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NCI National Clinical Trials Network

EA2212

ECOG-ACRIN cancer research group

For Patients with Gastric/Gastroesophageal Junction Cancer

EA2212 Available Through ECOG-ACRIN Cancer Research Group

A Randomized Phase II Study of Perioperative Atezolizumab +/- Chemotherapy in Resectable MSI-H/dMMR Gastric and Gastroesophageal Junction (GEJ) Cancer

Patient Population

See Section 3 for Complete Eligibility Details

- Age ≥ 18 years; ECOG PS 0-2; adequate lab values
- Must have histologically/cytologically confirmed diagnosis of gastric or gastroesophageal junction adenocarcinoma that is MSI-H/dMMR (microsatellite instability-high/ mismatch repair deficient) as determined per protocol
- Must have previously untreated localized gastric, or Siewert type II or III GEJ adenocarcinoma. Tumors must be T2 or greater primary lesion or be any T stage with the presence of positive locoregional lymph nodes– N+ (clinical nodes) without evidence of metastatic disease
- Amenable to surgical resection with therapeutic intent
- No contraindications to FLOT or mFOLFOX/CAPOX
- No prior potentially curative surgery for carcinoma of the stomach/GEJ; no prior chemotherapy, targeted small molecule therapy, or radiation therapy for MSI-H/dMMR gastric and GEJ cancer
- Must not receive any other standard anti-cancer therapy or experimental agent concurrently with the study drugs
- Recovered from clinically significant AEs of their most recent therapy/intervention prior to randomization
- Must have chest/abdomen/pelvis CT completed within 4 weeks prior to randomization
- May not have received prior treatment with an immune checkpoint inhibitor (anti-PD-1, anti-PDL-1 anti-PDL-2, anti-CTLA4 monoclonal antibody)
- Must not have active autoimmune disease or history of autoimmune disease that might recur, which may affect vital organ function or require immune suppressive treatment including systemic corticosteroids (see protocol for details)
- Must not have known interstitial lung disease that is symptomatic or may interfere with the detection or management of suspected drug-related pulmonary toxicity; must not have known history of pneumonitis
- No known history of active TB
- No allogenic bone marrow/stem cell/solid organ transplant

Treatment Plan

See Section 5 for Complete Treatment Details

- Treatment must start within 14 days after randomization
- All patients will undergo neoadjuvant therapy, followed by surgery, then adjuvant therapy (with the same treatment that was assigned neoadjuvantly) followed by atezolizumab
- **Arm A (chemotherapy + atezolizumab):** Patients will receive one of the following (physician's choice) before proceeding to surgery:
  - ◊ 4 cycles (1 cycle = 14 days) of FLOT chemotherapy + atezolizumab OR
  - ◊ 4 cycles (1 cycle = 14 days) of mFOLFOX chemotherapy + atezolizumab OR
  - ◊ 3 cycles (1 cycle = 21 days) of CAPOX chemotherapy + atezolizumab
- **Arm B (atezolizumab):** Patients will receive 3 cycles (1 cycle = 21 days) of atezolizumab before surgery
- Surgery (approach per surgeon discretion, per protocol) must be performed up to 12 weeks post completion of neoadjuvant therapy
  - ◊ Prior to surgery, patients must be restaged with a CT chest/abdomen/pelvis to assess for disease progression; if metastatic disease is identified, patients will not go on to resection and will discontinue study treatment
  - ◊ For patients that need salvage surgery, the extent and timing will be per the patient's providers
- Adjuvant therapy should start within 4-10 weeks after surgery
  - ◊ Arm A: patients will receive the same chemotherapy regimen selected preoperatively; following completion of chemotherapy + atezolizumab, patients will receive 6 cycles (1 cycle = 21 days) of atezolizumab
  - ◊ Arm B: patients will receive 9 cycles (1 cycle = 21 days) of atezolizumab

Study Chair:
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Patient Enrollment

All Sites: Oncology Patient Enrollment Network (OPEN), https://open.ctsu.org/open

