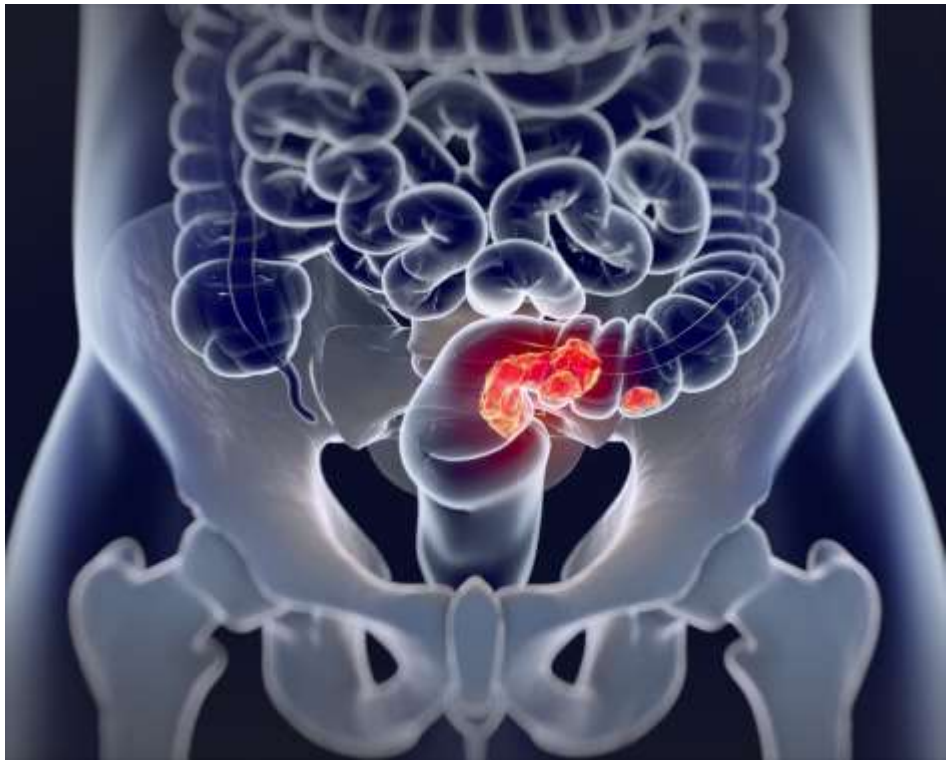
Preoperative ChemoRT in locally advanced rectal cancer



Dr Piyush Kumar

Panel Moderator

Panelists

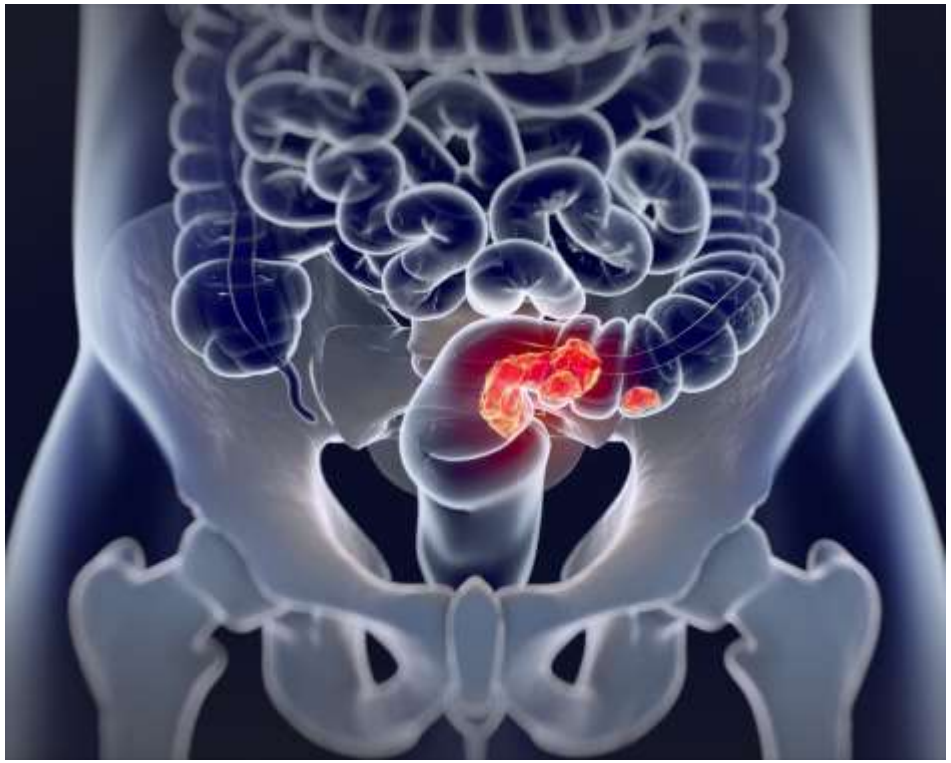
- **Dr Avilash Banerjee**, Yashoda Hospital, Somajiguda, Hyderabad
- **Dr Pamela Sen**, IMS-BHU, Varanasi
- **Dr Pragna GS**, KMC, Manipal
- **Dr Neelema PG**, Government Kilpauk Medical College, Chennai
- **Dr Sanyamita Jain**, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly

Methodology

- **Formation of whatsapp group**
- **Posting of questions to understand the topic of discussion**
- **Case scenarios selected by PGs from their institute**
- **Questions for each case scenario formed by 2 PGs as per allotment**
- **Answers to each question by each PG**

What was my role ?

Preoperative ChemoRT in locally advanced rectal cancer



Dr Piyush Kumar

Data Moderator

Case Discussion 1

- Sixty two years female, retired school teacher, presented with chief complaints of two month history of intermittent rectal bleeding, changes in bowel habits (alternating diarrhea and constipation), and a sensation of incomplete evacuation.
- Past Medical History: Hypertension (on medication for 8 years)
- No known history of colorectal cancer in the family
- Physical examination reveals mild tenderness on palpation of the lower abdomen, no palpable masses or hepatomegaly.
- Digital rectal examination (DRE) reveals an indurated lesion in the lower rectum, about 6 cm from the anal verge, which is hard and fixed, with no obvious involvement of the perianal skin

- **Colonoscopy Findings:**

- Lesion Location: Lower rectum (6 cm from anal verge).
- A large, irregular, ulcerated mass with raised edges and central necrosis, measuring approximately 4 cm in diameter. The mucosa surrounding the lesion appears inflamed, with a friable texture. The lesion partially obstructs the lumen, with narrowing of the rectal canal. No other polyps or lesions were identified throughout the colon.

- **Biopsy**: Moderately differentiated adenocarcinoma of the rectum.

- **CT Scan of the Abdomen and Pelvis:**
  - A **rectal mass** measuring 4 x 3.5 cm is seen at the lower rectum, involving the muscularis propria, with signs of **extramural extension** into the mesorectal fat.
  - **No distant metastases** are noted in the liver, lungs, or bones.
  - **Perirectal lymphadenopathy** is noted, with multiple enlarged lymph nodes in the mesorectum, the largest being 1.5 cm in size.
  - **No bowel perforation** or free intraperitoneal air is observed.
  - Mild **rectal wall thickening** and **abnormal mesorectal fat** suggest T3 stage.
  - The **pelvic organs** (uterus, ovaries) appear normal, with no evidence of direct spread to adjacent organs.

- **MRI of the Rectum (Pelvic MRI):**
  - A **5 cm circumferential mass** is identified in the distal rectum, about 6 cm from the anal verge, with **T3** characteristics (extending through the muscularis propria into the mesorectal fat).
  - The lesion appears to be **fixed** to the surrounding structures, which suggests **local invasion**.
  - **Mesorectal lymphadenopathy** is confirmed with several enlarged nodes (largest measuring 1.8 cm) located at the 3 o'clock and 9 o'clock positions in the mesorectum.
  - There is **no evidence of peritoneal carcinomatosis** or bladder involvement.
  - The **circumferential resection margin (CRM)** appears **involved**, with the tumor extending within 1 mm of the CRM

- **CT Chest:**
  - No evidence of pulmonary metastasis.
  - No significant pleural effusion or lymphadenopathy.

