


Coversheet for Network Site Specific Group Agreed Documentation

This sheet is to accompany all documentation agreed by Pan Birmingham Cancer Network Site Specific Groups. This will assist the Network Governance Committee to endorse the documentation and request implementation.

Document Title	Guideline for the referral and management of patients with squamous cell carcinoma of the anus
Document Date	June 2010
Document Purpose	This Guidance has been produced to support the management of patients with squamous cell carcinoma of the anus
Authors	Ian Geh: Consultant Clinical Oncologist, University Hospitals NHS Foundation Trust. Lara Barnish Deputy Director of Nursing, Pan Birmingham Cancer Network.
References	See document
Consultation Process	Colorectal Network Site Specific Group
Review Date (must be within three years)	June 2013
Approval Signatures: Network Site Specific Group Clinical Chair	
Date Approved by Network Governance Committee June 2010	

Guidelines for the Management of Squamous Cell Carcinoma of the Anus

Version History

Version	Summary of change	Date Issued
Draft 0.1	First draft	11.05.07
Draft 0.2	Amended following discussion with Ian Geh	15.05.07
Draft 0.3	Amended following review of cancer measures	06.08.07
Version 1	Endorsed by Pan Birmingham Cancer Network Governance Committee	24.09.07
Version 1.1	Prepared for Review	23.02.09
Version 1.2	With Ian Geh Changes	April 2010
Version 1.3	Reformatted / comments by LB. for comments by IG	14.04.2010
Version 1.4	With comments from IG. for consultation with the colorectal NSSG	22.04.10
Version 1.5	Approved by the NSSG.	11.05.10
Version 1.6	Minor changes made by LB and IG. For submission to the Clinical Guidelines sub group.	20.05.10
Version 2.0	Agreed by the Clinical Governance Sub Group with the proviso that the section on follow-up can be supported by the Network. LB to email Don Milligan.	15.06.10
Version 2.0	Response received from Don Milligan	16.06.10

Summary of Changes since Version One

- Additional staging tests that may be required.
- Additional detail for the chemo-radiotherapy, follow-up and the management of treatment failure.

1. Scope of the Guideline

This guidance makes recommendations for the referral and management of patients with squamous cell carcinoma (SCC) of the anus.

2. Guideline Background

Anal cancers are rare tumours with complex treatment pathways. In order to deliver optimal treatment, NICE (2004) recommends that these should be managed by one designated MDT per Cancer Network. This is to enable the expertise to be developed within the MDT and to allow for adequate numbers to audit outcomes. The Specialist Anal Cancer MDT for the Pan Birmingham Cancer Network is based at University Hospital Birmingham NHS Foundation Trust (UHBFT). See decision tree (Appendix I).

Guideline Statements

3 Referral

Patients with colorectal symptoms should be referred for investigation to their local colorectal unit. Specific symptoms include rectal pain and bleeding, change in bowels, visible or palpable mass. (See rapid access referral from, Appendix 2).

4. Diagnosis and investigations

4.1 Diagnosis is made by biopsy / local excision of the mass and histology, and can be carried out by the local colorectal cancer teams.

4.2 Histology can include:

- a) Squamous cell carcinoma, variants include cloacogenic (basaloid) carcinoma and verrucous carcinoma
- b) Adenocarcinoma
- c) Melanoma
- d) Non-Hodgkin's lymphoma (more common in HIV+ patients)

} These cancers
will not be covered
in this document

4.3 Staging:

4.3.1 Initial investigations

- a) Bloods (FBC, U+Es, LFTs)
- b) HIV test if considered at risk
- c) Biopsy +/- EUA
- d) MRI pelvis
- e) CT chest, abdomen, pelvis
- f) 18-FDG PET/CT may be used for solving uncertainties seen on CT or MRI

