Real-World Performance of a Comprehensive Genomic Profiling Test Optimized for Small Tumor Samples

Scott A. Tomlins
Strata Oncology, Ann Arbor, MI.

Daniel H. Hovelson
Strata Oncology, Ann Arbor, MI.

Jennifer M. Suga
Kaiser Permanente, Dept of Medical Oncology, Vallejo, CA.

Daniel M. Anderson
Metro-Minnesota Community Oncology Research Consortium (MMCORC), St Louis Park, MN.

Han A. Koh
Kaiser Permanente, Bellflower, CA.

See next page for additional authors

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Scott A. Tomlins, MD, PhD, Daniel H. Hovelson, PhD, [...], and Daniel R. Rhodes, PhD

Abstract

PURPOSE

Tissue-based comprehensive genomic profiling (CGP) is increasingly used for treatment selection in patients with advanced cancer; however, tissue availability may limit widespread implementation. Here, we established real-world CGP tissue availability and assessed CGP performance on consecutively received samples.

MATERIALS AND METHODS

We conducted a post hoc, nonprespecified analysis of 32,048 consecutive tumor tissue samples received for StrataNGS, a multiplex polymerase chain reaction (PCR)–based comprehensive genomic profiling (PCR-CGP) test, as part of an ongoing observational trial (NCT03061305). Sample characteristics and PCR-CGP performance were assessed across all tested samples, including exception samples not meeting minimum input quality control (QC) requirements (< 20% tumor content [TC], < 2 mm^2 tumor surface area [TSA], DNA or RNA yield < 1 ng/μL, or specimen age > 5 years). Tests reporting ≥ 1 prioritized alteration or meeting TC and sequencing QC were considered successful. For prostate carcinoma and lung adenocarcinoma, tests reporting ≥ 1 actionable or informative alteration or meeting TC and sequencing QC were considered actionable.

RESULTS

Among 31,165 (97.2%) samples where PCR-CGP was attempted, 10.7% had < 20% TC and 59.2% were small (< 25 mm^2 tumor surface area). Of 31,101 samples evaluable for input requirements, 8,089 (26.0%) were exceptions not meeting requirements. However, 94.2% of the 31,101 tested samples were successfully reported, including 80.5% of exception samples. Positive predictive value of PCR-CGP for *ERBB2* amplification in exceptions and/or sequencing QC-failure breast cancer samples was 96.7%. Importantly, 84.0% of tested prostate carcinomas and 87.9% of lung adenocarcinomas yielded results informing treatment selection.

CONCLUSION

Most real-world tissue samples from patients with advanced cancer desiring CGP are limited, requiring optimized CGP approaches to produce meaningful results. An optimized PCR-CGP test, coupled with an inclusive exception testing policy, delivered reportable results for > 94% of samples, potentially expanding the proportion of CGP-testable patients and impact of biomarker-guided therapies.

INTRODUCTION

Molecular profiling of patient tumor specimens is increasingly important as more therapies are indicated in biomarker-defined patient populations.[1] Next-generation sequencing (NGS) is the diagnostic method of choice to assess relevant biomarkers simultaneously from formalin-fixed paraffin-embedded (FFPE) tumor tissue[2-10] or circulating cell-free DNA (cfDNA) liquid biopsy sample.[11-14] The US Center for Medicare and Medicaid Services has deemed tissue-based comprehensive genomic profiling (CGP) by NGS—which includes evaluation of single-nucleotide variants, short insertions and deletions (indels), copy number amplifications and deep deletions, gene fusions, microsatellite instability (MSI), and tumor mutation burden (TMB)—medically necessary for patients with advanced solid tumors (NCD CAG-00450N and LCD L38045).

CONTEXT

Key Objective

Comprehensive genomic profiling (CGP) on tumor tissue can guide treatment for patients with advanced solid tumors. Whether tissue requirements for leading tests (eg, ≥ 25 mm^2 tumor surface area and ≥ 20% tumor content) limit adoption and affect real-world performance is unclear. Here, we determined tissue characteristics and CGP performance in > 30,000 consecutively received tissue samples tested by polymerase chain reaction (PCR)–based comprehensive genomic profiling.

Knowledge Generated

Among > 30,000 consecutively tested tissue samples, 59% had < 25 mm^2 tumor surface area and 11% had < 20% tumor content. PCR-based CGP and a broad exception testing policy (performing testing on samples not meeting minimum input requirements) successfully reported 94% of samples, including 81% of such exception samples.

Relevance

The majority of samples received for tissue-based CGP testing in a real-world cohort are small. An optimized PCR-CGP test and testing of exception samples may increase the proportion of patients who can undergo tissue CGP to guide biomarker-based therapies.

Successful FFPE tissue CGP requires nucleic acid isolation of adequate quantity and quality from tumor cells. Challenges affecting real-world CGP applicability include minute specimens, samples with low tumor content (TC), and low-quality nucleic acid (affected by sample age and fixation).[15] To maximize reportability, most CGP tests have tumor size (generally in mm^2 of tumor surface area [TSA]), TC, and nucleic acid yield or input requirements.[3,5,15] However, tissue CGP test failure rates of 30%-50% in clinical trial cohorts, where testing is attempted on all received samples (or those received below input requirements are considered failures), suggest that current CGP approaches, which are largely based on hybrid capture (HC) library preparation, may only be applicable for a subset of specimens.[16-20]

Herein, we characterized sample attributes of > 30,000 consecutive real-world samples submitted for CGP and the performance of a multiplex polymerase chain reaction (PCR)–based CGP test, StrataNGS, applied to consecutively received and tested samples, including those below sample input requirements.