- **Assessment**:
  - Tumor stage: **T3N1M0** (locally advanced rectal cancer with regional lymph node involvement but no distant metastasis)

Question (Dr Avilash)

- Why were both CT and MRI done for this case

EVALUATION OF COMPARATIVE ROLE OF CT SCAN AND MRI IN LOCAL STAGING OF RECTAL CANCER

Drashty Rameshbhai Chauhan[1], Bhavya Jayeshbhai Chauhan[2], Rupal Bhimabhai Vadhiya[3], Jigna Thakorbhai Patel[4]

[1]Assistant Professor, Department of Radiology, Gujarat Cancer and Research Institute, Gujarat, India.
[2]Resident, Department of Radiology, Gujarat Cancer and Research Institute, Gujarat, India.
[3]Resident, Department of Radiology, Gujarat Cancer and Research Institute, Gujarat, India.
[4]Resident, Department of Radiology, Gujarat Cancer and Research Institute, Gujarat, India.

CONCLUSION

Both modalities CT and MRI are useful for characterisation of features of rectal carcinoma. CECT examination is useful as initial cost and time are less. It is an effective tool for diagnosing and staging rectal malignancy but there are certain characteristics of rectal tumours such as initial stage of rectal malignancy (T1, T2), mesorectal fascia involvement and lymph node assessment in which MRI is superior compared to CT.

Question for all

- What are the specific features you are looking for in MRI pelvis

MRI of Rectal Cancer: Tumor Staging, Imaging Techniques, and Management

MRI helps the radiologist *(a)* describe the tumor location and morphology, *(b)* provide its T and N categories, *(c)* detect the presence of extramural vascular invasion, and *(d)* identify its relationship with surrounding structures, including the sphincter complex and involvement of the mesorectal fascia. These features help diagnose locally advanced rectal tumors (categories T3c-d, T4, N1, and N2), for which neoadjuvant chemoradiotherapy (CRT) is indicated. In

Diagnostic accuracy of preoperative magnetic resonance imaging in predicting curative resection of rectal cancer: prospective observational study

MERCURY Study Group

Results 354 of the 408 patients had a clear circumferential resection margin (87%, 95% confidence interval 83% to 90%). Specificity for prediction of a clear margin by magnetic resonance imaging was 92% (327/354, 90% to 95%). High

- To visualize mesorectal fascia (to predict distance for surgical margins)
- To look for involvement of pelvic floor muscles
- To predict Circumferential Resection Margin (CRM) & Tumor Regression Grade (TRG)
- To categorize low rectal cancers based on tumour closeness to internal sphincter plane, thus decide on NACRT or Surgery

Question (Dr Pamela)

- Role of PET CT in this case

FDG-PET/CT is not routinely indicated

- FDG-PET/CT does not supplant a contrast-enhanced diagnostic CT or MRI and should only be used to evaluate an equivocal finding on a contrast-enhanced CT or MRI scan or in patients with strong contraindications to IV contrast administration

Question (Dr Sanyamita)

- Optimum investigations to be done

Question to all

- Any other investigations to be suggested

Work up

After histopathological diagnosis by biopsy

- MMR/MSI testing
- Colonoscopy
- Consider proctoscopy
- Chest CT and abdominal CT or MRI
- Endorectal ultrasound (*if MRI is contraindicated or inconclusive, or for superficial lesions*)
- CBC, chemistry profile, CEA
- Fertility risk discussion / counseling in appropriate patients
- FDG-PET/CT scan is not indicated

- dMMR
- pMMR
- MSS
- MSI

- dMMR - MSI
- pMMR - MMS

Question (Dr Neelema)

- How will you proceed with this case for treatment?

