SAFETY

Surveillance After Extremity Tumor Surgery

Randomization Guidelines

Version 2.0

This study is registered on ClinicalTrials.gov

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Document History

Date (DD-MMM-YY)	Author(s)	Version No.	Description of Amendment(s)
28-MAY-20	Tricia Schneider	1.0	Initial Version
31-JAN-22	Tess Hudson	2.0	Updated figures

1.0 Introduction

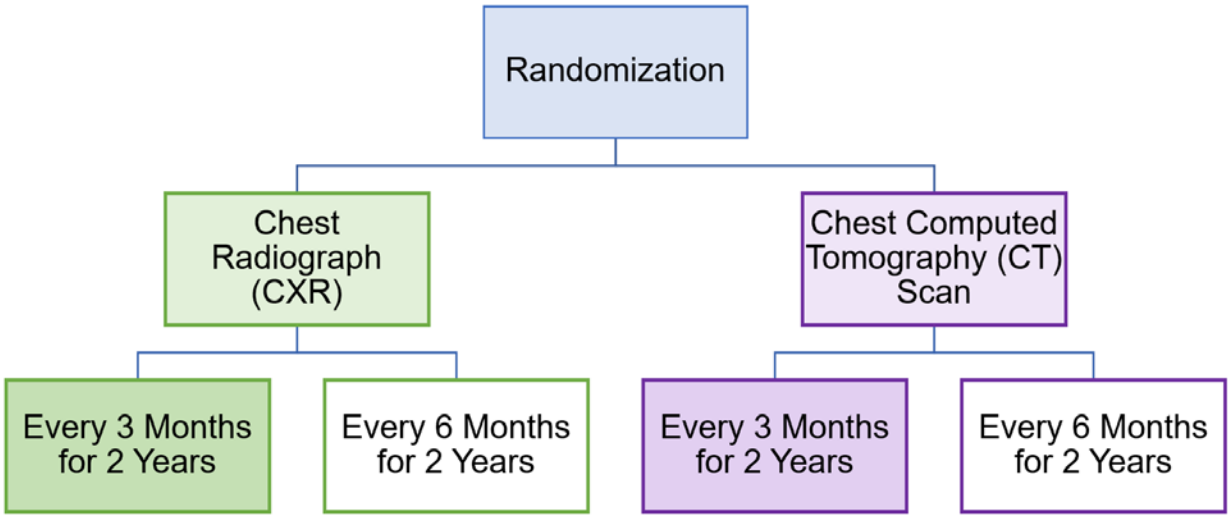
The purpose of this document is to provide guidance on trial randomization for the **S**urveillance **AF**ter **E**xtremity **T**umor surger**Y** (SAFETY) trial. Clinical site personnel should review this document prior to beginning study enrolment and refer to it when questions arise. If clinical site personnel have questions regarding the randomization procedures, they should contact the Project Manager at the Methods Center via email and / or telephone.

2.0 Trial Design

This trial follows a 2X2 factorial randomized controlled trial (RCT) design. Participants are the unit of randomization. Factorial RCTs simultaneously evaluate the effectiveness of two or more treatments. This study was designed as a factorial RCT as there are no known or expected interactions between surveillance frequency and imaging modality. Participants will first be randomized to one of the two thoracic imaging modalities being evaluated (i.e., chest radiograph [CXR] vs. chest computed tomography (CT) scan). Participants will then be randomized to one of the two surveillance frequencies being evaluated (i.e., every three months vs. every six months). Therefore, participants will be randomized to one of four treatment / surveillance groups (**FIGURE 1**):

- Clinical assessment and CXR every three months for two years; or
- Clinical assessment and CXR every six months for two years; or
- Clinical assessment and chest CT scan every three months for two years; or
- Clinical assessment and chest CT scan every six months for two years.

