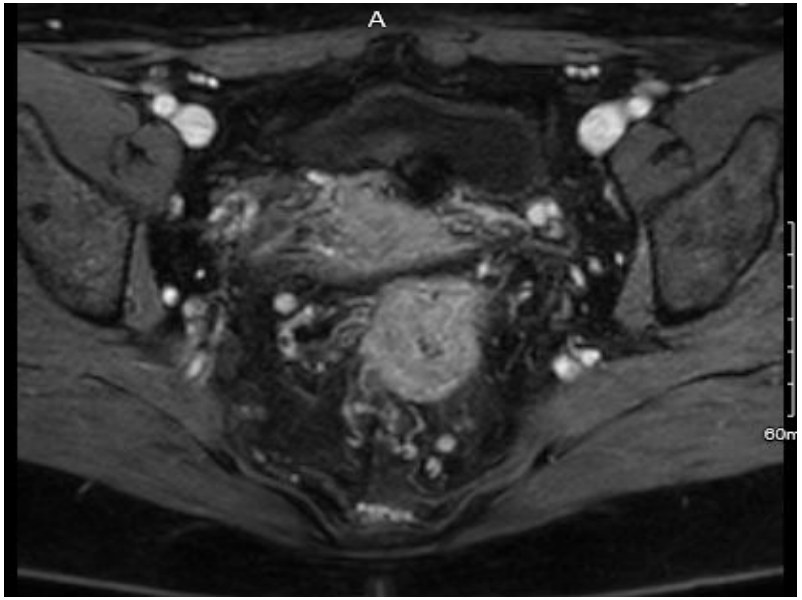
Metastatic Disease

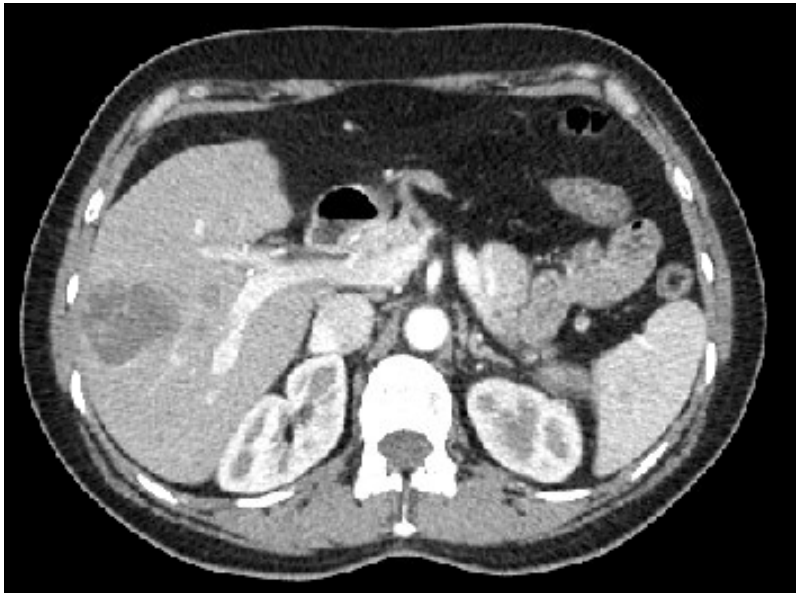
Case-Based Panel Discussion

Case 1

48 yo female presented in August 2019 with blood per rectum and underwent colonoscopy demonstrating an ulcerated mass in the distal rectum, extending from just above the anal verge to 7cm. Biopsy demonstrates MSI stable, moderately differentiated adenocarcinoma. No other polyps or masses noted. CEA 9.5

Staged with MRI pelvis, CT CAP, PET/CT: cT3 cN2 cM1a





No family history of CRC, any role for hereditary testing?

Molecular profiling:

BIOMARKER	METHOD	RESULT
KRAS	**NGS**	**Mutation Not Detected**
NRAS	**NGS**	**Mutation Not Detected**
BRAF	NGS	Mutation Not Detected

CANCER TYPE RELEVANT BIOMARKERS

Biomarker	Method	Result
MSI	NGS	Stable
Tumor Mutational Burden		Intermediate | 9 Mutations/Mb
ERBB2 (Her2/Neu)	CNA-NGS	Amplification Not Detected
PIK3CA	NGS	Mutation Not Detected

