

# Multidisciplinary Care of *BRAF*-Mutant Stage III Melanoma: A Physicians Perspective Review

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**Key Words.** Melanoma • *BRAF* • Multidisciplinary care • Diagnosis • Patient journey

## ABSTRACT

Prognosis among patients with stage III melanoma can vary widely depending on the risk of disease relapse. Therefore, it is vital to optimize patient care through accurate diagnosis and staging as well as thoughtful treatment planning. A multidisciplinary team (MDT) approach, which involves active collaboration among physician specialists across a patient's disease journey, has been increasingly adopted as the standard of care for treatment of a variety of cancers, including melanoma. This review provides an overview of MDT care principles for patients with *BRAF*-mutant-positive, stage III cutaneous melanoma and summarizes current literature, clinical experiences, and institutional best practices. Therapeutic goals from dermatologic, surgical, and medical oncologist perspectives regarding MDT care throughout a patient's disease course are discussed. Additionally, the role of each specialty's involvement in testing

for predictive biomarkers at relevant time points to facilitate informed treatment decisions is discussed. Last, instances of successful MDT treatment of other cancers and key lessons to optimize MDT patient care in cutaneous melanoma are provided. Several aspects of MDT patient care are considered vital, such as the importance of staging via pathological examination and imaging, biomarker testing, and interdisciplinary physician and patient engagement throughout the course of treatment. Use of MDTs has the potential to improve patient care in cutaneous melanoma by improving the speed and accuracy of diagnosis, implementing a personalized treatment plan early on, and being proactive in adverse event management. Physician perspectives described in this review may lead to better outcomes, quality of life, and overall patient satisfaction. *The Oncologist* 2021;26:e1644–e1651

**Implications for Practice:** As more cancer therapies emerge, it is critical to optimize patient care and treatment planning. The multidisciplinary team (MDT) approach, which involves active collaboration among specialists, has led to encouraging survival results in multiple cancer types. As MDT care becomes more widely adopted in the treatment of melanoma, accurate diagnosis and staging are important, as clinical outcomes for stage III disease vary widely by substage. Because ~50% of melanomas harbor *BRAF* mutations, testing is important for an informed treatment decision. Interdisciplinary physician-patient engagement throughout the course of treatment can improve comorbidity and adverse event management to optimize patients' treatment journeys.

## INTRODUCTION

Cutaneous melanoma is one of the most common cancers, with an estimated 100,350 new cases diagnosed in the U.S. in 2020 [1, 2]. Melanoma is staged using the tumor, node, metastasis (TNM) system [3, 4]. "T" refers to primary

tumor depth of invasion and ulceration status. "N" refers to regional lymph node metastases and presence of in-transit, satellite, and/or microsatellite metastases. "M" refers to distant metastases and integrates elevated lactate

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dehydrogenase levels—an independent, adverse prognostic factor in melanoma [3, 5].

Patients with disease localized to the skin (stages I–II) are managed with wide surgical excision and have a generally favorable prognosis [3, 6]. The 5-year melanoma-specific survival (MSS; i.e., survival until death from melanoma) rate for stage I to IIA disease ranges from 94% to 99%; stages IIB and IIC have lower 5-year MSS rates of 87% and 82%, respectively [3]. In patients with stage III melanoma, four pathological stage groups exist (IIIA, IIB, IIC, IIID) as determined by T and N ratings, with considerable variability in prognosis by disease substage [3, 4]. Recurrence risk increases and long-term survival decreases with advancing disease stage [3, 4, 7]. The 5-year MSS rate is 77% for all patients with stage III melanoma [3]. However, the 5-year MSS rates for stages IIIA, IIB, IIC, and IIID are 93%, 83%, 69%, and 32%, respectively [3], demonstrating a wide range of prognosis in these patients.