MATERIALS AND METHODS

Patient Cohort

All samples received for testing from February 13, 2017, to June 25, 2020, from the Strata Trial (NCT03061305), a 100,000-patient observational study for patients with advanced solid tumors, were included. Sample, sequencing quality control (QC) metrics, and clinically reported biomarker results were retrieved from StrataPOINT, a de-identified Strata Trial Results Database (Data Supplement).

CGP Testing

Samples were tested with StrataNGS, the current version of which is a 429-gene polymerase chain reaction–based comprehensive genomic profiling (PCR-CGP) laboratory-developed test for FFPE tumor tissue samples performed on coisolated DNA and RNA, which has been validated on more than 1,900 FFPE tumor samples, and is covered for Medicare beneficiaries ([21,22] and Tomlins et al, manuscript submitted). Earlier StrataNGS versions used during the described study period (Data Supplement) were essentially the same, but only report prioritized mutations from 57 genes (v3) or did not include TMB (v2)[22]; as specimen requirements have not changed, all received samples during the described study period were included.

StrataNGS requires one FFPE block or 10 × 5 µm-thick unstained slides. Minimum sample input QC requirements are TSA ≥ 2 mm^2, TC ≥ 20%, time from sample acquisition < 5 years, and ≥ 1 ng/µL for both DNA and RNA; however, samples not meeting these requirements but with identifiable and isolatable tumor are deemed exceptions and testing is attempted. PCR-CGP data are processed using in-house–developed bioinformatics pipelines and sequencing QC assessments are performed per variant type and a final molecularly informed TC is determined. For samples failing ≥ 1 sequencing QC assessments or with a final TC < 20% (the StrataNGS limits of detection [LOD] for most alteration types), positive alterations may still be called via an expert molecular pathology review process; however, other alterations cannot be definitively ruled out, thus yielding a partial test result. Additional test details and sample QC metric definitions are provided in the Data Supplement; the formal analytical and clinical validation of the current test is described separately (Tomlins et al manuscript submitted).

Reportability, Actionability, and Positive Predictive Value

Tests with ≥ 1 reported prioritized alteration or passing all sequencing QC assessments and having TC ≥ 20% were considered successfully reported. Pan-cancer actionability is described in the Data Supplement. For prostate cancer and non–small-cell lung cancer (NSCLC) adenocarcinoma specific analyses, only reports that could rule in (by being positive for an actionable or exclusionary biomarker) or rule out (by passing all sequencing QC metrics and TC > 20%) biomarker-directed therapy were considered informative, as described in the Data Supplement.

RESULTS

Characteristics of Samples Received for CGP

CGP testing was performed by a single Clinical Laboratory Improvement Amendments–certified, College of American Pathologists–accredited laboratory (Strata Oncology, Ann Arbor, MI) as part of an observational clinical trial evaluating the impact of solid tumor sequencing in the advanced-cancer setting using a previously validated PCR-CGP test (StrataNGS). Across 28 diverse US health systems, 31,165 consecutive unique solid-tumor samples (from 30,565 unique patients) were received for CGP testing between February 13, 2017, and June 25, 2020; an additional 883 samples (Fig 1A) were rejected for various reasons, most commonly scant or no identifiable tissue or tumor (Data Supplement). Rejected samples were excluded from further analysis.

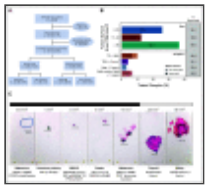

FIG 1.

(A) Breakdown of consecutive PCR-CGP tests ordered from a single commercial clinical sequencing provider between February 13, 2017, and June 25, 2020, including the number of samples rejected before testing, the number of tests performed, the number of ...

Sample characteristics from all 31,165 consecutively tested samples are shown in Table 1, with demographics in the Data Supplement. Notably, 10.7% of tested samples had a final TC < 20% (Table 1), a common minimum TC requirement for CGP tests (including the PCR-CGP test), because corresponding LOD can preclude exclusion of certain variants or variant types below that TC.[3,5] Only 40.8% of samples had TSA ≥ 25 mm^2, with 44.7% of samples having ≤ 10 mm^2 TSA (Table 1). Importantly, TSA ≥ 25 mm^2 is the minimum TSA requirement for several leading commercial HC-CGP tests, including the only US Food and Drug Administration (FDA)–approved tissue CGP companion diagnostic device (FoundationOne CDx).[3,5,23,24]

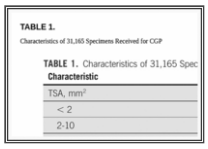
TABLE 1.
Characteristics of 31,165 Specimens Received for CGP
TABLE 1. Characteristics of 31,165 Spec
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TABLE 1.

Characteristics of 31,165 Specimens Received for CGP

As expected, the majority of samples were from biopsies (57.2%); however, cytology cell blocks from fine-needle aspirations and fluid cytology comprised 7.8% of samples (Table 1). As expected, nucleic acid yield was associated with TSA; as among samples with < 2 mm^2 TSA, only 44.5% and 51.7% yielded > 1 ng/μL DNA and RNA, respectively (Data Supplement).

