

# ASCO special article

# Rationale and Design of the Targeted Agent and Profiling Utilization Registry Study

executive summary

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**Purpose** Case reports and small prospective trials suggest that administering targeted therapies to patients with advanced cancer and an identified genomic target may be associated with clinical benefit. The Targeted Agent and Profiling Utilization Registry (TAPUR) study, a phase II prospective, nonrandomized, multibasket pragmatic clinical trial, aims to identify signals of drug activity when US Food and Drug Administration–approved drugs are matched to prespecified genomic targets in patients with advanced cancer, outside of approved indications.

**Methods** Patients eligible to participate in TAPUR are age  $\geq 12$  years and have advanced measurable or evaluable solid tumors, multiple myeloma, or B-cell non-Hodgkin lymphoma. Eligible participants are matched to any of the 16 US Food and Drug Administration–approved study drugs based on protocol-specified genomic inclusion and exclusion criteria. Genomic profiling from any Clinical Laboratory Improvement Amendments–certified, College of American Pathologists–accredited laboratory is acceptable. The treating physician selects the treatment from the available study therapies or consults with the TAPUR Molecular Tumor Board. Participants are placed into multiple parallel cohorts defined by tumor type, genomic alteration, and drug. The primary study end point within each cohort is objective response or stable disease of at least 16 weeks duration. Secondary end points include safety, progression-free survival, and overall survival.

**Results** More than 1,000 participants have thus far been registered, and more than 800 have been treated with a TAPUR study drug. Two study cohorts have permanently closed to enrollment because of lack of antitumor activity, and 12 have expanded to the second stage of enrollment after promising preliminary activity.

**Conclusion** The TAPUR study will describe the efficacy and toxicity of the targeted drugs used outside of their approved indications when matched to a somatic genomic variant.

## INTRODUCTION

Evidence is building through reports of clinical trials, case reports, and clinical anecdotes to suggest that patient outcomes may be improved when a targeted agent is matched to a genomic alteration present in a patient's tumor.<sup>1-6</sup> Clinical reports to date suggest that 30% to 80% of advanced solid tumors harbor potentially actionable genomic variants.<sup>7-10</sup>

In a meta-analysis of 570 phase II studies of new anticancer agents, Schwaederle et al<sup>11</sup> examined response rate (RR), progression-free survival (PFS), and overall survival (OS) for 32,149 patients who received a personalized treatment strategy versus those who did not. Multivariable

analysis demonstrated that the personalized approach consistently and independently correlated with higher median RR (31% *v* 10.5%;  $P < .001$ ), prolonged median PFS (5.9 *v* 2.7 months;  $P < .001$ ), and improved OS (13.7 *v* 8.9 months;  $P = .001$ ). In a similar approach, Jardim et al<sup>12</sup> analyzed registration trials for agents approved by the US Food and Drug Administration (FDA) between 1998 and 2013. Analysis of experimental arms in 112 registration trials demonstrated that therapy assigned based on a biomarker selection strategy was associated with higher RRs (48% *v* 23%;  $P < .001$ ) and longer PFS (median, 8.3 *v* 5.5 months;  $P = .002$ ) and OS (median, 19.3 *v* 13.5 months;  $P = .04$ ). Tsimberidou et al<sup>13</sup> reported results

of the MD Anderson Cancer Center experience of genomic profiling of patients with solid tumors with advanced disease, the IMPACT (Initiative for Molecular Profiling and Advanced Cancer Therapy) study. Of 1,144 patients analyzed, 40.2% had  $\geq$  one genomic variant. Of the patients who received a targeted therapy matched to a genomic variant, the median PFS and OS times were 3.9 and 11.4 months, respectively, compared with 2.2 and 8.6 months, respectively, for patients who did not receive a matched targeted therapy. The MOSCATO-01 (Molecular Screening for Cancer Treatment Optimization; ClinicalTrials.gov identifier: NCT01566019) trial enrolled patients with treatment-resistant progressive metastatic cancers with lesions accessible to biopsy to perform genomic profiling.<sup>14</sup> This study compared PFS using therapy based on genomic assessment with PFS for the most recent therapy during which the patient had experienced disease progression. Of 1,035 adult patients enrolled, 843 had molecular profiling successfully performed. An actionable variant was identified in 411 patients (49%), and 199 patients actually received a matched therapy. The PFS2/PFS1 ratio was  $> 1.3$  in 33% of evaluable patients (63 of 193), representing 7% of the overall study population. At Indiana University, 43% of patients with advanced cancer treated with a genomically guided therapy attained a PFS2/PFS1 ratio  $> 1.3$  compared with 5.3% of patients whose treatment was not guided by genomic profiling.<sup>15</sup> A retrospective matched cohort study conducted by investigators at Intermountain Health reported that patients with advanced cancer treated according to their tumor genomic profile had a median PFS twice as long as that of a matched control group treated at physician discretion (22.9 *v* 12 weeks).<sup>16</sup>

