ANNUAL

Advances and Innovations in Endoscopic Oncology and Multidisciplinary Gastrointestinal Cancer Care

TNT and Organ Preservation: To Resect or Not to Resect?

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Disclosures

- I do not have any relevant financial relationships.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content

Objectives

Define complete response, partial response and incomplete response

Understand the risks of organ preservation with a partial response

Use available data to drive treatment decisions in organ preservation with a partial response

“Induction”

“Consolidation”

PRODIGE TRIAL

pCR 28.4%
Distant Met 20%

pCR 14.3%
Distant Met 26.8%

Same OS
Same Operative Complications

Triplet Chemotherapy TRIAL

pCR 28%
3 yr DFS 76%

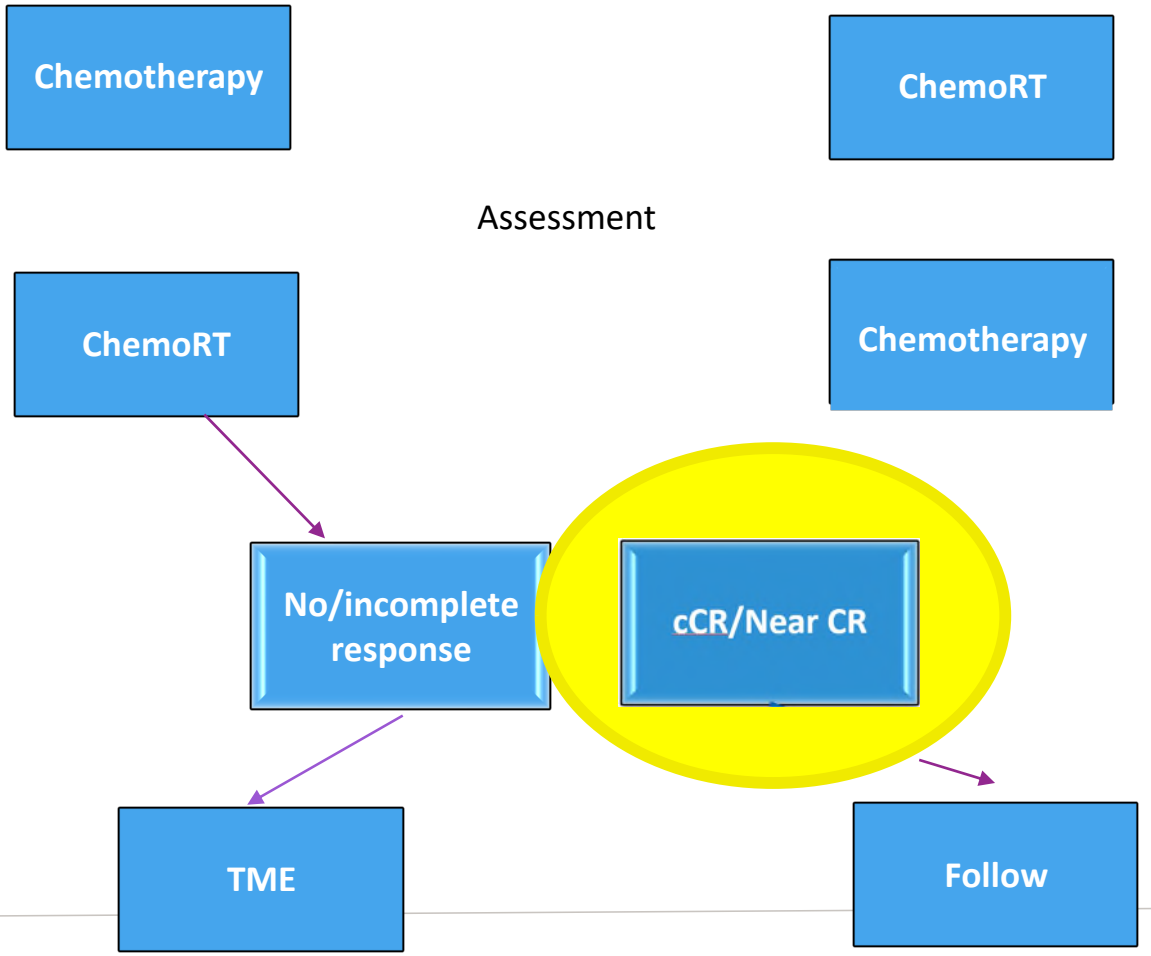
pCR 13%
3 yr DFS 69%

Same Operative Characteristics

Organ Preservation Strategy 2: TNT and observation (OPRA)

Induction

Consolidation



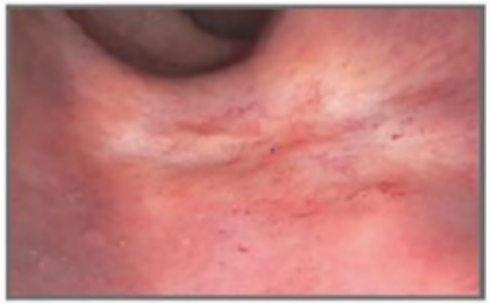
PRIMARY ENDPOINT: 3-year DFS

OPRA: Study Protocol

cCR
Clinical Complete Response

Endoscopy:
- Flat, white scar
- Telangiectasia
- No ulceration or nodularity

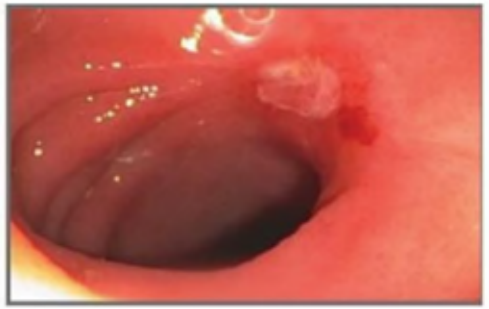
DRE:
- Normal



cCR
Near Complete Response

Endoscopy:
- Irregular mucosa
- Small nodules or minor mucosal abnormality
- Superficial ulceration
- Mild persisting erythema

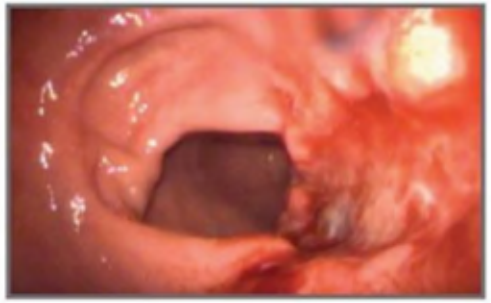
DRE:
- Smooth induration or minor mucosal abnormality



iCR
Incomplete Response

Endoscopy:
- Visible tumor

DRE:
- Palpable tumor nodules



OPRA results

OPRA: Long Term Results

Lessons Learned

74% offered W&W

36% regrowth
94% within 2 years
99% within 3 years

R0 resection rates the same between immediate and salvage TME

13% developed mets even with sustained CR

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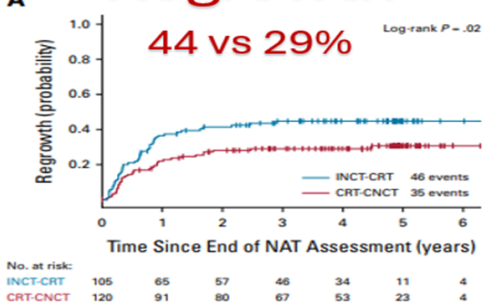
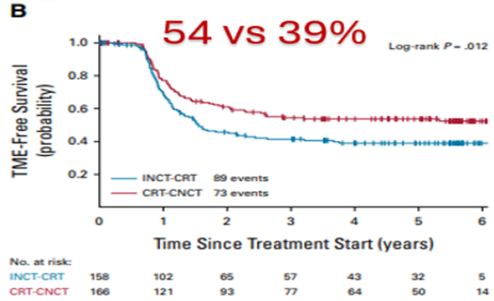
Regrowth

44 vs 29%

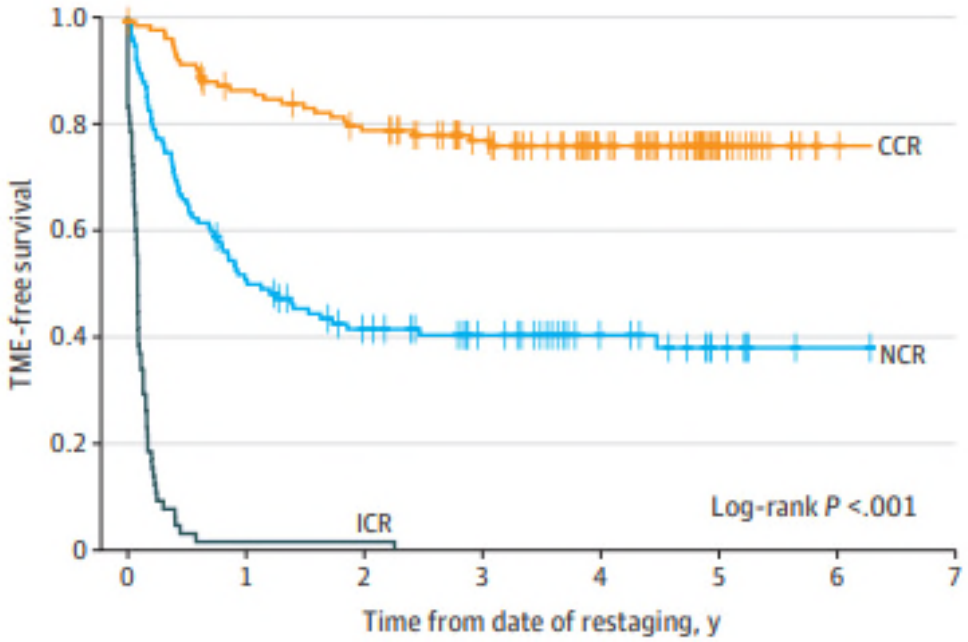


Organ Preservation

54 vs 39%



OPRA : Long Term Results



- Local regrowth at 2 years
- cCR 20%
- nCR 49%
- Organ preservation: 47%
- cCR 77%
- nCR 40%
- iCR 5% (1 ref, 2 mets)
- DFS: 74%
- cCR 88%
- pCR 69%
- iCR 56%

JAMA Net Open .2024; 7(1):e2350903

OPRA : Accuracy of Endoscopy & MRI

Diagnostic performance identifying a true response (TR) for patients with a cCR or nCR (Panel A) and patients with cCR only (Panel B).

	A			B		
Parameter (%) (Patients positive for a TR)	Endoscopy (n=217)	MRI (n=229)	Endoscopy & MRI (n=125)	Endoscopy (n=114)	MRI (n=109)	Endoscopy & MRI (n=68)
Accuracy	65	60	66	72	63	75
Sensitivity	96	95	99	64	54	71
Specificity	33	23	27	80	73	80
Positive predictive value	60	57	62	77	68	81
Negative predictive value	88	81	95	68	60	70
Positive PTP	60	57	62	77	68	81
Negative PTP	12	20	5.3	33	40	30

PTP= posttest probability.

J Clin Oncol 2024;42:S3.

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2023
pMMR/MSS Rectal Cancer

NCCN Guidelines Index
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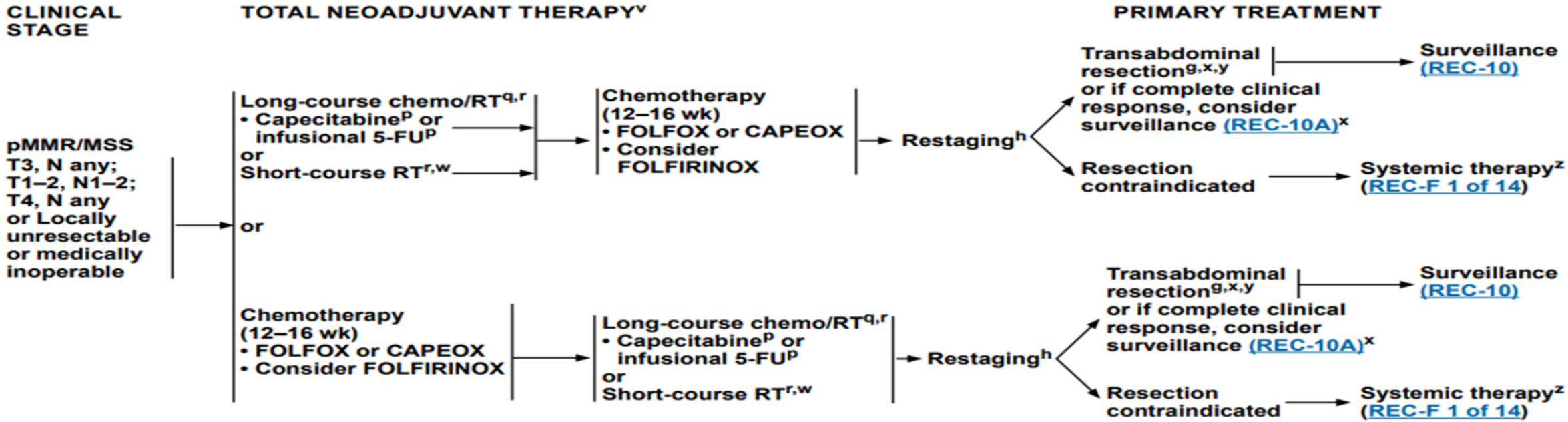
Discussion



[g] Principles of Surgery (REC-C).
[h] Principles of Imaging (REC-A).
[p] Bolus 5-FU/leucovorin/RT is an option for patients not able to tolerate capecitabine or infusional 5-FU.
[q] Principles of Perioperative Therapy (REC-D).
[r] Principles of Radiation Therapy (REC-E).
[v] In select cases (eg, a patient who is not a candidate for intensive therapy) neoadjuvant therapy with chemo/RT or RT alone may be considered prior to surgery.
[w] Evaluation for short-course RT should be in a multidisciplinary setting, with a discussion of the need for downstaging and the possibility of long-term toxicity.
[x] In those patients who achieve a complete clinical response with no evidence of residual disease on digital rectal examination (DRE), rectal MRI, and direct endoscopic evaluation, a "watch and wait," nonoperative (chemotherapy and/or RT) management approach may be considered in centers with experienced multidisciplinary teams. The degree to which risk of local and/or distant failure may be increased relative to standard surgical resection has not yet been adequately characterized. Decisions for nonoperative management should involve a careful discussion with the patient of their risk tolerance.
[y] For select patients who may be candidates for intraoperative RT (IORT), see Principles of Radiation Therapy (REC-E).
[z] FOLFIRINOX is not recommended in this setting.

