Guideline Resource Unit
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Early-Stage Rectal Cancer

Effective Date: January 2025

Background

A patient may be predisposed to develop colorectal cancer by a hereditary condition (e.g.: hereditary non-polyposis colon cancer, familial adenomatous polyposis) or a personal history of either inflammatory bowel disease (e.g.: Crohn's disease, ulcerative colitis) or adenomatous polyps. Over 60 percent of colorectal cancers arise without a clearly identifiable predisposing factor, however.

After a diagnosis of colorectal cancer, prognosis depends upon the stage at diagnosis; that is, prognosis is better with less penetration of the tumor into the bowel wall, fewer involved regional lymph nodes, and no evidence of metastatic disease.

Because the prognosis is better when colorectal cancer is identified at an earlier stage, because of the relatively high incidence of colorectal cancer, and because of the simplicity and accuracy of screening tests, screening for colorectal cancer represents an important component of routine care for all adults aged fifty years or older, or in the case of patients with a family history of colorectal cancer, at age 40 or 10 years before the youngest affected family member, whichever comes first. This is especially important in patients with first-degree relatives with colorectal cancer.

This guideline was developed to outline the management recommendations for patients with rectal cancer (adenocarcinoma) amenable to resection with curative intent.

Guideline Questions

- What are the recommendations for the diagnostic workup and staging of adult patients with rectal cancer amenable to resection with curative intent?
- What are the treatment recommendations for adult patients with rectal cancer amenable to resection with curative intent?
- What is the optimal timing of surgery following neoadjuvant treatment for rectal cancer?

Search Strategy

This guideline was developed to promote evidence-based practice in Alberta. It was compiled from the results of randomized controlled trials and systematic reviews, derived from an English language and relevant term search of PubMed and MEDLINE from 1990 forward. It takes into consideration related information presented at local, national, and international meetings as well as the Alberta Provincial Gastrointestinal Tumour Team's interpretation of the data.

Target Population

The recommendations outlined in this guideline apply to adults (18+ years) with early stage rectal cancer. Different principles may apply to pediatric patients.

Recommendations and Discussion

Diagnostic Work-up

- In addition to a digital rectal examination (DRE), biopsy via endoscopy, and CT (chest, abdomen, pelvis), magnetic resonance imaging (MRI) of the pelvis is strongly recommended[1] to provide additional information about the extent of the disease (e.g. depth of penetration, lymph node involvement, fixation to adjacent structures).
- Pathological assessment of mismatch repair status (currently performed reflexively in Alberta).
- Transrectal endoscopic ultrasound can provide complementary information to MRI, especially when there is uncertainty between T1 and T2 tumors, T2 versus early T3 tumours, or if a lymph node assessment or guided biopsy is required. It can also be used for patients with contraindications to MRI.
- For patients with locally advanced disease who undergo neoadjuvant therapy, restaging CT (chest, abdomen, pelvis) and/or MRI should be strongly considered, as it can potentially aid in identifying patients who have had a complete clinical response and may be candidates for watchful waiting, and may also identify the rare patient who progresses or develops metastatic disease while on neoadjuvant therapy.

Stage Information

- Clinical staging should be performed according to the AJCC TNM – 8th Edition (Appendix A).

Goals of Therapy

The goals of therapy are to render the patient free of disease, to delay or prevent recurrence, and to preserve anal sphincter, urinary, and sexual function.

Recommendations

- A multidisciplinary team is required to define and provide the optimal care for a patient with rectal cancer. It should generally be composed of surgeons, radiologists, both radiation and medical oncologists, and ideally pathologists.
- All patients with rectal cancer should consider treatment on a clinical trial, if available.

- To precisely dissect the rectum and para-rectal lymph nodes within the mesorectal envelope and to obtain an optimal circumferential radial margin (CRM), surgery should *only* be performed by a surgeon experienced with the total mesorectal excision technique (TME).[2,3]
- If sufficient rectum distal to the cancer permits a colorectal or coloanal anastomosis, perform a radical *en bloc* excision of the rectum by low anterior resection. Otherwise, perform an APR.

Table 2. Recommendations for Treatment of Patients with Rectal Cancer Amenable to Resection.