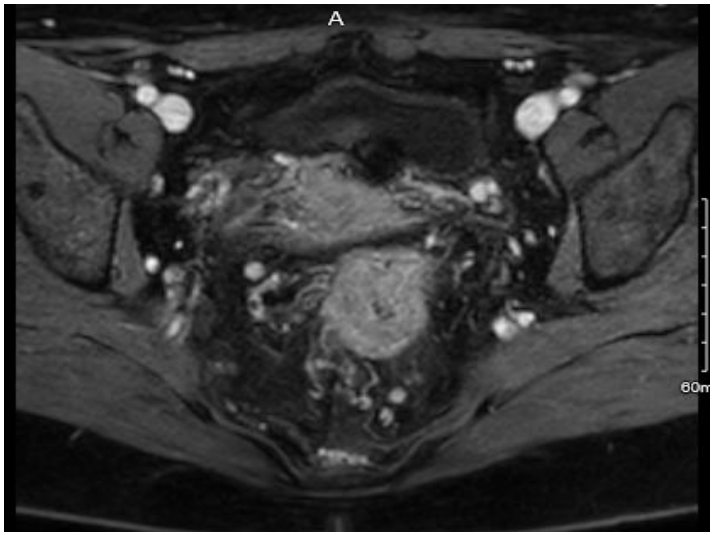
OTHER FINDINGS (see page 2 for additional results)

Biomarker	Method	Result
AMER1	NGS	Mutated, Pathogenic
		Exon 2 | p.R497*

OTHER FINDINGS (cont) (see page 2 for additional results)

Biomarker	Method	Result
APC	NGS	Mutated, Pathogenic
		Exon 12 | p.R499*
EP300	NGS	Mutated, Pathogenic
		Exon 27 | p.S1441fs
TP53	NGS	Mutated, Pathogenic
		Exon 5 | p.R175H

In this 48yo female with cT3 cN2 cM1a, MSI stable, KRAS WT rectal cancer, what is the recommended treatment strategy?



Points of Discussion:

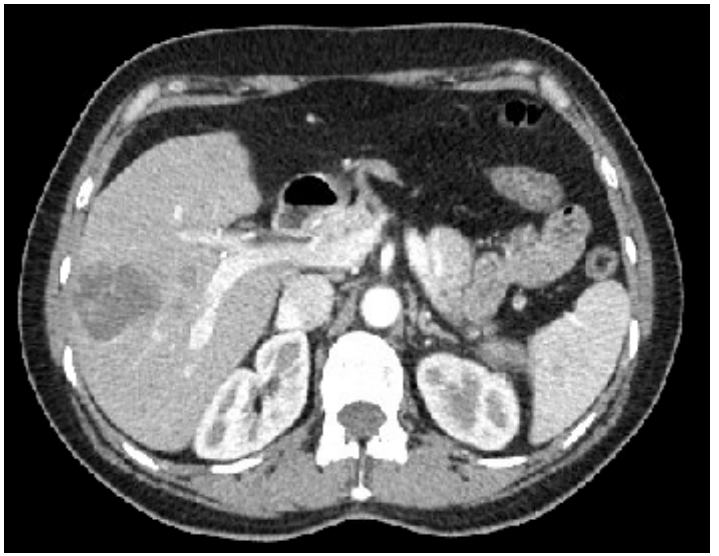
Chemotherapy – when and what type?

Biologic? If so what?

Radiation therapy? Long vs Short?

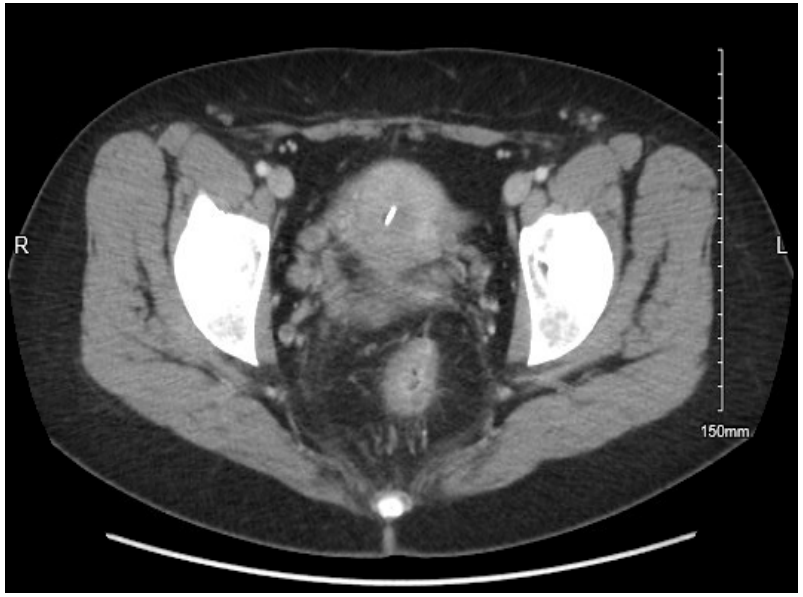
Liver directed therapy?

