Embedding Clinical Cancer Research in Health Care Delivery: ASCO's Pragmatic Studies

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Disclosures

- I am an employee of ASCO
- I have nothing else to disclose

Prioritization and Principles for ASCO Research

- Fills an important knowledge gap in the cancer care setting
- Research questions that ASCO is uniquely poised to address
- Engages patients and their advocates in all aspects of the research process.
- Unlikely to be pursued by other organizations (e.g., cooperative groups, industry)

Knowledge Gaps in Personalized Cancer Care (1)

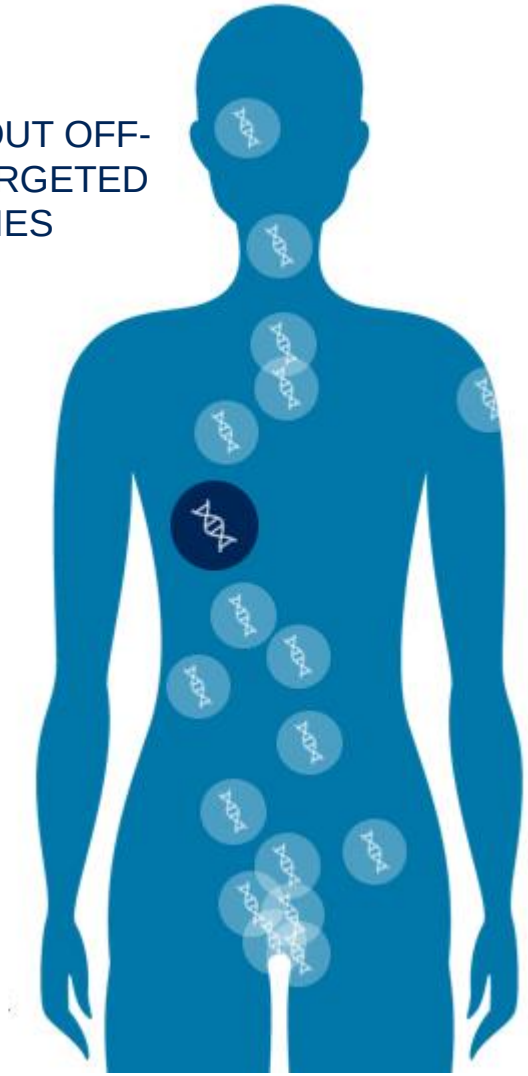
How can we bring precision medicine to all cancer patients?
Are targeted anti-cancer agents efficacious in off-label cancer types?

- Increasing emphasis on personalized and precision medicine
- Increasing number of targeted agents
- Precision medicine requires new knowledge that is not easily accessible in many cancer care settings
- ASCO's answer: The TAPUR Study
  - Provide access to targeted agents via a trial protocol
  - Help sites utilize genomic reports to identify treatment options
  - Rapid turn-around of findings from completed trial cohorts

