

INNOVATE, COLLABORATE: TRANSFORM



ASTRO'S 61ST ANNUAL MEETING

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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

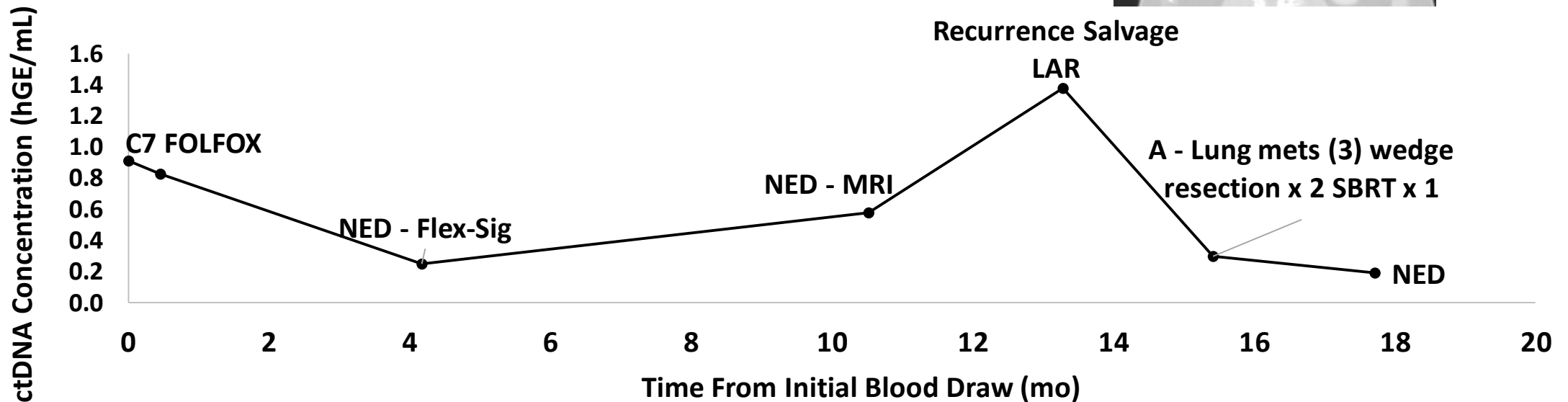
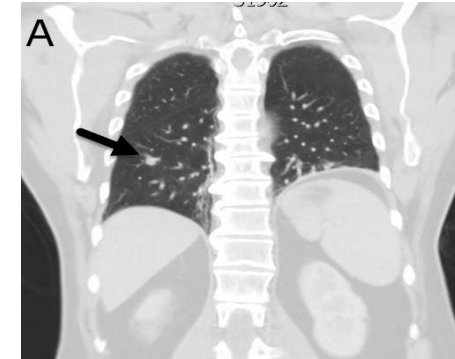
- Non-operative management of locally-advanced esophageal and rectal cancer is becoming more prevalent
- Highly sensitive and specific serum biomarkers of treatment response are needed – ctDNA monitoring shows great promise

