Targeted Agent and Molecular Profiling Registry (TAPUR)

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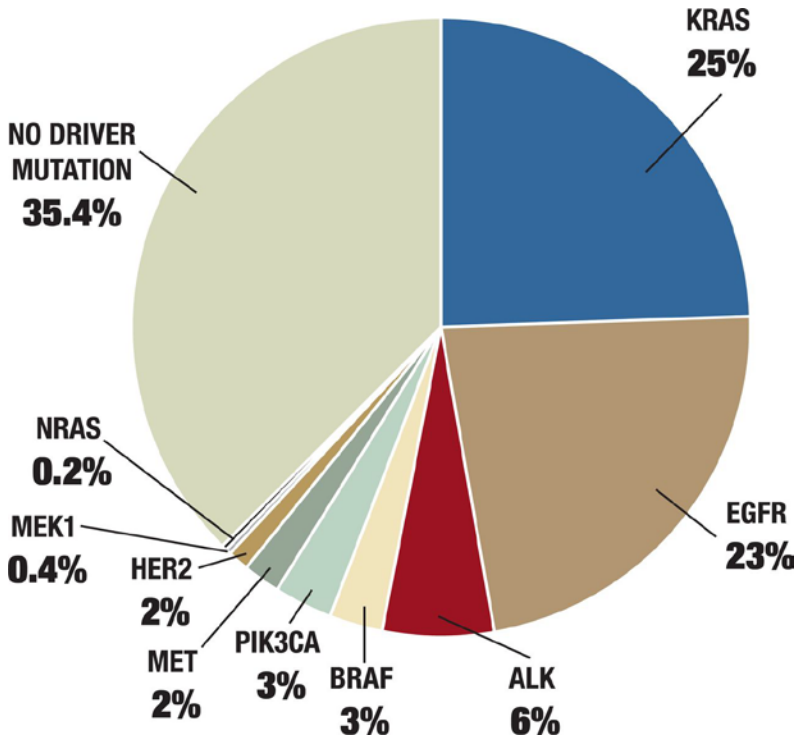
Presented at National Cancer Policy Forum Workshop on Policy Issues in the Development and Adoption of Molecularly Targeted Therapies for Cancer, November 10, 2014

Problem

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

Matching Drugs to Mutations



Genotypes of NSCLC

Clin Cancer Res 18 (Suppl 1) S67. Nov 1, 2012

Potential Treatments

- Crizotinib (ALK TKI)
- Erlotinib (EGFR TKI)
- Lapatinib, Afatinib (EGFR/HER2)
- Onartuzumab (MetMAb)
- Tivantinib (cMET TKI)
- Selumetinib (MEK1/2)
- Trametenib (MEK1/2)
- Vemurafenib (BRAF)

Potential Drug Sources

- Commercial drug used within indication
- Commercial drug used off label (reimbursement?)
- Clinical trial participation
- Expanded access program (company sponsor or individual patient IND)

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Proposed Solution: A Facilitated Access Program and Registry

- Facilitate patient access to marketed, targeted agents against common aberrations
- Create a registry of administered treatment and patient outcomes
- Participants: Patients, physicians, pharma, payers, FDA

What's Required?

Pharma provides drugs.

