A PILOT STUDY TO EVALUATE THE CLINICAL AND IMMUNOLOGICAL EFFECTS OF INCORPORATING A CD40-AGONISTIC ANTIBODY INTO THE MULTIMODALITY TREATMENT OF RESECTABLE ESOPHAGEAL AND GE JUNCTION CANCERS

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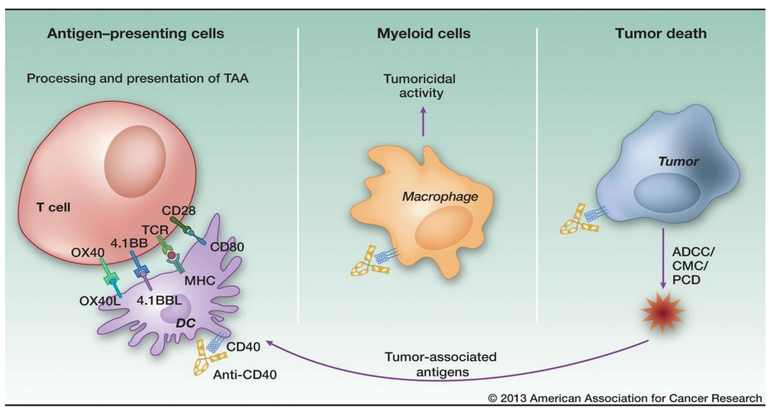
BACKGROUND

- Trimodality therapy (neoadjuv chemoRT → surgery) represents the standard of care for patients with resectable esophageal and GE junction cancers, but relapse rates remain high
- Immuno-oncology agents have established efficacy in the treatment of advanced/metastatic esophagogastric cancers, with recent accelerated FDA approval of pembrolizumab for this indication (PD-L1 positive tumors)



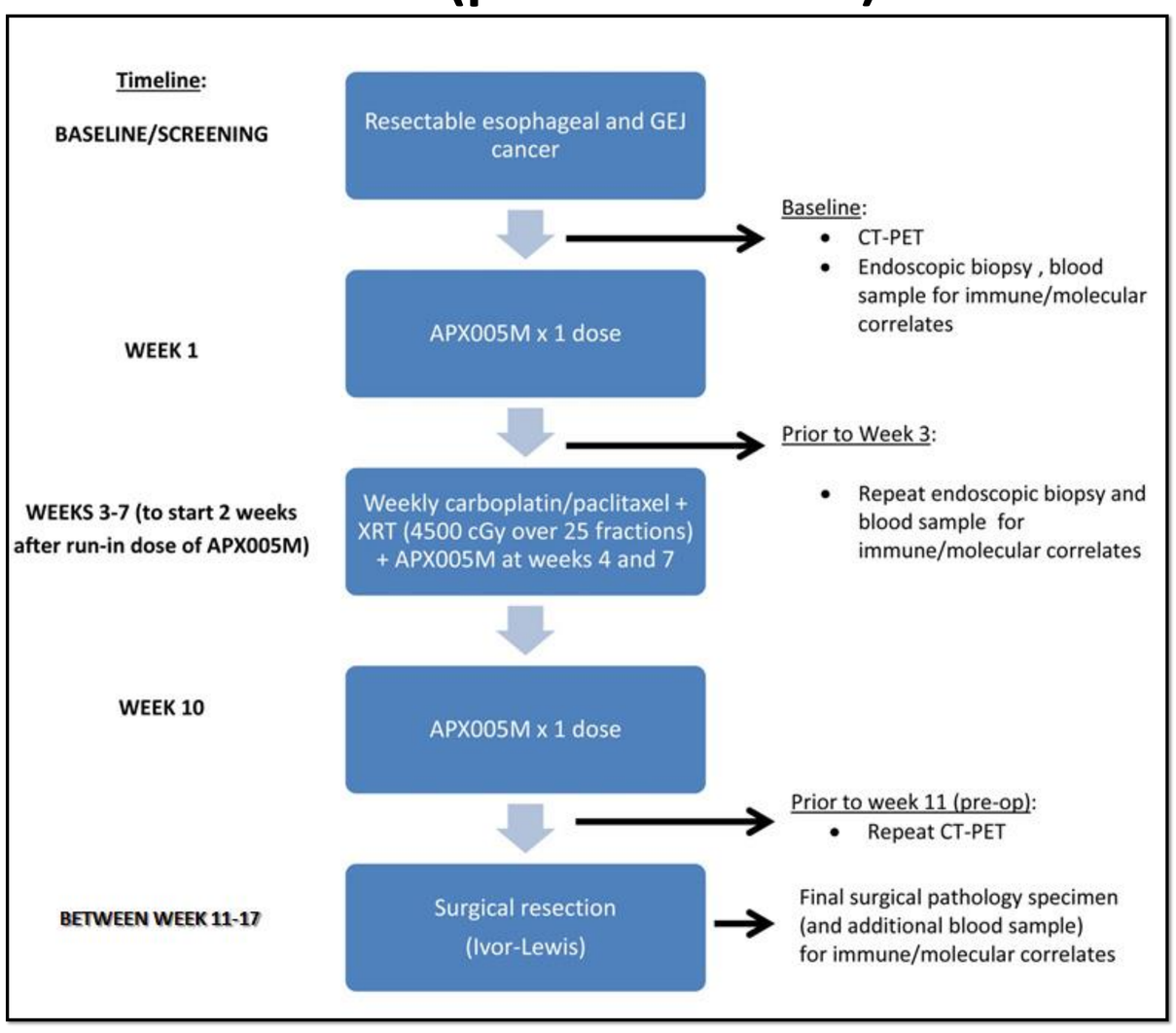
(Vonderheide and Glennie, *Clin Cancer Res* 2013)