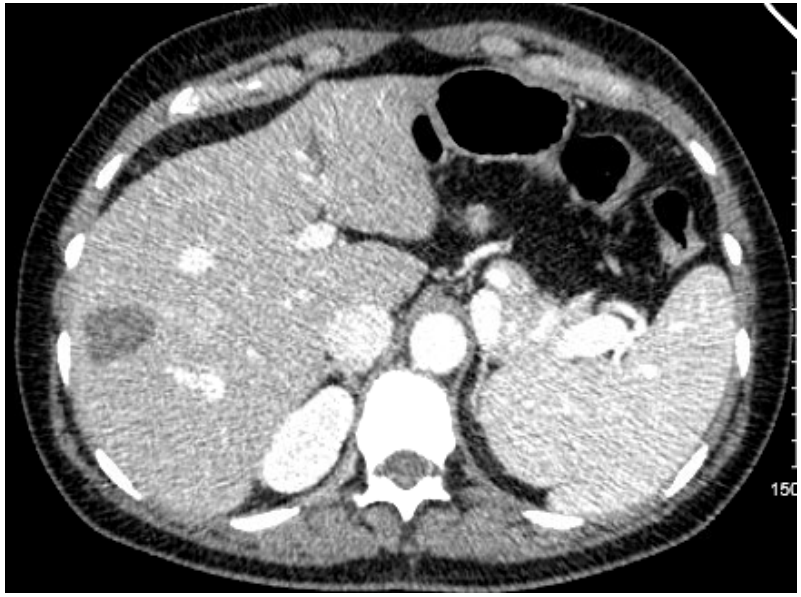
Sequencing of resections?



Received FOLFOX x 6 (Bevacizumab given with cycles 1-4)

Liver metastasis decreased in size by approximately 50%. Decreased thickening of rectal wall mass and reduction in size of mesorectal lymph nodes. CEA 9.5 to 1.6





Next step?

December 2019 - Resection of segment 6/7 hepatic metastasis

Pathology: 5% viable tumor, all margins free of tumor (7mm – closest parenchymal margin).

Uneventful recovery

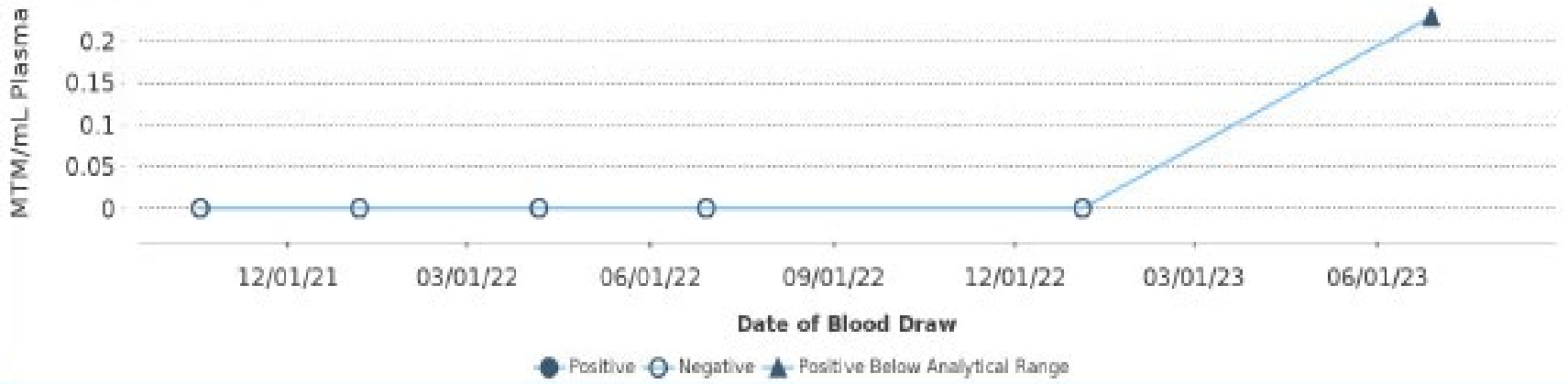
Received 50.4 Gy XRT with concomitant Xeloda
May 2020 – patient undergoes APR and TAH/BSO

Pathology: ypT3 ypN1a (1/11), well differentiated adenocarcinoma
All margins negative, - PNI, - LVI, - extramural tumor deposits
Treatment effect: residual cancer with evident tumor regression, present in small groups of cancer cells (Ryan score 2/3).

