



## Editorial

## Consensus Guidelines for the Management of Melanoma during the COVID-19 Pandemic: Surgery, Systemic Anti-cancer Therapy, Radiotherapy and Follow-up

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The current COVID-19 pandemic has major implications for the ability to deliver normal care for patients. Although Sir Simon Stevens, Chief Executive of NHS England, recommends 'referrals, diagnostics and treatment to be brought back to pre-pandemic levels at the earliest opportunity', there is still a need to manage the challenges of the heightened risk of COVID-19 for patients and staff.

Local situations will vary and determine the capacity and capability to manage patients, but care should not significantly deviate from current recognised high standards. This may be particularly relevant for surgical procedures. The specialist skin cancer multidisciplinary team should continue to advise with attendance done remotely.

Decisions on systemic therapy may also need to be modified. Targeted therapy with dabrafenib and trametinib is associated with a high risk of fever and malaise, which mimic COVID-19 symptoms. Although the majority of patients do not require hospitalisation, the possibility of COVID-19 infection must now be considered. Patients with fever should be advised to stop treatment, take paracetamol and self-isolate. If their symptoms promptly resolve on stopping the drug, they can discontinue self-isolation at 48 h. Early testing for SARS-CoV-2 should be implemented as soon as possible in accordance with national guidelines.

Treatment for immune toxicity may require immunosuppression and use of acute medical services, including respiratory support. Significant immune toxicity is common with combination immunotherapy, frequently leading to hospital admission. The same toxicities are seen for single agent PD-1 inhibitors, although much less frequently. Older

patients and those with significant comorbidity are at greater risk of severe complications from COVID-19 infection, so minimising other potential contributory risk factors is particularly important.

Radiotherapy is less commonly used for malignant melanoma. However, it may be considered for palliation of symptoms and some other rarer indications [1]. When used, modified fractionation should be considered and the benefits carefully weighed against the risk of exposure to the virus.

These guidelines on how to manage patients with melanoma during the COVID-19 pandemic, taking into consideration the risks patients face from cancer, cancer-related treatment complications and infection, represent the consensus view of a number of senior melanoma clinicians.

### General Interventions to Minimise and Manage the Impact of COVID-19

- Reduce the need for patients to visit the hospital, i.e. congregating in waiting areas, contamination of radiology machines etc.
- Clinic lists should be screened in advance. Review how frequently patients need to be seen and, where possible, routine reviews should be replaced by a telephone or video call.
- Consider how treatments are prescribed, dispensed and administered. Where possible, choose a treatment that minimises the risk of admission to hospital due to risk of treatment-related toxicity.
- Consider hypofractionated radiotherapy regimens, including single exposure in palliative radiotherapy to reduce the number of visits to hospital.

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- Review requirements for routine imaging.
- Clearly record all changes in standard management in the patient record and document discussion with the patient/family.

## Surgery

- Excision of any suspicious lesion should be with a 2 mm margin and could be provided by a general practitioner/local multidisciplinary team. It is recognised that there could be an increased number of non-malignant lesions excised.
- Sentinel node biopsies (SNBx) should continue to be offered to patients with pT1b-pT4b melanomas; however, capacity will be reduced. Therefore, patients with pT2b-pT3b melanomas should be prioritised first, followed by the addition of pT4a-pT4b and finally pT1b-pT2a as capacity is restored to normal.
- If SNBx have to stop all together, primaries on the extremities could have a 1 cm wide local excision and the potential for a delayed SNBx. Lymphatic drainage is more predictable in the limbs and closure of these defects is normally possible with a linear scar, which is least likely to interfere with lymphatic drainage. Head and neck and truncal primaries have greater variability in their lymphatic drainage and delayed SNBx may not be appropriate.
- Recurrent lesions causing significant morbidity should be prioritised, such as fungating tumour, pain, involvement of critical structures or situations where delayed surgery would lead to loss of control at that site.
- Further details are available from the British Association of Plastic Reconstructive and Aesthetic Surgeons [2].

## Systemic Anti-cancer Therapy and Radiotherapy Prioritisation

The aim is to continue to deliver all appropriate treatments to patients who require them. The National Institute for Health and Care Excellence (NICE) and NHS England have published tables prioritising systemic anti-cancer therapy and radiotherapy [3,4]. Tables 1 and 2 outline 'Priority Levels' for certain treatments.

## Proposals

### Systemic Anti-cancer Therapy for Metastatic Disease

- For patients starting immunotherapy, the majority should start single agent PD-1 inhibitor. Consideration should be given to choosing 6-weekly pembrolizumab with a telephone call at 2–3 weeks.
- For those patients with much higher risk disease (e.g. bulky liver metastases, asymptomatic brain metastases), combination immunotherapy is still appropriate (Priority Level 2). Consider home administration where possible and appropriate.
- For patients requiring BRAF targeted therapy, consideration should be given to choosing encorafenib and binimetinib because of the lower chance of symptoms that mimic COVID-19 infection.
- Treatment frequency and supervision
  - Immunotherapy: a one cycle break is acceptable in patients on treatment for >3 months. Patients require blood tests at the missed cycle timepoint and a telephone review.
  - Targeted therapy: aim for continuous treatment; patients stable on treatment beyond 4 months can safely be dispensed 8 weeks of drug without blood tests in between.

