Cancer Tumor Clinic: The University of California San Diego Moores
Cancer Center Experience with a Precision Therapy Approach

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Background. Patients with rare tumors may lack approved treatments and clinical trial access. Although each rare tumor is uncommon, cumulatively they account for approximately 25% of cancers. We recently initiated a Rare Tumor Clinic that emphasized a precision medicine strategy.

Materials and Methods. We investigated the first 40 patients presenting at the Rare Tumor Clinic. Next-generation sequencing (NGS) of tissue and plasma-derived, circulating-tumor DNA (ctDNA), and protein markers were assessed.

Results. Median age was 58 years (range, 31–78 years); 70% (28/40) were women; median number of previous systemic therapies was 2 (range 0–7). The most common diagnoses were sarcoma (n = 7) for solid tumors and Erdheim-Chester disease (n = 5) for hematologic malignancies. Twenty distinct diagnoses were seen. Examples of ultrarare tumors included ameloblastoma, yolk sac liver tumor, ampullary cancer, and Castleman’s disease. Altogether, 32 of 33 patients (97%) with tissue NGS and 15 of 33 (45%) with ctDNA sequencing harbored ≥1 alteration. Overall, 92.5% of patients (37/40) had ≥1 actionable target based on either genomic (n = 32) or protein (n = 27) markers. In total, 52.5% (21/40) received matched therapy; 52.4% (11/21) achieved stable disease (SD) ≥6 months (n = 3), partial remission (PR; n = 6), or complete remission (CR; n = 2). Matched therapy resulted in significantly longer progression-free survival compared with last prior unmatched therapy (hazard ratio 0.26, 95% confidence interval 0.10–0.71, p = .008).

Conclusion. Identifying genomic and protein markers in patients with rare/ultrarare tumors was feasible. When therapies were matched, >50% of patients attained SD ≥6 months, PR, or CR. Further precision medicine clinical investigations focusing on rare and ultrarare tumors are urgently needed. The Oncologist 2018;23:171–178

Implications for Practice: Although rare tumors are infrequent by definition, when all subtypes of rare cancers are combined, they account for approximately 25% of adult malignancies. However, patients with rare tumors may lack approved treatments and clinical trial access. This paper describes an institutional a Rare Tumor Clinic focused on a precision medicine strategy. Performing genomics and protein analyses was feasible amongst patients with rare cancers. Over 50% of patients attained SD ≥6 months, PR, or CR when they received matched therapy (genomically targeted and/or immunotherapy). Further studies investigating the efficacy of the precision therapy approach among rare tumors are warranted.

INTRODUCTION

In 2012, there were 14.1 million new cases of cancer and 8.2 million cancer-related deaths worldwide, making cancer one of the most common causes of death [1]. Among diverse cancer subtypes, certain cancers fall into the category of rare tumors. The definition of rare tumors differs depending on the country. For example, in the U.S., rare tumors are defined as those with an incidence of fewer than 15 cases per 100,000 per year; in Europe and Japan, 6 cases per 100,000 per year; however, incidence of fewer than 15 cases per 100,000 per year is a widely accepted definition [2–5]. Among rare tumors, cancers with prevalence of fewer than 2,000 or incidence of fewer than 2 cases per 100,000 are referred to as ultrarare tumors [6, 7].

Although each type of rare tumor is uncommon by definition, when all subtypes of rare cancers are combined, they account for 22%–25% of all adult tumors [2, 3]. Hence the overall burden of rare tumors is significant. Clinical management of rare malignancies can be challenging due to lack of information, which can lead to difficulty making the diagnosis, as well as a shortage of therapeutic options that are approved by the U.S. Food and Drug Administration (FDA) and experimental options.
in clinical trials. Rare cancers can also be scientifically challenging to study, and substantial parts of the literature regarding rare cancers are case reports, single-institution case series, or smaller multicenter case series rather than phase III randomized trials [3]. Thus, patients with rare cancers tend to lack novel therapeutic approaches such as those with a targeted therapy. Conceivably due to these limitations, patients with rare tumors are reported to have lower 5-year overall survival when compared with those with common tumors (47% vs. 66%) [2]. To overcome these challenges, in-depth understanding of the biology of rare tumors is required.