FIGURE 1. SAFETY TRIAL FACTORIAL DESIGN



3.0 Randomization

Once clinical site personnel identify an eligible patient and the patient consents to participate in the study, the patient can be randomized. The SAFETY trial utilizes an internet-based randomization system (www.randomize.net) to assign each enrolled participant to one of the four treatment / surveillance groups. Site research personnel will **not** be blinded to treatment / surveillance allocation as they will be responsible for the coordination of follow-up visits and

imaging, as well as following the participants in clinic. Similarly, participants will also **not** be blinded to treatment / surveillance allocation. Randomization will occur in random permuted blocks with varying block sizes of four and eight. Participants will be stratified according to **clinical site** and **peri-operative chemotherapy** status (yes vs. no). Once the participant is randomized, the randomization system will display the surveillance regimen to which the participant has been allocated.

4.0 Accessing the Randomization System

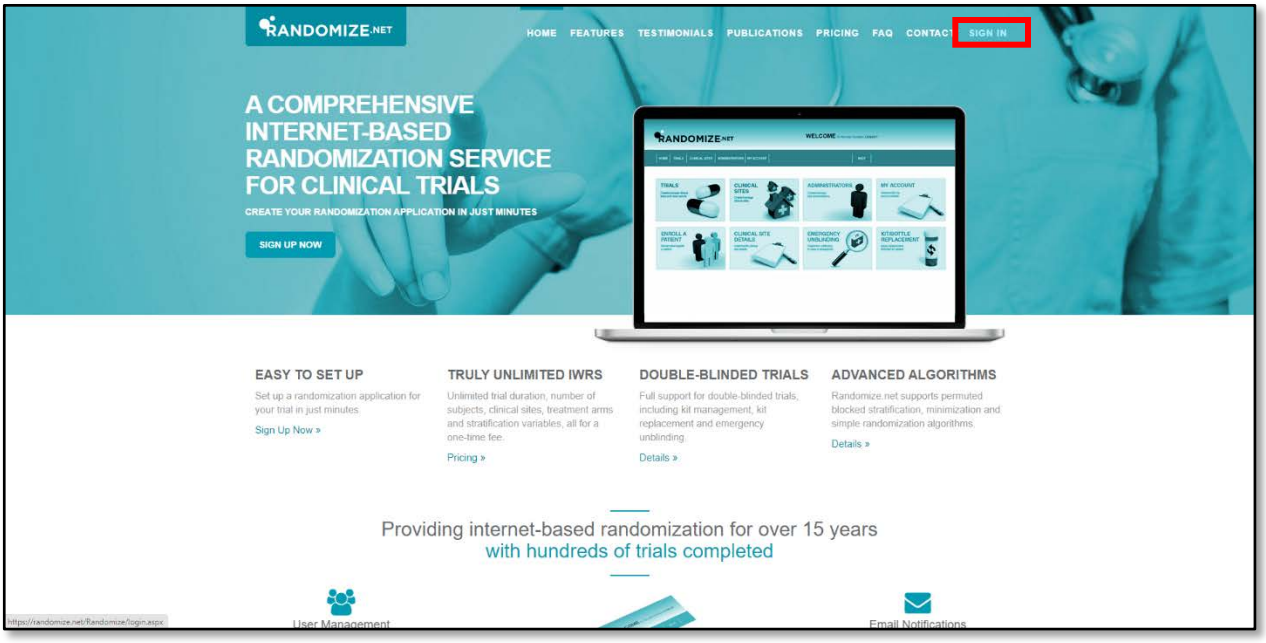
REMINDER: Please wait to randomize the patient until the first clinic visit at which all treatment is complete, the patient's surgical wound has been deemed healed or stable and the plan for post-treatment surveillance has been discussed.

Upon study initiation at an institution, Methods Center personnel will assign participating site-specific login credentials (username and password) to the randomization system. These unique login credentials will be required in order to access the study randomization system.

