

Targeted Agent and Profiling Utilization Registry

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Disclosure Information

Richard L. Schilsky, MD

- I have no financial relationships to disclose
- I will discuss off label use of various anti-cancer drugs in the context of a research study.

Problem

- Patient with advanced cancer; no standard Rx options
- Genomic profile test performed
- Potentially actionable variant detected
- How to get the drug?
- How to learn from the treatment?

Overall Goals of TAPUR

- To learn from the real world practice of prescribing targeted therapies to patients with advanced cancer whose tumor harbors a genomic variant known to be a drug target
- To educate oncologists about implementation of precision medicine in clinical practice

TAPUR Study Primary Objective

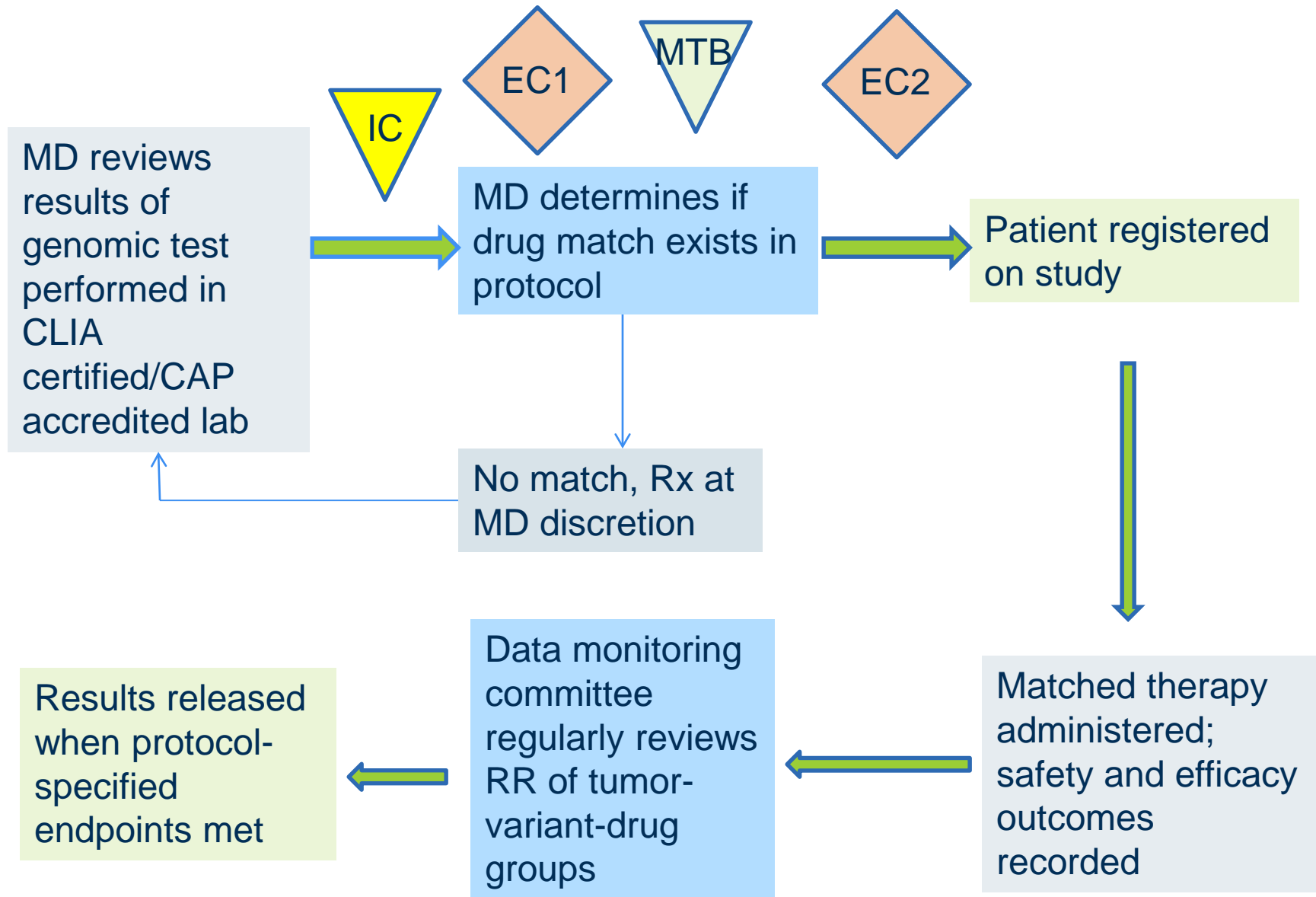
- To describe the anti-tumor activity and toxicity of commercially available, targeted anti-cancer drugs prescribed for treatment of patients with advanced solid tumors, B cell NHL or MM with a genomic variant known to be a drug target or to predict sensitivity to a drug.