**Table 1**  
Systemic anti-cancer therapy prioritisation during the COVID-19 emergency

Indication	Comment	Priority level
First-line metastatic disease <ul style="list-style-type: none"> <li>• Single agent PD-L1 inhibitor</li> <li>• Combination ipilimumab and nivolumab for high risk features such as bulky liver metastases or asymptomatic brain metastases</li> <li>• Combination BRAF and MEK inhibitor therapy</li> </ul>	Considered the highest priority given the major impact on long-term survival, with a median expected 5-year survival of about 50%	2
Second-line metastatic disease for patients with a BRAF mutation	Effective second-line treatments available (targeted therapy or immunotherapy), although outcomes not as good as for first line	2
Second-line metastatic disease for patients without a BRAF mutation and all subsequent lines of treatment	Have a poor outcome and lower priority	6
Adjuvant therapy	Has a major impact on risk of recurrence. Data currently too immature to show an impact on overall survival, although very likely. Considered Priority Level 2, but lower than first-line treatment for metastatic disease	2

**Table 2**  
Radiotherapy prioritisation during the COVID-19 emergency

Indication	Comment	Priority level
Palliative radiotherapy	Alleviation of symptoms has potential to reduce burden on other healthcare services. Consider using single fraction or shorter fractionated schedules	4
Metastatic spinal cord compression	For patients who have useful salvageable neurological function	2
Stereotactic radiosurgery for brain metastases	If delay to treatment would lead to neurological deterioration or possible need for surgery For palliative intervention	2 4

### Systemic Anti-cancer Therapy for Adjuvant Therapy

- Patients with a BRAF mutation should be offered adjuvant dabrafenib and trametinib to minimise the risk of requirement for immunosuppression to manage treatment-related toxicity.
- Patients who are BRAF wild type should be offered 6-weekly adjuvant pembrolizumab [5].
- Consider limiting adjuvant therapy to patients with the highest risk disease (stage IIIC and IIID). The absolute benefit is considered a lower priority for resected stage IIIA and IIIB patients [6].
- Treatment breaks as for metastatic disease (see above).

### Definitive Radiotherapy

- Where definitive radiotherapy is used, modified fractionation should be considered.
- Radiotherapy for rarer indications, such as lentigo maligna, lentigo maligna melanoma and melanoma *in situ*, should be deferred for 2–3 months. These patients are generally elderly and should avoid hospitals wherever possible.

### Adjuvant Radiotherapy

- In cases when surgical margins were inadequate and further surgery is not a viable option, radiotherapy may be considered, but should be carefully assessed to balance the risk of exposure to the virus against the risks of local recurrence.
- Patients with closely excised melanoma at high risk of recurrence could have clinical review by their surgeon/dermatologist in 3–4 months to consider the possibility of further surgery or, if not possible, postoperative radiotherapy.
- Adjuvant nodal radiotherapy should be considered in regional metastases from mucosal primaries but not offered routinely in cutaneous melanoma primaries.

### Palliative Radiotherapy

- For standard palliative radiotherapy (excluding brain metastases) consider 20 Gy in four fractions instead of 20 Gy in five fractions, 30 Gy in eight fractions instead of 30 Gy in 10 fractions or a single fraction of 8–10 Gy (e.g. bleeding or fungating skin nodules).
- Consider stereotactic radiotherapy for patients with brain metastases if a delay to treatment would lead to neurological deterioration or a need for surgery and as a palliative intervention (although lower priority). For further guidance for stereotactic radiosurgery (SRS) during the COVID-19 pandemic please refer to [7].
- In some patients, best supportive care may be the most appropriate management.

### Routine Imaging

- Consider substituting computed tomography of the head for magnetic resonance imaging of the brain to minimise the number of visits, i.e. one visit for computed tomography of the head, thorax, abdomen, pelvis.
- The frequency of surveillance imaging should continue as current standard, but consider extending the period between follow-up scans according to local availability.

## Conclusion

These guidelines are not evidence based but a consensus view of senior melanoma clinicians. They are designed to help decision making rather than limit choice and physicians should interpret them as they feel appropriate for their local circumstances and priorities.

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## Conflicts of interest

P.C. Lorigan reports personal fees and other from BMS, personal fees from Merck, personal fees and other from Novartis, personal fees and other from GSK, personal fees and other from Amgen, personal fees and other from Chugai, outside the submitted work.

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