The North of Scotland Clinical Management Guideline for Colorectal Cancer is currently under review and may not be fully reflective of all current practices.
General Principles

In order to ensure accurate data capture and opportunity for peer review:
- All patients (including those who decline, or are considered clinically not suitable for active treatment) should be registered with the appropriate local colorectal cancer MDT.
- In advance of any patient being discussed at the specialist weekly Colorectal Cancer MDT, it is important to have taken steps at the earliest to establish a cancer diagnosis as well as an indication of clinical staging (see page 7 and 8).

In addition to any other specialist referrals that may be clinically indicated depending on individual patients circumstances, all patients should be formally referred to the relevant Clinical Nurse Specialist at the earlier opportunity. This allows for assessment and ongoing specialist advice, education, support and co-ordination of care for the patient throughout the treatment pathway.

At all stages through the pathway:
- Any treatment plans during their presentation be discussed with the patient
- Patients should be provided with written information and treatment summaries should be provided
- Primary care should be notified of patients pathway progress
- Where available, clinical trials should always be considered the preferred option for eligible patients

SACT regimens will be numbered throughout this document and descriptions of these will be found on page 6 (please see refer to SACT regimen spreadsheet in the interim).

Confirm Diagnosis

The specific diagnostic tests can be found on each pathway page.

Pathology

For biopsy:
- Site
- Type
- Differentiation

For resection (in addition to above):
- Margin status
- Nodal involvement
- Local invasion
- Background abnormalities
- Extramural venous invasion
- Assess for genetic markers

Resection reports should conform to RCPath dataset proforma and use TNM 8

Other Considerations

- Bowel function
- Performance Status (ECOG and/or ASA)
Pathology confirmed colorectal polyp cancer → All patients CT chest, abdomen and pelvis. → Discuss at MDT including imaging review → If clear on imaging → Completely excised → Adverse pathological features → Consider surgical resection → Consider further surveillance/follow-up as per local protocol/guidelines for T1 cancer → Determine further clinical management according to individual findings and patient fitness/preferences.
Confirmed Diagnosis:
- History and examination
- FBC, LFT, U&E, CEA
- Full colonic exam with removal/biopsy of other endoluminal abnormality
- CT C/A/P

MDT Review → Primary resectable?

Yes → Surgery

Potentially curative

MDT Review
Determine post-operative management

Stage I

Stage II Low risk

Stage II High risk

Stage III

No → Consider palliative surgical and oncological options

- Consider neo-adjuvant chemotherapy – 3, 4, 8, 10, 11, 12, 13, 17
- Request biomarkers
- DPYD genotyping pre-5-FU

Follow up

Stage III

Consider adjuvant chemotherapy – 1, 2, 3, 4, 5, 6, 7 (aim for treatment within 8 weeks)

DPYD genotyping pre-5-FU

---

a Request biomarkers – RAS, BRAF, MSI

b Low risk – absence of high risk factors

c High risk – Consider LN number; pT4 disease; tumour perforation; vascular invasion; threatened margin and tumour differentiation (scoring systems may aid decision making)
Confirmed Diagnosis
Rectal adeno-carcinoma (≤ 15cm from Anal verge):
- History and examination
- DRE
- Biopsy and biomarkers
- Endoscopic Assessment
- CT C/A/P
- Thin slice MRI pelvis - to assess the risk of local recurrence determined by anticipated resection margin, tumour and lymph node staging, unless contraindicated.
- FBC, LFT, U&E, CEA

Low risk
- Surgery (local excision in selected patients)

Moderate risk
- Consider neo-adjuvant therapy: 3, 4, 8, 10, 11, 12, 13, 17
- ChemoRT
- Short/long course RT
- Chemotherapy Review DPYD genotyping

High risk
- Requires neo-adjuvant therapy: 3, 4, 8, 10, 11, 12, 13, 17
- ChemoRT
- Short/long course RT
- Chemotherapy Review DPYD genotyping

8-10 week reassessment:
- MRI pelvis
- CT C/A/P
- DRE
- Consider sigmoidoscopy

Active Surveillance (see page 8)

Low risk
- Stage I
- Stage II Low risk
- Stage III

Moderate risk
- Stage II High risk
- Consider adjuvant chemotherapy
- 1, 2, 3, 4, 5, 6, 7 Review DPYD genotyping

High risk
- Stage III
- Consider other chemotherapy or exenteration surgery
- CRM still involved

Follow up

a Low risk – Clear Margins cT1, cT2 or cT3 and no lymph node involvement

b Moderate risk - Involved Margins ≥cT3b in which the potential surgical margin is not threatened; any suspicious lymph node not threatening the surgical resection margin; presence of extramural vascular invasion – indicates high risk of distant recurrence

c High risk – Involved Margins / Locally Advanced: Clinical fixity; radiology suggest R0 resection unlikely; tumour encroachment/ breach of mesorectal fascia; ≥T2 at or below levator origin; a threatened (<1 mm) or breached resection margin; low tumour encroaching onto the intersphincteric plane or with levator involvement. Consideration should be given to pelvic exenteration (refer to appropriate MDT).
**Metastatic Colorectal Cancer**