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

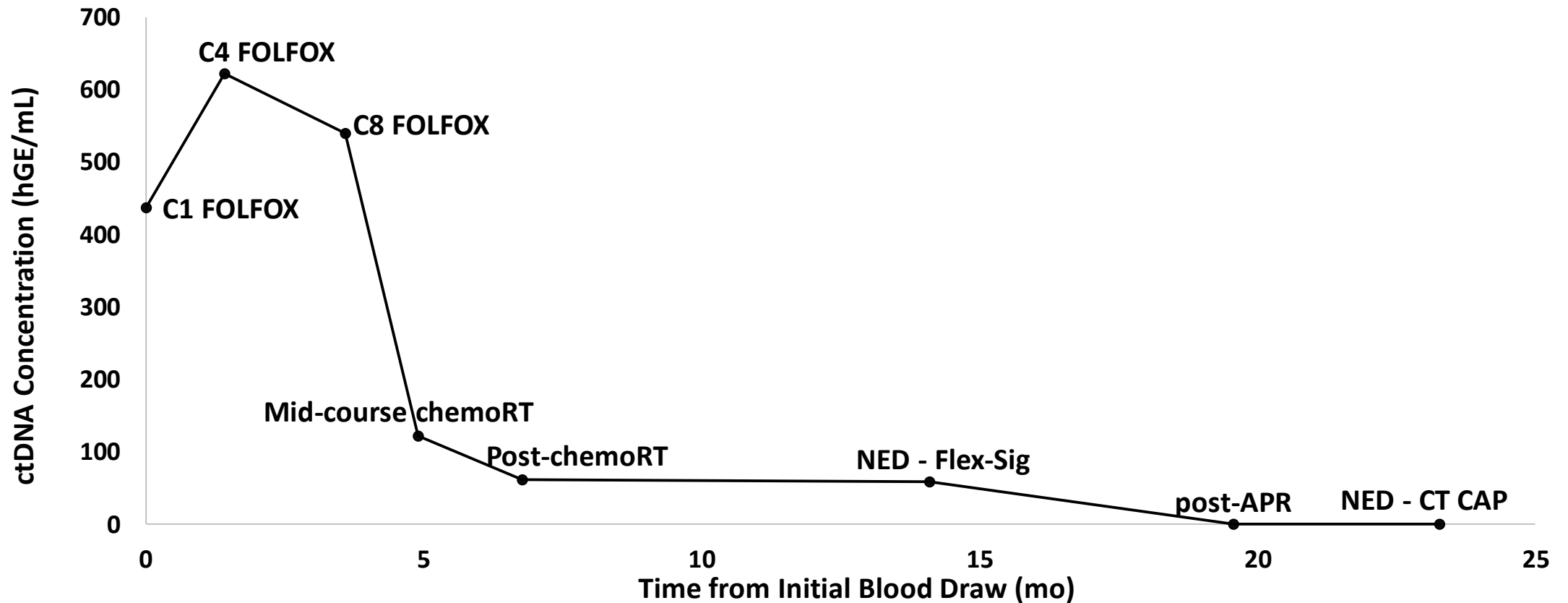
Persistent ctDNA precedes clinical recurrence with 8 month lead-time

cT2N1M0 rectal adenocarcinoma



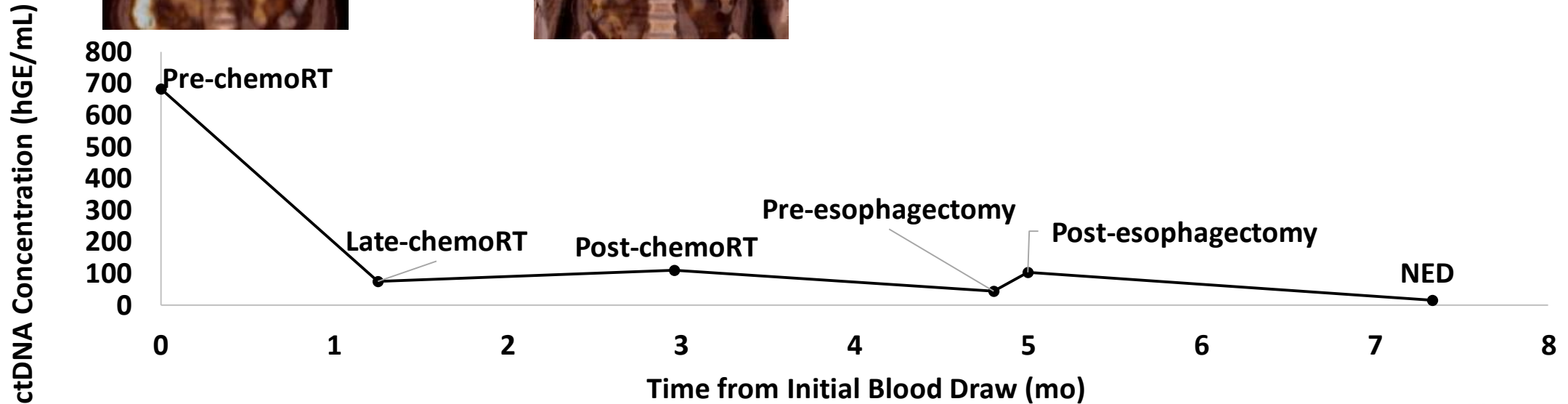
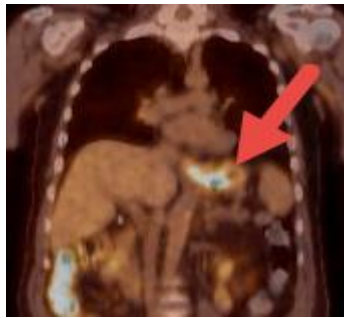
Persistent ctDNA precedes clinical recurrence with 5 month lead-time

