NICE National Institute for Health and Care Excellence

NICE guideline

Melanoma: assessment and management

NICE guideline

Published: 29 July 2015
www.nice.org.uk/guidance/ng14

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

Contents

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

This guideline is the basis of QS130.

Overview

This guideline covers the assessment and management of melanoma (a type of skin cancer) in children, young people and adults. It aims to reduce variation in practice and improve survival.

Who is it for?

- Healthcare professionals working in primary, secondary and tertiary care
- People with melanoma and their families and carers

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

Introduction

Melanoma is the third most common skin cancer in the UK. It accounts for more cancer deaths than all other skin cancers combined. In 2011 there were 13,348 new cases of melanoma and 2209 deaths from melanoma.

Although melanoma is more often diagnosed in older people, it is increasingly affecting younger people. More than 900 adults aged under 35 are now diagnosed with melanoma annually in the UK, and it is the second most common cancer in adults aged between 25 and 49. Melanoma therefore leads to more years of life lost overall than many more common cancers.

Most melanomas occur in people with pale skin. The risk factors are skin that tends to burn in the sun, having many moles, intermittent sun exposure and sunburn.

This guideline addresses areas where there is uncertainty or variation in practice. It contains recommendations on:

- assessing and staging melanoma, including the use of sentinel lymph node biopsy
- treating stages 0–IV melanoma, including adjuvant chemotherapy and immunotherapy
- treating in-transit melanoma metastases
- treating metastatic melanoma
- follow-up after treatment for melanoma.

The guideline also includes advice on managing vitamin D levels and drug therapy for intercurrent conditions in people diagnosed with melanoma.

The guideline covers suspected or newly diagnosed cutaneous melanoma (including vulval and penile melanoma) in children, young people and adults. However, there was insufficient high-quality evidence on which to make specific recommendations for vulval and penile melanoma.

It does not cover primary ocular melanoma or melanoma arising in mucosal sites.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

Safeguarding children

Remember that child maltreatment:

- is common
- can present anywhere
- may co-exist with other health problems, including melanoma.

See the NICE guideline on child maltreatment for clinical features that may be associated with maltreatment.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

Key priorities for implementation

The following recommendations have been identified as priorities for implementation. The full list of recommendations is in section 1.

See implementation: getting started for information about putting the recommendations on dermoscopy, managing suboptimal vitamin D levels, sentinel lymph node biopsy and completion lymphadenectomy into practice.

Communication and support

- To help people make decisions about their care, follow the recommendations on communication, information provision and support in NICE's guideline on improving outcomes for people with skin tumours including melanoma, in particular the following 5 recommendations:
  - 'Improved, preferably nationally standardised, written information should be made available to all patients. Information should be appropriate to the patients' needs at that point in their diagnosis and treatment, and should be repeated over time. The information given must be specific to the histopathological type of lesion, type of treatment, local services and any choice within them, and should cover both physical and psychosocial issues.'
  - 'Those who are directly involved in treating patients should receive specific training in communication and breaking bad news.'
  - 'Patients should be invited to bring a companion with them to consultations.'
  - 'Each LSMDT [local hospital skin cancer multidisciplinary team] and SSMDT [specialist skin cancer multidisciplinary team] should have at least one skin cancer clinical nurse specialist (CNS) who will play a leading role in supporting patients and carers. There should be equity of access to information and support regardless of where the care is delivered.'
  - 'All LSMDTs and SSMDTs should have access to psychological support services for skin cancer patients.'

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

Assessing melanoma

Dermoscopy and other visualisation techniques

- Assess all pigmented skin lesions that are either referred for assessment or identified during follow-up in secondary or tertiary care, using dermoscopy carried out by healthcare professionals trained in this technique.

Photography

- For a clinically atypical melanocytic lesion that does not need excision at first presentation in secondary or tertiary care:
  - use baseline photography (preferably dermoscopic) **and**
  - review the clinical appearance of the lesion, and compare it with the baseline photographic images, 3 months after first presentation to identify early signs of melanoma.

Taking tumour samples for genetic testing

- If targeted systemic therapy is a treatment option, offer genetic testing using:
  - a secondary melanoma tissue sample if there is adequate cellularity **or**
  - a primary melanoma tissue sample if a secondary sample is not available or is of inadequate cellularity.

Managing suboptimal vitamin D levels

- Measure vitamin D levels at diagnosis in secondary care in all people with melanoma.

Staging investigations

Sentinel lymph node biopsy

- Consider sentinel lymph node biopsy as a staging rather than a therapeutic procedure for people with stage IB–IIC melanoma with a Breslow thickness of more than 1 mm, and give them detailed verbal and written information about the possible advantages and disadvantages, using table 1.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

Table 1 Possible advantages and disadvantages of sentinel lymph node biopsy

Possible advantages of sentinel lymph node biopsy	Possible disadvantages of sentinel lymph node biopsy
The operation helps to find out whether the cancer has spread to the lymph nodes. It is better than ultrasound scans at finding very small cancers in the lymph nodes.	The purpose of the operation is not to cure the cancer. There is no good evidence that people who have the operation live longer than people who do not have it.
The operation can help predict what might happen in the future. For example, in people with a primary melanoma that is between 1 and 4 mm thick: • around 1 out of 10 die within 10 years if the sentinel lymph node biopsy is negative • around 3 out of 10 die within 10 years if the sentinel lymph node biopsy is positive.	The result needs to be interpreted with caution. Of every 100 people who have a negative sentinel lymph node biopsy, around 3 will subsequently develop a recurrence in the same group of lymph nodes.
People who have had the operation may be able to take part in clinical trials of new treatments for melanoma. These trials often cannot accept people who haven't had this operation.	A general anaesthetic is needed for the operation.
	The operation results in complications in between 4 and 10 out of every 100 people who have it.

Managing stage III melanoma

Completion lymphadenectomy

- Consider completion lymphadenectomy for people whose sentinel lymph node biopsy shows micro-metastases and give them detailed verbal and written information about the possible advantages and disadvantages, using table 2.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

Table 2 Possible advantages and disadvantages of completion lymphadenectomy

Possible advantages of completion lymphadenectomy	Possible disadvantages of completion lymphadenectomy
Removing the rest of the lymph nodes before cancer develops in them reduces the chance of the cancer returning in the same part of the body.	Lymphoedema (long-term swelling) may develop, and is most likely if the operation is in the groin and least likely in the head and neck.
The operation is less complicated and safer than waiting until cancer develops in the remaining lymph nodes and then removing them.	In 4 out of 5 people, cancer will not develop in the remaining lymph nodes, so there is a chance that the operation will have been done unnecessarily.
People who have had the operation may be able to take part in clinical trials of new treatments to prevent future melanoma. These trials often cannot accept people who have not had this operation.	There is no evidence that people who have this operation live longer than people who do not have it.
	Having any operation can cause complications.

Adjuvant radiotherapy

- Do not offer adjuvant radiotherapy to people with stage IIIB or IIIC melanoma unless a reduction in the risk of local recurrence is estimated to outweigh the risk of significant adverse effects.

Follow-up after treatment for melanoma

Follow-up for all people who have had melanoma

- Consider personalised follow-up for people who are at increased risk of further primary melanomas (for example people with atypical mole syndrome, previous melanoma, or a history of melanoma in first-degree relatives or other relevant familial cancer syndromes).

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

Follow-up after stage IIC melanoma with no sentinel lymph node biopsy or stage III melanoma

- Consider surveillance imaging as part of follow-up for people who have had stage IIC melanoma with no sentinel lymph node biopsy or stage III melanoma and who would become eligible for systemic therapy as a result of early detection of metastatic disease if:
  - there is a clinical trial of the value of regular imaging **or**
  - the specialist skin cancer multidisciplinary team agrees to a local policy and specific funding for imaging 6-monthly for 3 years is identified.

Take into account the possible advantages and disadvantages of surveillance imaging and discuss these with the person, using table 3.

Table 3 Possible advantages and disadvantages of surveillance imaging

Possible advantages of surveillance imaging (having regular scans)	Possible disadvantages of surveillance imaging (having regular scans)
If the melanoma comes back (recurrent melanoma), it is more likely to be detected sooner. It is possible that this could lead to a better outcome by allowing treatment with drugs (such as immunotherapy drugs) to start earlier.	Although early drug treatment of recurrent melanoma might improve survival, there is currently no evidence showing this.
Some people find it reassuring to have regular scans.	Some people find that having regular scans increases their anxiety.
	Scans expose the body to radiation, which can increase the risk of cancer in the future.
	Scans of the brain and neck increase the risk of developing cataracts.
	Scans of the chest cause a very small increase in the risk of thyroid cancer.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

Possible advantages of surveillance imaging (having regular scans)	Possible disadvantages of surveillance imaging (having regular scans)
	Scans may show abnormalities that are later found to be harmless, causing unnecessary investigations and anxiety.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

Stages of melanoma

The stages of melanoma referred to in this guideline were based on the American Joint Committee on Cancer's (AJCC) Melanoma of the skin staging (7th edition).

Staging of primary melanoma can be carried out in 2 steps. The initial staging is based on the histopathological features reported by the pathologist looking at the microscopic sections of the tumour. The melanoma is staged as 0–IIC, based on factors such as the thickness of the tumour and the presence or absence of ulceration. In many hospitals in the UK, this first step is followed by the option of a second, which is a sampling of the lymph nodes most likely to contain secondary melanoma cells (sentinel lymph node biopsy). If a sentinel lymph node biopsy is performed and microscopic disease is detected, the melanoma becomes stage III. If no microscopic disease is detected then the initial stage is used.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

1 Recommendations

The following guidance is based on the best available evidence. The full guideline gives details of the methods and the evidence used to develop the guidance.

These recommendations cover suspected and diagnosed melanoma. All recommendations relate to children, young people and adults unless specified otherwise.

People have the right to be involved in discussions and make informed decisions about their care, as described in NICE's information on making decisions about your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.1 Communication and support

1.1.1 To help people make decisions about their care, follow the recommendations on communication, information provision and support in NICE's guideline on improving outcomes for people with skin tumours including melanoma, in particular the following 5 recommendations:

- 'Improved, preferably nationally standardised, written information should be made available to all patients. Information should be appropriate to the patients' needs at that point in their diagnosis and treatment, and should be repeated over time. The information given must be specific to the histopathological type of lesion, type of treatment, local services and any choice within them, and should cover both physical and psychosocial issues.'
- 'Those who are directly involved in treating patients should receive specific training in communication and breaking bad news.'
- 'Patients should be invited to bring a companion with them to consultations.'

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

- 'Each LSMDT [local hospital skin cancer multidisciplinary team] and SSMDT [specialist skin cancer multidisciplinary team] should have at least one skin cancer clinical nurse specialist (CNS) who will play a leading role in supporting patients and carers. There should be equity of access to information and support regardless of where the care is delivered.'

- 'All LSMDTs and SSMDTs should have access to psychological support services for skin cancer patients.'

1.1.2 Follow the recommendations on follow-up in NICE's guideline on improving outcomes for people with skin tumours including melanoma, in particular the following 2 recommendations:

- 'All patients should be given written instruction on how to obtain quick and easy access back to see a member of the LSMDT/SSMDT when necessary.'

- 'All patients should be given both oral and written information about the different types of skin cancer and instruction about self-surveillance.'

1.1.3 Give people with melanoma and their families or carers advice about protecting against skin damage caused by exposure to the sun while avoiding vitamin D depletion.

1.1.4 Carry out a holistic needs assessment to identify the psychosocial needs of people with melanoma and their needs for support and education about the likelihood of recurrence, metastatic spread, new primary lesions and the risk of melanoma in their family members.

1.1.5 Follow the recommendations on communication and patient-centred care in NICE's guideline on patient experience in adult NHS services.

1.2 Assessing melanoma

Dermoscopy and other visualisation techniques

See implementation: getting started for information about putting recommendation 1.2.1 into practice.

1.2.1 Assess all pigmented skin lesions that are either referred for assessment or identified during follow-up in secondary or tertiary care, using dermoscopy

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

carried out by healthcare professionals trained in this technique.

1.2.2 Do not routinely use confocal microscopy or computer-assisted diagnostic tools to assess pigmented skin lesions.

Photography

1.2.3 For a clinically atypical melanocytic lesion that does not need excision at first presentation in secondary or tertiary care:

- use baseline photography (preferably dermoscopic) **and**
- review the clinical appearance of the lesion, and compare it with the baseline photographic images, 3 months after first presentation to identify early signs of melanoma.

Assessing and managing atypical spitzoid lesions

1.2.4 Discuss all suspected atypical spitzoid lesions at the specialist skin cancer multidisciplinary team meeting.

1.2.5 Make the diagnosis of a spitzoid lesion of uncertain malignant potential on the basis of the histology, clinical features and behaviour.

1.2.6 Manage a spitzoid lesion of uncertain malignant potential as melanoma.

Taking tumour samples for genetic testing

1.2.7 If targeted systemic therapy is a treatment option, offer genetic testing using:

- a secondary melanoma tissue sample if there is adequate cellularity **or**
- a primary melanoma tissue sample if a secondary sample is not available or is of inadequate cellularity.

Genetic testing in early-stage melanoma

1.2.8 Do not offer genetic testing of stage IA–IIB primary melanoma at presentation except as part of a clinical trial.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

1.2.9 Consider genetic testing of stage IIC primary melanoma or the nodal deposits or in-transit metastases for people with stage III melanoma.

1.2.10 If insufficient tissue is available from nodal deposits or in-transit metastases, consider genetic testing of the primary tumour for people with stage III melanoma.

1.3 Managing suboptimal vitamin D levels

See implementation: getting started for information about putting recommendations 1.3.1 and 1.3.2 into practice.

1.3.1 Measure vitamin D levels at diagnosis in secondary care in all people with melanoma.

1.3.2 Give people whose vitamin D levels are thought to be suboptimal advice on vitamin D supplementation and monitoring in line with local policies and NICE's guideline on vitamin D.

1.4 Managing concurrent drug treatment

1.4.1 Do not withhold or change drug treatment for other conditions, except immunosuppressants, on the basis of a diagnosis of melanoma.

1.4.2 Consider minimising or avoiding immunosuppressants for people with melanoma.

1.5 Staging investigations

Sentinel lymph node biopsy

See implementation: getting started for information about putting recommendation 1.5.2 into practice. NICE has also produced an option grid to support discussions with people about sentinel lymph node biopsy.

1.5.1 Do not offer imaging or sentinel lymph node biopsy to people who have stage IA melanoma or those who have stage IB melanoma with a Breslow thickness of 1 mm or less.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

1.5.2 Consider sentinel lymph node biopsy as a staging rather than a therapeutic procedure for people with stage IB–IIC melanoma with a Breslow thickness of more than 1 mm, and give them detailed verbal and written information about the possible advantages and disadvantages, using table 4.

Table 4 Possible advantages and disadvantages of sentinel lymph node biopsy

Possible advantages of sentinel lymph node biopsy	Possible disadvantages of sentinel lymph node biopsy
The operation helps to find out whether the cancer has spread to the lymph nodes. It is better than ultrasound scans at finding very small cancers in the lymph nodes.	The purpose of the operation is not to cure the cancer. There is no good evidence that people who have the operation live longer than people who do not have it.
The operation can help predict what might happen in the future. For example, in people with a primary melanoma that is between 1 and 4 mm thick: • around 1 out of 10 die within 10 years if the sentinel lymph node biopsy is negative • around 3 out of 10 die within 10 years if the sentinel lymph node biopsy is positive.	The result needs to be interpreted with caution. Of every 100 people who have a negative sentinel lymph node biopsy, around 3 will subsequently develop a recurrence in the same group of lymph nodes.
People who have had the operation may be able to take part in clinical trials of new treatments for melanoma. These trials often cannot accept people who haven't had this operation.	A general anaesthetic is needed for the operation.
	The operation results in complications in between 4 and 10 out of every 100 people who have it.

Imaging

1.5.3 Offer CT staging to people with stage IIC melanoma who have not had sentinel

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

lymph node biopsy, and to people with stage III or suspected stage IV melanoma.

1.5.4 Include the brain as part of imaging for people with suspected stage IV melanoma.

1.5.5 Consider whole-body MRI for children and young people (from birth to 24 years) with stage III or suspected stage IV melanoma.

1.6 Managing stages 0–II melanoma

Excision

1.6.1 Consider a clinical margin of at least 0.5 cm when excising stage 0 melanoma.

1.6.2 If excision for stage 0 melanoma does not achieve an adequate histological margin, discuss further management with the multidisciplinary team.

1.6.3 Offer excision with a clinical margin of at least 1 cm to people with stage I melanoma.

1.6.4 Offer excision with a clinical margin of at least 2 cm to people with stage II melanoma.

Imiquimod for stage 0 melanoma

In July 2015 the use of topical imiquimod in recommendations 1.6.5 to 1.6.6 and 1.7.7 to 1.7.8 was off label for these indications and for use in children and young people. See NICE's information on prescribing medicines.

1.6.5 Consider topical imiquimod to treat stage 0 melanoma in adults if surgery to remove the entire lesion with a 0.5 cm clinical margin would lead to unacceptable disfigurement or morbidity.

1.6.6 Consider a repeat skin biopsy for histopathological assessment after treatment with topical imiquimod for stage 0 melanoma, to check whether it has been effective.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

1.7 Managing stage III melanoma

Completion lymphadenectomy

See implementation: getting started for information about putting recommendation 1.7.1 into practice. NICE has also produced an option grid to support discussions with people about completion lymphadenectomy.

1.7.1 Consider completion lymphadenectomy for people whose sentinel lymph node biopsy shows micro-metastases and give them detailed verbal and written information about the possible advantages and disadvantages, using table 5.

Table 5 Possible advantages and disadvantages of completion lymphadenectomy

Possible advantages of completion lymphadenectomy	Possible disadvantages of completion lymphadenectomy
Removing the rest of the lymph nodes before cancer develops in them reduces the chance of the cancer returning in the same part of the body.	Lymphoedema (long-term swelling) may develop, and is most likely if the operation is in the groin and least likely in the head and neck.
The operation is less complicated and safer than waiting until cancer develops in the remaining lymph nodes and then removing them.	In 4 out of 5 people, cancer will not develop in the remaining lymph nodes, so there is a chance that the operation will have been done unnecessarily.
People who have had the operation may be able to take part in clinical trials of new treatments to prevent future melanoma. These trials often cannot accept people who have not had this operation.	There is no evidence that people who have this operation live longer than people who do not have it.
	Having any operation can cause complications.

Lymph node dissection

1.7.2 Offer therapeutic lymph node dissection to people with palpable stage IIIB–IIIC melanoma or nodal disease detected by imaging.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

Adjuvant radiotherapy

1.7.3 Do not offer adjuvant radiotherapy to people with stage IIIA melanoma.

1.7.4 Do not offer adjuvant radiotherapy to people with stage IIIB or IIIC melanoma unless a reduction in the risk of local recurrence is estimated to outweigh the risk of significant adverse effects.

Palliative treatment for in-transit metastases

1.7.5 Refer the care of all people with newly diagnosed or progressive in-transit metastases to the specialist skin cancer multidisciplinary team (SSMDT).

1.7.6 If palliative treatment for in-transit metastases is needed, offer palliative surgery as a first option if surgery is feasible.

1.7.7 If palliative surgery is not feasible for people with in-transit metastases, consider the following options:

- systemic therapy (for more information see recommendations 1.8.5–1.8.9)
- isolated limb infusion
- isolated limb perfusion
- radiotherapy
- electrochemotherapy in line with NICE's interventional procedure guidance on electrochemotherapy for metastases in the skin from tumours of non-skin origin and melanoma
- CO_2 laser
- a topical agent such as imiquimod.

Palliative treatment for superficial skin metastases

1.7.8 Consider topical imiquimod to palliate superficial melanoma skin metastases.

For all technology appraisal guidance relevant to this section, see therapies for unresectable or metastatic stage III melanoma in the NICE Pathway on melanoma.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

Genomic biomarker-based treatment

The point at which to use genomic biomarker-based therapy in solid tumour treatment pathways is uncertain. See treating stage III melanoma in the NICE Pathway on melanoma.

1.8 Managing stage IV melanoma

Management of oligometastatic stage IV melanoma

1.8.1 Refer the care of people who appear to have oligometastatic melanoma to the specialist skin cancer multidisciplinary team (SSMDT) for recommendations about staging and management.

1.8.2 Consider surgery or other ablative treatments (including stereotactic radiotherapy or radioembolisation) to prevent and control symptoms of oligometastatic stage IV melanoma in consultation with site-specific MDTs (such as an MDT for the brain or for bones).

Brain metastases

1.8.3 Discuss the care of people with melanoma and brain metastases with the SSMDT.

1.8.4 Refer people with melanoma and brain metastases that might be suitable for surgery or stereotactic radiotherapy to the brain and other central nervous system tumours MDT for a recommendation about treatment.

Systemic anticancer treatment

Targeted treatments

1.8.5 For adults, see NICE's technology appraisal guidance on dabrafenib for treating unresectable or metastatic BRAF V600 mutation-positive melanoma.

Dabrafenib has a marketing authorisation in the UK in monotherapy for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation.

1.8.6 For adults, 'Vemurafenib is recommended as an option for treating BRAF V600

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

mutation-positive unresectable or metastatic melanoma only if the manufacturer provides vemurafenib with the discount agreed in the patient access scheme'. [This recommendation is from NICE's technology appraisal guidance on vemurafenib for treating locally advanced or metastatic BRAF V600 mutation-positive malignant melanoma.]

Vemurafenib has a UK marketing authorisation for 'the treatment of adult patients with BRAF V600 mutation-positive unresectable or metastatic melanoma'.

Immunotherapy

1.8.7 For adults, see NICE's technology appraisal guidance on ipilimumab for previously treated advanced (unresectable or metastatic) melanoma and ipilimumab for previously untreated advanced (unresectable or metastatic) melanoma.

Ipilimumab has a UK marketing authorisation for 'the treatment of advanced (unresectable or metastatic) melanoma in adults'.

Cytotoxic chemotherapy

1.8.8 Consider dacarbazine for people with stage IV metastatic melanoma if immunotherapy or targeted therapy are not suitable.

In July 2015 this use was common in UK clinical practice, but was an off-label use of dacarbazine. See NICE's information on prescribing medicines.

1.8.9 Do not routinely offer further cytotoxic chemotherapy for stage IV metastatic melanoma to people previously treated with dacarbazine except in the context of a clinical trial.

For all technology appraisal guidance relevant to this section, see systemic anticancer therapies for stage IV melanoma in the NICE Pathway on melanoma.

Genomic biomarker-based treatment

The point at which to use genomic biomarker-based therapy in solid tumour treatment pathways is uncertain. See treating stage IV melanoma in the NICE Pathway on melanoma.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

1.9 Follow-up after treatment for melanoma

Follow-up for all people who have had melanoma

1.9.1 Perform a full examination of the skin and regional lymph nodes at all follow-up appointments.

1.9.2 Consider personalised follow-up for people who are at increased risk of further primary melanomas (for example people with atypical mole syndrome, previous melanoma, or a history of melanoma in first-degree relatives or other relevant familial cancer syndromes).

1.9.3 Consider including the brain for people having imaging as part of follow-up after treatment for melanoma.

1.9.4 Consider imaging the brain if metastatic disease outside the central nervous system is suspected.

1.9.5 Consider CT rather than MRI of the brain for adults having imaging as part of follow-up or if metastatic disease is suspected.

1.9.6 Consider MRI rather than CT of the brain for children and young people (from birth to 24 years) having imaging as part of follow-up or if metastatic disease is suspected.

1.9.7 Provide psychosocial support for the person with melanoma and their family or carers at all follow-up appointments.

1.9.8 All local follow-up policies should include reinforcing advice about self-examination (in line with recommendation 1.1.2), and health promotion for people with melanoma and their families, including sun awareness, avoiding vitamin D depletion (in line with recommendation 1.1.3), and NICE's guideline on stop smoking interventions and services.

1.9.9 Continue to manage drug treatment for other conditions in line with recommendations 1.4.1 and 1.4.2 after treatment for melanoma.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

Follow-up after stage 0 melanoma

1.9.10 Discharge people who have had stage 0 melanoma after completion of treatment and provide advice in line with recommendation 1.9.8.

Follow-up after stage IA melanoma

1.9.11 For people who have had stage IA melanoma, consider follow-up 2–4 times during the first year after completion of treatment and discharging them at the end of that year.

1.9.12 Do not routinely offer screening investigations (including imaging and blood tests) as part of follow-up to people who have had stage IA melanoma.

Follow-up after stages IB–IIB melanoma or stage IIC melanoma (fully staged using sentinel lymph node biopsy)

1.9.13 For people who have had stages IB–IIB melanoma or stage IIC melanoma with a negative sentinel lymph node biopsy, consider follow-up every 3 months for the first 3 years after completion of treatment, then every 6 months for the next 2 years, and discharging them at the end of 5 years.

1.9.14 Do not routinely offer screening investigations (including imaging and blood tests) as part of follow-up to people who have had stages IB–IIB melanoma or stage IIC melanoma with a negative sentinel lymph node biopsy.

Follow-up after stage IIC melanoma with no sentinel lymph node biopsy or stage III melanoma

1.9.15 For people who have had stage IIC melanoma with no sentinel lymph node biopsy, or stage III melanoma, consider follow-up every 3 months for the first 3 years after completion of treatment, then every 6 months for the next 2 years, and discharging them at the end of 5 years.

1.9.16 Consider surveillance imaging as part of follow-up for people who have had stage IIC melanoma with no sentinel lymph node biopsy or stage III melanoma and who would become eligible for systemic therapy as a result of early detection of metastatic disease if:

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

- there is a clinical trial of the value of regular imaging **or**
- the specialist skin cancer multidisciplinary team agrees to a local policy and specific funding for imaging 6-monthly for 3 years is identified.

Take into account the possible advantages and disadvantages of surveillance imaging and discuss these with the person, using table 6. NICE has also produced an option grid to support these discussions.

Table 6 Possible advantages and disadvantages of surveillance imaging

Possible advantages of surveillance imaging (having regular scans)	Possible disadvantages of surveillance imaging (having regular scans)
If the melanoma comes back (recurrent melanoma), it is more likely to be detected sooner. It is possible that this could lead to a better outcome by allowing treatment with drugs (such as immunotherapy drugs) to start earlier.	Although early drug treatment of recurrent melanoma might improve survival, there is currently no evidence showing this.
Some people find it reassuring to have regular scans.	Some people find that having regular scans increases their anxiety.
	Scans expose the body to radiation, which can increase the risk of cancer in the future.
	Scans of the brain and neck increase the risk of developing cataracts.
	Scans of the chest cause a very small increase in the risk of thyroid cancer.
	Scans may show abnormalities that are later found to be harmless, causing unnecessary investigations and anxiety.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

Follow-up after stage IV melanoma

1.9.17 Offer personalised follow-up to people who have had stage IV melanoma.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

2 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future.

2.1 Techniques for confirming a diagnosis in people with suspected atypical spitzoid melanocytic lesions

In people with reported atypical spitzoid lesions, how effective are fluorescence in-situ hybridization (FISH), comparative genomic hybridization (CGH) and tests to detect driver mutations compared with histopathological examination alone in predicting disease-specific survival?

This should be investigated in a prospective diagnostic study. Secondary outcomes should include sensitivity, specificity, accuracy, positive predictive value, disease-specific survival and progression-free survival.

Why this is important

Atypical spitzoid lesions continue to be diagnostically challenging. There are no reliably reproducible histological, immunohistochemistry or molecular features that allow exact typing and prognostic assessment of these lesions. The current 'gold standard' is histological examination with expert review, but it is not always possible to distinguish spitzoid melanoma from benign spitzoid melanocytic lesions.

Current molecular technologies such as FISH and CGH provide some help, but the results are difficult to interpret and may not be conclusive. Understanding and mapping changes in molecular pathways could predict outcome and inform individual treatment planning.

2.2 Surgical excision for people with lentigo maligna

For people with lentigo maligna (stage 0 in sun-damaged skin, usually on the face) how effective is Mohs micrographic surgery, compared with excision with a 0.5 cm clinical margin, in preventing biopsy-proven local recurrence at 5 years?

This should be investigated in a randomised controlled trial. Secondary outcomes should include

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

cosmetic and functional outcomes.

Why this is important

Mohs micrographic surgery is a microscopically controlled surgical technique designed to allow complete excision of the tumour with minimal tissue loss. The technique can be useful for people with lentigo maligna because their lesions can be very large and located in a cosmetically sensitive site where surgery may cause significant scarring. However, the histological detection of small numbers of melanocytes at the edge of a sample is difficult, and can lead to false negative results. In addition, lentigo maligna may occur in an area of field change with a risk of skip lesions at the edge. Therefore, although Mohs micrographic surgery may ensure complete excision of lentigo maligna, it can be accompanied by the recurrence of a similar lesion in adjacent skin.

2.3 Follow-up surveillance imaging

In people treated for high-risk stage II and III melanoma, does regular surveillance imaging improve melanoma-specific survival compared with routine clinical follow-up alone?

This should be investigated in a randomised controlled trial. Secondary outcomes should include time to recurrence, site of recurrence, proportion of people receiving active therapy at recurrence, cost effectiveness and quality of life.

Why this is important

Until recently there have been no effective therapies for metastatic melanoma and no strong rationale for early detection of relapse through surveillance imaging. However, new, effective targeted treatments and immunotherapy agents are now available and further treatments are likely to become available in the near future. In particular, immunotherapy can offer long-term disease-free survival but takes a number of months to take effect. In this situation, early detection of relapse may identify people likely to be fit enough to receive the treatment for long enough to benefit.

Although early detection of relapse through surveillance imaging might appear likely to improve outcomes, there is no evidence to confirm this. In addition, routine imaging has resource implications and involves more hospital visits and increased radiation exposure for the person.

2.4 Vitamin D supplementation

In people with stage I–III melanoma does vitamin D supplementation improve overall survival?

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

This should be investigated in a placebo-controlled randomised trial. Secondary outcomes should include disease-specific survival and toxicity, including the development of renal stones and hypercalcaemia.

Why this is important

It has been reported that suboptimal levels of vitamin D at diagnosis are common in people with melanoma from the north of England and that higher levels are associated with lower melanoma-related mortality. However, vitamin D levels are higher in leaner, fitter people and the nature of the relationship between vitamin D levels and melanoma survival is unclear.

There are 2 adjuvant trials of vitamin D supplementation listed as active currently, 1 in Italy and 1 in Australia. However, there are many uncertainties about the design of vitamin D trials, which might become clearer in the next few years. These include the dose of vitamin D, use of concurrent aspirin therapy and the baseline level at which vitamin D supplementation would be started.

2.5 The effect of drug therapy for concurrent conditions on melanoma survival

In people diagnosed with melanoma what is the effect of drug therapy to treat concurrent conditions on disease-specific survival?

This should be investigated in a national prospective cohort study. Secondary outcomes should include overall survival and quality of life.

Why this is important

Drugs such as immunosuppressants and those used to treat conditions such as diabetes have effects that may affect survival in people with melanoma. For example metformin, the most frequently prescribed drug for type 2 diabetes, is thought to reduce overall cancer rates in people with diabetes but to increase mortality from melanoma in the approximately 40% of these people who have a somatic BRAF mutation.

There is a need to balance the risk of melanoma deaths with the benefits from the most effective treatment of the concurrent conditions. But there is currently no evidence to inform this decision.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

Implementation: getting started

While developing this guideline, the Guideline Development Group identified 10 recommendations in 6 areas as key priorities for implementation. This section highlights 3 of those areas that could have a significant impact on practice and be challenging to implement. They have been identified with the help of stakeholders and members of the Guideline Development Group, using the criteria outlined in developing NICE guidelines: the manual, section 9.4. See the section on Finding more information for details of where to get help to address these challenges.

Challenge 1 – Using dermoscopy (dematoscopy) to assess pigmented lesions

See recommendation 1.2.1.

Potential benefits of implementation

Dermoscopy performed in secondary care by suitably trained specialists is both more sensitive and more specific in classifying skin lesions than clinical examination with the naked eye alone. It lessens the chance of missing a diagnosis of melanoma and reduces the number of unnecessary surgical procedures to remove benign lesions.

Challenges for implementation

For healthcare professionals in secondary care skin cancer clinics:

- Using dermoscopy routinely. Dermoscopy is integral to most dermatology services but is thought to be less commonly used in some clinics, for example clinics staffed by plastic and reconstructive surgeons.

For healthcare professionals who assess pigmented lesions:

- Developing competencies in assessment.
- Gaining experience in dermoscopy through regular practice.
- Including formal training in dermoscopy in their continuing professional development and revalidation work.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

- Gaining access to new equipment (in some areas).

For relevant royal colleges and speciality training organisations:

- Including dermoscopy in speciality training curricula for healthcare professionals who assess pigmented lesions.

Making the changes happen

Commissioners of services could:

- Include provision of dermoscopy in local service specifications.

Providers of secondary skin cancer clinics could:

- Arrange for healthcare professionals who assess pigmented lesions to have formal training in dermoscopy. There are a range of academic institutions that deliver national and local courses.
- Routinely provide experiential training for staff in specialist clinics. This could include competency-based assessment.
- Include reference to ongoing experience and competency in the appraisals of healthcare professionals who perform dermoscopy.

The relevant royal colleges, supported by the speciality training organisations, could:

- Include dermoscopy where relevant in their specialty training curricula, and look at the specialty training curriculum for dermatology from the Joint Royal Colleges of Physicians Training Board as an example.
- Consider developing work-based assessments for measuring competency in the use of dermoscopy.

Challenge 2 – Measuring vitamin D levels and advising on supplementation

See recommendations 1.3.1 and 1.3.2.

Potential benefits of implementation

Measuring vitamin D levels at diagnosis allows healthcare professionals to identify people with

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

melanoma whose vitamin D levels are low and who might benefit from supplementation in line with national policies, as well as people with high vitamin D levels who do not need supplementation and in whom supplementation might be harmful. Knowing a person's vitamin D level will also improve the accuracy of the advice given to them about the risks and benefits of sunlight exposure.

Challenges for implementation

For dermatologists (and possibly oncologists) in skin cancer multidisciplinary teams:

- Measuring vitamin D levels routinely at diagnosis of melanoma.
- Developing expertise in interpreting vitamin D levels.
- Providing advice about vitamin D supplementation if needed.

Making the changes happen

Dermatologists (and possibly oncologists) in skin cancer multidisciplinary teams could:

- Refer to the Scientific Advisory Committee on Nutrition for information on vitamin D supplementation.
- Refer to NICE's pathway on vitamin D: increasing supplement use among at-risk groups, which covers vitamin D supplementation in people with low or no exposure to the sun.
- Listen to the podcast produced by NICE to explain the evidence behind the recommendations on vitamin D and its supplementation.
- Use the Advice for melanoma health care teams – vitamin D and melanoma produced by GenoMEL (the Melanoma Genetics Consortium).

Challenge 3 – Considering sentinel lymph node biopsy and completion lymphadenectomy

See recommendations 1.5.2 and 1.7.1.

Potential benefits of implementation

Considering sentinel lymph node biopsy (SLNB) for people who have stage IB–IIC melanoma with a Breslow thickness of more than 1 mm, and discussing the possible advantages and disadvantages with them, will enable people with these melanomas to make an informed decision about whether

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

or not to have this procedure. Those who choose to have SLNB may benefit from more accurate staging, giving a better indication of outcome (including survival and risk of relapse). SLNB is more sensitive than ultrasound, so lymphatic spread may be diagnosed earlier. In addition, people who have SLNB may be able to participate in clinical trials of new treatments.

Similarly, discussing the possible advantages and disadvantages of completion lymphadenectomy with people who have a positive SLNB will enable them to make an informed decision about whether or not to have this procedure after SLNB. Completion lymphadenectomy can reduce the chance of the melanoma returning and may enable the person to participate in clinical trials of new treatments.

Challenges for implementation

For clinicians in skin cancer multidisciplinary teams:

- Explaining the value of SLNB as a staging tool to people with melanoma, because there are no clear survival benefits from it.
- Providing comprehensive information about the possible advantages and disadvantages of having the procedure.
- Explaining the benefits of proceeding to completion lymphadenectomy to people with a positive SLNB result.

For commissioners:

- Providing SLNB in services.

Making the changes happen

Clinicians in skin cancer multidisciplinary teams could:

- Listen to the explanation of the evidence behind the SLNB recommendations on the NICE podcast.
- Use the decision aid option grids that NICE has produced to help discuss the possible risks and benefits of having SLNB and, for people with a positive SLNB, proceeding to completion lymphadenectomy.

Commissioners could:

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

- Ensure that service specifications include provision of SLNB. This may not be delivered locally.
- Visit the NICE local practice collection to see examples of SLNB services.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

Finding more information and committee details

You can see everything NICE says on this topic in the NICE Pathway on melanoma.

To find NICE guidance on related topics, including guidance in development, see the NICE webpage on skin cancer.

For full details of the evidence and the guideline committee's discussions, see the full guideline. You can also find information about how the guideline was developed, including details of the committee.

NICE has produced tools and resources to help you put this guideline into practice. For general help and advice on putting our guidelines into practice, see resources to help you put NICE guidance into practice.

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).

Update information

Minor changes since publication

May 2021: We added links to the NICE Pathway on melanoma for information on genomic biomarker-based therapy in solid tumour treatment pathways.

July 2019: We added option grids to help with discussion of potential treatments. Links added to the NICE Pathway on melanoma to sections 1.7 and 1.8 to link to the latest NICE technology appraisal guidance on these topics.

ISBN: 978-1-4731-1322-0

Accreditation

© NICE 2021. All rights reserved. Subject to Notice of rights (https://www.nice.org.uk/terms-and-conditions#notice-of-rights).