North of Scotland Clinical Management Guideline (CMG): Anal Cancer Approved 21/12/20

Document Control

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General Principles

- Where available, clinical trials should always be considered as the preferred option for all eligible patients
- Patients must be involved in all decision-making relating to their care with informed consent required for patients undergoing treatment
- A list of SACT regimens is provided. Full regional SACT Protocols will be developed and linked to from this document.

North Cancer Alliance

For symptoms of suspected Colorectal Cancer, please refer to the Scottish Referral Guidelines for Suspected Cancer

Anal Cancer: Background

- The anal canal is approximately 4cm long and extends from the junction of the puborectalis portion of the levator ani musle and the external anal sphincter to the anal verge.
- The proximal portion of the anal canal (ie the area of transition from the rectal mucosa to the squamous mucosa on the hair-bearing anal margin and which is referred to as the 'transitional zone') is quite variable between patients.
- In some patients, the distinction between the anal squamous mucosa and the rectal glandular mucosa is clear and abrupt, where in other it is less so.
- The biology and prognosis of keratinizing and non-keratinizing squamous cell carcinomas of the anal canal are similar. As there is no easily identifiable landmark between the rectum and anus, clinicians should rely on the pathologic classification of tumours in the area rather than the surgical or endoscopic classification.
- Adenocarcinomas of the anal canal share the same natural history as rectal adenocarcinomas and should be managed accordingly.
- Lymphatic drainage of anal cancers is dependent on the anatomic site of origin and patients with anal cancer should therefore undergo both physical and radiographic examination of both the perirectal and paravertebral nodes and the inguinal and femoral lymph nodes.

Diagnosis

- The following guidelines are only for squamous cell cancer of the anus, which is the most common type of anal cancer: Adenocarcinoma of the anus is treated in the same way as rectal cancers and should be managed accordingly.
- It is important to establish a definitive diagnosis earliest and an indication of clinical staging (see page 6) in advance of patient being discussed at the locally agreed appropriate specialist weekly colorectal/lower GI cancer MDT

Confirm Diagnosis

- Full history & physical examination including DRE and examination of both groins/inguinal regions
- Blood profile (ie FBC, U+E, LFTs)
- Proctoscopy, EUA and biopsy
- Staging CT of chest, abdomen and pelvis
- MRI of pelvis
- FDG PET scan after MDT discussion
- Colposcopy (in female patients) if indicated

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Histology

- Site
- Type
- Grade
- Infiltration pattern
- Depth of invasion
- Cytology

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Other Considerations

- HIV testing
- Infertility and potential fertility preservation strategies should be discussed with
  -all male patients
  -all female patients of child bearing age
- Effective contraception should also be discussed with all patients due to have pelvic radiotherapy
- Performance Status assessment
- Assessment/documentation of bowel function

Due to the nature of their presenting disease and likely treatment, all patients should be referred to the colorectal clinical nurse specialist (CNS) after cancer diagnosis for assessment and ongoing specialist advice, education, support and coordination of care for patient and their relatives throughout the treatment pathway.

In line with best principles, at all stages throughout the treatment pathway:

- Any treatment plans should be discussed with patients and relatives during their preparation
- Patients and their relatives should be provided with written information
- Primary care should be notified of patients pathway progress
- Treatment summaries should be provided