Pan-Tumor CGP Experience

Given our previous experience that PCR-CGP could often deliver partial results even in very poor quality samples, CGP was attempted on *all* 31,165 tumor samples using the PCR-CGP test, including exception samples not passing input requirements (those with TC < 20%, TSA < 2 mm^2, specimen age > 5 years, or DNA and/or RNA concentration < 1 ng/μL); median turnaround time from sample receipt to report release was 7 business days (interquartile range 6-9). Of these 31,165 samples, 31,101 (99.8%) were evaluable for passing sample input requirements and were further considered for assessing sample characteristic impact on PCR-CGP reportability (Fig 1A and Data Supplement).

As shown in Figure 1 and the Data Supplement, 29,293 of 31,101 (94.2%) samples were successfully reported, defined as having at least one reported prioritized alteration or passing all sequencing QC assessments and ≥ 20% final TC. Among the 23,012 (74.0%) samples passing all input requirements, 22,782 (99.0%) were successfully reported. Reportability did not vary by sample size (Fig 1B and Data Supplement), demonstrating that this PCR-CGP test is suitable for minute samples with ≥ 2 mm^2 TSA when other input requirements are met. Notably, among 8,089 (26.0%) exception samples, 6,511 (80.5%) were still successfully reported (Figs 1A and 1B). Samples with TC < 20% comprised the largest (10.7%) and poorest performing exception category (68.2% successfully reported), as expected given that < 20% TC samples automatically fail QC because of the overall

LOD, and thus all such samples without reported prioritized alterations are deemed test failures (not reported) as the presence of variants cannot be excluded. Samples not meeting other input requirements had decreased reportability (85.9%-90.1%) relative to QC-passing samples, but again, reportable results were still provided for most (Fig 1B). The impact of sample characteristics on individual variant class performance is described in the Data Supplement. Representative successfully tested samples across the TSA range are shown in Figure 1C, and results stratified by cancer type and potential biomarker–based actionability are shown in Figure 2. Clinicopathologic and biomarker findings from all samples are provided (Data Supplement).

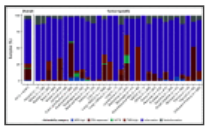

FIG 2.

Pan-cancer assessment of potential actionability from PCR-CGP testing. All sample QC input-evaluable samples profiled between January 1 and June 25, 2020 (n = 8,241), were stratified by tumor type and assigned to one actionability class on the basis of ...

To address the positive predictive value (PPV) of prioritized biomarkers reported from exception and/or sequencing QC samples, we determined the PPV of PCR-CGP for *ERBB2* amplification in all exception and/or sequencing QC-failure breast cancer samples with orthogonal clinical *ERBB2* amplification status. As shown in the Data Supplement, the PPV in these 60 samples was 96.7%, similar to 98.5% PPV for *ERBB2* amplifications determined in the PCR-CGP test clinical validation (only including sample and sequencing QC-passing samples; Tomlins et al, manuscript in review); genomic data from a true-positive 1.5-mm^2, TC-exception sample are shown in Figure 3. Likewise, an example report from a successfully reported TC-exception NSCLC sample harboring expert-reviewed prioritized *TP53* mutation and *EML4-ALK* fusion is shown in the Data Supplement. Additionally, as shown in the Data Supplement, biomarker frequencies were highly correlated (overall Pearson $r = 0.990$; per tumor type $r = 0.897$-0.999) to those from MSK-IMPACT, an independent, large, single-institution, advanced solid-tumor profiling experience using an FDA-cleared HC-CGP test.[7] Lastly, no significant changes in the percentage of samples meeting sample QC metrics or reportability were observed across the study period, consistent with continued desire for CGP testing of challenging tissue samples (Data Supplement).

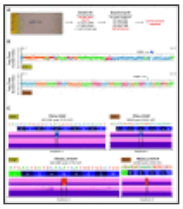

FIG 3.

Underlying genomic data supporting a reported *ERBB2* amplification in a breast cancer TC and tumor size exception sample. (A) Hematoxylin and eosin slide from a 1.5-mm^2 TSA lung biopsy from a patient with metastatic breast cancer submitted for PCR-CGP. ...

Prostate Carcinoma Experience

The FDA approval of pembrolizumab for all advanced microsatellite instability–high (MSI-H) solid tumors and the approval of rucaparib (for *BRCA1/2*) and olaparib (for *BRCA1/2*, *ATM*, and 11 other potential homologous recombination deficiency [HRD] genes) for metastatic castration-resistant prostate cancer led the National Comprehensive Cancer Network to recommend MSI-H and HRD gene testing for all men with metastatic castration-resistant prostate cancer given relatively high frequency of these alterations.[17,25-30]

As shown in Figure 4A and the Data Supplement, among 1,344 prostate cancer samples, although the overall exception proportion was similar to the pan-tumor input-evaluable cohort (33.7% *v* 26.0%), prostate cancer had the highest frequency of age exception samples (10.9%) and overall frequency of samples age > 5 years (14.9%; Data Supplement), consistent with the frequent delay between diagnosis and recurrence after definitive therapy and/or androgen deprivation therapy. To assess therapy selection performance, we separated reports into those yielding informative therapy selection results (able to rule in or out biomarker-guided therapy) for MSI status and HRD gene (*BRCA1*, *BRCA2*, and *ATM*) alterations and those yielding noninformative results where additional testing (eg, either by liquid biopsy or obtaining and testing another sample) would be required. Overall, 84.0% of prostate cancer samples yielded informative results (including 60.9% of exception samples; Fig 4B and Data Supplement). Importantly, the positive MSI-H and HRD biomarker rate was similar between samples meeting input requirements versus exceptions (14.7% *v* 12.6%; Fig 2B and Data Supplement). Together, this suggests that approximately 84% of patients with advanced prostate cancer desiring CGP have sufficient tissue samples for informative PCR-CGP, minimizing the potential need to obtain and test a new sample or pursue liquid biopsy testing (Fig 4C).