Secondary Objectives

- To record the treatment-related adverse events.
- To create a prospective database of patient outcomes following treatment.
- To create a prospective database of commercially available tumor genome profiling tests used by clinical oncologists in the usual care setting.
- To determine the concordance of the treatment plan proposed by the treating oncologist with that recommended by the molecular tumor board in applicable situations.

TAPUR Eligibility

- Patients with advanced solid tumors, B cell NHL and multiple myeloma for whom no standard treatment options exist
- Adequate organ function; PS 0-2
- Results available from a genomic test (FISH, PCR, NGS, WES, IHC for gene expression) performed in a CLIA certified, CAP accredited lab. Labs located or offering services to residents of NY must also have NY State accreditation. Test should be registered with NIH Genetic Test Registry.



TAPUR Matching Rules

- Specific genomic inclusion and exclusion criteria included for each drug
- Matching at variant level if possible
- Automated rules engine approves/rejects match proposed by treating MD
- If no match proposed or match rejected, treating MD may consult TAPUR MTB
- MTB identifies TAPUR drugs or other options based on tumor genomics

Study Endpoints and Analysis

- Primary endpoint: ORR per standard response criteria or SD at 16 w
- Other endpoints: PFS, OS, time on treatment, grade 3-5 AEs per CTCAE, SAEs
- Each tumor type-gene-drug is a “group”
- Enroll 10 patients/group. If ≤ 1 response, stop
- If at least 2 responses, enroll additional 18
- 7 or more responses/28, further study
- 85% power to conclude activity if true RR is 35% and a Type 1 error rate of 10%

Participating Drug Companies

Newest additions:



Previously joined:



Targeted Agent and
Profiling Utilization
Registry Study



Drugs Available in TAPUR

Pharmaceutical Company (Number of Drugs)	Drug(s) Provided for TAPUR Study
AstraZeneca (1)	Olaparib
Bayer (1)	Regorafenib
Bristol-Meyers Squibb (1)	Dasatinib
Eli Lilly (1)	Cetuximab
Genentech (6), with support for Erlotinib from Astellas	Erlotinib, Trastuzumab + Pertuzumab, Vemurafenib + Cobimetinib, Vismodegib
Merck (1)	Pembrolizumab
Pfizer (6)	Axitinib, Bosutinib, Crizotinib, Palbociclib, Sunitinib, Temsirolimus

Supporting Vendors



- **Syapse Precision Medicine Software**
 - Electronic data collection platform & study workflows



- **Illumina NextBio**
 - Knowledge base provider



- **Cardinal Health Specialty Pharmacy**
 - Central drug distribution

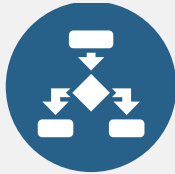
Syapse-TAPUR Platform Automates Study Workflows

syapse

MD reviews genomic test results & study eligibility criteria



Automatic check for drug-variant match in protocol



Yes

No

MD confirms eligibility criteria; enters pre-treatment data; ASCO approves Cohort



Ordering of targeted therapy



Response assessment & adverse event reporting



Query & data mining by ASCO, pharma partners



Knowledge base provider sends analysis to MTB



TAPUR MTB reviews knowledge base provider's recommendation

syapse

Treatment Proposal Form

Instructions: Complete this form to record the treating physician's proposed genomic variant-TAPUR study drug match for the patient. The treating physician should consult with Table 7-1 in the TAPUR protocol for acceptable genomic variant-TAPUR study drug matches. If the treating physician does not have a proposed genomic variant-TAPUR study drug match, this must also be recorded on this form prior to request of review by the Molecular Tumor Board.