Rapid technological advancements have revolutionized the way we evaluate and diagnose patients’ cancer. The standard evaluation is based on the light microscope, but more recently the “molecular microscope,” which includes comprehensive genomic interrogation by techniques such as next-generation sequencing (NGS), transcriptomics, and protein analyses, has been exploited [8]. Consequently, the way clinical trials are conducted is also transforming from a “one-size-fits-all” approach to a more customized, precision strategy that incorporates basket or umbrella trials, each of which are applicable even in patients with rare cancers. (A basket trial focuses on a specific mutation across multiple cancer types; an umbrella trial focuses on a specific type of cancer.) One example is the basket/umbrella study using imatinib among diverse cancers known to express imatinib-sensitive tyrosine kinases [9]. This study showed responses among multiple rare malignancies, including dermatofibrosarcoma protubersans (response rate [RR] 83%, targeting PDGFRB), hypereosinophilic syndrome (RR 43%, targeting PDGFRB/KIT), myeloproliferative disorders (RR 57%, targeting PDGFRB), and systemic mastocytosis (RR 20%, targeting PDGFRB/KIT), which facilitated FDA approval of imatinib for these rare and ultrarare disease conditions [9]. Furthermore, a basket trial with vemurafenib in BRAF V600 mutation-positive cancers also demonstrated clinical benefit among patients with rare cancers (RR of 43% for Erdheim-Chester disease or Langerhans’ cell histiocytosis [9], hypereosinophilic syndrome [9], and systemic mastocytosis [9], and RR of 29% for anaplastic thyroid cancer) [10]. Moreover, accumulating evidence from clinical trials and large-scale meta-analyses suggests that the matched targeted therapy approach (biomarker-based) can achieve better outcomes when compared with a non-biomarker-based approach [11–14].

Based on the unmet need for novel treatments for patients with rare cancers, we have initiated a Rare Tumor Clinic that emphasized a precision medicine strategy utilizing genomic and protein analysis to guide individualized therapy. Herein, we report our preliminary experience across patients as well as an illustrative case highlighting the successful use of ErbB2-targeting therapy in an ultrarare tumor.

**Materials and Methods**

**Patients**

We investigated clinical characteristics and treatment outcomes among patients presenting at the Rare Tumor Clinic at the University of California, San Diego (UCSD) Moores Cancer Center (n = 40). This study was performed in accordance with the guidelines of the UCSD Internal Review Board (PREDICT [Profile Related Evidence Determining Individualized Cancer Therapy] protocol; NCT02478931) an investigational studies for which the patients gave consent.

**Target Identification Through Next-Generation Sequencing and Protein Analysis**

When available, we performed NGS on both tissue and plasma (circulating-tumor DNA [ctDNA]) to seek actionable genomic alterations. Protein markers were also analyzed as appropriate. The majority of tissue NGS were performed at Foundation Medicine with assay panels of 236 or 315 genes according to previously reported methods in a laboratory certified by Clinical Laboratory Improvement Amendments (CLIA; n = 31; Cambridge, MA, www.foundationmedicine.com) [15–17]. This method of sequencing allows for detection of copy number alterations, gene rearrangements, and somatic mutations with 99% specificity and >99% sensitivity for base substitutions at ≥5 mutant allele frequency and >95% sensitivity for copy number alterations. A threshold of ≥8 copies for gene amplification was used. A smaller subset of patients had tissue NGS done using other platforms, including UCSD (n = 2, 397 genes), NanOmiics (n = 2, 434 genes; Culver City, CA, http://www.