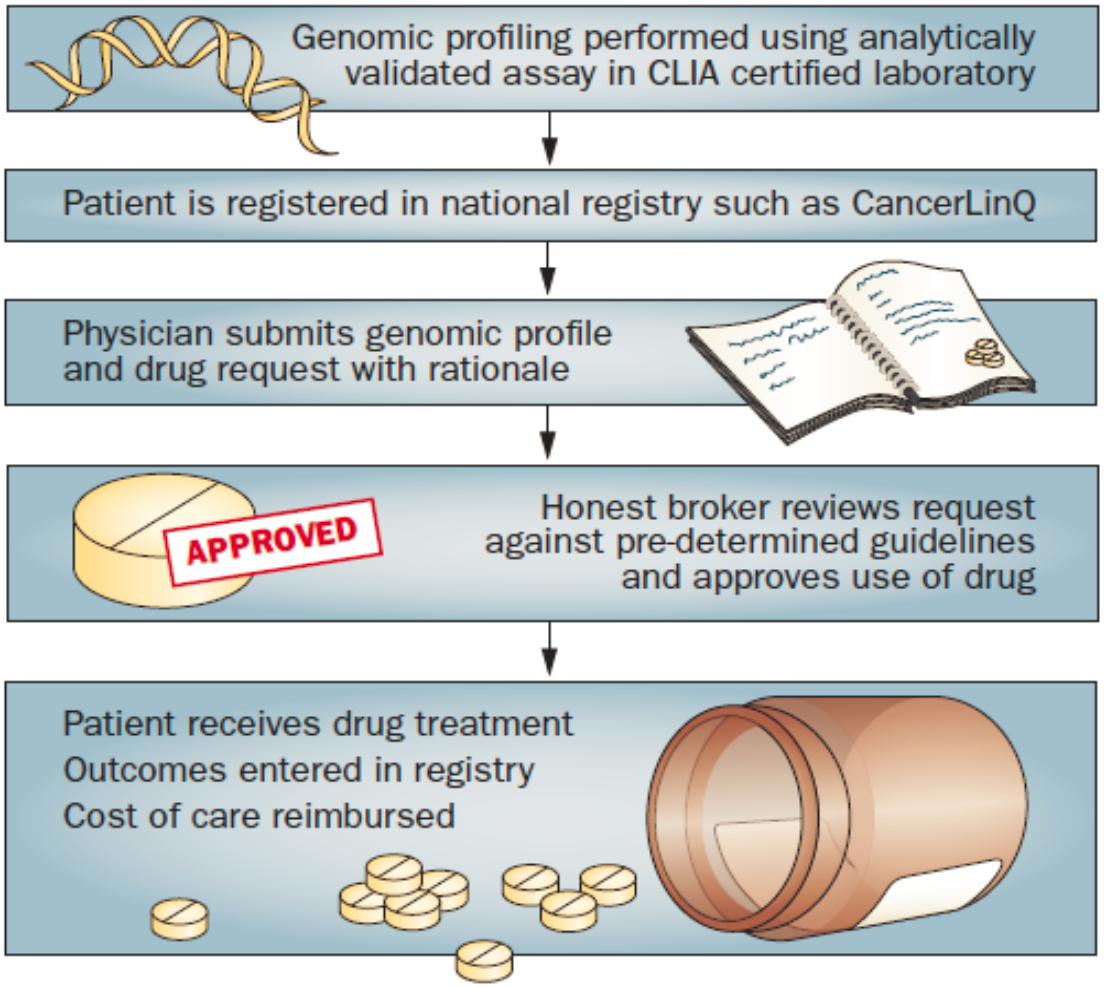
Patient agrees to data collection.

Physician submits required follow-up data.

CMS/commercial payers reimburse treatment costs.

Third party (ASCO) provides honest broker and hosts the outcomes registry.

How Might It Work?



Schilsky, Nature Rev. Clin. Oncol., 2014.

TAPUR Study Primary Objectives

- To describe the anti-tumor activity and toxicity of commercially available, targeted anti-cancer drugs used off label for treatment of patients with advanced solid tumors with a known genomic variant.

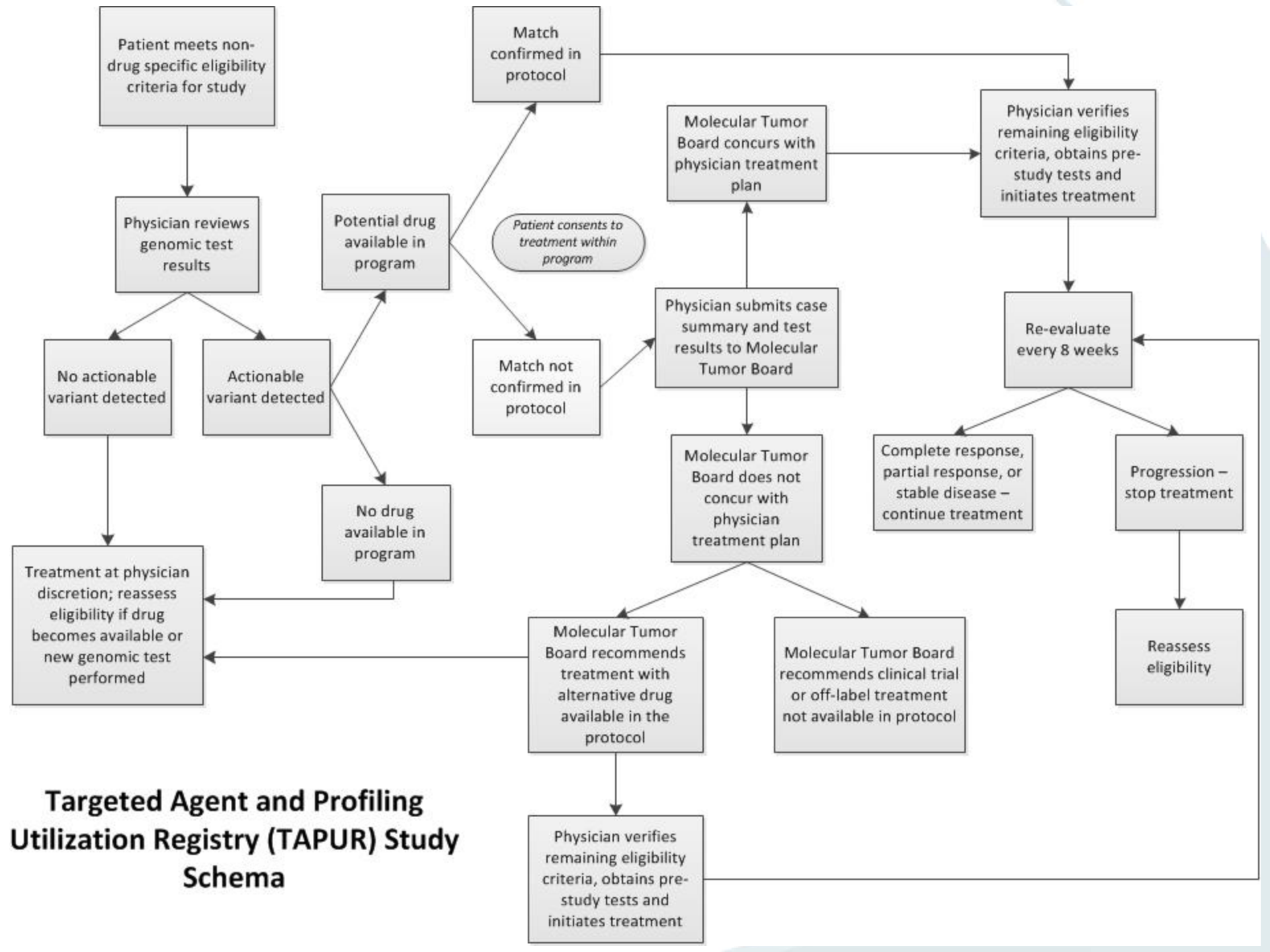
- To facilitate patient access to commercially available, targeted anti-cancer drugs of potential efficacy prescribed off label for treatment of patients with an advanced solid tumor with a known genomic variant.

