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FAST FACTS

EA2324: A Randomized Phase II/III Trial of Intraperitoneal Paclitaxel Plus Systemic Treatment vs Systemic Treatment Alone in Gastric Carcinomatosis – STOPGAP II

Eligibility Criteria

NOTE: This protocol has a two-step registration process. Once a patient is registered to Step 0, the site should promptly schedule the surgery for the diagnostic laparoscopy and make preparations to randomize to Step 1.

NOTE: Please refer to Section 4.2.6 for additional information regarding the intraoperative Step 1 randomization process.

Eligibility Criteria – Step 0 Registration

1. Patient must be at least 18 years of age.
2. Patient must have an ECOG performance status of 0-1.
3. Patient must have histologically or cytologically confirmed microsatellite stable (MSS) or Mismatch Repair (MMR) protein expression proficient primary gastric or gastroesophageal adenocarcinoma (Siewert 3) with synchronous cytology positive disease (cyt+) OR peritoneal carcinomatosis detected by imaging, laparoscopy or laparotomy. Patients with microsatellite instability-high (MSI-H/dMMR) Mismatch Repair deficient disease are not eligible.
4. Patient must have received a minimum of 3 months and a maximum of 6 months of first line systemic treatment.
5. Patient must be registered to Step 0 within 4 weeks of the last dose of first line systemic therapy. Patient must not have any ongoing significant adverse events that would prohibit them from undergoing a diagnostic laparoscopy procedure followed by further systemic and intraperitoneal therapy.
6. Patient must have no evidence of small or large bowel obstruction other than gastric outlet obstruction due to primary malignancy.
7. Patient must have no evidence of solid organ metastases except for ovarian metastases. Baseline imaging must be done within 30 days prior to Step 0 registration.
8. Patient must have no evidence of clinically significant radiologic peritoneal disease progression during first line systemic therapy.
9. Patient must have no evidence of extensive retroperitoneal lymph node metastases not amenable to resection during gastrectomy.
10. Patient must have no history of prior surgery that would preclude safe diagnostic laparoscopy and port placement.
11. Patient must have no evidence of massive ascites on imaging or history of two therapeutic paracentesis with drainage of more than 1.0 liter of ascites each time in 30 days prior to Step 0 registration.

12. 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 II or better.
13. Patient must not have any uncontrolled intercurrent illness or any other significant condition(s) that would make this protocol unreasonably hazardous.
14. Patient must not have any known contraindications or drug allergies to the protocol treatment agents: Paclitaxel, 5-Fluorouracil, or Leucovorin.
15. Patient must have adequate organ and marrow function as defined below (these labs must be obtained ≤ 30 days prior to Step 0 registration):

    - Leukocytes ≥ 2,000/µL

      Leukocytes:_____ Date of Test:_____
    - Absolute neutrophil count (ANC) ≥ 1,500/µL

      ANC:_____ Date of Test:_____
    - Platelets ≥ 75,000/µL

      Platelets:_____ Date of Test:_____
    - Total bilirubin ≤ 1.5 institutional upper limit of normal (ULN). If patient has Gilbert's Syndrome, total bilirubin must be < 2.0 mg/dL

      Total Bilirubin:_____ Institutional ULN:_____

      Date of Test:_____

      Gilbert's Syndrome_____ (Yes or No)
    - AST(SGOT) and ALT(SGPT) ≤ 3.0 × institutional ULN

      AST:_____ Institutional ULN:_____
    - Date of Test:_____

      ALT: _____Institutional ULN:_____
    - Creatinine Clearance ≥ 30 mL/min (estimated using Cockcroft and Gault formula or measured) See Appendix VII for calculation information.

      Creatinine Clearance _____Date:_____
    - Hemoglobin ≥ 8 g/dL

      Hemoglobin _____Date of Test:_____
    - Serum Albumin ≥ 2.5 g/dL

      Serum Albumin _____Date of Test:_____
16. Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months of Step 0 registration are eligible for this trial.
17. For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated.

18. 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.
19. 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.
20. Patient must not be pregnant or breast-feeding due to the potential harm to an unborn fetus and possible risk for adverse events in nursing infants with the treatment regimens being used.

    All patients of childbearing potential must have a blood test or urine study within 14 days prior to Step 0 registration to rule out pregnancy.

    A patient of childbearing potential is someone, regardless of whether they have undergone tubal ligation, who meets the following criteria: 1) has achieved menarche at some point, 2) has not undergone a hysterectomy or bilateral oophorectomy; or 3) has not been naturally postmenopausal (amenorrhea following cancer therapy does not rule out childbearing potential) for at least 24 consecutive months (i.e., has had menses at any time in the preceding 24 consecutive months).