Treatment for *BRAF*-mutant stage III melanoma depends on whether the tumor is surgically resectable or unresectable [6]. Patients with resectable melanoma typically undergo surgery to remove the primary tumor and regional lymph nodes [6]. Because of a high 5-year risk of relapse in patients with stage III melanoma, ranging from 48% to 85% [7], patients with *BRAF*-mutant melanoma are often treated with adjuvant therapy, including immunotherapy (e.g., ipilimumab, nivolumab, or pembrolizumab) or targeted therapy (e.g., dabrafenib plus trametinib), following surgery to mitigate risk of relapse [6]. In patients with unresectable disease, first-line therapy is either immunotherapy or targeted therapy [6]. The incidence rate of stage III melanoma has increased in recent years, from 1.14 per 100,000 people in 2010 to 1.36 per 100,000 in 2014 [8], stressing the need for effective treatments.

In 2015, ipilimumab (at 10 mg/kg) was the first checkpoint inhibitor (CPI) approved as adjuvant therapy for patients with stage III melanoma following resection (Table 1) [9–11]. Subsequently, additional CPIs (e.g., nivolumab and pembrolizumab), with improved clinical benefits and tolerability profiles, have been approved as adjuvant therapy for melanoma with lymph node involvement following resection (Table 1) [12–19]. Nivolumab and pembrolizumab also induced clinical responses in patients with *BRAF* V600-mutant disease [13, 17]. However, no predictive biomarkers of clinical response to CPIs exist. Unlike in other solid tumors, the use of programmed cell death ligand-1 expression as a biomarker to guide treatment selection in melanoma is not supported by current evidence, and its use in clinical practice remains controversial [6, 20, 21].

Targeted therapy also significantly improved outcomes in patients with *BRAF* V600-mutant, resected stage III melanoma. The phase III COMBI-AD study of 1-year adjuvant therapy with dabrafenib plus trametinib versus placebo in resected, high-risk, stage III melanoma with *BRAF* V600E/K mutations showed increased relapse-free survival compared with placebo (Table 1) [22–24]. No clear guidelines exist on the comparative effectiveness of *BRAF* and *MEK* targeted therapy versus CPIs in patients with *BRAF*-mutant

stage III melanoma. As a result, several factors must be considered in order to individualize adjuvant treatment, including risk of relapse, presence of comorbidities, risk of treatment-related adverse events (TRAEs), and patient preferences.

Despite recent treatment advancements, further improvement is needed to improve efficacy and duration of response. For example, the combination of CPIs and targeted therapy is being investigated to help achieve these goals [25–27]. In addition, comprehensive patient case management using a multidisciplinary team (MDT) is a promising approach to optimize patient care and treatment selection.

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### OVERALL IMPORTANT CONSIDERATIONS FOR MDTs

Patient care has increasingly relied on MDTs comprising various physician specialists (e.g., dermatologists, surgeons, pathologists, oncologists, and/or radiologists) who discuss patient cases at regularly occurring panels or tumor boards [28–39]. MDTs can optimize patient care in multiple ways, including increasing accuracy of diagnosis, personalizing treatment selection, and being proactive in adverse event (AE) management [32]. These measures have the potential to improve outcomes, preserve quality of life, and increase overall patient satisfaction [32, 33]. Newer MDT approaches focus on interdisciplinary physician and patient engagement throughout the course of disease to enhance communication, share decision-making, improve comorbidity and AE management, and increase touchpoints to individually monitor patients [36].

MDTs can be used throughout a patient's treatment journey, from initial presentation to treatment and follow-up. To ensure that each member of the MDT can contribute fully, it is important to define necessary patient information to help direct treatment strategies and relapse surveillance. Tumor characteristics that inform staging and prognosis, such as tumor thickness, ulceration, mitotic rate, margin status, microsatellitosis, lymphovascular invasion, and sentinel node involvement [6], should be readily available to the MDT. In high-risk patients with stage II and III disease, imaging (e.g., radiographic, ultrasound, computed tomography [CT], and positron emission tomography [PET]) and genomic test results, including *BRAF* mutation status, should also be shared to guide treatment decisions and trial enrollment, if appropriate. Additionally, because patients may come under MDT care following initial workup with their primary care physician or other specialists, it is important to determine whether all recommended workup has been completed for each patient to ensure that the MDT has all the relevant information to create the patient's treatment plan. Based on our experiences in treating melanoma, best practices to optimize the treatment journey for patients with *BRAF*-mutant stage III melanoma are summarized in Figure 1. This review highlights key information, such as referral patterns and clinical characteristics, to be shared among MDT members to guide treatment throughout the patient journey and during long-term follow-up care.