Despite these encouraging findings to support the strategy of matching drugs to a tumor molecular profile, the initial report of a prospective study of this approach has raised questions about its utility. Le Tourneau et al<sup>17</sup> published the results of a randomized phase II trial comparing therapy on the basis of tumor molecular profiling versus physician choice of therapy in patients with refractory cancer. Approximately 25 genomic targets were assessed in tumor biopsies and could be matched to 11 commercially available targeted drugs provided in the study. The median PFS was 2.3 months for the

matched therapy arm and 2.0 months for the physician choice arm ( $P = .41$ ).

The availability of FDA-approved agents targeted against specific genomic alterations along with the widespread availability of tumor genomic profiling tests is fueling off-label prescribing of targeted anticancer drugs based on genomic profiling in patients with advanced cancer, but with no means or incentive to collect or report the outcomes of patients treated. ASCO decided to sponsor its first clinical trial to attempt to fill this knowledge gap. This article will describe the rationale and design of the Targeted Agent and Profiling Utilization Registry (TAPUR) study, a large pragmatic precision medicine basket trial with the overarching goal of describing the efficacy and toxicity of targeted anticancer drugs used outside of their approved indications for treatment of patients with advanced cancer based on a tumor genomic profile.

## METHODS

### Objectives

The primary objective of TAPUR is to evaluate the antitumor activity of commercially available targeted anticancer drugs used outside of their FDA-approved indications for treatment of patients with advanced solid tumors, multiple myeloma, or B-cell non-Hodgkin lymphoma with a genomic alteration known to be a drug target. Secondary objectives include determination of PFS, OS, and safety.

### Design

The TAPUR study is a phase II prospective, non-randomized, open-label clinical trial that aims to define signals of drug activity. The primary study outcome is antitumor activity, defined as tumor response at  $\geq 8$  weeks or stable disease (SD) at  $\geq 16$  weeks from the time of enrollment. For patients with solid tumors, response is defined as complete or partial response by Response Evaluation Criteria in Solid Tumors (RECIST; version 1.1).<sup>18</sup> For patients with non-Hodgkin lymphoma, response is defined according to the Lugano criteria.<sup>19,20</sup> For patients with multiple myeloma, response is defined according to the International Myeloma Working Group Uniform Response Criteria.<sup>21,22</sup> All serious adverse events (SAEs) and grade 3 to 5 treatment-related AEs are reported using the National Cancer

**Table 1.** List of Available TAPUR Study Treatments for Adults and Pediatric Patients

Study Drug	Population to Which Available
Axitinib	Adults and children age 12-17 years
Bosutinib	Adults only
Cetuximab	Adults and children age 12-17 years
Crizotinib	Adults and children age 12-17 years
Dasatinib	Adults and children age 13-17 years
Erlotinib	Adults and children age 12-17 years
Nivolumab + ipilimumab	
Olaparib	Adults and children age 16-17 years
Palbociclib	Adults only
Pembrolizumab	Adults and children age 12-17 years
Regorafenib	Adults and children age 12-17 years
Sunitinib	Adults and children age 12-17 years
Temsirolimus	Adults and children age 12-17 years
Trastuzumab + pertuzumab	Adults only
Vemurafenib + cobimetinib	Adults only
Vismodegib	Adults and children age 12-17 years

NOTE. Adults defined as those age  $\geq 18$  years.

Abbreviation: TAPUR, Targeted Agent and Profiling Utilization Registry.

Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE; version 4.0). The study includes participants as young as 12 years of age with a tumor harboring a genomic alteration known to be a target of or to predict sensitivity to at least one of the 16 therapeutic options available in the study (Table 1). Patients may not be matched to treatments that are already FDA approved for their cancer type. Eligible participants must have a tumor genomic variant identified on a test performed in a laboratory that has certification under the Clinical Laboratory Improvement Amendments and accreditation by the College of American Pathologists. Patients are matched to at least one of the available study treatments through a set of protocol-defined genomic matching rules or after review of a participant case by the TAPUR Molecular Tumor Board (MTB). Participants are then placed into one of the multiple parallel cohorts defined by study drug, genomic alteration, and tumor type as shown in Figure 1. The study uses Simon's optimal two-stage design for cohort analysis.