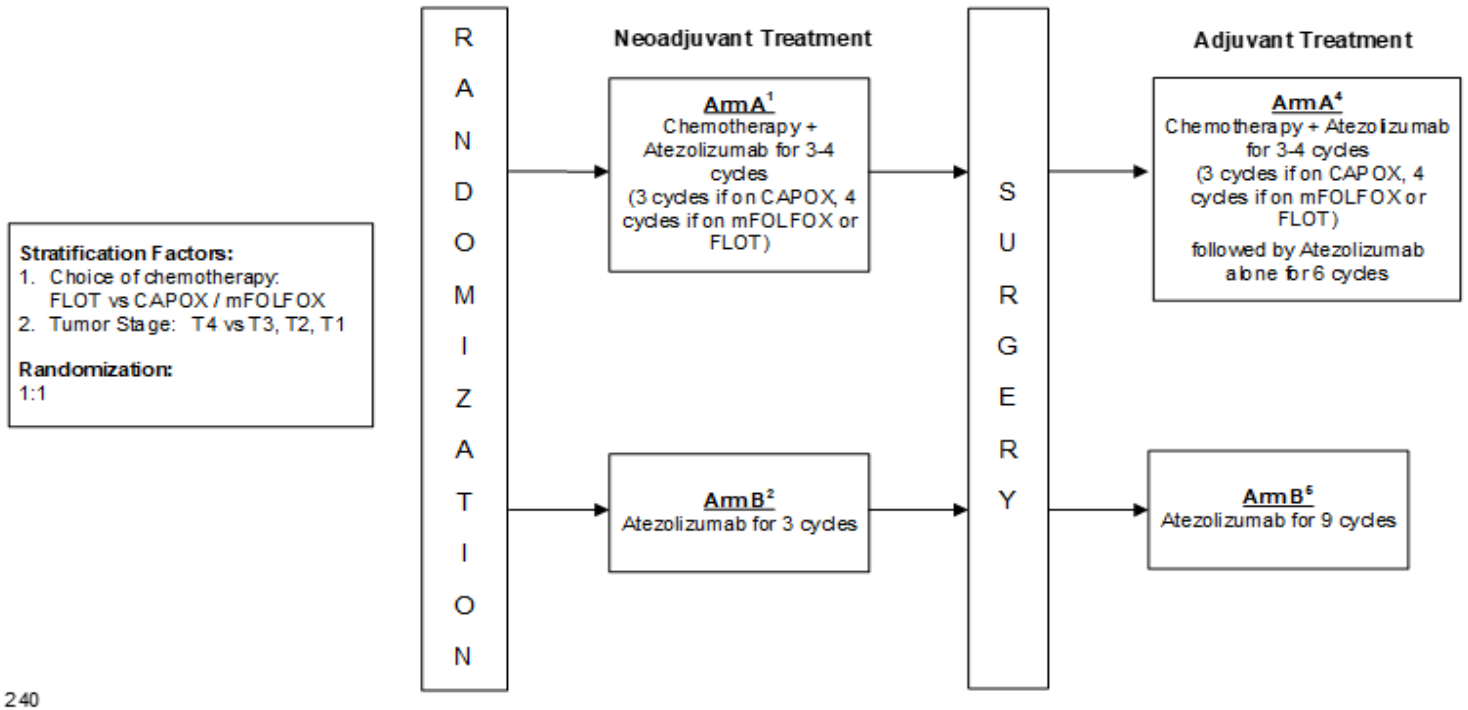
Protocol Information

ECOG-ACRIN Operations-Boston: 857-504-2900, http://ecog-acrin.org (Member Login)

Please Enroll Your Eligible Patients!

EA2212

Schema



N = 240

1. Arm A Neoadjuvant: Prior to randomization, the treatment physician must select one of the following chemotherapy regimens outlined below (see Section 5.2 for detailed administration guidelines).

   Arm A Option 1 FLOT: Day 1 Docetaxel 50 mg/m^2 IV, Oxaliplatin 85 mg/m^2 IV, Leucovorin 200 mg/m^2 IV, Fluorouracil (5-FU) 2600 mg/m^2 IV continuous infusion over 24 hours, Atezolizumab 840mg mg IV. Repeat cycle every 14 days for 4 cycles.

   Arm A Option 2 mFOLFOX: Day 1 Oxaliplatin 85 mg/m^2 IV, Leucovorin 400 mg/m^2 IV, Fluorouracil (5-FU) bolus of 400 mg/m^2 followed by Fluorouracil (5-FU) 2400 mg/m^2 IV continuous infusion over 46 hours, Atezolizumab 840mg mg IV. Repeat cycle every 14 days for 4 cycles.

   Arm A Option 3 CAPOX: Day 1 Oxaliplatin 130 mg/m^2 IV infusion and Atezolizumab 1200mg IV; Capecitabine 1000 mg/m^2 twice a day by mouth on Days 1-14 of each cycle. Repeat cycle every 21 days for 3 cycles.

2. Arm B Neoadjuvant: Day 1 Atezolizumab 1200 mg IV. Repeat cycle every 21 days for 3 cycles.

3. Surgery: Refer to Section 5.2.4 for details for those patients that do not go on to surgery

4. Arm A Adjuvant: The same regimen used in the neoadjuvant setting will be used in the adjuvant setting. Repeat cycle every 14 days for 4 cycles for FLOT +Atezolizumab or mFLOFOX + Atezolizumab and repeat cycle every 21 days for 3 cycles for CAPOX + Atezolizumab. After adjuvant Chemotherapy + Atezolizumab is complete, patient will receive Atezolizumab 1200mg mg IV alone for 6 cycles.

5. Arm B Adjuvant: Day 1 Atezolizumab 1200 mg IV. Repeat cycle every 21 days for 9 cycles.