ASCO TAPUR™

Targeted Agent and Profiling Utilization Registry Study

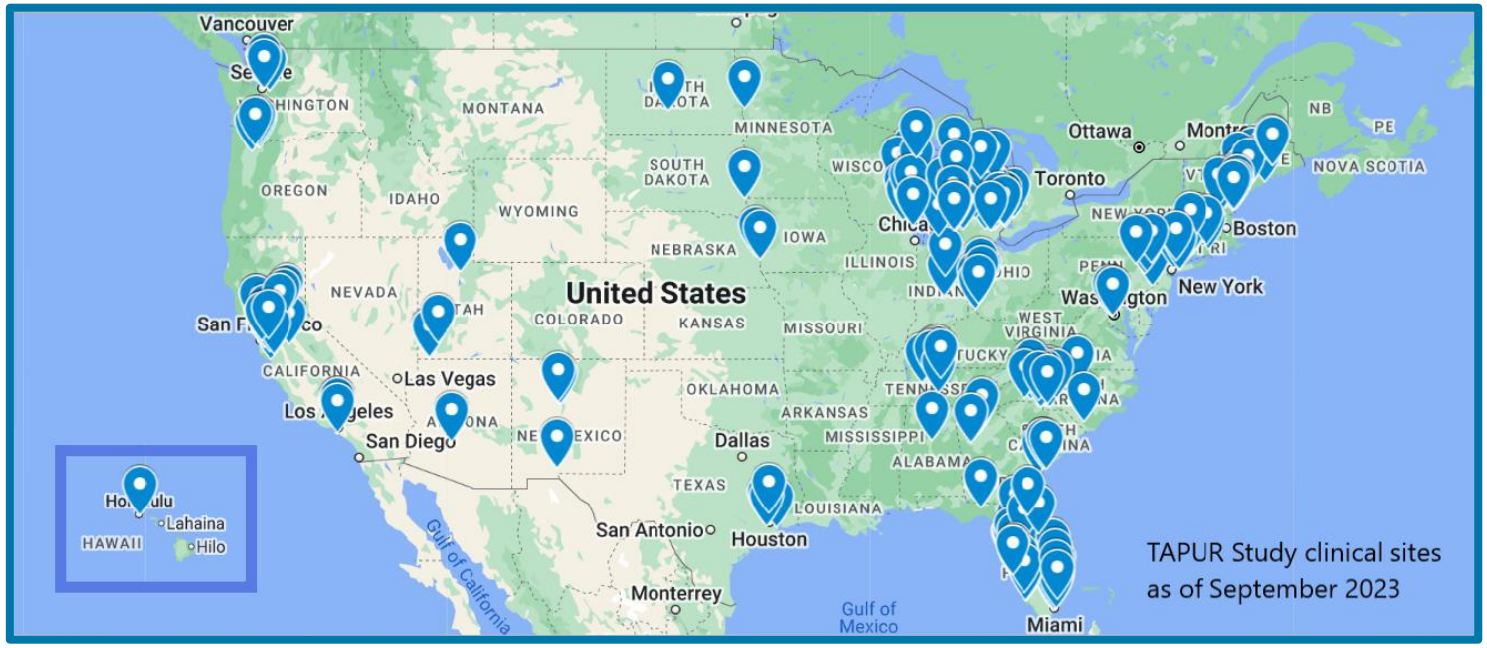
UNMET NEED:
KNOWLEDGE ABOUT OFF-LABEL USE OF TARGETED CANCER THERAPIES



- Precision medicine phase II basket trial
- Aims to describe the safety and efficacy of FDA-approved, targeted anti-cancer drugs prescribed for treatment of patients with advanced cancer that has a potentially actionable genomic alteration.
- **Key**: off-label uses of FDA-approved drugs
- The problem TAPUR trial addresses: many of the target-drug-tumor site combinations are left unstudied.
  - Small patient populations mean small market potential (so pharma trials unlikely)
  - **Yet, doctors prescribe off-label for patients.**
    - Lacking adequate evidence
    - Results are not captured or understood.

Working with Sites: The TAPUR Study Network

- More than 80% of TAPUR sites are community based
- How?
  - Protocol developed with many pragmatic elements
  - Easy implementation in all sites
  - Do-able for sites with fewer research staff/resources.
- Leads to more representative patient population
- Provides access to patients who otherwise may not have access to participate in trials