TAPUR was designed independently by ASCO staff and volunteer leaders, with input from patient advocates, community-based investigators, the initial collaborating pharmaceutical companies, and the ASCO Cancer Research Committee. The study protocol was reviewed by the FDA

and determined to be exempt from investigational new drug regulations. The study was registered on ClinicalTrials.gov (NCT02693535) before study launch.

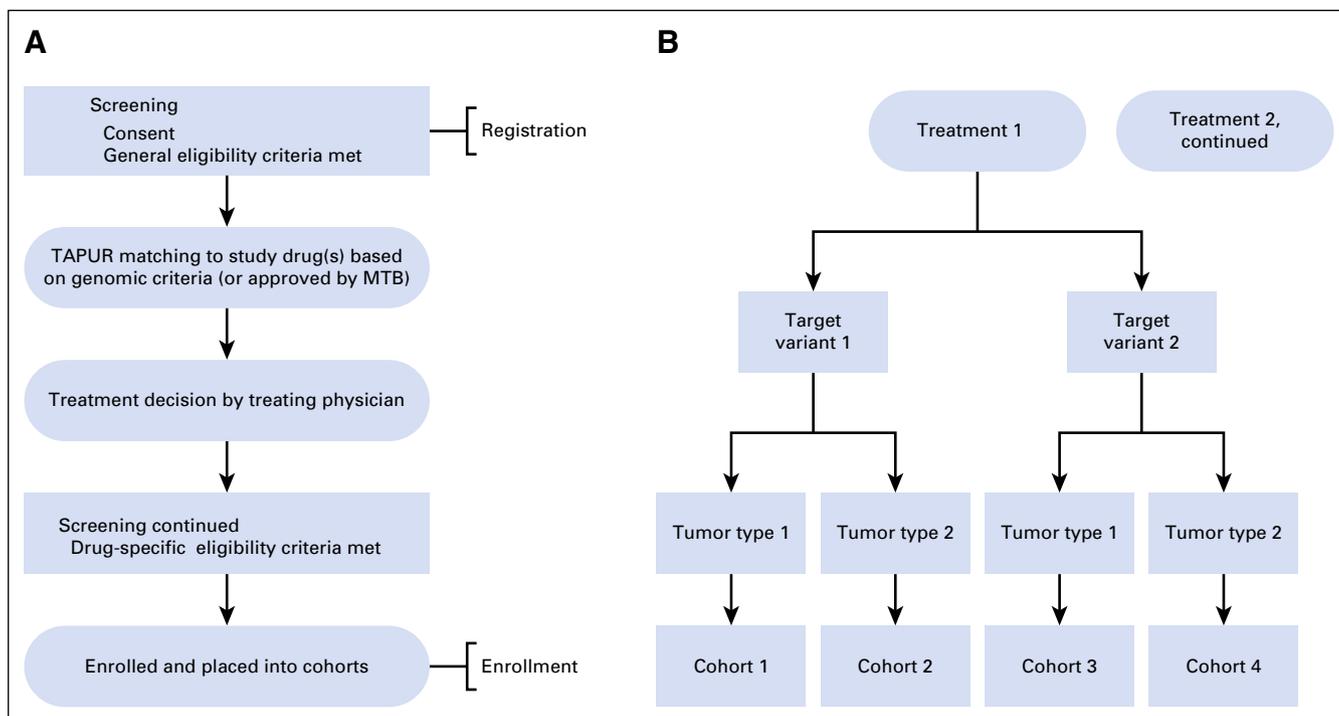
A data and safety monitoring board (DSMB), consisting of a group of independent experts not involved in the conduct of TAPUR, meets biannually to monitor the study data and outcomes. Their primary functions include assessing the safety and efficacy of study treatments, safeguarding the interests and safety of trial participants, and ensuring that study results are both credible and reported to the medical community in a timely manner. The DSMB reviews all cohorts once stage one enrollment is complete and recommends cohorts for either closure or expansion. For expanded cohorts, it will review all final cohort analyses and make recommendations regarding release of the cohort data.

### Study Population and Recruitment

The pragmatic approach of TAPUR allows for broad eligibility criteria, including Eastern Cooperative Oncology Group performance status of 0 to 2, age  $\geq 12$  years, prior malignancies or positive HIV status, and previously treated but clinically stable brain metastases. Major eligibility criteria are summarized in Table 2. TAPUR inclusion and exclusion criteria comport fully with recently published recommendations by ASCO and Friends of Cancer Research for broadening eligibility criteria for cancer clinical trials.<sup>23</sup> Participating sites include both academic and community centers.

