Cutaneous Melanoma Treatment Regimens

Clinical Trials: The NCCN recommends cancer patient participation in clinical trials as the gold standard for treatment.

Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced healthcare team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are only provided to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data becomes available. The National Comprehensive Cancer Network Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The NCCN makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

Note: All recommendations are category 2A unless otherwise indicated.

▶Stage IIIA (SLN-positive) or Stage IIIB/C/D (SLN-positive)[1,a]

REGIMEN	DOSING
Adjuvant Therapy	
Preferred Regimens	
Dabrafenib/Trametinib (for patients with disease characterized by *BRAF* V600-activating mutation) (Category 1 for AJCC 7th edition stage IIIA with SLN metastasis >1 mm or stage IIIB/C disease)[2-6,a-c]	**Days 1-28:** Dabrafenib 150mg orally twice daily **Days 1-28:** Trametinib 2mg orally once daily. Repeat cycle every 4 weeks for 12 cycles.
Nivolumab (Category 1 for AJCC 7th edition stage IIIB/C disease)[7-11,a,d,e]	**Day 1:** Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks for 1 year. **OR** **Day 1:** Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks for 1 year.
Pembrolizumab (Category 1 for AJCC 7th edition stage IIIA with SLN metastasis >1 mm or stage IIIB/C disease)[12-15,a,e,f]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for 1 year. **OR** **Day 1:** Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for 1 year.

▶Stage IIIA (Clinically Positive Nodes)[1]

Adjuvant Therapy	
Preferred Regimens	
Dabrafenib/Trametinib (for patients with disease characterized by *BRAF* V600-activating mutation) (Category 1)[2-6,b,c]	**Days 1-28:** Dabrafenib 150mg orally twice daily **Days 1-28:** Trametinib 2mg orally once daily. Repeat cycle every 4 weeks for 12 cycles.
Nivolumab (Category 1)[7-11,d,e]	**Day 1:** Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks for 1 year. **OR** **Day 1:** Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks for 1 year.
Pembrolizumab (Category 1)[12-15,e,f]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for 1 year. **OR** **Day 1:** Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for 1 year.

continued

Cutaneous Melanoma Treatment Regimens

▶Stage III (Clinical Satellite in-Transit)[1]

REGIMEN	DOSING
Limited Resectable Disease	
Initial Treatment	
Intralesional Talimogene Laherparepvec[16-18,a]	**Day 1:** Talimogene laherparepvec up to 4 mL at a concentration of 10^6 (1 million) plaque-forming units (PFU) per mL, administered in multiple injections intralesional starting with the largest lesions. Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated. Administer for one 3-week cycle, **followed by:** **Day 1:** Talimogene laherparepvec up to 4 mL at a concentration of 10^8 (100 million) PFU/mL, administered in multiple injections intralesional starting with any new lesions that have developed since previous treatment. Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated. Repeat cycle every 2 weeks.
Systemic Therapy; see Systemic Therapy (See adjuvant therapy)	
Adjuvant Therapy if NED Following Local Therapy[a]	
Preferred Regimens	
Dabrafenib/Trametinib (for patients with disease characterized by *BRAF* V600-activating mutation)[2-6,b,c]	**Days 1-28:** Dabrafenib 150mg orally twice daily **Days 1-28:** Trametinib 2mg orally once daily. Repeat cycle every 4 weeks for 12 cycles.
Nivolumab (Category 1)[7-11,d,e]	**Day 1:** Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks for 1 year. **OR** **Day 1:** Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks for 1 year.
Pembrolizumab[12-15,e,f]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for 1 year. **OR** **Day 1:** Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for 1 year.
Unresectable Disease	
Initial Treatment	
Preferred Regimens	
Systemic Therapy; see Systemic Therapy for Metastatic or Unresectable Disease	
Local Therapy Options	
Intralesional Aldesleukin (Interleukin-2) (Category 2B)[19-21]	Aldesleukin (interleukin-2) 0.6 – 6 million units intralesional three times a week. Repeat weekly.
Intralesional Talimogene Laherparepvec (Category 1)[16-18,a]	**Day 1:** Talimogene laherparepvec up to 4 mL at a concentration of 10^6 (1 million) PFU per mL, administered in multiple injections intralesional starting with the largest lesions. Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated. Administer for one 3-week cycle, **followed by:** **Day 1:** Talimogene laherparepvec up to 4 mL at a concentration of 10^8 (100 million) PFU/mL, administered in multiple injections intralesional starting with any new lesions that have developed since previous treatment. Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated. Repeat cycle every 2 weeks.
Topical Imiquimod (for superficial dermal lesions) (Category 2B)[22-24]	**Days 1-28:** Imiquimod 5% cream topical to lesions twice daily. Repeat cycle every 4 weeks.

