Title: Systemic Anti-Cancer Therapy (SACT) guidelines for the management of patients with anal cancer

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Links to other policies: NICaN Anal SACT protocols

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Authorisation of Systemic Anti-Cancer Therapy (SACT) Guidelines for Anal Malignancies

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<th>Written by Systemic Guidelines Author</th>
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<tr>
<td>Dr Richard Park, Consultant Clinical Oncologist &amp; Dr Robert Harte Consultant Clinical Oncologist</td>
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<th>Dr Martin Eatock, Consultant Medical Oncologist, chair of the NICaN Drugs &amp; Therapeutics committee</th>
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These SACT guidelines are being submitted by the author on behalf of the GI oncologists group.
1.0 INTRODUCTION / PURPOSE OF POLICY

1.1 Background
Cancers arising from the anal canal and anal margin are uncommon. The annual incidence was 0.65 per 100,000 in England in 2007. There are on average 17 new cases of invasive squamous cell carcinoma (SCC) of the anal canal and margin in Northern Ireland (NI) each year (NI Cancer Registry, 2009). Other rare tumours are encountered (e.g. melanoma, lymphoma and sarcoma) and their management is not covered in this guideline. Surgery is typically used as a first-line treatment for small anal margin tumours which can be curative. For most tumours the recommended treatment is chemoradiation (CRT). A minority of patients for whom CRT is inappropriate may be considered for surgery (see below).

1.2 Purpose
This guidance has been produced to support:
• The management of patients with suspected Anal cancer
• The management of patients diagnosed with Anal cancer

Treatment decisions are made by weighing a range of factors, which cannot all be accounted for in a single clinical management guideline. This guidance provides a description of the range of treatment options available for a clinical scenario. Individual clinical management strategies are best discussed at a multidisciplinary meeting (MDM). The Management of patients with suspected and diagnosed Colorectal Cancer is out with this guidance as is contained within the NICaN Colorectal Cancer Guidance.

2.0 SCOPE OF THE POLICY
This document is aimed at all clinical staff involved in the management of patients with anal cancer.

3.0 ROLES/RESPONSIBILITIES
It is the responsibility of all clinical staff involved in the management of patients with anal cancer to familiarise themselves with these guidelines.

4.0 KEY POLICY PRINCIPLES

4.1 Referral for specialist treatment
All patients with a new diagnosis of anal cancer should be reviewed through the Regional MDT before treatment. The core membership of the MDT includes pathologist, radiologist, clinical oncologists and colorectal surgeons, with dedicated MDT coordinator, nursing and data management support. The MDT should have a defined relationship with other specialist groups (e.g. plastic surgery, urological and gynaecological surgical oncologists, genitourinary and palliative medicine).

Following the histological confirmation of an anal canal cancer and discussion
by the unit GI MDT, patients should be referred within one working day to the Regional MDT using CAPPS and e-mail/ Referral Proforma. (See Appendix Referral and management Pathway)

4.2 Pre-treatment assessment

**Unit GI MDT**
- Initial clinical assessment
- Examination and biopsy
- Discussion of pathology
- Decision for regional MDT referral
- Request CT chest/abdomen/pelvis

**Regional Anal Canal MDT discussion**
- Review clinical summary
- Review pathology
- Review available imaging
- Propose initial management plan (including required additional investigations to complete staging – see Appendix 2)

**Regional Anal Canal MDT member assessment**
- Clinical examination (including Performance Status)
- Full blood count
- Urea and electrolytes
- Liver function tests
- Additional investigations as per MDT discussion (e.g. CT, MRI, PET, FNA of clinically suspicious lymphadenopathy)
- in HIV positive cases seek advice from GUM clinic on current status/medication
- Confirm appropriateness of initial management plan
- Consider trial recruitment (if available)
- Explanation of proposed treatment
- Update referring MDT/GP

4.3 Management

The standard radical treatment for SCC of the anal canal and margin is primary CRT.

4.3.1 Standard CRT

**Patient Selection**
- Any T stage, node +ve,
- T2-4, node –ve
- Fit for radical CRT
Treatment Regimen
Radiotherapy
Phase I – 30.6 Gy/17 fractions/3.4 weeks to large parallel opposed fields
Phase II – 19.8 Gy/11 fractions/2.2 weeks to planned volume (GTV+ margin).

Chemotherapy
Mitomycin 12mg/m² D1, Fluorouracil 1000mg/m² D1-4 and D29-32
Alternatively,
Mitomycin 12mg/m² D1, Capecitabine 825mg/m² bd on radiotherapy days only.

4.3.2 Modified CRT (with radical intent in patients who are not suitable for standard treatment)

**Modified** CRT schedules may be considered for patients with early stage tumours (T1N0 – T1/2 post R1 resection) or those unfit for standard treatment on the basis of general fitness.

Radiotherapy field is GTV plus 3cm margin in all directions (as per phase II above).
For anal margin tumours a direct field may be used.
Dose prescription - 30Gy/15 fractions/3 weeks.