Endoscopic Predictors of Residual Tumor After Total Neoadjuvant Therapy: A Post Hoc Analysis From the Organ Preservation in Rectal Adenocarcinoma Trial

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On Behalf of the OPRA Consortium

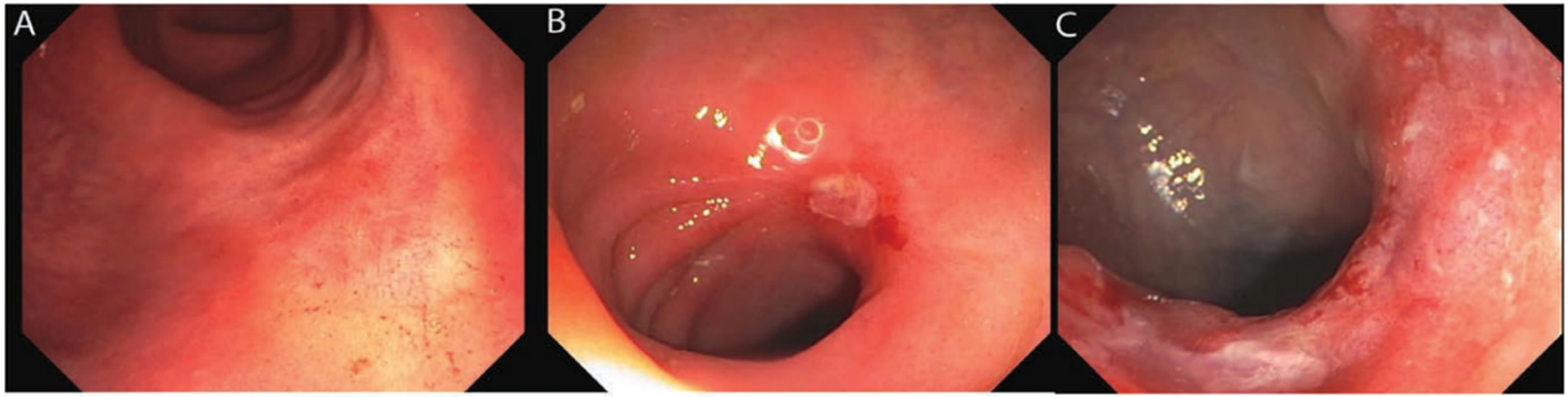


FIGURE 1. Representative endoscopic images of a cCR, nCR, and iCR. A, A flat white scar with telangiectasia demonstrating a cCR. B, A small, well-demarcated ulcer without other polypoid growth illustrating an nCR. C, Gross, residual tumor indicative of an iCR. cCR = clinical complete response; iCR = incomplete clinical response; nCR = near complete clinical response.

OPRA: Post Hoc Analysis of Endoscopy

TABLE 5. Multivariable logistic regression: predictors of residual tumor among nCRs

Variables	*OR*	*95% CI*	*p*
Induction TNT	2.25	0.94–5.54	0.068
Ulcer	4.71	1.63–15.8	**0.003**
Nodularity	1.96	0.8–5.05	0.144
Irregular mucosa	2.65	1.06–7.02	**0.036**

Multivariable logistic regression analysis of predictors of residual tumor among nCRs. Variables for the model were chosen using backward selection. Bolded numbers are statistically significant.
nCR = near complete responder; TNT = total neoadjuvant therapy.

Dis Colon Rectum 2024;67:369-376.

SURVEILLANCE

DW-MRI q6 mo x3 yr then q 1 yr

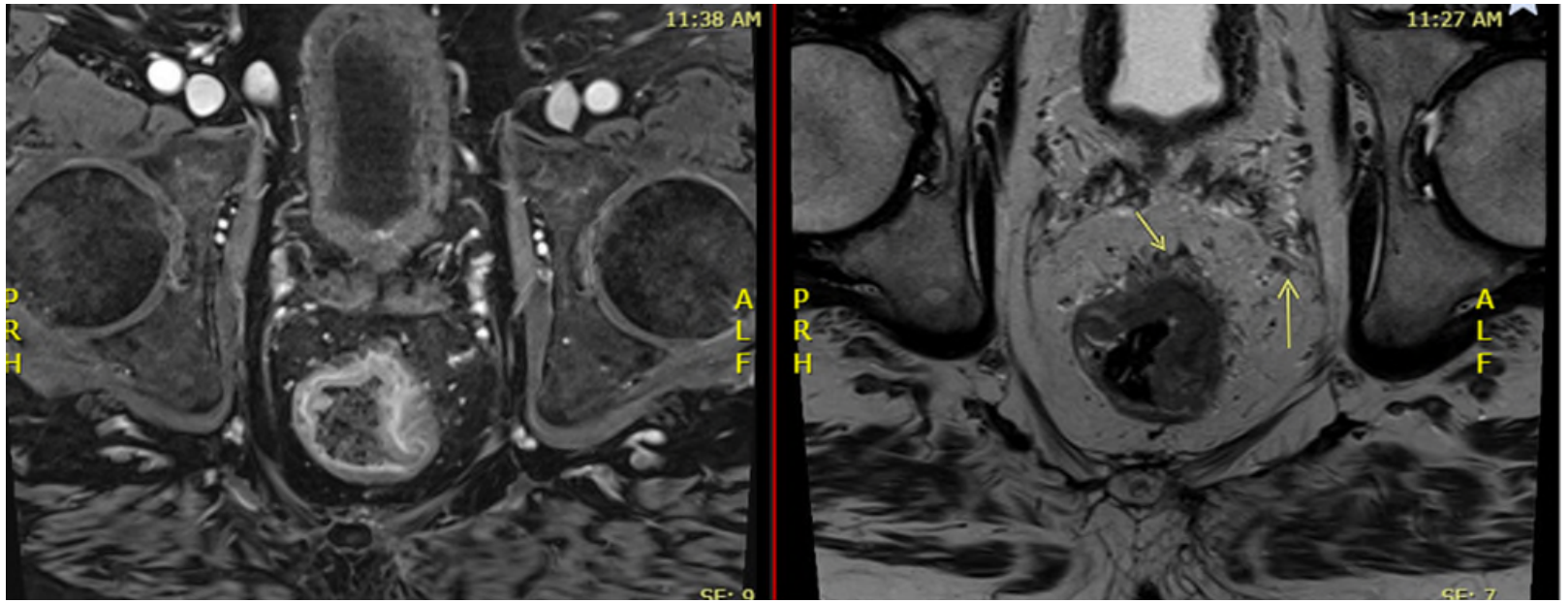
Flex sig q4 mo x3 yr then q 6mo

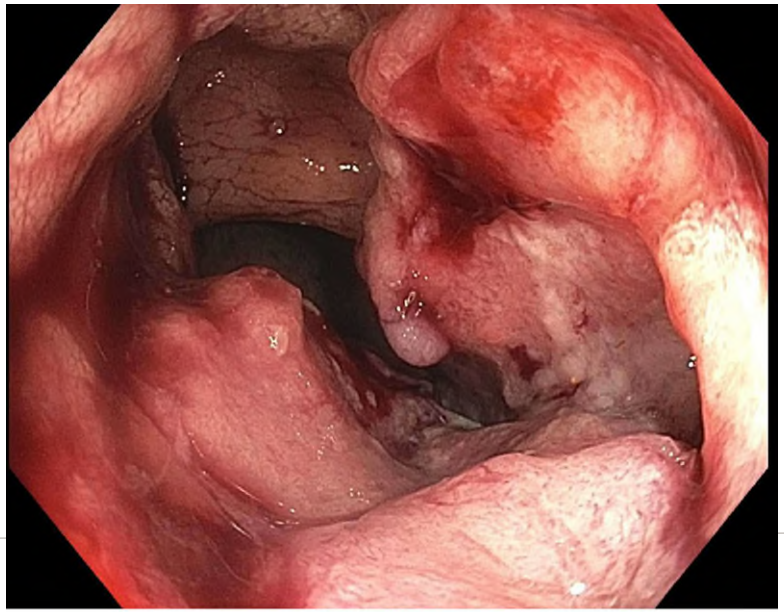
CEA q3 mo x2 yr/q6mo x 2 yr

CT CAP Annually

Case 1

- 72 yr old man
- rectal cancer, concurrent prostate ca
- MRI: T3N0
- Early EMVI (arrow)
- Borderline left anterior LN (arrow)
- Consolidation TNT ending May 2023





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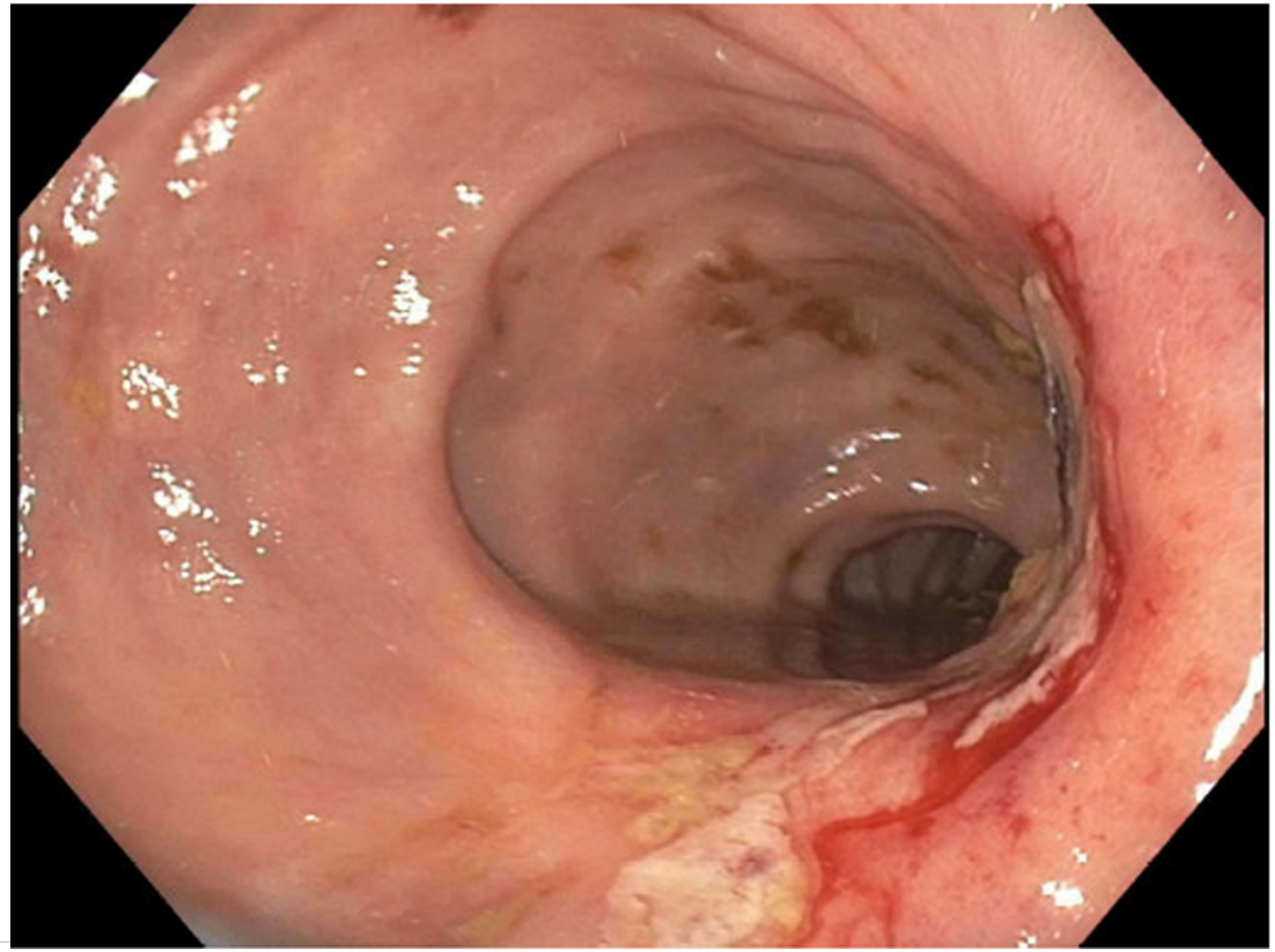

