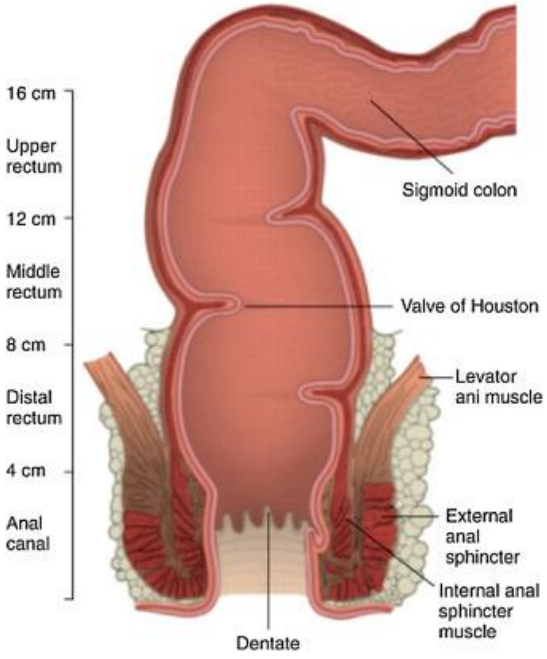
RECTAL CANCER

GENERAL OVERVIEW AND ANATOMICAL DEFINITION

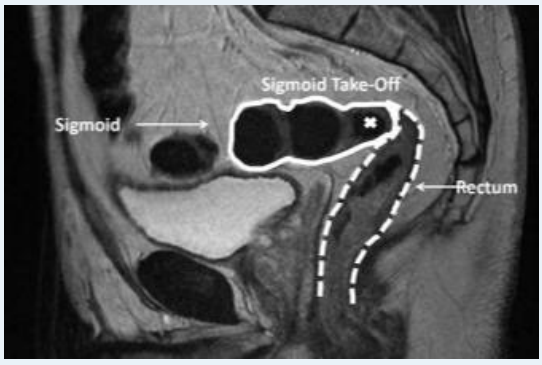
- **Treatment principle.** Management is driven by tumour height, MRI-defined local risk, sphincter/intersphincteric involvement, nodal burden and patient goals, especially organ preservation.
- **Definition of the rectum.** Use the MRI-defined sigmoid take-off as the preferred upper boundary. A fixed distance of ~15 cm from the anal verge is useful clinically but is less reproducible.
- **Classical height.** Upper/proximal ≈10–15 cm, middle ≈5–10 cm and low/distal <5 cm from the anal verge; always report exact height and relation to the peritoneal reflection.
- **Symptoms.** Rectal bleeding, altered bowel habit, tenesmus, anaemia, rectal mass or incidental/asymptomatic presentation.
- **Biology.** Determine MMR/MSI in all newly diagnosed rectal adenocarcinomas; this has hereditary implications and can profoundly change treatment in dMMR/MSI-H locally advanced disease.



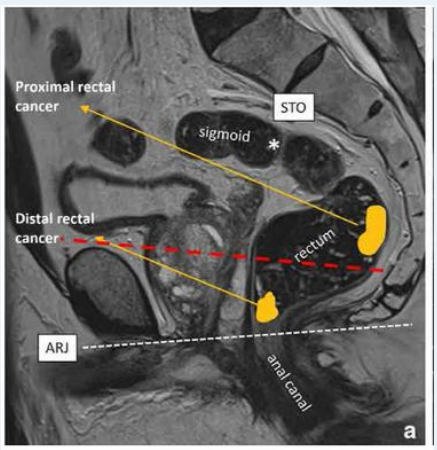
Classical anatomical subdivision.

MRI LANDMARKS FOR UPPER VERSUS LOWER RECTUM

- **Sigmoid take-off (STO).** The point where the sigmoid colon turns anteriorly away from the sacrum is the preferred imaging landmark for the upper border of the rectum.
- **Low/distal tumour assessment.** Report distance from the anal verge, relation to the anorectal junction and sphincter complex, and whether the intersphincteric plane is involved.



Sigmoid take-off on sagittal MRI.



MRI landmarks distinguishing proximal and distal rectal tumours.

