Care pathway: Anorectal mucosal melanoma

Possible Anorectal mucosal melanoma?
Refer to Box 1

REFERRAL

Refer to a colorectal surgeon or a pigmented lesion clinic via the urgent cancer referral pathway (e.g. the 2-week wait pathway). [In regions benefiting from local dermatological expertise, it is acceptable for suspicious skin lesions in the perianal area to be referred to a dermatologist rather than a colorectal surgeon.]

DIAGNOSIS

- Make diagnosis of the primary by excision or punch biopsy depending on the size and site of the lesion.
- Patients who present with an anorectal lesion and palpable groin lymph node(s) should have pathological confirmation either by FNA or core biopsy of the suspicious node(s).

DIAGNOSIS OF ANORECTAL MUCOSAL MELANOMA

- YES
- NO → Follow other guidelines

STAGING INVESTIGATIONS

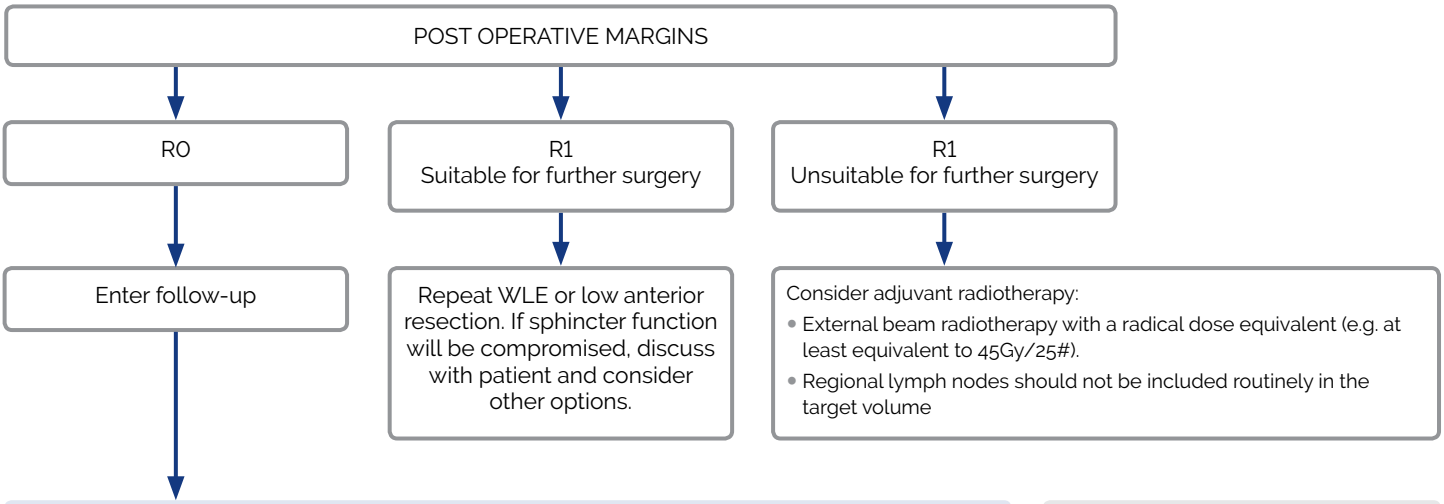
- Local staging should be as for common tumours at the anatomical site (anus, rectum) and include:
  - External inspection/examination
  - Palpation of inguinal lymph nodes
  - Digital examination
  - EUA
  - Proctoscopy +/- flexible sigmoidoscopy
  - MRI pelvis.
- Investigations looking for systemic disease are those generic for all anatomical sites including CT of the thorax, abdomen, and pelvis, including the groins. Consider MRI or CT of brain.
- If major surgery (i.e. surgery involving more than WLE and/or lymph node dissection) is being considered perform a PET-CT scan.
- Record histological features – see Box 2
- Molecular Testing should occur as soon as practical, ideally at the time of first diagnosis.
- Test for BRAF, C-KIT, NRAS, GNAQ, GNA11.

SURGICAL PLANNING

- Surgery to be carried out only in centres regularly performing complex anorectal surgery and regularly managing complex melanoma within a specialist melanoma MDT
- Assess patient's baseline anorectal function
- Assess resectability on the basis of the staging investigations
- The aim is to achieve an R0 (microscopically clear > 1mm) margin in the least radical fashion (i.e. with local excision).
- Sentinel lymph node biopsy is only recommended if it directs adjuvant treatment or clinical trial entry. Following a positive sentinel node there is the option of following the patient by clinical examination +/- ultrasound. Completion of the nodal dissection should be performed depending on emerging data and/or consensus opinion.

- WLE predicted to impact significantly on continence
  - NO
    - Resectable with no locoregional lymph nodes → WLE aiming for R0 margin
    - Resectable with metastatic regional lymph nodal disease → WLE aiming for R0 margin + lymphadenectomy
  - YES → Discuss with patient → Consider an APR
- Resectable with isolated mesorectal lymph nodes → Perform PET-CT and MRI of the brain to exclude low volume metastatic disease → Consider low anterior resection or APR
- Irresectable or metastatic disease → Consider other management options including:
  - Systemic therapies (see recommendations for metastatic disease)
  - Close observation depending on the clinical scenario
  - Surgery only for palliation
  - Adjuvant radiotherapy:
    - External beam radiotherapy with a radical dose equivalent (e.g. at least equivalent to 45Gy/25#)
    - Regional lymph nodes should not be included routinely in the target volume

POST OPERATIVE MARGINS



FOLLOW-UP

- All patients should have rapid access to clinical review between appointments or after discharge if they have any concerns
- If appropriate, discuss the advantages and disadvantages of surveillance imaging as set out in NG14 1.9.16 http://optiongrid.org/option-grids/pdf/63/en_gb
- All patients following potentially curative treatment or treatment for relapse should be followed up as follows:

