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Melanoma and COVID-19: A narrative review focused on treatment

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Abstract

Melanoma is the most severe form of skin cancer and its incidence has increased over the past few decades. COVID-19 pandemic affected the diagnosis and management of many diseases including melanoma. In this study, we aimed to provide a review focused on the diagnosis and management of melanoma in the era of COVID-19. A comprehensive search was conducted on PubMed, Web of Science, and Google Scholar databases using the keywords "melanoma," "coronavirus," "COVID 19," and "SARS-CoV-2." The relevant guidelines published by the European Society for Medical Oncology and the National Comprehensive Cancer Network were also included. The current guidelines recommend that surgical interventions for new diagnosis of invasive primary melanoma, patients with postoperative complications, wide resection and sentinel lymph node biopsy for newly diagnosed T3-T4 melanoma, and planned surgical procedures for patients in neo-adjuvant trials should be prioritized. Surgical treatment of T3/T4 melanomas should be prioritized over T1/T2 melanomas except for any melanoma in which large clinical residual lesion is visible. Adjuvant therapies can be postponed for up to 12 weeks depending on the local center circumstances. PD-1 inhibitor monotherapy is recommended for patients starting immunologic therapy. Combination immunotherapy is still considered suitable for patients with higher-risk disease. Encorafenib and binimetinib should be prioritized for patients requiring BRAF-targeted therapy due to the lower chance of symptoms mimicking COVID-19 infection.

KEYWORDS

coronavirus, COVID 19, melanoma, SARS-CoV-2

1 | INTRODUCTION

Melanoma, a neoplasm of melanocytes, is the most severe form of skin cancer. Although it was formerly thought to be uncommon, the incidence has increased over the past few decades.[1] COVID-19 is a very contagious infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 outbreak, which caused thousands of deaths, has been declared a pandemic by the World Health Organization on March 2020.[2] Due to the COVID-19 crisis, many scheduled medical and surgical activities have been suspended. This interruption to the health care system can negatively affect the diagnosis and management of melanoma. Neglecting melanoma throughout the outbreak may be associated with increased rates of mortality, morbidity, and health care expenses. In this study, we provide a narrative review focused on the diagnosis and management of melanoma in the era of COVID-19.

2 | METHODS

This narrative review includes searching PubMed, Google Scholar, and Web of Science databases using the keywords "melanoma," "coronavirus," "COVID 19," and "SARS-CoV-2." The search was supplemented by manual searching of reference lists of included articles. A total of 15 relevant articles was identified. The search was updated in July 2020. The guidelines provided by the European Society for Medical Oncology and the National Comprehensive Cancer Network were also included.

