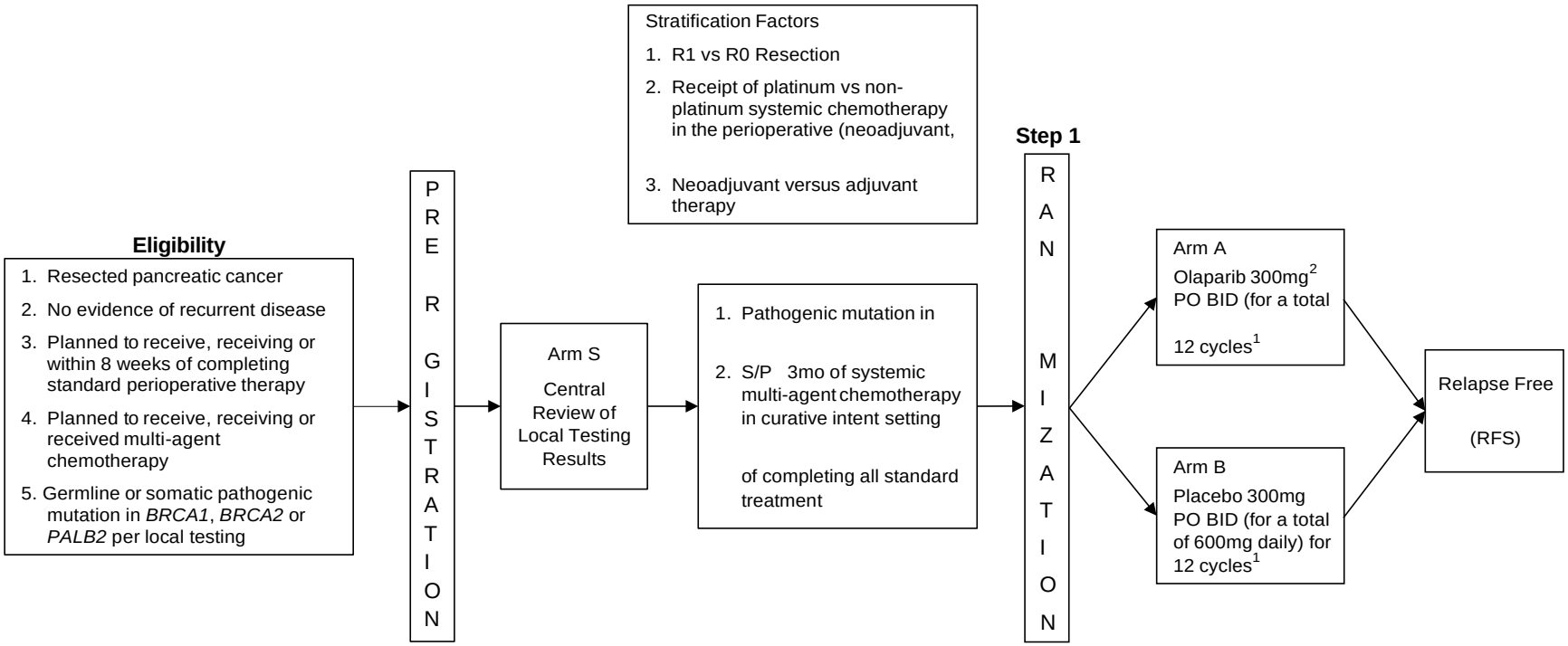
Schema



[1] One cycle = 4 weeks

[2] Olaparib is supplied in either 100 mg or 150 mg tablets

NOTE: Please note that when a patient has been successfully randomized, the confirmation of randomization will indicate that the patient is on Arm X. The patient will actually be randomized to Arm A or B, but as this is a double-blind trial, that information cannot be displayed.

3. Selection of Patients

Each of the criteria in the checklist that follows must be met in order for a patient to be considered eligible for this study. Use the checklist to confirm a patient's eligibility. For each patient, this checklist must be photocopied, completed and maintained in the patient's chart.

In calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test is done on a Monday, the Monday four weeks later would be considered Day 28.

