FAST FACTS

S1900A: LOH high and/or deleterious BRCA1/2 mutation – Rucaparib

5.1 Sub-Study Specific Criteria

a. Sub-Study Specific Disease Related Criteria/Laboratory Criteria

1. Patients must be assigned to **S1900A**. **S1900A** biomarker eligibility defined as LOH high and/or deleterious BRCA1/2 mutation is as follows using the FMI tissue- assay:

Biomarker-positive group	Alteration type	Eligible alteration
LOH	Loss of Heterozygosity (LOH)	Genomic LOH ≥ 21%
BRCA	Homologous Recombination Deficiency (HRD)	Deleterious mutations in BRCA1 or BRCA2

2. Patients must not have had prior treatment with any PARP inhibitor, including rucaparib, talazoparib, veliparib, olaparib, or niraparib. For information and a list of PARP inhibitors, please consult the S1900A – Poly Polymerase Inhibitors, Scott et al., 2015 JCO ref from the link on the S1900A protocol abstract page of the SWOG (http://swog.org) or CTSU (https://www.ctsu.org) websites.
3. Patients must be able to take oral medications.
4. Patients with known ≥ Grade 3 hypercholesterolemia must be ≤ Grade 2 (≤400 mg/dL) within 28 days prior to sub-study registration. (Fasting cholesterols is required to be performed pre-registration only in those patients where clinically indicated.) Note: Use of medication to lower cholesterol is acceptable. Caution should be noted for the use of certain statin drugs. See Section 3.1c.3.

≥ Grade 3 hypercholesterolemia ("cholesterol high") is defined by NCI CTCAE v5 as blood cholesterol measurement > 400 mg/dL

b. **Sub-Study Specific Prior/Concurrent Therapy Criteria**

1. Patients must not be planning to receive any concurrent chemotherapy or small molecular or hormonal therapy within 21 days and biologics (e.g. bevacizumab, necitumumab or ramucirumab) or immunotherapy within 28 days prior to sub-study registration and while receiving treatment on this study. Concurrent use of hormones for non-cancer-related conditions (e.g., insulin for diabetes and hormone replacement therapy) is acceptable.

5.2 Common Eligibility Criteria for all Sub-Studies

a. **Disease Related Criteria**

1. Patients must not have EGFR sensitizing mutations, EGFR T790M mutation, ALK gene fusion, ROS 1 gene rearrangement, and BRAF V600E mutation unless they have progressed following all standard of care targeted therapy.

2. Patients must not have documented evidence of acute hepatitis or have an active or uncontrolled infection.
3. Patients with a known history of HIV seropositivity:
    - Must have undetectable viral load using standard HIV assays in clinical practice.
    - Must have CD4 count ≥ 400/mcL.
    - Must not require prophylaxis for any opportunistic infections (i.e., fungal, mAC, or PCP prophylaxis).
    - Must not be newly diagnosed within 12 months prior to sub-study registration.

b. **Prior/Concurrent Therapy Criteria**

1. Patients must have progressed (in the opinion of the treating physician) following the most recent line of therapy.
2. Patients must not have received any prior systemic therapy (systemic chemotherapy, immunotherapy or investigational drug) within 21 days prior to sub-study registration. Patients must have recovered (≤ Grade 1) from any side effects of prior therapy. Patients must not have received any radiation therapy within 14 days prior to sub-study registration. (See Section 5.2c.2 for criteria regarding therapy for CNS metastases).