RECTAL CANCER

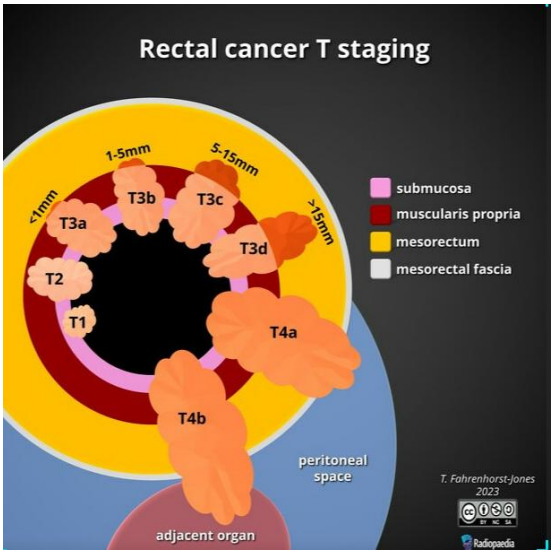
STAGING AND MRI RISK STRATIFICATION

INITIAL WORK-UP

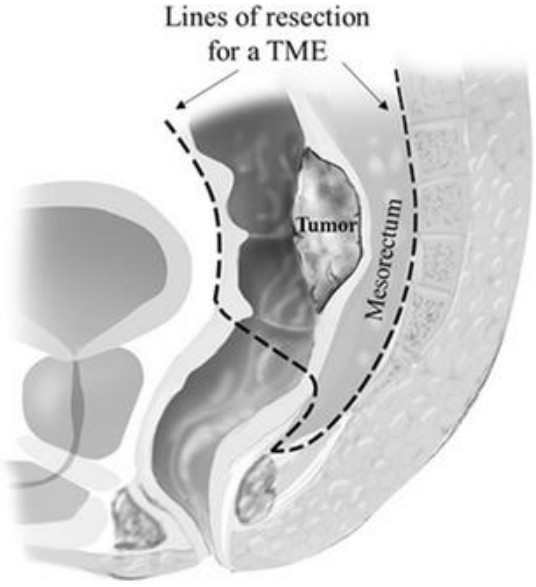
- **Local staging.** High-resolution rectal MRI is mandatory; add digital rectal examination and endoscopy. Endorectal ultrasound is useful mainly for selected early T1/T2 lesions.
- **Systemic staging.** Contrast-enhanced CT thorax/abdomen/pelvis. Obtain baseline CEA and routine laboratory assessment.
- **MRI report should include.** Tumour height, cT stage and extramural depth, cN stage, mesorectal fascia (MRF)/predicted CRM, extramural venous invasion (EMVI), tumour deposits, lateral pelvic nodes, peritoneal reflection and sphincter/intersphincteric involvement.

AJCC 8 — TNM definitions

Primary tumour (T)	Regional lymph nodes (N)	Metastasis (M)
TX: cannot be assessed T0: no primary tumour Tis: carcinoma in situ T1: invades submucosa T2: invades muscularis propria T3: extends through muscularis propria into perirectal tissues T4a: penetrates visceral peritoneum T4b: invades adjacent organs/structures	NX: cannot be assessed N0: no regional LN N1a: 1 positive LN N1b: 2–3 positive LN N1c: tumour deposits without positive regional LN N2a: 4–6 positive LN N2b: ≥7 positive LN	M0: no distant metastasis M1a: one organ/site, no peritoneal metastasis M1b: ≥2 organs/sites, no peritoneal metastasis M1c: peritoneal metastasis ± other sites



MRI T3 subcategories: a <1 mm, b 1–5 mm, c 5–15 mm, d >15 mm extramural extension.



TME plane and mesorectal envelope.

KEY PROGNOSTIC / TREATMENT-SELECTING MRI FEATURES

- **MRF / CRM.** MRF threatened/involved when tumour, malignant node or tumour deposit is close to the mesorectal fascia; this is a major driver for neoadjuvant treatment.
- **EMVI and tumour deposits.** Both identify higher systemic relapse risk and support treatment intensification.
- **Lateral pelvic lymph nodes.** Report suspicious internal iliac/obturator nodes separately; discuss in specialist MDT.

RECTAL CANCER

EARLY AND UPPER-THIRD RECTAL CANCER

GENERAL SURGICAL PRINCIPLES

- **Local excision.** For carefully selected low-risk cT1N0 lesions, transanal local excision (TEM/TAMIS) or endoscopic resection can be curative.
- **Completion TME.** Recommend when pT1 adverse features are present (e.g. deeper submucosal invasion, poor differentiation, lymphovascular invasion, tumour budding or involved/uncertain margin).
- **Radical surgery.** TME is standard for mid/low rectal cancer; partial mesorectal excision (PME) is appropriate for selected upper-third tumours. Sphincter preservation requires an oncologically safe distal/intersphincteric plane.
- **Pathology.** Aim to assess ≥12 regional lymph nodes and document CRM, distal margin and quality of the mesorectal specimen.