4.3.2 Staging is classified using the UICC TNM system

5. Management

- 5.1 All patients with a diagnosis of SCC of the anus, including those who have undergone local excision, should be referred to, and discussed in, the specialist anal cancer multidisciplinary meeting at UHBFT.
- 5.2 Small anal margin tumours (T1 or early T2) suitable for complete excision without damage to the anal sphincters should be managed by local excision and followed up closely afterwards. These patients should be assessed and managed by the anal cancer specialist team.
- 5.3 For all other SCCs of the anal canal and margin with no evidence of metastases outside the pelvis, CRT should be the primary treatment.
- 5.4 Patients with metastatic disease outside the pelvis may benefit from palliative CRT (30-45 Gy in 15-25 fractions with 1-2 cycles mitomycin C/5FU) to the pelvis to control local symptoms.
- 5.5 Abdominoperineal resection is no longer the primary treatment modality of choice for anal canal SCC, unless chemoradiotherapy (CRT) is contraindicated (e.g. previous radiotherapy to the pelvis).
- 5.6 All patients who are not suitable for local excision should be considered for synchronous chemoradiotherapy, unless this is contraindicated.
- 5.7 Two randomised trials (UKCCCR and EORTC) [2,3] have demonstrated the superiority of synchronous chemoradiotherapy (CRT is the primary treatment of anal canal and margin SCC.
- 5.8 The NCRI ACT II trial used a lower dose of radiotherapy to the primary tumour and uninvolved lymph nodes to reduce acute toxicity. This enabled the phase II boost to commence immediately after completion of phase I without the 6 week gap which was necessary in the UKCCCR trial. The ACT II trial compared mitomycin C / 5FU against cisplatin /5FU given with radiotherapy, with or without 2 cycles of maintenance cisplatin / 5FU after completion of CRT in a 2 x 2 trial design. Early results of this trial which recruited 940 patients showed identical complete response of 95% with cisplatin or mitomycin C, and the 2 cycles of cisplatin / 5FU given after completion of CRT did not improve disease-free survival further [4].
- 5.9 The ACT II trial radiotherapy protocol has defined a new standard of care for the UK. It has achieved the highest complete response rate ever published in the largest trial ever completed for this rare cancer.

5.10 Preparation for CRT:

5.10.1 Patients with advanced tumours causing obstruction, incontinence, extensive pain and skin ulceration and female patients with vaginal invasion should be defunctioned. An end colostomy is usually performed, as the likelihood of these patients being subsequently reversed is small (approximately 20%).

5.10.2 Sperm banking should be offered to male patients if appropriate.

5.10.3 PAP smear of the uterine cervix should be performed in female patients prior to commencement of radiotherapy. Patients with abnormal smears should be referred for gynaecological assessment.

5.11 CRT Protocol (based on ACT II)

5.11.1 Radiotherapy Planning

Patients will be planned using the CT simulator. Patient should be in the prone position with a distended bladder. Radio-opaque wire marker should be placed at the anal verge by the attending clinician. If tumour or soft tissue induration is visible in the perineum, the extent of these should also be marked with radio-opaque wires. Tissue equivalent bolus material of appropriate size and thickness must be made and placed over the perineum and inguinal lymph nodes (particularly in thin patients with very little subcutaneous fat) to build up the surface dose of the radiotherapy. Planning CT scan of the entire pelvis should be taken at 3 mm slice intervals, making sure the inferior limit extends at least 8 cm below the markers.

The gross tumour volume (GTV) of the primary tumour and involved lymph nodes should be contoured on the individual CT images, with the aid of the staging CT and MRI scans (18-FDG PET/CT if performed).

5.11.2 Phase I Planning Target volume (PTV)

Superior border: 1-2 cm above inferior aspect of the sacroiliac joints. The superior border of the PTV will be standardised UNLESS pelvic lymph nodes are seen on the CT/MRI scan or the primary tumour extends to within 3cm of this border, in which case the border is recommended to extend 3cm above the upper limit of known macroscopic disease.

Lateral border: To cover fully both inguinal lymph node regions. In practice, the PTV border is lateral to the acetabulum.

Inferior border: 3 cm below the anal margin (for disease confined to the anal canal only) or 3 cm below most inferior extent of tumour (for anal margin tumours).

Field arrangement: Parallel opposed anterior and posterior fields. Consider a 3 field planned volume throughout for tumours (T1 and small T2) of the anal canal at low risk of inguinal lymph node involvement.

5.11.3 Phase II PTV

This will usually be with a 3 field planned volume to include the primary tumour and involved pelvic lymph nodes, with a 3 cm margin in all directions. If the inguinal node(s) are involved, a parallel opposed anterior and posterior field arrangement (as in phase I) will have to be used.

A direct electron beam to the perineum may be possible for small tumours (T1 or small T2) at the anal margin. Some bolus will be needed to bring increase the surface dose to 100%, depending on the energy of the electrons used. There will be stand off from the electron applicator to the tumour. This will need to be taken into account when calculating the monitor units. There is also a higher risk of geographical miss if the stand off is significant. Therefore, selection of suitable patients for electrons is essential.

