Effects of smoking on treatment efficacy and clinical outcomes in the S1602 Phase III Non-Muscle Invasive Bladder Cancer (NMIBC) Study

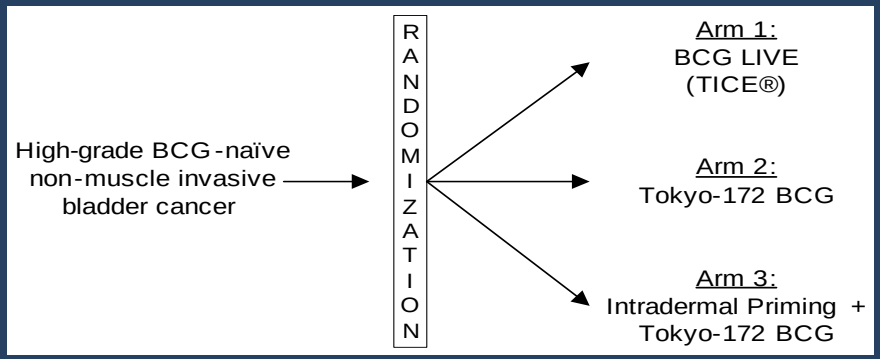
Background

- Cigarette smoking is an established risk factor for bladder cancer, yet the impact of current smoking or smoking history on the course of the disease is not well-understood.
- There is published evidence that smoking may interact with intravesical BCG immunotherapy which is the standard of care for patients high grade NMIBC.
- A prospective smoking study embedded in a large, multicenter clinical trial such as S1602 will provide more definitive evidence regarding the relationship of smoking, treatment and patient outcomes.
- Nearly half of patients with high grade NMIBC will experience recurrence and/or disease progression within 5 years. Treatment for progressive disease includes cystectomy or chemo-radiotherapy, which contributes to a severe decline in quality of life and overall survival.

S1602 - Phase III Bladder Cancer Trial

- A Randomized Trial to Evaluate the Influence of BCG Strain Differences and T Cell Priming with Intradermal BCG Before Intravesical Therapy for BCG-Naïve High-Grade Non-Muscle Invasive Bladder Cancer

- Co-Primary Aims
  - A) Test non-inferiority of the Tokyo BCG strain
  - B) Test superiority of addition of Priming



- 924 patients randomized and follow-up for 5 years
- Planned activation December 2016

Aims

- Evaluate the associations of smoking status (current vs. former vs. never smokers), cumulative smoking exposure and time since smoking cessation with patient outcomes.
- Evaluate whether efficacy of BCG strain (TICE® vs. Tokyo) is modified by measures of smoking exposure (status, cumulative exposure, timing of cessation).
- Estimate adverse event profiles for each of the 3 treatment arms by smoking status variables.
- Test changes in urinary cytokine levels after BCG vary by smoking exposure variables.

Assessments and Timing

- A Goal – Minimal additional data collection impact.
- C-TUQ core items 1, 4, 5, and 6 will be used to assess baseline smoking status and cumulative smoking exposure.
- Extension items 13 and 14 will be added, along with the 4 core items, to the follow-up questionnaires to capture attempts to quit smoking.
- Exposure will be measured at study entry and then again at 1 year and 2 years post-randomization.

C-TUQ Items

- **Baseline and cumulative exposure (C-TUQ items 1, 4, 5 and 6)**
  - **Smoked at least 100 cigarettes in your entire life (Y / N)**
  - **Total years smoked**
  - **Cigarettes smoked / day**
  - **Time since last smoked a cigarette**
- **Attempts to quit (C-TUQ items 13 and 14)**
  - **Have your cancer doctors advised you to quit smoking cigarettes?**
  - **In the past 30 days, have you been trying to quit smoking cigarettes?**

Status

- Additional forms have been implemented in RAVE EDC system
- The baseline forms are part of the Initial Form Set (IFS) and are part of institutional data performance requirements
- Institutions are informed of follow-up assessments through an “expectation” system

Comments

- Provides feasibility results and specific data to answer specified questions
- Serves as a test case since there are likely other disease studies (outside of lung) where the limited additional data collection burden is justified
- Another goal to add very limited (at least baseline) questions much more broadly across NCTN studies
- Opens up opportunities for future smoking related research questions