<table>
<tr><th>Stage</th><th>Recommendations</th></tr>
<tr><td>Stage 0</td><td>• Perform local or transanal excision.[4]
• No adjuvant systemic therapy is indicated.</td></tr>
<tr><td>Stage I</td><td>• If sufficient rectum distal to the cancer permits a colorectal or coloanal anastomosis, and the patient has good continence, perform a radical en bloc excision of the rectum by low anterior resection. Otherwise, perform an abdominoperineal resection (APR) Particularly in patients who would require APR, consideration could be made to total neoadjuvant therapy to try to achieve a complete clinical response and allow for watchful waiting – all of these patient should be reviewed at a multidisciplinary tumor group, and must understand the risk of recurrence and the critical importance of close surveillance if this strategy is employed.
• In a carefully selected patient with low-risk T_1 disease who accepts an increased risk of tumor recurrence, a prolonged period of post-operative surveillance, and a decreased success after salvage surgery, consider transanal excision.[2,5,6] A T_1 rectal cancer is considered “low-risk” if the tumors is well or moderately well differentiated, and has no evidence of lymphovascular invasion, perineural invasion, or high grade tumor budding. Depth of invasion into the submucosa is not possible for pathologists to report accurately.
• No adjuvant systemic therapy is indicated.</td></tr>
<tr><td>Stage II / III</td><td>Neoadjuvant therapy is the preferred approach: This is a rapidly evolving field. See schema[Link]

<table>
<tr><th>Recommendation</th><th>Strength of Recommendation</th><th>Quality of Evidence</th></tr>
<tr><td>For patients with stage II-III rectal cancer, neoadjuvant RT is recommended (short course or long course chemoradiation) due to similar efficacy and patient reported quality of life (QoL) outcomes.</td><td>Strong</td><td>High</td></tr>
<tr><td>For patients with stage II rectal cancer at lower risk of recurrence, omission of RT is conditionally recommended after MDT discussion. These include: cT3a/b = 1-3 mm extramural tumor spread N0 tumor >10 cm from anal verge (as per surgeon) and Crm ≥2mm and no EMVI.</td><td>Conditional</td><td>Moderate</td></tr>
<tr><td>For patients with cT2N1, cT3N0, cT3N1 rectal cancer, MRF clear, candidate for sphincter sparing, oxaliplatin based chemotherapy for 3 months followed by restaging, and omission of RT if the tumor responds (≥20%) can be considered.*</td><td>Conditional</td><td>High</td></tr>
</table>
*Note: The CONVERT trial included patients with cT2N+ or cT3-T4aNany tumors as well as patients with tumors within 5cm from the anal verge. The PROSPECT trial did not include T4a or tumors within 5 cm of the anal verge.[7,8] For patients with tumors within 5 cm of the anal verge and where downstaging is required, pre-operative treatment with</td></tr>
</table>

Stage	Recommendations
	radiation +/- preoperative chemotherapy will be the preferred option. Patients had adjuvant chemotherapy after surgery: PROSPECT – 8 cycles of adjuvant FOLFOX were suggested CONVERT – adjuvant CAPOX 4 cycles (6 months total perioperatively)

- **Long course chemoradiation**[7, 9,10]**:** long-course pre-operative radiotherapy (50 Gy in 25 fractions or 50.4 Gy in 28 fractions) with either protracted venous infusion 5-Fluorouracil (225 mg/m^2 per day by ambulatory infusion pump during the entire period of radiation therapy[11]) or Capecitabine (825 mg/m^2 po BID).[12]
- Surgery should be performed 6-11 weeks after having completed long course radiation.[13]
- Long-course chemoradiation may be more appropriate for low rectal cancers compared to short-course RT. Pre-operative CRT is associated with a lower rate of grade 3/4 acute toxicities, long-term toxicities, and local recurrence, but no difference in five-year overall survival when compared to post-operative CRT.[9]
- **Short course radiation**: Patients with rectal cancer amenable to surgical resection can be offered short-course pre-operative RT (25 Gy in five fractions).[13-15] Surgery should be performed within one week or delayed until 4-8 weeks after the end of RT.
- Short course RT may be preferred for elderly patients[16] [Level II Evidence]. Elderly patients with a good performance status can be considered for the other pre-operative treatment options mentioned here. Multidisciplinary discussion is recommended.
- **Total neoadjuvant therapy** (TNT)[17,18] refers to the use of multiagent chemotherapy and RT prior to surgery. In a systematic review and meta-analysis of seven studies, TNT was associated with a higher rate of pathological complete response (pCR) and improved disease-free survival compared to neoadjuvant long-course CRT and adjuvant chemotherapy.[19] Among patients with a higher risk of locoregional recurrence, TNT is strongly recommended after multidisciplinary discussion.