UPPER-THIRD / PROXIMAL RECTAL CANCER — PRACTICAL UZA APPROACH

- **Low-risk cT1–T3, MRF clear, no EMVI/high-risk nodes.** Primary surgery is usually preferred; radiotherapy can often be omitted.
- **Selected cT2N+ or cT3 disease suitable for sphincter-sparing surgery.** Neoadjuvant FOLFOX/CAPOX with selective chemoradiotherapy is a validated option in PROSPECT-like patients; use only when MRI risk is appropriate and the MDT is comfortable omitting routine pelvic RT.
- **High-risk upper-third disease / cT4.** Use a risk-adapted neoadjuvant strategy (chemotherapy or TNT) according to MRF, nodal burden, EMVI and resectability.

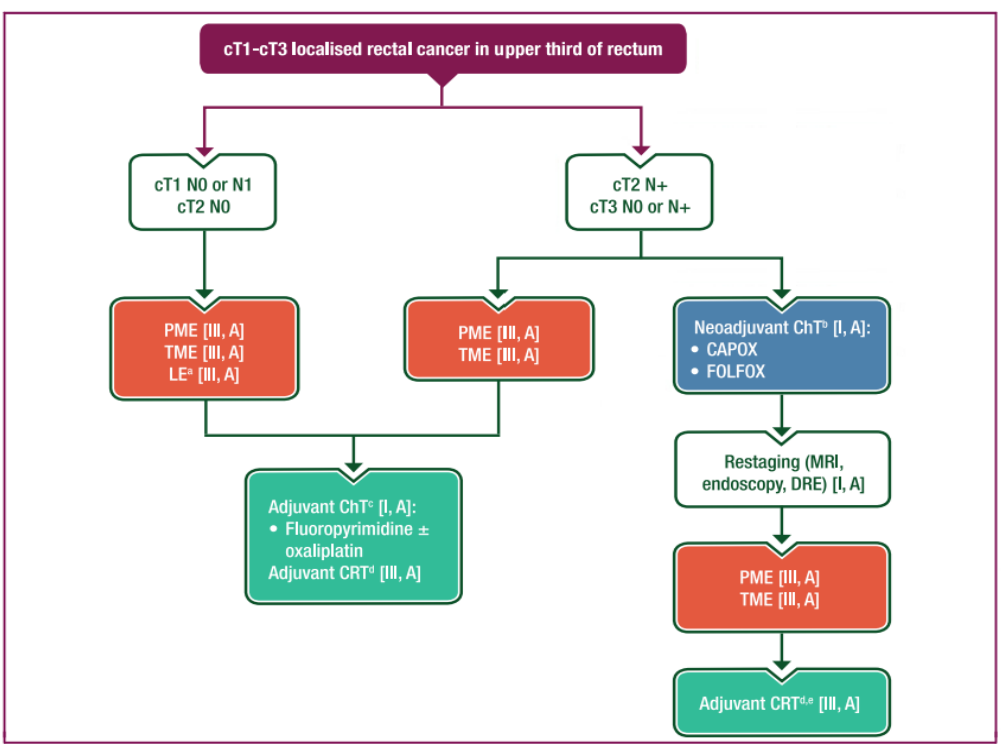


Figure 1. Management of cT1-cT3 localised rectal cancer located in the upper third of the rectum.
Purple: algorithm title; orange: surgery; blue: systemic anticancer therapy or their combination; turquoise: nonsystemic anticancer therapies or a combination of treatment modalities; white: other aspects of management and nontreatment aspects.
c, clinical; CAPOX, capecitabine—oxaliplatin; ChT, chemotherapy; CRM, circumferential resection margin; CRT, chemoradiotherapy; DRE, digital rectal examination; FOLFOX, leucovorin—5-fluorouracil—oxaliplatin; LE, local excision; MRF, mesorectal fascia; MRI, magnetic resonance imaging; N+, node positive; p, pathological; PME, partial mesorectal excision; RT, radiotherapy; TME, total mesorectal excision.
[a]For low-risk tumours (pT1 without unfavourable pathological features).
[b]Salvage RT is recommended in case of intolerance to, or progression on, neoadjuvant ChT [I, A].
[c]Only following PME or TME alone, according to clinical risk assessment.
[d]Only in case of CRM positivity, pT4b, pN2 with extracapsular spread close to the MRF or poor-quality TME in patients who did not receive preoperative RT.
[e]Adjuvant ChT may be considered, but its clinical value is not proven [V, C].