continued

Cutaneous Melanoma Treatment Regimens

▶Stage III (Clinical Satellite in-Transit)[1] (continued)

REGIMEN	DOSING
Unresectable Disease (continued)	
Adjuvant Therapy if NED Following Local Therapy[a]	
Dabrafenib/Trametinib (for patients with disease characterized by *BRAF* V600-activating mutation) (Category 2B)[2-6,b,c]	**Days 1-28:** Dabrafenib 150mg orally twice daily **Days 1-28:** Trametinib 2mg orally once daily. Repeat cycle every 4 weeks for 12 cycles.
Nivolumab (Category 2B)[7-11,d,e]	**Day 1:** Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks for 1 year. **OR** **Day 1:** Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks for 1 year.
Pembrolizumab (Category 2B)[12-15,e,f]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for 1 year. **OR** **Day 1:** Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for 1 year.

▶Stage IV Metastatic Disease[1]

Oligometastatic Disease	
Adjuvant Therapy if NED Following Initial Treatment[a]	
Preferred Regimens	
Nivolumab (Category 1)[7-11,d,e]	**Day 1:** Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks for 1 year. **OR** **Day 1:** Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks for 1 year.
Pembrolizumab[12-15,e,f]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for 1 year. **OR** **Day 1:** Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for 1 year.
Other Recommended Regimens	
Dabrafenib/Trametinib (for patients with disease characterized by *BRAF* V600-activating mutation) (Category 2B)[2-6,b,c]	**Days 1-28:** Dabrafenib 150mg orally twice daily **Days 1-28:** Trametinib 2mg orally once daily. Repeat cycle every 4 weeks for 12 cycles.
Encorafenib/Binimetinib (for patients with disease characterized by *BRAF* V600-activating mutation) (Category 2B)[25-27,b,c]	**Days 1-28:** Encorafenib 450mg orally once daily **Days 1-28:** Binimetinib 45mg orally every 12 hours. Repeat cycle every 4 weeks.
Nivolumab + Ipilimumab followed by Nivolumab (Category 2B)[7,9,28-31,d,g]	**Day 1:** Nivolumab 1mg/kg IV over 30 minutes, **followed by:** **Day 1:** Ipilimumab 3mg/kg IV over 90 minutes. Repeat every 3 weeks for 4 cycles, **followed by:** **Day 1:** Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks. **OR** **Day 1:** Nivolumab 1mg/kg IV over 30 minutes, **followed by:** **Day 1:** Ipilimumab 3mg/kg IV over 90 minutes. Repeat every 3 weeks for 4 cycles, **followed by:** **Day 1:** Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks.
Vemurafenib/Cobimetinib (for patients with disease characterized by *BRAF* V600-activating mutation) (Category 2B)[32-35,b,c]	**Days 1-28:** Vemurafenib 960mg orally twice daily **Days 1-21:** Cobimetinib 60mg orally once daily. Repeat cycle every 4 weeks.

continued

Cutaneous Melanoma Treatment Regimens

▶Stage IV Metastatic Disease[1] (continued)

REGIMEN	DOSING
Oligometastatic Disease (continued)	
Useful in Certain Circumstances	
Ipilimumab (if prior exposure to anti–PD-1 therapy)[28,36-39,a,g]	**Day 1:** Ipilimumab 3mg/kg IV over 90 minutes. Repeat cycle every 3 weeks for 4 cycles.
Widely Disseminated Disease	
Preferred Regimens	
Systemic Therapy; see Systemic Therapy for Metastatic or Unresectable Disease	
Useful in Certain Circumstances: Extracranial Lesions	
Intralesional Talimogene Laherparepvec[16-18,a]	**Day 1:** Talimogene laherparepvec up to 4 mL at a concentration of 10^6 (1 million) PFU per mL, administered in multiple injections intralesional starting with the largest lesions. Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated. Administer for one 3-week cycle, **followed by:** **Day 1:** Talimogene laherparepvec up to 4 mL at a concentration of 10^8 (100 million) PFU/mL, administered in multiple injections intralesional starting with any new lesions that have developed since previous treatment. Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated. Repeat cycle every 2 weeks.

▶Recurrent Disease[1]

Local Satellite in-Transit Recurrence	
Initial Treatment for Limited Resectable Disease	
Intralesional Talimogene Laherparepvec[16-18,a]	**Day 1:** Talimogene laherparepvec up to 4 mL at a concentration of 10^6 (1 million) PFU per mL, administered in multiple injections intralesional starting with the largest lesions. Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated. Administer one 3-week cycle, **followed by:** **Day 1:** Talimogene laherparepvec up to 4 mL at a concentration of 10^8 (100 million) PFU/mL, administered in multiple injections intralesional starting with any new lesions that have developed since previous treatment. Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated. Repeat cycle every 2 weeks.
Systemic Therapy; see Systemic Therapy (See adjuvant therapy options)	
Adjuvant Therapy if NED Following Initial Treatment[a]	
Preferred Regimens	
Dabrafenib/Trametinib (for patients with disease characterized by *BRAF* V600-activating mutation)[2-6,b,c]	**Days 1-28:** Dabrafenib 150mg orally twice daily **Days 1-28:** Trametinib 2mg orally once daily. Repeat cycle every 4 weeks for 12 cycles.
Nivolumab[7-11,d,e]	**Day 1:** Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks for 1 year. **OR** **Day 1:** Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks for 1 year.
Pembrolizumab[12-15,e,f]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for 1 year. **OR** **Day 1:** Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for 1 year.
Useful in Certain Circumstances	
Ipilimumab (if prior exposure to anti–PD-1 therapy)[28,36-39,a,g]	**Day 1:** Ipilimumab 3mg/kg IV over 90 minutes. Repeat cycle every 3 weeks for 4 cycles.

continued

Cutaneous Melanoma Treatment Regimens

▶Recurrent Disease[1] (continued)

