FAST FACTS

NRG-GY037, A Phase III Study of Induction Pembrolizumab and Chemotherapy Followed by Chemoradiation and Pembrolizumab vs Chemoradiation and Pembrolizumab Both Followed by Pembrolizumab for High Risk Locally Advanced Cervical Cancer

3.1 On Study Guidelines

- The below language provides guidelines for inclusivity of patients with known HIV, HBV, and/or HCV infection]:
    - For patients with known HIV, HBV, and/or HCV infection: HIV-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial.
    - For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated.
    - Patients with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are currently on treatment, they are eligible if they have an undetectable HCV viral load.
- Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial.
- The effects of pembrolizumab on the developing human fetus are unknown. For this reason and because other therapeutic agents and radiation used in this trial are known to be teratogenic, participants of child-bearing potential must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) during study therapy and for 12 months following the completion of study therapy. Should a participant become pregnant or suspect pregnancy while participating in this study, they should inform their treating physician immediately.

Eligibility Criteria

3.2.1 Documentation of Disease

- Patients must have pathologically confirmed newly diagnosed cervical cancer. Eligible pathologic types: squamous cell carcinoma, adenocarcinoma, adenosquamous cell carcinoma

3.2.2 Definition of Disease

- Patients must have pathologically confirmed newly diagnosed cervical cancer. Eligible pathologic types: squamous cell carcinoma, adenocarcinoma, adenosquamous cell carcinoma

- Patients must have locally advanced cervical cancer (LACC) with T3 or T4 disease with or without lymph node involvement (see Appendix 1 for FIGO and TMN staging):
    - IIIA (T3aN0M0)
    - IIIB (T3bN0M0)
    - IIIC1(T3aN1M0, T3bN1M0)
    - IIIC2 (T3aN2M0, T3bN2M0)
    - IVA (T4aN0M0, T4aN1M0, T4aN2M0)

- No prior hysterectomy defined as removal of the entire uterus. NOTE: prior partial/subtotal hysterectomy for reasons other than cervical cancer are eligible to participate in the study. No plan to perform a hysterectomy as part of initial cervical cancer therapy.

- No paraaortic lymph node (PALN) metastases above the T12/L1 interspace.
    - *Note: Nodal status can be confirmed by imaging (CT, MRI, or PET/CT), fine needle aspirate/core biopsy, extra peritoneal biopsy, laparoscopic biopsy, or lymphadenectomy.*

    - Radiologic Definition of Lymph node staging:
      N1:
      - *One or more pelvic lymph nodes with short axis diameter of ≥ 15 mm (axial plane) by CT or MRI, and/or*
      - *One or more pelvic lymph nodes with short axis diameter of ≥ 10 mm and SUVmax ≥ 2.5 by FDG-PET*

      N2:
      - *One or more para-aortic lymph node with short axis diameter of ≥ 15 mm (axial plane) by CT or MRI, and/or*
      - *One or more para-aortic lymph node with short axis diameter of ≥ 10 mm and SUVmax ≥ 2.5 by FDG-PET.*

3.2.3 Prior Treatment

- No prior definitive surgical, radiation, or systemic therapy for cervical cancer.
- No prior immunotherapy.
- No prior pelvic radiation therapy for any disease

3.2.4 Age ≥ 18

3.2.5 ECOG Performance Status of ≤ 2 *See Appendix II for performance status criteria*

3.2.6 Not Pregnant and Not Nursing

3.2.7 Required Initial Laboratory Values

- Adequate hematologic function defined as follows:
  - Absolute neutrophil count (ANC) ≥ 1,500 cells/mm3
  - Platelets ≥ 100,000 cells/mm3
  - Hemoglobin ≥ 8 g/dl (Note: The use of transfusion or other intervention to achieve Hgb ≥ 8 g/dl is acceptable).

- Adequate renal function defined as follows:
  - Creatinine clearance (CrCL) of ≥50 mL/min by the Cockcroft-Gault formula

$$\text{CrCl (mL/min)} = \frac{[140 - \text{age (years)}] \times \text{weight (kg)}}{72 \times \text{creatinine (mg / dL)}} \quad \{\times 0.85 \text{ for female patients}\}$$

- Adequate hepatic function defined as follows:
  - Total bilirubin ≤ 1.5 x institutional upper limit of normal (ULN) (patients with known Gilbert's disease who have bilirubin level ≤ 3 x institutional ULN may be enrolled)
  - AST and ALT ≤3 x institutional ULN

- Adequate cardiac function defined as follows:
  - Patients with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification. To be eligible for this trial, patients should be class 2B or better (see Appendix IV: New York Heart Association (NYHA) Functional Classification).

3.2.8 Comorbid Conditions

- No active infection requiring parenteral antibiotics.