Chemotherapy – Mitomycin 12mg/m² D1, Fluorouracil 1000mg/m² D1-4.

4.4 Surgical approaches

- Anorectal excision when CRT contra-indicated (e.g. previous pelvic RT, renal transplant, significant pre-existing bowel disease)
- Local excision of some small tumours
- Defunctioning ileostomy/colostomy
- Block dissection of inguinal nodes
- Salvage surgery

4.5 Palliative therapy

Palliative radiotherapy, chemotherapy or surgery may be considered for patients unsuitable for radical treatment, either with advanced disease at presentation or recurrence. The approach used will vary according to disease and patient factors and usually will require MDT discussion.

Cisplatin and fluorouracil are used for the treatment of relapsed/metastatic squamous cell carcinoma of the anal canal and margin.

Cisplatin 80mg/m² D1, Fluorouracil 1000mg/mg² D1-4.
21day cycle. Give up to a maximum of 5 cycles.
4.6 Follow up

Clinical follow up is undertaken by the team delivering radical therapy in order to:
- Allow detection and appropriate management of severe treatment related morbidity
- Detect local recurrence amenable to salvage surgery (greatest risk period 12-36 months)
- Allow audit of outcome of current protocols

Those who experience marked acute toxicity post CRT will be seen weekly in the Cancer Centre until severe symptoms have settled.

Post treatment response assessment should take place 4 weekly until complete response (CR) is achieved. If clinical examination is too uncomfortable or persistent or recurrent local disease is suspected, then examination under anaesthetic should be considered. Biopsy following CRT is only advised where there is a residual mass and the clinical suspicion is of persistent or recurrent disease and after MDT discussion. Each assessment will comprise clinical examination including DRE, with CT at the end of year 1. Further imaging will be requested as indicated.

4.7 Standard follow up schedule after radical treatment

- 4 weekly until clinical complete response and acute toxicity resolved, then
- 3 monthly until end of year 2, then
- 4 monthly until end of year 3, then
- 6 monthly until end of year 5

Recurrence after 5 years of continuing complete clinical response is rare, and patients can usually be discharged from regular follow up at this point.

5.0 IMPLEMENTATION OF POLICY

5.1 Dissemination
This policy will be agreed by all consultant oncologists treating patients with SACT for Anal cancer. The guideline will form the basis for development of the SACT regimen specific protocols. It will be available on the intranet for use by all doctors, nurses and pharmacists involved in all stages of SACT assessment and delivery in patients with anal cancer.

6.0 MONITORING

Use of these guidelines will be monitored using audit.
7.0 EVIDENCE BASE /REFERENCES


8.0 CONSULTATION PROCESS

Consultation and review is via the authors and the NICaN Colorectal group.
Appendix 1 – Referral and management Pathway

Unit GI MDT
- Clinical assessment and biopsy
- Local GI MDT discussion
- Refer to Regional MDT (Including patient details, clinical summary, relevant pathology and radiology reports)
- Initiate staging investigations (CT +/- MRI)

Regional Anal Canal MDT
- Review clinical summary
- Review Pathology
- Review Imaging
- Agreement Management plan
- Update referring clinician and GP

Post MDT
- Clinical assessment (history, examination, performance status)
- Arrange outstanding staging investigations
- Review and initiate management plan
- Update referring clinician and GP
Appendix 2 – TNM staging

TNM staging (7th edition 2010)

Tumour
- Tx Primary tumour cannot be assessed
- Tis Carcinoma in situ
- T1 Tumour 2cm or less
- T2 Tumour >2cm – 5cm
- T3 Tumour >5cm
- T4 Tumour invades other organ (vagina, urethra, bladder, sacrum)

Nodes
- Regional nodes are perirectal, internal iliac and inguinal.
- Nx Regional nodes cannot be assessed
- N0 No regional node metastases
- N1 Metastasis in perirectal node(s)
- N2 Metastasis in unilateral internal iliac and/or inguinal node(s)
- N3 Metastasis in perirectal and inguinal nodes and/or bilateral internal iliac or inguinal

Metastasis
- M0 No metastasis
- M1 Metastasis present (unilateral or bilateral)
- T4 Tumour invades other organ (vagina, urethra, bladder, sacrum)

Nodes
- Regional nodes are perirectal, internal iliac and inguinal.
- Nx Regional nodes cannot be assessed
- N0 No regional node metastases
- N1 Metastasis in perirectal node(s)
- N2 Metastasis in unilateral internal iliac and/or inguinal node(s)
- N3 Metastasis in perirectal and inguinal nodes and/or bilateral internal iliac or inguinal

Metastasis
- M0 No metastasis
- M1 Metastasis present (unilateral or bilateral)
10.0 **EQUALITY STATEMENT**
In line with duties under the equality legislation (Section 75 of the Northern Ireland Act 1998), Targeting Social Need Initiative, Disability discrimination and the Human Rights Act 1998, an initial screening exercise to ascertain if this policy should be subject to a full impact assessment has been carried out. The outcome of the Equality screening for this policy is:

- Major impact □
- Minor impact □
- No impact. √