2.1 | Melanoma diagnosis and surgery in the era of COVID-19

Melanoma causes 6850 deaths per year in the United States and mortality is directly associated with tumor stage. Nearly 90% of melanomas progress through a radial growth period and can be excised before they metastasize.[3] Therefore, early diagnosis is crucial for survival rates. The current proposal for confirmed melanoma treatment is within 3 to 4 weeks following diagnosis to improve survival. In a study of 986 patients with melanoma who were managed with wide local excision, the timing from biopsy to wide local excision did not remarkably affect overall survival on multivariable analysis.[4] On the other hand, a retrospective study using the National Cancer Data Base reported notably worse survival for patients with stages I to III melanoma who experienced a delay of more than 2 months from diagnosis to final surgical management compared with patients treated within 2 months of diagnosis.[5] Another study of National Cancer Data Base similarly reported that delays of more than 30 days from biopsy to final surgery were associated with worse survival for patients with early melanoma.[6] Tejero-Vasaquez and Nagore developed a rate of growth model to estimate the effect of COVID-19 lockdown on melanoma thickness and prognosis.[7] They randomly selected 1000 melanomas with a known rate of growth from a database and the tumors were classified according to thickness based on the melanoma staging criteria of the American Joint Committee on Cancer. For each case, a rate of growth was used to predict tumor thickness after a diagnostic delay of 1 to 3 months. Then 5- and 10-year survival rates for the patients were calculated and classified into diagnostic groups. The authors concluded that in the absence of appropriate care for melanoma patients in the lockdown circumstances, the health care system could see a remarkable rise in melanoma upstaging cases and health care expenses.[7] Another recent study comparing detection rates of melanoma before and during the UK Government-mandated lockdown showed that melanoma detection rates were higher during the lockdown. Most cases represented early or thin melanomas. The authors concluded that this outcome highlights the significance of continued skin cancer services during the COVID-19 lockdown.[8] All these data indicate that an obstacle in melanoma diagnosis and treatment can be associated with increased rates of morbidity and mortality. Furthermore, the management of higher-stage diseases requires higher costs. Pandemic-related delays in melanoma diagnosis and management may have serious consequences on the economic burden of the disease. In this context, we suggest that individuals who have any new lesions or have noticed changes in their existing lesions should be encouraged to apply to the dermatology outpatient clinic. Surgical procedures for the diagnosis of melanoma and scheduled surgical interventions should not be postponed for more than 3 months. Recurrent melanomas associated with significant morbidity should be prioritized. Lesions with the involvement of essential structures or locations where postponed surgery would cause loss of control should be removed without delay. Sentinel node biopsies should also continue to be recommended to patients with pT1b-pT4b melanomas. Patients with pT2b-pT3b melanomas should be prioritized first until the capacity is returned to routine. Head-neck and truncal melanomas have higher variability in their lymphatic drainage. Postponed sentinel node biopsies for these locations may be associated with decreased survival.[9] ESMO[10] and NCCN[11] published specific guidelines detailing surgical and medical priorities for patients with melanoma during the COVID-19 pandemic. Tables 1-3 are summarized the specific recommendations included in these guidelines.

Another important issue is the safety of the patient and surgeon during the surgery. Cutaneous surgery is deemed low to medium risk surgery. This remains right in the current circumstances, but only when the patient can properly wear a surgical mask. In this regard, for procedures on the face, dermatological surgery can be considered as a high-risk procedure. Hence, wearing high protection mask (FFP3) during surgery on the facial area is recommended. For the other body areas, FFP2 masks can be considered as suitable protection equipment. Standardized consent forms should be adapted to inform patients of the risk of being infected with SARS-CoV-2 during the procedure.[12]

2.2 | Teledermatology and melanoma in the era of COVID-19

Diagnosing and managing pigmented skin lesions usually need face-to-face visits. However, teledermatology care could be delivered to those who are fearful of visiting clinics for the risk of infection.[13] Teledermatology services may also be used for patients at higher risk of SARS-CoV-2 infection, including those with chronic disorders or under immunosuppression. The teledermatology care can be delivered using the real-time videoconferencing method or the patient's prerecorded images with accompanying medical history. Whether a patient is suitable for virtual melanoma examination should be evaluated personally based on their access to a smart device and Internet connection, and risk factors associated with COVID-19. For patients, they would be required teledermoscopy, this will add further costs or equipment, which will need to be addressed. To render an accurate diagnosis using teledermatology and teledermatoscopy, a standardized guide for patients to obtain high-quality macroscopic and dermatoscopic images should be provided.[14] In a recent randomized controlled trial comparing patients using self-skin examination with or without a mobile dermoscope at home, both groups had a high level

TABLE 1 European Society for Medical Oncology recommendation concerning outpatient visits and surgical priorities for patients with melanoma[10]

High priority	Medium priority	Low priority
Outpatient visit priorities		
-New diagnosis of invasive primary melanoma, except that tumor is in situ or T1a and wide excision has been done -Post-operative patients with complications	-Established patients with new symptoms related to treatment -Dyspnea, grade 2 or higher diarrhea or new-onset neurological symptoms in patients on immuno-oncology, and fever that does not resolve with treatment interruption in patients on BRAF inhibitor or MEK inhibitor prompts for SARS-CoV-2 testing -Post-operative patients without complications -Visits between two treatments for patients on immunologic therapies (refer to telemedicine)	-Patients with no active treatment or melanoma survivors (refer to telemedicine) -Patients with dysplastic naevi syndrome or other risk factors -Psychological support visits (refer to telemedicine)
Priorities for surgery in primary melanoma		
-Any curative excision for stage III melanoma -Wide resection and sentinel lymph node biopsy for newly diagnosed T3 and T4 melanoma -Surgical treatment of complications related to surgical procedures -Planned surgical procedures for patients in neo-adjuvant trials	-Wide resection and sentinel lymph node biopsy for newly diagnosed T1b and T2 melanoma -Wide excision alone for T1a or lower melanoma -Excision of oligo-metastatic disease	None

of sensitivity (>75%) and specificity (>87%) in identifying suspicious lesions. In the teledermoscopy group, no melanoma was overlooked by the subjects.[15]

According to the NCCN, telemedicine evaluation should be preferred for new patients if possible; complete history and physical examination can be postponed for up to the day of surgery.[11]

2.3 | Melanoma screening in the era of COVID-19

Planning and implementing screening campaigns for skin cancer are essential in order to identify malignant lesions early. The American Academy of Dermatology skin cancer screening program has confirmed the value of screening in the early detection of skin cancers.[16] Melanoma screening campaigns canceled due to preventive measures during pandemic probably led to a delay in diagnoses of skin cancer.[13,17] Therefore, public health institutions should keep efficiency during this outbreak and offer effective solutions to build alternative models of screening campaigns to ensure melanoma prevention with safe conditions. Alternative models of screening campaigns should rely on the same principles as the usual ones. These campaigns should include training patients about sun protection through a media campaign on TV and Internet sources; information about how to recognize suspicious and dangerous lesions, and how to do self-examination, shared through the websites, mobile applications, and social media platforms. Furthermore, face-to-face visits should be scheduled with a limited number of patients each day through a unique e-mail or call center provided by the organizing institute.[17]

2.4 | The impact of COVID-19 on the course of advanced melanoma

Metastatic melanoma is one of the most difficult cancers to manage and usually has a poor outcome. Recently, targeted therapy and immunotherapy have opened a new horizon in the treatment of advanced melanoma. Most of the advanced melanoma cases are managed with targeted therapy or immunotherapy including pembrolizumab, nivolumab, ipilimumab, dabrafenib, trametinib, vemurafenib, cobimetinib, encorafenib, and binimetinib.[18] The impact of COVID-19 on the course of advanced melanoma is not well known. However, few studies suggested that COVID-19 may have no substantial impact on the course of the disease. In a retrospective study including 50 patients with melanoma infected with SARS-CoV-2, mortality rates from COVID-19 by melanoma treatment type were found to be 16%, 15%, and 36% for patients on immunotherapy, targeted therapy, and for those that were not on active treatment, respectively. The authors concluded that anti-programmed cell death-1 therapy does not surpass the global risk of death in this group.[19] In another study including 80 patients with metastatic melanoma under immune checkpoint inhibition (62 nivolumab and 18 pembrolizumab), a total of 57 patients maintained treatment without interruptions, while 16 delayed their treatment for one or two cycles.

TABLE 2 European Society for Medical Oncology recommendation concerning priorities for adjuvant systemic therapies for stage III melanoma, systemic treatments for inoperable stage III/IV melanoma, and radiotherapy for inoperable stage III/IV Melanoma[10]

High priorities	Medium priorities	Low priorities
Priorities for adjuvant systemic therapies for stage III melanoma		
-Maintenance of treatment in the setting of a clinical trial, provided patient benefits outweigh risks, with possible modification of procedures without influencing patient safety and study conduct	-Adjuvant targeted or immunologic treatments for patients with high-risk stage III disease	-Any adjuvant therapy for sentinel lymph node deposit of less than 1 mm or stage III A
-Adjuvant therapies can be postponed for up to 12 weeks depending on the local center circumstances -Adjuvant BRAF inhibitor/MEK inhibitor can be started and the following switch to adjuvant immuno-oncology therapies can be considered -Double dosing with double period to reduce visits is recommended for patients on programmed cell death protein-1 blockade: pembrolizumab 400 mg every 6 weeks and nivolumab 480 mg every 4 weeks with one inter-cure visit in telemedicine with blood exams performed in a laboratory near to the patient if a COVID-19-protected facility is accessible, otherwise at the center under current measures -For patients on tyrosine kinase inhibitors: refer follow-up visits to telemedicine with blood exams performed in a laboratory near to the patient if a COVID-19-protected facility is accessible, otherwise at the center under current measures -Inclusions in adjuvant and neo-adjuvant trials should be limited to prevent more visits to the center		
Priorities for systemic treatments for inoperable stage III/IV melanoma		
-Targeted therapies or immunologic therapies for inoperable stage III or IV melanoma -Maintenance of treatment in the setting of a clinical trial, provided patient benefits outweigh risks, with possible modification of procedures without influencing patient safety and study conduct	None	None
-For patients on immuno-oncologic therapy, the small numerical benefit of ipilimumab/nivolumab compared with programmed cell death protein-1 single agent has to be weighed against increased grade III/IV immune-related adverse event and the risk related to steroid use. The CheckMate 511 regimen (ipilimumab 1 mg/kg and nivolumab 3 mg/kg) can be considered on a case-by-case basis -Double dosing with double period to reduce visits is recommended for patients on programmed cell death protein-1 blockade: pembrolizumab 400 mg every 6 weeks and nivolumab 480 mg every 4 weeks with one inter-cure visit in telemedicine with blood exams performed in a laboratory near to the patient if a COVID-19-protected facility is accessible, otherwise at the center under current measures -Patients on immuno-oncologic therapies with symptoms of pneumonitis on computerized tomography scans should be tested for SARS-CoV-2 before administrating corticosteroids -For patients on tyrosine kinase inhibitors: refer follow-up visits to telemedicine with blood exams performed in a laboratory near to the patient if a COVID-19-protected facility is accessible, otherwise at the center under current measures -It is recommended to avoid corticosteroids as much as possible (Administer conservatively as much as possible)		
Priorities for radiotherapy for inoperable stage III/IV melanoma		
-Stereotactic radiosurgery for metastatic brain lesions -Threatening lesion, for example, fracture or bleeding risk -Acute spinal cord compression	-Irradiation of symptomatic metastases	-Adjuvant radiotherapy after radical lymphadenectomy for local control -Radiotherapy for asymptomatic and not threatening metastatic lesions

The remaining seven patients suspended treatment due to progression, completion of schedule, or were lost to follow-up. The author stated that none of the patients under immune checkpoint inhibition developed SARS-CoV-2 infection.[20]

In the current literature, a few cases of COVID-19 developed in patients with melanoma have also been reported. Schmidle et al reported a 47-year-old female contracting COVID-19 while receiving adjuvant immunotherapy with the PD1-antagonist nivolumab for completely resected stage IV melanoma.[21] The patient did not reveal any severe symptoms like shortness of breath or a decrease in oxygen saturation during the course of the disease. Fever resolved within 3 days. No treatment for COVID-19 was needed; however, nivolumab was suspended as a precautionary measure. Two weeks after the beginning of COVID-19 symptoms, SARS-CoV-2-IgG antibodies suggesting immunization were identified.[21] Yekedüz et al reported a 75-year-old female metastatic melanoma (BRAF wild-type) patient with multiple comorbidities, contracting SARS-CoV-2 infection.[22] The patient developed severe respiratory symptoms related to COVID-19 while she was on nivolumab. She was discharged with a good clinical condition on the fifth day of the favipiravir and hydroxychloroquine treatment. However, she died because of the chronic cardiac problems 10 days later being discharged.[22] Gómez-Caminero-López et al reported a 66-year-old patient with Clark level V melanoma.[23] The patient developed a low-grade fever and dyspnea, and PCR confirmed SARS-CoV-2 infection. The patient died 4 days after the diagnosis of COVID-19. The authors did not provide any information with regard to treatment.[23]

Serzan et al reported a 65-year-old stage IV melanoma patients with lung and brain metastases. The patient was on combined

TABLE 3 National Comprehensive Cancer Network recommendation concerning the management of melanoma during the COVID-19 pandemic[11]