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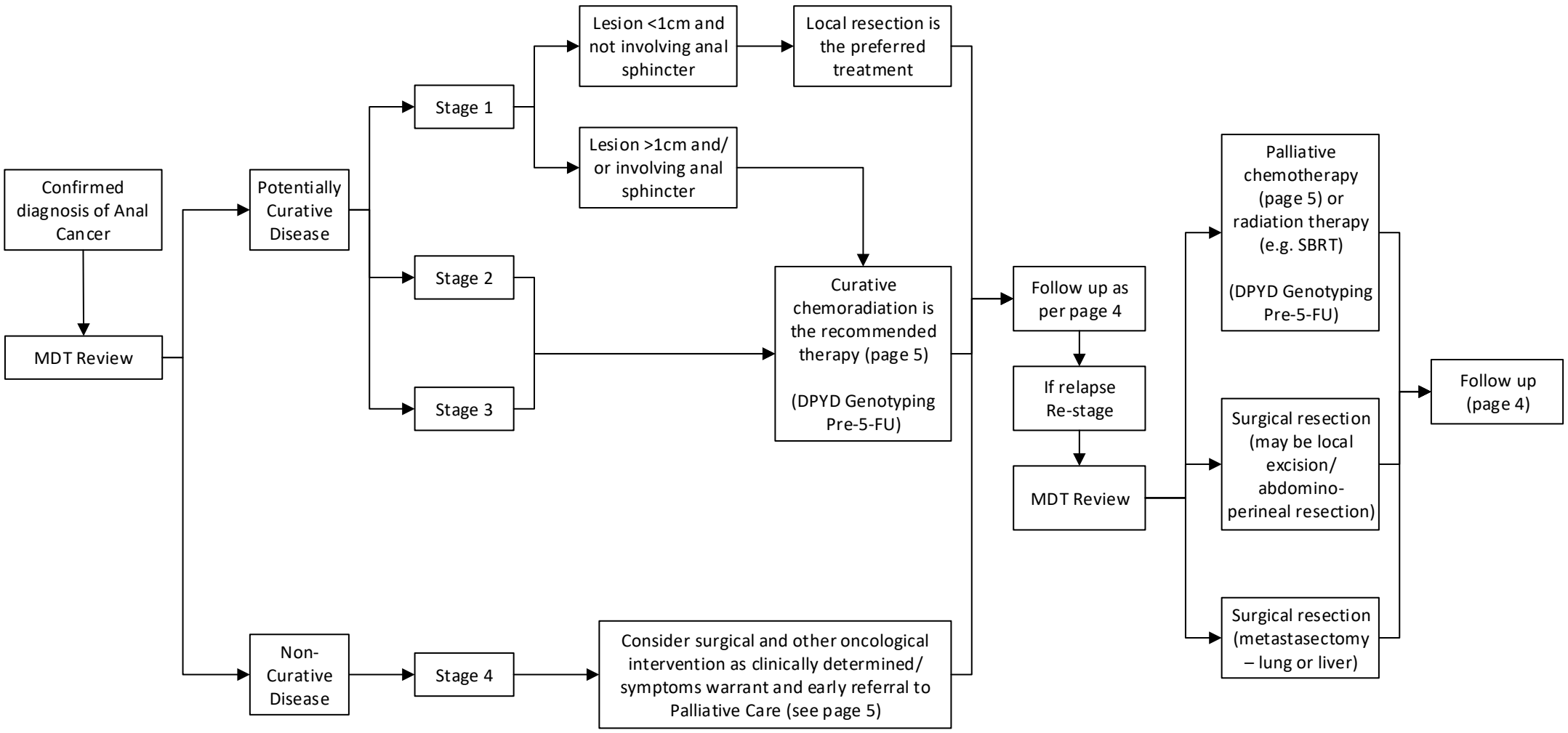
Initial Evaluation | **Clinical Stage** | **Primary Treatment** | **Follow-up** | ***Relapse***



General Guidance Notes

Acute radiation reaction side effects
(normally settle 2-3 weeks after completing treatment)

Common effects:
- Diarrhoea
- Proctitis (ie inflammation of the lining of the rectum)
- Lethargy
- Desquamation (ie the shedding of the outer layers of the skin)
- Urinary frequency

Late radiation reaction side effects
(normally commence after 6 months)

Possible effects:
- Anal dysfunction
- Persistent proctitis (usually improves after 12-18 months)
- Change in bowel habit
- Telangiectasia (ie dilated blood vessels near the surface of the skin or mucous membranes)
- Vaginal fibrosis (ie fibrous tissue adhesions in the vagina, hence the use of dilators during & after treatment)
- Erectile dysfunction
- Infertility
- Urethral fibrosis/stricture

Follow-up for Anal Canal Tumours

Excepting where patients are participating in a clinical trial (where separate guidance may exist), all other patients should attend an Outpatient Clinic for first follow-up 4-6 weeks after treatment completion.