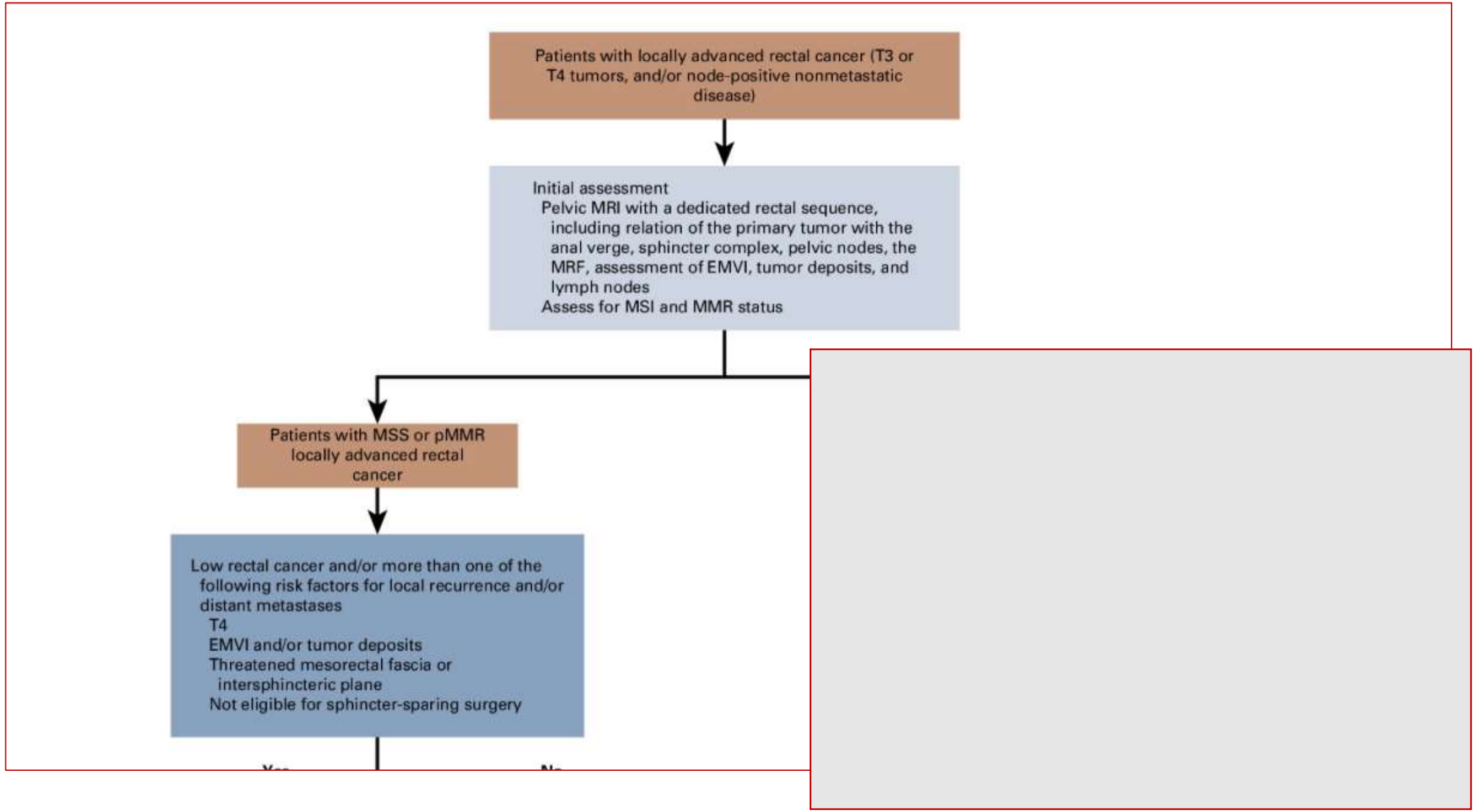
Question to all

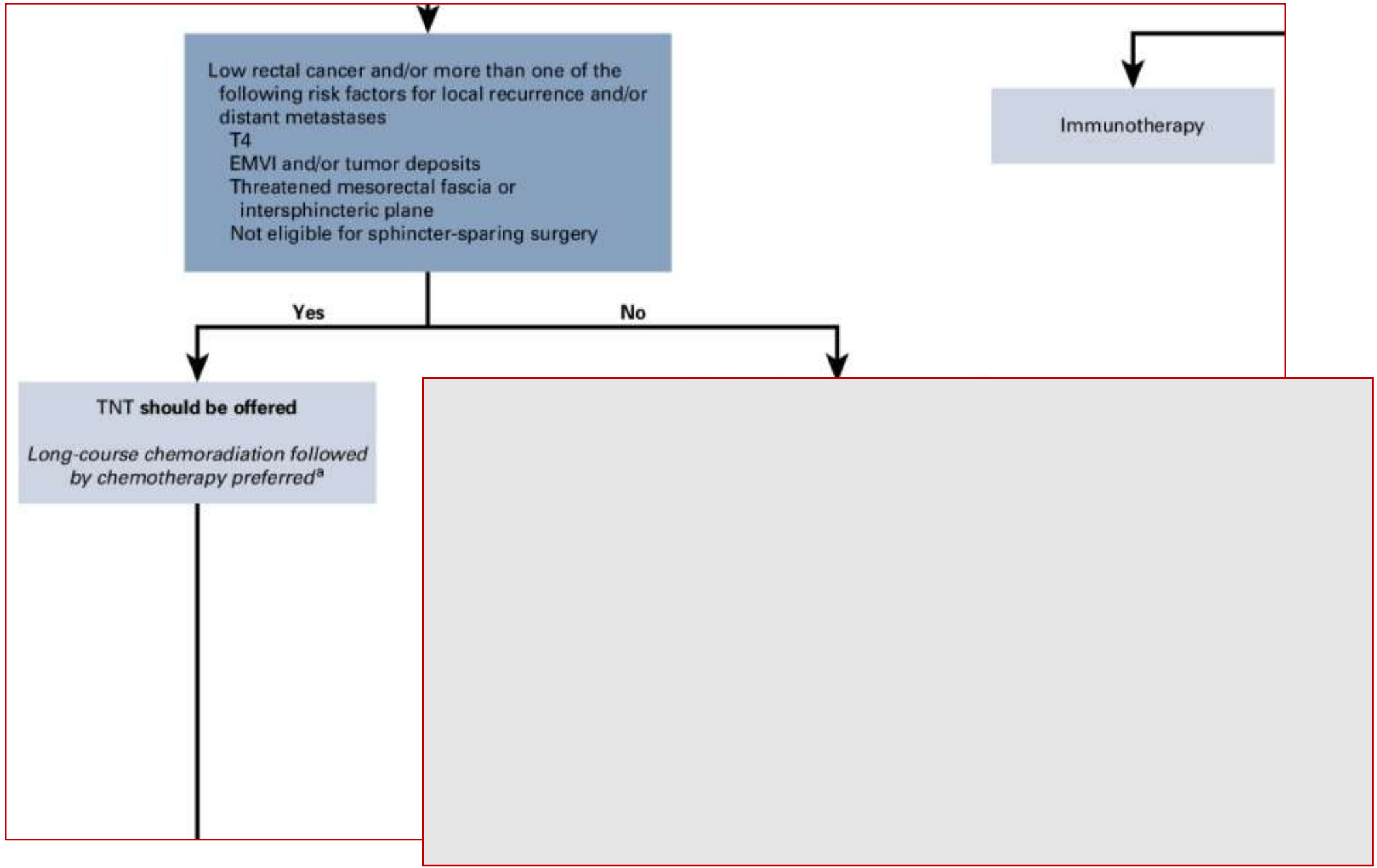
- Your suggestions regarding different aspects

ASCO Special Articles

Management of Locally Advanced Rectal Cancer: ASCO Guideline

Aaron J. Scott, MD[1]; Erin B. Kennedy, MHSc[2]; Jordan Berlin, MD[3]; Gina Brown, MBBS, MD[4]; Myriam Chalabi, MD, PhD[5]; May T. Cho, MD[6]; Mike Cusnir, MD[7]; Jennifer Dorth, MD[8]; Manju George, DVM, PhD[9]; Lisa A. Kachnic, MD[10]; Hagen F. Kennecke, MD[11]; Jonathan M. Loree, MD[12]; Van K. Morris, MD[13]; Rodrigo Oliva Perez, MD, PhD[14]; J. Joshua Smith, MD, PhD[15]; Matthew R. Strickland, MD[16]; and Sepideh Gholami, MD, MAS[17]