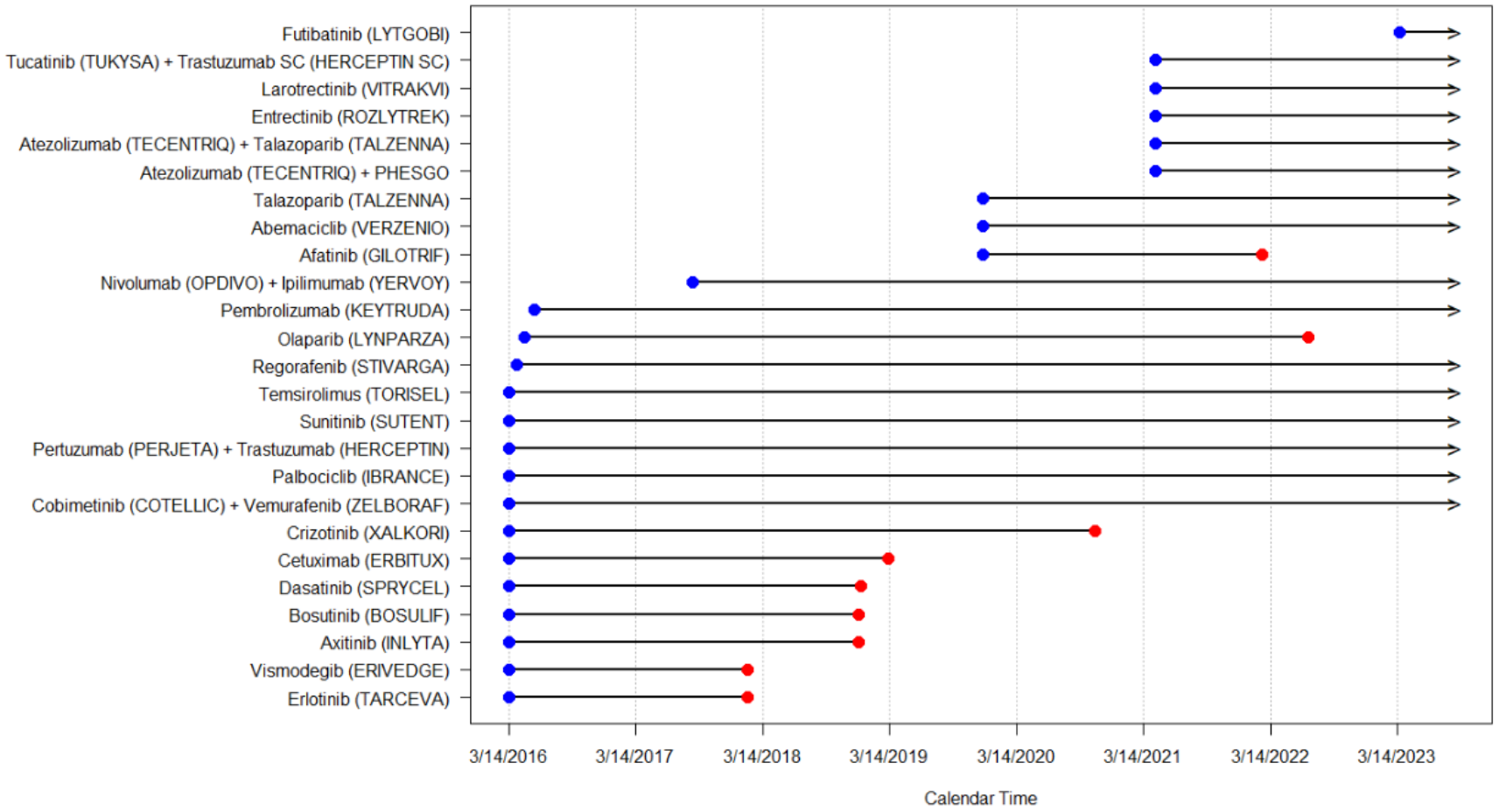


As of September 19, 2023:

- 267 sites in 28 states
- Consented 3984 participants and 2738 participants have received study treatment

Working with Industry: 10 Companies Have (or Had) Treatments on TAPUR

25 treatments have been available on TAPUR



Knowledge Gap in Personalized Cancer Care (2)

For this patient, what is the right dose of this anti-cancer treatment? Should we "start low, go slow?"

- Doses of oncology drugs are too high for many patients to tolerate
- Evidence is scant about the efficacy of lower doses.
- Maximum tolerated dose (MTD) paradigm is incorrect dose finding approach for targeted and immunotherapy agents
- Many clinicians start drugs at lower doses, especially for older patients (>65 yrs old)
- Surveys of clinicians and RWD provide data on practice patterns but not comparison of safety and efficacy outcomes.
- Solution?: Titrated dosing vs. FDA indicated dosing
- Trial Setting: CDK4/6 inhibitors in patients 65 and older newly diagnosed metastatic HR+/HER2- breast cancer, in combination with endocrine therapy.
- Why this setting?
  - Some evidence supporting lower doses comparable in adjuvant setting
  - Reasonably large patient population

CDK4/6 Dosing Knowledge (CDK) Trial

Hypothesis: "Titrating" dose of CDK4/6 inhibitors (i.e., starting with lower dose and increasing as tolerated) could allow older patients to tolerate treatment better, stay on treatment longer, and derive more benefit from treatment

Schema:

- Arm 1: **Indicated Dose.** Start at FDA approved dose for palbociclib (125 mg) or ribociclib (600 mg)
- Arm 2: **Titrated Dose.** Start at lower dose palbociclib (100 mg or 75 mg) or ribociclib (400 or 200 mg) and escalate as tolerated

