This document was published on 24 March 2020. Please check www.rcr.ac.uk/cancer-treatment-documents to ensure you have the latest version. This document is the collaborative work of oncologists and their teams, and is not a formal RCR guideline or consensus statement.

Guidelines for follow-up and SACT for melanoma during COVID-19 pandemic

Authors: Pippa Corrie, Avinash Gupta, Mark Harries, James Larkin, Paul Lorigan, Paul Nathan, Mark Middleton, Christian Ottensmeier and Lisa Pickering

Contents

Background 2

Interventions to minimise and manage the impact of COVID-19 2

SACT prioritisation 3

SACT melanoma – metastatic disease 3

SACT melanoma - adjuvant therapy 3

Proposals 3

Metastatic disease 3

Adjuvant therapy 4

Routine imaging 4

This document was published on 24 March 2020. Please check www.rcr.ac.uk/cancer-treatment-documents to ensure you have the latest version. This document is the collaborative work of oncologists and their teams, and is not a formal RCR guideline or consensus statement.

Background

The worsening COVID-19 pandemic is likely to have major implications on the ability to deliver normal care for patients. This document identifies some of the strategies that can be taken to minimise the impact on melanoma patients and the healthcare system.

Targeted therapy and immunotherapy have different toxicity profiles with which clinicians are now very familiar. Targeted therapy with dabrafenib and trametinib (the UK market leader) is associated with a high risk of fever, rigors and malaise which mimic COVID-19 symptoms. While the majority of patients are normally managed symptomatically with supportive care meds, dose interruptions and reductions, and don't require admission to hospital, the possibility of COVID-19 infection must now be considered. Patients calling for advice with fever and pyrexia should be told to stop treatment, take ibuprofen and paracetamol and self-isolate. However, if the patients are well, they will not need to be admitted. If their symptoms promptly resolve on stopping drug they can discontinue self-isolation at 48 hrs.

Significant immune toxicity is common with combination immunotherapy, frequently leading to hospital admission requiring immune suppression and use of acute medical services including respiratory support. The same toxicities are seen for single agent PD-1 inhibitors though much less frequently. Immune suppression is likely to lead to patients being more susceptible to COVID-19 infection. Older patients and those with significant co-morbidities are more at risk of severe complications of COVID-19 infection and so minimising other potential contributory risk factors is particularly important in this patient group.

The guidance provided below is based on limited evidence and may require to be updated over time, but is intended to help melanoma specialist teams manage their service effectively during this unprecedented period.

Interventions to minimise and manage the impact of COVID-19

1. Reduce need for patients to visit the hospital i.e. reduce footfall in hospital, congregating in waiting areas, contamination of radiology machines, exposure to other patients and staff etc.

2. Clinic lists should be screened in advance. Where possible, routine reviews should be deferred and replaced by a telephone call.

3. Review how frequently patients need to be seen in clinic and how treatments are prescribed, dispensed and administered.

4. Where possible, choose a treatment that minimises the risk of admission to hospital due to risk of treatment-related toxicity

5. Minimise treatment-related toxicity that could be confused for or worsen COVID-19 infection (fever, cough, breathlessness and pneumonitis) and would compete for acute medical support

6. Review requirements for routine imaging

SACT prioritisation

The aim is to continue to deliver all appropriate treatments to those patients who require them. However, we should consider any changes we can make now that will help reduce the impact of the COVID-19 pandemic. Furthermore, there is a real possibility that if the situation deteriorates dramatically, we will have to prioritise which SACT needs to be delivered. Prioritisation of SACT is happening across most centres.

SACT melanoma – metastatic disease

Treatment of first line metastatic disease is considered the highest priority, given the major impact on long term survival, with median expected 5-year survival of approximately 50%.

Treatment of second line metastatic disease in patients with a BRAF mutation and so with an effective second line treatment (targeted therapy or immunotherapy) is also considered a priority, though the outcomes are not as good as for first line.

Second line treatments in patients without a BRAF mutation and all subsequent lines of treatment have a poor outcome and so is a lower priority.

SACT melanoma – adjuvant therapy

Adjuvant therapy has a major impact on risk of recurrence. The data for adjuvant immunotherapy is currently too immature to show an impact on overall survival, although this is very likely. Adjuvant therapy is offered to patients with a wide range of prognosis and the absolute benefit in earlier Stage III patients is low. For these reasons, adjuvant therapy is considered a lower priority for resected stage IIIA and IIIB patients, and overall a lower priority than first line treatment for metastatic disease.

There is currently no consensus on which adjuvant treatment to offer patients with a BRAF mutation. This choice should now be informed by the risk of toxicity requiring immunosuppression or respiratory support.

Proposals

Metastatic disease

1. First line metastatic disease is the highest priority for treatment.
2. Second line metastatic disease in patients with a BRAF mutation is also considered a high priority
3. Second line treatment in patients without a BRAF mutation and all subsequent lines of treatment have a poor outcome and so are a lower priority
4. 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.
5. For those patients with much higher risk disease e.g. bulky liver metastases, asymptomatic brain metastases, combination immunotherapy is still appropriate.

6. Consider home administration where possible and appropriate.

7. For patients requiring BRAF targeted therapy, consideration should be given to choosing encorafenib and binimetanib because of the lower chance of symptoms that mimic COVID-19 infection.

8. Metastatic disease - treatment frequency and supervision

    - Immunotherapy: 1 cycle break is acceptable in patients on treatment for >3/12. Patients require blood tests at missed cycle time-point and 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

Adjuvant therapy

9. Adjuvant therapy is considered a lower priority than first line metastatic disease

10. Patients with a BRAF mutation should be offered adjuvant dabrafenib and trametinib.

11. Patients who are BRAF WT should be offered 6 weekly adjuvant pembrolizumab.

12. Consider limiting adjuvant therapy to patients with the highest risk disease (stage IIIC and IIID)

13. Immunotherapy

    - If necessary, interrupt treatment for 1 cycle length (4-6 weeks) in patients who have had at least 3/12 treatment. Require blood tests at missed cycle time-point and telephone review

14. Targeted therapy

    - Dispense 2/12 at a time for patients who have been established on treatment for four months or more. Patients do not require blood tests in between.

Routine imaging

15. Consider substituting CT head for MR brain to minimise number of visits, i.e. one visit for CT head, thorax, abdomen, pelvis

16. Frequency of surveillance imaging

    - Surveillance imaging will continue as current standard. However, consider extending period between follow-up scans according to local availability.