- Eligibility criteria used in pivotal trials of total neoadjuvant therapy :[20]

RAPIDO	cT4 cN2 disease (4 or more nodes positive) Distance between tumor and mesorectal fascia on MRI <=1 mm Lateral lymph node >= 1 cm (internal iliac, external iliac, obturator or common iliac) Extramural vascular invasion
STELLAR*/PRODIGE	cT3-4 (STELLAR/PRODIGE) and/or N+, distal or middle tumors (STELLAR)

- Radiation may be short course (RAPIDO, STELLAR) or long course chemoradiation.

Recommendations for patients with rectal cancer undergoing neoadjuvant therapy	Strength of Recommendation	Quality of Evidence
For patients with tumor factors associated with increased risk of local recurrence, long course chemoradiation is preferred over short course[21]. Risk factors include cT3 tumors (< 5 cm from	Conditional	Moderate

Stage	Recommendations		
	anal verge), mrCRM < 2 mm, cT4, presence of mrEMVI, lateral pelvic nodes The choice of long course chemoRT or short course RT is determined by patient and clinical factors. **Neoadjuvant therapy is the preferred approach:** This is a rapidly evolving field. See schema**[Link]**		
	Multiagent chemotherapy is recommended (for suitable patients) • **before or after long course ChemoRT or** • **after short course RT** Delivery of chemotherapy prior to chemoRT is recommended for patients receiving FOLFIRINOX or in settings where initiation of radiation may be delayed[21].	Strong	Strong
	For patients receiving neoadjuvant chemotherapy as component of TNT, up to 16 weeks of FOLFOX or CAPOX is recommended).* [20,22,23]	Strong	Strong
	6 cycles of FOLFIRINOX can be considered for highly selected patients prior to long course chemoRT(PRODIGE)[24]^	Conditional	Strong

***The STELLAR trial used 4 cycles of CAPOX after short course RT and 2 cycles of CAPOX AFTER surgery. In RAPIDO, 9 cycles of FOLFOX were given after short course RT.

^In highly selected patients, **FOLFIRINOX x 3 months** followed **by long course chemoRT** was utilized as total neoadjuvant therapy in PRODIGE 23. After surgery, **3 months adjuvant chemotherapy** was recommended regardless of pathological stage (capecitabine or FOLFOX). This strategy resulted in an improvement in overall survival compared to standard chemoradiation (7 year OS 76.1% with chemoRT vs 81.9% with FOLFIRINOX and CRT, p 0.033 restricted mean survival time).[24] FOLFIRINOX is associated with increased toxicity compared to FOLFOX and there is an ongoing trial evaluating the two neoadjuvant chemotherapy regimens.

- **Adjuvant therapy after neoadjuvant** treatment: adjuvant chemotherapy options are extrapolated from colon cancer based on the final pathology, see the Clinical Practice Guideline for Early-Stage Colon Cancer.
    - After short course RT: 6 months of adjuvant chemotherapy is recommended
    - After long course CRT: 4 months of adjuvant chemotherapy is recommended
    - Adjuvant chemotherapy may be considered for patients who received total neoadjuvant therapy

Adjuvant therapy for patients who have upfront surgery

- If a patient with rectal cancer undergoes a low anterior resection or an abdominoperineal resection without pre-operative radiotherapy, offer two months of adjuvant chemotherapy (as for colon cancer), then radiotherapy (4,500 to 5,400 cGy in twenty-five to thirty fractions) with either concurrent protracted venous infusion 5-Fluorouracil (225 mg/m^2 per day by ambulatory infusion pump)[9] or Capecitabine (825 mg/m^2 po BID)[12] and then two additional months of adjuvant chemotherapy (as for colon cancer).[25-27] Radiation may be omitted after multidisciplinary discussion.