- No live vaccine within 30 days prior to registration. Examples of live vaccines include, but are not limited to, the following: measles, mumps, rubella, varicella/zoster (chicken pox), yellow fever, rabies, BCG, and typhoid vaccine. Seasonal influenza vaccines for injection are generally killed virus vaccines and are allowed; however, intranasal

- No diagnosis of immunodeficiency or is 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 registration.

- No active autoimmune disease that has required systemic treatment in past 2 years (i.e., with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (e.g., thyroxine, insulin, or

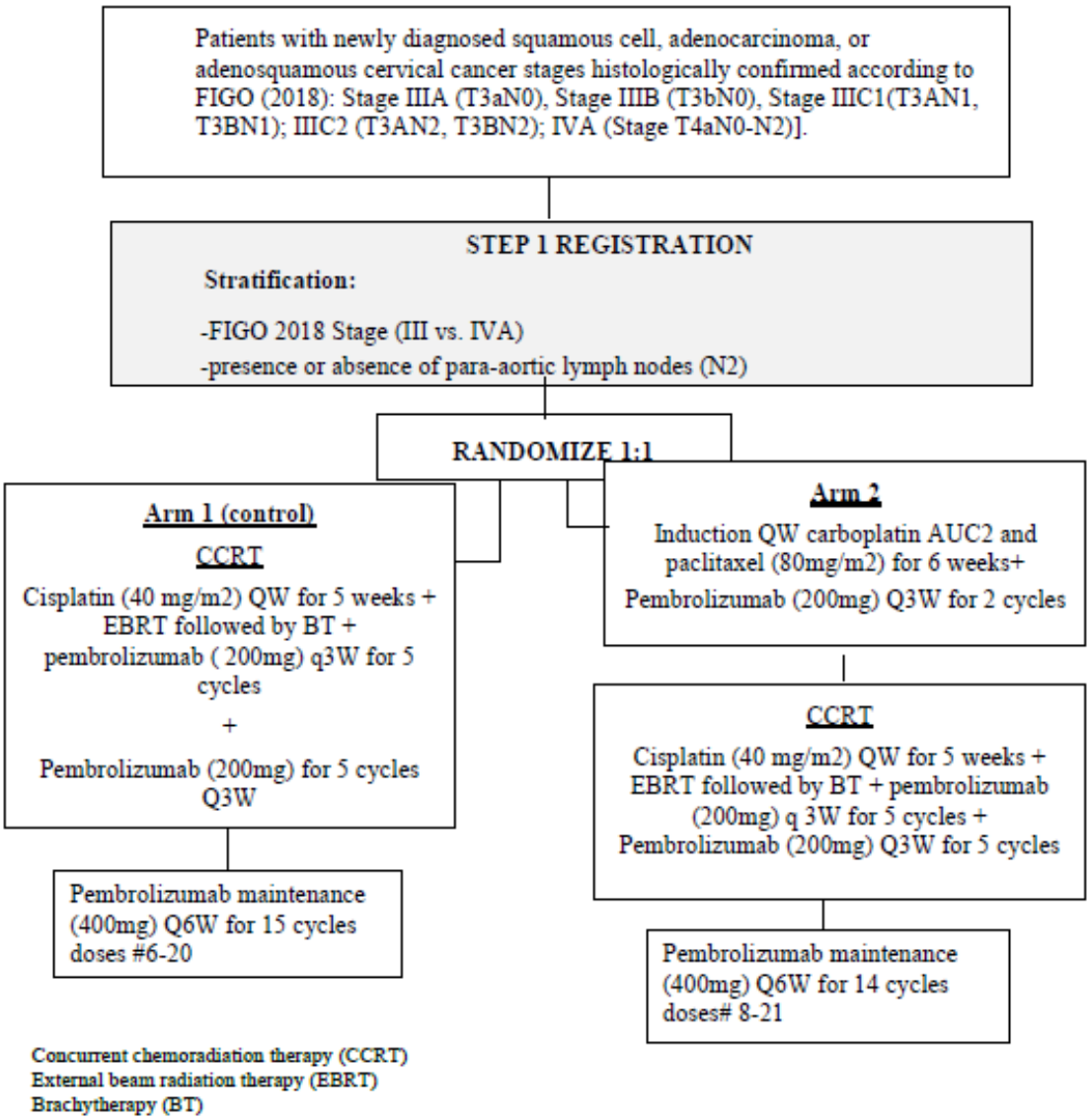
physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) is not considered a form of systemic treatment and is allowed.

- No history of (non-infectious) pneumonitis that required steroids, or current pneumonitis.

3.2.9 Allergies

- No history of allergic reaction to the study agent(s) or compounds of similar chemical or biologic composition to the study agent(s) (or any of its excipients).

NRG-GY037
SCHEMA



Concurrent chemoradiation therapy (CCRT)
External beam radiation therapy (EBRT)
Brachytherapy (BT)