Strata PATH™: A multicohort, non-randomized, open-label phase 2 trial to explore efficacy and safety of FDA-approved cancer therapies in novel biomarker-guided patient population

Abstract #CT059

Kat Kwiatkowski[1], Laura E. Lamb[1], Scott A. Tomlins[1], D. Bryan Johnson[1], Daniel H. Hovelson[1], Nickolay Khazanov[1], Benjamin J. Bulen[1], Travis Reeder[1], Daniel R. Rhodes[1]

[1]Strata Oncology, Ann Arbor, MI

Lorem ipsum

Purpose

The Strata Precision Indications for Approved Therapies (Strata PATH; Protocol STR-004-001; NCT05097599) trial is a non-randomized open-label, prospective pan-tumor therapeutic trial designed to evaluate the efficacy and safety of multiple FDA-approved cancer therapies in new, biomarker-guided patient populations. Enrollment into a cohort of this basket trial is based on novel biomarkers including DNA, quantitative RNA expression and novel multivariate algorithms that account for both tumor and tumor microenvironment variables hypothesized to predict improved therapeutic response. The therapeutic classes evaluated in Strata PATH include targeted therapies, antibody-drug conjugates, immunotherapies, and angiogenesis inhibitors.

Trial Design

Key eligibility criteria are pathologically confirmed solid tumor. The study is currently enrolling traditionally defined metastatic, relapsed, refractory, or advanced stage III or IV solid tumors that have exhausted standard of care options. Patients are assigned to treatment by tumor type and biomarker status (Table 1). All patients will be treated until disease progression, unacceptable toxicity, patient/physician decision to withdraw, or 3 years of treatment from the date of consent. Primary Outcome measure includes overall response rate (ORR) as assessed by the investigator according to RECIST version 1.1. Secondary outcome measures include ctDNA response, Duration of Response (DoR), Time to Treatment Discontinuation (TTD), Time to Next Treatment (TTNT), Overall Survival (OS), safety, and ctDNA Response Rate. Enrollment is ongoing with 35 participants per cohort for up to 20 cohorts (700 participants total).

Summary

Strata PATH provides the next important step forward in precision medicine, guiding clinical trial and therapy selection by expanding biomarker testing to quantifiable RNA expression and multivariant algorithm based molecular testing.

Additional Information

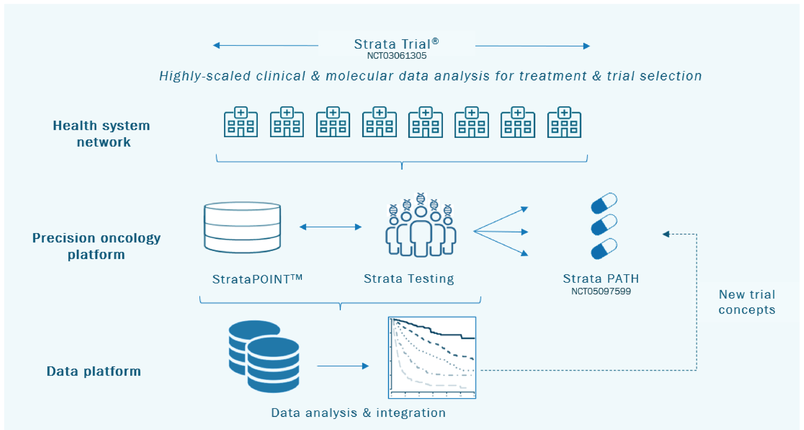
Questions?
Contact Laura Lamb, PhD at Laura.Lamb@strataoncology.com

Trial information?
Contact Kat Kwiatkowski, PhD at Kat.Kwiatkowski@strataoncology.com

