Uveal Melanoma National Guidelines

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Reason for development

• Concern from patient groups and clinicians regarding variation in management, referral pathways and access to treatments.

• Comparatively small evidence base compared with more common cancers yet often strong opinions regarding interventions.

• Guidelines represent an attempt to make evidence based recommendations. Where evidence lacking GDG made expert consensus statements.
Methods

• Support and funding from Melanoma Focus
• Formation of Guideline Development Group (GDG) comprised of patients, patient organisations and clinicians from the specialities caring for UM patients.
• Search, appraisal and review of evidence presented to the GDG
• Discussion of evidence and formulation of recommendations based on evidence and members experience
• Consultation on draft guideline and subsequent revisions
• Application for NICE accreditation of methods
• Publication
Guideline Development Group

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Recommendations

*Patient Choice and Shared decision-making*

- All specialist surgical ocular oncology multidisciplinary teams (MDTs) should collaborate to produce an information leaflet on the options available nationally. [GPP]

- All available procedural and treatment options, local, national and international should be discussed with the patient. [GPP]

- The risks and benefits of any procedures and treatments being considered should be fully discussed with the patient, including their impact on quality of life. [GPP]
Service Configuration

• Supra-regional specialist multi-disciplinary teams (MDT), using a network model, should be established.

• For advanced disease, the specialist MDT should include an oncologist, interventional radiologist, a diagnostic radiologist a histopathologist, a liver surgeon and a clinical nurse specialist, all with experience in treating uveal melanoma and with direct links to ocular surgical oncology centres. [GPP]

• Any molecular testing should be carried out within an accredited molecular pathology laboratory.[GPP]

• A national register, based on a standardised minimum data set, should be established where details of every patient with a diagnosis of uveal melanoma are entered, with follow-up data collected at least annually. [GPP]
General Guidance

• All local recurrences of the primary uveal melanoma should be reported to the surgical ocular oncology centre where treatment for the primary tumour took place. [GPP]

• All Optometrists and Ophthalmologists should receive training in the recognition of uveal melanoma, in order to allow earlier detection and timely referral of patients with uveal melanoma. [GPP]

• Each surgical ocular oncology centre should audit their results and share them nationally. [GPP]

• The suspected diagnosis of uveal melanoma by the referring clinician should follow the same pathways as for any other suspected cancer. The ocular oncology centre should be notified within 48 hours of presentation and the patient seen by the specialist within two weeks. Grade C
General Guidance

• Suspicious lesions or lesions diagnosed as uveal melanoma should be referred to a consultant surgical ocular oncologist in one of the surgical oncology centres for ocular malignancies. Grade D

• Specimens should be reported by an ophthalmic pathologist within a specialist centre. [GPP]

• All patients with a new diagnosis of uveal melanoma should be offered referral to a medical or clinical oncologist with a specialist interest in the disease. [GPP]

• Patients should be informed about and recruited into clinical trials wherever possible. [GPP]

• Patients should be offered the opportunity to participate in uveal melanoma specific research. With patient consent, samples should be taken surplus to diagnostic requirements and stored in an ethically-approved quality biobank for research purposes. [GPP]
Management of the Primary Tumour

• Pre-operative investigations
• Make a diagnosis of uveal melanoma using ophthalmoscopy, fundus photography and conventional ocular ultrasound. Grade A
• Ciliary body melanoma should be imaged with Ultrasound Biomicroscopy or anterior segment optical coherence tomography. Grade D
• If the clinical diagnosis is uncertain following the above-mentioned techniques then diagnostic biopsy should be considered and balanced against potential risks of the procedure [GPP]
• Fine needle aspiration biopsy can be performed either with a direct transcleral approach or using a transvitreal approach. Grade D
Management of the Primary Tumour

• *Staging before primary treatment*

• A decision on staging should be made based on the individual circumstances of the patient, but staging should not delay the primary management of the tumour. [GPP]

• Staging should be considered in the following circumstances:

• The patient is at particularly high risk because of the clinical features of their presentation.

