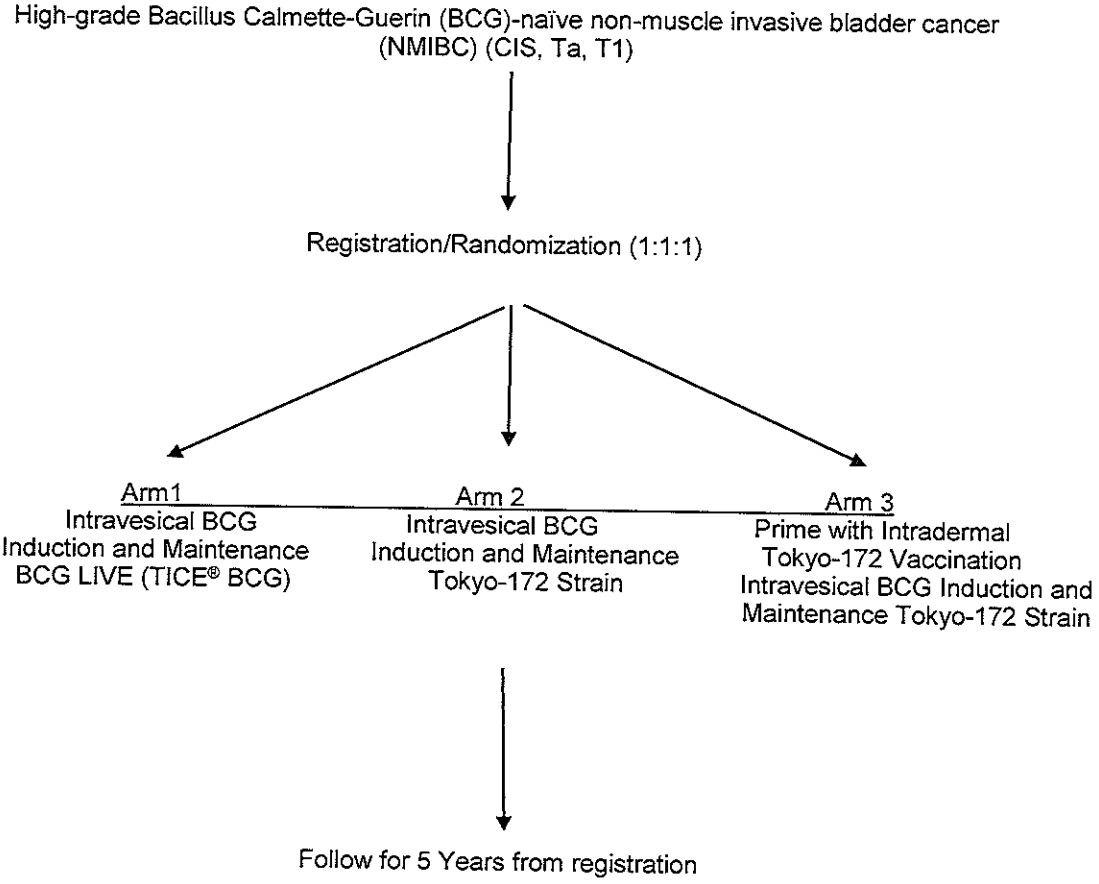
SCHEMA


High-grade Bacillus Calmette-Guerin (BCG)-naïve non-muscle invasive bladder cancer (NMIBC) (CIS, Ta, T1)
Registration/Randomization (1:1:1)
Arm1
Intravesical BCG Induction and Maintenance BCG LIVE (TICE® BCG)
Arm 2
Intravesical BCG Induction and Maintenance Tokyo-172 Strain
Arm 3
Prime with Intradermal Tokyo-172 Vaccination Intravesical BCG Induction and Maintenance Tokyo-172 Strain
Follow for 5 Years from registration

5.0 ELIGIBILITY CRITERIA

Each of the criteria in the following section must be met in order for a patient to be considered eligible for registration. Use the spaces provided to confirm a patient's eligibility. For each criterion requiring test results and dates, please record this information on the Onstudy Form and submit via Medidata Rave® (see Section 14.0). Any potential eligibility issues should be addressed to the Data Operations Center in Seattle at 206/652-2267 prior to registration.