cT3N1 rectal adenocarcinoma



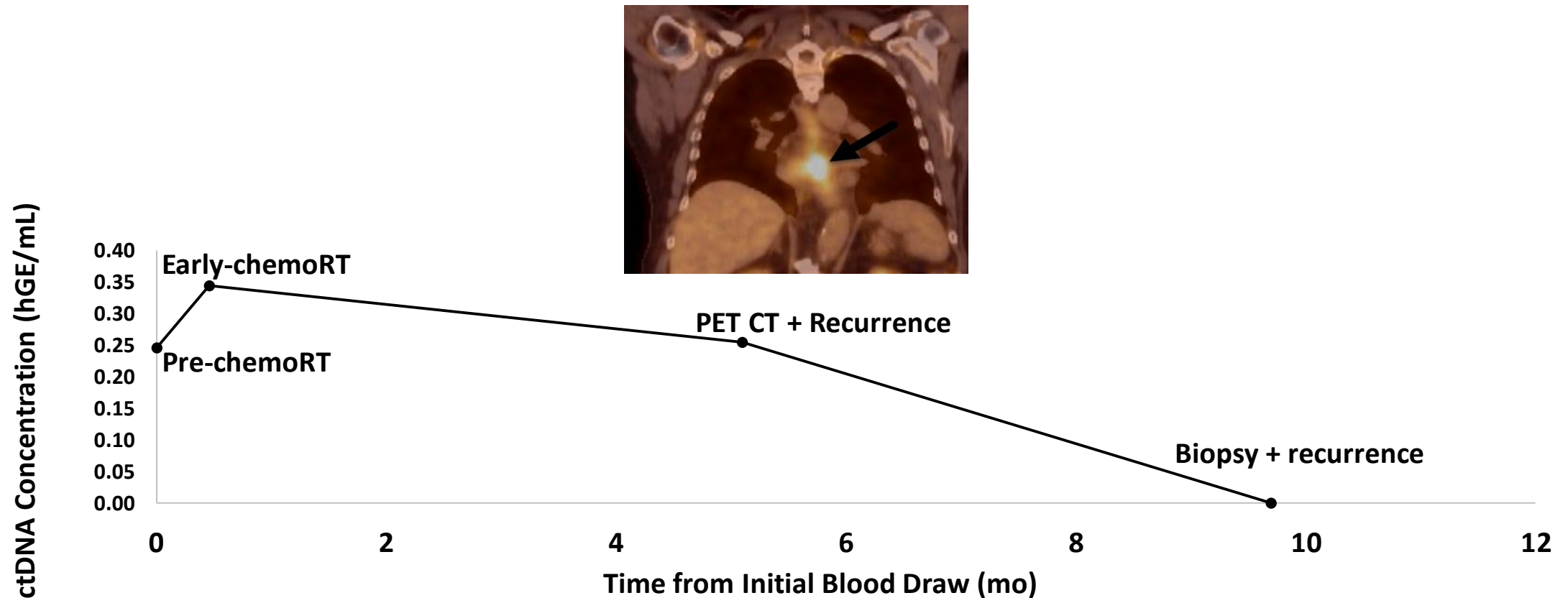
ctDNA declines with neoadjuvant chemoRT and after resection