**Table 1. Patient characteristics (n = 40)**

| Patient characteristics | n (%) |
|-------------------------|-------|
| Age, years, median, range | 58, 31–87 |
| Gender | | |
| Men | 12 (30%) |
| Women | 28 (70%) |
| Number of previous systemic therapies, median, range | 2, 0–7 |
| Cancer diagnosis | | |
| Castleman’s disease | 4 (10%) |
| Erdheim-Chester disease | 5 (12.5%) |
| High-grade serous ovarian cancer | 4 (10%) |
| Basal cell carcinoma | 2 (5%) |
| Carcinoma of unknown primary | 2 (5%) |
| Papillary serous carcinoma of ovary | 2 (5%) |
| Metaplastic carcinoma of breast | 2 (5%) |
| Other | 12 (30%) |
| Number of targetable genomic or protein anomalies per patient, median, range | |
| Tissue NGS (n = 33)^3 | 3, 0–15 |
| ctDNA (n = 15) | 3, 1–13 |
| IHC (n = 29) | 6, 0–12 |

^3 Sarcoma includes one each of the following: desmoid tumor, endometrial stroma sarcoma, myxofibrosarcoma, liposarcoma, chondrosarcoma, angiosarcoma of breast, and fibromyxoid sarcoma.

^4 Other includes one each of the following: amillary carcinoma, ameloblastoma, anal squamous cell carcinoma, melanocytic sarcoma, neuroendocrine tumor of the uterine cervix, yolk sac tumor, thymoma, fallopian cancer, adenoid cystic carcinoma, ocular melanoma, glioblastoma multiforme, and myoepithelial carcinoma.

^5 Three patients had tissue NGS using two different panels. Abbreviations: ctDNA, circulating-tumor DNA; IHC, immunohistochemistry; NGS, next-generation sequencing.
Blood-derived ctDNA analysis was performed by Guardant Health (n = 33; Redwood City, CA, www.guardanthealth.com), a CLIA-certified laboratory, with assay panels of 54, 68, or 70 genes, as previously described [18]. All ctDNA was sequenced, including somatic ctDNA and the germline ctDNA derived from leukocyte lysis. Germline alterations were filtered out and not reported. The assay reports single nucleotide variants in all genes and selected copy number amplifications, fusions, and indel events [18].

Most protein analyses with immunohistochemistry (IHC) were performed at Caris Life Sciences (n = 25; Irving, TX, www.carismolecularintelligence.com). The IHC markers to be tested were selected by the treating physician. Selected protein death-ligand 1 (PD-L1) testing was performed through Pathline (n = 5) or Emerge (n = 11; Ramsey, NJ, www.pathline-emerge.com/).

Endpoints and Statistical Methods
Descriptive statistics were used to summarize the patient characteristics. Progression-free survival (PFS) was measured using the method of Kaplan and Meier [19] and defined as the time interval between the start of therapy and the date of disease progression or removal from therapy for any reason, whichever occurred first. Patients who were progression-free (for PFS) at the time of last follow-up were censored on that date. Response to therapy was evaluated using the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 [20].

RESULTS
Patient Characteristics
Among 40 patients who presented to the Rare Tumor Clinic, the median age was 58 years (range 31–78 years). Seventy percent of patients were women (28/40). The median number of
previous systemic therapies was 2 (range 0–7). The most common diagnosis was sarcoma (n = 7, 17.5%) followed by Erdheim-Chester disease (12.5% [5/40]), Castleman’s disease (10% [4/40]) and high-grade serous ovarian cancer (10% [4/40]). Overall, 20 distinct diagnoses were seen. Thirty patients had ultrarare tumors, including ameloblastoma, yolk sac liver tumor, ampullary cancer, Castleman’s disease, and desmoid tumor (Table 1 and supplemental online Table 1).

Target Identification with Tissue NGS, ctDNA, and IHC Among Patients with Rare Tumors
Among 40 patients who presented to the Rare Tumor Clinic, 37 patients (92.5%) had at least one theoretically actionable target (by either an FDA-approved or an investigational agent) detected by either tissue NGS, ctDNA, or IHC or similar test (supplemental online Tables 1, 2, and 3).