5.11.4 Radiotherapy dose and fractionation

Phase I	30.6 Gy in 17 fractions over 23 days
Phase II	19.8 Gy in 11 fractions over 15 days

Radiotherapy should start on a Monday (Tuesday is acceptable if Bank Holiday week).
Treat as category I (compensate for missed days).

No gap between phase I and phase II.

Clinical oncologist **must** see the patient on the treatment unit on day 1 or 2 of radiotherapy to check adequate coverage of the inferior border and to ensure appropriate placement of bolus over the perineum and any involved lymph nodes.

5.11.5 Chemotherapy

- | | |
|----------------|---|
| a. 5FU | 1000 mg/m ² iv over 24 hours
days 1-4 and 29-32 |
| b. Mitomycin C | 12 mg/m ² iv bolus
day 1 only
dose reduce to 10 mg/m ² if > 70yrs
dose reduce to 8 mg/m ² if GFR 50-59 ml/min |

- c. Chemotherapy to start at least 1 hour prior to radiotherapy, at commencement of each cycle.
- d. Chemotherapy rota reference: o-rota 92 (Mito/5FU + RT)

5.12 RT alone (T1N0M0 anal margin tumours)

Most T1 anal margin SCCs are suitable for local excision and this should be the recommended treatment. Radical radiotherapy alone may be appropriate in selected patients. A dose of 35 Gy in 5 fractions over 1 week using a direct electron field may be used. Some bolus will be needed to bring increase the surface dose to 100%, depending on the energy of the electrons used. There will be stand off from the electron applicator to the tumour. This will need to be taken into account when calculating the monitor units. There is also a higher risk of geographical miss if the stand off is significant. Therefore, the selection of suitable patients for electrons is essential.

5.13 Follow up

5.13.1 After completion of curative treatment, patients will be offered follow up by one or more members of the UHBFT MDT, however, patients who have had local excision for an early (low recurrence risk) cancer or anal intraepithelial neoplasia (AIN) may be referred back to the referring team. Patients wishing to have their follow up care locally will be referred back to their local hospital.

Patients for palliative care only will be referred back to the referring team.

- a) Follow up clinic appointment at 4-6 weeks after completion of CRT. Skin reaction may not have settled sufficiently to allow for adequate clinical evaluation of response.
- b) Assess patient by recording symptoms, bowel and urinary function, abdominal examination including palpation of inguinal lymph nodes, digital rectal examination on each clinic visit. Vaginal examination if appropriate. Continue follow up at 4-6 week intervals until complete clinical response (cCR) achieved. If at 3-4 months cCR not achieved, arrange EUA and biopsy.
- c) On achieving cCR, extend clinic appointments to 2-3 month intervals until 12 months from completion of CRT.
- d) Between 12 and 24 months, clinic appointments at 3-4 month intervals.
- e) Beyond 24 months, clinic appointments at 6 month intervals to at least 5 years.
- f) Restaging CT chest, abdomen, pelvis may be performed in high risk patients at 12 and 24 months if deemed appropriate.

5.14 Management of Treatment Failure

5.14.1 Locoregional failure (either failure to achieve cCR or locoregional recurrence following cCR) accounts for the majority of treatment failures. Very few patients develop distant metastatic disease, particularly in the absence of locoregional failure.

5.14.2 On suspicion of locoregional failure, confirmation by biopsy should be sought. The patient should be restaged with a CT scan of the chest, abdomen and pelvis. The extent of locoregional disease should be assessed by an MRI scan of the pelvis. Results of investigations should be reviewed and discussed in the Anal Cancer MDM, in order to make an appropriate management recommendation.

5.14.3 Distant metastatic disease is usually incurable but may respond temporarily to palliative chemotherapy.

5.14.4 Palliative Chemotherapy.

Patient with a good Performance Status should be offered 5FU / cisplatin (4-day).

5.14.5 Salvage Surgery should be considered for locoregional failure.

- a) EUA to confirm residual or recurrent disease by biopsy and to assess local extent of disease and surgical options.
- b) Restage with CT scan of chest, abdomen, pelvis and MRI of pelvis. If salvage resection remains an option, 18-FDG PET/CT to exclude sites of occult metastatic disease.
- c) Review and discuss in Anal Cancer MDM. Surgical procedure will need to be carefully planned with plastic surgeons and sometimes gynaecologists, urologists, vascular surgeons etc.

