The Update on the Gastroesophageal Cancer Care and Research at OSU

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The James

THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER

Creating a Cancer-free World.
One Person, One Discovery at a Time.
Gastrointestinal Medical Oncology at OSU

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Goals

• Incidence and Survival of Gastroesophageal Cancers
• The Diagnostic Process of Gastroesophageal Cancers
• Treatment of Localized Esophageal and Esophagogastric Junction (GEJ) Cancers
• Treatment of Localized Gastric Cancer
• Ongoing Research for Gastroesophageal Cancers at James
• Treatment of Metastatic Gastroesophageal Cancers
Age Standardized Incidence Rate of Esophageal Adenocarcinoma & Squamous Cell Carcinoma in Men

Schlottmann et al. Esophageal cancer. July 2018
Age Standardized Incidence Rate of Esophageal Adenocarcinoma & Squamous Cell Carcinoma in Women

Schlottmann et al. Esophageal cancer. July 2018
Probability of Developing Cancer (2014-2016) in the United States

- Breast (female): 12.8%
- Prostate: 11.6%
- Lung and bronchus: 6.3%
- Colorectum: 4.4%
- Pancreas: 1.6%
- Oral cavity and pharynx: 1.2%
- Liver and intrahepatic bile duct: 1%
- Stomach: 0.9%
- Esophagus: 0.5%
- Testis: 0.4%
Five-year relative survival (2009-2015) in the United States

Prostate: 98%
Testis: 95%
Breast (female): 90%
Oral cavity and pharynx: 65%
Colorectum: 64%
Stomach: 32%
Esophagus: 20%
Lung and bronchus: 19%
Liver and intrahepatic bile duct: 18%
Pancreas: 9%
The Diagnosis of Esophageal, Gastroesophageal Junction (GEJ) and Gastric Cancers

Accurate staging is essential:

- EGD with biopsy
- Endoscopic Ultrasound for tumor (T) and nodal (N) staging
- PET scan to rule out disease spreading (M)
- Laparoscopic exam to rule out disease spreading to the peritoneum
Gastroesophageal Cancer Molecular Subtypes

Squamous Cell Carcinoma

Adenocarcinoma

J Kim et al. Nature 2017
Current Treatment for Esophageal and GEJ Cancers in the US

- **cT1 N0**
  - Endoscopic resection +/- ablation;
  - Esophagectomy

- **cT2-3 or any nodal positive**
  - Concurrent chemotherapy with radiation
  - Surgery
Standard of Care for Esophageal and Gastroesophageal Junction (GEJ) Cancers: Preoperative Chemoradiation

CROSS Trial

SCC or Adenocarcinoma of Esophageal +GEJ
T1N1M0
T2-3N0-1M0
PS 0-2

N=188

Chemoradiotherapy (Carboplatin/paclitaxel)
N=178

Esophagectomy alone

Esophagectomy

Van Hagen et al. NEJM 2012; Shapiro et al. Lancet Oncology 2015
Overall Survival for Patients with Locoreginal Esophageal and GEJ Cancers: Preoperative Chemoradiation

Van Hagen et al. NEJM 2012; Shapiro et al. Lancet Oncology 2015
Ongoing Clinical Trials: How Can We Improve the Treatment for Patients with Esophageal or GEJ Adenocarcinomas Who Are NOT Surgical Candidates?
Phase I Trial with Expansion Cohort of OBP-301 (Telomelysin\textsuperscript{TM}) and Definitive Chemoradiation for Patients with Locally Advanced Esophageal and Gastroesophageal Adenocarcinoma Who Are Not Candidates for Surgery

Dr. Eric Miller  
Radiation Oncology

Dr. Terence Williams  
Radiation Oncology

Dr. Ning Jin  
Medical Oncology

Dr. Georgios Papachristou  
Gastroenterology
Rationale: Phase I Trial with Expansion Cohort of OBP-301 and Definitive Chemoradiation for Patients with Locally Advanced Esophageal and GEJ Adenocarcinoma Who Are Not Candidates for Surgery

• Oncolytic immunotherapy employs viruses that are designed to preferentially lyse cancer cells and trigger anti-tumor immunity.

• In OBP-301-003-CV (OBP-301 + Radiation phase I/II study), OBP-301 was combined with radiation in Japanese esophageal cancer patients who were not candidates for surgery or chemoradiation. Toxicities were manageable.

• OBP-301 may sensitize the infected tumor cells to radiation.