To gain access to the randomization system, follow these steps:

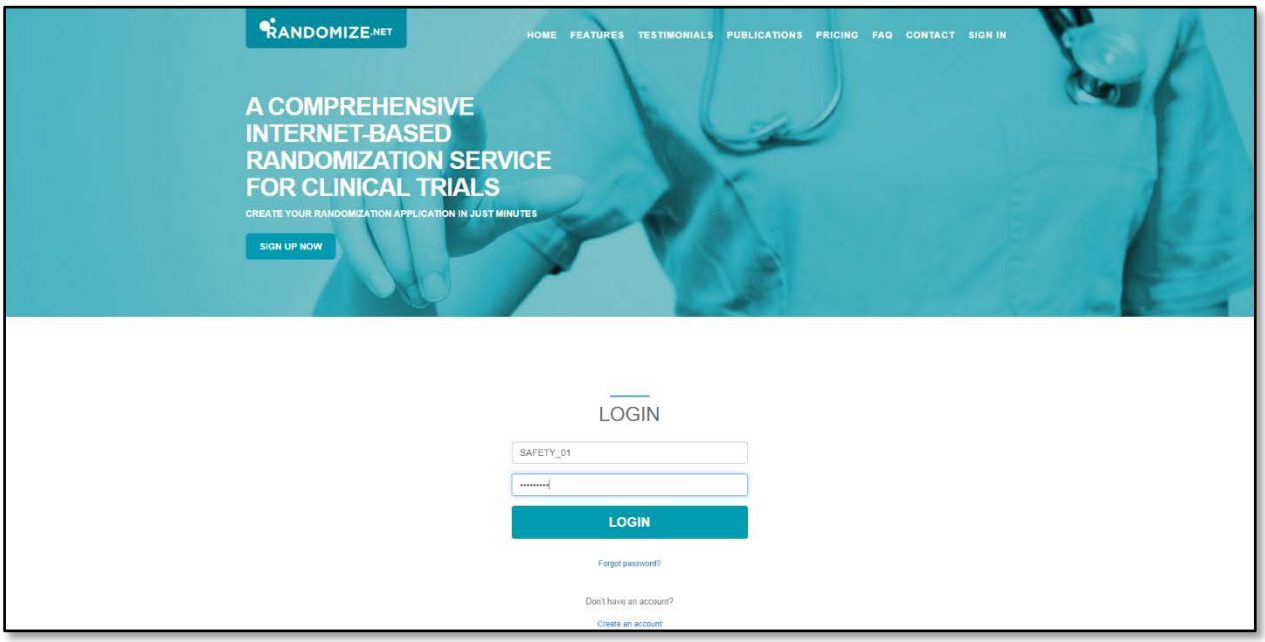
1. Navigate to www.randomize.net.
2. Click the *Sign In* button in the top right-hand corner of the randomization system Welcome Screen (see **FIGURE 2**).