ECOG-ACRIN Patient No. _____

Patient's Initials (L, F, M) _

Physician Signature and Date _____

NOTE: CTEP Policy does not allow for the issuance of waivers to any protocol specified criteria (http://ctep.cancer.gov/protocolDevelopment/policies_deviations.htm). Therefore, all eligibility criteria listed in Section 3 must be met, without exception. The registration of individuals who do not meet all criteria listed in Section 3 can result in the participant being censored from the analysis of the study, and the citation of a major protocol violation during an audit. All questions regarding clarification of eligibility criteria must be directed to the Group's Executive Officer (EA.ExecOfficer@jimmy.harvard.edu) or the Group's Regulatory Officer (EA.RegOfficer@jimmy.harvard.edu).

NOTE: Institutions may use the eligibility checklist as source documentation if it has been reviewed, signed, and dated prior to registration/randomization by the treating physician.

3.1 Eligibility Criteria for Step 0 (Pre-Registration)

_____3.1.1 Patient must be ≥18 years of age on day of consent.

_____3.1.2 Patient must have an ECOG Performance Status of 0-2.

_____3.1.3 Patient must have a diagnosis of pancreatic cancer and have successfully undergone a curative intent surgical resection and must have no evidence of recurrent disease as determined by the investigator.

NOTE: This includes patients with adenocarcinoma, acinar carcinoma, squamous cell carcinoma adenosquamous and variants thereof. Patients with neuroendocrine tumors are excluded from enrolling.

_____3.1.4 Patient must be planning to receive, be receiving or be within 8 weeks of having completed at least three combined months (i.e., 12 weeks) of perioperative (neoadjuvant, adjuvant or a combination of both) systemic, multi-agent chemotherapy.Patients may have had up to 6 months of perioperative systemic therapy as deemed appropriate by their primary treating medical team (patients can have received radiation or chemoradiation in addition to this 6 month course).

_____ 3.1.5 Patient must have a known pathogenic or likely pathogenic germline or somatic mutation in *BRCA1, BRCA2*, or *PALB2*, as determined by a Clinical Laboratory Improvement Amendments (CLIA) certified or equivalently-accredited laboratory. Mutations must be considered pathogenic or likely pathogenic by a reference database such as ClinVar or OncoKb.org.

3.2 Eligibility Criteria for Step 1 (Randomization)

_____ 3.2.1 Patient must have met the eligibility criteria outlined in Section 3.1.

_____3.2.2 Patient must have undergone at least 3 combined months (i.e., 12 weeks) of perioperative (neoadjuvant, adjuvant or a combination of both) systemic, multi-agent chemotherapy. Patients may have had up to 6 months of perioperative systemic therapy as deemed appropriate by their primary treating medical team (patients can have received radiation or chemoradiation in addition to this 6 months course).

_____3.2.3 Central expert reviewer must have determined the patient eligible for randomization after review of local genetic testing reports.

_____3.2.4 If mutation in *BRCA1, BRCA2* or *PALB2* was identified in tumor tissue and the patient has not previously undergone germline testing, the patient must agree to undergo germline testing.

_____ 3.2.5 Patient must have no evidence of recurrent or metastatic pancreatic cancer at the time of randomization as documented by baseline scans obtained ≤ 4 weeks prior to randomization.

_____ 3.2.6 Patient must not have previously had evidence of progressive pancreatic cancer while receiving platinum-based therapy

_____ 3.2.7 Patient must be ≥ 21 days (three weeks) from their last treatment (including chemotherapy or radiotherapy) but ≤ 56 days (eight weeks) from their last treatment. Patients who have received neoadjuvant and/or adjuvant radiotherapy are eligible.

_____ 3.2.8 Patient must have recovered from any adverse events due to prior anti-cancer therapy (i.e., have no residual toxicities > Grade 1 with the exception of alopecia and/or neuropathy).

_____ 3.2.9 Patient must not be receiving any other investigational agents at the time of randomization and while on protocol treatment.

_____3.2.10 Patient must not have any history of allergic reactions attributed to compounds of similar chemical or biological composition to olaparib.

_____3.2.11 Patient must not have any personal history of myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML). Patients with myelodysplastic syndrome/acute myeloid leukaemia or with features suggestive of MDS/AML.

_____3.2.12 Patient must not have any uncontrolled gastrointestinal disorder that would, in the opinion of the investigator, interfere with the ingestion or absorption of olaparib.

_____ 3.2.13 Patient must not be pregnant or breast-feeding due the potential harm to an unborn fetus and possible risk for adverse events in nursing infants with the treatment regimens being used.

All patients of childbearing potential must have a blood test or urine study within 14 days prior to randomization to rule out pregnancy. A patient of childbearing potential is defined as anyone, regardless of sexual orientation or whether they have undergone tubal ligation, who meets the following criteria: 1) has achieved menarche at some point, 2) has not undergone a hysterectomy or bilateral oophorectomy; or 3) has not been naturally postmenopausal (amenorrhea following cancer therapy does not rule out childbearing potential) for at least 24 consecutive months (i.e., has had menses at any time in the preceding 24 consecutive months).

Patient of child bearing potential?_____(Yes or No)

Date of blood test or urine study: _____

_____3.2.14 Patients of childbearing potential and sexually active patients must not expect to conceive or father children by using accepted and effective method(s) of contraception or abstaining from sexual intercourse for the duration of their participation in the study and for 1 month after the last dose of protocol treatment for female patients and for 3 months after the last dose of protocol treatment for male patients. Patients must also not donate sperm while on protocol treatment and for 3 months after the last dose of protocol treatment. Patients must also not breast-feed while on protocol treatment and for 3 months after the last dose of protocol treatment.

_____3.2.15 Patient must have adequate organ and marrow function as defined below: (labs must be obtained ≤ 14 days prior to randomization):

_ Leukocytes ≥ 3,000/mcL

Leukocytes:_____Date of Test:_____

_____ Absolute neutrophil count ≥ 1,500/mcL

ANC:_____Date of Test:_____

_____ Platelets ≥ 100,000/mcL

Platelet:_____Date of Test:_____

_ Hemoglobin ≥ 10.0 g/dL with no blood transfusion in the past 28 days

Hgb:_____Date of Test:_____

_____ Total bilirubin ≤ 1.5 institutional upper limit of normal (ULN) except in patients with Gilbert's syndrome. Patients with Gilbert's syndrome may enroll if direct bilirubin ≤ 2.5 X ULN of the direct bilirubin

Total bilirubin:_____Institutional total bilirubin ULN:

_____

Date of Test: _____

Patient with Gilbert's syndrome? _ (Yes or No)

If yes, Direct bilirubin:_____Institutional direct bilirubin ULN:_____

_____AST(SGOT)/ALT(SGPT) ≤ 2.5 X institutional ULN

ALT:_____Institutional ULN:_____

Date of Test:_____

AST:_____ Institutional ULN:_____

Date of Test:_____

_____Creatinine ≤ 1.5 institutional ULN OR calculated Cockcroft Gault creatinine clearance > 50 mL/min/1.73 m^2.

Serum creatinine_____Institutional ULN:_____

Or

Creatinine clearance:_____Date of Test:_____

_____3.2.16 Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial.

_____3.2.17 For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated.

_____3.2.18 Patients with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are currently on treatment, they are eligible if they have an undetectable HCV viral load.

_____3.2.19 Patient must not have resting ECG indicating uncontrolled, potentially reversible cardiac conditions, as judged by the investigator (e.g., unstable ischemia, uncontrolled symptomatic arrhythmia, congestive heart failure, QTc prolongation >500 ms, electrolyte disturbances, etc.) or have congenital long QT syndrome.

_____3.2.20 Concomitant use of known potent CYP3A4/5 inhibitors such as ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, telithromycin, clarithromycin and nelfinavir is prohibited. See Section 8.1.13 for more details.

_____3.2.21 Patients who are being actively treated for an ongoing concurrent malignancy are ineligible, with the exception of those receiving adjuvant hormone therapies and those receiving topical therapies for skin cancers.

_____3.2.22 Patient must not have, in the opinion of the investigator, any other concurrent medical condition that would prevent the patient from complying with the study procedures.

_____3.2.23 Patient must not be considered a poor medical risk due to a serious, uncontrolled medical disorder, non-malignant systemic disease or active, uncontrolled infection. Examples include, but are not limited to, uncontrolled ventricular arrhythmia, recent (within 3 months) myocardial infarction, uncontrolled major seizure disorder, unstable spinal cord compression, superior vena cava syndrome, extensive interstitial bilateral lung disease on High Resolution Computed Tomography (HRCT) scan or any psychiatric disorder that prohibits obtaining informed consent.

_____ 3.2.24 Patient must have the ability to understand and the willingness to sign a written informed consent document, or have legally authorized representative provide authorization to participate.

_____ 3.2.25 Patient must not have had major surgery within 2 weeks prior to randomization and patients must have recovered from any effects of any major surgery.

_____ _____

Physician Signature Date

OPTIONAL: This signature line is provided for use by institutions wishing to use the eligibility checklist as source documentation.