Patients with locally advanced rectal cancer (T3 or T4 tumors, and/or node-positive nonmetastatic disease)
Initial assessment
Pelvic MRI with a dedicated rectal sequence, including relation of the primary tumor with the anal verge, sphincter complex, pelvic nodes, the MRF, assessment of EMVI, tumor deposits, and lymph nodes
Assess for MSI and MMR status
Patients with MSS or pMMR locally advanced rectal cancer
Low rectal cancer and/or more than one of the following risk factors for local recurrence and/or distant metastases
T4
EMVI and/or tumor deposits
Threatened mesorectal fascia or intersphincteric plane
Not eligible for sphincter-sparing surgery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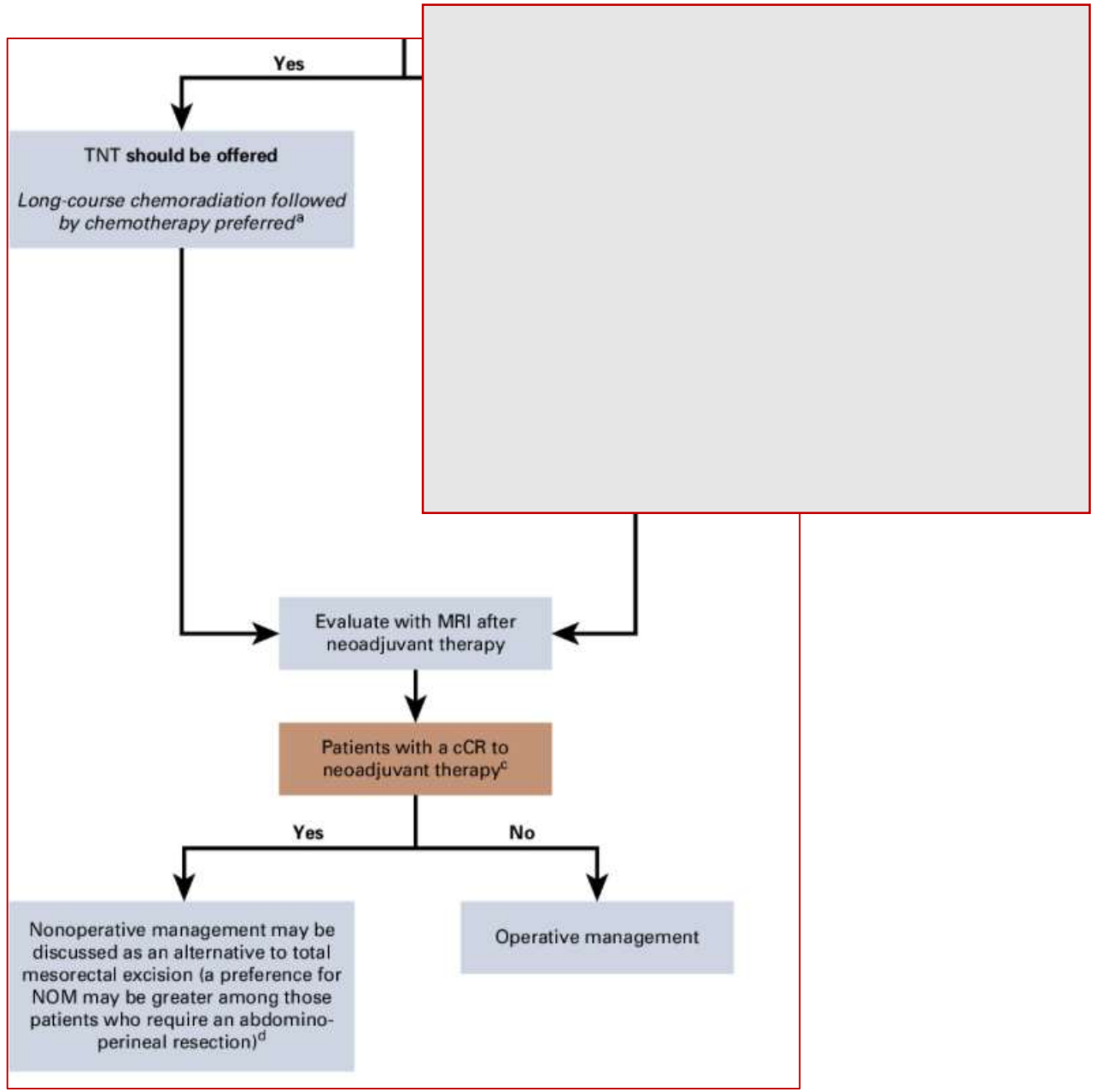
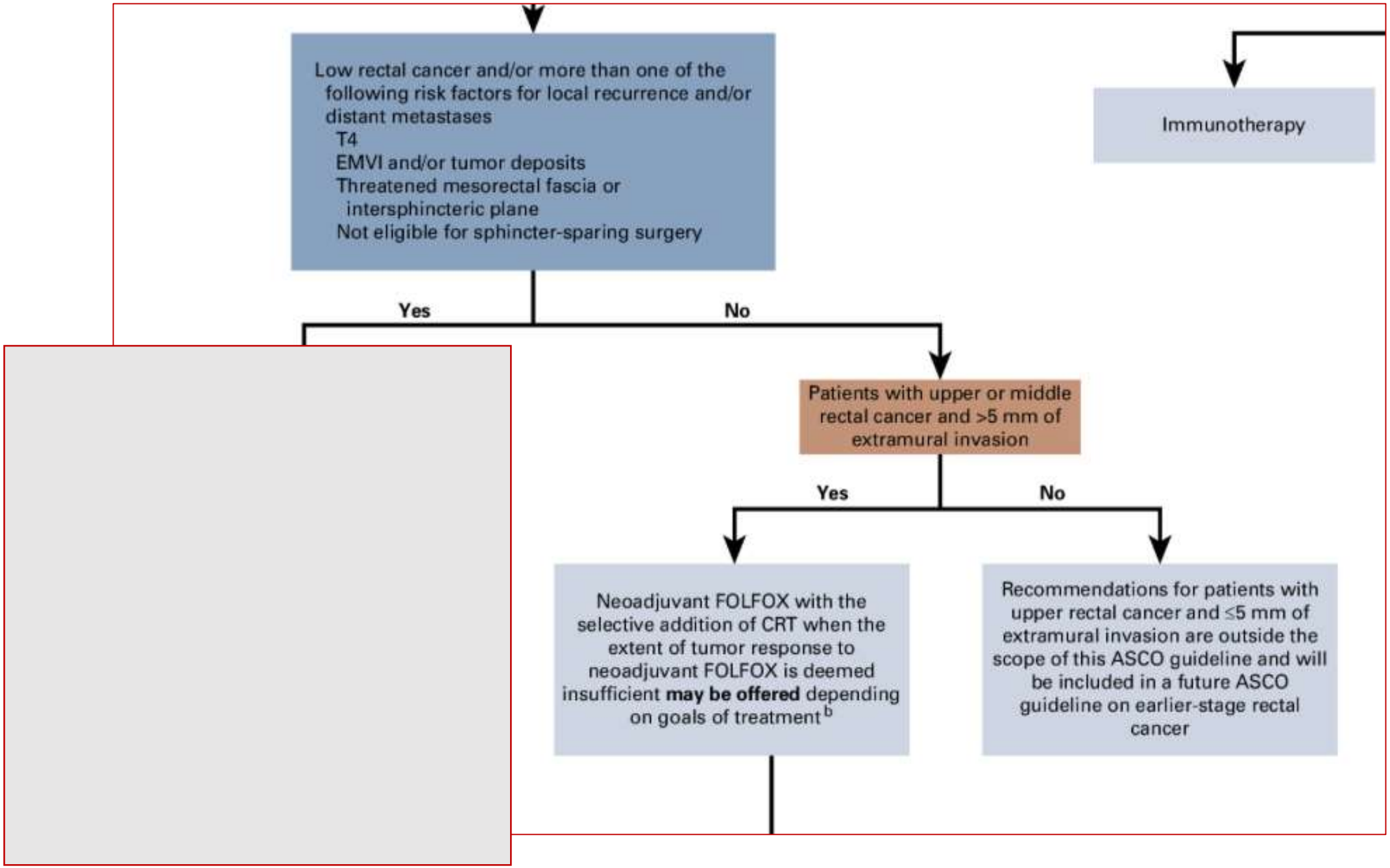
Threatened mesorectal fascia or intersphincteric plane
Not eligible for sphincter-sparing surgery
Immunotherapy
Yes
No
TNT **should be offered**
Long-course chemoradiation followed by chemotherapy preferred[a]