FIGURE 2. RANDOMIZE.NET WELCOME SCREEN



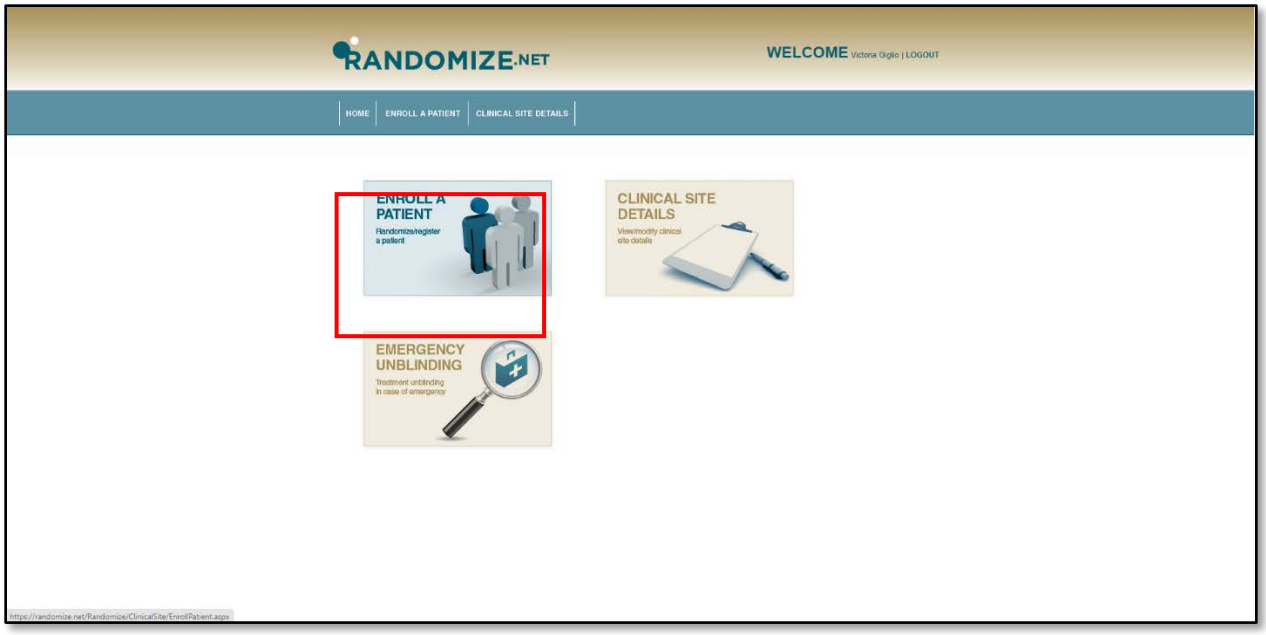
3. Enter your site's unique login credentials (assigned by the Methods Center) and then click the *Login* button (see **FIGURE 3**).

FIGURE 3. RANDOMIZE.NET LOGIN SCREEN



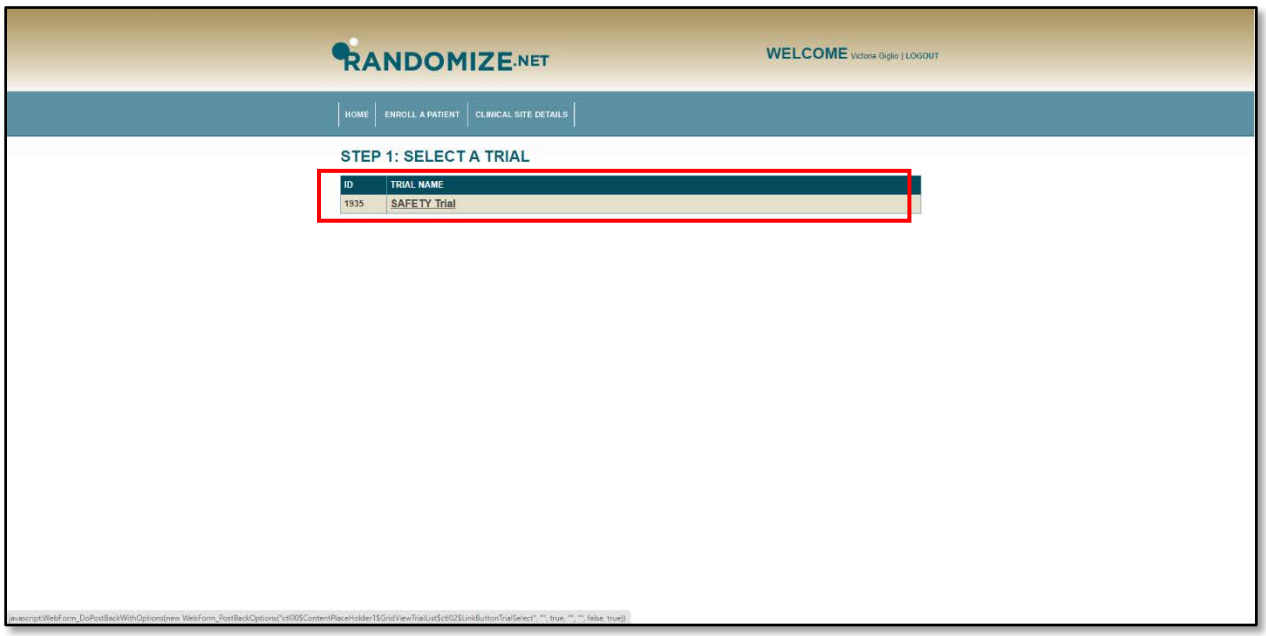
4. Once on the Home Screen, click the *Enroll a Patient* button to begin the randomization process (see **FIGURE 4**).