TAPUR Study Secondary Objectives

- To record the treatment-related adverse events.
- To create a prospective registry of patient outcomes following off label treatment.
- To create a prospective registry 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.

TAPUR Eligibility

- Patients with advanced solid tumors (and possibly myeloma) for whom no standard treatment options exist
- Adequate organ function; PS 0-2
- Results available from a genomic test (FISH, PCR, NGS) performed in a CLIA certified, CAP accredited lab that has obtained a McKesson Z code. Labs located or offering services in NY must also have NY State accreditation



Targeted Agent and Profiling Utilization Registry (TAPUR) Study Schema

Why the Molecular Tumor Board?

- Protect patients from inappropriate treatment based on incorrect interpretation of molecular test results.
- Protect patients from inappropriate treatment based on misunderstanding of drug action.
- Compare physician selection and treatment choice to honest broker recommendation.
- Maintain compliance with FDA rules about promotion of off label use.

Making the Match

Box 1 | Proposed definition of clinically actionable variants and criteria for drug selection

Definition of clinically actionable variants

- Gene variant is the target of an approved drug for any cancer indication
- Activating mutations in genes upstream of the molecular target of an approved drug
- Inactivating mutations in genes that result in unique susceptibility to a specific molecular intervention (for example, *BRCA1* mutation and PARP inhibitors)
- Other genes of interest that have appropriate justification for selection based on published scientific evidence regarding susceptibility to a specific molecular targeted therapy

Criteria for drug selection

- Level 1: Agent met a clinical end point (objective response, progression-free survival or overall survival) in a clinical trial testing the agent in the patient's tumour type harbouring the mutation of interest
- Level 2: Agent is commercially available for use in any tumour type with the specific genomic variant identified in the patient's tumour
- Level 2: Agent demonstrated evidence of clinical activity against the patient's tumour type based on published literature
- Level 3: Agent demonstrated preclinical evidence of antitumour activity and evidence of target inhibition in model systems of patient's tumour type

Possible Actions of MTB

- Concur with MD plan
- Recommend treatment with other drug in protocol targeting selected variant
- Recommend treatment with other drug in protocol targeting other variant
- Recommend off label treatment with drug not in protocol
- Recommend clinical trial

Study Endpoints and Analysis

- Primary endpoint: ORR per RECIST
- Other endpoints: PFS, OS, time on treatment, grade 3-5 AEs per CTCAE, SAEs
- Each tumor type-variant-drug is a “group”
- Enroll 8 patients/group. If no responses, stop
- If at least 1 response, enroll additional 16
- 4 or fewer responses/24, no interest
- 85% power and an alpha error rate of 7.8%

Data Collection

- Patient demographics to confirm eligibility
- Genomic test performed and results
- Proposed treatment
- MTB recommendation
- Patient most recent prior treatment and best response
- Efficacy: ORR, PFS, OS, time on treatment
- Safety: SAEs, Gr 3-5 AEs

Who Benefits?

- **Patients** receive targeted agent matched to molecular profile
- **Physicians** receive interpretation of molecular test results, guidance in treatment recommendations and access to drugs
- **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 additional safety data

Issues for Discussion

- Will the data be reliable?

- How might it be used?

  - Hypothesis generation to inform new studies?
  - Label modification, e.g., for safety issues?
  - Label expansion, e.g., for new indications?
  - Compendia/guideline modifications?
  - Reimbursement policy, expand or reduce coverage?
  - Doctor-patient decision-making?