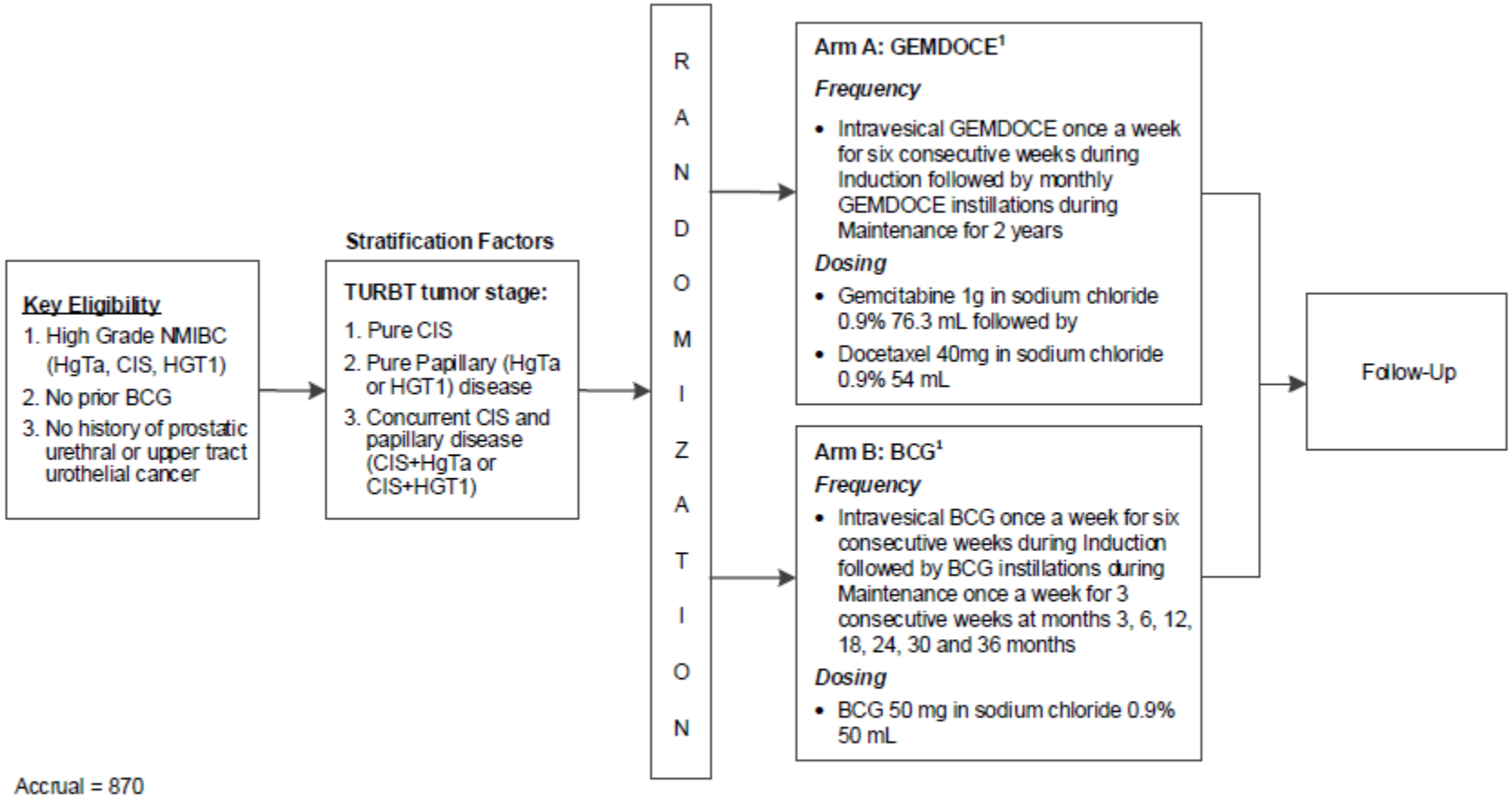
Schema



Accrual = 870

1. Please refer to Section 5.1 for detailed instructions on Arm A and B intravesical therapy procedures.

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 randomization by the treating physician.