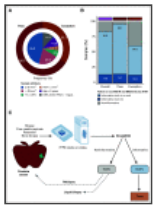

FIG 4.

(A) Donut plot characterizing the composition of consecutively tested, sample input characteristic-evaluable prostate cancer samples (n = 1,344) from the overall PCR-CGP test cohort. The outer ring indicates the percentage of samples meeting (pass: dark ...

NSCLC Adenocarcinoma Experience

CGP is especially relevant in NSCLC given the large number of recommended biomarkers required to guide therapy (Data Supplement). Among 1,144 NSCLC adenocarcinoma samples, the exception proportion was greater than the overall pan-tumor cohort (40.6% *v* 26.0%), with 21.6% having TC < 20% and 12.1% having TSA < 2 mm^2 (Fig 5A and Data Supplement). Yet, 87.9% of NSCLC adenocarcinoma samples yielded informative (able to rule in or out biomarker-guided therapy) results (Fig 5B and Data Supplement), including 98.4% of samples meeting input requirements and 72.6% of exceptions. Importantly, overall informative biomarker frequencies in this NSCLC adenocarcinoma cohort were similar to those observed in NSCLC adenocarcinoma from the MSK-IMPACT cohort (Pearson correlation coefficient $r^2 = 0.96$, $P < .001$; Figs 5C and Data Supplement).

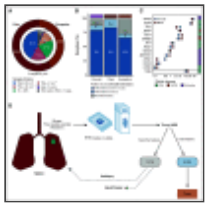

FIG 5.

(A) Donut plot characterizing the composition of consecutively tested, sample input characteristic-evaluable NSCLC adenocarcinoma samples (n = 1,142) from the overall PCR-CGP test cohort. The outer ring indicates the percentage of samples meeting (pass: ...

Like prostate cancer, TC < 20% NSCLC adenocarcinoma samples had the lowest informative rate (Data Supplement), as negative results cannot be definitively asserted in this sub-LOD setting, which can particularly affect detection of nonmutation biomarkers given the frequent difficulty of knowing the true TC in the absence of TC-defining mutations. However, in contrast to the low actionable biomarker frequency in prostate cancer, actionable or informative biomarkers are frequent in NSCLC adenocarcinoma. Hence, the positive informative biomarker detection rate in NSCLC adenocarcinoma TC-exception samples (58.7%) is only marginally less than that in samples meeting input requirements (82.0%), and all other sample exception groups had positive detection rates of 79.7%-81.2% (Data Supplement). These results suggest that approximately 88% of patients with advanced NSCLC adenocarcinoma desiring CGP have sufficient tissue samples for informative PCR-CGP, minimizing the potential need for rebiopsy or liquid biopsy (Fig 5C).

DISCUSSION

Herein, we present the tissue characteristics and PCR-CGP test performance from more than 30,000 consecutively tested solid-tumor samples from patients with advanced cancer submitted from 28 diverse US health systems through a multi-institutional observational clinical trial. Importantly, testing during the study period was not restricted by tumor type and was provided at no cost to patients. Sites were provided with minimal sample submission requirements and PCR-CGP testing was attempted for essentially all samples with identifiable tumor, providing a unique view on real-world tumor tissue availability and CGP test performance.

Unexpectedly, we found that most submitted samples were limited, with 10.7% having < 20% TC and 44.7% with TSA ≤ 10 mm^2. Despite these challenges, PCR-CGP reported results for 94.2% of all tested tumor samples, including 80.5% of exception samples not meeting input criteria. Specifically, among NSCLC adenocarcinoma, we found that limited tissue was even more pronounced with 21.6% of samples having < 20% TC and an additional 12.1% having < 2 mm^2 TSA; however, PCR-CGP testing successfully reported treatment selection informative results in 87.9% of samples. Similar results were observed in prostate carcinoma, where despite a substantially lower positive informative biomarker rate, PCR-CGP produced treatment selection informative results in 84.0% of samples.

We attribute PCR-CGP's high reportability rates to two main factors. First, multiplex PCR-based CGP library preparation method enabled minimal input (eg, TSA 2 mm^2) versus leading commercially available HC-CGP tests requiring ≥ 25 mm.[2,3,5,23,24] Notably, only 40.8% of samples in our total received cohort met this requirement and the proportion was even smaller in input-evaluable NSCLC samples (23.6%, lung—NSCLC; Data Supplement). Consistent with these findings, in clinical trials testing available FFPE tissue samples from patients with advanced NSCLC or CRPC, HC-CGP failure rates of approximately 30%-40% have been reported.[16-20] Thus, the PCR-CGP test, with its lower input requirements, has the potential to expand the proportion of testable tumor samples.