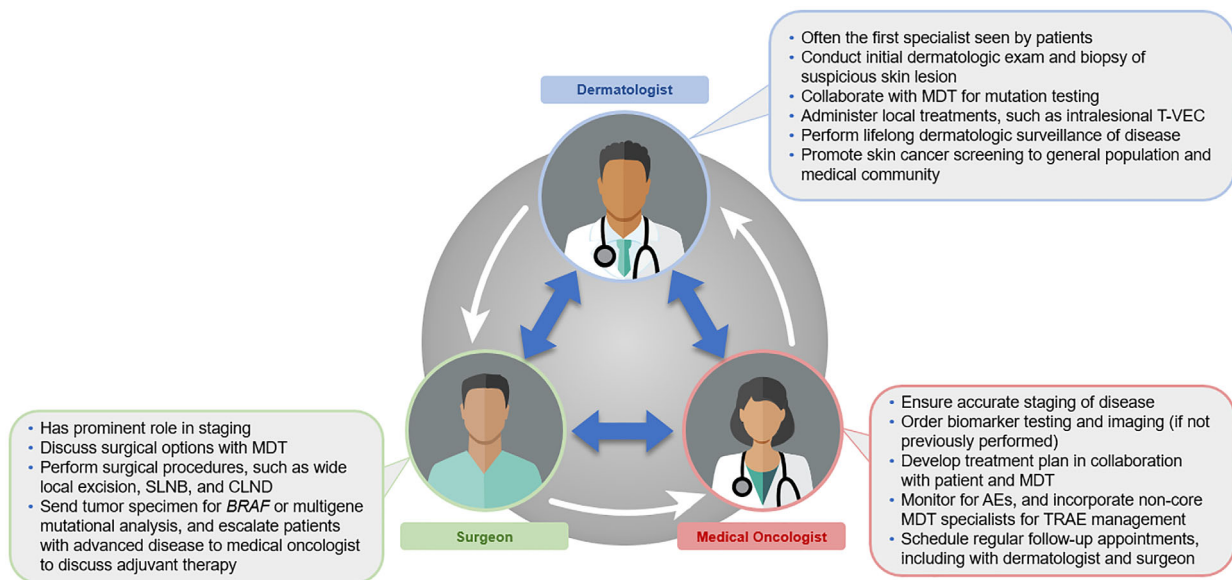
**Table 1.** Summary of clinical trials of adjuvant therapy in advanced melanoma