c. **Clinical/Laboratory Criteria**

1. Patients must have measurable disease (see **S1900A** Section 10.1) documented by CT or MRI. The CT from a combined PET/CT may be used to document only non-measurable disease unless it is of diagnostic quality as defined in **S1900A** Section 10.1c. Measurable disease must be assessed within 28 days prior to sub-study registration. Pleural effusions, ascites and laboratory parameters are not acceptable as the only evidence of disease. Non-measurable disease must be assessed within 42 days prior to sub-study registration. All disease must be assessed and documented on the Baseline Tumor Assessment Form. Patients whose only measurable disease is within a previous radiation therapy port must demonstrate clearly progressive disease (in the opinion of the treating investigator) prior to registration. See **S1900A** Section 15.0 and **LungMAP** Appendix 18.2 for guidelines and submission instructions for required central radiology review. CT and MRI scans must be submitted for central review via TRIAD.
2. Patients must have a CT or MRI scan of the brain to evaluate for CNS disease within 42 days prior to sub-study registration. Patient must not have leptomeningeal disease, spinal cord compression or brain metastases unless: (1) metastases have been locally treated and have remained clinically controlled and asymptomatic for at least 14 days following treatment, and prior to registration, AND (2) patient has no residual neurological dysfunction and has been off corticosteroids for at least 24 hours prior to sub-study registration.
3. Patient must not have had a major surgery within 14 days prior to sub-study registration. Patient must have fully recovered from the effects of prior surgery in the opinion of the treating investigator.
4. Patients must have an ANC ≥ 1,500/mcl, platelet count ≥ 100,000 mcl, and hemoglobin ≥ 9 g/dL obtained within 28 days prior to sub-study registration.

5. Patients must have adequate hepatic function as defined by serum bilirubin ≤ Institutional Upper Limit of Normal (IULN) and either ALT or AST ≤ 2 x IULN within 28 days prior to sub-study registration (if both ALT and AST are done, both must be ≤ 2 IULN). For patients with liver metastases, bilirubin and either ALT or AST must be ≤ 5 x IULN (if both ALT and AST are done, both must be ≤ 5 x IULN).
6. Patients must have a serum creatinine ≤ the IULN OR or calculated creatinine clearance ≥ 50 mL/min using the following Cockroft-Gault Formula. This specimen must have been drawn and processed within 28 days prior to sub-study registration:
    - Calculated Creatinine Clearance = (140 - age) X (actual body weight in kg†)
    - 72 x serum creatinine*
    - Multiply this number by 0.85 if the patient is a female.
    - † The kilogram weight is the patient weight with an upper limit of 140% of the IBW.
7. Actual lab serum creatinine value with a minimum of 0.8 mg/ dL.
8. Patients must have Zubrod performance status 0-1 (see **S1900A** Section 10.4) documented within 28 days prior to sub-study registration.
9. Patients must not have any Grade III/IV cardiac disease as defined by the New York Heart Association Criteria (i.e., patients with cardiac disease resulting in marked limitation of physical activity or resulting in inability to carry on any physical activity without discomfort), unstable angina pectoris, and myocardial infarction within 6 months, or serious uncontrolled cardiac arrhythmia (see **S1900A** Appendix 18.1).
    - Pre-study history and physical exam must be obtained within 28 days prior to sub-study registration.
10. No other prior malignancy is allowed except for the following: adequately treated basal cell or squamous cell skin cancer, in situ cervical cancer, adequately treated Stage I or II cancer from which the patient is currently in complete remission, or any other cancer from which the patient has been disease free for five years.
11. Patients must not be pregnant or nursing. Women/men of reproductive potential must have agreed to use an effective contraceptive method during the study and 6 months after completion of study treatment. A woman is considered to be of "reproductive potential" if she has had menses at any time in the preceding 12 consecutive months. In addition to routine contraceptive methods, "effective contraception" also includes heterosexual celibacy and surgery intended to prevent pregnancy (or with a side-effect of pregnancy prevention) defined as a hysterectomy, bilateral oophorectomy or bilateral tubal ligation. However, if at any point a previously celibate patient chooses to become heterosexually active during the time period for use of contraceptive measures outlined in the protocol, he/she is responsible for beginning contraceptive measures during the study and 6 months after study completion.

5.3 Specimen Submission Criteria

a. Patients must agree to have blood specimens submitted for circulating tumor DNA (ctDNA) as outlined in Section 15.0.
b. Patients must also be offered participation in banking and in the correlative studies for collection and future use of specimens as described in **S1900A** Section 15.0.

Version Date

SCHEMA