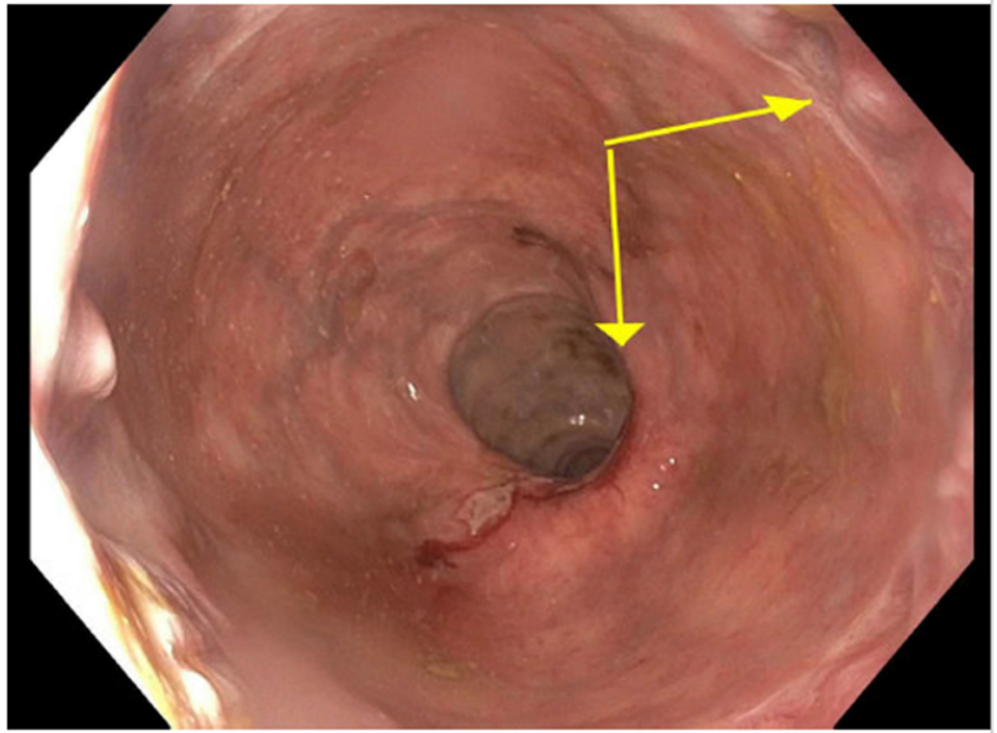

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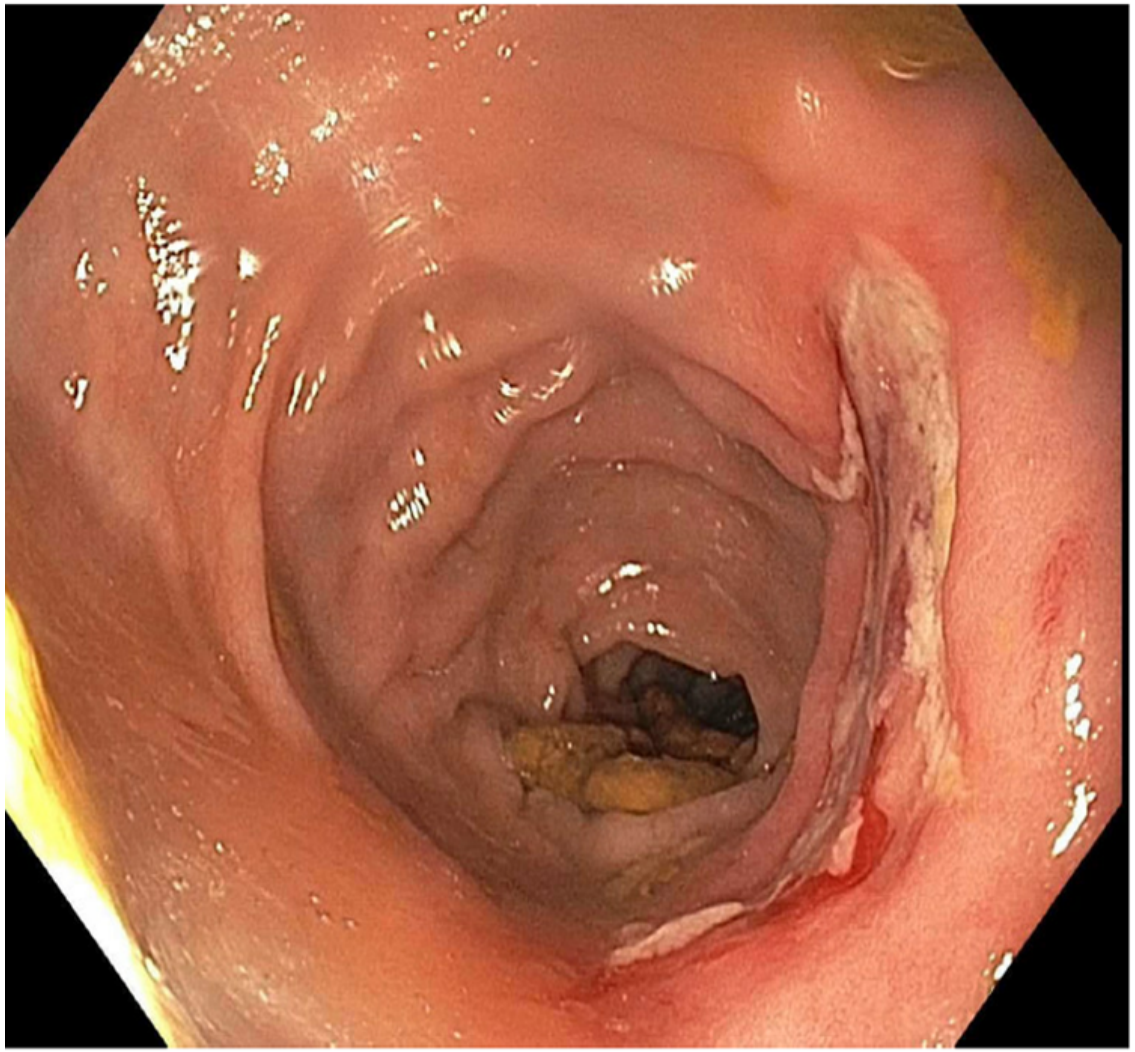

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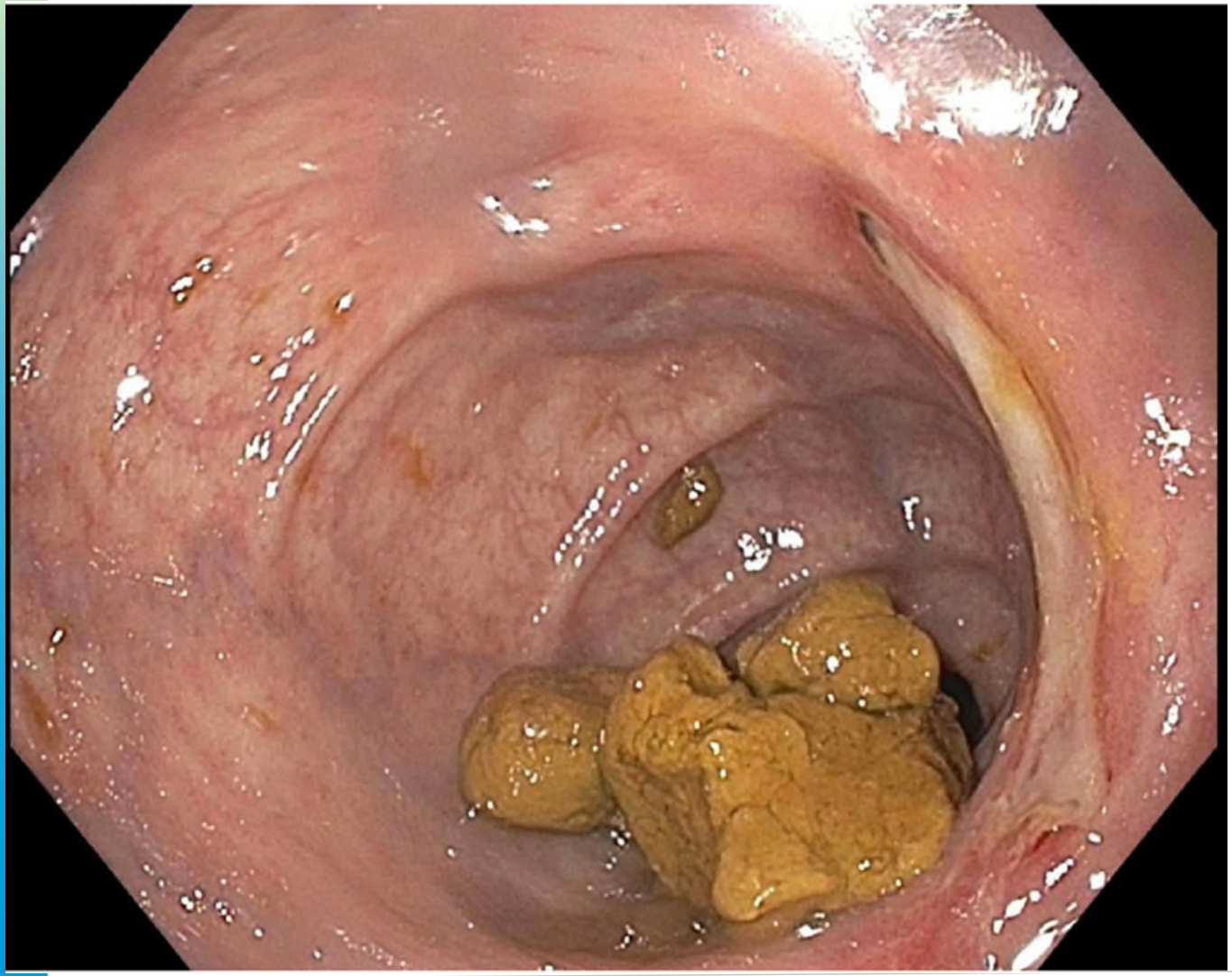
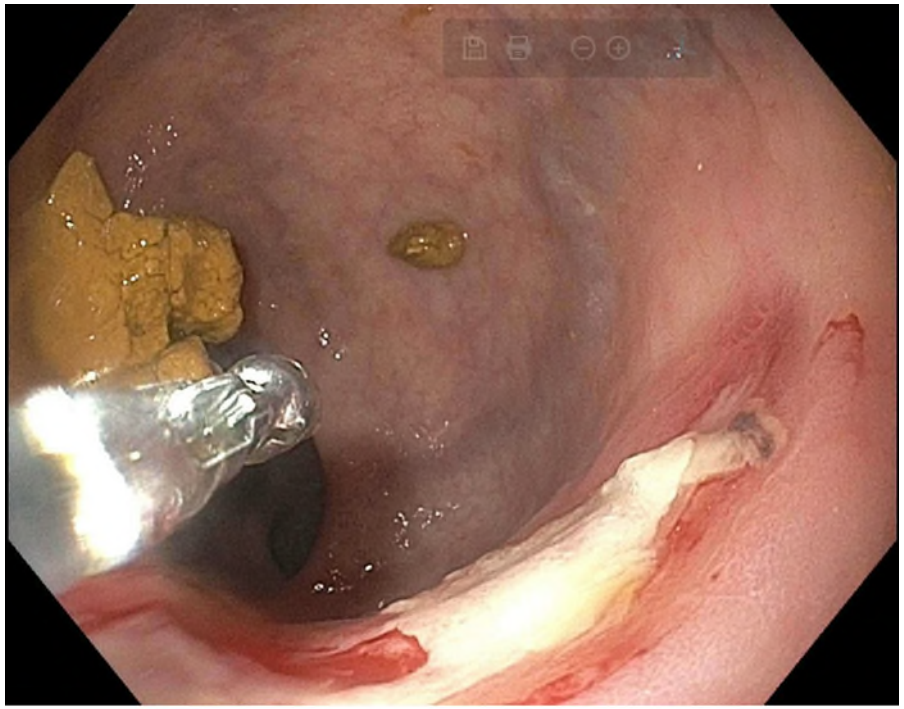
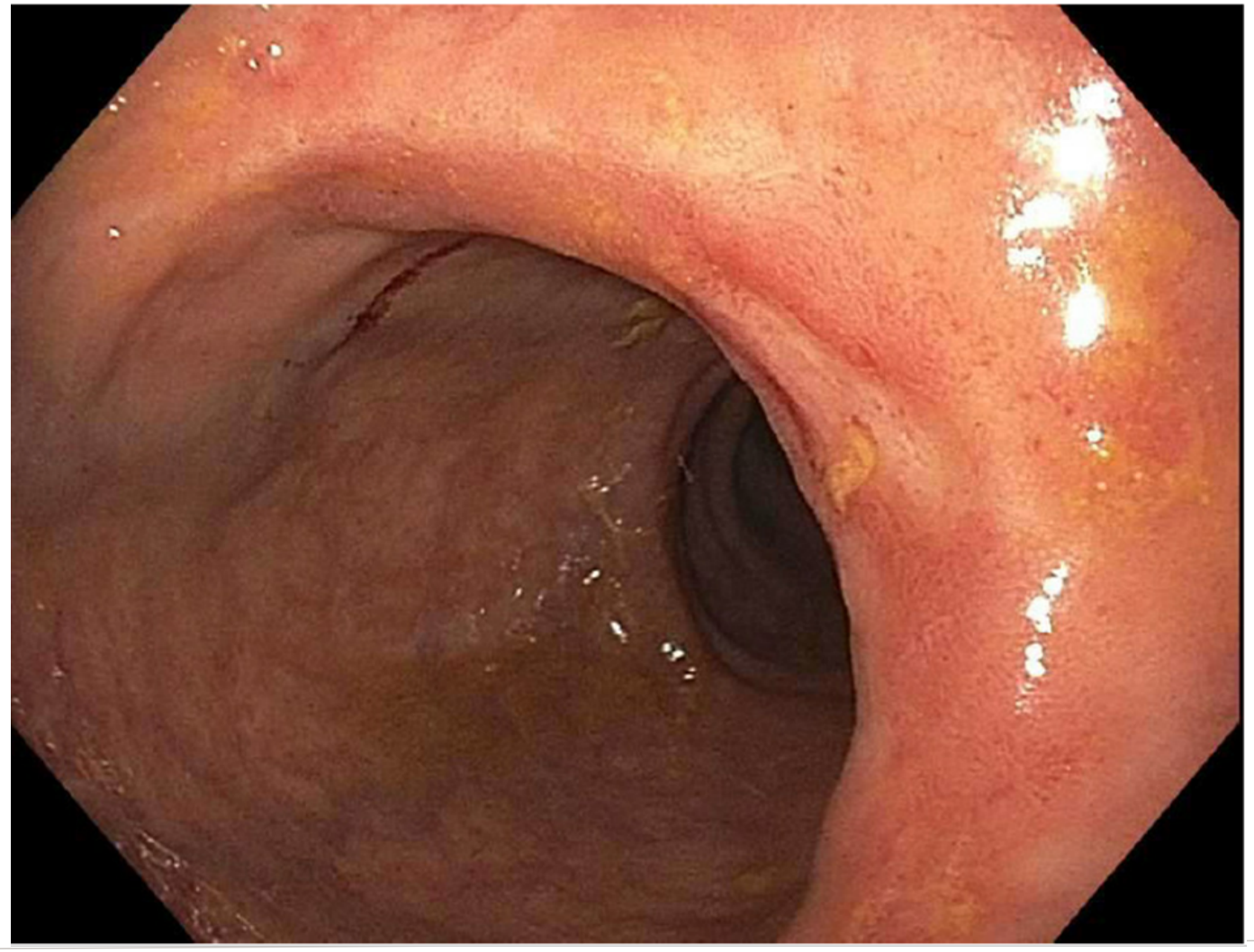