Yes
TNT should be offered
Long-course chemoradiation followed by chemotherapy preferred[a]
Evaluate with MRI after neoadjuvant therapy
Patients with a cCR to neoadjuvant therapy[c]
Yes
No
Nonoperative management may be discussed as an alternative to total mesorectal excision (a preference for NOM may be greater among those patients who require an abdomino-perineal resection)[d]
Operative management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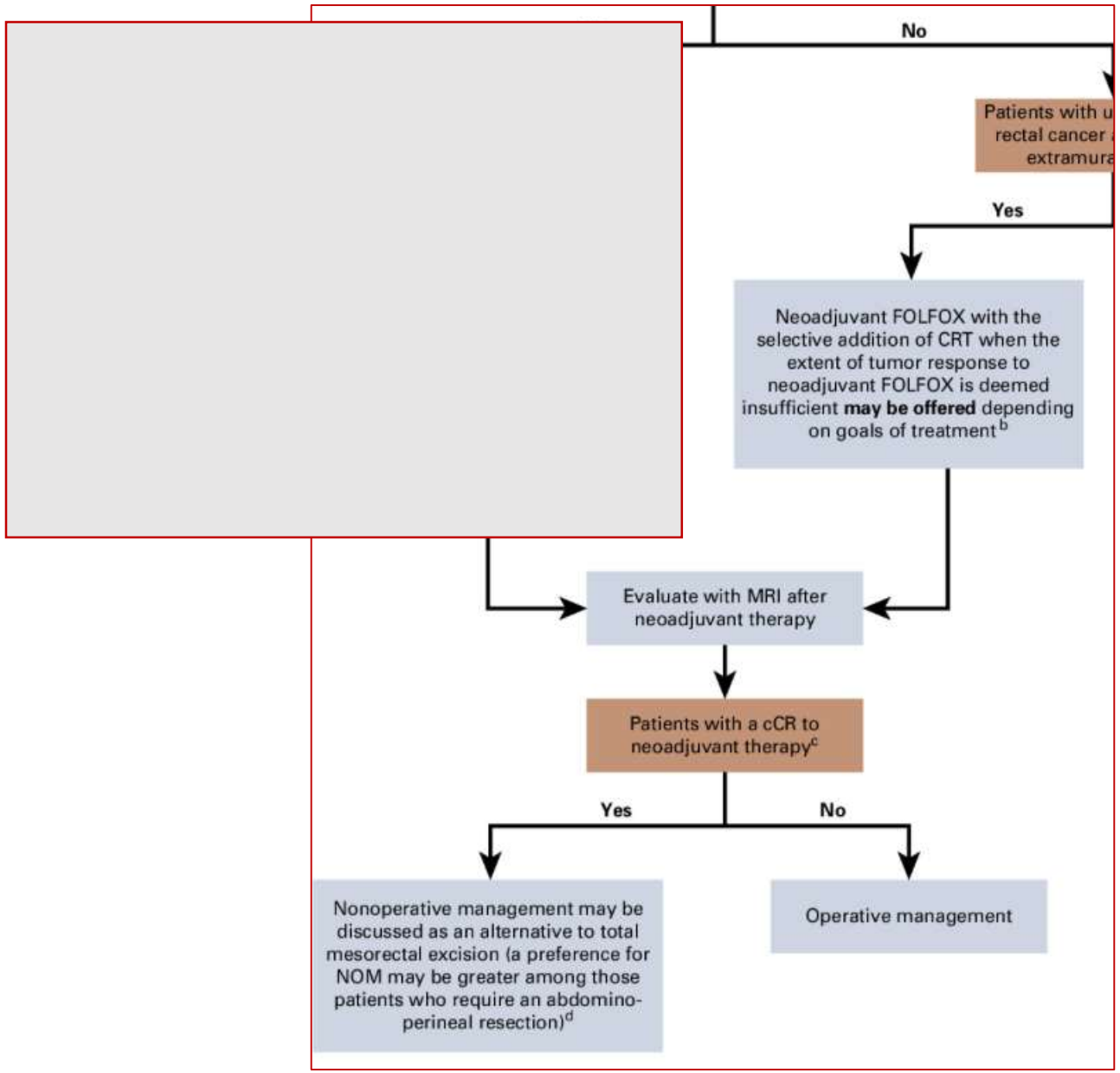
T4
EMVI and/or tumor deposits
Threatened mesorectal fascia or intersphincteric plane
Not eligible for sphincter-sparing surgery
Immunotherapy
Yes
No
Patients with upper or middle rectal cancer and >5 mm of extramural invasion
Yes
No
Neoadjuvant FOLFOX with the selective addition of CRT when the extent of tumor response to neoadjuvant FOLFOX is deemed insufficient **may be offered** depending on goals of treatment [b]
Recommendations for patients with upper rectal cancer and ≤5 mm of extramural invasion are outside the scope of this ASCO guideline and will be included in a future ASCO guideline on earlier-stage rectal cancer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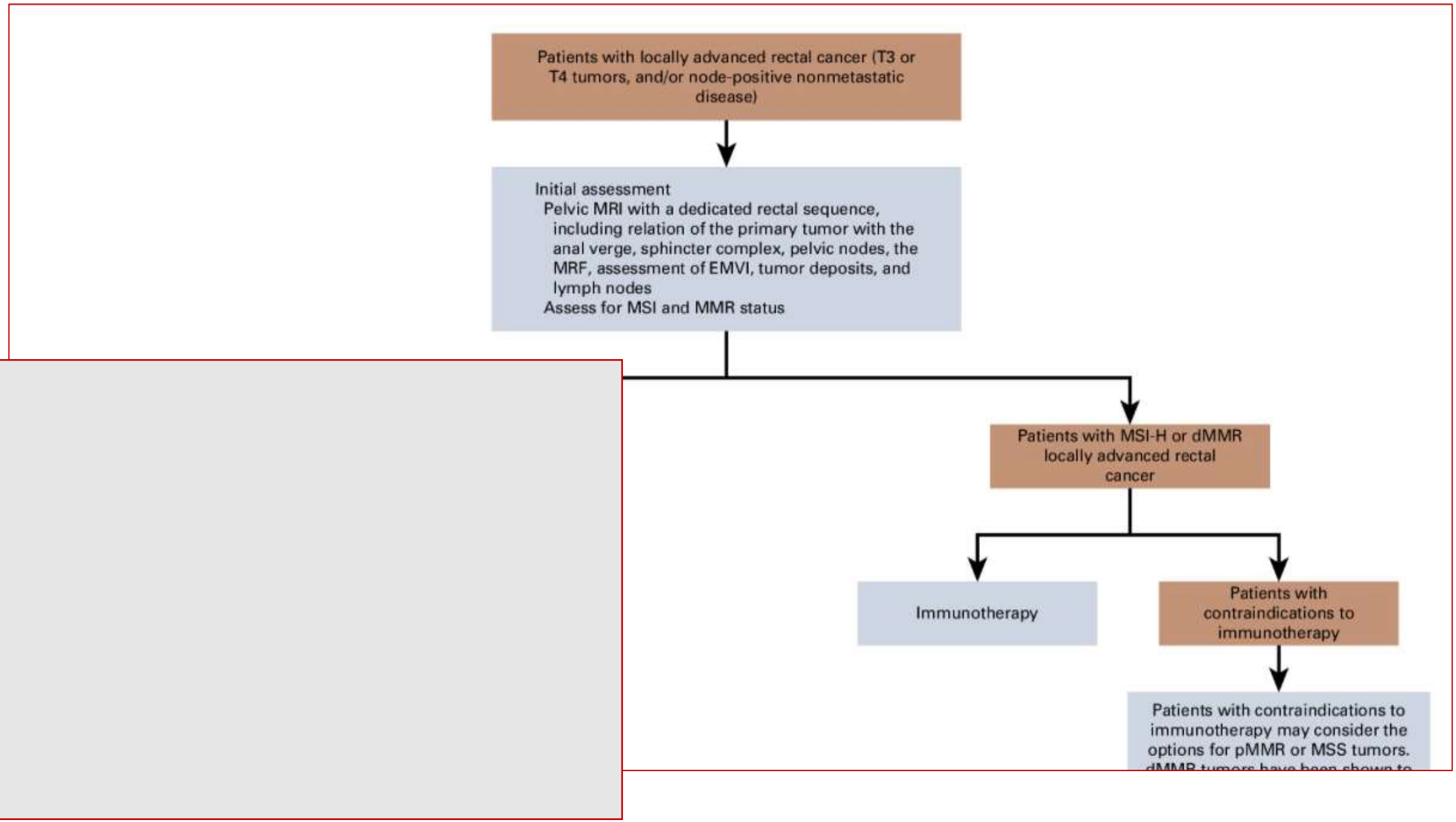
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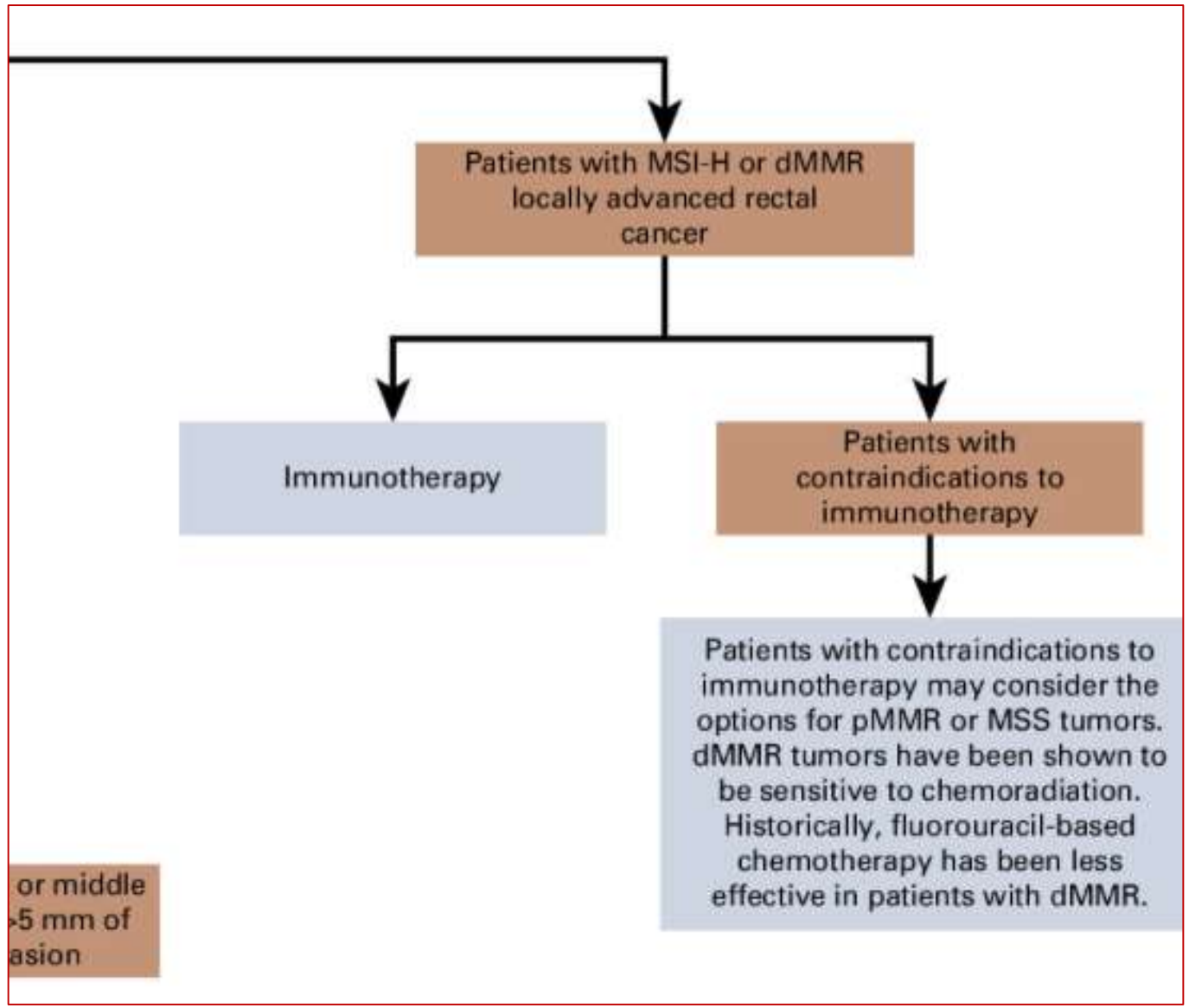
Immunotherapy
Patients with contraindications to immunotherapy
Patients with contraindications to immunotherapy may consider the options for pMMR or MSS tumors.