FIGURE 4. RANDOMIZE.NET HOME SCREEN



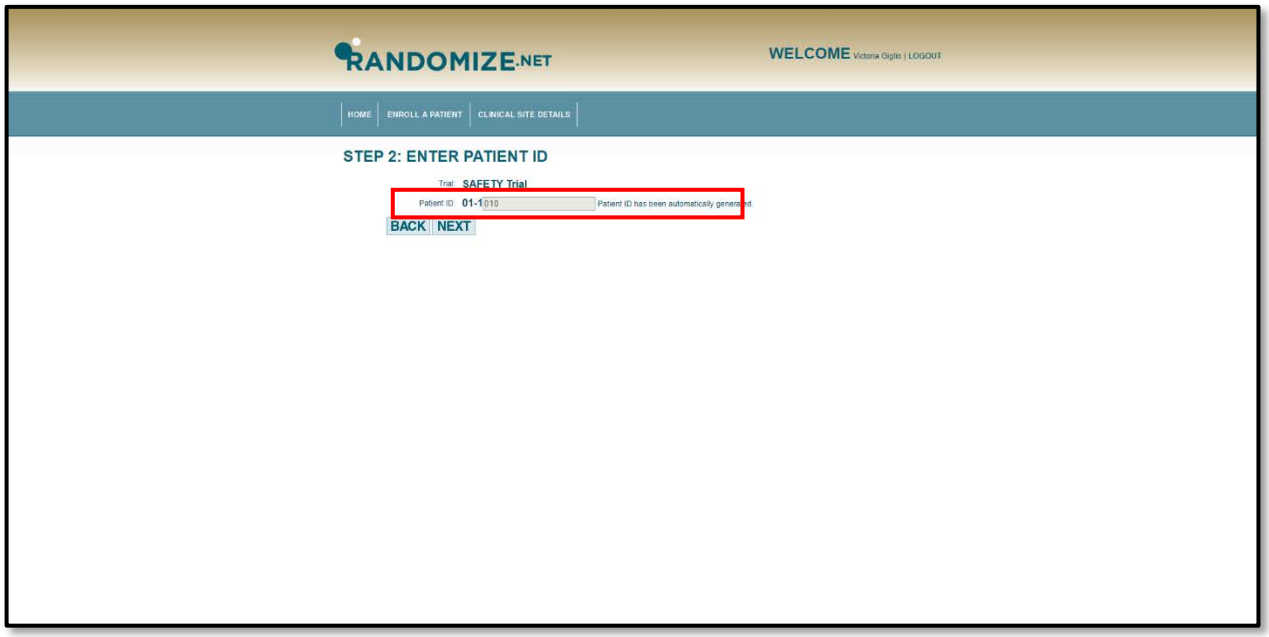
5. Select the SAFETY trial (see **FIGURE 5**).