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 4 weeks later would be considered Day 28. This allows for efficient patient scheduling without exceeding the guidelines. **If Day 60 or 90 falls on a weekend or holiday, the limit may be extended to the next working day.**

SWOG Patient No._____

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

5.1 Disease Related Criteria

____ a. Patients must have histologically proven Ta, carcinoma in situ (CIS) or T1 stage urothelial cell carcinoma of the bladder within 90 days prior to registration.

____ b. Patients must have had all grossly visible papillary tumors removed within 30 days prior to registration or cystoscopy confirming no grossly visible papillary tumors within 30 days prior to registration.

____ c. Patients with T1 disease must have cross-sectional imaging of abdomen/pelvis demonstrating no evidence of metastatic disease (MRI or CT scan) within 90 days prior to registration. Patients with T1 disease must have re-resection confirming ≤ T1 disease within 90 days prior to registration.

____ d. Patients must have high-grade bladder cancer as defined by 2004 WHO/ISUP classification. *(17)*

____ e. Patients must not have pure squamous cell carcinoma or adenocarcinoma.

____ f. Patients' disease must not have micropapillary components.

____ g. Patients must have no evidence of upper tract (renal pelvis or ureters) cancer confirmed by one of the following tests performed within 90 days prior to registration: CT urogram, intravenous pyelogram, MR urogram, or retrograde pyelograms.

____ h. Patients must not have nodal involvement or metastatic disease.

____ i. 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. Patients with localized prostate cancer who are being followed by an active surveillance program are also eligible.

____ j. Patients must have a Zubrod performance status of 0-2 (see Section 10.5).

SWOG Patient No._____

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

5.2 Prior/Concurrent Therapy Criteria

____ a. Patients must not have received prior intravesical BCG.

____ b. Patients must not be taking oral glucocorticoids at the time of registration.

____ c. Patients must not be planning to receive concomitant biologic therapy, hormonal therapy, chemotherapy, surgery, or other cancer therapy while on study.

5.3 Clinical/Laboratory Criteria

____ a. Patients must not have known history of tuberculosis.

____ b. Patients must be PPD negative within 90 days prior to registration. PPD negativity is defined as < 10 mm diameter induration (palpable, raised hardened area) in the volar forearm at 48-72 hours following injection with standard tuberculin dose (5 units, 0.1 ml). See Section 18.1 for more information

____ c. Patients must be ≥ 18 years of age.

____ d. Prestudy history and physical must be obtained within 90 days prior to registration. Patients must have a complete blood count (CBC) and basic metabolic panel including creatinine, potassium, chloride, BUN, CO_2 and glucose within 28 days prior to registration.

____ e. Patients must not be pregnant or nursing as the use of BCG is not recommended during pregnancy. Women/men of reproductive potential must have agreed to use an effective contraceptive method. 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.

5.4 Specimen Submission Criteria

____ a. Patients must be offered the opportunity to participate in specimen banking for future studies, to include translational medicine studies, outlined in Section 15.0.

5.5 Patient Reported Outcomes (PRO) Submission Criteria

____ a. Patients who can complete PRO forms in English or Spanish must complete the baseline Bladder Cancer Index, EORTC QLQ-C30 and AUASS forms.

5.6 Regulatory Criteria

____ a. Patients must be informed of the investigational nature of this study and must sign and give written informed consent in accordance with institutional and federal guidelines.

____ b. As a part of the OPEN registration process (see Section 13.3 for OPEN access instructions) the treating institution's identity is provided in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered in the system.

5.7 Site Criteria

____ a. Treating physician must confirm availability and access to BCG LIVE (TICE® BCG).