A. Rectum, biopsy:

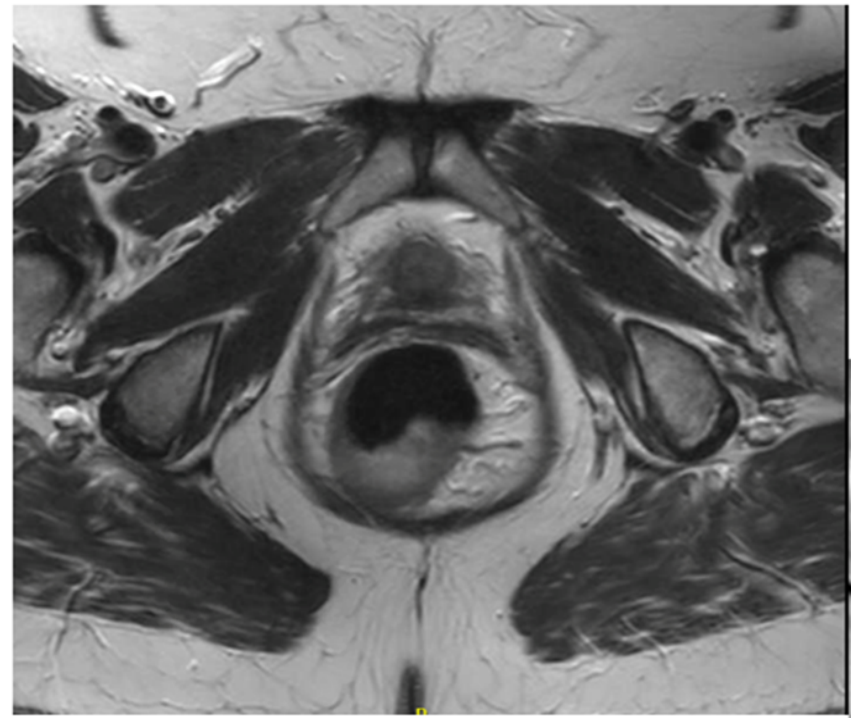
- Rectal mucosa with reactive changes and fibrinopurulent ulcer exudate
- Negative for malignancy

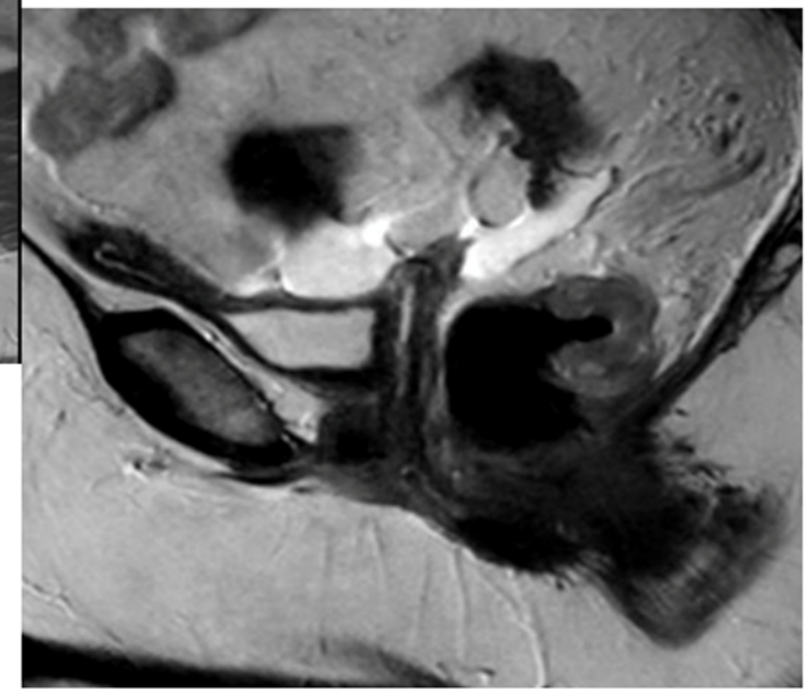
- Flex sig June 2024



Case 2

T3c N+ mid rectal tumor with EMVI
CRM: Primary rectal tumor does not threaten the mesorectal fascia.
Metastatic node 1.5mm from mesorectal fascia without invasion.





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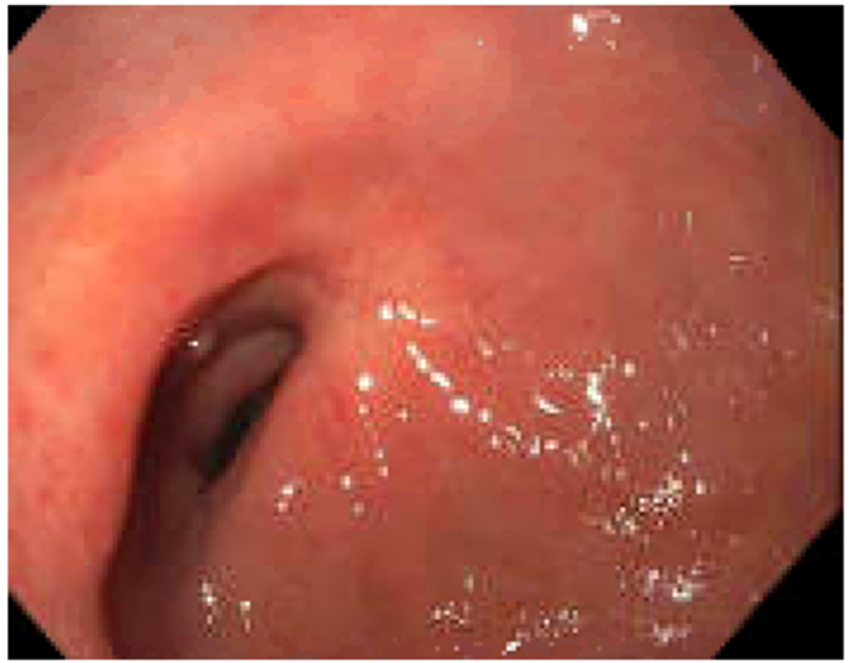

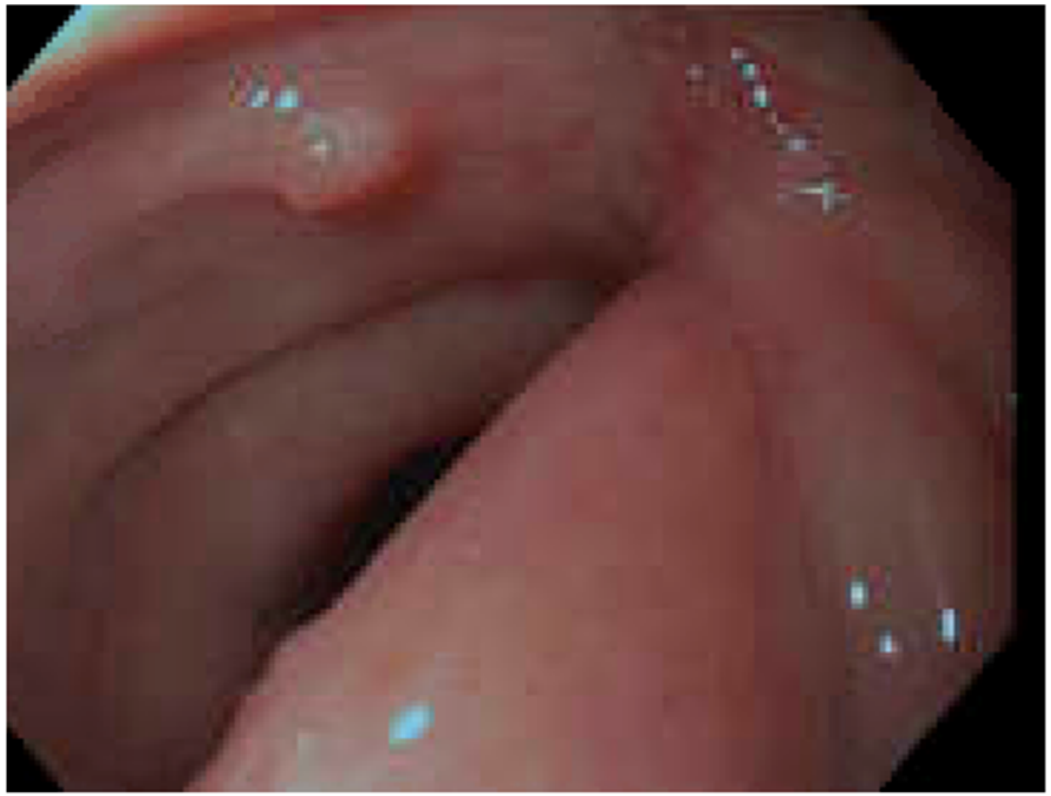

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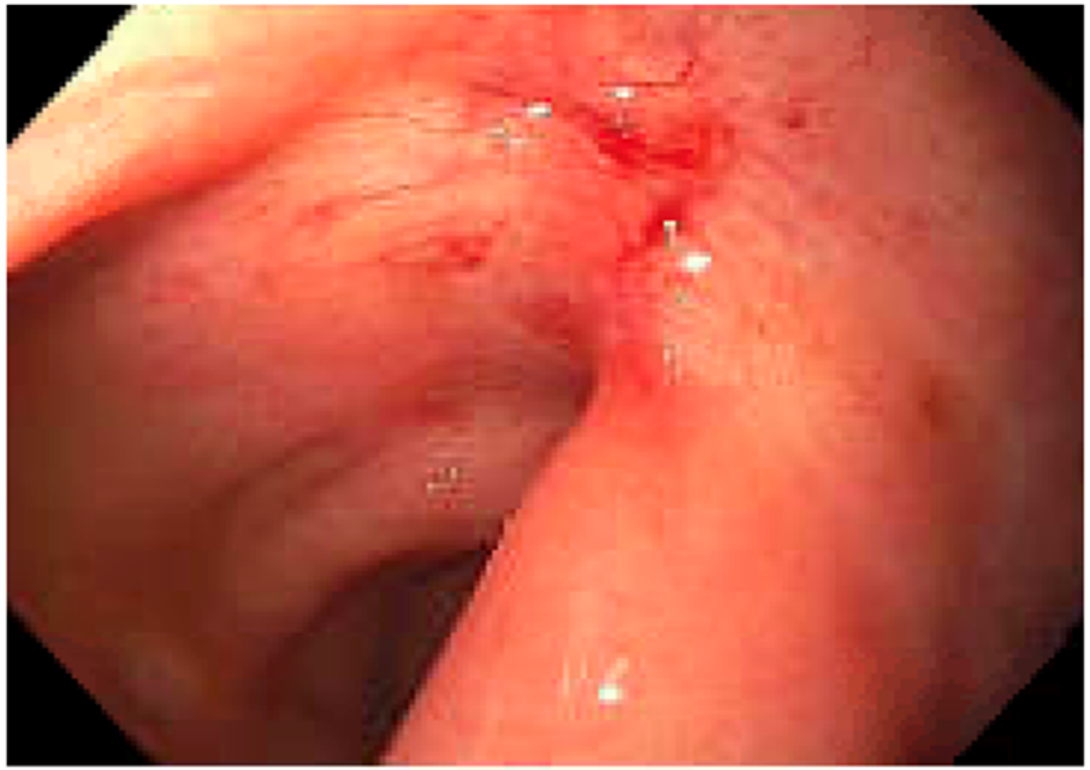