<table>
<tr><th>Stage</th><th>Recommendations</th></tr>
<tr><td></td><td>• As long as resection of a metachronous polyp, second colorectal cancer, or metastasis to liver or lung is appropriate, surveillance is recommended (see Clinical Practice Guideline for Colorectal Cancer Surveillance).</td></tr>
<tr><td>Stage II-III patients who decline surgery</td><td>• Non-operative management is an area of active research and has never been compared to the standard options listed above.
• For patients who decline surgery or have a contraindication to surgery and are willing to undergo intense post-treatment surveillance, curative-intent non-operative management (NOM) can be considered after multidisciplinary discussion.
• Whenever possible, NOM with patient enrollment in a clinical trial is preferred.
• The most widely accepted NOM would follow the OPRA protocol[28] with concurrent long-course CRT with 50-56 Gy followed by FOLFOX or CAPOX. NOM is not guaranteed; approximately one-quarter of patients require surgery due to an incomplete treatment response following repeat assessment 4-12 weeks after NOM.
• The optimal surveillance strategy has not been determined. It is time and resource intense. The importance of adhering to the surveillance investigations should be emphasized to patients who desire a NOM approach.
Surveillance in patients undergoing non-operative management following complete clinical response to neoadjuvant therapy (OPRA)
<table>
<tr><th></th><th colspan="14">Months Post-Treatment</th></tr>
<tr><th>Follow-up</th><th>4</th><th>6</th><th>8</th><th>12</th><th>16</th><th>18</th><th>20</th><th>24</th><th>30</th><th>36</th><th>42</th><th>48</th><th>54</th><th>60</th></tr>
<tr><td>MRI</td><td></td><td>x</td><td></td><td>x</td><td></td><td>x</td><td></td><td>x</td><td></td><td>x</td><td></td><td>x</td><td></td><td>x</td></tr>
<tr><td>CT (CAP)</td><td></td><td></td><td></td><td>x</td><td></td><td></td><td></td><td>x</td><td></td><td>x</td><td></td><td>x</td><td></td><td>x</td></tr>
<tr><td>Sigmoidoscopy</td><td>x</td><td></td><td>x</td><td>x</td><td>x</td><td></td><td>x</td><td>x</td><td>x</td><td>x</td><td>x</td><td>x</td><td>x</td><td>x</td></tr>
<tr><td>DRE</td><td>x</td><td></td><td>x</td><td>x</td><td>x</td><td></td><td>x</td><td>x</td><td>x</td><td>x</td><td>x</td><td>x</td><td>x</td><td>x</td></tr>
<tr><td>CEA</td><td>x</td><td></td><td>x</td><td>x</td><td>x</td><td></td><td>x</td><td>x</td><td>x</td><td>x</td><td>x</td><td>x</td><td>x</td><td>x</td></tr>
</table></td></tr>
<tr><td>Locally recurrent cancer after treatment</td><td>• Care should be directed by the Multidisciplinary Gastrointestinal Tumor Team.
• If the recurrence is not amenable to surgical resection, see Clinical Practice Guideline for Metastatic Colorectal Cancer.</td></tr>
<tr><td>Stage IV or or with unresectable disease, or are medically inoperable</td><td>• See Integrating an Early Palliative Approach into Advanced Cancer Care
• All patients with metastatic disease should be evaluated for the potential of being resectable, particularly those with only liver involvement, and should be assessed by a hepatobiliary surgeon, ideally with the multidisciplinary tumor group.
• See Clinical Practice Guideline for Metastatic Colorectal Cancer. For chemotherapy treatment options
• Consider palliative radiotherapy for local symptoms.
•</td></tr>
</table>

Pathologic Assessment

Please refer to the Pathway for detailed information about pathologic assessment.