6. Patient Information and Counselling

6.1 All patients, and with their consent, their partners will be given access to appropriate written information during their investigation and treatment, and on diagnosis will be given the opportunity to discuss their management with a clinical nurse specialist who is a member of the relevant MDT. The patient should have a method of access to the specialist anal cancer team at all times.

6.2 Access to psychological support will be available if required. All patients should undergo a holistic needs assessment and onward referral as required.

7 Clinical Trials

- 7.1 Wherever possible, patients who are eligible should be offered the opportunity to participate in National Institute for Health Research portfolio clinical trials and other well designed studies.
- 7.2 When a trial is only open at one Trust in the Network, patients should be offered referral for trial entry. A list of studies available at each Trust is available from Pan Birmingham Cancer Research Network. Email: PBCRN@westmidlands.nhs.uk
- 7.3 Patients who have been recruited into a clinical trial will be followed up as defined in the protocol

8 Palliative Care

Palliative care services will be made available to all patients as deemed appropriate by the MDT.

Monitoring of the Guideline

Implementation of the guidance will be considered as a topic for audit by the NSSG in 2012.

References

1. NICE, 2004, Improving Outcomes in Colorectal Cancers. National Institute for Clinical Excellence, London.
2. UKCCRC. Epidermoid anal cancer: results from the UKCCCR randomised trial of radiotherapy alone versus radiotherapy, 5-fluorouracil, and mitomycin. UKCCCR Anal Cancer Trial Working Party. UK Co-ordinating Committee on Cancer Research. Lancet 1996; 348: 1049-54.
3. Bartelink H, Roelofsen F, Eschwege F et al. Concomitant radiotherapy and chemotherapy is superior to radiotherapy alone in the treatment of locally advanced anal cancer: results of a phase III randomized trial of the European Organization for Research and Treatment of Cancer Radiotherapy and Gastrointestinal Cooperative Groups. J Clin Oncol 1997; 15: 2040-9.
4. R. James, S. Wan, R. Glynne-Jones A randomized trial of chemoradiation using mitomycin or cisplatin, with or without maintenance cisplatin/5FU in squamous cell carcinoma of the anus (ACT II). J Clin Oncol 2009; 27:18 (suppl; abstr LBA4009).

Authors

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Approval Date of Network Site Specific Group Date May 2010