3.1 Eligibility Criteria

_____3.1.1 Patient must be ≥ 18 years of age.

_____3.1.2 Patient must not have any prior or current history of muscle-invasive (i.e., T2, T3, T4), locally advanced unresectable, or metastatic urothelial carcinoma as assessed on radiographic imaging obtained within 90 days prior to randomization. The radiographic imaging includes a CT Scan OR MRI of the abdomen/pelvis with intravenous contrast.

NOTE: If a patient's renal function does not permit the administration of intravenous contrast, either a CT scan or MRI of the abdomen/pelvis without intravenous contrast is acceptable.

NOTE: Patients with a history of non-invasive (Ta, Tis) upper tract urothelial carcinoma that has been definitively treated with at least one post-treatment disease assessment (i.e., either cytology, biopsy, or imaging) that demonstrates no evidence of residual disease are eligible.

_____3.1.3 Patient must have histologically confirmed high-grade non-muscle invasive urothelial carcinoma of the bladder (HgTa, HGT1, CIS, HgTa + CIS, or HGT1 + CIS stage) on transurethral resection of bladder tumor (TURBT) obtained within 90 days prior to randomization.

_____3.1.4 Patient must have all visible papillary tumor resected by the treating urologist at the site registering the patient to this protocol prior to randomization. If the treating urologist did not perform the TURBT as outlined in Section 3.1.3, the treating urologist must perform a cystoscopy within 28 days prior to randomization to confirm the absence of visible papillary disease.

_____3.1.5 Patient must have not received prior intravesical therapy for bladder cancer, with the exception of perioperative chemotherapy at the time of TURBT.

_____3.1.6 Patients with high grade T1 disease must have undergone a restaging TURBT within 90 days prior to Step 1 randomization.

NOTE: Patients with high grade T1 disease who undergo a restaging TURBT that shows no residual cancer in the restaging TURBT specimen are eligible.

_____ 3.1.7 Patient must not have pure squamous cell carcinoma or adenocarcinoma.

_____3.1.8 Patient must not have any component of neuroendocrine carcinoma (i.e., small cell or large cell).

_____3.1.9 Patient must not have any component of sarcomatoid, micropapillary, or plasmacytoid variant histology.

_____3.1.10 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.

_____3.1.11 Patient must have ECOG Performance Status 0-2.

_____3.1.12 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: _____

_____ 3.1.13 Patient must not expect to conceive or father children by using an accepted and effective method(s) of contraception or by abstaining from sexual intercourse for the duration of their participation in the study. In addition,patients on Arm A must continue contraception measures for six months after the last dose of GEMDOCE for patients of child-bearing potential and continue for three month after the last dose of GEMDOC for male patients with partners of child-bearing potential. All patients must not breastfeed during their time on protocol treatment.

_____3.1.14 Patient may have received prior systemic gemcitabine or docetaxel use if it was for a non-bladder malignancy.

_____3.1.15 Patient must not have a history of severe hypersensitivity reactions to docetaxel or drugs formulated with polysorbate 80.

_____3.1.16 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.

_____3.1.17 Patient must have adequate organ and marrow function as defined below (these labs must be obtained ≤ 28 days prior to randomization):

_____Leukocytes ≥ 3,000/mcL

Leukocytes:_____Date of Test:_____

_____Absolute neutrophil count (ANC) ≥ 1,500/mcL

ANC:_____Date of Test:_____

_____Platelets ≥ 70,000/mcL

Platelets:_____Date of Test:_____

_____Total Bilirubin ≤ institutional upper limit of normal (ULN)

Total Bilirubin:_____Institutional ULN:_____

Date of Test:_____

_____AST(SGOT)/ALT(SGPT) ≤ 3.0 × institutional ULN

AST:_____Institutional ULN:_____

Date of Test:_____

ALT:_____Institutional ULN:_____

_____3.1.18 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.

_____3.1.19 For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated.

_____3.1.20 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.

_____3.1.21 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.

_____ _____

Physician Signature Date

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