Tissue NGS
Among 40 patients with rare tumors, 33 patients underwent tissue NGS. Most patients had tissue NGS through Foundation Medicine (n = 31); others had NGS through the laboratory at NantOmics (n = 2), UCSD (n = 2), and Washington University (n = 1). Three patients had NGS using two different panels. (See Materials and Methods section for assay details.) Among those 33 patients, the most common alteration was in the TP53 gene (45.5% [15/33]), followed by CDKN2A/B loss (12.1% [4/33]), FRS2 amplification (12.1% [4/33]), MDM2 amplification (12.1% [4/33]), RB1 alteration (12.1% [4/33]), and KRAS alteration (12.1% [4/33];
detected by ctDNA, all 15 had detectable alterations detected per patient was 3 (range 1–14; Table 1 and supplemental online Table 1). Of the 33 patients evaluable by an FDA-approved drug. Median PFS was 19.7 months for matched therapy and 3.5 months for last prior unmatched therapy (HR 0.26, 95% CI 0.10–0.71; p = .008). Abbreviations: CI, confidence interval; HR, hazard ratio.

Fig. 1A and supplemental online Table 4). The median number of alterations detected per patient was 3 (range 0–24; Table 1 and supplemental online Table 1). The median number of alterations that were potentially targetable with either an FDA-approved or an investigational agent was 3 per patient (range 0–15; supplemental online Tables 1 and 3). Among 33 patients who had tissue NGS, 32 patients had theoretically actionable aberrations. One patient, ID13 (supplemental online Tables 1 and 3), had BRAF V600E mutation detected by polymerase chain reaction, but tissue NGS failed to reveal the same mutation. Of the 33 patients, 32 (97%) had an alteration targetable by an FDA-approved drug (supplemental online Tables 1 and 3).

Blood-Derived ctDNA
ctDNA was evaluated in 33 patients using panels of 54 to 70 genes (see Materials and Methods). Among those 33 patients, 15 had detectable, nonsynonymous, characterized alterations. The most common alteration was in the TP53 gene (21.2% [7/33]), followed by BRAF amplification (18.2% [6/33]), MYC amplification (15.2% [5/33]), and MET amplification (12.1% [4/33]; Fig. 1B and supplemental online Table 5). Among 15 patients with detectable ctDNA alterations, the median number of alterations detected per patient was 3 (range 1–14; Table 1 and supplemental online Table 1). The median number of alterations that were potentially targetable with either an FDA-approved or an investigational agent was 3 per patient (range 1–13; Table 1 and supplemental online Tables 1 and 3). Of the 15 patients who were found to have alterations detected by ctDNA, all 15 had ≥1 alterations potentially targetable by an FDA-approved drug. Of the 33 patients evaluated for ctDNA, 27 patients had both ctDNA and tissue NGS analyses. Concordances between ctDNA and tissue NGS for commonly altered genes were 66.7% (18/27) for TP53, 74.1% (20/27) for BRAF, 88.9% (24/27) for MYC, and 85.2% (23/27) for MET alterations (supplemental online Table 6).

Protein Immunohistochemistry
Among patients who had IHC testing, most had IHC performed by Caris Life Sciences (n = 25). Occasionally, PD-L1 testing was performed through Pathline (22C3 antibody; n = 5) or Emerge (SP142 antibody; n = 11). Altogether, 29 patients had IHC testing, 27 of whom were found to have potentially actionable IHC results (Table 1). Two patients (IDs 20 and 28, Table 1) who did not have actionable IHC only had PD-L1 testing, which was negative. The most common potentially actionable IHC result was RRM1 negative (81.0% [17/21]), followed by ERCC1 negative (70.8% [17/24]), TLE3 positive (70.6% [12/17]), and TOPO1 positive (66.7% [16/24]; Fig. 1C and supplemental online Table 2 show implications of test results). Among 29 patients, the median number of hypothetically druggable IHC results per patient was 6 (range 0–12; Table 1, supplemental online Tables 1 and 2). All IHC results were potentially targetable with FDA-approved agents (supplemental online Table 2).