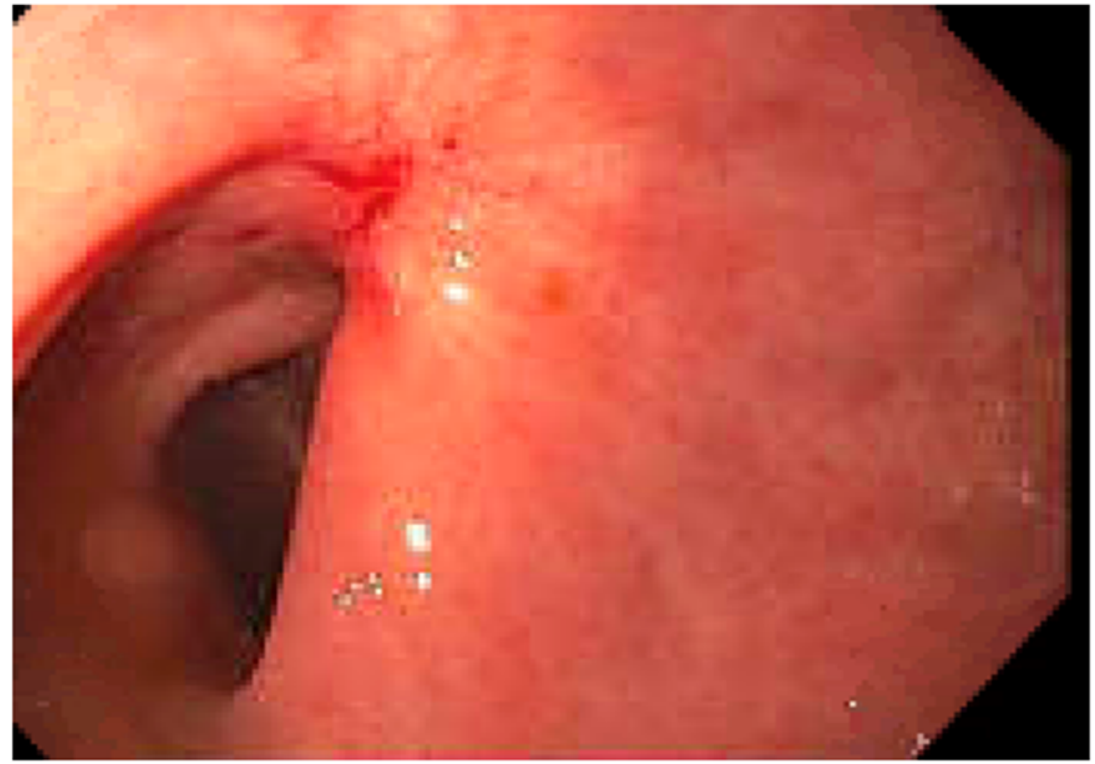

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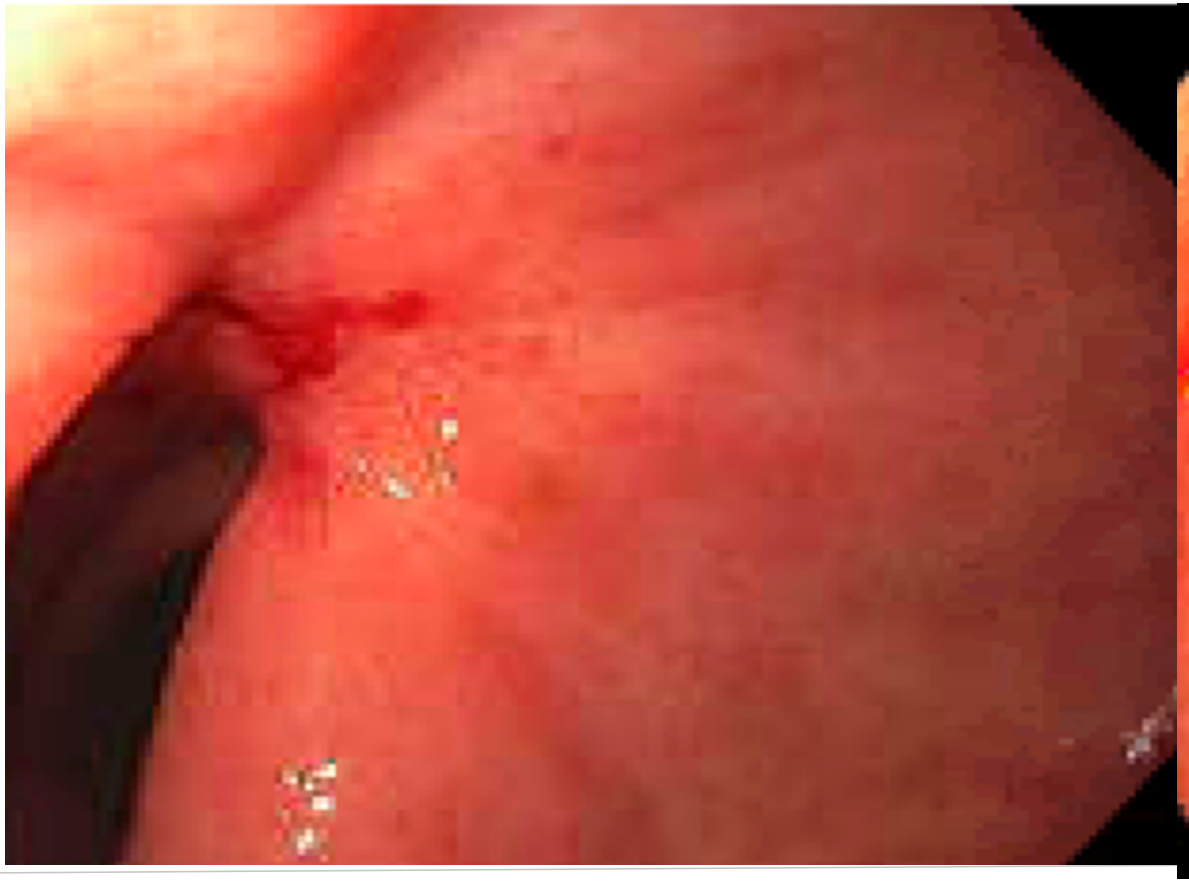
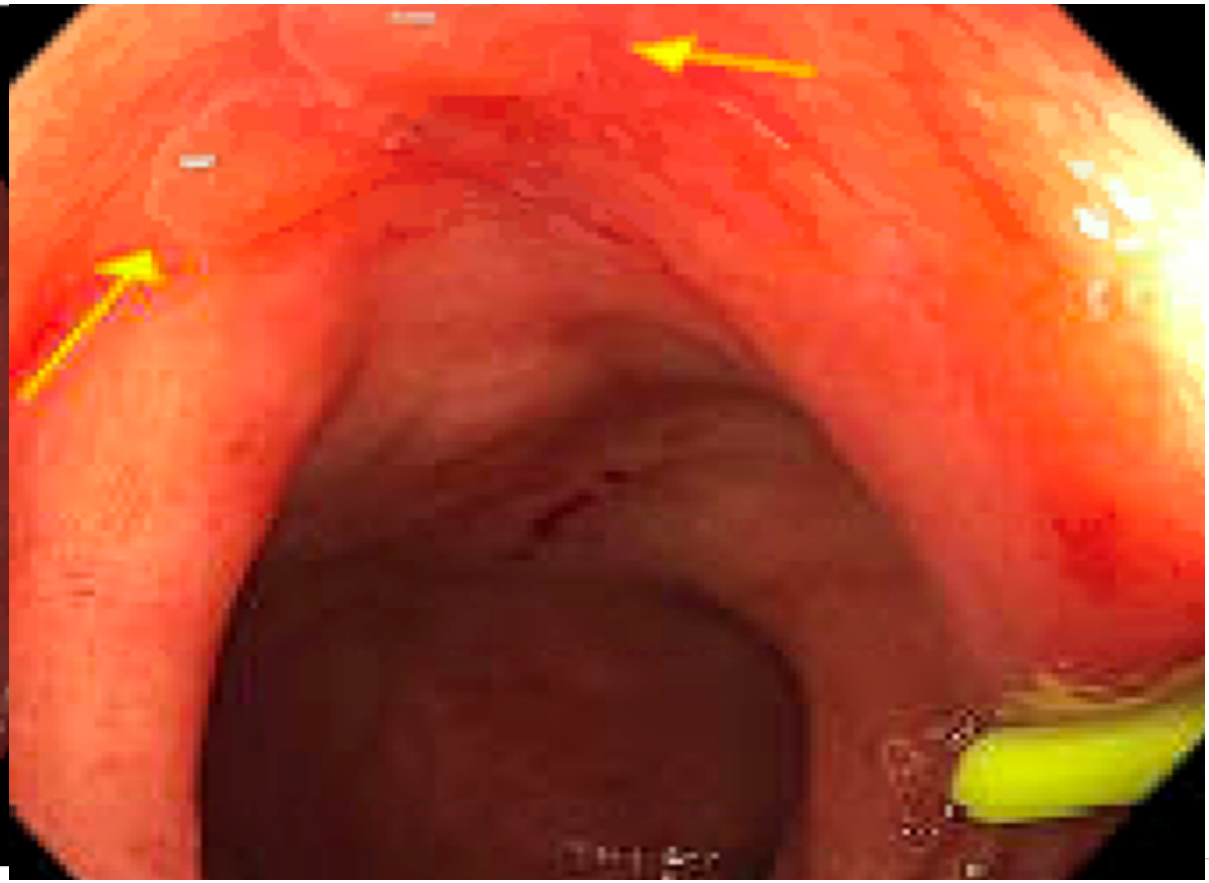
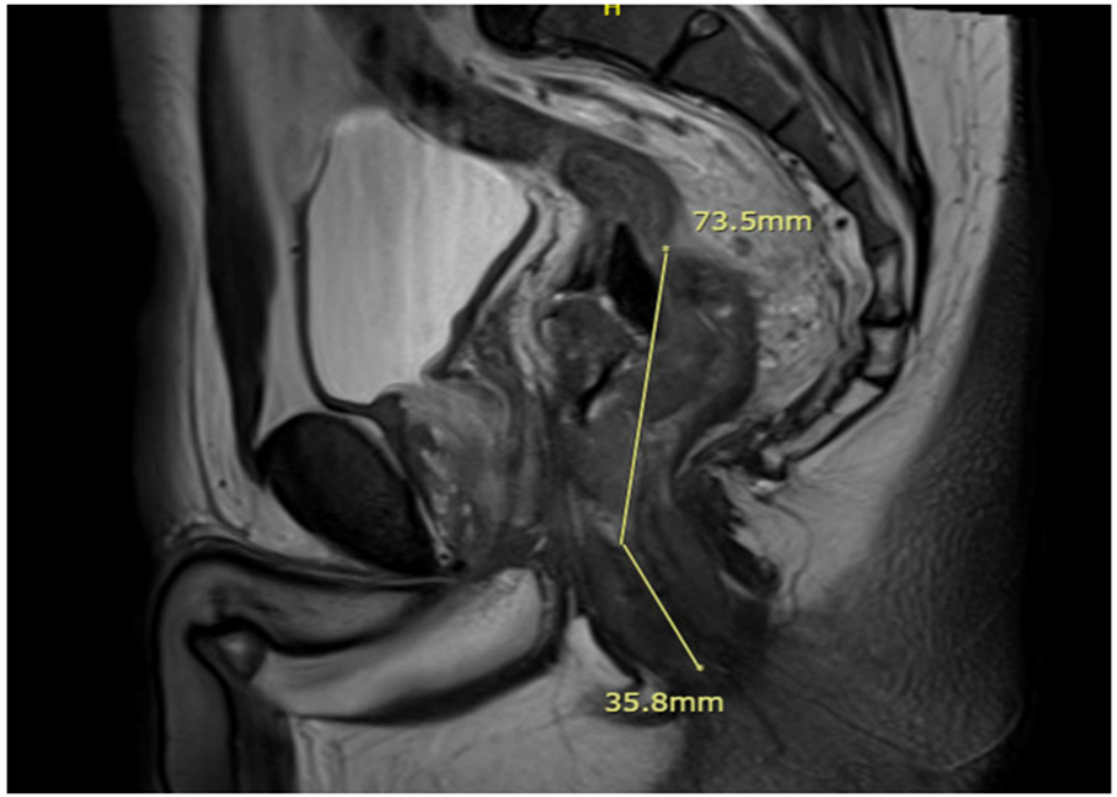




Case 3

T3b N+ Circumferential low rectal tumor with involvement of the internal anal sphincter, numerous surrounding tumor deposits and lymph nodes. No definite EMVI.
CRM: Involved: tumor <1 mm.
Sphincter involvement: Present.