ESMO 2025 algorithm for cT1–cT3 localised upper-third rectal cancer .

RECTAL CANCER

MIDDLE / LOWER RECTUM AND LOCALLY ADVANCED DISEASE

INTERMEDIATE-RISK MIDDLE / LOWER RECTAL CANCER

- **cT2N+ / cT3 N0–N1, MRF clear.** Options include neoadjuvant chemo, long-course chemoradiotherapy or selected primary TME depending on tumour height, organ-preservation goals and MRI risk.
- **When organ preservation is a major goal.** Long-course chemorRT followed by consolidation chemo is attractive because it maximises clinical complete response and TME-free survival in OPRA.
- **Distal tumours.** Assess sphincter/intersphincteric involvement carefully; organ-preservation strategies should be discussed early, before committing to abdominoperineal resection.

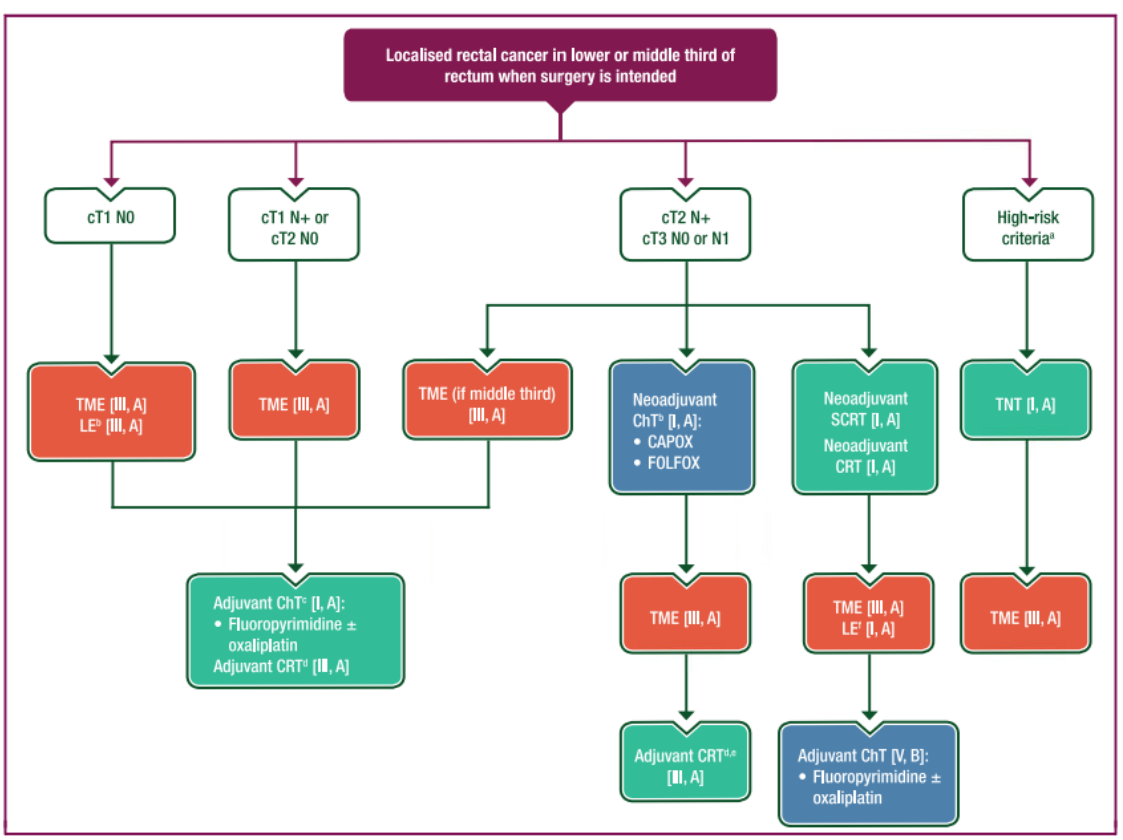


Figure 3. Management of localised rectal cancer located in the lower or middle third of the rectum when surgery is intended.
Purple: algorithm title; orange: surgery; blue: systemic anticancer therapy or their combination; turquoise: nonsystemic anticancer therapies or a combination of treatment modalities; white: other aspects of management and nontreatment aspects.
c, clinical; CAPOX, capecitabine—oxaliplatin; ChT, chemotherapy; CRM, circumferential resection margin; CRT, chemoradiotherapy; EMVI+, extramural venous invasion; FOLFOX, leucovorin—5-fluorouracil—oxaliplatin; LE, local excision; LN+, involved lymph nodes; MRF, mesorectal fascia; mrMRF+, involved or threatened mesorectal fascia; N+, node positive; p, pathological; RT, radiotherapy; SCRT, short-course radiotherapy; TME, total mesorectal excision; TNT, total neoadjuvant therapy.
[a]cT4, cN2, mrMRF+, EMVI+, lateral LN+.
[b]Salvage RT is recommended in case of intolerance to, or progression on, neoadjuvant ChT [I, A].