Second, as PCR-CGP can generate some data on nearly all samples and because of our belief that even a single biomarker may be highly actionable (regardless of the ability to assess all CGP variant classes), we used a liberal exception testing policy, where we attempted testing on nearly all samples with identifiable tumor, even if not meeting all input requirements. To maximize actionable insights from the available tissue, this necessitated PCR-CGP bioinformatic pipeline development and QC metrics optimized for minute, low-quality samples, and reporting included expert-level variant review. As expected, low-TC samples were the most challenging (68.2% reportability), given the inability to exclude the presence of alterations in such samples on the basis of test LOD (data and an example report from two such samples are shown in Fig 3 and the Data Supplement2). Likewise, samples failing more than one sample QC metric were less frequently reportable (Data Supplement), which may guide decisions on rebiopsy or liquid biopsy testing. However, the high PPV (96.7%) for *ERBB2* amplification in exception and/or sequencing QC-failure breast cancer samples supports the potential clinical utility of our approach.

Liquid biopsy represents an alternative CGP methodology when no tissue is available or procurement is difficult. Although highly specific for treatment selection,[16] as evidenced by the recent FDA approval of both the FoundationOne Liquid CDx and Guardant360 CDx cfDNA CGP tests, cfDNA sensitivity is challenged by the lack of circulating tumor DNA in some patients and differentiating an informative negative test from a lack of detectable cfDNA (eg, does an NSCLC cfDNA test identifying a *TP53* mutation at 0.5% variant allele frequency [VAF] exclude the possibility of an *EGFR* exon 19 deletion?) given the prevalence of clonal hematopoiesis (CHIP) and the poor PPV of de novo alterations at VAFs < 1%.[31-36] For example, in NSCLC, the Guardant360 CDx test showed only 67.4%-77.7% positive predictive agreement versus tissue-based *EGFR* testing (exon 19 deletions/p.L858R/p.T790M).[33] In prostate cancer, liquid biopsy may be particularly appealing in patients with very old diagnostic tissue or bone-only disease.[37] Encouragingly, sensitivity for actionable *BRCA1/2* mutations was 93% in a comparison of cfDNA FoundationACT/One Liquid versus FoundationOne tissue testing in CRPC rucaparib screening studies; however, cfDNA-exclusive mutations had low VAF relative to cfDNA-based TC,[38] suggesting that they may be subclonal and thus of unclear therapeutic relevance. Likewise, *BRCA2* deep deletion detection is critical but challenging as detection (via tissue or cfDNA) requires 30%-40% TC; however, < 25% of patients in the cfDNA-based rucaparib studies had ≥ 35% cfDNA TC[38] versus 79.5% of the 2,045 prostate cancer samples having ≥ 35% tissue TC herein. Last, CHIP is particularly relevant in prostate cancer as a recent cfDNA-based laboratory-developed test found 10% of men harbored CHIP variants in olaparib-associated HRD genes, most frequently *ATM*.[39] These results complicate interpreting efficacy of poly (ADP-ribose) polymerase inhibitor trials enrolling men with cfDNA-based *ATM* variants[40] and olaparib treatment selection. Hence, these issues highlight the difficult decisions clinicians face when deciding between tissue versus liquid testing.[36,37]

A limitation of our study is the lack of head-to-head testing with HC-based tissue tests and/or liquid biopsy testing, necessitating carefully designed future studies to directly compare real-world performance. Likewise, patients with noninformative PCR-CGP testing in this cohort were not followed to determine whether rebiopsy or liquid biopsy was pursued and impact on clinical management. Additionally, the PCR-CGP test used herein does not report a global HRD assessment.[41] Last, PCR-CGP testing treatment response has not been determined, and thus, our approach's clinical impact is unclear.

The growing compendium of biomarker-guided targeted therapies and immunotherapies makes clear the importance of CGP for treatment selection in patients with advanced cancer. Our study demonstrates that although most patients desiring CGP in a real-world cohort have challenging tissue specimens, optimized approaches including PCR-CGP and broadly testing sample exceptions can maximize actionable information.

Notes

Scott A. Tomlins

Employment: Strata Oncology

Leadership: Strata Oncology

Stock and Other Ownership Interests: Strata Oncology, Javelin Oncology

Consulting or Advisory Role: Janssen, Astellas Medivation, Strata Oncology

Research Funding: Astellas Medivation

Patents, Royalties, Other Intellectual Property: I am a coinventor on a patent issued to the University of Michigan on ETS gene fusions in prostate and am included in the royalty stream. The diagnostic field of use was licensed to Hologic/Gen-Probe (who sublicensed some rights to Ventana/Roche) and is licensed to LynxDx. I am a coinventor on a patent issued to Strata Oncology related to MSI determination and checkpoint inhibitor benefit

Travel, Accommodations, Expenses: Strata Oncology, Genzyme

Daniel H. Hovelson

Employment: Strata Oncology

Elizabeth C. Dees

Consulting or Advisory Role: Novartis, Strata Oncology, G1 Therapeutics

Research Funding: Novartis, Genentech/Roche, Pfizer, Merck, H3 Biomedicine, Meryx Pharmaceuticals

Travel, Accommodations, Expenses: G1 Therapeutics

Mark E. Burkard

Consulting or Advisory Role: Pointcare genomics, Strata Oncology, Novartis

Research Funding: AbbVie, Strata Oncology, Puma Biotechnology, Loxo, Merck, Arcus Ventures, Apollomics, Elevation Oncology, Genentech

Patents, Royalties, Other Intellectual Property: I have a patent for implantable/localized drug delivery device that can sample the tumor microenvironment and deliver drug, I have a patent for a method to detect recombination events with CRISPR-mediated editing, and I have a patent for conducting expansion microscopy without specialized equipment