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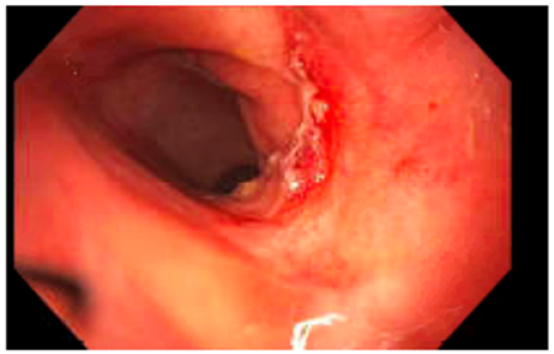

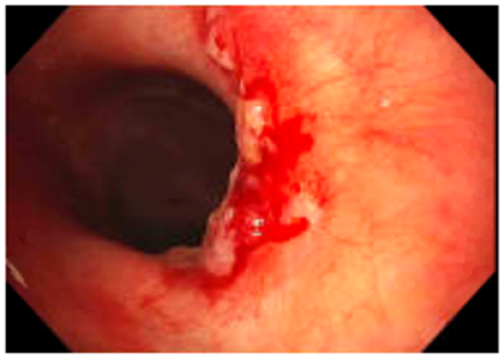

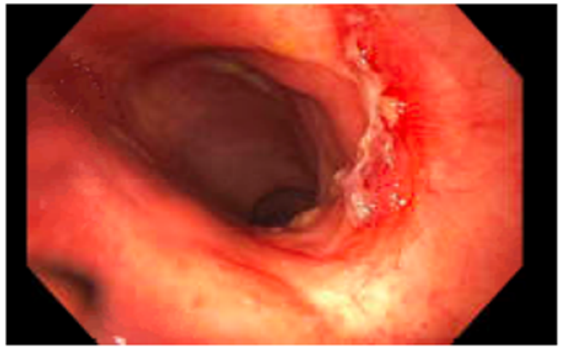

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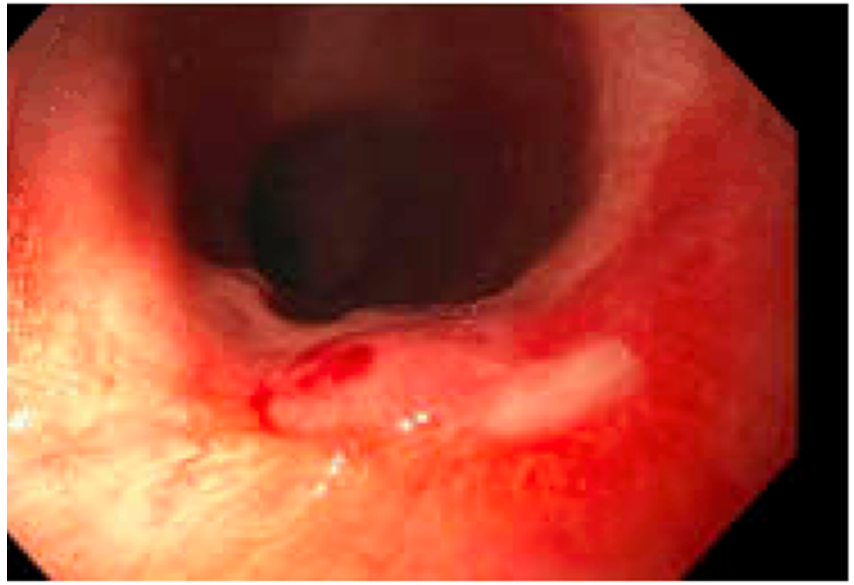

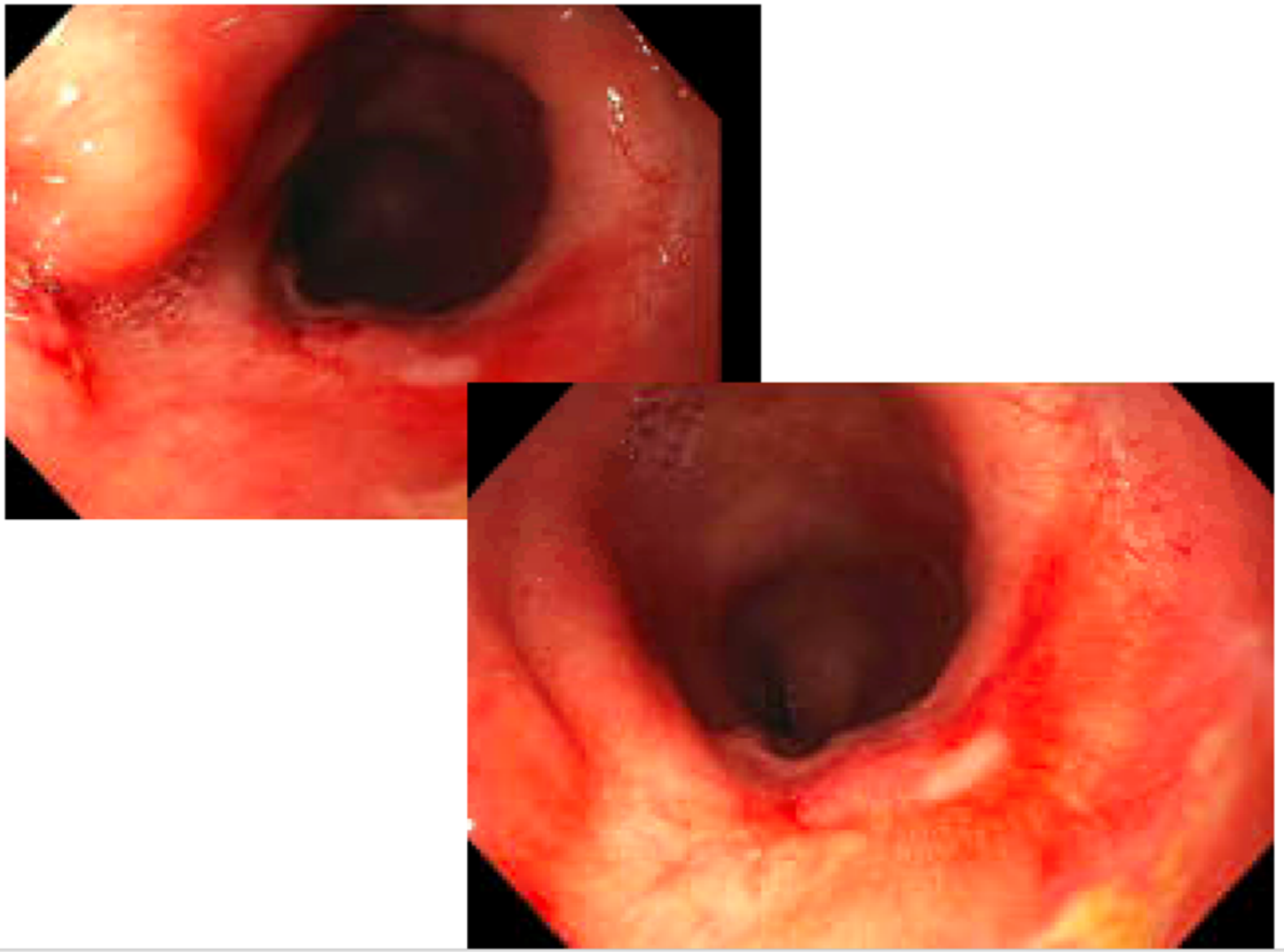

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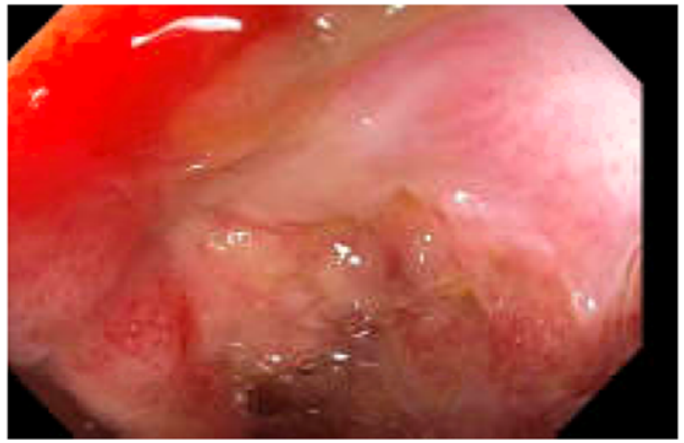

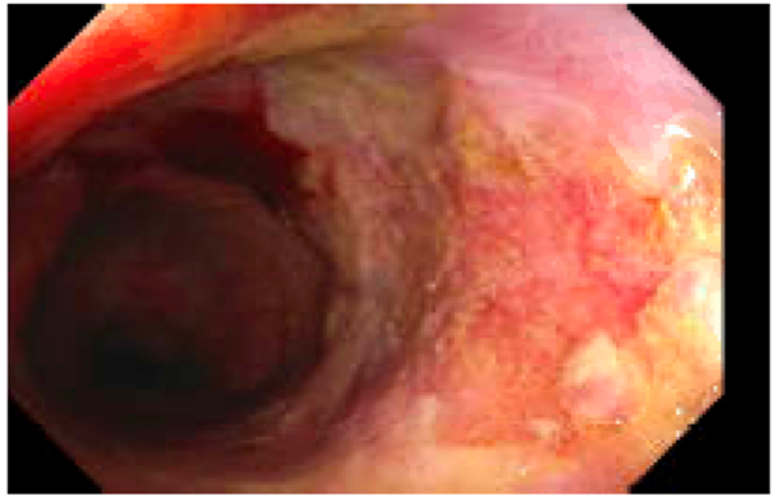

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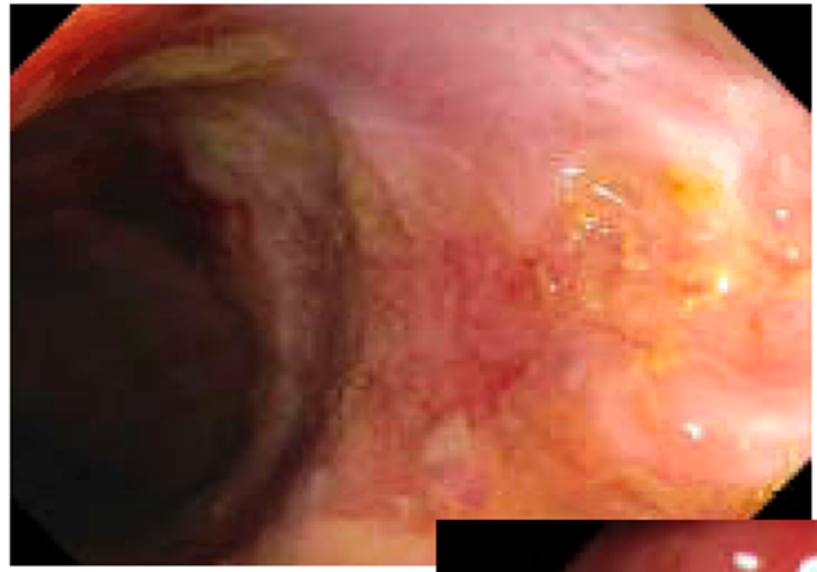

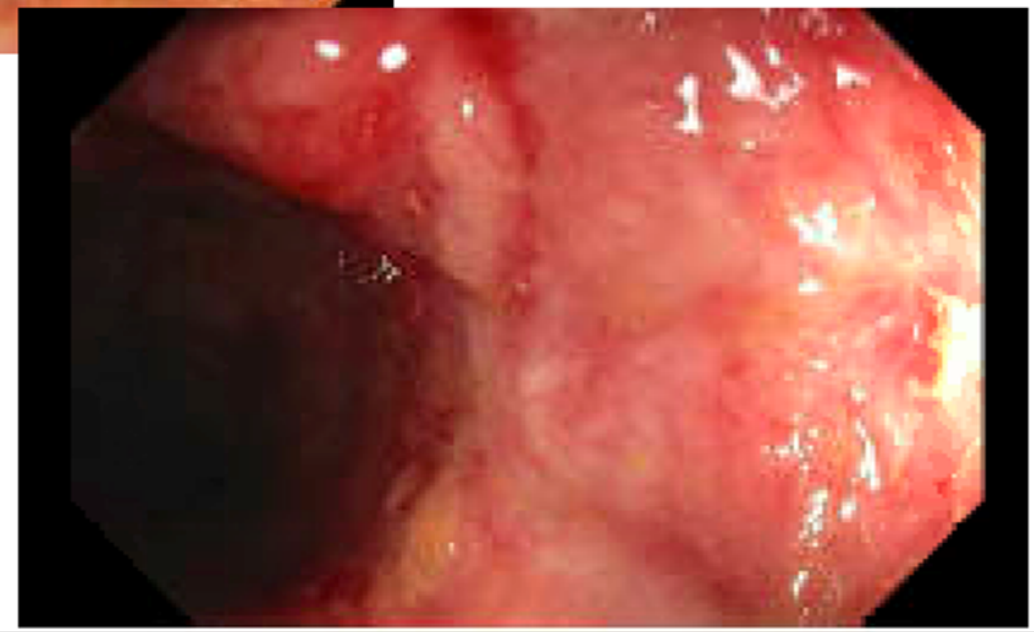

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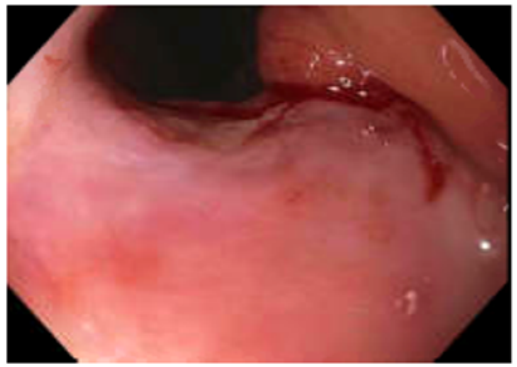