cT3N1 esophageal adenocarcinoma



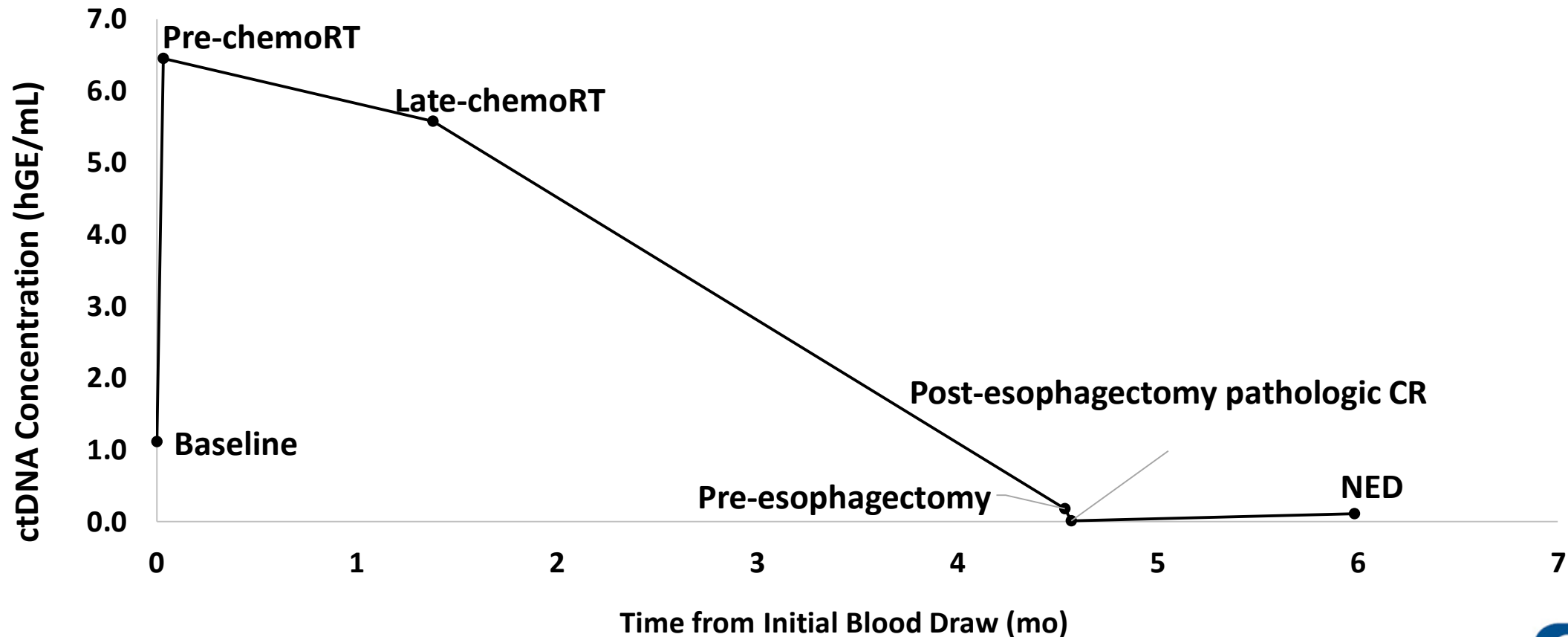
ctDNA undetectable at time of recurrence

cT3Nx esophageal adenocarcinoma



Absence of ctDNA associated with pCR

cT2N0 esophageal adenocarcinoma



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