Approval Date by the Clinical Governance Committee Date June 2010

Approval Signatures

Pan Birmingham Cancer Network Clinical Governance Committee Chair

Name: Doug Wulff



Signature Date June 2010

Pan Birmingham Cancer Network Manager

Name: Karen Metcalf



Signature Date June 2010

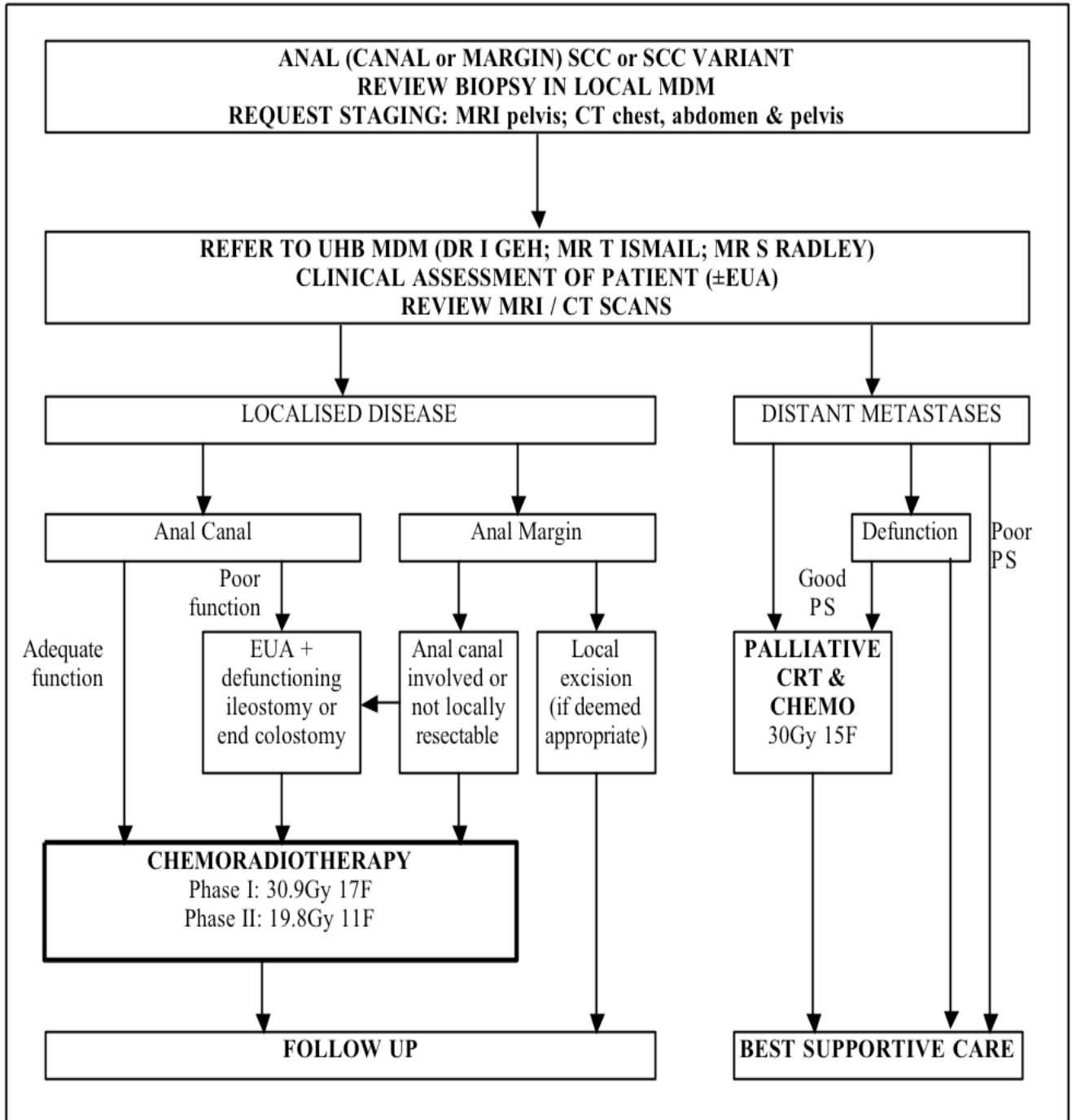
Network Site Specific Group Clinical Chair

Name: Rob Church

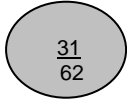


Signature Date June 2010

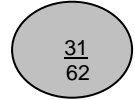
Appendix 1 – Anal Cancer Decision Tree



Appendix 2 – 2 WW form



URGENT



URGENT

URGENT REFERRAL FOR SUSPECTED COLORECTAL CANCER (Version 2.0)

If you wish to include an accompanying letter, please do so. *On completion please FAX to the number below.*

These forms should only be used for suspected cancer and in conjunction with the NICE Referral Guidelines for Suspected Cancer, June 2005

Patient Details

GP Details (inc Fax Number)

Surname	Gender	Fax No:
Forename		
D.O.B.		
Address		
Postcode		Date of Decision to Refer
Telephone		Date of Referral
NHS No		GP Signature
Hospital No		
Interpreter?		

Do not use this form for patients who do not meet the criteria. Please use a routine letter.

Relevant information: (Check as appropriate)

Notes

- 6 weeks rectal bleeding > 60 years
- 6 weeks change in bowel habit (looser stools/ increased stool frequency) > 60 years
- 6 weeks bleeding and change of bowel habit (looser stools/ increased stool frequency) > 40 years
- Right sided abdominal mass
- Rectal mass
- Unexplained iron deficiency anaemia (<11g males and <10g in post menopausal females)

Clinical Details

History/Examination/Investigations.....

Medication

Diabetes mellitus? Y / N Insulin? Y / N Oral hypoglycaemic? Y / N

For Hospital Use

Appointment Date Clinic Attending

Was the referral appropriate Yes No (if no please give reason)

COLORECTAL CLINICS WITH RAPID ACCESS FACILITIES

Hospital	Tel	Fax
City	0121 507 5805	0121 507 5075
Good Hope	0121 424 7476	0121 424 7376
Heartlands and Solihull	0121 424 5000	0121 424 5001
Queen Elizabeth (UHBFT)	0121 627 2485	0121 460 5800
Sandwell	0121 507 3834	0121 507 3723
Walsall Manor	01922 721172 ext 6876 or 7227	01922 656773

- Please discard all other Colorectal Urgent Referral Forms -