v.10/17/24 (Add. #7)

NCI National Clinical Trials Network

EA2183

ECOG-ACRIN cancer research group

For Patients with Oligometastatic HER2- EGA

Please Enroll Your Eligible Patients!

EA2183 Available Through ECOG-ACRIN Cancer Research Group

A Phase III Study of Consolidative Radiotherapy in Patients with Oligometastatic HER2 Negative Esophageal and Gastric Adenocarcinoma (EGA)

Patient Population

See Section 3 for complete eligibility criteria

- ≥ 18 years of age, ECOG PS 0-1, and adequate lab values
- Histologically confirmed HER2- metastatic esophageal/ gastric adenocarcinoma (AJCC 8th ed.) with known PDL1 CPS expression
- Must have received 3-6 months of first-line systemic therapy for advanced disease within 4 weeks of randomization; must have at least stable disease, with no evidence of progression on first-line systemic therapy
- Must have oligometastatic disease at the time of diagnosis of metastatic disease, and prior to initiation of first-line systemic therapy, which is defined as:
  - ◊ 1-5 radiologically visible metastatic lesions (not sites), in addition to the primary site
  - ◊ Anatomically defined lymphadenopathy will be considered as 1 metastatic lesion
  - ◊ No radiologically evident peritoneal metastasis
- Must have received at least 2 chemotherapy agents during first-line treatment
- Consultation with radiation oncology must be performed; prior palliative/definitive radiation/chemoradiation to the primary site is allowed
- Patients who had prior definitive treatment for early stage EGA are eligible as long as recurrent disease developed at least 6 months after prior therapy completion (see protocol for details)
- Major surgery must be completed ≥ 4 weeks prior to randomization
- Patients with CNS metastasis are not eligible
- Must not have uncontrolled intercurrent illness (see protocol for details)
- Must not receive live vaccines within 4 weeks of randomization (see protocol for details)

Treatment Plan

See Section 5 for complete treatment details

Eligible patients will have received 3-6 months of standard first-line systemic therapy. Patients will be randomized to one of the following arms:

- **Arm X**: Consolidative XRT followed by systemic therapy
- **Arm Y**: Consolidative systemic therapy

Systemic Therapy: For both arms, systemic therapy after randomization will be chosen by the treating physician

- ◊ Chemotherapy + immunotherapy: [FOLFOX; CAPOX; CF] + [nivolumab or pembrolizumab]

or

- ◊ Chemotherapy alone: FOLFOX; CAPOX; CF; FLOT; FOLFIRI

- Systemic therapy dosing will be per SOC
- Chemotherapy: dose reduction, modification, re-escalation, or chemotherapy agent stoppages because of cumulative toxicities (e.g., oxaliplatin-induced neuropathy) are permitted
- Immunotherapy: No dose reductions to nivolumab or pembrolizumab are permitted
- Patients may remain on study treatment with chemotherapy alone if immunotherapy is permanently discontinued due to toxicities

Radiation Therapy: Administered using external beam photon RT, with 3D-CRT, IMRT, SBRT, SRS, or photon therapy, per treating radiation oncologist. Proton therapy is also permitted

- XRT must be performed at a participating study site
- Total dose and fractionation will be at the discretion of the treating radiation oncologist
- Patients without prior RT to the primary tumor should be treated with up to 45 Gy in 15 fractions
- To allow adequate recovery for Arm X patients, systemic therapy should start 2-4 weeks after the completion of XRT

