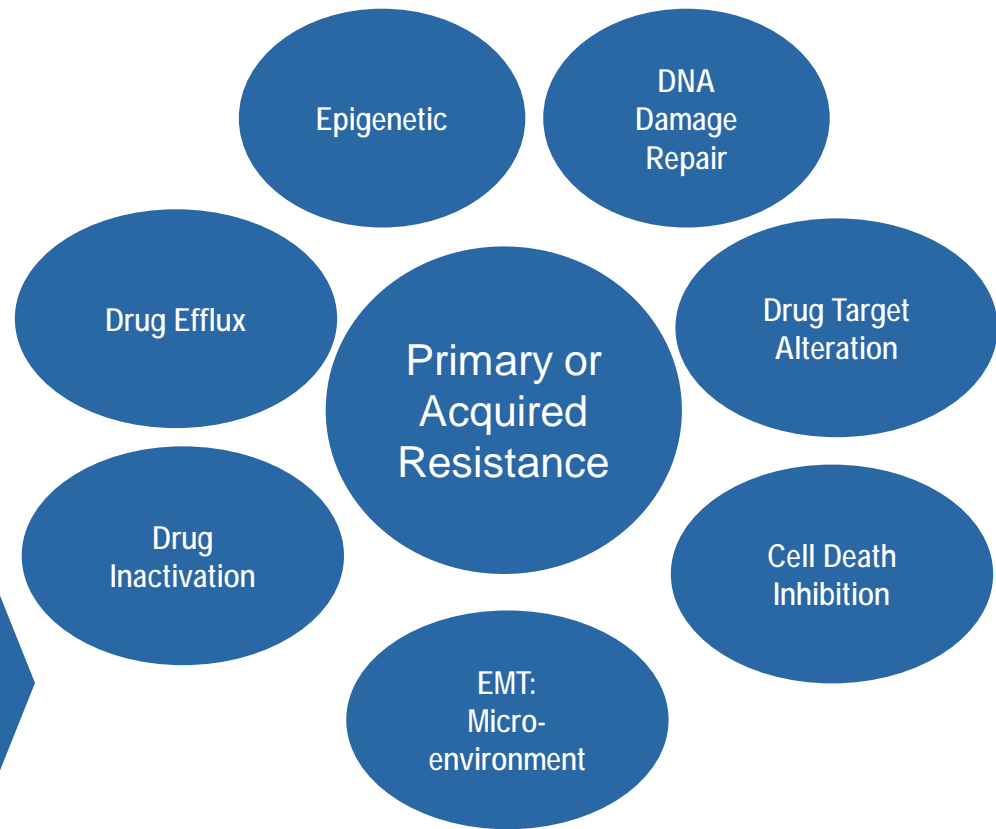
NCI Virtual Drug Formulary

- Access to investigational drugs for investigator initiated studies is difficult and time consuming, often the cost-benefit of negotiating an agreement with a Pharmaceutical Collaborator is prohibitive or so difficult and time consuming that the study is never initiated.
- This process is especially burdensome for multi-agent combinatorial studies, and more burdensome still when one or both of those agents are investigational and proprietary to different collaborators.
- Major roadblock to precision medicine clinical trials

NCI Virtual Drug Formulary: Proposal

- Create a system within the NCI that leverages our existing mechanisms to provide Collaborator Investigational agent for investigator held INDs
- The program will have the following characteristics:
 - ✓ Easy to access with a “menu” of agents to choose from
 - ✓ Quick and simple process that ensures rapid turn around times
 - ✓ Utilizes pre-existing agreements/infrastructure that current Pharmaceutical Collaborators are already familiar with
- Agents will be provided for both clinical and pre-clinical studies (although perhaps by different mechanisms)
- INDs will be held by investigators/institutions, not CTEP
- Large base of agents for investigators to access
- Agreement terms will be standardized or pre-approved in such a way as to substantially decrease the transactional costs of study initiation: mtg ASCO

Mechanisms of Resistance To Targeted Cancer Therapeutics



- Broad range of mechanisms
- Until recently, tools to interrogate possibilities in vivo quite limited
- Resistance to single agents inevitable: 1^o or acquired; requires combinations but data to provide in vivo molecular rationale for the combination (both therapy & toxicity) not often available

Precision Medicine Initiative for Oncology:

2. Understand & overcome resistance to targeted drugs, drug combinations, and immunotherapy

Employ clinical materials from drug resistant patients and exceptional responders for molecular analysis, leading to rational studies of targeted combinations

- ✓ Create a repository of molecularly analyzed samples of resistant disease and expand the use of tumor profiling methods such as circulating tumor cells (CTCs) and fragments of tumor DNA in blood to understand and monitor disease progression
- ✓ Evaluate mechanisms of resistance and sensitivity in patients enrolled on clinical trials of targeted agents and immunotherapy
- ✓ STAY TUNED

Precision Medicine Initiative for Oncology:

3. Improve pre-clinical models for evaluating targeted therapeutics and immunotherapy

- ✓ Develop new cancer models to identify the heterogeneity of resistance mechanisms
- ✓ Use preclinical modeling to determine the effectiveness of new combinations of novel molecularly targeted investigational agents and immunotherapy
- ✓ "Administrative supplements (for CCSGs) to support research in canine immunotherapy via collaboration of NCI-designated Cancer Centers and Veterinary Medical Colleges"—issued April 12, 2016
- ✓ "Administrative supplements (for CCSGs, SPOREs, NCTN, and UM1 grantees) to support collaborative research efforts to enhance preclinical drug development and preclinical clinical trials utilizing patient derived xenograft (PDX) models"—issued May 2, 2016

Precision Medicine Initiative for Oncology:

4. Create national cancer database to integrate genomic information with clinical response and outcome

- ✓ Establish NCI's Genomic Data Commons (GDC) to facilitate the identification of subtypes of cancers and potential new drug targets
- ✓ Develop secure, flexible, meaningful, interoperable interfaces to provide for the analysis of large-scale cancer genomic and clinical data
- ✓ Establish a sustainable infrastructure for cancer genomic data to allow for the analysis of multiple data types, multi-scalar data, and temporal data

Questions?



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