[c]Following TME alone, according to clinical risk assessment.
[d]Only in case of CRM positivity, pT4b, pN2 with extracapsular spread close to the MRF or poor-quality TME in patients who did not receive preoperative RT.
[e]Adjuvant ChT may be considered, but its clinical value is not proven [V, C].
[f]Patients with baseline cT2 or cT3a N0 tumours.

ESMO 2025 algorithm for localised middle/lower-third rectal cancer when surgery is intended.

HIGH-RISK FEATURES THAT FAVOUR TNT

- cT4 disease, cN2, involved/threatened MRF, EMVI-positive disease, clinically relevant tumour deposits and/or suspicious lateral pelvic nodes.
- For fit patients, TNT is preferred over a chemotherapy-after-surgery strategy because systemic treatment is completed preoperatively and response can guide organ preservation.

RECTAL CANCER

TOTAL NEOADJUVANT THERAPY — KEY EVIDENCE

PRODIGE 23 — LONG-COURSE CRT-BASED TNT

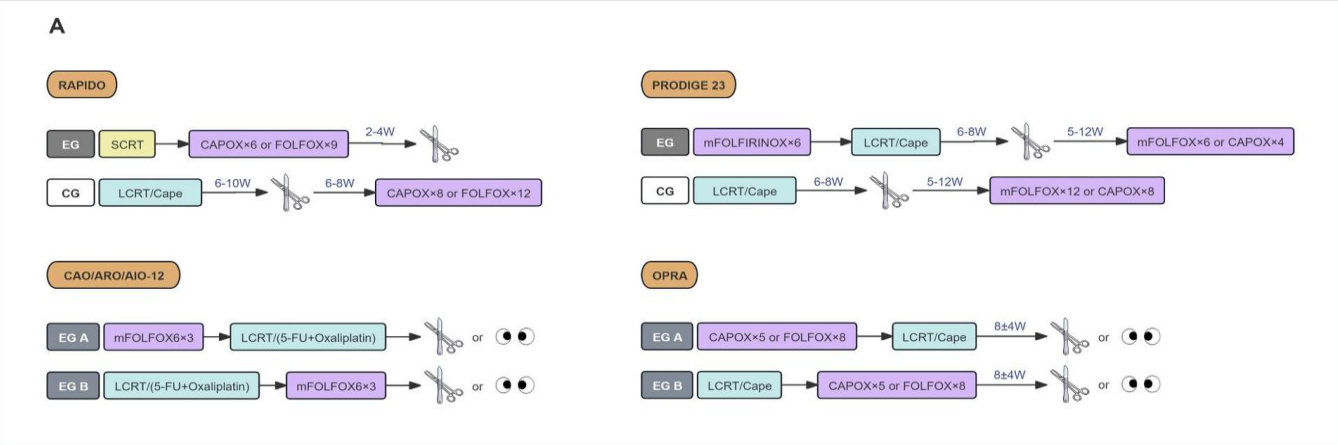
- **Regimen.** 6 cycles mFOLFIRINOX → long-course chemoradiotherapy → TME → shorter adjuvant chemotherapy.
- **Long-term outcome.** At ~7 years, DFS 67.6% vs 62.5%, MFS 79.2% vs 72.3% and OS 81.9% vs 76.1% versus standard chemoradiotherapy followed by surgery/adjuvant chemotherapy.
- **UZA interpretation.** Strong option for fit cT3/4 patients, particularly when systemic relapse risk is high.

RAPIDO — SHORT-COURSE RT-BASED TNT

- **Regimen.** 5×5 Gy → CAPOX/FOLFOX → TME.
- **Benefit.** Reduced disease-related treatment failure and distant metastases in high-risk MRI-defined disease.
- **Caveat.** At 5 years, locoregional recurrence after R0/R1 resection was higher with the RAPIDO experimental strategy (10% vs 6%). This local-control signal should be considered when choosing between TNT schedules.