### Study Treatment Decision

Once a potential participant is identified, the clinical site obtains informed consent and registers the participant in the TAPUR electronic data capture (EDC) platform as shown in Figure 1. The TAPUR EDC is a Web-based data entry system where all study data are entered and treatment matches are surfaced based on genomic profiling test results, according to a prespecified set of genomic inclusion and exclusion criteria (hereafter referred to as the matching rules). If a study drug is identified and the drug-specific inclusion and exclusion criteria are met, the clinical site completes the drug-specific informed consent process and enrolls the participant in the study. Treatment begins, and



**Fig 1.** Participant registration, enrollment, and cohort assignment process. (A) Process by which participants are registered and enrolled in the study. (B) Organization of the cohorts for analysis, which are grouped by treatment, targeted variant, and tumor type. TAPUR, Targeted Agent and Profiling Utilization Registry.

all protocol-specified evaluations must be performed and data reported in the EDC.

### MTB

Treating physicians may choose to consult with the TAPUR MTB when no or multiple treatment matches surface within the TAPUR matching rules or if the treating physician would like to propose a treatment match outside of the matching rules. The MTB, composed of clinical oncologists, molecular pathologists, and patient advocates, reviews the genomic test results, pathology reports, and clinical histories of submitted patient cases and identifies potential treatment matches among the study treatments. The MTB may also suggest off-study treatments for consideration. Of more than 1,000 patients registered in TAPUR thus far, approximately 23% have been referred for MTB review by their treating physicians. Of the patient cases reviewed by the MTB, approximately 65% resulted in identification of a study drug option.

### Treatment Schedule and Interval of Evaluations

Study treatments are administered according to the recommended starting dose and schedule described in the package insert of each drug. Adjustments in dosage and scheduling are

permitted at the discretion of the treating physician in accordance with the recommended dose modifications contained in the approved prescribing information. Management of AEs is performed according to institutional standards of care, informed by the package insert.

Tumor measurements and radiologic evaluations and evaluation of clinical disease status are performed every 8 weeks after initiation of treatment for the first 16 weeks, and then every 12 weeks if the treatment continues, and at the end of study treatment, if possible. Study treatment is continued until progressive disease is documented.

After progression of disease during any study treatment, participants may be reassessed to determine eligibility for treatment with another study drug after a minimum of 30 days has elapsed from the last dose of the previous drug and any AEs have resolved to grade  $\geq 2$  or stabilized. All general and drug-specific eligibility criteria must be reconfirmed, and the participant must sign a new drug-specific consent form.

### AE and SAE Criteria

AEs and SAEs measured by the NCI CTCAE must be reported once a participant has received at least one dose of study treatment. Collection and reporting of qualifying AEs continue until

**Table 2.** Summary of Major Inclusion and Exclusion Criteria for Registration

Criterion
<b>Inclusion</b>
Patient (age ≥ 12 years*) with a histologically proven locally advanced or metastatic solid tumor, multiple myeloma, or B-cell non-Hodgkin lymphoma who is no longer benefitting from standard anticancer treatment or no such treatment is available or indicated
ECOG performance status of 0 to 2 and acceptable organ function defined per protocol
Patients must have measurable or evaluable disease (per RECIST version 1.1 for solid tumor, Lugano criteria for non-Hodgkin lymphoma, or International Myeloma Working Group criteria for multiple myeloma)
Results must be available from a genomic test or IHC test for protein expression performed in a CLIA-certified, CAP-accredited, and New York State-accredited (for laboratories offering services to residents of New York) laboratory
Patient must have a tumor genomic profile for which treatment with one of the FDA-approved targeted anticancer treatments included in this study has potential clinical benefit based on the genomic criteria
Ability to understand and the willingness to sign a written informed consent/assent document
<b>Exclusion</b>
Ongoing toxicity of CTCAE grade ≥ 2, other than peripheral neuropathy, related to antitumor treatment that was completed within 4 weeks before registration; patients with ongoing peripheral neuropathy of CTCAE grade ≥ 3 will be excluded
Patient is receiving any other anticancer treatment
Female patients who are pregnant or nursing; male patients who refuse to practice barrier contraception methods
Patients with primary brain tumors are excluded; patients with known progressive brain metastases determined by serial imaging or declining neurologic function in the opinion of the treating physician are not eligible; patients with previously treated brain metastases are eligible, provided that they have not experienced a seizure or had a clinically significant change in neurologic status within the 3 months before registration; all patients with previously treated brain metastases must be clinically stable for at least 1 month after completion of treatment and off steroid treatment for 1 month before study enrollment
Patients with preexisting cardiac conditions, including uncontrolled or symptomatic angina, uncontrolled atrial or ventricular arrhythmias, or symptomatic congestive heart failure, are not eligible
Patients with LVEF known to be < 40% are not eligible
Patients with stroke (including TIA) or acute myocardial infarction within 4 months before the first dose of study treatment are not eligible
Patients with any other clinically significant medical condition that in the opinion of the treating physician makes it undesirable for them to participate in the study or that could jeopardize compliance with study requirements, including but not limited to ongoing or active infection, significant uncontrolled hypertension, severe psychiatric illness situations, or anticipated or planned anticancer treatment or surgery

NOTE. This list includes only major eligibility criteria.