• In addition, OBP-301 may also potentiate systemic anti-tumor immune responses, which may also prevent distant spreading.
Trial Design for NRG-GI007

1. EUS
2. PET/CT
3. Chemoradiation with Intra-tumor Injections of Oncolytic Virus
4. EGD
5. Post-XRT PET/CT
6. Observation
Inclusion criteria

• Adenocarcinoma of the esophagus or GEJ within 90 days prior to registration.
• Performance Status of 0-1.
• Must have a tumor that is amenable to intra-tumoral injection.
• Patients must, in the opinion of a thoracic surgeon and/or multidisciplinary team, not be a candidate for surgery but are candidates for chemoradiation.
• Patients must have adequate blood, kidney, and liver function.

Please consult your treating physician, if you are recently diagnosed with locally advanced E/GEJ cancer to consider this trial enrollment!
Current Treatment for Gastric Cancer in the US

- **cT1 N0**
  - Endoscopic resection or surgery

- **cT2-3 or nodal positive**
  - Chemotherapy then surgery then chemotherapy
  - Surgery then adjuvant chemotherapy and radiation
  - Upfront chemotherapy and radiation then surgery

Favored
Current Standard Care for Peri-operative Chemotherapy in Gastric Cancer (FLOT4)

Al-Batran et al. The Lancet. 2019
Ongoing Research for Gastric Cancer at the James

- **cT1 N0**: Endoscopic resection or surgery
- **cT2-3 or nodal positive**
  - Chemotherapy then surgery then chemotherapy
  - Surgery then adjuvant chemotherapy and radiation
  - Upfront chemotherapy and radiation, then surgery

Research Interest
Total Neoadjuvant Therapy for the Treatment of Gastroesophageal Junction (GEJ) and Gastric Cancers

Dr. Ning Jin
Medical Oncology

Dr. Dayssy A. Diaz
Radiation Oncology

Dr. Jordan Cloyd
Surgical Oncology

Dr. Michael Knopp
Radiology

Dr. Chadwick Wright
Radiology
Rationale: Total Neoadjuvant Therapy for the Treatment of Gastroesophageal Junction (GEJ) and Gastric Cancers

- Chemotherapy prior to surgery can improve outcome in gastric cancer.
- Postoperative chemoradiation can improve outcome compared to surgery alone in gastric cancer.
- Chemotherapy and chemoradiation before surgery will ensure adequate treatment delivery and may be feasible in gastric cancer.
- The use of digital PET imaging to adapt treatment volumes has the potential to decrease radiation toxicity.
Trial Design of Total Neoadjuvant Therapy in GEJ and Gastric Cancer

1. Baseline PET scan
2. Chemotherapy
3. Post-treatment PET
4. Chemoradiation (PET will be used to define the boost volume)
5. Post-XRT PET
6. Surgery
Inclusion criteria

- Patients with biopsy proven, cT2N0-T4aN3M0 (TNM 8th edition), gastric or GEJ adenocarcinoma.
- Evaluation with EUS and staging laparoscopy prior to enrollment is strongly recommended.
- Patients should be ≥18 years old.
- ECOG performance status ≤ 2.
- Patients must have adequate blood, kidney, and liver function.

Please consult your treating physician, if you are recently diagnosed with locally advanced gastric cancer to consider this trial enrollment!
Systemic Therapies for Metastatic (Stage IV) Esophageal, GEJ and Gastric Cancers

- FOLFOX +/- Trastuzumab
- Paclitaxel + Ramucirumab Or Immunotherapy if PD-L1 ≥10
- Immunotherapy Irinotecan TAS102

Clinical Trials

Palliative Care

The James
Immunotherapy in Upper GI Cancers

- PD-L1 expression on tumor cells suppresses immune surveillance, permitting tumor growth.
- Pembrolizumab is a humanized antibody that
  - Binds to PD-1 with high affinity, preventing PD-1 from binding to its ligands
  - Has demonstrated robust antitumor activity and manageable toxicity in multiple cancers
Pembrolizumab is Approved in Third Line for Patients with GEJ and Gastric Adenocarcinomas with PD-L1 ≥ 1

Median OS: 5.6 months

Fuchs et al. JAMA Oncol. 2018 (Keynote-059)
Pembrolizumab is Approved in Second Line for Patients with Esophageal Squamous Cell Carcinoma with PD-L1 ≥ 10

**Overall Survival (PD-L1 CPS ≥10)**

Median OS: 9.3 months in patients receiving pembrolizumab vs. 6.7 months receiving chemotherapy

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Kojima et al. J. Clin Oncol. 2019 (Keynote-181)
Conclusion

- The treatment of gastroesophageal cancer is complex with unfavorable clinical outcomes.
- At James, we have developed a multidisciplinary team to conduct clinical trials to improve the treatment efficacy in upper GI cancers.
- Immunotherapy holds promise in this field.
Thank You

To learn more about Ohio State’s cancer program, please visit cancer.osu.edu or follow us in social media: