NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

Malignant melanoma: assessment and management of malignant melanoma

1.1 Short title

Malignant Melanoma

2 The remit

The Department of Health has asked NICE to develop a clinical guideline on assessment and management of malignant melanoma.

3 Clinical need for the guideline

3.1 Epidemiology

a) Melanoma is the third commonest skin cancer in the UK. However, it is the cause of more cancer deaths than all other skin cancers combined. In 2010 there were 2,746 deaths from skin cancer in the UK. This included 2,203 deaths from melanoma and 546 from other forms of skin cancer.

b) In 2010, 12,818 people in the UK were diagnosed with melanoma. Although the disease is more common in older age groups it is often diagnosed in younger people and is the second most common cancer in the 15 - 34 year age group.

c) The incidence of melanoma is rising rapidly and is predicted to increase by 50% in the next 15 years. This is the fastest increase in incidence for any cancer. The incidence of melanoma is strongly related to intermittent sun exposure in the fair skinned.

d) The mortality rates for melanoma are also rising rapidly especially in older men. In 2010, 62% of melanoma deaths were in people aged 65 years and over and 5% of deaths were in the 15-39 year age group.

e) There appear to be variations in survival across different cancer networks, and poorer survival may be attributable to late presentation and/or delays in diagnosis and initial treatment.

3.2 Current practice

a) The majority of melanomas are initially diagnosed by dermatologists with 41% of cases being referred via the two week wait process.

b) Primary melanoma is treated by complete excision, pathological analysis and subsequent wide local excision. There remains some uncertainty about optimal final excision margins and this topic is the subject of current research.

c) Imaging for staging purposes is not indicated for patients with stage 1 and 2 disease. In some parts of the UK, sentinel node biopsy is offered to selected patients as a staging tool but has not been shown to confer any survival advantage and there remains uncertainty about its cost effectiveness. There is thought to be variation in practice in the use of CT and PET imaging for patients with more advanced disease.

d) Adjuvant chemotherapy and immunotherapy are not indicated and continue to be the subject of research trials. Adjuvant radiotherapy for stage IIIB and IIIC melanoma is used in some centres but with little supporting evidence.

e) Cutaneous metastases are excised if it is technically feasible. Multiple cutaneous metastases confined to one limb may be treated by a number of modalities including isolated limb infusion and isolated limb perfusion.

f) Some patients with small numbers of apparently localised metastases to other organs may also be offered surgical resection, although this is not supported by randomised trial evidence.

g) Patients whose metastatic melanoma carries *BRAF* mutations may be treated with specific BRAF inhibitors (BRAFi). These drugs have a very rapid effect on tumours but unfortunately the majority of patients develop resistance and the tumour relapses. Use of the drug is associated with an increased survival of around 6 months.

h) Patients with systemic metastases whose tumours are not found to be *BRAF* mutated are usually treated with dacarbazine but response rates are low.

i) Radiotherapy may be used to treat isolated cerebral metastases and for palliation.

4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, 'Further information').

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

a) Children, young people and adults with suspected melanoma.

b) Children, young people and adults with newly diagnosed cutaneous melanoma, including vulval and penile melanoma.

c) Subgroups identified as needing specific consideration will be considered during development of the guideline.

4.1.2 Groups that will not be covered

a) People with primary ocular melanoma.

b) People with melanoma arising in mucosal sites.

4.2 Healthcare setting

a) All settings in which NHS-funded care is provided.

4.3 Clinical management

4.3.1 Key clinical issues that will be covered

a) The specific information and support needs of patients and carers with melanoma at the point of diagnosis, during and after treatment.

b) The best approach to increasing diagnostic accuracy and appropriate prompt excision.

c) The best approach for mutation testing of tumours for prognostic and predictive purposes.

d) The most effective method of staging melanoma:

   i. the role of sentinel lymph node biopsy in newly diagnosed melanoma

   ii. imaging for newly diagnosed and recurrent melanoma

e) The most effective surgical treatment for stage I-II melanoma.

f) The most effective surgical treatment for stage III melanoma.

g) The indications for adjuvant radiotherapy for stage III melanoma after resection.

h) The most effective treatment for in-transit melanoma metastases.

i) The role of surgery and stereotactic radiotherapy in stage IV melanoma.

j) The role of chemotherapy in the treatment of metastatic melanoma.

k) The optimum methods and frequency of follow-up for patients with melanoma.

l) The role of measuring Vitamin D levels and of supplementation in people who have been diagnosed with melanoma.

m) The role of imiquimod in the treatment of melanoma.

n) The risks associated with concurrent drug therapy in patients with melanoma. (for example, immunosuppressants)

4.3.2 Clinical issues that will not be covered

a) Referral from primary care with suspected malignant melanoma. [This will be covered by "Suspected Cancer" the update of "Referral guidelines for suspected cancer" (NICE clinical guideline 27).

b) Education, awareness and prevention of melanoma.

c) Ipilimumab for the treatment of Stage III or IV Melanoma. (This is the subject of an ongoing NICE technology appraisal).

d) Vemurafenib for the treatment of BRAF V600 mutation positive, unresectable metastatic melanoma. (This is the subject of an ongoing NICE technology appraisal).

e) Ipilimumab for the treatment of previously untreated unresectable stage III or IV Melanoma. (This is the subject of an ongoing NICE technology appraisal).

f) End of life care.

g) Complementary therapies.

4.4 Main outcomes

a) Overall survival.

b) Disease-free survival.

c) Melanoma-related morbidity.

d) Melanoma-related mortality.

e) Treatment-related morbidity.

f) Treatment-related mortality.

g) Psychological wellbeing.

h) Number and length of admissions to hospital after diagnosis.

i) Number and severity of adverse events.

j) Health-related quality of life.

k) Cost effectiveness

l) Patient reported outcomes

4.5 Review questions

Review questions guide a systematic review of the literature. They address only the key clinical issues covered in the scope, and usually relate to interventions, diagnosis, prognosis, service delivery or patient experience. Please note that these review questions are draft versions and will be finalised with the Guideline Development Group.

a) What are the specific information and support needs of patients and carers:

- at the point of first diagnosis
- during treatment
- after treatment (including follow-up and at discharge)?

b) What is the diagnostic accuracy of dermoscopy, history taking and visual examination for the identification of melanoma?

c) Is the accuracy of current tests for melanoma affected by reader experience? (for example comparing consultants with trainees).

d) Is photography an effective method by which to monitor progression of pigmented lesions?

e) What is the most effective testing strategy to identify tumours with genetic mutations which may respond to targeted therapies?

f) What is the most appropriate tumour block (primary or secondary) on which to carry out genetic testing to identify patients who might benefit from targeted therapies?

g) Does genetic mutation targeted therapy improve outcomes in patients with melanoma?

h) Does the timing of genetic testing influence the outcomes for a patient who may benefit from targeted therapies (early stage (I-IIIA) versus late stage (IIIB-IV)?

i) Should sentinel lymph node biopsy be available to all patients with newly diagnosed melanoma?

j) What it the most effective surgical treatment for stage I-II melanoma to achieve clear margins and improved patient outcomes?

k) What are the appropriate margins when surgically treating stage I-II melanoma?

l) What is the most effective surgical treatment for stage III melanoma?

m) Who should carry out surgery for stage III melanoma?

n) What is the effectiveness of adjuvant radiotherapy for stage III melanoma in patients who have undergone curative resection?

o) What is the most effective treatment for in-transit melanoma metastases? (For example, surgery, isolated limb infusion, isolated limb perfusion, palliative radiotherapy, cryotherapy, electro-chemotherapy)

p) What is the effectiveness of surgery or stereotactic radiotherapy compared with systemic chemotherapy in the treatment/management of stage IV melanoma?

q) How effective is surgery in the treatment of oligometastaic disease?

r) What are the factors which indicate the use of dacarbazine in patients with stage IV melanoma?

s) What is the effectiveness of temozolomide compared with dacarbazine in the treatment of patients with stage 4 metastatic melanoma? (Temozolomide is subject to agreement with the NICE Technology Appraisal programme).

t) In asymptomatic patients who have undergone treatment with curative intent for melanoma, what is the optimal method(s), frequency and duration of follow-up?

u) What is the optimal setting for follow-up of asymptomatic patients who have undergone treatment with curative intent for melanoma?

v) What are the indications for imaging for brain metastasis as part of follow-up in asymptomactic patients?

w) Is CT or MRI the most appropriate method of imaging for brain metastasis as part of follow-up for asymptomatic patients?

x) Do vitamin D levels at diagnosis and during follow up predict cancer related and/or bone related outcomes for patients with melanoma?

y) How should sub-optimal vitamin D levels be managed in patients with melanoma (including supplements and monitoring)?

z) How effective are topical treatment(s) (for example imiquimod) in the treatment of melanoma?

aa) What is the most effective approach to the management of the risks associated with concurrent drug therapies in patients diagnosed with melanoma (e.g. Immunosuppressant, L-dopa, Metformin)?

4.6 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see ‘Further information’).

4.7 Status

4.7.1 Scope

This is the consultation draft of the scope. The consultation dates are 4 January 2013 to 1 February 2013.

4.7.2 Timing

The development of the guideline recommendations will begin in May 2013.

5 Related NICE guidance

5.1 Published guidance

5.1.1 NICE guidance to be updated

This guideline will not update or replace any NICE guidance.

5.1.2 NICE guidance to be incorporated

This guideline will not incorporate any NICE guidance.

5.1.3 Other related NICE guidance

- Vemurafenib for treating locally advanced or metastatic BRAF V600 mutation-positive malignant melanoma. NICE technology appraisal guidance 269 (2012).
- Ipilimumab for previously treated advanced (unresectable or metastatic) melanoma. NICE technology appraisal guidance 268 (2012).
- Neutropenic sepsis: prevention and management of neutropenic sepsis in cancer patients. NICE clinical guideline 151 (2012).
- Opioids in palliative care: safe and effective prescribing of strong opioids for pain in palliative care of adults. NICE clinical guideline 140 (2012).
- Patient experience in adult NHS services: improving the experience of care for people using adult NHS services. NICE clinical guideline 138 (2012).
- The MIST Therapy system for the promotion of wound healing in chronic and acute wounds. NICE medical technologies guidance 5 (2011).
- Endoscopic radical ingurial lymphadenectomy. NICE interventional procedure guidance 398 (2011).
- Skin cancer prevention: Information, resources and environmental changes. NICE public health guidance 32 (2011).
- Ambulight photodynamic therapy for the treatment of non-melanoma skin cancer. NICE medical technologies guidance 6 (2011).
- Skin Tumours including melanoma. NICE cancer service guidance (2010)
- Medicines Adherence: involving patients in decisions about prescribed medicines and supporting adherence. NICE clinical guideline 76 (2009).
- Surgical site infection: prevention and treatment of surgical site infection. NICE clinical guideline 74 (2008).
- Photodynamic therapy for non-melanoma skin tumours (including premlignant and primary non-metastatic skin lesions). NICE interventional procedure guidance 155 (2006).
- Intralesional photocoagulation of subcutaneous congenital vascular disorders. NICE interventional procedure guidance 90 (2004).

- Improving supportive and palliative care for adults with cancer. NICE cancer service guidance (2004).

5.2 Guidance under development

NICE is currently developing the following related guidance (details available from the NICE website):

- Implementing Vitamin D guidance. NICE public health guidance. Publication expected June 2014.
- Melanoma (previously untreated unresectable stage III or IV) Ipilimumab. NICE technology appraisal guidance 74. Publication expected August 2013.
- Suspected Cancer: Recognition and management of suspected cancer in children, young people and adults (update).NICE clinical guideline. Publication date to be confirmed.
- Sunlight exposure: benefits and safety. NICE public health guidance. Publication date to be confirmed.
- Melanoma (Advanced & Metastatic) Temozolomide. NICE technology appraisal guidance 316 (Suspended).

6 Further information

Information on the guideline development process is provided in the following documents, available from the NICE website:

- 'How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS'
- 'The guidelines manual'.

Information on the progress of the guideline will also be available from the NICE website.