Uneventful recovery - Followed by 3 months CapeOx

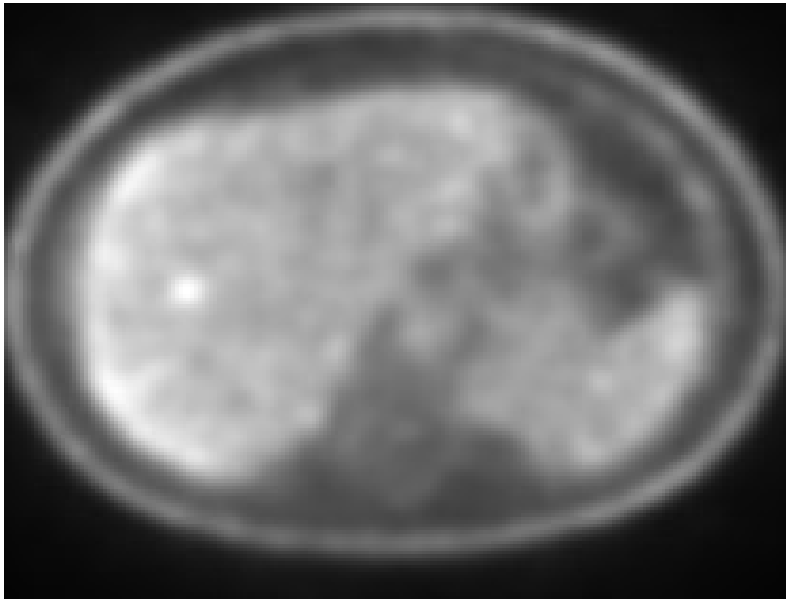
Remained NED by imaging and CEA, ctDNA from completion of treatment in September 2020 until June 2023.

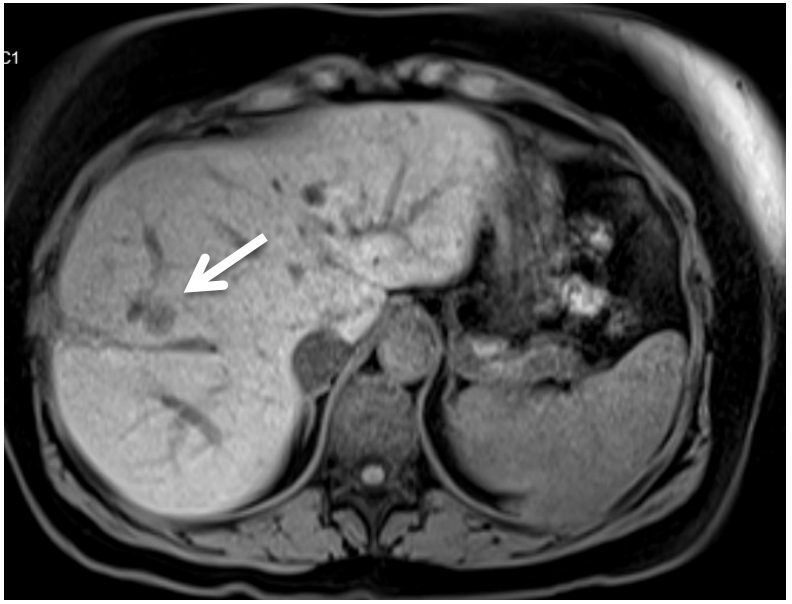
Historical Results



Date	Reported MTM/mL
Jun 28, 2023	0.23
Jan 04, 2023	0.00
Jun 29, 2022	0.00
Apr 06, 2022	0.00
Jan 06, 2022	0.00
Oct 18, 2021	0.00

PET/CT demonstrates isolated liver metastasis.
MRI liver 1.2 x 1.8 x 1.6 cm isolated liver metastasis





Management?

Case 2

65 yo male underwent initial screening colonoscopy in December 2019.
Found to have 11 polyps from cecum though sigmoid colon.
10 of the 11 polyps are removed via snare polypectomy with pathology demonstrating tubular and tubulovillous adenomas with no dysplasia.