Study	Stage <sup>a</sup>	Phase	Experimental Groups	Results
<b>EORTC 18071</b> [9, 12] Median follow-up: 6.9 years	IIIA, IIIB, or IIIC	III	<ul style="list-style-type: none"> <li>Ipi: 10 mg/kg</li> <li>Placebo</li> </ul>	<p><b>RFS</b></p> <ul style="list-style-type: none"> <li>Median RFS               <ul style="list-style-type: none"> <li>Ipi: 26.1 months</li> <li>Placebo: 17.1 months</li> </ul> </li> <li>3-year RFS               <ul style="list-style-type: none"> <li>Ipi: 46.5%</li> <li>Placebo: 34.8%</li> </ul> </li> <li>7-year RFS               <ul style="list-style-type: none"> <li>Ipi: 39.2%</li> <li>Placebo: 30.9%</li> </ul> </li> </ul> <p><b>OS</b></p> <ul style="list-style-type: none"> <li>Median OS               <ul style="list-style-type: none"> <li>Ipi: NE</li> <li>Placebo: 7.8 years</li> </ul> </li> <li>7-year OS               <ul style="list-style-type: none"> <li>Ipi: 60.0%</li> <li>Placebo: 51.3%</li> </ul> </li> </ul>
<b>North American Intergroup E1609</b> [11] Median follow-up: 57.4 months	IIIB, IIIC, M1a, M1b	III	<ul style="list-style-type: none"> <li>Ipi3: 3 mg/kg</li> <li>HDI</li> <li>Ipi10: 10 mg/kg</li> </ul>	<p><b>RFS</b></p> <ul style="list-style-type: none"> <li>Median RFS</li> <li>Ipi3: 4.5 years</li> <li>HDI: 2.5 years<sup>b</sup></li> <li>Ipi10: 3.9 years</li> </ul> <p><b>OS</b></p> <ul style="list-style-type: none"> <li>5-year OS</li> <li>Ipi3: 72%</li> <li>HDI: 67%<sup>b</sup></li> <li>Ipi10: 70%</li> </ul>
<b>CheckMate 238</b> [13-16] Minimum follow-up: 48 months	IIIB, IIIC, or IV	III	<ul style="list-style-type: none"> <li>Nivo: 3 mg/kg</li> <li>Ipi: 10 mg/kg</li> </ul>	<p><b>RFS</b></p> <ul style="list-style-type: none"> <li>Median RFS               <ul style="list-style-type: none"> <li>Nivo: NR</li> <li>Ipi: 24.9 months</li> </ul> </li> <li>1-year RFS               <ul style="list-style-type: none"> <li>Nivo: 70.5%</li> <li>Ipi: 60.8%</li> </ul> </li> <li>2-year RFS               <ul style="list-style-type: none"> <li>Nivo: 62%</li> <li>Ipi: 51%</li> </ul> </li> <li>3-year RFS               <ul style="list-style-type: none"> <li>Nivo: 58%</li> <li>Ipi: 45%</li> </ul> </li> <li>4-year RFS               <ul style="list-style-type: none"> <li>Nivo: 52%</li> <li>Ipi: 41%</li> </ul> </li> </ul> <p><b>OS</b></p> <ul style="list-style-type: none"> <li>3-year OS               <ul style="list-style-type: none"> <li>Nivo: 82%</li> <li>Ipi: 82%</li> </ul> </li> <li>4-year OS               <ul style="list-style-type: none"> <li>Nivo: 78%</li> <li>Ipi: 77%</li> </ul> </li> </ul>
<b>KEYNOTE-054</b> [17-19] Median follow-up: 3.5 years	IIIA, IIIB, or IIIC	III	<ul style="list-style-type: none"> <li>Pem: 200 mg</li> <li>Placebo</li> </ul>	<p><b>RFS</b></p> <ul style="list-style-type: none"> <li>Median RFS               <ul style="list-style-type: none"> <li>Pem: NR</li> <li>Placebo: 20.4 months</li> </ul> </li> <li>1-year RFS               <ul style="list-style-type: none"> <li>Pem: 75.4%</li> <li>Placebo: 60.2%</li> </ul> </li> <li>2-year RFS               <ul style="list-style-type: none"> <li>Pem: 68.3%</li> <li>Placebo: 47.1%</li> </ul> </li> <li>3.5-year RFS               <ul style="list-style-type: none"> <li>Pem: 59.8%</li> <li>Placebo: 41.4%</li> </ul> </li> </ul> <p><b>OS</b></p> <p>Study ongoing</p>
<b>COMBI-AD</b> [23-25] Median follow-up: 5 years	IIIA, IIIB, or IIIC	III	<ul style="list-style-type: none"> <li>D (150 mg) + T (2 mg)</li> <li>Placebo</li> </ul>	<p><b>RFS</b></p> <ul style="list-style-type: none"> <li>Median RFS               <ul style="list-style-type: none"> <li>D+T: NR</li> <li>Placebo: 16.6 months</li> </ul> </li> <li>1-year RFS               <ul style="list-style-type: none"> <li>D+T: 88%</li> <li>Placebo: 56%</li> </ul> </li> <li>2-year RFS               <ul style="list-style-type: none"> <li>D+T: 67%</li> <li>Placebo: 44%</li> </ul> </li> <li>3-year RFS               <ul style="list-style-type: none"> <li>D+T: 59%</li> <li>Placebo: 39%</li> </ul> </li> <li>4-year RFS               <ul style="list-style-type: none"> <li>D+T: 55%</li> <li>Placebo: 38%</li> </ul> </li> <li>5-year RFS               <ul style="list-style-type: none"> <li>D+T: 52%</li> <li>Placebo: 36%</li> </ul> </li> </ul> <p><b>OS</b></p> <ul style="list-style-type: none"> <li>Median OS               <ul style="list-style-type: none"> <li>D+T: NR</li> <li>Placebo: NR</li> </ul> </li> <li>3-year OS               <ul style="list-style-type: none"> <li>D+T: 86%</li> <li>Placebo: 77%</li> </ul> </li> </ul>