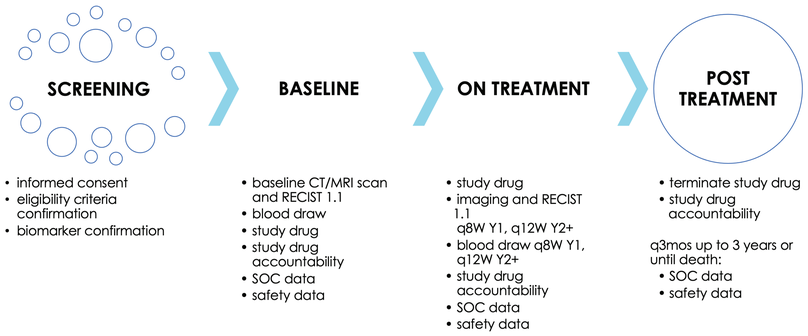
Scan using your phones camera for PDF of poster

Conflict of Interest Disclosure: All authors are equity holders and/or employees for Strata Oncology. ST and DR are equity holders in Javelin Oncology. ST previously served as a consultant to Strata Oncology and has consulted for Astellas/Medivation and Janssen. He has received research (to University of Michigan) funding from Astellas and has received travel support from the Prostate Cancer Foundation. All authors affirm that this abstract will not be used to sell a particular product or service.

Figure 1. Strata Oncology Development Paradigm - Strata Oncology's precision oncology development framework incorporates a feedback loop including molecular data paired with clinical outcomes to accelerate the impact of precision oncology



Study Schematic



Study Population

Inclusion Criteria:

1. Male or female > 18 years of age.
2. Pathologically confirmed solid tumor.
3. Participants must be able to follow study visit schedule and be willing to provide peripheral blood samples at the indicated time points.
4. CGP results need to be from a test conducted in a CLIA approved laboratory and archival formalin-fixed, paraffin-embedded (FFPE) tumor tissue is required for confirmatory testing of non-Strata test results unless otherwise indicated within the cohort-specific protocol criteria.
5. Biomarker positive for the defined cohort.
6. Individuals with non-primary, treated or stable brain metastases must show no radiographic evidence of progression within 4 weeks prior to consent.
7. Adequate bone marrow, organ function & laboratory parameters as determined by the treating physician unless otherwise indicated within the cohort-specific protocol criteria.
8. Adequate cardiac function:
   a. Left ventricular ejection fraction (LVEF) ≥ 50%.
   b. QTc interval ≤ 470 ms (females) or ≤ 450 ms (males) average preferred.

Exclusion Criteria:

1. Receiving another anticancer therapy.
2. Major surgery within 4 weeks prior to study entry.
3. Has received a systemic anticancer therapy within 3 weeks of first study dose.
4. Individuals with a history of a second malignancy are ineligible except for the following circumstances:
   a. Individuals with a history of other malignancies are eligible if they have been disease-free for at least 3 years or are deemed by the investigator to be at low risk for recurrence of that malignancy.
   b. Individuals with the following cancers that have been diagnosed and treated within the past 3 years are eligible: cervical/prostate carcinoma in situ, superficial bladder cancer, non-melanoma cancer of the skin.
   c. Patients with other cancers diagnosed within the past 3 years and felt to be at low risk of recurrence should be discussed with the study principal investigator to determine eligibility.
5. Participant has a primary central nervous system tumor.
6. A woman of childbearing potential who has a positive urine pregnancy test (within 72 hours) prior to treatment. If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test will be required.
7. Females who are pregnant or nursing or plan to become pregnant or anyone unwilling to use contraception for the duration of treatment.
8. Ongoing toxicity of CTCAE grade >2, other than peripheral neuropathy, related to anticancer therapy that was completed within 4 weeks of consent.
9. Ongoing peripheral neuropathy of CTCAE grade >3
10. History of stroke including transient ischemic attack (TIA) or acute myocardial infarction within 6 months of consent.
11. Participant has a known history of human immunodeficiency virus (HIV), Hepatitis B or known active Hepatitis C virus infection.
12. Medical condition that would place the patient at risk as a result of blood donation, such as bleeding disorder.
13. Any other clinically significant medical condition that, in the opinion of the treating physician, makes participation undesirable, including but not limited to ongoing or active infection, significant uncontrolled hypertension, or severe psychiatric illness.