Michael Guarino

Stock and Other Ownership Interests: Johnson and Johnson, Johnson and Johnson

Travel, Accommodations, Expenses: McKesson, ARMO BioSciences, AstraZeneca, BMS, De Novo Pharmaceuticals

Marc R. Matrana

Consulting or Advisory Role: Strata Oncology

Speakers' Bureau: Bristol Myers Squibb, AstraZeneca, Merck, Eisai, Genentech, Janssen, Exelixis

Eddy S. Yang

Consulting or Advisory Role: Strata Oncology, AstraZeneca, Bayer, Clovis Oncology, Lilly

Research Funding: Lilly, Novartis, Clovis Oncology, Puma Biotechnology

Benjamin M. Parsons

Consulting or Advisory Role: Celgene, Amgen, AstraZeneca

Speakers' Bureau: Amgen, Celgene, AstraZeneca

Open Payments Link: https://openpaymentsdata.cms.gov/physician/795031

Michael A. Thompson

Stock and Other Ownership Interests: Doximity

Consulting or Advisory Role: Celgene, VIA Oncology, Takeda, GlaxoSmithKline, Strata Oncology, Syapse, Adaptive Biotechnologies, AbbVie, GRAIL, Epizyme, Janssen Oncology

Research Funding: Takeda, Bristol Myers Squibb, TG Therapeutics, Cancer Research and Biostatistics, AbbVie, PrECOG, Strata Oncology, Lynx Biosciences, Denovo Biopharma, ARMO BioSciences, GlaxoSmithKline, Amgen

Patents, Royalties, Other Intellectual Property: UpToDate, Peer Review for Plasma Cell Dyscrasias (Editor: Robert Kyle)

Travel, Accommodations, Expenses: Takeda, GlaxoSmithKline, Syapse

Other Relationship: Doximity

Open Payments Link: https://openpaymentsdata.cms.gov/physician/192826/summary

William J. Edenfield

Consulting or Advisory Role: Chimerix

Suresh Nair

Stock and Other Ownership Interests: Moderna Therapeutics, Novavax, Biontech, Gilead Sciences

Research Funding: Bristol Myers Squibb, Merck, Nektar

Adedayo Onitilo

Consulting or Advisory Role: Kite, a Gilead company, Envision Communications

Speakers' Bureau: GlaxoSmithKline, Puma Biotechnology, Kite/Gilead, AbbVie

Robert Siegel

Research Funding: Merck, Mirati Therapeutics, GRAIL, Altor BioScience, Galera Therapeutics, Apollomics, Strata Oncology, Arcus Biosciences, Bristol Myers Squibb, Cancer Insight, Puma Biotechnology, Conjupro Biotherapeutics, Razor Genomics, Sanofi, Seattle Genetics

Other Relationship: American Board of Internal Medicine (ABIM)

William J. Irvin

Research Funding: Merck, Altor BioScience, Odonate Therapeutics, Boston Biomedical, Novartis, Pfizer, Seattle Genetics, Altor BioScience, AstraZeneca

Arvinda Padmanabhan

Speakers' Bureau: Clovis Oncology, Roche

Anneliese Gonzalez

Research Funding: Novartis, Radius Health, Astellas Pharma

Paul Harms

Research Funding: Q32 Bio

Jennifer Hipp

Employment: Strata Oncology

Stock and Other Ownership Interests: Strata Oncology

Consulting or Advisory Role: PathAI

Kat Kwiatkowski

Employment: Strata Oncology

Stock and Other Ownership Interests: Strata Oncology, Epizyme, Loxo, Editas Medicine, Intuitive Surgical

Khalis Mitchell

Employment: Strata Oncology

Stock and Other Ownership Interests: Mirati Therapeutics

Javed Siddiqui

Consulting or Advisory Role: Strata Oncology, LynxDx

Hana Vakil

Employment: Strata Oncology

Stock and Other Ownership Interests: Strata Oncology

D. Bryan Johnson

Employment: Strata Oncology

Stock and Other Ownership Interests: Strata Oncology

Daniel R. Rhodes

Employment: Strata Oncology, Javelin Oncology

Leadership: Strata Oncology, Javelin Oncology

Stock and Other Ownership Interests: Strata Oncology, Javelin Oncology

Patents, Royalties, Other Intellectual Property: I am paid royalties from the University of Michigan on license revenues related to a patent on prostate cancer gene fusions

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DISCLAIMER

Authors who are employed by the study sponsor Strata Oncology were involved in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation of the manuscript; and the decision to submit the manuscript for publication.

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De-identified participant and molecular data (including raw data) are made available to all Strata Trial partnered institutions. De-identified participant and biomarker data are provided in the Data Supplement.

