RANDOMIZED PHASE III TRIAL OF MFOLFIRINOX +/- NIVOLUMAB VS. FOLFOX +/- NIVOLUMAB FOR FIRST-LINE TREATMENT OF METASTATIC HER2-NEGATIVE GASTROESOPHAGEAL ADENOCARCINOMA

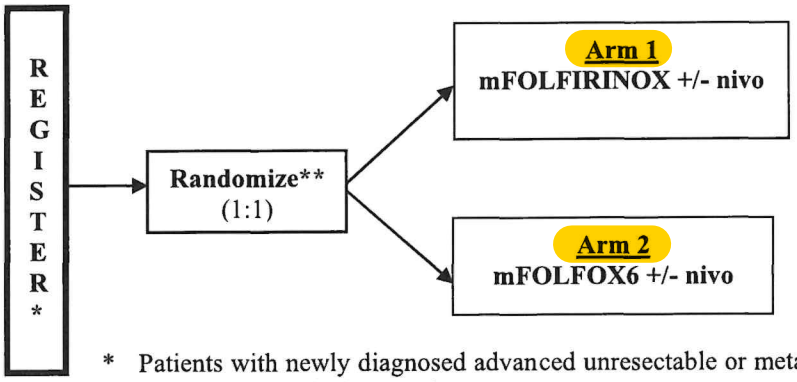
Eligibility Criteria (see Section 3.0)

- HER2 negative gastroesophageal adenocarcinoma with known PD-L1 CPS
- Measurable disease or non-measurable but evaluable disease as defined by RECIST 1.1
- No prior treatment for metastatic disease (see Section 3.2 for prior neoadjuvant and/or adjuvant therapy parameters)
- Not pregnant and not nursing
- Age ≥ 18 years
- ECOG performance status 0 or 1
- 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.
- No allogeneic tissue/organ transplant
- No known Gilbert's Syndrome or known homozygosity for UGAT1A1*28 polymorphism
- No grade ≥ 2 peripheral neuropathy, neurosensory toxicity, or neuromotor toxicity per CTCAE v5.0 regardless of causality
- No medical condition such as uncontrolled infection, uncontrolled diabetes mellitus or cardiac disease which, in the opinion of the treating physician, would make this protocol unreasonably hazardous for the patient.
- No active autoimmune disease requiring systemic treatment with disease modifying agents or immunosuppressive drugs within 6 months.
- No history of noninfectious pneumonitis requiring steroids

Required Initial Laboratory Values

ANC	≥ 1500/mm^3
Platelet count:	≥ 100,000/mm^3
Creatinine:	≤ 1.5 x upper limit of normal (ULN) OR
Calc. creatinine clearance	≥ 30 mL/min
Total bilirubin:	≤ 1.5 x ULN
AST/ALT:	≤ 3 x ULN (< 5 x ULN if clearly attributable to liver metastases)

Schema



* Patients with newly diagnosed advanced unresectable or metastatic HER2 negative gastric, GEJ, esophageal adenocarcinoma

** Stratification: Tumor location (gastric vs GEJ vs esophagus); Measurable disease vs not; planned nivo use vs not; PD-L1 CPS ≥ 5 vs < 5.

Patients will be treated using 14-day cycles until disease progression or discontinuation of treatment for other reasons (e.g. unacceptable adverse events, withdrawal, etc.); oxaliplatin will be given up to 12 cycles.