A. Treatment Proposal

1. Does the treating physician have a treatment proposal for a study drug on TAPUR?...

Yes No

2. Which TAPUR study drug does the treating physician propose the patient receive?

- | | | |
|---|---|--|
| <input type="radio"/> Ado-trastuzumab emtansine (KADCYLA) | <input type="radio"/> Axitinib (INLYTA) | <input type="radio"/> Bosutinib (BOSULIF) |
| <input type="radio"/> Cetuximab (ERBITUX) | <input type="radio"/> Crizotinib (XALKORI) | <input type="radio"/> Dasatinib (SPRYCEL) |
| <input type="radio"/> Erlotinib (TARCEVA) | <input type="radio"/> Olaparib (LYNPARZA) | <input type="radio"/> Palbociclib (IBRANCE) |
| <input type="radio"/> Regorafenib (STIVARGA) | <input type="radio"/> Sunitinib (SUTENT) | <input type="radio"/> Temsirolimus (TORISEL) |
| <input type="radio"/> Vemurafenib (ZELBORAF) | <input type="radio"/> Vismodegib (ERIVEDGE) | |

* Note, the decision should be informed by the genomic profiling test results of the patient's tumor and review of Table 7-1 in the TAPUR protocol outlining acceptable genomic matches to TAPUR study drugs.

3. Please indicate the genomic variant identified to match the patient to the study medication selected above.

4. Do you plan to submit a request for review by the TAPUR Molecular Tumor Board?*

Yes No

* Note: If there is a pre-specified match defined in the protocol identified and confirmed with the automated matching rules engine in the Syapse-TAPIR application, Molecular Tumor Board review is not required.

Keep going 50%

A. Treatment Proposal

Signature

Adverse Event Reporting Form – AE Form

Instructions: Complete this form to record any TAPUR study participant adverse or serious adverse events. Only those events that occur starting with the Baseline Cycle 1 Day 1 Visit should be reported. A separate form is required for each event. All protocol-defined serious adverse events and CTCAE v4.0 Grade 3-5 adverse events that are possibly, probably or definitely related to the study drug, whether expected or not, must be recorded on this form. All deaths, regardless of attribution, must be documented on this form. Record the severity grade for each adverse event per the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE version 4.0). The criteria can be found at: <http://ctep.cancer.gov/reporting/ctc.html>. For previously reported ongoing or resolved events, complete a separate, new AE Follow-up Form. Do not update original form.

Serious adverse events must be reported to the ASCO TAPUR study team within 24 hours of the site learning of the event. Submission of this form will serve as notification to the study team. For any questions, contact the ASCO TAPUR study team or email TAPURSAE@asco.org.

Adverse events must also be reported by each participating site investigator, according to their local policy and procedures, to the Institutional Review Board (IRB) responsible for oversight of their participants.

A. Event Information

1. Date of event onset:*

 yyyy-mm-dd

2. Assessment of expectedness:*

Expected

Unexpected

3. Event description*

Note: Enter event term OR MedDRA code.

a. Event term using CTCAE v4.0 terminology or MedDRA v12.0 Code:

A. Event Information

B. Concomitant Drugs (drugs taken within 2 weeks before event onset)

C. Event Narrative

D. Confirmation of Review

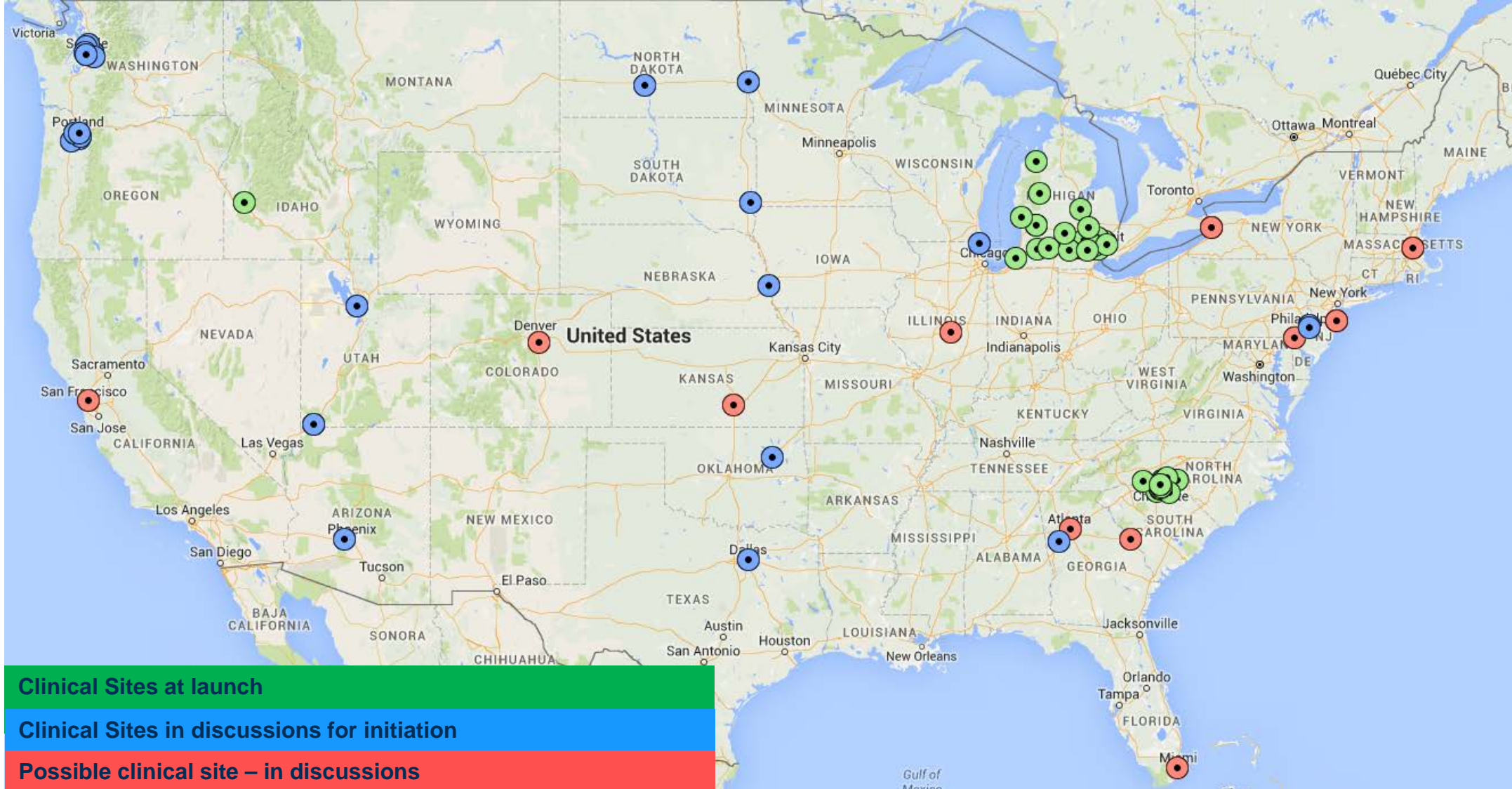
Comments

Signature

Clinical Sites at Study Launch

- **Cancer Research Consortium of West Michigan**
 - Site PI: Kathleen J. Yost, M.D.
 - Grand Rapids, MI; 9 participating sites in MI
- **Carolinas HealthCare System Levine Cancer Institute**
 - Site PI: Edward S. Kim, M.D.
 - Charlotte, NC; 13 participating sites in NC & SC
- **Michigan Cancer Research Consortium**
 - Site PI: Philip J. Stella, M.D.
 - Ann Arbor, MI; 11 participating sites in MI & ID
- **University of Michigan**
 - Site PI: Ajjai Alva, MBBS
 - Ann Arbor, MI; 1 participating center in MI

