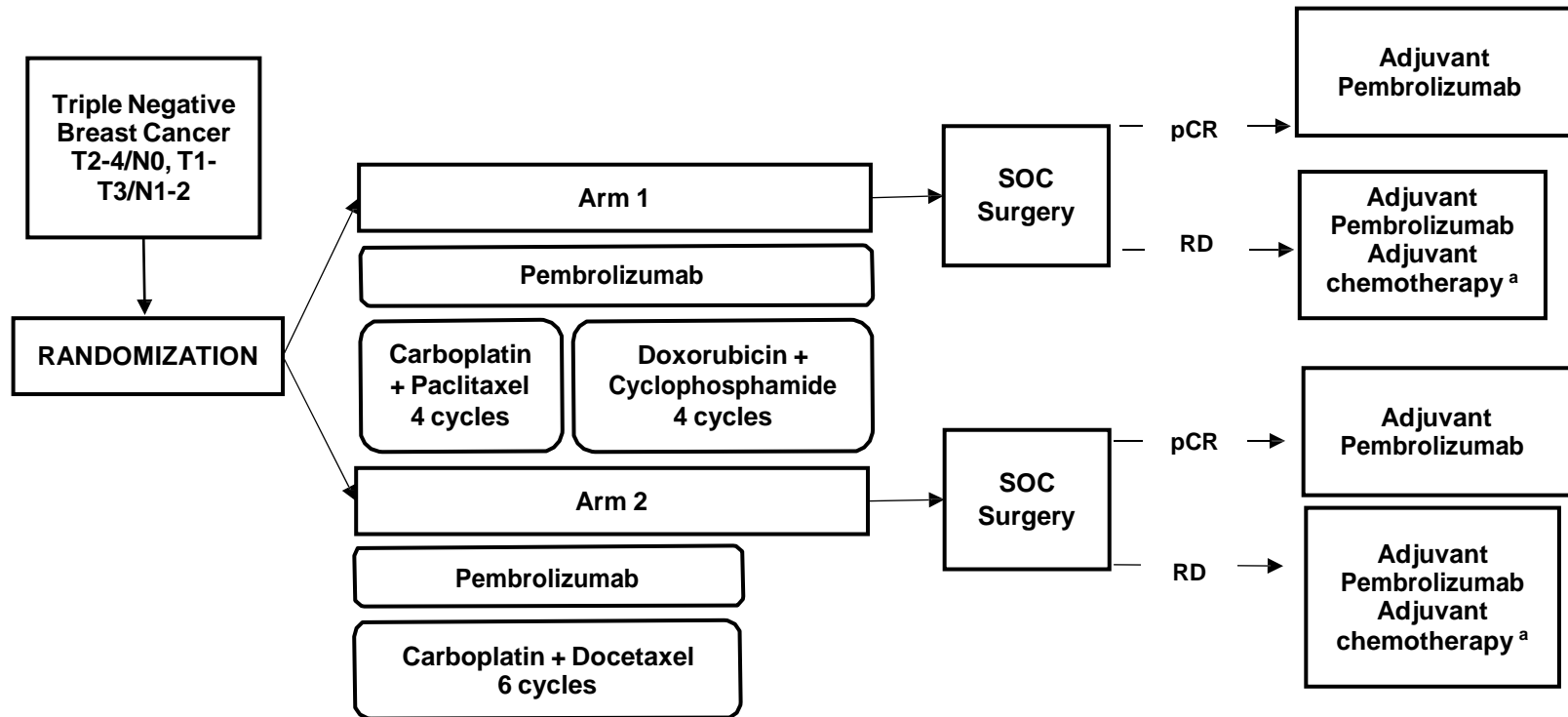


SCHEMA



^a Treating investigator discretion. See [Section 7.4b](#).

5.0 ELIGIBILITY CRITERIA

Each of the criteria in the following section must be met in order for a participant to be considered eligible for registration in OPEN. [Section 5](#) may be printed and used to by the site, but is not to be uploaded in RAVE (unless specially stated). 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 SWOG SDMC in Seattle at 206/652-2267 or breastquestion@crab.org prior to registration.