<sup>a</sup>Patients with stage IIIA melanoma per the American Joint Committee on Cancer *Cancer Staging Manual* 7th Edition were included if they had sentinel lymph node metastasis >1 mm.

<sup>b</sup>Data for the first-step comparison (Ipi3 vs. HDI) are listed. Data for the second-step comparison (Ipi10 vs. HDI) are as follows: median RFS with HDI: 2.4 yr; 5-yr OS with HDI: 65%.

Abbreviations: D, dabrafenib; HDI, high-dose interferon; Ipi, ipilimumab; NE, not estimable; Nivo, nivolumab; NR, not reached; OS, overall survival; Pem, pembrolizumab; RFS, relapse-free survival; T, trametinib.



**Figure 1.** Best practices for the ideal treatment journey of patients with *BRAF*-mutant stage III melanoma. The most common patient journey (dermatologist to surgeon to medical oncologist) is indicated by the white arrows. However, it is important to note that not all patients are first seen by a dermatologist. Therefore, staging must be performed or verified by each member of the MDT. Communication among the MDT (blue arrows) is vital for optimal patient care. Abbreviations: AE, adverse event; CLND, completion lymph node dissection; MDT, multidisciplinary team; SLNB, sentinel lymph node biopsy; T-VEC, talimogene laherparepvec; TRAE, treatment-related adverse event.

### DERMATOLOGIST PERSPECTIVE (DR. CORNELIUS)

Although there are multiple points of entry into care for patients with melanoma, dermatologists are often the first specialists to evaluate patients with suspected melanoma and perform a biopsy. Referral to a dermatologist early in patient care is also important for managing cutaneous toxicities and detecting locoregional recurrence and second primaries. Pathology should be read by a pathologist with expertise in pigmented lesions, preferably a dermatopathologist, so that the appropriate synoptic pathology report is recorded. Once a melanoma diagnosis is confirmed, a patient should be referred to a surgical oncologist or medical oncologist, depending on the disease stage, to determine the optimal next steps including surgical resection and/or the need for systemic therapies. Mohs surgery may be considered in appropriately selected stage 0 disease for cosmetically sensitive areas with the goal of tumor clearance and achievement of appropriate surgical margins. Wide local excision (using appropriate margins) for T1 tumors that do not require a sentinel lymph node biopsy can be performed by dermatologists and dermatological surgeons as well. If patients come to the MDT through outside referral by a primary care physician, they may first be treated by a surgeon or medical oncologist, with assurance that a dermatologist will be enlisted in their ongoing care.