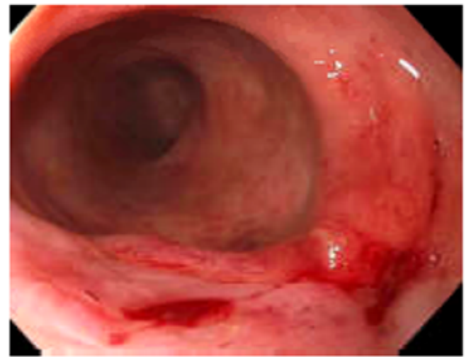

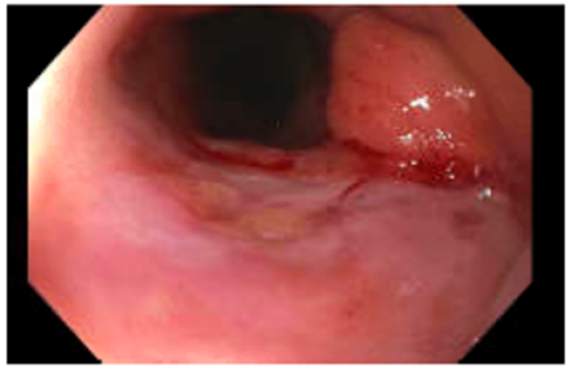

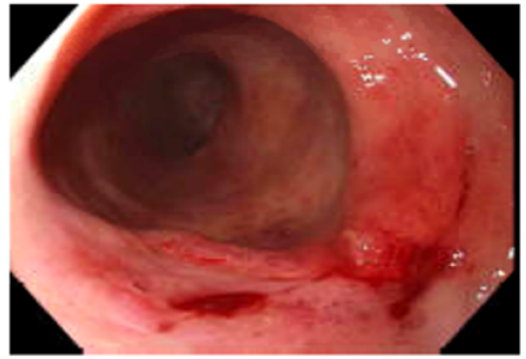

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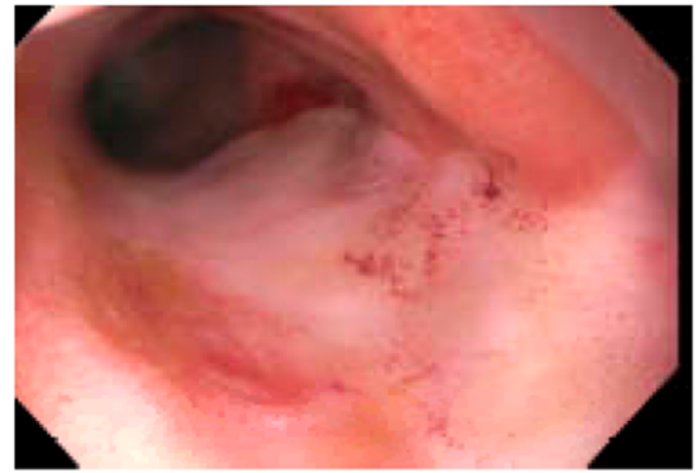

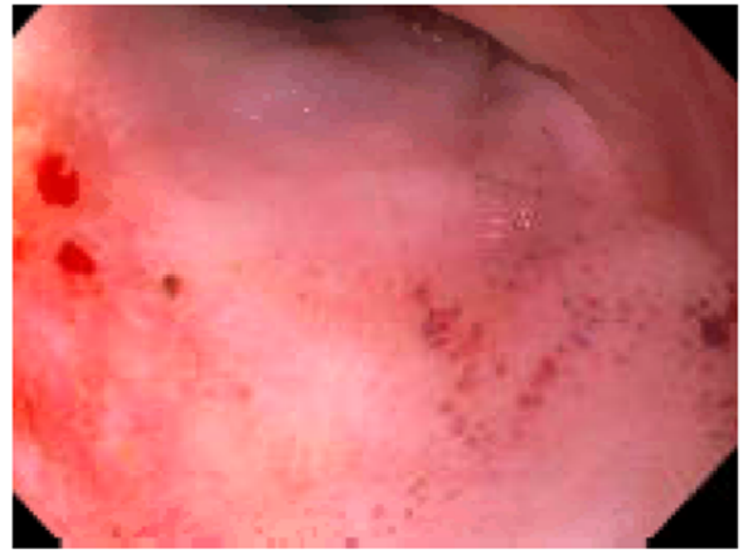

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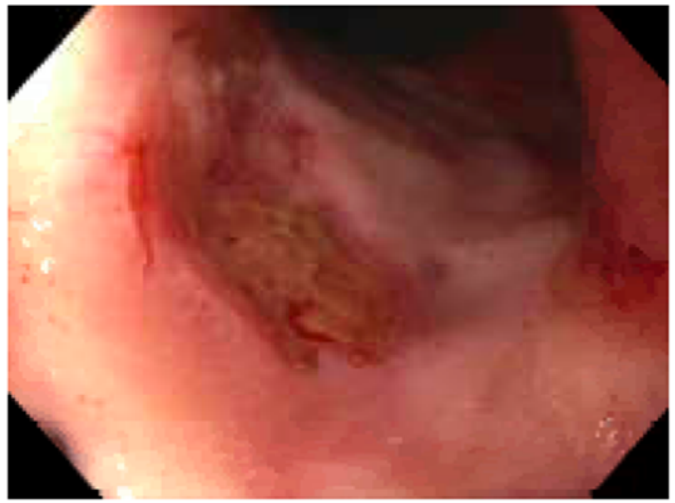
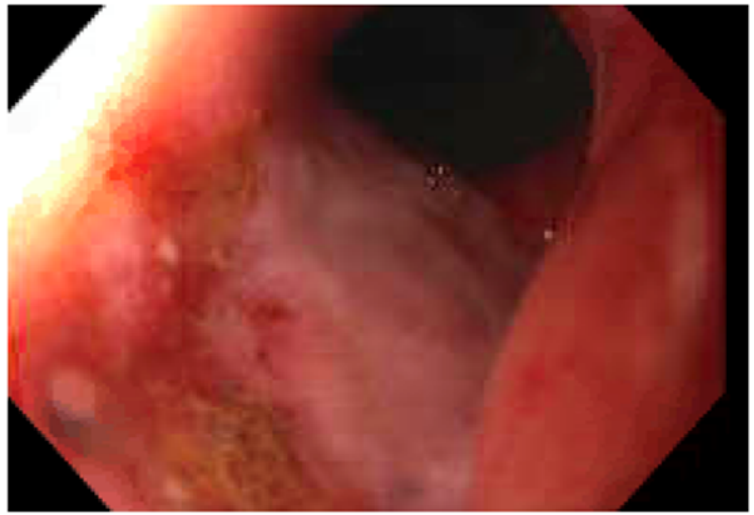
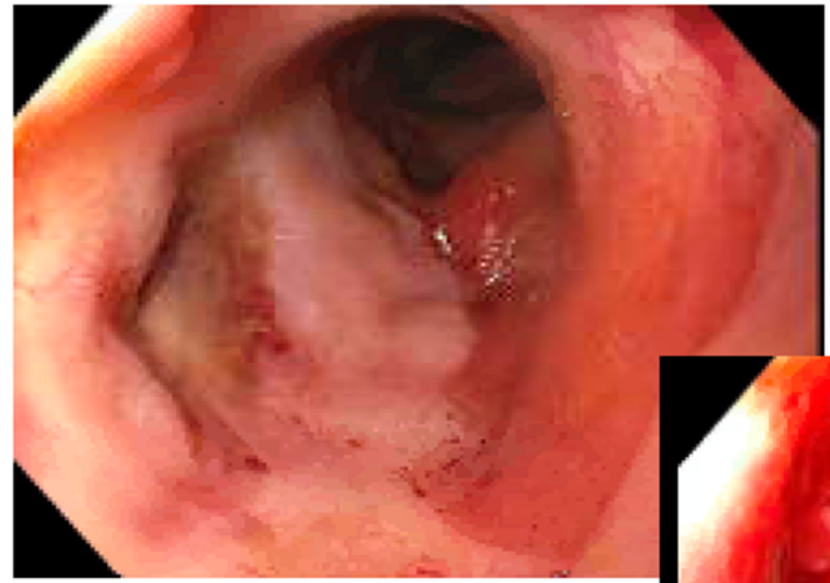
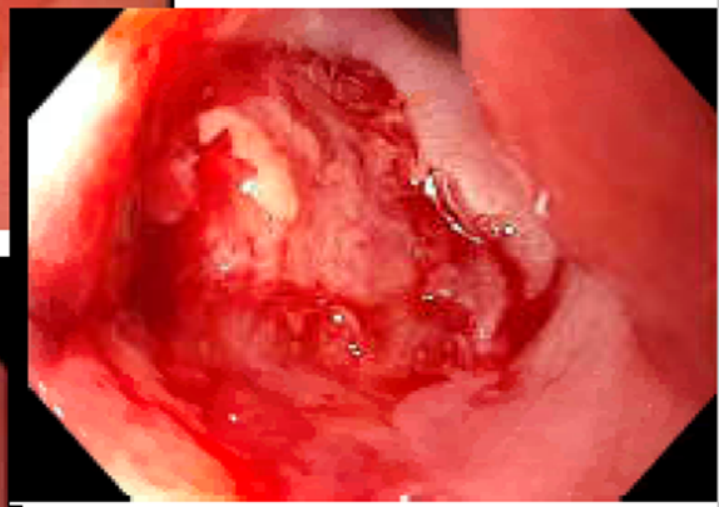
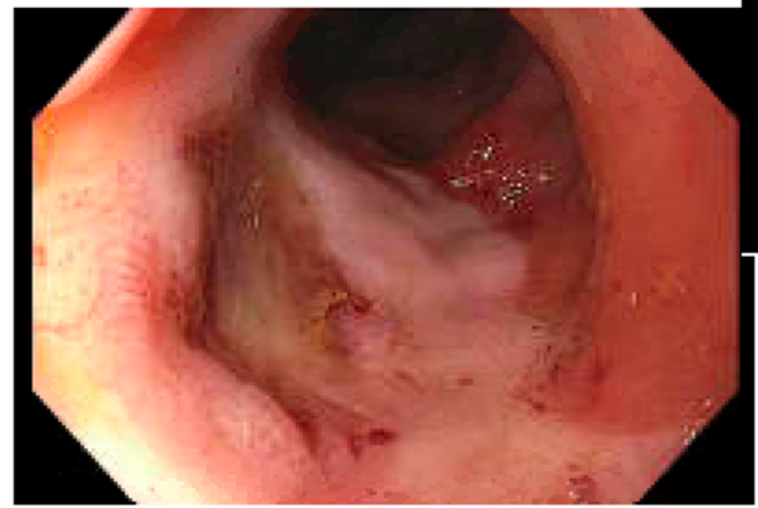






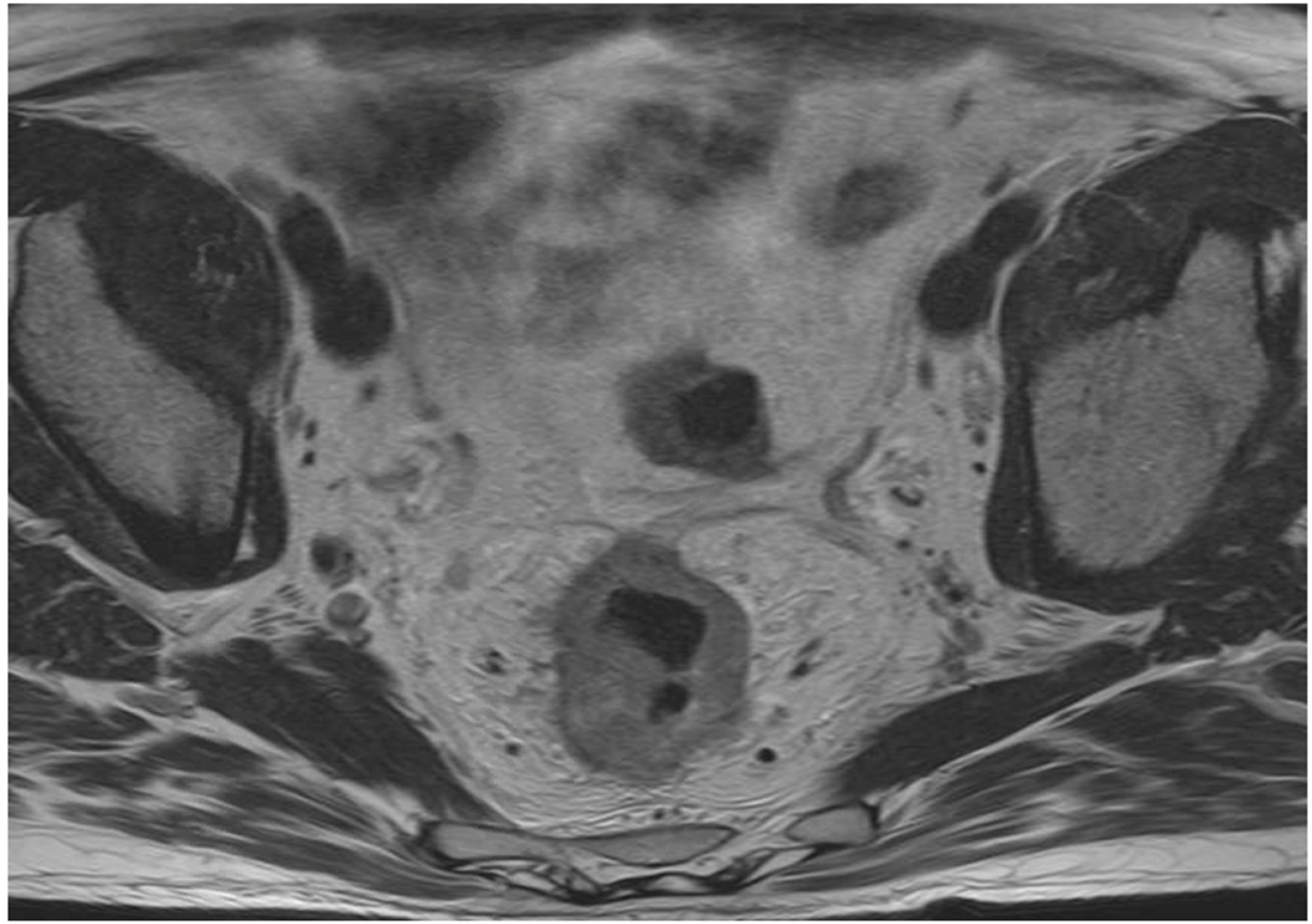




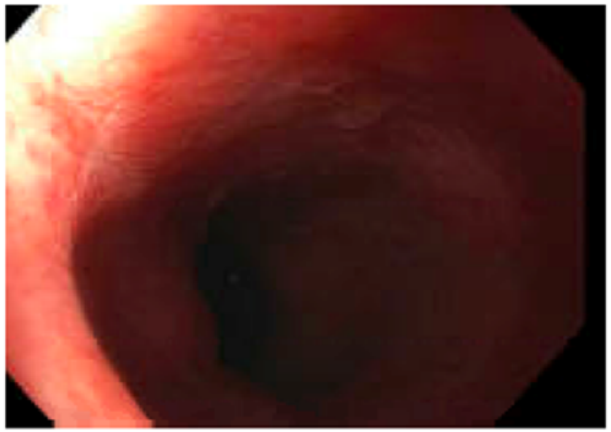
T3c upper to mid rectal neoplasm without EMVI

