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Table 1: Summary of guideline recommendations regarding pre-operative management of rectal cancer

Guideline	**Year**	**Disease stage/risk factors**				
		Very early	**Early**	**Intermediate**	**Locally advanced**	**Advanced**
		cT1-2 N0	**cT1-2 N1-2 or cT3a/b N0 CRM clear** **No EMVI**	**cT3a/b N0 low tumour** **cT3a/b N1/2 if mid-high tumour** **No EMVI**	**cT3c/d N0-2 CRM clear; very low tumour; EMVI positive**	**cT4; lateral nodes involved; CRM threatened/involved**
NICE [331]	2020	Surgery alone (local excision or TME)	Pre-operative SCRT or LCRT followed by TME for T3 or N1-2		Pre-operative SCRT or LCRT followed by surgery	Pre-operative SCRT or LCRT followed by surgery
ESMO [3129]	2017	TEM if no adverse features* (TME used as salvage if needed) TEM + perioperative LCRT if adverse features Local RT (contact or brachytherapy) is an alternative to local surgery, alone or with LCRT	TME If cT1 or elderly/frail, may consider TEM	TME May use SCRT or LCRT pre-operatively if good quality excision cannot be achieved	Pre-operative SCRT or LCRT followed by TME (pre-operative RT used to improve local recurrence rates rather than improve resectability)	Pre-operative LCRT followed by TME SCRT plus FOLFOX chemotherapy followed by TME
NCCN [320]	2020	TEM	Pre-operative SCRT or LCRT followed by TME plus adjuvant CAPOX/FOLFOX		Pre-operative SCRT or LCRT followed by TME plus adjuvant	TNT `(Consider FOLFOXIRI as choice of systemic chemotherapy if T4 N1-

		If adverse features* or T2 disease, do salvage TME (+/- CAPOX/FOLFOX) Or use LCRT/SCRT. If no disease post-RT then observe or CAPOX/FOLOX. If disease still present do TME (+/- CAPOX/FOLFOX) If TME for T1/2 disease reveals T3N0, then: LCRT+ CAPOX/FOLFOX or CAPOX/FOLFOX + LCRT or CAPOX/FOLFOX or observe If TME for T1/2 disease reveals T4N0 or T1-4N1-2, then: CAPOX/FOLFOX + LCRT or LCRT + CAPOX/FOLFOX	Or TNT (see below for definition) followed by TME	CAPOX/FOLFOX Or TNT (see below for definition) followed by TME NB. “Watch and wait” may be an alternative to TME for those with a cCR”	2) followed by TME NB. Watch and wait may be an alternative to TME for those with a cCR IORT may be considered at the time of TME

ASTRO [342]	2020	Surgery alone May consider pre-operative LCRT for low tumours to aid sphincter preservation	Pre-operative SCRT or LCRT followed by TME Consider omission of pre-operative RT for T3a/b N0, EMVI negative, CRM clear, >10 cm from anal verge	Pre-operative SCRT or LCRT followed by TME If cT3 low (≤5cm from anal verge) tumour, consider CAPOX/FOLFOX before or after LCRT or after SCRT	Pre-operative SCRT or LCRT followed by TME Consider neoadjuvant CAPOX/FOLFOX chemotherapy in addition to pre-operative LCRT or SCRT for risk factors (T3 ≤5 cm from anal verge; CRM <2 mm; N2; EMVI positive

CAPOX, capecitabine and oxaliplatin; CRM, circumferential resection margin; EMVI, extramural vascular invasion; FOLFOX, 5-fluorouracil and oxaliplatin; FOLFOXIRI, 5-fluorouracil, oxaliplatin and irinotecan; IORT, intra-operative radiotherapy; LCRT, long course radiotherapy; RT, radiotherapy; SCRT, short course radiotherapy; TME, total mesorectal excision; TEM, Transanal endoscopic microsurgery; TNT, Total neoadjuvant therapy – this involves SCRT or LCRT followed by CAPOX/FOLFOX chemotherapy (approx. 12-16 weeks) or CAPOX/FOLFOX chemotherapy (approx. 12-16 weeks) followed by SCRT or LCRT (NCCN guideline definition); cCR, complete clinical response
*Adverse features following TEM include: positive margins, sub-mucosal spread, poorly differentiated tumour, lymphovascular invasion. ESMO considers involvement of the middle third of the sub-mucosal layer (or lower) to be an adverse feature (≥sm2) while NCCN considers involvement of the lower third (sm3) to be an adverse feature