Clinical Outcome Among Patients Who Presented at Rare Tumor Clinic
Among patients who presented to the Rare Tumor Clinic (n = 40), 21 received matched targeted therapy and were assessable for response (Fig. 2, supplemental online Table 3, and supplemental online Fig. 1). Other patients (n = 19) were not included in response assessment due to the following reasons: treatment had not yet been started or it was too early for first response assessment (n = 6), underlying disease was stable or in remission with prior systemic therapy (n = 6), the patient had undergone surgical management and was on surveillance (n = 4), or the patient had poor performance status that obviated being treated (n = 3).

Among 21 patients who underwent matched targeted therapy, 14.3% (3/21) attained SD (stable disease) ≥6 months, 28.6% (6/21) had partial response (PR), and 9.5% (2/21) achieved complete response (CR), for a total of 52.4% of patients with SD ≥6 months, PR, or CR. Median PFS with matched therapy was 19.6 months (range 0.99+ to 26.1+ months) (Fig. 2, supplemental online Table 3, and supplemental online Fig. 1).

Twelve of the 21 patients were evaluable to compare the therapeutic outcome of matched therapy with last prior unmatched therapy. (Nine were not evaluable for the following reasons: matched therapy was the first-line therapy [n = 5], prior therapy was matched therapy [n = 3], and prior therapy was given in an adjuvant setting [n = 1].) Among those evaluable patients who could be assessed for matched versus last prior unmatched therapy, matched therapy had statistically significant improvement in PFS when compared with last prior unmatched therapy (hazard ratio [HR] 0.26, 95% confidence interval [CI] 0.10–0.71, p = .008, median PFS 19.7 vs. 3.5 months; Fig. 3). Eight of 12 patients (66.7%) had PFS ratio of ≥1.3 (range 0.23–5.60; PFS of matched therapy divided by PFS of last prior unmatched therapy) [21] (supplemental online Fig. 2). On the other hand, no patient achieved PFS ratio of ≥1.3 when subsequent unmatched therapy was administered (range 0.17–1.19; n = 6 were evaluable).

Patient with Ampullary Carcinoma Managed with Matched Therapy Based on Tissue DNA
A 68-year-old woman with ampullary carcinoma presented with recurrent disease of the lung 5 years after completing perioperative management with neoadjuvant and adjuvant chemotherapy. Biopsy of the lung mass confirmed metastatic ampullary carcinoma. Further analysis with tissue NGS revealed multiple alterations, including ERBB2 amplification...
gests that most patients may need an individualized precision genomic makeup [24–26]. Understanding that each individual

example, patients with adenocarcinoma of the lung are now subdivided based on their underlying molecular characteristics, including KRAS (30%), EGFR (10–15%), BRAF (7%), MET (7%), ROS1 (2%), ALK (1%), and RET (<1%) mutations [22]. Although adenocarcinoma of the lung diagnosed by standard microscopic exam is categorized as one of the most common cancers (incidence of 62 per 100,000 per year [23]), patients with ROS1, ALK, and RET alterations comprise infrequent subgroups of this malignancy. Furthermore, through the lens of the “molecular microscope,” each individual can have a distinct and complex genomic makeup [24–26]. Understanding that each individual has a unique molecular portfolio is important because it suggests that most patients may need an individualized precision therapy approach rather than the canonical strategy based on histological commonalities [11–14].