Diagnostic biopsy priorities
Excisional/complete saucerization biopsy should be preferred with the intent to excise the clinical lesion
Broad shave biopsy should be done for larger suspected melanoma in situ and lentigo maligna
Provide telemedicine care for new patients if possible; complete anamnesis and physical examination can be postponed for up to the day of surgical procedure
Wide excision priorities
Postpone wide excision of melanoma in situ for up to 3 months
Postpone wide excision of T1 melanoma for up to 3 months even for a positive border on biopsy, as long as the bulk of the lesion has been excised. If a large residual lesion is visible, perform a total excisional biopsy with narrow surgical margins or elliptical excision with 1 cm surgical margins in the outpatient setting
Postpone wide excision for up to 3 months for invasive melanomas of any depth, for which the previous biopsy showed clear histopathological margins or just peripheral transection of the in situ component
Surgical treatment of T3/T4 melanomas should be prioritized over T1/T2 melanomas except for any melanoma in which large clinical residual lesion is visible
Depending on operating room capacities, consider sentinel lymph node biopsy for melanomas thicker than 0.8 mm. Sentinel lymph node biopsy may be postponed for up to 3 months unless wide in the operating room is scheduled, in which case wide excision and sentinel lymph node biopsy may be done at the same time
Delay follow-up visits in surgically excised, asymptomatic patients with stages 0, I, II melanoma for at least 3 to 6 months
Prefer telemedicine for follow-up visits
Delay imaging examination in asymptomatic stage IIB/IIC patients for at least 3 to 6 months
Stage 3 melanoma
Delay completion lymph node dissection following a positive SLNB and perform regional nodal ultrasound examination or other imaging methods as appropriate
Delay follow-up imaging for 3 to 6 months in asymptomatic, surgically resected patients who are not administered systemic treatment
Delay follow-up imaging for 3 months for patients who are on systemic adjuvant treatment without clinical evidence of disease
Delay therapeutic lymph node excision in the setting of clinically palpable regional nodes, and suggest neoadjuvant systemic treatments (immune checkpoint blockade or BRAF/MEK inhibitors) instead. Exceptions are when metastatic nodes are penetrating a vital structure, when neoadjuvant treatment is not possible, and when the systemic treatment has already failed
Neoadjuvant considerations include higher-dose pembrolizumab (400 mg intravenous for one to two cycles every 6 weeks), two cycles of nivolumab (480 mg intravenous every 4 weeks), BRAF/MEK inhibitors for 8 weeks followed by surgery, preoperative administration of two cycles of ipilimumab 3 mg/kg and nivolumab 1 mg/kg. Surgery should be done 8 to 9 weeks after the start of neoadjuvant treatment
Short-time follow-up with imaging may be required. Consider ongoing immunologic therapy over surgery for patients with clinical/radiologic improvement
Metastatic excisions should be postponed unless the patient is symptomatic and patients should be maintained on systemic treatment. Depending on hospital resources, the use of talimogene laherparepvec for cutaneous/nodal/in-transit metastasis should be carefully considered and, if possible, delayed until the pandemic wanes. A single dose of irradiation may be beneficial for large symptomatic metastatic lesions
For clinical monitoring of stage III patients who are not on treatment, the physician in charge may postpone the follow visit up to 3 months and/or prefer telemedicine
Stage III melanoma adjuvant therapy
Adjuvant therapy may be delayed up to 12 weeks from the time of the definitive surgical excision of melanoma. Adjuvant therapy has not been confirmed to increase melanoma survival and should be suspended during the COVID-19 pandemic for patients with less than 50% risk of disease relapse
The regimens that are the least taxing on the health care system and patient should be preferred
Adjuvant alternatives include Nivolumab 480 mg intravenous every 4 weeks for 1 year, pembrolizumab 200 mg intravenous every 3 weeks for 1 year, pembrolizumab 400 mg intravenous every 6 weeks for 1 year, BRAF/MEK inhibitors following current NCCN Guidelines for Cutaneous Melanoma
While dabrafenib/trametinib is the evidence-based option, alternative BRAF/MEK inhibitor regimens (encorafenib/binimetinib or vemurafenib/cobimetinib) may be preferred in the case of limited drug supply
Symptom checks using telemedicine are recommended with fewer clinic visits
Stage IV melanoma
The toxicity of the regimen selected should be cautiously considered on a case-by-case basis and the agents with the least toxicity should be preferred. Single-agent anti-programmed cell death-1 is recommended over combination ipilimumab/nivolumab during the pandemic because of possible worsening of COVID-19, need for corticosteroids or other immunosuppressive agents that may negatively affect patients with COVID-19, and increased consumption of resources for visits due to toxic reactions or follow-up