Abbreviations: CAP, College of American Pathologists; CLIA, Clinical Laboratory Improvement Amendments; CTCAE, Common Terminology Criteria for Adverse Events; ECOG, Eastern Cooperative Oncology Group; FDA, US Food and Drug Administration; IHC, immunohistochemistry; LVEF, left ventricular ejection fraction; RECIST, Response Evaluation Criteria in Solid Tumors; TIA, transient ischemic attack.

\*Restrictions apply. Not all therapies are available for patients age < 18 years. Refer to Table 1.

30 days after the last dose of study drug. Events not resolved at the end of study treatment require follow-up every 30 days until the event resolves to CTCAE grade ≤ 2.

TAPUR requires reporting of CTCAE grade 3 to 4 AEs that are possibly, probably, or definitely related to the study treatment, whether expected or not. All SAEs, regardless of grade, relatedness to study drug, or expectedness, must also be reported, including all deaths.

## End Points

The primary end point is objective response at ≥ 8 weeks or SD documented at ≥ 16 weeks. Participants who have measurable disease present at baseline and have received at least one dose of study treatment are considered evaluable for response. Participants who have lesions present at baseline that are evaluable but do not meet the definition of measurable disease and receive at least one dose of study treatment are assessed on

**Table 3.** TAPUR Study Milestones

Date	Milestone
March 14, 2016	Study launch at 37 clinical site locations with 14 study drugs
March 2016	First participant registered (consented)
April 2016	First participant enrolled; two additional drugs added for total of 16 study drugs
May 2016	Additional drug added for total of 17 study drugs
August 2016	100th participant registered
November 2016	100th participant enrolled
April 2017	33 clinical sites added for total of 70 locations
June 2017	500th participant registered
August 2017	Additional therapy added for 19 study drugs
September 2017	First cohort reaches stage one
November 2017	500th participant enrolled
December 2017	43 clinical sites added for total of 113 locations
February 2018	1,000th participant registered
March 2018	10th cohort reaches stage one

Abbreviation: TAPUR, Targeted Agent and Profiling Utilization Registry.

the basis of the presence, absence, or unequivocal progression of the lesions. Participants who have no tumor evaluation beyond baseline and are alive with no signs of progressive disease at the time of leaving the study will be replaced in their cohort with another participant.

Secondary end points include grade 3 to 5 AEs and SAEs, PFS, response duration, and OS. PFS is defined as the time from initiation of treatment to documented disease progression or death resulting from any cause, whichever occurs first. Response duration is defined as time from documentation of partial or complete response until objective tumor progression. OS is defined as time from initiation of treatment until death resulting from any cause.

### Statistical Considerations

For each cohort, Simon's optimal two-stage design is used. The null hypothesis is that the probability of objective response or SD of at least 16 weeks duration is 15%, versus the alternative hypothesis that it is at least 35%. Power and type I error rate are assumed to be 85% and 0.10 (one sided), respectively. Under these assumptions, in the first stage, 10 participants are entered. If  $\geq$  two participants experience objective response or SD of at least 16 weeks duration, an additional 18 participants are enrolled; otherwise, the cohort is permanently closed. After 28 participants in the cohort have been observed for the primary outcome, if seven or more participants achieve

objective response or SD of at least 16 weeks duration, the null hypothesis will be rejected, and we will declare that the study drug is active in the cohort of participants defined by tumor type and genomic alteration. This design has a 54% chance of early stopping if the null hypothesis is true.