Patients with MSI-H or dMMR locally advanced rectal cancer
Immunotherapy
Patients with contraindications to immunotherapy
Patients with contraindications to immunotherapy may consider the options for pMMR or MSS tumors. dMMR tumors have been shown to be sensitive to chemoradiation. Historically, fluorouracil-based chemotherapy has been less effective in patients with dMMR.
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Annals of Oncology 28 (Supplement 4): iv22–iv40, 2017
doi:10.1093/annonc/mdx224

CLINICAL PRACTICE GUIDELINES

Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

R. Glynne-Jones[1], L. Wyrwicz[2], E. Tiret[3,4], G. Brown[5], C. Rödel[6], A. Cervantes[7] & D. Arnold[8], on behalf of the ESMO Guidelines Committee*

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†Approved by the ESMO Guidelines Committee: August 2002, last update May 2017. This publication supersedes the previously published version—Ann Oncol 2013; 24 (Suppl. 6): vi81–vi88.

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Table 6. Recommended choice of treatment options within TNM risk category of primary rectal cancer without distant metastases

Risk group	TN substage	Possible therapeutic options	Further considerations
Very early	cT1 sm1 N0 (on ERUS and MRI)	Local excision (TEM) If pT1 and no adverse features, TEM is sufficient If adverse histopathology (sm ≥ 2, G3, V1, L1), requires radical resection (TME) as standard	Alternatively, in the case of adverse features on pathology, TEM plus salvage (or adjuvant) CRT in perioperative high-risk patients (but unproven benefit—with high risk of local recurrence for pT2)
Early (Good)	cT1-cT2; cT3a/b if middle or high, N0 (or also cN1 if high), MRF clear, no EMVI	Surgery (TME) alone is standard. If unexpected poor prognostic signs on histopathology (CRM+, extranodal/N2), consider postoperative CRT/CT (see postoperative recommendations in Table 7)	For fragile, high-risk patients or those rejecting radical surgery (CRT with evaluation, local excision or if achieving cCR, 'watch-and-wait', organ preservation)
Intermediate	cT3a/b very low, levators clear, MRF clear or cT3a/b in mid- or high rectum, cN1-2 (not extranodal), no EMVI	Surgery (TME) alone is a standard only if good-quality mesorectal resection assured (and local recurrence ≤0.5% or, if not, preoperative SCPRT (5×5 Gy) or CRT followed by TME	If CRT is given and cCR is achieved, 'watch-and-wait' in high-risk patients for surgery may be considered
Bad	cT3c/d or very low localisation levators threatened, MRF clear cT3c/d mid-rectum, cN1–N2 (extranodal), EMVI+, limited cT4aN0	Preoperative SCPRT (5×5cGy) or CRT followed by TME, depending on need for regression	If CRT and cCR achieved, 'watch-and-wait' in high-risk patients may be considered
Advanced (Ugly)	cT3 with any MRF involved, any cT4a/b, lateral node+	Preoperative CRT followed by surgery (TME and more extended surgery if needed due to tumour overgrowth), or preoperative SCPRT (5×5 Gy) plus FOLFOX and delay to surgery	Alternatively, 5×5 Gy alone with a delay to surgery in fragile/elderly or in patients with severe comorbidity who cannot tolerate CRT

Other factors besides T and N stages are relevant, such as EMVI, MRF involvement, distance from the anus and sphincters, size of mesorectum and patient characteristics. Patient preferences are also important.

cCR, clinical complete response; CRM, circumferential resection margin; CRT, chemoradiotherapy; CT, computed tomography; EMVI, extramural vascular invasion; ERUS, endoscopic rectal ultrasound; FOLFOX, leucovorin/fluorouracil/oxaliplatin; MRF, mesorectal fascia; MRI, magnetic resonance imaging; SCPRT, short-course preoperative radiotherapy; TEM, transanal endoscopic microsurgery; TME, total mesorectal excision; TNM, tumour, node, metastasis.

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Question (Dr Pragna)

- Any other option in terms of
  - Choice of alternate chemotherapy
  - Non surgical approach (TNT)

Alternate chemotherapy regimes

- **mFOLFOX**

Oxaliplatin 85 mg/m2 IV, day 1, leucovorin 400 mg/m2 IV day 1, 5-FU 400 mg/m2 IV bolus on day 1, followed by 1200 mg/m2/day x 2 days (total 2400 mg/m2 over 46–48 hours) continuous infusion. Repeat every 2 weeks to a total of 6 mo perioperative therapy.

- **CAPEOX**

Oxaliplatin 130 mg/m2 IV day 1. Capecitabine 1000 mg/m2 PO twice daily for 14 days every 3 weeks. Repeat every 3 weeks to a total of 6 months perioperative therapy.

- **FOLFIRINOX**

Oxaliplatin 85 mg/m² IV on day 1, leucovorin 400 mg/m² IV over 2 hours on day 1, irinotecan 180 mg/m² IV over 30–90 minutes on day 1, 5-FU 400 mg/m² IV push day 1, 5-FU 1200 mg/m²/day x 2 days (total 2400 mg/m² over 46 hours) continuous infusion.

Repeat every 2 weeks.

- **Modified FOLFIRINOX9**

Oxaliplatin 85 mg/m² IV on day 1, leucovorin 400 mg/m² IV over 2 hours on day 1, irinotecan 150 mg/m² IV over 30–90 minutes on day 1, 5-FU 1200 mg/m²/day x 2 days (total 2400 mg/m² over 46 hours) continuous infusion. Repeat every 2 weeks.

Dosing Schedules for Concurrent Chemotherapy / RT

- **RT + continuous infusion 5-FU**

5-FU 225 mg/m2 IV over 24 hours daily on days 1–5 or days 1–7 for 5 weeks with RT

- **RT + capecitabine**

Capecitabine 825 mg/m2 PO BID, Monday–Friday, on days of radiation treatment only, throughout the duration of RT (typically 28–30 treatment days)

- **RT + 5-FU/leucovorin**

5-FU 400 mg/m2 IV bolus + leucovorin 20 mg/m2 IV bolus for 4 days during weeks 1 and 5 of RT

ALTERNATE THERAPY

- **dMMR/MSI-H, T3, N any; T1–2, N1–2; T4, N any or Locally unresectable or medically inoperable-**
    - Checkpoint inhibitor immunotherapy for up to 6 months ***Dostarlimab or Nivolumab or Pembrolizumab***
- Re-evaluate disease status every 2–3 months
- If Persistent disease at 6 months - then proceed with CRT (LC or SC)

TNT

January 9, 2024

Organ Preservation and Survival by Clinical Response Grade in Patients With Rectal Cancer Treated With Total Neoadjuvant Therapy- A Secondary Analysis of the OPRA Randomized Clinical Trial

January 9, 2024

Organ Preservation and Survival by Clinical Response Grade in Patients With Rectal Cancer Treated With Total Neoadjuvant Therapy- A Secondary Analysis of the OPRA Randomized Clinical Trial

- Patients randomized to (induction chemotherapy followed by chemoradiation) or (chemoradiation followed by consolidation chemotherapy)
- Tumor response was assessed 8 (±4) weeks after TNT by digital rectal examination and endoscopy and categorized by clinical tumor response grade. A 3-tier grading schema that stratifies clinical tumor response into clinical complete response (CCR), near complete response (NCR), and incomplete clinical response (ICR) was devised to maximize patient eligibility for OP.
- The 3-year probability of OP was 77% (95% CI, 70%-85%) for patients with a CCR and 40% (95% CI, 32%-51%) for patients with an NCR ($P < .001$). Clinical tumor response grade was associated with disease-free survival, local recurrence-free survival, distant metastasis-free survival, and overall survival.
- In this secondary analysis of a randomized clinical trial, most patients with a CCR after TNT achieved OP, with few developing tumor regrowth.