We have utilized the personalized matched targeted therapy approach at the Rare Tumor Clinic (Fig. 2, supplemental online Tables 1, 2, and 3). Overall, among 21 patients who received a matched therapy, 52.4% (11/21) attained SD ≥6 months, PR, or CR (14.3% [3/21], SD ≥6 months; 28.6% [6/21], PR; and 9.5% [2/21], CR) with a median PFS of 19.6 months (range 0.99+ to 26.1+ months). Median overall survival from initiation of matched therapy has not reached (range 12.1 to 29.21 months) (Fig. 2 and supplemental online Table 3). Moreover, the matched therapy approach had a statistically significant improvement in PFS when compared with last prior unmatched therapy (HR: 0.26, 95% CI: 0.10–0.71, p = .008; median PFS 19.7 vs. 3.5 months [n = 12 evaluable patients]); Fig. 3). Our pilot experience with the matched targeted therapy approach in rare cancers suggests feasibility in a Rare Tumor Clinic.

Among our patients with exceptional responses was an individual diagnosed with ampullary carcinoma. Her tumor harbored an ERBB2 amplification, and her disease was successfully managed with anti-human epidermal growth receptor 2 therapy (trastuzumab and pertuzumab; PR, 59% decrease, with PFS of 15.2+ months). Examples of a successful matched targeted therapy approach also include patients treated with immunotherapy. Recent literature suggests that high tumor mutation burden (TMB) status, high microsatellite instability (MSI-high) and the expression/amplification of PD-L1 can be predictive of response to immune checkpoint inhibitors [27, 28]. We have treated three patients with aggressive, advanced/metastatic ultrarare malignancies (two with advanced/metastatic basal cell cancers and one with high-grade, large-cell neuroendocrine gynecologic cancer) with PD-1 inhibitors based on the genomic information (n = 3 patients with high TMB, one of whom also had PDL1 amplification; n = 1 with both high TMB and MSI-high); all had remarkable responses (n = 1 with CR and n = 2 with PR; Fig. 2, supplemental online Tables 1 and 3, ID #4, 16, and 21) [29, 30].

Figure 4. Patient with ampullary carcinoma and ERBB2 amplification treated with anti-human epidermal growth receptor 2 therapy (trastuzumab and pertuzumab). A 68-year-old woman with ampullary carcinoma presented with recurrent disease to lung 5 years after the completion of perioperative therapy with neoadjuvant chemotherapy (5-fluorouracil, irinotecan, and oxaliplatin) followed by Whipple procedure and adjuvant 5-fluorouracil. Biopsy of lung mass confirmed metastatic ampullary carcinoma. Tissue next-generation sequencing revealed alterations, including ERBB2 amplification. Patient received trastuzumab and pertuzumab, demonstrating partial response. Left: Computerized axial tomography (CAT) scan of chest before treatment. Right: CAT scan 14 months after the treatment, showing about 59% reduction in size of lung mass (per Response Evaluation Criteria in Solid Tumors, version 1.1). Progression-free survival = 15.2+ months (supplemental online Table 1, ID #1).

(supplemental online Table 1, ID #1). Matched therapy with a combination of trastuzumab and pertuzumab was initiated after consent (protocol: My Pathway, NCT02091141). The patient achieved a partial response (59% reduction per RECIST 1.1). Treatment is ongoing after 15+ months of therapy (Fig. 4). There was no significant toxicity.

**DISCUSSION**

Here we report our preliminary experience in the Rare Tumor Clinic at the UCSD Center for Personalized Cancer Therapy (n = 40 patients). When available, genomics and protein analyses were performed to guide a precision therapy strategy (supplemental online Table 1). Overall, 37 patients (92.5%) had at least one potentially actionable target (by either an FDA-approved or an investigational agent) by genomics (from tissue and/or blood) as well as protein analyses, indicating that this approach is feasible among patients with rare tumors (supplemental online Tables 1, 2, and 3).