Clinical Site Expansion Plan



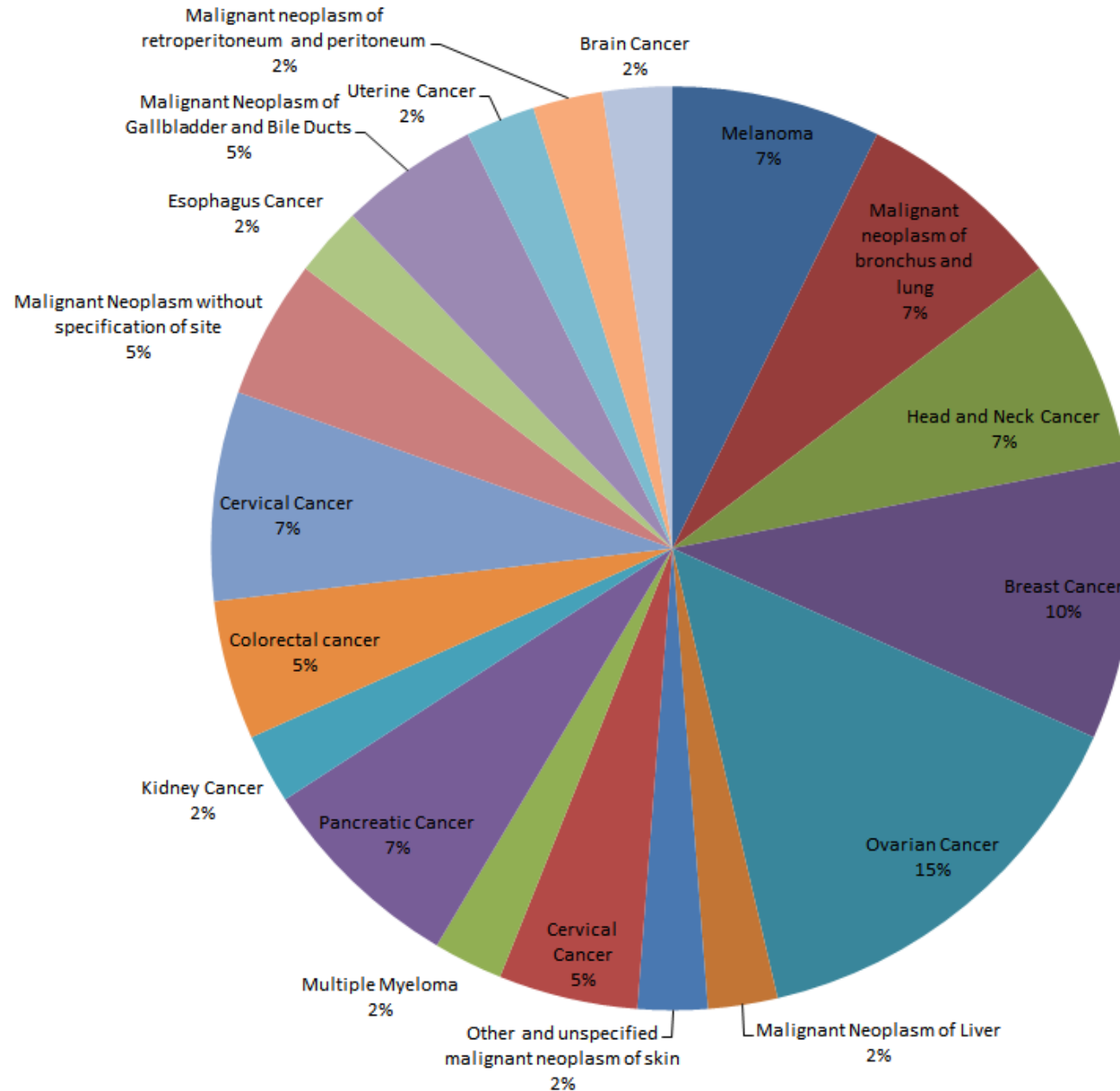
TAPUR Oversight Groups

- **Steering Group**
- **Dr. Edward S. Kim**, Carolinas HealthCare System, *Chair*
 - **Dr. Richard L. Schilsky**, TAPUR PI, *Vice Chair*
- **Molecular Tumor Board**
- **Dr. Mark Kris**, Memorial Sloan Kettering Cancer Center, *Chair*
 - **Dr. Vered Stearns**, Johns Hopkins Sidney Kimmel Comprehensive Cancer Center, *Chair-Elect*
 - **Dr. Anna Berry**, Swedish Cancer Institute, *Vice Chair*
 - **Dr. Gary Schwartz**, Columbia University Medical Center, *Vice Chair*
- **Data & Safety Monitoring Board**
 - **Janet Dancey, M.D.**, Canadian Cancer Trials Group, *Chair*
 - **Yael P. Mosse, M.D.**, Children's Hospital of Philadelphia
 - **Gina R. Petroni, PhD**, University of Virginia Public Health System
 - **Deborah E. Collyar**, Patient Advocates RSCH

