**Management of**

**Gastro- intestinal Cancers**

**RECTAL CANCER (adenocarcinoma)**

**Workup:** Digital rectal examination (and rigid sigmoidoscopy if available)

Complete colonoscopyawith multiple (8) biopsies

Serum CEA

Local staging: MRI pelvisb (Endorectal ultrasound in early tumorsc)

Metastatic workup: CECT scan abdomen, CECT thorax/chest X-rayd

PET scan can be considered only in select indicationse

**All patients need to be evaluated by a Multidisciplinary team**

To discuss Ovarian Transposition & Sperm banking in eligible patients before neoadjuvant radiation

**Very early rectal cancer**

**cT1N0**

**Disseminated Metastatic disease**

Never Resectable

**Limited metastatic disease**

**Advanced rectal cancer**

**cT3-4/ N1-2/ MRF involved/ EMVI+**

**Early rectal cancer**

**cT1-2N0, MRF clear, no EMVI**

**See individual flow charts**

aIf complete colonoscopy cannot be performed before treatment, then a colonoscopy should be done within 6 months of surgery

bHigh resolution phased array external MRI with minimum strength 1.5 T with T2W non-fat suppressed sequences orthogonal to tumor and in low rectal cancers, scans parallel and perpendicular to anal canal; Add Diffusion weighted imaging; NO ENDORECTAL MRI; No contrast enhanced T1 weighted sequences or any fat suppressed sequences.

cEndorectal ultrasound is indicated ONLY when suspecting a T1 tumor and contemplating a transanal endoscopic microsurgery (TEM)

dThere is no clear evidence for superiority of CECT chest over a chest X-ray and the latter may be an alternative in a resource constrained setting

ePETCT in initial staging is indicated ONLY in the following 4 scenarios : a) in established hepatic metastases to rule out extrahepatic disease when radical surgery is planned, b) when metastases are suspected but not confirmed on CT , c) when CEA is very high at presentation (>200ng/ml) & d) when MRI reveals extensive extramural venous invasion (EMVI) which is an adverse prognostic factor for distant mets.

**Very early rectal cancer**

cT1N0

**Early rectal cancer**

cT1-2N0, MRF clear, no EMVI

Suitable for local excision

 **No**

**Yes**

TMEc

Local excision (TEM/transanal excision)

pT1-2, N0, CRM-

pT1-4, N1-2 or CRM+

pT3N0, CRM-

pT2

pT1

 **Adverse featuresa**

Chemoradiation followed by systemic chemotherapyd

No

Yes

pT1-2/pT3a-b, N0, CRM -

N1-2/ >pT3b/ CRM positive

Chemoradiationb

 TME

aAdverse features include >sm2, Grade 3, lymphovascular invasion

bIf pT2 after local excision, chemoradiation may be considered in patients who are poor risk for TME or refuse surgery

cIn very low rectal cancer, neoadjuvant chemoradiation may be considered before TME even in pT1-2 if sphincter preservation is to be attempted

cIn pT3N0 after TME, role of systemic chemotherapy after adjuvant chemoradiation is unclear

dAdjuvant therapy may be avoided in patients with pT3N0 disease with <5mm extension into the mesorectum and negative CRM

TEM- transanal endoscopic microsurgery; TME- total mesorectal excision; CRM- circumferential resection margin; EMVI- extramural venous invasion

**Surveillance**

**Locally Advanced rectal cancer**

cT3-4, N0-2/ MRF involved/ EMVI+

**Upper third rectum**

**Lower third rectum**

**Middle third rectum**

cT3a-b, N0-1, no EMVI, MRF clear

cT3c-d/ cT4/ N2/ MRF involved/ EMVI+

cT3a-b, N0-2, MRF clear, no EMVI

cT3c-d, N0-2, MRF clear/ EMVI+

Any cT3 with involved MRF/ cT4/ lateral pelvic node on MRI

cT3a-d, cN0-2, MRF clear, EMVI±

Neoadjuvant chemoradiation

**OR**

Short course RTb

**OR**

Total Neoadjuvant Therapy (TNT)

(see Appendix A)

Neoadjuvant chemoradiation

**OR**

Short course RTb

**OR**

Total Neoadjuvant Therapy (TNT)

(see Appendix A)

Neoadjuvant chemoradiation

**OR**

short course RTb

**OR**

Total Neoadjuvant Therapy (TNT)

(see Appendix A)

Neoadjuvant chemoradiation

**OR**

Short course RTb

**OR**

Total Neoadjuvant Therapy (TNT)

(see Appendix A)