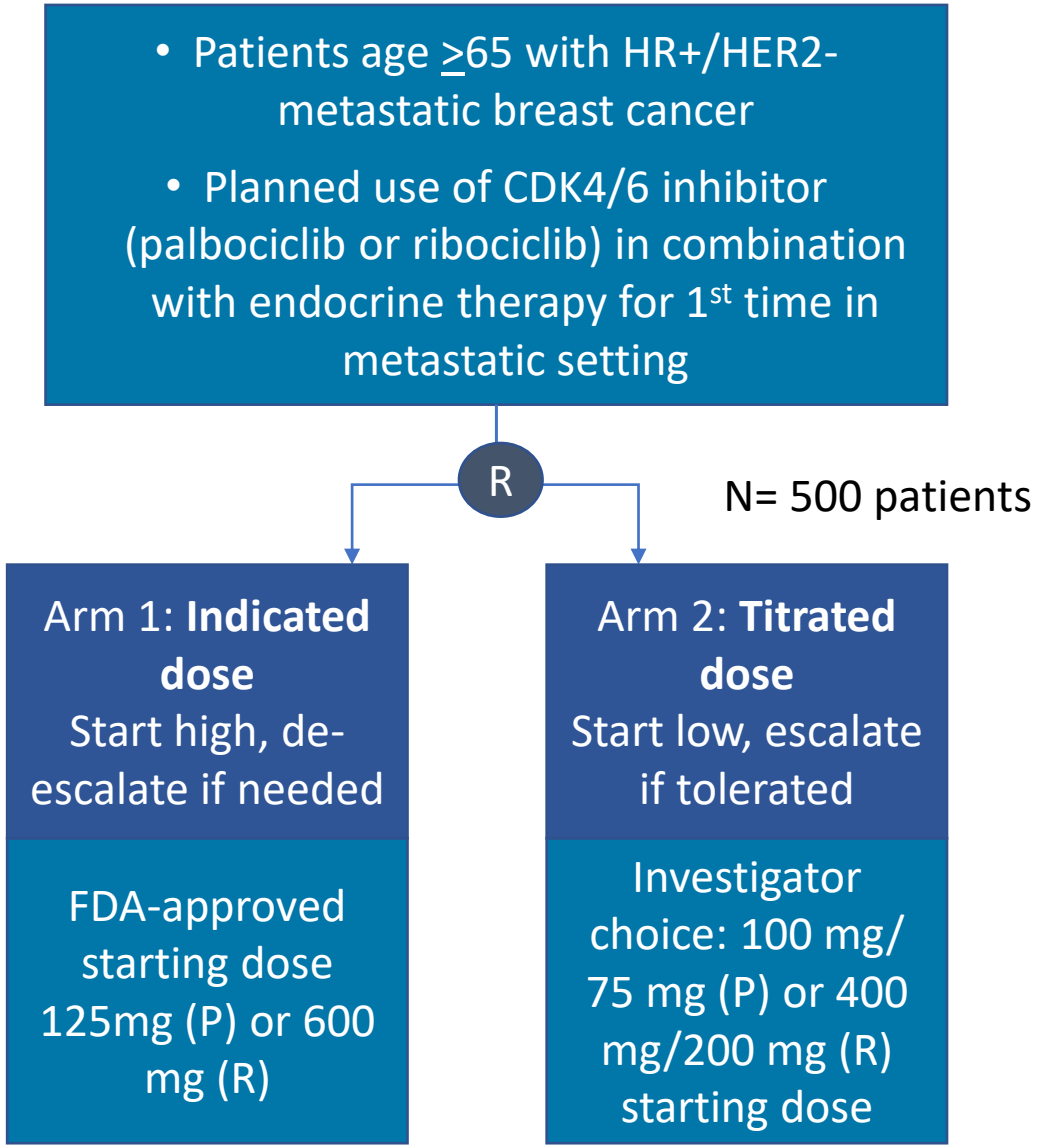
Choice of palbociclib or ribociclib made by clinician prior to randomization

Primary objective:

To compare **time to discontinuation** of CDK4/6 inhibitor

Secondary objectives address tolerability, quality of life, cumulative dose, efficacy, and healthcare utilization.

Funded by Patient Centered Outcomes Research Institute (PCORI): Funding commences 11/1/23.



Working with sites: CDK Study Network

- Both dosing approaches are in regular use
- Pragmatic protocol
  - Mimics standard of care
  - Simple primary outcome: time to treatment discontinuation
  - Limited data collection
- Site selection process
  - Detailed site questionnaire
  - Want balance of community vs. academic sites
  - Overlapping with TAPUR sites

Dosing Platform Study?

- Long-term goal: evaluate other already approved agents with dosing and schedule questions
- Questions:
  - Can patients stay on therapy longer if at lower doses?
  - Do lower doses still benefit patients who may otherwise not get any treatment (due to tolerance concerns)?

Drugs with evidence of overdosing

Drug	Current Dosage	Recommended Dosage
Ibrutinib	420 mg	140 mg
Erlotinib	150 mg	25–100 mg
Dasatinib	100 mg	50 mg
Pembrolizumab	200 mg	2 mg/kg
Abiraterone	1,000 mg fasting	250 mg with food
Lapatinib	1,250 mg fasting	500 mg with food
Pazopanib	800 mg fasting	400–600 mg with food
Nivolumab	Every 2–4 weeks	Every 8–12 weeks
Atezolizumab	Every 2–4 weeks	Every 8–12 weeks
Pembrolizumab	Every 3–6 weeks	Every 8–12 weeks

From https://optimalcancercare.org/ which was adapted Seritella et al. (2020, Clinical Pharmacology and Therapeutics) 108(3))

Final Thoughts

- Our projects are addressing uncertainties existing in current clinical care with FDA approved agents
  - Mechanism for controlling bias (randomization in CDK Study)
  - Mechanism for systematic data collection
- Personalized medicine does not require complex protocols
- Including pragmatic trial elements allow more sites to participate in research
- Making protocols accessible encourages inclusion and equity in patient populations