(Continues)

TABLE 3 (Continued)

It is currently not well known how patients with COVID-19 on immune checkpoint blockade will respond to the expected immune-related adverse events. Patients on immune checkpoint blockade could undergo more severe therapy-related adverse events during their treatment course and that treatment of immune-related adverse events with corticosteroids or other immunosuppressive agents may negatively affect patients with COVID-19
Single-agent anti-programmed cell death-1 should be discussed for each patient with no brain metastasis
The lowest frequency dosing scheme of available regimens should be preferred (Nivolumab 480 mg intravenous every 4 weeks or pembrolizumab 400 mg intravenous every 6 weeks)
Nivolumab/ipilimumab combination induces grade 3 to 4 immune-related adverse events more than twice as frequent as single-agent anti-programmed cell death protein-1 therapy, usually requiring high-dose and prolonged corticosteroid or other immunosuppressants, hospitalization, and emergency department visits. Hence, decisions concerning combination vs single-agent therapy should be tailored to patient characteristics and with the awareness of limited capacity to handle toxic reactions
A combination of ipilimumab 1 mg/kg and nivolumab 3 mg/kg every 3 weeks for four infusions, with following consideration for single-agent nivolumab therapy, is associated with lower incidences of immune-mediated toxic reactions
Stage IV melanoma with brain metastasis
The combination of nivolumab/ipilimumab has a high rate of intracranial durable responses, similar to the extracranial activity of these agents. The risk of immune-related adverse events is the same as for patients with no metastatic brain lesions and may be reduced by the alternative dosing of ipilimumab 1 mg/kg and nivolumab 3 mg/kg in the four cycles of induction treatment. In patients with BRAF wild-type melanoma, this regimen may be the most rational approach for patients with asymptomatic and small metastases who do not need corticosteroids for perilesional edema
Patients with larger, symptomatic metastasis, and/or metastasis requiring corticosteroids should undergo stereotactic radiosurgery
BRAF/MEK inhibitors should be considered for patients with BRAF V600-mutated melanoma and brain metastasis
General advice in the case of limited drug supply
Drug supplies may become limited throughout the pandemic; accordingly, the following recommendations can be considered
Dabrafenib/trametinib can be used instead of encorafenib/binimetinib or vemurafenib/cobimetinib combinations
Encorafenib/binimetinib or vemurafenib/cobimetinib combinations can be used instead of dabrafenib/trametinib
BRAF inhibitor monotherapy can be used in the case of a limited supply of MEK inhibitor
In patients progressing beyond standard immune checkpoint blockade and targeted therapy, hospice care should be considered since chemotherapy provides only limited benefit
Oral temozolomide is the favorite option if palliative chemotherapy is considered, as it would restrict resource consumption and contact with the health care system

nivolumab and ipilimumab immunotherapy.[24] He developed early-onset severe dyspnea associated with acute coronavirus HKU1 (non-COVID-19) infection, with diffuse pneumonitis evidenced computerized tomography scan. He was managed with corticosteroids leading to the resolution of pneumonitis on control imaging. The author concluded that diffuse pneumonitis may be associated with exacerbated immune-mediated toxicity due to immune checkpoint inhibitors.[24]

2.5 | Management of advanced melanoma in the era of COVID-19 pandemic

There are no evidence-based guidelines for the management of melanoma in the era of COVID-19. However, several guidelines designed to help making clinical decisions have been published. The recommendations contained in these guidelines should be interpreted by physicians as they feel suitable for their local conditions and priorities.