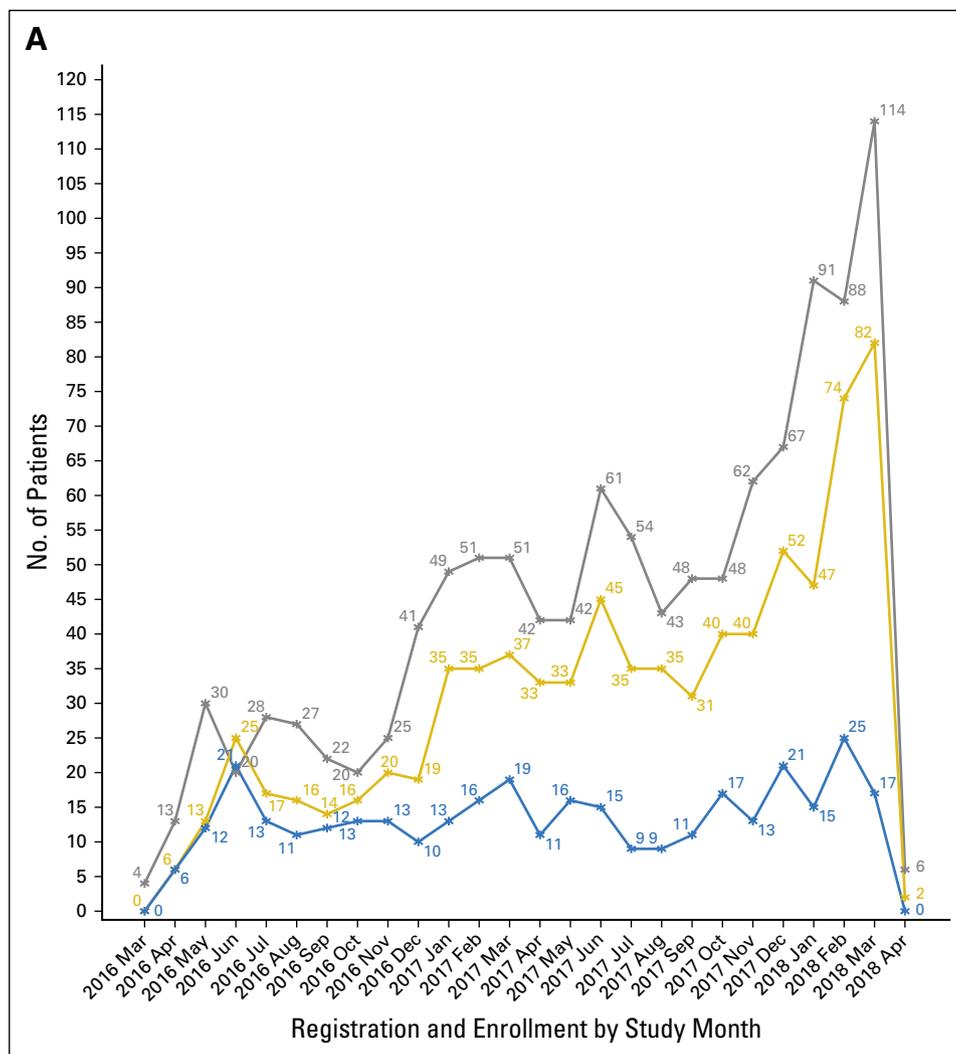
Estimates of the RR and 95% CI will be presented for each cohort upon closure (at either stage one or stage two).<sup>24</sup> The Kaplan-Meier method will be used to estimate the duration of response, PFS, and OS distributions.

## RESULTS

Table 3 summarizes key study milestones. Figure 2 shows participant registration and enrollment by month and the rate of creation of new cohorts (Fig 2A). Figure 2 also shows the distribution of genomic targets by tumor type (Fig 2B) and study drug (Fig 2C), highlighting the heterogeneity of genomic targets and tumor types, resulting in 336 unique cohorts at the time of this writing. As summarized in Table 4, thus far, 12 cohorts have expanded to the second stage of enrollment, and two cohorts have been permanently closed after stage one.

## DISCUSSION

Precision medicine approaches to cancer care have clearly revolutionized the treatment of