Dermatologists should remain active MDT members throughout all stages of diagnosis and treatment. The interval for dermatologic evaluations should be based on disease stage and time from initial diagnosis, as outlined in the National Comprehensive Cancer Network guidelines [6]. Patients with melanoma are at higher risk for subsequent primary tumors, other nonmelanoma skin cancers, and local-regional recurrence. Dermatologic surveillance should be lifelong and a

routine part of the dermatologic follow-up for new primary lesions, nodal recurrence, and dermal metastases. Additionally, cutaneous TRAEs (e.g., new primary tumors and cutaneous eruptions [including bullous diseases and pruritus]) are common and best managed by dermatologists, with the goal of maintaining the treatment regimen. Dermatologists may also actively participate in administering oncolytic viral therapy, such as talimogene laherparepvec, to cutaneous and subcutaneous metastases, if determined appropriate by the MDT [6].

Last, dermatologists should consider the value and appropriate use of skin cancer screening. Two large-scale studies have demonstrated the benefit of skin cancer screening in lowering skin cancer burden. The German SCREEN study, which evaluated >360,000 people over a 5-year period, found that population-based skin cancer screening was associated with a subsequent decrease in melanoma mortality [40]. However, this decrease was not maintained over a longer follow-up time [41]. Therefore, this is an area of constant evaluation, and a revised version of the U.S. Preventive Services Task Force (USPSTF) is currently addressing this issue. Another study confirmed the value of screening with the additional finding that sensitivity and specificity of melanoma detection were highest in skin examinations performed by dermatologists versus physician assistants [42]. Nonetheless, the USPSTF concluded that there was insufficient evidence to support wide-scale skin cancer screening from a cost-benefit perspective and, most importantly, when determining effect on melanoma mortality [43]. Guidelines have been developed using current data that support appropriate risk-based cancer screening for individuals at highest risk [44, 45]. Among patients clinically diagnosed with melanoma by the American Academy of Dermatology–sponsored SPOT Me skin cancer screening program, 75% were classified as high risk [45]. For patients aged 35–75 years with

a personal or family history of melanoma, genetic predisposition, high-risk phenotype, and/or ultraviolet radiation overexposure, the USPSTF guidelines recommend a total body skin examination at least annually [44].

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### **SURGEON PERSPECTIVE (DR. FIELDS)**

Surgeons have a prominent role in melanoma staging and may perform a variety of surgical procedures depending on biopsy findings. The MDT can discuss whether surgical resection is possible and, if so, which procedure to perform. Surgical options include wide local excision (WLE) to remove cancerous lesions and nearby skin tissue (e.g., surgical margin of 0.5–2.0 cm depending on tumor thickness) and sentinel lymph node biopsy (SLNB). Completion lymph node dissection (CLND) is an option in patients with a positive SLNB [6]. The results of the DeCOG-SLT and MSLT-II trials have led to avoidance of CLND in many stage III melanomas after a positive SLNB, provided that there is adequate surveillance of the involved nodal basin [46, 47]. CLND should be discussed for patients with gross melanoma with nodal involvement or referred to a neoadjuvant therapy clinical trial in which an MDT can best optimize the plan of care. If CLND is not performed, patients are followed up closely per clinical trial protocols, with routine ultrasound of the at-risk nodal basin and clinical examination every 3–4 months during the first 2 years, then every 6 months during years 3–5 [6, 46, 47]. Currently, CLND is only recommended for patients outside of the DeCOG-SLT and MSLT-II trial criteria or patients who fit the trial criteria but are unable to comply with the trial surveillance program. In these circumstances, we may recommend CLND, especially in the head and neck or axilla regions where the morbidity of CLND is less than in the groin [48, 49]. A dermatologist or primary care physician may refer patients for WLE and SLNB after a biopsy is performed. Patients with a positive SLNB are classified as stage III, and adjuvant therapy is recommended after resection in high-risk patients (stage IIIB/C/D and select, higher-risk stage IIIA with SLN metastasis >1 mm) [6]. If a patient is diagnosed as stage III by a surgeon, MDT discussions should be expedited regarding next steps, including *BRAF* mutation testing (if not previously performed) and consideration of adjuvant therapy and/or subsequent surgery, with the goal of preventing clinical recurrence. Adjuvant radiation therapy may also be considered; however, studies of adjuvant radiation for highest-risk melanoma have only demonstrated improvements in reducing the risk of local relapse but have failed to show significant benefits in relapse-free survival (RFS) or overall survival (OS). Retrospective studies showed improvement in locoregional disease control and regional recurrence rates in patients with advanced melanoma who received radiotherapy following surgery [50–52]. A later randomized trial found improvement in the risk of lymph-node field relapse but no differences in RFS or OS with adjuvant radiotherapy compared with postoperative observation in patients with regional lymph node metastases with high-risk features of recurrence [53].