TNTCRT PHASE III — JCO 2026

- **Population.** Stage II/III high-risk LARC: cT4, cN2, MRF involvement, or cT3c-d with EMVI.
- **Result.** Long-course RT with uninterrupted doublet chemotherapy improved 3-year DFS (74.8% vs 66.0%), metastasis-free survival and pCR (26.4% vs 9.8%) versus conventional chemoradiotherapy.
- **Toxicity.** More grade ≥3 toxicity during the neoadjuvant phase, but overall severe toxicity and major postoperative complications were similar.



TNT schedules in key clinical trials (Zhou et al., Crit Rev Oncol Hematol. 2026; original figure retained).

RECTAL CANCER

ORGAN PRESERVATION AND WATCH-AND-WAIT

WATCH-AND-WAIT AFTER CLINICAL COMPLETE RESPONSE

- **Current position.** Watch-and-wait is now an accepted option for carefully selected patients with a clinical complete response in an experienced centre with structured surveillance.
- **Response assessment.** Combine digital rectal examination, endoscopy and high-quality MRI. A near-complete response may mature with additional observation; avoid declaring failure too early when continued regression is documented.
- **OPRA.** Five-year DFS was similar between induction and consolidation TNT, but TME-free survival was higher when chemoradiotherapy was followed by consolidation chemotherapy (54% vs 39%). Most local regrowth occurred in the first 2 years.
- **Salvage.** TME after local regrowth can provide outcomes comparable to TME performed immediately after incomplete response when regrowth is detected during close surveillance.

EARLY RECTAL CANCER — CONTACT X-RAY BRACHYTHERAPY (OPERA)

- **Population.** Selected operable cT2–cT3b low/mid rectal adenocarcinoma, tumour <5 cm, cN0 or small cN1.
- **Five-year data.** Organ preservation remained higher with contact X-ray brachytherapy boost than external-beam boost (79% vs 56%); benefit was greatest for tumours <3 cm.
- **Practical note.** Requires dedicated expertise/equipment and is not a universal UZA standard; consider referral when organ preservation is a major goal.

dMMR / MSI-H LOCALLY ADVANCED RECTAL CANCER

- **Evidence.** Single-agent dostarlimab produced an exceptional clinical complete response signal in the original phase II study; larger confirmatory AZUR-1 is ongoing.
- **UZA practical approach.** Identify dMMR/MSI-H at diagnosis and discuss upfront PD-1 blockade in the rectal MDT/clinical-trial context before standard TNT, particularly when organ preservation is a priority.
- **Belgian access — August 2026.** Dostarlimab is not EMA-authorised for localised rectal cancer and is not reimbursed in Belgium for this indication; access would require a clinical trial or specific non-standard access pathway.

RECTAL CANCER

cT4 UPPER-THIRD DISEASE AND PRACTICAL ALGORITHM

cT4 UPPER-THIRD RECTAL CANCER

- **Goal.** Achieve an R0 resection while controlling early systemic relapse risk.
- **Neoadjuvant options.** FOLFOX/CAPOX-based chemotherapy, or TNT including pelvic RT when MRF is threatened/involved, downsizing is needed, or local control is a major concern.
- **Restaging.** Repeat MRI and endoscopic/DRE assessment before surgery; surgical planning should be revisited in the multidisciplinary rectal cancer team.