**Confirmed Diagnosis**
- Stage IV liver, lung, peritoneal mets
- Pathology review
- History and examination
- DRE
- Endoscopic Assessment
- CT C/A/P and MRI pelvis
- Consider PET CT
- KRAS, NRAS, BRAF, MSI testing
- DPYD genotyping
- FBC, LFTs, U&Es, CEA

**MDT Review** → **Resectable primary?** →  
- Yes/ 
  metastases detected in follow-up → **Resectable metastases** (consider MRI liver) → **Neo-adjuvant chemotherapy**  
  RAS Wild Type – 3, 4, 8, 10, 11, 12, 13, 15  
  RAS Mutant – 3, 4, 8, 17  
- No → **Non-resectable oligometastatic disease**

**Chemotherapy 1st Line Options**
- RAS Wild Type – 1, 2, 3, 4, 8, 10, 11, 12, 13, 15
- RAS Mutant – 1, 2, 3, 4, 8, 17
- 5, 6, and 14 can be considered in particular situations
- BRAF mutant – 17

**Chemotherapy 2nd Line Options**
- 1, 2, 3, 4, 8, 9, 17
- 5, 6, 14, 16 can be considered in particular situations

**Chemotherapy 3rd Line Options**
- Consider re-challenge (1,2,3,4, 14) depending on treatment free interval
- 18
- MSI – Consider Pembrolizumab/Nivolumab via PACS2 application - unlicensed

**Consider:**
1. Synchronous resection
2. Sequential resection of primary followed by met
3. Resection of primary followed by 3 months adjuvant chemotherapy 3, 4 then resection of met (if high risk primary e.g. heavy nodal burden or T4)
4. If resectable peritoneal mets, consider referral for CRS +/- HIPEC

**Consider:**
1. Synchronous resection of primary and met
2. Resection of primary followed by met
3. Resection not possible – consider alternative chemotherapy

**Consider:**
1. Palliative resection
2. Palliative bypass
3. Stent
4. (Chemo) Radiotherapy
5. Chemotherapy

**Consider Radio Frequency Ablation (RFA) or stereotactic XRT (currently within RCT)**

**Confirmed Diagnosis:**
- Stage IV liver, lung, peritoneal mets
- Pathology review
- History and examination
- DRE
- Endoscopic Assessment
- CT C/A/P and MRI pelvis
- Consider PET CT
- KRAS, NRAS, BRAF, MSI testing
- DPYD genotyping
- FBC, LFTs, U&Es, CEA
<table>
<thead>
<tr>
<th>No</th>
<th>SACT Protocol/Regimen Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Capecitabine</td>
</tr>
<tr>
<td>2</td>
<td>5-Fluorouracil (Modified de Gramont)</td>
</tr>
<tr>
<td>3</td>
<td>mFolfox 6 (where m = modified)</td>
</tr>
<tr>
<td>4</td>
<td>Capox</td>
</tr>
<tr>
<td>5</td>
<td>Raltitrexed + oxaliplatin</td>
</tr>
<tr>
<td>6</td>
<td>Raltitrexed</td>
</tr>
<tr>
<td>7</td>
<td>5-Fluorouracil (continuous infusion)</td>
</tr>
<tr>
<td>8</td>
<td>Folfiri</td>
</tr>
<tr>
<td>9</td>
<td>Folfiri + Aflibercept</td>
</tr>
<tr>
<td>10</td>
<td>Folfiri + Cetuximab</td>
</tr>
<tr>
<td>11</td>
<td>Folfox + Cetuximab</td>
</tr>
<tr>
<td>12</td>
<td>Folfox + Panitumumab</td>
</tr>
<tr>
<td>13</td>
<td>Folfiri + Panitumumab</td>
</tr>
<tr>
<td>14</td>
<td>Irinotecan</td>
</tr>
<tr>
<td>15</td>
<td>Irinotecan + Cetuximab</td>
</tr>
<tr>
<td>16</td>
<td>Irinotecan + Aflibercept</td>
</tr>
<tr>
<td>17</td>
<td>Folfoxiri</td>
</tr>
<tr>
<td>18</td>
<td>Lonsurf (trifluridine with tipiracil)</td>
</tr>
<tr>
<td>19</td>
<td>Capecitabine with radiotherapy</td>
</tr>
</tbody>
</table>
## TNM Staging for Colorectal Cancer (8th Edition; 2017)

### Primary Tumour (T)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumour cannot be assessed</td>
</tr>
<tr>
<td>To</td>
<td>No evidence of primary tumour</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ: invasion of lamina propria</td>
</tr>
<tr>
<td>T1</td>
<td>Tumour invades submucosa</td>
</tr>
<tr>
<td>T2</td>
<td>Tumour invades muscularis propria</td>
</tr>
<tr>
<td>T3</td>
<td>Tumour invades subserosa or into non-peritonealised pericolic or perirectal tissues</td>
</tr>
</tbody>
</table>