NCI policy does not allow for waiver of any eligibility criterion (http://ctep.cancer.gov/protocolDevelopment/policies_deviations.htm).

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 participant scheduling without exceeding the guidelines. **If Day 0 or 21 falls on a weekend or holiday, the limit may be extended to the next working day.**

5.1 Disease Related Criteria

- a. Participants must have histologically confirmed ER-negative, PR-negative, and HER2-negative breast cancer (TNBC) defined as ER<5%, PR<5%, and HER2 negative (per 2020 ASCO CAP guidelines).

NOTE: Participants with weakly ER or PR positive disease, defined as ER and/or PR between 1-4% by immunohistochemistry, are eligible if adjuvant endocrine therapy is not recommended/planned by the treating physician.

- b. Participants must have AJCC 8 anatomic tumor clinical stage either
 - T2-T4, N0, M0 or
 - T1-T3, N1-2, M0.

Note: All participants with clinically suspicious nodes must undergo core needle biopsy or fine needle biopsy per standard clinical practice to pathologically confirm nodal status.

- c. Participants must have breast and axillary imaging with mammogram and/or ultrasound and/or MRI within 49 days prior to randomization.

Note: Participants with bilateral invasive breast cancer are eligible if both breast cancers are ER-negative, PR-negative, and HER2-negative provided they meet the other eligibility criteria.

- d. Participants must not have T4/N+, any N3, or inflammatory breast cancer.
- e. Participants must not have metastatic disease (M1).

5.2 Prior/Concurrent Therapy Criteria

- a. Participants must not have received prior systemic therapy or radiation therapy with curative intent for the current breast cancer
- b. Participants must not have had previous definitive ipsilateral breast surgery for the current breast cancer
- c. Participants must not have current or anticipated use of other investigational agents while participating in this study
- d. Participants must not have history of allergic reactions attributed to compounds of similar chemical or biologic composition as study agents
- e. Participants must not have severe hypersensitivity (\geq grade 3) to pembrolizumab or any of its excipients.
- f. Participants must not have received prior therapy with an anti-PD-1, anti-PD-L1, or anti-PD-L2 agent or with an agent directed to another stimulatory or co-inhibitory T-cell receptor (e.g. CTLA-4, OX-40, CD137).
- g. Participants must not be currently participating in or have participated in a study of an investigational agent or used an investigational device within 28 days prior to randomization.

5.3 Clinical/Laboratory Criteria

- a. Participants must be \geq 18 years old.
- b. Participants must have Zubrod Performance Status of 0-2 (see [Section 10.10](#)).
- c. Participants with evidence of peripheral neuropathy must have it at \leq Grade 1, by CTCAE v. 5.0, within 28 days prior to randomization.
- d. Participants must have a complete medical history and physical exam within 28 days prior to randomization.
- e. Participants must have adequate organ and marrow function as defined below within 28 days prior to randomization:
 - Hemoglobin \geq 9.0 g/dL or \geq 5.6 mol/L
 - leukocytes \geq 3 x 10³/uL
 - absolute neutrophil count \geq 1.5 x 10³/uL
 - platelets \geq 100 x 10³/uL
 - total bilirubin \leq 1.5x institutional upper limit of normal (IULN), OR direct bilirubin \leq IULN for participants with total bilirubin >1.5x IULN (unless history of Gilbert's disease. Participants with history of Gilbert's disease must have total bilirubin \leq 5 x institutional IULN).
 - AST and ALT \leq 3 x institutional ULN

- f. Participants must have a serum creatinine \leq the IULN OR calculated creatinine clearance \geq 50 mL/min/1.73m² using the following Cockcroft-Gault Formula. This specimen must have been drawn and processed within 28 days prior to registration:

$$\text{Calculated Creatinine Clearance} = \frac{(140 - \text{age}) \times (\text{weight in kg})}{72 \times \text{serum creatinine}} \dagger$$

Multiply this number by 0.85 if the participant is a female.