Thereafter:
- 3 monthly follows ups (Year 1-2)
- 6 monthly follow ups (Year 3)
- Annually (Years 4 & 5)
- Consider annual colposcopy as appropriate

Follow-up MRI (pelvis) will be carried out at 3 and 6 months. Follow-up CT (chest/abdo/pelvis) will be carried out at 12 months. All time points are from the completion of CRT

If evidence of persistent disease then requires EUA and biopsy (only after MDT discussion) then, re-staging including FDG PET
If localised, then for salvage surgery
If metastatic, consider options & patients wishes

SACT Regimens

SACT Regimen – Curative		
Mitomycin/capecitabine + RTX	1 cycle	Mitomycin 12mg/m2 IV (day 1) Capecitabine 825mg/m2 Oral Twice daily (Mon-Fri for 6 weeks)
Mitomycin/5-Fluorouracil + RTX	1 cycle	Mitomycin 12mg/m2 IV (day 1) 5-Fluorouracil 1000mg/m2 continuous IV infusion - Days 1-4 (week 1) and Days 29-32 (week 5)
Cisplatin/5-Fluorouracil	1 cycle	Cisplatin 60mg/m2 IV (day 1) 5-Fluorouracil 1000mg/m2 continuous IV infusion - Days 1-4 (week 1) and Days 29-32 (week 5)

SACT Regimen – Palliative		
Carboplatin/Paclitaxel	6 cycles (every 21 days)	Carboplatin AUC 5 IV (day 1) Paclitaxel 175mg/m2 IV (day 1)
Cisplatin/5-Fluorouracil	6 cycles (every 21 days)	Cisplatin 60mg/m2 IV (day 1) 5-Fluorouracil 1000mg/m2 continuous IV infusion (Days 1-4 of each cycle)
Carboplatin/Paclitaxel	**6 cycles** (every 28 days)	Carboplatin AUC 5 IV (day 1) Paclitaxel 80mg/m2 IV (days 1, 8, 15)
Cisplatin/capecitabine	6 cycles (every 21 days)	Cisplatin 60mg/m2 IV (day 1) Capecitabine 625mg/m2 Oral Twice daily (Days 1-21)

TNM Staging for Anal Cancer (8th Edition; 2017)		
Primary Tumour (T)		
TX	Primary tumour cannot be assessed	
To	No evidence of primary tumour	
Tis	Carcinoma in situ, Bowen disease, high grade squamous intraepithelial lesion (HSIL), anal intraepithelial neoplasia II–III (AIN II–III)	
T1	Tumour 2 cm or less in greatest dimension	
T2	Tumour more than 2 cm but not more than 5 cm in greatest dimension	
T3	Tumour more than 5 cm in greatest dimension	
T4	Tumour of any size invades adjacent organ(s) e.g. vagina, urethra, bladder*	
Notes	*Direct invasion of the rectal wall, perianal skin, subcutaneous tissue, or the sphincter muscle(s) alone is not classified as T4	
Regional Lymph Nodes (N)		
NX	Regional lymph nodes cannot be assessed	
N0	No regional lymph node metastasis	
N1	**N1**	Metastasis in regional lymph node(s)
	N1a	Metastases in inguinal, mesorectal, and/or internal iliac nodes
	N1b	Metastases in external iliac nodes
	N1c	Metastases in external iliac and in inguinal, mesorectal and/or internal iliac nodes
Distant Metastasis (M)		
M0	No distant metastasis	
M1	Distant metastasis	

Definitions

CNS	Cancer Nurse Specialist
CT	Computed Tomography
DRE	Digital Rectal Exam
EUA	Examination Under Anaesthetic
FBC	Full blood count
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma Virus
LFT	Liver Function Test
MDT	Multi-Disciplinary Team
MRI	Magnetic Resonance Imaging
PET CT	Positron Emission Tomography
SACT	Systemic Anti-Cancer Therapy
U&Es	Urea & Electrolytes