TMEa

TME

pT1-3N0, CRM-

pT4/ N1-2/ CRM+

pT1-3N0, CRM-

pT1-3N1-2, CRM-

pT4/ CRM+

Restaging

Adjuvant chemoradiation

Restagingc

Adjuvant chemoradiation

TMEd

TMEd

**Surveillancef (see below for footnote)**

Systemic chemotherapy

Systemic chemotherapy

**Metastatic disease**

**Disseminated metastatic disease/ unfit or unwilling for aggressive treatment (no potential for cure)**

**Unresectable liver/ lung metastasis Fit and willing for aggressive treatment**

**Limited resectable liver/ lung metastasis** **Fit and willing for aggressive treatment (potential for cure)**

Systemic conversion chemotherapy ± biological agents(see Appendix C)

Diversion stoma if obstructed

-Supportive care as appropriate

-Palliative systemic therapy may be offered after discussion

-Maintain continuum of care

-Encourage enrolment in clinical trials

Advanced primary with involved MRF

Resectable primary with clear MRF

Metastasis remains unresectable

Metastases becomes resectable

Perioperative chemotherapy (see Appendix B)

Perioperative chemotherapy

SCRT **OR** Chemoradiation

Resect metastasis

SCRT followed by additional chemotherapy**OR**

Chemoradiation

SCRT **OR** Chemoradiation

Consider alternative local therapy for metastasis

Palliative RT to primary if indicated

Continue systemic therapy

Synchronous or staged resection of primary and metastasis

SCRT **OR** Chemoradiation

Synchronous or staged resection of primary and metastasis

resection of primary

Complete remaining chemotherapy if any

Footnote for advanced rectal cancer:

aFor upper rectal tumors, a partial mesorectal excision with 5cm distal mesorectal clearance is sufficient

bSurgery after short course RT may be performed within 5-7 days or after 6-8 weeks, the latter being associated with less morbidity

cRestaging is usually performed 4-6 weeks after short course RT and 6-8 weeks after chemoradiation. A high-resolution phased array external MRI without endorectal coil is usedfor local staging, surgical planning and defining resection margins. A CT thorax and abdomen for restaging is optional since it changes the management in <7% of patients. A PET-CT may be considered optional if an exenterative procedure is planned.

dSurgery is usually performed 6-12 weeks after chemoradiation. Watch and wait is an option in patients who achieve clinical, radiological and serological complete response after neoadjuvant chemoradiation and willing for intensive surveillance protocol.

eRole of systemic chemotherapy in patients who have received neoadjuvant chemoradiation or short course RT is controversial and is to be discussed with the patient. Patients with residual disease post TME will usually be offered adjuvant chemotherapy (FOLFOX/CAPOX/Capecitabine/5FU) to complete total 6 months of perioperative chemotherapy. Patients with pathological CR can be kept on surveillance after surgery.

fSurveillance-Clinical examination and Serum CEA every 3-6 months for first 5 years and then annually/ at the discretion of the physician; CECT abdomen/pelvis and Chest X-ray/CT Thorax annually for 3 years and thereafter only if clinically indicated; Colonoscopy to be performed 1 year after surgery if complete colonoscopy done upfront (if not done, then colonoscopy to be done within 6 months of surgery) and thereafter once in 5 years or when indicated clinically. Routine surveillance is not required in early stage disease or if the patient is not a candidate for surgery or systemic therapy if recurrence is diagnosed.

Appendix B

A TNT like approach to be considered in these patients with goal of delivering upfront systemic therapy to tackle the metastases whereas the goal of radiation is to achieve local control.

Perioperative chemotherapy in patients with resectable synchronous lung/liver metastases can be one of the following:-

FOLFOX/CAPOX (preferable)

FOLFIRINOX (in young, fit patients)

Appendix C

These patients are treated with intensive systemic therapy in an attempt to convert the disease to a resectable stage. They should undergo evaluation for resection every 2 months while on systemic therapy.

Systemic chemotherapy choices in these patients can be

* CAPOX/FOLFOX/FOLFIRI/FOLFIRINOX

Targeted therapy/Biological agents may be added to the systemic chemotherapy backbone based on KRAS/NRAS/BRAF mutation status

* Cetuximab/Panitumumab (if RAS/RAF wild type)
* Bevacizumab

Appendix A (TNT)

There are two TNT treatment approaches

1. Induction chemotherapy first f/b chemoRT/SCRT

OR

1. chemoRT/SCRT first f/b consolidation chemotherapy

(which of these two approaches are better is unclear; however there is some preliminary evidence that chemoRT f/b consolidation have better RT completion rates, more pathological CR and better organ preservation rates)

1. Local RT can be either SCRT or Long course chemoRT with capecitabine or infusional 5 FU
2. Chemotherapy choices (12 to 16 weeks) – FOLFOX/CAPOX/FOLFIRINOX

Adjuvant chemotherapy may be delivered after surgery with CAPOX/FOLFOX/Capecitabine/5FU\_leucovirin; such that the total perioperative chemotherapy does not exceed 6 months