† The kilogram weight is the participant weight with an upper limit of 140% of the IBW.

* Actual lab serum creatinine value with a minimum of 0.7 mg/dL.

- g. Participants must have adequate cardiac function. Participants must have left ventricular ejection fraction \geq 50% as assessed by either ECHO or MUGA assessed within 28 days prior to registration. Participants with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, must have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification (see [Section 18.1](#)) and must be class 2B or better.
- h. Participants with known human immunodeficiency virus (HIV)-infection must be on effective anti-retroviral therapy at randomization and have undetectable viral load test on the most recent test results obtained within 6 months prior to randomization.
- i. Participants with evidence of chronic hepatitis B virus (HBV) infection must have undetectable HBV viral load while on suppressive therapy on the most recent test results obtained within 6 months prior to randomization, if indicated.

Note: No testing for Hepatitis B is required unless mandated by local health authority.

- j. Participants with a history of hepatitis C virus (HCV) infection must have been treated and cured. Participants currently being treated for HCV infection must have undetectable HCV viral load test on the most recent test results obtained within 6 months prior to randomization, if indicated.

Note: No testing for Hepatitis C is required unless mandated by local health authority.

- k. Participants with history of diabetes must not have uncontrolled diabetes in the opinion of the treating investigator.
- l. Participants must not have uncontrolled hypertension in the opinion of the treating investigator.
- m. Participants must not have had a major surgery within 14 days prior to randomization. Participants must have fully recovered from the effects of prior major surgery in the opinion of the treating investigator.
- n. Participants must not have severe or active infections within 14 days prior to Randomization, including but not limited to hospitalization for infection, bacteremia, or severe pneumonia.
- o. Participants must not have a diagnosis of immunodeficiency and be receiving chronic systemic steroid therapy (in dosing exceeding 10 mg daily of prednisone equivalent) or any other form of immunosuppressive therapy within 7 days prior to randomization.

- p. Participants must not have active autoimmune disease that has required systemic treatment in 2 years prior to randomization (i.e., with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (e.g., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) is not considered a form of systemic treatment.
- q. Participants must not have a history of (non-infectious) pneumonitis that required steroids, or has current (non-infectious) pneumonitis.
- r. Participants must not have received a live vaccine within 30 days prior to randomization. Examples of live vaccines include, but are not limited to, the following: measles, mumps, rubella, varicella/zoster (chicken pox), yellow fever, rabies, Bacillus Calmette–Guérin (BCG), and typhoid vaccine. Seasonal influenza vaccines for injection are generally killed virus vaccines and are allowed; however, intranasal influenza vaccines (e.g., FluMist®) are live attenuated vaccines and are not allowed.
- s. Participants must not have a prior or concurrent malignancy whose natural history or treatment (in the opinion of the treating physician) has the potential to interfere with the safety or efficacy assessment of the treatment regimen.
- t. Participants must not be pregnant or nursing. Individuals who are of reproductive potential must have agreed to use an effective contraceptive method with details provided as a part of the consent process. A person who has had menses at any time in the preceding 12 consecutive months or who has semen likely to contain sperm is considered to be of "reproductive potential." In addition to routine contraceptive methods, "effective contraception" also includes refraining from sexual activity that might result in pregnancy and surgery intended to prevent pregnancy (or with a side-effect of pregnancy prevention) including hysterectomy, bilateral oophorectomy, bilateral tubal ligation/occlusion, and vasectomy with testing showing no sperm in the semen.

5.4 Additional Criteria

- a. Participants must have one (1) physical 4–5-micron single H&E slide from the archival pretreatment diagnostic biopsy available for submission, as outlined in [Section 15.2](#).
- b. Participants must be offered the opportunity to participate in specimen banking as outlined in [Section 15.3](#). With participant consent, specimens must be collected and submitted via the SWOG Specimen Tracking System as outlined in [Section 15.4](#).
- c. Participants who can complete questionnaires in English, Spanish, or French must be offered the opportunity to participate in the Patient-Reported Outcome study as outlined in [Section 15.5](#).