FIGURE 5. RANDOMIZE.NET ENROLL A PATIENT SCREEN



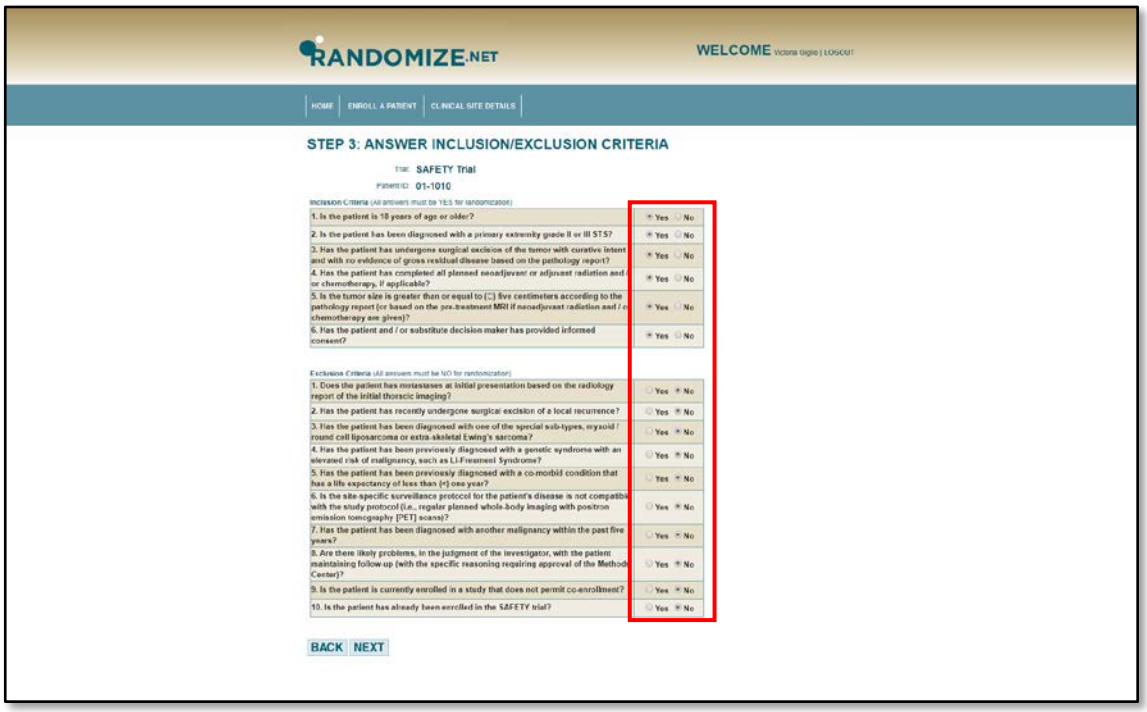
6. A Participant ID will be automatically generated. Record the Participant ID and click the *Next* button (see **FIGURE 6**).

FIGURE 6. RANDOMIZE.NET PARTICIPANT GENERATOR



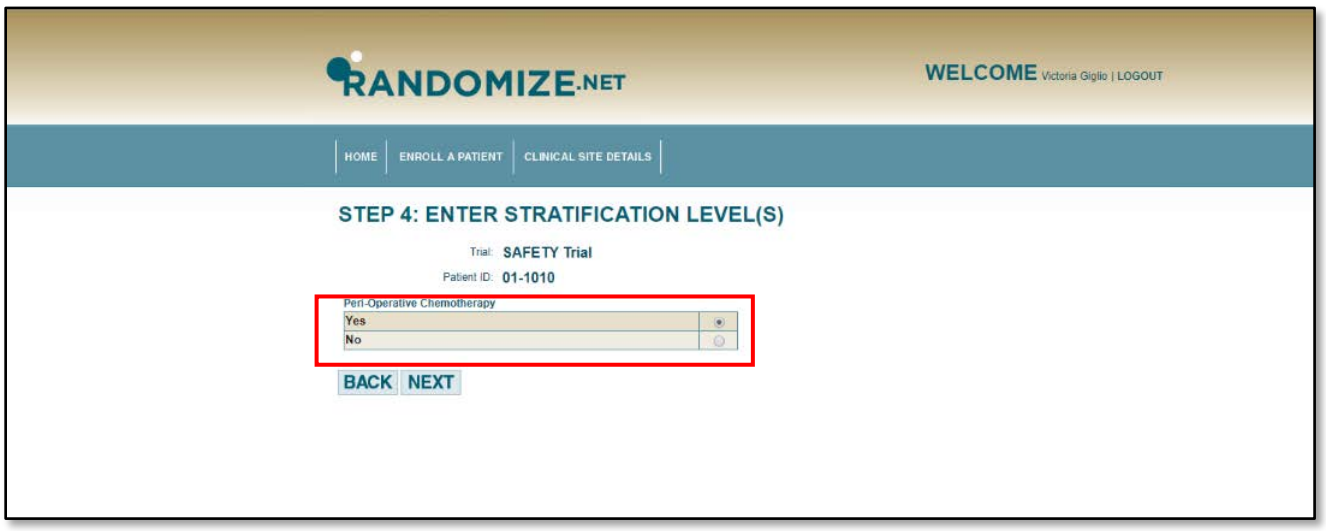
7. Review the eligibility criteria to ensure that the participant meets all inclusion criteria and does **not** meet any of the exclusion criteria. Select 'Yes' or 'No' for each criterion and then click the *Next* button (see **FIGURE 7**).