• The patient is particularly anxious and requires reassurance [GPP]
Prognostication

Prognostic factors include clinical, morphological and genetic features. The following should be recorded:

- Age
- Gender
- Tumour location
- Tumour height
- Tumour Largest basal diameter
- Ciliary body involvement
- Extraocular melanoma growth (macroscopic)

The following features should be recorded if tissue is available:

- Cell type (modified Callender system)
- Mitotic count (number/40 high power fields in H&E stained sections)
- Presence of extravascular matrix patterns (particularly closed connective tissue loops; enhanced with Periodic acid Schiff staining). Grade A
- Presence of extraocular melanoma growth (size, presence or absence of encapsulation). [GRADE A]
Prognostication

**Prognostic biopsy**

- There should be a fully informed discussion with all patients, explaining the role of biopsy including the benefits and risks. The discussion should include:
  - Risk of having the biopsy
  - Limitations of the investigation
  - Benefits for future treatments (including possible recruitment to trials)
  - Impact on quality of life
  - Recruitment to trials
  - Follow-up [GPP]
Treatment

• Recommendations regarding:

  • Radiotherapy – Plaque Brachytherapy (Ruthenium 106, Iodine 125), Proton Beam, Stereotactic radiosurgery

  • Phototherapy – Transpupllary thermotherapy, Photodynamic Therapy

  • Surgery – Exoresection, Endoresection, Enucleation, Exenteration
Surveillance

• Led by the supra-regional specialist multidisciplinary team. [GPP]

• All patients, irrespective of risk, should have a holistic assessment to discuss the risk, benefits and consequences of entry into a surveillance programme. The discussion should consider risk of false positives, the emotional impact of screening as well as the frequency and duration of screening. An individual plan should be developed. [GPP]

• Prognostication and risk prediction should be based on the best available evidence, taking into account clinical, morphological and genetic cancer features. [GPP]

• Patients judged at high-risk of developing metastases should have 6-monthly life-long surveillance incorporating a clinical review, nurse specialist support and liver-specific imaging by a non-ionising modality. [GPP]

• Liver function tests alone are an inadequate tool for surveillance. Grade C
Metastatic disease

**Staging**

Patients should have whole body staging (chest, abdomen and pelvis) with CT scan or PET CT. Grade D

Brain imaging should not be carried out in the absence of symptoms. [GPP]

Patients who have symptomatic bony pain should have a bone scan to assess the presence of bony disease. [GPP]

Contract enhanced MRI with diffusion weight imaging should be used to stage liver disease when assessing operability. Grade D
Metastatic disease - Prognostication

This minimum data set should be collected for all patients with systemic disease (Stage IV) for future validation:
Metastatic Tumour Burden (site, diameter and number),
LDH, ALP, GGT, Bilirubin
Presence or absence of ascites
Gender
Age
Performance status,
DFS following definitive primary therapy. [GPP]

A tissue sample should be taken to confirm the diagnosis of metastatic uveal melanoma unless contraindicated. [GPP]
Curative (R0) resection is the most important positive prognostic factor following liver resection. [GPP]
Metastatic disease

• Patients should be considered for clinical trials wherever possible and be informed of available trial options at other centres. [GPP]

• Patients with good performance status (PS 0-2) who decline trials or for whom no suitable clinical trials are available should be offered systemic treatments and managed in specialist centres with appropriate oncology expertise in uveal melanoma. [GPP]

• Specialist centres should be involved in treatment decisions and review, but a patient may prefer to receive supportive care and systemic treatment locally. [GPP]

• For patients with technically resectable disease, assessment for curative intent hepatic resection should be offered. Grade D

• Pre-operative diagnostic laparoscopy should be performed in patients with radiologically resectable liver metastases, as many of these patients will have a miliary pattern of disease. Grade D
Metastatic disease

• Patients with liver predominant disease should be considered for regional therapy. Grade D

• Regional or systemic treatments may be considered in patients with liver dominant disease where resection is not suitable. [GPP]

• Loco-regional treatment for the management of oligometastatic disease (i.e. when metastases are limited to a single or limited number of organs) should be considered. This may include surgery, stereotactic treatment or other forms of ablation.[GPP]

• Ipilimumab can be offered in the UK following NICE approval of this drug for use in melanoma generically.
• *Surveillance following liver treatment*

• Patients treated with curative intent should be followed with regular (3-4 monthly) hepatic MRI and CT of chest, abdomen and pelvis. [GPP]

• Patient outcomes for this selected group should be collected centrally and prospectively. [GPP]
Summary

• Guidelines represent the first evidence based approach to identify standards of care in uveal melanoma
• UK focused but international contribution and review
• Provide support for improvement in pathways and practice

• Thank you to GDG members, Nancy Turnbull and Melanoma Focus