As mentioned, each case of rare cancer is rare by definition; however, when all the subtypes of rare cancers are included, they account for one-fourth of all adult tumors, making “rare” tumors a rather common condition [2, 3]. Moreover, in the current era of genomic typing [8], common tumors are being subdivided into rare subsets or even n-of-one conditions [2, 3]. For example, patients with adenocarcinoma of the lung are now subdivided based on their underlying molecular characteristics, including KRAS (30%), EGFR (10–15%), BRAF (7%), MET (7%), ROS1 (2%), ALK (1%), and RET (<1%) mutations [22]. Although adenocarcinoma of the lung diagnosed by standard microscopic exam is categorized as one of the most common cancers (incidence of 62 per 100,000 per year [23]), patients with ROS1, ALK, and RET alterations comprise infrequent subgroups of this malignancy. Furthermore, through the lens of the “molecular microscope,” each individual can have a distinct and complex genomic makeup [24–26]. Understanding that each individual has a unique molecular portfolio is important because it suggests that most patients may need an individualized precision genomic approach rather than the canonical strategy based on histological commonalities [11–14].

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At the Rare Tumor Clinic, although more than half of the cases demonstrated SD ≥ 6 months, PR, or CR with the matching approach, it is important to note that not all patients had favorable clinical outcomes despite rationally selected treatments (Fig. 2 and supplemental online Table 3). Interestingly, we have previously shown that a high Matching Score (number of alterations matched with targeted therapies divided by total number of alterations identified) is independently associated with improvement in all outcome parameters [31, 32]. The number of patients in the current pilot study in our Rare Tumor Clinic is still too small to calculate the impact of a Matching Score, but this is planned for future reports. There are several other limitations to the current report. This study was performed retrospectively, and 20 different cancer types were included in this study, precluding a more in-depth analysis of any one histology. However, the diversity of tumors could suggest that the conclusions are generalizable across different rare tumors.

**CONCLUSION**

We have demonstrated that genomic and protein analysis to direct therapy is feasible among patients with rare and ultrarare tumors. Most patients (37/40 [92.5%]) had at least one actionable target detected by either genomics or protein analyses (supplemental online Tables 1, 2, and 3). Among patients who received matched targeted therapy, >50% of patients had SD ≥ 6 months, PR, or CR (Fig. 2 and supplemental online Table 3). Moreover, matched targeted therapy had a statistically significant improvement in PFS when compared with last prior unmatched therapy (HR: 0.26, 95% CI: 0.10–0.71, p = .008; Fig. 3). These pilot study results may be important because patients with rare and ultrarare tumors often have no FDA-approved treatments and may be ineligible for clinical trials. For this reason, we (Southwest Oncology Group/National Cancer Institute) recently initiated the national Dual Anti-CTLA-4 and anti-PD-1 blockade in Rare Tumors (DART) immunotherapy trial for rare cancers (NCT02834013). Further studies investigating the efficacy of an individualized precision therapy approach in patients with rare/ultrarare neoplasms are needed.

**ACKNOWLEDGMENTS**

This work was supported in part by the Joan and Irwin Jacobs Fund and by National Cancer Institute grant P30 CA016672 (R.K.).

**AUTHOR CONTRIBUTIONS**

Shumei Kato, Razelle Kurzrock

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See http://www.TheOncologist.com for supplemental material available online.

Editor’s Note:
See the related commentary, “Trailblazing Precision Oncology for Rare Tumor Subtypes,” by Kevin Shee and Todd W. Miller on page 143 of this issue.

For Further Reading:
Todd C. Knepper, Gillian C. Bell, J. Kevin Hicks et al. Key Lessons Learned from Moffitt’s Molecular Tumor Board: The Clinical Genomics Action Committee Experience. The Oncologist 2017;22:144–151; first published on February 8, 2017.

Implications for Practice:
It is clear that the increasing practicality of genetic tumor sequencing technology has led to its incorporation as part of routine clinical practice. Subsequently, many cancer centers are seeking to develop a personalized medicine services and/or molecular tumor board to shepherd precision medicine into clinical practice. This article discusses the key lessons learned through the establishment and development of a molecular tumor board and personalized medicine clinical service. This article highlights practical issues and can serve as an important guide to other centers as they conceive and develop their own personalized medicine services and molecular tumor boards.