### pT4 Stages

- **pT4** Tumour directly invades other organs or structures and/or perforates visceral peritoneum
- **pT4a** Tumour perforates visceral peritoneum
- **pT4b** Tumour directly invades other organs or structures

### Notes

- **a** Tis includes cancer cells confined within the mucosal lamina propria (intramucosal) with no extension through the muscularis mucosae into the submucosa
- **b** Invades through to visceral peritoneum to involve the surface
- **c** Direct invasion in T4b includes invasion of other organs or segments of the colorectum by way of the serosa, as confirmed on microscopic examination, or for tumours in a retroperitoneal or subperitoneal location, direct invasion of other organs or structures by virtue of extension beyond the muscularis propria.
- **d** Tumour that is adherent to other organs or structures, macroscopically, is classified cT4b. However, if no tumour is present in the adhesion, microscopically, the classification should be pT1-3, depending on the anatomical depth of wall invasion.
<table>
<thead>
<tr>
<th>Regional Lymph Nodes (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
</tr>
<tr>
<td>N0</td>
</tr>
<tr>
<td>N1</td>
</tr>
<tr>
<td>N1a</td>
</tr>
<tr>
<td>N1b</td>
</tr>
<tr>
<td>N1c</td>
</tr>
<tr>
<td>N2</td>
</tr>
<tr>
<td>N2a</td>
</tr>
<tr>
<td>N2b</td>
</tr>
</tbody>
</table>

**Notes**

* Tumour deposits (satellites) are discrete macroscopic or microscopic nodules of cancer in the pericolic or perirectal adipose tissue’s lymph drainage area of a primary carcinoma that are discontinuous from the primary and without histological evidence of residual lymph node or identifiable vascular or neural structures. If a vessel wall is identifiable on H&E, elastic or other stains, it should be classified as venous invasion (V1/2) or lymphatic invasion (L1). Similarly, if neural structures are identifiable, the lesion should be classified as perineural invasion (Pn1). The presence of tumour deposits does not change the primary tumour T category, but changes the node status (N) to pN1c if all regional lymph nodes are negative on pathological examination.

<table>
<thead>
<tr>
<th>Distant Metastasis (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
</tr>
<tr>
<td>M1</td>
</tr>
<tr>
<td>M1a</td>
</tr>
<tr>
<td>M1b</td>
</tr>
<tr>
<td>M1c</td>
</tr>
</tbody>
</table>
### Definitions

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA</td>
<td>American Surgeons Association</td>
</tr>
<tr>
<td>CAP</td>
<td>Chest, abdomen and pelvis</td>
</tr>
<tr>
<td>CEA</td>
<td>Carcino-embryonic antigen</td>
</tr>
<tr>
<td>CRM</td>
<td>Circumferential Resection Margin</td>
</tr>
<tr>
<td>CRS</td>
<td>Cyto-Reductive Surgery</td>
</tr>
<tr>
<td>CT</td>
<td>Computed Tomography</td>
</tr>
<tr>
<td>DPYD</td>
<td>Dihydropyrimidine Dehydrogenase Deficiency</td>
</tr>
<tr>
<td>DRE</td>
<td>Digital Rectal Examination</td>
</tr>
<tr>
<td>ECOG</td>
<td>East Coast Oncology Group</td>
</tr>
<tr>
<td>ERUS</td>
<td>Endoscopic Rectal Ultrasound</td>
</tr>
<tr>
<td>FBC</td>
<td>Full blood count</td>
</tr>
<tr>
<td>KRAS</td>
<td>Kirsten Rat Sarcoma</td>
</tr>
<tr>
<td>LFT</td>
<td>Liver Function Tests</td>
</tr>
<tr>
<td>LN</td>
<td>Lymph Nodes</td>
</tr>
<tr>
<td>MDT</td>
<td>Multi-Disciplinary Team</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>PACS2</td>
<td>Peer Approved Clinical System</td>
</tr>
<tr>
<td>PET</td>
<td>Positive Emission Tomography</td>
</tr>
<tr>
<td>RFA</td>
<td>Radio Frequency Ablation</td>
</tr>
<tr>
<td>R0</td>
<td>Resection for cure or complete remission</td>
</tr>
<tr>
<td>R1</td>
<td>Microscopic residual tumour</td>
</tr>
<tr>
<td>R2</td>
<td>Macroscopic residual tumour</td>
</tr>
<tr>
<td>SACT</td>
<td>Systemic Anti-Cancer Therapy</td>
</tr>
<tr>
<td>TEMS</td>
<td>Trans-anal Endoscopic Microsurgery</td>
</tr>
<tr>
<td>TNT</td>
<td>Total Neo-adjuvant Therapy</td>
</tr>
<tr>
<td>U&amp;Ees</td>
<td>Urea &amp; Electrolytes</td>
</tr>
</tbody>
</table>
References

Loughrey MB, Quirke P, Shepherd NA. Dataset for histopathological reporting of colorectal cancer. The Royal College of Pathologists 2018.


Adjuvant/Neo-adjuvant Chemotherapy

2nd/3rd Line Chemotherapy