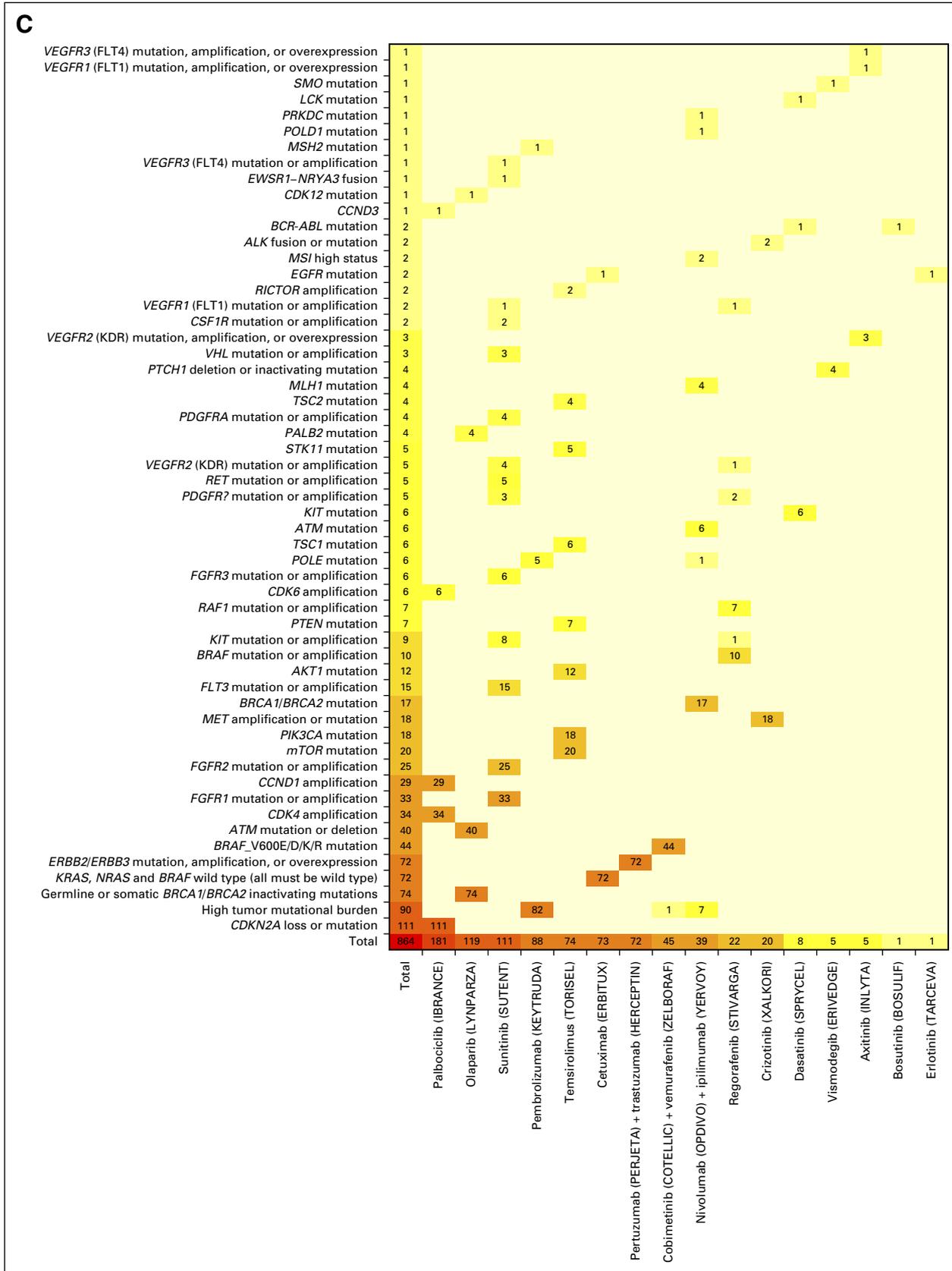
**Fig 2.** Targeted Agent and Profiling Utilization Registry (TAPUR) study registration, enrollment, and cohort creation by (A) month, (continued on next page)

many cancers that are driven by specific molecular alterations that can be targeted with drugs that inhibit aberrant signaling pathways in tumor cells. Thus, the targeting of *BCR-ABL* alterations in chronic myeloid leukemia, *FLT3* alterations in acute myeloid leukemia, *EGFR* mutations and *ALK* translocations in non-small-cell lung cancer, *BRAF* mutations in melanoma and non-small-cell lung cancer, and human epidermal growth factor receptor 2 overexpression in breast and gastric cancers, among others, represent examples of the successful application of precision medicine approaches in clinical oncology that have extended the lives of many patients.<sup>1,25-30</sup> Interest in precision medicine has been further fueled by reported responses ranging from modest to exceptional when targeted treatments are selected based on large-scale genomic tumor profiling.<sup>5</sup> The

widespread availability of commercial next-generation sequencing tests presents opportunities for patients who have exhausted standard treatment options to pursue treatments with investigational agents or approved drugs prescribed outside of their labeled indications.

The TAPUR study stemmed from the recognition that the rapid dissemination of genomic profiling provides an opportunity to learn from the application of precision cancer medicine in practice while at the same time providing a framework for clinical decision support for clinical oncologists who are struggling to interpret the complex genomic data they now confront in practice. Thus, the study was designed to closely replicate real-world clinical practice, with broad eligibility criteria that comport with recent recommendations,<sup>23</sup> minimum necessary





**Fig 2.** (Continued) (C) IBRANCE (Pfizer, New York, NY), LYNPARZA (AstraZeneca, Wilmington, DE), SUTENT (Pfizer), KEYTRUDA (Merck, Kenilworth, NJ), TORISEL (Pfizer), ERBITUX (Eli Lilly, Indianapolis, IN), PERJETA (Genentech, South San Francisco, CA), HERCEPTIN (Genentech), COTELLIC (Genentech), ZELBORAF (Genentech), OPDIVO (Bristol-Myers Squibb, New York, NY), YERVOY (Bristol-Myers Squibb), STIVARGA (Bayer, Whippany, NJ), XALKORI (Pfizer), SPRYCEL (Bristol-Myers Squibb), ERIVEDGE (Genentech), INLYTA (Pfizer), BOSULIF (Pfizer), and TARCEVA (Genentech). MSI, microsatellite instability; NHL, non-Hodgkin lymphoma.