TNT FLB WNW

original reports

Organ Preservation in Patients With Rectal Adenocarcinoma Treated With Total Neoadjuvant Therapy

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CONCLUSION Organ preservation is achievable in half of the patients with rectal cancer treated with total neoadjuvant therapy, without an apparent detriment in survival, compared with historical controls treated with chemoradiotherapy, TME, and postoperative chemotherapy.

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CRT FLB WNT

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Sign in

Curative chemoradiation for low rectal cancer: Primary clinical outcomes from a multicenter phase II trial.

quency grade 2 was seen in four patients. **Conclusions:** The vast majority of patients with low rectal cancer can be cured by modern radiotherapy 62 Gy in 28 fractions with excellent patient-reported outcomes, toxicity, tumor control, and survival. The treatment is feasible in a multicenter setting. We suggest this approach as a standard of care option. Clinical trial information: NCT02438839. Research Sponsor: The Danish Cancer Society.

Question for all

Radiotherapy details

- Short versus long
- Doses
- Technique

Short versus long Course

- ***Short course**:*
- Typically one week to surgery [Swedish, Dutch, MRC, Polish I, TROG], less pCR. Excellent compliance.
- [Stockholm III] - less surgical complications when surgery at 4-6w than at 1w after SC-RT
- [Polish II, Stockholm III] utilized ~6w after short course, but still only had 10-15% pCR. Less surgical complications.
- Cost effective analysis suggests short courses cost half as much for 1 QALY than long courses
- *SC RT for patients who are candidates for LAR upfront, as there is suggestion of LC-RT having better conversion to sphincter sparing surgery per German Rectal Cancer Study above (19→ 39%).*
- SC-RT is likely also an ideal treatment for patients with metastatic disease.

Short versus long Course

Long course:

- Typically 6-8w until surgery, therefore better pCR.
- Do not wait more than 11w [GRECCAR-6], though may wait up to 4 mo without increased post-surgical complications so long as chemo is given as a bridge between conventionally fractionated CCRT and surgery.
- [TIMING trial], the exemplary trial to follow for patients desiring non-operative management. Most non-operative data such as from Brazil does not give adjuvant chemotherapy and ~30% will eventually have LR or DM, which is why TIMING trial is ideal as it mandates chemotherapy after CCRT.

Case Discussion 2

- Forty two year old male, farmer by occupation presented with bleeding per rectum on and off since 4 months and altered bowel habits since 6 months
- No familial history of colorectal cancers.
- No previous surgical history.
- Habits: No history of tobacco chewing, non-smoker non-alcoholic.
- Investigations: CBC normal, Tumor marker: CEA: 16.4 ng/mL
- Colonoscopy- Circumferential growth from 10-15cm from anal verge, Scope couldn't passed beyond.

- **Biopsy -** moderately differentiated adenocarcinoma
- **MRI –**
  - 6.8 * 1.3 cm irregular thickening in mid and upper rectum upto rectosigmoid , 5.5 cm from anal verge.
  - No lymph nodal enlargement.

Diagnosis - Carcinoma middle+upper third rectum (T2/3 N0 M0)

- **Rx received -** (after tumor board discussion)
- Total neoadjuvant therapy (4cycles of oxaliplatin and 7 cycles of Capacitabine 500mgm2 BD completed on 03/09/2024)
- With RT-50gy/25#, by IMRT.

- **MRI (post TNT)-**

Minimally diffusion restricted T2hyperintense circumferential wall thickening of length -2.6cm, thickness-1.6cm in mid rectum
No e/o MRF involvement
No e/o pelvic/Paraaortic lymphadenopathy intermediate response to NACRT

- **CEA**

Pre TNT-16. 40
Post TNT-2. 70

- **Pt. Underwent Surgery within 4 weeks.**

- **Surgery done -**Open low anterior resection with diversion transverse loop colostomy
- **HPE-**
  - No e/o viable cancer cells (complete response-score 0)
  - All margins negative for invasive carcinoma (Proximal-16cm, Distal-2cm, Circumferential-2.9cm)
  - Proximal and distal dougnut- free of tumor
- **Re-presented in TB -** Tumour board plan **-** observation.

Question to all

<u>Some questions should be answered thru first case discussion</u>

- Should we undergo PET CT in this case
- Alternative chemotherapy regime which can be used
- Timing of surgery

Question (Dr Pamela)

Discussion on some new questions

- Role of tumor marker CEA

Prognostic value of changes in serum carcinoembryonic antigen levels for preoperative chemoradiotherapy response in locally advanced rectal cancer

- Patients with preoperative serum CEA levels ≤ 5 ng/mL - good treatment response, with 20.0% of patients achieving pCR.
- Pre- and post-CRT CEA levels difference ≥ 5 ng/mL - associated with a good response.

Diseases. 2021 Mar 17;9(1):21. doi: 10.3390/diseases9010021

Diagnostic and Prognostic Value of CEA and CA19-9 in Colorectal Cancer

Leilani Lakemeyer [1], Silvia Sander [2], Mathias Wittau [1], Doris Henne-Bruns [1], Marko Kornmann [1], Johannes Lemke [1,*,†]

CEA and CA19-9 separately and combined and a multivariate analysis was performed. The 5-year overall survival was significantly shorter in patients with a CEA or CA19-9 level ≥200 compared to patients with an increased, but <200, or normal level (CEA: 69%/44%/7%; CA19-9: 66%/38%/8%). Patients with both tumor markers increased also showed a remarkably shorter 5-year survival rate (CEA+/CA19-9+: 23%). The multivariate analysis emphasizes these results (*p*-value < 0.0001). Patients with both tumor markers elevated had the shortest 5-year recurrence-free survival rate, followed by patients with either CEA or CA19-9 elevated (CEA-/CA19-9-: 79%; CEA+/CA19-9; CEA-/CA19-9+: 65%; CEA+/CA19-9+: 44%). In conclusion, measuring CEA and CA19-9 preoperatively in CRC patients is reasonable and could be useful as a prognostic factor.

CEA

- Change in pre and post treatment – prognostic value ?
- Significance when increases in follow up

Question (Dr Pragna)

Discussion on some new questions

- Is there an option of upfront surgery, rather than neoadjuvant chemoRT in this case

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CLINICAL PRACTICE GUIDELINES

Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

R. Glynne-Jones[1], L. Wyrwicz[2], E. Tiret[3,4], G. Brown[5], C. Rödel[6], A. Cervantes[7] & D. Arnold[8], on behalf of the ESMO Guidelines Committee*

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†Approved by the ESMO Guidelines Committee: August 2002, last update May 2017. This publication supersedes the previously published version—Ann Oncol 2013; 24 (Suppl. 6): vi81–vi88.