AUTHOR CONTRIBUTIONS

Conception and design: Scott A. Tomlins, Kat Kwiatkowski, D. Bryan Johnson, Daniel R. Rhodes

Administrative support: Khalis Mitchell

Provision of study materials or patients: Jennifer M. Suga, Elizabeth C. Dees, Mark E. Burkard, Michael Guarino, Jamil Khatri, Malek M. Safa, Eddy S. Yang, Benjamin M. Parsons, Jennifer N. Slim, Michael A. Thompson, William J. Edenfield, Adedayo Onitilo, Robert Siegel, Alan Miller, William J. Irvin, Abdul Hai Mansoor, Andrew Kellum, Paul Harms

Collection and assembly of data: Scott A. Tomlins, Jennifer M. Suga, Daniel M. Anderson, Han A. Koh, Elizabeth C. Dees, Brendan McNulty, Mark E. Burkard, Michael Guarino, Jamil Khatri, Malek M. Safa, Marc R. Matrana, Eddy S. Yang, Alex R. Menter, Jennifer N. Slim, Michael A. Thompson, Leon Hwang, William J. Edenfield, Suresh Nair, Adedayo Onitilo, Alan Miller, Timothy Wassenaar, William Schulz, Arvinda Padmanabhan, Anneliese Gonzalez, Andrew Kellum, Paul Harms, Jayson Falkner, Andrew Fischer, Jennifer Hipp, Kat Kwiatkowski, Lorena Lazo de la Vega

Data analysis and interpretation: Scott A. Tomlins, Daniel H. Hovelson, Elizabeth C. Dees, Eddy S. Yang, Benjamin M. Parsons, Michael A. Thompson, William J. Edenfield, Robert Siegel, William J. Irvin, Vallathucherry Harish, Stephanie Drewery, Travis Reeder, Javed Siddiqui, Hana Vakil, D. Bryan Johnson

Manuscript writing: All authors

Final approval of manuscript: All authors

Accountable for all aspects of the work: All authors

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

Scott A. Tomlins

Employment: Strata Oncology

Leadership: Strata Oncology

Stock and Other Ownership Interests: Strata Oncology, Javelin Oncology

Consulting or Advisory Role: Janssen, Astellas Medivation, Strata Oncology

Research Funding: Astellas Medivation

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Travel, Accommodations, Expenses: Strata Oncology, Genzyme

Daniel H. Hovelson

Employment: Strata Oncology

Elizabeth C. Dees

Consulting or Advisory Role: Novartis, Strata Oncology, G1 Therapeutics

Research Funding: Novartis, Genentech/Roche, Pfizer, Merck, H3 Biomedicine, Meryx Pharmaceuticals

Travel, Accommodations, Expenses: G1 Therapeutics

Mark E. Burkard

Consulting or Advisory Role: Pointcare genomics, Strata Oncology, Novartis

Research Funding: AbbVie, Strata Oncology, Puma Biotechnology, Loxo, Merck, Arcus Ventures, Apollomics, Elevation Oncology, Genentech

Patents, Royalties, Other Intellectual Property: I have a patent for implantable/localized drug delivery device that can sample the tumor microenvironment and deliver drug, I have a patent for a method to detect recombination events with CRISPR-mediated editing, and I have a patent for conducting expansion microscopy without specialized equipment

Michael Guarino

Stock and Other Ownership Interests: Johnson and Johnson, Johnson and Johnson

Travel, Accommodations, Expenses: McKesson, ARMO BioSciences, AstraZeneca, BMS, De Novo Pharmaceuticals

Marc R. Matrana

Consulting or Advisory Role: Strata Oncology

Speakers' Bureau: Bristol Myers Squibb, AstraZeneca, Merck, Eisai, Genentech, Janssen, Exelixis

Eddy S. Yang

Consulting or Advisory Role: Strata Oncology, AstraZeneca, Bayer, Clovis Oncology, Lilly

Research Funding: Lilly, Novartis, Clovis Oncology, Puma Biotechnology

Benjamin M. Parsons

Consulting or Advisory Role: Celgene, Amgen, AstraZeneca

Speakers' Bureau: Amgen, Celgene, AstraZeneca

Open Payments Link: https://openpaymentsdata.cms.gov/physician/795031

Michael A. Thompson

Stock and Other Ownership Interests: Doximity

Consulting or Advisory Role: Celgene, VIA Oncology, Takeda, GlaxoSmithKline, Strata Oncology, Syapse, Adaptive Biotechnologies, AbbVie, GRAIL, Epizyme, Janssen Oncology

Research Funding: Takeda, Bristol Myers Squibb, TG Therapeutics, Cancer Research and Biostatistics, AbbVie, PrECOG, Strata Oncology, Lynx Biosciences, Denovo Biopharma, ARMO BioSciences, GlaxoSmithKline, Amgen

Patents, Royalties, Other Intellectual Property: UpToDate, Peer Review for Plasma Cell Dyscrasias (Editor: Robert Kyle)

Travel, Accommodations, Expenses: Takeda, GlaxoSmithKline, Syapse

Other Relationship: Doximity

Open Payments Link: https://openpaymentsdata.cms.gov/physician/192826/summary

William J. Edenfield

Consulting or Advisory Role: Chimerix

Suresh Nair

Stock and Other Ownership Interests: Moderna Therapeutics, Novavax, Biontech, Gilead Sciences

Research Funding: Bristol Myers Squibb, Merck, Nektar

Adedayo Onitilo

Consulting or Advisory Role: Kite, a Gilead company, Envision Communications

Speakers' Bureau: GlaxoSmithKline, Puma Biotechnology, Kite/Gilead, AbbVie

Robert Siegel

Research Funding: Merck, Mirati Therapeutics, GRAIL, Altor BioScience, Galera Therapeutics, Apollomics, Strata Oncology, Arcus Biosciences, Bristol Myers Squibb, Cancer Insight, Puma Biotechnology, Conjupro Biotherapeutics, Razor Genomics, Sanofi, Seattle Genetics

Other Relationship: American Board of Internal Medicine (ABIM)