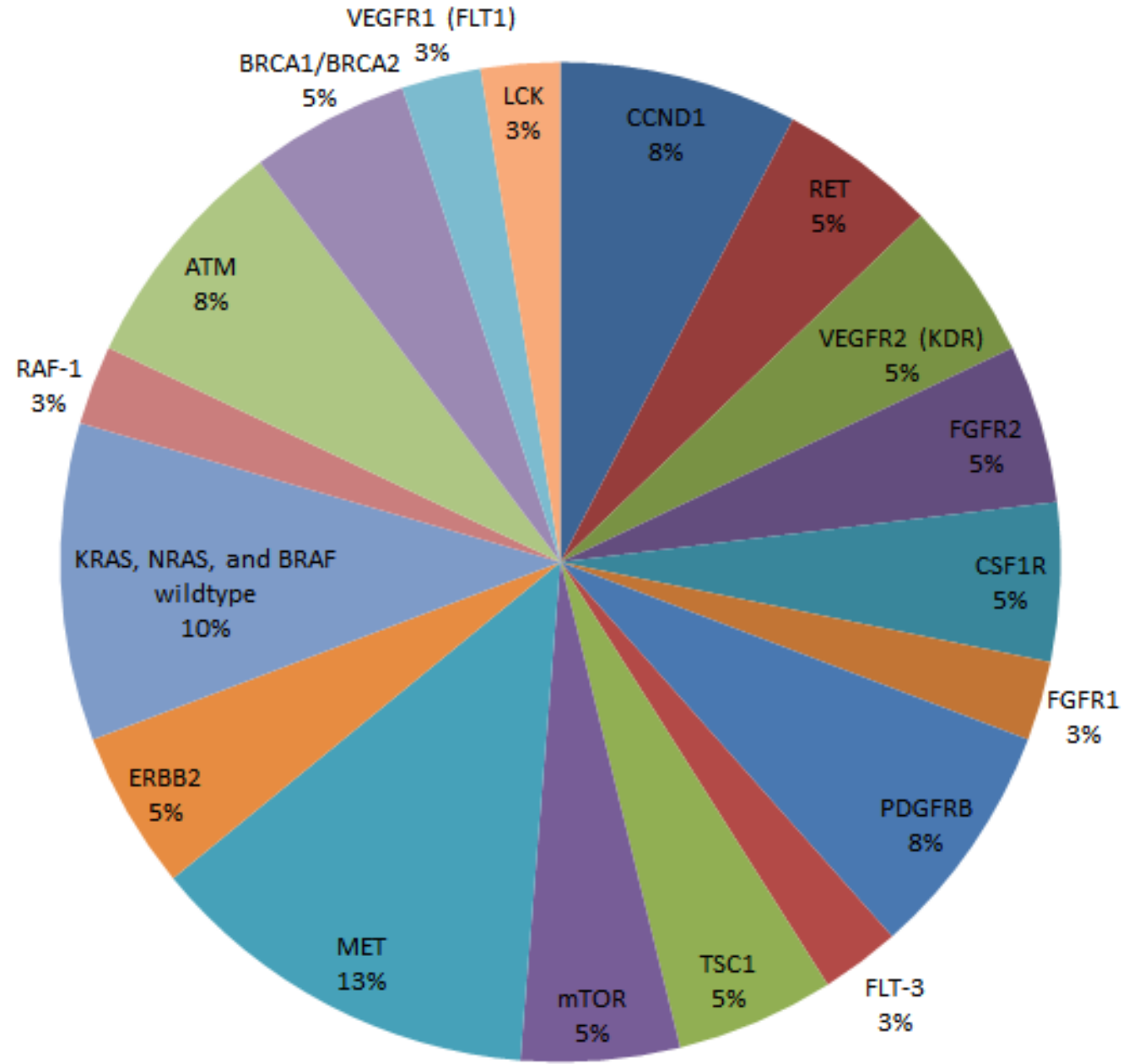
Key Milestones

- FDA reviewed and determined TAPUR Study IND-exempt (08/31/15)
- Chesapeake Institutional Review Board approval (02/09/16)
- Registered on ClinicalTrials.gov
 - NCT ID# 02693535 granted (02/20/16)
- *TAPUR Study Launch 03/14/16*
- 72 participants registered as of 07/08/16
- 44 patients on treatment as of 07/08/16

Frequency of Tumor Types in TAPUR (N=44)



Frequency of Genomic Aberrations in TAPUR (N=44)