Table 6. Recommended choice of treatment options within TNM risk category of primary rectal cancer without distant metastases

Risk group	TN substage	Possible therapeutic options	Further considerations
Very early	cT1 sm1 N0 (on ERUS and MRI)	Local excision (TEM) If pT1 and no adverse features, TEM is sufficient If adverse histopathology (sm ≥ 2, G3, V1, L1), requires radical resection (TME) as standard	Alternatively, in the case of adverse features on pathology, TEM plus salvage (or adjuvant) CRT in perioperative high-risk patients (but unproven benefit—with high risk of local recurrence for pT2)
Early (Good)	cT1-cT2; cT3a/b if middle or high, N0 (or also cN1 if high), MRF clear, no EMVI	Surgery (TME) alone is standard. If unexpected poor prognostic signs on histopathology (CRM+, extranodal/N2), consider postoperative CRT/CT (see postoperative recommendations in Table 7)	For fragile, high-risk patients or those rejecting radical surgery (CRT with evaluation, local excision or if achieving cCR, 'watch-and-wait', organ preservation)
Intermediate	cT3a/b very low, levators clear, MRF clear or cT3a/b in mid- or high rectum, cN1-2 (not extranodal), no EMVI	Surgery (TME) alone is a standard only if good-quality mesorectal resection assured (and local recurrence ≤0.5% or, if not, preoperative SCPRT (5×5 Gy) or CRT followed by TME	If CRT is given and cCR is achieved, 'watch-and-wait' in high-risk patients for surgery may be considered
Bad	cT3c/d or very low localisation levators threatened, MRF clear cT3c/d mid-rectum, cN1–N2 (extranodal), EMVI+, limited cT4aN0	Preoperative SCPRT (5×5cGy) or CRT followed by TME, depending on need for regression	If CRT and cCR achieved, 'watch-and-wait' in high-risk patients may be considered
Advanced (Ugly)	cT3 with any MRF involved, any cT4a/b, lateral node+	Preoperative CRT followed by surgery (TME and more extended surgery if needed due to tumour overgrowth), or preoperative SCPRT (5×5 Gy) plus FOLFOX and delay to surgery	Alternatively, 5×5 Gy alone with a delay to surgery in fragile/elderly or in patients with severe comorbidity who cannot tolerate CRT

Other factors besides T and N stages are relevant, such as EMVI, MRF involvement, distance from the anus and sphincters, size of mesorectum and patient characteristics. Patient preferences are also important.

cCR, clinical complete response; CRM, circumferential resection margin; CRT, chemoradiotherapy; CT, computed tomography; EMVI, extramural vascular invasion; ERUS, endoscopic rectal ultrasound; FOLFOX, leucovorin/fluorouracil/oxaliplatin; MRF, mesorectal fascia; MRI, magnetic resonance imaging; SCPRT, short-course preoperative radiotherapy; TEM, transanal endoscopic microsurgery; TME, total mesorectal excision; TNM, tumour, node, metastasis.

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		y surgery (TME ry if needed due r preoperative OX and delay to	Alternatively, 5×5 Gy alone with a delay to surgery in fragile/elderly or in patients with severe comorbidity who cannot tolerate CRT

from the anus and sphincters, size of mesorectum and patient characteristics. Patient preferences are also important.

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Question to all

Discussion on some new questions

- What are the radiotherapy volumes (CTV)
- Advantage of technique ?

Clinical Practice Guideline

Radiation Therapy for Rectal Cancer: Executive Summary of an ASTRO Clinical Practice Guideline

Jennifer Y. Wo, MD,[a] Christopher J. Anker, MD,[b] Jonathan B. Ashman, MD, PhD,[c] Nishin A. Bhadkamkar, MD,[d] Lisa Bradfield, BA,[e] Daniel T. Chang, MD,[f] Jennifer Dorth, MD,[g] Julio Garcia-Aguilar, MD,[h] David Goff,[i] Dustin Jacqmin, PhD,[j] Patrick Kelly, MD,[k] Neil B. Newman, MD, MS,[l] Jeffrey Olsen, MD,[m] Ann C. Raldow, MD, MPH,[n] Erika Ruiz-Garcia, MD,[o] Karyn B. Stitzenberg, MD,[p] Charles R. Thomas Jr, MD,[q] Q. Jackie Wu, PhD,[r] and Prajnan Das, MD, MS, MPH[s,*]

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What are the appropriate treatment volumes, dose-constraints, and techniques for patients treated with RT?

For patients with cT3-4 and/or cN+ rectal cancers, the task force recommends including the rectum, mesorectal nodes, presacral nodes, internal iliac nodes, and obturator nodes in the clinical target volume (CTV). If the primary tumor invades anterior structures or organs, nodal drainage may extend via the lymphatics of the involved organ.[71] Therefore, for patients with rectal tumors invading the prostate, seminal vesicles, cervix, vagina, and/or bladder, inclusion of the external iliac nodes in addition to the rectum, mesorectal nodes, presacral nodes, internal iliac nodes, and obturator nodes is conditionally recommended. Although lesions that extend to the anal canal can spread to the inguinal and external iliac nodes, limited data supports the inclusion of these lymph node regions in the CTV for patients with rectal cancer involving the anal canal.[71,81] Therefore, for patients with rectal tumors that extend into the anal canal, inclusion of the inguinal and external iliac nodes in addition to the rectum, mesorectal nodes, presacral nodes, internal

Elective Clinical Target Volumes for Conformal Therapy in Anorectal Cancer: An RTOG Consensus Panel Contouring Atlas

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Purpose—To develop a Radiation Therapy Oncology Group (RTOG) atlas of the elective clinical target volume (CTV) definitions to be used for planning pelvic intensity-modulated radiotherapy (IMRT) for anal and rectal cancers.

Methods and Materials—The Gastrointestinal Committee of the RTOG established a task group (the nine physician co-authors) to develop this atlas. They responded to a questionnaire concerning three elective CTVs (CTVA: internal iliac, pre-sacral and peri-rectal nodal regions for both anal and rectal case planning; CTVB: external iliac nodal region for anal case planning and for selected rectal cases; CTVC: inguinal nodal region for anal case planning and for select rectal cases), and to outline these areas on individual computed tomography images. The imaging files were shared via the Advanced Technology Consortium. A program developed by one of the co-authors (IEN) utilized binomial maximum-likelihood estimates to generate a 95% group consensus contour. The computer-estimated consensus contours were then reviewed by the group and modified to provide a final contouring consensus atlas.

Results—The panel achieved consensus CTV definitions to be used as guidelines for the adjuvant therapy of rectal cancer and definitive therapy for anal cancer. The most important difference from

Technique advantage

iliac nodes, and obturator nodes is conditionally recommended.

Modulated RT techniques like intensity modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT) have the potential to reduce treatment-associated side effects to bladder, large bowel and small bowel by reducing the dose to these organs. In the RTOG 0822 phase 2 trial[82] of preoperative chemo-radiation, using IMRT in combination with capecitabine and oxaliplatin did not reduce the rate of gastrointestinal toxicity compared with conventional radiation in a prior trial, RTOG 0247.[83] However, additional studies and a meta-analysis report that IMRT and VMAT result in reduced toxicity versus 3-D conformal radiation therapy.[72-77]

Modern planning techniques like 3-D conformal radiation therapy and IMRT/VMAT produce plans that are more conformal but less robust to daily variations in setup. This is particularly true of IMRT/VMAT because of the creation of concave dose distributions designed precisely to follow the contour of the target and spare critical structures. Recognizing the lack of published data,

Question (Dr Sanyamita)

Discussion on some new questions

- Role of adjuvant chemotherapy
- Indications

ADJUVANT CHEMOTHERAPY

- In colon cancer, adjuvant ChT has an established role for patients with ‘high-risk’ stage II and stage III disease.
- Patients with rectal cancer were specifically excluded from most phase III adjuvant studies because of the potential toxicity and confounding impact of RT or CRT
- After surgery alone for rectal cancer, individual trials and meta-analyses indicate that there is a benefit for adjuvant 5-FU- based ChT in terms of DFS and OS, but the magnitude of benefit is smaller than for colon cancer.
- It is unclear whether the initial clinical (yc) or patho-logical (yp) stage should be used to determine the risk/benefit of adjuvant treatment.

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Table 7. Potential indications for postoperative chemoradiotherapy if preoperative chemoradiotherapy not given

Sufficient and necessary	Insufficient and unnecessary
CRM $\leq$ 1 mm	pT1/pT2
pT4b	pT3
pN2 extracapsular spread close to MRF	CRM $>$ 2 mm
Extranodal deposits (N1c)	pT4a above peritoneal reflection
pN2 if poor mesorectal quality/defects	pN1
	If good quality smooth intact mesorectum
Sufficient	
pN2 low tumours within 4 cm of anal verge (risk of involved LPLN)	
Extensive extramural vascular invasion/ perineural invasion close to MRF	
Borderline sufficient	
pN2 in mid/upper rectum if good mesorectal quality	
CRM 1–2 mm	
Circumferential obstructing tumours	

CRM, circumferential resection margin; LPLN, lateral pelvic lymph node; MRF, mesorectal fascia.

Take home message

Every Panelist to say one liner…..

Thank you