FIGURE 7. RANDOMIZE.NET ELIGIBILITY CRITERIA CONFIRMATION



8. Select the correct response for the stratification variable (i.e., peri-operative chemotherapy) and then click the *Next* button to confirm that all information is correct for the participant (see **FIGURE 8**).

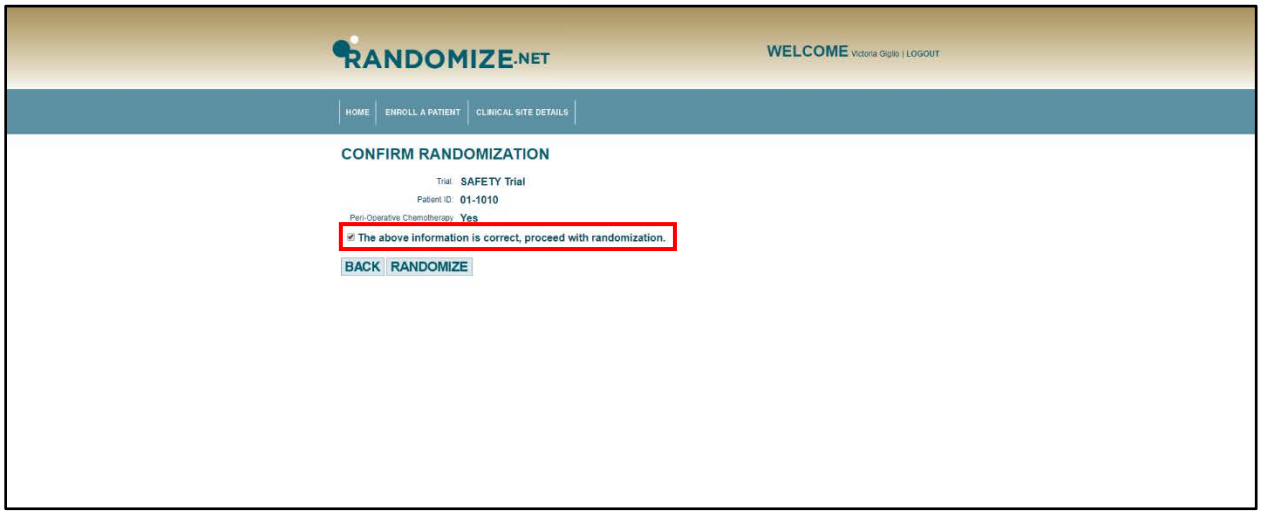
FIGURE 8. STRATIFICATION VARIABLE CONFIRMATION



REMINDER: At this point, please ensure all information is correct as clicking the *Randomize* button will complete the randomization process.