A 3cm polyp at 50cm (splenic flexure) is biopsied but is endoscopically Unresectable. The pathology from this biopsy is reported as “at least intra-mucosal adenocarcinoma” arising within a tubulovillous adenoma.

He has Factor V Leiden, no family history of colon cancer, grandfather with a history of “stomach cancer.”

CT with no evidence of metastatic disease, CEA 5.0

Role for hereditary testing based on colonoscopy findings?

Surgical recommendations?

Underwent left hemicolectomy in February 2020. At time exploration there is a “marble size” firm nodule in the omentum of near the splenic flexure, which was excised and confirmed to be metastatic disease on intra-operative frozen section analysis. No other sites of disease Identified.

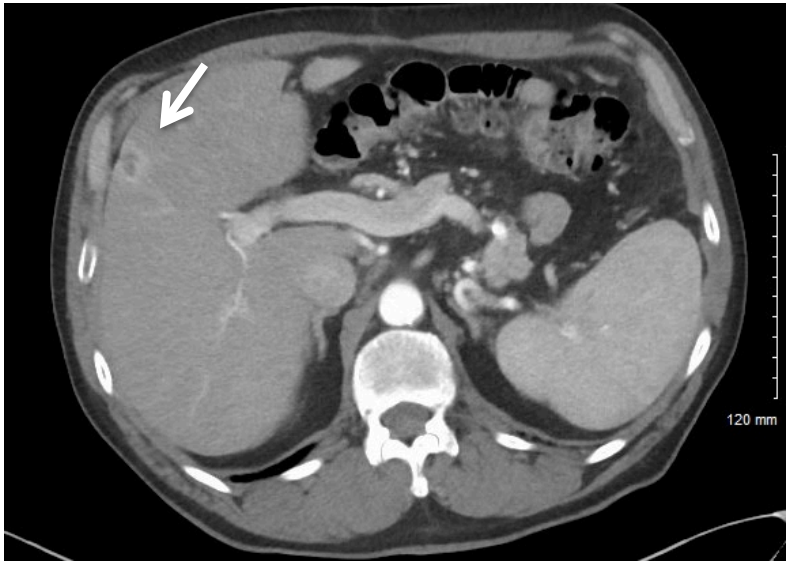
Final pathology: T3 N1b (3/12) M1c (2.2cm omental implant)
low grade adenocarcinoma with mucinous features, R0, +LVI, -PNI.
IHC with loss of MLH1 and PMS2, BRAF Wild Type, TMB 19.3
Germline testing negative for Lynch.

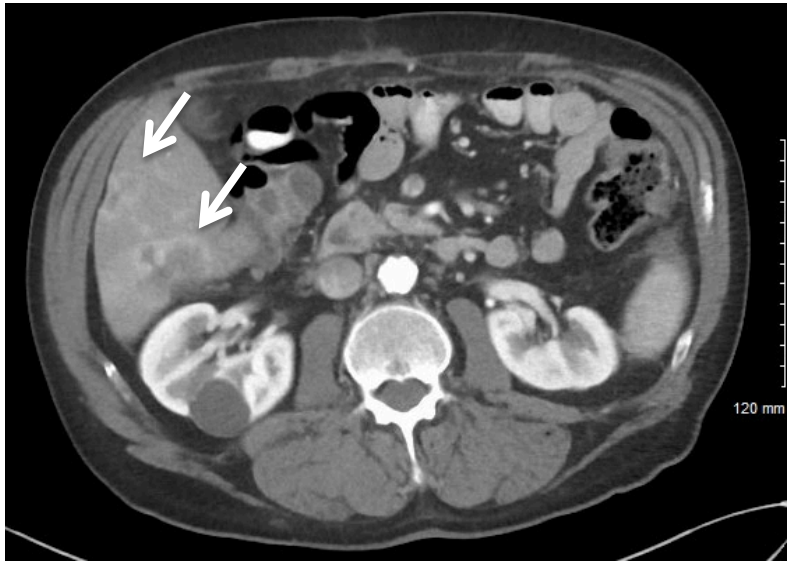
Post-operative Imaging?

Post-operative therapy for this patient?

Role of ctDNA in this setting?