Debate is ongoing regarding the value of CLND, as a recent study reported that CLND did not increase MSS

versus observation at a 3-year follow-up ( $86 \pm 1.3\%$  vs.  $86 \pm 1.2\%$ , respectively;  $p = .42$ ) but increased lymphedema (24.1% vs. 6.3%, respectively;  $p < .001$ ) [46]. Additionally, CLND frequency has been decreasing [47], and it is unclear whether CLND is still the standard of care in nonclinically positive stage III melanoma [54]. In patients with clinically positive stage III node(s), WLE of the primary tumor and therapeutic CLND are recommended. MDTs can clarify the need for CLND in individual patients. As stated above, CLND is recommended for patients unable to adhere to frequent follow-up protocols needed to monitor the at-risk nodal basin [6]. However, as the implementation of CLND in patients with positive SLN biopsy becomes less frequent, more patients will be at increased risk for later regional relapse. An MDT discussion would be expected to optimize the plan for care in an individual patient and help determine whether CLND may still be indicated for some patients based on disease extent or other risk factors.

*BRAF* mutation testing should be obtained as early as possible in any patients with known nodal metastatic disease, including positive SLN biopsy or more advanced nodal disease, to inform treatment selection of neoadjuvant therapy. Neoadjuvant systemic therapy, preferably in the context of a clinical trial, should be considered in patients with borderline resectability of nodes in patients with lymphadenopathy or with a very high risk of recurrence after lymphadenectomy [6].

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### **ONCOLOGIST PERSPECTIVE (DR. TARHINI)**

Because of the wide survival range among patients with stage III melanoma [3], there is heightened emphasis on accurate staging, especially if not done by preceding specialists. Oncologists should ensure that comprehensive and accurate clinical staging has been performed and order additional workup as clinically indicated. Once pathological disease staging has been confirmed, biomarker testing and imaging are recommended if not completed previously. Assessing *BRAF* mutational status is essential during the initial workup. Immunohistochemistry may be used as a rapid screening test prior to treatment selection, with a turnaround time of approximately 24–48 hours. Confirmatory testing using polymerase chain reaction–based diagnostic or multigene panel sequencing, with a longer turnaround time of 5–10 days, may be used subsequently or instead of immunohistochemistry [6]. Currently, gene expression profiling (GEP) to differentiate melanomas at low versus high risk for metastasis is not the standard of care. Recent meta-analysis testing the prognostic ability of two melanoma GEP tests, DecisionDx-Melanoma and MelaGenix, correctly classified recurrences with stage I disease in only 29% and 32%, respectively [55]. Based on these and other published results, the Melanoma Prevention Workshop Group acknowledges the need for further research to better quantify the association of GEP tests with melanoma outcomes and recommends avoiding routine use of GEP testing until prospective studies support their clinical utility [56]. Therefore, at this time, current molecular techniques should not replace standard of care pathological staging procedures [6]. PET-CT or CT scans for patients with stage III disease and magnetic resonance imaging of the

brain for higher-risk patients (stages IIIC and IIID) are ordered. In patients who do not undergo CLND following an initial positive SLNB, ultrasound imaging of the draining nodal basin is performed regularly for surveillance during follow-up. Overall, it is important that an MDT member orders imaging along with medical evaluations.