    Patient of childbearing potential? _____ (Yes or No)

    Date of blood test or urine study: _____

21. Patient must not expect to conceive or father children by using accepted and effective method(s) of contraception (or by abstaining from sexual intercourse) for the duration of their participation in the study. Arm A patients must adhere to the contraceptive requirements outlined in the product specific package inserts while on protocol treatment. Arm B patients must continue contraceptive measures for at least 3 months after the last dose of protocol treatment. In addition, both Arm A and Arm B patients who continue with targeted agents must adhere to the contraceptive requirements outlined in the product specific package inserts while on protocol treatment.

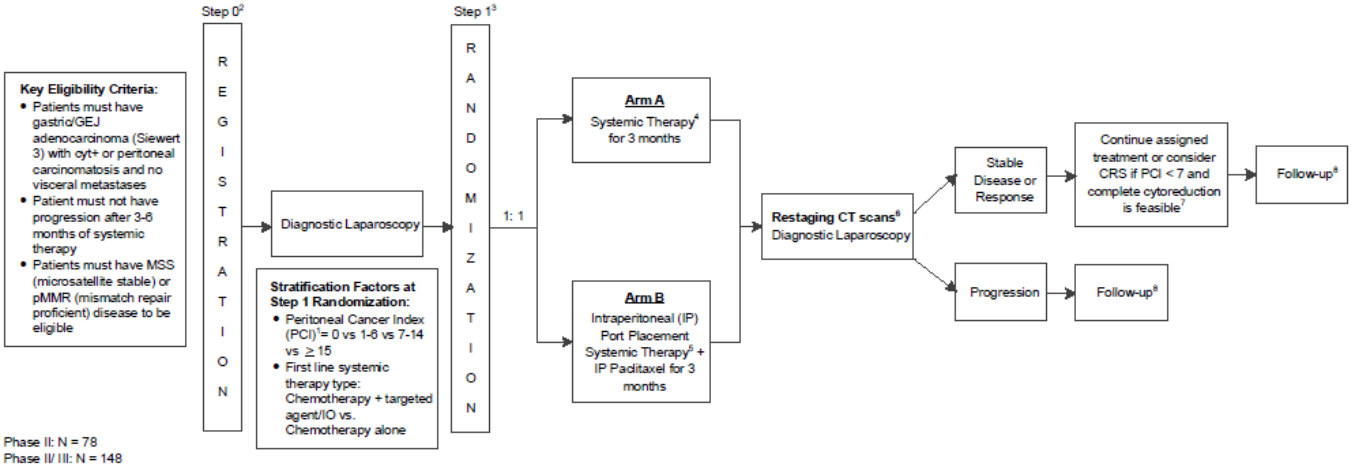
22. Patient must have the ability to understand and the willingness to sign a written informed consent document. Patients with impaired decision-making capacity (IDMC) who have a legally authorized representative (LAR) or caregiver and/or family member available will also be considered eligible.

Eligibility Criteria – Step 1 Randomization

1. Patient must have undergone a diagnostic laparoscopy with peritoneal lavage performed and aspiration for cytology obtained.

2. The extent of peritoneal disease burden must have been assessed during the diagnostic laparoscopy with the Peritoneal Cancer Index (PCI) available (see Appendix V).
3. Patient must not have extensive intraabdominal adhesions that preclude safe placement of the intraperitoneal port.

SCHEMA



1. See Appendix V for the PCI Calculator.
2. Step 0 is where patients will be fully consented and eligibility confirmed. Patients must by registered to Step 0 within 4 weeks after the last dose of first line therapy. The diagnostic laparoscopy must be planned and scheduled within 4 weeks of Step 0 registration
3. Patient are randomized 1:1. All patients will be randomized **in the operating room** after the PCI score has been calculated by the surgeon. All sites must be prepared for the intraoperative randomization process by ensuring all of the procedures outlined in Section 4.2.6 and Appendix VI are in place ahead of time. Patients who are randomized to Arm B will then undergo insertion of the intraperitoneal port at the time of diagnostic laparoscopy. EA2234 protocol treatment to start within 4 weeks of Step 1 randomization.
4. Arm A patients will receive any standard of care systemic therapy. Patient may also receive targeted therapies/immunotherapy. See Section 5.1.2. for additional details.
5. Arm B patients will receive systemic therapy consisting of 5-FU, Leucovorin and IV Paclitaxel in addition to IP Paclitaxel. Patient may also receive targeted therapies/immunotherapy. See Section 5.1.1 for additional details.
6. Restaging scans with CT and/or diffusion weighted MRI with contrast will be completed after 12 weeks (+/- 2 weeks) of protocol therapy and will continue to be obtained every 4 cycles thereafter. Diagnostic laparoscopy may be considered for surgical decision making at this time.
7. Patients will continue treatment until progression, intolerance/unacceptable toxicity, or cytoreduction.
8. See Sections 5.7 and 7.1 for additional details on follow up.