Protocol Title: Randomized, Phase III Trial to Evaluate the Efficacy and Safety of MK-3475 (Pembrolizumab) as Adjuvant Therapy for Triple Receptor-Negative Breast Cancer with ≥ 1 cm Residual Invasive Cancer or Positive Lymph Nodes (ypN+) After Neoadjuvant Chemotherapy

Target Population: Stages 0–IIIC Triple Negative Breast Cancer

Summary: To compare Invasive Disease-Free Survival (IDFS) of patients with Triple-Negative Breast Cancer (TNBC) who have either ≥ 1 cm residual Invasive Breast Cancer and / or positive lymph nodes (> ypN+) after neoadjuvant chemotherapy randomized to receive 1 Year of MK-3475 (Pembrolizumab) adjuvant therapy compared to no MK-3475 (Pembrolizumab), in both the entire study population and also in the PD-L1 positive subset.

Key Inclusion Criteria:
- Histologically confirmed TNBC, defined as ER Negative, PR Negative, and HER2 Negative with residual invasive breast cancer after completion of neoadjuvant chemotherapy.
  - Patients must NOT have Metastatic Disease (i.e., must be M0).
- Patients must have a complete axillary lymph node dissection after neoadjuvant chemotherapy if the patient had a documented pathologic involvement of axillary nodes before neoadjuvant chemotherapy and had:
  - Sentinel node biopsy after neoadjuvant chemotherapy with positive sentinel node(s).
  - Only 1 sentinel lymph node removed after neoadjuvant chemotherapy.
- Patients must have ≥ 5, available unstained slides from the residual (post-neoadjuvant) invasive tumor in primary site or lymph node to be submitted within 7 Days after registration to determine PD-L1 expression.
- Patients must have had neoadjuvant chemotherapy followed by surgery.
  - Patients who cannot complete all planned treatment cycles for any reason are considered high risk and therefore are eligible for the study if they have residual disease.
- Patients may receive post-operative (adjuvant) chemotherapy for up to 24 Weeks of duration after completion of surgery at the discretion of the treating physician.
  - Adjuvant chemotherapy, if administered, must have been completed within 35 Days prior to screening registration and must be given prior to radiation.
- Patients must have completed their final breast surgery (rendering them free from disease) with clear resection margins for invasive cancer and ductal carcinoma in situ (DCIS) within 90 Days prior to screening registration for patients not receiving post-operative (adjuvant) chemotherapy, or within 210 Days prior to screening registration for patients who have completed post-operative (adjuvant) chemotherapy.
- Patients for whom radiation therapy (RT) to affected breast or chest wall and regional nodal areas is clinically indicated, should receive RT after randomization when possible or concomitantly with MK-3475 (Pembrolizumab) if randomized to experimental arm.
  - However, RT administered prior to registration is also allowed.
- Patients must not have had prior immunotherapy with anti-PD-L1, anti-PD-1, anti-CTLA4 or similar drugs.
- Patients must not have active autoimmune disease that has required systemic treatment in past 2 Years.
- Patients must not have received live vaccines within 30 Days prior to registration.
- Patients must not have known active Hepatitis B Virus (HBV) or Hepatitis C Virus (HCV) infection prior to registration.
  - However, patients who have completed curative therapy for HCV are eligible.
- Patients with Human Immunodeficiency Virus (HIV) infection are eligible if they meet the following criteria: CD4 counts ≥ 350 mm³, serum HIV viral load of < 25,000 IU/ml, and treated on a stable antiretroviral regimen.

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For additional information: https://clinicaltrials.gov/ct2/show/NCT02954874