REGIMEN	DOSING
Local Satellite in-Transit Recurrence (continued)	
Initial Treatment for Unresectable Disease	
Preferred Regimens	
Systemic Therapy; see Systemic Therapy for Metastatic or Unresectable Disease	
Local Therapy Options	
Intralesional Talimogene Laherparepvec (Category 1)[16-18,a]	**Day 1**: Talimogene laherparepvec up to 4 mL at a concentration of 10^6 (1 million) PFU per mL, administered in multiple injections intralesional starting with the largest lesions. Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated. Administer for one 3-week cycle, **followed by:** **Day 1:** Talimogene laherparepvec up to 4 mL at a concentration of 10^8 (100 million) PFU/mL, administered in multiple injections intralesional starting with any new lesions that have developed since previous treatment. Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated. Repeat cycle every 2 weeks.
Intralesional Aldesleukin (Interleukin-2) (Category 2B)[19-21]	Aldesleukin (interleukin-2) 0.6 – 6 million units intralesional three times a week. Repeat weekly.
Topical Imiquimod (for superficial dermal lesions) (Category 2B)[22-24]	**Days 1-28:** Imiquimod 5% cream topical to lesions twice daily. Repeat cycle every 4 weeks.
Adjuvant Therapy if NED Following Local/Regional Therapy[a]	
Preferred Regimens	
Dabrafenib/Trametinib (for patients with disease characterized by *BRAF* V600-activating mutation) (Category 2B)[2-6,b,c]	**Days 1-28:** Dabrafenib 150mg orally twice daily **Days 1-28:** Trametinib 2mg orally once daily. Repeat cycle every 4 weeks for 12 cycles.
Nivolumab (Category 2B)[7-11,d,e]	**Day 1:** Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks for 1 year. **OR** **Day 1:** Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks for 1 year.
Pembrolizumab (Category 2B)[12-15,e,f]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for 1 year. **OR** **Day 1:** Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for 1 year.
Useful in Certain Circumstances	
Ipilimumab (if prior exposure to anti–PD-1 therapy) (Category 2B) [28,36-39,a,g]	**Day 1:** Ipilimumab 3mg/kg IV over 90 minutes. Repeat cycle every 3 weeks for 4 cycles.
Nodal Recurrence	
Adjuvant Therapy if No Previous Lymph Node Dissection	
Preferred Regimens	
Dabrafenib/Trametinib (for patients with disease characterized by *BRAF* V600-activating mutation) (Category 1)[2-6,b,c]	**Days 1-28:** Dabrafenib 150mg orally twice daily **Days 1-28:** Trametinib 2mg orally once daily. Repeat cycle every 4 weeks for 12 cycles.
Nivolumab (Category 1)[7-11,d,e]	**Day 1:** Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks for 1 year. **OR** **Day 1:** Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks for 1 year.

continued

Cutaneous Melanoma Treatment Regimens

▶Recurrent Disease[1] (continued)

REGIMEN	DOSING
Nodal Recurrence (continued)	
Adjuvant Therapy if No Previous Lymph Node Dissection (continued)	
Preferred Regimens (continued)	
Dabrafenib/Trametinib (for patients with disease characterized by *BRAF* V600-activating mutation) (Category 1)[2-6,b,c]	**Days 1-28:** Dabrafenib 150mg orally twice daily **Days 1-28:** Trametinib 2mg orally once daily. Repeat cycle every 4 weeks for 12 cycles.
Nivolumab (Category 1)[7-11,d,e]	**Day 1:** Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks for 1 year. **OR** **Day 1:** Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks for 1 year.
Pembrolizumab (Category 1)[12-15,e,f]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for 1 year. **OR** **Day 1:** Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for 1 year.
Useful in Certain Circumstances	
Ipilimumab (if prior exposure to anti–PD-1 therapy) [28,36-39,a,g]	**Day 1:** Ipilimumab 3mg/kg IV over 90 minutes. Repeat cycle every 3 weeks for 4 cycles.
Adjuvant Therapy for Resectable Nodal Recurrence Following Previous Lymph Node Dissection	
Preferred Regimens	
Dabrafenib/Trametinib (for patients with disease characterized by *BRAF* V600-activating mutation) (Category 1)[2-6,b,c]	**Days 1-28:** Dabrafenib 150mg orally twice daily **Days 1-28:** Trametinib 2mg orally once daily. Repeat cycle every 4 weeks for 12 cycles.
Nivolumab (Category 1)[7-11,d,e]	**Day 1:** Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks for 1 year. **OR** **Day 1:** Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks for 1 year.
Pembrolizumab (Category 1)[12-15,e,f]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for 1 year. **OR** **Day 1:** Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for 1 year.
Useful in Certain Circumstances	
Ipilimumab (if prior exposure to anti–PD-1 therapy)[28,36-39,a,g]	**Day 1:** Ipilimumab 3mg/kg IV over 90 minutes. Repeat cycle every 3 weeks for 4 cycles.
Adjuvant Therapy for Unresectable Nodal Recurrence Following Previous Lymph Node Dissection	
Preferred Regimens	
Systemic Therapy; see Systemic Therapy for Metastatic or Unresectable Disease	
Useful in Certain Circumstances	
Intralesional Talimogene Laherparepvec[16-18,a]	**Day 1:** Talimogene laherparepvec up to 4 mL at a concentration of 10^6 (1 million) PFU per mL, administered in multiple injections intralesional starting with the largest lesions. Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated. Administer for one 3-week cycle, **followed by:** **Day 1:** Talimogene laherparepvec up to 4 mL at a concentration of 10^8 (100 million) PFU/mL, administered in multiple injections intralesional starting with any new lesions that have developed since previous treatment. Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated. Repeat cycle every 2 weeks.