Table 1. Study Objectives

	Cohort	Biomarker profile	Therapy	Excluded cancer(s)*	Frequency	Status
DNA-based						
Primary driver mutation or fusion	A	ALK + ROS1 gene fusions	lorlatinib	NSCLC	0.1%	Active
	B	BRAF p.V600X mutations	encorafenib+binimetinib	Melanoma, colorectal, p.V600E in thyroid or NSCLC	0.5%	Active
	C	BRCA1/2 or PALB2 biallelic LoF	talazoparib	HER2- breast	0.7%	Active
Strata RNA Expression						
Target RNA expression	D	Her2 overexpression score positive	fam-trastuzumab deruxtecan	Breast, gastric, GEJ	3.7%	Paused**
Proprietary Algorithm						
Multivariant signature	E	Nectin-4 expression score high	enfortumab vedotin	Urothelial	7%	Paused**
	F	Trop2 treatment response score high	sacituzumab govitecan	TNBC, HR+/HER2- BC, mUC, NSCLC, SCLC, Head & Neck, CRC, endometrial	18%	Activation Q2 2023
	G	Immunotherapy response score high	pembrolizumab	Approved pembrolizumab indications	6.8%	Activation Q2 2023
	H	Angiogenesis inhibitor treatment response score high	axitinib	RCC, alveolar soft part sarcoma, and solitary fibrous tumors	3%	Activation Q2 2023

NSCLC = non-small cell lung cancer, GEJ = gastroesophageal junction adenocarcinoma, TNBC = triple negative breast cancer, mUC = metastatic urothelial cancer, SCLC = small cell lung cancer, CRC = colorectal cancer, RCC = renal cell carcinoma

*CNS and multiple primary cancers are not eligible for any cohorts

** Does not affect any currently enrolled study participants

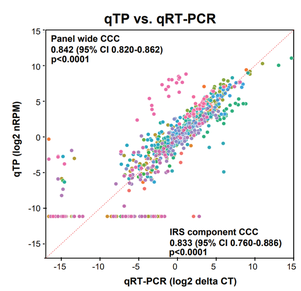
Table 2. Study Endpoints

Primary Endpoint	• Objective response rate (ORR)
Secondary Endpoints	• Duration of response (DoR) • Time to treatment discontinuation (TTD) • Time to next treatment (TTnT) • ctDNA response • Overall survival (OS) • Incidence of SAEs

Table 3. Study Objectives

Primary Objectives	• Assess the clinical activity of anti-cancer therapies in participants with pre-specified biomarker profiles.
Secondary Objectives	• Assess the duration of response in anti-cancer therapies in participants with pre-specified biomarker profiles. • Evaluate ctDNA response rate at additional timepoints for participants who received anti-cancer therapies with pre-specified biomarker profiles. • Evaluate overall survival (OS) for participants who received an anticancer therapy with pre-specified biomarker profiles. • Monitor and characterize the overall safety for participants in each of the biomarker cohorts. • Assess the molecular response of anti-cancer therapies in participants with pre-specified biomarker profiles
Exploratory Objectives	• Explore the relationship between serial ctDNA measurement and participant response to therapy.

Figure 2. Science behind the biomarkers: Cohort RNA biomarkers are highly correlated with RNA expression



Example: Cohort G and the Immuotherapy Response Score (IRS)

The clinical accuracy of the quantitative RNA expression (qTP) component of the Immunotherapy Response Score (IRS) was first determined by determining target gene expression concordance with hydrolysis probe based qRT-PCR through representational validation on 24 FFPE tumor samples. Expression of included individual target gene amplicons (n=32) are shown by color. The concordance correlation coefficient for the panel-wide validation as well as only the four IRS expression biomarkers (PD-L1, PD1, ADAM12 and TOP2A) are shown. The line of equality is shown.