When treatment plans are being developed, an open and trustworthy patient-physician relationship is essential for optimal patient care. Oncologists should discuss available treatment options and provide educational materials and information on support groups, and also refer patients to reliable online resources regarding their chosen systemic therapy. Information related to disease status and the adjuvant care plan should be shared with specialists who are not part of the core MDT, as they may be involved with managing preexisting comorbidities arising from primary disease and/or any TRAEs, such as fatigue, diarrhea, rash, pyrexia, and immune-mediated AEs [6, 13, 17, 22]. For example, patients who receive immunotherapy may experience endocrine-related complications, such as hypo- or hyperthyroidism [17]; thus, periodic discussions with an endocrinologist are helpful in managing these conditions. During surveillance follow-up visits, collaboration with other MDT specialists will provide the highest level of care. Most surgeons prefer to see patients at distinct intervals and continue to be part of the team; dermatologic evaluations are often lifelong. It is therefore essential that efforts be made to guarantee involvement of all MDT members during patient follow-ups.

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## DISCUSSION

MDTs are increasingly used to improve patient care and meaningfully engage all specialists during the patient's treatment journey. Each specialist has a distinct role in the treatment of patients with *BRAF*-mutant stage III melanoma. Mutual communication and collaboration among MDT members can ensure that all standard of care measures are performed, no matter which specialist first sees a patient. As MDTs become more prevalent in the treatment of melanoma, they will assist in building consensus on future aspects of care, such as how to appropriately image high-risk patients, determine the best time for genetic counseling, and develop guidelines on gene expression profiling.

MDT care in other cancers has led to improved clinical care and survival. In a 10-year study of >14,000 patients with symptomatic invasive breast cancer in western Scotland, MDT care was introduced in one health board area (greater Glasgow) but not in adjacent areas [33]. In the 5 years before introduction of MDT care, breast cancer mortality was 11% higher in the greater Glasgow area than in the nonintervention areas [33]. However, after MDT care was introduced, breast cancer mortality was 18% lower in the greater Glasgow area than in the nonintervention areas [33]. In patients with high-grade glioma, MDT care resulted in an earlier start of radiotherapy and higher median overall survival than in patients who did not receive MDT care (18.7 vs 11.9 months, respectively) [28]. In patients with Dukes stage C colorectal

cancer, MDT care was an independent predictor of survival and resulted in more patients receiving adjuvant chemotherapy, with improved 3-year overall survival compared with those who did not receive MDT care (66% vs. 58%, respectively) [34].

In recent years, more cancer clinics have implemented an MDT treatment model to improve clinical outcomes in patients with various malignancies. Additionally, health care cost-saving benefits were observed in melanoma management because of the more efficient usage pattern of health care resources within an MDT clinic [57, 58]. Although the scope and scale of these teams may vary by institution and cancer type, the end goal is to enhance multidisciplinary communication to optimize and individualize patient care. However, despite evidence supporting the benefits of the MDT care model, there can be barriers to successful development and implementation. Physician availability, financial compensation, administrative support, difficulties with communication, and record keeping are all potential impediments to optimal MDT care [31]. It is important to clearly define the roles and responsibilities of each specialist on an MDT and develop seamless referral and communication procedures to ensure that patients are receiving the best care for their disease.

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## CONCLUSION

MDTs are valuable for all patients regardless of their disease stage, as they provide quality patient care through open communication and collaboration among specialists who manage patients with melanoma. This provides patients with comfort that their disease is being optimally managed to achieve superior disease-related outcomes with respect to relapse-free and overall survival. As the use of adjuvant immunotherapy and targeted therapy is increasing in patients with stage III disease, decisions related to staging, molecular testing, surgical procedures, and treatment are evolving. Therefore, we believe that MDT patient care is becoming more important for this patient population. In addition, data on the value of systemic therapy for stage III and even earlier stages of melanoma are rapidly emerging. Treatment patterns and outcomes for patients with nonmetastatic melanoma vary greatly and are an area of focused clinical trials. As a result, fostering multidisciplinary care discussions at all stages of melanoma has the potential to optimize care resulting in the best outcomes possible.

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