September 2020 (7 months after colon resection)
3 discrete hepatic metastases, CEA 23



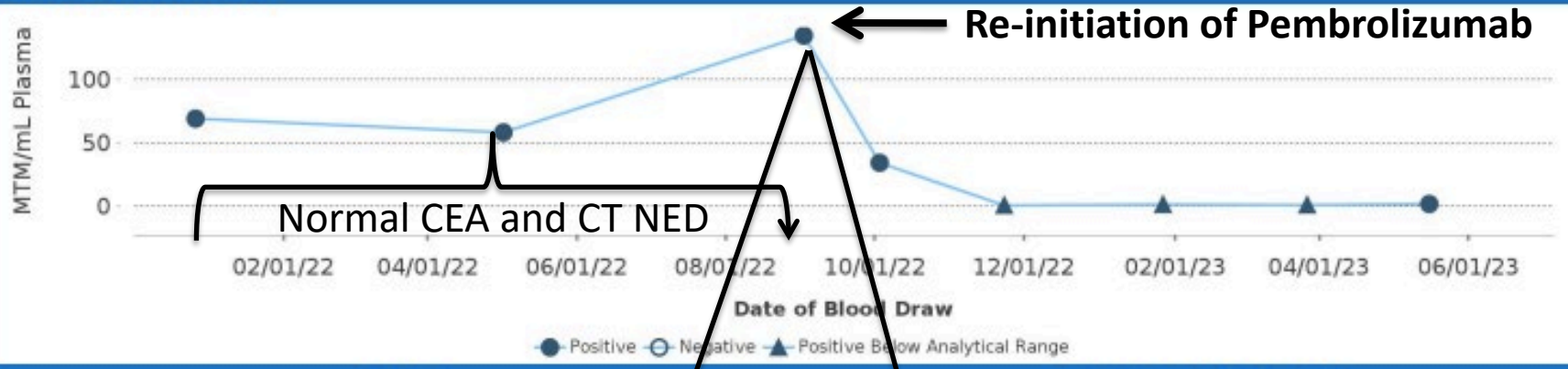


Recommended systemic therapy?

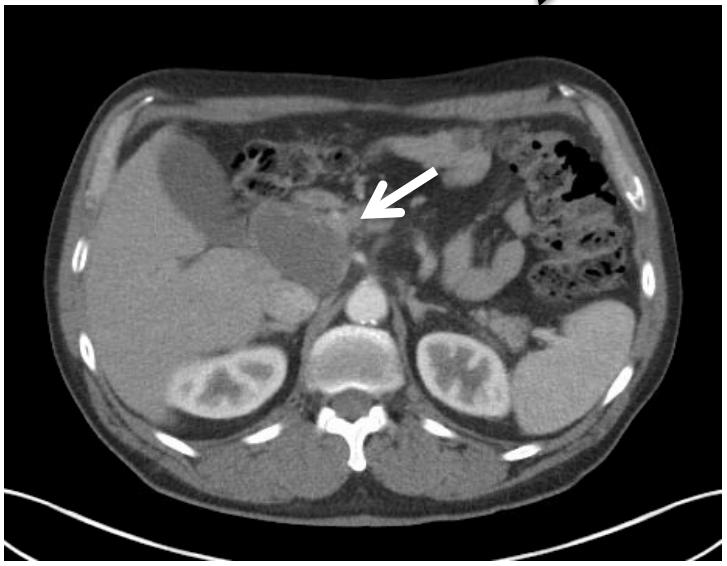
Any role for liver directed therapy?

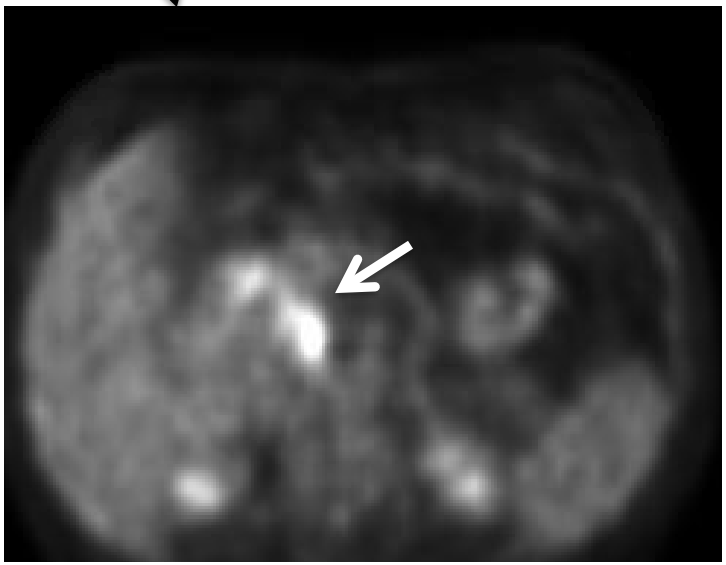
September 2020, started on single agent Pembrolizumab, which is continued until April 2021 – held for pneumonitis