continued

Cutaneous Melanoma Treatment Regimens

▶Systemic Therapy for Metastatic or Unresectable Disease[1]

REGIMEN	DOSING
First-Line Therapy	
Preferred Regimens	
Dabrafenib/Trametinib (for patients with disease characterized by *BRAF* V600-activating mutation) (Category 1)[2-6,b,c]	**Days 1-28:** Dabrafenib 150mg orally twice daily **Days 1-28:** Trametinib 2mg orally once daily. Repeat cycle every 4 weeks.
Encorafenib/Binimetinib (for patients with disease characterized by *BRAF* V600-activating mutation) (Category 1)[25-27,b,c]	**Days 1-28:** Encorafenib 450mg orally once daily **Days 1-28:** Binimetinib 45mg orally every 12 hours. Repeat cycle every 4 weeks.
Nivolumab (Category 1)[7-11,d,e]	**Day 1:** Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks. **OR** **Day 1:** Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks.
Nivolumab + Ipilimumab followed by Nivolumab (Category 1)[7,9,28-31,d,g]	**Day 1:** Nivolumab 1mg/kg IV over 30 minutes, **followed by:** **Day 1:** Ipilimumab 3mg/kg IV over 90 minutes. Repeat every 3 weeks for 4 cycles, **followed by:** **Day 1:** Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks. **OR** **Day 1:** Nivolumab 1mg/kg IV over 30 minutes, **followed by:** **Day 1:** Ipilimumab 3mg/kg IV over 90 minutes. Repeat every 3 weeks for 4 cycles, **followed by:** **Day 1:** Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks.
Pembrolizumab (Category 1)[12-15,e,f]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks. **OR** **Day 1:** Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks.
Vemurafenib/Cobimetinib (for patients with disease characterized by *BRAF* V600-activating mutation) (Category 1)[32-35,b,c]	**Days 1-28:** Vemurafenib 960mg orally twice daily **Days 1-21:** Cobimetinib 60mg orally once daily. Repeat cycle every 4 weeks.
Other Recommended Regimens	
Pembrolizumab/Low-dose Ipilimumab (Category 2B)[12,28,40,e-g]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes, **followed by:** **Day 1:** Ipilimumab 1mg/kg IV. Repeat cycle every 3 weeks for 4 cycles, **followed by:** **Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for up to 2 years **OR** **Day 1:** Pembrolizumab 400mg IV over 30 minutes Repeat cycle every 6 weeks for up to 2 years.
Vemurafenib/Cobimetinib + Atezolizumab (for patients with disease characterized by *BRAF* V600-activating mutation)[32,33,41,42,b,c,h]	**Days 1-21:** Vemurafenib 960mg orally twice daily, **followed by:** **Days 22-28:** Vemurafenib 720mg orally twice daily **Days 1-21:** Cobimetinib 60mg orally once daily Administer one 4-week cycle, **followed by:** **Days 1-28:** Vemurafenib 720mg orally twice daily **Days 1-21:** Cobimetinib 60mg orally daily **Days 1,15:** Atezolizumab 840mg IV over 60 minutes. Repeat cycle every 4 weeks.