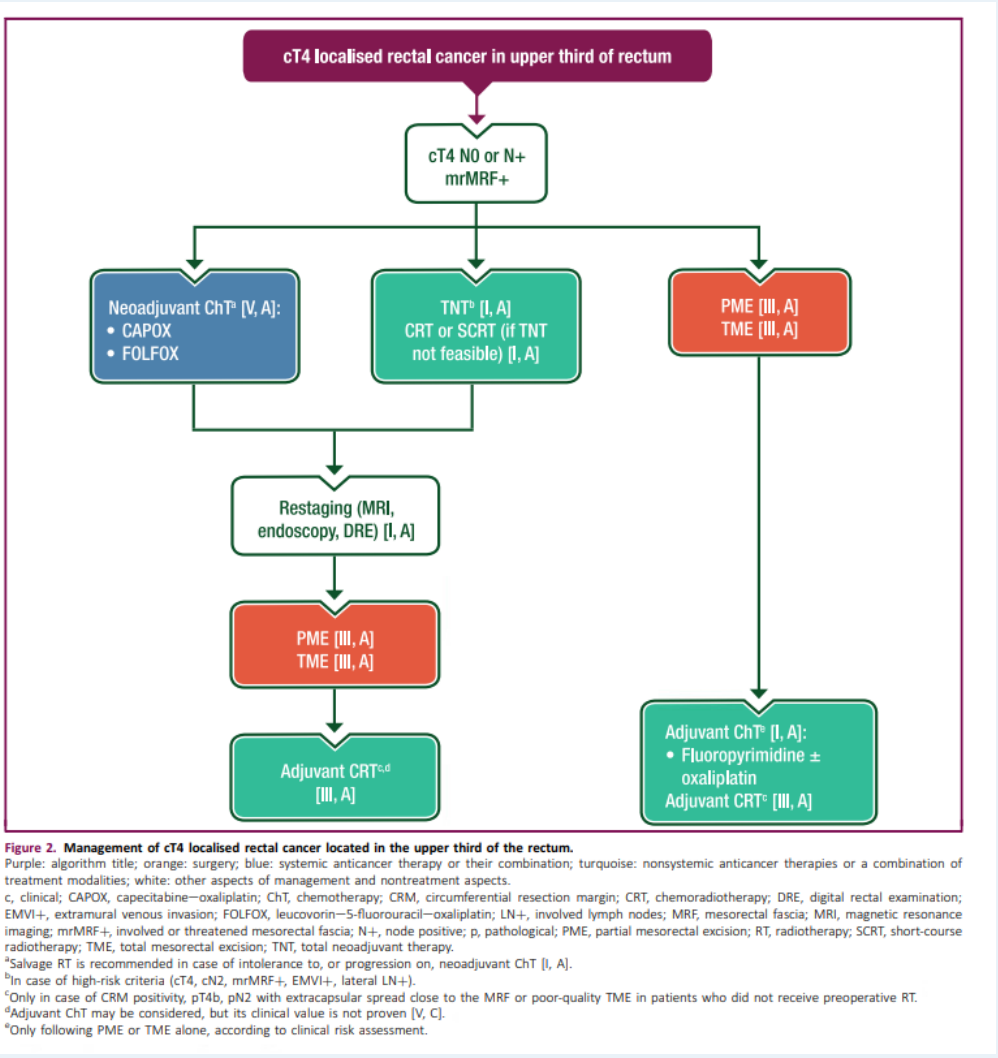


Figure 2. Management of cT4 localised rectal cancer located in the upper third of the rectum.
Purple: algorithm title; orange: surgery; blue: systemic anticancer therapy or their combination; turquoise: nonsystemic anticancer therapies or a combination of treatment modalities; white: other aspects of management and nontreatment aspects.
c, clinical; CAPOX, capecitabine—oxaliplatin; ChT, chemotherapy; CRM, circumferential resection margin; CRT, chemoradiotherapy; DRE, digital rectal examination; EMVI+, extramural venous invasion; FOLFOX, leucovorin—5-fluorouracil—oxaliplatin; LN+, involved lymph nodes; MRF, mesorectal fascia; MRI, magnetic resonance imaging; mrMRF+, involved or threatened mesorectal fascia; N+, node positive; p, pathological; PME, partial mesorectal excision; RT, radiotherapy; SCRT, short-course radiotherapy; TME, total mesorectal excision; TNT, total neoadjuvant therapy.
[a]Salvage RT is recommended in case of intolerance to, or progression on, neoadjuvant ChT [I, A].
[b]In case of high-risk criteria (cT4, cN2, mrMRF+, EMVI+, lateral LN+).
[c]Only in case of CRM positivity, pT4b, pN2 with extracapsular spread close to the MRF or poor-quality TME in patients who did not receive preoperative RT.
[d]Adjuvant ChT may be considered, but its clinical value is not proven [V, C].
[e]Only following PME or TME alone, according to clinical risk assessment.

ESMO 2025 algorithm for cT4 localised upper-third rectal cancer.

UZA SUMMARY — WHICH PATIENT NEEDS WHAT?

- **Very early low-risk cT1.** Local excision/endoscopic approach.
- **Upper-third low-risk.** Primary surgery; avoid routine RT.
- **PROSPECT-like intermediate risk.** Neoadjuvant FOLFOX/CAPOX with selective RT is reasonable.
- **Mid/low intermediate risk + organ-preservation goal.** Prefer long-course CRT-based strategy, often with consolidation chemotherapy.
- **MRI high-risk (T4/N2/MRF+/EMVI+/lateral nodes).** TNT.
- **dMMR/MSI-H.** Discuss upfront immunotherapy strategy before conventional TNT; reimbursement/access must be addressed.