Historical Results

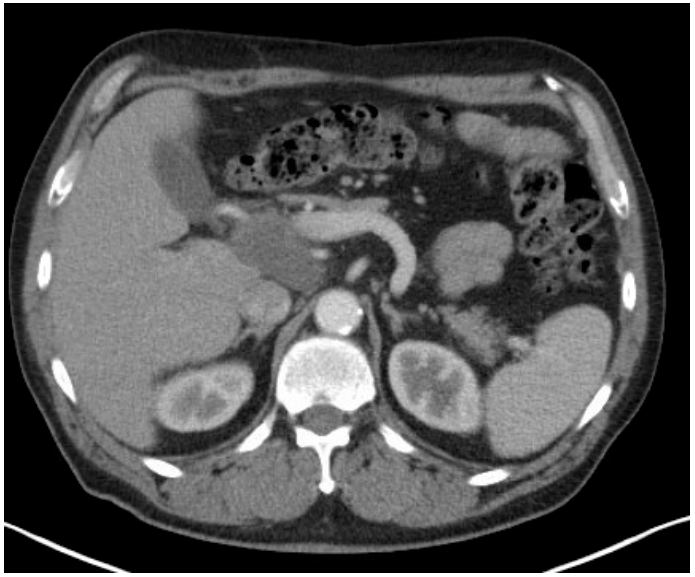


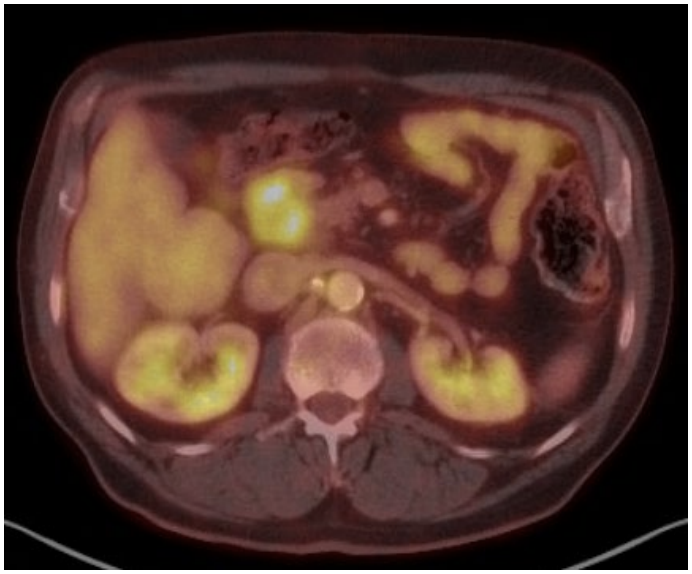
Date	Reported MTM/mL
May 16, 2023	1.42
Mar 27, 2023	0.58
Jan 27, 2023	0.99
Nov 23, 2022	0.29
Oct 03, 2022	34.03
Sep 02, 2022	134.64
May 02, 2022	58.07
Dec 27, 2021	68.97





After 9 months of treatment, imaging remains stable with portacaval node as the only radiographic site of disease.