continued

Cutaneous Melanoma Treatment Regimens

▶Systemic Therapy for Metastatic or Unresectable Disease[1] (continued)

REGIMEN	DOSING
Second-Line or Subsequent Therapy	
Preferred Regimens	
Dabrafenib/Trametinib (for patients with disease characterized by *BRAF* V600-activating mutation)[2-6,b,c]	**Days 1-28:** Dabrafenib 150mg orally twice daily **Days 1-28:** Trametinib 2mg orally once daily. Repeat cycle every 4 weeks.
Encorafenib/Binimetinib (for patients with disease characterized by *BRAF* V600-activating mutation)[25-27,b,c]	**Days 1-28:** Encorafenib 450mg orally once daily. **Days 1-28:** Binimetinib 45mg orally every 12 hours. Repeat cycle every 4 weeks.
Nivolumab[7-11,d,e]	**Day 1:** Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks. **OR** **Day 1:** Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks.
Nivolumab + Ipilimumab followed by Nivolumab[7,9,28-31,d,g]	**Day 1:** Nivolumab 1mg/kg IV over 30 minutes, **followed by:** **Day 1:** Ipilimumab 3mg/kg IV over 90 minutes. Repeat every 3 weeks for 4 cycles, **followed by:** **Day 1:** Nivolumab 240mg IV over 30 minutes. Repeat cycle every 2 weeks. **OR** **Day 1:** Nivolumab 1mg/kg IV over 30 minutes, **followed by:** **Day 1:** Ipilimumab 3mg/kg IV over 90 minutes. Repeat every 3 weeks for 4 cycles, **followed by:** **Day 1:** Nivolumab 480mg IV over 30 minutes. Repeat cycle every 4 weeks.
Pembrolizumab[12-15,e,f]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks. **OR** **Day 1:** Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks.
Pembrolizumab/Low-dose Ipilimumab (for tumors that have progressed after prior anti-PD-1 therapy)[12,28,40,a,e-g]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes, **followed by:** **Day 1:** Ipilimumab 1mg/kg IV. Repeat cycle every 3 weeks for 4 cycles, **followed by:** **Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks for up to 2 years **OR** **Day 1:** Pembrolizumab 400mg IV over 30 minutes. Repeat cycle every 6 weeks for up to 2 years.
Vemurafenib/Cobimetinib (for patients with disease characterized by *BRAF* V600-activating mutation)[32-35,b,c]	**Days 1-28:** Vemurafenib 960mg orally twice daily. **Days 1-21:** Cobimetinib 60mg orally once daily. Repeat cycle every 4 weeks.
Other Recommended Regimens	
High-dose Aldesleukin (Interleukin-2)[19,43,44,i]	**Days 1-5:** Aldesleukin (interleukin-2) 600,000units/kg IV over 15 minutes every 8 hours for a total of 14 doses. Repeat every 6-12 weeks for a maximum of 5 cycles. The course is repeated one time after 6-9 days of rest for a total of 2 courses per cycle. **OR** **Days 1-5:** Aldesleukin (interleukin-2) 720,000 units/kg IV over 15 minutes every 8 hours for a total of 14 doses. Repeat every 6-12 weeks for a maximum of 5 cycles. The course is repeated one time after 6-9 days of rest for a total of 2 courses per cycle.
Ipilimumab (if prior exposure to anti–PD-1 therapy)[28,36-39,a,g]	**Day 1:** Ipilimumab 3mg/kg IV over 90 minutes. Repeat cycle every 3 weeks for 4 cycles.

continued

Cutaneous Melanoma Treatment Regimens

▶Systemic Therapy for Metastatic or Unresectable Disease[1] (continued)

