SWOG | CANCER RESEARCH NETWORK

September 16, 2019

TO: ALL NATIONAL CLINICAL TRIALS NETWORK (NCTN) MEMBERS

FROM: SWOG Operations Office (protocols@swog.org)

RE: **S1602**, "A Phase III 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." Drs.: RS Svatek, AS Alva, SP Lerner, JJ Meeks and S Gilbert.

MEMORANDUM

Study Chair: Robert S. Svatek, M.D.
Phone number: 210/567-5676
Fax: 210/616-6868
E-mail: S1602question@swog.org

IRB Review Requirements
(√) Patient Notification Required
(√) Expedited Review Allowed

MEMORANDUM

Enclosed please find an "Investigator Letter" and a "Patient Information Letter" pertaining to the recent possible contamination of the diluent packaged with the Intradermal Tokyo BCG used for priming Arm 3 of **S1602**.

We ask that you please read the attached "Investigator Letter" for specific patient notification instructions.

This memorandum serves to notify the NCI, the CIRB, and the SWOG Statistics and Data Management Center.

cc: PROTOCOL & INFORMATION OFFICE
Satoshi Kodama– JBL
Christine Richardson – Consultant
Elliot Lee – McKesson Specialty Health

SWOG CANCER RESEARCH NETWORK

INVESTIGATOR LETTER

Date: September 16, 2019

To: **S1602** Participating Investigators

From: Robert S. Svatek, M.D. – S1602 Study Chair
Ian M. Thompson, Jr., M.D. – SWOG Genitourinary Committee Chair

RE: Diluent packaged in kits with Intradermal Tokyo BCG for use in **S1602**: "A Phase III Randomized Trial to Evaluate the Influence Of BCG Strain Differences and T Cell Priming with Intradermal BCG Before Intravesical Therapy for BCG-Naive High-Grade Non-Muscle Invasive Bladder Cancer."

S1602 was temporarily closed to new patient accrual on August 28, 2019, following notification from Japan BCG Laboratory (JBL), the vaccine manufacturer, of a potential contamination of the diluent packaged with the Tokyo BCG Intradermal Vaccine. The diluent was used for priming patients assigned to Arm 3.

The World Health Organization released the following information regarding the contamination; "During the packaging operation, a foreign matter was detected in one ampoule of diluent. A visual inspection of the total number of this lot (89,992 ampoules) was conducted. As a result, two additional ampoules of foreign matter were found. In total, three ampoules were detected from the lot. A foreign particle was also detected in one ampoule out of 87,647 from another lot. The main component of the foreign matter is ethylene propylene rubber/styrene butadiene rubber, carbonate and inorganic silicon compound.

A recall procedure was triggered by JBL in order to adhere to Japanese pharmacopoeia requirements and to comply with Japan's legislation. However, it should be highlighted that recall procedure was triggered on all lots of diluent with remaining shelf-life in countries even though no particles could be found in the retained samples of the distributed lots. As of today, no complaint regarding foreign matter was reported from the lots distributed so far. Since the diluent is terminally sterilized, the sterility of the product is ensured, regardless of presence or absence of foreign matter. The incidence rate per lot was calculated as 0.0011% - 0.0033%, which, in the risk assessment analysis, is considered as an extremely low incidence (less than 0.01%). Evaluation of adverse drug reactions did not provide any evidence of a change in the safety profile of the vaccine. Finally, it should be emphasized that the presence of foreign particles is a visible defect and as such, it can be detected by the vaccinator."

Patients who were registered to treatment on Arm 3 of **S1602** from 6/20/18 to 8/28/19 must be notified of the potential contamination of the diluent given with their intradermal Tokyo BCG vaccine. The attached "Patient Information Letter" may be used for patient notification. Documentation that this information has been provided to the patient must be retained in the patient's research record on site and will be subject to verification at the time of a Quality Assurance audit. This notification and the "Patient Information Letter" will be forwarded to the NCI Central Institutional Review Board (CIRB) by SWOG. If the NCI CIRB is not the IRB of Record for the study at your site, you should forward the information to the appropriate local IRB of Record for the study at your site.

Enrollment of new patients to **S1602** is temporarily closed, until replacement Tokyo BCG vaccine with new diluent is available for shipment to sites. Sites will be notified when the newly repackaged vaccine is available and when the study is re-opened to accrual.

Patients currently receiving treatment on **S1602** should continue to receive treatment and the study follow-up per the study protocol as only the intradermal Tokyo BCG diluent was potentially contaminated. The disease assessment and data submission schedule must continue to be followed as specified in the protocol.

Patients who are currently receiving Arm 3 protocol treatment must be notified as soon as possible.

Please direct questions to:
Eligibility/Data Submissions: guquestion@crab.org
Protocol/Regulatory: vgarcia@swog.org
S1602 Treatment-related/Medical: **S1602**Question@swog.org

Thank you for your continued participation in the **S1602** trial.

*[Patient Letter: For all patients registered to Arm 3 of **S1602**]*

PATIENT INFORMATION LETTER

S1602, "A Phase III Randomized Trial to Evaluate the Influence Of BCG Strain Differences and T Cell Priming with Intradermal BCG Before Intravesical Therapy for BCG-Naive High-Grade Non-Muscle Invasive Bladder Cancer."

You are taking part in a research study testing the Tokyo version of BCG and injection of intradermal BCG vaccine before BCG is instilled in the bladder for BCG-Naïve high-grade non-muscle invasive bladder cancer. This study is known as S1602. You were informed at the time of your enrollment in the study in your Consent Form that you would be given any new information that might affect your health and/or your willingness to continue in the study.

In August 2019, the manufacturer of the Tokyo BCG vaccine notified us as leaders of the study that there was a potential foreign material in less than 0.01% of the saline (1 defect in every 100,000 units of saline) used to make the vaccine. The sterility of the saline is ensured, regardless of presence or absence of foreign material. There is no evidence of a change in the safety of the vaccine that you received. Finally, you should be aware that this foreign material would be visible to the person administering the BCG vaccine.

At this time, we do not believe this potential contamination posed a safety risk to anyone who received the vaccine. We will notify you immediately if we learn this is not true.

Your future treatments and tests can continue as planned and do not change as a result of this.

We greatly appreciate your participation in the trial. The results from this research study will contribute to the knowledge of how best to treat patients with non-muscle invasive bladder cancer. You should discuss any questions you have about this "Patient Information Letter" with your study doctor.

Thank you very much for your participation.

Sincerely,

Robert S. Svatek, M.D.
Ian M. Thompson, Jr., M.D.