References

1. Battersby N, How P, Moran B, et al. Prospective Validation of a Low Rectal Cancer Magnetic Resonance Imaging Staging System and Development of a Local Recurrence Risk Stratification Model: The MERCURY II Study. *Annals of surgery*. 2016 Apr 2016;263(4)doi:10.1097/SLA.0000000000001193
2. Nascimbeni R, Burgart LJ, Nivatvongs S, Larson DR. Risk of lymph node metastasis in T1 carcinoma of the colon and rectum. *Diseases of the Colon & Rectum*. 2002;45(2):200-206.
3. Phang PT. Total mesorectal excision: technical aspects. *Canadian Journal of Surgery*. 2004;47(2):130-137.
4. Bailey HR, Huval WV, Max E, Smith KW, Butts DR, Zamora LF. Local excision of carcinoma of the rectum for cure. *Surgery*. 1992;111(5):555-561.
5. Bentrem DJ, Okabe S, Wong WD, et al. T1 adenocarcinoma of the rectum: transanal excision or radical surgery? *Annals of Surgery*. 2005;242(4):472-477.
6. Kikuchi R, Takano M, Takagi K, et al. Management of early invasive colorectal cancer. Risk of recurrence and clinical guidelines. *Diseases of the Colon & Rectum*. 1995;38(12):1286-1295.
7. Mei W, Wang X, Li Y, et al. Neoadjuvant Chemotherapy With CAPOX Versus Chemoradiation for Locally Advanced Rectal Cancer With Uninvolved Mesorectal Fascia (CONVERT): Initial Results of a Phase III Trial. *Annals of surgery*. 04/01/2023 2023;277(4)doi:10.1097/SLA.0000000000005780
8. Schrag D, Shi Q, Weiser M, et al. Preoperative Treatment of Locally Advanced Rectal Cancer. *The New England journal of medicine*. 06/04/2023 2023;doi:10.1056/NEJMoa2303269
9. Sauer R, Becker H, Hohenberger W, et al. Preoperative versus postoperative chemoradiotherapy for rectal cancer. *The New England journal of medicine*. 2004;351(17):1731-1740. doi:351/17/1731 [pii]
10. Wong RK, Berry S, Spithoff K, et al. Preoperative or postoperative therapy for stage II or III rectal cancer: an updated practice guideline. *Clinical oncology (Royal College of Radiologists (Great Britain))*. 2010;22(4):265-271. doi:10.1016/j.clon.2010.03.002 [doi]
11. O'Connell MJ, Martenson JA, Wieand HS, et al. Improving adjuvant therapy for rectal cancer by combining protracted-infusion fluorouracil with radiation therapy after curative surgery. *New England Journal of Medicine*. 1994;331(8):502-507.
12. Hofheinz RD, Wenz F, Post S, et al. Chemoradiotherapy with capecitabine versus fluorouracil for locally advanced rectal cancer: a randomised, multicentre, non-inferiority, phase 3 trial. *Lancet Oncology*. 2012;13(6):579-588. doi://dx.doi.org/10.1016/S1470-2045(12)70116-X
13. Francois Y, Nemoz CJ, Baulieux J, et al. Influence of the interval between preoperative radiation therapy and surgery on downstaging and on the rate of sphincter-sparing surgery for rectal cancer: the Lyon R90-01 randomized trial. *Journal of Clinical Oncology*. 1999;17(8):2396.
14. Cedermark B, Dahlberg M, Glimelius B, Påhlman L, Rutqvist L, Wilking N. Improved survival with preoperative radiotherapy in resectable rectal cancer. *The New England journal of medicine*. 04/03/1997 1997;336(14)doi:10.1056/NEJM199704033361402
15. Kapiteijn E, Marijnen CA, Nagtegaal ID, et al. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer. *The New England journal of medicine*. 2001;345(9):638-646. doi:10.1056/NEJMoa010580 [doi]
16. François E, De Bari B, Ronchin P, et al. Comparison of short course radiotherapy with chemoradiotherapy for locally advanced rectal cancers in the elderly: A multicentre, randomised, non-blinded, phase 3 trial. *European journal of cancer (Oxford, England : 1990)*. 2023 Feb 2023;180doi:10.1016/j.ejca.2022.11.020
17. Liu S, Jiang T, Xiao L, et al. Total Neoadjuvant Therapy (TNT) versus Standard Neoadjuvant Chemoradiotherapy for Locally Advanced Rectal Cancer: A Systematic Review and Meta-Analysis. *The oncologist*. 2021 Sep 2021;26(9)doi:10.1002/onco.13824
18. Kong J, Soucisse M, Michael M, et al. Total Neoadjuvant Therapy in Locally Advanced Rectal Cancer: A Systematic Review and Metaanalysis of Oncological and Operative Outcomes. *Annals of surgical oncology*. 2021 Nov 2021;28(12)doi:10.1245/s10434-021-09837-8
19. Kasi A, Abbasi S, Handa S, et al. Total Neoadjuvant Therapy vs Standard Therapy in Locally Advanced Rectal Cancer: A Systematic Review and Meta-analysis. *JAMA network open*. 12/01/2020 2020;3(12)doi:10.1001/jamanetworkopen.2020.30097
20. Bahadoer R, Dijkstra E, van Etten B, et al. Short-course radiotherapy followed by chemotherapy before total mesorectal excision (TME) versus preoperative chemoradiotherapy, TME, and optional adjuvant chemotherapy in locally advanced rectal cancer (RAPIDO): a randomised, open-label, phase 3 trial. *The Lancet Oncology*. 2021 Jan 2021;22(1)doi:10.1016/S1470-2045(20)30555-6