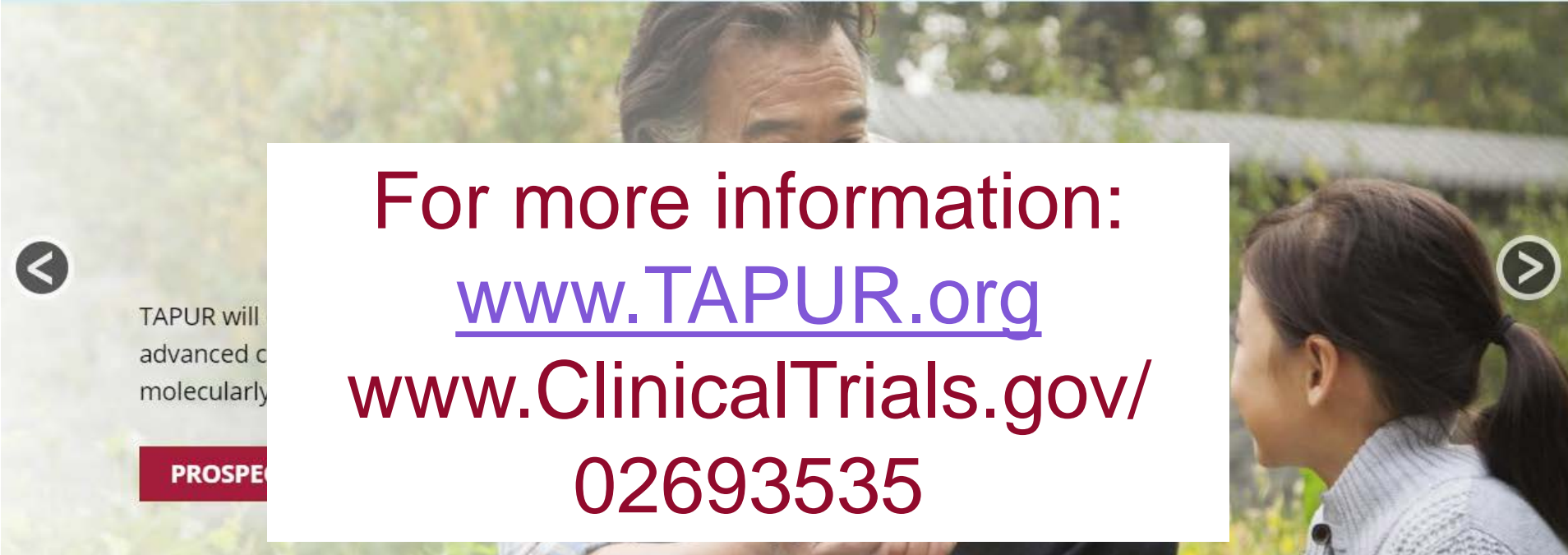


TAPUR Sub-study: Physician Perceptions & Use of Molecular Testing Survey

- **Goal:** Examine physician perspectives of genomic testing as it relates to
 - Conditions for ordering
 - Concerns/barriers to ordering
 - Anticipated use of test results
 - Confidence in interpreting and describing test results
 - Patient education and disclosure
 - Clinician and patient expectations
 - Frequency of reimbursement
- Collaboration with Research Advocacy Network

Who Benefits if TAPUR Succeeds?

- **Patients** receive targeted agent matched to tumor genomic profile; drugs at no cost
- **Physicians** receive guidance in interpretation of genomic test results and treatment options, access to drugs, clinical data on off-label use
- **Pharma** receives data on drug use and outcomes to inform R&D plans and life cycle management
- **Payers** receive data on test and drug use and outcomes to inform future coverage decisions
- **Regulators** receive data on extent and outcomes of off label drug and test use and real world safety data



About the Study

The **Targeted Agent and Profiling Utilization Registry (TAPUR) Study** is a non-randomized clinical trial that aims to describe the performance (both safety and efficacy) of commercially available, targeted anticancer drugs prescribed for treatment of patients with advanced cancer that has a potentially actionable genomic variant. The study also aims to simplify patient access to approved targeted therapies that are contributed to the program by collaborating pharmaceutical companies, catalogue the choice of genomic profiling test by clinical oncologists and learn about the utility of registry data to develop hypotheses for additional clinical trials.

Who Benefits?