Recommendations for management of Cutaneous Malignant Melanoma during COVID19 pandemic.

The following recommendations have been written as a proposal to guide melanoma treating physicians in treatment decisions on their patients during this pandemic, taking in account the current scientific data. This document can be adapted when new information is available.

As a general recommendation we must strictly adhere to the general rules of prevention and protection against COVID19 infection and the controlled access to the hospital.

We recommend to patients to follow the general protective measures available and regularly update on the (info coronavirus) webpage.

Primary Cutaneous Melanoma:

- Attempt excisional/ complete biopsy whenever possible with the intent to remove the clinical lesion. As per standard practice.
- Delay wide excision up to 3 months for invasive melanomas of any depth, for which previous biopsy had clear histological margins or only peripheral transection of the in situ component is acceptable at the condition that current access to surgical treatment is difficult or impossible or safety of the patient with regards to SARS-CoV-2 infection during the procedure cannot be guaranteed.
- Aim for complete resection in case of incomplete biopsy.
- Sentinel lymph node biopsy may be delayed for up tot 3 months unless wide excision is planned earlier, in which case Sentinel lymph node biopsy may be performed in the same time. Delay of surgical treatment is acceptable at the condition that current access to surgical treatment is difficult or impossible or safety of the patient with regards to SARS-CoV-2 infection during the procedure cannot be guaranteed.

Stage III melanoma (N+):

- In the absence of clinically detectable metastatic draining lymph nodes (palpation, US, CT, PET, MR imaging) there is no indication to perform immediate elective complete lymph node dissection following a positive Sentinel Lymph node biopsy, as per current guidelines. Perform radiological surveillance as appropriate, (US surveillance every 2 months as performed in the MSLT-II trial).
- In the case of clinically palpable regional nodes, need for lymphadenectomy has to be evaluated on a case by case basis, taking into account patient characteristic, availability of surgery, and safety of the patient with regards to SARS-CoV-2 infection

during the procedure. Systemic treatment, including treatment with anti-PD-1 immune checkpoint blockade or BRAF/MEK inhibitors can be considered as a neo-adjuvant treatment option. In case of BRAF V600-mutant melanoma, treatment with BRAF-/MEKi is recommended over anti-PD-1 therapy because of the higher short-term protection against disease progression (awaiting surgical CLND) and lower risk of irreversible adverse events necessitating immune suppressive therapy. In case of neo-adjuvant therapy, short interval imaging and follow-up is indicated . Neo-adjuvant therapy with the ipilimumab/nivolumab combination is not recommended given the high incidence of irAE and need of immunosuppressive therapy that could potentially increase the risk for complicated SARS-CoV-2 infection.

Stage III adjuvant therapy:

- Unless the fact that there are some controversies about COVID19 and use of immune checkpoint inhibitors, at this timepoint there is no clear scientific evidence for a negative impact of this treatment on the incidence and course of COVID19 infection.
- Adjuvant treatment with anti PD1 antibodies should be continue when started, in the absence of flu-like symptoms or known COVID19 infection.
- We recommend to choose regimen which needs less hospital visits or patient contacts, however make sure to surveil the wellbeing of patients by telephone contact at least every 2 weeks since patients may be more reluctant to report irAE because of fear of being hospitalized

  Nivolumab 480mg every 4 weeks

  Pembrolizumab 400mg IV every 6 weeks

- There is currently no evidence of negative impact of use of Dabrafenib-Trametinib on the incidence and course of COVID19 infection. Consider screening patients for SARS-CoV-2 infection at the incidence of potential overlapping symptomatology e.g pyrexia, gastrointestinal symptoms, muscle pain….
- Consider postpone the start of adjuvant up to 12 weeks after definitive surgery.

Stage IV melanoma:

- Unless the fact that there are some controversies about COVID19 and use of immune checkpoint inhibitors, at this timepoint there is no clear evidence for a negative impact of this treatment on the risk for SARS-CoV-2 infection or its outcome. For this reason, treatment should be continued taking all possible measures to prevent infection.

- For patients with a complete or deep partial response, interruption of treatment can be considered after a minimal duration of therapy of at least 6 months A worse outcome was observed when electively stopping treatment before 6 months of therapy (Jansen et al A of Oncology 2019)
- For newly diagnosed patients, choice of treatment must be made after consideration of risk of side effects. In general, single-agent anti PD1 antibody is preferred over combination Ipilimumab-Nivolumab due to the higher risk of immune mediated toxicity for which corticosteroids/other immunosuppressants are needed.
- Current standards of care should not be changed at the exception of initiating therapy with the ipilimumab/nivolumab regimen (at the exception of patients with melanoma brain metastases without BRAFV600 mutation or uveal primary melanoma). On an individual basis choose the therapy schedule which needs less hospital visits and patient contacts; , however make sure to surveil the wellbeing of patients by telephone contact at least every 2 weeks since patients may be more reluctant to report irAE because of fear of being hospitalized

  Nivolumab 480mg every 4 weeks

  Pembrolizumab 400mg IV every 6 weeks

- There is no evidence of negative impact of use of Dabrafenib-Trametinib, Encorafenib/Binimetinib or Vemurafenib/Cobimetinib on the incidence and course of COVID19 infection. Consider screening patients for SARS-CoV-2 infection at the incidence of potential overlapping symptomatology e.g pyrexia, gastrointestinal symptoms, muscle pain….

Guidelines made by collaboration of B. Neyns, O. Bechter, JF Baurain, V. Kruse, S. Aspenslagh and A. Rutten.

References:

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- www.fitcancer.fr
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