21. Scott AJ, Kennedy EB, Berlin J, et al. Management of Locally Advanced Rectal Cancer: ASCO Guideline. *J Clin Oncol*. Oct 2024;42(28):3355-3375. doi:10.1200/jco.24.01160
22. Jin J, Tang Y, Hu C, et al. Multicenter, Randomized, Phase III Trial of Short-Term Radiotherapy Plus Chemotherapy Versus Long-Term Chemoradiotherapy in Locally Advanced Rectal Cancer (STELLAR). *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 05/20/2022 2022;40(15)doi:10.1200/JCO.21.01667
23. Benson AB, Venook AP, Adam M, et al. NCCN Guidelines® Insights: Rectal Cancer, Version 3.2024. *J Natl Compr Canc Netw*. Aug 2024;22(6):366-375. doi:10.6004/jnccn.2024.0041
24. Conroy T, Etienne P, Rio E, Evesque L, Mesgousez-Nebout N, Vendrely V. Total neoadjuvant therapy with mFOLFIRINOX versus preoperative chemoradiation in patients with locally advanced rectal cancer: 7-year results of PRODIGE 23 phase III trial, a UNICANCER GI trial. *J Clin Onc*. 2023;41(17_suppl):LBA3504.
25. Krook JE, Moertel CG, Gunderson LL, et al. Effective surgical adjuvant therapy for high-risk rectal carcinoma. *New England Journal of Medicine*. 1991;324(11):709-715.
26. Sargent DJ, Wieand HS, Haller DG, et al. Disease-free survival versus overall survival as a primary end point for adjuvant colon cancer studies: individual patient data from 20,898 patients on 18 randomized trials. *Journal of Clinical Oncology*. 2005;23(34):8664-8670.
27. Sargent DJ, Patiyil S, Yothers G, et al. End points for colon cancer adjuvant trials: observations and recommendations based on individual patient data from 20,898 patients enrolled onto 18 randomized trials from the ACCENT Group. *Journal of Clinical Oncology*. 2007;25(29):4569-4574.
28. Garcia-Aguilar J, Patil S, Gollub M, et al. Organ Preservation in Patients With Rectal Adenocarcinoma Treated With Total Neoadjuvant Therapy. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 08/10/2022 2022;40(23)doi:10.1200/JCO.22.00032

Appendix A: 8th Edition Colon and Rectum Cancer Staging

Stage	Depth of Tumour Penetration		Regional Lymph Node Involvement		Metastases	
Stage 0	T_{is}	Carcinoma *in situ*, intramucosal carcinoma (involvement of lamina propria with no extension through muscularis mucosae)	N_0	No regional lymph node involvement	M_0	No distant metastasis
Stage I	T_1	Invades submucosa (through muscularis mucosa but not into muscularis propria)	N_0	No regional lymph node involvement	M_0	No distant metastasis
	T_2	Invades muscularis propria	N_0	No regional lymph node involvement	M_0	No distant metastasis
Stage II_A	T_3	Invades through muscularis propria into pericolorectal tissues	N_0	No regional lymph node involvement	M_0	No distant metastasis
Stage II_B	T_{4a}	Invades* through visceral peritoneum (including gross perforation of bowel through tumour and continuous invasion of tumour through areas of inflammation to surface of visceral peritoneum)	N_0	No regional lymph node involvement	M_0	No distant metastasis
Stage II_C	T_{4b}	Directly invades* or adhere§ to adjacent organs or structures	N_0	No regional lymph node involvement	M_0	No distant metastasis
Stage III_A	T_{1-2}	As described above	N_1	1-3 regional lymph nodes positive (tumour in lymph nodes measuring ≥0.2 mm), or any number of tumour deposits are present and all identifiable lymph nodes are negative	M_0	No distant metastasis
			N_{1c}	No regional lymph nodes positive, but tumor deposits in subserosa, mesentery, nonperitonealized pericolic, or perirectal/mesorectal tissues		
	T_1	Invades submucosa	N_{2a}	4-6 regional lymph nodes positive	M_0	No distant metastasis
Stage III_B	T_{3-4a}	As described above	N_1	1-3 regional lymph nodes positive (tumour in lymph nodes measuring ≥0.2 mm), or any number of tumour deposits are present and all identifiable lymph nodes are negative	M_0	No distant metastasis
			N_{1c}	No regional lymph nodes positive, but tumor deposits in subserosa, mesentery,		

Stage	Depth of Tumour Penetration		Regional Lymph Node Involvement		Metastases	
				nonperitonealized pericolic, or perirectal/mesorectal tissues		
	T_{2-3}	As described above	N_{2a}	4-6 regional lymph nodes positive	M_0	No distant metastasis
	T_{1-2}	As described above	N_{2b}	≥7 regional lymph nodes positive	M_0	No distant metastasis
Stage III_C	T_{4a}	Penetrates to surface of visceral peritoneum	N_{2a}	4-6 regional lymph nodes positive	M_0	No distant metastasis
	T_{3-4a}	As described above	N_{2b}	≥7 regional lymph nodes positive	M_0	No distant metastasis
	T_{4b}	Directly invades or is adherent to other organs or structures	N_{1-2}	As described above	M_0	No distant metastasis
Stage IV_A	T_{any}	As described above	N_{any}	As described above	M_{1A}	Metastasis to 1 site or organ without peritoneal metastasis
Stage IV_B	T_{any}	As described above	N_{any}	As described above	M_{1B}	Metastasis to ≥ 2 sites or organs without peritoneal metastasis
Stage IV_c	T_{any}	As described above	N_{any}	As described above	M_{1c}	Metastasis to peritoneal surface identified alone or with other site or organ metastases