William J. Irvin

Research Funding: Merck, Altor BioScience, Odonate Therapeutics, Boston Biomedical, Novartis, Pfizer, Seattle Genetics, Altor BioScience, AstraZeneca

Arvinda Padmanabhan

Speakers' Bureau: Clovis Oncology, Roche

Anneliese Gonzalez

Research Funding: Novartis, Radius Health, Astellas Pharma

Paul Harms

Research Funding: Q32 Bio

Jennifer Hipp

Employment: Strata Oncology

Stock and Other Ownership Interests: Strata Oncology

Consulting or Advisory Role: PathAI

Kat Kwiatkowski

Employment: Strata Oncology

Stock and Other Ownership Interests: Strata Oncology, Epizyme, Loxo, Editas Medicine, Intuitive Surgical

Khalis Mitchell

Employment: Strata Oncology

Stock and Other Ownership Interests: Mirati Therapeutics

Javed Siddiqui

Consulting or Advisory Role: Strata Oncology, LynxDx

Hana Vakil

Employment: Strata Oncology

Stock and Other Ownership Interests: Strata Oncology

D. Bryan Johnson

Employment: Strata Oncology

Stock and Other Ownership Interests: Strata Oncology

Daniel R. Rhodes

Employment: Strata Oncology, Javelin Oncology

Leadership: Strata Oncology, Javelin Oncology

Stock and Other Ownership Interests: Strata Oncology, Javelin Oncology

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Scott A. Tomlins, MD, PhD, [1] Daniel H. Hovelson, PhD, [1] Jennifer M. Suga, MD, [2] Daniel M. Anderson, MD, MPH, [3] Han A. Koh, MD, [4] Elizabeth C. Dees, MD, MSc, ScM, [5] Brendan McNulty, MD, [6] Mark E. Burkard, MD, PhD, [7] Michael Guarino, MD, [8] Jamil Khatri, MD, [8] Malek M. Safa, MD, [9] Marc R. Matrana, MD, [10] Eddy S. Yang, MD, PhD, [11] Alex R. Menter, MD, [12] Benjamin M. Parsons, DO, [13] Jennifer N. Slim, DO, [14] Michael A. Thompson, MD, PhD, [15] Leon Hwang, MD, [16] William J. Edenfield, MD, [17] Suresh Nair, MD, [18] Adedayo Onitilo, MD, [19] Robert Siegel, MD, [20] Alan Miller, MD, [21] Timothy Wassenaar, MD, [22] William J. Irvin, MD, [23] William Schulz, MD, [24] Arvinda Padmanabhan, MD, [25] Vallathucherry Harish, MD, [26] Anneliese Gonzalez, MD, [27] Abdul Hai Mansoor, MD, [28] Andrew Kellum, MD, [29] Paul Harms, MD, PhD, [30] Stephanie Drewery, BS, [1] Jayson Falkner, PhD, [1] Andrew Fischer, BS, [1] Jennifer Hipp, MD, PhD, [1] Kat Kwiatkowski, MPH, PhD, [1] Lorena Lazo de la Vega, PhD, [1,31] Khalis Mitchell, MS, [1] Travis Reeder, MLS, [1] Javed Siddiqui, MS, [1] Hana Vakil, MD, [1] D. Bryan Johnson, MSEE, [1] and Daniel R. Rhodes, PhD [1]

[1]Strata Oncology, Ann Arbor, MI
[2]Kaiser Permanente, Dept of Medical Oncology, Vallejo, CA

[3]Metro-Minnesota Community Oncology Research Consortium (MMCORC), St Louis Park, MN

[4]Kaiser Permanente, Bellflower, CA

[5]The University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, NC

[6]UNC Rex Healthcare, Raleigh, NC

[7]University of Wisconsin Carbone Cancer Center, Madison, WI

[8]ChristianaCare's Helen F. Graham Cancer Center & Research Institute, Newark, DE

[9]Kettering Cancer Center, Kettering, OH

[10]Ochsner Cancer Institute, New Orleans, LA

[11]University of Alabama at Birmingham, Birmingham, AL

[12]Kaiser Permanente Medical Group, Denver, CO

[13]Gundersen Health System, La Crosse, WI

[14]MultiCare, Auburn, WA

[15]Advocate Aurora Health Care, Milwaukee, WI

[16]Kaiser Permanente Mid Atlantic, Rockville, MD

[17]Prisma Health Cancer Institute, Greenville, SC

[18]Lehigh Valley Health Network, Allentown, PA

[19]Marshfield Clinic, Marshfield WI

[20]Bon Secours St Francis Cancer Center, Greenville, SC

[21]SCL Health Colorado, Broomfield, CO

[22]ProHealth Care, Waukesha, WI

[23]Bon Secours St Francis Medical Center Midlothian, Midlothian, VA

[24]Swedish American, Rockford, IL

[25]Baptist Health, Lexington, KY

[26]High Point Medical Center, High Point, NC

[27]UT Health-Memorial Hermann Cancer Institute, Houston, TX

[28]Kaiser Permanente Northwest, Portland, OR

[29]North Mississippi Medical Center, Tupelo, MS

[30]University of Michigan Health Systems, Ann Arbor, MI

[31]Current address: Brigham & Women's Hospital, Boston, MA

Scott A. Tomlins, MD, PhD, Strata Oncology, 8192 Jackson Rd, Suite A, Ann Arbor, MI 48103; e-mail: scott.tomlins@strataoncology.com.

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