REGIMEN	DOSING
Second-Line or Subsequent Therapy (continued)	
Useful in Certain Circumstances	
Albumin-bound Paclitaxel[45,46]	**For chemotherapy-naive patients:** **Days 1,8,15:** 150mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks. **OR** **For previously treated patients:** **Days 1,8,15:** 100mg/m^2 IV over 30 minutes. Repeat cycle every 4 weeks.
Binimetinib (for patients with *NRAS*-mutated tumors that have progressed after immune checkpoint inhibitors) (Category 2B)[26,47]	**Days 1-28:** Binimetinib 45mg orally every 12 hours. Repeat cycle every 4 weeks.
Cisplatin/Vinblastine/ Dacarbazine (Category 2B)[48-51]	**Days 1-4:** Cisplatin 20mg/m^2 IV over 30 minutes daily **Days 1-4:** Vinblastine 1.2mg/m^2 IV over 5-10 minutes daily **Day 1:** Dacarbazine 800mg/m^2 IV over 60 minutes. Repeat cycle every 3 weeks.
Dacarbazine[50,52,53]	**Day 1:** Dacarbazine 850-1,000mg/m^2 IV over 60 minutes. Repeat cycle every 3 weeks.
Entrectinib (for patients with *NTRK* gene fusion-positive tumors)[54,55]	**Days 1-28:** Entrectinib 600mg orally once daily. Repeat cycle every 4 weeks.
Imatinib (for patients with tumors of activating KIT mutations)[56,57]	**Days 1-28:** Imatinib 400mg orally twice daily. Repeat cycle every 4 weeks.
Ipilimumab/Intralesional Talimogene Laherparepvec (Category 2B)[16,28,58,a,g]	**Day 1 (Week 1):** Talimogene laherparepvec up to 4mL at a concentration of 10^6 (1 million) PFU per mL, administered in multiple injections intralesional starting with the largest lesions. Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated. Administer 1 cycle, **followed by:** **Day 1 (Week 4):** Talimogene laherparepvec up to 4 mL at a concentration of 10^8 (100 million) PFU/mL, administered in multiple injections intralesional starting with any new lesions that have developed since previous treatment. Prioritize injection of remaining lesion(s) based on lesion size until maximum injection volume is reached or until all injectable lesion(s) have been treated. Repeat cycle every 2 weeks. **Day 1 (Week 6):** Ipilimumab 3mg/kg IV over 90 minutes. Repeat cycle every 3 weeks for up to 4 cycles.
Larotrectinib (for patients with *NTRK* gene fusion-positive tumors)[59,60]	**Days 1-28:** Larotrectinib 100mg orally twice daily. Repeat cycle every 4 weeks.
Paclitaxel[61-64]	**Days 1,8,15:** Paclitaxel 80mg/m^2 IV over 60 minutes. Repeat cycle every 4 weeks.
Paclitaxel/Carboplatin[61,65-67]	**Days 1,8,15:** Paclitaxel 100mg/m^2 IV over 60 minutes, **followed by:** **Days 1,8,15:** Carboplatin AUC 2 IV over 30 minutes. Repeat cycle every 4 weeks. **OR** **Day 1:** Paclitaxel 225mg/m^2 IV over 3 hours, **followed by:** D**ay 1:** Carboplatin AUC 6 IV over 30 minutes. Repeat cycle every 3 weeks.

continued

Cutaneous Melanoma Treatment Regimens

▶Systemic Therapy for Metastatic or Unresectable Disease[1] (continued)

REGIMEN	DOSING
Second-Line or Subsequent Therapy (continued)	
Useful in Certain Circumstances (continued)	
Pembrolizumab + Lenvatinib (Category 2B)[12,68,69,f]	**Day 1:** Pembrolizumab 200mg IV over 30 minutes. Repeat cycle every 3 weeks, **with:** **Days 1-28:** Lenvatinib 20mg once daily. Repeat cycle every 4 weeks.
Temozolomide[70,71]	**Days 1-5:** Temozolomide 150-200mg/m^2 orally daily. Repeat cycle every 4 weeks.