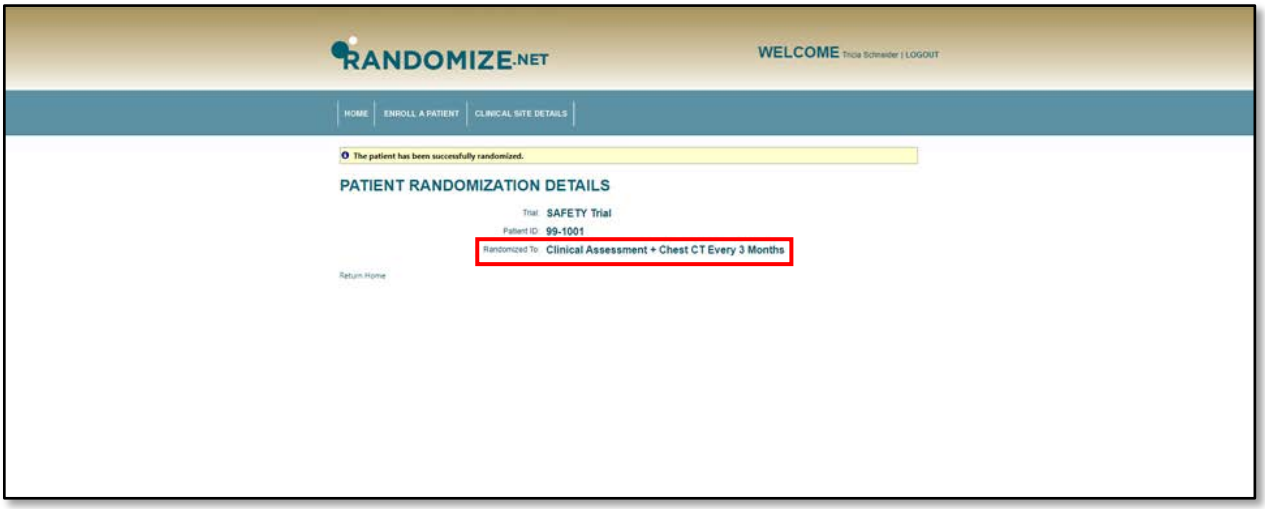
9. The randomization system will direct you to a Randomization Confirmation Screen, which will display the Participant ID and the participant's peri-operative chemotherapy status (see **FIGURE 9**).

FIGURE 9. RANDOMIZE.NET RANDOMIZATION CONFIRMATION SCREEN



10. The randomization system will direct you to the Randomization Details Screen, which will display the Participant ID, as well as the surveillance frequency and imaging modality to which the participant was allocated (see **FIGURE 10**).

FIGURE 10. RANDOMIZE.NET RANDOMIZATION DETAILS SCREEN



5.0 Submission of the Randomization Form

It is the responsibility of the clinical site personnel to submit the **Randomization Form** by entering the data into the study database. The clinical site personnel should retain the original **Randomization Form** in the appropriate SAFETY Participant Binder (if paper case report forms are being used).

6.0 Troubleshooting

6.1 Forgetting Your Site's Login Credentials

If you have forgotten your login credentials and it is during regular office hours, please contact the SAFETY Primary Project Manager at the Methods Center via mobile or email. See the **Methods Center Contact Information** document in the Study Resource Binder for contact details.

6.2 Difficulties with the Randomization System

If you experience difficulties with the randomization system, please check the web address (www.randomize.net) to ensure that it has been correctly entered. If the web address has been correctly entered, try refreshing the webpage after a few minutes. If you are still experiencing difficulties, please call www.randomize.net at (613)-366-4796 or email them at info@randomize.net.

6.3 Forgetting the Treatment Allocation After Exiting the Randomization System

If you exited the randomization system prior to documenting the treatment / surveillance allocation to which the participant was assigned and have forgotten which treatment / surveillance regimen the participant was to receive, please reference the confirmation email that was sent by the randomization system. Alternatively, you can contact the SAFETY Project Manager at the Methods Center to request that the confirmation email be forwarded to you.

6.4 Accessing the Randomization System More than Once for the Same Participant

If the randomization system has been accessed more than once for the same participant, please inform the Methods Center immediately. Please use the **first** treatment / surveillance allocation assigned to the participant.

7.0 Frequently Asked Questions

This section provides clarification and guidance on the randomization process. Please contact the Methods Center if you have any questions about the randomization of a particular participant in the trial.

7.1 What if we discover that a participant is ineligible after randomization?

Participants who are identified after randomization as being ineligible will be included and followed in the same way as eligible randomized participants, following the 'intention-to-treat' principle. If an ineligible participant is randomized, and this participant does not receive the allocated surveillance regimen, a **Protocol Deviation Form** should be completed. Once a participant is randomized, they must be included in the study.