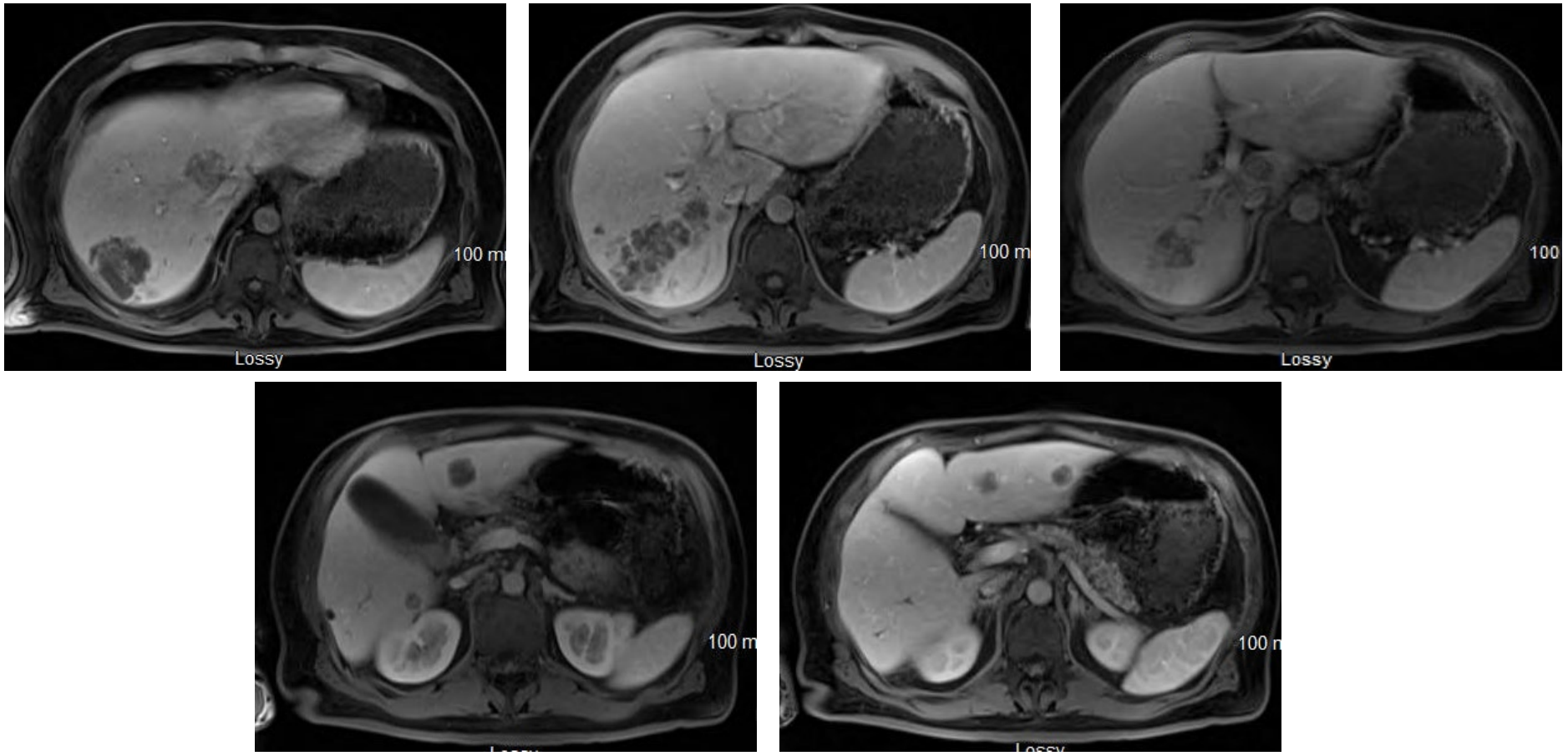
Management – continue Pembrolizumab, SBRT, Surgery, Other?

Case 3

51yo male required urgent ex-lap, sigmoid colectomy, and creation of colostomy for obstructing sigmoid mass/stricture. CT at the time of presentation reveals diffuse hypodense hepatic masses concerning for metastatic disease.

Pathology reveals T3 N1c M1a, Grade 2, adenocarcinoma, +LVI, -PNI + tumor budding (high >10 buds/hotspot), MSI-stable on IHC.

51yo male with left-sided, MSI stable left-sided colon cancer with diffuse liver metastases. ECOG 0



If no actionable targets (RAS WT, BRAF WT) – best 1st line therapy?

51yo male with left-sided, MSI stable left-sided colon cancer with diffuse liver metastases. ECOG 0

Biomarker	Method	Analyte	Result
KRAS	Seq	DNA-tumor	Mutation Not Detected
NRAS	Seq	DNA-tumor	Mutation Not Detected
BRAF	Seq	DNA-tumor	Mutation Not Detected
BRAC2	Seq	DNA-tumor	Pathogenic variant Exon 11 p.E1307

First Line Therapy?

What if tumor is right-sided?

51yo male with left-sided, MSI stable left-sided colon cancer with diffuse liver metastases. ECOG 0

Biomarker	Method	Analyte	Result
KRAS	Seq	DNA-tumor	Mutation Exon 12 p.G12C
BRAF	Seq	DNA-tumor	Mutation Not Detected
ERBB2 (Her2/Neu)	CAN-Seq	DNA-Tumor	Amplified

First Line Therapy?