[a] **AJCC**, American Joint Committee on Cancer; **IL**, interleukin; **NED**, no evidence of disease; **PFU**, plaque-forming unit; **PD-1**, programmed cell death 1, **SLN**, sentinel lymph node.

[b] Regular dermatologic evaluation and referral to a dermatologist or provider experienced in the diagnosis and management of cutaneous manifestations of targeted therapy is recommended. *BRAF* inhibitors are associated with cutaneous squamous cell carcinoma, extreme photosensitivity, and other dermatologic toxicities, which occur much less frequently with concurrent *MEK* inhibitors.

[c] Pyrexia (defined as a temperature of ≥38.5°C) is a common side effect of combining *BRAF* and *MEK* inhibitors and occurs less frequently with *BRAF* inhibitor monotherapy. The pyrexia is episodic, and onset is often 2 to 4 weeks following the start of therapy, with a median duration of 9 days. Pyrexia may be associated with child, night sweats, rash, dehydration, electrolyte abnormalities, and hypotension. Stopping or holding BRAF/MEK inhibitor combination therapy at the onset of pyrexia will often interrupt the episode, and treatment can be resumed with full-dose *BRAF/MEK* inhibitors upon cessation of pyrexia and pyrexia-related symptoms. Upon re-exposure to *BRAF/MEK* inhibitors, repeat pyrexia events can occur, but grade >3 events are uncommon. In occasional instances of prolonged or severe pyrexia not responsive to discontinuation of *BRAF/MEK* inhibitors, low-dose steroids (prednisone 10 mg/day) can be used. Patients with pyrexia should be advised to use antipyretics as needed and increase fluid intake.

[d] Nivolumab may cause severe, life-threatening immune-mediated adverse events, including pneumonitis, colitis, hepatitis, renal failure and nephritis, endocrinopathy, and encephalitis. While most of these reactions occur during treatment, some occur weeks to months after discontinuation of treatment. In the setting of immune-mediate reactions, nivolumab therapy may be held; for severe reactions, therapy should be permanently discontinued and high-dose systemic corticosteroids should by initiated according to specific recommendations in the drug package insert.

[e] Weight-based dosing has also been studied and could be considered based on patient-specific factors. Review drug package insert for specific dosing recommendations.

[f] Pembrolizumab may cause severe, life-threatening immune-mediated adverse events, including pneumonitis, colitis, hepatitis, hypophysitis, renal failure and nephritis, and endocrinopathy. While most of these reactions occur during treatment, some occur weeks to months after discontinuation of treatment. In the setting of immune-mediate reactions, pembrolizumab therapy may be held; for severe reactions, therapy should be permanently discontinued and high-dose systemic corticosteroids should by initiated according to specific recommendations in the drug package insert.

[g] Ipilimumab may cause severe, life-threatening immune-mediated adverse events, including enterocolitis, hepatitis, dermatitis (including toxic epidermal necrolysis), neuropathy, and endocrinopathy. While most of these reactions occur during treatment, some occur weeks to months after discontinuation of treatment. In the setting of immune-mediate reactions, ipilimumab therapy may be held; for severe reactions, therapy should be permanently discontinued and high-dose systemic corticosteroids should by initiated according to specific recommendations in the drug package insert.

[h] Atezolizumab may cause severe, life-threatening immune-mediated adverse events, including pneumonitis, colitis, hepatitis, hypophysitis, and endocrinopathy. While most of these reactions occur during treatment, some occur weeks to months after discontinuation of treatment. In the setting of immune-mediate reactions, atezolizumab therapy may be held; for severe reactions, therapy should be permanently discontinued and high-dose systemic corticosteroids should by initiated according to specific recommendations in the drug package insert.

[i] High-dose IL should not be used in patients with inadequate organ reserve, poor performance status, or untreated or active brain metastases. IL-2 may be considered for patients with small brain metastases and without significant peritumoral edema (Category 2B). Therapy should be restricted to an institution with medical staff experienced in the administration and management of these regimens.

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