*Direct invasion in T4 includes invasion of other organs or other segments of the colorectum as a result of direct extension through the serosa, as confirmed on microscopic examination (for example, invasion of the sigmoid colon by a carcinoma of the cecum) or, for cancers in a retroperitoneal or subperitoneal location, direct invasion of other organs or structures by virtue of extension beyond the muscularis propria (ie, respectively, a tumour on the posterior wall of the descending colon invading the left kidney or lateral abdominal wall; or a mid or distal rectal cancer with invasion of prostate, seminal vesicles, cervix, or vagina).

§Tumour that is adherent to other organs or structures, grossly, is classified cT4b. However, if no tumour is present in the adhesion, microscopically, the classification should be pT1-4a depending on the anatomical depth of wall invasion. The V and L classification should be used to identify the presence or absence of vascular or lymphatic invasion whereas the PN prognostic factor should be used for perineural invasion.

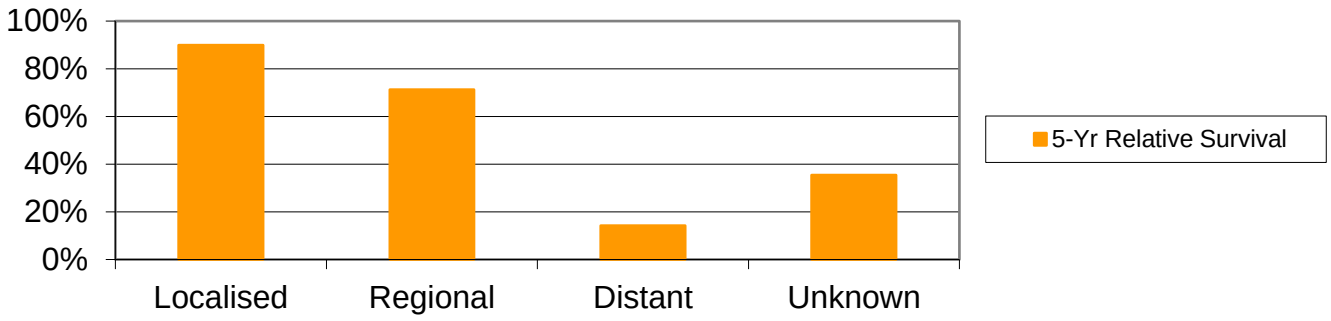
Appendix B:

Table 1. Scenarios where radiation may be omitted after multidisciplinary discussion

Criteria	Source
cT2N1, cT3N0-1 rectal cancer amenable to sphincter sparing surgery	The PROSPECT trial demonstrated non-inferiority of standard chemoradiation compared to preoperative FOLFOX and selective chemoradiation for patients who had <20% reduction in tumour size (Level I)
cT3a/b N0 tumours that are >10cm from the anal verge and with mrCRM ≥2mm and no mrEMVI.	ASTRO guidelines

Appendix C:

Figure 1. Observed survival rates with adenocarcinoma of rectum by SEER summary stage. Data from SEER 18 2009-2015, All Races, Both Sexes.



Appendix C:

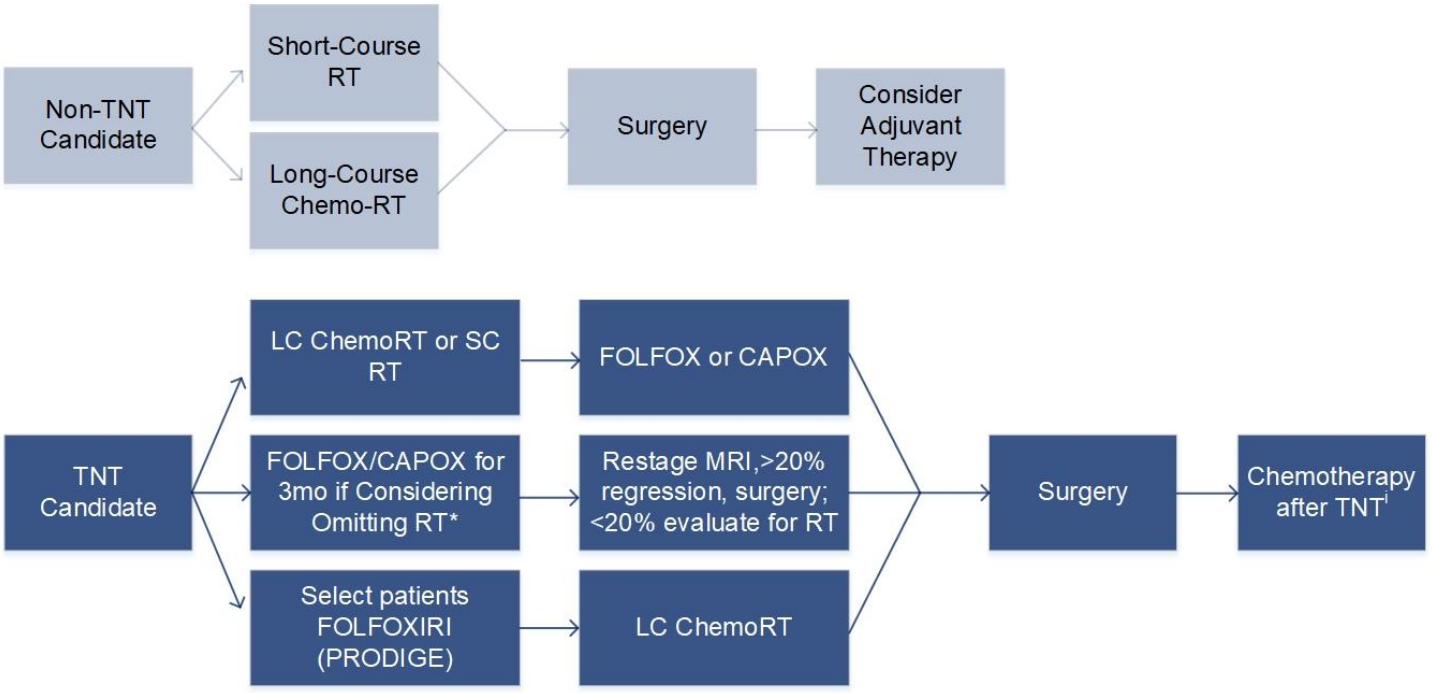


Figure 2. Treatment schema for stage II/III Rectal cancer.

[i]The STELLAR trial used 4 cycles of CAPOX after short course RT and 2 cycles of CAPOX AFTER surgery.
[i]FOWARC FOLFOX 4-6 cycles prior to surgery, 6-8 cycles after surgery
*****In suitable patients, **FOLFIRINOX x 3 months** followed **by long course chemoRT** was utilized as total neoadjuvant therapy in PRODIGE 23. After surgery, **3 months adjuvant chemotherapy** was recommended regardless of pathological stage (capecitabine or FOLFOX). This strategy resulted in an improvement in overall survival compared to standard chemoradiation (7 year OS 76.1% with chemoRT vs 81.9% with FOLFIRINOX and CRT, p 0.033 restricted mean survival time).[22] FOLFIRINOX is associated with increased toxicity compared to FOLFOX and there is an ongoing trial evaluating the two neoadjuvant chemotherapy regimens.

Development and Revision History

This guideline was developed by a multidisciplinary working group comprised of members from the Alberta Provincial GI Tumour Team, external participants identified by the Working Group Lead, and a methodologist from the Guideline Resource Unit. The draft guideline was externally reviewed and endorsed by members of the Alberta Provincial GI Tumour Team who were not involved in the guideline's development, including surgical oncologists, radiation oncologists, medical oncologists, gastroenterologists, nurses, pathologists, and pharmacists. A detailed description of the methodology followed during the guideline development process can be found in the Guideline Resource Unit Handbook.

This guideline was originally developed in 2009.

Maintenance

A formal review of the guideline will be conducted in Fall 2025. If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

Abbreviations

AJJ, American Joint Committee; APR, Abdominoperineal resection; CAP, College of American Pathologists; CEA, Carcinoembryonic antigen; CRM, Circumferential resection margin; CT, Computed tomography; DRE, Digital rectal examination; FDG-PET, Fluorodeoxyglucose positron emission tomography; ME, Mesorectal excision; MRI, Magnetic resonance imaging; TME, Total mesorectal excision; TS, Tumour specific.

Disclaimer

The recommendations contained in this guideline are a consensus of the Alberta Provincial Gastrointestinal Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

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Conflict of Interest Statements

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