Study Chair:
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Patient Enrollment (Oncology Patient Enrollment Network [OPEN])

https://open.ctsu.org/open 1-888-823-5923

Protocol Information (ECOG-ACRIN Operations – Boston)

http://ecog-acrin.org (Member Login) 1-857-504-2900

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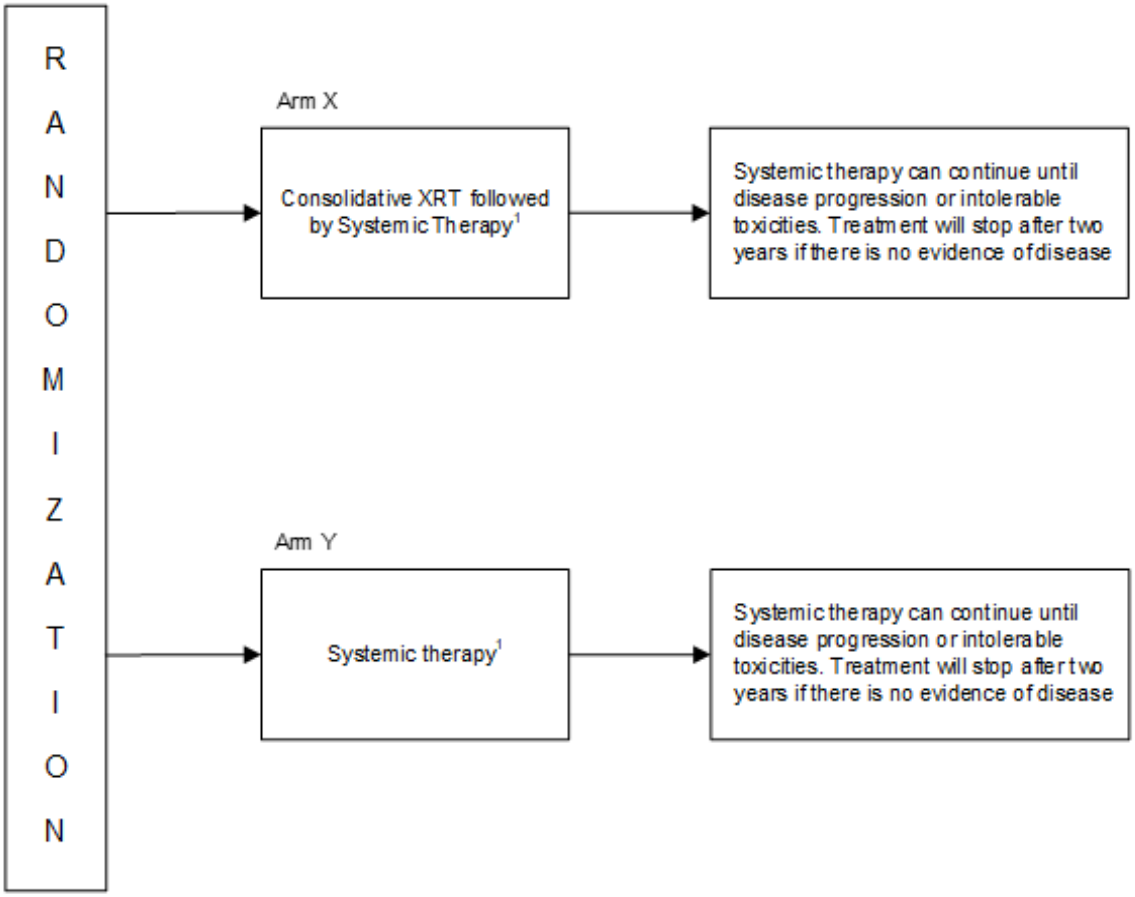
Schema

Stratification Factors:

- Number of metastatic sites: 1-2 vs. 3 or more at the time of diagnosis of advanced disease.
- Prior use of anti-PD1 agents (IO) during first-line treatment of advanced disease vs. no prior IO during first-line treatment of advanced disease
- Triplet vs. doublet first-line chemotherapy backbone



N = 216

1. Systemic therapy will consist of standard FDA approved systemic therapy for HER2 negative esophageal and gastric adenocarcinoma as per NCCN guidelines and with the options outlined in Section **5.1**. The selection of the systemic therapy regimen used is at the discretion of the treating physician and in agreement with the patient. Once the regimen has been declared and started, patients may not switch to another regimen option.