**Table 4.** TAPUR Study Initial Cohort Expansions and Closures

Study Drug	Tumor Type	Variant
Expansion to stage two		
Cetuximab	Ovarian cancer	<i>KRAS</i> , <i>NRAS</i> , and <i>BRAF</i> wild type
Cobimetinib + vemurafenib	Colorectal cancer	<i>BRAF_V600E/D/K/R</i> mutation
Olaparib	Breast cancer Colorectal cancer	Germ line or somatic <i>BRCA1/BRCA2</i> inactivating mutations <i>ATM</i> mutation or deletion
Palbociclib	Head and neck cancer Soft tissue sarcoma Malignant neoplasm of bronchus and lung	<i>CDKN2A</i> loss or mutation <i>CDK4</i> amplification <i>CDKN2A</i> loss or mutation
Pembrolizumab	Breast cancer Colorectal cancer Uterine cancer	High tumor mutational burden High tumor mutational burden High tumor mutational burden
Pertuzumab + trastuzumab	Colorectal cancer	<i>ERBB2/ERBB3</i> mutation, amplification, or overexpression
Sunitinib	Breast cancer	<i>FGFR1</i> mutation or amplification
Closed at stage one		
Palbociclib	Pancreatic cancer Malignant neoplasm of gallbladder and bile ducts	<i>CDKN2A</i> loss or mutation

Abbreviation: TAPUR, Targeted Agent and Profiling Utilization Registry.

data collection, and discretion left to the treating physician regarding choice of which tumor biospecimen to interrogate and which genomic profiling test to use. However, TAPUR uses standard treatment response and toxicity criteria for assessment of efficacy and toxicity outcomes, structured data collection, protocol-specified evaluation times, and a standard Simon's two-stage statistical design to assess the primary end point as well as an independent DSMB to provide recommendations on cohort expansion and closure. Importantly, the study also provides educational opportunities and clinical decision support tools to treating physicians in the form of protocol-specified genomic matching rules and access to an MTB to assist in interpretation of genomic test reports.

Although study results are not yet available, preliminary information about the status of certain cohorts suggests that the study can provide meaningful information. The expansion of some cohorts provides confidence that TAPUR can detect signals of drug activity when such activity is known to exist. Thus, the expansion of the olaparib cohort in patients with breast cancer whose tumors harbor *BRCA1* or *BRCA2* mutations is supported by clinical trial data and the recent

FDA approval of olaparib in such patients, and the expansion of the trastuzumab-pertuzumab cohort in patients with colorectal cancer with human epidermal growth factor receptor 2-overexpressing tumors is consistent with data recently reported.<sup>31,32</sup> Furthermore, the expansion of the pembrolizumab cohorts in patients with breast, uterine, and colorectal cancers with high tumor mutational burden is consistent with the activity of this class of agents in other tumor types with high tumor mutation loads.<sup>33</sup> Finally, in view of recent interest in histology-agnostic targeted drug development exemplified by the FDA approval of pembrolizumab in all microsatellite instability-high or mismatch repair deficient advanced solid tumors, it is interesting to note that the TAPUR cohorts of palbociclib in pancreatic cancer and gallbladder/bile duct cancers bearing *CDKN2A* alterations were closed after the first stage of enrollment, whereas cohorts comprising the same drug and genomic alteration in patients with non-small-cell lung cancer and head and neck cancer have been expanded to the second stage of enrollment.<sup>34</sup>

Many challenges were encountered in the development and launch of TAPUR, including defining the genomic matching rules, estimating

enrollment rates when the frequency of genomic targets was not well defined for many tumor types, identifying clinical launch sites that routinely used genomic profiling, arranging for drug distribution, and building an experienced clinical trial management team to operate the study. However, the launch of the TAPUR study by ASCO illustrates both the opportunity

for medical professional societies to learn from observing the clinical work of their members and the feasibility of doing so through the development of pragmatic clinical trials.

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**Manuscript writing:** All authors

**Final approval of manuscript:** All authors

#### AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

##### Rationale and Design of the Targeted Agent and Profiling Utilization Registry Study

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## Appendix

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