- Targeting **CD40**, a costimulatory molecule found on APCs, represents a promising cancer immunotherapeutic strategy
  - Activation results in improved antigen processing and presentation and cytokine release from activated APCs, enhancing T cell responses
  - CD40 expressed on many tumor cells; activation induces tumor cell apoptosis and inhibition of tumor growth
  - **APX005M** (Apexigen, San Carlos, CA) is a humanized IgG1 anti-CD40 agonistic antibody that binds to CD40 with high affinity; FIH phase I testing established safety and dose-dependent activation of APCs and T cells
- **This represents the first study to evaluate a CD40 agonistic mAb in combination with chemoRT in the neoadjuvant setting for this disease**

KEY ELIGIBILITY CRITERIA

- Histologically proven squamous cell carcinoma or adenocarcinoma of the esophagus or GE junction
- Surgically resectable (T1-3 N0-1 by endoscopic ultrasound)
- ECOG performance status 0-1
- Adequate hematological, renal, and hepatic parameters
- No prior exposure to any immuno-oncology agents
- No autoimmune disorder or chronic steroid dependency

STUDY SCHEMA (planned n = 16)



Notes re treatment: Carboplatin AUC 2, paclitaxel 50 mg/m2, APX005M 0.3 mg/kg; up to 2 dose reductions allowed.
During concurrent rx, APX005M dose offset from chemo by 2-3 days.

STUDY OBJECTIVES

- To establish the **safety** and **feasibility** of combining APX005M with standard-of-care chemoradiation in the neoadjuvant setting for patients with resectable esophageal/GEJ cancers.
- To assess the efficacy of this combination as measured by **pathologic complete response rate**.

STUDY CORRELATIVES

(*to be measured at baseline and at serial time points*):

- **Tissue Multiplex IHC** for both APC (B cell, dendritic cell, macrophage) and T cell activation
- **Blood and tissue flow** for APC and T cell activation
- **TCR sequencing** for T cell repertoire diversity

ClinicalTrials.gov Identifier: **NCT03165994**
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