Patient and Tumor-Specific Multiplexed Circulating Tumor DNA Response to Multi-Modality Therapy for Esophageal and Rectal Cancer: Preliminary Results of a Pilot Study

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Background

• Non-operative management of locally-advanced esophageal and rectal cancer is becoming more prevalent

• Highly sensitive and specific serum biomarkers of treatment response are needed – ctDNA monitoring shows great promise
Design

• Plasma specimens were collected at baseline, throughout neoadjuvant therapy, immediately prior to surgery and in follow up.

• Plasma samples underwent:
  • WES and library preparation
  • Somatic variants called using MuTect (1.1.4, Broad Institute)
  • SNV calls filtered to identify bait target sites
  • DIDA-Seq error-correction libraries prepared as per Butler et al., 2019
Persistent ctDNA precedes clinical recurrence with 8 month lead-time

cT2N1M0 rectal adenocarcinoma

Recurrence Salvage

A - Lung mets (3) wedge resection x 2 SBRT x 1

NED - Flex-Sig

NED - MRI

LAR
Persistent ctDNA precedes clinical recurrence with 5 month lead-time

cT3N1 rectal adenocarcinoma

- C1 FOLFOX
- C4 FOLFOX
- C8 FOLFOX
- Mid-course chemoRT
- Post-chemoRT
- NED - Flex-Sig
- post-APR
- NED - CT CAP

ctDNA Concentration (hGE/mL)

Time from Initial Blood Draw (mo)
ctDNA declines with neoadjuvant chemoRT and after resection

cT3N1 esophageal adenocarcinoma

ctDNA Concentration (hGE/mL) vs. Time from Initial Blood Draw (mo)

Pre-chemoRT, Late-chemoRT, Post-chemoRT, Pre-esophagectomy, Post-esophagectomy, NED
ctDNA undetectable at time of recurrence

cT3Nx esophageal adenocarcinoma
Absence of ctDNA associated with pCR

cT2N0 esophageal adenocarcinoma

- Pre-chemoRT
- Late-chemoRT
- Pre-esophagectomy
- Post-esophagectomy pathologic CR
- Baseline
- NED
Conclusions

• CtDNA associated with treatment response, confirming pCR and predicts local recurrences with significant clinical lead times.

• Tumor heterogeneity and high tumor mutational burden may reduce sensitivity.

• High sensitivity ctDNA detection could initiate early salvage surgery in non-operative patients and improve early detection of locally progressive or metastatic disease.
Questions