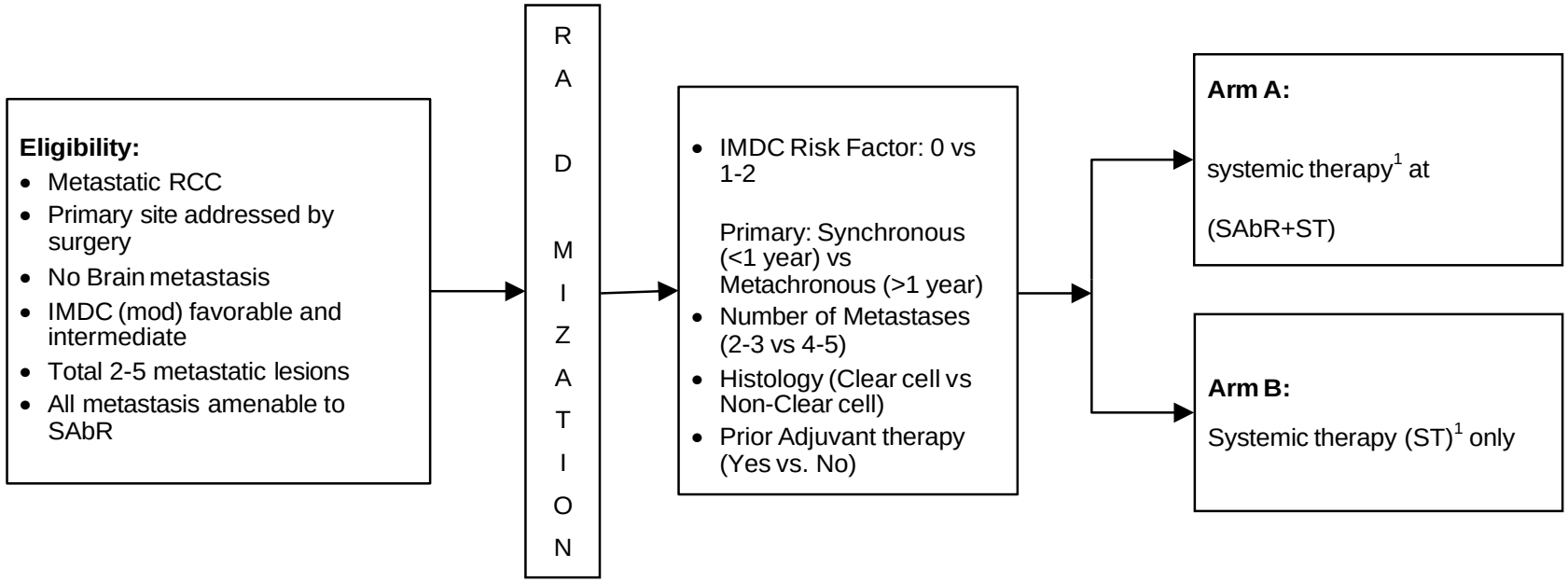
Schema



Accrual Goal = 472

Cycle Length = assessments will be done every 3 months

1. Systemic therapy will consist of standard FDA approved first line systemic therapy for renal cell carcinoma, as per NCCN guidelines and with the options outlined in Section 5.1.2. The selection of the systemic therapy regimen used is at the discretion of the treating physician and in agreement with the patient. Once the regimen has been declared and started, patients may not switch to another regimen option.

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, and require reporting to the IRB of record as non-compliance.

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

_____ 3.1.1 Patient must be ≥ 18 years of age.

_____ 3.1.2 Patient must have a pathologically (histologically or cytologically) proven diagnosis of renal cell carcinoma (RCC) prior to randomization.

_____ 3.1.3 Patient may have any RCC histology except a histology that has a sarcomatoid component.

_____ 3.1.4 Patient must have primary site addressed by local therapy. If the primary RCC is intact, the patient must undergo local treatment to the primary before randomization.

_____ 3.1.5 Patient must not have brain metastases.

_____ 3.1.6 Patient must have favorable or intermediate International Metastatic RCC Database Consortium (IMDC) risk (0-2) at the time of randomization (refer to Appendix III for modified IMDC risk categories).

_____ 3.1.7 Patient must have a total of between 2 and 5 metastatic lesions, as defined by RECIST criteria in Section 6.1.2 with imaging obtained within 45 days prior to randomization.

_____ 3.1.8 Patient must have a documentation from a radiation oncologist confirming that all sites are amenable to SAbR

_____ 3.1.9 Patient may have received prior therapy in the adjuvant setting as long as potential trial participants have recovered from clinically significant adverse events of their most recent therapy/intervention prior to enrollment.

_____ 3.1.10 Patient must not have metastasis involving the following locations: ultra-central (within 2cm of carina) lung, invading gastrointestinal tract (such as esophagus, stomach, intestines, colon, rectum), skin, and scalp.

_____ 3.1.11 Patient must not have received any prior systemic therapy (except for adjuvant setting, see 3.1.9) for metastatic RCC.

_____ 3.1.12 Patient must not have severe, active comorbidity defined as any of the following:

- Active autoimmune disease requiring ongoing therapy including systemic treatment with corticosteroids (> 10 mg daily prednisone equivalents) or other immunosuppressive medications daily. Inhaled steroids and adrenal replacement steroid doses > 10 mg daily prednisone equivalents are permitted in the absence of active autoimmune disease.
- History of severe allergic, anaphylactic or other hypersensitivity reactions to chimeric or humanized antibodies
- Active tuberculosis (PPD response without active TB is allowed)
- Uncontrolled hypertension (systolic BP >190mmHg or diastolic BP >110mmHg)
- Major surgery within 30 days prior to randomization
- Any serious (requiring hospital stay or long term rehab) non-healing wound, ulcer, or bone fracture within 30 days prior to randomization
- Any arterial thrombotic (STEMI, NSTEMI, CVA, etc.) events within 180 days prior to randomization
- Moderate or severe hepatic impairment (child-Pugh B or C)
- Untreated PE or DVT is not allowed. Treated PE or DVT is allowed > 30 days from diagnosis and when not resulting in respiratory impairment.
- Unstable cardiac arrhythmia within 180 days prior to randomization
- History of abdominal fistula, gastrointestinal perforation, intra-abdominal abscess, bowel obstruction, or gastric outlet obstruction within 180 days prior to randomization
- History of or active inflammatory bowel disease.
- Malabsorption syndrome within 30 days prior to randomization

_____ 3.1.13 Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial.

_____ 3.1.14 Patients with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification. To be eligible for this trial, patients should be class 2B or better.

_____3.1.15 Patient must not be pregnant or breast-feeding due to 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: _____

_____3.1.16 Patient must not expect to conceive or father children by using accepted and effective method(s) of contraception or by abstaining from sexual intercourse for the duration of their participation in the study and for 6 months after the last dose of protocol treatment.

_____3.1.17 Patient must have the ability to understand and the willingness to sign a written informed consent document. Patients with impaired decision-making capacity (IDMC) who have a legally authorized representative (LAR) or caregiver and/or family member available will also be considered eligible.

_____ 3.1.18 Patient must have a ECOG Performance Status 0-2.

_____3.1.19 Patients must have adequate organ and bone marrow function as per the recommended guidelines and the respective FDA package insert required for the systemic therapy chosen by the treating oncologist. We recognize that patients may have varying levels of renal and liver function that will impact which systemic therapy is appropriate for the patient. We do not require all patients to have specific baseline laboratory thresholds but do ask the treating oncologist to attest that the patient has adequate organ and bone marrow function to safely receive one of the first line systemic therapies listed in the protocol as a standard of care treatment option.

_____3.1.20 Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months of

randomization are eligible for this trial. Testing for HIV is not required for entry onto the study.

_____3.1.21 For patients with history of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated. If no previous history, testing for HBV is not required for entry onto the study.

_____3.1.22 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. If no previous history, testing for HCV is not required for entry onto the study.

_____3.1.23 In order to participate in the QOL portion of the protocol, the patient must speak English or Spanish.

NOTE: Sites cannot translate the associated QOL forms.

_____ _____

Physician Signature Date

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