Site of relapse	First three years	Years 3-5
Loco-regional	3 monthly clinical examination including: • External inspection/examination • Palpation of inguinal lymph nodes • Digital examination • Proctoscopy • Sigmoidoscopy (as required)	6 monthly clinical examination including: • External inspection/examination • Palpation of inguinal lymph nodes • Digital examination
Systemic	• 3-monthly clinical examination according to that used for other malignant tumours at the primary site • Baseline CT thorax, abdomen, pelvis including groins 2-3 months post-surgery • 6-monthly CT thorax, abdomen, pelvis including groins • 6-monthly CT or MRI of brain (to be discussed with the patient)	• 6-monthly clinical examination according to that used for other malignant tumours at the primary site • 12-monthly CT thorax, abdomen and pelvis including groins • 12-monthly CT or MRI of brain (to be discussed with the patient).

- From years 6-10 patients should be given an annual appointment for clinical examination or open rapid access if available
- Patients should be discharged at year 10

ADJUVANT SYSTEMIC TREATMENT

- Choice guided by the most contemporary data.
- Emerging data in cutaneous melanoma supports the use of immunotherapy agents and BRAF targeted treatments in the adjuvant setting and consideration should be given for its use in AUG melanoma.

BOX 1

SIGNS AND SYMPTOMS OF POSSIBLE AR MELANOMA

- Bleeding per rectum
- Pain
- Mass or swelling
- Palpable lymph nodes (e.g. in the groin) associated with anal symptoms
- Irregularly outlined pigmented or non-pigmented macule, papule, patch or nodule with or without ulceration
- Atypical haemorrhoids
- Polyps
- Unexplained lumps

Be aware that the presenting symptoms of anorectal melanoma may be similar to those of rectal cancer. The following may also be symptoms of ano-rectal melanoma:

- Change in continence
- Persistent itching (pruritus)
- Constipation/diarrhoea (change in bowel habit)
- Tenesmus

BOX 2

The following histological features of the primary should be included in all reports:

- macroscopic size of the tumour
- vertical tumour depth
- presence/absence of ulceration
- cytomorphological subtype (i.e. spindle, epithelioid, mixed)
- presence/absence of perineural and/or lymphatic invasion
- involvement of surrounding structures;
- confirmation of the diagnosis of melanoma with immunostaining with a melanocytic marker;
- involvement (or not) of surgical resection margins with either invasive melanoma or melanoma in situ: this may often require immunostaining with a melanocytic marker where there are surgery-induced artefacts.

Additional features such as presence/absence of pigmentation, presence/absence of necrosis, presence/absence and the composition of an accompanying inflammatory infiltrate could also be noted

The presence/absence of lymph node/distant metastases should be recorded according to the anatomical site using the 'N' and 'M' components of the AJCC/TNM system, as if the melanoma were a carcinoma

METASTATIC DISEASE

Treatment

1. The choice of systemic treatment should be guided by the most contemporary data.
2. Use single agent anti- PD1 antibodies in patients with unresectable Stage III or Stage IV tumours, taking into account any contraindications to this therapy.
3. Consider combination immunotherapy, e.g. anti-CTLA and anti-PD(L)1 monoclonal antibodies in selected fit patients.
4. The data demonstrates lower response rates from immunotherapy in mucosal melanoma compared to cutaneous melanoma therefore the significant toxicity of combination immunotherapy needs to be carefully discussed with the patient.
5. Consider BRAF + MEK inhibitors as a treatment option for the small number of patients with BRAF mutated unresectable Stage III or Stage IV AUG melanoma.
6. In patients with targetable mutations, consider immunotherapy as the preferred first line option unless the patient has a poor performance status and/or symptomatic bulky disease. However, this is a grey area and the correct sequence of immunotherapy/ targeted therapy is yet to be robustly defined by clinical trials.
7. Not all C-KIT mutations are successfully targeted. Therefore if one is identified, the patient needs to be carefully counselled that testing for a C-KIT mutation may not change their management. Funding for a C-KIT inhibitor would have to be sought and might not be obtained. This also needs to be discussed with the patient. However, the presence of a C-KIT mutation may facilitate entry into clinical trials.
8. There is insufficient evidence to recommend the routine use of chemotherapy or bio-chemotherapy in the treatment of metastatic disease. Such evidence as there is suggests low response rates.
9. Palliative radiotherapy can be considered alongside immunotherapy without interruption of the immunotherapy. Patients receiving BRAF inhibitors and palliative radiotherapy should have their systemic therapy withheld during RT. There is currently no data to suggest increased rates of toxicity. This is a consensus view which is the subject of ongoing research.
10. Other palliative options for skin metastases that could be considered include
    - Electrochemotherapy for metastases in the skin from tumours of non-skin origin and melanoma (IPG446) https://www.nice.org.uk/guidance/ipg446
    - Talimogene laherparepvec for treating unresectable metastatic melanoma (TA410) https://www.nice.org.uk/guidance/ta410
11. For management of supportive care refer to NICE guidance CSG4 https://www.nice.org.uk/guidance/csg4

Follow-up

If there is/has been loco-regional or metastatic disease, follow-up should include CT thorax, abdomen and pelvis including groins, and MRI or CT of brain should usually be at 3-monthly intervals for patients treated with immunotherapy, and 2-monthly intervals for those treated with targeted agents. In patients who have responded or whose disease has not progressed, after 2-3 years the interval between scans can be extended to 6 months up to year 5, and then annually up to year 10.