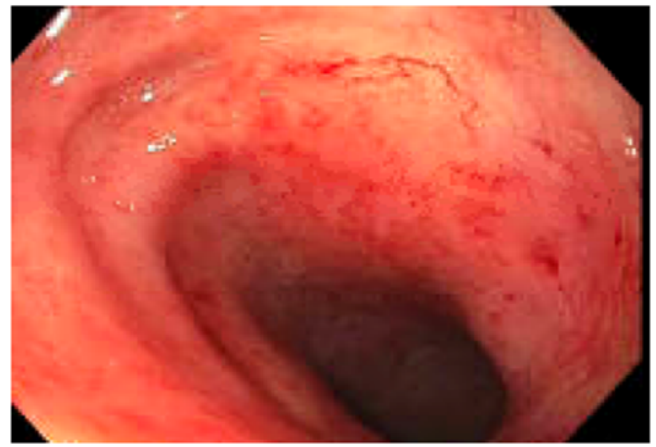
CRM: Clear: tumor margin >2 mm.

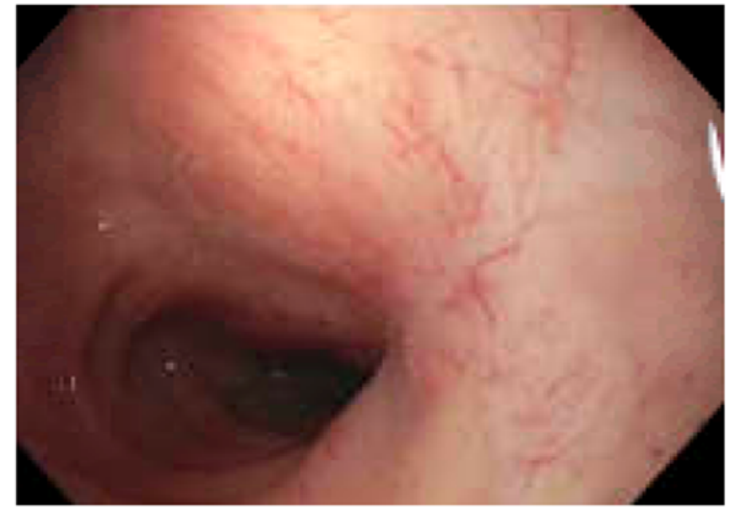
Sphincter involvement: Absent.

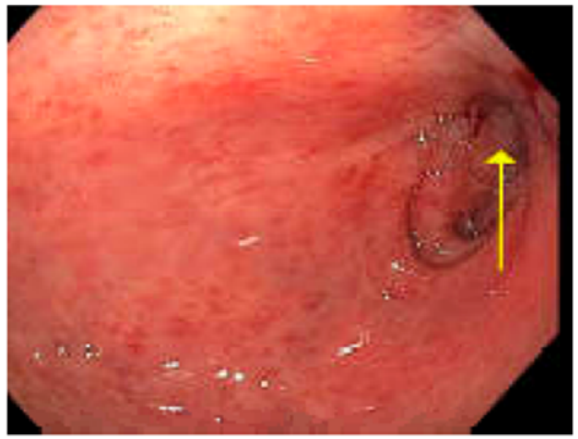


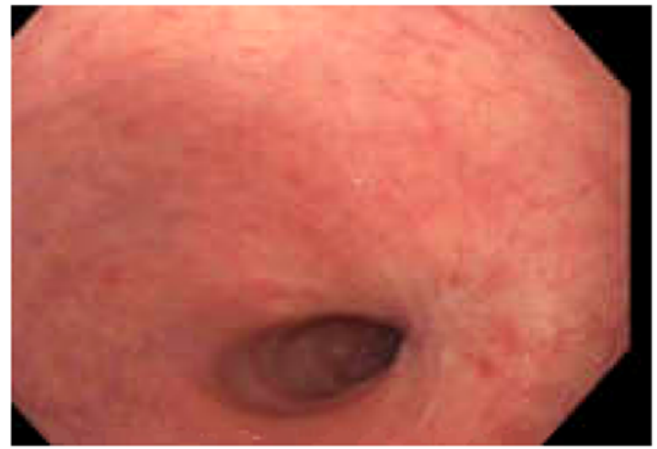
Flex sig years 1 and 2

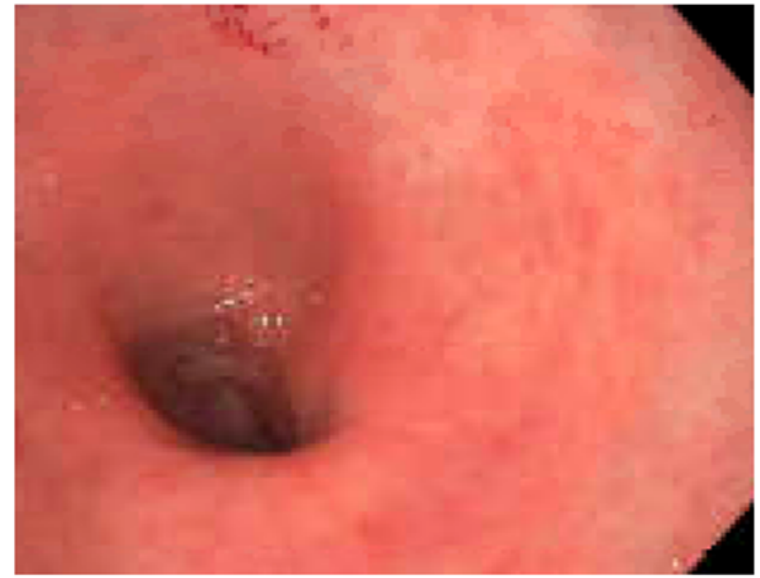




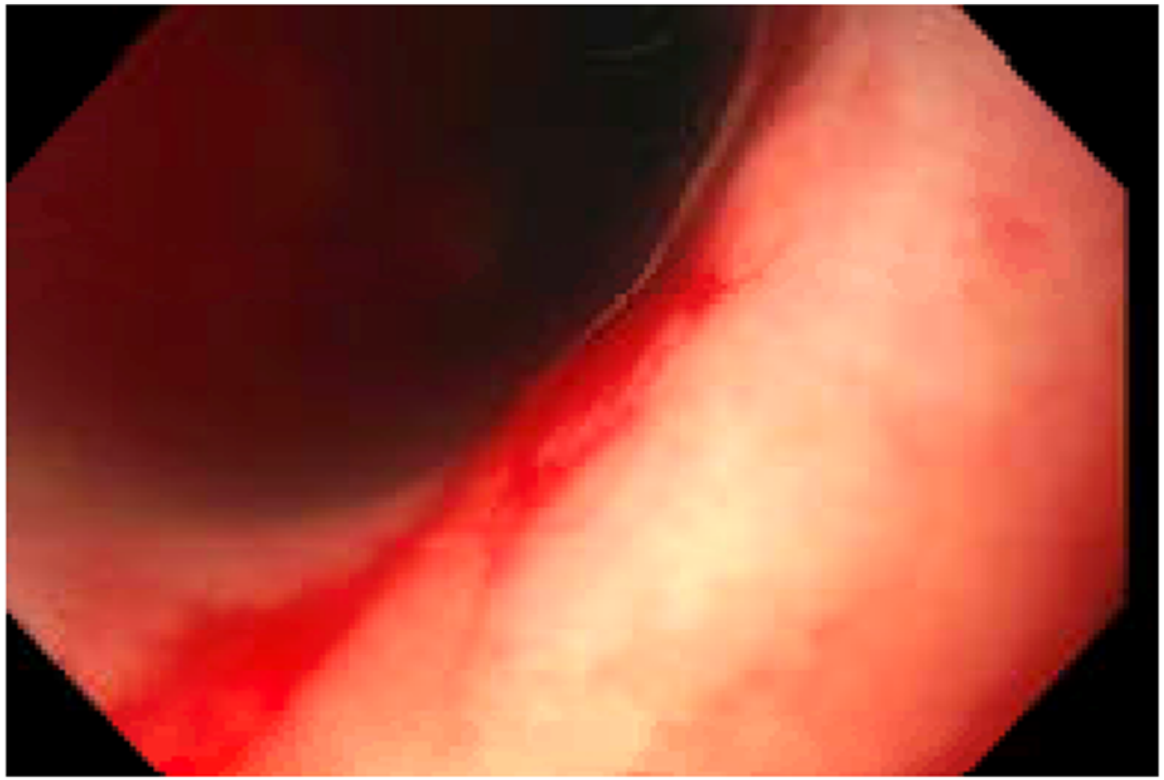


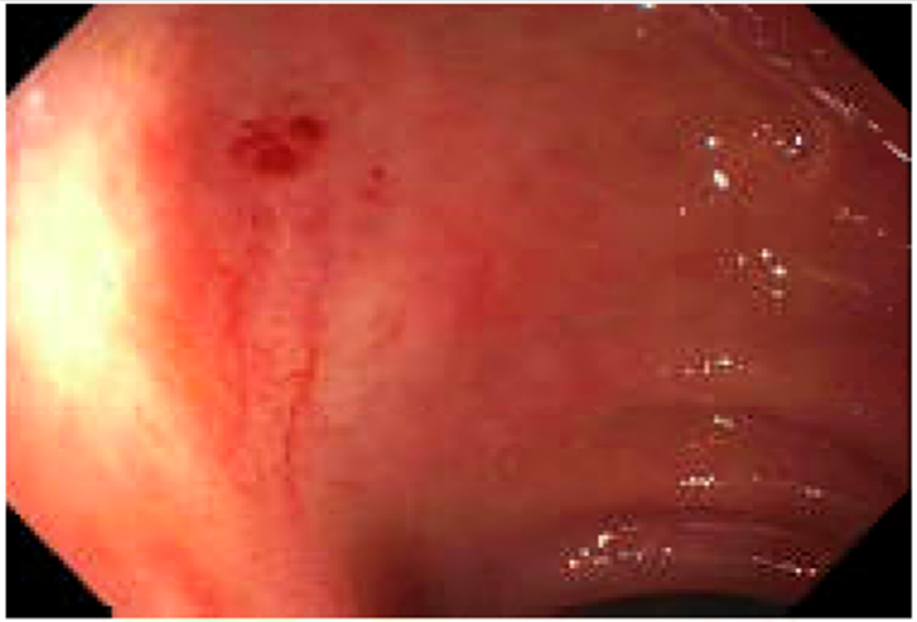


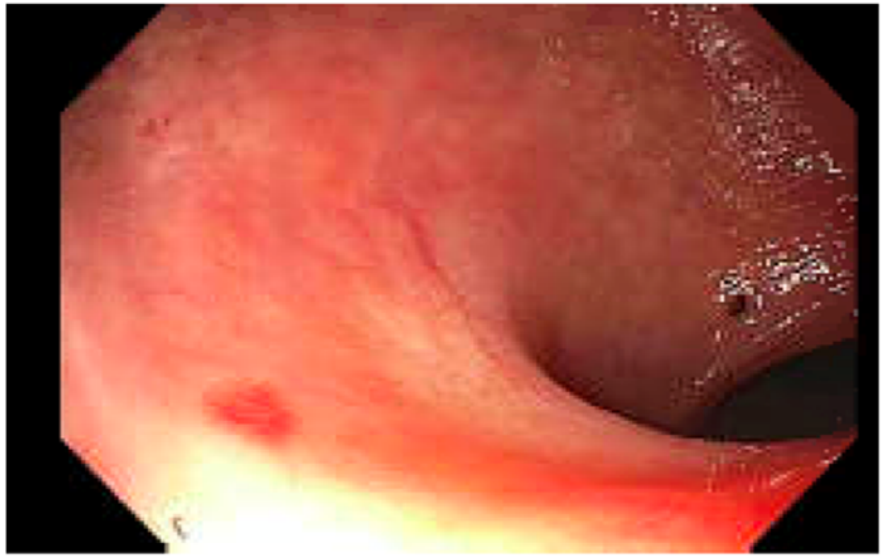




Flex sig through 4 years of surveillance







Summary

- Consolidation type TNT makes post-TNT observation possible in over half of patients
- Institutions need to define the tolerance for risk with partial clinical response
- Patients with pCR need close follow up, especially with high-risk features like ulcer, nodularity and irregular mucosa

Thank you!