In a UK-based consensus guideline for the management of melanoma during the COVID-19 pandemic, the authors have recommended PD-1 inhibitor monotherapy for patients starting immunologic therapy. Combination immunotherapy has been considered still suitable for patients with higher-risk disease. Encorafenib and binimetinib have been deemed as preferred agents for patients requiring BRAF-targeted therapy due to the lower chance of symptoms mimicking COVID-19 infection.[19] The recommendations of this guideline are summarized in Table 4.

ESMO recommended that all communications and discussions with other health care providers and with patients preferably be held by phone rather than face-to-face. Decisions for treatment initiation or maintenance should be discussed with both uninfected patients and COVID-19 positive patients after the explanation of proper risk/benefit. All patients undergoing surgery, radiotherapy, chemotherapy, or immunotherapy should be tested for COVID-19 before each treatment period. Adjuvant therapies that are thought to significantly increase survival should be prioritized in patients with resected high-risk disease. The advantages and disadvantages of palliative treatments and the option of "therapy holidays" should also be discussed with patients.[25] ESMO has published a guide detailing surgery, radiotherapy, and medical treatment priorities for patients with melanoma during the COVID-19 pandemic. According to this guideline, the priorities are classified as high, medium, and low.[10]

TABLE 4 The recommendations of the UK-based expert consensus guideline by Nahm et al for the management of melanoma during the COVID-19 pandemic[9]

Adjuvant therapy
PD-1 inhibitor monotherapy is recommended for patients starting immunologic therapy
Combination immunotherapy is still suitable for patients with higher-risk disease
Encorafenib and binimetinib should be prioritized for patients requiring BRAF targeted therapy due to the lower chance of symptoms mimicking COVID-19 infection
Patients with a BRAF mutation should be advised adjuvant dabrafenib and trametinib to reduce the risk of the need for immunosuppressive therapy due to treatment-related toxic reactions
Six-weekly adjuvant pembrolizumab is recommended for patients with BRAF wild-type melanoma
Limiting adjuvant therapy to patients with stage IIIC and IIID melanoma should be considered
Radiotherapy
Modified fractionation should be considered where definitive radiotherapy is used
Radiotherapy lentigo maligna, lentigo maligna melanoma, and melanoma in situ should be postponed for 2 to 3 months
Adjuvant nodal radiotherapy is not offered routinely in primary cutaneous melanoma, but it should be considered for regional metastases from mucosal primaries
For standard palliative radiotherapy in patients with no brain metastasis 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 to 10 Gy
Stereotactic radiotherapy should be considered for patients with brain metastases if the suspension of treatment may cause neurological deterioration or a requirement for surgery
Routine imaging
The frequency of follow-up imaging should remain as current standards but extending the intervals between follow-up scans should be considered depending on local availability

NCCN has also published a guide including a list of recommendations for patients with melanoma during the COVID-19 pandemic.[11] NCCN guide has focused on the management of advanced melanoma with a special emphasis on adjuvant therapies. The guideline additionally included general advice in the case of limited drug supply.[11] The recommendations of ESMO and NCCN are summarized in Tables 1-3.

3 | CONCLUSIONS

There are limited data about the impact of COVID-19 on the course of melanoma and related treatments. However, some treatment regimens and follow-up modifications can be considered to ensure the safety of patients and to reduce the burden on the health care system during the pandemic. The options should be discussed with the patient and communication with teledermatology should be preferred where possible and appropriate. Ongoing treatment regimens should be re-evaluated on a case-by-case basis, depending on local circumstances.

AUTHOR CONTRIBUTIONS

Ömer Faruk Elmas, Abdullah Demirbaş, Serkan Düzayak, Mustafa Atasoy: Literature searching, designing and writing the manuscript. Ömer Faruk Elmas, Abdullah Demirbaş, Mustafa Atasoy, Ümit Türsen, Torello Lotti: Substantial contributions to conception and design, interpretation of data. Ömer Faruk Elmas, Abdullah Demirbaş, Ümit Türsen, Torello Lotti: Editing, revising and final approval of the manuscript.

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