RECTAL CANCER

WHAT'S NEW? — 2024–2026

PRACTICE-CHANGING / PRACTICE-INFORMING UPDATES

- **ESMO 2025 guideline.** Formalises a more risk-adapted approach by tumour height and MRI features: less routine RT for upper-third/low-risk disease and greater use of TNT/organ preservation in selected mid-low/high-risk tumours.
- **PRODIGE 23 long-term update (Ann Oncol. 2024).** Demonstrates a significant long-term overall-survival advantage for mFOLFIRINOX-based TNT, strengthening this regimen as a preferred option in fit LARC patients.
- **OPRA long-term update (JCO. 2024).** Confirms durable organ preservation in approximately half of patients and supports CRT followed by consolidation chemotherapy when watch-and-wait is a major treatment goal.
- **OPERA 5-year update (Ann Oncol. 2025).** Confirms sustained organ-preservation benefit of contact X-ray brachytherapy boost in selected early low/mid rectal tumours.
- **TNTCRT phase III (JCO. 2026).** Long-course RT plus uninterrupted doublet chemotherapy improved DFS, MFS and pCR in MRI high-risk LARC.
- **dMMR/MSI-H rectal cancer.** The dostarlimab signal remains paradigm-shifting, but the strategy is still off-label in Europe for localised rectal cancer; multicentre confirmatory AZUR-1 is ongoing.

IMPORTANT CAVEATS

- **RAPIDO.** Excellent systemic-control data, but the 5-year locoregional recurrence signal argues against assuming that all TNT schedules are interchangeable.
- **Watch-and-wait.** Requires experienced multidisciplinary response assessment and intensive surveillance; the highest regrowth risk is during the first 2 years.
- **Avoid overtreatment.** Not every stage II/III tumour needs pelvic RT or full TNT; MRI-defined risk, tumour height and organ-preservation goals should drive treatment intensity.

RECTAL CANCER

SELECTED REFERENCES

1. Hofheinz RD, et al. Localised rectal cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol. 2025;36(9):1007-1024.
2. Schrag D, et al. Preoperative treatment of locally advanced rectal cancer (PROSPECT). N Engl J Med. 2023;389(4):322-334.
3. Conroy T, et al. Total neoadjuvant therapy with mFOLFIRINOX versus preoperative chemoradiotherapy in locally advanced rectal cancer: long-term PRODIGE 23 results. Ann Oncol. 2024;35(10):873-881.
4. Bahadoer RR, et al. Short-course radiotherapy followed by chemotherapy before TME versus preoperative chemoradiotherapy in locally advanced rectal cancer (RAPIDO). Lancet Oncol. 2021;22(1):29-42.
5. Dijkstra EA, et al. Locoregional failure during and after short-course radiotherapy followed by chemotherapy and surgery: 5-year RAPIDO follow-up. Ann Surg. 2023;278(4):e766-e772.
6. Garcia-Aguilar J, et al. Organ preservation in patients with rectal adenocarcinoma treated with total neoadjuvant therapy (OPRA). J Clin Oncol. 2022;40(23):2546-2556.
7. Verheij FS, et al. Long-term results of organ preservation in the randomized phase II OPRA trial. J Clin Oncol. 2024;42(5):500-506.
8. Gerard JP, et al. Contact X-ray brachytherapy boost for organ preservation in early cT2-cT3 rectal adenocarcinoma (OPERA). Lancet Gastroenterol Hepatol. 2023;8(4):356-367.
9. Baron D, et al. Five-year results of the OPERA trial. Ann Oncol. 2025;36(2):208-215.
10. Cercek A, et al. PD-1 blockade in mismatch repair-deficient, locally advanced rectal cancer. N Engl J Med. 2022;386(25):2363-2376.
11. Cercek A, et al. AZUR-1: dostarlimab monotherapy in untreated stage II/III dMMR/MSI-H locally advanced rectal cancer. Clin Colorectal Cancer. 2025;24(2):325-330.
12. Wang X, et al. Total neoadjuvant therapy with long-course radiotherapy versus chemoradiotherapy in high-risk locally advanced rectal cancer (TNTCRT). J Clin Oncol. 2026. doi:10.1200/JCO-25-03110.
13. Scott AJ, et al. Management of locally advanced rectal cancer: ASCO Guideline. J Clin Oncol. 2024;42(28):3355-3375.
14. Current Belgian reimbursement text for dostarlimab (Jemperli). BCFI/RIZIV; checked 18 August 2026.